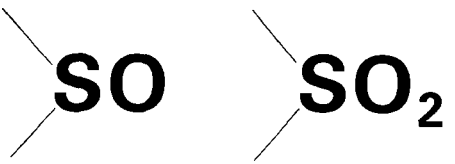
The chemistry of **sulphones and sulphoxides**

THE CHEMISTRY OF FUNCTIONAL GROUPS

A series of advanced treatises under the general editorship of Professor Saul Patai

The chemistry of alkenes (2 volumes)
The chemistry of the carbonyl group (2 volumes)
The chemistry of the ether linkage
The chemistry of the amino group
The chemistry of the nitro and nitroso groups (2 parts)
The chemistry of carboxylic acids and esters
The chemistry of the carbon–nitrogen double bond
The chemistry of amides
The chemistry of the cyano group
The chemistry of the hydroxyl group (2 parts)
The chemistry of the azido group
The chemistry of the acyl halides
The chemistry of the carbon–halogen bond (2 parts)
The chemistry of the quinonoid compounds (2 volumes, 4 parts)
The chemistry of the thiol group (2 parts)
The chemistry of the hydrazo, azo and azoxy groups (2 parts)
The chemistry of amidines and imidates
The chemistry of cyanates and their thio derivatives (2 parts)
The chemistry of diazonium and diazo groups (2 parts)
The chemistry of the carbon–carbon triple bond (2 parts)
The chemistry of ketenes, allenes and related compounds (2 parts)
The chemistry of the sulphonium group (2 parts)
Supplement A: The chemistry of double-bonded functional groups (2 parts)
Supplement B: The chemistry of acid derivatives (2 parts)
Supplement C: The chemistry of triple-bonded functional groups (2 parts)
Supplement D: The chemistry of halides, pseudo-halides and azides (2 parts)
Supplement E: The chemistry of ethers, crown ethers, hydroxyl groups and their sulphur analogues (2 parts)
Supplement F: The chemistry of amino, nitroso and nitro compounds and their derivatives (2 parts)
The chemistry of the metal–carbon bond (4 volumes)
The chemistry of peroxides
The chemistry of organic selenium and tellurium compounds (2 volumes)
The chemistry of the cyclopropyl group



The chemistry of **sulphones and sulphoxides**

Edited by

SAUL PATAI

and

ZVI RAPPOPORT

The Hebrew University, Jerusalem

and

CHARLES STIRLING

University College, Bangor

1988

JOHN WILEY & SONS

CHICHESTER–NEW YORK–BRISBANE–TORONTO–SINGAPORE

An Interscience ® Publication

Library of Congress Cataloging-in-Publication Data:

The Chemistry of sulphones and sulphoxides.
(The Chemistry of functional groups)
'An Interscience publication.'
1. Sulphones. 2. Sulphoxides. I. Patai, Saul. II. Rappoport, Zvi. III. Stirling, C. J. M. (Charles James Matthew) IV. Series.
QD305.S6C46 1988 546'.7232 87-8290

ISBN 0 471 91588 2

British Library Cataloguing in Publication Data:

The Chemistry of sulphones and sulphoxides.—
(The chemistry of functional groups).
1. Sulphoxides 2. Sulphones
I. Patai, Saul II. Rappoport, Zvi
III. Stirling, C.J.M. IV. Series
547'.065 QD341.S6

ISBN 0 471 91588 2

Printed and bound in Great Britain by Anchor Brendon, Colchester, Essex

Contributing authors

Z. B. Alfassi	Department of Nuclear Engineering, Ben-Gurion University of the Negev, Beer Sheva 84102, Israel
K. K. Andersen	Department of Chemistry, University of New Hampshire, Durham, NH 03824, USA
M. R. F. Ashworth	Fachbereich 13.5, Universität des Saarlandes, D-6600 Saarbrucken, FRG
S. Braverman	Department of Chemistry, Bar-Ilan University, Ramat-Gan 52100, Israel
N. Brot	Roche Institute of Molecular Biology, Roche Research Center, Nutley, NJ 07110, USA
M. Chanon	Université d'Aix-Marseille III, Laboratoire de Chimie Inorganique Moléculaire, UA 126-CNRS, 13397 Marseille, Cédex 13, France
C. Chatgilialoglu	Istituto dei composti del carbonio contenti eteroatomi e loro applicazioni, CNR, Ozzano Emilia, Bologna, Italy
J. Drabowicz	Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Department of Organic Sulphur Compounds, 90-362 Lódź, Boczna 5, Poland
H. Fujihara	Department of Chemistry, The University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan
N. Furukawa	Department of Chemistry, The University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan
A. Gavezzotti	Dipartimento di Chimica Fisica ed Elettrochimica e Centro CNR, Università di Milano, Milan, Italy
J. S. Grossert	Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada, B3H 4J3
I. Hargittai	Structural Chemistry Research Group of the Hungarian Academy of Sciences, Eötvös University, PO Box 117, Budapest, H-1431, Hungary

J. T. Herron — Chemical Kinetics Division, National Bureau of Standards, Gaithersburg, MD 20899, USA

J. Hoyle — Chemistry-Soils Department, Nova Scotia Agricultural College, PO Box 550, Truro, Nova Scotia, Canada, B2N 5E3

A. Kaji — Department of Chemistry, Faculty of Science, Kyoto University, Sakyo, Kyoto 606, Japan

P. Kiełbasinski — Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Department of Organic Sulphur Compounds, 90-362 Lódź, Boczna 5, Poland

M. Mikołajczyk — Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Department of Organic Sulphur Compounds, 90-362 Lódź, Boczna 5, Poland

S. Oae — Okayama University of Science, 1-1 Ridai-cho, Okayama 700, Japan

K. Pihlaja — Department of Chemistry, University of Turku, SF 20500 Turku 50, Finland

G. H. Posner — Department of Chemistry, The Johns Hopkins University, Baltimore, MD 21218, USA

A. Samat — Université d'Aix-Marseille III, Laboratoire de Chimie Inorganique Moléculaire, UA 126-CNRS, 13397 Marseille, Cédex 13, France

K. Schank — Fachrichtung 13.2 Organische Chemie, Universität des Saarlandes, D-6600 Saarbrücken, FRG

J. Shorter — Department of Chemistry, The University, Hull, HU6 7RX, UK

J. Simonet — Laboratoire d'Electrochimie, CNRS, Université de Rennes 1, France

I. W. J. Still — Department of Chemistry, University of Toronto, Erindale Campus, Mississauga, Ontario, Canada, L5L 1C6

K. Tanaka — Department of Chemistry, Faculty of Science, Kyoto University, Sakyo, Kyoto 606, Japan

Y. Uchida — Department of Applied Chemistry, Osaka Institute of Technology, Asahi-ku, Osaka 535, Japan

H. Weissbach — Roche Institute of Molecular Biology, Roche Research Center, Nutley, NJ 07110, USA

U. Zoller — Haifa University, Oranim, Israel

Foreword

In a set of volumes on sulphur-containing functional groups, the volume on the sulphonium group appeared in 1981 (in two parts). The present volume deals with sulphones and sulphoxides and further volumes, one on derivatives of sulphinic acids and another on derivatives of sulphenic acids, are now in the course of preparation, with a volume on sulphonic acid derivatives planned for the more distant future.

Chapters were planned on 'Structural chemistry of solids'; 'NMR and ESR'; 'Carbon acidity'; 'Syntheses and uses of isotopically labelled compounds' and on 'Pyrolysis' in this volume, but did not materialize. We will try to fill these gaps in a future supplementary volume.

The coverage of literature in most chapters is up to the middle or end of 1986.

We would be very grateful to readers who would let us know about mistakes or omissions in this volume or in other volumes in the Functional Groups series.

Jerusalem

SAUL PATAI
ZVI RAPPOPORT

Bangor
December 1987

CHARLES STIRLING

The Chemistry of Functional Groups
Preface to the Series

The series 'The Chemistry of Functional Groups' is 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 functional group treated and on the effects which it exerts on the chemical and physical properties, primarily in the immediate vicinity of the group in question and secondarily on the behaviour of the whole molecule. For instance, the volume *The Chemistry of the Ether Linkage* deals with reactions in which the C—O—C group is involved, as well as with the effects of the C—O—C group on the reactions of alkyl or aryl groups connected to the ether oxygen. It is the purpose of the volume to give a complete coverage of all properties and reactions of ethers in as far as these depend on the presence of the ether group but the primary subject matter is not the whole molecule, but the C—O—C functional group.

A further restriction in 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 as well as textbooks (i.e. in books which are usually found in the chemical libraries of universities and research institutes) should not, as a rule, be repeated in detail, unless it is necessary for the balanced treatment of the subject. Therefore each of the authors is asked *not* to give an encyclopaedic coverage of his subject, but to concentrate on the most important recent development 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.

With these restrictions, it is realized that no plan can be devised for a volume that would give a *complete* coverage of the subject 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-reference between the chapters of each volume. In this manner, sufficient freedom is given to each author to produce readable quasi-monographic chapters.

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

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

(b) One or more chapters dealing with the formation of the functional group in question, either from groups present in molecule, or by introducing the new group directly or indirectly.

(c) Chapters describing the characterization and characteristics of the functional groups, i.e. a chapter dealing with qualitative and quantitative methods of determination including chemical and physical methods, ultraviolet, infrared, nuclear magnetic resonance and mass spectra: a chapter dealing with activating and directive effects

exerted by the group and/or a chapter on the basicity, acidity or complex-forming ability of the group (if applicable).

(d) Chapters on the reactions, transformations and rearrangements which the functional group can undergo, either alone or in conjunction with other reagents.

(e) Special topics which do not fit any of the above sections, such as photochemistry, radiation chemistry, biochemical formations and reactions. Depending on the nature of each functional group treated, these special topics may include short monographs on related functional groups on which no separate volume is planned (e.g. a chapter on 'Thioketones' is included in the volume *The Chemistry of the Carbonyl Group*, and a chapter on 'Ketenes' is included in the volume *The Chemistry of Alkenes*). In others cases certain compounds, though containing only the functional group of the title, may have special features so as to be best treated in a separate chapter, as e.g. 'Polyethers' in *The Chemistry of the Ether Linkage*, or 'Tetraaminoethylenes' in *The Chemistry of the Amino Group*.

This plan entails that the breadth, depth and though-provoking nature of each chapter will differ with the views and inclinations of the author 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, it was decided to publish certain volumes in several parts, without giving consideration to the originally planned logical order of the chapters. If after the appearance of the originally planned parts of a volume it is found that either owing to non-delivery of chapters, or to new developments in the subject, sufficient material has accumulated for publication of a supplementary volume, containing material on related functional groups, this will be done as soon as possible.

The overall plan of the volumes in the series 'The Chemistry of Functional Groups' includes the titles listed below:

The Chemistry of Alkenes (two volumes)
The Chemistry of the Carbonyl Group (two volumes)
The Chemistry of the Ether Linkage
The Chemistry of the Amino Group
The Chemistry of the Nitro and Nitroso Groups (two parts)
The Chemistry of Carboxylic Acids and Esters
The Chemistry of the Carbon–Nitrogen Double Bond
The Chemistry of the Cyano Group
The Chemistry of Amides
The Chemistry of the Hydroxyl Group (two parts)
The Chemistry of the Azido Group
The Chemistry of Acyl Halides
The Chemistry of the Carbon–Halogen Bond (two parts)
The Chemistry of the Quinonoid Compounds (two parts)
The Chemistry of the Thiol Group (two parts)
The Chemistry of Amidines and Imidates
The Chemistry of the Hydrazo, Azo and Azoxy Groups (two parts)
The Chemistry of Cyanates and their Thio Derivatives (two parts)
The Chemistry of Diazonium and Diazo Groups (two parts)
The Chemistry of the Carbon–Carbon Triple Bond (two parts)
Supplement A: The Chemistry of Double-bonded Functional Groups (two parts)
The Chemistry of Ketenes, Allenes and Related Compounds (two parts)
Supplement B: The Chemistry of Acid Derivatives (two parts)
Supplement C: The Chemistry of Triple-Bonded Functional Groups (two parts)

Supplement D: The Chemistry of Halides, Pseudo-halides and Azides (two parts)
Supplement E: The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and their Sulphur Analogues (two parts)
The Chemistry of the Sulphonium Group (two parts)
Supplement F: The Chemistry of Amino, Nitroso and Nitro Groups and their Derivatives (two parts)
The Chemistry of the Metal–Carbon Bond (four volumes)
The Chemistry of Peroxides
The Chemistry of Organic Se and Te Compounds (two volumes)
The Chemistry of the Cyclopropyl Group (two parts)
The Chemistry of the Quinonoid Compounds Vol. 2 (two parts)

Titles in press:

The Chemistry of Organic Silicon Compounds
The Chemistry of Enones
Supplement A2: The Chemistry of Double-bonded Functional Groups

Titles in preparation:

The Chemistry of Enols
The Chemistry of Sulphinic Acids, Esters and Derivatives
The Chemistry of Sulphenic Acids, Esters and Derivatives

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 started, let along continued, without the support of many persons. First and foremost among these is Dr Arnold Weissberger, whose reassurance and trust encouraged me to tackle this task. The efficient and patient cooperation of several staff-members of the Publishers also rendered me invaluable aid (but unfortunately their code of ethics does not allow me to thank them by name). Many of may friends and colleagues in Israel and overseas helped me in the solution of various major and minor matters, and my thanks are due to all of them, especially to Professor Z. Rappoport. Carrying out such a long-range project would be quite impossible without the non-professional but none the less essential participation and partnership of my wife.

The Hebrew University
Jerusalem, ISRAEL

SAUL PATAI

Contents

List of Abbreviations Used

Ac	acetyl (MeCO)
acac	acetylacetone
Ad	adamantyl
All	allyl
An	anisyl
Ar	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*-dimethylformamide
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	tolyl(MeC_6H_4)
Tos	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, pp. 305–322) will also be used in their unabbreviated forms, both in the text and in structures.

We are sorry for any inconvenience to our readers. However, the rapidly rising costs of production make it absolutely necessary to use every means to reduce expenses—otherwise the whole existence of our Series would be in jeopardy.

CHAPTER 1

General and theoretical aspects

A. GAVEZZOTTI

Dipartimento di Chimica Fisica ed Elettrochimica e Centro CNR, Università di Milano, Milan, Italy

I. QUALITATIVE MOLECULAR ORBITAL THEORY

A. General Remarks

It is often stated that organic structure and reactivity can be understood in quantum chemical terms, and that molecular orbitals are the key to this understanding. It is also true, however, that theoretical chemists are sometimes uninterested in real chemical problems, and that organic chemists hardly understand or disregard altogether the results of quantum chemical calculations. Intermediate languages are needed to bridge this gap.

The main obstacle that stands in the way is the mathematical complexity of rigorous quantum chemical methods, and the accompanying difficulty in the interpretation of the results; approximate methods and pictorial representations may then be called for. Qualitative molecular orbital theories started with the Hückel approach to π-systems; a more systematic and successful approach to organic reactivity was provided by the Extended Hückel method and the Woodward–Hoffmann orbital symmetry conservation rules. Today, large computing facilities are available, but, for the reasons mentioned in the opening sentences, *ab initio* calculations are less appealing to the practicing chemist, and, as such, are not providing more immediate chemical understanding. It is still useful, therefore, to derive approximate wavefunctions for organic molecules on the basis of symmetry and overlap only. The following will illustrate how this can be done for sulphoxide and sulphone systems, starting from the very beginning. At the cost of including here and there some fairly obvious concepts, the procedure will be exposed in its entirety.

B. Basis Orbitals

1. Atomic orbitals (AO)

These are the basis functions with which every chemist becomes acquainted during early training. Mathematically, they are represented by Slater-type orbitals (STO) or gaussian-

TABLE 1. Analytical form of atomic orbitals[a]

$$\psi = QAr^{[n-(l+1)]}\exp(-\zeta t)f(x,y,z)$$

Slater orbitals: $A = [(2\zeta)^{2n+1}/(2n!)]^{1/2}$; $t = r$

Gaussian orbitals: $A = [(2/\pi)^{1/2}2^{2n+1}/(2n-1)!!]^{1/2}\zeta^{(2n+1)/4}$

$t = r^2$

Orbital	Q	$f(x,y,z)$
s	0.282095	1
p_x, p_y, p_z	0.488603	x, y, z
d_z^2	0.315392	$3z^2 - r^2$
d_{xy}, d_{xz}, d_{yz}	1.092548	xy, xz, yz
$d_{x^2-y^2}$	0.546274	$x^2 - y^2$

[a] n and l are quantum numbers, x, y, z are cartesian coordinates and $r = (x^2 + y^2 + z^2)^{1/2}$; $f(x,y,z)$ is the function of coordinates that results from the angular part of the orbital. For gaussian orbitals, $n = 1, 2, 3$ is always used for s, p and d functions, respectively.

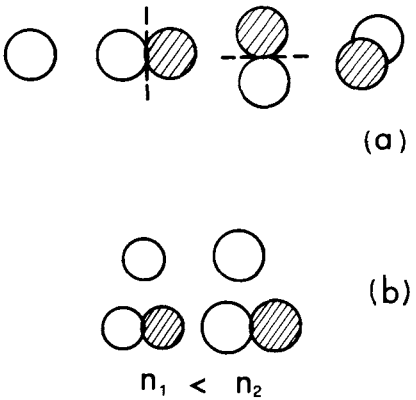


FIGURE 1. (a) Atomic orbitals with angular quantum number 0 (s orbitals, left) and 1 (p orbitals, right). (b) Diffuseness in space according to principal quantum number n.

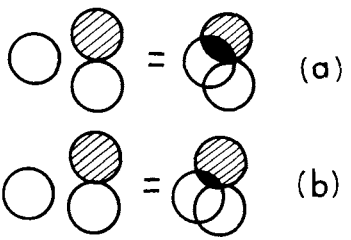


FIGURE 2. (a) s + p overlap equals zero: positive (white) and negative (black) areas cancel. (b) Overlap $\neq 0$.

type orbitals (GTO); the analytical forms are shown in Table 1. They have 0, 1, 2,... nodal planes, according to the angular quantum number being 0, 1, 2,... (Figure 1a). Their radial diffuseness increases with the principal quantum number n: thus, a 3p function of sulphur will have the same angular properties as a 2p function of oxygen, but will be more diffuse in space (Figure 1b). Since some AOs have nodal planes, some overlap integrals are identically zero by symmetry, the positive overlap exactly cancelling the negative one (Figure 2).

2. *Fragment orbitals (FO)*

Atomic orbitals can be combined to give fragment orbitals[1], that is, orbitals which are delocalized over a molecular fragment, such as CH_2 and CH_3, or over small molecules, such as H_2S and SO_2. The combinations are done on the basis of symmetry only. It is useful (but not strictly necessary) to proceed via hybrid orbitals, when both s and p AOs are involved. Figure 3 gives some self-explanatory examples. It is understood that whenever these fragments occur in a complex molecule their FOs will interact (again according to symmetry) with the FOs of the neighbouring groups.

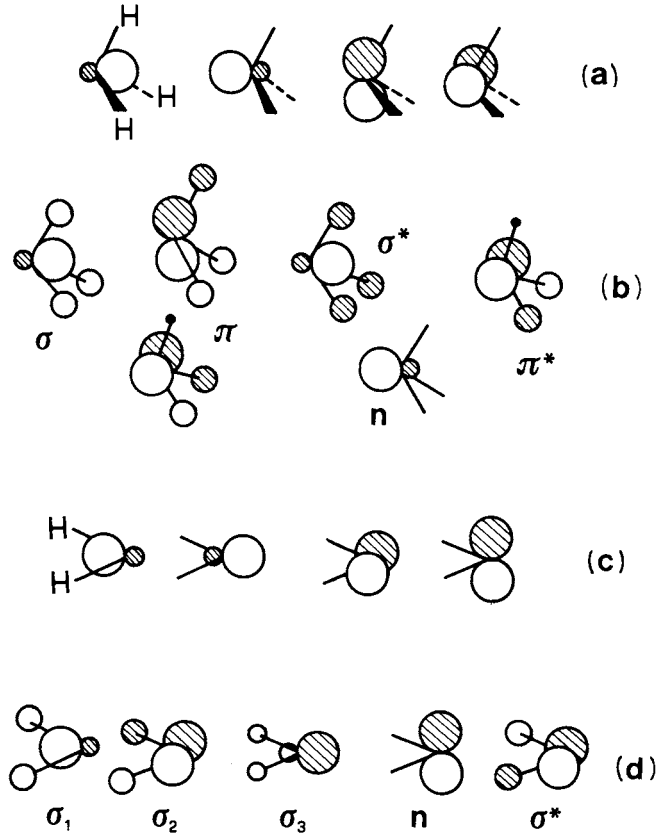


FIGURE 3. (a) Two sp hybrids (left) and two p orbitals on carbon. (b) Combination of the above with three s functions on hydrogen: the FOs of CH_3. (c) Same as (a), preparing sulphur for the FOs of H_2S, shown in (d).

3. *Bond orbitals and lone pairs*

Starting from hybrid orbitals, it is possible to construct bond orbitals by using normalized combinations. For every couple of hybrids pointing to each other along a bond direction, a bond–antibond pair can be obtained[2]:

$$b = 1/\sqrt{2}(h_1 + h_2)$$
$$a = 1/\sqrt{2}(h_1 - h_2)$$

Hybrids that do not point along bond directions are said to host 'lone pair' electrons. Figure 4 gives some examples.

The reader will be aware at this point (for example, by comparing the H_2S orbitals of Figures 3 and 4) that the final result is not unique, this being of course consistent with the qualitative character of these methods. The symmetry properties are, however, preserved,

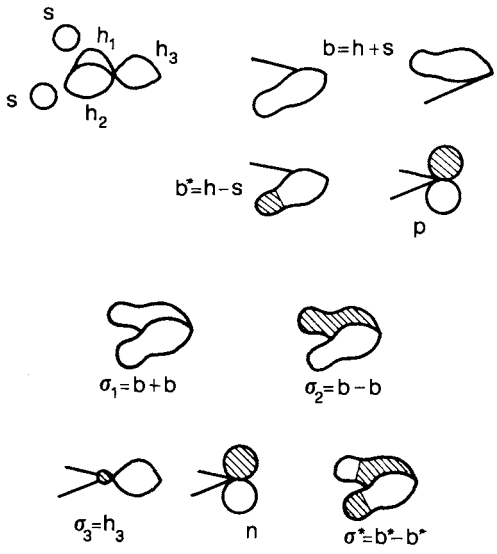


FIGURE 4. Top left: three hybrids, h_i, on sulphur and two s orbitals on hydrogen forming bond orbitals, b and b*; below, combination of BOs to give again the orbitals of H_2S (compare with Figure 3d). In this view, n and σ_3 are 'lone pair' orbitals.

and they are the same as could be found by any rigorous molecular orbital calculation. In particular, the very concept of 'lone pair' orbital is not uniquely defined in MO theory, but depends on the particular type of localization procedure to which the basis orbitals (or the final molecular orbitals) have been subjected.

The total molecular energy is invariant to all transformations involving basis orbitals, just as any physical event is invariant under any transformation of coordinates. But just as the proper choice of coordinates helps in visualizing physical events, so the choice of the proper orbital basis is helpful in visualizing molecular properties.

C. Molecular Orbitals (MO)

The canonical molecular orbitals of any molecule can by obtained by computer calculations. All MO methods involve the diagonalization of a secular matrix. It can be said that by moving from AOs to FOs to BOs basis sets one proceeds through the various stages of this diagonalization process, as the number of non-zero off-diagonal overlap matrix elements decreases.

We wish to list here the rules one may follow in combining partial orbitals, POs (AO, FO, BO) into approximate molecular orbitals.

(1) Recognize molecular symmetry planes and axes. Even approximate, or local symmetry elements may be useful. One should not step back just because, formally, the molecule has no symmetry elements. A methyl and an ethyl substituent, or chlorine and bromine substituent, can be equated. Substituents that disrupt the molecular symmetry but have trivial electronic requirements may be deleted.

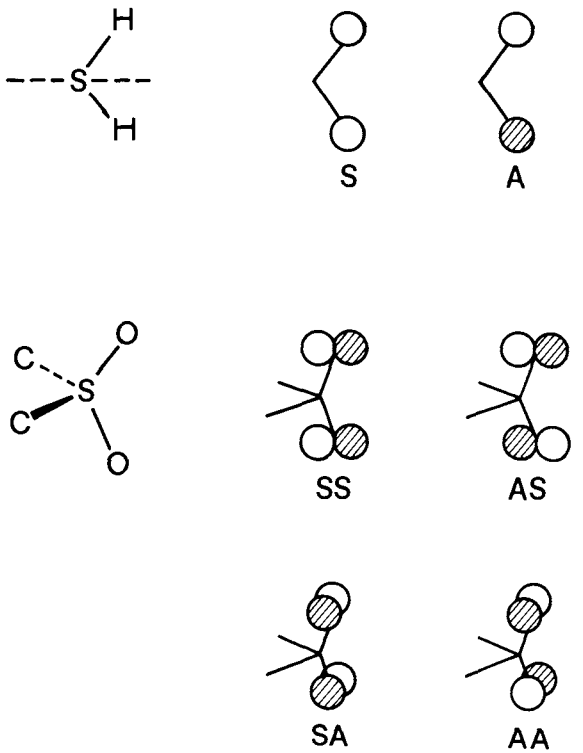


FIGURE 5. Symmetry-adapted combinations of two 1s hydrogen AOs (labelled symmetric or asymmetric with respect to the plane perpendicular to the HSH plane); and of the p orbitals of oxygens, where the labels are with respect to planes CSC and OSO.

(2) Form symmetry-adapted combinations (SAC) of POs. This is accomplished by combining couples into in-phase and out-of-phase pairs across symmetry elements. Figure 5 shows examples.

(3) Classify each PO or SAC as asymmetric (A) or symmetric (S) with respect to a given symmetry element, according to whether the orbital changes sign or not across that symmetry element.

(4) Combine POs with the same symmetry label(s) to form approximate MOs. From each couple, an in-phase and an out-of-phase combination must again be obtained. POs whose symmetry is such that they cannot mix, will remain as non-bonding orbitals. The in-phase combination will have a lower energy than the out-of-phase one.

The resulting MOs must meet the requirement that they be either (entirely) symmetric or (entirely) asymmetric with respect to each symmetry element; this provides a quick check of wrong combinations. The MOs have the following properties:

(1) A MO which has a nodal surface crossing a bond is antibonding (or vice versa, bonding) for that bond; when the MO is filled, the bond is weakened (strengthened), when it is emptied, by ionization or excitation or reaction, the bond is strengthened (weakened).

(2) A MO which has lobes of opposite sign into close contact is destabilized; if a

molecular deformation produces such an effect, the energy of that MO will rise. The opposite holds for contacts between lobes of the same sign.

All conclusions drawn from the above reasoning depend on the assumption (among others) that two-electron properties may be neglected. In particular, conclusions on total molecular energies drawn from MO inspection are sensitive to this point. The reader's attention is however drawn to the following points:

(1) A fairly large amount of information can be derived from such simple and inexpensive methods.

(2) These arguments go hand in hand with Extended Hückel Theory (EHT), both being based on overlap (symmetry) considerations. In fact, an EHT calculation will provide almost exactly the same results as a skilful use of the qualitative MO building scheme we have provided in this section.

(3) The Woodward–Hoffmann orbital symmetry rules rest very much on the same foundations; to the extent to which the total molecular energy changes parallel orbital energy changes, the reaction barriers arise from the need to correlate orbitals of the same symmetry in reactants and products. In reactions, bonds are broken and formed; in such bond stretching processes, bonding MOs are destabilized by bond lengthening, and antibonding MOs are destabilized by bond shortening.

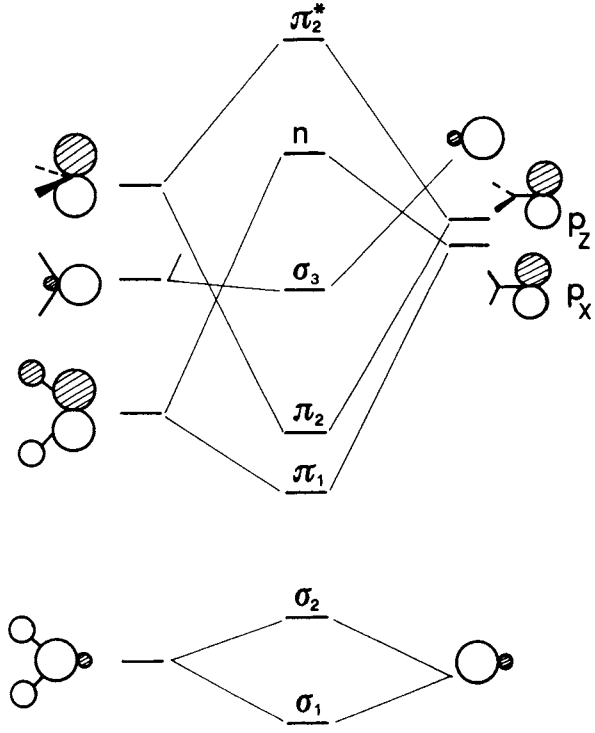


FIGURE 6. The MOs of H_2S (left) combining with the two sp hybrids and two p orbitals of oxygen to give the MOs of H_2SO (shown in Figure 7).

II. THE MOLECULAR ORBITALS OF SIMPLE SULPHUR COMPOUNDS

A. H_2S and H_2SO

In H_2S (see Figure 3d) the s and p_y orbitals of sulphur have been combined into two sp hybrids, and interact with the in-phase SAC of H_2 to give σ_2 and σ_3; p_x interacts with the out-of-phase SAC to give σ_2 and σ^*, while p_z is a non-bonding orbital. The reader may work out for himself what the MOs of H_2S would be if all three p orbitals of sulphur had been combined into sp^3 hybrids. σ_1 and σ_2 are S—H bonding, σ_3 is almost non-bonding, n is totally non-bonding, and σ^*, the lowest unoccupied molecular orbital (LUMO), is S—H antibonding.

Figure 6 illustrates how, on the same grounds, the AOs of oxygen combine with the MOs of H_2S to give the MOs of H_2SO. Figure 7 shows the shapes of these MOs, together with the changes in energy that accompany planarization. Notice how, on going from planar to pyramidal geometry, π_1 and π_1^* are stabilized (positive lobes on H and oxygen

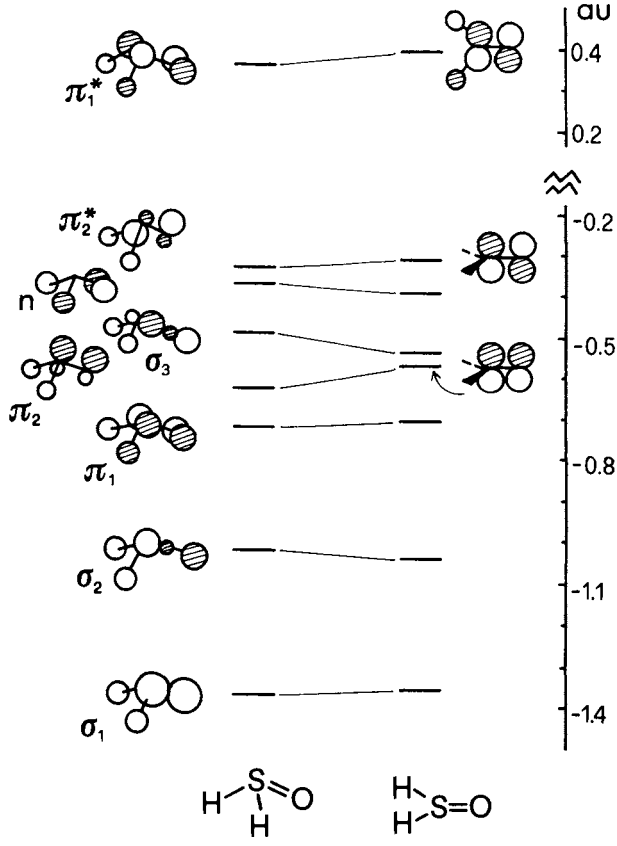


FIGURE 7. The MOs of H_2SO, and the energy changes after planarization. MO energies are from *ab initio* calculations as described in Section IV.C.1.

are brought together), as are π_2 and π_2^*, which gain some H—S overlap—forbidden by symmetry in the planar conformation; see Figure 2a. In n and σ_2 lobes of opposite sign are brought closer, and the MOs are destabilized.

In a slightly different approach, π_1, n and π_1^* can be seen as the three possible combinations ($+ + +$, $+ 0 -$, $+ - +$) of the p_x orbitals of oxygen and sulphur and the out-of-phase SAC of H_2.

B. SO_2 and H_2SO_2

Figure 8a shows how the SACs for the O_2 group can be formed, with their symmetry labels. Again, two sp hybrids have been constructed first. Figure 8b shows the MOs of

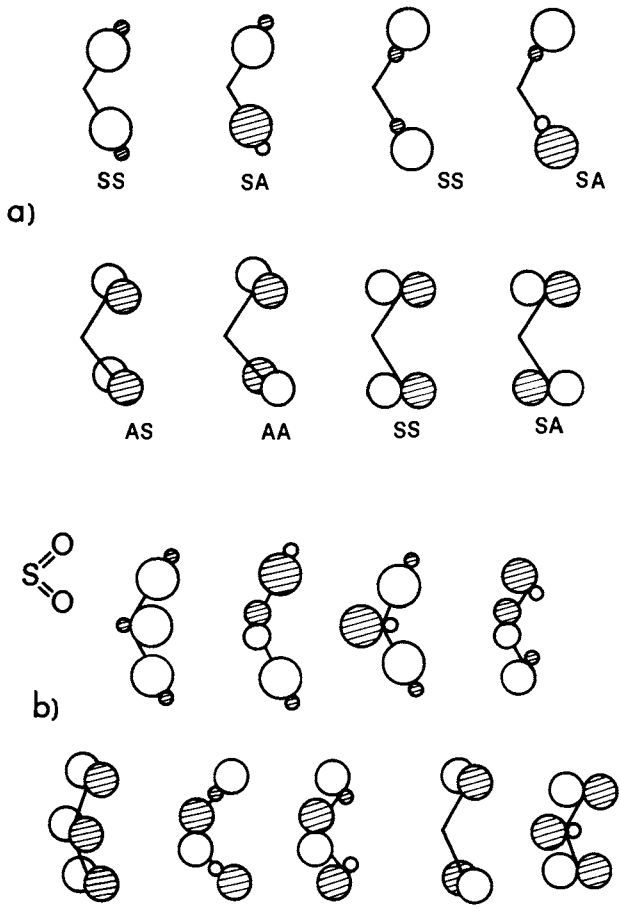


FIGURE 8. (a) Symmetry-adapted combinations of sp hybrids and of p orbitals on the oxygens of an OXO group. Symmetry labels are with respect to the OXO plane and to the plane perpendicular to it. (b) Combinations of these SACs with two sp hybrids and two p orbitals on sulphur to give the MOs of SO_2.

SO_2. Figure 9 shows how the SACs of O_2 can be coupled to the MOs of H_2S to give the MOs of H_2SO_2, for each symmetry block, but the reader may work out the equivalent case, in which the MOs of SO_2 are combined with the SACs of H_2. The final result must be qualitatively the same; the MO shapes are given in Figure 10. Within the AS block, it is easy to recognize that the number of nodal surfaces increases from 1 to 4 as the energy rises.

The highest occupied MO (HOMO) is S—O σ-antibonding, and S—H non-bonding. The LUMO is S—O π-antibonding and S—H antibonding. On this basis, it can be predicted that promotion of one electron from the HOMO to the LUMO will cause S—H bond weakening, and, since the σ-effects are stronger than the π-ones (σ overlap is larger than π overlap), the overall result will be an S—O bond strengthening (decrease of antibonding effects).

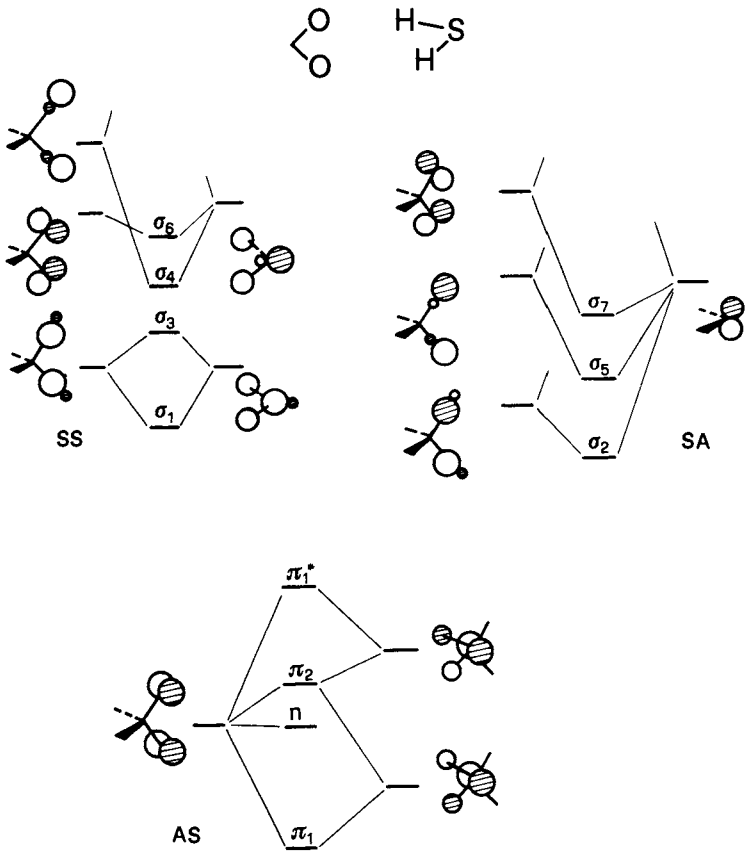


FIGURE 9. SACs of the OXO group (Figure 8a) interacting with the MOs of H_2S to give the MOs of H_2SO_2, for each symmetry block (labels with respect to OXO and HSH planes, respectively).

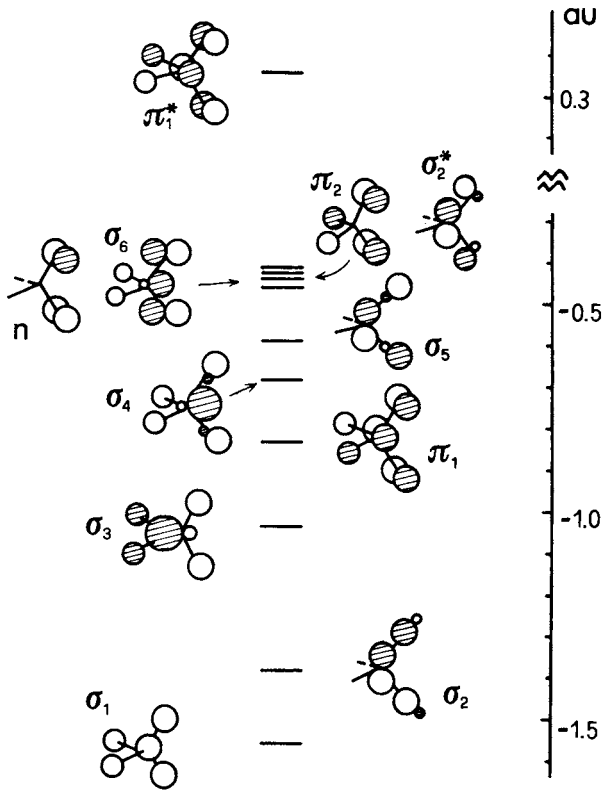


FIGURE 10. MOs of H_2SO_2. Energies from *ab initio* calculations as described in Section IV.C.1. σ_2* is the HOMO.

III. ANALYSIS OF MOLECULAR ORBITAL RESULTS

A. Wavefunction

Many of the figures given in Section II are actually simplified plots of the molecular orbitals. From any MO calculation, these are given by a set of coefficients, c_{ij}, in the linear combination of AOs χ_j (LCAO):

$$\psi_i = \sum_i c_{ij}\chi_j$$

The total wavefunction, Ψ, is an antisymmetrized product of the one-electron functions ψ_i (a Slater determinant). The ψ_i are called one-electron functions since they depend on the coordinates of only one electron; this approximation is embedded in all MO methods. The effects that are missing when this approximation is used go under the general name of electron correlation.

The Ψ lends itself to the usual probabilistic interpretation, that is, $\Psi\Psi^* d\tau$ is equal to the probability of finding an electron in the volume element $d\tau$; thus, a plot of this quantity as a

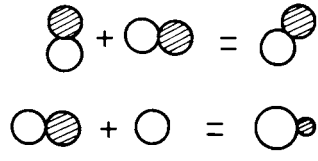


FIGURE 11. Combination of p orbitals on the same center resulting in rotation; combination of s and p orbitals on the same center resulting in a 'hybrid' orbital.

function of r will give the electron distribution in the molecule. If there are unpaired spins, then $\Psi_\alpha{}^2 - \Psi_\beta{}^2$ will give the spin density. If atomic electron distributions are subtracted from the molecular electron density, then bond electron density maps can be obtained. By a few mathematical manipulations, the electron density can be converted into the electrostatic potential around the molecule, which can be used to discuss reactivity to charged species. According to basic quantum mechanical principles, if a is an observable to which is associated an operator $\hat{A}$, then

$$\langle a \rangle = \int \Psi \hat{A} \Psi^* d\tau$$

is the expectation value of observable a. Thus, any molecular property can be obtained (at least in principle) in this way.

A graphical representation of the MOs can be obtained by drawing AOs on each atomic center, with signs as given by the LCAO coefficients. Combinations of AOs on the same center and with the same angular quantum number (for $l > 0$, i.e., p or d orbitals) merely represent rotations of AOs. A combination of AOs on the same center but with different angular quantum numbers (e.g., s and p orbitals) will yield the MO equivalent of 'hybrids'. Figure 11 shows what is meant by the above. For a final touch, the size of the AOs in the drawings can be made proportional to the magnitude of the coefficients—although care should be taken to avoid the impression that this represents the actual spatial size of the AOs or MOs, since that also depends on the diffuseness of the AO (see Section I.B.1).

B. MO Energies and Ionization Potentials

Molecular electrons can be allocated to molecular orbitals according to a sort of aufbau principle. In this line of thought, the orbital energies E_i can be assimilated to the ionization potentials of electrons in the orbitals. Of course, the MO energies are not independent of electron occupancies, and electron rearrangements occur after one electron is ejected; a better approximation to ionization energies can therefore be obtained by running two separate MO calculations, one for the ground state and one for the ion.

The total electronic energy is given by

$$E_{el} = 2\sum_i E_i - \sum_{i,j}(2J_{ij} - K_{ij})$$

where the sums are over occupied orbitals, and J_{ij} and K_{ij} are the two-electron parts of the Fock matrix. These make the difference between the total electronic energy and the sum of the energies of occupied MOs. They are neglected in semiempirical MO methods like Extended Hückel, where the total energy must be taken as the sum over occupied MO energies.

The energies of the highest occupied MO (HOMO) and of the lowest unoccupied MO

(LUMO) lend themselves to the following interpretation. A high-lying filled orbital contains electrons that are likely to drop to more stable energies when interacting with other molecules or fragments; therefore, a system with such electrons can be classified as a donor, or a base. Vice versa, a low-lying unfilled orbital will readily accept electrons under the same conditions, and qualifies a molecule as an acceptor, or an acid. Such reasoning clearly applies better on a relative than on an absolute basis. Along these lines, one then proceeds to the perturbational approach to molecular reactivity.

Electronic excitation energies can be approximated by differences between filled and empty orbital energies. Again, however, a more accurate treatment requires a separate calculation for the ground and excited state (represented by two different Slater determinants).

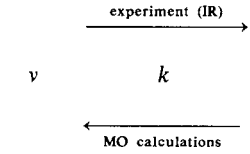
C. Total Energies: Conformational and Vibrational Analysis

Conformational analysis can be carried out by MO calculations by comparing the total energies of different conformations. Program packages which automatically (and analytically) compute the derivatives of the total energy, and minimize it, are by now available.

Vibrational analysis can be performed, although in an approximate way, as follows. The total energy is computed along vibrational displacement coordinates, and the curvatures are interpreted as force constants. Of course, there is no unique way to define these coordinates, but a particularly convenient choice for this type of calculation are the symmetry coordinates. These have the advantage that they are easily interpretable in chemical terms, as bond stretches or angle bends; and in many cases, by preserving molecular symmetry, they help saving computing time. Figure 12 shows some of these coordinates for dimethyl sulphoxide and dimethyl sulphone, and Table 2 lists their analytical expressions and the (experimental) values of the force constants. In the harmonic approximation, the deformation energy can be written as

$$E_{\text{def}} = \tfrac{1}{2} k_{ii} S_i^2$$

along symmetry coordinate S_i. Note that the force constants carry two indices, since also cross terms are included. The path connecting experimental vibrational frequencies to energies can be schematized as follows:



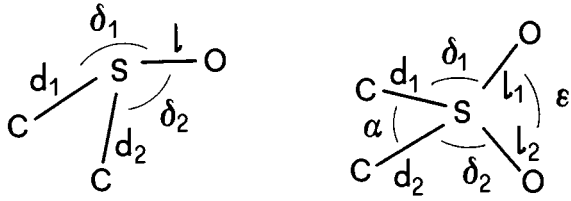


FIGURE 12. Molecular internal coordinates (bond lengths and angles) to be combined in symmetry coordinates (see Table 2).

TABLE 2. Analytical expressions for some symmetry coordinates[a] in dimethyl sulphoxide and dimethyl sulphone[b]

Coordinate	Expression	Force constant
Dimethyl sulphoxide		
S_7	l(S—O stretch)	7.16
S_{10}	$1/\sqrt{2}(d_1 + d_2)$ (sym C—S stretch)	2.87
S_{11}	$1/\sqrt{2}(\delta_1 + \delta_2)$ (sym CSO bending)	1.42
S_{12}	α (CSC bending)	1.36
S_{22}	$1/\sqrt{2}(d_1 - d_2)$ (asym C—S stretch)	2.59
S_{23}	$1/\sqrt{2}(\delta_1 - \delta_2)$ (asym CSO bending)	1.12
Dimethyl sulphone		
S_5	$1/\sqrt{2}(l_1 + l_2)$ (sym S—O stretch)	9.02
S_7	$1/\sqrt{2}(d_1 + d_2)$ (sym C—S stretch)	3.42
S_8	$1/\sqrt{2}(\varepsilon - \alpha)$ ('squashing')	1.76
S_{20}	$1/\sqrt{2}(d_1 - d_2)$ (asym C—S stretch)	3.08
S_{24}	$1/\sqrt{2}(l_1 - l_2)$ (asym S—O stretch)	10.21

[a]All data in this table are from G. Geiseler and G. Hanschmann, *J. Mol. Struct.*, **8**, 293 (1971).
[b]Refer to Figure 12 for the symbols. The force constants are in mdyn/Å.

D. Population Analysis

Molecular orbitals are functions defined over all space, vanishing only at infinity, and hence they are by definition delocalized over the whole molecule. But chemical significance relies on bond strengths and atomic charges. Therefore, some form of electron apportioning among the crucial molecular regions may be looked for. The most popular scheme for such a subdivision goes under the name of Mulliken population analysis. Given two atoms, r and s, and two atomic orbitals, χ_r and χ_s, one may have a function:

$$\psi = c_r\chi_r + c_s\chi_s$$

The population, N, of this function (usually equal to two electrons) is equal to:

$$N\int \psi^2 d\tau = Nc_r^2 + Nc_s^2 + 2Nc_rc_sS_{rs} = Nc_r^2 + Nc_s^2 + \mathrm{BOP}_{rs}$$

where S_{rs} is the overlap integral, and BOP_{rs} is called the bond overlap population along the r–s bond. This population can be divided into σ and π components, according to whether the AO combination is σ or π in character. If the rather crude assumption is made that half the electrons of the BOP pertain to each of the atoms (in fact, they will be more displaced towards the more electronegative center), sums can be carried out over occupied MOs to give total atomic charges (the Nc_r^2 term plus half of the BOP).

The BOP is interpreted as being correlated with the number of electrons in the bonding region between atoms, and hence to bond strength. Occupancy of bonding MOs (Section III.C) gives positive contributions to the BOP (c_r and c_s have the same sign), while the opposite is true for antibonding MOs. Caution must be exerted when using BOPs, as briefly summarized below:

(1) Do not expect a single-bond BOP to be equal to two, and so on for multiple bonds.

(2) A negative BOP can usually be interpreted as a repulsive interaction in valence-only MO calculations; in all-electron calculations, strongly antibonding core MOs are occupied, and negative BOPs are likely to occur even between strongly bound atoms.

(3) BOPs and atomic charges by population analysis are very sensitive to changes in the MO formulation and to the approximations (e.g. CNDO, EHT), and even to small basis set changes.

(4) BOPs and charges should be used only in a relative sense, among groups of similar molecules and, especially, using the same MO method and the same basis set.

(5) The BOP is sensitive to changes in bond length, as is the integral S_{rs}; inductive effects on bond strength can be gauged by BOP changes, but better so at constant bond length.

IV. VALENCE MO TREATMENT OF SULPHOXIDE AND SULPHONE COMPOUNDS

A. Pseudopotential Methods

The traditional valence-only MO schemes are Extended Hückel and CNDO with its subsequent modifications. Present-day computing facilities make it possible to move one step further, to the *ab initio* treatment of valence electrons through the use of pseudopotential (PP) methods. The essentials of such methods will be illustrated in the following, through a description of the NOCOR formulation[3], which will then be used for extensive calculations on sulphoxide and sulphone systems. The general concepts exposed in the foregoing sections will be illustrated by many examples.

In the NOCOR scheme, the following basic assumptions are made:

(1) The core electrons are replaced by a gaussian expansion which reproduces electrostatic and exchange core–valence interactions.

(2) The Fock matrix:

$$\boldsymbol{F}_{ij} = \boldsymbol{H}_{ij} + \boldsymbol{G}_{ij}$$

includes a correction to the one-electron matrix $\boldsymbol{H}_{ij}$, while all valence two-electron integrals are explicitly calculated. Therefore:

$$\boldsymbol{F}_{ij}^{(\mathrm{PP})} = \boldsymbol{H}_{ij}^{(\mathrm{PP})} + \boldsymbol{G}_{ij}^{(\mathrm{VALENCE})}$$

(3) All core–valence two-electron integrals are neglected.

TABLE 3. Coefficients (c_i) and exponents (α_i) of the 3G expansion for sulphur valence orbitals, and coefficients and exponents for the 6G expansion of the radial pseudopotential

3s		3p	
c_i	α_i	c_i	α_i
−0.494516	3.261907	−0.183835	6.780058
0.784269	0.334195	0.618104	0.441699
0.343541	0.125902	0.483497	0.127364

Pseudopotential	
c_i	α_i
0.300912	36.5903
0.413952	6.34650
0.057473	5.23282
−0.046591	2.07437
0.016197	0.55086
0.010162	0.05048

TABLE 4. Orbital energies and relative stabilities of atomic states for sulphur[a]

State		E(3s)	E(3p)	Relative energy
^{3}P	DZ-AE	−0.87897	−0.43694	—
	HF-AE	−0.87955	−0.43737	0
	PP	−0.87662	−0.43178	0
^{1}D	HF-AE	−0.88589	−0.41535	+0.0527
	PP	−0.87662	−0.40479	+0.0540
^{1}S	HF-AE	−0.89552	−0.38344	+0.1304
	PP	−0.87662	−0.36431	+0.1349

[a]DZ: double-zeta STO; HF: Hartree–Fock limit STO; AE: all electrons; PP: pseudopotential, this calculation. Energies are in a.u., and DZ and HF results are from Reference 4.

Obviously, the advantages of such methods increase with increasing atomic numbers; for first-row elements, the gain is negligible; for sulphur, these formulations are already reasonably time-saving. For the compounds which will be considered in the following sections, the computational effort is not substantially higher than in CNDO-type methods, with the advantage of an *ab initio* treatment of valence electrons. Any computing facility that allows extensive EHT calculations will also allow medium- to large-size PP calculations, for a reasonable expense.

The starting point to obtain a PP and basis set for sulphur was an accurate double-zeta STO atomic calculation[4]. A 24 GTO and 16 GTO expansion for core s and p orbitals, respectively, was used. For the valence functions, the STO combination resulting from the atomic calculation was contracted and re-expanded to 3G. The radial PP representation was then calculated and fitted to six gaussians, serving both for s and p valence electrons, although in principle the two expansions should be different. Table 3 gives the numerical details of all these functions.

The goodness of the PP representation can be checked by comparing the all-electron and PP orbital energies and relative stability of atomic states. The comparison is shown in Table 4, and is seen to be very satisfying. For a balanced treatment, also the carbon and oxygen atoms were treated by a PP, as described in previous work[5]. 3d functions were not introduced in the sulphur basis set, mainly because they were not deemed necessary for the illustrative purposes of this chapter. Also, the derivation of a PP representation for polarization functions is not a straightforward matter. The next section is devoted to the discussion of this point.

B. The Role of 3d Orbitals on Sulphur

The role of 3d polarization functions in molecular orbital calculations will be explained by a simple example, based on the SO_2 molecule. The symmetric bond stretch energy (symmetry coordinate S_5, Table 2) was calculated by our minimal basis set–PP approach, without d functions, yielding the result shown in Figure 13. The equilibrium bond distance is much too large, and the atomization energy is negative (the molecule is calculated to be unstable with respect to the free atoms). An all-electron calculation on the same molecule[6] gave excellent results for both quantities, when 3d functions were included in the basis set. It appears that they strengthen and shorten the S—O bond by allowing d-π back-bonding, through a coupling with oxygen p functions in the loosely-bonding or antibonding outer

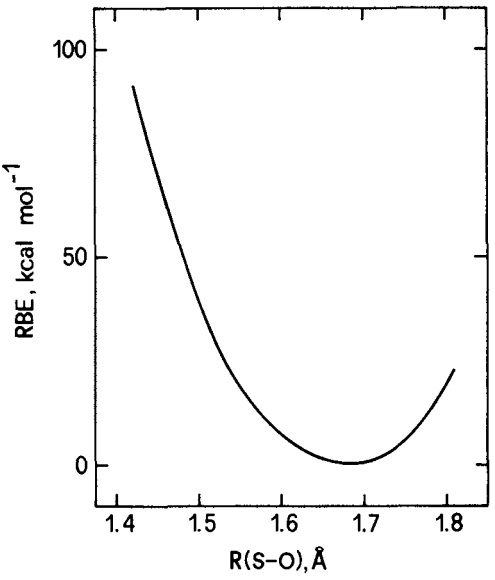


FIGURE 13. Relative binding energy, RBE, along the symmetric bond stretching in SO_2. PP calculations without 3d orbitals.

orbitals. In H_2S, where these interactions are impossible, 3d orbitals were found to be less crucial. Similar results were obtained in a PP study of SO_2[7], where it was also found that the SÔS bond angle prediction was less sensitive to d functions; this angle was calculated as 112.7° without, and 118.4° with 3d functions. Other studies[8] showed that also the C—S bond distance in CH_3SH was well reproduced without 3d functions; again, the dissociation energy of SO_2 was calculated as − 56.4 without, and 104.7 kcal mol^{-1} with 3d functions. A correct description of the energetics of the S—O bond therefore requires the use of these functions on sulphur; on the other hand, Table 5 reports calculated MO energies for SO_2, and it can be seen that they are fairly well reproduced even without 3d orbitals.

TABLE 5. Molecular orbital energies (a.u.) in SO_2

AE, no 3d[6]	AE, 3d[6]	PP	Experimental IP[6]
−0.468	−0.466	−0.424	0.460
−0.480	−0.491	−0.456	0.485
−0.525	−0.516	−0.517	0.496
−0.673	−0.649	−0.649	0.609
−0.671	−0.676	−0.696	—
−0.694	−0.677	−0.702	—
−0.873	−0.856	−0.880	—
−1.428	−1.393	−1.439	—
−1.550	−1.498	−1.581	—

TABLE 6. Calculated equilibrium geometries[9] for dimethyl sulphoxide[a]

Parameter	Basis set STO-3G	STO-4-31G	3G + d	Experimental
r(S=O)	1.82	1.73	1.49	1.48
r(S—C)	1.81	1.81	1.82	1.81
S=O bend	70.6	69.7	62.7	64.5
CSC angle	97.9	97.9	94.4	96.4

[a] Å and degree units are used here.

More definite evidence comes from an MO study of the S—O stretching in dimethyl sulphoxide[9], where three basis sets were employed: a STO-3G one (I), a 4-31G one (double-zeta, II) and a 3G + d one (III). Table 6 reports the main results; the small effect of the double-zeta, and the dramatic effect of the 3d functions, are clearly visible. Notice also how the C—S bond length and the bond angles are by far less sensitive to basis set changes.

The qualitative arguments we shall produce in the next sections are not affected by the lack of d functions in the sulphur basis set. This statement will be supported in detail by comparison of PP results with all-electron plus 3d ones, for the three-membered ring sulphur compounds (see Section IV.C.3).

C. Molecular Orbital Calculations: Results

1. H_2S, H_2SO, H_2SO_2

Table 7 shows the calculated properties of the molecules in this series. The molecular geometries were inferred from available data for H_2S and dimethyl sulphone. Methane

TABLE 7. Orbital energies and population analysis (from PP MO calculations) and assumed geometries[20] for hydrides[a]

Parameter	H_2S	H_2SO	H_2SO_2	Methane
HOMO (IP)	−0.401	−0.335	−0.426	−0.571
LUMO	0.388	0.360	0.355	0.680
q_S total	−0.322	0.450	1.255	−0.457[b]
s	1.766[c]	1.626	1.418	—
p	4.556[c]	3.925	3.327	—
BOP(S—H)	0.713	0.633	0.553	0.785[d]
BOP(S—O)	—	0.285	0.438	—
q_H	0.161	0.131	0.091	—
q_O	—	−0.711	−0.719	—
r(S—H)	1.34	1.34[e]	1.34[e]	—
r(S—O)	—	1.48[f]	1.44[g]	—
HŜH	92	92[e]	92[e]	—
OŜH	—	107[f]	—	—
OŜO	—	—	120[g]	—

[a] Energies are in a.u., charges (q) and BOPs in electrons, distances in Å and angles in degrees.
[b] On CH_2.
[c] Total number of electrons; 2 and 4 in neutral sulphur.
[d] BOP (C—H).
[e] Assumed as in H_2S.
[f] Assumed as in dimethyl sulphoxide.
[g] Assumed as in dimethyl sulphone.

was also considered, with the same basis set and pseudopotential, as the saturated aliphatic analogue in the HXH series ($X = CH_2$).

2. *Dimethyl sulphide, dimethyl sulphoxide, dimethyl sulphone*

Table 8 gives the complete population analysis for these molecules. Propane has been added for the same reason for which methane was considered above. Figure 14 gives the MOs of dimethyl sulphoxide, and Figure 15 the topmost ones of dimethyl sulphone.

A few comments apply. The σ manifold at the bottom of the MO energy spectrum of these molecules mainly consists of S—O and S—C bonding orbitals; at least one S—O antibonding orbital is however occupied. Note how these electron-rich molecules must occupy a large number of non-bonding or antibonding MOs near the top of the band, the more so for sulphoxides than for sulphones, since the number of electrons increases more slowly than the number of total (and hence also of non-repulsive) AO combinations. Thus, the HOMO of dimethyl sulphoxide is a π^* orbital, both C—S and S—O antibonding, while in the sulphone the HOMO is a moderately antibonding (actually almost non-bonding) orbital.

3. *Ethylene episulphide, sulphoxide and sulphone*

Table 9 shows the PP MO results for this interesting series of highly strained three-membered cyclic molecules. Here a detailed comparison is possible with the best results of an all-electron study, including d functions[10] (also reported in Table 9). An analysis of this table reveals how all trends in population analysis, both in charges and overlap populations, are the same in the AE + d and in the simple PP calculations, with very few and very minor exceptions. PP predicts a charge donation to the aliphatic groups, while AE predicts a withdrawal, mainly due to the availability of d orbitals on sulphur, which can allocate extra electronic charge. As outlined in the general notes on population analysis (Section III.D) comparisons should be carried out on a relative basis; and,

TABLE 8. Orbital energies and population analysis (from PP MO calculations) and assumed geometries[20] for dimethyl derivatives[a]

Parameter	$(CH_3)_2S$	$(CH_3)_2SO$	$(CH_3)_2SO_2$	Propane
HOMO (IP)	−0.343	−0.305	−0.401	−0.495
LUMO	0.369	0.342	0.357	0.562
q_S total	0.092	0.828	1.574	−0.005[b]
s	1.703	1.578	1.375	—
p	4.205	3.595	3.052	—
BOP(C—S)	0.582	0.471	0.387	0.634[c]
BOP(S—O)	—	0.402	0.547	—
$q_{(CH_3)}$	−0.046	−0.054	−0.060	0.002
q_O	—	−0.720	−0.727	—
r(C—S)[d]	1.80	1.80	1.80	1.54[c]
r(S—O)	—	1.48	1.44	—
CŜC	98.8	98.8	104	109.5[e]
OŜC	—	106	—	—
OŜO	—	—	120	—

[a]Energies are in a.u., charges (q) and BOPs in electrons, distances in Å and angles in degrees.
[b]On CH_2.
[c]C—C.
[d]Average value used for the three compounds.
[e]CĈC.

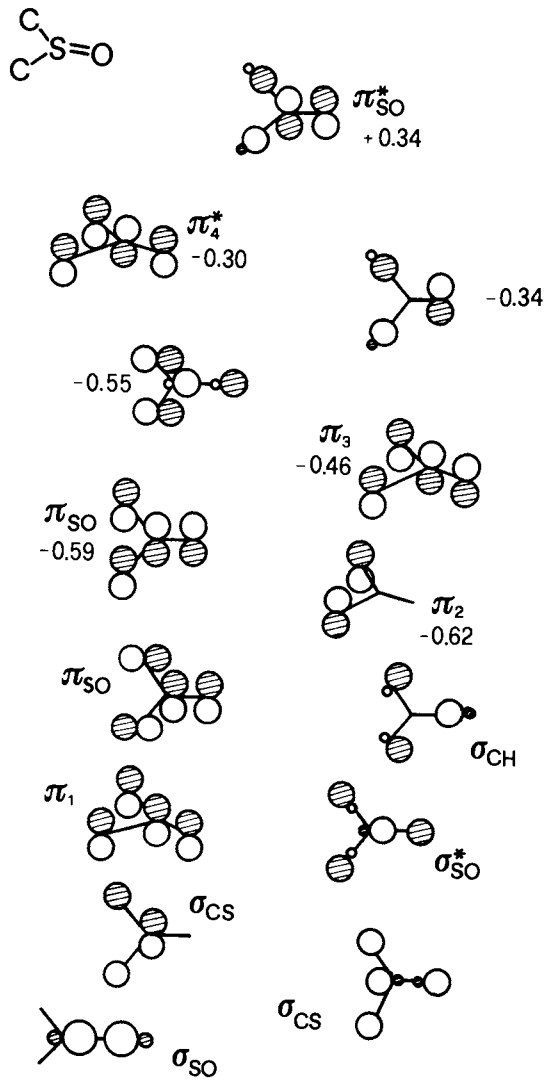


FIGURE 14. The MOs of dimethyl sulphoxide. Hydrogen atom contributions are not shown; they can be inferred from the FOs of CH_3, Figure 3b.

presumably, neither result is to be trusted on an absolute basis. Both kinds of calculations predict that the number of electrons on the methyl groups will increase on going from the sulphide to the sulphoxide and to the sulphone.

All other results are consistent with the picture of d orbitals as electron acceptors that strengthen the S—O bond. S—O BOPs are larger, and C—S ones are smaller, in the calculations with d orbitals; C—C BOPs show a decrease as the number of oxygen atoms

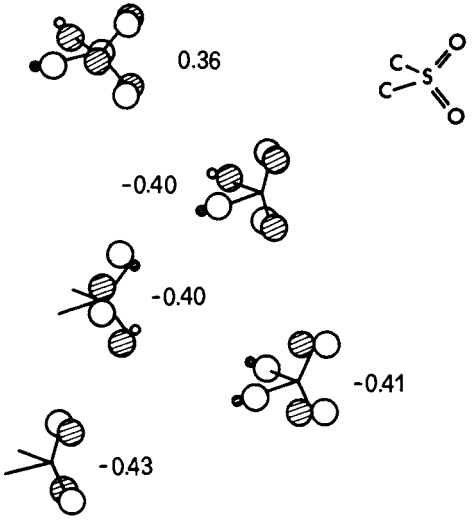


FIGURE 15. Topmost MOs of dimethyl sulphone. See also caption to Figure 14.

increases, but the AE result shows unreasonable negative C—C BOPs. Finally, the charges on oxygen are smaller in the calculations with d orbitals, due to the decreased sulphur-to-oxygen electron transfer.

Figure 16a shows the topmost valence orbitals of these molecules, and Figure 16b the comparison between calculated and observed values for the ionization potentials in the episulphide. The PP MO energies are invariably shifted downwards with respect to the spectrum of the observed IPs; this is a well-known effect, depending jointly on the minimal basis set and the PP representation. Keeping this in mind, the calculations offer a reasonably good guide to the true IP values. Finally, it may be noted that the HOMO of the episulphone, which has a very long C—C distance, is almost equal to that of the open-chain dimethyl sulphone molecule.

4. Trimethylene sulphide, sulphoxide and sulphone

Table 10 and Figure 17 carry all the necessary information. Since the only experimental geometry available is that for the sulphoxide, the ring geometry was kept constant in all three compounds, while OCS and OSO angles and S—O distances were taken from the analogous dimethyl derivatives.

5. Analysis of trends

Figure 18 shows in graphical form the trends which were obtained for the population analysis, on going from hydrocarbons to sulphides, sulphoxides and sulphones, and on changing the strain of the molecules by changing the ring size. The C—S (or H—S) BOPs decrease steadily, and are smaller than the corresponding C—C (or C—H) BOPs in the hydrocarbons; the C—S (or H—S) bond is apparently weaker than the C—C (or C—H) ones. At the same time, a strong increase in S—O BOP is consistently observed on going

TABLE 9. Orbital energies and population analysis (from PP MO calculations) and assumed geometries[20] for ethylene episulphide, sulphone and sulphoxide[a]

Parameter			
HOMO (IP)	−0.370	−0.350	−0.404
	−0.350	−0.355	−0.387
LUMO	0.205	0.187	0.225
q_S total	0.073	0.799	1.571
	−0.157	0.542	0.938
s	1.799	1.640	1.353
	1.878	1.699	1.267
p	4.127	3.561	3.075
	4.139	3.322	2.907
d[b]	0.140	0.437	0.888
BOP(C—C)	0.481	0.439	0.293
	0.278	0.111	−0.039
BOP(C—S)	0.445	0.342	0.305
	0.353	0.203	0.232
BOP(S—O)	—	0.436	0.530
	—	0.721	0.969
q_{CH_2}	−0.037	−0.067	−0.100
	0.079	0.050	0.037
q_O	—	−0.664	−0.673
	—	−0.590	−0.496
r(C—S)	1.822[c]	1.822	1.731
r(C—C)	1.505[c]	1.505	1.588
r(S—O)	—	1.483	1.439
CŜC	48.8[c]	48.8	54.6
OŜC	—	110.2	—
OŜO	—	—	121.4

[a] For each entry, the PP result is given above, the AE + d result[10] is given below. Energies are in a.u., charges (q) and BOPs in electrons, distances in Å and angles in degrees.
[b] AE result only.
[c] Assumed equal to the sulphoxide.

from the sulphoxides to the sulphones. The analysis of the top part of Figure 18 seems therefore to imply that the S—O bond becomes stronger than the C—S bond in sulphones.

Surprisingly enough, the effect of ring strain on the electronic structure of the —SO and —SO_2 groups is rather small. Sulphur charges and S—O BOPs are almost constant in the ring compounds and in the dimethyl derivatives. The only exception is a substantially weaker C—S bond (lower BOP) in ethylene episulphoxide.

The sulphone group does not perturb very much the hydrocarbon part of the molecules by inductive effects; the charges on CH_3 or CH_2 groups are rather small. The S—O bond in all sulphones (except H_2SO_2) is about as strong as in SO_2 itself (see the S—O BOPs in Figure 18b).

Charge distribution analysis reveals that, on the average, 0.7 electrons are donated by sulphur to each oxygen atom to which it is attached, be it in sulphoxide or sulphone molecules. About two-thirds of this donation goes through p orbitals. This picture might be changed by the introduction of d orbitals in the sulphur basis set. Judging from the results in Table 9, these orbitals do reduce the overall sulphur-to-oxygen electron

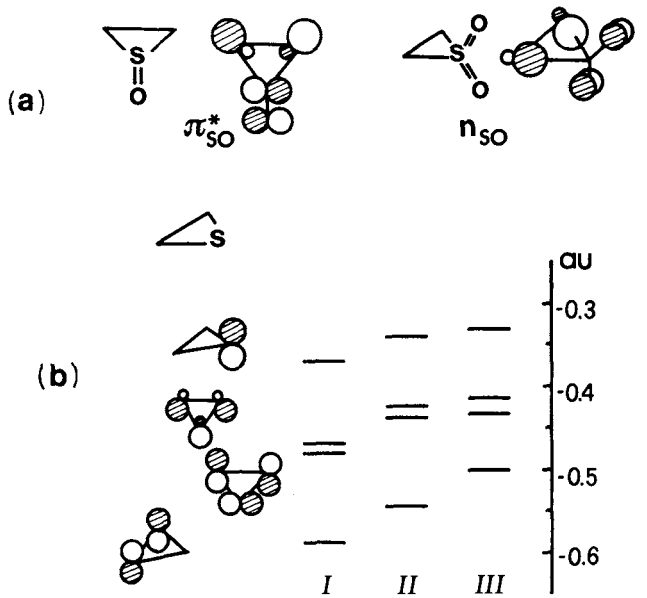


FIGURE 16. (a) The HOMO of ethylene episulphoxide and episulphone. (b) The energy spectrum at the top of the band for ethylene episulphide: I, PP; II, AE calculations (Reference 10); III, experimental values.

donation by about 30%, but leave unchanged the s and p charges calculated on sulphur. Their effect adds up to the s and p effects without apparently perturbing them. To summarize what has already been said about d orbital occupancy throughout this chapter, these orbitals act as electron sinks, where part of the total charge in electron-rich S—O bonds in poured, thus reducing the effects of the occupancy of antibonding orbitals. The fact that experimental geometries are accurately reproduced only when 3d orbitals are used supports the view that 3d orbital occupancy in sulphur is a true physical effect, and not just a computational artifact. The historical perspective of this problem[11,12] also lends support to this view.

The plots in Figure 19 show again the effect of the occupancy of antibonding orbitals in sulphur compounds: the HOMO is invariably destabilized with respect to the corresponding hydrocarbon HOMOs. Although LUMO energies (vacant orbital energies) are to be trusted less than those of occupied orbitals, LUMO stabilization and HOMO–LUMO gap reduction are clearly seen. The strained three- and four-membered ring compounds have more stable LUMOs; the lowest HOMO–LUMO gap is obtained for the ethylene episulphoxide molecule. The HOMO stabilization on going from sulphoxides to sulphones has already been discussed (see Section III.C.2) in terms of antibonding versus non-bonding character of these molecular orbitals.

6. *Barriers to planarization in sulphoxides*

In principle, an accurate calculation of these barriers should require full geometry optimization for the planar molecule. This is no easy task, however, and the result is very

TABLE 10. Orbital energies and population analysis (from PP MO calculations) and assumed geometries[20] (see text) for trimethylene sulphide, sulphoxide and sulphone[a]

Parameter			
HOMO (IP)	−0.351	−0.328	−0.405
LUMO	0.261	0.246	0.242
q_S total	0.092	0.827	1.557
s	1.760	1.603	1.383
p	4.148	3.570	3.060
BOP(C—S)	0.567	0.456	0.388
BOP(C—C)	0.623	0.614	0.617
BOP(S—O)	—	0.446	0.550[b]
			0.542
q_{CH_2}	α −0.061	−0.087	−0.106
	β 0.031	0.022	0.032
q_O	—	−0.674	−0.692[b]
			−0.686
r(C—S)	—	1.836	—
r(C—C)	—	1.540	—
r(S—O)	—	1.475	1.44[c]
CŜC	—	75.7	—
OŜO	—	—	120[c]
OŜC	—	113.4	—

[a]Energies are in a.u., charges (q) and BOPs in electrons, distances in Å and angles in degrees.
[b]There are two kinds of oxygen, since the ring is puckered.
[c]As in dimethyl sulphone.

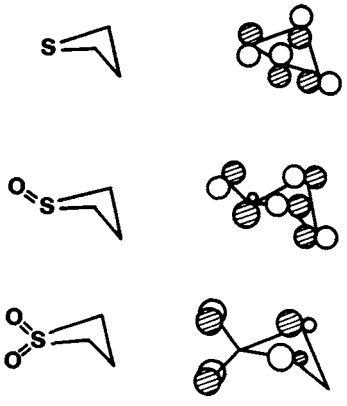


FIGURE 17. The HOMO in trimethylene sulphide, sulphoxide and sulphone, to be compared with the ones for the strained rings (Figure 16) and for the open-chain derivatives (Figures 14 and 15).

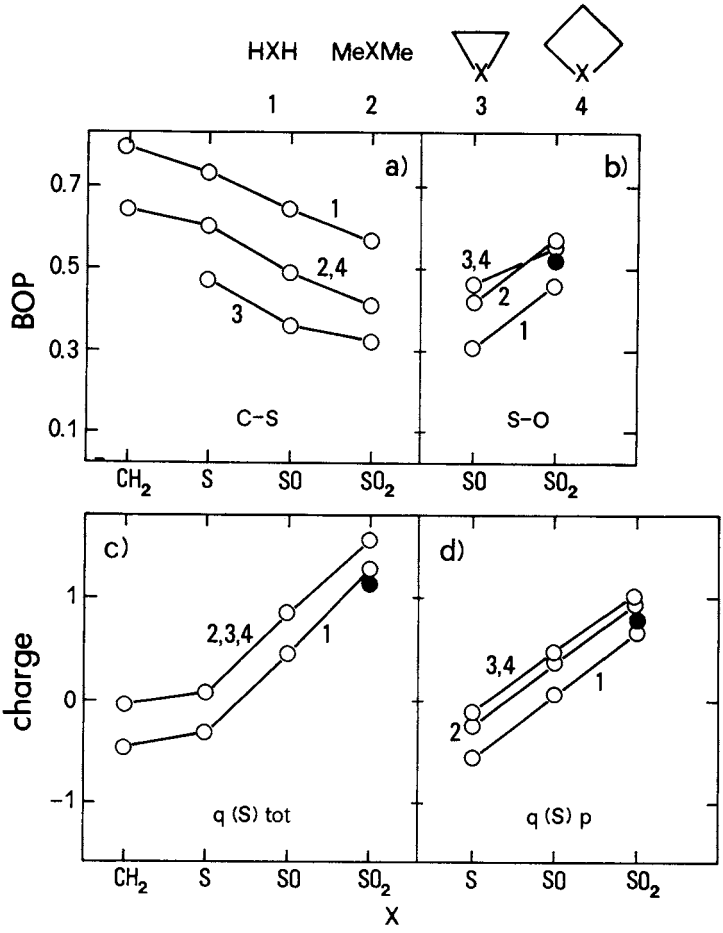


FIGURE 18. (a) C—S bond overlap population as a function of molecular geometry; (b) the same for the S—O BOP. (c) Total charge on sulphur, and (d), p-part of the charge. The black dots are the values for the SO_2 molecule itself.

sensitive to the choice of the basis set. We shall give in the following some qualitative arguments, based on calculations without geometry optimization, and in which the planar geometry was simulated by leaving all bond lengths and the CSC angle constant.

A simple analysis can be conducted using the S—O p–p BOPs, orbital by orbital. Table 11 shows these data. The x BOP is almost unaffected, since the planarization takes place in the nodal plane of these functions. The y BOP is drastically increased in the planar form, due to the favourable σ-type overlap; on the contrary, the z BOP becomes negative, due to the occupancy of π_2^* (see Figure 7) which is strongly antibonding in the planar form. A small increase in antibonding BOP comes also from the σ-block, however; this is more difficult to analyze in detail, being dispersed over many MOs. These lines of reasoning for H_2SO carry over to the other sulphoxide molecules here studied.

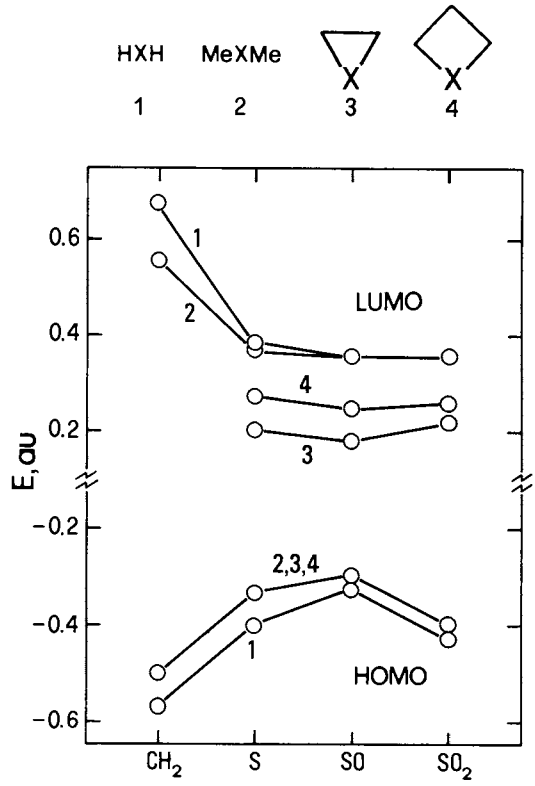


FIGURE 19. Trends in HOMO and LUMO for the molecules considered.

An accurate MO study of the inversion barrier in dimethyl sulphoxide[9] showed that the height of the calculated barrier is much more sensitive to the overall quality of the basis set, and to geometry optimization, than to the presence of 3d functions. This study predicts an S—O bond lengthening to 1.55 Å, and the best estimate of the barrier is 39.9 kcal mol^{-1}. This was the difference in energy between optimum planar and pyramidal

TABLE 11. S—O BOP in the p block for the planarization of H_2SO[a]

BOP type	Planar	Pyramidal
p_x–p_x	0.125	0.104
p_y–p_y	0.321	−0.035
p_z–p_z	−0.180	0.274
Total p	0.266	0.343
Total s + p	0.163	0.285

[a] x is along the S=O bond and y in the HSH plane.

TABLE 12. Energy and population analysis differences on going from pyramidal to planar sulphoxides by PP MO calculations

Molecule	ΔE^a	ΔBOP(C—S)	ΔBOP(S—O)	$\Delta q_S{}^b$
H_2SO	24.8	−0.005	−0.122	−0.160
$(CH_3)_2SO$	26.5	0.016	−0.124	−0.150
Ethylene episulphoxide	55.3	0.051	−0.221	−0.220
Trimethylene sulphoxide	36.0	0.018	−0.149	−0.180
Thiophen *S*-oxide	10.5[c]	—	—	—

[a] kcal mol^{-1} units.
[b] Negative values mean electron gain.
[c] All-electron MO calculation of Reference 13.

geometries (optimized with d functions) calculated by a double-zeta basis set without d functions.

Table 12 shows the results of our simplified calculations. A shortening of the C—S bonds, and a lengthening of the S—O ones, are clearly suggested by the changes in BOPs upon planarization. The sulphur atom is seen to recover almost all of the electrons lost by the S—O BOP. The variation in S—O BOP is exactly parallel to the increase in barrier height. Thus, even from the qualitative data in Table 12, it appears that the barrier to planarization arises mostly from a loss in S—O bond strength. In conjugated systems, this effect can be compensated by a gain in π-electron delocalization. Such was the case in thiophene *S*-oxide, for which an all-electron MO study[13] revealed a substantially lower barrier (see Table 12).

D. Further Remarks

What has been reported in the previous subsections does not amount to an exhaustive review of the existing literature on MO calculations for sulphones and sulphoxides—which is, anyway, not particularly rich. It must be said that the treatment of the S—O bond poses special problems, and is therefore less attractive for the theoretical chemist. A search was nevertheless conducted, and what follows provides nearly all the existing entry points to the theoretical literature of sulphone and sulphoxide compounds.

Wolfe[14] has provided a critical review, dealing with sulphur-containing carbanions, including a discussion of general theoretical methods for sulphur compounds. Hoffmann and coworkers[15] have published a qualitative MO analysis of the bonding in three-membered sulphur-containing rings, with some Extended Hückel calculations, and a masterful use of many of the orbital coupling arguments that have been summarized in this chapter. An exotic (for the theoretical chemist) molecule like F_2SO_2 has been treated by an *ab initio* calculation including bond polarization functions[16]. On the semiempirical side, the CNDO method was used for the conformational analysis of dimethyl sulphone[17], and again for three-membered cycles[18]; direct comparisons between CNDO and *ab initio* results have been reported[19].

The correlation of structural and vibrational parameters, and a detailed analysis of structural trends based on the available wealth of electron diffraction, microwave and X-ray structural studies on sulphoxides and sulphones, have been reported by Hargittai in a comprehensive study[20] which will stand for a long time as a milestone in the structural

chemistry of sulphur compounds. References to other theoretical activities on sulphur compounds are also abundant there.

V. STERIC PARAMETERS FOR SULPHOXIDE AND SULPHONE GROUPS

A. Molecular Wavefunction vs. Molecular Shape

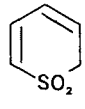
As outlined in Section III.A, knowledge of the molecular wavefunction implies knowledge of the electron distribution. By setting a threshold value for this function, the molecular boundaries can be established, and the path is open to a definition of molecular shape. A quicker, but quite effective, approach to this entity is taken by assuming that each atom in a molecule contributes an electron sphere, and that the overall shape of a molecular object results from interpenetration of these spheres. The necessary radii can be obtained by working backwards from the results of MO calculations[21], or from some kind of empirical fitting[22].

Once the size and shape of a molecule or of a molecular group are known, steric properties can be described in terms of space filling and mutual avoidance. Two basic quantities can be useful in this procedure, namely, the molecular volume, V_M[23] and the molecular free surface, S_M[24]. Both result from simple geometric calculations, given the molecular geometry and the so-called van der Waals or non-bonded atomic radii. It is important to remind here that all these arguments can be applied intra- or intermolecularly; the values of the atomic radii that apply in the two cases may be quite different. The following discussion will only concern the intermolecular part of the problem. The results will then be useful to interpret the molecular behaviour in condensed phases.

B. Volume and Surface of >SO and >SO_2 Groups

Table 13 lists these quantities for the simple molecules which have been previously considered in the MO calculations. Both V_M and S_M can be apportioned among the atoms in the molecule, and average atomic or group contributions can be obtained. A particularly attractive feature of these average contributions is that they are scarcely sensitive to small conformational changes or molecular deformations, so that they are additive over a rather large range of molecular geometries. By using the X-ray molecular structures of **1**[25] and **2**[26].

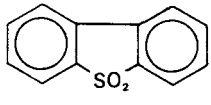
$CH_3SO_2CH_2CH_2SO_2CH_3$ (1)



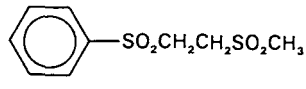
(2)

the group contributions of >CH_2 and =CH— groups α to the sulphur atom can be obtained; these are shown in Table 14, together with the group contributions derived from the data in Table 13, and some data taken from previous work[23,24].

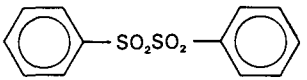
A number of sulphoxide and sulphone compounds, whose molecular structure was determined by X-ray analysis, was considered next[27–32].



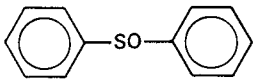
(3)



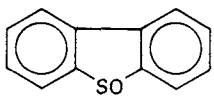
(4)



(5)



(6)



(7)

CH_3SOCH_3

(8)

TABLE 13. Free surface (Å^2) and volume (Å^3) for atoms in sulphur compounds, and total surface and volume[a]

Molecule	S	O	C	Total
H_2S	30.9	—	—	47.7
	22.5	—	—	29.0
CH_3SCH_3	22.3	—	13.6	90.3
	17.5	—	16.0	63.5
	26.6	—	12.6	79.0
	17.7	—	12.6	52.1
	24.1	—	10.5	95.4
	17.8	—	12.8	69.3
H_2SO	23.8	15.0	—	55.6
	20.5	7.6	—	34.6
CH_3SOCH_3	15.2	15.0	13.6	98.2
	15.6	7.6	16.0	69.1
	19.6	15.1	12.6	87.0
	15.7	7.6	12.6	57.8
	17.1	15.0	10.5[b]	103.3
	15.8	7.6	12.8	74.9
SO_2	26.4	14.7	—	55.8
	20.4	7.4	—	35.2
H_2SO_2	16.6	14.7	—	62.8
	18.5	7.4	—	39.8
$CH_3SO_2CH_3$	7.6	14.7	14.0	106.
	13.5	7.4	16.0	74.3
	11.1	14.7	12.8	93.4
	13.0	7.4	12.6	62.2
	9.8	14.7	10.5	111.
	13.8	7.4	12.8	80.1

[a] For each entry, the surface is above and the volume below.
[b] For the α methylene group.

TABLE 14. Group volumes (V in Å^3) and surfaces (S in Å^2) for fragments α to sulphur, and for sulphoxide and sulphone groups

Group	V	S
SO	23.2	30.2
SO_2	28.2	36.5
$-CH_3$	23.0	34.0
$>CH_2$	17.1	20.8
$=CH-$	14.8	18.6
C_6H_5[a]	78.6	94.9
$\equiv CH$[a]	18.1	27.8
$>C=O$[a]	18.2	22.3
$\diagup\!\!\diagdown CH$[a]	11.5	10.9

[a] Data from References 23 and 24, for general organic compounds.

The volume and surface of **3–8** were calculated, and were found to agree with those obtained from sums over group increments within 1%. Thus, it can be stated that the group increments in Table 14 are transferable quantities.

C. Molecular Surface and Ring Strain

There is one important case in which S_M is not constant for a given group, and that is when the group appears as a member of a strained ring system. In that case, the atomic

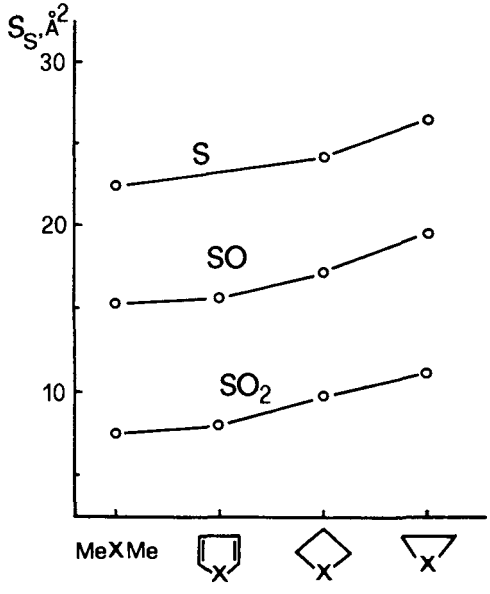


FIGURE 20. The free surface on the sulphur atom, S_s (Å^2), as a function of ring strain for sulphide, sulphoxide and sulphone molecules.

surface is a sensitive gauge of that strain. The point is demonstrated in Figure 20; the free surface on the sulphur atom increases as the ring strain increases. The curves in Figure 20 can be used to judge the amount of strain the $>SO$ or $>SO_2$ groups are subject to in any given ring.

D. Packing Energies of Sulphoxide and Sulphone Crystals

The packing energy of an organic crystal can be easily calculated by a lattice sum over pairwise interactions. The potential parameters for these calculations are summarized in Table 15. The packing energy is usually a quite accurate estimate of the crystal sublimation energy.

As already anticipated, the molecular surface we calculate is useful in describing condensed state properties. There is a steady linear relationship between S_M and packing energy for organic crystals[24], and the sulphoxide and sulphone compounds make no

TABLE 15. Parameters A, B, C for the intermolecular interatomic potentials[a] (energies in kcal mol^{-1}) and van der Waals radii used in surface and volume calculations (Å)[23,24]

Interaction	A	B	C	R_{vdW}
	$E = A\exp(-BR) - CR^{-6}$			
S···S	235000	3.49	2346	1.80
O···O	77700	4.18	259.4	1.40
C···C	71600	3.68	421	1.75
H···H	4900	4.29	29	1.17

[a] Mixed interactions by geometric average on A and C, and by arithmetic average on B.

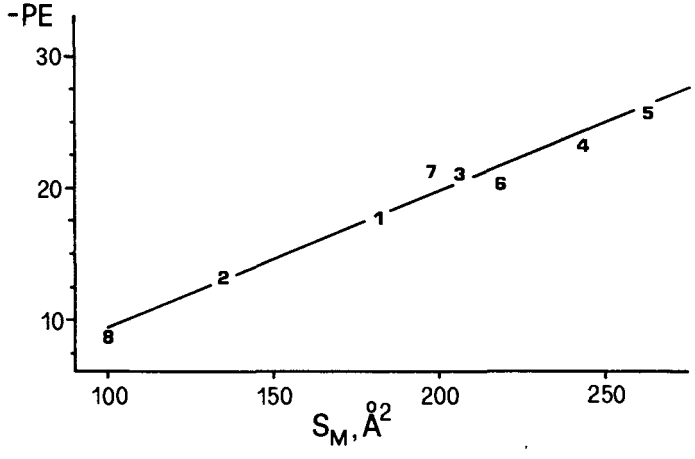


FIGURE 21. Packing energy, PE (kcal mol^{-1}; at 10 Å cutoff in the lattice sums), as a function of total molecular free surface, S_M, in compounds **1**–**8**.

exception, as shown in Figure 21. By a joint use of Table 14 (to calculate S_M) and Figure 21, the sublimation energy of sulphur-containing crystals can be estimated.

Due to the presence of the polar groups, the sulphoxide and sulphone crystals appear to be less tightly packed than the corresponding saturated hydrocarbons. The overall index of packing efficiency is the Kitaigorodski packing coefficient, C_K[22]; it is obtained by dividing the molecular volume by the total volume of the crystal cell. This quantity is on the average a little higher than 0.7 in organic crystals; the average C_K of compounds **1–8** is only 0.69.

VI. ACKNOWLEDGEMENT

The author thanks G. A. Pagani, Università di Milano, for fruitful discussions.

VII. REFERENCES

1. W. L. Jorgensen and L. Salem, *The Organic Chemist's Book of Orbitals*, Academic Press, New York, 1973, Chap. 1.
2. A. Gavezzotti and L. S. Bartell, *J. Amer. Chem. Soc.*, **101**, 5142 (1979).
3. C. S. Ewig and J. R. Van Wazer, *J. Chem. Phys.*, **63**, 4035 (1975); C. S. Ewig, R. Osman and J. R. Van Wazer, *J. Chem. Phys.*, **66**, 3557 (1977).
4. E. Clementi and C. Roetti, *At. Data Nucl. Data Tables*, **14**, 177 (1974).
5. A. Gavezzotti, G. F. Tantardini and M. Simonetta, *Chem. Phys.*, **105**, 333 (1986).
6. B. Roos and P. Siegbahn, *Theoret. Chim. Acta (Berl.)*, **21**, 368 (1971).
7. S. Huzinaga and M. Yoshimine, *J. Chem. Phys.*, **68**, 4486 (1978).
8. J. B. Collins, P. v. R. Schleyer, J. S. Binkley and J. A. Pople, *J. Chem. Phys.*, **64**, 5142 (1976).
9. P. G. Mezey and A. Kapur, *Can. J. Chem.*, **58**, 559 (1980).
10. M.-M. Rohmer and B. Roos, *J. Amer. Chem. Soc.*, **97**, 2025 (1975).
11. S. Oae, in *Organic Sulphur Chemistry, Theoretical and Experimental Advances* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Elsevier, Amsterdam, 1985, pp. 1–67.
12. F. Bernardi, I. G. Csizmadia, A. Mangini, H. B. Schlegel, M.-H. Whangbo and S. Wolfe, *J. Amer. Chem. Soc.*, **97**, 2209 (1975).
13. M. H. Palmer and R. H. Findlay, *J. Chem. Soc., Perkin Trans. 2*, 1223 (1975).
14. S. Wolfe, in *Organic Sulfur Chemistry, Theoretical and Experimental Advances* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Elsevier, Amsterdam, 1985, pp. 133–190.
15. R. Hoffmann, H. Fujimoto, J. R. Swenson and C. C. Wan, *J. Amer. Chem. Soc.*, **95**, 7644 (1973).
16. P. G. Burton and N. R. Carlsen, *Chem. Phys. Letters*, **46**, 48 (1977).
17. G. Robinet, F. Crasnier, J.-F. Labarre and C. Leibovici, *Theoret. Chim. Acta (Berl.)*, **25**, 259 (1972).
18. K. Tatsumi, Y. Yoshioka, K. Yamaguchi and T. Fueno, *Tetrahedron*, **32**, 1705 (1976).
19. H.-L. Hase, C. Müller and A. Schweig, *Tetrahedron*, **34**, 2983 (1978).
20. I. Hargittai, *The Structure of Volatile Sulphur Compounds*, Reidel, Dordrecht, 1985.
21. M. M. Francl, R. F. Hout and W. J. Hehre, *J. Amer. Chem. Soc.*, **106**, 563 (1984).
22. A. I. Kitaigorodski, *Molecular Crystals and Molecules*, Academic Press, New York, 1973, Chap. 1.
23. A. Gavezzotti, *J. Amer. Chem. Soc.*, **105**, 5220 (1983).
24. A. Gavezzotti, *J. Amer. Chem. Soc.*, **107**, 962 (1985).
25. F. Mo and O. Berg, *Acta Chem. Scand.*, **A36**, 657 (1982).
26. E. Boelema, G. J. Visser and A. Vos, *Rec. Trav. Chim. Pays-Bas*, **86**, 1275 (1967).
27. L. R. Kronfeld and R. L. Sass, *Acta Crystallogr.*, **B24**, 981 (1968).
28. F. Mo and A. Gaasdal, *Acta Crystallogr.*, **B36**, 2349 (1980).
29. C. T. Kiers and A. Vos, *Rec. Trav. Chim. Pays-Bas*, **91**, 126 (1972).
30. S. C. Abrahams, *Acta Crystallogr.*, **10**, 417 (1957).
31. J. A. Hashmall, V. Horak, L. E. Khoo, C. O. Quicksall and M. K. Sun, *J. Amer. Chem. Soc.*, **103**, 289 (1981).
32. R. Thomas, C. B. Shoemaker and K. Eriks, *Acta Crystallogr.*, **21**, 12 (1966).

CHAPTER 2

Structural chemistry of gaseous sulfoxides and sulfones

ISTVÁN HARGITTAI

Structural Chemistry Research Group of the Hungarian Academy of Sciences, Eötvös University, PO Box 117, Budapest, H-1431, Hungary

I. INTRODUCTION

Sulfoxides and sulfones have long been important in chemistry and their structural chemistry has been vigorously pursued during the past few decades. Today, they rank among the most studied classes of compounds, although that is not to say that further studies are unwarranted. However, a remarkable amount of structural data has been accumulated, making this area of study fruitful ground for concerted use of experimental and theoretical efforts. Thus, in addition to describing large numbers of individual structures and observing fairly general trends in structural variations, it is also becoming possible to understand the origins of these structures and their variations.

Of the two classes, the sulfones have received more study, but there is enough information on the sulfoxides to provide a meaningful comparison between them. Such a comparison is made more complete by including the corresponding sulfides and indeed the sulfone/sulfoxide/sulfide structural variations will be one of the central considerations of our treatment.

Another important consideration is the comparison between gaseous and crystalline sulfoxides and sulfones. Such a comparison may yield information about intermolecular interactions in the crystal[1]. Unfortunately, very few data are yet available for confident use in such comparisons. The first requirement is, of course, that the same compound has been investigated both in the gaseous state and in the crystal. In addition, it is necessary that all the structural data correspond to the same physical meaning (cf. Reference 1). When these conditions are fulfilled, interesting conclusions[2] may be reached on the basis of even small differences.

The differences in structural parameters originating from different techniques and referring to different states have been mentioned in a similar review on cyanates and isocyanates[3]. A more detailed discussion can be found elsewhere[4].

In this review, structural information on sulfoxides and sulfones is presented with emphasis on recent results and on structural variations. It is our intention that the discussion reflect the characteristic patterns of this area rather than provide an encyclopedic coverage. However, for the simplest, most fundamental, substances we are aiming at complete coverage as well.

Our discussion concentrates on experimental information providing some insight into the difficulties and limitations of these studies. In places, results from quantum chemical calculations will be invoked for comparison; however, a critical analysis of the application of these methods to sulfones and sulfoxides is beyond the scope of this section. As in previous reviews in this series[3,6,7], we shall be concerned primarily with the geometrical aspects of molecular structures.

For both sulfoxides and sulfones, the length of the S=O bond is the most important structural parameter. The sulfone group, in addition, has the bond angle O=S=O and the corresponding O···O nonbonded distance. The R—S=O and R—S—R bond angles and the lengths of R—S bonds in R_2SO sulfoxides and R_2SO_2 sulfones are the other geometrical parameters to consider. It is of interest to examine the changes in these parameters as the nature of the R group varies.

Two qualitative models have been successful in accounting for many of the structural changes in sulfoxides and sulfones[5]. One is the *V*alence *S*hell *E*lectron *P*air *R*epulsion (VSEPR) theory[8], while the other approach involves considerations of nonbonded ligand/ligand interactions[9].

The changes in the sulfur–carbon bonds appear to be especially sensitive to the nature of the R groups[10]. As R is usually a group of atoms, the relative conformation of these groups in terms of torsion angles with respect to the S—C bonds is often important.

II. GASEOUS STRUCTURES

A comprehensive and critical compilation has been published relatively recently on gas-phase molecular geometries of sulfur compounds including sulfoxides and sulfones[5]. This book covers the literature up to about 1980 and contains virtually all structures determined experimentally, up to that date, either by electron diffraction or microwave spectroscopy. Here we shall highlight only some of the most important observations from that source[5] and shall discuss recent results in more detail.

A. Sulfoxides

In addition to organic sulfoxides, R_2SO, thionyl halides, X_2SO, are considered here on account of the fundamental importance of their structures. Both thionyl fluoride, F_2SO, and thionyl chloride, Cl_2SO, have been repeatedly investigated by electron diffraction and microwave spectroscopy. The bond configuration of all sulfoxides is characterized by a pyramidal arrangement as shown in Figure 1. In terms of the VSEPR theory, this is an

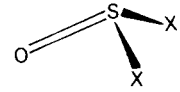


FIGURE 1. The pyramidal bond configuration of sulfoxides.

TABLE 1. Bond lengths (r_g) and bond angles (r_a) of thionyl halides from electron diffraction

	SOF_2	$SOCl_2$	$SOBr_2$
S=O (Å)	1.421(3)	1.443(5)	1.449(4)
S—X (Å)	1.585(3)	2.077(6)	2.255(5)
O=S—X (deg)	106.2(2)	106.4(6)	107.6(2)
X—S—X (deg)	92.3(3)	96.2(7)	98.2(2)
Ref.	12	13	14

AX_3E structure with three ligands and one lone pair of electrons around the central sulfur atom. The pyramidal bond configuration is part of the tetrahedral electronic configuration. The structure of Figure 1 possesses one symmetry plane (Point Group; C_s), and it is a general observation that the XSX angle is smaller than the OSX angle[11]. This result is fully consistent with VSEPR predictions according to which an angle involving multiple bond(s) will be greater than an angle involving single bonds only. Also from VSEPR theory, the angles involving the lone electron pair (E), i.e. the OSE and XSE angles, should be greater than the ideal tetrahedral value (109.5°) and, in particular, the OSE angle should be the largest of all. There is no experimental information about these angles but they can be estimated from quantum chemical calculations[16]. For example, the computed angles involving the lone pair are 109.5° for FSE and 125.8° for OSE in thionyl fluoride.

By virtue of C_s symmetry, the geometry of an X_2SO molecule is determined by the two independent bond lengths (X—S and S—O), and the two bond angles (X—S—X and O—S—X). All four parameters are listed for SOF_2, $SOCl_2$ and $SOBr_2$ in Table 1. Only the electron diffraction results are quoted here, but they are in good agreement with available microwave spectroscopy results for thionyl fluoride and thionyl chloride[15].

The lengths of the S—F, S—Cl and S—Br bonds gradually increase with increasing ligand size. The most noteworthy features of the thionyl fluoride structure are the relatively short S=O bond and small FSF angle as compared with S=O bonds and XSX angles of the other two thionyl halides. VSEPR considerations offer a straightforward explanation in that the great electronegativity of fluorine draws electron density in the sulfur–fluorine bond away from the vicinity of the central sulfur atom. Thus, the repulsions of the SF bonding pair for the other electron pairs are diminished, resulting in a shorter S=O and a smaller FSF angle. Accordingly, the OSF angle of SOF_2 should also be smaller than those of the other thionyl halides; the relatively large experimental errors for these measurements may conceal this change.

The geometrical variations shown by dimethyl sulfoxide, $(CH_3)_2SO$, and its perfluoro derivative, $(CF_3)_2SO$, are fully consistent with the above observations. A molecular model is shown in Figure 2 and the main geometrical parameters are given in Table 2. The S=O bond is shorter and the CSC angle is smaller in the perfluoro derivative than in dimethyl sulfoxide and even the change in the OSC angle is quite pronounced. It should be noted that the trifluoromethyl ligand is bulky, and although this size would tend to increase the bond angles and lengthen the bonds about the sulfur atom, the observed changes display none of these features, indicating that the effect of the electron pair repulsions prevails. The most striking differences between the two compounds is in the length of the S—C bonds; the CH_3/CF_3 substitution stretches this bond considerably. Similar changes accompany the CH_3/CF_3 substitution in sulfones, as will be seen in the next Section. This bond-length variation has been attributed, in simple terms, to the difference between the electron-

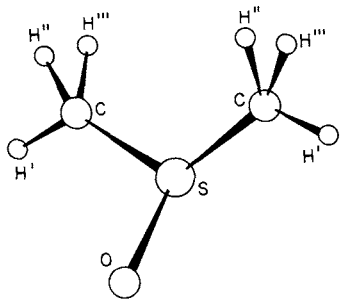


FIGURE 2. The molecular model of dimethyl sulfoxide. The following C—H lengths (Å), S—C—H bond angles (deg) and τ(C—S—C—H) torsional angles (deg) were determined from microwave spectra by Typke[17]:

C—H′	1.05(4)	SCH′	108(2)	τ'	1.6(9)
C—H″	1.098(3)	SCH″	107.8(2)	τ''	123.2(4)
C—H‴	1.071(8)	SCH‴	110.6(2)	τ'''	243.6(3).

releasing ability of the methyl group and the electron-withdrawing ability of the trifluoromethyl group[19,20] (see also later).

A degree of asymmetry has been established for the individual methyl groups in dimethyl sulfoxide[17]. This effect appears in the lengths of the three C—H bonds, in the S—C—H bond angles, and in the three torsion angles, τ(C—S—C—H); the values are given in the caption to Figure 2. The position of the hydrogen atom *anti* to the nonadjacent S—C bond is the least accurately determined of the three, but the asymmetry is definitely real. The differences of τ relative to 0, 120 and 240°, respectively, indicate a slight deviation from a symmetrical staggered form. The S=O bond is also staggered with respect to the C—H bonds of the methyl groups, and the dihedral angle S=O/CSC is 65° (Figure 3). The overall conformation of $(CF_3)_2SO$ is similar to that of dimethyl sulfoxide, but real deviations from the most symmetrical arrangement have not been established by the electron diffraction analysis as they were in the microwave spectroscopic investigation of $(CH_3)_2SO$. The torsional variation detected for the CF_3 groups is practically the same as the experimental error of the determination, 5(4)°. However, there seems to be a well-established tilt between the C_3 axis of the CF_3 groups and the S—C bond direction, viz.

TABLE 2. Sulfur bond configuration in dimethyl sulfoxide and its perfluoro derivative in the gaseous state

	$(CH_3)_2SO$ (r_z) microwave spectroscopy	$(CF_3)_2SO$ (r_a) electron diffraction
S=O (Å)	1.485(6)	1.469(4)
O=S—C (deg)	106.6(1)	104.5(11)
S—C (Å)	1.808(4)	1.885(4)
C—S—C (deg)	96.6(2)	94.0(2)
Ref.	17	18

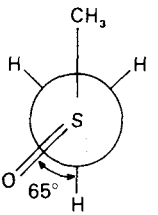


FIGURE 3. The conformation of dimethyl sulfoxide: projection along one of the S—C bonds.

3.6(5)°; the direction of the tilt indicates repulsion between the two CF_3 groups[18]. This feature is consistent with observations for a large series of sulfides with CH_3 or CF_3 substituents[5].

For diphenyl sulfoxide, $(C_6H_5)_2SO$, only the bond lengths could be determined with certainty; S=O 1.489(5) and S—C 1.804(6) Å (both are r_a)[21]. Among models in which the two torsional angles about the C—S bonds were constrained to have equal absolute values, the most probable conformation seems to be one in which the benzene rings are nearly perpendicular to the CSC plane. This model has C_s symmetry (Figure 4), and bond angles CSC 94° and OSC 108°. An early X-ray crystallographic study of diphenyl sulfoxide yielded CSC 97.3° and OSC 106.1° witn rather uncertain bond lengths[22], but with a conformation similar to that described above, although there was no crystallographically imposed symmetry.

The prevailing conformer (Figure 5) of *N,N'*-sulfinil-bis(dimethylamine), $(CH_3)_2NS(O)N(CH_3)_2$, is analogous to the staggered form of dimethyl sulfoxide; however, the presence of other, less abundant forms could not be excluded on the basis of the electron diffraction analysis[23]. The sulfur bond configuration is characterized by the following parameters (r_a): S=O 1.480(9), S—N 1.693(4) Å; NSN 97(1), and OSN 105.5(8)°.

The sulfur bond configurations of ethylene sulfoxide, $(CH_2)_2SO$, and trimethylene sulfoxide, $(CH_2)_3SO$, are shown in Figures 6 and 7, respectively. For the latter, details of

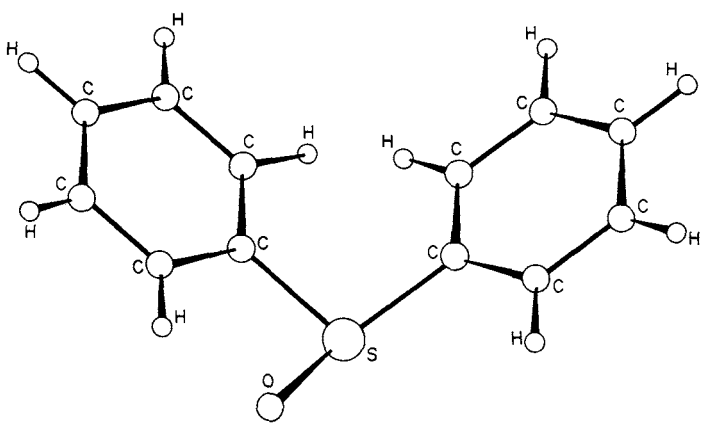


FIGURE 4. The molecular model of diphenyl sulfoxide (C_s point group): the benzene rings are nearly perpendicular to the CSC plane.

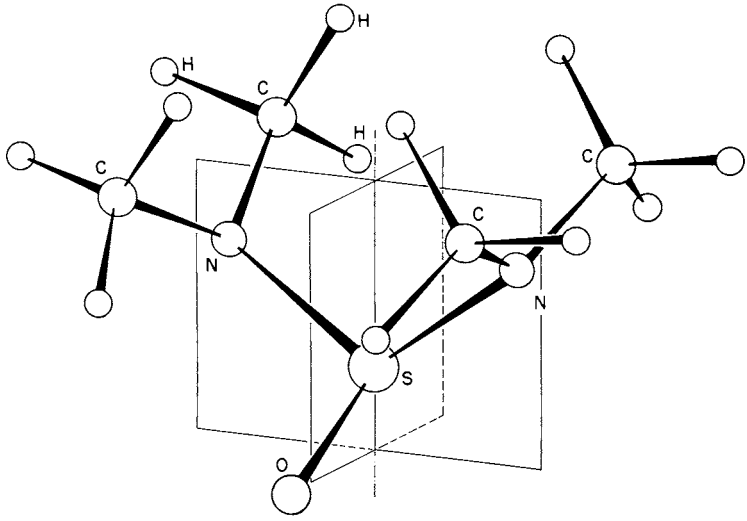


FIGURE 5. The molecular model of *N*, *N'*-sulfinil-bis(dimethylamine).

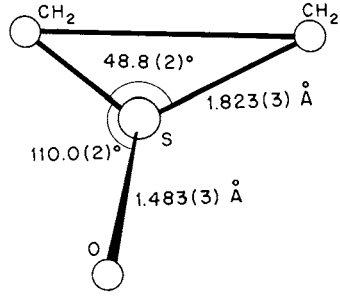


FIGURE 6. The sulfur bond configuration of ethylene sulfoxide[24,25].

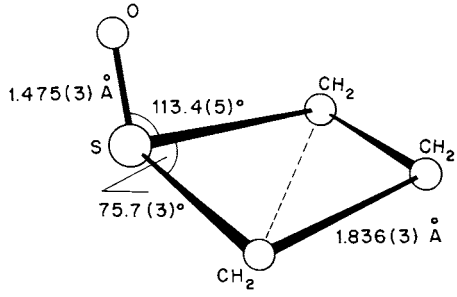


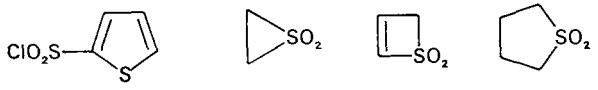
FIGURE 7. The sulfur bond configuration of trimethylene sulfoxide[26,27].

ring puckering and methylene group orientation have also been determined from microwave spectra[26,27].

B. Sulfones

Sulfone molecular structures, including sulfuryl halides, have been repeatedly reviewed through the late seventies[28] and early eighties[5]. Scheme 1 contains a list of the compounds discussed in these references. While the structures of these compounds will be discussed, recent structural information that was not included in the above compilations will be described initially. The relevant substances are listed in Table 3 along with the S=O bond lengths and OSO bond angles.

F_2SO_2	Cl_2SO_2	$(CH_3)_2SO_2$
$O(SO_2F)_2$	$ClSO_2CF_3$	$(CH_3O)_2SO_2$
FSO_2Cl	$ClSO_2CCl_3$	$(CH_2{=}CH)_2SO_2$
FSO_2Br	$ClSO_2OCH_3$	$(C_6H_5)_2SO_2$
$(FO_2SO)_2SO_2$	$ClSO_2CH_3$	$[(CH_3)_2N]_2SO_2$
	$ClSO_2CH{=}CH_2$	
	$ClSO_2C_6H_5$	
	$(ClSO_2)_2NH$	
	$ClSO_2N(CH_3)_2$	
	$ClSO_2NCO$	



SCHEME 1

The conformations of H_2NSO_2F and $HC(SO_2F)_3$ as a result of rotation about single bonds are shown in Figure 8 by projection formulas. The S—C bond length in the latter is 1.831(5) Å.

The overall geometry of pentafluorobenzenesulfonyl chloride, $C_6F_5SO_2Cl$[29], is similar to that of benzenesulfonyl chloride, $C_6H_5SO_2Cl$[40,41]. The molecular structure is shown in Figure 9. A comparison of the geometries of these two molecules reveals that the most noteworthy differences are the lengthening of the S—C bond, the shortening of the S—Cl bond, and the opening of the CSCl bond angle upon substitution of C_6H_5 by C_6F_5.

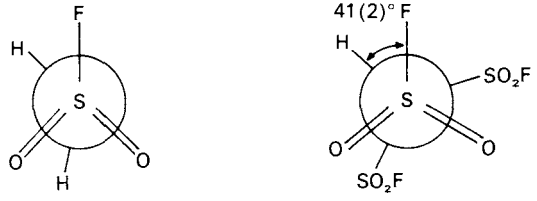


FIGURE 8. The torsional forms of H_2NSO_2F and $HC(SO_2F)_3$ shown by projections representing views along the S—N and S—C bonds, respectively[28].

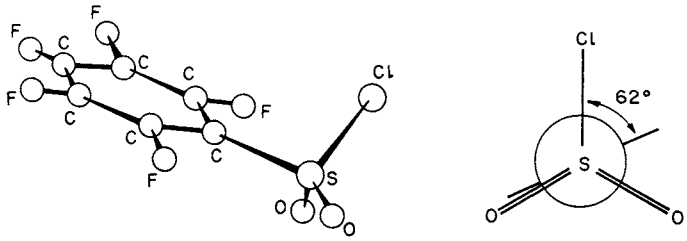


FIGURE 9. The molecular model and torsional form of pentafluorobenzene sulfonyl chloride[29]. The projection formula represents a view along the S—C bond.

	$C_6H_5SO_2Cl$	$C_6F_5SO_2Cl$
r_g(C—S), Å	1.765(9)	1.798(6)
∠ CSCl (deg.)	101.2	105(1)
r_g(S—Cl), Å	2.049(8)	2.027(5)

The change in the C—S bond length can again be related to the greater electron-withdrawing ability of the C_6F_5 group as compared with the C_6H_5 group. The effect is, however, smaller in this case than that observed upon substitution of CH_3 by CF_3, indicating a smaller susceptibility of the phenyl group to structural changes as a result of hydrogen/fluorine substitution[29].

The geometry of the triflic acid (trifluoromethanesulfonic acid) molecule[30], CF_3SO_2OH, is consistent with that of analogous molecules. The S—C bond length, 1.832(3) Å, is intermediate between those in CF_3SO_2Cl[42] and CH_3SO_2Cl[43]. The conformation is staggered about the C—S bond (Figure 10). The electron diffraction analysis indicated a deviation of about 10° from the symmetrical arrangement shown in Figure 10. If this difference is interpreted as a result of averaging over torsional vibrations about the C—S bond, then the barrier to rotation can be estimated as 15 kJ mol^{-1} [44]. Similar conformational properties were displayed by CCl_3SO_2Cl[45].

The molecular point groups of $(CF_3)_2SO_2$, $(CCl_3)_2SO_2$ and $(CBr_3)_2SO_2$ can be either C_{2v} or C_2 according to electron diffraction and vibrational spectroscopic data. The molecular model and projection formula for $(CCl_3)_2SO_2$ are shown in Figure 11. The molecular geometry of the bromine derivative has not been determined but its vibrational

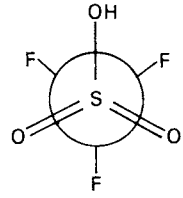


FIGURE 10. The staggered conformation of triflic acid[30]. The projection formula represents a view along the S—C bond.

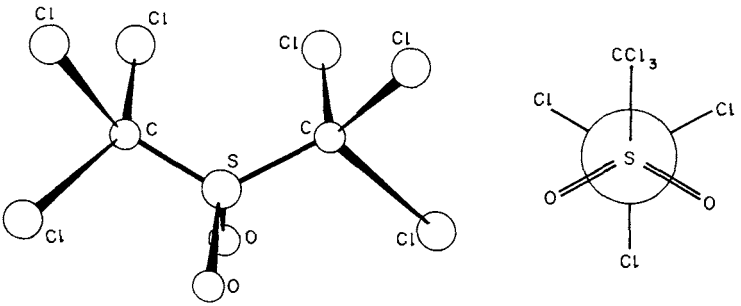


FIGURE 11. The molecular model (C_{2v} point group) and torsional form of $(CCl_3)_2SO_2$[31]. The projection formula represents a view along one of the S—C bonds.

spectra are consistent with those of the chlorine analog[31]. It is of interest to compare the C—S bond lengths and C—S—C bond angles in dimethyl sulfone and its two halogenated analogs:

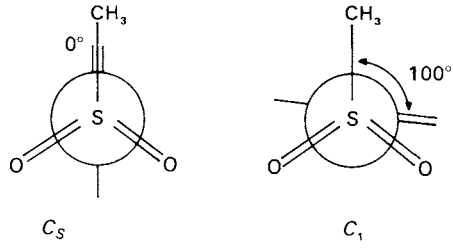
	$(CH_3)_2SO_2$	$(CF_3)_2SO_2$	$(CCl_3)_2SO_2$
S—C, Å	1.771(4)	1.858(5)	1.894(5)
C—S—C (deg)	102.6(9)	102.2(8)	109.8(4)
Reference	46	35	31

The lengthening of the S—C bond upon CH_3/CF_3 substitution has been interpreted by the electron-withdrawing ability of the trifluoromethyl group as compared to the electron-releasing ability of the methyl group. According to this interpretation, the S—C bond of $(CCl_3)_2SO_2$ would be expected to be of intermediate length. However, it has the longest S—C bond of all three substances. The greater lengthening of the S—C bond in $(CCl_3)_2SO_2$ may be due to the strong steric effects from the two bulky trichloromethyl groups. The shortest Cl···Cl nonbonded distance involving atoms in different CCl_3 groups is 3.31(1) Å, which is considerably less than twice the van der Waals radius of chlorine, viz. 3.60 Å. Valence shell electron-pair repulsion considerations would not account for the large C—S—C bond angle as compared with the analogous angles in the other two molecules. Thus, the extremely long S—C bond and the very large C—S—C angle of $(CCl_3)_2SO_2$ may be a result of nonbonded chlorine/chlorine repulsions. It should also be noted that the OSC angle of $(CCl_3)_2SO_2$, 106.5(3)°, is smaller than the CSC angle. This is an exception to the general observation for sulfones concerning the relationship among the sulfur bond angles, i.e.

$$O{=}S{=}O > O{=}S{-}X > X{-}S{-}X$$

as predicted by the VSEPR theory. This relationship follows from the greater repulsions by multiple bonds as compared to the repulsions by single bonds.

As has been observed for other vinyl sulfones[47,48], eclipsed forms prevail in the gaseous state of vinyl methyl sulfone, $CH_2{=}CHSO_2CH_3$[33], and α-bromovinyl methyl sulfone, $CH_2{=}CBrSO_2CH_3$[36]. The former appears as a mixture of two conformers in a 1:1 ratio (Figure 12). Although the environments of the two S—C bonds are different in each of these substances, it is difficult to distinguish their lengths from electron diffraction data. The mean bond lengths are 1.775 and 1.765 Å in the two compounds, respectively. Bromomethyl methyl sulfone, $CH_2BrSO_2CH_3$[36], has a staggered form with r(S—C) 1.784 Å as mean value. The C—S—C bond angles in all three molecules are in the range of 103–104°.



C_S C_1

FIGURE 12. Two stable torsional forms of vinyl methyl sulfone[33]. The projection formulas represent a view along the S—C(vinyl) bonds.

Methanesulfonic acid dimethylamide, $CH_3SO_2N(CH_3)_2$[34], has a staggered conformation (Figure 13) analogous to those of tetramethylsulfonyl diamide, $(CH_3)_2NSO_2N(CH_3)_2$[49], and *N*,*N*-dimethylsulfamoyl chloride, $(CH_3)_2NSO_2Cl$[50]. The S—C bond length and C—S—N angle are 1.771(12) Å and 106(1)°, respectively.

The electron diffraction analysis of 1,2-bis(methylsulfonyl)ethane, $CH_3SO_2CH_2CH_2SO_2CH_3$[38], yielded a limited amount of structural information. However, this substance has also been studied by X-ray crystallography[51,52], and the two sets of data offer a possibility for comparison. The molecular model is shown in Figure 14.

As regards rotation about the central C—C bond, an *anti* or nearly *anti* SCCS orientation was established in both gas and solid phases. Two different models for the rotation about the C—S bonds were equally consistent with the gas-phase experimental data. In one model, one of the CCSC chains had an *anti* orientation while the other chain approximated a *syn* orientation. In the other model, the CSCCSC skeleton had an inversion center with the CSC planes being essentially perpendicular to the SCCS plane. This second model was similar to the conformation in the crystal phase and is the one shown in Figure 14. The choice of model did not influence appreciably the refinement of the other parameters in the electron diffraction analysis. The S=O bond length from the electron diffraction study (Table 3) is in excellent agreement with that found from the low-temperature X-ray data[52]. The C—C bond found in the gas is longer, r_g 1.561(12) Å, than that measured in the crystal, 1.522 Å. Only the mean S—C bond length could be determined accurately (1.789 Å) for the molecules in the gas phase. When the lengths were

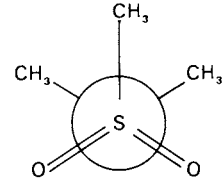


FIGURE 13. The staggered conformation of methanesulfonic acid dimethylamide[34]. The projection formula represents a view along the S—N bond.

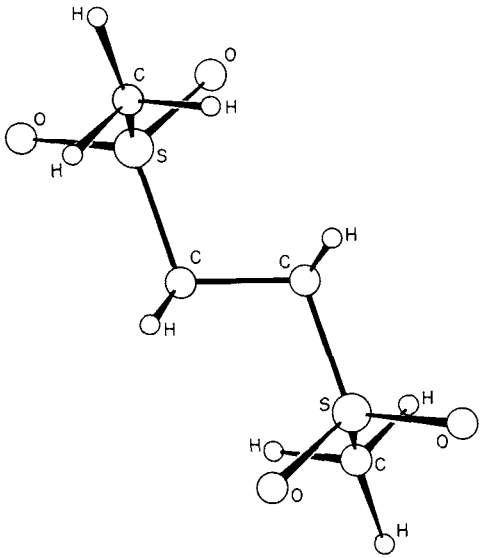


FIGURE 14. The molecular model of 1,2-bis-(methylsulfonyl)ethane.

refined separately, values for $H_3C—S$ and $—H_2C—S$ bonds of 1.772(25) and 1.808(25) Å were obtained, but the high uncertainty makes the results of limited value. However, assuming that the $H_3C—S$ bond has the same length as that found in other similar molecules (1.77 Å), the lengthening of the $—H_2C—S$ bond seems to be fairly well established. Nevertheless, the mean S—C bond length in the crystal, 1.77 Å, was found to be shorter than the mean length in the gas.

TABLE 3. Sulfonyl molecular geometries not yet considered in Reference 5; all gas-phase electron diffraction studies

Compound	r(S=O) (Å)	O=S=O (deg)	Ref.
H_2NSO_2F	1.412(3)	123.4(23)	28
$C_6F_5SO_2Cl$	1.415(3)	123.6(10)	29
$HC(SO_2F)_3$	1.416(3)	123.0(5)	28
CF_3SO_2OH	1.418(2)	122.0(13)	30
$(CCl_3)_2SO_2$	1.419(3)	120.8(10)	31
$HOSO_2OH$	1.422(10)	123.3(10)	32
$CH_3SO_2CH=CH_2$	1.429(4)	120.0(15)	33
$CH_3SO_2N(CH_3)_2$	1.431(5)	118.0(9)	34
$(CF_3)_2SO_2$	1.435(3)	122.9(26)	35
$BrCH_2SO_2CH_3$	1.437(3)	116.8(12)	36
$CH_2=CBrSO_2CH_3$	1.438(4)	121.6(26)	36
$BrCH—CH_2$ $\vert \quad \vert$ $CH_2—SO_2$	1.442(3)	121.5(5)	37
$(CH_3SO_2CH_2)_2$	1.443(3)	119.0	38
$C_6H_5SO_2CH_3$	1.444(3)	118.4(6)	39

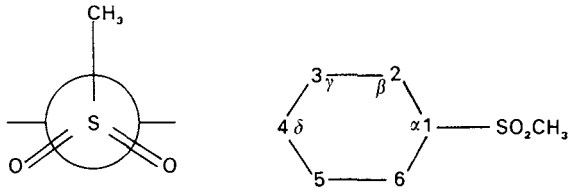


FIGURE 15. The ('perpendicular') torsional form of methyl-phenyl sulfone. The projection formula represents a view along the S—C(phenyl) bond. The other drawing shows the labels of the benzene ring angles.

There are several interesting questions relating to the structure of methyl phenyl sulfone, $C_6H_5SO_2CH_3$[39]. The first concerns the S—C bond lengths. Dimethyl sulfone[46] and diphenyl sulfone[21] have practically the same S—C bond lengths, viz. 1.771(4) and 1.772(5) Å, respectively. Methyl phenyl sulfone provided the opportunity to determine the lengths of these bonds in the same molecule; the results [S—CH_3 1.785(12) and S—C_6H_5 1.771(12) Å] were consistent with previous findings if the relatively large experimental errors were taken into account. Another question concerned the conformational behavior of methyl phenyl sulfone. In the gas phase, this molecule was shown to have a so-called 'perpendicular' form (Figure 15) which shows no appreciable deviation from a symmetric structure. This conformation was also found in crystalline methyl phenyl sulfone[53]. The deformation of the benzene ring under the influence of the methylsulfonyl substituent has also been investigated. The angular changes (Figure 15), unfortunately determined with large uncertainties, are consistent with the presence of an electronegative substituent. As the crystal structure of methyl phenyl sulfone was not investigated in sufficient detail, the molecular structure of methyl phenyl sulfone as determined in the gas phase has been compared with the molecular structure of *p*-methylsulfonylbenzoic acid, $CH_3SO_2C_6H_4COOH$, found in the crystal[54]. While *p*-methylsulfonylbenzoic acid is

TABLE 4. Selected molecular parameters of methyl phenyl sulfone (from gas-phase electron diffraction) and *p*-methylsulfonylbenzoic acid (from X-ray crystallography)

	$C_6H_5SO_2CH_3$	*p*-$CH_3SO_2C_6H_4COOH$[a]
C—C (Å)[b]	1.399(3)	1.398
S—C_6H_5 (Å)	1.771(12)	1.771
S—CH_3 (Å)	1.785(12)	1.768
S=O (Å)	1.445(3)	1.452
CSC (deg)	103.9(7)	103.6
OSO (deg)	118.4(6)	118.7
C_6H_5SO (deg)	108.2(4)	108.6
CH_3SO (deg)	108.6(6)	108.2
α (deg)	121.9(13)	122.0
β (deg)	118.9(8)	118.9
γ (deg)	119.6(7)	119.6
δ (deg)	121.2(7)	120.9

[a] Standard deviations are 0.002 Å for bond distances, 0.07–0.14° for bond angles.
[b] Mean value.

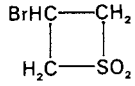
TABLE 5. Selected molecular parameters (Å, deg) of 3-bromo-λ^6-thietane 1,1-dioxide in the gas phase[37] and in the crystal[56]

	Gas	Crystal[a]
C—C Å	1.567(6)	1.525
S—C (Å)	1.801(4)	1.793
S=O (Å)	1.442(3)	1.410(mean)
Br—C (Å)	1.933	1.940
CCS (deg)	89.2(5)	87.9
CSC (deg)	80.4(4)	82.2
CCC (deg)	95.8(7)	101.3
OSO (deg)	121.5(5)	116.2
CCC/CSC (deg)	25.0(14)	9.0

[a] The estimated standard deviations for bond distances are 0.01–0.02 Å and for bond angles, 0.6–1.4°.

clearly a different molecule, the structural influence of the —COOH substituent on the benzene ring is negligibly small[55]. Most of the gas-phase and crystal-phase data are in excellent agreement as demonstrated in Table 4. An exception is the S—CH_3 bond distance which appears to be about 0.02 Å shorter in the crystal. The quoted X-ray diffraction results refer to high-2θ refinement and include corrections for librations[54].

The molecular geometry of 3-bromo-λ^6-thietane 1,1-dioxide, $C_3H_5BrO_2S$,



was determined in the gas phase by electron diffraction[37] and in the crystal by X-ray diffraction[56]. Some selected molecular parameters are presented in Table 5; the ring is more puckered, the C—C bond is longer, and the SO_2 group is more open in the gas phase than the corresponding results obtained from the crystal.

An earlier electron diffraction investigation of sulfolane, $CH_2CH_2CH_2CH_2SO_2$[57], has been augmented by a microwave spectroscopic analysis[58]. While the electron diffraction data were approximated by a half-chair and an envelope model (Figure 16), the microwave spectra could also be interpreted in terms of an essentially planar ring. The apparent inconsistency was resolved[59] by considering the planar moments in a relatively large series of sulfone molecules and by a comparison with the structure of ethylene episulfone (thiirane 1,1-dioxide), and additional evidence was provided for the planarity or near planarity of the sulfolane ring. This conclusion, however, refers to the equilibrium structure, whereas the effective structure obtained directly in an electron diffraction

FIGURE 16. The half-chair and envelope models of sulfolane.

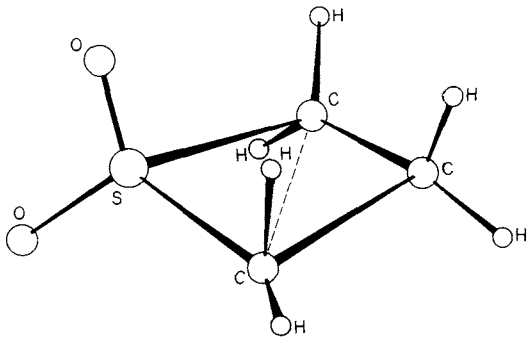
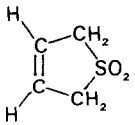
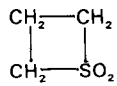


FIGURE 17. The molecular model of trimethylene sulfone with a considerably puckered four-membered ring[61].

analysis, by averaging over all intramolecular vibrations, may very well be a nonplanar half-chair or envelope. The microwave spectra of 2,5-dihydrothiophene *S,S*-dioxide showed[60] that the puckering motion has a double minimum potential function with a considerable barrier to the planarity of the ring. Low-resolution microwave spectra of trimethylene sulfone indicated a puckered four-membered ring conformation with a dihedral angle of about 43° (Figure 17)[61].





With the review of recent results completed, the data in Table 3 and the geometry of the SO_2 group will be discussed. An empirical relationship correlating S=O bond length, r (Å), and O=S=O bond angle, 2α (°), for a series of XSO_2Y sulfones was communicated in a previous study[5],

$$2\alpha = -147.7r + 331.7 \qquad (\sigma = 0.6°).$$

The S=O bonds shorten and the O=S=O bond angles open as more electronegative ligands are attached to the SO_2 group. The above relationship was based on data for a sample of only eleven compounds. However, all the data included in this study referred to free molecules which were studied by the same technique in the vapor phase, viz. electron diffraction, and most of the data originated from the same laboratory. The empirical relationship correlating 2α and r gave nearly the same predictions as the trigonometrical expression

$$2\alpha = 2\sin^{-1}(2.484/2r)$$

in which 2.484 Å corresponds to the nonbonded O···O distance. This expression utilizes the remarkable phenomenon of the O···O distance being constant in a relatively large series of sulfonyl derivatives. It was suggested[5] that this result indicates that the nonbonded oxygen–oxygen interactions may be as important in determining the geometry of the sulfone group as the bonded interactions considered in the valence shell electron-pair repulsion model[8]. It was further suggested that the emerging pattern of results can be visualized by a tetrahedral arrangement of the XSO_2Y molecule with the

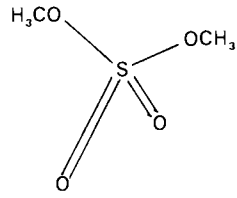


FIGURE 18. The molecular model of dimethyl sulfate.

sulfur atom in the center of the tetrahedron and the two oxygen atoms at two of the apexes. As the two ligands are changed, the two oxygen atoms remain in their position, while the sulfur atom may move up and down along the vector corresponding to the bisector of the O=S=O angle.

In addition, this observation of the constancy of O···O nonbonded distances had great value in both electron diffraction[62] and microwave spectroscopic[63] determinations of sulfonyl molecular structures. At the same time it was realized that a constancy of a nonbonded distance could be valid only within certain limits in a large series of compounds. It was emphasized, and should be reiterated, that both bonded *and* nonbonded interactions contribute to the determination of sulfonyl group geometry. An obvious indication that nonbonded interactions alone could not be responsible for the dimensions found is that the constant O···O distance of 2.48 Å is considerably larger than twice the 1,3-nonbonded radius of oxygen, viz. 1.13 Å, postulated empirically[9]. In fact, dimethyl sulfate[64] provides an example of a molecule in which three different O···O nonbonded distances occur (Figure 18). These distinct distances are associated with S=O/S=O, S=O/S—O and S—O/S—O interactions and are 2.48, 2.42 and 2.37 Å, respectively; these variations are indicative of diminishing bonded interactions. Unfortunately, no adequate quantum chemical calculations have yet been carried out on these systems to investigate the relative importance of bonded and nonbonded interactions.

Somewhat more attention has been paid to the constant values for fluorine–fluorine nonbonded distances in a large series of compounds containing CF_3 groups. The mean of the F···F nonbonded distances in 40 molecules was 2.162 Å with a standard deviation of 0.008 Å[65]. It may be noted that the molecules containing CF_3 groups discussed earlier in this review have the following F···F distances, $(CF_3)_2SO$ 2.162 Å, CF_3SO_2OH 2.163 Å and $(CF_3)_2SO_2$ 2.159 Å. The accumulated empirical information on F···F distances has been augmented by semiempirical quantum chemical calculations[66,67], the results of which were in agreement phenomenologically with the experimental data. However, energy partitioning calculations indicated that the constancy of nonbonded distances was a consequence of dominant bonding interactions and occurred as changes in bond lengths and bond angles were compensated[67].

In recent years the number of relatively simple sulfonyl molecules for which geometry has been determined in the vapor phase has increased considerably. The additional data are listed in Table 3. At this point there are a total of 40 geometries for sulfonyl compounds that have been determined in the vapour phase; all of them are indicated in the $r \sin \alpha$ versus $r \cos \alpha$ plot in Figure 19. While this number corresponds to a much larger sample of data than that considered previously, unfortunately the accuracy and the experimental sources are much more variable than for the smaller sample; therefore, no rigorous conclusions should be drawn on the basis of these data. It is remarkable, however, that the mean O···O nonbonded distance of the 40 geometries is the *same*, 2.484 Å, as in the smaller

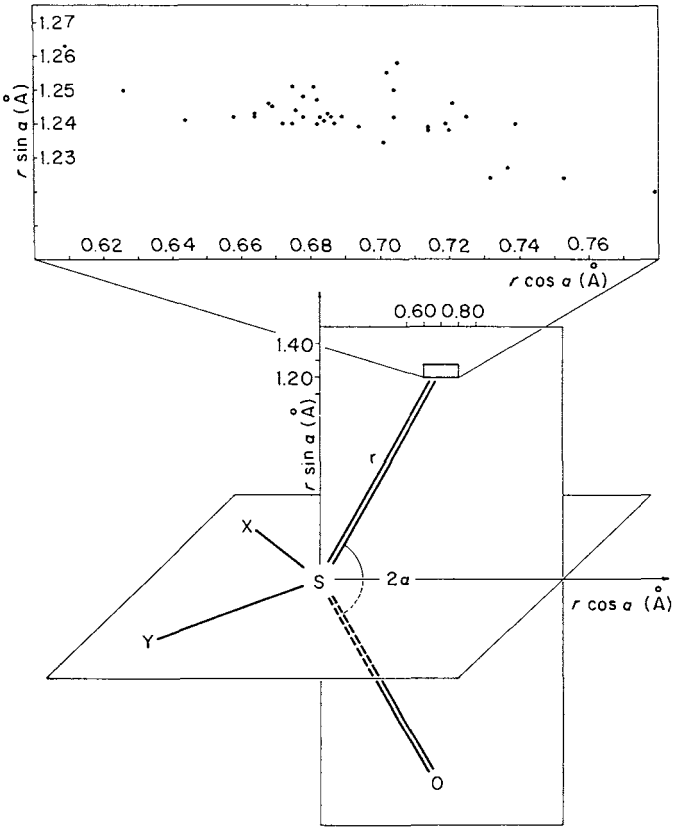


FIGURE 19. Molecular configuration of XSO_2Y sulfonyl derivatives and the $r \sin \alpha$ versus $r \cos \alpha$ plot characterizing the variations of O···O nonbonded distances with changing S=O length (r) and O=S=O angle (2α).

sample! The spread indicated by a relatively large standard deviation ($\sigma = 0.017$ Å) is much greater than that obtained from the 9 microwave spectroscopic studies ($\sigma = 0.004$ Å) originally selected[5]. More importantly, a closer scrutiny of the data depicted in Figure 19 reveals an *uneven* scatter of points around the imaginary horizontal line, $r \sin \alpha = 1.242$ Å. There is a tendency for declination of the plot in Figure 19 in the region of increasing $r \cos \alpha$ values. In this direction bonds get generally longer, accompanied by angular closing in agreement with diminishing electron-pair repulsions. The bond lengthening and angular closing could be such as to maintain the constancy of the O···O distance. That this constancy is not maintained, and the O···O distance tends to decrease in this region, is indicative that bonded interactions prevail in importance over the nonbonded ones in determining these structures.

C. Sulfone/Sulfoxide/Sulfide Comparison

The S—F bonds gradually lengthen in the SO_2F_2, SOF_2, SF_2 series, viz. 1.530(2), 1.585(3) and 1.592(1) Å, respectively, while for other S—X bonds a definite lengthening

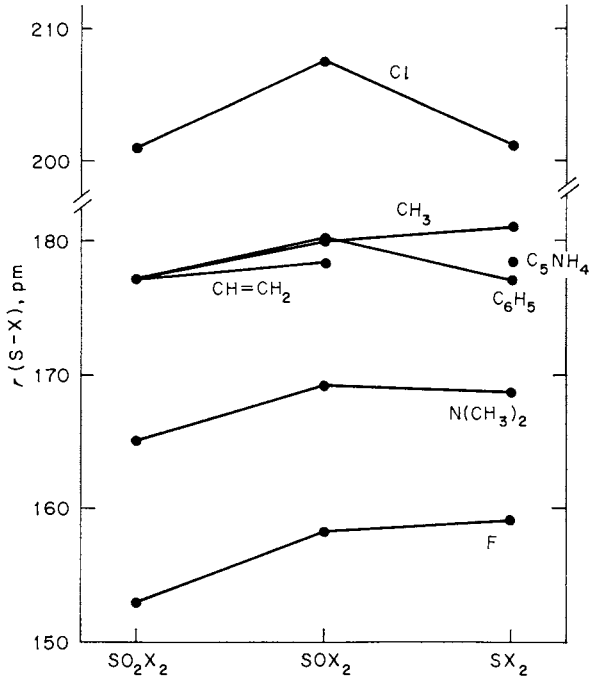


FIGURE 20. Sulfur bond lengths in analogous sulfones/sulfoxides/sulfides with various ligands (cf. Reference 5).

from sulfone to sulfoxide is often followed by a shortening in the sulfide, or the bond length remains the same on going from the sulfoxide to the sulfide. The variation in the lengths for some bonds in analogous sulfones, sulfoxides and sulfides is illustrated in Figure 20. These changes in the bond lengths are paralleled by angular variations in the XSX angle of the SO_2X_2, SOX_2, SX_2 series. This bond angle always decreases when going from a sulfone to the analogous sulfoxide, whereas from sulfoxide to sulfide there is an increase in the values (Figure 21). These variations will be discussed later.

The C—S bond lengths vary upon changing carbon valence states. However, the sulfones and sulfoxides show less sensitivity to these changes than the analogous sulfides[10]. These effects can be illustrated by considering the C—S bond lengths (Å) in analogous dimethyl and diphenyl derivatives:

$(CH_3)_2SO_2$	1.771(4)	$(CH_3)_2SO$	1.808(4)	$(CH_3)_2S$	1.807(2)
$(C_6H_5)_2SO_2$	1.772(5)	$(C_6H_5)_2SO$	1.804(6)	$(C_6H_5)_2S$	1.771(5)

It has been noted[5,10] that the length of a C—S bond depends also on the nature of the atoms or groups bonded to the carbon atoms. In this context, the sulfones and sulfoxides show greater sensitivity than the sulfides[10], as is demonstrated by the following examples of C—S bond lengths (A):

$(CH_3)_2SO_2$	1.771(4)	$(CH_3)_2SO$	1.808(4)	$(CH_3)_2S$	1.807(2)
$(CF_3)_2SO_2$	1.858(5)	$(CF_3)_2SO$	1.885(4)	$(CF_3)_2S$	1.819(3)

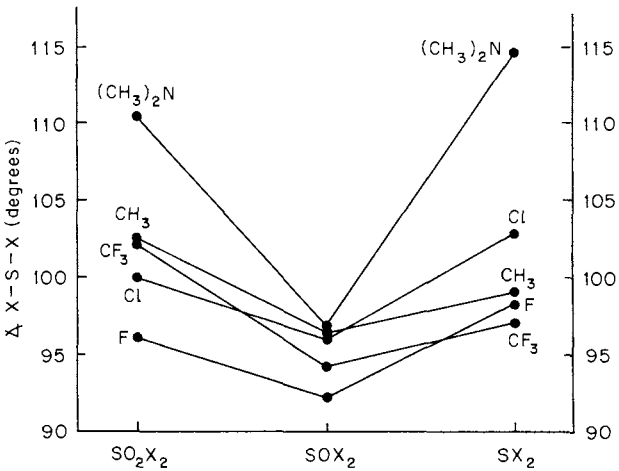


FIGURE 21. Sulfur bond angles in analogous sulfones, sulfoxides and sulfides with various ligands (cf. Reference 5).

The sulfur atoms in sulfones and sulfoxides are considered hypervalent, i.e. having formal valences 6 and 4, respectively. In this situation, the *d*-orbitals have been found to be true valence orbitals[68]. However, when *d*-orbitals are included in calculations, they are shown to be merely polarization functions. In general, however, the inclusion of *d*-orbitals improves the agreement of calculated structures with experiment, and are often necessary to reach reasonable results for sulfones and sulfoxides[69,70]. The effect of changing the atom bonded to carbon upon the C—S bond length in sulfones has been examined, e.g. CH_3SO_2Cl versus CF_3SO_2Cl. While relatively little *d*-orbital participation was found in these bonding situations, even small variations in this *d*-orbital participation was accompanied by considerable change in bond lengths. The experimental C—S bond lengths and the calculated so-called CS(*d*) partial Wiberg indexes are plotted in Figure 22 for a few sulfonyl chloride molecules[70]. The CS(*d*) partial Wiberg index is related to the amount of *d*-orbital participation in bonding, and a pattern of C—S bond shortening with increasing CS(*d*) partial Wiberg index is noted. Although *d*-orbital participation has usually been associated with the double-bond character of S=O bonds in hypervalent sulfur bonding, the above trend suggests that sulfur *d*-orbitals contribute to hyperconjugative $d\pi$–$p\pi$ bonding in addition to the usual C—S σ-bond, and, accordingly, changes are observed in the C—S bond lengths.

Quantum chemical calculations have also been instrumental in accounting for the experimentally observed bond-angle variations in the sulfone/sulfoxide/sulfide series (Figure 21)[5]. In terms of the VSEPR theory, these systems can be described by the general formulas AX_4, AX_3E and AX_2E_2 (Figure 23). Virtually all geometrical variations in these series could be described on the basis of electron-pair repulsions invoking a simple set of rules referring to the differences in repulsion strength of a bonding pair versus a lone pair, single bonds versus multiple bonds, and of bonds to ligands with different electronegativities. However, an apparent discrepancy is noted in terms of these considerations. While the decrease in the XSX angles in sulfoxides as compared with those in sulfones was consistent with VSEPR considerations, it would have been expected that this angle should further decrease in the analogous sulfides. However, this latter decrease was not observed in the experimental data. An explanation for this apparent anomaly may be as follows: for

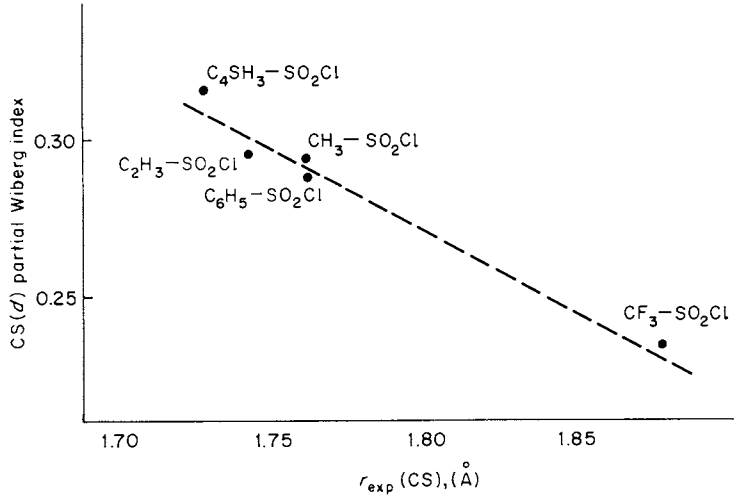


FIGURE 22. Partial CS(*d*) Wiberg indexes characterizing *d*-orbital participation plotted against the experimentally determined S—C bond lengths in some sulfonyl derivatives[70].

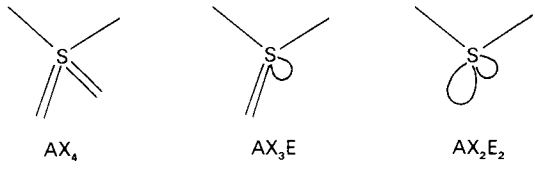


FIGURE 23. Representation of sulfones, sulfoxides and sulfides as AX_4, AX_3E, and AX_2E_2 systems.

general applicability of VSEPR considerations[71,72], not only the *bond* angle variations but also the angles of the *lone pairs* must be considered. Whereas the values of the bond angles XSX in the sulfone/sulfoxide/sulfide series can be determined both by experiment and by theoretical calculations, the angles made by the lone pairs in these systems can be obtained only from computation[16]. The situation is especially complicated in the case of sulfides where three kinds of interactions are present: bond/bond, bond/lone pair and lone pair/lone pair.

Finally, results in this field can be used to estimate electronegativities. It was noted above that, depending on the nature of the ligands X and Y, the S=O bond lengths and OSO bond angles change in a well-understood manner. Accordingly, the geometrical variations detected in the sulfonyl group offer a rather sensitive tool for estimating group electronegativities[73,74].

III. REFERENCES

1. M. Hargittai and I. Hargittai, *Physics and Chemistry of Minerals*, **14**, 413 (1987).
2. I. Hargittai and M. Hargittai, in *Molecular Structure and Energetics* (Eds. J. F. Liebman and A. Greenberg), Vol. 2, Chap. 1, VCH Publishers, New York, 1987, pp. 1–35.

3. I. Hargittai and I. C. Paul, in *The Chemistry of Cyanates and their Thio Derivatives* (Ed. S. Patai), Part 1, Chap. 2, John Wiley and Sons, Chichester, 1977, pp. 69–129.
4. I. Hargittai and W. J. Orville-Thomas (Eds.), *Diffraction Studies on Non-Crystalline Substances*, Elsevier, Amsterdam, New York, 1981.
5. I. Hargittai, *The Structure of Volatile Sulphur Compounds*, Reidel Publ. Co., Dordrecht–Boston–Lancaster, 1985.
6. I. C. Paul, in *The Chemistry of the Thiol Group* (Ed. S. Patai), John Wiley and Sons, Chichester, 1974.
7. I. Hargittai and B. Rozsondai, in *The Chemistry of Organic Selenium and Tellurium Compounds* (Eds. S. Patai and Z. Rappoport), Chap. 3, John Wiley and Sons, Chichester, 1986, pp. 63–155.
8. R. J. Gillespie, *Molecular Geometry*, Van Nostrand Reinhold, London, 1972.
9. L. S. Bartell, *J. Chem. Phys.*, **32**, 827 (1960); *J. Chem. Educ.*, **45**, 754 (1968).
10. I. Hargittai, in *Organic Sulfur Chemistry* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Chap. 2, Elsevier, Amsterdam–Oxford–New York–Tokyo, 1985, pp. 68–132.
11. Until recently, an erroneous structure for $SOCl_2$ has been widely used in the literature according to which ClSCl 114° and OSCl 106°. These angles originated from an early (1938) electron diffraction work in which values smaller than 114° were simply not tested for ClSCl. Modern techniques of electron diffraction structure analysis are more reliable in avoiding such artifacts.
12. I. Hargittai and F. C. Mijlhoff, *J. Mol. Struct.*, **16**, 69 (1973).
13. I. Hargittai, *Acta Chim. Acad. Sci. Hung.*, **60**, 231 (1969).
14. J. Brunvoll, I. Hargittai and B. Rozsondai, *J. Mol. Struct.*, **84**, 153 (1982).
15. S. Suzuki, M. Yamaguchi, M. Onda, T. Sakaizumi, O. Ohashi and I. Yamaguchi, *J. Mol. Struct.*, **73**, 41 (1981).
16. A. Schmiedekamp, D. W. J. Cruickshank, S. Skaarup, P. Pulay, I. Hargittai and J. E. Boggs, *J. Amer. Chem. Soc.*, **101**, 2002 (1979).
17. V. Typke, *Z. Naturforsch.*, **33a**, 842 (1978).
18. H. Oberhammer, R. C. Kumar, G. D. Knerr and J. M. Shreeve, *Inorg. Chem.*, **20**, 3871 (1981).
19. E. A. Robinson and R. Aroca, *Spectrochim. Acta*, **34A**, 1249 (1978).
20. I. Mayer and I. Hargittai, *Z. Naturforsch.*, **34a**, 911 (1979).
21. B. Rozsondai, J. H. Moore, D. C. Gregory and I. Hargittai, *J. Mol. Struct.*, **51**, 69 (1979).
22. S. C. Abrahams, *Acta Crystallogr.*, **10**, 417 (1957).
23. I. Hargittai and L. V. Vilkov, *Acta Chim. Acad. Sci. Hung.*, **63**, 143 (1970).
24. S. Saito, *Bull. Chem. Soc. Japan*, **42**, 663 (1969).
25. W. F. White and J. E. Wollrab, *Chem. Phys. Letters*, **3**, 25 (1969).
26. J. W. Bevan, A. C. Legon and D. J. Millen, *J. Chem. Soc., Chem. Commun.*, 659 (1974).
27. J. W. Bevan, A. C. Legon and D. J. Miller, *Proc. R. Soc. (London)*, **A354**, 435 (1977).
28. J. Brunvoll, M. Kolonits, C. Bliefert, K. Seppelt and I. Hargittai, *J. Mol. Struct.*, **78**, 307 (1982).
29. E. Vajda and I. Hargittai, *Z. Naturforsch.*, **38a**, 765 (1983).
30. G. Schultz, I. Hargittai and R. Seip, *Z. Naturforsch.*, **36a**, 917 (1981).
31. M. Hargittai, E. Vajda, C. J. Nielsen, P. Klaeboe, R. Seip and J. Brunvoll, *Acta Chem. Scand. A*, **37**, 341 (1983).
32. R. L. Kuczkowski, R. D. Suenram and F. J. Lovas, *J. Amer. Chem. Soc.*, **103**, 2561 (1981).
33. V. A. Naumov, R. N. Ziatdinova and E. A. Berdnikov, *Zh. Strukt. Khim.*, **22**(3), 89 (1981).
34. V. A. Naumov, R. N. Garaeva and G. G. Butenko, *Zh. Strukt. Khim.*, **20**(6), 1110 (1979).
35. H. Oberhammer, G. D. Knerr and J. M. Shreeve, *J. Mol. Struct.*, **82**, 143 (1982).
36. V. A. Naumov and R. N. Ziatdinova, *Zh. Strukt, Khim.*, **24**(3), 48 (1983).
37. J. Brunvoll, J. F. Chiang and I. Hargittai, *Acta Crystallogr.*, **C42**, 94 (1986).
38. J. Brunvoll and I. Hargittai, *Acta Chem. Scand. A*, **39**, 667 (1985).
39. J. Brunvoll, O. Exner, I. Hargittai, M. Kolonits and P. Scharfenberg, *J. Mol. Struct.*, **117** (1984).
40. J. Brunvoll and I. Hargittai, *J. Mol. Struct.*, **30**, 361 (1976).
41. B. P. Van Eijck, I. Hargittai and I. Mayer, *J. Mol. Struct.*, **61**, 301 (1980).
42. J. Brunvoll, M. Kolonits and I. Hargittai, *Z. Naturforsch.*, **33a**, 1236 (1978).
43. M. Hargittai and I. Hargittai, *J. Chem. Phys.*, **59**, 2513 (1973).
44. L. V. Vilkov, N. P. Penionzhkevich, J. Brunvoll and I. Hargittai, *J. Mol. Struct.*, **43**, 109 (1978).
45. J. Brunvoll, I. Hargittai and R. Seip, *Z. Naturforsch.*, **33a**, 222 (1978).
46. M. Hargittai and I. Hargittai, *J. Mol. Struct.*, **20**, 283 (1974).
47. J. Brunvoll and I. Hargittai, *Acta Chim. Acad. Sci. Hung.*, **94**, 333 (1977).

48. I. Hargittai, B. Rozsondai, B. Nagel, P. Bulcke, G. Robinet and J.-F. Labarre, *J. Chem. Soc., Dalton Trans.*, 861 (1978).
49. I. Hargittai, E. Vajda and A. Szöke, *J. Mol. Struct.*, **18**, 381 (1973).
50. I. Hargittai and J. Brunvoll, *Acta Chem. Scand. A*, **30**, 634 (1976).
51. F. Mo and Ø. Berg, *Acta Chem. Scand. A*, **36**, 657 (1982).
52. F. Mo, private communication on the low-temperature X-ray diffraction analysis of the 1,2-bis(methylsulfonyl)ethane crystal.
53. L. G. Vorontsova, *Kristallografiya*, **10**, 187 (1965).
54. J. Brunvoll, M. Colapietro, A. Domenicano, C. Marciante and I. Hargittai, *Z. Naturforsch.*, **39b**, 607 (1984).
55. A. Domenicano and P. Murray-Rust, *Tetrahedron Letters*, 2283 (1979).
56. J. F. Chiang, *Acta Cryst.*, **C39**, 737 (1983).
57. V. A. Naumov, V. N. Semashko and S. A. Shaidulin, *Zh. Strukt. Khim.*, **14**, 595 (1973).
58. J. L. Alonso, *J. Mol. Struct.*, **73**, 71 (1981).
59. I. Hargittai, *J. Mol. Struct.*, **77**, 313 (1981).
60. J. L. Alonso and D. G. Lister, *J. Chem. Soc., Chem. Commun.*, 93 (1982).
61. J. L. Alonso, *An. Quim. A*, **79**, 19 (1983).
62. For electron diffraction, the nonbonded distances of the tetrahedral sulfur bond configurations in sulfonyl molecules are closely spaced and cause strong correlation among the relevant parameters. Assuming one of them (O···O) to be known can greatly facilitate the determination of the rest of the parameters (see more details in Reference 5).
63. For simple sulfones, the planar moment of the molecule is determined by the positions of the oxygen atoms, thus the knowledge of the O···O distance may considerably aid the assignment of rotational transitions (see more details in Reference 5).
64. J. Brunvoll, O. Exner and I. Hargittai, *J. Mol. Struct.*, **73**, 99 (1981).
65. I. Hargittai, *J. Mol. Struct.*, **54**, 287 (1979).
66. C. Glidewell and A. Y. Meyer, *J. Mol. Struct.*, **72**, 209 (1981).
67. A. I. Kiss and I. Hargittai, *Z. Naturforsch.*, **37a**, 134 (1982).
68. I. Mayer, Satellite Symp. of the 5th ICQC 'Molecular Structure and Reactivity', Toronto, 1985, *J. Mol. Struct.*, THEOCHEM, **34**, 81 (1987).
69. R. J. Boyd and J. P. Szabo, *Can. J. Chem.*, **60**, 730 (1982).
70. I. Mayer, M. Révész and I. Hargittai, *Acta Chim. Acad. Sci. Hung.*, **114**, 159 (1983).
71. I. Hargittai, *Inorg. Chem.*, **21**, 4334 (1982).
72. I. Hargittai and B. Chamberland, in *Symmetry, Unifying Human Understanding* (Ed. I. Hargittai), Pergamon Press, New York and Oxford, 1986, pp. 1021–1038.
73. I. Hargittai, *Z. Naturforsch.*, **34a**, 755 (1979).
74. I. Hargittai and C. Bliefert, *Z. Naturforsch.*, **35b**, 1053 (1980).

CHAPTER 3

Stereochemistry, conformation, and chiroptical properties of sulfoxides

KENNETH K. ANDERSEN

Department of Chemistry, University of New Hampshire, Durham, NH 03824, USA

I. INTRODUCTION

The stereogenic sulfur atom in sulfoxides is usually configurationally stable at room temperature; thus, sulfoxides may be chiral based on this property alone[1]. In fact, there are many examples of optically active sulfoxides of both synthetic and natural origin. This chapter reviews the important methods for obtaining optically active sulfoxides, and discusses some reactions at sulfur which either leave the coordination number at three or increase it to four, generally with preservation of optical activity. It also describes briefly some recent studies on the conformational analysis and chiroptical properties of sulfoxides.

Several recent reviews will be helpful to those who wish to pursue these topics in more depth. Nudelman[2] collected over 800 references from 1926, the year when optically active sulfoxides were first reported, through 1979. His review is in five parts with the first four being reprints from the literature[3–6]. Solladie[7] in his review (140 references up to 1979) on the use of optically active sulfoxides in asymmetric syntheses included a valuable discussion on the configurational stability of sulfoxides and some experimental directions on how to prepare optically active sulfoxides. Additional information is reported in his chapter on the addition of chiral nucleophiles to aldehydes and ketones[8]. Cinquini and coworkers[9] reviewed more recent advances in the stereochemistry of optically active sulfoxides (128 references up to May, 1983) also emphasizing their use in asymmetric synthesis. Cinquini[10] also reviewed asymmetric C—C bond formation mediated by homochiral sulfoxides. Posner[11] reviewed the addition of organometallic reagents to chiral vinylic sulfoxides (39 references up to 1983) and, in a chapter of this present monograph, expands upon the subject. Chiral organosulfur compounds, in general, were reviewed by Mikolajczyk and Drabowicz[12] in 1982 (326 references up to 1980). Barbachyn and Johnson[13] discussed optical activation and utilization of compounds containing chiral sulfur centers (ca. 170 references up to 1984). Kresze[14], in his 1985 contribution in Houben-Weyl on the chemistry of sulfoxides, described the preparation of several optically active sulfoxides. All of these authors reference numerous earlier review articles some of which will be cited in this chapter when appropriate.

This review is not comprehensive but emphasizes the more recent literature through 1985 into early 1986. References to earlier work are included in an affort to make the subject understandable to those unfamiliar with past research and also to cover topics not touched upon in recent publications. The term optically active is used here in the sense that the chiral molecule under discussion is nonracemic but not necessarily enantiomerically pure. The terms homochiral and optically pure are used synonymously with enantiomerically pure.

II. METHODS FOR OBTAINING OPTICALLY ACTIVE SULFOXIDES

A. Resolution of Sulfoxides

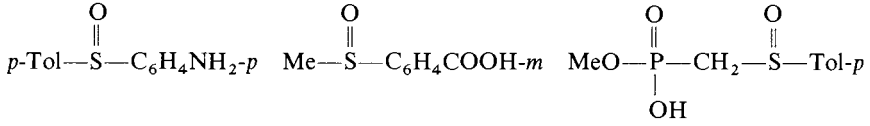
Racemic mixtures of sulfoxides have often been separated completely or partially into the enantiomers. Various resolution techniques have been used, but the most important method has been via diastereomeric salt formation. Recently, resolution via complex formation between sulfoxides and homochiral compounds has been demonstrated and will likely prove of increasing importance as a method of separating enantiomers. Preparative liquid chromatography on chiral columns may also prove increasingly important; it already is very useful on an analytical scale for the determination of enantiomeric purity.

The numerous examples of optically active sulfoxides reflect their configurational stability. Optically active sulfoxides resist thermal racemization by pyramidal inversion, so

once obtained they are stable[7,15]. Allyl sulfoxides are an exception; they racemize rapidly via a [2,3]-sigmatropic rearrangement. Hydrogen chloride in organic solvents also racemizes sulfoxides, so it is prudent to avoid contact between sulfoxides and chloride ions in strongly acidic media. Bases usually do not racemize sulfoxides, but there are a few exceptions in the cases of some organolithium reagents. Light can also racemize sulfoxides, but this is not a problem under ordinary laboratory conditions.

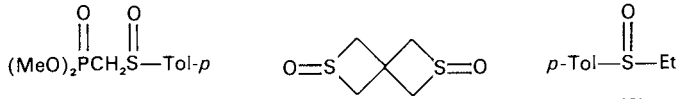
1. Diastereomer formation

Sulfoxides were first prepared in optically active form in 1926 by the classical technique of diastereomeric salt formation followed by separation of the diastereomers by recrystallization[16,17]. Sulfoxides **1** and **2** were treated with *d*-camphorsulfonic acid and brucine, respectively, to form the diastereomeric salts. These salts were separated by crystallization after which the sulfoxides were regenerated from the diastereomers by treatment with acid or base, as appropriate. Since then numerous sulfoxides, especially those bearing carboxyl groups, have been resolved using this general technique.



(**1**) (**2**) (**3**)

Sulfoxides without amino or carboxyl groups have also been resolved. Compound **3** was separated into enantiomers via salt formation between the phosphonic acid group and quinine[18]. Separation of these diastereomeric salts was achieved by fractional crystallization from acetone. Upon passage through an acidic ion exchange column, each salt was converted to the free acid **3**. Finally, the tetra-ammonium salt of each enantiomer of **3** was methylated with methyl iodide to give sulfoxide **4**. The levorotatory enantiomer was shown to be completely optically pure by the use of chiral shift reagents and by comparison with a sample prepared by stereospecific synthesis (see Section II.B.1). The dextrorotatory enantiomer was found to be 70% optically pure.



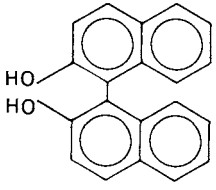
(**4**) (**5**) (**6**)

Molecules having only a sulfoxide function and no other acidic or basic site have been resolved through the intermediacy of metal complex formation. In 1934 Backer and Keuning[19] resolved the cobalt complex of sulfoxide **5** using *d*-camphorsulfonic acid. More recently Cope and Caress[20] applied the same technique to the resolution of ethyl *p*-tolyl sulfoxide (**6**). Sulfoxide **6** and optically active 1-phenylethylamine were used to form diastereomeric complexes; i.e., (+)- and (−)-*trans*-dichloro(ethyl *p*-tolyl sulfoxide) (1-phenylethylamine) platinum(II). Both enantiomers of **6** were obtained in optically pure form. Diastereomeric platinum complexes formed from racemic methyl phenyl (and three *para*-substituted phenyl) sulfoxides and D-*N*,*N*-dimethyl phenylglycine have been separated chromatographically on an analytical column[21]. A nonaromatic example, cyclohexyl methyl sulfoxide, did not resolve.

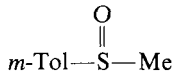
Recrystallization of a 1:1 molecular complex formed from several sulfoxides and (*R*)-(+)-2,2′-dihydroxy-1,1′-binaphthyl (**7**) allowed resolution of the former[22]. Conversely, using the optically pure sulfoxide, it was possible to resolve racemic bis-naphthol **7**.

Methyl *m*-tolyl (**8**), ethyl *m*-tolyl, methyl *n*-butyl and methyl *n*-propyl sulfoxides were obtained in 100% e.e. This method was less successful when applied to methyl phenyl sulfoxide (5% e.e.) or to methyl isobutyl and methyl ethyl sulfoxides (25% e.e.). No complexes were formed between methyl *o*-tolyl, methyl *p*-tolyl, methyl 2-butyl and methyl isopropyl sulfoxides so these compounds could not be resolved using **7**. A crystal structure of the 1:1 complex formed between **7** and **8** revealed that the partners were linked by OH—OS hydrogen bonds in endless zig-zag chains[23]. More recently, 2-chloroethyl *m*-tolyl sulfoxide (**9**) has been resolved using **7**[24].

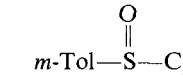
Kagan and coworkers determined and studied in detail the crystal structure of a 1:1 molecular complex between (*R*)-methyl *p*-tolyl sulfoxide (**10**) and (*S*)-*N*-(3,5-dinitrobenzoyl)-1-phenylethylamine (**11**). They suggested that amide **11**, which had been used as a chiral solvating agent for sulfoxides, might find use as a resolving agent for these compounds[25].



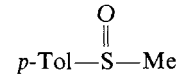
(**7**)



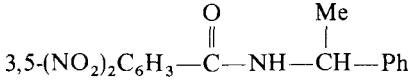
(**8**)



(**9**)



(**10**)

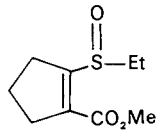


(**11**)

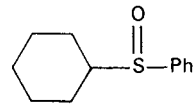
2. Chromatography

Chiral sulfoxides with at least one sulfur-bonded aryl group have been separated by liquid chromatography into the enantiomers[26]. Some of the columns employed, which are commercially available, used (*R*)-*N*-(3, 5-dinitrobenzoyl)phenylglycine bonded to silica as the chiral stationary phase with 2-propanol serving as the eluent[27]. This method of resolution is useful for analytical purposes in determining enantiomeric purity but less so for preparative work because of the larger columns required. A chiral recognition model was formulated based on the known configurations of the stationary phase and methyl aryl sulfoxides. This model predicts that the *R*-enantiomer should be most tightly bound to the stationary phase and thus elute last from the column. The nonaromatic sulfoxide, methyl 2-ethylsulfinylcyclopentene-1-carboxylate (**12**), was also resolved, but the elution order of the enantiomers could not be determined, since their configurations are unknown.

Yamagishi[28] partially resolved cyclohexyl phenyl sulfoxide (**13**) by means of high-performance liquid chromatography (HPLC). Earlier he had established that the nickel chelate $Ni(phen)_3^{2+}$ was adsorbed on the surface of the clay, montmorillinite, as an alternating sequence of enantiomers rather than as a single stereoisomer. A clay-chelate adduct prepared using only one of these enantiomers left 50% of the clay surface unoccupied. In some cases, this adduct was capable of selectively adsorbing one of a pair of aromatic enantiomers. A column packing prepared from such an adduct coated on silica gel allowed partial resolution of sulfoxide **13**.



(12)



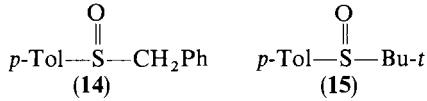
(13)

3. *Inclusion compounds*

Cyclodextrins, toroidal molecules composed of **6**, **7** and **8** D-glucose units, are now commercially available at reasonable cost. They form inclusion compounds with a variety of molecules and often differentially include sulfoxide enantiomers[29,30]. This property has been used to partially resolve some benzyl alkyl, phenyl alkyl and *p*-tolyl alkyl sulfoxides. The enantiomeric purities after one inclusion process ranged from 1.1% for *t*-butyl *p*-tolyl sulfoxide to 14.5% for benzyl *t*-butyl sulfoxide. Repeating the process on methyl *p*-tolyl sulfoxide (**10**) increased its enantiomeric purity from 8.1% to 11.4%; four recrystallizations raised the value to 71.5%. The use of cyclodextrins in asymmetric oxidations is discussed in Section II.C.1 and in the resolution of sulfinate esters in Section II.B.1.

4. *Preferential crystallization of enantiomers*

Seeding a supersaturated solution of a racemic modification with a crystal of one of the enantiomers sometimes results in the preferential crystallization of that enantiomer, especially if the modification crystallizes as a racemic mixture (conglomerate) rather than as a racemate (racemic compound). Dissolution of additional racemic modification, added after some of the first enantiomer has been removed, leads at lower temperature to a supersaturated solution from which the other enantiomer may be obtained by preferential crystallization upon seeding. By repeating this process in a cyclic way, seeding the supersaturated solution first with one enantiomer and then with the other and adding racemic modification in between, both enantiomers may be obtained in favorable cases; e.g., this procedure has been used to resolve amino acids and their derivatives[31]. Recently, this procedure, which is presently under active investigation, has been applied to the resolution of benzyl *p*-tolyl sulfoxide (**14**) and *t*-butyl *p*-tolyl sulfoxide (**15**)[32]. Preferential crystallization has certain advantages as a technique: no chemical transformations are needed as is usually the case in other techniques, the yields are high, and the method is suitable for large-scale industrial use. Of course, the sulfoxide must be crystalline and crystallize as a racemic mixture rather than as a racemate.



(14) (15)

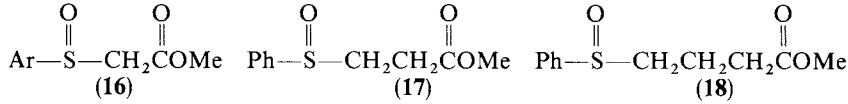
5. *Selective extraction*

Selective or preferential extraction of diastereomeric salts formed from sulfoxide carboxylic acids and alkaloids in water relative to the reciprocal diastereomeric salts has been studied[33].

6. *Kinetic resolution*

Numerous reactions of racemic sulfoxides with chiral reagents have been accomplished[2,12]. These examples of kinetic resolution usually lead to sulfoxides of low enantiomeric purity, but there are some exceptions.

The hydrolysis of seven alkyl arenesulfinylalkanoates by the bacterium *Corynebacterium equi* IFO 3730 studied by Ohta and coworkers[34] are recent examples of kinetic resolutions which give sulfoxides of high enantiomeric purity and in reasonable yield. Compounds **16a**, **16b** and **16c** were recovered in 30 to 43% yield and in 90 to 97% e.e. The *S* enantiomers underwent hydrolysis more rapidly than the *R* isomers. Sulfoxide **17** was isolated in 22% yield and 96% e.e., but sulfoxide **18** was completely metabolized. Esters other than methyl gave inferior results. The acids formed upon hydrolysis, although detected, were for the most part further metabolized by the bacterium.



(16) **(17)** **(18)**

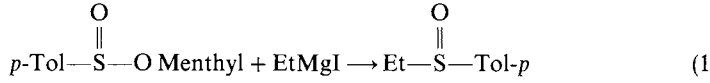
(a) Ar = Ph

(b) Ar = *p*-Tolyl

(c) Ar = *p*-ClC_6H_4

B. Nucleophilic Substitution at Tricoordinate Sulfur(IV)

In 1925, Phillips[35] prepared the first example of an optically active sulfinate ester, (−)-menthyl *p*-toluenesulfinate (**19**), which was subsequently shown to be of configuration *S* at sulfur. One year later, Gilman and coworkers[36] showed that treatment of ethyl and *n*-butyl *p*-toluenesulfinates with benzylmagnesium chloride and phenylmagnesium bromide, respectively, gave the corresponding benzyl and phenyl *p*-tolyl sulfoxides. Curiously, even though Gilman praised Phillips' work in a footnote, it was not until thirty-six years later that anyone reacted an optically active sulfinate ester with a Grignard reagent. In 1962, Andersen[37] treated sulfinate ester **19** with ethylmagnesium iodide to obtain (*R*)-(+)-ethyl *p*-tolyl sulfoxide (**6**) thus demonstrating for the first time that optically active sulfoxides can be produced from optically active sulfinate esters (equation 1). This Grignard–sulfinate ester reaction, often referred to as the Andersen synthesis, method or procedure[9,12,13,38,39], was shown to be a fairly general method for preparing optically active sulfoxides. The method has since been improved and its scope extended. A variety of nucleophilic reagents, other than classical Grignard reagents, as well as a variety of other tricoordinate S(IV) precursors, besides sulfinate esters, have been used. In spite of some disadvantages, the reaction of organometallic reagents with optically active sulfinate esters is the most often used method for preparing optically active sulfoxides although oxidative methods for preparing these compounds have been greatly improved in recent years and might become the method of choice (see Section II.C).



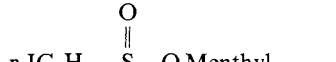
(19) **(6)** (1)

1. Sulfinate esters

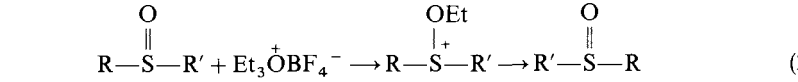
Preparation of the appropriate optically active sulfinate ester is initially required for reaction with a Grignard or other organometallic reagent. If the method is to produce homochiral sulfoxides, the precursor sulfinate ester must be optically pure. An exception to this statement occurs if the reaction yields a partially racemic sulfoxide which can be recrystallized to complete optical purity.

Preparation of enantiomerically pure sulfinate esters has most often been accomplished by making menthyl esters of arenesulfinic acids, particularly of *p*-toluenesulfinic acid. This

preparation leads to diastereomers epimeric at sulfur, but usually the epimer with configuration *S* is crystalline and can be isolated and recrystallized to complete optical purity. If both epimers are crystalline, as is the case for the menthyl *p*-iodobenzenesulfinates (**20**), then fractional crystallization may lead to their separation[40]. If the desired epimer is liquid and the undesired epimer solid, this situation may be reversed by using (+)- instead of the usual (−)-menthol as done by Goldberg and Sahli[41]. Both alcohols are commercially available, as are the sulfinate esters. The configuration at sulfoxide sulfur may also be inverted to give the enantiomer or epimer using Johnson's method; i.e., alkylation at oxygen using a trialkyloxonium salt followed by hydrolysis with aqueous base (equation 2)[13]. Occasionally this method fails[40]. During hydrolysis, the hydroxide ion does not attack exclusively at sulfur (inversion) but also at the alkyl carbon (C—O bond cleavage with retention at sulfur). Thus, the e.e. of the inverted sulfoxide is somewhat less than that of the starting isomer (see Section II.A)[13,43].

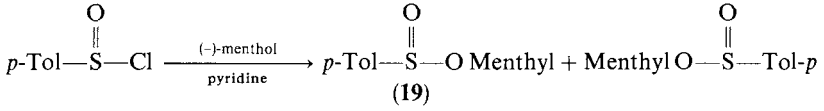


(20)

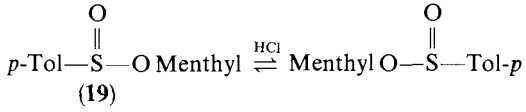


(2)

Arenesulfinate esters are usually prepared from an arenesulfinyl chloride and an alcohol in ether and pyridine. The arenesulfinyl chloride is usually prepared from the sodium arenesulfinate which is made by reduction of the arenesulfonyl chloride, preferably by aqueous sodium sulfite[44]. After the crystalline sulfinate epimer has been removed by filtration, the equilibrium between the epimers remaining in the mother liquor may be reestablished by the addition of hydrogen chloride as shown by Herbrandson and Cusano[40]. In this way the yield of the least soluble diastereomer may be increased beyond that which exists in the original reaction mixture (Scheme 1). Solladie[7] prepared sulfinate ester **19** in 90% yield using this technique and published the details of his procedure. Estep and Tavares[45] also published a convenient recipe for this method, although their yields were somewhat lower than Solladie's.



(19)

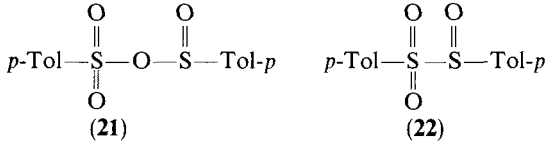


(19)

SCHEME 1

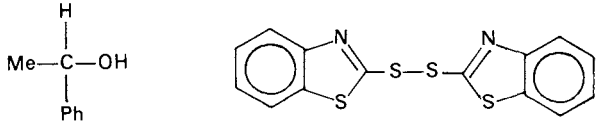
As an alternative, Harpp and coworkers[46] reacted benzenesulfinyl chloride with the trimethylsilyl derivative of menthol to form the diastereomeric esters in 91% yield; the epimer of configuration *R* could be isolated by crystallization in unspecified yield. Grossert and coworkers[47] prepared ester **19** in 51% yield as a mixture of diastereomers by treating *p*-toluenesulfonyl chloride with sodium *p*-toluenesulfinate in DMF containing menthol. It was postulated that initial nucleophilic attack by the sulfinate oxygen on the sulfonyl sulfur atom gave the mixed sulfonate–sulfinate anhydride **21**, which then reacted

with the menthol to give sulfinate ester **19**. It is also possible to prepare ester **19** and other *p*-toluenesulfinates without the use of sulfinyl chlorides by treating the alcohol with *p*-tolylsulfinyl *p*-tolyl sulfone (**22**) in the presence of pyridine[48].

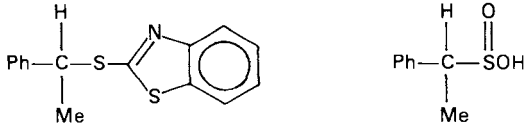


(**21**) (**22**)

Ueno and coworkers[49] have developed a procedure for the synthesis of chiral sulfinic acids. Treatment of (*R*)-(+)-**23** with disulfide **24** and tributylphosphine in THF gave (*S*)-(−)-**25**. Compound **25** was oxidized with potassium permanganate to the sulfone, which was then reduced to the sulfinic acid, (*S*)-(−)-**26**, by treatment with sodium borohydride. Conversion of **26** or an analog to an ester would lead to diastereomers. If these epimers could be separated, then they would offer a path to homochiral sulfoxides with stereogenic carbon and sulfur atoms.

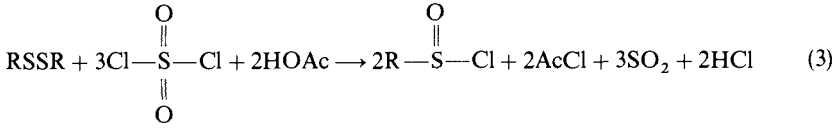


(**23**) (**24**)



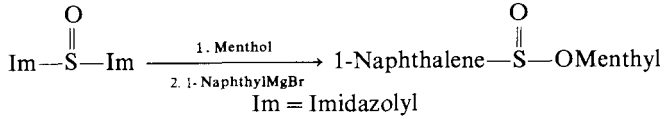
(**25**) (**26**)

Sulfinyl chlorides may be prepared from the corresponding thiols or disulfides by oxidative reactions rather than by reductions of sulfonyl compounds. A recent example, which improves the earlier procedure of Douglass, is given by equation (3)[50]. The chemistry of sulfinic acids and their derivatives has been reviewed[51,52,53].



(3)

Solladie and coworkers avoided the use of a sulfinyl chloride when they prepared (−)-menthyl 1-naphthalenesulfinate in an overall yield of 45% by the reaction of thionyl diimidazole, obtained from imidazole and thionyl chloride, with 0.7 equivalent of (−)-menthol followed by 1 equivalent of 1-naphthylmagnesium bromide (equation 4).

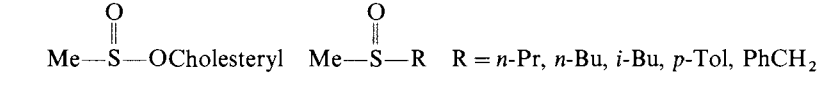


Im = Imidazolyl

(4)

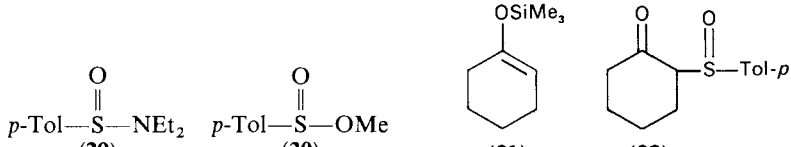
Although menthyl esters, especially **19**, are most often used to prepare sulfoxides, esters derived from optically active alcohols other than menthol have been prepared[55]. Ridley and Smal[56] prepared arenesulfinic esters of 1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranose. Unfortunately, these diastereomers were oils, except for the mesityl derivative, with the major epimer having configuration *R* at sulfur and so they offered no advantage over the menthyl esters. Separation of the epimers by chromatography failed.

A major problem with the sulfoxide synthesis using menthyl sulfinates is its failure to produce optically pure dialkyl sulfoxides. The prerequisite menthyl alkanesulfinates are oils which have resisted separation into the individual epimers. The menthyl phenyl methanesulfinates are an exception; the *R* epimer is crystalline[57]. One solution to this problem, at least for preparing methyl alkyl sulfoxides, was achieved using cholesteryl methanesulfinates (**27**)[58]. Both epimers were crystalline and could be separated by fractional crystallization, although in poor yield. Treatment of the epimers with *n*-propyl, *n*-butyl, isobutyl, *p*-tolyl and benzyl magnesium halides yielded the respective methyl alkyl sulfoxides (**28**) in greater than 95% e.e. and in 32 to 53% yields.



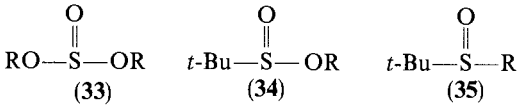
(**27**) (**28**)

An alternative to forming epimeric alkyl arene- or alkanesulfinates is to prepare optically active sulfinate esters with sulfur as the only asymmetric center. Hiroi and coworkers[59] have transformed (*S*)-(+)-*N*,*N*-diethyl *p*-toluenesulfinamide (**29**) into a variety of alkyl and alkenyl *p*-toluenesulfinates, such as **30**, with high stereospecificity under mild conditions by treating **29** with alcohols using boron trifluoride etherate as the catalyst. Since the sulfinamide is prepared from sulfinate ester **19**, this synthesis, although valuable as a source of other sulfinate esters, might appear at first not particularly useful as a step in sulfoxide synthesis. However, the boron trifluoride catalyzed reaction of ester *S*-**30** (93% e.e.) with enol silyl ether **31** derived from cyclohexanone gave **32** in 95% yield and with 92% e.e.[60]. The reaction proceeded with inversion of configuration at sulfur.



(**29**) (**30**) (**31**) (**32**)

Mikolajczyk and coworkers have summarized other methods which lead to the desired sulfinate esters[61]. These are asymmetric oxidation of sulfenamides, kinetic resolution of racemic sulfinates in transesterification with chiral alcohols, kinetic resolution of racemic sulfinates upon treatment with chiral Grignard reagents, optical resolution via cyclodextrin complexes, and esterification of sulfinyl chlorides with chiral alcohols in the presence of optically active amines. None of these methods is very satisfactory since the esters produced are of low enantiomeric purity. However, the reaction of dialkyl sulfites (**33**) with *t*-butylmagnesium chloride in the presence of quinine gave the corresponding methyl, ethyl, *n*-propyl, isopropyl and *n*-butyl 2,2-dimethylpropane-1-yl sulfinates (**34**) of 43 to 73% enantiomeric purity in 50 to 84% yield. This made available sulfinate esters for the synthesis of *t*-butyl sulfoxides (**35**).

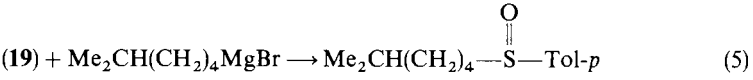


(33) (34) (35)

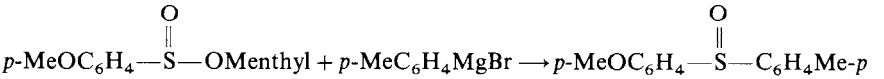
Originally the Grignard–sulfinate ester synthesis of sulfoxides was run in diethyl ether, the solvent in which the Grignard reagent was prepared. Tetrahydrofuran has also frequently been used[7]. However, substitution of benzene for the ether significantly improved the yields of sulfoxides[62]. Toluene has also been used and may be a satisfactory substitute for the more hazardous benzene[63]. Besides organomagnesium halides, other organometallic reagents based on lithium, copper, zinc and cadmium have been used with success[39]. Examples are given throughout this chapter and the one by Posner.

Some examples of the reaction of various nucleophilic reagents, generally organometallic reagents, with sulfinate esters are given in the following paragraphs, which are arranged according to the nature of the organic moiety of the reagent beginning with aryl and alkyl groups.

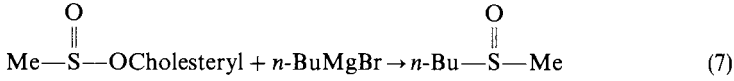
Aryl- and alkyl-magnesium halides were the first reagents used to form sulfoxides from sulfinate ester **19** and related (−)-menthyl arenesulfinates (equations 5[64], 6[65], 7[58] and 8[66]). Whereas optically pure esters produced the homochiral sulfoxides shown in equations (5), (6) and (7), the ester shown in equation (8) was an oily mixture of four diastereomers which led to formation of a *meso* sulfoxide and a *d,l* pair enriched in one enantiomer. A homochiral sulfoxide was obtained by fractional crystallization.



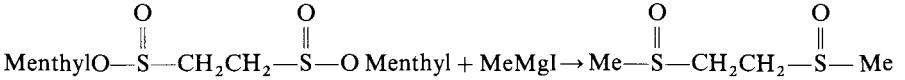
(5)



(6)



(7)

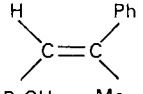


(8)

Occasionally, sulfinate ester **19** has been resistant to reaction with an organometallic reagent. The Grignard prepared by Raguse and Ridley from **36** did not react with ester **19** even in refluxing tetrahydrofuran, but a 34% yield of the desired sulfoxide was obtained when the solvent was changed to benzene. A similar yield was obtained using the organolithium reagent at −78° in tetrahydrofuran[67]. Sometimes the fault may lie not in the unreactivity of the ester but in the inability to form the organometallic reagent; e.g., Nieuwenhuyse and Louw[66] were unable to convert **37** (X = Br or Cl) into the organomagnesium or lithium halide. Kresze and coworkers reported that the Grignard prepared from (*E*)-1-bromo-3-phenyl-2-butene (**38**) did not react with ester **19** although

the reagent prepared from 1-bromo-3-phenylbutane (**39**) did[68].

$(o\text{-}BrC_6H_4OCH_2CH_2)_2O$ (**36**) $MeSCH_2CH_2X$ (**37**)



(**38**)

(**39**)

Sulfoxides may react with the organometallic reagents used to form them. Sometimes this leads to undesired sulfide formation, but occasionally such reactions have synthetic usefulness even in the synthesis of sulfoxides. Furukawa, Oae and coworkers have studied the reaction of Grignard reagents with sulfoxides. Treatment of a 3- or 4-pyridyl phenyl or 4-quinolyl phenyl sulfoxide with phenylmagnesium bromide led to the formation of the corresponding heterocyclic Grignard reagents whose presence could be shown by their reactions with aldehydes, ketone or sulfinate ester **19**, e.g. equation (9)[69]. Earlier work by Johnson had demonstrated that one homochiral sulfoxide could be transformed into another by ligand exchange with an organolithium reagent[13]. Oae and coworkers have also studied ligand coupling reactions occurring in the reaction of heteroaryl sulfoxides with organometallic reagents (see Section II.B.2)

$$\text{3-Pyridyl—}\overset{\overset{O}{\|}}{S}\text{—Ph} \xrightarrow[\text{2. (19)}]{\text{1. PhMgBr}} \text{3-Pyridyl—}\overset{\overset{O}{\|}}{S}\text{—Tol-}p \qquad (9)$$

In an endeavor to improve the yields in the Grignard synthesis, primarily by avoiding sulfide formation, Harpp and coworkers[46] treated some sulfinate esters with organocuprates in ether. Three examples of the synthesis of homochiral sulfoxides were given. (+)-*R*-Methyl phenyl sulfoxide was produced in 16% yield from (−)-menthyl benzenesulfinate. (+)-*R*-Methyl and (+)-*R*-phenyl *p*-tolyl sulfoxides were produced in yields of 55 and 59%, respectively, from sulfinate ester **19**. In spite of statements in recent review articles that organocopper lithium reagents give cleaner, presumably sulfide-free products in the Grignard synthesis, this seems not to be generally so. In fact, in several reactions with racemic sulfinates, Harpp and coworkers obtained only sulfide. Posner and Tang[70] found that treatment of ester **19** with isopropenylmagnesium bromide/10% cuprous iodide in THF gave 30 to 40% sulfide whereas the Grignard alone gave no sulfide.

Allyl sulfoxides are unique in that they undergo reversible [2, 3]-sigmatropic rearrangements to give sulfenate esters. Mislow and coworkers found that allyl *p*-tolyl sulfoxide (**40**) racemized via sulfenate (**41**) at conveniently measured rates at 50–70°, which is significantly below the 190–220° required to racemize sulfoxides by the pyramidal inversion mechanism[71]. In the synthesis of 1-alkenyl sulfoxides by means of the Horner–Wittig reaction of **4**, rearrangement of the carbon–carbon double bond from the 1 to the 2 position occurred, presumably via the anion, to give allylic sulfoxides (equation 10)[18]. The anion derived from **40** has been used in asymmetric synthesis[72,73].

$CH_2{=}CHCH_2\text{—}\overset{\overset{O}{\|}}{S}\text{—Tol-}p$ (**40**) $CH_2{=}CHCH_2\text{—S—O—Tol-}p$ (**41**)

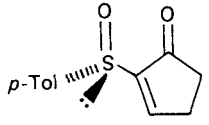
$$(MeO)_2PCH_2{-}S{-}Tol\text{-}p \xrightarrow[2.\ Me_2C=O]{1.\ n\text{-}BuLi} Me_2C{=}CH{-}S{-}Tol\text{-}p + CH_2{=}C(Me)CH_2{-}S{-}Tol\text{-}p \quad (10)$$

1-Alkenyl sulfoxides (**42** and **43**) were first prepared in optically active form by Mulvaney and Ottaviani[74], described in an article overlooked by most workers in the field, and a year later by Stirling and coworkers[75] through the reaction of the appropriate vinyl Grignard reagent with sulfinate ester **19**. Both groups studied the addition of nucleophiles to the carbon–carbon double bond[74,76]. More recently, Posner and coworkers reported a similar synthesis of (*E*)-1-alkenyl sulfoxides, e.g. **44** and **45**[70,77,78]. In the synthesis of **45**, the carbonyl group was first protected as the ketal prior to metallation of the 2-bromo-2-cyclopentenone with *n*-butyllithium. Hogen-Esch[79], Marino[80] and their coworkers have also prepared alkenyl *p*-tolyl sulfoxides from ester **19**.

$CH_2{=}CH{-}S{-}Tol\text{-}p$ (**42**)

$CH_2{=}C(Me){-}S{-}Tol\text{-}p$ (**43**)

E-$C_6H_{13}CH{=}CH{-}S{-}Tol\text{-}p$ (**44**)



(**45**)

Two other approaches to 1-alkenyl sulfoxides which do not use vinyl Grignard reagents have been developed. Mikolajczyk and coworkers prepared homochiral sulfoxide **41** from the reaction of dimethylphosphorylmethyllithium with sulfinate ester **19** and also by resolution (see Section II.A.1). The anion of **41** underwent addition to various carbonyl compounds to give not only the expected 1-alkenyl sulfoxides, but also often to give the corresponding allylic compounds as mentioned above (equation 10)[18]. In an effort to circumvent the problems associated with the Horner–Wittig method as well as the unavailability of 1-halo-1-alkenes, Kosugi and coworkers[63] prepared (*E*)-1-alkenyl *p*-tolyl sulfoxides from 1-alkynyl *p*-tolyl sulfoxides by stereoselective hydroalumination (equations 11 and 12).

$$RC{\equiv}CMgBr \xrightarrow{(19)} RC{\equiv}C{-}S{-}Tol\text{-}p \quad (11)$$

$$RC{\equiv}C{-}S{-}Tol\text{-}p + i\text{-}Bu_2AlH \longrightarrow RCH{=}CH{-}S{-}Tol\text{-}p \quad (12)$$

Allenyl and 1- and 2-alkynyl sulfoxides have also been prepared by reaction of organomagnesium halides with sulfinate ester **19**. 1-Alkynyl *p*-tolyl sulfoxides were prepared in good yield from 1-alkynylmagnesium halides plus ester **19** in toluene (equation 11)[63]. The corresponding organolithium compound was unsatisfactory as a

reagent; it added to the initially formed acetylenic sulfoxide whereas the Grignard reagent did not. Ether, THF and benzene were said to be unsatisfactory reaction solvents, although Stirling and coworkers earlier had prepared what was apparently the first example of an 1-alkynyl sulfoxide, 1-hexynyl *p*-tolyl sulfoxide, in ether in 70% yield[81]. When ester **19** was treated with Grignard reagents prepared from 2-alkynyl halides in ether, separable mixtures of allenyl and 2-alkenyl *p*-tolyl sulfoxides (**46a** and **46b**) were formed in which **46a** usually predominated (equation 13)[81]. Allenyl sulfoxides may prove useful in asymmetric synthesis[63].

$$MeC{\equiv}CCH_2MgBr \longrightarrow \underset{\textbf{(46a)}}{CH_2{=}C{=}C(Me)(O)S{-}Tol\text{-}p} + \underset{\textbf{(46b)}}{MeC{\equiv}CCH_2S(O){-}Tol\text{-}p} \qquad (13)$$

Active methylene compounds may be sulfinylated by reaction of their enolate anions with sulfinate ester[7-11]. This reaction has been investigated much in recent years and the compounds resulting from it have been of considerable use in asymmetric synthesis (see the chapter by Posner). Examples of the sulfinylation are given in the following paragraphs.

Schneider and Simon[82] prepared β-ketosulfoxides **47a** and **47b** by sulfinylation of the dianions of the methyl acetoacetates **48a** and **48b** with sulfinate ester **19** followed by decarboxylation of the intermediate products (Scheme 2). Apparently this avoids racemization experienced by others in the direct synthesis of these compounds[9]. β-Ketosulfoxides are also available from the reaction of the anion derived from methyl *p*-tolyl sulfoxide with esters (see Section II.E). They can also be obtained, in some cases, through the hydrolysis of α-sulfinylhydrazones whose synthesis is described below. Mention has already been made of the synthesis of 2-*p*-tolylsulfinylcycloalkanones such as **32**.

$$\underset{\textbf{(19)}}{p\text{-Tol}{-}S(O){-}O\,Menthyl} + \underset{\textbf{(48)}}{MeC(O){-}CH(R){-}C(O)Me} \xrightarrow[\text{2. } n\text{-BuLi, } -40\,^{\circ}C]{\text{1. NaH/THF}}$$

(a) R = H
(b) R = Et

$$p\text{-Tol}{-}S(O){-}CH_2C(O)CH(R)C(O)Me \xrightarrow[\text{2. HCl, } CH_2Cl_2]{\text{1. KOH, MeOH}} \underset{\textbf{(47)}}{p\text{-Tol}{-}S(O){-}CH_2C(O)CH_2R}$$

(a) R = H
(b) R = Et

SCHEME 2

Esters and amides may be sulfinylated. Addition of a mixture of *t*-butyl acetate and sulfinate ester **19** to a THF–ether solution of magnesium diisopropylamide led to the formation of (*R*)-(+)-*t*-butyl *p*-toluenesulfinylacetate (**49**) in 90% yield (equation 14)[7]. *t*-Butyl propanoate and butanoate also underwent this sulfinylation to give **50** and **51** in yields of 68 and 45%, respectively[83]. The diastereomeric ratio was 1:1 for **50** and 3:7 for **51**. These esters may also be obtained by alkylation of **49**. Similarly, treatment of α-lithio-*N*,*N*-dimethylacetamide with sulfinate ester **19** gave (*R*)-(+)-*N*,*N*-dimethyl-*p*-toluenesulfinylacetamide (**52**) (equation 15)[84].

$$RCH_2COBu\text{-}t \xrightarrow[(19)]{i\text{-}Pr_2NMgBr} p\text{-Tol}—S(=O)—CH(R)C(=O)Bu\text{-}t \quad (14)$$

(**49**) R = H
(**50**) R = Me
(**51**) R = Et

$$LiCH_2C(=O)NMe_2 \xrightarrow{(19)} p\text{-Tol}—S(=O)—CH_2C(=O)NMe_2 \quad (15)$$

(**52**)

Enolates derived from various imino compounds have been sulfinylated in reactions analogous to those shown by equations (14) and (15). Some representative examples are shown in equations 16–18. Here again, these compounds have been utilized in asymmetric syntheses. Addition of sulfinate ester **19** to a THF suspension of α-lithio-*N*,*N*-dimethylhydrazones, derived from readily available hydrazones of aldehydes and ketones, leads to α-sulfinylhydrazones in good yield, e.g. **53** and **54** (equations 16 and 17)[85,86]. Compounds **53** and **54** were obtained in a 95/5 and 75/25 *E*/*Z* ratio, respectively. The epimer ratio of compound **53** was 55/45. Five other examples were reported with various *E*/*Z* and epimeric ratios.

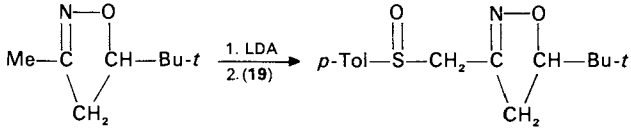
$$EtCH{=}NNMe_2 \xrightarrow[2.\,(19)]{1.\,LDA} p\text{-Tol}—S(=O)—CH(Me)CH{=}NNMe_2 \quad (16)$$

(**53**)

$$MeCEt(=NNMe_2) \xrightarrow[2.\,(19)]{1.\,LDA} p\text{-Tol}—S(=O)—CH_2CEt(=NNMe_2) \quad (17)$$

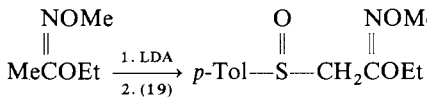
(**54**)

4,5-Dihydroisoxazolines also underwent sulfinylation in an analogous manner and yielded compounds useful in asymmetric synthesis (equation 18)[87–89]. The *R* configuration at sulfur was fixed by the configuration of the starting ester assuming, as is usually done, that the sulfinylation proceeds with inversion at sulfur. Diastereomers were formed without any great bias in ratios ranging from 40/60 to 46/54 for six examples. Separation of these isomers was readily accomplished by chromatography after which the sulfinyl group could be removed in nearly quantitative yield by reductive desulfurization with sodium amalgam to yield enantiomerically pure 4,5-isoxazolines. α-Alkylation to the sulfinyl group followed by desulfinylation and hydrolysis yielded β-hydroxy ketones of high enantiomeric purity.



(18)

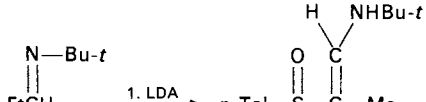
The lithium enolate of ethyl *N*-methoxyacetimidate (**55**) was also successfully sulfinylated by treatment with sulfinate ester **19** (equation 19)[87]. Sulfoxide **56** was used in an asymmetric synthesis of some β-hydroxy esters.



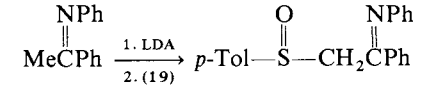
(19)

(**55**) (**56**)

β-Enamino and β-imino sulfoxides are formed by the reaction of lithioenamines with sulfinate ester **19**[90]. In the six examples reported, enamines were formed exclusively in three cases (equation 20), a mixture of enamines and imines in two cases, and an imine exclusively in one case (equation 21).

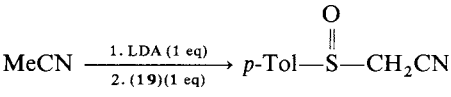


(20)



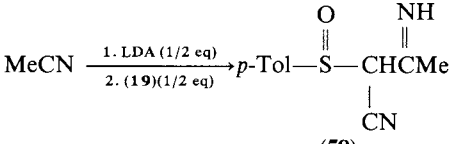
(21)

α-Cyanosulfoxides such as **57** were produced from sulfinate ester **19**, nitriles and LDA present in a 1:1:1 ratio (equation 22)[91]. When the ratio of reactants was changed to 1:2:1, α-cyano-β-iminosulphoxides such as **58** were obtained (equation 23). In this latter case, the nitrile underwent self-condensation and it was this product which reacted with **19** to give **58**. The anion of **57** was shown to be unreactive toward acetonitrile so it could not have been the source of **58**.



(22)

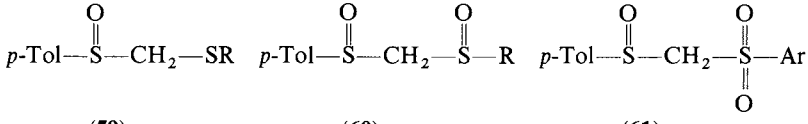
(**57**)



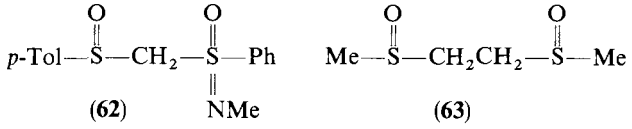
(23)

(**58**)

Various sulfur compounds have been sulfinylated by treatment of the appropriate carbanion with sulfinate ester **19**. Compounds **59**[92], **60**[93], **61**[94] and **62**[95] were prepared in this way, β-disulfoxides (**63**) have also been prepared, as shown earlier by equation (8).

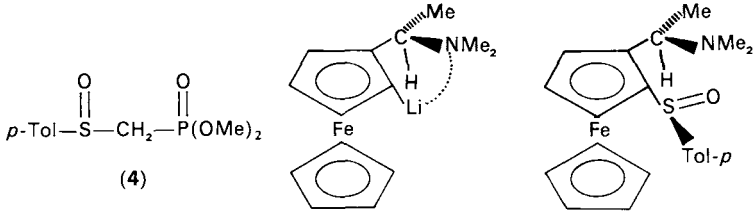


(**59**) (**60**) (**61**)



(62) (63)

An α-phosphoryl sulfoxide (**4**) has also been prepared by the reaction of the appropriate carbanion with sulfinate ester **19** (see also Section II.A.1)[18]. Ugi and coworkers prepared (*S*, *R*, *S*)-**65** by reaction of (*R*, *R*)-**64** with ester **19**. The (*S*, *S*, *R*) diastereomer was prepared from (*S*, *S*)-**64**[96].

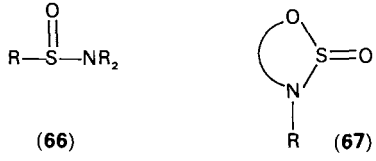


(4) (*R*,*R*-**64**) (*S*,*R*,*S*-**65**)

In view of the successful preparation of so many homochiral sulfoxides via the reaction of nucleophilic species with sulfinate ester **19**, it appears likely that the reaction is capable of extension to provide still more examples of potentially useful sulfoxides.

2. *Other tricoordinate sulfur(IV) compounds*

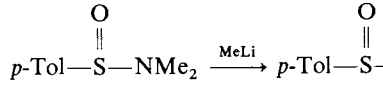
Although carbanionic and enolate species are most often sulfinylated using sulfinate esters, particularly homochiral ester **19**, other tricoordinate S(IV) compounds may be used in their place. Sulfinamides (**66**) and cyclic sulfite ester-amides (**67**) are two examples of such compounds.



(66) (67)

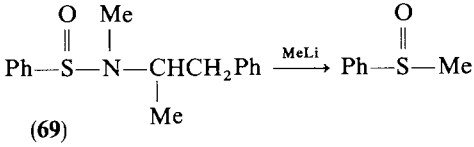
Sulfinamides react with organolithium reagents to give sulfoxides[7,12,15]. For example, sulfinamide **68** reacted with methyllithium, but not dimethylmagnesium iodide or dimethylcadmium, with inversion of configuration at sulfur to give sulfoxide **10** (equation 24)[97]. In one case, even though the sulfinamide (**69**) was diastereomerically pure, the sulfoxide produced from it was not, being formed in 90 to 92% enantiomeric purity (equation 25)[98]. Racemization of the sulfoxide by the methyllithium is a possible explanation for this loss of enantiomeric purity, although it is possible to obtain homochiral methyl *p*-tolyl sulfoxide from the reaction of methyllithium with sulfinate ester **19**; i.e. without racemization by the methyllithium[97]. Sulfinamides are more prone to racemization (or epimerization) than are sulfinate esters[97], although bulky groups on nitrogen appear to increase resistance towards racemization[99]. Furthermore, enantiomerically pure sulfinamides are often obtained from sulfinate ester **19**. Thus, they usually do not offer an advantageous route to sulfoxides compared to sulfinate esters. Schroeck and Johnson[100] obtained sulfinamides from sulfoximines by treating the latter with

aluminium amalgam (equation 26)[13,101]. Homochiral sulfoximines are available by resolution and by several other means. Recently, optically active sulfinamides have been prepared by the ene reaction of optically active alkenes with *N*-sulfinyl compounds such as *N*-sulfinyl-*p*-toluenesulfonamide (equation 27)[68,102].



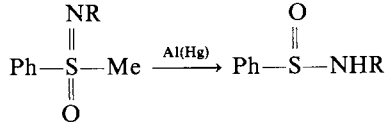
(24)

(68) (10)

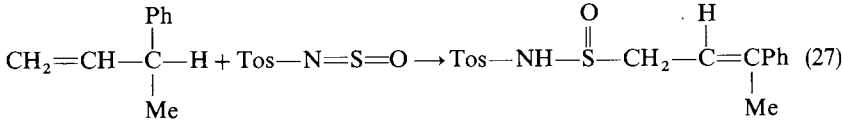


(25)

(69)

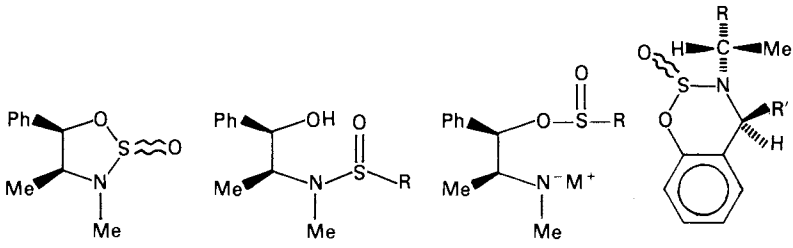


(26)



(27)

Wudl and Lee[103] treated *l*-ephedrine with thionyl chloride to obtain diastereomeric 3,4-dimethyl-5-phenyl-2-oxo-1,2,3-oxathiazolidines (**70**) epimeric at sulfur. Reaction of one epimer of **70** with either an organo-lithium or -magnesium reagent yielded a sulfinamide (**71**), which upon treatment with an excess of a second organometallic reagent yielded a sulfoxide of high optical purity. This procedure was complicated in the first step by a competing reaction. Initial O—S rather than N—S bond cleavage led to a sulfinate ester (**72**). An intramolecular O to N sulfinyl shift with retention at sulfur followed to give sulfinamide **71**. This intramolecular process decreased the optical purity of the resulting sulfinamide, most of which was formed directly with inversion upon O—S bond cleavage, consequently lowering the enantiomeric purity of any sulfoxide produced in a later step.



(70) (71) (72) (73)

Hiroi and coworkers[104–106] extended and improved the procedure of Wudl and Lee by preparing epimeric benzoxathiazine-2-oxides (**73**) via the reaction of homochiral amino-

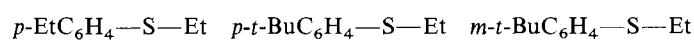
phenols with thionyl chloride. When R was α-naphthyl, one epimer was greatly favored thermodynamically. Treatment of this epimer with phenylmagnesium bromide followed by treatment with an alkyllithium gave alkyl phenyl sulfoxides of good enantiomeric purity.

C. Asymmetric Oxidation

The earliest attempts to obtain optically active sulfoxides by the oxidation of sulfides using oxidants such as chiral peracids did not fare well. The enantiomeric purities obtained were very low. Biological oxidants offered great improvement in a few cases, but not in others. Lately, some very encouraging progress has been made using chiral oxaziridines and peroxometal complexes as oxidants. Newer developments in the use of both chemical oxidants and biological oxidants are described below.

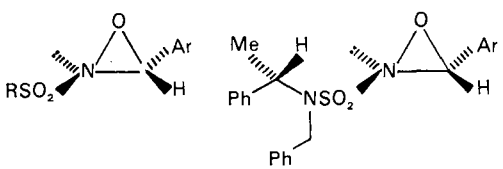
1. Chemical oxidants

Asymmetric oxidation of sulfides by direct oxygen transfer from optically active peracids gives sulfoxides of low enantiomeric purity, usually only a few percent[107,108]. (See Reference 42 for an interesting example of the oxidation of a sulfide in a chiral molecule by an achiral oxidant.) Recently, in a variation of this technique, Czarnik[109] and Drabowicz and Mikolajczyk[110] oxidized sulfides with various oxidizing agents in the presence of cyclodextrins. Czarnik oxidized **74**, **75** and **76** in such a way that half or more of the sulfide remained unreacted. Sulfide **76** when treated with aqueous solutions of hydrogen peroxide, *m*-chloroperbenzoic acid, *t*-butyl hydroperoxide or iodosobenzene diacetate gave the sulfoxide in 0 to 34% e.e. depending on the oxidant and the type of cyclodextrin used. Drabowicz and Mikolajczyk restricted their oxidant to hydrogen peroxide and used pyridine as a solvent. They observed e.e. values ranging from 0 to 30% in the oxidation of thirteen dialkyl and alkyl aryl sulfides.

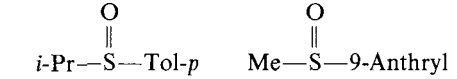


(**74**) (**75**) (**76**)

Chiral 2-sulfonyloxaziridines (**77**) and 2-sulfamyloxaziridines (**78**), developed by Davis and coworkers[111–113], were used successfully in the oxidation of similar substrates. The oxidations of isopropyl *p*-tolyl sulfide and methyl 9-anthryl sulfide to their respective sulfoxides, **79** and **80**, using **78** as an oxidant gave greater than 90% yields with 65 and 68% e.e., respectively. Davis pointed out that even though the enantiomeric purities obtained using **77** and **78** are sometimes rather low, these compounds are nevertheless useful synthetic reagents if the sulfinate ester–Grignard reaction is not applicable. Since the oxaziridines have well-defined active sites, they are also useful in assigning absolute configurations to sulfoxides and related compounds, such as thiosulfinates, which can be obtained using **77** and **78** as oxidants. Recently, some chiral sulfamyloxaziridines afforded **80** in 91% e.e. It appears that these oxidants rival the peroxotitanium complexes described below[113]. These two classes of oxidants and peracids share a similarity in mechanism[111a].



(**77**) (**78**)

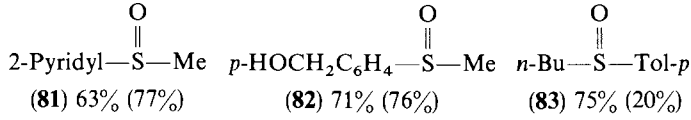


(**79**) (65%) (**80**) (68%)

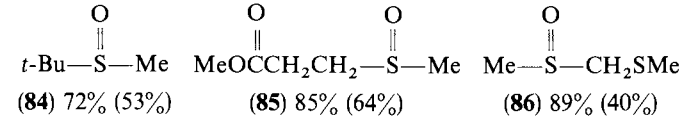
Significant improvements in asymmetric oxidations were made by Modena and, especially, by Kagan, and their coworkers. Both groups used chiral peroxotitanium complexes patterned after the Sharpless reagent as the oxidants.

Modena, Di Furia and Curci investigated the use of $MoO_2(acac)_2$ and $VO(acac)_2$ in the presence of *t*-butyl alcohol and a chiral alcohol in a benzene–toluene solvent mixture to oxidize methyl *p*-tolyl and methyl phenyl sulfides to the sulfoxides[114]. The enantiomeric purities were low, the highest values being 9–10% obtained using $VO(acac)_2$ and (−)-menthol. More recently, Di Furia and colleagues[115] investigated other molybdenum and vanadium complexes and, in particular, a modified Sharpless reagent (a titanium complex). Using a 1:4:2 ratio of Ti(OPr-*i*)$_4$/(+)-diethyl tartrate/*t*-BuOOH in methylene chloride at − 20° instead of the 1: > 1.2:1.5–2.0 ratio recommended for oxidation of allylic alcohols[116], methyl *p*-tolyl sulfoxide was obtained in 88% e.e. It is noteworthy that the sulfide sulfur atom, unlike the oxygen atom of allylic alcohols, does not complex strongly with the titanium. 1,3-Dithiolanes, 1,3-dithianes and 1,3-oxothiolane have also been oxidized to the corresponding monosulfoxides using the modified reagent as a route to optically active carbonyl compounds[115b].

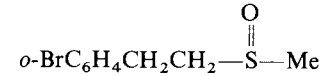
Kagan and coworkers have also developed a efficient asymmetric oxidation of sulfides to sulfoxides using a stoichiometric amount of a modified Sharpless reagent and applied it extensively[108]. Oxidation of methyl *p*-tolyl sulfide by the standard Sharpless reagent in methylene chloride at − 20° gave racemic sulfoxide (41%) and sulfone (17%). The outcome of the oxidation was drastically changed for the better when one equivalent of water was added. An 84% enantiomerically pure sulfoxide was obtained in 90% yield. Increasing the molar ratio of diethyl tartrate to 2 increased the e.e. to 90%. Kagan oxidized almost thirty alkyl aryl and alkyl methyl sulfides to the sulfoxides in good chemical yield and with enantiomeric purities generally from 50 to 91%, most often at the higher end of this range. The method is particularly useful in obtaining dialkyl sulfoxides, which are hard to prepare by other methods, and those containing phenolic OH, COOMe, CH_2OH, NO_2 and pyridyl groups. These groups do not interfere. Using tartrate of configuration (*R*, *R*) or (*S*, *S*) allows synthesis of either of the sulfoxide enantiomers. The reaction is also amenable to scale-up. More recently, the oxidation has been extended to sulfoxides functionalized with Cl, CN, —CH=CH_2 or COOR groups and to a methionine derivative with good results. Cyclopropyl phenyl sulfide was oxidized to sulfoxide of 95% enantiomeric purity[117]. Nonlinear effects were observed in the oxidation of methyl *p*-tolyl sulfide (and some other compounds) by reagents prepared from diethyl tartrate samples of different enantiomeric purity; i.e. a plot of e.e. of the tartrate versus e.e. of the sulfoxide was curved[118]. Kagan presented some possible mechanistic schemes which account for the nonlinearity and pointed out that 'great caution is needed in interpreting the results of an asymmetric synthesis not using enantiomerically pure reagent or catalysts'. He has recently reviewed his work, discussed a possible mechanism for the oxidation, and pointed out that methyl *p*-tolyl sulfoxide of 99% e.e. can be obtained by recrystallizing a sample of lesser purity from hexane[119]. The asymmetric oxidation of disulfides to thiosulfinates, of sulfenamides to sulfinamides, and of sulfenates to sulfinates has also been studied[120]. Some examples of sulfoxides prepared using the modified reagent are given by structures **81**–**86** together with the yields and enantiomeric purities, in parentheses. Beckwith and Boate[121] made use of the modified Sharpless reagent to prepare (**R**)-**87** from the sulfide in greater than 96% e.e.



(**81**) 63% (77%) (**82**) 71% (76%) (**83**) 75% (20%)

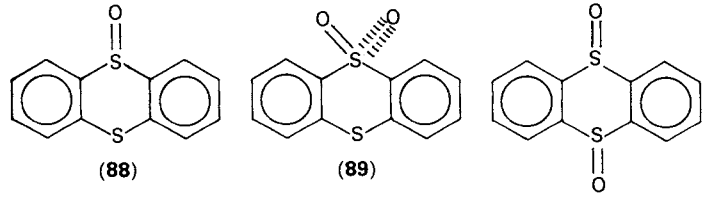


(**84**) 72% (53%) (**85**) 85% (64%) (**86**) 89% (40%)



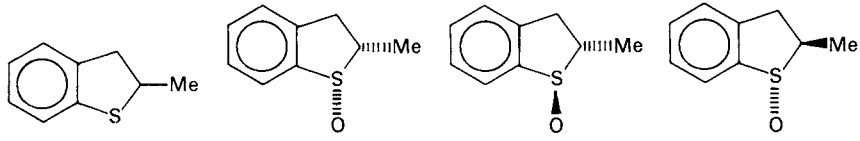
(**87**)

Adam and Lohray[122] have used thianthrene 5-oxide (**88**) as a mechanistic probe in oxidations with transition metal peroxides. They oxidized **88** with various diperoxo complexes of chromium, molybdenum and tungsten and formulated a plausible mechanism on the basis of the products formed, **89** and **90**.

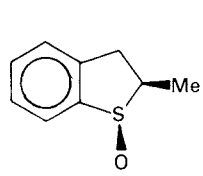


(**88**) (**89**) (**90**)

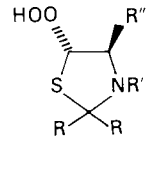
Takata and Ando have investigated the oxidation of racemic 2-methyl-2,3-dihydrobenzothiophene (**91**) to the stereoisomeric sulfoxides (**92**–**95**). They used optically active hydroperoxides (**96**), with and without added $Ti(OPr\text{-}i)_4$, and the modified Sharpless reagent, presumably based on naturally occurring tartaric acid although this was not explicitly stated in their article[123,124]. Slightly more than two moles of racemic sulfide **91** were oxidized by one mole of oxidant with predominant formation of the *trans* sulfoxides **93** and **94**. Usually more than 90% of the sulfoxides were *trans*. Hydroperoxide **96** gave up to 72% e.e. for the formation of (*1S,2R*)-**94** whereas the modified Sharpless reagent gave (*1R,2S*)-**93** in 82% e.e. That is, the two reagents showed opposite enantioselectivities but similar diastereoselectivities. Changing the configuration of the tartrate ester in the Sharpless reagent should, of course, cause the selectivities to be the same.



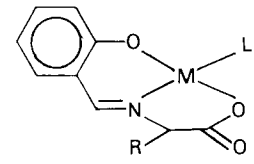
(**91**) (**92**) (**93**) (**94**)



(95)



(96)



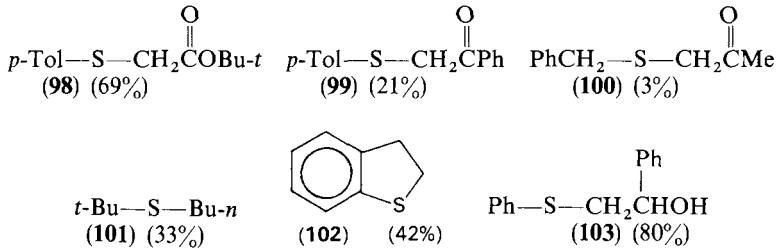
(97)

Colona and coworkers oxidized a variety of alkyl aryl and heterocyclic sulfides to the sulfoxides using *t*-butyl hydroperoxide and a catalytic amount of a complex (**97**) derived from a transition metal and the imines of L-amino acids. Of the metals (M = TiO, MoO_2, VO, Cu, Co, Fe), titanium gave the highest e.e. (21%), but molybdenum was the most efficient catalyst. The sulfoxides were accompanied by considerable sulfone[125].

Sugimoto and coworkers[126,127] oxidized a number of alkyl phenyl, alkyl *p*-tolyl and alkyl benzyl sulfides to sulfoxides using sodium metaperiodate or hydrogen peroxide in the presence of one-third mole of bovine serum albumin (BSA) at pH > 9 in a biomimetic approach. Enantiomeric purities from 1 to 81% were observed. It was postulated that the sulfides were bound in the chiral hydrophobic binding domains of the BSA where one of the pairs of enantiotopic lone pairs was attacked by the reagent. Oxidation of alkyl phenyl sulfides with sodium metaperiodate resulted in predominant formation of *R*-sulfoxides whereas the closely related alkyl *p*-tolyl sulfides yielded the *S*-sulfoxides. Binding of the oxidant as well as the sulfides was suggested as necessary to explain the predominant formation of *R*-sulfoxides from both the alkyl phenyl and alkyl *p*-tolyl sulfides when hydrogen peroxide was the oxidant.

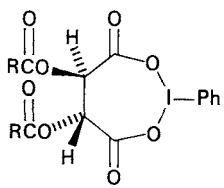
Kinetic resolution was also investigated. Racemic sulfoxides were oxidized, and at 50% completion of reaction, the remaining sulfoxides were found to be enantiomerically enriched (1 to 33% e.e.). By using a large excess of hydrogen peroxide, the two processes were combined. That is, a 5 molar excess of hydrogen peroxide gave less than 5% sulfone, but a 10 molar excess gave an increasing amount with a consequent increase or decrease in the optical purity of the sulfoxide. For example, oxidation of isopropyl phenyl sulfide over 12 hours led to a 78% yield of sulfoxide whose optical purity remained at 62% during this period. As time went on, the yield of sulfoxide decreased to 47% due to overoxidation to the sulfone, but the optical purity increased to 93%. The oxidation of *n*-butyl and isobutyl phenyl sulfides gave similar results. But this combination of steps was not always favorable. Overoxidation of *n*-butyl *p*-tolyl sulfide caused the enantiomeric purity to decrease from 17 to 13% as the chemical yield fell from 79 to 57%.

Colonna and coworkers[128,129] also investigated the use of BSA-sodium metaperiodate in the oxidation of sulfides, but they used only one-twentieth of a mole of BSA, a catalytic amount, rather than the one-third used by Sugimoto. Some of the sulfides oxidized are depicted by **98** to **103** with the e.e. values in parentheses. The reactions were carried out at room temperature by stirring a heterogeneous mixture of BSA (0.05 mole), substrate (1 mole) and sodium metaperiodate (2 mole) in a borate buffer at pH 9. On the basis of circular dichroism (CD) and UV studies, they concluded that the large amounts of sodium metaperiodate modified the conformation of the BSA and thus the bonding of the sulfides to the protein. This might explain the difference in behavior observed by Sugimoto and Colonna. At the relatively low ratio of periodate to BSA used by the former, a significant decrease in enantioselectivity below pH 8 was observed, whereas Colonna found no significant dependence between pH 5 to 11. The high molecular weight of BSA is a distinct disadvantage to the large-scale use of this method. Colonna used 3.3 g, a catalytic amount, to oxidize one mmol, approximately 0.2 g, of sulfide.



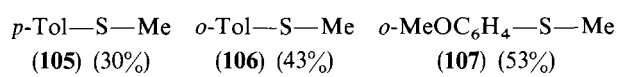
The resolution of cyclohexyl phenyl sulfoxide by chromatography on a δ-tris(1,10-phenanthroline)nickel(II)–montmorillonite column was described in Section II.A.2[28]. Oxidation of an aqueous suspension of cyclohexyl phenyl sulfide, adsorbed on this clay–chelate complex, by sodium metaperiodate on a micromolar scale proceeded in over 90% yield and gave up to 78% e.e.[130]. Several other sulfides were also oxidized in a similar fashion. Methyl and ethyl sulfides gave sulfoxides with 0 and 9% e.e., respectively. The results with sulfides bearing bulkier alkyl groups, *n*-butyl, 2-butyl and benzyl phenyl sulfides, were better, the sulfoxides being obtained in 75, 65 and 70% e.e., respectively. An attempt to carry out the reaction on a larger scale (0.6 mmol) gave only 45% e.e.

Imamoto and Koto[131] prepared some interesting chiral oxidants (**104**) by the reaction of iodosylbenzene with tartaric anhydride. Methyl *p*-tolyl sulfide (**105**) was oxidized by **104c** to the sulfoxide in 80% yield with 40% e.e. Methyl *p*-tolyl, *o*-tolyl and *o*-anisyl sulfides (**105**–**107**) were oxidized by **104a** to their sulfoxides with the enantiomeric purities shown.



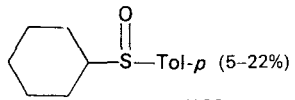
(**104**)

(**a**) R = Me
(**b**) R = Ph
(**c**) R = *t*-Bu



Komori and Nonaka[132,133] electrochemically oxidized methyl, isopropyl, *n*-butyl, isobutyl, *t*-butyl and cyclohexyl phenyl sulfides (**108**) and cyclohexyl *p*-tolyl sulfide (**109**) to their sulfoxides using a variety of polyamino acid-coated electrodes to obtain the range of e.e. values shown in parentheses. The highest enantiomeric purities were obtained using an electrode doubly coated with polypyrrole and poly(L-valine), an electrode which also proved the most durable of those prepared.

R—S—Ph (**108**) R = Me, (1–2%), *i*-Pr (28–77%), *n*-Bu (6–20%), *i*-Bu (16–44%), *t*-Bu (3–93%), cyclohexyl (17–54%)



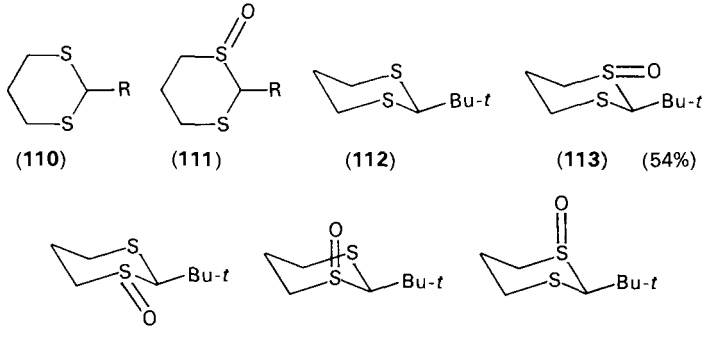
(**109**)

2. Biological agents

A number of studies describing the oxidation of sulfides to sulfoxides by biological oxidizing agents have been published over the years[2,9,13,107]. Microbial systems are often

able to transform sulfides to sulfoxides of high enantiomeric purity on a preparative scale. Enzymes of mammalian origin also yield sulfoxides, but have proved less suitable for large-scale use.

Boyd, Drake and coworkers investigated the structure and absolute stereochemistry of sulfoxides (**111**) produced by fungal monooxygenase-catalyzed oxidation of 2-alkyl-1,3-dithianes (**110**) using three fungi, *Aspergillus foetidus*, *Mortierella isabellina* and a *Helminthosporium* species[134]. Previous studies had shown that the monooxygenase fungal enzymes could differentiate between the prochiral faces associated with a sulfur atom in acyclic and cyclic sulfides. The highest optical yield, 72%, was obtained in the oxidation of **112** by the *Helminthosporium* fungus. Four sulfoxides (**113**–**116**) were produced in the relative amounts shown in parentheses. The pro-*S* thioalkyl group was preferred to the pro-*R* group by 68 to 32% during equatorial oxidation whereas the pro-*R* group was favored over the pro-*S* group by 85 to 15% during axial oxidation. Addition of racemic sulfoxides to each of the fungi in turn showed that preferential removal of one enantiomer could account for the stereoselectivity observed in some of the oxidations, but not in the case just described. In this case, recovered sulfoxide was still racemic. The authors stated that this was the first evidence that monooxygenase enzymes can stereochemically differentiate between prochiral thioalkyl groups during sulfoxide formation.



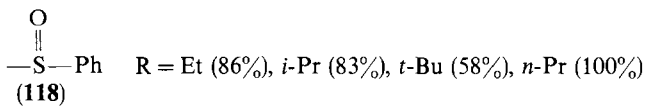
(**110**) (**111**) (**112**) (**113**) (54%)

(**114**) (26%) (**115**) (17%) (**116**) (3%)

Holland and coworkers[135] investigated the oxidation of ten *para*-substituted methyl phenyl sulfides (**117**) and five alkyl phenyl sulfides (**118**) to their respective sulfoxides by the fungus *Mortierella isabellina*. Earlier, the authors had proposed that cytochrome P-450 dependent monooxygenase enzymes of the fungus were responsible for oxidation at sulfur. The present study was carried out to determine the effects of *para* substitution on the enantiomeric purity of the sulfoxides obtained. Optical yields ranged from 20 to 100% and are listed by their precursor sulfides below in parentheses. The e.e. values obtained from isosteric sulfides **117** (H vs. F, MeO vs. Et, Me vs. CN) were compared. In these three instances, higher e.e. values were obtained for the molecule with the most electron-withdrawing group. Sulfone formation occurred in the two instances where X = NO_2 and Br. Racemic sulfoxides added in these two cases were recovered quantitatively, so direct oxidation of the sulfoxides could not have been the source of the sulfones. The authors proposed that the sulfides bind specifically to the enzyme but are oxidized non-stereospecifically. This non-stereospecific oxidation might be the result of a loose active site in which oxidation can occur on either face of the sulfide. A radical cation, whose reactivity is dependent on the *para* substituents as well as on steric effects and whose formation is slow compared to its demise, was proposed as an intermediate.

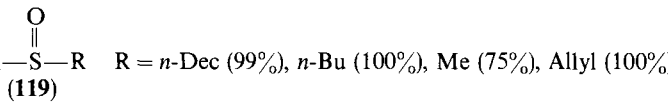
p-XC_6H_4—S—Me (**117**)

X = H (58%), Me (46%), Et (90%), *i*-Pr (84%), *t*-Bu (76%), MeO (72%), NO_2 (20%), F (70%), Cl (90%), Br (100%), CN (80%)

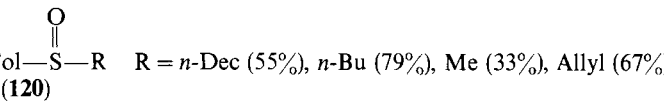


(**118**)

Ohta and coworkers[136] used a bacterium, *Corynebacterium equi* IFO 3730, rather than a fungus, to oxidize eight alkyl phenyl and *p*-tolyl sulfides to their respective sulfoxides (**119**, **120**) of configuration *R*. Virtually all of the sulfur compounds were accounted for as the sum of uncreacted sulfide, sulfoxide and sulfone. The enantiomeric purities of the sulfoxides obtained were quite good and are shown below in parentheses. The formation of the allyl sulfoxides in high optical purity is noteworthy. The authors believe that the sulfoxides were formed by enantioselective oxidation of the sulfides rather than by enantioselective oxidation of racemic sulfoxides, since the yield of sulfoxides was greater than 50% in five of the ten oxidations reported (see also Reference 34).



(**119**)

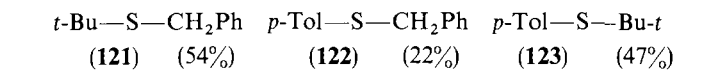


(**120**)

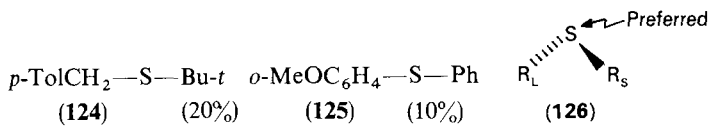
Purified mammalian- and bacterial-derived enzymes were used by Oae, Walsh and their coworkers to oxidize sulfides to sulfoxides. The emphasis in these studies was on the characteristics of the enzymes rather than on the use of the enzymes to prepare homochiral sulfoxides.

Walsh and coworkers oxidized ethyl *p*-tolyl sulfide on an analytical scale to the *S*-sulfoxide of 64% enantiomeric purity using a bacterial flavoenzyme cyclohexanone monooxygenase derived from *Acinetobacter*[137]. Using a flavin adenine dinucleotide containing monooxygenase purified from hog liver microsomes yielded the *R*-sulfoxide of 90% enantiomeric purity. HPLC on a column containing a 3,5-dinitrobenzoyl-D-phenylglycine chiral stationary phase was used to determine the optical purity of the sulfoxides.

Oae and coworkers oxidized several diaryl, dialkyl and alkyl aryl sulfides to their corresponding sulfoxides using purified cytochrome P-450 obtained from rabbit liver microsomes[138]. In agreement with expectations, this enzyme did not exhibit much stereospecificity. Some examples including the observed e.e. values are shown by **121**–**125**. A model was proposed to account for the absolute configurations of the sulfoxides produced (**126**). The sulfur atom is preferentially oxidized from the direction indicated.



(**121**) (54%) (**122**) (22%) (**123**) (47%)



(**124**) (20%) (**125**) (10%) (**126**)

D. Asymmetric Reduction

In principle, it should be possible to selectively reduce one of the enantiomers in a racemic sulfoxide mixture; that is, an asymmetric kinetic resolution via reduction should

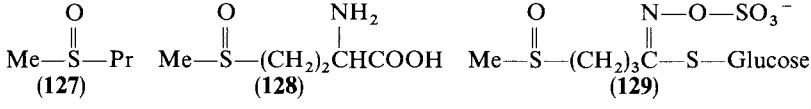
be possible. Several examples of this approach are mentioned in the review by Mikolajczyk and Drabowicz[12].

E. Structure Modification of Chiral Sulfoxides

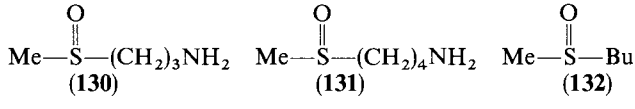
An optically active sulfoxide may often be transformed into another optically active sulfoxide without racemization. This is often accomplished by formation of a new bond to the α-carbon atom, e.g. to the methyl carbon of methyl *p*-tolyl sulfoxide. To accomplish this, an α-metallated carbanion is first formed at low temperature after which this species may be treated with a large variety of electrophiles to give a structurally modified sulfoxide. Alternatively, nucleophilic reagents may be added to a homochiral vinylic sulfoxide. Structurally more complex compounds formed in these ways may be further modified in subsequent steps. Such transformations are the basis of many asymmetric syntheses and are discussed in the chapter by Posner and in earlier reviews[7-11].

F. Natural Sources of Sulfoxides

Even though sulfoxides, presumably homochiral, occur frequently in plants and animals, they are usually not obtained in quantity from such sources[139,140]. However, Kjær and Malver[141] developed routes to (*S*)- and (*R*)-methyl propyl sulfoxides (**127**) of high optical purity from (+)-L-methionine sulfoxide (**128**) and 3-methylsulfinylpropylglucosinolate (**129**), respectively. Sulfoxide **128** was obtained by resolution, but sulfoxide **129**, which is commercially available as glucoiberin, was isolated by extraction from the commercially available seeds of the ornamental *Iberis amara*. Sulfoxides **128** and **129** were converted to the enantiomeric aminosulfoxides, (*S*)- and (*R*)-**130**. Each enantiomer of **130** was subsequently deaminated to give (*R*)- and (*S*)-**127**, respectively. The deamination procedure was also successful in converting (*R*)-4-methylsulfinylbutylamine (**131**), obtained by resolution, to the corresponding sulfoxide, (*R*)-**132**. Since ω-aminoalkyl methyl sulfoxides are available from glucosinolates, common in many plants, Kjær and Malver proposed that their procedure is general for the preparation of methyl alkyl sulfoxides (see also Reference 58).



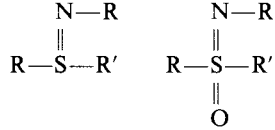
(127) **(128)** **(129)**



(130) **(131)** **(132)**

G. Sulfoxides from Sulfilimines and Sulfoximines

Optically active sulfoximines (**133**) and sulfilimines (**134**) may be converted to optically active sulfoxides[12,142].



(133) **(134)**

Optically active sulfilimines are available by resolution and by treatment of the corresponding sulfide with *t*-butyl hypochlorite in the presence of menthol and an amide. Thus, treatment of an equimolar mixture of a diaryl sulfide, menthol and pyridine in acetonitrile at $-25\,^{\circ}C$ with *t*-butyl hypochlorite followed by addition of a molar equivalent of sodium *p*-toluenesulfonamide yielded optically active *N*-tosyl diaryl sulfilimines of 14 to 47% enantiomeric purity in 34 to 88% yield (equations 28 and 29)[142]. Resolution may be accomplished either by treating basic *N*-unsubstituted sulfilimines with optically active acids and fractionally crystallizing the resulting diastereomers or by seeding a supersaturated solution of *N*-substituted sulfilimines with a crystal of one enantiomer following the procedure described in Section II.A.4. Sulfilimines undergo alkaline hydrolysis to the corresponding sulfoxide (equation 30) with complete inversion of configuration.

$$\mathrm{Ar{-}S{-}Ar' + \textit{t}\text{-}BuOCl + menthol \longrightarrow Ar{-}\overset{+}{S}(O\,Menthyl){-}Ar'} \tag{28}$$

$$\mathrm{Ar{-}\overset{+}{S}(O{-}Menthyl){-}Ar' + \textit{p}\text{-}TolSO_2NHNa \longrightarrow Ar'{-}S(N{-}Ts){-}Ar} \tag{29}$$

$$\mathrm{\textit{p}\text{-}Tol{-}S(N{-}Ts){-}Me + NaOH \longrightarrow \textit{p}\text{-}Tol{-}S(O){-}Me} \tag{30}$$

Optically active sulfoximines are available from sulfilimines by oxidation, which occurs with retention of configuration at sulfur, or, preferably, by resolution of a racemic mixture[13,142]. Although sulfoximines may also be prepared from sulfoxides, this is not of concern here. Akutagawa and coworkers[143] showed that *N*-unsubstituted sulfoximines are cleanly converted in quantitative yield to the corresponding sulfoxides by treatment with an equimolar amount of *t*-butyl nitrite (equation 31). Since (*S*)-(+)-methyl phenyl sulfoximines gave (*S*)-(−)-methyl phenyl sulfoxide with complete retention of configuration, it is presumed that this reaction proceeds with retention in general. This procedure could be quite useful in those cases where homochiral sulfoxides are not available by the sulfinate ester–Grignard method or by asymmetric oxidation. Of course, a resolution of the prerequisite sulfoximine is required if this method is to be successful. Preparation of the racemic sulfoximine is usually easily achieved.

$$\mathrm{R{-}S(O)(NH){-}R + \textit{t}\text{-}BuONO \longrightarrow R{-}S(O){-}R} \tag{31}$$

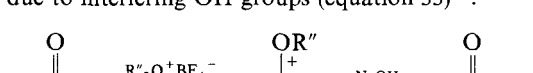
III. STEREOCHEMISTRY OF REACTIONS AT SULFOXIDE SULFUR

Many reactions are known which involve the sulfur atom in sulfoxides and other tricoordinate S(IV) species. Three situations are common in these reactions, i.e. the sulfur atom may remain tricoordinate, its coordination number may be reduced to two, or it may be increased to four. If the sulfur atom is rendered dicoordinate, it can no longer be stereogenic so such transformations will not be considered here. Reactions which leave the coordination number at three usually take place with inversion of configuration or

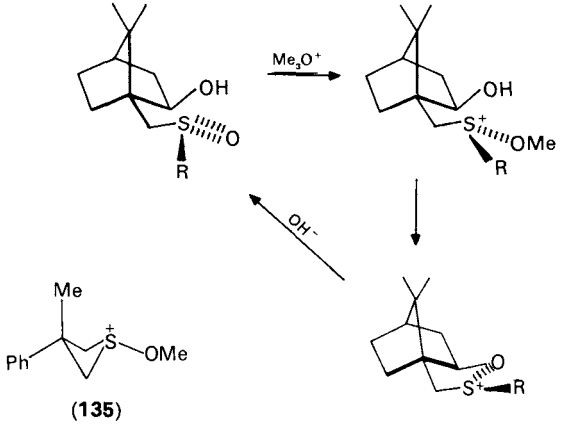
racemization, although there are a few cases where retention has been observed. Most of these reactions can be classified as nucleophilic substitution at sulfur, that is, one of the three ligands is replaced by a nucleophile. Recent research by Mikolajczyk and coworkers on substitution at sulfur in sulfinamides indicates that retention is perhaps not as rare or unusual as previously believed[144] (see also Reference 14). Reactions which increase the coordination number to four usually occur with retention or racemization. They occur by the addition of an electrophile to the lone electron pair on sulfur. The stereochemistry of these processes is described in the reviews by Mikolajczyk and Drabowicz[12,144], Barbachyn and Johnson[13], Tillet[15], Laur[39] and Kice[145]. Only a few illustrative examples and some recent results will be mentioned here.

A. Reactions Which Leave the Coordination Number at Three

Johnson and McCants[146] devised a very valuable method for inverting the configuration of sulfoxides by alkylating the sulfinyl oxygen and then displacing the alkoxy group by treatment with base (equation 32). Although O-alkylation usually takes place quite well and does not effect the configuration at sulfur, the hydrolysis step has a problem, i.e. S—O bond cleavage is not exclusive. A few percent C—O bond cleavage occurs which leads to retention at sulfur, thus lowering the enantiomeric or diastereomeric purity of the product. For example, hydroxide ion reacted at sulfur of methoxysulfonium salt **135** only about 12 times faster than it did at carbon[43]. Occasionally Johnson's method fails to yield an inverted sulfoxide due to interfering OH groups (equation 33)[42].



(32)

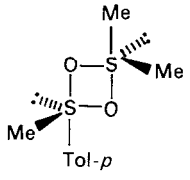


(33)

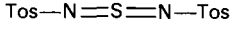
(135)

Only relatively few nucleophilic substitution reactions at sulfur proceed with retention. Oae found that (*R*)-(+)-methyl *p*-tolyl sulfoxide exchanged ^{18}O with dimethyl sulfoxide at 150 °C much faster than it racemized; thus, the exchange took place with retention. A cyclic intermediate, **136**, was proposed to account for this behavior[12,147]. The same sulfoxide was found to react with *N*,*N*′-ditosylsulfurdiimide, **137**, with either retention or inversion depending on the reaction conditions. Christensen[148] observed retention in benzene whereas Cram and coworkers[149] found that inversion took place in pyridine. A four-membered ring intermediate, **138**, was postulated to account for the retention, whereas a

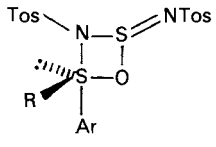
six-membered ring containing two molecules of reagent and the sulfoxide was postulated to account for the inversion. These and some additional examples are discussed by Mikolajczyk and Drabowicz[12].



(136)

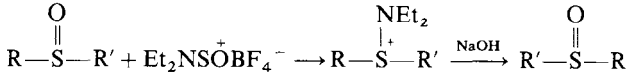


(137)

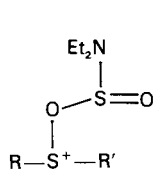


(138)

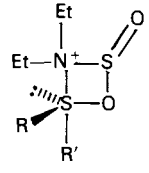
Mikolajczyk and coworkers investigated the stereochemistry of the reaction of *N*-ethyl-*N*-sulfinylethanaminium tetrafluoroborate with four sulfoxides, a reaction originally discovered by Kresze (equation 34)[12,150]. The stereochemistry of the aminosulfonium salts was determined by basic hydrolysis to the corresponding sulfoxides, presumably with complete inversion of configuration. Two dialkyl sulfoxides, methyl isobutyl sulfoxide and methyl *n*-butyl sulfoxide, reacted with 83 and 71% retention, respectively. Methyl *p*-tolyl sulfoxide reacted with 6% retention whereas phenyl *p*-tolyl sulfoxide was completely racemized. Initial formation of an adduct, **139**, was proposed. This adduct then closed to a four-membered ring sulfurane, **140**, with the nitrogen atom in the apical position. After Berry pseudorotation to place the oxygen in the apical position, sulfurane **141** lost sulfur dioxide to give the aminosulfonium salt. A low barrier to pyramidal inversion was suggested to explain the racemization observed for the methyl and phenyl *p*-tolyl sulfoxides. An achiral dication was proposed as an alternative explanation.



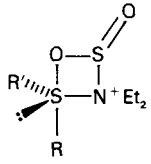
(34)



(139)

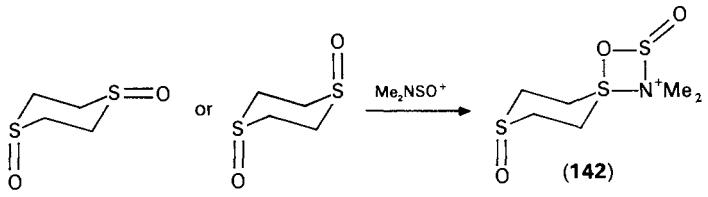


(140)

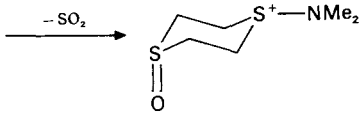


(141)

More recently Schwöbel and coworkers[151] carried out a similar study, but using three pairs of *cis* and *trans* six-membered cyclic sulfoxides. For each pair, the same aminosulfonium salt was obtained (equations 35 and 36). Each axial sulfinyl group was transformed into an equatorial S—NMe_2 group with inversion. Each equatorial sulfinyl group was transformed into an equatorial S—NMe_2 group with retention. The aminosulfonium salts were analyzed by basic hydrolysis to the sulfoxides with inversion as described above. This surprising stereochemistry was rationalized as follows. Each pair of sulfoxide diastereomers was postulated to yield a cyclic sulfurane with the nitrogen apical. These initially formed sulfuranes rapidly underwent turnstile pseudorotations to yield a common more-stable NMR-observable sulfurane, **142**, with an oxygen apical. Sulfurane **142** then lost sulfur dioxide to give the same aminosulfonium salt regardless of the *cis–trans* stereochemistry of the starting sulfoxide.

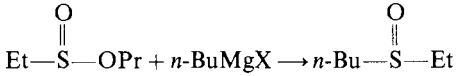


(35)

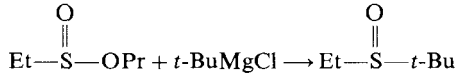


(36)

Perhaps the most interesting of recent developments in research on the stereochemistry of nucleophilic substitution at sulfur comes from the work of Mikolajczyk and Drabowicz[152]. They found that the reaction of sulfinate esters with Grignard reagents does not necessarily proceed with inversion of configuration in all cases as commonly believed (equations 37 and 38). Thus (*S*)-(−)-*n*-propyl ethanesulfinate gave (*S*)-(+)-ethyl *n*-butyl sulfoxide with inversion but (*R*)-(−)-ethyl *t*-butyl sulfoxide with retention when treated with the appropriate Grignard reagent. No four-membered ring intermediate can be invoked, as was done above, to explain the observed retention. Perhaps pseudorotation of an intermediate may account for this unusual stereochemistry much in the way it was proposed to explain retention in substitution at sulfur of sulfinamides[144].



(37)

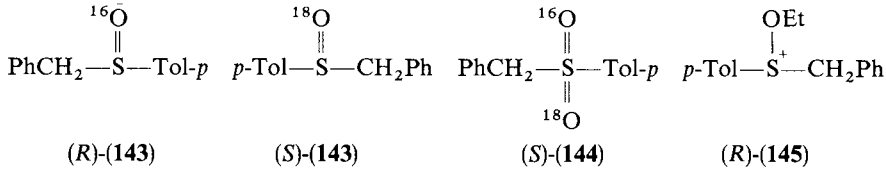


(38)

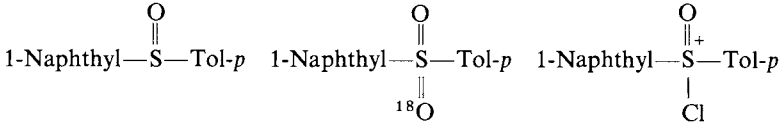
B. Reactions Which Increase the Coordination Number to Four

There are a number of reactions which transform a tricoordinate S(IV) into a tetracoordinate S(VI) group. Sulfoxides, for example, can be oxidized to sulfones. If a peroxy acid is used as the oxidant, the reaction proceeds with retention at sulfur. It is commonly assumed that the peroxy oxygen is added to sulfur's unshared pair of electrons without effecting sulfur's configuration. Normally, sulfone sulfur is not stereogenic, but if one of the oxygen atoms is replaced by an isotope, ^{17}O or ^{18}O, then it becomes so. Several oxidations of sulfoxides to sulfones involving ^{18}O have been carried out beginning with Stirling's oxidation of (*R*)-(+)-benzyl *p*-tolyl sulfoxide (**143**) to (*S*)-(−)-benzyl *p*-tolyl sulfone (**144**) using peroxyacetic acid[153]. Cinquini achieved the same stereospecific incorporation of ^{18}O by treating sulfoxide (*R*)-(+)-**143** with triethyloxonium tetrafluoroborate to form alkoxysulfonium salt (*R*)-**145** then hydrolyzing (*R*)-**145** to sulfoxide (*S*)-(−)-**143** with ^{18}O-labeled hydroxide ion[154]. Then sulfoxide (*S*)-(−)-**143** was oxidized to sulfone (*S*)-(−)-**144** using *m*-chloroperbenzoic acid. (*S*)-(−)-*p*-Tolyl 1-naphthyl sulfoxide (**146**) was transformed into (*R*)-(+)-*p*-tolyl 1-naphthyl sulfone (**147**) in a similar way. Alternatively, sulfoxide **146** was treated with iodosobenzene dichloride, ^{18}O-labeled water and pyridine to give sulfone (*S*)-(−)-**147**. In this case, intermediate **148** was thought to be formed with retention, but hydrolyzed with inversion. Thus, even though oxidation of

sulfoxides to sulfones has been observed to proceed with retention or inversion, the first step involves a retentive electrophilic addition to the lone pair on sulfur.



(*R*)-(**143**) (*S*)-(**143**) (*S*)-(**144**) (*R*)-(**145**)



(*S*)-(**146**) (*R*)-(**147**) (*R*)-(**148**)

Addition of nitrogen to the lone pair of sulfoxides or of oxygen to the lone pair of sulfilimines is quite common and leads to sulfoximines (see also Section II.G). Such reactions have been reviewed[12,13].

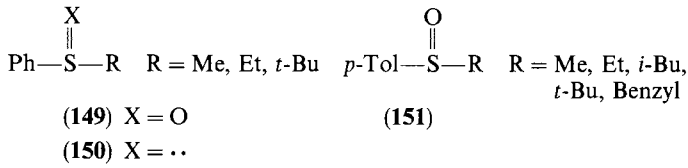
IV. CONFORMATIONAL ANALYSIS OF SULFOXIDES

The conformations of both acyclic and cyclic sulfoxides have been studied with investigations of six-membered cyclic sulfoxides being particularly prominent. Hargittai[155] has written a review, entitled 'Geometrical variations in free organic sulfur molecules', in which the conformations of simple sulfoxides in the vapor state are discussed. This review is based upon results obtained from electron diffraction and microwave spectroscopy and not X-ray crystallography. Structural data, taken from the literature into 1970 and based on various physical techniques including X-ray crystallography, are presented in Laur's review[39]. Allinger has developed a force field for sulfoxides, so molecular mechanics calculations (MM2) have now been applied to sulfoxide-containing molecules[156,157].

A. Acyclic Sulfoxides

Tai[156] applied MM2 to the ten dialkyl sulfoxides possible when the alkyl groups are restricted to methyl, ethyl, isopropyl and *t*-butyl, and calculated that only one or two conformations exist in substantial amount (> 20%) for each molecule.

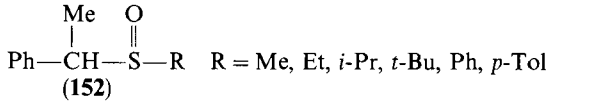
^{13}C NMR and photoelectron spectra of sulfoxides **149** and **151** were used to examine how their conformations depended on the size of the alkyl group, R[158]. In contrast to **150**, the sulfide analogs of **149**, the size of R seemed to have little influence on the conformation around the aryl–sulfur bond. That is, the methyl group of methyl phenyl sulfide preferred an orientation such that the S-methyl bond lay in the plane of the phenyl ring. As the size of R was increased from methyl to *t*-butyl, this bond was rotated out of the plane, tending toward 90°, due to interference between R and the *ortho* hydrogens. But for the corresponding sulfoxide, the S-methyl bond preferred to be roughly perpendicular to the plane, and so steric effects were not very important. Sulfoxides **149** and **151** prefer approximately the same conformations regardless of the size of R, in agreement with conclusions reached earlier by others[159].



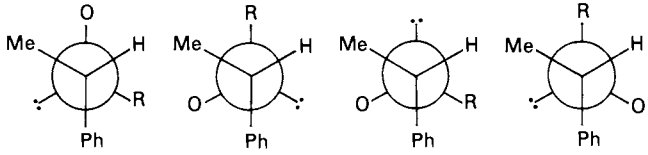
(**149**) X = O (**151**)

(**150**) X = ··

Nishio and coworkers investigated the conformations of several acyclic sulfoxides by NMR spectroscopy, largely by computer simulation of lanthanide-induced chemical shifts using $Eu(fod)_3$, but also by the use of X-ray, ORD-CD and dipole-moment studies. They concluded that for a series of alkyl 1-phenylethyl sulfoxides (**152**), the phenyl and alkyl groups preferred the *gauche* conformation with the alkyl and methyl groups *anti* (**153** and **155**). This preference was regardless of R or the configuration at sulfur. However, when R was methyl, ethyl or isopropyl, **154** and **156** also contributed substantially to the conformer populations[160].

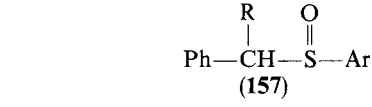


(**152**)



(**153**) (**154**) (**155**) (**156**)

Similar conclusions were reached for sulfoxides **157**. Conformation **158** was preferred for (*RS/SR*)-**157** but with some contribution from conformer **159**. The (*RR/SS*) diastereomers preferred the reverse; conformer **161** was preferred to **160**[161]. An attractive force between Ph/Ar and Ph/R was thought to be the primary factor in determining the conformational preference of sulfoxides **152** and **157**. MM2 calculations were carried out on a series of molecules of general structure PhCHR—X—R′ with X equal to CHOH, C=O, S and S=O[157]. The main conformers of these molecules have the Ph (or aryl) and R′ (alkyl) groups *gauche*. The calculations supported the existence of CH-π attractive interactions with minor contributions from other effects.

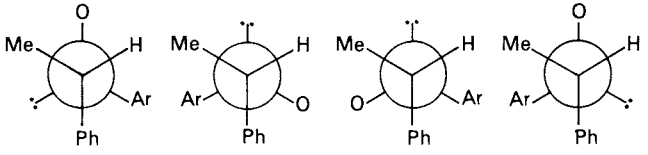


(**157**)

(**a**) R = Me, Ar = Ph

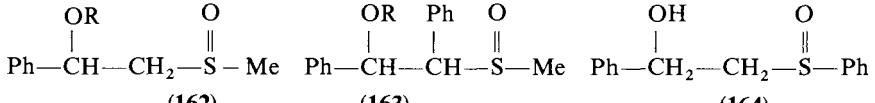
(**b**) R = Me, Ar = *p*-Tol

(**c**) R = Et, Ar = Ph



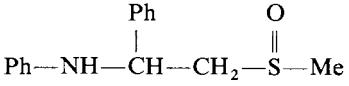
(**158**) (**159**) (**160**) (**161**)

Ruano and coworkers studied the conformational preferences of the diastereomeric sulfoxides **162** and of their O-methyl and O-acetyl derivatives by ^1H NMR and IR spectroscopy[162]. Configurational assignments made to diastereomers **162**, based on the effect of dilution and solvent polarity on the coupling constants, were later confirmed by X-ray crystallography[163]. Conformational analyses of the related diastereomeric sulfoxides **163** and of their O-menthyl and O,O-acetyl derivatives were also carried out[164]. A donor–acceptor interaction between the oxygen and the sulfur was invoked to explain the different behavior observed for the diastereomers epimeric at sulfur. Earlier assignments made to the closely related sulfoxides **164** by others were concluded to be in error. Ruano and coworkers also established the conformational preferences of the two diastereomers of **165** and their change upon protonation at nitrogen[165].



(162) **(163)** **(164)**

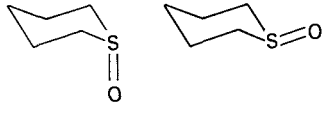
R = H, Me, OAc



(165)

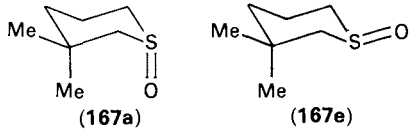
B. Cyclic Sulfoxides

The conformational energies of several mono- and dimethyl-substituted thiane-1-oxides (**166–171**) have been investigated by Barbarella and coworkers[166] using ^{13}C and ^{17}O NMR. A discussion of earlier conformational studies of thiane-1-oxides is given in this article. The ^{17}O chemical shifts for the axial oxygens were found at higher fields than the shifts observed for the equatorial oxygens. Integration of peaks obtained using low-temperature ^{13}C NMR in CD_2Cl_2 and in THF-d_8 gave the proportion of axial and equatorial S=O conformers. The spectrum of sulfoxide **166** was also determined in CD_3OD, $(CD_3)_2CO$, $CDCl_3$ and CHF_2Cl. The axial conformer, **166a**, was favored over the equatorial conformer, **166e**, by about three to one in methanol, acetone and tetrahydrofuran. In methylene chloride neither conformer was favored. In chloroform and in difluorochloromethane the equatorial conformer was favored by 55 to 45.

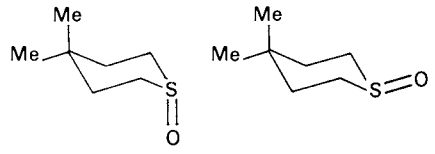


(166a) **(166e)**

Of all the solvents, THF gave the greatest amount of axial conformer for sulfoxides **166**, **167** and **168**. For **167**, the axial conformer was not detected in methylene chloride, but was present to the extent of 20% in THF. For **168**, the amount of axial conformer increased from 75 to over 95%.

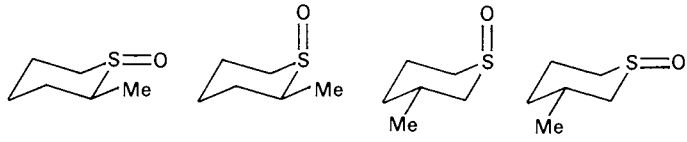


(167a) **(167e)**

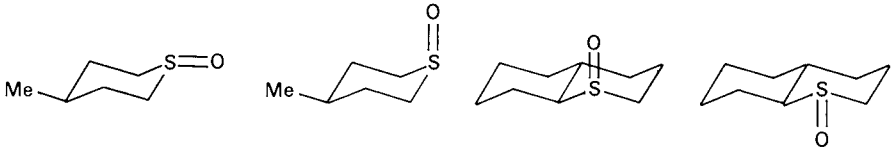


(168a) (168e)

The preference for the axial position in unhindered thiane-1-oxides has been known for some time. The spectra of the *cis* and *trans* isomers of the 2-, 3- and 4-methyl thiane-1-oxides, **169–171**, were also measured. It was concluded from the ^{13}C chemical shifts that the methyl groups preferred the equatorial positions. A comparison of the ^{17}O chemical shifts obtained for sulfoxides **169–174** with those obtained for the *cis* and *trans* sulfoxide isomers of *trans*-1-thiadecalin, **175** and **176**, was consistent with this proposal. Sulfoxide **175** with the S=O axial gave a shift about 17 ppm upfield from that of its equatorial isomer **176**. For sulfoxides **169–174**, the conformers proposed to have the S=O axial gave shifts that were upfield from those of the supposed equatorial conformers. For *trans*-3, *trans*-5-dimethylthiane-1-oxide (**177**) with the oxygen axial, the ^{17}O signal was 21 ppm upfield from the signal observed for the equatorial oxygen in *cis*-3, *cis*-5-dimethylthiane-1-oxide (**178**).



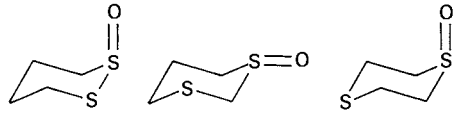
(169) (170) (171) (172)



(173) (174) (175) (176)

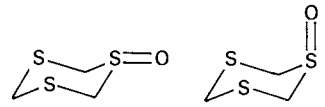
(177) (178)

The conformational preference of the monosulfoxides of 1,2-, 1,3- and 1,4-dithianes (**179–181**) were determined by NMR experiments which included variable-temperature studies, double irradiation, solvent effects and the influence of lanthanide shift reagents[167]. For **179** and **181**, the axial conformers were the dominant species in CD_3OD, but for **180**, the equatorial conformer was in excess.



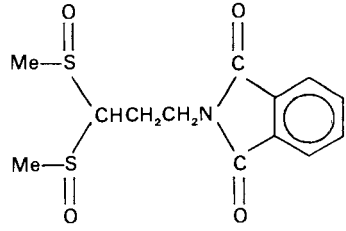
(179) (180) (181)

The conformational preference of 1,3,5-trithiane-1-oxide has been determined in solution and in the solid state[168]. ^{13}C and dynamic ^{1}H NMR studies indicated that the S=O bond is equatorial (**182**) in solution, as did molecular mechanics calculations. Surprisingly, the axial conformation (**183**) is preferred in the crystalline state.



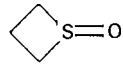
(182) (183)

Although perhaps not strictly a conformational study, the structure of the gem-disulfoxide **184** was determined by X-ray crystallography[169]. A comparison of the structural parameters so measured with ^{1}H and ^{13}C NMR chemical shifts led the authors to conclude that chemical shifts should allow configurational assignments to be made to related sulfoxides.



(184)

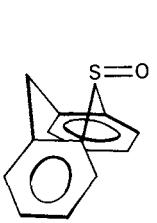
The conformation of thietane-1-oxide (**185**), determined from its ^{1}H NMR spectrum taken in a nematic solvent, was found to have the oxygen equatorial and to be strongly puckered with an angle of puckering of about 38°, in agreement with the results of a microwave study[170].



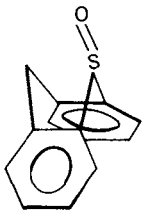
(185)

Ternay and coworkers examined the conformations of thioxanthene-10-oxide (**186**) and related compounds. They found that oxygen preferred the pseudoequatorial position, **186e**, but that the amount of pseudoaxial conformer, **186a**, increased when the oxygen was complexed with iodine monochloride or trifluoroacetic acid[171].

Barbarella and coworkers[172] have studied the conformational properties of thiolane-1-oxide (**187**), its mono- and di-methyl derivatives (**188–194**) and *trans*-2-thiahydrindane-2-oxide (**195**) using force-field calculations and ^{1}H, ^{13}C and ^{17}O NMR. They concluded that the overall conformational preference depends on the substituents and their locations

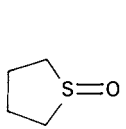


(186e)

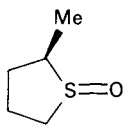


(186a)

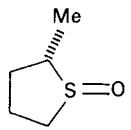
which makes conformational analysis of these rings difficult. Their force-field calculations did not support the preferred existence of an envelope conformation with sulfur at the tip and the oxygen axial.



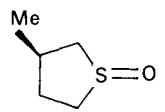
(187)



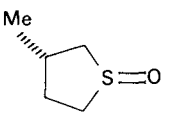
(188)



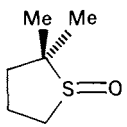
(189)



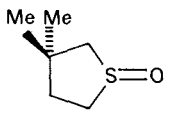
(190)



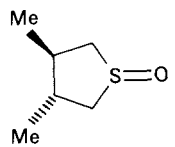
(191)



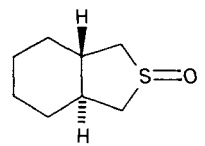
(192)



(193)



(194)



(195)

V. CHIROPTICAL PROPERTIES OF SULFOXIDES

Laur[39] has reviewed investigations of the chiroptical properties of sulfoxides carried out in the 1960s. Mikolajczyk and Drabowicz[12] briefly discuss some chiroptical properties of chiral sulfur compounds. They also list the rules, developed by Mislow and coworkers, that correlate signs of Cotton effects with absolute configurations for methyl alkyl sulfoxides, alkyl aryl sulfoxides and menthyl arenesulfinates. These rules have been extended by others. For example, the absolute configuration was assigned to the sulfoxide function in the biologically active mold metabolite sparsomycin by Ottenheijm and coworkers[173] in this way and confirmed by X-ray. The Cotton effects for some monosulfoxides of 1,3-dithianes of known absolute configuration also agreed with the predictions of Mislow[134]. The ORD and CD spectra of vinyl *p*-tolyl sulfoxide and 2-phenylethyl *p*-tolyl sulfoxide have been measured and are also in accord with Mislow's rules[74]. Ugi and coworkers investigated the ORD spectra of dimethylferrocenyl sulfoxides, e.g. **64** and **65**[96].

VI. REFERENCES

1. K. Mislow and J. Siegel, *J. Amer. Chem. Soc.*, **106**, 3319 (1984).
2. A. Nudelman, *The Chemistry of Optically Active Sulfur Compounds*, Gordon and Breach, New York, 1984.

3. A. Nudelman, *Int. J. Sulfur Chem.*, **6**, 1 (1971).
4. A. Nudelman, *Int. J. Sulfur Chem.*, **7**, 241 (1977).
5. A. Nudelman, *Phosphorus Sulfur*, **2**, 51 (1976).
6. A. Nudelman, *Phosphorus Sulfur*, **9**, 1 (1980).
7. G. Solladie, *Synthesis*, 184 (1981).
8. G. Solladie, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Vol. 2, Chap. 6, Academic Press, New York, 1983, pp. 157–199.
9. M. Cinquini, F. Cozzi and F. Montanari, in *Organic Sulfur Chemistry* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Chap. 7, Elsevier, Amsterdam, 1985, pp. 355–407.
10. M. Cinquini, *Phosphorus Sulfur*, **24**, 39 (1985).
11. G. H. Posner, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Vol. 2, Chap. 8, Academic Press, New York, 1983, pp. 225–241.
12. M. Mikolajczyk and J. Drabowicz, in *Topics in Stereochemistry* (Eds. N. Allinger, E. Eliel and S. Wilen), Vol. 13, Wiley, New York, 1982, pp. 333–468.
13. M. R. Barbachyn and C. R. Johnson, in *Asymmetric Synthesis* (Eds. J. D. Morrison and J. W. Scott), Vol. 4, Chap. 2, Academic Press, New York, 1984, pp. 227–261.
14. G. Kresze, in *Methoden der Organischen Chemie (Houben–Weyl)* (Ed. D. Klamann), Vol. E11, Georg Thieme Verlag, Stuttgart, 1985, pp. 669–886.
15. J. G. Tillet, *Chem. Rev.*, **76**, 747 (1976).
16. P. W. B. Harrison, J. Kenyon and H. Phillips, *J. Chem. Soc.*, 2079 (1926).
17. J. D. Morrison, in *Asymmetric Synthesis* (Ed. J. D. Morrison) Vol. 1, Chap. 1, Academic Press, New York, 1983, pp. 1–12.
18. M. Mikolajczyk, W. Midura, S. Grzejszczak, A. Zatorski and A. Chefczynska, *J. Org. Chem.*, **43**, 473 (1978).
19. H. J. Backer and K. J. Keuning, *Rec. Trav. Chim. Pays-Bas*, **53**, 798 (1934).
20. A. C. Cope and E. A. Caress, *J. Amer. Chem. Soc.*, **88**, 1711 (1966).
21. M. Goldman, Z. Kustanovich, S. Weinstein, A. Tishbee and E. Gil-Av, *J. Amer. Chem. Soc.*, **104**, 1093 (1982).
22. F. Toda, K. Tanaka and S. Nagamatsu, *Tetrahedron Letters*, **25**, 4929 (1984); see also patent, cited in *Chem. Abstr.*, **105**, 133347b (1986), to F. Toda and K. Tanaka, Jpn. Kokai Tokkyo Koho JP 61 36,254 [8636,254].
23. F. Toda, K. Tanaka and T. C. W. Mak, *Chem. Letters*, 2085 (1984).
24. F. Toda and K. Mori, *J. Chem. Soc., Chem. Commun.*, 1059 (1986).
25. P. Charpin, E. Dunach, H. B. Kagan and F. R. Theobald, *Tetrahedron Letters*, **27**, 2989 (1986).
26. W. H. Pirkle and J. Finn, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Vol. 1, Chap. 6, Academic Press, New York, 1983, pp. 87–124.
27. S. Allenmark, L. Nielsen and W. H. Pirkle, *Acta Chem. Scand. B*, **37**, 325 (1983).
28. A. Yamagishi, *J. Amer. Chem. Soc.*, **107**, 732 (1985).
29. M. Mikolajczyk and J. Drabowicz, *J. Amer. Chem. Soc.*, **100**, 2510 (1978).
30. J. Drabowicz and M. Mikolajczyk, in *Proceedings of the First International Symposium on Cyclodextrins* (Ed. J. Szejtli), Reidel, Dordrecht, 1982, pp. 205–215; *Chem. Abstr.*, **98**, 71128g (1983).
31. S. Yamada, M. Yamamoto and I. Chibata, *J. Org. Chem.*, **40**, 3360 (1975).
32. B. F. Bonini, P. Carisi, G. Maccagnani, G. Mazzanti, P. Zani and G. Gottarelli, *Abstracts of Papers, 12th International Symposium on the Organic Chemistry of Sulfur*, Nijmegen, The Netherlands, 29 June–4 July, 1986, p. PA 25; P. Zani, private communication.
33. J. Rabai, *Abstracts of Papers, 12th International Symposium on the Organic Chemistry of Sulfur*, Nijmegen, The Netherlands, 29 June–4 July, 1986, p. PB7.
34. H. Ohta, Y. Kato and G. Tsuchihashi, *Chem. Letters*, 217 (1986).
35. H. Phillips, *J. Chem. Soc.*, **127**, 2552 (1925).
36. H. Gilman, J. Robinson and N. H. Beaber, *J. Amer. Chem. Soc.*, **48**, 2715 (1926).
37. K. K. Andersen, *Tetrahedron Letters*, 93 (1962).
38. T. Durst, in *Comprehensive Organic Chemistry* (Ed. D. Neville Jones), Vol. 3, Part 11.6, Pergamon Press, Oxford, 1979, pp. 121–156.
39. P. H. Laur, in *Sulfur in Organic and Inorganic Chemistry* (Ed. A. Senning), Chap. 24, Dekker, New York, 1972, pp. 91–390.
40. H. F. Herbrandson and C. M. Cusano, *J. Amer. Chem. Soc.*, **83**, 2124 (1961).

41. S. I. Goldberg and M. S. Sahli, *J. Org. Chem.*, **32**, 2059 (1967).
42. O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle and G. Modena, *J. Org. Chem.*, **51**, 1457 (1986).
43. M. Buza, K. K. Andersen and M. D. Pazdon, *J. Org. Chem.*, **43**, 3827 (1978).
44. L. Field and C. D. Clark, *Org. Syntheses, Coll. Vol. IV*, 674 (1963).
45. R. E. Estep and D. F. Tavares, *Int. J. Sulfur Chem.*, **8**, 279 (1973).
46. D. N. Harpp, B. T. Friedlander, C. Larsen, K. Steliou and A. Stockton, *J. Org. Chem.*, **43**, 3481 (1978).
47. J. S. Grossert, P. K. Dubey and T. Elwood, *Can. J. Chem.*, **63**, 1263 (1985).
48. R. B. Boar and A. C. Patel, *Synthesis*, 585 (1982).
49. Y. Ueno, A. Kojima and M. Okawara, *Chem. Letters*, 2125 (1984).
50. J. -H. Youn and R. Herrmann, *Tetrahedron Letters*, **27**, 1493 (1986).
51. K. K. Andersen, in *Comprehensive Organic Chemistry* (Ed. D. Neville Jones), Vol. 3, Part 11.18, Pergamon Press, Oxford, 1979, pp. 317–329.
52. E. Wenschuh, K. Dolling, M. Mikolajczyk and J. Drabowicz, *Z. Chem.*, **20**, 122 (1980).
53. E. Krauthaussen, in *Methoden der Organischen Chemie (Houben–Weyl)* (Ed. D. Klamann), Vol. E 11, Georg Thieme Verlag, Stuttgart, 1985, pp. 614–664.
54. G. Demailly, C. Greck and G. Solladie, *Tetrahedron Letters*, **25**, 4113 (1984).
55. M. M. Green, M. Axelrod and K. Mislow, *J. Amer. Chem. Soc.*, **88**, 862 (1966).
56. D. D. Ridley and M. A. Smal, *Aust. J. Chem.*, **35**, 495 (1982).
57. M. Axelrod, P. Bickart, J. Jacobus, M. M. Green and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4835 (1968).
58. K. K. Andersen, B. Bujnicki, J. Drabowicz, M. Mikolajczyk and J. B. O'Brien, *J. Org. Chem.*, **49**, 4070 (1984).
59. K. Hiroi, R. Kitayama and S. Sato, *Synthesis*, 1040 (1983).
60. K. Hiroi and N. Matsuyama, *Chem. Letters*, 65 (1986).
61. J. Drabowicz, S. Legedz and M. Mikolajczyk, *J. Chem. Soc., Chem. Commun.*, 1670 (1985).
62. J. Drabowicz, B. Bujnicki and M. Mikolajczyk, *J. Org. Chem.*, **47**, 3325 (1982).
63. H. Kosugi, M. Kitaoka, K. Tagami and H. Uda, *Chem. Letters*, 805 (1985).
64. D. G. Farnum, T. Veysoglu, A. M. Carde, B. Duhl-Emswiler, T. A. Pancoast, T. J. Reitz and R. T. Carde, *Tetrahedron Letters*, 4009 (1977).
65. K. K. Andersen, W. Gaffield, N. E. Papanikolaou, J. W. Foley and R. I. Perkins, *J. Amer. Chem. Soc.*, **86**, 5637 (1964).
66. H. Nieuwenhuyse and R. Louw, *J. Chem. Soc., Perkin Trans. 1*, 839 (1973).
67. B. Raguse and D. D. Ridley, *Aust. J. Chem.*, **37**, 2059 (1984).
68. R. Bussas, H. Munsterer and G. Kresze, *J. Org. Chem.*, **48**, 2828 (1983).
69. N. Furukawa, T. Shibutani, K. Matsumara, H. Fujihara and S. Oae, *Tetrahedron Letters*, **27**, 3899 (1986).
70. G. H. Posner and P.-W. Tang, *J. Org. Chem.*, **43**, 4131 (1978); the rotation of **42** prepared from **19** was reported as (−) rather than as (+), the correct sign (personal communication from G. H. Posner).
71. P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4869 (1968).
72. D. H. Hua, G. Sinai-Zingde and S. Venkataraman, *J. Amer. Chem. Soc.*, **107**, 4088 (1985).
73. D. H. Hua, *J. Amer. Chem. Soc.*, **108**, 3835 (1986).
74. J. E. Mulvaney and R. A. Ottaviani, *J. Polym. Sci.*, **8**, 2293 (1970).
75. D. J. Abbott, S. Colonna and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 471 (1971).
76. D. J. Abbott, S. Colonna and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 1*, 492 (1976).
77. G. H. Posner, E. Asirvatham and S. F. Ali, *J. Chem. Soc., Chem. Commun.*, 542 (1985).
78. M. Hulce, J. P. Mallamo, L. L. Frye, T. P. Kogan and G. H. Posner, *Org. Synth.*, **64**, 196 (1986).
79. M. A. Buese and T. E. Hogen-Esch, *J. Amer. Chem. Soc.*, **107**, 4509 (1985).
80. J. P. Marino and A. D. Perez, *J. Amer. Chem. Soc.*, **106**, 7643 (1984).
81. M. Cinquini, S. Colonna, F. Cozzi and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 1*, 2061 (1976).
82. F. Schneider and R. Simon, *Synthesis*, 582 (1986).
83. G. Solladie, F. Matloubi–Moghadam, C. Luttmann and C. Mioskowski, *Helv. Chim. Acta*, **65**, 1602 (1982).

84. R. Annunziata, M. Cinquini, F. Cozzi, F. Montanari and A. Restelli, *J. Chem. Soc., Chem. Commun.*, 1138 (1983).
85. L. Banfi, L. Colombo, C. Gennari, R. Annunziata and F. Cozzi, *Synthesis*, 829 (1982).
86. R. Annunziata, M. Cinquini, F. Cozzi and A. Restelli, *J. Chem. Soc., Perkin Trans. 1*, 2293 (1985).
87. M. Cinquini, F. Cozzi and A. Gilardi, *J. Chem. Soc., Chem. Commun.*, 551 (1984).
88. R. Annunziata, M. Cinquini, F. Cozzi and A. Restelli, *J. Chem. Soc., Chem. Commun.*, 1253 (1984).
89. R. Annunziata, M. Cinquini, A. Gilardi and F. Cozzi, *Synthesis*, 1016 (1983).
90. R. Annunziata, M. Cinquini, A. Restelli and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 1183 (1982).
91. R. Annunziata, M. Cinquini, S. Colonna and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 614 (1981).
92. L. Colombo, C. Gennari and E. Narisano, *Tetrahedron Letters*, 3861 (1978).
93. N. Kunieda, J. Nokami and M. Kinoshita, *Bull. Chem. Soc. Japan*, **49**, 256 (1976).
94. R. Annunziata, M. Cinquini and F. Cozzi, *Synthesis*, 535 (1979).
95. R. Annunziata, M. Cinquini and F. Cozzi, *Synthesis*, 767 (1982).
96. R. Hermann, G. Hubener and I. Ugi, *Tetrahedron*, **41**, 941 (1985).
97. S. Colonna, R. Giovini and F. Montanari, *J. Chem. Soc., Chem. Commun.*, 865 (1968).
98. J. Jacobus and K. Mislow, *J. Chem. Soc., Chem. Commun.*, 253 (1968).
99. M. Mikolajczyk, J. Drabowicz and B. Bujnicki, *Tetrahedron Letters*, **26**, 5699 (1985).
100. C. W. Schroeck and C. R. Johnson, *J. Amer. Chem. Soc.*, **93**, 5305 (1971).
101. S. G. Pyne, *J. Org. Chem.*, **51**, 81 (1986).
102. S. W. Remiszewski, R. R. Whittle and S. W. Weinreb, *J. Org. Chem.*, **49**, 3243 (1984).
103. F. Wudl and T. B. K. Lee, *J. Amer. Chem. Soc.*, **95**, 6349 (1973).
104. K. Hiroi, S. Sato and R. Kitayama, *Chem. Letters*, 1595 (1980).
105. K. Hiroi, R. Kitayama and S. Sato, *Heterocycles*, **15**, 879 (1981).
106. K. Hiroi, S. Sato and R. Kitayama, *Chem. Pharm. Bull.*, **31**, 3471 (1983).
107. J. D. Morrison and H. S. Mosher, *Asymmetric Organic Reactions*, Chap. 8, Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1971, pp. 336–373.
108. P. Pitchen, E. Dunach, M. N. Deshmukh and H. B. Kagan, *J. Amer. Chem. Soc.*, **106**, 8188 (1984).
109. A. W. Czarnik, *J. Org. Chem.*, **49**, 924 (1984).
110. J. Drabowicz and M. Mikolajczyk, *Phosphorus Sulfur*, **21**, 245 (1984).
111. (a) F. A. Davis, J. M. Billmers, D. J. Gosciniak, J. C. Towson and R. D. Bach, *J. Org. Chem.*, **51**, 4240 (1986).
(b) F. A. Davis, J. P. McCauley, Jr. and M. E. Harakal, *J. Org. Chem.*, **49**, 1465 (1984).
(c) F. A. Davis and J. M. Billmers, *J. Org. Chem.*, **48**, 2672 (1983).
(d) F. A. Davis, R. H. Jenkins, Jr., S. B. Awad, O. D. Stringer, W. H. Watson and J. Galloy, *J. Amer. Chem. Soc.*, **104**, 5412 (1982).
112. F. A. Davis and R. H. Jenkins, Jr, in *Asymmetric Synthesis* (Eds. J. D. Morrison and J. W. Scott), Vol. 4, Chap. 4, Academic Press, New York, 1984, pp. 313–353.
113. F. A. Davis, J. P. McCauley, Jr., S. Chattopadhyay, M. E. Harakal, W. H. Watson and I. Tavanaiepour, *Abstracts of Papers, 12th International Symposium on the Organic Chemistry of Sulfur*, Nijmegen, The Netherlands, 29 June–4 July, 1986, p. L10.
114. F. Di Furia, G. Modena and R. Curci, *Tetrahedron Letters*, 4637 (1976).
115. (a) F. Di Furia, G. Modena and R. Seraglia, *Synthesis*, 325 (1984).
(b) O. Bortolini, F. Di Furia, G. Licini, G. Modena and M. Rossi, *Tetrahedron Letters*, **27**, 6257 (1986).
116. B. E. Rossiter, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Vol. 5, Chap. 7, Academic Press, New York, 1985, pp. 193–246.
117. (a) E. Dunach and H. B. Kagan, *Nouv. J. Chim.*, **9**, 1 (1985).
(b) H. B. Kagan, E. Dunach, M. Deshmukh and P. Pitchen, *Chem. Scripta*, **25**, 101 (1985).
(c) P. Pitchen and H. B. Kagan, *Tetrahedron Letters*, **25**, 1049 (1984).
118. C. Puchot, O. Samuel, E. Dunach, S. Zhao, C. Agami and H. B. Kagan, *J. Amer. Chem. Soc.*, **108**, 2353 (1986).
119. (a) H. B. Kagan, *Phosphorus Sulfur*, **27**, 127 (1986).
(b) H. B. Kagan, E. Dunach, C. Nemecek, P. Pitchen, O. Samuel and S.-H. Zhao, *Pure Appl. Chem.*, **57**, 1911 (1985).
120. C. Nemecek, E. Dunach and H. B. Kagan, *Nouv. J. Chim.*, **10**, 761 (1986).
121. A. L. J. Beckwith and D. R. Boate, *J. Chem. Soc., Chem. Commun.*, 189 (1986).
122. W. Adam and B. B. Lohray, *Angew. Chem., Int. Ed. Engl.*, **25**, 188 (1986).
123. T. Takata and W. Ando, *Tetrahedron Letters*, **27**, 1591 (1986).

124. T. Takata and W. Ando, *Bull. Chem. Soc. Japan*, **59**, 1275 (1986).
125. S. Colonna, private communication.
126. T. Sugimoto, T. Kokubo, J. Miyazaki, S. Tanimoto and M. Okano, *Bioinorg. Chem.*, **10**, 311 (1981).
127. T. Sugimoto, T. Kokubo, J. Miyazaki, S. Tanimoto and M. Okano, *J. Chem. Soc., Chem. Commun.*, 402 (1979).
128. S. Colonna, S. Banfi, R. Annunziata and L. Casella, *J. Org. Chem.*, **51**, 891 (1986).
129. S. Colonna, S. Banfi, F. Fontana and M. Sommaruga, *J. Org. Chem.*, **50**, 769 (1985).
130. A. Yamagishi, *J. Chem. Soc., Chem. Commun.*, 290 (1986).
131. T. Imamoto and H. Koto, *Chem. Letters*, 967 (1986).
132. T. Komori and T. Nonaka, *J. Amer. Chem. Soc.*, **106**, 2656 (1984).
133. T. Komori and T. Nonaka, *J. Amer. Chem. Soc.*, **105**, 5690 (1983).
134. B. J. Auret, D. R. Boyd, E. S. Cassidy, R. Hamilton, F. Taylor and A. F. Drake, *J. Chem. Soc., Perkin Trans. 1*, 1547 (1985).
135. H. L. Holland, H. Popperl, R. W. Ninniss and P. C. Chenchaiah, *Can. J. Chem.*, **63**, 1118 (1985).
136. H. Ohta, Y. Okamoto and G. Tsuchihashi, *Chem. Letters*, 205 (1984).
137. D. R. Light, D. J. Waxman and C. Walsh, *Biochemistry*, **21**, 2490 (1982).
138. T. Takata, M. Yamazaki, K. Fujimori, Y. H. Kim, T. Iyanagi and S. Oae, *Bull. Chem. Soc. Japan*, **56**, 2300 (1983).
139. A. Kjær, *Pure Appl. Chem.*, **49**, 137 (1977).
140. A. Kjær, *Tetrahedron*, **30**, 1551 (1974).
141. A. Kjær and O. Malver, *Chem. Scripta*, **20**, 42 (1982).
142. (a) S. Oae and N. Furukawa, *Sulfilimines and Related Derivatives*, Chap. 7, ACS Monograph 179, American Chemical Society, Washington, D.C., 1983, pp. 247–275.
(b) K. Kikuchi, N. Furukawa, M. Moriyama and S. Oae, *Bull. Chem. Soc. Japan*, **58**, 1934 (1985).
143. K. Akutagawa, N. Furukawa and S. Oae, *Phosphorus Sulfur*, **19**, 369 (1984).
144. M. Mikolajczyk, *Phosphorus Sulfur*, **27**, 31 (1986).
145. J. L. Kice, *Adv. Phys. Org. Chem.*, **17**, 65 (1980).
146. C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 5404 (1965).
147. S. Oae, M. Yokoyama, M. Kise and N. Furukawa, *Tetrahedron Letters*, 4131 (1968).
148. B. W. Christensen, *J. Chem. Soc., Chem. Commun.*, 597 (1971).
149. D. J. Cram, J. Day, D. R. Rayner, D. M. von Schriltz, D. J. Duchamp and D. C. Garwood, *J. Amer. Chem. Soc.*, **92**, 7369 (1970).
150. J. Drabowicz, B. Bujnicki and M. Mikolajczyk, *J. Org. Chem.*, **46**, 2788 (1981).
151. A. Schwöbel, G. Kresze and M. A. Perez, *Liebigs Ann. Chem.*, 72 (1985).
152. M. Mikolajczyk and J. Drabowicz; reported by JD at the 12th International Symposium on the Organic Chemistry of Sulfur, 29 June–4 July, 1986, Nijmegen, The Netherlands and personal communication.
153. C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963).
154. R. Annunziata, M. Cinquini and S. Colonna, *J. Chem. Soc., Perkin Trans 1*, 2057 (1972).
155. I. Hargittai, in *Organic Sulfur Chemistry* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Chap. 2, Elsevier, Amsterdam, 1985, pp. 68–132.
156. J. C. Tai, *J. Comput. Chem.*, **2**, 161 (1981).
157. M. Hirota, T. Sekiya, K. Abe, H. Tashiro, M. Karatsu, M. Nishio and E. Osawa, *Tetrahedron*, **39**, 3091 (1983).
158. M. Mohraz, W. Jian-qi, E. Heilbronner, A. Solladie-Cavallo and F. Matloubi-Moghadam, *Helv. Chim. Acta*, **64**, 97 (1981).
159. H. Bock and B. Solouki, *Chem. Ber.*, **107**, 2299 (1974).
160. Y. Kodama, S. Zushi, K. Nishihata and M. Nishio, *J. Chem. Soc., Perkin Trans. 2*, 1306 (1980).
161. K. Kobayashi, Y. Kodama, M. Nishio, T. Sugawara and H. Iwamura, *Bull. Chem. Soc. Japan*, **55**, 3560 (1982).
162. E. Brunet, J. L. Garcia Ruano, M. A. Hoyos, J. L. Rodriguez, P. Prados and F. Alcudia, *Org. Magn. Reson*, **21**, 643 (1983).
163. M. A. Hoyos, S. Martinez and S. Garcia Blanco, *Acta Cryst. C*, **39**, 118 (1983).
164. E. Brunet, J. L. Garcia Ruano, M. C. Martinez, J. H. Rodriguez and F. Alcudia, *Tetrahedron*, **40**, 2023 (1984).
165. E. Brunet, M. C. Carreno, M. T. Gallego, J. L. Garcia Ruano and F. Alcudia, *J. Chem. Soc., Perkin Trans. 2*, 937 (1983).
166. G. Barbarella, P. Dembech and V. Tugnoli, *Org. Magn. Reson.*, **22**, 402 (1984).

167. E. Juaristi, J. Guzman, V. V. Kane and R. S. Glass, *Tetrahedron*, **40**, 1477 (1984).
168. R. F. Bryan, F. A. Carey and S. M. Peckler, *J. Org. Chem.*, **45**, 5136 (1980).
169. M. Poje and E. F. Paulus, *Tetrahedron*, **38**, 3623 (1982).
170. G. Fronza, R. Mondelli and S. Bradamante, *J. Magn. Reson.*, **36**, 343 (1979).
171. A. L. Ternay, Jr., D. Craig and H. R. O'Neal, *J. Org. Chem.*, **45**, 1520 (1980).
172. G. Barbarella, S. Rossini, A. Bongini and V. Tugnoli, *Tetrahedron*, **41**, 4691 (1985).
173. H. C. J. Ottenheijm, R. M. J. Liskamp, P. Helquist, J. W. Lauher and M. S. Shekhani, *J. Amer. Chem. Soc.*, **103**, 1720 (1981).

CHAPTER 4

Thermochemistry of sulfoxides and sulfones

JOHN T. HERRON

Chemical Kinetics Division, National Bureau of Standards, Gaithersburg, MD 20899, USA

I. INTRODUCTION

This chapter is a review of the experimental data on the thermochemistry of sulfoxides and sulfones and the use of such data in developing estimation methods, deriving bond strengths, and interpreting data on the thermal stability and chemical kinetics of these species. For the purposes of this review, sulfoxides and sulfones will be taken to mean any compound containing the SO or SO_2 group. Thus, data are given for cyclic compounds containing those groups as well as for the sulfites and sulfates.

Almost all of the directly measured thermochemical data for the sulfoxides, sulfones, sulfites and sulfates are due to the work of Busfield and Mackle and their coworkers at the University of Leeds and The Queens University, Belfast[1–14]. This work involved measurement of enthalpies of combustion, fusion and vaporization. It is the basis of the subsequent compilations of Benson and coworkers[15], Cox and Pilcher[16] and Pedley, Naylor and Kirby[17]. The data given by the latter are used as the basic data set in the present work. Corrections and omissions are noted in the next section. Data on additional compounds were sought by searching the IUPAC Bulletin of Thermochemistry and Thermodynamics for the years 1980–1983[18], and by searches of Chemical Abstracts.

Other major sources of data on the thermochemistry of sulfur-containing compounds are the review by Benson[19], which is of particular value in evaluating data on radicals and other labile species, and the review of the present author on the thermochemistry of the inorganic S—O—F compounds[20].

Where no data exist, one wishes to be able to estimate thermochemical quantities. A simple and convenient method to do that is through the use of the method of group additivity developed by Benson and coworkers[15,21,22]. The earlier group values are revised here, and new group values calculated to allow extension of the method to sulfites and sulfates. In addition, a method based on the constancy of S—O bond dissociation energies is applied.

The only quantity considered here is the enthalpy of formation, $\Delta_f H^0$, at 298.15 K. Data are given in units of kJ mol^{-1}. The conversion factor 1 thermochemical calorie $\equiv$ 4.1840 joules was used.

Data on entropies and heat capacities, which are available only for dimethyl sulfoxide and dimethyl sulfone, can be found elsewhere[19].

II. THERMOCHEMICAL DATA FROM COMBUSTION AND REACTION CALORIMETRY

The thermochemical data for the sulfoxides, sulfones, sulfites and sulfates, derived from calorimetric measurements, are given in Tables 1–5. All entries in the tables were checked by examination of the original sources. Where available, data are given for the gas phase and either the liquid (lq) or solid (c) phase. Preference was given to gas and liquid phase data.

Some additions and corrections have been made. The data given here for *t*-butyl ethyl sulfoxide were not included in either Cox and Pilcher[16] or Pedley, Naylor and Kirby[17]. The latter authors give data for a compound identified as ethyl methyl sulfate (sulfuric acid ethyl methyl ester), which is identified in Cox and Pilcher[16] and in the original article[23] as

TABLE 1. Thermochemical data for sulfoxides[a]

Formula, Name(s)	$\Delta_f H^0$/kJ mol^{-1}	
	Condensed	Gaseous
C_2H_6OS, Dimethyl sulfoxide (Sulfinylbismethane)	-204.2 ± 0.7(lq)	-151.3 ± 0.8
$C_4H_{10}OS$, Diethyl sulfoxide (1, 1′-Sulfinylbisethane)	-268.0 ± 0.9(lq)	-205.6 ± 1.5
$C_5H_{10}OS$, Allyl ethyl sulfoxide [3-(Ethylsulfinyl)-1-propene]	-173.3 ± 0.8(lq)	-103.7 ± 1.9
$C_6H_{14}OS$, Dipropyl sulfoxide (1, 1′-Sulfinylbispropane)	-329.4 ± 0.9(lq)	-254.9 ± 1.5
$C_6H_{14}OS$, *t*-Butyl ethyl sulfoxide [(2-Ethylsulfinyl)-2-methylpropane]	-348.5 ± 0.8(lq)	-274.1 ± 1.6[b]
$C_{12}H_{10}OS$, Diphenyl sulfoxide (1, 1′-Sulfinylbisbenzene)	9.7 ± 1.0(c)	106.8 ± 3.1
$C_8H_{20}ON_2S$, *N*,*N*′-Thionylbis(diethylamine)	-322.2 ± 5.9(lq)[c]	-277.0 ± 7.0[d]

[a] Ref. 17, except as noted.
[b] Ref. 8.
[c] Ref. 16. The empirical formula was given as $C_4H_{10}ON_2S$.
[d] Ref. 15. From data on liquid, and an estimated enthalpy of vaporization.

TABLE 2. Thermochemical data for alkyl sulphones[a]

Formula, Name(s)	$\Delta_f H^0$/kJ mol^{-1} Condensed	Gaseous
$C_2H_6O_2S$, Dimethyl sulfone (Sulfonylbismethane)	-450.1 ± 0.7(c)	-373.1 ± 3.0
$C_3H_8O_2S$, Ethyl methyl sulfone [(Methylsulfonyl)ethane]	-486.4 ± 0.7(c)	-408.3 ± 3.0
$C_4H_6O_2S$, Divinyl sulfone (1,1′-Sulfonylbisethene)	-204.7 ± 3.5(lq)	-150.9 ± 3.6
$C_4H_8O_2S$, Allyl methyl sulfone [3-(Methylsulfonyl)-1-propene]	-385.1 ± 1.1(lq)	-305.6 ± 2.8
$C_4H_{10}O_2S$, Diethyl sulfone (1,1′-Sulfonylbisethane)	-515.5 ± 0.7(c)	-429.3 ± 2.6
$C_4H_{10}O_2S$, Isopropyl methyl sulfone [2-(Methylsulfonyl)propane]	-504.3 ± 1.2(lq)	-434.0 ± 2.8
$C_5H_{10}O_2S$, Allyl ethyl sulfone [3-(Ethylsulfonyl)-1-propene]	-406.0 ± 1.0(lq)	-322.3 ± 2.7
$C_5H_{12}O_2S$, Butyl methyl sulfone [1-(Methylsulfonyl)butane]	-535.8 ± 0.8(lq)	-459.7 ± 2.6
$C_5H_{12}O_2S$, *t*-Butyl methyl sulfone [2-(Methylsulfonyl)-2-methylpropane]	-556.0 ± 2.8(c)	-473.5 ± 3.8
$C_6H_{14}O_2S$, Dipropyl sulfone (1,1′-Sulfonylbispropane)	-548.2 ± 0.8(lq)	-468.3 ± 2.6
$C_6H_{14}O_2S$, *t*-Butyl ethyl sulfone [2-(Ethylsulfonyl)-2-methylpropane]	-578.0 ± 1.4(c)	-491.4 ± 2.8
$C_8H_{18}O_2S$, Dibutyl sulfone (1,1′-Sulfonylbisbutane)	-610.2 ± 2.0(c)	-509.8 ± 3.2
$C_8H_{18}O_2S$, Diisobutyl sulfone [1,1′-Sulfonylbis(2-methylpropane)]	-625.2 ± 0.8(lq)	-535.6 ± 2.6
$C_8H_{18}O_2S$, Di-*t*-butyl sulfone {2-[(1,1-Dimethylethyl)-sulfonyl]2-methylpropane}	-640.4 ± 2.3(c)	-546.3 ± 3.7
$C_7H_{16}O_4S_2$, 2,2-Bis(ethylsulfonyl)propane	-881.5 ± 3.8(c)	
$C_8H_{20}O_2N_2S$, *N*,*N*′-Sulfurylbis(diethylamine)	-636.6 ± 9.2(lq)[b]	-581.6 ± 10.3[c]

[a] Ref. 17, except as noted.
[b] Ref. 16. The empirical formula was given as $C_4H_{10}O_2N_2S$.
[c] Ref. 15. From data on liquid, and an estimated enthalpy of vaporization.

isopropyl hydrogen sulfate. The latter designation is used here. In the next section it will be shown, using the method of group additivity, that the compound could not be ethyl methyl sulfate, and if it is isopropyl hydrogen sulfate, the value is not reliable.

III. ESTIMATION OF THERMOCHEMICAL PROPERTIES

A. Group additivity

A powerful and readily applied method for the estimation of thermochemical properties for gas phase species is that of group additivity developed by Benson and his coworkers[15,21,22]. The method is based on the observation that the thermochemical properties of a molecule can be represented as a sum of contributions from the individual groups which make up the molecule. The method of defining groups and arriving at group

TABLE 3. Thermochemical data for aromatic sulphones[a]

Formula, Name(s)	$\Delta_f H^0$/kJ mol^{-1} Condensed	Gaseous
$C_7H_8O_2S$, Methyl phenyl sulfone [(Methylsulfonyl)benzene]	-345.4 ± 0.9(c)	-253.4 ± 3.1
$C_8H_8O_2S$, Phenyl vinyl sulfone [(Ethenylsulfonyl)benzene]	-199.3 ± 2.2(lq)	-129.0 ± 3.1
$C_8H_{10}O_2S$, Methyl *p*-tolyl sulfone [1-Methyl-4-(methylsulfonyl)benzene]	-373.1 ± 0.8(c)	-273.1 ± 3.4
$C_8H_{10}O_2S$, Benzyl methyl sulfone {[(Methylsulfonyl)methyl]benzene}	-371.2 ± 1.6(c)	-272.1 ± 3.3
$C_9H_8O_2S$, (1-Propynylsulfonyl)benzene	-52.2 ± 4.1(c)	43.2 ± 4.8
$C_9H_8O_2S$, (2-Propynylsulfonyl)benzene	-68.8 ± 2.6(c)	36.2 ± 3.6
$C_9H_8O_2S$, Allenyl phenyl sulfone [(1, 2-Propadienylsulfonyl)benzene]	-103.7 ± 5.1(c)	1.8 ± 5.6
$C_9H_{10}O_2S$, *p*-Tolyl vinyl sulfone [1-(Ethenylsulfonyl)-4-methylbenzene]	-233.5 ± 2.9(lq)	-162.3 ± 3.9
$C_{10}H_{10}O_2S$, 1-Methyl-4-(1-propynylsulfonyl)benzene	-93.2 ± 3.2(c)	10.1 ± 4.1
$C_{10}H_{10}O_2S$, 1-Methyl-4-(2-propynylsulfonyl)benzene	-106.8 ± 3.2(c)	0.7 ± 4.1
$C_{10}H_{10}O_2S$, 1-Methyl-4-(1, 2-propadienylsulfonyl)benzene	-145.6 ± 3.8(c)	-32.6 ± 4.6
$C_{10}H_{12}O_2S$, Allyl *p*-tolyl sulfone [1-Methyl-4-(2-propenylsulfonyl)benzene]	-299.1 ± 2.4(c)	-203.3 ± 3.8
$C_{10}H_{12}O_2S$, (*E*)-1-Methyl-4-(1-propenylsulfonyl)benzene	-288.4 ± 1.7(lq)	-208.9 ± 2.1
$C_{10}H_{12}O_2S$, 1-Methyl-4-(1-methylethenylsulfonyl)benzene	-285.4 ± 2.0(c)	-196.7 ± 3.2
$C_{11}H_{14}O_2S$, 1-Methyl-4-(3-butenylsulfonyl)benzene	-339.4 ± 1.4(c)	-226.0 ± 3.2
$C_{11}H_{14}O_2S$, 1-Methyl-4-(2-butenylsulfonyl)benzene	-348.3 ± 1.8(c)	-240.8 ± 3.1
$C_{11}H_{14}O_2S$, 1-Methyl-4-(1-butenylsulfonyl)benzene	-326.8 ± 0.8(lq)	-229.8 ± 2.8
$C_{11}H_{14}O_2S$, 1-Methyl-4-(2-methyl-1-propenylsulfonyl)benzene	-331.0 ± 1.4(lq)	-239.8 ± 2.8
$C_{11}H_{14}O_2S$, 1-Methyl-4-(2-methyl-2-propenylsulfonyl)benzene	-348.2 ± 1.3(c)	-241.5 ± 3.2
$C_{12}H_{10}O_2S$, Diphenyl sulfone (1, 1′-Sulfonylbisbenzene)	-225.0 ± 1.6(c)	-118.7 ± 3.3
$C_{14}H_{12}O_2S$, *trans*-Phenyl styryl sulfone [(*E*)-(2-Phenylethenyl)sulfonylbenzene]	-140.0 ± 2.9	-35.0 ± 4.8
$C_{14}H_{14}O_2S$, Di-*p*-Tolyl sulfone [1,1′-Sulfonylbis(4-methylbenzene)]	-311.3 ± 0.8	-201.7 ± 3.1
$C_{14}H_{14}O_2S$, Dibenzyl sulfone	-282.6 ± 1.2(c)	-157.1 ± 3.2
$C_{15}H_{14}O_2S$, *cis*-Styryl *p*-tolyl sulfone [(*Z*)-1-Methyl-4-(2-phenylethenyl)sulfonylbenzene]	-156.2 ± 4.3(lq)	-60.0 ± 5.1
$C_{15}H_{14}O_2S$, *trans*-Styryl *p*-tolyl sulfone [(*E*)-1-Methyl-4-(2-phenylethenyl)sulfonylbenzene]	-162.9 ± 4.7(lq)	-69.6 ± 5.3
$C_{12}H_{10}O_4S_2$, Diphenyl disulfone	-643.2 ± 1.6(c)	-481.3 ± 4.5

[a] Ref. 17.

values has been described in detail previously[15], and a 'best' set of values is given by Benson[22]. Revisions and extensions have been given for other groups such as the peroxides[24]. Benson and coworkers[15,22] provided values for groups found in sulfoxides and sulfones. These are revised and expanded here to permit estimation of the enthalpies of formation of the sulfoxides, sulfones, sulfites and sulfates. The group values were calculated using the experimentally derived enthalpy of formation data given in Tables 1–5, and the group contributions for the C—H—O compounds given in Ref. 22. The group contributions obtained here are based on a somewhat larger data base than that used by

TABLE 4. Thermochemical data for heterocyclic sulphones[a]

Formula, Name(s)	$\Delta_f H^0$/kJ mol^{-1}	
	Condensed	Gaseous
$C_3H_4O_2S$, 2*H*-Thiete 1, 1-dioxide	-208.2 ± 1.0(c)	-124.6 ± 2.7
$C_4H_6O_2S$, 2, 5-Dihydrothiophene 1, 1-dioxide	-318.9 ± 1.3(c)	-256.2 ± 2.8
$C_4H_6O_2S$, 2, 3-Dihydrothiophene 1, 1-dioxide	-323.5 ± 1.7(c)	-262.0 ± 3.1
$C_5H_8O_2S$, 2, 5-Dihydro-2-methylthiophene 1, 1-dioxide	-359.9 ± 2.0(c)	-299.2 ± 3.2
$C_5H_8O_2S$, 2, 5-Dihydro-3-methylthiophene 1, 1-dioxide	-355.9 ± 2.1(c)	-291.9 ± 3.3

[a] Ref. 17.

TABLE 5. Thermochemical data for sulfites and sulfates[a]

Formula, Name(s)	$\Delta_f H^0$/kJ mol^{-1}	
	Condensed	Gaseous
H_2SO_3, Sulfurous acid		-531.4 ± 12.6[b]
$C_2H_6O_3S$, Dimethyl sulfite (Sulfurous acid dimethyl ester)	-523.6 ± 1.1(lq)	-483.4 ± 2.0
$C_3H_8O_3S$, Ethyl methyl sulfite (Sulfurous acid ethyl methyl ester)	-567.5 ± 1.2(lq)	-524.0 ± 2.1
$C_4H_{10}O_3S$, Diethyl sulfite (Sulfurous acid diethyl ester)	-600.7 ± 0.9(lq)	-552.2 ± 1.9
$C_6H_{14}O_3S$, Dipropyl sulfite (Sulfurous acid dipropyl ester)	-646.8 ± 1.2(lq)	-588.3 ± 2.1
$C_8H_{18}O_3S$, Dibutyl sulfite (Sulfurous acid dibutyl ester)	-693.1 ± 4.0(1q)	-625.3 ± 4.4
H_2SO_4, Sulfuric acid		-735.1 ± 8.4[c]
$C_2H_6O_4S$, Dimethyl sulfate (Sulfuric acid dimethyl ester)	-735.5 ± 1.0(lq)	-687.0 ± 1.9
$C_3H_8O_4S$, Isopropyl hydrogen sulfate	-898.1 ± 1.5(lq)	-854[d]
$C_4H_{10}O_4S$, Diethyl sulfate (Sulfuric acid diethyl ester)	-813.2 ± 1.1(lq)	-756.3 ± 2.0
$C_6H_{14}O_4S$, Dipropyl sulfate (Sulfuric acid dipropyl (ester)	-859.0 ± 1.3(lq)	-792.0 ± 2.1
$C_8H_{18}O_4S$, Dibutyl sulfate (Sulfuric acid dibutyl ester)	-904.6 ± 2.6(lq)	-828.9 ± 3.1

[a] Ref. 17, except as noted.
[b] Ref. 19.
[c] Ref. 37.
[d] Ref. 16. Unreliable, see text.

Benson and coworkers[15], and the values differ somewhat. The differences probably reflect the small differences in the enthalpies of formation of the parent compounds used in the two cases (i.e., the differences between enthalpies of formation compiled by Benson and coworkers[15] and those compiled by Pedley, Naylor and Kirby[17]) as well as different approaches to deriving the group contributions. The major differences probably arise from the different values used for the relevant enthalpies of fusion and vaporization. It should be emphasized that the derivation of group contributions is not purely quantitative in nature, and that subjective elements enter into the selection of molecules to be used to

derive group contributions. The broadest possible selection of molecules for inclusion in the calculations was made here.

The group contributions are given in Table 6. The group values were used to predict the enthalpy of formation of every compound in Tables 1–5 (except for those containing nitrogen). The estimated values were then compared to the experimental values. The agreement was usually to within about 10 kJ mol^{-1}. The worst cases were for butyl methyl sulfone, *t*-butyl methyl sulfone and 1-methyl-4-(1-methylethenylsulfonyl)benzene, for which the deviations were 12.4, 14.0 and 12.3 kJ mol^{-1}, respectively. The average deviation was 4.4 kJ mol^{-1}.

Some of the group values in Table 6 are taken directly from Ref. 19, and in some cases were derived using estimated enthalpies of formation of parent compounds. The latter are less reliable than the other values in the table. Similarly, some of the group values derived here (see Section IV) are based on estimates of enthalpies of formation of parent compounds. All such numbers are enclosed in brackets to indicate their greater uncertainty.

Corrections for *gauche* configurations and *cis* isomers are given in the footnotes to Table 6. Corrections for ring structures are given in Table 8. The sources of the ring correction terms are discussed in Section IV.

To illustrate the practical application of the method, consider the molecule discussed in the previous section which was identified as either ethyl methyl sulfate or isopropyl hydrogen sulfate. Using the group contributions given in Table 6, one calculates that for ethyl methyl sulfate ($C_2H_5OSO_2OCH_3$) $\Delta_f H^0 = -718.3$ kJ mol^{-1}, and for isopropyl

TABLE 6. Group values for $\Delta_f H^{0a}$

Group	$\Delta_f H^0$/kJ mol^{-1}	Group	$\Delta_f H^0$/kJ mol^{-1}
C—(SO)(H)$_3$	−42.17[b]	C$_t$—(SO$_2$)	177.1
C—(C)(SO)(H)$_2$	−29.16	C$_B$—(SO$_2$)[b]	15.48
C—(C)$_2$(SO)(H)	[−21.3]	C$_d$—(C)(SO$_2$)	64.01
C—(C)$_3$(SO)	−9.28	C$_d$—(SO$_2$)(H)	51.7
C—(C$_d$)(SO)(H)$_2$	−27.56	SO$_2$—(C)$_2$	−288.7
C$_B$—(SO)	15.48[b]	SO$_2$—(C)(C$_d$)	−316.8
SO—(C)$_2$	−66.95	SO$_2$—(C)(C$_B$)	−289.1
SO—(C)(C$_B$)	[−72.0]	SO$_2$—(C$_d$)$_2$	−306.7
SO—(C$_B$)$_2$	−66.95	SO$_2$—(C$_d$)(C$_B$)[b]	−296.3
SO—(O)$_2$	[−213][c]	SO$_2$—(C$_t$)(C$_B$)[b]	−296.3
O—(SO)(H)	−158.6[b]	SO$_2$—(C$_B$)$_2$	−296.3
O—(C)(SO)	−92.6	SO$_2$—(C$_B$)(SO$_2$)	−325.2
C—(SO$_2$)(H)$_3$	−42.17[b]	SO$_2$—(O)$_2$	−417.3
C—(C)(SO$_2$)(H)$_2$	−32.1	O—(SO$_2$)(H)[b]	−158.6
C—(C)$_2$(SO$_2$)(H)	−18.76	O—(C)(SO$_2$)	−91.4
C—(C)$_3$(SO$_2$)	−2.1	O—(SO$_2$)$_2$	[−4][c]
C—(C$_d$)(SO$_2$)(H)$_2$	−29.49	O—(O)(SO$_2$)	[3][c]
C—(C)(C$_d$)(SO$_2$)(H)	−71.99		
C—(C$_t$)(SO$_2$)(H)$_2$	16.36		
C—(C$_B$)(SO$_2$)(H)$_2$	−29.8		

[a] This work, except as noted. Corrections for geometric isomers from Ref. 19: *cis* = 4.1; alkane *gauche* = 3.4; alkene *gauche* = 2.1. This reference also gives other correction terms and discusses their application.

[b] Certain irreducible groups are assigned values following the procedure outlined in Ref. 15. Group assignments are as follows: C—(SO$_2$)(H)$_3$ = C—(SO)(H$_3$) = C—(CO)(H)$_3$; C$_B$—(SO) = C$_B$—(SO$_2$) = C$_B$—(CO); O—(SO$_2$)(H) = O—(SO)(H) = O—(C)(H); SO$_2$—(C$_t$)(C$_B$) = SO$_2$—(C$_d$)(C$_B$) = SO$_2$—(C$_B$)$_2$.

[c] Ref. 19.

hydrogen sulfate $[(CH_3)_2CHOSO_2OH]$ $\Delta_f H^0 = -782.2\,kJ\,mol^{-1}$. These may be compared with the experimental value of $-854\,kJ\,mol^{-1}$ (based on the reported[16] enthalpy of formation for the substance in the liquid state of $-898.1\,kJ\,mol^{-1}$ and an estimated enthalpy of vaporization of $44\,kJ\,mol^{-1}$). Clearly, the experimental data do not refer to ethyl methyl sulfate. If the experimental data are for isopropyl hydrogen sulfate, however, the gross difference between the estimated and experimental data suggests that the experimental data are unreliable.

B. S—O Bond Dissociation Energies

The data of Tables 1–5 in conjunction with data for the enthalpies of formation of the relevant sulfides[17] allow us to calculate S—O bond dissociation energies (BDE) for the sulfoxides, sulfones and sulfates. These are shown in Table 7. For the C—H—O—S compounds the values are remarkably consistent for a given series. Based on the data for the hydrocarbon radical pairs listed in the table, the average bond dissociation energies are: $(R^1O)(R^2O)SO—O = 453$, $R^1R^2SO—O = 470$, and $R^1R^2S—O = 373\,kJ\,mol^{-1}$. Thus if there are data available for the sulfide or sulfone, the enthalpy of formation of the corresponding sulfoxide is readily calculated. For example, the enthalpy of formation of isopropyl methyl sulfoxide is calculated to be $-214.5\,kJ\,mol^{-1}$ using the sulfide and $-213\,kJ\,mol^{-1}$ using the sulfone. From the average value of $-213.8\,kJ\,mol^{-1}$ the group value for $C—(C)_2(SO)(H)$ is estimated to be $-21.3\,kJ\,mol^{-1}$. In the same way, the enthalpy of formation of methyl phenyl sulfoxide is estimated to be $-29.6\,kJ\,mol^{-1}$ and the group value $SO—(C)(C_B)$ is estimated to be $-72.0\,kJ\,mol^{-1}$. For ethyl methyl sulfoxide, the enthalpy of formation can be calculated from data on the sulfone, the sulfide, and by group additivity. The values so obtained are -187, -183 and $-181\,kJ\,mol^{-1}$, respectively, in good agreement. In the case of di-*t*-butyl sulfoxide, the agreement is not as good, the corresponding three values being -325, -313 and $-339\,kJ\,mol^{-1}$. Further use will be made of this method of estimating enthalpies of formation when the properties of the cyclic compounds are considered in Section IV.

The data are of little practical use in the case of the sulfite–sulfate pairs, since the available experimental data cover the identical radical pairs for both sets of compounds.

TABLE 7. S—O bond dissociation energies in sulfoxides, sulfones, sulfates and related compounds[a]

		Bond dissociation energy/kJ mol^{-1}		
R^1	R^2	$R^1R^2S—O$	$R^1R^2SO—O$	$(R^1O)(R^2O)SO—O$
H	H			453
CH_2[b]	CH_2[b]	382	477	
CH_3	CH_3	363	471	453
C_2H_5	C_2H_5	371	473	453
C_2H_5	C_3H_5	371	468	453
C_3H_7	C_3H_7	378	463	453
C_2H_5	t-C_4H_9	375	466	
C_4H_9	C_4H_9			452
Ph	Ph	374	475	
F	F	477[c]	514[c]	

[a] Calculated from data in Tables 1–5, and $\Delta_f H^0$ of atomic oxygen of $249.2\,kJ\,mol^{-1}$.
[b] For cyclo-C_2H_4S and cyclo-C_2H_4SO.
[c] Calculated from data in Ref. 20.

However, the fact that the derived S—O bond dissociation energy in sulfuric acid is identical to that found in the acid derivatives, strongly supports the estimated enthalpy of formation for gas-phase sulfurous acid given by Benson[18].

IV. ESTIMATED ENTHALPIES OF FORMATION FOR CYCLIC COMPOUNDS

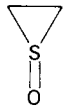
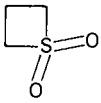
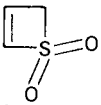
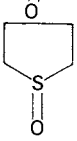
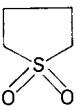
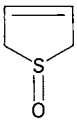
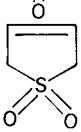
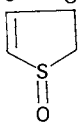
The cyclic compounds of interest here are those containing a sulfur atom as a ring constituent. The experimental data for these compounds are given in Table 4. There are two ways of estimating properties for additional compounds: by group additivity knowing the correction for the particular ring (usually equal to the ring strain energy), or by use of the S—O bond dissociation energy argument. The ring correction for the 2,5-dihydrothiophene ring can be determined from data in Table 4 on 2,5-dihydrothiophene-1,1 dioxide and 2,5-dihydro-2-methylthiophene 1,1-dioxide and group values from Table 6, to be 19.2 kJ mol^{-1}. This is very close to the ring correction term for the corresponding sulfide[18] of 20.9 kJ mol^{-1}. In the same way, the ring correction for 2*H*-thiete 1,1-dioxide is estimated to be 114.9 kJ mol^{-1}. Extending these arguments to a series of typical ring structures, leads to the estimated enthalpies of formation and derived ring correction terms given in Table 8. As expected, the ring correction terms are similar to those found for the corresponding sulfides[18], and in the absence of other data, the ring correction terms for the sulfides should be used.

V. PYROLYSIS OF SULFOXIDES AND SULFONES

The pyrolysis of sulfones and, to a lesser extent, sulfoxides is of considerable practical interest in synthetic organic chemistry[25–27]. However, there are almost no quantitative data on the kinetics of these processes. Benson[19] has reviewed the kinetics and derived bond dissociation energies for a limited number of compounds. More recently, McMillen and Golden[28] have reviewed the data on bond dissociation energies and recommended 'best' values. The most important source of data on bond energies is the work of Busfield and Ivin[1] on the pyrolysis of dimethyl, methyl allyl and methyl benzyl sulfones using the toluene carrier flow technique. Because of problems inherent in that particular technique, the data have been reinterpreted[19,28,29] to yield bond dissociation energies differing somewhat from the original values. Accepting the interpretation of McMillen and Golden[28] for the bond dissociation energies we can calculate the enthalpy of formation of the CH_3SO_2 radical as shown in the first three entries of Table 9. The average of the three values, -251 kJ mol^{-1}, can then be used in conjunction with data from Tables 2 and 3, and radical enthalpies of formation from McMillen and Golden[28], to calculate bond dissociation energies for other sulfones containing the CH_3SO_2 group. For example, as shown in Table 9, the bond dissociation energy in methyl phenyl sulfone for the process leading to the formation of $Ph + CH_3SO_2$ is calculated to be 331 kJ mol^{-1}.

The activation energy for the reaction $(PhSO_2)_2 \rightarrow 2PhSO_2$ has been reported[30] to be 172 kJ mol^{-1}, from which the enthalpy of formation of $PhSO_2$ can be calculated as shown in Table 9. This is supported by the work of Baechler and coworkers[31] on the (1,3)-allylic rearrangement in β-methylallyl phenyl sulfone in which bond cleavage was postulated to be the rate-determining step with a reported activation energy of 186 kJ mol^{-1}. Reinterpreting that work by choosing a more realistic A factor of $\log A = 15.5$ (A in units of s^{-1}), and using the reported rate constant at 423 K, the activation energy is estimated to be 169 kJ mol^{-1}. If the reaction is $PhSO_2CH_2C(CH_3)=CH_2 \rightarrow PhSO_2 + CH_2C(CH_3)=CH_2$, then using group values from Table 6 to estimate the enthalpy of formation of the sulfone, and an estimated enthalpy of formation of $CH_2C(CH_3)=CH_2$ of 126 kJ mol^{-1}, it can be estimated that $\Delta_f H^0(PhSO_2) = -164$ kJ mol^{-1}, in good agreement with the value derived from the study of the decomposition of $(PhSO_2)_2$ given in Table 9. Using an

TABLE 8. Estimated enthalpies of formation and ring correction values for cyclic sulfoxides and sulfones

Compound	$\Delta_f H^0$/kJ mol^{-1} [a]	Ring correction/kJ mol^{-1}	Selected/kJ mol^{-1}
	−42	83	83
	−263		83
	−63	82.5	83
	−284		83
	96		115
	−124.6[b]	114.9	115
	−158	8.5	8
	−379		8
	−36		19
	−256.2[b]	19.2	19
	−37		19

[a] Estimated from S=O BDE, except as noted.
[b] From Table 4.

TABLE 9. Bond energies in sulfoxides and sulfones, and enthalpies of formation of sulfinyl and sulfonyl radicals

R^1	R^2	BDE(R^1—R^2)/ kJ mol^{-1}	$\Delta_f H^0(R^1)$[a]/ kJ mol^{-1}
CH_3SO_2	CH_3	280	−241
CH_3SO_2	CH_2=$CHCH_2$	208	−262
CH_3SO_2	$PhCH_2$	221	−251
CH_3SO_2	Ph	331	[−251][b]
$C_2H_5SO_2$	C_2H_5	280	−258
$(CH_3)_2CHCH_2SO_2$	CH_3CH=CH	201	−339
$PhSO_2$	$PhSO_2$	172	−156[c]
$PhSO_2$	$CH(CH_3)CH$=CH_2	169	−164
$PhSO_2$	Ph	288	[−160][b]
$PhSO_2$	CH_3	240	[−160][b]
CH_3SO	CH_3	230	−68
CH_2SO[d]	CH_2[d]	229	
PhSO	$CD_2C(CH_3)$=CH_2	45	151

[a] Calculated from the BDE and the $\Delta_f H^0(R^2)$ taken from Ref. 28, except as noted.
[b] Value used to calculate BDE.
[c] See text.
[d] In the cyclic compound thiirane 1-oxide. See text for meaning of BDE in this case.

average value of $\Delta_f H^0(PhSO_2) = -160\,kJ\,mol^{-1}$, other bond dissociation energies for compounds containing the $PhSO_2$ group are readily calculated as shown in Table 9. Of particular interest is the bond dissociation energy in methyl phenyl sulfone for the process leading to the formation of $PhSO_2 + CH_3$, which is estimated to be $240\,kJ\,mol^{-1}$, $91\,kJ\,mol^{-1}$ less than for the process leading to the formation of $Ph + CH_3SO_2$.

The pyrolysis of allyl *sec*-butyl sulfone was studied by Myong and coworkers[32], who reported an activation energy for a free radical (bond scission) reaction of $201\,kJ\,mol^{-1}$. If the reaction is $CH_3CH{=}CHSO_2CH_2CH(CH_3)_2 \rightarrow CH_3CH{=}CH + (CH_3)_2CHCH_2SO_2$, then on the basis of an enthalpy of formation of allyl *sec*-butyl sulfone calculated using group additivity and the measured activation energy, one estimates the enthalpy of formation of the $(CH_3)_2CHCH_2SO_2$ radical given in Table 9.

In the case of the sulfoxides there are even fewer data available for use in deriving bond energies. Benson[19] has reinterpreted data on the pyrolysis of dimethyl sulfoxide[33] to estimate the bond dissociation energy for $CH_3SO{-}CH_3$ shown in Table 9. Support for that value comes from a study of the pyrolysis of thiirane 1-oxide[34], in which the activation energy for decomposition in chlorobenzene solution was found to be $146\,kJ\,mol^{-1}$. This is a measure of the C—S bond dissociation energy in the cyclic molecule. For the corresponding linear molecule, the bond dissociation energy is equal to the bond dissociation energy in the cyclic molecule plus the ring correction value (strain energy). If the latter is taken to be $83\,kJ\,mol^{-1}$ (see Table 8), we obtain a value for the bond dissociation energy of $229\,kJ\,mol^{-1}$ in agreement with the value derived from the analysis of the dimethyl sulfoxide pyrolysis (see Table 9). The bond dissociation energy for thiirane 1-oxide of $57\,kJ\,mol^{-1}$ reported by Nishitani and coworkers[35] is clearly incorrect. For any reasonable choice of a pre-exponential factor for the reaction, it would imply that the lifetime of the thiirane 1-oxide would be too short to permit the observations.

The study by Baechler and coworkers[31], cited above, also provided data on the (1,3)-allylic rearrangement in β-methylallyl phenyl sulfoxide. Using the same approach as was used in reinterpreting the sulfone data, the activation energy is estimated to be $151\,kJ\,mol^{-1}$, and $\Delta_f H^0(PhSO) = 45\,kJ\,mol^{-1}$.

Mislow and coworkers[36] studied the thermal racemization of benzyl *p*-tolyl sulfoxide, which they interpreted in terms of a bond scission mechanism. They reported an activation energy of 184 kJ mol^{-1} and a pre-exponential factor of $\log A = 18.8$ (A in units of s^{-1}). Benson[19] reinterpreted this data by choosing a more reasonable value for A of $\log A = 15.5$ and, using the rate constants, calculated an activation energy of 151 kJ mol^{-1}. From this he calculated the enthalpy of formation of PhSO. Repeating the calculations one finds that the activation energy is 158 kJ mol^{-1}. However, the reaction does not involve formation of PhSO, rather the mechanism is p-$CH_3C_6H_4SOCH_2Ph \rightarrow$ p-$CH_3C_6H_4SO + PhCH_2$. There are no thermochemical data available for the parent compound, and no radical enthalpy of formation has been derived.

VI. CONCLUSIONS

There have been no significant additions to the body of thermochemical data on the sulfoxides, sulfones, sulfites and sulfates since the work of Busfield, Mackle and coworkers in the 1960s. The uncertainty in their data is in the 4–6 kJ mol^{-1} range. The best estimation methods have uncertainties in the 6–10 kJ mol^{-1} range. The chemical kinetic data on pyrolysis reactions have an even higher degree of uncertainty, and this is clearly the area where there is the greatest need for more reliable data if the interpretation of the mechanisms of sulfoxide and sulfone pyrolysis reactions are to be put on a quantitative basis.

VII. ACKNOWLEDGEMENT

This work was supported by the Office of Standard Reference Data of the National Bureau of Standards.

VIII. REFERENCES

1. W. K. Busfield and K. J. Ivin, *Trans. Faraday Soc.*, **57**, 1044 (1961).
2. W. K. Busfield, H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 1054 (1961).
3. W. K. Busfield, K. J. Ivin, H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 1058 (1961).
4. W. K. Busfield, K. J. Ivin, H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 1064 (1961).
5. H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 1070 (1961).
6. H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 1521 (1961).
7. H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 1873 (1961).
8. H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **57**, 2119 (1961).
9. H. Mackle and P. A. G. O'Hare, *Trans. Faraday Soc.*, **60**, 506 (1964).
10. H. Mackle and D. V. McNally, *Trans. Faraday Soc.*, **65**, 1738 (1969).
11. H. Mackle and W. V. Steele, *Trans. Faraday Soc.*, **65**, 2053 (1969).
12. H. Mackle, D. V. McNally and W. V. Steele, *Trans. Faraday Soc.*, **65**, 2060 (1969).
13. H. Mackle and W. V. Steele, *Trans. Faraday Soc.*, **65**, 2069 (1969).
14. H. Mackle and W. V. Steele, *Trans. Faraday Soc.*, **65**, 2073 (1969).
15. 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).
16. J. D. Cox and G. Pilcher, *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, New York, 1970.
17. J. B. Pedley, R. D. Naylor and S. P. Kirby, *Thermochemical Data of Organic Compounds*, Chapman and Hall, New York, 1986.
18. R. M. Freeman (Ed.), *Bulletin of Chemical Thermodynamics*, IUPAC Commission on Thermodynamics, **23** (1980); **24** (1981); **25** (1982); **26** (1983), Thermochemistry, Inc., Stillwater, OK.
19. S. W. Benson, *Chem. Rev.*, **78**, 23 (1978).
20. J. T. Herron, *J. Phys. Chem. Ref. Data*, **16**, 1 (1987).
21. S. W. Benson and J. H. Buss, *J. Chem. Phys.*, **29**, 546 (1958).

22. S. W. Benson, *Thermochemical Kinetics*, Wiley, New York, 1976.
23. S. G. Entelis, G. V. Korovina and N. M. Chirkov, *Dokl. Akad. Nauk SSSR*, **134**, 856 (1960).
24. A. C. Baldwin, in *The Chemistry of Functional Groups, Peroxides* (Ed. S. Patai), Wiley, New York, 1983.
25. E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, 1978.
26. R. F. C. Brown, *Pyrolytic Methods in Organic Chemistry*, Academic Press, New York, 1980.
27. F. Vogtle and L. Rossa, *Angew. Chem., Int. Ed. Engl.*, **18**, 515 (1979).
28. D. F. McMillen and D. M. Golden, *Ann. Rev. Phys. Chem.*, **33**, 493 (1982).
29. S. W. Benson and H. E. O'Neal, *Kinetic Data on Gas Phase Unimolecular Reactions*, NSRDS-NBS 21, U.S. Government Printing Office, Washington, 1970.
30. J. L. Kice and N. E. Pawlowski, *J. Amer. Chem. Soc.*, **86**, 4898 (1964).
31. R. D. Baechler, P. Bentley, L. Deuring and S. Fisk, *Tetrahedron Letters*, **23**, 2269 (1982).
32. S. O. Myong, L. W. Linder, Jr., S. C. Seike and R. D. Little, *J. Org. Chem.*, **50**, 2244 (1985).
33. F. C. Thyrion and G. Debecker, *Int. J. Chem. Kinet.*, **5**, 583 (1973).
34. G. E. Hartzell and J. N. Paige, *J. Amer. Chem. Soc.*, **88**, 2616 (1966).
35. E. Nishitani, K. Fududa and I. Tanaka, *Bull. Chem. Soc. Japan*, **58**, 3475 (1985).
36. E. G. Miller, D. R. Rayner, H. T. Thomas and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4861 (1968).
37. M. W. Chase, Jr., C. A. Davies, J. R. Downey, Jr., D. J. Frurip, R. A. McDonald and A. N. Syverud, *JANAF Thermochemical Tables*, 3rd ed., *J. Phys. Chem. Ref. Data*, **14**, Suppl. 1 (1985).

CHAPTER 5

Detection and determination of sulphones and sulphoxides

M. R. F. ASHWORTH

Fachbereich 13.5, Universität des Saarlandes, D-6600 Saarbrucken, FRG

I. INTRODUCTION

In a contribution dealing with two related compound classes, space could be saved by treating them together in domains where they display close similarities. However, the only spheres where this applies to sulphones and sulphoxides are elemental sulphur determination and chromatography. The former is too unspecific to be considered for inclusion in this chapter. Chromatographic behaviour is determined by the whole molecule, but the widespread use of chromatographic methods does justify its treatment. At the risk of a very little duplication it has been deemed more suitable to provide separate accounts of the two compound classes.

II. SULPHONES

Most analytical work on sulphones has naturally been concerned with the compounds synthesized for special purposes, e.g. sulphonal, trional and tetronal as sedatives and hypnotics; Sulphenone (4-chlorodiphenyl sulphone) and Tedion (2,4,4′,5′-tetrachlorodiphenyl sulphone) as acaricides; 4,4′-diaminodiphenyl sulphone as an antileprotic. In choosing examples preference has been given to methods devoted to more than a single sulphone.

Some publications have described studies of sulphones together with representatives of other compound classes, such as sulphoxides, sulphides and ethers. As a rule only those are mentioned in which sulphone examples make up at least about one quarter of the total.

The following subdivision has been adopted in this section: oxidation methods; reduction methods; pyrolysis to SO_2; addition to activated double bonds; spectroscopic methods; chromatographic methods.

A. Oxidation Methods

Since the sulphone group contains sulphur in its highest oxidation state, specific analytical procedures based on controlled oxidation are not possible. The complete molecule can be submitted to oxidative degradation, e.g. in the elemental sulphur determination, methods for which, as stated above, will not be included here.

B. Reduction Methods

Reduction of sulphones to S(IV) or S(II) is more feasible but this can be accomplished by only the strongest reducing agents. For instance, neither Ti(III) nor zinc, with or without alkali, nor hydriodic acid is successful. Alkali metals are effective at high temperatures (up to 500 °C) leading to sulphide ion, as in the Lassaigne procedure for detecting sulphur in organic compounds, or the so-called Zimmermann quantitative sulphur determination.

Reduction to S(IV) is the basis of two spot tests of Feigl, although these apply to other S(VI) classes, e.g. sulphonamides. Thus Feigl and Lenzer[1] fused the sample with alkali to yield sulphite, then treating with hydrochloric acid and warming to expel sulphur dioxide; they detected the latter with nickel(II) hydroxide on test paper, which yielded ultimately the black Ni(IV) oxyhydrate (see also Section C). In the other test Feigl[2] fused the sample with sodium formate/alkali, cooled and acidified with sulphuric acid to liberate sulphur dioxide in this case also. This was detected by a ferric chloride/potassium ferricyanide reagent which yielded a blue colour (Prussian, Turnbull's).

Polarographic reduction

The polarography of sulphones has been fairly extensively studied, sometimes with an analytical bias and sometimes with more theoretical interest. It is generally accepted that a two-electron reduction takes place, to sulphinate:

$$Ar_2SO_2 + 2e + H_2O \rightarrow ArSO_2^- + ArH + OH^-$$

The two principal categories of compounds studied have been diaryl or aryl alkyl sulphones (not dialkyl sulphones, which are polarographically not reducible) and S-dioxides of certain heterocyclic compounds, such as thiophene (also benzo- and dibenzothiophenes) and phenothiazines. The first named have half-wave potentials in the region of -2.0 V, the thiophene dioxides near -1.0 V. Some examples of each category may be given.

a. Diaryl and aryl alkyl sulphones. Mairanovskii and Neiman[3] studied methyl phenyl and diphenyl sulphones also containing halogen substituents, in 50% ethanol and with tetraethylammonium iodide as supporting electrolyte. Their half-wave potentials were exceptionally low, between about -1.3 and -1.0 V. They claimed a four-electron reduction, to organic sulphide. Levin and Shestov[4] found half-wave potentials of the order of -2.0 V for diphenyl sulphone and its *p*-sulphonic acid derivative, working also in 50% ethanol and with tetraethylammonium iodide; the sulphonic acid showed a slightly lower reduction potential in water instead of the 50% ethanol, using the same electrolyte. Diphenyl sulphone, also with a dimethylamino substituent, methyl phenyl and chloromethyl phenyl sulphones were studied in 75% dioxan containing tetramethylammonium chloride by Horner and Nickel[5]; their potentials were also of the order of -2.0 V, the last-named compound also exhibiting a wave at -1.7 V, probably due to reduction of the chloro group. Shestov and Osipova[6] investigated a series of diphenyl sulphones with sulphonic acid, chloro- and methyl-substituents and also dinaphthyl sulphones, in 80% ethanol containing tetraethylammonium iodide or hydroxide as supporting electrolyte. Their half-wave potentials ranged from -1.6 to -2.28 V. Bowers and Russell[7] polarographed diaryl and methyl phenyl sulphones in 50% ethanol containing tetramethylammonium bromide. Some 26 *m*- and *p*-substituted methyl phenyl sulphones were studied polarographically by Manoušek and coworkers[8].

Differential pulse polarography in dimethyl sulphoxide–benzene(3:2) using tetrabutylammonium perchlorate as supporting electrolyte was carried out on aromatic sulphones by Cox and Przyjazny[9]. They also performed cathodic stripping voltammetry, reducing to sulphonate by controlled-potential electrolysis in dimethyl sulphoxide–water(4 + 1) at a mercury pool electrode, using the same electrolyte as above; the sulphonate was determined at a silver electrode. Recently Oelschläger and Modrack[10] determined sulphides by oxidation with hydrogen peroxide to sulphones and then carrying out polarography in 50–90% methanol with tetraethylammonium bromide or iodide or lithium chloride as electrolyte.

b. Thiophene and other heterocyclic dioxides. Smith and colleagues[11] reduced polarographically benzothiophene dioxide in 50% ethanol containing ammonium chloride and found half-wave potentials of about -1.2 V. They also investigated halogen-substituted (Cl-, Br-) derivatives, which showed an extra wave at -0.92 to -0.97 V, probably halogen reduction. Drushel and Miller[12] also investigated alkylthiophene and benzothiophene dioxides, in benzene–methanol(3:2) containing tetrabutylammonium iodide, and found half-wave potentials between -1.0 and -1.3 V. Thiophene dioxide, from oxidation of thiophene with hydrogen peroxide, was reduced polarographically by Jaworski and Bogaczek[13] in dimethylformamide (the solvent from the oxidation) and with tetrabutylammonium iodide as supporting electrolyte; the half-wave potential was -1.4 V. Jaworski and coworkers[14] polarographed benzothiophene dioxide in pyridine–acetic acid (1:1) and obtained a half-wave potential of -0.8 V. Gerdil and Lucken[15] carried out polarography in anhydrous dimethylformamide on dibenzothiophenone dioxide and thianthrene tetroxide and their methyl derivatives (also on diphenyl sulphone). The polarographic behaviour of the dioxides of phenothiazine and of benzo- and dibenzophenothiazines was studied by Kudryavtseva and colleagues[16] in ethanol containing tetramethylammonium chloride; they reported half-wave potentials in excess of -2.0 V. In dilute (3%) acetic acid, in which the phenothiazines were present as phenothiazonium salts, reduction was easier (-0.8 to -1.0 V).

Some polarographic work has been performed on sulphones in which, evidently, other functional groups suffered reduction. Thus the vinyl group rather than the sulphone group of methyl vinyl sulphone was reduced polarographically[17,18]. The unsaturated group of α,β-unsaturated sulphones was also reduced[19]. Halogen substituents have been

reduced in various polarographic studies on sulphones. Examples are chloro- and bromo-substituted thiophene dioxides[11], chloromethyl phenyl sulphone[5], chlorophenyl sulphones[6], Tedion[20], and bis(4-chlorophenyl)sulphone in the presence of 4-chlorobenzenesulphonyl chloride which was previously destroyed with tetraethylammonium hydroxide[21].

C. Pyrolysis to Sulphur Dioxide

This should be possible, especially with cyclic sulphones. Feigl and Costa Neto[22] tested for sulphones by pyrolysis and detection of the sulphur dioxide with nickel(II) hydroxide, which yielded the black nickel(IV) oxyhydrate $NiO(OH)_2$. Mashkina and Savostin[23] adapted this in a quantitative procedure for sulpholenes. They decomposed at 375 °C in a steel tube and determined the sulphur dioxide gas chromatographically on a firebrick column, impregnated with 20% dinonyl phthalate or sulpholane, at 50 °C, using hydrogen as carrier gas. Volodina and coworkers[24] likewise pyrolysed sulphones but at 700–750 °C, in a quartz tube in a current of nitrogen. This was led into a reagent of sodium tetrachloromercurate, Na_2HgCl_4, which reacted with the sulphur dioxide to give the $[Hg(SO_3)_2]^{2-}$ ion; the latter was evaluated by adding a fuchsine/formaldeyde reagent and measuring light absorbance at 560 nm after 30 min reaction time.

D. Addition to Activated —C=C— Bonds

Obtemperanskaya and Kareva[25] determined α,β-unsaturated ketones and sulphones by adding sodium sulphite to the sample in *p*-dioxan. After 5–10 min they titrated with standard sulphuric acid potentiometrically or to thymolphthalein:

$$—C{=}C—SO_2— + SO_3^{2-} + H_2O \longrightarrow —\underset{{}^{-}O_3S}{C}—\underset{H}{C}—SO_2— + OH^-$$

As mentioned in Section B, under polarography, α,β-unsaturated sulphones undergo reduction of the double bond.

E. Spectroscopic Methods

1. Infrared

The few analytical procedures based on infrared measurements have been of commercial products. Thus bis(4-chlorophenyl)sulphone, a by-product in the (former) manufacture of DDT, was determined by Downing and coworkers[26] by measurements at the stronger infrared absorption band at 1160 cm^{-1}. Tedion was determined by Gunther and colleagues[27] on and in citrus fruit by extraction with chloroform, removing interfering substances by oxidation with chromic acid (Tedion was stable) and then measuring the infrared absorption in carbon disulphide solution also at 1160 cm^{-1}. Goto and Sato[28] used Gunther's procedure for the same purpose.

2. Ultraviolet

Detection in HPLC by ultraviolet absorption is commonplace and does not merit special mention here (see Section F.1 below). There appear to be only few quantitative procedures for sulphones which are based on measurements of UV absorption. The final stage in a determination of the acaricide Sulphenone by Shuman[29] was differential measurement of the absorption at 230, 240 and 250 nm in isooctane solution. Kashiwa and

Ito[30] determined Tedion through the difference between absorption at 250 and 277 nm after thin-layer chromatographic separation and elution with methanol.

3. Mass spectrometry

Some studies have been made of the mass spectra of cyclic sulphones[31], sulphones of aromatic heterocycles[32], and benzothiazole *S*-dioxide[33]. A direct analytical application does not appear to be known.

4. X-ray emission

Yasuda and Kakiyama[34] used this method to determine sulphone residues in petroleum pitches and related materials.

F. Chromatographic Methods

1. Column, paper, liquid and thin-layer chromatography

Longenecker[35] separated aminosulphones by paper chromatography using as mobile phase benzene–cyclohexane(1:1) or benzene saturated with water; visualization was via the amino group (diazotization and coupling). O'Donnell[36] separated sulphur compounds in an asphalt sample by oxidizing to sulphones with hydrogen peroxide and then eluting from an alumina column with alcohol. TLC of sulphones (also sulphoxides, thiols and sulphides) was carried out[37] on alumina layers, impregnated with 5% dinonyl phthalate and methanol–water–pyridine(5:1:1) as mobile phase. Kashiwa and Ito[30] determined Tedion by TLC on an alumina plate with hexane–diethyl ether(9:1), ultimately eluting the spots and determining the Tedion through measurements in the ultraviolet region. Ackermann and Spranger[38] studied oxidation metabolites (sulphones and sulphoxides) of Systox-type thiophosphate esters, $(CH_3O)_2P(=O$ or $=S)—O$ (or $—S)—CH_2CH_2SCH_3$ (the last sulphur atom was oxidized); they employed silica gel G or B layers and the solvent mixture toluene–methanol–isopropanol–acetonitrile–water(40:16:16:20:9).

Fishbein and Fawkes[39] investigated the TLC of 20 aliphatic and aromatic sulphones (also sulphoxides and sulphides); they used layers of silica gel DF-5 and, as mobile phases, 2.5% acetone in benzene and toluene–ethyl acetate(1:1), testing various spray agents (in no way specific for sulphones). Tedion and Sulphenone were separated by Giacobini and Lemetre[20] in two-dimensional TLC on silica gel G-2, the mobile phases being cyclohexane–benzene–chloroform(55:5:40) and cyclohexane–ethyl acetate(95:5); they visualized with ethanolic fluorescein and concluded with polarographic determination. Sulphones from the oxidation of vacuum gas oils were separated by Drushel and Sommers[40] on a silica gel column, activated at 135 °C; after having eluted sulphur-free aromatics with benzene, the sulphones were eluted with dioxan and characterized by physical methods. Finley and Kaiser[41] separated aminosulphones and isomeric aryl sulphonamides with ethyl acetate–benzene(20:8) on silica gel or alumina thin layers containing a fluorescent indicator. In a study of the oxidation of thiols and sulphides Novitskaya and coworkers[42] separated sulphones containing hydroxyl groups on alumina layers with various mobile phases, such as chloroform, ethanol, diethyl ether, acetone, hexane, acetone–carbon tetrachloride(1:4) and acetone–hexane(1:1). Tatsumi and colleagues[43] separated dihydroxydiphenyl sulphone from phenol and benzenesulphonic acid through TLC with the mobile phase benzene–acetone(1:1), visualizing with iodine vapour.

Mital and Jain[44] investigated phenothiazine sulphones containing various substituents

(nitro-, chloro-, bromo- and methyl-groups) on silica gel G layers, using the solvent mixtures hexane–benzene(2:8), carbon tetrachloride–acetone(9:1) and carbon tetrachloride–methanol(95:5); the spots were directly visible in daylight. Gordon and Peters[45] carried out chromatography of 4,4′-diaminodiphenyl sulphone and its mono- and di-acetylated derivatives on dry silica gel in a microbore column, using anhydrous ethyl acetate; they monitored the effluent at 280 nm and related peak areas with amounts. Gordon and coworkers[46] identified and determined impurities from preparation of the anti-leprotic drug 4,4′-diaminodiphenyl sulphone (such as 4-aminodiphenyl sulphone, 2,4′-diaminodiphenyl sulphone) by extraction with 70% ethanol and ultimate HPLC on a silica-gel-packed column with a mobile phase of chloroform–carbon tetrachloride(7:3); the eluate was subsequently evaporated, taken up in dichloroethane and evaluated by fluorescence measurements at 405, 375 and 350 nm (for the two impurities mentioned and the drug itself, respectively). Oxidation products of bis(*p*-nitrophenyl) sulphide (sulphones, sulphoxides) were separated[47] by means of TLC on silica gel with the mobile phase hexane–acetone–benzene–methanol(60:36:10:1).

Ivanov and colleagues[48] controlled the synthesis of 2,7-diaminodibenzothiophene dioxide (used in the production of heat-resistant plastics) by TLC on silica gel N (activated for 10 min at 100 °C) with the mobile phase hexane–acetone–light petroleum–benzene–methanol(20:40:10:10:1). Cheung and Lim[49] also investigated contaminants in commercial 4,4′-diaminodiphenyl sulphone (e.g. the 4-amino-, 2,4′-diamino- and 4-amino-4′-chlorodiphenyl sulphones) with the aid of TLC on silica gel layers, with chloroform–diethyl ether–methanol(7:2:1). As well as employing GLC, Cox and Przyjazny[50] carried out HPLC of various organic sulphur compounds, including sulphones, on Bondapak C_{18} Corasil columns at ambient temperature and using the mobile phases methanol–water(3:2, 1:1 and 7:13); they detected the compounds through absorption in the ultraviolet and amperometrically. Singhal and coworkers[51] studied the TLC of heterocyclic sulphones on silica gel G, taking as mobile phase the upper layer of benzene–ethanol–ammonia solution(7:2:1); some diazepine derivatives were separated more efficiently with benzene–ethanol–ammonia solution(27:11:12) and benzene–chloroform(3:2).

Dinaphthyl sulphone was the sole sulphone representative in a study of organic products in tannery effluents, carried out by Thruston and McGuire[52]; after having extracted with dichloromethane they performed HPLC on Zorbax CH with a solvent gradient from hexane to dichloromethane-methanol and UV recording at 254 and 280 nm. Gidoh and colleagues[53] used HPLC to separate three anti-leprosy drugs and their principal metabolites in serum. Bis(4-aminophenyl)sulphone and its metabolites could be separated on a Bondapak C_{18} column with 20% aqueous acetonitrile and detecting at 296 nm. Besides using GLC, Udris and coworkers[54] performed TLC on silica gel–gypsum(87:13), impregnated with Rhodamine 6G as fluorescent indicator, and using the solvent mixture hexane–acetone–light petroleum–benzene–methanol–25% aqueous ammonia(100:200:50:50:5:2) to identify and determine bis(4-aminophenyl)-sulphone and separate it from the impurities 4-amino-4′-chlorodiphenyl sulphone and 4-chlorodiphenyl sulphone. Yoshii and colleagues[55] separated isomers of bis(hydroxyphenol)sulphone on Zorbax SIL with hexane–chloroform(2:3) for 21 min, then chloroform–isopropanol(99:1); the order of elution was 2,2′-, 2,3′-, 2,4′-, 3,3′-, 3,4′- and 4,4′-, detection being in the UV range at 254 and 290 nm.

2. *Gas chromatography*

Most of the examples concern substituted diphenyl sulphones, with the anti-leprotic agent 4,4′-diaminodiphenyl sulphone taking a prominent place. Cates and Meloan[56] separated aliphatic, aromatic and cyclic sulphones using helium carrier gas and thermal

conductivity detection, and tested out several columns; the best was found to be 20% Carbowax 1500 or 200-M on Gas-Chrome Z at 200 °C or 225–250 °C. Cates[57] studied mixtures of sulphones, sulphoxides and amines, also using thermal conductivity and flame ionization detectors with temperature programming. Dimethyl and tetramethylene sulphones with the corresponding sulphoxides and sulphides were investigated by Wallace and Mahon[58], who used a column of Chromosorb W, impregnated with 20% Polyethylene glycol 20 MM; the carrier gas was helium, detection with FID and the best temperatures were found to be 25–205 °C for the dimethyl compounds and 70–168 °C for the tetramethylene compounds. Kazinik[59] separated diphenyl, phenyl *p*-tolyl and di-*p*-tolyl sulphones (with the corresponding ethers and some esters also) on a 5% SKT silicone/Celite 545 column at 170 °C (for the sulphones) employing argon as carrier gas and FID. With coworkers the same author[60] separated high-boiling amines derived from diphenyl sulphone (also from biphenyl and diphenyl sulphide), likewise with argon and FID but using a Celite 545 column at 200–290 °C with 20% Apiezon L. Ob'edkova and colleagues[61] separated derivatives of diphenyl sulphone containing methyl- and chloro-substituents on a column of 1% neopentyl glycol succinate on Chromosorb W AW-DMCS at 220–240 °C; carrier gas was nitrogen with detection using FID.

Mixtures of 4,4′-diaminodiphenyl sulphone and the mono- and di-acetylated derivatives were converted by Burchfield and coworkers[62] to corresponding iodides (through diazotization and treatment with potassium iodide), which were subjected to GLC; the column was of Gas-Chrom Q containing 3% Poly-A-103 at 285 °C, carrier gas was nitrogen and detection by electron capture. Ob'edkova and colleagues[63] studied mixtures of aromatic hydrocarbons, sulphonyl chlorides and sulphones in reaction mixtures from preparation of 4,4′-dichlorodiphenyl sulphone; they employed a column of 4% SKTV-dimethylvinylsilicone on Polychrom-1, with temperature programming from 50 to 200 °C at 40°/min, nitrogen carrier gas and FID. Kochetkova and coworkers[64] determined sulphones in petroleum from waste waters; they used a column of Kromatom N-AW, impregnated with 5% Apiezon L, at 275 °C, helium carrier gas and FID. To compare with the HPLC method. Przyjazny and coworkers[65] tried GLC and obtained better separation of thiols, sulphoxides and sulphones on a temperature-programmed column of 1.5% OV-17 + 1.95% OV-20 on Chromosorb W and with flame photometric detection. Yamano and Yoshimura[66] extracted urinary metabolites, such as methyl propyl, 2-hydroxypropyl methyl and 3-hydroxypropyl methyl sulphones with ethyl acetate, carried out clean-up on a silica gel column and ultimately GLC on 1% SE-60 on Chromosorb W in nitrogen and with FID. Identification and determination of 4,4′-diaminodiphenyl sulphone (containing also 4-amino-4′-chlorodiphenyl and 4-chlorodiphenyl sulphones) was performed[54] on a column of 20% Lucoprene G-1000 on Chromaton N-AW at 280 °C, with argon carrier gas and FID.

Shakhtman and coworkers[67] carried out gas-solid chromatographic separation of *cis/trans* pairs, including 1-phenylsulphonyl-2-(phenylthio)ethene and ethyl-ω-styryl sulphone; they used a graphitized C-black column at 230 °C, nitrogen carrier gas and FID.

III. SULPHOXIDES

The sulphoxide group is more amenable to chemical analytical methods than the sulphone group. Controlled oxidation and reduction are possible:

$$R_2SO_2 \xleftarrow[\text{oxidation}]{} R_2SO \xrightarrow[\text{reduction}]{} R_2S$$

Further, sulphoxides are weak bases reacting with protons, for example:

$$R_2S{=}O + H^+ \rightleftharpoons R_2S{=}\overset{+}{O}H \leftrightarrow R_2\overset{+}{S}{-}OH$$

Some further chemical methods, mainly for detection of sulphoxides (e.g., in visualization), are based on reactions of other functional groups present in the molecule, or on the molecule as a whole.

In general, the publications cited here pertain to methods valid for several sulphoxides, even though some other compound classes may have been studied at the same time. However, many methods for dimethyl sulphoxide alone are also given on account of the considerable current importance of this compound.

A subdivision similar to that for sulphones has been adopted: oxidation methods; reduction methods; methods dependent on basic properties; complex formation with inorganic salts; spectroscopy; chromatography.

A. Oxidation Methods

Most methods of oxidation to sulphones involve classical reagents and the standard procedure has been to use a measured amount of oxidation reagent in excess and to determine the unused amount by back-titration, nearly always with iron(II).

Sub-classification is most convenient according to the reagent:

1. Dichromate

Stelmach[68] determined dimethyl sulphoxide with this reagent, quantitative reaction requiring 1 h. Savant and coworkers[69] determined dimethyl sulphoxide and diphenyl sulphoxide and also some copper sulphoxide perchlorate complexes by heating for 10–12 min with dichromate/sulphuric acid and back-titrating with ferrous ammonium sulphate. A very similar procedure was adopted by Satyanarayana Rao[70]. Moravek and Vlačil[71] tested several methods for determining aromatic sulphoxides, including the use of excess dichromate and back-titrating with ferrous ammonium sulphate.

2. Permanganate

Douglas[72] investigated heats of formation of dimethyl sulphoxide (and also of the sulphone) and proposed in a footnote that it could be determined by 5-min reaction with potassium permanganate/sulphuric acid, then adding excess iron(II) sulphate and finally titrating with permanganate. The same principle was used by Krishnan and Patel[73] to determine dimethyl sulphoxide in various complexes (with perchlorates of titanyl, zirconyl and thorium), and by Krull and Friedmann[74] to determine the same compound but using only dilute sulphuric acid and 5-min reaction.

3. Chloramine T or B

Aravamudan and Venkappayya[75] oxidized dimethyl sulphoxide in acetate buffer of pH 4 to 4.5 and with a reaction time of only 1 min. They then added potassium iodide and acid and titrated with thiosulphate the iodine liberated by unused reagent. They reported that cerium(IV) and Cr(VI) were much less effective oxidizing reagents for the sulphoxide. A very similar procedure was used by Rangaswama and Mahadevappa[76] to determine dimethyl sulphoxide and numerous other compounds with chloramine B.

4. Other oxidising agents

Böhme[77] employed excess monoperphthalic acid in diethyl ether to oxidize dibenzyl and benzyl ethyl sulphoxides. Reaction time was 24 h at -15 to $+10$ °C, after which he added potassium iodide and water and titrated the iodine set free with thiosulphate. Dickenson[78] oxidized dimethyl sulphoxide in malt, wort or beer with $Na_2S_2O_5$. In

contrast to all previously mentioned procedures, in which unused reagent was determined, the organic reaction product, dimethyl sulphide, was evaluated gas chromatographically.

B. Reduction Methods

A wider range of reagents is encountered here than with oxidation. In this case, too, the customary conclusion has been determination of unused reagent.

1. Halide ion/acid

This is evidently the most popular method of reduction depending on the reaction:

$$R_2S{=}O + 2I^-(Br^-) + 2H^+ \longrightarrow R_2S + H_2O + I_2(Br_2)$$

Thus Karaulova and Gal'pern[79] were able to detect 10 μg of dibenzyl sulphoxide through the iodine appearing with hydriodic acid reagent. Sulphoxides on paper chromatograms were visualized by Thompson and coworkers[80] using a spray of sodium iodide, hydrochloric acid and starch; colour development needed some 15 min, however. De Marco[81] likewise visualized down to 5 μg sulphoxide on paper chromatograms through the brown spots obtained with a potassium iodide/hydrochloric acid reagent. Tiberg[82] detected the —SO— group in oxidation products of ethylene thioglycollic acid with HBr in glacial acetic acid, which gave the brown bromine colour.

Some quantitative procedures may be mentioned. Larsson[83] determined 'thionyl' compounds with potassium iodide in glacial acetic acid containing more than 1% water; after 5 min the iodine set free was titrated with thiosulphate. Toennies and Kolb[84] studied methionine sulphoxide and reported that it quantitatively yielded iodine from aqueous sodium iodide/perchloric acid within 1 h; the iodine could be titrated with thiosulphate. Jančík and Körbl[85] determined some sulphoxides with a potassium iodide/hydrochloric acid reagent and 5 min reaction time. A mixture of 57% hydriodic acid and glacial acetic acid(1:20) was used by Hogeveen and Montanari[86] to determine dialkyl, diaryl and alkyl aryl sulphoxides; the reaction mixture was left in the dark in an atmosphere of hydrogen for 30–40 min (some needed longer). In both these last two procedures the final titration was with thiosulphate. Allenmark[87] modified the procedure by dissolving the sulphoxide (e.g., dimethyl, dibenzyl) in acetic acid and then adding potassium iodide and acetyl chloride. After stirring for 2–5 min hydrochloric acid was added, and then thiosulphate titration was carried out. The reaction series is evidently:

$$R_2S{=}O + CH_3COCl \longrightarrow R_2\overset{+}{S}{=}O \quad Cl^- \xrightarrow{2I^-} R_2S + CH_3COO^- + I_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad COCH_3$$

It is probable that the test of Wolski[88] for sulphoxides depends on the first reaction. He used acetyl chloride or bromide; the product from the former gave a red colour with nitrite ion, absorption maximum at 545 nm, and the latter gave a yellowish-orange colour directly. The method was used also by Besyadetskaya and colleagues[89] to determine dimethyl sulphoxide in ointments.

Hydrobromic instead of hydriodic acid has also been used in quantitative work. Thus Larsson[83] evaluated 'thionyl' compounds with a hydrobromic acid/acetic acid reagent, then adding potassium iodide and titrating with thiosulphate.

2. Titanium(III)

Barnard and Hargrave[90] reduced sulphoxides in glacial acetic acid (or *t*-butanol, or benzene) with excess titanium(III) by heating for 1 h at 80 °C. They then extracted the

sulphides with carbon tetrachloride and determined unused titanium(III) by adding excess iron(III) and titrating the iron(II) with dichromate. They also titrated the excess titanium(III) directly with iron(III) to thiocyanate indicator. Legault and Groves[91] blamed inefficient extraction of the sulphides for the low results with more polar sulphoxides; accordingly they added ammonium sulphate to the aqueous solution and extracted twice with *n*-butanol and three times with carbon tetrachloride. Gawargious[92] adapted the titanium method to the micro scale, using titanium(III) sulphate and reducing in the presence of ammonium thiocyanate and sodium acetate for 20 min at 70 °C (aromatic sulphoxides) or 1 h at 90 °C (aliphatics). He then acidified strongly, extracted sulphides with carbon tetrachloride or *n*-butanol, and finally titrated unused reducing agent with ferric alum.

3. *Tin(II)*

Glynn[93] quantitatively reduced sulphoxides by boiling for 45 min in an atmosphere of carbon dioxide with a fairly strongly acid solution of stannous chloride; unused reagent was back-titrated with ferric alum to potassium indigotrisulphonate. Anness[94] determined dimethyl sulphoxide in aqueous solution by reduction with stannous chloride on a boiling water bath, but the final stage was gas chromatographic determination of the dimethyl sulphide on 10% Triton X-305 on Chromosorb G AW DMCS at 100 °C in nitrogen carrier gas and using a sulphur-specific detector.

4. *Metal hydrides*

Okuno and coworkers[95] determined sulphoxides in petroleum fractions by reduction with lithium aluminium hydride and determining the increase in sulphide content spectrophotometrically. In work on isolation and characterization of sulphur compounds in high-boiling petroleum fractions, Drushel and Sommers[96] included a procedure for partial oxidation of sulphur compounds to sulphoxides, separating these with benzene on silica gel and then reducing them again with lithium aluminium hydride to the sulphides, which were analysed by physical methods, such as mass spectrometry, nuclear magnetic resonance, ultraviolet absorption and also thin-layer chromatography. Andreae[97] reduced dimethyl sulphoxide in aqueous solution with sodium borohydride [also with chromium(II) chloride] and ultimately determined the sulphide by gas chromatography. In one procedure, 16.5% silicone oil DC 550 on Chromosorb W AW DMCS was used, with helium gas and FID; in the other, the column was of 5% OV-3 on the same support but with flame photometric detection.

5. *Other chemical reducing agents*

A test of Safronov[98] for sulphoxides depends on reaction with a leuco compound derived from mixing an indole derivative (tryptophan), glyoxalic acid and fairly concentrated hydrochloric acid. Heating at 95 °C yielded a violet colour, turning blue within 15 min. This principle has been adapted by Vlačil and Huynh Dong Khanh[99] to determine low concentrations of dibenzyl sulphoxide. They prepared a leuco compound from L-tryptophan and *N*-dimethylaminobenzaldehyde; this yielded a coloured product, evaluated at 620 nm after 40 min at 50 °C. Turkevich and colleagues[100] identified dimethyl sulphoxide in biological fluids by heating to 70–80 °C for 5 min with benzyl alcohol-ammoniacal silver nitrate; a grey precipitate of silver, presumably due to formation of benzaldehyde by oxidation of the alcohol by sulphoxide, was the positive result.

Drushel and Sommers[96] also used zinc/hydrochloric acid and Andreae[97] chromium(II) chloride for reduction of sulphoxides.

6. Polarography

Sulphoxides (except dialkyl sulphoxides) appear to be polarographically reducible to the sulphides in a two-electron change:

$$R_2S{=}O + 2e + 2H^+ \rightarrow R_2S + H_2O$$

Bowers and Russell[7] studied the polarography of methyl phenyl and diphenyl sulphoxides in 50% ethanol using tetramethylammonium bromide as supporting electrolyte. The half-wave potential exceeded -2.0 V. They demonstrated the formation of the sulphide by physical methods, such as spectrophotometry. A linear relation between diffusion current and concentration was reported, although the authors mentioned no analytical possibility. Some heterocyclic sulphoxides (of phenothiazine and its benzo- and dibenzo-derivatives) were studied by Kudryavtseva and coworkers[16] in ethanolic tetramethylammonium chloride solution. Their reduction potentials were also about -2.0 V, but in acid solution (e.g. 3% perchloride acid), where the phenothiazines were present as salts, reduction was easier (-0.8 to -1.0 V). Porter and Beresford[101] investigated the polarography of chlorpromazine and its sulphoxide and bromo derivatives, finding a reduction wave for the sulphoxide at -0.75 V in dilute hydrochloric acid, suitable for quantitative determination. Johansson and Persson[102] made a polarographic study of 2-(5-methylbenzimidazolyl)-1-(2-pyridylethyl)sulphoxide (also of the corresponding sulphide and an *N*-oxide) in tablets extracted with ethanol. They recorded differential pulse polarograms between -0.6 and -1.4 V in 40% ethanol + phosphate buffer of pH 7.7. This enabled the sulphoxide to be determined. They quoted a four-electron reduction:

$$\begin{matrix} R{-}S{=}O \\ | \\ R' \end{matrix} + 4e + 4H^+ \rightarrow R'SH + RH + H_2O$$

where R = 1-(2-pyridylethyl) and R′ = 2-(5-methylbenzimidazolyl).

C. Methods Dependent on Basic Properties

Since the fifties publications have appeared dealing with the direct titration of sulphoxides in non-aqueous solution, mostly with perchloric acid in acetic acid. Both Streuli[103] and Wimer[104] used acetic anhydride as solvent for the sample and potentiometric end-point indication. Perchloric acid in acetic acid–acetic anhydride(1:1) was the former's reagent and he included dimethyl sulphoxide among the samples of weak bases. The latter titrated with perchloric acid in dioxan and tested aliphatic, aromatic and heterocyclic sulphoxides. Bezinger and coworkers[105] used conditions similar to those of Wimer; they dissolved less easily soluble compounds in nitromethane, dioxan or chlorobenzene, then diluting with the acetic anhydride. Karaulova and colleagues[106] employed a micro-version of Wimer's procedure to titrate sulphoxides derived from oxidation of sulphides in middle petroleum distillates (the aim of the work was sulphide determination). Data to compare with the results of infrared measurements were obtained by Štefanać and Verbić[107] using Wimer's method. After removing stronger bases in petroleum fractions on cation exchange resins, Okuno and colleagues[95] titrated weaker bases potentiometrically with perchloric acid in acetic anhydride; physical methods (IR, NMR) and reduction with lithium aluminium hydride showed that these bases were non-aromatic sulphoxides. Kolthoff and colleagues[108] performed spectrophotometric titration (*m*-cresolsulphophthalein as indicator) of weak bases (including dimethyl sulphoxide) in acetonitrile with perchloric acid. Dimethyl sulphoxide in aqueous solution was determined by Khazova and Bogomolov[109] by adding acetic anhydride and titrating potentiometrically with perchloric acid in dioxan. Puchalsky[110] determined sulphides by

oxidizing with hydrogen peroxide in glacial acetic acid to sulphoxides, then adding acetic anhydride and titrating potentiometrically with perchloric acid in acetic acid. Berčík and coworkers[111] titrated various basic compounds, including dimethyl sulphoxide, with perchloric acid in acetic anhydride, using an activated carbon electrode in the potentiometric procedure. Pačigová and Veselý[112] correlated sulphoxide concentrations from titration with perchloric acid in dioxan with those obtained from infrared measurements at 1050 cm^{-1}. Dioctyl sulphoxide was among the examples tested by Kiričenková and Švec[113], who described a semi-automatic titration device for potentiometric titration in acetic anhydride with perchloric acid in anhydrous dioxan. In their comparison of various methods for determining sulphoxides, Moravek and Vlačil[71] found that potentiometric titration with perchloric acid was the best. Thompson and coworkers[114] used the basic properties of sulphoxides in a separation method for aliphatic sulphides; they first oxidized these to sulphoxides with *t*-butyl hypochlorite and then extracted the sulphoxides formed with 80% sulphuric acid (subsequently reducing these to the sulphides again).

D. Complex Formation with Inorganic Salts

Some analytical use has been made of the tendency of sulphoxides to form complexes with inorganic salts. Thus Hucker and Hoffmann[115] determined radioactive dimethyl sulphoxide in the presence of the sulphone by first measuring the radioactivity of both in chloroform, then adding additional, inactive sulphoxide and precipitating the total sulphoxide with stannic chloride. The precipitate was centrifuged and the residual activity in the supernatant, due only to the sulphone, was measured, enabling the radioactivity and hence amount of sulphoxide to be obtained by difference. Roland and Duyckaerts[116] titrated dihexyl sulphoxide (also tributylphosphine and tributylphosphine oxide) in dry 1,2-dichloroethane with the Lewis acids stannic chloride and bromide and titanium(IV) chloride, using malachite green (C. I. Basic Green 4) or crystal violet (C. I. Basic Violet 3) as indicators. Stannic chloride was the best titrant and malachite green the preferred indicator.

A determination of dimethyl sulphoxide by Dizdar and Idjaković[117] is based on the fact that it can cause changes in the visible absorption spectra of some metal compounds, especially transition metals, in aqueous solution. In these solutions water and sulphoxide evidently compete for places in the coordination sphere of the metal ions. The authors found the effect to be largest with ammonium ferric sulphate, $(NH_4)_2SO_4 \cdot Fe_2(SO_4)_3 \cdot 12H_2O$, in dilute acid and related the observed increase in absorption at 410 nm with the concentration of dimethyl sulphoxide. Neither sulphide nor sulphone interfered. Toma and coworkers[118] described a method, which may bear a relation to this group displacement in a sphere of coordination. They reacted sulphoxides (also cyanides and carbon monoxide) with excess sodium aquapentacyanoferrate^{II} (the corresponding amminopentacyanoferrate complex was used) with which a 1:1 complex is formed. In the sulphoxide determination they then titrated spectrophotometrically with methylpyrazinium iodide, the cation of which reacts with the unused ferrate^{II} complex to give a deep blue ion combination product (absorption maximum at 658 nm).

E. Spectroscopy

1. Infrared

Barnard and colleagues[119] reported a powerful absorption band at 1040 cm^{-1} for sulphoxides, where absorption was proportional to concentration. Oba[120] utilized this wavelength for a rapid determination of the synergistic insecticide 'Sulfox-Cide', 1,2-

methylenedioxy-4-(2-octylsulphonylpropyl)benzene, in aerosols. Štefanać and Verbić[107] compared titration of sulphoxides with perchloric acid (see Section C) with their determination by infrared measurement in chloroform at 1040 cm^{-1}. Dimethyl sulphoxide in sucrose esters was determined by Zajic and Bareš[121] from infrared measurement at 1060 or 954 cm^{-1}. Snyder and coworkers[122] showed the presence of aliphatic sulphoxides in some high-boiling petroleum fractions through the infrared absorption at 1030 cm^{-1}. Okuno and colleagues[95] also regarded absorption at 1040 cm^{-1} as evidence of identification of non-aromatic sulphoxides in petroleum fractions. An approximate correlation between infrared absorption at 1050 cm^{-1} and sulphoxide content of certain viscous oil fractions was found by Pačigová and Veselý[112].

2. *Ultraviolet*

Absorption in this range is less directly related to the sulphoxide group. Haus and coworkers[123] determined the insecticide 'Sulfox-Cide' (see the preceding subsection) by measurements at 288 and 254 nm (maximum and minimum, respectively).

3. *Nuclear magnetic resonance*

An example of determination of dimethyl sulphoxide (in solutions and ointments) was given by Kram and Turczan[124]. They recorded the NMR spectra at 60 MHz of the sulphoxide in methanol + water or chloroform and integrated the peaks; the amount of sulphoxide was calculated from the ratio of its peak area to that of methanol.

4. *Fluorescence*

Tompsett[125] determined phenothiazine drugs in blood serum by extraction, oxidation with hydrogen peroxide to sulphoxide and evaluation spectrofluorimetrically.

F. Chromatography

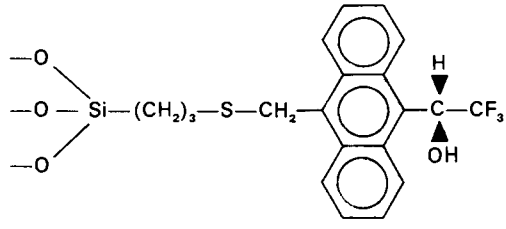
1. *Column, paper, liquid, thin-layer and ion exchange chromatography*

In a study of sulphides in petroleum distillates, Karaulova and coworkers[106] converted them to sulphoxides with hydrogen peroxide in acetic acid and adsorbed these products on silica gel from aqueous solution; they could be eluted with ethanol. Horák and Pecka[126] separated aliphatic and aromatic sulphoxides on a strongly acid cation exchanger, Dowex 50 in the H^+-form. The sample was added in benzene solution; aromatic and benzyl sulphoxides passed through and the aliphatic sulphoxides were subsequently eluted with ethanol. Ackerman and Spranger[38] separated sulphoxide metabolites of Systox-type thiophosphate esters by thin-layer chromatography on silica gel G or B, using the solvent mixture toluene–methanol–isopropanol–acetonitrile–water(40:16:16:20:9). Among various visualization reagents which they tested, potassium hexachloroplatinate was found to be the best, yielding yellow spots on a pink background. Mixtures of unsymmetrical sulphoxides were separated by Prinzler and colleagues[37] on alumina, impregnated with 5% dinonyl phthalate and using the mobile phase methanol–water–pyridine(5:1:1). Karaulova and coworkers[127] studied symmetrical and unsymmetrical aliphatic, aromatic and heterocyclic sulphoxides on alumina layers with the solvent mixture acetone–carbon tetrachloride(1:4), visualizing with iodine vapour. Thin-layer chromatography of sulphoxides (also sulphones and sulphides) was carried out by Fishbein and Fawkes[39] on silica gel DF-5 with the mobile phase benzene–acetone(40:1) or toluene–ethyl acetate(1:1); they also tested numerous spray reagents, the

best of which were tetracyanoethylene and 2, 3-dichloro-5, 6-dicyano-1, 4-benzoquinone, both followed by exposure to ammonia vapour.

Prinzler and Tauchmann[128] performed TLC of some aliphatic sulphoxides on alumina layers, using benzene–methanol(9:1) (a study of the effect of layer humidity). Prinzler and coworkers[129] also studied dialkyl, methyl alkyl, ethyl alkyl and alkyl phenyl sulphoxides on alumina, also in reversed phase systems with dinonyl phthalate impregnation. The solvents used were benzene–pyridine(20:1) or dioxan or, in the reversed-phase system, methanol–water–pyridine(5:1:1) as used in the work mentioned above. Sulphoxides were obtained from high-boiling petroleum fractions by Drushel and Sommers[96] by applying a benzene solution to a silica gel column, eluting the hydrocarbons with further benzene and finally the sulphoxides with benzene-methanol. Krull and Friedmann[74] separated dimethyl sulphoxide from amino acids and other acids on, respectively, Dowex 50-X8 in the H^+-form and Dowex 1-X8 in the carbonate form; the sulphoxide was eluted first. Higher-boiling petroleum fractions (b.p. 250–500 °C) were passed through Duolite C-10 cation exchange resin by Okuno and colleagues[95]; this retained bases, including sulphoxides, which were obtained by successive elution with n-pentane, benzene-methanol and 10% diisopropylamine in methanol (the nitrogen bases were retained on the column). Novitskaya and coworkers[42] separated sulphoxides (also sulphones) from the oxidation of thiols and sulphides by using TLC on alumina and various mobile phases (chloroform, ethanol, diethyl ether, acetone, hexane, carbon tetrachloride–acetone(4:1), hexane–acetone(1:1)).

Popova and colleagues[47] carried out TLC of oxidation products of 4, 4′-dinitrodiphenyl sulphide (the sulphoxide and sulphone) on silica gel + a fluorescent indicator, using hexane–acetone–benzene–methanol(60:36:10:1) as solvent mixture. Morris[130] performed GLC and TLC of dimethyl sulphoxide. For the latter, he applied a 6% solution of the sample in methanol to silica gel and developed with methanol–ammonia solution(200:3), visualizing with 2% aqueous Co^{II} thiocyanate–methanol(2:1). HPLC separations of chiral mixtures of sulphoxides have been carried out. Thus Pirkle and coworkers[131,132] reported separations of alkyl 2, 4-dinitrophenyl sulphoxides and some others on a silica-gel (Porosil)-bonded chiral fluoroalcoholic stationary phase, with the structure:



The solvent used was hexane–isopropanol(4:1). Later, Allenmark and colleagues[133] obtained enantioselective HPLC retention of a series of alkyl carboxymethyl sulphoxides (and other sulphoxides and classes) on a column of (*R*)-*N*-(3, 5-dinitrobenzoyl)phenylglycine covalently bound via an amide bond (CSP 1), or ionically bound (CSP 2), to 3-aminopropylsilica; the mobile phase was again hexane–isopropanol(4:1, or, also 19:1) and determination carried out at 254 or 280 nm. The sulphoxides were better resolved on CSP 2.

2. *Gas chromatography*

Cates and Meloan[56] separated aliphatic and aromatic sulphoxides on Carbowax 20M

or 1500 on Chromosorb Z or silanised diatomaceous earth at 200–250 °C; helium was the carrier gas and detection by thermal conductivity. Cates[57] studied the GC separation of sulphoxides, sulphones and amines with detection through thermal conductivity or flame ionisation and temperature programming. Reaction mixtures of thiols and sulphoxides (in a kinetic study) were analysed using GLC by Wallace and Mahon[134], on Chromosorb W impregnated with 20% Carbowax 20 MM; helium carrier gas and FID were employed. The same authors[58] reported GLC of dimethyl (at 25 to 205 °C) and tetramethylene sulphoxides (at 70 to 168 °C) in the presence of the corresponding sulphides and sulphones, also on Chromosorb W carrying Carbowax 20 MM. As before, helium was the carrier gas and detection by FID. Paulin and coworkers[135] determined dimethyl sulphoxide in plasma and cerebrospinal fluid by GLC on a column of 20% Carbowax 20 M on Chromosorb P at 160 °C, with hydrogen, helium or air as carrier gas and FID. Dimethyl sulphoxide in butanol was determined by Stuart [136] in a temperature-programmed (100 to 150 °C) column of 20% Carbowax 20M–SE 20(1:4) on Teflon 6 + Chromosorb P(1:1); here, too, helium gas and FID were employed. Variali[137] determined dimethyl sulphoxide in benzene or toluene by GLC on 20% Carbowax 20M–SE 20(1:4) on silanized Chromosorb P–Chromosorb T(1:1), or on glass beads–Chromosorb T(1:1), the beads coated with 0.2% Carbowax 20 M–SE 20(2:3) and the Chromosorb T with 10% of this same mixture; this column gave less tailing. Seager and Stone[138] determined dimethyl sulphoxide in aqueous solution by GSC on Porapak T at 190 °C in a stainless steel column, using helium gas and FID or thermal conductivity detection.

Impurities in dimethyl sulphone (which included the sulphoxide) were determined by Kazinik and coworkers[139] on a column of 20% poly(butanediol adipate) and 4% phosphoric acid on Celite 545 at 170 °C; carrier gas was argon and FID detection. Awwad and Sarkissian[140] determined dimethyl sulphoxide in mixtures with benzene, toluene and xylenes in an extract from Iraq Powerformate on a column of 7.5% SE-30 + 0.5% Carbowax 20 M on Chromosorb W; the temperature was programmed from 90 to 140 °C at 20°/min, carrier gas was nitrogen, and FID. Dimethyl sulphoxide in the presence of dimethyl sulphate was determined[141] by GLC on 15% PEGS on Chromosorb W, using heat conductivity detection. Foul-smelling sulphur compounds emitted by Kraft pulp mills, and including dimethyl sulphoxide, were subjected by Pszonka[142] to GLC on 20% tritolyl phosphate on Gas-Chrom Q; deactigel separated the compounds also but results were poorly reproducible. Kimura and coworkers[143] separated metabolites of *p*-dichlorobenzene in rats (including 2, 5-dichlorodiphenyl sulphoxide) by subjecting tissue extracts to GLC on a Chromosorb W AW DMCS column, impregnated with 5% DEGS and at 170 °C; carrier gas was nitrogen and detection by electron capture.

Turkevich and coworkers[144] determined dimethyl sulphoxide in aqueous solution by GLC on 15% Carbowax 20 M on Chromosorb N AW-DMCS at 180 °C; nitrogen and FID were used, and diethyl sulphoxide as internal standard. Ogata and Fujii[145] determined urinary dimethyl sulphoxide (and sulphone) by extracting with chloroform and then performing GLC on temperature-programmed (80 to 200 °C at 10°/min) Shimalite W impregnated with 5% polyoxymethylene glycol 20 M; dimethyl sulphide served as internal standard. In the GLC determination of dimethyl sulphoxide by Morris[130], 3% OV-1 on Gas-Chrom Q at 60 °C was used, with dual FID and nitrogen carrier gas; an internal standard of 2% toluene in methanol was used. Dimethyl sulphoxide in serum and other body fluids was determined by Garretson and Aitchison[146] in a final GLC stage on a silanised glass column of 20% Carbowax 20 M on Supelcoport, temperature programmed from 155 to 170 °C at 30°/min; FID and nitrogen were used. Makovskaya and colleagues[147] determined dimethyl sulphoxide in solutions from production of some types of fibre; they used a column of Chromaton N-AW, coated with 15% Apiezon L, at 150 °C, argon carrier gas and FID.

IV. REFERENCES

1. F. Feigl and A. Lenzer, *Mikrochim. Acta*, **1**, 129 (1937).
2. F. Feigl, in *Spot Tests in Organic Analysis*, Elsevier, London, 1966, p. 85.
3. S. G. Mairanovskii and M. B. Neiman, *Dokl. Akad. Nauk SSSR*, **87**, 805 (1952).
4. E. S. Levin and A. P. Shestov, *Dokl. Akad. Nauk SSSR*, **96**, 999 (1954).
5. L. Horner and H. Nickel, *Chem. Ber.*, **89**, 1681 (1956).
6. A. P. Shestov and N. A. Osipova, *Zh. Obshch. Khim.*, **27**, 2790 (1957).
7. R. C. Bowers and H. D. Russell, *Anal. Chem.*, **32**, 405 (1960).
8. O. Manoušek, O. Exner and P. Zuman, *Collect. Czech. Chem. Commun.*, **33**, 3988 (1968).
9. J. A. Cox and A. Przyjazny, *Anal. Lett.*, **10**, 1131 (1977).
10. H. Oelschläger and G. Modrack, *Arch. Pharm.*, **318**, 431 (1985).
11. C. P. Smith, H. G. Sprague and O. C. Elmer, *Anal. Chem.*, **25**, 793 (1953).
12. H. V. Drushel and J. F. Miller, *Anal. Chem.*, **30**, 1271 (1958).
13. M. Jaworski and J. Bogaczek, *Chem. Anal. (Warsaw)*, **9**, 231 (1964).
14. M. Jaworski, J. Bogaczek and J. Dziekan, *Chem. Anal. (Warsaw)*, **10**, 1291 (1965).
15. R. Gerdil and E. A. X. Lucken, *Mol. Phys.*, **9**, 529 (1965).
16. N. A. Kudryavtseva, Z. V. Pushkareva and V. F. Gryazev, *Zh. Obshch. Khim.*, **35**, 14 (1965).
17. C. W. Johnson, C. G. Overberger and W. J. Seagers, *J. Amer. Chem. Soc.*, **75**, 1495 (1953).
18. A. A. Pozdeeva, S. G. Mairanovskii and L. K. Gladkova, *Elektrokhimiya*, **3**, 1127 (1967).
19. B. A. Arbuzov and E. A. Berdnikov, *Dokl. Akad. Nauk SSSR*, **171**, 860 (1966).
20. V. Giacobini and G. Lemetre, *Chim. Ind. (Milan)*, **48**, 479 (1966).
21. M. M. Filimonova, V. E. Gorbunova and V. F. Durneva, *Zh. Anal. Khim.*, **33**, 1829 (1978).
22. F. Feigl and Costa Neto, in *Spot Tests in Organic Analysis*, Elsevier, London, 1966, p. 229.
23. A. V. Mashkina and Yu. A. Savostin, *Neftekhimiya*, **5**, 760 (1965).
24. M. A. Volodina, M. Abdukarimova, T. A. Gorshkova, V. G. Borodina and V. N. Zhardetskaya, *Vestn. Mosk. Univ. Khim.*, **23**, 114 (1968).
25. S. I. Obtemperanskaya and G. P. Kareva, *Vestn. Mosk. Univ. Khim.*, **15**, 121 (1974).
26. J. R. Downing, W. V. Freed, I. F. Walker and G. D. Patterson, *Ind. Eng. Chem., Anal. Ed.*, **18**, 464 (1946).
27. F. A. Gunther, R. C. Blinn and J. H. Barkley, *J. Agr. Food Chem.*, 7, 104 (1959).
28. S. Goto and R. Sato, *Bunseki Kagaku*, **12**, 238 (1963).
29. H. Shuman, *J. Assoc. Offic. Agr. Chemists*, **40**, 274 (1957).
30. T. Kashiwa and F. Ito, *Bunseki Kagaku*, **14**, 1019 (1965).
31. D. S. Weinberg, C. Stafford and M. W. Scoggins, *Tetrahedron*, **24**, 5409 (1968).
32. J. Heiss, K.-P. Zeller and B. Zech, *Tetrahedron*, **24**, 3255 (1968).
33. H. Hettler, H. M. Schiebel and H. Budzikiewicz, *Org. Mass Spectrom.*, **2**, 1117 (1969).
34. S. Yasuda and H. Kakiyama, *Bunseki Kagaku*, **29**, 447 (1980).
35. W. H. Longenecker, *Anal. Chem.*, **21**, 1402 (1949).
36. G. O'Donnell, *Anal. Chem.*, **23**, 894 (1951).
37. H. Prinzler, D. Pape, H. Tauchmann, M. Teppke and C. Tzscharnke, *Ropa Uhlie*, **8**, 13 (1960).
38. H. Ackermann and D. Spranger, *J. Chromatogr.*, **17**, 608 (1965).
39. L. Fishbein and J. Fawkes, *J. Chromatogr.*, **22**, 323 (1966).
40. H. V. Drushel and A. L. Sommers, *Anal. Chem.*, **39**, 1819 (1967).
41. T. K. Finley and R. S. Kaiser, *J. Chromatogr.*, **39**, 195 (1969).
42. N. N. Novitskaya, L. E. Zhuravieva and L. P. Ivanova, *Zh. Anal. Khim.*, **24**, 470 (1969).
43. T. Tatsumi, H. Ishiwatari and S. Sakurai, *Kinzoku Hyomen Gijutsu*, **20**, 591 (1969).
44. R. L. Mital and S. K. Jain, *J. Chromatogr.*, **47**, 546 (1970).
45. G. R. Gordon and J. H. Peters, *J. Chromatogr.*, **47**, 269 (1970).
46. G. R. Gordon, D. C. Ghoul and J. H. Peters, *J. Pharm. Sci.*, **64**, 1205 (1975).
47. A. G. Popova, A. V. Ivanov and Z. A. Lerman, *Zh. Anal. Khim.*, **31**, 408 (1976).
48. A. V. Ivanov, A. G. Popova and N. A. Lakomova, *Zh. Anal. Khim.*, **31**, 404 (1976).
49. A. P. Cheung and P. Lim, *J. Pharm. Sci.*, **66**, 1723 (1977).
50. J. A. Cox and A. Przyjazny, *Anal. Lett.*, **10**, 869 (1977).
51. R. K. Singhal, S. Kumar, R. Grover and B. C. Joshi, *Acta Cienc. Indica*, **4**, 122 (1978).
52. A. D. Thruston, jr. and J. M. McGuire, *Biomed. Mass Spectrom.*, **8**, 47 (1981).
53. M. Gidoh, S. Tsutsumi and S. Takitani, *J. Chromatogr.*, **223**, 379 (1981).

54. N. V. Udris, V. P. Morazova, A. Sh. Glaz, Yu. D. Grudtsun, N. A. Lakomova, V. F. Boronin and D. A. Novokhatka, *Zh. Anal. Khim.*, **38**, 306 (1983).
55. Y. Yoshii, T. Hirashima and O. Manabe, *Bunseki Kagaku*, **32**, 87 (1983).
56. V. E. Cates and C. E. Meloan, *J. Chromatogr.*, **11**, 472 (1963).
57. V. E. Cates, *Diss. Abstr.*, **24**, 49 (1963).
58. T. J. Wallace and J. J. Mahon, *Nature (London)*, **201**, 817 (1964).
59. E. M. Kazinik, *Zh. Anal. Khim.*, **25**, 2054 (1970).
60. E. M. Kazinik, G. A. Gudkova, L. Ya. Mesh, T. A. Shcheglova and A. V. Ivanov, *Zh. Anal. Khim.*, **26**, 1920 (1971).
61. L. V. Ob'edkova, Yu. A. Moskvichev and G. S. Mironov, *Zh. Anal. Khim.*, **28**, 1425 (1973).
62. H. P. Burchfield, E. E. Storrs, R. J. Wheeler, V. K. Bhat and L. L. Green, *Anal. Chem.*, **45**, 916 (1973).
63. L. V. Ob'edkova, Yu. A. Moskvichev, G. S. Mironov and I. M. Rubleva, *Zh. Anal. Khim.*, **31**, 201 (1976).
64. R. P. Kochetkova, S. A. Eppel, R. I. Sidorov and G. P. Kolisnyk, *Khim. Tekhnol. Topl. Masel*, 48 (1976).
65. A. Przyjazny, R. Staszewski and J. A. Cox, *Chem. Anal. (Warsaw)*, **26**, 147 (1981).
66. S. Yamano and H. Yoshimura, *J. Pharmacobio-Dyn.*, **5**, 97 (1982).
67. R. I. Shakhtman, B. A. Rudenko, E. N. Prilezhaeva and V. A. Krongauz, *J. Chromatogr.*, **104**, 409 (1975).
68. K. Stelmach, *Chem. Anal. (Warsaw)*, **11**, 627 (1966).
69. V. V. Savant, J. Gopalakrishnan and C. C. Patel, *Z. Anal. Chem.*, **238**, 273 (1968).
70. V. R. Satyanarayana Rao, *Current Sci.*, **38**, 385 (1969).
71. J. Moravek and F. Vlačil, *Chem. Listy*, **73**, 750 (1979).
72. T. B. Douglas, *J. Amer. Chem. Soc.*, **68**, 1072 (1946).
73. V. Krishnan and C. C. Patel, *J. Inorg. Nucl. Chem.*, **26**, 2201 (1964).
74. L. H. Krull and M. Friedmann, *J. Chromatogr.*, **26**, 336 (1967).
75. G. Aravamudan and D. Venkappayya, *Talanta*, **15**, 704 (1968).
76. Y. H. S. Rangaswama and D. S. Mahadevappa, *Indian J. Chem., Sect. A*, **17**, 602 (1979).
77. H. Böhme, *Chem. Ber.*, **70**, 379 (1937).
78. C. J. Dickenson, *J. Inst. Brewing (London)*, **87**, 16 (1981).
79. E. N. Karaulova and G. D. Gal'pern, *Zh. Obshch. Khim.*, **29**, 3033 (1959).
80. J. F. Thompson, W. N. Arnold and C. J. Morris, *Nature (London)*, **197**, 380 (1963).
81. C. De Marco, *Nature (London)*, **198**, 683 (1963).
82 Å. Tiberg, *Chem. Ber.*, **49**, 2024 (1916).
83. E. Larsson, *Svensk Kem. Tidskr.*, **49**, 264 (1937).
84. G. Toennies and J. J. Kolb, *J. Biol. Chem.*, **128**, 399 (1939).
85. F. Jančík and J. Körbl, *Česk. Farm.*, **11**, 305 (1962).
86. H. Hogeveen and F. Montanari, *Gazz. Chim. Ital.*, **94**, 176 (1964).
87. S. Allenmark, *Acta Chem. Scand.*, **20**, 910 (1966).
88. T. Wolski, *Chem. Anal. (Warsaw)*, **14**, 1319 (1969).
89. A. I. Besyadetskaya, N. S. Oleiovskaya, I. A. Dmukhovskya, A. S. Lipkovskii, A. I. Ostroumova and A. V. Stroganova, *Farm. Zh. (Kiev)*, 56 (1980).
90. D. Barnard and K. R. Hargrave, *Anal. Chim. Acta*, **5**, 536 (1951); **6**, 23 (1952).
91. R. R. Legault and K. Groves, *Anal. Chem.*, **29**, 1495 (1957).
92. Y. A. Gawargious, *Microchem. J.*, **16**, 673 (1971).
93. E. Glynn, *Analyst (London)*, **72**, 248 (1947).
94. B. J. Anness, *J. Sci. Food Agr.*, **32**, 353 (1981).
95. I. Okuno, D. R. Latham and W. E. Haines, *Anal. Chem.*, **39**, 1830 (1967).
96. H. V. Drushel and A. L. Sommers, *Anal. Chem.*, **39**, 1819 (1967).
97. M. O. Andreae, *Anal. Chem.*, **52**, 150 (1980).
98. A. P. Safronov, *Zh. Anal. Khim.*, **18**, 548 (1963).
99. F. Vlačil and Huynh Dong Khanh, *Collect. Czech. Chem. Commun.*, **44**, 1908 (1979).
100. N. M. Turkevich, E. V. Vladzimirskaya, S. I. Tereshchuk and M. F. Tomashevskaya, *Farmatsiya (Moscow)*, **26**, 33 (1977).
101. G. S. Porter and J. Beresford, *J. Pharm. Pharmacol.*, **18**, 223 (1966).
102. B.-L. Johansson and B. Persson, *Anal. Chim. Acta*, **102**, 121 (1978).

103. C. A. Streuli, *Anal. Chem.*, **30**, 997 (1958).
104. D. D. Wimer, *Anal. Chem.*, **30**, 2060 (1958).
105. N. N. Bezinger, G. D. Gal'pern and M. A. Abdurakhmanov, *Zh. Anal. Khim.*, **16**, 91 (1961).
106. E. N. Karaulova, G. D. Gal'pern and B. A. Smirnov, *Tetrahedron*, **18**, 1115 (1962).
107. Z. Štefanać and A. Verbić, *Z. Anal. Chem.*, **232**, 113 (1967).
108. I. M. Kolthoff, N. K. Chantooni and S. Bhownik, *Anal. Chem.*, **39**, 1627 (1967).
109. I. V. Khazova and B. D. Bogomolov, *Izv. Vyssh. Ucheb. Zaved. Les. Zh.*, **13**, 92 (1970).
110. C. B. Puchalsky, *Anal. Chem.*, **41**, 843 (1969).
111. J. Berčík, M. Cakrt and Z. Hladký, *Chem. Zvesti*, **24**, 290 (1970).
112. D. Pačigová and V. Veselý, *Ropa Uhlie*, **12**, 123 (1970).
113. S. Kiričenková and A. Švec, *Chem. Listy*, **67**, 311 (1973).
114. C. J. Thompson, H. J. Coleman, R. H. Hopkins and H. T. Rall, *J. Chem. Eng. Data*, **9**, 293 (1964).
115. H. E. Hucker and E. A. Hoffmann, *Experientia*, **22**, 855 (1966).
116. G. Roland and G. Duyckaerts, *Anal. Chim. Acta*, **68**, 323 (1974).
117. Z. Dizdar and Z. Idjaković, *Talanta*, **19**, 1217 (1972).
118. H. E. Toma, E. Giesbrecht and J. M. Malin, *Anais Acad. Brasil. Cienc.*, **48**, 41 (1976).
119. D. Barnard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).
120. T. Oba, *Bunseki Kagaku*, **9**, 601 (1962).
121. J. Zajic and M. Bareš, *Fette, Seifen, Anstrichm.*, **69**, 393 (1967).
122. L. R. Snyder, B. E. Buell and H. E. Howard, *Anal. Chem.*, **40**, 1303 (1968).
123. J. B. Haus, L. Manolev and R. W. Price, *J. Assoc. Offic. Agr. Chemists*, **48**, 569 (1965).
124. T. C. Kram and J. W. Turczan, *J. Pharm. Sci.*, **57**, 651 (1968).
125. S. L. Tompsett, *Acta Pharmacol. Toxicol.*, **26**, 298 (1968).
126. V. Horák and J. Pecka, *J. Chromatogr.*, **14**, 97 (1964).
127. E. N. Karaulova, T. S. Bobruiskova and G. D. Gal'pern, *Zh. Anal. Khim.*, **21**, 893 (1966).
128. H. W. Prinzler and H. Tauchmann, *J. Chromatogr.*, **29**, 142 (1967).
129. H. W. Prinzler, H. Tauchmann and C. Tzscharnke, *J. Chromatogr.*, **29**, 151 (1967).
130. W. A. Morris, *Anal. Chem.*, **53**, 916 (1981).
131. W. H. Pirkle and D. W. House, *J. Org. Chem.*, **44**, 1957 (1979).
132. W. H. Pirkle, D. W. House and J. M. Finn, *J. Chromatogr.*, **192**, 143 (1980).
133. S. Allenmark, L. Paelsen and W. H. Pirkle, *Acta Chem. Scand, Ser. B*, **37**, 325 (1983).
134. T. J. Wallace and J. J. Mahon, *J. Amer. Chem. Soc.*, **86**, 4099 (1964).
135. H. J. Paulin, J. B. Murphy and R. E. Larson, *Anal. Chem.*, **38**, 651 (1966).
136. R. A. Stuart, *J. Gas Chromatogr.*, **4**, 388 (1966).
137. G. Variali, *Rass. Chim.*, **22**, 47 (1970).
138. S. L. Seager and L. C. Stone, *J. Chromatogr. Sci.*, **9**, 438 (1971).
139. E. M. Kazinik, G. A. Gudkova, L. Ya, Mesh, T. A. Shcheglova and A. V. Ivanov, *Tr. Vses. Nauch.-Issled. Proekt, Inst. Monomerov*, **3**, 135 (1972).
140. A. M. Awwad and T. M. Sarkissian, *J. Chromatogr. Sci.*, **15**, 487 (1977).
141. N. M. Turkevich, S. I. Tereshchuk and O. M. Tereshchuk, *Farmatsiya (Moscow)*, **27**, 79 (1978).
142. B. Pszonka, *Przeglad Papier*, **34**, 357 (1978).
143. R. Kimura, T. Hayashi, M. Sato, T. Aimoto and T. Murata, *J. Pharmacobio-Dyn.*, **2**, 237 (1979).
144. N. M. Turkevich, S. I. Tereshchuk and O. M. Tereshchuk, *Farmatsiya (Moscow)*, **28**, 33 (1979).
145. M. Ogata and T. Fujii, *Ind. Health*, **17**, 73 (1979).
146. S. E. Garretson and J. P. Aitchison, *J. Anal. Toxicol.*, **6**, 76 (1982).
147. N. V. Makovskaya, N. I. Zubkova and I. N. Agranovskii, *Khim. Volokna*, **24**, 55 (1982).

CHAPTER 6

Mass spectra of sulfoxides and sulfones

KALEVI PIHLAJA

Department of Chemistry, University of Turku, SF 20500 Turku 50, Finland

I. INTRODUCTION

Since the classical paper of Meyerson and coworkers[1] in 1964 on the electron impact(EI) mass spectra of diaryl sulfones, only some more than one hundred original reports dealing with the mass spectra of sulfoxides and sulfones have been published. These data have been reviewed quite extensively, most recently by Khmel'nitskii and Efremov[2] in a review on 'The rearrangements in sulfoxides and sulfones induced by electron impact' and by Porter[3]. Several less comprehensive surveys have also been presented[4–7]. Since Reference 2 and to a lesser extent Reference 4 cover the EI mass spectra of alkyl and aryl sulfoxides and sulfones up to 1974 fairly completely, and Reference 3 together with Reference 2 the mass spectra of heterocyclic sulfoxides and sulfones and their nitrogen-containing counterparts up to 1980, the present chapter will mainly concentrate on the most recent developments and some complementary material not described in the above-mentioned reviews.

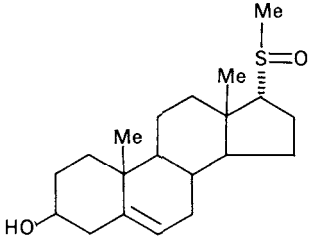
Sometimes the mass spectra of related sulfoxides and sulfones have been discussed very compactly in the original literature. In these cases a detailed discussion on both will appear under the heading sulfoxides, but will be mentioned also in context with sulfones.

II. MASS SPECTRA OF SULFOXIDES

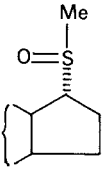
A. Aliphatic Sulfoxides

Dodson and coworkers[8] inspected the EI mass spectra of 3β-hydroxy-20-thia-17(α and β)-pregnen-5-ene oxides (**1–4**) in the light of their absolute configurations. By comparing the ion abundances in reactions (1A)–(1C) (equation 1) it was possible to draw conclusions about the rates of these reactions and hence about the configurations of the starting sulfoxides.

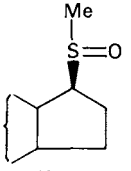
The elimination of $HX(X = SOCH_3, SCH_3)$ from the $[M - STol]^+$ and $[MH - HSTol]^+$ cations $(Tol = CH_3C_6H_4)$ from **5–9** under electron impact and chemical ionization depends strongly on the spatial orientation of the vicinal substituents[9]. The intensity of the $[M - STol]^+$ ion is appreciably higher when X and Y are *cis* than when they are *trans*. The stereochemistry of the sulfoxide group is not important since **7** and **8** exhibit very similar spectra. The elimination of $HSOCH_3$ occurs more easily from **7** and **8**



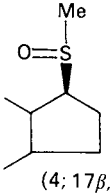
(1; 17α, *S*)



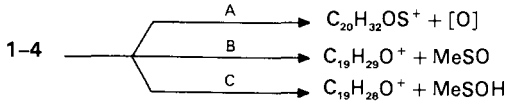
(2; 17α, *R*)



(3; 17β, *S*)

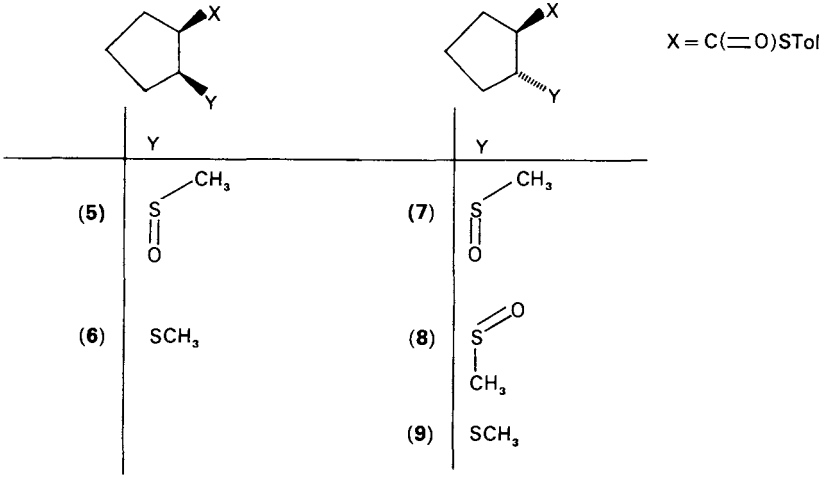


(4; 17β, *R*)



(1)

(two available *cis*-hydrogens) than from **5** (one *cis*-hydrogen), as can be seen from the relative intensities of the $[M-(STol+HX)]^+$ ions (75, 68 and 34%, respectively). Correspondingly, the $[MH-HSTol-HX]^-$ ion forms the base peaks in the CH_4-chemical ionization spectra of **7** and **8** but not in that of **5**[9].

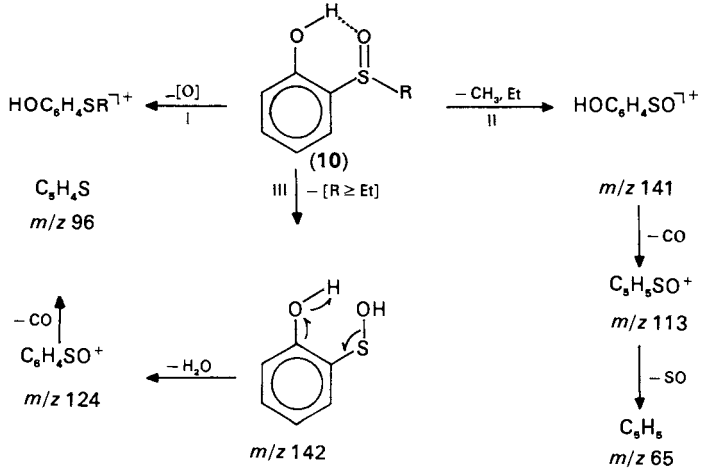


Potzinger and coworkers[9b] determined ionisation and appearance energies for the molecular and major fragment ions of several dialkylsulfoxides, R^1SOR^2 (R^1 = Me; R^2 = Me, Et, *i*-Pr, and *i*-pentyl and $R^1 = R^2$ = Et or *i*-Pr). In addition to the evaluation of dissociation energies in the ions and their enthalpies of formation, a value of 280 $\pm$ 30 kJ mol^{-1} for the C—S dissociation energy in neutral dialkyl sulfoxides was derived.

B. Alkyl Aryl Sulfoxides

Pedersen and coworkers[10] studied the EI mass spectra of several alkyl 2-hydroxyphenyl sulfoxides (**10**) and found that, contrary to methyl phenyl sulfoxide[2,11] and the corresponding sulfones[10], they do not show any abundant skeletal rearrangement ions (see Section III). This is obviously due to an *ortho* effect as shown in structure **10**.

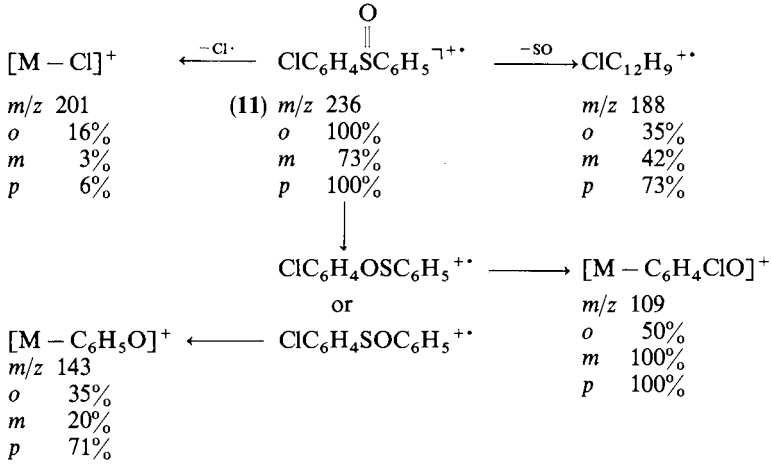
The loss of an oxygen atom from the molecular ions of **10** occurs also to some extent and is most pronounced when R = CH_3 (route I in equation 2). The predominant fragmentation route of methyl and ethyl 2-hydroxyphenyl sulfoxides is II (equation 2) which, however, is not important when R > Et. Ethyl 2-hydroxyphenyl sulfoxide undergoes also fragmentation via route III, which is the main path of fragmentation when R > Et[10].



(2)

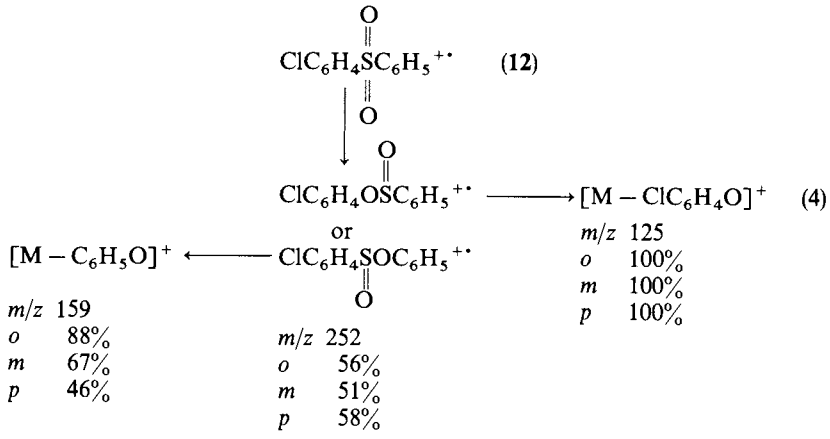
C. Diaryl Sulfoxides

The loss of Cl· from the molecular ion of *ortho*-chlorodiphenyl sulfoxide (*o*-**11**) has been found to be significantly greater than from the *meta*- and *para*-isomers (equation 3)[12]. This observation is best explained by an *ortho* effect in accord with a tight activated complex.



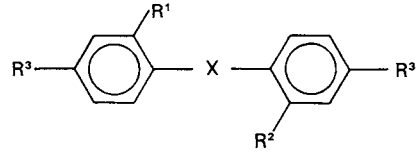
(3)

The other fragmentation pathways are typical for diaryl sulfoxides[1-4,6,11]. A corresponding *ortho* effect was found in chlorodiphenyl ethers and sulfides but not in sulfones[12] (**12**) were the sulfinate ester rearrangements[1-4,6,11] and the consequent formation of the *m/z* 125 and *m/z* 159 ions suppress the other possible fragmentations of the molecular ions (equation 4). It is also noteworthy that the ratio [*m/z* 125]:[*m/z* 159] increases with increasing distance between the chlorine and the sulfur (equation 4).

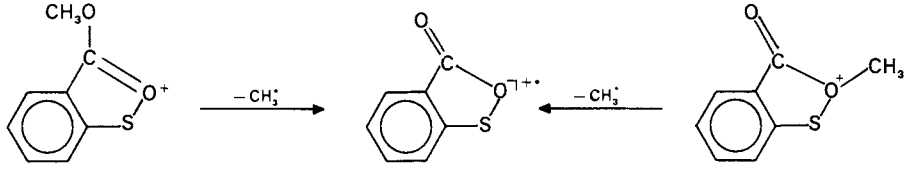


(4)

The main primary fragment ions of diaryl sulfoxides **13** and **14** have the structures **16a** or **16b** ($C_8H_7SO_2^{+\cdot}$, *m/z* 167) and the ion *m/z* 152 (**17**) can be obtained from both by the loss of $CH_3^{\cdot}$ (equation 5)[13]. Ions **16a** and **16b** are formed from the sulfenate ester structure of the molecular ions of **13** and **14** through a cyclization process and a simultaneous loss of the other OAr part. A similar *ortho* effect is not possible in **15** and hence its most intense ion is $M^{+\cdot}$ (23% of the total ionization in comparison with 2.7 and 0.6% for **13** and **14**, respectively) and its primary fragments are typical for a normal diaryl sulfoxide.



	X	R^1	R^2	R^3
(**13**)	SO	$COOCH_3$	H	H
(**14**)	SO	$COOCH_3$	$COOCH_3$	H
(**15**)	SO	H	H	$COOCH_3$

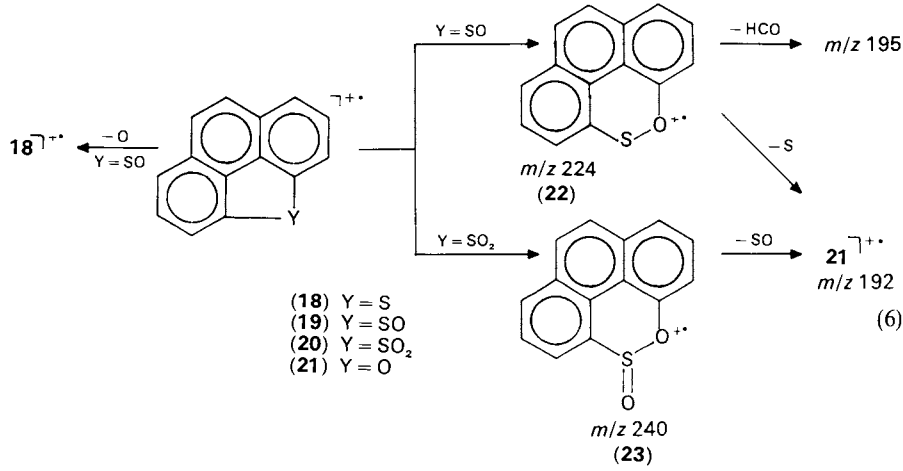


(**16a**) (**17**) (**16b**) (5)

Efremov and coworkers[14] observed that electron-donating groups promote the sulfoxide–sulfonate ester rearrangement[1–4,6,11] in the molecular ions of 2,4-dinitrophenyl phenyl sulfoxides. At 12 eV the dissociation of the unisomerized molecular ion dominates, supporting the view that the formation of the sulfonate ions is a high-energy process. Surprisingly, a small amount of SO_2 elimination occurred also. This could be explained by a migration of one of the oxygen atoms of the nitro group at position 2 to the sulfur atom in order to form a sulfonium ion and then eliminate SO_2.

D. Sulfoxide Function in a Heterocycle

Phenanthro[4,5-b,c,d]thiophene 4-oxide (**19**) and 4,4-dioxide (**20**)[15] undergo first the well-known sulfenate (**22**) or sulfinate ester (**23**) rearrangements[1–4,6], respectively (equation 6). The sulfoxide loses an oxygen atom and enters the fragmentation pathway of **18** or loses HCO (more likely in two steps) from **22**. Both sulfenate and sulfinate ions can fragment further via **21** after losing a sulfur atom or eliminating SO[5], respectively.

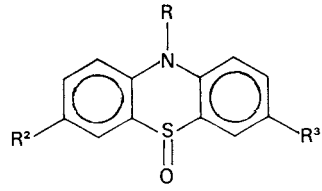


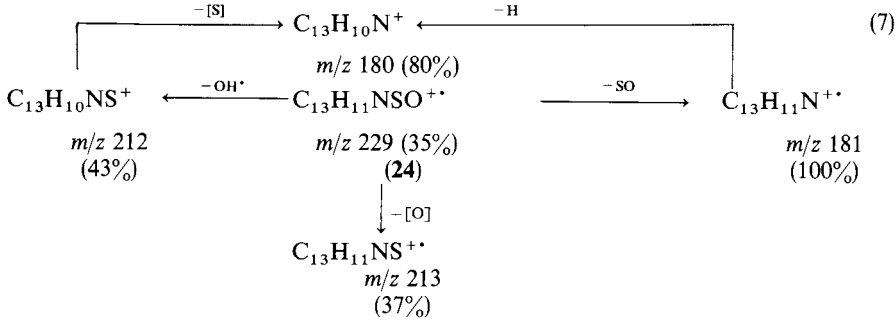
(6)

Characteristic for the EI mass spectra of 10-methylphenothiazine-5-oxide (**24**, equation 7), 10-butyl-3,7-dinitrophenothiazine-5-oxide (**25**, equation 8) and 10-butyl-3-nitro-7-chlorophenothiazine-5-oxide (**26**, equation 9) are eliminations of an oxygen atom, an ·OH radical and SO[16a]. The loss of an oxygen atom is roughly of the same importance in all three cases, but the elimination of SO from **24** is far more significant than from **25** and **26**, in which the main primary fragmentation occurs via the elimination of the ·OH radical (equations 7–9). This can be explained by the nonplanar conformation of the phenothiazine ring[17] and the *extra* and *intra* configurations of the *N*-substituent[16,17]. For **24** both configurations are possible, whereas **25** and **26** favor greatly the *extra* form where the elimination of ·OH can involve the *S*-oxygen and a hydrogen of the alkyl group. Later on Taulov and coworkers extended their studies to five more 5-oxides[16b] ($R^1 = CH_3$, Et, Pr; $R^2 = Cl$; $R^3 = NO_2$ and $R^1 = —CH_2CH=CH_2$; $R^2 = R^3 = H$) and seven 5,5-dioxides[16c] ($R^1 = CH_3$, Et, $—CH_2CH=CH_2$, $—C\equiv C—CH_3$; $R^2 = R^3 = H$ and $R^1 = Et$; $R^2 = Cl$; $R^3 = NO_2$) and reconfirmed their earlier conclusions (see also p. 145).

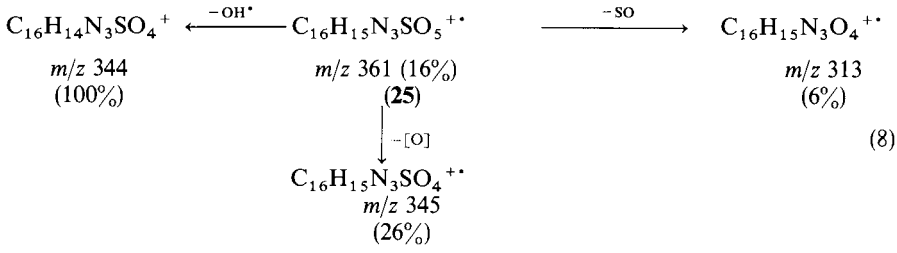
Klemm and coworkers[18a] prepared some isomeric chlorinated 2,3-dihydrothieno-[2,3-*b*]pyridine 1-oxides and reported their EI mass spectra at 70 eV. Only one isomer (**30**) was isolated in the case of the 5-ethyl derivative the mass spectrum of which

	R^1	R^2	R^3
24	CH_3	H	H
25	Bu	NO_2	NO_2
26	Bu	Cl	NO_2

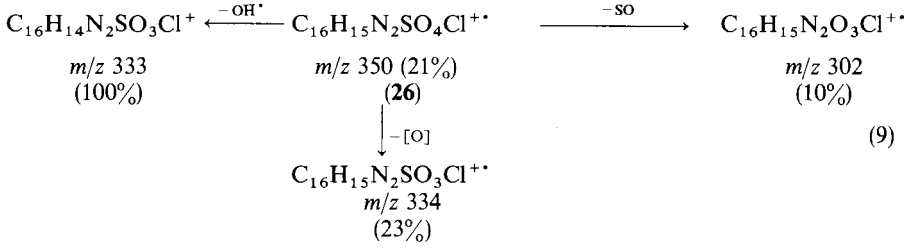




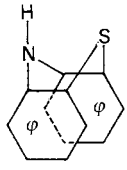
(7)



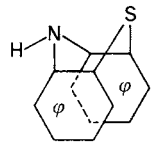
(8)



(9)

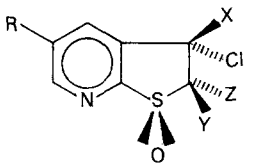


H-*extra*



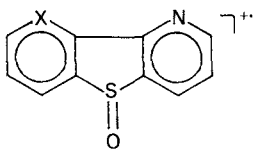
H-*intra*

resembled closely that of **27**. Accordingly, it was concluded that **27** and **30** have similar configurations since the mass spectrum of **28** differed appreciably from that of **27**. The loss of HClO from the molecular ion corresponds to the second most abundant peak (*m/z* 169) in the spectrum of **28** whereas in **27** its contribution is only 6%. Similarly, **29** shows 16% of $[M - HClO]^{+\cdot}$ but **30** less than 5%.



	X	Y	Z	R
(**27**)	H	Cl	H	H
(**28**)	H	H	Cl	H
(**29**)	Cl	Cl	H	H
(**30**)	H	Cl	H	Et

Both benzothieno[3,2-*b*]pyridine 5-oxide (**31**) and thieno[3,2-*b*:4,5-*b'*]dipyridine 5-oxide (**32**) exhibit competitive loss of oxygen either as an atom or as carbon monoxide after initial skeletal rearrangement, e.g. to sulfenate esters (equation 10)[18b]. These results together with some data for *N*-oxides indicate that the presence of an intense $[M - 16]^{+\cdot}$ peak is not diagnostic for the latter only.



(**31**) X = CH *m/z* 201 (100%)

(**32**) X = N *m/z* 200 (100%)
(or sulfenate esters)

$-CO \rightarrow C_{10}H_7NS^{+\cdot}$ *m/z* 173 (33%)

$-[O] \rightarrow C_{11}H_7NS^{+\cdot}$ *m/z* 185 (47%)

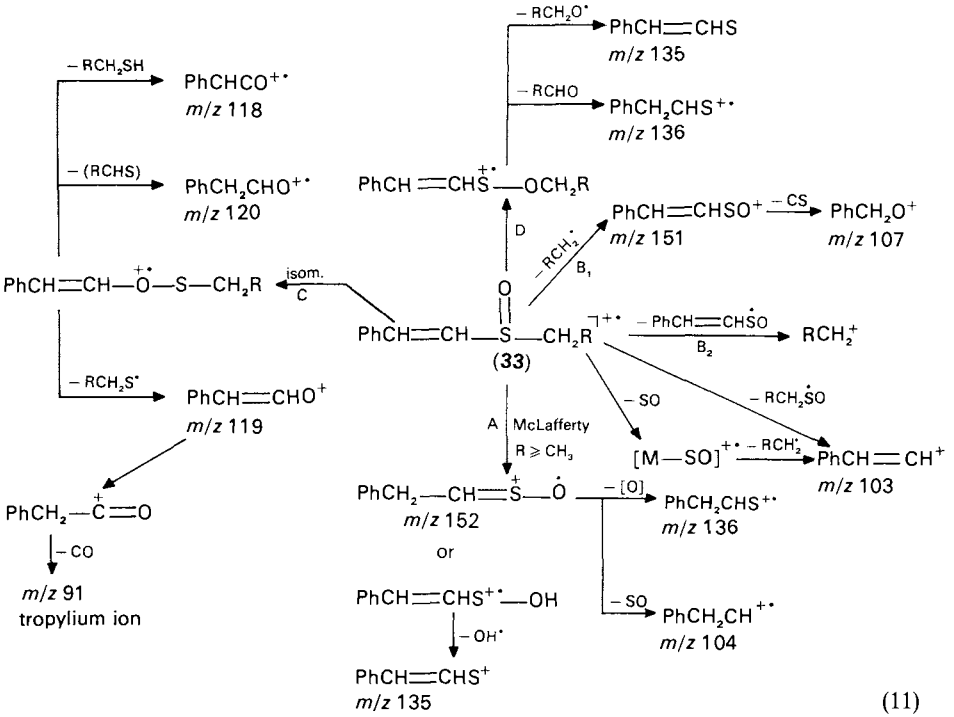
$-[O] \rightarrow C_{10}H_6N_2S^{+\cdot}$ *m/z* 186 (26%)

$-CO \rightarrow C_9H_6N_2S^{+\cdot}$ *m/z* 174 (31%)

(10)

E. Alkyl Styryl Sulfoxides

Alkene elimination (A), alkyl loss (B), styryl (C) and alkyl migrations (D) dominate the EI mass spectra of *Z*- and *E*-alkyl styryl sulfoxides (**33**)[19]. The situation at 12 eV has been summarized in equation (11). The direct cleavage of an alkyl group (route B_1) occurs easily in compounds with shorter alkyl chains ($RCH_2 \leqslant C_3H_7$) whereas the formation of *m/z* 152 ion (route A) becomes predominant when $RCH_2 \geqslant C_3H_7$. In some cases the carbonium ion RCH_2^+ (e.g. $PhCH_2CH_2^+$, route B_2) but not the styryl sulfinyl ion retains the positive charge during the fragmentation of the C—S bond. In general, hydrogen migrations both to the benzylic carbon and to the sulfinyl oxygen together with alkene elimination are the most facile processes. The former are also a unique feature for alkyl styryl sulfoxides as compared with other sulfoxides[1-3]. Styryl (route C) and alkyl (route D, especially when R = H) migrations are also significant mainly in compounds with shorter alkyl chains, which is comparable to methyl styryl and aryl styryl sulfoxides[2,20]. Some formation of $[M - O]^{+\cdot}$ and $[M - OH]^+$ ions also occurred and in the case of phenyl styryl derivatives the $[M - SO]^{+\cdot}$ ion formed the base peak of the spectrum and the $[M - SOH]^+$ peak was about one-third of it. No big difference was observed in the spectra of the *E*- and *Z*-isomers.



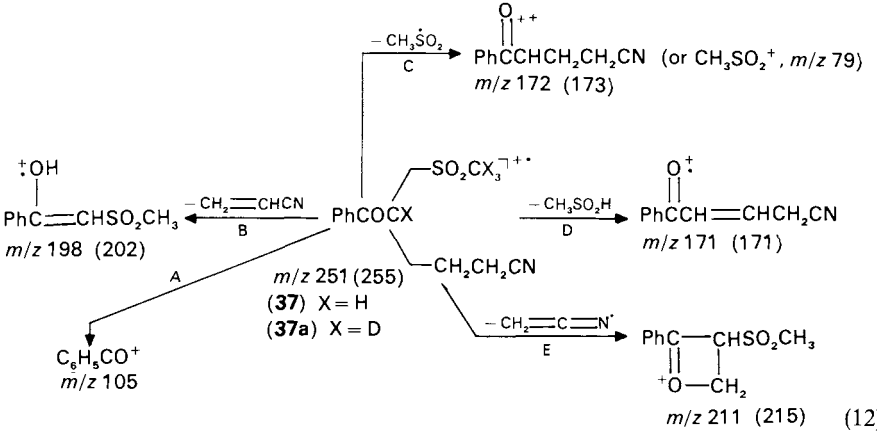
(11)

III. MASS SPECTRA OF SULFONES

A. Dialkyl Sulfones

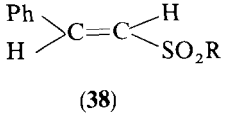
The EI mass spectra of $[RCH_2CH_2]_2SO_2$ where R = —$CONH_2$ (**34**), —$COOCH_3$ (**35**) and —CN (**36**) have been reported[21]. Sulfone **34** gave no peak for the molecular ion (*m/z* 208) and did not fragment initially at the sulfone linkage but gave the ion $CONH_2^+$ (*m/z* 44) as the base peak and further fragmentations via $[M - CONH_2]^+$ ion. No molecular ion was found in the case of **35** either, although its fragmentation was dominated by a rupture of the sulfone linkage leading to the base peak at *m/z* 151. The sulfone–sulfinate ester rearrangement occurs also, as shown by ions at *m/z* 135 and 103. Sulfone **36** gave also a weak $M^{+\cdot}$ peak and ions *m/z* 118 and 54 as a result of a direct sulfone cleavage. Some extrusion of SO_2 from **36** was also probable.

Diller and Bergmann[22] studied the fragmentation of γ-methylsulfonyl-γ-benzoylbutyronitrile (**37**, equation 12) under electron bombardment and found that the formation of $[C_6H_5CO]^+$ ion, *m/z* 105 (route A), predominated as with other phenyl ketones. A McLafferty rearrangement produces the ion *m/z* 198 (route B) parallell to the photolysis of **37**[23]. Also, the loss of CH_3SO_2 (route C) corresponds to a photolytic path. It should be mentioned, however, that the relative abundances of *m/z* 198 and 172 are rather low at 70 eV. Two more primary fragmentations are of importance, namely the elimination of CH_3SO_2H (route D) leading to *m/z* 171 and the loss of $CH_2CN\cdot$ giving the ion *m/z* 211 (route E). All the above pathways were confirmed by observing the respective ions in the spectrum of the tetradeuterio derivative (**37a**; *m/z* values in parentheses).



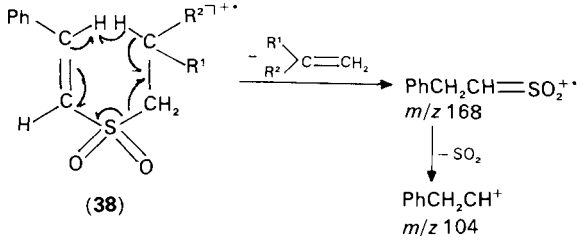
(12)

(*E*)-1-Alkylsulfonyl-2-phenylethenes[24a] (alkyl styryl sulfones, **38**) exhibit an interesting rearrangement (when R > CH_3) where a β-hydrogen of the alkyl group migrates to the styryl carbon via a six-membered transition state (equation 13) which then gives an alkene and an intermediate ion, *m/z* 168. The ion *m/z* 104 is then obtained from the latter via the loss of SO_2. Another major process is the styryl migration (sulfinate ester formation[1–4,6]) which leads to the ions *m/z* 103 and *m/z* 119, which together with the ion *m/z* 104 dominate the fragmentation at 12 eV.



(**38**)

R = Me, Et, *i*-Pr, $CH(CH_3)CD_3$, Pr, Bu, *i*-Bu, $PhCH_2CH_2$



(**38**) (13)

Corina and coworkers[24b] also gave the ten ion listings for the EI mass spectra of $CH_3SO_2CH_2COR$ (R = —$CH_2CH_2COOCH_3$, —$(CH_2)_6COCH_2Cl$ or —$(CH_2)_{14}CH_3$) in context of their studies on the GC and GC/MS of various methane thiolsulphonates.

B. Alkyl Aryl Sulfones

Pedersen and coworkers[10] investigated the EI mass spectra of several 2-hydroxyphenyl alkyl sulfones (**39**) and sulfoxides (Section II.B). The methyl derivative seemed to fragment only via sulfinate ester formation giving the primary product ions *m/z* 157 and 109 (equation 14). Obviously hydrogen bonding between the *ortho* hydroxyl and the sulfone sulfur makes the loss of CH_3SO_2 difficult in contrast to the situation in methyl phenyl sulfone[11]. The sulfinate ester rearrangement is not important when R > Et in **39**.

Furthermore, R = Et is the only case where the direct formation of the ion *m/z* 140 from $M^{+\cdot}$ (*m/z* 186) was supported by a metastable ion corresponding to the elimination of ethanol from *m/z* 186. The fragmentation of **39** (R > Et) can be summarized as in equation (15). The formation of the ion *m/z* 94 was not confirmed by metastable ions. The loss of SO_2 from the molecular ions was not found practically at all. Aryl methyl sulfones[25] (**40**) form $[Aryl\ SO_2]^+$ and [Aryl] ions by simple cleavages. $[Aryl\ O]^+$ and $[Aryl\ OH]^+$ ions via aryl migration (**40a**) and to much lesser extent $[Aryl\ SO]^+$ ions via alkyl migration (**40b**) (equation 16). The mode of fragmentation of **40a** depended strongly on the nature of R. Electron-donating groups promote the cleavage reaction by stabilizing the $[Aryl\ O]^+$ ions whereas the nitro group favors a hydrogen rearrangement (equation 17) to the exclusion of the $4\text{-}O_2NC_6H_4O^+$ formation.

$2\text{-}HOC_6H_4SO_2R$ R = Me, Et, Pr, *i*-Pr, Bu, *i*-Bu, *s*-Bu, *t*-Bu,
(**39**) *i*-Pe, $CH_2CH{=}CHCH_3$, CH_2Ph, $CH(CH_3)Ph$

$2\text{-}HOC_6H_4OS(=O)CH_3^{+\cdot}$ $\xrightarrow{-CH_3\cdot}$ $2\text{-}HOC_6H_4O\overset{+}{S}{=}O$

m/z 172 (−$CH_3SO\cdot$) → $2\text{-}HOC_6H_4O^+$ *m/z* 109

m/z 157 (−SO_2) → $C_6H_5O^+$ *m/z* 93

m/z 157 (−SO) → $2\text{-}HOC_6H_4O^+$ *m/z* 109 (14)

$2\text{-}HOC_6H_4SO_2R^{+\cdot}$

? → $C_6H_6O^+$

−(R—H)· → $2\text{-}HOC_6H_4SO_2H^{+\cdot}$ *m/z* 158

R > Et → R^+

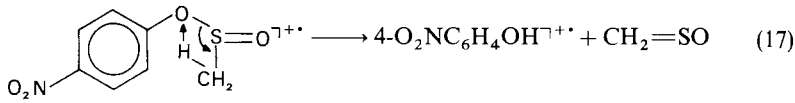
$2\text{-}HOC_6H_4SO_2H^{+\cdot}$ (−SO_2, ?) → *m/z* 94

$2\text{-}HOC_6H_4SO_2H^{+\cdot}$ (−H_2O·) → $C_6H_4SO_2^{+\cdot}$ *m/z* 140 $\xrightarrow{-SO}$ $C_6H_4O^{+\cdot}$ *m/z* 92 (15)

$4\text{-}RC_6H_4SO_2CH_3^{+\cdot}$ (**40**) → $4\text{-}RC_6H_4OS(=O)CH_3^{+\cdot}$ (**40a**)

$4\text{-}RC_6H_4S(=O)OCH_3^{+\cdot}$ (**40b**) (16)

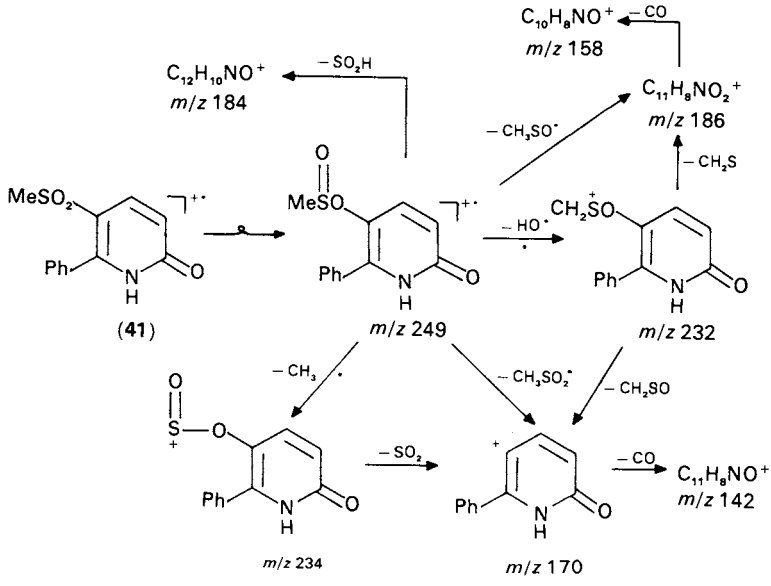
R = OMe, Me, H, Cl, Br, NO_2



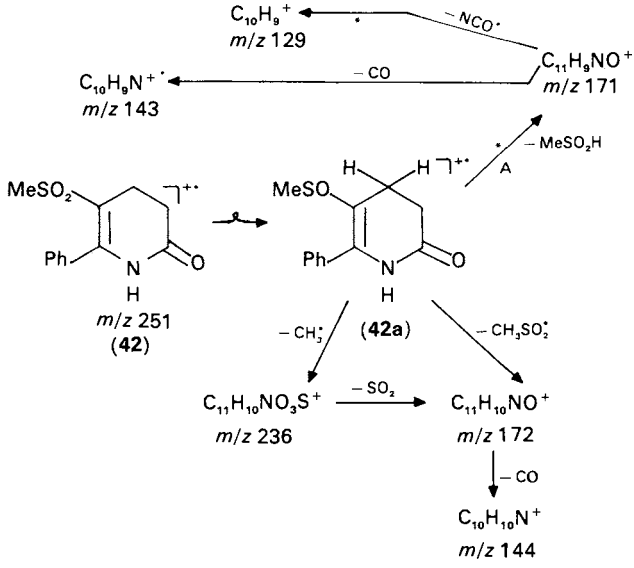
$\longrightarrow 4\text{-}O_2NC_6H_4OH^{+\cdot} + CH_2{=}SO$ (17)

The primary fragmentations of 5-methylsulfonyl-6-phenyl-2-pyridone (**41**) and its 3,4-dihydro analogue (**42**) are dominated by the methylsulfonyl substituent and not by the pyridone moiety[26]. Equation (18) summarizes the most important primary fragmentations and shows that the pyridone ions *m/z* 186 and 170 yield the pyrrole-type ions *m/z* 158 and 142 only after the sulfonyl side-chain has been broken off. Since the mass spectrum

of 6-phenyl-2-pyridone[26] does not show a $[M - OH]^+$ peak it is obvious that the oxygen of the OH radical released from **41** originates from the sulfonyl group. Also, derivatives monodeuteriated at N or at position 3 support this view and indicate also that the OH hydrogen comes from the phenyl ring or the methyl group. Furthermore, direct loss of SO_2H seems to occur from the sulfinate ester form of **41**.



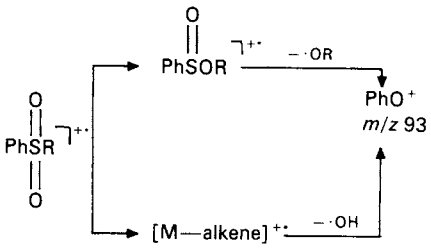
(18)



(19)

The base peak at *m/z* 172 in the 70 eV EI mass spectrum of **42** (equation 19) is due to the loss of CH_3SO_2H from the rearranged molecular ion (**42a**). The spectra of the *N*- and 3-deuteriated derivatives of **42** spoke for the 4-methylene group as a possible source of the acid hydrogen. A similar mechanism has been reported for dialkyl sulfones[27]. The fragment *m/z* 171 then yields pyrrole, *m/z* 143 via the loss of CO and a fragment *m/z* 129 by losing NCO·. Some loss of $CH_3SO_2^{\bullet}$ (or stepwise losses of $CH_3^{\bullet}$ and SO_2) led to the formation of the ion *m/z* 172 (for the possible structure cf. equation 18)[25] obviously via **42a**. The ion *m/z* 172 in turn was the precursor of the pyrroline ion, *m/z* 144. The loss of CO as that of $CH_3SO^{\bullet}$ are only of minor importance, which indicates that the partial loss of the aromaticity of the pyridone ring (i) does not weaken significantly the predominance of the methylsulfonyl substituent in the primary fragmentations but (ii) enhances remarkably route A (equation 19). The fairly intense ions at *m/z* 104 for both **41** and **42** were given the structure $PhC{\equiv}\overset{+}{N}H$.

Jones and Tebby[28] confirmed the presence of peaks corresponding to ArOH and/or ArO ions in the spectra of alkyl aryl sulfones supporting the facile migration of the aryl group from sulfur to oxygen[1-4,6,11]. They also emphasized that the formation of ArSO (M − OR) ions[11] becomes more evident as the branching of the alkyl group increases (equation 20). An alternative pathway was also suggested for the formation of these ions—an alkene elimination accompanied by a loss of HO radical. An interesting observation was also the loss of a methyl radical from the protonated molecular ions of ethyl phenyl and ethyl tolyl sulfones (13 and 50%, respectively)[28].



R	%M⁺·	%[M − OR]⁺
Me	29	0
Et	83	19
i-Pr	39	26
t-Bu	6	35

(20)

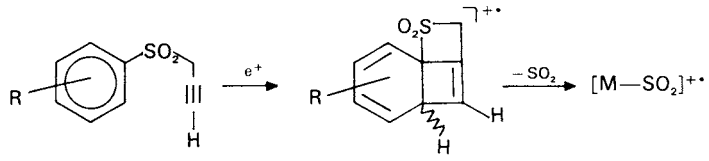
C. Aryl Unsaturated Alkyl Sulfones

1. Aryl propynyl sulfones

The title compounds (**43**)[29] eliminated SO_2 very easily, possibly via an intramolecular 2 + 2 addition in the molecular ion (equation 21). Peaks corresponding to the sulfone–sulfinate rearrangement[2,4-6,11] were all of relatively low intensity ($\leq 12\%$ at 20 eV). The 2 + 2 addition preceding the loss of SO_2 (equation 21) finds further support (i) in the easy extrusion of SO_2 from other derivatives of thiete dioxide[30,31], (ii) in the low intensities of the $[M - SO_2]^{+\bullet}$ ions of 2-Me and 2,6-diMe derivatives of **43** (i.e. blocking of *ortho* positions), and (iii) in the lack of SO_2 elimination in the case of aryl butynyl sulfones (**44**) where, on the contrary, the sulfinate ester rearrangement (equation 22) prior to fragmentation has a major role.

2. Derivatives of 1,4-bis(arylsulfonyl)-2-butyne and 1,6-bis(arylsulfonyl)-2,4-hexadiyne

Compounds **45** exhibit, in addition to sulfone–sulfinate rearrangements[1,2,4-6,11], alkyl sulfone cleavages[4,6,27], intramolecular Smiles-type rearrangements[33] and extrusion of SO_2[3,5,29,30], an exceptional mode of remote group interaction which leads to the loss of



(43) (43a) (21)

		R = H	4-Me	3-Me	2-Me
%[M − SO_2]$^{+\cdot}$	20 eV	68	60	62	19
Base peak	20 eV	$ArSO_2^+$	Ar^+	Ar^+	Ar^+

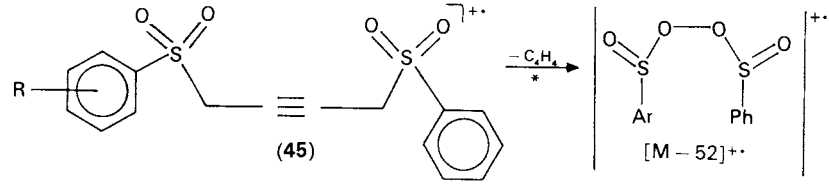
2,6-diMe	4-Cl	3-Me, 4-Br	3,4-diCl	2,5-diCl
12	48	55	41	100(15eV)
Ar^+	$ArSO_2^+$	$ArSO_2^+$	$ArSO_2^+$	[M − SO_2]$^{+\cdot}$

$$PhSO_2CH_2C{\equiv}CCH_2R^{\urcorner+\cdot} \longrightarrow PhS(O)CH_2C{\equiv}CCH_2R^{\urcorner+\cdot} \qquad (22)$$

(44) (44a)

		R = H	Cl	OTol-*p*	SO_2cyclohexyl	SO_2Ph
[M—SO_2]$^{+\cdot}$	20 eV	27	0	0	1	0
$ArSO^+$	20 eV	47	18	100	92	100
[M − ArSO]$^+$	20 eV	2	1	7	0	77

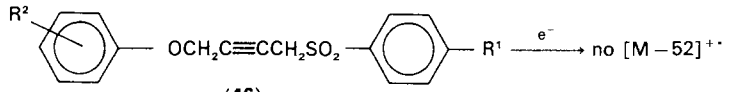
the four carbon chain, C_4H_4, separating the two sulfone moieties (equation 23)[32]. This direct interaction pathway, but not an *ortho* Claisen rearrangement, was supported by the observations that (i) aryl propynyl sulfones do not undergo thermal Claisen rearrangements[34] and (ii) compounds **46** do not show the [M − 52] ion under electron impact. Furthermore, compounds **47** formed readily [M − 54] ions and their dideuteriated counterparts **48** [M − 56] ions. The route M$^{+\cdot}$ → [M − 52]$^{+\cdot}$ → $ArSO_2^+$ for **45** was also substantiated by metastable peaks. Later Thyagarajan and coworkers[35] found additional



	a	b	c	d	e	f	g
R	4-Me	3-Me	2-Me	4-*t*-Bu	H	4-OMe	4-Cl

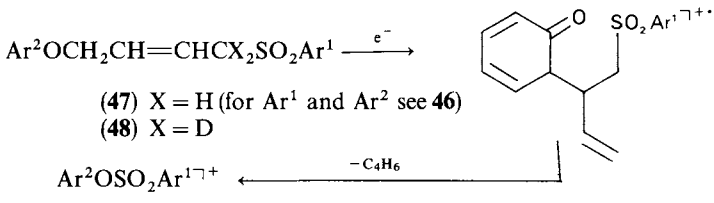
(23a)

evidence to the above direct interaction pathway (equation 23) by investigating the EI mass spectra of some 1,6-bis(arylsulfonyl)-2,4-hexadiynes where the extra triple bond would make a direct interaction process impossible. Accordingly, none of the bis-sulfones **49** showed a loss of C_6H_4 in addition to commonly predictable modes of fragmentation mentioned above. Hence no *ortho* Claisen rearrangement occurred either. Instead, compounds **49** produced peaks for $[M-SO_2]^{+\cdot}$ and $[M-2SO_2]^{+\cdot}$ (equation 23c) obviously via thiete dioxide type intermediates as in the case of aryl propynyl sulfones[29] (Section III.C.1). In most cases elimination of SO from the parent ion was also observed[35] in accord with the sulfinate rearrangements.



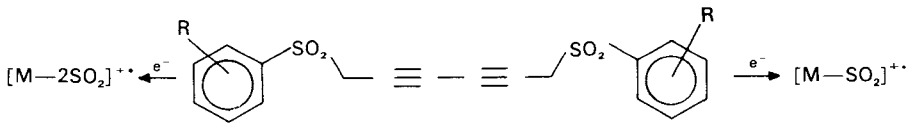
(**46**)

	a	**b**	**c**	**d**
R^1	2-naphthyl	4-Br	4-*t*-Bu	4-Cl
R^2	H	Me	H	Me



(**47**) X = H (for Ar^1 and Ar^2 see **46**)
(**48**) X = D

(23b)



(**49**)

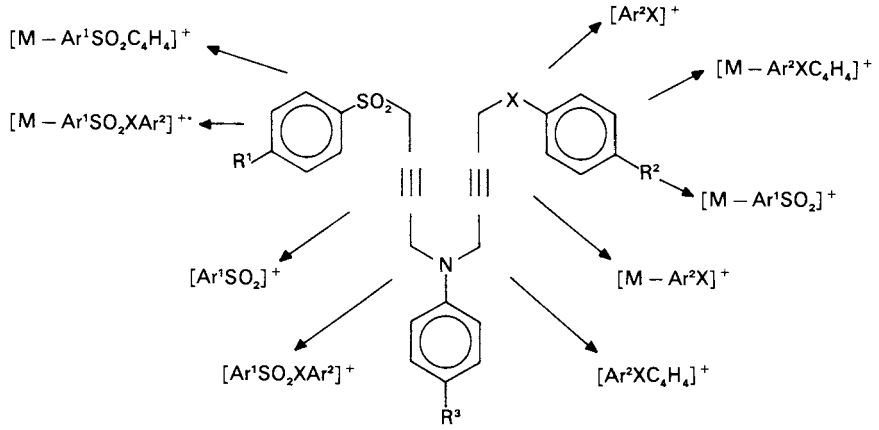
(23c)

R = H, 4-Me, 4-MeO, 4-Cl, 4-Br, 3,4-diCl, 3-Me, 4-Br

3. *N-(4'-Arylsulfonyl-2'-butynyl)-N-(4''-arylthio-2''-butynyl)- and N,N-bis(4'-arylsulfonyl-2'-butynyl)anilines*

In addition to the expectable bond fissions leading to the formation of $[M-Ar^1SO_2]^+$, $[M-Ar^2X]^+$, $[M-Ar^1SO_2C_4H_4]^+$, $[M-Ar^2XC_4H_4]^+$, $[Ar^1SO_2]^+$ and $[ArS]^+$ ions (equation 24), *N*-(4'-arylsulfonyl-2'-butynyl)-*N*-(4''-arylthio-2''-butynyl)- (**50**)[36] and *N*,*N*-bis(4'-arylsulfonyl-2'-butynyl)anilines (**51**)[37] display a concerted or fast consecutive elimination of the arylsulfonyl (Ar^1SO_2) and Ar^2X (X = S or SO_2) moieties yielding the abundant $[M-Ar^1SO_2XAr^2]^{+\cdot}$ ions. The latter (**51**) exhibit also the sulfone–sulfinate ester rearrangement as could be concluded from the intense $[ArSO]^+$ and $[ArO]^+$ ions, whereas the former do not undergo skeletal rearrangements at all[36]. Metastable peaks and

B/E scans established that the $[M - Ar^1SO_2SAr^2]^{+\cdot}$ ions from **50** are formed by the losses of Ar^2S from $[M - Ar^1SO_2]^+$ and Ar^1SO_2 from $[M - Ar^2S]^+$ and fragmented further via losses of a hydrogen atom, $\cdot R^3$, $\cdot C_2H_3$ and C_4H_4. In the case of **51** the $Ar^1SO_2SO_2Ar^2$ moiety, however, is lost *directly* from the molecular ion and the resulting sulfur-free fragments are exactly the same as those for the corresponding sulfides[37], where a similar concerted elimination of the two arylthio groups takes place.



(50) X = S (24)

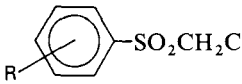
	a	b	c	d	e	f	g	h
R^1	Cl	Cl	Cl	Cl	Cl	H	Cl	H
R^2	H	CH_3	H	CH_3	Cl	Cl	Cl	Cl
R^3	H	H	CH_3	CH_3	CH_3	CH_3	CH_3O	CH_3O
$[M - Ar^1SO_2SAr^2]^{+\cdot}$/%	72	75	86	99	56	93	48	56

(51) X = SO_2

	a	b	c	d	e	f
$R^1 = R^2$	Cl	Cl	CH_3	CH_3	Br	Br
R^3	CH_3O	CH_3	CH_3O	CH_3	CH_3O	CH_3
$[M - Ar^1SO_2SO_2Ar^2]^{+\cdot}$/%	5	30	10	12	—	18

4. Aryl allyl and aryl propenyl sulfones and some arylsulfonylbutenes

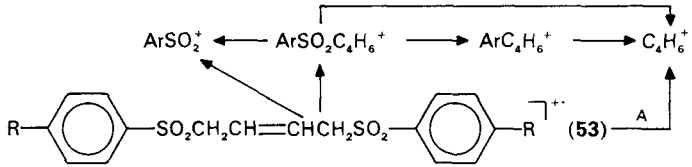
a. Aryl allyl sulfones. These compounds (**52**)[38] displayed three principal modes of fragmentation, namely C—S bond cleavage[4], sulfone–sulfinate ester rearrangement[1,2,4–6,11] and extrusion of SO_2[29]. Some hydrogen migration to the sulfone group occurred also, as could be concluded from the presence of abundant $[M - SO_2H]^+$ peaks in most of **52a–g**.



(52)

	a	b	c	d	e	f	g
R	4-Me	4-Cl	4-NH_2	3-Me	4-$NHCOCH_3$	H	2-CH_3

b. 1,4-bis(Arylsulfonyl)-2-butenes. The EI mass spectra of **53** (equation 25)[38] were dominated by the direct losses of the $ArSO_2^+$ and $ArSO_2C_4H_6^+$ ions and the subsequent elimination of SO_2 leading to the ion $ArC_4H_6^+$. No direct extrusion of SO_2 was observed as in the case of **43** and **52**. The mass spectral behavior of 1-aryloxy-2-butenyl-4-arylsulfones (**54**), however, was parallel to that of **53**. Here, as in **53**, $C_4H_6^{+\cdot}$, *m/z* 54, may arise also directly from the molecular ion (route A in equation 25) via the remote group interaction first observed in 2-butynyl-1,4-diarylsulfones[32] (equation 23). In other words, the remote group interaction resulting in the loss of C_4H_6 from the molecular ion overrides the extrusion of SO_2 when the allylic double bond is surrounded by more than one readily ionizable functional group capable of bonding by remote interaction. The above conclusions found support in the finding that **54** deuteriated at CH_2 α to the sulfone group releases $C_4H_6D_2$, *m/z* 56[38].



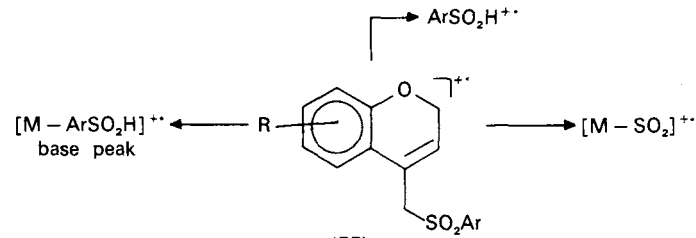
(25)

	a	b	c	d
R	Cl	Br	H	CH_3

$Ar^1OCH_2CH{=}CHCH_2SO_2Ar^2$ (**54**)

	a	b	c	d
Ar^1	Ph	Ph	*p*-MeC_6H_4	*p*-MeC_6H_4
Ar^2	2-naphthyl	*p*-*t*-BuC_6H_4	*p*-ClC_6H_4	*p*-BrC_6H_4

If the rotational freedom of the aryloxy group is restricted, as in 4-[(arylsulfonyl)methyl]-2*H*-1-benzopyranes (**55**), the remote group interaction is not possible anymore and these derivatives fragment mainly by ejecting $ArSO_2H$ and SO_2[38] (equation 26).

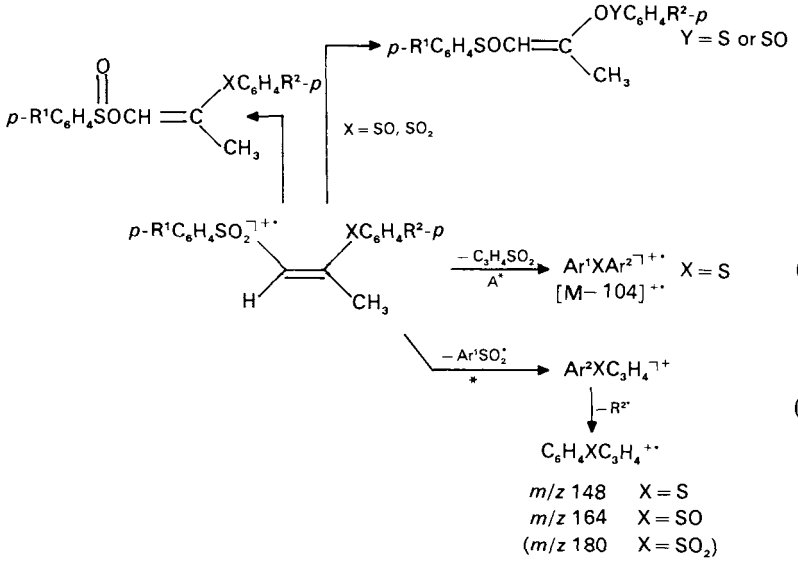


(26)

(**55**)

	a	b	c	d	e	f	g
R	4-Cl	4-Cl	H	4-Cl	4-Cl	*o*-Me	4-Cl
Ar	4-$MeOC_6H_4$	4-BrC_6H_4	4-ClC_6H_4	4-*t*-BuC_6H_4	4-$CH_3C_6H_4$	2-naphthyl	Ph

5. Aryl propenyl sulfones and Smiles rearrangement



(56) X = S		(57) X = SO		(58) X = SO_2	
R^1	R^2	R^1	R^2	R^1	R^2
Cl	Br	Cl	Br	Cl	Br
Cl	OMe	Br	Br	Cl	OMe
Br	Br	Cl	Cl	Br	Br
Cl	Cl	Cl	Me	Cl	Cl
Cl	Me	Me	Cl	Cl	Me
Me	Cl			Me	Me
Me	Me				

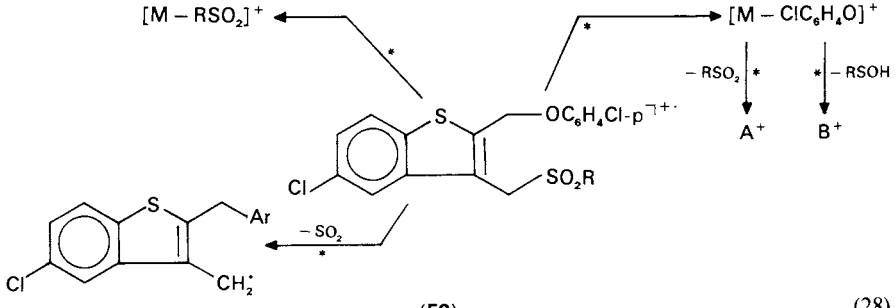
Both *cis*- and *trans*-1-arylsulfonyl-2-arylsulfenyl propenes (**56**) underwent a Smiles rearrangement under electron impact at 20 and 70 eV and formed a diarylsulfide ion $[M - 104]^{+\cdot}$ (equation 27a)[39] through a process where a bond between the $R^1C_6H_4$ group and the sulfide sulfur is formed and a rearomatization occurs by a loss of the neutral thiirene dioxide or a simultaneous expulsion of SO_2 and propyne. The ion *m/z* 148 was also obtained from all of the sulfonyl-sulfides, **56** (equation 27b) and here the loss of R^2 seemed to be related to the bond strength[39]. In addition to the above compounds **56** exhibited some simple cleavages before and after sulfone–sulfinate rearrangements.

In contrast to **56** the sulfonyl-sulfoxides (**57**) did not give the fragment $[M - 104]^{+\cdot}$ at all and the relative abundance of the ion *m/z* 164 which is analogous to the *m/z* 148 fragment (equation 27b) was also remarkably reduced, obviously due to the loss of the lone pair electrons on the sulfur via oxidation. Instead **57** gave various simple cleavages, in general similar to those of **56** and sulfonyl–sulfinate and sulfinyl–sulfenate rearrangements were also present.

Disulfones (**58**) showed no formation of the $[M - 104]^{+\cdot}$ or *m/z* 180 either (equations 27a and 27b, respectively) but fragmented mainly via the well-known sulfone–sulfinate rearrangement. Vinyl migration predominates in all of the above rearrangements

of **56–58** since there is no evidence of $C_6H_4O^+$, i.e. of aryl migration (see also Section II.E). The double bond geometry had hardly any effect on the mass spectra of **56–58**[39].

A Smiles rearrangement (equation 28) was also responsible for the secondary loss of SO_2 in the EI induced fragmentation of 2-(*p*-chlorophenoxymethyl)-3-arylsulfonylmethyl-5-chlorobenzo(*b*)thiophenes (**59**) but not in their 3-alkylsulfonylmethyl derivatives[33]. In the latter, the loss of RSO_2 from the molecular ions and those of RSO_2 and RSOH from the $[M - ClC_6H_4O]^+$ ions are the predominant routes of fragmentation.



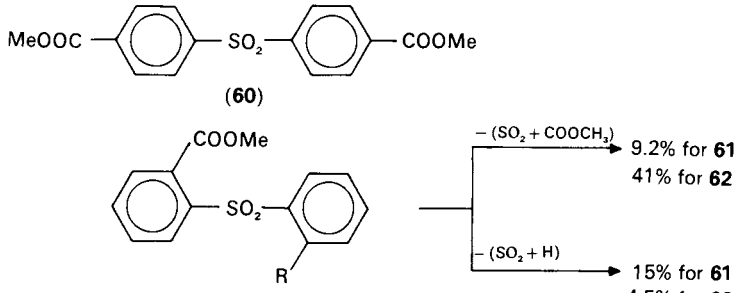
(**59**) (28)

	a	b	c	d	e
R	*p*-ClC_6H_4	2,5-diClC_6H_3	*p*-MeC_6H_4	*p*-BrC_6H_4	2-MeC_6H_4

	f	g	h	i	j
R	3-Me,4-BrC_6H_3	2,6-diMeC_6H_3	Cyclohexyl	Pr	Bu

D. Diaryl Sulfones and *Ortho* Effects

Bihari and coworkers[13] studied the EI mass spectra of compounds **60–62**. In the case of the *p*-substituted compound **60** an aryl migration followed by the S—OAryl bond rupture led to the most abundant ions, as could be expected[1,2,4–6,11]. The sulfone–sulfinate arrangement in the *ortho*-substituted compounds **61** and **62** was suppressed by a new mode of fragmentation resulting in very abundant $[M - (SO_2 + H)]^+$ and $[M - (SO_2 + COOCH_3)]^+$ ions. The formation of these ions involves an attack of an oxygen from the *o*-COOR group on the *ortho* position of the other aryl group which gives condensed cyclic structures (equation 29). Chlorodiphenyl sulfones[12] did not exhibit any special *ortho* effect (Section II.C).

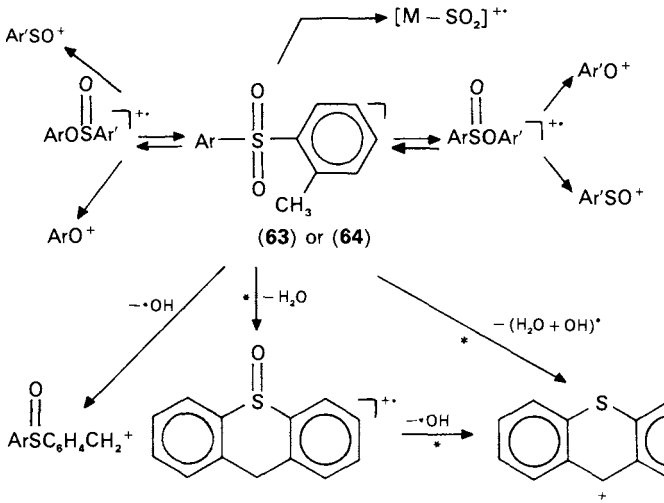


(**60**)

(**61**) R = H (29)

(**62**) R = COOMe

Efremov and coworkers investigated the mass spectra of 18 methyl-substituted diphenyl (**63**)[40] and substituted phenyl mesityl sulfones (**64**)[41]. The mass spectra of practically all the compounds showed by the rearrangement ions $[M-OH]^+$, $[M-H_2O]^{+\cdot}$ and $[M-(H_2O+OH)]^+$, the relative abundances of which depend on the position of the substituent in the phenyl moiety (*ortho* effect). It was also evident that in **63** the introduction of the first methyl substituent clearly decreases the contribution of the sulfone sulfinate isomerization (equation 30) to their fragmentation whereas the further substitution had little or no effect on the isomerization process in both **63**[40] and **64**[41].



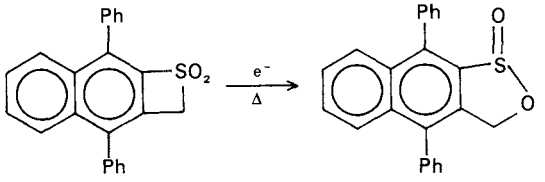
(30)

The rearrangement ions $[M-OH]^+$, $[M-H_2O]^{+\cdot}$ and $[M-H_2O+OH]^+$ (equation 30) were not present if **63** had no *ortho* methyl substituent but they were present in all of **64**. Accordingly, at least one of the eliminated hydrogens must be supplied by the methyl group and not by the aromatic rings. Some formation of $[M-SO_2]^{+\cdot}$ occurred also in both **63** and **64**.

E. Sulfone Function in a Heterocycle

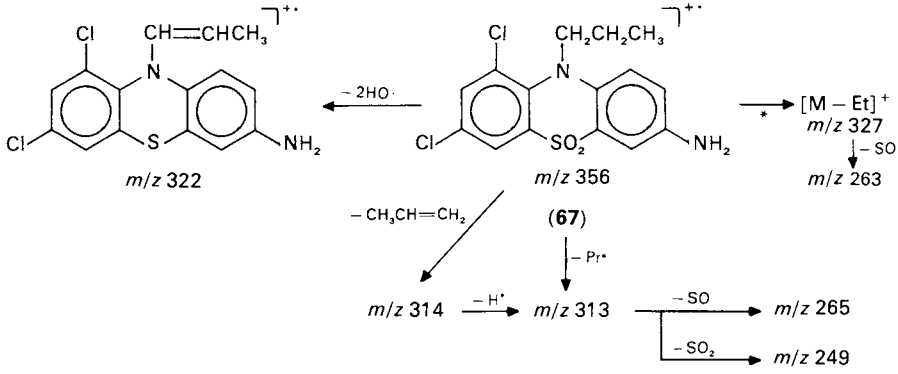
1. *Positive ion mass spectra of cyclic sulfones*

Phenanthro[4, 5-*b*, *c*, *d*]thiophene-4, 4-dioxide (**20**) fragments mainly via the cyclic sulfinate ester[15] (Section II.D). Naphthothiete sulfone (**65**) rearranges also to a cyclic sulfinate (**66**) prior to fragmentation, as shown by the similarities in their EI mass spectra[30]. The parent SO ion at *m/z* 308 which was much less pronounced for **65** than for **66** (10 vs. 54%) indicated, however, that the former does not decompose exclusively via **66**.



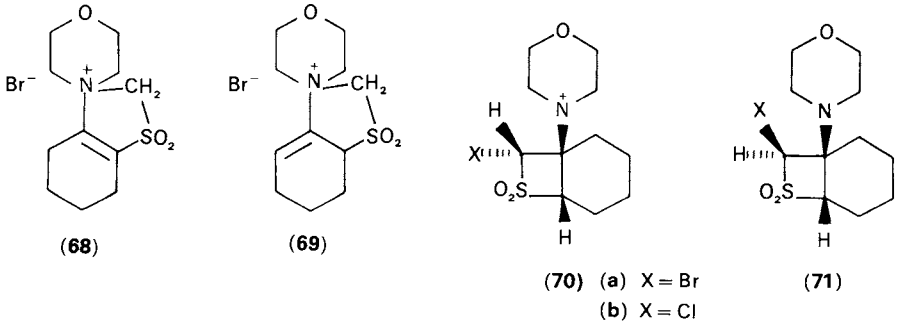
(**65**) (**66**)

In the mass spectrum of 10-propyl-3-amino-7,9-dichlorophenothiazine-5-sulfone (**67**) the molecular ion is quite intense, but the base peak is formed by the loss of Et from the propyl side-chain[16]. The other primary and secondary fragmentations are summarized in equation (31). The loss of two OH radicals (H_2O_2) can occur favorably from the *extra* configuration of **67** (cf. Section II.D).



(31)

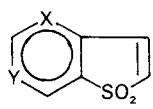
Goralski and Evans[42] stated the EI mass spectra of **68–71** to be in accord with their structures.



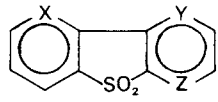
Klemm and coworkers[18b] studied the spectra of several thienopyridine sulfones (**72–78**) and found that it is possible to distinguish by mass spectrometry between a sulfone function and a combination of two sulfoxide or *N*-oxide functions in the same molecule[15]. For instance, compound **77** forms **78** losing the *N*-oxygen atom, since except for the molecular ion their mass spectra are very similar. Compound **78** rearranges prior to fragmentation to the two possible cyclic sulfinates (**80** and **81**), which then fragment further by losing SO and CNO, respectively.

Sulfone **74** (*m/z* 217, 100%) loses SO and then ketene, giving the ions *m/z* 169 (15%) and *m/z* 127 (10%)[15]. Another pathway begins with the cyclic sulfinate rearrangements (cf. **80** and **81**) and continues with a loss of CHO radical, giving the ions *m/z* 188 (11%). Sulfone **75** is symmetric and its mass spectrum is dominated by the cyclic sulfinate ester rearrangement, leading to the ions *m/z* 137 (C_6H_3NSO, 46%) and *m/z* 109 (C_5H_3NS, 83%), consecutively.

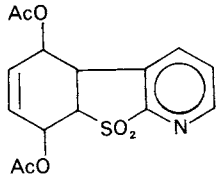
The molecular ion of **79** is of very low intensity and the most abundant peak in its mass spectrum corresponds to Ac^+. Losses of AcOH, ketene and SO_2 are also observed. The



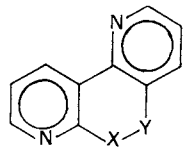
	X	Y
(72)	N	CH
(73)	CH	N



	X	Y	Z
(74)	CH	N	CH
(75)	N	N	CH
(76)	CH	CH	N
(77)	N→O	CH	N
(78)	N	CH	N



(79)



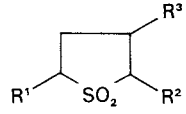
	X	Y
(80)	SO	O
(81)	O	SO

peak at *m/z* 217, $[M-2HOAc]^{+\cdot}$ can have the structure of **76** since the peaks corresponding to the most abundant ones in its mass spectrum, namely *m/z* 169, $[M-SO]^{+\cdot}$ (38%), *m/z* 162, $[M-(CO+HCN)]^{+\cdot}$ (33%), *m/z* 147, $C_9H_7S^+$ (47%) and *m/z* 127, $[M-SO_2CN]^+$ (39%) were also detectable in that of **76**.

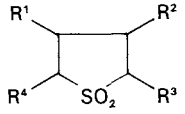
The mass spectrum of thieno[3,2-*c*]pyridine 1,1-dioxide (**73**) resembles closely that of **72**[43], the most important ions being $M^{+\cdot}$ (*m/z* 167, 54%), $[M-CHO]^+$ (*m/z* 138, 100%), $[M-SO]^{+\cdot}$ (*m/z* 119, 13%) and $C_5H_4NS^+$ (*m/z* 110, 26%).

2. *Negative ion mass spectra of cyclic sulfones*

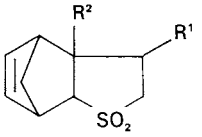
Furlei and coworkers[44] studied the negative ion mass spectra of several cyclic sulfones (**82–98**) upon dissociative electron capture and concluded that the negative molecular ions were notably stabilized by the introduction of electron-withdrawing substituents and/or unsaturation. Some difference was found in the negative ion mass spectra of configurational isomers (**85** vs. **86** and **87** vs. **88**) in contrast to the situation in their positive ion spectra. A strong SO_2 ion (*m/z* 64) was observed also for all the compounds studied.



	R^1	R^2	R^3	Configuration
(82)	H	H	H	–
(83)	CH_2=CH—	CH_2=CH—	H	?
(84)	CH_2=CH—	CH_2=CH—	CH_3	?
(85)	CH_2=C(CH_3)—	CH_2=CH—	H	*trans*
(86)	CH_2=C(CH_3)—	CH_2=CH—	H	*cis*
(87)	CH_2=C(CH_3)—	CH_2=C(CH_3)—	H	*trans*
(88)	CH_2=C(CH_3)—	CH_2=C(CH_3)—	H	*cis*



	R^1	R^2	R^3	R^4
(89)	H	=O	H	H
(90)	CH_3	=O	H	H
(91)	H	=O	H	CH_3
(92)	$C_8H_{17}SO_2$	H	H	H
(93)	H	=O	=CHPh	H
(94)	C_4H_9S—	=O	=CHPh	H
(95)	$C_8H_{17}S$—	=O	=CHPh	H
(96)	$C_8H_{17}S$—	H	H	H



	R^1	R^2
(97)	=O	H
(98)	H	$C_6H_{13}SO_2$—

F. Mass Spectra of Disulfones

1. β-Disulfones

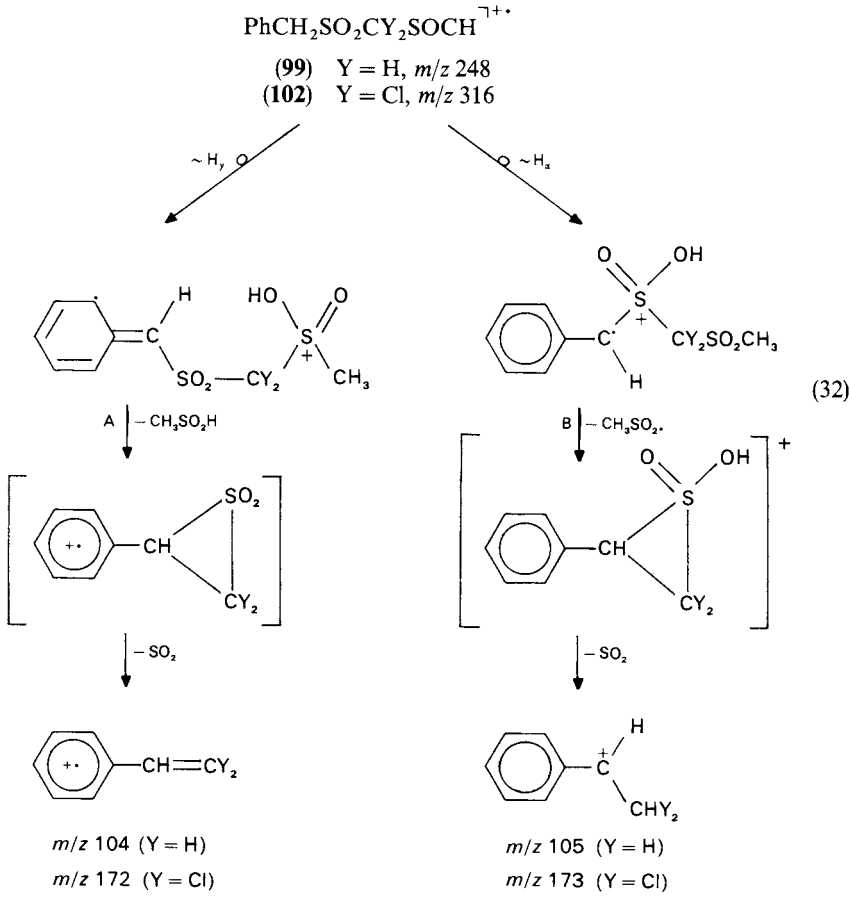
Langler and coworkers[45,46] studied the Ramberg–Bäcklund process[47] in the fragmentation of some β-disulfones (**99–105**). The mass spectra of these compounds are dominated by the tropylium ions as expected, but in addition to them and their fragmentation products a pair of ions at *m/z* 104/105 (172/173 when Y = Cl) were observed[45,46]. The compositions of the latter ions were C_8H_8 (or $C_8H_6Cl_2$) and C_8H_9 (or $C_8H_7Cl_2$) as shown by high-resolution measurements. By studying the mass spectra of compounds **99–103** it was first concluded that at least half of the *m/z* 104 ions came from a different source than the *m/z* 105 ions[45]. Since there is little reason to believe that one or other sulfonyl group, e.g. in **99**, ionizes more readily, routes A and B in equation (32) rationalize the independent appearance of the ions *m/z* 104 and 105, respectively. The former especially is very similar to the Ramberg–Bäcklund rearrangement of α-halosulfones[47]. The above postulation finds further support in the EI mass spectra of **106** and **107**, which do not exhibit the ions *m/z* 104/105 at all.

$PhCX_2SO_2CY_2SO_2CZ_3$

	X	Y	Z
(99)	H	H	H
(100)	D	H	H
(101)	H	D	H
(102)	H	Cl	H
(103)	H	H	D
(104)	H	H	$-CZ_3 = -Ph$
(105)	H	H	$-CZ_3 = -CH_2Cl$

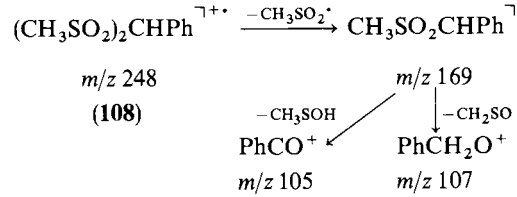
$PhCH_2XCH_2SO_2CH_3$

(106) X = S
(107) X = SO



(32)

In contrast to the situation in **106** and **107**, the mass spectra of both **104** and **105** show the presence of the expected ions at *m/z* 104 and 105[46]. In particular, the spectrum of **104** demonstrates that C-5 of, for instance, **99** is not contained in the *m/z* 104/105 ions in the mass spectrum of the latter, in agreement with the pathways shown in equation (32). Also $(CH_3SO_2)_2CHPh$ (**108**), which is isomeric with **99**, was prepared and its mass spectrum recorded. The latter includes the ion $CH_3SO_2CHPh^{+}$ (*m/z* 169) which fragments further to give the ions *m/z* 107 and *m/z* 105 (equation 33) of which the latter has different composition from that of the ions *m/z* 105 in the spectra of **99–105** and **103–105**, and hence the latter must be formed as shown in route **B** of equation (32).



(33)

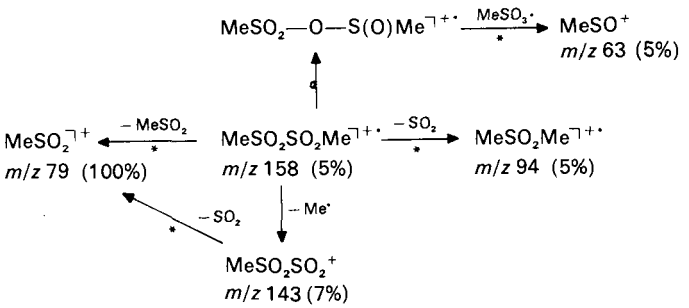
It is interesting to note here that two α-mesyl sulfonyl chlorides (**109** and **110**) have been found to exhibit a fragmentation process shown in equation (34)[48a].

$$CH_3SO_2CX_2SO_2Cl^{\neg+\cdot} \xrightarrow{-CH_3SO_2} X_2CSO_2Cl^{\neg+} \xrightarrow{-SO_2} X_2CCl^{\neg+} \qquad (34)$$

(**109**) X = H; *m/z* 192 (0%)	*m/z* 113 (5.5%)	*m/z* 49 (13%)
(**110**) X = Cl; *m/z* 260 (0%)	*m/z* 115 (1.8%)	*m/z* 51 (4.3%)
	m/z 181 (0.5%)	*m/z* 117 (83.3%)
	m/z 183 (0.47%)	*m/z* 119 (79.2%)
	m/z 185 (0.16%)	*m/z* 121 (26.4%)
		m/z 123 (2.8%)

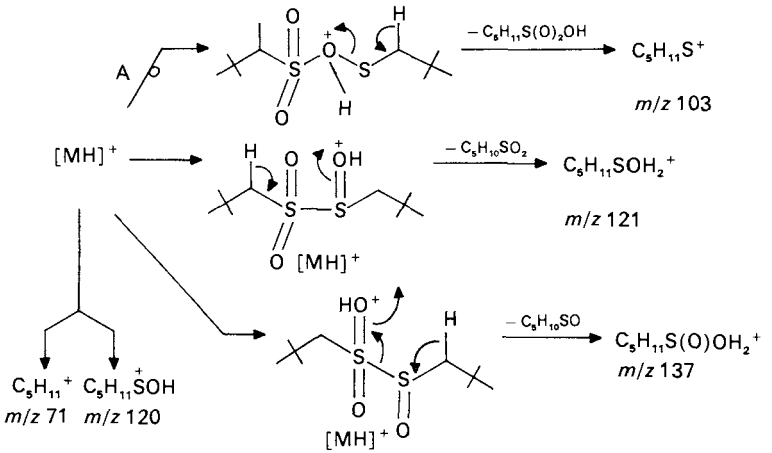
2. Sulfinyl sulfones and α-disulfones

Dimethyl α-disulfone forms the fragments shown in equation (35) under electron impact at 70 eV. The fragmentation processes are closely related to the thermal[48d] and photochemical[48e] results reported for diaryl α-disulfones. In contrast to $MeSO_2SMe$, $MeSO_2SO_2Me$ shows no indication of the formation of $MeS(OH)_2^{+}$[48b].



(35)

Freeman and Angeletakis[48c] studied the isobutane chemical ionization and EI induced mass spectra of 2, 2-dimethylpropyl 2, 2-dimethylpropanesulfinyl sulfone. In the former (equation 36) the main peaks are $[MH]^+$ *m/z* 255 (58%), $[MH + 1]^{+\cdot}$ *m/z* 256 (7%), [MH



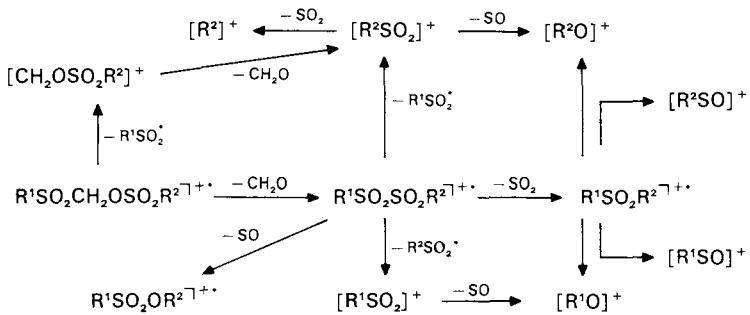
(36)

$+2]^+$ *m/z* 257 (8%), $C_5H_{13}SO_2^+$ *m/z* 137 (68%), $C_5H_{13}SO^+$ *m/z* 121 (100%), $C_5H_{11}SOH^+$ *m/z* 120 (96%), $C_5H_{11}S^+$ *m/z* 103 (43%) and $C_5H_{11}^+$ *m/z* 71 (100%) and in the latter $M^{+\cdot}$ *m/z* 254 (0.2%), $C_5H_{11}^+$ *m/z* 71 (100%), $SO_2^{+\cdot}$ *m/z* 64 (21%), $C_4H_9^+$ *m/z* 57 (96%), $C_4H_8^+$ *m/z* 56 (39%) and $C_4H_7^+$ *m/z* 55 (54%). In the CI spectrum fragment *m/z* 103 arises from the rearranged $[MH]^+$ ion (protonated sulfenyl sulfonate, route A in equation 36) by loss of 2,2-dimethylpropanesulfonic acid[48c]. Loss of thioaldehyde (C_4H_9CHS) and the formation of protonated 2,2-dimethylpropanesulfonic acid (*m/z* 153, 11%) are also possible via route A.

G. Some Miscellaneous Sulfones

1. Arylsulfonylmethyl sulfonates

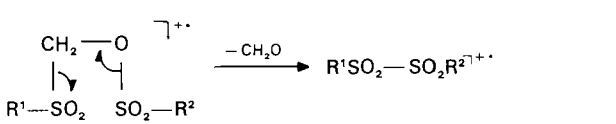
Graafland and coworkers[49] studied the EI mass spectra of 12 arylsulfonylmethyl sulfonates (**111–122**) at 70 eV and found them to fragment via the generalized pattern given in equation (37). All the reactions shown were supported by metastables. In general, the intensity of the $M^{+\cdot}$ peak was very low except with **121** and **122** (28 and 6%, respectively). The base peak was usually $[R^1SO_2]^+$ or $[R^2SO_2]^+$, but in the case of **112** and **121** it was $[R^1]^+$ and in the case of **122**, CF_3^+.



(37)

	R¹	R²		R¹	R²
(111)	Ph	*p*-$CH_3C_6H_4$	**(117)**	*p*-$CH_3C_6H_4$	2,3,6-$(O_2N)_3C_6H_2$
(112)	*p*-$CH_3C_6H_4$	Ph	**(118)**	*p*-$CH_3OC_6H_4$	*p*-$CH_3C_6H_4$
(113)	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	**(119)**	*p*-$O_2NC_6H_4$	*p*-$CH_3C_6H_4$
(114)	*p*-$CH_3C_6H_4$	*p*-$CH_3OC_6H_4$	**(120)**	*m*-ClC_6H_4	*p*-$CH_3C_6H_4$
(115)	*p*-$CH_3C_6H_4$	*p*-ClC_6H_4	**(121)**	*p*-$CH_3C_6H_4$	CF_3
(116)	*p*-$CH_3C_6H_4$	*p*-$O_2NC_6H_4$	**(122)**	*p*-$O_2NC_6H_4$	CF_3

The most interesting feature in the spectra of the above compounds is the presence of an intense peak for $[M-CH_2O]^{+\cdot}$ (except with **117** and **121**), the identity of which was checked by means of accurate mass measurements and deuteriation of the central methylene group. The following mechanism was proposed to explain the loss of CH_2O which governs very much also the consequent fragmentations (equation 38):



(38)

In order to find further support to this mechanism[49] (equation 38) the ratio of the intensities of two metastable decompositions of the $[M - CH_2O]^{+\cdot}$ ion of **113**, namely

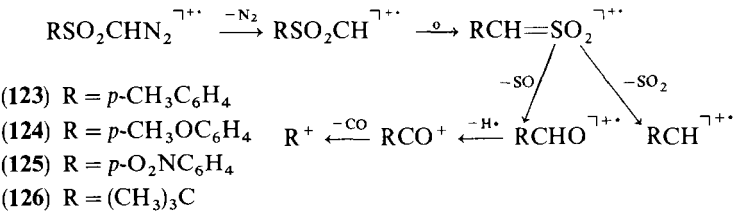
$$m/z\ 310 \xrightarrow{-R^1SO_2} m/z\ 155 \quad \text{and} \quad m/z\ 310 \xrightarrow{-SO} m/z\ 262$$

were determined. They were equal to those of di-*p*-tolyl disulfone (p-$CH_3C_6H_4SO_2$—$SO_2C_6H_4CH_3$-p) indicating that the molecular ion of the latter and the $[M - CH_2O]^{+\cdot}$ ion from **113** are likely to be identical, or at least consist of the same mixtute of structures[50].

The formation of the $[M - CH_2SO_2]^{+\cdot}$ ions (compounds **111–113, 115** and **116**) and of the $[M - CH_2SO_3]^{+\cdot}$ ions (compounds **114** and **117**) are at least partly two-step processes, since metastables could be observed for the losses of SO and SO_2, respectively. In the case of **122** the $[M - SO_2]^{+\cdot}$ ion was present (9%) and a metastable was observed for the formation of $[M - CH_2SO_3]^{+\cdot}$ from it but not via the $[M - CH_2O]^{+\cdot}$ ion[49].

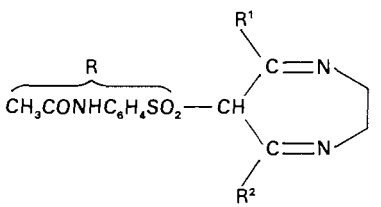
2. α-Diazosulfones

It has been reported that α-diazosulfones (**123–126**) do fragment via $[M - N_2]^{+\cdot}$ intermediates[51] although the peaks corresponding to these ions are not present in their EI mass spectra. The above view was supported by the metastables for m/z 168 → 104 (**123**), m/z 184 → 136 (**124**) and m/z 134 → 106 (**126**). A possible fragmentation pathway is outlined in equation (39) although it does not explain the formation of the $[M - N_2 - CO]^{+\cdot}$ ion (m/z 106), which is one of the main fragments of **126**; **126** does not give fragments $[M - N_2—SO]^{+\cdot}$ and $[M - N_2—SO—H]^{+}$ at all.

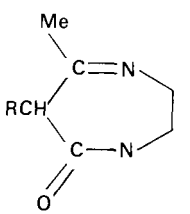


(**123**) R = p-$CH_3C_6H_4$
(**124**) R = p-$CH_3OC_6H_4$
(**125**) R = p-$O_2NC_6H_4$
(**126**) R = $(CH_3)_3C$ (39)

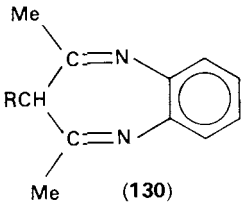
In this context it should be mentioned that some fragmentation data for compounds **127–131**[52] and **132–143**[53] have also been given. Compounds **127–131** do not exhibit peaks for the parent ions at all. Their base peaks are m/z 93 (anilinium ion, compounds **127–129**) and m/z 172 ($[M - R]^+$, compounds **130–131**).



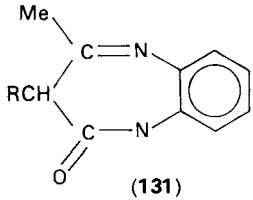
	R^1	R^2
(**127**)	Me	Me
(**128**)	Me	Ph



(**129**)



(130)

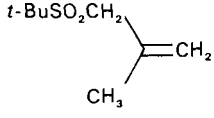


(131)

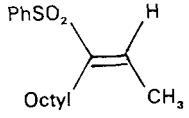
$RSO_2CH_2C(CH_3)_2CH_2C(=CH_2)CHXSO_2R$ t-$BuSO_2CHXCH(CH_3)Ph$

	R	X
(132a)	t-Bu	H
(132b)	p-$CH_3C_6H_4$	H
(132c)	p-$CH_3C_6H_4$	D

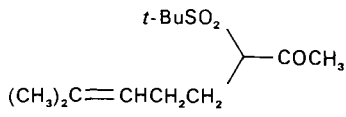
(133) X = H
(134) X = CH_3



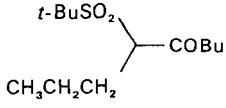
(135)



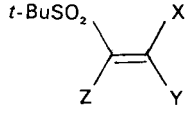
(136)



(137)



(138)



(139)–(143)

	X	Y	Z
(139*E*)	H	Me	$Me_2C{=}CHCH_2CH_2$
(139*Z*)	Me	H	$Me_2C{=}CHCH_2CH_2$
(140*E*)	H	Hexyl	Me
(141*E*)	H	Me	Hexyl
(141*Z*)	Me	H	Hexyl
(142*E*)	H	Bu	Pr
(142*Z*)	Bu	H	Pr
(143*E*)	H	Me	Me

IV. MASS SPECTRA OF SOME ENVIRONMENTALLY AND PHARMACEUTICALLY SIGNIFICANT SULFOXIDES OR SULFONES

A. Sulfoxides

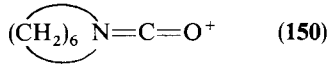
1. Carbamoyl sulfoxides

Most of the carbamoyl sulfoxides studied (**144–149**)[54] did not give measurable molecular ions although the $[M-O]^+$ ion was observed in each case(0.1–0.6%).

$R^1SOCONR_2^2$

	R^1	R^2		R^1	R^2
(144)	Et	Pr	**(147)**	p-$ClC_6H_4CH_2$	Et
(145)	Et	$-(CH_2)_6-(=R_2^2)$	**(148)**	Ph	Me
(146)	Et	*i*-Bu	**(149)**	p-ClC_6H_4	Me

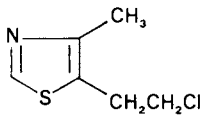
The fragmentation patterns were quite similar to those of the precursor thiocarbamates, i.e. the base peak was $R_2^2NCO^+$ or $R^{2\,1+}$ and major ions R^2NHCO^+, R^+ and $R^{2\,1+}$. Ions RSO^+ and $RSOH^{+\cdot}$ (1–8%) were unique to the sulfoxides. In the case of **145** most of the fragments arise, however, from the precursor ion **150**.



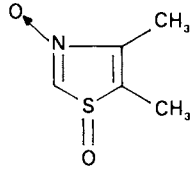
(150)

2. 4,5-Dimethylthiazole-N-oxide-S-oxide and two phenothiazine sulfoxides

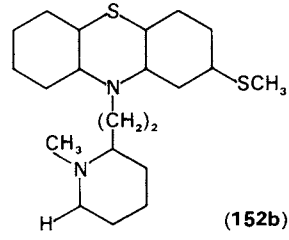
When studying the metabolic fate of chloromethiazole (**151**) in healthy male subjects Offen and coworkers[55a] separated a novel metabolite, $C_5H_7NO_2S$, which was shown to be 4,5-dimethylthiazole-*N*-oxide-*S*-oxide (**152**). Its EI mass spectrum showed a molecular ion at *m/z* 145, $[M-15]^+$ ion at *m/z* 130 and $[M-OH]^+$ ion at *m/z* 128. The major secondary fragments were due to the *m/z* 130 and 128 ions through the loss of CO and SO (*m/z* 102 and 100 and *m/z* 82, respectively). The isobutane chemical ionization spectrum of **152** included the $[M+1]^+$ ion at *m/z* 146 and the major fragment ion at *m/z* 130.



(151)



(152a)



(152b)

Papadopoulos and Crammer[55b] studied the sulphoxide intermediates of thioridazine (**152b**) in man.

B. Sulfones

1. Metabolites in the degradation of Demeton S-methyl sulfoxide by soil microorganisms

Ziegler and coworkers[56] observed that the title compound (**153**) formed, during degradation by *Pseudomonas putida* 1453 and *Nocardia sp.* DSM 43252, several sulfone metabolites (**154–158**) which were identified by comparing their EI mass spectra with those recorded for the synthesized reference compounds. Only **154** and **156** showed peaks for molecular ions in their EI mass spectra. The highest *m/z* values in the spectra shown[56] were accounted for by the loss of Me (**154**), EtSO (**155**), $EtSO_2$ (**156**), Et and EtO (**157**) and $EtSO_2$ (**158**). Cleavage of the ethoxy group from **157** is possible only after a sulfoxide–sulfenate ester rearrangement[1–4,6]. It was also observed that **156** and **158** split off two molecules of ethanesulfinic acid with the formation of the alkenes *m/z* 212 (58%) and *m/z* 180 (26%) and divinyl disulfide, $[CH_2{=}CHS]_2$, and divinyl sulfide, $[CH_2{=}CH]_2S$, respectively.

$(H_3CO)_2P(=O)SCH_2CH_2S(=O)CH_2CH_3$ **(153)**

$CH_3CH_2SO_2CH_2CH_2SH$ **(154)**

$[CH_3CH_2S(=O)CH_2CH_2S]_2$ **(155)** $[CH_3CH_2SO_2CH_2CH_2S]_2$ **(156)**

$[CH_3CH_2S(=O)CH_2CH_2]_2S$ **(157)** $[CH_3CH_2SO_2CH_2CH_2]_2S$ **(158)**

The field desorption mass spectra of **154–158** always showed the ions $[M+1]^+$, $[M+2]^+$ and $[M+3]^+$ in addition to the molecular ions which were the base peaks. No fragment peaks were seen in the latter spectra.

2. Polychloromethylsulfonylbiphenyls

Mizutani and coworkers[57a] confirmed the presence of polychloro(methylsulfonyl)biphenyls (**159–170**) as sulfur-containing metabolites of chlorobiphenyls (Cl-BP) in the feces of mice based on both GLC-mass spectrometry and chemical derivatization. In some cases comparison with authentic samples (**161** and **162**) was also made. When preparing **161** and **162**, 2, 5-dichloro-3-(methylsulfonyl)aniline, 2, 5-dichloro-1-iodo-3-(methylsulfonyl)benzene and 2,2′,5,5′-tetrachloro-3,3′-bis(methylsulfonyl)biphenyl were also obtained and their four peak EI mass spectra reported[57a]. Similar data were given for the corresponding 4-substituted intermediates, which were involved in the preparation of **162**. Also 2,4′,5-trichloro-2′-(methylsulfonyl)-biphenyl was prepared and its four peak mass spectra given. Metabolites **163** and **164** were also identified by comparison with the authentic standards.

(159)	2,3′,5-Cl_3-3-$MeSO_2$-BP	**(165)**	2,3′,5,5′-Cl_4-3-$MeSO_2$-BP
(160)	2,3′,5-Cl_3-4-$MeSO_2$-BP	**(166)**	2,3′,5,5′-Cl_4-4-$MeSO_2$-BP
(161)	2,4′,5-Cl_3-3-$MeSO_2$-BP	**(167)**	2,2′,3,4,5′-Cl_5-3′-$MeSO_2$-BP
(162)	2,4′,5-Cl_3-4-$MeSO_2$-BP	**(168)**	2,2′,3,4,5′-Cl_5-4′-$MeSO_2$-BP
(163)	2,2′,4,4′-Cl_4-6-$MeSO_2$-BP	**(169)**	2,2′,4,5,5′-Cl_5-3′-$MeSO_2$-BP
(164)	2,2′,4,4′-Cl_4-5-$MeSO_2$-BP	**(170)**	2,2′,4,5,5′-Cl_5-4′-$MeSO_2$-BP

The 3- or 3′-isomers gave in general a $[M-CH_2SO]^+$ (7–13% relative abundance, r.a.) but no $[M-Me]^+$ peaks, whereas the 4- or 4′-isomers exhibited $[M-MeSO]^+$ (17–39% r.a.) and $[M-Me]^+$ (3–6% r.a.) peaks[57,58]. These observations together with some complementary data served as criteria for the tentative assignment of the structures **159**, **160** and **165–170**.

Bergman and coworkers[59] synthesized 28 methylsulfonylpolychlorobiphenyls and studied the influence of the position of the sulfur-containing group on the EI-induced fragmentation. The ions $[CH_3SO]^+$, *m/z* 63 and $[CH_3SO_2]^+$, *m/z* 79 were always dominant but the $[M-CH_3SO]^+$ and $[M-CH_3SO_2]^+$ ions could also be seen. In all cases the loss of CH_3SO_2Cl, $[M-114]^{+\bullet}$, gave intense peaks (11–100% r.a.). 2-$MeSO_2$-derivatives with a 2-chloro substituent (**171, 173, 175** and **177**) show a strong loss of the chlorine atom. Formation of a dibenzofuran structure ($M-SOCH_3Cl$) occurs also in the 2-methylsulfonyl derivatives after a sulfone–sulfinate rearrangement[1–4,6,11]. Compounds **178–198** gave ions $[M-91]^+$ due to loss of $[CH_3SO+CO)$ which, together with the lack of the above-mentioned dibenzofuran ion, differentiate these sulfones from compounds **171–177**. The differentiation of the 3-$MeSO_2$ and 4-$MeSO_2$ biphenyls is not easy by the mass spectrometric data alone although the $[M-CH_3SO]^+$ ion is always at least somewhat more abundant for the latter[59].

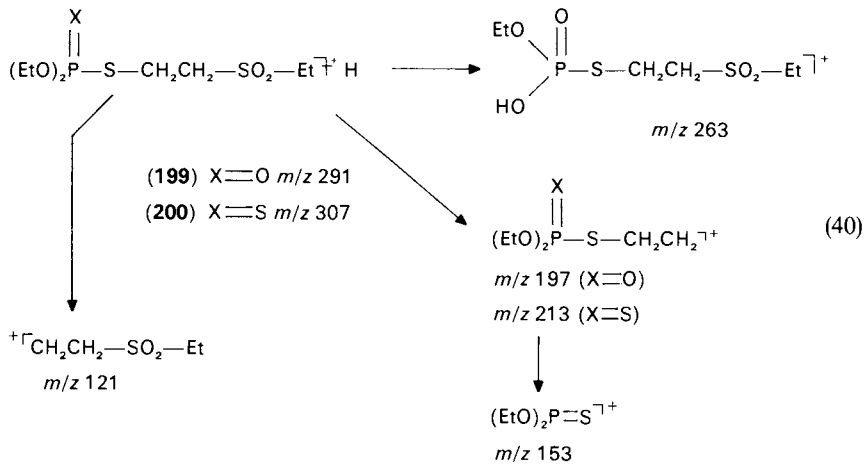
Recently Haraguchi and coworkers[57b] synthesized and characterized 86 methylsulfonyl derivatives of polychlorinated biphenyls. Their mass spectrometric conclusions were parallel to the previous ones[57a,58,59].

Dichloro-2-$MeSO_2$-BP	Trichloro-2-$MeSO_2$-BP	Dichloro-3-$MeSO_2$-BP
(171) 2′,5′-	**(176)** 3′,4′,5′-	**(178)** 2′,5′,-
(172) 3′,4′-	**(177)** 2′,3′,4′-	**(179)** 3′,4′-
(173) 2′,3′-		**(180)** 2′.3′-
(174) 3′,5′-		**(181)** 2′,6′-
(175) 2′,4′-	Trichloro-3-$MeSO_2$-BP	**(182)** 2′,4′-
	(184) 3′,4′,5′-	**(183)** 3′,5′-
	(185) 2′,3′,4′-	
Dichloro-4-$MeSO_2$-BP	Trichloro-4-$MeSO_2$-BP	Tetrachloro-4-$MeSO_2$-BP
(186) 2′,5′-	**(192)** 3′,4′,5′-	**(195)** 2,2′,5,5′-
(187) 3′,4′-	**(193)** 2′,3′,4′-	**(196)** 2,2′,4′,5-
(188) 2′,3′-	**(194)** 2,4′,5-	**(197)** 2,3′,4′,5-
(189) 2′,6′-		
(190) 2′,4′-	**(198)** 2,2′,4′,5,5′-Cl_5-4-$MeSO_2$-BP	
(191) 3′,5′-		

By treating groups of mice with 2,4′,5-trichlorobiphenyl and [^{35}S]cysteine or [^{35}S]methionine the formation of 4-[^{35}S]methylsulfonyl-2,4′,5-trichlorobiphenyl (**194**) was indicated and shown to deposit in the lungs. GC-MS analysis confirmed the presence of **194** as the minor component[60].

3. *Demeton-S-sulfone*

An unknown analytical response in lettuce was detected[61] and thought to contain P and S. The initial GC/MS CI CH_4 data were dominated by ions at *m/z* 121, 197 and 291 (equation 40). The GC/MS CI NH_3 data, however, indicated that perhaps the molecule had a higher molecular weight of 306 (MH^+ equal to *m/z* 307, cf. equation 40). Comparison with the CI CH_4 and CI NH_3 spectra of demeton-S- (**199**) and demeton-*O*-sulfones showed, however, that the retention time and mass spectra of the former only matched the unknown (except the omission of the ion at *m/z* 307). On another stationary phase (OV-101) limited mass scanning of the ion at *m/z* 121 revealed a second unknown (**200**) eluting at 4.2 min (the major unknown, i.e. demeton-*S*-sulfone at 3.0 min). The molecular weight of **200** was believed to be 306. Because of the presence of ions at *m/z* 121,



(40)

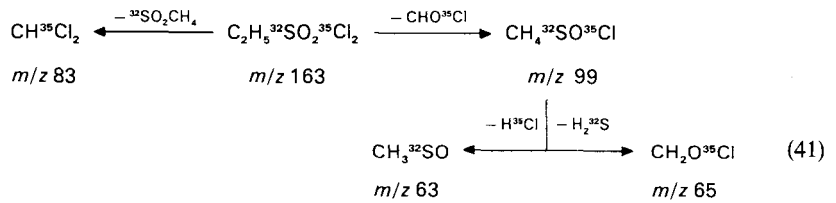
153 and 213 (197 + 16) the second and minor unknown was tentatively identified as the corresponding phosphorodithioate disulfoton sulfone (**200**)[61]. Some reference data can also be found in *Mass Spectral Data Compilation of Pesticides and Industrial Chemicals*[62].

4. 1,1-Dichlorodimethyl sulfone

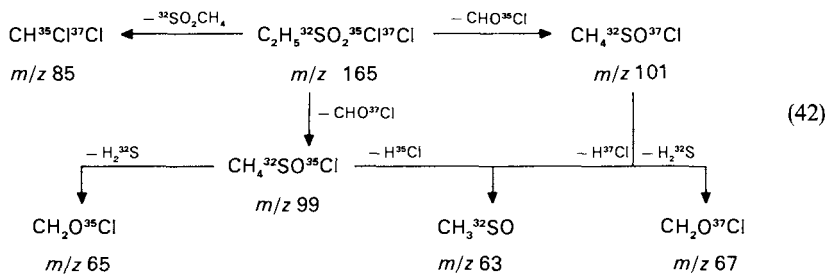
Lindström and Schubert[63] applied GC-MS, GC-MS-MS and direct inlet MS-MS to determine 1,1-dichlorodimethyl sulfone (**201**, DDS) in aquatic organisms outside a pulp mill bleach plant. Both GC-MS-MS and direct inlet MS-MS of tissue extracts of fish and mussel appeared to be sensitive, selective and fast techniques for the determination of DDS.

Only three ions of relatively high intensities were formed under electron impact, namely *m/z* 83 ($CH^{35}Cl^{35}Cl$; 100%), *m/z* 85 ($CH^{37}Cl^{35}Cl$; 66%) and *m/z* 87 ($CH^{37}Cl^{37}Cl$; 11%).

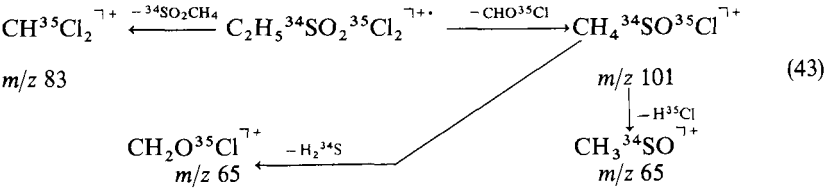
By CH_4-chemical ionization two predominant ions from DDS were formed in the ion source: *m/z* 163 (M + 1) and *m/z* 165 (M + 3), which were accelerated and separated in the first quadrupole. Decomposition by collision activation with argon then occurred in the second quadrupole and the resulting daughter ions were separated in the third quadrupole to give rise to collision-induced spectra (equations 41–43). When carrying out the analysis with a solid inlet MS-MS system (TSQ) it was observed that, when operating TSQ in the multiple ion detection mode and selecting the ions *m/z* 63, 83, 85, 99 and 101, only in the third quadrupole was there no interference from other *m/z* 163 and 165 precursor ions[63].



(41)



(42)

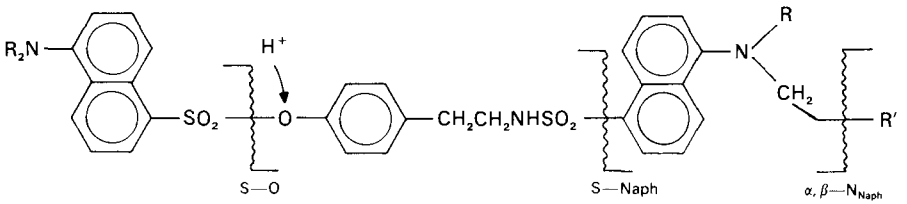


(43)

V. SULFONES WITH N—S BONDS

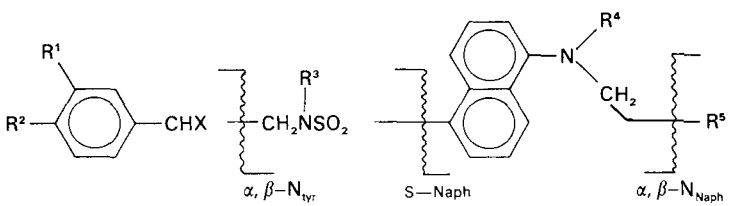
A. Sulfonamides

Davis[64a] prepared 5-dimethyl-, -diethyl-, -dipropyl-, -dibutyl- and -dipentylamino-naphthalene-1-sulfonyl derivatives of tyramine (**202–206**) and other biogenic amines and recorded their mass spectra to improve their quantitation. In the case of compounds **202–206** the major fragmentations included, in addition to α,β-N_{Naph} cleavage (equation 44), the breakages of the sulfate–oxygen (S—O) bond and the sulfur–naphthalene (S—Naph) bond. The intensity variations from one scan to another were, however, considerable and hence the sulfate ester linkage was avoided by methylating the phenolic oxygen atom or oxygen and nitrogen atoms after first derivatizing the nitrogen atom selectively with the dialkylaminonaphthalenesulfonyl chloride[64a]. Compounds **207–212**, e.g., were prepared in this way. The major types of fragmentation are shown in equation (45). The relative intensities of the molecular ions varied from 20 to 40%. The mixed derivatives exhibited a unique ion as the base peak and also improved the sensitivity substantially. Compound **208** seemed to be the best derivative studied[64a].



(44)

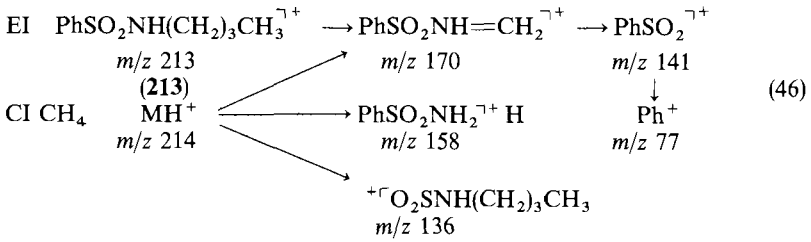
	R	R′		R	R′
(**202**)	Me	H	(**205**)	Bu	Pr
(**203**)	Et	Me	(**206**)	Pentyl	Bu
(**204**)	Pr	Et			

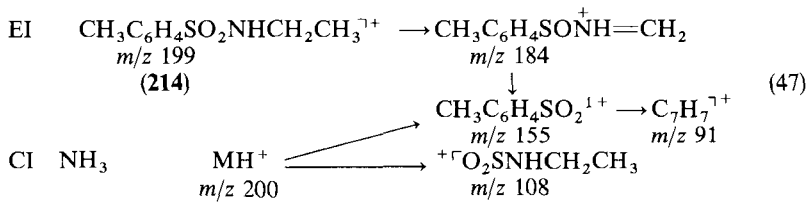


(45)

	R^1	R^2	R^3	R^4	R^5	X
(**207**)	H	H	H	Bu	Pr	H
(**208**)	H	CH_3O	CH_3	Bu	Pr	H
(**209**)	CH_3O	H	CH_3	Bu	Pr	H
(**210**)	H	CH_3O	CH_3	Bu	Pr	H
(**211**)	CH_3O	CH_3O	CH_3	Bu	Pr	H
(**212**)	H	CH_3O	CH_3	Bu	Pr	OH

Application of EI, CI NH_3 and CI CH_4 mass spectrometry[61] to the identification of a contaminant (**213**) in anhydrous sodium sulfate used for regulatory pesticide analysis revealed the fragmentation pathways shown in equation (46) which are typical for *N*-alkyl substituted sulfonamides[64b] (*m/z* 170) with benzene as the aromatic nucleus (*m/z* 158, *m/z* 136). The lack of an ion at *m/z* 91 (the tropylium ion) also strongly suggested that there were no methylene or methyl groups directly attached to the aromatic ring. Similarly, a pesticide analysis of samples of dried apple rings[61] revealed three unknown analytical responses. All three compounds gave the same ions but in different relative abundances. One of the contaminants gave the EI and CI NH_3 spectra given in equation (47) on the basis of which this compound was 4-methyl-*N*-ethylbenzenesulfonamide. This was also verified by a reference compound[61,64b]. The other two structures were assumed to be the *meta* and *ortho* counterparts of **214**.



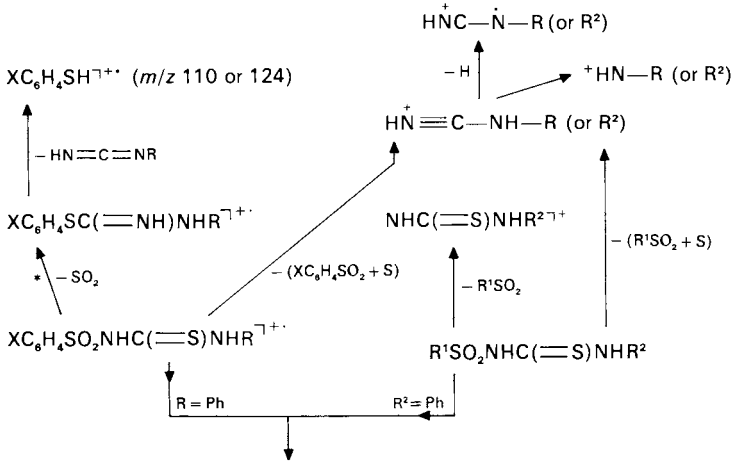


B. Arene- and Alkanesulfonylthioureas

Duffield and coworkers[65] studied the EI- induced mass spectra of five arene- (**215–219**) and four alkane sulfonylthioureas (**220–223**) and observed two rearrangement processes, namely loss of SO_2 from **215–219** and the elimination of $ArSO_2$ and RSO_2 with the thione sulfur atom from **215–223**. The other fragmentations involved simple bond cleavages with and without hydrogen transfer (equation 48). The loss of H_2S was evident for all the compounds studied except **221** and **222**. It was, however, found to be a thermal and not an ionization process.

C. Sulfonylhydrazides

As a result of some contradictory observations in earlier reports[66,67] Kascheres and Van Fossen Bravo[68] reinvestigated the mass spectra of a series of substituted benzenesulfonylhydrazines (**224–236**). All the compounds give molecular ions, which are moderately abundant for compounds **224–232** (X electron donating) but very weak for compounds **233–236** (X electron withdrawing). The main fragmentations corresponded to loss of $N_2H^{\bullet}$ and/or N_2H_2 from the rearranged molecular ions, as confirmed by mass analyzed ion kinetic energy (MIKE) spectra. The consequent $[M-29]^+$ or $[M-30]^{+\bullet}$ ions were abundant for compounds **224–228** and **231**, of medium intensity for compounds **229**, **230**,



(48)

	R	X		R¹	R²
(215)	Ph	H	(220)	Me	Et
(216)	Ph	*p*-Me	(221)	Pr	Et
(217)	Me	H	(222)	Pr	Bu
(218)	Et	H	(223)	Me	Ph
(219)	Pr	H			

232 and **233**, and weak for **234–235**. An $[M - SO_2]^{+\cdot}$ ion was of significance only for **233–235** (14–25%) although it was observed in the spectra of all the compounds ($\leqslant 2\%$). All the hydrazides exhibited also a simple S—N bond cleavage with retention of the charge on nitrogen, i.e. the formation of the N_2H_3 ion (*m/z* 31). This cleavage was favoured by electron-withdrawing substituents.

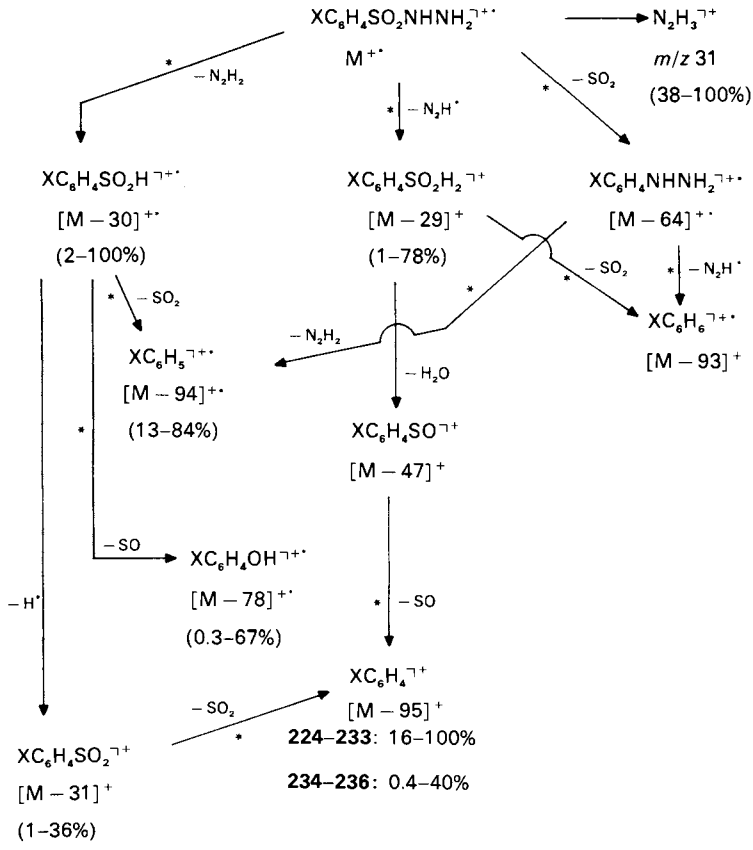
$XC_6H_4SO_2NHNH_2$

	X		X		X
(224)	H	(228)	2-OMe	(233)	4-COOH
(225)	4-Me	(229)	4-Br	(234)	4-NO_2
(226)	4-OMe	(230)	4-Cl	(235)	3-NO_2
(227)	3-OMe	(231)	4-NHAc	(236)	2-NO_2

$2,4,6\text{-}Me_3C_6H_2SO_2NHNH_2$
(**232**)

It is interesting to note that a plot of σ values for the substituents X vs $\log Z/Z_0$ for *m/z* 31 gave a good linear Hammett correlation with a $\rho = +0.52$, in agreement with an earlier observation[67]. Of the three nitro derivatives (**234–236**) 2-nitrobenzenesulfonylhydrazide (**236**) exhibits a seven times more intense $[M - 30]^{+\cdot}$ ion than the 4- and 3-nitro derivatives (**234** and **235**), obviously because of a facile rearrangement of a hydrazide hydrogen to an oxygen of the 2-nitro group (equation 49). The low intensity of the $[M - SO_2]^{+\cdot}$ ion from **236** in comparison with that from **234** and **235** could in turn be due to

steric inhibition by the *ortho* nitro group. Some other *ortho* effects were also speculated on the basis of the MIKE-spectra.

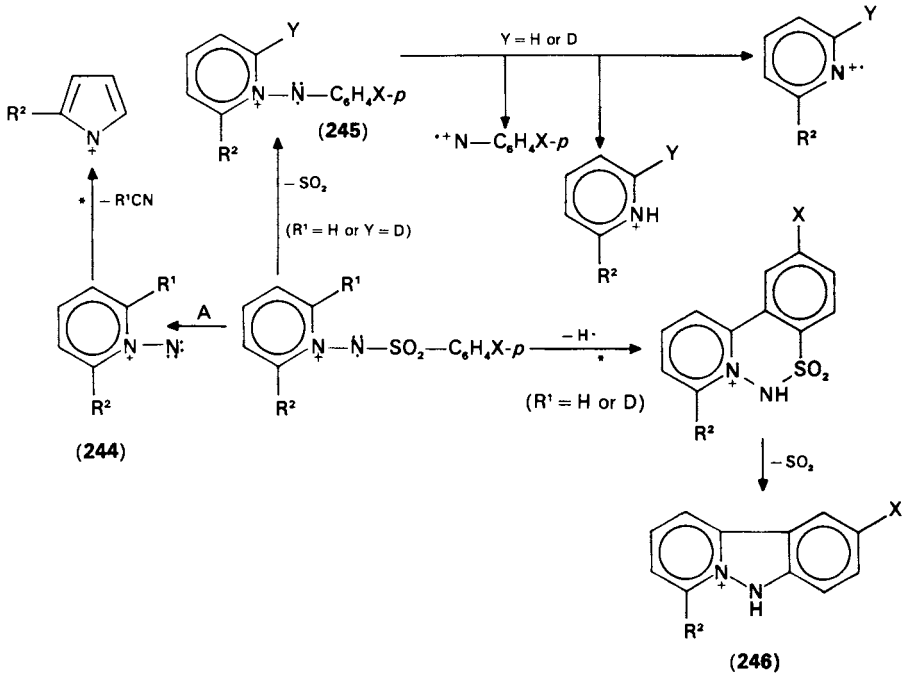


(49)

D. *N*-Arenesulfonyliminopyridinium Betaines

Characteristic for the fragmentation of the title compounds (**237**–**243**)[69] are a very facile N—S bond cleavage (route A in equation 50 giving rise to **244**) as in sulfonylhydrazides (Section V.C) and skeletal rearrangements accompanied by the extrusion of SO_2 from the $M^{+\cdot}$ and $[M-1]^+$ ions to the ionized *N*-aryliminopyridinium betaines (**245**, compounds **237**–**239**) or *N*-imino-2-benzylpyridinium betaines (**247**, compounds **240**–**243** in equation 52) and azacarbazoles (**246**), respectively[69]. Ion **244** decomposes further by elimination of HCN and via the loss of R^1N and HCN, as shown in equation (51). The sequence $M^{+\cdot}$ (**240**–**243**) → **247** → **248** (equation 52) is supported by the fact that *N*-imino-α-alkylpyridinium betaines can lose an NH_2 radical due to the operation of an *ortho* effect[70].

The mechanistic conclusions described in equations (50)–(52) were all supported by the observations related to the deuterium labelling, metastables and accurate mass measurements[69].

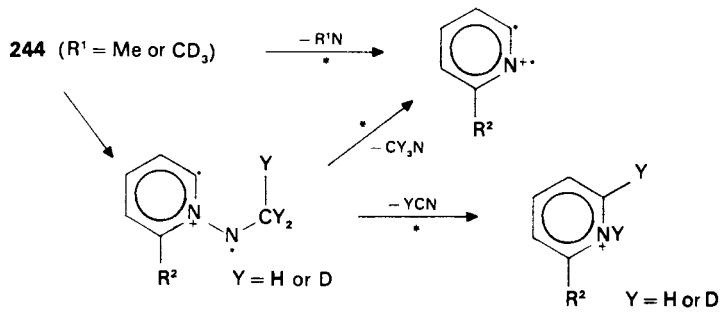


(50)

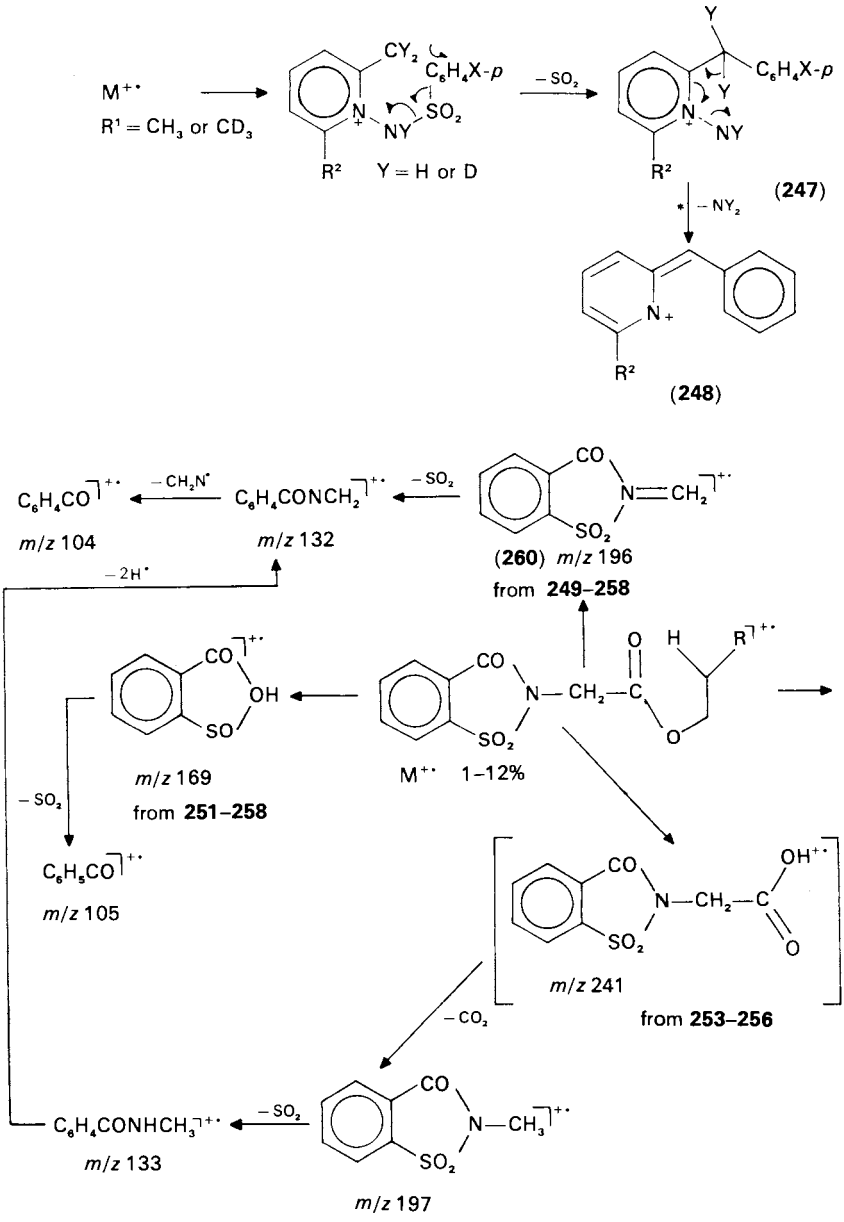
	X	R^1	R^2
(237a)	H	H	H
(237b)	H	D	D
(237c)*	H	D	D
(238)	Me	H	H
(239)	Cl	H	H

	X	R^1	R^2
(240)	H	Me	H
(241a)	H	Me	Me
(241b)	H	CD_3	CD_3
(242)	Me	Me	Me
(243)	Cl	Me	Me

* d_5-pyridinium



(51)


M+·
R1 = CH3 or CD3
CY2
C6H4X-p
SO2
NY
R2
Y = H or D
− SO2
Y
(247)
* − NY2
(248)
(52)
C6H4CO+·
− CH2N·
C6H4CONCH2+·
m/z 104
m/z 132
− SO2
(260) m/z 196
from 249–258
− 2H·
CO
OH
SO
m/z 169
from 251–258
M+· 1–12%
O
H
R+·
OR+·
(259)
− SO2
C6H5CO+·
m/z 105
OH+·
m/z 241
from 253–256
− CO2
C6H4CONHCH3+·
m/z 133
CH3+·
m/z 197

E. 2-Substituted 2*H*-1,2-Benzisothiazolin-3-one 1,1-Dioxide

Svoboda and coworkers[71] prepared several 2-substituted 2*H*-1,2-benzisothiazolin-3-ones (**249–258**; R = Me, $C_6H_5CH_2$, CH_3COCH_2, $C_6H_5COCH_2$, CH_3OCOCH_2, $CH_3OCH_2CH_2OCOCH_2$, $CH_3CH_2OCH_2CH_2OCOCH_2$, $C_6H_5OCH_2CH_2OCOCH_2$, $CH_3OCOCH(CH_3)$ and $CH_3CH_2OCOCH_2CH_2CH_2$, respectively) and discussed their EI mass spectra. The course of fragmentation depends substantially on the character of the N-substituent, as can be seen from equation (53). The ion *m/z* 241, an outcome of McLafferty rearrangement in **253–256**, was not very numerous since the ion **259** retains the charge although the former gives also ion *m/z* 197. The ion *m/z* 196 (**260**) can be formed in all cases and acts as a precursor for ions *m/z* 132 and 104, respectively. The ion *m/z* 197 is equal to $[\mathbf{249}]^{+\cdot}$ and can hence give ions **260** (*m/z* 196) and then *m/z* 132 → *m/z* 104. Alternatively, *m/z* 197 gives *m/z* 133 via loss of SO_2 and then *m/z* 132 → *m/z* 104[72]. The formation of *m/z* 105 was explained by elimination of SO_2 from the ion *m/z* 169, which can be obtained from the parent ions of **251–258** by a rearrangement analogous to that described for phthalic acid ester[4]. See also the report by Gillis[73].

VI. REFERENCES

1. S. Meyerson, H. Drews and E. K. Fields, *Anal. Chem.*, **36**, 1294 (1964).
2. R. A. Khmel'nitskii and Yu. A. Efremov, *Russ. Chem. Rev.*, **46**, 46 (1977).
3. Q. N. Porter, *Mass Spectrometry of Heterocyclic Compounds*, 2nd ed., Wiley, New York, 1985, Chap. 8, pp. 358, 361–362, 366–367, 370; Chap. 9, pp. 374–375, 379–380, 391–392, 397, 399, 407, 409, 412–413, 415–416; Chap. 10, pp. 430, 440–441, 444; Chap. 11, pp. 458, 461–462, 464.
4. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, Chap. 19, Holden-Day, San Francisco, 1967, pp. 552–566.
5. P. Brown and C. Djerassi, *Angew. Chem., Int. Ed. Engl.*, **6**, 490 (1967).
6. J. H. Bowie, B. K. Simons and S.-O. Lawesson, *Rev. Pure Appl. Chem.*, **19**, 71 (1969).
7. R. G. Cooks, *Org. Mass Spectrom.*, **2**, 481 (1969).
8. R. M. Dodson, P. J. Cahill and V. C. Nelson, *Chem. Commun.*, 620 (1968).
9. (a) R. Lüdersdorf, K. Praefcke and H. Schwarz, *Org. Mass Spectrom.*, **13**, 179 (1978).
   (b) P. Potzinger, H.-U. Stracke, W. Küpper and K. Gollnick, *Z. Naturforsch.* **30a**, 340 (1975).
10. A. O. Pedersen, G. Schroll, S.-O. Lawesson, W. A. Laurie and R. I. Reed, *Tetrahedron*, **26**, 4449 (1970).
11. J. H. Bowie, D. H. Williams, S.-O. Lawesson, J. O. Madson, C. Nolde and G. Schroll, *Tetrahedron*, **22**, 3515 (1966).
12. I. Granoth, *J. Chem. Soc., Perkin Trans. 2*, 1503 (1972).
13. M. Bihari, J. Tamás, I. Kapovits and J. Rábai, *Adv. Mass Spectrom.*, **7B**, 1362 (1978).
14. Yu. A. Efremov, A. G. Popova, R. A. Khmel'nitskii, A. Ya. Kaminskii and N. V. Fedyainov, *J. Org. Chem. USSR*, **16**, 1072 (1980).
15. L. H. Klemm, D. R. McCoy and D. R. Olson, *J. Heterocycl. Chem.*, **7**, 1347 (1970).
16. (a) D. Simov and I. G. Taulov, *Org. Mass Spectrom.*, **5**, 1133 (1971).
    (b) I. G. Taulov, J. Tamás, J. Hegedüs-Vajda and D. Simov, *Acta Chim. Acad. Sci. Hung.*, **105**, 109 (1980).
    (c) I. G. Taulov, J. Tamás, J. Hegedüs-Vajda and D. Simov, *Acta Chim. Acad. Sci. Hung.*, **105**, 117 (1980).
17. J. P. Malrieu and B. Pulman, *Theor. Chim. Acta*, **2**, 293 (1964).
18. (a) L. H. Klemm, R. E. Merrill and F. H. W. Lee, *J. Heterocycl. Chem.*, **11**, 535 (1974).
    (b) L. H. Klemm, S. Rottschaefer and R. E. Merrill, *J. Heterocycl. Chem.*, **12**, 1265 (1975).
19. L. K. Liu and F.-T. Luo, *Org. Mass Spectrom.*, **18**, 22 (1983).
20. T. H. Kinstle and W. R. Oliver, *Org. Mass Spectrom.*, **6**, 699 (1972).
21. H. W. Gibson and D. A. McKenzie, *J. Org. Chem.*, **35**, 2994 (1970).
22. D. Diller and F. Bergmann, *Org. Mass Spectrom.*, **12**, 294 (1977).
23. D. Diller and F. Bergmann, *J. Org. Chem.*, **37**, 2147 (1972).
24. (a) L. K. Liu and C. T. Hong, *Org. Mass Spectrom.*, **13**, 675 (1978).
    (b) D. L. Corina, D. P. Bloxham and G. K. Cooper, *J. Chromatogr.*, **198**, 287 (1980).
25. I. Pratanata, L. R. Williams and R. N. Williams, *Org. Mass Spectrom.*, **8**, 175 (1974).
26. F. Bergmann and D. Diller, *Org. Mass Spectrom.*, **12**, 338 (1977).

27. R. T. Aplin and K. Bailey, *J. Chem. Soc. (B)*, 513 (1967).
28. I. W. Jones and J. C. Tebby, *Phosphorus Sulfur*, **5**, 57 (1978).
29. D. K. Bates and B. S. Thyagarajan, *Int. J. Sulfur Chem.*, **3**, 57 (1973).
30. D. C. Dittmer, R. S. Henion and N. Takashina, *J. Org. Chem.*, **34**, 1310 (1969).
31. D. C. Dittmer and R. Glassman, *J. Org. Chem.*, **35**, 999 (1970).
32. B. S. Thyagarajan, D. K. Bates, K. C. Majumdar and P. Brown, *Int. J. Sulfur Chem.*, **8**, 551 (1976).
33. B. S. Thyagarajan and K. C. Majumdar, *Phosphorus Sulfur*, **1**, 55 (1976).
34. C. J. M. Stirling, *Chem. Commun.*, 131 (1967).
35. B. S. Thyagarajan, P. E. Glaspy, E. Baker and P. Brown, *Org. Mass Spectrom.*, **15**, 224 (1980).
36. P. E. Glaspy, R. A. Hancock and B. S. Thyagarajan, *Org. Mass Spectrom.*, **20**, 281 (1985).
37. B. S. Thyagarajan, P. E. Glaspy and P. Brown, *Org. Mass Spectrom.*, **15**, 22 (1980).
38. B. S. Thyagarajan, K. C. Majumdar and D. K. Bates, *Phosphorus Sulfur*, **1**, 67 (1976).
39. C. J. Hill, B. S. Thyagarajan, D. K. Bates and R. J. Spangler, *Org. Mass Spectrom.*, **12**, 379 (1977).
40. Yu. A. Efremov, R. A. Khmel'nitskii and N. V. Fedyainov, *J. Org. Chem. USSR*, **16**, 95 (1980).
41. Yu. A. Efremov and N. V. Fedyainov, *J. Org. Chem. USSR*, **18**, 1679 (1982).
42. C. T. Goralski and T. E. Evans, *J. Org. Chem.*, **37**, 2080 (1972).
43. L. H. Klemm and R. E. Merrill, *J. Heterocycl. Chem.*, **9**, 293 (1972).
44. I. I. Furlei, V. K. Mavrodiev, E. E. Shul'ts, R. V. Kunakova, U. M. Dzhemilev and G. A. Tolstikov, *Izv. Akad. Nauk, Ser. Khim.*, no. 11, 2477 (1985).
45. W. R. Hardstaff and R. F. Langler, *Org. Mass Spectrom.*, **10**, 215 (1975).
46. R. F. Langler, W. S. Mantle and M. J. Newman, *Org. Mass Spectrom.*, **10**, 1135 (1975).
47. L. A. Paquette, *J. Amer. Chem. Soc.*, **86**, 4085, 4089, 4383 (1964).
48. (a) W. R. Hardstaff, R. F. Langler and M. J. Newman, *Org. Mass Spectrom.*, **9**, 1156 (1974).
(b) E. Block, M. D. Bentley, F. A. Davis, I. B. Douglass and J. A. Lacadie, *J. Org. Chem.*, **40**, 2770 (1975).
(c) F. Freeman and C. N. Angeletakis, *Org. Mass Spectrom.*, **17**, 114 (1982).
(d) J. L. Kice and N. A. Favstritsky, *J. Org. Chem.*, **35**, 116 (1970).
(e) M. Kobayashi, K. Tanaka and H. Minatano, *Bull. Chem. Soc. Japan*, **45**, 2906 (1972).
49. T. Graafland, J. B. F. N. Engberts and W. D. Weringa, *Org. Mass Spectrom.*, **10**, 33 (1975).
50. T. W. Shannon and F. W. McLafferty, *J. Amer. Chem. Soc.*, **88**, 5021 (1966).
51. O. Luinenburg, J. B. F. N. Engberts and W. D. Weringa, *Org. Mass Spectrom.*, **9**, 837 (1974).
52. D. Gupta and B. C. Joshi, *Anal. Chem. Symp. Ser.*, **12**, 143 (1983).
53. J.-L. Fabre, M. Julia and J.-N. Verpeaux, *Bull. Soc. Chim. Fr.*, 762 (1985).
54. C. K. Tseng and J. F. Bolow, *J. Agric. Food Chem.*, **25**, 1383 (1977).
55. (a) C. F. Offen, M. J. Frearson, K. Wilson and D. Burnett, *Xenobiotica*, **15**, 503 (1985).
(b) A. S. Papadopoulos and J. L. Crammer, *Xenobiotica*, **16**, 1097 (1986).
56. W. Ziegler, G. Engelhardt, P. R. Wallnöfer, L. Oehlmann and K. Wagner, *J. Agric. Food Chem.*, **27**, 1102 (1980).
57. (a) T. Mizutani, K. Yamamoto and K. Tajima, *J. Agric. Food Chem.*, **26**, 862 (1978).
(b) K. Haraguchi, H. Kuroki and Y. Masuda, *J. Agric. Food Chem.*, **35**, 178 (1987).
58. T. Mio, K. Sumino and T. Mizutani, *Chem. Pharm. Bull.*, **24**, 1958 (1976).
59. Å. Bergman, B. Jansson and I. Bamford, *Biomed. Mass Spectrom.*, **7**, 20 (1980).
60. Å. Bergman, I. Brandt, Y. Larsson and C. A. Wachtmeister, *Chem.-Biol. Interact.*, **31**, 65 (1980).
61. T. Cairns, E. G. Siegmund, R. A. Jacobson, T. Barry, G. Petzinger, W. Morris and D. Heikes, *Biomed. Mass Spectrom.*, **10**, 301 (1983).
62. T. Cairns, E. G. Siegmund and R. A. Jacobson, *Mass Spectral Data Compilation of Pesticides and Industrial Chemicals*, Food and Drug Administration, Los Angeles, 1981.
63. K. Lindström and R. Schubert, *J. High. Res. Chrom., Chrom. Commun.*, **7**, 68 (1984).
64. (a) B. A. Davis, *Biomed. Mass Spectrom.*, **6**, 149 (1979) and references cited therein.
(b) G. M. Singer, W. Lijinsky and W. T. Rainey, Jr., *Org. Mass Spectrom.*, **10**, 473 (1975).
65. A. M. Duffield, G. Djerassi, R. Neidlein and E. Heukelbach, *Org. Mass Spectrom.*, **2**, 641 (1969).
66. E. Dynesen, S.-O. Lawesson, G. Schroll, J. H. Bowie and R. G. Cooks, *J. Chem. Soc. (B)*, 15 (1968).
67. F. Balza and N. Duran, *Org. Mass Spectrom.*, **8**, 413 (1974).
68. C. Kascheres and R. Van Fossen Bravo, *Org. Mass Spectrom.*, **14**, 293 (1979).
69. M. Ikeda, S. Kato, Y. Sumida and Y. Tamura, *Org. Mass Spectrom.*, **5**, 1383 (1971).
70. M. Ikeda, N. Tsujimoto and Y. Tamura, *Org. Mass Spectrom.*, **5**, 935 (1971).
71. J. Svoboda, J. Paleček and V. Dědek, *Coll. Czech. Chem. Commun.*, **51**, 1304 (1986).
72. C. R. Rasmussen, *J. Org. Chem.*, **39**, 1554 (1974).
73. R. G. Gillis, *Aust. J. Chem.*, **36**, 2161 (1986).

CHAPTER 7

Synthesis of open-chain sulfones

KURT SCHANK

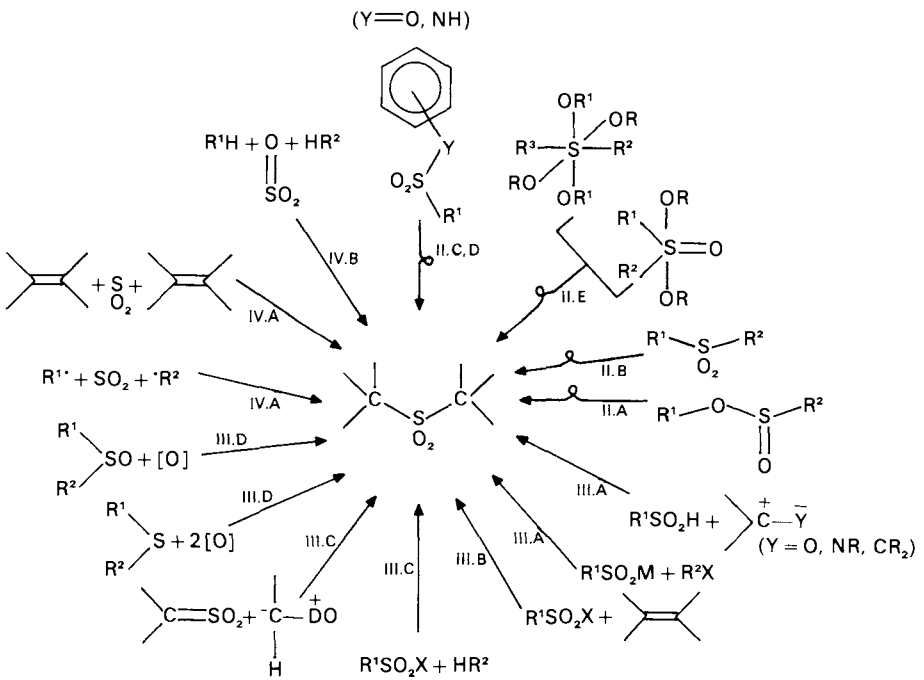
Fachrichtung 13.2 Organische Chemie, Universität des Saarlandes, D-6600 Saarbrücken, FRG

I. INTRODUCTION

Sulfones have been prepared by three principally different strategies: *One-component methods* include various isomerizations, rearrangements under degradation, and hydrolysis of oxygen-substituted dialkyl (diaryl) sulfuranes(VI).

Two-component methods represent the most widely applied principles in sulfone syntheses, including C—S bond formation between carbon and RSO_2 species of nucleophilic, radical or electrophilic character as well as oxidations of thioethers or sulfoxides, and cheletropic reactions of sulfur dioxide. *Three-component methods* use sulfur dioxide as a binding link in order to connect two carbons by a radical or polar route, or use sulfur trioxide as an electrophilic condensation agent to combine two hydrocarbon moieties by a sulfonyl bridge with elimination of water.

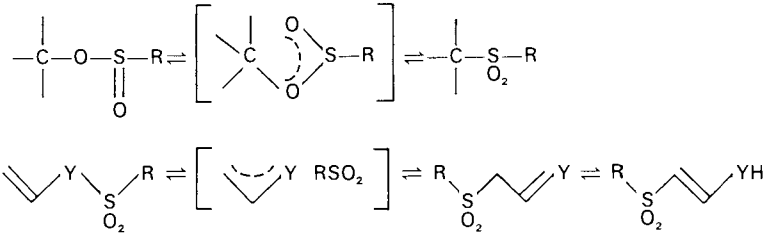
Scheme 1 presents a general survey on methods discussed in this chapter. References 1–5 are a selection of some recently published comprehensive reviews.



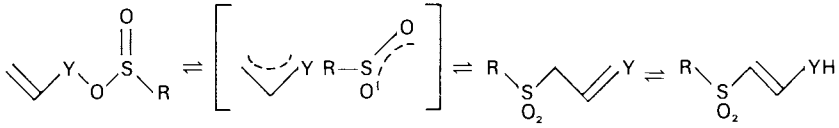
SCHEME 1. Syntheses of sulfones.

II. ONE-COMPONENT METHODS

The most important types of these methods are the isomerizing rearrangements. According to whether the reaction occurs at the sulfone site or at the carbon site on the one hand, or at both sites on the other, one should distinguish between *unifold* and *twofold* transformations (Schemes 2 and 3).



SCHEME 2. Unified types.

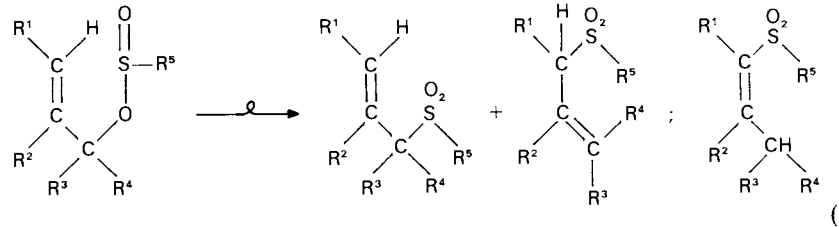


SCHEME 3. Twofold types.

The nature of the initial bond cleavage (homolytic, heterolytic, or by a concerted pathway) cannot be generalized because it depends on substituent effects and/or reaction conditions.

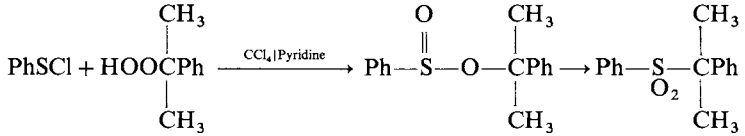
A. Sulfinate–Sulfone Rearrangements

This reaction type has been intensely studied[6–10]. The application of highly polar solvents, catalysis with tertiary amines[11] or with acids[6,12,13], mesomeric stabilization of intermediate carbenium ions[6,11,14–16] (allylic and benzylic systems; propargylic systems[17–21]) as well as derivatives of sulfinic acids with increasing acidity[15,22] usually indicate an ionic pathway (intra- and/or inter-molecular):



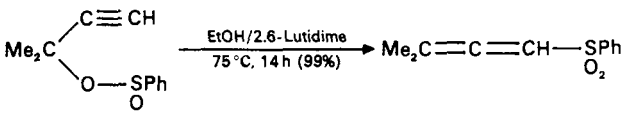
(1)

Principally, both unifold and twofold transformation types ensue in these cases. A unifold transformation occurs in the case of the rearrangement of cumyl benzenesulfinate, which arises from the conversion of cumyl hydroperoxide with benzenesulfenyl chloride[23] (equation 2). Closely related sulfoxylate–sulfone rearrangements, which pass intermediate sulfinate steps similarly, are equally known[24,25].



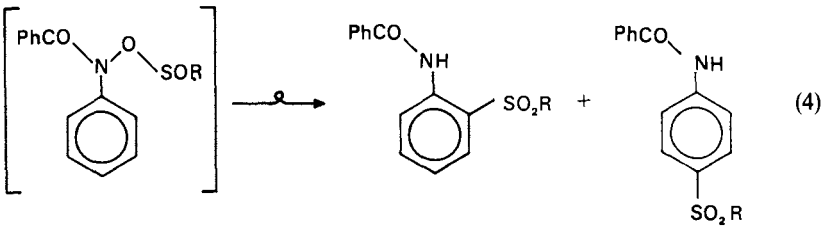
(2)

A neat twofold transformation, obviously a consequence of a sigmatropic [2.3]rearrangement rather than by an ionic pathway, occurs in the case of a propargyl sulfinate[20] (equation 3).



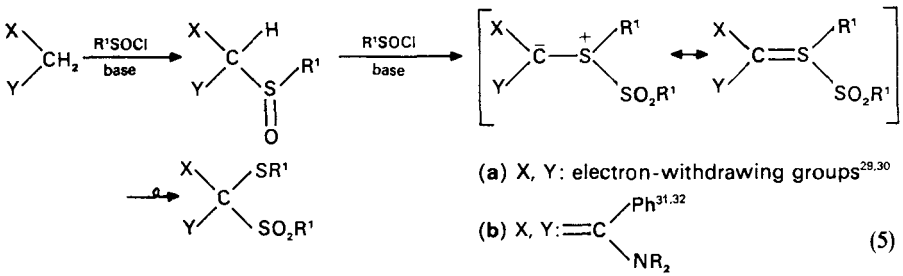
(3)

Allyl sulfones formed from allyl sulfinates (cf. equation 1) can easily tautomerize to give α,β-unsaturated sulfones[26]; in cases for which R^1, R^2 are part of an (hetero) aromatic system, this tautomerization occurs spontaneously. Similarly, sulfinic acid esters from *N*-phenylhydroxamic acids as reactive intermediates rearrange to give *o*-(major part) and *p*-sulfonylanilines (minor part)[27]:



(4)

Another type of sulfinate–sulfone rearrangement similar to the Pummerer rearrangement takes place in the course of treating α-morpholinostyrenes or reactive methylene compounds with sulfinyl chlorides in the presence of bases. The intermediate sulfoxides are rearranged by further sulfinyl chloride through a sulfinyloxysulfonium ylide stage[28] (equation 5).



(a) X, Y: electron-withdrawing groups[29,30]

(b) X, Y: =C(Ph[31,32])NR2

(5)

B. Sulfone–Sulfone Rearrangements*

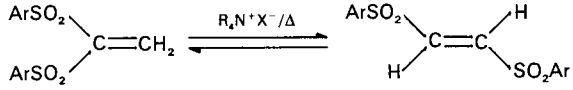
Rearrangements of this type are unifold transformations, which show [1.*n*]shifts of the sulfonyl group within the carbon moiety.

1. [1.2]Rearrangements

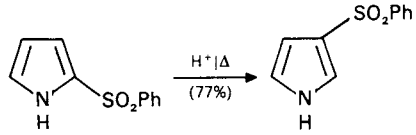
The simplest rearrangement of this type represents the vinylidene disulfone–vinylene disulfone rearrangement[33–35], which has been reported to proceed equally in both

*See also Chapter 13.

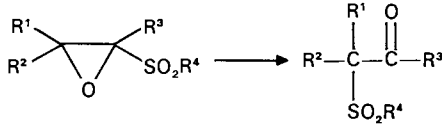
directions[36] (equation 6). Possibly the anti-Michael addition, which has been found to proceed beside the normal Michael addition in the course of the addition of nucleophiles to α,β-unsaturated sulfones[37], plays here a deciding role. *o*-Sulfonyl substituents in pyrroles suffer similar acid catalyzed 1,2-migrations[38] (equation 7). In contrast to these reactions, in the subsequent rearrangements additional changes in the molecular structure accompany 1.2-sulfonyl migrations. Acid catalysis yields β-oxo sulfones from sulfonyl-substituted oxiranes[39–46a] (equation 8). Whether α-oxo carbenium ions[46b] are participating in this reaction is unknown. However, in a case in which oxirane ring opening dominated a primary sulfonyl elimination, the β-oxo sulfonyl system has been formed without sulfonyl migration[47] (equation 9). In another type of β-oxo sulfone derivative, mineral acid catalysis yields only a normal hydrolysis reaction whereas dilute acetic acid catalyzes an unexpected concerted [1.2]sulfonyl[1.4]acyl shift[48] (equation 10).



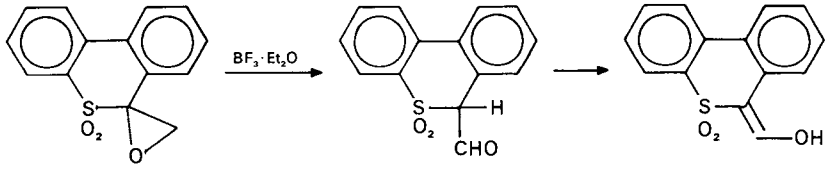
(6)



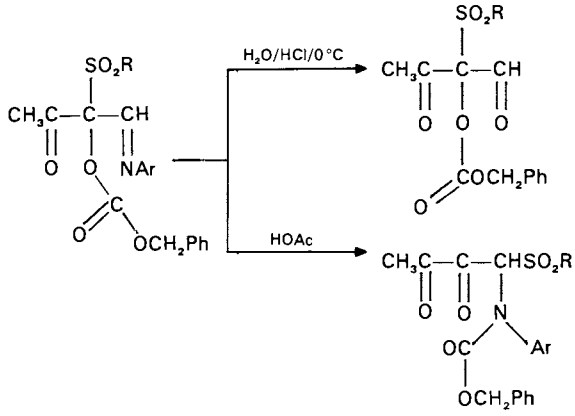
(7)



(8)



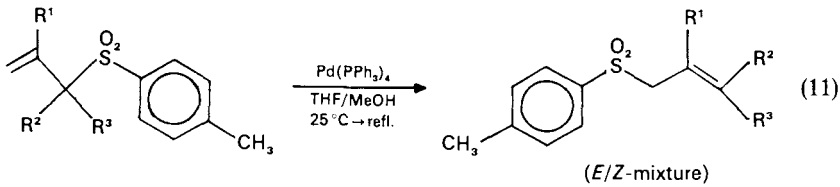
(9)



(10)

2. [1.3]Rearrangements

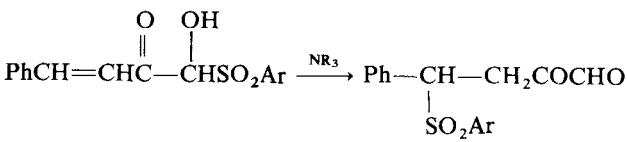
In allyl sulfones 1, 3-migrations of the sulfonyl group take place thermally[49–51] or Pd(0)-catalyzed[52] (equation 11).



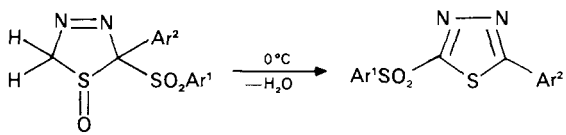
(11)

3. [1.4]Rearrangements

Reactions of this type have been observed without (equation 12)[53] and with (equation 13)[54] additional condensation.



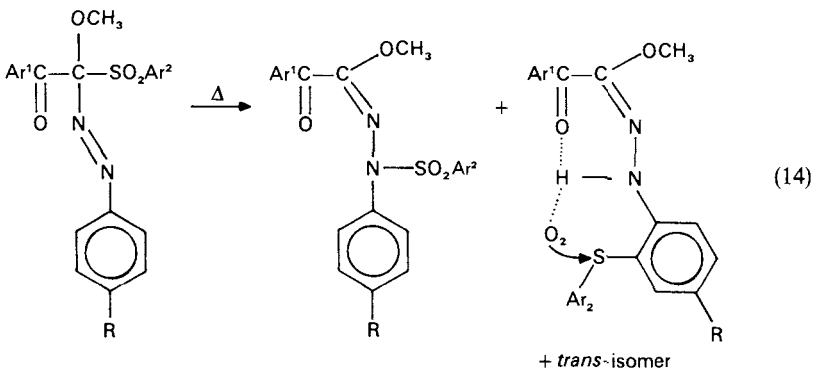
(12)



(13)

4. [1.5]Rearrangements

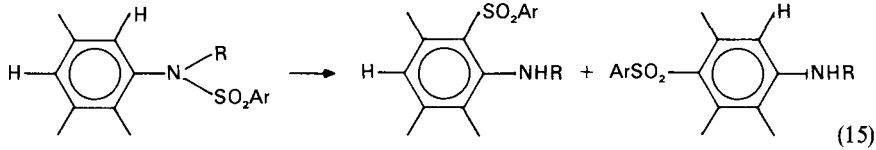
Reaction products of concomitant anionotropic 1, 3-shifts to nitrogen and 1, 5-shifts to carbon of sulfonyl groups in azo coupling products of α-methoxy β-oxo sulfones have been found under thermal conditions[55,56] (equation 14).



(14)

C. Sulfonanilide–Anilinosulfone Rearrangement[57]

Sulfonanilides suffer 1, 3- and 1, 5-shifts of the sulfonyl group under various conditions. The reactions may be spontaneous[58–60], thermal[61,62], photochemical[62,63], base-catalyzed[61,64,65], acid-catalyzed[66–69] or oxidative[70] (equation 15).



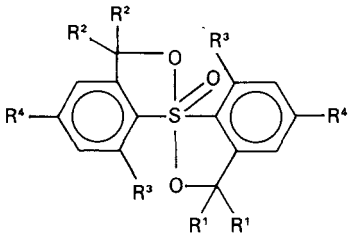
(15)

D. Arene Sulfonate–Aryl Sulfone (Sulfone-Fries) Rearrangement[71]

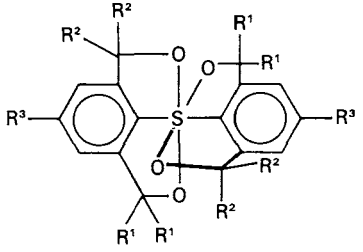
This rearrangement ensues principally according to the same scheme as shown in equation 15 yielding *o*- and/or *p*-sulfonyl-substituted phenols. Yields under Friedel–Crafts conditions are poor[72]; only under photochemical conditions[73] or in exceptional cases[74] are the yields over 10–25%.

E. Isomerization of Oxysulfuranes

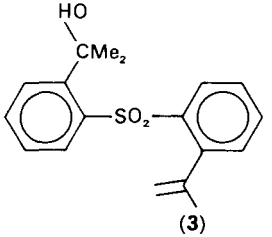
The interesting work of Martin and coworkers[75–77] on oxygen-substituted sulfuranes(VI) 10-S-4 and 12-S-6 species made available for the first time quasi 'mono- and bis-acetals' of sulfones (**1** and **2**). Proton-catalyzed fragmentation of **1b** led to the sulfone isomer **3**[76]; the corresponding fragmentation of **2a** gave, depending on reaction conditions, the isomeric sulfone **4** or a mixture of the sulfone isomers **4** and **5**[77].



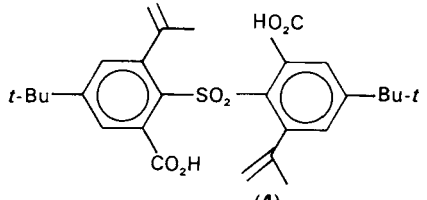
(**1**) (**a**) $R^1 = R^2 = CF_3$; $R^3 = H$; $R^4 = t$-Bu[75]
(**b**) $R^1 = R^2 = Me$; $R^3 = R^4 = H$[76]
(**c**) $R^1 = R^2 = Me$; $R^4 = t$-Bu; $R^3 = CO_2Et$, CH_2OH, $C(CH_3)_2OH$[77]



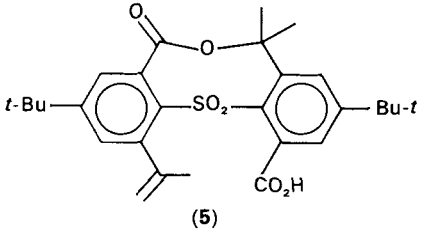
(**2**) (**a**) $R^1 = Me$; R^2, $R^2 = O$; $R^3 = t$-Bu[77]
(**b**) $R^1 = R^2 = Me$; $R^3 = t$-Bu[77]



(**3**)



(**4**)



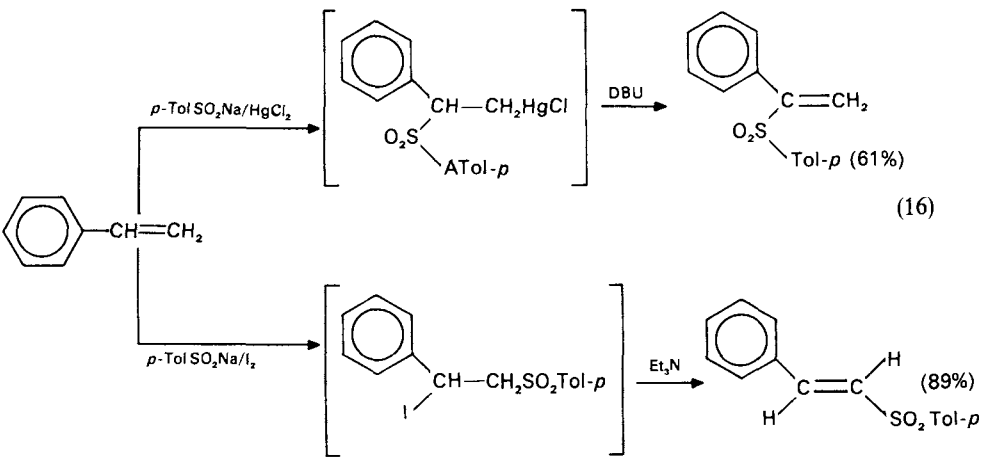
(**5**)

III. TWO-COMPONENT METHODS

A. S-Substitution of Sulfinate Nucleophiles with C-Electrophiles

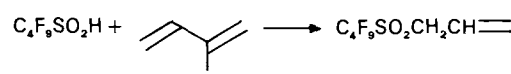
1. Addition of sulfinic acids (or salts) to unactivated C=C double bonds

Usually, isolated C=C double bonds do not react with sulfinic acids or their salts to form sulfones. Exceptions represent the 'chloropalladiosulfonylation' of dicyclopentadiene[78] and the 'sulfonylmercuration' of 1-alkenes[79] (equation 16). Interestingly, the corresponding 'iodosulfonylation' yields the regioisomeric sulfone[79]. Further investigations concerning the mechanism of this second reaction which could involve the addition of intermediately formed tosyl iodide (cf. Section III.B.1) are announced.

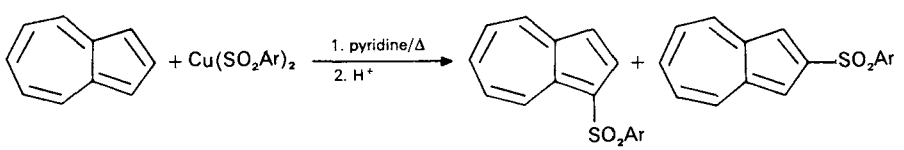


(16)

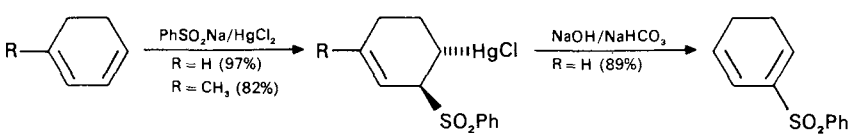
Additions of sulfinic acids to polyenes ('hydrosulfonylation'), however, proceed with very strong acids[80] or under catalysis of Pd complexes[81] (equation 17). With copper(II) arenesulfinates, azulene has been oxidatively sulfonylated in the 1- and 2-positions of the five-membered ring[82] (equation 18). The 'sulfonylmercuration' has also been applied with success to conjugated dienes[83] (equation 19).



(17)



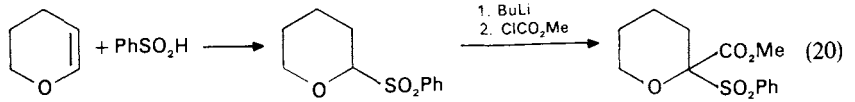
(18)



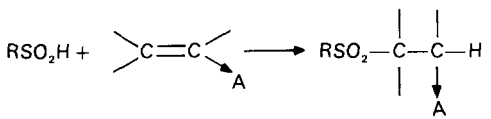
(19)

2. Addition of sulfinic acids to polar C=C double bonds

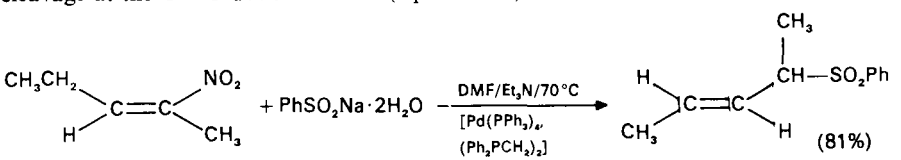
Polarization of C=C double bonds can be effected by adjacent electron donor[84] (equation 20) or electron acceptor systems. In the second case, a large number of Michael-acceptor olefins have been added successfully to sulfinic acids[85] (equation 20a). Table 1 gives a survey on this addition[86–93].



(20)

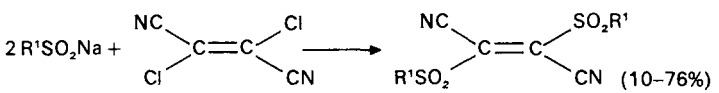


Some particular features should be mentioned. Instead of Michael additions, α-nitroolefins are reported to yield allyl sulfones under Pd catalysis[94] (equation 21). Halogenated acceptor-olefins can substitute halogen β to the acceptor by *ipso*-substitution with sulfinate (equation 22[95], equation 23[96]) or can lose halogen α to the acceptor in the course of a secondary elimination occurring β to the introduced sulfonyl groups[97] (equation 24). On the other hand, the use of hydrated sodium sulfinates can lead to cleavage at the C=C double bond[98] (equation 25).



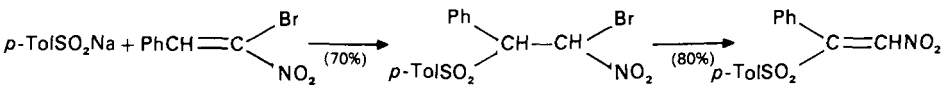
(21)

$$PhSO_2H + ClCH{=}CHNO_2 \longrightarrow PhSO_2CH{=}CHNO_2\ (72\%) \qquad (22)$$

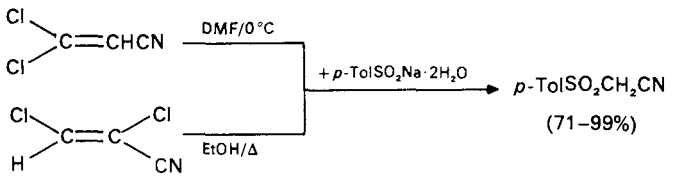


(23)

(R^1 = alkyl, allyl, benzyl, aryl)

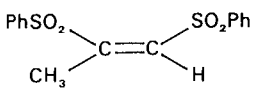
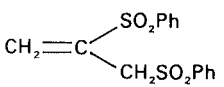


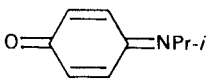
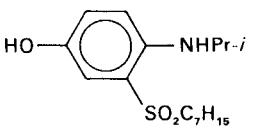
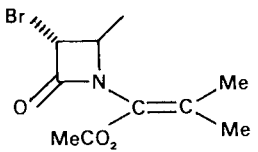
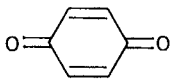
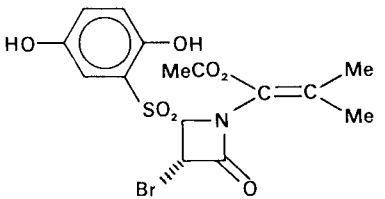
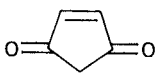
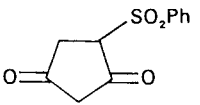
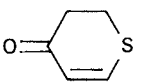
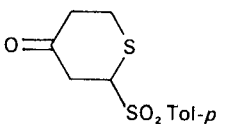
(24)



(25)

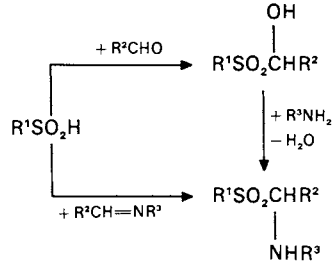
TABLE 1. Sulfones from sulfinic acids RSO_2H and acceptor-substituted olefins, acetylenes or quinones

R	Michael acceptor	Sulfone	Yield (%)	Ref.
p-Tol	$CH_3CH{=}CHCHO$	*p*-TolSO_2CHCH_2CHO (CH$_3$)	84	86
p-Tol	$CH_2{=}CHCOCH_3$	*p*-Tol$SO_2CH_2CH_2COCH_3$	92	87
p-ZC_6H_4 (Z = H, Me, NHAc, Br, Cl)	$PhCH{=}CHCOCH_2NO_2$	*p*-$ZC_6H_4SO_2CH(Ph)CH_2COCH_2NO_2$	40–55	88
Ph	1. $CH_2{=}CHCONEt_2$ 2. P_4S_{10}	$PhSO_2CH_2CH_2CSNEt_2$	90	89
p-$O_2NC_6H_4$	$PhCH{=}CHNO_2$	*p*-$O_2NC_6H_4SO_2CHCH_2NO_2$ (Ph)	83	90
p-Tol	$CH_2{=}C(SO_2Ph)_2$	*p*-Tol$SO_2CH_2CH(SO_2Ph)_2$	95	91
Ph	$CH_3C{\equiv}CSO_2Ph$		84	92
Ph	$CH_2{=}C{=}CHSO_2Ph$		73	92

C_7H_{15}-			92	93a
			78	93b
Ph			98	93c
p-Tol			94	93d

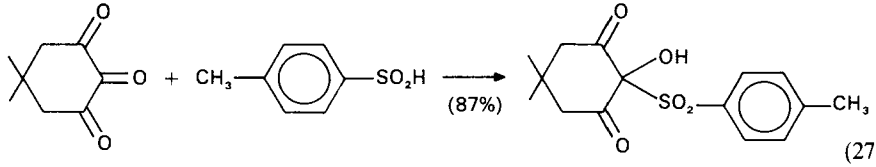
3. Addition of sulfinic acids to polar C=Y double bonds

Polar C=Y double bonds (Y = NR, O, S) with electrophilic carbon have been added to sulfinic acids under formation of sulfones. As in the preceding section one must distinguish between carbonyl groups and their derivatives on the one hand, and carboxylic acids (possessing leaving groups at the electrophilic carbon) on the other. Aldehydes[99–101] of sufficient reactivity—especially mono-substituted glyoxals[102,103]—and their aryl or arylsulfonyl imines[104] have been added to sulfinic acids (in a reversible equilibrium) to yield α-hydroxy or α-amino sulfones; the latter could also be obtained from the former in the presence of primary amines[99,100] (equation 26).



(26)

In the case of the carbonyl group of cyclohexanone, two flanking carbonyl groups were necessary to afford the corresponding adduct[104] (equation 27). In the course of tertiary amine- or silica gel-catalyzed rearrangements of benzyl (and related) thiosulfonates to α-monosulfonylated dibenzyl (and related disulfides[105], an intermediate carbophilic S-addition of sulfinate to a thioaldehyde as reactive intermediate according to equation 27a must have taken place. The intermediacy of the thioaldehydes could be proved by trapping with cyclopentadiene after base-catalyzed fragmentation of **7** at room temperature.



(27)

$$R^2CH_2SSO_2R^1 \xrightarrow[SiO_2(c,d)]{Et_3N(a,b)\text{ or}} \left[R^2\underset{\underset{S}{\|}}{CH} + R^1SO_2H \longrightarrow R^2\underset{\underset{SH}{|}}{CH}SO_2R^1 \right]$$

(6)

$$\xrightarrow[-R^1SO_2H]{+6} R^2CH_2SS\underset{\underset{R^2}{|}}{C}HSO_2R^1 \qquad (27a)$$

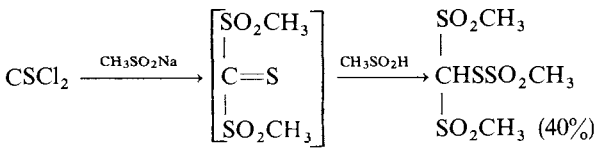
(7)

$R^1 = p$-Tol; R^2 = (**a**) p-$O_2NC_6H_4$ (95%) (**b**) Ph (78%)
(**c**) COC_6H_4Br-p (~ 100%) (**d**) CO_2Et (~ 100%)

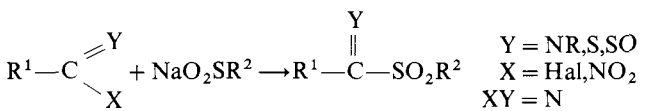
An inverse addition of sulfinic acid to a thiocarbonyl group could have taken place with the reactive intermediate **8**, which should arise from thiophosgene and methanesulfinic acid (sodium salt)[106] (equation 28). The first step of this reaction represents an S-acylation

of the ambident sulfinate anion, which occurs only with thiono or imino derivatives of acyl halides and related species; acyl halides themselves[107,108] react with sulfinate anions under O-substitution followed by disproportionation of the initially formed mixed anhydride[109].

Table 2 surveys different types of addition–elimination sequences (equation 29).

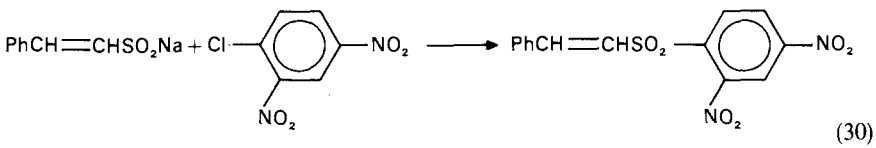


(8) (28)

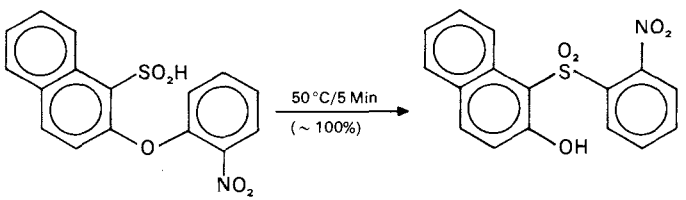


(29)

Nucleophilic substitutions of halogen by the addition–elimination pathway in electron-deficient six-membered hetarenes by sulfinate anions under formation of sulfones have been described earlier[120]. The corresponding electron-poor arenes behave similarly[121] (equation 30). A special type of this reaction represents the inverse Smiles rearrangement in equation 31[122].



(30)

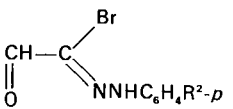
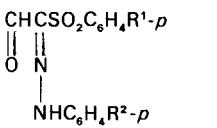
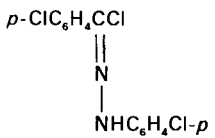
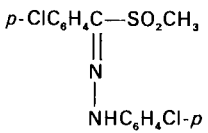
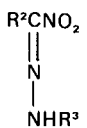
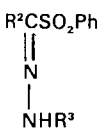
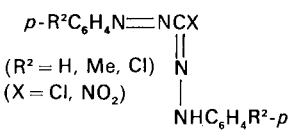
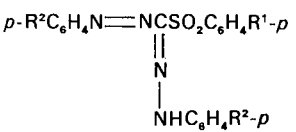


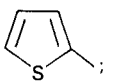
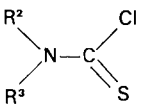
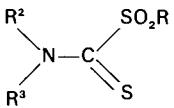
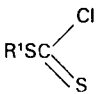
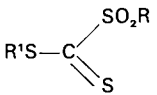
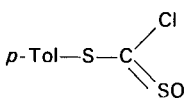
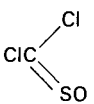
(31)

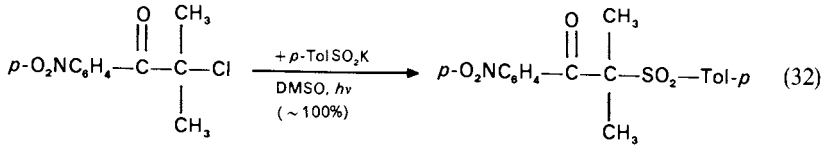
4. Nucleophilic displacement of sp^3-carbon bonded halide and related leaving groups

The usual sulfone synthesis by displacement of halide by sulfinate is assumed to have a nucleophilic S_N2 mechanism[123]. However, in special cases of alkyl halides with additional, electron-withdrawing substituents a radical substitution pathway has been observed[124–127] (equation 32). Correspondingly, substitutions under formation of sulfones take place with α-nitroalkyl iodides[125] or bromide[126] as well as with α-nitroalkyl thiocyanates[127]. Related reactions are the co-oxidations of sulfinates and anions of nitroalkanes yielding sulfones under the influence of iodine[128], hexacyanoferrate(III)[129–131], caroate[131], and peroxidisulfate[129,130] as oxidants. Further radical sulfone formations from sulfinic acids are shown in the examples[132–136] for arylation and alkenylation in equations 33–35.

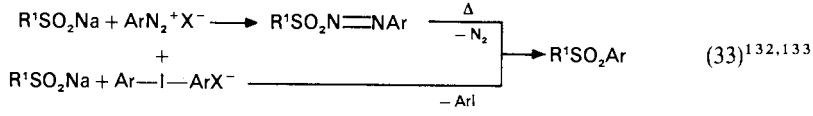
TABLE 2. Sulfones from S-acylations of sulfinate anions RSO_2^-

R	Acylation reagent	Sulfone	Yield (%)	Ref.
p-$R^1C_6H_4$ (R^1 = H, Me, Cl)			50–70	110
Me			33	111 (110)
Ph			/	112
p-$R^1C_6H_4$ (R^1 = H, Me)			/	113

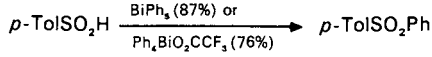
Ph	$Br_2C{=}N{-}N{=}CBr_2$	$(PhSO_2)_2C{=}N{-}N{=}C(SO_2Ph)_2$	93	114
p-$R^1C_6H_4$ (R^1 = H, OMe, Hal, NHAc)	Cl—C≡N	*p*-$R^1C_6H_4SO_2CN$	92–97	115
Me—;  ; *p*-$R^1C_6H_4$ (R^1 = H, Hal, NO_2)	 R^2, R^3 = Alkyl, Aryl		10–71	116
Me–; Ph–; 1-Adamantyl-			7–70	117, 118
p-Tol		*p*-TolSCH$_2$SO$_2$Tol-*p*	81	119
p-Tol		(*p*-TolSO$_2$)$_2$CH$_2$	80	119



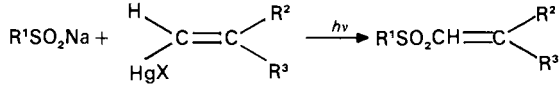
(32)



(33)[132,133]

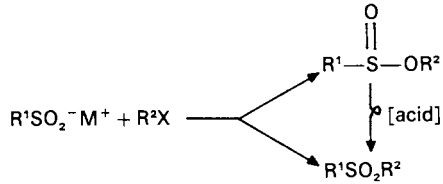


(34)[134]



(35)[135,136]

Alkylation of the ambident sulfinate ions by variation of alkylating agent, countercation, solvent, and reaction conditions has been the subject of extensive investigations previously as well as today, since sulfone synthesis by S-alkylation is probably the most important method[137]. Usually, alkyl halides have been used in order to synthesize sulfones, in combination with sodium, potassium or silver salts of sulfinic acids in protonic solvents (ethanol, dipropylene glycol[138], polyglycol[139], or water) at elevated temperature; however, by using α-halogeno ethers instead of alkyl halides, protonic solvents as well as solvents of a too enhanced polarity must be avoided, since they lead to undesired side-reactions[140–142]. On the other hand, sulfinates from weaker sulfinic acids are more favorable on account of their higher S-nucleophilicity[143] than those of very strong sulfinic acids. Sulfinate esters are obtained primarily in the latter cases as products of kinetic control and can be easily rearranged to their sulfone isomers under acid catalysis[22,143] (equation 36). Table 3 gives a survey of sulfones generated by this method.



(36)

The conversions of α-halogeno carbonyl compounds seem to be of particular interest. α-Halogeno monocarbonyl compounds are able to yield sulfones by either a radical[124–127] or a nucleophilic (Table 3[148–150,153,156,157]) pathway. This proves to be correct also for α-halogeno β,β-dicarbonyl compounds[158] with certain limitations. In the case of α-halogeno β,β,β-tricarbonyl compounds, however, the halogen is so strongly positive that it is reductively eliminated by means of a sulfinate to form a sulfonyl halide. In a subsequent reaction, this sulfonyl halide reacts as an electrophilic derivative of a sulfonic acid and attacks the simultaneously formed enolate anion on oxygen according to the scheme of a Schotten–Baumann reaction (equation 37). On the other hand, enolates are

TABLE 3. Sulfones from sulfinates R^1SO_2M and alkyl halides

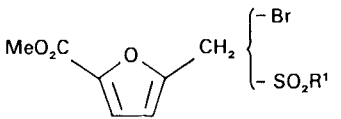
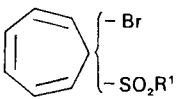
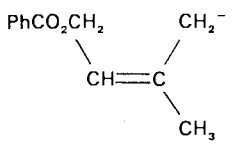
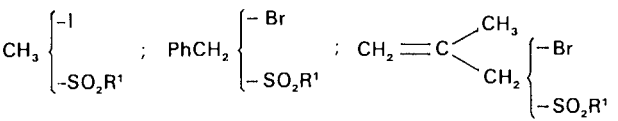
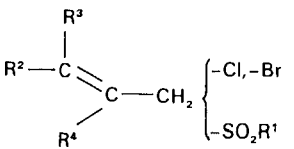
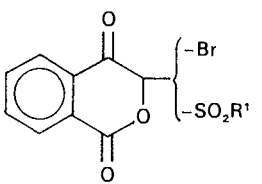
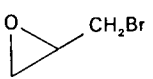
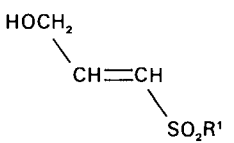
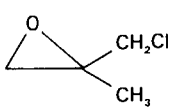
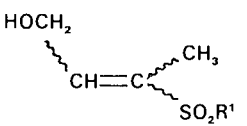
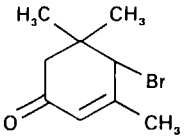
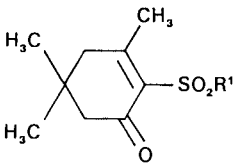
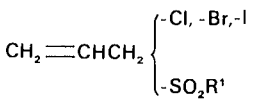
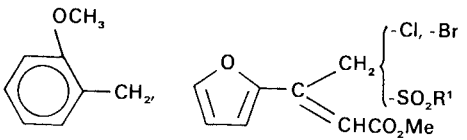
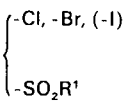
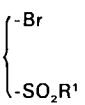
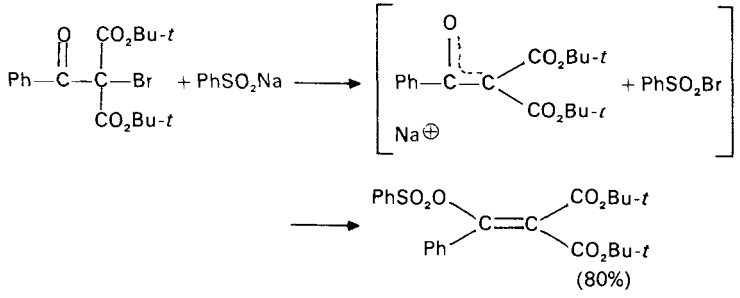
R^1	M	R^2X and $R^2SO_2R^1$ or rearranged sulfones	Yield (%)	Ref.
CCl_3	Na		45	144
C_4H_9	$\frac{1}{2}Mg$		/	145
p-$NO_2C_6H_4$	Na		/	145
	MgBr		75–80	146
p-RC_6H_4— (R = H, Br)	Na		63–89 ($E+Z$)	147
p-RC_6H_4 (R = H, Cl, OMe, NO_2)	Na		40–54	148

TABLE 3. (Contd.)

R^1	M	R^2X and $R^2SO_2R^1$	or rearranged sulfones	Yield (%)	Ref.
Ph	Amberlyst A-26	$CH_3\{$-I, $-SO_2R^1$; $C_8H_{17}\{$-I, $-SO_2R^1$; $PhCOCH_2\{$-I, $-SO_2R^1$; $EtO_2CCH_2\{$-Br, $-SO_2R^1$		83–100	149
p-Tol	Bu_4N (PTC)	C_6H_{13}, $PhCH_2$, C_7H_{15}, Et, 2-C_7H_{15}, $CH_2{=}C(CH_3)CH_2$, $CH_2{=}CHCH_2$, CH_3COCH_2, $CH_3CH(CO_2Et)$, ICH_2, $Cl(CH_2)_3\{$-Cl, -Br, -I; $-SO_2R^1$		≦94	150
				81	150
				95 ($E/Z = 65:35$)	150

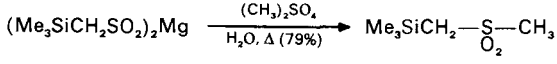
p-Tol	Na			65	151
p-Tol	Bu_4N (PTC)	Me, $MeOCH_2$, *p*-ClC_6H_4, $NCCH_2$, $BrCH_2$, $PhCOCH_2$, $(CH_3)_2CH$, 		59–96	152, 153
p-Tol	Na			94,74	154, 155
p-RC_6H_4 (R = H, Me, OMe, Cl, NO_2)	Li, K, Na	$R^2COCH(OMe)$  (R^2: Me, *t*-Bu, Aryl)		20–60	156
o-$O_2NC_6H_4$	Na	NaO_2CCH_2 		91	157

able to yield sulfones with sulfonyl halides (cf. Section III.C.2)[159].

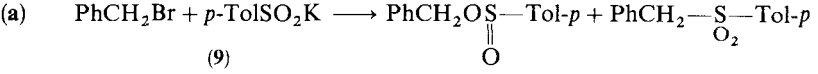


(37)

In connection with alkylations of ambident sulfinates by alkyl halides, manifold efforts have been made to find rules for either O- or S-alkylations. In the course of these investigations various leaving groups instead of halides as well as different reaction conditions have been applied: Sodium arenesulfinate and trimethyloxonium tetrafluoroborate yield O-substitution[160], whereas phase-transfer catalysis (PTC) conversion of potassium benzene sulfinate with trialkylsulfonium salts leads to S-substitution[161,162]. A comparative investigation of the reaction of 4-toluenesulfinate (as free acid, as sodium salt or as silver salt) describes exclusive S-substitution with methyl iodide and exclusive or at least predominant O-substitution with diazomethane, dimethyl sulfate and methyl tosylate[163,164]. On the other hand, 4-toluenesulfinic acid has been found to be O- and S-alkylated with diazoalkanes[165–167], and magnesium trimethylsilylmethanesulfinate has been described to furnish the corresponding sulfone with dimethyl sulfate[168] (equation 38). Recently, investigations on the effects of cryptands with regard to the O- and S-selectivity in the alkylation of sulfinic acids have been reported[169]:

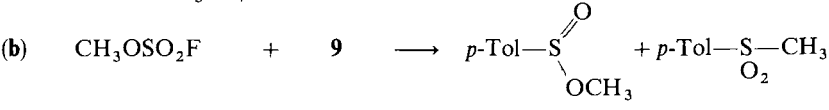


(38)



(9)

conditions:			
1. CH_2Cl_2/20 h	0%	0%
2. C_6H_6/18-crown-6/2.5 h	0%	96%
3. CH_3CN/20 h	0%	95%



	(10)	(11)
conditions:		
1. CH_2Cl_2/2 h	40%	60%
2. CH_2Cl_2/18-crown-6/2 h	70%	30%
3. CH_2Cl_2/cryptofix(222), 2 h	83%	17%
4. HMPA/2 h	100%	0%

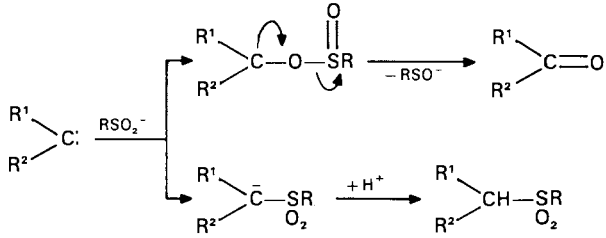
(c)	$CH_3\overset{+}{S}Ph_2\ ClO_4^-$	+ **9**	⟶	**10**	+	**11**
	conditions:	1. CH_2Cl_2/24 h		44%		56%
		2. CH_2Cl_2/18-crown-6/2 h		40%		60%
(d)	$CH_3\overset{+}{S}Ph_2\ ClO_4^-$ (O)	+ **9**	⟶	**10**	+	**11**
	conditions:	1. CH_2Cl_2/24 h		56%		44%
		2. CH_2Cl_2/18-crown-6/2 h		25%		75%
		3. DMF/26 h		24%		76%

Dimethyl methanephosphonate has been successfully applied in synthesis of aryl methyl sulfones[170]. In the above-mentioned cases, the alkylating agents contained as efficient leaving groups either anions of very strong acids (halide, sulfate, sulfonate, phosphonate) or onium cations (diazonium, oxonium, sulfonium, oxosulfonium ions). However, weaker leaving groups can also be used[137b,137e] on condition that the adjacent alkyl group assists in expelling such groups. Thus in connection with benzyl and allyl groups, sulfinyloxy[171,172] and acetoxy groups without[173] and with metal catalysis [Ni(0)[174], Pd(0)[175–179]] have been applied. Generally, syntheses of allyl sulfones afford isomers, however, the relative rates can be directed[175,177]. Table 4 summarizes some nucleophilic displacements of varying weak leaving groups by sulfinate.

Sulfone exchanges by more nucleophilic sulfinates have also been reported[196].

5. *Addition of sulfinic acids (or salts) to carbenes*

Normal carbenes with two carbon substituents are highly reactive electrophiles ("hard acids") and add to sulfinates on oxygen[197,198]; decomposition of such sulfinyloxy carbanions yields carbonyl compounds and sulfenates[199]. On the other hand, carbenes which are deactivated by one or two π-donor substituents add to sulfinates on sulfur yielding sulfonyl stabilized carbanions; the latter are usually protonated in the course of work-up (equation 39). As to the reaction of haloforms with sulfinates in the presence of bases, it is noteworthy that only *one* halogen is able to be substituted by sulfinate under formation of α-halogen sulfones, as is the case with methylene halide[150,152,205–207] (cf. Table 3). After introduction of the sulfonyl group instead of one halogen, the remaining halogens are strongly positivated and cannot be substituted by a second sulfonyl group; on the other hand, excess of sulfinate can dehalogenate α-halogeno sulfones[207]. However, if the positivating effect of the sulfonyl group is internally compensated by an appropriate electron-releasing substituent[203], α-elimination of halide becomes possible again and a β-disulfone may be formed.



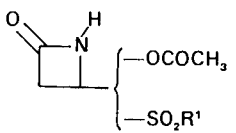
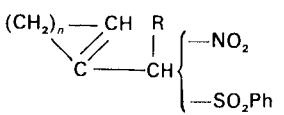
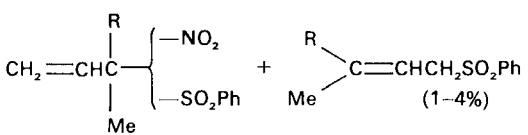
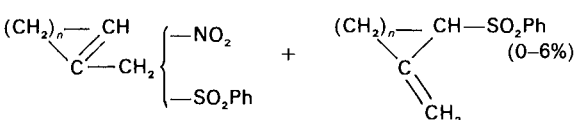
(39)

(a) R^1R^2 = Cl, Br; R = *t*-Bu, CH_2Ph, Ph, *p*-ZC_6H_4(Z = Me, Cl), 2-Naphthoyl[200,201]

(b) R^1 = OMe; R^2 = CO_2Me; R = *p*-Tol[202]

(c) R^1 = OMe; OEt, OPh, SMe, SPh; R = *p*-ZC_6H_4(Z = Me, Cl)[203,204]

TABLE 4. Sulfones from nucleophilic displacement of different weak leaving groups by sulfinates R^1SO_2M

R^1	MX	R^2X and $R^2SO_2R^1$ or rearranged sulfone	Yield (%)	Ref.
Et, CH_2Ph, 4-Tol, 3-$NO_2C_6H_4$, 4-Cl-3-MeC_6H_3	HOAc		61–95	180
p-Tol	HOAc	CH_3SCH_2 {—$OCOCH_3$ (from DMSO and Ac_2O); —SO_2Tol-*p* ("MMT-Sulfone")}	71	181
Ph	$NaNO_2$	 [Pd(PPh_3)$_4$-catalysis] (R = H, *n* = 2, 3; R = Me, *n* = 3)	70–75	182
Ph	$NaNO_2$	 (R = C_6H_{13}, $CH_2CH_2COCH_3$, $CH_2CH_2CO_2CH_3$)	76–96	182 (cf. 94)
Ph	$NaNO_2$	 (*n* = 3–6)	65–92	183

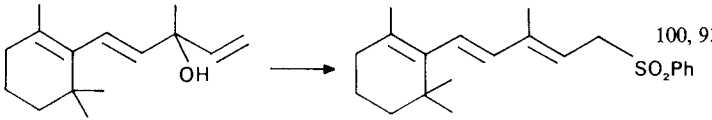
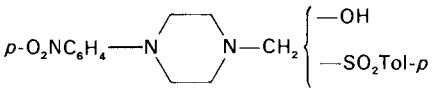
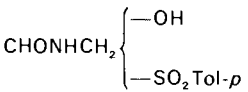
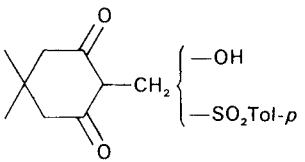
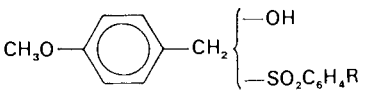
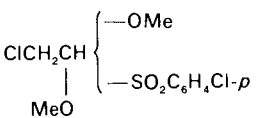
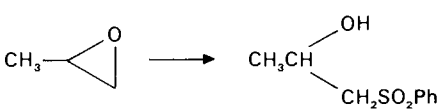
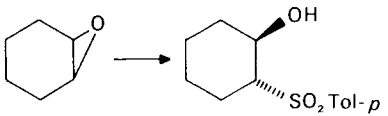
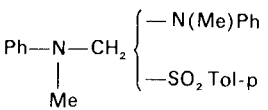
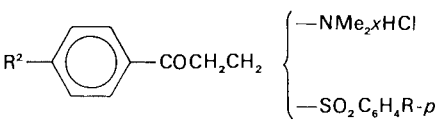
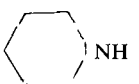
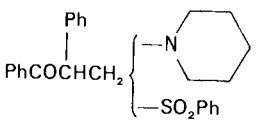
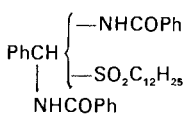
Ph	H_2O		100, 93	184 185
p-Tol	H_2O		77	186
p-Tol	H_2O		55	187
p-Tol	H_2O		95	188
RC_6H_4	H_2O		74–92	189
p-RC_6H_4 (R = H, Me, Cl)	MeOH		57	190
p-ClC_6H_4	ROH		83	191

TABLE 4. (Contd.)

R^1	MX	R^2X and $R^2SO_2R^1$ or rearranged sulfone	Yield (%)	Ref.
p-Tol	ROH		89	150
p-Tol	PhNHMe		51	192
p-RC_6H_4 (R = H, Me, OMe, NO_2, Cl, NH_2, NHAc)	Me_2NH (*x*HCl)	 (R^2 = H, Me, OMe, Cl)	*a*	193
Ph			83	194 (cf. 186)
$C_{12}H_{25}$	$PhCONH_2$		27	195 (cf. 192)

[a]Yields partially in g.

In this connection it should be mentioned that dihalogenomethyl methyl ethers did not furnish the expected β-disulfone nor the α-halogeno sulfones as preliminary steps in appreciable amounts; surprisingly, sulfonyl halides have been isolated as main products of these conversions[208]:

$$CH_3OCHX_2 + p\text{-}TolSO_2Na \longrightarrow p\text{-}TolSO_2X \quad [X = Cl(34\%),\ Br\ (59\%)]$$

B. Radical Addition of Sulfonic Acid Derivatives to Unsaturated Systems

1. Halosulfonylation

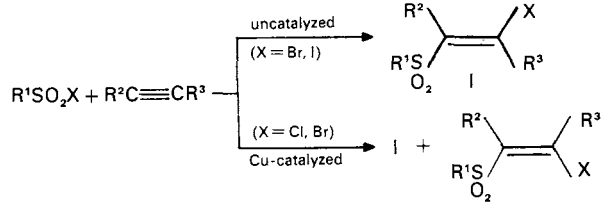
As a consequence of facile homolytic cleavages, sulfonyl halides (I > Br > Cl; F unsuitable) are able to add to unsaturated C—C systems. To prevent (or reduce) competing polymerizations, the additions of sulfonyl chlorides have been recommended to be carried out in the presence of copper(I/II) salts (Asscher–Vofsi reaction[209,210]). Comprehensive surveys have been published[211] on the resulting β-halogeno sulfones (or their vinyloguous compounds) as well as on their dehalogenation products (vinyl sulfones, 1-sulfonyl-1,3-dienes, etc.). Table 5 reviews a series of sulfonyl halide additions and facile hydrogen halide eliminations.

Some details on the course of these reactions should be emphasized:

(1) Sulfonyl chlorides are added in the presence of copper(I)- or copper(II)-chloride exclusively[212], however, mostly in the further presence of triethylamine hydrochloride[213–220], especially in additions to conjugated systems[214–218].

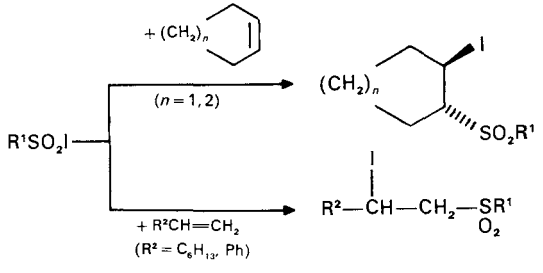
(2) Copper salts may be replaced also by other catalysts[221–224].

(3) Sulfonyl bromides and iodides react similarly[217,218,225]; copper-salt catalysis in these cases facilitates the additions but is not absolutely necessary; however, it influences the stereochemistry of the additions. Addition of sulfonyl iodides[226] as well as the uncatalyzed thermal addition of sulfonyl bromides[227] to *alkynes* leads to an exclusive *trans*-addition, whereas $CuBr_2$ catalysis in the latter case causes the formation of *cis*-addition products to some extent (11–16%); correspondingly, copper-salt catalysis in sulfonyl chloride additions to alkynes leads to the formation of a mixture of *Z,E*-isomers[228,229] (equation 40).



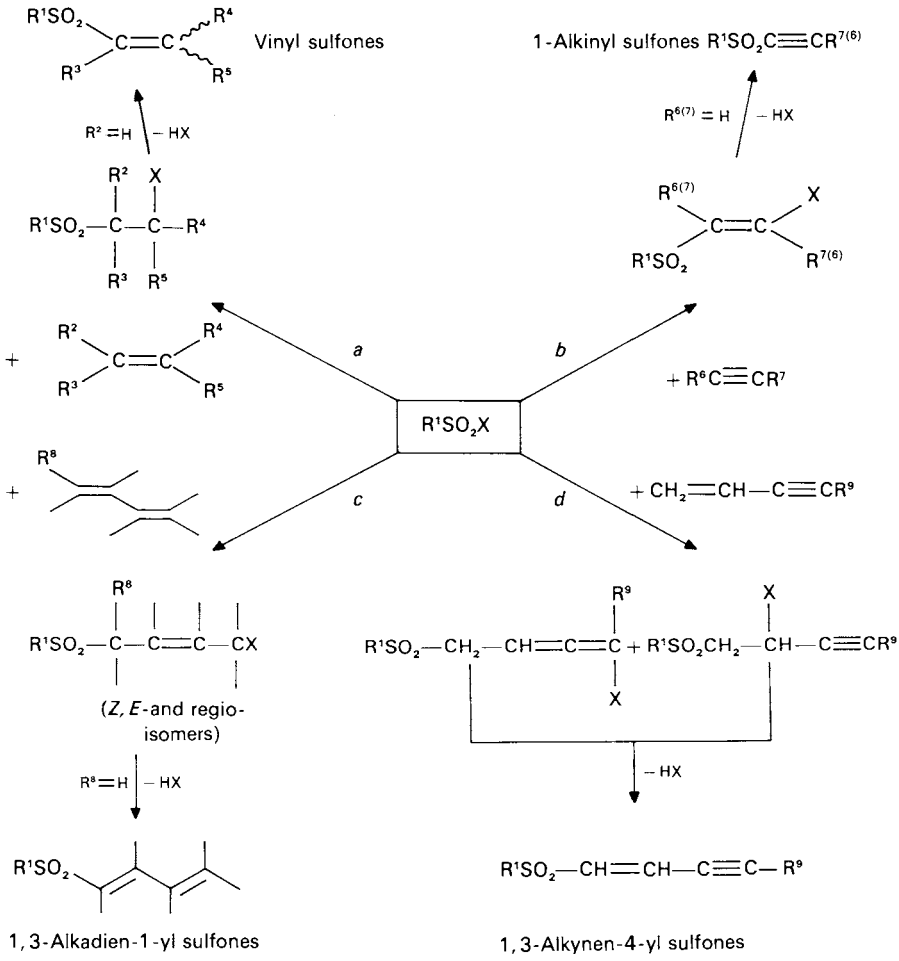
(40)

(4) Addition of sulfonyl iodide to alkenes ensues stereo- and regiospecifically[231] (equation 41).



(41)

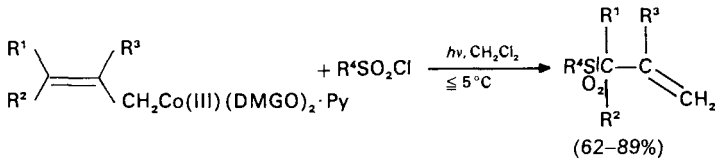
TABLE 5. Survey of sulfonyl halide additions to unsaturated systems and hydrogen halide eliminations to unsaturated sulfones



[a]References 209, 210, 212, 214, 215, 217, 218, 220, 230, 231; cf. 79.
[b]References 213, 226–229.
[c]References 210, 214, 215, 220.
[d]Reference 216.

Table 6 gives a selection of reactions of sulfonyl halides with different unsaturated systems.

Recently, Co(III)–allyl complexes have been described to be sulfonylated regiospecifically by sulfonyl halides under irradiation[232] (equation 42). Similarly, allyl methyl sulfone has been obtained from allyltrimethylsilane under copper(I) catalysis[213].



(42)

DMGO = Dimethylglyoximate

R^1, R^2 = H; R^3 = Me

R^1 = Me; R^2, R^3 = H

R^1 = Me; R^2, R^3 = H

R^1, R^2 = Me; R^3 = H

R^4 = *p*-FC_6H_4; 2,4,5-$Cl_3C_6H_2$

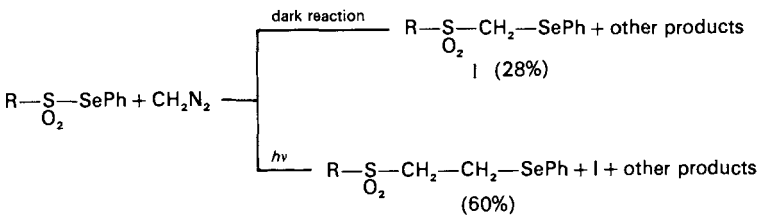
2. Thio- and seleno-sulfonylation

In the same manner as described before, arenesulfonyl thiocyanates are able to show self-addition to conjugated systems yielding sulfones[243,244]. More important, however, is that reactions of selenosulfonates with unsaturated systems as well as with nucleophilic carbon have been proved.

In the first step of the Arndt–Eistert homologation of carboxylic acids, the nucleophilic carbon of diazomethane replaces chloride from the corresponding carboxylic acid chloride. If the evolved hydrogen chloride is not removed, the initially formed diazomethyl ketone is immediately transformed to the corresponding chloromethyl ketone under evolution of molecular nitrogen. Principally, this reaction represents an insertion of a methylene group into the carbon–chlorine bond of the acid chloride (equation 43). This reaction sequence proceeds with sulfenic and sulfinic acid chlorides too, but it does not occur with sulfonyl chlorides[245] (although this is controversial[246] (equation 44)). However, if the sulfonyl chloride is replaced by the corresponding selenosulfonate, an insertion takes place both in a dark reaction and under irradiation[247] (equation 45). The addition of selenosulfonates to unsaturated C—C bonds appears to be of particular interest, because the introduced seleno function can be easily removed by oxidation yielding vinyl or alkynyl sulfones. Additions have been performed with alkenes[248–250], alkynes[251–255], and allenes[256,257]. Table 7 gives a survey on these reactions.

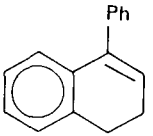
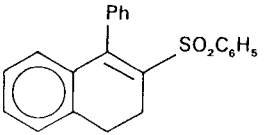
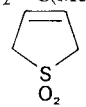
$$RC(=O)Cl + CH_2N_2 \xrightarrow[-N_2]{} RC(=O)CH_2Cl \qquad (43)$$

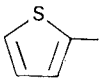
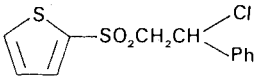
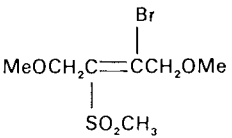
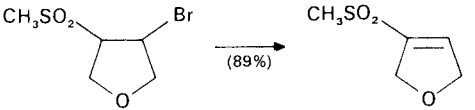
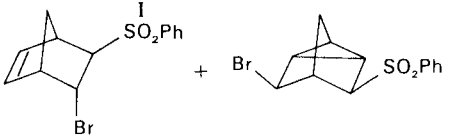
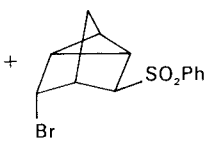
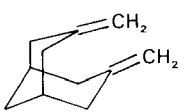
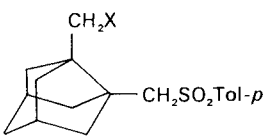
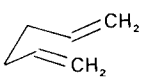
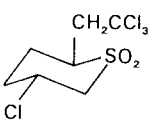
$$RSO_2Cl + CH_2N_2 \xrightarrow[-N_2]{} RSO_2CH_2Cl \qquad (44)$$



(45)

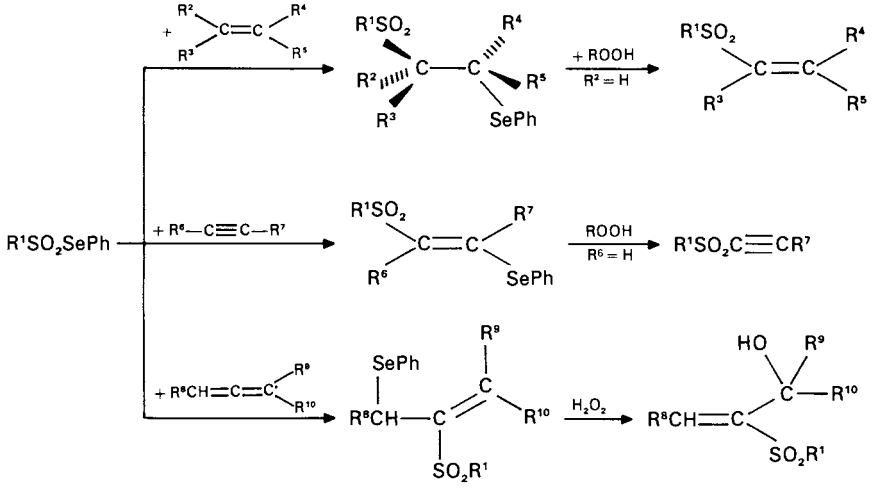
TABLE 6. Sulfones from unsaturated systems and sulfonyl halides R^1SO_2X by radical routes

R^1	X	Unsaturated C—C compound	Catalyst	Sulfone	Yield (%)	Ref
CH_3	Cl	$Me_3SiCH{=}CH_2$	*a*	$Me_3SiCHClCH_2SO_2CH_3$ → $Me_3SiCH{=}CHSO_2CH_3$	70	213
C_6H_5	Cl	*p*-$ZC_6H_4OCH{=}CH_2$ (Z = Me, OMe, Hal)	*b*	*p*-$ZC_6H_4OCHClCH_2SO_2C_6H_5$	40–95	222, 223
		$CH_3CH{=}CHCH_3$ (*Z* + *E*)	*c*	$CH_3CHClCH(CH_3)SO_2C_6H_5$ (diastereomers)	51	209, 233
						
p-Tol	Cl	$CH_2{=}CH_2$	*c*	*p*-$TolSO_2CH_2CH_2Cl$ + *p*-$TolSO_2CH{=}CH_2$	95	220
		$CH_2{=}CH{-}CH{=}CH_2$	*c*	*p*-$TolSO_2CH_2CH{=}CHCH_2Cl$	95	220
		$CH_2{=}C(Me){-}CH{=}CH_2$	*a*	mixture of 3 sulfones	82	214
			*c*	*p*-$TolSO_2CH_2CH{=}CHCH_2Cl$	67	210
		$PhCH{=}CH_2$	*d*	*p*-$TolSO_2CH{=}CHPh$	86 36	221a, 234 234
		$Ph_2C{=}CH_2$	*d*	*p*-$TolSO_2CH{=}CPh_2$	59	213
		$PhC{\equiv}CH$	*c* *c*	*p*-$TolSO_2CH{=}C(Cl)Ph$ *E*/*Z*: 92/8 *E*/*Z*: 35/65	88 85	235 235
p-$ClCH_2C_6H_4$	Cl	$CH_2{=}CH_2$	*c*	*p*-$ClCH_2C_6H_4SO_2CH_2CH_2Cl$ + *p*-$ClCH_2C_6H_4SO_2CH{=}CH_2$	90	220
p-$O_2NC_6H_4$	Cl	$PhC{\equiv}CH$	*c*	*p*-$O_2NC_6H_4SO_2CH{=}C(Cl)Ph$ *E*/*Z*: 93/7 *E*/*Z*: 42/58	94 92	235 235

	Cl	$PhCH{=}CH_2$	*c*		93	219, 236
CH_3	Br	$MeOCH_2C{\equiv}CCH_2OMe$	*f*		59	237
			*g*		95	237
p-Tol	I	$PhCH{=}C{=}CH_2$	/	*p*-$TolSO_2CH_2C{=}CHPh$	80	238
Ph	Br		/			
					8, 32, 24	239
p-Tol	Cl Br		/		70 96	240 241
CCl_3	Cl		/		14	242

Catalysts: [a]CuCl/Et_3NHCl; [b]AIBN/*hv*; [c]$CuCl_2$/Et_3NHCl; [d]$Ru[PPh_3]Cl_2$/Bu_3N; [e]CuCl/CH_3CN; [f]*t*-BuOOH/$ZnCl_2$; [g]H_2O_2/*t*-BuOOH/$ZnCl_2$/Et_3N.

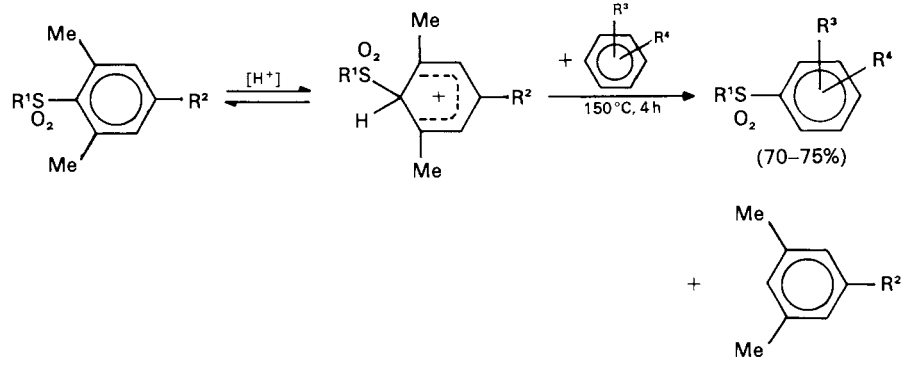
TABLE 7. Sulfones from unsaturated C—C systems and selenosulfonates



It is noteworthy that in these selenosulfonylations, the direction of the addition is opposite to the corresponding additions of sulfonyl iodides to allenes (cf. Table 7 in Reference 238).

C. S-Substitution of Sulfonyl Electrophiles with C-Nucleophiles

In principle, sulfonyl compounds bearing highly-electron-accepting substituents are able to transfer the sulfonyl group as an electrophile. Thus, the exchange of aryl substituents in methyl aryl sulfones under catalysis of trifluoromethanesulfonic acid takes place[258] (equation 46). This reaction represents a further example for the reversibility of Friedel–Crafts reactions.



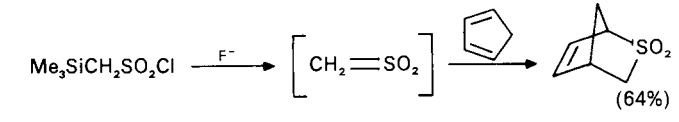
$R^1 = Me$ $R^3 = H, Me, OMe, OEt, OPh$

$R^2 = H, Me, Ph$ $R^4 = H, Me$ (46)

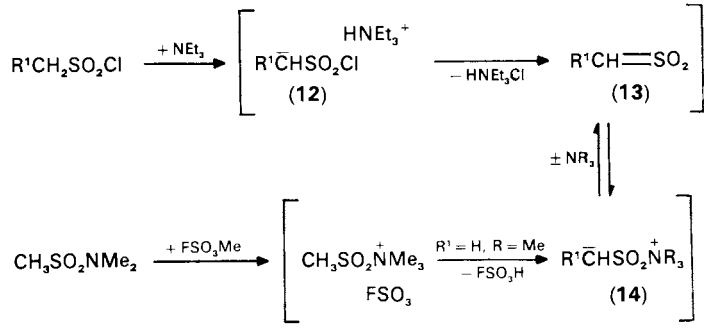
Normally, reactive derivatives of sulfonic acids serve to transfer electrophilic sulfonyl groups[259]. The most frequently applied compounds of this type are sulfonyl halides, though they show an ambiguous reaction behavior (cf. Section III.B). This ambiguity is additionally enhanced by the structure of sulfonyl halides and by the reaction conditions in the course of electrophilic sulfonyl transfers. On the one hand, sulfonyl halides can displace halides by an addition–elimination mechanism; on the other hand, as a consequence of the possibility of the formation of a carbanion α to the sulfonyl halide function, sulfenes can arise after halide elimination and show electrophilic as well as dipolarophilic properties.

1. *Sulfene reactions*

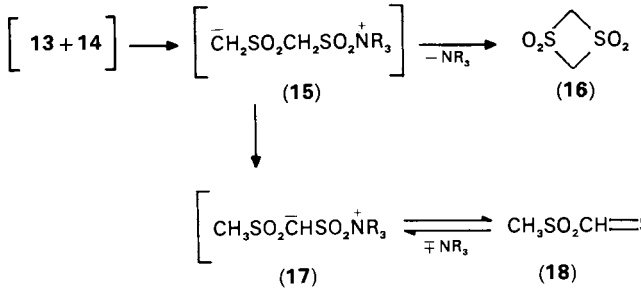
Recent investigations show that *free* sulfenes arise from fluoride-induced fragmentation of trimethylsilylmethanesulfonyl chloride, as could be proved by trapping in the course of a Diels–Alder reaction[260] (equation 47). Usually, generation of sulfenes[261] starts from sulfonyl halides with at least one α hydrogen and tertiary bases, where the ammonium ylide **14** dominates over **13**. Mixtures of **13** and **14** may also be obtained by N-alkylation of methanesulfonic acid dimethylamide[262] (equation 48). In the absence of efficient trapping reagents[263], the intermediates **12**, **13** and **14** are able to react with each other in different ways. With $R^1 = H$, **13** and **14** may yield **15**, which undergoes either ring closure to the cyclic disulfone **16**[264] or proton migration to yield **17** (equation 49). On the other hand, **17**



(47)

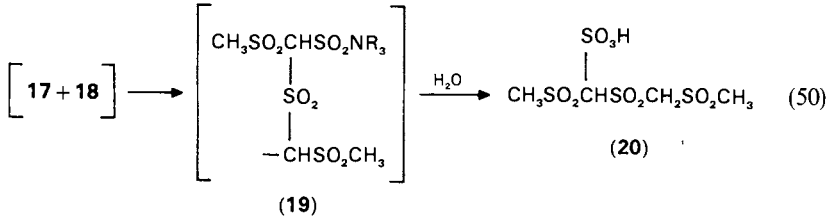


(48)

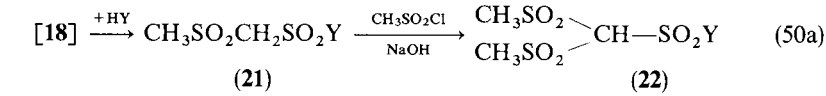


(49)

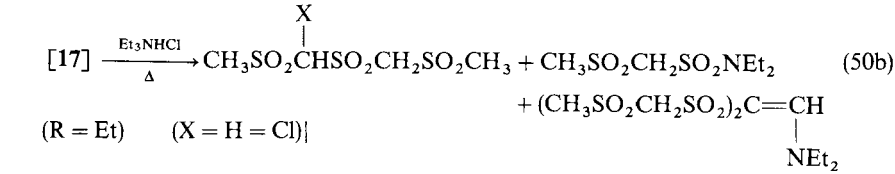
and **18** exhibit the same equilibrium as **13** and **14** as well as addition to yield **19**[265] which in turn is hydrolyzed to give **20** (equation 50). The sulfonyl sulfene **18** can be trapped by appropriate (proton activated) nucleophiles[262,263,265] to furnish **21**, which is further mesylated to **22**[263,265] (equation 50a). At −40 °C the sulfene oligomerizations become slower from step to step; the ylide **17** proves to be storable in acetonitrile at this temperature for several days without significant decomposition[266]. On thermolysis, the products in equation 50b have been identified.



(50)

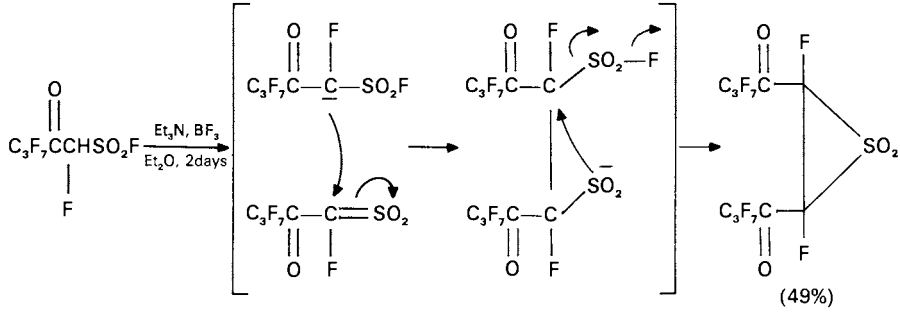


(50a)



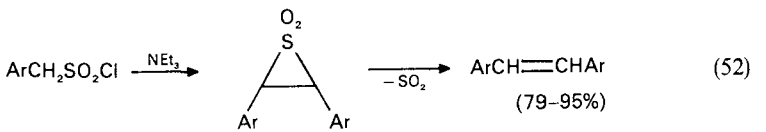
(50b)

The sulfene reactions discussed above use C—S bonds for dimerizations and oligomerizations. However, starting with appropriate substituents R^1 (equation 48: R^1 = aryl, acyl), more stabilized anions **12** are obtained, which react with their corresponding sulfenes **13** under C—C bond formation followed by ring closure to a three-membered ring sulfone (Wedekind–Staudinger reaction)[267] (equation 51). In most cases these thiirane *S*,*S*-dioxides extrude sulfur dioxide[268] under formation of olefins[269] (equation 52). In the case of the conversion of cinnamylsulfonyl chloride, a mixture of *Z* and *E* 1,2-bis(*trans*-β-styryl)thiirane *S*,*S*-dioxides is formed. The *E* isomer undergoes ring enlargement to give a seven-membered ring sulfone[269] (equation 53). On the other hand, reductive ring opening of *Z*-2,3-diphenylthiirane *S*,*S*-dioxide yields the open-chain

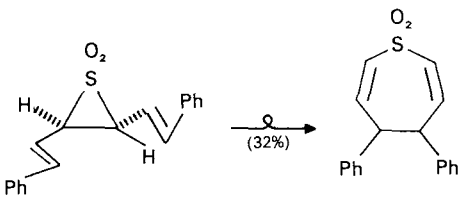


(51)

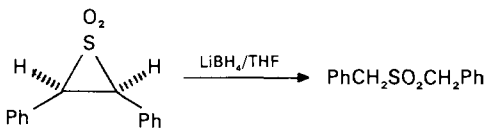
dibenzyl sulfone[270a] (equation 54). Lewis-acid-catalyzed insertion of thiirane 1, 1-dioxide into α-halo ethers also furnishes open-chain sulfones[270b] (equation 55). In most cases sulfenes are trapped *in situ* with appropriate reagents containing reactive C=C double bonds (equation 56). The four-membered ring sulfones thus obtained by [2 + 2]cycloaddition will be treated in another chapter of this volume. It should be mentioned, however, that in special cases facile hydrolytic cleavages of the initially formed thietane *S*, *S*-dioxides occur with formation of open-chain sulfones[273,274] (equations 57 and 58).



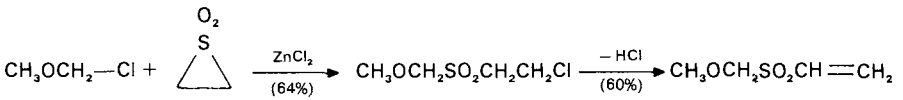
(52)



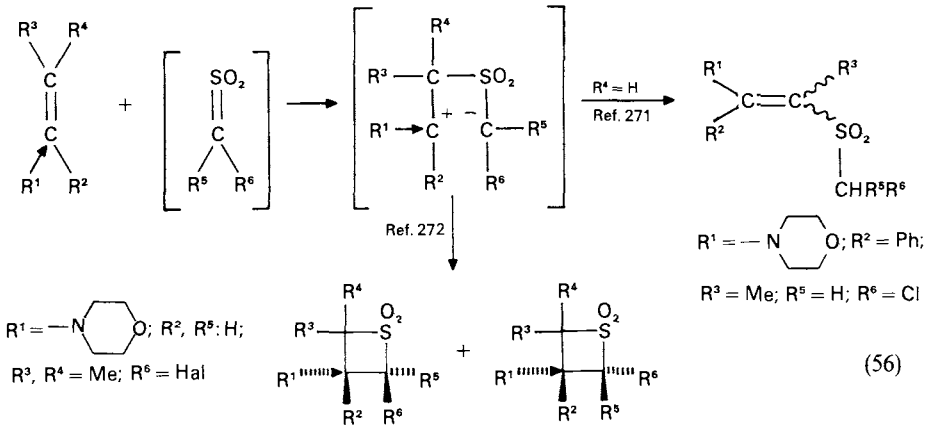
(53)



(54)

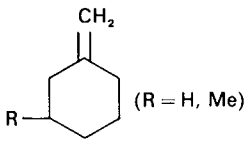
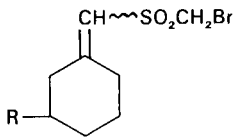
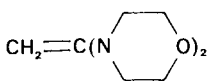
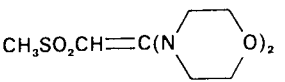
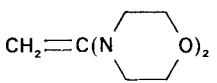
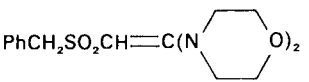
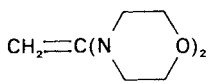
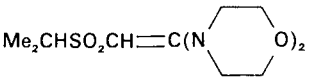
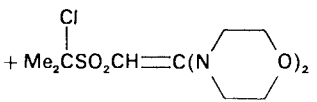
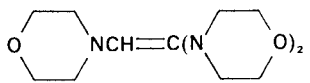
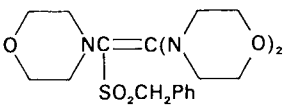
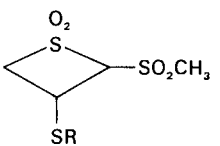


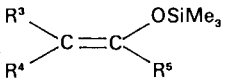
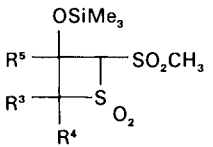
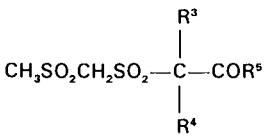
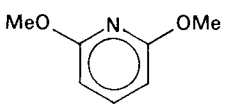
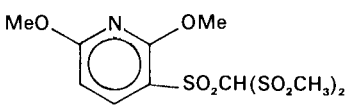
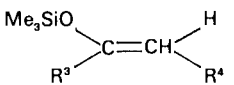
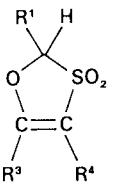
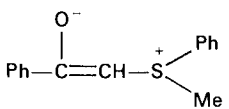
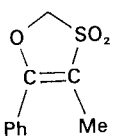
(55)



(56)

TABLE 8. (Partly) open-chain sulfones from sulfenes and their dimers

$R^1R^2CHSO_2X$ R^1	R^2	X	Unsaturated compound	Base (solvent)	Sulfone	Yield (%)	Ref.
Br	H	Br		Et_3N		*a*	275
H	H	Cl		(DMF)		58	276
Ph	H	Cl		(DMF)		60	276
Me	Me	Cl		Et_2NH(DMF)			
						8,12	276
Ph	H	Cl		Et_3N		26	277
H	H	Cl	CH_2=CHSR (R = Me, Et, Bu, *t*-Bu, *c*-C_6H_{11})	Et_3N		32–75	278

H	H	Cl		Et_3N (EtOH/MeCN)		7–53	279
						7–68	
H	H	Cl		Et_3N		80	280
H, Me	Cl, Br, I	Br		DBN		≤ 70	281
Me	H	Cl		Et_3N		36	282

[a]Obtained only as intermediate.

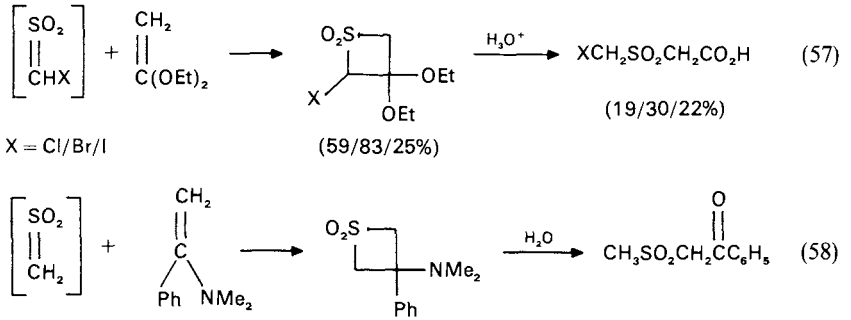


Table 8 gives a survey on some selected syntheses of (partly) open chain sulfones from sulfenes.

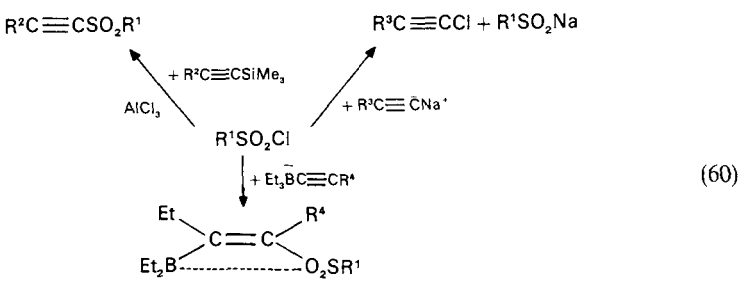
2. Halide substitution in sulfonyl halides

Besides radical additions to unsaturated C—C bonds (Section III.B.1) and sulfene reactions (see above), sulfonyl halides are able to furnish sulfones by nucleophilic substitution of halide by appropriate C-nucleophiles. Undesired radical reactions are suppressed by avoiding heat, irradiation, radical initiators, transition-element ion catalysis, and unsuitable halogens. However, a second type of undesired reaction can occur by transfer of halogen instead of sulfonyl groups[283–286] (which becomes the main reaction, e.g. with sulfuryl chloride). Normally, both types of undesired side-reaction can be avoided by utilizing sulfonyl fluorides.

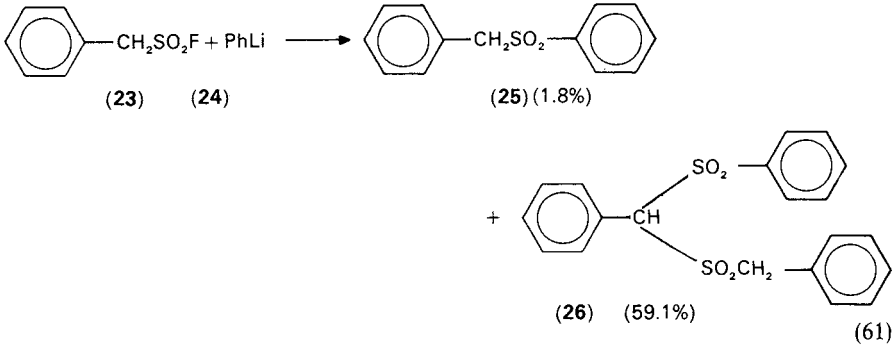
a. Friedel–Crafts related sulfonylations. Sulfonylations of arenes by sulfonyl halides under Friedel–Crafts conditions have been reviewed frequently[288]. Appropriate catalysts are Lewis acids (e.g. $AlCl_3$[289], SbX_5[290], $FeCl_3$[291]) or heteropolyacids[292] (equation 59). In some special cases, cyclopropane[293] and olefins[294] as well as silyl and stannyl compounds[295] are also sulfonylated under Lewis acid catalysis.

$$ArH + RSO_2X \xrightarrow[-HX]{\text{catalyst}} ArSO_2R \tag{59}$$

b. Sulfonylation of reactive carbon nucleophiles. Whereas bis(trimethylsilyl)acetylene exhibits sulfone formation under Friedel–Crafts catalysis[295b], sodium acetylides are halogenated by arenesulfonyl chlorides, bromides and iodides[296] under simultaneous formation of sodium arenesulfinates. On the other hand, complexation of the nucleophilic carbon by triethylborane and subsequent conversion with sulfonyl chlorides leads to a regiospecific sulfonylation of the vicinal carbon atom[297] (equation 60).

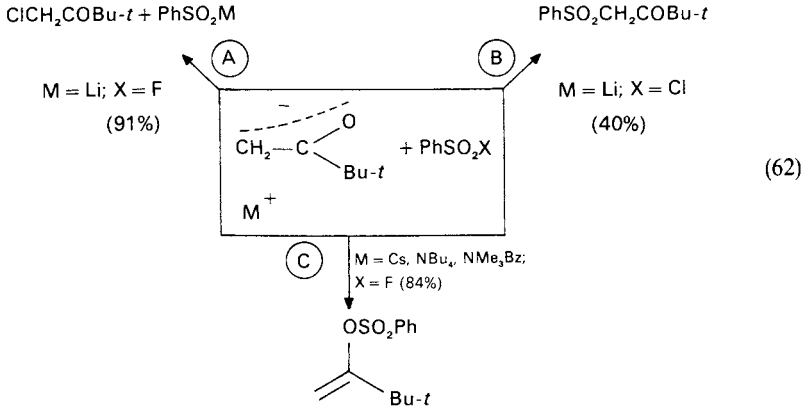


Whereas aryl Grignard compounds afford good yields of sulfones with sulfonyl fluorides[298,299], phenyllithium is mainly chlorinated by α-toluene-sulfonyl chloride; on the other hand, the corresponding fluoride yields only a trace of the expected monosulfonylation product, while the main product is **26** obtained by twofold sulfonylation[300] (equation 61).



(61)

Corresponding 1,1-disulfones have been obtained from alkyl Grignard and alkyllithium compounds with tosyl fluoride[301]. From diarylcadmium compounds and aromatic[302] as well as aliphatic[303] sulfonyl chlorides, the formation of sulfones in moderate yields has been reported. Obviously, these reactions follow a radical pathway shown by the additional formation of chloroarenes as well as diaryls. A similar sulfone synthesis from diarylmercury compounds and tosyl iodide[304] has been investigated earlier. Conversions of a twofold ambiguity occur with enolates and arenesulfonyl halides depending on the counter-cation on the one hand, as well on the halogen on the other. Whereas enolates with partly shielded oxygen undergo C-chlorination with sulfonyl chloride (route A; see equation 62) and C-sulfonylation with sulfonyl fluoride[284] (route B), free enolate ions act as O-nucleophiles and yield enol sulfonates with sulfonyl fluoride[305] (route C).

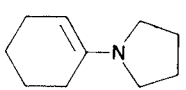
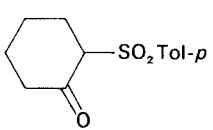


(62)

In connection with route A, the formation of sulfones from sulfinates and α-haloketones on the one hand, and of isomeric enol sulfonates on the other (cf. Section III.A.4), should be pointed out.

Table 9 gives a summary of sulfonylations of several types of C-nucleophiles with

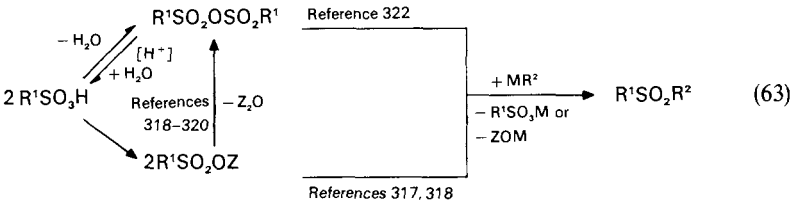
TABLE 9. Sulfones R^1SO_2X from different C-nucleophiles and sulfonyl halides

R^1SO_2X R^1	X	C-nucleophile	Sulfone	Yield	Ref.
p-BrC_6H_4	F	PhMgBr	*p*-$BrC_6H_4SO_2Ph$	91	299
$PhCH_2$	F	PhMgBr	$PhCH_2SO_2Ph$	88	298 (299)
CH_3	Cl	$(MeO_2C)_2CHNa$	$(MeO_2C)_2CHSO_2CH_3$	58	306
CF_3	F	$(EtO_2C)_2CHNa$	$(EtO_2C)_2CHSO_2CF_3$	86	307a
CF_3^-	F	$CH_3SO_2CH_2MgBr$	$CF_3SO_2CH_2SO_2CH_3$	70	307b
C_4H_9	F	$(EtO_2C)_2CHNa$	$(EtO_2C)_2CHSO_2C_4H_9$	80	307a
CH_3	Cl	$CH_3COC^-HCO_2Me$ Na^+	$CH_3CO(MeO_2C)CHSO_2CH_3$	15	306 (308)
		C_6H_5Co $C_6H_5COC^-HCO_2Et$ Na^+	$C_6H_5CO(EtO_2C)CHSO_2CH_3$	26	308
		$(C_6H_5CO)_2CHNa$	$(C_6H_5CO)_2CHSO_2CH_3$	26	308
p-Tol	F	CH_3CH_2MgBr	$CH_3CH(SO_2Tol\text{-}p)_2$	83	301
		$CH_2{=}PPh_3$	*p*-$TolSO_2CH{=}PPh_3$	74	309
		$PhCH{=}PPh_3$	*p*-$TolSO_2C(Ph){=}PPh_3$	12	309
$MeCH_2$	F	$PhCH{=}PPh_3$	$PhCH_2SO_2C(Me){=}PPh_3$ (rearrangement product!)	94	310
t-$BuCH_2$	F	$PhCH{=}PPh_3$	*t*-$BuCH_2SO_2C(Ph){=}PPh_3$	77	310
p-An	F	CH_2SOMe_2	*p*-$AnSO_2\dot{C}HSOMe_2$	91	311
p-Tol	Cl			54	312
		$PhC(OSiMe_3){=}CH_2$	$PhCOCH_2SO_2Tol\text{-}p$	66	313

sulfonyl halides. In this connection, it should be mentioned that organocobalt complexes yield sulfones with sulfonyl chlorides, however, under photochemical conditions[314,315].

3. *Sulfonic acid anhydrides and esters*

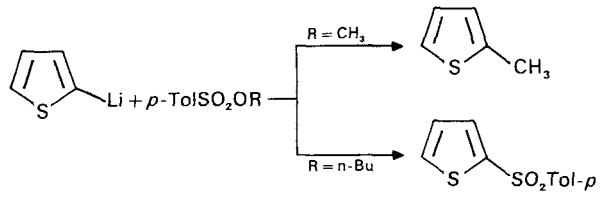
Sulfonic acids themselves are unfit for electrophilic transfer of sulfonyl groups because of the poor nucleofugality of the hydroxide anion. However, the high acidity obviously leads to an equilibrium between the acids and their anhydrides and water, from which water can be removed either by special reaction conditions (i.e., azeotropic distillation with appropriate solvents) or chemically with anhydride forming agents[316] (equation 63). sulfonic acid anhydride sulfonylations are compiled in Table 10.



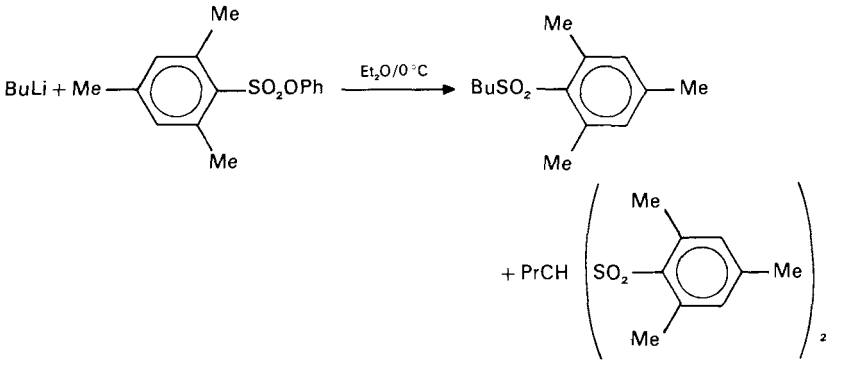
(63)

$Z = ClO_3$[317] SO_3H[318] COR[3 319] $SOCl$[320] etc.; M = H, Na, MgX (X = Br, OEt) etc.; R^2 = nucleofugal groups

The formation of halogenation products from Grignard reagents and sulfonic acid anhydrides is the result of an oxidative reaction pathway[323,327]. This side-reaction can be reduced by using sulfonic acid esters, however, in these cases alkylations[328] as well as twofold sulfonylations[329] (cf. corresponding results with sulfonyl fluorides[301]) are competing (equations 64 and 65).

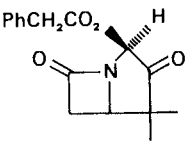
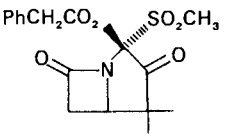


(64)



(65)

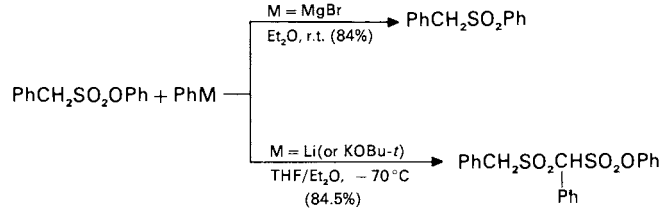
TABLE 10. Sulfones from different C-nucleophiles and sulfonic acid anhydrides $(R^1SO_2)_2O$

R^1	C-Nucleophile	Sulfone	Yield (%)	Ref.
CH_3	*p*-AnCH=PPh_3	*p*-$AnCH_2SO_2CH{=}PPh_3$ (rearranged product!)	61	310
			/	321
	C_6H_4Z-*p* (Z = Me, OMe)	$CH_3SO_2C_6H_4Z$-*p*	53,70	322
CF_3	$PhCH_2MgCl$	$PhCH_2SO_2CF_3$[+ $PhCH_2Cl$ (13%)]	87	323
	PhC≡CMgBr	$PhC{\equiv}CSO_2CF_3$[+ PhC≡CBr (63%)]	5	323
	PhC≡CLi	$PhC{\equiv}CSO_2CF_3$	72	324
	TolH	*p*-$TolSO_2CF_3$ + *o*-$TolSO_2CF_3$	46 + 23	325
C_4F_9	PhC≡CLi	$PhC{\equiv}CSO_2C_4F_9$	28	326
Ph	C_6H_4Z-*p* (Z = H, Br)	$PhSO_2C_6H_4Z$-*p*	99,74	327

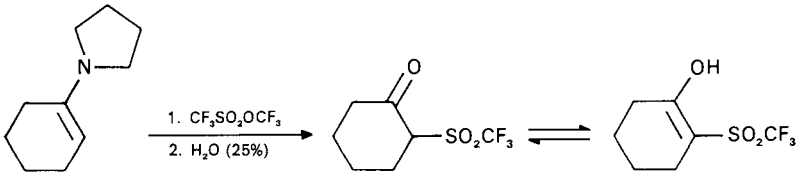
Interestingly, in the latter case no sulfone formation was observed in THF at $-70\,^{\circ}C$[330]. By ^{18}O-labelling of menthyl phenylmethanesulfonate, sulfone formation through a possible sulfene mechanism could be excluded[331]. Reasonable to good yields of sulfones can be obtained by conversion of organolithium compounds with aryl arenesulfonates[332] (equation 66). Whereas phenyl phenylmethanesulfonate and phenylmagnesium bromide furnish the expected sulfone[333], phenyllithium functions as a base[334] causing a Claisen-like sulfonic acid ester condensation which ensues equally under the influence of potassium *t*-butoxide[334] (equation 67). Activated alkyl sulfonates like trifluoromethyl trifluoromethanesulfonate[335] and β-sultones[336] have been utilized to transfer sulfonyl groups to C-nucleophiles (equations 68 and 69).

$$R^1Li + p\text{-}R^2C_6H_4SO_2OPh \xrightarrow[-25\rightarrow+25\,^{\circ}C]{Et_2O} R^1SO_2C_6H_4R^2\text{-}p \qquad (66)$$

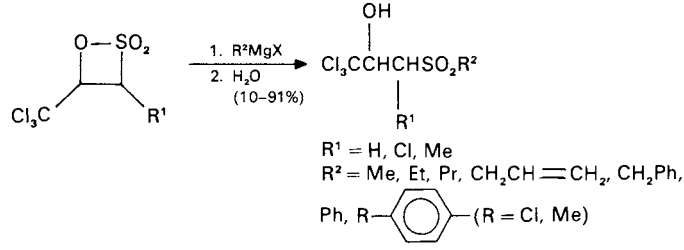
(36–98%, 21 examples)



(67)



(68)

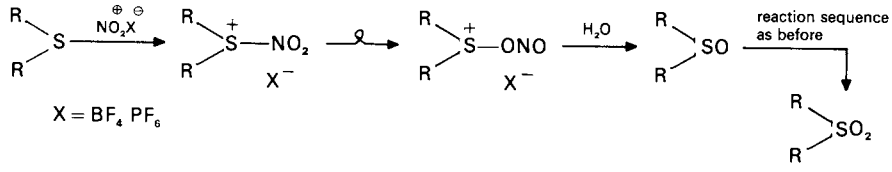


(69)

D. Sulfones by S-Oxidation[336]

The most widely applied method to prepare sulfones is the oxidation of thioethers. In the course of these oxidations sulfoxides must occur as intermediates. However, since oxidation mechanisms for thioethers and sulfoxides are partly different, these oxidations will be discussed separately. A recently published method[337,338] allows oxidation of a

thioether to its sulfoxide without formation of the corresponding sulfone (equation 70). The nitrito sulfonium intermediate is unable to react a second time with the nitrosyl salt. However, after hydrolysis the so-obtained sulfoxide yields the corresponding sulfone in a similar way.



(70)

The usual oxidizing agents transfer oxygen (or halogens and related species with subsequent hydrolysis) stepwise to the sulfur of thioethers: Rates of step A compared with those of step B are faster with electrophilic oxidation agents (peroxy acids); inversely, rates of step B compared with those of step A are faster with nucleophilic oxidation agents (peroxy anions)[339-341].

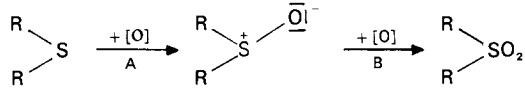
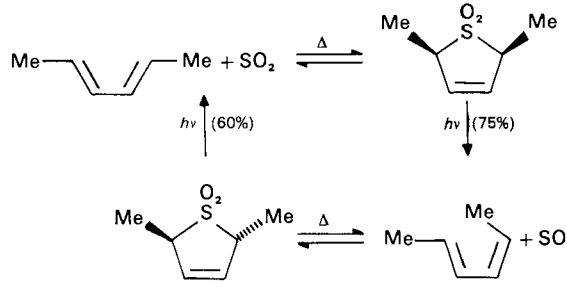


Table 11 affords a survey on oxidation methods of thioethers and sulfoxides.

E. Sulfolene Reaction[428] and Related Cycloadditions

These methods use sulfur dioxide as a building block, generally for cyclic sulfones. However, since several variations allow the preparation of open-chain sulfones too (Section III.D), several selected examples will be presented here.

By a sequence of thermal and photochemical steps in the course of a simple sulfolene reaction, stereospecific isomerizations are possible[429-431] (equation 71). On the other



(71)

hand, in the presence of an appropriate catalyst [consisting of 1 $Pd(acac)_2 + 3PPh_3 + 2AlEt_3$] reaction of sulfur dioxide and butadiene leads to sulfolanes with unsaturated groups in α-, α'-position[432,433]:

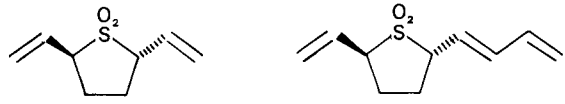


TABLE 11. Oxidation of thioethers and sulfoxides by various methods

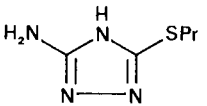
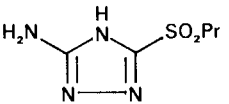
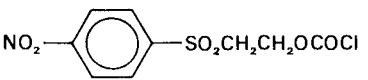
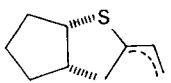
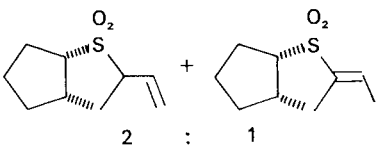
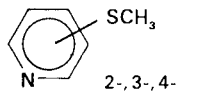
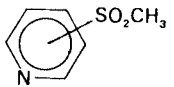
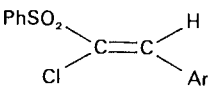
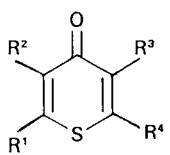
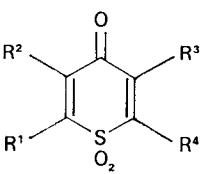
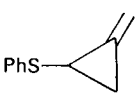
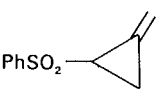
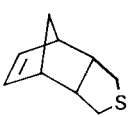
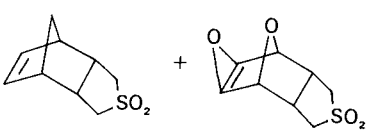
Thioether or sulfoxide	Oxidation conditions (and remarks)	Sulfone	Yield (%)	Ref.*
R^1SR^2 (R^1, R^2 = Et, CH_2Ph; R^1—R^2 = —$(CH_2)_n$— $n = 5, 6$)	$O_2/h\nu$ [TPP] (yields of sulfoxides 36–88%)	$R^1SO_2R^2$	7–33	342
MeSOMe	$O_2/h\nu$[TPP]	$MeSO_2Me$	99	343 (344)
MeSOMe	$^1O_2$	$MeSO_2Me$	/	345, 346
MeSPh	O_3 (1.85 mol only)	$MeSO_2Ph$	97	347
PhSOPh	KO_2/18-crown-6/$(EtO)_2POCl$	$PhSO_2Ph$	73	348 (349)
	H_2O_2/100 °C		47	350
p-$O_2NC_6H_4SCH_2CH_2OH$	1. H_2O_2; 2. $COCl_2$		100	351
$RS(CH_2)_nOH$ (R = Alkyl)	H_2O_2/HCl or HBr	$RSO_2(CH_2)_nCl$ (or Br)	60–85	352
	H_2O_2/THF, 0 °C	 2 : 1	92	353 (354–357)
MeSMe	H_2O_2/EtOH/NaOH	$MeSO_2Me$	98	358 (359)
R^1SR^2	H_2O_2/V_2O_5	$R^1SO_2R^2$	52–79	360

TABLE 11. (Contd.)

Thioether or sulfoxide	Oxidation conditions (and remarks)	Sulfone	Yield (%)	Ref.*
 2-, 3-, 4-	H_2O_2/Na_2WO_4		76,99,36	361 (362,363)
R^1SR^2	H_2O_2/SeO_2	$R^1SO_2R^2$	73–100	364
R^1SR^2	H_2O_2/ArSeOH	$R^1SO_2R^2$	98–100	365 (353)
MeSMe	$H_2O_2/PhCH_2CN$	$MeSO_2Me$	100	366
PhSPh	$H_2O_2/FeCl_3$/dry MeCN (with molar amount: 100% sulfoxide)	$PhSO_2Ph$	100	367
$PhSCH{=}CH_2$	H_2O_2/HOAc/70 °C	$PhSO_2CH{=}CH_2$	78	368
$PhSCHPO(OEt)_2$ | Cl	1. H_2O_2/HOAc (or MCPBA); 2. NaH/THF; ArCHO		77–90	369
	H_2O_2/HOAc/100 °C		63–69	370
	H_2O_2/HOAc		80	371 (372)
R^1SR^2	sodium perborate	$R^1SO_2R^2$	91–99	373
	$KHSO_5/KHSO_4/K_2SO_4$ (oxone)		80 + 20	374 (372)

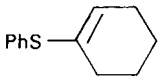
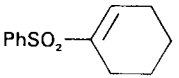
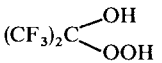
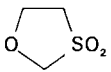
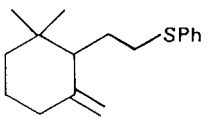
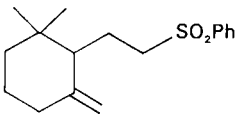
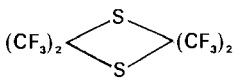
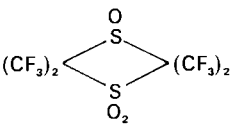
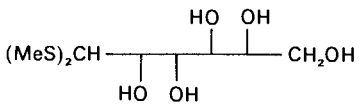
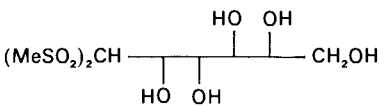
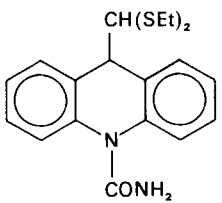
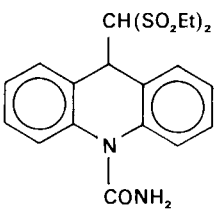
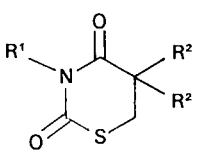
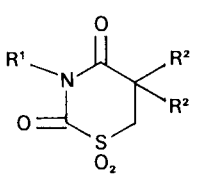
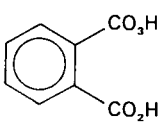
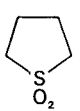
$R^1R^2R^3CSOCH_2CH{=}CH_2$	$KHSO_5/KHSO_4/K_2SO_4$	$R^1R^2R^3CSO_2CH_2CH{=}CH_2$	31–54	375
	$KHSO_5$		98	376a
$(EtO)_2P(=O)CH_2SPh$	$KHSO_5$	$(EtO)_2P(=O)CH_2SO_2Ph$	94	376b
PhSPh		$PhSO_2Ph$	98	377
PhSPh	Me_3COO^-	$PhSO_2Ph$	90	378 (372)
	$Me_3COOH/MnO_2(acac)_2$		72	372
	$Me_3SiOOSiMe_3/80\,°C$		83	379 (372)
$MeSCMe_2CN$	CH_3CO_3H	$MeSO_2CMe_2CN$	95	380 (381)
R^1SR^2	CF_3CO_3H	$R^1SO_2R^2$	58–99	382 (383,384)
	$CF_3SO_3H/20\,°C$		47	384
	$CF_3SO_3H/30\,°C$		56	384

TABLE 11. (Contd.)

Thioether or sulfoxide	Oxidation conditions (and remarks)	Sulfone	Yield (%)	Ref.*
	$C_2H_5CO_3H$		94	385
$(p\text{-}O_2NC_6H_4)_2SO$	$PhCO_3H$ (kinetic measurements)	$(p\text{-}NO_2C_6H_4)_2SO_2$		386
PhSPh	$C_6F_5CO_3H$	$PhSO_2Ph$	92	387
	$3\text{-}ClC_6H_4CO_3H/CHCl_3/-40\,°C$ (MCPBA)		64	388
	$3\text{-}ClC_6H_4CO_3H/CHCl_3/-40\,°C$ (MCPBA)		31–100	389 (372, 390)
$(MeS)_2CHCO_2Me$		$(MeSO_2)_2CHCO_2Me$	78	391 (372,392)
	Resin-CO_3H	 (+ sulfoxide)	/	393

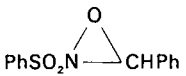
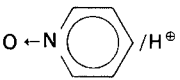
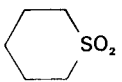
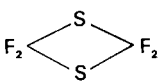
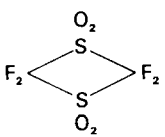
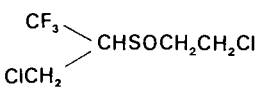
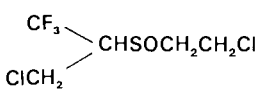
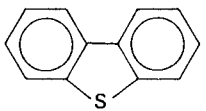
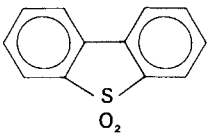
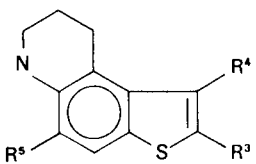
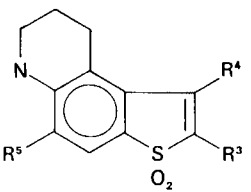
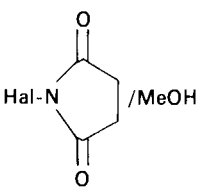
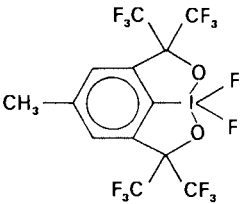
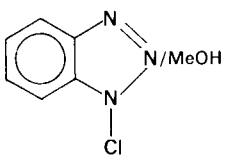
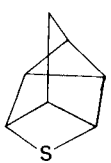
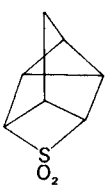
MeSPh		$MeSO_2Ph$ (+ sulfoxide, 20%)	80	394 (395)
MeSOMe		$MeSO_2Me$	94	396
PhSPh	RuO_4	$PhSO_2Ph$	70	397
PhSOPh	RuO_4	$PhSO_2Ph$	93	397
	OsO_4 (oxidizes sulfoxides faster)		58	398
CH_3SOCH_2OMe	MnO_4^-	$CH_3SO_2CH_2OMe$	68	399 (372, 400, 401)
R^1SR^2	1. $NaIO_4$; 2. $KMnO_4/MgSO_4$	$R^1SO_2R^2$	75–93	402
MeSPh	$Zn(MnO_4)_2/SiO_2$	$MeSO_2Ph$	92	403
$ClCH_2CH_2STol\text{-}p$	$KMnO_4/H^+$	$ClCH_2CH_2SO_2Tol\text{-}p$	83	404 (405,406)
	CrO_3/HNO_2		15	407 (372)
	CrO_3/H_2SO_4 (60%)		75	408
ArSAr	1. F_2/Neon; 2. H_2O	$ArSO_2Ar$	/	409

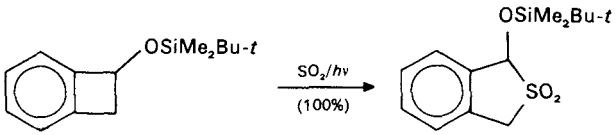
TABLE 11. (Contd.)

Thioether or sulfoxide	Oxidation conditions (and remarks)	Sulfone	Yield (%)	Ref.*
	1. Cl_2; 2. H_2O		93	410 (372)
CH_3SOCH_3	Br_2/OH^-	$CBr_3SO_2CBr_3$	88	411 (412)
$PhCH_2SOCHPh_2$	SO_2Cl_2/CaO	$PhCH_2SO_2CHPh_2$	80	413 (414,415)
	NaOCl		47–53	416 (372)
$(ClCH_2CH_2)_2S$	$Ca(OCl)_2$	$(ClCH_2CH_2)_2SO_2$	22	417
ArSAr		$ArSO_2Ar$	/	418
PhSPh	$PhICl_2/H_2O$/pyridine	$PhSO_2Ph$	100	419
PhSPh	$PhI(OCOCF_3)_2$	$PhSO_2Ph$	91	420

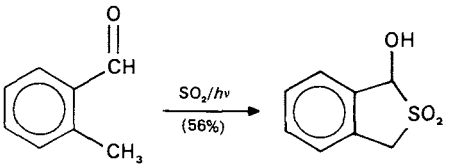
$(4\text{-}ClC_6H_4)_2S$		$(4\text{-}ClC_6H_4)_2SO_2$ (+ sulfoxide 53%)		21	421
PhSOPh	$PhIO_2/VO(acac)_2$	$PhSO_2Ph$		73	422
MeSOMe	Chloroamine T	$MeSO_2Me$		100	423a (424,425)
MeSOMe	Disproportionation	$MeSO_2Me$		/	423b
MeSOPh		$MeSO_2Ph$		97	426
	$NaIO_4$		(+ sulfoxide 32%)	47	427 (410,372)

*References in brackets contain material for further reading.

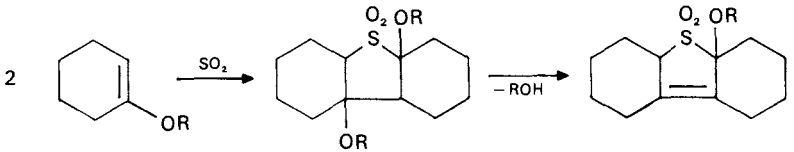
A direct insertion of sulfur dioxide into a C—C bond has been observed under photochemical conditions[434] (equation 72); a related CH insertion followed by an intramolecular sulfinate to carbonyl addition yields the same system[434] (equation 73). A further sulfolene synthesis utilizes a three-component reaction; see equation 74 (cf. Section IV below)[435].



(72)

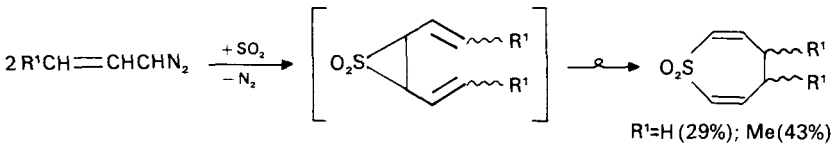


(73)



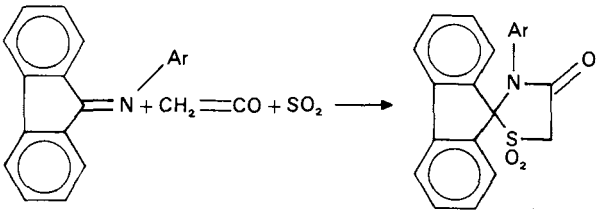
(74)

Other interesting three-component cycloadditions are the following: Sulfur dioxide and diazo compounds lead to episulfones (equation 75)[436]—in a special case to 4,5-dihydrothiepine *S,S*-dioxides[437]; sulfur dioxide, ketene, and arylimine lead to thiazole derivatives[438] (equation 76); sulfur dioxide, quinone, and alkenes lead to benzoxathiane derivatives[439] (equation 77).

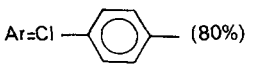


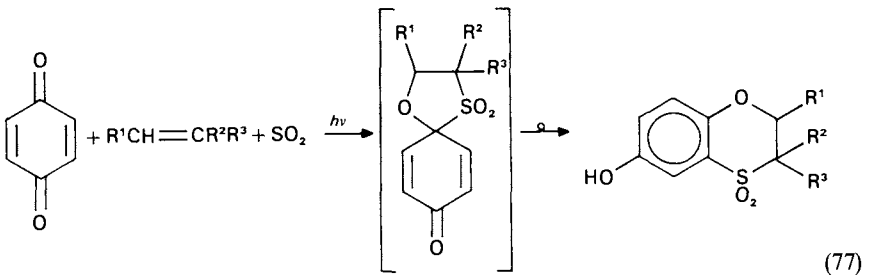
R¹=H (29%); Me(43%)

(75)



(76)



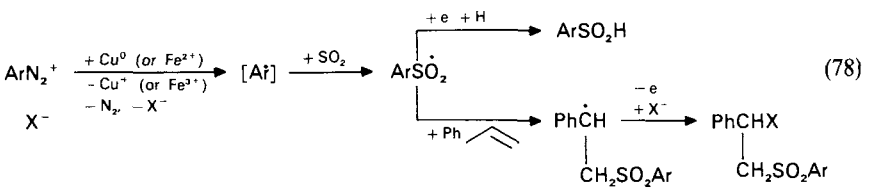


(77)

IV. THREE-COMPONENT METHODS

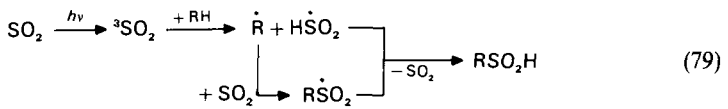
A. Additions to Sulfur Dioxide

Sulfur dioxide (see above) as well as $^3SO_2$, $SO_2^{\cdot\ominus}$, and $\{SO_2^{2\ominus}\}$ have been used as building blocks in three-component sulfone syntheses. It has long been known that aromatic sulfinic acids are easily available from diazonium salts and sulfur dioxide under copper catalysis[440]. Mechanistically, aryl radicals as reactive intermediates add to sulfur dioxide generating arenesulfonyl radicals, which either take up an electron (or hydrogen) yielding a sulfinic acid or add to an olefinic double bond yielding final β-halogenated alkyl aryl sulfones[441] (equation 78).

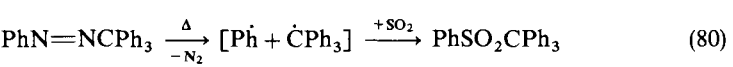


(78)

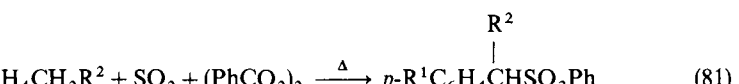
The free-radical reaction may be equally initiated by photoactivated sulfur dioxide ($^3SO_2$)[442] (equation 79). On the other hand, polysulfones are obtained by radical copolymerization of appropriate olefins with sulfur dioxide[443–449], and similarly, uptake of sulfur dioxide by a radical-pair formed by nitrogen extrusion from an azo compound yields the corresponding sulfone[450] (equation 80). Correspondingly, alkylbenzenes, dibenzoyl peroxide, and sulfur dioxide yield sulfones under thermal conditions[451]



(79)

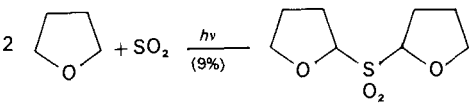


(80)



(81)

(equation 81). A combination between equation 79 and equations 80 and 81 affords the formation of an α-sulfonyl bisether[452]:



Beside these free radical reactions of sulfur dioxide, its electrophilic reactions generating sulfinates with organometallic compounds[453,454] or sulfinic acids with arenes under Friedel–Crafts conditions[455] are well known. To complete these three-component syntheses, the sulfinates prepared first are transformed to sulfones by reactions with appropriate electrophiles, discussed earlier in this chapter, i.e. equation 82.

$$R^1M + SO_2 \longrightarrow R^1SO_2M \xrightarrow[-MX]{+R^2X} R^1SO_2R^2 \tag{82}$$

The electrophilic character of sulfur dioxide does not only enable addition to reactive nucleophiles, but also to electrons forming sulfur dioxide radical anions which possess the requirements of a captodative[456] stabilization (equation 83). This electron transfer occurs electrochemically[457] or chemically under Leuckart–Wallach conditions (formic acid/tertiary amine[458,459], by reduction of sulfur dioxide with 1-benzyl-1,4-dihydronicotinamide[460] or with Rongalite[461]. The radical anion behaves as an efficient nucleophile and affords the generation of sulfones with alkyl halides[462–464] and Michael-acceptor olefins[458–460] (equations 84 and 85).

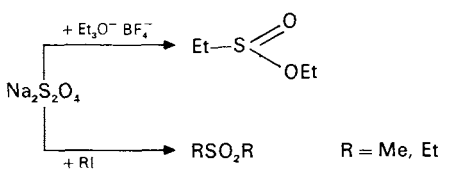
$$SO_2 + e \longrightarrow \bar{O}{-}\dot{S}{=}O \longleftrightarrow \dot{O}{-}\bar{S}{=}O \tag{83}$$

$$R^1X + \dot{S}O_2^- \xrightarrow[-X^-]{} \left[R^1\dot{S}O_2 \xrightarrow[-SO_2]{+SO_2^-} \right] R^1SO_2^- \xrightarrow{+R^2X} R^1SO_2R^2 \tag{84}$$

$$2\begin{matrix} R^1 \\ R^2 \end{matrix}\!\!>\!C{=}CH_2 \quad 2\dot{S}O_2^- + 2H^+ \xrightarrow[-SO_2]{} \begin{matrix} R^1 \\ R^2 \end{matrix}\!\!>\!CHCH_2SO_2CH_2CH\!<\!\begin{matrix} R^1 \\ R^2 \end{matrix} \tag{85}$$

Between sulfur dioxide radical anions, dithionite, and sulfoxylate/sulfite there exists a pH-dependent equilibrium[465] (equation 86). Therefore, dithionite has been used as a source of sulfoxylate in order to prepare sulfinate and hence sulfones. Alkylation with triethyl oxonium fluoroborate leads to ethyl ethanesulfinate, alkyl iodides lead to symmetrical sulfones[466] (equation 87).

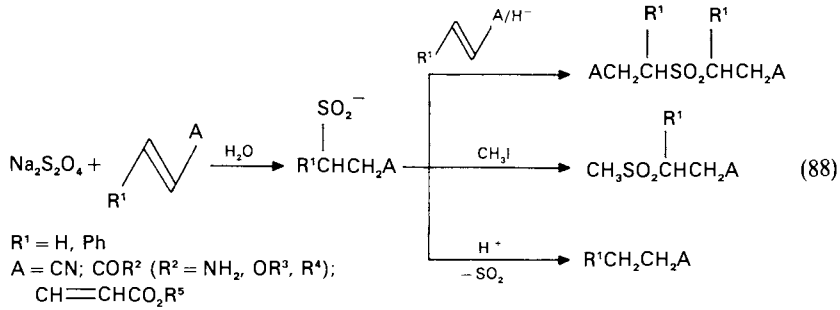
$$2\,\dot{S}O_2^- \rightleftharpoons S_2O_4^{2-} \xrightleftharpoons{\pm H_2O} HSO_2^- + HSO_3^- \tag{86}$$



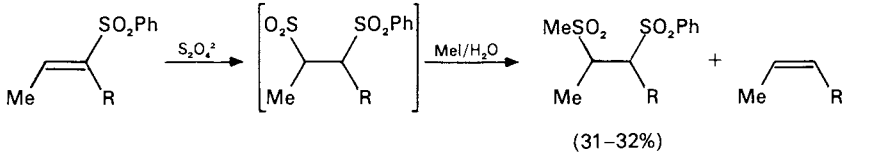
(87)

On the other hand, Michael-acceptor olefins add to the sulfoxylate stage from dithionite, yielding a sulfinate intermediate which yields, according to the reaction

conditions, symmetrical[467] or unsymmetrical sulfones[468,469], or which is decomposed under loss of sulfur dioxide (excess dithionite and PTC conditions) furnishing a hydrogenation product[465] (equation 88). Interestingly, α,β-unsaturated sulfones as acceptor olefins show formation of γ-disulfones in the same way, however, instead of a hydrogenation of the double bond as side-reaction, the formation of olefins has been observed[470] (equation 89). Principally, the same reactions as discussed above have been realized utilizing formamidino sulfinic acid[467] or Rongalite[461,467,471].



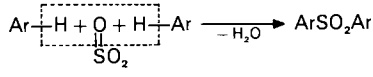
(88)



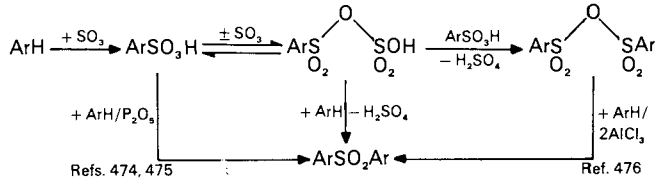
(89)

B. Condensations of Hydrocarbons with Sulfur Trioxide and its Derivatives

It has been known[472] that sulfones are side-products in the course of sulfonation of arenes with sulfur trioxide or its derivatives. Generally, this reaction may be expressed by equation 90. Mechanistic investigations have indicated[473] that this reaction follows the pathway shown in equation 91.



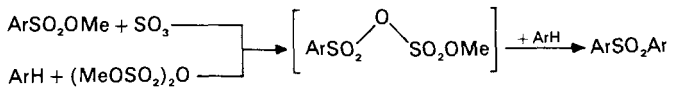
(90)



(91)

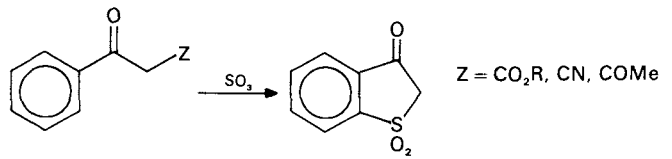
An important role must be attributed to intermediate mixed anhydrides of sulfonic acids and mineral acids; sulfonic acid anhydrides are reported to need Friedel–Crafts conditions to generate sulfones[327,476]. Instead of arenesulfonic acids, their methyl esters may undergo insertion of sulfur trioxide[477,478] yielding mixed anhydrides, which in turn furnish

sulfones in good yields (equation 92). On the other hand, the same reactive intermediate is also accessible from the sulfur trioxide insertion product of dimethyl sulfate and an arene[477].

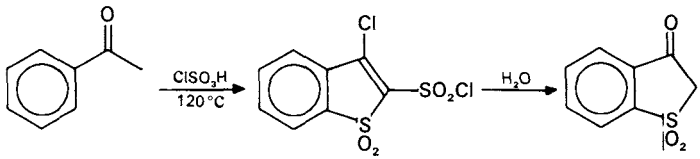


(92)

Using sulfur trioxide a nucleophilic aliphatic carbon and an aromatic nucleus may be connected by a sulfonyl bridge[479] (equation 93). Instead of sulfur trioxide, sulfuric acid or chlorosulfonic acid is utilized mostly. The procedures differ mainly by the manner in which the water is eliminated[480]; e.g., a mixture of sulfuric acid and trifluoroacetic anhydride was used recently[481]. Similarly to equation 93, 3-oxo-2, 3-dihydrobenzothiophene 1, 1-dioxide is available from acetophenone and chlorosulfonic acid[482] (equation 94).



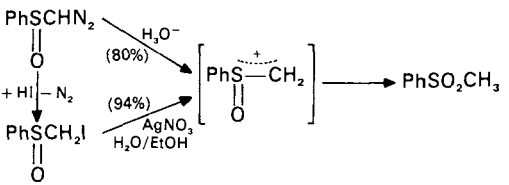
(93)



(94)

V. MISCELLANEOUS METHODS

In the course of the hydrolysis of an α-diazomethyl sulfoxide, a redox-disproportionation through an intermediate sulfinyl carbenium ion occurs[483] (equation 95). Sulfone formation has been observed in the course of several extrusion reactions. As shown in Section IV.A, a radical pair generated by extrusion of nitrogen may be trapped by sulfur dioxide under formation of a sulfone bridge[450]. Heating diazosulfinates (frequently and incorrectly designed as "azosulfones") yields directly sulfones after thermal extrusion of nitrogen, because the sulfone moiety is already incorporated into the starting molecule[484,485] (equation 96). In a related reaction, arenesulfonyl radicals are simultaneously generated by thermolysis of sulfonyl bromides or iodides in the presence of a radical pair obtained by extrusion of nitrogen from an azo compound[487] (equation 97).



(95)

$$ArSO_2N{=}NCF_3 \xrightarrow[-N_2]{\Delta} ArSO_2CF_3 \quad (40\%) \tag{96}$$

$$p\text{-TolSO}_2\text{X} + \text{PhN}{=}\text{NCPh}_3 \xrightarrow[\substack{-\text{N}_2\\-\text{PhX}}]{\Delta} p\text{-TolSO}_2\text{CPh}_3 \quad \text{X} = \text{Br (56\%), I (78\%)}$$

A corresponding extrusion of sulfur dioxide from disulfones has been reported[486] (equation 98). Extrusions of sulfur have also been observed from thiolsulfinates yielding sulfones[488,489].

Oxidative cleavage of oxosulfonium ylides[490] as well as of sulfoximines[491] leads to sulfone formation. In the course of oxidations of dialkoxy sulfuranes(IV) by hydrogen peroxide[492] or *t*-butyl hydroperoxide[493], sulfone formation takes place (equation 99).

$$\underset{\text{O}_2\ \text{O}_2}{\text{PhCH}_2\text{S—SCH}_2\text{Ph}} \xrightarrow[-\text{SO}_2]{\Delta} \underset{(12\%)}{\text{PhCH}_2\text{SO}_2\text{CH}_2\text{Ph}} + \underset{\text{(main product)}}{\text{PhCH}_2\text{CH}_2\text{Ph}} \qquad (98)$$

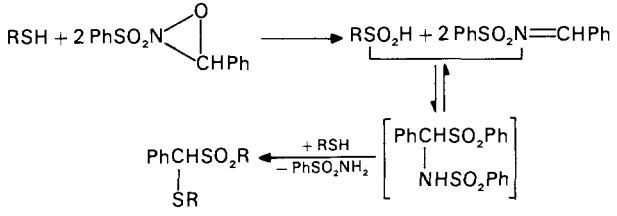
$$\begin{matrix}\text{Ph}\\ \text{Ph}\end{matrix}\!\!>\!\text{S(OR)}_2 \xrightarrow[-75\,^\circ\text{C}]{t\text{-BuOOH}} \underset{(88\%)\quad \text{R} = \text{C(CF}_3)_2\text{Ph}}{\text{PhSO}_2\text{Ph}} \qquad (99)$$

Electrochemical oxidation of disulfides and trapping of intermediately formed sulfinates by alkylation yields sulfones in good yields[494].

A very surprising sulfone formation has been investigated by Oae and coworkers[495]. On heating *p*-toluenesulfinic acid with dimethylaniline in ethanol for 15 h, the reaction mixture shown in equation 100 has been obtained. Obviously, the observed products arise from an equilibrium between the sulfinic acid and its pseudo-anhydride (disulfide trioxide), which is able to attack the amine nitrogen and degrade the tertiary amine corresponding to a Polonovsky reaction[496].

$$\begin{aligned} p\text{-TolSO}_2\text{H} + \text{PhNMe}_2 \longrightarrow\ & \underset{\text{O}_2\quad(34\%)}{p\text{-TolSCH}_2\text{C}_6\text{H}_4\text{NMe}_2} + \underset{\text{O}_2\quad(2\%)}{p\text{-TolSCH}_2\text{C}_6\text{H}_4\text{NHMe}} \\ & + p\text{-TolSC}_6\text{H}_4\text{NMe}_2 + \underset{\text{O}_x\ (x=0,2)}{p\text{-TolS—STol-}p} \\ & + \underset{\text{O}}{\underset{\|}{p\text{-TolSO}_3\text{H}}} \end{aligned} \qquad (100)$$

An interesting sulfone formation occurs when thiols are oxidized with a two-molar amount of 2-(benzenesulfonyl)-3-phenyloxaziridine[497]:



R = *t*-Bu

According to reaction conditions, formation of either the sulfinic acid or the α-thiolated sulfone could be observed (up to 80%); the intermediate α-sulfonylamino sulfone proved to be unstable.

VI. REFERENCES

1. K. Schank in *Methoden der Organischen Chemie* (*Houben-Weyl*), 4th ed., Vol. E11 (Ed. D. Klamann), Thieme, Stuttgart, 1985, p. 1129.

2. T. Durst in *Comprehensive Organic Chemistry*, Vol. 3 (Eds. D. H. R. Barton and W. D. Ollis), Pergamon, Oxford, 1979, p. 171.
3. P. D. Magnus, *Tetrahedron*, **33**, 2019 (1977).
4. W. E. Truce, T. C. Klingler and W. W. Brand in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, London, 1977, p. 527.
5. I. Haiduc and K. J. Wynne in *Methodicum Chimicum*, Vol. 7 (Eds. H. Zimmer and K. Niedenzu), Thieme, Stuttgart, 1976, p. 745.
6. H. H. Wragg, J. S. McFayden and T. U. Stevens, *J. Chem. Soc.*, 3603 (1958).
7. S. Braverman and C. Simons, *Mech. React. Sulfur Compd.*, **2**, 101 (1967).
8. S. Braverman, *Int. J. Sulfur Chem. C*, **6**, 149 (1971).
9. D. J. Raber, J. M. Harris and P. v. R. Schleyer in *Ions and Ion Pairs in Organic Reactions*, Vol. 2 (Ed. M. Szwarc), Wiley–Interscience, New York, 1974, p. 318.
10. K. Hiroi, R. Kitayama and S. Sato, *J. Chem. Soc., Chem. Commun.*, 1470 (1983).
11. S. Braverman and T. Globerman, *Tetrahedron*, **30**, 3873 (1974).
12. A. C. Cope, D. E. Morrison and L. Field, *J. Amer. Chem. Soc.*, **72**, 59 (1950).
13. (a) D. Darwish and R. McLaren, *Tetrahedron Letters*, 1231 (1962).
    (b) R. W. Hoffmann and W. Sieber, *Ann. Chem.*, **703**, 96 (1967).
14. S. Braverman and S. Steiner, *Isr. J. Chem.*, **5**, 267 (1967).
15. S. Braverman and H. Manor, *Phosphorus Sulfur*, **2**, 213, 215 (1976).
16. P. A. Grieco and D. Boseler, *Synth. Commun.*, **5**, 315 (1975).
17. S. Braverman and H. Mechoulam, *Isr. J. Chem.*, **5**, 71 (1967).
18. C. J. M. Stirling, *Chem. Commun.*, 131 (1967).
19. G. Smith and C. J. M. Stirling, *J. Chem. Soc. (C)*, 1530 (1971).
20. S. Braverman and H. Mechoulam, *Tetrahedron*, **30**, 3883 (1974).
21. M. Ohmori, S. Yamada, H. Takayama and K. Ochi, *Tetrahedron Letters*, **23**, 4709 (1982).
22. J. B. Hendrickson and P. L. Skipper, *Tetrahedron*, **32**, 1627 (1976).
23. H. Kropf, M. Ball and A. Gilberz, *Ann. Chem.*, 1013 (1974).
24. G. Büchi and R. M. Freidinger, *J. Amer. Chem. Soc.*, **96**, 3332 (1974).
25. H. W. Gibson and D. A. McKenzie, *J. Org. Chem.*, **35**, 2994 (1970).
26. A. H. Klazinga and A. Vos, *Recl. Trav. Chim. Pays-Bas*, **92**, 360 (1973).
27. A. Heesing, W. Kleine-Homann and W. Müllers, *Chem. Ber.*, **113**, 152 (1980).
28. K. Schank, in Ref. 1, p. 1190.
29. G. A. Russell and E. T. Sabourin, *J. Org. Chem.*, **34**, 2336 (1969).
30. K. Schank and S. Bügler, *Sulfur Letters*, **1**, 63 (1982).
31. K. Schank, *Ann. Univ. Sarav., Math.-Naturwiss. Fak.*, **16**, 35, 43 (1981); *Chem. Abstr.*, **96**, 5730 (1982).
32. S. Bügler, Diplomarbeit, Universität Saarbrücken, 1980.
33. V. M. Neplyuev and I. M. Bazavova, *Zh. Org. Khim.*, **17**, 2231 (1981); *Chem. Abstr.*, **96**, 68494 (1982).
34. H. Stetter and K. Steinbeck, *Ann. Chem.*, 1315 (1974).
35. A. R. Friedman and D. R. Graber, *J. Org. Chem.*, **37**, 1902 (1972).
36. N. P. Petukhova, N. E. Dontsova, E. N. Prilezhaeva and V. S. Bogdanov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 474 (1984).
37. F. Benedetti, S. Fabrissi and A. Risaliti, *Tetrahedron*, **39**, 3887 (1983); for further literature see K. Schank, in Ref. 1, p. 1270.
38. J. De Sales, R. Greenhouse and J. M. Muchowski, *J. Org. Chem.*, **47**, 3668 (1982).
39. A. Jończyk and T. Radwan-Pytlewski, *Chem. Letters*, 1557 (1983).
40. K. Kubo, N. Ito, Y. Isomura and M. Murakami, *Chem. Pharm. Bull.*, **28**, 1131 (1980).
41. M. J. Farrell, T. Durst and J. M. J. Frechet, *Tetrahedron Letters*, 203 (1979).
42. C. R. Johnson, K. Mori and A. Nakanishi, *J. Org. Chem.*, **44**, 2065 (1979).
43. T. Durst, K.-C. Tin, F. de Reinach-Hirtzbach, J. M. Descesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).
44. L. Thijs, A. Houwen-Claasen and B. Zwanenburg, *Phosphorus Sulfur*, **6**, 303 (1979).
45. D. F. Tavares, R. E. Estep and M. Blezard, *Tetrahedron Letters*, 2373 (1970).
46. (a) T. Durst and K.-C. Tin, *Tetrahedron Letters*, 2369 (1970).
    (b) X. Creary, *Acc. Chem. Res.*, **18**, 3 (1985).
47. K. Schank and F. Werner, *Ann. Chem.*, 1739 (1983).

48. G. Bouillon, *Dissertation*, Saarbrücken, 1982; K. Schank, G. Bouillon and V. Schramm, in preparation.
49. S. O. Myong, L. W. Linder, S. C. Seike and R. D. Little, *J. Org. Chem.*, **50**, 2244 (1985).
50. R. D. Baechler, P. Bentley, L. Deuring and S. Fisk, *Tetrahedron Letters*, 2269 (1982).
51. P. Lin and G. H. Whitham, *J. Chem. Soc., Chem. Commun.*, 1102 (1983).
52. K. Inomata, Y. Murata, H. Kato, Y. Tsukahara, H. Kinoshita and H. Kotake, *Chem. Letters*, 931 (1985).
53. K. Schank, *Chem. Ber.*, **103**, 3087 (1970).
54. B. Zwanenburg and A. Wagenaar, *Tetrahedron Letters*, 5009 (1973).
55. W. Jeblick and K. Schank, *Ann. Chem.*, 1727 (1976).
56. W. Jeblick and K. Schank, *Ann. Chem.*, 1096 (1977).
57. For review literature see K. Schank, in Ref. 1, p. 1191; W. E. Truce, T. C. Klingler and W. W. Brand in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, London, 1977, p. 543; F. Muth in *Methoden der Organischen Chemie (Houben-Weyl-Müller)*, 4th ed., Vol. 9, Thieme, Stuttgart, 1955, p. 640.
58. W. Bradley and J. D. Hannon, *Chem. Ind. (London)*, 540 (1959).
59. M. Rai, S. Kumar, K. Krishnan and A. Singh, *Chem. Ind. (London)*, 26 (1979).
60. A. Singh, S. Kumar, M. R. Manrao and B. Kaur, *J. Indian Chem. Soc.*, **59**, 673 (1982).
61. D. Hellwinkel and M. Supp, *Angew. Chem., Int. Ed. Engl.*, **13**, 270 (1974); *Tetrahedron Letters*, 1499 (1975).
62. M. Z. A. Badr, M. M. Aly and A. M. Fahmy, *J. Org. Chem.*, **46**, 4784 (1981).
63. H. Nozaki, T. Okada, R. Noyori and M. Kawanisi, *Tetrahedron*, **22**, 2177 (1966).
64. D. Hellwinkel, R. Lenz and F. Lämmerzahl, *Tetrahedron*, **39**, 2073 (1983).
65. D. Nagarathnam and P. C. Srinivasan, *Indian J. Chem.*, **B22**, 1050 (1983).
66. T. N. Gerasimova, V. A. Bushmelev and V. A. Koptyuk, *Zh. Org. Khim.*, **1**, 1667 (1965); *Chem. Abstr.*, **64**, 626 (1966).
67. S. S. Shrimali, N. D. Sharma, S. Kumar and B. C. Joshi, *Rev. Roum. Chim.*, **23**, 613 (1978).
68. R. Grover and B. C. Joshi, *J. Indian Chem. Soc.*, **56**, 1220 (1979).
69. S. S. Shrimali, A. Iyer, R. K. Singhal, D. Kishere and B. C. Joshi, *Rev. Roum. Chim.*, **24**, 597 (1979); *Chem. Abstr.*, **92**, 146474 (1980).
70. K. S. Burmistrov, N. V. Toropin, S. I. Burmistrov and S. V. Loban', *Zh. Org. Khim.*, **17**, 2460 (1981); *Chem. Abstr.*, **96**, 85158 (1982).
71. For review literature see K. Schank, in Ref. 1, p. 1191.
72. B. S. Patwa and A. R. Parikh, *J. Indian Chem. Soc.*, **53**, 602 (1976).
73. H. Dürr in *Methoden der Organischen Chemie (Houben-Weyl)*, 4 ed., Vol. IV/5b, Thieme, Stuttgart, 1976, p. 1047.
74. A. Erndt and M. Zubek, *Rocz. Chem.*, **50**, 973 (1976); *Chem. Abstr.*, **86**, 72151 (1977).
75. (a) J. C. Martin and E. F. Perozzi, *J. Amer. Chem. Soc.*, **96**, 3155 (1974).
    (b) W. Y. Lam, E. N. Duesler and J. C. Martin, *J. Amer. Chem. Soc.*, **103**, 127 (1981).
76. L. J. Adzima and J. C. Martin, *J. Amer. Chem. Soc.*, **99**, 1657 (1977).
77. W. Y. Lam and J. C. Martin, *J. Amer. Chem. Soc.*, **103**, 120 (1981).
78. (a) Y. Tamaru and Z. Yoshida, *J. Org. Chem.*, **44**, 1188 (1979).
    (b) O. S. Andell, J.-E. Bäckvall and C. Moberg, *Acta Chem. Scand., Ser. B*, **40**, 184 (1986).
79. K. Inomata, T. Kobayashi, S. Sasaoka, H. Kinoshita and H. Kotake, *Chem. Letters*, 289 (1986).
80. DOS 2.926.671 (1981), Bayer AG; inv. M. Hanack and T. Stoll; *Chem. Abstr.*, **94**, 191778 (1981).
81. For summarized references see K. Schank, in Ref. 1, p. 1159.
82. V. A. Nefedov, L. V. Kryuchkova and L. K. Tarygina, *Zh. Org. Khim.*, **13**, 1735 (1977); *Chem. Abstr.*, **87**, 201180 (1977); for further literature see Reference 80.
83. O. S. Andell and J.-E. Bäckvall, *Tetrahedron Letters*, 4555 (1985).
84. (a) S. V. Ley, B. Lygo and A. Wonnacott, *Tetrahedron Letters*, **26**, 535 (1985).
    (b) S. V. Ley, B. Lygo, F. Sternfeld and A. Wonnacott, *Tetrahedron*, **42**, 4333 (1986).
85. For summarized references see:
    (a) K. Schank, in Ref. 1, p. 1160.
    (b) T. Durst, in Ref. 2, p. 177.
    (c) W. E. Truce, T. C. Klingler and W. W. Brand, in Ref. 3, p. 538.
    (d) I. Haiduc and K. J. Wynne, in Ref. 5, p. 749.

(e) A. Schöberl and A. Wagner in *Methoden Organischen Chemie (Houben-Weyl-Müller)*, 4th ed., Vol. 9, Thieme, Stuttgart, 1955, p. 234.
86. G. K. Cooper and L. J. Dolby, *J. Org. Chem.*, **44**, 3414 (1979).
87. J. Fayos, J. Clardy, L. J. Dolby and T. Farnham, *J. Org. Chem.*, **42**, 1349 (1977).
88. S. I. Tsaikova and D. I. Aleksiev, *Zh. Org. Khim.*, **22**, 444 (1986).
89. S. De Lombaert and L. Ghosez, *Tetrahedron Letters*,**25**, 3475 (1984).
90. P. Messinger, *Arch. Pharm. (Weinheim, Ger.)*, **306**, 458 (1973).
91. I. M. Bazavova, V. M. Neplyuev and M. O. Lozinskii, *Zh. Org. Khim.*, **18**, 865 (1982); *Chem. Abstr.*, **97**, 91851 (1982).
92. C. J. M. Stirling, *J. Chem. Soc.*, 5856 (1964).
93. (a) K. Bailey, B. R. Brown and B. Chalmers, *Chem. Commun.*, 618 (1967).
(b) H. Maruyama and T. Hiraoka, *J. Org. Chem.*, **51**, 399 (1986).
(c) M. A. Lapitskaya, T. A. Manukina and K. K. Pivnitskii, *Zh. Org. Khim.*, **22**, 872 (1986).
(d) H. Matsuyama, Y. Miyazawa, and M. Kobayashi, *Chem. Letters*, 433 (1986).
94. R. Tamura, K. Hayashi, M. Kakihana, M. Tsuji and D. Oda, *Chem. Letters*, 229 (1985).
95. D. I. Aleksiev, *Zh. Org. Khim.*, **12**, 2038 (1976); *Chem. Abstr.*, **85**, 192285 (1976).
96. E. L. Martin, *J. Amer. Chem. Soc.*, **85**, 2449 (1963).
97. D. I. Aleksiev, *Zh. Org. Khim.*, **11**, 211, 908 (1975); *Chem. Abstr.*, **83**, 9378, 9380 (1975).
98. B. Miller and M. V. Kalnins, *Tetrahedron*, **23**, 1145 (1967).
99. H. Bredereck and E. Bäder, *Chem. Ber.*, **87**, 129 (1954).
100. H. Bredereck, E. Bäder and G. Höschele, *Chem. Ber.*, **87**, 784 (1954).
101. E. Bäder and H. D. Bermann, *Chem. Ber.*, **88**, 41 (1955).
102. K. Schank, *Chem. Ber.*, **99**, 48 (1966).
103. K. Schank, *Chem. Ber.*, **103**, 3087 (1970).
104. C. Lick, *Dissertation*, Saarbrücken, 1983.
105. G. W. Kirby, A. W. Lochead and G. N. Sheldrake, *J. Chem. Soc., Chem. Commun.*, 1469 (1984); cf. A. Senning, *Synthesis*, 412 (1980).
106. (a) N. H. Nilsson, C. Jacobsen and A. Senning, *J. Chem. Soc., Chem. Commun.*, 658 (1970).
(b) N. H. Nilsson and A. Senning, *Org. Prep. Proced. Int.*, **12**, 229 (1980).
107. M. Kobayashi, *Bull. Chem. Soc. Japan*, **39**, 967 (1966).
108. K. Schank, *Ann. Chem.*, **702**, 75 (1967), see p. 85.
109. K. Schank and F. Werner, *Phosphorus Sulfur*, **8**, 335 (1980).
110. I. M. Bazavova, V. M. Neplyuev and R. G. Dubenko, *Zh. Org. Khim.*, **11**, 2388 (1975); *Chem. Abstr.*, **84**, 43534 (1976).
111. J. Perronnet and P. Girault, *Bull. Soc. Chim. Fr.*, 2843 (1973).
112. A. S. Shawali, H. M. Hassaneen and S. M. Sherif, *J. Heterocycl. Chem.*, **17**, 1745 (1980).
113. A. O. Abdelhamid, I. M. Abbas, M. A. Abdallah, A. A. Fahmi and A. S. Shawali, *J. Heterocycl. Chem.*, **22**, 813 (1985).
114. J. Diekmann, *J. Org. Chem.*, **30**, 2272 (1965); US. Pat. 3.332.936 (1967), Du Pont, Inv. J. Diekmann, *Chem. Abstr.*, **68**, 59304 (1968).
115. J. M. Cox and R. Gosh, *Tetrahedron Letters*, 3351 (1969).
116. N. H. Nilsson, C. Jacobsen, O. N. Sørensen, N. K. Haunsøe and A. Senning, *Chem. Ber.*, **105**, 2854 (1972).
117. N. H. Nilsson and A. Senning, *Chem. Ber.*, **107**, 2345 (1974).
118. E. Fanghänel, K.-H. Kühnemund and A. M. Richter, *Synthesis*, 319 (1984).
119. G. E. Veenstra and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, **95**, 28 (1976).
120. O. R. Roblin, Jun., J. H. Williams and G. W. Anderson, *J. Amer. Chem. Soc.*, **63**, 1930 (1941); see W. E. Truce, T. C. Klingler and W. W. Brand, in Ref. 4, p. 527, 536; C. J. M. Stirling, *Int. J. Sulfur Chem.*, **B6**, 277, 285 (1971).
121. N. Kharasch, E. M. May and F. R. Mayo, *J. Org. Chem.*, **3**, 175 (1939).
122. R. R. Coats and D. T. Gibson, *J. Chem. Soc.*, 442 (1940).
123. In this connection attention should be paid to the principally possible reaction sequence corresponding to the so-called RARP mechanism: C. Y. Meyers, W. S. Matthews, L. L. Ho, V. M. Kolb and T. E. Parady in *Catalysis in Organic Syntheses 1977* (Ed. G. V. Smith), Academic Press, New York, 1977, p. 197.
124. G. A. Russell and F. Ros, *J. Amer. Chem. Soc.*, **107**, 2506 (1985).
125. N. Kornblum, M. M. Kestner, S. D. Boyd and L. C. Cattran, *J. Amer. Chem. Soc.*, **95**, 3356 (1973).
126. B. R. Fishwick, D. K. Rowles and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 835 (1983).

127. S. I. Al-Khalil and W. R. Bowman, *Tetrahedron Letters*, **24**, 2517 (1983).
128. J. L. Kelley, E. W. McLean and K. F. Williard, *J. Heterocycl. Chem.*, **14**, 1415 (1977).
129. Z. Matacz, H. Piotrowska and T. Urbanski, *Pol. J. Chem.*, **53**, 187 (1979); *Chem. Abstr.*, **91**, 19811 (1979).
130. N. Kornblum, H. K. Singh and W. I. Kelly, *J. Org. Chem.*, **48**, 332 (1983).
131. L. C. Garver, V. Grakauskas and K. Baum, *J. Org. Chem.*, **50**, 1699 (1985).
132. F. Muth in *Methoden der Organischen Chemie (Houben-Weyl-Müller)*, 4 Ed., Vol. 9, Thieme, Stuttgart, 1955, p. 334.
133. F. M. Beringer, A. Brierley, M. Drexler, E. M. Gindler and C. C. Lumpkin, *J. Amer. Chem. Soc.*, **75**, 2708 (1953).
134. D. H. R. Barton, J.-C. Blazejewski, B. Charpiot and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 503 (1981).
135. J. Hershberger and G. A. Russell, *Synthesis*, 475 (1980).
136. W. Sas, *J. Chem. Soc., Chem. Commun.*, 862 (1984).
137. (a) C. M. Suter in *Organic Chemistry of Sulfur*, Wiley, New York, London, 1944; unaltered reprint by Intra-Science Research Foundation, Santa Monica, 1969, p. 667.
(b) C. J. M. Stirling, *Int. J. Sulfur Chem.*, **B6**, 277, 285 (1971).
(c) W. E. Truce, T. C. Klingler and W. W. Brand, in Ref. 4, p. 536.
(d) T. Durst, in Ref. 2, p. 174.
(e) E. Wenschuh and K. Dölling, *Z. Chem.*, **20**, 122 (1980).
(f) K. Schank, in Ref. 1, p. 1145.
138. J. M. Kauffman, *J. Chem. Eng. Data*, **14**, 498 (1969).
139. K. Sukata, *Bull. Chem. Soc. Japan*, **57**, 613 (1984).
140. K. Schank, *Ann. Chem.*, **714**, 117 (1968).
141. K. Schank and A. Weber, *Synthesis*, 367 (1970).
142. K. Schank and A. Weber, *Chem. Ber.*, **105**, 2188 (1972).
143. J. B. Hendrickson, D. A. Judelson and T. Chancellor, *Synthesis*, 320 (1984).
144. A. Jurašek, J. Kováč and R. Belko, *Collect. Czech. Chem. Commun.*, **45**, 746 (1980).
145. M. Hanack and A. Kühnle, *Tetrahedron Letters*, **22**, 3047 (1981).
146. E. V. Polunin, A. M. Moiseenkov and A. V. Semenovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1354 (1981); *Chem. Abstr.*, **95**, 132235 (1981).
147. B. M. Trost and N. R. Schmuff, *J. Amer. Chem. Soc.*, **107**, 396 (1985).
148. M. Adler and K. Schank, *Chem. Ber.*, **111**, 2859 (1978).
149. J. V. Weber, M. Schneider, D. Paquer and P. Faller, *Sulfur Letters*, 45 (1985).
150. J. K. Crandall and C. Pradat, *J. Org. Chem.*, **50**, 1327 (1985).
151. L. D. Markley, *J. Org. Chem.*, **38**, 3417 (1973).
152. G. E. Veenstra and B. Zwanenburg, *Synthesis*, 519 (1975).
153. J. Wildeman and A. M. van Leusen, *Synthesis*, 733 (1979).
154. I. H. Sanchez and M. A. Aguilar, *Synthesis*, 55 (1981).
155. K. Špirkova, J. Kováč, V. Konečny, M. Dandarova and M. Černayova, *Collect. Czech. Chem. Commun.*, **45**, 142 (1980).
156. (a) K. Schank, *Ann. Chem.*, **714**, 117 (1968); **716**, 87 (1968).
(b) K. Schank and A. Weber, *Chem. Ber.*, **105**, 2188 (1972).
157. Z. Courtin, H.-R. von Tobel and G. Auerbach, *Helv. Chim. Acta*, **63**, 1412 (1980).
158. C. Kowal, I. Czernicka and Z. Eckstein, *Przem. Chem.*, **62**, 401 (1983); *Chem. Abstr.*, **100**, 85351 (1984).
159. I. Fleming and C. R. Owen, *J. Chem. Soc., Chem. Commun.*, 1402 (1970).
160. M. Kobayashi, *Bull. Chem. Soc. Japan*, **39**, 1296 (1966).
161. B. Badet, M. Julia and M. Ramirez-Muñoz, *Synthesis*, 926 (1980).
162. M. Julia, D. Lavé, M. Mulhauser, M. Ramirez-Muñoz and D. Uguen, *Tetrahedron Letters*, **24**, 1783 (1983).
163. J. S. Meek and J. S. Fowler, *J. Org. Chem.*, **33**, 3422 (1968).
164. N. V. Kondratenko, V. P. Sambur and L. M. Yagupolskii, *Zh. Org. Khim.*, **7**, 2382 (1971); *Chem. Abstr.*, **76**, 58544 (1972).
165. M. Kobayashi, H. Minato and H. Fukuda, *Bull. Chem. Soc. Japan*, **46**, 1266 (1973).
166. H. Dorn and H. Graubaum, *Z. Chem.*, **15**, 437 (1975).
167. G. A. Russell and F. Ros, *J. Amer. Chem. Soc.*, **104**, 7349 (1982).
168. E. Wenschuh, W. Radeck, A. Porzel, A. Kolbe and S. Edelmann, *Z. Anorg. Allg. Chem.*, **528**, 138 (1985).

169. M. Kobayashi and K. Toriyabe, *Sulfur Letters*, 117 (1985).
170. P. Sutter and C. D. Weis, *Phosphorus Sulfur*, **4**, 335 (1978).
171. N. Kornblum, P. Ackermann and R. T. Swiger, *J. Org. Chem.*, **45**, 5294 (1980).
172. L. M. Tolbert and S. Siddiqui, *Tetrahedron*, **38**, 1079 (1982).
173. A. Fischli and H. Mayer, *Helv. Chim. Acta*, **58**, 1492 (1975).
174. T. Cuvigny and M. Julia, *J. Organomet. Chem.*, **250**, C21 (1983).
175. K. Inomata, T. Yamamoto and H. Kotake, *Chem. Letters*, 1357 (1981).
176. U. M. Dzhemilev, R. V. Kunakova, R. L. Gaisin, G. A. Tolstikov and V. V. Siderova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 696 (1981); *Chem. Abstr.*, **95**, 97251 (1981).
177. M. Julia, M. Nel, A. Righini and D. Uguen, *J. Organomet. Chem.*, **235**, 113 (1982).
178. E. Keinan and Z. Roth, *J. Org. Chem.*, **48**, 1769 (1983).
179. G. P. Boldrini, D. Savoia, E. Tagliavini, C. Trombini and A. Umani-Ronchi, *J. Organomet. Chem.*, **268**, 97 (1984).
180. K. Clauss, D. Grimm and G. Prossel, *Ann. Chem.*, 539 (1974).
181. (a) K. Ogura, *Yuki Gosei Kagaku Kyokai Shi*, **42**, 1152 (1984).
(b) K. Ogura, N. Yahata, J.-I. Watanabe, K. Takahashi and H. Iida, *Bull. Chem. Soc. Japan*, **56**, 3543 (1983).
182. (a) N. Ono, I. Hamamoto, T. Yanai and A. Kaji, *J. Chem. Soc., Chem. Commun.*, 523 (1985).
(b) N. Ono, I. Hamamoto, T. Kawai, A. Kaji, R. Tamura and M. Kakihana, *Bull. Chem. Soc. Japan*, **59**, 405 (1986).
183. R. Tamura, K. Hayashi, M. Kakihana, M. Tsuji and D. Oda, *Tetrahedron Letters*, 851 (1985).
184. M. Julia and D. Arnoult, *Bull. Soc. Chim. Fr.*, 746 (1973).
185. D. Arnoult, P. Chabardes, G. Farge and M. Julia, *Bull. Soc. Chim. Fr.*, II-130 (1985).
186. H. Hellmann and G. Opitz, *Chem. Ber.*, **90**, 8 (1957).
187. T. Olijnsma, J. B. F. N. Engberts and J. Strating, *Recl. Trav. Chim. Pays-Bas*, **91**, 209 (1972).
188. H. Hellmann and K. Müller, *Chem. Ber.*, **98**, 638 (1965).
189. K. Schank, in Ref. 1, p. 1149; sulfones from diaryl- and triarylcarbinols: A. Schöberl and A. Wagner in *Methoden der Organischen Chemie (Houben-Weyl-Müller)*, 4th ed., Vol. 9, Thieme, Stuttgart, 1955, p. 233.
190. K. Schank and H.-G. Schmitt, *Chem. Ber.*, **110**, 3235 (1977).
191. I. W. J. Still and F. J. Ablenas, *Synth. Commun.*, **12**, 1103 (1983).
192. P. Messinger and J. Gompertz, *Arch. Pharm. (Weinheim, Ger.)*, **307**, 653 (1974).
193. O. R. Hansen and R. Hammer, *Acta Chem. Scand.*, **7**, 1331 (1953).
194. (a) P. Messinger, *Arch. Pharm. (Weinheim, Ger.)*, **306**, 603 (1973).
(b) P. Messinger and J. Gompertz, *Arch. Pharm. (Weinheim, Ger.)*, **308**, 737 (1975).
195. P. Messinger and H. Greve, *Arch. Pharm. (Weinheim, Ger.)*, **315**, 385 (1982).
196. F. Muth, in Ref. 132, p. 336.
197. H. Nozaki, R. Noyori and K. Sisido, *Tetrahedron*, **20**, 1125 (1964).
198. J. W. Wilt, C. A. Schneider, H. F. Dabek, Jr., J. F. Kraemer and W. J. Wagner, *J. Org. Chem.*, **31**, 1543 (1966).
199. W. Müller and K. Schank, *Chem. Ber.*, **111**, 2870 (1978).
200. W. Middelbos, J. Strating and B. Zwanenburg, *Tetrahedron Letters*, 351 (1971).
201. E. Gradoú, Z. Ejmocki and Z. Eckstein, *Pol. J. Chem.*, **55**, 469 (1981); *Chem. Abstr.*, **95**, 219834 (1981).
202. J. Gehlhaus and R. W. Hoffmann, *Tetrahedron*, **26**, 5901 (1970).
203. K. Schank, F. Schroeder and A. Weber, *Ann. Chem.*, 553 (1973).
204. F. Bellesia, R. Grandi, U. M. Pagnoni and R. Trave, *J. Chem. Res. (S)*, 112 (1981).
205. Z. Eckstein, E. Polubiec and D. Palut, *Przem. Chem.*, **47**, 544 (1968); *Chem. Abstr.*, **70**, 57343 (1968).
206. A. Schöberl and A. Wagner in *Methoden der Organischen Chemie (Houben-Weyl-Müller)*, 4th ed., Vol. 9, Thieme, Stuttgart, 1955, p. 233.
207. C. M. Suter, in Ref. 137a, p. 668.
208. K. Schank and F. Schroeder, *Phosphorus Sulfur*, **1**, 307 (1976).
209. M. Asscher and D. Vofsi, *J. Chem. Soc.*, 4962 (1964).
210. W. E. Truce, C. T. Goralski, L. W. Christensen and R. H. Bavry, *J. Org. Chem.*, **35**, 4217 (1970).
211. (a) K. Schank, in Ref. 1, p. 1180 and references cited therein.
(b) Bromides: P. S. Magee in *Sulfur in Organic and Inorganic Chemistry* (Ed. A. Senning), Vol. 4, M. Dekker, New York, 1982, p. 315.

(c) Iodides: L. Field and C. M. Lukehart in *Sulfur in Organic and Inorganic Chemistry* (Ed. A. Senning), Vol. 4, M. Dekker, New York, 1982, p. 356.
212. Y. Amiel, *J. Org. Chem.*, **36**, 3697 (1971).
213. J.-P. Pillot, J. Dunoguès and R. Calas, *Synthesis*, 469 (1977).
214. J. J. Burger, T. B. R. A. Chen, E. R. de Waard and H. O. Huisman, *Tetrahedron*, **36**, 723 (1980).
215. M. M. Tanaskov, M. D. Stadnichuk and L. V. Kekisheva, *Zh. Obshch. Khim.*, **50**, 1738 (1980); *Chem. Abstr.*, **94**, 3387 (1981).
216. E. Y. Kolosov and M. D. Stadnichuk, *Zh. Org. Khim.*, **18**, 2266 (1982); *Chem. Abstr.*, **98**, 125527 (1983).
217. M. D. Stadnichuk, T. B. Kryukova and A. A. Petrov, *Zh. Obshch. Khim.*, **45**, 838 (1975); *Chem. Abstr.*, **83**, 79319 (1975).
218. E. Y. Kolosov and M. D. Stadnichuk, *Zh. Org. Khim.*, **17**, 1184 (1981); *Chem. Abstr.*, **95**, 150094 (1981).
219. W. E. Truce and C. T. Goralski, *J. Org. Chem.*, **36**, 2536 (1971).
220. J. Sinnreich and M. Asscher, *J. Chem. Soc., Perkin Trans. 1*, 1543 (1972).
221. (a) N. Kamigata, H. Sawada and M. Kobayashi, *Chem. Letters*, 159 (1979).
(b) N. Kamigata, J. Ozaki and M. Kobayashi, *J. Org. Chem.*, **50**, 5045 (1985).
222. M. A. Vasil'eva, T. I. Bychkova, D. F. Kushnarev, T. I. Rozova and A. V. Kalabina, *Zh. Org. Khim.*, **13**, 283 (1977); *Chem. Abstr.*, **87**, 5551 (1977).
223. A. V. Kalabina, M. A. Vasil'eva and T. I. Bychkova, *Zh. Org. Khim.*, **15**, 268 (1979); *Chem. Abstr.*, **91**, 5004 (1979).
224. M. M. Tanaskov and M. D. Stadnichuk, *Zh. Obshch. Khim.*, **48**, 1140 (1978).; *Chem. Abstr.*, **89**, 41911 (1978).
225. M. M. Tanaskov and M. D. Stadnichuk, *Zh. Obshch. Khim.*, **45**, 843 (1975); *Chem. Abstr.*, **83**, 79320 (1975).
226. W. E. Truce and G. C. Wolf, *J. Org. Chem.*, **36**, 1727 (1971).
227. Y. Amiel, *J. Org. Chem.*, **39**, 3867 (1974).
228. Y. Amiel, *Tetrahedron Letters*, 661 (1971).
229. Y. Amiel, *J. Org. Chem.*, **36**, 3691 (1971).
230. L. K. Liu, Y. Chi and K. Y. Jen, *J. Org. Chem.*, **45**, 406 (1980).
231. L. M. Harwood, M. Julia and G. Le Thuillier, *Tetrahedron*, **36**, 2483 (1980).
232. B. D. Gupta, S. Roy and S. Sen, *Indian J. Chem.*, **B24**, 1032 (1985).
233. W. E. Truce and C. T. Goralski, *J. Org. Chem.*, **35**, 4220 (1970).
234. N. Kamigata, H. Sawada and M. Kobayashi, *J. Org. Chem.*, **48**, 3793 (1983).
235. Y. Amiel, *J. Org. Chem.*, **36**, 3697 (1971).
236. C. T. Goralski, *J. Org. Chem.*, **37**, 2354 (1972).
237. W. Böll, *Ann. Chem.*, 1665 (1979).
238. W. E. Truce and G. C. Wolf, *Chem. Commun.*, 150 (1969).
239. S. J. Cristol, J. K. Harrington and M. S. Singer, *J. Amer. Chem. Soc.*, **88**, 1529 (1966).
240. V. K. Gubernatov, B. E. Kogai and V. A. Sokolenko, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1874 (1983); *Chem. Abstr.*, **99**, 194486 (1983).
241. V. K. Gubernatov, B. E. Kogai, E. D. Korniets and V. A. Sokolenko, *Zh. Org. Khim.*, **19**, 2209 (1983); *Chem. Abstr.*, **100**, 209277 (1984).
242. M. R. Ashcroft, P. Bougeard, A. Bury, C. J. Cooksey, M. D. Johnson, J. M. Hungerford and G. M. Lampman, *J. Org. Chem.*, **49**, 1751 (1984).
243. G. C. Wolf, *J. Org. Chem.*, **39**, 3454 (1974).
244. M. M. Tanaskov, P. E. Starodub, M. D. Stadnichuk and E. A. Tanaskova, *Zh. Org. Khim.*, **17**, 1800 (1981); *Chem. Abstr.*, **96**, 6297 (1982).
245. A. M. van Leusen, J. Strating and D. van Leusen, *Tetrahedron Letters*, 5207 (1973).
246. B. Michel, J. F. McGarrity and H. Dahn, *Chimia*, **27**, 320 (1973).
247. T. G. Back, *J. Org. Chem.*, **46**, 5443 (1981).
248. R. A. Gancarz and J. L. Kice, *J. Org. Chem.*, **46**, 4899 (1981).
249. L. A. Paquette and G. D. Crause, *J. Org. Chem.*, **48**, 141 (1983).
250. Y.-H. Kang and J. L. Kice, *J. Org. Chem.*, **49**, 1507 (1984).
251. T. G. Back and S. Collins, *Tetrahedron Letters*, **22**, 5111 (1981).
252. T. G. Back and S. Collins, *J. Org. Chem.*, **46**, 3249 (1981).
253. T. Miura and M. Kobayashi, *J. Chem. Soc., Chem. Commun.*, 438 (1982).
254. T. G. Back, S. Collins and R. G. Kerr, *J. Org. Chem.*, **48**, 3077 (1983).

255. T. G. Back, S. Collins, U. Gokhale and K.-W. Law, *J. Org. Chem.*, **48**, 4776 (1983).
256. Y.-H. Kang and J. L. Kice, *Tetrahedron Letters*, **23**, 5373 (1982).
257. J. L. Kice and Y.-H. Kang, *Tetrahedron*, **41**, 4739 (1985).
258. A. M. El-Khawaga and R. M. Roberts, *J. Org. Chem.*, **50**, 3334 (1985).
259. K. Schank, in Ref. 1, p. 1165 and references cited therein.
260. E. Block and M. Aslam, *Tetrahedron Letters*, **23**, 4203 (1982).
261. (a) G. Opitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 107 (1967).
(b) N. H. Fischer, *Synthesis*, 393 (1970).
262. J. F. King and J. R. Du Manoir, *J. Amer. Chem. Soc.*, **97**, 2566 (1975).
263. A. Senning, *Synthesis*, 211 (1973).
264. G. Opitz and H. R. Mohl, *Angew. Chem., Int. Ed. Engl.*, **8**, 73 (1969).
265. J. S. Grossert and M. M. Bharadwaj, *J. Chem. Soc., Chem. Commun.*, 144 (1974).
266. K. Rieth and G. Opitz, *Phosphorus Sulfur*, **6**, 257 (1979); G. Opitz, private communication, 1983.
267. A. F. Ermolov, A. F. Eleev, A. P. Kutepov and G. A. Sokol'skii, *Zh. Org. Khim.*, **22**, 222 (1986).
268. Cf. three-membered ring sulfones as intermediates of the Ramberg–Bäcklund reaction: L. A. Paquette, *Org. React.*, **25**, 1 (1977).
269. J. Nakayama, M. Tanuma, Y. Honda and M. Hoshino, *Tetrahedron Letters*, **25**, 4553 (1984).
270. (a) S. Matsumura, T. Nagai and N. Tokura, *Tetrahedron Letters*, 3929 (1966).
(b) E. Vilsmaier and B. Hloch, *Synthesis*, 428 (1971).
271. P. Del Buttero, S. Maiorana, G. D. Andreetti, G. Boccelli and P. Sgarabotto, *J. Chem. Soc., Perkin Trans. 2*, 809 (1975).
272. (a) P. Del Buttero and S. Maiorana, *J. Chem. Soc., Perkin Trans. 1*, 2540 (1973).
(b) W. E. Truce and J. F. Rach, *J. Org. Chem.*, **39**, 1109 (1974).
273. W. Ried and J. Paraškevová, *Sulfur Letters*, **1**, 79 (1983).
274. L. N. Koikov, P. B. Terent'ev and N. S. Kulikov, *Zh. Org. Khim.*, **17**, 1087 (1981); *Chem. Abstr.*, **95**, 219928 (1981).
275. E. Block, V. Eswarakrishnan and K. Gebreyes, *Tetrahedron Letters*, **25**, 5469 (1984).
276. R. H. Hasek, R. H. Meen and J. C. Martin, *J. Org. Chem.*, **30**, 1495 (1965).
277. H. Böhme and W. Höver, *Ann. Chem.*, **748**, 59 (1971).
278. E. N. Prilezhaeva, N. P. Petukhova, V. I. Kurilkin, A. U. Stepanyants and V. P. Lezina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1827 (1974); *Chem. Abstr.*, **81**, 169369 (1974).
279. A. G. Shipov and Y. I. Baukov, *Zh. Obshch. Khim.*, **56**, 126 (1986).
280. J. S. Grossert, J. Hoyle, M. M. Bharadwaj and T. S. Cameron, *J. Chem. Soc., Chem. Commun.*, 1175 (1982).
281. E. Block, M. Aslam, R. Iyer and J. Hutchinson, *J. Org. Chem.*, **49**, 3664 (1984).
282. H. Nozaki, M. Takaku and Y. Hayashi, *Tetrahedron Letters*, 2303 (1967).
283. J. A. Hyatt and A. W. White, *Synthesis*, 214 (1984).
284. E. Hirsch, S. Hünig and H.-U. Reißig, *Chem. Ber.*, **115**, 399 (1982).
285. K. Schank, F. Schroeder and A. Weber, *Ann. Chem.*, 553 (1973).
286. R. Stroh in *Methoden der Organischen Chemie* (*Houben-Weyl-Müller*), 4th ed., Vol. V/3, Thieme, Stuttgart, 1962, p. 897.
287. F. Muth, in Ref. 132, p. 588.
288. (a) C. M. Suter, in Ref. 137a, p. 673.
(b) F. R. Jensen in *Friedel-Crafts and Related Reactions* (Ed. G. A. Olah), Vol. III/2, Interscience, New York, London, Sydney, 1964, p. 1319.
(c) W. E. Truce, T. C. Klingler and W. W. Brand, in Ref. 4, p. 532.
(d) T. Durst, in Ref. 2, p. 175.
(e) F. Effenberger, *Angew. Chem., Int. Ed. Engl.*, **19**, 151 (1980).
289. J. A. Hyatt and A. W. White, *Synthesis*, 214 (1984).
290. (a) G. A. Olah and H. C. Lin, *Synthesis*, 342 (1974).
(b) G. A. Olah, H. C. Lin and A. Germain, *Synthesis*, 895 (1974).
291. Y. A. Moskvichev, L. A. Sizyk, S. K. Kramerova and G. S. Mironov, *Zh. Org. Khim.*, **18**, 163 (1982); *Chem. Abstr.*, **96**, 162242 (1982).
292. K. Nomiya, Y. Sugaya and M. Miwa, *Bull. Chem. Soc. Japan*, **53**, 3389 (1980).
293. D. J. Abraham and W. E. Truce, *J. Org. Chem.*, **28**, 2901 (1963).
294. (a) S. Tanimoto, S. Yasuda and M. Okano, *Yuki Gosei Kagaku Kyokai Shi*, **28**, 1041 (1970); *Chem. Abstr.*, **74**, 76124 (1971).

(b) T. Imagawa, G. L, Gard, T. W. Mix and I. M. Shreeve, *Inorg. Chem.*, **22**, 969 (1983).
295. (a) S. N. Bhattacharya, C. Eaborn and D. R. M. Walton, *J. Chem. Soc. (C)*, 1367 (1969).
(b) S. N. Bhattacharya, B. M. Josiah and D. R. M. Walton, *Organometal. Chem.*, **1**, 145 (1971).
296. (a) M. Bourguel and R. Truchet, *C. R. Acad. Sci.*, **190**, 753 (1930).
(b) R. Truchet, *Ann. Chim. (Paris)*, **16**, 309 (1931).
297. G. H. L. Nefkens and B. Zwanenburg, *Phosphorus Sulfur*, **6**, 221 (1979).
298. Y. Shirota, T. Nagai and N. Tokura, *Tetrahedron*, **25**, 3193 (1969).
299. A. I. Khodair, A. A. Abdel-Wahab and A. M. El-Khawaga, *Z. Naturforsch. B*, **33**, 403 (1978).
300. Y. Shirota, T. Nagai and N. Tokura, *Tetrahedron*, **23**, 639 (1967).
301. H. Fukuda, F. J. Frank and W. E. Truce, *J. Org. Chem.*, **28**, 1420 (1963).
302. A. I. Khodair, A. Swelim and A. A. Abdel-Wahab, *Phosphorus Sulfur*, **2**, 165 (1976).
303. A. I. Khodair, A. Swelim and A. A. Abdel-Wahab, *Phosphorus Sulfur*, **2**, 169 (1976).
304. (a) F. C. Whitmore and N. Thurman, *J. Amer. Chem. Soc.*, **45**, 1069 (1923).
(b) Ferrocenyl sulfones: A. N. Nesmeyanov, E. G. Perevalova and O. A. Nesmeyanova, *Dokl. Akad. Nauk SSSR*, **119**, 288 (1958); *Chem. Abstr.*, **52**, 14579 (1958); *Izv. Akad. Nauk SSSR, Ser. Khim.*, 47 (1962); *Chem. Abstr.*, **57**, 12532 (1962).
305. E. Hirsch, S. Hünig and H.-U. Reißig, *Chem. Ber.*, **115**, 3687 (1982).
306. H. Böhme, R. Braun and L. Häfner, *Ann. Chem.*, **744**, 15 (1971).
307. (a) P. I. Ogoiko, V. P. Nazaretyan, A. Y. Il'chenko and L. M. Yagupol'skii, *Zh. Org. Khim.*, **16**, 1397 (1980); *Chem. Abstr.*, **94**, 30145 (1981).
(b) J. B. Hendrickson, G. J. Boudreaux and P. S. Palumbo, *J. Amer. Chem. Soc.*, **108**, 2358 (1986).
308. H. Böhme and H. Fischer, *Chem. Ber.*, **76**, 92, 99 (1943).
309. A. M. van Leusen, B. A. Reith, A. J. W. Iedema and J. Strating, *Recl. Trav. Chim. Pays-Bas*, **91**, 37 (1972).
310. B. A. Reith, J. Strating and A. M. van Leusen, *J. Org. Chem.*, **39**, 2728 (1974).
311. W. E. Truce and G. D. Madding, *Tetrahedron Letters*, 3681 (1966).
312. M. E. Kuehne, *J. Org. Chem.*, **28**, 2124 (1963).
313. Y. Kuroki, S. Murai, N. Sonoda and S. Tsutsumi, *Organomet. Chem. Synth.*, **1**, 465 (1972).
314. A. E. Crease, B. D. Gupta, M. D. Johnson, E. Bialkowska, K. N. V. Duong and A. Gaudemer, *J. Chem. Soc., Perkin Trans. 1*, 2611 (1979).
315. P. Bougeard, A. Bury, C. J. Cooksey, M. D. Johnson, J. M. Hungerford and G. M. Lampman, *J. Amer. Chem. Soc.*, **104**, 5230 (1982).
316. For a summary, see K. Schank, in Ref. 1, p. 1136, 1165.
317. (a) F. Muth, in Ref. 132, p. 590, 673.
(b) F. Klages and F. E. Malecki, *Ann. Chem.*, **691**, 15 (1961).
318. N. H. Christensen, *Acta Chem. Scand.*, **18**, 954 (1964).
319. M. H. Karger and Y. Mazur, *J. Org. Chem.*, **36**, 528 (1971).
320. F. Muth, in Ref. 132, p. 552.
321. M. Shibuya, T. Inoue, Y. Jinbo and S. Kubota, *Heterocycles*, **19**, 188 (1982).
322. E. E. Gilbert, *J. Org. Chem.*, **28**, 1945 (1963).
323. X. Creary, *J. Org. Chem.*, **45**, 2727 (1980).
324. R. S. Glass and D. L. Smith, *J. Org. Chem.*, **39**, 3712 (1974).
325. J. B. Hendrickson and K. W. Bair, *J. Org. Chem.*, **42**, 3875 (1977).
326. F. Massa, M. Hanack and L. R. Subramanian, *J. Fluorine Chem.*, **19**, 601 (1982).
327. L. Field, *J. Amer. Chem. Soc.*, **74**, 394 (1952).
328. S. Gronowitz and P. Pedaja, *Chem. Scripta*, **15**, 187 (1980).
329. W. E. Truce and B. Van Gemert, *Phosphorus Sulfur*, **6**, 309 (1979).
330. W. E. Truce and B. Van Gemert, *J. Amer. Chem. Soc.*, **100**, 5525 (1978).
331. M. A. Sabol and K. K. Andersen, *J. Amer. Chem. Soc.*, **91**, 3603 (1969).
332. (a) W. H. Baarschers, *Can. J. Chem.*, **54**, 3056 (1976).
(b) J. D. Stewart and H. W. Pinnick, *Heterocycles*, **25**, 213 (1987).
333. Y. Shirota, T. Nagai and N. Tokura, *Tetrahedron Letters*, 3299 (1967).
334. W. E. Truce and L. W. Christensen, *J. Org. Chem.*, **35**, 3968 (1970).
335. W. Hanefeld and D. Kluck, *Synthesis*, 229 (1981).
336. (a) K. Schank, in Ref. 1, p. 1194.
(b) W. E. Truce, T. C. Klingler and W. W. Brand, in Ref. 4, p. 529.
(c) I. Haiduc and K. J. Wynne in *Methodicum Chimicum* (Ed. F. Korte), Vol. 7, G. Thieme, Stuttgart, 1976, p. 751.

(d) A. Schöberl and A. Wagner in *Methoden der Organischen Chemie (Houben-Weyl-Müller)*, 4th ed., Vol. 9, Thieme, Stuttgart, 1955, p. 227.
(e) C. M. Suter, in Ref. 137a, p. 660.
337. G. A. Olah, B. G. B. Gupta and S. C. Narang, *J. Amer. Chem. Soc.*, **101**, 5317 (1979).
338. G. A. Olah and B. G. B. Gupta, *J. Org. Chem.*, **48**, 3585 (1983).
339. F. Montanari, M. Cinquini and U. Folli, *Mech. React. Sulfur Compd.*, **3**, 121 (1968).
340. R. Curci and J. O. Edwards in *Organic Peroxides* (Ed. D. Swern), Vol. 1, Wiley–Interscience, New York, 1970, pp. 230, 243.
341. Y. Sawaki, H. Kato and Y. Ogata, *J. Amer. Chem. Soc.*, **103**, 3832 (1981).
342. T. Takata, K. Ishibashi and W. Ando, *Tetrahedron Letters*, **26**, 4609 (1985).
343. G. O. Schenck and C. H. Krauch, *Chem. Ber.*, **96**, 517 (1963).
344. R. S. Davidson and J. L. Pratt, *Tetrahedron Letters*, **24**, 5903 (1983).
345. Y. Sawaki and Y. Ogata, *J. Amer. Chem. Soc.*, **103**, 5947 (1981).
346. C. Gu, C. S. Foote and M. L. Kacher, *J. Amer. Chem. Soc.*, **103**, 5949 (1981).
347. D. Barnard, *J. Chem. Soc.*, 4547 (1957).
348. A. Miura, M. Nojima and S. Kusabayashi, *J. Chem. Soc., Chem. Commun.*, 1352 (1982).
349. H. Gampp and S. J. Lippard, *Inorg. Chem.*, **22**, 357 (1983).
350. K. Sasse and H. Niedrig, *Angew. Chem., Int. Ed. Engl.*, **20**, 780 (1981).
351. C. A. A. Claesen, A. M. A. Pistorius and G. I. Tesser, *Tetrahedron Letters*, 3859 (1985).
352. A. R. Derzhinskii, L. D. Konyushkin and E. I. Prilezhaeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1116 (1982); *Chem. Abstr.*, **97**, 109519 (1982).
353. K. C. Nicolaou, R. L. Magolda, W. J. Sipio, N. E. Barnette, Z. Lysenko and M. M. Joullié, *J. Amer. Chem. Soc.*, **102**, 3784 (1980). (Cf. also ref. 354–357).
354. W. M. Weigert, W. Merk, H. Offermanns, G. Prescher, G. Schreyer and O. Weiberg, *Chem.-Ztg.*, **99**, 106, 116 (1975).
355. H. Kropf, A. Weickmann and K.-P. Zeller in *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., Vol. IV/1a (Ed. H. Kropf), Thieme, Stuttgart, 1981, pp. 286, 292.
356. G. A. Russell and J. M. Pecoraro, *J. Org. Chem.*, **44**, 3990 (1979).
357. *Warning* in the use of a H_2O_2/acetone mixture: A. D. Brewer, *Chem. Brit.*, **11**, 335 (1975).
358. H. Böhme and U. Sitorus, *Chem.-Ztg.*, **96**, 37 (1972).
359. A. O. Pedersen, G. Schroll, S.-O. Lawesson, W. A. Laurie and R. I. Reed, *Tetrahedron*, **26**, 4449 (1970).
360. H. Kropf, A. Weickmann and K.-P. Zeller, in Ref. 355, p. 224.
361. C. S. Giam, K. Kikukawa and D. A. Trujillo, *Org. Prep. Proced. Int.*, **13**, 137 (1981).
362. R. A. Sheldon and J. K. Kochi in *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, 1981, p. 392.
363. H. S. Schultz, H. B. Freyermuth and S. R. Buc, *J. Org. Chem.*, **28**, 1140 (1963).
364. J. Drabowicz, P. Lyzwa and M. Mikolajczyk, *Phosphorus Sulfur*, **17**, 169 (1983).
365. (a) H. J. Reich, F. Chow and S. L. Peake, *Synthesis*, 299 (1978).
(b) H. J. Reich in *Organic Chemistry, A Series of Monographs* (Ed. W. S. Trahanovsky), Vol. 5-C, *Oxidations in Organic Chemistry*, Academic Press, New York, 1978, pp. 1, 9.
366. Y. Sawaki and Y. Ogata, *Bull. Chem. Soc. Japan*, **54**, 793 (1981).
367. H. Sugimoto and D. T. Sawyer, *J. Org. Chem.*, **50**, 1784 (1985).
368. L. A. Paquette and R. V. C. Carr, *Org. Synth.*, **64**, 157 (1985).
369. I. Yamamoto, T. Sakai, S. Yamamoto, K. Ohta and K. Matsuzaki, *Synthesis*, 676 (1985).
370. A. M. Plotnikov, A. D. Shebaldova and V. G. Kharchenko, *Khim. Geterotsikl. Soedin.*, 1489 (1985).
371. A. Weber and M. Neuenschwander, *Angew. Chem., Int. Ed. Engl.*, **20**, 774 (1981).
372. K. Schank, in Ref. 1, pp. 1195, 1199.
373. A. McKillop and J. A. Tarbin, *Tetrahedron Letters*, **24**, 1505 (1983).
374. R. Bloch, J. Abecassis and D. Hassan, *J. Org. Chem.*, **50**, 1544 (1985).
375. J. Holoch and W. Sundermeyer, *Chem. Ber.*, **119**, 269 (1986).
376. (a) B. M. Trost and D. P. Curran, *Tetrahedron Letters*, **22**, 1287 (1981).
(b) T. A. Blumenkopf, *Synth. Commun.*, **16**, 139 (1986).
377. B. Ganem, A. J. Biloski and R. P. Heggs, *Tetrahedron Letters*, **21**, 689 (1980).
378. R. Curci, F. DiFuria and G. Modena, *J. Chem. Soc., Perkin Trans. 2*, 603 (1978).
379. P. Kocienski and M. Todd, *J. Chem. Soc., Chem. Commun.*, 1078 (1982).
380. J. Rouchaud, C. Moons and J. Meyer, *Bull. Soc. Chim. Fr. II*, 411 (1980).

381. B. Plesničar in *Organic Chemistry, A Series of Monographs* (Ed. W. S. Trahanovsky), Vol. 5-C, *Oxidations in Organic Chemistry*, Academic Press, New York, 1978, pp. 211, 280.
382. C. G. Venier, T. G. Squires, Y.-Y. Chen, G. P. Hussmann, J. C. Shei and B. F. Smith, *J. Org. Chem.*, **47**, 3773 (1982).
383. R. Liotta and W. S. Hoff, *J. Org. Chem.*, **45**, 2887 (1980).
384. A. Elsäßer, W. Sundermeyer and D. S. Stephenson, *Chem. Ber.*, **118**, 116 (1985).
385. R. Barker and D. L. MacDonald, *J. Amer. Chem. Soc.*, **82**, 2297 (1960).
386. R. Curci and J. O. Edwards in *Organic Peroxides* (Ed. D. Swern), Vol. 1, Wiley, Interscience, New York, 1970.
387. U. M. Dzhemilev, N. S. Vostrikov, A. M. Moiseenkov and G. A. Tolstikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1320 (1981); *Chem. Abstr.*, **95**, 167877 (1981).
388. T. Scholl and H. J. Roth, *Arch. Pharm. (Weinheim, Ger.)*, **318**, 634 (1985).
389. W. Hanefeld, *Ann. Chem.*, 1627 (1984).
390. J. Nakayama, H. Machida, R. Saito and M. Hoshino, *Tetrahedron Letters*, **26**, 1983 (1985).
391. H. Böhme and M. Junga, *Ann. Chem.*, **758**, 132 (1972).
392. A. R. Derzhinskii, V. E. Kalugin and E. N. Prilezhaeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1384 (1984).
393. C. R. Harrison and P. Hodge, *J. Chem. Soc., Perkin Trans. 1*, 2252 (1976).
394. F. A. Davis, R. Jenkins, Jr. and S. G. Yocklovich, *Tetrahedron Letters*, 5171 (1978).
395. F. A. Davis and J. M. Billmers, *J. Org. Chem.*, **48**, 2672 (1983).
396. M. E. C. Biffin, J. Miller and D. B. Paul, *Tetrahedron Letters*, 1015 (1969).
397. C. Djerassi and R. R. Engle, *J. Amer. Chem. Soc.*, **75**, 3838 (1953).
398. H. B. Henbest and S. A. Khan, *Chem. Commun.*, 1036 (1968).
399. G. W. Gokel, H. M. Gerdes and D. M. Dishong, *J. Org. Chem.*, **45**, 3634 (1980).
400. N. A. Noureldin and D. G. Lee, *J. Org. Chem.*, **47**, 2790 (1982).
401. *Warning!* Explosions with benzyltriethylammonium permanganate: J. Graefe and R. Rienäcker, *Angew. Chem., Int. Ed. Engl.*, **22**, 625 (1983).
402. S. T. Purrington and A. G. Glenn, *Org. Prep. Proced. Int.*, **17**, 227 (1985).
403. S. Wolfe and C. F. Ingold, *J. Amer. Chem. Soc.*, **105**, 7755 (1983).
404. D. Klamann and H. Bertsch, *Chem. Ber.*, **88**, 201 (1955).
405. Y. Ueno, A. Kojima and M. Okawara, *Chem. Letters*, 2125 (1984).
406. R. Schork and W. Sundermeyer, *Chem. Ber.*, **118**, 1415 (1985).
407. R. Seelinger and W. Sundermeyer, *Angew. Chem., Int. Ed. Engl.*, **19**, 203 (1980).
408. A. V. Fokin, A. F. Kolomiets, S. N. Shkurak, N. V. Kondrashov and F. M. Mukhametshin, *Zh. Org. Khim.*, **21**, 2337 (1985).
409. I. Ruppert, *Angew. Chem., Int. Ed. Engl.*, **18**, 880 (1979).
410. A. K. Sen and G. Chattopadhyay, *Indian J. Chem.*, **B17**, 222 (1979).
411. L. A. Carpino and J. R. Williams, *J. Org. Chem.*, **39**, 2320 (1974).
412. Y. Ueno, T. Miyano and M. Okawara, *Bull. Chem. Soc. Japan*, **53**, 3615 (1980).
413. C. Y. Meyers and G. J. McCollum, *Tetrahedron Letters*, 289 (1973).
414. (a) T. Durst and K. C. Tin, *Can. J. Chem.*, **49**, 2374 (1971).
(b) T. Durst, in Ref. 2, pp. 171–172.
415. I. Tabushi and H. Kitaguchi in *Synthetic Reagents* (Ed. J. S. Pizey), Vol. 4, Ellis Horwood, Chichester, 1981, p. 360.
416. K. S. Sharma, R. Parshad and V. Singh, *Indian J. Chem.*, **B17**, 342 (1979).
417. S. Vassart and R. Jadot, *Bull. Soc. Chim. Belg.*, **74**, 565 (1965).
418. R. Harville and S. F. Reed, *J. Org. Chem.*, **33**, 3976 (1968).
419. G. Barberi, M. Cinquini, S. Colonna and F. Montanari, *J. Chem. Soc. (C)*, 659 (1968).
420. D. Barbas, S. Spyroudis and A. Varvoglis, *J. Chem. Res. (S)*, **6**, 186 (1985).
421. T. T. Nguyen, R. Y. Amey and J. C. Martin, *J. Org. Chem.*, **47**, 1024 (1982).
422. R. Barret, F. Pautet, M. Daudon and B. Mathian, *Sulfur Letters*, 127 (1985).
423. (a) D. K. Padma, R. A. Shaw, A. R. Vasudeva Murthy and M. Woods, *Int. J. Sulfur Chem.*, **A1**, 243, 248 (1971).
(b) D. Martin and H. G. Hauthal in *Dimethylsulfoxid*, Akademie Verlag, Berlin, 1971, p. 324.
424. K. Ganapathy and P. Jayagandhi, *Int. J. Chem. Kinet.*, **15**, 129 (1983).
425. With sodium *N*-bromobenzenesulfonamide: D. S. Mahadevappa, S. Anada, A. S. A. Murthy and K. S. Rangappa, *Tetrahedron*, **40**, 1673 (1984).
426. W. D. Kingsbury and C. R. Johnson, *Chem. Commun.*, 365 (1969).

427. D. J. H. Smith, J. D. Finlay, C. R. Hall and J. J. Uebel, *J. Org. Chem.*, **44**, 4757 (1979).
428. (a) S. D. Turk and R. L. Cobb in *Organic Chemistry, A Series of Monographs, 1,4-Cycloaddition Reactions: The Diels-Alder Reaction in Heterocyclic Synthesis* (Ed. J. Hamer), Vol. 8, Academic Press, New York, 1967, p. 13.
(b) T. Durst, in Ref. 2, p. 178.
429. W. L. Mock, *J. Amer. Chem. Soc.*, **88**, 2857 (1966).
430. S. D. McGregor and D. M. Lemal, *J. Amer. Chem. Soc.*, **88**, 2858 (1966).
431. J. Saltiel and L. Metts, *J. Amer. Chem. Soc.*, **89**, 2232 (1967).
432. U. M. Dzhemilev, R. V. Kunakova, Y. T. Struchkov, G. A. Tolstikov, F. V. Sharipova, L. G. Kuz'mina and S. R. Rafikov, *Dokl. Akad. Nauk SSSR, Ser. Khim.*, **250**, 105 (1980); *Chem. Abstr.*, **92**, 197499 (1980).
433. U. M. Dzhemilev, R. V. Kunakova, F. V. Sharipova, G. A. Tolstikov and L. V. Spirikhin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 475 (1981); *Chem. Abstr.*, **95**, 42869 (1981).
434. (a) J. L. Charlton and T. Durst, *Tetrahedron Letters*, **25**, 2663 (1984); 3413 (1985).
(b) T. Durst, E. C. Kozma and J. L. Charlton, *J. Org. Chem.*, **50**, 4829 (1985).
435. D. Masilamani, E. H. Manahan, J. Vitrone and M. M. Rogić, *J. Org. Chem.*, **48**, 4918 (1983).
436. N. H. Fischer, *Synthesis*, 393 (1970).
437. L. A. Paquette and S. Maiorana, *J. Chem. Soc., Chem. Commun.*, 313 (1971).
438. Z. Lysenko and M. M. Joullié, *J. Org. Chem.*, **41**, 3925 (1976).
439. R. M. Wilson and S. W. Wunderly, *J. Amer. Chem. Soc.*, **96**, 7350 (1974); **104**, 4429 (1982).
440. F. Muth, in Ref. 132, p. 320.
441. (a) V. M. Naidan and G. D. Naidan, *Zh. Obshch. Khim.*, **50**, 2611 (1980); *Chem. Abstr.*, **94**, 191834 (1981).
(b) With conjugated dienes see: V. M. Naidan, G. D. Naidan, S. G. Drozdova and V. M. Musienko, *Zh. Obshch. Khim.*, **55**, 391 (1985).
442. J. Sherwell and J. M. Tedder, *J. Chem. Soc., Perkin Trans. 2*, 1076 (1978).
443. F. Dawans and G. Lefèbre, *Rev. Inst. Fr. Pet. Ann. Combust. Liq.*, **16**, 941 (1961); *Chem. Abstr.*, **57**, 7077 (1962).
444. S. Nakajima and Y. Minoura, *Yuki Gosei Kagaku Kyokai Shi*, **24**, 806 (1966); *Chem. Abstr.*, **65**, 17061 (1966).
445. E. Spingler, *Plastica*, **19**, 269 (1966); *Chem. Abstr.*, **65**, 17130 (1966).
446. F. Riehl, *Hydrocarbon Process*, **46**, 161 (1967); *Chem. Abstr.*, **66**, 95625 (1967).
447. V. V. Lapshin, *Plast. Massy*, **1**, 74 (1967); *Chem. Abstr.*, **66**, 105518 (1967).
448. K. J. Ivin and M. Navratil, *Int. J. Sulfur Chem.*, **C6**, 97 (1971).
449. C. S. Marvel, *Sulfur Rep.*, **3**, 71 (1983).
450. H. Takeuchi, T. Nagai and N. Tokura, *Tetrahedron*, **25**, 2987 (1969).
451. C. M. M. da Silva Corrêa, A. S. Lindsay and W. A. Waters, *J. Chem. Soc. (C)*, 1872 (1968).
452. H. Takeuchi, T. Nagai and N. Tokura, *Bull. Chem. Soc. Japan*, **46**, 695 (1973).
453. F. Muth, in Ref. 132, p. 325.
454. E. Krauthausen, in Ref. 1, p. 623.
455. F. Muth, in Ref. 132, p. 324.
456. H. G. Viehe, Z. Janousek and R. Merenyi, *Acc. Chem. Res.*, **18**, 148 (1985).
457. P. Bruno, M. Caselli and A. Traini, *J. Electroanal. Chem. Interfacial Electrochem.*, **113**, 99 (1980); *Chem. Abstr.*, **93**, 227496 (1980).
458. Ger. Pat. 1.222.048 (1966), Bayer AG., Inv.: K. Wagner; *Chem. Abstr.*, **65**, 13545 (1966).
459. H. W. Gibson and D. A. McKenzie, *J. Org. Chem.*, **35**, 2994 (1970).
460. W. F. Jarvis and D. C. Dittmer, *J. Org. Chem.*, **48**, 2784 (1983).
461. W. F. Jarvis and D. C. Dittmer, Abstr. Nr. 51, Org. Chem. Div. 189th *Am. Chem. Soc. Nat. Meet.*, Miami Beach/Fl., 1985.
462. D. Knittel and B. Kastening, *J. Appl. Electrochem.*, **3**, 291 (1973).
463. D. Knittel and B. Kastening, *Ber. Bunsenges. Phys. Chem.*, **77**, 833 (1973).
464. D. Knittel, *Monatsh. Chem.*, **113**, 37 (1982); **117**, 359 (1986).
465. F. Camps, J. Coll and J. Guitart, *Tetrahedron*, **42**, 4603 (1986).
466. (a) K. Matsuo, M. Kobayashi and H. Minato, *Bull. Chem. Soc. Japan*, **43**, 260 (1970).
(b) E. Wellisch, E. Gipstein and O. J. Sweeting, *J. Polym. Sci.*, **B2**, 35 (1964).
467. R. Kerber and J. Starnick, *Chem. Ber.*, **104**, 2035 (1971).
468. S.-K. Chung, *J. Org. Chem.*, **46**, 5458 (1981).

469. F. Camps, J. Coll, A. Guerrero, J. Guitart and M. Riba, *Chem. Letters*, 715 (1982).
470. M. Julia, H. Lauron, J.-P. Stacino and J.-N. Verpeaux, *Tetrahedron*, **42**, 2475 (1986).
471. P. Messinger and H. Greve, *Synthesis*, 259 (1977).
472. F. Muth, in Ref. 132, p. 493.
473. (a) H. Cerfontain, A. Telder and L. Vollbracht, *Recl. Trav. Chim. Pays-Bas*, **83**, 1103 (1964).
(b) N. H. Christensen, *Acta Chem. Scand.*, **18**, 954 (1964).
474. H. J. Sipe, Jr., D. W. Clary and S. B. White, *Synthesis*, 283 (1984).
475. M. Ueda, K. Uchiyama and T. Kane, *Synthesis*, 323 (1984).
476. However: E. E. Gilbert, *J. Org. Chem.*, **28**, 1945 (1963).
477. R. Joly, R. Bucourt and J. Mathieu, *Recl. Trav. Chim. Pays-Bas*, **78**, 527 (1959).
478. Y. A. Moskvichev, Y. E. Shapiro, S. K. Kramerova, L. A. Sizyk, I. V. Shutova, E. M. Alov and G. S. Mironov, *Zh. Org. Khim.*, **18**, 330 (1982); *Chem. Abstr.*, **96**, 199215 (1982)
479. (a) W. Ried and G. Oremek, *Chem.-Ztg.*, **104**, 12 (1980).
(b) W. Ried and G. Oremek, *Ann. Chem.*, 619 (1981).
(c) F. Arndt, A. Kirsch and P. Nachtwey, *Chem. Ber.*, **59**, 1074 (1926).
480. I. Haiduc and K. J. Wynne in Ref. 5, p. 748.
481. T. E. Tyobeka, R. A. Hancock and H. Weigel, *J. Chem. Soc., Chem. Commun.*, 114 (1980).
482. D. D. Chapman, *Heterocycles*, **21**, 597 (1984).
483. C. G. Venier, F. A. Wing, Jr. and H. J. Barager, *Tetrahedron Letters*, **21**, 3159 (1980).
484. A. Sekiya and T. Umemoto, *Chem. Letters*, 1519 (1982).
485. N. Kamigata and M. Kobayashi, *Sulfur Rep.*, **2**, 87 (1982), p. 109.
486. L. O. Farng and J. L. Kice, *J. Org. Chem.*, **46**, 2599 (1981).
487. C. M. M. DaSilva Corrêa and M. A. B. C. S. Oliveira, *J. Chem. Soc., Perkin Trans. 2*, 711 (1983).
488. J. P. Weidner and S. S. Block, *Synthesis*, 583 (1970).
489. D. N. Harpp, J. Adams, J. G. Gleason, D. Mullins and K. Stelliou, *Tetrahedron Letters*, 3989 (1978).
490. W. Ando, S. Kohmoto, H. Miyazaki, K. Nishizawa and H. Tsumaki, *Photochem. Photobiol.*, **30**, 81 (1979).
491. T. Abe and J. M. Shreeve, *Inorg. Chem.*, **20**, 2432 (1981).
492. L. D. Martin and J. C. Martin, *J. Amer. Chem. Soc.*, **99**, 3511 (1977).
493. P. D. Bartlett, T. Aida, H.-K. Chu and T. S. Fang, *J. Amer. Chem. Soc.*, **102**, 3515 (1980).
494. C. Degrand and H. Lund, *Acta Chem. Scand., Ser. B*, **33**, 512 (1979).
495. S. Oae, O. Yamada and T. Maeda, *Bull. Chem. Soc. Japan*, **47**, 166 (1974).
496. J. C. Craig and K. K. Purushothaman, *Tetrahedron Letters*, 5305 (1969).
497. F. A. Davis and R. L. Billmers, *J. Amer. Chem. Soc.*, **103**, 7016 (1981).

CHAPTER 8

Synthesis of sulphoxides

JOZEF DRABOWICZ, PIOTR KIEŁBASINSKI AND MARIAN MIKOŁAJCZYK

Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Department of Organic Sulphur Compounds, 90–362 Łódź, Boczna 5, Poland

I. INTRODUCTION

Earlier methods for the synthesis of sulphoxides have been reviewed up to 1955 by Schöberl and Wagner in 'Houben–Weyl'[1]. A new edition of the sulphur volume of this series contains a comprehensive review of the chemistry of sulphoxides by Kresze in which preparative procedures have also been collected up to 1982[2]. As a rule, small chapters presenting very briefly the standard procedures used for the preparation of sulphoxides are parts of organic chemistry textbooks[3,4]. More detailed, but still far from exhaustive, are surveys of the sulphoxide syntheses in the books devoted to the chemistry of organic sulphur compounds. For example, such compilations of the sulphoxide syntheses may be found in *Organic Chemistry of Sulphur* edited by Oae[5] and in the book by Block, *Reactions of Organosulfur Compounds*[6]. The synthesis of sulphoxides is also discussed by Johnson and Sharp in their review on the chemistry of sulphoxides[7] and more recently by Drabowicz and Mikołajczyk in a review article on the synthesis of sulphoxides[8]. Moreover, the synthetic procedures used for the preparation of the particular groups of sulphoxides are included in many other reviews which have been published in the last two decades[2].

The purpose of the present chapter is to provide an up-to-date review of methods which may be applied for the synthesis of both achiral and chiral (racemic and optically active) sulphoxides as well as their derivatives. Since the synthesis of optically active sulphoxides is based on many special procedures, it was found necessary to separate the syntheses of achiral and racemic sulphoxides from those of optically active ones.

Some limitations of the subject surveyed have been necessary in order to keep the size of the chapter within the reasonable bounds. Accordingly, to make it not too long and readable, the discussion of the methods of the sulphoxide synthesis will be divided into three parts. In the first part, all the general methods of the synthesis of sulphoxides will be briefly presented. In the second one, methods for the preparation of optically active sulphoxides will be discussed. The last part will include the synthetic procedures leading to functionalized sulphoxides starting from simple dialkyl or arylalkyl sulphoxides. In this part, however, the synthesis of achiral, racemic and optically active sulphoxides will be treated together. Each section and subsection includes, where possible, some considerations of mechanistic aspects as well as short comments on the scope and limitations of the particular reaction under discussion.

II. SYNTHESIS OF ACHIRAL AND RACEMIC SULPHOXIDES

A. Oxidation of Sulphides

The oldest and generally applied sulphoxide synthesis consists of the oxidation of sulphides to sulphoxides. This reaction was reported for the first time by Märcker[9] as early as 1865. He found that treatment of dibenzyl sulphide with nitric acid afforded the corresponding dibenzyl sulphoxide in a high yield. Since that time the oxidation of

sulphides to sulphoxides has been the subject of extensive studies and a number of useful synthetic procedures are now available. They will be discussed below.

1. Oxidation by hydrogen peroxide

The simplest procedure for oxidation of sulphides to sulphoxides used till now involves the oxidation of sulphides with hydrogen peroxide alone or in the presence of various catalysts (equation 1).

$$R{-}S{-}R^1 + H_2O_2 \longrightarrow R{-}\underset{\underset{O}{\|}}{S}{-}R^1 + H_2O \qquad (1)$$

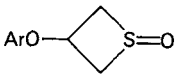
The major difficulty encountered in the preparation of sulphoxides by this method is a facile over-oxidation to the corresponding sulphones.

a. Hydrogen peroxide. Since 1908, when Gazdar and Smiles[10] reported that sulphides may be almost quantitatively oxidized to sulphoxides by hydrogen peroxide in acetone, this solvent has been commonly used as a reaction medium[11–13]. The only drawback is the relatively long reaction time needed for completion of the oxidation. This limitation may be simply overcome by the use of methanol as solvent[14]. It was found that various sulphoxides can be obtained selectively by keeping the corresponding sulphides with 2–4 equivalents of hydrogen peroxide in methanol solution at room temperature for 1 to 75 h depending on the structure of the starting sulphide. The use of methanol as solvent makes this oxidation procedure preparatively simple because the work-up is limited only to the addition of water to the reaction mixture and extraction of the resultant solution with chloroform. Since oxidation with hydrogen peroxide is very mild, it can be successfully applied to the preparation of acid-sensitive sulphoxides, such as allyl sulphoxide (Table 1) or silyl-substituted vinyl sulphoxides of structure **1**[15].

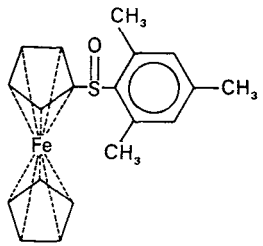
$$R_3Si(CH_2)_n\underset{\underset{O}{\|}}{S}CH{=}CH_2$$

(1)

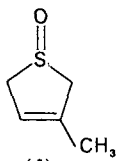
Thietane sulphoxide **2** was isolated in 65% yield after treatment of the parent sulphide with hydrogen peroxide[16]. Mesityl ferrocenyl sulphoxide **3** and the corresponding



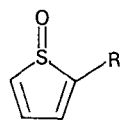
(2)



(3)



(4)



(5)

TABLE 1. Oxidation of sulphides to sulphoxides, R^1R^2SO, with hydrogen peroxide

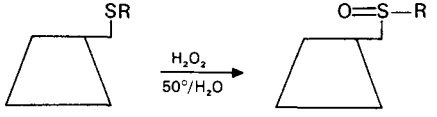
R^1	R^2	Solvent[b]	Reaction time (h)	Yield (%)	Ref.
Me	*n*-Bu	M	1	99	14
n-Bu	*n*-Bu	M	2	83	14
t-Bu	*t*-Bu	A	24	c	13
i-Am[a]	*i*-Am[a]	A	24	45	10
$PhCH_2$	$PhCH_2$	A	48	75	10
$PhCH_2$	Me	A	12	77	11
Ph	Me	A	24	c	12
Ph	Me	M	18	99	14
Ph	Ph	A	24	c	12
Ph	Ph	M	170	50	14
p-Tol	CH_2NO_2	A	120	25	11
Me	CH_2CO_2Et	A	72	87	11
Me	$CH(Me)CH{=}CH_2$	A	24	c	13
Me	$CH(Et)CH{=}CH_2$	A	24	c	13

[a]Am = C_5H_{11}.
[b]M = methanol, A = acetone.
[c]Not given.

sulphone were obtained in almost equivalent amounts after oxidation of the starting sulphide with hydrogen peroxide in methanol – water/potassium hydroxide solution at pH 7–9[17].

3-Methyl-2, 5-dihydrothiophene was converted into the corresponding *S*-oxide **4** in 57% yield after treatment with 30% excess of hydrogen peroxide for 60 h. By the same procedure the sulphoxides **5** derived from thiophene and its α-substituted analogues were also prepared[18].

Recently, 6-alkylsulphinyl β-cyclodextrins **6** were obtained from the corresponding sulphides by oxidation with dilute aqueous hydrogen peroxide[19] (equation 2).

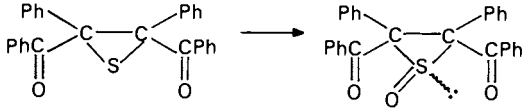


(2)

(**6**) (**a**) R = Me
(**b**) R = *n*-Pr

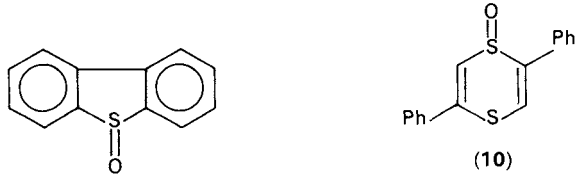
b. Oxidation by hydrogen peroxide in the presence of catalysts. Oxidation of sulphides by hydrogen peroxide has been found to be subject to catalysis. In 1908 Hinsberg[20] used acetic acid as a catalyst. He found that sulphides may be oxidized to sulphoxides in very high yields by hydrogen peroxide in acetone/acetic acid mixture or in acetic acid alone. Later on, it was found that sulphuric and perchloric acids[21] function also as efficient catalysts. The main drawback of the acid-catalyzed oxidation is a relatively long reaction time and a facile over-oxidation to the corresponding sulphones. However, by means of this procedure some sulphoxides of more than routine interest were prepared. For instance, Dittmer and Levy[22] reported that oxidation of dibenzoylstilbene episulphide **7** with hydrogen peroxide in acetic acid gave two diastereoisomeric sulphoxides **8**

(equation 3).

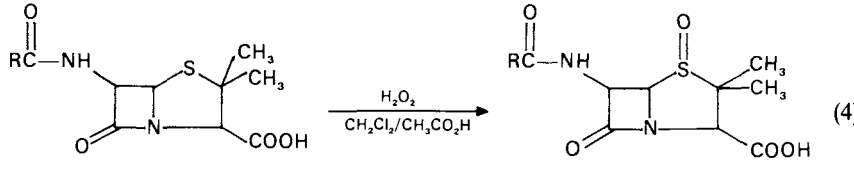


(7) (8) (3)

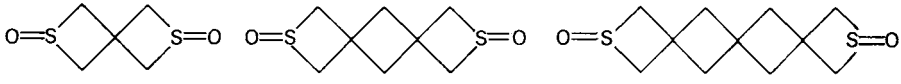
Dibenzothiophen *S*-oxide **9**[23] and 2,5-diphenyl-1,4-dithiacyclohexadiene-1-oxide **10**[24] were prepared from the corresponding sulphides by treatment with hydrogen peroxide in the presence of acetic acid. Selective oxidation of the penicillin derivative **11** to *S*-oxide **12** was achieved using hydrogen peroxide in methylene chloride solution containing 5 equivalents of acetic acid[25] (equation 4). Another interesting example is the synthesis of disulphoxides **13**, **14** and **15** which were obtained by oxidation of the parent sulphides with two equivalents of hydrogen peroxide in acetic acid at room temperature[26]. It was demonstrated that substantial through-bond interactions of the sulphur lone electron pairs occur in these structures. Treatment of α-pyridyl sulphides with hydrogen peroxide in acetic acid gave exclusively sulphoxides **16** in very good yields[27]. Similarly, oxidation of dithioacetals[28,29] resulted in the formation of the corresponding *S*-monooxides **17**. Apart from acids, few other compounds were found to be effective catalysts for the hydrogen peroxide oxidation of sulphides to sulphoxides. Thus, sulphides are oxidized to sulphoxides with hydrogen peroxide in absolute *t*-butyl alcohol containing a catalytic amount of vanadium pentoxide at 15°. The conversion of sulphides and sulphoxides to sulphones takes place only at 45 °C in the presence of this catalyst[30]. Yields of sulphoxides (Table 2) are good even in the oxidation of labile sulphides such as α-chlorosulphides and α-acetoxysulphides. Also thiirane-1-oxides **18** may be prepared by this procedure in 55–60% yields.



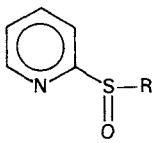
(9) (10)



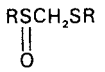
(11) (12) (4)



(13) (14) (15)

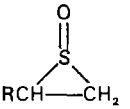


(16)



(17)

R = Me, Et, Bu



(18)

(a) R = H

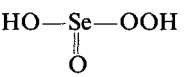
(b) R = CH_2OH

Vanadium pentoxide and mercuric oxide were used as catalysts for the hydrogen peroxide oxidation of bis(phenylthio)methane to its monooxide **17a**[31] (equation 5). From the synthetic point of view, it is interesting to note that vanadium pentoxide, in addition to its catalytic action, functions also as an indicator in this reaction. In the presence of hydrogen peroxide, the reaction mixture is orange while in the absence of hydrogen peroxide a pale yellow colour is observed. Thus, it is possible to perform the oxidation process as a titration ensuring that an excess of oxidant is never present.

$$PhSCH_2SPh \xrightarrow[V_2O_5]{H_2O_2} Ph{-}\underset{\underset{O}{\|}}{S}{-}CH_2SPh \qquad (5)$$

(17a)

A highly selective and rapid oxidation of sulphides to sulphoxides occurs when hydrogen peroxide/selenium dioxide system is used[32]. The reaction takes place immediately upon addition of a solution of hydrogen peroxide and selenium dioxide to a solution of a sulphide in methanol at room temperature. Yields of sulphoxides (Table 2) are in the range between 80 and 95%. It is most probable that perseleninic acid **19** is the true oxidizing agent.



(19)

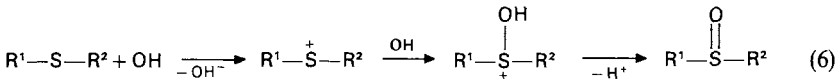
It is interesting to note that Reich and coworkers[33] reported the conversion of methyl

TABLE 2. Catalyzed oxidation of sulphides to sulphoxides, R^1R^2SO, with hydrogen peroxide

R^1	R^2	Catalyst	Yield (%)	Ref.
n-Bu	*n*-Bu	SeO_2	90	32
t-Bu	*t*-Bu	$TiCl_3$	98	35
$PhCH_2$	$PhCH_2$	V_2O_5	62	30
$PhCH_2$	$PhCH_2$	SeO_2	88	32
$PhCH_2$	$PhCH_2$	$TiCl_3$	98	35
Ph	Me	SeO_2	95	32
Ph	Me	$TiCl_3$	100	35
Ph	Ph	V_2O_5	60	30
Ph	Ph	SeO_2	92	32
Ph	Ph	$TiCl_3$	100	35
$C_{12}H_{25}$	CH_2Cl	V_2O_5	69	30
Ph	CH_2Cl	V_2O_5	73	30
CH_2CO_2Me	CH_2CO_2Me	V_2O_5	49	30
Dibenzothiophene		$TiCl_3$	99	35

phenyl sulphide to the corresponding sulphoxide by means of phenylperseleninic acid and Melnikov[34] found that sulphides may be oxidized to sulphoxides by refluxing with selenium dioxide for a few hours in chloroform.

A rapid and clean oxidation of sulphides to sulphoxides can also be carried out using the titanium(III) trichloride/hydrogen peroxide reagent[35]. On a milimole scale, the oxidation takes place in a time shorter than 20 min upon addition of a solution of hydrogen peroxide to a solution of the sulphide and titanium(III) trichloride in methanol at room temperature. It was suggested that the formation of a sulphoxide in this reaction resulted from a direct coupling of the hydroxy radical with cation radical **20** formed at the sulphur atom of the sulphide (equation 6).

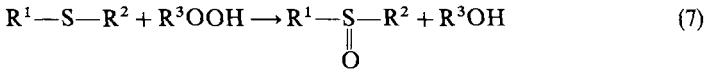


(6)

(20)

2. Oxidation with organic peroxides

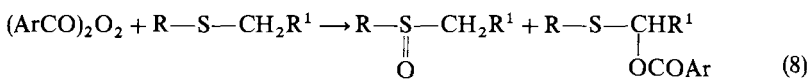
Benzoyl hydroperoxide was used for the conversion of divinyl sulphide into divinyl sulphoxide by Levin[36] as early as 1930. In 1954 Bateman and Hargrave[37] reported that saturated sulphides may be oxidized to sulphoxides by means of cyclohexyl or *t*-butyl hydroperoxide. These authors found that in both polar and non-polar solvents oxygen transfer occurred to give quantitative yields of sulphoxides over a wide range of experimental conditions according to equation 7. It was also reported[38] that a quantitative yield of sulphoxides was obtained from the reaction of unsaturated sulphides with *t*-butyl and cyclohexyl hydroperoxides in methanol. With *t*-butyl hydroperoxide in benzene the sulphoxide yield was in no case stoichiometric, varying from 90 to 5% under the condition chosen.



(7)

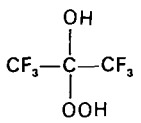
R^3 = *t*-Bu or cyclohexyl

Horner and Jürgens[39] reported that benzoyl peroxides **21** in the presence of sulphides decompose to give sulphoxides and α-acyloxysulphides **22** (equation 8). The latter compounds are undoubtedly formed as a result of the Pummerer reaction. The oxidation reaction leading to sulphoxides has been shown to be an ionic process[40]. However, till now it has not found wider synthetic applications. Ganem and coworkers[41] showed that 2-hydroperoxyhexafluoro-2-propanol **23** formed *in situ* from hexafluoroacetone and

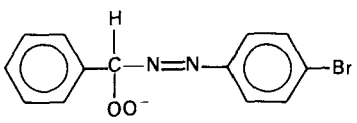


(8)

(21) **(22)**



(23)



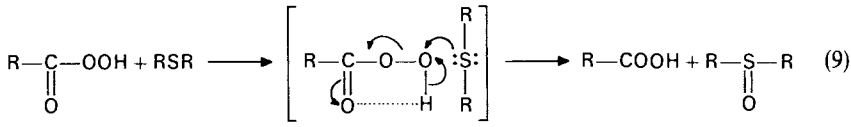
(24)

hydrogen peroxide is a convenient reagent for the conversion of sulphides into the corresponding sulphoxides under mild conditions. The reaction takes place quickly below room temperature affording sulphoxides almost quantitatively. The first oxidation of sulphides to sulphoxides under basic conditions was achieved using diazohydroperoxide anion **24**[42].

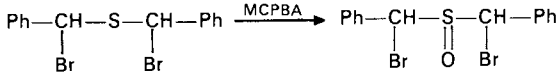
3. *Oxidation with peracids*

It is well established that organic peroxides are much stronger oxidizing agents than hydrogen peroxide. Among them organic peracids are strong oxidants even in the cold[43]. Levin[44] as early as 1928 commented on the ease with which organic sulphides may be oxidized to sulphoxides by perbenzoic acid at room temperature. Since that time, a variety of other peracids have been used for this conversion[2].

Based on the kinetic studies, a mechanism for this oxidation was proposed[45] which involves a nucleophilic attack by the sulphide on a cyclic hydrogen-bonded form of the peracid (equation 9). Since oxidation using peracids occurs under very mild conditions, it can be successfully applied to the preparation of base sensitive sulphoxides. Thus, di(α-bromobenzyl) sulphoxide **25**, which is very labile in the presence of a base, was obtained by careful oxidation of α-di(α-bromobenzyl) sulphide by means of *m*-chloroperbenzoic acid (MCPBA)[46] (equation 10).



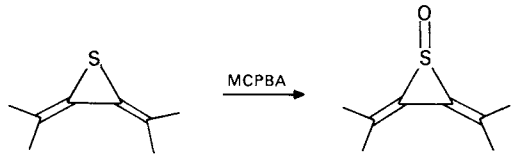
(9)



(10)

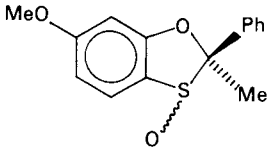
(25)

Oxidation of a thiiraneradialene with equimolar amounts of MCPBA in CH_2Cl_2 at about 0 °C gave the corresponding thiiraneradialene *S*-oxide **26** in a quantitative yield[47] (equation 11). 5-Membered heterocyclic sulphoxides such as 1,3-benzoxathiolane sulphoxide **27**, 1,3-benzdithiolane sulphoxide **28** and 1,3-dithiolane sulphoxide **29** were readily obtained from their sulphide precursors by oxidation with MCPBA in dichloromethane solution[48].

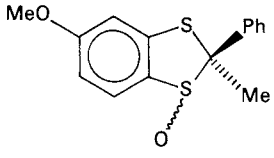


(11)

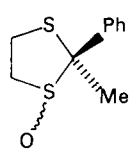
(26)



(27)



(28)



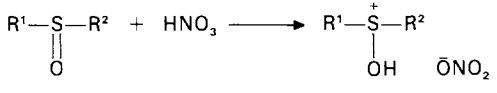
(29)

The use of optically active peracids for asymmetric oxidation of sulphides will be discussed in Section III dealing with the synthesis of optically active sulphoxides.

4. Oxidation with nitrogen-containing compounds

a. Nitric acid. Märcker[9] in 1865 first showed that dibenzyl sulphide may be oxidized to the corresponding sulphoxide by nitric acid of a proper strength. Soon after, this oxidant was used for the preparation of dialkyl sulphoxides[49]. More recently alkyl aryl[50] and long-chain dialkyl sulphoxides[51] were prepared by oxidation of parent sulphides with nitric acid in acetic anhydride. The first preparation of polyfluoroalkyl sulphoxides involved the oxidation of trifluoromethyl methyl sulphide with concentrated nitric acid to give trifluoromethyl methyl sulphoxide in 30% yield[52]. Later on, it was found that by the use of fuming nitric acid and longer reaction time the yields of perfluoroalkyl sulphoxides may be increased[53].

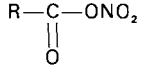
A detailed study revealed that sulphides may react with nitric acid to give sulphoxides, sulphones and their nitro derivatives[54]. However, under suitable conditions the nitric acid oxidation of sulphides leads to a selective formation of sulphoxides. This is probably due to the formation of a sulphonium salt **30** which is resistant to further oxidation[50] (equation 12).



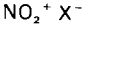
(12)

(**30**)

b. Organic nitrates and nitronium salts. In 1976 Low and coworkers[55] reported that organic nitrates, which were known as nitrating agents, have also oxidative properties. They found that acyl nitrates **31** react rapidly with dialkyl and arylalkyl sulphides at $-78°$ to give sulphoxides in very high yields (Table 3).



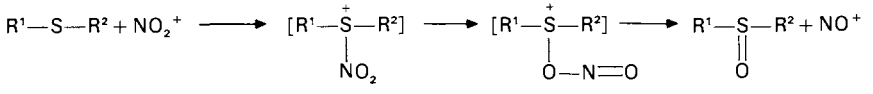
(**31**) (**a**) R = Me (**b**) R = Ph



(**32**) (**a**) $X = PF_6$ (**b**) $X = BF_4$

Olah and coworkers[56] found that treatment of dialkyl, arylalkyl and diaryl sulphides with nitronium hexafluorophosphate (or tetrafluoroborate) **32** at $-78°$ in methylene chloride resulted in the formation of sulphoxides in moderate to high yields (Table 3). In the oxidation of diphenyl sulphide which affords diphenyl sulphoxide in 95% yield, small amounts of the ring nitration products (*o*- and *p*-nitrophenyl phenyl sulphides) were formed. However, diphenyl sulphone and nitrophenyl phenyl sulphoxide were not detected among the reaction products.

It was proposed that an initially formed *S*-nitrosulphonium ion **33** rearranges into the *S*-nitritosulphonium ion **34**, which is then stabilized by loss of NO^+ ion to give the corresponding sulphoxide (equation 13).

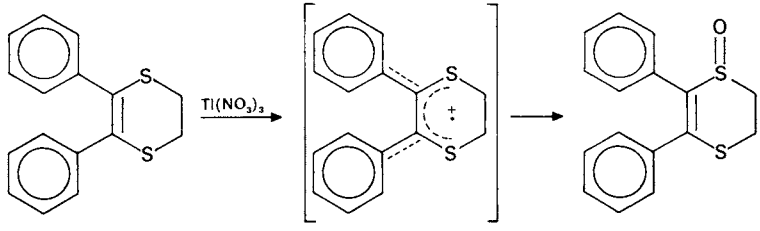


(**33**) (**34**) (13)

TABLE 3. Oxidation of sulphides to sulphoxides, R^1R^2SO, with nitrogen-containing oxidants

R^1	R^2	Oxidant	Yield (%)	Ref.
Me	Me	$MeCONO_3$	100	55
Me	Me	$PhCONO_3$	95	55
Me	Me	NO_2PF_6	46	56
Et	Et	$MeCONO_3$	83	55
Et	Et	$PhCONO_3$	100	55
Et	Et	NO_2PF_6	90	56
Et	Et	$Tl(NO_3)_3$	86	57
Et	Et	N_2O_4	95	64
n-Pr	*n*-Pr	NO_2PF_6	95	56
n-Pr	*n*-Pr	$Tl(NO_3)_3$	92	57
n-Pr	*n*-Pr	N_2O_4	100	64
Me	Ph	$MeCONO_3$	85	55
Me	Ph	$PhCONO_3$	100	55
Me	Ph	NO_2PF_6	89	56
Ph	Ph	NO_2PF_6	61	56
Ph	Ph	$Tl(NO_3)_3$	82	57
p-ClC_6H_4	*p*-ClC_6H_4	NO_2PF_6	90	57

c. Inorganic nitrates. It was reported[57] that reaction of dialkyl and arylalkyl sulphides with an excess of thallium(III) nitrate at room temperature in a chloroform–acetic acid (3:1) solution afforded the corresponding sulphoxides in high yields (Table 3). However, in a chloroform–acetic anhydride (3:1) solution the exclusive formation of sulphones was observed. 2,3-Diphenyl-5,6-dihydro-1,4-dithiin **35** on treatment with 1.2 equivalent of thallium(III) nitrate in chloroform–methanol (1:1) solution at room temperature gave the corresponding sulphoxide **36** in 72% yield within 15 min (equation 14). The ESR spectrum of the reacting solution indicated the presence of the cation radical **37**. Therefore, the formation of **36** in this reaction was suggested to proceed by a one-electron oxidation mechanism.



(35) **(37)** **(36)**

Ceric ammonium nitrate was also used as an efficient reagent for the conversion of diaryl sulphides into the corresponding sulphoxides under very mild conditions[58]. Over-oxidation, even in the presence of an excess of the reagent, was not observed. However, this reagent is not suitable for the oxidation of sulphides possessing α-hydrogens. This is most probably due to the Pummerer reaction which occurs in the presence of cerium(III) nitrate. An improved procedure utilizing catalytic amounts of cerium(IV) salt together with a cooxidant (BrO_3^-), which recycles the spent cerium(III)ions, avoided this limitation and can be applied also to the oxidation of dialkyl sulphides[59].

d. Nitrogen tetroxide. The first report on oxidation of organic sulphur compounds by 'nitrous fumes' was published by Pummerer[60] in 1910. In 1927 Bell and Bennett[61] reported that oxidation of 1,4-dithiane by this reagent gave predominantly the *trans*-isomer of 1,4-dithiane β-disulphoxide and a little of the *cis*-isomer of 1,4-dithiane α-disulphoxide. This observation was later confirmed by Whitaker and Sisler[62]. Horner and Hübenett[63] reported also on the use of dinitrogen tetroxide in carbon tetrachloride for oxidation of methyl phenyl sulphide to the corresponding sulphoxide. Soon after, liquid dinitrogen tetroxide was used for the selective oxidation of dialkyl sulphides to sulphoxides[64]. It was also found that dinitrogen tetroxide forms molecular addition compounds with dialkyl sulphoxides. Most probably, the formation of such addition compounds may prevent further oxidation at sulphur. Dinitrogen tetroxide may be used for oxidation of α-chlorosulphides, provided that the formation of N_2O_3 is prevented by scavenging the reaction mixture with oxygen[65].

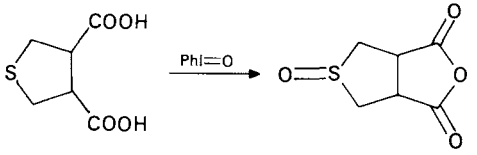
5. Oxidation with trivalent iodo compounds

a. Iodosobenzene. Ford-Moore[66] reported that iodosobenzene is a very convenient reagent for the conversion of β-hydroxy and β-chlorosulphides **38** to the corresponding sulphoxides **39** (equation 15). An interesting example of the oxidation of cyclic dicarboxylic acids *cis*-**40** and *trans*-**40** by iodosobenzene has been described by Takaya and coworkers[67]. They found that treatment of *trans*-acid **40** with iodosobenzene gave the expected sulphoxide. However, oxidation of *cis*-**40** was accompanied by dehydration and afforded sulphoxide **41** (equation 16).

$$XCH_2CH_2{-}S{-}CH_2CH_2X + PhI{=}O \longrightarrow XCH_2CH_2{-}\underset{\underset{O}{\|}}{S}{-}CH_2CH_2X + PhI \qquad (15)$$

(38)
(a) X = OH
(b) X = Cl

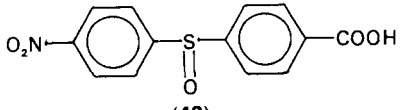
(39)



(16)

cis-(**40**) (**41**)

b. Iodobenzene diacetate. Iodobenzene diacetate was used by Szmant and Suld[68] for the preparation of *p*-(nitrophenylsulphinyl)benzoic acid **42**. The oxidation of the starting sulphide in boiling acetic acid for 24 h with an equivalent amount of iodobenzene diacetate gave sulphoxide **42** in 90% yield. Later on, oxidation of benzyl phenyl and dibenzyl sulphide by this reagent was found to be much less efficient and afforded the corresponding sulphoxides in 51 and 21% yields, respectively[69].



(**42**)

c. Iodobenzene dichloride. Montanari and coworkers[70] found that sulphides are selectively oxidized to sulphoxides by iodobenzene dichloride in aqueous pyridine according to equation (17). The reaction is almost instantaneous at a temperature below 0° and affords a wide range of aliphatic, aromatic and heterocyclic sulphoxides in yields over 80%. Iodobenzene dichloride is only a controlled source of chlorine. The reaction proceeds via an electrophilic attack of the chlorine at the divalent sulphur to afford a chlorosulphonium salt **43**. This salt is then decomposed by nucleophilic attack of water giving the sulphoxide (equation 18). This procedure is suitable for the synthesis of sulphoxides containing ^{18}O in the sulphinyl group.

$$R^1—S—R^2 + PhICl_2 + 2C_5H_5N + H_2O \longrightarrow R^1—\underset{\underset{O}{\|}}{S}—R^2 + PhI + 2C_5H_5H\cdot HCl \qquad (17)$$

$$R^1—S—R^2 + PhICl_2 \longrightarrow R^1—\overset{+}{\underset{\underset{Cl}{|}}{S}}—R^2 \xrightarrow{H_2O} R^1—\underset{\underset{O}{\|}}{S}—R^2 \qquad (18)$$

(43)

6. *Oxidation with metaperiodates*

In 1962, Leonard and Johnson[71] described the selective oxidation of sulphides to sulphoxides by sodium metaperiodate (equation 19). This reaction is general in scope and may be applied to the preparation of acyclic, cyclic, aliphatic, aromatic and heterocyclic sulphoxides. Typically, the reaction is carried out at 0° in methanol–water solution and is complete in 3–24 h affording yields of about 90% or higher (Table 4). However, in some cases this reagent does not work efficiently. Thus, the attempted oxidation of methyl heptafluoropropyl sulphide with aqueous sodium periodate at temperatures in the range 5–20° gave unchanged reactants[53]. Moreover, when the reaction was carried out at 100° for 7 days

TABLE 4. Oxidation of sulphides to sulphoxides, R^1R^2SO, by metaperiodates, MIO_4

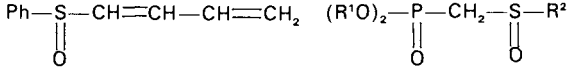
R^1	R^2	M	Solvent (%)	Yield (%)	Ref.
Et	Et	Na	M/W[a]	65	71
Me	Ph	Na	M/W[a]	99	71
Me	Ph	Na/Al_2O_3	EtOH	88	79
Me	Ph	Bu_4N	$CHCl_3$	86	78
$PhCH_2$	$PhCH_2$	Na	M/W[a]	96	71
$PhCH_2$	$PhCH_2$	Na/SiO_2	CH_2Cl_2	66	80
t-Bu	*t*-Bu	Na/Al_2O_3	EtOH	85	79
CH_2=CH—CH_2	CH_2=CH—CH_2	Na/Al_2O_3	EtOH	87	79
Bz	*i*-Pr	Na/Al_2O_3	EtOH	85	79
Ph	Ph	Na	M/W[a]	98	71
Ph	Ph	Na/Al_2O_3	EtOH	90	79
Ph	Ph	Bu_4N	$CHCl_3$	72	78
	Thiane	Na	M/W[a]	99	71
	Thiane	Bu_4N	$CHCl_3$	90	78
p-Tol	*p*-Tol	Bu_4N	$CHCl_3$	70	78

[a]M/W = methanol–water solution.

the unchanged sulphide (80%) and heptafluoropropyl sulphone were isolated. No trace of sulphoxide was detected under these conditions [53].

$$R^1—S—R^2 + NaIO_4 \longrightarrow R^1—\underset{\underset{O}{\|}}{S}—R^2 + NaIO_3 \tag{19}$$

Oxidation of phenyl hexyl sulphide with sodium metaperiodate gave also only a trace amount of the corresponding sulphoxide[72]. On the other hand, Hall and coworkers[73] prepared benzylpenicillin and phenoxymethyl penicillin sulphoxides from the corresponding benzyl esters by oxidation with sodium metaperiodate in dioxane solution with a phosphate buffer. A general procedure for the synthesis of penicillin sulphoxides was reported later by Essery and coworkers[74] which consists in the direct oxidation of penicillins or their salts with sodium metaperiodate in aqueous solution at pH 6.5–7.0. 1-Butadienyl phenyl sulphoxide **44**[75] and α-phosphoryl sulphoxides **45**[76] were also prepared by the same procedure.

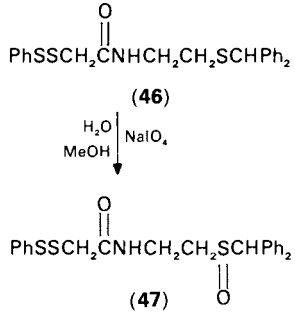


(44) **(45)**

R^1 = Me, Et

R^2 = Me, Ph, *p*-Tol

The selective oxidation of the sulphide grouping in the presence of the disulphide bond was observed when a methanolic solution of amide **46** was treated with an aqueous solution of sodium metaperiodate[77] (equation 20).



(46) **(47)** (20)

Water insoluble tetrabutylammonium metaperiodate, which can be prepared from sodium metaperiodate and tetrabutylammonium hydrogen sulphate in aqueous solution, was found to be a useful reagent for the selective oxidation of sulphides in organic solvents[78]. The reaction was generally carried out in boiling chloroform and gave dialkyl, alkyl aryl and diaryl sulphoxides in yields which are comparable with those reported for sodium metaperiodate in aqueous methanol solution (Table 4). In the case of diaryl sulphoxides, the yields decrease with prolonged reaction time.

Alumina supported sodium metaperiodate, which can be prepared by soaking the inorganic support with a hot solution of sodium metaperiodate, was also found to be a very convenient reagent for the selective and clean oxidation of sulphides to sulphoxides[79]. The oxidation reaction may be simply carried out by vigorous stirring of this solid oxidant with the sulphide solution at room temperature. As may be expected for such a procedure, solvent plays an important role in this oxidation and ethanol (95%) was found to be

superior to benzene, THF and chloroform. It should be noted that dibenzothiophen was not oxidized by this reagent even after 48 h.

Silica gel supported sodium metaperiodate was used for the selective oxidation of dibenzyl sulphide[80]. Metaperiodate anion soaked on strongly basic-ion-exchange resins Amberlite IRA-904 or Amberlyst A-26 was found to be able to oxidize sulphides into the corresponding sulphoxides in 82–99% yield[81].

7. *Oxidation with halogens and compounds containing 'electropositive' halogens*

a. Halogens. Molecular halogens have long been known to form addition compounds with organic sulphides which may be chlorosulphonium salts or sulphuranes **48**. These can be subsequently hydrolyzed to sulphoxides as shown in equation 21. However, it was recognized very early that undesirable side-reactions very often predominate over the sulphoxide formation[23,82]. Thus, oxidation of dimethyl sulphide with chlorine in water gave α-chloromethyl sulphoxides[83]. Treatment of mono-, di- and trichloromethyl sulphides **49** with chlorine in acetic acid–water mixture afforded the corresponding sulphoxides **50** in good yields[84]. On the other hand, the reaction of dichloro- and trichlorosulphoxides **50** with chlorine in methylene chloride gave exclusively the corresponding sulphinyl chlorides **51**, resulting from cleavage of the carbon–sulphur bond[85] in **50** (equation 22). In the case of aryl sulphides, halogenation of the aromatic ring was also observed[86].

$$R^1\text{—}S\text{—}R^2 + X_2 \rightleftharpoons \left[R^1\overset{+}{S}R^2XX^- \rightleftharpoons R^1R^2SX_2\right] \xrightarrow{H_2O} R^1\text{—}\underset{\underset{O}{\|}}{S}\text{—}R^2 + 2HX \qquad (21)$$

(**48**)

$$R\text{—}S\text{—}R^1 \xrightarrow[H_2O/AcOH]{Cl_2} R\text{—}\underset{\underset{O}{\|}}{S}\text{—}R^1 \xrightarrow[CH_2Cl_2]{Cl_2} R\text{—}\underset{\underset{O}{\|}}{S}\text{—}Cl \qquad (22)$$

(**49**) (**50**) (**51**)

for **b** and **c**

(**a**) $R^1 = CH_2Cl$

(**b**) $R^1 = CHCl_2$

(**c**) $R^1 = CCl_3$

With bromine as an oxidant the formation of by-products may be easily prevented by carrying out the oxidation under appropriate conditions. For example, Oae and coworkers[87] reported oxidation of a number of sulphides with the complexes of bromine and tertiary amines in 70% aqueous acetic acid as solvent. They found that pyridine-bromine and 1,4-diazabicyclo[2,2,2]octane-bromine complexes gave satisfactory results in terms of yields and purity of sulphoxides (Table 5). It was demonstrated[88,89] that sulphoxides (dialkyl, aryl alkyl, diaryl, α-phosphoryl, *S*-oxides of penicillin) can be obtained in high yields and free of the above-discussed side-products if the reaction of sulphides with bromine or chlorine as well as the subsequent hydrolysis of the addition compounds is carried out under two-phase conditions (CH_2Cl_2/H_2O) using potassium hydrogen carbonate as a base. This procedure was applied also for the preparation of sulphoxides containing ^{18}O in the sulphinyl group. However, the ^{18}O content in the sulphoxide formed was much lower than that of ^{18}O in the water used for the reaction. More recently, a modified two-phase oxidation procedure was developed which allows one to synthesize ^{18}O labelled sulphoxides with no loss of ^{18}O enrichment. It involves the use of pyridine instead of potassium hydrogen carbonate as hydrogen bromide acceptor[90].

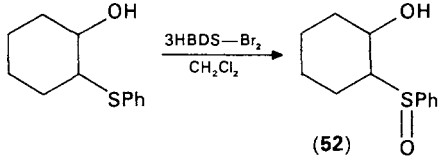
TABLE 5. Oxidation of sulphides to sulphoxides, R^1R^2SO, with bromine

R^1	R^2	Reaction conditions	Yield (%)	Ref.
Me	*n*-Pr	$Br_2/H_2O/CH_2Cl_2/KHCO_3$	85	89
Me	*n*-Bu	$Br_2/H_2O/CH_2Cl_2/KHCO_3$	90	89
Ph	Me	$Br_2/H_2O/CH_2Cl_2/KHCO_3$	97	89
Ph	Me	Br_2/HBDS[a]/CH_2Cl_2	85	72
p-Tol	Me	$Br_2/Py/H_2O/AcOH$	85	87
$PhCH_2$	$PhCH_2$	$Br_2/H_2O/CH_2Cl_2/KHCO_3$	97	89
$PhCH_2$	$PhCH_2$	Br_2/HBDS[a]/CH_2Cl_2	92	72
$PhCH_2$	Ph	$Br_2/Py/H_2O/Ac$	65	87
$PhCH_2$	$PhCH_2$	$Br_2/Py/H_2{}^{18}O/CH_2Cl_2$	90	90
Ph	Ph	$Br_2/H_2O/CH_2Cl_2/KHCO_3$	95	89
Ph	Ph	Br_2/HBDS[a]/CH_2Cl_2	18	72
Ph	Ph	$Br_2/Py/H_2O/AcOH$	95	87
CH_3	CH_2Cl	Br_2/HBDS/CH_2Cl_2	78	72
Ph	C_6H_{13}	Br_2/HBDS/CH_2Cl_2	85	72
C_6H_{13}	C_6H_{13}	Br_2/HBDS/CH_2Cl_2	90	72

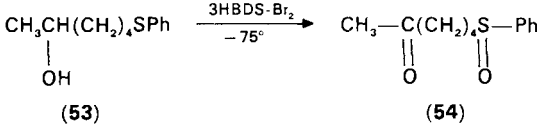
[a]HBDS = hexabutyldistannoxane.

Ueno and coworkers[72] described a procedure in which oxidation of sulphides by bromine can be carried out under anhydrous conditions. They found that treatment of sulphides with bromine and then with hexabutyldistannoxane (HBDS) in organic solvent (room temperature, 1–2 h) afforded sulphoxides in high yields (Table 5) without sulphone contaminations (equation 23). This procedure has a special value for the oxidation of hydrophobic sulphides such as hexyl phenyl sulphide and dihexyl sulphide because, for example, oxidation of the former with sodium metaperiodate gave a trace amount of the corresponding sulphoxide. It is interesting that α-(phenylthio) cyclohexanol after treatment with $HBDS/Br_2$ reagent gave 2-(phenylsulphinyl)cyclohexanol (**52**) in 87% yield (equation 24), whereas acyclic hydroxysulphide **53** was cleanly converted by this reagent to the corresponding ketosulphoxide **54** in almost quantitative yield (equation 25).

$$R^1{-}S{-}R^2 + Br_2 + (Bu_3Sn)_2O \longrightarrow R^1{-}\underset{\underset{O}{\|}}{S}{-}R^2 + 2Bu_3SnBr \qquad (23)$$



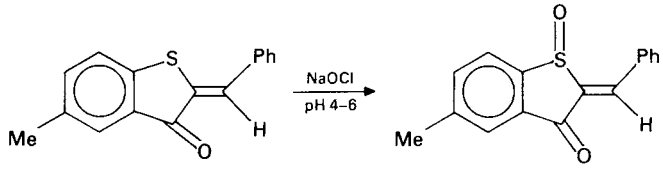
(52) (24)



(53) (54) (25)

The rate of formation of sulphoxides from sulphides and iodine in aqueous solution has been found to be relatively slow. It may be, however, accelerated by certain nucleophiles, such as phthalate ion[91], hydrogen phosphate ion[91] and β-cyclodextrin phosphate ion[92]. The selective oxidation of *N*-acetylmethionine[93] and *N*-acetylmethionine methyl ester[94] to the corresponding *S*-oxides was achieved using iodine in the presence of dicarboxylate ions.

b. Hypochlorites. In the chemical literature there is only a single report on the use of an inorganic hypochlorite (NaOCl) for the selective oxidation of sulphides to sulphoxides. Reamonn and O'Sullivan[95] found that the reaction of 2-benzylidene 2,3-dihydro-5-methylbenzo [*b*] thiophen-3-one gave the corresponding *S*-oxide **55** in a yield over 80% (equation 26). The most stable organic hypochlorite, *t*-butyl hypochlorite, was first used for the oxidation of sulphides in 1964. Skell and Epstein[96] showed that sulphides react with this compound at low temperature to give at first alkoxysulphonium salt **56** which then decomposes to sulphoxides at room temperature (equation 27). Later on, it was found that *t*-butyl hypochlorite in methanol is a very convenient reagent for selective oxidation of cyclic[97], acyclic[98] and β-hydroxy[99] sulphides. Oxidation of cyclic sulphides **57** by this reagent gave in all cases *cis*-sulphoxide **58**[97] (equation 28).

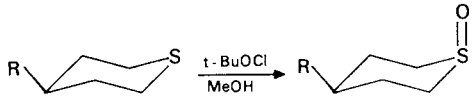


(26)

(55)

$$R^1—S—R^2 + BuOCl \longrightarrow [R^1R^2\dot{S}(OBu\text{-}t)Cl^-] \longrightarrow R^1—\underset{\underset{O}{\|}}{S}—R^2 \qquad (27)$$

(56)



(28)

(57) **(58)**

The reaction of sulphides **59** bearing an ethynyl or a carbomethoxy group α to sulphur with *t*-butyl hypochlorite in methanol or ethanol gives high yields of the corresponding α-alkoxy sulphides (**60**) rather than sulphoxides[98] (equation 29). Oxidation of benzo[b]thiophene with *t*-butyl hypochlorite in *t*-butyl alcohol at 30–40° gave the corresponding 2-chloro-1-benzothiophen-1-oxide **61** in 45% yield[100] (equation 30).

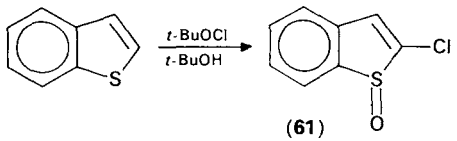
$$Ar—S—CH_2X \xrightarrow[MeOH \text{ or } EtOH]{t\text{-}BuOCl} Ar—S—\underset{\underset{OR}{|}}{CH}—X \qquad (29)$$

(59) **(60)**

(**a**) X = C≡CH

(**b**) X = CO_2Me

R = Me or Et



(61) (30)

c. N-Halo compounds. Oae and coworkers[101] reported that aromatic sulphides gave the corresponding sulphoxides in high yields (Table 6) on treatment with one equivalent of *N*-bromosuccinimide (NBS) in a dioxane–water (7:3) solution at room temperature. However, the reaction of NBS with dialkyl and aryl alkyl sulphides under the same experimental conditions resulted in a C—S bond cleavage and gave no sulphoxides. On the other hand, aryl fluoromethyl sulphides when reacted with one equivalent of NBS in methanol or THF containing a few drops of water afforded cleanly the corresponding α-fluoromethyl sulphoxides[102].

It was reported earlier that even dialkyl sulphides are efficiently oxidized to sulphoxides without a concomitant C—S bond cleavage by NBS or *N*-chlorosuccinimide (NCS) when the reaction is performed in anhydrous methanol at low temperature[103]. *N*-Chloro-Nylon-6, 6 in methanol–water or dioxane–water[104] and *N*-bromo-ε-caprolactam in water or alcohols[105] were also used successfully for oxidation of sulphides.

Sulphides are quickly and efficiently converted into sulphoxides by 1-chlorobenzotriazole (NCBT) in methanol at $-78°$[106]. However, this reagent cannot be used for the oxidation of *t*-butyl sulphide and dibenzyl sulphide since C—S bond cleavage takes place.

In the reaction between chloramine B and di-(2-chloroethyl)sulphide in aqueous solvents simultaneous formation of di(2-chloroethyl)sulphoxide and the corresponding sulphimide, $PhSO_2N{=}S(CH_2CH_2Cl)$, was observed[107]. The amount of sulphoxide increased on increasing the concentration of water in the reaction mixture.

d. Sulphuryl chloride. Traynelis and coworkers[108] showed that the low-temperature reaction of sulphuryl chloride with sulphides leads to the formation of the chlorine–sulphide complexes which are then converted to the corresponding sulphoxides by

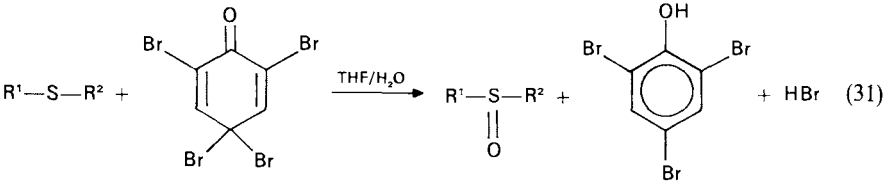
TABLE 6. Oxidation of sulphides to sulphoxides, R^1R^2SO, using *N*-halo compounds

R^1	R^2	*N*-halo compound[a]	Solvent	Yield (%)	Ref.
Me	Me	NCS	MeOH	62	103
Et	Et	NBS	MeOH	65	103
n-Pr	*n*-Pr	NBS	MeOH	76	103
$PhCH_2$	$PhCH_2$	NCS	MeOH	86	103
$PhCH_2$	Ph	NCS	MeOH	82	103
Ph	Ph	NCS	MeOH	93	103
Ph	Ph	NBS	H_2O	75	101
$PhCH_2$	Et	NBS	D/H_2O[b]	85	101
i-Pr	*i*-Pr	NCBT	MeOH	87	106
Ph	Me	NCBT	MeOH	92	106
p-Tol	CH_2F	NBS	$MeOH/H_2O$	85	102
Ph	CH_2F	NBS	$MeOH/H_2O$	83	102
$p\text{-}ClC_6H_4$	CH_2F	NBS	$MeOH/H_2O$	79	102
$p\text{-}O_2NC_6H_4$	CH_2F	NBS	$MeOH/H_2O$	81	102

[a]NCS = *N*-chlorosuccinimide; NBS = *N*-bromosuccinimide; NCTB = 1-chlorobenzotriazole.
[b]D = dioxane.

treatment with ethanol. Yields of sulphoxides are in the range of 60–95%. Hojo and coworkers[109] found that oxidation of aryl alkyl and diaryl sulphides with equivalent amount of sulphuryl chloride in the presence of wet silica gel at room temperature gave sulphoxides in almost quantitative yield without formation of any chlorinated products. With dialkyl and benzyl sulphides, this reaction should be carried out at ice-bath temperature in order to avoïd α-chlorination. Allylic sulphoxides were also prepared by this procedure without chlorination at the allylic position.

e. 2,4,4,6-Tetrabromocyclohexadienone. Sulphides could be oxidized efficiently to the corresponding sulphoxides uncontaminated by sulphones by means of 2,4,4,6-tetrabromocyclohexadienone **62** in dioxane–water or tetrahydrofuran–water solution at room temperature[110] (equation 31).

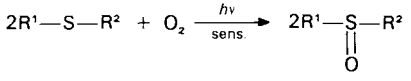


(31)

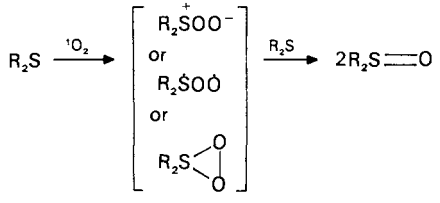
(62)

8. Photochemical oxidation

Photochemical synthesis of sulphoxides was reported for the first time by Foote and Peters[111] in 1971. They found that dialkyl sulphides undergo smoothly dye-photosensitized oxidation to give sulphoxides (equation 32). This oxidation reaction has been postulated to proceed through an intermediate adduct **63**, which could be a zwitterionic peroxide, a diradical or cyclic peroxide, which then reacts with a second molecule of sulphide to give the sulphoxide (equation 33).



(32)

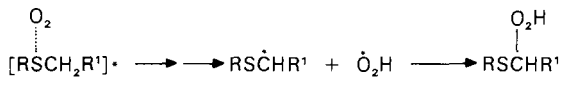


(33)

(63)

Direct photooxidation of aliphatic sulphides in hexane solution and as solids gave sulphoxides in a quantitative yield. Only di-*t*-butyl sulphide was not oxidized under these conditions[112]. The appearance of an intense absorption band ($\lambda_{max} = 300$ nm) on saturating liquid sulphides with oxygen provides evidence for the formation of a charge-transfer (C.T.) complex **64** between oxygen as an electron acceptor and sulphur as an electron donor, as a primary step in this reaction. It was suggested that the excited C.T. complex **64** leads to an α-alkylthioalkyl radical **65** capable of combining with a

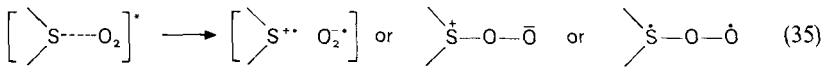
hydroperoxide radical **66** and forming sulphide peroxides **67** (equation 34).



(34)

(64) (65) (66) (67)

Although this mechanism could explain the inertness of di-*t*-butyl sulphide towards oxidation due to the absence of α-hydrogen atoms, it was later ruled out by Tezuka and coworkers[113]. They found that diphenyl sulphoxide was also formed when diphenyl sulphide was photolyzed in the presence of oxygen in methylene chloride or in benzene as a solvent. This implies that α-hydrogen is not necessary for the formation of the sulphoxide. It was proposed that a possible reactive intermediate arising from the excited complex **64** would be either a singlet oxygen, a pair of superoxide anion radical and the cation radical of sulphide **68** or zwitterionic and/or biradical species such as **69** or **70** (equation 35).



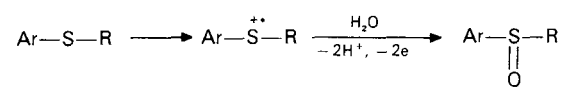
(35)

(64a) (68) (69) (70)

The formation of *cis* and *trans* 3-*t*-butylsulphinylcyclobutanes and *cis* and *trans* 4-*t*-butylsulphinylcyclohexanes in the photochemical oxygen transfer from aza-aromatic *N*-oxides to the corresponding sulphides has been reported by Boyd and coworkers[114]. The results are consistent with a transition state involving oxaziridine intermediate where partial bonding of the oxygen atom to the ring nitrogen atom is maintained during the oxygen transfer process.

9. *Electrochemical oxidation*

An interesting preparation of sulphoxides involves the electrochemical oxidation of sulphides. It was found[115,116] that anodic oxidation of aromatic sulphides leads to the formation of cation radicals **71** which react with water to give the corresponding sulphoxides in yields exceeding in many cases 80% (equation 36). Thus, in acetic acid–water (8:2) solution an electrochemical oxidation of diphenyl sulphide in the presence of perchlorate or chloride anions gave diphenyl sulphoxide almost quantitatively[117,118]. Dibenzothiophene-1-oxide **9** was obtained[119] in 100% yield by oxidation of dibenzo thiophene in the same solvent mixture. Electrooxidation of methyl phenyl sulphide in acetonitrile–water solution in the presence of lithium perchlorate gave methyl phenyl sulphoxide in 74% yield[120]. However, oxidation of phenyl triphenylmethyl sulphide under the same conditions gave products arising from the cleavage of the C—S bond[120]. Oxidation of 1,4-di(methylthio)benzene in methanol–THF (5:1) solution in the presence of tetramethylammonium perchlorate on platinum electrode gave selectively methyl 4-(methylthio)phenyl sulphoxide in 83% yield[121].

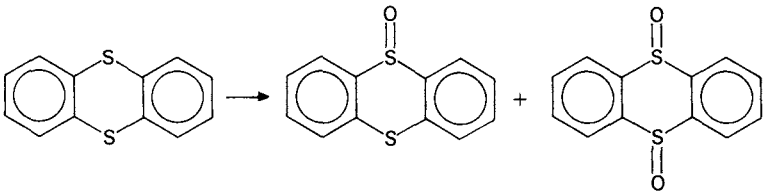


(36)

(71)

Oxidation of thiantrene **72** in acetic acid–water (8:2) mixture in the presence of perchloric acid on silver electrode afforded thiantrene 5-oxide **73** when electrolysis is carried out at 1.5 V or a mixture of *cis* and *trans* thiantrene 5,10-dioxide **74** in 44 and 28%

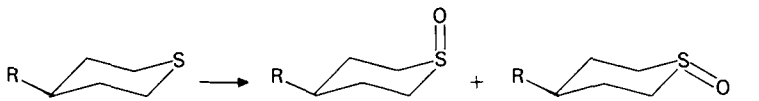
yield, respectively, together with the corresponding sulphone (13%), sulphoxide-sulphone (10%) and disulphone (5%) at 1.6 V[122] (equation 37).



(37)

(72) (73) (74)

Stereoselective conversion of a thiane **57** to the corresponding *trans*-thiane-1-oxide **58** was achieved by bromonium ion mediated electrooxidation while a preferential formation of the *cis*-sulphoxide **58** was observed under acidic electrolysis[123] (equation 38).



(38)

(57) *cis*-(58) *trans*-(58)

$R = p\text{-}ClC_6H_4$

10. Oxidation by miscellaneous reagents

Chromic acid oxidation of sulphides to sulphoxides was reported in 1926[124]. However, this oxidation procedure is not selective and sulphone formation was observed[125]. When pyridine was used as a solvent the sulphone formation was strongly reduced[126].

Oxidation of di-*n*-butyl sulphide with activated manganese dioxide in light petroleum gave di-*n*-butyl sulphoxide exclusively[126]. However, the reaction was very slow at room temperature. This reagent is also suitable for oxidation of diallyl sulphides although, after 76 h, diallyl sulphoxide was isolated in 13% yield only.

Oxidation of dibenzyl and methyl phenyl sulphides by lead tetraacetate in acetic acid was also reported[127].

Selenoxides readily convert dialkyl sulphides into sulphoxides in acetic acid solution being themselves reduced to selenides[128] (equation 39). The yields of sulphoxides are strongly dependent on the steric requirements of the alkyl groups. The reaction does not occur in methanol and benzene. Recently, the photochemical oxygen transfer from selenoxides to sulphides was reported by Tezuka and coworkers[129]. They found that photolysis of a mixture of selenoxide (diphenyl or dibenzoselenophene oxide) with dialkyl and aryl alkyl sulphides in methanol gave the corresponding sulphoxides in good yields (78–97%) along with the deoxygenated aromatic selenide. Sulphones were not formed under any reaction conditions and diphenyl sulphide was unsusceptible to photooxidation with these selenoxides. It was proposed that an excited selenoxide molecule interacts with the sulphide to form a bimolecular intermediate which collapses to a sulphoxide and selenide.

$$R^1\text{—}S\text{—}R^2 + R\text{—}\underset{\underset{O}{\|}}{Se}\text{—}R \longrightarrow R^1\text{—}\underset{\underset{O}{\|}}{S}\text{—}R^2 + R\text{—}Se\text{—}R \qquad (39)$$

Clean and selective oxidation of dibenzyl and dibutyl sulphides to the corresponding

sulphoxides by aromatic seleninic acid in the presence of a strong acid catalyst in acetonitrile solution was reported by Faehl and Kice[130]. The stoichiometry of the reaction is described by equation 40.

$$R_2S + 2/3\ ArSeO_2H \xrightarrow{H^+} R_2S{=}O + 1/3\ ArSe{-}SeAr + 1/3\,H_2O \qquad (40)$$

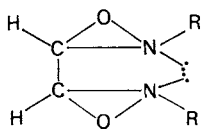
Diphenyl sulphoxide was obtained when a solution of diphenyl sulphide was treated with potassium hydrogen sulphate in ethanol and acetic acid[131].

Dialkyl and alkyl aryl sulphides are converted into the corresponding sulphoxides on oxidation with ozone[132,133]. This method was found to be highly stereoselective. For instance, thianes **57** gave the corresponding *trans*-sulphoxides **58** exclusively[97]. However, the formation of sulphones as by-products is very difficult to avoid. For example, the reaction of di-(2-hydroxyethyl)sulphide with 1.5 equivalent of ozone gave a 1:1 mixture of the corresponding sulphoxide and sulphone[134]. ω-(Chloroalkyl)phenyl sulphoxides were also prepared by ozonolysis of the corresponding sulphides in 55–74% yields[135]. Catalytic oxidation of sulphides by oxygen in the presence of metal catalysts such as metal oxides or metal sulphides was found to occur in the gas phase at higher temperatures and/or higher pressure[2,136]. Generally, the yields of sulphoxides are good, however, the corresponding sulphones are always formed as by-products.

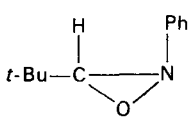
Recently, Davis and coworkers[137] reported the selective oxidation of sulphides under aprotic conditions by 2-arenesulphonyl-3-aryloxaziridines **75**. The reaction (equation 41) is instantaneous at room temperature giving sulphoxides in yields exceeding 80% (equation 41). The structure of oxaziridine is decisive in this reaction. Thus, the stable oxaziridines **76** were found to give the sulphoxides in a very low yield (5–7%) only. Moreover *E*-2-*t*-butyl-3-phenyl oxaziridine **77** failed to undergo any detectable reaction with methyl *p*-tolyl sulphide even on heating for more than 48 h at 60 °C[138]. The rapid oxidation of sulphides by oxaziridine **75** is therefore due to the presence of the 2-arenesulphonyl group which apparently increases the electrophilicity of the oxaziridine oxygen atom. As a result, the first step of the oxidation, namely a nucleophilic attack by the sulphur atom on the oxaziridine oxygen atom, is strongly accelerated[114,138].

$$Ar^2SO_2N(O)CHAr^1 + R^1{-}S{-}R^2 \longrightarrow R^1{-}S(=O){-}R^2 + Ar^2SO_2N{=}CHAr^1 \qquad (41)$$

(**75**)



(**76**)



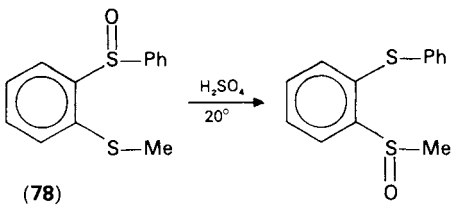
(**77**)

R = *t*-Bu, *c*-Hex

Intermolecular exchange of the sulphinyl oxygen atom between sulphoxide and sulphide (equation 42) may also have preparative value, at least in some special cases. Thermal, non-catalyzed exchange, usually between dimethyl sulphoxide as the oxygen donor and various sulphides, occurs above 160 °C and gives the corresponding sulphoxides in moderate to high yields[139,140]. This reaction is subject to acid catalysis[140]. For example, di-ω-alkanesulphinyl alkanes were prepared in 25–85% yield by the oxidation of the corresponding sulphides with dimethyl sulphoxide in the presence of 2–

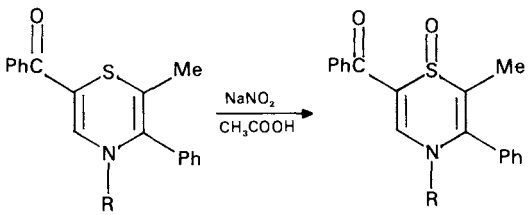
6 mol% of hydrogen chloride[141]. Another example is the intramolecular oxygen exchange reaction in sulphoxide **78** which occurs at room temperature in the presence of sulphuric acid[142] (equation 43). Oxidation of sulphides to sulphoxides by 3-iodosylbenzoic acid is highly selective in the presence of dichlorotris(triphenylphosphine)ruthenium[143]. Selective oxidation of sulphides by iodosobenzene catalyzed by manganese/or iron(III) tetraphenylporphynato complexes was also recently described[144].

$$R^1—\overset{\overset{O}{\|}}{S}—R^2 + R^3_2S \longrightarrow R^3—\overset{\overset{O}{\|}}{S}—R^3 + R^1—S—R^2 \qquad (42)$$



(78) (43)

Interesting oxidation of thiazines **79** with sodium nitrite in acetic acid was found to give the corresponding sulphoxides **80** in 67% yield[145] (equation 44).



(79) (80) (44)

B. Cooxidation of Alkenes and Thiols

Kharasch and coworkers[146] were the first to show that thiols and olefins cooxidize in an atmosphere of oxygen at room temperature to yield substituted 2-sulphinylethanols **81** (equation 45). Later on, it was demonstrated that α-mercapto-substituted hydroperoxides are formed as intermediates. Thus, Oswald[147] found that cooxidation of thiophenol with styrene gave the corresponding β-mercaptohydroperoxide **82** which subsequently underwent rearrangement to 2-phenylsulphinyl-α-phenylethanol **83** (equation 46).

$$R—CH=CH_2 + R'SH \xrightarrow{O_2} R'\overset{\overset{O}{\|}}{S}CH_2\underset{\underset{OH}{|}}{CHR} \qquad (45)$$

(81)

$$PhCH=CH_2 \xrightarrow[O_2]{PhSH} PhCH(OOH)CH_2SPh \longrightarrow PhCH(OH)CH_2\overset{\overset{O}{\|}}{S}Ph \qquad (46)$$

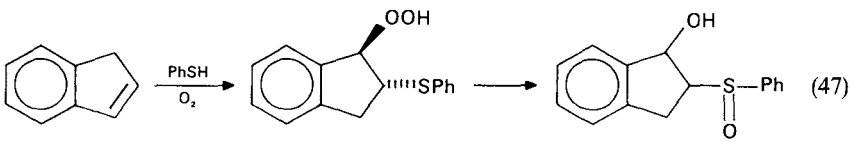
(82) (83)

TABLE 7. Formation of β-hydroxysulphoxides, $RCH(OH)CH_2—SOR^1$, via cooxidation of alkenes, $RCH=CH_2$, and thiols, R^1SH

R	R^1	Conditions	Yield (%)	Ref.
$AcOCH_2$	p-ClC_6H_4	FL[a]	92	151
$AcOCH_2$	Ph	FL[a]	54	151
$HOCH_2$	p-Tol	FL[a]	90	151
$PhOCH_2$	p-Tol	FL[a]	80	151
$ClCH_2$	p-Tol	FL[a]	79	151
$PhCH_2$	p-Tol	FL[a]	83	151
n-Pr	p-Tol	V_2O_5[b]	67	151
n-Pr	p-Tol	$VO(acac)_2$[b]	66	151
Ph	Ph	X[c]$(acac)_2$[b]	23	151
Ph	p-Tol	X[c]	73	150
Ph	$PhCH_2$	X[c]	21	150
Ph	t-Bu	X[c]	36	150
CN	Ph	X[c]	96	150

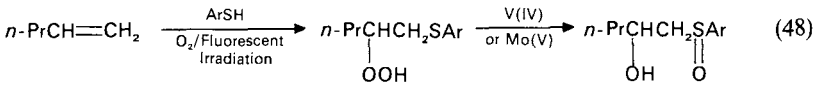
[a]Irradiation with a black-light fluorescent lamp.
[b]As catalyst.
[c]Reaction carried out using sodium chloride or potassium bromide as catalysts.

The cooxidation of thiophenol with indene by air in hydrocarbon solvents provides 1-hydroperoxy-2-phenylthioindane **84** in 77% yield. Subsequent rearrangement afforded a mixture of *trans* and *cis* 2-phenylsulphinyl-1-indanols **85**[148,149] (equation 47).

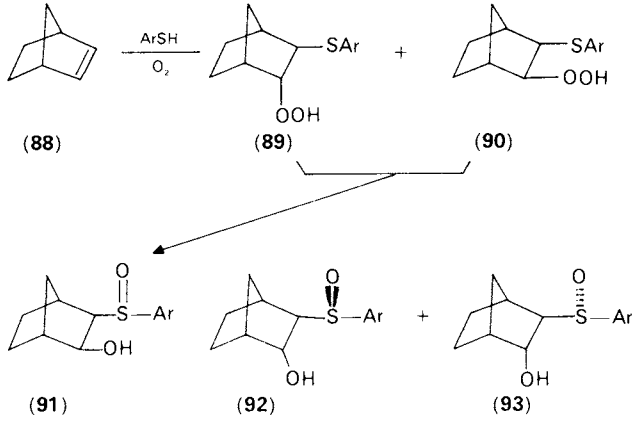


(84) (85) (47)

The cooxidation reaction is strongly accelerated by chloride and bromide ions[150]. Tsuchihashi and coworkers[151] reported that irradiation with a black-light fluorescent lamp is effective and most suitable for the direct cooxidation of arenethiols and α, β-unsaturated nitriles and unsaturated allylic esters affording the corresponding β-hydroxysulphoxides (Table 7). On the other hand, the cooxidation of pentene-1 and aromatic thiols with simultaneous fluorescent irradiation afforded the corresponding β-hydroperoxy sulphides **86** in good yields. It was found that these peroxides can be converted into hydroxysulphoxides **87** by stirring the reaction mixture in the presence of catalytic amounts of vanadium(IV) or molybdenum(V) complexes (equation 48). The stereochemistry of this reaction was a subject of detailed investigations of Beckwith and coworkers[152] who established that norbornene **88** and *p*-toluenethiol interact in the presence of oxygen by a free radical chain mechanism to give a mixture of isomeric



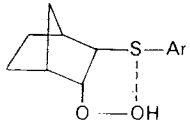
(86) (87) (48)



SCHEME 1

hydroperoxy sulphides **89** and **90** which, on rearrangement, gave the corresponding hydroxy sulphoxides as major products. Of the two possible diastereoisomeric exo, exo hydroxy sulphoxides, only one (**91**) was detected. On the other hand, both of the possible diastereoisomeric endo, exo compounds **92** and **93** were detected, but one was formed in very much higher yield than the other (Scheme 1).

These results may easily be rationalized by assuming that the formation of hydroxy sulphoxides **91**, **92** and **93** from hydroperoxysulphides **89** and **90** is an intramolecular oxidation–reduction reaction proceeding through a five-membered transition state **94**. However, an alternative intermolecular mechanism in which the approach of the oxidant is directed by the hydroperoxy or the hydroxy function in the reductant cannot be excluded.



(**94**)

C. Reaction of Organometallic Compounds with Sulphurous Acid Derivatives

Strecker[153] reported in 1910 that the reaction of thionyl chloride with two equivalents of phenylmagnesium bromide or benzylmagnesium bromide afforded diphenyl or dibenzyl sulphoxides, respectively (equation 49; Table 8). The corresponding sulphides are formed as by-products of this reaction. Recently, other sulphoxides were prepared by this procedure[154,155]. It should be pointed out that this rather simple approach to the synthesis of symmetrical sulphoxides has not yet found wider application.

$$2RMgX + SOCl_2 \longrightarrow R{-}\overset{\overset{O}{\|}}{S}{-}R \qquad (49)$$

Strecker[153] was also the first to show that diethyl sulphite reacts with two equivalents of Grignard reagent in ether solution to yield symmetrical sulphoxides (equation 50). Bert[156]

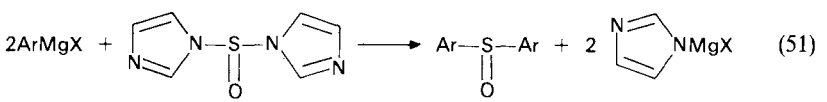
TABLE 8. Formation of sulphoxides, $R_2S{=}O$, from the reaction of Grignard reagents with sulphurous acid derivatives, SOX_2

X	R	Yield (%)	Ref.
Cl	Ph	*a*	153
Cl	$PhCH_2$	*a*	153
Cl	*c*-C_6H_{11}	85	154
Cl	*p*-$MeOC_6H_4$	42	154
OEt	Ph	*a*	153
OEt	$PhCH_2$	*a*	153
OBu-*n*	Ph	40	157
OPh	Ph	74	157
Im[b]	Ph	35	158
Im[b]	*p*-MeC_6H_4	40	158
Im[b]	*p*-$MeOC_6H_4$	60	158
Im[b]	2,4,6-$Me_3C_6H_2$	84	158
Im[b]	*p*-$Me_2NC_6H_4$	50	158

[a]Not given.
[b]*N*-Imidazoyl.

has recommended the use of di-*n*-butyl sulphite as a starting material for the preparation of sulphoxides. However, Gilman and coworkers[157] prepared diphenyl sulphoxide only in 40% yield using this sulphite and found that the reaction of diphenyl sulphite with phenylmagnesium bromide gave diphenyl sulphoxide in 74% yield. Symmetrical diaryl sulphoxides were prepared by Bast and Andersen[158] by the reaction of *N*,*N*-thionyl diimidazole **95** with appropriate Grignard reagents (equation 51).

$$2RMgX + (EtO)_2SO \longrightarrow R{-}\underset{\underset{O}{\|}}{S}{-}R + 2EtOMgX \qquad (50)$$



(**95**)

D. Reaction of Organometallic Compounds with Sulphinic Acid Derivatives

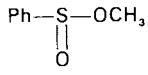
1. Sulphinic acid esters

Gilman and coworkers[157] first reported that the reaction between *p*-toluenesulphinates **96** and Grignard reagents produced sulphoxides in about 60% yield (equation 52).

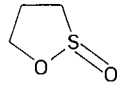
$$p\text{-Tol}{-}\underset{\underset{O}{\|}}{S}{-}OR + R^1MgX \longrightarrow p\text{-Tol}{-}\underset{\underset{O}{\|}}{S}{-}R^1 + ROMgX \qquad (52)$$

(**96**) R = Et, *n*-Bu; R^1 = Ph, $PhCH_2$

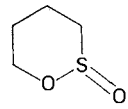
Detailed study of the reaction of methyl benzenesulphinate **97** and two cyclic sulphinates **98** and **99** with a number of Grignard reagents was carried out by Harpp and coworkers[159].



(**97**)



(**98**)



(**99**)

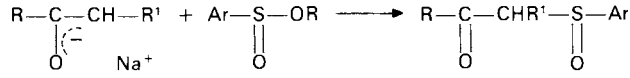
It was found that all the reactions gave the corresponding sulphoxides in moderate to good yields, but the conditions must be very carefully selected, otherwise considerable quantities of sulphides and other impurities are formed. The presence of the impurities can make purification of the reaction products difficult and thus severely limits the synthetic utility of the reaction. It was also indicated that the use of organocopper reagents in place of the Grignard compounds is advantageous and leads to sulphoxides in higher yields.

Reaction of alkyl phenylmethanesulphinates **100** with *n*-butyllithium in tetrahydrofuran at $-80\,^{\circ}C$ afforded the corresponding benzyl *n*-butyl sulphoxide[160] (equation 53). Preparation of optically active sulphoxides by this reaction will be discussed later in this chapter.

$$PhCH_2{-}\overset{\overset{O}{\|}}{S}{-}OR + n\text{-BuLi} \longrightarrow PhCH_2{-}\overset{\overset{O}{\|}}{S}{-}Bu\text{-}n \qquad (53)$$

(**100**) R = Et, *i*-Pr, *n*-Bu

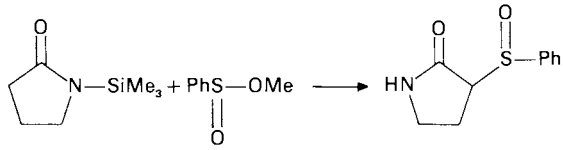
As an extension of the reaction of sulphinates with organometallic compounds, the Claisen-type condensation between ketone enolate anions **101** and arenesulphinates may be considered. It was found[161,162] that this reaction provides an interesting synthetic approach to α-ketosulphoxides **102** (equation 54; Table 9).



(54)

(**101**) (**102**)

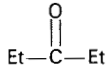
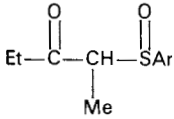
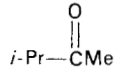
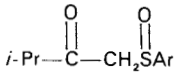
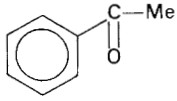
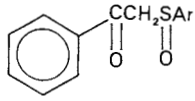
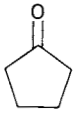
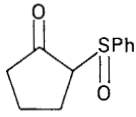
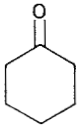
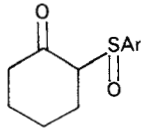
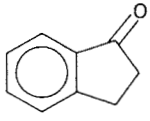
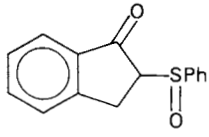
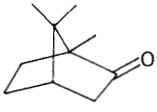
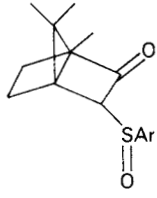
Direct sulphinylation of 1-trimethylsilyl-2-pyrrolidone **103** with methyl benzenesulphinate was found to give the sulphoxide **104** in 67% yield[163] (equation 55). Few sulphinylsulphones **105** were prepared by treatment of arylsulphinates with the carbanions generated from dimethyl[164] or methyl *p*-tolyl sulphones[162] (equation 56). The hydrolytically and thermally unstable α-silylmethyl sulphoxides **106** were prepared[165] in high yield by the reaction of methyl arenesulphinates with the Grignard reagent obtained from halomethyltrialkylsilanes (equation 57). It was found[166] that the sulphoxide **106a** is sufficiently stable for study of its metallation provided care is taken in its preparation and it is stored at temperatures below $0\,^{\circ}C$. It is interesting that trimethylgermylmethyl phenyl sulphoxide **107**, prepared in 78% yield in a similar way to its silicon analogue, was found to be thermally stable[165] (equation 58).

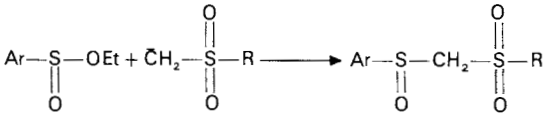


(55)

(**103**) (**104**)

TABLE 9. α-Ketosulphoxides from the reaction of methyl arenesulphinates, ArSOOMe, with carbonyl compounds

Carbonyl compounds	Ar	α-Ketosulphoxide	Yield (%)	Ref.
	Ph		77	162
	p-Tol		65	161
	*p*-Tol		52	161
	Ph		70	162
	p-Tol		57	161
	Ph		74	161
	*p*-Tol		74	162
	Ph		49	161
	Ph		60	162
	Ph		50	162
	p-Tol		67	161



(56)

(**105**)

R = Me or *p*-Tol

$$Ar—\overset{\overset{O}{\|}}{S}—OMe + R_3SiCH_2MgX \longrightarrow Ar—\overset{\overset{O}{\|}}{S}—CH_2SiR_3 \quad (57)$$

(106) (a) Ar = Ph
(b) Ar = *p*-Tol

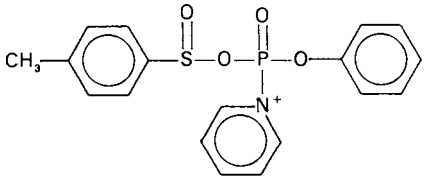
$$Ph—\overset{\overset{O}{\|}}{S}—OMe + Me_3GeCH_2MgCl \longrightarrow Ph—\overset{\overset{O}{\|}}{S}—CH_2GeMe_3 \quad (58)$$

(107)

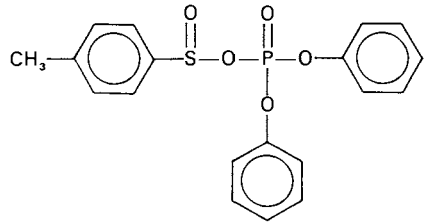
2. Mixed anhydrides of sulphinic acids

Few racemic alkyl *p*-tolyl sulphoxides were prepared in rather low yields (16–40%) by the reaction of Grignard reagents with mixed anhydrides **108**, **109** and compound **110** formed *in situ* from *p*-toluenesulphinic acid and 3-phthalimidoxy-1,2-benzoisothiazole 1,1-dioxide[167] (equation 59). The mixed anhydrides **109** or **110** when reacted with cyclopentene and cyclohexene enamines **111** gave the corresponding α-ketocycloalkyl sulphoxides **112** in low yields (10–41%) along with small amounts of several by-products such as disulphides and thiosulphonates[167] (equation 60).

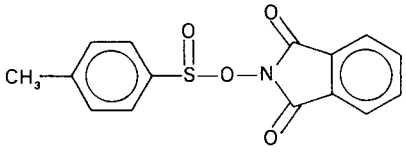
$$\textbf{108} \text{ or } \textbf{109} \text{ or } \textbf{110} + RMgX \longrightarrow p\text{-Tol}—\overset{\overset{O}{\|}}{S}—R \quad (59)$$



(108)



(109)



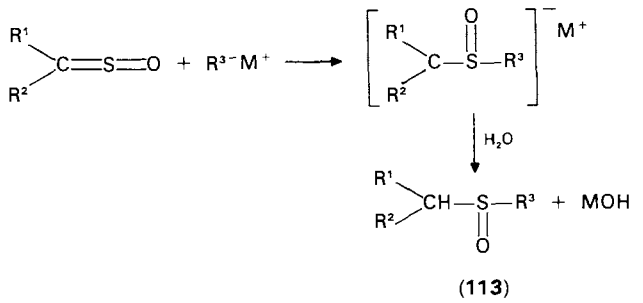
(110)

$$\textbf{109 or 110} + (CH_2)_n\text{(NR}^2\text{)} \longrightarrow p\text{-TolS(O)}\text{-}(CH_2)_n\text{(O)} \quad (60)$$

(111) (a) $n = 0$ (112)
(b) $n = 1$

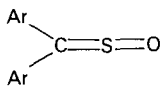
3. Sulphines

Addition of organometallic compounds to sulphines should lead to the formation of sulphoxides **113** (equation 61). Schultz and Schlessinger[168] and Venier and coworkers[169] studied the reaction of diaryl sulphines **114** as well as the sulphines **115** and **116** derived from dibenzotropone and fluorenone, respectively, with alkyl and aryllithium reagents. They found that treatment of **114** and **115** with an equivalent of the lithium reagent in benzene solution at 25° gave the corresponding sulphoxides in 70–80% yields, whereas the reaction of methyllithium with sulphine **116** gave a mixture of various products from which the expected sulphoxides were isolated in a low yield. On the other hand, the reaction of **116** with *n*-butyllithium was more efficient and gave *n*-butyl-(9-fluorenyl)sulphoxide in 65% yield[169]. A series of α-substituted sulphoxides containing functional groups such as CH_2SOMe, CH_2CN and $CH(Et)CONEt_2$ were prepared by the Zwanenburg group from diaromatic sulphines and the appropriate carbanions[170]. Zwanenburg and coworkers[171] have also described the synthesis of dithioacetal *S*-oxides **118a** and α-sulphonyl sulphoxides **118b** which result from the reaction between sulphines **117** and alkyllithium reagents (equation 62). The reaction of thioketene *S*-oxides **119** with phenyllithium is, however, less effective and leads to the formation of α,β-unsaturated sulphoxides **120** in low (20–35%) yields[172] (equation 63). Treatment of sulphine **121** with the Grignard reagents or organolithium compounds derived from sulphones, ketones or nitriles afforded α,β-unsaturated-α-thiomethyl sulphoxides **122**[173] (equation 64).

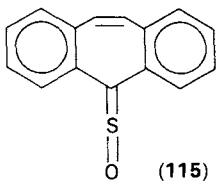


(61)

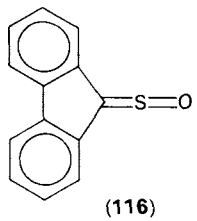
(113)



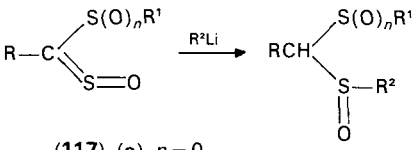
(114)



(115)



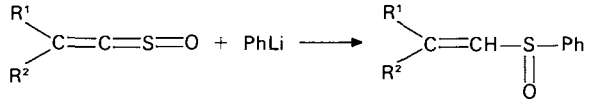
(116)



(62)

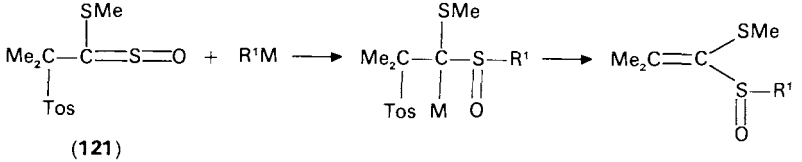
(117) (a) $n = 0$
(b) $n = 2$

(118) (a) $n = 0$
(b) $n = 2$



(63)

(119) (120)

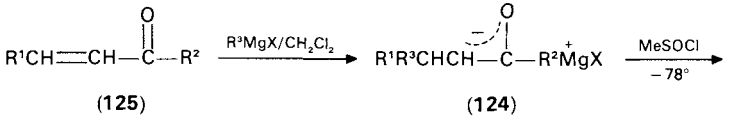


(64)

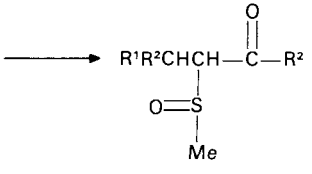
(121) (122)

4. Sulphinyl chloride

Few α-ketosulphoxides **123** were prepared by trapping the enolate anions **124**, which are generated by the Michael addition of Grignard reagents to easily available α, β-unsaturated carbonyl compounds **125**, with methanesulphinyl chloride[174] (equation 65).



(125) (124)



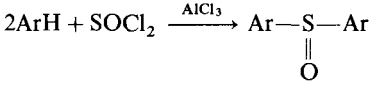
(65)

(123)

E. Reaction of Aromatic Derivatives and Compounds Containing Active Hydrogen with Sulphinyl Chlorides

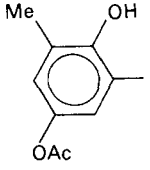
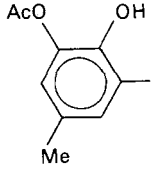
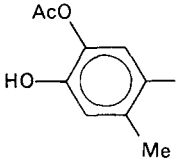
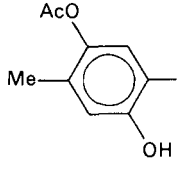
1. Thionyl chloride

In 1887 Colby and McLaughlin[175] found that treatment of benzene with thionyl chloride in the presence of aluminium trichloride produces diphenyl sulphoxide probably via benzenesulphinyl chloride. Later on, some other diaryl sulphoxides were prepared by this procedure[176–180] (equation 66; Table 10). Highly reactive aromatic compounds such as naphthyl ethers react with thionyl chloride in the absence of a catalyst[181].



(66)

TABLE 10. Diaryl sulphoxides, Ar_2SO, from aromatic compounds and thionyl chloride in the presence of $AlCl_3$

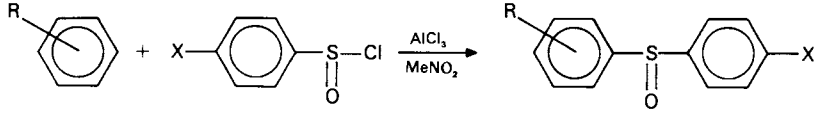
Ar	Yield (%)	Ref.
Ph	50	176
p-ClC_6H_4	*a*	177
p-MeC_6H_4	*a*	178
p-FC_6H_4	75	180
	*a*	179
	*a*	179
	*a*	179
	*a*	179

[a]Not given.

2. *Sulphinyl chlorides*

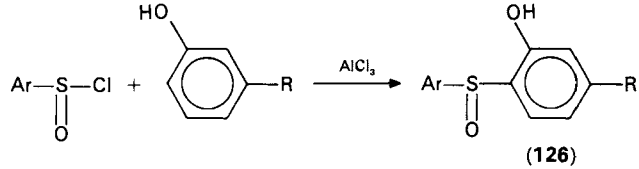
In spite of the fact that phenyl *p*-tolyl sulphoxide had been prepared[182] from benzene and *p*-toluenesulphinyl chloride as long ago as 1926, the preparation of sulphoxides by the reaction of aromatic compounds with sulphinyl chlorides is relatively unexplored. Douglas and Farah[183] reported a 26% yield of methyl phenyl sulphoxide from benzene and methanesulphinyl chloride in the presence of aluminium trichloride. Olah and Nishimura[184] carried out detailed investigation of the aluminium chloride catalyzed arenesulphinylation of benzene and polymethylbenzenes in nitromethane (equation 67). It was found that the reaction is of high selectivity, indicating that the sulphinylating agent is

obviously a very weak electrophile. These observations are in contrast with the previously reported data on sulphonylation and indicate the different nature of both reactions.



(67)

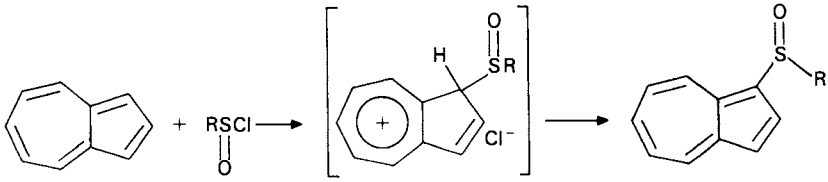
Hydroxy substituted diaryl sulphoxides **126** were prepared by the condensation of *m*-substituted phenols with arenesulphinyl chlorides in the presence of aluminium trichloride[185] (equation 68).



(68)

(**126**)

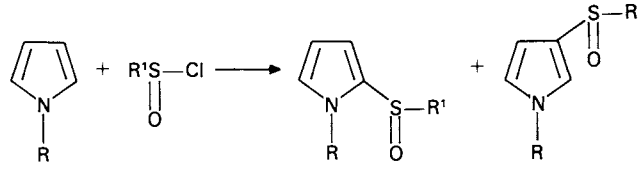
1-Azulyl sulphoxides **127** have also been prepared by a reaction involving a direct electrophilic substitution on the azulene ring by alkane- or arenesulphinyl chlorides[186] (equation 69). Preparation of the methyl and phenyl sulphoxides of 4,6,8-trimethylazulene and 4,6,8-tri-isopropylazulene by this method resulted in fair yields (57–72%). However, the substitution on azulene itself gave only low yields of the corresponding sulphoxides.



(69)

(**127**)

Reaction of pyrrole and *N*-methylpyrrole **128** with arene and alkanesulphinyl chlorides gave the corresponding 2-sulphinylpyrroles **129** as major products only when their interaction with the hydrogen chloride formed was eluded[187] (equation 70). When this precaution was not taken the sulphoxides **129** underwent a remarkably facile acid-promoted rearrangement to the isomeric 3-sulphinylpyrroles **130**. Whereas the formation of 3-substituted **130** could not be prevented when sulphinyl chlorides were used, (*N*-phenylsulphinyl)succinimide **131a** reacted with a variety of pyrroles **128** in dichloromethane at room temperature to give the corresponding 2-sulphinylpyrroles **129** in good yields

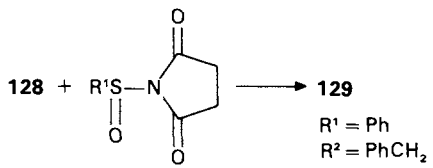


(70)

(**128**) (**a**) R = H
(**b**) R = Me

(**129**) (**130**)

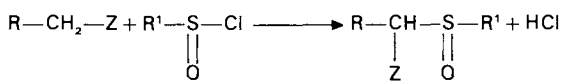
(equation 71). In contrast to the imide **131a**, (*N*-phenylmethanesulphinyl) succinimide **131b** did not react with pyrroles **128** at room temperature. However, at 72 °C in benzene this reaction occurred and 2-phenylmethanesulphinylpyrroles **129** could be isolated in a low yield. Reaction of compounds **132** containing active hydrogen atoms with sulphinyl chlorides may also be considered as a method for the synthesis of α-substituted sulphoxides **133** (equation 72).



(71)

(131) (**a**) $R^1 = Ph$

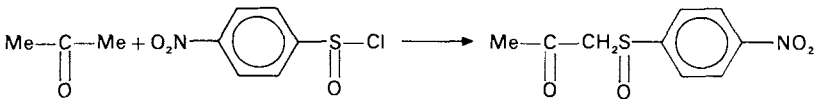
(**b**) $R^1 = PhCH_2$



(72)

(132) **(133)**

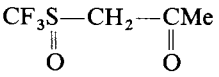
Up to now this possibility was applied for the preparation of α-ketosulphoxides. The first formation of α-ketosulphoxides in the reaction between a ketone and sulphinyl chloride was reported by Oae and Ikura[188] in 1966. They prepared *p*-nitrobenzenesulphinyl chloride and identified it by means of its reaction product with acetone which had the analytical composition of α-sulphinylacetone **134** (equation 73).



(73)

(134)

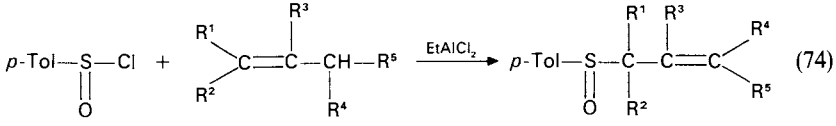
It was reported[189] later that *o*-nitrobenzenesulphinyl chloride reacts with acetone, acetophenone and dimedone giving the corresponding α-sulphinylketones in about 80% yield. Unstable trifluoromethylsulphinylacetone **135** was generated *in situ* in the reaction between trifluoromethanesulphinyl chloride and acetone which served both as reactant and solvent[190].



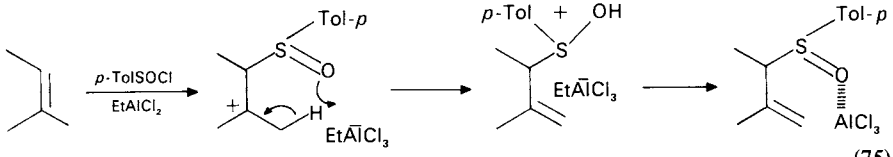
(135)

The ethylaluminium dichloride-catalyzed reaction of *p*-toluenesulphinyl chloride with alkenes **136** successfully applied[191] for the synthesis of allylic sulphoxides **137** (equation 74) may also be regarded formally as a reaction of sulphinyl chlorides with compounds containing active hydrogen atom. Treatment of an alkene **136** with one equivalent each of ethylaluminium dichloride and *p*-toluenesulphinyl chloride at room temperature gave the corresponding **137**. This reaction is very general and proceeds in

good yields with a variety of alkenes. Mechanistically, it may formally be classified as an ene reaction which proceeds through the intermediates shown in equation 75. The proposed mechanism was supported by the fact that α-pinene, which easily undergoes concerted ene reactions, gave a complex mixture of products arising from rearrangement of the intermediate carbocation.

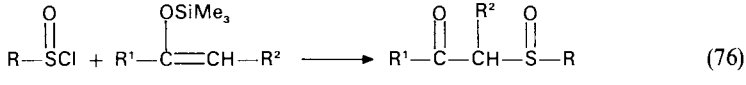


(136) (137) (74)



(75)

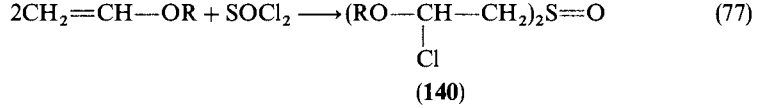
The addition of sulphinyl chlorides to trimethylsilyl enol ether **138** affording α-ketosulphoxides **139** (equation 76) represents an extension of the reaction of sulphinyl chlorides with ketones. This reaction has attracted attention only recently. Sergeev and coworkers[192] reported that treatment of sulphinyl chlorides with acyclic enol ethers afforded α-ketosulphoxides **139** in good to excellent yields. Meanwell and Johnson[193] observed that in the case of cyclic enol ethers the corresponding sulphoxides were formed only in very low yields. They found, however, that the introduction of an equivalent amount of a Lewis acid into the reaction mixture markedly promotes the desired reaction, whereas the use of catalytic amounts of a Lewis acid led to a substantial reduction in the yield. This is most probably due to the formation of a complex between the α-ketosulphoxide and the Lewis acid.



(138) (139) (76)

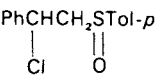
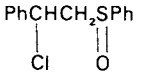
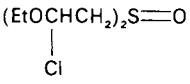
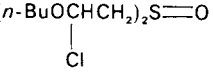
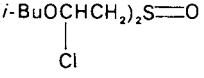
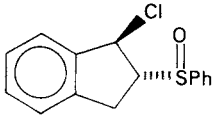
F. Addition of Sulphinyl Chlorides to Unsaturated Compounds

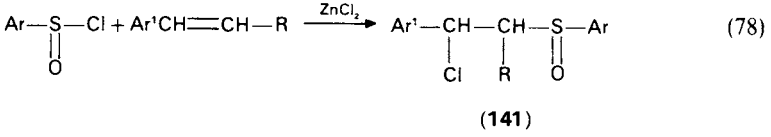
Thionyl chloride and enol ethers react to give high yields (Table 11) of di(β-chloro-β-alkoxyethyl)sulphoxides[194] **140** (equation 77). *p*-Toluenesulphinyl chloride and benzenesulphinyl chloride react with a variety of conjugated aromatic olefins in the presence of zinc chloride to give 1-chloro-1-phenyl-2-arenesulphinylethanes **141** in moderate to good yields[195] (equation 78; Table 11). The addition to indene occurs with anti stereochemistry to give *trans*-1-chloro-2-phenylsulphinylindene[195]. Benzenesulphinyl chloride reacts also with non-conjugated olefins under high pressure (2.5 kbar) to give the corresponding sulphinylethanes in very high yields[196].



(140) (77)

TABLE 11. β-Chlorosulphoxides from sulphinyl chlorides, RSOCl, and unsaturated compounds, $R^1CH{=}CH_2$

R	R^1	Sulphoxide	Yield (%)	Ref.
p-Tol	Ph		40	195
Ph	Ph		80	195
Cl	EtO		97	194
Cl	*n*-BuO		80	194
Cl	*i*-BuO		90	194
Ph	Indene		37	195

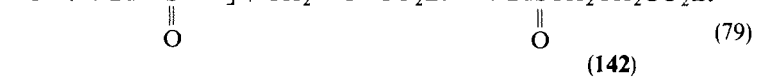


(78)

(141)

G. Addition of Sulphenic Acids to Unsaturated Compounds

t-Butanesulphenic acid generated thermally from di-*t*-butyl sulphoxide adds readily at room temperature to ethyl acrylate giving an adduct which was identified as ethyl β-(*t*-butanesulphinyl)propionate[197] **142** (equation 79). Addition of *t*-butanesulphenic acid to methyl propiolate gave bis-adduct **143** by a double addition–elimination reaction[197]. Block and O'Connor[198] showed that pyrolysis of alkane thiosulphinates affords alkanesulphenic acids which can be trapped by alkynes leading to α,β-unsaturated sulphoxides **144** in moderate to high yields (equation 80; Table 12).



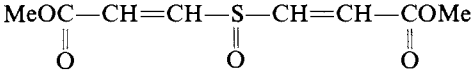
(79)

(142)

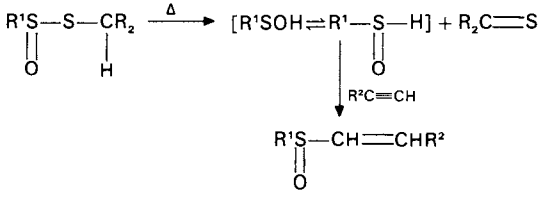
TABLE 12. Synthesis of *E*-α,β-unsaturated sulphoxides, $R^1S(O)CH{=}CHR^2$, by addition of sulphenic acids, R^1SOH, to alkynes, $R^2C{\equiv}CH$

Sulphenic acid precursor	R^1	R^2	Yield (%)	Ref.
MeS(O)SMe	Me	CO_2Me	65	198
EtS(O)SEt	Et	CO_2Me	76	198
i-PrS(O)SMe	*i*-Pr	CO_2Me	49	198
t-BuS(O)SBu-*t*	*t*-Bu	CO_2Me	56	198
EtS(O)SEt	Et	Ph	91	198
EtS(O)SEt	Et	C_5H_{11}-*n*	33	198
PhS(O)N=CHPh	Ph	CO_2Me	70	199
m-$XC_6H_4S(O)N{=}CHC_6H_4X$-*p*[a]	*m*-$NO_2C_6H_4$	CO_2Me	82	199
m-$XC_6H_4S(O)N{=}CHMe$[a]	*m*-$NO_2C_6H_4$	CO_2Me	72	199
$PhS(O)CH_2CH_2CN$	Ph	C_6H_{13}-*n*	94	200
$MeS(O)CH_2CH_2CN$	Me	C_6H_{13}-*n*	86	200
$PhS(O)CH_2CH_2CN$	Ph	CH_2OH	82	200
$PhS(O)CH_2CH_2CN$	Ph	CH_2SMe	52	200
$MeS(O)CH_2CH_2CN$	Me	CH_2SMe	50	200
$PhS(O)CH_2CH_2CN$	Ph	CH_2Br	36	200

[a] $X = NO_2$.



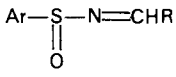
(143)



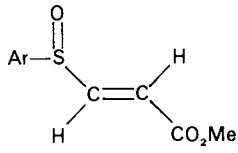
(80)

(144) $R^2 = CO_2Me$, Ph, n-C_5H_{11}

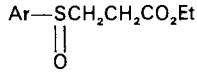
Davis and coworkers[199] found another convenient way to generate arenesulphenic acids by the thermolysis of *N*-alkylidenearenesulphinamides **145**. On heating **145** for 24 h at 80–115° in methyl propiolate or ethyl acrylate it afforded methyl *trans*-arenesulphinylacrylates **146** and ethyl arenesulphinylpropionate **147**, respectively, in high yields.



(145)



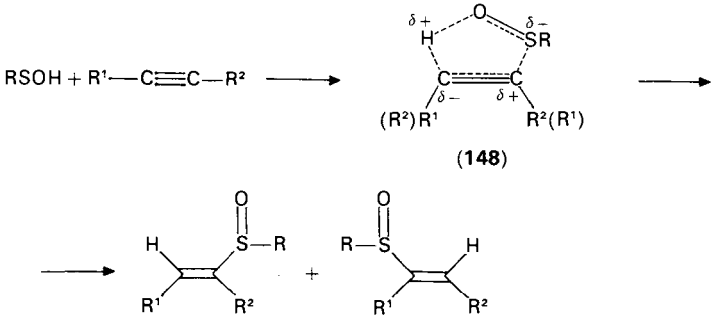
(146)



(147)

Jones and coworkers[200] found that a variety of sulphenic acids may be generated by thermolysis of the readily available β-cyanosulphoxides (equation 81) and observed their highly regiospecific addition also to non-conjugated alkynes (Table 12). As expected for a pericyclic mechanism, the reaction afforded the product of a stereospecific *cis*-addition. However, the regioselectivity of the addition suggests that the partial carbon–sulphur bond in the transition state **148** is polarized in such a way that the carbon atom has some cationic character (equation 82).

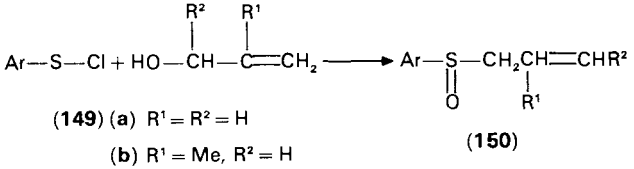
$$R{-}\underset{\underset{O}{\|}}{S}CH_2\underset{\underset{H}{|}}{C}HCN \longrightarrow RSOH + CH_2{=}CHCN \tag{81}$$



(82)

H. Rearrangement of Sulphenic Acid Esters

The spontaneous rearrangement of allyl *p*-toluenesulphenates to allyl sulphoxides was independently recorded by Mislow and coworkers and Braverman and Stabinsky. Mislow and colleagues[201] have demonstrated that simple allyl alcohols such as **149**, on conversion to the corresponding lithium alkoxides followed by treatment with arenesulphenyl chlorides, may be smoothly transformed at room temperature via the sulphenate esters into allylic sulphoxides **150** (equation 83). Braverman and Stabinsky[202] have found that when the more reactive trichloromethanesulphenyl chloride is treated with allyl alcohol and pyridine in ether at −70°, it affords trichloromethyl allyl sulphoxide and not allyl trichloromethanesulphenate as reported by Sosnovski[203] (equation 84).



(**149**) (**a**) $R^1 = R^2 = H$
(**b**) $R^1 = Me$, $R^2 = H$

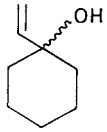
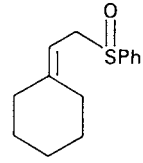
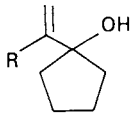
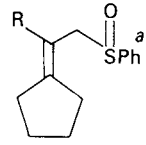
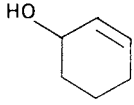
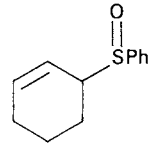
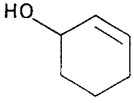
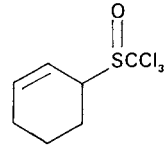
(**150**)

(83)

$$Cl_3C{-}SCl + CH_2{=}CH{-}CH_2OH \xrightarrow[-70°]{C_5H_5N} Cl_3C{-}\underset{\underset{O}{\|}}{S}CH_2{-}CH{=}CH_2 \tag{84}$$

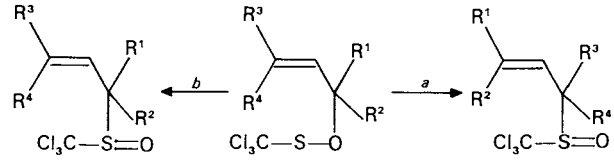
The allyl sulphenate–allyl sulphoxide rearrangement is a general reaction and is applicable to structurally diverse allyl alcohols[204,205] (Table 13). Mechanistically, it represents a typical example of a [2,3]-sigmatropic rearrangement as shown by the detailed investigations of Mislow and Braverman and their coworkers.

TABLE 13. Synthesis of allyl sulphoxides from sulphenyl chlorides, RSCl, and allyl alcohols

R	Alcohol	Sulphoxide	Yield (%)	Ref.
Ph			80	204
Ph			80	204
Ph			80	204
Cl_3C			*b*	205
Me	$CH_2{=}CHCH_2OH$	$MeSCH_2CH{=}CH_2$ (O)	*b*	205
Cl_3C	$CH_2{=}CHCH_2OH$	$Cl_3CSCH_2CH{=}CH_2$ (O)		202

[a]R = H or Me.
[b]Not given.

Braverman and Grendi[206] have shown that, depending on the type of substitution, allylic trichloromethanesulphenates undergo rearrangement to allylic trichloromethyl sulphoxides by one of two different pathways (equation 85). Rearrangement according to route *a* has been observed with allyl, crotyl and α,α-dimethylallyl sulphenates. It occurs



(85)

spontaneously at low temperature and it is reversible and believed to proceed by a concerted intramolecular mechanism. On the other hand, the corresponding cinnamyl and γ,γ-dimethylallyl esters have been found to form the sulphoxides via route *b*. This process takes place only at higher temperatures and could be explained by a dissociation–recombination mechanism. The conversion of benzyl *p*-toluenesulphenate to benzyl *p*-tolyl sulphoxide, which requires temperature above 110 °C, may also be considered to take place by such a mechanism[201].

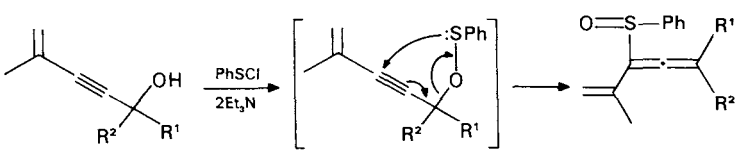
Rearrangement of acetylenic sulphenates to the allenic sulphoxides **151** was discovered when the synthesis of propargylic ester of trichloromethanesulphenic acid **152** was attempted[207] (equation 86). This reaction is of general scope and gives very good yields of allenic sulphoxides (Table 14) from structurally diverse alcohols and various sulphenyl chlorides[208–210]. Reaction of alkynols **153** with benzenesulphenyl chloride in the presence of triethylamine afforded nearly quantitative yields of the corresponding allenic sulphoxides **154** via the initially formed sulphenate esters **155** which undergo a [2, 3]-sigmatropic propargylic rearrangement[211] (equation 87).

$$Cl_3C{-}S{-}Cl + HOCH_2{-}C{\equiv}CH \xrightarrow{C_5H_5N} [Cl_3C{-}SOCH_2C{\equiv}CH] \quad (86)$$

(**152**)

$$Cl_3C{-}\underset{\underset{O}{\|}}{S}{-}CH{=}C{=}CH_2$$

(**151**)

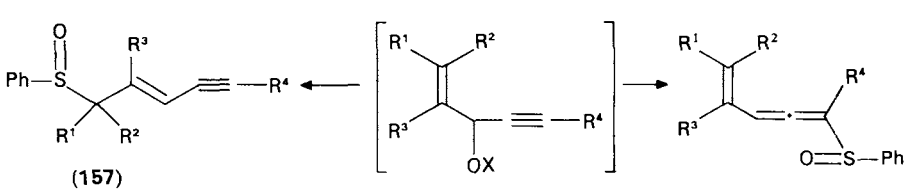


(87)

(**153**) (**155**) (**154**)

(**a**) $R^1 = R^2 = H$
(**b**) $R^1 = H$; $R^2 = Me$
(**c**) $R^1 = R^2 = Me$

Reaction of alkynols **156** with benzenesulphenyl chloride afforded either the vinylacetylene sulphoxides **157** or the allene sulphoxides **158** depending upon the substitution pattern of alkynols **156**. Vinylacetylene sulphoxides **157** result from a [2, 3]-allylic rearrangement of the sulphenate ester **159** (equation 88). In the case of the cyclic

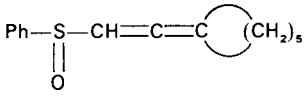
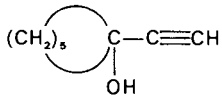
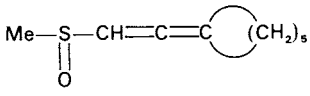
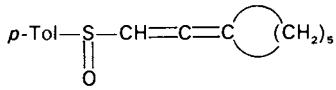
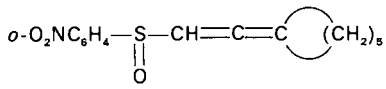
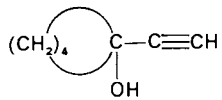
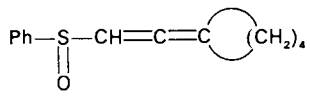
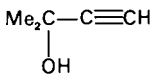
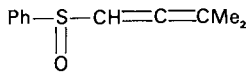
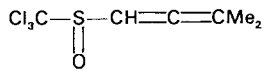
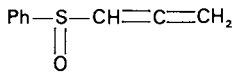
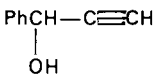
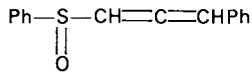
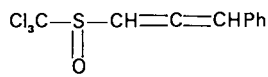
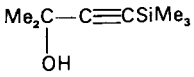
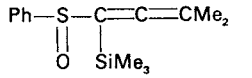


(**157**)

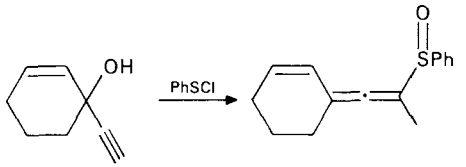
(**156**) X = H (**158**)

(**159**) X = SPh (88)

TABLE 14. Allenic sulphoxides from propargylic alcohols and sulphenyl chlorides, RSCl

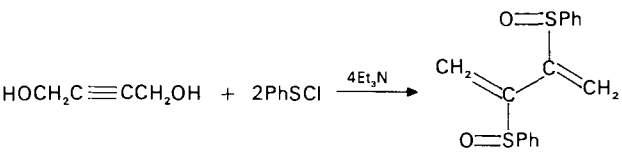
R	Alcohol	Sulphoxide	Yield (%)	Ref.
Ph			75	208
Me			30	208
p-Tol			73	208
o-$O_2NC_6H_4$			48.5	208
Ph			52	208
Ph			48	208
Cl_3C			75	207
Ph	$HOCH_2C{\equiv}CH$		50	208
Ph			50	207
Cl_3C			70	207
Ph			56	211

unsaturated alcohol **160** the vinylallene sulphoxide **161** was formed[210] as the only product (equation 89). The reaction of acetylenic diol **162** with two equivalents of benzenesulphenyl chloride afforded the corresponding unsaturated disulphoxide **163** in 76% yield[212] (equation 90).



(89)

(**160**) (**161**)

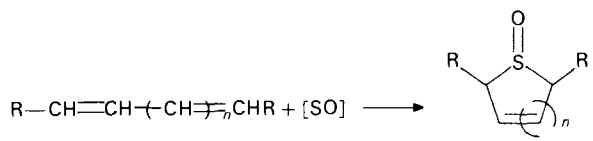


(90)

(**162**) (**163**)

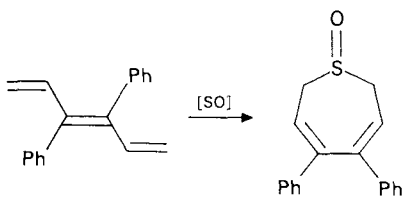
I. Cycloaddition of Sulphur Monoxide and Sulphines to Unsaturated Compounds

Dodson and Sauers[213] were the first to show that sulphur monoxide generated *in situ* by thermolysis of thiirane *S*-oxide could be trapped by dienes or trienes in the form of 2,5-dihydrothiophene *S*-oxide **164a** or 2,7-dihydrothiepin *S*-oxide **164b** (equation 91). For the reactions carried out in boiling toluene yields of the cyclic sulphoxides were usually in the range between 20 and 40%; equimolar amounts of isoprene and thiirane *S*-oxide in refluxing toluene gave 3-methyl-3 thiolene *S*-oxide in 83% yield[214]. A low yield (7%) of 4,5-diphenyl-2,7-dihydrothiepin-1-oxide **165** was observed when 3,4-diphenyl-1,3,5-hexatriene **166** was reacted with sulphur monoxide[215] (equation 92). The thermal reaction of cyclooctatetraene and thiirane *S*-oxide in boiling xylene resulted in the formation (30% yield) of the cycloaddition product **167** to which the anti configuration was assigned[216].



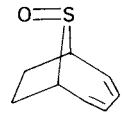
(91)

(**164**) (**a**) $n = 1$
(**b**) $n = 2$



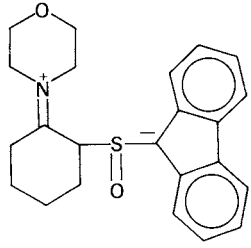
(92)

(**166**) (**165**)



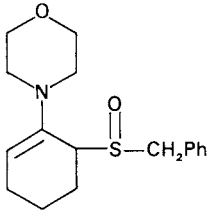
(**167**)

Due to the presence of a heterocumulene unit, sulphines may be considered as a group of compounds which are able to undergo cycloaddition reactions. Reaction of sulphines with enamines and phosphorus ylides reported by Sheppard[217] and Trippett[218] and their coworkers may be considered formally as an example of [2 + 2] cycloaddition. In fact, Sheppard and Dickman[217] obtained a 1:1 adduct from thiofluorenone *S*-oxide and 1-morpholinocyclohexene to which they assigned the dipolar sulphoxide structure **168**.

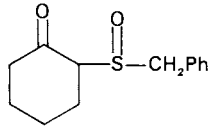


(**168**)

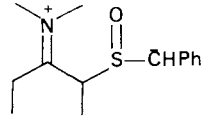
Phenylsulphine prepared *in situ* from phenylmethanesulphinyl chloride and triethylamine reacted with 1-morpholinocyclohexene to form the addition product **169** having the enamine structure[218]. A similar experiment with phenylsulphine and 2-pyrrolidinocyclohexene gave only 2-phenylmethanesulphinyl cyclohexanone **170**. The latter is most probably formed by hydrolysis of the corresponding enamine sulphoxide upon isolation. The reaction of sulphines with enamines is apparently a stepwise process involving the transient formation of the dipolar intermediate **171** which is stabilized by proton transfer, giving the enamine sulphoxide.



(**169**)



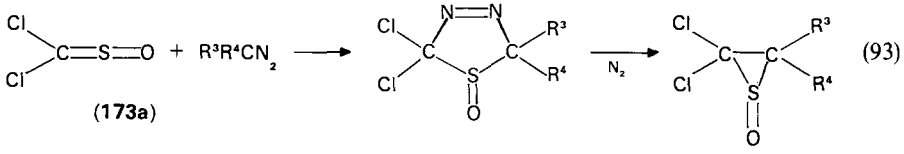
(**170**)



(**171**)

The possibility of a [2 + 3] cycloaddition of sulphines was first suggested by Zwanenburg and coworkers[219]. They obtained relatively stable dichloroepisulphoxide **172** from the reaction of dichlorosulphine **173a** with diazo compounds and proposed that it arises from the initially formed cycloaddition product **174** by nitrogen elimination (equation 93). The stability of the thiadiazoline *S*-oxides **174** strongly depends upon the nature of all substituents. Thus, the cycloaddition reaction of aromatic sulphines such as thiobenzophenone *S*-oxide and thiofluorenone *S*-oxide with diazopropane leads to thiadiazoline *S*-oxides in high yield. Diazomethane reacts more sluggishly and in most cases a complex mixture of various products was formed. Only thiofluorenone *S*-oxide

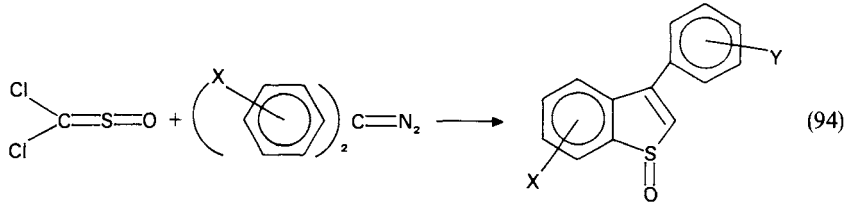
gave the expected cycloadduct in 50% yield[220,221].



(93)

(173a) (174) (172)

Treatment of dichlorosulphine **173a** with diaryldiazomethanes **175** gives derivatives of 2-chlorobenzo[*b*]thiophene *S*-oxide[222] **176** (equation 94). It was proposed that the reaction is initiated by a [2 + 3] dipolar cycloaddition reaction of dichlorosulphine **173a** affording thiadiazoline *S*-oxides **174a** which then lose nitrogen to form episulphoxides **177**. Spontaneous cyclization of the latter leads to the chlorosulphoxides **176** (equation 95). Diarylsulphines **173b**, when dissolved in aprotic solvents such as pentane or ether and treated with aryldiazomethanes **178**, gave smoothly the episulphoxides **179** in good yields[223] (equation 96). It was suggested that the reaction is a two-step process involving the formation of the diazonium intermediate **180** which undergoes cyclization by intramolecular nucleophilic attack, nitrogen being a leaving group. However, the formation of **179** via the thiadiazoline *S*-oxide intermediate cannot be excluded (equation 97).

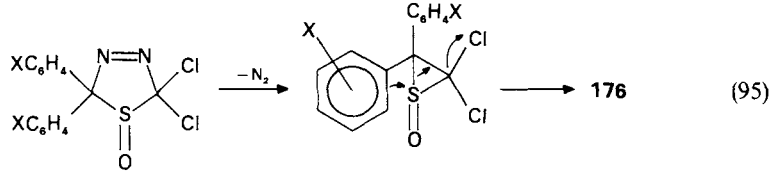


(94)

(173a) (175) (176)

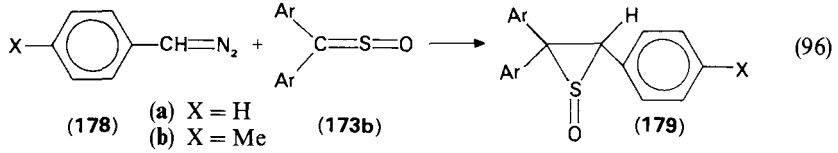
(**a**) X = H
(**b**) X = 4-Me
(**c**) X = 4-Cl
(**d**) X = 4-OMe
(**e**) X = 3-OMe

X	Y
(**a**) H	H
(**b**) 6-Me	4-Me
(**c**) 6-Cl	4-Cl
(**e**) 5-OMe	3-OMe



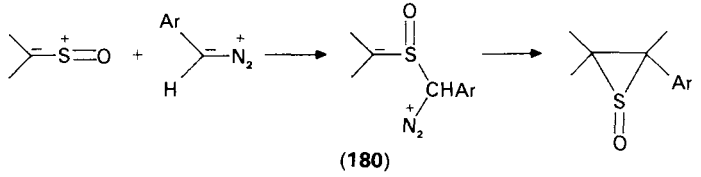
(95)

(174a) (177)



(96)

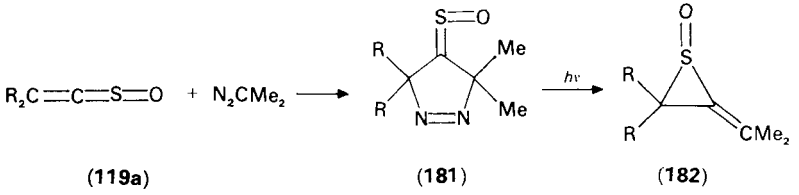
(178) (**a**) X = H (**b**) X = Me (173b) (179)



(97)

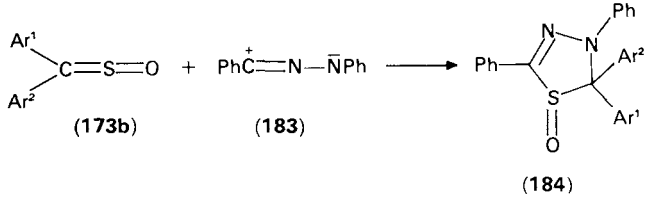
(180)

Thioketene *S*-oxides **119a** react smoothly with diazopropane to give good to excellent yields of a 1:1 adduct **181** resulting from the [2 + 3] cycloaddition across the C=C bond of the heterocumulene[224]. Photolysis of this adduct in benzene or carbon tetrachloride results in rapid elimination of nitrogen and formation of episulphoxide **182** (equation 98). Heterocyclic compounds containing the sulphoxide function have also been prepared by [1 + 3] dipolar cycloaddition of sulphines to nitrilimines. Thus, diaryl sulphines **173b**, upon heating for two hours in boiling benzene with diphenylnitrilimine **183** [generated *in situ* by the action of triethylamine on *N*-(α-chlorobenzylidene)-*N'*-phenyl hydrazine], gave 1,3,4-thiadiazoline *S*-oxides **184** in 58–92% yields[225] (equation 99). The reaction of the pure geometrical isomers of unsymmetrical diarylsulphines **173b** ($Ar^1 \neq Ar^2$) with **183** in refluxing benzene gave either the same single diastereoisomeric adduct or a mixture of both diastereoisomers. However, it was demonstrated that the cycloaddition is completely stereospecific and that the steric integrity is lost by a ring opening–ring closure of the cycloaddition product **184**.



(98)

(119a) (181) (182)

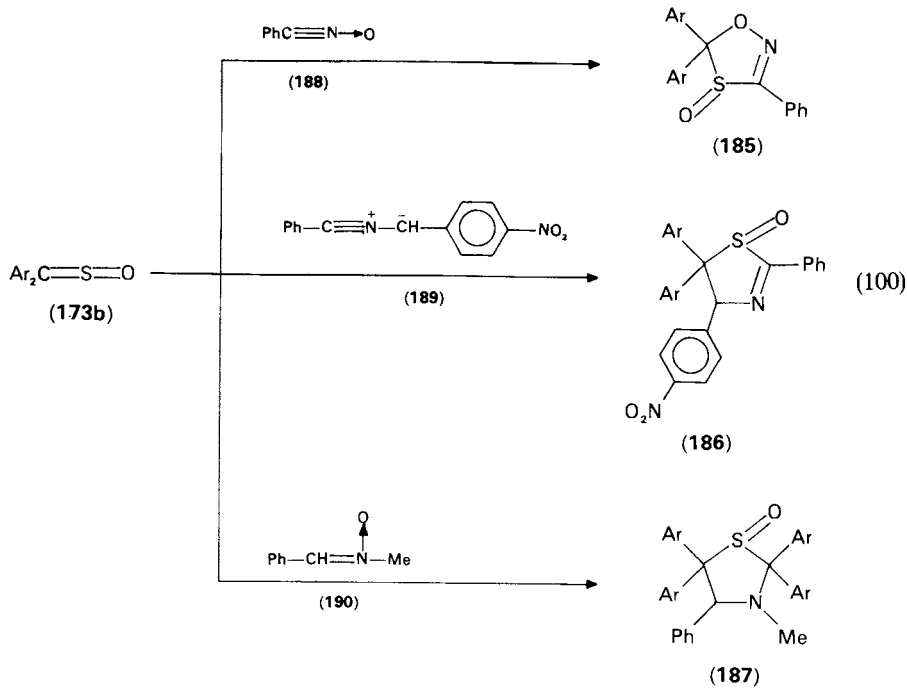


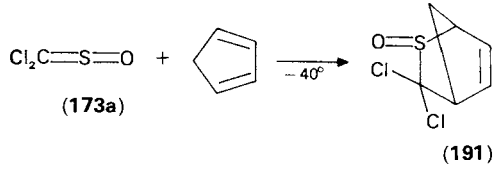
(99)

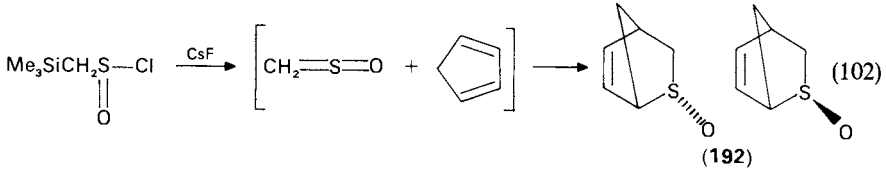
(173b) (183) (184)

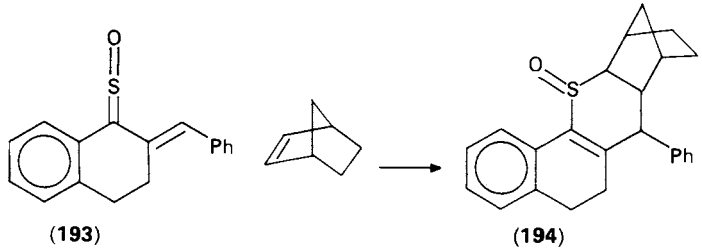
Heterocyclic sulphoxides of general structure **185**, **186** and **187** have been prepared by cycloaddition of diarylsulphines **173b** to nitrile oxides **188**[226], nitrile ylides **189**[227] and nitrones **190**[228], respectively (equation 100).

Sulphines may react as dienophiles with 1,3-dienes with the formation of cyclic sulphoxides. Unstable 2,2-dichloro-5,6-dihydro-2*H*-thiin-1-oxide **191** was formed in an exothermic reaction between **173a** and cyclopentadiene at −40 °C[219] (equation 101). The simplest, parent sulphine, $CH_2=S=O$, prepared *in situ* by treatment of α-trimethylsilylmethanesulphinyl chloride with cesium fluoride, reacts with cyclopentadiene to give bicyclic, unsaturated sulphoxide **192** as a mixture of two diastereoisomers in a 9:1 ratio[229] (equation 102). On the other hand, α,β-unsaturated sulphine **193** (generated by thermolysis of 2-benzylidene-1-thiotetralone dimer *S*-oxide) in boiling toluene behaves as a 1,3-diene and was trapped by norborene forming sulphoxide **194** in 78% yield[230] (equation 103).


PhC≡N→O
(188)
(185)
Ph—C≡N—CH—NO2
(189)
(186)
Ar2C=S=O
(173b)
(100)
Ph—CH=N—Me
(190)
(187)


Cl2C=S=O
(173a)
−40°
(191)
(101)


Me3SiCH2S—Cl
CsF
CH2=S=O
(192)
(102)


Ph
(193)
(194)
(103)

J. Hydrolysis of Sulphimines

Hydrolysis of sulphimines has rather limited application as a route to racemic sulphoxides. Hydrolysis of *S,S*-diethyl-*p*-toluenesulphonylsulphilimine **195** gave the corresponding sulphonamide and an oily substance believed to be diethyl sulphoxide because of a facile formation of diethyl sulphide upon reduction[231] (equation 104). Hydrolysis of unsubstituted dimethylsulphilimine and diethylsulphilimine is very rapid and gives the corresponding sulphoxides in high yields[232]. According to Oae and coworkers[233] alkaline hydrolysis of alkyl *p*-tolyl *N*-tosylsulphilimines **196** results in the predominant formation of α-alkoxyalkyl sulphides **197** (equation 105).

$$p\text{-TolSO}_2\text{N=SEt}_2 \xrightarrow{H_2O} p\text{-TolSO}_2\text{NH}_2 + \text{Et}_2\text{S=O} \qquad (104)$$

(195)

$$p\text{-Tol—S(=NTos)—CHR}_2 \xrightarrow[ROH]{OH^-} p\text{-Tol—S(OR}^1\text{)—CR}_2 + p\text{-Tol—S(=O)—CHR}_2 \qquad (105)$$

(196) **(197)**

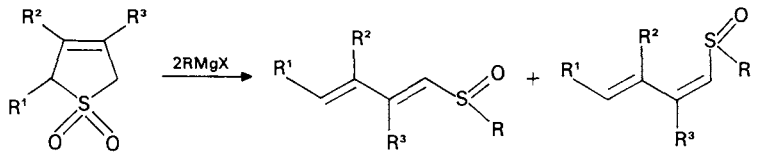
K. From Organic Sulphur Compounds of Higher Oxidation State

An interesting synthesis of sulphoxides involving the reaction of Grignard reagents with sulphonyl chlorides or ethyl chlorosulphonate was reported by Hepwort and Chapham[234] in 1921. They found that treatment of benzenesulphonyl chloride with an excess of phenylmagnesium bromide gave diphenyl sulphoxide as the major reaction product (equation 106). The reaction of ethyl chlorosulphate with PhMgBr, EtMgBr and $PhCH_2MgCl$ afforded the corresponding symmetrical sulphoxides in substantial quantities[234] (equation 107). The reaction of arenesulphonyl chlorides with trialkylaluminium or alkylaluminium chloride was found to give alkyl aryl sulphoxides together with the corresponding sulphides[235] (equation 108). It was reported that sulpholene **198** reacts with two moles of alkyl or arylmagnesium halides to produce isomeric butadienylic sulphoxides **199** in which the *Z*-configuration around the double bond α,β to sulphur predominated[236] (equation 109). Also bicyclic sulphones **200** afforded 1,4-dienylic sulphoxides **201** in 35–58% yield[236] upon treatment with two moles of phenylmagnesium bromide (equation 110). The formation of the dienylic sulphoxides **199** and **201** may be explained by the assumption that the reaction takes place in two steps. The first step is the formation of the sulphinate salt **202** through ring opening of an anion **203**, and the second involving the reaction with another Grignard molecule to form sulphoxides **199** or **201** (equation 111). The latter reaction is similar to that of sulphinic esters with Grignard reagents.

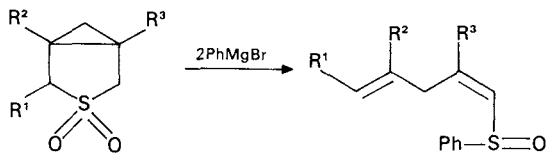
$$\text{PhSO}_2\text{Cl} + \text{PhMgBr} \longrightarrow \text{Ph—S(=O)—Ph} \qquad (106)$$

$$\text{EtOSO}_2\text{Cl} + \text{RMgX} \longrightarrow \text{R—S(=O)—R} \qquad (107)$$

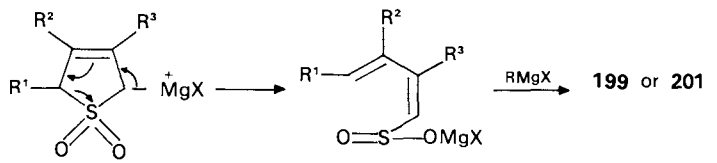
$$\text{ArSO}_2\text{Cl} \xrightarrow[\text{or } R_nAlCl_{3-n}]{R_3Al} \text{Ar—S(=O)—R} + \text{Ar—S—R} \qquad (108)$$



(198) (199) (109)

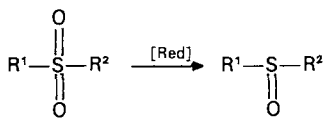


(200) (201) (110)

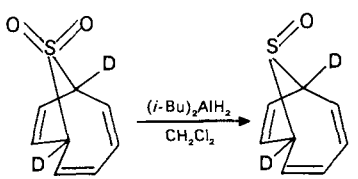


(203) (202) (111)

Since sulphones **204** are easily available compounds one would expect that they could be used as starting materials for the preparation of sulphoxides via the selective removal of one oxygen atom from the sulphonyl group (equation 112). Up to now, there is only one example reported of a direct reduction of a sulphone to a sulphoxide. The bicyclic dideuterio sulphone **205** after 24 h treatment with three-fold excess of diisobutyl aluminium hydride in boiling dichloromethane gave the corresponding sulphoxide **206** in 36% yield[237] (equation 113). A two-step procedure for the selective reduction of sulphones to sulphoxides, which involves an initial reaction of sulphone **204** with aryldiazonium tetrafluoroborate **207** to form aryloxysulphoxonium salt **208** and its subsequent reduction (equation 114), was alluded to by Shimagaki and coworkers[238] and

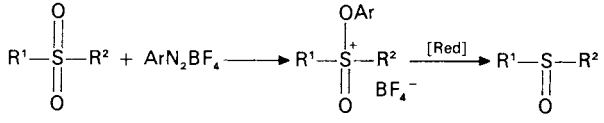


(204) (112)



(205) (206) (113)

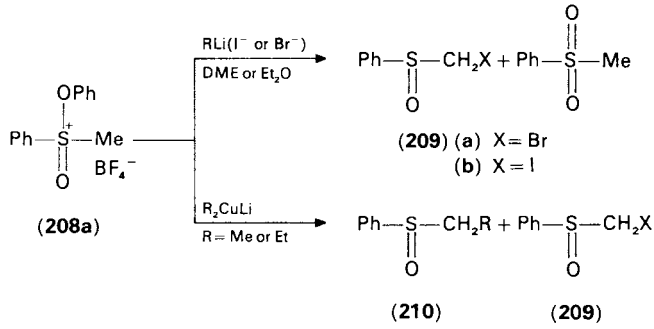
studied in detail by Still and his coworkers[239]. Methyl phenyl sulphone was converted into methyl phenyl sulphoxide by this procedure using benzenediazonium tetrafluoroborate **207a** as an arylating reagent and hydrogen sulphide or benzyl mercaptan in the presence of pyridine as the reductant[238]. Few other sulphones were reduced in a similar way via an initial reaction with 4-chlorobenzenediazonium tetrafluoroborate and subsequent reduction of the aryloxysulphonium salts **208b** with sodium borohydride/alumina[239].



(114)

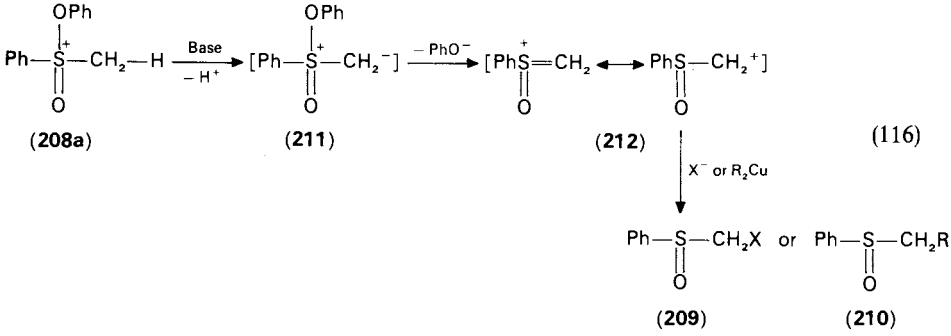
(204) (207) (208) (a) Ar = Ph (b) Ar = *p*-ClC$_6$H$_4$

The reaction of sulphoxonium salt **208a** with alkyllithium prepared from alkyl iodides or bromides gave the corresponding α-halogenosulphoxides **209** in 45–77% yields along with methyl phenyl sulphone[238] (equation 115). Lithium dimethylcopper prepared from methyl iodide, lithium and cuprous iodide afforded ethyl phenyl sulphoxide **210** (R = Me) in 69% yield. On the other hand, lithium diethylcopper prepared from ethyl iodide gave α-iodosulphoxide **209b** in 71% yield as a single reaction product (equation 115). The formation of α-halogenosulphoxides **209** and α-alkylmethyl derivatives **210** in the reaction of sulphoxonium salt **208a** with organocopper reagents results from the reaction sequence given in equation 116. Deprotonation of **208a** by a base leads to a very unstable ylide **211** which undergoes spontaneous decomposition to the phenoxide anion and a sulphoxonium ion **212**. The latter is trapped by nucleophiles (X^- or R^-) present in the reaction mixture to form the final reaction product **209** and/or **210**.



(208a) (209) (a) X = Br (b) X = I (210)

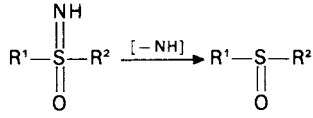
(115)



(208a) (211) (212) (209) (210)

(116)

Deimination of sulphoximines **213** as a method of synthesis of racemic sulphoxides (equation 117) has no synthetic value. However, this approach has been applied for the synthesis of optically active sulphoxides and will be discussed in the next part of this chapter.

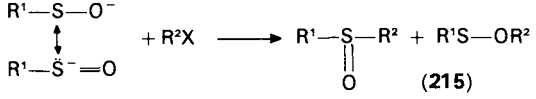


(117)

(213)

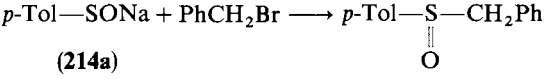
L. Alkylation of Sulphenate Anion

Anion **214** derived from sulphenic acid may be described by two mesomeric forms in which the negative charge is concentrated on the oxygen or sulphur atom and it shows a typical ambident reactivity. In accord with the HSAB concept[240], its alkylation may be expected to occur either on the sulphur atom to give the corresponding sulphoxides or on the oxygen atom to form sulphenate esters **215** (equation 118). The sulphoxide to sulphenate ratio depends mainly on the 'hardness' of the alkylating reagents. Thus, alkylation of sodium *p*-toluenesulphenate **214a**, formed by alkaline hydrolysis of *p*-toluenesulphenyl chloride, with benzyl bromide gave benzyl *p*-tolyl sulphoxide as the only product[241] (equation 119).



(118)

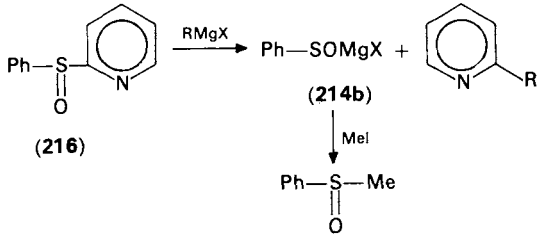
(214) (215)



(119)

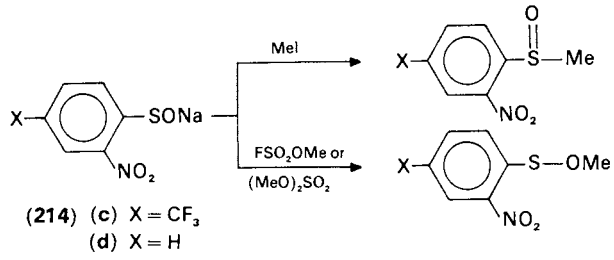
(214a)

The magnesium salt of benzenesulphenic acid **214b**, obtained by the reaction of pyridyl sulphoxide **216** with a Grignard reagent, gave upon alkylation with methyl iodide almost quantitatively methyl phenyl sulphoxide[227] (equation 120). The sulphenate anions **214c** and **214d**, generated by the base-catalysed hydrolysis of the corresponding disulphides or sulphenate esters, undergo *S*-methylation with methyl iodide, but predominant *O*-methylation with 'harder' methylation agents such as methyl fluorosulphonate and dimethyl sulphate[242] (equation 121). Alkylation of the sulphenate anion **214e**, obtained by the addition of lithium-cyclohexanone enolate to sulphine **173c**, gave the corresponding 1-aryl-3-oxo-1-alkenyl sulphoxides in high yields[243] (equation 122).



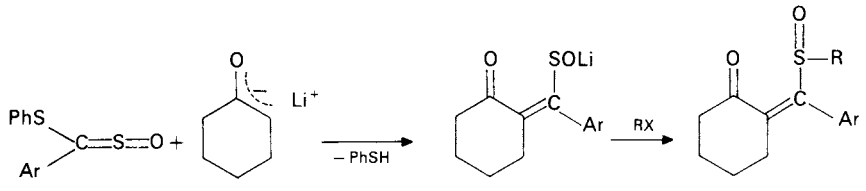
(120)

(216) (214b)



(214) (c) X = CF_3
(d) X = H

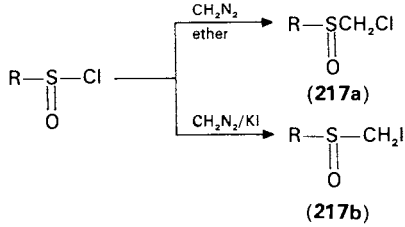
(121)



(173c) (214e) (122)

M. Miscellaneous Methods

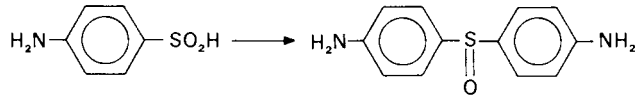
Reaction of diazomethane with sulphinyl chlorides has been known since 1957[244]. Effective procedures for the synthesis of α-halogenosulphoxides **217** based on this reaction were reported by Venier and coworkers[245,246]. Treatment of alkane or arenesulphinyl chlorides with diazomethane in ether solution gives α-chlorosulphoxides **217a** in 70–90% yields. When the same reaction was carried out in the presence of iodide anion it yielded the corresponding iodo derivatives **217b** in high yields (equation 123). Bromomethyl trichloromethyl sulphoxide was isolated in 15% yield after treatment of trichloromethanesulphinyl bromide with diazomethane[247] (equation 124).



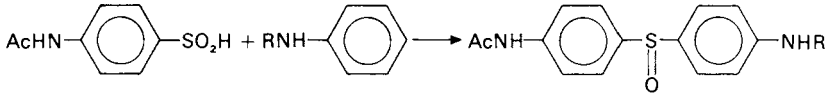
(123)

$$Cl_3C—\underset{\underset{O}{\|}}{S}—Br + CH_2N_2 \longrightarrow Cl_3C—\underset{\underset{O}{\|}}{S}—CH_2Br \qquad (124)$$

Heating of *p*-aminobenzenesulphinic acid for a few hours gives the corresponding *p,p'*-diaminophenyl sulphoxide in 57% yield[248] (equation 125). The thermal reaction of 4-acetamidobenzenesulphinic acid with N-alkylanilines affords the corresponding (4-acetamidophenyl)(4'-alkylaminophenyl)sulphoxides[249] (equation 126). Passing a stream of sulphur dioxide through a mixture of benzene and aluminium chloride at reflux temperature afforded diphenyl sulphoxide as a single reaction product[175].

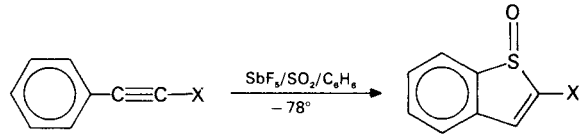


(125)



(126)

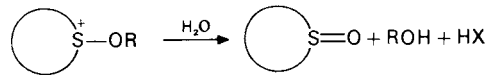
Few 1-benzothiophene-*S*-oxides **218** were obtained in moderate yields by treatment of 1-arylacetylenes **219** with sulfur dioxide and benzene in the presence of antimony pentafluoride[250] (equation 127). A series of cyclic sulphoxides have been prepared by hydrolysis of the corresponding alkoxy sulphonium salts **220**[251–254] (equation 128). Syn-sulphoxide **221** was obtained in a low yield (15–20%) in the reaction of the dianion of cyclooctatetraene **222** with thionyl chloride[255] (equation 129).



(127)

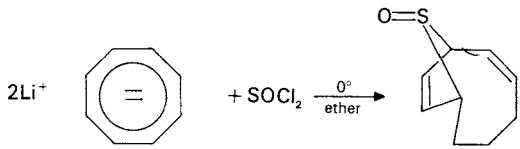
(219) **(218)**

(**a**) X = Cl
(**b**) X = Br
(**c**) X = Ph



(128)

(220)



(129)

(222) **(221)**

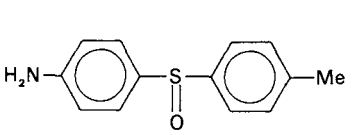
III. SYNTHESIS OF OPTICALLY ACTIVE SULPHOXIDES

Chiral sulphoxides are the most important group of compounds among a vast number of various types of chiral organosulphur compounds. In the first period of the development of sulphur stereochemistry, optically active sulphoxides were mainly used as model compounds in stereochemical studies[256]. At present, chiral sulphoxides play an important role in asymmetric synthesis, especially in an asymmetric C—C bond formation[257]. Therefore, much effort has been devoted to elaboration of convenient methods for their synthesis. Until now, optically active sulphoxides have been obtained in the following ways: optical resolution, asymmetric synthesis, kinetic resolution and stereospecific synthesis. These methods are briefly discussed below.

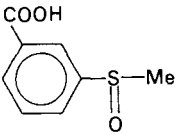
A. Optical Resolution

1. Classical resolution

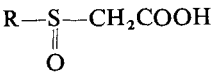
Since the pioneering work of Harrison and coworkers[258] on the resolution of 4-aminophenyl 4-tolyl sulphoxide **223** and carboxyphenyl methyl sulphoxide **224** into their enantiomeric forms via formation and crystallization of the diastereoisomeric salts with d-camphorsulphonic acid and brucine, respectively, this technique has been used frequently for the preparation of selected sulphoxides in optically active form[259]. Suszko and his collaborators[260] and later Janczewski and his group published[261] a large number of papers on the synthesis, resolution and optical properties of α-substituted sulphinylacetic acid derivatives of the general structure **225**. 1, 6- and 1, 8-naphthalenedisulphinylacetic acid **226** and **227** were resolved into their enantiomeric forms using the carboxylic groups for the salt formation with optically active amines[262].



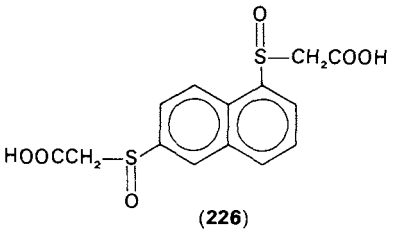
(223)



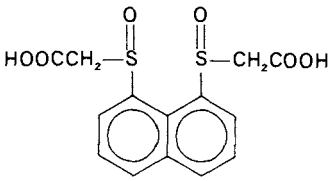
(224)



(225)

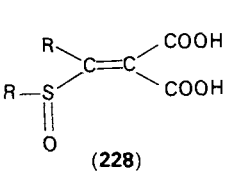


(226)

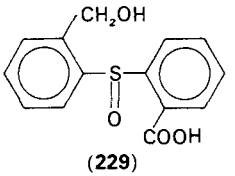


(227)

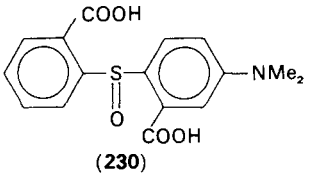
Bohman and Allenmark[263] resolved a series of sulphoxide derivatives of unsaturated malonic acids of the general structure **228**. The classical method of resolution via formation of diastereoisomeric salts with cinchonine and quinine has also been used by Kapovits and coworkers[264] to resolve sulphoxides **229**, **230**, **231** and **232** which are precursors of chiral sulphuranes. Mikołajczyk and his coworkers[265] achieved optical resolution of sulphoxide **233** by utilizing the phosphonic acid moiety for salt formation with quinine. The racemic sulphinylacetic acid **234**, which has a second centre of chirality on the α-carbon atom, was resolved into pure diastereoisomers by Holmberg[266]. Racemic 2-hydroxy- and 4-hydroxyphenyl alkyl sulphoxides were separated via the diastereoisomeric 2- or 4-(*tetra*-O-acetyl-D-glucopyranosyloxy)phenyl alkyl sulphoxides **235**. The optically active sulphoxides were recovered from the isolated diastereoisomers **235** by deacetylation with base and cleavage of the acetal[267]. Racemic 1,3-dithian-1-oxide **236**



(228)

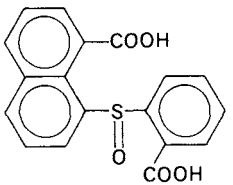


(229)

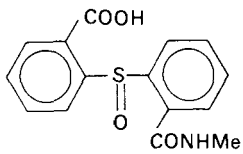


(230)

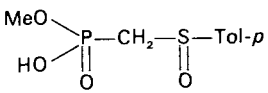
was resolved by a two-step procedure involving the addition of the 2-lithio derivative of **236** to (+) camphor followed by separation of the diastereoisomeric alcohols and regeneration of the optically active sulphoxide **236** with potassium hydroxide in *t*-butyl alcohol[268].



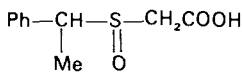
(231)



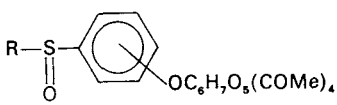
(232)



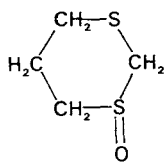
(233)



(234)



(235)



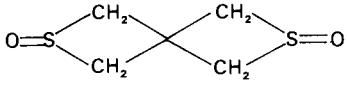
(236)

It is well known that spontaneous resolution of a racemate may occur upon crystallization if a chiral molecule crystallizes as a conglomerate. With regard to sulphoxides, this phenomenon was observed for the first time in the case of methyl *p*-tolyl sulphoxide[269]. The optical rotation of a partially resolved sulphoxide (via β-cyclodextrin inclusion complexes) was found to increase from $[\alpha]_{589} = +11.5°$ (e.e. 8.1%) to $[\alpha]_{589} = +100.8$ (e.e. 71.5%) after four fractional crystallizations from light petroleum ether. Later on, few optically active ketosulphoxides of low optical purity were converted into the pure enantiomers by fractional crystallization from ethyl ether-hexane[270]. This resolution by crystallization was also successful for racemic benzyl *p*-tolyl sulphoxide and *t*-butyl phenyl sulphoxide[271].

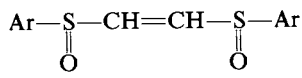
2. *Non-classical resolution*

In addition to the classical resolution of racemic sulphoxides via diastereoisomeric salts or derivatives, illustrated above, other so-called non-classical procedures are known to be useful for the resolution of racemic sulphoxides that do not contain acidic or basic functional groups. For the first time this technique was reported in 1934 by Becker and Keuning[272] who resolved 2,5-dithiaspiro[3,3]heptane-2,5-dioxide **237** by means of a cobalt complex with d-camphorsulphonic acid as a ligand. The total resolution of ethyl *p*-tolyl sulphoxide was achieved through the formation and separation of the diastereoisomeric complexes with *trans*-dichloroethylene platinum(II) containing optically active α-phenylethylamine as a ligand[273]. Due to its conceptual simplicity, the direct chromatographic separation of racemic sulphoxides on chiral columns may be considered as a convenient route leading to enantiomeric forms. Montanari and coworkers[274] found

that racemic unsaturated vinyl disulphoxide **238** may be partially resolved by this method on activated α-lactose.

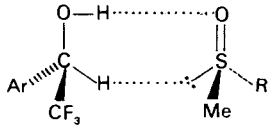


(**237**)

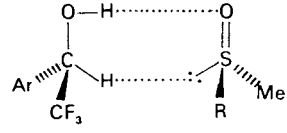


(**238**)

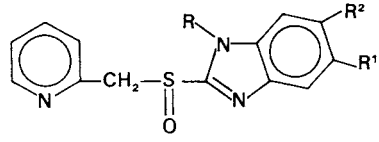
Wudl reported[275] that a polymer prepared from optically active methyl *p*-styryl sulphoxide may also be used as a chiral support in chromatographic resolution of racemic sulphoxides. In an extension of their studies on the NMR determination of enantiomeric purity and absolute configuration of chiral sulphoxides, Pirkle and House introduced recently a silica-gel-bonded chiral fluoroalcoholic stationary phase for the direct separation of racemic sulphoxides[276]. This chromatographic resolution is conceptually based on three types of stereochemically dependent interactions between the chiral fluoroalcoholic moiety of the stationary phase and the racemic sulphoxides to be separated. One assumes that the preferred conformation of the diastereoisomeric solvates **239a** and **239b** is stabilized by hydrogen bonding between the hydroxy and sulphinyl group, by interaction between the weakly acidic methine proton of the fluoroalcohol and the lone electron pair on sulphur (carbinyl hydrogen bonding), and also to some extent by interaction between the aromatic rings (R = Ar). Racemic phenyl vinyl sulphoxide was resolved by high-performance liquid chromatography on (+) poly-(triphenylmethyl)methacrylate column with methanol–water (8:2) mixture as eluent[277]. The stationary phase composed of (*R*)-*N*-(3,5-dinitrobenzoyl) phenyl glycine bound to aminopropyl silica was used for the resolution of a series of alkyl aryl sulphoxides[278]. Pharmacologically active racemic sulphoxides **240** were resolved by the affinity chromatography technique based on enantioselective interactions with immobilized bovine serum albumin[279].



S_C (**239a**) R_S



S_C (**239b**) S_S

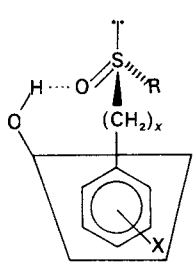


(**240**)

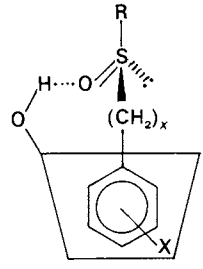
The gas chromatographic separation of some sulphoxide enantiomers was observed on quartz fused silica capillaries coated with the chiral silicon phase chirasil-val[280].

A different non-classical approach to the resolution of sulphoxides was reported by Mikołajczyk and Drabowicz[269,281]. It is based on the fact that sulphinyl compounds very easily form inclusion complexes with β-cyclodextrin. Since β-cyclodextrin as the host molecule is chiral, its inclusion complexes with racemic guest substances used in an excess are mixtures of diastereoisomers that should be formed in unequal amounts. In this way a series of alkyl phenyl, alkyl *p*-tolyl and alkyl benzyl sulphoxides has been resolved. However, the optical purities of the partially resolved sulphoxides do not exceed 22% after

a single inclusion process. Moreover, the optical purities of the included sulphoxides are strongly dependent on the nature of the aromatic ring and the alkyl group connected to the sulphinyl sulphur atom. The stereoselectivity of the inclusion is also dependent on the pH of the solution in which the formation of the inclusion complexes takes place, as well as on the presence of the water-miscible solvents like methanol, acetone or dioxane acting as hydrogen bond acceptors. The stereoselectivity of the inclusion of sulphoxides into β-cyclodextrin was also affected by the addition of inorganic salts to the water solution. The relationship between the stereospecificity of inclusion of sulphoxides into β-cyclodextrin and the structure of the preferentially included sulphoxide was rationalized by assuming that two inclusion complexes **241a** and **241b** are concurrently formed in a ratio that depends on the nature of alkyl and aryl substituents connected with the sulphinyl sulphur atom. In the case of *t*-butyl aryl, isopropyl and *n*-butyl *o*-tolyl sulphoxides, the inclusion complex **241b** is favoured for steric reasons.

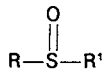


(241a)



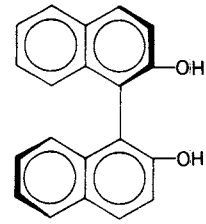
(241b)

A new approach to the resolution of sulphoxides **242** was recently reported by Toda and coworkers[282]. It takes advantage of the fact that some sulphoxides form crystalline complexes with optically active 2,2′-dihydroxy-1,1-binaphthyl **243**. When a two-molar excess of racemic sulphoxide **242** was mixed with one enantiomeric form of binaphthyl **243** in benzene-hexane and kept at room temperature for 12 h, a 1:1 complex enriched strongly in one sulphoxide enantiomer was obtained. Its recrystallization from benzene followed by chromatography on silica gel using benzene-ethyl acetate as eluent gave optically pure sulphoxide. However, methyl phenyl sulphoxide was poorly resolved by this procedure and methyl *o*-tolyl, methyl *p*-tolyl, *s*-butyl methyl and *i*-propyl methyl sulphoxides did not form complexes with **243**.



(242)

(a) R = *m*-MeC_6H_4, R^1 = Me
(b) R = *m*-MeC_6H_4, R^1 = Et
(c) R = *n*-Bu, R^1 = Me
(d) R = *n*-Pr, R^1 = Me



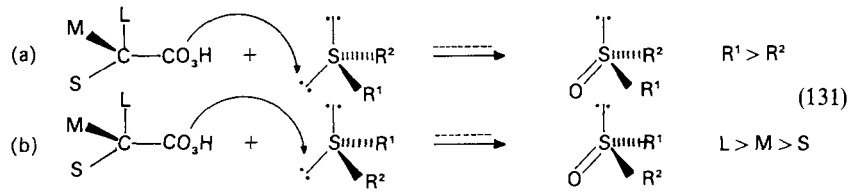
(243)

B. Asymmetric Synthesis

A convenient and simple route to chiral sulphoxides is an asymmetric oxidation of prochiral sulphides by optically active oxidizing reagents.

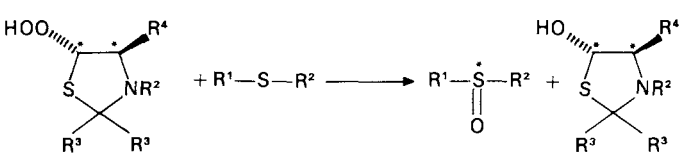
In 1960, Montanari[283] and Balenovic[284] and their coworkers described independently the first asymmetric oxidation of sulfides with optically active peracids. However, the sulphoxides were formed in this asymmetric reaction (equation 130) with low optical purities, generally not higher than 10%. The extensive studies of Montanari and his group on peracid oxidation indicated that the chirality of the predominantly formed sulphoxide enantiomer depends on the absolute configuration of the peracid used. According to Montanari[283], the stereoselectivity of the sulphide oxidation is determined by the balance between one transition state (a) and a more hindered transition state (b) in which the groups R^1 and R^2 at sulphur face the moderately and least hindered regions of the peracid, respectively (equation 131).

$$R^1—S—R^2 + \overset{*}{R}—\overset{O}{\overset{\|}{C}}—OOH \longrightarrow R^1—\overset{O}{\overset{\|}{\underset{*}{S}}}—R^2 + \overset{*}{R}—COOH \qquad (130)$$



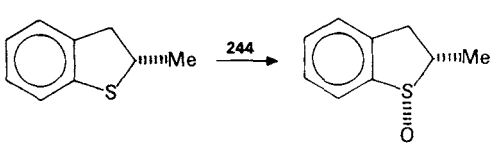
(131)

Optically active hydroperoxides **244** were found[285] to oxidize prochiral sulphides into the corresponding sulphoxides in higher optical yields (up to 27%) in comparison with those observed with peracids (equation 132). Moreover, the optical purity of the sulphoxides formed may be enhanced by addition of $Ti(OPr\text{-}i)_4$. The oxidation of racemic 2-methyl-2,3-dihydrobenzothiophene **246** with these peroxides gave a mixture of *cis* and *trans*-sulphoxides **247** (equation 133). In all cases of the oxidation with the hydroperoxide alone the formation of the *trans*-isomer was strongly preferred and the e.e. value (up to 42%) of the *cis*-isomer was always higher than that of the *trans*-isomer. Moreover, the addition of $Ti(OPr\text{-}i)_4$ furthermore promoted the selective formation of the *trans*-sulphoxide **247** and remarkably enhanced the e.e. value of both isomers.



(132)

(**244**) (**245**)



(133)

(**246**) *cis*-(**247**) *trans*-(**247**)

The standard Sharpless reagent [$Ti(OPr\text{-}i)_4$/(*R*, *R*)-diethyl tartrate (DET)/*t*-BuOOH] oxidizes methyl *p*-tolyl sulphide into a mixture of racemic sulphoxide and sulphone[286].

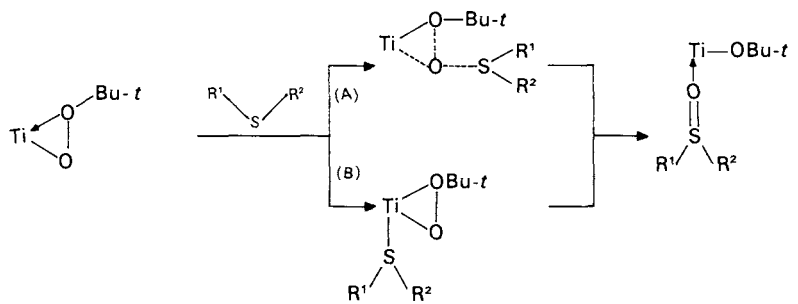
TABLE 15. Asymmetric oxidation of sulphides, R^1SR^2, to optically active sulphoxides, $R^1R^2S{=}O$

R^1	R^2	Oxidant[a]	Yield (%)	$[\alpha]_{589}$	e.e. (%) (conf.)	Ref.
Me	*p*-Tol	A	90	+132.0	91.0(*R*)	286
Me	*p*-Tol	B	60	+128.5	88.3(*R*)	287
Me	*p*-Tol	C	46	+ 93.5	64.5(*R*)	287
Me	*p*-Tol	D			31.0(*S*)	292
Me	Ph	A	80	+130.0	89.0(*R*)	286
Me	*p*-ClC_6H_4	A	95	+ 97.0	78.0(*R*)	286
Me	*p*-BrC_6H_4	A	70	+ 77.0	80.0(*R*)	286
Et	*p*-Tol	A	71	+139.0	74.0(*R*)	286
i-Pr	*p*-Tol	A	56	+111.0	63.0(*R*)	286
i-Pr	*p*-Tol	*b*			23.0(*S*)	292
n-Bu	*p*-Tol	A	75	+ 38.0	20.0(*R*)	286
Me	*n*-C_8H_{17}	A	77	− 44.0	71.0	286
Me	*t*-Bu	A	72	− 2.1	53.0(*R*)	286
Me	*c*-Hex	A	67	− 44.3	54.0	286

[a]A: Ti(OPr-*i*)$_4$ + (*R*,*R*)-diethyl tartrate + H_2O + *t*-BuOOH (1:2:1:1.1) in methylene chloride; B: Ti(OPr-*i*)$_4$ + (*R*,*R*)-diethyl tartrate + *t*-BuOOH (1:4:2) in 1,2-dichloroethane; C: Ti(OPr-*i*)$_4$ + (*R*,*R*)-diethyl tartrate + *t*-BuOOH (1:4:2) in toluene.
[b]Sulphonyloxaziridine **250a** (Ar = 2-chloro-5-nitrophenyl).

However, this reagent, modified by addition of one molar equivalent of water, was found by Kagan and coworkers[286] to give a new homogeneous reagent [Ti(OPr-*i*)$_4$/DET/*t*-BuOOH/H_2O] which is able to oxidize various types of alkyl aryl sulphides to the corresponding chiral sulphoxides with e.e. in the range of 80–90% in a predictable manner. In the case of dialkyl sulphoxides the e.e. values ranged between 50–71% (Table 15).

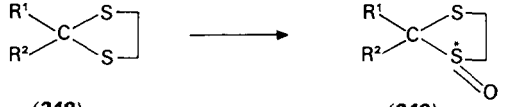
Based on detailed kinetic investigations, a tentative mechanism for this asymmetric oxidation was proposed (Scheme 2) according to which optically active sulphoxides may be formed by two pathways: external attack on the sulphur atom by the chiral titanium hydroperoxide (path A) or coordination of sulphur to titanium prior to the oxidation step (path B). Although paths A and B could not be distinguished experimentally, the temperature effect was tentatively ascribed to a change of the mechanism, path A being predominant above − 20 °C and path B becoming competitive at lower temperatures (or vice versa).



SCHEME 2

A closely related asymmetric synthesis of chiral sulphoxides, which involves a direct oxidation of the parent sulphides by *t*-butylhydroperoxide in the presence of metal catalyst and diethyl tartrate, was also reported by Modena and Di Furia and their coworkers-[287,288]. The effect of the reaction parameters such as metal catalyst, chiral tartrate and solvent on the optical yield does not follow a simple pattern. Generally, the highest optical purities (up to 88%) were observed when reactions were carried out using $Ti(OPr\text{-}i)_4$ as a metal catalyst in 1,2-dichloroethane.

The modified Sharpless reagent was also successfully applied[288] for the asymmetric oxidation of a series of 1,3-dithiolanes **248** to their *S*-monooxides **249** (equation 134). It was observed that the optical induction on sulphur (e.e. from 68 to 83%) is not significantly affected by the substituents R^1 and R^2. Asymmetric oxidation of a few aryl methyl sulphides by organic hydroperoxides in the presence of a catalytic amount of the optically active Schiff base–oxovanadium(IV) complexes gave the corresponding sulphoxides with e.e. lower than 40%[289].

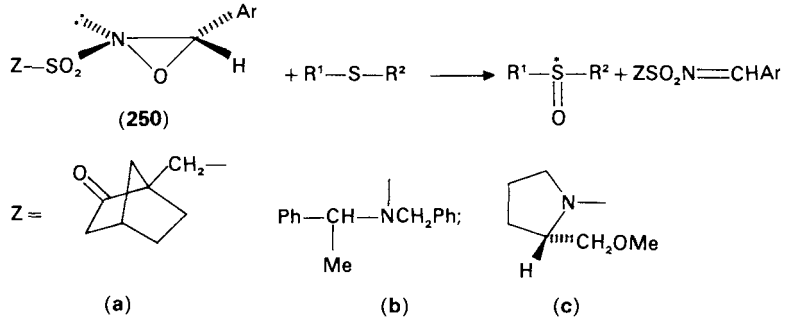


(134)

(248) **(249)**

In contrast to the asymmetric procedures discussed above, the metal-catalyzed oxidation of alkyl aryl sulphides by *t*-butylhydroperoxide carried out in a chiral alcohol gives rise to chiral sulphoxides of low optical purity[290] (e.e. 0.6–9.8%). Similarly, a very low asymmetric induction was noted when prochiral sulphides were oxidized by sodium metaperiodate in chiral alcohols as solvents[291].

Chiral 2-sulphonyloxaziridines **250a** and 2-sulphamyloxaziridines **250b,c** represent another type of efficient asymmetric oxidizing reagent which has recently been used by Davis and coworkers[292] for the synthesis of chiral sulphoxides (equation 135). It was established that the sulphoxide absolute configuration was determined by the configuration of the oxaziridine three-membered ring and that non-bonded steric interactions in the transition state were responsible for the asymmetric induction. The increased enantioselectivity exhibited by 2-sulphonyl and 2-sulphamyloxaziridines, in comparison to peracids or hydroperoxides, is most likely a manifestation of the closer proximity of the oxaziridine substituents to the reactive centre. In oxaziridines the oxygen atom, which undergoes transfer to sulphur, is located in a rigid three-membered ring and is one bond removed from the carbon and nitrogen chiral centres.



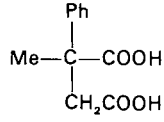
(135)

(250) **(a)** **(b)** **(c)**

Formation of optically active sulphoxides was found to occur during oxidation of sulphides in the presence of chiral catalysts. Thus, the oxidation of benzyl methyl sulphide

with iodine suspended in (*R*)-2-methyl-2-phenylsuccinic acid **251** buffer gives optically active benzyl methyl sulphoxide having 6.35% optical purity[293] (equation 136).

$$PhCH_2—S—Me \xrightarrow[water]{I_2/KI + \mathbf{251}} PhCH_2—\overset{*}{\underset{\|}{S}}(O)—Me \qquad (136)$$



(251)

β-Cyclodextrin mediated oxidation of prochiral sulphides by achiral oxidation reagents leads also to optically active sulphoxides (e.e. up to 30%). When oxidation was carried out in pyridine the highest optical purities were obtained[294] with hydrogen peroxide, whereas in water the best results were observed with *m*-chloroperbenzoic acid[295].

Much higher asymmetric induction was observed in the two-phase oxidation of simple alkyl aryl and diaryl sulphides[296], substituted alkyl aryl sulphides[297] and dithioacetals of formaldehyde[298] by sodium metaperiodate in the presence of proteins such as bovine serum *γ*-globulin and egg albumin. Optical purities of the sulphoxides so formed ranged between 20 and 85%.

Very low asymmetric induction (e.e. 0.3–2.5%) was noted when unsymmetrical sulphides were electrochemically oxidized on an anode modified by treatment with (−)camphoric anhydride or (*S*)-phenylalanine methyl ester[299]. Much better results were obtained with the poly(L-valine) coated platinum electrodes[300]. For example, *t*-butyl phenyl sulphide was converted to the corresponding sulphoxide with e.e. as high as 93%, when electrode coated with polypyrrole and poly(L-valine) was used.

In contrast to asymmetric oxidation of unsymmetrical sulphides with chiral chemical oxidants, microbiological oxidation (equation 137) usually gives much better results. In 1962, optically active benzyl phenyl sulfoxide with 18% optical purity was prepared[301] by oxidation of the parent sulphide via fermentation with Aspergillus niger, NRRL 337. Asymmetric induction during oxidation of 7-α-methylthioandrostane to the corresponding sulphoxide by fermentation with Calonectria decora (CBS) was also observed[302]. Later on, Henbest and coworkers found[303] that the chemical yield and stereoselectivity of the oxidation by Aspergillus niger depend on the structure of the sulphide and on the efficiency with which the enzymatic oxidation system can accommodate the reacting sulphide substrate. The highest optical purity (99%) was observed in the case of *t*-butyl *p*-tolyl sulphoxide and the lowest (32%) for methyl *p*-tolyl sulphoxide. Very recently oxidation of some alkyl aryl sulphides by Mortierella Isabellina RRLL 1757[304,305], and Helminthosporium sp., NRRL 4671[304], was found to give the corresponding sulphoxides with almost 100% optical purity.

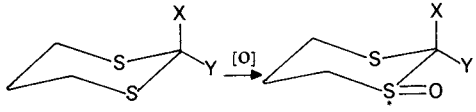
$$R^1—S—R^2 \xrightarrow{\text{microorganism}} R^1—\overset{*}{\underset{\|}{S}}(O)—R^2 \qquad (137)$$

However, (−)-(*S*)-*p*-tolylthio-(*p*-tolyl) sulphinylmethane **252** was obtained in 20% e.e. from gem-disulphide **253** using Helmintosporium cultures[306] (equation 138). With this culture much higher asymmetric induction was observed when 1,3-dithianes **254** substituted or unsubstituted at carbon 2 were used as substrates (equation 139). Whereas the optical yield of the (−)-(*S*)-monosulphoxide **255** (X = Y = H) was about 14% only, this

value increased up to 72% for 2-alkyl substituted dithianes **255**[307].

$$p\text{-Tol—S—CH}_2\text{—S—Tol-}p \xrightarrow{[O]} p\text{-Tol—}\overset{\overset{O}{\|}}{\overset{\cdot}{S}}\text{—CH}_2\text{—S—Tol-}p \qquad (138)$$

(253) **(252)**



(139)

(254) **(255)**

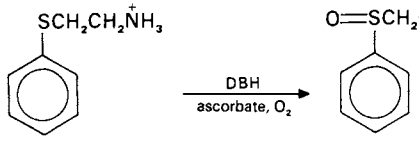
X, Y = H, Me, *t*-Bu

Stereoselective oxygen transfer to the sulphur atom of alkyl aryl sulphides catalyzed by 2-flavoenzyme monooxygenases afforded optically active sulphoxides in high optical yields[308]. For instance, with ethyl *p*-tolyl sulphide as substrate cyclohexanone monooxygenase from Actinetobacter produces predominantly (−)-(*S*)-sulphoxide with 64% e.e. In contrast, FAD-containing dimethylaniline monooxygenase purified from hog liver microsomes affords (+)-(*R*)-enantiomer of this sulphoxide with 90% optical purity[308].

Asymmetric oxidation of this sulphide was also catalyzed by two isocytochromes P 450 purified from phenobarbital induced rat liver[309]. Both P 450 isocytochromes, termed PB-1 and PB-4, when reconstituted with purified rat liver NADPH-cytochrome P 450 reductase and cytochrome b_5 afforded ethyl *p*-tolyl sulphoxide with *S*-configuration at the sulphur atom. In the case of PB-1 optical purity of this sulphoxide was 58% whereas with PB-4 it was 78%.

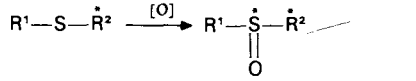
The oxidation of a series of cyclic and acyclic sulphides by cytochrome P 450 from rabbit liver gave sulphoxides with *R*-configuration at sulphur. The maximum of the e.e. value (53.8%) was observed for benzyl *t*-butyl sulphoxide[310].

Dopamine β-hydroxylase (DBH), a copper-containing monooxygenase present in a variety of mammalian tissues, catalyzes the conversion of the protonated 2-aminoethyl phenyl sulphide **256** to the corresponding optically active sulphoxide **257**[311] (equation 140). Formation of diastereoisomeric sulphoxides is also observed when sulphides that are chiral at carbon are reacted with achiral oxidizing agent (equation 141). This internal asymmetric induction was first described by Cram and Pine[312] in 1963. They oxidized (*R*)-2-octyl phenyl sulphide with *t*-butyl hydroperoxide and found that two diastereoisomeric sulphoxides **258** were formed in a 1.6:1 ratio. More recently, Nishihata and Nishio[313] investigated the oxidation of optically active 1-phenylethyl alkyl(phenyl) sulphides with various oxidizing agents. In every reaction studied the predominantly formed diastereoisomeric sulphoxide **259** was shown to have the S_CR_S configuration. Moreover, the diastereoisomeric ratio was not significantly affected by a change in the nature of the oxidant. In a series of alkyl derivatives, the product ratio (S_CR_S)-**259** to (S_CS_S)-**259** varies from 3.1 for R = Me to 49 for R = *t*-Bu. Asymmetric induction was also observed when chiral alkyl aryl sulphides were oxidized either with *N*-chloro-*p*-toluenesulphonamide or with *t*-butyl hypochlorite and TosNHNa[314].



\+ dehydroascorbate (140)

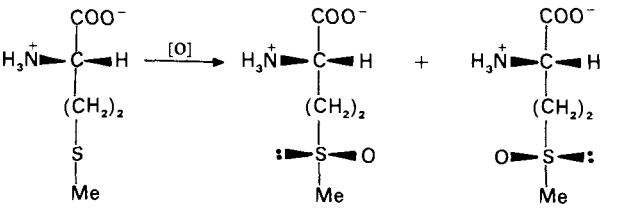
(256) **(257)**, $[\alpha]_{589} = -240°$



(141)

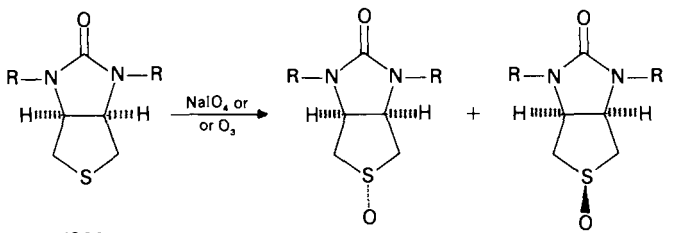
(258) (259)

The oxidation of (*S*)-methionine **260** with hydrogen peroxide was found to give the corresponding diastereoisomeric sulphoxides **261** in nearly equal amounts[315] (equation 142). However, the use of $HAuCl_4$ as oxidant[316] provides a method for the completely stereospecific conversion of (S_C)-**260** into the methionine sulphoxide (S_CS_S)-**261**. A high asymmetric induction at sulphur was observed in the oxidation of the bicyclic sulphide **262**. Marquet and her coworkers[317] reported that treatment of **262**, which is the key intermediate in the total synthesis of biotin, with sodium metaperiodate or ozone gave the two diastereoisomeric sulphoxides *cis*-**263** and *trans*-**263** in a 9:1 ratio (equation 143). The oxidation of esters of *o*-methylthiobenzoic acid **264** containing a chiral alkoxy group by achiral peracids gave **265** which, after hydrolysis, gave optically active *o*-methylsulphinylbenzoic acid **266**[318] (equation 144). The use of 2, 4, 6-trimethylperbenzoic acid and bulky alkyl groups in the ester moiety lead to the highest optical purity of this sulphoxide (40%).



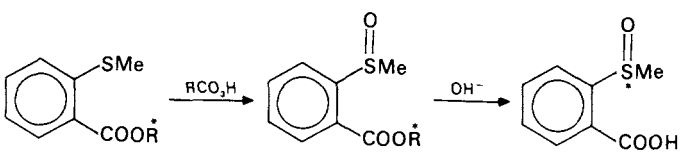
(*S*)-(**260**) (S_CS_S)-(**261**) (S_CR_S)-(**261**)

(142)



(**262**) *cis*-(**263**) R = $PhCH_2$, $CH_2{=}CH{-}CH_2$ *trans*-(**263**)

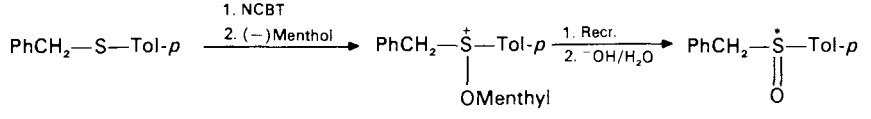
(143)



(**264**) (**265**) (**266**)

(144)

Chiral alcohols have also been used in an asymmetric synthesis of sulphoxides based on halogenation of sulphides. Johnson and coworkers have found[319] that the reaction of benzyl *p*-tolyl sulphide with *N*-chlorobenzotriazole (NCBT) followed by addition of (−) menthol and silver tetrafluoroborate afforded diastereoisomeric menthoxysulphonium salts **267** which, upon recrystallization and hydrolysis, gave benzyl *p*-tolyl sulphoxide with 87% optical purity (equation 145). More recently, Oae and coworkers reported[320] that optically active diaryl sulphoxides (e.g. up to 20%) were formed either by hydrolysis or thermolysis of the corresponding diaryl menthoxysulphonium salts prepared *in situ* from diaryl sulphides using (−) menthol and *t*-butyl hypochlorite.



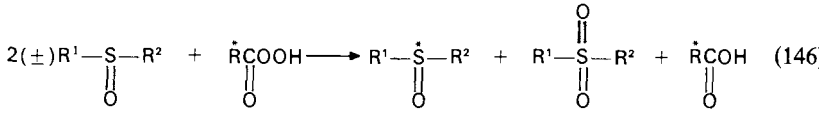
(**267**) (145)

Optically active sulphoxides were also obtained in low optical and chemical yields by the oxidation of prochiral sulphides with *N*-bromocaprolactam and a chiral alcohol as a solvent[321], or by treatment of sulphides with chiral *N*-chlorocaprolactam and water as oxidant[322].

C. Kinetic Resolution of Sulphoxides

The well-known fact that enantiomers exhibit different reactivity towards chiral reagents has been used to obtain optically active sulphoxides in a process which is called kinetic resolution. Kinetic resolution of sulphoxides usually involves either oxidation to the corresponding sulphones or reduction to sulphides by means of proper chiral oxidizing or reducing agents.

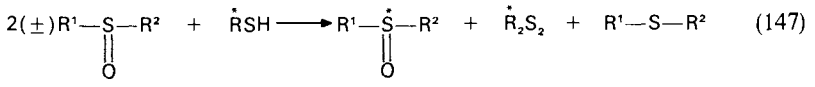
The first oxidative kinetic resolution of racemic sulphoxides was accomplished in the reaction with a deficiency of chiral peracids affording a mixture of optically active sulphoxide and achiral sulphone[323,324] (equation 146). However, the very low optical purity (up to 5%) of the recovered sulphoxides constitutes a serious limitation of this procedure. A more effective kinetic resolution of methyl *p*-tolyl sulphoxide and *t*-butyl phenyl sulphoxide was observed when these sulphoxides were oxidized with a half molar equivalent of the oxaziridine diastereoisomer **250**[325]. The optical purity of the recovered sulphoxides was in the range 0.5 to 23%. The hydrogen peroxide oxidation of racemic sulphoxides carried out in the presence of bovine serum albumin (BSA) is even more efficient[317]. For example, isobutyl phenyl sulphoxide left after partial oxidation of a racemate was optically active and the optical purity increased as the reaction proceeded. After 75% conversion its optical purity was 69%. As expected, relatively high optical purity (up to 30%) of sulphoxides was noted when they were exposed to growing cultures of Aspergillus niger[318]. In connection with asymmetric oxidation of sulphides to sulphoxides, it is interesting to note that the sulphoxide enantiomer formed preferentially in the asymmetric oxidation of a sulphide undergoes slower oxidation to sulphone. Thus, when the oxidation of alkyl phenyl sulphides with sodium metaperiodate in the presence of BSA was carried out for a long time, the optical purity of the *R*-enriched alkyl phenyl sulphoxides increased gradually as the amount of sulphoxides decreased, reaching a constant value of about 90% after 96 h, when the sulphoxides yields were about 45%[326].



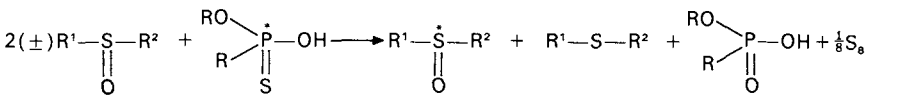
(146)

When racemic 1,3-dithiane *S*-monoxide **236** was exposed to the action of the microorganisms, a kinetic resolution took place and (−)-(*S*)-**236** was obtained with 10% e.e.[327].

The first reductive kinetic resolution of racemic sulphoxides was reported by Balenovic and Bregant[328]. They found that L-cysteine reacted with racemic sulphoxides to produce a mixture of L-cystine, sulphide and non-reduced optically active starting sulphoxide (equation 147). Mikołajczyk and Para[329] reported that the reaction of optically active phosphonothioic acid **268** with racemic sulphoxides used in a 1:2 ratio gave the non-reduced optically active sulphoxides, however, with a low optical purity (equation 148). It is interesting to note that a clear relationship was found between the chirality of the reducing P-thioacid **268** and the recovered sulphoxide. Partial asymmetric reduction of racemic sulphoxides also occurs when a complex of $LiAlH_4$ with chiral alcohols[330], as well as a mixture of formamidine sulphinic acid with chiral amines, are used as chiral reducing systems[331].

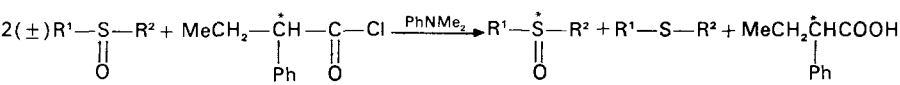


(147)

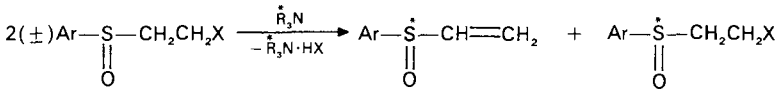


(**268**) (148)

A very interesting approach to optically active sulphoxides, based on a kinetic resolution in a Pummerer-type reaction with optically active α-phenylbutyric acid chloride **269** in the presence of *N*,*N*-dimethylaniline, was reported by Juge and Kagan[332] (equation 149). In contrast to the asymmetric reductions discussed above, this procedure afforded the recovered sulphoxides in optical yields up to 70%. Chiral α,β-unsaturated sulphoxides **270** were prepared via a kinetic resolution elaborated by Marchese and coworkers[333]. They found that elimination of HX from racemic β-halogenosulphoxides **271** in the presence of chiral tertiary amines takes place in an asymmetric way leading to both sulphoxides **270** and **271**, which are optically active (optical yields up to 20%) with opposite configurations at sulphur (equation 150).



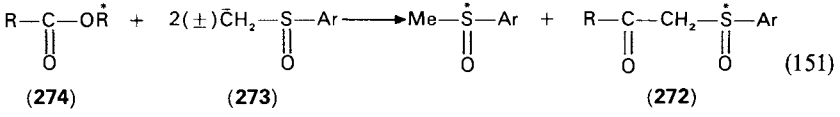
(**269**) (149)



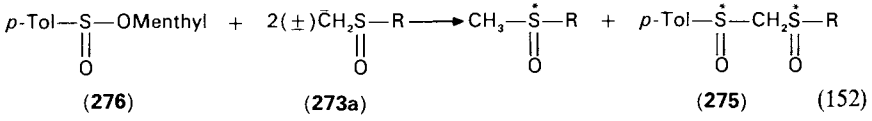
(**271**) (**270**) (**271**) (150)

The preparation of enantiomerically enriched α-ketosulphoxides **272** was also based on a kinetic resolution involving the reaction of the carbanion **273** derived from racemic aryl methyl sulphoxides with a deficiency of optically active carboxylic esters **274**[334] (equation 151). The degree of stereoselectivity in this reaction is strongly dependent on the nature of both the group R and the chiral residue R* in **274**. Thus, the α-ketosulphoxide formed in the reaction with menthyl esters had an optical yield of 1.3% for R = Et. In the

case of R = Bu-*t*, the optical yield was increased to 71.5%. In a similar way optically active α-disulphoxides **275** were obtained starting from diastereoisomerically pure menthyl *p*-toluenesulphinate **276** and the racemic sulphoxide carbanions **273a**[335] (equation 152).



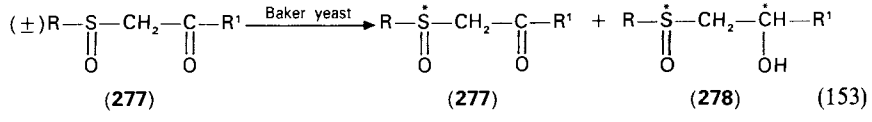
(274) (273) (272) (151)



(276) (273a) (275) (152)

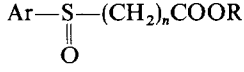
A kinetic resolution of racemic sulphoxides was observed in the reduction by chiral polyiminoalanes. The efficiency of this process depends on the molecular structure of the polyiminoalane. With open pseudo-cubic tetra [*N*-(1-phenylethyl)]imidoalane, unreacted sulphoxides were isolated in enantiomeric enrichment up to 75%. Optical purity was shown to increase with increasing the reaction temperature, a maximum enrichment being observed between 55 and 70 °C[336].

A kinetic resolution was also observed in the reduction of racemic α-ketosulphoxides **277** by fermenting yeast[337] (equation 153). Both the starting ketones **277** and the corresponding β-hydroxysulphoxides **278** formed have been recovered in almost enantiomerically pure form.



(277) (277) (278) (153)

Enzyme mediated hydrolysis of racemic arenesulphinyl alkanoates **279** may also be considered as a method of kinetic resolution. Racemic sulphoxides **279** incubated in the presence of Carynebacterium equi IF 3730 was found to give recovered sulphoxide in optically active form with e.e. higher than 90%[338].



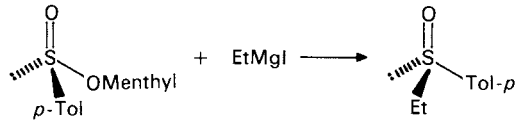
(279)

Partial photochemical decomposition of racemic alkyl aryl sulphoxides in the presence of chiral amines as sensitizers gave non-decomposed sulphoxides in optically active form with optical purity of about 3%[339]. The report[340] on the use of cholesteric liquid crystalline reaction media to change the enantiomeric composition of racemic sulphoxides at high temperatures could not be reproduced[341].

D. Stereospecific Synthesis

A great achievement of the stereochemistry of organosulphur compounds was the stereoselective synthesis of optically active sulphoxides developed by Andersen in 1962[342]. This approach to sulphoxides of high optical purity, still most important and widely used,

is based on the reaction of the diastereoisomerically pure (or strongly enriched in one diastereoisomer) menthyl arene(alkane)sulphinates with Grignard reagents. (+)-(*R*)-Ethyl *p*-tolyl sulphoxide **280** prepared from (−)-(*S*)-menthyl *p*-toluenesulphinate **276** and ethylmagnesium iodide (equation 154) was the first optically active sulphoxide obtained by this method[342].



(154)

(−)-(*S*)-(**276**) (+)-(*R*)-(**280**)

The Andersen sulphoxide synthesis is general in scope and a large number of chiral alkyl aryl and diaryl sulphoxides became available from (−)-(*S*)-**276** and other optically active sulphinates[343–346] (Table 16).

Usually, the reaction of arenesulphinates with Grignard reagents is carried out in ethyl ether solution. However, in this solvent chiral sulphoxides are formed in moderate or low yields depending on the structure of both the sulphinic esters and the Grignard reagents. Harpp and coworkers[159] carried out detailed studies on this reaction and found that the reaction conditions must be carefully selected, otherwise considerable quantities of impurities, which are difficult to separate, are formed. They also found that the use of lithium-copper reagents (R_2CuLi) instead of Grignard reagents gives a cleaner conversion of sulphinates to sulphoxides. However, in this case also the yields of sulphoxides were in the range between 16 and 59%. Chiral sulphoxides of greater chemical and optical purity and in higher yields are obtained when the reactions of menthyl sulphinates with Grignard reagents are carried out in a benzene solution[347]. It is interesting to note that in this solvent the yields of sulphides formed as by-products are much lower.

The synthesis of chiral dialkyl sulphoxides of high optical purity from diastereoisomeric alkanesulphinates has a serious limitation because the sulphinates are not

TABLE 16. Synthesis of optically active sulphoxides, *p*-TolS(O)R, from *O*-menthyl *p*-toluenesulphinate (−)-(*S*)-**276**

$[\alpha]_{589}$[a], deg	Conditions	R	Yield (%)	$[\alpha]_{589}$[a], deg	Ref.
−198.0	$MeMgI/Et_2O$	Me	*b*	+145.5	343
−195.0	MeMgI/PhH	Me	82	+150.1	347
−210.0	Me_2CuLi/Et_2O	Me	55	+143.2	159
−198.0	$EtMgBr/Et_2O$	Et	*b*	+187.5	343
−195.0	EtMgBr/PhH	Et	92	+198.0	347
−198.0	*i*-$PrMgBr/Et_2O$	*i*-Pr	22	+176.5	343
−195.0	*i*-PrMgBr/PhH	*i*-Pr	40	+173.2	347
−198.0	*n*-$BuMgBr/Et_2O$	*n*-Bu	*b*	+187.0	343
−195.0	*n*-BuMgBr/PhH	*n*-Bu	73	+186.0	347
−195.0	PhMgBr/PhH	Ph	88	+ 20.0	347
−210.0	Ph_2CuLi/Et_2O	Ph	52	+ 20.7	159
−198.0	*o*-$TolMgBr/Et_2O$	*o*-Tol	*b*	− 89.1	343
−198.0	*m*-$TolMgBr/Et_2O$	*m*-Tol	*b*	+ 15.1	343

[a] In acetone solution.
[b] Not given.

epimerically pure at sulphur[343,344,348]. For example, diastereoisomeric menthyl methanesulphinates are oils which cannot be separated into pure diastereoisomers. It was found[349], however, that substitution of cholesterol for menthol leads to crystalline cholesteryl methanesulphinates **281** which, after separation by crystallization into pure diastereoisomers and upon treatment with alkyl Grignard reagents, yielded alkyl methyl sulphoxides **282** of high enantiomeric purity (equation 155). In accord with the original Andersen assumption[342], the reactions of Grignard reagents with arene(alkane)sulphinates proceed with a full inversion of configuration at the sulphinyl sulphur atom. This steric course was firmly established by Mislow[350] and other investigators[351,352]. However, it was recently found that the reactions of alkyl *t*-butanesulphinates with methylmagnesium halides and alkyl methanesulphinates with *t*-butylmagnesium chloride are not fully stereoselective[353].

$$\underset{\textbf{(281)}}{Me{-}\overset{\overset{O}{\|}}{\overset{\cdot}{S}}{-}OCholesteryl} + RMgX \longrightarrow \underset{\textbf{(282)}}{R{-}\overset{\overset{O}{\|}}{\overset{\cdot}{S}}{-}Me} \qquad (155)$$

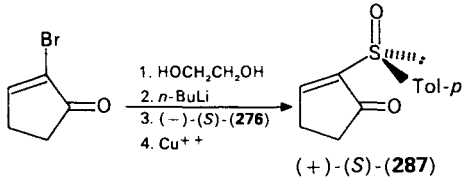
The stereospecific conversion of menthyl arenesulphinates into chiral aryl methyl sulphoxides may also be achieved by means of methyllithium[354–356]. The reaction of methyllithium with diastereoisomerically[356] or enantiomerically[355] pure arenesulphinamides **283** was found to give optically active aryl methyl sulphoxides **284** (equation 156). The preparation of optically active sulphoxides **285** and **286**, which are chiral by virtue of isotopic substitution (H → D and $^{12}C \rightarrow {}^{13}C$, respectively), involves the reaction of the appropriate non-labelled menthyl sulphinates with fully deuteriated methyl magnesium iodide[357] (equation 157) and with benzylmagnesium chloride prepared from benzyl chloride labelled with carbon ^{13}C[358] (equation 158).

$$\underset{\textbf{(283)}}{Ar{-}\overset{\overset{O}{\|}}{\overset{\cdot}{S}}{-}NR_2} + MeLi \longrightarrow \underset{\textbf{(284)}}{Ar{-}\overset{\overset{O}{\|}}{\overset{\cdot}{S}}{-}Me} \qquad (156)$$

$$CH_3{-}\overset{\overset{O}{\|}}{S}{-}OMenthyl + CD_3MgI \longrightarrow \underset{\textbf{(285)}}{CH_3{-}\overset{\overset{O}{\|}}{S}{-}CD_3} \qquad (157)$$

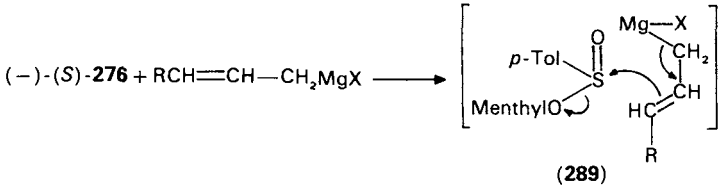
$$Ph^{12}CH_2{-}\overset{\overset{O}{\|}}{S}{-}OMenthyl + Ph^{13}CH_2MgCl \longrightarrow \underset{\textbf{(286)}}{Ph^{12}CH_2{-}\overset{\overset{O}{\|}}{S}{-}{}^{13}CH_2Ph} \qquad (158)$$

Further utility of the Andersen sulphoxides synthesis is demonstrated by the preparation of optically active unsaturated sulphoxides which were first prepared by Stirling and coworkers[359] from sulphinate **276** and the appropriate vinylic Grignard reagents. Later on, Posner and Tang[360] prepared in a similar way a series of (*E*)-1-alkenyl *p*-tolyl sulphoxides. Posner's group accomplished also the synthesis of (+)-(*S*)-2-(*p*-tolylsulphinyl)-2-cyclopentenone **287**, which is a key compound in the chiral synthesis of various natural products[361] (equation 159).

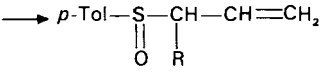


(+)-(*S*)-(**287**) (159)

Treatment of (−)-(*S*)-**276** with allyl Grignard reagents gives optically active allylic sulphoxides **288**. This reaction, however, involves an allylic rearrangement via transition state **289** as evidenced by Mislow and his collaborators[362] (equation 160).

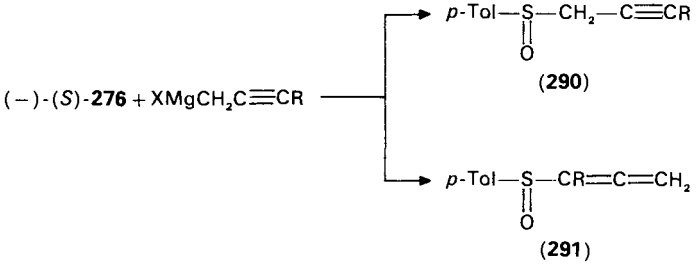


(**289**)



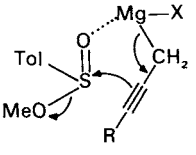
(**288**) (160)

A closely related reaction of (−)-(*S*)-**276** with the Grignard reagents obtained from α-acetylenic halides leads to the formation of mixtures of acetylenic sulphoxides **290** and allenic sulphoxides **291**[363] (equation 161). The latter compounds are most probably formed via transition state **292**, which is analogous to **289**. On the other hand, hex-1-ynyl *p*-tolyl sulphoxide **293** is smoothly prepared from hex-1-ynylmagnesium bromide and (−)-(*S*)-**276**[363] (equation 162).



(**290**)

(**291**) (161)



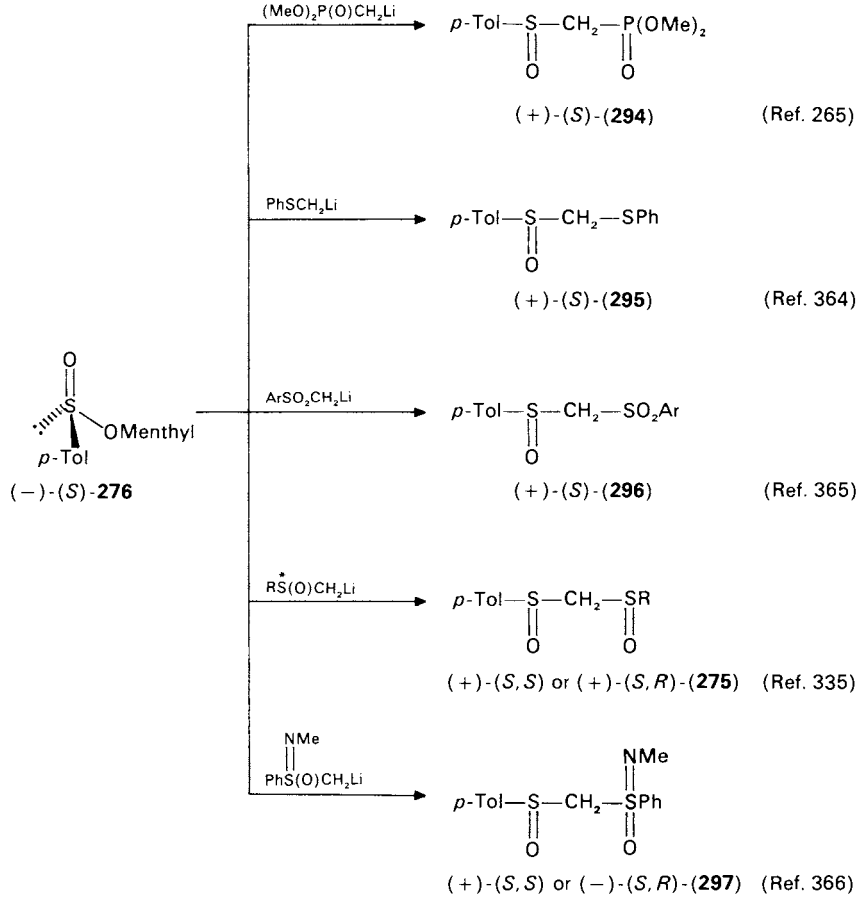
(**292**)

$$(-)\text{-}(S)\text{-}\mathbf{276} + \text{BrMgC}{\equiv}\text{C—Bu-}n \longrightarrow p\text{-Tol—}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{—C}{\equiv}\text{C—Bu-}n \qquad (162)$$

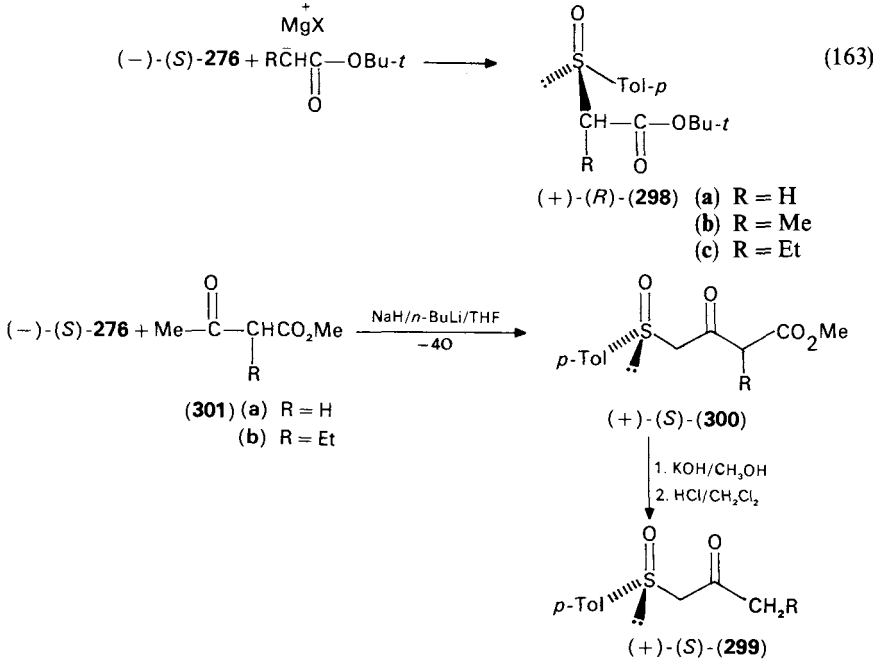
(293)

The Andersen sulphoxide synthesis allows one also to synthesize a variety of α-heteroatom substituted sulphoxides starting from α-heteroatom stabilized carbanions and (−)-(*S*)-**276**. The selected examples shown in Scheme 3 are the best illustration of the generality of this approach. The reaction of enolates or enolate like species with (−)-(*S*)-**276** has been used for the synthesis of optically active α-carbalkoxy sulphoxides. For example, treatment of (−)-(*S*)-**276** with the halogenomagnesium enolates of *t*-butyl acetate, *t*-butyl propionate or *t*-butyl butyrate resulted in the formation of (+)-(*R*)-*t*-butyl *p*-toluenesulphinylcarboxylates **298**[367] (equation 163).

Two chiral *p*-tolylsulphinylmethyl ketones **299** were prepared by decarboxylation of optically active sulphinyl ketoesters **300** which were obtained from (−)-(*S*)-**276** and the

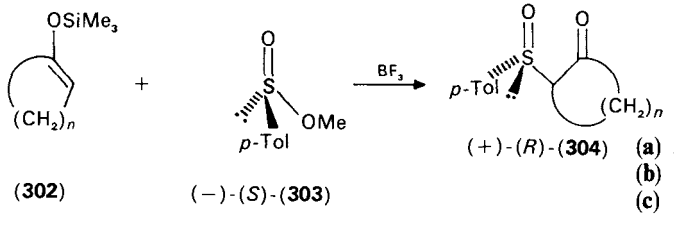


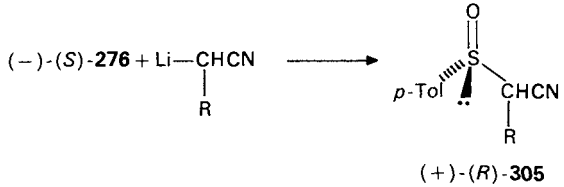
SCHEME 3



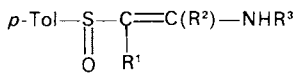
SCHEME 4

dianion derived from methyl acetoacetate **301**[368] (Scheme 4). The acid-catalyzed reaction of enol silyl ethers of cyclic ketones **302** with chiral methyl *p*-toluenesulphinate (−)-(*S*)-**303** was found[369] to be a very convenient and general entry to optically active α-sulphinylketones **304** (equation 164). Boron trifluoride etherate, titanium tetrachloride and tin tetrachloride were applied as acidic catalysts. The highest chemical and optical yields were obtained with boron trifluoride. The reaction of α-cyanocarbanions with (−)-(*S*)-**276** afforded the corresponding α-cyanoalkyl *p*-tolyl sulphoxides (+)-(*R*)-**305** in high chemical yield and optical purity[370] (equation 165). In the reaction of α-lithiated imines

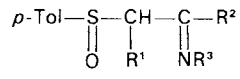




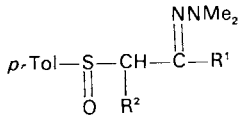
with this sulphinate, optically active β-enamino **306** and/or β-iminosulphoxides **307** were formed[371]. In an analogous way, optically active α-sulphinylhydrazones **308** were prepared from (−)-(*S*)-**276** and α-metallated *N*,*N*-dimethylhydrazones[372].



(**306**)

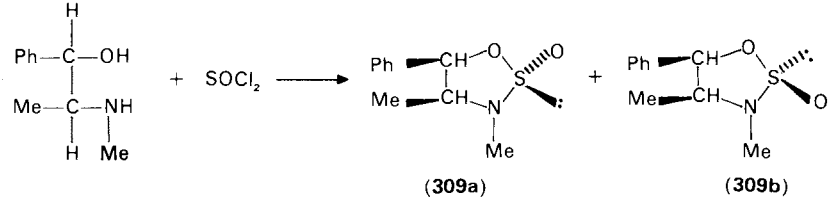


(**307**)

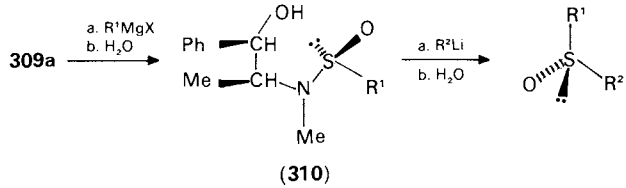


(**308**) R¹, R² = H, Alkyl, Aryl

A highly stereoselective cleavage of the S—O bond in cyclic diastereoisomeric amidosulphites **309** by Grignard reagents followed by highly stereoselective cleavage of the S—N bond with alkyllithium reagents in the formed chiral sulphinamides **310**, are the key steps in the stereospecific synthesis of chiral sulphoxides reported by Wudl and Lee[373] (Scheme 5). The precursor amidosulphite **309** was easily prepared from 1-ephedrine and thionyl chloride. It is interesting to note that the order of introduction of the groups R^1 and R^2 determines the configuration of the optically active sulphoxides formed.



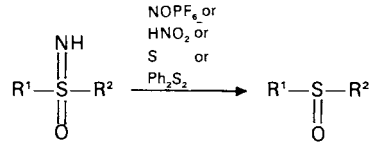
(**309a**) (**309b**)



(**310**)

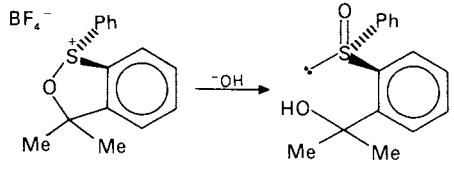
SCHEME 5

A different approach to optically active sulphoxides of high optical purity involves the stereospecific deimination of optically active sulphoximides **213**. These compounds are sufficiently basic and are easily resolved into enantiomers through the formation of the diastereoisomeric salts with optically active sulphonic acids[374]. The stereospecific conversion of sulphoximides **213** into the corresponding sulphoxides was acheived by a low-temperature reaction with nitrosyl hexafluorophosphate or nitrous acid[375]. An alternative deimidation procedure consists in heating at 160 °C with elemental sulphur or diphenyl disulphide (equation 166). All these procedures afford chiral sulphoxides with retention of configuration at the sulphur atom[376].

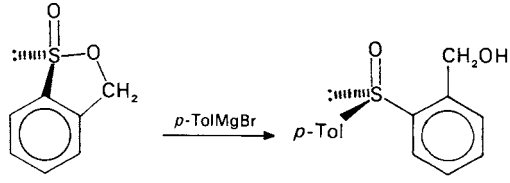


(213) (166)

Optically active sulphoxides **311** and **312** have been prepared stereospecifically either by hydrolysis of the optically active sulphonium salt **313** or by the reaction of *p*-tolyl magnesium bromide with optically active sulphinate **314**, respectively[377] (equations 167 and 168).



(+)-(*S*)-(**313**) (−)-(*S*)-(**311**) (167)



(+)-(*S*)-(**314**) (+)-(*R*)-(**312**) (168)

IV. FUNCTIONALIZATION OF SULPHOXIDES

Functionalization of organic substituents adjacent to the sulphoxide moiety constitutes an important method of the synthesis of a variety of sulphoxides, which are not available by the methods described in the previous sections. Such transformations enable one to synthesize a large number of very sophisticated sulphoxides which are required for special purposes or serve as a source of many sulphur-free organic compounds.

Since a great number of such transformations were described in the chemical literature, only selected examples of general importance will be presented here. This section will consist of the following parts: reactions of the sulphoxide α-carbanions; introduction, substitution, transformation and elimination of heteroatomic groups attached to organic substituents in sulphoxides; additions to unsaturated sulphoxides; other modifications of organic substituents in sulphoxides.

A. Reactions of the Sulphoxide α-Carbanions

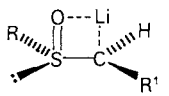
1. Generation of carbanions

Formation of α-sulphinyl carbanions has been widely investigated[378,379]. Several bases have been found to be suitable for the generation of these carbanions, including the use of

methyllithium and LDA which enable formation of carbanions at low temperatures. On the other hand, *n*-butyllithium and *t*-butyllithium must be used with caution since they can cause cleavage of the carbon–sulphur bond, resulting in an exchange of the organic substituent[380,381]. Other basic reagents, such as sodium hydride, sodium or potassium *t*-butoxide, though also effective, particularly for a generation of the methylsulphinyl carbanion in DMSO solution, may cause in some cases side-reactions leading to undesired products arising from condensation reactions of the carbanions formed. Sodium amide in liquid ammonia, when used in an appropriate excess, generates a dianion[382].

Generation of anions α to the sulphinyl group takes place also in 1-alkenyl sulphoxides and can easily be achieved by using such bases as LDA[383–385], *t*-BuLi[386] and *n*-BuLi (for allenyl sulphoxides)[387].

In contrast to the early theoretical work of Rauk and coworkers[388], ^{13}C-NMR investigations had revealed that the metallated carbon atom in the α-sulphinyl carbanion is nearly planar[389,390]. A four-centre chelate structure **315** has been proposed for α-lithiosulphoxides, and it is believed to be responsible for the planar configuration of the anionic carbon atom[389] and for the greater stability of α-sulphinyl carbanions in comparison with α-sulphenyl carbanions[391]. This chelation favours one of the two diastereoisomeric carbanions and for this reason α-sulphinyl carbanions react with electrophiles in a highly stereoselective manner (see below).



(315)

A detailed discussion of the different acidities of the diastereotopic α-methylene protons in sulphoxides, as well as of the stereochemistry of reactions of sulphoxide α-carbanions with electrophilic reagents is beyond the scope of this chapter. A recent review by Wolfe pertinent to these problems is available[392].

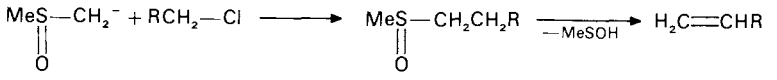
2. *Reactions of α-sulphinyl carbanions with electrophiles*

a. General remarks. Reactions of α-sulphinyl carbanions with electrophilic reagents have been widely applied, usually at one of the stages in multistep syntheses of organic compounds. Very often the sulphinyl moiety which served as a carbanion stabilizing group is finally removed giving sulphur-free products.

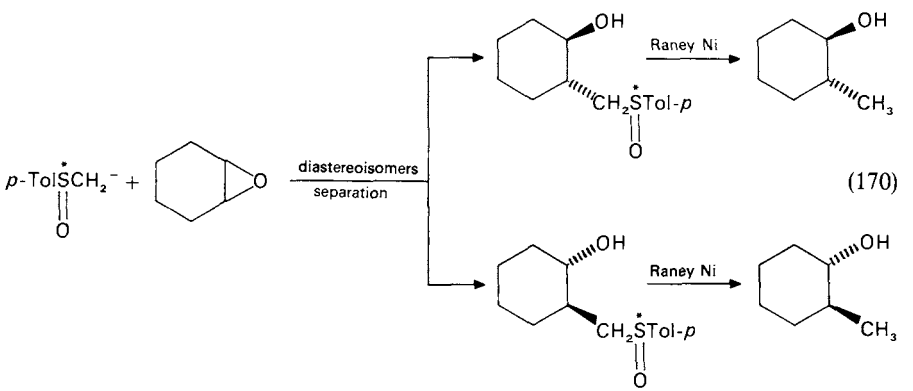
In this section alkylation, Michael additions, hydroxyalkylation (reaction with carbonyl compounds), aminoalkylation, acylation and some other reactions of α-sulphinyl carbanions will be discussed.

b. Alkylation of α-sulphinyl carbanions. Simple alkylation of α-sulphinyl carbanions is usually used as a first step in a sequence of reactions leading to sulphur-free organic compounds. Entwistle and Johnstone[393] and later Trost and Bridges[394] obtained in this way a variety of alkenes via the well-known elimination of sulphenic acid (equation 169). Oxiranes react with α-sulphinyl carbanions to give γ-hydroxy sulphoxides[395–397]. The reaction of the anion of optically active methyl *p*-tolyl sulphoxide with cyclohexene oxide was used by Tsuchihashi and coworkers for the synthesis of optically active 2-hydroxy-1-methylcyclohexanes[398] (equation 170). Guittet and Julia alkylated phenyl lithiomethyl sulphoxide with methallyl chloride to obtain the homoallyl sulphoxide **316** which, after subsequent treatment with a base and an oxirane, gave the γ-hydroxysulphoxide **317**. The latter underwent elimination of benzenesulphenic acid to give (*E*)-hotrienol **318**, a

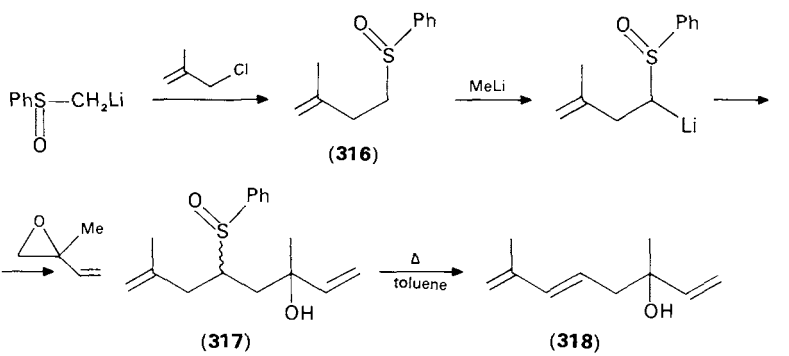
naturally occurring monoterpene[395] (equation 171).



(169)



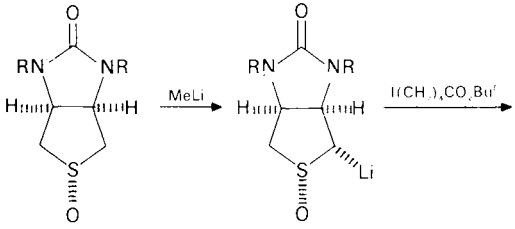
(170)



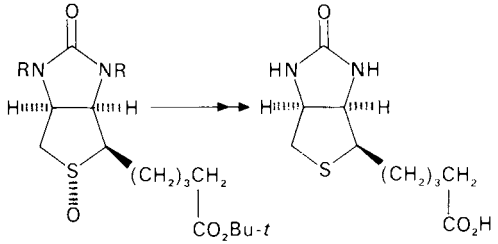
(171)

An interesting application of alkylation of α-sulphinyl carbanions was reported by Marquet and coworkers[317] in their total synthesis of biotine **321** (equation 172). The carbanion **319** generated by MeLi in a HMPT–THF or HMPT–diglyme mixture was alkylated by *t*-butyl ω-iodovalerate. The reaction was highly stereoselective and a single isomer with a side-chain *trans* to the S—O bond was obtained. It must be stressed, however, that the choice of the base and the solvent is crucial for the alkylation yield. More recently, a high diastereoselection (80%) was observed in the alkylation of α-sulphinyl anion with α-bromomethyl acrylate. In this case also the choice of the base appears to be decisive—the highest asymmetric induction is found when metallation of the sulphoxide is carried out by using highly hindered bases, e.g. lithium tetramethylpiperidine[399] (equation 173).

It has been found that aryl groups can also be introduced into the α-position of sulphoxides. Corey and Chaykovsky have demonstrated that chlorobenzene reacts at room temperature with an excess of sodium methylsulphinyl carbanion to give methyl benzyl sulphoxide in 41% yield. The authors believe that a benzyne intermediate may be involved in the reaction[400,401] (equation 174).

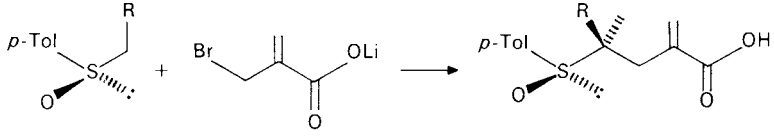


(263) (319)

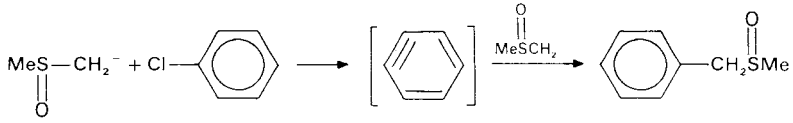


(320) (321)

(172)



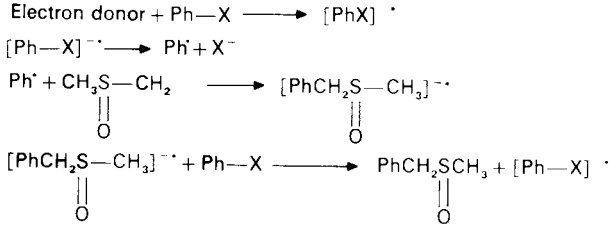
(173)



(174)

A similar goal can be achieved using the conditions of the $S_{RN}1$ reaction. The anion of DMSO is generated by $NaNH_2$ in DMSO and the $S_{RN}1$ reaction is initiated by sunlight[402] (Scheme 6).

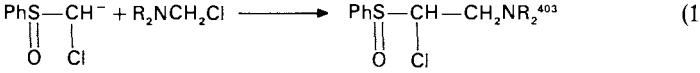
Alkylation of carbanions of α-halogenomethyl sulphoxides enables one to elongate the alkyl chain[403–406] (equations 175 and 176). α-Chlorosulphoxides react with nitroarenes in



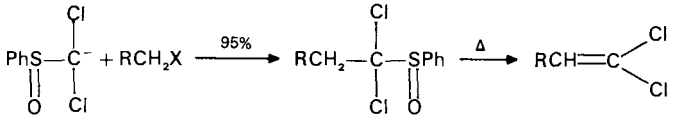
SCHEME 6

the presence of bases B (powdered NaOH in DMSO, NaOH in liquid ammonia, Bu_4NOH in *o*-dichlorobenzene or 50% aq NaOH + Bu_4NHSO_4 in benzene) to give the corresponding sulphoxides **322** in yields of 45–68% via the so-called 'vicarious substitution'[407] (equation 177). Nitrobenzyl phenyl sulphoxides serve as a source of a variety of nitroarenes (e.g. equation 178).

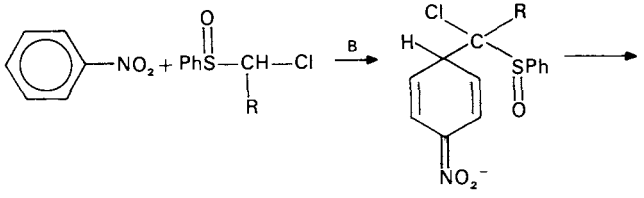
Carey and Hernandez have reported that phenyl trimethylsilylmethyllithio sulphoxide reacts with alkyl iodides to give the corresponding phenyl α-trimethylsilylalkyl sulphoxides[166] (equation 179).



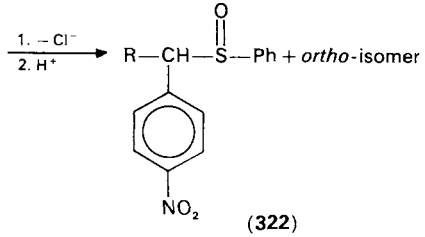
(175)



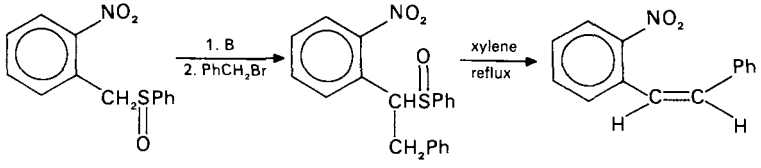
(176)



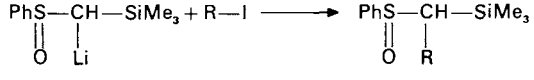
(177)



(322)



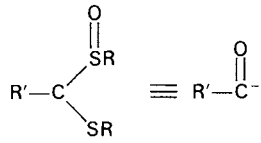
(178)



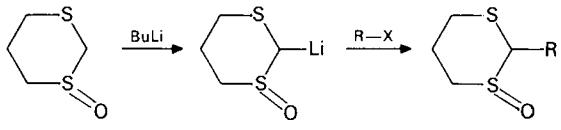
(179)

From the synthetic point of view the most important α-sulphinyl carbanions are the anions derived from dithioacetal *S*-oxides which may be considered as synthons of acyl

anions (for reviews see References 408 and 409).



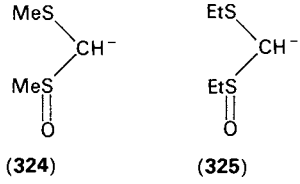
Carlson and Helquist[410] were the first to perform the alkylation of 2-lithio 1,3-dithian-*S*-oxide **323** (equation 180). The yields of this reaction appeared, however, to be low. In spite of the fact that dithian-*S*-oxides have been intensively investigated[268,411], their synthetic applications are rather limited.



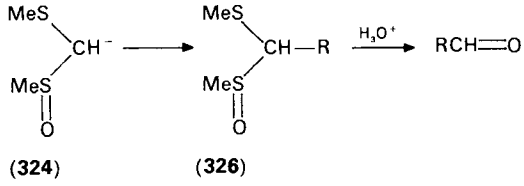
(180)

(236) **(323)**

The anions of alkyl alkylthiomethyl sulphoxides have found a much broader application. Methyl methylthiomethyl sulphoxide **324** was first introduced by Ogura and Tsuchihashi in 1971[412] and ethyl ethylthiomethyl sulphoxide **325** was synthesized by Schlessinger and coworkers in 1973[413]. Ogura and Tsuchihashi performed alkylation of **324** and obtained a series of substituted dithioacetal monoxides **326** which were then hydrolysed to the corresponding aldehydes (equation 181; Table 17)[412].



(324) **(325)**



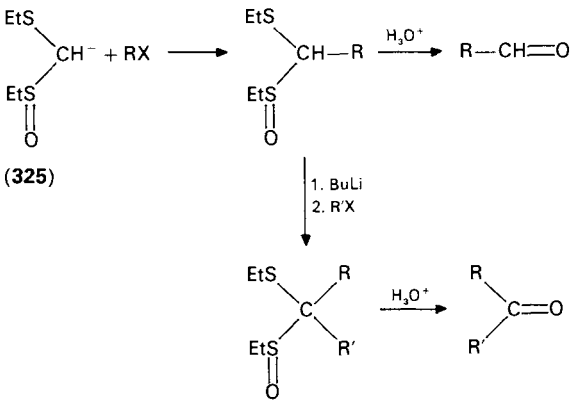
(181)

(324) **(326)**

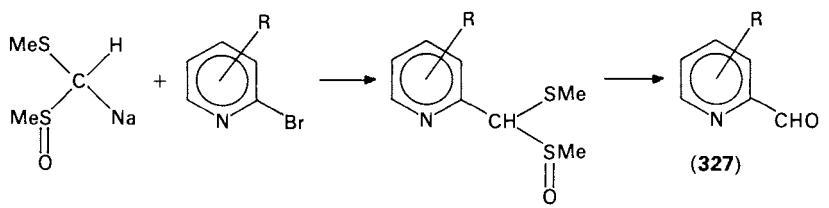
TABLE 17. Alkylation of the methyl methylthiomethyl sulphoxide anion **324**

Halide	Yield of sulphoxide **326** (%)	Yield of aldehyde (%)
MeI	92	84
n-C_4H_9I	72	91
$PhCH_2Br$	92	88
p-$BrC_6H_4CH_2Br$	37	88

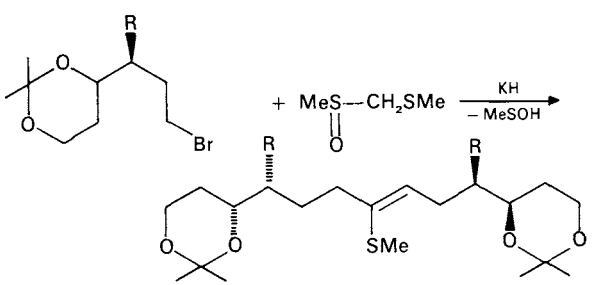
Schlessinger and coworkers[413] claim that the use of ethyl ethylthiomethyl sulphoxide **325** leads to much better yields of the alkylation products. In fact, all the alkylated products were obtained from **325** in yields exceeding 95%. Moreover, the anion **325** may undergo a double alkylation, which enables one to obtain not only aldehydes but also the corresponding ketones (equation 182). Schill and Jones performed a similar cycle of reactions using sodium hydride as a base[29]. Newcome and coworkers reacted methyl methylthiosodiomethyl sulphoxide with bromopyridines and obtained, after hydrolysis, the corresponding pyridine aldehydes **327**[414] (equation 183). Evans and colleagues utilized the alkylation of **324** as a key reaction in their synthesis of the ionophore antibiotic A-23187 (equation 184)[415]. Marshall and Wuts described a method of the synthesis of hexahydronaphthalenol **328** which involves the alkylation of **325**[416] (equation 185). Dithioacetal *S*-oxides undergo easily cycloalkylation reaction when reacted with α,ω-dihalogenoalkanes[417–419] (equations 186, 187). This reaction has been applied to the synthesis of optically active 4-hydroxycyclopentenone **329**[420] (equation 188).



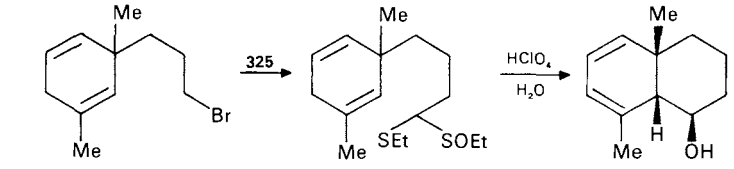
(182)



(183)

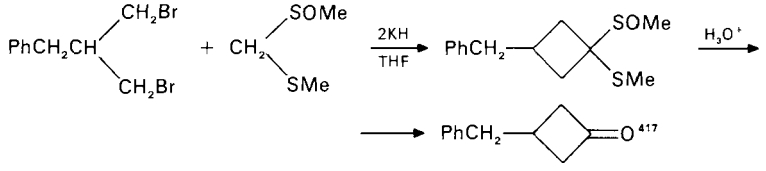


(184)

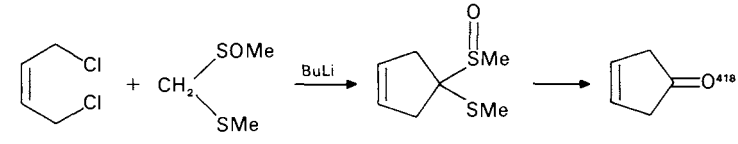


(185)

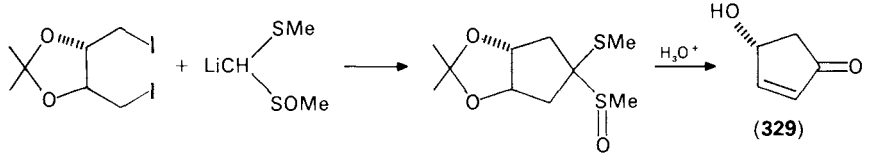
(328)



(186)



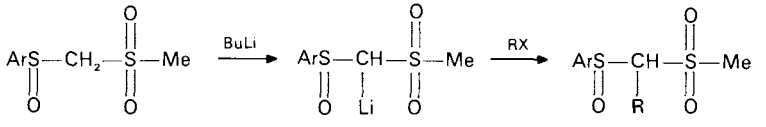
(187)



(329)

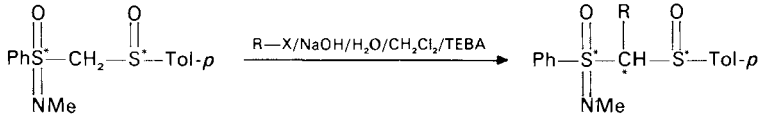
(188)

Similarly to simple sulphoxides, aryl methylsulphonylmethyl sulphoxides **330** undergo facile alkylation[164] (equation 189). Annunziata and Cinquini have used a chiral analogue of sulphonyl sulphoxides, i.e. phenyl *p*-tolylsulphinylmethyl sulphoximine **297** having two chiral moieties, both capable of inducing optical activity at the α-carbon atom[366] (equation 190). The reaction of the diastereoisomerically pure **297** with alkyl halides was performed under phase-transfer catalytic conditions and resulted in a high asymmetric induction on the α-carbon atom (Table 18). It is interesting to note that the sulphinyl group in **297** exerts the stronger effect on asymmetric induction[366].



(189)

(330)



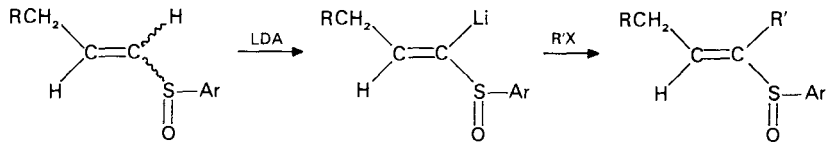
(190)

(297)

TABLE 18. Asymmetric alkylation of **297**

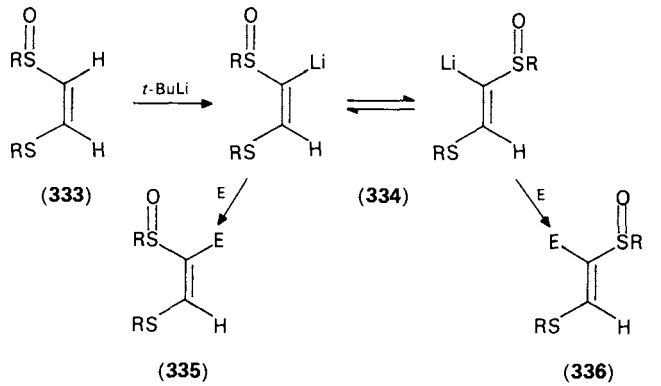
Substrate **297**	Alkyl halide	Yield, alkylated product (%)	Diastereoisomeric ratio
(+)-(*S*,*S*)	$H_2C{=}CH{-}CH_2Br$	93	100:0
(−)-(*S*,*R*)	$H_2C{=}CH{-}CH_2Br$	87	83:17
(+)-(*S*,*S*)	$PhCH_2Br$	77	100:0
(−)-(*S*,*R*)	$PhCH_2Br$	79	80:20
(+)-(*S*,*S*)	$HC{\equiv}C{-}CH_2Br$	91	100:0
(−)-(*S*,*R*)	$HC{\equiv}C{-}CH_2Br$	73	100:0
(+)-(*S*,*S*)	EtBr	80	100:0
(−)-(*S*,*R*)	EtBr	82	80:20
(+)-(*S*,*S*)	EtI	70	100:0
(+)-(*S*,*S*)	*n*-BuBr	30	100:0

As mentioned above, 1-alkenyl aryl sulphoxides can effectively be α-lithiated by treatment with a slight excess of LDA in THF at −78°. The 1-(arylsulphinyl)alkenyllithium reagents **331** so generated react cleanly and rapidly with a variety of electrophiles to give 1-substituted 1-alkenyl sulphoxides **332** in high yields (equation 191).



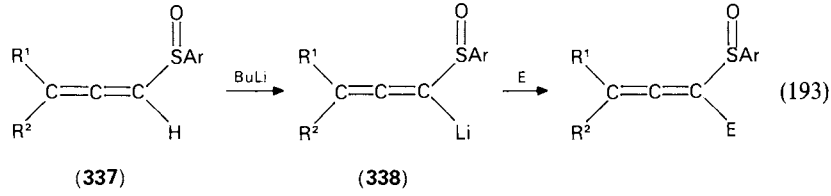
(**331**) (**332**) (191)

α-Sulphinylalkenyl carbanions appeared to be configurationally unstable. Hence, alkylation of *E*- and *Z*-1-alkenyl sulphoxides leads almost exclusively to the corresponding *E*-2-alkenyl sulphoxides[383–385]. The monosulphoxide **333** obtained from *Z*-dimercaptoethylene gives on treatment with *t*-BuLi α-deprotonated species **334**. The latter are configurationally labile and therefore their reaction with electrophiles affords the two products **335** and **336**[386] (equation 192). Allenyl sulphoxides **337** are also readily metallated at the α-position with BuLi to give the corresponding lithio-derivatives **338**



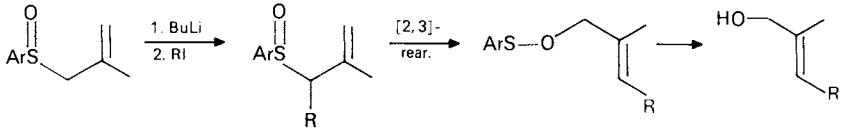
(**333**) (**334**) (**335**) (**336**) (192)

which may react with various electrophiles[387] (equation 193). α-Sulphinyl carbanions, generated easily from 2-alkenyl sulphoxides **339** by BuLi or LDA, can be alkylated. However, the resulting products **340** undergo a [2,3] sigmatropic rearrangement to the corresponding sulphenates **341**. The latter give, after desulphurization, a variety of allylic alcohols[421–426] (equation 194). This method has been applied to the synthesis of 3-hydroxycycloalkenes[423] (equation 195) and terpene alcohols[424] (equation 196).

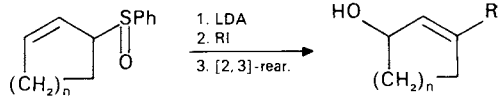


(193)

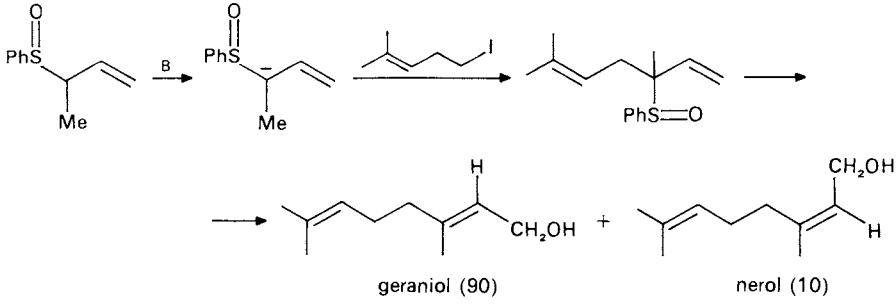
(337) (338)



(339) (340) (341) (194)



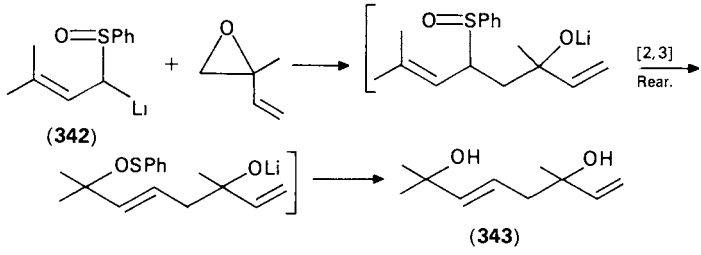
(195)



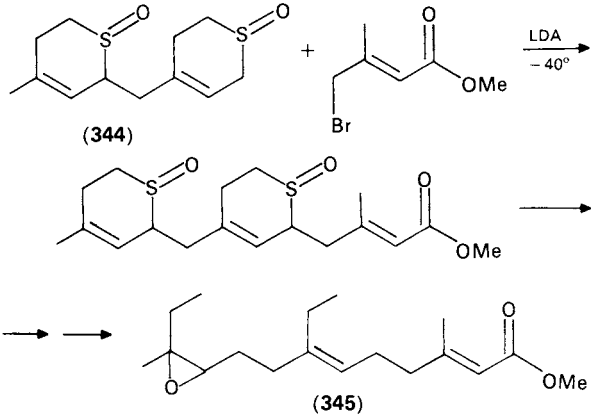
geraniol (90) nerol (10)

(196)

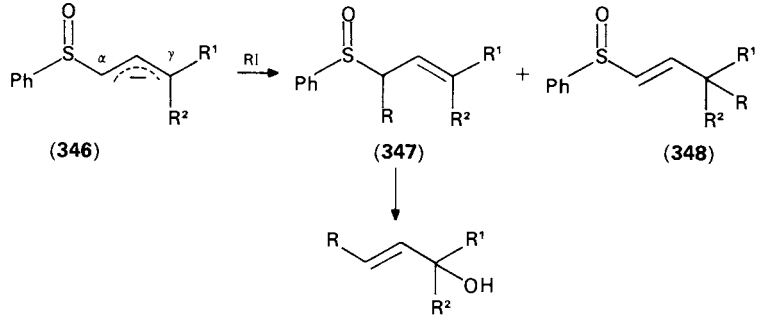
The reaction of the phenylsulphinyl allylic lithium α-carbanion **342** with oxiranes was found by Guittet and Julia to give, after rearrangement and desulphurization, dihydroxydienes **343**[427] (equation 197). Demoute and coworkers have described the alkylation reaction of a very sophisticated 2-alkenyl sulphoxide **344** as a part of the total synthesis of a juvenile hormone **345**[428] (equation 198). Since the allylic sulphoxide carbanion has an ambident character, the alkylation may occur sometimes also at the γ-position. This direction of alkylation is observed in the case of acyclic allylic sulphoxide anions **346**, and results in the formation of the corresponding allylic sulphoxide **347** and vinylic sulphoxide **348**[423] (equation 199).



(197)

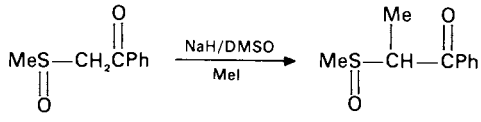


(198)



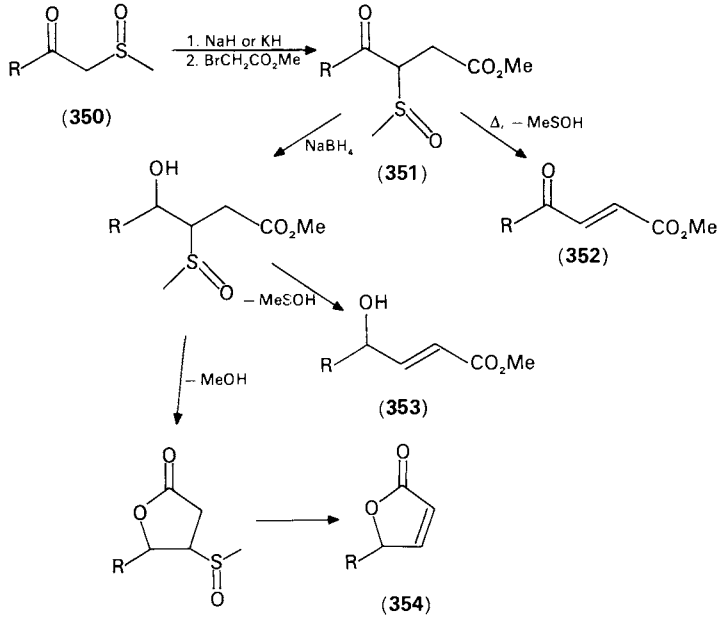
(199)

Alkylation of α-ketosulphoxides **349** creates many interesting synthetic possibilities, since it proceeds easily and allows one to introduce a large number of substituents. The α-ketosulphoxide anion is usually generated by means of sodium or potassium hydride[429] (equation 200). It is also possible to carry out the alkylation of α-ketosulphoxides under phase transfer catalysis conditions, using the $CH_2Cl_2/Bu_4NHSO_4/NaOH$ aq system[430].



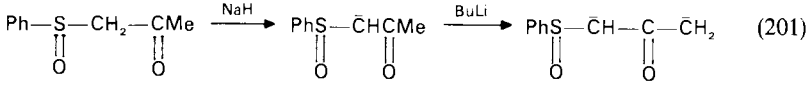
(200)

Bartlett has reported on the alkylation of α-ketosulphoxides **350** with methyl bromoacetate. The product obtained **351** was further transformed into β-keto or γ-hydroxy-α,β-unsaturated esters **352** and **353** and butenolides **354** and other organic compounds[431] (Scheme 7). It is also possible to generate a dianion **355** from α-ketosulphoxides by a subsequent addition of NaH and BuLi[432–434] (equation 201). It undergoes exclusive alkylation at the γ-carbon atom and the α-phenylsulphinyl ketones formed undergo, in turn, a ready elimination of benzenesulphenic acid affording alkyl vinyl ketones[433,434]. The generality of this approach is illustrated by the examples collected in Table 19 (see equation 202 in the table).



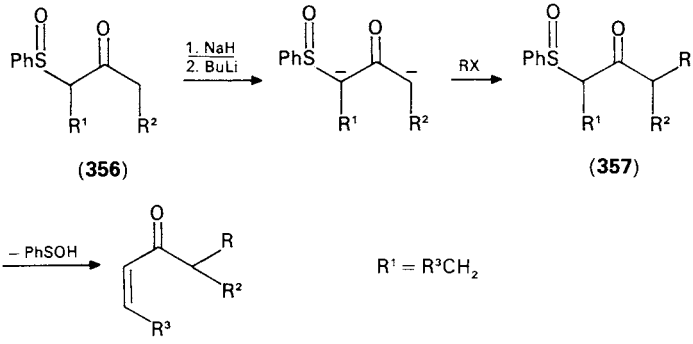
SCHEME 7

The anions derived from α-sulphinyl carboxylic esters **358** can also be easily generated by NaH or LDA[435–437]. Their reaction with alkyl halides gives monoalkylated products **359** which can be transformed into α,β-unsaturated esters **360** (equation 203; Table 20). When a second equivalent of NaH and alkyl halide is added either in one step or in a two-step procedure, the α,α-dialkylated esters can be prepared[436]. The reaction of the anions of α-sulphinyl carboxylic esters with π-allylpalladium complexes **361** (directly available from the corresponding olefins) leads to substitution at the allylic position of an olefin[437–439] (equation 204). In sharp contrast to the highly stereospecific behaviour of the methylene protons of benzyl methyl sulphoxide, the reactivity of the two diastereotopic methylene protons in arylsulphinylacetates is comparable. Solladie and coworkers[367] have investigated the alkylation of optically active *t*-butyl *p*-tolylsulphinylacetate and α-substituted



(201)

TABLE 19. Alkylation of the dianions of α-ketosulphoxides **356**



(202)

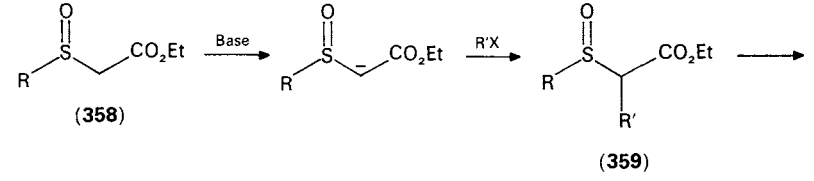
R^1	R^2	R—X	Yield of **357** (%)	Refs.
H	H	n-$C_6H_{13}Br$	79	432
H	H	$C_6H_5CH_2Br$	73	432
H	H	$CH_2{=}CHCH_2Br$	64	432
CH_3	H	$C_6H_5CH_2Br$	72	433
CH_3	H	MeI	65	433
CH_3	H	n-BuI	84	433
CH_3	H	Geranyl chloride	71	433
CH_3	H	$CH_3C(Cl){=}CHCH_2Cl$	70	433
CH_2—CH_2		$C_6H_5CH_2Br$	50	434
CH_2—CH_2		n-BuI	65	434
CH_2—CH_2		EtI	60	434
CH_2—CH_2		$CH_3C(Cl){=}CHCH_2$— Cl	34	434

TABLE 20. Alkylation of α-sulphinyl carboxylic esters **358**

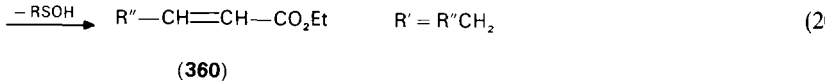
R	R′	Base	Yield of **359**	or **360**	Refs.
CH_3	n-Pr	NaH/DMSO	60		436
CH_3	n-Bu	NaH/DMSO	54		436
CH_3	CH_2Ph	NaH/DMSO	73		436
CH_3	Et	NaH/DMSO	82		436
CH_3	CH_2CO_2Et	NaH/DMSO	65		
Ph	CH_2Ph	NaH or LDA in HMPT		30	437
Ph	$MeO_2CCH_2(CH_2)_4$	NaH or LDA in HMPT		82	437
Ph	$(CH_2)_9$	NaH or LDA in HMPT		80	442

analogues (+)-(*R*)-**298** and found that the stereoselectivity of the alkylation is very poor, being lower than 42:58. Moreover, the alkylation has been found to proceed only when BuLi was used as a base and methyl iodide as an alkylating agent[367].

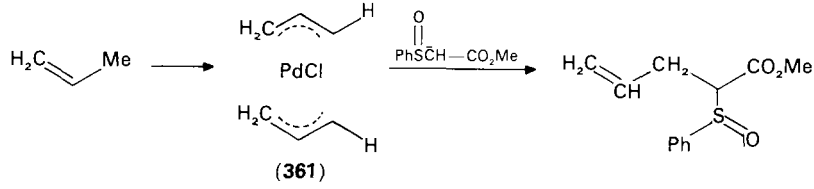
The dianion of 2-carboxyethyl phenyl sulphoxide **362** undergoes alkylation at the α-position to the sulphinyl group[440,441] (equation 205).



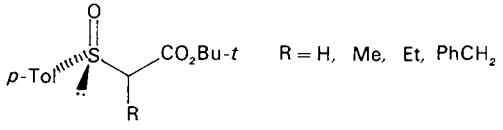
(358) (359)



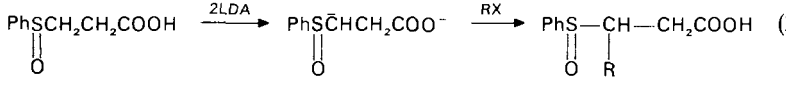
(360) (203)



(361) (204)



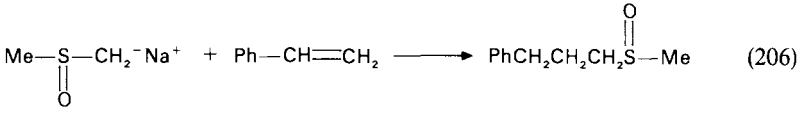
(+)-(*R*)-(**298**)



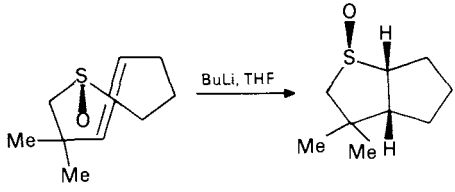
(**362**) (205)

c. Michael addition of α-sulphinyl carbanions. The addition of a variety of α-sulphinyl carbanions to activated alkenes can be easily achieved. Thus, methylsulphinylmethyl carbanion obtained from dimethyl sulphoxide adds even to such unusual Michael acceptors as styrenes (equation 206), although in some cases undesired side-reactions may prevail[442-444]. Treatment of *E*-homoallylic eight- to ten-membered ring sulphoxides with BuLi in THF results in a transannular addition of the α-sulphinyl carbanion generated to the *E*-double bond, leading to bicyclic products[445] (equation 207). Alkynes react with α-sulphinyl carbanions to yield 2-alkenyl sulphoxides **363**[446] (equation 208). α-Sulphinyl carbanions add to unsaturated ketones in a 1,4-manner, leading to γ-sulphinyl ketones **364**[447-449] (equation 209). Boger and Mullican have exploited this reaction, followed by a subsequent aldol condensation, for the synthesis of annelated phenols[447] **365** (equation 210). Hauser and Rhee used the reaction for the synthesis of regioselectively constructed naphthalenes[448] and anthracenes **366**[449] (equation 211). The reaction of α-sulphinyl carbanions with α,β-unsaturated esters proceeds in a similar way[450,451]. Ghera and Ben-David have found that the conjugated addition of α-sulphinyl carbanions to ethyl

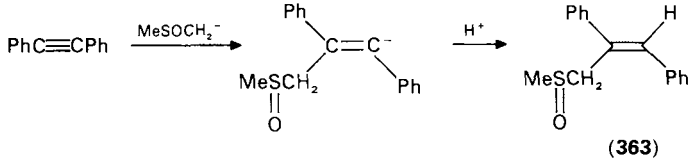
4-bromocrotonate is followed by displacement of bromide anion which affords cyclopropanecarboxylates **367**[452] (equation 212). The anions derived from (*R*) and (*S*) deacetoxycephalosporanate 1-oxides **368** afford, under very mild conditions, the Michael adducts with acrylonitrile[452] (equation 213). α-Ketosulphoxide carbanions **369** undergo facile Michael reaction with α,β-unsaturated esters, ketones and nitriles[453,454] (equation 214). When an excess of a base and the Michael acceptor is used, the products of a double addition are obtained[453]. The dianion of β-ketosulphoxides **370** reacts with α,β-



(206)

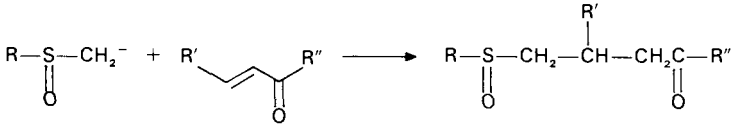


(207)



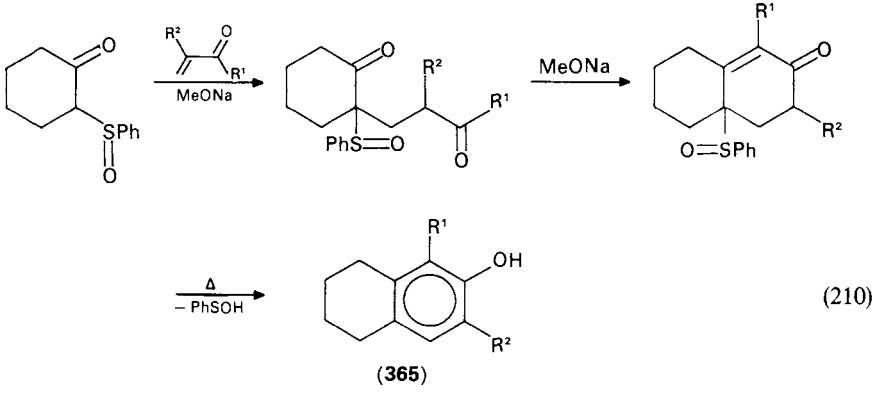
(208)

(**363**)



(209)

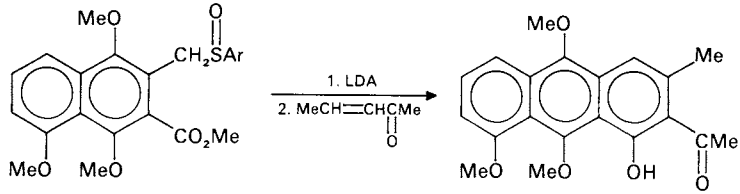
(**364**)



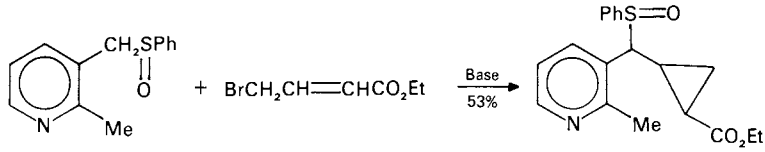
(210)

(**365**)

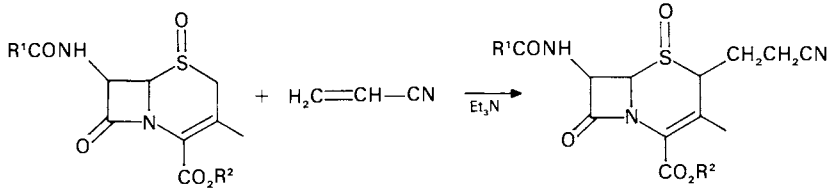
unsaturated carbonyl compounds to give the products of both 1,4- and 1,2-additions **371** and **372**, respectively[432] (equation 215). The carbanion derived from α-sulphinyl acetate



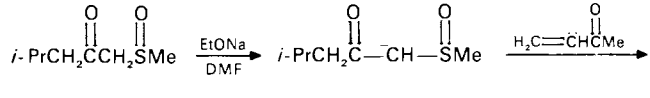
(**366**) (211)



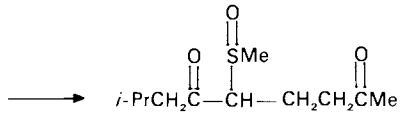
(**367**) (212)



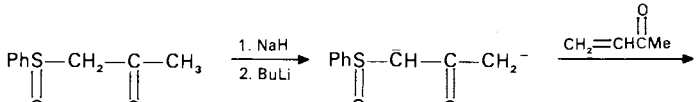
(**368**) (213)



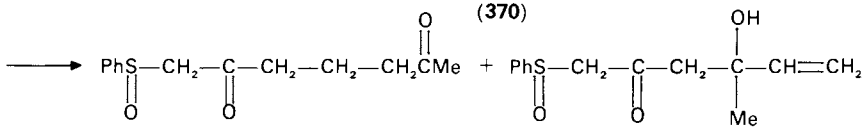
(**369**)



(214)

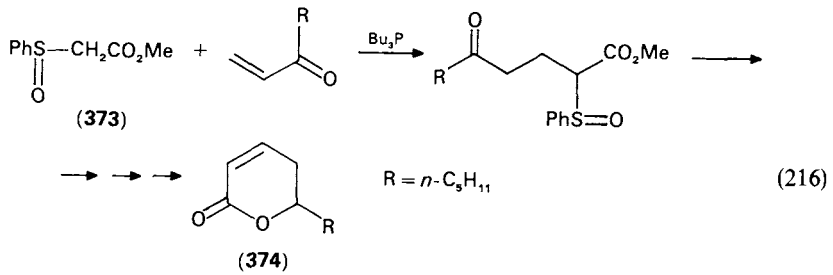


(**370**)

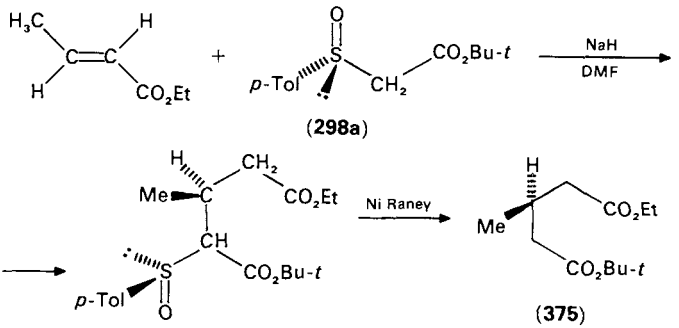


(**371**) (35%) (**372**) (65%) (215)

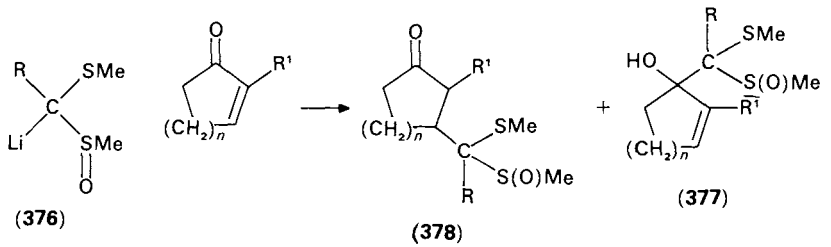
373 adds easily to α,β-unsaturated carbonyl compounds[436,455,456]. The reaction has been applied, among others, to the synthesis of α,β-unsaturated δ-lactones[456] **374** (equation 216). Michael addition of the enolate anion generated from (+)-(*R*) *t*-butyl α-*p*-toluenesulphinylacetate **298a** to α,β-unsaturated esters occurs with asymmetric induction and the optical purity of a newly created asymmetric carbon centre in **375** varies from 12 to 24%[457] (equation 217). In the reaction of the lithium salts of dithioacetal monoxides **376** with α,β-unsaturated carbonyl compounds the products of both 1,2-(**377**) and 1,4-(**378**) additions are formed (equation 218; Table 21)[458].



(216)



(217)



(218)

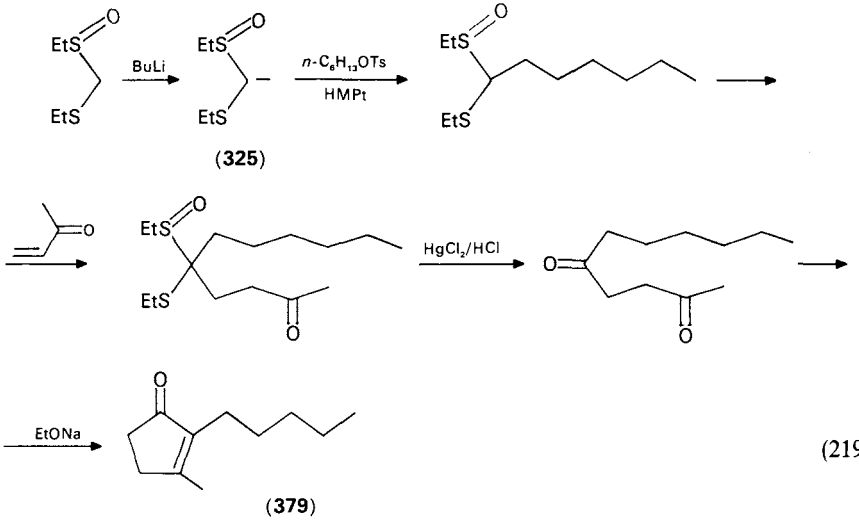
TABLE 21. Addition of dithioacetal monoxide lithium salts **376** to cyclic α,β-unsaturated ketones

R	R^1	*n*	Temp (°C)	Total yield (%)	**378**:**377** Ratio
H	H	1	−78	79	72:28
Me	H	1	−78	89	68:32
Me	H	1	0	68	28:72
H	CH_2Ph	1	−78	68	29:71
H	$(CH_2)_6CO_2Me$	1	−78	73	30:70
H	H	2	−78	75	9:91

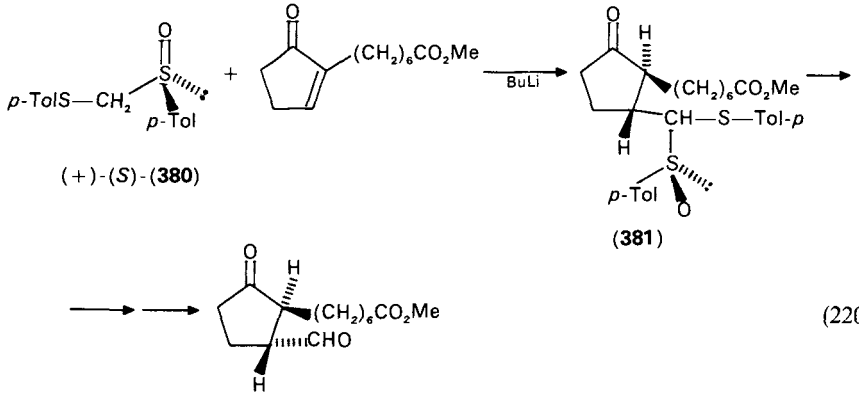
The ratio of the 1,2- to 1,4-adducts depends on several factors and the following general conclusions may be formulated[458]:

1. In the case of cyclohexenone the product of 1,2-addition always prevails.
2. In the case of cyclopentenone derivatives introduction of a substituent at the 2-position reduces the yield of 1,4-adduct.
3. Higher temperatures promote 1,2-addition.
4. The presence of HMPT promotes 1,4-addition[459].

Ethyl ethylthiomethyl sulphoxide anion **325** has been found to give better yield of 1,4-adducts compared with its methyl analogue[460]. This anion has been used by Schlessinger and coworkers as a key reagent in the synthesis of 1,4-dicarbonyl precursors of naturally occurring cyclopentenones, e.g. dihydrojasmone[461] **379** (equation 219). Michael addition of the anion of optically active (+)-(*S*)-*p*-tolyl *p*-tolylthiomethyl sulphoxide **380** to the properly substituted cyclopentenone constitutes an important step in the asymmetric synthesis of optically active cyclopentenone **381**, which is a precursor of 11-deoxy-ent-prostanoids[462] (equation 220). The reaction proceeds with a high β- and γ-asymmetric induction (92%), but with a poor α-stereoselection (52:48).

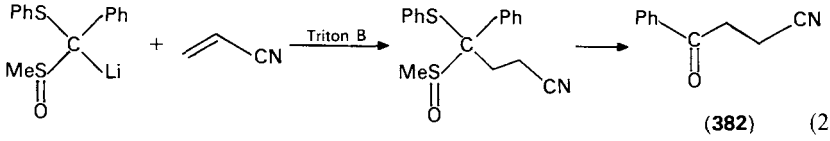


(219)

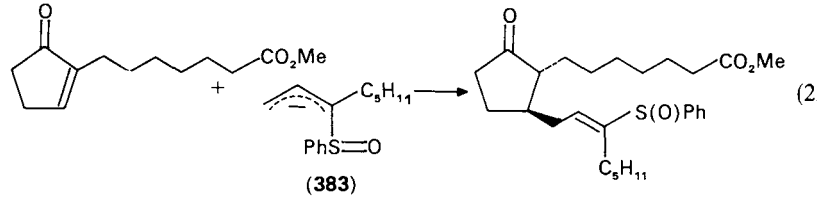


(220)

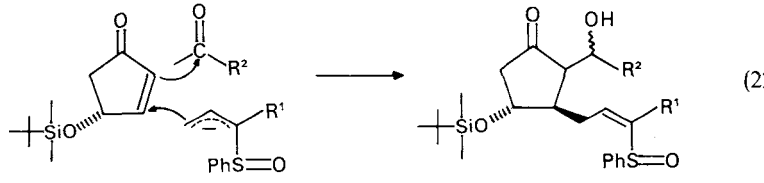
Dithioacetal monoxides undergo Michael addition to acrylonitrile. The addition products are easily converted into γ-ketonitriles[171] **382** (equation 221). Benzenesulphinyl allylic carbanions **383** derived from the corresponding allylic sulphoxides react selectively at the γ-position with a variety of cycloalkenones to give the 1,4-adducts[463–466] (equation 222). Recently, Nokami and coworkers have synthesized some prostaglandin analogues via a three-component coupling process involving 1,4-addition of phenylsulphinyl allylic carbanion (equation 223)[467].



(**382**) (221)

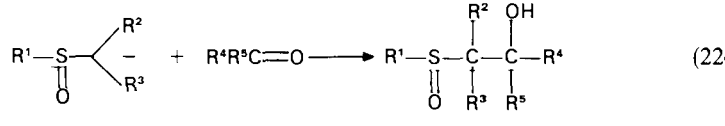


(**383**) (222)



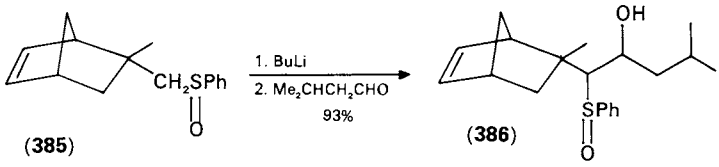
(223)

d. Hydroxyalkylation of α-sulphinyl carbanions and synthesis of vinyl sulphoxides. α-Sulphinyl carbanions undergo an aldol-type condensation with carbonyl compounds affording β-hydroxyalkyl sulphoxides **384** (equation 224).



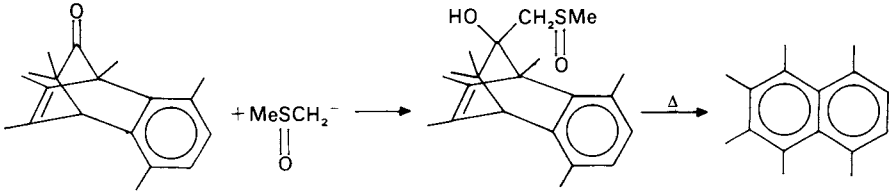
(**384**) (224)

Corey and Chaykovsky were the first to investigate the reaction of dimethyl sulphoxide anion (dimsyl anion) with aldehydes and ketones[400,401]. They found that the reaction with non-enolizable carbonyl compounds results in the formation of β-hydroxyalkyl sulphoxides in good yields (e.g. Ph_2CO—86%, PhCHO—50%). However, with enolizable carbonyl compounds, particularly with cycloalkanones, poor yields of hydroxyalkyl products are observed (e.g. camphor—28%, cyclohexanone—17%, but cycloheptanone—unusually—64%)[401]. The reaction with cyclopentanone does not afford the desired β-hydroxy compound at all[468], while the reaction of the carbanion of sulphoxide **385** with isobutyraldehyde gives the corresponding β-hydroxy sulphoxide **386**[469] in high yield (equation 225).

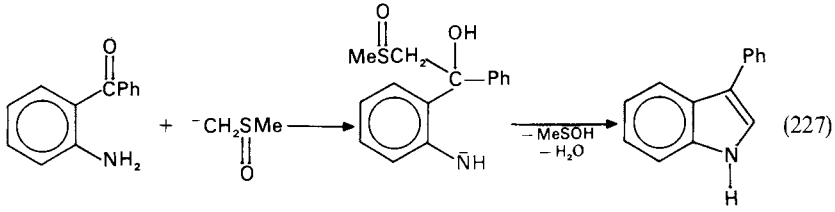


(385) (386) (225)

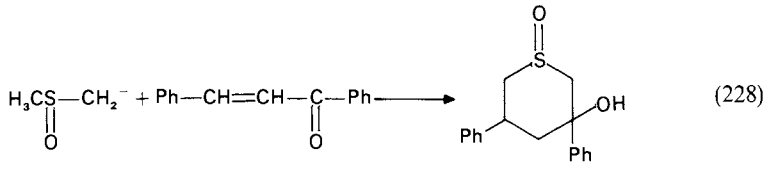
The reaction has been applied for the synthesis of a variety of β-hydroxyalkyl sulphoxides, which then served as the source of other organic compounds. Hart and Oku synthesized in this way polymethylnaphthalenes **387**[470] (equation 226). 2-Aminobenzophenone reacts with dimsyl anion to give, after subsequent condensation and elimination of methanesulphenic acid, 3-phenylindole **388**[471] (equation 227). 3-Hydroxy-3, 5-diphenylthiane-1-oxide **389** can be obtained from dimsyl anion and benzalacetophenone via a Michael addition and subsequent intramolecular aldol-type condensation[472] (equation 228). Smith and coworkers reacted the carbanion of *tert*-butyl isopropyl sulphoxide **390** with diaryl ketones and obtained the corresponding β-hydroxy sulphoxides **391** which were then transformed via β-sultines **392** into substituted olefins[473] (equation 229). 4*H*-1, 4-Benzothiazine 1-oxides **394** are readily prepared via lithiation of 2-acylaminophenyl sulphoxides **393** followed by subsequent annelation[474] (equation 230). A very efficient conversion of aldehydes and ketones to the one-carbon homologous allyl alcohols (equation 231) involves an initial reaction of sulphoxide anions with carbonyl compounds[475] (compare References 520 and 521). It is interesting to note that γ-lactones, e.g. **395**, react with dimsyl anion without opening of the lactone ring and give the corresponding β-hydroxy sulphoxides **396**[476] (equation 232).



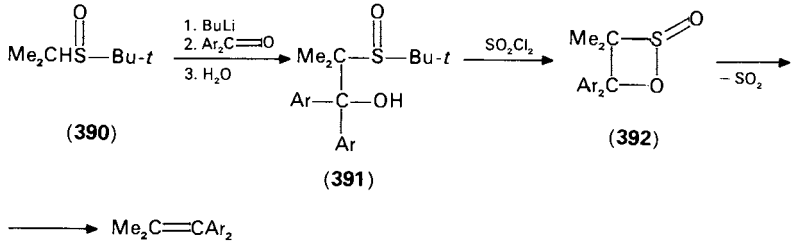
(387) (226)



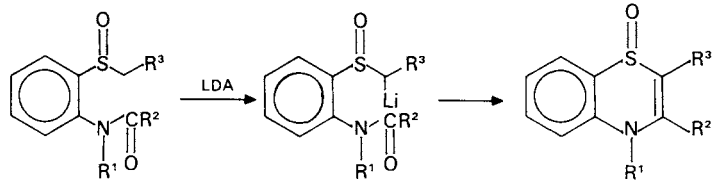
(388) (227)



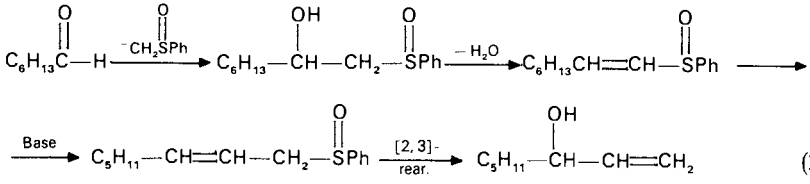
(389) (228)



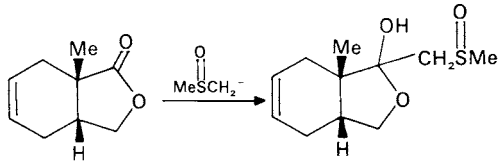
(390) (391) (392) (229)



(393) (394) (230)

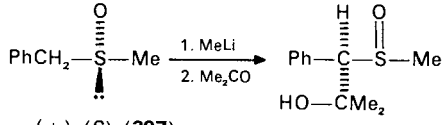


(231)

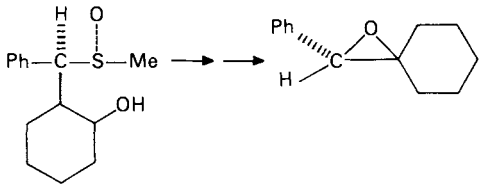


(395) (396) (232)

Durst and coworkers were the first to report the condensation of chiral α-sulphinyl carbanions with carbonyl compounds[477]. They found that metallation of (+)-(*S*)-benzyl methyl sulphoxide **397** followed by quenching with acetone gives a mixture of diastereoisomeric β-hydroxy sulphoxides **398** in a 15:1 ratio (equation 233). The synthesis of optically active oxiranes was based on this reaction (equation 234). In this context, it is interesting to point out that condensation of benzyl phenyl sulphoxide with benzaldehyde gave a mixture of four β-sulphinyl alcohols (40% overall yield), the ratio of which after immediate work-up was 41:19:8:32[478].

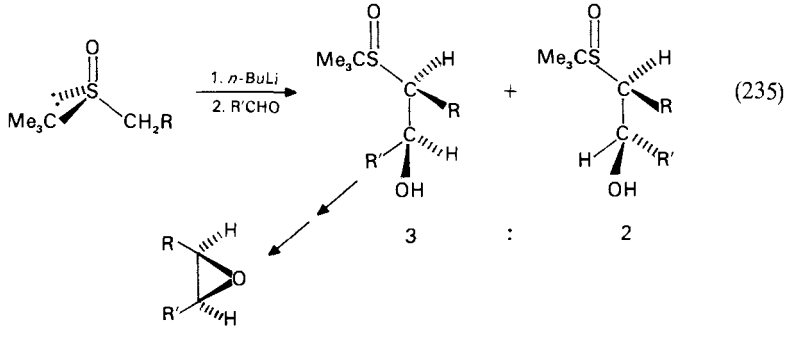


(+)-(*S*)-(**397**) (*R*,*S*)-(**398**) (233)

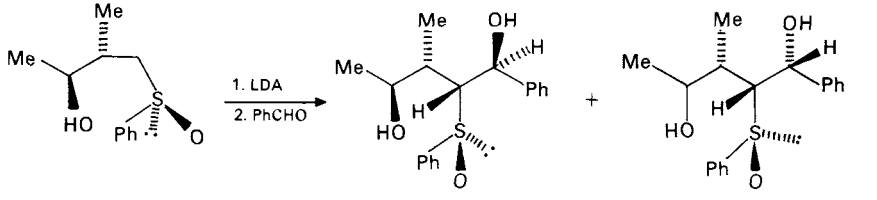


(234)

Condensation of optically active alkyl *t*-butyl sulphoxides with aldehydes gives the corresponding product in a diastereoisomeric ratio 3:2. This reaction has been used for the stereospecific synthesis of optically active oxiranes, among them, a sex-attractant (+)-disparlure[479] (equation 235). The reaction of aldehydes with γ-hydroxyalkyl sulphoxide **399** having three chiral centres provides useful methodology for generating 1,2- and 1,3-asymmetry[480]. The diastereoisomeric ratio observed upon rapid deprotonation of **399** with LDA at −78 °C, quenching with benzaldehyde and work-up at −78 °C, was 91:9 (equation 236). However, the diastereoisomer of **399** with the opposite configuration at sulphur leads to a mixture of four possible stereoisomers in a 67:17:13:3 ratio. This indicates that the carbanion configuration is dependent on the asymmetry at the β-position as well as on the chirality of sulphur[480].



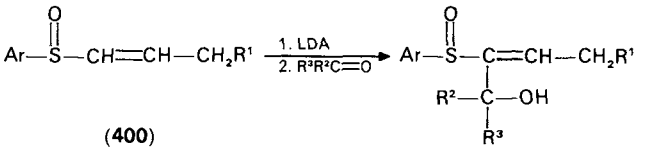
(235)



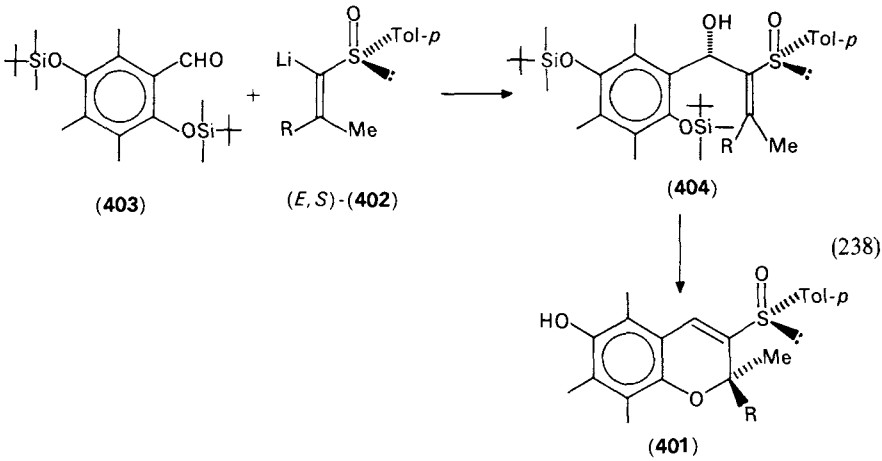
(**399**) 91 : 9 (236)

The carbanions of 1-alkenyl sulphoxides **400** also react with carbonyl compounds to give the corresponding condensation products[384] (equation 237). Solladie and Moine have used this type of reaction in their enantiospecific synthesis of the chroman ring of α-tocopherol **401**. Addition of the lithio reagent **402** to the aldehyde **403** affords the allylic alcohol **404** in 75% yield as a sole diastereoisomer[481] (equation 238).

α-Lithio derivatives of optically active *E*-β-silyloxy-α,β-unsaturated sulphoxides **405** were reacted with gaseous carbon dioxide, followed by the introduction of *p*-toluenesulphonic acid to allow desilylation and cyclization, affording 2-*p*-toluenesulphinylbutenolides **406** in 50–65% yield[482] (equation 239).

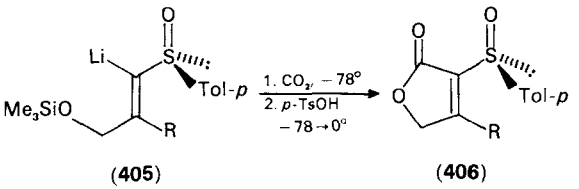


(400) (237)



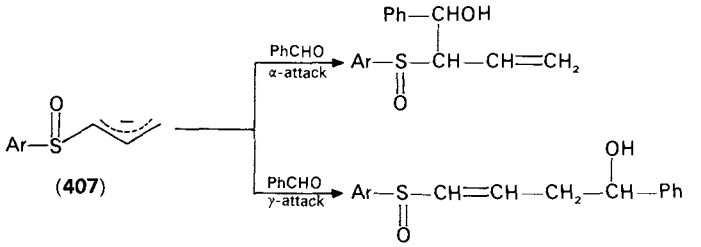
(403) (*E*,*S*)-(402) (404) (238)

(401)



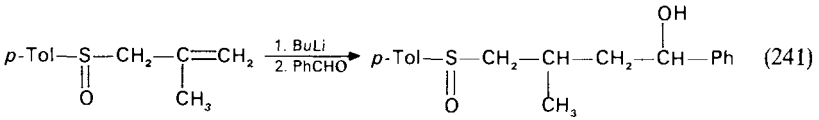
(405) (406) (239)

Addition of the anions of allyl aryl sulphoxides **407** to benzaldehyde proceeds readily and affords a mixture of products resulting from both α- and γ-attack of the allyl anion[483] (equation 240). In the case of the α-attack a mixture of all four possible diastereoisomers is observed, while in the case of the γ-attack, the diastereoisomer ratio exceeds 2:1.



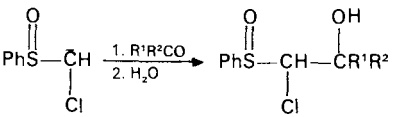
(407) (240)

In contrast, the anion of *p*-tolyl (2-methyl)-2-propenyl sulphoxide **408** reacts with benzaldehyde exclusively at the γ-position[426] (equation 241).

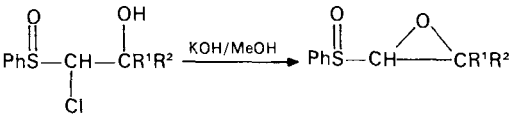


(408) (241)

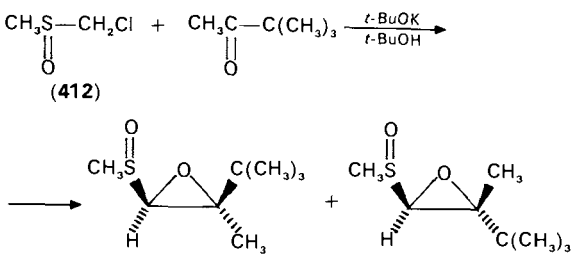
Reaction of the carbanion of chloromethyl phenyl sulphoxide **409** with carbonyl compounds yields the corresponding β-hydroxy adducts **410** in 68–79% yield. Each of these compounds appears to be a single isomer[484] (equation 242). Treatment of adducts **410** with dilute potassium hydroxide in methanol at room temperature gives the epoxy sulphoxides **411** (equation 243). The ease of this intramolecular displacement of chloride ion contrasts with a great difficulty in displacing chloride ion from chloromethyl phenyl sulphoxide by external nucleophiles[484]. When chloromethyl methyl sulphoxide **412** is reacted with unsymmetrical ketones in the presence of potassium *tert*-butoxide in *tert*-butanol oxiranes are directly formed as a mixture of diastereoisomers[485] (equation 244). α-Sulphinyl epoxides **413** rearrange to α-sulphinyl aldehydes **414** or ketones, which can be transformed by elimination of sulphenic acid into α,β-unsaturated aldehydes or ketones[486–489] (equation 245). The lithium salts (**410a**) of α-chloro-β-hydroxyalkyl



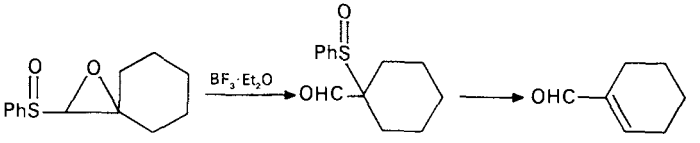
(409) (410) (242)



(410) (411) (243)

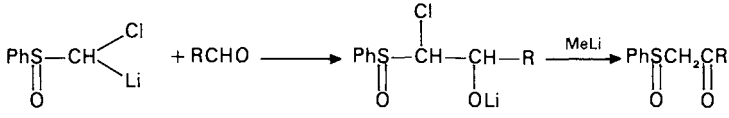


(412) 3 1 (244)



(413) (414) (245)

sulphoxides **410** obtained from the condensation of α-lithio-α-chloroalkyl sulphoxides **409** with carbonyl compounds can be transformed into various organic compounds[490,491]. Of interest is that elimination of chloride anion by base used in excess leads to α-sulphinylketones **415**[492] (equation 246).

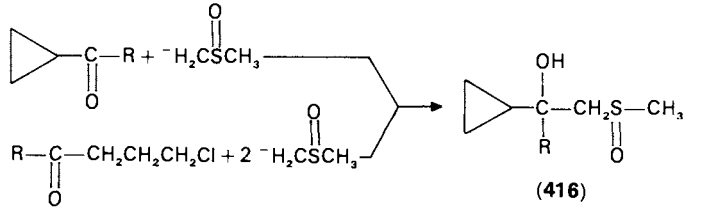


(246)

(409) **(410a)** **(415)**

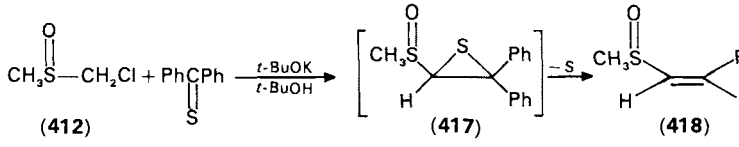
2-Cyclopropyl-2-hydroxyalkyl sulphoxides **416** can be obtained either by addition of an α-sulphinyl carbanion to a cyclopropyl ketone, or from alkyl 3-chloropropyl ketones and two moles of an α-sulphinyl carbanion[493] (equation 247).

Reaction of thiobenzophenone with chloromethyl methyl sulphoxide **412** does not give the expected 2,2-diphenyl-3-methylsulphinylthiirane **417**, but the α,β-unsaturated sulphoxide **418** in a 38% yield[485] (equation 248).



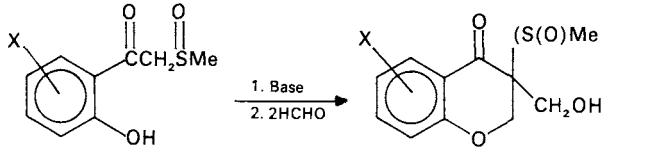
(247)

(416)



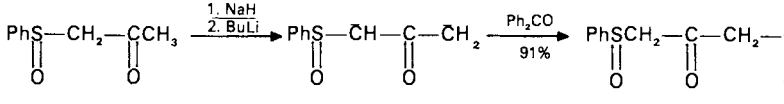
(412) **(417)** **(418)**

α-Ketosulphoxides react with aldehydes in the presence of base to give the expected α-condensation products. For example, when *o*-hydroxy-ω-(methanesulphinyl) acetophenones **419** were allowed to react with two moles of formaldehyde in the presence of base, 3-(hydroxymethyl)-3-(methanesulphinyl)-4-chromanones **420** were obtained as a result of the α-condensation[494] (equation 249). A dianion of phenylsulphinylacetone **355** reacts with carbonyl compounds at the more reactive γ-position[432,495] (equation 250).



(249)

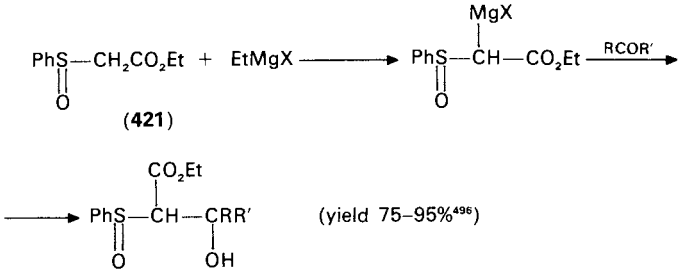
(419) **(420)**



(355)

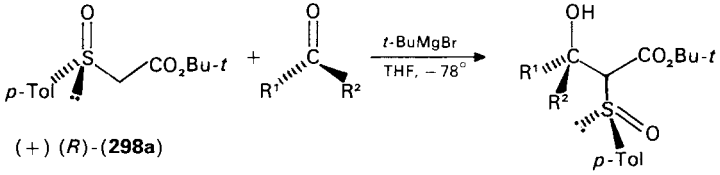
(250)

Reaction of α-sulphinyl carboxylic esters **421** with carbonyl compounds has usually been performed using a Grignard reagent as a base. No condensation products are obtained using *t*-butyllithium or sodium hydride[367,496,497] (equation 251). The condensation products formed are convenient starting materials for the synthesis of α,β-unsaturated esters and β-ketones[497].

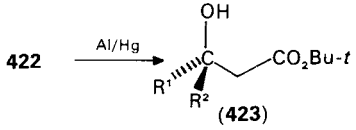


(421) (251)

Reaction of optically active α-sulphinyl acetate **298a** with prochiral carbonyl compounds proceeds with a high asymmetric induction[367,498,499], the degree of which depends on the nature of substituents at the carbonyl group (equation 252; Table 22)[498]. The β-hydroxy sulphoxides **422** formed may be transformed to optically active β-hydroxycarboxylic esters **423**[367] (equation 253) and optically active long-chain lactones **424**[499] (equation 254). Corey and coworkers have used this method to introduce a chiral centre at C-3 in their synthesis of maytansin[500], and Papageorgiou and Benezra for the synthesis of chiral α-hydroxyalkyl acrylates **425**[501] (equation 255).



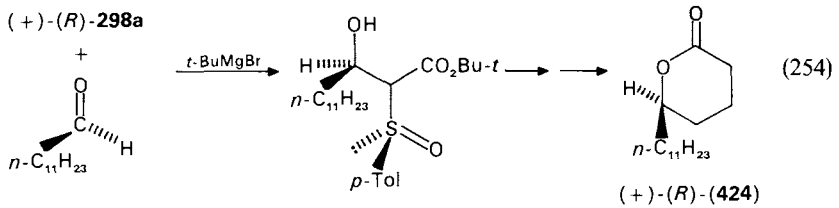
(+) (*R*)-(**298a**) (**422**) (252)



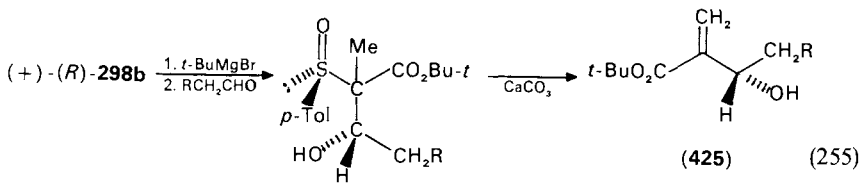
(**423**) (253)

TABLE 22. Reaction of *t*-butyl *p*-toluenesulphinylacetate **298a** with carbonyl compounds

R^1	R^2	Yield of **422** (%)	Asymmetric induction (%)
H	Ph	85	91
Me	Ph	75	68
Ph	CF_3	75	20
H	*n*-C_7H_{15}	80	86
Me	*c*-Hex	88	95

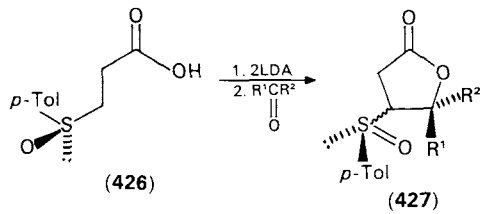


(254)



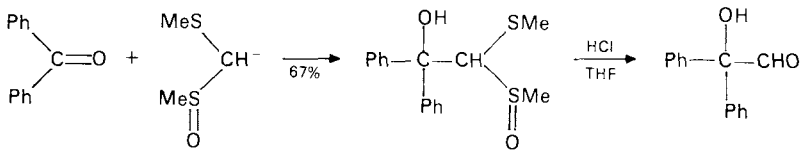
(255)

Addition of the dianion of β-sulphinylcarboxylic acids to carbonyl compounds leads to the formation of the corresponding hydroxy derivatives which undergo spontaneous cyclization to give γ-lactones[440]. Bravo and coworkers have found that when optically active (+)-(*R*)-3-(*p*-toluenesulphinyl)propionic acid **426** is used for this reaction, the corresponding diastereoisomeric β-sulphinyl-γ-lactones **427** are formed in a ratio which is dependent on the substituents in the carbonyl component[441,502,503] (equation 256).



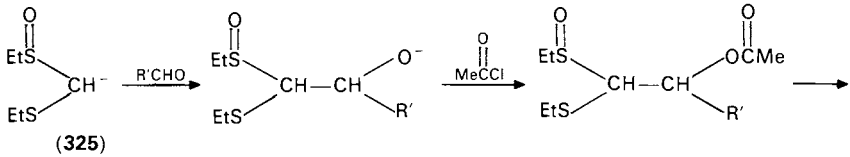
(256)

Dithioacetal monoxide anions react with carbonyl compounds in a similar way affording the corresponding α-hydroxy aldehyde dithioacetal oxides **428**. Ogura and Tsuchihashi, who performed this reaction for the first time using the anion of methyl methylthiomethyl sulphoxide **324**, obtained in this way a series of α-hydroxyaldehydes **429**[504] (equation 257).

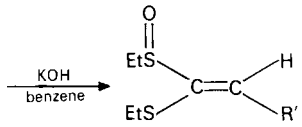


(257)

The use of ethyl ethylthiomethyl sulphoxide in this reaction leads to the desired addition products in much better yields (95–97%). These products were then converted into ketene dithioacetal monoxide derivatives **430** by a sequence of reactions (equation 258)[505]. Reaction of 2-lithio-1,3-dithiane-1-oxide with benzophenone affords a mixture of the diastereoisomeric tertiary alcohols **431** in a ratio which is temperature dependent (*cis*:*trans* changes from 3:1 at −78 °C to 1:1 at room temperature)[268].

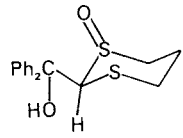


(325)



(430)

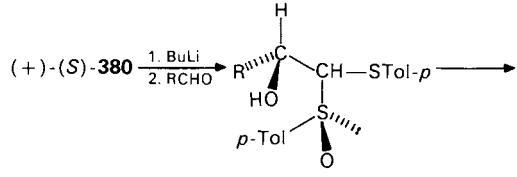
(258)



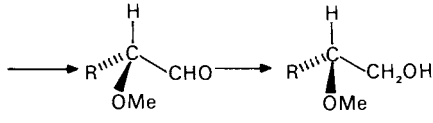
(431)

Condensation of the carbanion of optically active *p*-tolyl *p*-tolylthiomethyl sulphoxide **380** with benzaldehyde and phenylacetaldehyde produces the corresponding sulphoxides **432** which are converted into optically active α-methoxy aldehydes **433** and alcohols **434** with enantiomeric excess of 70% and 46%, respectively[506,507] (equation 259).

α-Sulphinyl carbanions have been used for the synthesis of vinyl sulphoxides. It was found that α-sulphinylacetates **435a** and α-ketosulphoxides **435b** easily undergo Knoevenagel condensation with aldehydes in the presence of piperidine to give the corresponding α,β-unsaturated sulphoxides **436** (equation 260; Table 23)[508,509]. The Knoevenagel condensation of α-sulphinylacetates with carbonyl compounds is also efficient when sodium hydride and zinc chloride are used[510].

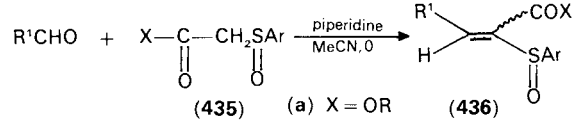


(432)



(433) (434)

(259)



(435) (a) X = OR (b) X = R (436)

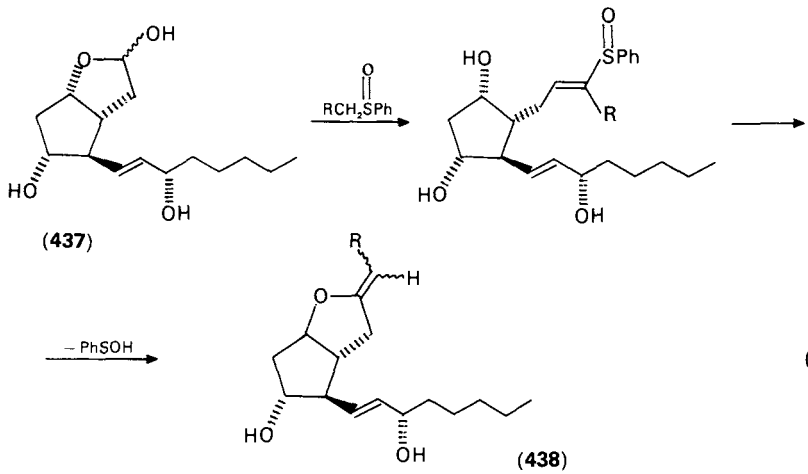
(260)

TABLE 23. Knoevenagel condensation of α-sulphinylacetates **435a** and α-ketosulphoxides **435b** with aldehydes

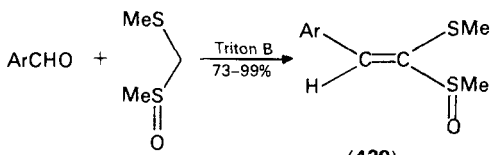
R^1	X	Ar	Yield (%)	Configuration of the product
n-Bu	OMe	*p*-ClC_6H_4	70	*E*
n-Bu	*t*-OBu	Ph	67	*E*
i-Pr	OMe	*p*-ClC_6H_4	90	*E*
Ph	OMe	Ph	85	*E*
n-Bu	Ph	Ph	61	*E*
n-Bu	Me	Ph	68	*Z*

The Knoevenagel condensation of α-lithiosulphoxides with hemiacetal **437** has been used to synthesize PGI_2 analogues **438**[511] (equation 261). The Knoevenagel-type condensation of dithioacetal monoxides with substituted benzaldehydes has been performed using Triton B as a base and gave the corresponding ketene dithioacetal monoxides **439**[512,513] (equation 262).

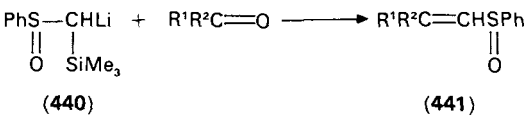
α-Lithio-α-trimethylsilyl sulphoxides **440** undergo the Peterson reaction with saturated or α,β-unsaturated carbonyl compounds to afford α,β-unsaturated sulphoxides **441** in 66–78% yield[166] (equation 263). The limitation of this approach to the synthesis of vinyl sulphoxide is the low or moderate chemical stability of the starting material **440**.



(261)

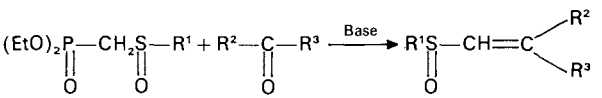


(262)



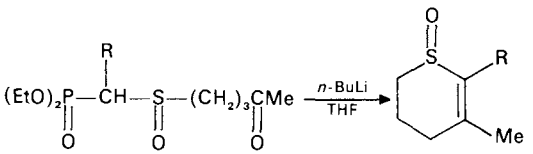
(263)

The Horner–Wittig reaction of α-phosphoryl sulphoxides **442**, which are chemically stable, results in the formation of α,β-unsaturated sulphoxides **443** in high yields[514,515] (equation 264). The reaction has been found to be non-stereoselective, mixtures of *E* and *Z* isomers being formed from aldehydes and unsymmetrical ketones[515–518]. In the case of aromatic aldehydes this reaction can also be advantageously performed in a two-phase catalytic system[516,517], even without the usual PTC catalysts[518] (Table 24). Intramolecular Horner–Wittig reaction of α-phosphoryl-δ-oxosulphoxides **444** leads to α,β-unsaturated cyclic sulphoxides **445**[519] (equation 265). Starting from optically active *O,O*-



(264)

(442) **(443)**



(265)

(444) **(445)**

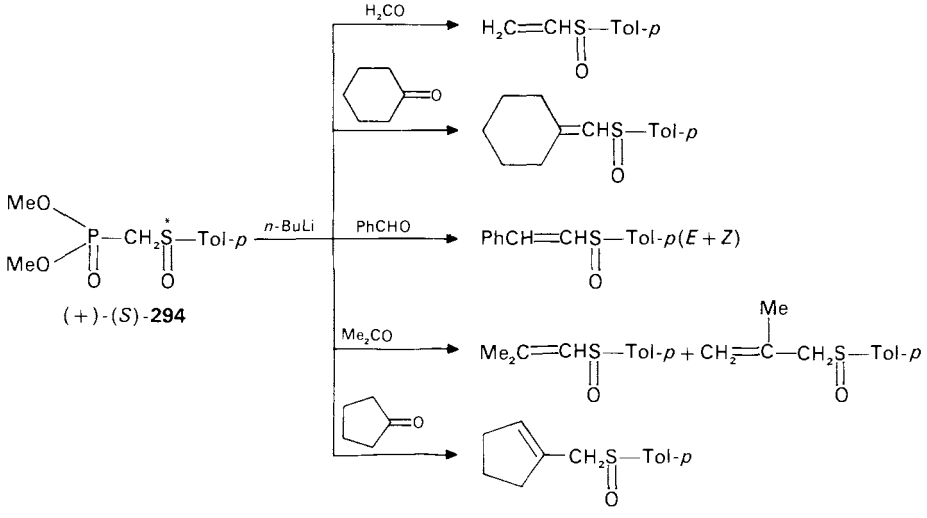
R = H, yield 60%
R = Me, yield 74%

TABLE 24. *Synthesis of vinyl sulphoxides* **443** *from α-phosphoryl sulphoxides* **442**

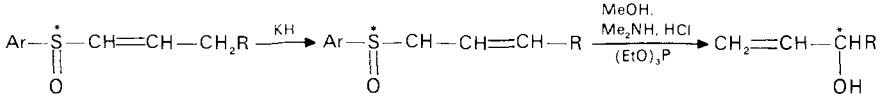
R^1	R^2	R^3	Base	Yield (%)	*E*:*Z* ratio	Refs.
Me	Ph	Ph	BuLi	84	—	515
Me	—$(CH_2)_4$—		BuLi	50	—	515
Me	—$(CH_2)_4$—		BuLi	81	—	515
Me	—$(CH_2)_6$—		BuLi	81	—	515
Me	H	Ph	BuLi	70	58:42	515
Me	H	2,4-$Cl_2C_6H_3$	BuLi	80	45:55	515
Me	H	*p*-MeC_6H_4	BuLi	72	54:46	515
Me	H	*p*-$Me_2NC_6H_4$	BuLi	75	82:18	515
Me	Me	Ph	BuLi	70	45:55	515
Me	Me	2,4-$Cl_2C_6H_3$	BuLi	51	27:73	515
Me	H	Ph	A[b]	51	70:30	516
Ph	H	Ph	A[b]	54	83:17	516
Ph	H	*p*-ClC_6H_4	A[b]	57		516
Ph	H	*p*-$MeOC_6H_4$	A[b]	48		516
Ph	H	Ph	B[b]	53	82:18	518
Me	H	Ph	B[b]	51	77:23	518
$CH=CR^2R^3$	H	Ph	A[b]	60	95:5[a]	517
$CH=CR^2R^3$	H	*p*-ClC_6H_4	A[b]	62	92:8[a]	517
$CH=CR^2R^3$	H	*p*-ClC_6H_4	A[b]	58	87:13[a]	519
$CH=CR^2R^3$	H	*p*$MeOC_6H_4$	A[b]	68	97:3[a]	517

[a] *E,E*:*E,Z* ratio.
[b] A: 50% NaOH/TEBA (PTC); B: 50% NaOH without catalyst.

dimethylphosphorylmethyl *p*-tolyl sulphoxide **294**, optically active vinyl sulphoxides have been obtained (Scheme 8)[265,520]. In the case of carbonyl compounds having a hydrogen atom in the α-position, allylic sulphoxides are also formed, however, with a great extent of racemization. Vinyl sulphoxides can be totally converted into allylic sulphoxides by means of a base, which has been applied to the synthesis of optically active allyl alcohols[520,521] (compare Reference 475; see equation 266).



SCHEME 8

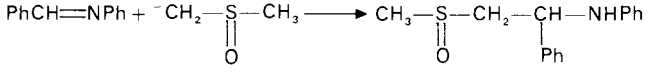


e.e. 0–60%

(266)

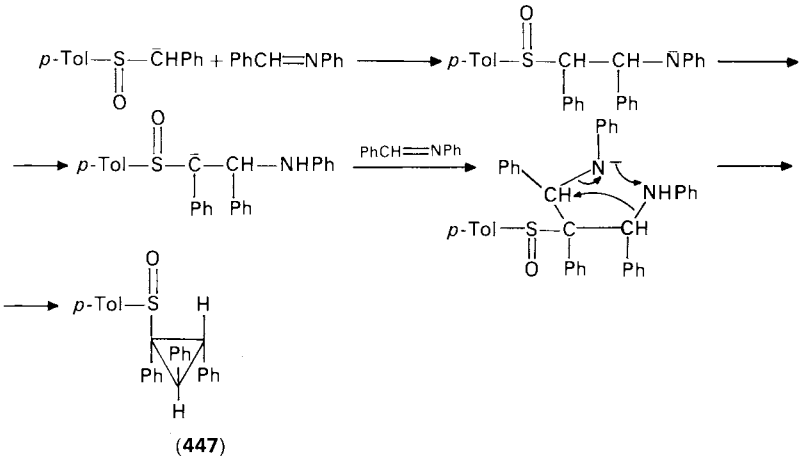
e. Aminoalkylation of α-sulphinyl carbanions. Aminoalkylation of α-sulphinyl carbanions takes place when they are treated with compounds having a double or triple carbon–nitrogen bond.

In this way benzalaniline reacts with dimsyl anion to give β-anilinosulphoxide **446** in 92% yield[401] (equation 267). Nudelman and Cram have found that the analogous reaction with the carbanion of benzyl *p*-tolyl sulphoxide is more complex and leads to the formation of substituted cyclopropyl sulphoxides **447** (equation 268)[522]. The carbanion derived from cyclohexanone dimethyldithioacetal *S*-oxide **448** gives β-mercaptoanilines derivatives on treatment with iminoketones and further elaboration[523] (equation 269).



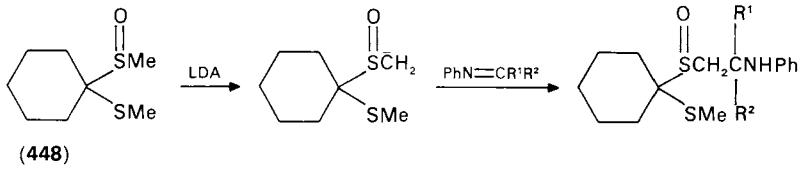
(267)

(446)

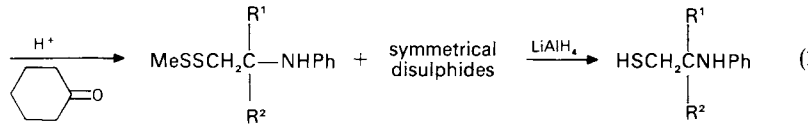


(268)

(447)

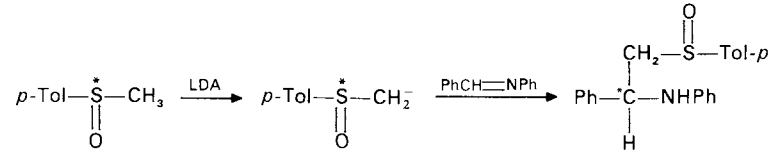


(448)

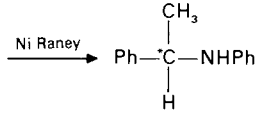


(269)

Reaction of benzylideneaniline with optically active methyl *p*-tolyl sulphoxide **449** in the presence of lithium diethylamide produces the corresponding *β*-anilinosulphoxide **450** with 100% asymmetric induction. Its reductive desulphurization with Raney nickel leads to the enantiomerically pure amine **451**[524] (equation 270). When the same optically active



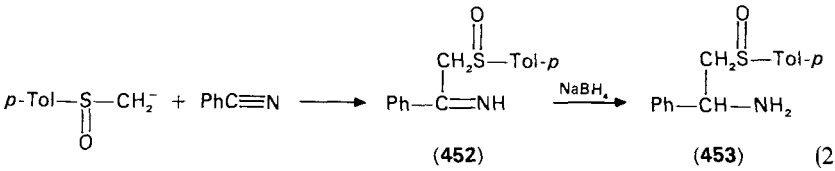
(449) (450)



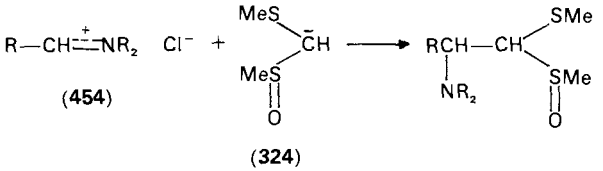
(270)

(451)

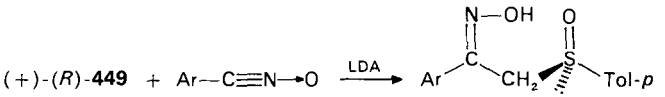
sulphoxide anion is treated with benzonitrile and the addition product **452** is then reduced with $NaBH_4$, 2-amino-2-phenylethyl *p*-tolyl sulphoxide **453** is formed as a 1:1 mixture of both diastereoisomers[524] (equation 271). Iminium salts **454** react with α-sulphinyl carbanions in a similar way as the free imines[525] (equation 272). Reaction of enantiomerically pure (+)-(*R*)-methyl *p*-tolyl sulphoxide **449** with LDA and then with nitrile oxides **455** affords optically active β-oximinosulphoxides **456** in a good yield (equation 273). The adducts have a *Z*-configuration around the C=N double bond[526]. The same anion reacts with nitrones **457** to afford optically active hydroxylamines **458** with very high β-stereoselectivity (equation 274). The diastereoisomeric ratio of the products varies from 75:25 to 100:0, being the highest for R = *t*-Bu[526].



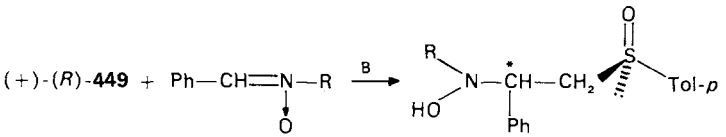
(452) (453) (271)



(454) (324) (272)

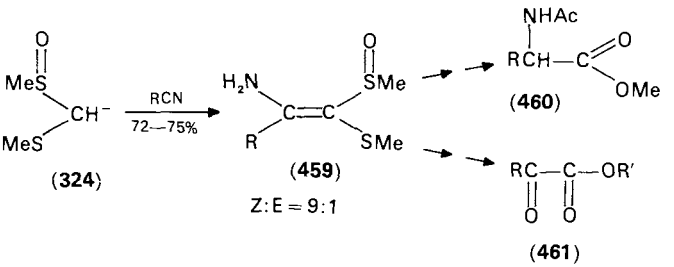


(455) (456) (273)



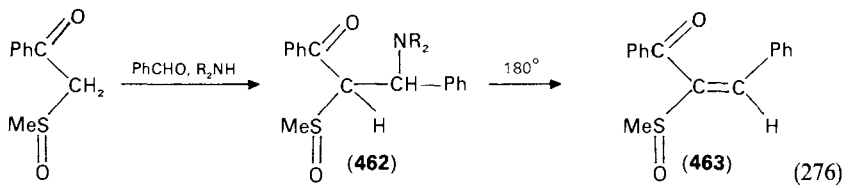
(457) (458) (274)

Enaminosulphoxides **459** have been obtained in the reaction of the carbanion of methyl methylthiomethyl sulphoxide **324** with nitriles. This procedure has been applied for converting nitriles into α-aminoacids **460**[527] and α-ketoacids **461**[528] (equation 275).



(324) (459) Z:E = 9:1 (460) (461) (275)

Sulphoxides also undergo Mannich-type condensation when reacted with aldehydes and secondary amines or their salts. In some cases, stable Mannich bases **462** can be isolated. They undergo amine elimination upon heating to give the corresponding α,β-unsaturated sulphoxides **463**[164,529] (equation 276).

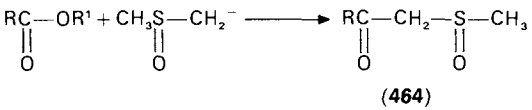


(276)

Cephalosporin (S_S)-sulphoxides give 2-exomethylene derivatives under Mannich reaction conditions but the corresponding (R_S)-sulphoxides fail to react[530,531].

f. Acylation of α-sulphinyl carbanions. Synthesis of β-oxosulphoxides. α-Ketosulphoxides have found very broad application in organic synthesis (see, for example, Reference 532). For this reason, a great deal of examples of their syntheses appear in the chemical literature. The main approach to this class of functionalized sulphoxides involves the reaction of α-sulphinyl carbanions with carboxylic esters or acyl halides.

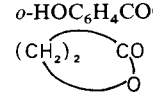
The first reports on this reaction were published almost simultaneously by Russell and coworkers[533] and Corey and Chaykovsky[534], who reacted dimsyl anion with a variety of carboxylic esters and obtained the corresponding α-ketosulphoxides **464** in high yields (equation 277; Table 25).



(464)

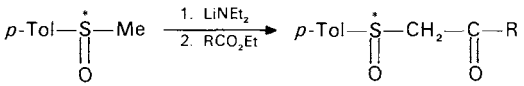
(277)

TABLE 25. Reaction of dimsyl anion with carboxylic esters

Ester	Yield of **464** (%)	Refs.
PhCOOEt	72	533
PhCOOEt	79	534
p-$MeOC_6H_4COOEt$	98	534
α-Naphthyl-COOEt	98	534
α-Furyl-COOEt	71	534
Cyclohexyl-COOEt	98	534
n-$C_5H_{11}COOEt$	70	534
n-$C_{17}H_{35}COOEt$	98	534
$MeOOC(CH_2)_nCOOMe$	55	535
X-*o*-OH-C_6H_3COOEt[a]	28–88	494
p-$MeOC_6H_4COOMe$	71	533
p-MeC_6H_4COOMe	72	533
o-HOC_6H_4COOMe	18	533
	95	536

[a]X: additional substituent in the ring.

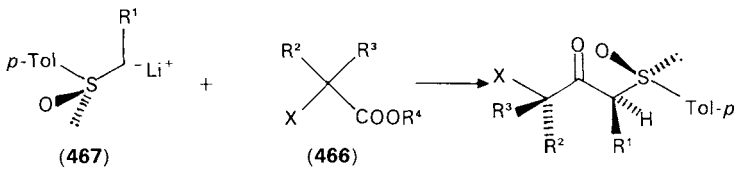
Optically active α-ketosulphoxides **465** have also been obtained in this way starting from the carbanion derived from optically active sulphoxide **449**[537,538] (equation 278).



(278)

(**449**) (**465**)

Even with α-halocarboxylic acid esters **466** the attack of α-sulphinyl carbanion **467** takes place at the carbonyl carbon atom and not at the α-carbon atom and the corresponding α-halo-α-sulphinyl ketones **468** are obtained in high yields[539,540] (equation 279).

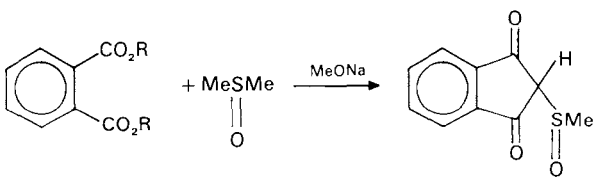


(279)

(**467**) (**466**) (**468**)

X = Cl, Br, F

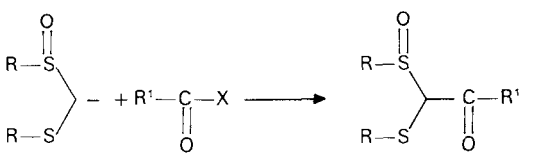
When phthalates are added to a solution of sodium methoxide in DMSO 2-(methanesulphinyl)-1,3-indanone **469** is readily formed[541] (equation 280).



(280)

(**469**)

Acylation of the anions of dithioacetal monoxides proceeds in a similar way leading to the desired products **470** in 83–92% yield[505,542] (equation 281).

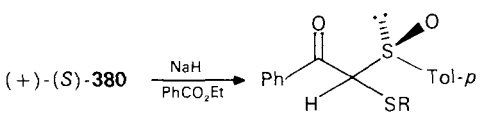


(281)

R = Ph, Me, Pr
X = Cl, OEt

(**470**)

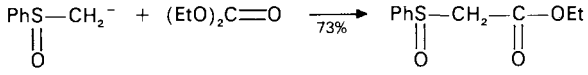
Treatment of the optically active dithioacetal monoxide **380** with ethyl benzoate in the presence of sodium hydride gives the benzoylated product **471** as a diastereoisomeric mixture, in the thermodynamically controlled (65:35) ratio[543] (equation 282).



(282)

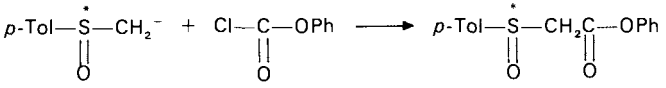
(**471**)

α-Sulphinyl acetates **472** or **473** can be obtained in the reaction of α-sulphinyl carbanions either with diethyl carbonate[496] (equation 283) or with phenyl chloroformate[500] (equation 284). The carbanions of 1-alkenyl sulphoxides **474** react with carbon dioxide and LDA and after subsequent alkylation afford the corresponding α,β-unsaturated α-sulphinylcarboxylic esters **475**[544] (equation 285); see also equation 239 and Reference 482.



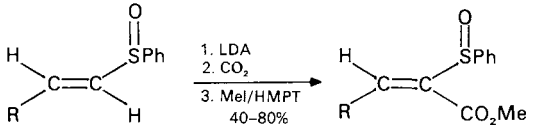
(283)

(**472**)



(284)

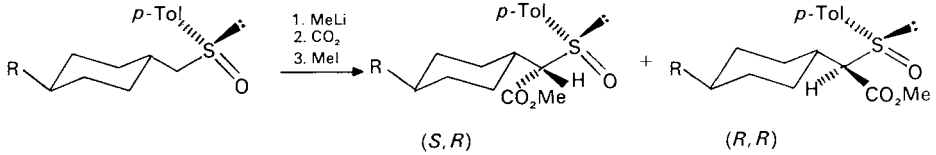
(**473**)



(285)

(**474**) (**475**)

Solladie and coworkers[545] confirmed the earlier result of Nishihata and Nishio[546] that the carbonation of the α-sulphinyl carbanion proceeds under kinetic control with retention of configuration at the metallated carbon atom. However, they also found that the stereochemical outcome of this reaction depends on other factors. They observed that 90% of asymmetric induction may be achieved under kinetic control (reaction time < 0.5 min) by using a base with low content of lithium salts, a result consistent with an electrophilic assistance by the lithium cation (equation 286)[545].



(*S*,*R*) : (*R*,*R*)

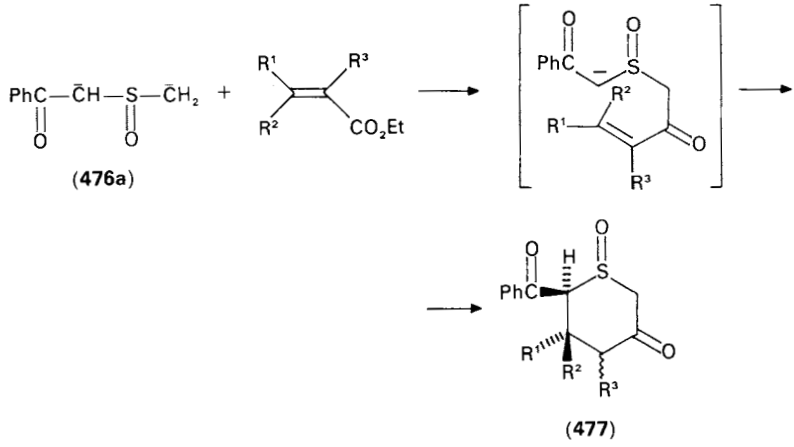
95 : 5 (286)

The α,α′-dianions of α-ketomethyl sulphoxides **476** react with esters exclusively at the α′-position[547] (equation 287). With α,β-unsaturated esters these anions afford substituted 3-oxothian-1-oxides **477** the products of annelation[548] (equation 288).

(287)

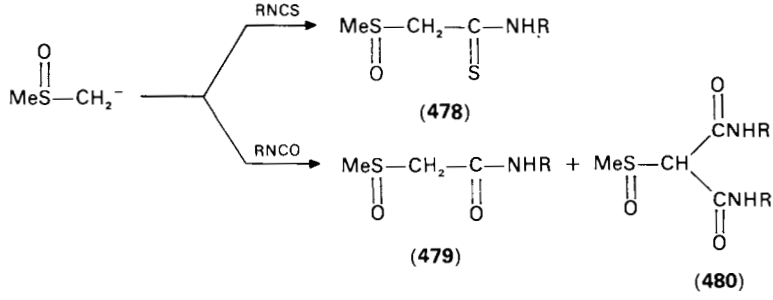
(**476**)

Reaction of dimsyl anion with isothiocyanates gives α-thioamidosulphoxides **478** in 12–59% yield, whereas with isocyanates it affords a mixture of α-amidosulphoxides **479** and methylsulphinylmalonoamides **480**, the products of a double addition[549] (equation 289).

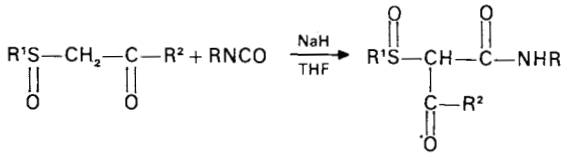


(476a) (477) (288)

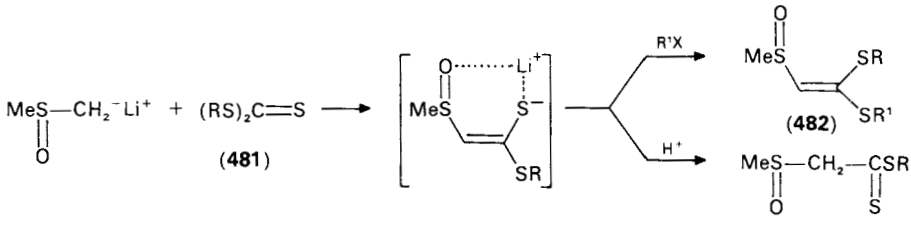
In contrast, α-ketosulphoxides react with isocyanates to give the products of a mono-addition only[550] (equation 290). Reaction of dimsyl anion with trithiocarbonates **481** followed by alkylation results in the formation of (methylsulphinyl)ketene dithioacetals **482**[551] (equation 291).



(478) (479) (480) (289)

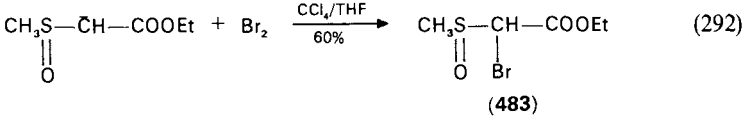


(290)



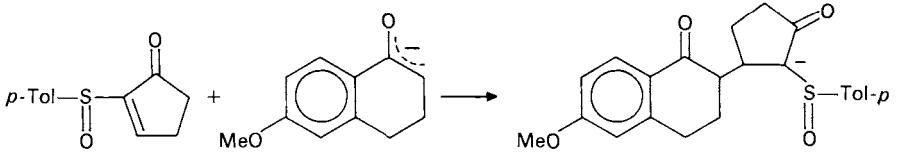
(481) (482) (291)

g. Other reactions of α-sulphinyl carbanions. α-Sulphinyl carbanions can also react with heteroatomic electrophiles. When a solution of bromine in CCl_4 is added to the α-sulphinylacetate anion in THF the corresponding α-bromo-α-sulphinyl acetate **483** is formed[436] (equation 292). Reaction of 1-cyclopentenone sulphoxide **484** with the enolate ion derived from 6-methoxytetralone **485**, followed by fluorination with perchloryl fluoride, gives the α-fluorinated α-ketosulphoxide **486**[552] (equation 293). Treatment of alkyl phenyl sulphoxides in THF with LDA and a dropwise addition of the anion formed to an excess of chlorotrimethylsilane results in the formation of α-trimethylsilylalkyl phenyl sulphoxides **487** in 85–95% yield[553] (equation 294). It must be stressed, however, that the use of NaH in DMSO as a base does not lead to the desired product[554].

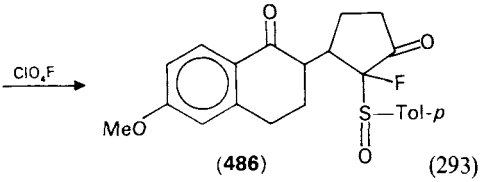


(292)

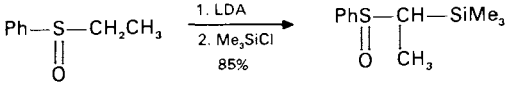
(**483**)



(**484**) (**485**)



(**486**) (293)

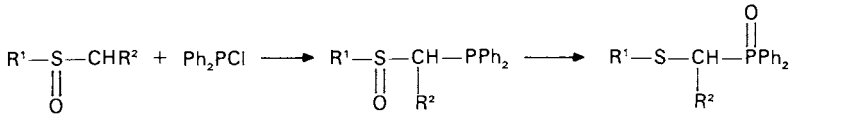


(294)

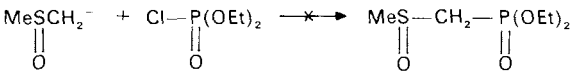
(**487**)

diast. ratio 10:1

Chlorodiphenylphosphine **488** reacts with α-sulphinyl carbanions to give α-sulphinylphosphines **489** which undergo ready isomerization to α-sulphenylphosphine oxides **490**[555] (equation 295). The report of Almog and Weissman that α-sulphinyl carbanions react with phosphorochloridates **491** to give α-phosphoryl sulphoxides[514] **492** calls for correction (equation 296). Actually, the phosphorylation occurs at the oxygen atom of the ambident dimsyl anion, and is followed by the Pummerer-type reaction affording diethylphosphoric acid and tetraethyl pyrophosphate among other products[76].



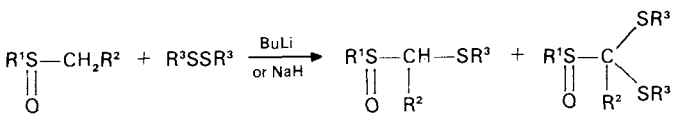
(**488**) (**489**) (**490**) (295)



(296)

(491) (492)

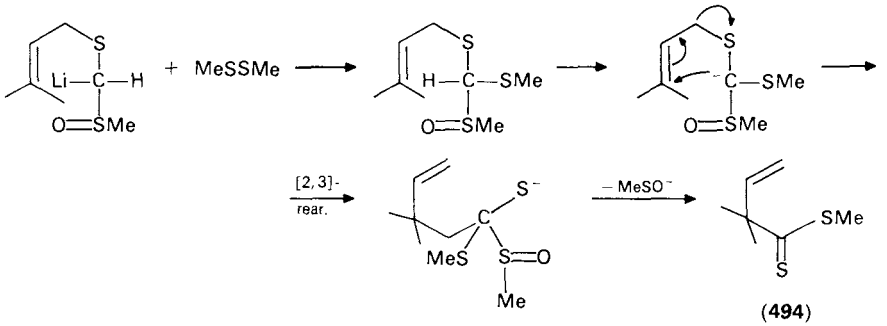
Reaction of sulphoxides with disulphides **493** in the presence of BuLi or NaH yields mono-, and disulphenylated products (equation 297). The formation of monosulphenylated sulphoxide as the main reaction product (55%) takes place only when Et_2S_2, sulphoxide and BuLi are used in a 1:3:3 ratio[556].



(297)

(493)

Julia and coworkers have utilized the sulphenylation reaction in the synthesis of β,γ-unsaturated dithiocarboxylates **494**, via the reaction sequence shown in equation 298[557].



(494)

(298)

Racemic or optically active β-disulphoxides can be obtained via a facile one-step procedure from arenesulphinic esters and α-sulphinyl carbanions[558] or by oxidation of α-sulphinyl carbanions[559].

B. Introduction, Substitution, Transformation and Elimination of Heteroatomic Groups at Organic Substituents in Sulphoxides

1. α-Halogenation of sulphoxides

Sulphoxides having at least one hydrogen at the α-carbon atom can be converted into the corresponding α-halogenosulphoxides upon treatment with a variety of electrophilic halogenating reagents. In many cases the reaction is carried out in the presence of bases which act as hydrogen halides trapping agents (equation 299). The presence of bases protects both the substrates and products from undesired side-reactions, such as the Pummerer rearrangement. For the synthesis of α-chlorosulphoxides the following halogenating reagents have been used: chlorine in the presence of bases (mainly pyridine)[560–564], nitrosyl chloride (NOCl) in the presence of pyridine[565–567], *N*-chlorosuccinimide[566,568–572], sulphuryl chloride[562,563,573–575], dichloroiodobenzene ($PhICl_2$)[564,576–579], *t*-butyl hypochlorite[562,563,567,576], *N*-chlorobenzotri-

azole[570,571,576,578,580,581] and *N*-chlorosulphoximine[565,582].

$$R^1\text{—}S(=O)\text{—}CHR^2R^3 + [X] \longrightarrow R^1\text{—}S(=O)\text{—}CR^2R^3 + H\text{—}X \qquad (299)$$

α-Bromosulphoxides have been synthesized by bromination of sulphoxides with bromine[566,570,571,576–579,583,584] or with a mixture of bromine with *N*-bromosuccinimide[585] in the presence of pyridine. In the latter case, NBS is considered to regenerate bromine (being the true brominating agent) by reaction with the hydrogen bromide formed. Another procedure for the synthesis of α-bromosulphoxides involves the reaction of α-sulphinyl carbanion with bromine[436] (see Section IV.A.2.g). An interesting preparative modification is a solid-phase silica-gel catalyzed α-halogenation of alkyl aryl sulphoxides with *N*-halosuccinimides[572].

α-Iodomethyl sulphoxides **495** can be obtained via exchange of chloride anion by iodide in α-chloromethyl sulphoxides[586] (equation 300).

$$Ar\text{—}S(=O)\text{—}CH_2Cl + KI \longrightarrow Ar\text{—}S(=O)\text{—}CH_2I \qquad (300)$$

(495)

The stereochemistry, kinetics and mechanism of α-halogenation of sulphoxides have been widely investigated[587,588] and exhaustively reviewed[257,589]. Therefore, they will not be discussed here.

2. *Substitution of heteroatomic groups by hydrogen atoms*

The title reaction may be accomplished by using various reducing agents. Thus benzyl α,α-dichlorobenzyl sulphoxide **496** was reduced to a mixture of diastereoisomeric benzyl α-chlorobenzyl sulphoxides **497** by means of $(Me_2N)_3P/Et_3N$ in aqueous solvent, Bu_3SnH, Ph_3P/Et_3N in methanol and $CrCl_2$[590] (equation 301). Similarly, dichlorobis(phenylsulphinyl)methane is reduced to the corresponding monochloro derivative[591].

Aryl α-bromomethyl sulphoxides **498** are reduced by $Co_2(CO)_8/Al_2O_3$ to aryl methyl sulphoxides (equation 302). This procedure appeared to be unsuitable for reducing α-chlorosulphoxides[592].

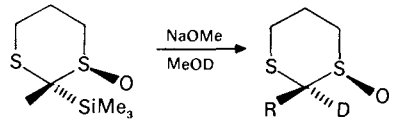
$$PhCH_2\text{—}S(=O)\text{—}CCl_2Ph \longrightarrow PhCH_2\text{—}S(=O)\text{—}CH(Cl)\text{—}Ph \qquad (301)$$

(496) **(497)**

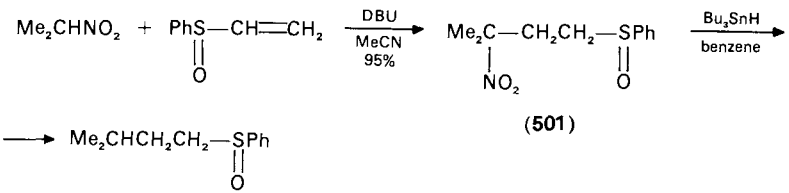
$$ArS(=O)\text{—}CH_2\text{—}Br \xrightarrow[80\text{–}100\%]{Co_2(CO)_8/Al_2O_3} ArS(=O)\text{—}CH_3 \qquad (302)$$

(498)

The stereospecific base-cleavage of the trimethylsilyl group in 1,3-dithiane 1-oxides **499** enables to obtain the specifically deuteriated products **500**[593] (equation 303). A nitro group in γ-nitroalkyl sulphoxides **501** (obtained by the Michael addition of nitroalkanes to α,β-unsaturated sulphoxides) is replaced by hydrogen by means of tributyltin hydride (equation 304). This reagent does not affect the sulphinyl function. The overall procedure provides an efficient method for the conjugate addition of alkyl groups to α,β-unsaturated sulphoxides[594].



(499) (500) (303)

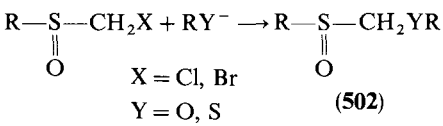


(501) (304)

3. *Nucleophilic substitution of α-halogen atoms in α-halosulphoxides*

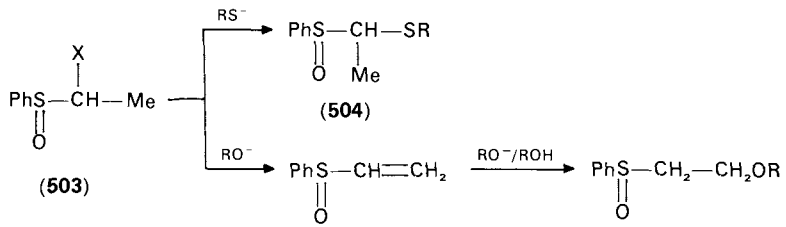
α-Chloroalkyl sulphoxides have been found to be extremely inert in nucleophilic substitution reactions. They are less reactive than *n*-BuCl by a factor of 10^2 [595]. Nevertheless, substitution of the α-halogen has been successfully carried out by several nucleophiles.

The mechanism of the nucleophilic substitution of α-halogenosulphoxides depends on structural factors and the nature of a nucleophile[596] and may occur according to two competitive mechanisms: a direct S_N2 substitution[597] and an elimination–addition process[577]. Thus, chloromethyl[570,598] and bromomethyl[599] sulphoxides react with alkoxide and mercaptide anions via an S_N2 mechanism to give the corresponding α-alkoxy and α-alkylthiomethyl sulphoxides **502**, respectively (equation 305). Optically active α-alkoxymethyl and α-alkylthiomethyl sulphoxides can also be obtained in this way[570,599].

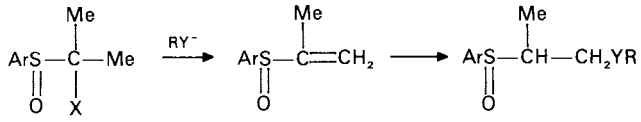


(502) (305)

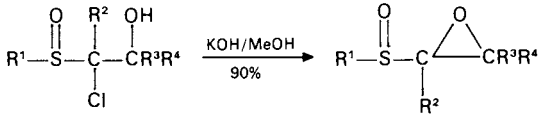
On the other hand, in the case of α-halogenoethyl sulphoxides **503** an S_N2-type displacement occurs with mercaptide anions and leads to α-alkylthioethyl sulphoxides **504**, while the elimination–addition mechanism is operative with alkoxide anions, affording β-alkoxyethyl sulphoxides[577,596] **505** (equation 306). Finally, the reaction of 1-halogeno-1-methylethyl derivatives with both nucleophiles mentioned above occurs via the elimination–addition mechanism[596] (equation 307). The substitution reaction can also take place intramolecularly (equation 308) and it proceeds very easily (cf. Section IV.A.2.c)[484,600].



(503) (504) (505) (306)



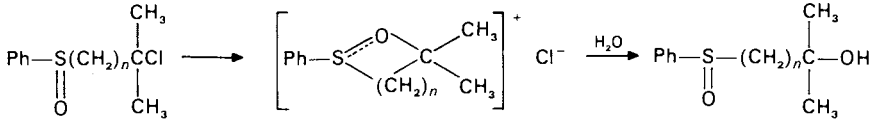
(307)



(308)

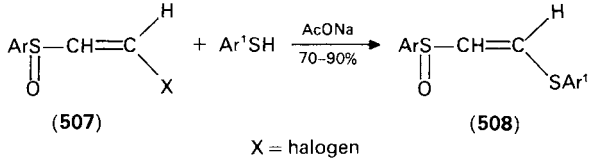
4. Nucleophilic substitution in halogenosulphoxides having a halogen atom in another position

Based on kinetic investigations the solvolysis of ω-chloroalkyl sulphoxides **506** in 80% ethanol was found to proceed via a cyclic intermediate formed via anchimeric assistance of the sulphinyl oxygen atom[601,602]. For a solvolysis of 4-halogenothian-1-oxides see Reference 603 (equation 309).

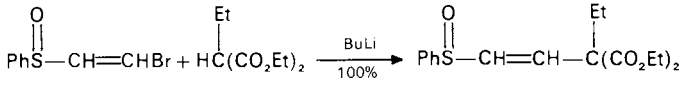


(309)

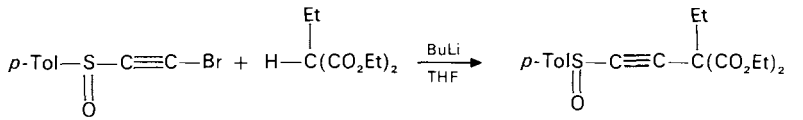
β-Halogenovinyl sulphoxides **507** react with arylthiols in basic solution to give the corresponding β-arylthiovinyl aryl sulphoxides **508**, i.e. the products of a formal nucleophilic substitution at the olefinic carbon atom[604] (equation 310). Similarly, 2-bromovinyl phenyl sulphoxide **509** reacts with the anions of 1, 3-dicarbonyl compounds to give the corresponding β-substitution products **510**[605] (equation 311). Addition of β-bromoethynyl sulphoxide **511** to a mixture of diethyl ethylmalonate and BuLi in THF gives the corresponding substituted ethynyl sulphoxides **512** in 72% yield[605] (equation 312). These reactions probably proceed via a nucleophilic addition–elimination process (cf. Section IV.C.2.b).



(310)



(311)

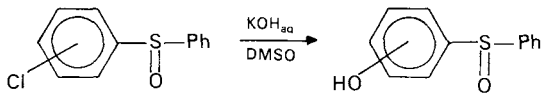


(511) (512) (312)

5. Substitution at the aromatic ring in aryl sulphoxides

Halogenation of diphenyl or methyl phenyl sulphoxides by Cl_2 or Br_2 affords mainly *para*-halogeno derivatives, whereas the *meta*-isomers are formed in low percentages or not at all[606,607]. In contrast, nitration in concentrated sulphuric acid leads to *meta*-substitution whose extent increases with acidity of the medium (up to 100%)[608].

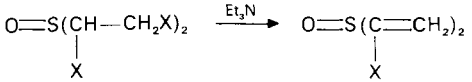
A phenylsulphinyl group has been found to promote the nucleophilic substitutions of chlorine at positions *ortho* and *para* to the aromatic ring (equation 313)[609].



(313)

6. Elimination of heteroatomic substituents in alkyl residue

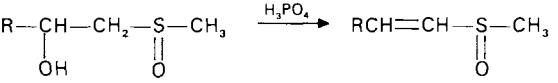
α,β-Dihalogeno sulphoxides **513** undergo dehydrohalogenation to afford α-halogeno-vinyl sulphoxides **514**[610] (equation 314).



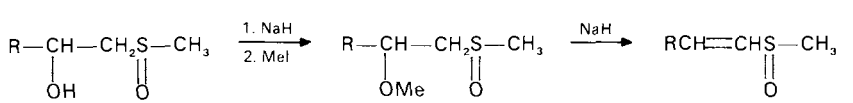
(513) (514) (314)

X = Cl, Br

β-Hydroxyalkyl sulphoxides **515** can be dehydrated either by treatment with phosphoric acid (equation 315) or by the alkylation with MeI in the presence of an excess of sodium hydride[611] (equation 316). For other dehydration reactions see References 475 and 505 (Section IV.A.2.d). For elimination of amines see References 164 and 529 (Section IV.A.2.e).

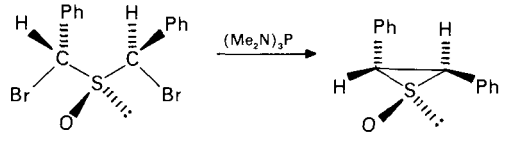


(515) (315)

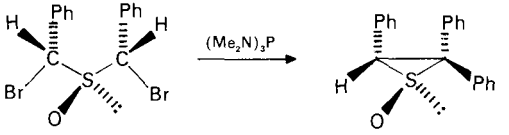


(515) (316)

α,α'-Dibromosulphoxides **516** when treated with $(Me_2N)_3P$ afford thiirane 1-oxides in 65% yield. The reaction is highly stereospecific and has been proven to occur with a double inversion (W elimination). Thus, the racemic sulphoxide yields the *trans*-thiirane 1-oxide **517** while the *meso* compound produces the *cis*, *anti*-thiirane 1-oxide **518**[612] (equation 317).

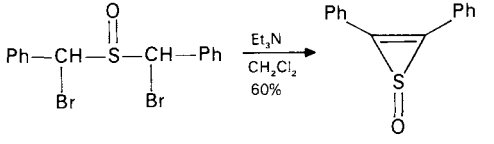


rac. (**516**) (**517**)



meso-(**516**) (**518**) (317)

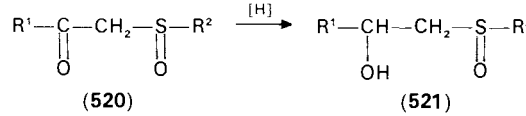
The synthesis of 2, 3-diphenylthiirene 1-oxide **519** has been accomplished by treatment of (±)-α, α′-dibromobenzyl sulphoxide **516** with a slight excess of triethylamine in boiling CH_2Cl_2[46] (equation 318).



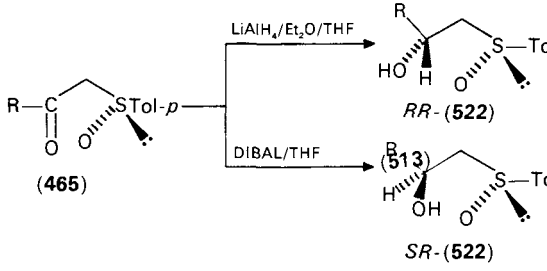
(**516**) (**519**) (318)

7. Reduction of β-oxosulphoxides

β-Oxosulphoxides **520** are reduced to β-hydroxysulphoxides **521** by several reagents, including $NaBH_4$[431,543,611], $LiAlH_4$[538,613–616] and DIBAL[615,616] (equation 319). Reduction of β-oxosulphoxides was found to be a highly stereoselective process. In the case of aryl β-oxosulphoxides $LiAlH_4$ has been found to give higher asymmetric induction than $NaBH_4$[538]. Moreover, Solladie and coworkers have found that reduction of β-oxosulphoxides of identical chirality at sulphur leads to the opposite stereochemistry at the β-carbon atom, depending on the reducing agent used. For instance, the diastereoisomeric ratio *RR*:*RS* changes from 90:10 to 0:100 when DIBAL/THF is used in place of $LiAlH_4/Et_2O/THF$[615] (equation 320). Very recently, the same authors reported

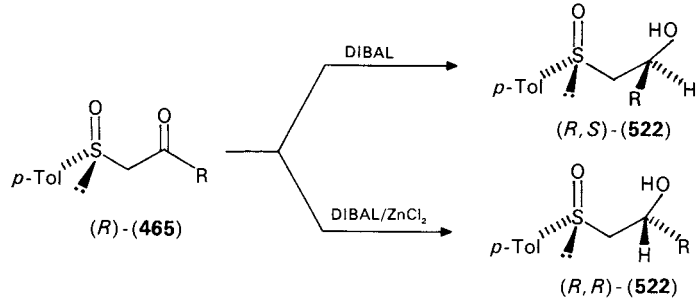


(**520**) (**521**) (319)



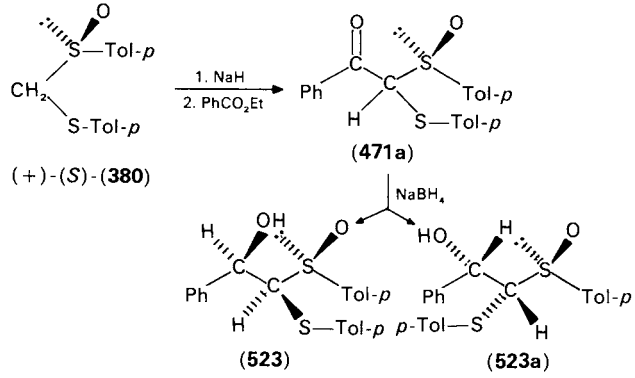
(**465**) *RR*-(**522**) (**513**) *SR*-(**522**) (320)

that, starting from one enantiomer of the β-oxosulphoxide **465**, β-hydroxysulphoxides **522** of opposite stereochemistry at the β-carbon atom can be prepared in a very high (up to 95%) diastereoisomeric purity using DIBAL or DIBAL/$ZnCl_2$ as reducing agents[616] (equation 321).



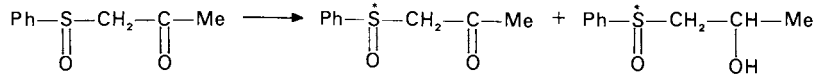
(321)

This procedure has been recently applied to the synthesis of L-lyxitol and the polyhydroxylated chain of amphotericin B[257]. Interesting results have also been obtained in the reduction of β-oxo derivatives of dithioacetal monoxides. In the reaction sequence of equation 322 two successive asymmetric inductions are involved. After the first reaction, involving acylation of the carbanion, a diastereoisomeric mixture in a 65:35 ratio is produced. When this mixture is reduced with $NaBH_4$ in MeOH–conc. aqueous solution of ammonia, among four possible diastereoisomeric alcohols, the stereoisomer **523** is obtained with a stereoselectivity of 98%[543]. Guanti and coworkers have found that the $LiAlH_4$ reduction of the same substrates at −78° in THF/ether leads to **523** with a stereoselectivity 99:1[613,614].



(322)

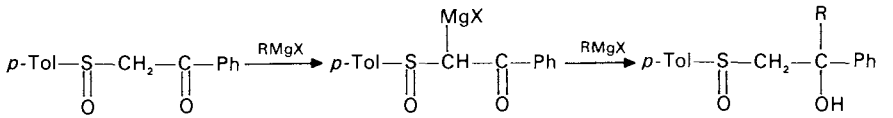
In the reduction of racemic β-ketosulphoxides (e.g. **464a**) with actively fermenting yeast (Saccharomyces cerevisiae) the enantiomers are reduced at sufficiently different rates to allow isolation of optically active β-hydroxy sulphoxide **524** and unreacted optically active β-ketosulphoxide with at least 95% optical purity[617,618] (equation 323).



(323)

A reverse reaction, i.e. oxidation of β-hydroxysulphoxides to β-ketosulphoxides, can be performed using active manganese dioxide[619].

Addition of an excess of a Grignard reagent to β-ketosulphoxide yields a mixture of the diastereoisomeric alcohols **525**[496] (equation 324).



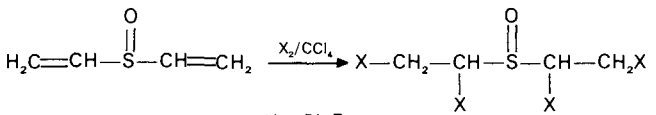
(**525**)

(324)

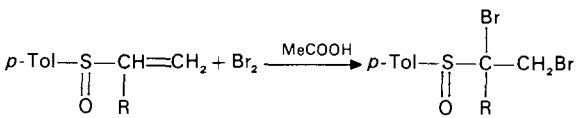
C. Additions to Unsaturated Sulphoxides

1. Electrophilic additions

Halogens add easily to α,β-unsaturated sulphoxides to afford α,β-dihalogenosulphoxides (e.g. equation 325)[620,621]. Addition of bromine to (+)-*p*-tolyl vinyl sulphoxides **526** (R = H or Me) gives the corresponding α,β-dibromo sulphoxides **527** with optical yields (α-induction) of 32% (R = H) and 43% (R = Me)[359] (equation 326). Reaction of *N*-bromosuccinimide with (+)-(*R*)-*E*-*p*-tolyl-2-styryl sulphoxide **528** in water or methanol gives diastereoisomeric mixtures of α-bromo-β-hydroxy (or methoxy) sulphoxides **529a** and **529b** in a very high diastereoisomeric ratio (90:10 for R = H and 95:5 for R = Me) (equation 327). This conversion may be considered as a formal electrophilic addition of hypobromous acid or methyl hypobromite, respectively[622]. For iodolactonisation of β-carboxy-β,γ-unsaturated sulphoxides by $I_2/NaHCO_3/H_2O$ see Reference 623. Addition of a variety of electrophiles E—X (Br_2, ArSCl, H_2O/HgO) to allenyl sulphoxides **530** takes place across the β,γ-double bond via a sulphoxonium salt **531** which, after subsequent hydrolysis, produces γ-hydroxy α,β-unsaturated sulphoxides **532**[208] (equation 328). Regioselectivity of hydrogenation of unsaturated sulphoxides depends on the reagents used (e.g. equation 329)[238].

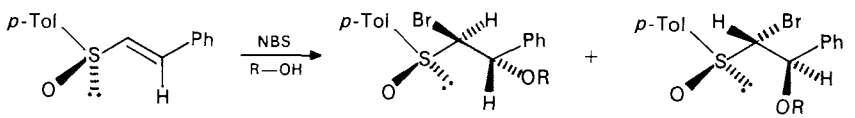


(325)



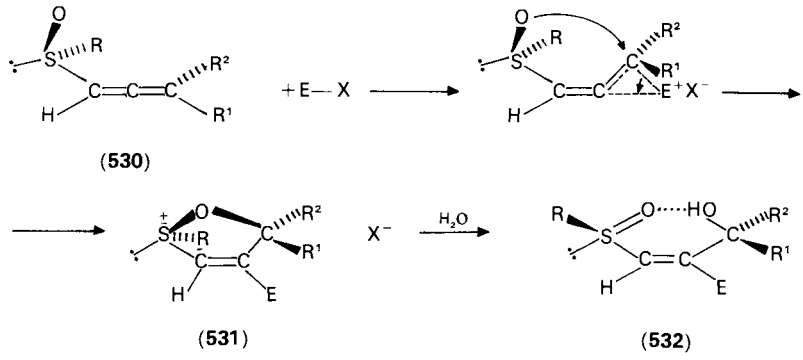
(**526**) (**527**)

(326)

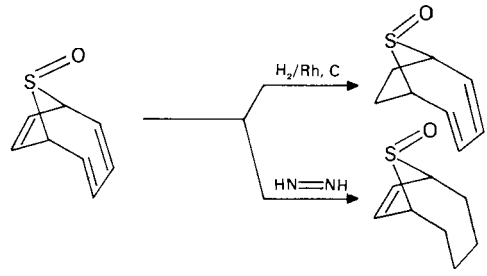


E, (+)-(*R*)-(**528**) (**529a**) (**529b**)

(327)



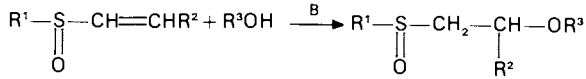
(328)



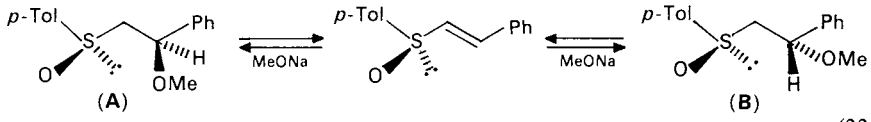
(329)

2. Nucleophilic additions

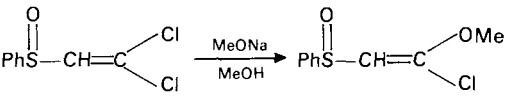
a. Addition of heteroatomic nucleophiles. Alcohols add to α,β-unsaturated sulphoxides in the presence of bases[624–626] (in some cases used in catalytic amounts)[627] to give β-alkoxy(aryloxy)ethyl sulphoxides in good to high yields (equation 330). (See also the discussion in Section IV.B.3. and References 577 and 596). It has been proven that the addition of alkoxides to α,β-unsaturated sulphoxides is a reversible, thermodynamically controlled process (equation 331)[624]. β,β-Dichlorovinyl phenyl sulphoxide **533** reacts with sodium methoxide to give β-chloro-β-methoxyvinyl phenyl sulphoxide **534** via addition of methoxide anion and subsequent elimination of chloride anion[628] (equation 332).



(330)

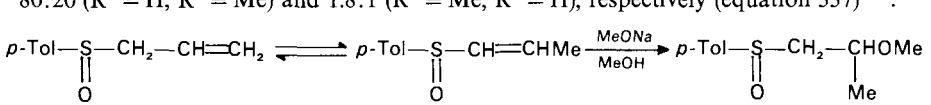


(331)

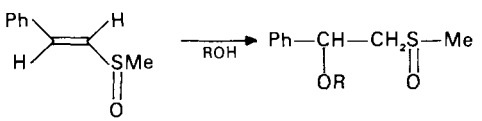


(533) (534) (332)

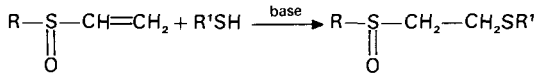
Allyl *p*-tolyl sulphoxide **535** reacts with sodium methoxide in methanol by initial prototropic isomerization and subsequent addition of methanol to give **536**[629] (equation 333). Protic solvents are photochemically incorporated by the open chain olefinic bond of *trans* methyl β-styryl sulphoxide **537** in a Markovnikov regiospecificity[630] (equation 334). Mercaptanes and thiophenols add to vinyl sulphoxides in a similar manner[625,627] (compare also Reference 604 and Section IV.B.3) to give β-alkylthio(arylthio)ethyl sulphoxides **538** (equation 335). Addition of deuteriated thiophenol (PhSD) to optically active *p*-tolyl vinyl sulphoxide is accompanied by a low asymmetric α-induction not exceeding 10% (equation 336)[359]. Addition of amines to vinyl sulphoxides proceeds in the same way giving β-aminoethyl sulphoxides in good to quantitative yields depending on the substituents at the vinyl moiety[359,627]. When optically active *p*-tolyl vinyl sulphoxides are used in this reaction, diastereoisomeric mixtures are always formed and asymmetric induction at the β- and α-carbon atoms is 80:20 ($R^1 = H$, $R^2 = Me$) and 1.8:1 ($R^1 = Me$, $R^2 = H$), respectively (equation 337)[359].



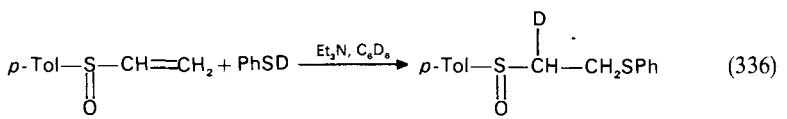
(535) (536) (333)



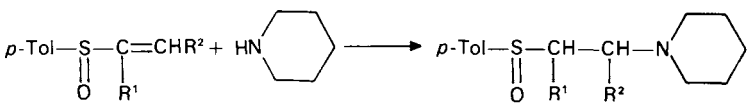
(537) R = Me, MeC=O (334)



(538) (335)



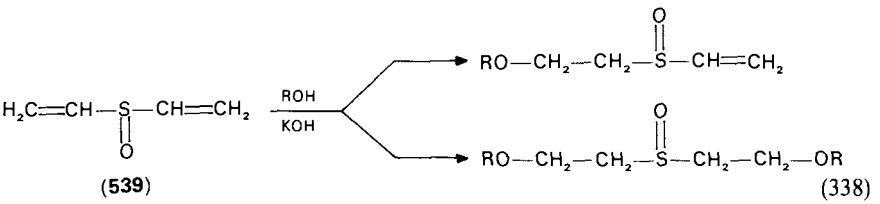
(336)



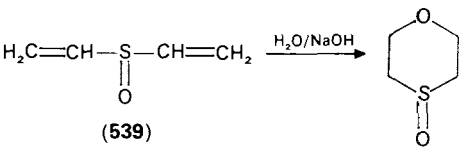
(337)

Addition of heteroatomic nucleophiles to divinyl sulphoxides gives mono and bifunctionalized products as well as compounds resulting from their cyclization. For

example, the reaction of divinyl sulphoxide **539** with alcohols in the presence of a base gives both mono- and diaddition products (equation 338)[631]. On the other hand, reaction of divinyl sulphoxide with dilute solution of NaOH leads to the cyclic 1,4-oxathian-4-oxide **540**[620] (equation 339).

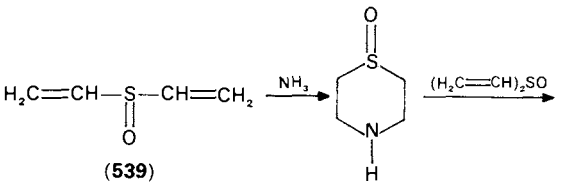


(**539**) (338)

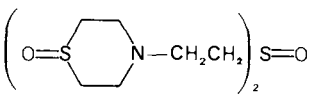


(**539**) (**540**) (339)

Similarly, the reaction of ammonia with an excess of **539** produces bis-[2-(1-oxotetrahydro-1,4-thiazin)-ethyl] sulphoxide **541**[632] (equation 340).

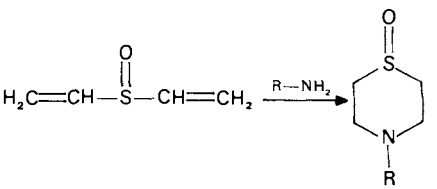


(**539**)

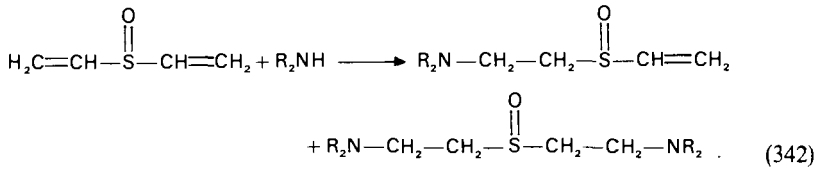


(**541**) (340)

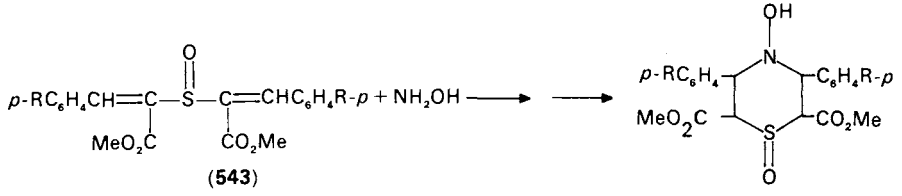
Monoalkylamines give only the cyclic products, i.e. *N*-alkyltetrahydro-1,4-thiazin-1-oxides **542** (equation 341), while dialkylamines afford the mono- and diaddition products (equation 342)[633]. Hydroxylamine undergoes double addition to substituted divinyl sulphoxides **543** to give thiazine 1-oxides **544**[634] (equation 343).



(**542**) (341)

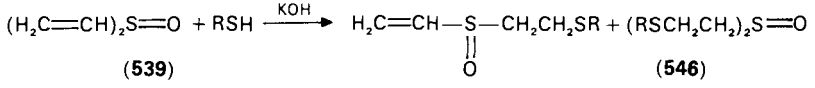


(342)



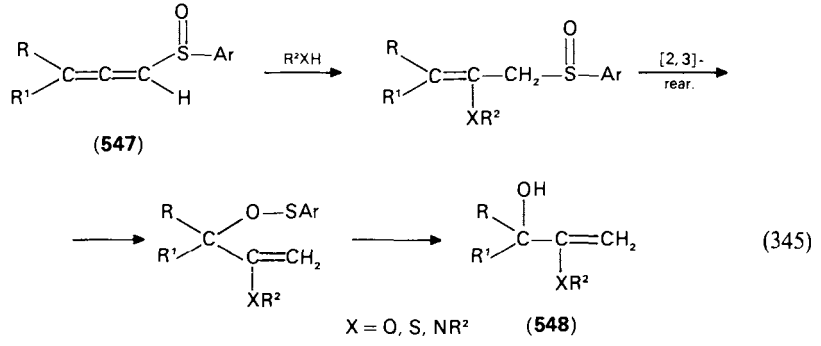
(543) (544) (343)

Mercaptanes add easily to divinyl sulphoxide in the presence of catalytic amounts of bases, giving β-alkylthioethyl vinyl sulphoxides **545** and β,β'-di(alkylthioethyl)sulphoxides **546** (equation 344). When an excess of divinyl sulphoxide is applied the reaction can be stopped at the stage of monoaddition[635,636].



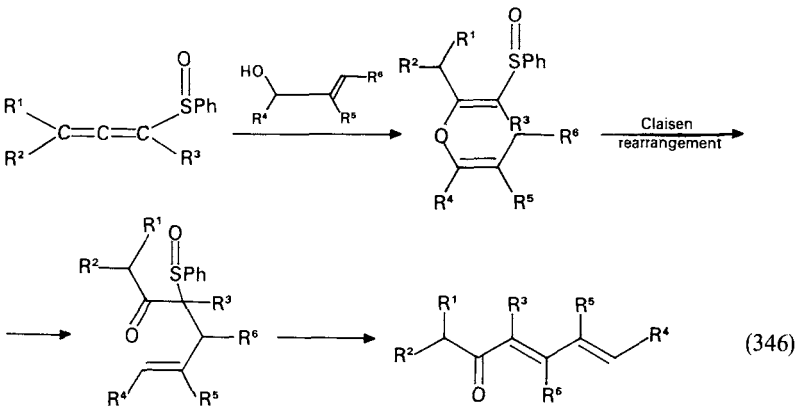
(539) (545) (546) (344)

Nucleophilic addition to allenyl sulphoxides **547** proceeds across the α,β-double bond to produce the corresponding β-substituted allylic sulphoxides which undergo readily a [2,3]-sigmatropic rearrangement affording substituted allyl alcohols[208,637] (equation 345). Under proper basic conditions, the initially formed allylic sulphoxides can rearrange to the corresponding vinyl sulphoxides which can be elaborated to 2,4-dienones **549** (equation 346)[638] and α-ketosulphoxides (equation 347)[639].



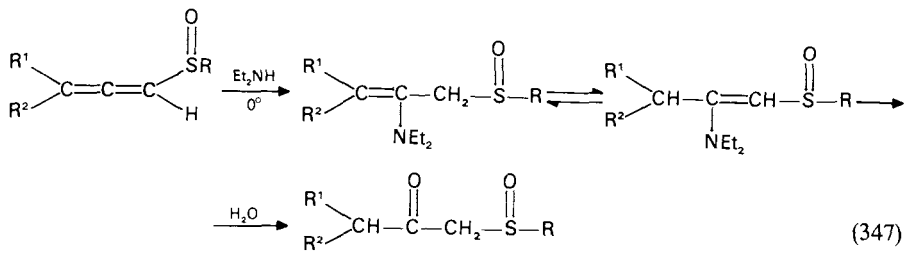
(547) (548) (345)

b. Michael addition to α,β-unsaturated sulphoxides. Michael addition to vinyl sulphoxides (equation 348) allows one to introduce a variety of organic units possessing acidic



(346)

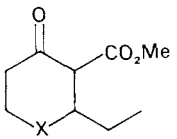
(549)



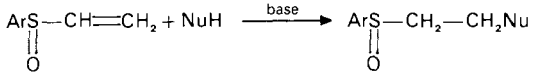
(347)

hydrogen. Selected examples are collected in Table 26. The reaction of (+)-*R-trans*-β-styryl *p*-tolyl sulphoxide with diethyl malonate gives a mixture of diastereoisomers **550**,

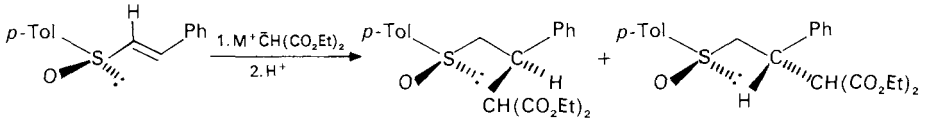
TABLE 26. Michael additions to aryl vinyl sulphoxides

Ar	Nu—H	Yield of adduct (%)	Refs.
p-Tol	$CH_2(CO_2Et)_2$	61	640, 641
p-Tol	$MeCOCH_2CO_2Et$	71	640, 641
Ph	Me_2CHNO_2	87	627
Ph	Me_2CHNO_2	95	594
Ph	$PhCH_2CH(Me)NO_2$	98	594
Ph	$EtCH(CO_2Et)_2$	95	627
p-ClC_6H_4	$Me_2CHCH(CO_2Et)CN$	80	627
Ar	 $X = (CH_2)_n$ $n = 4, 7, 10$	Yields and ratio of regioisomers depend on Ar and *n*	642

the ratio of which is strongly dependent on the nature of the counterion and solvent used[641] (equation 349).



(348)

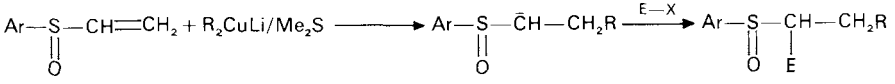


(550a) (550b)

(349)

Solvent	M^+	550a:550b ratio
EtOH	Na^+	81:19
EtOH	K^+	79:21
THF	K^+	55:45
THF	Na^+	36:64
THF	Li^+	22:78
THF/hexane	Li^+	21:79

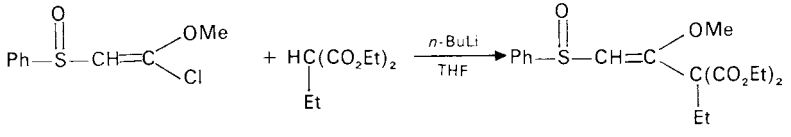
Dialkyl cuprates may also be added to aryl vinyl sulphoxides and the resulting α-sulphinyl carbanions can be treated with various electrophiles such as aldehydes, ketones and alkyl halides (equation 350)[643].



overall yields 13–75%

(350)

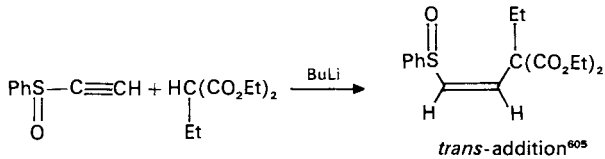
β-Halogenovinyl sulphoxides **551** react with nucleophiles to give β-substituted vinyl sulphoxides **552**. The first step in the reaction is a Michael addition, followed by an elimination of a halide anion[605,627] (equation 351).



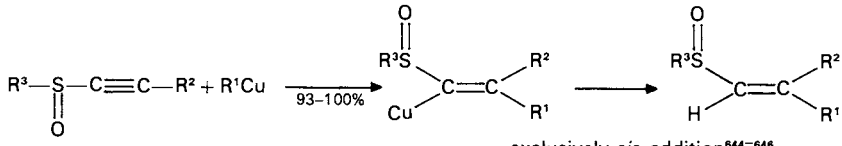
(551) (552)

(351)

Alkynyl sulphoxides **553**, **554** also behave as Michael acceptors and afford the corresponding β-substituted vinyl sulphoxides upon treatment with nucleophiles[605,644–646] (equations 352 and 353).

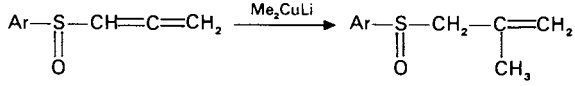


(553) (352)



(554) (353)

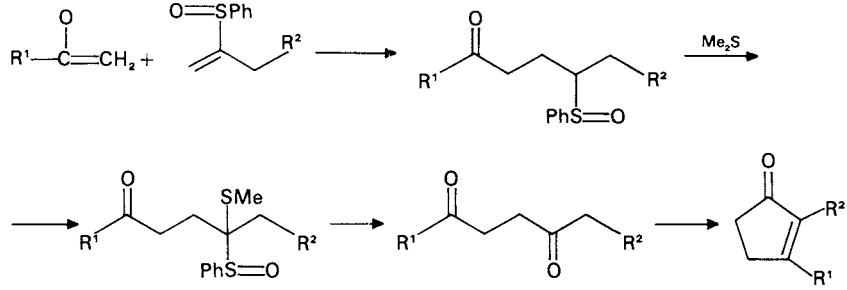
Alkylcopper reagents add to allenyl sulphoxides **555** to give the corresponding allylic sulphoxides **556** in moderate yields[647] (equation 354).



(354)

(**555**) (**556**)

Conjugate addition of enolate anions to α,β-unsaturated sulphoxides followed by a sulphoxide→ketone transformation were used for the preparation of 1,4-dicarbonyl compounds and cyclopentenone derivatives (equation 355)[648].

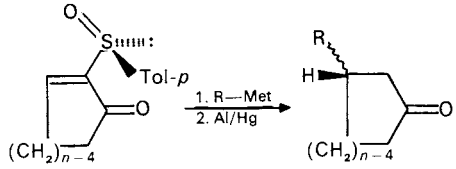


(355)

Posner and coworkers have published a series of papers in which they described a successful application of the Michael reaction between a variety of carbanionic reagents and chiral cycloalkenone sulphoxides **557** to the synthesis of chiral organic compounds (for reviews see References 257, 649, 650). In several cases products of very high optical purity can be obtained. Subsequent removal of the sulphinyl group, serving as a chiral adjuvant, leads to optically active 3-substituted cycloalkenones **558** (equation 356; Table 27).

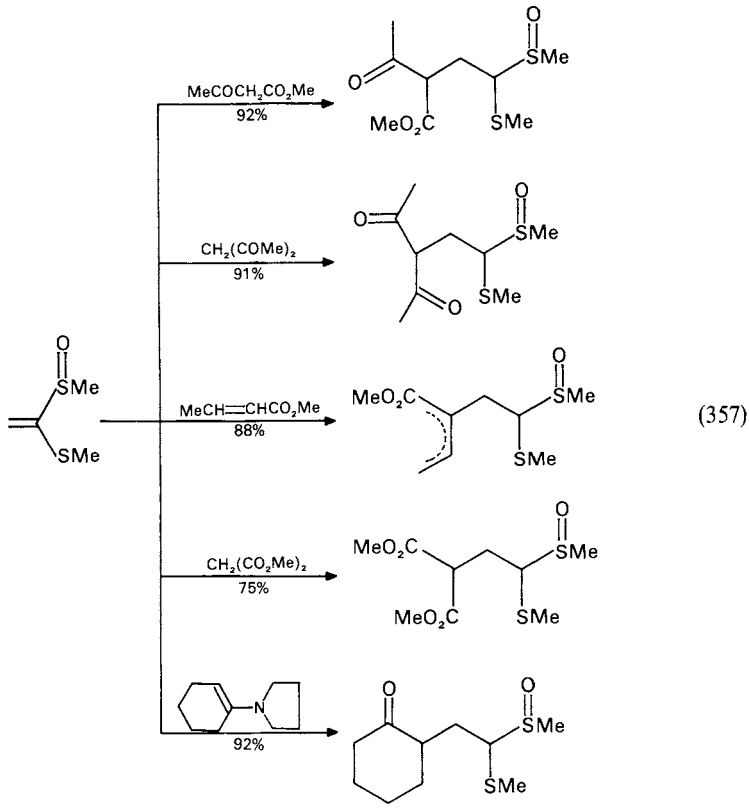
This approach has been found to be general and applicable also to the generation of a

chiral quaternary carbon centre[654] and for the synthesis of chiral 3-substituted 4-butanolides[653,655].



(557) (558) (356)

Schlessinger and coworkers described a conjugate addition of enolate species to ketene dithioacetal monoxides[656] (equation 357). Some of the products obtained were elaborated to dihydrojasmone[657], prostaglandins[658] and rethrolones[659].



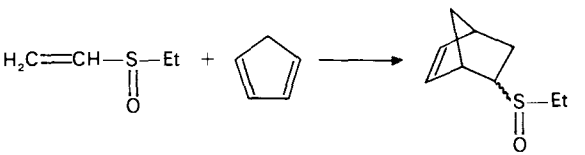
(357)

3. Cycloadditions

a. Diels–Alder reactions. Vinyl sulphoxides have been widely used as dienophiles in [2 + 4]-cycloaddition reactions. For example, in the reaction of vinyl sulphoxides with cyclopentadiene the corresponding diastereoisomeric mixture of bicyclo[2.2.1]-hepten-5-yl sulphoxides **559** is formed[660] (equation 358).

TABLE 27. Michael additions to chiral cycloalkenone sulphoxides **557**

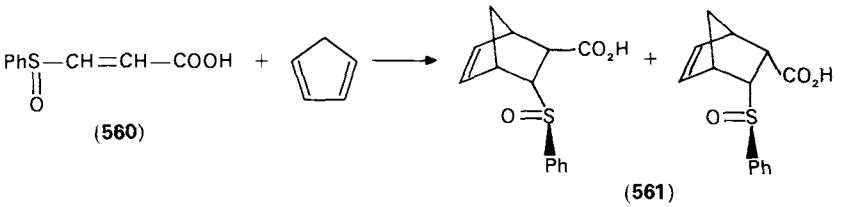
n	*R*-Met	Yield (%)	e.e. (%)	Abs. conf. of **588**	Refs
5	$ZnBr_2/MeMgI$	89	87	*R*	361, 650
5	$MeTi(OPr\text{-}i)_3$	90	90	*R*	361, 650
6	$ZnBr_2/MeMgBr$	95	62	*R*	361, 650
6	$MeTi(OPr\text{-}i)_3$	85	86	*R*	361, 650
5	$ZnBr_2/EtMgCl$	90	90	*R*	650, 651
5	$ZnBr_2/CH_2{=}CHMgBr$	75	98	*R*	650, 651
5	$ZnBr_2/PhMgCl$	70	92	*R*	650, 651
5	Me_2Mg	69	97	*S*	652
5	Et_2Mg	88	81	*S*	652
5	$(CH_2{=}CH)_2Mg$	74	57	*S*	652
5	Ph_2Mg	72	98	*S*	652
6	Me_2Mg	67	79	*S*	652
6	$(s\text{-}Bu)_2Mg$	67	62	*S*	652
5	$MeOC(=O)$	62	70	*S*	653
6	$CH(SiMe_3)Li$	95	95	*S*	653



(358)

(**559**) endo:exo = 3:1

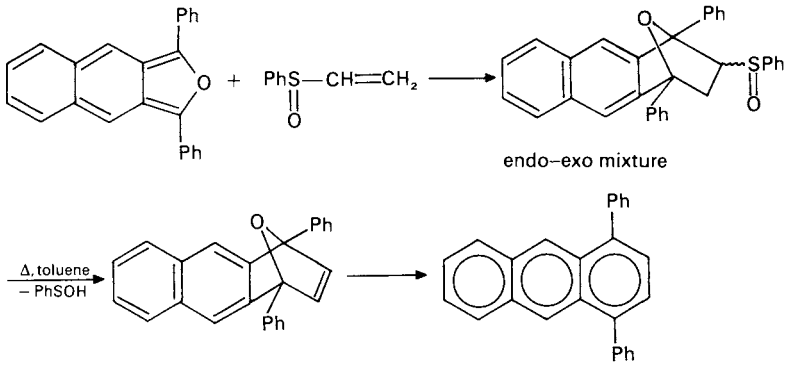
More detailed stereochemical studies on the Diels–Alder reaction between cyclopentadiene and 2-phenylsulphinylacrylic acid **560** revealed that the formation of endo-syn products **561** is strongly favoured (75–80%) over that of the endo-anti forms[661] (equation 359).



(**560**) (**561**)

(359)

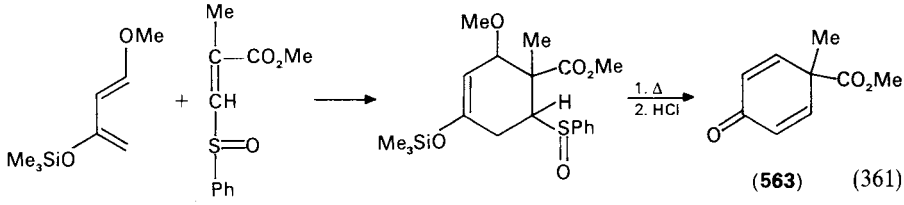
For a recent discussion on the stereochemical aspects of the Diels–Alder reaction with vinyl sulphoxides see References 662, 663. It should be pointed out that vinyl sulphoxides can be considered in [2 + 4]-cycloadditions as acetylene synthons since the sulphinyl moiety may be removed from the product by sulphenic acid elimination. Paquette and coworkers took advantage of this fact in the synthesis of properly substituted anthracenes **562**[664] (equation 360).



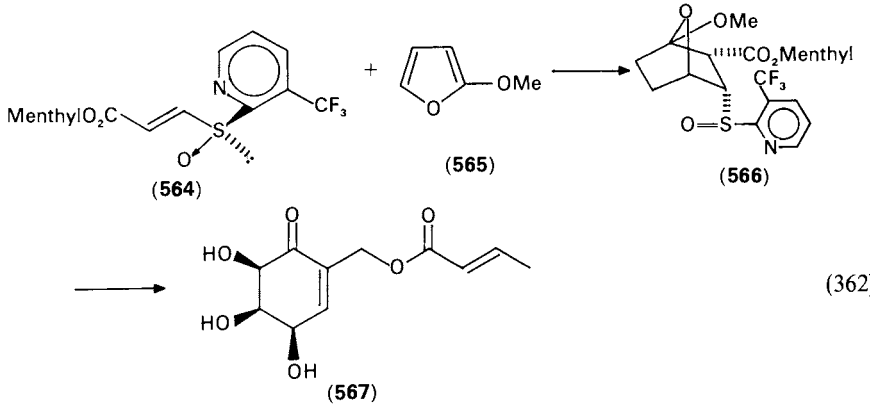
(360)

(562)

Danishefsky and coworkers using the same approach have synthesized substituted cyclohexadienones **563**[665,666] (equation 361). A highly stereoselective (96%) cycloaddition of diastereoisomerically pure (S_S)-menthyl 3-(3-trifluoromethylpyrid-2-ylsulphinyl)acrylate **564** to 2-methoxyfuran **565** leads to the cycloadduct **566** which was elaborated by Koizumi and coworkers to glyoxalase I inhibitor **567**[667] (equation 362).



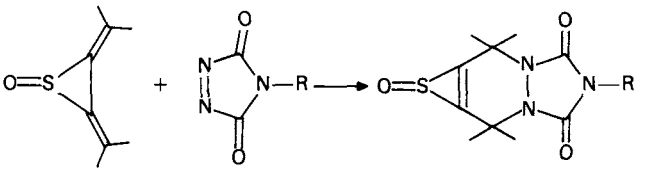
(563) (361)



(362)

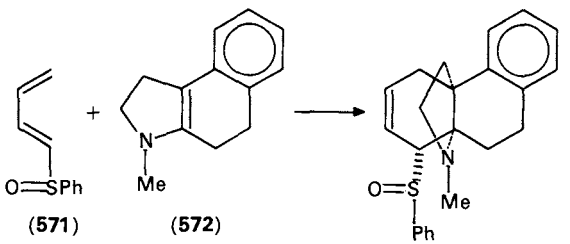
Divinyl sulphoxide was found to react with cyclopentadiene[668,669] or perchlorocyclopentadiene[670] to give a mixture of the monoaddition and diaddition products.

When the thiiranoradialene sulphoxide **568** was treated with an equimolar amount of 4-substituted 1, 2, 4-triazoline-3, 5-diones **569**, the adducts **570** were formed in quantitative yields[671] (equation 363).



(568) (569) (570) (363)

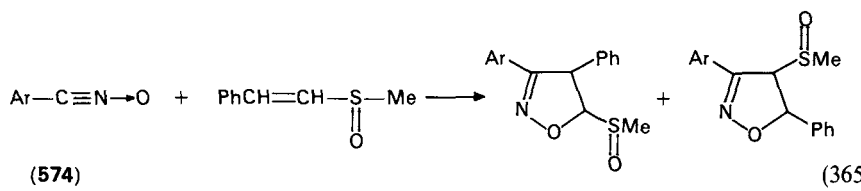
Butadienyl sulphoxides may be used as diene compounds in the Diels–Alder cycloadditions. For example, butadienyl phenyl sulphoxide **571** gives a mixture of diastereoisomeric sulphoxides **573** upon heating with an equimolar amount of *N*-methyl tetrahydrobenzindole **572**[672] (equation 364).



(571) (572) (573) (364)

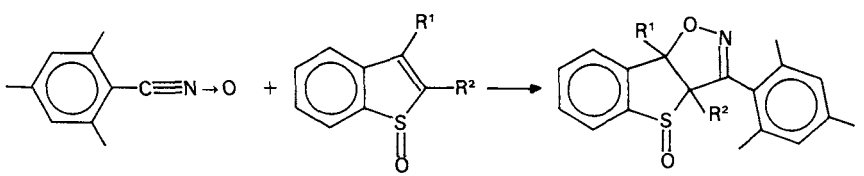
b. 1,3-Dipolar cycloadditions. Vinyl sulphoxides were also used as dipolarophiles in 1,3-dipolar cycloaddition reactions.

The cycloaddition of nitrile oxides **574** to vinyl sulphoxides usually produces a mixture of regio- and diastereoisomers. Their ratio is dependent on the nitrile oxide used and the configuration around the double bond in the starting sulphoxide (equation 365)[673].



(574) (365)

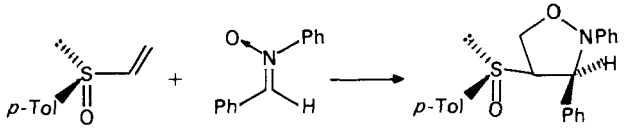
The 1,3-dipolar cycloaddition of mesitonitrile oxide **575** to benzo[*b*]thiophene *S*-oxides **576** in non-stereoselective and both *syn* and *anti* adducts **577** are obtained[674,675] (equation 366).



(575) (576) (577) (366)

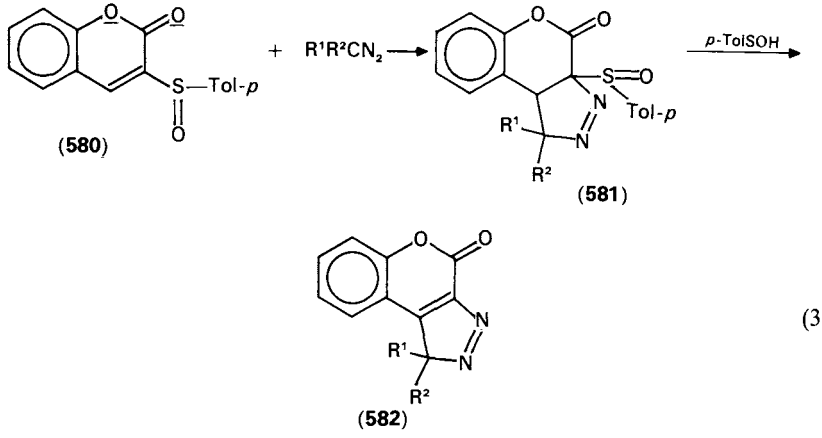
On the other hand, a very high asymmetric induction was observed in the 1,3-dipolar cycloaddition of (*R*)-(+)-*p*-tolyl vinyl sulphoxide **578** with acyclic nitrones. The reaction

depicted in equation 367 affords the product **579** in 57% yield and with 90% e.e.[676].



(578) (579) (367)

Diazoalkanes add to 3-*p*-toluenesulphinylcoumarin **580** to give the cycloaddition products **581**, which after elimination of *p*-toluenesulphenic acid afford 3-*H*-pyrazole derivatives **582**[677] (equation 368).



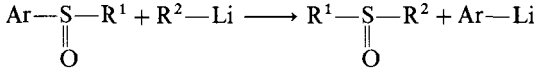
(580) (581) (582) (368)

D. Other Transformations of Organic Substituents in Sulphoxides

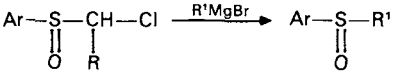
1. Exchange of organic substituents at the sulphinyl sulphur atom

The reaction of alkyllithium reagents with diaryl or alkyl aryl sulphoxides results in a displacement of the aromatic group by the alkyl group from the alkyllithium (equation 369)[380,381,479]. Johnson and coworkers[380] were the first to apply this reaction for the synthesis of optically active alkyl methyl sulphoxides. Later on, Durst and coworkers[381] found that the aromatic group which can best carry a negative charge is the most readily displaced, and that the lowest yields of displacement were observed when methyllithium was used as a nucleophilic reagent. The results are summarized in Table 28.

In the case of α-chloroalkyl aryl sulphoxides, the chloroalkyl group is easily replaced by an alkyl or aryl group of a Grignard reagent (equation 370). Bromomethyl sulphoxides react slowly and give the products in low yields, while iodomethyl sulphoxides are unreactive presumably due to steric hindrance (Table 29)[678].



(369)



(370)

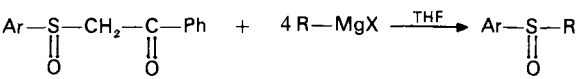
TABLE 28. Displacement of aryl groups in sulphoxides by alkyllithiums

Aryl	R^1	R^2	Yield (%)	Refs.
p-Tol	Me	*n*-Bu	84	380
p-Tol	Me	*t*-Bu	75	380
p-Tol	*n*-Bu	*t*-Bu	76	380
Ph	Me	*n*-Bu	83	380
Ph	Me	*t*-Bu	66	381
Ph	Me	Me	3	381
Ph	Et	*n*-Bu	35	381
Ph	Et	*t*-Bu	50	381
Ph	*i*-Pr	Me	0	381
Ph	*i*-Pr	*t*-Bu	38	381
Ph	CH_2Ph	Me	7	381
Ph	CH_2Ph	*n*-Bu	40	381
Ph	CH_2Ph	*t*-Bu	50	381
p-Tol	$(CH_2)_5CHMe_2$	*t*-Bu	100	479
Ph	CH_2Cl	Me	12	381
Ph	CH_2Cl	*n*-Bu	4	381
Ph	CH_2Cl	*t*-Bu	5	381
Ph	CH(Cl)Me	Me	36	381
Ph	CH(Cl)Me	*n*-Bu	22	381
Ph	CH(Cl)Me	*t*-Bu	9	381

TABLE 29. Displacement of chloroalkyl groups in sulphoxides by Grignard reagents[678]

Aryl	R	R^1	Yield (%)
Ph	H	Et	99
Ph	H	*i*-Pr	55
p-Tol	H	Et	93
Ph	H	Ph	96
p-ClC_6H_4	H	Ph	97
Ph	Me	*i*-Pr	80
p-Tol	Et	Et	80
Ph	H	CH_2Br	81

With α-ketosulphoxides a displacement of the enolate grouping by an excess of a Grignard reagent takes place only when the reaction is performed in THF (equation 371)[679].

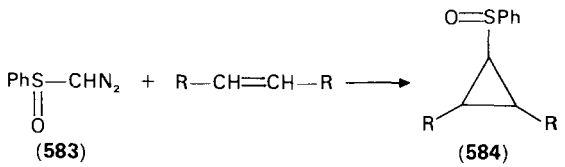


(371)

2. Formation and reactions of α-sulphinyl carbenes

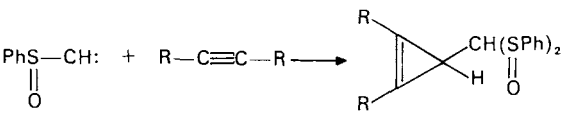
Phenyl diazomethyl sulphoxide **583** formed *in situ* from diazomethane and benzenesulphinyl chloride undergoes addition to olefins affording the corresponding cyclopropyl

sulphoxides **584** in 35–40% yield[680,681] (equation 372). The addition proceeds in a *trans*-manner and most probably via a singlet carbene. Reaction of the same carbene **585** with alkynes leads, however, to an unexpected product **586**[682] (equation 373).



(372)

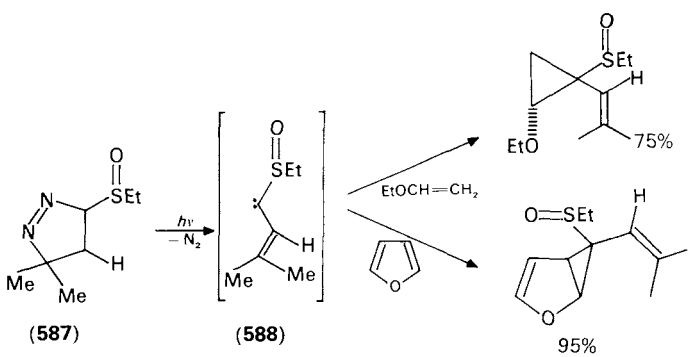
(583) (584)



(373)

(585) (586)

Photolysis of the sulphinyl-3*H*-pyrazole **587** in ether or methylene chloride leads to the formation of a relatively stable carbene **588** that can be identified by physical methods. When the irradiation is performed in ethyl vinyl ether or in furan, the expected cyclopropanes are formed smoothly and stereospecifically[683] (equation 374).

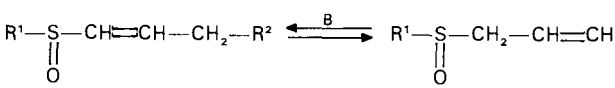


(374)

(587) (588) 75% 95%

3. *Rearrangement of substituents in sulphoxides*

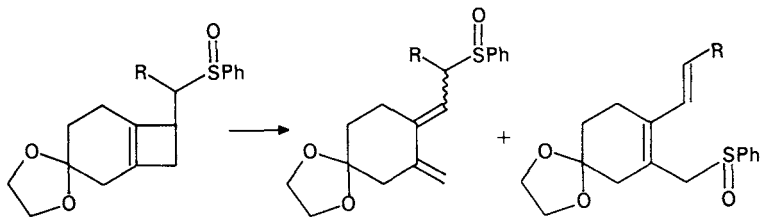
Double bond migration in vinylic and allylic sulphoxides can be achieved by using proper bases B (equation 375).



(375)

This reaction and its synthetic applications have been already described in previous sections (Section IV.A.2.d, References 475, 520, 521; Section IV.C.2.a, Reference 629).

Arenesulphinyl groups have been found to facilitate ring opening of cyclobutanes (equation 376)[684].



(376)

Anions of thietane-1-oxides **589** undergo ring contraction to give cyclopropyl sulphoxides **590**[685] (equation 377).

(377)

(589) **(590)**

V. REFERENCES

1. A. Schöberl and A. Wagner, in *Methoden der Organischen Chemie (Houben-Weyl)*, Vol. IX, 4th Ed. (Ed. E. Müller), George Thieme Verlag, Stuttgart, 1955, pp. 211–221.
2. G. Kresze, in *Methoden der Organischen Chemie (Houben-Weyl)*, Vol. 11E, 5th Ed. (Ed. D. Klamann), George Thieme Verlag, Stuttgart, 1985, pp. 669–886.
3. T. Durst, in *Comprehensive Organic Chemistry*, Vol. 3 (Ed. D. N. Jones), Pergamon, Oxford, 1979, pp. 121–156.
4. P. A. Lowe, in *Rodd's 'Chemistry of Carbon Compounds'*, Part 1A–B, Suppl. (Ed. M. P. Ansell), Elsevier, Amsterdam, 1985, pp. 109–129.
5. S. Oae, in *Organic Chemistry of Sulphur* (Ed. S. Oae), Plenum Press, London, 1977, pp. 383–471.
6. E. Block, *Reactions of Organosulfur Compounds*, Academic Press, 1978.
7. C. R. Johnson and J. C. Sharp, *Quart. Rep. Sulfur Chem.*, **4**, No 1 (1969).
8. J. Drabowicz and M. Mikołajczyk, *Org. Prep. Proced. Int.*, **14**, 45 (1982).
9. C. Märcker, *Ann. Chem.*, **136**, 891 (1865).
10. M. Gazdar and S. Smiles, *J. Chem. Soc.*, **93**, 1833 (1908).
11. S. Hunig and S. Boes, *Ann. Chem.*, **579**, 23 (1953).
12. D. Barnard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).
13. D. Barnard, L. Bateman, M. E. Cain, T. Colclough and J. I. Cunneen, *J. Chem. Soc.*, 5339 (1961).
14. J. Drabowicz and M. Mikołajczyk, *Synth. Commun.*, **11**, 1025 (1981).
15. M. F. Shostakowskii, N. V. Komarov and N. N. Vlasova, *Inter. Symp. Organosilicon Chem. Sci. Commun., Suppl. Prague*, 1965, p. 21; *Chem. Abstr.*, **65**, 8950 (1966).
16. M. Sander, *Monatsh. Chem.*, **96**, 896 (1965).
17. N. V. Drozd, V. A. Sozonova and A. N. Nesmeyanov, *Dokl. Akad. Nauk SSSR*, 159 (1964).
18. R. D. Obolentsev, V. G. Bukharov and M. M. Gerasimow, *Khim. Sera i Azotoorgan. Soedin., Akad. Nauk SSSR, Bashkirsk Filial*, **3**, 35 (1969); *Chem. Abstr.*, **57**, 5868c (1962).
19. K. Fujita, S. Ejima, T. Ueda, T. Imoto and H. R. Schulten, *Tetrahedron Letters*, **25**, 3711 (1984).
20. O. Hinsberg, *Chem. Ber.*, **41**, 2836 (1908).
21. A. Ceruiani, G. Modena and P. E. Todesco, *Gazz. Chim. Ital.*, **90**, 383 (1973).
22. D. C. Dittmer and G. C. Levy, *J. Org. Chem.*, **30**, 636 (1965).
23. A. H. Schlessinger and T. A. Mowny, *J. Amer. Chem. Soc.*, **73**, 2614 (1951).
24. H. H. Szmant and L. H. Alfonso, *J. Amer. Chem. Soc.*, **79**, 205 (1957).
25. C. R. Harrison and P. Hodge, *J. Chem. Soc., Perkin Trans. 1*, 2212 (1976).
26. A. D. Baeker, R. Scharfman and C. A. Stein, *Tetrahedron Letters*, **24**, 2957 (1983).

27. S. Oae, T. Kawi and N. Furukawa, *Tetrahedron Letters*, **25**, 69 (1984).
28. K. Ogura and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **45**, 2203 (1972).
29. G. Schill and P. R. Jones, *Synthesis*, 117 (1974).
30. F. E. Hardy, R. P. H. Speakman and P. Robson, *J. Chem. Soc. (C)*, 2334 (1969).
31. G. Tsuchihashi and K. Ogura, D.O.S. 2336817 (1974); *Chem. Abstr.*, **80**, 108 182 (1974).
32. J. Drabowicz and M. Mikołajczyk, *Synthesis*, 758 (1978).
33. H. J. Reich, F. Chow and S. L. Peake, *Synthesis*, 299 (1978).
34. N. N. Melnikov, *Usp. Khim.*, 443 (1936).
35. Y. Watanabe, T. Numata and S. Oae, *Synthesis*, 204 (1981).
36. L. Levin, *J. prakt. Chem.*, **127**, 77 (1930).
37. L. Bateman and K. R. Hargrave, *Proc. Roy. Soc. London, Ser. A.*, **224**, 389 (1954).
38. D. Barnard, *J. Chem. Soc.*, 489 (1956).
39. L. Horner and E. Jürgens, *Ann. Chem.*, **602**, 135 (1957).
40. W. A. Pryor and H. T. Bickley, *J. Org. Chem.*, **37**, 2885 (1972).
41. B. Ganem, A. J. Biloski and R. P. Heggs, *Tetrahedron Letters*, **21**, 689 (1980).
42. T. Tezuka and H. Suzuki, *J. Chem. Soc., Chem. Commun.*, 325 (1985).
43. R. Criegee, *Ann. Chem.*, **560**, 127 (1948).
44. L. Lewin, *J. prakt. Chem.*, **118**, 282 (1928).
45. C. G. Overberger and R. W. Cummins, *J. Amer. Chem. Soc.*, **75**, 4250 (1953).
46. L. A. Carpino and H. W. Chen, *J. Amer. Chem. Soc.*, **101**, 390 (1979).
47. W. Ando, Y. Haniu and T. Takata, *Tetrahedron*, **42**, 1989 (1986).
48. N. Ueda, H. Shimizu, T. Kataoka and H. Hori, *Tetrahedron Letters*, **25**, 757 (1984).
49. (a) A. Saytzeff, *Ann. Chem.*, **139**, 354 (1866); **144**, 148 (1867).
(b) E. Fromm, *Ann. Chem.*, **396**, 75 (1913).
(c) T. P. Hildtich, *J. Chem. Soc.*, **93**, 1618 (1908).
50. A. Polard and R. Robinson, *J. Chem. Soc.*, 3090 (1926); F. G. Bordwell and B. J. Boutan, *J. Amer. Chem. Soc.*, **79**, 717 (1957).
51. G. Laurence, *Compt. Rend. Acad. Sci., Ser. C*, **269**, 352 (1969).
52. L. M. Yagupolskii and A. G. Panteleimonov, *J. Gen. Chem. USSR*, **35**, 1123 (1965).
53. R. N. Haszeldine, R. B. Rigby and A. E. Tipping, *J. Chem. Soc., Perkin Trans. 1*, 676 (1973).
54. B. Ciocca and L. Canonica, *Gazz. Chim. Ital.*, **76**, 113 (1946); *Chem. Abstr.*, **46**, 7153 (1946); N. Marziano and A. Compagniani, *Ann. Chim. (Rome)*, **58**, 59 (1968); Y. Ogata and T. Kamei, *Tetrahedron*, **26**, 5567 (1970).
55. R. Low, H. P. W. Vermeeren, J. J. A. van Asten and W. J. Ultee, *J. Chem. Soc., Chem. Commun.*, 496 (1976).
56. G. A. Olah, B. G. Gupta and S. C. Narang, *J. Amer. Chem. Soc.*, **101**, 5317 (1979).
57. Y. Nagano, M. Ochiai, K. Kaneko, A. Maeda, K. Watanabe and E. Fujita, *Tetrahedron Letters*, 1345 (1977).
58. T. L. Ho and C. M. Wong, *Synthesis*, 562 (1972).
59. T. L. Ho, *Synth. Commun.*, **9**, 237 (1979).
60. R. Pummerer, *Chem. Ber.*, **43**, 1407 (1910).
61. E. Bell and G. Bennett, *J. Chem. Soc.*, 1978 (1927).
62. R. D. Whitaker and H. H. Sisler, *J. Org. Chem.*, **25**, 1038 (1960).
63. L. Horner and F. Hübenett, *Ann. Chem.*, **579**, 193 (1953).
64. C. C. Addison and J. C. Sheldon, *J. Chem. Soc.*, 2705 (1956).
65. R. D. Whitaker and C. L. Bennett, *Quart. J. Florida Acad. Sci.*, **28**, 137 (1965); *Chem. Abstr.*, **63**, 9436d (1965).
66. W. H. Ford-Moore, *J. Chem. Soc.*, 2126 (1949).
67. T. Takaya, H. Enyo and E. Imoto, *Bull. Chem. Soc. Japan*, **41**, 1032 (1968).
68. H. H. Szmant and G. Suld, *J. Amer. Chem. Soc.*, **78**, 3400 (1956).
69. K. C. Schreiber and V. P. Fernandez, *J. Org. Chem.*, **26**, 2910 (1961).
70. G. Barbieri, M. Cinquini, S. Colonna and F. Montanari, *J. Chem. Soc. (C)*, 659 (1969).
71. N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962); C. R. Johnson and J. E. Keiser, *Org. Synth.*, **46**, 78 (1966).
72. Y. Ueno, T. Inoue and M. Okawara, *Tetrahedron Letters*, 2413 (1977).
73. A. W. Chow, N. M. Hall and J. R. E. Hoover, *J. Org. Chem.*, **27**, 1381 (1962).
74. J. M. Essery, K. Dadabo, W. J. Gottstein, A. Hallastrand and L. C. Eheney, *J. Org. Chem.*, **30**, 4388 (1965).

75. D. A. Evans, C. A. Brygan and C. L. Sims, *J. Amer. Chem. Soc.*, **94**, 2891 (1972).
76. M. Mikołajczyk and A. Zatorski, *Synthesis*, 669 (1973).
77. R. G. Hiskey and M. A. Harpold, *J. Org. Chem.*, **32**, 3191 (1967).
78. E. Santaniello, A. Manzocchi and A. Farachi, *Synthesis*, 563 (1980).
79. K. T. Lin and Y. C. Tong, *J. Org. Chem.*, **43**, 2717 (1978).
80. D. N. Gupta, P. Hodge and J. E. Davies, *J. Chem. Soc., Perkin Trans. 1*, 2970 (1981).
81. C. R. Harrison and P. Hodge, *J. Chem. Soc., Perkin Trans. 1*, 509 (1982).
82. H. Kwart and R. K. Miller, *J. Amer. Chem. Soc.*, **78**, 5008 (1956).
83. C. F. Bennett, D. V. Goheen and W. S. MacGregor, *J. Org. Chem.*, **28**, 2485 (1963).
84. J. S. Grossert, W. R. Hardstaff and R. F. Langer, *Can. J. Chem.*, **55**, 421 (1977).
85. J. S. Grossert, W. R. Hardstaff and R. F. Langer, *J. Chem. Soc., Chem. Commun.*, 50 (1973).
86. T. Zinke and W. Frohneberg, *Chem. Ber.*, **43**, 837 (1910).
87. S. Oae, Y. Onishi, S. Kozuka and W. Tagaki, *Bull. Chem. Soc. Japan*, **39**, 364 (1966).
88. D. O. Spray, *Tetrahedron Letters*, 3717 (1972).
89. J. Drabowicz, W. Midura and M. Mikołajczyk, *Synthesis*, 39 (1979).
90. A. Okruszek, *J. Labelled Compd. Radiophram.*, **20**, 741 (1983).
91. T. Higuchi and K. H. Gensch, *J. Amer. Chem. Soc.*, **88**, 3874 (1966).
92. T. Eiki and W. Tagaki, *Chem. Letters*, 1063 (1980).
93. P. R. Young and L. S. Hsieh, *J. Org. Chem.*, **47**, 1419 (1982).
94. P. R. Young and M. Till, *J. Org. Chem.*, **47**, 1416 (1982).
95. L. L. S. Reamonn and W. I. O.'Sullivan, *J. Chem. Soc., Chem. Commun.*, 1012 (1976); L. L. S. Reamonn and W. I. O'Sullivan, *J. Chem. Soc., Perkin Trans. 1*, 1194 (1980).
96. P. S. Skell and M. F. Epstein, Abstracts 147th ACS Meeting, April 1964, Philadelphia, p. 26N.
97. C. R. Johnson and D. McCants Jr., *J. Amer. Chem. Soc.*, **87**, 1109 (1965).
98. L. S. Skattebol, B. Boulette and S. Solemen, *J. Org. Chem.*, **32**, 3111 (1967).
99. N. K. Sharma, F. de Reinach-Hirtzbach and T. Durst, *Can. J. Chem.*, **54**, 3012 (1976).
100. P. Geneste, J. Grimaud, J. L. Olive and S. N. Ung, *Tetrahedron Letters*, 2345 (1975).
101. W. Tagaki, K. Kikukawa, K. Ando and S. Oae, *Chem. Ind. (London)*, 1624 (1964).
102. K. M. More and J. Wemple, *Synthesis*, 791 (1977).
103. R. Harlville and S. F. Reed Jr., *J. Org. Chem.*, **33**, 3976 (1968).
104. Y. Sato, N. Kunieda and M. Kinoshita, *Chem. Letters*, 1023 (1972).
105. Y. Sato, N. Kunieda and M. Kinoshita, *Mem. Fac. Eng. Osaka City Univ.*, 101 (1974); *Chem. Abstr.*, **83**, 205875 (1975).
106. W. D. Kingsbury and C. R. Johnson, *J. Chem. Soc., Chem. Commun.*, 365 (1969).
107. J. Benes, *Coll. Czech. Chem. Commun.*, **28**, 1171 (1963).
108. J. Traynelis, Y. Yoshikawa, S. M. Tarka and J. R. Livingston Jr., *J. Org. Chem.* **38**, 3986 (1973).
109. M. Hojo and R. Masuda, *Tetrahedron Letters*, 613 (1976); M. Hojo, R. Masuda and K. Hakotani, *Tetrahedron Letters*, 1121 (1978).
110. V. Calo, F. Ciminale, G. Lopez and P. E. Todesco, *Int. J. Sulfur Chem.* [*A*], **1**, 130 (1971).
111. C. S. Foote and J. W. Peters, *J. Amer. Chem. Soc.*, **93**, 3795 (1971).
112. D. Sinnreich, H. Lind and H. Batzer, *Tetrahedron Letters*, 3541 (1976).
113. T. Tezuka, H. Suzuki and H. Miyazaki, *Tetrahedron Letters*, 1959 (1978).
114. M. N. Akhtar, R. D. Boyd, J. D. Neill and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1693 (1980).
115. H. J. Shine and L. Piette, *J. Amer. Chem. Soc.*, **84**, 4798 (1962).
116. G. S. Wilson, D. D. Swanson, J. T. Klug, R. S. Glass, M. D. Ryan and W. K. Musker, *J. Amer. Chem. Soc.*, **101**, 1040 (1979).
117. A. A. Haumffray and D. S. Houghton, *Electrochim. Acta*, **17**, 1435 (1972).
118. D. S. Houghton and A. A. Haumffray, *Electrochim. Acta*, **17**, 1421 (1972).
119. D. S. Houghton and A. A. Haumffray, *Electrochim. Acta*, **17**, 2145 (1972).
120. K. Uneyama and S. Tori, *Tetrahedron Letters*, 329 (1971).
121. P. Margaretha, *Helv. Chim. Acta*, **62**, 1978 (1979).
122. H. E. Imberger and A. A. Haumffray, *Electrochim. Acta*, **18**, 373 (1973).
123. M. Kimura, N. Kuriki, M. Inashi and Y. Sawaki, *Tetrahedron Letters*, **25**, 4665 (1984).
124. R. Knoll, *J. prakt. Chem.*, [2], **113**, 40 (1926).
125. H. H. Szmant and R. Lapiński, *J. Amer. Chem. Soc.*, **80**, 6883 (1958).
126. D. E. Edwards and J. B. Stenlake, *J. Chem. Soc.*, 3272 (1954).
127. H. Böhme, H. Fischer and R. Frank, *Ann. Chem.*, **563**, 54 (1949).

128. D. Barnard and D. T. Woodbridge, *Chem. Ind. (London)*, 1603 (1959); F. Ogura, Y. Yamamushi, T. Otsubo and H. Tanaka, *Bull. Chem. Soc. Japan*, **55**, 641 (1982).
129. T. Tezuka, H. Miyazaki and H. Suzuki, *Tetrahedron Letters*, 4885 (1978).
130. L. G. Faehl and J. L. Kice, *J. Org. Chem.*, **44**, 2357 (1979).
131. J. P. Gregorov and A. F. Levit, *Zh. Obshch. Khim.*, **33**, 544 (1963); *Chem. Abstr.*, **59**, 15064 (1963).
132. L. Horner, H. Schaefer and W. Ludwig, *Chem. Ber.*, **91**, 75 (1958).
133. D. Barnard, *J. Chem. Soc.*, 4547 (1957).
134. L. J. Hughens, T. D. McMin Jr. and J. C. Burleson, US Patent **3**, 114, 775 (1963); *Chem. Abstr.*, **60**, 6751a (1964).
135. F. G. Bordwell and W. T. Branner Jr., *J. Amer. Chem. Soc.*, **86**, 4645 (1964).
136. A. V. Mashkina and L. B. Aroleva, *Neftkhimia*, **8**, 414 (1968); *Chem. Abstr.*, **69**, 86270 (1968).
137. F. A. Davis, R. Jenkins Jr. and S. G. Yocklovich, *Tetrahedron Letters*, 5171 (1978).
138. D. M. Jerina, D. R. Boyd and J. W. Daley, *Tetrahedron Letters*, 457 (1970).
139. D. Barnard, *Chem. Ind. (London)*, 565 (1955).
140. S. Searles and H. R. Hays, *J. Org. Chem.*, **23**, 2028 (1958).
141. C. M. Hull and T. W. Barger, *J. Org. Chem.*, **40**, 3152 (1975).
142. T. Numata and S. Oae, *Int. J. Sulfur Chem., A*, **1**, 6 (1971).
143. P. Müller and J. Godoy, *Helv. Chim. Acta*, **66**, 1790 (1983).
144. T. Takata, R. Tajima and W. Ando, *Phosphorus and Sulfur*, **16**, 67 (1983).
145. K. Sugiyama, T. Ogawa and H. Hirano, *Yakugaku Zasshi*, **101**, 904 (1981); *Chem. Abstr.*, **96**, 85485 (1982).
146. M. S. Kharasch, W. Nudenberg and G. L. Mantell, *J. Org. Chem.*, **16**, 524 (1951).
147. A. A. Oswald, *J. Org. Chem.*, **26**, 842 (1961).
148. J. F. Ford, R. C. Pitkethly and V. O. Young, *Tetrahedron*, **4**, 325 (1958).
149. H. H. Szmant and J. J. Rigau, *J. Org. Chem.*, **37**, 447 (1972).
150. H. Bredereck, A. Wagner and K. Kottenhahn, *Chem. Ber.*, **93**, 2415 (1960).
151. S. Iriuchijima, K. Maniawa, T. Sakakibara and G. Tsuchihashi, *J. Org. Chem.*, **39**, 1170 (1974); S. Iriuchijima and G. Tsuchihashi, *Synthesis*, 401 (1975).
152. A. L. J. Beckwith and R. D. Wagner, *J. Org. Chem.*, **46**, 3638 (1981); A. L. J. Beckwith, J. R. Rodgers and R. D. Wagner, *Aust. J. Chem.*, **35**, 989 (1982).
153. A. Strecker, *Chem. Ber.*, **43**, 1131 (1910).
154. N. P. Volynskii, G. D. Galpern and V. V. Smolyaninov, *Neftkhimia*, *1*, 473 (1961); *Chem. Abstr.*, **57**, 1650h (1962).
155. V. Franzen, H. I. Joschek and G. Mertz, *Ann. Chem.*, **654**, 82 (1962).
156. H. Bert, *Compt. Rend. Acad. Sci.*, **178**, 1826 (1924).
157. H. Gilman, J. Robinson and N. Beaber, *J. Amer. Chem. Soc.*, **48**, 2715 (1926).
158. S. Bast and K. K. Andersen, *J. Org. Chem.*, **33**, 846 (1968).
159. D. N. Harpp, S. M. Vines, J. P. Montillier and T. H. Chan, *J. Org. Chem.*, **41**, 3987 (1976).
160. E. Wenschuh and H. Lankau, *Z. Chem.*, **13**, 427 (1973).
161. R. M. Coates and H. D. Pigott, *Synthesis*, 319 (1975).
162. H. J. Monteiro and J. P. de Souza, *Tetrahedron Letters*, 921 (1975).
163. P. A. Zoretic, P. Soja and N. D. Sinha, *J. Org. Chem.*, **43**, 1379 (1978).
164. H. Bohme and B. Clement, *Tetrahedron Letters*, 1737 (1979).
165. A. G. Brook and D. G. Anderson, *Can. J. Chem.*, **46**, 2115 (1968).
166. F. C. Carey and O. Hernandez, *J. Org. Chem.*, **38**, 2670 (1973).
167. Y. Nogushi, K. Kurogi, M. Sekioka and M. Furukawa, *Bull. Chem. Soc. Japan*, **56**, 349 (1983).
168. A. G. Schultz and R. H. Schlessinger, *J. Chem. Soc., Chem. Commun.*, 747 (1974).
169. C. G. Venier, C. G. Gibbs and P. T. Crane, *J. Org. Chem.*, **39**, 501 (1974).
170. J. A. Loontjes, M. van der Leij and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, **99**, 39 (1980).
171. G. E. Veenstra and B. Zwanenburg, *Tetrahedron*, **34**, 1585 (1978); B. Zwanenburg and P. Kiełbasiński, *Tetrahedron*, **35**, 169 (1979).
172. E. Schaumann and W. R. Klein, *Tetrahedron Letters*, 3457 (1977).
173. M. van der Leij, H. T. M. Strijtveen and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, **99**, 45 (1980).
174. T. Fujisawa, A. Noda, T. Kawara and T. Sato, *Chem. Letters*, 1159 (1981).
175. C. E. Colby and C. S. McLaughlin, *Ber.*, **20**, 195 (1887).
176. R. L. Shriner, H. C. Struck and W. J. Jorison, *J. Amer. Chem. Soc.*, **52**, 2060 (1930).
177. G. C. Hampson, H. Farmer and L. E. Sutton, *Proc. Roy. Soc. London, Ser. A*, **143**, 146 (1933).

178. C. W. N. Cumper, J. F. Read and A. I. Vogel, *J. Chem. Soc.*, 5860 (1965).
179. V. G. Kullkarni and G. V. Jadhar, *J. Indian Chem. Soc.*, **34**, 245 (1957); *Chem. Abstr.*, **51**, 17795c (1957).
180. J. Granoth, A. Kalair and Z. Pelah, *J. Chem. Soc. (C)*, 2424 (1969).
181. C. C. Silveradd, *Chem. Ind. (London)*, **45**, 36 (1926).
182. P. Courtot and P. Chffert, Dissertation, Nancy (1926); see Ref. 1, p. 217.
183. J. B. Douglas and B. S. Farah, *J. Org. Chem.*, **23**, 805 (1958).
184. G. A. Olah and J. Nishimura, *J. Org. Chem.*, **39**, 1203 (1974).
185. D. W. Chasar and T. M. Pratt, *Phosphorus and Sulfur*, **5**, 35 (1978).
186. L. L. Rephogle and J. R. Maynarol, *J. Org. Chem.*, **32**, 1909 (1967).
187. O. Carmona, R. Greenhouse, R. Landeros and J. Muchowski, *J. Org. Chem.*, **45**, 5336 (1980).
188. S. Oae and K. Ikura, *Bull. Chem. Soc. Japan*, **39**, 1306 (1966).
189. N. K. Chapovskaya, L. K. Knyazeva and N. S. Zefirov, *Zh. Org. Khim.*, 9, 1014 (1973); Eng. Ed. 1041 (1973).
190. C. A. Bunton and J. M. Shreeve, *Inorg. Chem.*, **16**, 1039 (1977).
191. B. B. Snider, *J. Org. Chem.*, **46**, 3155 (1981).
192. V. N. Sergeev, G. S. Zeitseva and Y. I. Baukov, *Zh. Obshch. Khim.*, **50**, 699 (1980); *Chem. Abstr.*, **93**, 132020 (1980).
193. N. A. Meanwell and C. R. Johnson, *Synthesis*, 283 (1982).
194. F. Effenberger and J. Daub, *Angew. Chem.*, **76**, 1435 (1964); F. Effenberger and J. Daub, *Chem. Ber.*, **102**, 104 (1969).
195. G. Glaros and S. Sullivan, *Synth. Commun.*, **6**, 495 (1976).
196. A. M. Moiseenkov, Lecture presented during VI International Conference on Organic Synthesis, Moscow, August 10–15, 1986.
197. J. R. Shelton and K. E. Davis, *J. Amer. Chem. Soc.*, **89**, 718 (1967).
198. E. Block and J. O'Connor, *J. Amer. Chem. Soc.*, **96**, 3929 (1974).
199. F. A. Davis, A. J. Friedman and U. K. Nadir *J. Amer. Chem. Soc.*, **100**, 2844 (1978).
200. D. N. Jones, P. D. Cottam and J. Davies, *Tetrahedron Letters*, 4977 (1979).
201. G. E. Miller, D. R. Rayner and K. Mislow, *J. Amer. Chem. Soc.*, **88**, 3139 (1966).
202. S. Braverman and Y. Stabinsky, *J. Chem. Soc., Chem. Commun.*, 270 (1967).
203. G. Sosnovsky, *J. Chem. Soc.*, 3139 (1956).
204. D. A. Evans, G. G. Andrews and C. L. Sims, *J. Amer. Chem. Soc.*, **93**, 4956 (1971).
205. N. S. Zefirov and F. A. Abdulvaleeva, *Vest. Mosk. Univ. Khim.*, **11**, 725 (1970); *Chem. Abstr.*, **74**, 125046 (1971); N. S. Zefirov and F. A. Abdulvaleeva, *Vest. Mosk. Univ. Khim.*, **24**, 135 (1969); *Chem. Abstr.*, **71**, 112345 (1969); N. S. Zefirov and F. A. Abdulvaleeva, *Zh. Org. Khim.*, 7, 947 (1971).
206. S. Braverman and B. Grendi, *Tetrahedron*, **30**, 2379 (1974).
207. S. Braverman and Y. Stabinsky, *Israel J. Chem.*, **5**, 125 (1967); *Chem. Abstr.*, **68**, 21379 (1968).
208. L. Horner and V. Binder, *Ann. Chem.*, **757**, 33 (1972).
209. G. Smith and C. J. M. Stirling, *J. Chem. Soc. (C)*, 1530 (1971).
210. I. Cutting and P. J. Parsons, *Tetrahedron Letters*, **24**, 4463 (1983).
211. E. M. G. A. van Kruchten and W. H. Okamura, *Tetrahedron Letters*, **23**, 1019 (1982).
212. S. Jeganthan and W. H. Okamura, *Tetrahedron Letters*, **23**, 4763 (1982).
213. R. M. Dodson and F. R. Sauers, *J. Chem. Soc., Chem. Commun.*, 1189, (1967).
214. P. Chao and D. M. Lemal, *J. Amer. Chem. Soc.*, **95**, 920 (1973).
215. R. M. Dodson and J. P. Nelson, *J. Chem. Soc., Chem. Commun.*, 1169 (1969).
216. A. G. Anastassiou and B. Y. H. Chao, *J. Chem. Soc., Chem. Commun.*, 979 (1971).
217. W. A. Sheppard and J. Dickman, *J. Amer. Chem. Soc.*, **86**, 1891 (1964).
218. A. M. Hamid and S. Trippett, *J. Chem. Soc. (C)*, 1612 (1968).
219. B. Zwanenburg, L. Thijs and J. Strating, *Tetrahedron Letters*, 4461 (1969).
220. B. Zwanenburg, A. Wagenaar, L. Thijs and J. Strating, *J. Chem. Soc., Perkin Trans. 1*, 73 (1973).
221. C. G. Venier and C. G. Gibbs, *Tetrahedron Letters*, **22**, 2293 (1972).
222. L. Thijs, J. Strating and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas.*, **91**, 1345 (1972).
223. B. F. Bonini and G. Maccagnani, *Gazz. Chim. Ital.*, **105**, 827 (1975).
224. E. Schaumann, H. Behr, G. Adiwidjaja, A. Tangerman, B. H. M. Lammerink and B. Zwanenburg, *Tetrahedron*, **27**, 219 (1981).
225. B. F. Bonini, G. Maccagnani, L. Thijs and B. Zwanenburg, *Tetrahedron Letters*, 3569 (1973);

B. F. Bonini, G. Maccagnani, G. Mazzanti, L. Thijs, G. E. Veenstra and B. Zwanenburg, *J. Chem. Soc., Perkin Trans. 1*, 1218 (1978).
226. B. F. Bonini, G. Maccagnani, G. Mazzanti, L. Thijs, H. P. M. M. Ambrosius and B. Zwanenburg, *J. Chem. Soc., Perkin Trans. 1*, 1468 (1977).
227. B. F. Bonini, G. Maccagnani, G. Mazzanti and B. Zwanenburg, *Gazz. Chim. Ital.*, **107**, 289 (1977).
228. B. F. Bonini, G. Maccagnani, G. Mazzanti, P. Petrini and B. Zwanenburg, *Gazz. Chim. Ital.*, **107**, 283 (1977).
229. E. Block and A. Wall, *Tetrahedron Letters*, **26**, 425 (1985).
230. T. Karakasa and S. Motoki, *Tetrahedron Letters*, 3961 (1979).
231. B. H. Nicolet and J. Willard, *Science*, **53**, 217 (1921).
232. R. Appel and W. Buechner, *Chem. Ber.*, **95**, 855 (1962).
233. H. Kobayashi, N. Furukawa, T. Aida and S. Oae, *Tetrahedron Letters*, 3109 (1971).
234. H. Hepwort and H. W. Chapham, *J. Chem. Soc.*, 1188 (1921).
235. H. Reinheckel and D. Jahnke, *Chem. Ber.*, **99**, 1718 (1966); H. Reinheckel and D. Jahnke, D.D.R.P. 51311 (1966); *Chem. Abstr.*, **66**, 104 821 (1967); R. Reinheckel and D. Jahnke, D.D.R.P., 1568 367 (1970); *Chem. Abstr.*, **74**, 141265 (1971).
236. Y. Gaoni, *Tetrahedron Letters*, 4521 (1977).
237. A. G. Anastassiou, J. C. Wetzel and B. Y. H. Chao, *J. Amer. Chem. Soc.*, **97**, 1124 (1975).
238. M. Shimagaki, H. Tsuchiya, Y. Ban and T. Oishi, *Tetrahedron Letters*, 3435 (1978).
239. I. W. J. Still and S. Szilagyi, *Synth. Commun.*, **9**, 923 (1979); I. W. L. Still and F. J. Ablenas, *J. Org. Chem.*, **48**, 1617 (1983).
240. R. G. Pearson, *Surv. Prog. Chem.*, **5**, 1 (1969); R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963).
241. E. Vinkler, F. Klivenyi and J. Pintye, *Acta Chim. (Budapest)*, **65**, 333 (1970); *Chem. Abstr.*, **74**, 3383 (1971).
242. D. R. Hogg and A. Robertson, *Tetrahedron Letters*, 3783 (1974); D. R. Hogg and A. Robertson, *J. Chem. Soc., Perkin Trans. 1*, 1125 (1979).
243. M. van der Leij and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, **99**, 49 (1980).
244. E. Ayca, *Rev. Fac. Sci. Iniv. Instanbul, Ser. C*, **22**, 371 (1957); *Chem. Abstr.*, **53**, 11287 (1959).
245. C. G. Venier, H. H. Hsieh and H. J. Barager III, *J. Org. Chem.*, **38**, 17 (1973).
246. C. G. Venier and H. J. Barager III, *J. Chem. Soc., Chem. Commun.*, 319 (1973); C. G. Venier and H. J. Barager III, *Org. Prep. Proced. Int.*, **6**, 77 (1974).
247. A. Senning, S. Kaae and C. Jacobsen, *Acta Chim. Scand.*, **22**, 3256 (1968).
248. P. Lapape, *Ann. Pharm. Fr.*, **28**, 181 (1970); *Chem. Abstr.*, **73**, 9854 (1970).
249. M. C. Koshla and N. Anand, *J. Sci. Ind. Res., Sect. B*, **16**, 69 (1957); *Chem. Abstr.*, **51**, 13804 (1957).
250. R. L. Fan, J. I. Dickstein and S. I., Miller, *J. Org. Chem.*, **47**, 2466 (1982).
251. C. R. Johnson and D. McCants Jr., *J. Amer. Chem. Soc.*, **87**, 5404 (1956); C. R. Johnson, *J. Amer. Chem. Soc.*, **85**, 1020 (1963).
252. R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 5644 (1969).
253. H. Hogeveen, G. Maccagnani and F. Montanari, *J. Chem. Soc. (C)*, 1585 (1966).
254. W. K. Musker, T. L. Wolford and P. B. Roush, *J. Amer. Chem. Soc.*, **100**, 6416 (1978).
255. L. D. Quin, N. S. Rao and J. Szewczyk, *Phosphorus and Sulfur*, **27**, 109 (1986).
256. M. Mikołajczyk and J. Drabowicz, *Top. Stereochem.*, **13**, 333 (1982); K. K. Andersen, *Int. J. Sulfur Chem., B*, **6**, 69 (1971); P. H. Laur, in *Sulfur in Organic and Inorganic Chemistry*, Vol. 3 (Ed. A. Senning), Dekker, New York, 1972, pp. 91–274.
257. G. Solladie, *Synthesis*, 185 (1981); S. Colonna, R. Annunziata and M. Cinquini, *Phosphorus and Sulfur*, **10**, 197 (1981); M. Cinquini, F. Cozzi and F. Montanari, in *Organic Sulphur Chemistry* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Elsevier, Amsterdam, 1985, pp. 355–407; G. Solladie, in *Perspectives in the Organic Chemistry of Sulphur* (Eds. B. Zwanenburg and A. J. H. Klunder), Elsevier, Amsterdam, 1987, pp. 293–314; G. H. Posner, in *Perspectives in the Organic Chemistry of Sulphur* (Eds. B. Zwanenburg and A. J. H. Klunder), Elsevier, Amsterdam, 1987, pp. 145–152.
258. P. W. B. Harrison, J. Kenyon and H. Phillips, *J. Chem. Soc.*, 2079 (1926).
259. For exhaustive compilation see: A. Nudelman, *Int. J. Sulfur Chem., B*, **6**, 1 (1971); *Int. J. Sulfur Chem., B*, **7**, 241 (1972); *Phosphorus and Sulfur*, **2**, 51 (1976).
260. W. Piechulek and Suszko, *Rocz. Chem.*, **13**, 520 (1933); M. Janczewski and J. Suszko, *Rocz. Chem.*, **26**, 394 (1952).

261. M. Janczewski, L. Goś and J. Jurczak, *Pol. J. Chem.*, **58**, 749 (1984) and earlier references.
262. M. Kiełczewski, *Bull. Acad. Pol. Sci., Ser. Chem.*, **14**, 813 (1966).
263. O. Bohman and S. Allenmark, *Ark. Kemi*, **31**, 299 (1969).
264. P. Huszthy, J. Kapovits, A. Kucsman and A. Radic, *Tetrahedron Letters*, 1553 (1978).
265. M. Mikołajczyk, W. Midura, S. Grzejszczak, A. Zatorski and A. Chefczyńska, *J. Org. Chem.*, **43**, 478 (1978).
266. B. Holmberg, *Ark. Kemi Min. Geol.*, **13A**, 1 (1939).
267. G. Wagner and S. Boehme, *Arch. Pharm.*, **257**, 2907 (1964).
268. R. F. Bryan, F. A. Carey, O. D. Dailey Jr., R. J. Maner and R. W. Miller, *J. Org. Chem.*, **43**, 90 (1978).
269. M. Mikołajczyk and J. Drabowicz, *J. Amer. Chem. Soc.*, **100**, 2510 (1978); M. Mikołajczyk, J. Drabowicz and F. Cramer, *J. Chem. Soc., Chem. Commun.*, 317 (1971).
270. N. Kunieda and M. Kinoshita, *Phosphorus and Sulfur*, **10**, 383 (1981).
271. B. F. Bonini, P. Carisi, M. Maccagnani, G. Mazzanti and P. Zani, 12th International Symposium on the Organic Chemistry of Sulphur, Nijmegen 1986, Abstracts of Paper, PA25.
272. H. J. Becker and K. J. Keuning, *Recl. Trav. Chim. Pays-Bas*, **53**, 798 (1934).
273. A. C. Cope and E. A. Caress, *J. Amer. Chem. Soc.*, **88**, 1711 (1966).
274. G. Farina, F. Montanari and A. Negrini, *Gazz. Chim. Ital.*, **89**, 1548 (1959).
275. F. Wudl, *Diss. Abstr.*, **28**, 2263 B (1968).
276. W. H. Pirkle and D. W. House, *J. Org. Chem.*, **44**, 1957 (1979).
277. Y. Okamoto, *Bull. Soc. Chem. Japan*, **57**, 1681 (1982).
278. S. Allenmark and S. Nilsen, *Acta Chim. Scand., Ser.* B, **37**, 325 (1983).
279. S. Allenmark, B. Bougren, H. Boren and A. Per, *Anal. Biochem.*, **136**, 293 (1984).
280. E. Bayer, E. Küsters, G. J. Nichelson and H. Frank, *J. Chromatogr.*, **320**, 393 (1985).
281. J. Drabowicz and M. Mikołajczyk, *Proceedings I Int. Symp. on Cyclodextrin* (Ed. J. Szejtli), Akademiai Kiado, Budapest, 1982, p. 205.
282. F. Toda, K. Tanaka and S. Nagamatsu, *Tetrahedron Letters*, **25**, 4929 (1984).
283. A. Mayer, F. Montanari and M. Tramontini, *Gazz. Chim. Ital.*, **90**, 739 (1960); A. Macconi, F. Montanari, M. Secci and M. Tramontini, *Tetrahedron Letters*, 607 (1961); U. Folli, D. Iarossi, F. Montanari and G. Torre, *J. Chem. Soc. (C)*, 1317 (1968).
284. K. Balenovic, N. Bregant and D. Francetic, *Tetrahedron Letters*, 20 (1960); K. Balenovic, I. Bregovic, D. Francetic, I. Monkovic and V. Tomasic, *Chem. Ind. (London)*, 469 (1961).
285. W. Ando and T. Takata, *Tetrahedron Letters*, **27**, 1591 (1986).
286. P. Pitchen, E. Dunach, M. N. Deshmukh and H. B. Kagan, *J. Amer. Chem. Soc.*, **106**, 8188 (1984); H. B. Kagan, *Phosphorus and Sulphur*, **27**, 127 (1986); E. Dunach and H. B. Kagan, *Nouv. J. Chim.*, **9**, 1 (1985).
287. F. Di Furia, G. Modena and R. Seraglia, *Synthesis*, 325 (1984).
288. O. Bartolini, F. Di Furia, G. Licini, G. Modena and M. Rossi, *Tetrahedron Letters*, **27**, 6257 (1986).
289. K. Nakajima, M. Kojima and J. Fujita, *Chem. Letters*, 1483 (1986).
290. F. Di Furia, G. Modena and R. Curci, *Tetrahedron Letters*, 4637 (1976).
291. K. T. Lin and Y. C. Tong, *J. Chem. Res. (S)*, 276 (1979).
292. F. A. Davis, J. P. McCauley Jr. and M. E. Harakal, *J. Org. Chem.*, **49**, 1465 (1984); F. A. Davis, R. H. Jenkins Jr., S. B. Awad and O. D. Stringer, *J. Amer. Chem. Soc.*, **104**, 5412 (1982); F. A. Davis, J. P. McCauley, Jr., S. Chattopadhyay, M. E. Harakal, W. H. Watson and I. Tavanaiepour, in *Perspectives in the Organic Chemistry of Sulfur* (Eds. B. Zwanenburg and A. J. H. Klunder), Elsevier, Amsterdam, 1987, pp. 153–165.
293. T. Higuchi, I. H. Pitman and K. H. Gensch, *J. Amer. Chem. Soc.*, **88**, 5676 (1966).
294. J. Drabowicz and M. Mikołajczyk, *Phosphorus and Sulfur*, **19**, 245 (1984).
295. A. W. Czernik, *J. Org. Chem.*, **49**, 924 (1984).
296. T. Sugimoto, T. Kokubo, J. Miyazaki, S. Tanimoto and M. Okano, *J. Chem. Soc., Chem. Commun.*, 402 (1979).
297. S. Colonna, S. Banfi, F. Fontana and M. Sommaruga, *J. Org. Chem.*, **50**, 769 (1985).
298. K. Ogura, M. Fujita and H. Iida, *Tetrahedron Letters*, **21**, 2233 (1980).
299. B. E. Firth, L. L. Miller, M. M. Mitani, T. Rogers, J. Lennox and R. W. Murray, *J. Amer. Chem. Soc.*, **98**, 8271 (1976); B. E. Firth and L. L. Miller, *J. Amer. Chem. Soc.*, **98**, 8272 (1976).
300. T. Komori and T. Nonaka, *J. Amer. Chem. Soc.*, **105**, 5690 (1983); T. Komori and T. Nonaka, *J. Amer. Chem. Soc.*, **106**, 2656 (1984).

301. R. M. Dodson, N. Newman and H. M. Tsuchiya, *J. Org. Chem.*, **27**, 2707 (1962).
302. C. E. Holmlund, K. J. Sax, B. E. Nielsen, R. E. Hartman, R. H. Evans, Jr. and R. H. Blank, *J. Org. Chem.*, **27**, 1468 (1962).
303. B. J. Auret, D. R. Boyd, H. B. Henbest and S. Ross, *J. Chem. Soc. (C)*, 2371 (1968).
304. E. Abushanab, D. Reed, F. Suzuki and C. J. Sih, *Tetrahedron Letters*, 3415 (1978).
305. H. L. Holland, H. Pöpperl, R. W. Ninniss and P. C. Chenchaiah, *Can. J. Chem.*, **63**, 1118 (1985).
306. B. J. Auret, D. R. Boyd, F. Breen, R. M. Green and P. M. Robinson, *J. Chem. Soc., Perkin Trans. 1*, 930 (1981).
307. B. J. Auret, D. R. Boyd, E. S. Cassioly, F. Turley, A. F. Drake and S. F. Mason, *J. Chem. Soc., Chem. Commun.*, 282 (1983).
308. D. R. Light, D. J. Waxman and C. Walsh, *Biochemistry*, **21**, 2490 (1982).
309. D. J. Waxman, D. R. Light and C. Walsh, *Biochemistry*, **21**, 2499 (1982).
310. T. Takata, M. Yamazaki, K. Fujimori, Y. H. Khim, T. Iyanagi and S. Oae, *Bull. Chem. Soc. Japan*, **56**, 2300 (1983).
311. S. W. May and R. S. Phillips, *J. Amer. Chem. Soc.*, **102**, 5981 (1980).
312. D. J. Cram and S. H. Pine, *J. Amer. Chem. Soc.*, **85**, 1096 (1963).
313. K. Nishihata and M. Nishio, *J. Chem. Soc., Perkin Trans. 2*, 758 (1973).
314. F. Ruff, G. Szabo, J. Vajda, J. Kövesdi and A. Kucsman, *Tetrahedron*, **36**, 1631 (1980).
315. B. W. Christensen and A. Kjaer, *J. Chem. Soc., Chem. Commun.*, 225 (1965).
316. E. Bordignon, L. Cattalini, G. Natile and A. Scatturin, *J. Chem. Soc., Chem. Commun.*, 878 (1973).
317. S. Lavielle, S. Bory, B. Moreau, M. Luche and A. Marquet, *J. Amer. Chem. Soc.*, **100**, 1558 (1978).
318. G. Barbieri, V. Davoli, I. Moretti, F. Montanari and G. Torre, *J. Chem. Soc. (C)*, 731 (1969).
319. C. R. Johnson, C. C. Bacon and W. D. Kingsbury, *Tetrahedron Letters*, 501 (1972).
320. M. Moriyama, S. Oae, T. Numata and N. Furukawa, *Chem. Ind. (London)*, 163 (1976).
321. M. Kinoshita, Y. Sato and N. Kunieda, *Chem. Letters*, 377 (1974).
322. Y. Sato, N. Kunieda and M. Kinoshita, *Chem. Letters*, 563 (1976).
323. M. Kobayashi and A. Yobe, *Bull. Chem. Soc. Japan*, **40**, 224 (1967).
324. U. Folli, D. Jarossi and F. Montanari, *J. Chem. Soc. (C)*, 2374 (1968).
325. F. A. Davis and J. M. Billmers, *J. Org. Chem.*, **48**, 2672 (1983).
326. T. Sugimoto, T. Kokubo, J. Miyazaki, S. Tamimoto and M. Okano, *Bioorg. Chem.*, **10**, 311 (1981); T. Sugimoto, T. Kokubo, J. Miyazaki and M. Okano, *J. Chem. Soc., Chem. Commun.*, 1052 (1979).
327. B. J. Auret, D. Boyd and H. B. Henbest, *J. Chem. Soc. (C)*, 2374 (1968).
328. K. Balenovic and N. Bregant, *Chem. Ind. (London)*, 1577 (1964).
329. M. Mikołajczyk and M. Para, *J. Chem. Soc., Chem. Commun.*, 1192 (1969).
330. M. Mikołajczyk and J. Drabowicz, *Phosphorus and Sulfur*, **1**, 301 (1976).
331. J. Drabowicz and M. Pacholczyk, *Phosphorus and Sulfur*, **10**, 233 (1976).
332. S. Juge and H. B. Kagan, *Tetrahedron Letters*, 2733 (1975).
333. G. Marchese, F. Naso and L. Ronzini, *J. Chem. Soc., Chem. Commun.*, 830 (1974).
334. N. Kunieda, H. Motoki and M. Kinoshita, *Chem. Letters*, 713 (1978).
335. N. Kunieda, J. Nokami and M. Kinoshita, *Bull. Chem. Soc. Japan*, **49**, 256 (1976).
336. R. Annunziata, G. Borgogno, F. Montanari, S. Quici and S. Cucinella, *J. Chem. Soc., Perkin Trans. 1*, 113 (1981).
337. R. L. Crumbie, B. S. Deol, J. E. Nemorin, and D. D. Ridley, *Aust. J. Chem.*, **31**, 1965 (1978).
338. H. Ohta, Y. Kato and G. Tsuchihashi, *Chem. Letters*, 217 (1986).
339. H. B. Kagan, G. Balavoine and A. Mardpour, *J. Mol. Evol.*, **4**, 41 (1974).
340. W. H. Pirkle and P. L. Rinaldi, *J. Amer. Chem. Soc.*, **99**, 3510 (1977).
341. C. Eskenazi, J. F. Nicoud and H. B. Kagan, *J. Org. Chem.*, **44**, 995 (1979).
342. K. K. Andersen, *Tetrahedron Letters*, 93 (1962).
343. K. Mislow, M. M. Green, P. Laur, J. P. Melillo, T. Simons and A. L. Ternay Jr., *J. Amer. Chem. Soc.*, **87**, 1958 (1965).
344. K. K. Andersen, *J. Org. Chem.*, **29**, 1953 (1964); K. K. Andersen, W. Gaffield, N. E. Papanikolaou, J. W. Foley and R. I. Perkins, *J. Amer. Chem. Soc.*, **86**, 5637 (1964).
345. C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963).
346. S. Oae and Y. H. Khim, *Bull. Chem. Soc. Japan*, **40**, 1716 (1967).
347. J. Drabowicz, B. Bujnicki, and M. Mikołajczyk, *J. Org. Chem.*, **47**, 3325 (1982).
348. D. D. Ridley and M. A. Small, *J. Chem. Soc., Chem. Commun.*, 505 (1981).

349. K. K. Andersen, B. Bujnicki, J. Drabowicz, M. Mikołajczyk and J. B. O'Brien, *J. Org. Chem.*, **49**, 4070 (1984).
350. M. Axelrod, P. Bickart, J. Jacobus, M. M. Green and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4835 (1968).
351. H. Hope, U. de la Camp, G. Homer, A. W. Messing and L. H. Sommer, *Angew. Chem.*, **81**, 619 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 612 (1969).
352. U. de la Camp and H. Hope, *Acta Crystallogr., Sect. B*, **26**, 846 (1970).
353. J. Drabowicz and M. Mikołajczyk, unpublished results.
354. J. Jacobus and K. Mislow, *J. Amer. Chem. Soc.*, **89**, 5228 (1967).
355. S. Colonna, R. Giovini and F. Montanari, *J. Chem. Soc., Chem. Commun.*, 865.(1968).
356. J. Jacobus and K. Mislow, *J. Chem. Soc., Chem. Commun.*, 253 (1968).
357. W. H. Pirkle and S. D. Beare, *J. Amer. Chem. Soc.*, **90**, 6250 (1968).
358. K. K. Andersen, S. Colonna and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 645 (1973).
359. D. J. Abbott, S. Colonna and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 1*, 492 (1976).
360. G. H. Posner and P. W. Tang, *J. Org. Chem.*, **43**, 4131 (1978).
361. G. H. Posner, J. P. Mallamo, M. Hulce and L. L. Frye, *J. Amer. Chem. Soc.*, **104**, 4180 (1982).
362. P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4869 (1968).
363. M. Cinquini, S. Colonna, F. Cozzi and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 1*, 2061 (1976).
364. G. L. Colombo, C. Gennari and E. Narisano, *Tetrahedron Letters*, 3861 (1978).
365. R. Annunziata, M. Cinquini and F. Cozzi, *Synthesis*, 535 (1979).
366. R. Annunziata, M. Cinquini and F. Cozzi, *Synthesis*, 767 (1982).
367. C. Mioskowski and G. Solladie, *Tetrahedron*, **36**, 227 (1980); G. Solladie, F. Matloubi-Maghadam, G. Luttmann and G. Mioskowski, *Helv. Chim. Acta*, **65**, 1602 (1982).
368. F. Schneider and R. Simon, *Synthesis*, 582 (1986).
369. K. Hiroi and N. Matsuyama, *Chem. Letters*, 65 (1986).
370. R. Annunziata, M. Cinquini, S. Colonna and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 614 (1981).
371. R. Annunziata, M. Cinquini, A. Restelli and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 1183 (1982).
372. L. Banfi, G. Colombo, R. Gennari, R. Annunziata and F. Cozzi, *Synthesis*, 829 (1982).
373. F. Wudl and T. B. K. Lee, *J. Amer. Chem. Soc.*, **95**, 6349 (1973).
374. R. Fusco and A. Tenconi, *Chim. Ind. (Milan)*, **47**, 61 (1965); *Chem. Abstr.*, **62**, 103576 (1965); C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **95**, 7418 (1973).
375. D. J. Cram, J. Day, D. R. Rayner, D. M. von Schriltz, D. J. Duchamp and D. C. Garwood, *J. Amer. Chem. Soc.*, **92**, 7369 (1970).
376. S. Oae, Y. Tsuchida and N. Furukawa, *Bull. Chem. Soc. Japan*, **46**, 648 (1973).
377. T. M. Balthazar and J. C. Martin, *J. Amer. Chem. Soc.*, **99**, 152 (1977).
378. T. Durst, *Adv. Org. Chem.*, **6**, 285 (1969).
379. T. Durst and R. Viau, *Intra-Sci. Chem. Rep.*, 7, 63 (1973).
380. J. P. Lockard, C. W. Schroeck and C. R. Johnson, *Synthesis*, 485 (1973).
381. T. Durst, M. J. LeBelle, R. Van den Elzen and K.-C. Tin, *Can. J. Chem.*, **52**, 761 (1974).
382. H. M. Moskowitz, J. Blanc-Guennee and M. M. Miocque, *Compt. Rend. Acad. Sci., Ser. C*, **267**, 898 (1968).
383. G. H. Posner, P. W. Tang and J. P. Mallamo, *Tetrahedron Letters*, 3995 (1978).
384. H. Okamura, Y. Mitsushira, M. Miura and H. Takei, *Chem. Letters*, 517 (1978).
385. H. Takei, H. Sugimura, M. Miura and H. Okamura, *Chem. Letters*, 1209 (1980).
386. R. R. Schmidt, H. Speer and B. Schmid, *Tetrahedron Letters*, 4277 (1979).
387. R. C. Cookson and P. J. Parsons, *J. Chem. Soc., Chem. Commun.*, 822 (1978).
388. A. Rauk, S. Wolfe and I. G. Csizmadia, *Can. J. Chem.*, **47**, 113 (1969).
389. G. Chassaing and A. Marquet, *Tetrahedron*, **34**, 1399 (1978).
390. R. Lett and G. Chassaing, *Tetrahedron*, **34**, 2705 (1978).
391. S. Nishi and M. Matsuda, *J. Amer. Chem. Soc.*, **101**, 4632 (1979).
392. S. Wolfe, in *Organic Sulphur Chemistry: Theoretical and Experimental Advances* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Elsevier, Amsterdam, 1985, pp. 133–190.
393. I. D. Entwistle and R. A. W. Johnstone, *J. Chem. Soc., Chem. Commun.*, 29 (1965).
394. B. M. Trost and A. J. Bridges, *J. Org. Chem.*, **40**, 2014 (1975).
395. E. Guittet and S. Julia, *Synth. Commun.*, **9**, 317 (1979).
396. H. Fillion and A. Boucherle, *Bull. Soc. Chim. Fr.*, 2699 (1972).

397. N. K. Sharma, F. Jung and T. Durst, *Tetrahedron Letters*, 2863 (1973).
398. G. Tsuchihashi, S. Iriuchijma and M. Ishibashi, *Tetrahedron Letters*, 4605 (1972).
399. P. Bravo, G. Resnati and F. Viani, *Tetrahedron Letters*, **26**, 2913 (1985).
400. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **84**, 866 (1962).
401. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).
402. S. Rajan and K. Muralimohan, *Tetrahedron Letters*, 485 (1978).
403. H. Böhme and W. Stammberger, *Justus Liebigs Ann. Chem.*, **754**, 56 (1971).
404. V. Reutrakul and P. Thamnusan, *Tetrahedron Letters*, 617 (1979).
405. V. Reutrakul and K. Herunsalee, *Tetrahedron Letters*, **24**, 527 (1983).
406. V. Reutrakul and V. Rukachaisirikul, *Tetrahedron Letters*, **24**, 725 (1983).
407. M. Makosza, J. Goliński and J. Pankowski, *Synthesis*, 40 (1983).
408. B. T. Gröbel and D. Seebach, *Synthesis*, 357 (1977).
409. S. Grzejszczak and M. Mikołajczyk, *Wiad. Chem.*, **34**, 337 (1980).
410. R. M. Carlson and P. M. Helquist, *J. Org. Chem.*, **33**, 2596 (1968).
411. F. A. Carey, O. D. Dailey, Jr. and O. Hernandez, *J. Org. Chem.*, **41**, 3979 (1976).
412. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 3151 (1971).
413. J. E. Richman, J. L. Herrmann and R. H. Schlessinger, *Tetrahedron Letters*, 3267 (1973).
414. G. R. Newcome, J. M. Robinson and J. D. Sauer, *J. Chem. Soc., Chem. Commun.*, 410 (1974).
415. D. A. Evans, C. E. Sacks, R. A. Whitney and N. G. Mandel, *Tetrahedron Letters*, 727 (1978).
416. J. A. Marshall and P. G. M. Wuts, *Synth. Commun.*, **7**, 233 (1977).
417. K. Ogura, M. Yamashita, M. Suzuki and G. Tsuchihashi, *Tetrahedron Letters*, 3653 (1974).
418. K. Ogura, M. Yamashita, S. Furukawa, M. Suzuki and G. Tsuchihashi, *Tetrahedron Letters*, 2767 (1975).
419. K. Ogura, M. Yamashita, M. Suzuki, S. Furukawa and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **57**, 1637 (1984).
420. K. Ogura, M. Yamashita and G. Tsuchihashi, *Tetrahedron Letters*, 759 (1976).
421. P. A. Grieco, *J. Chem. Soc., Chem. Commun.*, 702 (1972).
422. P. A. Grieco and R. S. Finkelhor, *J. Org. Chem.*, **38**, 2245 (1973).
423. D. A. Evans, G. C. Andrews, T. T. Fujimoto and D. Wells, *Tetrahedron Letters*, 1385 (1973).
424. D. A. Evans, G. C. Andrews, T. T. Fujimoto and D. Wells, *Tetrahedron Letters*, 1389 (1973).
425. D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974).
426. K. Koosha and M.-L. Capmau, *Compt. Rend. Acad. Sci., Ser. C*, **279**, 585 (1974).
427. E. Guittet and S. Julia, *Synth. Commun.*, **11**, 723 (1981).
428. J.-P. Demoute, D. Hainaut and E. Toromanoff, *Compt. Rend. Acad. Sci., Ser. C*, **277**, 49 (1973).
429. P. G. Gassman and G. D. Richmond, *J. Org. Chem.*, **31**, 2355 (1966).
430. B. Clement, *Chem. Zeitung*, **104**, 368 (1980).
431. P. A. Bartlett, *J. Amer. Chem. Soc.*, **98**, 3305 (1976).
432. I. Kuwajima and H. Iwasawa, *Tetrahedron Letters*, 107 (1974).
433. P. A. Grieco, D. Boxler and C. S. Pogonowski, *J. Chem. Soc., Chem. Commun.*, 497 (1974).
434. P. A. Grieco and C. S. Pogonowski, *J. Chem. Soc., Chem. Commun.*, 72 (1975).
435. N. Petragnani and M. Yonashiro, *Synthesis*, 521 (1982).
436. J. J. A. van Asten and R. Louw, *Tetrahedron Letters*, 671 (1975).
437. B. Trost, P. Conway, P. E. Strege and T. J. Dietsche, *J. Amer. Chem. Soc.*, **96**, 7165 (1974).
438. B. M. Trost and K. K. Leung, *Tetrahedron Letters*, 4197 (1975).
439. B. M. Trost, L. Weber, P. Strege, T. J. Fullerton and T. J. Dietsche, *J. Amer. Chem. Soc.*, **100**, 3426 (1978).
440. K. Iwai, H. Kosugi, A. Miyazaki and H. Uda, *Synth. Commun.*, **6**, 357 (1976).
441. P. Bravo, P. Carrera, G. Resnati and C. Ticozzi, *J. Chem. Soc., Chem. Commun.*, 19 (1984).
442. C. Walling and L. Bollyky, *J. Org. Chem.*, **29**, 2699 (1964).
443. R. Baker and M. J. Spillett, *J. Chem. Soc., Chem. Commun.*, 757 (1966).
444. B. G. James and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1204 (1974).
445. V. Ceré, C. Paolucci, S. Pollicino, E. Sandri and A. Fava, *J. Chem. Soc., Chem. Commun.*, 764 (1981).
446. I. Iwai and J. Ide, *Chem. Pharm. Bull.*, **13**, 663 (1965).
447. D. L. Boger and D. Mullican, *J. Org. Chem.*, **45**, 5002 (1980).
448. F. M. Hauser and R. F. Rhee, *J. Org. Chem.*, **43**, 178 (1978).
449. F. M. Hauser and R. P. Rhee, *J. Amer. Chem. Soc.*, **101**, 1628 (1979).
450. H. Nozaki, T. Mori and M. Kawanishi, *Can. J. Chem.*, **46**, 3767 (1968).

451. E. Ghera and Y. Ben-David, *Tetrahedron Letters*, 4603 (1979).
452. D. H. Bremmer and M. M. Campbell, *J. Chem. Soc., Chem. Commun.*, 538 (1976).
453. G. A. Russell and L. A. Ochrymowicz, *J. Org. Chem.*, **34**, 3624 (1969).
454. O. P. Vig, K. L. Matta, J. M. Sehgal and S. D. Sharma, *J. Indian Chem. Soc.*, **47**, 894 (1970).
455. A. Jaxa-Chamiec, P. G. Sammes and P. D. Kennewell, *J. Chem. Soc., Perkin Trans. 1*, 170 (1980).
456. T. Yoshida and S. Saito, *Chem. Letters*, 1587 (1982).
457. F. Matloubi and G. Solladie, *Tetrahedron Letters*, 2141 (1979).
458. K. Ogura, M. Yamashita and G. Tsuchihashi, *Tetrahedron Letters*, 1303 (1978).
459. L. Colombo, C. Gennari, G. Resnati and C. Scolastico, *Synthesis*, 74 (1981).
460. L. Herrmann, J. E. Richman and R. H. Schlessinger, *Tetrahedron Letters*, 3271 (1973).
461. L. Herrmann, J. E. Richman and R. H. Schlessinger, *Tetrahedron Letters*, 3275 (1973).
462. L. Colombo, C. Gennari, G. Resnati and C. Scolastico, *J. Chem. Soc., Perkin Trans. 1*, 1284 (1981).
463. L. L. Vasileva, V. I. Melnikova, E. T. Gainullina and K. K. Pivnitsky, *Zh. Org. Khim.*, **16**, 2618 (1980).
464. M. R. Binns, R. K. Haynes, T. L. Houston and W. R. Jackson, *Aust. J. Chem.*, **34**, 2465 (1981).
465. J. Nokami, T. Ono, A. Iwao and S. Wakabayashi, *Bull. Chem. Soc. Japan*, **55**, 3043 (1982).
466. L. L. Vasileva, V. I. Melnikova and K. K. Pivnitsky, *Zh. Obshch. Khim.*, **52**, 2651 (1982).
467. J. Nokami, T. Ono, S. Wakabayashi, A. Hazato and S. Kurizumi, *Tetrahedron Letters*, **26**, 1985 (1985).
468. W. T. Comer and D. L. Temple, *J. Org. Chem.*, **38**, 2121 (1973).
469. D. Heisler, F. Jung, J. P. Vevert and J. J. Riehl, *Tetrahedron Letters*, 4879 (1976).
470. H. Hart and A. Oku, *J. Org. Chem.*, **37**, 4269 (1972).
471. P. Bravo, G. Gaudiano and P. P. Ponti, *Chem. Ind. (London)*, 253 (1971).
472. J. A. Gautier, M. Mioque, M. Plat, H. Moskowitz and J. Blanc-Gueneé, *Compt. Rend. Acad. Sci., Ser. C*, **269**, 839 (1969).
473. M. D. M. Gray, D. R. Russell, D. J. H. Smith, T. Durst and B. Gimbarzevsky, *J. Chem. Soc., Perkin Trans. 1*, 1826 (1981).
474. F. Babudri, S. Florio, A. M. Vitrani and L. Di Nunno, *J. Chem. Soc., Perkin Trans. 1*, 1899 (1984).
475. R. W. Hoffmann, S. Goldmann, N. Maak, R. Gerlach, F. Frickel and G. Steinbach, *Chem. Ber.*, **113**, 819 (1980).
476. B. M. Trost and C. H. Miller, *J. Amer. Chem. Soc.*, **97**, 7182 (1975).
477. T. Durst, R. Viau, R. Van den Elzen and C. H. Nguyen, *J. Chem. Soc., Chem. Commun.*, 1334 (1971).
478. C. H. Kingsbury, *J. Org. Chem.*, **37**, 102 (1972).
479. D. G. Farnum, T. Veysoglu, A. M. Carde, B. Duhl-Emswiler, T. A. Pancoast, T. J. Reitz and R. T. Carde, *Tetrahedron Letters*, 4009 (1977).
480. D. R. Williams, J. G. Phillips and J. C. Huffman, *J. Org. Chem.*, **46**, 410 (1981).
481. G. Solladie and G. Moine, *J. Amer. Chem. Soc.*, **106**, 6097 (1984).
482. R. A. Holton and H.-B. Kim, *Tetrahedron Letters*, **27**, 2191 (1986).
483. D. J. Antonjuk, D. D. Ridley and M. A. Small, *Austr. J. Chem.*, **33**, 2635 (1980).
484. T. Durst, *J. Amer. Chem. Soc.*, **91**, 1034 (1969).
485. G. Tsuchihashi and K. Ogura, *Bull. Chem. Soc. Japan*, **45**, 2023 (1972).
486. T. Durst and K.-C. Tin, *Tetrahedron Letters*, 2369 (1970).
487. D. F. Tavares, R. E. Estep and M. Blezard, *Tetrahedron Letters*, 2373 (1970).
488. V. Reutrakul and W. Kanghae, *Tetrahedron Letters*, 1377 (1977).
489. D. F. Taber and B. P. Gunn, *J. Org. Chem.*, **44**, 450 (1979).
490. V. Reutrakul and W. Kanghae, *Tetrahedron Letters*, 1225 (1977).
491. V. Reutrakul, A. Tiensripojamarn, K. Kusamran and S. Nimgirawath, *Chem. Letters*, 209 (1979).
492. I. Kuwajima and Y. Fukuda, *Tetrahedron Letters*, 327 (1973).
493. M. Madesclaire, D. Roche and D. Chatonier, *Synthesis*, 828 (1981).
494. S. Klutchko, M. P. Cohen, J. Shabel, Jr. and M. Jon Strandtmann, *J. Heterocycl. Chem.*, **11**, 183 (1974).
495. P. A. Grieco and C. S. Pogonowski, *J. Org. Chem.*, **39**, 732 (1974).
496. N. Kunieda, J. Nokami and M. Kinoshita, *Tetrahedron Letters*, 3997 (1974).
497. J. Nokami, N. Kunieda and M. Kinoshita, *Tetrahedron Letters*, 2179 (1975).
498. C. Mioskowski and G. Solladié, *J. Chem. Soc., Chem. Commun.*, 162 (1977).

499. G. Solladié and F. Matloubi-Moghadam, *J. Org. Chem.*, **47**, 91 (1982).
500. E. J. Corey, L. O. Weigel, A. R. Chamberlin, H. Cho and D. H. Hua, *J. Amer. Chem. Soc.*, **102**, 6613 (1980).
501. C. Papageorgiou and C. Benezra, *Tetrahedron Letters*, **25**, 1303 (1984).
502. A. Albinati, P. Bravo, F. Ganazzoli, G. Resnati and F. Viani, *J. Chem. Soc., Perkin Trans. 1*, 1405 (1986).
503. P. Bravo and G. Resnati, in *Perspectives in the Organic Chemistry of Sulfur* (Eds. B. Zwanenburg and A. J. H. Klunder), Elsevier, Amsterdam, 1987, pp. 89–103.
504. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 2681 (1972).
505. J. H. Herrmann, J. E. Richman, P. J. Wepplo and R. H. Schlessinger, *Tetrahedron Letters*, 4707 (1973).
506. L. Colombo, C. Gennari, C. Scolastico, G. Guanti and E. Narisano, *J. Chem. Soc., Chem. Commun.*, 591 (1979).
507. L. Colombo, C. Gennari, C. Scolastico, G. Guanti and E. Narisano, *J. Chem. Soc., Perkin Trans. 1*, 1278 (1981).
508. R. Tanikaga, M. Nishida, N. Ono and A. Kaji, *Chem. Letters*, 781 (1980).
509. R. Tanikaga, T. Tamura, Y. Nozaki and A. Kaji, *J. Chem. Soc., Chem. Commun.*, 87 (1984).
510. Q. B. Cass, A. A. Jaxa-Chamiec and P. G. Sammes, *J. Chem. Soc., Chem. Commun.*, 1248 (1981).
511. G. Galambosz, V. Simonidesz, J. Ivanics, K. Horvath and G. Kovacs, *Tetrahedron Letters*, **24**, 1281 (1983).
512. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 1383 (1972).
513. K. Ogura, Y. Ito and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **52**, 2013 (1979).
514. J. Almog and B. A. Weissman, *Synthesis*, 164 (1973).
515. M. Mikołajczyk, S. Grzejszczak and A. Zatorski, *J. Org. Chem.*, **40**, 1979 (1975).
516. M. Mikołajczyk, S. Grzejszczak, W. Midura and A. Zatorski, *Synthesis*, 278 (1975).
517. M. Mikołajczyk, M. Popielarczyk and S. Grzejszczak, *Phosphorus and Sulfur*, **10**, 369 (1981).
518. M. Mikołajczyk, S. Grzejszczak, W. Midura and A. Zatorski, *Synthesis*, 396 (1976).
519. M. Mikołajczyk, M. Popielarczyk and S. Grzejszczak, *Z. Chem.*, **24**, 377 (1984).
520. R. W. Hoffmann and N. Maak, *Tetrahedron Letters*, 2237 (1976).
521. K. Bischofberger and J. R. Bull, *J. Chem. Soc., Chem. Commun.*, 1051 (1982).
522. A. Nudelman and D. J. Cram, *J. Org. Chem.*, **34**, 3659 (1969).
523. K. Ogura, S. Furukawa and G. Tsuchihashi, *Synthesis*, 202 (1976).
524. G. Tsuchihashi, S. Iriuchijima and K. Maniwa, *Tetrahedron Letters*, 3389 (1973).
525. L. Duhamel, P. Duhamel and N. Mancelle, *Bull. Soc. Chim. Fr.*, 331 (1974).
526. R. Annuziata and M. Cinquini, *Synthesis*, 929 (1982).
527. K. Ogura and G. Tsuchihashi, *J. Amer. Chem. Soc.*, **96**, 1960 (1974).
528. K. Ogura, N. Katoh, I. Yoshimura and G. Tsuchihashi, *Tetrahedron Letters*, 375 (1978).
529. H. Böhme and B. Clement, *Arch. Pharm. (Weinheim)*, **312**, 531 (1979).
530. I. G. Wright, C. W. Ashbrook, T. Goodson, G. V. Kaiser and E. M. van Heyningen, *J. Med. Chem.*, **14**, 420 (1971).
531. J. Cs. Jaszberenyi, I. Petrikovics, E. T. Gunda and S. Hosztafi, *Acta Chim. Acad. Sci. Hung.*, **110**, 81 (1982).
532. G. A. Russell and L. A. Ochrymowicz, *J. Org. Chem.*, **35**, 764 (1970).
533. H.-D. Becker, G. J. Mikol and G. A. Russell, *J. Amer. Chem. Soc.*, **85**, 3410 (1963).
534. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **86**, 1639 (1964).
535. Y. Yamamoto and H. Nozaki, *Bull. Chem. Soc. Japan*, **45**, 1167 (1972).
536. H. Nozaki, T. Mori and M. Kawanishi, *Can. J. Chem.*, **46**, 3767 (1968).
537. N. Kunieda, J. Nokami and M. Kinoshita, *Chem. Letters*, 369 (1974).
538. R. Annunziata, M. Cinquini and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 1687 (1979).
539. P. Bravo and G. Resnati, *Tetrahedron Letters*, **26**, 560 (1985).
540. P. Bravo, E. Piovosi and G. Resnati, *Synthesis*, 579 (1986).
541. H.-D. Becker and G. A. Russell, *J. Org. Chem.*, **28**, 1896 (1963).
542. K. Ogura, S. Furukawa and G. I. Tsuchihashi, *Chem. Letters*, 659 (1974).
543. K. Ogura, M. Fuijita, T. Inaba, T. Takahashi and H. Iida, *Tetrahedron Letters*, **24**, 503 (1983).
544. G. H. Posner, J. P. Mallamo and K. Miura, *J. Amer. Chem. Soc.*, **103**, 2886 (1981).
545. G. Solladie, R. Zimmermann and R. Bartsch, *Tetrahedron Letters*, **24**, 755 (1983).
546. K. Nishihata and M. Nishio, *Tetrahedron Letters*, 1695 (1976).
547. Y. Tamura, H. Shindo, J. Uenishi and H. Ishibashi, *Chem. Pharm. Bull.*, **27**, 3186 (1979).

548. Y. Tamura, H. Shindo and H. Ishibashi, *J. Heterocycl. Chem.*, **17**, 1637 (1980).
549. M. von Strandtmann, S. Klutchko, D. Connor and J. Shavel, Jr., *J. Org. Chem.*, **36**, 1742 (1971).
550. P. Messinger and C. Kunnick, *Arch. Pharm. (Weinheim)*, **318**, 1086 (1985).
551. M. Yokoyama, M. Hayashi and T. Imamoto, *Chem. Letters*, 953 (1982).
552. G. H. Posner and L. L. Frye, *J. Fluorine Chem.*, **28**, 151 (1985); *Chem. Abstr.*, **104**, 109 129 (1986).
553. E. Vedejs and M. Mullins, *Tetrahedron Letters*, 2017 (1975).
554. A. G. Brook and D. G. Anderson, *Can. J. Chem.*, **46**, 2115 (1968).
555. E. Vedejs, H. Mastalerz, G. P. Mejer and D. W. Powell, *J. Org. Chem.*, **46**, 5253 (1981).
556. B. Wladislaw and L. Marzorati, *An. Acad. Bras. Cienc.*, **51**, 245 (1979); *Chem. Abstr.*, **92**, 41503 (1980).
557. V. Ratovelomanana, Ch. Huynh and S. Julia, *Compt. Rend. Acad. Sci., Ser. C*, **280**, 1327 (1975).
558. N. Kunieda, J. Nokami and M. Kinoshita, *Chem. Letters*, 871 (1973).
559. C. A. Maryanoff, B. E. Maryanoff, R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, **95**, 5839 (1973).
560. G. Tsuchihashi and S. Iriuchijima, *Bull. Chem. Soc. Japan*, **43**, 2271 (1970).
561. D. Martin, A. Berger and R. Peschel, *J. Prakt. Chem.*, **312**, 683 (1970).
562. S. Iriuchijima, M. Ishibashi and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **46**, 921 (1973).
563. J. Klein and H. Stollar, *J. Amer. Chem. Soc.*, **95**, 7437 (1973).
564. S. Bory, R. Lett, B. Moreau and A. Marquet, *Compt. Rend. Acad. Sci., Ser. C*, **276**, 1323 (1973).
565. R. N. Loeppky and D. C. K. Chang, *Tetrahedron Letters*, 5415 (1968).
566. F. Jung, K. C. Tin and T. Durst, *Int. Sulfur Chem.*, **8**, 1 (1973).
567. S. Iriuchijima and G. Tsuchihashi, *Tetrahedron Letters*, 5259 (1969).
568. G. Tsuchihashi and K. Ogura, *Bull. Chem. Soc. Japan*, **44**, 1726 (1971).
569. K. Ogura, J. Imaizumi, H. Iida and G. Tsuchihashi, *Chem. Letters*, 1587 (1980).
570. M. Cinquini, S. Colonna and F. Montanari, *J. Chem. Soc., Chem. Commun.*, 1441 (1970).
571. M. Cinquini, S. Colonna, R. Fornasier and F. Montanari, *J. Chem. Soc., Perkin Trans. 1*, 1886 (1972).
572. J. Drabowicz, *Synthesis*, 831 (1986).
573. K. C. Tin and T. Durst, *Tetrahedron Letters*, 4643 (1970).
574. G. Tsuchihashi, K. Ogura, S. Iriuchijima and S. Tomisawa, *Synthesis*, 89 (1971).
575. T. Durst and K. C. Tin, *Can. J. Chem.*, **49**, 2374 (1971).
576. M. Cinquini, S. Colonna and F. Montanari, *J. Chem. Soc., Perkin Trans. 1*, 1719, 1723 (1974).
577. M. Cinquini and S. Colonna, *J. Chem. Soc., Perkin Trans. 1*, 1883 (1972).
578. P. Calazavara, M. Cinquini, S. Colonna, R. Fornasier and F. Montanari, *J. Amer. Chem. Soc.*, **95**, 7431 (1973).
579. R. Annunziata, and S. Colonna, *J. Chem. Soc., Perkin Trans. 1*, 1052 (1977).
580. M. Cinquini and S. Colonna, *Synthesis*, 259 (1972).
581. D. Landini and A. Maia, *J. Chem. Soc., Perkin Trans. 2*, 218 (1975).
582. H. Morita, H. Itoh, N. Furukawa and S. Oae, *Chem. Letters*, 817 (1978).
583. S. Iriuchijima and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **46**, 929 (1973).
584. A. Garbesi and A. Fava, *J. Org. Chem.*, **42**, 4029 (1977).
585. S. Iriuchijima and G. Tsuchihashi, *Synthesis*, 588 (1970).
586. M. Hojo, R. Masuda, T. Saeki and S. Uyeda, *Synthesis*, 697 (1976).
587. M. Cinquini, S. Colonna and D. Landini, *J. Chem. Soc., Perkin Trans. 2*, 296 (1972).
588. J. Klein, *Chem. Letters*, 359 (1979).
589. F. Montanari, in *Organic Sulphur Chemistry* (Ed. C. J. M. Stirling), Butterworths, London, 1975, p. 181.
590. B. B. Jarvis and M. M. Evans, *J. Org. Chem.*, **39**, 643 (1974).
591. B. B. Jarvis and H. E. Fried, *J. Org. Chem.*, **40**, 1278 (1975).
592. H. Alper and M. Gopal, *J. Org. Chem.*, **48**, 4380 (1983).
593. F. A. Carey, O. O. Dailey, Jr., O. Hernandez and R. Tucker, *J. Org. Chem.*, **41**, 3975 (1976).
594. N. Ono, H. Miyake, A. Kamimura, N. Tsukui and A. Kaji, *Tetrahedron Letters*, **23**, 2957 (1982).
595. M. Hojo and Z. Yoshida, *J. Amer. Chem. Soc.*, **90**, 4496 (1968).
596. M. Cinquini, S. Colonna, D. Landini and A. M. Maia, *J. Chem. Soc., Perkin Trans. 2*, 996 (1976).
597. M. Cinquini, D. Landini and A. Maia, *J. Chem. Soc., Chem. Commun.*, 734 (1972).
598. K. Ogura and G. Tsuchihashi, *J. Chem. Soc., Chem. Commun.*, 1689 (1970).
599. T. Numata and S. Oae, *Bull. Soc. Chem. Japan*, **45**, 2794 (1972).
600. T. Durst, K. C. Tin, F. de Reinach-Hirtzbach, J. M. Decesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).

601. F. Montanari, R. Danieli, H. Hogeveen and G. Maccagnani, *Tetrahedron Letters*, 2685 (1964).
602. M. Cinquini, S. Colonna and F. Montanari, *Tetrahedron Letters*, 3181 (1966).
603. J. C. Martin and J. J. Uebel, *J. Amer. Chem. Soc.*, **86**, 2936 (1964).
604. F. Montanari and A. Negrini, *Gazz. Chim. Ital.*, **89**, 1543 (1959).
605. I. Hori and T. Oishi, *Tetrahedron Letters*, 4087 (1979).
606. C. Carpanelli, G. Gaiani and G. Leandri, *Gazz. Chim. Ital.*, **100**, 618 (1970).
607. A. C. Boicelli, R. Danieli, A. Mangini, A. Ricci and G. Pirazzini, *J. Chem. Soc., Perkin Trans. 2*, 1343 (1974).
608. N. C. Marziano, E. Maccarone, G. M. Cimino and R. C. Passerini, *J. Org. Chem.*, **39**, 1098 (1974).
609. S. Oae and Y. H. Khim, *Bull. Chem. Soc. Japan*, **40**, 1716 (1967).
610. E. Molenaar and J. Strating, *Recl. Trav. Chim. Pays-Bas*, **87**, 49 (1968).
611. G. A. Russell, E. Sabourin and G. J. Mikol, *J. Org. Chem.*, **31**, 2854 (1966).
612. B. B. Jarvis, S. D. Dutkey and H. L. Amman, *J. Amer. Chem. Soc.*, **94**, 2136 (1972).
613. G. Guanti, E. Narisano, L. Banfi and C. Scolastico, *Tetrahedron Letters*, 817 (1983).
614. G. Guanti, E. Narisano, F. Pero, L. Banfi and C. Scolastico, *J. Chem. Soc., Perkin Trans. 1*, 189 (1984).
615. G. Solladie, C. Greck, G. Demailly and A. Solladie-Cavallo, *Tetrahedron Letters*, **23**, 5047 (1982).
616. G. Solladie, G. Demailly and C. Greck, *Tetrahedron Letters*, 435 (1985).
617. R. L. Crumbie, D. D. Ridley and G. W. Simpson, *J. Chem. Soc., Chem. Commun.*, 315 (1977).
618. R. L. Crumbie, B. S. Deol, J. E. Nemorin and D. D. Ridley, *Aust. J. Chem.*, **31**, 1965 (1978).
619. G. A. Russell and H.-D. Becker, *J. Amer. Chem. Soc.*, **85**, 3406 (1963).
620. J. R. Alexander and H. McCombie, *J. Chem. Soc.*, 1973 (1931).
621. E. G. Kataev and F. R. Tantasheva, *Zh. Obshch. Khim.*, **33**, 2307 (1963).
622. G. Tsuchihashi, S. Mitamura and K. Ogura, *Tetrahedron Letters*, 455 (1974).
623. H. Hogeveen, G. Maccagnani and F. Montanari, *J. Chem. Soc. (C)*, 1585 (1966) and references cited therein.
624. G. Tsuchihashi, S. Mitamura and K. Ogura, *Tetrahedron Letters*, 2469 (1973).
625. M. Shostakovskii, E. N. Prilezhaeva, L. V. Tsymbal, R. Y. Tolchinskaya and N. G. Starova, *Zh. Obshch. Khim.*, **31**, 2496 (1961).
626. J. E. Mulvaney and R. A. Ottaviani, *J. Polym. Sci.*, **8**, 2293 (1970).
627. R. Tanikaga, H. Sugihara, K. Tanaka and A. Kaji, *Synthesis*, 299 (1977).
628. H. Kinoshita, I. Hori, T. Oishi and Y. Ban, *Chem. Letters*, 1517 (1984).
629. D. J. Abbott and C. J. M. Stirling, *J. Chem. Soc. (C)*, 818 (1969).
630. N. Miyamoto, K. Utimoto and H. Nozaki, *Tetrahedron Letters*, 2895 (1972).
631. N. K. Gusarova, B. A. Trofimov, G. G. Efremova and S. V. Amosova, *Zh. Org. Khim.*, **17**, 2272 (1981).
632. B. A. Trofimov, N. K. Gusarova, S. V. Amosova, G. G. Efremova, S. M. Ponomareva and L. M. Sinegovskaya, *Zh. Org. Khim.*, **17**, 1980 (1981).
633. B. A. Trofimov, N. K. Gusarova, G. G. Efremova, A. N. Nikolskaya and S. V. Amosova, *Zh. Org. Khim.*, **17**, 1984 (1981).
634. H. Yamamura and H. H. Otto, *Arch. Pharm. (Weinheim)*, **318**, 193 (1985).
635. B. A. Trofimov, N. K. Gusarova, G. G. Efremova, S. V. Amosova, F. P. Kletsko, N. N. Vlasova and M. G. Voronkov, *Zh. Org. Khim.*, **16**, 2538 (1980).
636. M. G. Voronkov, F. P. Kletsko, N. N. Vlasova, N. K. Gusarova, G. G. Efremova, V. V. Keiko and B. A. Trofimov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1690 (1978).
637. R. Annunziata, M. Cinquini and A. Restelli, *J. Chem. Soc., Perkin Trans. 1*, 1183 (1982).
638. R. C. Cookson and R. Gopalan, *J. Chem. Soc., Chem. Commun.*, 608 (1978).
639. H.-J. Altenbach and H. Soicke, *Justus Liebigs Ann. Chem.*, 1096 (1982).
640. G. Tsuchihashi, S. Mitamura, S. Inoue and K. Ogura, *Tetrahedron Letters*, 323 (1973).
641. G. Tsuchihashi, S. Mitamura and K. Ogura, *Tetrahedron Letters*, 855 (1976).
642. J. Bruhn, H. Heimgartner and H. Schmid, *Helv. Chim. Acta*, **62**, 2630 (1979).
643. H. Sugihara, T. Tanikaga, K. Tanaka and A. Kaji, *Bull. Chem. Soc. Japan*, **51**, 655 (1978).
644. W. E. Truce and M. J. Lusch, *J. Org. Chem.*, **39**, 3174 (1974).
645. P. Vermeer, J. Meijer and C. Eylander, *Recl. Trav. Chim. Pays-Bas*, **93**, 240 (1974).
646. W. E. Truce and M. J. Lusch, *J. Org. Chem.*, **43**, 2252 (1978).
647. J. Berlan and K. Koosha, *J. Organomet. Chem.*, **153**, 107 (1978).

648. P. J. Brown, D. N. Jones, M. A. Khan, N. A. Meanwell and P. J. Richards, *J. Chem. Soc., Perkin Trans. 1*, 2049 (1984).
649. G. H. Posner, J. P. Mallamo, K. Miura and M. Hulce, *Pure Appl. Chem.*, **53**, 2307 (1981).
650. G. H. Posner, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Academic Press, New York, 1983, p. 225.
651. G. H. Posner, M. Hulce, J. P. Mallamo, S. A. Drexler and J. Clardy, *J. Org. Chem.*, **46**, 5244 (1981).
652. G. H. Posner and M. Hulce, *Tetrahedron Letters*, **25**, 379 (1984).
653. G. H. Posner, M. Weitzberg, T. G. Hamill, E. Asirvatham, H. Cun-Leng and J. Clardy, *Tetrahedron*, **42**, 2919 (1986).
654. G. H. Posner, T. P. Kogan and M. Hulce, *Tetrahedron Letters*, **25**, 383 (1984).
655. G. H. Posner, T. P. Kogan, S. R. Haines and L. L. Frye, *Tetrahedron Letters*, **25**, 2727 (1984).
656. J. L. Herrmann, G. R. Kieczykowski, R. Romanet, P. J. Wepplo and R. H. Schlessinger, *Tetrahedron Letters*, 4711 (1973).
657. B. Cazes, C. Huynh, S. Julia, V. Ratovelomanana and O. Ruel, *J. Chem. Res. (S)*, 68 (1978).
658. G. R. Kieczykowski, C. S. Pogonowski, J. E. Richman and R. H. Schlessinger, *J. Org. Chem.*, **42**, 175 (1977).
659. R. F. Romanet and R. H. Schlessinger, *J. Amer. Chem. Soc.*, **96**, 370 (1974).
660. E. N. Prilezhaeva, L. V. Tsymbal and M. F. Shostakovskii, *Dokl. Akad. Nauk SSSR*, **138**, 1122 (1961).
661. S. Ghersetti, H. Hogeveen, G. Maccagnani, F. Montanari and F. Taddei, *J. Chem. Soc.*, 3718 (1963).
662. O. DeLucchi, N. Lucchini, C. Marchiaro, G. Valle and G. Modena, *J. Org. Chem.*, **51**, 1457 (1986).
663. Y. Arai, S. Kuwayama, Y. Takeuchi and T. Koizumi, *Synth. Commun.*, **16**, 233 (1986).
664. L. A. Paquette, R. E. Moerck, B. Harirchian and P. D. Magnus, *J. Amer. Chem. Soc.*, **100**, 1597 (1978).
665. S. Danishefsky, R. K. Singh and T. Harayama, *J. Amer. Chem. Soc.*, **99**, 5810 (1977).
666. S. Danishefsky, T. Harayama and R. K. Singh, *J. Amer. Chem. Soc.*, **101**, 7008 (1979).
667. H. Takayama, K. Hayashi and T. Koizumi, *Tetrahedron Letters*, **27**, 5509 (1986).
668. E. G. Kataev and F. R. Tantasheva, *Dokl. Akad. Nauk SSSR*, **141**, 1101 (1961).
669. E. N. Prilezhaeva, V. A. Azovskaya and M. F. Shostakovskii, *Zh. Obshch. Khim.*, **35**, 35 (1965).
670. E. N. Prilezhaeva, V. A. Azovskaya, L. V. Tsymbal, E. N. Guryanova, G. Andrianova and M. F. Shostakovskii, *Zh. Obshch. Khim.*, **35**, 39 (1965).
671. W. Ando, Y. Hanyu, T. Takata and K. Ueno, *J. Amer. Chem. Soc.*, **104**, 4981 (1982).
672. D. A. Evans, C. A. Bryan and C. L. Sims, *J. Amer. Chem. Soc.*, **94**, 2891 (1982).
673. P. Caramella, E. Albini, T. Bandiera, A. Corsico Coda, P. Grünanger and M. Albini, *Tetrahedron*, **39**, 689 (1983).
674. P. Geneste, R. Durand and D. Pioch, *Tetrahedron Letters*, 4845 (1979).
675. A. Bened, R. Durand, D. Pioch, P. Geneste, J.-P. Declercq, G. Germain, J. Rambaud, R. Roques, C. Guimon and G. P. Guillouzo, *J. Org. Chem.*, **47**, 2461 (1982).
676. T. Koizumi, H. Hirai and E. Yoshii, *J. Org. Chem.*, **47**, 4004 (1982).
677. F. M. Dean and B. K. Park, *Tetrahedron Letters*, 4275 (1974).
678. M. Hojo, R. Masuda, T. Saeki, K. Fujimori and S. Tsutsumi, *Synthesis*, 789 (1977).
679. J. Nokami, N. Kunieda and M. Kinoshita, *Chem. Letters*, 249 (1977).
680. C. G. Venier, H. J. Barager III and M. A. Ward, *J. Amer. Chem. Soc.*, **97**, 3238 (1975).
681. C. G. Venier and M. A. Ward, *Tetrahedron Letters*, 3215 (1978).
682. C. G. Venier and H. Beckhaus, *Tetrahedron Letters*, 109 (1978).
683. M. Franck-Neumann and J.-J. Lohmann, *Angew. Chem., Int. Ed. Engl.*, **16**, 323 (1977).
684. T. Kametani, M. Tsubuki, H. Nemoto and K. Suzuki, *J. Amer. Chem. Soc.*, **103**, 1256 (1981).
685. D. N. Jones, T. P. Kogan, R. F. Newton and S. Smith, *J. Chem. Soc., Chem. Commun.*, 589 (1982).

CHAPTER 9

Cyclic sulfones and sulfoxides

URI ZOLLER
Haifa University, Oranim, Israel

The following chapter constitutes a walk on the trail of cyclic sulfones and sulfoxides, an intriguing and interesting class of compounds, that displays a variety of novel and unique properties, particularly when of small ring size.

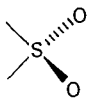
Several theoretical and experimental characteristics of the sulfone and sulfoxide groups are substantially modified when these are incorporated within a cyclic array. As a rule, the smaller the ring size the larger the deviation from the 'normal' expected properties and behavior of the sulfone and sulfoxide groups.

This chapter is an attempt to present a balanced treatment of the subject, concentrating on recent developments in the area and emphasizing the chemistry of small-ring sulfones and sulfoxides as a particular distinct category within the chemistry of the sulfone and sulfoxide functional groups.

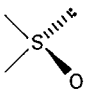
Section III in the chapter is based on Reference 2, whereas Section V is relatively short since a recently published book[279] adequately covers the relevant topics.

I. PREFACE

The generation, structure, physical and chemical properties of the closely-related sulfone (**1**) and sulfoxide (**2**) functional groups have been thoroughly described and discussed in this volume.



(**1**)



(**2**)

In view of the fact that the chemistry of ring compounds has played a considerable role in the development of modern organic chemistry, the following question is definitely relevant: Do *cyclic* sulfones and sulfoxides envisioned as a particular distinct category within this class of compounds contribute uniquely—in their own right—to the understanding of the characteristics and chemistry of the sulfone and sulfoxide functionalities and their role in organic chemistry?

Small ring compounds represent a fair portion of strained organic systems[1] in which the geometry of sp^3 and that of sp^2 carbons have been distorted from the ideal configurations. Foremost among these reactive molecules are the small ring heterocycles, such as thiirane and thiirene oxides and dioxides[2].

The introduction of heteroatoms into cyclic systems produces significant variations in the molecular geometry that reflect the changes in covalent radii, relative electronegativity and effective hybridization. Consequently, there are changes in the bonding and the physico-chemical characteristics of these heterocyclic systems—particularly in small ring systems.

Cyclic systems have frequently been used in studies of chemical bonding and reactivity, reaction mechanisms and a variety of other problems of interest to chemists[3]. Their utility depends on the changes in the carbon–carbon and the carbon–heteroatom bonds as well as on steric and electronic effects that result from the introduction of heteroatoms into the system. Indeed, the carbon–heteroatom bond length in small rings shows an effective increase with increasing heteroatom electronegativity[4], in line with a

potential facile ring opening involving these bonds. Thus, the presence of a heteroatom, coupled with the strain in the system, makes the hetero-three- to five-membered rings (relatively) easily cleavable: both electrophiles and nucleophiles as well as thermally and photochemically induced reactions are expected to initiate facile ring opening.

The presence of one or more sulfone and/or sulfoxide functions within a ring system also adds a new dimension of intrinsic difficulty concerning the synthesis, the stability–reactivity, and the stereo- and regio-selectivity of the reactions of these heterocycles. Clearly, the geometrical constraints impart particular features to these molecules in terms of structural and conformational chemistry, energy, strain energy, bonding, charge distribution and, consequently, in terms of the potential unique characteristics of the sulfone and sulfoxide groups incorporated in them. Based on accumulated evidence, the special contribution of cyclic sulfones and sulfoxides to the understanding of the various aspects of the chemistry of these two closely-related functional groups deserves a special treatment. Correlations and/or discrepancies between theoretical or 'educated' predictions and experimental results concerning the cyclic sulfone and sulfoxide systems will be described, and this treatment will provide an excellent setting for studying and understanding the following:

(a) The consequences of the inclusion of the sulfone and sulfoxide groups in a cyclic array as far as generation, structural-physical/spectral properties, bonding, energies, activating and directive effects, chemical stability and chemical reactivity are concerned.

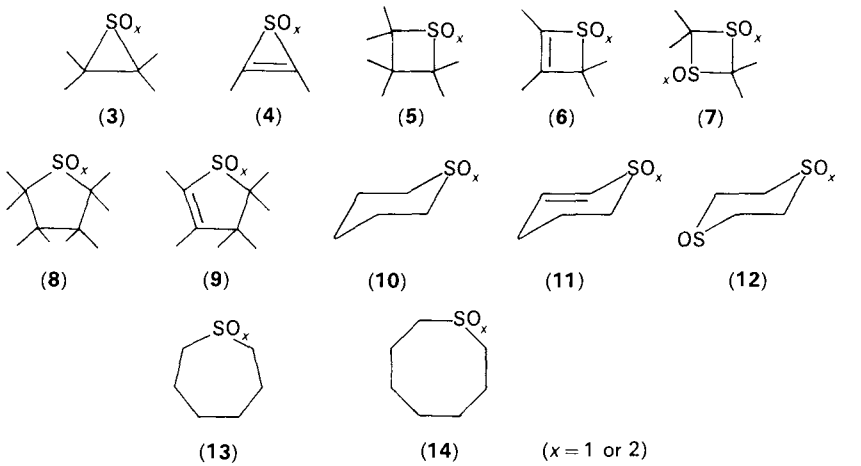
(b) The nature and some fundamental aspects of carbon–carbon and carbon–sulfur bonds in general, and in sulfur-containing small-ring heterocycles in particular.

(c) The particular role played by d-orbitals in cyclic strained systems containing the sulfoxide and/or sulfone functional group.

II. INTRODUCTION: SCOPE AND LIMITATIONS

The first member of the three-membered ring sulfones was synthesized about 70 years ago[5], and its unsaturated analogue has been known for only 20 years[6]. Since the mid-sixties, an explosive expansion in the chemistry of some of these small- to middle-sized sulfone and sulfoxide heterocycles has taken place.

To date, all saturated and unsaturated three- and larger-membered ring sulfones and sulfoxides (e.g., thiirane (**3**), thiirene (**4**), thietane (**5**), thiete (**6**), dithietane (**7**), thiolane (**8**), thiolene (**9**), thiane (**10**), thiene (**11**), dithiane (**12**), thiepane (**13**), thiocane (**14**), and their unsaturated analogues as well as isomers and closely-related systems) have been synthesized and their chemistry well-established.



Heterocycles of type **3–14** containing either additional nonsulfur heteroatom or nonsulfone/sulfoxide functional groups (other than double bonds) within the ring skeleton, have been excluded from being treated because of the overwhelming amount of material and since we wanted to emphasize the effects which these two functional groups exert on the chemical and physical properties of the systems.

Similarly, only selected cyclic systems containing more than one sulfoxide or sulfone groups have been included and discussed here, primarily in the thietane (i.e. 1,2- and 1,3-dithietanes) and thiane (i.e. 1,2-, 1,3- and 1,4-dithianes) series. The criterion for the inclusion of these multifunctional heterocycles was their contribution to the understanding of the physical properties and chemical reactivity of cyclic sulfones and sulfoxides, and the effects of these groups on either their immediate vicinity or on the behavior of the whole molecule.

Three-membered saturated and unsaturated sulfone and sulfoxide rings comprise a unique class of compounds[2] among the cyclic sulfone and sulfoxide series, due to the greatest distortion from the optimal (normal) bond lengths and angles of their counterparts in the open-chain and/or greater than eight-membered heterocycle series. Consequently, their preparation constitutes a special synthetic challenge, and their physicochemical properties are expected and, indeed, have been found to be different from those of other cyclic sulfones and sulfoxides. Therefore, the three-membered sulfones and sulfoxides are to be treated together. Cyclic sulfones and sulfoxides having a ring size of greater than eight have not been included, assuming that beginning with nine-membered rings the chemistry of the acyclic sulfones and sulfoxides has actually been approached.

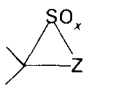
The field of cyclic sulfones and sulfoxides also provides a challenge for further investigations. Four possible directions for future research are as follows:

(a) the synthesis and study of three-membered rings incorporating sulfone or sulfoxide and an additional heteroatom (e.g. **15a**)[7,8];

(b) the synthesis and study of small-ring sulfamides and sulfurous diamides (e.g. **15b**) and closely related systems[9];

(c) the synthesis and study of thiapropellanes (e.g., **15c**)[10];

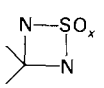
(d) the use of cyclic sulfones and sulfoxides as synthons in organic synthesis.



(15a)

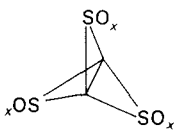
($x = 1$ or 2)

Z = NR, O, S, etc.



(15b)

($x = 1$ or 2)



(15c)

($x = 1$ or 2)

III. THREE-MEMBERED RING SULFOXIDES AND SULFONES

A. Introduction

The incorporation of the sulfoxide and sulfone functional groups within three-membered saturated and unsaturated ring systems (e.g. **3** and **4**) turns the latter into extremely interesting candidates for both theoretical and experimental investigation. The geometrical constraints are such that a unique combination of angles (tetrahedral, trigonal and dihedral), bond lengths (carbon–carbon, carbon–sulfur and sulfur–oxygen), strain energy and regio-proximity is obtained and reflected in the consequent physical and

chemical properties of these systems. In addition, some kind of 'aromaticity' can, in principle, be assigned to the unsaturated systems of type **4**[11], whereas the sulfoxides **4** ($x = 1$) can be considered as both pseudo-aromatic and 'classically' nonaromatic simultaneously[12] since they have, at least formally, a cyclic array or $4n\pi$ electrons predicted by theory to be highly unstable[13,14].

Although it may be experimentally impossible to distinguish and quantify the effect of each of the above factors separately within given three-membered ring systems, a comparison with the properties of higher ring systems (i.e., **5**–**14**) may provide an estimate of the contribution of the sulfone or the sulfoxide function to these properties.

The chemistry of three-membered rings containing oxidized sulfur starts with the work of Staudinger and Pfenninger[5] (equation 1).

$$R^1R^2CN_2 + SO_2 \longrightarrow [R^1R^2C{=}SO_2] \xrightarrow{R^1R^2C(CN)_2} R^1R^2C(\text{—}SO_2\text{—})CR^1R^2 \quad (1)$$

(3a)

The base-induced Ramberg–Bäcklund rearrangement[15] later initiated extensive mechanistically[16]- and synthetically[17]-oriented investigations, and played a significant role not only with respect to the study of thiirane dioxides (**3b**), but also contributed substantially to the present state of the art concerning three-membered rings containing sulfur[2] (equation 2).

$$R^1R^2CSO_2CR^3R^4 \xrightarrow[-HX]{\text{base}} R^1R^2C(\text{—}SO_2\text{—})CR^3R^4 \xrightarrow{(-SO_2)} R^1R^2C{=}CR^3R^4 \quad (2)$$

(H, X)

X = halogen

R^1, R^2, R^3, R^4 = H, alkyl, aryl

(3b)

Following the pioneering mechanistic studies conducted by Bordwell[18] and Neureiter[19], the physical and chemical properties of the thiirane dioxides could be established, as well as several significant aspects of their chemistry.

Thiirane oxides (**3**; $x = 1$) were rather rare and not well characterized until about 20 years ago[20]. Since 1965 synthetic methods for their preparation have been consistently and systematically explored[2]. They are rather thermodynamically stable compounds—compared to their closely-related thiirane dioxides—provided they have an *anti*-configuration with respect to the substituents and the sulfinyl oxygen. Also they are more resistant than the corresponding sulfones toward ring opening by either nucleophiles or electrophiles.

The first substituted thiirene dioxides[21] and thiirene oxides[22] (e.g. **4**; $x = 2$ and $x = 1$, respectively) were synthesized and characterized by Carpino and coworkers, while the parent thiirene oxide and dioxide are not known to date. However, the successful syntheses of the substituted unsaturated systems **4** opened the door to an extensive research involving the theoretical and experimental aspects of this class of intriguing compounds[2], particularly as far as the unique role and characteristics of their sulfone and sulfoxide groups are concerned.

Regardless of the question concerning the 'Hückel aromatic nature' of these nonbenzenoid systems, in which aromatic effects, if any, would require transmission through d-orbitals of the sulfur atom[11,23], the accumulated chemical and spectral evidence clearly suggests that both thiirene dioxides and thiirene oxides are unique systems with regard to their fundamental molecular structure and electronic configuration[2]. Thus, both the fascinating question of π-d bonding in conjugative unsaturated sulfone systems and the aromatic or nonaromatic nature of sulfone- and sulfoxide-containing unsaturated

heterocycles may be addressed and studied using thiirene dioxides and oxides as a model. It is noteworthy that thiirene oxides are remarkably stable, both thermally and toward electrophiles, relative to their saturated analogues (3) in spite of their additional strain[12]. It should be pointed out, however, that three-membered rings containing a sulfur atom are generally more stable than other three-membered rings. This is probably due to a lower strain energy for the former, apparently associated with the capacity of the sulfur atom to better accommodate the extra strain of the small ring compared with either the carbon atom or other second-row heteroatoms[2].

B. Structure and Physical Properties

1. Molecular orbital calculations

Ab initio molecular orbital calculations[24] of the parent cyclic thiirane oxide and dioxide (3; $x = 1$ and 2) have been carried out recently[25], using the Gaussian 76 program[26]. The geometries were optimized at the STO-3G* level[27] in which a manifold of five d-type functions, consisting of one second-order Gaussian each, was added to the minimal STO-3G basis set[28] for the second-row sulfur atom. The r(CH) and ⟨HCH have been fixed at their experimental values. The results were compared with those obtained for the equilibrium geometries of the open sulfones XSO_2Y where $X = Y = H$ or CH_3[25]. The relevant data are summarized in Table 1 together with data obtained from previous theoretical studies of cyclic sulfoxides and sulfones in which the structural parameters were determined by using *ab initio* MO-SCF[29], extended Hückel[30], and MNDO[31,32] calculations. In all of these theoretical studies, the importance and the necessity of including d-functions of the hypervalent sulfur (as a second-row atom) in the sulfone or sulfoxide group in the calculations was clearly demonstrated[29,32,33]. In fact, in those cases in which the 3d AO's of the sulfur atom were neglected in the calculations, the results obtained are clearly unsatisfactory compared to the results obtained either by alternative theoretical calculation procedures (which include the d-orbitals) or by experiment.

Two major trends are apparent from the data in Table 1. First, in both the acyclic and cyclic series, there is a lengthening of the sulfur–oxygen bond in going from the sulfones to

TABLE 1. Calculated bond lengths[a] and angles[b] in three-membered ring sulfone and sulfoxide and their acyclic analogues

	Geometrical parameters					
Molecule[c]	r(SO)	r(CS)	r(CC)	⟨OSO	⟨CSC	⟨CSO
Thiirane 1,1-dioxide	1.456 (1.452)[f]	1.757 (1.755)	1.560 (1.590)	—	52.7	115.0
Thiirane 1-oxide	1.474 (1.504)	1.788 (1.822)	1.515 (1.505)	—	50.1	114.9
Dimethyl sulfone[d]	1.455	1.818	—	124.3	98.5	107.8
Dimethyl sulfoxide[e]	1.522	1.791	—	—	141.8	123.8

[a] Bond lengths in Å.
[b] Angles in deg.
[c] Ref. 25 for the first three molecules and Ref. 32 for the fourth one.
[d] Point group C_{2v}.
[e] Point group C_s.
[f] Data in parentheses are from a previous study[29] in which a medium-size contracted Gaussian basis set was used in the calculations.

the sulfoxides, although this tendency is less pronounced in the cyclic series. Second, the carbon–carbon bond in the thiirane dioxide is substantially longer than that of the thiirane oxide or that of ordinary carbon–carbon σ bonds, whereas the carbon–sulfur bond in the cyclic oxide is longer than that of the cyclic sulfone, in contrast to the trend in the acyclic counterparts. The first feature should manifest itself in the increased capacity of the three-membered sulfoxides—compared with that of the three-membered sulfones—to serve as nucleophiles via the sulfoxide oxygen in appropriately designed chemical reactions. The second feature should lead to a relatively easy opening of the carbon–carbon bond in thiirane dioxides.

The group of Hoffmann and coworkers[30] concluded that the long C—C bond of thiirane dioxide is due to the effective population of the π^* level of the ethylene fragment through a low-lying orbital ($3b_2$ of π symmetry) in SO_2, and to the action of the 3d-orbitals in SO_2 as effective acceptors, thus depopulating the orbital of C_2H_4. The combination of these two effects leads to a weakening of the carbon–carbon bond. Consequently, the cleavage of this bond in the thiirane dioxide should be disrotatory, but conrotatory in the thiirane itself. The binding mechanism in the thiirane 1-oxide was also interpreted in terms of a donor-acceptor complex between ethylene and the SO fragment. It turns out that two factors are important in explaining the calculated structural features in thiirane oxides and dioxides: the donor–acceptor strength of the sulfoxide and the sulfone moieties, respectively, and the 3d sulfur orbital participation[29,30]. The extraordinary length of the carbon–carbon bond, which has been quoted to be the longest known[34], is best explained in terms of the latter. However, there is no evidence for an increased 3d S population in strained sulfur compounds like thiirane oxides. Although, in principle, the lowest-energy conformations of sulfones as well as sulfoxides would assume a staggered arrangement about the carbon–sulfur bond, the unique geometrical constraints applied when these groups are incorporated in a three-membered ring array should be reflected in both the total energy of the strained systems and in the net atomic charges of all the atoms involved. These two parameters may be used for predicting the relative thermodynamical stability and chemical reactivity of the cyclic sulfones and sulfoxides, on the one hand, in comparison to their acyclic counterparts, on the other. Selected relevent STO-3G* total energies and net atomic charges based on the Mulliken population analysis procedure[35] are given in Table 2. As could be expected, the total energy content of the cyclic molecule increases and the polarity of its sulfone group decreases compared with those of the acyclic counterpart dimethyl sulfone. Given the changes in carbon–carbon and the carbon–sulfur bond lengths and the strain energy embodied in the cyclic sulfone, which is clearly reflected in its total energy, it is not simple to estimate the 'net effect' of the decreased polarity of the

TABLE 2. Calculated total energies (au) and atomic charges of three-membered ring sulfone and sulfoxide and their acyclic counterparts (after Reference 25)

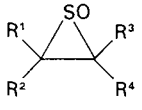
		Net atomic charges			
Molecule	Total Energy	S	O	C	H
Thiirane 1,1-dioxide	−617.98137 −624.678[c]	+0.35	−0.24	−0.12	+0.09
Thiirane 1-oxide	−544.15393 −549.994[c]	+0.27	−0.31	−0.14	+0.08[a] 0.09[b]
Dimethyl sulfone	−619.11196	+0.40	−0.27	−0.19	+0.08

[a]The hydrogen atoms on the oxygen side of the CSC plane.
[b]The hydrogen atoms on the opposite side of the CSC plane.
[c]Ref. 29. MO-SCF calculations using medium-size contracted Gaussian basis set.

sulfonyl group on the predicted chemical reactivity of the whole system including the functional group itself, nor to test experimentally the conclusions reached.

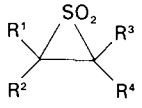
2. Experimental geometrical parameters

The geometric parameters of the three-membered ring sulfones and sulfoxides have been determined via X-ray diffraction techniques and gas-phase microwave spectroscopy. The accumulated data for some selected thiirane and thiirene oxides and dioxides (**16–19**) as well as for the corresponding thiirane (**20**) and the acyclic dimethyl sulfone (for the sake of comparison) are given in Table 3, together with the calculated values.



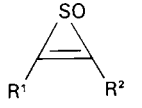
(**16**)

(**a**) $R^1 = R^2 = R^3 = R^4 = H$
(**b**) $R^1 = R^3 = CH_3$; $R^2 = R^4 = H$



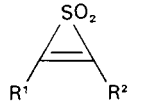
(**17**)

(**a**) $R^1 = R^2 = R^3 = R^4 = H$
(**b**) $R^1 = R^3 = CH_3$; $R^2 = R^4 = H$



(**18**)

(**a**) $R^1 = R^2 = C_6H_5$

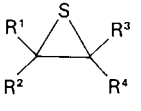


(**19**)

(**a**) $R^1 = R^2 = CH_3$
(**b**) $R^1 = R^2 = C_6H_5$

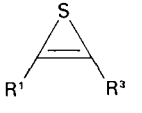
As in the acyclic series, there is a lengthening of the sulfur–oxygen bond as the sulfur is oxidized from the sulfoxide to the sulfone in both the thiirane (i.e. **16a** → **17a**) and the thiirene (i.e. **18a** → **19b**) series. Unexpected, however, is the substantial decrease in the OSO angle of the sulfone group in thiirenes compared with that of the thiiranes (e.g. ⟨OSO of **19a** is smaller than ⟨OSO of **17a**) and that of the corresponding acyclic dimethyl sulfone. There appears to be no simple explanation for this trend.

A unique characteristic feature of the cyclic three-membered ring sulfones and sulfoxides is the dramatic increase in the length of the carbon–carbon single bonds and the carbon–carbon double bonds in the series of thiirane–thiirane oxide–thiirane dioxide (**20a** → **16a** → **17a**), and thiirene–thiirene oxide–thiirene dioxide (**21** → **18a** → **19b**).



(**20**)

(**a**) $R^1 = R^2 = R^3 = R^4 = H$
(**b**) $R^1 = R^3 = CH_3$; $R^2 = R^4 = H$



(**21**)

$R^1 = R^2 = Ph$

There is a concomitant decrease in the length of the carbon–sulfur bonds in the thiirene series, but irregularity is apparent in the decrease of the carbon–sulfur bond in the thiirane series. Thus, *r*(CS) **19b** ⟨ *r*(CS) **18a** and *r*(CS) **17a** ⟨ *r*(CS) **16a**, but the carbon–sulfur bond lengths of **20a** and its oxide (**16a**) are essentially identical.

The above relationships between the thiiranes (**20**) and their dioxides (**17**) are reminiscent of those between cyclopropane and cyclopropanone[44]. The entire phenomena of the C—C bond lengthening and the concomitant C—S bond shortening in the three-membered ring sulfones and sulfoxides can be accounted for in terms of the sulfur 3d-orbital participation and the variation in the donor–acceptor capacities of the S, SO and SO_2[29,30]. The variations of the calculated valence-state orbital energies, together with the corresponding variations of the C—C overlap populations, can be used to understand the discontinuous variations of the C—C and the C—S bond lengths in the series thiiranes –

TABLE 3. Experimental geometries of selected acyclic and three-membered sulfones and sulfoxides (**16–19**)

Molecule	Functional group	Geometrical parameters							Method of determination[a]	Ref.
		r(SO)	r(CS)	r(CC)	⟨OSO	⟨CSC	⟨CCS	⟨CSO		
17a	SO_2	1.439	1.731	1.590	121.26	54.7	62.7		M	36
			1.76	1.586					M	34
		(1.456)[b]	(1.757)[b]	(1.560)[b]		(52.7)[b]				
17b	SO_2	1.720	1.588			54.6	62.0		X	4
		(1.730)[b]	(1.60)[b]						X	37
16a	SO	1.483	1.822	1.504		48.8	65.6		X	38
		(1.474)[b]	(1.788)[b]	(1.515)[b]						
19a	SO_2	1.449	1.692	1.333	114.8	46.4			X	39
19b	SO_2	1.444; 1.453	1.703; 1.716	1.354	116.1	46.7	66.2; 67.2		X	39
18a	SO	1.467	1.784	1.305		42.9	68.5; 68.6	114.9; 115	X	39
$(CH_3)SO_2$	SO_2	1.432; 1.435	1.777; 1.771		121.0; 119.7	103.3; 102.6			M	40
		(1.455)[b]	(1.818)[b]		(124.3)[b]	(98.5)[b]				
SO_2[c]		1.431			119.3					41
$(CH_3)_2SO$	SO	1.477	1.810			96.4		106.7		38,42
20a[d]	S		1.815	1.484		48.3	65.9		M	4,43
20b[d]	S		1.820	1.492		48.4	65.8		X	4

[a] X = X-ray diffraction technique; M = microwave spectroscopy.
[b] Values in parentheses are the calculated geometries (see Table 1).
[c] Point group C_{2v}.
[d] Data for this ring are included for comparison.

thirane oxides – thiirane dioxides[29]. In contrast, extended Hückel calculations[30] showed continuous changes along this series, the C—S population increasing and the C—C population decreasing.

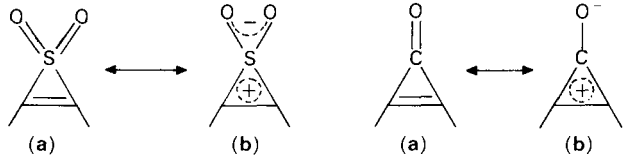
Clearly, there exists a good agreement between theoretical predictions (and calculations) based on the participation of sulfur 3d-orbitals and available experimental results. Thus, the important role of the sulfur d-orbitals in determining the structure and, consequently, the chemistry of sulfones and sulfoxides in general, and of strained small-ring sulfones and sulfoxides in particular, has been established.

It is illuminating to note that only very minor (and probably insignificant) differences can be detected as far as the r(SO) and ⟨OSO in the cyclic and acyclic sulfones and sulfoxides [i.e. **17a** versus $(CH_3)_2SO_2$ and SO_2; and **16a** versus $(CH_3)_2SO$] are concerned. The same is true concerning the r(SO) in the sulfoxide and sulfone groups in the thiirene series (i.e. **18a** and **19a**), compared with that of the acyclic analogues [i.e. $(CH_3)_2SO$ and $(CH_3)_2SO_2$, respectively].

The apparent insensitivity of the SO_2 bond lengths (and CNDO/S[45] and CNDO/2[46] calculations of oxygen charge densities) to structural variations in the carbon skeleton portion of the molecule might well be due to an 'insulating effect' of the LUMO sulfur d-orbitals; that is, that electronic interactions between the carbon framework and sulfur can occur without appreciable change in the oxygen–sulfur interactions. Consequently, the sulfur–oxygen bond distance provides an unsatisfactory measure of, e.g., d-π electron interactions. In contrast, the dramatic changes in the carbon–carbon bond lengths (from 1.305 Å in **18a** to 1.354 Å in **19b** and from 1.784 Å for the carbon–sulfur bond in **18a** to 1.709 Å for this bond in **19b**) were interpreted in terms of substantial π-delocalization[39]. It should be pointed out, however, that several 'ordinary' cyclic sulfones have been found to have shorter carbon–sulfur lengths than those of the corresponding sulfoxides[47].

3. *Theoretical treatment and interpretations*

The structural features and the spectroscopic characteristics of the thiirene dioxide system (**22**) are of special theoretical interest since, on the basis of analogy with cyclopropenone (**23**), it is a possible nonbenzenoid aromatic system with all the physical and chemical implications involved. Aromatic and/or conjugative effects, if any, require transmission through the d-orbitals of the sulfur atom.



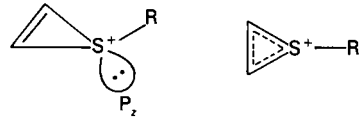
(22) (23)

Conjugation of the π-electrons of the carbon–carbon double bond with the LUMO sulfur 3d-orbitals would be expected to stabilize the Hückel $4n+2$ ($n=0$) array of π-electrons in the thiirene dioxide system. No wonder, therefore, that the successful synthesis of the first member in this series (e.g. **19b**)[21] has initiated and stimulated several studies[11,39,45,46,48,49], the main objective of which was to determine whether or not thiirene dioxides should be considered to be aromatic (or 'pseudo-aromatic') and/or to what extent conjugation effects, which require some sort of π-d bonding in the conjugatively unsaturated sulfones, are operative within these systems. The fact that the sulfur–oxygen bond lengths in thiirene dioxides were found to be similar to those of other SO_2-containing compounds, *does not* corroborate a Hückel-type π-delocalization

illustrated by structure **22b**. Understandably, the chemistry and reactivity of the thiirene dioxides and their sulfone functional group are contingent on the structural characteristics.

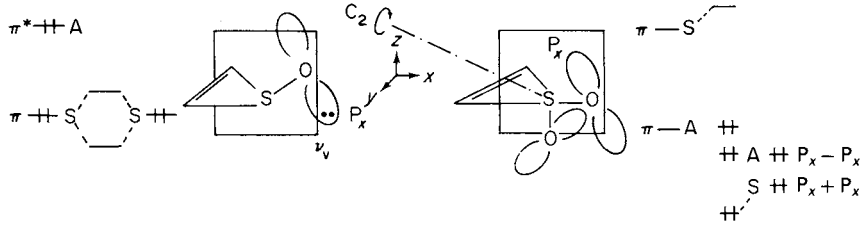
Similar considerations apply to the thiirene oxide system (**18**), since in this case too the sulfur's 3d-orbitals have the potential of interacting with the 2p-orbitals of both the adjacent carbon and oxygen atoms. Such an interaction should facilitate some kind of conjugation of the carbon–carbon double-bond π-electrons with the formally unoccupied 3d-orbitals, which in turn would give rise to Hückel-type stabilization associated with cyclic array of $4n + 2$ ($n = 0$) π-electrons.

The question of sulfur d-orbital involvement in chemical bonding centers about their 'size' (radial distribution) in potential bonding situations. This size depends mainly upon the net charge (oxidation state)[50]: the greater the oxidation state of sulfur, the greater the importance of d-orbitals in overlap transmission of electronic effects via π-conjugation. The high-lying d_{xz}-orbital of proper symmetry contracts in volume and descends in energy as the oxidation state of the thiirene sulfur increases[51]. Thus, the available d_{xz}-orbital would permit electron delocalization from the ethylene fragment into sulfur and might permit a thiirenium cation (**24**) as a potential nonbenzenoid 'aromatic' molecule with a nonzero carbon–sulfur π-bond order (cf. **25**), whereas the lower order of geometry would allow the p_z electron pair to mix in the not large orthogonal *S*-function and assume a nonbonding rather than antibonding role.



(24) **(25)**

Analogous effects may allow 'aromatic' assignments to the thiirene 1-oxide and dioxide, and may be demonstrated through the interaction diagrams given below[52].

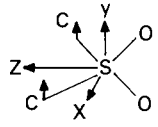


Employing a C_2 symmetry in the case of the thiirene 1-dioxide and remembering that the spiro-operator that mixes the fragment orbitals gives nonzero matrix elements only if these orbitals are symmetric to the C_2 operation[53], the net result is stabilizing. On the other hand, thiirene 1-oxide suffers a homoconjugative destabilization.

Based on experimental results and complementary calculations, an out-of-plane π-delocalization is suggested for thiirene dioxides[39]. As far as the thiirene oxide is concerned, theoretical calculations[11] predict possible spiroconjugative-type[53] interaction between the $\pi^*_{C=C}$ orbital of the ring and the π-orbitals of the SO (which leads to aromatic stabilization and a π charge transfer backward from the SO to the C=C). There exists, however, a rather strong destabilization effect, due to the $\pi^*_{SO}(d_{xz})$-orbital.

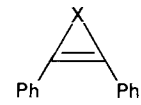
In order to justify the validity of ketone–sulfone analogies, a series of CNDO/2 calculations on a number of model cyclic unsaturated sulfones and ketones was

undertaken[46]. It was found that: (a) only little charge separation occurs in thiirene dioxides; (b) the difference in charge density on oxygen in the series of ketones is not reproduced by the sulfones; and (c) in contrast to cyclopropenone, thiirene dioxide is a weak acceptor in hydrogen bonding. It was concluded[46] that a comparison of cyclic unsaturated sulfones and ketones is of little value, and that although the d_{yz}-orbital of the sulfur atom (**26**) can and does promote resonance structures (e.g. **22b**) analogous to the predominant polar resonance structures in ketones (e.g. **23b**), the d_{xy}-orbital has a contrary effect of comparable magnitude.



(**26**)

The thiirene dioxide system was investigated by an analysis of the inductive and conjugative interactions between the carbon–carbon (C=C) and the sulfonyl (SO_2) subunits and consideration of the possible 'aromaticity' of this species[45]. By using a method which makes it possible to distinguish inductive from conjugative effects[48], the C=C—SO_2 interactions could be evaluated and compared to the results obtained by analyzing the UV photoelectron spectra of thiirene dioxides[45]. Both approaches revealed a strong hyperconjugative interaction between the occupied C=C MO and an occupied SO_2 σ-MO_1, and a modest mixing between the former and a vacant SO_2 σ^* which is a nearly pure sulfur d-AO. The π-σ^* interaction is responsible for a small π charge transfer from the carbon–carbon double bond to the sulfonyl unit. In spite of this charge transfer being much smaller in magnitude than in the corresponding cyclopropenone, it was concluded that thiirene dioxide does have a tendency to exhibit properties expected of an 'aromatic' model. However, the degree (but not the nature) of this tendency is much smaller for thiirene dioxides than for the corresponding ketones. In a complementary study[49], the photoelectron spectra of 2,3-diphenyl-substituted compounds (**27**) were interpreted and analyzed in terms of inductive and conjugative interactions between the subunits C=C and X. The values obtained were compared with theoretical data obtained by using the 'cut-off' procedure[48,54].



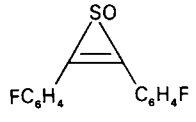
X = CH_2, CO, C=S, SO, SO_2

(**27**)

The calculated CNDO/2 inductive (I) and CNDO/2 conjugative (C) effects of **27** were found to be -0.35 and 0.04, -0.45 and 0.1, and -0.95 and 0.06 eV for X = CO, SO and SO_2, respectively. The corresponding aromaticities (conjugation energies) and the π charge transfer from the PhC=CPh segment to X were calculated to be -52.84 and 245.4×10^{-3}, -22.05 and 82.2×10^{-3}, and -21.84 and 81.4×10^{-3} kcal mol^{-1}, respectively[49]. Although the values obtained for either the sulfoxide or the sulfone (**27**, X = SO and X = SO_2) are surprisingly comparable in magnitude, the results suggest that these phenyl-substituted molecules are likely (somewhat) aromatic as their parent systems are. Interestingly, the corresponding experimental I and C values for **27** (X = CO and SO)[49] were found to be at least 1.5–2.5 times greater than the calculated spiroconjugation in

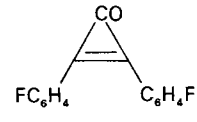
thiirene dioxide which was found to be negligible relative to hyperconjugation, and the influence of d-orbitals of sulfur on the electronic structure of this system was shown to be rather pronounced. Both aromaticity orders derived from the *ab initio* and CNDO/S charge transfer values concur and agree with the CNDO/S conjugation energy order, and both suggested thiirene dioxides to be aromatic in nature at least to some extent[11].

Following the work of Taft[55] and coworkers on fluorobenzenes which permitted the isolation of the inductive (σ_I) and conjugative (σ_R) effects, the σ values of 2, 3-di-*meta*- and *para*-fluorophenylthiirene oxides (**28a,b**) were calculated (based on the measured shielding parameters of these compounds)[56] and compared with the σ values of corresponding bis(*meta*- and *para*-fluorophenyl) cyclopropenones (**29a,b**).



(28)

(a) *m*-FC_6H_4
(b) *p*-FC_6H_4



(29)

(a) *m*-FC_6H_4
(b) *p*-FC_6H_4

These comparisons of σ_R (0.16 and 0.25 for **18** and **29**, respectively) showed, as expected, that the extent of the electron-withdrawing conjugative effect increases in the order thiirene oxide < thiirene dioxide < cyclopropenone. Although this result agrees with earlier studies on the relative order of conjugative interaction in simple vinyl sulfoxides and sulfones compared with that of enones, it is not pertinent to the question of whether these are simple conjugative interactions or *cyclic* conjugative effects with transmission through the sulfur atom[11,23c,45,46,56].

Standard CNDO/2 calculations on models of thiirenes have been performed[39] in an attempt to obtain a picture of their bonding. Both the atomic charge densities and bond indices of the parent thiirene, thiirene oxide and thiirene dioxide have been calculated using model parameters. While the trends in the carbon–carbon and carbon–sulfur bond indices agree qualitatively with the trends observed in the experimental bond lengths, the sulfur–oxygen indices predicted that the sulfoxide distance should be smaller than the sulfone distance—in contrast to the experimental results. Thus, it was concluded[39] that the calculated oxygen charge densities and sulfur–oxygen bond orders provide an insensitive measure of d-π electron interactions, and that the in-plane carbon p_z-orbitals are primarily responsible for the bond-length variations. The contributions of the out-of-plane carbon p_y–sulfur interactions to the carbon–sulfur bond orders in the thiirene series suggest that π-delocalization may be of a magnitude comparable to that of the cyclopropenones.

Based on the geometries of three-membered ring heterocycles as determined by X-ray and gas-phase methods, it could be demonstrated[4] that in saturated three-membered heterocycles similar to **3**, the carbon–carbon bond length decreases linearly with increasing heteroatom electronegativity whereas the carbon–heteroatom bond shows an effective increase as the electronegativity of the heteroatom increases. The above is applicable to the series sulfones–sulfoxides **3** if the relative electronegativities of the two functional groups are being considered. These effects are explicable in terms of interaction of the heteroatom with ethylene[29,30,57] and are analogous to the formation of metalacyclopropanes[58,59].

The experimental carbon–carbon and carbon–sulfur bond-length values for the series **3** and **4** are in good agreement with the calculated values both in the saturated and unsaturated sulfones and sulfoxides (Table 1 and 3). Thus, it appears that the carbon–

carbon double bonds in the series **4** also vary with electronegativity in a systematic manner. Clearly, variations in the electronic distribution in the three-membered ring sulfones and sulfoxides leave their trace in the molecular geometry and ultimately in the chemistry of these systems.

On the basis of a naive analogy with cyclopropenones, the ground-state aromatic stabilization of which has been recently reconfirmed, some kind of 'aromaticity' can, in principle, be assigned to these systems when Z = SO or SO_2, assuming a possibility for transmission of electronic effects via π-conjugation.

The thiirene oxide system is of particular interest due to it being simultaneously both a potentially nonbenzenoid aromatic $(4n+2)\pi$ and antiaromatic $4n\pi$ Hückel system.

Since it is clear that the presence of an unshared pair of electrons on the sulfur of the sulfoxide group leads to no special instability in the case of the known thiirene oxides (i.e., **18a**, **28a,b** and the first alkyl-substituted thiirene oxide **30** recently synthesized[60]), the reduced antiaromatic properties of the thiirene oxides relative to that of thiirenes have been manifested experimentally. As far as the possibility of electron-attracting conjugative stabilization involving the sulfur atom in thiirene oxides is concerned, the experimental evidence accumulated so far is not decisive. Thus, the chemical shift of the vinylic carbon of 2,3-diphenylthiirene 1-oxide (**18a**) was found to be 137.3 ppm (downfield from Me_4Si) and those of the corresponding diphenyl and dimethyl sulfones (**19b**, **19a**) to be 158.9 and 167.4 ppm, respectively[12], compared with the reported values of 148.5 and 157.9 for the 2,3-diphenyl- and 2,3-dimethylcyclopropenones.

To summarize, based on both theoretical and experimental results, the following conclusions emerge[12]:

(i) Conjugative interactions and/or cyclic π-delocalizations are small compared with closely related systems.

(ii) No significant antiaromatic destabilizing effects can be ascribed to the sulfur unshared pair of electrons.

(iii) The oxygen moiety in the sulfoxide function should not be expected to be highly reactive.

4. *Spectroscopic characteristics and characterization*

a. Infrared. The infrared spectrum is the best available technique for determining the presence of both the sulfone and the sulfoxide functional groups within a given molecule. Although the sulfur–oxygen stretching frequencies of both the sulfone and the sulfoxide groups give rise to absorption peaks within the fingerprint region (that is $<1400\,cm^{-1}$), their location is characteristically fixed, and they are typically strong so as to dominate the spectrum and thus are easily identifiable.

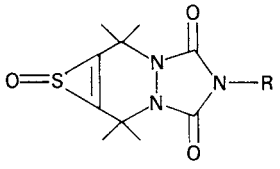
As in the acyclic series, saturated three-membered ring sulfones and sulfoxides (i.e. thiirane dioxides and thiirane oxides) exhibit stretching frequencies typical of sulfones and sulfoxides: at about 1320 (asymmetric) and 1160 cm^{-1} (symmetric) for the former[61,62] and 1050–1090 cm^{-1} for the latter[63], with the exact location being somewhat dependent on the nature of substituents on the α-carbons. Some representative data of IR absorptions of the SO_2 and SO groups in thiirane and thiirene oxides and dioxides are given in Table 4. It appears that the constraints of the three-membered saturated ring have little effect on the stretching frequencies of both sulfone and sulfoxide groups incorporated in it. The situation is entirely different, however, as far as the IR spectra of both thiirene dioxides and thiirene oxides are concerned (Table 4). Thus, the most striking feature of the data in Table 4 is, undoubtedly, the anomalous asymmetric stretching[64] frequency of the SO_2 group in thiirene dioxides. Usually, an internal correlation is observed between the asymmetric and symmetric stretching frequencies of the SO_2 group in sulfones as well as in

TABLE 4. Selected IR stretching frequencies of sulfone and sulfoxide groups in thiirane and thiirene dioxides and oxides

Compound		IR frequencies[a] Asymmetric		Symmetric	Ref.
Thiirane dioxide	**17a**	1310		1160	2,36,62
Thiirane dioxide	**17c**	1328[c]		1168[c]	61
	(R^1 = Cl; R^2 = R^3 = R^4 = H)				
Thiirane dioxide	**17d**	1346[b]		1160[b]	21
	(R^1 = R^3 = Ph; R^2 = R^4 = H)				
Thiirane dioxide	**19a**	1256		1166	6
Thiirene dioxide	**19b**	1279[b]		1167[b]	6,21
Thiirene dioxide	**28a**	1250[c]		1149[c]	2,22
Thiirane oxide	**16a**		1060		63
Thiirane oxide	**16b**		1080, 1065[d]		63
Thiirane oxide	**16c**		1065		63
	(R^1 = R^3 = Ph; R^2 = R^4 = H)				
Thiirene oxide	**18a**		1061		22
	18b		1065		22
	30[e]		1115[f]		60

[a] cm^{-1}.
[b] In CCl_4.
[c] In Nujol.
[d] Two isomers; *syn*; *anti*.
[e] Dialkyl-substituted thiirene oxide (six-membered ring fused)[60].
[f] In KBr.

other compounds containing the sulfonyl group. In contrast, thiirene dioxides show a marked shift of the asymmetric absorption to lower frequencies (compared with other sulfones) without a correlated shift of the symmetric band to higher frequencies. The net result is that the Bellamy–Williams correlation[65] no longer holds for these compounds. Although the reason for this phenomenon is not yet clear, it appears that the ring strain alone cannot be responsible for this effect[6]. However, the π-d interactions of the type discussed in the previous section may provide a satisfactory explanation. It is interesting to note that a characteristic feature of the cycloadducts of thiirene oxide with 4-substituted 1,2,4-triazoline-3,5-diones (e.g. the six-membered ring fused thiirene *S*-oxide **30**) is that their stretching vibrational absorption due to the sulfur–oxygen bond appears at the unusually high frequency of 1115 cm^{-1}. This value indicates a surprisingly short S—O bond length, the shortest found for any type of sulfoxide (1.4583 Å by X-ray analysis)[60]. Apparently, this S—O bond shortening reflects the combined effect of ring fusion and alkyl substitution.



(**30**)

(**a**) R = Me

(**b**) R = Ph

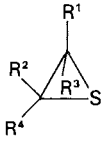
b. ^1H and ^{13}C NMR spectroscopy. Proton- and carbon-13 NMR spectroscopy have found wide application in organosulfur chemistry[63,66,67]. In both cases, as expected, the inductive- and the directionally-dependent anisotropic effects of the sulfonyl and the sulfoxyl groups play a major role[67,68] cyclic systems included[2,69,70].

The order of magnitude of α-proton shifts for a particular ring size is generally S < SO < SO_2, in accord with the inductive effects of these functional groups[66]. Shielding in the three-membered series is probably dominated by bond and group anisotropies that distinguish it from the other sulfur-containing ring systems[70].

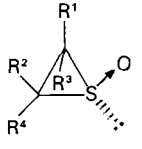
Thus, the positions of the three-membered ring proton signals of thiirane dioxides depend upon the environment of these protons[71] and the solvents used[72] and are not uniquely indicative of this class of compounds. The high field shift of the three-membered ring protons of thiirane dioxides compared with the α-protons in the four- and higher-membered sulfone rings may be partly due to the diamagnetic anisotropy of the three-membered ring[73].

^1H NMR techniques have been extensively used in determining both the configuration and the stereochemistry of thiirane oxides, e.g., in making the choice between isomers obtained in the preparation of the oxides. Configuration assignments have been made, based on the expected anisotropy effect of the S—O bond. In certain six-, five- and four-membered ring sulfoxides, a β-hydrogen which is *syn* to the S—O bond experiences a profound deshielding effect, while a β-hydrogen which is *anti* to the S—O (i.e. *syn* to the lone pair of the sulfur atom) suffers from a shielding effect as compared with the same protons of the parent sulfide[69,74].

Indeed, the validity of this approach and analogy was unequivocally demonstrated[63] by an examination of the NMR characteristics of 2,2-dimethylthiirane (**31a**), *cis*-2,3-dimethylthiirane (**31b**), *trans*-2,3-dimethylthiirane (**31c**), and their corresponding sulfoxides (**32a–c**).



(31)



(32)

(a) $R^1 = R^3 = CH_3$, $R^2 = R^4 = H$

(b) $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$

(c) $R^1 = R^4 = CH_3$, $R^2 = R^3 = H$

The chemical shifts of the H-methyl groups in thiiranes **31a, 31b** and **31c** were found to be $\delta = 1.59, 1.44$ and 1.45, respectively. The chemical shifts of the β-anti-methyl hydrogens (i.e. those of R^3) where found to be $\delta = 1.25, 1.23$ and 1.27 in **32a–c** compared with $\delta = 1.74$ and 1.64 for *syn*-R^1-hydrogens in **32a** and **31c**, respectively[63,75]. The consistency of the deshielding effect in accordance with the position of the β-hydrogens in ring sulfoxides is thus apparent. These observations validate the applicability of the S—O anisotropy rule to the three-membered ring system.

Although a remarkable upfield or downfield shift of a β-proton in a rigid system depending on the direction of the S—O bond was established in many cases, the same behavior was not observed for the hydrogens directly attached to the three-membered thiirane oxide ring (e.g. $\delta = 1.85$ and 1.89 for R^3 in **31b** and **32b**, respectively). Occasionally, the shielding and deshielding effects of the S—O bond are compensating each other at these hydrogens. The principle has been used successfully, however, to assign the configuration of a number of aryl-substituted thiirane oxides.

All the above chemical shift-based assignments were further confirmed by solvent-induced shift studies[63,76]. The geminal coupling constants in thiirane oxide (− 6.4 Hz) and 2-methylthiirane oxide (− 6.0 Hz) were appreciably more negative than those in thiirane (− 0.7 Hz) and 2-methylthiirane (− 0.8 Hz), respectively[76]; the trend to greater negative value of J_{gem} with increasing group electronegativity of the heteroatom is the converse of the usual NMR behavior of three-membered heterocycles. The vicinal coupling constants for the *syn*-protons, namely 11.5 and 11.7 Hz, in thiirane oxide were also abnormal[77]. These facts were interpreted in terms of the Pople–Bothner-By model for spin coupling[78]. However, the larger ^3J values for thiirane oxide were ascribed to greater electronegativity of the SO compared with that of S in thiiranes. In general, the opposite effect is found in other three-membered heterocycles: an increase in ^3J is found as the electronegativity of the heteroatom decreases[79] and the magnitude of $^3J_{CH}$ roughly parallels $^3J_{HH}$ in this series of compounds[80].

The vinylic hydrogen in 2-methylthiirene dioxide resonates at $\delta = 8.99$[81], a particularly low magnetic field. This low value may reflect the combined inductive and anisotropic effects of the sulfone group with the anisotropic effect of the carbon–carbon double bond. Consequently, this high deshielding of the ring hydrogen cannot be considered as evidence for the assumed partial aromaticity assigned to the thiirene dioxides[6,11,39].

Several trends have emerged in the extensive carbon-13 NMR spectroscopy data that have been accumulated for sulfones and sulfoxides. Based on many studies of cyclic systems—particularly five- and six-membered ring sulfur compounds—these trends were shown to generally apply equally to both the cyclic and acyclic systems[70]. Thus: (a) oxidation of a sulfide to a sulfone results in a 20–25 ppm downfield chemical shift for sp^3-hybridized α-carbon atoms and 4–9 ppm upfield shift for β-carbons[82,83], and (b) there is very little difference between the chemical shifts of α-carbon atoms of sulfones and sulfoxides[84,85] despite the difference in the inductive effects of these two functional groups[70]. A difference is observed, however, in the ^1H chemical shift of related cyclic sulfoxides and sulfones[70].

The ^{13}C NMR data for representative three-membered sulfones and sulfoxides are given in Table 5. The chemical shifts of the sp^3-hybridized α-carbon in the parent thiirane[70] and the five-membered ring[86] sulfide, sulfoxide and sulfone are 18.1, 31.7, 54.3 and 51.1, respectively, whereas those of cyclopropenone, diphenylcyclopropenone and dimethylcyclopropenone are 169.0[87], 148.7[88] and 157.9, respectively.

In contrast to the insignificant differences between the carbon chemical shifts of cyclic

TABLE 5. Ring carbon-13 chemical shifts of three-membered sulfones and sulfoxides

Compound	Chemical shift (ppm)[a]	Ref.
Thiirane oxide **16a**	33.8	70
Thiirane dioxide **17a**	31.6	70
2,3-Diphenylthiirene oxide **18a**	137.3	12
Alkyl-substituted fused thiirene oxide **30a**	15.3	60
2,3-Diphenylthiirene dioxide **19b**	158.9	12
2,3-Dimethylthiirene dioxide **19a**	167.4	12

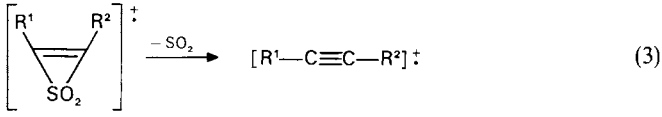
[a]Downfield from $(CH_3)_4Si$ in $CDCl_3$.

sulfones and sulfoxides in the saturated series, there is a noticeable downfield shift (14–22 ppm) of the α-carbon in the sulfones compared to sulfoxides in the thiirene series. In comparing the carbon shifts of the thiirene oxides and dioxides with the cyclopropenone system, we note very similar patterns (e.g., about 9 ppm difference in the shifts of alkyl- and aryl-substituted vinylic carbons). Similarly, the positions of the methyl and H absorption in the NMR spectrum of 2-methylthiirene dioxides are comparable to those observed for methylcyclopropenone (2.70 and 8.70, respectively)[89]. Hence, the differences in the ^{13}C chemical shift values found for the thiirene oxides and dioxides suggest a higher degree of aromaticity of the dioxides compared with that of the sulfoxides[12]. However, the magnitude of this conjugative effect (and, consequently, the relative degree of 'aromaticity') remains an open question, since the inductive effect (and, also, possibly the anisotropic effect)[70] is clearly reflected in the observed difference.

Interestingly, the oxygen-17 chemical shifts for the thiirane oxide (**16a**) and thiirane dioxide (**17a**) were found to be 71 and 111 ppm (downfield from natural-abundance ^{17}O in H_2O), respectively. The oxygen-17 shift reveals that this oxygen is the most highly shielded oxygen atom so far reported[80,70].

c. Mass spectroscopy. The extrusion of sulfur dioxide and of sulfur monoxide is a characteristic of these systems[2,6,15–18,63] and should be reflected in their mass spectra.

Verification of the molecular weight of thiirene dioxides by mass spectrometry, employing the conventional electron-impact (EI) ionization method, has been unsuccessful due to the absence or insignificant intensity of molecular ion peaks in their mass spectra. The base peak is rather characteristic, however, and corresponds to the formation of the disubstituted acetylene ion by loss of sulfur dioxide[91] (equation 3).

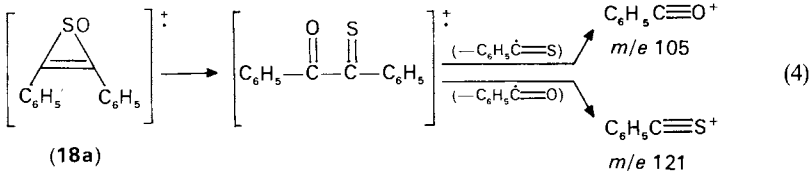


(19) (3)

In fact, considerable thermal decomposition may precede ionization as suggested by the fact that only the relatively volatile 2, 2-dimethylthiirene dioxide gave any evidence for the molecular ion. Retention of the positive charge with the sulfone function is responsible for the ion at *m/e* 64 (SO_2^+).

Similarly, a common feature in the mass spectrum of thiirene oxides is the high abundance of the substituted acetylene ion (e.g. $[PhC{\equiv}CPh]^+$) formed by elimination of sulfur monoxide. In fact, this ion constitutes the base peak in the spectrum of **18a** whereas the molecular ion has a rather insignificant intensity (0.25% Σ of M^+)[91].

The other ions are products of the further decomposition of the diphenylacetylene ion (*m/e* 178), or the fragmentation products of the monothiobenzyl[92] ion as depicted in equation 4[93].



(18a) (4)

The use of the chemical ionization (CI) mass spectrometry technique[94] in the case of

thiirene dioxides proved to be very useful, in that by using different reagent gases (i.e. methane, isobutane, ammonia and dimethylamine) the relative abundance of molecular adduct ions have been enhanced and thus the molecular weight of the thiirene dioxides investigated could be established[91]. Thus, the formation of $(R^1C{\equiv}CR^2 + H)^+$ and $(SO_2 + H)^+$ in the methane CI spectra occurred via the elimination of SO_2 from $(M + H)^+$. Here, too, the acetylenic ion dominated the spectra. Similar results were obtained with the other reagent gases.

Similarly, methane CI spectrum of **18a** was found to be dominated by the $(C_6H_5C{\equiv}CC_6H_5 + H)^+$ ion. A distinct molecular ion species at *m/e* value corresponding to $(M + H)^+$ was observed in the methane mass spectra of this thiirene oxide (26% Σ 40). Furthermore, the relative intensity of the $(M + H)^+$ peak of **18a** was shown to increase substantially in the isobutane and dimethyl amine CI mass spectra[91].

C. The Sulfone and Sulfoxide Functionality in Three-Membered Ring Systems: Activating and Directive Effects

There are several unique features associated with the sulfone and the sulfoxide groups relating to their activating, directive, stabilizing and destabilizing effects as well as to their interrelationships with adjacent functional groups. The incorporation of these groups within a cyclic array imparts some extra strain-originated conformational-torsional constraints as well as steric-originated rigidity (and/or enhanced proximity between certain atoms) to these systems, the ultimate result being a substantial modification of the sulfone and sulfoxide functionality compared with that of acyclic systems.

The following features associated with the sulfoxide and sulfone functional groups in thiirane and thiirene oxides and dioxides are to be discussed:

1. Thermal elimination of SO_2 and SO (SO_2 and SO as leaving groups).
2. Acidity of α-hydrogens (sulfonyl and sulfoxy carbanions).
3. Electrophilicity of the SO_2 and SO groups (reaction with bases/nucleophiles).
4. Nucleophilicity of the SO_2 and SO groups (the reaction of the sulfoxy oxygen with electrophiles).
5. The (formal) Michael addition of nucleophiles to thiirene oxides and dioxides (formally vinyl sulfoxides and sulfones).
6. Miscellaneous (formation of complexes, and configuration induced by the sulfoxide group).

In all of the above, the activating, directive and stabilizing–destabilizing effects are similar in principle to those in the acyclic systems. However, the *magnitude* of these effects *per se*, or in conjunction with other characteristics of the systems in point, are considerably different and, consequently, the ultimate chemical results may be different.

1. Thermal elimination of SO_2 and SO

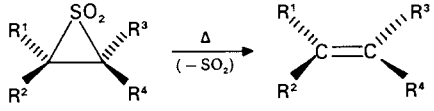
In principle the higher the oxidation state of the sulfur atom, the better its 'leaving capacity'; that is, the sulfonyl group is a better leaving group than the sulfoxy group, which in turn is a better leaving group than the unoxidized divalent sulfur. The enhanced polarizability of the oxidized groups, combined with the high electronegativity of the attached oxygen atom(s) which generates a partial positive charge on the sulfur atom, turn these groups into efficient 'sink' for the bonding electrons of the adjacent carbon atoms. Furthermore, the carbon–sulfur bond is weaker than ordinary carbon–carbon bonds, sulfur dioxide is a resonance-stabilized unit, and sulfur monoxide in its triplet ground state can easily be generated from suitable sulfoxides[95], possibly through the thermally allowed concerted nonlinear chelatropic process[96].

Hence, one would expect the thermal elimination of sulfur dioxide or of sulfur monoxide

to be a facile process. However, elimination of SO_2 or SO from acyclic sulfones and sulfoxides is not ordinarily observed. Both are very stable compounds, and elimination requires either appropriate chemical modifications in the case of sulfones or the presence of a β-carbon carrying at least one hydrogen atom in the case of sulfoxides[97].

The situation is entirely different in the three-membered ring sulfones and sulfoxides: the facile thermolytic elimination of SO_2 from the former is probably their most distinctive (and dominant) chemical reaction, whereas the loss of SO from the latter characterizes both the thiirane and thiirene series[2].

Thus, most thiirane dioxides slowly decompose near room temperature and rapidly at about 80° or above their melting points to give, stereospecifically, the related alkenes and sulfur dioxide[2,18,19,71] (equation 5).



(5)

(17) (33)

(c) $R^1 = R^3 = H$, $R^2 = R^4$ = alkyl or aryl

(d) $R^1 = R^4 = H$, $R^2 = R^3$ = alkyl or aryl

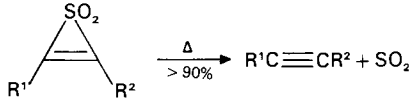
This thermal fragmentation is so facile that only under inert atmosphere and very low temperatures can the rate of decomposition be reduced sufficiently so as to make the systematic study of these molecules possible.

Several mechanistic explanations[98]—including both concerted symmetry-allowed nonlinear chelatropic paths[96], and nonconcerted stepwise mechanisms (such as that in which a diradical species is involved[99])—have been advanced to accommodate the stereospecific experimental results[2,17a,73,99].

The SO_2 eliminations follow first-order rates and were found to correlate surprisingly well with the ionizing power of the medium. Also, the rates are base-accelerated, albeit the effect is rather small[99].

The formation of alkenes from thiirane dioxides may not be stereospecifically controlled in the presence of a sufficiently strong base and sufficiently acidic protons in the three-membered ring. Under such conditions (essentially those typical for the Ramberg–Bäcklund reaction), epimerization via a carbanion intermediate produces an equilibrium mixture of thiirane dioxides[19,99] and consequently a mixture of *cis*- and *trans*-alkenes.

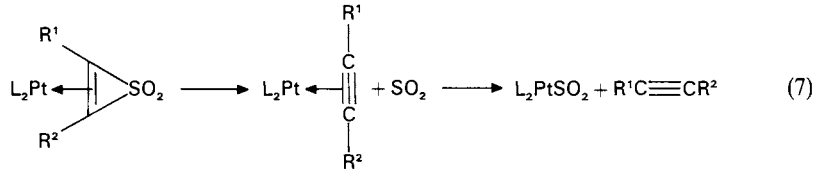
Thermal decomposition of thiirene dioxides results in the extrusion of sulfur dioxide and the formation of the corresponding acetylenes in high yields[6,21,100,101] (equation 6). Kinetic studies[100,101] of this thermally-induced extrusion showed it to be facilitated by electron-donating substituents (e.g. alkyl groups). In addition, the data which correlate best with the sum of σ_p^+ substituent constants suggest that a free radical, stepwise, rather than a nonlinear, symmetry-allowed, concerted extrusion mechanism[96] is operable. Interestingly, the thermal elimination of SO_2 from the thiirene oxide **19b** to give diphenylacetylene was found to be 10^4 slower than the elimination of SO_2 from the thiirane dioxide analogue **17** to give *trans*-stilbene[102].



(6)

(19) (34)

The transition-metal catalyzed decomposition of thiirene dioxides has been also investigated primarily via kinetic studies[103]. Zerovalent platinum and palladium complexes and monovalent iridium and rhodium complexes were found to affect this process, whereas divalent platinum and palladium had no effect. The kinetic data suggested the mechanism in equation 7.



(7)

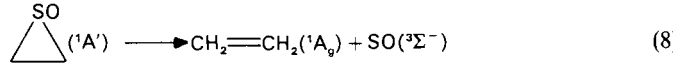
(35) (36) (34)

Since a similarity between the rates of decomposition of thiirene dioxide complexes and those of thiirane dioxides was found, it was suggested[103] that upon coordination the carbon–carbon bond order of thiirene dioxides decreases and the ligand becomes thiirane dioxide-like. The role of the metal is thus to 'saturate' the carbon–carbon double bond so that the reactivity of the coordinated thiirene dioxide approaches that of the thermally less stable thiirane dioxide.

The higher strain energy in thiirene dioxides (**19**) compared to thiirane dioxides (**17**) is obvious. Yet, the elimination of sulfur dioxide from the latter is significantly faster than one would expect for a thermally allowed concerted process. Consequently, either aromatic-type conjugative stabilization effects are operative in thiirene dioxides[2,112] or the relative ease of SO_2 elimination reflects the relative thermodynamic stability of the (diradical?)[99] intermediates involved in the nonconcerted stepwise elimination process.

It has been generally assumed that thermal decomposition of thiirane oxides proceeds stereospecifically to the corresponding olefins by elimination of sulfur monoxide, possibly through a concerted nonlinear chelatropic reaction[96] with retention of configuration of the liberated olefin.

Pyrolysis of the parent thiirane oxide **16a** monitored by microwave spectroscopy led to the conclusion that the sulfur monoxide is generated in its triplet ground state, although the singlet state ($^1\Delta$) cannot be excluded completely[38] (equation 8). A later study presented evidence, based on the stereoselective addition to dienes of sulfur monoxide generated from thiirane oxide as well as thermochemical data, that the ground state $^3\Sigma^-$ is formed exclusively[104].

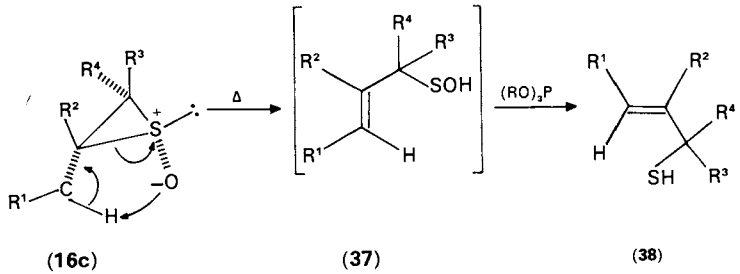


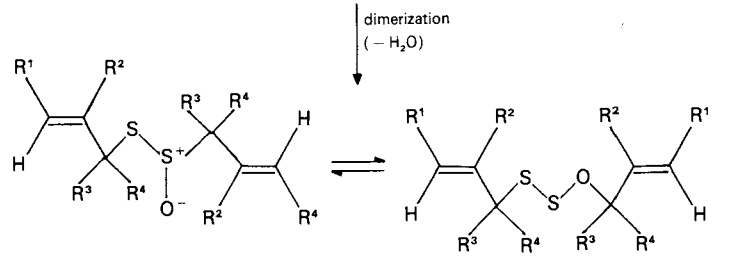
(8)

(**16a**)

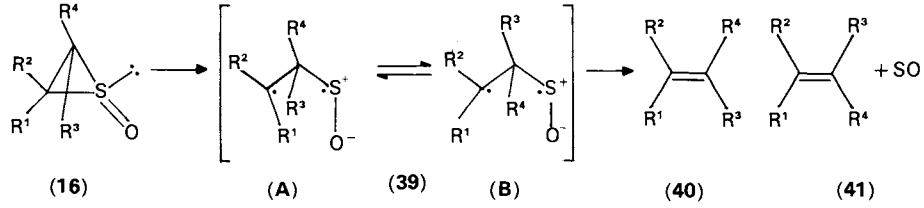
In the presence of a suitably disposed β-hydrogen—as in alkyl-substituted thiirane oxides such as **16c**—an alternative, more facile pathway for thermal fragmentation is available[63a,105]. In such cases the thiirene oxides are thermally rearranged to the allylic sulfenic acid, **37**, similarly to the thermolysis of larger cyclic[106] and acyclic[97] sulfoxides (see equation 9). In sharp contrast to this type of thiirane oxide, *mono*- and *cis*-disubstituted ones have no available hydrogen for abstraction and afford on thermolysis only olefins and sulfur monoxide[63a]. However, rapid thermolysis of thiirane oxides of type **16c** at high temperatures (200–340 °C), rather than at room temperature or lower, afforded mixtures of *cis*- and *trans*-olefins with the concomitant extrusion of sulfur monoxide[105]. The rationale proposed for all these observations is that thiirane oxides may thermally

decompose by two routes: the first is a facile rearrangement to a sulfenic acid when the stereochemistry is favorable (as shown in equation 9), and the second is a pathway of higher activation energy which leads through a partially stereospecific route to the olefins and sulfur monoxide[105] (equation 10).





(9)



(**d**) $R^1 = R^4 = CH_3$, $R^2 = R^3 = H$ (**g**) $R^1 = R^4 = H$, $R^2 = R^3 = C_6H_5$

(**e**) $R^1 = R^3 = H$, $R^2 = R^4 = D$ (**h**) $R^1 = R^3 = H$, $R^2 = R^4 = C_6H_5$

(**f**) $R^1 = R^4 = H$, $R^2 = R^3 = D$ (10)

Thermolysis of **16e,f** in either solution or gas phase (150–350 °C) gave deuteriated ethylenes (i.e. **40e** from **16e** and **41f** from **16f**) with about 95% retention of stereochemistry[107]. Similarly, pyrolysis of the stereoisomeric 2,3-diphenylthiirane oxides **16g,h** proceeded smoothly to yield stilbenes and sulfur monoxide in more than 70% yield[108]. The extrusion of SO from the *trans*-isomer proceeds almost stereospecifically, while that from the *cis*-isomer occurs with complete loss of stereochemistry. This indicates the intervention of a stepwise mechanism, and not a symmetry-allowed nonlinear chelatropic reaction[96]. Based on the fact that all attempts to trap the intermediate with 1,3-dipolarophiles were in vain, whereas a 1:1 adduct was obtained in good yield (about 60%) with the carbon radical scavenger di-*p*-anisyl thioketone, a mechanistic scheme as depicted in equation 10 has been proposed[108]. Although the radical intermediates are capable of internal rotation about the carbon–carbon bond, for the 2,3-diphenyl case (i.e. **16g,h**), the rotation would be

restricted owing to the steric repulsion of the two phenyl groups, with the *trans*-conformer of **39** being thermally favored.

All the above indicates that thiirane oxides are not unusual in their thermal behavior when compared with their higher or lower oxidized analogues, and suggests analogous modes of extrusion of S, SO and SO_2 from the sulfur-containing three-membered rings. Although a stereochemically rather rigid 'biradical' **39** of the type proposed in the thermolysis of thiiranes[109] and thiirane dioxides[99] may account mechanistically for the results, a significant contribution of a concerted process cannot be ruled out.

The symmetric diarylthiirene oxides (**18**) are much more thermally stable than the corresponding saturated thiiranes and unsaturated thiirene dioxides. Thus, the thiirene oxide **18a** shows only slight decomposition after 24 hours of reflux in benzene, whereas the analogous sulfone **19b** fragments completely to SO_2 and diphenylacetylene after less than six hours under the same conditions[110]. Irradiation of the oxide **18a**, however, does result in the elimination of sulfur monoxide and formation of diphenylacetylene. Its thermolysis at 130 °C afforded benzil as the only isolable product[22], implying that SO is not being eliminated in this thermolytic process.

It is highly probable that the lesser stability of thiirene dioxides compared with that of the thiirene oxides simply reflects the more facile extrusion of sulfur dioxide relative to that of sulfur monoxide. In fact, the same effect is probably operative in the case of the *cis*- and *trans*-diphenylthiirane oxides (**16g,h**)[110] compared with *cis*- and *trans*-diphenylthiirane dioxides (**17d,e**)[99]: the former were found to be more stable toward thermal decomposition than the latter.

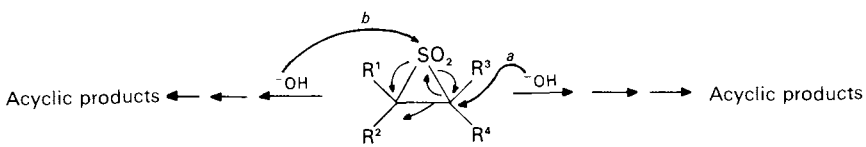
2. *Acidity of (sulfonyl and sulfoxy) α-hydrogens*

Two major factors are responsible for the acidity of the hydrogens attached to carbon atoms alpha to sulfonyl and sulfoxy groups. The first is the strong inductive effect of these highly electronegative functional groups (the effect of the sulfone being greater than that of the sulfoxide), and the second is the capacity of the adjacent partially positively charged sulfur atom to stabilize the developing α-carbanion via the expansion of its valence shell involving p–d orbital interaction.

The question arises whether there are any unique characteristics associated with the acidity of α-hydrogens when the sulfone or the sulfoxide group is incorporated within a three-membered ring system.

Based on extensive studies associated with the Ramberg–Bäcklund rearrangement[15] and its mechanism[2,16–19,111,112], including the treatment of thiirane oxides with bases, the following conclusions emerge:

The nucleophilic attack of strong bases (e.g. hydroxide ion, alkoxide ions and carbanions) on either the α-carbon[111] or the sulfur atom of the sulfone group[99,113] of the thiirane dioxides is the initial key step that is responsible for the subsequent ring opening and further reaction. The formation of a three-membered α-sulfonyl carbanion is not observed in these cases (equation 11).

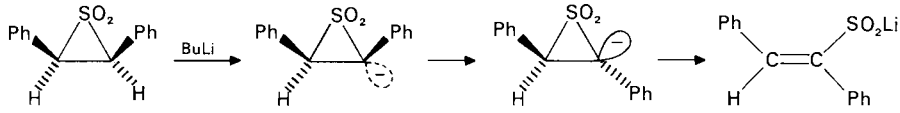


(**17**)

R^1 or R^2 or R^3 or R^4 = H (11)

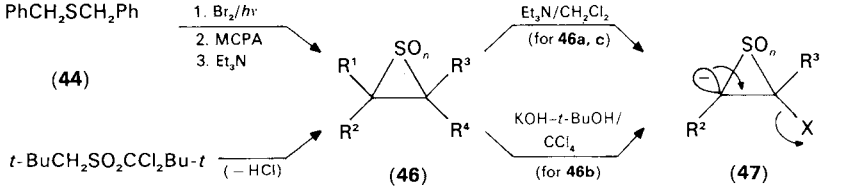
The reaction of thiirane dioxides with reagents that are weak nucleophiles but strong

bases, however, does lead to the formation of α-carbanions. Thus, for example, the formation of the sulfinate **43** was interpreted[99,111] in terms of a carbanion intermediate (**42**) which rearranges with inversion of configuration as illustrated in equation 12.



(**16c**) (**a**) (**42**) (**b**) (**43**) (12)

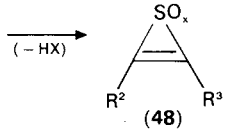
Clearly, strain energy, the unique sp^3 hybridization of both carbons and sulfur in the three-membered ring thiiranes, the relative stability of α-carbanions, and the substitution pattern on the one hand, and both the nucleophilicity/basicity ratio and steric hindrance of the attacking base on the other, play significant roles in determining the course of reaction between three-membered sulfones containing α-hydrogens and bases[2]. With weakly nucleophilic bases and thiirane dioxides whose substituents either stabilize an adjacent carbanion (e.g. aryl groups), or sterically hinder nucleophilic attack on the substituted carbon (e.g. *t*-butyl groups), the α-sulfonyl carbanion forms, leading to a product in which the three-membered ring skeleton is preserved intact. The above explains the accessibility of the thiirene dioxide[6] and thiirene oxide[22] systems when a modified Ramberg–Bäcklund procedure is used under mild conditions. This leads to several unique compounds otherwise difficult to obtain[112] as illustrated in equation 13. In all of these cases, the formation of α-sulfonyl or α-sulfoxy carbanions (**47**) is the key step.



$R^4 = H$, $R^4 = Br$ or Cl
(**a**) $n = 2$; $R^2 = R^3 = Ph$
(**b**) $n = 2$; $R^2 = R^3 = t$-Bu
(**c**) $n = 1$; $R^2 = R^3 = Ph$

X = Br or Cl
$n = 1$ or 2

(13)



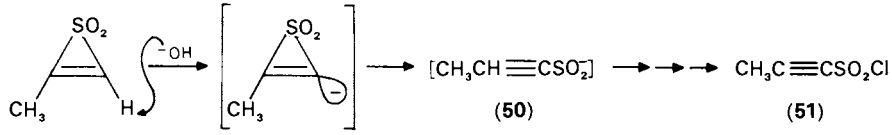
(**48**)

(**a**) $n = 2$; $R^2 = R^3 = Ph$
(**b**) $n = 2$; $R^2 = R^3 = t$-Bu
(**c**) $n = 1$; $R^2 = R^3 = Ph$

Significantly, (a) α-sulfonyl carbanions of thiirane dioxides, generated from the latter in the presence of strong bases such as potassium *t*-butoxide[19] and alkoxide ions[99], do epimerize to relieve steric repulsion between substituents as in **42** above; and (b) the α-hydrogen in aryl-substituted three-membered sulfoxides (e.g. **46c**) are sufficiently acidic to

form carbanions, in spite of the decreased capacity of the sulfoxide group to stabilize an adjacent carbanion compared to sulfones[2].

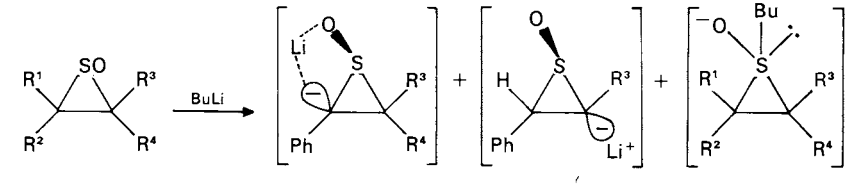
The issue of the acidity of α-hydrogens in thiirene oxides and dioxides is dealt with only in the dioxide series, since neither the parent, nor any mono-substituted thiirene oxide, is known to date. Thus the study of the reaction of 2-methylthiirene dioxide (**19c**) with aqueous sodium hydroxide revealed that the hydroxide ion is presumably diverted from attack at the sulfonyl group (which is the usual pattern for hydroxide ion attack on thiirene dioxides) by the pronounced acidity of the vinyl proton of this compound[113] (see equation 14).



(**19c**) (**49**) (**50**) (**51**) (14)

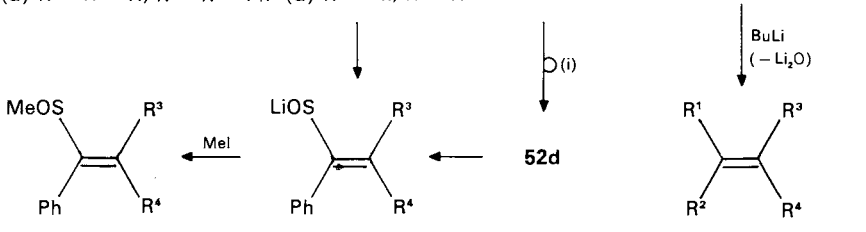
Although sulfinate (**50**) was not actually isolated, its intermediacy was established by trapping as the isolable sulfonyl chloride **51**, which suggests the formation of the α-sulfonyl vinyl carbanion **49** as the first species along the reaction route.

The formation of α-sulfoxy carbanions in thiirane oxides is possibly analogous to the formation of α-sulfonyl carbanions in the thiirane dioxide series. The reaction of the three-membered ring oxide (e.g. **16**) with a weakly nucleophilic strong base such as BuLi will provide the sulfoxy carbanion (i.e. **52** and **53**) competitively only in the presence of carbanion stabilizing substituents (e.g. aryl groups) since: (a) the capacity of the sulfoxide group to stabilize an α-carbanion is less than that of the sulfone; and (b) the competing route, in which the sulfur is being attacked nucleophilically by the base, is evidently more favorable in sulfoxides than in sulfones. On the other hand, the chelation of the Li^+ to the sulfoxide oxygen would give preference to the formation of *syn* carbanion and to epimerization (inversion) of the sterically unfavorable carbanion. An illustrative example for all the above is given in equation 15[114].



(**16**) (**52**) (**53d**) (**54c, d**)

(**c**) $R^1 = R^3 = H$, $R^2 = R^4 = Ph$ (**c**) $R^3 = H$, $R^4 = Ph$
(**d**) $R^1 = R^4 = H$, $R^2 = R^3 = Ph$ (**d**) $R^3 = Ph$, $R^4 = H$ (15)



(**56c, d**) (**55c, d**) (**57c, d**)

To summarize: under favorable conditions the acidity of α-hydrogens facilitates the generation of α-sulfoxy and α-sulfonyl carbanions in thiirane and thiirene oxides and dioxides as in acyclic sulfoxides and sulfones. However, the particular structural constraints of three-membered ring systems may lead not only to different chemical consequences following the formation of the carbanions, but may also provide alternative pathways not available in the case of the acyclic counterparts for hydrogen abstraction in the reaction of bases.

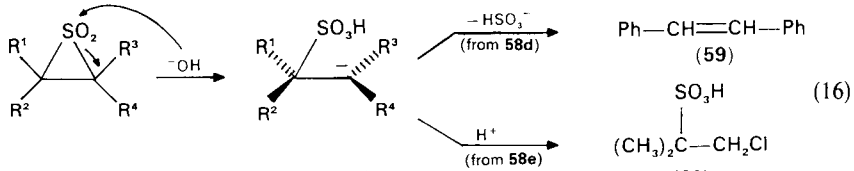
3. *Electrophilicity of the SO_2 and SO group (reaction with bases/nucleophiles)*

A direct attack of nucleophiles on the sulfur atom of the sulfone or sulfoxide group in acyclic or large-ring sulfones and sulfoxides is rather rare, or unknown, excluding metal hydride reductions and/or reductive deoxygenations. The situation is completely different in the three-membered ring systems.

The elimination of sulfur dioxide from thiirane dioxides leading to the corresponding alkenes is not the only result of base-induced reactions; other products are also formed. This fact raises the question of the mechanistic pathway of this reaction. In general, the thiirane dioxide is treated with a large excess of the base in an appropriate solvent for several hours at room temperature or below. Bases commonly used are 2N NaOH (in water), $NaOCH_3$ (in methanol), t-BuO^-K^+ (in t-BuOH) and BuLi (in tetrahydrofuran) or KOH–CCl_4 (in t-BuOH)[16–19,99,112,113].

A nucleophilic attack of the hydroxide (or the alkoxide) ions on the *sulfur* atom of the thiirane dioxide ring to give sulfonic acids or similar intermediates, which then decompose to alkenes and bisulfite ion, has been suggested for these reactions[16–17,99].

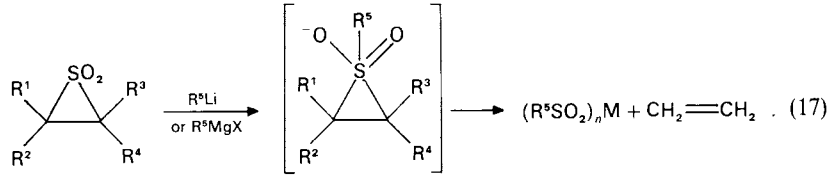
Sulfonic acids (e.g. **58**) should be sufficiently stable to be isolated and identified, as proved to be the case in the Ramberg–Bäcklund rearrangement of 2-halothiirane dioxide[115] (equation 16).



(16)

(**d**) $R^1 = R^3 = H$; $R^2 = R^4 = Ph$
(**e**) $R^1 = R^2 = CH_3$; $R^3 = H$; $R^4 = Cl$

Similarly, the reaction of the parent thiirane dioxide, the 2-chloro- and 2,3-*cis*-dimethylthiirane dioxides with either Grignard or alkyl lithium reagents, has been studied extensively. The fair-to-good yields of the sulfinates (**62**) obtained (48–82%), accompanied by ethylene (or the corresponding alkenes for substituted thiirane dioxide), have been interpreted in terms of initial nucleophilic attack of the base on the sulfur atom as depicted in equation 17[116].



(17)

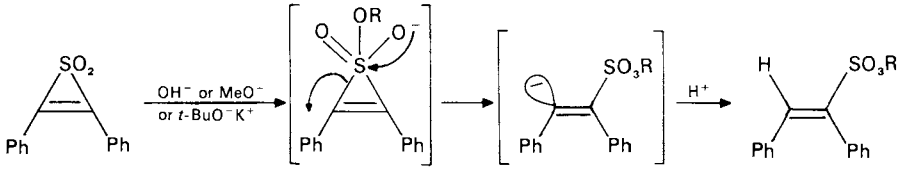
(**17a**) $R^1 = R^2 = R^3 = R^4 = H$

(**61**) $R^5 = CH_3$ or n-C_4H_9

(**62**) M = Li or Mg

An initial attack of a lithium reagent on the sulfur atom of **16**, leading to alkenes, has been discussed in the previous section. The similarity in the chemical consequences of the electrophilicity of both the sulfone and sulfoxide functional groups in strained three-membered ring systems is thus established.

As expected, the treatment of thiirane dioxides with strong bases resulted in ring opening to give the corresponding alkenesulfonic acids (or sulfonates) with retention of the original stereochemistry. These results are best accounted for in terms of initial attack of the nucleophilic base on the electrophilic sulfur with concomitant ring opening as shown in equation 18[99,102].



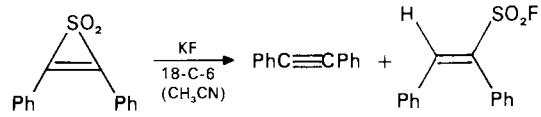
(19b) **(63)** **(64a–c)** **(65a,b)**

(a) R = H
(b) R = CH_3
(c) R = *t*-Bu (18)

Although a radical mode of ring opening cannot be excluded[102], the initial formation of the common sulfurane intermediate **63** does take account of both products obtained, the sulfonic acids/sulfonates **65** and the diphenylacetylene (**66**), and the expected temperature dependence of the ratio **65/66**. Also, the formation of the sulfurane (**63**) explains the similar results obtained in applying the KOH–CCl_4 system to the *in situ*-generated *n*-butyl- and *t*-butyl-substituted thiirene dioxides[117].

Treatment of **19b** with phenylmagnesium bromide gives diphenylacetylene (**66**) and the salt of benzenesulfinic acid[6,21]. Lithium aluminium hydride reacts with **19b** similarly. These ring-opening reactions are similar to the reactions of organometallic reagents with the analogous thiirane dioxides (equation 17 above).

Finally, the reaction of **19b** with potassium fluoride in the presence of a crown-ether phase-transfer agent[118] to yield the sulfonyl fluoride **67** and diphenylacetylene[119] belongs to the same category in which a nucleophile (F^- in this case) attacks the electrophilic sulfur of the sulfone group (equation 19).



(19b) **(66)** **(67)** (19)

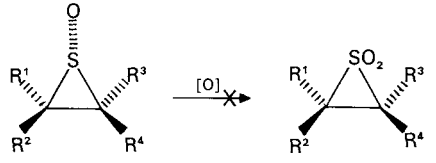
To summarize: in contrast to the observed nucleophilic attack of strongly basic nucleophiles on the sulfonyl and sulfoxy sulfur of the three-membered ring sulfones and sulfoxides, the acyclic sulfone and sulfoxide groups are attacked by nucleophiles only with difficulty[120]. Although the precise reason for this difference is as yet not clear, it is most probably associated with the geometry, electronic structure, bonding and strain energy of the cyclic compounds.

4. Nucleophilicity of the SO_2 and SO groups

Both the sulfone and the sulfoxide groups are characteristically electrophilic based on the increasing electropositivity of the sulfur atom in proportion to its oxidation state. Therefore, the nucleophilicity of these groups can be discussed only in terms of the nucleophilicity of either the trivalent sulfur atom, still having a pair of nonbonding electrons, or the oxygen atom in the sulfoxides.

Oxidation of thiirane and thiirene oxides to the dioxides is the best method to obtain the sulfones. Indeed, in the acyclic, or large-ring systems, the sequence sulfide → sulfoxide → sulfone is by far the easiest method to prepare sulfoxides and sulfones. The situation is different in the three-membered ring series: Thus, oxidation of thiiranes to the oxides by either perbenzoic acid or *m*-chloroperbenzoic acid under mild conditions affords the corresponding thiirane sulfoxides in almost quantitative yield[2,63,75,121]. However, further oxidation to the sulfone is rather limited since the thermally and/or chemically sensitive sulfones cannot survive the reaction conditions employed. With more stable thiirane oxides having the *anti*-configuration of the substituent(s) and the sulfinyl oxygen, steric hindrance may prevent a smooth oxidation under mild conditions. The following constitutes an illustrative example.

All attempts to oxidize either *cis*- or *trans*-di-*t*-butylthiirane oxides failed[122] (see equation 20). Reagents investigated included *m*-chloroperbenzoic acid, sodium peroxide, hydrogen peroxide, ozone and aqueous potassium permanganate. The *cis* oxide was resistant to oxidation (apparently steric hindrance), and the *trans* isomer was consumed with excess oxidizing agent but no identifiable products could be isolated.



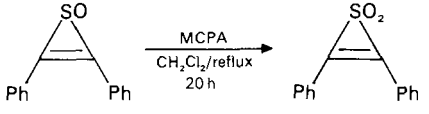
(20)

(**16i,j**) (**17i,j**)

(i) $R^1 = R^3 = H$, $R^2 = R^4 = t$-Bu

(j) $R^1 = R^4 = H$, $R^2 = R^3 = t$-Bu

In contrast to thiirane oxides, the electrophilic oxidation of thiirene oxides to thiirene dioxides is feasible, probably because both the starting material and the end product can survive the reaction conditions (equation 21).



(20–30% yield) (21)

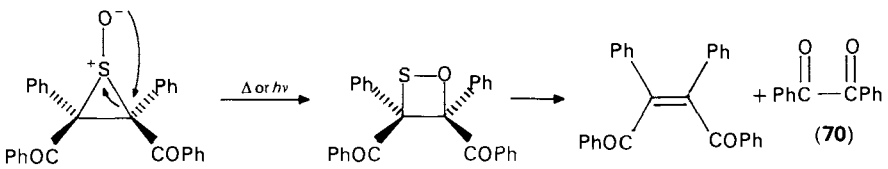
(**18a**) (**19b**)

To what extent the above suggests that the sulfoxide sulfur of thiirene oxides is more nucleophilic than that of thiirane oxides remains an open question.

There are several reactions in which the sulfoxy *oxygen* exhibits its nucleophilicity, the most noticeable being the thermal rearrangement of thiirane oxides (in the presence of a suitable disposed β-hydrogen) to allylic sulfenic acids[2,63,105] (see equation 9 in Section III.C.1).

In the following transformations, the nucleophilic oxygen of the sulfoxide group plays a

key role. Thus, a mechanism which involves ring expansion of the sulfoxide was suggested[123] to account for the formation of the products in the thermolysis and photolysis of the thiirane oxide **16k**. The stereochemistry around the sulfur atom has no effect on the ultimate results (see equation 22).

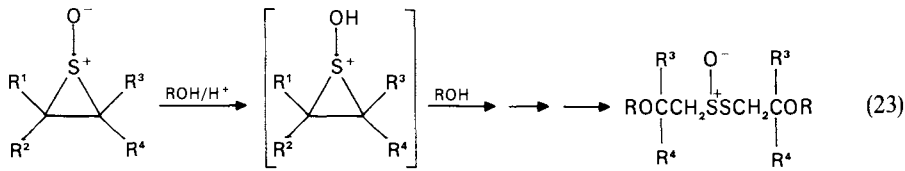


(16k) (68) (69)

(22)

Expansions of cyclic sulfones to cyclic sulfinates are known[124], and a similar mechanistic pathway of the expansion of the three-membered ring to a four-membered ring has been suggested for the photolytic fragmentation of the 2, 3-diphenylthiirene oxide **18a**[22].

The first step in the acid-catalyzed ring opening of thiirane oxides[125,126] is the proton attachment to the oxygen as illustrated in equation 23. The ring opening is generally stereospecific, with inversion occurring at the ring-substituted carbon attacked by the nucleophile[126]. A preferential attack on the unsubstituted carbon was observed with thiols as nucleophiles.

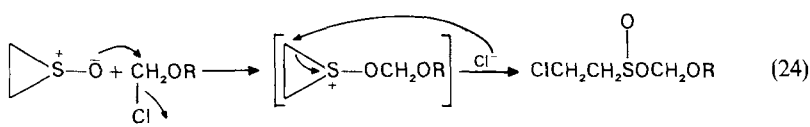


(16m,n) (71) (72) (23)

(m) $R^1 = R^2 = H$, $R^3 = R^4 = Me$ R = Me, Et, *i*-Pr, etc.

(n) $R^1 = R^2 = R^3 = H$, $R^4 = Ph$

A mechanism analogous in many ways to that of the acid-catalyzed ring opening reaction was advanced for the reaction of the thiirane oxide with alkyl chloromethyl ethers[127]. The first step is the displacement of the chloride by the sulfoxy oxygen (equation 24). In view of the above mechanistic interpretation, it is quite surprising that the parent thiirane oxide (**16a**) was found to be protonated on sulfur and *not* at oxygen in FSO_3H–SbF_6 at −78 °C, according to NMR studies[128].

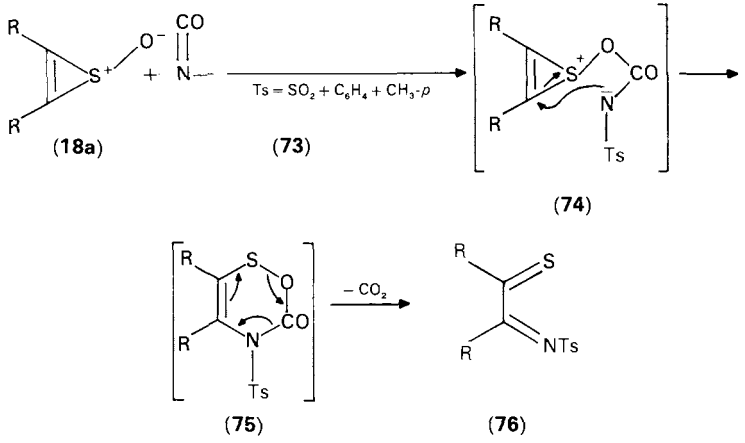


(16a) (24)

Theoretical considerations (previously discussed in Section III.B.3) predict the oxygen moiety in the sulfoxide function of thiirene oxides to be relatively nonreactive[12], that is, less nucleophilic than the sulfoxy oxygen of either thiirane oxides or ordinary acyclic sulfoxides.

The sulfoxide function in the diphenylthiirene oxide (**18a**) did react with the particularly

electrophilic[129] *p*-toluenesulfonyl and chlorosulfonyl isocyanates[12]. Hence, refluxing **18a** with isocyanate **73** in methylene chloride for 24 hours resulted in the isolation of imine **76** due, most probably, to the mechanistic sequence given in equation 25[12].



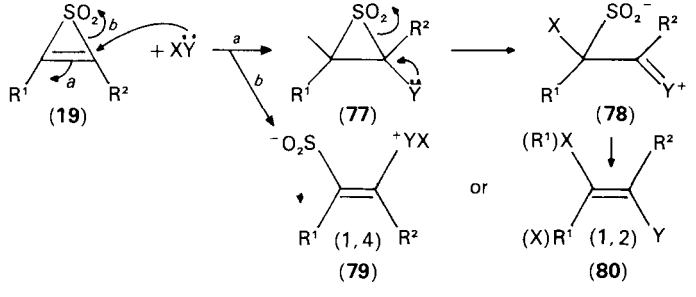
(25)

The successful deoxygenation of the sulfoxide **18a**[12] by either hexachlorodisilane as the reducing agent, or diiron nonacarbonyl according to the deoxygenation–complexation route[130], can also be rationalized in terms of electrophilic attack of the reagents used on the nucleophilic sulfoxy oxygen.

In conclusion, any electrophilic attack on the sulfoxide function in thiirene oxides must overcome a substantial energy barrier. Indeed, many oxidative reagents that proved to react smoothly with acyclic sulfoxides[131] left the thiirene oxides intact under comparable reaction conditions. Thus, there is a good correlation between theoretical predictions and experimental results in this case[2,12].

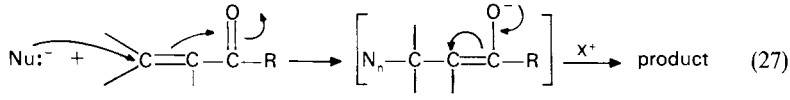
5. *The (formal) Michael addition of nucleophiles to thiirene oxides and dioxides*

α,β-Unsaturated sulfones[132], like other alkenes substituted with electron-withdrawing groups[133], are susceptible to nucleophilic additions across the carbon–carbon double bond. Thiirene dioxides are no exception and they do undergo the expected addition with soft nucleophiles. Formally, these may be categorized as Michael additions. However, these additions in the thiirene dioxide series are accompanied by ring cleavage (of one of the carbon–sulfur bonds) *sometimes* followed, as a consequence, by a loss of a sulfur dioxide unit, as shown in equation 26. The mechanistic patterns in the scheme, however, should not be considered as proven.



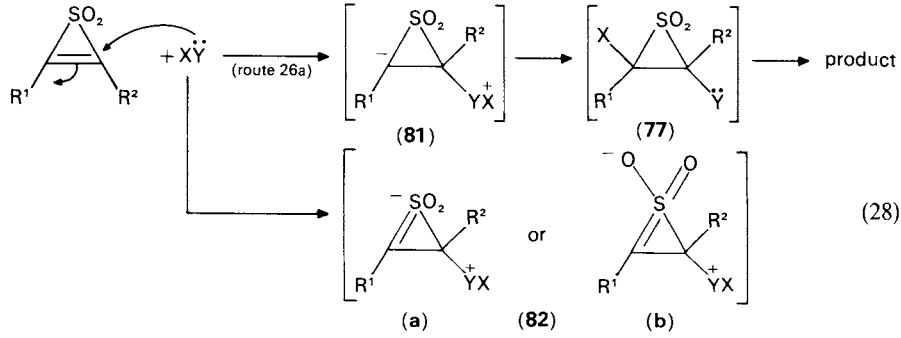
(26)

Michael addition is a 1,4-addition reaction of a nucleophile to an α,β-unsaturated system in which the double bond is conjugated with a carbonyl group, enabling the formation of the corresponding enolate as an intermediate (equation 27).



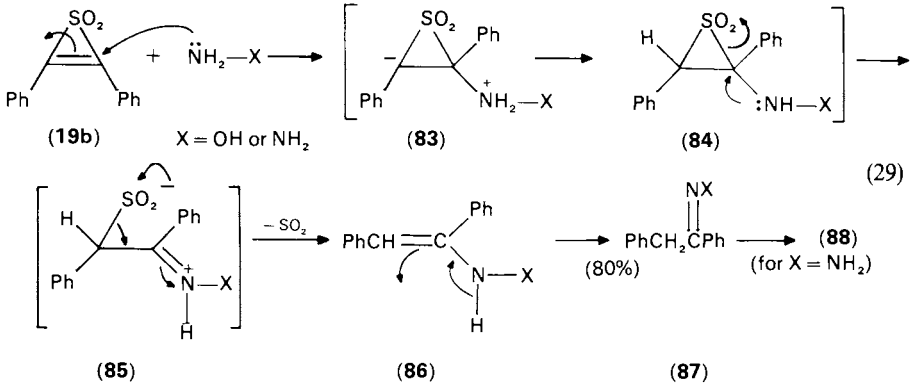
(27)

Clearly, an analogous 1,4-type conjugation cannot be operative in the three-membered ring thiirene dioxides for two major reasons: (a) there is an 'insulating effect' of the LUMO sulfur d-orbitals; that is, electronic interactions between the carbon framework and sulfur are not extended into the sulfur–oxygen interactions (see Sections III.B.2, 3); and (b) the intermediacy of a carbon–sulfur double bond (i.e. **82a**) within the three-membered ring framework is highly unlikely (equation 28). Consequently, the nucleophilic addition of XŸ proceeds either by route *a* or route *b* (equation 26) with the intermediacy of the stabilized α-sulfonyl carbanion **81** along route *a*. Therefore, only 1,2-additions to the double bond via route *a* (equation 26) may be categorized as 'Michael additions' and will be treated as such.



(28)

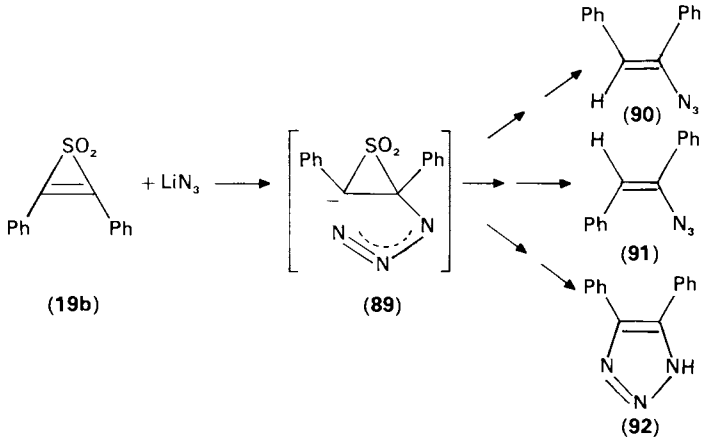
An illustrative example of the Michael reaction is that of the thiirene dioxide **19b** with either hydroxylamine or hydrazine to give desoxybenzoin oxime (**87**) and desoxybenzoin azine (**88**), respectively, in good yields[6] (see equation 29). The results were interpreted in terms of an initial nucleophilic addition to the α,β-unsaturated sulfone system, followed by loss of sulfur dioxide and tautomerization. Interestingly, the treatment of the corresponding thiirene oxide (**18a**) with hydroxylamine also afforded **86** (as well as the dioxime of benzoin), albeit in a lower yield, but apparently via the same mechanistic pathway[6].



(29)

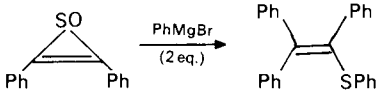
Although the nucleophilic addition of secondary amines to thiirene dioxides can be interpreted as following the same mechanistic pathway, the reaction was found to be second order in amine[119] (which is typical for the addition of amines to olefins in appropriate solvents[132,133]), and the addition is *syn*. As a result, mechanisms with a cyclic-concerted addition across the carbon–carbon bond, or a stepwise addition involving two molecules of amine per one molecule of thiirene dioxide, have been proposed.

In a similar manner, the reaction of **19b** with lithium azide[135] to give the *cis*- and *trans*-vinyl azides (i.e. **90**, **91**) and triazole **92** can be rationalized by assuming an initial stepwise 'Michael-type' nucleophilic addition of the azide ion to the carbon–carbon double bond, followed by protonation or rearrangement/transformations including inversion of the initially formed α-sulfonyl carbanion[134] (equation 30). The products obtained in the reaction of **19b** with equimolar acyl-substituted sulfonium ylids such as $(CH_3)_2\overset{+}{S}\overset{-}{C}HCOAr$[135] were also rationalized in terms of an initial attack of the ylid carbon on the vinylic carbon of the thiirene dioxide leading to an α-sulfonyl carbanion analogous to **89**, which through further transformations results in a novel ring enlargement of the original thiirene dioxide.



(30)

Finally, obtaining olefin **93** from the reaction of thiirene oxide **18a** with two equivalents of phenylmagnesium bromide may be a consequence of the initial nucleophilic 'Michael-type' addition of the latter across the carbon–carbon double bond of the cyclic sulfone[22] (see equation 31).



(31)

Thus, like α,β-unsaturated ketones and sulfones, both thiirene dioxides and thiirene oxides are preferentially attacked by the less basic nucleophiles on the vinylic carbon atom[2]. This would lead to formally 1,4 Michael-type adducts and/or other products resulting from further transformations following the initial formation of the α-sulfonyl and α-sulfoxy carbanions.

6. *Miscellaneous*

a. Complexation with transition metal complexes. Zerovalent platinum and palladium complexes of the thiirene dioxides can be easily prepared by ligand exchange with

platinum complexes of the type L_2PtX at ambient temperature[81] (see equation 32).

(32)

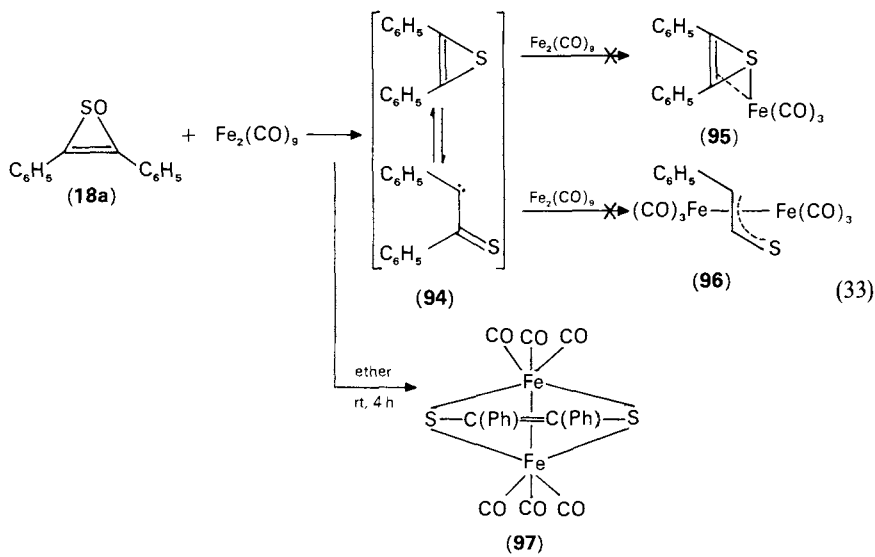
(19) (35)

(a) $R^1 = R^2 = CH_3$
(b) $R^1 = R^2 = Ph$
(c) $R^1 = H$, $R^2 = CH_3$
(d) $R^1 = CH_3$, $R^2 = Ph$

$L = Ph_3P$
$X = Ph_3P$, $CH_2{=}{=}CH_2$, CS_2

Of all attempted thiirene dioxides, only **19c** coordinated to Vaska's complex [*trans*-$IrL_2(CO)Cl$]. The structural assignments were based on both IR and NMR spectroscopy (i.e. coupling constants), according to which both the platinum and the palladium complexes of thiirene dioxides **19a,c** were isolated at temperatures below 0 °C. Attempts to isolate the complexes with **19b,d** failed, presumably due to the reduced availability of the π-electrons of the carbon–carbon double bond in these substituted thiirene oxides for interaction with the vacant LUMO of the metal, or their enhanced tendency to lose SO_2 thermally. Indeed, the zerovalent palladium and platinum complexes as well as monovalent rhodium and iridium complexes were found[81] to catalyze the decomposition of thiirene dioxide, whereas divalent platinum and palladium complexes had no effect. The capacity of SO_2 to serve as a ligand in metal complexes is well known, and obtaining the stable complex L_2PtSO_2 in the above-catalyzed SO_2 elimination from thiirene dioxides (see equation 7) is probably a major driving force for the reaction to occur. At any rate, the sulfone group appears to be only indirectly involved in the complexation of thiirene dioxides to transition metals.

Unexpectedly, neither direct complexation nor the deoxygenated complexes **95** or **96**[136,137] were observed in the reaction of diphenylthiirene oxide (**18a**) with iron nonacarbonyl. Instead, the red organosulfur–iron complex **97**[138] was isolated[12], which required the cleavage of three carbon–sulfur bonds in the thiirene oxide system (see equation 33). The mechanism of the formation of **97** from **18a** is as yet a matter of speculation.

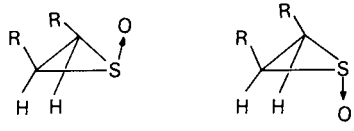


(33)

b. Configuration induced by the sulfoxide group. The asymmetry of the sulfoxide group gives rise to *syn–anti* configurations in cyclic substituted sulfoxides involving the sulfoxy oxygen and the substituents.

A systematic study[63a] in which substituted thiiranes were oxidized to the corresponding thiirane oxides determined the geometrical position of the oxygen atom by complete NMR and microwave analysis.

Mono- and *cis*-di-substituted thiirane oxides can theoretically exist in the *syn*- (*s*) and *anti*- (*a*) configurations shown below:

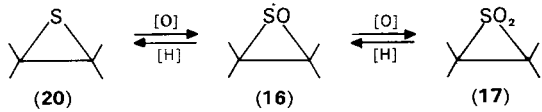


The oxidizing agent (organic peracid) usually attacks the sulfur from the less hindered side of the substrate to produce the less hindered oxidation product as a major isomer[139].

Thus, the observed stereoselectivity means the exclusive formation of the *anti*-isomer (*a*). This conclusion was confirmed by NMR analysis[63] (see Section III.B.4.b) and, clearly, can be extended and generalized with respect to larger cyclic sulfoxide systems.

D. The Synthesis of Three-Membered Ring Sulfones and Sulfoxides

Oxidation of the sulfur in thiiranes (**20**) to the corresponding sulfoxides (i.e. **16**) and further oxidation to the sulfones (**17**) is formally analogous to the sequence sulfides → sulfoxides → sulfones in the acyclic or large ring series (equation 34).

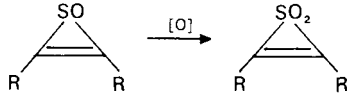


(34)

Also, the reduction of sulfones **17** to the sulfoxides **16** would seem to be the method of choice for the preparation of the latter, provided the former are readily available.

Unfortunately, although sulfoxides **16** are accessible via the oxidation of thiiranes **20** under controlled mild reaction conditions[2,63,121,122], their direct oxidation to the sulfones **17** is impractical, since the thermodynamically unstable sulfones would lose SO_2 under the reaction conditions. On the other hand, the treatment of the sensitive three-membered ring sulfones with either appropriate reducing agents (e.g. metal hydrides like $LiAlH_4$) or deoxygenation agents (e.g. $Cl_3SiSiCl_3$[140], $Et_3N{\cdot}SO_2$[141], $Fe(CO)_9$[12,130]) would result in reduction up to the sulfide state (i.e. **20**) followed, possibly, by the destruction of the three-membered ring system. In fact, there is no known method available for reducing the sulfones to sulfoxides even in the acyclic series, due to the very fast reduction of the sulfoxide to the sulfide.

The situation is even more problematic in the unsaturated series: the elusive thiirenes[2,142] cannot serve as starting materials for the synthesis of thiirene oxides **18** via direct oxidation, and the laborious synthetic method used to prepare the most commonly known and studied aryl-substituted thiirene oxides[2,22] **18** does not make the latter attractive as starting materials for preparing the corresponding thiirene dioxides[19]. Fortunately there are much better and versatile methods available[2] for the synthesis of the sulfones **19** (equation 35).

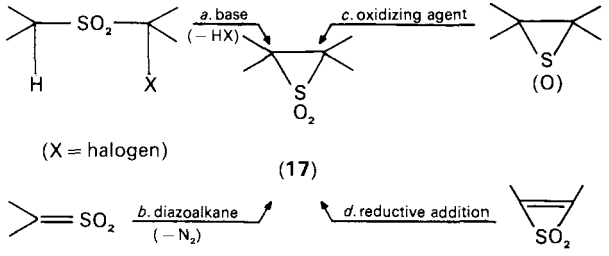


(18) (19) (35)

Similarly, also for the transformation **18** → **19**, different strategies have been developed, which will be presented and discussed below.

1. Thiirane dioxides

Due to the instability of thiirane dioxides, only a few methods are available for their practical preparation. Of the routes summarized in the scheme below[2] (equation 36), only *a* and *b* have practical value and generalizability. Route *b* appears to be the method of choice.



(36)

Route *a* represents the classic Ramberg–Bäcklund reaction, the most thoroughly studied of all the routes[2,15–19,99,117]. Under the basic reaction conditions employed, the *in situ* generated three-membered ring would undergo further transformations, mainly loss of SO_2. This route, however, turns out to be very productive in the preparation of aryl-substituted thiirene dioxides[6] and oxides[22] due to the relative thermal stability and survivability of the latter in the presence of weakly nucleophilic organic bases (see later).

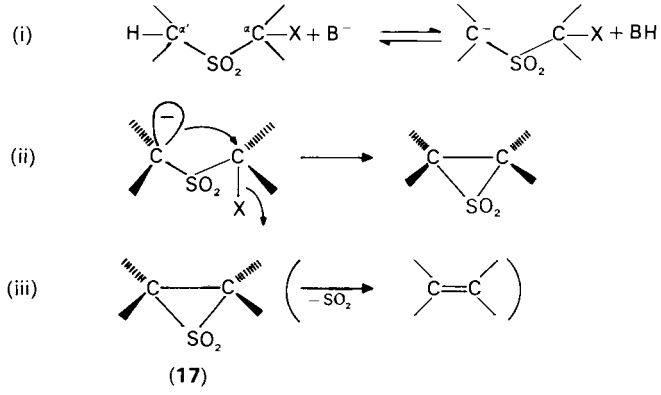
Route *b* involves the formation of one carbon–carbon bond and one carbon–sulfur bond. It belongs to the category of sulfene chemistry[143]. Sulfene intermediates react readily with diazoalkanes to produce, after the loss of nitrogen, thiirane dioxides. So far, this appears to be the method of choice for the preparation of thiirane dioxides of all types.

Route *c* involves the oxidation of thiiranes through the corresponding sulfoxides to the dioxide stage. The problems associated with this route have been discussed above, and its scope was shown to be rather limited.

Route *d* is a hydrogenation of thiirene dioxides. Since the preparation of thiirene dioxides is rather laborious, and many of them are prepared from the corresponding thiirane oxides[6], this method has practically no preparative value, and the only example reported is the reduction of **18a** to *cis*- **17d** in a very low yield (8%)[21].

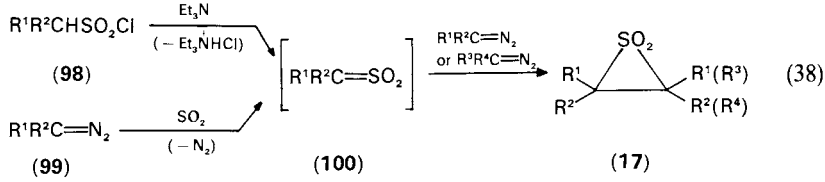
a. From α-halosulfones and strong bases. Typically, the bases applied are sodium hydroxide, sodium alkoxides and *t*-BuO^-K^+. The reaction is generally depicted as in Scheme 37[17b].

Actually, thiirane dioxides (**17**) have so far never been isolated in these reactions; *cis*- and *trans*-olefins were the main products, and all attempts to obtain the three-membered ring system and prevent the loss of SO_2 failed. Hence, the method can be used only for the *in situ* formation of intermediates.



(37)

b. Via sulfenes and diazoalkanes. The best method for the synthesis of thiirane dioxides is the interception with diazoalkanes of sulfenes generated *in situ* through dehydrohalogenation of sulfonyl chlorides containing α-hydrogens[143]. Alternatively, sulfenes can be generated by the reaction of diazoalkanes with sulfur dioxide[5], and with a second mole of a diazoalkane give thiirane dioxides (equation 38).



(38)

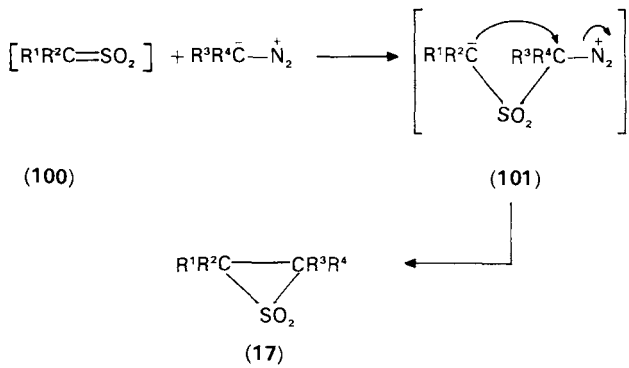
In a typical procedure[61,144] the sulfonyl chloride in ether is added to an etheral solution of the diazoalkane and triethylamine. Filtration and evaporation gives the relatively pure thiirane dioxide. Further purification can be easily achieved by recrystallizations preferentially *below* room temperature in order to avoid fragmentation of the product into sulfur dioxide and the olefin. In general, when the temperature of the above reaction is lowered, the yields are improved without a drastic decrease in reactivity[144]. Many thiirane dioxides have been successfully synthesized through this method and a detailed list of them can be found elsewhere[2].

The use of excess diazoalkane in its reaction with sulfur dioxide will necessarily lead to symmetrically substituted thiirane dioxides. When monoalkyl or monoaryl diazoalkanes are used, mixtures of *cis*- and *trans*-isomers are formed[18,19,99].

The *cis/trans* ratio of the products varies significantly with the polarity of the reaction medium: the higher the polarity of the solvent, the lower is the yield of the *cis*-product.

Another procedure[145] consists of bubbling of sulfur dioxide through a chilled solution of diazomethane in ether[146]. Evaporation of the solvent leaves the crude thiirane dioxide, which can be further purified by either distillation under reduced pressure or recrystallization. The formation of the thiirane dioxides is usually accompanied by formation of the corresponding olefins, along with small amount of ketazines.

The mechanism of this reaction is not known. However, some evidence[18,98,143] suggests the mechanism (equation 39) with the zwitterion **101** as a key intermediate. This is in accord with the known favored attack of nucleophiles at the sulfur atom of sulfenes[143].



(100) (101) (39)

(17)

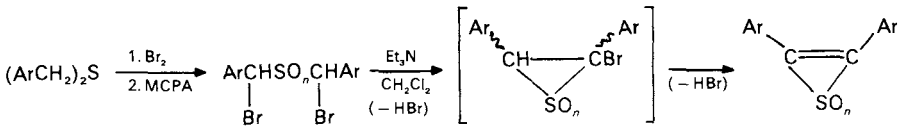
The stereochemistry of the ring product (**17**) was rationalized in terms of the attraction and repulsion between the involved substituents[98]. The accompanying olefins may be formed via carbene intermediates (arising from α-elimination of SO_2 from sulfene), and the intermediacy of thiadiazoline dioxide (from sulfene and diazoalkane) explains the formation of the ketazine side-products. Thiadiazoline, on its part, may be formed directly by the cyclization of zwitterion **101**.

As stated before, routes *c* and *d* (equation 36)[6,21] have very limited value.

2. *Thiirene dioxides*

a. Via modified Ramberg–Bäcklund reaction. The Ramberg–Bäcklund method is extremely useful for the preparation of thiirene dioxides[6,147] as well as of thiirene oxides[21] and other three-membered ring sulfone systems (e.g. thiadiaziridine dioxides)[100,101].

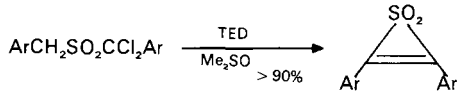
Most thiirene dioxides (and oxides) have been prepared through a modified Ramberg–Bäcklund reaction as the last crucial cyclization step, as illustrated in equation 40 for the benzylic series[6,22]. Synthesis of thiirene dioxides requires two major modifications of the originally employed reaction: first, the inorganic base has to be replaced by the less basic and less nucleophilic triethylamine[6,21]; and second, the aqueous media has to be substituted by an aprotic organic solvent (e.g. methylene chloride). Under these mild reaction conditions the isolation of aryl-substituted thiirene dioxides (and oxides) is feasible[6,22]. In fact, this is the most convenient way for the preparation of the aryl-disubstituted three-membered ring sulfones and sulfoxides[2].



(102) (103) (**18**) $n=1$ (**19**) $n=2$

(40)

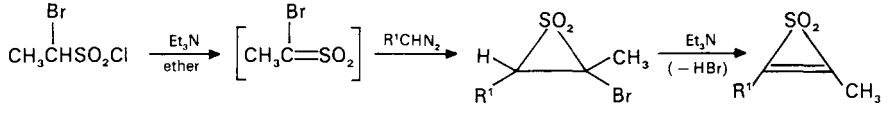
In a similar way, diarylthiirene dioxides can be prepared by the reaction of triethylenediamine (TED) or DABCO with α,α-dichlorobenzyl sulfones at ambient temperatures[100] (equation 41).



(104) (19) (41)

Ar = C_6H_5, *p*-ClC_6H_4, *p*-MeC_6H_4

b. Via sulfenes and diazoalkanes. This route for the preparation of alkyl-substituted thiirene dioxides is based on the interception of *in situ*-generated sulfenes with diazoalkanes[143,144]. The 2-halo-substituted thiirane dioxide ring thus formed is treated with a base to yield the required thiirene dioxide through dehydrohalogenation[6,113] (see equation 42).



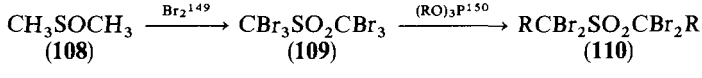
(105) (106) (107) (19)

(**a**) $R^1 = CH_3$
(**c**) $R^1 = H$
(**d**) $R^1 = C_6H_5$

(42)

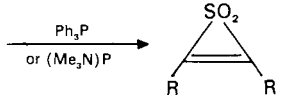
However, alcohol-free solutions of diazomethane[146] must be used to avoid destruction of the intermediate sulfene and a stronger base such as 1, 5-diazabicyclo [4.3.0] non-5-ene is required for the final dehydrohalogenation step to obtain sulfones **19a,d**.

c. By debromination of tetrabromosulfones. This route to dialkylthiirene dioxides from tetrabromosulfones (see equation 43) is of particular significance, since it can be used on a large scale, and makes dialkylthiirene dioxides as easily obtainable as the diaryl-analogues. Both dimethyl- and diethyl-thiirene dioxides have been thus prepared[148].



(108) (109) (110) (43)

(**a**) R = Me
(**e**) R = Et



(**19a,e**)

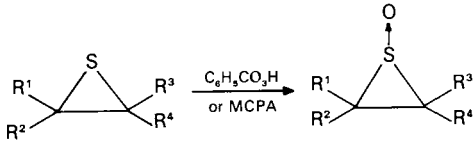
3. Thiirane oxides

To date, several well-established methods are available for the convenient preparation of thiirane oxides, the two main ones being the controlled oxidation of thiiranes[63a] and the reaction of sulfenes with diazoalkanes[63b].

a. By oxidation of thiiranes. The controlled oxidation of thiiranes to the corresponding thiirane oxides is a well-established process[63a,65].

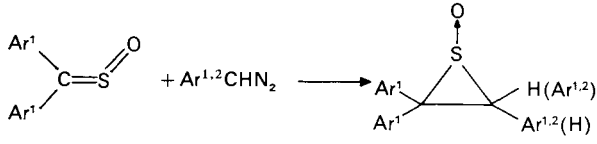
Following the isolation of the parent thiirane oxide **16a** by the oxidation of thiirane with either sodium metaperiodate[95] or with the *t*-BuOH–H_2O–V_2O_5 system[151], a systematic study was undertaken[63a,75] to establish a reliable and general method for the oxidation of thiiranes to thiirane oxides. Iodosobenzene, *t*-butyl hypochlorite, N_2O_4, H_2O_2 and organic peracids have been examined.

Either perbenzoic acid or *m*-chloroperbenzoic acid are the reagents of choice and methylene chloride is the preferred solvent for the oxidation under mild conditions[63a,75] (equation 44). Equimolar amounts of the reactants are used and the oxidation is completed within minutes. The reaction affords an essentially pure solution of the sulfoxide in almost quantitative yield[63a,75]. The thiirane oxides have the *anti*-configuration with respect to the substituent(s) and sulphinyl oxygen[63a,75]. Considering the steric hindrance of substituents in the peracid oxidation, the preferential formation of the *anti*-isomer is to be expected. However, there is no significant deuterium isotope effect on the regioselectivity of the sulfoxidation of *cis*-dideuteriothiirane; both stereoisomers of the corresponding thiirane oxide are formed in equal amounts[107].



(20) (16) (44)

b. Via sulfines and diazoalkanes. This is the most important nonoxidative method for the preparation of thiirane oxides, particularly aryl-substituted ones. Thus, diaryl sulphines dissolved in aprotic solvents such as pentane or ether give the thiirane oxides in good yields in a smooth reaction with aryldiazomethanes, as illustrated in equation 45[2,63b]. A mechanism analogous to that operative in the reaction of sulfenes with diazoalkanes to give thiirane dioxides (equation 39) is probable.



(111) (112) (16) (*syn* and *anti*) (45)

If reaction conditions are chosen in such a way that the products crystallize from the cooled reaction mixture, it is possible to obtain pure products even in the cases of sensitive three-membered ring sulfoxides.

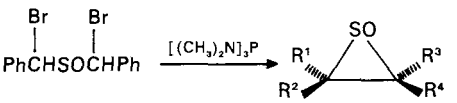
All the asymmetric thiirane oxides which have been obtained through this procedure are mixtures of the two possible *cis*- and *trans*- (*syn*- and *anti*-) configurations, but the *anti*-isomer predominates.

Any attempt to separate the two components by the usual chromatographic methods failed owing to the instability of the thiirane oxides, which easily lose sulfur monoxide to give the corresponding olefins[152].

c. By ring closure of α,α′-dibromobenzyl sulfoxides. A general, efficient nonoxidative route for the preparation of diaryl-substituted thiirane oxides involves the photolytic

bromination of dibenzyl sulfide followed by the oxidation of the isolable intermediate dibromosulfide (**113**) to the corresponding mixture of benzylic α,α'-dibromosulfoxides (**114**). 1,3-elimination of bromine from the dibromide by treatment with *tris*(dimethylamino)phosphine provides the three-membered ring sulfoxide stereospecifically[153] (equation 46).

$$PhCH_2SCH_2Ph \xrightarrow[h\nu]{Br_2} \underset{\textbf{(113)}}{PhCHBrSCHBrPh} \xrightarrow{MCPA}$$



(46)

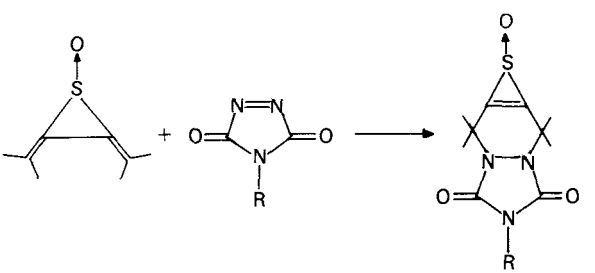
(**114**) (**16**)

(**a**) *meso*-dibromo (*anti*) (**c**) $R^1 = R^3 = Ph$ (from **114a**)
(**b**) (±)-α,α'-dibromo (*trans*) (**d**) $R^1 = R^4 = Ph$ (from **114b**)

4. Thiirene oxides

a. Aryl substituted. A general route for the preparation of thiirene oxides involves the reaction of benzylic α,α'-dibromosulfoxides with excess triethylamine in refluxing methylene chloride for 24–48 hours[22]. In fact, all known aryl-substituted thiirene oxides have been synthesized through this modified Ramberg–Bäcklund procedure (equation 40). This route, however, is laborious, lengthy, and the overall yield is rather low (16–20%)[2].

b. Alkyl substituted. The first (and so far the only known) synthesis of alkyl-substituted thiirene oxides[60] involves the [2 + 4] cycloaddition of equimolar amounts of thiiranoradialene sulfoxide **115**[154] and the superdienophile **116**, to yield the sulfoxide system **30**[60] (equation 47).



(47)

(**115**) (**116**) (**30a, b**)

(**a**) R = CH_3
(**b**) R = C_6H_5

All attempts to prepare other [2 + 4] cycloadducts of sulfoxides **115** with dienophiles such as maleic anhydride, ethyl azodicarboxylate, etc., have failed[60]. A method for preparing ordinary alkyl-substituted thiirene oxides (e.g. **18**; $R^1 = R^2 =$ alkyl) is still lacking.

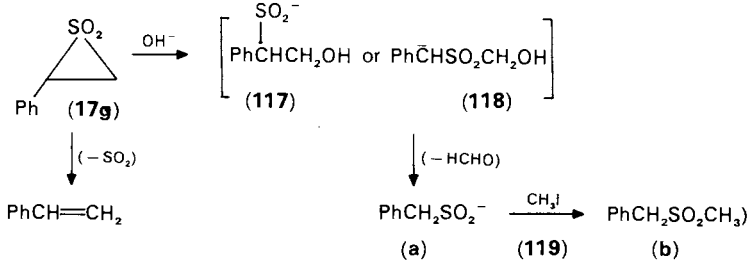
E. Selected Chemical Reactions and Transformations

Selected additional reactions, transformations, or rearrangements of three-membered ring sulfones and sulfoxides will follow. The criteria for selection is the direct or indirect involvement of the functional groups in the reaction.

1. Nucleophilic attack on carbon in thiirane and thiirene dioxides and oxides

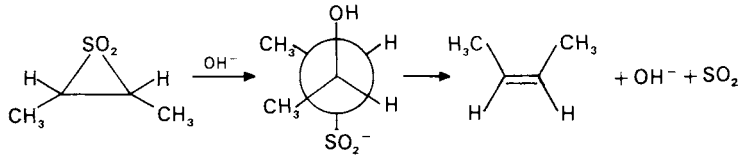
a. With strong bases. The rupture of thiirane and thiirene dioxides generated *in situ* under the Ramberg–Bäcklund rearrangement conditions has been extensively studied[15–19,99,112] and thoroughly discussed[2,154], alkenes and acetylenes, respectively, being the major products. The involvement of the sulfone group in these transformations is obvious either as the site of primary attack by the base, or as an 'electron sink' for the bonding carbon–sulfur bond electrons, following the nucleophilic attack of the base on the carbon or the initial formation of the corresponding α-sulfonyl carbanion. Of all the above, only the base-induced formation of α-sulfonyl carbanions is known in the acyclic systems.

In the presence of aqueous sodium hydroxide, 2-phenylthiirane dioxide gives styrene and the sulfinate **119**. These results have been interpreted[111] in terms of initial *nucleophilic* attack of hydroxide ion at the *carbon atom* in the 3-position of the three-membered ring in addition to sulfur dioxide elimination (see equation 48).



(48)

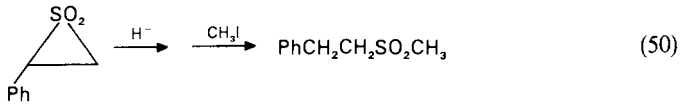
Similarly, the stereospecific formation of *cis*-2-butene from *cis*-2, 3-dimethylthiirane dioxide[19] may be rationalized in terms of a stereospecific ring opening to give the threo-sulfinate **120** which, in turn, decomposes stereospecifically to yield the *cis*-alkene, hydroxide ion and sulfur dioxide[73]. The parent thiirane dioxide fragments analogously to ethylene, hydroxide ion and sulfur dioxide (equation 49).



(49)

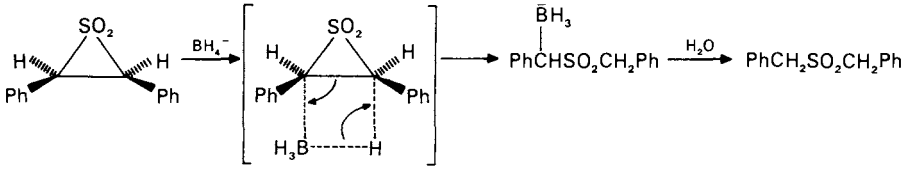
It was further confirmed that although the fragmentation pattern is dependent on the substitution pattern, most thiirane dioxides formed *in situ* decompose rapidly and stereospecifically under alkaline conditions to yield the corresponding alkenes with *retention* of configuration[156].

b. With metal hydrides. A closely related nucleophilic ring opening is the selective attack on the 2-carbon atom by the hydride ion ($LiAlH_4$ or $LiBH_4$)[115] as shown in equation 50.

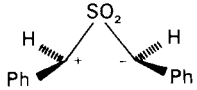


(17g) (122) (50)

In general, reductive cleavage of the carbon–carbon bond in thiirane dioxides can be accomplished[115] by the typical nucleophilic reducing agents, lithium and sodium borohydrides, and lithium aluminium hydride. Thus, 2,3-*cis*-diphenylthiirane afforded 45% yield of dibenzyl sulfone with either $LiBH_4$ or $NaBH_4$, but only between 0–10% with $LiAlH_4$. The reduction of 2,2,3,3-tetraphenylthiirane dioxide gave the corresponding open sulfone in 68% yield, whereas the reduction of 2-phenylthiirane dioxide with the same reagents (equation 50) gave no carbon–carbon cleavage product, but rather a carbon–sulfur fission product (a sulfinic acid salt). Based on these results and solvent effects, the mechanism shown in equation 51 has been proposed[155], although others involving either an activated zwitterion (**126**) or a simple S_N2 hydride attack on the phenyl-substituted carbon cannot be excluded.



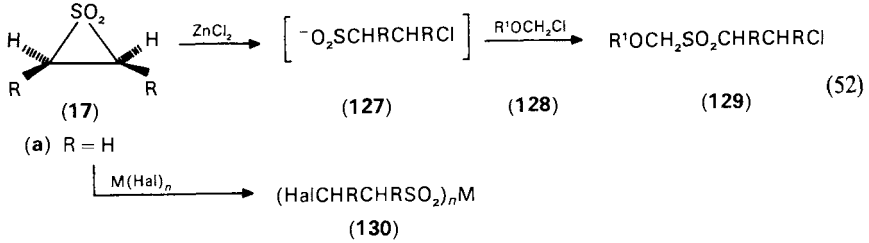
(17d) (123) (124) (125)



(126) (51)

There is no clear reason to prefer either of these mechanisms, since stereochemical and kinetic data are lacking. Solvent effects also give no suggestion about the problem. It is possible that the carbon–carbon bond is weakened by an increasing number of phenyl substituents, resulting in more carbon–carbon bond cleavage products, as is indeed found experimentally. All these reductive reactions of thiirane dioxides with metal hydrides are accompanied by the formation of the corresponding alkenes via the 'usual' elimination of sulfur dioxide.

c. With metal halides. Reaction of the parent thiirane dioxide with chloromethyl ethers in the presence of zinc chloride gave alkoxymethyl 2-chloroethyl sulfones (**129**), presumably through the intermediacy of the chlorosulfinate (**127**)[128] (equation 52).



(17) (127) (128) (129) (52)

(a) R = H

(130)

The zinc chloride is acting here as a Lewis acid. Similarly, thiirane dioxides react with metal halides such as lithium and magnesium chlorides, bromides and iodides in ether or THF to give the halo-metal sulfinates (**130**) in fair yields[157].

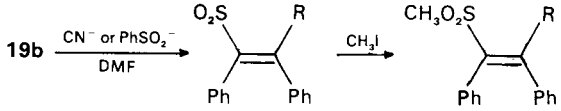
d. With soft nucleophiles. Phosphines react rapidly with thiirene dioxides to give the corresponding betaines (**132**) in essentially quantitative yield[119,158] (equation 53).

(53)

(**19b**) (**131**) (**132**)

(**a**) $R^1 = R^2 = R^3 = NMe_2$
(**b**) $R^1 = R^2 = R^3 = Bu$
(**c**) $R^1 = R^2 = Et$; $R^3 = Ph$
(**d**) $R^1 = R^2 = Ph$; $R^3 = CH_3$

Cyanide and benzenesulfinate ions react with thiirene dioxides in an analogous manner (equation 54).



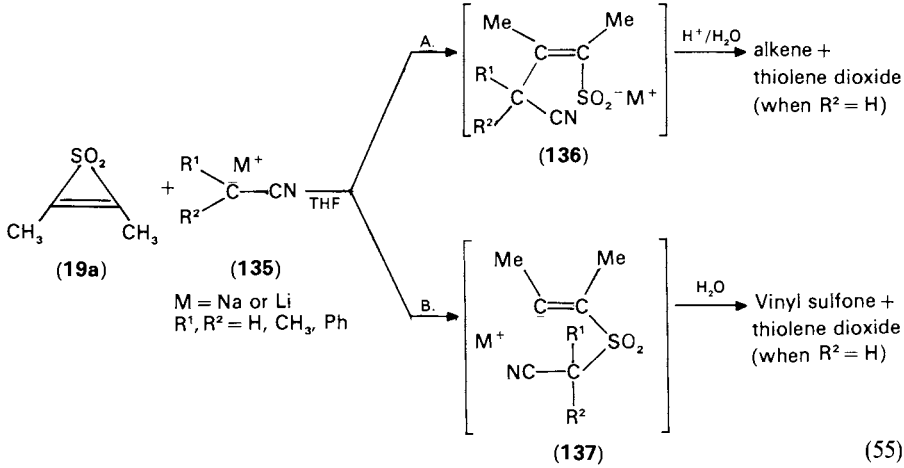
(54)

(**133**) (**134**)

(**a**) R = CN
(**b**) $R = PhSO_2$

The stereochemistry of the electrocyclic ring opening following the attack of the nucleophile on the vinylic carbon appears to be governed by the principle of least motion[159,60].

α-Metalated nitriles (**135**) attack thiirene dioxides nucleophilically; the latter act as ambident electrophiles. The two intermediates formed (**136** and **137**) yield both alkenes and sulfur-containing heterocycles, depending on whether or not the starting metalated nitriles contain an α-hydrogen atom[135] (equation 55).

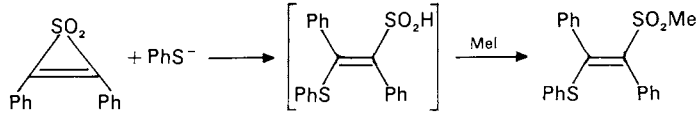


(55)

(**19a**) (**135**) (**136**) (**137**)

M = Na or Li
R^1, R^2 = H, CH_3, Ph

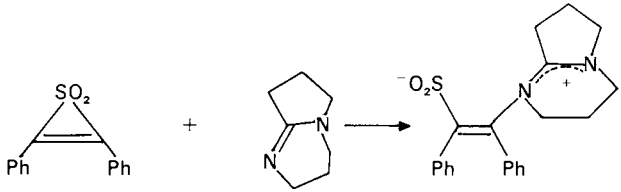
The softer, less basic potassium bromide and iodide did not react with the thiirene dioxide **19b**. The latter was also inert towards potassium thiocyanate, selenocyanate or nitrile. It did react, however, with potassium thiophenoxide in DMF at room temperature to yield, most probably, the vinyl sulfinate **138** isolated as the corresponding sulfone[39] (equation 56).



(19b) (138) (139) (56)

The isolation of the *E*-isomer **139** was in fact unexpected, since all tetrasubstituted olefins previously obtained from thiirene dioxide have been assigned the *cis*-configuration with respect to the two phenyl substituents based on the principle of least motion during the ring opening to olefins[159,160]. It might well be, therefore, that the *E*-isomer is obtained through the isomerization of the initially formed *Z*-isomer.

Although thiirene dioxides do not react with typical tertiary amines like triethylamine, they do react with the amidine 1,5-diazobicyclo-[4.3.0]-non-5-ene (DBN) to give a 1:1 adduct betaine[119,158] **141**, analogously to the reaction of thiirene dioxides with soft nucleophiles (equation 57).

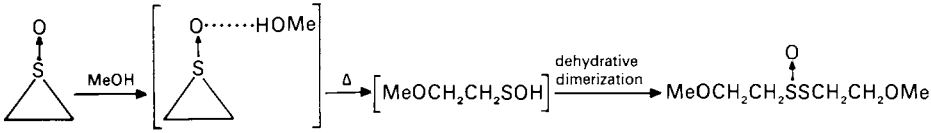


(19b) (140) (141) (57)

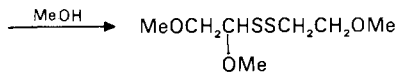
Interestingly, it appears that thiirene oxides also react with amidines (e.g. DBU) in a similar way[2].

2. Acid-catalyzed ring opening of thiirane oxides

The reaction of **16a** on heating with methanol to give the sulfenic acid intermediate **142** and the sulfinate **143** (which was further transformed into the disulfide **144**) was interpreted in terms of the mechanism shown in equation 58[161].



(16a) (142) (143) (58)



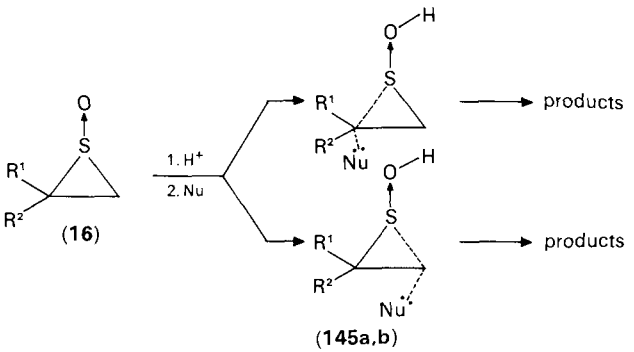
(144)

Presumably, the heterolytic scission of the carbon–sulfur bond in the oxide is assisted by the hydrogen bonding, in addition to the inherent strain of the three-membered ring.

Under the reaction conditions the initially formed thiosulfinate (**143**) is quantitatively transformed into the disulfide **144** by a Pummerer-type rearrangement[125].

The above reaction is a convincing example of an intermolecular hydrogen abstraction leading essentially to the same result as obtained in the pyrolysis of alkyl-substituted thiirane oxides through an intramolecular β-elimination of hydrogen.

The mechanistic interpretation of the acid-catalyzed ring opening reaction of thiirane oxides[125] is based on the push–pull mechanism[162] with a transition state in which the bonded hydrogen atom plays a major role (see equation 59).

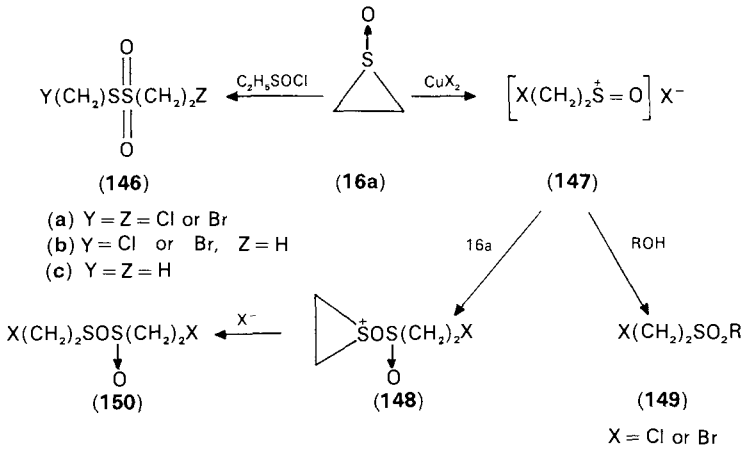


(59)

The above explains the key roles of: (a) the nucleophilicity of the nucleophile; (b) the substituent(s); (c) the polarity of the reaction medium; and (d) the the bulkiness of the nucleophile, in determining the regio- and stereo-specificity of the reaction. The reaction of alkyl chloromethyl ethers with thiirane oxides to give sulfenic esters[128] appears to be mechanistically analogous.

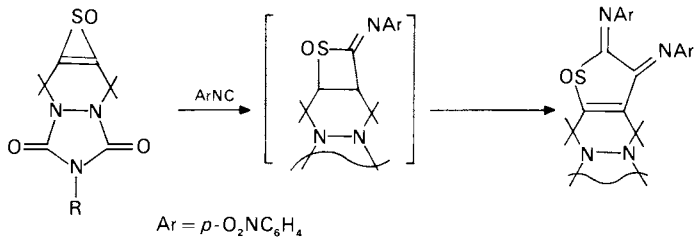
3. *Reactions of thiirane oxides with metal salts*

Whereas acyclic sulfoxides form complexes with various metal salts, thiirane oxides react with copper(II) chloride or bromide[163] in benzene at room temperature to give the thiolsulfonate **146a**. In alcoholic solution below 0 °C the major products are sulfinates (**149**). Similar results are obtained in the reaction of thiirane oxides with ethanesulfinyl chloride[163] as summarized in equation 60.



(60)

The formation of the 2, 3-diiminosulfoxide **152** by the insertion of two moles of isonitrile into the carbon–sulfur bond of **30**[164] (equation 61) can be naively considered as related to the transformation **16a** → **147** → **148**.



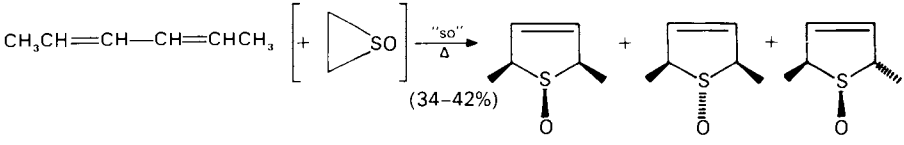
(30) (151) (152) (61)

4. Thermolysis of thiirane and thiirene oxides

The thermolysis of acyclic- and/or six- and larger ring sulfoxides to yield olefins and sulfenic acids is well documented[97,106]. The formation of allylic sulfenic acids and thiosulfinates in the thermolysis of thiirane oxides containing hydrogen on the α-carbon of the ring substituent (which is *syn* to the S—O bond) has been discussed previously in terms of β-elimination of hydrogen, which is facilitated by relief of strain in the three-membered ring (Section III.C.1).

The thermolysis of thiirane oxides not having β-hydrogens available for extraction has been shown, through an elegant study[104], to generate triplet sulfur monoxide[95] that could be trapped stereospecifically with dienes[165].

Thus the reaction of the three geometrical isomers of 2,4-hexadiene with thiirane oxide afforded the three related 3-thiolene *S*-oxides **154** depicted in equation 62[104].



(153)	(16a)		(154)	
(a) *trans–trans*	⟶	0	87	13
(b) *cis–trans*	⟶	*Trace*	5	95
(c) *cis–cis*	⟶	20	19	61

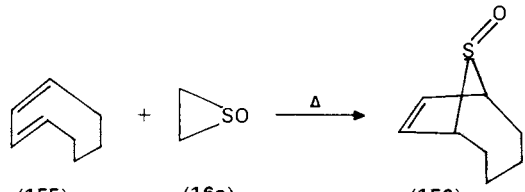
(% extrapolated to zero reaction time)

(62)

The above stereoselective additions of SO to dienes could have been predicted from its ground triplet state.

Stereochemical control at sulfur is detectable only in methyl *cis*-sulfoxide, of course, but it is noteworthy that the methyl *cis*-sulfoxide from **153a** is exclusively the less-stable isomer **154**-*t*, *t*.

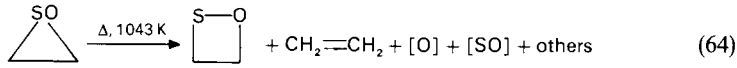
The high stereoselectivity of the SO—diene reaction is further demonstrated in reaction 63, where essentially only one sulfoxide (**156**) was formed[104].



(155) (16a) (156) (63)

Interestingly, preliminary calculations (3–21G* basis set) estimate the ΔH_f of the triplet SO (and ethylene) generation from the parent thiirane oxide (**16a**) to be about 18 kcal mol^{-1} [166].

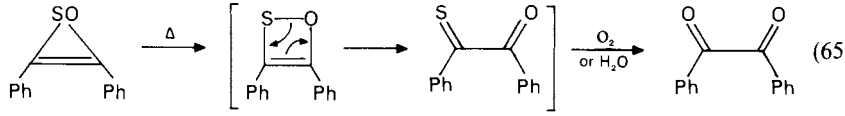
The thermolysis of **16a** has been studied[167] by the flash vacuum thermolysis-field ionization mass spectrometry technique[168] in the temperature range 1043–1404 K. Evidence was presented that the ring enlargement product 1, 2-oxathietane **157** is being formed (sulfoxide–sulfenate rearrangement) alongside atomic oxygen extrusion and sulfur monoxide elimination (among others; see equation 64). The extrusion of atomic oxygen from organic sulfoxides has been previously reported[169]. It should be pointed out, however, that the rupture of the semipolar S—O bond requires about 90 kcal mol^{-1} [170], compared to about 18 kcal mol^{-1} [166] required for the extrusion of the triplet SO.



(16a) (157) (64)

Also, the isolation of benzil **160** as the only product in the thermolysis of thiirene oxide **18a** at 130 °C was rationalized[22] in terms of initial ring expansion (sulfoxide–sulfenate rearrangement) followed by rearrangement to monothiobenzil **159**. The latter might be expected to undergo hydrolysis or air oxidation to give benzil **160** (equation 65).

Support for the initial ring expansion (**18a** → **158**) can be inferred from the fact that benzil was also isolated (although in low yield) in the electrochemical reduction of the thiirene oxide **18a**[171].



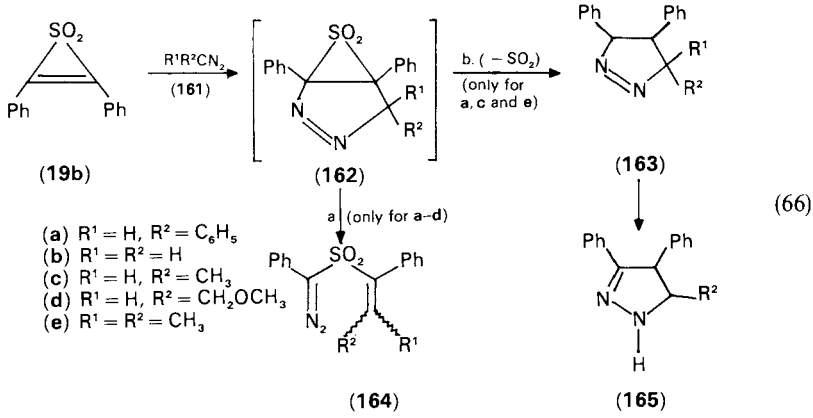
(18a) (158) (159) (160) (65)

5. Cycloaddition reactions

As formal α, β-unsaturated sulfones and sulfoxides, respectively, both thiirene dioxides (**19**) and thiirene oxides (**18**) should be capable, in principle, of undergoing cycloaddition reactions with either electron-rich olefins or serving as electrophilic dipolarophiles in 2 + 3 cycloadditions. The ultimate products in such cycloadditions are expected to be a consequence of rearrangements of the initially formed cycloadducts, and/or loss of sulfur dioxide (or sulfur monoxide) following the cycloaddition step, depending on the particular reaction conditions. The relative ease of the cycloaddition should provide some indication concerning the extent of the 'aromaticity' in these systems[2].

a. Thiirene dioxides. The [2 + 2] and [2 + 3] cycloaddition capability of thiirene dioxides (**19**) has been extensively explored[2,6,134,135,172–175].

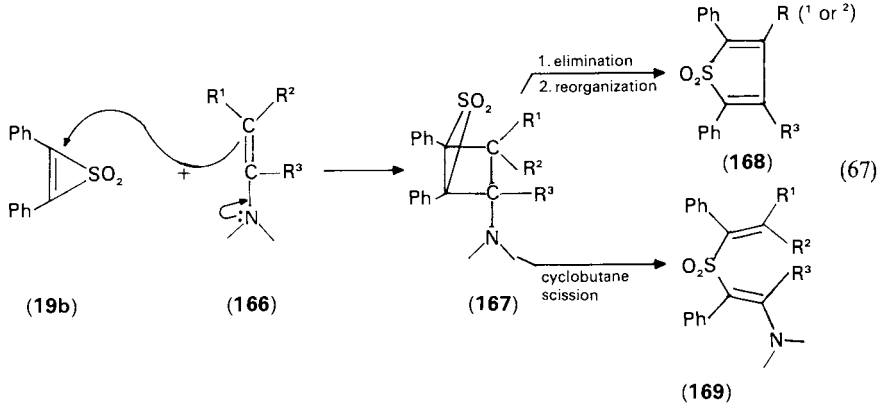
The cycloaddition of thiirene dioxide with phenyldiazomethane gave 3,4,5-triphenylpyrazole (**165a**) and the acyclic α-diazobenzyl 1,2-diphenylvinyl sulfone (**164a**), both suggested to originate in the common 1,3-dipolar cycloaddition intermediate **162**[6] (equation 66). Diphenylthiirene dioxide reacts similarly with other diazoalkanes (**161b–e**).



(66)

The ring-opening process leading to **164** (route a) is analogous to that which has been demonstrated to follow the cycloadditions of tosyl azide to certain enamines[176]. Similar results have been reported for the reaction of 2,3-diphenylcyclopropenone with 2-diazopropane[177]. Other 1,3-dipolar cycloadditions with thiirene dioxides could also be affected (see below).

Thiirene dioxides readily react with an entire spectrum of enamines to provide novel acyclic and cyclic systems[172]. These products result mostly from carbon–carbon or carbon–sulfur bond cleavage in the intermediate 'fused' thiirane dioxide **167** (equation 67).



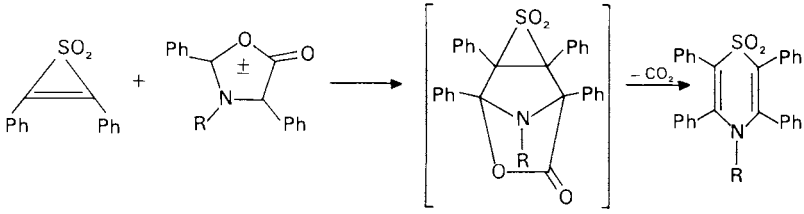
(67)

The synthetic potential of such transformations for the preparation of medium-size heterocycles[172] has been discussed elsewhere[2]. It is generally accepted that the reaction between thiirene dioxides and enamines is a stepwise (nonconcerted) thermal [2 + 2] cycloaddition. However, a concerted [4 + 2] cycloaddition, in which the lone pair of the enamine nitrogen atom participates, cannot be excluded.

In general, the above cycloadditions are exothermic and occur much faster than those of

enamines with cyclopropenones. Perhaps this is further evidence for the lack of substantial aromatic character of thiirene dioxides (at least compared to cyclopropenones).

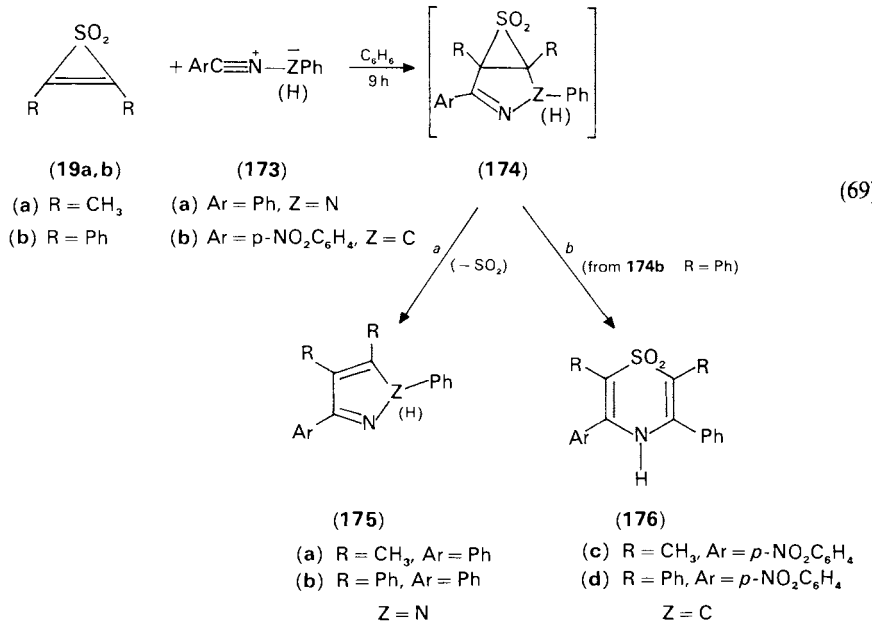
1, 3-Dipolar cycloadditions with thiirene dioxides as dipolarophiles have been conducted, leading (after extrusion of various small stable molecules) to a variety of heterocycles as illustrated in equation 68[174]. These results suggest the cycloaddition of **170** across the 2, 3-double bond of the thiirene dioxide to give the intermediate **171** which is followed by both carbon dioxide extrusion (preferentially to sulfur dioxide extrusion), and cleavage of the three-membered ring. In contrast, the reaction of thiirene dioxide **19b** with a six-membered mesoinoic compound[178] or with pyridinium ylids[173] is known to give adducts resulting from extrusion of sulfur dioxide.



(68)

(**19b**) (**170**) (**171**) (**172**)

Similar cycloadditions between thiirene dioxides and 1, 3-dipoles generated *in situ* give heterocycles which result from either loss of sulfur dioxide or from the three-membered ring opening of the initially formed adduct (e.g. **174**). Such cycloadditions with nitrilium imides (**173a**) and nitrile ylids (**173b**) are illustrated in equation 69[175].

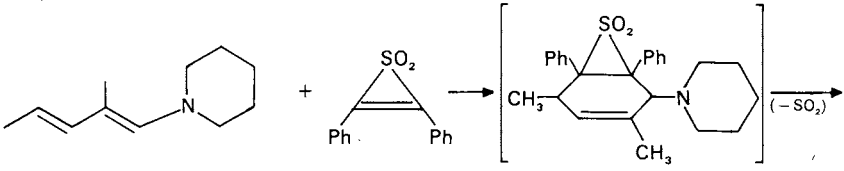


(69)

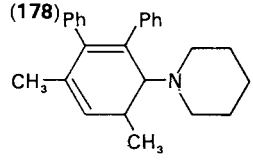
Ready extrusion of sulfur dioxide from fused thiirane dioxides is well known and was observed in the formation of pyrazoles from **19b** and diazoalkanes[6,179]. A ring expansion

similar to that depicted in route *b* (equation 69) was reported for the 1:1 cycloadduct of **19b** and azide ion[134] as well as in analogous cycloadditions[174].

Interestingly, benzonitrile oxide does not react with thiirene dioxide **19b** even in boiling benzene, whereas the electron-rich diene 1-piperidino-2-methyl-1, 3-pentadiene (**177**) does react under the same reaction conditions to give the expected six-membered [4 + 2] cycloadduct **178**, accompanied by sulfur dioxide extrusion and 1, 3-hydrogen shift to form the conjugated system **179**[175] (equation 70).



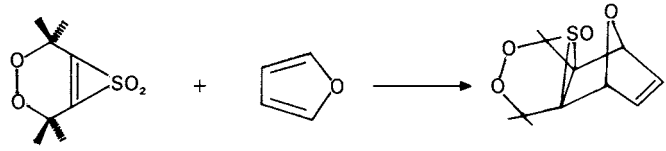
(177) (19b) (178) (70)



(179)

b. Thiirene oxides. Treatment of thiirene oxide **18a** with phenyldiazomethane in ether results in the formation of the pyrazole **165** which arises by loss of sulfur monoxide from a labile cycloadduct analogous to **162**[6], which in turn is obtained from the cycloaddition of the corresponding thiirene dioxide (i.e. **19b**) with the diazoalkane[6].

When the bicyclic thiirene oxide **180**[164] is dissolved in excess furan, a single crystalline *endo*-cycloadduct (**182**) is formed stereospecifically (equation 71)[164]. This is the first propellane containing the thiirane oxide moiety. Clearly, the driving force for its formation is the release of the ring strain of the starting fused-ring system **180**. In contrast, **18a** did not react with furan even under 'forcing' conditions.



(180) (181) (182) (71)

IV. FOUR-MEMBERED RING SULFOXIDES AND SULFONES

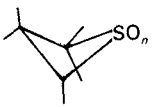
A. Introduction

The unique characteristics of three-membered ring sulfoxides and sulfones raise the question: Are the major features observed in the three-membered ring series extended into the still small and strained four-membered ring series, or will the latter be more reminiscent of the larger ring and acyclic sulfoxides and sulfones?

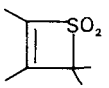
The less strain energy inherent in the four-membered ring sulfoxides and sulfones, their less distorted geometries and the lack of potential 'aromatic'-type conjugation effects make the comparison of their physical and chemical properties with other cyclic and

acyclic counterparts meaningful and susceptible to experimental testing, and also turn them into interesting candidates for theoretical investigation. Thus, for example, the puckered structure established for this class of oxides and dioxides[180] imparts a unique dimension to the uncertainty regarding the role of d-orbitals acting as polarization functions[3,24] in molecules containing second-row atoms, particularly sulfur[181]. In certain cases, such as the four-membered ring thietane and dithietane (oxides, dioxides, trioxides and tetroxides included), the special symmetry of d-functions may be required to span the irreducible representations of occupied orbitals in the molecule[182], and to determine whether or not d-orbitals are used in bonding in these puckered bent or planar cyclic systems[183].

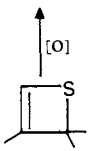
The preparation and investigation of the thietane oxide system (**5a**) is largely associated with stereochemical and conformational studies[66,74,184,185]. The investigation of the thietane dioxides (**5b**) is substantially related to the chemistry of sulfenes[143,186,187], the [2 + 2] cycloaddition of which with enamines is probably the method of choice for the synthesis of **5b**[186,187]. The study of the thiete dioxide system (**6**) evolved, at least in part, from the recognition that the unstable thiete system **183** can be uniquely stabilized when the sulfur in the system is transformed into the corresponding sulfone[188,189], and that the thiete dioxide system is very useful in cycloadditions[190] and thermolytic[191] reactions. The main interest in the dithietane oxides and dioxides (**7**) appears to lie in the synthetic challenge associated with their preparation, as well as in their unique structural features and chemical behavior under thermolytic conditions[192].



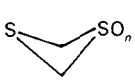
(5)
(a) $n = 1$
(b) $n = 2$



(6)



(183)



(184)
(a) $n = 1$
(b) $n = 2$

(7)
(a) $n = 1$
(b) $n = 2$

Whereas the transformations thietane → thietane oxide → thietane dioxide are easy to perform[192], as is the reverse transformation thietane dioxides → thietanes[188], no method of reducing the sulfonyl group to a sulfoxy group is available as yet.

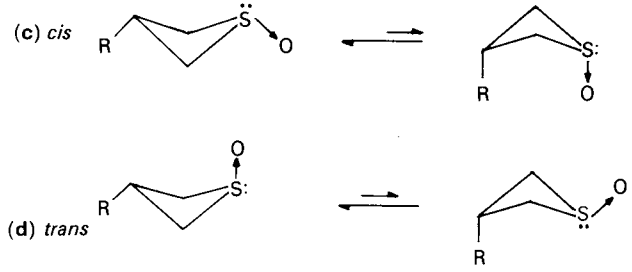
Although one finds, as expected, a regular change of physical and chemical properties in going from thietanes to their oxides and dioxides, or in going from thiirane oxides and dioxides to the four-, five- and six-membered sulfoxides and sulfones, there are some unusual effects associated with the four-membered ring series. An example is the unusual sulfonyl-oxygen deshielding and β-carbon shielding[70], as revealed by carbon-13 and oxygen-17 NMR spectroscopy. This suggests unique structural characteristics, which may be relevant to structure, bonding and charge distribution in these systems.

B. Structure and Physical Properties

1. Conformation and stereochemistry of thietane oxides and dioxides

It is well-documented that the thietane ring is puckered[193] and an energy barrier exists to planarity. Hence two conformations must be considered for each isomer of the *cis*- and

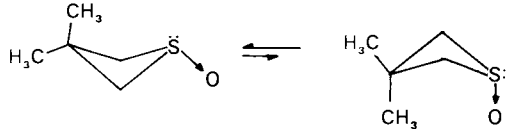
trans-3-substituted thietane oxides; the sulfinyl oxygen, nonetheless, exerts equatorial preference[74]. This preference may be attributed to a 1,3-cross ring, nonbonded interaction between the axial β-hydrogen and axial sulfinyl oxygen in the less-favored isomer. Apparently the nonbonded electron pair on sulfur has a lesser steric requirement. Stereochemical assignments could be made for a series of 3-substituted thietane oxides based on their NMR spectra[66]. Both isomers prefer conformations with the ring-substituent equatorial, as shown in equation 72. Interestingly, this preference is not affected significantly by changes of substituents in the 3-position[184], although the nature of the substituent may have a small effect on the degree of ring puckering. Based on dipole-moment studies, it was concluded[193b] that ring puckering decreases in the order: sulfide (axial)1, 1-sulfoxide, sulfone.



(72)

(5c,d)

The same equatorial preference is also manifested in the 3,3-disubstituted thietane oxides[66,194]. Thus, the NMR spectra of **5e,f** contain two Me singlets at 1.23 and 1.30 ppm and two methylene multiplets at 3.03 and 3.53 ppm (in $CDCl_3$). The large difference in the chemical shifts of the axial and equatorial α-methylene hydrogens is characteristic of an axial nonbonded electron pair on sulfur (conformation **5e**; equation 73). This conformational preference is corroborated by the *small* differences in the chemical shifts of the two methyl groups, and fits the contention that 1,3-diaxial interactions are responsible for this ultimate result. Certainly, these interactions are greater in the conformer **5f**.



(73)

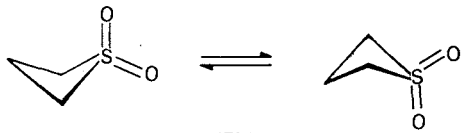
(e) (5) (f)

The preference for conformer **5e** has also been established for 3-alkyl-3-aryl thietane oxides[194], based mainly on the analysis of the AA'BB' spin system of the ring hydrogens in the NMR spectrum.

The NMR spectra of the corresponding dimethyl sulfide and dimethyl sulfone consist of two singlets at 1.27, 2.92 and 1.43, 3.80 ppm, respectively (in $CDCl_3$), most probably implying a rapid interconversion of puckered conformations[66].

The proton spectra analysis of thietane, thietane oxide and thietane dioxide at 100 and 300 MHz in the temperature range -140 to 190 °C confirmed the puckered structure for the oxide (**5a**) with the sulfinyl oxygen in the equatorial orientation, as inferred from chemical-shift considerations[180]. It appears that the repulsive-type 1,3-interactions between the oxygen and the 3-substituents[184] are operating between oxygen and the axial proton on C-3 in the unsubstituted thietane oxide (**5a**). For the thietane dioxide (**5b**;

equation 74), the NMR data are in agreement with either a planar structure or, more likely, a rapid interconversion between two equivalent conformers, as is the case for the unsubstituted thietane[180].

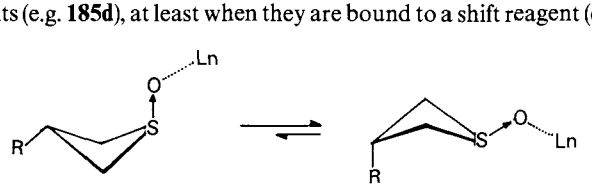


(74)

(5b)

Interestingly, the crystal structures of 3-substituted thietane and thietane dioxides[180] showed that in the solid state they exist in the puckered structure, with the S—O bond equatorial in the oxides and the 3-substituent *axial* for the *trans*-isomers, contrary to what has been quoted before[66,195]. Thus, the claim that conformer **5c** is predominant in the solutions of the *trans*-isomer needs to be re-examined.

A study[195] based on the NMR lanthanide-induced shifts (LIS) for a series of *cis*- and *trans*-3-substituted, and 3,3-disubstituted thietane oxides concluded that all *cis*-substituted oxides (**5c**; $R = CH_3$, *t*-Bu and aryl) exist *exclusively* in the diequatorial conformation. The *trans*-3-substituted isomers (**185**) prefer the equatorial oxygen conformation ($R = CH_3$, 86%; *t*-Bu, 65–75%; aryl, 75%), which means an *axial* preference for the substituents (e.g. **185d**), at least when they are bound to a shift reagent (equation 75).



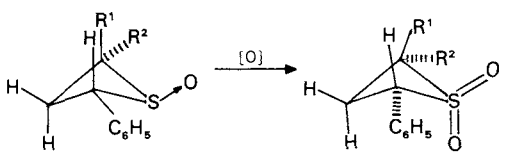
(75)

(c) **(d)**

(185)

Based on NMR chemical shift assignments and the use of recorded spin–spin coupling constants ($J_{m,n}$), it was determined[193c] that in both 2,4-diphenyl-substituted thietane oxides (**186a,b**) the dominant conformers are those in which the S—O bond is *equatorial* and, therefore, in the *trans*-2,4-isomer[186] one phenyl group (i.e. R^1) is *syn*-axial to the S—O bond, whereas in the *cis*-2,4-diphenyl isomer **186b** both phenyls are *anti*-equatorial to the S—O bond.

The consequences with respect to the corresponding thietane dioxides are straightforward: in the *trans*-isomer, **187a**, one phenyl group (i.e. R^1) is necessarily axial, whereas in the isomer **187b** both substituents are equatorial (equation 76). Clearly these preferred conformations minimize the potential repulsive interaction between 1,3-diaxial substituents[66].



(76)

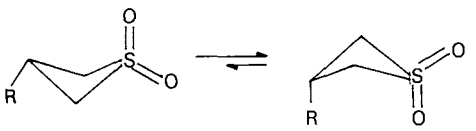
(186) **(187)**

(a) $R^1 = C_6H_5$, $R^2 = H$
(b) $R^1 = H$, $R^2 = C_6H_5$

The crystal structure of the *cis*-oxide **186b**[196] was shown (as expected) to be a flattened molecule as the benzene rings extend in an equatorial direction from the puckered thietane ring. The latter has a pucker angle of 41.9°, which is in good agreement with the value of 39.7° calculated for this molecule[193c] by using the Barfield–Karplus (spin–spin, coupling-based) equation[197].

It might well be that, compared with other thietane oxide systems, the larger pucker angle here is due to the two bulky 2,4-phenyl substituents that tend toward equatorial conformation.

The NMR spectra of 3-substituted thietane dioxides (**188**; equation 77) have been analyzed at 300 and 100 MHz using a LAOCN program, and provided evidence for a slight puckering of the four-membered ring and a preferred *axial* orientation (i.e. **188b**) of the 3-substituents[198]. The NMR measurements in the range between − 135 and + 150 °C indicate an increase in the population of the less-stable equatorially substituted isomer with increasing temperature. These results are in accord with an axial preference of the substituents in the analogous *trans*-3-substituted thietane oxides, as previously established[185].



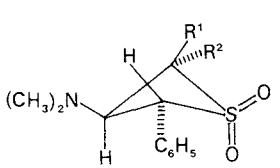
(77)

($\mathbf{a}_{(1-3)}$) (**188**) ($\mathbf{b}_{(1-3)}$)

R = OH, Cl, OCOMe

X-ray analyses of solid **188** have shown that the angles of the puckering of the four-membered sulfones are small and that the substituents are always axial, as in solution[198]. As far as the 3-substituted thietane dioxide is concerned, the axial preference of the substituent is unexpected (although not unprecedented[199]) and difficult to account for, since the equatorial preference (i.e. **188a**) would have been predicted based on steric considerations; that is, the 1-O, 3-R diaxial repulsive interactions. Attractive-type interactions between the electronegative 3-substituents and the axial sulfonyl-oxygen are very difficult to advocate. It is, therefore, noteworthy that NMR study of the parent thietane dioxide (**5b**) in a nematic phase solvent[200] showed the four-membered sulfone to have a *planar* or slightly distorted average vibration conformation with a low barrier to ring planarity. The thietane oxide, however, exists preferentially in one strongly puckered conformation (angle of puckering about 38°) with the oxygen in equatorial orientation.

As one would expect, the tri-substituted *cis–trans*-2,4-diaryl-3-dimethylaminothietanes (**187c,d**) were shown by NMR to have all three substituents in pseudoequatorial positions with the remaining hydrogens in axial positions[202].



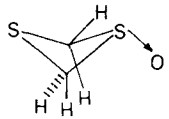
(**187**)

(**c**) R^1 = H, R^2 = Ar (*cis*)

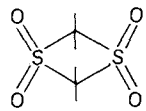
(**d**) R^1 = Ar, R^2 = H (*trans*)

The structures of four-membered rings are of considerable interest, owing in part to the low-frequency ring puckering vibration[203]. The comparison of the structures and conformational preferences of thietane oxides and dioxides discussed above with those of dithietane oxides and dioxides is therefore appropriate and will follow.

The gas-phase structure of 1,3-dithietane 1-oxide (**189**) has been determined from its microwave spectrum and the spectra of eight isotopic modifications[192]. The ring is puckered, the angle between the two CSC planes being 39.3° with the oxygen equatorial.



(189)



(7b)

The oxide **189** displays short nonbonded sulfur–sulfur and carbon–carbon distances (2.600 and 2.372 Å, respectively). Nonetheless, the sulfur–oxygen bond (1.473 Å) and the angle of pucker appear to be normal compared to the data presented above for the thietane oxides[180,197,200,204].

The structure of 1,3-dithietane tetroxide **7b** has been shown by X-ray diffraction methods to be planar and almost square[192], the molecule being located on a crystallographically required center of symmetry at the center of the four-membered ring, with the planes of the SO_2 and CH_2 groups essentially perpendicular to the plane of the four-atom ring (89.9° and 85°, respectively). Again, these results are in accord with previous studies that established the planarity (or near planarity) of the analogous thietane dioxides[180,198]. It appears that the inclusion of a second sulfur atom, a sulfoxide, or a sulfone group in the four-membered ring thietane oxides and dioxides (in a 1,3 relationship) does not alter the conformational preferences of the latter, nor does it cause any unusual anomalies as far as the particular geometrical parameters (e.g. bond lengths and angles) of these molecules are concerned (see Section IV.B.2 below).

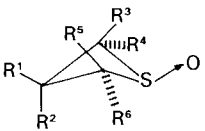
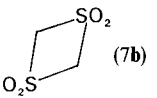
2. *Experimental geometrical parameters*

The crystal structures of several thietane oxides have been determined. Bond lengths and angles are given in Table 6.

The data indicate no exceptional intermolecular contacts nor any unusual bond lengths and bond angles in the compounds studied. The structures and conformational preferences are consistent with those derived from NMR studies. The slight deviation of the pucker angle in the thietane oxide **186b** (41.9°), compared to that of the other oxides cited, may be accounted for by the two bulky phenyl substituents tending toward equatorial conformations. Interestingly, however, the pucker angles of 3-substituted thietane dioxides (i.e. $\mathbf{188}_{(1-3)}$; R = OH, Cl, OCOMe) were found by X-ray studies[198,208] to be 6.8°, 9.3° and 7.9°, respectively. This means that the ring of thietane dioxides is approaching planarity, whereas that of the 1,3-dithietane tetroxides is actually planar and almost square[192], at least in the case of the parent tetroxide **7b**. Intramolecular nonbonded S···S and C···C distances are 2.590 Å and 2.524 Å, respectively. The former short value is similar to what was found for the nonbonded S···S distance in the oxide **189**[192].

3. *Theoretical treatment and interpretations*

a. NMR-based calculations. Both the dihedral angles HCCH and the angles of pucker of *cis*- and *trans*-2-4-diphenylthietane oxides (**186a,b**) have been calculated[193c] by using

TABLE 6. Bond lengths[a] and bond angles[b] in selected thietane oxides  (**5**;**186**) and 1, 3-dithietane tetroxide  (**7b**)

Compound	*r*SO	*r*SC	*r*CC	⟨CSC	⟨OSC	⟨SCC	⟨CCC	⟨OSO	Pucker angle	Ref.
5d; $R^1 = R^3 = R^4 = R^5 = R^6 = H$, $R^2 = CO_2H$	1.52	1.835[c]	1.59[d]	78	110.5[e]	89.5[f]	94	—	35	205
	1.526	1.842	1.529	76.6	112.0	90.2	96.6	—	27	206
5c; $R^2 = R^3 = R^4 = R^5 = R^6 = H$, $R^1 = p\text{-}BrC_6H_4$	1.482	1.84[c]	1.54	—	118	—	—	—	33	195
5d; $R^1 = R^3 = R^4 = R^5 = R^6 = H$, $R^2 = p\text{-}BrC_6H_4$	1.492	1.83[c]	1.52	—	116	—	—	—	32	195
5e; $R^1 = R^2 = CH_3$, $R^3 = R^4 = R^5 = R^6 = H$	—	—	—	—	—	—	—	—	27	206
186b; $R^1 = R^2 = R^3 = R^5$, $R^4 = R^6 = C_6H_5$	1.466	1.847	1.565	76.5	114.1	86.9	93.9	—	41.9	196
186c; $R^1 = R^4 = R^5 = H$, $R^2 = C_6H_{13}$, $R^3 = CH_3$, $R^6 = CH_2OH$	1.502	1.844[c]	1.552[d]	76.5	112.5[e]	90.4[f]	94.7	—	29	207
7b	1.434[g]	1.808[c]	—	88.5	111.1	91.5[h]	—	119.4		

[a] In Å.
[b] Degrees (°).
[c] An average of value obtained from the S—C_2 and S—C_4 distances.
[d] An average value obtained from the two relevant C—C bonds.
[e] An average value obtained from the two (or four) relevant OSC angles.
[f] An average value obtained from the relevant SSC angles.
[g] An average value obtained from the two relevant S—O bond lengths.
[h] ⟩SCS.

their NMR spectra, some previously published data concerning bond lengths and angles in the thietane–thietane oxide series[205,209], and the Karplus–Barfield equation[197] of the form $^3J_{H,H'} = A\cos^2\phi + B\cos\phi + C$.

Thus, the dihedral angles of the *trans*-oxide (**186a**) were calculated to be 91.0°, 36.5°, 26.5° and 154° for $\langle R^2CCH^3$, $\langle R^2CCH^4$, $\langle H^2CCH^3$ and H^2CCH^4, respectively; and 31.6° and 159.1° for $\langle R^1CCH^3$ and R^1CCH^4, respectively, in the *cis*-oxide **186b**.

The pucker angle of **186b** was calculated to be 39.7° and that of **5d** ($R^2 = CO_2H$) to be 29.7°[193c]. These results are in excellent agreement with the experimental values of 41.9° and 27° obtained via X-ray studies[196,206] as can be seen in Table 6. For the corresponding *cis*-thietane dioxide (i.e. **187b**) the above procedure gave an angle of pucker of 35°, a value that is highly questionable in view of the tendency toward planarity of the four-membered ring in thietane dioxides.

Similar calculations have been applied to the 3-substituted thietane dioxide series (i.e. **188**$_{(1-3)}$)[198], assuming that only the constant C in the Karplus equation should be significantly affected by the substituents and by the oxidation state of sulfur. The results thus obtained were in poor agreement with X-ray data.

It is difficult to decide whether the discrepancy between the calculated and experimental data is due to a different conformational preference of the thietane dioxides in the liquid and the solid phase, or to the crude approximations included in the Karplus–Barfield equation. However, the relationship between vicinal coupling constants and dihedral angles appears qualitatively valid in thietane oxides and dioxides, particularly if trends instead of exact values are discussed[193c]. At any rate thietane dioxides, 1,3-dithietane dioxides and tetroxides maintain either planarity[192] or a slightly distorted average vibrating conformation with a low barrier to ring planarity[198].

b. Photoelectron (PE) spectra and their assignments. The PE spectrum of 1,3-dithietane 1-oxide **189** is best discussed by comparison with thietane oxide, since the large perturbation S → SO can be replaced by the isovalent and electronic one, $CH_2 \rightarrow S$[192].

The three highest occupied orbitals of sulfoxides are the lone pairs n_s and n_o, as well as the π_{SO} bond[210]. The 1,3-dithietane 1-oxide adds a 'lone-pair' ionization and destabilizes the n_o and π_{SO} radical-cation states compared with thietane oxide. According to a hyperconjugative MO model, the n_s^+ combination in 1,3-dithietane is destabilized by about 1 eV relative to the basis orbital energy $\alpha(n_s)$ due to the combination with the

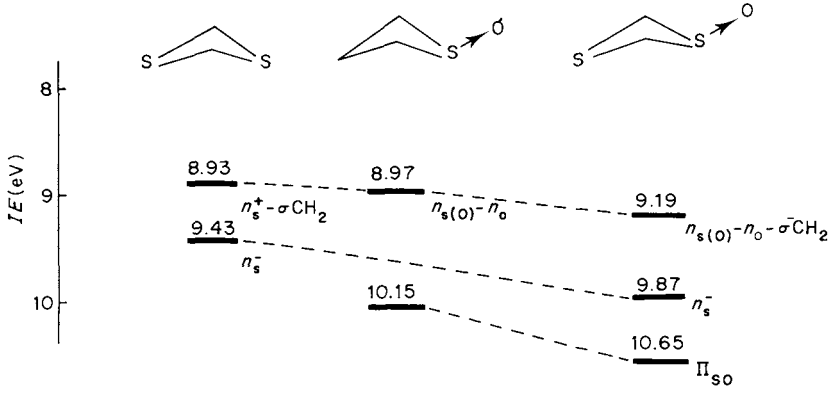
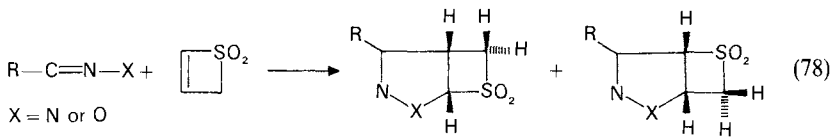


FIGURE 1. Sulfur lone-pair and π_{SO} ionization patterns in 1,3-dithietane, thietane oxide and 1,3-dithietane oxide.

$\sigma_{CH_2}(b_{2u})$ orbital[210]. In the 1,3-dithietane 1-oxide both sulfur 'lone-pair' ionizations are further increased by the oxygen substitution. In thietane oxide both n_o and π_{SO} ionizations are lowered by the $S \rightarrow CH_2$ substitution, whereas a $CH_2 \rightarrow SO$ replacement splits the n_o and π_{SO} ionizations and increases their center of gravity. The radical-cation-state correlation shown in Figure 1[192] is supported both by EHMO and modified CNDO calculations based on the known structural parameters[211]. Similar considerations and interpretations have been applied for the PE spectra of 1,3-dithietane dioxide and 1,3-dithietane tetroxide (**7b**) and their assignments.

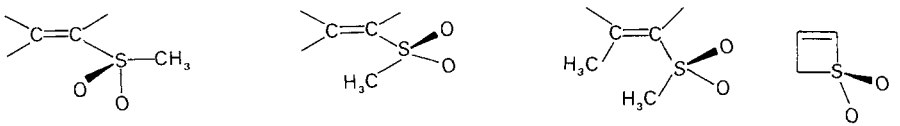
c. Theoretical investigation on cycloaddition of thiete dioxides. Cycloaddition of nitrile oxides, diazoalkanes and nitrones with thiete dioxide[213] (**6b**) show regiochemical characteristics markedly different from those observed for acyclic vinyl sulfones[212]. This difference constituted a good basis for a theoretical study of regioisomerism of these cycloaddition reactions[214].



(78)

(190) (6b) (A) (191) (B)

The charge-transfer stabilization energy, calculated according to the Klopman–Salem perturbational approach in the CNDO/2 approximation[215], provided results that are able to account for the experimental trends of the ratio between the two isomers (i.e. **191A,B**; equation 78)[214]. The change of regiochemistry in the cycloadditions of the four-membered cyclic sulfone (**6b**) compared to that of the acyclic vinyl sulfone, can be explained in terms of its locked *cis–syn*-structure. Such a *cis–syn*-structure occurs also in open vinyl sulfones (**193**), but is not locked in them. An example of predicted regiochemistry differences between the 'open' and the cyclic sulfones in the cycloaddition reaction with $PhC{\equiv}N \rightarrow O$ is given below [based on the calculated stabilization energy differences $\Delta\Delta E = \Delta E(\mathbf{B}) - \Delta E(\mathbf{A})$][214]:



(192a) (192b) (193) (6b)

$10^{-3}\Delta\Delta J\,mol^{-1}$: + 2.84(**A**) + 0.402(**A**) + (**B**) − 1.548(**B**) − 0.963(**B**)

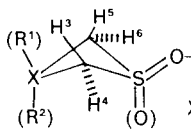
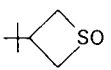
Thus, formation of one isomer only in the cycloaddition is expected when the following holds: $-0.84 > \Delta\Delta E > 1.25 \times 10^3\,J\,mol^{-1}$, whereas $-0.84 < \Delta\Delta E < 1.25 \times 10^3\,J\,mol^{-1}$ corresponds to a mixture of variable isomer ratios.

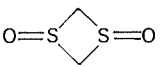
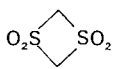
Predictions obtained by using the frontier orbital approximation[213] were unsuccessful, apparently due to inadequacies in these MO calculations mostly involving the energy gap between HO of the dipole and LU of the dipolarophile.

4. Spectroscopic characteristics and characterization

a. ^1H and ^{13}C NMR spectroscopy. NMR spectroscopy is the technique most often applied to the study and characterization of four-membered ring sulfoxides and

TABLE 7. ^{1}H and ^{13}C NMR chemical shifts and coupling constants of four-membered sulfoxides and sulfones

 X = C or S	Chemical shifts δ			Coupling constants							Refs.
	$^{1}H_{(\alpha-C)}$	$^{13}C_{\alpha}$	$R^{1or2} = H$	gemH^3H^4	*trans*H^3H^6	*cis*H^4H^6	*cis*H^3H^5	gemH^1H^2 (X = C; $R^1 = R^2 = H$)	*trans*H^2H^3 (X = C; $R^1 = R^2 = H$)	*cis* H^1H^3	
	3.09[a], 3.46[a]	52.7[b]	1.95, 2.27[a]	−10.29	−0.95	6.10	−0.57	−12.69[a]	+12.53[a]	+12.53[a]	180, 192
(*cis* & *trans*-) 	{*cis*- 2.83[c], 3.42[c] {*trans*- 3.52, 3.62[d]		1.93 3.07								66 66
	4.09[a]	65.6[b]	2.14	−14.0	−1.24		2.24(av.)	−12.63[a]	+6.33[a]	+10.34[a]	180,192
	3.80[d], 3.56[e]										66
MeCOO 	4.19[d], 4.57[d]	71.73[d]		−14.48	−1.19	3.76	2.87			7.93	198

	4.23[f], 3.37, 3.73[g],	53.1	−7.53[h]	0.73[i]	5.56	0.005[i]	192
	5.27[f,j]	68.4					192
(*cis*-) 	4.78, 5.72[j]	69.1	−13.40[h]	1[i]	3.76[i]	1[i]	192
(*trans*-) 	4.97[j]	69					192
	6.40[h]	92.1					192

[a] In $(CD_3)_2CO$.
[b] α-Carbon.
[c] Multiplet in CCl_4.
[d] In $CDCl_3$.
[e] In C_6H_6.
[f] In $(CD_3)_2SO$.
[g] In C_6D_6.
[h] Negative sign assumed.
[i] Sign unknown.
[j] In CF_3COOH.

sulfones[66,70,74,180,184,185,192–203,216]. Chemical shifts and coupling constants have been used for structural, conformational and stereochemical assignments and preferences and for the establishment of the four-membered ring sulfone effect[70,216].

^1H and ^{13}C chemical shifts and coupling constants of some selected representative four-membered ring sulfoxides and sulfones are given in Table 7.

Stereochemical assignments for a series of 3-substituted thietane oxides (**5c,d**) were made, based on the equatorial preference of the oxygen–sulfur bond[76] and on the large chemical-shift-difference characteristic of the α-methylene hydrogens in the *cis*-isomer, and the significant relative deshielding of the β-hydrogen in the *trans*-isomer[66]. The stereochemical assignments were confirmed by the aromatic solvent-induced shifts (ASIS)[217]. Protons on the opposite side of the ring to the sulfinyl oxygen in thietane oxides undergo larger ASIS than those on the same side of the ring[194]. The preference of the equatorial orientation by the sulfur–oxygen bond has also been established for 3,3-disubstituted thietane oxides based on similar interpretation of the NMR data including the appearance of the resonance of the axial hydrogens (in line with that of the hydrogen *anti* to the 'lone pair' on sulfur) in the sulfoxide at higher field compared with the resonance of the equatorial hydrogens. Indeed, the α-proton *trans* diaxial to the nonbonded electrons on sulfur always appears at higher field than the equatorial α-proton in cyclic sulfoxides[66].

The proton spectra of thietane oxide (**5a**) and thietane dioxide (**5b**) have been studied in order to evaluate whether the oxidation at the sulfur atom changes the established 35° puckering of the ring[218], and whether a correlation is possible between structure and NMR parameters[180].

The analysis of the spectral data indicates for thietane oxide a preferred puckered structure with the sulfinyl oxygen in the equatorial orientation. The ring inversion rate is fast enough to average the coupling constant values, but the strongly puckered structure is the most populated. The data for thietane dioxide are in agreement with either a planar structure, or with two rapid interconverting equivalent conformers.

Thorough analysis of the coupling constants suggests that vicinal and cross-ring coupling can be valuable when used for stereochemical assignments in thietane oxides and dioxides, provided one takes into consideration the conformational changes and the substituent effects[180].

All of the above conclusions have been confirmed in an NMR study of **5a** and **b** in the nematic phase[201]. The results confirmed the effective C_{2v} symmetry of the dioxide as expected for a planar-ring geometry or for rapidly interconverting slightly bent structures, with a low barrier to ring planarity. The NMR-based experimental values and the calculated ring parameters (D_{ij}) were found to be in very good agreement in both the oxide and the dioxide ring systems. The angle of puckering for **5a** has been estimated to be approximately 38°[201] as compared with 34.67° obtained from microwave results[219].

Following a detailed NMR study of the 3-substituted thietane dioxides **188** it was concluded that the three-bond coupling constants ^3J can be safely used for stereochemical assignments in this series; in particular the $^3J_{R^1H^4} < 4$Hz (Table 7, $R^1 = H$, $X = C$) is consistent with an equatorial–equatorial interaction. This indicates an axial preference for the 3-substituent R (i.e. **188b**) in both liquid and solid phases, and also suggests that the ring is puckered[198].

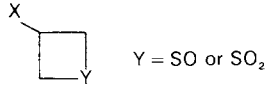
The previously discussed conformational study of 3-substituted thietane oxides using lanthanide shift reagents[185] corroborates the conclusions derived from other NMR studies and suggests that all *trans*-3-substituted thietane oxides prefer an equatorial oxygen conformation when the thietane oxides are bound to shift reagents.

A useful comparison of the ^{13}C shifts for acyclic and cyclic five- and six-membered sulfur compounds has been made[86,220], but data on cyclic sulfur compounds of other ring sizes are rather limited. Typically, oxidation of sulfide to a sulfone results in 20–25 ppm

downfield shift for the α-carbon and 4–9 ppm upfield shift for the β-carbon[70]. Surprisingly, there is very little difference between the α-carbon shifts of sulfoxides and sulfones.

The chemical shifts of the unsubstituted α-carbons of thietane oxides and dioxides (Table 7) are about 53 ppm for the former and about 67 ppm for the latter. The value of the α-carbon chemical shifts of the 1, 3-dithietane disulfoxides (*cis* and *trans*) is about 69 ppm [near that of the four-membered thietane(mono)-dioxide], whereas the chemical shift of the α-carbon of the parent 1, 3-thietane tetroxide is about 92 ppm. In comparing the above values with the chemical shift of the α-carbon in thietane, which is about 26 ppm[70], one can see that there is about 40 ppm downfield shift in going from the thietane to its dioxide and an additional 25 ppm downfield shift in going to the tetroxide. The difference between the α-carbon chemical shifts of the sulfones and sulfoxides is 13–15 ppm. The shift of 28.0 ppm for the β-carbon in thietane decreases to 10.4 ppm in the sulfoxide and to 5.8 in the sulfone. Effects of this order of magnitude are not observed in other cyclic sulfones and sulfoxides. There is some parallel to this anomalous 'four-membered ring-sulfone effect'[216] in the downfield chemical shifts of the α-protons and upfield chemical shift of the β-protons in the four-membered ring sulfones (4.09 and 2.14 ppm, respectively, compared with 3.21 and 2.94 ppm for the thietane[221]). In the other ring systems the order of α-proton shifts is in accord with the inductive effect: sulfenyl < sulfinyl (average) < sulfonyl[70]. The 'four-membered ring effect'[192] is also reflected in the considerable deshielding of the sulfonyl oxygens in the thietane dioxide as determined via the oxygen-17 chemical shifts (182 ppm compared with 111 and 165 ppm in three- and five-membered ring sulfones, respectively[70]). It should be pointed out that the nonequivalence of the two sulfone oxygens may be observed[70]. For oxygen-17 shifts, the sulfoxides also show the same trend. The effect appears to be general for other sulfonyl and sulfoximino groups in saturated four-membered rings[70]. In contrast, carbon-13 shifts in cycloalkanes[222] and thiacycloalkanes[70] and nitrogen-15 shifts in azacycloalkanes[223] do not show an anomaly at the four-membered ring. The origin of the 'four-membered ring sulfone effect' remains an unanswered question, but it may be related to perturbation of the sulfur atoms, which might have an unusual dependence on the state of oxidation when incorporated in four-membered rings.

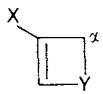
Carbon-13 chemical shifts of the α- and β-carbon atoms of various unsubstituted and 3-substituted thietane oxides and dioxides have been recorded and correlated by the equations $\delta_\alpha = a_y + b_x$ and $\delta_\beta = a_x + b_y$ where a and b are parameters characteristic of the sulfoxide or sulfone (y) and the substituent (x)[216]. The values of the substituent parameters were found to parallel those which determine the effect on the ^{13}C chemical shifts when hydrogen is replaced by a substituent[224].



In four-membered ring sulfones, the α-carbon–hydrogen coupling constants J(CH) were shown to be similar to those of the corresponding sulfoxides and sulfides. The β-carbon–hydrogen coupling constants are sensitive to the nature of the substituent X, but no special β effect is observed. Interestingly, thietes (**6b**) also reveal the 'four-membered ring sulfone effect'. *Trans*-3-substituted thietane oxides show a greater downfield shift for the β-carbon atom than the *cis*-isomer (Table 8). Except for the four-membered ring anomaly, the experimental data are in accord with the expected trends in cyclic sulfides, sulfoxides and sulfones.

b. Infrared, mass and UV spectra. The strong IR absorptions are 1030–1070 for sulfoxides and 1130–1160 and 1300–1350 cm^{-1} for sulfones[225]. Here the four-membered

TABLE 8. Chemical shifts (ppm)[a] and coupling constants for selected thietanes, thietane oxides and dioxides  (after Reference 216)

Y	X	α-C	β-C	^1J(α-CH)	^1J(β-CH)	a_y	b_y
S	H	26.16	28.17	145.7	135.9	27.95	24.13
SO	H	52.80	10.40	148.1	139.4	50.39[b]	18.67[b]
SO_2	H	65.57	5.8	145.2	144.3	64.97	7.17
S	Ph	32.00	44.07	146.7	131.4		
SO	Ph	56.24[b]	33.39[b,c]	147.7[b]	—		
SO_2	Ph	71.87	24.46	147.7	146.6		
S	OH	38.67	67.33	147.4	150.7		
SO	OH	59.90[b]	63.80[b]	149.1[b]	151.3[b]		
SO_2	OH	74.09[b]	52.67[d]	145.8	161.6		
							
S	Ph	35.79					
SO_2	Ph	69.87					

[a] In $CDCl_3$.
[b] For the *trans*-isomer.
[c] 27.11 ppm for the *cis*-isomer.
[d] In $(CD_3)_2CO$.

ring sulfoxides and sulfones were found to be within the 'normal' ranges[66,185,193c,202,216,226,227]

Mass spectrometry was applied in conjunction with thermolysis studies leading mainly to sulfines[192,228] and rearranged products[229] with four-membered sulfoxides and to a loss of sulfur dioxide with sulfones[192,193c,230]. The fragmentation pattern of thietes under electron impact can be explained by the sequential loss of the elements of sulfur monoxide and oxygen from an intervening cyclic sulfinate intermediate[189].

The combination of the flash vacuum pyrolysis (FVP) technique[169] with mass spectrometry proved to be particularly useful in identification and characterization of both the fragmentation/rearrangement patterns, intermediates and/or final products formed (see Section IV.E.1). Usually, no structures are indicated in the mass spectra, although ionization and appearance potential can, in principle, provide structural information.

In view of the limited capacity of the sulfur atom in the sulfoxide and sulfone functional groups to transmit conjugative effects due to the 'insulating effect' of the LUMO sulfur d-orbitals[45,46,56], the application of the UV technique even in the case of the cyclic vinyl sulfones (e.g. thiete dioxides **6b**) cannot be expected to find extensive use. UV spectra of substituted thiete dioxides in which an extended conjugated system (e.g. **194**) exists in the molecule, did provide useful information for structure elucidation[231]. However, the extent

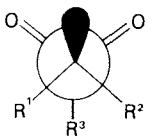
(a) **(194)** (b)

R = H, Cl, NO_2

of participation (if at all) of the sulfone group in the chromophoric conjugated system (and consequently in determining λ_{max} and ε) in **194** cannot be estimated without further UV studies with similar or closely related thiete dioxide systems.

C. Acidity and p*K* Values

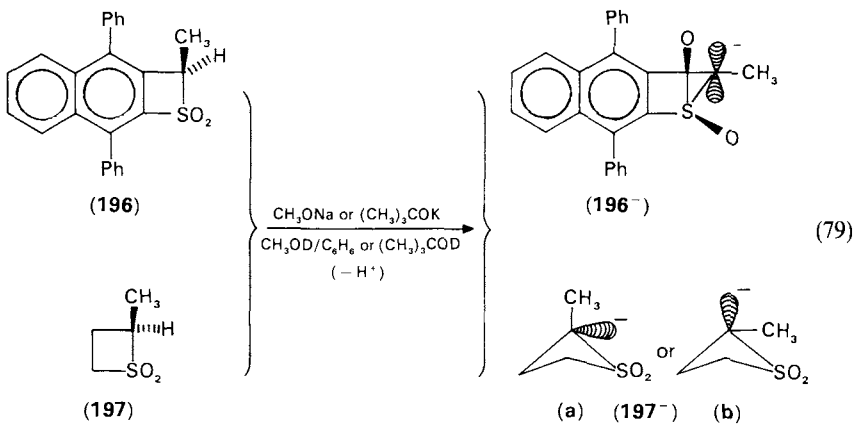
The inductive and electrostatic effects, steric constraints and conjugative interactions are the major factors that determine the configurational stability of α-sulfonyl carbanions[227]. These are thought to be pyramidal with appreciable electrostatic inhibition to racemization by way of inversion[232]. LCAO-MO-SCF calculations have indicated the conformer **195** in which the lone pair is directed along the bisector of the OSO angle to be the most stable in acyclic sulfones[232c].



(**195**)

Stereochemical constraints in cyclic sulfones and sulfoxides impart increased weight to strain and conformational factors in the generation of carbanions and their stability, causing distinct differences between the behavior of cyclic and open-chain systems[233], due primarily to the prevention of extensive rotation about the C_α—S bond, which is the major way that achiral carbanions racemize. Study of the α-H/D exchange rate k_e and the racemization rate k_α may provide information concerning the acidity-stereochemical relationships in optically active cyclic sulfone and sulfoxide systems.

Rate constants for H/D exchange and activation parameters (k_e and k_α) have been measured for the optically active thietane dioxides **196** and **197**[227]. The k_e/k_α values for ethoxide and *t*-butoxide-catalyzed reactions were found to be 0.88–1.02 and 0.6–0.67, respectively, with **197** undergo ring exchange/racemization about 10^5 times slower than the former. Racemization occurs concurrently with exchange in **196** in which extensive delocalization by the aromatic system stabilizes the negative charge of the α-sulfonyl carbanion (**196**$^-$). Also, the shift of the α methyl group from an eclipsed to a staggered conformation (with respect to the sulfonyl oxygen) in passing from **196** to its carbanion results in a relief of steric strain that contributes to the rate acceleration compared with the process in **197** (equation 79).

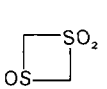


(79)

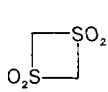
197 enjoys greater conformational mobility than **196**, and the k_e/k_α values (0.60–0.67) are in agreement with two mechanistic possibilities reflecting either exchange with net inversion (from **197**-**a**) or a blend of inversion without exchange (*iso*inversion), inversion and racemization processes (from **197**-**b**). Both enthalpy and entropy factors are involved in these processes, which are solvent-dependent. Nevertheless, it might well be that the dominance of k_α over k_e in the thietane dioxide series reflects the low barrier to ring planarity in the four-membered ring[180,198,200] once the α-sulfonyl carbanion has been formed.

Both the isomerization and the H/D exchange rates were shown to be dependent on the nature of the α-halogen substituent (I > Br > Cl) in a series of *cis*- and *trans*-2-halo-3-morpholino-4,4-dimethylthietane dioxides[234]. The observed k_e/k_α values of about 1 for the *cis*-isomers demonstrate that the relief of strain energy (particularly in the more sterically hindered *cis*-series), through the formation of the α-sulfonyl carbanion and its inversion, promotes both exchange and isomerization. A plausible explanation for the greater H/D exchange rate in the *trans*-isomers can be envisaged in the particular position of the exchanging proton with respect to the sulfonyl OSO angle. The dependence of the H/D exchange rate of a proton α to sulfonyl or sulfinyl groups on its orientation relative to these groups is well established[232d].

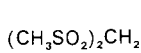
Ring-strain effects are known to enhance the acidity of hydrogens in α positions to functional groups capable of stabilizing a negative charge[233]. A comparison of the pK_a values[192] (in DMSO) of the sulfoxide-sulfone **7c** and the disulfone **7b**, 13.8 and 12.5 ± 0.08 respectively, with 15.0 ± 0.02 for **198** and 15.5 for **199**[235], demonstrates that similar effects are most probably operative in the cyclic thietane sulfoxide and sulfone systems. Both the 1,3-dithietane oxide (**184a**)[192] and the tetroxide **7b**[236] have been shown to undergo ready H/D exchange with $NaOD/D_2O$. Analysis of deuteriated **184a** indicated a 6:1 preference of 'axial' monodeuteriation over 'equatorial' monodeuteriation, in contrast to the predictions of the 'gauche effect theory' of greater reactivity for the quasi-equatorial protons gauche to both the S—O bond and the lone pair of sulfur[237].



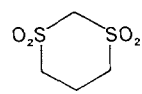
(**7c**)



(**7b**)



(**198**)



(**199**)

(**184a**)

Both thermal- and acid-induced equilibrations of 3,3-disubstituted thietane oxides were very slow ($K_{eq} \approx 10^{-5}\ s^{-1}$)[194]. The results suggest that thietane oxides are similar to the various acyclic sulfoxides with respect to the rates of thermally induced pyramidal inversion at sulfur[238], and that this inversion process, therefore, does not interfere significantly in the above exchange/racemization studies.

It is noteworthy that in spite of the demonstrated acidity of the α-hydrogens in thietane oxides and dioxides, attempted mono- or dialkylations of these systems have been unsuccessful thus far.

D. The Synthesis of Four-membered Ring Sulfoxides and Sulfones

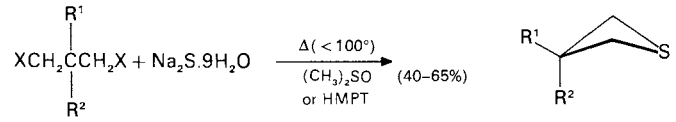
1. *Thietane oxides*

The method of choice for preparing thietane oxides is the oxidation of thietanes. This can be conducted using hydrogen peroxide, sodium hypochloride[194], sodium metaperiodate[66], $NaIO_4$[74c] and *m*-chloroperbenzoic acid[185].

The thietanes are most often prepared through ring closure of 1,3-dibromides or 1,3-disulfonate esters[193c,239,240], through fusion of cyclic carbonate esters of 1,3-diols with

thiocyanate ion[241], by base-induced cyclization of substituted 1,3-chlorothiols[193c], or by reduction of thietane 1,1-dioxides[74,143,242].

A typical sequence is described in equation 80[194,243].



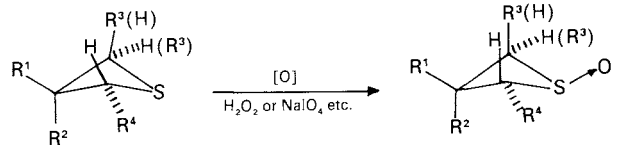
(80)

(200)

X = Br or $OSO_2C_6H_5$

(201a)

Oxidation of the thietanes provides thietane oxides (equation 81).



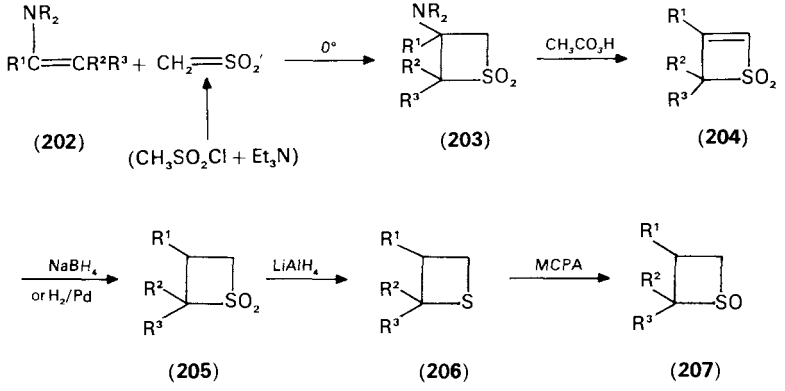
(81)

(201b, c) (5)

The oxidation results in mixtures of *cis*- and *trans*-isomers, the ratio of which is primarily sterically controlled[74]. The oxidant appears to approach the sulfur atom preferentially from the least-sterically hindered direction, so that the thermodynamically least stable isomers may occasionally predominate[74,194,244].

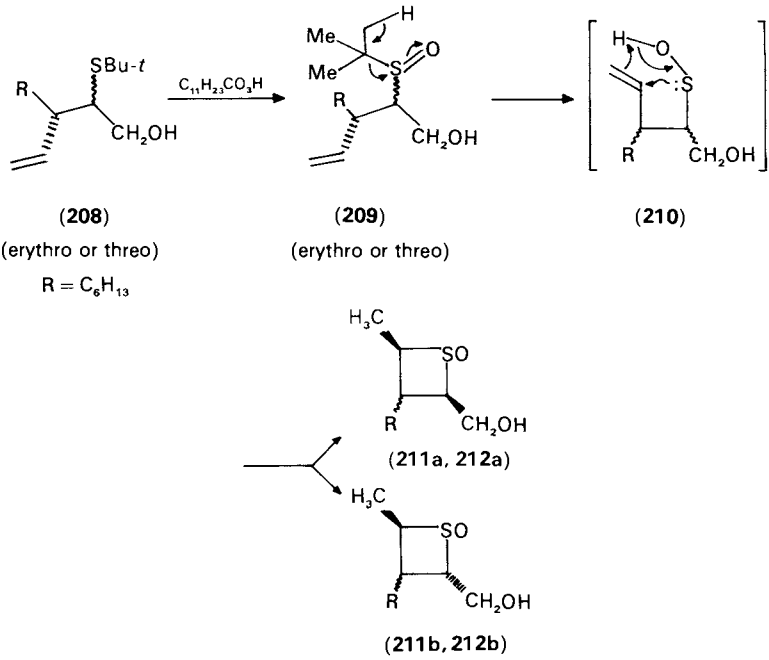
The base-induced cyclization of 1,3-chlorothiols to thietane[193c,226] followed by the oxidation of the latter is analogous in all respects to the strategy described above.

Thiete sulfones may be[74b] converted to the corresponding saturated thietanes and followed by oxidation of the latter to the desired sulfoxides[185] (equation 82). By chromatography, the mixture (**207**) can be separated to the *cis* and *trans* isomers.



(82)

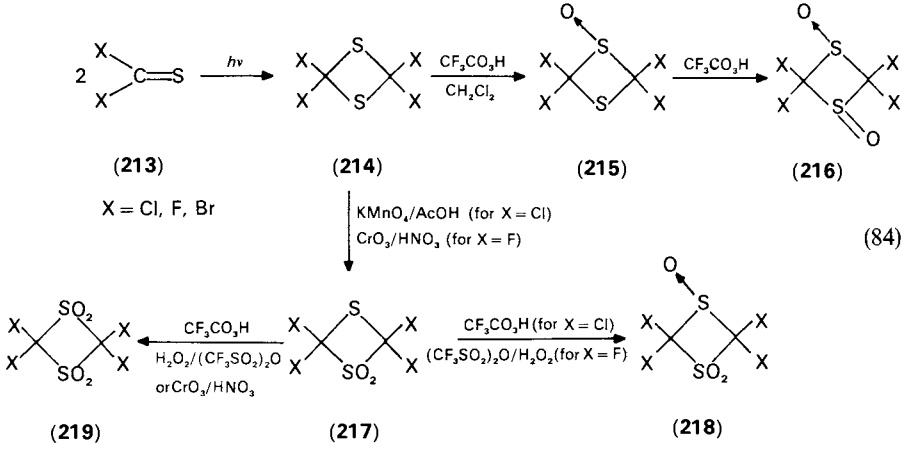
The addition of sulfenic acids to olefins[207] has been successfully applied in the synthesis of thietanoprostanoids, the thietane analogues of prostaglandin[245]. The general synthetic scheme is presented in equation 83[207]. The key step is the thermolysis of either *erythro*- or *threo*-2-*t*-butylsulphinyl-3-vinyl-1-ol (**209**) to give the corresponding alkenesulfenic acids **210**, which cyclize spontaneously to a mixture of stereoisomeric thietane oxides.



(83)

The synthesis takes advantage of the well-documented sulfoxide → sulfenate rearrangement[97,106], as well as of its retro-process, leading to cyclization and formation of the desired four-membered ring sulfoxide system (i.e. **211**, **212**). A closely related ring enlargement is based on the reversibility of this rearrangement and has found wide use in penicillin chemistry[246].

The syntheses of perhalogenated dithiethanes and their oxidation products (**214–219**) have been recently reported[247]. The method is based on the photochemical dimerization of thiophosgen or its fluoro- and bromo-analogues followed by partial oxidation with trifluoroperacetic acid to the desired sulfoxides (or sulfones)[248] as shown in equation 84.

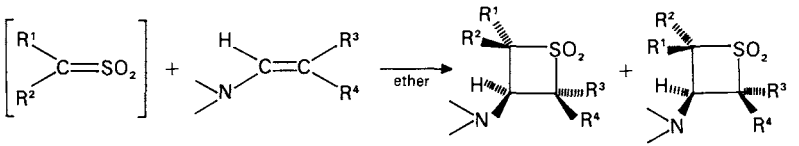


(84)

2. Thietane dioxides

Given any thietane, oxidation of the sulfur to a sulfone with peracids[202,203] or H_2O_2[74c] is straightforward and in most cases neither intervenes chemically with other sites nor alters the structural features or stereochemistry of the thietane ring.

It appears, however, that the most used strategy for the preparation of thietane dioxides is the [2 + 2] cycloaddition of enamines (**202**) with *in situ*-generated sulfenes (**220**)[74,143,186–188,202,242] to give β-aminothietane sulfones (equation 85).



(**220**) (**202**) (**a**) (**221**) (**b**)

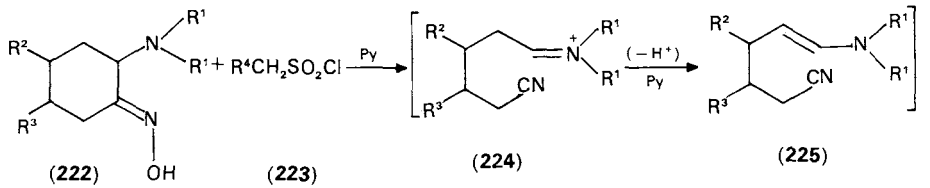
R^1 = Ar, Alkyl, ArCO, CO_2Et, CN, Hal $R^3 = R^4$ = Alkyl (*trans*) (*cis*)

$R^2 = CH_3$ or H (85)

Although the yields of the above reactions are high and the procedure is simple[186], there are some apparent disadvantages: the selection of the sulfene substituents R^1 and R^2 is limited, depending on the availability of the sulfonyl chloride precursors; the cycloaddition leads to a mixture of *cis*- and *trans*-substituted thietane dioxides; the cycloaddition reaction is reversible[202]; and several further transformations are necessary if a dioxide without 3-*N*-substituent is required.

The steric outcome in the above cyclization can be explained on the basis of either a zwitterionic intermediate[186,202] or a concerted [π2s + π2s] process[248], depending on the nature of the reactants[186]. Definite predictions are practically impossible as yet. The more stable *trans*-isomers (i.e. **221a**) can be obtained by stirring the isomeric mixture with catalytic amounts of potassium *t*-butoxide in *t*-butyl alcohol for several days[186].

A closely related procedure for preparing thietane dioxides is the one-step conversion of cyclic α-amino ketoximes (**222**) to 2-(ω-cyanoalkyl)-3-dialkylaminothietane dioxides (**226**), with *trans*-orientation of the substituents[249] (equation 86).



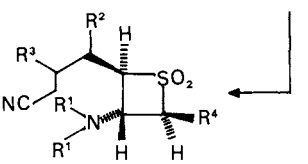
(**222**) (**223**) (**224**) (**225**)

(**a**) $R^2 = R^3 = H$

(**b**) $R^2 = H$, $R^3 = t$-Bu

(**c**) $R^2 = t$-Bu, $R^3 = H$

$R^4 = H$ or C_6H_5 (86)

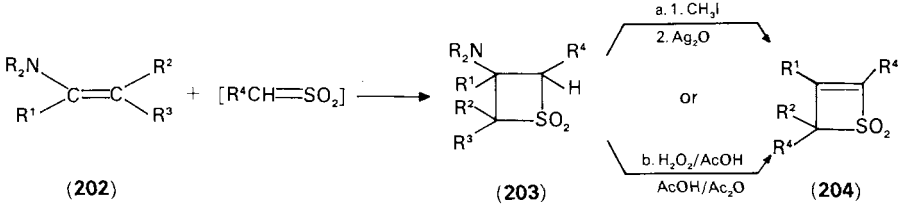


(**226**)

The scope of the above is rather limited, mainly because of the need to prepare the starting ketoximes **222** and the resultant specific pattern of the sulfone product.

3. *Thiete dioxides*

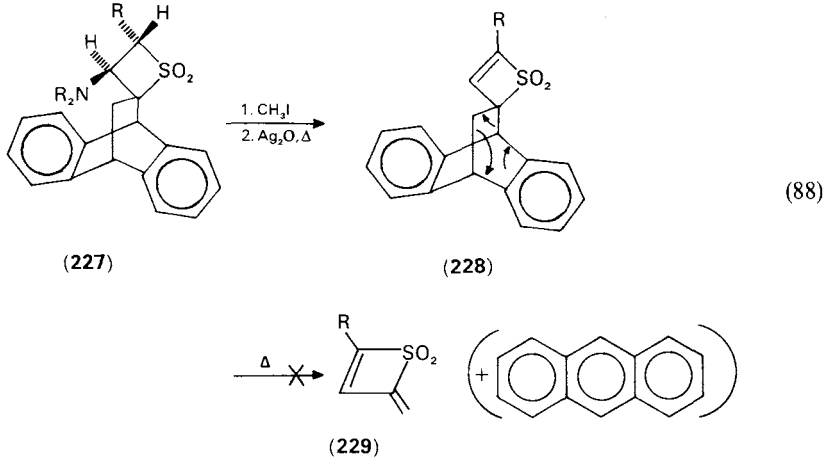
Practically speaking, almost all syntheses of these systems are based on the enamine–sulfene cycloaddition reaction[143,250]. The thietane sulfone thus obtained yields, by elimination of R_2NH, the desired unsaturated, four-membered sulfone system[187–189,231,250,251] (equation 87).



(202) (203) (204)

(87)

An attempted synthesis via a retro Diels–Alder route failed, due to the instability of the thiete sulfones at the temperatures required to remove the anthracene blocking group[189] (equation 88).

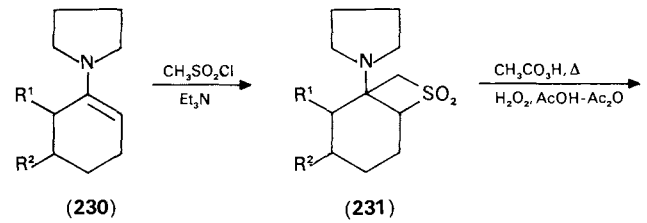


(227) (228) (229)

(88)

The Hofmann degradation approach (equation 87a) suffers from the fact that some aminothietane dioxides (**203**) display a propensity for ring cleavage when treated with methyl iodide, particularly when R^2 or R^3 are electron-withdrawing substituents[189]. *N*-oxide degradation, on the other hand, appears to be quite general, albeit giving rise to mixtures of isomeric thiete dioxides [189,250]. Hofmann degradations readily take place in water suspensions even without heating[188] and this method is probably the most convenient (and most used) to prepare thiete dioxides.

Thiete dioxides, in which the double bond is incorporated into an aromatic system (i.e. **234**), are made via the same strategy depicted in equation 87, except that the system is aromatized only at the last step[250–253] (equation 89).

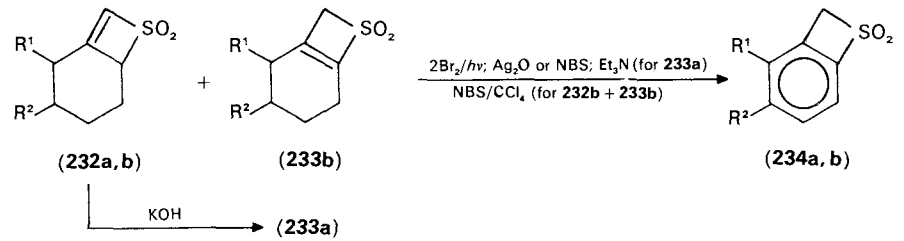


(230) (231)

(a) $R^1 = R^2 = H$

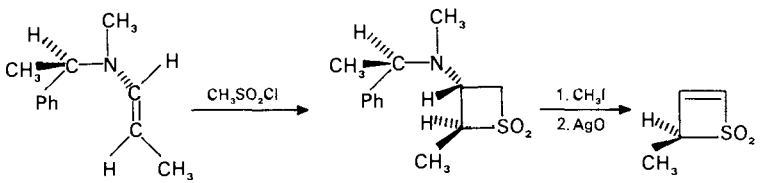
(b) $R^1R^2 =$ 

(89)



(232a,b) (233b) (234a,b) (233a)

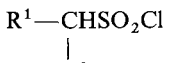
Asymmetric induction and the synthesis of optically active thietane and thiete dioxides can be achieved via the basic strategy depicted above (equation 87), by using optically active enamine in the first (2 + 2) cycloaddition[187] (equation 90). α-Halo and α,α-dihalo



(90)

R(+)(235) (236) S(+)(237)

thiete dioxides can be readily prepared by using α-halo and α,α-dihalosulfonyl chlorides (**238**) within the scheme of equation 87[254].

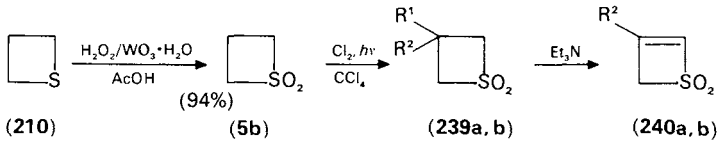


(**238**)

$R^1 = H, Cl, Br$

$R^2 = Cl, Br, I$

A preparation of 3-substituted thiete dioxides takes advantage of the commercial availability of the parent four-membered thietanes. The latter is oxidized to the sulfone, which in turn is photochemically mono- or di-chlorinated in the 3-position. The 3-chlorothietane dioxide (**239a**) can be easily transformed into the thiete dioxide, whereas the 3,3-dichloro homolog is transformed into the 3-chloro-2*H*-thiete 1,1-dioxide (**240b**)[255] (equation 91). **240b** reacts with carbanions, amines, alcohols and thiols to give the corresponding 3-substituted thiete dioxides[255].



(91)

E. Selected Chemical Reactions and Transformations

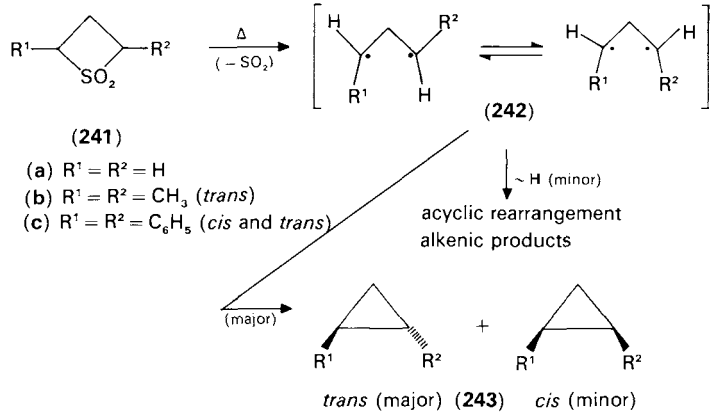
Several typical reactions of cyclic sulfoxides or sulfones are not observed in the acyclic and large-ring sulfoxide and sulfone analogues, or if they are, they take a different path. In such cases the effect of the cyclic sulfoxide or sulfone function is at least partially a consequence of the particular stereochemical constraints of the cyclic array.

1. Thermolysis

Acyclic sulfoxides fragment into olefins and sulfenic acids on thermolysis[97]. Cyclic sulfoxides exhibit essentially the same ready mode of fragmentation[106].

The main result of the thermolysis of the three-membered ring sulfoxides and sulfones is the extrusion of the sulfur monoxide and the sulfur dioxide moieties (Section III.C.1)[99,105]. Only in the presence of a suitably disposed β-hydrogen does the ordinary sulfoxide-sulfenic acid fragmentation take place in the thiirane oxide series (equation 9).

The dominant pattern for the thermal fragmentation of thietane dioxides involves extrusion of sulfur dioxide leading to a 1,3-diradical (i.e. **242**) which closes to final products, mainly cyclopropanes, accompanied by rearrangement products resulting from hydrogen migration within the diradical[191,193c,230,256–258] (equation 92).

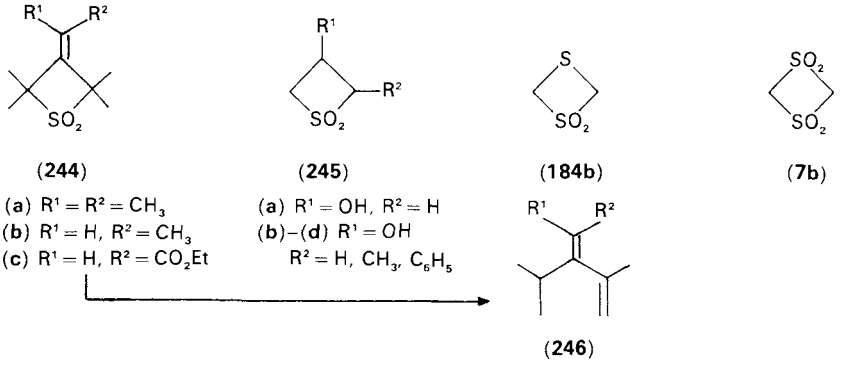


(92)

The reaction is not stereospecific and the product mixture of the *cis*- and *trans*-cyclopropane isomers (when applicable)[193c,230] approximates the expected equilibrium mixture at the temperatures of the pyrolysis[259].

Analogous results are obtained in the pyrolysis of 3-alkylidene-2, 2, 4, 4-tetramethylene-thietane dioxides[256] (**244**), 3-hydroxy and 3-keto thietane dioxides (**245**)[191], and 1,3-dithietane dioxides and tetroxides (**184b** and **7b**)[192]. The extrusion of both CO and SO_2 and the two SO_2 moieties in **245b–d** and **7b**, respectively, to give ethylene, the formation of

diene **246** in the pyrolysis of **244a–c**, of acetone in the pyrolysis of **245a**, and of thirane in the pyrolysis of **184b**, are all consistent with a mechanism involving a trimethylene radical intermediate.



(**244**) (**245**) (**184b**) (**7b**)

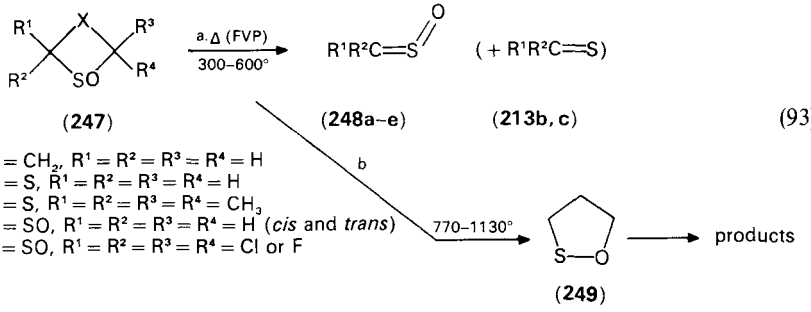
(**a**) $R^1 = R^2 = CH_3$
(**b**) $R^1 = H$, $R^2 = CH_3$
(**c**) $R^1 = H$, $R^2 = CO_2Et$

(**a**) $R^1 = OH$, $R^2 = H$
(**b**)–(**d**) $R^1 = OH$
$R^2 = H$, CH_3, C_6H_5

(**246**)

The reaction appears to take place via homolysis of the carbon–sulfur bond, facilitated by both ring strain and the relative ease of the SO_2 extrusion, to give the 1,3-diradical in an overall retro 3 + 1 process[258]. The latter can either ring close to form cyclopropanes (or cyclopropanones, or thiiranes, or thiirane dioxides, that may undergo further transformations) or, depending on the substitution pattern, give rise to hydrogen migrations (and/or other rearrangements) to yield stable unsaturated acyclic products.

In contrast, thermolyses of the four-membered ring sulfoxides do not eliminate sulfur monoxide[260] but undergo, almost exclusively, a retro 2 + 2 decomposition [simultaneous for a concerted ($\sigma_a^2 + \sigma_s^2$) process or stepwise for a process involving 1,4-diradical] leading to the generation of sulfines (i.e. **248**)[192,228,247a]. The formation of these low-molecular-weight, reactive, short-lived species can be detected by either mass spectrometry, microwave or photoelectron spectroscopy techniques[192], or through the actual trapping, isolation and identification of the final products (equation 93).



(**247**) (**248a–e**) (**213b, c**) (93)

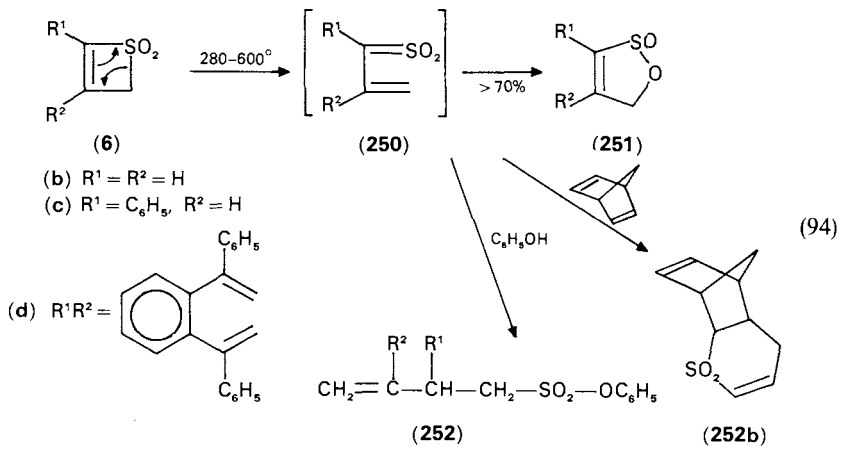
(**a**) $X = CH_2$, $R^1 = R^2 = R^3 = R^4 = H$
(**b**) $X = S$, $R^1 = R^2 = R^3 = R^4 = H$
(**c**) $X = S$, $R^1 = R^2 = R^3 = R^4 = CH_3$
(**d**) $X = SO$, $R^1 = R^2 = R^3 = R^4 = H$ (*cis* and *trans*)
(**e**) $X = SO$, $R^1 = R^2 = R^3 = R^4 = Cl$ or F

(**249**)

One exception to the above general fragmentation pattern is the formation of the ring-rearranged sulfenate (**249**) in the gas-phase thermolysis of thietane oxide (**247a**) at elevated temperatures[229]. Although the temperature of this thermolysis is considerably higher than those used in the other studies, it is difficult to account for the (not totally unprecedented[191]) difference in the results.

Stepwise decomposition of thietane oxides should be influenced by the relative stabilities of the developing radical centers, whereas the subsequent selection between

retro (3 + 1) and (2 + 2) routes should be influenced by the relative stability of the developing π systems. The stabilization of an adjacent (α-) radical center is in the order S > SO > SO_2, while the order of leaving abilities is the reverse, SO_2 > SO > S. Based on what is known of thermal ring opening of cyclobutenes (retro 2 + 2 intramolecular cycloaddition)[96], and on the behavior of thietane oxides and dioxides under pyrolytic conditions, the thermolyses of thiete sulfones have been explained in terms of a retro (2 + 2) concerted process, leading initially to sulfene intermediates, which can be trapped or are further rearranged under the reaction conditions to yield the observed final products[191,257,261] (equation 94).

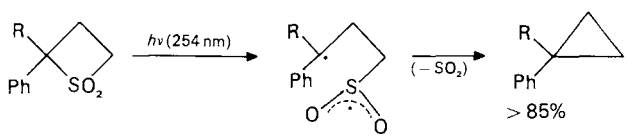


(94)

The formation of cyclic sulfinic esters (sultines) from vinyl sulfenes is known[191], and the trapping of the expected intermediate vinyl sulfene in the thermolysis of thiete dioxide (**6b** and **194**) has been convincingly achieved[231,262]. Specifically, thermolysis of thiete dioxide **6b** in the presence of norbornenes gave cycloadducts of the Diels–Alder type (i.e. **252b**), resulting from the trapping of the vinyl sulfene formed. The accumulated evidence thus supports the proposed mechanism for these thermolytic reactions.

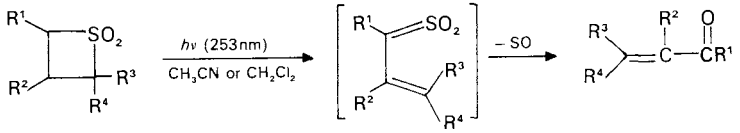
2. *Photolysis*

The photolyses of several 2-alkyl-2-phenylthietane dioxides in dichloromethane or methanol afforded excellent yields of 1-substituted 1-phenylcyclopropanes apparently via the same mechanism as in the parallel thermolyses[263a] (equation 95).



(95)

The phenyl substitution provides both the chromophore necessary for photoactivity and the stabilization of the initially formed radical. The reported photochemical extrusion of SO from 2,2,4,4-tetraacetylthietane[263b] to give the corresponding cyclopropane appears to be a unique case associated with the particular features of the irradiated molecule.



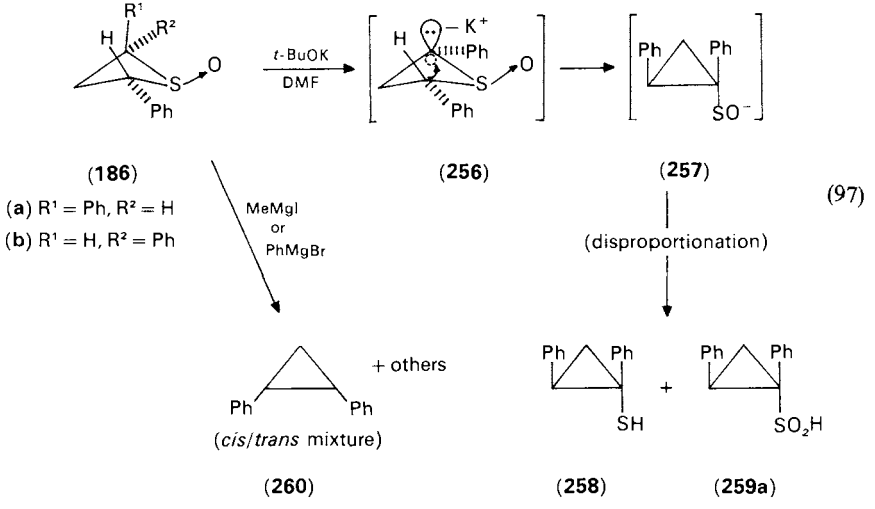
(6e) (250b) (255) (96)

The photolysis of various substituted thiete dioxides under similar conditions resulted in the formation of the unsaturated ketones (**255**)[264], most probably via a vinyl sulfene intermediate followed by a loss of sulfur monoxide as shown in equation 96. The same results were obtained in the thermolysis of **6e** ($R^1 = R^3 = Ph$; $R^2 = R^4 = H$)[231], which further demonstrates that similar mechanisms are operative in thermolyses and photolyses of thietane dioxides and thiete dioxides.

3. Rearrangements

Molecular rearrangements such as that of Stevens[248,265] or the sulfoxide → sulfinic acid, Ramberg–Bäcklund[15] or sultone → sultine rearrangements, are quite common in these classes of compounds.

Rearrangements closely resembling the Stevens rearrangement[248,265] have been investigated by applying Grignard reagents or potassium *t*-butoxide in dimethylformamide (low availability of protons) to *cis*- and *trans*-2,4-diphenylthietane oxides and dioxides[266,267]. The main results are summarized in equation 97 and 98.



(**186**) (**256**) (**257**) (97)

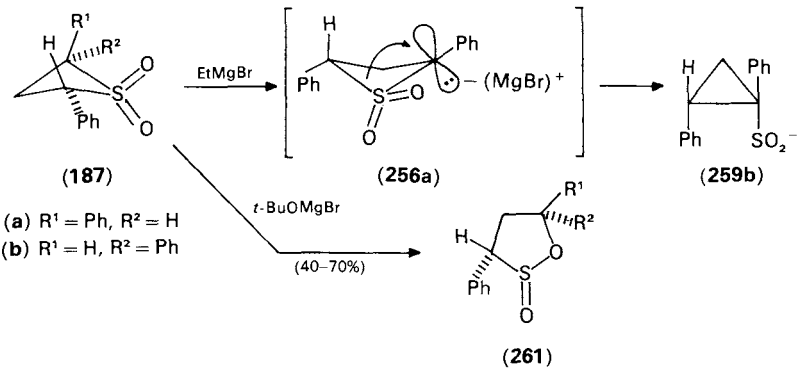
(**a**) $R^1 = Ph$, $R^2 = H$

(**b**) $R^1 = H$, $R^2 = Ph$

(**260**) (**258**) (**259a**)

Both (*cis*- and *trans*-) isomers rearrange stereospecifically to the *cis*-rearranged cyclopropane product (i.e. **257**), the processes being apparently controlled by the same *cis*-anion intermediate (i.e. **256**)

The α-sulfonyl carbanion (**256a**) rapidly formed from either isomer is stabilized by rearrangement to the *trans*-1,2-diphenylcyclopropane sulfinate (**259b**), so that the overall result is a highly stereoselective rearrangement process. In line with previous results, the ring enlargement (i.e. **187** → **261**) induced by the *t*-BuOMgBr is an example of a stereospecific sulfone → sultine rearrangement in a cyclic system.



(187)
(a) $R^1 = Ph$, $R^2 = H$
(b) $R^1 = H$, $R^2 = Ph$

(256a)

(259b)

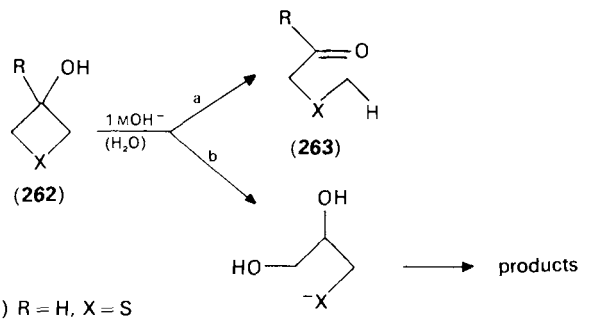
(261)

(98)

The relative stabilities of the species involved appear to be responsible for the stereochemical outcomes. Relief of ring strain must play a role in determining the course of the reaction. An explanation for the different reaction paths on using different Grignard reagents must wait further experimentation.

4. Eliminative fission of the thietane ring

The role of strain in determining reactivity in base-induced eliminative fission of the thietane ring (equation 99a), the nature of the transition state for ring opening, and the competition between eliminative fission and nucleophilic substitutive ring fission (equation 99b) have been recently studied[268]. The rates of eliminative fission were found to be 5×10^{-5} and $6 \times 10^{-1} - 6 \times 10^{-3}$ $M^{-1} s^{-1}$ for the thietane oxides (**262b,d**) and thietane dioxides (**262c,e**), respectively. The thietane **262a** under these conditions undergoes the substitutive ring fission alternative (equation 99b) at higher temperatures and at a slower rate. Thus, the reactivity is to be associated with the capacity of the functional group to stabilize a carbanion adjacent to the carbon that is detached in the ring cleavage. The observed accelerations, compared with rates of about 10^{-9} in the cyclobutanol series[269], are presumably offset by the lower strain energy of thietane (81.9 kJ mol^{-1}) compared with that of cyclobutane (106.2 kJ mol^{-1}). By comparison of the reactivities of the cyclic sulfoxide and sulfone (**262d,e**) with those of their acyclic counterparts [e.g., about 10^{-8} and



(262)

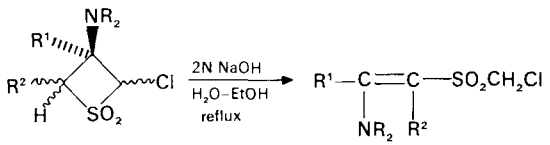
(263)

(264)

(99)

(a) R = H, X = S
(b) R = H, X = SO
(c) R = H, X = SO_2
(d) R = C_6H_5, X = SO
(e) R = C_6H_5, X = SO_2

10^{-5} for $C_6H_5C(OH)HCH_2XCH_3$; X = SO and SO_2, respectively], the effect of ring strain is estimated at about 5×10^4 for the sulfoxide and sulfone [268]. The increased rate of fission in the phenyl-substituted thietanes reflects the apparent relief of larger amounts of ring strain in these cases (as a result of increased initial steric interactions between ring hydrogens and substituents). Other 3,3-disubstituted thietane dioxides were shown to undergo base-induced eliminative ring fission similar to that discussed above. The ring opening is observed only if position 4 is mono-substituted (so that a carbanion can be formed there), and position 3 is di-substituted (to make the α,β dehydrohalogenation impossible)[270] (equation 100).

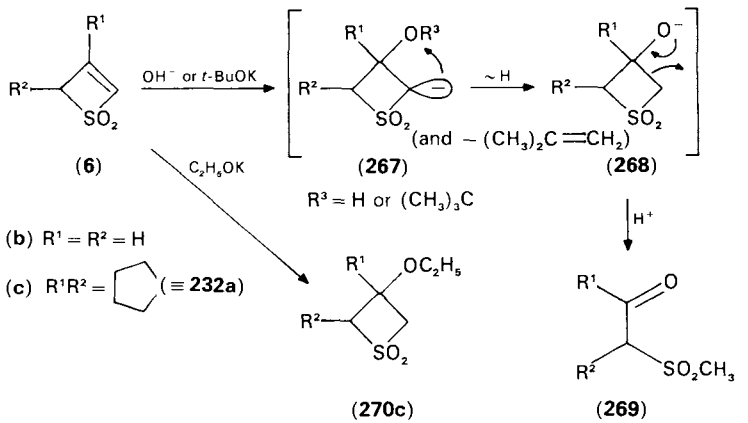


(100)

(265) (266)

(a) $R^1 = C_6H_5$, $R^2 = H$
(b) $R^1 = C_6H_5$, $R^2 = CH_3$

Base-induced eliminative ring fission, in which both the double bond and the sulfone function take part, has been observed in thiete dioxides[253]. The reaction can be rationalized in terms of initial Michael-type addition to the double bond of the ring vinyl sulfone, followed by a reverse aldol condensation with ring opening. The isolation of the ether **270c** in the treatment of **6c** with potassium ethoxide (since the transformation **267** → **268** is not possible in this case) is in agreement with the reaction mechanism outlined in equation 101[253].



(101)

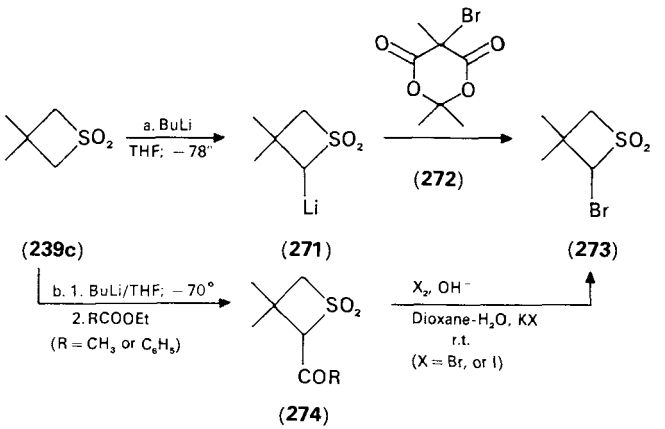
Interestingly, isomerization of the double bond in thiete sulfones can be accomplished by their treatment with strong bases (e.g. KOH) in aprotic solvents[253].

5. α-Halogenation

The α-halogenation of sulfones is not a straightforward reaction, since (a) the carbon is at best partially positively charged due to the strong electron-withdrawing capacity of the

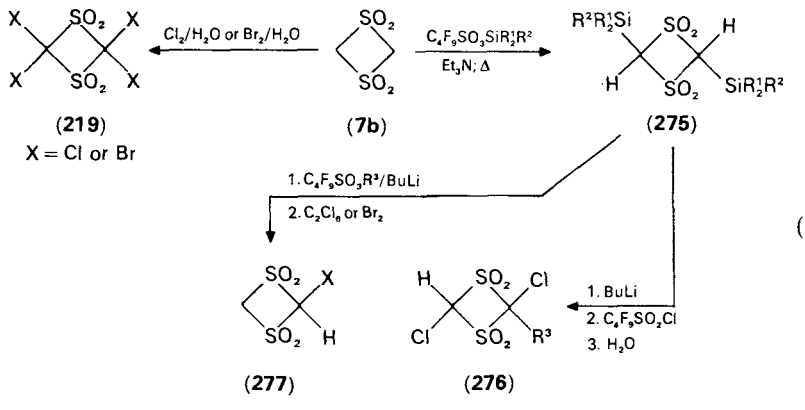
adjacent sulfone group; (b) the α-hydrogens are nonenolizable; and (c) some steric hindrance is expected to be exerted by the sulfone oxygens on the approaching halogenating agent. The α-halogenation of various acyclic and bicyclic sulfones can be achieved, however, by the halogenation of the initially generated α-sulfonyl carbanions[271].

The lithio-α-carbanion readily generated by the treatment of thietane dioxides with BuLi failed to react with all conventional halogenating agents (Br_2, Cl_2, NBS or *N*-chlorobenzotriazole)[272]. Successful halogenation could be affected, however, by treating the α-carbanion with the 5-methyl, 5-bromo derivative of Meldrum's acid **272**[272,273]. Thietane dioxides can be monoacylated by using esters and employing essentially the same procedure. The resulting monoacylthietane dioxides (i.e. **274**) can be easily transformed to the corresponding α-halothietane dioxides by treatment with basic aqueous solutions of the desired halogen (equation 102b)[274].



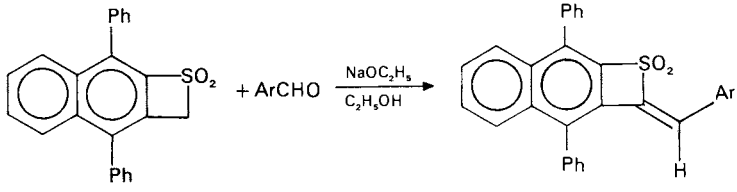
(102)

The 1,3-dithietane tetroxides (**7b**) readily undergo tetra-α-halogenation[275] with either Br_2 or Cl_2, but not with I_2. Partial α-halogenation in this series can be accomplished indirectly by starting from either 2,4-bis(trimethylsilyl)- or 2,4-bis(*t*-butyldimethylsilyl)-1,3-dithietane tetroxides (**275**) as shown in equation 103[275]. In all of the above reactions one takes advantage of the highly acidic α-hydrogens and, consequently, the



(103)

facile *in situ* formation of the reactive α-sulfonyl carbanions. By analogy to α-halogenation, condensations of thiete dioxides with aldehydes yields α-methylidene thiete sulfones (**279**). Here again the particularly acidic α-hydrogen and the formation of the stabilized α-carbanion[227] have been utilized[276] (equation 104).

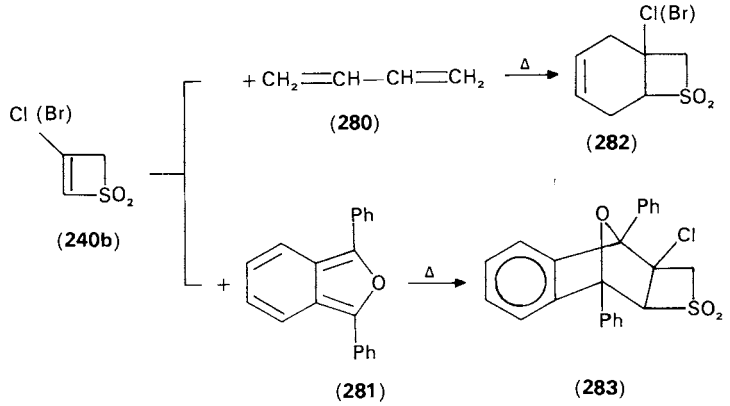


(104)

(**196a**) (**278**) (**279**)

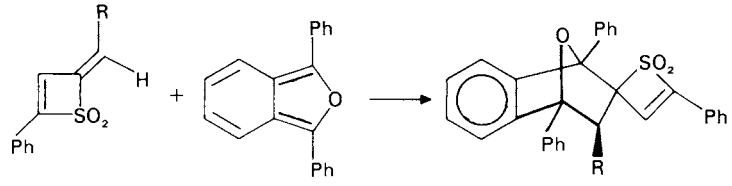
6. Cycloaddition reactions

Based on the high dienophilicity of acyclic vinyl sulfones one should expect thiete dioxides to exhibit similar properties. Indeed, several Diels–Alder (2 + 4) cycloadditions with thiete dioxide as dienophile are known. For example, 1,3-butadiene and 1,3-diphenylisobenzofuran react with 3-chloro- or 3-bromo-thiete dioxides to afford the corresponding 1:1 Diels–Alder cycloadducts[255,277] (equation 105).



(105)

Equimolar quantities of methylidene thiete (**284a**) and phenylisobenzofuran afforded a *single* crystalline spiro-cycloadduct (**285a**), and a similar result was obtained with thiete **284b**[242b] (equation 106). Clearly, the Diels–Alder additions with these thietes prefer (essentially exclusively) the involvement of the exocyclic double bond as the dienophile, which suggests steric control (associated with the bulky sulfone group) in the transition states. Inspection of the two theoretically possible transition states[242b] indeed corroborates this conclusion. Irradiation of thiete dioxide **284a** afforded a single crystalline *trans*-photodimer (as far as the two sulfonyl groups are concerned) with the cycloaddition having occurred between the two *exo*cyclic double bonds of the monomers. This photodimerization is a symmetry-allowed (2 + 2) cycloaddition[248] in which the high degree of symmetry observed in the process is a consequence of an arrangement with the minimal steric interference of the two sulfone groups in the most favorable transition state.



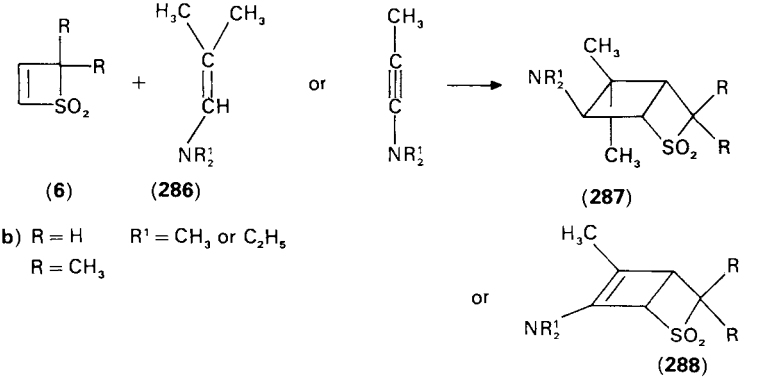
(106)

(284)
(a) R = H
(b) R = Ph

(281)

(285a,b)

As expected, 1:1 (2 + 2) cycloadducts are obtained in the reactions of thiete dioxides with some typical electron-rich olefins, e.g. enamines and ynamines, although this cycloaddition has not proven to be general[190].



(107)

(6)

(b) R = H R = CH_3

(286) $R^1 = CH_3$ or C_2H_5

(287)

(288)

The steric effect generated by the gem-dimethyl group of the thietane ring on the adjacent sp^2 carbon atom makes the cycloaddition in these cases more sluggish compared with those of the parent thietane dioxide (**6b**)[190]. These cycloadditions provide a convenient entry into the strained thiabicyclo [2.2.0] hexane system (e.g. **287**, **288**; equation 107).

Cycloadditions of the 1,3-dipolar nitrile oxides and diazoalkenes to acyclic vinyl sulfones are in general highly selective, the particular regioisomer formed depending on the substituents of both reactants[213,214]. Nitrones, on the other hand, tend to yield mixtures of the two possible isomers (see equation 78).

3 + 2 Cycloadditions of nitrones, nitrile oxides or diazo compounds to thiete dioxides do not show the high stereoselectivity observed with acyclic vinyl sulfones, and mixtures of the two possible adducts are formed[213,214,278]. The charge-transfer stabilization energy calculated according to the Klopman–Salem perturbational approach[215] is able to account for the experimental trends of the isomer ratio in terms of the major stereochemical structural differences between the acyclic vinyl sulfones and the four-membered ring sulfones[214] (see Section IV.B.3).

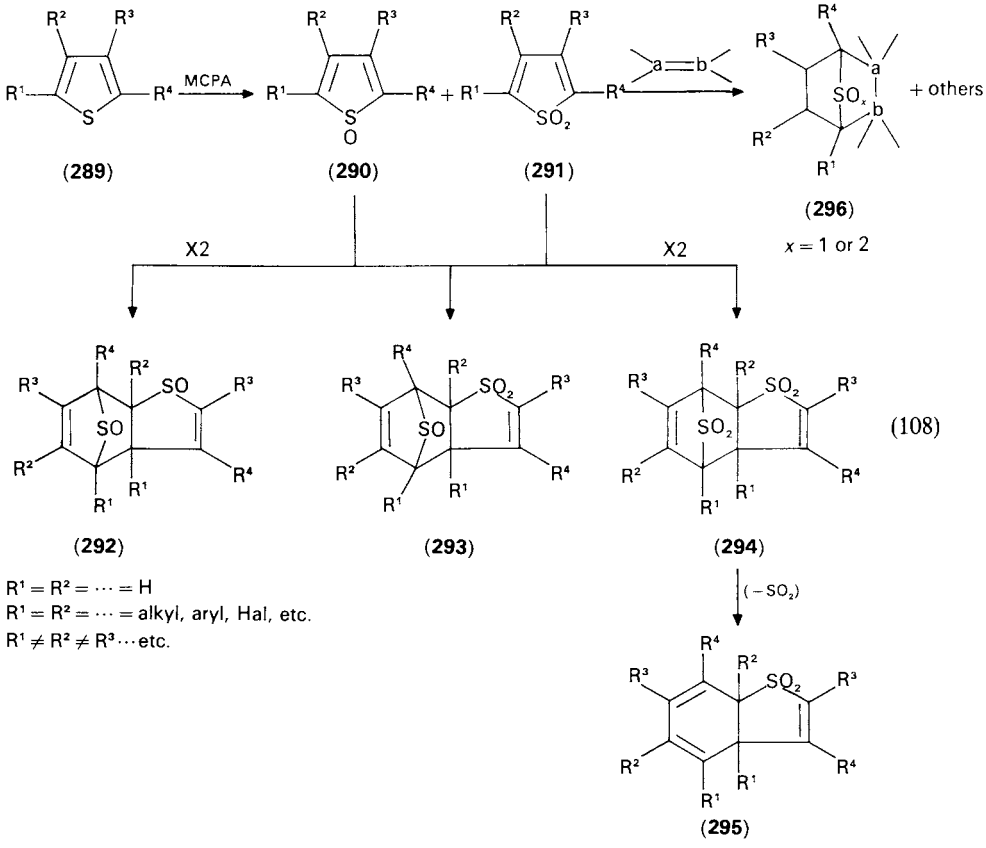
V. FIVE-MEMBERED RING SULFOXIDES AND SULFONES

A. Introduction and Scope

The enormous literature of five-membered ring systems containing sulfur primarily describes the synthesis, properties and chemistry of thiophene and its derivatives[279].

Thiophene oxides and dioxides have recently been thoroughly reviewed[280,281].

Oxidation of thiophene to the corresponding oxide and dioxide, i.e. **290** and **291** (MCPA appears to be the reagent of choice[282,283]) results in loss of aromaticity in the latter, giving rise to the formation of reactive electron-deficient diene systems 'locked' in the cisoid configuration. It is not surprising, therefore, that the bulk of the chemistry associated with these molecules involves either self-Diels–Alder-type cycloadditions of the *in situ*-generated oxidized reactive species, or their facile cycloaddition with both dienophiles and dienes as illustrated in equation 108[280,281]. Diene character and tendency toward Diels–Alder additions were calculated to be less for thiophene oxides than for thiophene dioxides[284], the ready dimerization of the latter being rationalized in terms of second-order perturbation theory[285] and spiro-conjugation[53a]. Experimentally, however, thiophene oxide is much more reactive as a diene than thiophene dioxide[286,287].



(108)

The existence or nonexistence of conjugative effects involving the sulfone group in thiophene dioxides (a problem analogous to that in thiirene oxide and dioxide systems[2,11]) has been the subject of many studies resulting, nonetheless, in no unequivocal conclusion[280].

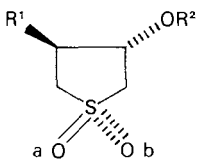
Here, only few selected aspects associated with these systems, particularly those having generalizability and/or which provide a better understanding of the sulfoxide and sulfone functionality within cyclic systems (and/or not dealt with in References 280 and 281) will be

briefly reviewed. The discussion of five-membered ring sulfoxides and sulfones containing additional heteroatom(s) and/or sulfoxide or sulfone groups is beyond the scope of this chapter.

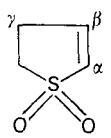
B. Physical Studies (NMR, IR and p*K*)

Oxygen-17 NMR spectroscopy has an immense potential for structural analysis of cyclic sulfoxides and sulfones as well as for providing insight into the nature of bonding within these two functional groups[288]. Indeed, in addition to data concerning the ^{17}O NMR chemical shifts for several cyclic sulfoxides and sulfones, ^{17}O NMR chemical shift differences between several diastereotopic sulfonyl oxygens in both cyclic and acyclic systems have been reported[70,289].

The ^{17}O NMR spectra of 4-alkoxythiolane dioxides (**297**) indicate that the sulfonyl oxygens have little influence on the chemical shifts of the 'etheral' oxygen, but that the sulfonyl oxygens are diastereotopic, with the chemical shift differences ($\Delta\delta_{a,b}$) being independent of the structure of the alkyl group in the moiety[280]. The oxygen *cis* to the alkoxy *oxygen* (O_b) was shown to be the more deshielded.



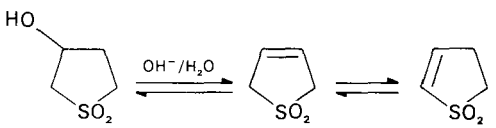
(**297**)



(**298**)

$R^1 = H,\ OCH_3,\ OC_2H_5,\ OC_3H_7^i,$ etc.
$R^2 =$ alkyl

Although the $\Delta\delta_{a,b}$ (i.e. $\delta O_b - \delta O_a$) was rather small (≈ 1.55 ppm), the shift-reagent $Eu(fod)_3$ enhances the ^{17}O chemical difference substantially, and shifts both oxygens upfield (the least sterically hindered sulfonyl oxygen is more responsive to the shielding). α,β but not β,γ unsaturation in the molecule [i.e., the double bond in thiolene (**298**)] deshielded the sulfonyl oxygens, in both five- and six-membered rings[290]. The utility of ^{17}O NMR in the thiolene dioxide series was further demonstrated by the determination of the base-induced equilibrium in equation 109. ^1H NMR has been used to assign configuration to stereoisomeric sulfoxides. The chemical shift of the β-hydrogen was found to be strongly dependent on the spatial relationship between the β-hydrogen and the sulfoxide group. The field effect and the magnetic anisotropy of the sulfoxide group result in deshielding of the β-proton in the *cis*-position to the sulfoxide oxygen[291].



(6%) (56%) (38%)

(**297b**) (**299**) (**298**) (109)

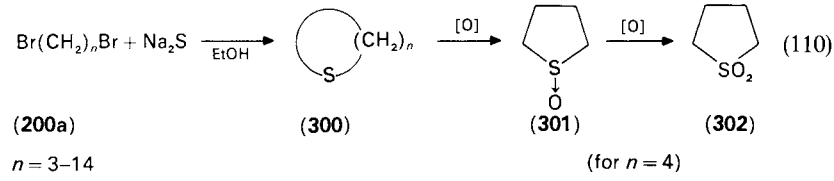
A long-range proton coupling, which was found to be transmitted by a sulfone group in thiolane dioxide systems[292], is apparently facilitated by a nonbonding *p*-orbital on one of the sulfone oxygen atoms. This phenomenon is of interest for saturated cyclic systems.

IR spectra of thiolane oxides in the solid phase were shown to be most outstandingly different in the sulfoxide region depending on the particular crystalline state/structure[291b], a fact which can be used to advantage for conformational analysis. Also, as one could expect, the sulfoxide absorptions indicate strong hydrogen bonding.

Finally, since besides the inductive effect of the sulfoxide and the sulfone functional groups, hydrogen bonding, field effects and steric effects to solvation may or may not work in the same direction, the pK_α values can be useful in assigning configurations of suitable pairs of stereoisomeric sulfoxide and sulfone carboxylic acids[291].

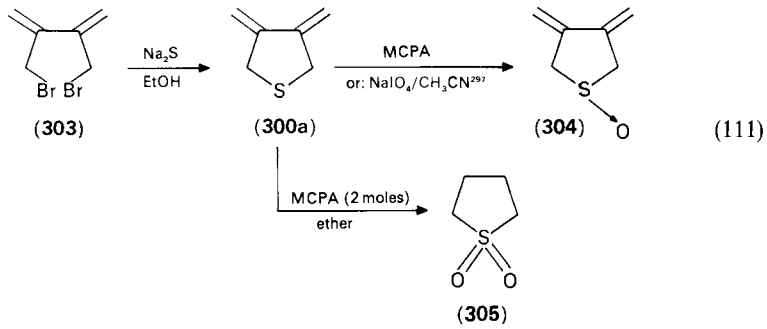
C. The Synthesis of Five-membered Ring Sulfoxides and Sulfones

The reaction of α,ω-dihaloalkanes with sulfide ion under high dilution conditions is the method of choice for the synthesis of five- and six-membered ring sulfides[243,293]. The oxidation of the formed thiolanes to the corresponding thiolane sulfoxides and/or sulfones by common oxidizing agents is simple and straightforward. This synthetic sequence constitutes the common route for the synthesis of sulfur-containing cyclic systems having ring size of four up to fifteen[243] (and most probably even more; see equation 110). The method has been successfully applied to prepare several 3,4-dimethylenethiolanes[294] that are interesting as starting materials in numerous cycloadditions or as potential precursors of the tetramethylenemethane biradical[295] through the thermal or photolytic extrusion of sulfur monoxide or dioxide[296] (equation 111).



(200a) (300) (301) (302) (110)

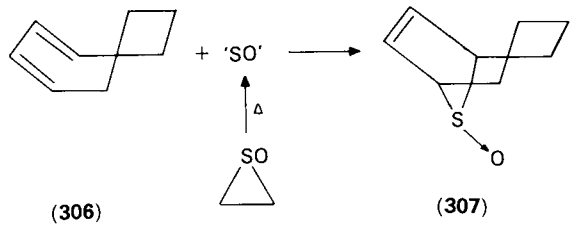
$n = 3$–14 (for $n = 4$)



(303) (300a) (304) (111)

(305)

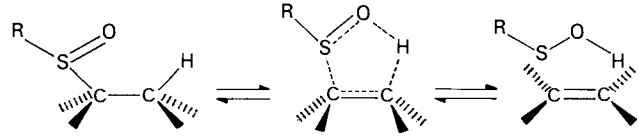
Two attractive routes to thiolene oxide and dioxide are the diene-SO[104] and diene-SO_2[298] cycloadditions, respectively. These cycloadditions are highly stereoselective at both carbons of the diene systems and at sulfur (see equation 62 for specifics) which, in the case of sulfoxide formation, proceed via attack of triplet SO on the diene. Equation 112 shows an example of such a cycloaddition[104]. The overall yields are significantly improved by running the cycloadditions in the absence of oxygen and by the use of excess diene.



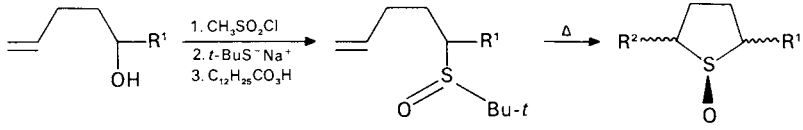
(306) (307) (112)

Since sulfoxides and sulfones are versatile synthetic intermediates, and since in both the thiolene oxide and dioxides the reverse dethionylation[114] (– SO), and cheletropic extrusion of sulfur dioxide[296], respectively, readily take place thermally, these cycloadditions are expected to find a useful place in organic synthesis. It should be kept in mind, however, that the retrograde SO-diene reaction and interconversion of the thiolene oxides compete effectively against SO extrusion on heating, and that diene isomerization accompanies the forward reaction (SO + diene).

A method for the stereospecific synthesis of thiolane oxides involves the pyrolysis of derivatives of 5-*t*-butylsulfinylpentene (**310**), and is based on the thermal decomposition of dialkyl sulfoxides to alkenes and alkanesulfenic acids[299] (equation 113). This reversible reaction proceeds by a concerted *syn*-intramolecular mechanism[246,300] and thus facilitates the desired stereospecific synthesis[301]. The stereoelectronic requirements preclude the formation of the other possible isomer or the six-membered ring thiane oxide (equation 114). Bicyclic thiolane oxides can be prepared similarly from a cyclic alkene[301].



(308) (113)



(309) (310) (301) (114)

(a) $R^1 = H$

(b) $R^1 = CH_3$

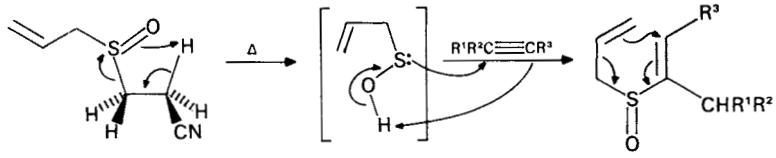
(a) $R^1 = H$, $R^2 = cis\text{-}CH_3$ (with reference to O)

(b) $R^1 = R^2 = cis\text{-}CH_3$

(c) $R^1 = trans\text{-}CH_3$, $R^2 = cis\text{-}CH_3$

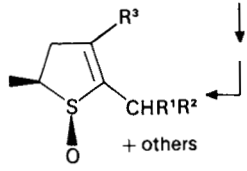
A closely related method is the thermolysis of 1-allylsulfinyl-2-cyanoethane in alkynes, which leads to the formation of thiolane oxide derivatives via consecutive pericyclic reactions[302]. The low yield and formation of mixtures are somewhat compensated for by the convenience, but its practicality is as yet rather limited (equation 115).

It is noteworthy that, based on the sulfoxide–sulfenic acid rearrangement, the readily accessible 1, 3-dithiolane systems (**316**) may be utilized (equation 116) as an efficient entry into the 1, 4-dithiane series[303], including the construction of carbocyclic fused systems[304]. The oxidation of the dithienes **318** to the corresponding sulfoxides (**319** and **320**) and sulfones is a simple, straightforward process.

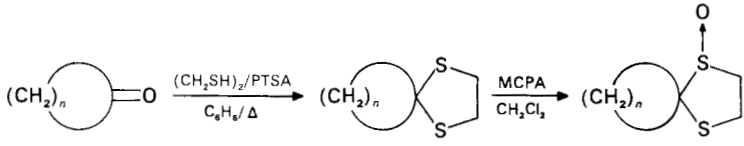


(311) (312) (313) (115)

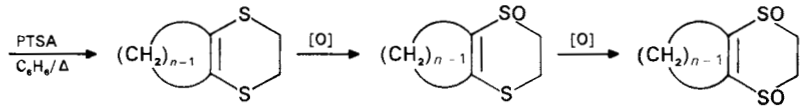
$R^1 = H$, $R^2 = C_6H_{11}$
$R^3 = H$ or CO_2Me



(314)

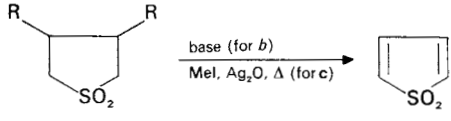


(315) (316) (317) (116)



(318) (319) (320)

Similarly, the most common method of preparing the substituted, fully unsaturated thiolane system, e.g. thiophene dioxides, is by direct oxidation of the readily available substituted thiophenes with hydrogen peroxide, perbenzoic acid and *m*-chloroperbenzoic acid[280–283]. Alternatively, thiophene dioxides are conveniently prepared via the 'double elimination' methodology[280,305] illustrated in equation 117.



(117)

(321)

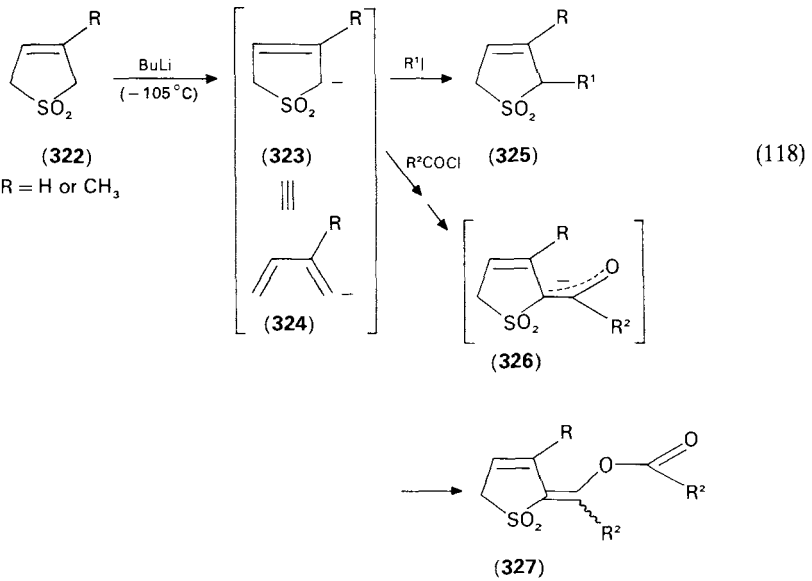
(**302a**) R = Br or Cl

(**302b**) $R = NMe_2$

D. Selected Chemical Reactions

1. Alkylation/acylation of 3-thiolenes

Treatment of 3-thiolenes with BuLi provides the 2-anion **323**, which may act as a butadiene 1-anion equivalent (i.e. **324**)[306]. Treatment of **323** with alkyl halide gives the 2-alkylated product (**325**) in high yield[306,307] (see equation 118). Acylation of **323** leads to the products **327** in which the acylated anions formed *in situ* under the basic conditions have undergone further acylation[306].



(118)

The success of the above alkylation and acylations, without obtaining ring-opening products[308], extends the usefulness of this method particularly when the anion **323** is being used in a regio- and stereo-specific manner[306,309]. Thus, the combination of direct alkylation and thermal extrusion of sulfur dioxide provides an ideal route for the preparation of terminally substituted conjugated dienes.

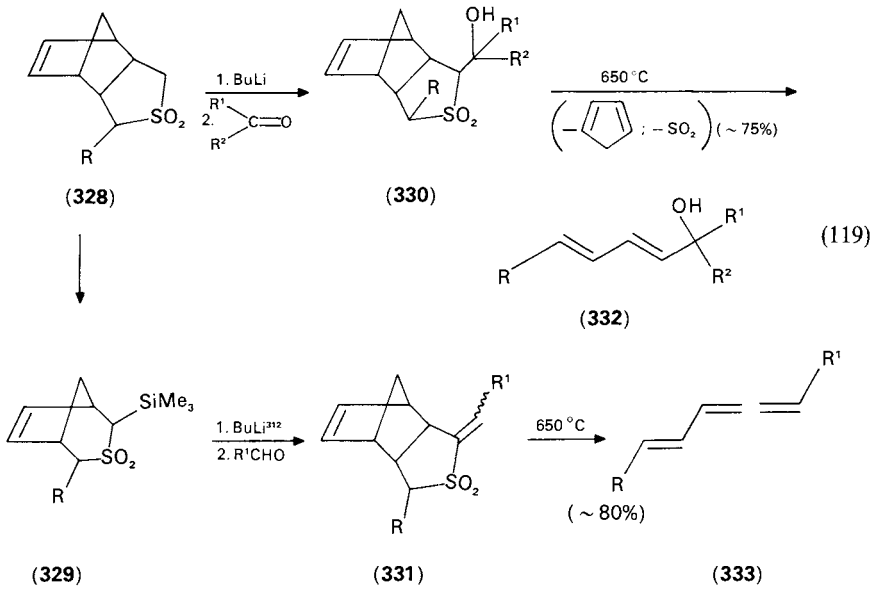
2. Functionalization of conjugated dienes

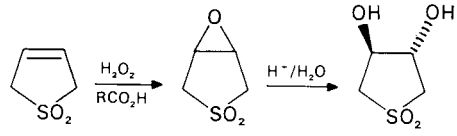
Based on the facile formation and reactivity of **323**, and the retro Diels–Alder reaction of **325**[306,310], a simple procedure has been developed for the stereoselective synthesis of functionalized conjugated dienes as well as vinylallenes[311] (see equation 119).

3. Epoxidation of thiolene dioxides

When 3-thiolene dioxide is treated with hydrogen peroxide, the corresponding epoxide is obtained[313]. The 3,4-*trans*-diols can be obtained by hydrolysis under acidic conditions (equation 120).

The cycloaddition reactions of thiophene oxides and dioxides (**290** and **291**[280,281]) have already been discussed (Section V.A).





(120)

VI. SIX-MEMBERED RING SULFOXIDES AND SULFONES

The distorted sp^3 angles at both carbon and sulfur atoms in small ring sulfoxides and sulfones approach their 'normal' size beginning with the thianes. Consequently, the characteristics and chemical behavior of six- and higher-membered sulfoxides and sulfones are expected to be similar to those of the acyclic counterparts. However, in view of the constraints imposed by the cyclic array, three issues deserve study:

(a) The chair (twist) boat conformational preference/equilibrium once the sulfur atom is incorporated into the cyclohexane ring skeleton, and the physical-chemical consequences of the various conformations adopted by the molecule.

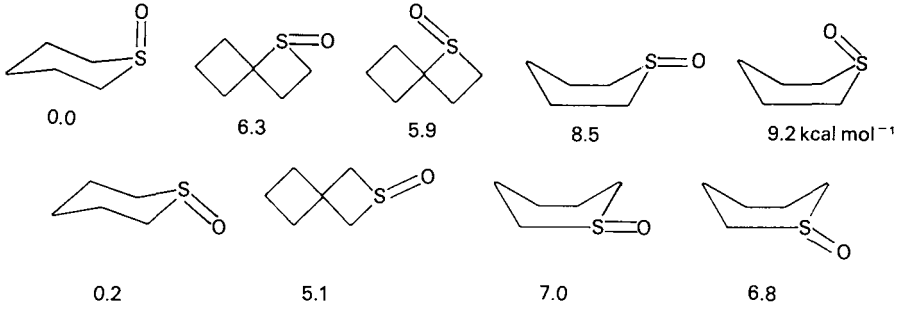
(b) The axial/equatorial orientation of the sulfur–oxygen bond in thiane sulfoxides and the direction/orientation preferences in reactions in which sulfoxide or sulfone groups are involved.

(c) The role of steric hindrance in modifying and/or altering the course of reactions in thianes compared to those in analogous acyclic systems.

A. Conformational Analysis

The molecular mechanics method[314] has been applied to the calculation of conformational properties of the thiane, dithiane and trithiane oxide systems[315], which are

expected to differ considerably from those of cyclohexane[316]. It was calculated that the chair form of thiane oxide is more stable than the twist form by more than 5 kcal mol^{-1}, and for the chair, the axial orientation of the oxygen atom is more stable than the equatorial by about 0.15 kcal mol^{-1} [315].



Other studies have also established the preference of the chair conformation with the oxygen in the axial position[317,318]; the rationale for this preference is different from the 'attractive interaction between the sulfoxide oxygen and the *syn*-axial hydrogens' proposed previously[318b]. Rather, a *repulsion* effect is advocated[315]: the equatorial oxygen is squeezed between four vicinal hydrogens, while there are only two corresponding repulsions if it is in the axial position. The correlation between the predicted[315] and observed[318a] conformational/orientational preferences in 3,3-dimethylthiane oxide (e.g., equatorial preference in the chair conformation) corroborates this interpretation. The axial preferences of the sulfur–oxygen bond in the thiane oxide is reversed in 3,3-dimethylthiane oxide because of the *syn*-axial interaction. 4,4-Dimethylthiane oxide, however, maintains a predominance of the axial isomers as deduced from the analysis of NMR data[318a].

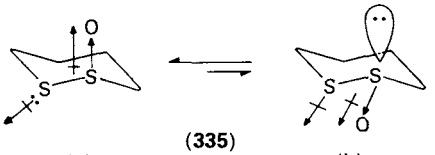
The same preferences have been calculated[315] and observed[319] in the 1,2-dithiane oxide system. Although the chair forms are also more stable than the twist or boat in 1,3-, 1,4-dithianes and 1,3,5-trithianes, the preference of the oxygen is highly variable, depending on steric and electronic interactions.

Examination of the NMR spectrum of thiane 3,3,5,5-d_4 oxide enabled the estimation of the axial/equatorial equilibrium constant[317]. The value was found to be 1.62 (at $-90\,^{\circ}C$), corresponding to a free-energy difference of 0.175 kcal mol^{-1}, which is in good agreement with field force calculations[315].

The substitution of a heteroatom for an α-sulfoxy methylene group substantially increases the preference for an axial orientation of the sulfoxide oxygen[320], despite the smaller space requirement of the sulfur with its lone pairs, compared to that of a methylene group[321], at least in the case of 1,3-dithiolane oxides. The substituting heteroatom, therefore, should decrease the conformation stability (i.e. lower the barrier to chair–chair interconversion).

Based on NMR data that were interpreted in terms of one conformationally pure form of the 1,2-dithiane oxide **335** that is not undergoing interconversion, it was suggested[319] that the strong axial preference of the sulfur–oxygen bond results from a dipolar interaction; that is, an unfavorable dipolar arrangement in the case of the equatorial orientation is relieved with the sulfur–oxygen bond adopting an axial configuration (an anomeric effect; equation 121).

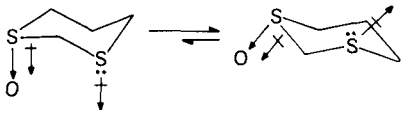
The conformational preferences of six-membered cyclic sulfoxides are strongly dependent upon the nature of the other ring atoms, especially in 1- and 3-positions[322]. Indeed, molecular mechanics calculations indicate that most of the energy difference between the



(335)

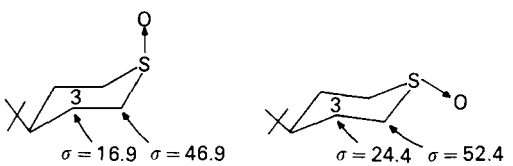
(a) (b) (121)

equatorial and axial conformations of **336** arises from dipole–dipole interactions[315], which explains the preference for conformation **336b** (see equation 122).



(a) (**336**) (b) (122)

X-ray structure determination of *cis*- and *trans*-2-phenyl-1,3-dithiane oxides showed them to adopt chair conformations with equatorial phenyl groups, and demonstrated the importance of transannular dipolar interactions as structure determinants[323]. The analysis of ^{1}H- and ^{13}C-NMR parameters of the thiane-3-one oxides reveals the chair conformation and axial preference of the sulfur–oxygen bond[85,324]. Introduction of a sulfur at the remaining β-position of these systems increases the amount of the equatorial conformer. It was concluded that orbital–orbital interactions may well be dominant factors in these systems, since simple steric and dipolar effects are not sufficient to account for the observed differences[324]. ^{1}H- and ^{13}C-NMR studies showed that the *axial* S=O conformers indeed dominate the conformational equilibria of 1,2- and 1,4-dithiolane oxides, whereas the *equatorial* is more stable than the axial by 0.64 kcal mol^{-1} ($\Delta G°$ at -80 °C) in 1,3-dithiolane oxides. Since a solvent effect was not observed, it appears that dipole/dipole interactions do not control this equilibrium[326]. The marked sensitivity of carbon-13 NMR shifts to the orientation of the sulfonyl oxygen in six-membered ring sulfoxides (**10**) (the largest effect being about 7.5 ppm shielding at C-3,5 of the axial conformer relative to the equatorial; i.e. **10b** vs. **10c**) permits facile stereochemical assignments within this series[326]. This upfield shift can be interpreted in terms of the 'gauche γ' steric shift[327]. The difference in the 'β' effect (shielding of C-2,6) must have a different origin. A difference in the shifts of the axial and equatorial oxygens was found in the ^{17}O-NMR spectra of 4-heterosubstituted thiolane dioxides[290]. However, incomplete knowledge regarding various effects on sulfonyl oxygen shifts weakens the stereochemical assignments of the sulfone oxygens. Nevertheless, the *cis*- and *trans*-isomers of methyl-substituted thiane oxides are readily identified by ^{13}C and ^{18}O NMR, the latter approach being particularly useful[327]. Thus, the ^{17}O signals of *axial* SO groups are found several ppm *upfield* of the equatorial counterparts. The fact that the axial/equatorial ratio of thiane oxides is solvent-dependent is relevant to the stereochemistry of α-methylation or chlorination of cyclic sulfoxides, which depend on the orientation of the sulfoxide oxygen (see Section VI.C below).

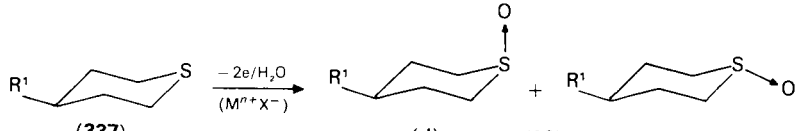


(b) (**10**) (c)

B. The Synthesis of Six-Membered Ring Sulfoxides and Sulfones

The oxidation of thianes to the corresponding sulfoxides and sulfones is a matter of routine.

Electrochemical oxidation of 4-aryl-substituted thiane in aqueous organic solvents containing various halide salts as electrolytes gave selectively the *trans*-sulfoxide (**10e**). Under acidic conditions a preferential formation of the *cis*-sulfoxide was attained[328]. The stereoselective potential of this method for the oxidation of cyclic sulfides[139,329] is apparent (equation 123).

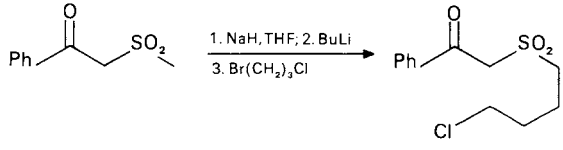


(123)

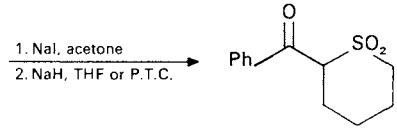
(337) (d) (10) (e)

$R^1 = p\text{-}ClC_6H_4$ M = Li, Mg, Bu_4N; X = Br, Cl; $n = 1, 2$

The 1,3-dianions formed across the sulfone[330] of β-ketosulfones may be selectively dialkylated[331] with an α,ω-dihalide and thus cyclize to give 2-ketothiane dioxides[332]. Due to its polarity, the 2-keto-substituent (or other polar group in the 2-position) adopts the axial orientation[332] (equation 124).



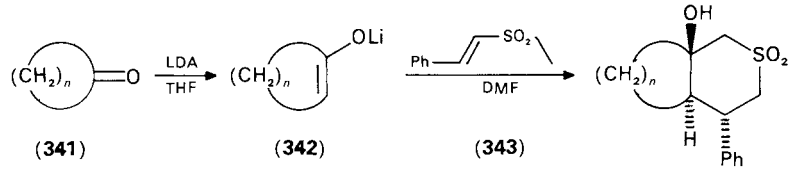
(338) (339) (124)



(340)

The application of vinyl sulfones as synthones has been restricted since conversion of the sulfonyl group to another functional moiety is generally difficult.

A useful method of utilizing vinyl sulfones (specifically methyl styryl sulfones) for the preparation of thiane dioxides in good yields is illustrated in equation 125[333].



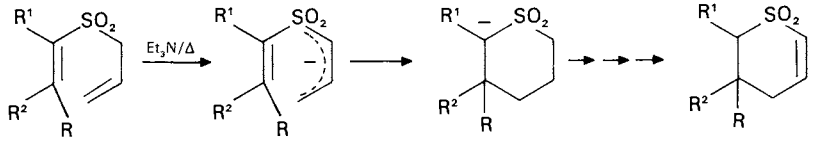
(125)

(341) (342) (343) (344)

$n = 3\text{–}5$

It appears that the ketone enolates add to the vinyl sulfone, followed by a condensation that leads to the thiane sulfone. The latter may be desulfonylated to provide olefins[333,334].

Similarly, enamino vinyl sulfones (**345**) can undergo a thermally allowed electrocyclic reaction between the termini of the enaminic double bond and the allyl sulfonyl portion in the intermediate anion (**346**) to afford α,β-unsaturated thiene dioxides (**348**) as shown in equation 126[335].

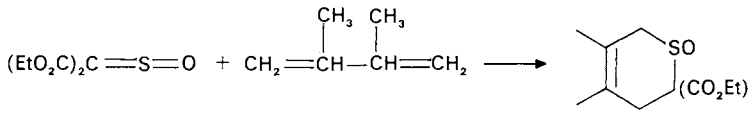


(126)

(**345**) (**346**) (**347**) (**348**)

R = Morpholine

β,γ-Unsaturated sulfoxides (e.g. 3-thiene oxides) can be prepared by trapping of the *in situ*-generated **349** with dienes in a Diels–Alder-type reaction (equation 127)[336].



(127)

(**349**) (**350**) (**351**)

The trapping of both sulfines and sulfenes with dienes is probably the method of choice for the preparation of 3-thiene oxides and dioxides, respectively[143,337].

C. Selected Chemical Transformations

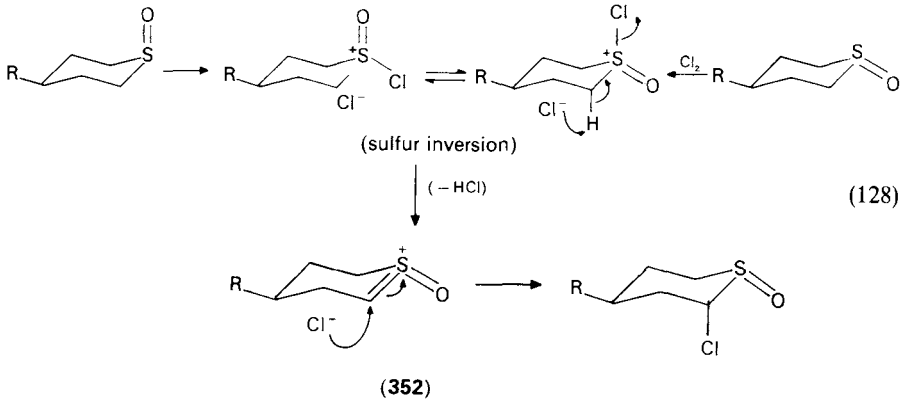
1. α-Halogenation of thiane oxides

Whereas α-chlorination of sulfones usually constitutes a problem, thiane oxides are easily chlorinated at the α-position by a wide spectrum of chlorinating agents[338]. The mechanism is similar to that with carbonyl groups[339].

Several studies[338,340–342] show that the chlorination does not proceed, as assumed previously[343], by proton abstraction followed by reaction of the carbanion thus formed, with electrophilic chlorine. A mechanism involving a chlorooxosulfonium ion formed by attack of a positive chlorine species on sulfur was shown to be more likely[344].

The chlorination gave α-chlorosulfoxides with the chloride atom in the *axial* and the oxygen atom in the *equatorial* position, independent of the configuration at the sulfur of the starting material[338,340,341]. Furthermore, thietane oxides containing small substituents undergo ring inversion to place the oxygen in the equatorial position before being halogenated axially[338,340]. The mechanism shown in equation 128 takes into account all the experimental results. The steric course is rationalized on the basis of *trans*-axial elimination of hydrogen chloride, followed by an *axial* addition of chloride ion to the α-carbon. The 'inverted ylide' **352** must have a nonplanar structure around sulfur[338].

The comparison of the results of α-halogenation with those of α-methylation of six-membered ring sulfoxides[345] reveals that similar factors are operative and determine the stereochemical outcomes in both cases.

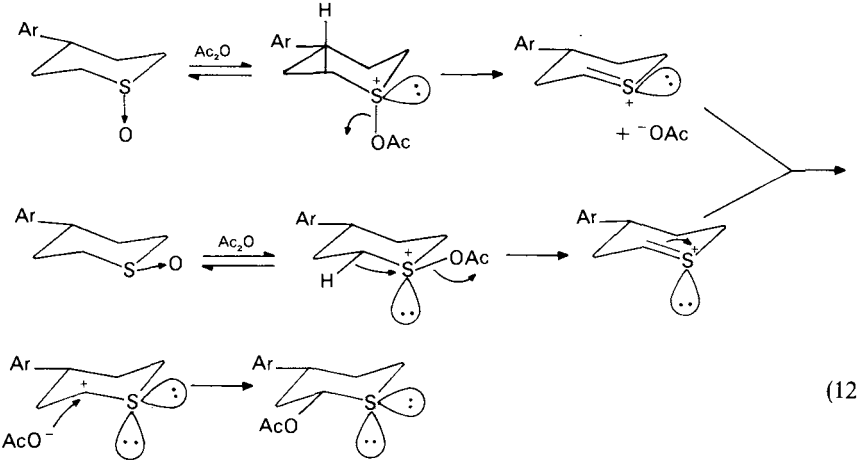


(128)

(352)

2. Pummerer rearrangement

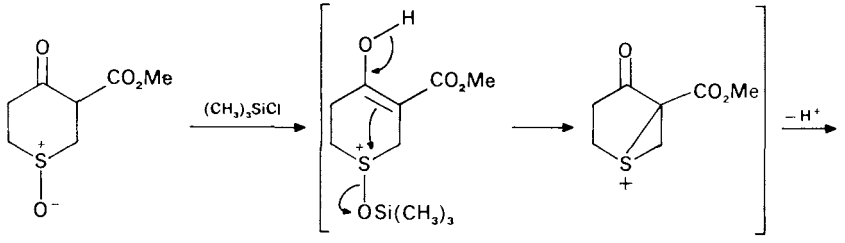
The Pummerer reaction[346] of conformationally rigid 4-aryl-substituted thiane oxides with acetic anhydride was either stereoselective or stereospecific, and the rearrangement is mainly intermolecular, while the rate-determining step appears to be the E2 1,2-elimination of acetic acid from the acetoxysulfonium intermediates formed in the initial acetylation of the sulfoxide. The thermodynamically controlled product is the axial acetoxy isomer, while the kinetically controlled product is the equatorial isomer that is preferentially formed due to the facile access of the acetate to the equatorial position[347]. The overall mechanism is illustrated in equation 129.



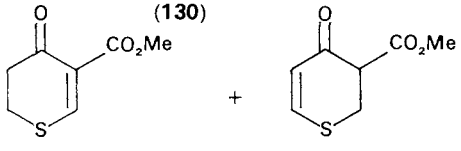
(129)

Chlorotrimethylsilane-induced Pummerer rearrangements effect the transformation of 4-ketothiane oxides into the corresponding α,β-unsaturated thianes[348], apparently via the formation and subsequent deprotonation of thiiranium intermediates rather than by the conventional sulfocarbonium mechanism depicted in equation 129.

The reaction appears to be facilitated by a γ-carbonyl group. In the absence of this activation, sulfoxide deoxygenation[349] appears to be the favored reaction pathway[348] (equation 130).



(353) (354) (355) (130)



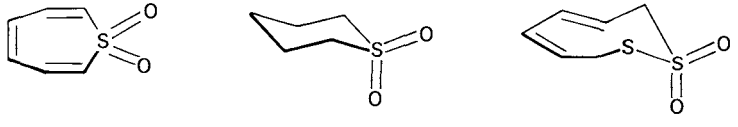
(major) (minor)

(356) (357)

VII. MEDIUM-SIZE RING SULFOXIDES AND SULFONES

In principle, the properties and chemical behavior of cyclic sulfoxides and sulfones having a ring size of seven and up are expected to be quite similar to those of the analogous acyclic systems.

This is actually observed, except when either potentially aromatic molecules such as thiepin dioxide (**358**) or when (relatively) sterically/conformationally rigid systems are involved.

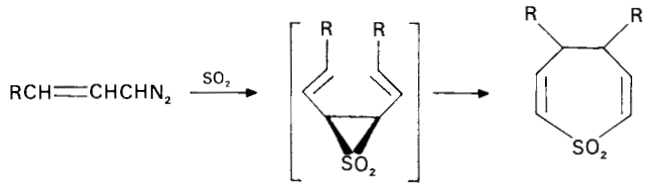


(**358**) (**10b**) (**359**)

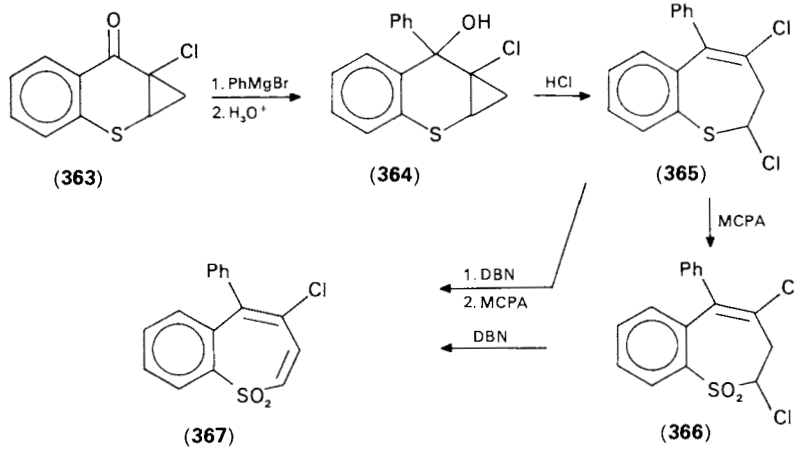
Thus, the crystal structure of the eight-membered ring dithiocin dioxide **359** indicates that the eight-membered ring is a pseudo-chair in which the 'pseudo-axial' sulfur–oxygen bond of the sulfone group is significantly shorter (1.352 Å vs. 1.475 Å) than the 'pseudo-equatorial' one[350]. *Ab initio* STO-3G* molecular orbital calculations for both this molecule and the six-membered thiane dioxide (**10b**) (for the sake of comparison) have been conducted[25]. Limited geometry optimization of the axial and equatorial S—O bonds in the chair conformations of the six- and eight-membered rings **10b** and **329** leads to bond lengths of 1.46 Å in *both* molecules, with the difference between the two S—O bonds in each molecule being less than 0.01 Å, in spite of the difference in ring size, and even when a sulfur atom has been incorporated adjacent to the sulfone group in the eight-membered ring. Consequently, axial and equatorial S—O bond lengths in these systems are predicted not to differ significantly in the gas phase[350]. Indeed, X-ray crystal structure determination of the seven-membered ring 1,3-dithiazine tetroxide system indicates that all the S—O bonds of the two sulfone groups in the molecule are essentially identical[351]. If a difference does exist in the solid state, it must be associated with crystal packing forces, which lead to deformation of sulfur moieties as suggested by relevant molecular calculations[352].

The common route for the synthesis of medium-size ring sulfoxides and sulfones is oxidation of the corresponding cyclic sulfides[70], which are obtained from the interaction of α,ω-dihaloalkanes with sulfide ion in fair to good yields[243] (equation 110).

Other less general routes to the medium-size ring sulfoxide and sulfone systems do exist, but each one is specific to a particular ring size and to the specifically desired structural features of the target molecule. Equations 131 and 132 are two examples[353,354] of such syntheses.



(360) (361) (362) (131)



(363) (364) (365) (132)

(367) (366)

VIII. ACKNOWLEDGEMENTS

The hospitality of the Department of Chemistry and Professor James P. Kutney at the University of British Columbia, Vancouver, Canada, during the time of writing this chapter is highly appreciated. I am indebted to the secretarial staff of the Department, Ms. Carolyn Delheij-Joyce in particular, for their extensive and patient input in the typing and production, and to Professor Manfred Reinecke for his help and useful suggestions.

IX. REFERENCES

1. J. F. Liebman and A. Greenberg, *Strained Organic Molecules*, Academic Press, New York, 1978.
2. U. Zoller, in *Small-ring Heterocycles* (Ed. A. Hassner), Wiley, New York, 1983, pp. 333–660.
3. K. B. Wiberg, *Acc. Chem. Res.*, **17**, 379 (1984).
4. F. H. Allen, *Tetrahedron*, **38**, 2843 (1982).

5. H. Staudinger and F. Pfenninger, *Chem. Ber.*, **49**, 1941 (1916).
6. L. A. Carpino, L. V. McAdams, III, R. H. Rynbrant and J. W. Spiewak, *J. Amer. Chem. Soc.*, **93**, 476 (1971).
7. H. Quast and F. Kees, *Chem. Ber.*, **114**, 774 (1981).
8. J. C. Sheehan, U. Zoller and D. Ben-Ishai, *J. Org. Chem.*, **39**, 1817 (1974).
9. U. Zoller and P. Rona, *Tetrahedron Letters*, **26**, 6813 (1985).
10. U. Zoller, E. Block and L. Radom, Unpublished results.
11. H. L. Hase, C. Müller and A. Schweig, *Tetrahedron*, **34**, 2983 (1978).
12. U. Zoller, *J. Org. Chem.*, **50**, 1107 (1985).
13. R. Breslow, *Acc. Chem. Res.*, **6**, 393 (1973).
14. W. A. Lathan, L. Radom, P. C. Hariharan, W. J. Hehre and J. A. Pople, *Fortschr. Chem. Forsch.*, **40**, 1 (1973).
15. L. Ramberg and B. Bäcklund, *Arkiv Kemi Mineral Geol.*, **13A**, No. 27 (1940); *Chem. Abstr.*, **34**, 4725 (1940).
16. (a) F. G. Bordwell, in *Organosulfur Compounds* (Ed. M. J. Janssen), Wiley, New York, 1967, pp. 271–284.
    (b) L. A. Paquette, R. E. Wingard, Jr., J. C. Philips, G. L. Tompson, L. K. Read and J. Clardy, *J. Amer. Chem. Soc.*, **93**, 4508 (1971).
17. (a) L. A. Paquette, *Acc. Chem. Res.*, **1**, 209 (1968).
    (b) S. W. Schneller, *Int. J. Sulfur Chem.*, **8**, 583 (1976).
    (c) N. H. Fischer, *Synthesis*, 393 (1970).
18. F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **73**, 5187 (1951).
19. N. P. Neureiter, *J. Amer. Chem. Soc.*, **88**, 558 (1966).
20. C. D. Dittmer and G. C. Levy, *J. Org. Chem.*, **30**, 636 (1965).
21. L. A. Carpino and L. V. McAdams, III, *J. Amer. Chem. Soc.*, **87**, 5804 (1965).
22. L. A. Carpino and H-W. Chen, *J. Amer. Chem. Soc.*, **101**, 390 (1979).
23. (a) M. J. Dewar, *The Molecular Orbital Theory of Organic Chemistry*, McGraw-Hill, New York, 1969, pp. 430–440.
    (b) K. A. R. Mitchell, *Chem. Rev.*, **69**, 157 (1969).
    (c) N. D. Epiotis, R. L. Yates, F. Bernardi and S. Wolfe, *J. Amer. Chem. Soc.*, **98**, 5435 (1976).
24. W. J. Hehre, L. Radom, P. v. R. Schleyer and J. A. Pople, *An Initio Molecular Orbital Theory*, Wiley, New York, 1986.
25. R. L. Boyd and J. P. Szabo, *Can. J. Chem.*, **60**, 730 (1982).
26. J. S. Binkley, R. A. Whitehead, P. C. Hariharan, R. Seeger and J. A. Pople. *QCPE*, **11**, 368 (1978).
27. J. B. Collins, P. v. R. Schleyer, J. S. Binkley and J. A. Pople, *J. Chem. Phys.*, **64**, 5142 (1976).
28. W. J. Hehre, R. F. Stewart and J. A. Pople, *J. Chem. Phys.*, **51**, 2657 (1969).
29. M. M. Rohmer and B. Roos, *J. Amer. Chem. Soc.*, **97**, 2025 (1975).
30. R. Hoffman, H. Fujimoto, J. R. Swenson and C.-C. Wan. *J. Amer. Chem. Soc.*, **95**, 7644 (1973).
31. M. J. S. Dewar and W. Thiel, *J. Amer. Chem. Soc.*, **99**, 4899 (1977).
32. M. J. S. Dewar and M. L. McKee, *J. Comput. Chem.*, **4**, 84 (1983).
33. R. J. Boyd, A. Gupta, R. F. Langler, S. P. Lownie and J. A. Pincock, *Can. J. Chem.*, **58**, 331 (1980).
34. H. Kim, *J. Chem. Phys.*, **57**, 1075 (1972).
35. R. S. Mulliken, *J. Chem. Phys.*, **23**, 1833, 1841 (1955).
36. Y. Nakano, S. Saito and Y. Morino, *Bull. Chem. Soc. Japan*, **43**, 368 (1970).
37. R. Desiderato and R. L. Sass, *Acta Cryst.*, **23**, 430 (1967).
38. S. Saito, *Bull. Chem. Soc. Japan*, **42**, 663, 667 (1969).
39. H. L. Ammon, L. Fallon and L. A. Plastas, *Acta Cryst.*, **B32**, 2171 (1976).
40. I. Hargittai, *Sulfone Molecular Structures*, Lecture Notes in Chemistry, Vol. 6, Springer-Verlag, Berlin, 1978.
41. J. K. G. Watson, *J. Mol. Spectrosc.*, **48**, 479 (1973).
42. H. Dreizler and G. Dendi, *Z. Naturforsch.*, **19A**, 512 (1964).
43. K. Okiye, C. Hirose, D. Lister and J. Sheridan, *Chem. Phys. Letters*, **24**, 111 (1974).
44. (a) J. M. Pochan, J. E. Baldwin and W. H. Flygare, *J. Amer. Chem. Soc.*, **91**, 1896 (1969).
    (b) F. H. Allen, *Acta Cryst.*, **B35**, 2331 (1979).
45. C. Müller, A. Schweig and H. Vermeer, *J. Amer. Chem. Soc.*, **97**, 982 (1975).
46. F. de Jong, A. J. Noorduin, T. Bouwman and M. J. Janssen, *Tetrahedron Letters*, 1209 (1974).
47. (a) M. L. Ziegler, J. Weiss, H. Schildknecht, N. Grund and H.-E. Sasse, *Liebigs Ann.*, 1702 (1973).

(b) G. L. Hardgrove, J. S. Bratholdt and M. M. Lein, *J. Org. Chem.*, **39**, 246 (1974).
(c) S. S. C. Chu, *Acta Cryst.*, **B31**, 1082 (1975).
48. (a) C. Müller, A. Schweig and H. Vermeer, *Angew. Chem., Int. Ed. Engl.*, **13**, 273 (1974).
(b) W. Schäfer, A. Schweig, G. Maier, T. Sayrac and K. J. Crandall, *Tetrahedron Letters*, 1213 (1976).
49. C. Müller, A. Schweig and H. Vermeer, *J. Amer. Chem. Soc.*, **100**, 8058 (1978).
50. C. A. Coulson, in *Proceedings of the Robert A. Welch Foundation Conference on Chemical Research, XVI, Theoretical Chemistry*, 1973, pp. 61–97.
51. D. W. J. Cruickshank, B. C. Webster and M. A. Spinnter, *Int. J. Quantum Chem.*, **15**, 225 (1967).
52. E. M. Burgess, private communication.
53. (a) H. E. Simmons and T. Fukunaga, *J. Amer. Chem. Soc.*, **89**, 5208 (1967).
(b) A. Schweig, U. Weidner, D. Hellwinkel and W. Krapp, *Angew. Chem., Int. Ed. Engl.*, **12**, 310 (1973).
54. (a) N. C. Baird, *Theor. Chim. Acta*, **16**, 239 (1970).
(b) C. Müller, A. Schweig, M. P. Cava and M. V. Lashmikantharmi, *J. Amer. Chem. Soc.*, **98**, 7187 (1976).
55. J. W. Rakshys, R. W. Taft and W. A. Sheppard, *J. Amer. Chem. Soc.*, **90**, 5236 (1968).
56. (a) A. Sreitweiser, Jr. and J. E. Williams Jr., *J. Amer. Chem. Soc.*, **97**, 191 (1975).
(b) W. Schafer, A. Schweig, K. Dimroth and H. Kantor, *J. Amer. Chem. Soc.*, **98**, 4410 (1976).
57. G. L. Delker, Y. Wang, G. D. Stucky, R. L. Lambert Jr., C. K. Haas and D. Seyferth, *J. Amer. Chem. Soc.*, **98**, 1779 (1976).
58. M. J. S. Dewar, *Bull. Chem. Soc. Japan*, **18**, 279 (1951).
59. J. K. Stalick and J. A. Ibers, *J. Amer. Chem. Soc.*, **92**, 5333 (1970).
60. W. Ando, Y. Hanyu, T. Takata and K. Ueno, *J. Amer. Chem. Soc.*, **104**, 4981 (1982).
61. L. Paquette and L. S. Wittenbrook, *Org. Synth.*, **49**, 18 (1969).
62. G. M. Kuzyants and V. T. Aleksanyan, *J. Struct. Chem. USSR*, **13**, 576 (1972).
63. (a) K. Kondo and A. Negishi, *Tetrahedron*, **27**, 4821 (1971).
(b) B. F. Bonini, A. Capelli, G. Maccagani and G. Mazzanti, *Gazz. Chim. Italic*, **105**, 827 (1975).
64. (a) D. Bernard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).
(b) W. Grey and Stephenson, *Spectrochim. Acta*, **16**, 1312 (1960).
(c) E. A. Robinson, *Can. J. Chem.*, **39**, 247 (1961).
65. L. J. Bellamy and R. L. Williams, *J. Chem. Soc.*, 863 (1957).
66. W. O. Siegel and C. R. Johnson, *Tetrahedron*, **27**, 341 (1971).
67. P. B. Salmon, R. Nagarajan and R. M. Dodson, *Chem. Commun.*, 552 (1967).
68. (a) F. A. Carey, O. D. Dailey Jr. and W. C. Hutton, *J. Org. Chem.*, **43**, 96 (1978), and references cited therein.
(b) E. L. Eliel and K. M. Pietrusiewicz, in *Topics in Carbon-13 NMR Spectroscopy*, Vol. 3 (Ed. G. C. Levy), Chap. 3, Wiley, New York, 1979.
69. (a) B. J. Hutchinson, K. K. Andersen and A. R. Katritzky, *J. Amer. Chem. Soc.*, **91**, 3839 (1969).
(b) J. J. Rigau, C. C. Bacon and C. R. Johnson, *J. Org. Chem.*, **35**, 3655 (1970).
70. E. Block, A. A. Bazzi, J. B. Lambert, S. M. Wharry, K. K. Andersen, D. C. Dittmer, B. H. Patwardhan and D. J. H. Smith, *J. Org. Chem.*, **45**, 4807 (1980).
71. N. H. Fischer, *Synthesis*, 393 (1970).
72. M. Veyama, K. Tori and M. Fukuyama, *Org. Magn. Reson.*, **4**, 441 (1972).
73. T. Kempe, Ph.D. Dissertation, Royal Institute of Technology, Denmark, 1974.
74. (a) C. R. Johnson and W. O. Siegel, *J. Amer. Chem. Soc.*, **91**, 2796 (1969).
(b) C. R. Johnson and W. O. Siegel, *J. Org. Chem.*, **35**, 3657 (1970).
(c) C. W. Wucherpfennig, *Tetrahedron Letters*, 765 (1970).
75. K. Kondo, A. Nagishi and M. Fukuyama, *Tetrahedron Letters*, 2461 (1969).
76. (a) M. Ohtsuru, K. Tori and M. Fukuyama, *Tetrahedron Letters*, 2877 (1970).
(b) M. Ueyama and K. Tori, *Nippon Kagaku Zasshi*, **92**, 741 (1971).
77. R. W. Mitchell, F. A. Hartmann and J. A. Merritt, *J. Mol. Spectrosc.*, **31**, 388 (1969).
78. J. Pople and A. Bothner-By, *J. Chem. Phys.*, **42**, 1338 (1965).
79. C. A. Kingsbury, D. L. Durham and R. Hutton, *J. Org. Chem.*, **43**, 4696 (1978).
80. (a) V. Solkan and N. Sergeyev, *Org. Magn. Reson.*, **6**, 200 (1974).
(b) M. Cooper and S. Manatt, *J. Amer. Chem. Soc.*, **91**, 6325 (1969).
81. D. N. Reinhoudt, C. G. Kouwenhoven and J. P. Visser, *J. Organomet. Chem.*, **57**, 403 (1973).

82. D. Lee, J. C. Keifer, R. P. Rooney, T. B. Garner and S. A. Evans, Jr., *J. Org. Chem.*, **44**, 2580 (1979).
83. S. W. Bass and S. A. Evans, Jr., *J. Org. Chem.*, **45**, 710 (1980).
84. Mc. Crachren and S. A. Evans, Jr., *J. Org. Chem.*, **44**, 3551 (1979).
85. M. S. Puar, G. C. Rovnyak, A. I. Cohen, B. Toeplitz and J. Z. Gougotas, *J. Org. Chem.*, **44**, 2513 (1979).
86. G. Barbarella, P. Dembech, A. Garbesi and A. Fava, *Org. Magn. Reson.*, **8**, 108 (1976).
87. M. Suda and S. Masamune, *Chem. Commun.*, 504 (1974).
88. P. J. Stang, G. Mass, D. L. Smith and J. A. McCloskey, *J. Amer. Chem. Soc.*, **103**, 4837 (1981).
89. R. Breslow and L. J. Altman, *J. Amer. Chem. Soc.*, **88**, 504 (1966).
90. T. St. Armour and D. Fiat, *Bull. Magn. Reson.*, **1**, 118 (1980).
91. (a) P. Vouros and L. A. Carpino, *J. Org. Chem.*, **39**, 3777 (1974).
    (b) P. Vouros, *J. Heter. Chem.*, **12**, 21 (1975).
92. D. C. Dittmer and G. E. Kuhlman, *J. Org. Chem.*, **35**, 4224 (1970).
93. H. H. Jaffé, *Acc. Chem. Res.*, **2**, 136 (1969).
94. F. A. Field, *Acc. Chem. Res.*, **1**, 42 (1968).
95. G. E. Hartzell and J. N. Paige, *J. Amer. Chem. Soc.*, **88**, 2616 (1966); *J. Org. Chem.*, **32**, 459 (1967).
96. R. B. Woodward and R. Hoffman, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).
97. J. R. Shelton and K. E. Davis, *Int. J. Sulfur Chem.*, **8**, 197 (1973).
98. T. Nagai, H. Namikoshi and N. Tokura, *Tetrahedron*, **24**, 3267 (1968).
99. F. G. Bordwell, J. M. Williams, E. B. Hoyt, Jr. and B. B. Jarvis, *J. Amer. Chem. Soc.*, **90**, 429 (1968).
100. J. C. Philips, J. V. Swisher, D. Haydukewych and O. Morales, *Chem. Commun.*, 22 (1971).
101. J. C. Philips and O. Morales, *Chem. Commun.*, 713 (1977).
102. F. G. Bordwell, J. M. Williams, Jr. and B. B. Jarvis, *J. Org. Chem.*, **33**, 2026 (1968).
103. D. N. Reinhoudt, C. G. Kouwenhoven and J. P. Visser, *J. Organomet. Chem.*, **57**, 403 (1973).
104. (a) D. M. Lemal and P. Chao, *J. Amer. Chem. Soc.*, **95**, 922 (1973).
    (b) D. M. Lemal and P. Chao, *J. Amer. Chem. Soc.*, **95**, 920 (1973).
105. J. E. Baldwin, G. Hofle and Se Chun Choi, *J. Amer. Chem. Soc.*, **93**, 2810 (1971).
106. D. N. Jones, D. R. Hill and D. A. Lewton, *Tetrahedron Letters*, 2235 (1975).
107. W. G. L. Albersberg, K. Peter and C. Vollhardt, *J. Amer. Chem. Soc.*, **99**, 2792 (1977).
108. K. Kondo, M. Matsumoto and A. Negishi, *Tetrahedron Letters*, 2131 (1972).
109. E. M. Lown, H. S. Sandhu, H. E. Gunning and O. P. Strausz, *J. Amer. Chem. Soc.*, **90**, 7164 (1968).
110. L. A. Carpino and H.-W. Chen, *J. Amer. Chem. Soc.*, **93**, 785 (1971).
111. S. Matsumura, T. Nagai and N. Tokura, *Bull. Chem. Soc. Japan*, **41**, 2672 (1968).
112. C. Y. Meyers, in *Topics in Organic Sulfur Chemistry* (Ed. M. Tisler), University Press, Ljubljana, Yugoslavia, 1978, pp. 207–260.
113. L. A. Carpino and R. H. Rynbrandt, *J. Amer. Chem. Soc.*, **88**, 5682 (1966).
114. B. F. Bonini, G. Maccagani, G. Mazzanti and P. Piccinelli, *Tetrahedron Letters*, 3987 (1979).
115. L. A. Paquette, L. S. Wittenbrook and V. V. Kane, *J. Amer. Chem. Soc.*, **89**, 4487 (1967).
116. E. Vilsmaier, R. Tropitzsch and O. Vostrowsky, *Tetrahedron Letters*, 3987 (1974).
117. C. Y. Meyers, W. S. Mathews, G. J. McCollum, L. L. Ho and H. H. Duy, Heterocycles, **9**, 1486 (1978).
118. W. P. Weber and G. W. Gokel, *Phase Transfer Catalysis in Organic Synthesis*, Springer-Verlag, New York, 1977.
119. B. B. Jarvis, W. P. Tong and H. L. Ammon, *J. Org. Chem.*, **40**, 3189 (1975).
120. R. V. Vizgert, *Russ. Chem. Rev.*, **32**, 1 (1963).
121. W. Ando, Y. Hanyu, Y. Kumamoto and T. Takata, *Tetrahedron*, **42**, 1989 (1986).
122. P. Raynolds, S. Sonnebelt, S. Bakker and R. M. Kellog, *J. Amer. Chem. Soc.*, **96**, 3146 (1974).
123. D. C. Dittmer, G. E. Kuhlmann and G. C. Levy, *J. Org. Chem.*, **35**, 3676 (1970).
124. D. C. Dittmer, R. S. Henion and N. Takashina, *J. Org. Chem.*, **34**, 1310 (1969).
125. G. E. Masner, A. D. Mesure and J. G. Tillet, *Tetrahedron Letters*, 3153 (1968).
126. K. Kondo, A. Negishi and I. Ojima, *J. Amer. Chem. Soc.*, **94**, 5786 (1972).
127. G. A. Olah and P. J. Szilagyi, *J. Org. Chem.*, **36**, 1121 (1971).
128. E. Vilsmaier and B. Holch, *Synthesis*, 590 (1971).
129. J. K. Rasmussen and A. Hassner, *Chem. Rev.*, **76**, 389 (1976).

130. (a) H. Alper and E. C. H. Keung, *Tetrahedron Letters*, 53 (1970).
(b) M. Rosenblum and C. Gatsonis, *J. Amer. Chem. Soc.*, **89**, 5064 (1967).
(c) W. L. Chow, J. Fossey and R. A. Perry, *Chem. Commun.*, 501 (1972).
131. (a) L. A. Carpino, P. H. Terry and S. D. Thatte, *Tetrahedron Letters*, 3329 (1964).
(b) R. Breslow, J. Posner and A. Krebs, *J. Amer. Chem. Soc.*, **85**, 234 (1963).
132. S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 343 (1967).
133. S. Patai and Z. Rappoport, in *The Chemistry of Alkenes* (Ed. S. Patai), Interscience, New York, 1964, p. 8.
134. B. B. Jarvis, G. P. Stahy and H. L. Ammon, *Tetrahedron Letters*, 3781 (1978).
135. Y. Yoshida, M. Komatsu, Y. Oshiro and T. Agawa, *J. Org. Chem.*, **44**, 830 (1979).
136. P. G. Mente and C. W. Rees, *Chem. Commun.*, 418 (1972).
137. K. H. Pannel, A. J. Mayr, R. Hoggard and R. C. Pettersen, *Angew. Chem., Int. Ed. Engl.*, **19**, 63 (1980).
138. N. Schrauzer, V. P. Mayweg, H. W. Fink and W. Heinrich, *J. Amer. Chem. Soc.*, **88**, 4604 (1966).
139. C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 1109 (1965).
140. K. Newmann, G. Zon and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7012 (1969).
141. G. A. Olah, Y. D. Vanker and M. Arvanaghi, *Synthesis*, 984 (1979).
142. (a) M. Torres, A. Clement, J. E. Bertie, H. E. Gunning and O. P. Straus, *J. Org. Chem.*, **43**, 2490 (1978).
(b) R. K. Gosavi and O. P. Straus, *Can. J. Chem.*, **61**, 2596 (1983).
143. G. Opitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 107 (1967).
144. N. Fischer and G. Opitz, *Org. Synth.*, **48**, 106 (1968).
145. (a) G. Hesse, E. Reichold and S. Majmudar, *Chem. Ber.*, **90**, 2106 (1957).
(b) G. Hesse and S. Majmudar, *Chem. Ber.*, **93**, 1129 (1960).
146. F. Arndt, *Org. Synth.*, Coll. Vol. II, 165 (1950).
147. A. Carpino and L. V. McAdams, III, *Org. Synth.*, **50**, 65 (1970).
148. L. A. Carpino and J. R. Williams, *J. Org. Chem.*, **39**, 2321 (1974).
149. (a) W. V. Farrar, *J. Chem. Soc.*, 508 (1956).
(b) H. Liebig, *German patent*, 1,256,216; *Chem. Abstr.*, **69**, 18609 (1969).
150. K. Szabo, *U.S. patent*, 3,106,585; *Chem. Abstr.*, **60**, 2841b (1964). *U.S. patent*, 3,294,845; *Chem. Abstr.*, **67**, 11210c (1967).
151. F. E. Hardi, P. R. Speckman and P. Robson, *J. Chem. Soc. (C)*, 2334 (1969).
152. B. F. Bonini and G. Maccagani, *Tetrahedron Letters*, 3585 (1973).
153. B. B. Jarvis, S. S. Duthey and H. L. Ammon, *J. Amer. Chem. Soc.*, **94**, 2136 (1972).
154. L. A. Paquette, *Org. React.*, **25**, 1 (1977).
155. S. Matsumura, T. Nagai and N. Tokura, *Bull. Chem. Soc. Japan*, **41**, 635 (1968); *Tetrahedron Letters*, 3929 (1966).
156. (a) C. Y. Meyers, W. S. Matthews, G. J. McCollum and J. C. Branca, *Tetrahedron Letters*, 1105 (1976).
(b) C. Y. Meyers, W. S. Matthews and G. J. McCollum, *Heterocycles*, **9**, 1486 (1978).
157. E. Vilsmaier, R. Tropitzsch and O. Vostrowsky, *Tetrahedron Letters*, 3275 (1974).
158. B. B. Jarvis and W. P. Tong, *Synthesis*, 102 (1975).
159. O. S. Tee, J. A. Altman and K. Yates, *J. Amer. Chem. Soc.*, **96**, 3141 (1974).
160. G. L. Hardgrove, J. S. Bratholdt and M. M. Lein, *J. Org. Chem.*, **39**, 246 (1974).
161. K. Kondo and A. Negishi, *Chem. Letters*, 1525 (1974).
162. L. A. Paquette, *Principles of Modern Heterocyclic Chemistry*, Benjamin, New York, 1968, p. 26.
163. K. Kondo, A. Negishi and G. Tsuchihashi, *Tetrahedron Letters*, 2743 (1969).
164. W. Ando, Y. Hanyu and T. Takata, *J. Org. Chem.*, **51**, 2122 (1986).
165. (a) R. M. Dobson and R. F. Sauers, *Chem. Commun.*, 1189 (1967).
(b) R. M. Dobson and J. P. Nelson, *Chem. Commun.*, 1159 (1969).
166. M. Tho, private communication, 1986.
167. L. Carlsen and H. Egsgaard, *J. Chem. Soc., Perkin Trans. 2*, 279 (1982).
168. L. Carlsen and H. Egsgaard, *Thermochim. Acta*, **38**, 47 (1980).
169. L. Carlsen, H. Egsgaard and K. N. Harpp, *J. Chem. Soc., Perkin Trans. 2*, 1166 (1981).
170. S. W. Benson, *Chem. Rev.*, **78**, 23 (1978).
171. A. J. Fry, K. Ankner and V. K. Handa, *Chem. Commun.*, 120 (1981).

172. (a) M. H. Rosen and G. Bonet, *J. Org. Chem.*, **39**, 3805 (1974).
(b) M. H. Rosen, I. Fingler and G. Bonet, *J. Med. Chem.*, **19**, 414 (1976).
173. Y. Hayasi, H. Nakamura and H. Nozaki, *Bull. Chem. Soc. Japan*, **46**, 667 (1973).
174. H. Matsujubo, M. Kojima and H. Kato, *Chem. Letters*, 1153 (1975).
175. M. Komatsu, Y. Yoshida, M. Uesaka, Y. Oshiro and T. Agawa, *J. Org. Chem.*, **49**, 1300 (1984).
176. R. Fusco, G. Bianchetti, R. Rocar and R. Ugo, *Chem. Ber.*, **96**, 802 (1963).
177. M. Franck-Neumann and C. Buchecker, *Tetrahedron Letters*, 2659 (1969).
178. K. T. Potts, A. J. Elliott and M. Sorm, *J. Org. Chem.*, **37**, 3838 (1972).
179. M. Regitz and B. Mathieu, *Chem. Ber.*, **113**, 1632 (1980).
180. C. Cistaro, G. Fronza, R. Mondelli, S. Bradamante and G. A. Pagani, *J. Magn. Reson.*, **15**, 367 (1974).
181. (a) R. S. Mulliken and B. Liu, *J. Amer. Chem. Soc.*, **93**, 6738 (1971).
(b) M. A. Ratner and J. R. Sabin, *J. Amer. Chem. Soc.*, **93**, 3542 (1971).
182. J. I. Musher, *J. Amer. Chem. Soc.*, **94**, 1370 (1972).
183. J. K. George and C. Trindle, *Int. J. Sulfur Chem.*, **8**, 83 (1973).
184. C. R. Johnson and W. O. Siegl, *Tetrahedron Letters*, 1879 (1969).
185. D. J. H. Smith, J. D. Finlay and C. R. Hall, *J. Org. Chem.*, **44**, 4757 (1979).
186. W. E. Truce and J. F. Rach, *J. Org. Chem.*, **39**, 1109 (1974).
187. L. A. Paquette and J. P. Freeman, *J. Amer. Chem. Soc.*, **91**, 7548 (1969).
188. P. L.-F. Chang and D. C. Dittmer, *J. Org. Chem.*, **34**, 2791 (1969).
189. L. A. Paquette, M. Rosen and H. Stucki, *J. Org. Chem.*, **33**, 3020 (1968).
190. L. A. Paquette, R. W. Houser and M. Rosen, *J. Amer. Chem. Soc.*, **35**, 905 (1970).
191. J. F. King, P. De Mayo, C. L. McIntosh, K. Piers and D. J. H. Smith, *Can. J. Chem.*, **48**, 3704 (1970).
192. E. Block, E. R. Corey, R. E. Penn, T. L. Renken, P. F. Sherwin, H. Bock, T. Hirabayashi, S. Mohmand and B. Solouki, *J. Amer. Chem. Soc.*, **104**, 3119 (1982).
193. (a) W. D. Keller, T. R. Lusebrink and C. H. Cederholm, *J. Chem. Phys.*, **44**, 782 (1966).
(b) B. A. Arbuzuv, O. N. Nuretdinova and A. N. Vereschagin, *Dokl. Akad. Nauk SSSR*, **172**, 591 (1967).
(c) R. M. Dodson, E. H. Jancis and G. Klose, *J. Org. Chem.*, **35**, 2520 (1970).
194. M. Buza, K. K. Andersen and M. D. Pazdon, *J. Org. Chem.*, **43**, 3827 (1978).
195. J. H. Barlow, C. R. Hall, D. R. Russell and D. J. H. Smith, *Chem. Commun.*, 133 (1975).
196. G. L. Hardgrove, Jr., J. S. Bratholdt and M. M. Lein, *J. Org. Chem.*, **39**, 246 (1974).
197. M. Barfield and M. Karplus, *J. Amer. Chem. Soc.*, **91**, 1 (1969).
198. C. Cistaro, G. Fronza, R. Mondelli, S. Bradamante and G. A. Pagani, *J. Magn. Reson.*, **17**, 219 (1975).
199. G. Wood, C. C. Barker and A. Kligerman, *Can. J. Chem.*, **51**, 3329 (1973).
200. J. W. Emsley and J. C. Lindon, *NMR Spectroscopy Using Liquid Crystal Solvents*, Pergamon, Oxford, 1975.
201. G. Fronza, R. Mondelli and S. Bradamante, *J. Magn. Reson.*, **36**, 343 (1979).
202. F. S. Abott, J. E. Coats and K. Haya, *J. Org. Chem.*, **42**, 3502 (1977).
203. T. B. Malloy, Jr., L. E. Baumann and L. A. Carreira, in *Topics in Stereochemistry* (Eds. E. L. Eliel and N. L. Allinger), Vol. XIV, Wiley–Interscience, New York, 1979.
204. J. W. Bevan, A. C. Legon and D. J. Millen, *Proc. R. Soc. London, Ser. A*, 354, 491–509 (1977).
205. (a) S. Allenmark, *Arkiv Kemi*, **26**, 73 (1966).
(b) R. M. Wing, J. J. Uebel and K. K. Andersen, *J. Amer. Chem. Soc.*, **95**, 6046 (1973).
206. S. Abrahamson and G. Rehnberg, *Acta Chem. Scand.*, **26**, 494 (1972).
207. D. N. Jones, T. P. Kogan, P. Murry-Rust, J. Murry-Rust and R. F. Newton, *J. Chem. Soc., Perkin Trans. 1*, 1325 (1982).
208. G. D. Andretti, G. Bocelli and P. Sgarabotto, *Cryst. Struct. Commun.*, **1**, 423 (1972); **2**, 323 (1973); **3**, 499 (1973).
209. D. O. Harris, H. W. Harrington, A. C. Luntz and W. D. Gwinn, *J. Chem. Phys.*, **44**, 3467 (1966).
210. (a) H. Bock and B. Solouki, *Chem. Ber.*, **107**, 2299 (1974).
(b) G. Wagner and H. Bock, *Chem. Ber.*, **109**, 68 (1976).
211. E Block, E. R. Corey, R. E. Penn, T. L. Renken and P. F. Sherwin, *J. Amer. Chem. Soc.*, **98**, 5715 (1976).
212. (a) W. E. Parham, F. D. Blake and D. R. Theissen, *J. Org. Chem.*, **27**, 2415 (1962).

(b) K. N. Houk, Y. M. Chang, R. W. Strozier and P. Caramella, *Heterocycles*, **7**, 793 (1977).
213. P. G. De Benedetti, C. De Micheli, R. Gandolfi, P. Gariboldi and A. Rastelli, *J. Org. Chem.*, **45**, 3646 (1980).
214. P. G. De Benedetti, S. Quartieri, A. Rastelli, M. De Amici, C. De Micheli, R. Gandolfi and P. Gariboldi, *J. Chem. Soc., Perkin Trans. 2*, 95 (1982).
215. (a) L. Salem, *J. Amer. Chem. Soc.*, **90**, 543 (1968).
(b) G. Klopman, *J. Amer. Chem. Soc.*, **90**, 223 (1968).
216. D. C. Dittmer, B. H. Patwardhan and J. T. Bartholomew, *Org. Magn. Resan.*, **18**, 82 (1982).
217. (a) P. B. Sollman, R. Nagarajan and R. M. Dodson, *Chem. Commun.*, 552 (1967).
(b) T. Ledaal, *Tetrahedron Letters*, 1683 (1968).
218. L. H. Sharpen and V. W. Laurie, *J. Chem. Phys.*, **49**, 221 (1968).
219. J. W. Bevan, A. G. Legon and D. Millen, *Chem. Commun.*, 659 (1974).
220. K. Kabinska, *Bull. Acad. Pol. Sci., Ser. Sci. Chim.*, **24**, 369 (1976).
221. C. Cistaro, G. Fronza, R. Mondelli, S. Bradamante and G. A. Pagani, *J. Magn. Reson.*, **15**, 257 (1974).
222. J. B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1972.
223. G. C. Levy and R. L. Lichter, *Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy*, Wiley, New York, 1979.
224. W. Wehrli and T. Wirthlin, *Interpretation of Carbon-13 NMR Spectra*, Heyden and Son, London, 1978.
225. J. R. Dyer, *Application of Absorption Spectroscopy of Organic Compounds*, Prentice-Hall, Inc., NJ, 1965.
226. F. A. Abbott and K. Haya, *Can. J. Chem.*, **56**, 71 (1978).
227. L. A. Paquette, J. F. Freeman and M. J. Wyvratt, *J. Amer. Chem. Soc.*, **93**, 3216 (1971).
228. E. Block, R. E. Penn, R. J. Olsen and P. F. Sherwin, *J. Amer. Chem. Soc.*, **98**, 1264 (1976).
229. L. Carlson, H. Egsgaard and D. N. Harpp, *J. Chem. Soc., Perkin Trans 2*, 1166 (1981).
230. B. M. Trost, W. L. Schinski, F. Chen and I. B. Mantz, *J. Amer. Chem. Soc.*, **93**, 676 (1971).
231. J. E. Coats and F. S. Abott, *J. Org. Chem.*, **42**, 3506 (1977).
232. (a) F. A. L. Anet, R. D. Trepka and D. J. Cram, *J. Amer. Chem. Soc.*, **89**, 357 (1967).
(b) A. Ratajczak, F. A. L. Anet and D. J. Cram, *J. Amer. Chem. Soc.*, **89**, 2072 (1967).
(c) S. Wolfe, A. Rauk and I. G. Csizmadia *J. Amer. Chem. Soc.*, **91**, 1567 (1969).
(d) R. R. Frazer, F. J. Schuber and Y. Y. Wigfield, *J. Amer. Chem. Soc.*, **94**, 8795 (1972).
233. (a) E. J. Corey, H. König and T. H. Lowry, *Tetrahedron Letters*, 515 (1962).
(b) D. J. Cram and T. A. Whitney, *J. Amer. Chem. Soc.*, **89**, 4651 (1967).
234. S. Bradamante, P. Del Buttero, D. Landini and S. Miorana, *J. Chem. Soc., Perkin Trans. 2*, 1676 (1974).
235. (a) F. G. Bordwell and W. A. Kirsh, referred to in Ref. 192.
(b) F. G. Bordwell, J. C. Branca, D. L. Hughes and W. N. Olmstead, *J. Org. Chem.*, **45**, 3305 (1980).
236. G. Opitz and H. R. Mohl, *Angew. Chem., Int. Ed. Engl.*, **8**, 73 (1969).
237. (a) G. Barbarella, A. Garbesi and A. Fava, *J. Amer. Chem. Soc.*, **97**, 5883 (1975).
(b) A. Rauk, S. Wolfe and I. G. Czismadia, *Can. J. Chem.*, **47**, 113 (1969).
238. D. R. Rayner, A. J. Gordon and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4854 (1968).
239. M. Sander, *Chem. Rev.*, **66**, 341 (1966).
240. (a) A. Biezais and G. Bergson, *Acta Chem. Scand.*, **18**, 815 (1964).
(b) M. S. Newmen, J. R. Leblank, H. A. Kames and G. Axelrad, *J. Amer. Chem. Soc.*, **86**, 868 (1964).
241. (a) N. Kharasch, *Int. J. Sulfur Chem.*, **8**, 649 (1976).
(b) L. A. Paquette and J. P. Freeman, *J. Org. Chem.*, **35**, 2249 (1970).
242. (a) W. E. Truce and P. N. Son, *J. Org. Chem.*, **30**, 71 (1965).
(b) L. A. Paquette and M. Rosen, *J. Org. Chem.*, **33**, 3027 (1968).
(c) D. C. Dittmer and F. A. Davis, *J. Amer. Chem. Soc.*, **87**, 2064 (1965).
(d) S. Searls, Jr., H. R. Hays and E. F. Lutz, *J. Org. Chem.*, **27**, 2828 (1962).
243. L. Mandolini and T. Vontor, *Synth. Commun.*, **9**, 857 (1979).
244. J. J. Rigau, C. C. Bacon and C. R. Johnson, *J. Org. Chem.*, **35**, 3655 (1970).
245. D. N. Jones, T. P. Kogan and R. F. Newton, *J. Chem. Soc., Perkin Trans. 1*, 1333 (1982).
246. R. D. G. Cooper, *J. Amer. Chem. Soc.*, **92**, 5010 (1970).
247. (a) M. Eschwey, W. Sundermeyer and D. S. Stephenson, *Chem. Ber.*, **116**, 1623 (1983).

(b) R. Seelinger and W. Sundermeyer, *Angew. Chem., Int. Ed. Engl.*, **19**, 203 (1980).
(c) R. Shork and W. Sundermeyer, *Chem. Ber.*, **118**, 1415 (1985).
248. R. B. Woodward and R. Hoffman, *The Conservation of Orbital Symmetry*, Academic Press, New York, 1970.
249. S.-C. Chen and Y. Chow, *Can. J. Chem.*, **52**, 2283 (1974).
250. (a) L. A. Paquette, J. P. Freeman and R. W. Houser, *J. Org. Chem.*, **34**, 2901 (1969).
(b) L. A. Paquette and M. Rosen, *J. Amer. Chem. Soc.*, **89**, 4102 (1967).
(c) L. A. Paquette and M. Rosen, *J. Org. Chem.*, **33**, 2130 (1968).
251. B. Lamm, *Acta Chem. Scand.*, **B29**, 332 (1975).
252. D. C. Dittmer and N. Takashina, *Tetrahedron Letters*, 3809 (1964).
253. D. C. Dittmer and F. A. Davis, *J. Org. Chem.*, **32**, 3872 (1967).
254. W. Reid and H. Bopp, *Chem. Ber.*, **111**, 1527 (1978).
255. T. C. Sedergran, M. Yokoyama and D. C. Dittmer, *J. Org. Chem.*, **49**, 2408 (1984).
256. R. J. Bushby, *J. Chem. Soc., Perkin Trans. 1*, 2513 (1975).
257. C. L. McIntosh and P. De Mayo, *Chem. Commun.*, 32 (1969).
258. (a) D. Cornell and W. Stang, *Int. J. Chem. Kinet.*, 7, 799 (1975).
(b) A. Padwa and R. Gruber, *J. Org. Chem.*, **35**, 1781 (1970).
259. R. J. Crawford and T. R. Lynch, *Can. J. Chem.*, **46**, 1457 (1968).
260. R. F. C. Brown, *Pyrolytic Methods in Organic Chemistry*, Academic Press, New York, 1980.
261. J. F. King, K. Piers, D. H. Smith, C. L. McIntosh and P. De Mayo, *Chem. Commun.*, 31 (1969).
262. D. C. Dittmer, J. E. McCaskie, J. E. Babiarz and M. V. Ruggeri, *J. Org. Chem.*, **42**, 1910 (1977).
263. (a) J. D. Finlay and D. J. H. Smith, *Synth. Commun.*, 579 (1978).
(b) S. Ito and J. Mori, *Bull. Chem. Soc. Japan*, **51**, 3403 (1978).
264. R. F. J. Langendries and F. C. De Schryver, *Tetrahedron Letters*, 4781 (1972).
265. U. Schöllkopf, *Angew. Chem., Int. Ed. Engl.*, **9**, 763 (1970).
266. (a) R. M. Dodson, P. D. Hammen and R. A. Davis, *J. Org. Chem.*, **36**, 2693 (1971).
(b) R. M. Dodson, P. D. Hammen, E. H. Jancis and G. Klose, *J. Org. Chem.*, **36**, 2698 (1971).
267. (a) R. M. Dodson and P. D. Hammen, *Chem. Commun.*, 1294 (1968).
(b) R. M. Dodson, P. D. Hammen and J. U. Fan, *J. Org. Chem.*, **36**, 2703 (1971).
268. D. J. Young and C. J. M. Stirling, *Chem. Commun.* (in press) (1987).
269. A. Bury, H. A. Earl and C. J. M. Stirling, *Chem. Commun.*, 393 (1985).
270. P. Del Buttero, S. Mavorana and M. Trautluft, *J. Chem. Soc., Perkin Trans. 1*, 1411 (1974).
271. E. J. Corey and E. Block, *J. Org. Chem.*, **34**, 1233 (1969).
272. J. P. Marino, *Chem. Commun.*, 861 (1973).
273. L. S. Melvin, Jr. and B. M. Trost, *J. Amer. Chem. Soc.*, **94**, 1790 (1972).
274. P. Del Buttero and S. Mavorana, *Synth. Commun.*, 333 (1975).
275. U. Rheude and W. Sundermeyer, *Chem. Ber.*, **116**, 1285 (1983); **114**, 3378 (1981).
276. D. C. Dittmer and J. M. Balquist, *J. Org. Chem.*, **33**, 1364 (1968).
277. D. C. Dittmer and T. Nelson, *J. Org. Chem.*, **41**, 3044 (1976).
278. D. C. Dittmer and R. Glassman, *J. Org. Chem.*, **35**, 999 (1970).
279. S. Gronowitz (Ed.), *Thiophene and its Derivatives* (Parts One and Two), Wiley, New York, 1985, 1986.
280. M. S. Raasch, in Ref. 279, Part One, pp. 571–627.
281. P. H. Benders, D. N. Reinhoudt and W. P. Trompenaars, in Ref. 279, Part One, pp. 716–744.
282. D. Mukhergee, L. C. Dunn and K. N. Houk, *J. Amer. Chem. Soc.*, **101**, 251 (1979).
283. J. L. Melles and H. J. Backer, *Rec. Trav. Chim. Pays-Bas*, **72**, 314 (1953).
284. M. H. Palmer and R. H. Findlay, *J. Chem. Soc., Perkin Trans. 2*, 1223 (1975).
285. E. W. Garbisch, Jr. and R. F. Sprecher, *J. Amer. Chem. Soc.*, **88**, 3434 (1966).
286. K. Torssell, *Acta Chem. Scand.*, **B30**, 353 (1976).
287. W. L. Mock, *J. Amer. Chem. Soc.*, **92**, 7610 (1970).
288. (a) W. G. Klemperer, *Angew. Chem., Int. Ed. Engl.*, **17**, 246 (1978).
(b) J.-P. Kintzinger, in *NMR-17 and Silicon 29* (Eds. P. Diehl, E. Fluck and R. Kosfeld), Springer-Verlag, New York, 1981, pp. 1–64.
289. J. C. Dyer, D. L. Harris and S. A. Evans, Jr., *J. Org. Chem.*, **47**, 3660 (1982).
290. T. H. Sammakia, D. L. Harris and S. A. Evans, Jr., *Org. Magn. Reson.*, **22**, 747 (1984).
291. (a) E. Jonsson, *Arkiv Kemi*, **26**, 357 (1967).
(b) E. Jonsson and S. Holmquist, *Arkiv Kemi*, **29**, 301 (1968).

292. L. A. Serenson and A. W. Serenson, *Tetrahedron Letters*, 1315 (1973).
293. C. Galli, G. Giovannelli, G. Illuminati and L. Mandolini, *J. Org. Chem.*, **44**, 1258 (1979).
294. S. Sadeh and Y. Gaoni, *Tetrahedron Letters*, 2365 (1973).
295. J. J. Gajewski and C. N. Shih, *J. Amer. Chem. Soc.*, **94**, 1675 (1972).
296. H. W. Gschwend and H. Haider, *J. Org. Chem.*, **37**, 59 (1972).
297. G. A. Russel and L. A. Ochrymowycz, *J. Org. Chem.*, **35**, 2106 (1970).
298. (a) S. D. McGregor and D. M. Lemal, *J. Amer. Chem. Soc.*, **88**, 2858 (1966).
(b) W. L. Mock, *J. Amer. Chem. Soc.*, **88**, 2857 (1966).
299. C. A. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, **82**, 1812 (1960).
300. (a) D. H. R. Barton, F. Comer, D. G. T. Greig, P. G. Sammes, C. M. Cooper, G. Hewitt and W. G. E. Underwood, *J. Chem. Soc.*, 3540 (1971).
(b) D. H. R. Barton, D. G. T. Greig, G. Lucente, P. G. Sammes, M. V. Taylor, C. M. Cooper, G. Hewitt and W. G. E. Underwood, *Chem. Commun.*, 1683 (1970).
301. D. N. Jones and D. A. Lewton, *Chem. Commun.*, 457 (1974).
302. R. Bell, P. D. Cottam, J. Davis, D. N. Jones and N. A. Meanwell, *Tetrahedron Letters*, **21**, 4379 (1980).
303. C. H. Chen, *Tetrahedron Letters*, 25 (1976).
304. C. H. Chen and B. A. Donatelli, *J. Org. Chem.*, **41**, 3053 (1976).
305. (a) W. J. Baily and E. W. Cummins, *J. Amer. Chem. Soc.*, **76**, 1932 (1954).
(b) D. Copland, D. Lever and W. B. Menzies, *Tetrahedron Letters*, 639 (1977).
(c) S. E. Reiter, L. C. Dunn and K. N. Houk, *J. Amer. Chem. Soc.*, **99**, 4199 (1977).
306. (a) T. S. Chou, H. H. Tso and L. C. Lin, *J. Org. Chem.*, **51**, 1000 (1986).
(b) T. S. Chou, H. H. Tso and L. J. Chang, *J. Chem. Soc., Perkin Trans. 1*, 515 (1985).
307. S. Yamada, H. Ohsawa and H. Takayama, *Chem. Letters*, 1003 (1983).
308. R. Block and J. Abeccasis, *Synth. Commun.*, **15**, 959 (1985), and references cited therein.
309. H. H. Tso, L. J. Chang, L. C. Lin and T. S. Chou, *J. Chin. Chem. Soc.*, **32**, 333 (1985).
310. R. Bloch and J. Abecassis, *Tetrahedron Letters*, **24**, 1247 (1983).
311. R. Bloch, D. Hassan and X. Mandard, *Tetrahedron Letters*, **24**, 4691 (1983).
312. D. J. Peterson, *J. Org. Chem.*, **33**, 780 (1968).
313. J. E. McCormick and R. S. McElhinney, *J. Chem. Soc., Perkin Trans. 1*, 1335 (1972).
314. (a) U. Burkert and N. L. Allinger, in *Molecular Mechanics*, ACS Monograph, American Chemical Society, 1982.
(b) J. E. Williams, P. J. Stang and P. v. R. Schleyer, *Ann. Rev. Phys. Chem.*, **19**, 531 (1968).
315. N. L. Allinger and J. Kau, *Tetrahedron*, **32**, 529 (1976).
316. (a) E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, *Conformational Analysis*, Wiley–Interscience, New York, 1965, pp. 36–126, 156.
(b) E. L. Eliel, *Angew. Chem. Int. Ed. Engl.*, **11**, 739 (1972).
317. J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).
318. (a) J. B. Lambert, D. S. Bailey and C. E. Mixan, *J. Org. Chem.*, **37**, 377 (1972).
(b) C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **86**, 2935 (1964).
319. D. N. Harpp and G. Gleason, *J. Org. Chem.*, **36**, 1314 (1971).
320. (a) H. F. van Worden and E. Havinga, *Rec. Trav. Chim. Pays-Bas*, **86**, 342 (1967).
(b) J. A. Deyrup and C. L. Moyer, *J. Org. Chem.*, **34**, 175 (1969).
321. E. L. Eliel and R. O. Hutchins, *J. Amer. Chem. Soc.*, **91**, 2703 (1969).
322. (a) E. L. Eliel, *Acc. Chem. Res.*, **3**, 1 (1970).
(b) J. B. Lambert and S. I. Featherman, *Chem. Rev.*, **75**, 611 (1975).
323. F. A. Carey, P. M. Smith, R. J. Maher and R. F. Bryan, *J. Org. Chem.*, **42**, 961 (1977).
324. K. Bergesen, B. M. Carden and M. J. Cook, *J. Chem. Soc., Perkin Trans. 2*, 1001 (1978).
325. E. Juaristi and J. Gusmán, *Tetrahedron*, **40**, 1477 (1984).
326. G. W. Buchanan and T. Durst, *Tetrahedron Letters*, 1683 (1975).
327. G. Barbarella, P. Dembech and V. Tugnoli, *Org. Magn. Reson.*, **22**, 402 (1984).
328. M. Kimura, N. Kuriki, M. Inaishi and Y. Sawaki, *Tetrahedron Letters*, **25**, 4665 (1984).
329. G. Barbieri, M. Cinguini, S. Colona and F. Montanari, *J. Chem. Soc. (C)*, 659 (1968).
330. J. S. Hubbard and T. M. Harris, *J. Amer. Chem. Soc.*, **102**, 2110 (1980).
331. (a) O. H. House and J. K. Larson, *J. Org. Chem.*, **33**, 61 (1968).
(b) P. D. Magnus, *Tetrahedron*, **33**, 2019 (1977).
332. J. S. Grossert, J. Boyle and D. L. Hooper, *Tetrahedron*, **40**, 1135 (1984).
333. K. Takaki, K. Nakagawa and K. Negoro, *J. Org. Chem.*, **45**, 4789 (1980).

334. P. J. Kocienski, B. Lythgoe and S. Ruston, *J. Chem. Soc., Perkin Trans. 1*, 829 (1978).
335. S. Bradamante, S. Maiorana and G. Pagani, *J. Chem. Soc., Perkin Trans. 1*, 282 (1972).
336. R. W. Saalfrank and W. Rost, *Angew. Chem., Int. Ed. Engl.*, **24**, 855 (1985).
337. (a) E. Block, in *Organic Sulfur Chemistry* (Eds. R. Kh. Freidlina and A. E. Skorova), Pergamon Press, Oxford, 1981.
(b) J. F. King, *Acc. Chem. Res.*, **8**, 10 (1975).
338. J. Klein and H. Stollar, *J. Amer. Chem. Soc.*, **95**, 7437 (1973) and references cited therein.
339. S. Wolfe, A. Rauk, L. M. Tei and I. G. Csizmadia, *J. Chem. Soc. (B)*, 136 (1971).
340. S. Iriuchijima, M. Ishibashi and G.-I. Tsuchihashi, *Bull. Chem. Soc. Japan*, **46**, 921 (1973).
341. M. Cinquini, S. Colonna and F. Montanari, *J. Chem. Soc., Perkin Trans. 1*, 1723 (1974).
342. H. Stollar and J. Klein, *J. Chem. Soc., Perkin Trans. 1*, 1763 (1974).
343. G. Tsuchihashi and S. Iruichijima, *Bull. Chem. Soc. Japan*, **43**, 2271 (1970).
344. T. Durst, K. Tin and M. J. V. Marcil, *Can. J. Chem.*, **51**, 1704 (1973).
345. R. Bory, B. Moreau and A. Marquet, *Tetrahedron Letters*, 4921 (1972) and references cited therein.
346. S. Oae and T. Numata, in *Isotopes in Organic Chemistry* (Eds. E. Buncel and C. C. Lee), Vol. 5, Chap. 2, Elsevier, New York, 1980.
347. S. Oae, O. Itoh, T. Numata and T. Yoshimura, *Bull. Chem. Soc. Japan*, **56**, 270 (1983).
348. (a) S. Lane, S. J. Quick and R. J. K. Taylor, *Tetrahedron Letters*, **25**, 1039 (1984).
(b) S. Lane, S. J. Quick and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 2549 (1984).
349. G. A. Olah and S. C. Narang, *Tetrahedron*, **38**, 2225 (1982).
350. G. H. Wahl, Jr., J. Bordner, D. N. Harp and J. G. Gleason, *Acta Cryst.*, **B29**, 2272 (1973).
351. J. S. Grossert, M. H. Bharadwaj, R. F. Langler, T. S. Cameron and R. E. Cordes, *Can. J. Chem.*, **56**, 1183 (1978).
352. P. G. Mezey and A. Kapur, *Can. J. Chem.*, **58**, 559 (1980).
353. L. A. Paquette and S. Miorana, *Chem. Commun.*, 313 (1971).
354. V. J. Traynelis, J. A. Schield, W. A. Lidley and D. W. H. MacDowell, *J. Org. Chem.*, **43**, 3379 (1978).

CHAPTER **10**

Electronic effects of the sulfinyl and sulfonyl groups

JOHN SHORTER

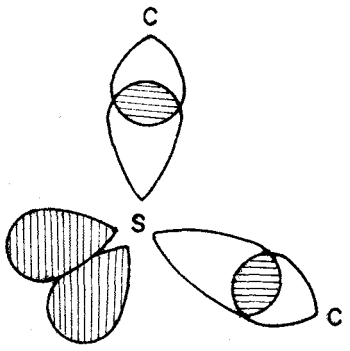
Department of Chemistry, The University, Hull, HU6 7RX, UK

I. INTRODUCTION

A. Sulfur Bonding[1,2]

The electronic structure of the sulfur atom in its ground state may be written as $1s^2 2s^2 2p^6 3s^2 3p_x^2 3p_y^1 3p_z^1$. When sulfur forms two single bonds to hydrogen, this may be pictured most simply in terms of the overlap of singly occupied 3p orbitals on sulfur with singly occupied 1s orbitals on hydrogen. Two doubly occupied, localized molecular orbitals of the σ-type are thereby formed. Two unshared pairs of electrons in the valence shell of the sulfur atom are left in the remaining 3p and the 3s orbital. In accord with this simple picture, the bond angle $\angle$HSH in hydrogen sulfide is approximately a right angle, actually 92° 20′. The slight opening-out of the angle is attributed to steric or electrical repulsion between the hydrogen atoms. (In water, for which the bonding involves 2p orbitals on oxygen, the bond angle is larger, 105°, due to the greater repulsion between the hydrogen atoms when attached to the smaller oxygen atom.) The S—C bonding in a dialkyl sulfide may be envisaged in an analogous way, singly occupied $2sp^3$ hybridized orbitals of carbon being involved. The greater steric repulsion between the alkyl groups opens-out the bond angle rather further than in hydrogen sulfide, e.g. in dimethyl sulfide it is 105°.

A slightly different way of picturing the formation of two single bonds by sulfur envisages the use of $3sp^3$ hybridized orbitals by sulfur. Thus the formation of dimethyl sulfide may be pictured in terms of the overlap of singly occupied $3sp^3$ hybridized orbitals on sulfur with singly occupied $2sp^3$ hybridized orbitals on carbon. Two doubly occupied, localized molecular orbitals of the σ-type are thereby formed. Two unshared pairs of electrons in the valence shell of the sulfur atom are left in the remaining $3sp^3$ orbitals. In accord with this picture, the bond angle $\angle$CSC in dimethyl sulfide is interpreted as essentially tetrahedral (109° 28′; see **1**).

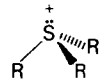


(1)

The contraction to 105° is explained by postulating that the repulsion between the unshared pairs of electrons is greater than between the shared pairs, thus opening-out the angle between the former and contracting the angle between the latter.

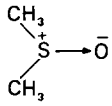
Viewed from the standpoint of molecular orbital theory, as it has developed during the last decade or so[3], the above simple pictures of the sulfur bonding in a dialkyl sulfide are somewhat naïve but they serve to introduce the subject and act as a basis for discussing the bonding in sulfoxides and sulfones. It will be convenient to use the second of the two pictures as the basis for further discussion, i.e. that involving the use of $3sp^3$ hybridized orbitals on sulfur.

The formation of a further single bond between sulfur and carbon, as in the trimethylsulfonium cation, may be pictured as involving a $3sp^3$ unshared pair orbital on sulfur and an empty $2sp^3$ orbital on carbon in a methyl cation. Thus the three σ bonds and the remaining unshared pair (in a $3sp^3$ orbital) in a trialkylsulfonium ion are distributed approximately tetrahedrally, i.e. the ion is pyramidal, with the sulfur atom at the apex (**2**).

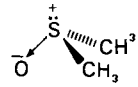


(**2**)

When the third bond is formed to oxygen rather than carbon, the situation is not so simple. The formation of dimethyl sulfoxide can be pictured initially in a way analogous to the above, an empty $2sp^3$ orbital on oxygen being involved. The bond between sulfur and oxygen is then a coordinate bond and the structure is appropriately written as **3** or **4**, with

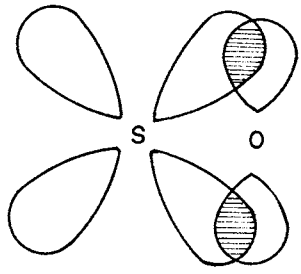


(**3**)



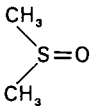
(**4**)

formal unit charges on sulfur and oxygen. At this point, however, the possible contribution of a 3d orbital on sulfur must be considered. One of the two electrons in an unshared pair $3sp^3$ orbital of dimethyl sulfide may be pictured as transferred to an appropriate 3d orbital, e.g. $3d_{xy}$. The oxygen atom is considered to be in a $2sp^2$ hybridized state, with two unpaired electrons, one in one of the $2sp^2$ orbitals and the other in the unhybridized $2p_y$ orbital. A σ bond is now formed by the end-on overlap of the singly occupied $3sp^3$ orbital of sulfur with the singly occupied $2sp^2$ orbital of oxygen, while a π(pd) bond is formed by the sideways overlap of the $3d_{xy}$ orbital of sulfur with the unhybridized $2p_y$ orbital of oxygen (see **5**).

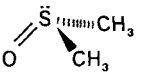


(**5**)

Considered in this way the structure of dimethyl sulfoxide involves a double bond and a valence shell of ten electrons for sulfur (**6** and **7**)[4,5].

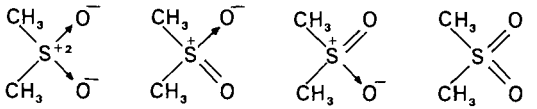


(**6**)



(**7**)

The formation of a further bond to oxygen, as in dimethyl sulfone, can be pictured in an analogous way to give tetrahedral structures involving various combinations of coordinate and double sulfur–oxygen bonds, **8–11**, with **9** and **10** having a valence shell of ten electrons and **11** one of twelve electrons for sulfur. In **8** there is a formal double positive charge on sulfur, with unit negative charges on each oxygen.



(**8**) (**9**) (**10**) (**11**)

The nature of the sulfur–oxygen bonds in sulfoxides and sulfones has been much discussed over many years[1]. One would expect the actual structures to be intermediate between the canonical structures **3** and **6**, and **8–11**, respectively, and that discussion would be about the relative contributions of the various canonical structures. In practice the emphasis has been on the extremes: is the sulfur–oxygen linkage in sulfoxides and sulfones essentially a coordinate bond or a double bond? Various lines of evidence have been considered to bear on this question and these will now be examined briefly[6].

The sulfur–oxygen bond length in sulfoxides and sulfones varies somewhat with the nature of the other groups attached to sulfur but is on average about 1.45 Å. This is much less than may be calculated as the sum of single-bond covalent radii, 1.60 Å, and even slightly less than the sum of the double-bond covalent radii, 1.49 Å. These and other pertinent bond length data, and also data from dipole moment measurements and thermochemistry, led Phillips and coworkers[7] to suggest that the sulfur–oxygen linkage in sulfoxides and sulfones may be appropriately represented as a double bond. However, the argument from bond lengths is not really clear-cut. The point at issue is not double bond *versus* single bond but double bond *versus* coordinate bond, the latter involving both a covalent and an ionic component. The charge separation could well be responsible for the contraction relative to the expected bond length for a sulfur–oxygen single linkage, particularly with sulfones in which the canonical structure involving two coordinate bonds **8** has two formal positive charges on sulfur.

The argument from dipole moments is similarly ambiguous. The bond moment of the sulfur–oxygen linkage in various simple sulfoxides and sulfones was originally[7] calculated from observed dipole moments to be about 2.4 D, but was later[8] recalculated as about 3.0 D. The bond moment of a sulfur–oxygen double bond in which the electrons were shared equally would, of course, be zero, while the full separation of unit charges to a distance of 1.45 Å in a coordinate bond would imply a bond moment of 6.96 D. The observed intermediate value may be explained for either type of bond by assuming an unsymmetrical distribution of bonding electrons. For the double bond the electrons must be shifted towards oxygen; for the coordinate bond, towards sulfur. Such shifts can readily be explained in terms of electronegativites of S *versus* O and of S^+ *versus* O^-.

Considerations of bond energies, which will not be entered into here[6], similarly do not give a clear answer to this structural problem. Studies of the infrared spectra of sulfoxides and sulfones enable force constants of the sulfur–oxygen bonds to be calculated with various groups attached to sulfur. Again, these have been variously interpreted and no clear indication as to the nature of the sulfur–oxygen bond emerges[6].

A small number of physical properties appears to provide more definite information: these are molecular refraction, parachor, and (in a more limited way) ultraviolet absorption[6].

The molecular refraction is a measure of the total polarizability of electrons in the molecule. It is to a considerable extent an additive function of bond refractions, with a double bond showing a substantial exaltation compared to the corresponding single bond. There is no evidence for such an exaltation in sulfoxides or sulfones, and one must conclude that the sulfur–oxygen bond therein is not a double bond but a coordinate bond. The bond refraction of this sulfur–oxygen coordinate bond actually appears to be somewhat lower than that of a sulfur–oxygen covalent single bond. This may be due to the strong electric field associated with the charge separation of the coordinate bond constraining the electrons in neighboring bonds and reducing the polarizability of the molecule as a whole[6].

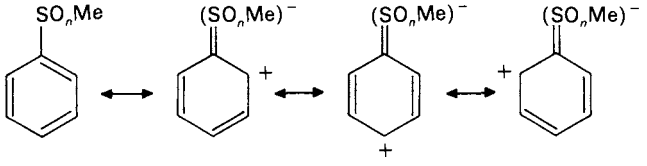
Sugden's parachor[9] is essentially a measure of the molar volumes of liquids at temperatures at which their surface tensions are equal. The parachor of a molecule is to a considerable extent an additive property of the contributing atoms but a double bond is associated with a substantial parachor increment. If the sulfur–oxygen bond in a sulfoxide or sulfone were a double bond, this should produce an increment in the parachor. In fact the observed values for the parachor of a considerable number of sulfoxides and sulfones are roughly equal to, or even slightly less than, the respective values calculated on the assumption that the sulfur–oxygen linkage therein is a single bond[6].

It should be mentioned finally that the ultraviolet spectra of simple sulfones (but not sulfoxides) provide evidence for the coordinate sulfur–oxygen bond. Double bonds characteristically lead to ultraviolet absorption somewhere in the range 200–400 nm. If the sulfur–oxygen linkage in sulfones were a double bond, it would be expected to give rise to at least a weak ultraviolet absorption. In fact dialkyl sulfones are transparent through the ultraviolet region, at least down to 200 nm. The electric field of the coordinate sulfur–oxygen bond may be presumed to constrain the electrons and thereby increase the excitation energy required for ultraviolet absorption. Evidence of this kind cannot be adduced for sulfoxides because the unshared electron pair may be excited by ultraviolet light[6].

In summary, therefore, one may say that all the evidence from bond lengths, dipole moments, bond energies, infrared spectra, molecular refraction, parachor and ultraviolet spectra may be satisfactorily interpreted in terms of a sulfur–oxygen bond which is largely, if not entirely, a coordinate bond. Some of the evidence for a coordinate bond is compelling; there is no compelling evidence for a sulfur–oxygen bond that is essentially a double bond. The dipole moment evidence, however, requires that the formal charges associated with the coordinate bond are partially neutralized by a shift of the bonding electrons away from the oxygen towards the sulfur. A recent highly sophisticated discussion of chemical bonding in higher main group elements agrees that the sulfur–oxygen bonds in sulfoxides and sulfones should be regarded as essentially coordinate rather than double bonds[3]. The necessity of supposing that the valence shell of sulfur can be expanded to ten or twelve electrons by the participation of 3d orbitals in the bonding may thus be avoided for dialkyl sulfoxides and sulfones. However, this is only a temporary respite in relation both to the behavior of a wide range of sulfoxides and sulfones and to a broader consideration of the chemistry of sulfur.

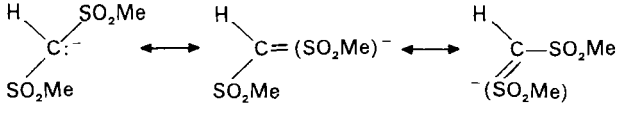
Thus the bonding in sulfur hexafluoride SF_6 has for a long time been considered to involve two of the 3d orbitals of sulfur, with the sulfur in a sp^3d^2 hybridized state and

having twelve electrons in its valence shell (see Pauling[10], who nevertheless expressed some doubts about the bonding role of d orbitals of the same principal quantum number as the s and p orbitals involved). There are also many other so-called hypervalent molecules formed by sulfur and its neighbors in the second row of the Periodic Table which appear to 'require' a bonding role of d orbitals, with 'octet expansion'. Of more immediate relevance to the present article on electronic effects is the possible bonding role of 3d orbitals and octet expansion for molecules in which sulfinyl or sulfonyl groups are attached to unsaturated systems or carbanionic centers. For example, in the case of PhSOMe or $PhSO_2Me$, and more particularly for some of their ring-substituted derivatives, there is much experimental evidence of various kinds that the benzene ring is conjugated with the bond linking it to the sulfur atom. Thus canonical structures of the types shown in **12a** and **b** must be regarded as contributing to the resonance hybrids. (For



(12) **(a)** $n = 1$
(b) $n = 2$

the sulfoxides there is a further complication connected with the lone pair of electrons on the sulfur, but we will not consider that at this stage.) Sulfonyl groups appear particularly able to stabilize adjacent carbanionic centers, for example in $:\bar{C}H(SO_2Me)_2$, and it seems appropriate to regard this species as a resonance hybrid of the canonical structures **13**. (In



(13)

passing it may be remarked that the analogous situations obtain for the sulfonio group[11].) Much of the experimental evidence that may be considered to support the importance of π(pd) bonding from carbon to sulfur in systems of these types will be presented and discussed later in this chapter.

At this point it must be said, however, that for many years there has been a school of thought among quantum chemists which maintains that it is not necessary to invoke a bonding role for the 3d orbitals of sulfur in some situations where this has been the traditional approach or, to put this more strongly, that it is not at all correct to do so[12,13]. (The same comment applies to the supposed bonding role of d orbitals in analogous situations for various other elements[14].) Such views did not seem to make much impact on organosulfur chemistry in general for a long time, but within the last decade there has been a move towards taking them more seriously[12–14]. This may be due partly to the accumulation of experimental evidence that d orbital bonding does not occur in certain examples for which it would traditionally have been invoked and partly to the results of *ab initio* molecular orbital calculations. It is certainly no longer appropriate to write about the electronic effects of sulfinyl and sulfonyl groups and ignore these views or refer to them only as an after-thought[11]. An attempt must therefore be made here to present the alternatives to invoking a bonding role for the 3d orbitals of sulfur, even though in the rest of the chapter there will be much reference to π(pd) bonding, albeit often in a historical context.

B. The Role of 3d Orbitals; Experimental Evidence

There is a vast literature in which many experimental results for sulfur in its various oxidation states are explained in terms of a bonding role of 3d orbitals. The subject has been extensively reviewed a number of times[15]. There is a corresponding literature for the neighbors of sulfur in the Periodic Table: silicon, phosphorus and chlorine[14]. The same situation holds for the higher members in the same Groups in respect of the participation of d orbitals of higher principal quantum number. The possibility of alternative explanations in terms of lower electronegativity, higher polarizability and larger atoms has rarely been considered. It is as if Pauling's postulate[10] of the bonding role of 3d orbitals in molecules such as SF_6 established an inviolable mode of thought on these matters. In so far as this mode of thought is relevant to the electronic effects of sulfinyl and sulfonyl groups we shall encounter it frequently later in this chapter. At this point we shall restrict ourselves to describing a few experimental results which appear to cast doubt on the bonding role of sulfur 3d orbitals. We will concentrate on examples involving sulfoxides and sulfones but there will also be brief mention of other sulfur compounds which are relevant in this connection.

The possibility of conjugative interaction between a vinyl group and SOMe or SO_2Me will first be considered[6]. The vinyl group is prone to enter into conjugative interaction with suitably attached groups. Thus the carbonyl stretching frequency $\bar{\nu}$(CO) for methyl vinyl ketone (pure liquid) is 1684 cm^{-1}, compared with 1715 cm^{-1} for acetone (pure liquid)[16]. This difference corresponds to the carbonyl group in methyl vinyl ketone acquiring enhanced single bond character through the participation of a polar canonical structure **14b**:

$$\underset{\textbf{(a)}}{CH_2{=}CH{-}\overset{\overset{O}{\|}}{C}{-}CH_3} \leftrightarrow \underset{\textbf{(b)}}{\overset{+}{C}H_2{-}CH{=}\overset{\overset{O^-}{|}}{C}{-}CH_3}$$

(14)

Further, $\bar{\nu}$(C=C) for the stretching of the double bond in an unconjugated vinyl group is about 1639 cm^{-1} but in methyl vinyl ketone it is 1621 cm^{-1}.

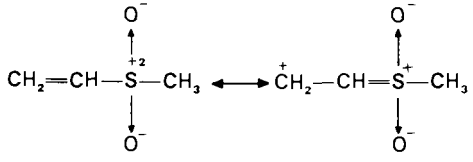
The behavior of $\bar{\nu}$(C=C) also indicates strong conjugation in methyl vinyl sulfide through the participation of one of the sulfur lone pairs in π(pp) bonding (cf. **15**). $\bar{\nu}$(C=C)

$$CH_2{=}CH{-}\ddot{\underset{\cdot\cdot}{S}}{-}CH_3 \leftrightarrow \bar{C}H_2{-}CH{=}\overset{+}{\underset{\cdot\cdot}{S}}{-}CH_3$$

(15)

is at 1587 cm^{-1}, compared with 1634 cm^{-1} in the unconjugated allyl methyl sulfide. For methyl vinyl sulfoxide $\bar{\nu}$(C=C) is 1613 cm^{-1}. In a sulfoxide the remaining lone pair on the sulfur still gives the possibility of π(pp) bonding but diminished in importance. For methyl vinyl sulfone $\bar{\nu}$(C=C) is 1626 cm^{-1}. In a sulfone π(pp) bonding involving sulfur is impossible but there is no sign of appreciable π(pd) bonding, which would lower $\bar{\nu}$(C=C) again through **16b**. In fact $\bar{\nu}$(C=C) is practically back to the value for allyl methyl sulfide, 1634 cm^{-1}.

Additional evidence for the absence of conjugation between a vinyl group and $-SO_2-$ is sometimes drawn from the observation that the sulfur–oxygen stretching vibrations are but little affected when the ethyl groups of diethyl sulfone are successively replaced by vinyl groups[17]. While this might be considered good evidence against conjugation if the sulfur–oxygen linkage is regarded as a double bond (cf. the C=O in methyl vinyl ketone), it is not such definite evidence against interaction between a vinyl group and the sulfur–oxygen



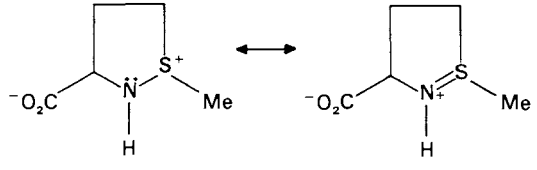
(a) (b)

(16)

coordinate bond. However, the absence of π(pd) bonding between a vinyl group and $—SO_2—$ is confirmed by thermochemical studies. The experimental heats of atomization of several vinyl sulfones (determined from heats of combustion) scarcely differ from those calculated from bond energies, e.g. for divinyl sulfone the values are 1217.1 and 1222.9 kcal mol^{-1} respectively[18]. (The small difference is in the wrong direction for an effect of conjugation.)

Carbanions are stabilized by electron-withdrawing groups attached to the center of negative charge and it is commonly supposed that ability to delocalize the charge through π bonding is particularly important, as for example with the nitro group. The sulfinyl and sulfonyl groups are certainly highly electron-withdrawing, as will be seen in detail later, and their ability to stabilize carbanions has traditionally been attributed particularly to π(pd) bonding, e.g. **13**. It has thus often been supposed that the tetrahedral distribution of bonds around the α-carbon in the sulfinyl or sulfonyl carbon acid gives place to the planar distribution of sp^2 carbon in the carbanion. However, it has long been known that reactions involving carbanions from optically active sulfones often proceed with high retention of configuration; this also occurs, but to a lesser extent, with sulfoxides[19]. These observations are most easily explained in terms of a pyramidal carbanion, with electrostatic inhibition of inversion, but various *ad hoc* explanations have been devised to maintain the supposed planar π(pd) bonded carbanion, e.g. hindrance to rotation around the C—S bond. There is now, however, considerable support for the pyramidal carbanion, with localized negative charge, stabilized by sulfinyl or sulfonyl groups. In this connection ^{13}C NMR studies have been very revealing[20]. Delocalization of negative charge and rehybridization of α-carbon from sp^3 to sp^2 is associated with a large downfield (positive) shift as between the carbon acid and its lithium salt, e.g. for 9-fluorenyllithium the shift is + 43.6 ppm, the carbanion being stabilized by extensive delocalization of charge into the aromatic rings. For $PhSOCH_2Li$ and $PhSO_2CH_2Li$ the ^{13}C shifts are − 11.9 and − 9.0 ppm respectively[21], rather similar to those shown by alkyllithiums, in which delocalization through conjugation is impossible, e.g. CH_3Li − 13 ppm. This was held to support that view that the sulfinyl and sulfonyl carbanions are pyramidal and stabilized by polarization of the sulfur rather than by π(pd) bonding.

We will give one further experimental example, not concerned with sulfoxides or sulfones, but which provides a strong warning against over-reliance on hypothetical π(pd) bonding of sulfur. Dehydromethionine might be expected to be stabilized by resonance involving such bonding, (**17**) with the N adopting planar geometry. In fact X-ray



(17)

crystallographic study shows that the geometry at the N is pyramidal[22]. This suggests that there is no π(pd) bonding between the N and the S. The authors point out that this system is essentially isoelectronic with a sulfonium ylide system, which may therefore behave similarly in this respect, i.e. the usually assumed resonance **18** may not be correct.

(18)

C. The Role of 3d Orbitals; Molecular Orbital Theory

There are two complementary lines of approach to examining the part played by 3d orbitals in molecular orbital theory and to appreciating current doubts as to their role. On the one hand, there is the question of 3d orbitals in relation to the basic formulation of molecular orbitals by overlapping atomic orbitals; on the other hand, there is the question of the effect of including or excluding 3d functions in molecular orbital calculations, particularly of the *ab initio* type. We shall consider each of these briefly in turn.

From the standpoint of angular distribution, 3d orbitals should have considerable overlap with suitably oriented 2s or 2p orbitals (or hybrid $2sp^2$ or $2sp^3$ orbitals) on ligand atoms. We have already seen one example of this in connection with the possible double sulfur–oxygen bond in sulfoxides and sulfones, involving π(pd) bonding, but there are several other types of overlap involving d orbitals and leading either to σ-bonding or π-bonding (or to non-bonding MO)[23]. We have also mentioned already the traditional formulation of SF_6 as involving sp^3d^2 hybridization, permitted by the angular distributions of the various orbitals[10].

But the angular distribution is only one part of what must be considered in connection with the overlap of d orbitals with orbitals on ligand atoms. The radial distribution is also extremely important, i.e. the size of the d orbital. Various estimates of the radial distributions of 3d orbitals for free atoms of the second short period, such as silicon, phosphorus and sulfur, suggest that these orbitals are far too diffuse for them to have any effective overlap with the orbitals of ligands. It is, however, possible to get over this difficulty in various ways, notably through the idea that the electrostatic field of the ligands induces d orbital contraction. This is in accord with the well-known observation that the higher valencies of phosphorus and sulfur, for example, are brought into play only by the most electronegative elements, e.g. SF_6 is extremely stable but there is no SCl_6, and SCl_4 is decomposed well below ambient temperature. From this point of view a π(pd) bonding component in the sulfur–oxygen bonds of sulfoxides and sulfones would not be ruled out. However, the hypothetical occurrence of such bonding when carbon is the ligand involved could not be justified in terms of 3d orbital contraction.

The other aspect of 3d orbitals which is important in relation to their possible role in bonding is their energy. If their energies are too far above those of the s or p orbitals in question, there will not be any effective 'mixing', leading to bonding of the σ or π type. 3d orbitals do tend to be of rather high energy but here again the electronegative nature of the ligand can be important and could lower the 3d orbital energies appropriately.

The foregoing discussion indicates that while there are difficulties in the way of a bonding role for 3d orbitals, for certain situations at least it is possible to conceive of ways in which these difficulties may be overcome. However, it is necessary to say that even for hypervalent molecules such as SF_6 which seem to 'require' the use of d orbitals, there are molecular orbital treatments not involving the use of d orbitals. In fact, as shown by Bent in an elegant exposition[12], the MO model of SF_6 involving the use of d orbitals is only one of several possibilities. The octahedral stereochemistry of SF_6, traditionally explained in

terms of the sp^3d^2 hybridization of sulfur[10], can actually be explained without reference to orbitals at all by electron-pair repulsion theory or by an ionic model of SF_6 as $S^{+6}(F^-)_6$. The SF_6 molecule can also be described by a MO model involving only fluorine atomic orbitals (giving either delocalized or localized molecular orbitals) or more conventionally in terms of delocalized molecular orbitals made up entirely of 3s and 3p orbitals on sulfur and 2p orbitals of fluorine. The last-mentioned typifies the most general treatment of these hypervalent molecules, i.e. MO models involving multicenter bonding. Such MO formulations are also possible for molecules of elements in the first short period and it must be presumed that packing difficulties prevent the existence of molecules such as OF_6.

We pass now to the question of the role of 3d functions in molecular orbital calculations. Doubts about this seem to have arisen in the later 1960s. In 1969 Coulson[24] questioned whether the finding of a small contribution from d functions in a MO calculation could be regarded as evidence for d orbital contributions to bonding, rather than the possibility of expressing polarization or perturbation of $p\pi$ orbitals in terms of a $d\pi$ component. Two early papers of considerable interest for the present chapter involved SCF-MO calculations on the hypothetical species $^-CH_2S(H)O$ and $^-CH_2S(H)O_2$ as models for sulfoxide- and sulfone-stabilized carbanions[25,26]. The results of these calculations supported the pyramidal carbanion, with conformational preferences governed by the minimizing of electrostatic repulsions, and no significant contribution of d orbital bonding to the stabilization by the sulfinyl or sulfonyl groups.

In the past two decades there have been several hundred molecular orbital studies of sulfur compounds, of increasing sophistication as the *ab initio* procedures have progressed and computers have improved. It is not possible to report, however, that a clear coherent picture of the role of d orbitals has emerged or is emerging from these calculations. For some time in the 1970s it seemed as though the concept of a bonding role for d orbitals was gradually fading away. There were many studies in which it was shown that the inclusion of d functions in the calculations made practically no difference to the results. Thus Streitwieser and Williams[27] made *ab initio* SCF calculations on CH_3SH and $^-CH_2SH$. Two different basis sets were tried: 'split shell' (SS) and 'split shell + d orbitals' (SS + d). The marked carbanion-stabilizing effect of sulfur was confirmed but the introduction of d orbitals affected the energies of CH_3SH and $^-CH_2SH$ almost equally. Hence the d orbitals have no effect on the proton affinity of $^-CH_2SH$. Calculation of electron density differences as between CH_3SH and $^-CH_2SH$ showed increased electron density on S in the carbanion, accommodated through the polarization of the polarizable sulfur electrons.

Another important and influential paper was by Bernardi and coworkers[28] (containing in its title the phrase 'the irrelevance of d orbital conjugation') and was a rather more elaborate study closely related to the above, since it concerned a non-empirical MO investigation of the reactions described in equation 1.

$$^-CH_2XH + H^+ \longrightarrow CH_3XH \longleftarrow H^+ + CH_3X^- \qquad (1)$$

for the systems X = O or S. Computations were performed with several basis sets containing either sp or spd functions on the heteroatoms. No evidence was found for the differences in behavior between the oxygen and sulfur systems being due to π(pd) bonding for sulfur. The importance of the polarizability of sulfur was again emphasized. The greater polarizability of sulfur compared with oxygen was attributed, at least in part, to the presence of low-lying d orbitals on sulfur. Thus the 'irrelevance' of d orbitals as such was not asserted, only that of their role in bonding. The same research group pursued these matters in later papers, with further rationalization of the characteristic behavior of sulfur without postulating π(pd) bonding[29].

In the later 1970s there were, however, some papers which asserted the importance of including d orbitals in the basis set in *ab initio* MO calculations. For instance, calculations

of binding energies and geometries of various molecules containing elements of the second short period found that satisfactory agreement with experimental values required the inclusion of 3d functions[30]. Around 1980 there was a new development stimulated by advances in computation enabling some of the restraints necessarily imposed on early *ab initio* MO calculations to be eliminated. Some of the systems previously investigated were re-examined, often by those who had been involved in the earlier work, and reappraisal of the situation regarding d orbitals was often involved. For example, improved computational procedures showed that sulfur 3d functions were essential for the proper description of the bonding in the α-thiocarbanions $^{-}CH_2SH$ and $^{-}CH_2SCH_3$[31]. The structures and proton affinities of CH_2SR_2, $^{-}CH_2SOR$, and $^{-}CH_2SO_2R$ (R = H or CH_3) were examined at the 3–21G* (d orbitals on sulfur) and 3–21G (no d orbitals on sulfur) levels, using 'gradient optimization procedures'[32]. The role of d orbitals was found to be important. In particular, for the sulfinyl and sulfonyl carbanions there is charge transfer from the n_c (carbon lone pair) orbital to the σ_{SR}* orbital and there is further an important stabilizing interaction involving the d_{xz} orbital of sulfur and σ_{SR}*. This is regarded as a d orbital polarization effect. Other *ab initio* studies (and also semiempirical studies of sulfonium ylides), which also find d orbitals to be important, are interpreted in terms of π(pd) bonding between S and C[33].

On the other hand, a very recent theoretical study of carbanions and lithium salts derived from dimethyl sulfone by Bors and Streitwieser[34] apparently confirms that d orbitals are not important in stabilizing the anion and that simple coulombic interactions play a dominant role, with significant charge polarization. Also, another study of α-heterosubstituted organolithium and organosodium compounds claims to show the 'energetic unimportance of second-row d orbital effects'[35]. The greater stabilization of carbanions by second-row than by first-row elements is attributed to greater electropositive character, more effective negative hyperconjugation and greater polarizability.

And finally, we may mention that 'a statistical analysis of the sulfur d orbital problem' has been carried out with dimethyl sulfoxide as a model compound[36]. 'The results provide a clear answer to the sulfur d orbital problem, since no simultaneous reproduction of experimental geometry and an adequate approximation to the variationally optimum total energy have been possible without including d polarization functions on sulfur'.

We must now decide on a policy for dealing, in the rest of this chapter, with the effects of sulfinyl and sulfonyl groups which were traditionally ascribed to π(pd) bonding between carbon and sulfur. It is clearly not possible at present to decide between the various alternative explanations that have been offered. The only sensible policy appears to be to use some fairly neutral descriptive term to cover the phenomena for which π(pd) bonding for long provided the conventional explanation. All parties seem to agree that these phenomena are all connected with a special build-up of electron density in the vicinity of sulfur, whatever may be the precise mechanism by which this occurs. To that extent it seems not unsuitable to refer to these phenomena as involving 'octet expansion' of sulfur and we will make some use of this term in appropriate context. It must, however, be understood that we do this as a convenient shorthand, without prejudice to the question of the precise mechanism whereby the 'octet expansion' occurs. In using this term we are essentially following in the footsteps of Bent[12]. But in the appropriate historical context we shall still refer to d orbital conjugation and π(pd) bonding.

D. Electronic Effects of Sulfinyl and Sulfonyl Groups and the Scope of this Chapter

The considerable dipole moment of the sulfur–oxygen bond[7,8] in the sense $S^{\delta+}—O^{\delta-}$ would be expected to result in these groups acting as strongly electron-attracting substituents with a similarity to CH_3CO, CN, NO_2, etc. Chemical evidence for such behavior has been known for many years. Thus the activation of a methylene or methyl

group adjacent to a sulfonyl group, was discovered almost a century ago. In 1889 Fromm found that bis(alkylsulfonyl)methanes would undergo halogenation on the central methylene group and also methylation by methyl iodide in the presence of alkali[37] (see also Fromm and coworkers)[38]. Such activation is, of course, connected with incipient formation of a hydrogen ion under the electron-attracting influence of the substituents. Direct evidence of ionization was provided by the observation that the same compounds dissolve in caustic alkali[39]. The solutions have an ultraviolet absorption *ca.* 200 nm, which is undoubtedly that of the anion $\bar{C}H(SO_2R)_2$, the parent sulfones being transparent in this region in neutral or acidic solution[40]. The pK_a value of bis(methylsulfonyl)methane in water at 25 °C was found to be 14[41]. Nearly half a century ago dimethyl sulfone in alkaline D_2O was shown to exchange its hydrogen for deuterium[42].

It has also been known for many years that sulfonyl groups, like carbonyl groups, promote the addition of nucleophilic reagents to carbon–carbon double bonds[43]. The *meta*-directing properties of the SO_2Me group in electrophilic aromatic substitution were discovered in the mid-1920s[44].

The acidifying influence of sulfinyl groups, although weaker than that of sulfonyl groups, has also long been recognized. Thus dibutyl sulfoxide in alkaline D_2O slowly exchanges hydrogen for deuterium[45]. The promotion of nucleophilic aromatic substitution by sulfinyl groups, analogous to the well-known effect exercised by nitro groups, has been known for half a century: Hammick and Williams showed in 1938 that *p*-iodophenyl phenyl sulfoxide was hydrolyzed by alkali under conditions in which the *meta* isomer was not affected[46].

The quantitative study of the electronic effects of sulfinyl and sulfonyl groups is naturally much concerned with the Hammett equation and its extensions. The next section therefore contains a summary of the salient features of the Hammett equation and cognate linear free-energy relationships. This prepares the ground for a discussion of the electronic effects (sigma values) of sulfinyl and sulfonyl groups attached to aromatic systems, including the transmission of electronic effects through —SO— and —SO_2— (rho values), and the *ortho*-effect in which electronic effects are moderated by steric and other influences. Later sections deal with substituent effects in aliphatic systems and the stabilization of carbanionic centers. Finally, there is a group of miscellaneous topics, including the influence of sulfinyl and sulfonyl groups on nucleophilic aliphatic substitution and nucleophilic and electrophilic aromatic substitution.

II. THE HAMMETT EQUATION[47]

A. Introduction

The Hammett equation is the best-known example of a linear free-energy relationship (LFER), that is, an equation which implies a linear relationship between free energies of reaction or activation for two related processes[48]. It describes the influence of polar *meta*- or *para*-substituents on reactivity for side-chain reactions of benzene derivatives.

The Hammett equation (1937)[49–51] takes the form of equation 2 or 3:

$$\log k = \log k^0 + \rho\sigma \tag{2}$$

$$\log K = \log K^0 + \rho\sigma \tag{3}$$

The symbol k or K is the rate or equilibrium constant, respectively, for a side-chain reaction of a *meta*- or *para*-substituted benzene derivative, and k^0 or K^0 denotes the statistical quantity (intercept term) approximating to k or K for the 'parent' or 'unsubstituted' compound. The *substituent constant* σ measures the polar (electronic) effect of replacing H by a given substituent (in the *meta*- or *para*-position) and is, in principle, independent of the nature of the reaction. The *reaction constant* ρ depends on the nature of

TABLE 1. Selected values[a] of σ, σ^+, and σ^- constants

Substituent	σ_m	σ_p	σ_p^+	σ_p^-
Me	−0.07	−0.17	−0.31	—
OMe	0.12	−0.27	−0.78	—
SMe	0.15	0.00	−0.60	0.21
OH	0.12	−0.37	−0.92	—
SH	0.25	0.15	—	—
NMe_2	−0.15	−0.63	−1.7	—
F	0.34	0.06	−0.07	—
Cl	0.37	0.23	0.11	—
CF_3	0.43	0.54	—	0.65
CN	0.56	0.66	—	0.88
NO_2	0.71	0.78	—	1.24
CO_2H	0.37	0.45	—	0.73

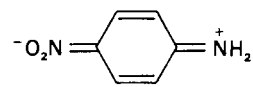
[a] These values, drawn from various sources, are presented solely for illustration. The table should not itself be used uncritically as a source of σ values for correlations. See rather References 50 and 79.

the reaction (including conditions such as solvent and temperature) and measures the susceptibility of the reaction to polar effects. Hammett chose the ionization of benzoic acids in water at 25 °C as a standard process. For this, ρ is defined as 1.000, and the value of σ for a given substituent is then $\log (K_a/K_a^0)$, where K_a is the ionization constant of the substituted benzoic acid and K_a^0 that of benzoic acid itself. Selected values of σ for well-known substituents are given in Table 1. They are readily interpreted qualitatively in simple electronic terms, i.e. through the inductive (I) effect and the resonance or conjugative (R) effect.

Jaffé (1953)[52] showed that while many rate or equilibrium data conform well to the Hammett equation (as indicated by the correlation coefficient), many such data are outside the scope of the equation in its original form and mode of application. Deviations are commonly shown by *para*-substituents with considerable $+R$ or $-R$ effect[53]. Hammett himself found that *p*-NO_2 ($+R$) showed deviations in the correlation of reactions of anilines or phenols. The deviations were systematic in that a σ value of *ca.* 1.27 seemed to apply, compared with 0.78 based on the ionization of *p*-nitrobenzoic acid. Other examples were soon discovered and it became conventional to treat them similarly in terms of a 'duality of substituent constants'.

When σ values based on the ionization of benzoic acid are used, deviations may occur with $+R$ *para*-substituents for reactions involving $-R$ electron-rich reaction centers, and with $-R$ *para*-substituents for reactions involving $+R$ electron-poor reaction centers. The explanation of these deviations is in terms of 'cross-conjugation', i.e. conjugation involving substituent and reaction center.

In the ionization of the *p*-nitroanilinium ion, the free base is stabilized by delocalization of electrons involving the canonical structure **19**. An analogous structure is not possible for



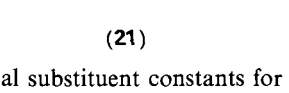
(19)

the *p*-nitroanilinium ion. In the ionization of *p*-nitrophenol, analogous delocalization is possible in both phenol and phenate species, but is more marked in the ion. Thus, in both

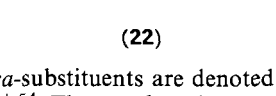
the aniline and the phenol system *p*-NO_2 is effectively more electron-attracting than in the ionization of benzoic acid, where the reaction center is incapable of a $-R$ effect, and indeed shows a small $+R$ effect (**20**).

(**20**)

An example of a reaction series in which large deviations are shown by $-R$ *para*-substituents is provided by the rate constants for the solvolysis of substituted *t*-cumyl chlorides, $ArCMe_2Cl$[54]. This reaction follows an S_N1 mechanism, with intermediate formation of the cation $ArCMe_2^+$. A $-R$ *para*-substituent such as OMe may stabilize the activated complex, which resembles the carbocation–chloride ion pair, through delocalization involving structure **21**. Such delocalization will clearly be more pronounced than in the species involved in the ionization of *p*-methoxybenzoic acid, which has a reaction center of feeble $+R$ type (**22**). The effective σ value for *p*-OMe in the solvolysis of *t*-cumyl chloride is thus -0.78, compared with the value of -0.27 based on the ionization of benzoic acids.



(**21**)



(**22**)

The special substituent constants for $+R$ *para*-substituents are denoted by σ^-, and those for $-R$ *para*-substituents are denoted by σ^+[54]. They are based respectively on the reaction series discussed above. Selected values are given in Table 1. Characteristic σ^- or σ^+ values are sometimes distinguished for *meta*-substituents also, but only for a minority of substituents which show very marked $+R$ or $-R$ effects do these differ significantly from ordinary σ values. The range of applicability of the Hammett equation is greatly extended by means of σ^- and σ^+, notably to nucleophilic (by σ^-) and to electrophilic (by σ^+) aromatic substitution.

However, the 'duality of substituent constants' and the attempt to deal with cross-conjugation by selecting σ^+, σ or σ^- in any given case is somewhat artificial. The contribution of the resonance effect of a substituent relative to its inductive effect must in principle vary continuously as the electron-demanding quality of the reaction center is varied, i.e. whether it is electron-rich or electron-poor. A 'sliding scale' of substituent constants would be expected for each substituent having a resonance effect and not just a pair of discrete values: σ^+ and σ for $-R$, or σ^- and σ for $+R$ substituents[55].

B. Multiparameter Extensions[56,57]

There are two main types of treatment, both involving multiparameter extensions of the Hammett equation, which essentially express the 'sliding scale' idea.

In the Yukawa–Tsuno equation (1959)[58] (equation 4), the sliding scale is provided by multiple regression on σ and $(\sigma^+ - \sigma)$ or $(\sigma^- - \sigma)$, depending on whether the reaction is more or is less electron demanding than the ionization of benzoic acid.

$$\log k = \log k^0 + \rho[\sigma + r^{\pm}(\sigma^{\pm} - \sigma)] \tag{4}$$

(There is a corresponding form of the equation for equilibria.) The quantity r^+ gives

the contribution of the enhanced $\pm R$ effect in a given reaction. (The equation was modified in 1966[59] to use σ^0 instead of σ values, see below, but the essential principles are unaltered.)

In the form of treatment developed by Taft and his colleagues since 1956[60–62], the Hammett constants are analyzed into inductive and resonance parameters, and the sliding scale is then provided by multiple regression on these. Equations 5 and 6 show the basic relationships.

$$\sigma_m = \sigma_I + 0.33\ \sigma_R(\mathrm{BA}) \tag{5}$$

$$\sigma_p = \sigma_I + \sigma_R(\mathrm{BA}) \tag{6}$$

The σ_I scale is based on alicyclic and aliphatic reactivities (see below), and the factor 0.33 in equation 5 is the value of a 'relay coefficient', α, giving the indirect contribution of the resonance effect to σ_m. However, the ionization of benzoic acids is not regarded as an entirely satisfactory standard process, since it is subject to some slight effect of cross-conjugation (see structure **22** above). Consideration of 'insulated series', not subject to this effect, e.g. the ionization of phenylacetic acids, is used as the basis of a σ^0 scale, which can be analyzed by equations 7 and 8[63]. (Note the different value of α.) By a different procedure Wepster and colleagues[55] devised an analogous σ^n scale (n = normal, i.e. free from the effects of cross-conjugation). Analysis of σ^+ and σ^- constants correspondingly involves $\sigma_R{}^+$ and $\sigma_R{}^-$.

$$\sigma_m{}^0 = \sigma_I + 0.5\ \sigma_R{}^0 \tag{7}$$

$$\sigma_p{}^0 = \sigma_I + \sigma_R{}^0 \tag{8}$$

Multiple regression on σ_I- and σ_R-type parameters employs the 'dual substituent-parameter' equation, which may be written as in equation 9[64].

$$\log(k/k^0) = \rho_I\sigma_I + \rho_R\sigma_R \tag{9}$$

For any given reaction series the equation is applied to *meta*- and *para*-substituents separately, and so values of ρ_I and ρ_R characteristic both of reaction and of substituent position are obtained. The various σ_R-type scales are linearly related to each other only approximately. In any given application the scale which gives the best correlations must be found[65].

Values of σ^0-, σ_I- and σ_R-type parameters for certain substituents are given in Table 2. It should be mentioned that Exner has developed a slightly different procedure for analyzing sigma values into inductive and resonance components, to which reference will be made later in this chapter[66].

The correlation analysis of spectroscopic properties in terms of σ_I- and σ_R-type parameters has been very important. Substituent effects on ^{19}F NMR shielding in

TABLE 2. Selected values[a] of σ^0-, σ_I- and σ_R-type constants

Substituent	$\sigma_m{}^0$	$\sigma_p{}^0$	σ_I	σ_R(BA)	$\sigma_R{}^0$	$\sigma_R{}^+$	$\sigma_R{}^-$
Me	−0.07	−0.15	−0.05	−0.12	−0.10	−0.25	—
OMe	0.06	−0.16	0.26	−0.53	−0.41	−1.02	—
NO_2	0.70	0.82	0.63	0.15	0.19	—	0.61
F	0.35	0.17	0.52	−0.46	−0.35	−0.57	—
Cl	0.37	0.27	0.47	−0.24	−0.20	−0.36	—

[a]See footnote to Table 1.

fluorobenzenes have been studied in great detail by Taft and colleagues[63,67,68]. For δ_m^F linear regression on σ_I is on the whole satisfactory, but a term in σ_R^0 with a small coefficient is sometimes introduced. The correlation analysis of δ_p^F, however, requires terms in both σ_I- and σ_R-type parameters, with σ_R^0 being widely applicable. Many new values of these parameters have been assigned from fluorine chemical shifts.

The correlation analysis of infrared data has been much examined by Katritzky, Topsom and colleagues[69,70]. Thus, the intensities of the ν_{16} ring-stretching bands of mono- and di-substituted benzenes may be correlated with the σ_R^0 values of the substituents and these correlations may be used to find new σ_R^0 values.

Finally, in this account of multiparameter extensions of the Hammett equation, we comment briefly on the origins of the σ_I scale. This had its beginning around 1956[62] in the σ' scale of Roberts and Moreland[71] for substituents X in the reactions of 4-X-bicyclo[2.2.2]octane-1 derivatives. However, at that time few values of σ' were available. A more practical basis for a scale of inductive substituent constants lay in the σ^* values for XCH_2 groups derived from Taft's analysis of the reactivities of aliphatic esters into polar, steric and resonance effects[62,72,73]. For the few σ' values available it was shown that σ' for X was related to σ^* for XCH_2 by the equation $\sigma' = 0.45\,\sigma^*$. Thereafter the factor 0.45 was used to calculate σ_I values of X from σ^* values of XCH_2[74].

III. SUBSTITUENT EFFECTS IN AROMATIC SYSTEMS

A. Sigma Values from Reactivity Studies

1. Alkylsulfinyl and alkylsulfonyl groups

Most of the information available concerns SOMe and SO_2Me. Bordwell and his colleagues were the leading pioneers in determining sigma values for these groups. The results of the main determinations of the ordinary Hammett σ constant and of the exalted constant σ^- are shown in Tables 3 and 4 respectively.

It will be convenient to take the work (in 1952) of Bordwell and Cooper (BC)[75] on the electronic effects of SO_2Me as the starting point of our discussion. The values of σ_m and σ_p, 0.65 and 0.72 respectively, as obtained from the ionization constants of substituted benzoic acids in 50% ethanol, are rather similar to the values for CN: 0.56 and 0.66 respectively (Table 1). The SO_2Me group is revealed as slightly less electron-attracting than the NO_2 group (values 0.71 and 0.78) and considerably more electron-attracting than the COMe group (values 0.35 and 0.43, also determined by BC). The order $\sigma_p > \sigma_m$ for CN, NO_2 and COMe is usually attributed to the operation of a $+R$ effect from the *para* position, i.e. π(pp) conjugation of the substituent with the benzene ring. In the extension of this explanation to the order $\sigma_p > \sigma_m$ for SO_2Me, the $+R$ effect is usually held to involve π(pd) conjugation but in accordance with our declared policy in Section I.C we will attribute a $+R$ effect for SO_2Me simply to octet expansion of sulfur.

BC raised the question of the conjugative ability of SO_2Me in connection with the enhanced electron-attracting effect displayed in its influence on the ionization of phenol or anilinium ion. (It should be noted that the symbol σ^- for substituents showing enhanced conjugation in connection with these processes was, in 1952, not yet in use.) The σ_m value for SO_2Me is perhaps slightly increased but the σ_p value is greatly increased to 0.98 for the influence of SO_2Me on the ionization of phenol and 1.13 for its influence on the anilinium ion (Table 4). BC pointed out that this exaltation was comparable with that observed for CN, COMe and NO_2 in similar situations and suggested that direct conjugation of substituent with reaction center was likewise indicated. For example, free *p*-methylsulfonylaniline (**23**) would be stabilized by resonance with a canonical structure involving a valence shell of ten electrons for sulfur (**24**), such a possibility being precluded

TABLE 3. Sigma values for SOMe and SO_2Me based on the ionization of benzoic acids and related processes

Authors	Year	Ref.	Method	ρ	SOMe		SO_2Me	
					σ_m	σ_p	σ_m	σ_p
Bordwell and Cooper	1952	75	pK_a, benzoic acids, 50% v/v EtOH—H_2O, 25 °C	1.464	—	—	0.65	0.72
Kloosterziel and Backer	1952	77	pK_a, benzoic acids, 50% v/v EtOH—H_2O, 25 °C	1.464	—	—	0.65	0.75
			H_2O, 25 °C	1.000	—	—	0.56	0.68
			k, benzoic acids + diazodiphenylmethane, EtOH, 26 °C	0.937	—	—	0.63	—
Price and Hydock	1952	76	k, ethyl benzoates + OH^-, 56% v/v Me_2CO—H_2O, 25 °C	2.373	0.52	0.54	0.65	0.76
			95% v/v BCS[a]—H_2O, 25 °C	2.4	0.49	0.45	0.67	0.71
Jaffé	1953	52	See main text	—	0.551	0.567	0.647	0.728
Bordwell and Boutan	1957	81	pK_a, benzoic acids, 50% v/v EtOH—H_2O, 25 °C	1.464	0.51	0.48	—	—
McDaniel and Brown	1958	82	See main text	—	0.52	0.49	0.60	0.72
van Bekkum, Verkade and Wepster	1959	55	See main text	—	—	—	0.678	0.686[b]
Barlin and Perrin	1966	83	See main text	—	0.52	0.49	0.678	0.72
Exner	1966	66	See main text	—	0.52	0.49	0.64	0.73
Yukawa, Tsuno and Sawada	1972	84	k, substituted-benzyl benzoates + OH^-, 70% v/v Me_2CO—H_2O, 25 °C	0.981	—	0.573[c]	0.697[c]	0.749[c]
			k, ethyl benzoates + OH^-, 85% v/v EtOH—H_2O, ? °C	?	—	0.564	0.659	0.721

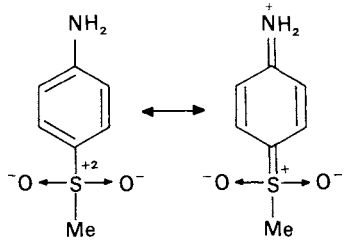
[a]Butyl cellosolve.
[b]σ^n value.
[c]σ^0 values.

TABLE 4. Sigma values for SOMe and SO_2Me based on the ionization of phenols or anilinium ions

Authors	Year	Ref.	Method	ρ	SOMe		SO_2Me	
					σ_m^-	σ_p^-	σ_m^-	σ_p^-
Bordwell and Cooper	1952	75	pK_a, phenols, H_2O, 25 °C	2.091	—	—	0.70	0.98
			pK_a, anilinium ions, H_2O, 25 °C	2.73	—	—	0.69	1.13
Kloosterziel and Backer	1952	77	pK_a, phenols, H_2O, 25 °C	2.008	—	—	—	1.16
			pK_a, anilinium ions, H_2O, 25 °C	2.73	—	—	0.68	1.14
	1953	78	pK_a, phenols, H_2O, 25 °C	2.091	—	—	—	0.98
Bordwell and Andersen	1953	80	pK_a, thiophenols, 48% v/v EtOH—H_2O, 25 °C	2.578	—	—	—	0.82
Jaffé	1953	52	See main text	—	—	—	—	1.049
Bordwell and Boutan	1957	81	pK_a, phenols, H_2O, 25 °C	2.091	0.53	0.73[a]	—	—
Barlin and Perrin	1966	83	See main text	—	—	—	—	0.92

[a]Recalculation by the present author from the relevant data yields 0.756.

for the *p*-methylsulfonylanilinium ion.



(23) (24)

BC referred to the spectroscopic evidence then available, that SO_2Me would conjugate with unsaturated systems under suitable circumstances, particularly in excited states.

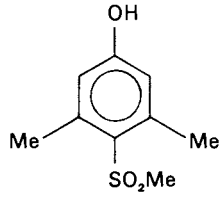
Work by other authors in 1952 essentially confirmed the results and interpretation of BC. Thus Price and Hydock (PH)[76] determined σ_m and σ_p for SO_2Me by studying the kinetics of saponification of substituted ethyl benzoates in two different solvents (Table 3). Both values of σ_m agreed closely with BC's value determined from benzoic acid ionization in 50% ethanol. PH's value for σ_p, 0.71, as determined through saponification in 95% butyl cellosolve agreed closely with BH's value 0.72. However, PH considered that the results for saponification in this solvent were less reliable than those involving 56% acetone, which yielded the value 0.76, appreciably higher than BC's. Kloosterziel and Backer (KB)[77] also determined the pK_a values for the benzoic acids in 50% ethanol, finding close agreement with other determinations of σ_m but obtaining a somewhat higher value of σ_p, 0.75, than that found by BC (Table 3). However, KB's determination of the pK_a values in water yielded rather lower values of both σ_m and σ_p, 0.56 and 0.68 respectively, although determination of σ_m by means of the kinetics of the reaction of benzoic acids with diazodiphenylmethane in ethanol found 0.63. There was thus some slight evidence of a solvent dependence of the σ_m and σ_p values of SO_2Me.

KB's determination of σ_p^- from the ionization of anilinium ions agreed closely with BC's (Table 4). The corresponding value for σ_m^- which KB record in their main table deviated markedly from BC's, but in their footnote 22 (added in proof) they concluded that this was in error and gave a new value of 0.68, in close agreement with BC's. There was a largely unresolved discrepancy between BC's and KB's values for σ_p^- determined from phenol ionization, 0.98 and 1.16 respectively, the latter agreeing closely with the anilinium ion value. The discrepancy may have been partly connected with disagreement as to the values of ρ and log k^0 for the ionization of phenols, but the bulk of the discrepancy remained unexplained. However, in a paper the following year KB[78] presented a σ_p^- value redetermined on the phenol system, which at 0.98 agreed exactly with BC's (Table 4).

There is thus some evidence that the enhancement of the $+R$ effect of *p*-SO_2Me is greater in the ionization of the anilinium ion than in the ionization of phenol. These two systems are often regarded as essentially equivalent as a basis for the definition of σ_p^- values, probably because the two values for the nitro group (on whose behaviour the 'duality of substituent constants' was largely founded), agree closely, 1.23 to 1.25 and 1.24 to 1.28 respectively. In fact, careful inspection of Exner's compilation[79] of σ_p^- values reveals various substituents for which discrepancies between the anilinium and phenol scales exist, e.g. CO_2R, 0.74 and 0.64; CN, 0.99 and 0.88; SCF_3, 0.64 and 0.57; SO_2CF_3, 1.65 and 1.36, respectively, as well as others for which there is good agreement or even a small discrepancy in the opposite direction. This may provide a warning that values determined on the basis of the two systems should not be mixed indiscriminately in correlations. Ideally only one of these systems should be chosen as the basis for the σ_p^- scale and the

other should be regarded as a system for treatment by the Yukawa–Tsuno equation[58,59] and other extensions of the Hammett equation[56]. (See Ehrenson and coworkers[65] on the $\sigma_{R(A)}^-$ and $\sigma_{R(P)}^-$ scales.) In this connection it may be mentioned that Bordwell and Andersen[80] found an even smaller apparent sigma value for *p*-SO_2Me from the ionization of thiophenols, namely 0.82; the value for *p*-NO_2 was also reduced to 1.00. The authors explained these results, compared to those for phenols, in terms of varying degrees of conjugation as between the substituents and the respective reaction centers, i.e. varying degrees of valence shell expansion in the case of SO_2Me.

Before we leave the enhancement of the $+R$ effect of SO_2Me by octet expansion, it is appropriate to mention its stereochemical aspect. This was examined by Kloosterziel and Backer in the later of their two papers to which reference has already been made[78]. They measured the pK_a value of 4-methylsulfonyl-3, 5-xylenol **25** and compared its acidity with that of 4-methylsulfonylphenol. Parallel measurements were made with 4-CN and 4-NO_2



(25)

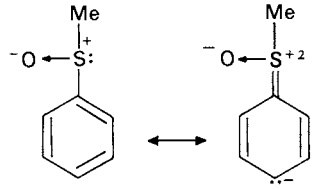
analogs. Effective sigma values σ (obs.) for the 3, 5-dimethyl compounds were thus obtained and compared with sigma values σ (calc.) computed on the assumption of a strict additivity of substituent effects. The results are shown in Table 5. The two *ortho*-methyl groups twist the nitro group very markedly out of the plane of the ring, thereby diminishing π(pp) conjugation and decreasing the acidity, this being the phenomenon commonly referred to as 'steric inhibition of resonance'. The π(pp) conjugation of the linear cyano group is not subject to any twisting effect of the *ortho*-methyls. The bulky methylsulfonyl group, however, must be subject to very strong steric interaction with the *ortho*-methyls. Nevertheless the interaction of this group with the benzene ring is apparently unaffected, a strict additivity of substituent effects on the acidity being observed. This is conventionally attributed to π(pd) conjugation not being subject to any requirement of a special orientation of SO_2Me relative to the plane of the benzene ring. It is sometimes pointed out that rotation about the ring–sulfur bond by 90° brings into line another 3d orbital of sulfur which can be used for π(pd) bonding; cf. the situation for p orbitals and π(pp) bonding. However, in view of current uncertainties about the bonding

TABLE 5. Ionization of 4-substituted-3, 5-xylenols[78]

Substituent(s)	σ (obs.)	σ (calc.)
3, 5-Me_2	−0.15	—
4-NO_2	1.29	—
4-NO_2-3, 5-Me_2	0.77	1.14
4-CN	0.92	—
4-CN-3, 5-Me_2	0.79	0.77
4-SO_2Me	0.98	—
4-SO_2Me-3, 5-Me_2	0.83	0.83

role of d orbitals we must simply say that the lack of so-called steric inhibition of resonance for SO_2Me means that octet expansion of sulfur, whatever its mechanism, is not affected by rotation about the ring–sulfur bond.

We turn now to the methylsulfinyl group SOMe. Here it is appropriate to start with the work of Price and Hydock (PH)[76], who included the effects of *m*- and *p*-SOMe in their work on ester saponification. The values of σ_m for the two solvent systems agree fairly well at 0.52 and 0.49, but there is a considerable discrepancy between the two values of σ_p at 0.54 and 0.45 (Table 3). The result is that for the measurements in 56% acetone $\sigma_m < \sigma_p$, while for 95% butyl cellosolve $\sigma_m > \sigma_p$. At all events it is clear that SOMe is rather less electron-attracting than SO_2Me, whether in the *meta*- or the *para*-position, and is not much more electron-attracting than COMe. In so far as the SOMe group contains only one $S^{\delta+}—O^{\delta-}$ dipole compared with two in SO_2Me a smaller electron-attracting effect of SOMe might be expected. Further, since the sulfur atom in SOMe has a lone pair of electrons there is the possibility, particularly in relation to the *para*-position, that the electron-attracting effect might be reduced by π(pp) bonding from sulfur to the benzene ring, (**26**) and (**27**), cf. SMe, for which the values of σ_m and σ_p are +0.15 and 0.00



(**26**) (**27**)

respectively[79]. Clearly there is no very great effect of π(pp) conjugation for SOMe (presumably the appearance of a notional double positive charge on S would operate against it, as in the case of the dimethylsulfonio group) but this could account for the order $\sigma_m > \sigma_p$, if real; cf. the halo substituents[79].

Bordwell and Boutan (BB)[81] carried out extensive work on the methylsulfinyl group in 1957. It must be emphasized that they found that the preparation of pure arylmethyl sulfoxides from arylmethyl sulfides by oxidation was not a trivial matter. The frequently recommended reagent, hydrogen peroxide in acetic acid, tended to give sulfoxides contaminated with appreciable quantities of sulfones, which could not be removed by fractional crystallization. Oxidation by nitric acid was found to be more satisfactory.

From the pK_a values of the substituted benzoic acids in 50% ethanol, BB determined σ_m and σ_p of SOMe to be 0.51 and 0.48 respectively. They thus essentially confirmed the σ_m value as determined by PH[76] and obtained a σ_p value which was closer to the lower value found by PH rather than the higher. The order is thus $\sigma_m > \sigma_p$ (just) but the authors refrained from attaching any particular significance to this. They were obviously much more impressed by the exaltation of σ_p in the effect of SOMe on the ionization of phenol, an increase of 0.25 (comparable with that observed for SO_2Me), while σ_m was essentially unaffected (Table 4). The exaltation was naturally attributed to valence shell expansion of sulfur to ten electrons. However, they were unable to obtain evidence for such conjugation in ultraviolet spectra. The behavior of SOMe in this respect resembled that of SMe rather than SO_2Me, which was attributed to conjugative interaction involving the sulfur lone pair in the photoexcited state. They looked for evidence of an enhanced effect of this kind by introducing + *R* groups such as NO_2 in the position *para* to SOMe, but failed to find it.

Having considered the main individual investigations of SO_2Me and SOMe in respect of their ordinary Hammett σ constants and of the exalted constant σ^-, we must examine

the treatment afforded to these in certain well-known reviews of the Hammett equation, associated with compilations of substituent constants.

In his 're-examination of the Hammett equation' Jaffé (1953)[52] provided values of σ_m and σ_p for both SOMe and SO_2Me as indicated in Table 3. In Jaffé's view the σ value for a given substituent should be chosen to give as good an account as possible of the entire available body of data relating to the influence of that substituent, rather than being based on behavior in some standard process. Thus the values given for many substituents involved the treatment and averaging of the results of several authors in each case. The disadvantage of this procedure is that important details such as the precision of the data and spread of results are not always apparent to the reader. Certainly the quotation of σ values to 3 places of decimals gives an over-optimistic impression as to reliability in many cases. The σ_m and σ_p values for SOMe are apparently based on the alkaline hydrolysis of ethyl benzoates in 60% acetone at 0 °C, drawing results from several different sources, with the work of E. Tommila and his colleagues being prominent. The values are decidedly higher than any values found by Price and Hydock[76] or Bordwell and Boutan[81]. The σ_m value for SO_2Me was based on considering seven different reactions and fits in fairly well with the various values discussed above. The values averaged are said to range from 0.560 to 0.683, which corresponds roughly to the situation in Tables 3 and 4. The value of σ_p for SO_2Me was based on considering four reactions and the value of 0.728 corresponds fairly well to what might be expected from Table 3. Jaffé also gives the value of 1.049 for the exalted constant (described as σ^* in the symbolism that was briefly in vogue around that time), which appears to be an average value for the effect in anilinium ions and phenols.

McDaniel and Brown (1958)[82] returned to an emphasis on the ionization of benzoic acids, preferably in water but failing that in some aqueous organic solvent, as providing the standard process for defining σ values. They thus favored Bordwell and Boutan's[81] results for *m*- and *p*-SOMe (Table 3; recalculation and slight adjustment of the σ values appears to have occurred), while for *m*- and *p*-SO_2Me they appear to have taken averages from the various measurements of Bordwell and Cooper[75] and of Kloosterziel and Backer[77], including the values for aqueous solution obtained by the latter authors. McDaniel and Brown[82] ascribed an uncertainty of 0.1 to all their final values for these groups.

In the 'simple re-evaluation of the Hammett $\rho\sigma$ relation' of Wepster and colleagues (1959)[55], SO_2Me plays a part in connection with the 'normal values' σ^n and this will be mentioned later in discussion of σ^o. For now we mention only that σ_m for SO_2Me is given as 0.678 ± 0.044 (with a difference of 0.100 between the lowest and highest of the four individual values averaged). This is rather greater than what one might expect from the data in Tables 3 and 4, and this is presumably due to Wepster's recalculation of ρ values according to the principles expounded in the review, i.e. the determination of the ρ value of a given reaction should involve only substituents for which no significant effect of cross-conjugation should occur.

In their article on the 'Prediction of the strengths of organic acids' Barlin and Perrin[83] accepted McDaniel and Brown's[82] σ values for *m*- and *p*-SOMe and *p*-SO_2Me, but prefer Wepster's[55] value for *m*-SO_2Me. They also quote 0.92 for the exalted constant for *p*-SO_2Me in phenols, but the basis for this is obscure.

Finally, in part V[66] of Exner's series on 'Studies of the Inductive Effect' SO_2Me is involved in the development of his views on the insignificance of the $+R$ effect for the influence of substituents on the ionization of benzoic acids. This work will be referred to again later in connection with σ_I and σ_R values for SOMe and SO_2Me. For now we mention that the article tabulates σ_m and σ_p values which have been subject to minor corrections to bring them into conformity (to within ± 0.01 σ units) with certain relationships between sigma values. For SO_2Me the values of σ_m and σ_p are 0.64 and 0.73 respectively (Table 3; these are very close to Jaffé's[52] average values), while for SOMe the

values are 0.52 and 0.49 respectively (essentially those recommended by McDaniel and Brown[82], on the basis of Bordwell and Boutan's[81] experimental results.)

One remaining matter for SOMe and SO_2Me which must be dealt with at this stage is the determination of 'normal' substituent constants, i.e. free from any effect of cross-conjugation. The ordinary Hammett σ constants affected by this are mainly those for *para*-substituents of $-R$ character. In so far as SO_2Me shows $+R$ behavior, no very striking difference between σ_p and σ_p^0 (Taft)[63] or σ_p^n (Wepster)[55] would be expected. The case of SOMe is not so clear: while this group, as we have seen, shows marked $+R$ behavior in respect of its effect on phenol ionization, there are slight indications of a small $-R$ effect on benzoic acid ionization.

Wepster and colleagues[55] included information about the 'normal' behavior only of SO_2Me. The σ_p^n value for SO_2Me is given as 0.686, based on the pK_a value of *p*-methylsulfonylbenzoic acid in 50% ethanol. This is considerably lower than the σ_p values on this basis given in Table 3, apparently due to Wepster having recalculated ρ for the ionization of benzoic acids in 50% ethanol as 1.57. Thus the outcome of Wepster's analysis is the characterization of SO_2Me by $\sigma_m = 0.678$ and $\sigma_p^n = 0.686$, which effectively destroys any analogy to the behavior of CN, MeCO or NO_2.

Yukawa and coworkers (1972)[84] determined σ^0 values from the rate constants for alkaline hydrolysis of *m*- and *p*-substituted-benzyl benzoates in 70% (v/v) aqueous acetone at 25 °C. σ_p^0 values for SOMe and SO_2Me were found to be 0.573 and 0.749 respectively. These were compared with 0.564 and 0.721, respectively, for σ_p values determined from the rate constants of alkaline hydrolysis of substituted ethyl benzoates in 85% aqueous ethanol. From these values there is no evidence for any $-R$ cross-conjugative effect of SOMe as a substituent in the benzoate moiety, which is eliminated when it is in the benzyl. However, both the values for SOMe are substantially higher than most of the σ_p values for SOMe which we have surveyed previously. For SO_2Me the order $\sigma_p^0 > \sigma_p$, if significant, finds no immediate explanation since σ_p^0 and σ_p should be equivalent for $+R$ substituents, but a similar relationship appears for some other $+R$ substituents, e.g. for NO_2, $\sigma_p^0 = 0.821$ and $\sigma_p = 0.78$. A value of 0.697 is given for σ_m^0 of SO_2Me. This is appreciably greater than the ordinary values of σ_m discussed above; again, there is no immediate explanation. The latter are supported by a new value of 0.659 based on the alkaline hydrolysis of ethyl benzoates in 85% ethanol. The use of systems in which the substituent is 'insulated' by methylene groups from the reaction center has, in fact, been criticized by Hoefnagel, Wepster and colleagues[85,86] for its tendency to lead to slightly exalted values of σ^0 for $+R$ substituents. They see an analogy to the very pronounced exaltations that occur in the effects of $+R$ substituents on the ionization of $ArXCH_2CO_2H$ with X = NH or O, when the observed σ value can approach σ^-, due to cross-conjugation of the $+R$ substituent with NH or O, e.g. for *p*-SO_2Me apparent σ values ranging from 0.87 to 1.11 were recorded. The suggestion is that CH_2 is capable of a slight interaction of this nature through its hyperconjugation.

In connection with 'normal' substituent constants it must finally be mentioned that SO_2Me was included in an elaborate statistical analysis of a large body of data relating to substituent effects in aromatic systems[87]. What are claimed to be 'normal' substituent constants emerge as $\sigma_m^0 = 0.69$ and $\sigma_p^0 = 0.73$, not greatly different from those determined by Yukawa and coworkers[84] or in the case of σ_p^0 from the ordinary σ_p value.

2. *Arylsulfinyl and arylsulfonyl groups*

Most of the information available concerns SOPh and SO_2Ph, with some about the effect of substituents in the phenyl. The most important data are summarized in Table 6.

Szmant and Suld[88] measured pK_a values for various substituted benzoic acids and phenols in 48% aqueous ethanol by potentiometric titration. Substituent constants

TABLE 6. Sigma values for SOPh and SO_2Ph

Authors	Year	Ref.	Method	ρ	SOPh	SO_2Ph
Szmant and Suld	1956	88	pK_a, benzoic acids, 48% v/v EtOH—H_2O 25 °C	1.460	σ_p, 0.465	σ_p, 0.70
			pK_a, phenols, 48% v/v EtOH—H_2O, 25 °C	2.48	—	σ_p^-, 0.95
			pK_a, anilinium ions	?	—	σ_p^-, 1.21[a]
Meyers	1963	90	pK_a, phenols, 48% v/v EtOH—H_2O, 25 °C	2.50	σ_m^-, 0.52 σ_p^-, 0.71	σ_m^-, 0.62 σ_p^-, 0.90
Bodor and Kövendi	1966	95	k, isonitrosation of *o*-nitroethylbenzenes	4.466	h^-	σ_p^0, 0.76
Exner	1966	66	See main text	—	— —	σ_m, 0.62 σ_p, 0.71
Exner	1978	79	Calculated from σ_I and σ_R^0	—	σ_m^0, 0.51 σ_p^0, 0.50	σ_m^0, 0.59 σ_p^0, 0.66

[a]Stated to be a tentative value.

determined in this way included σ_p values for SOPh and SO_2Ph of 0.465 and 0.70 respectively and a σ_p^- value for SO_2Ph of 0.95. These values indicate the behavior of SOPh and SO_2Ph to be very similar to SOMe and SO_2Me (Tables 3 and 4). The authors also gave a tentative value for σ_p^- of SO_2Ph, based on anilinium ions, of 1.21, again fairly close to the corresponding value for SO_2Me. Studies were also made of several substituted benzoic acids 4-(4′-$XC_6H_4SO_2$)$C_6H_4CO_2H$ and phenols 4-(4′-$XC_6H_4SO_2$)C_6H_4OH, with σ_p and σ_p^- values being tabulated for the substituted arylsulfonyl groups. There was particular interest in the effect of the 4′-NO_2 group, which appeared to *reduce* the acidity of 4-phenylsulfonylbenzoic acid. This was explained in terms of the hypothesis that the 4′-nitro group 'causes a greater double-bond character in the sulfur-oxygen bonds; the consequently smaller positive charge at the sulfur atom exerts a smaller electron-withdrawing effect on the benzoic acid moiety.' However, Meyers and coworkers[89] were unable to reproduce this result, for they found the acid concerned to be insufficiently soluble for potentiometric titration in 48% aqueous ethanol. The pK_a values in 80% aqueous acetone showed no 4′-NO_2 anomaly. These authors were able to reproduce other results of Szmant and Suld[88] for arylsulfonylbenzoic acids, and it is probable that most of the work of Szmant and Suld (including also that on the arylsulfonylphenols) is quite reliable.

Meyers and colleagues[89] found that the pK_a values of 4-(4′-$XC_6H_4SO_2$)$C_6H_4CO_2H$ and also of 4-$XC_6H_4SO_2CH_2CO_2H$ in 80% acetone gave good Hammett plots against the σ_p values of X. Meyers[90] also determined substituent constants from phenol ionization in 48% aqueous ethanol as follows: for SOPh the values of σ_p^- and σ_m^- were 0.71 and 0.52 respectively (cf. the values of Bordwell and Boutan[81] for SOMe, Table 4), and for SO_2Ph, 0.90 and 0.62 respectively (slightly lower than Bordwell and Cooper's[75] values for SO_2Me). A further compilation of substituent constants based on the ionization of arylsulfonyl substituted benzoic acids and phenols was provided by Meyers and coworkers[91].

The steric requirements of the enhanced interaction between arylsulfinyl or arylsulfonyl groups and the benzene ring in bis(4-hydroxyphenyl)sulfoxides or sulfones were examined by Oae and colleagues through the introduction of methyl groups in two or four of the positions *ortho* to SO or SO_2. As in the work described earlier for SO_2Me, effective values for the combined influence of the substituents σ (obs.) were determined and compared with σ (calc.) computed on the basis of strict additivity of substituent effects on the dissociation

of the phenol. In the earlier stages of this work[92] no evidence of 'steric inhibition of resonance' was found for the sulfoxides, or in similar studies of sulfonium chlorides, although such an effect was found for the related sulfides, in which π(pp) conjugation occurs. Studies of ultraviolet spectra gave similar indications. Later, however, doubts arose about the identity of the compounds involved in this study, so the work was repeated for newly prepared bis(4-hydroxyphenyl) sulfides, sulfoxides and sulfones[93]. First, and now also second, dissociation constants were measured, and studies of ultraviolet spectra were carried out. For the sulfinyl and sulfonyl groups essentially no steric inhibition of resonance was observed in the first dissociation or uv spectra, although there were slight indications of such an effect in the second dissociation. The latter was tentatively attributed to a steric problem in using 3d orbitals of the sulfur atom for the simultaneous conjugative stabilization of the two negative centers in the dianion. As before, steric inhibition of π(pp) resonance was observed for the sulfide system.

Hammett studies of the dissociation constants of benzoylacetanilides $XC_6H_4COCHZCONHC_6H_4Y$ permitted the determination of σ_p values for 4-$MeC_6H_4SO_2$ and 4-$NO_2C_6H_4SO_2$ as 0.63 and 0.76 respectively[94]. Qualitatively these values appear quite reasonable in relation to a value of 0.70 for SO_2Ph, but values of 0.67 and 0.83 respectively are suggested by Meyers and coworkers[91] and these stand in a more reasonable quantitative relationship to the above value for SO_2Ph.

What was claimed[79] to be a value of σ_p^0 of 0.76 for SO_2Ph was given by Bodor and Kövendi[95] on the basis of a kinetic study of the effect of *para-* substituents on the isonitrosation of *o*-nitroethylbenzene. However, there is no obvious reason why σ_p^0 should be greater than σ_p for this substituent.

Only a very limited number of the general articles on the Hammett equation associated with compilations of substituent constants (referred to previously in connection with SOMe and SO_2Me) give much attention to SOPh and SO_2Ph. Exner's paper of 1966[66] gives values of σ_m and σ_p for SO_2Ph of 0.62 and 0.71 respectively, based essentially on benzoic acid ionization, but possibly having been subjected to certain minor corrections, as explained previously. There is no earlier value based on benzoic acid with which to compare the former but it agrees closely with the σ_m^- value based on phenol ionization, and σ_m^- should differ but little from σ_m for this substituent. The σ_p value determined by Exner[66] agrees closely with the earlier value of 0.70 from Szmant and Suld[88]. Exner also gives pK_a data for substituted benzoic acids in 80% methyl cellosolve from which σ_m and σ_p values of 0.14 and 0.16 respectively can be calculated for CH_2SO_2Ph. These correspond very closely to the tabulated generalised values for CH_2SO_2R of 0.15 and 0.17 respectively. Thus the interposing of a methylene group between the sulfonyl function and the benzene ring produces a damping effect by a factor of somewhat over 4, rather higher than the damping factor of a methylene group in an aliphatic system, which is usually about 2.8[62].

Exner devoted some attention to SOPh and SO_2Ph in his extensive compilation of substituent constants of 1978[79]. For the former, however, values based directly on chemical reactivity were found to be few, as is already apparent in the present section, and so Exner considered it useful to give values based on appropriate summation of inductive and resonance constants (see Section III.B). These were considered to be 'normal' values, i.e. σ_m^0 and σ_p^0, of 0.51 and 0.50 respectively. Corresponding values for SO_2Ph were 0.59 and 0.66 respectively, both slightly smaller (for no obvious reason) than the chemically based values of σ_m and σ_p (and a value supposed to be of σ_p^0) quoted earlier in this section.

3. *Fluoroalkylsulfinyl and fluoroalkylsulfonyl groups*

These constitute the only category of substituted alkylsulfinyl and alkylsulfonyl groups for which there appears to be appreciable information. Compounds containing these groups have often been used in spectroscopic studies of inductive and resonance effects

TABLE 7. Sigma values for fluoroalkylsulfinyl and fluoroalkylsulfonyl groups

Substituent	Authors	Year	Ref.	Method[a]	σ_m or σ_m^-		σ_p or σ_p^-	
$SOCF_3$	Yagupol'skii and coworkers	1974	96	pK_a BA	0.63	—	0.69	—
				pK_a An	—	0.76	—	1.05
				From σ_I, σ_R	0.74	—	0.80	—
$SOCHF_2$	Sedova and coworkers	1969	97	See main text	0.54	—	0.58	—
	Yagupol'skii and coworkers	1974	96	From σ_I, σ_R	0.70	—	0.76	—
	Titov and coworkers	1971	98	pK_a An	—	—	—	0.93
SO_2CF_3	Exner	1966	66	pK_a BA[b]	0.80	—	0.91	—
	Sheppard	1963	99	pK_a BA	0.79	—	0.93	—
	Yagupol'skii and coworkers	1974	96	pK_a BA	0.76	—	0.96	—
				From σ_I, σ_R	0.88	—	1.04	—
	Titov and coworkers	1971	98	pK_a An	—	0.98	—	1.63
	Sheppard	1963	99	pK_a An	—	1.00	—	1.65
				pK_a Ph	—	0.92	—	1.36
SO_2CHF_2	Pollet and coworkers	1976	100	pK_a BA	0.75	—	0.86	—
	Titov and coworkers	1971	98	pK_a An	—	0.87	—	1.44
	Yagupol'skii and coworkers	1974	96	From σ_I, σ_R	0.73	—	0.87	—
SO_2CH_2F	Yagupol'skii and coworkers	1974	96	From σ_I, σ_R	0.66	—	0.77	—
	Titov and coworkers	1971	98	pK_a An	—	—	—	1.17
$SO_2CF_2CHF_2$	Lifshits and coworkers	1969	101	pK_a cyanine dyes	—	—	1.01	—
SO_2CF_2CHFCl					—	—	0.98	—
$SO_2CF_2CHFCF_3$					—	—	1.03	—
CH_2SOCF_3	Yagupol'skii and coworkers	1974	96	From σ_I, σ_R	0.25	—	0.24	—
$CH_2SO_2CF_3$				pK_a BA	0.29	—	0.31	—

[a]BA = benzoic acid; An = anilinium ion; Ph = phenol.

[b]Values subject to slight corrections to conform to certain relationships between sigma constants.

and such work will be dealt with in Section III.B. In the present section we shall concentrate on the determination of substituent constants from chemical reactivity, but there will be occasional mention of the use of σ_I and σ_R values to calculate σ values. The main data available are shown in Table 7.

There is little information for fluoro-substituted sulfinyl groups. Values of σ_m and σ_p for $SOCF_3$ based on benzoic acid ionization are 0.63 and 0.69 respectively[96], compared with values of about 0.52 and 0.49 for SOMe (Table 3). Thus the electronegative fluorine somewhat enhances the electron-attracting influence of the sulfinyl function and makes the order more definitely $\sigma_m < \sigma_p$, possibly by suppressing any tendency of the sulfur lone pair to engage in π(pp) conjugation. Values of σ_m^- and σ_p^- for $SOCF_3$ based on anilinium ion dissociation are 0.76 and 1.05 respectively[96]. An increase of 0.13 as between σ_m and σ_m^- is unusually high and it is possible that the values of σ_m and σ_p quoted above are somewhat too low. Determinations of σ_I- and σ_R-type constants by NMR and other methods[96] indicate that values of σ_m and σ_p of about 0.74 and 0.80 may be nearer the mark. There is a similar problem for $SOCHF_2$. Values of σ_m and σ_p based on spectroscopic studies of dimethylaminoazo dyes are 0.54 and 0.58 respectively[97], not very much higher than the corresponding values for SOMe. Again the indications from σ_I- and σ_R-type constants[96] are that σ_m and σ_p should be rather larger, at perhaps 0.70 and 0.76 respectively[79]. The σ_p^- value, based on anilinium ion, for this substituent is 0.93[98].

There is rather more information for fluoro-substituted sulfonyl groups, although there are various anomalies in it. The largest amount of data is for SO_2CF_3, which is one of the most powerfully electron-attracting groups known. Values of σ_m and σ_p, on the basis of benzoic acid ionization, range from 0.76 to 0.80 and from 0.91 to 0.96 respectively[66,96,99]. For the exalted constants σ^- based on anilinium ions, σ_m^- and σ_p^- values are 0.98[98], 1.00[99] and 1.63[98], 1.65[99] respectively, and based on phenol ionization[99] are 0.92 and 1.36 respectively. As for $SOCF_3$ there thus appears to be a marked exaltation of the substituent constant as between σ_m and σ_m^-, but in view of there being several studies of the behavior of *m*-trifluoromethylsulfonylbenzoic acid, it is difficult to claim that the above σ_m value is too low (cf. $SOCF_3$ above). For SO_2CHF_2, values of σ_m and σ_p based on benzoic acid are 0.75 and 0.86 respectively[100]. A greater difference between the σ_m values for SO_2CF_3 and SO_2CHF_2 might have been expected, but Exner considers that each of these values may be subject to an uncertainty of 0.1[79]. Values of σ_m^- and σ_p^- for SO_2CHF_2, based on anilinium ions, are 0.87 and 1.44 respectively[98]. For SO_2CH_2F the only chemically based value is for σ_p^- (from anilinium ions) at 1.17[98].

Stepwise fluorination of SO_2CH_3 is thus seen to lead to a continuous increase in σ_p^-: 1.13, 1.17, 1.44, 1.64, but the increments display no simple pattern. The effect of stepwise fluorination will be mentioned again later in connection with spectroscopically based substituent constants.

There is a little information regarding the behavior of highly fluorinated larger alkyl groups, based on pK_a values of cyanine dyes, as shown in Table 7[101]. It is perhaps surprising that the σ_p values attained do not greatly exceed that of SO_2CF_3. There are also σ values for CH_2SOCF_3 and $CH_2SO_2CF_3$, which naturally differ but little as between the *meta*- and the *para*-position (Table 7)[96]. On comparison with the substituent constants for $SOCF_3$ and SO_2CF_3 there is clearly shown the elimination of the $+R$ effect by the methylene group and also its damping influence on the inductive effect by a factor of about 3.

B. The Separation of Inductive and Resonance Effects; Substituent Constants from Spectroscopic Studies

The development of σ_I and σ_R-type scales of substituent constants has not, of course, been a consequence solely of spectroscopic studies of organic compounds. Its origins lie in

the analysis of chemically-based Hammett constants and in studies of the reactivity of aliphatic and alicyclic systems (see section II.B), but at an early stage the relationship of inductive and resonance parameters to spectroscopic quantities of various types acquired considerable importance. This aspect, as it concerns sulfinyl and sulfonyl groups, will be emphasized here; the more chemical aspects will receive some attention, and indeed we will start with these, but in particular, detailed matters relating to the basis of σ_I values in studies of aliphatic and alicyclic compounds will be deferred until Section IV.

1. *Inductive and resonance constants from reactivity studies*

Taft's earliest values of σ_I for substituents X were calculated from σ^* values of CH_2X through the relation $\sigma_I(X) = 0.45\ \sigma^*(CH_2X)$[60,74]. They included values for SOMe and SO_2Me of 0.52 and 0.59 respectively[60], cf. 0.58 for CN and 0.63 for NO_2. These values for SOMe and SO_2Me received satisfactory but rather limited testing in Taft and Lewis's examination of the general applicability of a fixed scale of inductive effects in the reactivities of *meta*- and *para*-substituted derivatives of benzene[60]. The corresponding paper on resonance effects[61] showed that no fixed scale of these was applicable, and ranges of $\bar{\sigma}_R^{para}$ and $\bar{\sigma}_R^{meta}$ values were tabulated. The only group mentioned of immediate interest for the present article was SO_2Me for which $\bar{\sigma}_R^{para}$ was given as 0.13 to 0.19 for 'benzoic class' reactivities and 0.16 to 0.51 for 'nucleophilic class' reactivities, the corresponding ranges for $\bar{\sigma}_R^{meta}$ being 0.01 to 0.08 and 0.08 to 0.11 respectively. It was, of course, the variability of resonance effects which ultimately led Taft and his associates to define four scales for resonance effects: σ_R^0, σ_R(BA), σ_R^+ and σ_R^-, each 'of limited generality' for a particular class of processes[65]. In this development the relationship of σ_I- and σ_R-type constants to spectroscopic quantities was of considerable importance but the crystallization of these ideas in the 1973 article[65] was still very largely chemically-based. We shall therefore now present and discuss the information concerning σ_I- and σ_R-type constants in that article which relates to sulfinyl and sulfonyl groups. The information is in Table 8.

The σ_I value for SOMe is slightly different from that given by Taft and Lewis[60]. The continuous increase in σ_I produced by attached electronegative atoms at S or C is, of course, to be expected. This also encourages octet expansion as measured by σ_R^0. The zero value for SOMe presumably means that any tendency to octet expansion [conventionally π(pd) conjugation] is essentially cancelled by the π(pp) conjugation of the sulfur lone pair. For these $+R$ substituents no exaltation of σ_R-type values in the direction $\sigma_R^0 \rightarrow \sigma_R$(BA) $\rightarrow \sigma_R^+$ would be expected. The table shows two σ_R^--type constants: $\sigma_{R(A)}^-$ based on anilinium ion dissociation and $\sigma_{R(P)}^-$ based on phenol dissociation. We have already remarked in connection with σ^- scales that the anilinium- and phenol-based scales do not coincide and we now see this reflected in the σ_R^- values. (Ehrenson and colleagues[65] regard the $\sigma_{R(A)}^-$ scale as more soundly based within the terms of their analysis.)

It is appropriate to mention here that Exner[66] carries out the separation of inductive

TABLE 8. σ_I and σ_R-type parameters from Ehrenson, Brownlee, and Taft[65]

Substituent	σ_I	σ_R^0	σ_R(BA)	σ_R^+	$\sigma_{R(A)}^-$	$\sigma_{R(P)}^-$
SOMe	0.50	0.00	0.00	0.00	—	0.17
SO_2Me	0.59	0.12	0.12	0.12	0.38	0.29
$SOCF_3$	0.64	0.08	0.08	0.08	—	—
SO_2CF_3[a]	0.84	0.24	(0.24)	—	0.57	0.41

[a]Values regarded as 'secondary' substituent parameters: σ_I value from ^{19}F NMR, and σ_R(BA) only a 'suggested' value.

and resonance effects in a way slightly different from the procedures of Taft and colleagues, consequent upon his view that (a) the inductive effect operates more powerfully from the *para*- than from the *meta*-position, and (b) that the aliphatic-based inductive scale requires a correction factor when applied to the analysis of σ_m and σ_p values. The result is that Exner's σ_R values (benzoic acid based) for SO_2Me, SO_2Ph, SO_2CHF_2 and SO_2CF_3 are all zero, i.e. these substituents normally exert no conjugative effect. (The same applies to well-known $+R$ substituents such as CN and NO_2.) A further result is that σ_R for SOMe becomes -0.17, indicating π(pp) conjugation, cf. SMe -0.24. The σ_R^- values for SO_2Me, SO_2CF_3 and SOMe at 0.29, 0.44 and 0.17 respectively, are not much different from Taft's $\sigma_{R(P)}^-$ values. Exner's different procedure should presumably tend to lead to smaller σ_R^- values but the situation is somewhat obscured by the existence of both $\sigma_{R(A)}^-$ and $\sigma_{R(P)}^-$. Taft and colleagues are critical of Exner's treatment[65].

A rival analysis of substituent effects into field (equivalent to inductive) and resonance components was proposed many years ago by Swain and Lupton[102], was later slightly corrected by Hansch and colleagues[103], and fairly recently has been substantially modified by Swain and colleagues[104]. Although Swain's treatment has found considerable application in certain quarters[105] it has also been subjected to trenchant adverse criticism, in both its original[105] and its recently modified form[106–109]. It has always been largely chemically-based, so it is appropriate to mention that SOMe and SO_2Me have featured in the forty-odd substituents included in the work, so their values of $\mathfrak{F}$ and $\mathfrak{R}$[102,103] or F and R[104] are available.

It should also be mentioned that SOMe and SO_2Me were among the substituents included in Dewar and Grisdale's analysis (1962) of σ_m and σ_p values into field and mesomeric components characterized by F and M, or F' and M' according to the procedure used[110]. The main purpose of this analysis was to predict sigma values for the various dispositions of substituent and reaction center in the naphthalene and biphenyl systems. At that time no data were available for testing the F and M or F' and M' values of SOMe and SO_2Me in this way, but pK_a values have subsequently been measured for most of the methylsulfonyl-1- and 2-naphthoic acids[111]. As is usually with tests of Dewar and Grisdale's treatment, agreement between predicted and observed results is patchy: quite good for some relative dispositions of substituent and reaction center, but only rather moderate to poor in others. SOMe and SO_2Me were not included in the improved version of the theory (1971)[112].

We defer the discussion of Charton's σ_I and σ_R values to Section IV.

2. *Sigma values from ^{19}F NMR*

This subject has been associated with the development of the σ_I- and σ_R-type scales almost from the start[74] (see Section II.B), but the first paper in which sulfinyl and sulfonyl groups played a part appears to have been one by Taft and coworkers in 1963[67]. The main object of this paper was to study the effect of solvent on the inductive order by ^{19}F NMR measurements on a large number of *meta*-substituted fluorobenzenes in a great variety of solvents. The relationship between the NMR shielding parameter and σ_I was established by means of selected systems as equation 10:

$$\int_{H}^{m\text{-}X} = (-7.10)\,\sigma_I + 0.60 \qquad (10)$$

For SOMe and SO_2Me the values of σ_I as determined through chemical reactivities in 'weakly protonic' solvents are quoted as 0.52 and 0.60 respectively. These provide a point of reference for consideration of the values determined through ^{19}F NMR studies. The values for these substituents as determined in 'normal' solvents are given as $+0.49$ and

+0.55 respectively. The term 'normal' solvent appears to embrace a wide variety of solvents of the non-hydrogen-bonding, or not markedly hydrogen-bonding, type. In hydrogen-bonding solvents the σ_I values are increased, the values of 0.62 ± 0.03 for SOMe and of 0.62 ± 0.04 for SO_2Me being quoted as relating to 'weakly protonic' solvents. Not too much quantitative significance should be attached to these values but they indicate that hydrogen-bonding of the solvent to the substituent enhances inductive electron withdrawal. This is confirmed by a value of 1.00 obtained for SOMe when trifluoroacetic acid was used as solvent.

In the related paper on ^{19}F screening parameters of *para*-substituted fluorobenzenes in relation to resonance effects, a few measurements for SOMe and SO_2Me were recorded but no use was made of them for calculation of σ_R-type parameters[68]. However, some years later, Sheppard and Taft[113] used these data (carbon tetrachloride solution) to calculate $\bar{\sigma}_R$ values through equation 11:

$$\int_{m\text{-X}}^{p\text{-X}} = -29.5\bar{\sigma}_R \tag{11}$$

(The left-hand side is the ^{19}F screening parameter for *p*-X relative to *m*-X, and $\bar{\sigma}_R$ is the effective σ_R-type parameter. For $-R$ substituents the $\bar{\sigma}_R$ values thereby obtained are considered to be ${\sigma_R}^0$ values, but $\bar{\sigma}_R$ values for $+R$ substituents are slightly enhanced by the cross-conjugation of the $-R$ F substituent with the $+R$ X group.) The $\bar{\sigma}_R$ values for SOMe and SO_2Me are 0.00 and 0.16 respectively, cf. 0.00 and 0.12 suggested by Ehrenson and coworkers for ${\sigma_R}^0$ [65]. ^{19}F-based values of σ_I and $\bar{\sigma}_R$ were also given for $SOCF_3$ as 0.68 and 0.13 respectively (cf. 0.64 for σ_1 and 0.08 for ${\sigma_R}^0$ [65]) and for SO_2CF_3 as 0.78 and 0.31 (cf. 0.84 for σ_1 and 0.24 for ${\sigma_R}^0$ [65]. The solvent for $SOCF_3$ was CCl_3F (infinite dilution) and for SO_2CF_3 was carbon tetrachloride.

The same substituents, together with those containing partially fluorinated methyl groups, have also been investigated by L. M. Yagupol'skii and colleagues. (There is a useful review by Yagupol'skii on the electronic nature of fluorine-containing substituents, to which reference has already been made[96].) Table 9 summarizes the main results from Taft[68,113], as already discussed, and from Yagupol'skii and colleagues[96,114]. It will be seen that a considerable range of values has been obtained for a given substituent in many instances. Successive fluorination tends to raise both σ_I and $\bar{\sigma}_R$, but the pattern is not very regular, and there is a distinct anomaly in the $\bar{\sigma}_R$ values lying in the order $SO_2Me > SO_2CH_2F$ from measurements in dichloroethane. There is also a marked tendency for σ_I values obtained by the use of this solvent to be higher than those obtained by use of carbon tetrachloride. Some members of the former set actually agree fairly closely with the σ_I values of Ehrenson and coworkers[65], i.e. for SO_2Me and SO_2CF_3. Yagupol'skii's $\bar{\sigma}_R$ values in the main show clear signs of some enhancement by cross-conjugation (cf. comment above for Taft's values). Yagupol'skii has determined ${\sigma_R}^0$ constants for some $+R$ substituents by comparing ^1H, ^{13}C and ^{19}F chemical shifts[115]. Values for SO_2Me, SO_2CF_3 and $SOCF_3$ are 0.14, 0.20 and 0.09 respectively, rather smaller than the $\bar{\sigma}_R$ values from ^{19}F measurements alone, and comparable with Ehrenson and coworkers[65] values of ${\sigma_R}^0$ (Table 8).

Kaplan and Martin's[116] determinations for phenylsulfinyl and phenylsulfonyl groups are of interest as showing practically no difference in σ_I values, with a very small negative $\bar{\sigma}_R$ for SOPh, cf. Taft's values for SOMe and SO_2Me.

Finally, in this section, we mention that Adcock and colleagues[117] have determined σ_I and $\bar{\sigma}_R$ values for several substituents including SO_2Me by studies of substituent chemical shifts in fluoronaphthalenes, and parallel studies with fluorobenzenes, in several solvents. The results are summarized in Table 10. The most significant finding appears to be the diminution in $\bar{\sigma}_R$ values as between the fluorobenzene and fluoronaphthalene probe for

TABLE 9. σ_I and $\bar{\sigma}_R$ values based on ^{19}F NMR

Substituent	Authors	Year	Ref.	Solvent	σ_I	$\bar{\sigma}_R$
SOMe	Taft and coworkers	1963	67	'normal'	0.49	—
	Sheppard and Taft	1972	113	CCl_4	—	0.00
SO_2Me	Taft and coworkers	1963	67	'normal'	0.55	—
	Sheppard and Taft	1972	113	CCl_4	—	0.16
$SOCF_3$	Sheppard and Taft	1972	113	CCl_3F	0.68	0.13
SO_2CF_3	Sheppard and Taft	1972	113	CCl_4	0.78	0.31
SOMe	Quoted by Yagupol'skii and coworkers	1974	96	?	0.49	0.00
$SOCHF_2$	Syrova and coworkers	1970	114	$C_2H_4Cl_2$	0.65	0.11
$SOCF_3$	Yagupol'skii and coworkers	1974	96	?	0.67	0.13
SO_2Me	Syrova and coworkers	1970	114	CCl_4	0.48	0.16
SO_2CH_2F					0.55	0.22
SO_2CHF_2					0.59	0.28
SO_2CF_3					0.73	0.31
SO_2Me	Syrova and coworkers	1970	114	$C_2H_4Cl_2$	0.60	0.18
SO_2CH_2F					0.66	0.04
SO_2CHF_2					0.73	0.30
SO_2CF_3					0.85	0.34
SOPh	Kaplan and Martin	1973	116	CCl_4	0.51	−0.01
SO_2Ph					0.52	0.14

TABLE 10. σ_I and $\bar{\sigma}_R$ constants for SO_2Me based on ^{19}F NMR in fluorobenzene and fluoronaphthalene systems[117]

System	Solvent	σ_I	$\bar{\sigma}_R$
Fluorobenzene	CCl_4[a]	0.55	0.16
	benzene	0.53	0.16
	DMF	0.50	0.16
Fluoronaphthalene	benzene	0.62	0.08
	DMF	0.56	0.09

[a]Reference 113.

SO_2Me and other + R substituents. It was suggested that these differences arise from the much larger substituent–probe interactions in *para*-substituted fluorobenzenes compared with 6-substituted 2-fluoronaphthalenes. Thus the fluoronaphthalene-based values of $\bar{\sigma}_R$ approximate to $\sigma_R{}^0$.

3. *The contribution of ^1H and ^{13}C NMR*

The electronic effects of many substituents have been examined by studies of PMR[118,119]; sulfinyl and sulfonyl groups have been included in some of these. For example, Socrates[120] measured the hydroxyl chemical shifts for 55 substituted phenols in carbon tetrachloride and in dimethyl sulfoxide at infinite dilution, and endeavored to

correlate these with the pK_a values in aqueous solution. The compounds studied included *m*- and *p*-methylsulfonylphenol.

Yukawa, Tsuno and their colleagues[121] have made studies more specifically related to determining substituent constants, which have included both methylsulfinyl and methylsulfonyl groups. Hydroxyl chemical shifts were determined for a large number of *m*- and *p*-substituted phenols in DMF and in DMSO. The results were treated by the LArSR relationship[121] (usually called the Yukawa–Tsuno equation, see Section II.B):

$$\Delta\delta = \rho(\sigma^0 + r\Delta\bar{\sigma}_R^-) \tag{12}$$

with $\rho = 1.655$ and $r = 0.639$ in DMF (correlation coefficient 0.9992), and $\rho = 1.530$ and $r = 0.673$ in DMSO (correlation coefficient 0.9990). About 30 points for 'well-behaved' substituents were involved in each case, the substituent constants being derived from earlier work by the principal authors[84], and based on chemical reactivities. However, a number of substituents did not conform to the above equation and it was considered that the electronic effects of these were influenced by interactions between substituent and solvent. These included *p*-SO_2Me, which in company with certain other $+R$ substituents exhibited a weaker electron attraction than expected from the correlation equation. This was attributed to the enhancement of the electron-attracting influence of *p*-SO_2Me by hydrogen-bonding to water in the aqueous organic solutions used for measuring substituent constants by studies of chemical reactivities, such hydrogen-bonding being, of course, absent in DMF or DMSO solution. It seems to the present author that the results tabulated for *m*-SO_2Me and *p*-SOMe indicate that these substituents also behave in this way, although the authors do not comment to this effect. The results of the PMR study in DMF are further used to calculate modified substituent parameters in DMF for $+R$ and $-R$ groups in connection with the authors' *Linear Substituent Free Energy (LSFE) Relationship*, and SO_2Me is included in the former category.

A later paper by Yukawa, Tsuno and colleagues[122] deals further with hydroxyl chemical shifts for substituted phenols and also for 4-substituted 2- and 3-cresols and 2, 6-xylenols in DMSO, SOMe and SO_2Me again being included among the substituents.

There have, of course, been many studies of ^{13}C substituent chemical shifts in substituted benzenes over the last decade or so, and these to a great extent reflect the electronic effects of the substituent concerned. Ewing[123] has compiled data to 1979 and included information (and references) for several sulfinyl and sulfonyl groups. He has also discussed the correlation of ^{13}C chemical shifts with substituent parameters[119]. For instance, in a discussion of $\delta(C_p)$ for various series *p*-XC_6H_4Y, with a given Y, the correlations of $\delta(C_p)$ with σ_p^+ of X are better than those with σ_p. The series include those with Y = SOMe and SO_2Me. In general, however, correlation of δ(C) values with σ_I- and σ_R-type parameters through the dual substituent-parameter equation is appropriate.

Taft and colleagues[124] measured $\delta(C_p)$ values for a large series of monosubstituted benzenes at high dilution in several solvents. The substituents included SOMe, SO_2Me and SO_2Ph. The results for cyclohexane and carbon tetrachloride were used as the basis for redefining σ_R^0 values through iterative application of the dual substituent-parameter equation. In this way, new σ_R^0 values for the above substituents were evaluated as 0.01, 0.12 and 0.09 respectively. The first two are very close to the σ_R^0 values of Ehrenson and coworkers[65], while the third is rather lower than the $\bar{\sigma}_R$ value of 0.14 determined from ^{19}F NMR by Kaplan and Martin[116], as might be expected. The $\delta(C_p)$ values obtained in $CDCl_3$, acetone, DMF and DMSO as solvents were used as the basis for discussing substituent–solvent interactions. The electron-attracting behavior of SOMe and SO_2Me is enhanced in $CDCl_3$ by these groups acting as hydrogen-bond acceptors. On the other hand, substituent–solvent interaction reduces their electron-attracting behavior in DMF and DMSO.

4. The contribution of infrared spectroscopy

The correlation of infrared frequencies or intensities with substituent constants has been practiced for many years[69]. In the earliest work the sigma constants used were variously σ, σ^+ and σ^-, and there was interest in which type of constant gave the best correlation of a given data set of frequencies or intensities. The findings could often be rationalized in terms of the nature of the infrared transition involved, although sometimes the correlations were not very good, with various deviant points. A good example of such work is a paper by Exner and Boček[125] on the frequencies and intensities of the C≡N stretching vibration of 71 *meta*- and *para*-substituted benzonitriles. The great range of substituents studied included SO_2Me and CH_2SO_2Ph.

However, in more recent years it has become usual to employ σ_I- or σ_R-type constants, either together in the dual substituent-parameter equation or individually in special linear regression equations which hold for particular infrared magnitudes. In this connection a long series of papers by Katritzky, Topsom and their colleagues on 'Infrared intensities as a quantitative measure of intramolecular interactions' is of particular importance. We will sample this series of papers, insofar as they help to elucidate the electronic effects of sulfinyl and sulfonyl groups.

Early work by these authors established a relationship between $A_{\text{mono}}{}^{1/2}$, the square root of the integrated absorbance of the ν_{16} ring bands in monosubstituted benzenes, and $\sigma_R{}^0$ for the substituents. The equation was usually written as follows[126]:

$$A_{\text{mono}} = 17{,}600(\sigma_R{}^0)^2 + 100 \tag{13}$$

Once the equation was well founded it became a tool for establishing a scale of resonance parameters based uniformly on infrared intensities, and particularly for measuring $\sigma_R{}^0$ values of substituents which had not been obtained in other ways. It should, of course, be noted that the above equation could not give the *sign* of $\sigma_R{}^0$ for any given substituent, since $\sqrt{(\sigma_R{}^0)^2}$ can be given a positive or a negative sign. The sign had to be decided on other grounds. For instance, it was later found that the integrated intensities of the ν_{16} vibration for *para*-disubstituted benzenes are correlated by the equation 14[127]:

$$A_{para} = 11{,}800(\sigma_R{}^0 1 - \sigma_R{}^0 2)^2 + 170 \tag{14}$$

provided the two substituents are not in donor–acceptor interaction. Suitable application of this equation enables the sign of a new $\sigma_R{}^0$ value to be determined.

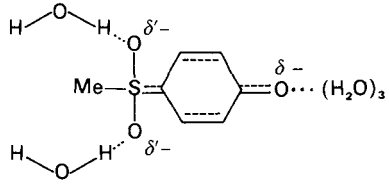
As far as sulfinyl and sulfonyl groups are concerned, one of the papers[126] recorded $\pm\sigma_R{}^0$ values for SOPh, SO_2Ph and SO_2Me as 0.065, 0.064 and 0.069 respectively, indicating little dependence on state of oxidation or nature of hydrocarbon moiety attached to sulfur. The finding of a significant resonance effect for SOPh contrasts with other evidence regarding sulfinyl groups, and the question of π(pp) *versus* π(pd) conjugation remained unanswered in the uncertainty as to the sign of $\sigma_R{}^0$. Sulfinyl and sulfonyl groups were further studied later in work on a series of *meta*- and *para*-substituted methyl phenyl sulfoxides and sulfones[128], which resolved the matter of signs. It was shown that whereas SO_2Me is a $+R$ group with a value of $\sigma_R{}^0$ equal to $+0.06$, SOMe is a $-R$ group, a net resonance donor, with a value of $\sigma_R{}^0$ equal to -0.07. However, studies of SOMe when placed *para* to a strong donor group found that it became a marked resonance acceptor, like SO_2Me in the same situation. The evidence from infrared intensities seems to stand largely alone in indicating $-R$ behavior for SOMe, but we may recall that Exner's characteristic procedure[66] for calculating σ_R values finds -0.17 for this substituent (see Section III.B.1).

The intensities of the stretching vibrations of monosubstituted ethylenes are also related to $\sigma_R{}^0$ values[129]. Studies of this system yielded a value of 0.072 for $\sigma_R{}^0$ of SO_2Me.

5. Recent experimental and theoretical studies

Many studies of substituent effects in gas-phase reactions have been carried out in recent years. It is hoped that, by comparing gas-phase and solution behavior, the role of the solvent in solution reactions will be clarified. Fujio and coworkers[130] have studied the gas-phase acidities relative to phenol of 38 *meta*- and *para*-substituted phenols by the ion cyclotron resonance (ICR) equilibrium constant method. Treatment of the results by linear free-energy relationships and comparisons with behavior in solution led to several interesting conclusions, but we must concentrate here on the implications for the electronic effects of sulfinyl and sulfonyl groups. A scale of 'inherent σ values' is based on the gas-phase measurements, and the values of σ_m(g) and σ_p^-(g) are compared with substituent constants for aqueous solutions, σ_m^n(aq) and σ_p^-(aq). A small number of 'select *meta*- and *para*-substituents' is identified for which σ_m(g) $\approx \sigma_m^n$(aq) and σ_p^-(g) $\approx \sigma_p^-$(aq) because these substituents do not act as hydrogen-bond acceptors in aqueous solution, e.g. Cl and CF_3. There are other substituents for which σ_m(g) $\approx \sigma_m^n$(aq), but for which σ_p^-(aq) deviates significantly from σ_p^-(g), e.g. CN and NO_2. There is a third category for which the aqueous solution σ values deviate markedly from the inherent σ values for both *meta*- and *para*-positions. Prominent among these are several + *R* substituents, including SOMe and SO_2Me, for which σ_m^n(aq) > σ_m(g) and σ_p^-(aq) > σ_p^-(g). [For CN and NO_2, σ_p^-(aq) is also > σ_p^-(g).] Values of these parameters for various substituents are shown in Table 11. The most important inference from this situation[130] is that 'the previously generally held view that σ_p^-(aq) values represent the inherent internal π-electron-acceptor ability of + *R* substituents must be incorrect. Instead, σ_p^-(aq) values are shown to involve a complex composite of field/inductive, internally enhanced π-electron delocalization and specific substituent HBA solvation assisted resonance effects.'

Thus, while the enhancement of the electron-attracting effect of SO_2Me by hydrogen bonding to water is fairly small in the *meta*-position, it is much larger in the *para*- position because of the delocalization of charge from O^- into the substituent in the anion. The situation may be represented schematically as **28**. It should be noted, however, that for



(28)

TABLE 11. Sigma values from measurements in the gas-phase and in aqueous solution[130]

Substituent	σ_m(g)	σ_m^n(aq)	σ_p^-(g)	σ_p^-(aq)
Cl	0.36	0.37	0.30	0.26
CF_3	0.48	0.47	0.59	0.56
SOMe	0.39	0.52	0.57	0.73
CN	0.65	0.61	0.83	0.99
SO_2Me	0.64	0.68	0.88	1.05
NO_2	0.72	0.71	1.04	1.23

SOMe the enhancement in the *meta*-position is almost as large as in the *para*-position. The authors go on to show the applicability of σ_p^-(g) values to certain *solution* processes, particularly those in non-aqueous solvents, but including the dissociation of thiophenols in 48% ethanol, the results of Bordwell and Andersen[80] to which reference has been made earlier (Section III.A.1). A separation of field/inductive and resonance effects is also essayed for the gas-phase acidities of the phenols, and SOMe and SO_2Me feature in the discussion. There is reference to a σ_R^0 value of + 0.07 for SOMe as an unpublished result of Adcock, Bromilow and Taft (cf. 0.00 from Ehrenson and coworkers[65] and − 0.07 from Katritzky, Topsom and colleagues[128].)

Recent studies have found enhanced substituent solvation assisted resonance effects in dipolar non-hydrogen bonding solvents[131]. For several + *R* substituents acidities of phenols in DMSO are well correlated with their gas-phase acidities. The substituents include *m*- and *p*-SOMe, *m*- and *p*-SO_2Me, *m*-SO_2CF_3 and *m*-NO_2. But there is very considerable enhancement of the effect of *p*-SO_2CF_3, *p*-NO_2 and various other *para*-substituents in DMSO solution.

Marriott and Topsom[132,133] have recently developed theoretical scales of substituent field and resonance parameters. The former correspond to the traditional 'inductive' parameters but these authors are firm believers in the field model of the so-called inductive effect and use the symbol σ_F[134]. The theoretical substituent field effect scale[132] is based on *ab initio* molecular orbital calculations of energies or electron populations of simple molecular systems. The results of the calculations are well correlated with σ_F values for a small number of substituents whose σ_F values on the various experimental scales (gas-phase, non-polar solvents, polar solvents) are concordant, and the regression equations are the basis for theoretical σ_F values of about 50 substituents. These include SOMe and SO_2Me at 0.37 and 0.60 respectively, which agree well with 'inherent best values in the literature' of 0.36 and 0.58. However, it should be noted that σ_I for SOMe is given as 0.50 by Ehrenson and coworkers[65].

The theoretical substituent resonance effect scale[133] is based on *ab initio* calculations of electron populations in substituted ethylenes. A suitable regression equation is again established by using standard substituents, but now the quantum mechanical quantity is correlated with infrared-based σ_R^0 values. This equation is then the basis for theoretical σ_R^0 values of more than 40 substituents including SOMe and SO_2Me at − 0.03 and 0.05 respectively. The latter agrees well with the infrared-based value of 0.06, and the former supports the occurrence of a − *R* effect as in the infrared value of − 0.07[128]; cf. the σ_R^0 value of 0.0 given by Ehrenson and coworkers[65].

Finally we mention the very recent development of a 'scale of directional substituent polarizability parameters' from *ab initio* calculations of polarizability potentials[135]. It is expected that this scale of σ_α values will prove of considerable utility in correlation analysis, often in association with σ_F values. The σ_α value of SO_2Me is given as − 0.62; cf. H, 0.00; NO_2, − 0.26; COMe, − 0.55; SMe, − 0.68; *t*-Bu, − 0.75.

C. The Transmission of Electronic Effects through —SO— and —SO_2—; Rho Values

Most studies of the transmission of electronic effects through —SO— and —SO_2— have involved examining the influence of substituents on the pK_a values of carboxylic acids and phenols of the types $XC_6H_4SO_nYC_6H_4CO_2H$ or $XC_6H_4SO_nC_6H_4OH$ where Y = CH_2 or CH=CH. There have been a few relevant spectroscopic studies.

We begin with studies of the pK_a values of substituted phenylmercapto-, phenylsulfinyl- and phenylsulfonyl-acetic acids. Pasto and Kent[136] found that phenylsulfinylacetic acid was a weaker acid than phenylsulfonylacetic acid in water, the pK_a values at 25 °C being 2.732 and 2.513 respectively. However, in aqueous ethanol or aqueous dioxan as solvent

the pK_a values of these acids increase curvilinearly and converge as the proportion of the organic component is increased, so that in highly non-aqueous mixtures phenylsulfinylacetic acid is stronger than phenylsulfonylacetic acid, e.g. the pK_a values for 80% v/v dioxan are 6.241 and 6.334 respectively. The authors attribute this behavior to the effect of solvent composition on intramolecular hydrogen bonding in phenylsulfonylacetic acid. This is a factor tending to stabilize the undissociated form of the acid and it becomes more pronounced in the less aqueous media. Internal hydrogen-bonding is considered to be much less important in the sulfinyl acid, which prefers a conformation in which the SO oxygen is remote from the carboxyl hydrogen.

In a related study Pasto and coworkers[137] determined Hammett ρ values for the effect of *meta*- and *para*-substituents on the above-named acids in water and in 50% dioxan–water. In water the ρ values for transmission through SCH_2, $SOCH_2$ and SO_2CH_2 were 0.300, 0.166 and 0.253 respectively and in the aqueous organic mixture, 0.622, 0.380 and 0.507. The superior transmitting power of the SCH_2 group was attributed to its greater polarizability [cf. also the corresponding ρ values (in water) for transmission by CH_2CH_2 and OCH_2, 0.237 and 0.226 respectively], the bonding of sulfur to oxygen reducing the polarizability of the sulfur atom. Also, the transmission of electronic effects 'may be partially shunted into the highly polar sulfur–oxygen bond instead of being directed entirely through the methylene group to the carboxyl group'. Within these terms, however, the order $SOCH_2 < SO_2CH_2$ for the ρ values would not be expected and the increased transmission through SO_2CH_2 was attributed to the intramolecular hydrogen bonding which has already been referred to. (It should be noted that some of the Hammett plots in this work are not very good.) Substituent effects in phenylsulfonylacetic acid were also studied by Meyers and colleagues[89].

Hogeveen[138] measured apparent acidity constants of substituted β-phenylthio-, β-phenylsulfinyl- and β-phenylsulfonyl-acrylic acids (*cis* and *trans*) in 50% v/v ethanol. The ρ values for transmission through SCH=CH, SOCH=CH and SO_2CH=CH were 0.531, 0.389 and 0.320 respectively for the *cis* acids and 0.652, 0.282 and 0.331 for the *trans* acids. These results were discussed in considerable detail and compared with those of pertinent related systems. Little importance was attached to the small differences between ρ values for *cis/trans* isomers, and the relative transmissions were taken as the mean ρ values: 0.59, 0.34 and 0.33. The superior transmission of SCH=CH was attributed to greater polarizability. The values for $pK_a(trans) - pK_a(cis)$ of isomeric acids were also discussed. For the sulfonyl acids this is almost constant at 0.1 unit; for the sulfinyl acids there is some variation about a mean value of 0.26 unit, and for the thio acids there is also some variation about a mean value of -0.15 unit. The differing behavior of the three systems in this respect was explained in terms of hypothetical conformations and electrostatic interactions therein.

The work so far described in this section has been further discussed by Thirot[139] in connection with his special linear free-energy treatment[140] in which a distinction is drawn between ρ_m and ρ_p.

Meyers and coworkers[141] measured the pK_a values of a number of arylthio-, arylsulfinyl- and arylsulfonyl-phenols. From their few results relating to the effects of 4'- R on 4-OH, Hogeveen[138] inferred that relative influence of substituents was about the same in the three series, contrasting with what he had found in his various series of acrylic acids. He attributed this to the compensation of the polarizability effect (see above) by the influence of π(pd) conjugation in the anions of the sulfinyl and sulfonyl series. Meyers and coworkers[141] were more interested in the effect of moving the OH from the 4- to the 2-position (see Section III.D).

Frankovkskii and Katsnel'son[142] determined the pK_a values (60% aqueous dioxan) for a series of 3'- or 4'-substituted *para*-phenylthio-, phenylsufinyl- and phenylsulfonyl- phenols, with a fixed chloro-substituent in the 2'-position. The ρ values for transmission through S, SO and SO_2 were 0.667, 0.402 and 0.565 respectively. This contrasts with the situation inferred by Hogeveen[138] from the results of Meyers and coworkers[141] (see above). It is, however, similar

to that obtaining in the ρ values for the substituted acetic acid series (see above), and casts doubt on the explanation of the order of ρ values $SOCH_2 < SO_2CH_2$ in terms of hydrogen-bonding[137]. In a later paper Katsnel'son and Frankovskii[143] found that the order of ρ values $SO < SO_2$ persisted in other aqueous organic solvents. These authors regarded the relative transmissions of SO and SO_2 as governed by several factors but attached first importance to π(pd) conjugation of the sulfur atom with the benzene rings, this being more marked with SO_2 than SO because of the contraction of the 3d orbitals by the two electronegative oxygen atoms. (This explanation would also hold for ρ values $SOCH_2 < SO_2CH_2$.)

Turning now to spectroscopic studies, we mention first a study by Hyne and Greidanus[144] of the transmission of electronic effects through diphenyl sulfides, sulfoxides and sulfones, and the corresponding methylphenyl compounds. The NMR response of the aromatic ring protons was determined as a function of the nature of the *para*- substituents and of the bridging group between the rings. The results suggested that a transmission mechanism is operative through S that is not effective through SO or SO_2.

Konovalov and colleagues[145] studied the chemical shifts of the CH_2 protons for a series of derivatives of arylsulfonylacetic acids and β-disulfones in DMSO or $CDCl_3$. The transmission of electronic effects through the SO_2 bridge was detected and attributed 'to the possibility of participation of the 3d orbitals of sulfur in the formation of the S=O bond and to the existence of $d\pi-p\pi$ conjugation'. The paper contains various references to related (mainly Soviet) work.

Very recently there has been an experimental and theoretical study of electronic substituent effects in 4-aminoaryl (4-substituted aryl) sulfones[146]. PMR, ^{13}C NMR and infrared measurements were involved and semi-empirical all-valence CNDO/2 calculations, with and without sulfur d orbitals, were carried out. Various correlations between spectral results and substituent constants are presented. There is good agreement between experimental and theoretical data, which does not depend on the inclusion or exclusion of the sulfur d orbitals from the calculations.

Infrared studies have also been involved in investigating the effect of introducing heterobridges between the rings of *para*-(4'-substituted phenyl)nitrobenzenes[147]. The symmetric and asymmetric stretching frequencies of the nitro group were measured. The transmission was best in the biphenylene system; for the bridged systems the order was $O > S > SO_2 > CO > NHCO$.

Finally, although strictly outside the scope of this chapter (and book), we mention a study of the transmission of electronic effects in *N*-alkylidene-sulfenamides, -sulfinamides and -sulfonamides, $XC_6H_4SO_nN{=}CHC_6H_4OH$-2, through measuring the PMR chemical shifts of the *o*-OH[148]. The ρ values lie in the order $S < SO > SO_2$ (cf. above) which is attributed to a complex interplay of factors.

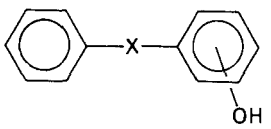
D. The *Ortho*-Effect of Sulfinyl and Sulfonyl Groups

The term *ortho*-effect has long been used to cover the peculiar influence of a substituent in the *ortho*-position to a reaction center, which often differs very markedly from that of the same substituent in the *meta*- or *para*-position[149–151]. Steric phenomena have long been recognized as playing a major part in the *ortho*-effect. Primary steric effects of various kinds, including steric hindrance to solvation or to the approach of the reagent, and secondary steric effects have been invoked. In certain systems hydrogen-bonding and other intramolecular interactions have been postulated.

Much effort has been devoted to the attempt to set up scales of σ_o values of general applicability. Only very limited success has been achieved in this direction[150] and it seems naïve to suppose that any simple LFER analogous to the Hammett equation could be successful in connection with the *ortho*-effect, except in rather limited and special situations. On the whole the various essays at scales of σ_o values have not involved sulfinyl or sulfonyl

groups. One exception to this was the attempt of Tribble and Traynham[152] to establish a scale of σ_o^- values based on the relative chemical shifts of OH in *ortho*-substituted phenols, $\Delta\delta_o$, dissolved in DMSO. A value of 0.92 was recorded for σ_o^- of SOMe but recalculation gives 0.88 when a slightly erroneous value for $\Delta\delta_o$ is corrected[153]. *o*-SOMe does not appear in any of the reactivity or spectral data with which the authors tested the applicability of their σ_o^- values.

More recently a comparison of the ^1H NMR chemical shifts and acidity constants of *o*-methylsulfinylphenol and *o*-hydroxyacetophenone showed that intramolecular hydrogen bonding is stronger for the carbonyl compound[154]. The effect of introducing bulky groups *ortho* to SOMe or COMe indicated 'that these have different intramolecular hydrogen bonding patterns and different stereochemical requirements for molecular stabilization when attached to an unsaturated system.' Thus *o*-methylsulfinylphenol is a stronger acid (pK_a, 7.60) than the *meta* and the *para* isomer (pK_a, 8.79 and 8.43 respectively), while *o*-acetylphenol is a weaker acid (pK_a, 10.22) than phenol itself (pK_a, 9.98) and the *meta* and *para* isomers are stronger (pK_a, 9.19 and 8.05 respectively). The unexpectedly high acidity of *o*-methylsulfinylphenol was attributed to anion stabilization through O^- interacting with the positive sulfur of the sulfinyl group, a type of interaction previously suggested by Meyers and coworkers[141] for *o*-hydroxyphenyl phenyl sulfoxide. The latter authors measured the pK_a values for the phenols with OH in the 2- or 4-position of **29**, where X = S, SO, SO_2 or CH_2.



(29)

Moving OH from 4- to 2-position slightly reduces the acidity for X = S or CH_2, but increases it for X = SO, the pK_a values (in 48% aqueous ethanol) being 9.17 and 9.04 respectively. This was attributed to the above interaction. On the other hand, moving OH from 4- to 2-position greatly reduces the acidity of the sulfone system (pK_a values 8.69 and 9.10 respectively) and this was attributed to an inescapable unfavorable interaction of the negative oxygens of SO_2 with the O^- in the anion.

Hojo and colleagues[155,156] have carried out numerous studies of *ortho*-effects, in particular on the ionizations of benzoic acids in DMSO–water mixed solvents. The *ortho*-effects are assessed by measuring the pK_a values of *ortho*- and *para*- substituted benzoic acids in solvents containing from 0 to 95% v/v DMSO and expressing the results as equation 15:

$$ortho\text{-effect} = \log K_o - \log K_p \tag{15}$$

Mininum *ortho*-effects tend to be observed at about 65% DMSO. The method has been applied to sulfur-containing substituents[156]. The pK_a values of the *ortho*-substituted acids in water are: SMe, 3.67; SOMe, 3.10; SO_2Me, 2.53. The *ortho*-effect of SMe is said to be merely of a steric nature, while that of SO_2Me is quite similar to that of NO_2, i.e. for both *o*-SMe and *o*-SO_2Me there is an acid-strengthening secondary steric effect (cf. below), but for *o*-SO_2Me, as for *o*-NO_2, there is in addition the effect of strong electron attraction close to the reaction center. The *ortho*-effect of SOMe is quite different. It increases steadily with increase in DMSO content of the solvent and this is explained by the strong stabilization of the benzoate anion by the field effect of the $S^{\delta+}$–$O^{\delta-}$ dipole. There is a similar but more striking effect for Me_2S^+. (It may be remarked in passing that the results of Hojo and coworkers reveal some solvent dependence of the σ_p values for SOMe and SO_2Me.) A later paper extends the work to ΔH^0 and ΔS^0 of ionization, and *o*- and *p*-SOMe are included in the systems studied[157]. Various correlations between the thermodynamic quantities are considered.

In recent years much progress in understanding the *ortho*-effect has been made through the multiple regression analysis of reactivity data in terms of substituent parameters which measure the electronic or steric effects of substituents[158,159]. This approach is essentially an extension of the dual substituent-parameter treatment of the effects of *meta*- and *para*-substituents as applied by Taft and coworkers[65]. One of the most extensive analyses of this type has been carried out by the present author and his colleagues[160] for the reaction between diazodiphenylmethane (DDM) and *ortho*-substituted benzoic acids in alcohols. The rate-determining step of this reaction involves a proton transfer from the carboxylic acid to DDM to form a diphenylmethanediazonium-carboxylate ion-pair; subsequent fast product-governing stages have been variously formulated. The analysis employs the extended Hammett equation in the form (16):

$$\log k = h + \alpha\sigma_I + \beta\sigma_R + \phi\upsilon \qquad (16)$$

σ_I and σ_R are respectively the inductive and resonance constants of Taft's analysis of ordinary composite Hammett constants (values obtained by Charton were used) and υ is the steric substituent constant developed by Charton[161,162]. The intercept term, h, notionally corresponds to log k for H as an *ortho*-substituent, but is not found in practice always to agree closely with the observed value of log k for the parent system.

To apply this equation, i.e. to determine the regression coefficients, it is necessary to select a set of substituents which can be expected to be 'well-behaved'. Particular problems may be caused for σ_R and υ by conformational effects. For the present discussion the main point of interest is that it proves possible to include SO_2Me among the 'well-behaved' substituents, 18 in number, by using $\sigma_I = 0.59$, $\sigma_R = 0.12$ and $\upsilon = 1.2$. This is presumably possible because there is no serious conformational (twisting about ring–S bond) dependence of the resonance effect. Further, the two negative oxygens and the methyl, being roughly the same size, give SO_2Me something of the symmetry of the *t*-Bu group, which has almost the same steric parameter, $\upsilon = 1.24$. For completeness we mention that the regression equations were established for data in eleven alcohols as solvents and were then used to assess the peculiar behavior of another 15 *ortho*-substituents in respect of conformational effects and intramolecular hydrogen bonding. The steric effect expressed by $\phi\upsilon$ is one of steric acceleration, i.e. it is a secondary steric effect concerned with the twisting of the carboxyl group out of the plane of the benzene ring. The work has been extended to seven aprotic solvents and in all cases *o*-SO_2Me is included[163].

Correlation analyses of this type have also been carried out in connection with the kinetics of the reaction of *ortho*-substituted benzoate ions with *para*-substituted phenacyl bromides[164] and of *ortho*-substituted benzoate ions with ethyl bromoacetate[165]. In all cases it is possible to include *o*-SO_2Me among the basic set of 'well-behaved' substituents.

IV. SUBSTITUENT EFFECTS IN ALIPHATIC AND ALICYCLIC SYSTEMS

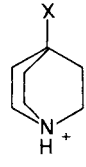
The electron-attracting influence of sulfinyl and sulfonyl groups in aliphatic systems has long been recognized. Thus pK_a values for phenylsulfinyl- and phenylsulfonyl-acetic acids were determined in 1934 to be 2.658 and 2.440 (at 25 °C respectively[166], cf. acetic acid, 4.75). Also, pK_a values (at 25 °C) for several 2-alkylsulfonylpropanoic acids were measured in 1937, e.g. 2.444 for the SO_2Me compound[167]. Such information was translated into the symbolism of linear free-energy relationships by Taft[62], who calculated a σ^* value of 1.32 for CH_2SO_2Me. Later, Chambers and Stirling[168] calculated a σ^* value of 1.37 for CH_2SO_2Ph. As already mentioned in Section II.B, Taft converted σ^* values to the σ_I scale through the equation $\sigma_I(X) = 0.45\ \sigma^*(CH_2X)$. Later, in the hands of Taft and other workers, the σ_I scale was extended to other sulfinyl and sulfonyl groups, particularly fluoro-substituted ones, but the basis of the σ_I scale in chemical reactivities has been increasingly overlaid by the contribution of ^{19}F NMR (Section III.B).

TABLE 12. σ_I and σ_R values tabulated by Charton[170]

Substituent	σ_I	σ_R
SO_2CF_3	0.71	0.21
$SOCF_3$	0.67	−0.03
SO_2Ph	0.56	0.12
SOPh	0.51	−0.07
SO_2Me	0.59	0.11
SOMe	Not given	0.00

Charton, however, has remained faithful to the pK_a basis of σ_I values for over 20 years[169]. For a detailed exposition of this, the reader should consult Charton's extensive review[170]. Here we must confine ourselves to saying that great importance is attached to the pK_a values of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and of substituted acetic acids, but, in all, about 80 series involving acid-base behavior make some contribution to the extensive tabulation of σ_I values. In Table 12 we show a selection of Charton's σ_I values that is relevant to the present Chapter, along with (for completeness) the corresponding σ_R values, which are essentially obtained by subtraction of σ_I values from the corresponding σ_p values (based on the ionization of 4-substituted benzoic acids). It must be emphasized that Charton's tables contain many qualifying footnotes and the values in Table 12 are presented only for illustrative purposes. We may note in passing that Charton's work gives some support to the view that sulfinyl groups can show appreciable $-R$ character (see Section III.B).

Charton's σ_I value for SO_2Me merits comment in that it is based not on the behavior of aliphatic or alicyclic carboxylic acids but on the pK_a values of 4-substituted quinuclidinium ions **30** in water. This system has been advocated by Grob and Schlageter[171] as

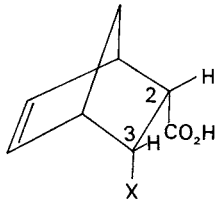


(30)

a suitable basis for comparing the inductive effects of substituents and they define a σ_I^q scale simply in terms of the effect of substituents on the pK_a value, i.e. for a substituent X, $\sigma_I^q = pK_a^H - pK_a^X$. The system is very sensitive to the inductive effects of substituents, so the numerical scale of σ_I^q is much more extended than that of σ_I. The value of σ_I^q for SO_2Me is 3.23, cf. COMe, 1.69; Cl, 2.51; CN, 3.04; NO_2, 3.48. There is an approximately rectilinear relationship between σ_I^q and Charton's σ_I, and the σ_I value for SO_2Me tabulated is derived from σ_I^q by applying an appropriate scaling factor.

Charton's σ_I values for SOPh and SO_2Ph are based on the pK_a values for phenylsulfinyl- and phenylsulfonyl-acetic acids[137], which we have already discussed in connection with the transmission of electronic effects by SO and SO_2 (Section III.C). These groups have also been the subject of a detailed study by Hogeveen and Montanari[172], who measured the pK_a values of some 3-phenylthio-, 3-phenylsulfinyl- and

3-phenylsulfonyl-bicyclo[2.2.1]hept-5-ene-2-carboxylic acids in 50% v/v ethanol–water, i.e. the norbornene system **31** and its three stereoisomers. Some related norbornane



(31)

derivatives were also studied. The effects of having the substituent and carboxyl group in the *exo* or *endo* disposition and, in the case of the sulfoxides, of the stereochemistry at sulfur were examined. In the *trans* series the normal order of inductive effects was observed, i.e. $SO_2Ph > SOPh > SPh > H$ (acidity constants of β-substituted propanoic acids were studied for comparison) but in the *cis* series the order was observed to be $SOPh > SO_2Ph > SPh > H$. The results were discussed in terms of the field effect, intramolecular hydrogen bonding, and steric hindrance to solvation. The same effects were invoked to explain minor differences in acidity arising from stereoisomerism at sulfur in the sulfoxides.

Finally it should be pointed out that Charton's σ_I values for $SOCF_3$ and SO_2CF_3 are based on pK_a values of substituted acetic acids determined by Orda and colleagues[173]. From the same results Yagupol'skii and coworkers[96] calculated σ^* values for CH_2SOCF_3 and $CH_2SO_2CF_3$ of 1.50 and 1.61 respectively, and from these they calculated values of σ^* for $SOCF_3$ and SO_2CF_3 of 4.20 and 4.50 by applying the methylene decremental factor 2.8. (If calculated from the σ_I values based on ^{19}F NMR, multiplication by 6.23 yields the σ^* values 4.17 and 4.55[96].)

V. STABILIZATION OF CARBANIONIC CENTERS BY SULFINYL AND SULFONYL GROUPS

A. Introduction

In the Introduction (Section I), some reference was made to the ability of sulfinyl and, particularly, of sulfonyl groups to stabilize adjacent carbanionic centers. It was indicated that while this has been traditionally ascribed to π(pd) bonding, the necessary planar distribution of bonds around the α-carbon is not supported unequivocally by the evidence, which is sometimes more clearly in favor of a pyramidal carbanion, with localized negative charge. In the latter case the stabilization of the carbanion by sulfinyl or sulfonyl groups is ascribed to polarization effects, maybe involving some octet expansion of sulfur including a role of d orbitals but not a π(pd) bonding role. Two recent papers typify the diversity of evidence. There has been an X-ray structure determination[174] of the dimer of [α-(phenylsulfonyl)benzyllithiumtetramethylethylenediamine]. The bond between the anionic carbon and sulfur is much shorter than a C—S bond in sulfones, approaching the length of a C=S bond. Also the distribution of bonds about that carbon is planar. Thus an important role of π(pd) bonding seems indicated. On the other hand, a study of the stereochemistry of alkylation of metallated allyl sulfones finds evidence for somewhat pyramidal carbanions, even though the presence of the allyl group should provide a further driving force for planarity by providing additional conjugation[175].

The ionization in water of carbon acids whose acidity is stimulated by SO_2Me groups was first studied more than forty years ago. In 1953 Pearson and Dillon[41] tabulated data

TABLE 13. Acidities of sulfones in DMSO at 25 °C[178]

Sulfone	pK_a	Sulfone	pK_a
$CH_3SO_2CH_3$	28.5	$(C_6H_5CH_2)_2SO_2$	22
$CH_3SO_2C_6H_5$	27	$[C_6H_5CH(CH_3)]_2SO_2$	23.5
$CH_3CH_2SO_2C_6H_5$	29		

derived from earlier work as follows: $MeSO_2Me$, $pK_a = 23$ (Hochberg and Bonhoeffer, 1939[42]); $(MeSO_2)_2CH_2$, $pK_a = 14$ (Schwarzenbach and Felder, 1944[176]); $(MeSO_2)_3CH$, strong acid[176]. Data were also presented for some compounds whose carbon acidity is due to the combined action of sulfonyl and carbonyl groups. The study of carbon acidity caused by sulfinyl groups appears to have started rather later. In 1965 Corey and Chaykovsky[177] discussed the formation and applications to organic synthesis of the methylsulfinyl carbanion, $MeSOCH_2^-$, and recognized that in ability to stabilize adjacent negative charge, SO groups were intermediate between NO_2, CO and SO_2 groups on the one hand and alkyl groups on the other.

In the last twenty years the behavior of carbon acids involving sulfonyl groups and, to a lesser extent, sulfinyl groups has been much studied. As an example of early work we mention that of Bordwell and coworkers[178] in 1967 on the pK_a values of several sulfones in dimethyl sulfoxide. As shown in Table 13, phenyl substitution increases the acidity and methyl substitution decreases it. There is an interesting contrast with nitro carbon acids, in which methyl substitution increases acidity, e.g. pK_a values in water of CH_3NO_2 and $CH_3CH_2NO_2$ are 10.2 and 8.6 respectively[41]. There is also an interesting contrast in the much greater effectiveness of NO_2 than SO_2Me in promoting the acidity of carbon acids, whereas the corresponding oxyacids, $HO{\cdot}NO_2$ and $HO{\cdot}SO_2Me$, are *both* strong acids. (Also, the electronic effects of NO_2 and SO_2Me as indicated by the various sigma constants are rather similar; Section III.) Bordwell and coworkers[178] explained the difference in terms of strong π(pp) bonding in $[CH_2NO_2]^-$, putting negative charge on oxygen, compared with weak π(pd) bonding in $[CH_2SO_2CH_3]^-$, putting negative charge on sulfur. The acidifying effect of methyl substitution in the nitro acids was attributed to the effect of CH_3 in stabilizing the C=N in $CH_2{=}NO_2^-$.

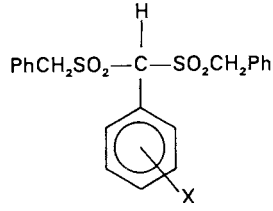
In this chapter it is clearly impossible to do more than sample the extensive literature on the carbon acidity of sulfinyl and sulfonyl compounds, as it illuminates the electronic effects of these groups, particularly in connection with linear free-energy relationships. There are three main areas to cover: first, as already indicated, equilibrium acidities (pK_a values); second, the kinetics of ionization, usually studied through hydrogen isotopic exchange; and finally, the kinetics of other reactions proceeding *via* carbanionic intermediates.

B. Equilibrium Acidities

Comparison of spectrophotometric and potentiometric methods of determining pK_a values in DMSO enabled Bordwell and colleagues[179] to establish an absolute scale of acidities in such solutions. On this scale the pK_a values of dibenzyl sulfone, methyl phenyl sulfone and dimethyl sulfone were raised to 23.95, 29.0, and 31.1 respectively (cf. Table 13). That of benzyl methyl sulfoxide was given as 29.0, and data were presented which indicated a value of 35.1 for DMSO. Thus the stabilizing effect of SO was about 4 pK_a units weaker than that of SO_2. For comparison, the pK_a values for a few other carbon acids on the same scale were: fluorene, 22.6; nitromethane, 17.2; acetone, 26.5. In a related paper[180], the pK_a value for methyl trifluoromethyl sulfone was given as 18.76, showing that the carbanionic stabilizing effect of SO_2CF_3 is approaching that of NO_2. Bordwell and coworkers[180]

attributed this to a much greater contribution of π(pd) bonding for SO_2CF_3 than SO_2CH_3, because of the contraction of the d orbitals of sulfur by the highly electronegative CF_3. They were aware of the climate of opinion against a bonding role for the d orbitals of sulfur and comment: 'It is also possible to describe the bonding in other ways; the one clear point emerging from the experimental results is that conjugation of sulfur in SO_2CF_3 with the carbanion is *strong*.' More recently (1980) Bordwell and colleagues[181] have drawn evidence from their work that carbanions of the type GH_2^- (where G is an electron-withdrawing group, including SOR and SO_2R among the possibilities) are planar, or nearly so. 'Acidity data indicate that the preferential generation of chiral, rather than achiral, planar α-sulfonyl carbanions is a consequence of a preferred kinetic pathway rather than an inherent greater thermodynamic stability.' This[181] and the previously mentioned paper[180] include information on the acidifying effects of sulfonyl groups on cyclopropyl compounds *c*-PrG.

There has been considerable interest in the effect of substituents in one or more attached benzene rings on the strengths of carbon acids in respect of applying the Hammett equation; systems involving SO_2Ph or SOPh have frequently been chosen for study. Thus Amel and Marek (1973)[182] measured the pK_a values (25 °C) of a series of phenyl phenacyl sulfones, 3- or 4-$XC_6H_4SO_2CH_2COC_6H_4Y$-4, in 95% ethanol. For both X and Y ordinary Hammett σ constants were applicable, the ρ values being 2.01 and 2.35 respectively. The positive ρ value for variation of the substituent in the phenylsulfonyl moiety was interpreted in terms of the enhancement of π(pd) bonding in the carbanion. Lee and Ang[183] studied the ionization of a series of α,α(benzylsulfonyl)toluenes **32** in 80% w/w DMSO–water, with *meta*- or *para*-substituents in the toluene moiety. The ρ value was 2.53



(32)

(25 °C) compared with 12 for substituted toluenes (in DMSO)[184], and this dramatic reduction in sensitivity was attributed to the very important role of the two SO_2CH_2Ph groups in delocalizing the carbanionic negative charge[185]. As might be expected, σ^- values were needed for conformity of *p*-CN and *p*-NO_2.

Kunieda and coworkers[186] measured the pK_a values of substituted α-phenylsulfinylacetophenones $XC_6H_4SOCH_2COC_6H_4Y$ in 50% ethanol. The ρ values are 1.32 for X and 2.68 for Y. The former was compared with 2.01 in the analogous sulfone system (see above[182]) and it was suggested that the lower value for XC_6H_4SO was due to a smaller π(pd) interaction.

Bordwell and colleagues have made various contributions in the general area of substituent effects in the benzene rings of carbon and other acids ionizing in DMSO. $ArCH_2SO_2Ph$ and $ArCH_2SO_2Me$, both with a ρ value 5.1, have been included in a recent summary of a dozen systems[187]. The ρ values for those acids in which the negative charge in the anion is concentrated primarily on the atom next to the phenyl ring fall mainly between 5.1 and 5.7, and there is no correlation between the pK_a values of the parent acids and the ρ values.

Very recently equilibrium ion-pair acidities of substituted diphenylmethanes have been measured in cyclohexylamine[188]. The *meta* series gives a normal Hammett plot ($\rho = 9.69$)

but the *para* series (including SO_2Me) is said not to fit 'in attempted correlations with σ^-, the Yukawa–Tsuno modification or dual substituent-parameter approaches.'

Studies of gas-phase acidities of carbon acids have appeared in the last ten years, including work on sulfones and sulfoxides[189]. The acidity of substituted methanes increases in the order

$$SOMe < CN < COMe < SO_2Me < COPh \leqslant SO_2Ph < NO_2.$$

The order is fairly similar to that observed for acidities in DMSO solution:

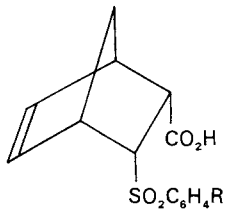
$$SOMe < CN < SO_2Me < SO_2Ph < COMe < COPh < NO_2,$$

but some pairs are reversed, indicating specific solvation effects. On average the acidities are attenuated by a factor of 1.3 in DMSO solution, but the sulfones and sulfoxides are more seriously affected.

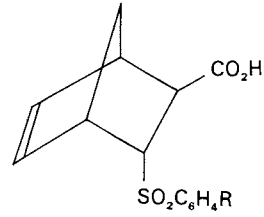
C. Kinetics of Ionization of Carbon Acids

During the past quarter of a century there have been numerous studies of the rates of ionization of sulfinyl and sulfonyl carbon acids[190]. Most of these have involved measuring the rate of base-catalyzed protium–deuterium exchange and often there have been parallel studies of rates of racemization or inversion. The interest of the investigators has been almost entirely in the stereochemical aspects of the processes. The two hydrogens of a CH_2 group α to SOR or SO_2R are diastereotopic and this character shows itself in different rates of ionization. Also, the environment of the ionizable hydrogens varies with the conformation of the sulfoxide or sulfone and their behavior is affected differently when the solvent or basic catalyst is varied. Thus the phenomena are very complicated and while the electronic effects of the sulfinyl and sulfonyl groups underlie all that is observed, there are a great many other factors that overlie them. Therefore there is little work in this area which can be said to be concerned primarily with elucidating the electronic effects of sulfinyl or sulfonyl groups. There have been repeated studies of the behavior of certain substrates, such as benzyl methyl sulfoxide (and related compounds) and 2-octyl phenyl sulfone, and studies of conformationally-fixed cyclic compounds have also been popular. The main interest has almost always been in establishing the nature of the intermediate carbanions, whether planar or pyramidal. It is in this connection that the studies are most relevant to the electronic effects of the sulfinyl or sulfonyl groups, i.e. whether the carbanion is stabilized by delocalization through conjugation, π(pd) bonding, octet expansion of sulfur, or whatever. As we have already seen, no very coherent picture has as yet emerged in these matters. We shall therefore not pursue them further. Some of these experimental and theoretical studies[190] will doubtless be dealt with by other authors elsewhere in this book.

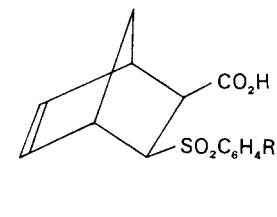
Of the studies which bear more particularly on electronic effects we mention first a study of the base-catalyzed H–D exchange in the 3-arylsulfonylbicyclo[2.2.1]hept-5-ene-2-carboxylic acids, *cis* (**33**), (**35**) and *trans* (**34**), and of the base-catalyzed inversion of the arylsulfonyl group in *cis* compounds (**33**) and (**35**)[191]. R comprised several *meta*- or *para*-



(**33**)



(**34**)



(**35**)

substituents and conformity to the Hammett equation was found for various rates of exchange or inversion. The ρ values for exchange (*ca.* 2.7) were larger than those for inversion (*ca.* 2.3). The operation of various external electrostatic and steric factors was discussed.

A study of the rates of water-catalyzed detritiation of six disulfonyl-activated carbon acids contains results of interest in connection with electronic effects[192]. Thus the carbanion stabilizing abilities of several groups as measured kinetically lie in the order $SO_2Ph > SO_2Et > SO_2Me$.

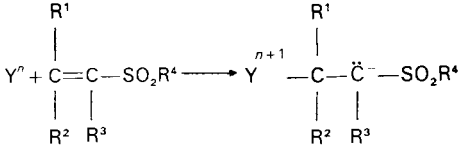
A final, rather different example which fits in appropriately here, in that it involves hydrogen exchange, is the measurement of equilibrium and rate constants for the base-catalyzed isomerization of unsaturated sulfides, sulfoxides and sulfones[193]:

$$CH_2{=}CH{-}CH_2X \rightleftharpoons CH_3{-}CH{=}CHX \tag{17}$$

where X = SR, SOR or SO_2R, R being Me, Et, *i*-Pr or *t*-Bu. The results (including discrimination between *cis* and *trans* isomeric products) were interpreted in terms of the electronic effect of the alkyl and of steric demands of sulfide, sulfoxide and sulfone groups.

D. Kinetics of Other Reactions Proceeding via Carbanionic Intermediates

It has long been known that α,β-unsaturated sulfones resemble α,β-unsaturated ketones and aldehydes in undergoing addition reactions with nucleophilic reagents[43]. These reactions are initiated by nucleophilic attack at the carbon β to the sulfone group:



(18)

where Y = RO^-, RS^-, CN^-, R_2NH, etc.; $n = -1$ or 0.

The stabilization of the carbanionic center on the α carbon atom by the sulfone group is no doubt an important factor promoting such reactions. Sulfoxides are capable of undergoing such reactions but are rather less prone to do so than sulfones.

McDowell and Stirling[194] studied electronic effects upon the reactivity of aryl vinyl sulfones towards amines. Rate constants for *t*-butylamine addition in ethanol at 25 °C were well correlated by the Hammett equation, with $\rho = 1.59$. Comparison of this with ρ values for H–D exchange mentioned above[191] suggested considerable carbanionic character in the transition state, perhaps in a concerted mechanism. Rates of addition of amines to alkenyl, allenyl and alkynyl *p*-tolyl sulfones have also been measured[195].

Although the point is not connected with carbanion formation, this is a convenient place to mention that *electrophilic* addition to the ethylenic double bond is greatly retarded in α,β-unsaturated sulfones. Thus the addition of chlorine to methyl vinyl sulfone in acetic acid at 25 °C is slower than that to ethyl acrylate by a factor of about 600[196]. This was attributed to the large electron-attracting inductive effect of SO_2Me compared with CO_2Et. Bromine addition to α,β-unsaturated sulfones is also somewhat slower than to β,γ-unsaturated sulfones by a factor of up to 20, depending on substrate and solvent[197,198]. This is not, however, considered to indicate significant conjugation of the sulfonyl group with the ethylenic link in the ground state of α,β-unsaturated sulfones.

Various reactions are promoted by sulfone groups through carbanion formation by proton loss from saturated systems. Thus there is base-catalyzed halogenation of suitable sulfones, analogous to the well-known halogenation of ketones. However, for the ketones the rate-determining step is the ionization, the halogenation of the enolate anion being

very fast, whereas for the sulfones there is an ionization pre-equilibrium and the halogenation is rate-limiting. A kinetic study of the bromination of six disulfones enabled rate constants for the attack of Br_2 and Br_3^- on the carbanions to be determined[199]. Ease of attack by Br_2 was in the order $SO_2Et > SO_2Me$, but the reverse order held for attack by Br_3^-.

Of considerable interest are sulfone promoted eliminations and cyclizations, which proceed *via* base-catalyzed removal of a proton from the carbon atom α to the sulfonyl group, e.g. equations 19 and 20.

$$ArSO_2CH_2CH_2X \xrightarrow{-HX} ArSO_2CH{=}CH_2 \tag{19}$$

$$ArSO_2CH_2CH_2CH_2X \xrightarrow{-HX} ArSO_2 \text{—}\triangleleft \tag{20}$$

Yano and Oae[200] studied the rates of base-catalyzed elimination of a series of *para*-substituted-phenyl β-chloroethyl sulfones in anhydrous acetonitrile with four nitrogen bases. Log k values for the parent sulfone correlated well with the pK_a values of the bases, while the ρ values (50 °C) for the reactions involving the various bases were Et_3N, 1.81; $Et_2NCH_2CH_2OH$, 1.75; $EtN(CH_2CH_2OH)_2$, 1.72; and $N(CH_2CH_2OH)_3$, 1.64. The ρ values thus decrease with decrease in the strength of the base and this was attributed to decreasing carbanionic character in the transition state. The authors considered the mechanism to be of the *E*2cb type, i.e. proton removal is rate-determining.

Goering and coworkers[201] studied the kinetics of base-promoted dehydrohalogenation of several series of *cis*- or *trans*-2-chlorocycloalkyl aryl sulfones. For the *trans*-2-chlorocyclohexyl series reacting with sodium hydroxide in 80% ethanol at 0 °C the ρ value was 1.42. The mechanism was considered to involve rate-determining carbanion formation, with the subsequent loss of chloride ion in a fast step.

The cyclization of aryl 3-chloropropyl sulfones by potassium *t*-butoxide in *t*-butyl alcohol at 30 °C (equation 20) has a ρ value of 2.32 for substituents in Ar[202]. This is considered by Bird and Stirling to indicate the formation of an intermediate carbanion which is essentially in equilibrium with the reactants. A recent review by Stirling[203] deals with structure-reactivity aspects of many sulfonyl promoted reactions of this type.

It should be mentioned here that if no other leaving group is present, sulfonyl can act as its own leaving group in hydroxide- or alkoxide-catalyzed elimination from sulfones. Carbanion formation is not involved in this but the promotion of the ionization of a C—H bond by the sulfonyl group is seen at the β-carbon rather than the α-carbon, e.g. equation 21.

$$\begin{array}{l} \quad H\text{-----}OH^- \\ \quad\ \vdots \\ R\text{—}CH\text{—}CH_2\text{—}SO_2R^1 \end{array} \longrightarrow RCH{=}CH_2 + \bar{S}O_2R^1 + H_2O \tag{21}$$

The course of such reactions (for example, the different products from an unsymmetrical sulfone) was investigated long ago by Ingold and colleagues[204].

Finally, we must mention the extensive work of Jarvis and colleagues on the kinetics of nucleophilic displacements on the halogen atoms of α-halosulfones[205]. The reactions studied have often been of the type of equation 22.

$$ArCHXSO_2Ph + PAr_3^1 + H_2O \xrightarrow{\text{aq. DMF}} ArCH_2SO_2Ph + HX + PAr_3^1O \tag{22}$$

and are believed to involve slow attack by the nucleophile PAr_3^1 on the halogen X to form intermediates $Ar\bar{C}HSO_2Ph$ and $PAr_3^1X^+$, followed by very fast reactions of the intermediates with water. The influence of various factors has been studied. Thus the effect

of *meta*- and *para*-substituents in Ar requires σ^- in Hammett correlation (as might be expected with a carbanion intermediate) and ρ values for X = Cl, Br and I are 2.23, 5.97 and 6.29 respectively (Ar^1 = Ph; 90% aqueous DMF, 25 °C)[206]. The correlation for X = Br was used to determine σ^- values for several groups including *p*-SO_2Me, for which the value 0.82 was obtained[207]. This is considerably lower than the value of 0.98 obtained by Bordwell and Cooper[75] (see Section III.A.1) based on the ionization of phenols, and in fact agrees with Bordwell and Anderson's[80] value based on the ionization of thiophenols, which is somewhat surprising.

The influence of substituents in Ar^1 is characterized by negative ρ values (plot based on ordinary Hammett σ constants)[208]. Reactions involving other types of phosphorus nucleophiles (e.g. PPh_2Alk)[208] and $ArSO_2^-$ ions as nucleophiles have also been studied[209]. The work has been extended to the study of α-azidosulfones but the reaction does not turn out to be analogous[210]. There is base-catalyzed abstraction of hydrogen ion from the α-carbon atom.

VI. MISCELLANEOUS TOPICS

A. Nucleophilic Aliphatic Substitution

Bordwell and Cooper[211] drew attention to the inertness of α-halosulfones and related compounds towards nucleophilic displacements of the halogen. Thus chloromethyl *p*-tolyl sulfone reacts with potassium iodide in acetone at less than one-fiftieth of the rate for *n*-butyl chloride. On the other hand, 1-(*p*-toluenesulfonyl)-3-chloro-1-propene reacts about 14 times faster than allyl chloride. This contrast (and other comparisons) led the authors to attribute the inertness of α-halosulfones to steric hindrance, which was eliminated when the sulfonyl group was more remote from the reaction center.

Meyers[212] collected together several examples of the anomalous behavior of sulfones in which the group was close to the reaction center and interpreted these in terms of the negative direct field effect of the SO_2 oxygen atoms (cf. Meyers and colleagues[141]).

A systematic study of the effect of various groups on the rates of the S_N2 reactions of aliphatic chlorides with potassium iodide in acetone was carried out by Bordwell and Brannen[213]. *n*-BuCl was taken as a standard of reactivity. Nearly all the electron-attracting groups studied, including SOPh and SO_2Ph, were mildly activating when introduced into the γ-position, i.e. in the substrates $X(CH_2)_3Cl$ (relative reactivities for SOPh, 2.6; SO_2Ph 3.6), but more diverse behavior appeared when the groups were in the β- or α-position, i.e. in $X(CH_2)_2Cl$ and XCH_2Cl. In the β-position SOPh remained mildly activating (2.7) but SO_2Ph became slightly deactivating (0.38), and in the α-position even SOPh became deactivating (0.25), while SO_2Ph (as mentioned above) was strongly deactivating (< 0.02). This behavior contrasted with that of COPh, which in the α-position became enormously activating (3.2×10^4). The retarding effect of α-SO_2Ph was now attributed to a combination of steric and O^- field effects.

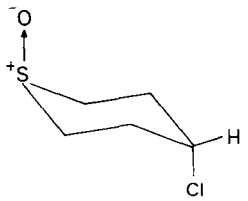
A further study of nucleophilic displacements α to sulfonyl groups was carried out by Bordwell and Jarvis[214]. This utilized the enhanced reactivities of nucleophiles in dipolar aprotic solvents such as DMF. Many nucleophiles were still rather reluctant to react with α-halosulfones but thiophenoxide ion reacted fairly readily with bromo- or chloro-methyl phenyl sulfone to give high yields of phenylthiomethyl phenyl sulfone, presumably by S_N2 displacement. However, while α-halobenzyl phenyl sulfones gave S_N2 reaction with this nucleophile in *anhydrous* DMF, in the presence of small amounts of protic solvent, large quantities of benzyl phenyl sulfone were produced. This appears to have been the start of Jarvis's extensive investigations of nucleophilic displacement on halogen to give α-sulfonyl carbanions (see Section V.D)[205–209].

Cinquini and coworkers[215] found that α-halogenomethyl sulfoxides react with *n*-PrO^-

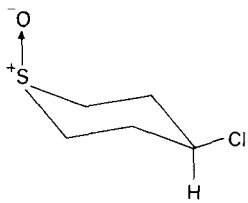
or EtS^- in propan-1-ol *via* S_N2 substitution; α-halogeno-ethyl and -isopropyl derivatives react more slowly and an elimination–addition reaction is of great importance[216]. The last-mentioned derivatives bear an obvious relationship to tertiary halides but no S_N1 mechanism appeared. The formation of carbocations is presumably greatly hindered by the SO moiety.

In the course of extensive studies of S_N2 reactions in dipolar aprotic solvents, Hayami and colleagues[217] studied chlorine isotopic exchange of (arylsulfonyl)chloromethanes, (arylsulfinyl)chloromethanes and 2-chloro-1-arylethanones in acetonitrile, i.e. $XC_6H_4YCH_2Cl$ with Y = SO_2, SO or CO. The results were compared with earlier work involving other moieties Y. For X = H, the order of reactivities with different Y's was S > none > SO > SO_2, in the ratios of about 10^8:3.3×10^7:3×10^2:1.0. It was suggested that the low reactivity of sulfinyl and sulfonyl derivatives might be due, at least in part, to an exothermic nucleophile-substrate association. The ρ values for different *para*-substituents X are Y = SO, 0.88; SO_2, 0.70 (cf. Section III.C), in interesting contrast to Y = S, −0.92, indicating that the role of C—Cl bond-formation is dominant for SO and SO_2 but that of bond-breaking is dominant for S.

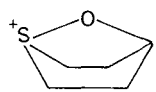
There is a special interest in the role of neighboring group participation by sulfinyl groups in nucleophilic aliphatic substitution. Thus Martin and Uebel[218] found that *trans*-4-chlorothiane-*S*-oxide **36** is solvolyzed (50% v/v aqueous ethanol, 140 °C) 630 times faster than the *cis* isomer **37**. This was attributed to the intervention of **38** for the former.



(36)



(37)



(38)

Cinquini and coworkers[219] studied the S_N1 solvolyses of $PhSO(CH_2)_nCMe_2Cl$, $n = 1, 2, 3$ or 4, in various aqueous organic solvents. In 80% aqueous DMF at 35 °C the rate constants for the various values of *n*, *seriatim*, relative to *t*-BuCl as 1.0, were 16:100:210:0.25, indicating clearly the occurrence of neighboring group participation for $n = 1$ to 3. In more aqueous media the effect was much less pronounced, e.g. the derivative with $n = 2$ was only 1.6 times more reactive than *t*-BuCl in 30% aqueous DMF. Analogous effects were not found in the sulfones $PhSO_2(CH_2)_nCMe_2Cl$, for which the ratios of rate constants (again that for *t*-BuCl is taken as unity) were 0.039:0.112:0.194:0.614 in 80% aqueous sulfolane, 35 °C. These results show largely the inhibitory effect of SO_2Ph on carbocation formation and the consequent favorable effect of interposing methylene groups. (It should be noted that the ratios for the sulfoxides in 80% aqueous sulfolane were qualitatively similar to those quoted above for 80% aqueous DMF: 25.6:46.7:163:1.1.)

The different behavior of sulfinyl and sulfonyl groups in this respect was also demonstrated by Barbieri and colleagues[220] in a study of the solvolysis of benzyl chloride with CH_2SOEt or CH_2SO_2Et in the *para*- or *ortho*-position. Moving CH_2SOEt from *para*- to *ortho*-position produced a considerable increase in reactivity, by a factor of about 100 in 80% aqueous sulfolane, while moving CH_2SO_2Et in the same way produced a decrease in reactivity of about 10%.

For a review of neighboring group participation by sulfinyl oxygen, see Montanari[221]. This special influence of sulfinyl groups on reactivity is, of course, due to the high polarity

of the sulfur–oxygen coordinate bond. This is also manifested in the behavior of sulfoxides as Brønsted and Lewis bases, characteristics which are much weaker in sulfones. The pK_a values of the protonated forms of common sulfoxides are in the region -2 to -3, as determined in aqueous solutions of strong acids[222], while those of sulfones are around -12[223]. Sulfoxides are also stronger bases than sulfones towards Lewis acids such as BF_3[224]. The distinctive pyrolyses of sulfoxides are caused by the basic nature of the sulfoxide oxygen atom[225]. Presumably the weaker basic (and nucleophilic) behavior of each oxygen in a sulfone is due to the adverse effect of the large positive charge on the sulfur (formally two units; see Section I.A) on the availability of the lone pairs of electrons of each oxygen.

B. Nucleophilic Aromatic Substitution

Sulfinyl and sulfonyl groups would be expected to activate the benzene ring towards nucleophilic substitution, as CN and NO_2 do, and an already-mentioned example of this (Section I.D) was discovered nearly half a century ago[46].

Miller[226] applied the Hammett equation to the rate constants for the reaction of 4-substituted 1-chloro-2-nitrobenzenes with OMe^- in methanol at 50 °C. σ^- values (denoted σ^* in accordance with the practice briefly in vogue at that time, 1956) were used for $+R$ substituents, and SO_2Me conformed well at a σ^- value of 1.049[52]. A σ^- value of 1.117 for SO_2Ph was derived from the Hammett plot, intermediate between the values based on phenol and anilinium ionizations by Szmant and Suld[88] at about the same time.

Oae and Khim[227] measured the rates of hydrolysis of chlorophenyl phenyl sulfoxides and sulfones with hydroxide ion in aqueous DMSO at 158 °C. Both SOPh and SO_2Ph were found to activate the nucleophilic substitution from *ortho*- and *para*-positions, but the effect of SO_2Ph was considerably larger than that of SOPh. The results were interpreted in terms of π(pd) conjugation in the intermediate complexes. In a later paper[228] it was shown that the introduction of a methyl group *ortho* to SOPh or SO_2Ph slightly retards the above and related reactions but this was attributed to the inductive effect of Me rather than steric inhibition of π(pd) conjugation (Section III.A.1).

When 4,4′-dichlorodiphenyl sulfone is treated with two equivalents of sodium hydroxide in aqueous DMSO, only one Cl is hydrolyzed[229]. Presumably the arylsulfonyl activating effect is eliminated by conjugation of O^- with the ring in the first hydrolysis product.

A long series of studies of aromatic nucleophilic substitution included the kinetics of reactions of 1-chloro-2,4-bis(trifluoromethylsulfonyl)benzene, 3-nitro-4-chlorophenyl trifluoromethyl sulfone and 2-chlorophenyl trifluoromethyl sulfone with sodium methoxide or ammonia in methanol[230]. The SO_2CF_3 group was found to have an enormous accelerating effect, in accord with the σ^- value of 1.65, based on the dissociation of anilinium ion[99]. Further examples of the promotion of nucleophilic aromatic substitution by fluoro-substituted sulfonyl groups are given by Yagupol'skii and coworkers[96].

Sulfinyl and sulfonyl groups can also act as leaving groups in aromatic nucleophilic substitution. The kinetics of hydrolysis of mononitrophenyl sulfoxides, sulfones and sulfonium methylsulfate by sodium hydroxide in 25% aqueous dioxan have been studied[231]. The mobility order is $SMe_2^+ \geqslant SO \approx SO_2$ for *p*-nitro-derivatives and $SO > SO_2$ for *o*-nitro-derivatives. The order $SO_2 > SO$ might have been expected on electronegativity grounds and the observed, rather small, effects are explained in terms of the interplay of electronic and steric effects, including the role of π(pd) conjugation. A mobility order $SOPh > SO_2Ph$ had been observed many years earlier by Bunnett and colleagues[232] in the reaction of 1-substituted 2,4-dinitrobenzenes with pyridine in methanol. The activation of sulfinyl and sulfonyl groups as leaving groups in nucleophilic substitution may also be accomplished by —N= in heterocycles such as pyridine,

pyrazine, quinoline, etc.[233]. Yagupol'skii and coworkers[96] give examples of the role of fluoro-substituted sulfinyl and sulfonyl groups as leaving groups.

The polarographic reduction of aryl methyl sulfones containing electron-attracting substituents in the benzene ring involves $MeSO_2^-$ as a leaving group. The process is thus a kind of aromatic nucleophilic substitution, the nucleophile being the electron[234]. The effect of *para*-substituents on the half-wave potentials exceeds that to be expected from the usual σ^- values. 3- and 4-SO_2Me were included in the study.

C. Electrophilic Aromatic Substitution

Sulfinyl and sulfonyl groups were involved in early studies of the directive effects of substituents in nitration and other reactions with electrophilic reagents. Thus Twist and Smiles[44] (in 1925) showed that nitration of phenyl methyl sulfone gave exclusively 3-nitrophenyl methyl sulfone. The results of bromination and sulfonation were analogous, so SO_2Me was established, like NO_2, as a *meta*-directing group.

The SOMe group became inadvertently involved in the disputes of the mid-1920s between R. Robinson and C. K. Ingold concerning the new electronic theory of organic chemistry[235]. Ingold and colleagues[236] found that *S*-methylthioguaiacol, 1-SMe-2-$OMeC_6H_4$, was nitrated (by nitric acid in acetic anhydride) in the 6-position to form what they believed to be 1-SMe-2-OMe-6-$NO_2C_6H_3$, i.e. the SMe, when adjacent to OMe, directed strongly to the *ortho*-position. This seemed to them a remarkable result but they were able to devise an explanation. They also found that the nitration of 2-methoxyphenyl methyl sulfone gave mainly the 5-nitro isomer, with some 3-nitro, in accord with the *meta*-directing effect of SO_2Me and the *ortho- para*-directing effect of OMe. The system was re-examined by Pollard and Robinson[237], who found that the product of the supposed nitration of *S*-methylthioguaiacol was in fact not a nitro compound at all but 2-methoxyphenyl methyl sulfoxide, i.e. the action of the nitric acid was to oxidize SMe to SOMe. The successive oxidation and nitration of *S*-methylthioguaiacol could be carried out by the action of cold fuming nitric acid and this produced largely 5-nitro-2-methoxyphenyl methyl sulfoxide, i.e. the nitration occurred mainly in the *para*-position to OMe and in the *meta*-position to SOMe. A correction note by Ingold and Ingold[238] appeared immediately following Pollard and Robinson's paper.

Ingold and coworkers[239] found that nitration of benzyl methyl sulfone produced only 30% of the *meta* derivative, and much *ortho* and *para* isomer. Presumably the *meta*-directing influence of SO_2Me is weakened by the intervening CH_2 group, which has itself some of the *ortho-para*-directing effect of a methyl group when attached to the ring.

Chatterjee and Robinson[240] studied the nitration of *m*-nitrophenyl benzyl sulfone, which occurred exclusively in the benzyl ring producing 25% *ortho*, 28% *meta* and 47% *para* isomer. Baldwin and Robinson[241] nitrated a series of phenyl alkyl sulfones $PhSO_2R$. When R = Me, 98.5% of *meta* derivative was found but the amount of *meta* isomer fell with the chain length and branching of the alkyl group. e.g. *n*-Bu, 85.7%; *i*-Pr, 80.0%. This was attributed to the electron repulsive influence of the higher alkyl groups.

Thus over half a century ago there was already a fair amount of information about the directive influence of sulfonyl groups but there appears to have been no information about sulfinyl groups in this respect before the 1950s, when Leandri and Pallotti[242] reported that the sulfinyl group was *para*-orienting in the nitration of aromatic sulfoxides. This was later confirmed for bromination[243]. It thus appears that in the highly electron-demanding reactions of electrophilic substitution the conjugative role of the remaining lone pair of electrons on the sulfur is important, i.e. SOR groups behave in a $-R$ fashion. We may recall at this point that while the σ_R(BA) and σ_R^0 substituent constants of SOMe are often taken to be zero, and σ_R^- is positive, 0.17[65], some authors have argued in favour of a small negative σ_R^0 value, -0.07, based on infrared spectroscopy[128]. Indeed, Charton[170] has

tabulated a distinctive σ_R^+ value of -0.10 for SOMe; cf. Ehrenson and coworkers[65], who take it to be zero.

In recent years the effect of sulfinyl groups on electrophilic substitution has been much studied. Marziano and colleagues[244] studied the kinetics of nitration of diphenyl sulfoxide in 83–100% sulfuric acid, measuring proportions of isomers and second-order rate coefficients (k_2), and calculating k_p, k_m and k_o. At the lower concentrations of sulfuric acid each individual *meta*-position is less reactive than each *para*-position but because there are four of the former and two of the latter, slightly more than 50% of the product is *meta* isomer. At higher acidities $k_m > k_p$, so that in 100% sulfuric acid the product contains over 80% *meta* isomer. The *ortho*-positions are always relatively unreactive. The rate constants increase with acidity up to *ca.* 90% sulfuric acid and then decrease again. The above and other features of the results are explained in terms of the competitive nitration of two species: Ph_2SO and $[Ph_2SOH]^+$, the former favoring *para* substitution and the latter *meta* substitution. A later paper from the same research group presented results on the nitration of methyl phenyl sulfoxide in sulfuric acid[245]. The results were broadly similar, although $k_m > k_p$ throughout, and *meta* nitration always predominates. PhSOMe is less reactive than Ph_2SO by a factor of about 10.

Isomer distributions for molecular bromination of methyl phenyl sulfoxide and molecular chlorination of diphenyl sulfoxide in various solvents show a great preponderance of *para* isomer in the product[246]. For chlorination in nitromethane at 25 °C there is a strong activating effect of SOPh and an effective σ^+ value of -0.19 is indicated. This is attributed to polarization of the sulfoxide group in the transition state, induced by the electrophilic reagent. On the other hand *p*-SOMe strongly retards the protodesilylation of methyl *p*-trimethylsilylphenyl sulfoxide in H_2SO_4–AcOH mixtures, possibly because of hydrogen bonding between the sulfinyl group and the acidic medium.

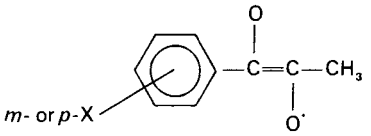
Thus it seems clear that, in the absence of interactions with the reaction medium, SOR groups behave as $-R$ substituents and activate electrophilic substitution. However, they are prone to protonation or at least to act as hydrogen bond acceptors, in which condition they behave as $+R$ substituents, deactivate electrophilic substitution and are *meta*-directing.

Finally, it may be mentioned that Yagupol'skii and coworkers[96] give isomer composition for nitration of $PhCH{:}CHSO_2CF_3$ as 27% *ortho*, 15.0% *meta* and 58.0% *para*. Thus the *ortho-para*-directing character of the vinyl group is only slightly modified by the presence of SO_2CF_3, in spite of the σ_m and σ_p values of $CH{:}CHSO_2CF_3$ being *positive* at 0.44 and 0.56 respectively, based on ^{19}F NMR values of σ_I and σ_R of 0.31 and 0.25.

D. Free Radicals

The effect of sulfur-containing substituents on free radicals appears to be a topic of current interest, so we will discuss it briefly insofar as it concerns sulfinyl and sulfonyl groups. Our discussion will refer mainly to a few recent papers, which usually contain copious references to earlier work; see also Block[247].

Work of several types has been carried out. As long ago as 1970 Strom and Norton[248] studied electron-withdrawal by substituents containing Group IV and Group VI elements through their effect on ESR methyl hyperfine splitting in 1-phenyl-1,2-propanesemidiones **39**.

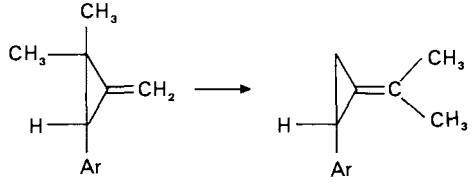


(**39**)

A good correlation with ordinary Hammett σ values was based on 16 'well-behaved' substituents, and *p*-SOMe conformed well to this. Various other substituents showed deviations which were attributed to enhanced + *R* effects. These included *p*-SPh and this was explained in terms of π(pd) bonding, which was thus taken to play no part in the effect of *p*-SOMe on the methyl hyperfine splitting. More recently several 4-substituted benzyl radicals of the type $RSO_nC_6H_4CH_2^{\cdot}$ ($n = 0$, 1 or 2; R = Me, Ph, Tol, COMe or OMe) have been examined by ESR spectroscopy[249]. The ability to delocalize spin density onto the substituent decreases in general as *n* increases and the effect of R depends on the oxidation state of sulfur. These authors have devised a new scale of substituent effects $\sigma_\alpha^{\cdot}$ (sigma dot alpha) on the basis of benzylic α-hydrogen hyperfine coupling constants. A few values are as follows: 4-SMe, 0.063; 4-SOPh, 0.026; 4-SOMe, 0.018; 4-SO_2Ph, 0.018; 4-SO_2Me, 0.005; H, 0.000; 3-Cl, −0.007; 3-CN, −0.026.

Another type of work is based on the measurement of oxidation potentials of carbanions. Thus Bordwell and Bausch[250] have measured these for the fluorenide ion and 21 substituted fluorenide ions in DMSO solution. The values of E_{ox} for 2-substituted fluorenide ions were found to give a good rectilinear plot against the corresponding pK_a values in DMSO for the conjugate acids. Various points and also some of those for 3-substituents deviated from this plot. These deviations are the basis of acidity-oxidation-potential (AOP) values (expressed in kcal mol^{-1}). The AOP, when related to the AOP for the parent fluorene system, indicates whether the radical (resulting from the oxidation of the carbanion) is specially stabilized by the substituent. There is such stabilization by 3-MeS and 3-PhS, but 2-SO_2Me, 2-SO_2Ph and 3-SO_2Ph conform well to the above-mentioned plot. On the other hand, 2-SOMe exerts a considerable radical destabilizing effect. Some other systems were also discussed. The work was extended to rate constants for electron-transfer from carbanions to 1,1-dinitrocyclohexane[251]. Substituted 9-phenylfluorenide ions were studied and linear correlations of log *k* with pK_a or E_{ox} were found. The substituents involved included SO_2Ph and SO_2Me.

Free radical substituent effects have also been probed through the kinetics of rearrangement of 3-aryl-2,2-dimethylmethylenecyclopropanes **40** to **41**[252]. The reaction



(40) **(41)**

proceeds *via* a singlet trimethylenemethane biradical. The rate constants for several sulfur-containing substituents (C_6D_6 as solvent, 80 °C) are in the order:

$$p\text{-SMe} \gg p\text{-SOMe} \approx p\text{-}SO_2\text{Me} > m\text{-SOMe} > \text{H} > m\text{-SMe} > m\text{-}SO_2\text{Me},$$

only an approximately three-fold range in reactivity being involved. The results indicate that the rate-enhancing effect (the stabilization of the biradical intermediate) is conjugative in nature. The stabilization is considered to involve the non-bonding electron pair of SMe and an effect involving vacant d orbitals is invoked for SOMe and SO_2Me, as well as for SMe.

Arising from studies of the photochemistry of benzenesulfonyl systems, extensive *ab initio* MO calculations have been made for various sulfonyl radicals and related species[253]. The STO-3G* basis set, which includes d-type polarization functions on second-row atoms, was used. The inclusion of d orbitals on sulfur was found to be very

important and the results suggest that the radical site in sulfonyl radicals is significantly delocalized over the entire functional group.

Finally, we mention that over 20 years ago acid dissociation constants of phenols with sulfur-containing substituents were determined for lowest triplet and first excited singlet states and compared with those for the ground state[254]. LFER treatment showed that the extent of electron-attracting conjugation by sulfinyl, sulfonyl and sulfonio groups was greatly enhanced in photo-excited states, while sigma constants for electronically excited sulfide groups were not usually appreciably different from those in the ground state. These findings were interpreted in terms of competing $-R$ and $+R$ conjugation [π(pp) and π(pd) respectively] for sulfide groups and $+R$ π(pd) conjugation for the other sulfur groups.

VII. REFERENCES

1. C. C. Price and S. Oae, *Sulfur Bonding*, Ronald Press, New York, 1962. (After a quarter of a century this is still a valuable source of information on matters related to bonding in sulfoxides, sulfones, and sulfonium ions.)
2. P. J. Durrant and B. Durrant, *Introduction to Advanced Inorganic Chemistry*, 2nd ed., Longmans, London, 1970, pp. 829–880.
3. W. Kutzelnigg, *Angew. Chem., Int. Ed. Engl.*, **23**, 272 (1984).
4. G. Cilento, *Chem. Rev.*, **60**, 147 (1960).
5. K. A. R. Mitchell, *Chem. Rev.*, **69**, 157 (1969).
6. Ref. 1, Chapters 3 and 4. (These give a very detailed account of the evidence for S→O *versus* S=O.)
7. G. M. Philips, J. S. Hunter and L. E. Sutton, *J. Chem. Soc.*, 146 (1945).
8. C. W. N. Cumper and S. Walker, *Trans. Faraday Soc.*, **52**, 193 (1956).
9. S. Sugden, *The Parachor and Valency*, Routledge, London, 1930.
10. L. Pauling, *The Nature of the Chemical Bond*, 2nd ed., Cornell, Ithaca, New York, 1940, p. 92.
11. J. Shorter in *The Chemistry of the Sulphonium Group* (Eds. C. J. M. Stirling and S. Patai), Chap. 9, Wiley, Chichester, 1981.
12. H. A. Bent, in *The Organic Chemistry of Sulfur* (Ed. S. Oae), Chap. 1, Plenum Press, New York, 1976.
13. E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, 1978. See especially pp. 18–21 and 44–50.
14. H. Kwart and K. King, *d-Orbitals in the Chemistry of Silicon, Phosphorus, and Sulfur*, Springer-Verlag, Berlin, 1977.
15. Cf. all the above-cited books on the organic chemistry of sulfur and many others.
16. Bond-stretching frequencies quoted here are from ref. 1 or standard compilations of infrared data.
17. Ref. 1, p. 77.
18. H. Mackle, D. V. McNally and W. V. Steele, *Trans. Faraday Soc.*, **65**, 2060 (1969).
19. See, for example, D. J. Cram, R. D. Trepka and P. St. Janiak, *J. Amer. Chem. Soc.*, **88**, 2749 (1966); also Ref. 13, pp. 50–56.
20. S. E. Browne, S. E. Asher, E. H. Cornwall, J. K. Frisoli, L. J. Harris, E. A. Salot, E. A. Sauter, M. A. Trecoske and P. S. Veale, Jr., *J. Amer, Chem. Soc.*, **106**, 1432 (1984).
21. G. Chassaing and A. Marquet, *Tetrahedron*, **34**, 1399 (1978).
22. R. S. Glass and J. R. Duchek, *J. Amer. Chem. Soc.*, **98**, 965 (1976).
23. Ref. 14, pp. 2–13 is relevant to all this discussion.
24. C. A. Coulson, *Nature*, **221**, 1106 (1969).
25. A. Rauk, S. Wolfe and I. G. Csizmadia, *Can. J. Chem.*, **47**, 113 (1969).
26. S. Wolfe, A. Rauk and I. G. Csizmadia, *J. Amer. Chem. Soc.*, **91**, 1567 (1969).
27. A. Streitwieser and J. E. Williams, *J. Amer. Chem. Soc.*, **97**, 191 (1975).
28. F. Bernardi, I. G. Csizmadia, A. Mangini, H. B. Schlegel, M.-H. Whangbo and S. Wolfe, *J. Amer. Chem. Soc.*, **97**, 2209 (1975).
29. e.g. F. Bernardi, H. B. Schlegel, M.-H. Whangbo and S. Wolfe, *J. Amer. Chem. Soc.*, **99**, 5633 (1977).

30. J. B. Collins, P. von R. Schleyer, J. S. Binkley and J. A. Pople, *J. Chem. Phys.*, **64**, 5142 (1976).
31. S. Wolfe, L. A. LaJohn, F. Bernardi, A. Mangini and G. Tonachini, *Tetrahedron Letters*, **24**, 3789 (1983).
32. S. Wolfe, A. Stolow and L. A. LaJohn, *Tetrahedron Letters*, **24**, 4071 (1983).
33. V. Král, Z. Arnold and Z. Havlas, *Collect. Czech. Chem. Commun.*, **46**, 883 (1981).
34. D. A. Bors and A. Streitwieser, Jr., *J. Amer. Chem. Soc.*, **108**, 1397 (1986).
35. P. von R. Schleyer, T. Clark, A. J. Kos, G. W. Spitznagel, C. Rohde, D. Arad, K. N. Houk and N. G. Rondan, *J. Amer. Chem. Soc.*, **106**, 6467 (1984).
36. P. G. Mezey and E.-C. Hass, *J. Chem. Phys.*, **77**, 870 (1982).
37. E. Fromm, *Liebigs Ann. Chem.*, **253**, 135 (1889).
38. E. Fromm, A. Forster and B. von Scherschewitzki, *Liebigs Ann. Chem.*, **394**, 343 (1912).
39. F. Arndt and C. Martius, *Liebigs Ann. Chem.*, **499**, 228 (1932).
40. E. A. Fehnel and M. Carmack, *J. Amer. Chem. Soc.*, **71**, 231 (1949).
41. R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1953).
42. J. Hochberg and K. F. Bonhoeffer, *Z. Phys. Chem.*, **184A**, 419 (1939).
43. For many examples, see Ref. 1, pp. 110–114.
44. R. F. Twist and S. Smiles, *J. Chem. Soc.*, **127**, 1248 (1925).
45. W. von E. Doering and A. K. Hoffmann, *J. Amer. Chem. Soc.*, **77**, 521 (1955).
46. D. L. Hammick and R. B. Williams, *J. Chem. Soc.*, 211 (1938).
47. This section is largely based on the previous account in Ref. 11, in which certain material was adapted (by kind permission of the Oxford University Press) from J. Shorter, *Correlation Analysis in Organic Chemistry; An Introduction to Linear Free-Energy Relationships*, Chap. 2, Oxford Chemistry Series, 1973.
48. J. Shorter, *Correlation Analysis of Organic Reactivity*, Chap. 1, Research Studies Press, Wiley, Chichester, 1982.
49. L. P. Hammett, *Physical Organic Chemistry*, 2nd ed., Chap. 11, McGraw-Hill, New York, 1970.
50. O. Exner, in *Advances in Linear Free Energy Relationships* (Eds. N. B. Chapman and J. Shorter), Chap. 1, Plenum Press, London, 1972.
51. Ref. 48, Chap. 3.
52. H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).
53. The symbol and sign conventions used for substituent effects in this chapter are those most frequently used by writers on correlation analysis in organic chemistry. *I* or *R* effects which withdraw electrons from the ring are regarded as positive. See Ref. 48, pp. 229–230 for a more detailed consideration of symbol and sign conventions.
54. H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958).
55. H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, **78**, 815 (1959).
56. J. Shorter, in *Correlation Analysis in Chemistry: Recent Advances* (Eds. N. B. Chapman and J. Shorter), Chap. 4, Plenum Press, New York, 1978.
57. Ref. 48, Chap. 3.
58. Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Japan*, **32**, 971 (1959).
59. Y. Yukawa, Y. Tsuno and M. Sawada, *Bull. Chem. Soc. Japan*, **39**, 2274 (1966).
60. R. W. Taft and I. C. Lewis, *J. Amer. Chem. Soc.*, **80**, 2436 (1958).
61. R. W. Taft and I. C. Lewis, *J. Amer. Chem. Soc.*, **81**, 5343 (1959).
62. R. W. Taft, in *Steric Effects in Organic Chemistry* (Ed. M. S. Newman), Chap. 13, Wiley, New York, 1956.
63. R. W. Taft, S. Ehrenson, I. C. Lewis and R. E. Glick, *J. Amer. Chem. Soc.*, **81**, 5352 (1959).
64. S. Ehrenson, *Prog. Phys. Org. Chem.*, **2**, 195 (1964).
65. S. Ehrenson, R. T. C. Brownlee and R. W. Taft, *Prog. Phys. Org. Chem.*, **10**, 1 (1973).
66. O. Exner, *Collect. Czech. Chem. Commun.*, **31**, 65 (1966).
67. R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen and G. T. Davis, *J. Amer. Chem. Soc.*, **85**, 709 (1963).
68. R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen and G. T. Davis, *J. Amer. Chem. Soc.*, **85**, 3146 (1963).
69. A. R. Katritzky and R. D. Topsom, in *Advances in Linear Free Energy Relationships* (Eds. N. B. Chapman and J. Shorter), Chap. 3, Plenum Press, London, 1972, and references cited therein.
70. G. P. Ford, A. R. Katritzky and R. D. Topsom, in *Correlation Analysis in Chemistry: Recent Advances* (Eds. N. B. Chapman and J. Shorter), Chap. 6, Plenum Press, New York, 1978.
71. J. D. Roberts and W. T. Moreland, *J. Amer. Chem. Soc.*, **75**, 2167 (1953).

72. Ref. 48, Chap. 4.
73. J. Shorter, in *Advances in Linear Free Energy Relationships* (Eds. N. B. Chapman and J. Shorter), Chap. 2, Plenum Press, London, 1972. See also Ref. 47, Chap. 3.
74. R. W. Taft, *J. Amer. Chem. Soc.*, **79**, 1045 (1957).
75. F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **74**, 1058 (1952).
76. C. C. Price and J. J. Hydock, *J. Amer. Chem. Soc.*, **74**, 1943 (1952).
77. H. Kloosterziel and H. Backer, *Rec. Trav. Chim. Pays-Bas*, **71**, 295 (1952).
78. H. Kloosterziel and H. Backer, *Rec. Trav. Chim. Pays-Bas*, **72**, 185 (1953).
79. O. Exner, in *Correlation Analysis in Chemistry: Recent Advances* (Eds. N. B. Chapman and J. Shorter), Chap. 10, Plenum Press, New York, 1978.
80. F. G. Bordwell and H. M. Andersen, *J. Amer. Chem. Soc.*, **75**, 6019 (1953).
81. F. G. Bordwell and P. J. Boutan, *J. Amer. Chem. Soc.*, **79**, 717 (1957).
82. D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).
83. G. B. Barlin and D. D. Perrin, *Quart. Rev.*, **20**, 75 (1966).
84. Y. Yukawa, Y. Tsuno and M. Sawada, *Bull. Chem. Soc. Japan*, **45**, 1198 (1972).
85. A. J. Hoefnagel, J. C. Monshouwer, E. C. G. Snorn and B. M. Wepster, *J. Amer. Chem. Soc.*, **95**, 5350 (1973).
86. A. J. Hoefnagel and B. M. Wepster, *J. Amer. Chem. Soc.*, **95**, 5357 (1973).
87. M. Sjöström and S. Wold, *Chem. Scripta*, **9**, 200 (1976).
88. H. H. Szmant and G. Suld, *J. Amer. Chem. Soc.*, **78**, 3400 (1956).
89. C. Y. Meyers, G. Moretti and L. Maioli, *J. Org. Chem.*, **27**, 625 (1962).
90. C. Y. Meyers, *Gazz. Chim. Ital.*, **93**, 1206 (1963).
91. C. Y. Meyers, B. Cremonini and L. Maioli, *J. Amer. Chem. Soc.*, **86**, 2944 (1964).
92. S. Oae and C. Zalut, *J. Amer. Chem. Soc.*, **82**, 5359 (1960).
93. S. Oae, M. Yoshihara and W. Tagaki, *Bull. Chem. Soc. Japan*, **40**, 951 (1967).
94. E. Pelizzetti and C. Verdi, *J. Chem. Soc., Perkin Trans. 2*, 808 (1973).
95. N. Bodor and A. Kövendi, *Rev. Roum. Chem.*, **11**, 413 (1966); *Chem. Abstr.*, **65**, 7011 (1966).
96. L. M. Yagupol'skii, A. Ya. Il'chenko and N. B. Kondratenko, *Usp. Khim.*, **43**, 64 (1974); *Russ. Chem. Rev.*, **43**, 32 (1974).
97. L. N. Sedova, L. Z. Gandel'sman, L. A. Alekseeva and L. M. Yagupol'skii, *Zh. Obschei Khim.*, **39**, 2057 (1969); *J. Gen. Chem. USSR.*, **39**, 2011 (1969).
98. E. V. Titov, N. G. Korzhenevskaya, L. M. Kapkan, L. N. Sedova, L. Z. Gandel'sman, Yu. A. Fialkov and L. M. Yagupol'skii, *Zh. Org. Khim.*, **7**, 2552 (1971); *J. Org. Chem. USSR.*, **7**, 2651 (1971).
99. W. A. Sheppard, *J. Amer. Chem. Soc.*, **85**, 1314 (1963).
100. R. Pollet, R. van Poucke and A. de Cat, *Bull. Soc. Chim. Belges*, **75**, 573 (1976).
101. E. B. Lifshits, L. M. Yagupol'skii, D. Ya. Naroditskaya and E. S. Kozlova, *Reakts. Spos. Org. Soedinenii*, **6**, 317 (1969); *Org. React. (Tartu)*, **6**, 133 (1969).
102. C. G. Swain and E. C. Lupton, Jr., *J. Amer. Chem. Soc.*, **90**, 4328 (1968).
103. C. Hansch, A. Leo, S. H. Unger, K. H. Kim, D. Nikaitani and E. J. Lien, *J. Med. Chem.*, **16**, 1207 (1973).
104. C. G. Swain, S. H. Unger, N. R. Rosenquist and M. S. Swain, *J. Amer. Chem. Soc.*, **105**, 492 (1983).
105. Ref. 56, pp. 144–155 examines the Swain–Lupton treatment in detail.
106. W. F. Reynolds and R. D. Topsom, *J. Org. Chem.*, **49**, 1989 (1984).
107. A. J. Hoefnagel, W. Oosterbeek and B. M. Wepster, *J. Org. Chem.*, **49**, 1993 (1984).
108. M. Charton, *J. Org. Chem.*, **49**, 1997 (1984).
109. C. G. Swain, *J. Org. Chem.*, **49**, 2005 (1984).
110. M. J. S. Dewar and P. J. Grisdale, *J. Amer. Chem. Soc.*, **84**, 3548 (1962).
111. R. N. Berezina, K. Kalfus and V. A. Koptyug, *Izv. Sib. Otd. Akad. Nauk USSR, Ser. Khim. Nauk*, **6**, 100 (1970); *Chem. Abstr.*, **75**, 5044 (1971).
112. M. J. S. Dewar, R. Golden and J. M. Harris, *J. Amer. Chem. Soc.*, **93**, 4187 (1971).
113. W. A. Sheppard and R. W. Taft, *J. Amer. Chem. Soc.*, **94**, 1919 (1972).
114. G. P. Syrova, L. N. Sedova, L. Z. Gandel'sman, L. A. Alekseeva and L. M. Yagupol'skii, *Zh. Org. Khim.*, **6**, 2285 (1970); *J. Org. Chem. USSR*, **6**, 2293 (1970).
115. G. P. Syrova, V. F. Bystrov, V. V. Orda and L. M. Yagupol'skii, *Zh. Obschei Khim.*, **39**, 1395 (1969); *J. Gen. Chem. USSR*, **39**, 1364 (1969).
116. L. J. Kaplan and J. C. Martin, *J. Amer. Chem. Soc.*, **95**, 793 (1973).

117. W. Adcock, J. Alste, S. Q. A. Rizvi and M. Aurangzeb, *J. Amer. Chem. Soc.*, **98**, 1701 (1976).
118. M. T. Tribble and J. G. Traynham, in *Advances in Linear Free Energy Relationship* (Eds. N. B. Chapman and J. Shorter), Chap. 4, Plenum Press, London, 1972.
119. D. F. Ewing, in *Correlation Analysis in Chemistry: Recent Advances* (Eds. N. B. Chapman and J. Shorter), Chap. 8, Plenum Press, New York, 1978.
120. G. Socrates, *Trans. Faraday Soc.*, **66**, 1052 (1970).
121. Y. Tsuno, M. Fujio, Y. Takai and Y. Yukawa, *Bull. Chem. Soc. Japan*, **45**, 1519 (1972).
122. M. Fujio, M. Mishima, Y. Tsuno, Y. Yukawa and Y. Takai, *Bull. Chem. Soc. Japan*, **48**, 2127 (1975).
123. D. F. Ewing, *Org. Magn. Reson.*, **12**, 499 (1979).
124. J. Bromilow, R. T. C. Brownlee, V. O. Lopez and R. W. Taft, *J. Org. Chem.*, **44**, 4766 (1979).
125. O. Exner and K. Boček, *Collect. Czech. Chem. Commun.*, **38**, 50 (1973).
126. R. T. C. Brownlee, R. E. J. Hutchinson, A. R. Katritzky, T. T. Tidwell and R. D. Topsom, *J. Amer. Chem. Soc.*, **90**, 1757 (1968).
127. P. J. Q. English, A. R. Katritzky, T. T. Tidwell and R. D. Topsom, *J. Amer. Chem. Soc.*, **90**, 1767 (1968).
128. N. C. Cutress, T. B. Grindley, A. R. Katritzky, M. Shome and R. D. Topsom, *J. Chem. Soc., Perkin Trans. 2*, 268 (1974).
129. A. R. Katritzky, R. F. Pinzelli, M. V. Sinnott and R. D. Topsom, *J. Amer. Chem. Soc.*, **92**, 6861 (1970).
130. M. Fujio, R. T. McIver, Jr. and R. W. Taft, *J. Amer. Chem. Soc.*, **103**, 4017 (1981).
131. M. Mashima, R. T. McIver, Jr., R. W. Taft, F. G. Bordwell and W. N. Olmstead, *J. Amer. Chem. Soc.*, **106**, 2717 (1984).
132. S. Marriott and R. D. Topsom, *J. Amer. Chem. Soc.*, **106**, 7 (1984).
133. S. Marriott and R. D. Topsom, *J. Chem. Soc., Perkin Trans. 2*, 1045 (1985).
134. W. F. Reynolds, A. Gomes, A. Maron, D. W. MacIntyre, A. Tanin, G. K. Hamer and I. R. Peat, *Can. J. Chem.*, **61**, 2376 (1983).
135. W. J. Hehre, C.-F. Pau, A. D. Headley, R. W. Taft and R. D. Topsom, *J. Amer. Chem. Soc.*, **108**, 1711 (1986).
136. D. J. Pasto and R. Kent, *J. Org. Chem.*, **30**, 2684 (1965).
137. D. J. Pasto, D. McMillan and T. Murphy, *J. Org. Chem.*, **30**, 2688 (1965).
138. H. Hogeveen, *Rec. Trav. Chim. Pays-Bas*, **83**, 813 (1964).
139. G. Thirot, *Bull. Soc. Chim. France*, 3559 (1967).
140. G. Thirot, *Bull. Soc. Chim. France*, 739 (1967).
141. C. Y. Meyers, G. Lombardini and L. Bonoli, *J. Amer. Chem. Soc.*, **84**, 4603 (1962).
142. Ch. S. Frankovskii and E. Z. Katsnel'son, *Zh. Org. Khim.*, **4**, 1631 (1968); *J. Org. Chem. USSR*, **4**, 1567 (1968).
143. E. Z. Katsnel'son and Ch. S. Frankovskii, *Zh. Org. Khim.*, **6**, 1696 (1970); *J. Org. Chem. USSR*, **6**, 1701 (1970).
144. J. B. Hyne and J. W. Greidanus, *Can. J. Chem.*, **47**, 803 (1969).
145. E. V. Konovalov, R. G. Dubenko, T. Ya. Lavrenyuk, V. M. Neplyuev and P. S. Pel'kis, *Zh. Org. Khim.*, **10**, 427 (1974); *J. Org. Chem. USSR*, **10**, 431 (1974).
146. P. G. De Benedetti, U. Folli, D. Iarossi and C. Frassineti, *J. Chem. Soc., Perkin Trans. 2*, 1527 (1985).
147. V. F. Andrianov, A. Ya. Kaminsky, A. V. Ivanov and A. V. Golikova, *Org. React. (Tartu)*, **21**, 180 (1984).
148. F. A. Davis, J. M. Kaminski, E. W. Kluger and H. S. Freilich, *J. Amer. Chem. Soc.*, **97**, 7085 (1975).
149. H. B. Watson, *Modern Theories of Organic Chemistry*, 2nd ed., Clarendon Press, Oxford, 1941, p. 241.
150. Ref. 73, p. 103.
151. P. Segura, *Chem. Rev.*, in preparation.
152. M. T. Tribble and J. G. Traynham, *J. Amer. Chem. Soc.*, **91**, 379 (1969).
153. Personal communication to J. Shorter.
154. U. Folli, D. Iarossi and F. Taddei, *J. Chem. Soc., Perkin Trans. 2*, 848 (1973).
155. M. Hojo, M. Utaka and Z. Yoshida, *Tetrahedron*, **27**, 2713 (1971).
156. M. Hojo, M. Utaka and Z. Yoshida, *Tetrahedron*, **27**, 4031 (1971).
157. M. Hojo, M. Utaka and Z. Yoshida, *Tetrahedron*, **27**, 5433 (1971).

158. Ref. 48, p. 112.
159. M. Charton, *Prog. Phys. Org. Chem.*, **8**, 235 (1971).
160. M. H. Aslam, A. G. Burden, N. B. Chapman, J. Shorter and M. Charton, *J. Chem. Soc., Perkin Trans. 2*, 500 (1981).
161. M. Charton and B. I. Charton, *J. Org. Chem.*, **43**, 1161 (1978), and earlier papers referred to therein.
162. M. Charton, in *Topics in Current Chemistry 114: Steric Effects in Drug Design* (Eds. M. Charton and I. Motoc), Springer-Verlag, Berlin, 1983, pp. 57–91.
163. M. H. Aslam, N. B. Chapman, J. Shorter and M. Charton, *J. Chem. Soc., Perkin Trans 2*, 720 (1981).
164. C. Srinivasan, A. Shunmugasundaram, M. Roja and N. Arumugam, *Ind. J. Chem.*, **23B**, 555 (1984).
165. C. Srinivasan, A. Shunmugasundaram and N. Arumugam, *J. Chem. Soc., Perkin Trans. 2*, 213 (1984).
166. H. D. Crockford and T. B. Douglas, *J. Amer. Chem. Soc.*, **56**, 1472 (1934).
167. A. Mellander, *Ark. Kemi, Mineral., Geol.*, **12A**, 16 (1937); *Chem. Abstr.*, **31**, 5763 (1937).
168. A. Chambers and C. J. M. Stirling, *J. Chem. Soc.*, 4558 (1965).
169. M. Charton, *J. Org. Chem.*, **29**, 1222 (1964).
170. M. Charton, *Prog. Phys. Org. Chem.*, **13**, 119 (1981).
171. C. A. Grob and M. G. Schlageter, *Helv. Chim. Acta*, **59**, 264 (1976).
172. H. Hogeveen and F. Montanari, *J. Chem. Soc.*, 4864 (1963).
173. V. V. Orda, L. M. Yagupol'skii, V. F. Bystrov and A. V. Stepanyants, *Zh. Obschei Khim.*, **35**, 1628 (1965); *J. Gen. Chem. USSR*, **35**, 1631 (1965).
174. G. Boche, M. Marsch, K. Harms and G. M. Sheldrick, *Angew. Chem., Int. Ed. Engl.*, **24**, 573 (1985).
175. B. M. Trost and N. R. Schmuff, *J. Amer. Chem. Soc.*, **107**, 396 (1985).
176. G. Schwarzenbach and E. Felder, *Helv. Chim. Acta*, **27**, 1701 (1944).
177. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).
178. F. G. Bordwell, R. H. Imes and E. C. Steiner, *J. Amer. Chem. Soc.*, **89**, 3905 (1967).
179. W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum and N. R. Vanier, *J. Amer. Chem. Soc.*, **97**, 7006 (1975).
180. F. G. Bordwell, N. R. Vanier, W. S. Matthews, J. B. Hendrickson and P. L. Skipper, *J. Amer. Chem. Soc.*, **97**, 7160 (1975).
181. F. G. Bordwell, J. C. Branca, C. R. Johnson and N. R. Vanier, *J. Org. Chem.*, **45**, 3884 (1980).
182. R. T. Amel and P. J. Marek, *J. Org. Chem.*, **38**, 3513 (1973).
183. T. W. S. Lee and K.-P. Ang, *Can. J. Chem.*, **57**, 853 (1977).
184. F. G. Bordwell, D. Algrim and N. R. Vanier, *J. Org. Chem.*, **42**, 1817 (1977).
185. K.-P. Ang and T. W. S. Lee, *Austr. J. Chem.*, **30**, 521 (1977).
186. N. Kunieda, Y. Fujiwara, J. Nokami and M. Kinoshita, *Bull. Chem. Soc. Japan*, **49**, 575 (1976).
187. F. G. Bordwell, R. J. McCallum and W. N. Olmstead, *J. Org. Chem.*, **49**, 1424 (1984).
188. A. Streitwieser, E. R. Vorpagel and C.-C. Chen, *J. Amer. Chem. Soc.*, **107**, 6970 (1985).
189. J. B. Cumming and P. Kebarle, *J. Amer. Chem. Soc.*, **100**, 1835 (1978).
190. N. H. Werstiuk and S. Banerjee, *Can. J. Chem.*, **63**, 2100 (1985), contains an extensive bibliography.
191. H. Hogeveen, G. Maccagnani, F. Montanari and F. Taddei, *J. Chem. Soc.*, 4101 (1964).
192. F. Hibbert, *J. Chem. Soc., Perkin Trans. 2*, 1289 (1973).
193. V. Sváta, M. Procházka and V. Bakos, *Collect. Czech. Chem. Commun.*, **43**, 2619 (1978).
194. S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 348 (1967).
195. S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 351 (1967).
196. I. R. C. McDonald, R. M. Milburn and P. W. Robertson, *J. Chem. Soc.*, 2836 (1950).
197. V. Baliah and Sp. Shanmuganathan, *J. Phys. Chem.*, **63**, 2016 (1959).
198. Sp. Shanmuganathan and V. Subramanian, *Trans. Faraday Soc.*, **63**, 911 (1967).
199. R. P. Bell and B. G. Cox, *J. Chem. Soc. (B)*, 652 (1971).
200. Y. Yano and S. Oae, *Tetrahedron*, **26**, 27 (1970).
201. H. L. Goering, D. I. Relyea and K. L. Howe, *J. Amer. Chem. Soc.*, **79**, 2502 (1957).
202. R. Bird and C. J. M. Stirling, *J. Chem. Soc. (B)*, 111 (1968).
203. C. J. M. Stirling, *Pure Appl. Chem.*, **56**, 1781 (1984).

204. G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 705 (1930) and earlier papers referred to therein.
205. B. B. Jarvis and B. A. Marien, *J. Org. Chem.*, **42**, 2676 (1977) (is Part 9 of the series).
206. B. B. Jarvis and J. C. Saukaitis, *J. Amer. Chem. Soc.*, **95**, 7708 (1973).
207. B. B. Jarvis, R. L. Harper and W. P. Tong, *J. Org. Chem.*, **40**, 3778 (1975).
208. B. B. Jarvis and B. A. Marien, *J. Org. Chem.*, **41**, 2182 (1976).
209. B. B. Jarvis and W. P. Tong, *J. Org. Chem.*, **41**, 1557 (1976).
210. B. B. Jarvis and P. E. Nicholas, *J. Org. Chem.*, **45**, 2265 (1980).
211. F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **73**, 5185 (1951).
212. C. Y. Meyers, *Tetrahedron Letters*, 1125 (1962).
213. F. G. Bordwell and W. T. Brannen, Jr., *J. Amer. Chem. Soc.*, **86**, 4645 (1964).
214. F. G. Bordwell and B. B. Jarvis, *J. Org. Chem.*, **33**, 1182 (1968).
215. M. Cinquini, D. Landini and A. Maia, *J. Chem. Soc., Chem. Commun.* 734 (1972).
216. M. Cinquini, S. Colonna, D. Landini and A. M. Maia, *J. Chem. Soc., Perkin Trans. 2*, 996 (1976).
217. J. Hayami, T. Koyanagi and A. Kaji, *Bull. Chem. Soc. Japan*, **52**, 1441 (1979).
218. J. C. Martin and J. J. Uebel, *J. Amer. Chem. Soc.*, **86**, 2936 (1964).
219. M. Cinquini, S. Colonna and F. Montanari, *Tetrahedron Letters*, 3181 (1966).
220. G. Barbieri, M. Cinquini and S. Colonna, *Boll. Sci. Fac. Chim. Ind. Bologna*, **26**, 309 (1968); *Chem. Abstr.*, **70**, 105593 (1969).
221. F. Montanari, *Int. J. Sulfur Chem. C*, **6**, 137 (1971).
222. D. Landini, G. Modena, G. Scorrano and F. Taddei, *J. Amer. Chem. Soc.*, **91**, 6703 (1969).
223. S. K. Hall and E. A. Robinson, *Can. J. Chem.*, **42**, 1113 (1964).
224. R. G. Laughlin, *J. Org. Chem.*, **25**, 864 (1960).
225. S. Oae, in *The Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, 1976, p. 427.
226. J. Miller, *Austr. J. Chem.*, **9**, 61 (1956).
227. S. Oae and Y. H. Khim, *Bull. Chem. Soc. Japan*, **40**, 1716 (1967).
228. S. Oae and Y. H. Khim, *Bull. Chem. Soc. Japan*, **42**, 1622 (1969).
229. R. N. Johnson and A. G. Farnham, *J. Pol. Sci., A-1*, **5**, 2415 (1967).
230. S. M. Shein, V. A. Ignatov, L. A. Kozorez and L. F. Chervatyuk, *Zh. Obschei Khim.*, **37**, 114 (1967); *J. Gen. Chem. USSR.*, **37**, 101 (1967).
231. A. Chisari, E. Maccarone, G. Parisi and G. Perrini, *J. Chem. Soc., Perkin Trans. 2*, 957 (1982).
232. J. F. Bunnett, E. W. Garbisch, Jr. and K. M. Pruitt, *J. Amer. Chem. Soc.*, **79**, 385 (1957).
233. G. B. Barlin and W. V. Brown, *J. Chem. Soc. (B)*, 1435 (1968), and earlier papers referred to therein.
234. O. Manoušek, O. Exner and P. Zuman, *Collect. Czech. Chem. Commun.*, **33**, 3988 (1968).
235. J. Shorter, *Nat. Product Rep.*, **4**, 61 (1987), Robinson Centenary Issue.
236. E. L. Holmes, C. K. Ingold and E. H. Ingold, *J. Chem. Soc.*, 1684 (1926).
237. A. Pollard and R. Robinson, *J. Chem. Soc.*, 3090 (1926).
238. C. K. Ingold and E. H. Ingold, *J. Chem. Soc.*, 3093 (1926).
239. C. K. Ingold, E. H. Ingold and F. R. Shaw, *J. Chem. Soc.*, 813 (1927).
240. B. Chatterjee and R. Robinson, *J. Chem. Soc.*, 2780 (1927).
241. W. A. Baldwin and R. Robinson, *J. Chem. Soc.*, 1445 (1932).
242. G. Leandri and M. Pallotti, *Bol. Sci. Fac. Chim. Ind. Bologna*, **13**, 48 (1955).
243. C. Carpanelli, G. Gaiani and G. Leandri, *Gazz. Chim. Ital.*, **100**, 618 (1970).
244. N. C. Marziano, E. Maccarone and R. C. Passerini, *J. Chem. Soc. (B)*, 745 (1971).
245. N. C. Marziano, E. Maccarone, G. M. Cimino and R. C. Passerini, *J. Org. Chem.*, **39**, 1098 (1974).
246. A. C. Boicelli, R. Danieli, A. Mangini, A. Ricci and G. Pirazzini, *J. Chem. Soc., Perkin Trans. 2*, 1343 (1974).
247. Ref. 13, Chap. 5.
248. E. T. Strom and J. R. Norton, *J. Amer. Chem. Soc.*, **92**, 2327 (1970).
249. D. D. M. Wayner and D. R. Arnold, *Can. J. Chem.*, **62**, 1164 (1984).
250. F. G. Bordwell and M. J. Bausch, *J. Amer. Chem. Soc.*, **108**, 1979 (1986).
251. F. G. Bordwell and M. J. Bausch, *J. Amer. Chem. Soc.*, **108**, 1985 (1986).
252. X. Creary and M. E. Mehrsheikh-Mohammadi, *J. Org. Chem.*, **51**, 1110 (1986).
253. R. J. Boyd, A. Gupta, R. F. Langler, S. P. Lownie and J. A. Pincock, *Can. J. Chem.*, **58**, 331 (1980).
254. E. L. Wehry, *J. Amer. Chem. Soc.*, **89**, 41 (1967).

CHAPTER **11**

Hydrogen bonding and complexing properties of R_2SO_2 and R_2SO

NAOMICHI FURUKAWA and HISASHI FUJIHARA

Department of Chemistry, The University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan

I. INTRODUCTION

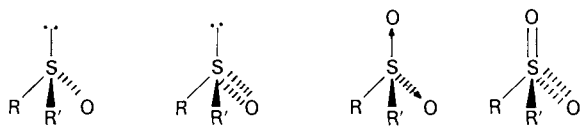
Sulphoxides and sulphones form hydrogen bonds with proton donors and association complexes with metallic salts by using either the oxygen atom or the sulphur atom in their S—O linkages. The capability for the formation of hydrogen bonds or complexes depends

TABLE 1. Bond lengths and bond angles of sulphoxides and sulphones

Compound	Bond distance (Å) S—C	S—O	Bond angle (deg)[a] C—S—C	C—S—O	Reference
$(CH_3)_2SO$	1.80	1.471	97.9	107.2 (X)	3
$(CH_3)_2SO$	1.799	1.485	96.6	106.7 (M)	4
$CH_3S(O)Ph$[b]	1.796	1.493	97.6	106.0 (X)	5
Ph_2SO	1.76	1.47	97.3	106.2 (X)	6
$(CH_3)_2SO_2$	1.781	1.473	104.8	108.5 (X)	7
$PhSO_2CH_3$	1.82	1.45	112	103, 108 (M)	8
$(p\text{-}ClC_6H_4)_2SO_2$	1.765	1.432	104.8	107.6 (X)	9

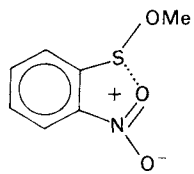
[a] X denotes X-ray crystallography and M microwave.
[b] Optically active compound.

remarkably on the nature of the S—O linkages in these compounds. The characters of the linkages in sulphoxides and sulphones have been argued for several decades, namely, whether the S—O bonds are semipolar single bonds (**A**) or double bonds (**B**) as shown below. The structures of several sulphoxides and sulphones have been determined by X-ray crystallographic analysis, electron or neutron diffraction methods and shown to have nearly tetrahedral configurations around the central sulphur atom.



Earlier, the detailed descriptions of the S—O bonds in sulphoxides and sulphones were summarized by Price and Oae[1] and also by Laur[2], and in the references cited in their work. Representative data on the X-ray structural analysis of sulphoxides and sulphones are given in Table 1.

These results demonstrate that the bond distances of the sulphur–oxygen bonds in sulphoxides and sulphones are between 1.43 and 1.49 Å. In general, the bond length of sulphoxides is slightly more than that of sulphones, and both are less than the sum of the single-bonded covalent radii of the sulphur and oxygen atoms (1.70 Å) but approximately equal the sum of the double-bonded covalent radii (1.49 Å). Pauling[10a] suggested that the contribution of covalent double-bond structures is important and significant in the sulphur–oxygen bonds in the sulphate ion. Furthermore, the observed values of 1.43–1.49 Å for the S—O bonds are much shorter than that of a single bond calculated by Schomaker and Stevenson (1.69 Å)[11] and are very close to the calculated double-bond length of 1.49 Å[12]. The sulphur–oxygen single-bond distance determined by X-ray crystallographic analysis of the sulphenate **1** was found to be 1.648 + 0.012 Å[13].



(**1**)

Although the S—O bond lengths in sulphoxides and sulphones seem to indicate that these are covalent double bonds, the dipole moments of these compounds obtained by calculation or by experimental measurements support the semipolar single-bond character in these compounds, and they should be represented as S→O, with about 66% ionic character[14,15].

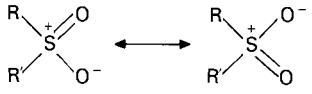
Infrared spectra provide further information as to the nature of the S—O bonds. Sulphoxides have an S—O stretching frequency band in the region of 1035–1070 cm^{-1} [16] while sulphones have two characteristic stretching frequency bands at 1100–1200 cm^{-1} and at 1300–1400 cm^{-1} due to symmetric (ν_{sym}) and asymmetric (ν_{asym}) frequencies, respectively[17].

Using these IR absorption frequency bands one can calculate the force constants (k) of the S—O bonds using equation 1[18].

$$k = 1.86 \times 10^5/(r - 0.88)^3, \quad \text{where } r \text{ is the bond length} \tag{1}$$

The force constants obtained for sulphoxides and sulphones are about 7×10^{-5} and 10×10^{-10} dyne cm^{-1}, respectively[17d]. The values of the force constants for sulphoxides are very similar to those of the N—O bond in pyridine N-oxides in which the k values are approximately $6–7 \times 10^5$ dyne cm^{-1} [19].

On the basis of these values one can conclude that, with increasing bond orders, the force constants rise, suggesting that the S—O bond of sulphoxides should have more semipolar character than that of sulphones. Furthermore, molecular diffraction measurements[20] and Parachors[21] for sulphoxides also suggest that the S—O bond in sulphoxides should have a semipolar single-bond representation while the S—O bond in sulphones is described by double bonds or better as the resonance hybride shown in Scheme 1.



SCHEME 1

The S—O bond in sulphoxides is well known to undergo facile reduction upon treatment with various mild reducing agents to give the corresponding sulphides[22], while the reduction of sulphones requires stronger reducing agents, such as $LiAlH_4$[23]. Furthermore, in the reduction of diphenyl sulphone initial treatment with phenyldiazonium salt converts the sulphone to the oxysulphonium salt, which then, by treatment with reducing agents, gives diphenyl sulphide[24]. Thus, these distinctions between the two types of sulphur–oxygen bonds in sulphoxides and sulphones are reflected not only in the chemical reactivity but also in the basicity and capability for hydrogen-bond formation of these compounds.

In this chapter we discuss three items associated strongly with the nature of the sulphur–oxygen bond in sulphoxides and sulphones. These are: (1) the nature and detection of hydrogen-bond formation of sulphoxides and sulphones with Lewis acids, and the relation between the strength of the hydrogen bond formed and the structure of these compounds, (2) protonation and measurements of the pK_a values of sulphoxides and sulphones in strong acidic media, (3) coordination and complex formation involving S—O bonds of sulphoxides and sulphones with metallic salts, including their use as NMR shift reagents and phase-transfer catalysts.

II. THE HYDROGEN BONDS OF SULPHOXIDES AND SULPHONES

A. Association of Dimethyl Sulphoxide

The hydrogen bond is a weak attractive force which operates between a proton and two electronegative atoms, such as

$$XH + Y \longrightarrow X \cdots H \cdots Y$$

The energy of the hydrogen bond ranges between 2 and 10 kcal mol^{-1}, but it is one of the most significant and fundamental chemical bonds observed in many molecules. Among various hydrogen bonds a weaker one is an intermolecular association which is recognized in pure liquids such as water, ammonia, alcohols and phenols. A stronger one is an intramolecular hydrogen bond occurring between two suitably located functional groups, such as in salicyl alcohol[10b]. The semipolar sulphur–oxygen linkages in sulphoxides and sulphones have a full or partial positive charge on the sulphur atom and a negative charge on the oxygen atom. Therefore, S—O bonds can interact or associate with various cationic and anionic reagents both through the sulphur and the oxygen atoms in these molecules. Evidence for intra- or inter-molecular association is found in the boiling points or melting points of sulphoxides (or sulphones) which are much higher than the corresponding sulphides. Some representative examples of the boiling points and densities of sulphides, sulphoxides and sulphones are shown in Table 2[25].

Another marked physical difference between sulphides and sulphoxides (or sulphones) is that sulphoxides (and lower alkyl sulphones) are hygroscopic and dissolve quite readily in water or protic solvents such as alcohols, and even more so lower alkyl or alkyl aryl sulphoxides are almost freely miscible with water. This can be accounted for by the formation of the strong hydrogen bond between the S—O bond in the sulphoxides and water molecules. Moreover, lower alkyl sulphoxides and sulphones such as dimethyl sulphoxide (DMSO) or sulpholene can dissolve a number of metallic salts, especially those of alkali and alkaline earth metals, and hence these compounds have been widely utilized as versatile and convenient solvents in modern organic chemistry[26] (Table 3).

TABLE 2. Boiling points and densities of sulphides, sulphoxides and sulphones

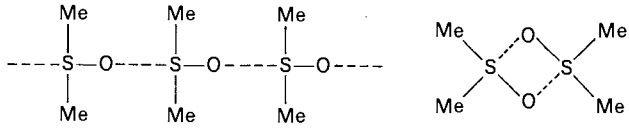
Compounds	Bp (Mp) (°C)	n_D^{20}
CH_3SCH_3	36.2 (−83)	0.846
$CH_3S(O)CH_3$	189 (18.45)	1.4787
$CH_3S(O)_2CH_3$	280–281	1.4733
$PhSCH_3$	80.0/11.5 mm Hg	1.5870
$PhS(O)CH_3$	75/0.01 mm Hg	1.5885
$PhS(O)_2CH_3$	(86.5–86.8)	
PhSPh	295–297 (−40)	1.6350
PhS(O)Ph	(70.0–70.3)	
$PhS(O)_2Ph$	378–379 (128–129)	
PhSHex-*c*	68.0–68.5/18 mm Hg	1.4945
PhS(O)Hex-*c*	88/0.05 mm Hg	1.5119
$PhS(O)_2$Hex-*c*	94.5–95/0.05 mm Hg	
$MeSCH_2CH{=}CH_2$	113.0–113.2/758	1.4712
$MeS(O)_2CH_2CH{=}CH_2$	99–99.5/13 mm Hg	1.4996
Thiane	140–142	1.5060
Thiane-1-oxide	90/1 mm Hg (60–61.5)	1.5080

TABLE 3. Solubility of salts in DMSO (g/100g DMSO) (after Reference 26)

Salt	Solubility	Salt	Solubility
$ZnNO_3H_2O$	550	$SnCl_2 \cdot 2H_2O$	40
$AgNO_3$	130	NH_4SCN	30
HgI_2	100	CdI_2	30
NH_4NO_3	80	$FeCl_3 \cdot 6H_2O$	30
$NiCl_2 \cdot 6H_2O$	60	NaI	30
NaCl	0.5	KI	16

The facile solubility of inorganic salts in DMSO is considered to be due to the strong solvation of the cations resulting in the formation of 'naked anions'.

The self-association of sulphoxides has been studied extensively in the case of DMSO. At room temperature, neat DMSO forms a chain-like polymeric intermolecular association complex with alternating sulphur and oxygen atoms, due to dipole–dipole interaction between the sulphur–oxygen bonds as shown in Scheme 2, left. However, the structure of the association complex of DMSO changes with changing temperature and dilution[27]. In general, DMSO forms a 1:1 head-to-tail complex in dilute solutions in non-polar solvents such as benzene (Scheme 2, right). The association has been proved by dipole moments, infra-red spectra, cryoscopic measurements and other data. The self-association of DMSO is thoroughly reviewed by Szmant[27a].

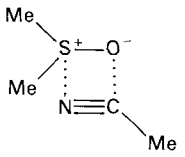


SCHEME 2. Association of DMSO.

The formation of similar complexes has been observed with other sulphoxides such as 2-thiaindane-2-oxide and butyl methyl sulphoxide, by NMR spectroscopy[28]. Furthermore, the facile oxygen transfer reaction between two different sulphoxides is postulated to proceed via formation of such 1:1 complexes between sulphoxides[29]. The structure of the complex or the aggregate or the self-association of DMSO has been judged by observing the infra-red stretching absorption band of the S—O group in various conditions. The IR stretching frequency band of the S—O group of DMSO appears at 1102–1103 cm^{-1} in the gas phase[30], and shifts to a lower wave number in dilute solutions of DMSO in non-polar solvents such as cyclohexane, carbon tetrachloride and carbon disulphide (to around 1070–1075 cm^{-1})[31].

Obviously, this shift implies the self-association of DMSO. Further frequency shifts to even lower wave numbers (1050–1000 cm^{-1}) are observed in both aprotic polar and protic solvents. In aprotic solvents such as acetonitrile and nitromethane, the association probably takes place between the S—O bond of DMSO and the —C≡N or the $—NO_2$ group in the molecules by dipole–dipole interaction as shown in Scheme 3[31,32]. Moreover, the stretching frequency for the S—O bond shifts to 1051 cm^{-1} in $CHCl_3$ and to 1010–1000 cm^{-1} in the presence of phenol in benzene or in aqueous solution[33]. These large frequency shifts are explained by the formation of hydrogen bonds between the oxygen atom in the S—O bond and the proton in the solvents. Thus, it has been

concluded that the magnitude of the frequency shifts for the S—O bond caused by the solvents changes according to the nature of the interactions operating between the S—O group and the solvents and increases from dipole induced dipole, through dipole–dipole and to hydrogen bonds.



SCHEME 3

The sites for complex formation in DMSO with inorganic salts depend remarkably on the nature of the metals involved in the salts. The alkali or alkali earth metallic salts form a complex with the oxygen atom in DMSO while Pd(II) or Pt(II) associates strongly at the sulphur atom. The IR frequency of the S—O bond of DMSO shifts to even lower wave numbers when associated with such metal cations as Li^+, Na^+ or Ca^{++}[34]. On the other hand, in the case of Pd(II) or Pt(II), the S—O frequency appears at higher wave numbers, at around 1100–1160 cm^{-1} [35]. These different shifts for the S—O frequency afford a convenient diagnosis to determine whether the cation associates with the oxygen or the sulphur atom in DMSO.

B. Hydrogen Bonds of Sulphoxides and Sulphones

1. The hydrogen bond of DMSO

The capability for hydrogen bonding of sulphoxides and sulphones with various alcohols and phenols has been investigated systematically and qualitatively by many workers. Various procedures were employed for the detection of hydrogen bonds in non-polar solvents such as CCl_4 or benzene, including infrared, ^1H and ^{19}F-NMR spectroscopy or other physical methods. The hydrogen bond of sulphoxides or sulphones with proton donors bearing a hydroxyl group are illustrated schematically in Scheme 4. The electronic state of the oxygen atoms in the S—O bond and in the hydroxyl compounds could affect significantly the stretching frequency of either the H—O bond in the donors or the S—O bond in the acceptors and hence becomes a measure of the strength of the inter- or intra-molecular hydrogen bond[36]. Thus, the magnitudes of the IR shifts from a standard compound in a series of related derivatives give a qualitative measure of the strengths of the hydrogen bond[37,38].

$$R_2S\rightarrow O + (H—O—R)_n \longrightarrow R_2S—O\cdots\cdots(H—O—R)_n$$

SCHEME 4. Hydrogen bond.

In order to test the relationship between the strength of the hydrogen bond and the OH frequency shift, Drago and his coworkers[39] have selected phenol as a standard compound in CCl_4 and reported the differences in the stretching frequency of the OH band (e.g., $\Delta\nu_{OH}$ values) of phenol by measuring the IR of phenol in the presence of a number of oxygen bases in CCl_4. They have proposed a linear relationship between $\Delta\nu_{OH}$ and the capability for the hydrogen bond of the H-bond acceptor and then calculated the equilibrium constants (K) and thermodynamic parameters for the hydrogen bond or the complex

TABLE 4. Thermodynamic data for formation of phenol adducts

	$\Delta\nu_{OH}$[a] (cm^{-1})	K(25 °C) ($1\,mol^{-1}$)	$-\Delta H^0$ ($kcal\,mol^{-1}$)
$(CH_3)_2SO$	340	182 ± 1	$6.5 \pm 0.2^{4.1}_{4.2}$
$(CH_3)_2SO$	350		
$(CH_2)_4SO$			7.0
$(CH_2)_4SO_2$		17.1 ± 0.7	4.9 ± 0.3
$(C_2H_5)_2S$			4.6
$(CH_3)_2CO$	193	13.5 ± 1.0	3.3 ± 0.5
CH_3CN	178	5.0 ± 0.2	3.2 ± 0.5
$CH_3CON(CH_3)_2$	342	134 ± 3	6.4 ± 0.2
$(CH_3)_3PO$	464	1480 ± 20	7.4 ± 0.5
$(C_2H_5)_3N$	553	89 ± 4	9.2 ± 0.1

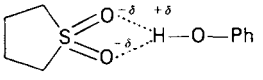
[a] Phenol $\Delta\nu_{OH} = 3609\,cm^{-1}$.

formation in the system[39]. Representative values for $\Delta\nu_{OH}$, equilibrium constants and enthalpy values are shown in Table 4. Based on the analysis of these values, they found a linear relationship between the enthalpy and the frequency shift for phenol-base adducts, and obtained the following empirical equation 2.

$$-\Delta H(kcal\,mol^{-1}) = 0.016\,\Delta\nu_{OH} + 0.63 \quad (2)$$

They also calculated ΔH values within $\pm 0.5\,kcal\,mol^{-1}$ by using the observed frequency shifts $\Delta\nu_{OH}$ and equation 1[40]. The thermodynamic data and $\Delta\nu_{OH}$ values shown in Table 4 provide information on the hydrogen bonding ability of several dipolar aprotic solvents including sulphoxides and sulphones with phenol. These results indicate that the capability for hydrogen bond formation of DMSO is of a magnitude similar to that of *N*,*N*-dimethylacetamide. Also, comparing the ΔH values for DMSO and tetramethylene sulphoxide, these two sulphoxides should be similar as acceptors. The parameters shown in Table 4 suggest that sulphones have lower capability for hydrogen bonding than the corresponding sulphoxides.

Drago and coworkers have stated that tetramethylene sulphone does not obey their proposed semi-empirical linear relationship, since this sulphone may form a hydrogen bond with phenol as shown in Scheme 5, involving both oxygen atoms of the sulphone[39b]. The donor abilities of other hydroxylic compounds have been studied by using DMSO as an acceptor and measuring the IR frequency shift of the O—H stretching band (ν_{OH}) in a non-polar solvent such as CCl_4, benzene or toluene. Representative results for the ΔH, $\Delta\nu_{OH}$ and association constants (K_{ass}) are summarized in Table 5,[51] which clearly demonstrates that the several C_A, E_A, C_B and E_B values are listed in Table 6.



SCHEME 5

Earlier, Ahland and coworkers[56] noticed that metal and metallic salts which form complexes with Lewis bases can be divided into two classes, namely one which interacts mostly with the donors bearing a first row element as a center and a second which coordinates preferentially with those of second and third row elements.

Pearson extended these concepts to a wide range of acids and bases and proposed the

TABLE 5. Hydrogen bond donor ability ($\Delta\nu_{OH}$) of hydroxylic compounds with DMSO in CCl_4

Compound	$\Delta\nu_{OH}(cm^{-1})$	K_{ass}	ΔH(kcal mol^{-1}) (calcd)	Reference
PhOH	350	250.2		53
	366	216	7.1(6.9)	43
	385			
	340	182 ± 1	6.5 ± 0.2	48
	359	229		
p-FC_6H_4OH	367		6.6(6.9)	43
	(356.6)			45
m-FC_6H_4OH	402		7.3(7.4)	43,46
p-ClC_6H_4OH	400		7.2(7.2)	43
m-$CF_3C_6H_4OH$	416		7.4(7.5)	43
t-BuOH	183		3.6(3.6)	44
CF_3CH_2OH	3.6	161.8	6.6(6.6)	43,47
$(CF_3)_2CHOH$	449		8.7(8.9)	43
	437			46,49
n-BuOH		15		48
n-$C_6H_{13}OH$	206		6.4	50
α-NaphOH	288			52
p-$NO_2C_6H_4OH$	439.4			53
3,5-$(CH_3)_2C_6H_3OH$	327.3			53
2,6-$(CH_3)_2C_6H_3OH$	274.6			53
H_2O	334			54

Calcd. values taken from Reference 43, based on the equation $-\Delta H = 0.0103\Delta\nu_{OH}(cm^{-1}) + 3.08(3)$.

TABLE 6. Acid and base parameters (E_A, C_A, E_B, C_B)[a]

Acid	C_A	E_A
I_2	1.00	1.00
C_6H_5OH	0.574(0.442)	4.70(4.33)
CH_3OH	0.14	3.41
C_2H_5OH	0.032	3.91
t-BuOH	0.095(0.300)	3.77(2.04)
$HCCl_3$	0.10(0.15)	5.11(3.31)
p-FC_6H_4OH	(0.446)	(4.17)
m-FC_6H_4OH	(0.506)	(4.42)
p-ClC_6H_4OH	(0.478)	(4.34)
m-CF_3	(0.530)	(4.48)
CF_3CH_2OH	(0.434)	(4.00)
$(CF_3)_2CHOH$	(0.509)	(5.56)
Base	C_B	E_B
Pyridine	6.92(6.40)	0.88(1.7)
$HCON(CH_3)_2$	2.73(2.48)	0.97(1.23)
CH_3COCH_3	0.66(2.33)	0.706(0.987)
CH_3SOCH_3	3.42(2.85)	0.969(1.34)
$(CH_2)_4SO$	3.30(3.16)	1.09(1.38)
$(C_2H_5)_2S$	7.78(7.40)	0.041(0.339)

[a] Parameters are taken from Reference 55. The values in parentheses are modified data taken from Reference 43.

TABLE 7. Enthalpies and $\Delta\nu_{OH}$ of bases and *t*-BuOH (measured in $C_2H_2Cl_4$) (after Reference 64)

Base	$-\Delta H^0$(kcal mol^{-1})	$\Delta\nu_{OH}$(cm^{-1})
Pyridine	4.3	247
Et_3N	5.2	344
CH_3CN	2.3	77
DMF	3.2	147
CH_3CO_2Et	2.4	73
CH_3COCH_3	2.7	98
DMSO	3.6	183
$C_2H_5OC_2H_5$	3.0	126

TABLE 8. $\Delta\nu_{OH}$ values for PhOH–base adducts

Acid	Base	$\Delta\nu_{OH}$(cm^{-1})[a]	$-\Delta H$ (Calcd)[b]
PhOH	CH_3CN	150	4.6(4.4)
	$(CH_3)_2CO$	193	5.1(5.3)
	DMF	345	6.1(6.4)
	Pyridine	465 ± 10	8.0(7.9)
	Et_3N	556 ± 20	9.1(9.2)
	DMSO	366	6.9(7.1)
p-ClC_6H_4OH	$MeCONMe_2$	376 ± 8	7.0(7.1)
	Pyridine	491 ± 8	8.1(8.1)
	DMSO	400	7.2(7.2)
m-$CF_3C_6H_4OH$	$MeCONMe_2$	391 ± 8	7.3(7.3)
	Pyridine	544	8.5(8.6)
	DMSO	416	7.4(7.5)

[a] Values calculated by equation 6.
[b] Values taken from Reference 43.

hard–soft acids–base concept (HSAB theory[57,58]). Klopman[59] has given a theoretical treatment of this concept based on molecular orbital calculations. The relation between hydrogen-bond donors and acceptors is based on a similar concept of these ideas and also on the Hammett relation[60] or the Edwards two-parameter equation[61].

Drago and coworkers have also calculated the enthalpy values for the formation of many complexes or hydrogen bonds by NMR[62] and calorimetric[63] techniques. For example, in a series of phenols or *t*-BuOH, they observed the IR frequency shifts ($\Delta\nu_{OH}$) of the hydroxyl compounds and found that a linear relationship exists between bases and individual acids. In Table 7 shows some ΔH values calculated by equation 2, and $\Delta\nu_{OH}$ values of *t*-BuOH[44] while in Table 8 frequency data $\Delta\nu_{OH}$ of various substituted phenols and the ΔH values are given.

Figures 1 and 2 present the linear relationships between these sets of bases and acids. The Hammett relationship is shown in Figure 3, based on the data in Table 8. The enthalpy values for the hydrogen bond give a straight line upon plotting against the Hammett substituent values of *p*-substituted phenols and the slopes become more steep with increasing capability for hydrogen bonding in the acceptor. DMSO and *N*,*N*-dimethylacetamide are shown to have similar capabilities for hydrogen bonding.

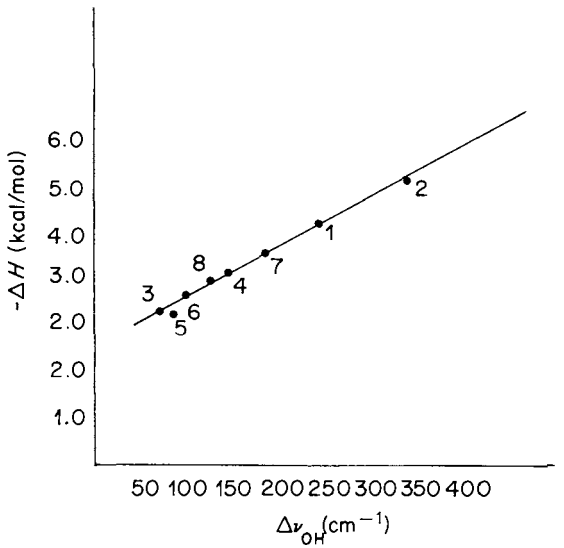


FIGURE 1. Linear enthalpy–frequency shift plot for *t*-BuOH adducts (from Table 7). 1:Pyridine, 2:Et_3N, 3:CH_3CO_2Et, 4:DMF, 5:CH_3CN, 6:$(CH_3)_2CO$, 7:DMSO, 8:Et_2O.

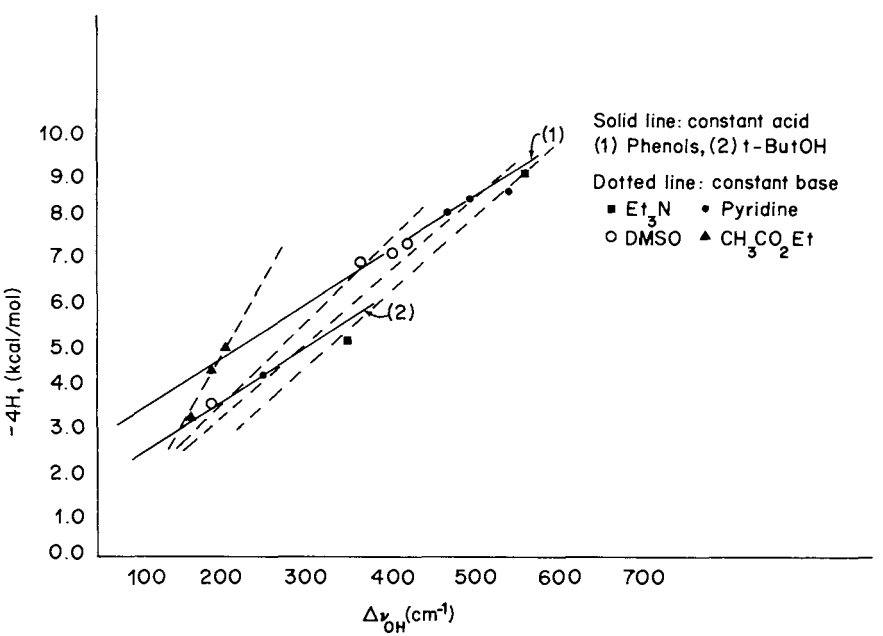


FIGURE 2. Constant-acid–constant-base frequency shift–enthalpy relationship.

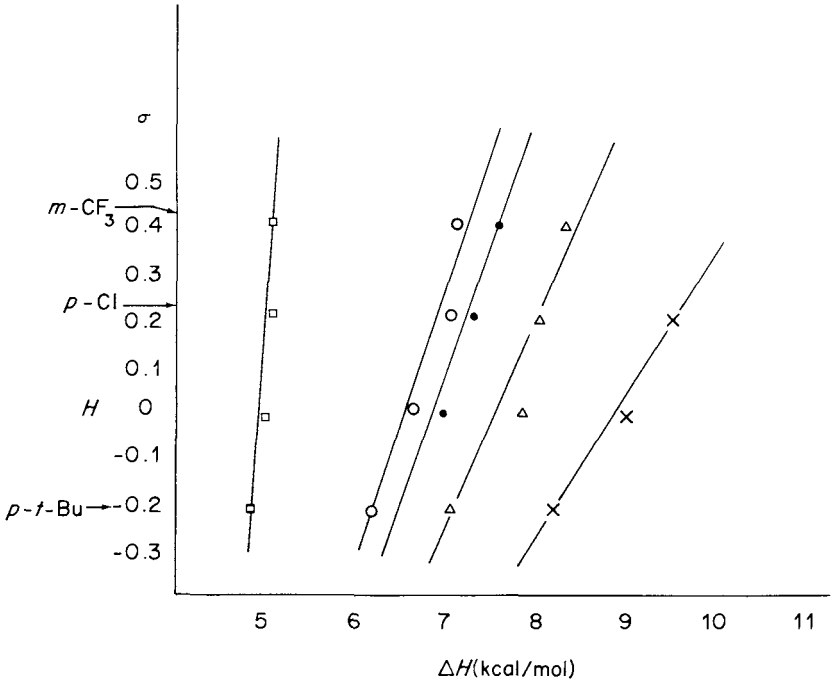


FIGURE 3. Hammett plots for bases and substituted phenols: □ refers to ethyl acetate, ○ *N,N*-dimethylacetamide, ● DMSO, Δ pyridine and × triethylamine.

The following empirical equations have been reported for series of bases with *t*-BuOH[64] or with *p*-substituted phenols[65a].

$$-\Delta H = 0.0106\, \nu_{OH} \pm 1.65 \qquad (t\text{-BuOH}) \tag{4}$$

$$-\Delta H = 0.0105\, \nu_{OH} \pm 2.99 \qquad (t\text{-PhOH}) \tag{5}$$

(error in ΔH, ± 0.22 kcal mol^{-1})

$$-\Delta H = 0.0103\, \nu_{OH} \pm 3.08 \qquad (16 \text{ bases}) \tag{6}$$

(In equations 5 and 6, ΔH values were obtained by a calorimetric method.)

These results clearly demonstrate that linear energy relationships can be established for the formation of hydrogen bonds between numerous Lewis bases (including sulphoxides) with Lewis acids.

In subsequent reports, Drago and coworkers studied hydrogen bonds while eliminating solvation effects by carrying out the experiments in poorly solvating media, such as CCl_4 or cyclohexane, for which dielectric constants are less than 2.3. In these solvents the conditions are similar to those in the gas phase. In order to test the validity of this assumption, the ΔH value of the interaction between *m*-fluorophenol and DMSO or EtOAc was treated in several non-polar solvents like CCl_4, *o*-$Cl_2C_6H_4$, and benzene with DMSO as a Lewis base (equation 7).

$$m\text{-}FC_6H_4OH\cdot EtOAc + DMSO \longrightarrow m\text{-}FC_6H_4OH\cdot DMSO + ETOAc \tag{7}$$

The enthalpy values of the displacement in the above solvents were calculated to be -2.0, -2.0 and -2.1 kcal mol^{-1}, i.e., practically identical within the experimental error. These observations verify the validity of the assumption for the cancellation of solvation effects in hydrogen bonds in non-polar solvents[65b,c]. Solvent effects on the hydrogen bond have been discussed by others[66a-c,80,82].

The ^{1}H NMR shifts of the OH proton in several hydroxyl compounds such as PhOH and fluoroalcohols[46,63] were measured in CCl_4 or CH_2Cl_2 in the presence of DMSO and other bases and compared to values obtained without bases. The ^{1}H NMR chemical shifts (δ values) give a good linear relationship against the enthalpy values obtained by equation 2 or by calorimetry[46]. In the case of PhOH as the donor, equation 8 is obtained.

$$\delta_{obs} = 0.748\,(\Delta H) - 4.68\,(\text{kcal mol}^{-1}) \tag{8}$$

Purcell and coworkers[46] obtained good correlations between the IR and ^{1}H NMR methods by the use of 1, 1, 1, 3, 3, 3-hexafluoropropanol and phenol as acids[46]. Taddei and colleagues[67] have reported that with $CHCl_3$ as the donor, a free energy relationship is established between the association constants and the ^{1}H NMR chemical shift values of $CHCl_3$ in the presence of Lewis bases. However, a non-linear relationship has been observed for several other Lewis bases and $CHCl_3$ by other authors[68].

Water was also investigated as a proton donor for the hydrogen bond with DMSO and other Lewis bases at infinite dilution detected by means of ^{1}H NMR[54,69]. A comparison of the hydrogen bonding ability of DMSO in various other aprotic solvents was presented by Delpuech[70] who measured the ^{1}H-NMR chemical shift of $CHCl_3$.

DMSO forms several association complexes with water containing different ratios of DMSO and water. Among those, the one having two molecules of H_2O and one DMSO is the most favoured. However, by increasing the concentration of DMSO, the composition of the aggregate becomes first a 1:1 complex and finally a 1:2 complex as shown in equation 9[71].

$$(H_2O)_x \cdot HOC \cdot DMSO \xrightarrow{DMSO} DMSO \cdot 2H_2O$$

$$\xrightarrow[\text{conc. } 0.3-0.5 \text{ mol/l}]{DMSO} DMSO \cdot H_2O \xrightarrow{DMSO\,0.5} DMSO \cdot H_2O \cdot DMSO \tag{9}$$

2. The hydrogen bond of sulphoxides and linear energy relationships

Recently, Kamlet and Taft introduced new elaborate parameters in order to explain the linear energy relationship for the formation of the hydrogen bond between HBA (hydrogen bond acceptor) and HBD (hydrogen bond donor). They treated several sulphoxides as HBA. The detailed presentations and actual treatments of these parameters have been described in their recent review article[72].

The evidence presented for the formation of hydrogen bonds with sulphoxides and sulphones was first reported by Barnard. Fabian and Koch, who measured the characteristic infra-red stretching frequency shifts of the S—O bond in the presence of MeOH in CCl_4[25]. Simultaneously the OH stretching band of MeOH at 3660 cm^{-1} undergoes a remarkable shift to ca. 3350 (in the presence of sulphoxides) or to 3515 cm^{-1} (in the presence of sulphones). The magnitudes of the frequency shifts for the S—O band could be correlated well with the proton affinity or the electron-donor ability of the oxygen atom in these molecules. The S—O stretching frequencies of several sulphoxides and sulphones and also percentage frequency decreases $-100\,\Delta\nu/\nu$ of each shift are shown in Table 9, from which it is seen that, in the S—O stretching shifts of the sulfoxides caused by the hydrogen bond, and there does not seem to be much difference

TABLE 9. Influence of H-bonding on IR stretching frequencies of sulphoxides and sulphones

Compound	Sulphoxide ($n = 1$)		Sulphone ($n = 2$)					
	ν CCl_4	$-100\Delta\nu/\nu$	ν_{sym} CCl_4	$-100\Delta\nu/\nu$ $CHCl_3$	$-100\Delta\nu/\nu$ CH_3OH	ν_{asym} CCl_4	$-100\Delta\nu/\nu$ $CHCl_3$	$-100\Delta\nu/\nu$ CH_3OH
cyclo-HexSO_nCH_3	1055	2	1144	0.6	0.9	1321	0.8	1.2
(cyclo-Hex)$_2SO_n$	—	—	1130	0.4	—	1312	0.8	0.8
$C_6H_5SO_nCH_3$	1055	1.9	1160	0.3	—	1334	1.2	1.6
$C_6H_5SO_nC_6H_5$	1055	1.6	1164	0.3	0.4	1336	1.3	1.6

The values $\Delta\nu/\nu$ indicate the shorter wave number shift and thus the larger the value, the stronger the H-bonding.
[a] Measured in $CHCl_3$ or in 0.2 mol MeOH solution.

between MeOH and $CHCl_3$ as solvents.

$$RR'S(O)_n + HX \longrightarrow RR'S(O)_n\text{—}HY \quad (10)$$

However, the S—O bands of sulfones in the presence of MeOH show a lower shift than in $CHCl_3$. This clearly indicates that sulphoxides form a stronger hydrogen bond with MeOH than do the corresponding sulphones. In $CHCl_3$ as a solvent, similar lower-frequency shifts of the S—O band in sulphoxides were also observed. Gramstad and his coworkers[73,74] have reported a quantitative treatment of the hydrogen bonding of sulphoxides with phenol in CCl_4 at constant concentrations of the solutes and they measured the IR frequency shift of the OH band in the phenol. The association constants for several sulphoxides with phenol (K_{ass}) at 20 °C and 50 °C were determined and the activation parameters for the association were also calculated by the standard method. The results are summarized in Table 10.

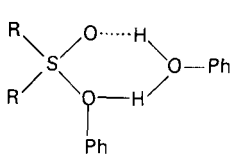
The association constants and thermodynamic parameters are correlated against $\Delta\nu_{OH}$ affording a good straight line within the experimental error. The linear relationship of ΔH vs $\Delta\nu_{OH}$ for various sulphoxides was also correlated with that obtained in the case of substituted nitrogen or organophosphorus compounds. As shown by the data in Table 10, the substituents attached on the sulphinyl sulphur atom affect very much the association constants which measure the magnitudes of the capability for the hydrogen bond. Normally, alkyl substituted sulphoxides associate more readily with a proton than those sulphoxides bearing aryl groups. This would be rationally accounted for by the higher basic character due to the inductive (+I) effect of the alkyl groups.

TABLE 10. Hydrogen bond of phenol to sulphoxides[a]

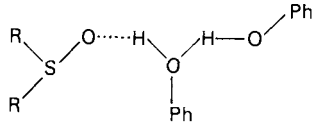
Sulphoxide	ν_{SO} (cm^{-1})	$\Delta\nu_{OH}$ (cm^{-1})	K_{ass}^{20} (l mol)	K_{ass}^{50} (l mol)	$\Delta\nu_{SO}$ (cm^{-1})
$(PrO)_2SO$	1211	154	6.9	4.0	
	1193				
$(EtO)_2SO$	1293	154	7.9	4.2	
	1192				
$(BuO)_2SO$	1210	162	8.2	5.1	
Ph_2SO	1052	294	70.4	28.1	15
	(1040)	(256)	(19)		
p-Tol_2SO	1053	320	105.1	39.4	18
	(1044)	(278)	(26)		
$(PhCH_2)_2SO$	1055	330	131.4	52.2	27
$(p$-$Ar)_2SO$	1042	299	(29)		
$(p$-$BrC_6H_4)_2SO$	1058	235	(6.5)		
$(p$-$NO_2C_6H_4)_2SO$	1060	179	(3.4)		
DMSO	1072	350	230.2	64.2	27
		(340)	(55)		
i-Pr_2SO	1058	360	209.7	83.2	13
$(CH_2)_4SO$	1034	370	233.5	77.6	19
Bu_2SO	1037	373	264.3	96.7	20
$(CH_2)_3SO$[b]	1092	128			
$(CH_2)_4SO$[b]	1035	161			
$(CH_2)_5SO$[b]	1053	155			
Et_2SO[b]	1066	167			

[a] Values in parentheses measured in toluene at 27 °C.
[b] Measured in MeOD.
All other values measured in CCl_4.

Szmant and coworkers[48] found a similar linear energy relationship between association constants of substituted diaryl sulphoxides and $\Delta\nu_{OH}$ of phenol in toluene, whereas Biscarini and coworkers[41] studied the effect of solvents on the self-association of phenol at rather high concentrations which might give rise to erroneous measurements of the IR frequency band of the OH, and which should, if possible, be avoided. Szmant[75] proposed that toluene is a better solvent than CCl_4 and cyclohexane in which self-association of phenol occurs at higher concentrations. He found that sulphoxides form two different association complexes, one composed of a 1:1 and the other of a 2:1 ratio of phenol and sulphoxide. Therefore, a correction in the derivation of the association constant should be required for the 1:1 complex between phenol and sulphoxide. The data of $\Delta\nu_{OH}$ and K_{ass}, at 27 °C in toluene, are shown in Table 10 in parentheses. The association constants of the *p*-substituted diaryl sulphoxides when plotted against Hammett σ constants (except the *p*-nitro derivative) give a good straight line with a ρ value of -0.65. The existence of a linear free energy relationship between K_{ass} and IR frequency shifts for the OH in phenol leads to the conclusion that the stronger the electron donating substituent, the stronger the hydrogen bond formed. Regarding the structure of the 2:1 complex described above, the formation of a six-membered cyclic structure (**A**) was proposed in Scheme 6 which is also presented in the case of formation of a dimer of DMSO[75,76], and which is more preferred than **B**.



(**A**)



(**B**)

SCHEME 6

A comparison of the ring size effect of the basicity of 4–6 membered cyclic sulphoxides with that of cyclic ketones was studied on the basis of the results obtained by measuring the IR frequency of the S—O bond in MeOD at 25 °C. The OD stretching shifts were correlated with the heats of mixing of the sulphoxides with MeOD which were determined independently by a calorimetric method[77]. The ring size effect thus determined is $6 > 5 > 4 >$ which is the same as in the hydrogen bonding capability of cyclic ketones, namely $7 > 6 > 5 > 4$. The hydrogen bonding ability (or basicity) of sulphoxides is suggested to be stronger than that of the corresponding carbonyl compounds.

Gramstad and coworkers[78] studied the formation of association complexes between $CHCl_3$ and *N*, *N*-disubstituted amides, four alkyl sulphoxides and diethyl sulphite in CCl_4 by following the ^1H NMR. The association constants (K_{ass}) were determined by equation 11[79],

$$\frac{C_a}{\delta_{obs}-\delta_f}=\frac{1}{\delta_x-\delta_f}(C_a+C_d-C_x)+\frac{1}{K_{ass}(\delta_x-\delta_f)} \tag{11}$$

where δ_{obs} is the chemical shift observed relative to TMS, δ_f the chemical shift of the non-bonded donor, δ_x the chemical shift of the donor proton in the complex, C_d the total concentration of proton donor, C_a the total concentration of proton acceptor, and C_x the total concentration of the donor in complexed form. Furthermore, the thermodynamic parameters ΔH and ΔS and also δ_x (the ^1H NMR chemical shift of $CHCl_3$ in a hydrogen bonded complex) were calculated. Based on these calculations, linear energy relationships

are established between δ_x and log K_{ass} or ΔH involving $CHCl_3$ with sulphoxides, amides or phosphine oxides and the following unified empirical equation is obtained:

$$-\Delta H(\pm 0.2\,\text{kcal mol}^{-1}) = 0.76\delta_x + 0.17 \tag{12}$$

Then the ΔH values of sulphoxides and amides were correlated with Taft's σ^* affording the following equation:

$$-\Delta H(\pm 0.2\,\text{kcal mol}^{-1}) = -0.34\Sigma\sigma^* + 1.7 \tag{13}$$

Phosphine oxides also fit equation 11, which indicates that their ability for hydrogen bonding with $CHCl_3$ is essentially electrostatic in nature.

Similarly, the K_{ass} determined by the ^1H NMR chemical shift of $CHCl_3$ in the presence of sulphoxides can be correlated well with the association constants obtained both on the basis of the IR stretching shift ($\Delta\nu_{OH}$) of phenol in the presence of sulphoxide and also with the ^{19}F NMR chemical shifts of *p*-fluorophenol (δ_x^F).

The following empirical equation is obtained for the hydrogen bond between $CHCl_3$ and phenol (equation 14):

$$\log K_{ass}^{50}(CHCl_3) = 0.40 \log K_{ass}^{50}(PhOH) - 0.85 \tag{14}$$

The results are in accordance with those obtained by Taft and colleagues[80,81]. These authors have measured the ^{19}F NMR chemical shifts of *p*-FC_6H_4OH in the presence of 60 bases including sulphoxides (DMSO, methyl phenyl, methyl *p*-nitrophenyl, diphenyl, tetramethylene sulphoxide) and determined the association constants K_f for the hydrogen bond shown in equation 15.

$$p\text{-}FC_6H_4OH + :B \overset{K_f}{\rightleftharpoons} p\text{-}FC_6H_4OH\cdots B \tag{15}$$

where $K_f = (\delta/\Delta)A_0\{A_0[1-(\delta/\Delta)][B_0-(\delta/\Delta)A_0]\}$, A_0 being the initial concentration of *p*-FC_6H_4OH, B_0 the initial base concentration and δ the averaged ^{19}F NMR chemical shift in ppm for the equilibrium mixture relative to that for 0.01 *M* *p*-FC_6H_4OH in CCl_4. The term δ/Δ indicates the limiting ^{19}F NMR shift (ppm) between that of the completely formed complex and the uncomplexed *p*-FC_6H_4OH. The log K_f values of various bases including sulphoxides in CCl_4 can be correlated well with the corresponding NMR δ values, suggesting that the linear energy relationship provides evidence for formation of the hydrogen bond in these systems. However, DMSO is an exception since it interacts with *p*-FC_6H_4OH by both the oxygen and fluorine atoms. The ^{19}F NMR (Δ) values are essentially independent of the temperature in CCl_4 and the intensity is not increased in polar solvents (e.g. $ClCH_2CH_2Cl$). This leads to the conclusion that only the formation of the hydrogen bonded complexes is an important process, while the contribution of ion pairs, such as $FC_6H_4O^-$—H^+B, can be excluded[80]. Taft and his coworkers[80] have introduced a new linear free-energy relationship (LFER) involving the formation constants of the hydrogen bond between various sets of bases and acids by using equation 16:

$$\log K_f = m(\log K_f)_0 + c \tag{16}$$

in which $(\log K_f)_0$ relates to the association constant of the hydrogen bond for *p*-FC_6H_4OH with bases in CCl_4 at 25 °C and log K_f relates to the corresponding constants of the reference acids. Both *m* and *c* are constants characteristic for the reference acids. The authors determined new base parameters pK_{HB}, which are a measure of the relative base strength in the hydrogen bond with alcohols and phenols, and which are defined as $pK_{HB} = \log(K_f)_0$, using the formation constants of the hydrogen bond of *p*-FC_6H_4OH and sulphoxides or other Lewis bases in CCl_4 at 25 °C. Selected values of *m* and *c* are presented in Table 11, and of pK_{HB} in Table 12.

TABLE 11. Values of m and c for acids in equation 16 (after Reference 80)

Acid	Temp. (°C)	m	c	No. of bases
2,2,2-CF_3CH_2OH	0	0.98	0.05	8 (DMSO, DPS)[a]
	25	0.92	−0.17	6 (DMSO, DPS)
	50	0.85	−0.34	8 (DMSO, DPS)
Phenol	20	0.94	−0.02	20 (DMSO, DPS)
	25	0.97	−0.13	14
	50	0.89	−0.31	20
C_6F_5OH	0	1.23	+0.63	8
	25	1.16	+0.32	6
	50	1.07	+0.08	7

[a] DPS denotes diphenyl sulphoxide.

TABLE 12. pK_{HB} values of several sulphur and phosphorus compounds at $pK_a = 0$

Base	pK_{HB}
$(EtO)_2SO$	0.98
$MeSOC_6H_4NO_2$-*p*	1.58
Ph_2SO	2.03
MeSOPh	2.15
$(PhCH_2)_2SO$	2.28
DMSO	2.53
Bu_2SO	2.60
Et_2S	0.11
n-Bu_2S	0.26
t-Bu_2S	0.21
Pyridine-*N*-oxide	2.76
$Ph_3P{-}O$	3.16

Furthermore, solvent, temperature and substituent effects on pK_{HB} are also presented and dual substituent parameters have been introduced into two carbonyl series: $(CH_3)_2NC(O)X$ ($X = CF_3, CH_2Cl, H, CH_3, NMe_2$) and $CH_3C(O)X$ ($X = CH_3CO, CF_3, H, F, CH_3, OCH_3, NMe_2$) and related to the following equation:

$$pK_{HB} = \sigma_I\rho_I + \sigma_R\rho_R \tag{17}$$

Interestingly, comparison of the values of pK_{HB} and the acidity constants pK_a in a series of the same family of compounds, such as carbonyl compounds, amines, pyridines and sulphoxides, shows that a good correlation exists between pK_{HB} and pK_a giving straight lines in each series of compounds with parallel slopes. This enables one to calculate the difference of the several pK_a values at the same pK_{HB} value, and vice versa. Thus, at $pK_a = 0$, pK_{HB} values of various functional groups were determined and are shown in Table 13.

A comparison of these pK_{HB} values at constant pK_a of the bases reveals that the most important factor which determines the correlation between the structure and the hydrogen bonding ability depends on the electronegativity of the acceptor atom in the Lewis bases employed. Thus, the strength of the basicities of the oxygen compounds described above is

TABLE 13. Comparison of pK_{HB} values of functional groups at $pK_a = 0$

Functional group	pK_{HB}
Prim. amine	−0.6
Pyridine	+0.5
Sulphide	+1.4
Ether	+1.7
Carbonyl	+2.4
Sulphoxide	+3.0
Nitrile	+3.4
Phosphine oxide	+3.9

arranged in the following decreasing order:

$$\geqslant N{\rightarrow}O > -{>}P{\rightarrow}O > > S{\rightarrow}O > C{=}O$$

By comparing pK_a and pK_{HB} values, Taft predicted the preferred sites for the hydrogen bond when two different functional groups are present and both may act as an acceptor for the hydrogen bond. Other applications of the pK_{HB} scale have also been described[81].

On the other hand, Arnett and his coworkers have reported both the enthalpies of the protonation (ΔH_i) and the hydrogen bond (ΔH_f) for acid–base reactions. They calculated H_i by measuring the association constants (K_{ass}) for the proton transfer (ionization) in a number of bases by using FSO_3H as the acid and determined ΔH_f by calorimetric measurements of the heat of dissolution of p-FC_6H_4OH in various hydrogen bond acceptors, including sulphoxides, in CCl_4[45,82]. They have also tried to correlate H_i and H_f for sulphoxides and for p-FC_6H_4OH with the pK_a values and the IR frequency shifts of p-fluorophenol in the case of hydrogen bond formation. The plots of ΔH_f vs ΔH_i and pK_a give good straight lines, indicating that a linear free energy relationship exists in these parameters. They have discussed the factors which affect the free energy relationships and the differences between the proton-transfer basicity and the hydrogen bonding ability. The results are summarized in Table 14.

Later, Taft and his coworkers examined the H-bonding donor ability of the amino protons in 4-nitroaniline and 4-nitrophenol as the hydrogen bond donors. They also tried

TABLE 14. Thermodynamic parameters of hydrogen-bonded complexes of p-FC_6H_4OH with sulphoxides and some other bases

Base	$K_f^{25°}$ ($l\,mol^{-1}$)	$\Delta\nu_f^\circ$ (cm^{-1})	$-\Delta H_f^\circ$ ($kcal\,mol^{-1}$)	$-\Delta H_i^\circ$ ($kcal\,mol^{-1}$)	pK_a
MeSOPh	140		6.3 ± 0.1	20.2 ± 1.0	−2.27
DMSO	346 ± 8	367	6.6 ± 0.1	26.5 ± 0.2	−1.80
Bu_2SO	400	384	6.9 ± 0.1	29.1 ± 0.1	−1.47
Ph_2SO	105 + 1	311	6.2 ± 0.3		
Bu_2S	1.8	261	3.44 ± 0.88		
Et_2S	1.3	263	3.63 ± 0.11	19.5 ± 0.3	
Acetone	15.4		5.59 ± 0.08		
$(CH_2)_4SO_2$		186		9.6 ± 0.3	
$(CH_2)_4SO$		380		29.1 ± 0.1	

to introduce new parameters for various solvents which work as acceptors for hydrogen bonds by measuring the intensities of the UV solvatochromic shifts for 4-nitroaniline relative to *N*,*N*-diethyl-4-nitroaniline. They used the UV method as an effective experimental tool for the establishment of a linear free energy relationship in the formation of hydrogen bonds between Lewis acids and more than one hundred Lewis bases[83–85]. They have also tried to introduce new parameters (β-values) in order to obtain accurate correlations between the hydrogen bonding donors and the acidity scales[86]. Infrared stretching frequency ν values for X—H (e.g., OH in p-FC_6H_4OH) in the donors are shown to have a linear relationship with β-values when using related bases as the hydrogen bond acceptors. Sulphoxides were found to belong to a family similar to carbonyl compounds and phosphine oxides[87]. The β-scales have been extended to include more than 150 compounds as acceptors. New linear free energy relationships have been also obtained between the β-scales and the ^{19}F NMR chemical shifts for p-FC_6H_4OH or 1-fluoroindole, and with the IR frequency shift of the OH group in PhOH, etc.

In the course of this study, the authors determined β-values for dibenzyl, methyl phenyl, methyl p-nitrophenyl, di-p-tolyl, di-isopropyl and tetramethylene sulphoxides and for diethyl, dipropyl and dibutyl sulphites. The β-scales are applied to the various reactions or the spectral measurements. The β-scales have been divided into either family-dependent (FD) types, which means two or more compounds can share the same β-scale, family-independent (FI) types. Consequently, a variety of β-scales are now available for various families of the bases, including 29 aldehydes and ketones, 17 carboxylic amides and ureas, 14 carboxylic acids esters, 4 acyl halides, 5 nitriles, 10 ethers, 16 phosphine oxides, 12 sulphinyl compounds, 15 pyridines and pyrimidines, 16 sp^3 hybridized amines and 10 alcohols. The enthalpies of formation of the hydrogen bond of 4-fluorophenol with both sulphoxides and phosphine oxides and related derivatives fit the empirical equation 18, where the standard deviation is $\gamma = 0.983$. Several averaged scales are shown in Table 15[88].

$$-\Delta H_f(4\text{-}FC_6H_4OH{:}HBA) = 3.16 + 4.49\,\beta \text{ kcal mol}^{-1} \quad (18)$$

Another different π^*-scale which indicates solvent dipolarity/polarizability and which is a measure of the ability of the solvent to stabilize a charge or a dipole by virtue of the dielectric effect, has been proposed for numerous Lewis bases including sulphoxides[89].

TABLE 15. β-Scales of phosphine oxides and sulphoxides (after Reference 87)

Compounds	β_{av}
DMSO	0.76
Ph_2SO	0.70
Bu_2SO	0.82
i-Pr_2SO	0.78
$(CH_2)_4SO$	0.80
$(PhCH_2)_2SO$	0.74
PhSOMe	0.71
p-$NO_2C_6H_4SOMe$	0.60
p-Tol_2SO	0.72
$(EtO)_2SO$	0.45
$(PrO)_2SO$	0.45
$(BuO)_2SO$	0.45
Ph_3PO	0.94
Me_3PO	1.02

A similar quantitative treatment of sulphoxides as hydrogen bonding acceptors has been obtained by comparing the IR frequency shift $\Delta\nu_{OH}$ of the C—I bond in an acetylenic iodide such as IC≡CI ($\Delta\nu_{C-I}$) due to formation of a C—T complex with phenol in various bases. This investigation suggests that sulphoxides belong to the same family as carbonyls, phosphine oxides, arsine oxides and their derivatives[90].

Recently, more detailed parameters for hydrogen bonding bases have been introduced and applied to many reactions demonstrating the existence of a linear free energy relationship between the hydrogen bonding donor and acceptor abilities and many kinetic or thermodynamic parameters[91].

DMSO can be used as a dipolar non-hydroxylic solvent for the measurement of pK_a values for various phenols bearing strongly electron-withdrawing substituents. These acidity scales in DMSO have been correlated with those in H_2O or in the gas phase[92].

In addition to the introduction of new parameters for sulphoxides with donors, the Badger–Bauer relationship has been re-investigated in detail by Filgueiras and coworkers[53]. The IR stretching shifts of both sulphoxides and phenols ($\Delta\nu_{S\cdots O}$ and $\Delta\nu_{OH}$) involved in the hydrogen bond, when plotted against ΔH values, give rise to a good linear relationship.

Other authors found that the enthalpies for the hydrogen bonding also give a good correlation against Hammett values. The linear free energy equations between $\Delta\nu_{OH}$, $\Delta\nu_{SO}$ and ΔH obtained in their investigations were as follows[93]:

$$-\Delta H = 0.0494\Delta\nu_{OH} + 11.59 \qquad (r = 0.985) \tag{19}$$

$$-\Delta H = 0.6954\Delta\nu_{SO} + 15.06 \qquad (r = 0.986) \tag{20}$$

$$\sigma_R = -0.1972\Delta H - 5.95 \qquad (r = 0.999) \tag{21}$$

The extrapolated $\Delta\nu_{OH}$ and $\Delta\nu_{SO}$ values for various phenol-sulphoxide systems are shown in Table 16.

Thiols have been also used as hydrogen bond donors, though they reduce the S—O bond of sulphoxides quite readily. The SH stretching shifts ($\Delta\nu_{SH}$) of thiophenol are ν_{SH} ($\Delta\nu_{SH}$) 2488 (97) with Et_2SO; 2515 (70) with PhS(O)Et; 2537 (48) with Ph_2SO, while the corresponding ν_{OH} of phenol are 3235 (385); 3285 (335); 3320 (300), respectively[94]. These studies show that phenol forms a stronger hydrogen bond with sulphoxides than thiophenol, and that the strength of the hydrogen bond between thiols and sulphoxides is in the following order: Et_2SO > PhSOEt > Ph_2SO.

Formation of hydrogen bonds between phenols and naphthols on the one hand, and dimethyl, divinyl, diphenyl sulphoxides and other sulphinyl or sulphonyl derivatives on the other, have also been documented in the literature[95–97].

TABLE 16. Extrapolated $\Delta\nu_{OH}$ and $\Delta\nu_{SO}$ values of phenol–sulphoxide systems (cm^{-1})

Sulphoxide	Phenol		*p*-FC_6H_4OH		*m*-FC_6H_4OH		*p*-$NO_2C_6H_4OH$	
	$\Delta\nu_{OH}$	$\Delta\nu_{SO}$	$\Delta\nu_{OH}$	$\Delta\nu_{SO}$	$\Delta\nu_{OH}$	$\Delta\nu_{SO}$	$\Delta\nu_{OH}$	$\Delta\nu_{SO}$
Bu_2SO	376.8	20.9	385.5	23.9	421.1	23.9	459.0	28.2
Pr_2SO	376.1	20.5	382.9	22.2	414.4	23.1	456.3	27.6
$(CH_2)_4SO$	370.3	20.4	377.2	22.0	406.7	22.7	441.7	27.0
DMSO	350.1	20.2	356.6	20.6	376.2	22.0	439.4	26.7
$(PhCH)_2SO$	314.3	—	332.3	—	373.8	—	408.7	—
p-Tol_2SO	297.8	15.8	306.3	17.1	333.4	17.7	392.9	23.7
Ph_2SO	291.6	15.3	297.6	16.5	323.6	17.1	382.2	21.2
(*p*-$ClC_6H_4)_2SO$	245.9	12.2	248.9	13.3	293.4	15.6	346.2	19.9

3. Sulphones as hydrogen bond acceptors

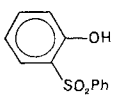
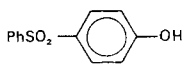
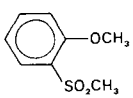
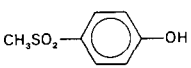
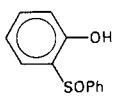
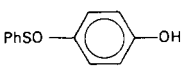
In contrast with the numerous investigations concerning hydrogen bonds involving sulphoxides as Lewis bases, only a few reports are available on hydrogen bonds with sulphones. Amstutz and his coworkers[98] have reported that *o*-hydroxyphenyl phenyl sulphone forms an intramolecular hydrogen bond which is much stronger than the intermolecular hydrogen bond formed in the case of the *p*-isomer. Several IR stretching frequencies of ν_{OH} and ν_{SO} bands are shown in Table 17.

Biscarini and his coworkers have investigated the IR spectra of mixtures of various sulphones and phenol in CCl_4. From the IR stretching frequencies of phenol (ν_{OH}) and sulphones (ν_{SO_2}), the equilibrium constants (K) for the hydrogen bond were calculated and $\Delta\nu_{OH}$ was found to be correlated linearly with the IR shifts $\Delta\nu_{SO_2}$ (both symmetric and antisymmetric frequency). The enthalpy values (ΔH) for these reactions have also been obtained and were plotted against Taft's σ^* constants to give a good straight line[99,100]. These results indicate that the Badger–Bauer relationship also holds in the hydrogen bond formation between sulphones and phenol. Furthermore, Engberts and his coworkers have investigated the hydrogen bonded complexes between phenol and 15 *p*-tolyl sulphones, *p*-TolSO_2X. The $\Delta\nu_{OH}$ values can be linearly correlated with $\Delta\nu_{SO_2}$ of the sulphones[101]. The substituents effect on $\Delta\nu$ is a linear function of Pauling's electronegativities π_i[102]. For example, the following linear energy relationships between $\Delta\nu$ and π_i have been obtained[103]

$$\Delta\nu = 491 - 88\sum\pi_i; \qquad \nu_{SO_2}^{asym} = 1153 + 44\sum\pi_i \tag{22}$$

The $\Delta\nu$ is also correlated linearly with ^{19}F of *p*-FC_6H_4X[103]. Besides these investigations, other linear free energy relationships for the hydrogen bond of sulphones with several

TABLE 17. IR frequencies of sulphoxides and sulphones (after Reference 98)

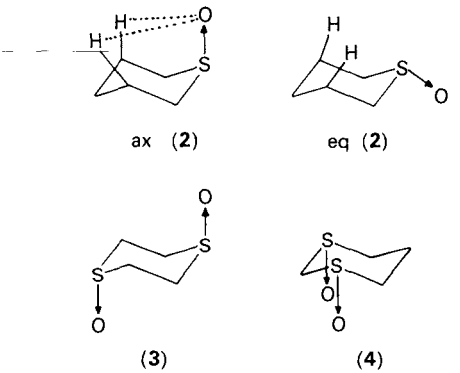
	$\nu_{OH}(cm^{-1})$	$\nu_{SO}(cm^{-1})$
	3292 (CCl_4) 3363 (nujol)	1138 (CCl_4) 1145 (nujol)
	3590 (CH_2Cl_2) 3417 (nujol)	1151 (CH_2Cl_2) 1154 (nujol)
		1151
		1150
		994
	3600 (weak)	

other donors such as amides, $CHCl_3$ or $CDCl_3$ have been published in the literature[104,105].

Intramolecular hydrogen bonds between sulphinyl or sulphonyl groups and hydroxyl groups have also been described[106,107]. The IR shifts ν_{SO} in these experiments were found at around 1005–1010 cm^{-1} [108–110]. Several other papers which describe hydrogen bonds of sulphoxides and sulphones are given in References 111–120.

C. The Influence of the Hydrogen Bond on the Conformation and Configuration of Sulphoxides

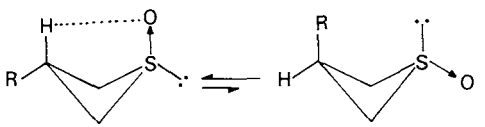
In the equilibrium mixtures of thiane oxide (**2**) and 1,3-, 1,4-dithiane dioxides (**3**) and (**4**), the axial conformers are present predominantly over the equatorial conformers at low temperatures ($-90\,°C$). For instance in the monoxide (**2**) a ratio of 62% axial and 48% equatorial conformers has been observed. The prevalence of the axial conformers in the sulphoxides (**2**) and (**4**) has been explained to be due to hydrogen bonds between the oxygen in the axial sulphinyl group and the hydrogen atom at the 3-position as shown in Scheme 7[121–127].



SCHEME 7

The ^1H NMR spectra of the epimeric cyclohexanols in DMSO reveal that the hydroxyl proton in the axial alcohol shows a resonance absorption at a higher field than in the equatorial one, indicating that the conformational effect of the hydrogen bond influences the ^1H NMR chemical shifts[128].

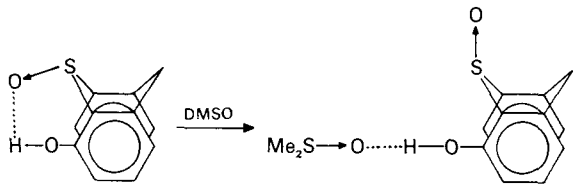
The stereochemistry of 3-substituted thietane-1-oxides (**5**) has been investigated by ^1H NMR and it was found that the sulphinyl oxygen atom occupies the axial position preferentially at equilibrium. This has been attributed to the hydrogen–oxygen attraction as shown in Scheme 8[128,129].



(**5**)

SCHEME 8

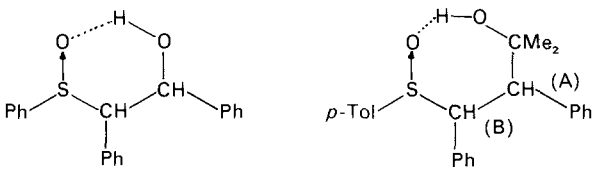
Evidence for direct effects of intramolecular hydrogen bonds on the conformational preferences of cyclic and acyclic sulphoxides having hydroxyl groups has been presented recently. Chasar studied the ^{1}H NMR spectra of thioxanthene 6-oxides and found that the 4-hydroxyl derivative (**6**) forms a strong intramolecular hydrogen bond in $CDCl_3$ which is efficient even on heating at 170 °C while this intramolecular hydrogen bond is broken in DMSO as a solvent, (**7**), where it is converted to an intermolecular hydrogen bond (Scheme 9). In the latter case the axial configuration of the S—O bond becomes predominant due to the steric repulsion between the S—O group and the hydrogen bond formed in DMSO with the alcoholic oxygen atom[130,131].



(**6**) in $CDCl_3$ (**7**) in DMSO

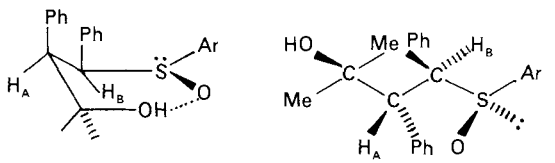
SCHEME 9

Kingsbury and his coworkers prepared β- and γ-hydroxy sulphoxides (**8**) and (**9**) (see Scheme 10). In the case of the sulphoxide (**9**), they could isolate four diastereoisomers (2 erythro and 2 threo isomers) and determine their favoured conformations by detailed analysis of their ^{1}H NMR and IR spectroscopy[132,133]. For example, the isomer (**9E**) having a lower melting point suggests that this is the erythro conformer ($\mathbf{9E_a}$) as shown in Scheme 11, while the higher melting erythro isomer is the non-hydrogen-bonding zigzag conformer ($\mathbf{9E_b}$). These conformations have been determined by the ^{1}H NMR coupling constants of H_A and H_B and chemical shifts of the O—H proton and also solvent effects. Intramolecular hydrogen bonding in cyclic sulphones has been demonstrated[134,135].



(**8**) (**9**)

SCHEME 10



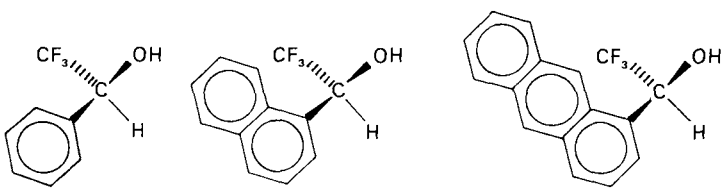
$J_{AB} = 2{,}8$ ($CDCl_3$) $J_{AB} = 12{,}3$ ($CDCl_3$)

($\mathbf{9E_a}$) ($\mathbf{9E_b}$)

SCHEME 11

Solvent effects on the ^1H NMR chemical shifts of sulphoxides in trifluoroacetic acid (TFA) have been reported and came to be an important technique for determination of the configuration and conformation of sulphoxides by comparing the ^1H NMR chemical shifts in CCl_4 and that in benzene. The hydrogen atoms nearest to the sulphinyl group are observed to suffer the largest deshielding effect in CF_3COOH. Thus the largest down-field shift is due to the generation of a partially charged centre on the sulphur atom in the sulphoxide as a result of the hydrogen bond with the oxygen atom in the sulphoxide and TFA[36-44]. Nishio determined the configurations of both erythro and threo isomers of α-phenethyl *p*-substituted phenyl sulphoxides based on the solvent shifts of the α-methine and the methyl protons in TFA, in benzene and in CCl_4[136-144]. The assignment was later found to be incorrect and amended to the opposite configurations[144]. This case shows how much care is needed in determining the conformations of acyclic sulphoxides, and this should be performed if possible on the basis of, e.g., X-ray crystallographic analysis[145].

The hydrogen-bonding ability in chiral alcohols bearing strongly electron-withdrawing groups such as CF_3 has been successfully applied for the determination of the configurations or enantiomeric excess of chiral sulphoxides by using NMR spectroscopy. These methods have been reviewed in detail by Pirkle[146]. A few examples of the alcohols



(*S*)-(+)-TFPE (*R*)-(+)-TFNE (*S*)-(+)-TFAE

SCHEME 12. Shift reagents.

used in the experiments are presented in Scheme 12. These alcohols are called (diamagnetic) 'chiral solvating agents (CSAs)'. Practically, when one treats enantiomeric solutes such as sulphoxides with one of the chiral solvating alcohols in a suitable solvent, one can observe the formation of association complexes that are diastereomeric and thus have different physical properties which can be differentiated by, e.g., ^1H NMR chemical shifts (equation 23):

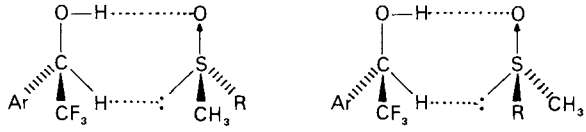
$$\begin{aligned} A + S &\overset{K_a}{\rightleftharpoons} As \\ A' + S &\underset{K_{a'}}{\rightleftharpoons} A'S \end{aligned} \tag{23}$$

The non-equivalent ^1H NMR magnitudes above lead to equation 24:

$$\Delta\delta = \frac{[AS]}{[A]}\delta AS - \frac{[A'S]}{[A']}\delta A'S \tag{24}$$

Thus, the enantiomeric contents in a pair of sulphoxides can be determined by the ^1H NMR chemical shifts in the methine or methylene protons in the two diastereomeric complexes which are stabilized by the hydrogen bond between the hydroxyl and the sulphinyl groups[147-151] (Scheme 13). Similarly, the enantiomeric purity and absolute configurations of chiral sulphinate ester can be determined by measuring the ^1H NMR shifts in the presence of the optically active alcohols[152].

Chiral recognition of enantiomeric sulphoxides by chiral alcohols was applied to the



SCHEME 13

resolution of racemic sulphoxides into the corresponding enantiomers by using a chromatographic technique based on chiral fluoroalcohols bonded to an appropriate stationary phase. This method is also based on preferred hydrogen bonding between the chiral alcohol and one of the enantiomers of the sulphoxides[153]. Similarly, the HPLC resolution of sulphoxides via diastereomeric Pt-complexes[*trans*-chloro[*N*,*N*-dimethyl-D-phenylglycine] (ethylene)Pt(II)] has been successfully performed and lead to the separation of enantiomers of sulphoxides $CH_3SOC_6H_4$-R-*p*[154].

D. Protonation of the Sulphinyl or Sulphonyl Oxygen Atoms and Basicities of Sulphoxides and Sulphones

Proton transfer reactions have similar characteristics to reactions involving the hydrogen bond. In structurally resembling compounds, a linear energy relationship between the enthalpy of the hydrogen bond and that of the proton transfer has been obtained in a series of groups such as carbonyl, sulphinyl, phosphoryl and pyridyl derivatives. However, a definite difference between these two reactions is that the transfer of a proton from an acid (AH) to a base (B) requires much energy and involves charged species which are solvated strongly.

$$AH + B \rightleftharpoons A^- + BH^+ \tag{25}$$

Sulphoxides undergo various acid catalyzed reactions on the sulphinyl sulphur atom, which were reviewed elsewhere[155]. Both sulphoxides and sulphones have been found to be weak bases and the determination of their pK_a values has generally been performed in strong acidic media such as concentrated sulphuric acid by means of cryoscopic measurements, UV spectroscopy or more accurately by ^1H NMR in strong acidic conditions. Earlier, cryoscopic conductivity and conductometric measurements of sulphoxides and sulphones have been performed by Gillespie[156–159], Szmant[160,161] and Hall[162] in concentrated sulphuric acid. Szmant determined the van't Hoff *i*-factors for various sulphoxides and sulphones and, on the basis of the observed *i*-factor of 4.7 in 100% sulphuric acid, he proposed that diphenyl sulphoxide generates sulphidonium cations while di-*p*-nitrophenyl sulphoxide gives the hydroxysulphonium ion as shown in the following equations[160,161]:

$$\begin{aligned}(C_6H_5)_2S{=}O + 3H_2SO_4 &\longrightarrow (C_6H_5)_2S^{++} + H_3O^+ + 3HSO_4^- \\ (NO_2C_6H_4)_2S{=}O + H_2SO_4 &\longrightarrow (NO_2C_6H_4)_2S^+ - OH + HSO_4^-\end{aligned} \tag{26}$$

However, Gillespie contested Szmant's results[158] and proposed that diaryl sulphoxides are initially protonated on the oxygen atom and then undergo a rather rapid sulphonation in the aromatic rings, and concluded that sulphoxides are stronger bases than sulphones.

Hall and Robinson[162] later reported pK_{BH^+} values of various sulphones obtained from equation 27, where H_o is the Hammett acidity function and K_b is calculated from (28).

$$H_o = pK_{HB^+} - \log[BH^+]/[B], \qquad H_o = pK_{BH^+} - \log K_B - \log[H_2SO_4] \tag{27}$$

$$K_{(H_2SO_4)} = K_b = \frac{[BH^+][HSO_4^-]}{[B]} \tag{28}$$

TABLE 18. pK_{HB^+} values of sulphones

Sulphones	$-pK_{BH^+}$
Me_2SO_2	12.27
Et_2SO_2	12,37
Pr_2SO_2	12.75
Bu_2SO_2	12.85
$(CH_2)_4SO_2$	12.88
Ph_2SO_2	13.4
$PhSO_2C_6H_4NO_2$-*p*	13.7

The pK_{BH^+} values plotted against the stretching frequencies of the SO in the sulphones afford a good straight line. Several $pK_{HB^+}(pK_a)$ values of sulphones are summarized in Table 18.

The pK_a values of various sulphoxides have been systematically determined by potentiometric titration in $(CH_3CO)_2O$—$HClO_4$ by Andersen and his coworkers[163]. They have correlated the pK_a values of dimethyl, methyl *m*- and *p*-substituted phenyl sulphoxides with Hammett σ values to give a ρ of 3.79. They have concluded that the protonation site might be the oxygen atom to form hydroxy sulphonium salts which undergo resonance stabilization with the benzene ring. At the same time, the pK_a value of DMSO has been reported by several others between 1.0 and -2.78[164–167]. Haake and his coworkers[168] also have reported measurement of the pK_a values of sulphoxides by the ^1H NMR method. However, two Italian groups have re-investigated the pK_a values and found that sulphoxides are not Hammett bases, and obtained the correct pK_a values of sulphoxides by using the Bunnett and Olsen equation (29)[169,170].

$$\log[BH^+]/[B] + H_0 = \phi(H_0 + \log[H^+]) + pK_{BH^+} \tag{29}$$

TABLE 19. pK_a values of sulphoxides

Sulphoxide	pK_a[a]
p-$ArSOCH_3$	-2.05 ($+0.76$[163])
p-$TolSOCH_3$	-2.22 ($+1.25$[163])
m-$TolSOCH_3$	-2.26
$PhSOCH_3$	-2.27 (-0.49[163], -3.38[168a])
p-$ClC_6H_4SOCH_3$	-2.45 (-1.57[163])
m-$ClC_6H_4SOCH_3$	-2.61 (-3.51[163])
p-$NO_2C_6H_4SOCH_3$	-2.96 (-3.51[163])
DMSO	-1.80 (0.91[163], 1.0[164], 0.0[165] -2.78[168b], -1.04[166])
t-BuSOMe	-1.62 (-1.47[173])
Bu_2SO	-1.47
$(PhCH_2)_2SO$	-2.03[172]
Ph_2SO	-2.54 (-3.58[163], -2.07[171], -3.19[172], -4.97[173])
p-Tol_2SO	-2.39 (-4.40[173])

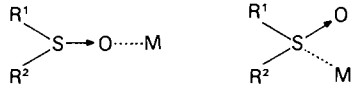
[a]Taken from Reference 170. The values are averaged ones obtained by UV and NMR methods in H_2SO_4 or $HClO_4$. Bunnett–Olsen's values, ϕ 0.4–0.6 in equation 29. This suggested that sulphoxides are not Hammett bases (J. F. Bunnett and F. P. Olsen, *Can. J. Chem.*, **44**, 1899 (1966))

They have also demonstrated that a linear energy relationship exists between pK_a values of sulphoxides and the hydrogen bonding ability which was determined by IR-stretching shift of the OH band in PhOH in CCl_4. Oae and coworkers[173] determined the pK_a values of diaryl sulphoxides and found that the substituent effect does not correlate with the Hammett σ values but approximately with the σ^+ values. The pK_a values thus obtained are summarized in Table 19.

III. COORDINATION COMPLEXES OF SULPHOXIDES AND SULPHONES WITH METALS

A. General Complexations of Sulphoxides

The chemistry involving metal coordination by sulphoxides was first reported in detail by Cotton[174] and by Drago[175]. The major findings of these studies are: (a) salts of most transition and many non-transition metal ions form adducts with sulphoxides; (b) stronger coordination bonds are formed with sulphoxides than with the corresponding sulphones; and (c) while most metal–sulphoxide bonds are established through the sulphinyl oxygen (**A**, Scheme 14), in a few cases [Pt(II) and Pd(II)] the bonds are formed through the sulphur atom (**B**).



(A) (B)

SCHEME 14

Several investigators[178–182] have studied the properties of DMSO as a solvent for inorganic salts and crystalline compounds were obtained with DMSO as a complexing agent. Many hexa-DMSO metal perchlorates[179–181], nitrates[183] and bromides[178] and a great number of adducts of metal halides[179–181,184–186] have been reported. The spectra in the visible region of coloured transition-metal perchlorate complexes of DMSO indicate an octahedral coordination of six DMSOs with the oxygen being the donor atom of the sulphoxide.

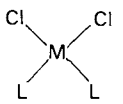
Diverse series of diphenyl sulphoxide (DPSO) complexes of Mn(II), Fe(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Ca(II), Al(II) and Mg(II) with various large anions have been reported[187–191]. The complexes have the general formula $M(DPSO)_6(Anion)_n$ where M is the metal cation. The reflection spectra in the visible and near-IR region indicate an octahedral configuration around the metal ion surrounded by the DPSO molecules. Comparison with the spectra of DMSO complexes shows that they have almost identical structures. IR spectra indicate that the oxygen atom in the sulphinyl group is the donor atom in all these complexes.

The ligand properties of a cyclic dithioether, 1,4-dithiane monosulphoxide (DTMSO), have been studied by physical measurements[192]. The infrared spectra indicate that the metal cation coordinates to the oxygen lone pair electrons of DTMSO. Both infrared and ligand-field spectra show the presence of octahedral ions $M(DTMSO)_6^{n+}$ in the compounds $M(DTMSO)_6(ClO_4)_n$ and $M(DTMSO)_6(BF_4)_n$. In the case of $M = Cu^{2+}$ these ions are distorted from the regular octahedral structure.

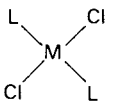
The infrared[174–176] and X-ray[175,193,194] studies demonstrate that though DMSO generally associates with metal cations through its oxygen atom, the donation by the sulphur atom is favoured for some cations, such as Pt(II) and Pd(II). However, Wayland

and Schramm[195] have suggested that both O and S coordination to Pd(II) may occur in the same complex e.g. $Pd(DMSO)_4^{2+}$.

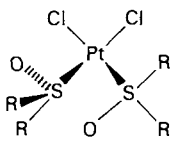
On the other hand, Kitching's group have reported that the IR and ^{1}H-NMR spectra of $PdCl_2L_2$ and $PtCl_2L_2$ [L = $(PhCH_2)_2S{=}O$, $Me_2S{=}O$, $PhCH_2S(O)Me$, $(MeS(O)CHMe_2$, $Et_2S{=}O$] support the S-bonded structures and configurations of the complexes shown in Scheme 15. Far-IR studies indicate that the Pd(II) complexes have uniformly the *trans* structure while the Pt(II) complexes have the *cis* one[196,197].



(M = Pt)



(M = Pd) (L = Sulphoxide)

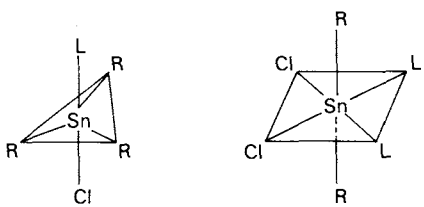


cis-$PtCl_2$ $[Et_2SO]_2$

SCHEME 15

The same group[198] characterized the complexes of methyltin halides with dibenzyl, diethyl and methyl benzyl sulphoxides. R_3SnCl forms complexes with one and R_2SnCl_2 with two donor molecules, and trigonal bipyramidal and octahedral structures, respectively, were suggested for these complexes as shown in Scheme 16.

IR spectra of these complexes suggest that the ligands are coordinated by the oxygen atom. The magnetic non-equivalence of the methylene groups due to flanking by the sulphur is influenced seriously by the oxygen coordination to the tin atom.



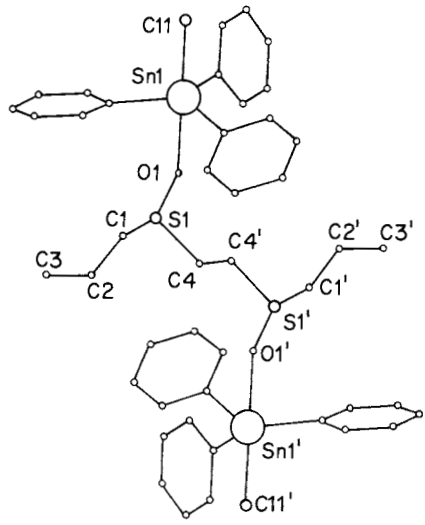
R = Me or Ph

L = sulphoxide

SCHEME 16

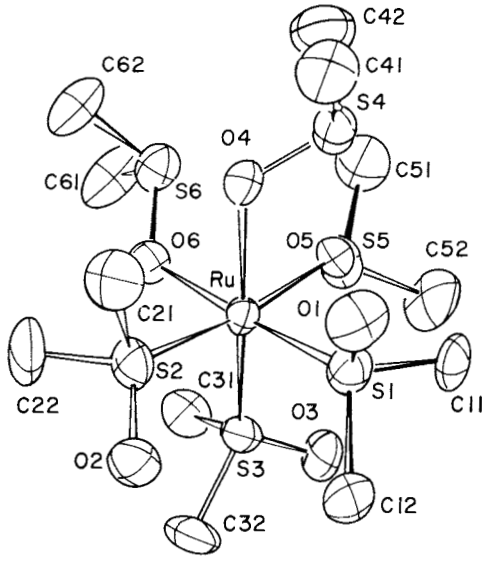
Filgueiras and coworkers[222] prepared the complex of a disulphoxide with triphenyltin chloride. The complex is a 2:1 adduct with two Ph_3SnCl units whose Sn atoms occupy the centre of the two trigonal bipyramids, as shown in Scheme 17.

Recently, Farrel and Oliveria[200] have studied the behaviour of *cis*-$[RuCl_2(Me_2SO)_4]$ and $[Ru(Me_2SO)_6](BF_4)_2$ in an aqueous solution. The crystal structure of the former shows that three Me_2SO ligands are S-bound and one is O-bound.



SCHEME 17. The structure of $(Ph_3SnCl)_2$rac-$(PrSOCH_2)_2$.

The second complex has been characterized by X-ray crystallography[223]. The ruthenium(II) atom is coordinated to three Me_2SO molecules via the oxygen atom and to three via the sulphur atom to give the irregular octahedral geometry as shown in Scheme 18.



SCHEME 18. A perspective view of $Ru(Me_2SO)_6^{2+}$.

TABLE 20

	S $2p_{3/2}$, eV	O 1s, eV	(O 1s-S $2p_{3/2}$), eV	Mode	ν(SO),[k] cm^{-1}
$NiCl_2 \cdot 3DMSO$	165.0	530.9	365.9	O	(940)[a] (992, *1037*, *1000*)[b] (1004, 999)[c]
$CoCl_2 \cdot 3DMSO$	165.0	531.0	366.0	O	(950)[a] (1002, *994*)[b] (999)[c]
$MnCl_2 \cdot 3DMSO$	165.1	530.9	365.8	O	(950)[a] (1004)[b]
$ZnCl_2 \cdot 2DMSO$	165.4	531.1	365.7	O	(952)[a]
$CuCl_2 \cdot 2DMSO$	164.7	530.4	365.7	O	(923)[a] (980, 987)[c]
$CdCl_2 \cdot DMSO$	165.1	530.7	365.6	O	(950)[a] (991)[c]
$HgCl_2 \cdot DMSO$	165.6	531.4	365.8	O	(1005, 1030)[c]
$SnCl_2 \cdot 2DMSO$	165.3	531.0	365.7	O	(920)[d]
$PtCl_2 \cdot 2DMSO$	165.6	530.5	364.9	S	(1157, 1134)[a] ($\sim$ 1110)[c] (1135, 1160)[e]
$Pd(DMSO)_4(BF_4)_2$	165.9	530.9	365.0	S	(1150, 1140, 920, 905)[f]
	165.1	530.9	365.8	O	(1150, 1140, 920, 905)[f]
$PdCl_2 \cdot 2DMSO$	165.5	530.6	365.1	S	(1120)[a] (1118)[c] (1116)[e] (1115)[g]
$AlCl_3 \cdot 6DMSO$	165.7	531.4	365.7	O	(1109)[c]
$FeCl_3 \cdot 2DMSO$	165.3	531.2	365.9	O	(933)[a] (981, 988)[c]
$PhCl_3 \cdot 3DMSO$	166.0	531.2	365.2	S	(1130, 1145)[g]
$SnCl_4 \cdot 2DMSO$	165.6	531.3	365.7	O	(915)[a] (907, 919)[h] (920, 905)[g]
$Sn(CH_3)_2Cl_2 \cdot 2DMSO$	164.4[j]	530.5[j]	366.1	O	(945) (944)[h]
DMSO	164.6[j]	529.9[j]	365.3		(1060)[i] (1055)[e]

[a] F. A. Cotton, R. Francis, and W. D. Horrocks, Jr., *J. Phys. Chem.*, **64**, 1534 (1960).
[b] Reference 175.
[c] Reference 179.
[d] J. S. Morrison and H. M. Heandle, *Inorg. Nucl. Chem.*, **29**, 393 (1967).
[e] Reference 197.
[f] Reference 195.
[g] Reference 199.
[h] Reference 184.
[i] Reference 174.
[j] Low-temperature spectra.
[k] Italic values of SO stretching frequencies are solution values. All others are for Nujol mulls.

In the formation of metal–dialkyl sulphoxide complexes, a shift of the S—O stretching frequency to lower wave numbers on binding to the oxygen atom and to higher values on binding to the sulphur atom has been established[174–177]. Although the S—O stretching mode generally gives rise to a distinct intense peak in the infrared spectrum, its location is often obscured or complicated by overlap or mixing with other bonds such as C—H rocking modes. Furthermore, in cases of sulphoxides having a phenyl group bound directly to the sulphur atom, the shift of the S—O stretching on complexation becomes so small that the determination of the binding site by infrared analysis is difficult or impossible. Su and Faller[199] have reported that a reliable method for determining the mode of binding of ambidentate sulphoxide ligands to the metals can be based upon a novel application of ESCA (Electron Spectroscopy for Chemical Analysis). Thus, the ionization potentials of electrons from inner shells of the sulphur and the oxygen atoms in a series of sulphoxide complexes were measured. These ionization potentials and the corresponding S—O stretching frequencies from the infrared measurements are given in Table 20.

Relative differences between S $2p_{3/2}$ and O 1 s ionization potentials show a characteristic separation for oxygen-bound and sulphur-bound sulphoxides. It is clearly shown in Table 20 that sulphur-bound complexes have (O 1 s–S $2p_{3/2}$) relative shifts of 365.0 eV, while oxygen-bound complexes have relative shifts of 365.8 eV. Infrared and X-ray crystallographic results also show that most neutral platinum and palladium dialkyl sulphoxide complexes contain metal–sulphur rather than metal–oxygen bonds, while first-row transition metals favour oxygen-bonded sulphoxide.

B. Sulphoxide Complexes of Actinoide (IV) Tetrachlorides

Complexes of actinoide tetrachlorides with sulphoxides $MCl_4 \cdot xR_2SO$ [R = Et, $x = 4$ (Th), 3 (Th, U or Np) and 2.5 (Np or Pu); R = Ph, $x = 4$ (Th, U, or Np) and 3 (U, Np, or Pu); R = $C_{10}H_7$, $x = 3$ (Th or U)] have been prepared[201,202]. In IR spectra, the shifts in the S=O stretching frequency of the ligand in all the sulphoxide complexes indicate that the ligands are bonded to the metal through the sulphoxide oxygen atom.

C. Sulphoxides as Polydentate Ligands

The behaviour of polydentate ligands containing sulphinyl groups has received much less attention. Giesbrecht and Osorio[203] have reported the coordination compounds of bivalent transition metal (Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Cu^{2+}, Zn^{2+}) perchlorates with 2,2′-sulphinyldiethanol (SDE).

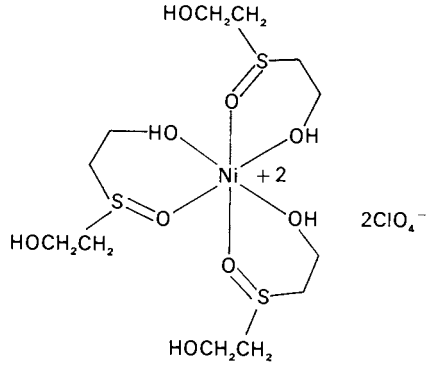
The sulphoxide (SDE) acts as a tridentate ligand in the 1:2 complexes and as bidentate ligand in the 1:3 complexes shown in Scheme 19.

Bidentate sulphoxides, such as 1,3-bis(methylsulphinyl)propane, 1,4-bis(methylsulphinyl)butane and 1,2-bis(ethylsulphinyl)ethane, have been synthesized and employed as ligands toward Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} [204]. All metal ions are bound to the ligands via the oxygen of the sulphoxide groups and are six-coordinate, as shown in Scheme 20, with the exception of Cu^{2+}, which is four-coordinate.

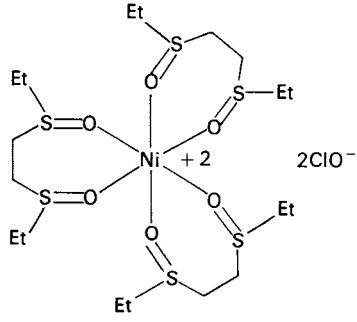
β-Ketosulphoxides, e.g. $PhCOCH_2SOCH_3$ as bidentate ligands, coordinate to sodium, barium, lead and mercury (Scheme 21a). On the other hand, metal–sulphoxide bonds for derivatives of platinum, palladium and mercury are different, and it has been proposed that the metal is bonded to the sulphinyl sulphur atom (Scheme 21b)[205].

West and colleagues[206] have reported the initial examples involving a N → O/S → O mixed donor ligand such as 2-(ethylsulphinyl)pyridine *N*-oxide for transition metal ion and lanthanide metal ion as shown in Scheme 22. Crystal field parameters based on

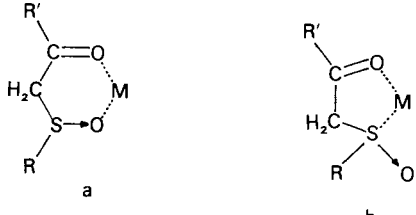
approximate octahedral symmetry are calculated for the Cr(III), Co(II) and Ni(II) complexes.



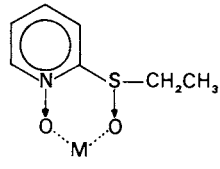
SCHEME 19



SCHEME 20



SCHEME 21



SCHEME 22

D. Extraction of Metal Ions with Sulphoxides and Sulphones

Sulphoxides and sulphones can be used as extractants for several metal ions such as U, Am, Pu, Cr, Zr, Np, Mo, Tm, Fe, Co from aqueous solutions[207-217].

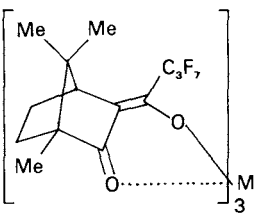
E. Coordination Complexes of Sulphones with Metals

A very few coordination complexes of tetramethylene sulphone $[(CH_2)_4SO_2]$ with transition metal ions have been prepared, and the coordinative ability of sulpholane is generally regarded as quite weak[224,225]. Sulpholane metal complexes should therefore serve as excellent precursors of the coordination compounds containing other weakly nucleophilic ligands.

F. Coordination of Sulphoxides with Shift Reagents

Optically active 2,2,2-trifluorophenylethanol, when used as NMR solvent, causes enantiomeric spectral dissimilarities for chiral episulphoxides: the relative field positions of non-equivalent NMR resonances are analyzed with respect to the absolute configuration of the solvated compounds[220].

The enantiomeric purity of optically active sulphoxides can be determined by chiral lanthanide shift reagents such as tris(3-trifluoroacetyl-*d*-camphorato)europium(III) and tris(heptafluorobutyryl-*d*-camphorato)europium(III)[218,219,221], the latter shown in Scheme 23.

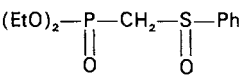


(M = Eu)

SCHEME 23

G. Sulphoxides as Phase Transfer Catalysts

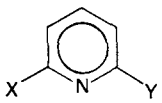
Sulphoxides can be used as phase transfer catalysts, for example, α-phosphoryl sulphoxides (Scheme 24) have been used as phase transfer catalysts in the two-phase alkylation of phenylacetonitrile or phenylacetone with alkyl halides and aqueous sodium hydroxide. However, they are considered to be inefficient catalysts for simple displacement reactions[226].



SCHEME 24

Recently, it has been reported that methyl 2-pyridyl sulphoxides (**10**) and related pyridyl derivatives (**11**) (see Scheme 25) are good phase transfer catalysts for S_N2 reactions of various primary or secondary alkyl halides in a two-phase reaction system and for the alkylation of phenylacetonitrile or phenylacetone with alkyl halides in liquid–liquid two-

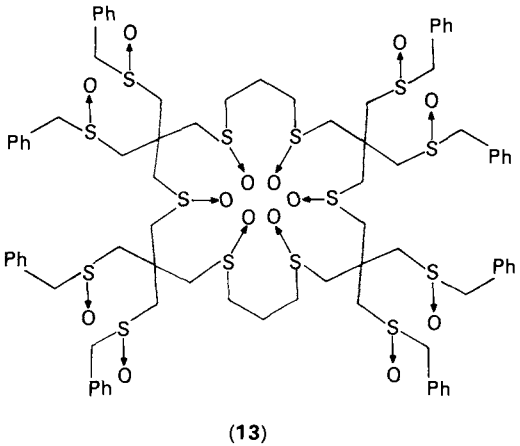
phase systems[227]. The catalytic activity of these sulphoxides can be attributed to initial coordination of the metal cation by the sulphinyl oxygen atom and the pyridyl nitrogen atom, resulting in transfer of nucleophiles from the aqueous phase to the organic phase. Thus, the nucleophile becomes a highly nucleophilic 'naked anion'.



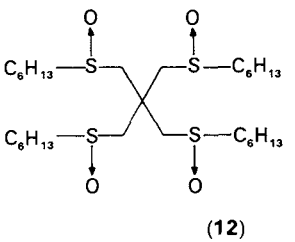
(**10**) X = H, Y = $CH_2S(O)Me$

(**11**) X = Y = $CH_2S(O)$ $(CH_2)_3S(O)$ $(CH_2)_3S(O)Me$

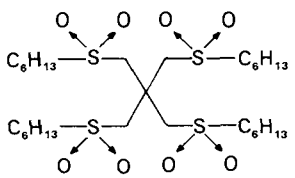
SCHEME 25



(**13**)



(**12**)



(**14**)

TABLE 21. Liquid–liquid two-phase alkylation catalyzed by various sulphoxides

$$PhCH_2COMe + RX \xrightarrow[50\%\ \text{aqueous NaOH}]{\text{Catalyst}} PhCH(R)COMe + NaX$$

RX	Catalyst (mol%)	Temp. (°C)	Time (h)	Yield (%)
EtI	(**13**) (1.0)	r.t.	0.9	92
EtI	(**12**) (1.0)	r.t.	1.5	94
EtI	(**14**) (1.0)	r.t.	4.0	89
EtI	*a* (1.0)	r.t.	5.0	14

[a] $C_{12}H_{25}S(O)C_{12}H_{25}$.

As expected, the compounds containing polysulphinyl groups have higher catalytic activities than the monosulphinyl compounds. For example, tetrakis(alkylsulphinylmethyl)methanes (**12**), 'octopus compounds' of a new type, have been synthesized[228]. The polysulphoxides **12** have been shown to serve as good phase-transfer catalysts which accelerate S_N2-type displacements of octyl bromide with various nucleophiles (thiocyanate, cyanide, phenoxide and thiolate) in solid–liquid two-phase systems. Alkylation of phenylacetonitrile with alkyl halides has also been carried out in liquid–liquid two-phase systems in the presence of the above sulphoxides to afford the corresponding monoalkylated products in high yields. Furthermore, the macrocyclic polythiaether polysulphoxides with benzylsulphinyl side-chains (**13**) have been found to work as excellent phase-transfer catalysts which promote alkylation of benzyl methyl ketone with alkyl halides in a liquid–liquid two-phase system (Table 21)[229]. Unlike the sulphoxides, the sulphone **14** was an ineffective catalyst. This lack of reactivity in the sulphone is believed to be due to the comparatively weak affinity of the sulphonyl groups for the metal cation.

IV. REFERENCES

1. C. C. Price and S. Oae, *Sulphur Bonding*, Ronald Press Co., New York, 1962.
2. P. H. Laur, in *Sulphur in Organic Chemistry* (Ed. A. Senning), Vol. 3, Marcel Dekker, New York, 1972, p. 91.
3. M. A. Viswamitra and K. K. Kannan, *Nature (London)*, **209**, 1016 (1966).
4. W. Feder, H. Dreizler, H. D. Rudolph and V. Typke, *Z. Naturforsch.*, **24a**, 266 (1966).
5. V. H. Hope, U. de la Camp, G. D. Homer, A. W. Messing and L. H. Sommer, *Angew. Chem.*, **81**, 619 (1969).
6. S. C. Abrahams, *Acta Crystallogr.*, **10**, 417 (1957).
7. D. A. Langs, J. V. Silverton and W. M. Bright, *J. Chem. Soc. (D)*, 1653 (1970).
8. L. G. Vorontsova, *Sov. Phys.-Crystallogr.*, **10**, 139 (1965).
9. J. G. Sime and S. C. Abrahams, *Acta Crystallogr.*, **13**, 1 (1960).
   R. G. Treuting and S. C. Abrahams, *Acta Crystallogr.*, **14**, 190 (1961).
10. (a) L. Pauling, *The Nature of the Chemical Bond*, Cornell Univ. Press, Ithaca, 1960, p. 240.
    (b) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell Univ. Press, Ithaca, 1957.
11. V. Schomaker and D. P. Stevenson, *J. Amer. Chem. Soc.*, **63**, 37 (1941).
12. Ref. 10a, p. 164.
13. W. C. Hamilton and S. J. Laplaca, *J. Amer. Chem. Soc.*, **86**, 2289 (1964).
14. C. W. N. Cumper and S. Walker, *Trans. Faraday Soc.*, **52**, 193 (1956).
15. (a) M. W. Lister and L. E. Sutton, *Trans. Faraday Soc.*, **35**, 495 (1939).
    (b) L. E. Sutton, R. G. A. New and J. B. Bentley, *J. Chem. Soc.*, 652 (1933).
    (c) E. N. Guryanova, *Zh. Fiz. Khim.*, **24**, 479 (1950).
    (d) C. W. N. Cumper, G. H. Jeffrey, J. Leichester, A. I. Vogel and S. Walker, *Research Correspondence Suppl. to Research (London)*, **8** (12), S65 (1955).
    (e) J. DeVries and W. H. Rodebush, *J. Amer. Chem. Soc.*, **53**, 2888 (1931).
    (f) Y. Toshiyasu, Y. Taniguchi, K. Kimura, R. Fujishiro, M. Yoshihara, W. Tagaki and S. Oae, *Bull. Chem. Soc. Japan*, **42**, 1878 (1969).
16. J. L. Bellamy, in *Organic Sulphur Compounds* (Ed. N. Kharasch), Vol. 1 Pergamon Press, New York, 1961, p. 47.
17. (a) V. H. Siebert, *Z. Anorg. Allg. Chem.*, **275**, 210, 223 (1954).
    (b) E. S. Waight, *J. Chem. Soc.*, 2440 (1952).
    (c) K. C. Schreiber, *Anal. Chem.*, **21**, 1168 (1949).
    (d) A. Simon and Kriegsmann, *Z. Physik. Chem.*, **204**, 369 (1955).
    (e) C. C. Price and H. Morita, *J. Amer. Chem. Soc.*, **75**, 4747 (1953).
    (f) C. C. Price and R. G. Gillis, *J. Amer. Chem. Soc.*, **75**, 4750 (1953).
18. G. Herzberg, *Molecular Spectra and Molecular Structure*, van Nostrand, New York, 1950.
19. G. Costa and P. Blasina, *Z. Phys. Chem.*, **4**, 24 (1955).
20. A. I. Vogel, *J. Chem. Soc.*, 1820, 1833 (1948).
21. A. I. Vogel and D. M. Cowan, *J. Chem. Soc.*, 16 (1943).

22. (a) T. Ho and C.-M. Wong, *Synth. Commun.*, 337 (1973).
(b) H. D. Durst, J. W. Zubrick and G. R. Kieczykowski, *Tetrahedron Letters*, 1777 (1974).
(c) W. P. Weber, P. Stromquist and T. I. Itoh, *Tetrahedron Letters*, 2595 (1974).
(d) M. Nojima, T. Nagata and N. Tokura, *Bull. Chem. Soc. Japan*, **48**, 1343 (1975).
(e) T. Numata, K. Ikura, Y. Shimano and S. Oae, *Org. Prep. Proced. Int.*, **8**, 119 (1976).
(f) R. G. Nuzzo, H. J. Simon and J. J. San Filippo, *J. Org. Chem.*, **42**, 568 (1977).
(g) Y. Akita, M. Inaba, H. Uchida and A. Ohta, *Synthesis*, 792 (1977).
(h) D. L. J. Clive, W. A. Kiel, S. M. Menchen and C.-K. Wong, *J. Chem. Soc., Chem. Commun.*, 657 (1977), 168 (1979).
(i) J. Drabowicz and M. Mikolajczyk, *Synthesis*, **138**, 542 (1978).
(j) H. S. D. Soysa and W. P. Weber, *Tetrahedron Letters*, 235, 1969 (1978).
(k) P. D. Baechler and S. K. Daley, *Tetrahedron Letters*, 101 (1978).
(l) G. A. Olah, B. G. B. Gupta and S. C. Narang, *J. Org. Chem.*, **43**, 4503 (1978); *Synthesis*, 58 (1979).
(m) I. W. J. Still, S. K. Hasan and K. Turnbull, *Can. J. Chem.*, **56**, 1423 (1978).
(n) T. Numata, H. Togo and S. Oae, *Chem. Letters*, 329 (1979).
(o) J. N. Denis and A. Krief, *J. Chem. Soc., Chem. Commun.*, 544 (1980).
(p) A. H. Schmidt and M. Russ, *Chem. Ber.*, **114**, 822 (1981).
(q) S. Kano, Y. Tanaka, E. Sugino and S. Hibino, *Synthesis*, 695 (1980).
(r) M. Wakisaka, M. Hatanaka, H. Nitta, M. Hatanaka and T. Ishimaru, *Synthesis*, 67 (1980).
(s) H. Suzuki, N. Sato and A. Osuka, *Chem. Letters*, 143 (1980).
(t) D. W. Chasar and J. P. Shockcor, *Phosphorus and Sulphur*, **8**, 187 (1980).
(u) G. Polumbo, C. Ferreri and R. Caputo, *Phosphorus and Sulphur*, **15**, 19 (1983).
(v) I. S. Alnaimi and W. P. Weber, *J. Organomet. Chem.*, **241**, 171 (1983).
(w) S. K. Chung and G. Han, *Synth. Commun.*, **12**, 903 (1982).
23. F. G. Bordwell and W. H. McKellin, *J. Amer. Chem. Soc.*, **73**, 2251 (1951).
24. I. W. J. Still and S. Szilagyi, *Synth. Commun.*, **9**, 923 (1979).
25. D. Barnard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).
26. (a) W. O. Ranky and D. C. Nelson, in *Organic Sulphur Compounds* (Ed. N. Kharash), Vol. 1, Pergamon Press, New York, 1961, p. 170.
(b) A. J. Parker, *Quart. Rep. Sulphur Chem.*, **3**, 185 (1968).
27. (a) R. H.Figueroa, E. Roig and H. H. Szmant, *Spectrochim. Acta*, **22**, 587 (1966).
(b) J. J. Lindberg, J. Kenttamaa and A. Nissema, *Suomen Kemistilehti*, **34B**, 98 (1961); **34B**, 156 (1961).
(c) R. F. Watson and J. F. Eastham, *J. Amer. Chem. Soc.*, **87**, 664 (1965).
28. K. Mislow, M. McGreen, P. Laur and D. R. Chrisholm, *J. Amer. Chem. Soc.*, **87**, 665 (1965).
29. S. Oae, M. Kise, M. Yokoyama and N. Furukawa, *Tetrahedron Letters*, 4131 (1968).
30. (a) F. A. Cotton, R. Francis and W. D. Horrocks, *J. Phys. Chem.*, **64**, 1534 (1960).
(b) L. J. Bellamy, C. P. Conduit, R. J. Pace and R. L. Williams, *Trans. Faraday Soc.*, **55**, 1677 (1959).
31. (a) T. Cairns, G. Eglinton and D. T. Gibson, *Spectochim. Acta*, **20**, 31 (1964).
(b) P. Biscarini and S. Ghersetti, *Gazz. Chim. Ital.*, **92**, 61 (1962).
32. (a) C. D. Ritchie, B. A. Bierl and R. J. Honour, *J. Amer. Chem. Soc.*, **84**, 4687 (1962).
(b) C. D. Ritchie and A. L. Pratt, *J. Amer. Chem. Soc.*, **86**, 1571 (1964).
33. S. Allenmark, *Acta Chem. Scand.*, **17**, 2715 (1963).
34. B. B. Wayland and R. F. Schramm, *Inorg. Chem.*, **8**, 971 (1969).
35. G. Kaufmann, M. J. F. Leroy and B. Pasche, *Bull. Soc. Chim. Fr.*, 3766 (1966).
36. (a) R. H. Gillette and F. Daniels, *J. Amer. Chem. Soc.*, **58**, 1139 (1936).
(b) D. Williams and W. Gordy, *J. Amer. Chem. Soc.*, **59**, 817 (1937). W. Gordy, *J. Chem. Phys.*, **7**, 93, 99 (1939); **8**, 170 (1940); **9**, 204 (1941).
(c) M. M. Davies and G. B. B. M. Sutherland, *J. Chem. Phys.*, **6**, 755 (1938).
37. M. Davies, *Ann. Rep.*, **43**, 5 (1946).
38. J. E. Gordon, *J. Org. Chem.*, **26**, 738 (1961).
39. (a) M. D. Joesten and R. S. Drago, *J. Amer. Chem. Soc.*, **84**, 2037, 2696, 3817 (1962).
(b) R. S. Drago, B. B. Wayland and R. L. Carlson, *J. Amer. Chem. Soc.*, **85**, 3125 (1963).
40. Earlier Badger and Bauer reported an empirical relationship between stretching frequencies of OH and enthalpy values: P. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937).
41. P. Biscarini, G. Galloni and S. Ghersetti, *Boll. Sci. Fac. Chim. Ind., Bologna*, **21**, 154 (1963).

42. T. Gramstad, *Spectrochim. Acta*, **19**, 829 (1963).
43. R. S. Drago, G. C. Vogel and T. E. Needham, *J. Amer. Chem. Soc.*, **93**, 6014 (1971).
44. R. S. Drago, N. O'Bryan and G. C. Vogel, *J. Amer. Chem. Soc.*, **92**, 3924 (1970).
45. E. M. Arnett, L. Joris, E. Mitchell, T. S. S. R. Murty, T. M. Gorrie and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **92**, 2365 (1970).
46. K. F. Purcell, J. A. Stikeleather and S. D. Brunk, *J. Amer. Chem. Soc.*, **91**, 4019 (1969).
47. A. D. Sherry and K. F. Purcell, *J. Phys. Chem.*, **74**, 3535 (1970).
48. R. H. Figueroa, E. Roig and H. H. Szmant, *Spectrochim. Acta*, **22**, 1107 (1966).
49. A. Kivinen, J. Murto and L. Kilpi, *Suomen Kemistilehti*, **40B**, 301 (1967).
50. C. P. Rader, *J. Amer. Chem. Soc.*, **88**, 1713 (1966).
51. H. H. Szmant, in *Dimethyl Sulfoxide* (Ed. S. W. Jacob), Vol. 1, Marcel Dekker, New York, 1971, p. 25.
52. P. Ruostesuo and J. Karhalainen, *Fin. Chem. Letters*, 210 (1979).
53. C. A. L. Filgueiras and O. G. F. Rocha, *Tetrahedron*, **38**, 1213 (1982).
54. J. R. Holmes, D. Kivelson and W. C. Drinkard, *J. Amer. Chem. Soc.*, **84**, 4677 (1962).
55. R. S. Drago and B. B. Wayland, *J. Amer. Chem. Soc.*, **87**, 3571 (1965).
56. S. Ahrland, J. Chatt and N. R. Davies, *Quart. Rev. (London)*, **12**, 265 (1958).
57. R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963).
58. T.-L. Ho, *Hard and Soft Acids and Bases Principle in Organic Chemistry*, Academic Press, New York, 1977.
59. G. Klopman, *Chemical Reactivity and Reaction Paths*, Wiley–Interscience, New York, 1974.
60. (a) L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940, p. 78.
    (b) R. W. Taft, Jr., in *Steric Effects in Organic Chemistry* (Ed. M. S. Newman), Chap. 13, Wiley, New York, 1956, p. 556.
61. J. O. Edwards, *J. Amer. Chem. Soc.*, **76**, 1541 (1954); **78**, 1819 (1956).
62. D. P. Eyman and R. S. Drago, *J. Amer. Chem. Soc.*, **88**, 1617 (1966).
63. T. D. Epley and R. S. Drago, *J. Amer. Chem. Soc.*, **89**, 5770 (1967).
64. R. S. Drago and T. D. Epley, *J. Amer. Chem. Soc.*, **91**, 2883 (1969).
65. (a) R. S. Drago, G. C. Vogel and T. E. Needham, *J. Amer. Chem. Soc.*, **93**, 6014 (1971).
    (b) R. S. Drago, M. S. Nozari and G. C. Vogel, *J. Amer. Chem. Soc.*, **94**, 90 (1972).
    (c) M. S. Nozari and R. S. Drago, *J. Amer. Chem. Soc.*, **94**, 6877 (1972).
66. (a) A. Allerhand and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **85**, 371 (1963).
    (b) S. D. Christian, K. O. Yeo and E. E. Tucker, *J. Phys. Chem.*, **75**, 2413 (1971).
    (c) S. D. Christian, R. Frech and K. O. Yeo, *J. Phys. Chem.*, **77**, 813 (1973).
67. P. Biscarini, L. Lunazzi and F. Taddei, *Boll. Sci. Fact. Chim. Ind., Bologna*, **22**, 67 (1964).
68. F. L. Slejko, R. S. Drago and D. G. Brown, *J. Amer. Chem. Soc.*, **94**, 9210 (1972).
69. S. F. Ting, S. M. Wang and N. C. Li, *Can. J. Chem.*, **45**, 425 (1967).
70. J. J. Delpuech, *Tetrahedron Letters*, 2111 (1965).
71. (a) J. J. Lindberg and R. Lauren, *Finska Kemistsamfundets Medd.*, **71**, 37 (1962).
    (b) E. Tommila and M. L. Murto, *Acta Chem. Scand.*, **17**, 1947 (1963).
    (c) J. Kenttamaa and J. J. Lindberg, *Suomen Kemistilehti*, **33B**, 32, 98, 104 (1960).
    (d) R. K. Wolford, *J. Phys. Chem.*, **68**, 3392 (1964).
72. M. J. Kamlet, J.-L. Abboud and R. W. Taft, *Prog. Phys. Org. Chem.*, **13**, 485 (1981).
73. (a) T. Gramstad, *Spectrochim. Acta*, **19**, 829 (1963).
    (b) T. Gramstad, *Spectrochim. Acta*, **19**, 497 (1963).
    (c) T. Gramstad, *Acta Chem. Scand.*, **15**, 1337 (1961).
    (d) G. Aksnes and T. Gramstad, *Acta Chem. Scand.*, **14**, 1485 (1960).
74. T. Gramstad and W. J. Fuglevik, *Acta Chem. Scand.*, **16**, 1369 (1962).
75. R. H. Figueroa, E. Roig and H. H. Szmant, *Spectrochim. Acta*, **22**, 587 (1966).
76. T. Cairns, G. Eglinton and D. T. Gibson, *Spectrochim. Acta*, **20**, 31 (1964).
77. (a) M. Tamres and S. Searles, Jr., *J. Amer. Chem. Soc.*, **81**, 2100 (1959).
    (b) M. Tamres, S. Searles, Jr., E. M. Leighly and D. W. Mohrman, *J. Amer. Chem. Soc.*, **76**, 3983 (1954).
78. T. Gramstad and O. Vikanes, *Spectrochim. Acta*, **28A**, 2131 (1972).
79. T. Gramstad and Ø. Mundheim, *Spectrochim. Acta*, **28A**, 1405 (1972).
80. (a) R. W. Taft, D. Gurka, L. Joris, P. v. R. Schleyer and J. W. Rakshys, *J. Amer. Chem. Soc.*, **91**, 4801 (1969).
    (b) P. R. Wells, S. Ehrenson and R. W. Taft, *Prog. Phys. Org. Chem.*, **6**, 147 (1968).

81. D. Gurka and R. W. Taft, *J. Amer. Chem. Soc.*, **91**, 4794 (1969). Related references are cited therein.
82. E. M. Arnett, E. J. Mitchell and T. S. S. R. Murty, *J. Amer. Chem. Soc.*, **96**, 3875 (1974).
83. J. Mitsky, L. Joris and R. W. Taft, *J. Amer. Chem. Soc.*, **94**, 3442 (1972).
84. M. J. Kamlet and R. W. Taft, *J. Amer. Chem. Soc.*, **98**, 377 (1976).
85. M. J. Kamlet and R. W. Taft, *J. Chem. Soc., Perkin Trans. 2*, 337 (1979).
86. (a) R. W. Taft and M. J. Kamlet, *J. Amer. Chem. Soc.*, **98**, 2886 (1976).
    (b) M. J. Kamlet and R. W. Taft, *J. Chem. Soc., Perkin Trans. 2*, 349 (1979).
87. M. J. Kamlet, A. Solomonovici and R. W. Taft, *J. Amer. Chem. Soc.*, **101**, 3734 (1979).
88. R. W. Taft, T. Gramstad and M. J. Kamlet, *J. Org. Chem.*, **47**, 4557 (1982).
89. M. J. Kamlet, J.-L. M. Abbound, M. H. Abraham and R. W. Taft, *J. Org. Chem.*, **48**, 2877 (1983).
90. (a) C. Laurence, M. Queignec-Cabanetos, T. Dziembowska, R. Queignec and B. Wojtkowiak, *J. Amer. Chem. Soc.*, **103**, 2567 (1981).
    (b) K. Niendort and R. Paetzold, *J. Mol. Struct.*, **19**, 693 (1973).
    (c) C. Laurence, G. Guiheneuf and B. Wojtkowiak, *J. Amer. Chem. Soc.*, **101**, 4793 (1979).
91. (a) R. W. Taft, M. H. Abraham, R. M. Doherty and M. J. Kamlet, *Prog. Phys. Org. Chem.*, **14**, 247 (1983).
    (b) R. W. Taft, M. H. Abraham, R. M. Doherty and M. J. Kamlet, *J. Amer. Chem. Soc.*, **107**, 3105 (1985).
    (c) J.-L. M. Abboud, K. Sraidi, G. Guiheneuf, A. Negro, M. J. Kamlet and R. W. Taft, *J. Org. Chem.*, **50**, 2870 (1985).
92. (a) M. Fujio, R. T. McIver, Jr. and R. W. Taft, *J. Amer. Chem. Soc.*, **103**, 4017 (1981).
    (b) M. Mashina, R. R. McIver, Jr., R. W. Taft, F. G. Bordwell and W. N. Olmstead, *J. Amer. Chem. Soc.*, **106**, 2717 (1984).
93. (a) F. G. Bordwell, R. J. McCallum and W. N. Olmstead, *J. Org. Chem.*, **49**, 1424 (1984).
    (b) T. Yokoyama, R. W. Taft and M. J. Kamlet, *J. Org. Chem.*, **51**, 3540 (1986).
94. A. Wagner, H. J. Beeher and K.-G. Kottenhahn, *Chem. Ber.*, **89**, 1708 (1956).
95. Y. L. Frolov, L. M. Sinegovskaya, N. K. Gusarova, V. V. Keiko, G. G. Efremova, S. V. Amosova and B. A. Trofimov, *Reakts. Sposobn. Org. Soedin*, **13**, 297 (1976); *Chem. Abstr.*, **86**, 71630s (1977).
96. V. V. Keiko, L. M. Sinegovskaya, Yu. L. Frolov, N. K. Gusarova and B. A. Trofimov, *Zh. Obsbch. Khim.*, **48**, 2347 (1978); *Chem. Abstr.*, **90**, 86530r (1979).
97. P. Ruostesuo and J. Karhalainen, *Finn. Chem. Letters*, 210 (1979); *Chem. Abstr.*, **93**, 7426x (1979).
98. E. D. Amstutz, I. M. Hunsberger and J. J. Chessick, *J. Amer. Chem. Soc.*, **73**, 1220 (1951).
99. P. Biscarini, G. Galloni and S. Ghersetti, *Boll. Sci. Fac. Chim. Ind., Bologna*, **21**, 180 (1963).
100. P. Biscarini, G. Galloni and S. Ghersetti, *Spectrochim. Acta*, **20**, 267 (1964).
101. J. W. Dallinga and J. B. F. N. Engberts, *Spectrochim. Acta*, **30A**, 1923 (1974).
102. L. Pauling, *J. Amer. Chem. Soc.*, **54**, 3570 (1932).
103. W. Adcock, M. J. S. Dewar and B. D. Gupta, *J. Amer. Chem. Soc.*, **95**, 7353 (1973).
104. A. N. Hambly and B. V. O'Grady, *Aust. J. Chem.*, **17**, 860 (1964).
105. K. Kabzinska and J. T. Wrobel, *Bull. Acad. Pol. Sci., Ser. Sci. Chim.*, **22**, 181 (1974); *Chem. Abstr.*, **81**, 90876q (1974).
106. K. B. Alves and L. Do Amaral, *Rev. Quim. Ind.*, **50**, 18 (1981); *Chem. Abstr.*, **95**, 131757m (1981).
107. U. Dawrowska, R. Stachura and J. Dabrowski, *Rocz. Chem.*, **44**, 1751 (1970); *Chem. Abstr.*, **74**, 93035f (1971).
108. T. M. Ivanova, L. I. Denisova and V. A. Batyakina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 435 (1971); *Chem. Abstr.*, **75**, 27606n (1971).
109. U. Folli, D. Iarossi and F. Taddei, *J. Chem. Soc., Perkin Trans. 2*, 848 (1973).
110. D. W. Chasar, D. J. Hunt and D. A. Lupyan, *Phosphorus and Sulphur*, **12**, 55 (1981).
111. A. B. Remizov and T. G. Mannafou, *Zh. Prikl. Spektrosk.*, **25**, 467 (1976); *Chem. Abstr.*, **86**, 29318w (1977).
112. A. B. Remizov, *Zh. Prikl. Spektrosk.*, **25**, 748 (1976); *Chem. Abstr.*, **86**, 71740c (1977).
113. S. Ghersetti, S. Giorgianni, A. Passerini and G. Spunta, *Spectrosc. Letters*, **9**, 427 (1976); *Chem. Abstr.*, **85**, 191701s (1976).
114. I. M. Bokhovkin, T. G. Antonova, B. K. Semenov and N. I. Shubina, *Zh. Obshch. Khim.*, **46**, 1000 (1976); *Chem. Abstr.*, **85**, 32317e (1976).
115. G. E. Binder and A. Schmidt, *Spectrochim. Acta*, **33A**, 815 (1977).

116. G. Fini and P. Mirone, *Spectrochim. Acta, part A*, **32A**, 625 (1976); *Chem. Abstr.*, **87**, 77339e (1976).
117. S. V. Dozmorov, Y. G. Slizhov and E. A. Krulikovskaya, *Zh. Priklad. Spektrosk*, **25**, 1129 (1976); *Chem. Abstr.*, **86**, 170545z (1977).
118. T. S. Cameron, R. J. Cummings and A. C. Knipe, *J. Chem. Soc., Perkin Trans. 2*, 802 (1976).
119. I. I. Mires, P. R. Olivato and B. Wladislaw, *J. Chem. Soc., Perkin Trans. 2*, 166 (1977).
120. V. K. Pogorelyi, T. B. Vishnyakova, V. N. Neplyuev and I. P. Gragerov, *Teor. Eksp. Khim.*, **15**, 406 (1979); *Chem. Abstr.*, **91**, 192629 (1979).
121. J. N. Baxter, J. Cymerman-Craig and J. B. Willis, *J. Chem. Soc.*, 669 (1955).
122. J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).
123. J. B. Lambert, R. G. Keske and D. K. Weary, *J. Amer. Chem. Soc.*, **89**, 5921 (1967).
124. D. Darwish and R. L. Tomilson, *J. Amer. Chem. Soc.*, **90**, 5938 (1968).
125. P. K. Claus, F. W. Vierhapper and R. L. Willer, *J. Org. Chem.*, **44**, 2863 (1979).
126. H. M. M. Shearer, *J. Chem. Soc.*, 1394 (1959).
127. C. Romers, C. Altona, H. R. Buys and H. Havinga, *Topics in Stereochem.*, **4**, 39 (1969).
128. W. O. Siegel and C. R. Johnson, *Tetrahedron*, **27**, 341 (1971).
129. R. M. Moriarty, *Topics in Stereochem.*, **8**, 271 (1974).
130. D. W. Chasar, *J. Org. Chem.*, **41**, 3111 (1976).
131. A. L. Ternay, Jr., J. Herrmann and B. A. Hayes, *J. Org. Chem.*, **45**, 189 (1980).
132. C. A. Kingsbury and R. A. Auerbach, *J. Org. Chem.*, **36**, 1737 (1971).
133. C. A. Kingsbury, V. W. Day and R. O. Day, *J. Org. Chem.*, **45**, 5255 (1980).
134. S. Fabrissin, S. Fatutta and A. Risaliti, *J. Chem. Soc., Perkin Trans. 1*, 1321 (1978).
135. G. V. Pavel and M. N. Tilichenko, *Zh. Org. Khim.*, **14**, 2369 (1978); *Chem. Abstr.*, **90**, 137626m (1979).
136. M. Nishio, *Chem. Commun.*, 562 (1968).
137. M. Nishio, *Chem. Pharm. Bull.*, **17**, 262, 274 (1969).
138. M. Nishio, *Chem. Commun.*, 51 (1969).
139. M. Nishio and K. Nishihata, *Chem. Commun.*, 1485 (1970).
140. W. Amann and Kresge, *Tetrahedron Letters*, 4909 (1968).
141. E. T. Strom, B. S. Snowden, Jr. and P. A. Toldan, *Chem. Commun.*, 50 (1969).
142. R. D. G. Cooper, P. V. DeMarco and D. O. Spry, *J. Amer. Chem. Soc.*, **91**, 1528 (1969).
143. D. H. R. Barton, F. Comer and P. G. Sammes, *J. Amer. Chem. Soc.*, **91**, 1529 (1969).
144. R. R. Fraser, T. Durst, M. M. McClory, R. Vian and Y. Y. Wigfield, *Int. J. Sulphur Chem.*, Part A, 133 (1971).
145. Y. Iitaka, Y. Kodama, K. Nishihata and M. Nishio, *Chem. Commun.*, 389 (1974).
146. (a) W. H. Pirkle and D. J. Hoover, *Topics in Stereochem.*, **13**, 263 (1982).
(b) W. H. Pirkle and S. D. Beare, *J. Amer. Chem. Soc.*, **90**, 6250 (1968).
147. W. H. Pirkle, S. D. Beare and R. L. Muntz, *Tetrahedron Letters*, 2295 (1974).
148. M. Bucciarelli, A. Forni, I. Moretti and G. Torre, *Tetrahedron*, **33**, 999 (1977).
149. T. A. Whitney and W. H. Pirkle, *Tetrahedron Letters*, 2299 (1974).
150. W. H. Pirkle and D. L. Sikkenga, *J. Org. Chem.*, **40**, 3430 (1975).
151. R. Lett and A. Marquett, *Tetrahedron*, **30**, 3379 (1974).
152. W. H. Pirkle and M. S. Hoekstra, *J. Amer. Chem. Soc.*, **98**, 1832 (1976).
153. W. H. Pirkle, D. W. House and J. M. Finn, *J. Chromatograph*, **192**, 143 (1980).
154. M. Goldman, Z. Kustanovich, S. Weinstein, A. Tishbee and E. Gil-Av, *J. Amer. Chem. Soc.*, **104**, 1093 (1982).
155. (a) S. Oae, *Quart. Rep. Sulphur Chem.*, **5**, 53 (1970).
(b) G. Modena, *Int. J. Sulphur Chem.*, 7, 95 (1972).
(c) G. Scorrano, *Acc. Chem. Res.*, **6**, 132 (1973).
156. R. J. Gillespie, *J. Chem. Soc.*, 2542 (1950).
157. R. J. Gillespie, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 2473 (1950).
158. R. J. Gillespie and R. C. Passerini, *J. Chem. Soc.*, 3850 (1956).
159. R. J. Gillespie and C. Solomons, *J. Chem. Soc.*, 1796 (1957).
160. H. H. Szmant and G. A. Brost, *J. Amer. Chem. Soc.*, **73**, 4175 (1951).
161. H. H. Szmant and R. L. Lapinski, *J. Amer. Chem. Soc.*, **74**, 4395 (1952).
162. S. K. Hall and E. A. Robinson, *Can. J. Chem.*, **42**, 1113 (1964).
163. K. K. Andersen, W. H. Edmonds, J. B. Biasotti and R. A. Strecker, *J. Org. Chem.*, **31**, 2859 (1966).

164. C. A. Streuli, *Anal. Chem.*, **30**, 997 (1958).
165. V. P. Nylen, *Z. Anorg. Allg. Chem.*, **246**, 227 (1941).
166. G. Wada, *Bull. Chem. Soc. Japan*, **42**, 890 (1969).
167. R. G. Laughlin, *J. Org. Chem.*, **25**, 864 (1960).
168. P. Haake, R. D. Cook and G. H. Hurst, *J. Amer. Chem. Soc.*, **89**, 2650 (1967).
169. N. C. Marziano, G. Cimino, U. Romano and R. C. Passerini, *Tetrahedron Letters*, 2833 (1969).
170. D. Landini, G. Modena, S. Scorrano and F. Taddei, *J. Amer. Chem. Soc.*, **91**, 6703 (1969).
171. P. O. I. Virtanen and J. Korpela, *Suomen Kemistilehti*, **B41**, 326 (1968).
172. C. Klofutar, F. Krasovec and M. Kusar, *Croat. Chem. Acta*, **40**, 23, (1968); *Chem. Abstr.*, **69**, 86163q (1968).
173. S. Oae, K. Sakai and N. Kunieda, *Bull. Chem. Soc. Japan*, **47**, 1964 (1969).
174. F. A. Cotton and R. Francis, *J. Amer. Chem. Soc.*, **82**, 2986 (1960).
175. D. W. Meek, D. K. Straub and R. S. Drago, *J. Amer. Chem. Soc.*, **82**, 6013 (1960).
176. J. Gopalakrishnan and C. C. Patel, *J. Sci. Ind. Res. (India)*, **27**, 475 (1968).
177. W. L. Reynolds, *Prog. Inorg. Chem.*, **12**, 1 (1970).
178. R. Francis and F. A. Cotton, *J. Chem. Soc.*, 2078 (1961).
179. J. Selbin, W. E. Bull and L. H. Holmes, *J. Inorg. Nucl. Chem.*, **16**, 219 (1961).
180. D. W. Meek, R. S. Drago and T. S. Piper, *Inorg. Chem.*, **1**, 285 (1962).
181. H. L. Schläfer and H. P. Opitz, *Z. Anorg. Allg. Chem.*, **313**, 178 (1961).
182. V. Krishnan and C. C. Patel, *J. Inorg. Nucl. Chem.*, **27**, 244 (1965).
183. D. K. Straub, R. S. Drago and J. T. Donoghue, *Inorg. Chem.*, **1**, 848 (1962).
184. H. G. Langer and A. H. Blut, *J. Org. Met. Chem.*, **5**, 289 (1966).
185. F. Fairbrother, K. H. Grundy and A. Thompson, *J. Less-Common Metals*, **10**, 38 (1966).
186. J. Selbin, M. Schober and J. D. Ortego, *J. Inorg. Nucl. Chem.*, **28**, 1385 (1966).
187. P. W. N. M. Van Leeuwen and W. L. Groeneveld, *Recl. Trav. Chim.*, **85**, 1173 (1966).
188. W. F. Currier and J. H. Weber, *Inorg. Chem.*, **6**, 1539 (1967).
189. J. H. Weber, *Inorg. Chem.*, **8**, 2813 (1969).
190. C. P. Prabhakaran and C. C. Patel, *J. Inorg. Nucl. Chem.*, **32**, 1223 (1970).
191. P. W. N. M. Van Leeuwen, *Recl. Trav. Chim.*, **86**, 201 (1967).
192. J. Reedijk, A. H. M. Fleur and W. L. Groeneveld, *Recl. Trav. Chim.*, **88**, 1115 (1969).
193. M. J. Bennett, F. A. Cotton and D. L. Weaver, *Acta Cryst.*, **23**, 581 (1967); **23**, 788 (1967).
194. D. A. Langs, C. R. Hare and R. G. Little, *J. Chem. Soc., Chem. Commun.*, 1080 (1967).
195. B. B. Wayland and R. F. Schramm, *Inorg. Chem.*, **8**, 971 (1969).
196. W. Kitching and C. J. Moore, *Inorg. Nucl. Chem. Letters*, **4**, 691 (1968).
197. W. Kitching, C. J. Moore and D. Doddrell, *Inorg. Chem.*, **9**, 541 (1970).
198. W. Kitching, C. J. Moore and D. Doddrell, *Aust. J. Chem.*, **22**, 1149 (1969).
199. C.-C. Su and J. W. Faller, *Inorg. Chem.*, **13**, 1734 (1974).
200. N. Farrel and N. G. De Oliveria, *Inorg. Chim. Acta*, **44**, L255-L256 (1980).
201. P. J. Alvey and K. W. Bagnall, *J. Chem. Soc., Dalton Trans.*, 2308 (1973).
202. P. J. Alvey, K. W. Bagnall, O. V. Lopez and D. Brown, *J. Chem. Soc., Dalton Trans.*, 1277 (1975).
203. E. Giesbrecht and V. K. Osorio, *J. Inorg. Nucl. Chem.*, **37**, 1322, 1409 (1975).
204. A. P. Zipp and S. K. Modan, *Inorg. Chim. Acta*, **22**, 49 (1977).
205. E. Boschmann, *J. Inorg. Nucl. Chem.*, **35**, 1025 (1973).
206. (a) E. W. Benson, R. E. Kohrman and D. X. West, *Inorg. Nucl. Chem. Letters*, **12**, 721 (1976). (b) L. J. Chartier, R. E. Kohrman and D. X. West, *J. Inorg. Nucl. Chem.*, **41**, 663 (1979).
207. A. Sambasiva and B. Ramachandra, *Ann. Chim. (Rome)*, **72**, 203 (1982).
208. Yu. I. Murinov, Yu. E. Nikitin, Yu. G. Kuvatov, A. M. Rozen, L. V. Spirikhim and E. E. Zaev, *Radiokhimiya*, **23**, 33 (1981); *Chem. Abstr.*, **94**, 145997f (1981).
209. B. F. Mvasoedov, N. P. Molochnikova, Yu. G. Kuvatov and Yu. E. Nikitin, *Radiokhimiya*, **23**, 43 (1981); *Chem. Abstr.*, **94**, 163421t (1981).
210. J. P. Shukla and M. S. Subramanian, *J. Radioanal. Chem.*, **60**, 403 (1980).
211. N. G. Afzaletdinova, *Issled. Obl. Khim. Vysokomol. Soedin. Neftekhim.*, 42 (1977), *Chem. Zbstr.*, **93**, 11328J (1980).
212. A. A. Goryachev and E. K. Kopkova, *Zh. Neorg. Khim.*, **25**, 1347 (1980); *Chem. Abstr.*, **93**, 32479z (1980).
213. V. S. Kolosnitsyn, *Issled. Obl. Khim. Vysokomol. Soedin. Neftekhim.*, 41 (1977); *Chem. Abstr.*, **92**, 170102b (1980).
214. J. P. Shukla, S. A. Pai and M. S. Subramanian, *J. Radioanal. Chem.*, **56**, 53 (1980).

215. M. Chakrabortty and S. R. Mohanty, *Radiochem. Radioanal. Letters*, **37**, 33 (1979).
216. V. V. Ramakrishna, S. K. Patil, L. K. Reddy and A. S. Reddy, *J. Radioanal. Chem.*, **47**, 57 (1978).
217. B. B. Misra and S. R. Mohanty, *Aust. J. Chem.*, **30**, 2297 (1977).
218. G. M. Whitesides and D. W. Lewis, *J. Am. Chem. Soc.*, **93**, 5915 (1971).
219. H. L. Goering, J. N. Eikenberry and G. S. Koermen *J. Am. Chem. Soc.*, **93**, 5913 (1971).
220. M. Bucciarell, A. Forni, I. Moretti and G. Torre, *Tetrahedron*, **33**, 999 (1977).
221. (a) H. L. Goering, J. N. Eikenberry, G. S. Koermer and C. J. Lattimer, *J. Amer. Chem. Soc.*, **96**, 1493 (1974).
(b) M. D. McCreary, D. W. Lewis, D. L. Wernick and G. M. Whitesides, *J. Amer. Chem. Soc.*, **96**, 1038 (1974).
222. C. A. L. Filgueiras, C. Celso, E. V. Marques and B. G. Johnson, *Inorg. Chim. Acta*, **59**, 71 (1982).
223. A. R. Davies, F. W. B. Einstein, N. P. Farrell, B. R. James and R. S. McMillan, *Inorg. Chem.*, **17**, 1965 (1978).
224. C. H. Langford and P. O. Langford, *Inorg. Chem.*, **1**, 184 (1962).
225. J. K. Hurst and H. Taube, *J. Amer. Chem. Soc.*, **90**, 1174 (1968).
226. M. Mikolajczyk, S. Grzjszczak, A. Zatorski, F. Montanari and M. Cinquini, *Tetrahedron Letters*, 3757 (1975).
227. N. Furukawa, S. Ogawa, T. T. Kawai and S. Oae, *J. Chem. Soc., Perkin Trans. 1*, 1833 (1984).
228. H. Fujihara, K. Imaoka, N. Furukawa and S. Oae, *J. Chem. Soc., Perkin Trans. 1*, 333 (1986).
229. H. Fujihara, K. Imaoka, N. Furukawa and S. Oae, *J. Chem. Soc., Perkin Trans. 1*, 465 (1986).

CHAPTER 12

Behavior of α-sulfinyl and α-sulfonyl carbanions

SHIGERU OAE

Okayama University of Science, 1-1 Ridai-cho, Okayama 700, Japan

YUZURU UCHIDA

Department of Applied Chemistry, Osaka Institute of Technology, Asahi-ku, Osaka 535, Japan

I. INTRODUCTION

This chapter describes the chemical behavior of α-sulfinyl and α-sulfonyl carbanions. The stereoelectronic effects of these sulfur-containing groups have been the subject of much controversy for more than a decade which has now gradually settled down. Meanwhile, the special features of the chemical behavior of these groups have been utilized for syntheses of thousands of useful organic substances. This chapter deals with the

stereochemistry of these sulfinyl and sulfonyl carbanions and with typical reactions of these species.

II. STEREOELECTRONIC EFFECTS OF SULFUR-CONTAINING GROUPS

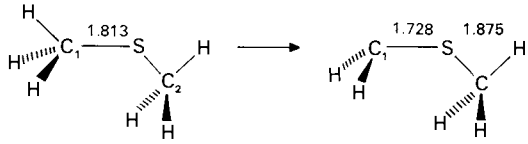
Sulfur-containing groups of various oxidation states have been known to enhance the acidity of α-methylene protons. This enhanced carbon acidity has been utilized effectively for syntheses of various useful organic compounds while the nature of this enhanced acidity has been studied extensively from theoretical viewpoints. Despite the lower electronegativity of the sulfur atom (2.5) than that of the oxygen atom (3.5), the α-thiocarbanion **1** bearing dicoordinate sulfur atom is known to be more stabilized than the corresponding α-oxycarbanion. This phenomenon, i.e., the marked stabilization of the α-thiocarbanion, was rationalized qualitatively on the basis of the following 3d-orbital resonance with sulfur atom (**1a**↔**1b**) until around 1970[1,2].

(**1a**) (**1b**)

However, many MO calculations showed that the contribution of 3d–2p π-bonding shown above may be rather insignificant in the stabilization of α-thiocarbanion **1a**[3–15]. Because of these numerous MO calculations which do not take into account the participation of 3d orbitals, experimentally significant works on the classical 3d-orbital resonance effect were unfortunately neglected. Only recently, however, Wolfe and coworkers recalculated the stereoelectronic behavior of CH_2SH_2, $^-CH_2\overset{+}{S}(CH_3)_2$, $^-CH_2SOR$ and $^-CH_2SO_2R$ using a new 3–21G* basis set which includes 3d orbitals on the sulfur atom, and found that their participation is quite significant in the stabilization of these α-sulfur carbanions[16,17]. Their calculation revealed that deprotonation of dimethyl sulfide ($r_{cs} = 1.813$ Å) gives the pyramidal carbanion, in which the C_1—S bond becomes shorter, i.e. 1.728 Å, while the S—C_2 bond becomes longer, i.e. 1.875 Å, as shown in Figure 1a. The following explanation was proposed. HOMO of the carbanion may be π-bonding around the C_1—S region and σ-antibonding around the C_2—S region, as shown in Figure 1a. However, mixing the d_{xz} atomic orbital of sulfur into this HOMO increases bonding between C_1 and S while decreasing antibonding between S and C_1. Thus, the 3d orbital may not interact directly with the nonbonding orbital of carbon atom but, by mixing with σ^*_{S-C}, HOMO energy may be lowered, as illustrated by Figure 1b.

For historical interest the earlier conclusion, derived from MO calculations without participation of 3d orbitals of the sulfur atom, may be briefly mentioned. If the stabilization of the α-thiocarbanion is caused by $n \rightarrow \sigma^*$ interaction, the interaction should be strictly conformationally controlled and hence the thiocarbanion of the *syn* conformation is expected to be far more stable than that of the *anti* conformation in Figure 2. Among many experimental observations which can be rationalized by the favorable $n_c \rightarrow \sigma^*$ interaction, two examples have been cited. One is the unstable nature of the $^-CH_2Cl$ anion, which cannot hyperconjugate owing to the lack of the σ^* orbital, and the other is the facile base-catalyzed bridge-head proton exchange of trithioorthoformate **2**, demonstrated by Oae and coworkers[18,19]. The bicyclic trithioorthoformate **2**, which gives the thiocarbanion that can assume the *anti* conformation, undergoes base-catalyzed proton exchange 10^3 times faster that the open-chain trithioorthoformate **3**, while lithiation of *m*-dithian was shown to take place only at the equatorial position[20].

Tricoordinate groups, such as sulfinyl (—SO—) and sulfonio ($—S^+R_2$), and a tetracoordinate group like sulfonyl ($—SO_2—$), possess partial positive charge on the central sulfur atom and hence are electron-withdrawing. The magnitude of the electron-



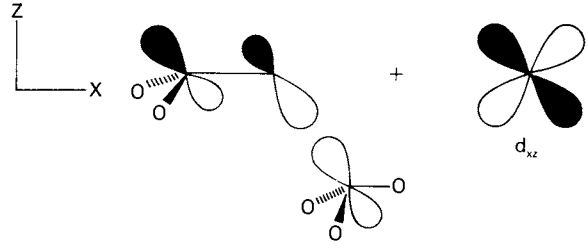


FIGURE 1a

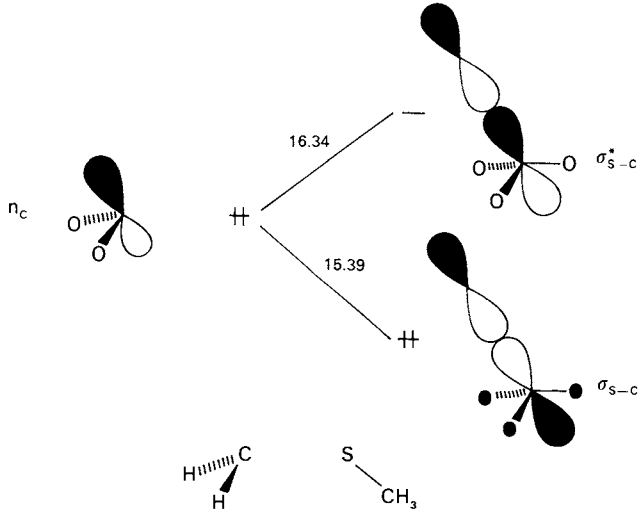
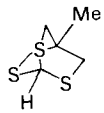


FIGURE 1b

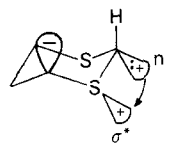
FIGURE 2



(2)

$HC(SEt)_2$

(3)



withdrawing effect of each of these groups can be seen comparatively from the data of pK_a values of substituted benzoic acids, shown in Tables 1 and 2.

Unfortunately, these data were not obtained under the same conditions. However, one can safely conclude that the sulfonio group ($-{}^+SR_2$) is the most electron-withdrawing, followed by the sulfonyl group ($-SO_2-$), and the least electron-withdrawing is the sulfinyl group (—SO—). The sulfonio group is more electron-withdrawing than the ammonio group ($-{}^+NR_3$).

There are also data on pK_a values of various substituted phenols, as shown in Table 3. The electron-withdrawing effect of the ammonio group is due only to its inductive effect and this can be seen in the higher acidity of the *m*-substituted compared with the *p*-substituted phenol; the value of $\sigma_p-\sigma_m$ is negative, -0.08. In contrast, all the tricoordinate and tetracoordinate sulfur groups exert a stronger electron-withdrawing effect from the *p*-position than from the *m*-position, as is evident from the positive values of $\sigma_p-\sigma_m$. This is the same trend as in the acid dissociations of nitrophenols, in which $\sigma_p-\sigma_m$ is $+0.53$. Obviously *p*-substituted sulfur-containing groups can conjugate with the phenolate ion by

TABLE 1. pK_a values of substituted benzoic acids in 50% ethanol at 25 °C

Substituent	pK_a	σ	Reference
H	5.73	0.00	21
p-NO_2	4.53	0.82	22
m-NO_2	4.66	0.72	22
p-$(CH_3)_3N^+$	4.42	0.88	23
m-$(CH_3)_3N^+$	4.22	1.02	23
p-CH_3SO_2	4.68	0.75	21, 24
m-CH_3SO_2	4.78	0.65	21, 24
p-CH_3SO	5.01	0.51	24, 25
m-CH_3SO	4.90	0.48	24, 25
p-C_6H_5SO	4.97	0.47	26
p-$C_6H_5SO_2$	4.63	0.70	26

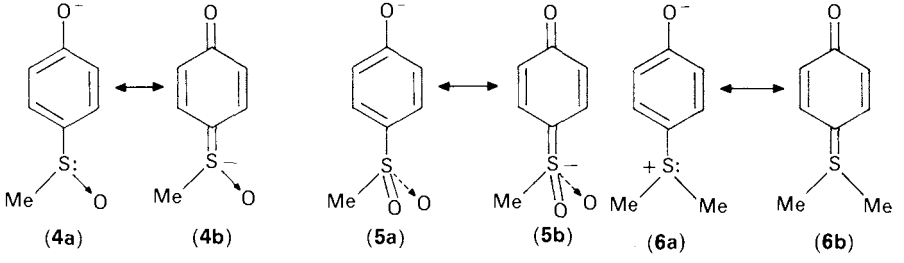
TABLE 2. pK_a values of *p*- and *m*-sulfonio- and sulfonyl-benzoic acids in water at 25 °C

Substituent	pK_a	σ	$\sigma_m-\sigma_p$	Reference
p-$(CH_3)_2S^+$	3.27	0.90		23
m-$(CH_3)_2S^+$	3.22	1.00	+0.10	23
m-CH_3SO_2	3.52	0.56		27
p-CH_3SO_2	3.64	0.68	+0.10	27

TABLE 3. pK_a values of substituted phenols in water at 25 °C

Substituent	pK_a	σ	$\sigma_p-\sigma_m$	Reference
m-CH_3SO	8.75	0.53		25
p-CH_3SO	8.28	0.73	+0.20	25
m-CH_3SO_2	8.40	0.70		21
p-CH_3SO_2	7.83	0.98	+0.28	21
m-$(CH_3)_2S^+$	7.67	1.00		25, 28
p-$(CH_3)_2S^+$	7.30	1.16	+0.16	25, 28
m-$(CH_3)_3N^+$	8.03	0.84		25, 28
p-$(CH_3)_3N^+$	8.35	0.76	−0.08	25, 28

resonance with the electron-withdrawing 3d orbital of sulfur, as illustrated by **4b**, **5b** and **6b**.



Although there has been some controversy related to the 3d-orbital resonance effect of sulfur-containing groups, these observations seem to support the conclusion that the 3d-orbital resonance with a sulfur atom becomes stronger as the positive charge on the sulfur atom increases, as suggested earlier[29]. The partial π-bond character of S—O linkage in sulfinyl and sulfonyl functions also seems to be in line with this argument[30]. Stereoangular nonsensitivity of the 2p–3d orbital overlap in forming the π-bond, suggested by Kimball[31], was also verified by subsequent work of Kloosterziel and Backer[32]. Generally, the additivity rule is valid for the Hammett σ-values if there is no steric inhibition of resonance. For example, the observed Σσ-value for 4-cyano-3,5-dimethyl calculated from the pK_a of phenol **7** is 0.79, which is in very good agreement with the calculated value (0.78). However, the Σσ-value for the 4-nitro-3,5-dimethyl groups calculated for phenol **8** is substantially different (by 0.37) from the calculated value, as shown below, obviously due to the steric inhibition of resonance interaction of the *p*-nitro group with the phenolate ion by the two *o*-methyl groups. However, in the acid dissociation of 4-methylsulfonyl-3,5-dimethylphenol **9**, both σ_{obs} and σ_{calc} are the same, indicating that there is no steric inhibition of resonance in the electron-accepting conjugation of the methylsulfonyl group with the phenolate ion. A similar nonsensitivity to steric inhibition of resonance is found in the pK_a values and σ values of 4-hydroxyphenyl sulfoxides and sulfones, as shown in Table 4. Similarly, there is no evidence for steric inhibition of resonance in the acid dissociations of substituted sulfoniophenols, as shown in Table 5. A similar phenomenon may be seen in the acid dissociations of 3,5-dichloro- and 3,5-dibromo-4-dimethylsulfoniophenols **10a** and **10b** and 3-methyl-4-dimethylsulfoniophenol **10c**, as observed in the data listed in Table 5[25,35].

TABLE 4. First pK_a values of bis(4-hydroxyphenyl)sulfoxides in 50% water–ethanol at 25 °C and related Hammett σ-values (after Reference 33)

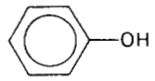
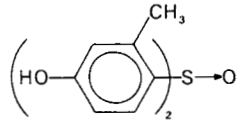
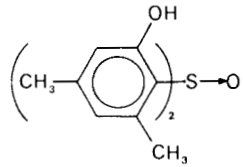
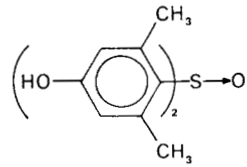
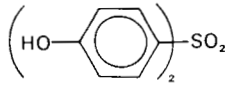
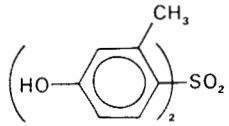
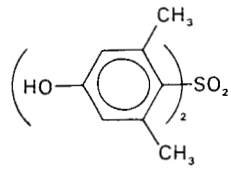
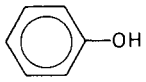
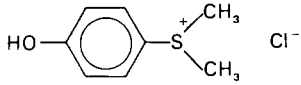
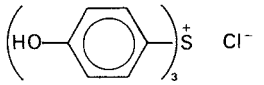
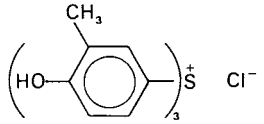
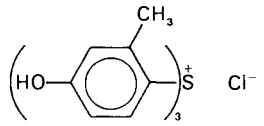
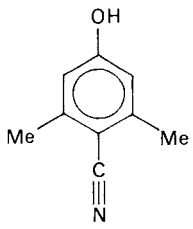
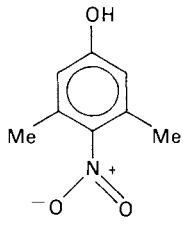
Phenol	pK_a	σ_{obs}	σ_{calc}
	11.22	0	
	9.09	0.78	
	9.28	0.71	0.71
	9.14		
	9.57	0.61	0.64
	8.52	0.99	
	8.77	0.90	0.92
	9.02	0.81	0.85

TABLE 5. First pK_a values of *p*-substituted sulfoniophenols in 39.93% ethanol at 25 °C and related Hammett σ-values (after Reference 34)

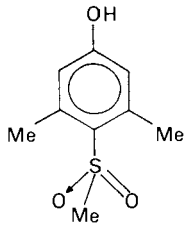
Phenol	pK_m	σ_{obs}	σ_{calc}
	10.59		
	7.72	1.19	
	7.02	1.48	
	7.39	1.32	1.34
	7.11	1.44	1.45



(7)

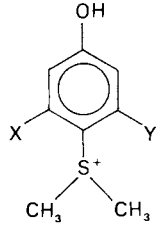


(8)



(9)

pK_a	8.21	8.25	8.13
σ_{obs}	0.79	0.77	0.83
σ_{calc}	0.78	1.14	0.83



(**10**) (**a**) X = Y = Cl
(**b**) X = Y = Br
(**c**) X = CH_3, Y = H

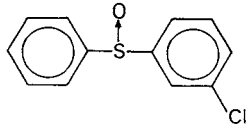
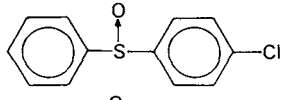
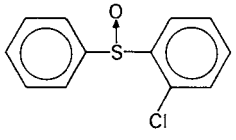
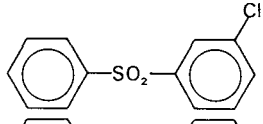
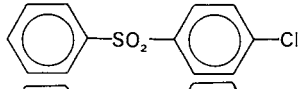
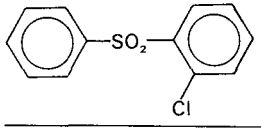
Electron-accepting conjugative effects of sulfinyl and sulfonio groups may be seen in a few experimental observations. For example, it was reported twenty years ago that *p*-iodophenyl sulfoxide reacted readily with alkali hydroxide whereas the *m*-isomer did not react under the same conditions[36]. More recent quantitative data on the electron-accepting effects of these tri- and tetra-coordinated sulfur-containing groups can be found in the quantitative data on reactivities, listed in Table 6.

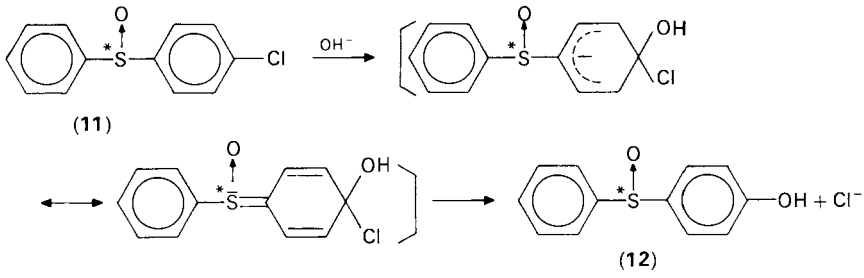
A *p*-$PhSO_2$ group enhances the electrophilic reactivity of chlorobenzene towards KOH far more than a *p*-PhSO group, and the *p*-isomer is much more reactive than the *m*-isomer in each group.

One interesting observation in this connection is that the *p*-sulfinylphenol **12** formed in the reaction of the optically active *p*-sulfinylchlorobenzene **11** with hydroxide ion was found to have retained completely the optical activity. This means that the electron-accepting conjugative interaction of the sulfinyl group with the benzene ring does not require any coplanarity with the latter, as has been suggested from the nonstereosensitivity of 3d-orbital resonance with sulfur-containing groups.

The electron-accepting conjugative effect of the sulfonio group is far greater than that of the sulfonyl group and even exceeds that of the nitro group, as can be observed from the

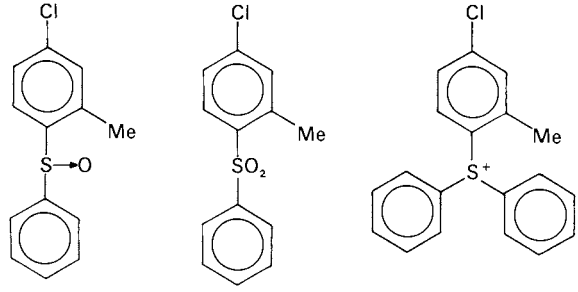
TABLE 6. Reactivities of *m*- and *p*-sulfur-containing substituted chlorobenzenes with KOH in 2:1 v/v DMSO–water (after Reference 36)

Compound	Relative reactivity	Relative reactivities of *o*-, *m*- and *p*-isomers of each group
	1	1
	81	81
	66	66
	450	1
	9,000	20
	4,600	10



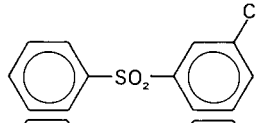
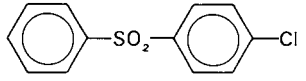
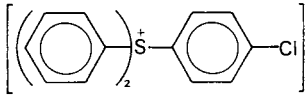
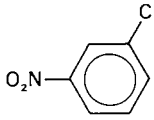
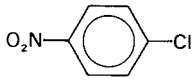
(11) (12)

data shown in Table 7. One *ortho* methyl group did not decrease appreciably the reactivities of phenylsulfinyl-, phenylsulfonyl- and diphenylsulfonio-chlorobenzenes, **15**, **16** and **17**, in their ethanolyses. The relative reactivities are 1/1.2 for **15/11**, 1/1.9 for **16/13**

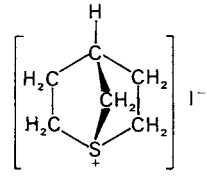


(15) (16) (17)

TABLE 7. Relative reactivities of *p*-substituted chlorobenzenes with KOH in 70% ethanol–water at 105 °C (after Reference 37)

Compound		Relative reactivity
		1
	(13)	24
	ClO_4^- (14)	8,215
		41
		2,600

and 1/1.8 for **17/14**, revealing clearly that the electron-accepting conjugative resonance interaction of these sulfur-containing groups does not suffer from steric inhibition to conjugative interaction by the *o*-methyl group[37]. A similar nonstereosensitivity for resonance was observed earlier in the relatively facile base-catalyzed H/D exchange of the bicyclic sulfonium compound **18** in D_2O, shown by Doering and Hoffmann[38]. There have been data on carbon acidities of various polysubstituted carbonyl-, cyano- and sulfonyl-methanes, as listed in Table 8.



(18)

Unlike the carbonyl group but similar to a cyano group, the sulfonyl group does not seem to suffer any steric hindrance of resonance, as exemplified by the smooth logarithmic increase in K_a values from the disulfonyl-substituted compound to the trisubstituted compound, despite the relatively large size of a methylsulfonyl compared to a carbonyl group. The markedly lower acidity of the bicyclic trisulfone is obviously due to the negative field effect of the six oxygen atoms sticking up on the same side of the *p*-orbital of the carbanion.

pK_a values of various sulfonylmethanes in DMSO, measured by Bordwell and coworkers[41-43] also revealed that the electron-accepting conjugative effect of a $PhSO_2$ group is nearly of the same order as that of a cyano group, as shown in Table 9. The

TABLE 8. Acid dissociation constants of α-substituted methanes at 25 °C in water (after References 28 and 39)

Compound	K_a	Compound	K_a
CH_3COCH_3	10^{-22}	$CH_3SO_2CH_3$	10^{-23}
$CH_2(COCH_3)_2$	1.0×10^{-9}	$CH_2(SO_2CH_3)_2$	1×10^{-14}
$CH(COCH_3)_3$	1.4×10^{-6}	$CH(SO_2CH_3)_3$	strong acid ($pK_a < 1$)
CH_3CN	10^{-25}	$HC(SO_2CH_2)_3CCH_3$	1.48×10^{-5}
$CH_2(CN)_2$	6.5×10^{-12}		
$CH(CN)_3$	Strong acid ($pK_a < 1$)		

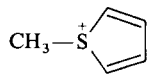
TABLE 9. pK_a values of various compounds in DMSO (after References 40–42)

Compound	pK_a	Compound	pK_a
$H_2C(CN)_2$	11.1	$PhSO_2CH_2OCH_3$	30.7
$PhSO_2CH_2CN$	12.0	$CH_3SO_2CH_3$	31.1
$PhSO_2CH_2SCH_3$	23.4	CH_3CN	31.3
$PhSO_2CH_3$	29.0	CH_3SOCH_3	35.1

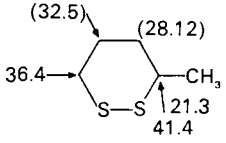
electron-accepting conjugative effect of a CH_3SO group is markedly lower (reflected by 4 pK_a units difference than that of a CH_3SO_2 group).

Unfortunately there are no measured pK_a values of sulfimido or sulfoximido substituted carboxylic acid or phenol for comparison with the effects of sulfinyl and sulfonyl groups, however, the NMR chemical shifts of the methylene protons of sulfilimine and sulfoximine have been compared and some representative data are listed in Table 10. In general, the proton signal of a methylene group attached to an electron-withdrawing group is shifted toward a lower field. However, despite the lower electron-withdrawing nature of an —S(O)—S— compared with an $—SO_2—S—$ group, the methyl proton in $—S(O)—SCH_3$ is shifted more to a lower field, i.e., by 2.67 ppm, than that in an $—SO_2—SCH_3$ group (i.e., by 2.60 ppm). Similar phenomena were observed for the two protons at α and β positions of the ethyl group in compounds **19–21**, and also in their ^{13}C NMR chemical shifts. By such comparisons of their ^{13}C chemical shifts the structures of four different oxidation products of 3-methyl-1,2-dithian **22**, namely **23–26**, can be elucidated[45].

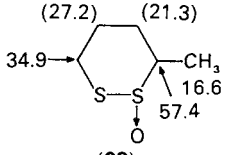
TABLE 10. NMR chemical shifts of methyl protons of various organosulfur compounds (after References 43 and 44)

Compound	δ (ppm)	Compound	δ (ppm)
$CH_3SCH_2SCH_3$	2.05	$CH_3SO_2SCH_3$	3.17
CH_3SCH_3	2.06	O ↑	
$(CH_3S)_3CH$	2.16	$CH_3SSO_2CH_3$	3.17
CH_3SSCH_3	2.30		
$CH_3SC_6H_5$	2.43		3.21
O ↑			
CH_3SOCH_3	2.46	$(CH_3)_2S^+—H\,SbCl_6^-$	3.27
$CH_3SO_2SCH_3$	2.60	$(CH_3)_2S^+—OCH_3\,ClO_4^-$	3.42
O ↑		O ↑	
CH_3SSCH_3	2.67	$(CH_3)_2S=NTs$	3.45
CH_3SO_2H	2.7	O ↑	
O ↑		$CH_3SF_2CF_3$	4.09
$CH_3SSO_2CH_3$	2.85	$(CH_3)_2S^+—OCH_3\,ClO_4^-$	4.25
$CH_3SO_2CH_3$	2.85	O ↑	
$(CH_3)_2S^+—C^-(CO_2CH_3)_2$	2.89	$(CH_3)_2S^+—OAr$	4.29
CH_3SO_3H	2.90	$N(CH_3)_2$ ↑	
$CH_3SO_2OCH_3$	2.95	CH_3S^+OAr ‖ O	4.44
O ↑			
CH_3SSCH_3	3.00		
$(CH_3)_3S^+\,ClO_4^-$	3.03		
$(CH_3)_2S(NH)_2$	3.06		
$CH_3SO_2C_6H_5$	3.10		

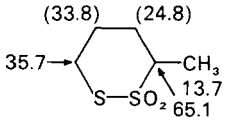
	$PhSSCH_2CH_3$ (19)		$PhS(O)SCH_2CH_3$ (20)		$PhSO_2SCH_2CH_3$ (21)	
^1H NMR δ (ppm)	2.71	1.29	3.13 3.16	1.43	3.00	1.28
^{13}C NMR δ (ppm)	32.6	14.1	27.6	15.9	30.5	14.1



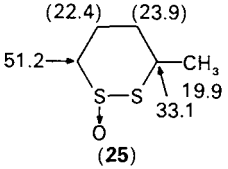
(22)



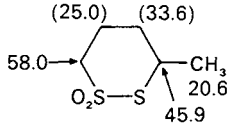
(23)



(24)



(25)

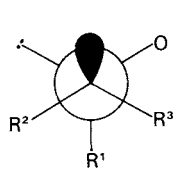


(26)

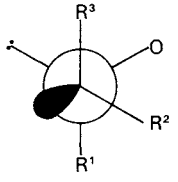
III. STEREOCHEMISTRY OF α-SULFINYL CARBANIONS

α-Sulfinyl carbanions are intrinsically diastereomeric since a chiral sulfinyl function is directly attached to the carbanionic center. Indeed, in the H/D exchange reaction of benzyl methyl sulfoxide with D_2O/NaOH the rates of H/D exchange of the two methylene protons were found to be different, pro-*R*-proton being exchanged preferentially from the *S*-chiral sulfoxide[46–49]. Conformation of the α-sulfinyl carbanion has been considered to be either pyramidal **27** or planar **28**, but always unsymmetrical. If the energy barrier for inversion of a pyramidal structure is relatively high, the asymmetry of the carbanion will be retained, whereas if the barrier for rotation around the C—S bond of the planar carbanion were relatively high, the asymmetry would also be maintained. An earlier *ab initio* MO calculation on a hypothetical molecule, the conjugate base ($^-CH_2SOH$) of hydrogen methyl sulfoxide, revealed that the most stable conformation of the carbanion is **29** in which the lone electron pair of the carbanion bisects the O—C lone pair angle and is more stable than **30** and **31** by 1.6 kcal mol^{-1} and 12 kcal mol^{-1}, respectively[50,51].

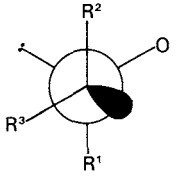
Recently, Wolfe and coworkers[50,51] recalculated the same molecule using a new 3–21G* basis set which includes the participation of 3d orbitals and revealed that the most



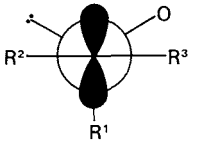
(27a)



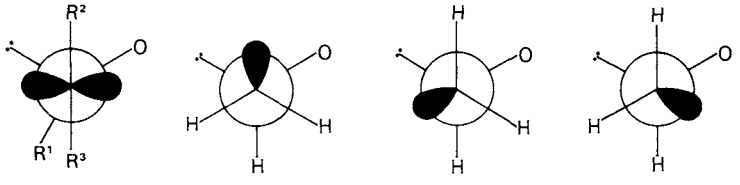
(27b)



(27c)

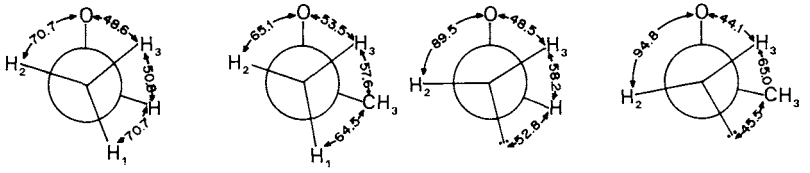


(28a)



(28b) (29) (30) (31)

stable conformation for CH_3SOH and CH_3SOCH_3 may be illustrated by the Newman projections of **32** and **33**, while those of the carbanions are given by **34** and **35**. This means that the α-sulfinyl carbanion is nonplanar and the H_1 proton on the opposite side of the S—O bond is removed preferentially. The same calculation also indicated that conformer **32** is 16.5 kcal mol^{-1}, and 17.2 kcal mol^{-1} more stable than conformers **29** and **31**, respectively[17]. This new MO calculation thus contradicts the earlier suggestion that the most stable carbanionic conformer is **29** but emphasizes the importance of the contribution of 3d-orbitals for the stabilization of α-sulfinyl carbanions.



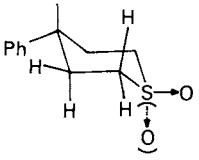
(32) (33) (34) (35)

Table 11 summarizes the relative conformation stabilities of various sulfinyl carbanions, based on the H/D exchange rates of the corresponding sulfinyl compounds **36–39**. The results are in good agreement with the order of stabilities obtained from the MO calculations using the 3–21G* basis set. This is remarkable, since the calculation did not take into consideration the solvent effect, despite the strong unsymmetrical solvation on the α-sulfinyl carbanion.

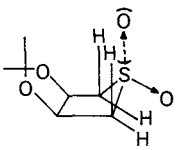
The relative ease of H/D exchange of the methylene protons of benzyl methyl sulfoxide is markedly influenced by the nature of the base and the solvent used, as shown in Table 12. The data reveal that rather high stereoselectivities can be observed when alkyllithium–THF is used.

TABLE 11. Relative stabilities derived from H/D exchange reactions of α-sulfinyl carbanions

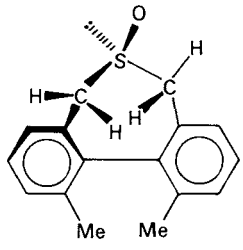
Compound	Solvent, M^+	Stability	References
$HSOCH_2^-$	Calc.	**27a** > **27b** > **27c**	50, 51
$HSOCH_2^-$	Calc.	**27b** > **27a** > **27c**	16
$CH_3SOCH_2^-$	Calc.	**27b** > **27a** > **27c**	16
36	CD_3OD, Na^+	**27b** > **27a**, **27a** > **27c**	52
	D_2O, Na^+	**27b** > **27a**, **27a** > **27c**	52
	t-BuOD, Na^+	**27a** ~ **27b** ~ **27c**	52
37	D_2O, Na^+	**27b** > **27a**	53
38	*t*-BuOD, K^+	**27a** > **27b**, **27c** > **27a**	54
	CD_3OD, Na^+	**27b** > **27a**, **27c** > **27a**	54
39	THF, *n*-BuLi	**27a** > **27b**	55



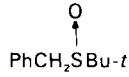
cis, trans-(**36**)



(**37**)



(**38**)



(**39**)

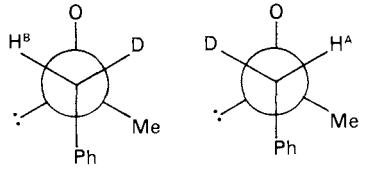
TABLE 12. Relative rates of H/D exchange of the diastereotopic protons in benzyl methyl sulfoxide and relative amount of **40** and **41** formed upon quenching of α-lithiobenzyl ethyl sulfone with D_2O (after Reference 56)

Solvent/base	Temp. (°C)	Relative rate H^A (Relative amounts) (**40**)	H^B (**41**)
D_2O/NaOD	24	14.2	1
CD_3OD/CD_3ONa	24	5.5	1
t-BuOD/*t*-BuONa	24	0.50	1
t-BuOD/*t*-BuOLi	24	0.22	1
DMSO/MeLi	24	(1.7)	(1)
Benzene/MeLi	24	(0.11)	(1)
THF/MeLi	24	(0.13)	(1)
THF/MeLi	−60	(0.50)	(1)

TABLE 13. Reactions of α-lithiosulfoxides with some electrophiles (in THF at −60 °C) (after Reference 49)

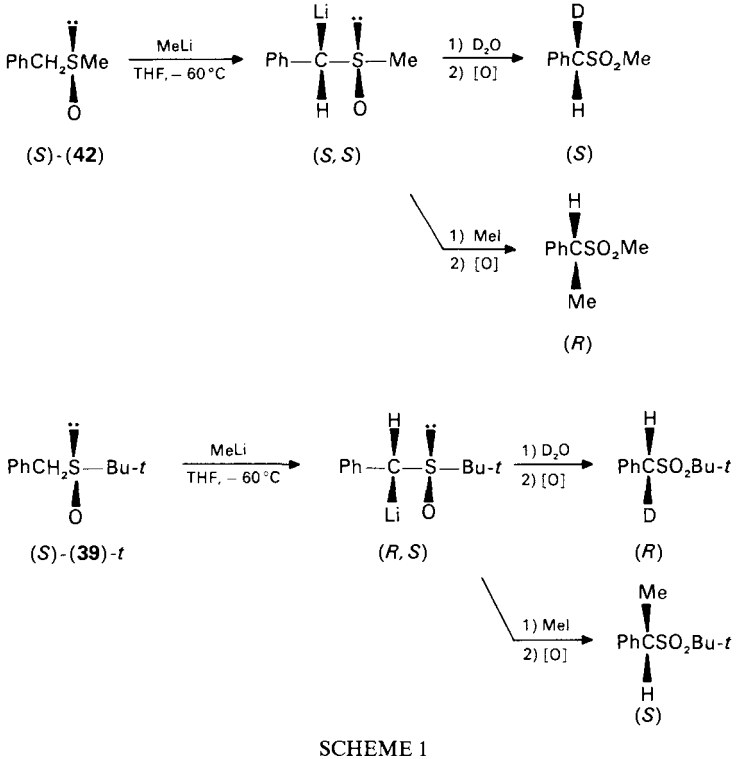
Lithiosulfoxide	Electrophile	Total yield (%)	Diastereomer ratio
$PhCH(Li)S(O)CH_3$	D_2O	85	15:1
	Acetone	75	15:1
	Cyclohexanone	72	15:1
	CH_3I	76	15:1
PhCH(Li)S(O)Bu-*t*	D_2O	90	99:1
	Acetone	77	99:1
	CH_3I	95	99:1
PhCH(Li)S(O)Ph	D_2O	80	1.5:1
	Cyclohexanone	85	1.5:1
	CH_3I	79	1.5:1
$CH_3CH(Li)S(O)Ph$	Acetone	81	13:1
	Benzophenone	73	12:1

Accordingly, there have been numerous studies on the stereochemistry of these α-sulfinyl carbanions[56–77]. Representative data on the reactions of α-lithiosulfoxides derived from benzyl sulfoxides with some electrophiles are listed in Table 13. Although the stereochemistry depends on the substituent on the sulfinyl function, the diastereomeric ratio remains the same regardless of the electrophile used for each sulfoxide.



(40) (41)

One interesting observation deduced from the data of Table 13 is that, despite the same diastereomeric ratio, the absolute configuration around the carbon atom of the major diastereomer changed with the electrophile used. In other words, the reactions of α-lithiobenzyl sulfoxides with D_2O[49,59] and its carbonylation[74] and carbonation[75] proceeded with retention of configuration, while methylation with CH_3I resulted in inversion[49,59]. The stereochemical study of these reactions was conducted with optically active benzyl sulfoxides **42** and **39** as shown in Scheme 1[49,58,60] and an interesting



SCHEME 1

TABLE 14. Diastereomeric ratios in the reaction of **44** with various electrophiles (after Reference 71)

Electrophile	Diastereomer ratio	
D_2O, CH_3OD or CH_3COOD	**45/46**	1/15
EtOD		1/5
t-BuOD		1/3
$CF_3COO^-NEt_3D^+$		1/2
D^+-sponge		1/1
MeI	**47/48**	19/1
$(MeO)_3PO$		1/1.5

question is how the stereochemical course of the substitution on the central carbon of the carbanion is controlled during these reactions. The effect of added lithium salt and that of strong solvating solvents on the stereoselectivity were therefore examined[61,65].

Recently, Marquet and coworkers[70] and Biellmann and Vicens[71] have shown independently that the sulfinyl-stabilized carbanion may be best described by sp^2 planar structure, chelated by the Li^+ ion, as illustrated by **43**. Very recently, the crystal structure of the 2:2 complex of lithiated α-phenylethyl phenyl sulfoxide with tetramethylethylenediamine has been shown to be dimeric, and each of the two lithium atoms to be chelated by two sulfinyl oxygen atoms and two diethylamino nitrogen atoms (Figure 3)[72]. This could be true only in the crystalline form, where there is chelation of two fairly strong nucleophiles. How this would effect the stereochemistry of the reaction with electrophiles is still unknown. The diastereomeric ratios in the reactions of α-lithiobenzyl methyl sulfoxide **44** with various electrophiles are listed in Table 14. One finds immediately that the stereoselectivity depends on the electron-donating ability of the electrophile used. For example, in the reaction of **44** with D_2O, which is an electron-donating solvent, D_2O would attack from the side of the lithium ion, while attack by CH_3I, which possesses a rather poor electron-donating ability, would be from the sterically unhindered and less solvated opposite site[71] (Figure 4). When the methylating reagent was $(CH_3O)_3PO$, which has a P—O linkage that can chelate strongly with the Li^+ ion, formation of compound **48** increased substantially, supporting the above argument[71]. Meanwhile, Marquet and

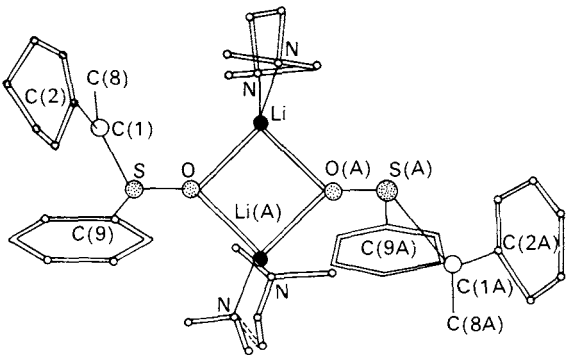


FIGURE 3

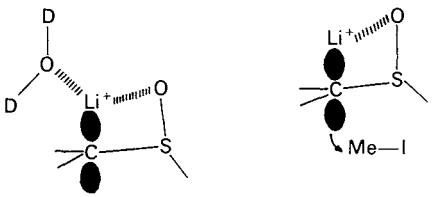


FIGURE 4

coworkers[70] also demonstrated that methylation of α-lithiated derivatives of *cis* and *trans*-4-*t*-butylthiacyclohexanes **49** and **52** proceeded similarly. The methylation of **50** with MeI took place mainly at the equatorial position, while that of **53** was mainly at the axial position (Table 15). The stereochemistry of methylation of these lithioderivatives was entirely opposite. All these observations suggest that such reactions proceed through a planar carbanion intermediate **43** which, upon reacting with $(CH_3O)_3PO$, would reach the transition state, shown in Figure 5, by chelating with the Li^+ ion. Such a chelated structure is in line with the results of Wolfe and coworkers[17], MO calculation using the 3–32G* basis set. According to their calculation, the lithium bridged structure **55** is the most stable, being 38.7 kcal mol^{-1} more stable than the structure **56** in which the Li^+ ion is

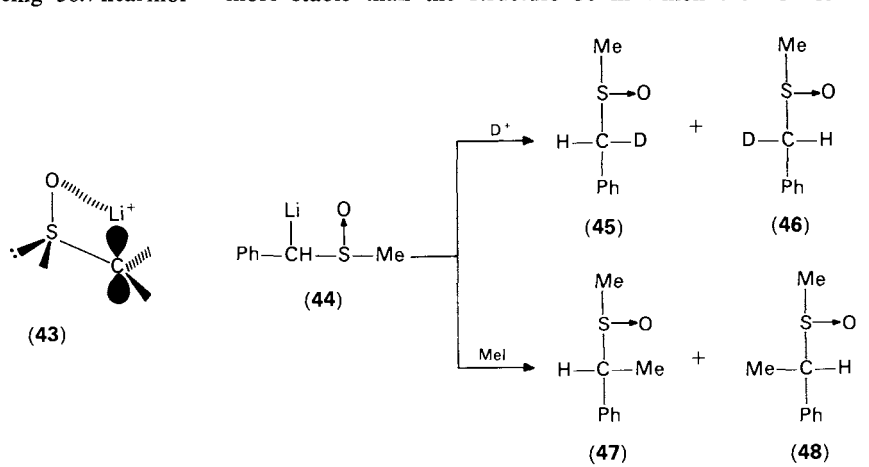


TABLE 15. Methylation of **50** and **53** at 20 °C (after Reference 70)

Alkylating agent	Medium	Ratio[a] **51a** / **51e**	Ratio[a] **54a** / **54e**
CH_3I	THF	20 / 80	100 / 0
$(CH_3O)_3PO$	THF	93 / 7	30 / 70
$(CH_3O)_3PO$	THF + 10 eq $LiClO_4$	40 / 60	92 / 8

[a]Isomer ratios were determined by GLC. The amount of α,α′-dimethyl derivative in these reactions was always less than 10%.

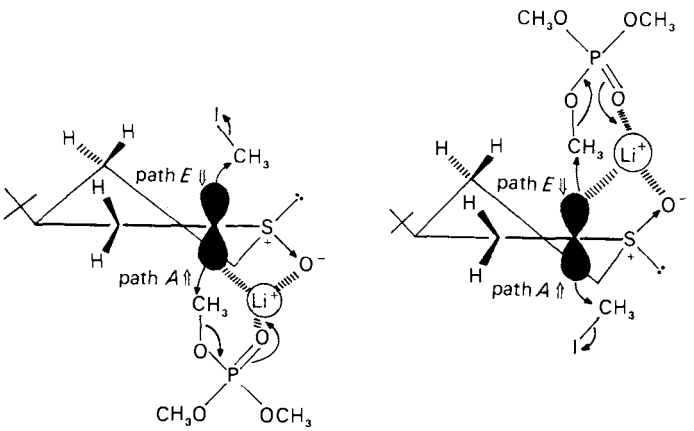
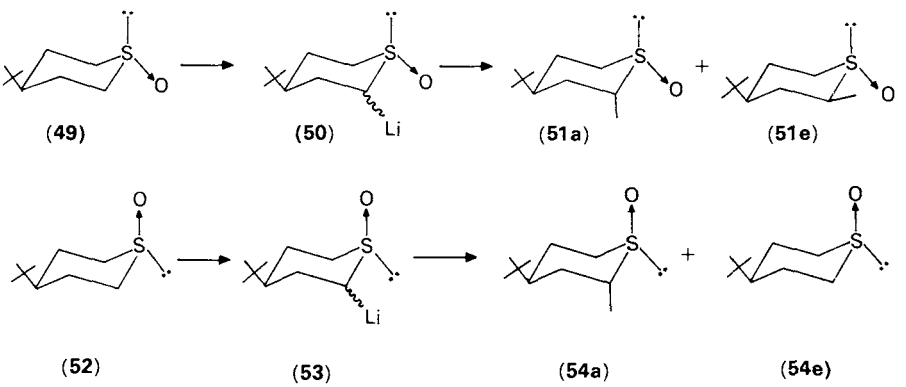
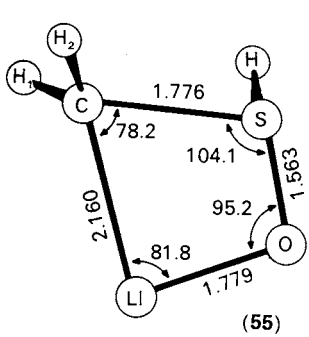


FIGURE 5

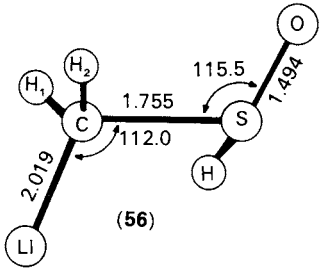
antiperiplanar to the S—O bond and 40 kcal.mol^{-1} more stable than structure **57**, in which the Li^+ ion is gauche to the S—O linkage. One interesting outcome of the calculation is that a second lithium ion is chelated to the sulfinyl oxygen atom and the C—Li bond is located at an antiperiplanar arrangement to the S—O bond in the most stable structure **58**. Therefore, with an excess of the Li^+ ion, the stereochemical behavior of the α-lithiated sulfoxide resembles that of the α-sulfinyl carbanion.



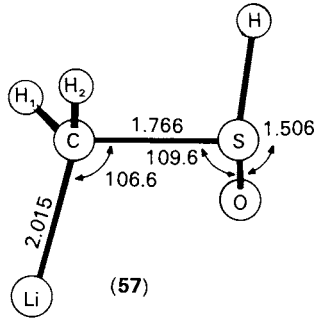
^1H and ^{13}C NMR spectra of α-lithiated sulfoxides suggest that the substituents at the α-carbon atom assume a planar sp^2 geometry[68,69,73]. However, there have been a few experimental observations which contradict this conclusion[76,77]. For example, the reaction of α-lithiothiane 1-oxide **59a** with oxirane gave mainly *trans*-2-(2-hydroxyethyl)-thiane 1-oxide **60a**, whereas a 9:1 *cis-trans* ratio of **60b** was obtained in the reaction of α-lithiothiane 1-oxide with the oxirane[76]. Furthermore, on methylation of α-lithiothiepane 1-oxide and α-lithiothiocane 1-oxide with methyl iodide, the *cis*-methylated products were the products formed in 15:1 and 5:1 excess, respectively, over the *trans* isomers[77]. If the α-lithiated sulfoxide would have the planar structure, such distinctive changes in stereoselectivity would not be expected.



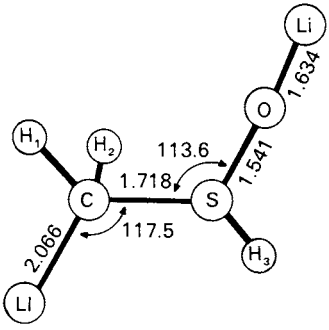
(55)



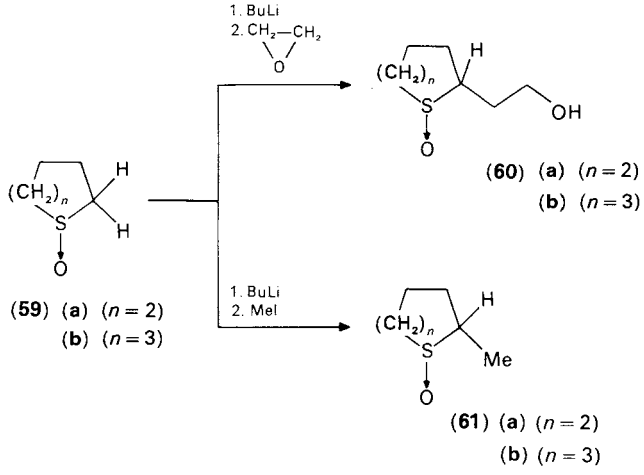
(56)



(57)



(58)



(59) (a) ($n = 2$)
(b) ($n = 3$)

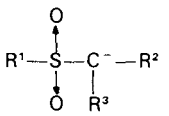
(60) (a) ($n = 2$)
(b) ($n = 3$)

(61) (a) ($n = 2$)
(b) ($n = 3$)

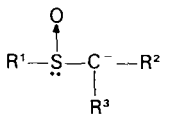
IV. STEREOCHEMISTRY OF α-SULFONYL CARBANIONS

Sulfur-containing groups at an α-position stabilize carbanions. All these species, i.e., the α-sulfonyl **62**[81–102], α-sulfinyl **63**[46–80], α-sulfenyl **64**[5,103,104] and α-sulfonio carbanions **65**[105–113], and those derived from sulfonates **66** and sulfonamides **67**[95] may retain their

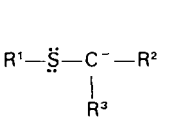
chirality during their reactions which usually end up with racemization. Especially noticeable is the remarkable stability of α-sulfonyl carbanions which retain the original configuration in reactions with electrophiles even when a typically racemizing solvent, such as DMSO, is used. For these sterically stable α-sulfur-containing substituted carbanions, two configurations are conceivable. One is a pyramidal (sp^3) structure **68** (of which the gauche form is believed to be the most stable) and the other is planar (sp^2) **69**. Racemization of the pyramidal form **68** is due to rotation around the C—S bond **68a** → **68b** followed by pyramidal inversion **68b** → **68c**, while that of the planar form **69** is caused by rotation around the C—S bond **69a** → **69b** → **69c**. In all these α-sulfur-stabilized carbanions **62–67**, both rotation around the C—S bond and pyramidal inversion should have fairly high energy barriers.



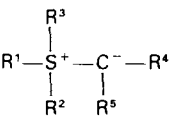
(62)



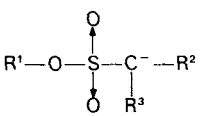
(63)



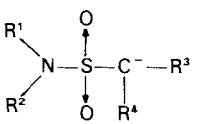
(64)



(65)

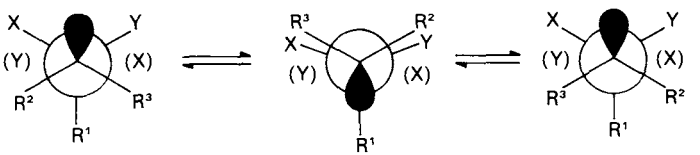


(66)



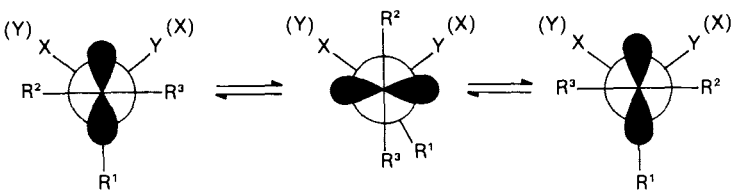
(67)

Pyramidal (sp^3) form



(68a) (68b) (68c)

Planar (sp^2) form



(69a) (69b) (69c)

Sulfonyl compound X = O, Y = O

Sulfinyl compound X = O, Y = :

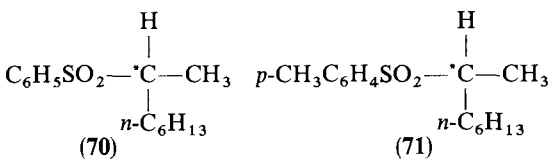
Sulfenyl compound X = :, Y = :

Sulfonium compound X = :, Y = R, Ar

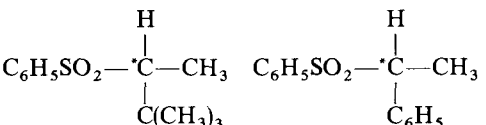
One commonly used procedure for studying the steric stability of the carbanion is comparison of the rate of base-catalyzed H/D exchange reaction (k_{ex}) on the chiral carbon with the rate of racemization (k_{rac}). By this comparison, inversion, racemization or

isoracemization can be detected. (1) When $k_{ex}/k_{rac} \gg 1$, the reaction should proceed through an intrinsically asymmetric carbanion and lead to retention of configuration. (2) When $k_{ex}/k_{rac} = 1$, the reaction proceeds through a symmetric carbanion and racemization is the net result[100]. It was found that in all the H/D exchange reactions, involving **62–67**, k_{ex}/k_{rac} was much larger than 1.

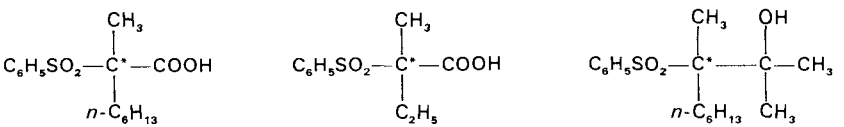
Some representative data on base-catalyzed H/D exchange reactions of several optically active sulfonyl compounds **70–73** are listed in Table 16. In all these reactions, $k_{ex}/k_{rac} \geqslant 10$. This means that the central carbon atoms of these intermediary α-sulfonyl carbanions retained to a large extent their steric configurations throughout the electrophilic substitutions. The decarboxylation of compounds **74** and **75** and the deacetonization of compound **76** were also shown to proceed with retention of configuration[86–89]. Although the stereoselectivity varied somewhat with the nature of the base and the solvent used for the reaction, the steric stability of the α-sulfonyl carbanion is in general much higher than that of the α-sulfinyl carbanion, which is somewhat vulnerable to the change of base and



(70) **(71)**



(72) **(73)**

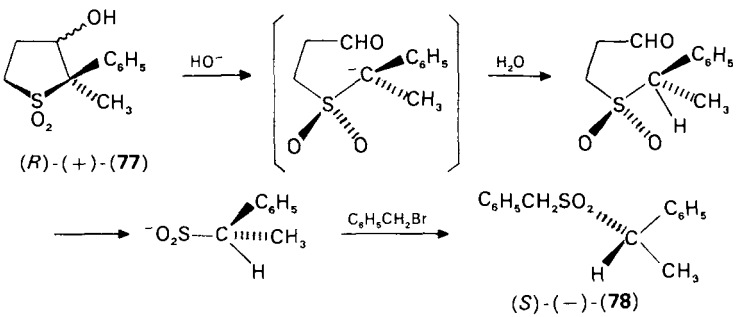


(74) **(75)** **(76)**

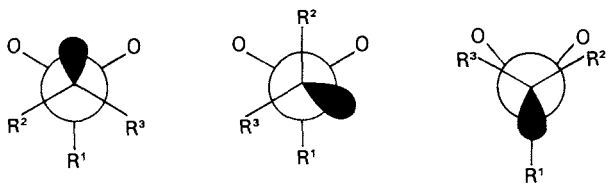
TABLE 16. Base-catalyzed H/D exchange reactions of sulfonyl compounds **70–73**

Compound	Solvent/base	Temp. (°C)	k_{ex}/k_{rac}	Ref.
70-d	CH_3OH/CH_3OK	100.6	10	81
70-d	CH_3OH/CH_3ONa	100	17	82
70-h	C_2H_5OD–D_2O	72	41	83
70-d	$(CH_3)_2SO$–CH_3OH/CH_3OK	25	10	81
70-h	$DOCH_2CH_2OD/DOCH_2CH_2OK$	100.6	14.5	81
70-d	$HOCH_2CH_2OH/HOCH_2CH_2OK$	100.6	32	81
70-d	$(CH_3)_3COH/(CH_3)_4NOH$	25	22–64	81
70-d	$(CH_3)_3COH/(CH_3)_3COK$	25	139–1980	81
71-d	CH_3OH/CH_3ONa	100	14	82
72-h	C_2H_5OD–D_2O	72	58	84
73-h	C_2H_5OD–D_2O	72	44	85

solvent. The intermediary α-sulfonyl carbanion apparently requires rather high energies both for rotation and for pyramidal inversion, regardless whether it is planar or pyramidal, thus affording the products with retention of configuration. This question then arises what would be the most stable configuration for the asymmetric α-sulfonyl carbanion. Earlier, Cram and Wingrove[87] considered that the most stable configuration of the α-sulfonyl carbanion is a pyramidal sp^3 hybrid structure, as shown by **79b** in which the lone electron pair on carbon atom lies anti to the S—O polar linkage, to avoid the electrostatic repulsion[87], though this contradicts the later preliminary *ab initio* calculation[4] which indicates the importance of the gauche interaction[88] favoring **79a** which is more stable than **79b**. Meanwhile, the base-catalyzed retro-aldol cleavage reaction of optically active 3-hydroxy-2-methyl-2-phenylthiolane 1,1-dioxide **77** was shown to proceed with 90–100% inversion of configuration[90]. This means that protonation took place from the same side as the two oxygen atoms of the adjacent SO_2 group. This stereospecificity may be due either to hydrogen-bonding between the protic solvent and the sulfonyl oxygen[90], or to the shielding of the *anti*-side of the S—O linkage of the carbanion by the leaving formyl group[80]. If the latter explanation accounts for the stereospecificity, the decarboxylation of compound **74** should also give the inverted product, because of the effective shielding by the leaving CO_2. However, the product was found to be formed with a 85–97% retention of configuration[86,87]. For formation of the inverted product, the pyramidal carbanion could have undergone fast pyramidal inversion to conformation **79a** or the reaction would have proceeded through formation of the unsymmetrically solvated planar carbanion **80a**[86].

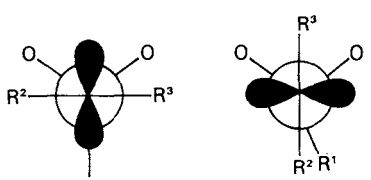


Pyramidal (sp^3) conformation (unsymmetrical)



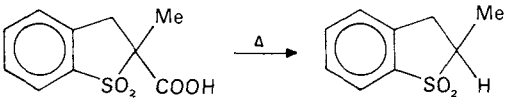
(79a) **(79b)** **(79c)**

Planar (sp^2) conformation (symmetrical)

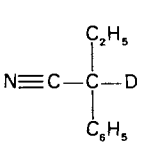


(80a) **(80b)**

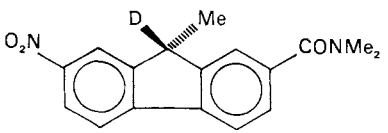
There has been an example in which decarboxylation of optically active cyclic sulfone gave completely racemic sulfone, i.e. the decarboxylation of **81** to afford **82** reported by Corey and colleagues[84] who assumed that the intermediary carbanion is planar. Meanwhile, Cram and Whitney[91] further extended their studies on the decarboxylation of the same compound and found that decarboxylation with a small amount of base in *t*-butanol proceeded with retention of configuration, that in ethylene gycol inversion was the main outcome, while in DMSO the reaction proceeded with racemization to afford **82**. Unlike the sulfones **70–73**, the base-catalyzed H/D exchange of sulfone **82** gave k_{ex}/k_{rac} values in the range 0.64–0.73; the rate of inversion is faster than that of exchange. In this reaction the cyclic carbanion formed from **82** is considered to be either planar or nearly planar, since in the reactions of **83** and **84** which would give planar or nearly planar carbanions, $k_{ex}/k_{rac} < 1$. It was suggested that the ring system enforces a conformation which destroys the electrostatic driving force for generating a pyramidal carbanion.



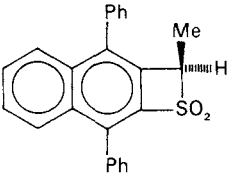
(81) (82)



(83)



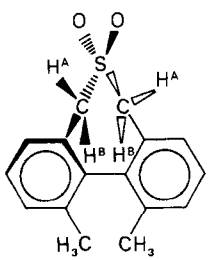
(84)



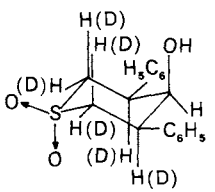
(85)

In the base-catalyzed H/D exchange of the four-membered cyclic sulfone **85**, the rate of exchange is slightly higher than that of racemization and the carbanion formed was also considered to be planar[101].

Fraser and Schuber[93] determined the rate constants, k_A and k_B, for the base-catalyzed H/D exchange of H_A and H_B protons of sulfone **86** and estimated the difference in the free energies of activation for **79a** and **79b** to be < 1.2 kcal mol^{-1}, based on the k_A/k_B value of 3 ± 0.5. In the base-catalyzed H/D exchange of **87**, $k_e/k_a = 1.6$, where k_e and k_a are the rate constants of H/D exchange of H_e and H_a, respectively. Based on the small k_e/k_a value, Brown and colleagues[94] suggested that if the carbanion is pyramidal, the steric stabilities of **79a** and **79b** are almost identical. Meanwhile, based on their ^{13}C-NMR study Chassaing and Marquet[73] proposed that the hybridization of the carbon atom of the sulfonyl carbanion, $PhSO_2CH_2^-$, would be between sp^2 and sp^3.



(86)



(87)

Earlier, Wolfe and colleagues[4] made a simple *ab initio* MO calculation of α-sulfonyl carbanion and proposed that the participation of 3d orbitals on the S atom would not contribute to its stabilization. They considered **79a** to be the most stable form, the energy difference between **79a** and **80a** being *ca.* 2.5 kcal mol^{-1} and that between **79a** and **79b** being *ca.* 4.1 kcal mol^{-1}, respectively. However, Bordwell and coworkers[102] pointed out that the minimal basis set calculation of Wolfe and colleagues may not be precise enough to discuss the small energy difference. Indeed, the recent calculation of Wolfe and colleagues on $^{-}CH_2SO_2H$, and $^{-}CH_2SO_2CH_3$ with the new 3–21G* basis set, disclosed clearly that the participation of 3d orbitals on the S atom does contribute to the stability of the α-sulfonyl carbanion[16,17].

V. REACTIONS OF α-SULFINYL CARBANIONS

Corey and Chaykovsky had discovered that dimethyl sulfoxide is converted to methylsulfinyl carbanion upon treatment with sodium hydride[114] and that this conjugate base of DMSO reacts with various electrophiles[115]. This finding has opened up various reactions with α-sulfinyl carbanions derived from sulfoxides, since the sulfinyl function can be removed either by thermolysis or by subjecting the compound to reductive desulfurization. Thus α-sulfinyl carbanions have become versatile synthetically useful reagents.

Sulfoxides (R^1—SO—R^2), which are tricoordinate sulfur compounds, are chiral when R^1 and R^2 are different, and α-sulfinyl carbanions derived from optically active sulfoxides are known to retain the chirality. Therefore, these chiral carbanions usually give products which are rich in one diastereomer upon treatment with some prochiral reagents. Thus, optically active sulfoxides have been used as versatile reagents for asymmetric syntheses of many naturally occurring products[116], since optically active α-sulfinyl carbanions can cause asymmetric induction in the C—C bond formation due to their close vicinity. In the following four subsections various reactions of α-sulfinyl carbanions are described: (A) alkylation and acylation, (B) addition to unsaturated bonds such as C=O, C=N or C≡N, (C) nucleophilic addition to α,β-unsaturated sulfoxides, and (D) reactions of allylic sulfoxides.

A. Alkylation and Acylation

Treatment of methylsulfinyl carbanion, commonly called dimsyl anion (**88**), with normal primary alkyl bromides, $CH_3(CH_2)_nCH_2Br$, gives alkyl methyl sulfoxides in excellent yields[117]. Refluxing these sulfoxides in DMSO gives generally vinylic products. However, the reaction of dimsyl anion with benzyl chloride was found not to give the corresponding sulfoxide but *trans*-stilbene, 3-phenylpropyl methyl sulfoxide and 1,2-diphenyl methyl sulfoxide[115,118]. Treatment of benzyl chloride with a strong base is known to give *trans*-stilbene[119], and hence the formation of 1,2-diphenyl methyl sulfoxide is considered to result from a further addition of dimsyl anion to *trans*-stilbene.

$$PhCH_2Cl + Na^{+}\,{}^{-}CH_2SOCH_3 \longrightarrow PhCH_2CH_2SOCH_3 + NaCl$$

(88)

$$PhCH_2CH_2SOCH_3 + Na^{+}\,{}^{-}CH_2SOCH_3 \longrightarrow PhCH{=}CH_2 + CH_3SONa + CH_3SOCH_3$$

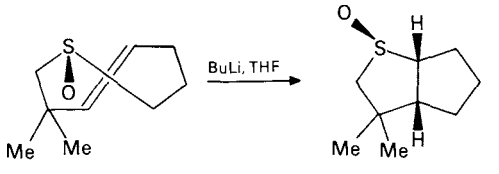
$$PhCH{=}CH_2 + Na^{+}\,{}^{-}CH_2SOCH_3 \longrightarrow Ph\bar{C}HCH_2CH_2SOCH_3\ Na^{+}$$

$$2PhCH_2Cl \xrightarrow{\text{base}} PhCH{=}CHPh$$

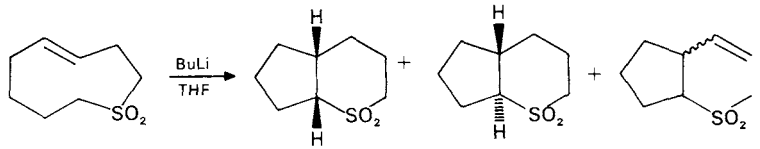
$$PhCH{=}CHPh + CH_3SONa \longrightarrow Ph\bar{C}H\underset{\displaystyle Ph}{\underset{|}{C}}HSOCH_3Na^{+}$$

In the reaction of **88** with β-phenethyl bromide, 1-phenethyl-3-phenylpropyl methyl sulfoxide and bis-3-phenylpropyl sulfoxide, besides 3-phenylpropyl methyl sulfoxide are obtained[118]. Sulfoxides, bearing a β-hydrogen to the sulfinyl function, give olefins upon thermolysis. Utilizing this reaction, Trost and Bridges[120] alkylated benzyl phenyl sulfoxide, 3,4-methylenedioxybenzyl phenyl sulfoxide, phenylthiomethyl phenyl sulfoxide, phenylsulfinylmethyl phenyl sulfoxide and cyanomethyl phenyl sulfoxide with alkyl, allyl and benzyl halides and subjected these sulfoxides to thermolysis, obtaining olefins in one-pot processes.

Dimsyl anion **88** is known to add to styrene, and to 1,1-diphenylethylene in the presence of a base, forming 3-arylpropyl methyl sulfoxides[121]. Treatment of (*E*)-3,3-dimethylthiacyclo-oct-4-ene-1-oxide **89** with *n*-BuLi gave exo-4,4-dimethyl-2-thiacyclo-[3.3.0]octane 2-oxide **90**, a bicyclic addition product of the internal double bond. A similar cyclization was observed in the reaction of **91** with *n*-BuLi[122].

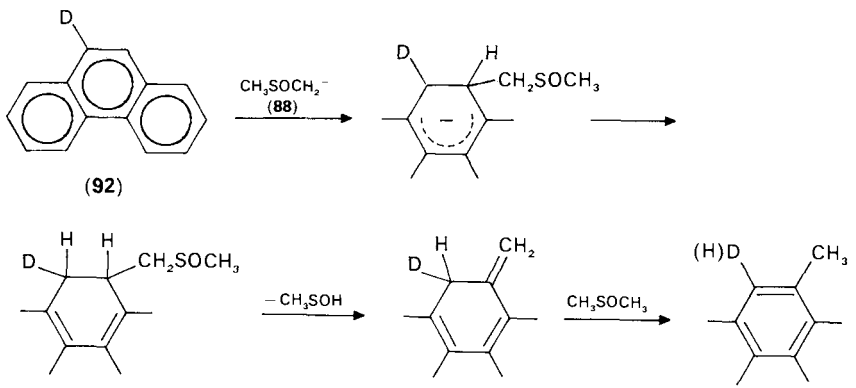


(**89**) (**90**)



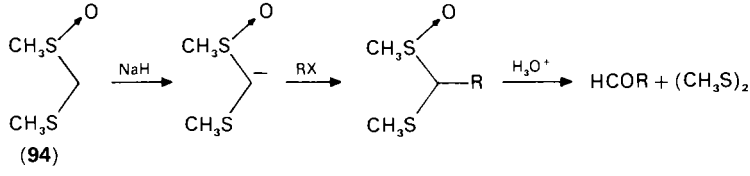
(**91**)

An interesting reaction of dimsyl anion **88** is the methylation of polyaromatic compounds. Thus naphthalene, anthracene, phenanthrene, acridine, quinoline, isoquinoline and phenanthridine were regiospecifically methylated upon treatment with potassium *t*-butoxide and DMSO in digyme or with sodium hydride in DMSO[123–125]. Since *ca.* 50% of D was found to remain in the monomethyl derivative **93** derived from 9-deuteriophenanthrene **92**, the mechanistic route shown in Scheme 2 was suggested[125].

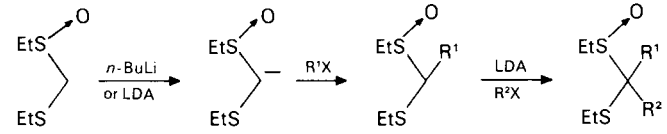


SCHEME 2

Carbanions formed from methyl methylthiomethyl sulfoxide **94** and ethyl ethylthiomethyl sulfoxide **95** were shown to be alkylated in excellent yields[126,127]. Treatment of **94** with *n*-BuLi or KH and subsequent reaction with 1, *n*-dihalo- or bis(tosyloxy)alkane gave 3-, 4-, 5- and 6-membered 1-methylsulfinyl-1-methylthiocycloalkanes[128–130]. Upon hydrolyses of these products, the corresponding aldehydes and ketones are obtained.

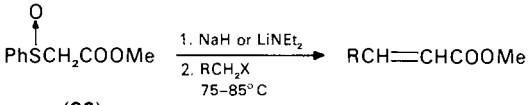


(**94**)

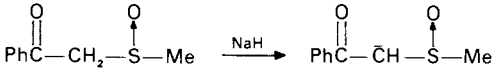


(**95**)

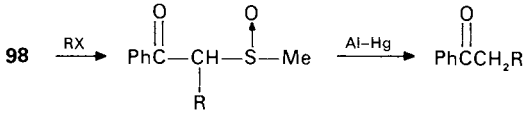
Methyl 2-phenylsulfinylacetate **96** and β-ketosulfoxides have been used for the syntheses of various ketones and derivatives of carboxylic acids[131–133]. For example, ω-(methylsulfinyl)acetophenone **97** have been converted to the corresponding ketone or to γ- and δ-ketoesters[134].

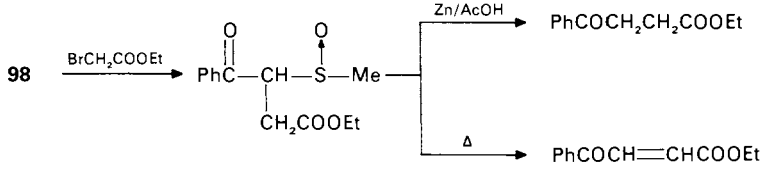


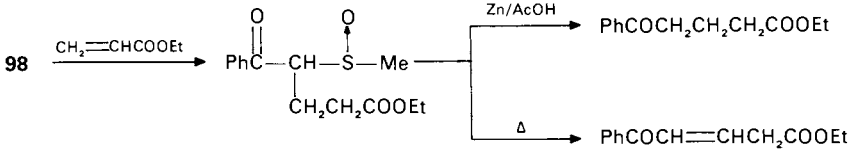
(**96**)



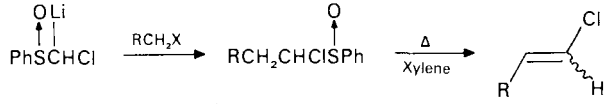
(**97**) (**98**)







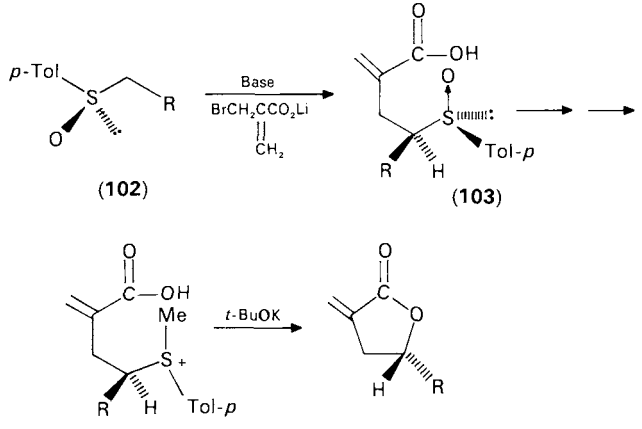
Lithiochloromethyl phenyl sulfoxide **99** was found to react with aryl or alkyl halides in the presence of one equivalent of hexamethylphosphoramide to afford alkylated products **100** in high yields[135]. Thermal decomposition of these products in the presence of a catalytic amount of hydroquinone in xylene gave the corresponding vinyl compounds **101**.



(**99**) (**100**) (**101**)

Durst and coworkers[49] found that treatment of either benzyl methyl sulfoxide or benzyl *t*-butyl sulfoxide with methyllithium gave the corresponding carbanion, which upon further treatment with D_2O or carbonyl compounds gave products with retention of configuration, while treatment with methyl iodide gave the methylated product of inverted configuration. Methylation with $(CH_3O)_3PO$ gave products with retention of configuration[61,70,71]. Biellmann and Vicens[71] and Marquet and coworkers[70] had suggested that the carbanions formed assumed planar structure **45** and that the regioselectivity depends on the electron-donating ability of the electrophile; e.g., D_2O with the nucleophilic oxygen reacts from the side of the Li, while the less nucleophilic methyl iodide attacks from the less sterically hindered side (Figure 4).

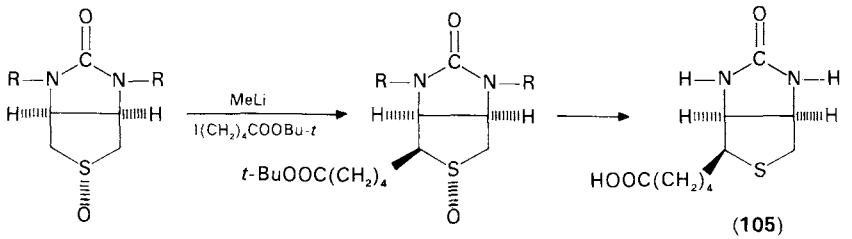
Recently, optically active (+)-(*R*)-methyl tolyl sulfoxide **102**, R = H was alkylated with a very high diastereoselectivity[136]. The sulfoxide was treated with either lithium diisopropylamide (LDA) or lithium tetramethylpiperidide (LTMP) to form the lithio-derivative, which upon subsequent reaction with lithium α-bromomethyl acrylate gave a mixture of two diastereomers of α-methylene-γ-sulfinylcarboxylic acid **103**. The use of the sterically highly hindered base, LTMP, gave the product with a higher diastereoselectivity. For example, the S_{c4}:R_{c4} ratio was 95:5 when R was the methyl group.



(**102**) (**103**)

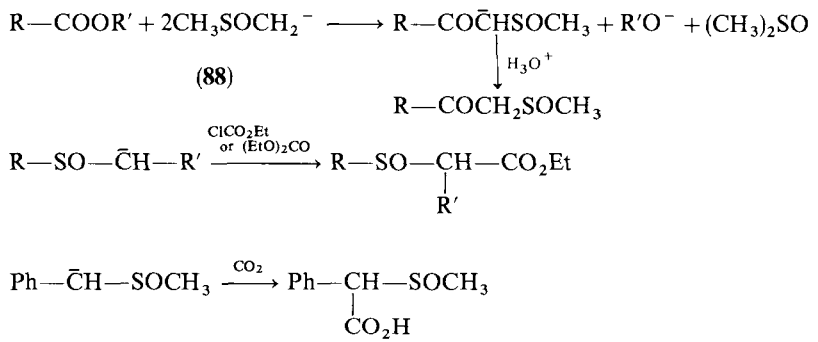
Five- and six-membered sulfoxides were shown to be alkylated with high stereoselectivities[70,76]. Marquet and coworkers[137] applied this reaction to synthesize *dl*-biotin **105** by stereoselective alkylation of sulfoxide **104**.

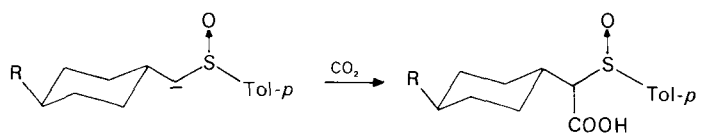
Dimsyl anion **88** reacts with esters of aromatic carboxylic acids and aliphatic acids which do not have a readily transferable proton, to give β-ketosulfoxides[114,133,138–141]. There are not many cases in which acyl chlorides were used[142,143]. However, the reaction



(104) (105)

of an α-sulfinyl carbanion with ethyl chloroformate or diethyl carbonate was found to give the corresponding α-sulfinyl esters[144]. Carbonation of α-sulfinyl carbanions afforded α-sulfinylacetic acids[75,145].

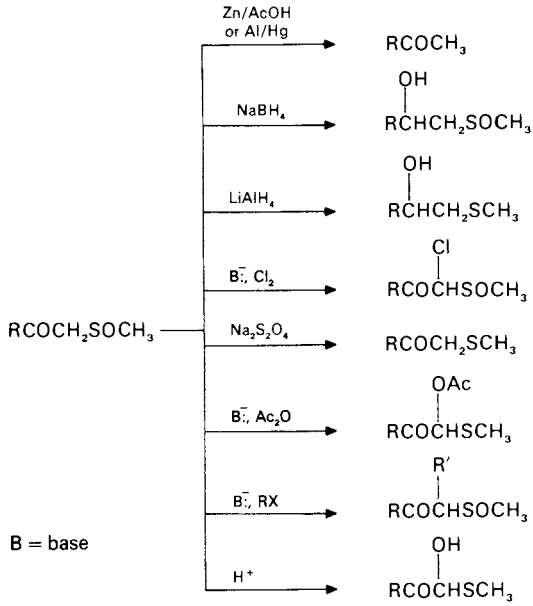




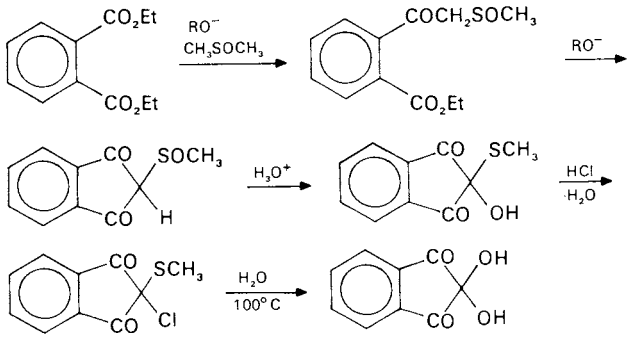
Desulfurization of β-ketosulfoxides with Zn/AcOH[134] or aluminium amalgam[133] can lead to the corresponding ketones. Other related reactions may be those shown in Scheme 3[146,147].

Russell and coworkers[147] had found that treatment of dimsyl anion **88** or of a similar methylsulfonyl carbanion with 1,2-, 1,3- and 1,4-dicarboxylic acid esters can give five- to seven-membered cyclic compounds. By this type of cyclization, they prepared ninhydrin hydrate **106** from diethyl phthalate[148,149].

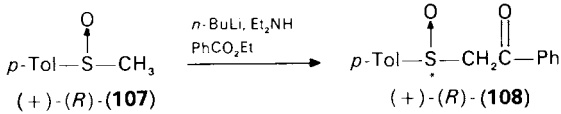
Carbanions derived from optically active sulfoxides react with esters, affording generally optically active β-ketoesters[116,150–153]. Kunieda and coworkers[151] revealed that treatment of (+)-(*R*)-methyl *p*-tolyl sulfoxide **107** with *n*-butyllithium or dimethylamine afforded the corresponding carbanion, which upon further reaction with ethyl benzoate gave (+)-(*R*)-α-(*p*-tolylsulfinyl)acetophenone **108**. They also found that the reaction between chiral esters of carboxylic acids (R^1COOR^*) and α-lithio aryl methyl sulfoxides gave optically active β-ketosulfoxides[154]. The stereoselectivity was found to be markedly influenced by the size of the R^1 group of the esters and the optical purity reached to 70.3% when R^1 was a *t*-butyl group.



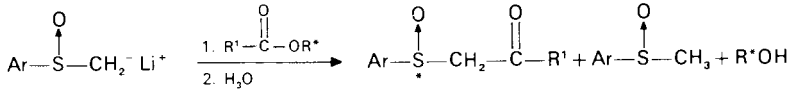
SCHEME 3



(**106**)

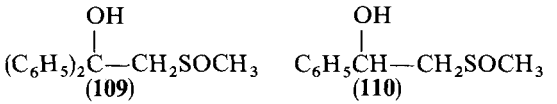


(+)-(*R*)-(**107**) (+)-(*R*)-(**108**)



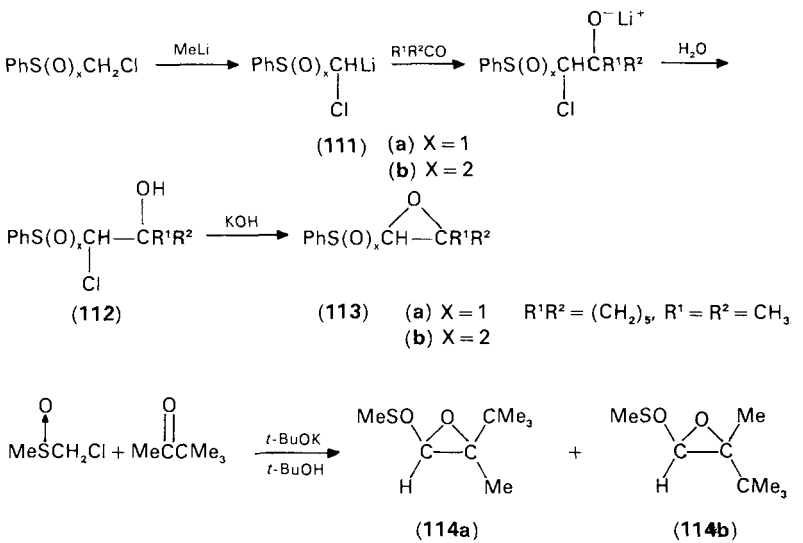
B. Addition to Unsaturated Bonds

Corey and Chaykovsky[114] found that the dimsyl anion reacts with benzophenone and benzaldehyde to afford the corresponding β-hydroxysulfoxides **109** and **110**. Thermal decomposition of these β-hydroxysulfoxides was shown to give α,β-unsaturated sulfoxides[155] or olefins[156,157]. Thus, the reaction of dimsyl anion with benzophenone at 100 °C gave 1,1-diphenylethylene, diphenylmethane, 1,1-diphenylcyclopropane and diphenylacetaldehyde, besides 1,1-diphenyl-2-methylthioethylene[156,157].



(109) **(110)**

Durst[158,159] extended this reaction to α-chloromethyl sulfoxides and sulphones and showed that the reaction of lithio derivative **111**, formed by treatment of α-chloromethyl phenyl sulfoxide (or of α-chloromethyl phenyl sulfone X = 2) with alkyllithium, with ketones afforded corresponding adducts **112** (or the corresponding sulfones) which upon further treatment with potassium hydroxide gave α-epoxysulfoxides **113** (or α-epoxysulfones). Direct formation of the α-epoxysulfoxide was then achieved by Tavares and coworkers[160] who found that chloromethyl *p*-tolyl sulfoxide can be treated directly with the carbonyl compound in the presence of potassium *t*-butoxide in *t*-butanol–ether mixture. Similar reactions of chloromethyl methyl sulfoxide with carbonyl and thiocarbonyl compounds were further developed by Tsuchihashi and Ogura[161] who found that treatment of chloromethyl methyl sulfoxide with potassium *t*-butoxide in the presence of unsymmetrical ketones, such as pinacolone or acetophenone, gave the two diastereomers **114a** and **114b** in a ratio of 3:1 and **115a** and **115b** in a ratio of 3:2. In these reactions, the thermodynamically unstable isomers, i.e. **114a** and **115a**, were found to form preferentially, suggesting that the carbanion attacks from the sterically least hindered site, when the sites of the substituents are different. A similar reaction took place between α-chloromethyl methyl sulfoxide and thiobenzophenone in the presence of *t*-BuOK affording in 38% yield α,β-unsaturated sulfoxide **117**, which is presumably formed by

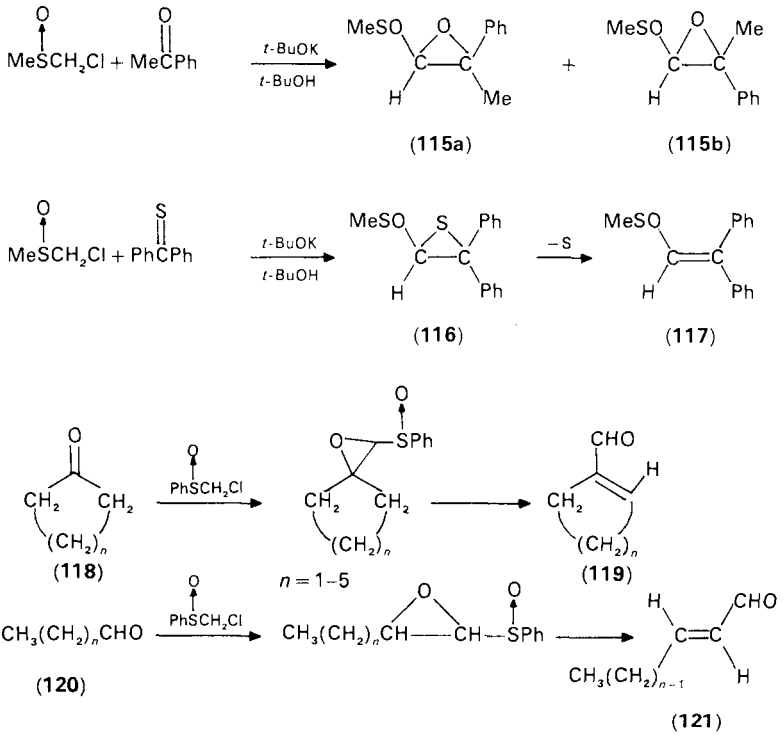


(111) (**a**) X = 1 (**b**) X = 2

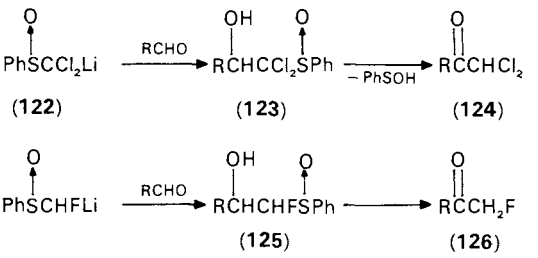
(112) **(113)** (**a**) X = 1 (**b**) X = 2 $R^1R^2 = (CH_2)_5$, $R^1 = R^2 = CH_3$

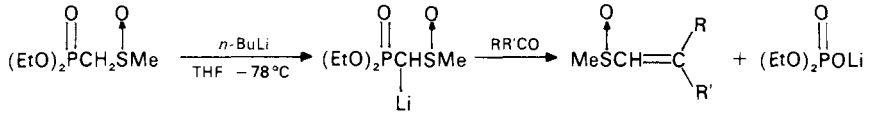
(114a) **(114b)**

extrusion of sulfur from the thiirane intermediate **116**. The epoxysulfoxides were shown to undergo acid-catalyzed or thermal decomposition to afford α,β-unsaturated aldehydes. This reaction was applied for the preparation of the α,β-unsaturated aldehydes **119** and **121**, by using the carbonyl compounds **118** and **120**[160,162].



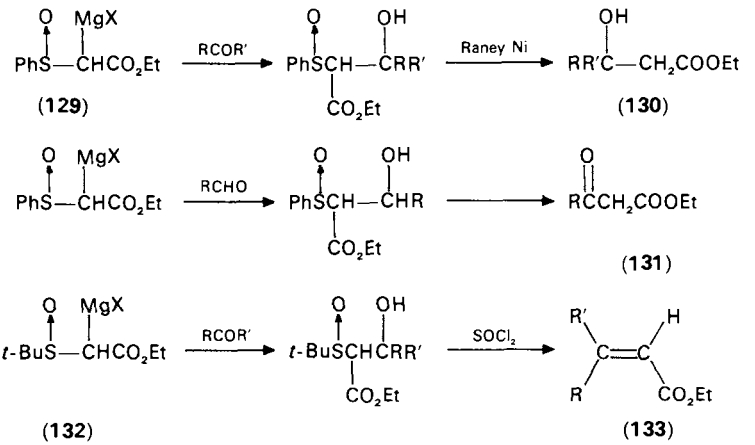
Treatment of α-dichloromethyl phenyl sulfoxide with lithium diisopropylamide in THF gave monolithiated derivative **122**, which upon further treatment with aldehyde afforded the β-hydroxy-α-dichlorosulfoxide **123**. Thermolysis of **123** gave dichloroketone **124**, by extruding benzenesulfenic acid as shown below[163,164]. Similarly, in the reaction of lithio-α-fluoromethyl phenyl sulfoxide and aldehyde, fluoromethyl ketone **126** was obtained, after thermolysis of the hydroxy intermediate **125**. Diethylphosphorylmethyl methyl sulfoxide was shown by Mikołajczyk and coworkers[165,166] to be lithiated with *n*-BuLi to intermediate **127**, which upon treatment with carbonyl compounds afforded the corresponding α,β-unsaturated sulfoxides **128** in good yields.





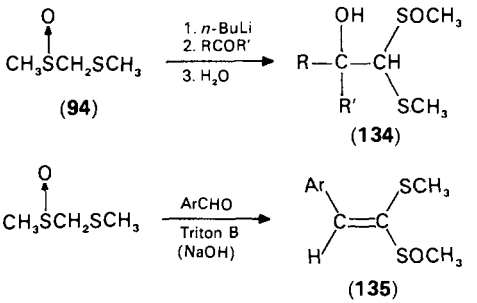
(127) (128)

Reaction of α-phenylsulfinyl acetate or ethyl α-(*t*-butylsulfinyl)acetate with one equivalent of ethylmagnesium bromide or iodide was shown to give the corresponding Grignard reagent **129** or **132**, which upon reaction with carbonyl compounds afforded the corresponding adducts. Thus Nokami and coworkers prepared ethyl β-hydroxycarboxylates **130**[167], β-keto esters **131**[168], α,β-unsaturated esters **133**[169] and other derivatives by this method.



(129) (130) (131) (132) (133)

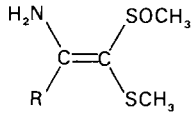
Methyl methylthiomethyl sulfoxide, commonly called FAMSO, has been regarded as a useful reagent for versatile organic syntheses. Utilization of FAMSO has been developed extensively by Ogura and colleagues, who have reported their work in numerous papers[126,130,170–183]. When the lithio-derivative was treated with a carbonyl compound, the α-hydroxyaldehyde dimethyl mercaptal *S*-oxide **134** was obtained[180]. Upon hydrolysis of **134**, α-hydroxyaldehydes and α-hydroxyketones are obtained. When benzyltrimethylammonium hydroxide (Triton B), potassium hydroxide or sodium hydroxide was used as a base, the reaction of **94** with aromatic aldehydes proceeds through a Knoevenagel-type condensation, eventually affording 2-aryl-1-(methylsulfinyl)-1-(methylthio)ethylene **135**, in good yields[180,181].



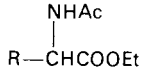
(94) (134) (135)

Ogura and colleagues have also shown that **135** can be further converted to various products such as arylacetic acids, their esters[181,182] and α-bromoarylacetic acid[183]. The condensation product of **94** with ketones can also be converted to the corresponding methyl ester by treatment with hydrogen chloride in methanol[184].

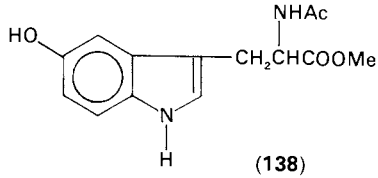
Treatment of the carbanion derived from **94** with nitriles was shown to give enaminesulfoxides **136**, which can be converted to α-ketoesters or α-ketoacylamides[185], besides the ester of *N*-acetylamino acid **137**. Using this reaction, the methyl ester of DL-*N*-acetyl-5-hydroxytryprophane **138** was synthesized[186].



(**136**)

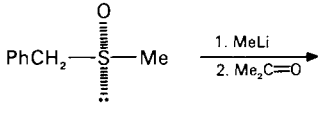


(**137**)

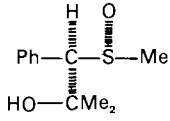


(**138**)

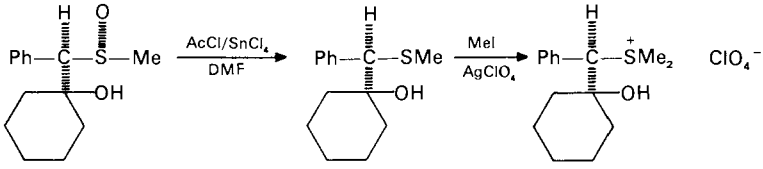
Optically pure (*S*)-benzyl methyl sulfoxide **139** can be converted to the corresponding α-lithio-derivative, which upon reaction with acetone gave a diastereomeric mixture (15:1) of the β-hydroxysulfoxide **140**. This addition reaction gave preferentially the product in which the configuration of the original carbanion is maintained. By this reaction, an optically active epoxy compound **142** was prepared from the cyclohexanone adduct **141**[187]. Johnson and Schroeck[188,189] succeeded in obtaining optically active styrene oxide by recrystallization of the condensation product of (+)-(*S*)-*n*-butyl methyl sulfoxide **143** with benzaldehyde.



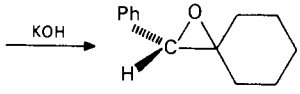
(*S*)-(**139**)



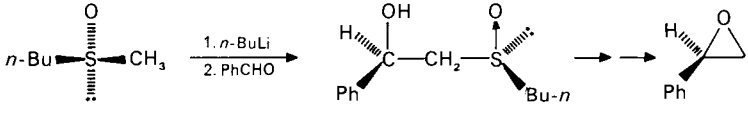
(*R*,*S*)-(**140**)



(*R*,*S*)-(**141**)

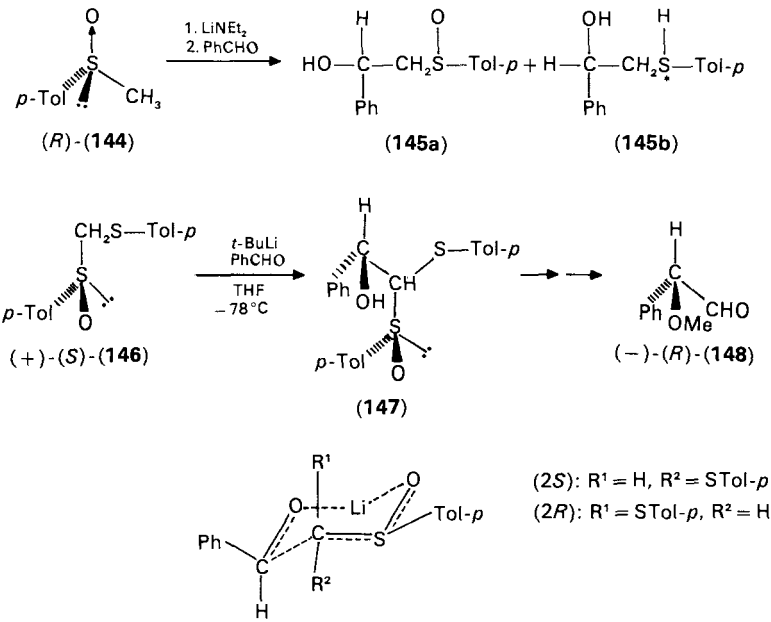


(*S*)-(**142**)



(+)-(*S*)-(**143**)

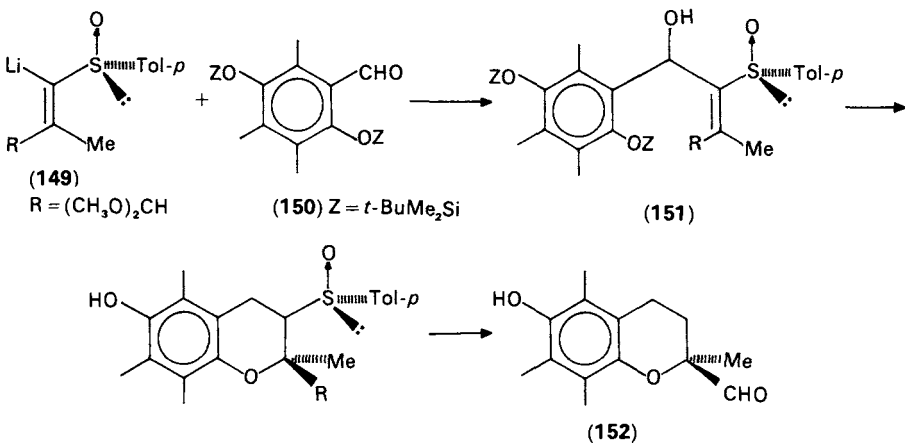
No stereoselectivity was observed in the formation of a 1:1 diastereomeric mixture of 2-hydroxy-2-phenylethyl *p*-tolyl sulfoxide **145** from treatment of (*R*)-methyl *p*-tolyl sulfoxide **144** with lithium diethylamide[190]. However, a considerable stereoselectivity was observed in the reaction of this carbanion with unsymmetrical, especially aromatic, ketones[191]. The carbanion derived from (*R*)-**144** was found to add to *N*-benzylideneaniline stereoselectivity, affording only one diastereomer, i.e. (R_s,S_c)-(+)-*N*-phenyl-2-amino-2-phenyl *p*-tolyl sulfoxide, which upon treatment with Raney Ni afforded the corresponding optically pure amine[192]. The reaction of the lithio-derivative of (+)-(*S*)-*p*-tolyl *p*-tolylthiomethyl sulfoxide **146** with benzaldehyde gave a mixture of 3 out of 4 possible isomers, i.e. (1*S*, 2*S*, 3*R*)-, (1*S*, 2*R*, 3*R*)- and (1*S*, 2*S*, 3*S*)-**147** in a ratio of 55:30:15. Methylation of the diastereomeric mixture, reduction of the sulfinyl group and further hydrolysis gave (−)-(*R*)-2-methoxy-2-phenylacetaldehyde **148** in 70% e.e. This addition is considered to proceed through a six-membered cyclic transition state, formed by chelation with lithium, as shown below[193,194].



Demailly and coworkers[195] found that the asymmetric induction increased markedly when optically active methyl pyridyl sulfoxide was treated with an aldehyde. They also synthesized (*S*)-chroman-2-carboxylaldehyde **152**, which is the cyclic ring part of α-tocopherol, by aldol-type condensation of the optically active lithium salt of α,β-unsaturated sulfoxide. Although the diastereomeric ratio of allylic alcohol **151** formed from lithium salt **149** and **150** was not determined, the reaction of **149** with salicylaldehyde gave the diastereomeric alcohol in a ratio of 28:72[196].

The reaction between the carbanion formed by treatment of optically active α-sulfinyl-ester **153**, with *t*-BuMgBr and carbonyl compounds, gives β-hydroxyester **154** in high optical yields[197–199].

When R^1 and R^2 are different as shown below, the carbanion approaches the ketone from the direction depicted by the arrow and gives preferentially one diastereomer over the other[197,200]. Using this carbanion, mevalolactone **155**[201], (+)-(*R*)-δ-*n*-hexadecalactone



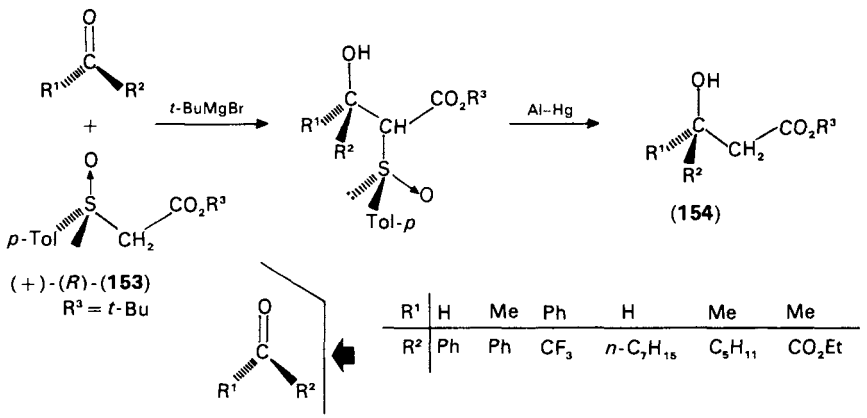
(149)
R = $(CH_3O)_2CH$

(150) Z = t-$BuMe_2Si$

(151)

(152)

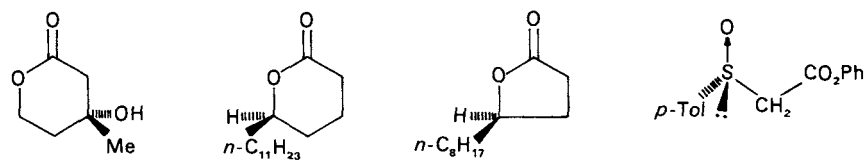
156, an insect pheromone and (+)-(*R*)-γ-*n*-dodecalactone (**157**)[202] were synthesized. Corey and coworkers[203] applied this reaction with phenyl (+)-(*R*)-α-(*p*-tolylsulfinyl)acetate **158** for the total synthesis of maytasin.



(+)-(*R*)-(**153**)
R^3 = t-Bu

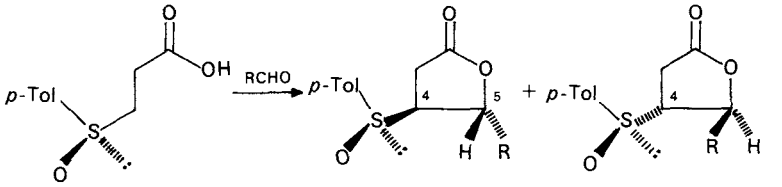
R^1	H	Me	Ph	H	Me	Me
R^2	Ph	Ph	CF_3	n-C_7H_{15}	C_5H_{11}	CO_2Et

(154)



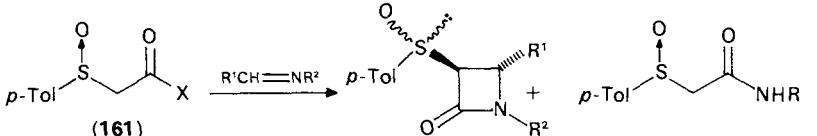
(−)-(*R*)-(**155**) (+)-(*R*)-(**156**) (+)-(*R*)-(**157**) (+)-(*R*)-(**158**)

Papageorgiou and Benezra[204] treated chiral t-butyl (−)-(*S*)- and (+)-(*R*)-2-(*p*-tolylsulfinyl)propionate with an aldehyde, then pyrolyzed the mixture and obtained chiral α-(hydroxyalkyl)acrylate in 75% e.e. Similarly, condensation of the anion of (+)-(*R*)-3-(*p*-tolylsulfinyl)propionic acid **159** with aldehydes was found to give the diastereomeric β-sulfinyl-γ-lactones, (+)-(S_{c4},R_{c5},R_s)-**160a** and (+)-(R_{c4},S_{c5},R_s)-**160b** in an approximate ratio of 60:40[205].



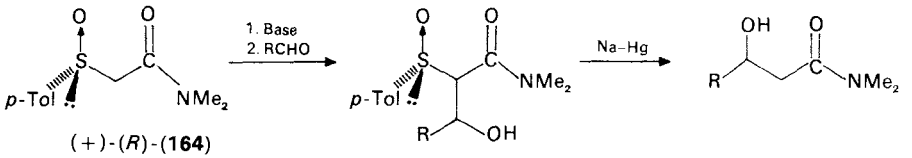
(159) (160a) (160b)

Reaction of *p*-nitrophenyl 2-(*p*-tolylsulfinyl)acetate **161** with aryl aldimines in the presence of imidazole was found to give β-lactams **162** and amides **163**[206]. In the cyclization, only the two 3,4-*trans* derivatives were formed out of a possible four diastereomeric pairs and, interestingly, the ratio of two diastereomeric pairs went up to 6.7:1. This means not only that internal asymmetric induction[207] affords the *trans* derivative, but that also a relatively high asymmetric induction took place during the reaction.

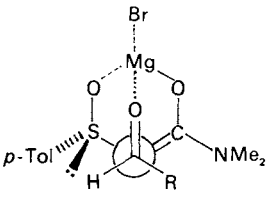


(161) X = *p*-$O_2NC_6H_4O$ (162) (163)

Annunziata and coworkers[208,209] treated (−)-(*S*)-menthyl *p*-toluenesulfinate with α-lithio *N*,*N*-dimethylacetamide and obtained (+)-(*R*)-sulfinylamide **164** which, upon further treatment with aldehyde in the presence of base, afforded the aldol condensation product. When they used *n*-BuLi the chiral discrimination in the resulting product was only 47%. However, when the base was *n*-BuMgBr, the product was formed with a very high stereoselectivity, i.e. 90–99%; the reaction is considered to proceed through the transition state **165**. Similarly, when enantiomerically pure (+)-(*R*)-*p*-tolylsulfinyl-*N*,*N*-dimethylthioacetamide was subjected to aldol condensation with aldehydes[210], β-hydroxythioacetamides were obtained in relatively high e.e. (40–90%) after desulfenylation. In this case, there is not much difference in e.e. of the resulting β-hydroxythioacetamides regardless of the difference in the base, which is either *t*-BuMgBr or *n*-BuLi. The β-hydroxythioacetamides have an (*S*)-configuration, regardless whether R is Me, *i*-Bu, *i*-Pr or *t*-Bu.

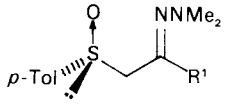


(+)-(*R*)-(**164**)

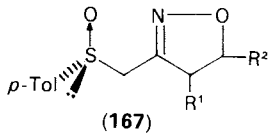


(**165**)

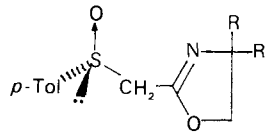
Other asymmetric syntheses, based on aldol condensation of chiral α-sulfinyl carbanions with carbonyl compounds, are the formation of β-hydroxyketones from β-sulfinylhydrazones **166**[211–214], of β,β′-dihydroxyketones from 3-(*p*-tolylsulfinylmethyl)-Δ^2-methylisoxalinones **167**[215], of β-hydroxyacids from 2-(*p*-tolylsulfinylmethyl)oxazolines **168**[216] and of β-hydroxyesters from ethyl-*p*-tolylsulfinyl-*N*-methoxyacetamide **169**[217].



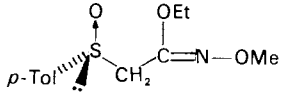
(**166**) R^1 = H, alkyl or aryl
R^2 = H or Me



(**167**)



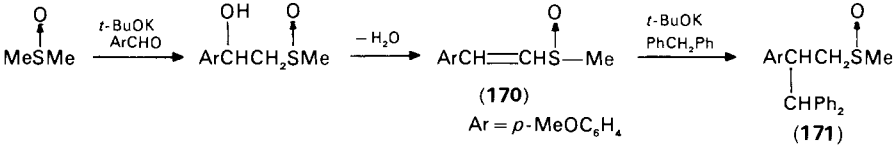
(**168**) R = H or Me



(**169**)

C. Nucleophilic Addition to α,β-Unsaturated Sulfoxides

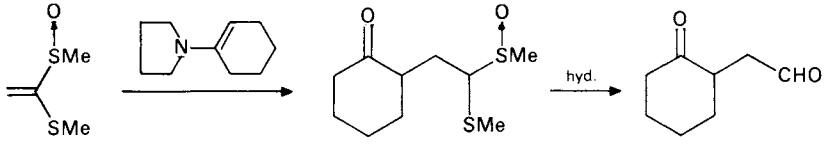
The Michael addition of nucleophiles to α,β-unsaturated sulfoxides creates initially α-sulfinyl carbanions by nucleophilic attack on the β-carbon atom. Russell and Becker[157] found that treatment of a mixture of diphenylmethane and anisaldehyde with potassium *t*-butoxide in DMSO gave at first the condensation product **170**, which upon Michael addition afforded the final product **171**.



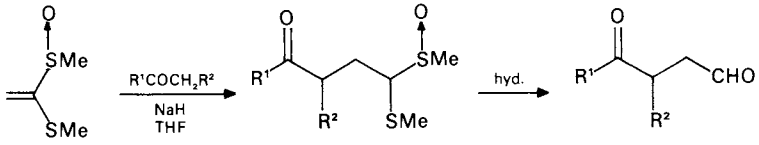
(**170**)
Ar = *p*-$MeOC_6H_4$

(**171**)

Hermann and colleagues[218,219] found that treatment of ketene thioacetal monoxides **172** and **173**, with enamines, sodium malonates, β-dicarbonyl compounds and lithio-

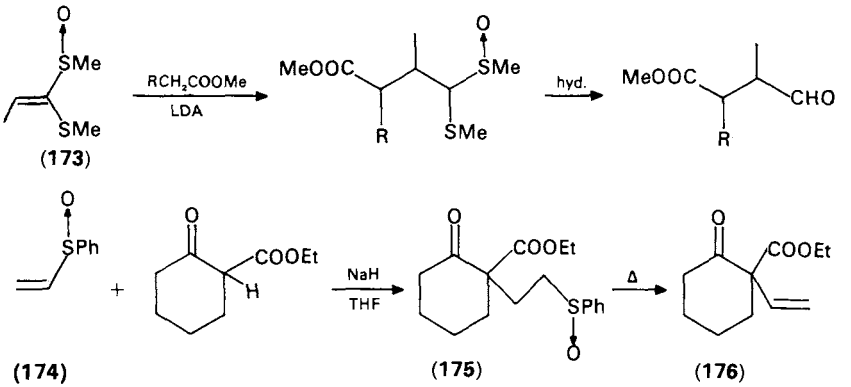


(**172**)

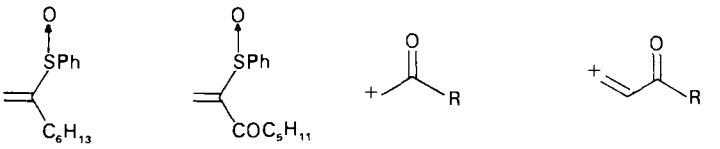


R^1 = Me or COOMe
R^2 = Ac or COOMe

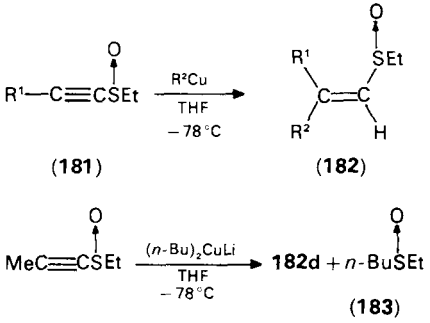
enolates of esters gave the corresponding Michael adducts in excellent yields in all cases. These adducts can be converted to the corresponding β-carbonylaldehydes upon perchloric-acid-catalyzed hydrolysis in a mixture of water with acetonitrile[218–220]. Phenyl vinyl sulfoxide **174** is a synthetic equivalent of the vinyl carbonium ion and hence the initial Michael addition to phenyl vinyl sulfoxide to form the adduct **175** and the subsequent thermolysis of **175** can give the corresponding vinyl compound **176**[221].



Alkenyl sulfoxides **177** and **178**, which can be readily prepared from 1-alkynes[222], provide synthones for the carbocations **179** and **180**. These synthones are useful for the simple construction of cyclopentenones and also in providing an electrophilic precursor for the β-side-chain on prostanoids[223,224].



Nucleophilic addition to acetylenic sulfoxides provides α,β-ethylenic sulfoxides. Treatment of **181** with monoalkyl-copper afforded nearly quantitatively β-alkylated α,β-ethylenic sulfoxides **182** through *cis*-addition to the triple bond. The reaction with lithium dimethylcuprate also afforded a similar adduct; however, the reaction with lithium di-*n*-butylcuprate was found to give a small amount of ethyl *n*-butyl sulfoxide **183** besides the



(a) $R^1 = R^2 = Me$
(b) $R^1 = R^2 = n\text{-}C_4H_9$
(c) $R^1 = Me$, $R^2 = n\text{-}C_4H_9$
(d) $R^1 = n\text{-}C_4H_9$, $R^2 = Me$

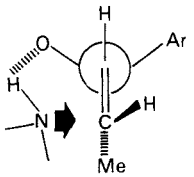
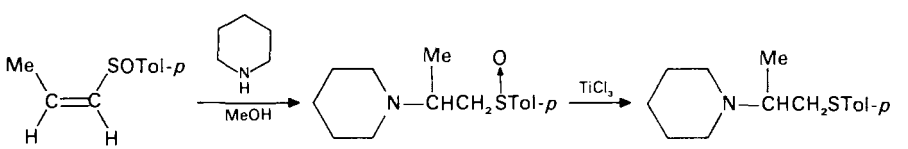


FIGURE 6

normal adduct. The sulfoxide **183** is considered to be formed by the nucleophilic attack of the *n*-butyl moiety of the cuprate on the S atom. Similar nucleophilic substitutions on the S atom are often observed when alkyllithiums or even Grignard reagents are used[225–227]. Reaction of ethynyl phenyl sulfoxide with diethyl ethylmalonate in the presence of *n*-butyllithium afforded the *trans*-adduct stereoselectively[228].

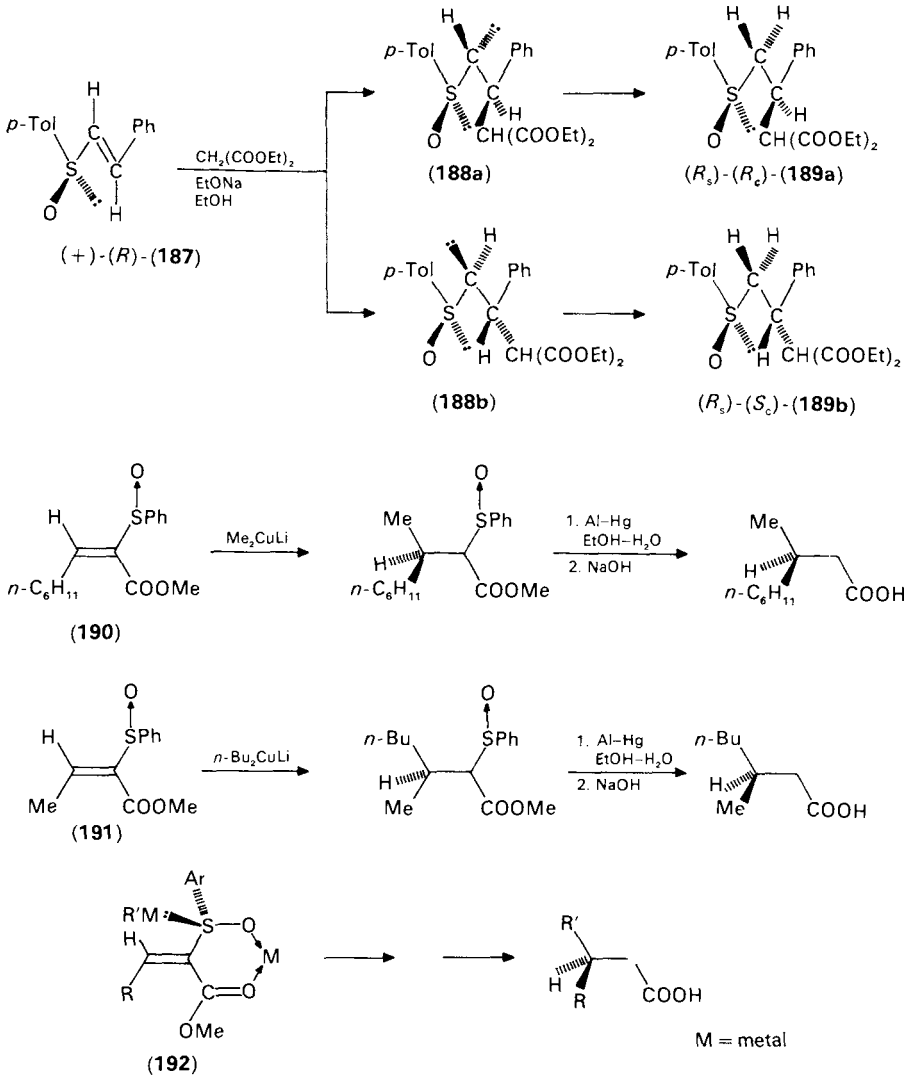
Abbott and coworkers[229] found that nucleophilic addition of amines to α,β-unsaturated sulfoxide gave asymmetrically induced adducts. For example, treatment of (*R*)-(−)-*cis*-propenyl *p*-tolyl sulfoxide **184** with piperidine in methanol gave a quantitative mixture of the diastereomeric adduct **185**. Reduction of this mixture gave (R_s)-(S_c)-2-piperidinopropyl *p*-tolyl sulfide **186** in 74% optical yield, suggesting that the amines attack from the opposite side of the bulky aryl group at the transition state, as shown above (Figure 6).



(184) **(185)** **(186)**

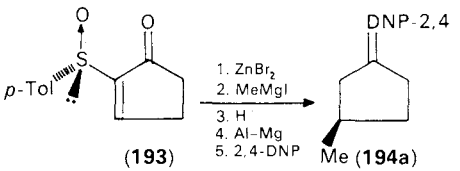
Tsuchihashi and coworkers[230] reported that *p*-tolyl vinyl sulfoxide reacted with diethyl malonate or with ethyl acetoacetate in the presence of sodium ethoxide in ethanol to afford the Michael adduct. The Michael addition of diethyl malonate to (+)-(*R*)-*trans*-β-styryl *p*-tolyl sulfoxide **187** was found to afford a diastereomeric mixture of (R_s)-(R_c)-**189a** and (R_s)-(S_c)-**189b** in the ratio of 8:2. In general, the stable conformer of an α-sulfinyl carbanion in a polar media has a structure in which the lone electron pair on the carbon atom is *trans* to the sulfinyl oxygen, namely the carbanion **188a** is more stable than **188b**[52,231]. Therefore, the stereoselectivity of the Michael addition would depend on the relative stabilities of the carbanions, **188a** and **188b**.

Another stereoselective β-alkylation was found by Posner and coworkers in the treatment of (*S*)-(+)-(*E*)-1-octenyl sulfoxide **190** and (*S*)-(+)-(*E*)-1-propenyl sulfoxide **191** with R_2CuLi. This reaction is believed to proceed through the chelated intermediate **192** and the addition would take place from the side of the nonbonding electron pair on the S atom, i.e., from the opposite side to the aryl group[232]. They also obtained (*R*)-(+)-3-methylcyclopentanone 2,4-dinitrophenylhydrazone in 53–83% chemical yields and 70–73% optical yields by first treating (*S*)-(+)-cyclopentenone *p*-tolyl sulfoxide **193** with one equivalent of various metal bromides (M = Ni, Co, Pd and Mg), followed by alkylation with methylmagnesium bromide or iodide, and subsequent reductive desulfurization and finally treatment with 2,4-dinitrophenylhydrazine to form the hydrazone. The best result was achieved when $ZnBr_2$ and methylmagnesium iodide were used, the chemical yield being 89% and the optical yield 72% of e.e. In the absence of the divalent metal salt, (*S*)-(−)-

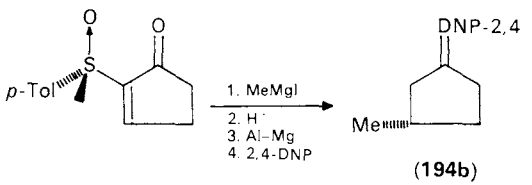


3-methyl adduct **194b** of opposite configuration was obtained in 76% chemical yield with 72% e.e. It is suggested that in the presence of metal ion (M) the sulfoxide assumes a chelated structure **195a** and hence alkylation take place from the side of the nonbonding electron pair to afford (*R*)-(+)-**194a**. In the absence of metal ion, the dipoles of the sulfinyl and the carbonyl functions would be in opposite directions as in **195b**, and hence the plane of the lone electron pair would lie in the opposite direction to that of the double bond and (*S*)-(−)-**194b** would be obtained[233,234]. Based on the above idea, Posner and Hulce[235] treated enantiomerically pure (*S*)-(+)-2-(arylsulfinyl)cycloalkenones with diorganomagnesium under carefully chosen conditions and obtained (*R*)- and (*S*)-3-substituted cycloalkanones with high e.e. A very high stereoselectivity was also observed in the addition reaction to (*S*)-(+)-2-(*p*-tolylsulfinyl)-2-butene-4-olide[236] or 3-methyl- and 3-*p*-

tolyl-2-(*p*-tolylsulfinyl)cyclopentenones[237] and this reaction was also applied for the synthesis of (−)-methyl jasmonate,[238] (−)-podorhizon[236] α-cuparenone[237] and enantiomerically pure steroid intermediates of natural configurations[239].

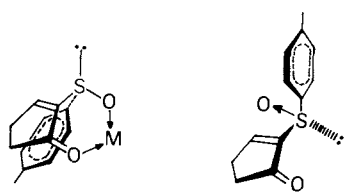


(193)



(194b)

2,4-DNP = 2,4-$(NO_2)_2C_6H_3$—NH—N

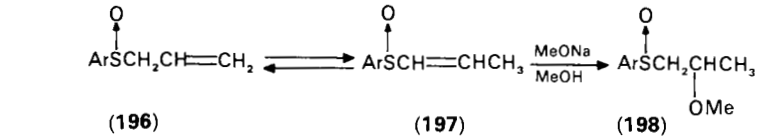


(195a) (195b)

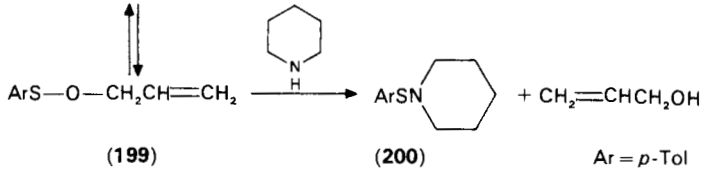
D. Reactions of Allylic Sulfoxides

The formation of a C—C bond via allylic carbanions bearing sulfur-containing groups has often been used recently. Among these reactions, allylic sulfoxides have been used for regio- as well as stereoselective organic syntheses. Abbott and Stirling[240] reported interesting reactions of allyl *p*-tolyl sulfoxide **196** with both methanolic sodium methoxide and piperidine. When **196** was treated with sodium methoxide in methanol, 2-methoxypropyl *p*-tolyl sulfoxide **198** was obtained, presumably by an initial prototropic isomerization of **198** to the vinylic sulfoxide **197** and subsequent nucleophilic addition. Treatment of **196** with piperidine afforded *N*-*p*-tolylsulfenylpiperidine **200** and allyl alcohol. This is considered to have proceeded through initial [2, 3]-sigmatropic rearrangement to form allyl *p*-toluenesulfenate **199** which, upon nucleophilic attack of piperidine, afforded the final product **200**.

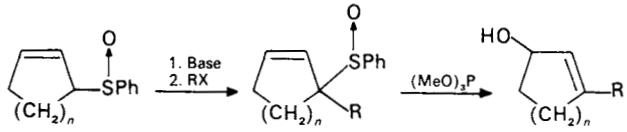
An allylic sulfenate, like **199**, is known to be in equilibrium with allylic sulfoxide,[241] like **196**, although its concentration is usually low[188]. Various allylic sulfoxides can be prepared by treatment of allylic alcohols with arenesulfenyl chlorides[242,243]. Evans and coworkers[243,244] prepared various allylic alcohols by treating the corresponding allylic sulfoxides with trimethyl phosphite. For example, the carbanion from a cycloalkenyl sulfoxide **201** was readily alkylated at the α-position by treatment with alkyl halide. The resulting alkylated derivative **202** was then treated with trimethyl phosphite and 3-substituted cycloalkenol was obtained. Alkylation of acyclic allylic sulfoxide **204** gave



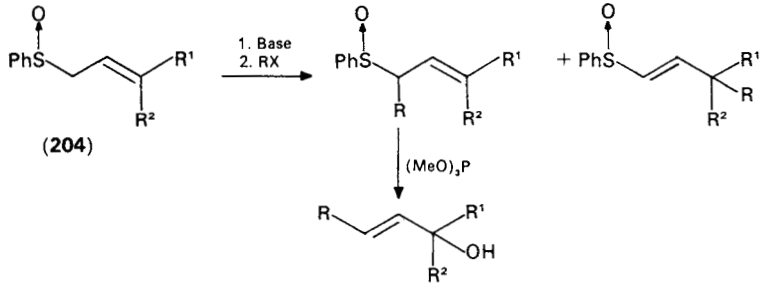
(196) (197) (198)



(199) (200) Ar = *p*-Tol

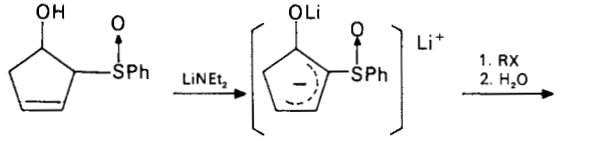


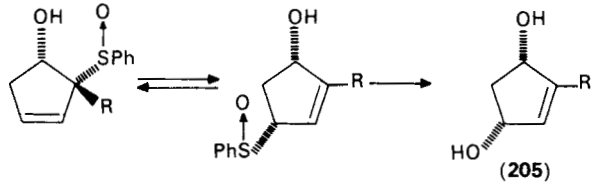
(201) (202) (203)



(204)

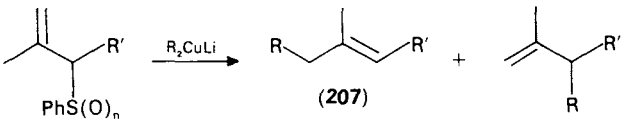
both α- and γ-alkylated products. This reaction has been applied for the syntheses of the sesquiterpene nuciferal[245] and of 1-alkyl-1-cyclopenten-*cis*-3, 5-diols **205**[246], which is the precursor of prostaglandins, and hence is quite useful.





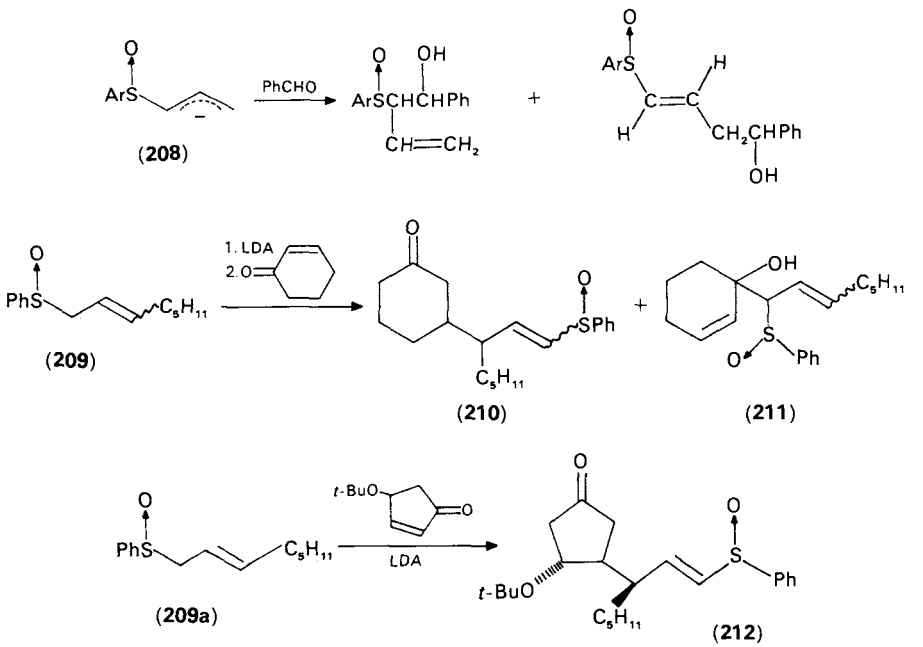
(205)

α-Substituted β-methyl allyl sulfoxides **206** and sulfones have been known to undergo regio- as well as stereoselective desulfurizative substitution upon treatment with lithium dialkylcuprates, affording predominantly the γ-(*E*)-adduct **207**. This process provides a new method for preparing trisubstituted (*E*)-olefins[247,248].

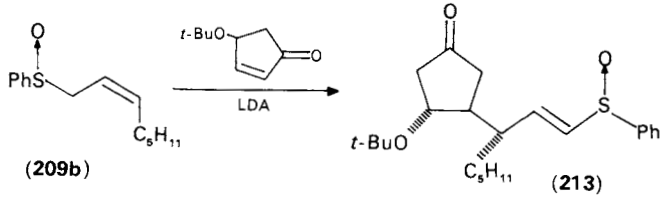


(**206**) (**a**) $n = 1$
(**b**) $n = 2$

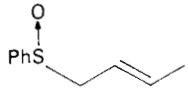
Addition of the carbanion formed from aryl allyl sulfoxides **208** to benzaldehyde was shown to proceed readily in moderate yields, affording a mixture of products resulting from α- and γ-attack on the allylic carbanion. All the γ-products possess the (*E*)-configuration around the double bond. Asymmetric induction in the addition generally resulted in major/minor diastereomer ratios which exceed 2:1[249]. The reaction of the carbanion from 1-(phenylsulfinyl)-2-octene **209** with 2-cyclohexenone was reported to give the 1,4-γ-adduct **210** and 1,2-α-adduct **211** in a ratio of 70:30[250]. According to Binns and coworkers[251] the conjugate addition of the carbanion from (*E*)- and (*Z*)-1-(phenylsulfinyl)-2-octene, **209a** and **209b**, to 4-*t*-butoxycyclopent-2-en-1-one proceeded stereoselectively forming (*E*)-vinylic sulfoxides **212** and **213**, respectively, as single diastereomers. A similarly high stereoselectivity was observed in the reactions of other allylic sulfoxides, **214**, **215** and **216**, with cyclic enones. The following ten-membered cyclic 'chair-chair' or '*trans*-decalyl'-like transition state **217** was proposed to account for the diastereospecific



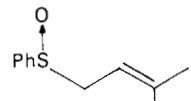
conjugate addition reactions of allylic carbanions bearing polar and charge-stabilizing groups in aprotic media[252]. Hua and colleagues[253], reported the regio- and stereochemical aspects of the reaction of the chiral carbanion derived from (+)-(*R*)-allyl *p*-tolyl sulfoxide **218** with various cyclic enones **219** and **220** and the utilization of these reactions in the asymmetric synthesis of (+)-hirsutene.



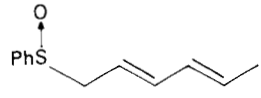
(209b) (213)



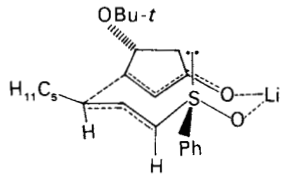
(214)



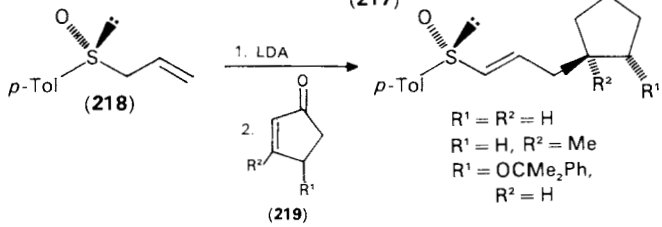
(215)



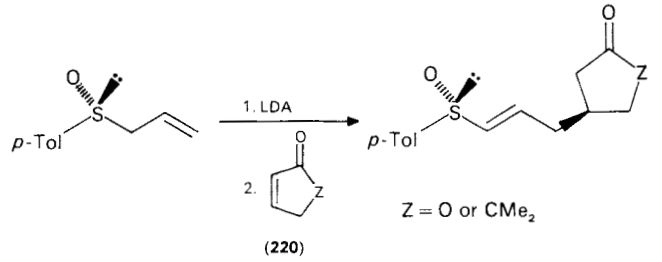
(216)



(217)



(218) (219)

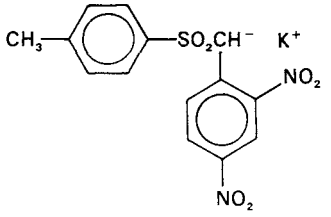


(220)

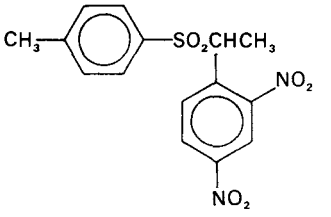
VI. REACTIONS OF α-SULFONYL CARBANIONS

The sulfonyl group has been known since the turn of the century to activate the α-methylene group. For instance, Fromm and Wittmann[254] found that 4-nitrophenyl benzyl sulfone reacted with methyl iodide in the presence of alcoholic sodium hydroxide to afford

the dimethyl derivative. Much later, Shriner and Greenlee[255] isolated the potassium salt of 2,4-dinitrobenzyl *p*-tolyl sulfone **221** which, upon treatment with methyl iodide, gave methylated product **222**.



(221)



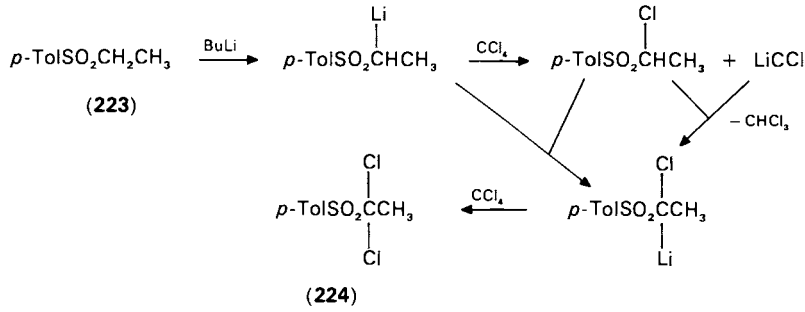
(222)

Before 1950, most of the reactions of α-sulfonyl carbanions were conducted with the corresponding magnesium compounds, mainly the Grignard reagents of sulfones[256–270]. The reactivities of these Grignard reagents were scrutinized by Kohler and coworkers and Field and coworkers in comparison with those of ordinary Grignard reagents, in the additions to carbonyl compounds[261–263,265], and to α,β-unsaturated aldehydes and ketones[263,269], in acylation[256,258,266] carbonation[257,260], alkylation[256], halogenolysis[257,259,268], and in the addition to carbon–nitrogen multiple bonds[266]. They were found to react similarly to the ordinary Grignard reagents. Since 1970, α-sulfonyl carbanions have been utilized extensively for organic syntheses and this is manifested in reviews[271,272]. α-Sulfonyl carbanions have been used for initial C—C bond formation and subsequent reductive desulfonation or elimination to form a double bond. Thus, many new syntheses via sulfones and useful reagents of sulfones have been developed. These reactions of α-sulfonyl carbanions are described in the following sections.

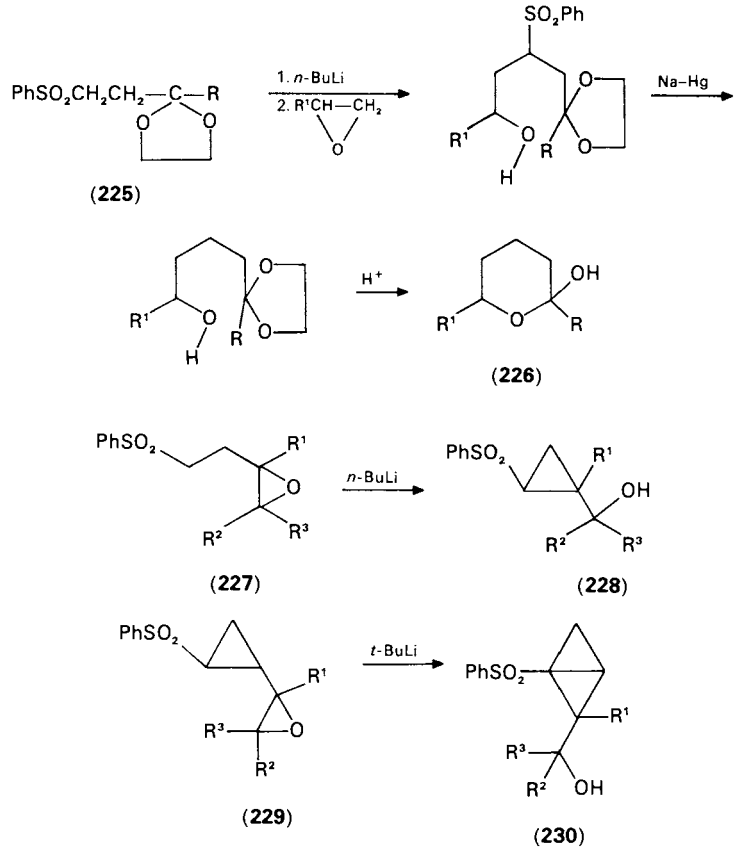
A. Alkylation and Acylation

In general, α-sulfonyl carbanions can be generated by treatment of alkyl sulfones with Grignard reagents or alkyllithium reagents. For example, treatment of alkyl aryl sulfones with Grignard reagents gave the corresponding α-halomagnesium derivatives[259–266]. Addition of appropriate nucleophiles to α,β-unsaturated sulfones also gives the corresponding α-sulfonyl carbanions. Other bases used to generate α-sulfonyl carbanions from the sulfones are LDA, lithium amide, sodium amide, potassium amide, sodium hydride and potassium alkoxides. Recently, α-sulfonyl carbanions were successfully generated by treatment of a solution of sulfones with condensed aqueous NaOH. α-Sulfonyl carbanions react with various alkyl, alkenyl and alkynyl halides[273,274]. However, their reaction with perhalogenated alkanes gives α-halogenated sulfones.[275,276] For example, treatment of ethyl *p*-tolyl sulfone **223** with an equimolar amount of *n*-butyllithium at −78 °C in THF, and subsequent treatment with 10-fold excess of carbon tetrachloride gave the corresponding dichlorinated sulfone **224**. This polyhalogenation has been considered to proceed via the path shown in Scheme 4[275]. The use of NaOH as the base in DMF was found to change the reaction pattern, affording only the monochlorinated sulfone[277].

In the reaction with epoxides, γ-hydroxysulfones are obtained[278–280]. For example, Kondo and coworkers[279] synthesized various δ-lactols **226** by treating sulfone acetals **225** with terminal epoxides as shown below. Dilithiated phenylsulfonylmethylene reacted with haloepoxide and afforded 3-(phenylsulfonyl)cycloalkanols[281]. Treatment of γ,δ-epoxysulfones **227** and **229** with *n*-butyllithium resulted in cyclization to form cyclopropane derivatives **228** and bicyclobutane **230**, respectively[282].

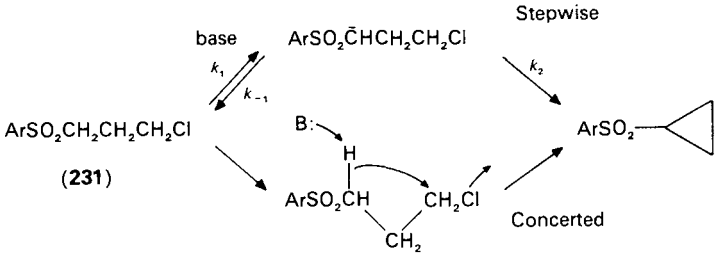


SCHEME 4



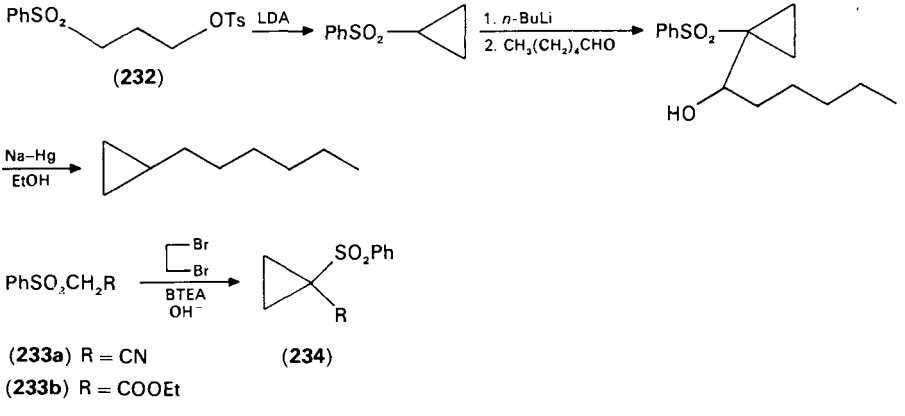
Aryl 3-chloropropyl sulfones **231** were shown to cyclize to aryl cyclopropyl sulfones upon treatment with *t*-BuOK in *t*-butanol[283] or with sodium amide in 1,2-dimethoxyethane[284]. Bird and Stirling[285] investigated the reaction of aryl 3-chloropropyl

sulfones with *t*-BuOK in *t*-butanol and found that it proceeds via a stepwise process involving an intermediate carbanion and not through a concerted process, as shown in Scheme 5.

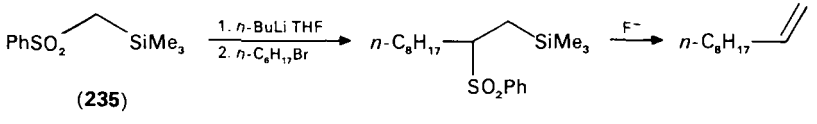


SCHEME 5

Cyclopropyl sulfones were shown to be obtained either by cyclization of γ-*p*-tosyloxy sulfones **232** with base[286,287] or by treatment of phenylsulfonylacetonitrile **233a** or ethyl phenyl sulfonyl acetate **233b** with 1,2-dibromoethane in the presence of benzyltriethylammonium chloride (BTEA) and alkali in good yields[288]. Chang and Pinnick[286] synthesized various cyclopropane derivatives **234** upon initial treatment of carbanions derived from cyclopropyl phenyl sulfone with either alkylating agents or a carbonyl compound and subsequent desulfonylation, as shown below.

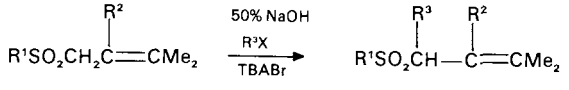


Treatment of α-sulfonyl carbanion with (iodomethyl)trimethylsilane gave β-trimethylsilyl sulfones[289–291]. Alkylation of β-trimethylsilyl sulfones **235** gave various β-trimethylsilyl sulfones[292]. The use of (iodomethyl)tributylstannane instead of (iodomethyl)trimethylsilane was shown to afford a tributylstannanyl derivative[293]. This compound has been used for syntheses of terminal olefins[289–293].



Alkylation of carbanions derived from allyl aryl sulfones **236** with alkyl halides is known

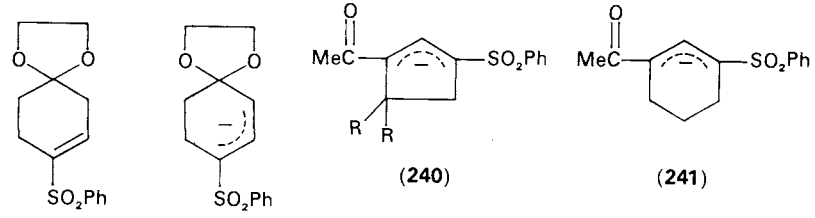
to result in a stereoselective alkylation at the α-position to the sulfonyl group[294–299]. Jończyk and Radwan-Pytlewski[298] achieved alkylation of allylic sulfones using a two-phase system of concentrated aqueous NaOH solution and a quaternary ammonium salt, such as tetrabutylammonium bromide (TBABr), as shown below.



(236) (237)

R^1 = Ph, R^2 = H
R^1 = Ph, R^2 = Me
R^1 = Me, R^2 = H

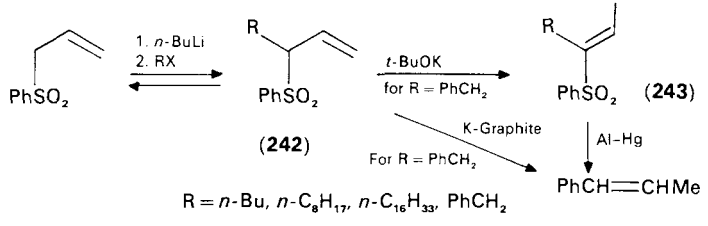
There have been many reports on the use of this method for the syntheses of vitamin A, methyl retinoic acid methyl ester, related derivatives, and polyenes[300–310].



(238) (239) (240) (241)

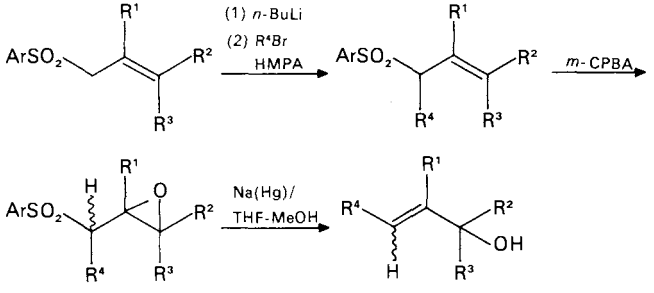
Carbanion **239** derived from vinyl sulfone **238** was shown to be alkylated regiospecifically at the α-carbon atom[311]. The carbanions **240** and **241** derived from δ-ketosulfones were shown to be alkylated at both α- and γ-carbons[312,313]. Alkylation of **240** gave α-alkylated products predominantly, while the α/γ ratio varied markedly by change of the alkylating agent in the reaction with **241**. For example, methylation with methyl iodide gave the products in the α/γ ratio of 72:28, while the α/γ ratio was 27:73 in the ethylation with ethyl bromide[312].

Allylic sulfones and α,β-unsaturated sulfones are known to be in equilibrium[314–319]. Allylic sulfones, such as **242**, isomerize to α,β-unsaturated sulfones **243** upon treatment with a catalytic amount of potassium *t*-butoxide in dry THF. The α,β-unsaturated sulfones can be converted to the corresponding olefins upon desulfonation with sodium amalgam[320] or aluminium amalgam[294,321]. Since treatment of allylic sulfones with potassium–graphite gives 2-alkenes, alkylation of allylic sulfones and subsequent desulfonation is a useful process for the synthesis of olefins, as shown in Scheme 6.



SCHEME 6

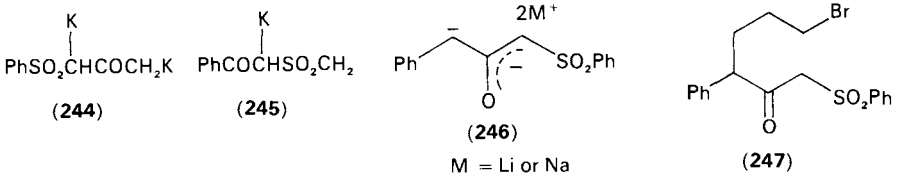
Koncienski[295] reported a new synthesis of allylic alcohols starting from the allylic sulfones via formation of epoxysulfones.



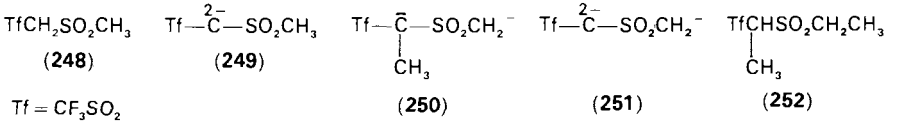
R^1, R^2, R^3 = H or Me, R^4 = *n*-hexyl, Ar = *p*-Tolyl

Both the α- and α′-hydrogens of dibenzyl sulfone were shown to be ionized by means of two equivalents of potassium amide in liquid ammonia[322].

Substitution of the α-methylene group with an electron-withdrawing group stabilizes the resulting α-sulfonyl carbanions markedly. Thus β-ketosulfones can be converted to the corresponding α-mono- and α,γ- or α,α′-dianions[323–327]. For example, treatment of phenylsulfonylacetone[323] or methyl phenacyl sulfone[324] with potassium amide in liquid ammonia gives rise to the formation of the corresponding dipotassio salts **244** and **245**. Alkylation and acylation of these dianions take place at the methylene terminal[323–327]. Upon quenching dianion **246** with 1,3-dibromopropane at −40 °C, **247** was obtained in 60–75% yield.



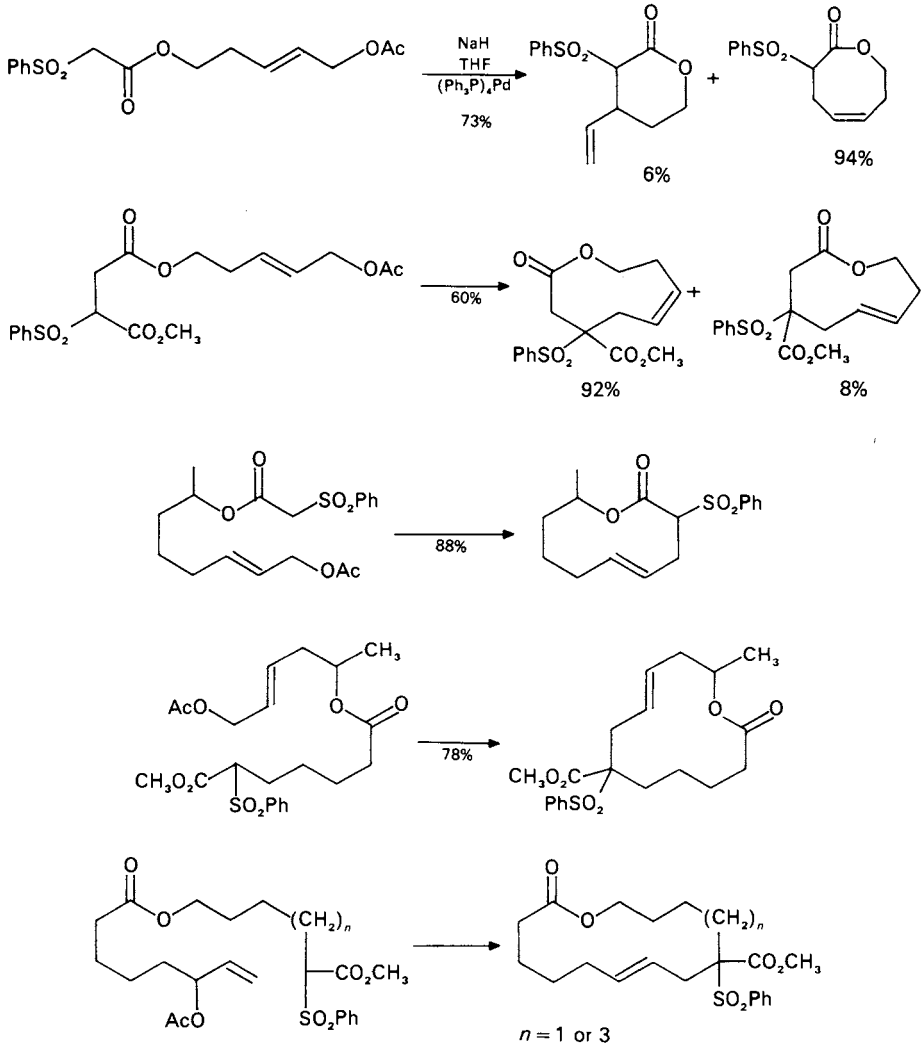
When methyltriflone **248** was treated with two equivalents of *n*-butyllithium at −50 °C in THF, α,α-dianion **249** is formed. After methylation of this dianion, further treatment with two equivalents of *n*-butyllithium gives the α,α′-dianion **250**. This dianion can be alkylated at the terminal carbon atom, like the dianions from ketosulfones. On reaction with three equivalents of *n*-butyllithium, **248** gives α,α,α′-trianion **251** which, upon methylation with methyl iodide, afforded methylated product **252**. Hendrickson and Palumbo[328] prepared cyclopentenone derivatives using **248** as the starting material.



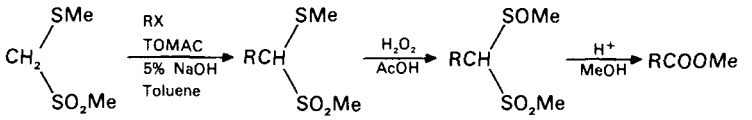
Tf = CF_3SO_2

Allylic acetates of either geranyl acetate or neryl acetate reacted with the sodium salt of methyl phenylsulfonyl acetate in the presence of tetrakis(triphenylphosphine palladium) affording the corresponding olefin, with a retained geometry at the primary carbon

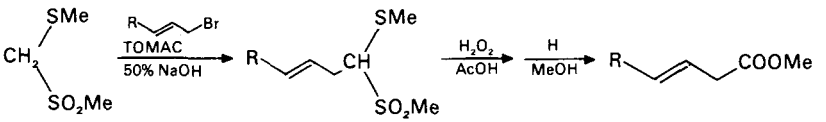
atom[329]. Trost and Verhoeven[330–332] applied this reaction for intramolecular cyclization and obtained medium-ring lactones and macrolides.



Ogura and coworkers[333] obtained alkyl and alkenyl derivatives **254**, **255** upon treatment of methyl methylthiomethyl sulfone **253** with alkyl or 2-alkenyl bromide under phase-transfer conditions using 50% aqueous NaOH. Interestingly, the reaction of **253** with 2-alkenyl bromides in HMPA in the presence of K_2CO_3–KI gave 1-alken-3-yl derivatives **256**. Oxidation of **254**–**256** to the *S*, *S*, *S*′-trioxides and subsequent treatment of the trioxides with hydrogen chloride in methanol gave the corresponding carboxylic esters. Dialkylation of **253** and subsequent hydrolysis gave cyclic and acyclic ketones[334]. Similarly, methylthiomethyl *p*-tolyl sulfone **257** is a useful reagent for the preparation of carboxylic esters and ketones[335]. Various methyl esters were synthesized using methyl

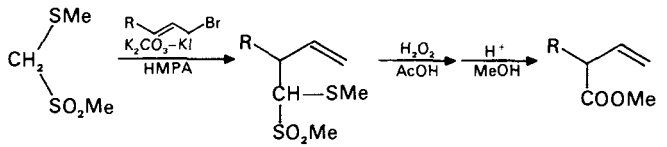


(253) (254)

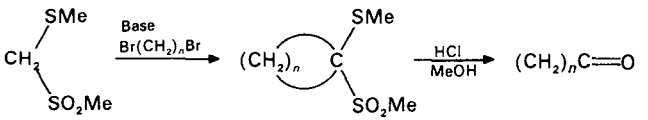


(253) (255)

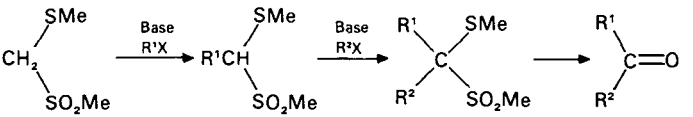
TOMAC = trioctylmethylammonium chloride



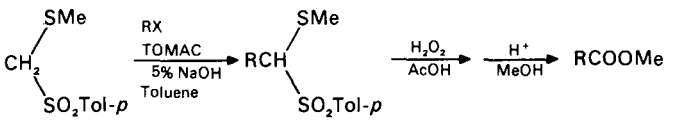
(253) (256)



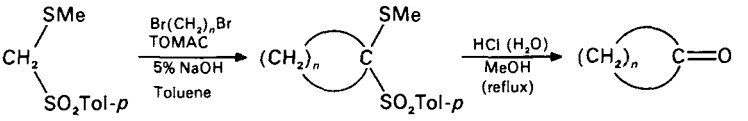
(253)



(253)



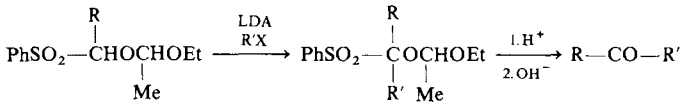
(257)



$n = 4, 5$

phenylsulfonylacetate. In this case good results were observed when the pH of the reaction mixture was controlled by addition of sodium hydrogen phosphate in the desulfonation step[336].

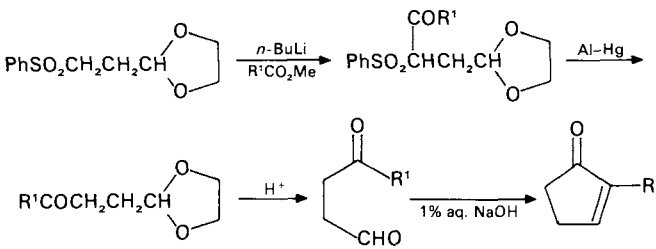
Tanaka and coworkers[337] reported successful syntheses of aldehydes and ketones using (1-ethoxyethoxy)methyl phenyl sulfone **258** and 1-(1-ethoxyethoxy)ethyl phenyl sulfone **259**, as shown in the following scheme.



(**258**) R=H
(**259**) R=Me

(Phenylsulfonyl)nitromethane is preferentially C-alkylated by benzylic halides and primary alkyl iodides, affording secondary α-nitrosulfones[338].

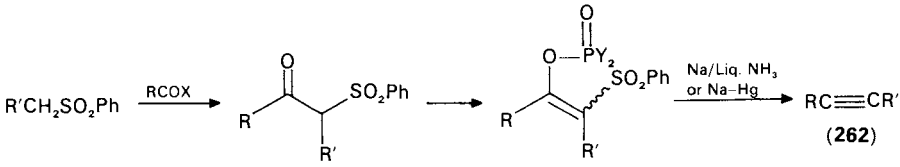
α-Sulfonyl carbanions give the corresponding β-ketosulfones upon reacting with acid chlorides[256,257,267,323,345] and esters[147,265,328,339–345]. The resulting β-ketosulfones are more acidic than the starting sulfones. Therefore, two equivalents of base is necessary to complete the reaction. Another procedure involves treatment of α,α-dilithio derivatives of alkyl aryl sulfones with one equivalent of acylating agent[341–345]. β-Ketosulfones readily undergo desulfonative reduction, and hence acylation is often applied as the initial step in the synthesis of carbonyl compounds. An example is the successful synthesis of cyclopentenone derivatives from 1,4-dicarbonyl compounds reported by Kondo and Tunemoto, as shown in Scheme 7[342].



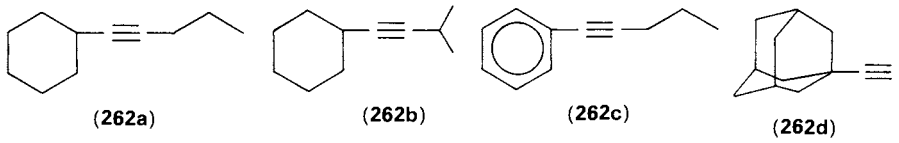
$R^1 = Me(CH_2)_5$, $Me(CH_2)_7$, $t\text{-}BuO_2C(CH_2)_7$; $R^2 = Me(CH_2)_4$, $Me(CH_2)_6$, $t\text{-}BuO_2C(CH_2)_6$

SCHEME 7

1-(*p*-Tolylsulfonyl)nonane and 1-(*p*-tolylsulfonyl)octane were converted by this method to 4-oxotridecanal and 4-oxododecanal, using α-sulfonyl carbanions and the pheromones of Japanese peach fruit moth (*Caposia niponensis Walshingham*) were obtained similarly in four steps[343]. Lythgoe and Waterhouse[345] and Bartlett and coworkers[346] found separately a procedure for the preparation of acetylenic compounds by reductive elimination of the enol phosphates of β-ketosulfones. β-Ketosulfones **260** derived from esters, acyl chloride or nitriles were converted to the corresponding enol phosphates **261** and further treatment of **261** with either sodium in liquid ammonia or sodium amalgam were shown by Bartlett and coworkers to afford mono- and di-substituted acetylenes **262** and eventually compounds **262a–g**[346].



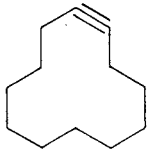
(260) (261) Y = OEt, OPh, NMe_2 (262)



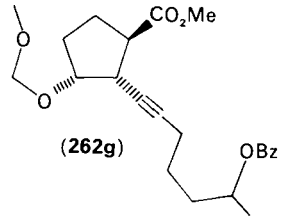
(262a) (262b) (262c) (262d)

$Me(CH_2)_{10}C{\equiv}CCHMe_2$

(262e)

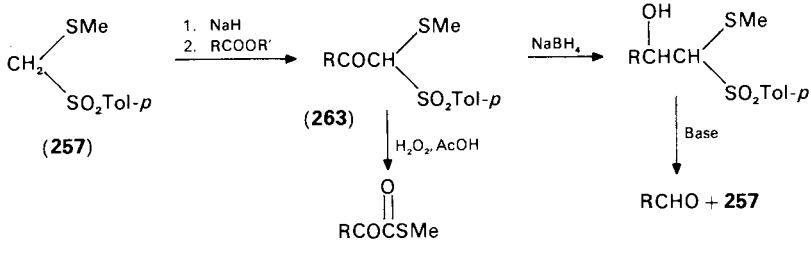


(262f)



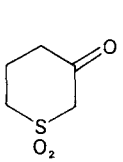
(262g)

Methylthiomethyl *p*-tolyl sulfone **257** was shown to react with various esters in the presence of excess NaH, affording compounds **263** which, upon reduction with $NaBH_4$ and further treatment with alkali, can be converted to the corresponding aldehydes[344]. Oxidation of **263** with hydrogen peroxide gives *S*-methyl α-ketocarbothioates **264**[335].

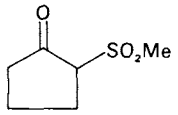


(257) (263) (264)

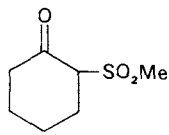
Reaction of sulfones, such as $CH_3SO_2(CH_2)_nCOOEt$ ($n = 2$–5), with sodium ethoxide were shown to result in elimination when $n = 2$ and in cyclization when $n = 3$–5. By this method, tetrahydrothiapyran-3-one-1-dioxide **265**, 2-methylsulfonylcyclopentanone **266** and 2-methylsulfonylcyclohexanone **267** were obtained[347]. Cyclization of ω-cyanosulfone, $CH_3SO_2(CH_2)_nC(CH_3)_2CN$, gave 4,4-dimethyltetrahydrothiophene-3-one dioxide **268** when $n = 1$, 2, 2-dimethyl-5-methylsulfonylcyclopentanone **269** when $n = 3$ and 2,2-dimethyl-6-methylsulfonylcyclohexanone **270** when $n = 4$[348].



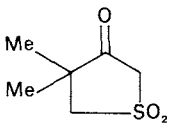
(265)



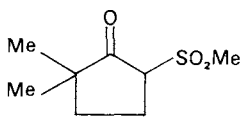
(266)



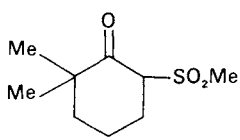
(267)



(268)

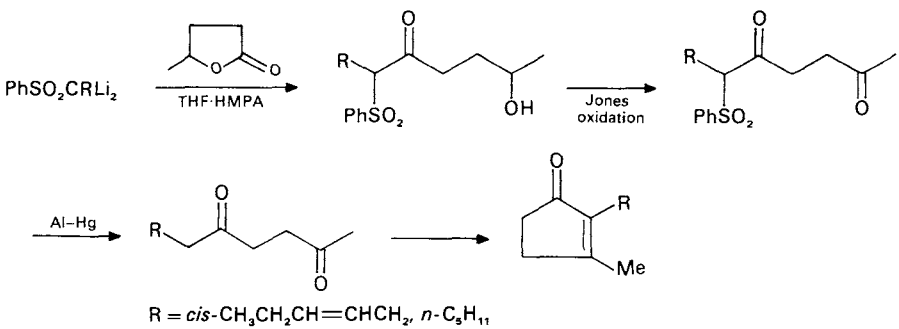


(269)



(270)

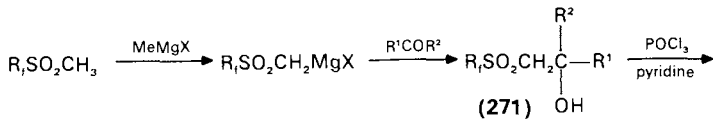
In the reaction of α-sulfonyl carbanion with lactones, the corresponding hydroxy-ω-ketosulfones were obtained[340,345,349–352]. Thus, various ω-hydroxyketones were shown by Umani-Ronchi and coworkers to be formed from the corresponding lactones. For example, the reaction of α,α-dilithioalkyl phenyl sulfones with lactones in THF at low temperatures afforded ω-hydroxy-β-ketosulfones which, upon desulfonylation with aluminium amalgam, gave the corresponding hydroxyketones[352]. This process was applied for the syntheses of *cis*-jasmone and dihydrojasmone by treating γ-valerolactone with *cis*-3-hexen-1-yl phenyl sulfone and *n*-hexyl phenyl sulfone[353].

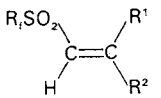


B. Addition to Unsaturated Bonds

Generally, in the nucleophilic addition to carbonyl groups, either magnesium compounds or alkali metal compounds (such as the Li, Na and K derivatives) are used. In some cases even potassium carbonate or piperidine were used as the base for condensation with sulfones. Good results were obtained when concentrated aqueous NaOH was used under phase-transfer conditions[288,297,333].

α-Halomagnesium derivatives of sulfones react like ordinary Grignard reagents and, with aldehydes and ketones, they afford hydroxysulfones in good yields[261–263,266]. Magnesium derivatives, obtained by treatment of trifluoromethylsulfonylmethane ($Rf = CF_3$) or nonafluorobutylsulfonylmethane ($Rf = C_4F_9$) with methylmagnesium halides (X = Cl, Br and I), were found to react with aldehydes or ketones to give β-hydroxysulfones **271**. Treatment of **271** with $POCl_3$ in the presence of pyridine afforded the corresponding vinyl triflones or vinyl nonaflones **272**[354].

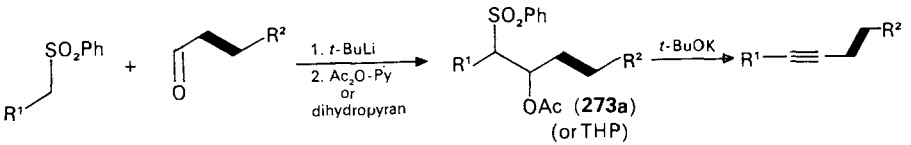


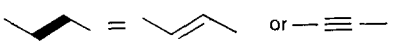


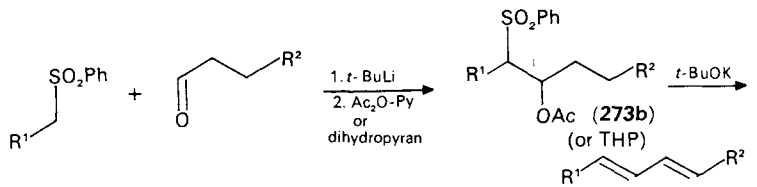
(272)

$R_f = CF_3$, C_4F_9

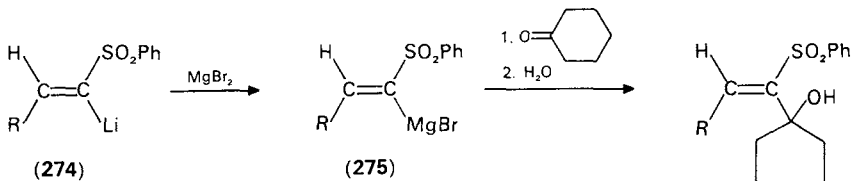
Treatment of acetylated or tetrahydropyranylated β-hydroxysulfones **273** with *t*-BuOK resulted in the formation of acetylenic or polyenic bonds[355,356].







In the reactions with enolizable carbonyl compounds, magnesium reagents give better results than lithium reagents. For example, in the reaction between vinyllithium reagents **274** and cyclohexanone, the yields of β-hydroxysulfones **276** were very low whereas, in the reaction with the magnesium reagent **275**, the β-hydroxysulfones was obtained in good yields[357].

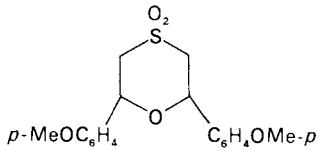


(274) (275) (276)

Ordinary Grignard reagents react with α,β-unsaturated carbonyl compounds and afford both 1,2-adduct and 1,4-adduct. However, methylsulfonylmethylmagnesium bromide[267] or *p*-tolylsulfonylmethylmagnesium bromide[270] gave only 1,2-adducts in the reaction with conjugated carbonyl compounds such as crotonaldehyde, cinnamaldehyde, *trans*-4-phenyl-3-buten-2-one, benzalacetophenone and 1,5-diphenyl-2,4-pentadien-1-one.

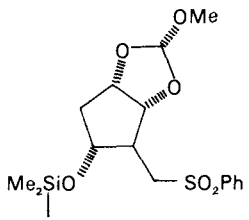
When a mixture of *p*-anisaldehyde and dimethyl sulfone was treated with excess potassium *t*-butoxide in DMF at 60–65 °C, bis-unsaturated sulfone **277** was obtained. In the reaction at 50 °C using a small amount of base, the main product was a heterocyclic compound, i.e., 2,4-di-*p*-methoxyphenyl-1,4-oxathiane 4,4-dioxide **278**[358].

(277)

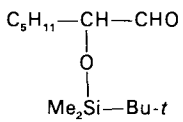


(278)

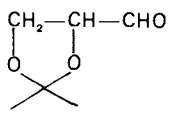
Condensation of sulfones with aromatic aldehydes in alkaline media readily gives β-hydroxysulfones, which can be dehydrated to the corresponding β-styrylsulfones[359]. In the condensation of the lithiated sulfones **279** with such aldehydes as **280**, **281** and **282**, addition of one equivalent of $BF_3 \cdot Et_2O$ prior to addition of the aldehydes was found to increase the yield of the reaction[360].



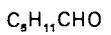
(279)



(280)



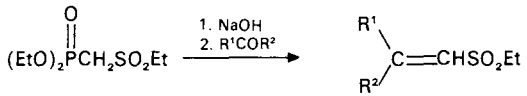
(281)



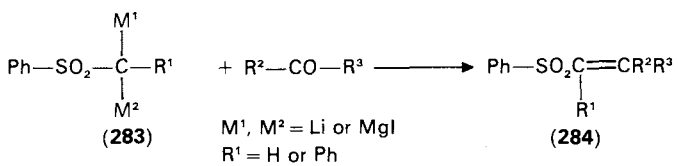
(282)

Bis(alkylsulfonyl)methanes[361,363] or bis(phenylsulfonyl)methane[362] readily reacted with aldehydes in the presence of bases to afford β-hydroxysulfones or bis-adducts. For example, bis(ethylsulfonyl)methane was found to react with salicylaldehyde in the presence of piperidine, affording 2-ethylsulfonylbenzofuran in a good yield[363].

In the base-catalyzed condensation of diethyl ethylsulfonylmethylphosphate with aldehydes or ketones, the corresponding α,β-unsaturated sulfones were obtained in good yields[297,364,365].



A similar Knoevenagel-type condensation takes place between methyl methylthiomethyl sulfone and aromatic aldehydes. In this reaction, use of K_2CO_3 (2 mol equiv) as base and refluxing in isopropanol gave the best result[178].

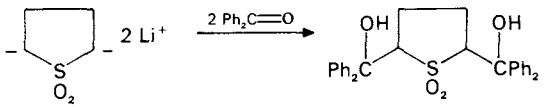


(283)

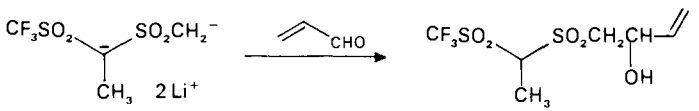
(284)

1,1-Dimetal derivatives **283** of alkyl and benzyl phenyl sulfones were found to react with aldehydes or ketones to give α,β-unsaturated phenyl sulfones **284** in good yields[366].

In the reaction of α,α'-dilithio salts **285** with benzophenone, di-condensation products were obtained[367], whereas in the reaction between the dianion **250** and acrolein only the mono-adduct was obtained[328].

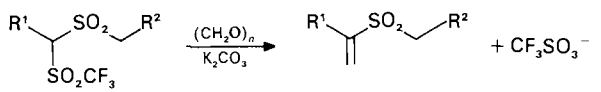


(**285**)

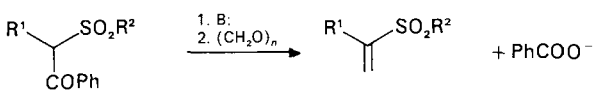


(**250**)

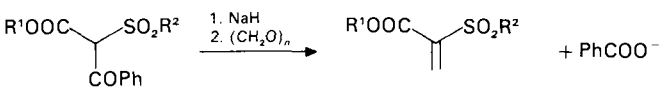
When the reaction between α-trifluoromethyl sulfone **286** and paraformaldehyde was carried out in the presence of potassium carbonate, the vinyl sulfone was obtained quantitatively upon elimination of triflate anion[368]. Such a deacylative methylenation was observed in the reaction between β-ketosulfones **287** and **288** and paraformaldehyde[369–371].



(**286**)

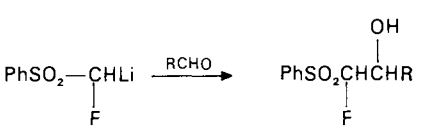


(**287**)

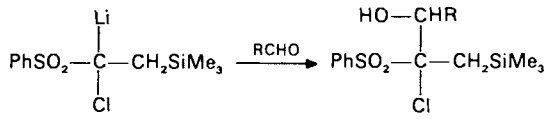


(**288**)

In the condensation reaction between chloro- and bromo-methyl aryl sulfones and carbonyl compounds, α-sulfonyloxiranes were obtained. In this condensation reaction, bases such as potassium *t*-butoxides[372], NaH[373] and aqueous concentrated hydroxide with benzyltriethylammonium chloride under two-phase condensation were used[374]. In the reaction with aldehydes only the *trans*-epoxide isomers resulted, whereas lithiofluoromethyl phenyl sulfone **289**[375] and **291**[376] were found to add to aldehydes affording β-hydroxysulfones **290** and **292**, respectively.

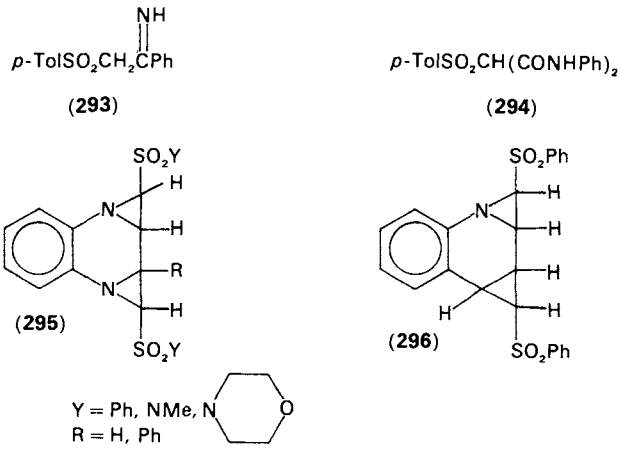


(**289**) (**290**)



(291) (292)

p-Tolylsulfonylmethylmagnesium bromide can add to the unsaturated carbon–nitrogen bond, such as in nitriles and isocyanates. For example, in the reaction with benzonitrile or phenyl isocyanate, 2-imino-2-phenylethyl *p*-tolyl sulfones **293** or *p*-tolylsulfonylmalonanilide **294** was obtained[266]. Quinoxalines and 1,5-, 1,6-, 1,7- and 1,8-naphthyridines reacted readily with chloromethyl phenyl sulfone and *N*,*N*-dialkyl chloromethanesulfonamides in the presence of base to afford tetracyclic bis-aziridines **295** and the cyclopropane-aziridine derivatives **296**[377].

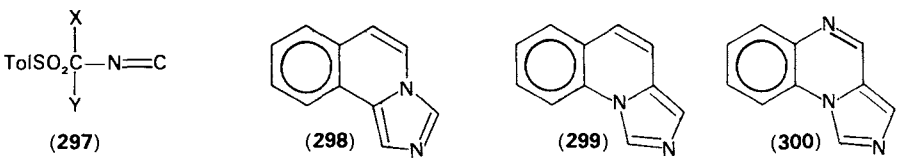


(293) (294)

(295) (296)

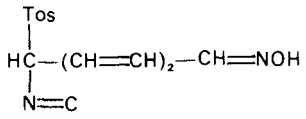
Y = Ph, NMe, N⟨O⟩
R = H, Ph

Mono- and dilithio derivatives of *p*-tosylmethyl isocyanide **297a** were shown to display interesting reactions. Reaction of the monoanion with unsaturated esters was shown to give pyrrole derivatives[378,379]. Dianion **297b** was found to add to the carbon–nitrogen double bonds of isoquinoline, quinoline and quinoxaline affording compounds **298**, **299** and **300**, respectively. In the reactions with pyridine *N*-oxide and pyridazine *N*-oxide, unstable open-chain products **301** and **302** were obtained[379].

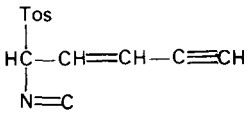


(297) (298) (299) (300)

(a) X = Y = H
(b) X = Y = Li
(c) X = Li, Y = H

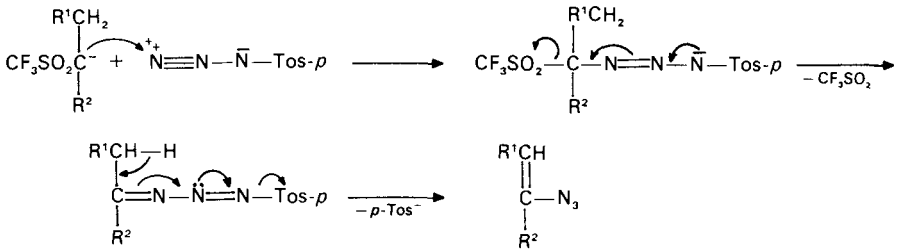


(301)

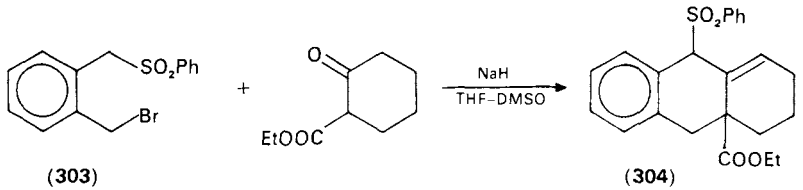


(302)

Triflones reacted with *p*-tolylsulfonyl azide in the presence of two equivalents of base (NaH/glyme) and afforded vinyl azides[380]. These azides were reduced with $LiAlH_4$ to afford the corresponding amines and, upon treatment with triethyl phosphite, they gave ketones after hydrolysis[381].

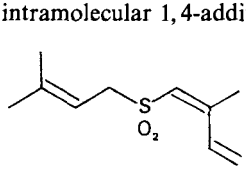


Bromosulfone **303** was found to react with ethyl cyclohexanone-2-carboxylate by preferential attack of the α-sulfonyl carbanion on the carbonyl group to give tricyclic compound **304**[382].

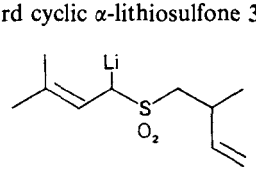


(303) (304)

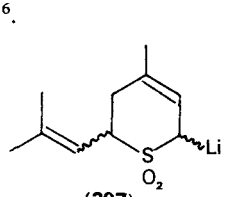
α-Sulfonyl carbanions were also found to react with electrophilic olefins. Allylic sulfones reacted with acrylonitrile[383], vinyl phenyl sulfones and *t*-butyl acrylate giving the corresponding α-adduct[384]. Benzyltriflone was shown to undergo a Michael addition to vinyl ketones in the presence of Et_3N in ethanol and also to acrylonitrile in the presence of EtO^- in ethanol. It also reacts with aldenydes in the presence of piperidine affording the Mannich-type reaction products[385]. Allylic sulfone **305** reacted with LDA at −78 °C in THF to form α-lithiosulfone **306** which, upon warming up to ca. −55 °C, underwent intramolecular 1,4-addition to afford cyclic α-lithiosulfone **307**[386].



(305)



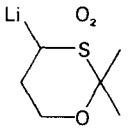
(306)



(307)

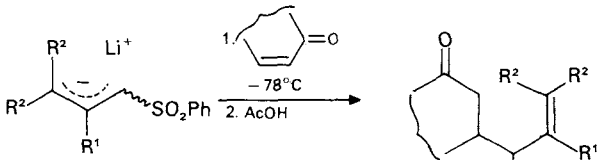
The lithio-derivative derived from cyclohexyl phenyl sulfone underwent 1,2-addition to cyclohexenylideneacetaldehyde or cinnamaldehyde to give the corresponding β-hydroxysulfones[387]. Reactions of 2,2-dimethyl-4-lithio-1,3-oxathiane 3,3-dioxide **308**

with various electrophiles were investigated. In the reaction with α,β-unsaturated ketones, 1,2-adducts were the main products, while in that with α,β-unsaturated esters, 1,4-adducts were mainly obtained[388].



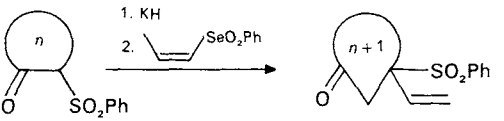
(308)

Carbanions derived from allylic sulfones **309** reacted with cyclohexenone, giving mainly 1,4-γ adducts[389]. When this reaction was carried out at a low temperature, 1,2-α-adducts were formed immediately and, upon raising the temperature, they rearranged to the 1,4-γ-adducts. The addition to acyclic and cyclic enones in HMPA gave almost completely the 1,4-adduct[390].



(309)

Potassium salts of cyclic ketosulfones of various size **310** ($n = 6$, 8, 12) reacted with phenyl (Z)-1-propenyl selenone affording cyclic ketosulfones **311** of various ring sizes ($n + 1$) having a vinyl group at the 3-position[391].



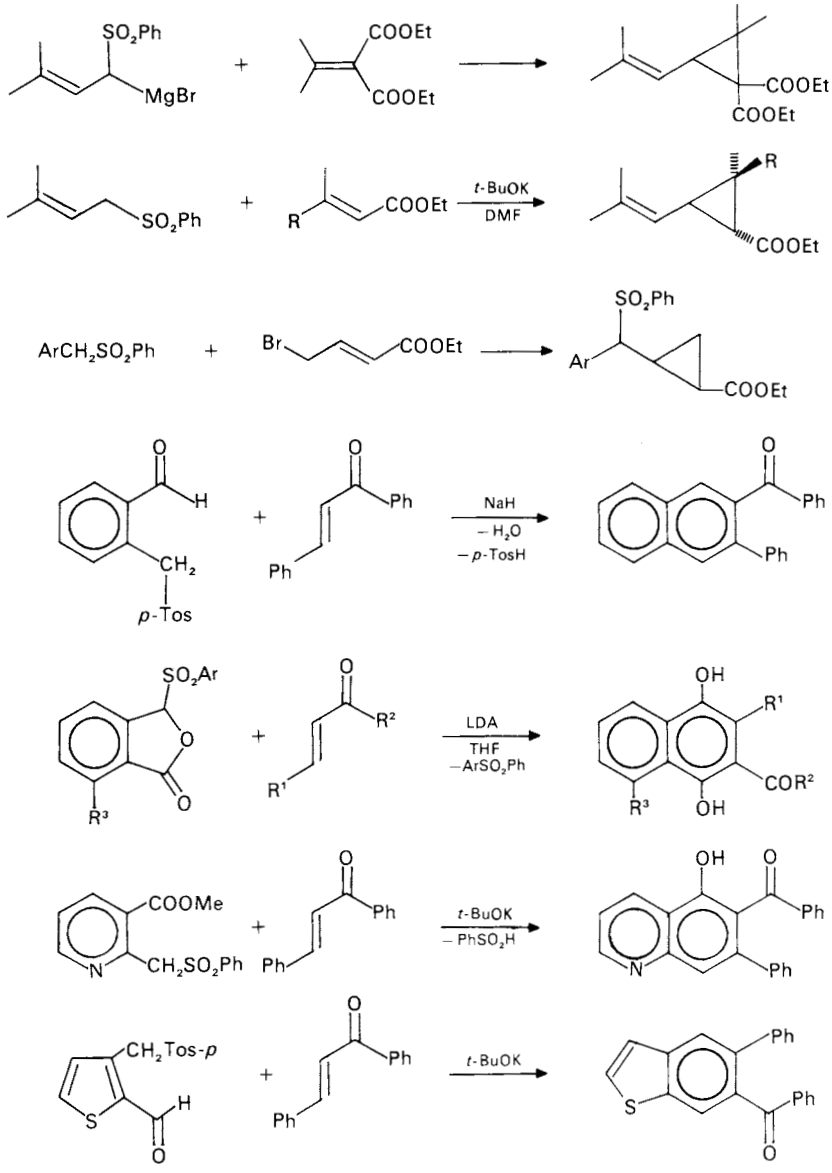
(310) (311)

Other reactions involving α-sulfonyl carbanions which afford cyclopropane derivatives or aromatic rings can be seen in the examples comprising Scheme 8[392–400].

C. Nucleophilic Addition to α,β-Unsaturated Sulfones

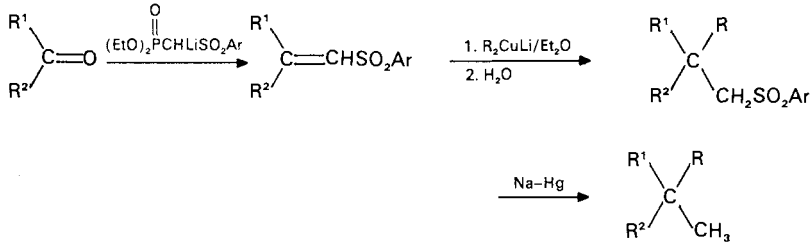
Nucleophilic addition to α,β-unsaturated sulfones has long been known. For example, treatment of divinyl sulfone with sodium hydroxide has been known to afford bis(β-hydroxyethyl) sulfone[401], while the reaction of α- and β-naphthyl allyl sulfones[402] and allyl benzyl sulfone[403] with alkali hydroxide or alkoxide gave β-hydroxy or alkoxy derivatives. In the latter reaction, the allyl group underwent prototropy to the 1-propenyl group, which in a subsequent step underwent nucleophilic attack[403]. Amines, alcohols and sulfides are known to add readily to α,β-unsaturated sulfones, and these addition reactions have been studied widely. In this section, the addition of carbon nucleophiles to α,β-unsaturated sulfones and the reactions of the resulting α-sulfonyl carbanions will be examined.

Vinyl sulfones, being good Michael acceptors, have been regarded as useful reagents for carbon–carbon bond formation. Nucleophiles used often are organometallic reagents, enamines and enolate anions and the Michael addition products are usually obtained in

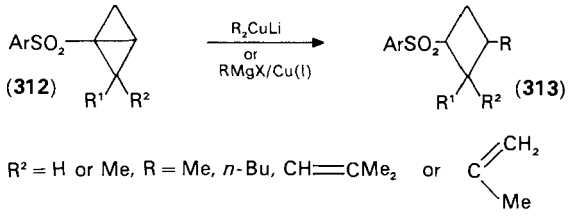


SCHEME 8

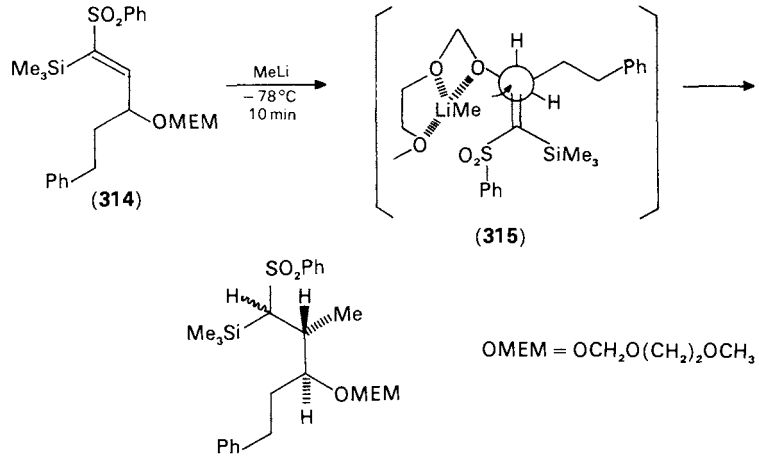
excellent yields. For example, treatment of α,β-ethylenic aryl sulfones with lithium dimethyl or dibutylcuprate afforded β-methylated or β-*n*-butylated sulfones in excellent yields. Posner and Brunelle[404,405] used this reaction for *gem*-dialkylation of aldehydes and ketones, as shown below.



The central C—C bond in bicyclo[1.1.0]butane has a high π-character and is known to behave as an olefin. Thus, 1-arylsulfonylbicyclobutanes **312** reacted with Grignard reagents in the presence of lithium dialkylcuprates or cuprous salts (Me_2S, CuBr or CuCl) giving 3-alkyl-1-arylsulfonylcyclobutanes **313**[406].

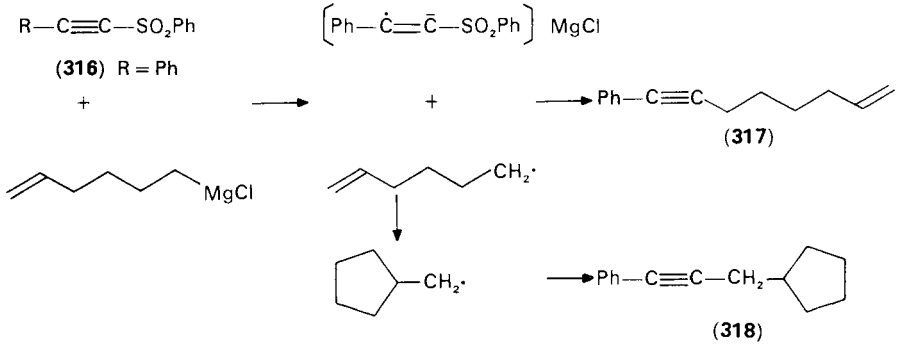


Isobe and coworkers[407] found an interesting diastereoselective heteroconjugate addition of methyllithium to **314**. The stereochemical control was considered to be determined at the stage of the intermediate **315**. Since methyllithium is considered to be coordinated strongly with the methoxyethoxymethoxyl (OMEM) group, the methyl anion would attack the β-carbon of the olefin only from one side, as shown below.

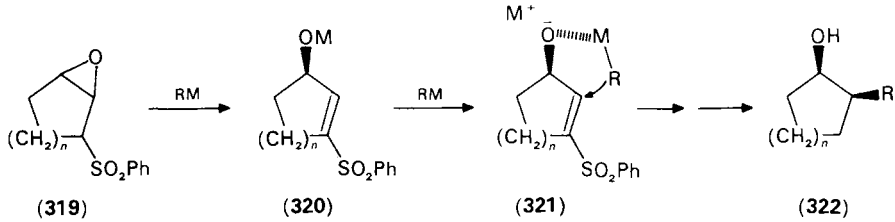


Lithium dibutylcuprate reacted with (*E*)-1,3-butadienyl *p*-tosyl sulfone affording (*Z*)-2-octenyl *p*-tosyl sulfone. In the reaction of allyl (*E*)- and (*Z*)-1,3-dibutadienyl sulfones with lithium dibutylcuprate or lithium (*Z*)-di(1-butenyl) cuprate, the major compound obtained was of (*Z*)-geometry around the 2,3-double bond, indicating that (*Z*)-selectivity is not so high in this reaction (56–79%)[408].

The nucleophilic addition of various lithium dialkyl- or diphenyl-cuprates to phenylsulfonylacetylenes was found to give mainly *E*-olefinic sulfones[409]. The mode of nucleophilic addition of organometallic reagents to acetylenic sulfone **316** was found to vary with the change of R and the organometallic reagent used in the following three reactions: (a) Michael addition (R = alkyl, aryl or Me_3Si), (b) mono- or dilithiation (R = Me or $R'CH_2$), and (c) alkylative desulfonylation (R = aryl and alkyl without α-hydrogen, Me_3Si, R'M = R'Li, R'MgX). The reaction of type (c) was found to proceed via a single-electron transfer (SET), namely, treatment of phenyl phenylethynyl sulfone (R = Ph) with 1.1 mol equivalent of 5-hexenylmagnesium chloride in THF afforded compounds **317** and **318** in the ratio 2:1. The formation of **318** has been considered to suggest the formation of 5-hexenyl radical, which would immediately cyclize to cyclopentylmethyl radical. Alkylative desulfonylation of this type appeared to take place in the treatment of vinylic sulfones, bearing the allyl, benzyl or *t*-butyl group with alkyllithium reagents of low electron affinities[410].



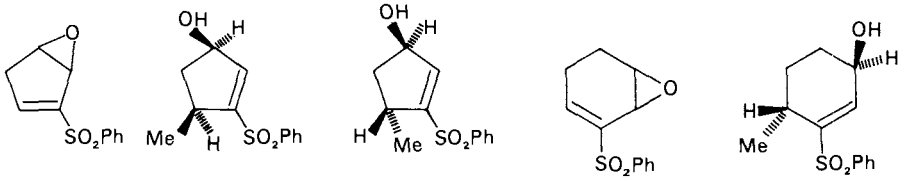
A similar stereospecific conjugate addition to epoxysulfone **323** was also observed[416] with Grignard reagents in the presence of nickel ion or palladium catalysts[411,412]. Methyllithium and *n*-butyllithium did not add to 1-propenyl phenyl sulfone nor to phenyl β-styryl sulfone but underwent lithiation at −95 °C[357,410]. However methyllithium, *n*-butyllithium, phenyllithium and Grignard reagents were shown to undergo conjugate addition to epoxysulfone **319** (*n* = 1–3). Since this addition gave *cis*-adducts **322**, the initial step is believed to form γ-oxide-α,β-unsaturated sulfones **320** which, in a subsequent step, undergo an intermolecular-assisted delivery of the reagent (cf. **321**) to afford the final product **322**[413–415].



(319) (320) (321) (322)

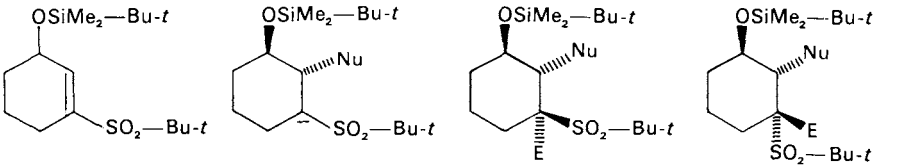
A similar stereospecific conjugate addition to epoxysulfone **323** was also observed[416]. When this reaction of **323** was carried out with methyllithium at −78 °C dichloromethane–diethyl ether (1:1) in the presence of lithium perchlorate, compounds **324** and **325** were obtained in a ratio of 95:5. On the other hand, in the treatment of **323**

with trimethylaluminium/methylcopper, only **325** was formed. Saddler and Fuchs[416] assumed that in the noncoordinating solvents, methyllithium undergoes direct addition via chelation to the epoxide forming an epoxide–lithium perchlorate complex, whereas in the reaction with methylcopper/trimethylaluminium formation of a THF-solvated epoxide–trimethylaluminium complex prevents the coordination with methylcopper which results in addition to the less sterically encumbered face. Treatment of epoxysulfone **326** with trimethylaluminium/methylcopper gave only **327** in 70% yield.



(323) **(324)** **(325)** **(326)** **(327)**

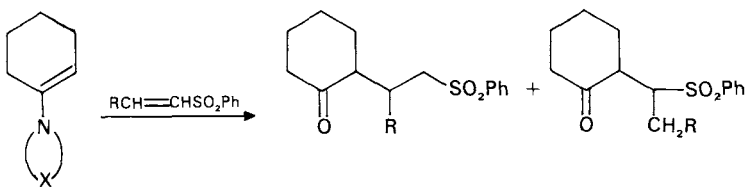
Potassium or lithium derivatives of ethyl acetate, dimethyl acetamide, acetonitrile, acetophenone, pinacolone and (trimethylsilyl)acetylene are known to undergo conjugate addition to 3-(*t*-butyldimethylsiloxy)-1-cyclohexenyl *t*-butyl sulfone **328**. The resulting α-sulfonyl carbanions **329** can be trapped stereospecifically by electrophiles such as water and methyl iodide[417]. When the nucleophile was an sp^3-hybridized primary anion ($Nu = CH_2Y$), the resulting product was mainly **330**, while in the reaction with (trimethylsilyl)acetylide anion the main product was **331**.



(328) **(329)** **(330)** **(331)**

E = H or Me
Nu = nucleophile

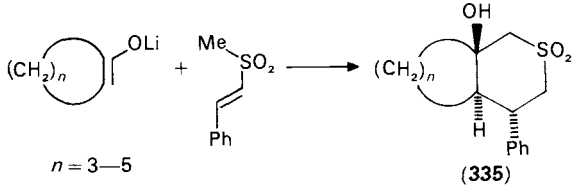
Phenyl vinyl sulfones reacted with cyclohexanone enamines **332** to afford adducts which, upon hydrolysis, gave 2-(2-phenylsulfonyl)alkylcyclohexanone **333a**[418,419]. However, in the reaction with phenyl styryl sulfone, two products **333b** and **334** were obtained by the nucleophilic attack at the β- and α-carbon atoms[420,421]. Steric effects, electrostatic interactions between the nitrogen atom of the enamine and the oxygen atoms of the sulfone group, and medium effects contribute to the regioselectivity of the reaction[422].



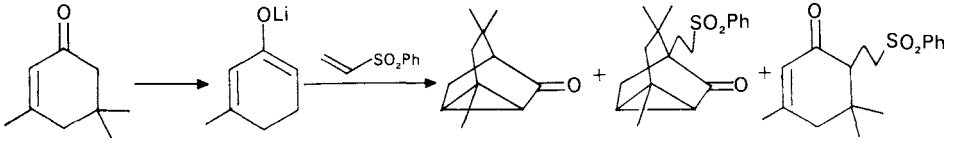
(332) **(333)** (**a**) R = H (**b**) R = Ph **(334)** R = Ph

X = CH_2OCH_2, $(CH_2)_2$ or $(CH_2)_3$

α-Sulfonyl carbanions, formed by nucleophilic addition to vinylic sulfones, were found to undergo cyclization upon reacting further with some functional groups within the molecule. Recently, ketone enolates were found to add to methyl styryl sulfone to afford cyclic products in good yields; treatment of methyl styryl sulfone with lithium cyclohexanone enolate in THF–DMF (1:2) at 80 °C give quantitatively 8a-hydroxy-4-phenyl-2-thiadecalin 2,2-dioxides **335**. By this reaction, 5–7 membered cycloalkanone enolates and acetone enolate were nicely converted to the corresponding cyclic sulfones[423]. In the reaction between isophorone lithium α′-enolate **336** and phenyl vinyl sulfone, tricyclooctanone **337** was formed along with **338** and **339**[424].



(335)

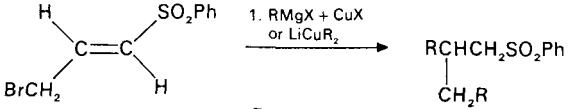


(336) (337) (338) (339)

Vinyl sulfone **340** was found to react with Grignard reagents, prepared from allyl bromide, propargyl bromide, 1-bromo-3-methyl-2-butene, bromobenzene and benzyl chloride and afforded the corresponding 2-substituted cyclopropyl phenyl sulfones **341**. In the reaction with Grignard reagents when R was a saturated alkyl group such as methyl, ethyl and *t*-butyl, corresponding cyclopropyl sulfones were not obtained. In the presence of a catalytic amount of a cuprous salt, the reaction with either Grignard reagents or lithium dialkylcuprate reagents was found to replace bromide and afforded the product **342** after further Michael addition[357].

(340) (341)

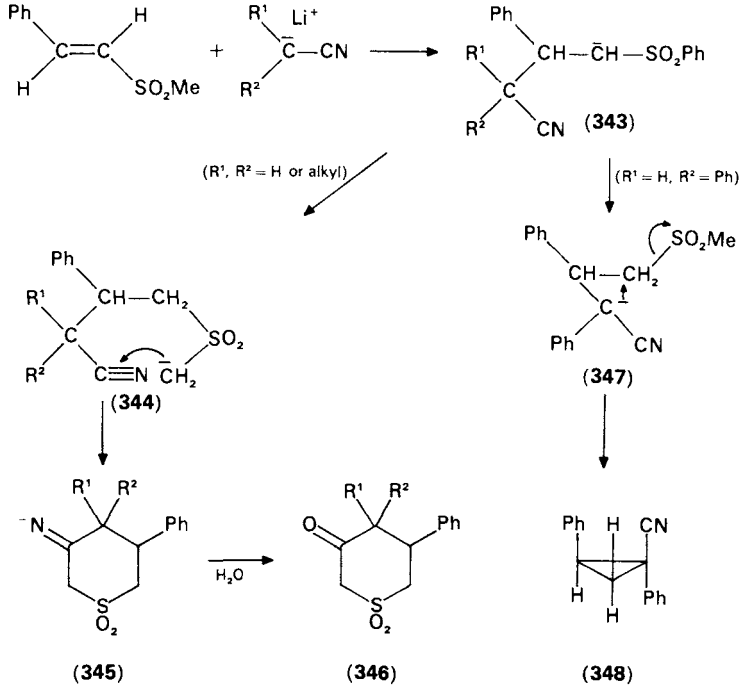
$R = CH_2{=}CHCH_2$, $HC{\equiv}CCH_2$, $CH_2{=}CHCMe_2$, Ph, $PhCH_2$



(340) (342)

Treatment of α-lithionitriles with vinylic sulfones resulted in the formation of cyclized products, i.e., 3-oxothian-1,1-dioxides **346** or cyclopropane derivatives **348**. When α-lithiated aliphatic nitriles were used, carbanions **343**, formed by the nucleophilic addition,

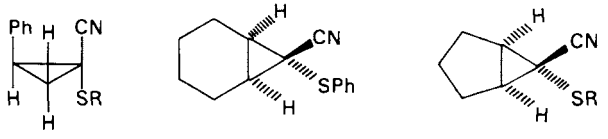
underwent intramolecular proton transfer to afford the stable carbanions **344**. The latter underwent further nucleophilic attack on the cyano group to form imines **345** that gave compounds **346** upon hydrolysis. In the reaction of the α-lithiophenylacetonitrile, carbanion **347** underwent intramolecular nucleophilic substitution to give cyclopropanes **348** (see Scheme 9).



(345) (346) (348)

SCHEME 9

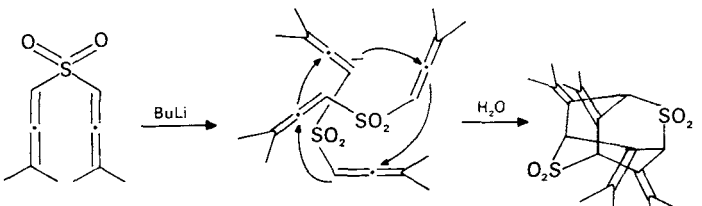
The cyclopropanation reactions were extended to the formation of cyclopropyl sulfides **349–353** in good yields[425].



(349) (351) (352)

(350) (353)

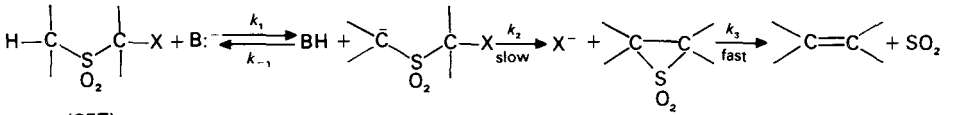
Treatment of diallenyl sulfone **354** with *n*-butyllithium resulted in a cyclodimerization to afford 2,6-dithiaadamantane derivative **356**. This dimerization is considered to be initiated by formation of the α-sulfonyl carbanion **355** and to proceed through a 'carbanion walk' or 'carbanion tour' process[426].



(354) **(355)** **(356)**

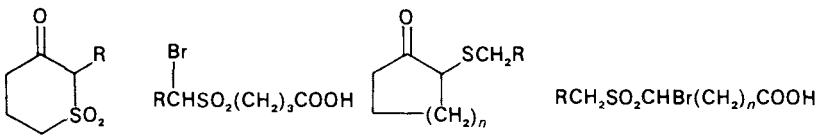
D. Ramberg–Bäcklund Reaction

Treatment of α-halosulfones **357** bearing α′-hydrogens with base gives olefins by extruding SO_2 from the episulfone intermediates **359**. The reaction was found by Ramberg and Bäcklund in 1940[427] and named after them, and it has been very useful for the preparation of tailor-made olefins. The reaction has been investigated in detail[428–431] and utilized widely for olefin syntheses. An excellent review on this reaction by Paquett[432] covers the literature up to 1975, so only recent studies are dealt with in this section. The generally accepted mechanistic path is shown below.



(357) **(358)** **(359)**

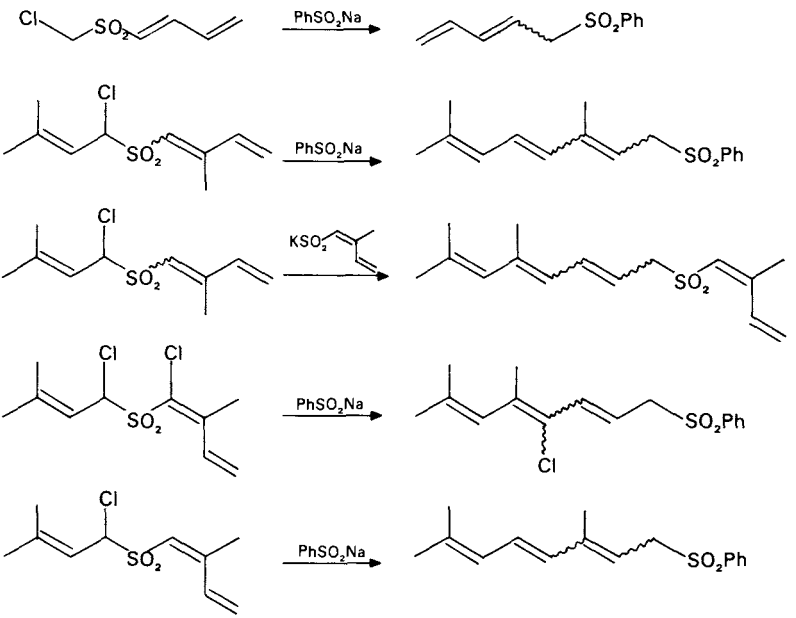
α-Halosulfones can be obtained upon treatment of the α-sulfonyl carbanion with electrophiles such as elemental bromine, iodine, *N*-chlorosuccinimide, cyanogen bromide and trichloromethanesulfonyl chloride. Treatment of sulfones with KOH or NaOH in CCl_4 is known also to afford the corresponding olefins in a one-pot process without isolating the intermediary chlorosulfones, according to Meyers and coworkers[433]. Meanwhile, Scholz[434] isolated α-bromomethylsulfones **361** in good yields upon treatment of cyclic ketosulfones **360** with aqueous NaOH–Br_2. A ring-opening reaction was found to occur upon treatment of α-(alkylthio)cycloalkanones **362** with NaOX (X = Br, Cl) to afford α-halosulfones **363**[435] which, upon further treatment with *t*-BuOK in DMSO, underwent the Ramberg–Bäcklund reaction to afford olefins with (*E*) configuration[434,435].



(360) **(361)** **(362)** **(363)**

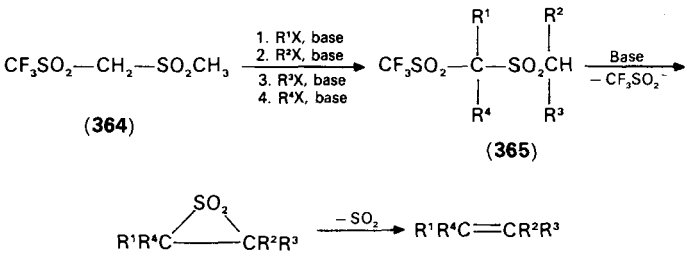
Since the Ramberg–Bäcklund reaction proceeds through the initial α-proton removal by base, followed by intramolecular nucleophilic substitution of α-carbanion **358** to form

episulfones **359**, if there is a good leaving group at the α-position of the sulfone, treatment of the sulfone with base would lead to the Ramberg–Bäcklund reaction after initial formation of the corresponding α′-anion. The α′-carbanions can be generated upon nucleophilic addition to α′, β′-unsaturated sulfones. Thus, Chen and coworkers carried out the Michael-addition-type Ramberg–Bäcklund reaction using sodium benzenesulfinate or potassium 1,3-butadienyl sulfinate[436] and obtained conjugated polyenes[436–438], as shown in Scheme 10.

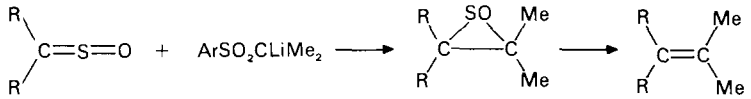


SCHEME 10

There have been Ramberg–Bäcklund-type reactions in which the leaving group is not a halide ion. For example, treatment of the polyalkylated methyl triflone **365** is known to result in a Ramberg–Bäcklund reaction forming the corresponding olefin. Since methyl triflone **364** can be alkylated successively regiospecifically at the two carbon atoms, Hendrickson and coworkers[439] used this reaction for the synthesis of some tailor-made olefins.

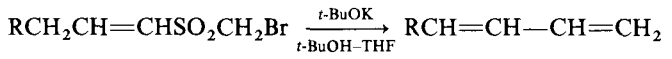


In the reaction between sulfines **366** and an α-sulfonyl carbanion, a Ramberg–Bäcklund reaction took place via formation of the intermediate **367**[440].

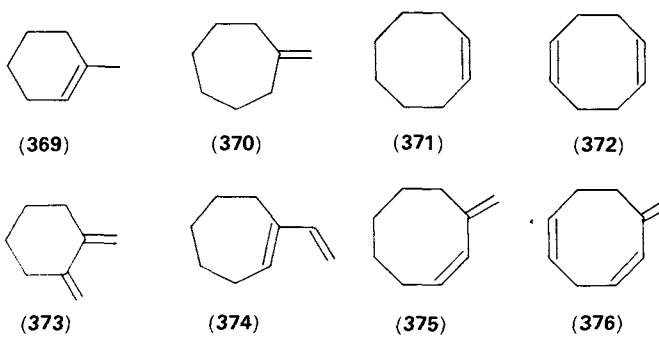


(366) (367)

Block and Aslam[441] reported a novel variant of the Ramberg–Bäcklund reaction in which α,β-unsaturated α′-bromoalkyl sulfones **368** afforded 1,3-dienes upon treatment with base. Since α′-bromoalkyl sulfones **368** can be obtained readily by the initial treatment of olefins with bromomethanesulfonyl bromide under photoirradiation and subsequent treatment with triethylamine, this reaction was utilized for preparation of dienes which contain one additional carbon over that of the corresponding olefin. Starting from the cyclic olefins **369–372** the 1,3-dienes **373–376** were obtained[442].



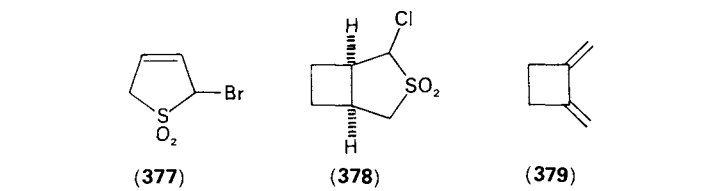
(368)



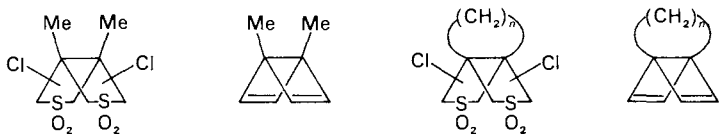
(369) (370) (371) (372)

(373) (374) (375) (376)

Treatment of halosulfones **377** and **378** with PhONa in diglyme resulted in the formation of butadiene and **379**[443]. Weinges and coworkers[444] reported that double Ramberg–Bäcklund reaction of isomeric dichlorodisulfone **380** gave 1,4-dimethyl-Dewar benzene **381** and *p*-xylene. The Ramberg–Bäcklund reactions of dichlorosulfones, **382** ($N = 2–5$), were carried out and 1,4-polymethylene-Dewar benzenes **383** ($n = 4, 5$) were obtained[445].

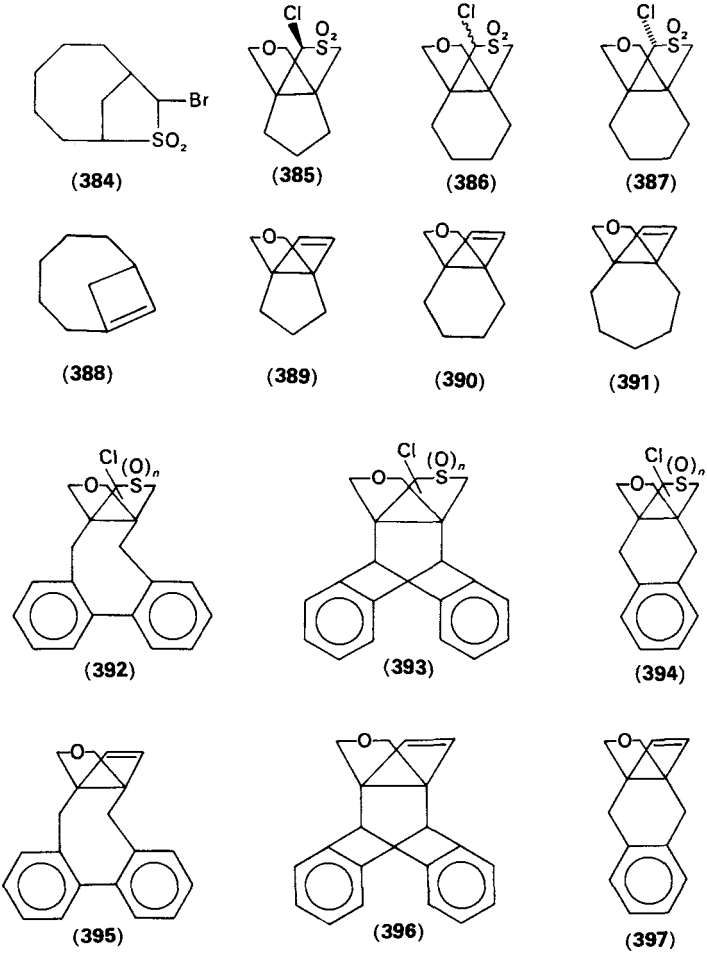


(377) (378) (379)

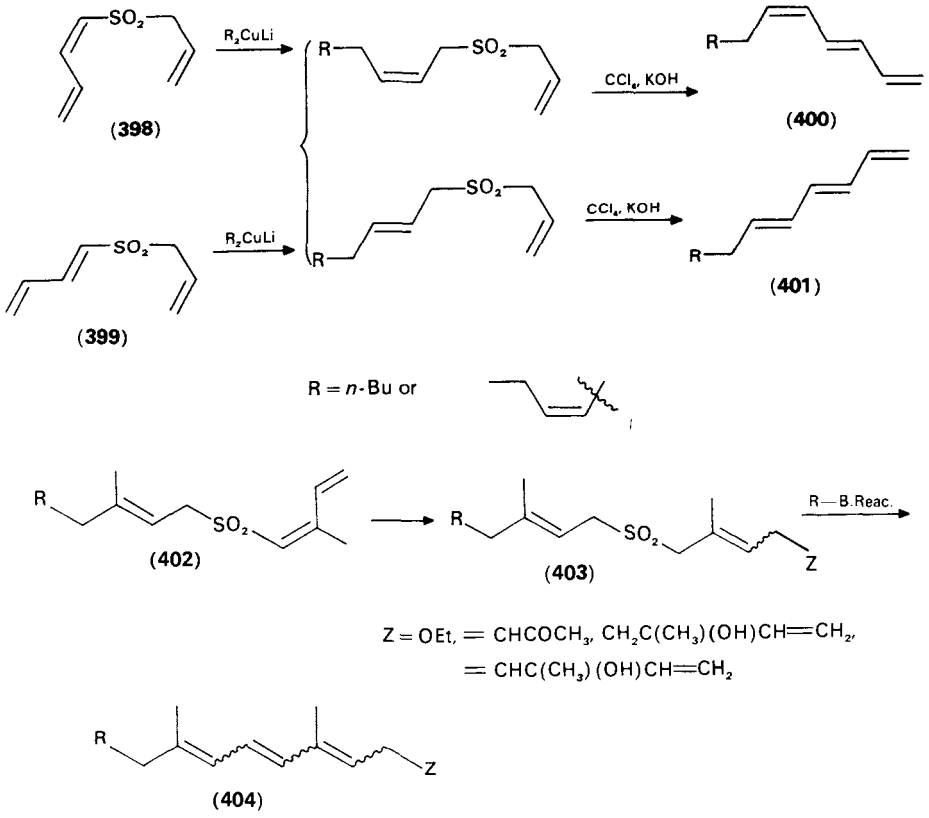


(380) (381) $n = 2–5$ (382) $n = 4, 5$ (383)

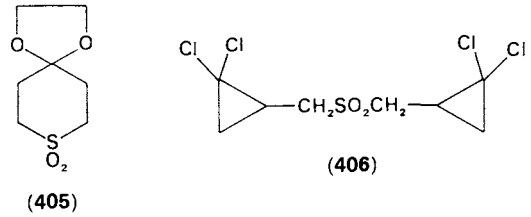
The Ramberg–Bäcklund reaction of compound **384** gave the Bredt olefin **388**, which was actually isolated[446]. By reaction of chlorosulfones **385–387** and **392–394** ($n = 2$) with potassium *t*-butoxide the corresponding oxaproperanes **392–397** were obtained by the Ramberg–Bäcklund reaction, but only in low yields[447,448]. In contrast, the reaction of the chlorosulfoxides **392**, **393** and **394** ($n = 1$) gave oxaproperanes **395**, **396** and **397** under analogous conditions in 85–90, 25 and 85% yields, respectively[447].



The Ramberg–Bäcklund reaction has been utilized for the preparation of polyenes. 1,3-Butadienyl allyl sulfones **398** and **399** were transformed into the tri- and tetra-enes **400** and **401** by alkylcuprate addition and the Ramberg–Bäcklund-type SO_2 extrusion[449]. Julia and coworkers[450] carried out the Michael addition of various nucleophiles such as ethanol, *t*-butyl acetoacetate and phenyl thioacetone to allyl dienyl sulfones **402** and then converted them to diallyl sulfones **403**. The sulfones were transformed into isoprenoid, **404** by the Ramberg–Bäcklund reaction.

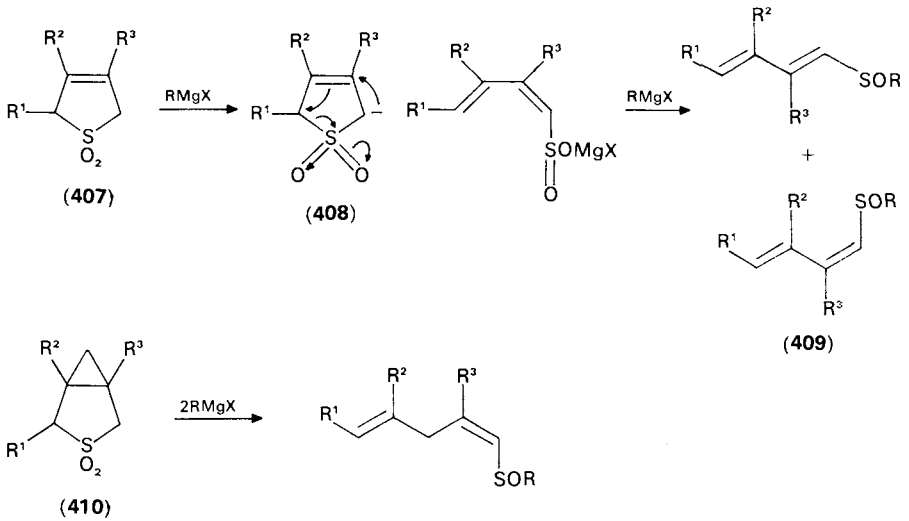


One-pot Ramberg–Bäcklund reaction of sulfones **405** and **406** with KOH in CCl_4-*t*-BuOH afforded the corresponding olefins[451,452].



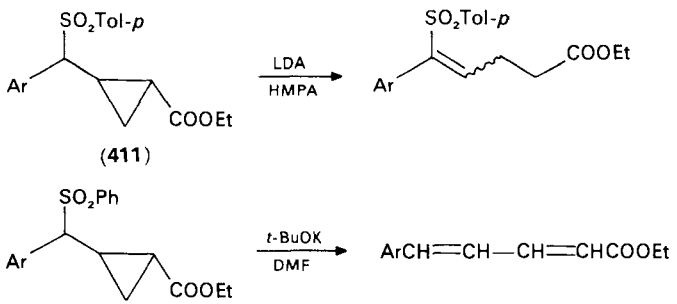
E. Miscellaneous Reactions of α-Sulfonyl Carbanions

The reaction of 2,5-dihydrothiophene 1,1-dioxide **407** with two equivalents of alkyl or arylmagnesium halide afforded 1,3-dienyl sulfoxides **409**[453]. This reaction has been considered to proceed via an initial ring-opening of the incipient anion **408** to form the corresponding sulfinate salt which reacted further with Grignard reagents, affording the sulfoxides. A similar ring-opening reaction was observed in the treatment of bicyclic sulfone **410** with Grignard reagents.



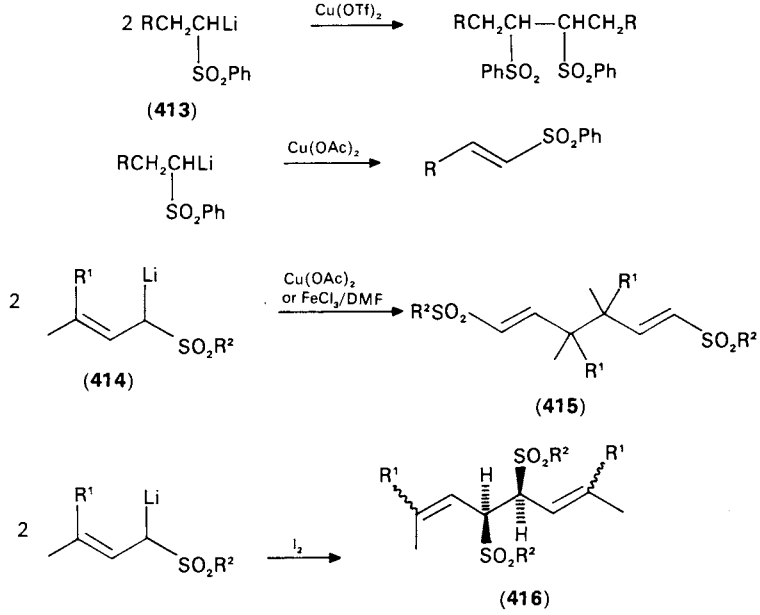
(407) (408) (409) (410)

Sulfone **411** gave the ring-opened product upon treatment with a catalytic amount of LDA in THF–HMPA, whereas treatment of **412** with *t*-BuOK in DMF resulted in ring-opening and elimination of a sulfinate anion[454].



(411) (412)

α-Lithiated benzyl phenyl sulfones undergo slow decomposition at room temperature in THF and afford 1,2-diarylethylenes. This decomposition reaction is promoted by elemental tellurium[455]. α-Sulfonyl carbanions are known to afford the corresponding disulfones upon coupling in the presence of cupric salts. Phenylsulfonylmethylmagnesium bromide was converted to 1,2-bis(phenylsulfonyl)ethane upon treatment with cupric chloride[268]. Julia and coworkers[456] reported that treatment of lithiated sulfones **413** with cupric triflate in the presence of isobutyronitrile gave the best result. The use of cupric acetate led to the formation of only *trans*-vinylic sulfone[457]. Obviously allylic sulfones **414** were oxidized in the presence of ferric chloride–dimethylformamide complex and afforded mainly 1,6-disulfones **415** by a 3,3′-coupling[268,456,458]. α-Sulfonyl carbanions also undergo coupling reaction with iodine. For example, treatment of the potassium salt of 2,4-dinitrobenzyl *p*-tolyl sulfone with iodine gave the corresponding dimers[255]. With an allylic sulfone **414**, a vicinal disulfone of *threo*-configuration **416** was formed presumably via formation of α-iodosulfone as intermediate[458].



α-Sulfonyl carbanions are known to undergo oxidative desulfonylation to form ketones upon treatment with molybdenum peroxide (MoO·Py·HMPA) in THF at −78 °C[459].

VII. REFERENCES

1. C. C. Price and S. Oae, *Sulfur Bonding*, The Ronald Press, New York, 1962, pp. 61–128.
2. Y. Yano and S. Oae, *3d Orbital Resonance in the Bivalent Sulfur Atom, Mechanisms of Reactions of Sulfur Compounds*, Vol. 4, Intra-Science, 1969, p. 167.
3. S. Wolfe, A. Rauk and I. G. Csizmadia, *J. Amer. Chem. Soc.*, **89**, 5710 (1967).
4. S. Wolfe, A. Rauk and I. G. Csizmadia, *J. Amer. Chem. Soc.*, **91**, 1567 (1969).
5. S. Wolfe, A. Rauk, L. M. Tel and I. G. Csizmadia, *Chem. Commun.*, 96, (1970).
6. A. Rauk, E. Buncel, R. Y. Moir and S. Wolfe, *J. Amer. Chem. Soc.*, **87**, 5498 (1965).
7. A. Rauk, S. Wolfe and I. G. Csizmadia, *Can. J. Chem.*, **47**, 113 (1968).
8. F. Bernardi, I. G. Csizmadia, A. Mangini, H. B. Schlegel, M.-H. Whangbo and S. Wolfe, *J. Amer. Chem. Soc.*, **97**, 2209 (1975).
9. N. D. Epiotis, R. L. Yates, F. Bernardi and S. Wolfe, *J. Amer. Chem. Soc.*, **98**, 5435 (1976).
10. C. A. Coulson, *Nature*, **221**, 1106 (1969).
11. J. B. Florey and L. C. Cusachs, *J. Amer. Chem. Soc.*, **94**, 3040 (1972).
12. J. I. Musher, *J. Amer. Chem. Soc.*, **94**, 1370 (1972).
13. A. Streitwieser, Jr. and J. E. Williams, Jr., *J. Amer. Chem. Soc.*, **97**, 191 (1975).
14. J. Fabian, P. Schönfeld and R. Mayer, *Phosphorus and Sulfur*, **2**, 151 (1976).
15. J. M. Lehn and G. Wipff, *J. Amer. Chem. Soc.*, **98**, 7498 (1976).
16. S. Wolfe, A. Stolow and L. A. Lajohn, *Tetrahedron Letters*, **24**, 4071 (1983).
17. S. Wolfe, F. Bernardi, I. G. Csizmadia and A. Mangini, in *Organic Sulfur Chemistry*, Elsevier, Amsterdam, 1985, pp. 133–190.
18. S. Oae, W. Tagaki and A. Ohno, *J. Amer. Chem. Soc.*, **83**, 5036 (1961).
19. S. Oae, W. Tagaki and A. Ohno, *Tetrahedron*, **20**, 427 (1964).
20. E. L. Eliel, A. A. Hartmann and A. G. Abatjoglou, *J. Amer. Chem. Soc.*, **96**, 1807 (1974).
21. F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **74**, 1058 (1952).

22. J. D. Roberts, E. A. McElhill and R. Armstrong, *J. Amer. Chem. Soc.*, **71**, 2923 (1949).
23. J. D. Roberts, R. A. Clement and J. J. Drysdale, *J. Amer. Chem. Soc.*, **73**, 2181 (1951).
24. C. C. Price and J. J. Hydock, *J. Amer. Chem. Soc.*, **74**, 1943 (1952).
25. F. G. Bordwell and P. J. Boutan, *J. Amer. Chem. Soc.*, **79**, 717 (1957).
26. H. H. Szmant and G. Suld., *J. Amer. Chem. Soc.*, **78**, 3400 (1956).
27. H. Kloosterziel and H. J. Backer, *Rec. Trav. Chim. Pays-Bas*, **71**, 295 (1952).
28. S. Oae and C. C. Price, *J. Amer. Chem. Soc.*, **80**, 3425 (1958).
29. D. P. Craig, A. Maccall, R. S. Nyholm, L. E. Orgel and L. E. Sutton, *J. Chem. Soc.*, 332 (1954).
30. D. P. Craig and E. A. Magnusson, *J. Chem. Soc.*, 4895 (1956).
31. G. E. Kimball, *J. Chem. Phys.*, **8**, 188 (1940).
32. H. Kloosterziel and H. J. Backer, *Rec. Trav. Chim. Pays-Bas*, **72**, 185 (1953).
33. S. Oae, M. Yoshihara and W. Tagaki, *Bull. Chem. Soc. Japan*, **40**, 959 (1967).
34. S. Oae and C. Zalut, *J. Amer. Chem. Soc.*, **82**, 5359 (1960).
35. S. Oae and C. C. Price, *J. Amer. Chem. Soc.*, **80**, 4938 (1958).
36. S. Oae and Y. H. Kim, *Bull. Chem. Soc. Japan*, **40**, 1716 (1967).
37. Y. H. Kim and S. Oae, *Bull. Chem. Soc. Japan*, **42**, 1622 (1969).
38. W. von E. Doering and A. K. Hoffmann, *J. Amer. Chem. Soc.*, **77**, 521 (1955).
39. R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2449 (1953).
40. F. G. Bordwell, W. S. Mathews and N. R. Vanier, *J. Amer. Chem. Soc.*, **97**, 442 (1975).
41. F. G. Bordwell, N. R. Vanier, W. S. Mathews, J. B. Hendrickson and P. L. Skipper, *J. Org. Chem.*, **97**, 7160 (1975).
42. F. G. Bordwell, M. Van Der Puy and N. R. Vanier, *J. Org. Chem.*, **41**, 1883, 1885 (1976).
43. N. F. Chamberlain and J. J. R. Reed, *The Analytical Chemistry of Sulfur and its Compounds* (Ed. J. H. Karchmer), Part III, Wiley (Interscience), New York, 1971.
44. E. Block, *Reaction of Organosulfur Compounds*, Academic Press, New York, 1978, p. 294.
45. T. Tanaka, Y. H. Kim, S. Oae and K. T. Suzuki, *Tetrahedron Letters*, 4303 (1978).
46. A. Rauk, E. Buncel, R. Y. Moir and S. Wolfe, *J. Amer. Chem. Soc.*, **87**, 5498 (1965).
47. J. E. Baldwin, R. E. Hacker and R. M. Scott, *J. Chem. Soc., Chem. Commun.*, 1415 (1969).
48. T. Durst and R. Viau, *Intra-Sci. Chem. Rep.*, **7**, 63 (1973).
49. T. Durst, R. Viau and M. R. McClory, *J. Amer. Chem. Soc.*, **93**, 3077 (1971).
50. A. Rauk, S. Wolfe and I. G. Csizmadia, *Can. J. Chem.*, **47**, 113 (1969).
51. S. Wolfe, A. Rauk and I. G. Csizmadia, *J. Amer. Chem. Soc.*, **89**, 5710 (1967).
52. B. J. Hutchinson, K. K. Andersen and A. R. Katritzky, *J. Amer. Chem. Soc.*, **91**, 3839 (1969).
53. R. Lett and A. Marquet, *Tetrahedron Letters*, 3255 (1971).
54. R. R. Fraser, F. J. Schuber and Y. Y. Wigfield, *J. Amer. Chem. Soc.*, **94**, 8795 (1972).
55. Y. Kodama, K. Nishihata and M. Nishio, *J. Chem. Soc., Perkin Trans. 2*, 1490 (1976).
56. T. Durst, R. R. Fraser, M. R. McClory, R. B. Swingle, R. Viau and Y. Y. Wigfield, *Can. J. Chem.*, **48**, 2148 (1970).
57. M. Nishio, *Chem. Commun.*, 562 (1968).
58. K. Nishihata and M. Nishio, *Tetrahedron Letters*, 4839 (1972).
59. K. Nishihata and M. Nishio, *Chem. Commun.*, 958 (1971).
60. R. Viau and T. Durst, *J. Amer. Chem. Soc.*, **95**, 1346 (1973).
61. J. F. Biellmann and J. J. Vicens, *Tetrahedron Letters*, 2915 (1974).
62. Y. Yamamoto and K. Maruyama, *J. Chem. Soc., Chem. Commun.*, 239 (1980).
63. R. R. Fraser and F. J. Schuber, *Chem. Commun.*, 397 (1969).
64. K. Nishihata and M. Nishio, *J. Chem. Soc., Perkin Trans. 2*, 1730 (1972).
65. T. Durst and M. Molin, *Tetrahedron Letters*, 63 (1975).
66. S. Bory, R. Lett, B. Moreau and A. Marquet, *Tetrahedron Letters*, 4921 (1972).
67. S. Bory and A. Marquet, *Tetrahedron Letters*, 4155 (1973).
68. R. Lett and A. Marquet, *Tetrahedron Letters*, 1579 (1975).
69. R. Lett, G. Chassaing and A. Marquet, *J. Organomet. Chem.*, 111, (1976).
70. G. Chassaing, R. Lett and A. Marquet, *Tetrahedron Letters*, 471 (1978).
71. J. F. Biellmann and J. J. Vicens, *Tetrahedron Letters*, 467 (1978).
72. M. Marsch, W. Maasa, K. Harms, G. Baum and G. Bashe, *Angew. Chem. Int. Ed.*, **25**, 1101 (1986).
73. G. Chassaing and A. Marquet, *Tetrahedron*, **34**, 1399 (1978).
74. T. Durst, R. Viau, R. Van Den Elzen and C. H. Nguyen, *Chem. Commun.*, 1334 (1971).
75. K. Nishihata and M. Nishio, *Tetrahedron Letters*, 1695 (1976).
76. V. Ceré, C. Paolucci, S. Pollicino, E. Sandri and A. Fava, *J. Org. Chem.*, **43**, 4826 (1978).

77. V. Ceré, S. Pollicino, E. Sandri and A. Fava, *Tetrahedron Letters*, 5239 (1978).
78. Y.-H. Khim, W. Tagaki, M. Kise, N. Furukawa and S. Oae, *Bull. Chem. Soc. Japan*, **39**, 2556 (1966).
79. D. J. Cram and S. H. Pine, *J. Amer. Chem. Soc.*, **85**, 1096 (1963).
80. D. J. Cram, R. D. Trepka and P. St. Janiak, *J. Amer. Chem. Soc.*, **88**, 2749 (1966).
81. D. J. Cram, D. A. Scott and W. D. Nielsen, *J. Amer. Chem. Soc.*, **83**, 3696 (1961).
82. H. L. Goering, D. L. Towns and B. Dittmar, *J. Org. Chem.*, **27**, 736 (1962).
83. E. J. Corey and E. T. Kaiser, *J. Amer. Chem. Soc.*, **83**, 490 (1961).
84. E. J. Corey, H. König and T. H. Lowry, *Tetahedron Letters*, 515 (1962).
85. E. J. Corey and T. H. Lowry, *Tetrahedron Letters*, 803 (1965).
86. D. J. Cram and A. S. Wingrove, *J. Amer. Chem. Soc.*, **84**, 1496 (1962).
87. D. J. Cram and A. S. Wingrove, *J. Amer. Chem. Soc.*, **85**, 1100 (1963).
88. S. Wolfe, A. Rauk, L. M. Tel and I. G. Csizmadia, *J. Chem. Soc. (B)*, 136 (1971).
89. J. E. Taylor and H. Verhoek, *J. Amer. Chem. Soc.*, **81**, 4537 (1959).
90. E. J. Corey and T. H. Lowry, *Tetrahedron Letters*, 793 (1965).
91. D. J. Cram and T. A. Whitney, *J. Amer. Chem. Soc.*, **89**, 4651 (1967).
92. H. P. Koch and W. E. Moffitt, *Trans. Faraday Soc.*, **47**, 7 (1951).
93. R. R. Fraser and F. J. Schuber, *Chem. Commun.*, 1474 (1969).
94. M. D. Brown, M. J. Cook, B. J. Hutchinson and A. R. Katritzky, *Tetrahedron*, **27**, 593 (1971).
95. D. J. Cram, R. D. Trepka and P. St. Janiak, *J. Amer. Chem. Soc.*, **86**, 2731 (1964).
96. S. Wolfe, *Acc. Chem. Res.*, **5**, 102 (1972).
97. J. N. Roitman and D. J. Cram, *J. Amer. Chem. Soc.*, **93**, 2225 (1971).
98. D. J. Cram, W. D. Nielsen and B. Rickborn, *J. Amer. Chem. Soc.*, **82**, 6415 (1960).
99. U. Folli, D. Iarosai, I. Moretti, F. Taddei and G. Torre, *J. Chem. Soc., Perkin Trans. 2*, 1655, 1658 (1974).
100. D. J. Cram, *Fundamentals of Carbanion Chemistry*, Academic Press, New York, 1965.
101. L. A. Paquette, J. P. Freeman and M. J. Wyvratt, *J. Amer. Chem. Soc.*, **93**, 3216 (1971).
102. F. G. Bordwell, J. C. Branca, C. R. Johnson and N. R. Vanier, *J. Org. Chem.*, **45**, 3884 (1980).
103. A. A. Hartman and E. L. Eliel, *J. Amer. Chem. Soc.*, **93**, 2572 (1971).
104. E. L. Eliel, A. Abatjoglou and A. A. Hartman, *J. Amer. Chem. Soc.*, **94**, 4786 (1972).
105. R. W. C. Cose, A. M. Davies, W. D. Ollis, C. Smith and I. O. Sutherland, *Chem. Commun.*, 293 (1969).
106. F. Bernardi, H. B. Schlegel, M.-H. Whangbo and S. Wolfe, *J. Amer. Chem. Soc.*, **99**, 5633 (1977).
107. S. Wolfe, P. Chamberlain and T. F. Garrard, *Can. J. Chem.*, **54**, 2847 (1976).
108. G. Barbarella, A. Garbesi and A. Fava, *J. Amer. Chem. Soc.*, **97**, 5883 (1975).
109. A. Garbesi, G. Barbarella and A. Fava, *Chem. Commun.*, 155 (1973).
110. G. Barbarella, A. Garbesi, A. Boicelli and A. Fava, *J. Amer. Chem. Soc.*, **95**, 8051 (1973).
111. D. M. Roush, E. M. Price, L. K. Templeton, D. H. Templeton and C. H. Heathcock, *J. Amer. Chem. Soc.*, **101**, 2971 (1979).
112. G. Barbarella, P. Dembech, A. Garbesi, F. Bernardi, A. Bottoni and A. Fava, *J. Amer. Chem. Soc.*, **100**, 200 (1978).
113. A. Garbesi, *Tetrahedron Letters*, 547 (1980).
114. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **84**, 866 (1962).
115. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).
116. G. Solladié, *Synthesis*, 185 (1981).
117. I. D. Entwistle and R. A. W. Johnstone, *Chem. Commun.*, 29 (1965).
118. I. D. Entwistle, R. A. W. Johnstone and B. J. Millard, *J. Chem. Soc. (C)*, 302 (1967).
119. F. W. Bergstrom and W. C. Fernelius, *Chem. Rev.*, **20**, 435 (1947).
120. B. M. Trost and A. J. Bridges, *J. Org. Chem.*, **40**, 2014 (1975).
121. C. Walling and L. Bollyky, *J. Org. Chem.*, **29**, 2699 (1964).
122. V. Cere, C. Paolucci, S. Polocino, E. Sandri and A. Fava, *J. Chem. Soc., Chem. Commun.*, 764 (1981).
123. P. A. Argabright, J. E. Hofmann and A. A. Schriesheim, *J. Org. Chem.*, **30**, 3233 (1965).
124. G. A. Russell and S. A. Weiner, *J. Org. Chem.*, **31**, 248 (1966).
125. H. Nozaki, Y. Yamamoto and R. Noyori, *Tetrahedron Letters*, 1123 (1966).
126. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 3151 (1971).
127. J. E. Richman, J. L. Herrmann and R. H. Sclessinger, *Tetrahedron Letters*, 3267 (1973).
128. K. Ogura, M. Yamashita and G. Tsuchihashi, *Tetrahedron Letters*, 759 (1976).

129. K. Ogura, M. Yamashita, M. Suzuki and G. Tsuchihashi, *Tetrahedron Letters*, 3653 (1974).
130. K. Ogura, M. Yamashita, M. Suzuki, S. Furukawa and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **57**, 1637 (1984).
131. B. M. Trost, W. P. Conway, P. E. Strege and T. J. Dietsche, *J. Amer. Chem. Soc.*, **96**, 7165 (1974).
132. M. Trost and K. K. Leung, *Tetrahedron Letters*, 4197 (1975).
133. P. G. Gassman and G. D. Richmond, *J. Org. Chem.*, **31**, 2355 (1966).
134. G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, **34**, 3624 (1969).
135. V. Reutrakul and P. Thamnusan, *Tetrahedron Letters*, 617 (1979).
136. P. Bravo, G. Resnati and F. Viani, *Tetrahedron Letters*, **26**, 2913 (1985).
137. S. Lavielle, S. Bory, B. Moreau, M. J. Luche and A. Marquet, *J. Amer. Chem. Soc.*, **100**, 1558 (1978).
138. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **86**, 1639 (1964).
139. H.-D. Becker, G. J. Mikol and G. A. Russell, *J. Amer. Chem. Soc.*, **85**, 3410 (1963).
140. A. Takeda, H. Hosisima and S. Torii, *Bull. Chem. Soc. Japan*, **39**, 1354 (1966).
141. T. L. Moore, *J. Org. Chem.*, **32**, 2786 (1967).
142. J. L. Herrmann, J. E. Richman, P. J. Wepplo and R. H. Schlessinger, *Tetrahedron Letters*, 4707 (1973).
143. G. Guanti, E. Narisano, L. Banfi and C. Scolastico, *Tetrahedron Letters*, 817 (1983).
144. J. J. A. van Asten and R. Louw, *Tetrahedron Letters*, 671 (1975).
145. G. Solladié, R. Zimmermann and R. Bartsch, *Tetrahedron Letters*, 755 (1983).
146. G. A. Russell, E. Sabourin and G. J. Mikol, *J. Org. Chem.*, **31**, 2854 (1966).
147. G. A. Russell and E. T. Sabourin, *J. Org. Chem.*, **34**, 2336 (1969).
148. G. A. Russell, E. T. Sabourin and G. Hamprecht, *J. Org. Chem.*, **34**, 2339 (1969).
149. H.-D. Becker and G. A. Russell, *J. Org. Chem.*, **28**, 1896 (1963).
150. R. Annunziata, M. Cinquini and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 1687 (1979).
151. N. Kunieda, J. Nokami and M. Kinoshita, *Chem. Letters*, 369 (1974).
152. G. Solladié, C. Greck, G. Demailly and A. Solladié-Cavallo, *Tetrahedron Letters*, 5047 (1982).
153. P. Bravo and G. Resnati, *Tetrahedron Letters*, **26**, 5601 (1985).
154. N. Kunieda, A. Suzuki and M. Kinoshita., *Bull. Chem. Soc. Japan*, **54**, 1143 (1981).
155. M. Chaykovsky and E. J. Correy, *J. Org. Chem.*, **28**, 254 (1963).
156. C. Walling and L. Bollysky, *J. Org. Chem.*, **28**, 256 (1963).
157. G. A. Russell and H.-D. Becker, *J. Amer. Chem. Soc.*, **85**, 3406 (1963).
158. T. Durst, *J. Amer. Chem. Soc.*, **91**, 1034 (1969).
159. T. Durst and K.-C. Tin, *Tetrahedron Letters*, 2369 (1970).
160. D. F. Tavares, R. E. Estep and M. Blezard, *Tetrahedron Letters*, 2373 (1970).
161. G. Tsuchihashi and K. Ogura, *Bull. Chem. Soc. Japan*, **45**, 2023 (1972).
162. V. Reutrakul and W. Kanghae, *Tetrahedron Letters*, 1377 (1977).
163. V. Reutrakul and K. Herunsalee, *Tetrahedron Letters*, **24**, 527 (1983).
164. V. Reutrakul and V. Rukachaisirikul, *Tetrahedron Letters*, **24**, 725 (1983).
165. M. Mikołajczyk, S. Grejszczak and A. Zatorsky, *J. Org. Chem.*, **40**, 1979 (1975).
166. M. Mikołajczyk, W. Midura, S. Grejszczak, A. Zatorski and A. Chefczyńska, *J. Org. Chem.*, **43**, 473 (1978).
167. N. Kunieda, J. Nokami and M. Kinoshita, *Tetrahedron Letters*, 3997 (1974).
168. J. Nokami, N. Kunieda and M. Kinoshita, *Tetrahedron Letters*, 2841 (1975).
169. J. Nokami, N. Kunieda and M. Kinoshita, *Tetrahedron Letters*, 2179 (1975).
170. K. Ogura and G. Tsuchihashi, *Chem. Letters* 659 (1974).
171. K. Ogura, M. Yamashita, H. Suzuki, S. Furukawa and G. Tsuchihashi, *Tetrahedron Letters*, 3653 (1974).
172. K. Ogura, M. Yamashita and G. Tsuchihashi, *Tetrahedron Letters*, 759 (1976).
173. K. Ogura, M. Yamashita and G. Tsuchihashi, *Tetrahedron Letters*, 1303 (1978).
174. K. Ogura, N. Katoh, I. Yoshimura and G. Tsuchihashi, *Tetrahedron Letters*, 375 (1978).
175. K. Ogura, M. Suzuki and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **53**, 1414 (1980).
176. K. Ogura, K. Arai and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **55**, 3669 (1982).
177. K. Ogura, M. Suzuki, J. Watanabe, M. Yoshimura, H. Iida and G. Tsuchihashi, *Chem. Letters*, 813 (1982).
178. K. Ogura, J. Watanabe, K. Takahashi and H. Iida, *J. Org. Chem.*, **47**, 5404 (1982).
179. K. Ogura, N. Yahata, K. Hashizume, K. Tsuyama, K. Takahashi and H. Iida, *Chem. Letters*, 767 (1983).

180. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 2681 (1972).
181. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 1383 (1972).
182. K. Ogura, Y. Ito and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **52**, 2013 (1979).
183. K. Ogura, S. Furukawa and G. Tsuchihashi, *Bull. Chem. Soc. Japan*, **48**, 2219 (1975).
184. K. Ogura, S. Mitamura, K. Kishi and G. Tsuchihashi, *Synthesis*, 880 (1979).
185. K. Ogura, N. Katoh, I. Yoshimura and G. Tsuchihashi, *Tetrahedron Letters*, 375 (1978).
186. K. Ogura and G. Tsuchihashi, *J. Amer. Chem. Soc.*, **96**, 1960 (1974).
187. T. Durst, R. Viau, R. Van Den Elzen and C. H. Nguyen, *Chem. Commun.*, 1334 (1971).
188. C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **93**, 5303 (1971).
189. C. R. Johnson, C. W. Schroeck and J. R. Shanklin, *J. Amer. Chem. Soc.*, **95**, 7424 (1973).
190. G. Tsuchihashi, S. Iriuchijima and M. Ishibashi, *Tetrahedron Letters*, 4605 (1972).
191. N. Kunieda, M. Kinoshita and J. Nokami, *Chem. Letters*, 289 (1977).
192. G. Tsuchihashi, S. Iriuchijima and K. Maniwa, *Tetrahedron Letters*, 3389 (1973).
193. L. Colombo, C. Gennari and C. Scolastico, *J. Chem. Soc., Chem. Commun.*, 591 (1979).
194. L. Colombo, C. Gennari and C. Scolastico, *J. Chem. Soc., Chem. Commun.*, 1278 (1981).
195. G. Demailly, C. Greck and G. Solladié, *Tetrahedron Letters*, **25**, 4113 (1984).
196. G. Solladié and G. Moine, *J. Amer. Chem. Soc.*, **106**, 6097 (1984).
197. C. Mioskowski and G. Solladié, *J. Chem. Soc., Chem. Commun.*, 162 (1977).
198. J. Solladié, F. M.-Moghadam, C. Luttmann and C. Mioskowski, *Helv. Chim. Acta*, **65**, 1602 (1982).
199. G. Solladié, *Synthesis*, 185 (1981).
200. C. Mioskowski and G. Solladié, *Tetrahedron*, **36**, 227 (1980).
201. E. Abushanab, D. Reed, F. Suzuki and C. J. Sih, *Tetrahedron Letters*, 3415 (1978).
202. G. Solladié and F. M.-Moghadam, *J. Org. Chem.*, **47**, 91 (1982).
203. E. J. Corey, L. O. Weigel, A. R. Chamberlin, H. Cho and D. H. Hua, *J. Amer. Chem. Soc.*, **102**, 6613 (1980).
204. C. Papageorgiou and C. Benezra, *Tetrahedron Letters*, **25**, 1303 (1984).
205. P. Bravo, P. Carrera, G. Resnati and C. Ticozzi, *J. Chem. Soc., Chem. Commun.*, 19 (1984).
206. G. Guanti, L. Banfi, E. Narisano and S. Thea, *J. Chem. Soc., Chem. Commun.*, 861 (1984).
207. P. A. Bartlett, *Tetrahedron*, **36**, 3 (1980).
208. R. Annunziata. M. Cinquini, F. Cozzi, F. Montanari and A. Restelli, *J. Chem. Soc., Chem. Commun.*, 1138 (1983).
209. R. Annunziata, M. Cinquini, F. Cozzi, F. Montanari and A. Restelli, *Tetrahedron*, **40**, 3815 (1984).
210. M. Cinquini, A. Manfredi, H. Molinari and A. Restelli, *Tetrahedron*, **41**, 4929 (1985).
211. L. Colombo, C. Gennari, G. Poli, C. Scolastico, R. Annunziata, M. Cinquini and F. Cozzi, *J. Chem. Soc., Chem. Commun.*, 403 (1983).
212. R. Annunziata, *Synthesis*, 702 (1984).
213. R. Annunziata, F. Cozzi and M. Cinquini, *J. Chem. Soc., Perkin Trans. 1*, 251 (1985).
214. R. Annunziata, M. Cinquini, F. Cozzi and A. Gilardi, *J. Chem. Soc., Perkin Trans. 1*, 255 (1985).
215. R. Annunziata, M. Cinquini, F. Cozzi and A. Restelli, *J. Chem. Soc., Chem. Commun.*, 1253 (1984).
216. R. Annunziata, M. Cinquini, A. Gilardi and F. Cozzi, *Synthesis*, 1061 (1983).
217. A. Bernardi, L. Colombo, C. Gennari and L. Prati, *Tetrahedron*, **40**, 3769 (1984).
218. J. L. Herrmann, G. R. Kieczykowski, R. F. Romanet, P. J. Wepplo and R. H. Schlessinger, *Tetrahedron Letters*, 4711 (1973).
219. J. L. Herrmann, G. R. Kieczykowski, R. F. Romanet and R. H. Schlessinger, *Tetrahedron Letters*, 4715 (1973).
220. G. R. Kieczykowski, C. S. Pogonowski, J. E. Richman and R. H. Schlessinger, *J. Org. Chem.*, **42**,
221. 175 (1977).
222. G. A. Koppel and M. D. Kinnick, *J. Chem. Soc., Chem. Commun.*, 473 (1975).
223. R. Bell, P. D. Cottam, J. Davies and D. N. Jones, *J. Chem. Soc., Perkin Trans. 1*, 2106 (1981). P. J. Brown, D. N. Jones, M. A. Khan and N. A. Meanwell, *Tetrahedron Letters*, **24**, 405 (1983).
224. P. J. Brown, D. N. Jones, M. A. Khan, N. A. Meanwell and P. P. Richards, *J. Chem. Soc., Perkin Trans. 1*, 2049 (1984).
225. W. E. Truce and M. J. Lusch, *J. Org. Chem.*, **39**, 3174 (1974).
226. W. E. Truce and M. J. Lusch, *J. Org. Chem.*, **43**, 2252 (1978).
227. S. Oae, *Croatica Chem. Acta*, **59**, 129 (1986).

228. I. Hori and T. Oishi, *Tetrahedron Letters*, 4087 (1979).
229. D. J. Abbott, S. Colonna and C. J. M. Stirling, *Chem. Commun.*, 471 (1971).
230. G. Tsuchihashi, S. Mitamura, S. Inoue and K. Ogura, *Tetrahedron Letters*, 323 (1973).
231. R. Lett, S. Bory, B. Horeau and A. Marquet, *Tetrahedron Letters*, 2855 (1971).
232. G. H. Posner, J. P. Mallamo and K. Miura, *J. Amer. Chem. Soc.*, **103**, 2886 (1981).
233. G. H. Posner, J. P. Mallamo, M. Hulce and L. L. Frye, *J. Amer. Chem. Soc.*, **104**, 4180 (1982).
234. G. H. Posner, L. L. Frye and M. Hulce, *Tetrahedron*, **40**, 1401 (1984).
235. G. H. Posner and M. Hulce, *Tetrahedron Letters*, **25**, 379 (1984).
236. G. H. Posner, T. P. Kogan, S. R. Haines and L. L. Frye, *Tetrahedron Letters*, **25**, 2627 (1984).
237. G. H. Posner, T. P. Kogan and M. Hulce, *Tetrahedron Letters*, **25**, 383 (1984).
238. G. H. Posner and E. Asirvatham, *J. Org. Chem.*, **50**, 2589 (1985).
239. G. H. Posner, M. Hulce, J. P. Mallamo, S. A. Drexler and J. Clardy, *J. Org. Chem.*, **46**, 5244 (1981).
240. D. J. Abbott and C. J. M. Stirling, *J. Chem. Soc. (C)*, 818 (1969).
241. R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, **92**, 2100 (1970).
242. P. Bickart, R. W. Carson, J. Jacobus, E. G. Miller and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4869 (1968).
243. D. A. Evans, G. C. Andrews and C. L. Sims, *J. Amer. Chem. Soc.*, **93**, 4956 (1971).
244. D. A. Evans, G. C. Andrews, T. T. Fujimoto and D. Wells, *Tetrahedron Letters*, 1385 (1973).
245. D. A. Evans, G. C. Andrews, T. T. Fujimoto and D. Wells, *Tetrahedron Letters*, 1389 (1973).
246. D. A. Evans, T. C. Crawford, T. T. Fujimoto and R. C. Thomas, *J. Org. Chem.*, **39**, 3176 (1974).
247. Y. Masaki, K. Sakuma and K. Kaji, *J. Chem. Soc., Chem. Commun.*, 434 (1980).
248. Y. Masaki, K. Sakuma and K. Kaji, *J. Chem. Soc., Perkin Trans. 1*, 1171 (1985).
249. D. J. Antonjuk, D. D. Ridley and M. A. Smal, *Aust. J. Chem.*, **33**, 2635 (1980).
250. J. Nokami, T. Ono, A. Iwao and S. Wakabayashi, *Bull. Chem. Soc., Japan*, **55**, 3043 (1982).
251. M. R. Binns, R. K. Haynes, A. A. Katsifis, P. A. Schober and S. Vonwiller, *Tetrahedron Letters*, **26**, 1565 (1985).
252. M. R. Binns, O. L. Chai, R. K. Haynes, A. A. Katsifis, P. A. Schober and S. C. Vonwiller, *Tetrahedron Letters*, **26**, 1569 (1985).
253. D. H. Hua, G. Sinal-Zingde and S. Venkataraman, *J. Amer. Chem. Soc.*, **107**, 4088 (1985).
254. E. Fromm and J. Wittmann, *Ber.*, **41**, 2270 (1908).
255. R. L. Shriner and S. O. Greenlee, *J. Org. Chem.*, **4**, 242 (1939).
256. E. P. Kohler and M. Tishler, *J. Amer. Chem. Soc.*, **57**, 217 (1935).
257. E. P. Kohler and H. Potter, *J. Amer. Chem. Soc.*, **57**, 1316 (1935).
258. E. P. Kohler and H. Potter, *J. Amer. Chem. Soc.*, **58**, 2166 (1936).
259. W. M. Ziegler and R. Connor, *J. Amer. Chem. Soc.*, **62**, 2596 (1940).
260. H. Gilman and F. J. Webb, *J. Amer. Chem. Soc.*, **71**, 4062 (1949).
261. L. Field, *J. Amer. Chem. Soc.*, **74**, 3919 (1952).
262. L. Field and J. W. McFarland, *J. Amer. Chem. Soc.*, **75**, 5582 (1953).
263. W. E. Truce and K. R. Buser, *J. Amer. Chem. Soc.*, **76**, 3577 (1954).
264. H. Potter, *J. Amer. Chem. Soc.*, **76**, 5472 (1954).
265. L. Field, *J. Amer. Chem. Soc.*, **78**, 92 (1956).
266. L. Field, J. E. Lawson and J. W. McFarland, *J. Amer. Chem. Soc.*, **78**, 4389 (1956).
267. V. Baliah and Sp. Shanmuganathan, *J. Org. Chem.*, **23**, 1233 (1958).
268. L. Field, J. R. Holsten and R. D. Clark, *J. Amer. Chem. Soc.*, **81**, 2572 (1959).
269. L. Field and E. T. Boyd, *J. Org. Chem.*, **26**, 1787 (1961).
270. J. W. McFarland and D. N. Buchanan, *J. Org. Chem.*, **30**, 2003 (1965).
271. P. D. Magnus, *Tetrahedron*, **33**, 2019 (1977).
272. J. F. Bielmann and J.-B. Ducep, *Org. React.*, **27**, 1 (1982).
273. K. Kondo and D. Tunemoto, *Tetrahedron Letters*, 1007 (1975).
274. C. G. M. Janssen, P. M. van Lier, H. M. Buck and E. F. Godefroi, *J. Org. Chem.*, **44**, 4199 (1979).
275. H. Kotake, K. Inomata, H. Kinoshita, Y. Sakamoto and Y. Kaneto, *Bull. Chem. Soc. Japan*, **53**, 3027 (1980).
276. J. Katenberg, E. R. de Waard and H. O. Huisman, *Tetrahedron*, **29**, 4149 (1973).
277. R. R. Regis and A. M. Doweyko, *Tetrahedron Letters*, **23**, 2539 (1982).
278. C. G. M. Janssen, P. M. van Lier, P. Schipper, L. H. J. G. Simons and E. F. Godefroi, *J. Org. Chem.*, **45**, 3159 (1980).
279. K. Kondo, E. Saito and D. Tunemoto, *Tetrahedron Letters*, 2275 (1975).

280. S. Torii, K. Uneyama and I. Kuwahara, *Bull. Chem. Soc. Japan*, **51**, 949 (1978).
281. J. J. Eisch, S. K. Dua and M. Behrooz, *J. Org. Chem.*, **50**, 3674 (1985).
282. Y. Gaoni, *Tetrahedron Letters*, 503 (1976).
283. H. E. Zimmerman and B. S. Thyagarajan, *J. Amer. Chem. Soc.*, **82**, 2505 (1960).
284. W. E. Truce and L. B. Lindy, *J. Org. Chem.*, **26**, 1463 (1961).
285. R. Bird and C. J. M. Stirling, *J. Chem. Soc. (B)*, 111 (1968).
286. Y.-H. Chang and H. W. Pinnick, *J. Org. Chem.*, **43**, 373 (1978).
287. R. Bird, G. Griffiths, G. F. Griffiths and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 2*, 579, (1982).
288. M. Takahashi, H. Suzuki and Y. Kata, *Bull. Chem. Soc. Japan*, **58**, 765 (1985).
289. P. J. Kocienski, *J. Org. Chem.*, **45**, 2037 (1980).
290. P. J. Kocienski and M. Todd, *J. Chem. Soc., Perkin Trans. 1*, 1777 (1983).
291. P. J. Kocienski and M. Todd, *J. Chem. Soc., Perkin Trans. 1*, 1783 (1983).
292. P. J. Kocienski, *Tetrahedron Letters*, **20**, 2649 (1979).
293. B. A. Pearlman, S. R. Putt and J. A. Fleming, *J. Org. Chem.*, **50**, 3622 (1985).
294. D. Savoia, C. Trombini and A. Umani-Ronchi, *J. Chem. Soc., Perkin Trans. 1*, 123 (1977).
295. P. J. Koncienski, *Tetrahedron Letters*, 441 (1979).
296. Y. Ueno, S. Aoki and M. Okawara, *J. Chem. Soc., Chem. Commun.*, 683 (1980).
297. D. F. Taber and S. A. Saleh, *J. Org. Chem.*, **46**, 4817 (1981).
298. A. Jończyk and T. Radwan-Pytlewski, *J. Org. Chem.*, **48**, 910 (1983).
299. K. Ogura, T. Iihama, K. Takahashi and H. Iida, *Tetrahedron Letters*, **25**, 2671 (1984).
300. M. Julia and D. Arnould, *Bull. Soc. Chim. Fr.*, 746 (1973).
301. P. S. Manchand, M. Rosenberger, G. Saucy, P. A. Wehrli, H. Wong, L. Chambers, M. P. Ferro and W. Jackson, *Helv. Chim. Acta*, **59**, 387 (1976).
302. A. Fischli, H. Mayer, W. Simon and H.-J. Stoller, *Helv. Chim. Acta*, **59**, 397 (1976).
303. G. L. Olson, H.-C. Cheung, K. D. Morgan, C. Neukom and G. Saucy, *J. Org. Chem.*, **41**, 3287 (1976).
304. P. Chabardes, J. P. Decor and J. Varagnat, *Tetrahedron*, **33**, 799 (1977).
305. S. C. Welch and J. M. Gruber, *J. Org. Chem.*, **47**, 385 (1982).
306. T. Mandai, H. Yamaguchi, K. Nishikawa, M. Kawada and J. Otera, *Tetrahedron Letters*, **22**, 761, 763 (1981).
307. T. Mandai, Y. Iuchi, K. Suzuki, M. Kawada and J. Otera, *Tetrahedron Letters*, **23**, 4721 (1982).
308. P. A. Grieco and Y. Maski, *J. Org. Chem.*, **39**, 2135 (1974).
309. A. Fischli and H. Mayer, *Helv. Chim. Acta*, **58**, 1584 (1975).
310. P. Kocienski and M. Todd, *J. Chem. Soc., Chem. Commun.*, 1078 (1982).
311. W. A. Kinney, G. D. Crouse and L. A. Paquette, *J. Org. Chem.*, **48**, 4986 (1983).
312. P. T. Lansbury and R. W. Erwin, *Tetrahedron Letters*, 2675 (1978).
313. B. M. Trost, N. R. Schmuff and M. J. Miller, *J. Amer. Chem. Soc.*, **102**, 5979 (1980).
314. J. Böeseken and E. de R. van Zuydewijn, *Proc. Acad. Sci. (Amsterdam)*, **40**, 23 (1937); *Chem. Abstr.*, **31**, 4953 (1937).
315. A. H. Raper and E. Rothstein, *J. Chem. Soc.*, 1027 (1963).
316. H. J. Backer and G. J. De Jong, *Rec. Trav. Chim. Pays-Bas*, **67**, 884 (1948).
317. E. A. Fehnel, *J. Amer. Chem. Soc.*, **74**, 1569 (1952).
318. D. E. O'Connor and W. I. Lyness, *J. Amer. Chem. Soc.*, **85**, 3044 (1963).
319. D. E. O'Connor and W. I. Lyness, *J. Amer. Chem. Soc.*, **86**, 3840 (1964).
320. V. Pascali and A. Umani-Ronchi, *J. Chem. Soc., Chem. Commun.*, 351 (1973).
321. J. F. Bielmann and J. B. Ducep, *Tetrahedron*, **27**, 5861 (1971).
322. C. R. Hauser and T. M. Harris, *J. Amer. Chem. Soc.*, **81**, 1134 (1959).
323. W. I. O'Sullivan, D. F. Tavares and C. R. Hauser, *J. Amer. Chem. Soc.*, **83**, 3453 (1961).
324. M. L. Miles and C. R. Hauser, *J. Org. Chem.*, **29**, 2329 (1964).
325. J. S. Grossert, J. Hoyle and D. L. Hooper, *Tetrahedron*, **40**, 1135 (1984).
326. H. M. Carroll and W. I. O'Sullivan, *J. Org. Chem.*, **30**, 2830 (1965).
327. F. Cooke and P. Magnus, *J. Chem. Soc., Chem. Commun.*, 519 (1976).
328. J. B. Hendrickson and P. S. Palumbo, *J. Org. Chem.*, **50**, 2110 (1985).
329. B. M. Trost and T. R. Verhoeven, *J. Org. Chem.*, **41**, 3215 (1976).
330. B. M. Trost and T. R. Verhoeven, *J. Amer. Chem. Soc.*, **99**, 3867 (1977).
331. B. M. Trost and T. R. Verhoeven, *Tetrahedron Letters*, 2275 (1978).
332. B. M. Trost and T. R. Verhoeven, *J. Amer. Chem. Soc.*, **101**, 1595 (1979).

333. K. Ogura, J. Watanabe and H. Iida, *Tetrahedron Letters*, **22**, 4499 (1981).
334. K. Ogura, M. Suzuki, J. Watanabe, M. Yamashita, H. Iida and G. Tsuchihashi, *Chem. Letters*, 813 (1982).
335. K. Ogura, N. Yahata, K. Hashizume, K. Tsuyama, K. Takahashi and H. Iida, *Chem. Letters*, 767 (1983).
336. B. M. Trost, H. C. Arndt, P. E. Strege and T. R. Verhoeven, *Tetrahedron Letters*, 3477 (1976).
337. K. Tanaka, S. Matsui and A. Kaji, *Bull. Chem. Soc. Japan*, **53**, 3619 (1980).
338. P. A. Wade, H. R. Hinney, N. V. Amin, P. D. Vail, S. D. Morrow, S. A. Hardinger and M. S. Saft, *J. Org. Chem.*, **46**, 765 (1981).
339. H. Stetter and R. Hesse, *Monatsh. Chem.*, **98**, 755 (1967) *Chem. Abstr.*, **67**, 73559 (1967).
340. H. O. House and J. K. Larson, *J. Org. Chem.*, **33**, 61 (1968).
341. E. M. Kaiser, L. E. Solter, R. A. Schwarz, R. D. Beard and C. R. Hauser, *J. Amer. Chem. Soc.*, **93**, 4237 (1971).
342. K. Kondo and D. Tunemoto, *Tetrahedron Letters*, 1397 (1975).
343. T. Yoshida and S. Saito, *Bull. Chem. Soc. Japan*, **55**, 3047 (1982).
344. K. Ogura, N. Yahata, K. Takahashi and H. Iida, *Tetrahedron Letters*, **24**, 5761 (1983).
345. B. Lythgoe and I. Waterhouse, *J. Chem. Soc., Perkin Trans. 1*, 2429 (1979).
346. P. A. Bartlett, F. R. Green III and E. H. Rose, *J. Amer. Chem. Soc.*, **100**, 4852 (1978).
347. W. E. Truce and R. H. Knospe, *J. Amer. Chem. Soc.*, **77**, 5063 (1955).
348. W. E. Truce, W. W. Bannister and R. H. Knospe, *J. Org. Chem.*, **27**, 2821 (1962).
349. L. J. Dolby, S. Esfandiari, C. A. Elliger and K. S. Marshall, *J. Org. Chem.*, **36**, 1277 (1971).
350. H. O. House, D. G. Melillo and F. J. Sauter, *J. Org. Chem.*, **38**, 741 (1973).
351. H. O. House, J. L. Haack, W. C. McDaniel and D. VanDerveer, *J. Org. Chem.*, **48**, 1643 (1983).
352. S. Cavicchioli, D. Savoia, C. Trombini and A. Umani-Ronchi, *J. Org. Chem.*, **49**, 1246 (1984).
353. M. C. Mussatto, D. Savoia, C. Trombini and A. Umani-Ronchi, *J. Org. Chem.*, **45**, 4002 (1980).
354. M. Hanack and K. Laping, *Tetrahedron Letters*, 4493 (1977).
355. T. Mandai, T. Yanagi, K. Araki, Y. Morisaki, M. Kawada and J. Otera, *J. Amer. Chem. Soc.*, **106**, 3670 (1984).
356. J. Otera, H. Misawa, T. Mandai, T. Onishi, S. Suzuki and Y. Fujita, *Chem. Letters*, 1883 (1985).
357. J. J. Eisch and J. E. Galle, *J. Org. Chem.*, **44**, 3279 (1979).
358. G. A. Russell, H.-D. Becker and J. Schoeb, *J. Org. Chem.*, **28**, 3584 (1963).
359. M. Julia, A. Righini and D. Uguen, *J. Chem. Soc., Perkin Trans. 1*, 1646 (1978).
360. B. Achmatowicz, E. Baranowska, A. R. Daniewski, J. Pankowski and J. Wicha, *Tetrahedron Letters*, **26**, 5597 (1985).
361. A. R. Friedman and D. R. Graber *J. Org. Chem.*, **37**, 1902 (1972).
362. L. A. Carpino, *J. Org. Chem.*, **38**, 2600 (1973).
363. M. L. Oftedahl, J. W. Baker and M. W. Dietrich, *J. Org. Chem.*, **30**, 296 (1965).
364. I. C. Popoff, J. L. Dever and G. R. Leader, *J. Org. Chem.*, **34**, 1128 (1969).
365. G. H. Posner and D. J. Brunelle, *J. Org. Chem.*, **37**, 3547 (1972).
366. V. Pascali and A. Umani-Ronchi, *J. Chem. Soc., Chem. Commun.*, 351 (1973).
367. W. E. Truce and T. C. Klinger, *J. Org. Chem.*, **35**, 1834 (1970).
368. J. B. Hendrickson and P. S. Palumbo, *Tetrahedron Letters*, **26**, 2849 (1985).
369. H. Kotake, K. Inomata and M. Sumita, *Chem. Letters*, 717 (1978).
370. Y. Ueno, H. Setoi and M. Okawara, *Chem. Letters*, 47 (1979).
371. E. Gipstein, C. G. Willson and H. S. Sachdev, *J. Org. Chem.*, **45**, 1486 (1980).
372. P. F. Vogt and D. F. Tavares, *Can. J. Chem.*, **47**, 2875 (1969).
373. F. Bohlmann and G. Haffer, *Chem. Ber.*, **102**, 4017 (1969).
374. A. Jończyk, K. Bańko and M. Makosza, *J. Org. Chem.*, **40**, 266 (1975).
375. M. Inbasekaran, N. P. Peet, J. R. McCarthy and M. E. LeTourneau, *J. Chem. Soc., Chem. Commun.*, 678 (1985).
376. C.-N. Hsiao and H. Shechter, *Tetrahedron Letters*, **23**, 3455 (1982).
377. J. Goliński, M. Makosza and A. Rykowski, *Tetrahedron Letters*, **24**, 3279 (1983).
378. A. M. van Leusen, H. Siderius, B. E. Hoogenhoom and D. van Leusen, *Tetrahedron Letters*, 5337 (1972).
379. S. P. J. M. van Nispen, C. Mensink and A. M. van Leusen, *Tetrahedron Letters*, **21**, 3723 (1980).
380. J. B. Hendrickson and P. L. Skipper, *Tetrahedron*, **32**, 1627 (1976).
381. J. B. Hendrickson, K. W. Bair and P. M. Keehn, *J. Org. Chem.*, **42**, 2935 (1977).
382. E. Ghera and Y. Ben-David, *Tetrahedron Letters*, **24**, 3533 (1983).

383. R. P. Welcher, *J. Org. Chem.*, **28**, 1712 (1963).
384. A. Jończyk and T. Radwan-Pytrlewski, *J. Org. Chem.*, **48**, 910 (1983).
385. J. B. Hendrickson, A. Giga and J. Wareing, *J. Amer. Chem. Soc.*, **96**, 2275 (1974).
386. J. J. Burger, T. B. R. A. Chen, E. R. De Waard and H. O. Huisman, *Tetrahedron*, **36**, 1847 (1980).
387. P. J. Kocienski, B. Lythgoe and S. Ruston, *J. Chem. Soc., Perkin Trans. 1*, 829 (1978).
388. K. Fuji, M. Node and Y. Usami, *Chem. Letters*, 961 (1986).
389. G. A. Kraus and K. Frazier, *Synth. Commun.*, **8**, 483 (1978).
390. M. Hirama, *Tetrahedron Letters*, **22**, 1905 (1981).
391. T. Sugawara and I. Kuwajima, *Tetrahedron Letters*, **26**, 5571 (1985).
392. M. Julia and A. Guy-Rouault, *Bull. Soc. Chim. Fr.*, 1411 (1967).
393. R. V. M. Campbell, L. Crombie, D. A. R. Findley, R. W. King, G. Pattenden and D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 897 (1975).
394. E. Ghera and Y. Ben-David, *Tetrahedron Letters*, 4603 (1979).
395. J. Wildeman, P. C. Borgen, H. Pluim, P. H. F. M. Rouwette and A. M. van Leusen, *Tetrahedron Letters*, 2213 (1978).
396. F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, **43**, 178 (1978).
397. F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, **44**, 2596 (1979).
398. F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, **45**, 3061 (1980).
399. L. Crombie, D. A. R. Findley and D. A. Whiting, *J. Chem. Soc., Chem. Commun.*, 1045 (1972).
400. A. M. van Leusen and J. W. Terpstra, *Tetrahedron Letters*, **22**, 5097 (1981).
401. A. E. Kretov, *J. Russ. Phys. Chem. Soc.*, **62**, 1 (1930); *Chem. Abstr.*, **24**, 4257 (1930).
402. J. Troger and K. Artmann, *J. Pr. Chem.*, **53**, 484 (1896).
403. E. Rothstein, *J. Chem. Soc.*, 684 (1934).
404. G. H. Posner and D. J. Brunelle, *Tetrahedron Letters*, 935 (1973).
405. G. H. Posner and D. J. Brunelle, *J. Org. Chem.*, **38**, 2747 (1973).
406. Y. Gaoni, *Tetrahedron Letters*, **23**, 5215 (1982).
407. M. Isobe, M. Kitamura and T. Goto., *Tetrahedron Letters*, 3465 (1979).
408. F. Näf, R. Decorzant and S. D. Escher, *Tetrahedron Letters*, **23**, 5045 (1982).
409. V. Fiandanese, G. Marchese and F. Naso, *Tetrahedron Letters*, 5131 (1978).
410. J. J. Eisch, M. Behrooz and J. E. Galle, *Tetrahedron Letters*, **25**, 4851 (1984).
411. J.-L. Fabre, M. Julia and J.-N. Verpeaux, *Tetrahedron Letters*, **23**, 2469 (1982).
412. J.-L. Fabre and M. Julia, *Tetrahedron Letters*, **24**, 4311 (1983).
413. P. C. Conrad and P. L. Fuchs, *J. Amer. Chem. Soc.*, **100**, 346 (1978).
414. J. C. Saddler, P. C. Conrad and P. L. Fuchs, *Tetrahedron Letters*, 5079 (1978).
415. D. L. Barton, P. C. Conrad and P. L. Fuchs, *Tetrahedron Letters*, **21**, 1811 (1980).
416. J. S. Saddler and P. L. Fuchs, *J. Amer. Chem. Soc.*, **103**, 2112 (1981).
417. P. R. Hamann and P. L. Fuchs, *J. Org. Chem.*, **48**, 914 (1983).
418. A. Risaliti, S. Fatutta and M. Forchiassin, *Tetrahedron*, **23**, 1451 (1967).
419. A. Risaliti, S. Fatutta, M. Forchiassin and C. Russo, *Ric. Sci.*, **38**, 827 (1968); *Chem. Abstr.*, **70**, 114688 (1969).
420. S. Fatutta and A. Risaliti, *J. Chem. Soc., Perkin Trans. 1*, 2387 (1974).
421. S. Fabrissin, S. Fatutta, N. Malusa and A. Risaliti, *J. Chem. Soc., Perkin Trans. 1*, 686 (1980).
422. F. Benedetti, S. Fabrissin and A. Risaliti, *Tetrahedron*, **40**, 977 (1984).
423. K. Takaki, K. Nakagawa and K. Negoro, *J. Org. Chem.*, **45**, 4789 (1980).
424. R. M. Cory and R. M. Renneboog, *J. Org. Chem.*, **49**, 3898 (1984).
425. T. Agawa, Y. Yoshida, M. Komatsu and Y. Ohshiro, *J. Chem. Soc., Perkin Trans. 1*, 751 (1981).
426. S. Braverman, D. Reisman and M. Sprecher, *Tetrahedron Letters*, 901 (1979).
427. L. Ramberg and B. Bäcklund, *Arkiv. Kemi Mineral. Goel*, **13A**, No. 24 (1949); *Chem. Abstr.*, **34**, 4725 (1940).
428. L. A. Paquette, in *Mechanisms of Molecular Migrations* (Ed. B. S. Thiagarajan), Vol. I, pp. 121–156.
429. L. A. Paquette, *Acc. Chem. Res.*, **1**, 209 (1968).
430. F. G. Bordwell, in *Organosulfur Chemistry* (Ed. M. J. Janssen), Interscience, New York, 1967, Chap. 16.
431. F. G. Bordwell, *Acc. Chem. Res.*, **3**, 281 (1970).
432. L. A. Paquette, *Org. React.*, **25**, 1 (1977).
433. C. Y. Meyers, A. M. Malte and W. S. Matthews, *J. Amer. Chem. Soc.*, **91**, 7510 (1969).
434. D. Scholz, *Chem. Ber.*, **114**, 909 (1981).

435. D. Scholz, *Liebigs Ann. Chem.*, 264 (1984).
436. T. B. R. A. Chen, J. J. Burger and E. R. de Waard, *Tetrahedron Letters*, 4527 (1977).
437. J. J. Burger, T. B. R. A. Chen, E. R. de Waard and H. O. Huisman, *Tetrahedron*, **37**, 417 (1981).
438. D. Scholz, and P. Burtscher, *Liebigs Ann. Chem.*, 517 (1985).
439. J. B. Hendrickson, G. J. Boudreaux and P. S. Palumbo, *Tetrahedron Letters*, **25**, 4617 (1984).
440. J. A. Loontjes, M. Van der Leij and B. Zwanenburg, *Rec. Trav. Chim. Pays-Bas*, **99**, 39 (1980); *Chem. Abstr.*, **93**, 4541f (1980).
441. E. Block and M. Aslam, *J. Amer. Chem. Soc.*, **105**, 6164 (1983).
442. E. Block and M. Aslam, *J. Amer. Chem. Soc.*, **105**, 6165 (1983).
443. R. Neidlein and H. Doerr, *Liebigs Ann. Chem.*, 1540 (1980).
444. K. Weinges, G.-U. Schwarz, M. Weber and G. Schilling, *Chem. Ber.*, **110**, 2961 (1977).
445. K. Weinges, H. Baake, H. Distler, K. Klessing, R. Kolb and G. Schilling, *Chem. Ber.*, **110**, 2978 (1977).
446. K. B. Becker and M. P. Labhart, *Helv. Chim. Acta*, **66**, 1090 (1983).
447. K. Weinges, J. Pill, K. Klessing and G. Schilling, *Chem. Ber.*, **110**, 2969 (1977).
448. K. Weinges, W. Kasel, J. Klein, G. Hubertus, H. Irngartinger, U. Huber-Patz and H. Rodewald, *Chem. Ber.*, **117**, 966 (1984).
449. F. Näf, R. Decorzant and S. D. Escher, *Tetrahedron Letters*, **23**, 5043 (1982).
450. M. Julia, D. Lave, M. Mulhauser, M. Ramirez-Muñoz and D. Uguen, *Tetrahedron Letters*, **24**, 1783 (1983).
451. H. Matsuyama, Y. Miyazawa, and Y. Takei and M. Kobayashi, *Chem. Letters*, 833 (1984).
452. K. A. Lukin, G. G. Bebikh and N. S. Zefirov, *Zh. Org. Khim*, **19**, 2523 (1983); *Chem. Abstr.*, **100**, 174296z (1984).
453. Y. Gaoni, *Tetrahedron Letters*, 4521 (1977).
454. A. Tomažič and E. Ghera, *Tetrahedron Letters*, **22**, 4349 (1981).
455. L. Engman, *J. Org. Chem.*, **49**, 3559 (1984).
456. M. Julia, G. Le Thuillier, Ch. Rolando and L. Saussine, *Tetrahedron Letters*, **23**, 2453 (1982).
457. J.-R. Baudin, M. Julia, C. Rolando and J.-N. Verpeaux, *Tetrahedron Letters*, **25**, 3203 (1984).
458. G. Buchi and R. M. Freidinger, *Tetrahedron Letters*, **26**, 5923 (1985).
459. R. D. Little and S. O. Myong, *Tetrahedron Letters*, **21**, 3339 (1980).

CHAPTER 13

Rearrangements involving sulfones

SAMUEL BRAVERMAN

Department of Chemistry, Bar-Ilan University, Ramat-Gan 52100, Israel

I. INTRODUCTION

Rearrangements involving sulfones have played an important role in the development of the chemistry of sulfones. It is therefore not surprising that all major literature surveys on sulfones[1–9], or their sulfinate precursors[10–14], also include a discussion of this subject.

However, while excellent and detailed coverage exists for certain rearrangements of general mechanistic and synthetic interest, such as, for example, the Ramberg–Bäcklund[15–18] or Smiles[19,20] rearrangement, the treatment of all other rearrangements is usually brief and partial. An attempt has therefore been made to provide the reader with a comprehensive and systematic survey of the literature dealing with rearrangements involving sulfones, some of which have never been reviewed before. An effort has also been made to scan the literature through 1986, as far as possible, and to cover the most significant aspects and most important advances, particularly work of the last two decades.

Rearrangements have been included in which sulfones participate not only as reactants but also as products. Reactions have been classified according to mechanism, but although the main emphasis has been on mechanism and stereochemistry, special attention to synthetic applications has also been given, wherever appropriate. Obviously, due to space limitations as well as the vast amount of work available, only selected and representative results of general importance, as judged by the concern of the reviewer, are presented below. Thus, the exclusion of a particular piece of work in no way passes judgement on its scientific value.

To a certain extent, the phenomenal expansion of organosulfur chemistry in recent years is also reflected in this review on rearrangements involving sulfones. It is hoped that this chapter, which is intended to serve all chemists, experts and students alike, will help them include its knowledge in their research programs, and will stimulate further creative work in the area.

II. REARRANGEMENTS OF SULFINATES TO SULFONES

A. Rearrangements of Alkyl and Benzyl Sulfinates to Sulfones

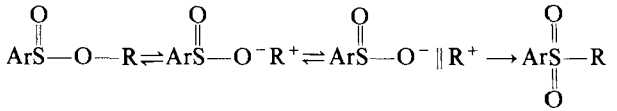
The rearrangement of esters of sulfinic acids to sulfones (equation 1) is one of the oldest and best studied rearrangements involving sulfones. However, although sulfinates were first prepared in 1885 by Otto and Rossing[21], and although the preparation of sulfones by heating sulfinic acids and alcohols under acidic conditions was reported by Hinsberg[22] in 1917, it was not before 1930 when Kenyon and Phillips[23] first reported that α-phenylethyl *p*-toluenesulfinate rearranged on standing to α-phenylethyl *p*-tolyl sulfone. Subsequently, Kenyon and coworkers[24] observed that this rearrangement was favored by an increase in solvent polarity and that in formic acid the optically active ester was converted to completely racemic sulfone. These results were considered as consistent with an ionic mechanism. Similarly, Stevens and coworkers[25] investigated the rearrangement of a number of sulfinates to sulfones and suggested an ionic mechanism. For example, no sulfone was obtained from the reaction of either methyl or benzyl *p*-toluenesulfinates, while the yield of sulfone was greater and the rate faster with the corresponding α,α-dimethylbenzyl than with α-methylbenzyl esters. It should also be pointed out that the driving force for the sulfinate to sulfone isomerization is the formation of the strong sulfur–oxygen bond in the sulfonyl group (112 kcal mol^{-1})[26], a result of back donation of a pair of nonbonding electrons from the oxygen atom into empty *d* orbitals of the sulfur atom, with consequent p_π–d_π overlap[27].

$$\mathrm{ArS(O)—O—R} \xrightarrow{\Delta} \mathrm{ArS(O)—R} \qquad (1)$$

Neither one of these reports provides any information with regard to the type of

ionization, i.e., ionization to free ions or ion pairs. The more recent, and mechanistically detailed investigations by Darwish and coworkers[28–33] prove quite useful in this respect, and may be regarded as the most important contribution in this field. These authors have examined the rearrangement of *t*-butyl[28], α-phenylethyl[28,29], α-(*p*-methoxyphenyl)ethyl[28,29], benzhydryl[28,30] 2-aryl-2-propyl[31] and trityl[32,33] 2,6-dimethylbenzenesulfinates under a variety of conditions. The main findings revealed by these investigations are as follows. The rate of rearrangement and solvolysis of the benzhydryl sulfinate showed a sensitivity to the ionizing power of the solvent similar to that shown in the solvolysis of the corresponding chloride[34], which is known to involve ionic intermediates. Similarly, the introduction of a methoxy group into the aromatic ring of the α-phenylethyl ester increased the rate of both rearrangement and solvolysis by four powers of ten. The size of this effect is indicative of an ionization mechanism[35].

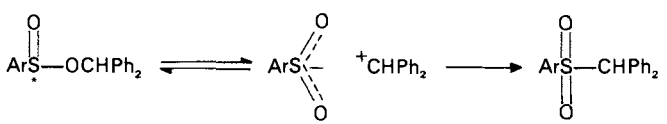
Several pieces of evidence indicate that sulfone is not formed by recombination of dissociated ions. For example, when the reactant was optically active, diastereomerically pure α-phenylethyl 2,6-dimethylbenzenesulfinate, the sulfone which was produced was also optically active and of over 95% retained configuration, but the ester recovered after partial reaction was a mixture of diastereomers.[36] Had dissociated ions been involved in the rearrangement to sulfone, the latter would have been expected to have lost most or all of the optical activity associated with the starting material. Further, the addition of 2,6-dimethylbenzenesulfinate anion to any of the systems did not increase the fraction of sulfone formed, as would have been expected if the ions were competing with solvent for the cation. Similarly, when *t*-butyl chloride, α-phenylethyl bromide or benzhydryl chloride were solvolyzed in the presence of lutidinium 2,6-dimethylbenzenesulfinate, no sulfone was formed[28], and no mixed products were obtained when benzhydryl 2,6-dimethylbenzenesulfinate was solvolyzed in the presence of the 4-methylbenzenesulfinate anion[30], thus no exchange of ions occurred during these reactions. Finally, even with the highly stable trityl cation produced during the rearrangement of trityl 2-methylbenzenesulfinate in acetonitrile, only 45% at most could be diverted to form trityl azide by the addition of tetrabutylammonium azide. Hence most of the sulfone appeared to be being produced from a species not readily trappable by azide ion. On the basis of these observations and other pertinent data, the mechanism which was proposed included the intermediacy of ion pairs[37], as shown in equation 2, where $ArSO_2^-R^+$ is a noncapturable intimate ion pair, and $ArSO_2^- \| R^+$ is a capturable solvent separated ion pair.



(2)

R = *t*-Bu, Ph_2CH, $PhCHCH_3$, Ph_3C

The ion pair mechanism initially suggested by Darwish and McLaren[28] (equation 2) has received further support from related studies conducted by several other investigators[38–42]. For example, Fava and coworkers[38] have reported that during isomerization in acetic acid, optically active benzhydryl *p*-toluenesulfinate loses optical activity at a rate which is about two and a half times faster than the rate of sulfone formation, thus indicating that return from an ion-pair species is occurring (equation 3).



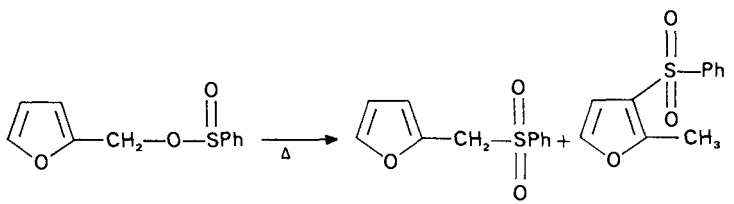
(3)

Braverman and coworkers[39–42] have studied the solvolysis and rearrangement of several benzyl and furfuryl sulfinates and reached similar conclusions with regard to the involvement of ion-pair intermediates. Thus, substitution of a *p*-hydrogen atom by a methoxy group in the benzyl group of benzyl arenesulfinates has been found to have a profound effect on the type of bond cleavage of these esters under solvolytic conditions. In contrast to benzyl arenesulfinate which undergoes solvolysis by sulfur–oxygen bond fission (equation 4), the solvolysis of the *p*-methoxybenzyl ester involves only carbon–oxygen bond fission and is accompanied by sulfone formation (equation 5)[39]. A kinetic study of the solvolysis and rearrangement revealed that the rate enhancement due to the *p*-methoxy group is approximately ten to the power of 4. The size of this effect, the great sensitivity to solvent ionizing power and other pertinent data are indicative of an ion-pair mechanism for the rearrangement of *p*-methoxybenzyl benzenesulfinate. Under nonsolvolytic conditions using formamide as solvent, the rearrangement of the *p*-methoxybenzyl ester is practically completed after two hours of heating on a steam bath.[39]

$$\mathrm{ArS(O)—OCH_2Ph + EtOH \xrightarrow{90^\circ} ArS(O)—OEt + PhCH_2OH} \qquad (4)$$

$$\mathrm{ArS(O)—OCH_2An\text{-}\mathit{p} + EtOH \xrightarrow{75^\circ} ArSO_2H + \mathit{p}\text{-}AnCH_2OEt + ArS(O)CH_2An\text{-}\mathit{p}} \qquad (5)$$

The rearrangement of furfuryl benzenesulfinate (**1**) appears of special interest. In contrast with the corresponding benzyl ester, this sulfinate was found to undergo a facile rearrangement to sulfone. Furthermore, in nonhydroxylic solvents a mixture of furfuryl phenyl sulfone (**2**) and 2-methyl-3-furyl phenyl sulfone (**3**) is obtained (equation 6)[40].

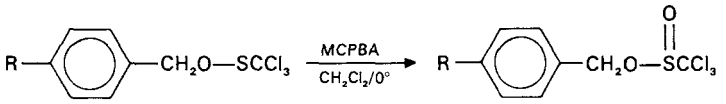


(6)

(**1**) (**2**) (**3**)

Since the ratio of the two sulfones **2** and **3** increases with the polarity of the solvent (from 1:4 in benzene to 16:1 in formamide) a possible concerted [2, 3]sigmatropic rearrangement for the formation of sulfone **3** was first considered. However, other evidence such as the effects of solvent and added salts seem to support an ionization mechanism, with the formation of the two sulfones by recombination from two different ion-pair species[40].

Interestingly, all the sulfinates considered so far were derived from arenesulfinic acids ($pK_a = 2.76$)[13]. Although considerably stronger than carboxylic acids, the ionization ability of their esters is much poorer than that of corresponding sulfonates. For this reason, and in view of the dramatic effect displayed by the trichloromethyl group on the reactivity of sulfenate esters in both solvolysis and rearrangement (see Chapter 14), Braverman and Duar[41] have investigated the reactivity of benzyl trichloromethanesulfinates. These esters (**5**) are easily and almost quantitatively obtained by oxidation of the corresponding sulfenates (**4**, equation 7).



(7)

(4) (5)

R = H, Me, Cl, NO_2

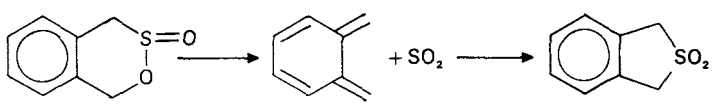
In sharp contrast with benzyl arenesulfinates which undergo ethanolysis with complete sulfur–oxygen bond fission (equation 4), the corresponding trichloromethanesulfinates undergo ethanolysis with exclusive carbon–oxygen bond fission (equation 8), and with a rate enhancement by a factor of 6 powers of ten. The unusual high reactivity of these esters, comparable to that of the corresponding tosylates[43], may be attributed to the high acid strength of Cl_3CSO_2H and the consequent high leaving group ability of its anion. On the other hand, the lack of rearrangement to sulfone under these conditions may reflect the lower nucleophilicity of the sulfur atom in this case. Also in contrast with benzyl arenesulfinates, these esters (**5**) undergo a facile rearrangement to sulfone on heating in polar nonhydroxylic solvents such as acetonitrile or nitromethane, in high yields (equation 9)[41b].

$$ArCH_2O—\overset{\overset{O}{\|}}{S}CCl_3 + EtOH \xrightarrow{32^\circ} ArCH_2OEt + Cl_3CSO_2H \tag{8}$$

$$ArCH_2O—\overset{\overset{O}{\|}}{S}CCl_3 \xrightarrow[4.5\,h]{MeCN,\ 100^\circ} ArCH_2\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}CCl_3 \tag{9}$$

In a similar study, Braverman and Manor[42] have prepared several benzyl trifluoromethanesulfinates(triflinates) in excellent yields using the method presented in equation 7. The reactivity of these esters entirely parallels that of the corresponding trichloro-analogues with respect to both solvolysis and rearrangement. It is worthwhile to mention the high reactivity of the *p*-anisyl esters, which rearrange to sulfones during their preparation at 0 °C[41,42]. At the same time, Hendrickson and Skipper[44] reported the rearrangement of a number of primary triflinates to the corresponding triflones. For example, heptyl triflinate rearranged to the corresponding sulfone on heating at 145° in HMPA for 4 h in 87% yield. This is in sharp contrast to the lack of reactivity of simple primary arenesulfinates. The triflones are of special interest for the synthetic chemist in the variety of ways they facilitate carbon–carbon bond construction, a subject already reviewed by Hendrickson[45].

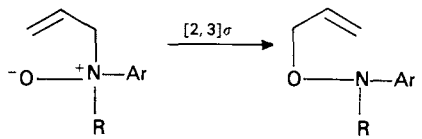
Finally, it should be of interest that the rearrangements of several cyclic benzylic sulfinates have also been described in the literature by Durst[46] and Hogeveen[47], and seem to proceed by a special two-step mechanism: retro-Diels–Alder extrusion of SO_2, followed by its chelotropic addition to the unstable quinodimethane intermediate (e.g. equation 10).



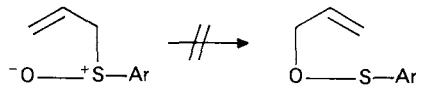
(10)

B. The [2, 3]Sigmatropic Rearrangement of Allylic Sulfinates to Sulfones

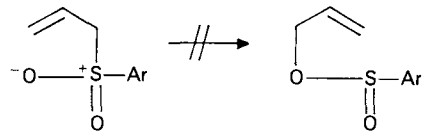
In 1950, Cope and coworkers[48] unsuccessfully attempted to use the well-known Meisenheimer rearrangement of *N*-allylamine oxides to *O*-allylhydroxylamines[49] in performing the formally analogous rearrangements of allyl aryl sulfoxides to allyl arenesulfenates and of allyl aryl sulfones to allyl arenesulfinates (equations 11–13).



(11)



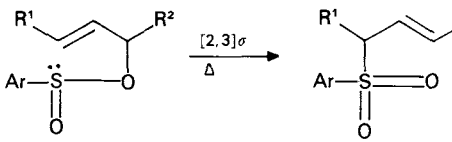
(12)



(13)

These authors[48] have also examined the thermal stability of allylic arenesulfinates. They found that allyl, crotyl and α-methylallyl benzenesulfinates on heating underwent rearrangement to sulfones in low yields, but were unable to reach a decision with regard to reaction mechanism, mainly because the last two esters gave the same product: crotyl phenyl sulfone.

Some ten years later, Darwish and Braverman[50,51] undertook a more extensive study of this rearrangement, which has revealed some unique features. These investigators examined the behavior of six different esters, namely allyl, crotyl, α-methylallyl, racemic and optically active α, γ-dimethylallyl, cinnamyl and α-phenylallyl 2, 6-dimethylbenzenesulfinates under various reaction conditions.



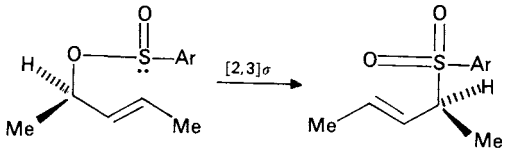
(6) (7)

	a	b	c	d	e	f
R^1	H	Me	H	Me	Ph	H
R^2	H	H	Me	Me	H	Ph

Ar = 2,6-$Me_2C_6H_3$

(14)

All these esters have been found to undergo rearrangement to sulfones in high yields even under solvolytic conditions (equation 14). This result seems of interest in view of the fact that under such conditions sulfinates in general undergo solvolysis with relatively little sulfone formation[28,39–42]. The second point of interest is that the rearrangement of unsymmetrically substituted allylic esters involves simultaneous isomerization of the allylic group. Similarly, optically active α, γ-dimethylallyl 2, 6-dimethylbenzenesulfinate rearranged to the corresponding optically active sulfone with practically complete inversion of configuration (equation 15)[50,51].



(15)

(**6d**) $[\alpha]_D^{25} + 3.86$ (**7d**) $[\alpha]_D^{25} + 7.02°$

It may be of interest to note that the stereospecific transformation shown in equation 15 has been cited as the first reported observation of an 1 → 3 chirality transfer[52]. It is evident that on rearrangement of optically active **6d** to **7d**, the chiral center at C-α is eliminated and a new one created at C-γ. The term 'self-immolative' asymmetric synthesis has also been used to describe syntheses of this kind[53]. As pointed out by Hoffmann[52], quantitative 1 → 3 chirality transfer will follow from the suprafacial[54,55] course of rearrangement, provided the reactant has a uniform configuration at the β,γ-double bond. This stereochemical prediction has also been confirmed by the results obtained in several other [2, 3]sigmatropic rearrangements, subsequently reported[56–58].

The evidence presented so far excludes the formation of dissociated ions as the principal precursor to sulfone, since such a mechanism would yield a mixture of two isomeric sulfones. Similarly, in the case of optically active ester a racemic product should be formed. The observed data are consistent with either an ion-pair mechanism or a more concerted cyclic intramolecular mechanism involving little change between the polarity of the ground state and transition state. Support for the second alternative was found from measurements of the substituent and solvent effects on the rate of reaction.

The relative rates of reaction for several different allylic systems are presented in Table 1. The data obtained by Vernon[59] on the formolysis of allyl chlorides have been used as a standard for ionization.

As one can see, the rate of rearrangement of the allylic arenesulfinates in 60% ethanol–water shows a marked sensitivity to the substitution of an α- or γ-hydrogen atom by an

TABLE 1. Relative rates of reaction of allylic 2, 6-dimethylbenzenesulfinates, chlorides, thiocyanates and thionbenzoates

	2, 6-Dimethyl-benzene-sulfinate[a]	Chloride[b]	Thiocyanate[c]	Thionbenzoate[d]
Allyl	1	1	1	1
Crotyl	36	3.5×10^3	15	6
α-Methylallyl	141	5.67×10^3	—	52
Cinnamyl	221	*ca.* 5×10^5	—	—
γ,γ-Dimethylallyl	—	*ca.* 1.5×10^7	150	—
α,α-Dimethylallyl	—	*ca.* 8×10^7	—	—
α,γ-Dimethylallyl	2.6×10^3	*ca.* 3×10^{8e}	—	—
α-Phenylallyl	*ca.* 2.1×10^4	*ca.* 2×10^{9e}	—	—

[a]The relative rates are based on the rate of rearrangement of allyl 2, 6-dimethylbenzenesulfinate in 60% ethanol–water at 90.0°, $k = 4.57 \times 10^{-6} s^{-1}$.

[b]Data taken from Reference 59.

[c]These values are based on the rate of allyl thiocyanate in acetonitrile at 60°, $k = 1.8 \times 10^{-5} s^{-1}$. Data of Reference 60.

[d]Allyl thionbenzoate in acetonitrile at 100° has $k = 5.67 \times 10^{-5} s^{-1}$. Data of Reference 61.

[e]These values were derived from data obtained in ethanol solvent (see p. 86 in Reference 50a).

alkyl or phenyl group, suggestive of a polar transition state. However, the large difference in sensitivity to substituent effects between the allylic chlorides and 2, 6-dimethylbenzenesulfinates, ranging between two and five powers of ten, tends to indicate that charge separation in the transition state in the rearrangement of sulfinates to sulfones is much smaller than in an ionization process.

The substituent effect data related to the rearrangement of the allylic 2, 6-dimethylbenzenesulfinates compares favorably with the corresponding data reported by Fava and coworkers[60] for the [3, 3]sigmatropic rearrangement of allylic thiocyanates to isothiocyanates in acetonitrile and by Smith[61] for the analogous rearrangement of allylic thionbenzoates to the thiolbenzoates in the same solvent. The rearrangement of the last two systems is believed to involve little change in charge separation between the ground state and transition state[60,61]. In order to test the solvent effect, equation 16, suggested by Winstein and coworkers[62], has been used:

$$\log k_{\text{reaction}} = a \log k_1 + b \tag{16}$$

where k_{reaction} and k_1 are the rate constants of the reaction being examined and that of ionization of *p*-methoxyneophyl *p*-toluenesulfonate, respectively. The *a* value in the above equation, which can be obtained graphically from a plot of $\log k_{\text{reaction}}$ vs. $\log k_1$, was suggested by these authors as a measure of relative sensitivity of a reaction to the ionizing power of the solvent.

As illustrated in Figure 1, $\log k$ for rearrangement of cinnamyl 2, 6-dimethylbenzenesulfinate, using dimethyl sulfoxide, acetonitrile, 12.5% acetic acid–dioxane and tetrahydrofuran as solvents at 90.0°, correlated quite well with $\log k$ for ionization of *p*-methoxyneophyl tosylate in the same solvents at 75.0°. The slope (*a* value) of the straight line is 0.30. A similar plot, obtained for allyl 2, 6-dimethylbenzenesulfinate, indicated an *a* value of 0.19. From the magnitude of these *a* values it is clear that the rearrangement of allylic 2, 6-dimethylbenzenesulfinates exhibits a low sensitivity to variation in solvent ionizing power, which is of the same order as that observed for the rearrangements of allylic thionbenzoates and azides ($a = 0.15$ and 0.12, respectively) believed to proceed by a cyclic intramolecular mechanism[61,63].

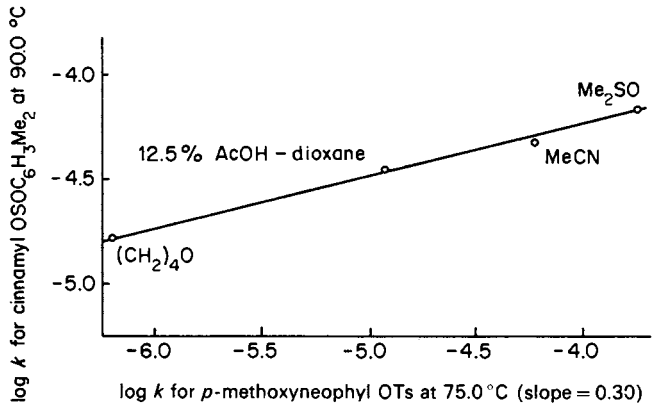
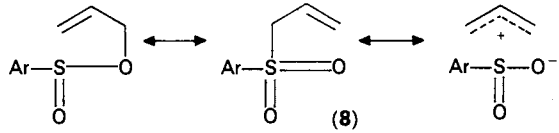


FIGURE 1. Plot of log *k* for rearrangement of cinnamyl 2, 6-dimethylbenzenesulfinate vs. log *k* for ionization of *p*-methoxyneophyl *p*-toluenesulfonate in 'nonhydroxylic' solvents.

On the basis of the evidence presented above as well as some other pertinent data (e.g. negative entropies of activation), Darwish and Braverman have suggested that the rearrangement of allylic 2,6-dimethylbenzenesulfinates (**6a–f**) to corresponding sulfones (**7a–f**) proceeds by a cyclic intramolecular mechanism involving a five-membered transition state which may be represented by a resonance hybrid (**8**) of the following resonance structures.

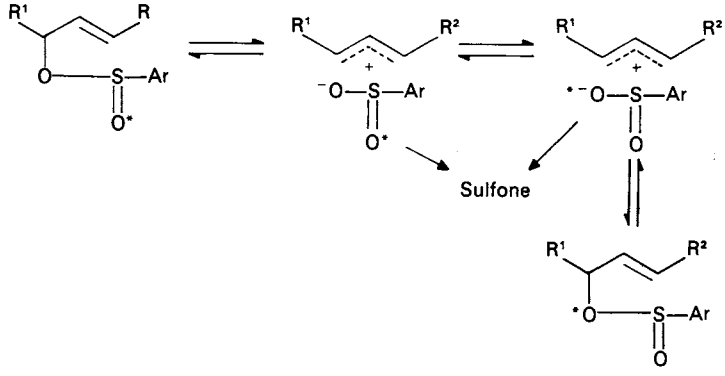


(**8**)

One would expect a graded sequence of transition states between the covalent and ionic structures. It is conceivable that with allyl 2,6-dimethylbenzenesulfinate in nonpolar solvents the covalent resonance structure of the transition state is the major contributor. It is also probable that replacement of a hydrogen of the allyl group by a carbenium ion-stabilizing substituent such as alkyl and phenyl groups, and the use of solvents of high ionizing power will enhance the contribution of the ionic resonance structure. It should be added that this is not only one of the first and best studied [2, 3]sigmatropic rearrangements[64], but it has also been used as a model for the prediction of the closely related [2, 3]sigmatropic rearrangements of allylic sulfenates to sulfoxides, propargylic sulfenates and sulfinates to allenic sulfoxides and sulfones[51], respectively, (see Chapter 14) as well as their corresponding selenium analogues[65].

Further support of the proposed mechanism can be found in several subsequent studies, including the most elegant investigation of oxygen-18 scrambling in the rearrangement of allylic arenesulfinates performed by Darwish and Armour[66], in order to determine the importance of the polar resonance structure of the transition state **8**. For this purpose, allylic arenesulfinates **6a–f** have been synthesized having an oxygen-18 label in the sulfinyl oxygen position. The esters which were recovered after partial reaction in ethanol, 60% ethanol or acetic acid were hydrolyzed and the excess oxygen-18 in the resulting alcohol was determined from the mass spectrum of the alcohol.

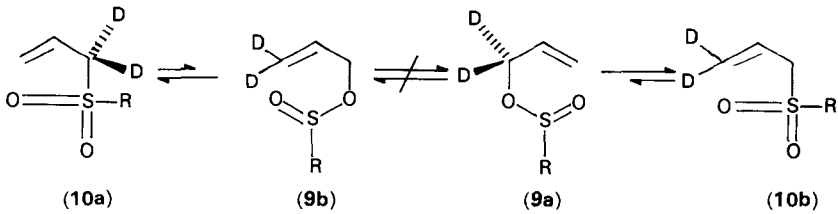
A general scheme for rearrangement of the arenesulfinate esters to sulfones involving an ionic intermediate which would result in scrambling of the oxygen-18 label in the ester is illustrated in equation 17. Excess oxygen-18 was not detected in the alcohols from the allyl, crotyl or α-methylallyl esters during reaction in any of the solvents examined, or in the alcohol from the α,γ-dimethylallyl ester during reaction in ethanol or 60% ethanol.



(17)

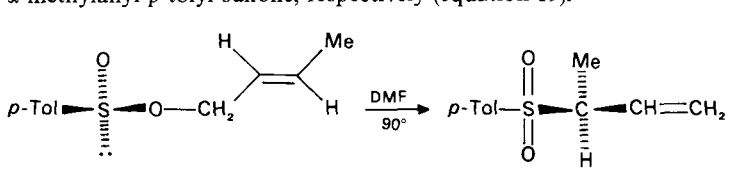
It has been suggested[66] that the rearrangement of these esters proceeds via a cyclic five-membered transition state in which bond-breaking and bond-making are sufficiently concerted that a discrete ionic intermediate is not involved. The presence of an ion-pair intermediate in the rearrangement of the cinnamyl ester would allow recombination of the α-carbon with either of the oxygens of the sulfinate anion. Such recombination of the ion pairs formed from the α,γ-dimethylallyl ester and the α-phenylallyl ester would lead to the formation of the diastereoisomer different from the starting ester. The experimental results from the rearrangement and scrambling of the α-phenylallyl ester are consistent with those calculated using a scheme allowing diastereoisomer interconversion. The incorporation of O-18 into the ether oxygen position during the rearrangement of the α,γ-dimethylallyl ester in acetic acid may arise by C—O bond fission to yield an ion pair followed by bond formation between the γ-carbon and sulfinyl-oxygen of the starting ester. This process is formally similar to rearrangement via a six-membered transition state and would lead to the formation of ester which was the same diastereoisomer as the starting material[66].

These results are in complete agreement with the mechanistic prediction mentioned above[51] with regard to the graded sequence of transition states between covalent and ionic structures, as a function of allylic substitution and solvent effects. The lack of any O-18 scrambling in the rearrangement of the allyl, crotyl and α-methylallyl esters is rather remarkable. A similar observation has been recently made by Little and coworkers[67] who prepared the deuterated sulfinate **9a** and analyzed the products obtained from its flash pyrolysis (254 °C, sealed tube, 41 and 105s). ^{1}H NMR analysis failed to indicate the presence of the isomerized sulfinate **9b** or sulfone **10a**; only sulfone **10b** was detected (equation 18). The lack of scrambling of the label in the sulfinate and the exclusive rearrangement to **10b** are again evidence for the concertedness of this [2,3]sigmatropic rearrangement even under such drastic conditions.



(18)

By modification of the elegant method of preparation of optically active sulfinates previously reported by Mikolajczyk and coworkers[68], an efficient stereospecific method for the conversion of readily available optically active sulfinamides to optically active sulfinates of inverted configuration at the sulfinyl function, has been recently reported by Hiroi and coworkers[69]. The same authors[70] subsequently reported the thermal rearrangement of several optically active *cis*- and *trans*-γ-substituted allylic *p*-toluenesulfinates to optically active chiral sulfones with high stereoselectivity. For example, *trans* and *cis* (*S*)-(−)-crotyl *p*-toluenesulfinates rearranged to optically active (*S*)-(+)- and (*R*)-(−)-α-methylallyl *p*-tolyl sulfone, respectively (equation 19).

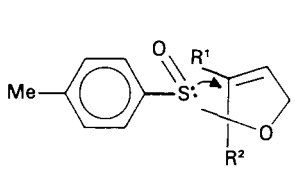


(19)

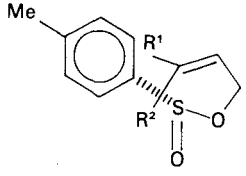
$[\alpha]_D = 4.4°$ (86.8% ee)

The complete retention of optical activity in the starting sulfinates recovered at any stage of the reaction, and the high stereoselectivity of the rearrangement are further evidence for the concertedness of the [2,3]sigmatropic rearrangement, in complete agreement with the results presented in equation 15.

The transfer of chirality from sulfur to carbon as well as the high stereoselectivity were explained by a preference of rearrangement through transition state **11a** over **11b** due to steric interference between the *p*-tolyl and α-alkyl group.



(11a)

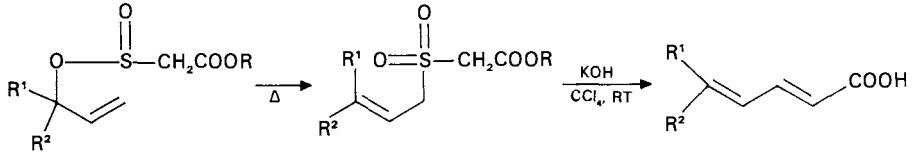


(11b)

Because of certain misconceptions with regard to the choice of solvent and the occurrence of sulfur–oxygen bond fission in hydroxylic solvents[69,70], it is important to emphasize that one can greatly reduce the rate of this competing process by the use of weak bases. In systems which can undergo facile C—O as well as S—O bond fission, it is possible to control the type of bond cleavage by choosing the appropriate base[71]. A remarkable illustration of this behavior is found in the ethanolysis of sulfinate **6a**. In anhydrous ethanol at 90.0° with acetate ion as the added base, **6a** yielded ethyl 2, 6-dimethylbenzenesulfinate plus a trace of sulfone **7a**. Under the same conditions but with 2, 6-lutidine the reaction was slower and sulfone **7a** was the only detectable reaction product[50a].

It has also been reported[44] that rearrangements of both α- and γ-propylallyl triflinates on heating in acetonitrile yield the same sulfone: γ-propylallyl triflone. Although the possibility of an ion-pair mechanism may be responsible for the lack of allylic rearrangement in one case as a result of the better leaving group ability of the triflinate anion as compared with the arenesulfinate anion, it is just as likely a consequence of the unbuffered conditions in which these reactions were performed. In this respect this is reminiscent of the results observed by Cope and coworkers[48] mentioned above which were also performed under nonbuffered conditions, and which could be simply corrected by the addition of 2, 6-lutidine[66b].

The synthetic utility of the allylic sulfinate–sulfone rearrangement is illustrated by the following two examples. Grieco and Boxler[72] have reported a relatively facile synthesis of conjugated dienoic acids by application of the Ramberg–Bäcklund method on the corresponding allylic sulfonoacetates (**12**) obtained in turn by rearrangement of their appropriate sulfinate precursors (equation 20).

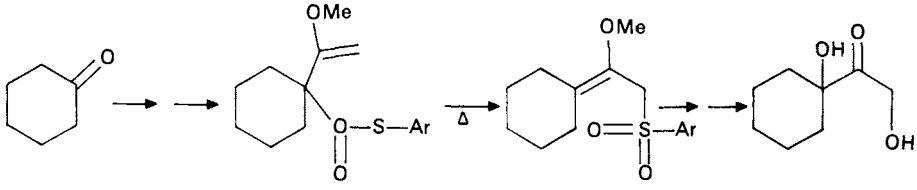


(12)

(20)

Baldwin and coworkers[73] have used the allylic sulfinate to sulfone rearrangement (**13** to **14**) for the development of a convenient route to the dihydroxyacetone unit, an

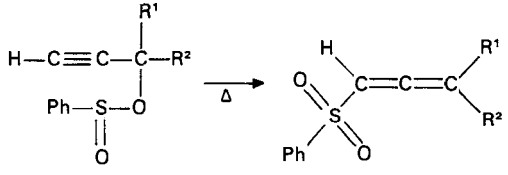
important structural feature in corticoid hormones, as well as other biologically active compounds (equation 21).



(13) (14) (21)

C. The [2, 3]Sigmatropic Rearrangement of Propargylic Arenesulfinates to Allenyl Aryl Sulfones

Following studies on the rearrangement of allylic arenesulfinates, Braverman and coworkers have investigated a number of natural extensions of this unique transformation, including the predictable [2, 3]sigmatropic rearrangements of allylic sulfenates to sulfoxides and of propargylic sulfenates and sulfinates to allenic sulfoxides and sulfones respectively. The last reaction is described below, while the other two are described in Chapter 14.



(15) (16) (22)

(a) $R^1 = R^2 = Me$ (d) $R^1 = H$, $R^2 = Ph$

(b) $R^1 = R^2 = H$ (e) $R^1 = Me$, $R^2 = Ph$

(c) $R^1 = H$, $R^2 = Me$

Rearrangements of propargylic systems to allenes in general have been widely studied and are well documented[74–78]. In 1966, Braverman and Mechoulam[79a] first reported the facile thermal rearrangement (equation 22) of α,α-dimethylpropargyl benzenesulfinate (**15a**) to γ,γ-dimethylallenyl phenyl sulfone (**16a**) thus indicating the occurrence of an 'allylic-shift' for this system as well, in spite of certain geometrical differences. The analogy between the rearrangement of allylic arenesulfinates, as described in the previous section, and the corresponding propargylic esters was further demonstrated by the almost exclusive rearrangement to sulfone even under solvolytic conditions, as well as by a low sensitivity of the rate of rearrangement to the change in the ionizing power of the solvent[79b].

As illustrated in Figure 2, $\log k$ for the rearrangement of α,α-dimethylpropargyl benzenesulfinate, using 80% ethanol, acetic acid, ethanol and acetonitrile as solvents at 75°, correlated quite well with $\log k$ for ionization of *p*-methoxyneophyl tosylate[72] in the same solvents and temperatures. The slope of the straight line is 0.28. From the magnitude of the *a* value thus determined (see equation 16), it is clear that the rearrangement of **15a** exhibits a low sensitivity to variation in solvent ionizing power, which is of the same order

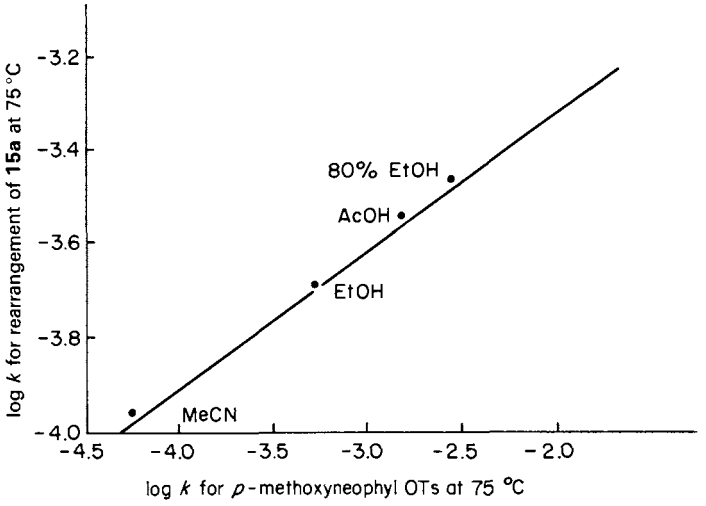
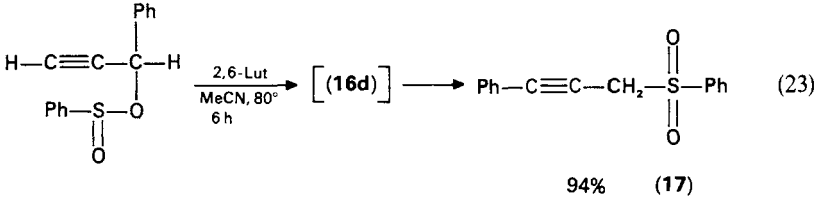


FIGURE 2. Plot of log k for rearrangement of α,α-dimethylpropargylbenzenesulphinate (**15a**) vs. log k for ionization of p-methoxyneophyl tosylate at 75°. Slope 0.28.

as that observed for the rearrangement of allylic sulfinates[50,51], thionbenzoates[61] and azides[63] ($a = 0.19$, 0.15 and 0.12, respectively) believed to proceed by a cyclic intramolecular mechanism.

The negative value of the entropy of activation ($\Delta S^{\ddagger} = -12.8$ eu) obtained for the reaction of **15a** in acetonitrile tends to support a highly ordered transition state, consistent with the operation of a concerted mechanism[79c]. Furthermore, the rate of rearrangement of **15a** in acetonitrile at 90° was 23 times faster than that of **15c**. The magnitude of the effect of substitution of an α-hydrogen by a methyl group, thus determined, is smaller by two powers of ten than the effect produced by a such a substitution in propargylic[81] and allylic[59] chlorides, reacting by ionization mechanisms.

As expected, the rearrangement of **15e** is quite analogous to that of **15a**. On the other hand, somewhat different behaviour has been observed with the secondary α-methyl and α-phenyl esters **15c** and **15d**. If the rearrangement is performed as usual in the presence of 2,6-lutidine, the initially formed γ-substituted allenyl sulfones (**16c**, **16d**) undergo a base catalyzed prototropic shift to the γ-substituted propargyl sulfones (**17**) (e.g., equation 23). Exclusion of the buffer altogether avoids this phenomenon but also results in some solvolysis and formation of α-phenyl propargyl sulfone as well. On the other hand, the presence of calcium carbonate as a heterogeneous phase drastically minimizes this problem. For example, heating of **15c** in MeCN for 85 h at 90° gave only the expected product (**16c**) in almost quantitative yield[79c]. In the light of the evidence presented above



(23)

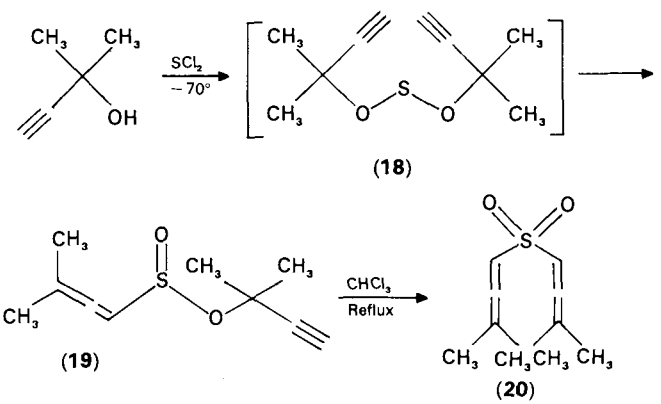
the authors[79] suggested that the rearrangement of propargylic sulfinates to allenyl sulfones proceeds by a concerted [2,3]sigmatropic shift[64] mechanism.

These observations on the rearrangement of propargylic arenesulfinates are confirmed by the work of Stirling and Smith[80] performed contemporaneously with that by Braverman and Mechoulam[79]. These authors reported that γ-deuteriopropargyl *p*-toluenesulfinate rearranged to α-deuterio *p*-tolyl sulfone on heating in chlorobenzene at 130°, and that under similar conditions *R*-(+)-α-methylpropargyl *p*-toluenesulfinate rearranged to (−)-γ-methylallenyl *p*-tolyl sulfone whose absolute configuration, predicted on the basis of a cyclic intramolecular mechanism, agrees with that calculated from the polarizability sequence of substituents attached to the allene system.

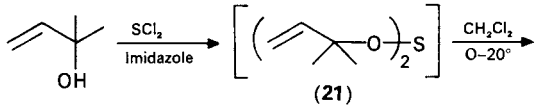
D. The Double [2,3]Sigmatropic Rearrangement of Allylic and Propargylic Sulfoxylates

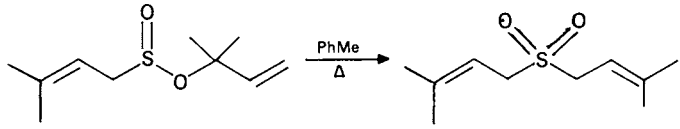
An interesting extension of the [2,3]sigmatropic rearrangements of allylic and propargylic sulfinates, discussed in the preceding two subsections, as well as the analogous rearrangements of allylic[82] and propargylic[51,83] sulfenates, is the double [2,3]sigmatropic rearrangement of the corresponding sulfoxylate esters, included in this section because of the formation of sulfones, as final products.

Braverman and Segev[84] first reported a convenient method for the preparation of conjugated diallenyl sulfones, involving a double [2,3]sigmatropic shift of propargylic sulfoxylates, as illustrated in equation 24. While the rearrangement of sulfinate **19** requires moderate heating for several hours, the rearrangement of its sulfoxylate precursor proceeds spontaneously even at low temperature. Diallenyl sulfone **20** was found to undergo some interesting thermal and ionic rearrangements to cyclic products[84]. Subsequently, Büchi and Freidinger[85] have reported the analogous rearrangement of allylic sulfoxylates to diallylic sulfones, as illustrated in equation 25. In this case too, the rearrangement of sulfinate **22** to the bisallyl sulfone **23** is best accomplished by brief reflux in toluene, while the formation of **22** itself takes place below room temperature. Previously, it has been reported that treatment of allyl alcohol with sulfur dichloride at −95° gave the corresponding sulfinate by rearrangement of the anticipated diallyl sulfoxylate[86,87]. The analogous rearrangement of allyl thiosulfoxylate to allyl thiosulfinate (equation 26), believed to represent the structure of allicin, the antibacterial principle of *Allium sativum* (garlic), has also been reported[88]. In this case, however, the rearrangement can be reversed by α-substitution in the product. A useful conversion of diallylic sulfones to the corresponding trienes, by way of the Ramberg–Bäcklund reaction, has also been described[85].

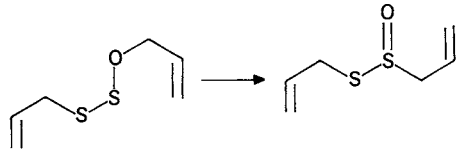


(24)





(25)

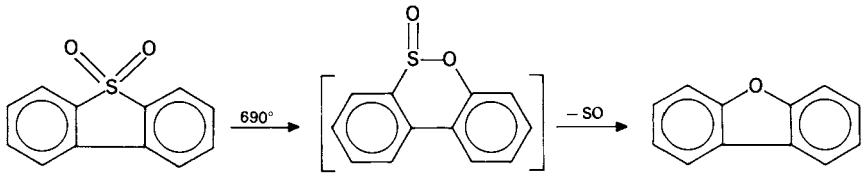


(26)

III. REARRANGEMENTS OF SULFONES TO SULFINATES

A. Thermal Rearrangements

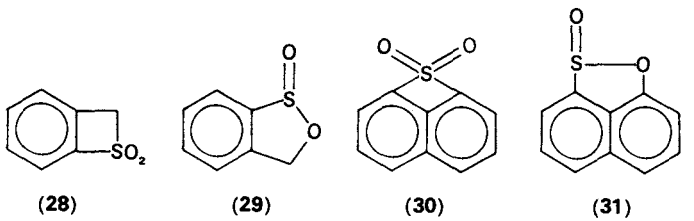
In contrast with the relatively facile thermal rearrangement of sulfinates to sulfones discussed in the preceding section, the reverse process is relatively, rarely encountered and is usually observed only at elevated temperatures. One of the first thermal sulfone to sulfinate isomerizations has been invoked by Fields and Meyerson[89] to occur during the pyrolysis of dibenzothiophene *S,S*-dioxide (**26**) to dibenzofuran, through elimination of sulfur monoxide from the sultine intermediate **27** (equation 27). More recently, the flash vapor-phase pyrolysis of various 2,5-dialkyl and diaryl thiophene-*S,S*-dioxides has also been shown to involve SO extrusion and formation of the corresponding furans in good yields[90].



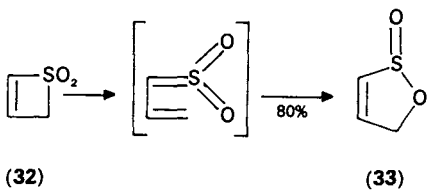
(27)

Several reports involving the rearrangement of cyclic four-membered α,β-unsaturated sulfones to the corresponding five-membered cyclic sulfinates (γ-sultines)[91] were subsequently published. For example, Dittmer and Nelsen[92] have observed the rearrangement of benzothiete 1,1-dioxide (**28**) to benzosultine **29** in 90% yield at 210°, while Hoffmann and Sieben[93] reported the gas-phase rearrangement of **30** to **31** at 300°. Contemporaneously, King and coworkers[94–96] have studied the thermal rearrangement of the parent molecules thiete 1,1-dioxide (**32**) to γ-sultine **33**, and rationalized their results in terms of a mechanism involving vinyl sulfene as a reactive intermediate, which is formed and reacts in a concerted manner (equation 28). This intermediate could be

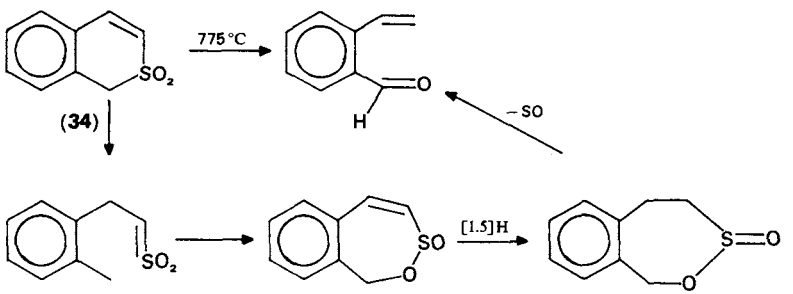
trapped by reaction with phenol, and the release of ring strain during its formation provides the driving force for the reaction. The flash-vacuum thermolysis of the benzothiopyran 1, 1-dioxide **34** was also suggested to involve a similar mechanism (equation 29)[97].



(28) **(29)** **(30)** **(31)**



(32) **(33)** (28)

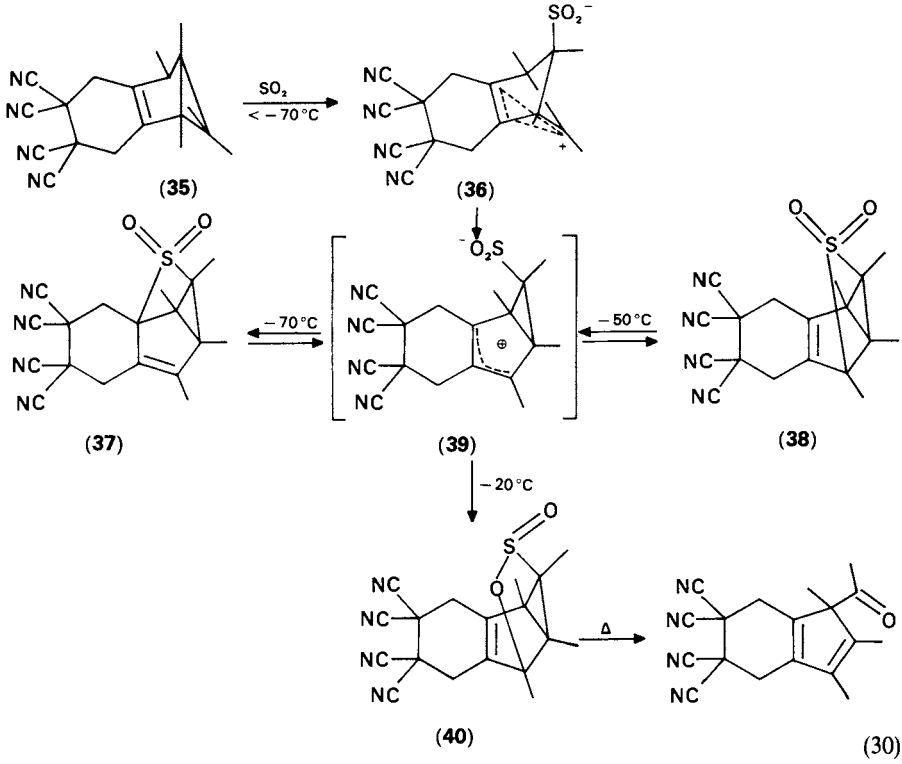


(34) (29)

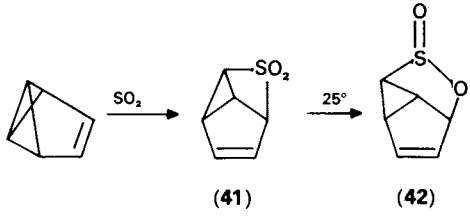
Recently, two extremely facile and unusual sulfone to sulfinate rearrangements were reported. Hogeveen and Zwart[98] treated the benzvalene derivative **35** with SO_2 at $-95\,^{\circ}C$ and observed the symmetric zwitterion **36**, which above $-70\,^{\circ}C$ rearranged to the sulfones **37** and **38**, presumably via the asymmetric zwitterion **39**. The two sulfones isomerized to the sultine derivative **40** at $-20\,^{\circ}C$, a sequence of reactions described as a chemical cascade (equation 30). Subsequently, Christl and coworkers[99] have reported the room-temperature rearrangement of cyclic sulfone **41** to sultine **42** (equation 31) believed to proceed by an ionic mechanism. Apparently, the release of ring strain present in the starting material provides considerable driving force for these rearrangements.

An interesting sulfone to sulfinate rearrangement has been observed by Schank and Schmitt[100] in the thermal fragmentation of α-alkoxysulfones, and is believed to involve an ion-pair mechanism (equation 32).

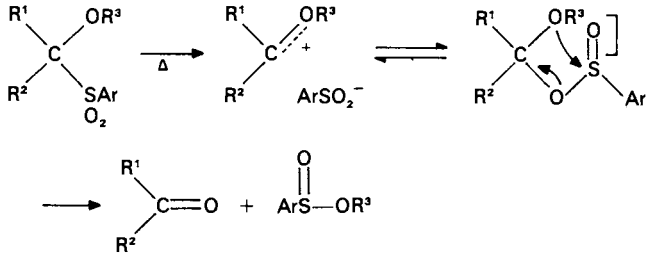
A similar mechanism may also be suggested for the thermal fragmentation of cyclic five-membered α-sulfonyl ethers to sulfur dioxide, alkenes and carbonyl compounds (equation 33)[101–103] as well as for the analogous rearrangement and fragmentation of trithioorthoacetate-*S*, *S*-dioxides (equation 34)[104].



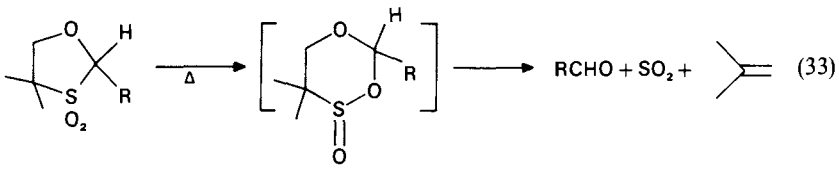
(30)

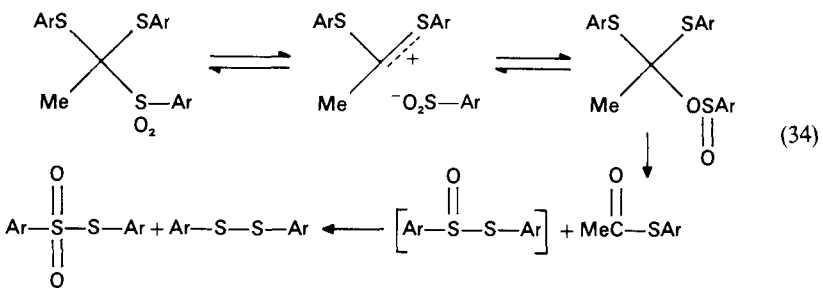


(31)



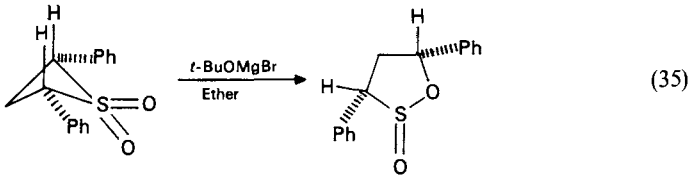
(32)



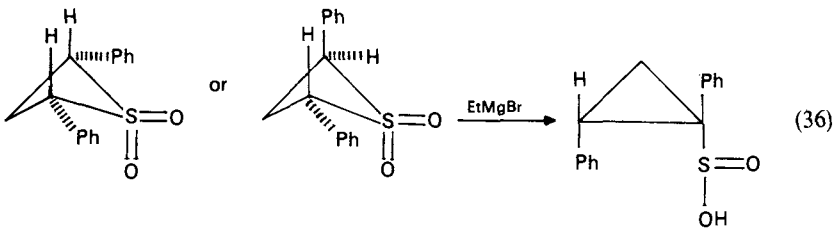


B. Carbanionic Rearrangements

Similar to the thermal rearrangements discussed in the previous subsection, the base-catalyzed rearrangements of cyclic four-membered sulfones to five-membered sulfinates have also been reported. For example, Dodson and coworkers[105] have observed the rearrangement of *cis*- and *trans*-2,4-diphenylthiethane 1,1 dioxides to *cis*- and *trans*-3,5-diphenyl-1,2-oxathiolane (2,3)-*cis*-2-oxides, respectively (equation 35), on treatment with *t*-butoxymagnesium bromide, which is stereospecific with respect to the phenyl group but stereoselective with respect to the oxygen atoms on sulfur.

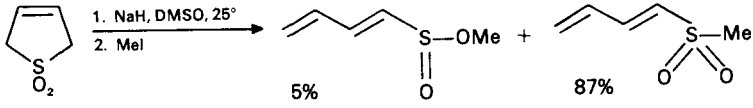


No firm decision, between an anion diradical mechanism and a concerted S→O 1,2-anionic shift, could be made from the available evidence[106]. Interestingly, the use of a stronger base such as ethylmagnesium bromide results in rearrangement to *trans*-1,2-diphenylcyclopropanesulfinic acid in highly stereoselective manner (equation 36)[107].



Under certain basic conditions 2,5-dihydrothiophene 1,1-dioxides undergo ring opening reactions[108,109] and the resulting buta-1,3-dienyl sulfinate ions may be alkylated

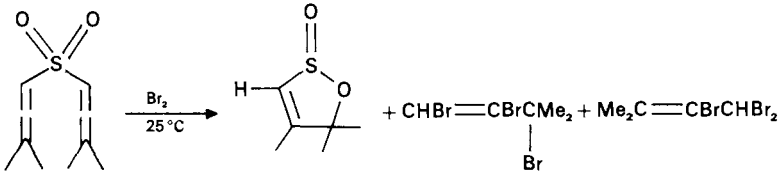
to the corresponding esters or sulfones (equation 37)[110].



(37)

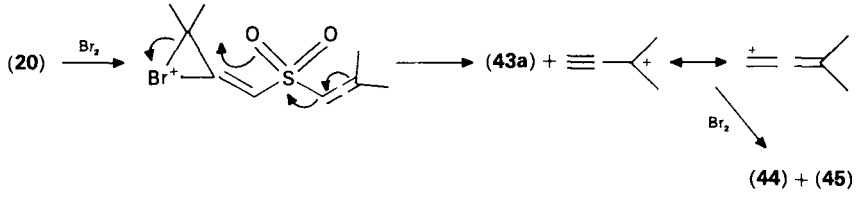
C. Electrophilic Rearrangements

Braverman and Reisman[111] have found that addition of a carbon tetrachloride solution of bromine to bis-γ,γ-dimethylallenyl sulfone **20** at room temperature unexpectedly resulted in spontaneous and quantitative fragmentation of the sulfone, with formation of the cyclic α,β-unsaturated sulfinate (γ-sultine) **43a** and the tribromo products **44** and **45** (equation 38). Analogously, treatment of the same sulfone with trifluoroacetic acid gives rise to γ-sultine **43b**. It is interesting to note that from a synthetic point of view it is not even necessary to prepare the diallenyl sulfone **20**, since one can use its sulfinate precursor (equation 24) to obtain exactly the same results, under the same conditions. The authors suggested that the fragmentation–cyclization of sulfone **20** may take place by the mechanism depicted in equation 39.



(20) **(43a)** X = Br; **(43b)** X = H **(44)** **(45)**

(38)

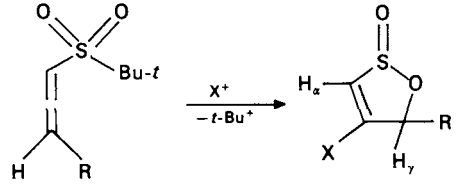


(39)

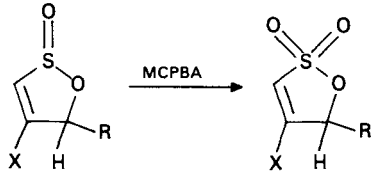
This mechanism is supported by several observations. First, treatment of either α,α-dimethylpropargyl or γ,γ-dimethylallenyl bromide with bromine gives the same mixture of **44** and **45** as obtained in the reaction of **20**. Second, reactions of the unsubstituted diallenyl sulfone did not result in the fragmentation–cyclization described above for sulfone **20** under the same conditions. Similarly, no γ-sultine was obtained on treatment of γ,γ-dimethylallenyl *p*-tolyl or methyl sulfone with bromine while γ,γ-dimethylallenyl *t*-butyl sulfone gave compound **43a** and *t*-butyl bromide. These results indicate that in the absence of a departing stable carbocation, such as α,α-dimethylpropargyl or *t*-butyl, no fragmentation and subsequent cyclization are possible under the mild conditions employed. However, further work has shown that this prerequisite is only required in the case of allenic sulfones and not of allenic sulfinates[112].

The conversion of sulfones to sulfinates under electrophilic conditions such as those described above appears to be unique. In continuation, a stereochemical study of this reaction has also been performed[113,114]. Racemic γ-methyl- and γ-*t*-butylallenyl *t*-butyl sulfones (**46, 47**) were prepared by [2, 3]sigmatropic rearrangement of the corresponding α-alkylpropargyl *t*-butylsulfinates. Optically active sulfones (−)-**46** ($[\alpha]_D^{25}$ −47.5°, yield 70%) and (−)-**47** ($[\alpha]_D^{25}$ −58.5°, yield 66%) were obtained by the elegant method of kinetic resolution[115], and were assigned the *R* absolute configuration by the use of the Lowe–Brewster rules[116] and the polarizability order $RSO_2 > H$ and alkyl > H. Treatment of these sulfones with bromine and methanesulfenyl chloride gave optically active γ-sultines **48–51**.

All the γ-sultines were obtained as diastereomeric mixtures (ca 1:1, by NMR), and each one of γ-sultines (+)-**49** and (+)-**51** (R = *t*-Bu) was separated into two diastereomers A and B by column chromatography. The oxidation of γ-sultines (−)-**49A** and (+)-**49B** to the corresponding optically active sultones (+)-**52A,B**, which lack a chiral sulfur, may be taken as proof that the observed optical activity in the sultines is also due to the γ-carbon. This result seems to exclude the intermediacy of vinylsulfene in the reaction mechanism, since its disrotatory closure would lead to racemic γ-carbon in the product.



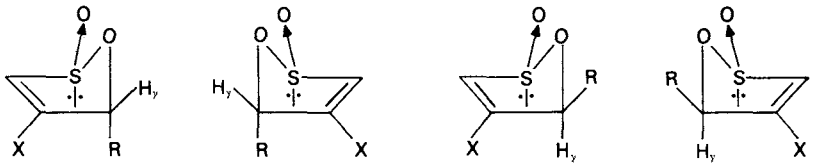
		$[\alpha]_D^{25}$, deg
(*R*)-(−)-(**46**), (**47**)	(**48**) X = Br, R = Me	+16.9
(**46**) R = Me	(**49**) X = Br, R = *t*-Bu	+15.6
(**47**) R = *t*-Bu	(**50**) X = MeS, R = Me	+23.7
	(**51**) X = MeS, R = *t*-Bu	+15.9



	$[\alpha]_D^{25}$, deg		$[\alpha]_D^{25}$, deg
(**49A**)	−17.0	(**52A**)	+9.8
(**49B**)	+75.8	(**52B**)	+12.6

The identity in sign and similarity in optical rotations of sultones (+)-**52A,B**, obtained from (−)-**49A** and (+)-**49B**, indicate that the absolute configuration of the γ-carbon in both sultones as well as in both sultines is the same. In conclusion, the authors suggested[113,114] that of the four possibilities shown below, γ-sultines **48A–51A** and **48B–51B** may be assigned the $(R)^C$–$(S)^S$ and $(R)^C$–$(R)^S$ absolute configurations, respectively. Although initiated by mechanistic interest, this study has also resulted in a new method for selective synthesis of

chiral α,β-unsaturated γ-sultines.

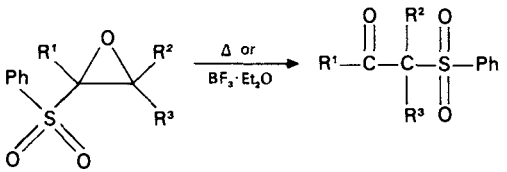


A $(R)^c—(S)^s$ A $(S)^c—(R)^s$ B $(S)^c—(S)^s$ B $(R)^c—(R)^s$

IV. 1,2- AND 1,3-REARRANGEMENTS OF SULFONES

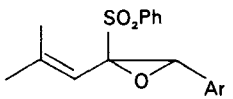
A. 1,2-Sulfonyl Migrations

The thermal and acid catalyzed rearrangements of α,β-epoxy sulfones **53** to β-carbonyl sulfones have been simultaneously reported by Durst[117], and Tavares[118] and their coworkers (equation 40). This 1,2-migration of the sulfonyl group is analogous to the migration of other electronegative groups such as, for example, the 1,2-acyl migration of α,β-epoxyketones[119]. The α,β-epoxysulfones are conveniently prepared by Darzens-type condensation between α-haloalkyl sulfones and carbonyl compounds with[120,121] or without[118,122] phase transfer catalysis. The temperature required for thermal rearrangement varied from less than 25 °C in **53** ($R^2 = R^3 = Ph$) to greater than 130 °C when $R^2 = R^3 =$ alkyl, as expected on the basis of relative stabilities of the intermediate carbenium ions. The rearrangement of sulfonyloxirane **54** takes place during chromatography with silica gel[123], while the rearrangement of sulfonyloxirane **55** was accompanied by desulfonylation to aldehyde **56**[120]. In a recent synthetic application of this rearrangement, Zwanenburg and coworkers[124] treated α-aryl-α-sulfonylacetaldehydes **57**, without being isolated, with various secondary amines to obtain the corresponding β-sulfonylenamines **58**, at room temperature. In another synthetic application a new route to medium-size sulfur-containing rings via a one-carbon ring enlargement was reported[120]. Thus the unsaturated sulfones **59**, which are readily prepared from the corresponding parent cyclic sulfones, alkyllithiums, and benzophenone followed by dehydration, gave directly the expanded β-keto sulfones **60** in greater than 90% yield upon refluxing in chloroform,

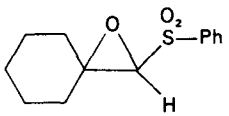


(40)

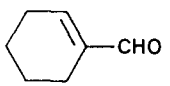
(53)



(54), Ar = $MeOC_6H_4$

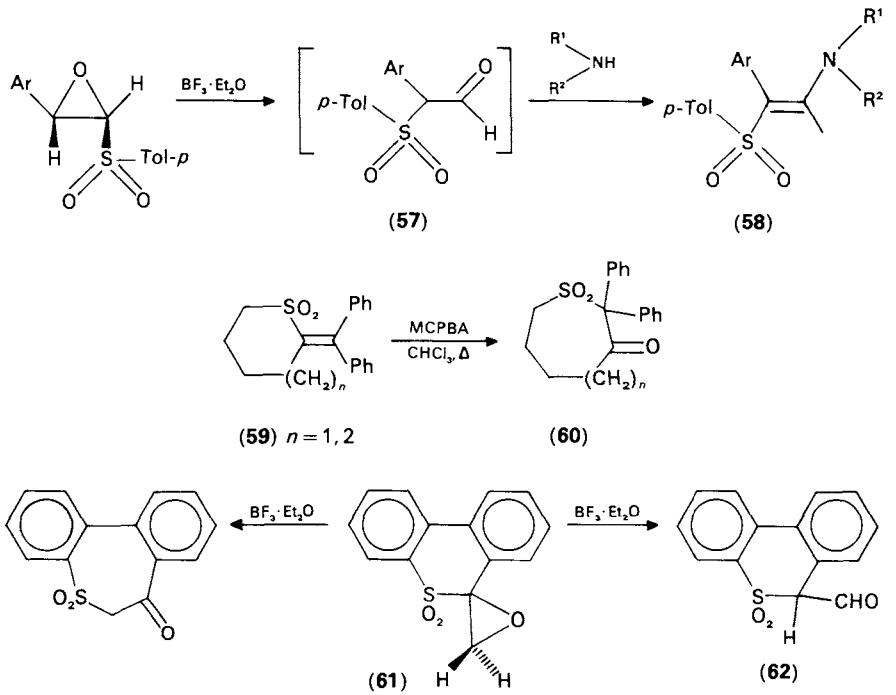


(55)

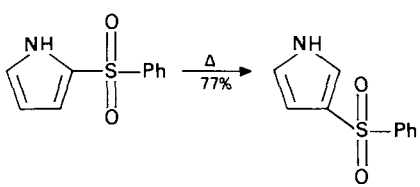


(56)

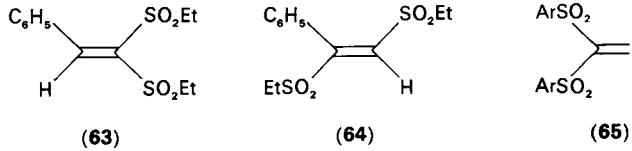
containing *m*-chloroperbenzoic acid. On the other hand, no ring enlargement could be observed in the rearrangement of the spiro sulfonyl oxirane **61**, due to competing hydride shift to aldehyde product **62**[125].



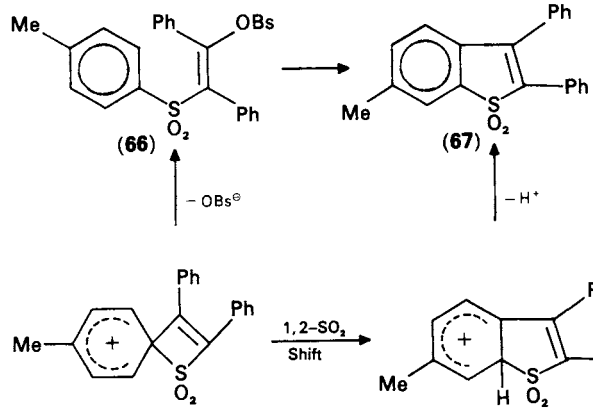
Several other 1,2-sulfonyl shifts have also been reported. For example, 2-arylsulfonylpyrroles rearrange upon heating with methanesulfonic acid in boiling 1,2-dichloroethane to the isomeric 3-arylsulfonylpyrroles (equation 41)[126]. Friedman and Graber[127] have shown that the piperidine-catalyzed Knoevenagel condensation between benzaldehyde and bis(ethylsulfonyl) methane gives not the reported[128] and expected β,β-bis(ethylsulfonyl)styrene (**63**) but stereospecifically rearranged (*E*)-α,β-bis(ethylsulfonyl)styrene (**64**), instead. The mechanism and stereochemistry of this reaction have also been discussed. Subsequently, similar rearrangement have been reported[129–131] including that of 1,1-bis(arylsulfonyl)ethene (**65**) to (*E*)-1,2-bis(arylsulfonyl)ethene[130]. Of special interest appears to be the 1,2-sulfonyl shift observed by Melloni and Modena[132] during the boron trifluoride-catalyzed cyclization of *trans*-1,2-diphenyl-2-arylsulfonylvinyl *p*-bromobenzenesulfonates (**66**) to benzo[*b*]thiophene 1,1-dioxides (**67**), in which the position of the methyl groups with respect to the sulfonyl group was different from that in the starting compound (equation 42).



(41)



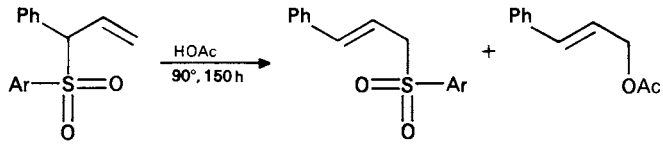
(63) (64) (65)



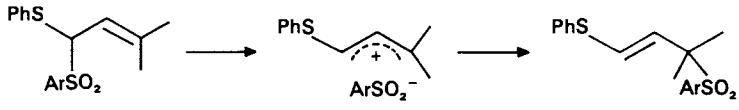
(42)

B. 1,3-Allylic Sulfonyl Migrations

The 1,3-rearrangement of allylic sulfones has received considerable attention due to its synthetic and mechanistic interest. The much cited paper by Cope and coworkers[48] has also been quoted[133] as an early precedent. This rearrangement was experimentally first observed by Darwish and Braverman[50] some ten years later. These authors found that α-phenylallyl 2,6-dimethylphenyl sulfone underwent considerable solvolysis and rearrangement to the corresponding γ-phenyl allyl sulfone, if the reaction solution in which it was formed was heated prolongedly (equation 43). For example, cinnamyl 2,6-dimethylbenzenesulfinate in buffered acetic acid with added sodium acetate, when heated for 150 h (330 half-lives) at 90° gave 15% cinnamyl acetate and a mixture of the two isomeric sulfones, of which 30% was cinnamyl 2,6-dimethylphenyl sulfone. These results seem to indicate an ion-pair mechanism for the observed solvolysis and rearrangement, but no further investigation of this slow thermal process was undertaken by these authors. Subsequently, Mislow and coworkers[134] reported that α-methylallyl *p*-tolyl sulfone rearranged slowly and partially to crotyl *p*-tolyl sulfone on standing at room temperature. Bordwell and Pagani[135] reported that rearrangement of the α-phenylthio substituted sulfone **68** to its allylic isomer **69** occured under mild conditions, methanolysis at 50° or on treatment with silica gel or alumina in benzene or chloroform. An ion-pair mechanism was suggested for this rearrangement also.

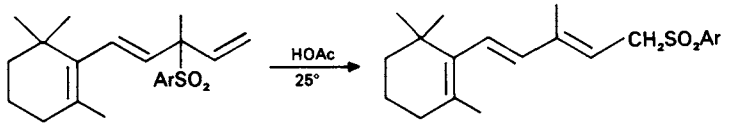


(43)



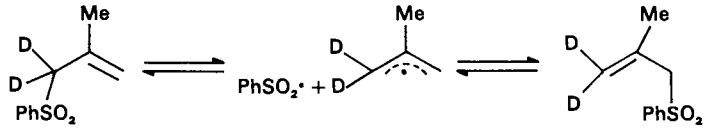
(68) (69)

Recently, a study of this rearrangement has been repeated and extended in order to determine the influence of α- and γ-substitution on the position of the **68**–**69** equilibrium in the presence of silica, and the utility of this reaction for a novel and convenient synthesis of highly substituted α,β-unsaturated ketones, by subsequent treatment with $CuCl_2$ in methanol–water[136]. An ion-pair mechanism can also be suggested for the facile rearrangement of sulfone **70** to **71**, a key intermediate in the Hoffmann–La Roche 'Sulfone Route' to Vitamin A[137].



(70) (71)

More recently, a number of reports dealing with 1,3-sulfonyl shifts which proceed by other mechanisms have been published. For example, Baechler and coworkers[138] suggested that the higher activation enthalpy observed for the isomerization of the deuterium labeled methallyl sulfone **72** in nitrobenzene at 150 °C as compared to the corresponding sulfide, together with the positive entropy of activation may be taken as evidence for a homolytic dissociation mechanism (equation 44). A similar mechanism has also been suggested by Little and coworkers[139] for the gas-phase thermal rearrangement of deuterium labelled allyl *sec*-butyl sulfone, which precedes its pyrolysis to alkene and sulfur dioxide.



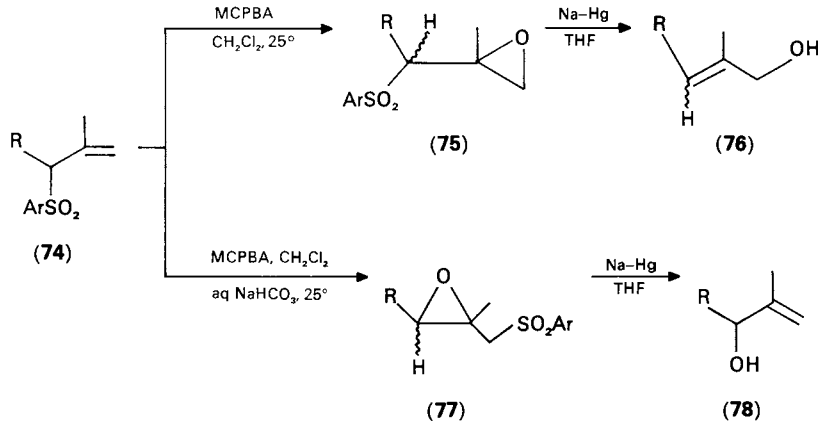
(44)

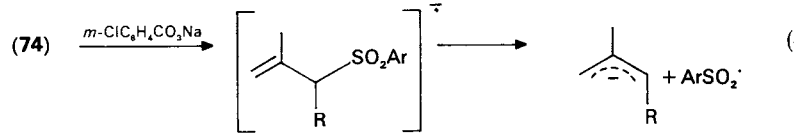
(72) $\Delta H^{\ddagger} = 44.4 \pm 4.2$ kcal mol^{-1} (73)

$\Delta S^{\ddagger} + 20.5 \pm 9.7$ eu

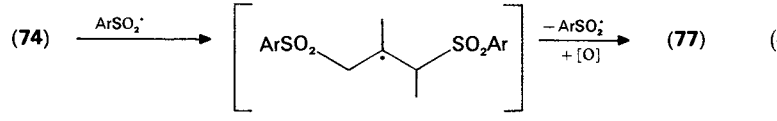
The reductive elimination of a variety of β-substituted sulfones for the preparation of di- and tri-substituted olefins (e.g. **75** to **76**)[140] and the use of allyl sulfones as synthetic equivalents of the allyl dianion $^{-}CH{=}CH{-}CH_2{}^{-}$, has prompted considerable interest in the [1,3]rearrangements of allylic sulfones[141–144]. Kocienski[141] has thus reported that while epoxidation of allylic sulfone **74** with MCPBA in CH_2Cl_2 at room temperature afforded the expected product **75**, epoxidation in the presence of two equivalents of $NaHCO_3$ afforded the isomeric β,γ-epoxysulfone **77**. Similar results were obtained with other α-mono- or di-substituted sulfones. On the other hand, the reaction of γ-substituted allylic sulfones results in the isomerization of the double bond, only. The following addition–elimination free radical chain mechanism has been suggested (equations 45, 46)[141]. In a closely related and simultaneously published investigation, Whitham and coworkers[142,143] reported the 1,3-rearrangement of a number of acyclic and cyclic allylic *p*-tolyl sulfones on treatment with either benzoyl peroxide in CCl_4 under reflux or with

sodium *p*-toluenesulfinate in aqueous acetic acid at 110 °C. Rearrangement is only successful in cases where the product sulfone is thermodynamically more stable than the starting material, e.g. isomerization of α,α-dimethylallyl (**79**) to γ,γ-dimethylallyl sulfone (**80**). A radical chain addition–elimination mechanism involving arenesulfonyl radicals has been proposed (equation 47). The same mechanism was also suggested[143] for the sulfinic acid catalyzed rearrangement of **79** to **80** previously reported by Julia and coworkers[144]. These authors[142,143] have also reported that heavily substituted allylic sulfones such as 1-methyl-2-cyclohexenyl *p*-tolyl sulfone only rearranged sluggishly under the benzoyl peroxide catalytic conditions, but underwent smooth allylic isomerization on being heated in 60% ACOH–H_2O at 110 °C, by an ion-pair dissociation–recombination mechanism. In an extension of these studies, the radical induced cyclization of some unsaturated allylic sulfones has also been reported[144]. A facile and efficient 1, 3-rearrangement of allylic sulfones catalyzed by $Pd(PPh_3)_4$ and its application to the synthesis of α,β-unsaturated ketones has also been reported[145,146]. The reaction is believed to involve a π-allyl complex[144,147] between the substrate and the palladium (0) catalyst.

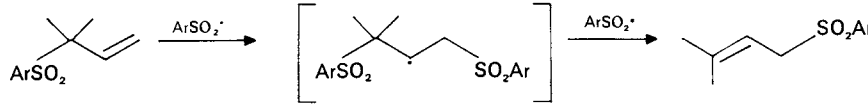




(45)

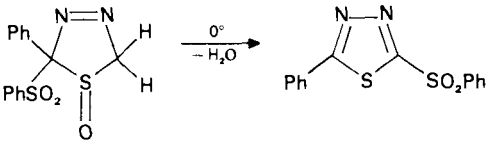


(46)



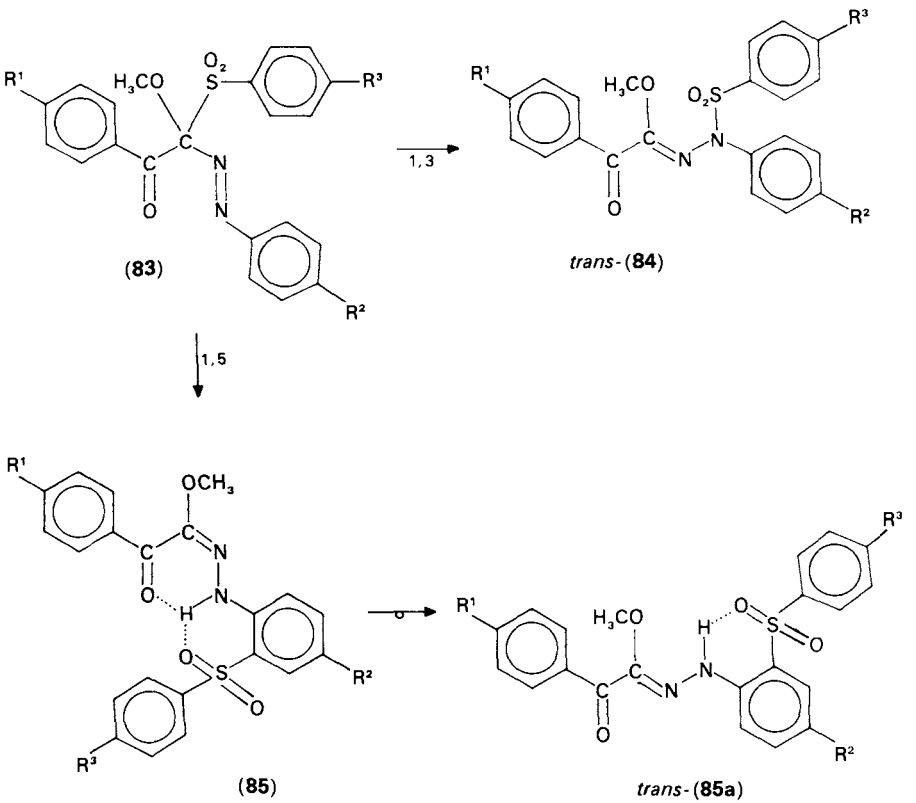
(47)

Zwanenburg and Wagenaar[148] have reported the rather unusual rearrangement of sulfone **81** to **82**, after standing overnight at 0°, and suggested an elimination–addition mechanism, via initial isomerization of Δ^3 to the Δ^2-thiazoline-oxide with subsequent elimination and readdition of sulfinic acid, followed by spontaneous loss of water in a Pummerer-type aromatization reaction.



(**81**) (**82**)

An interesting 1,3- and 1,5-heteroallylic sulfonyl migration has been observed by Jeblick and Schank[149,150]. For example, azasulfone **83** undergoes facile isomerization on heating in inert solvents. Sulfonamide **84** is the product of a formal 1,3-shift of the sulfonyl group. Simultaneously, *cis*-hydrazone **85**, produced by a corresponding 1,5-shift, is obtained and is isomerized in turn to the thermodynamically more stable *trans*-hydrazone **85a**, at slightly elevated temperatures. An ionic mechanism has been suggested by the authors.

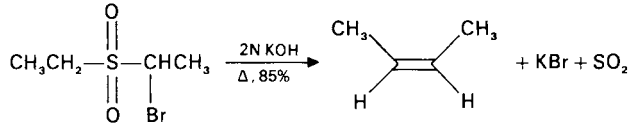


(**83**) *trans*-(**84**)

(**85**) *trans*-(**85a**)

V. THE RAMBERG–BÄCKLUND REARRANGEMENT

One of the most important reactions of sulfones in general is the Ramberg–Bäcklund rearrangement, which involves the conversion of α-halosulfones to olefins with accompanying loss of hydrogen halide and sulfur dioxide under basic conditions (equation 48)[151].

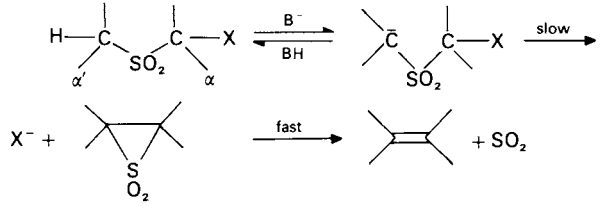


(48)

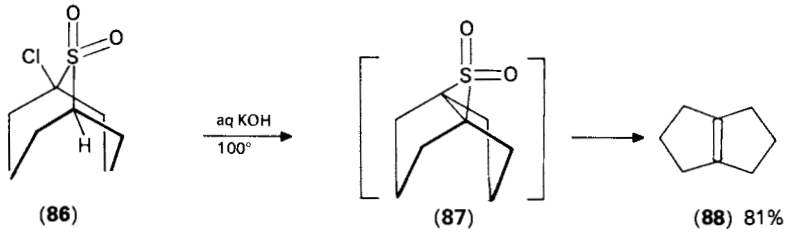
This process has received extensive attention in the past because of its considerable synthetic utility and mechanistic interest, and a number of excellent reviews by some leading contributors in the field such as Bordwell, Paquette and Meyers have been published during the last two decades[15–18,152–154]. Consequently, only the main features of this rearrangement and some of its latest developments are presented below.

A. Mechanism

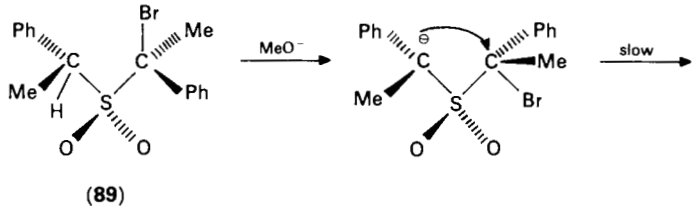
The general mechanism of the Ramberg–Bäcklund rearrangement is shown in equation 49. Kinetic investigations of the rearrangement of various α-halosulfones indicate that the reaction is second-order, first-order in both hydroxide ion and substrate[155–157]. Complete hydrogen–deuterium exchange at both α and α′ positions was found for the reaction of α-bromobenzyl benzyl sulfone with sodium methoxide in methanol-OD after one half-life[156]. This result suggests an initial rapid pre-equilibrium between the halosulfone and its anion. The unusually large leaving group effect observed with $PhCH_2SO_2CHXPh$, a Br:Cl rate ratio[156] of 620 at 0 °C, as well as the positive ρ values[158] for rearrangement of various $ArCHXSO_2CH_3$, provide supporting evidence that the second step involving the 1,3-displacement of halide ion and formation of the episulfone is rate determining. While no episulfone intermediate can be isolated under the usual reaction conditions, the availability of both symmetrical and asymmetrical episulfones by alternative methods[159] has established their stereospecific decomposition by chelotropic sulfur-dioxide extrusion[160–162]. The stereochemistry of the alkene product is therefore established during the second reaction step. Further stereochemical studies with both cyclic (equation 50)[162–164] as well as acyclic (equation 51)[165,166] α-halosulfones have established the high degree of stereoselectivity of this step involving inversion of configuration at both α and α′ reaction centers. Thus, the bridgehead α-halosulfone **86** with its W-geometry of α-Cl and α-H readily undergoes rearrangement under normal conditions, while the *erythro*-α-bromosulfone **89** gives stereoselectively the *cis*-stilbene derivative **90**. However, no support could be obtained in favor of a concerted mechanism for the 1,3-elimination reaction, since in the cases studied the $\Delta S^{\ddagger}$ terms have been positive, and since no rate enhancement could be observed in the rearrangement of α-bromosulfone **91** to acenaphthylene (**92**), in spite of the easily attained coplanar W-geometry of the H—C—SO_2—C—Br atoms in this substrate[167].

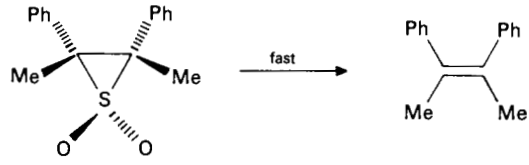


(49)

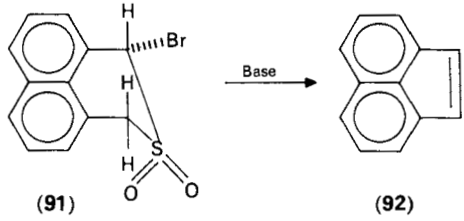


(50)

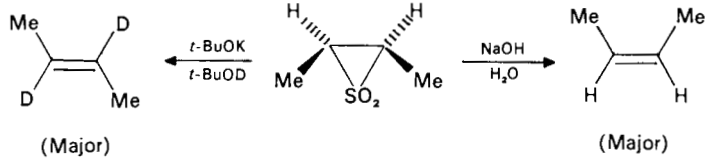




(51)



Finally, the most significant mechanistic feature of the Ramberg–Bäcklund rearrangement is the stereoselective formation of *cis*-olefin products, as a result of the preferential *cis*-positioning of the pair of *R* groups in the episulfone-forming transition state, variously attributed to London forces[168], to diastereoselectivity in carbanion formation[17,157,166], and to steric attraction[168]. However, with the use of stronger bases such as potassium *t*-butoxide[160], the *trans*-olefin predominates (equation 52), apparently due to prior epimerization of the kinetically favoured *cis*-episulfone, and subsequent loss of the sulfur dioxide. Similarly, when the episulfone intermediates possess unusually acidic

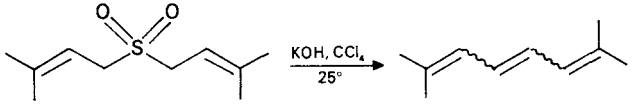


(52)

α-sulfonyl protons, isomerization to the *trans*-isomer will generally occur even with weaker base systems. Thus, benzyl α-chlorobenzyl sulfone is converted exclusively into *trans*-stilbene with sodium hydroxide in aqueous dioxane.

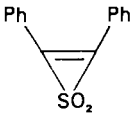
The preparation of α-halosulfones can be achieved by a variety of methods[18]. However, a useful development of the Ramberg–Bäcklund rearrangement that avoids the need to prepare the α-halosulfone in a separate step, is to treat a sulfone possessing both α- and α′-hydrogens with potassium hydroxide in carbon tetrachloride, which serves as the halogen source for *in situ* sulfone chlorination. The convenience of this method discovered by Meyers and coworkers[169] is sometimes offset by side-reactions due to polychlorination or dichlorocarbene addition to the generated olefin. For example, while dicyclohexyl sulfone gives dicyclohexylidene in 32% yield[169], benzhydryl sulfones react rapidly and quantitatively at room temperature or below, to give 1, 1-diarylalkenes (equation 53)[170]. Similarly, bis-allylic sulfones are also well-suited for this 'one-flask' olefin synthesis (equation 54)[72,85] with certain exceptions, such as di-β-retinyl sulfone. Conversion of the latter to β-carotene could, however, be achieved by treatment with butyllithium, and iodine or bromine[85]. On the other hand, di-*sec*-alkyl sulfones are converted into 1,1-dichlorocyclopropane derivatives by addition of dichlorocarbene to the initial products, while di-*n*-alkyl sulfones are transformed into *cis*-1,2-dialkylethenesulfonic acids, through dihalosulfone, and thiirene 1,1-dioxide intermediates[171–173]. Interestingly, while episulfones cannot usually be isolated from Ramberg–Bäcklund reactions because of the facility with which they lose SO_2, the thermally more stable thiirene 1,1-dioxides have been isolated from the reaction of α,α′-dihalosulfone with base (equation 55)[174]. However, a similar treatment of *bis*-α-bromophenacyl sulfone failed to give the corresponding thiirene 1,1-dioxide (**93**) and resulted in the formation of the 1,3-oxathiole 3,3-dioxide derivative **94**, which upon reduction with triphenylphosphine in refluxing methanol followed by alkaline cleavage was transformed to 5-phenyl-1,3-oxathiole 3,3-dioxide (**95**)[175]. These results are in agreement with a previous preparation of (**95**) from the reaction of chloromethyl phenacyl sulfone with base[176]. Reaction via enolate ions in these cases seems to compete with the normal Ramberg–Bäcklund rearrangement. 2, 3-Diarylthiirene 1,1-dioxides have also been isolated from the triethylenediamine-induced rearrangement of benzyl α, α-dichlorobenzyl sulfone, and undergo thermal decomposition to diarylacetylenes both in greater than 90% yield[177]. In addition to α,β-unsaturated sulfonic acids and acetylenes, vinyl chlorides are also likely products of the Ramberg–Bäcklund rearrangement of α,α- and α,α′-dihalosulfones. The nature of the products formed depends upon the structure of the sulfone and reaction conditions[18]. The formation of sulfonic acids as major products has also been observed in the rearrangement of α,α,α-trichloromethyl sulfones under normal conditions[18].

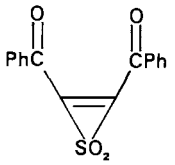
$$Ph_2CHSO_2CHMe_2 \xrightarrow[t\text{-BuOH}]{KOH,\ CCl_4} Ph_2C{=}CMe_2 \quad 100\% \qquad (53)$$



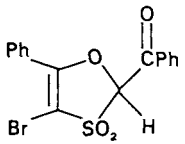
(54)

$$PhCHBrSO_2CHBrPh \xrightarrow[CH_2Cl_2]{Et_3N} \qquad (55)$$

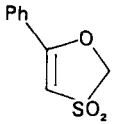




(93)



(94)

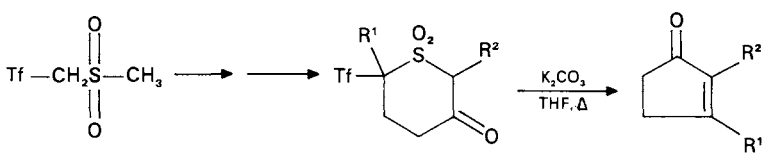


(95)

In recent years a number of modifications and extensions of the original Ramberg–Bäcklund reaction have been described. For example, Hartman and Hartman[178] have found that α-halosulfones readily undergo the Ramberg–Bäcklund rearrangement at room temperature under phase transfer catalysis conditions to afford olefinic products in good to excellent yields (equation 56). Substitution of halogens by other leaving groups in the starting materials has also been investigated. For example, Meyers and coworkers[179] have reported that, unexpectedly, a rate ratio for k_{OTs}/k_{Cl} of 0.0011 was observed in 1, 3-eliminations of (tosyloxy)methyl benzyl sulfone and chloromethyl benzyl sulfone in *t*-BuOK/*t*-BuOH at 25 °C. On the other hand, Hendrickson and coworkers[180] have found that the trifluoromethanesulfinate(triflinate) anion can be used as an efficient leaving group. These authors have also suggested the use of α-trifyl dimethyl sulfone (**96**) as a reagent which allows successive polyalkylation of the two carbons with regio control. Subsequent Ramberg–Bäcklund rearrangement of the product with loss of triflinate anion and extrusion of sulfur dioxide affords a new general olefin synthesis. This method has been successfully applied to the synthesis of several natural products, including dihydrojasmone (**97**, equation 57)[181]. In a related study β-ketosulfones have been found to form dianions and are alkylated at both α- and α′-sulfonyl positions. Brominating cleavage gives α-bromosulfones which, by Ramberg–Bäcklund rearrangement, form olefins[182,183]. The synthesis of the sex pheromone of the Mediterranean Fruit Fly (6-nonen-1-ol), starting from 2-(methylsulfonyl)cyclohexanone, has also been described[182].

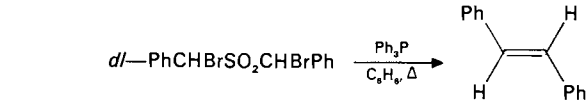
$$PhCH_2SO_2CH_2Cl \xrightarrow[\text{Aliquat}-336,\ 25°,\ 90\,\text{min}]{10\%\ NaOH/CH_2Cl_2} PhCH{=}CH_2 \qquad (56)$$

82%



(96) $Tf = CF_3SO_2$ (97) $R^1 = C_5H_{11}$, $R^2 = Me$ (57)

In another variation of the Ramberg–Bäcklund rearrangement the 1, 3-elimination reaction is induced by nucleophilic attack on halogen, rather than induced by base. This reaction is also highly stereoselective and inversion at both reaction sites has been observed[184,185]. For example, reaction of *dl*-α-bromobenzyl sulfone with triphenylphosphine in refluxing benzene gave 96% of *trans*-stilbene, whereas the corresponding *meso* isomer gave 95% of *cis*-stilbene under comparable conditions (equation 58). Similarly, the synthesis of 2, 3-dialkylthiirene 1, 1-dioxides via debromination of *bis*-α, α-dibromoalkyl sulfones by means of trisubstituted phosphines has been reported[186].

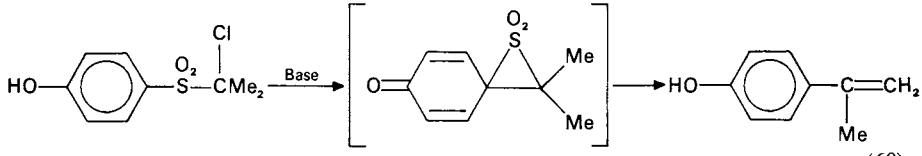


96% (58)

In one of its early extensions, the vinylogous equivalent of the Ramberg–Bäcklund rearrangement, *cis*- or *trans*-2-bromo-3-pentenyl benzyl sulfone was converted into 1-phenyl-2-methyl-1,3-pentadiene[187]. More recently, Block and coworkers[188,189] have described a complementary version of the preceding vinylogous or 1,5-Ramberg–Bäcklund rearrangement, whereby α,β-unsaturated bromomethyl sulfones are converted into 1,3-dienes with base. Since these sulfones can be made from olefins by addition of readily accessible bromomethanesulfonyl bromide followed by dehydrobromination, the overall process is a three-step transformation of olefins into 1,3-dienes bearing one more carbon atom (equation 59). An energetically unfavorable 1,7-Ramberg–Bäcklund rearrangement has also been observed when *p*-hydroxyphenyl α-haloalkyl sulfones were heated with one equivalent of base (equation 60)[190].

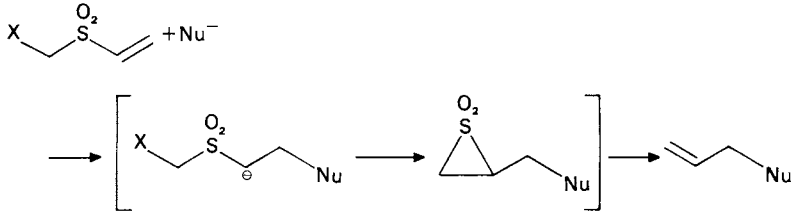
$$RCH_2CH{=}CH_2 + BrCH_2SO_2Br \xrightarrow[30\text{min},\,-20^\circ]{h\nu,CH_2Cl_2} RCH_2CHBrCH_2SO_2CH_2Br$$

$$\xrightarrow[0^\circ]{Et_3N} RCH_2CH{=}CHSO_2CH_2Br \xrightarrow[-20^\circ]{t\text{-BuOK}} RCH{=}CH{-}CH{=}CH_2 \qquad (59)$$



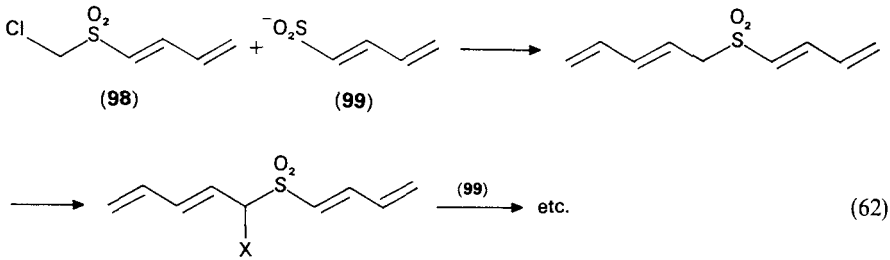
(60)

An attractive alternative of the Ramberg–Bäcklund procedure which circumvents the need of a strong base for the formation of the α-sulfonyl carbanion intermediate, involves addition of a suitable nucleophile to α-haloalkyl sulfones carrying a Michael acceptor system attached to the α′ position (equation 61)[191]. Furthermore, since vinyl sulfones are known to be excellent Michael acceptors, and sulfinate anions are good nucleophiles, the reaction of halomethyl vinyl or dienyl sulfones with sulfinate anions can be expected to unite two chain extension methods in one operation. The authors have named this approach the Michael induced Ramberg–Bäcklund (MIRB) synthesis. A convenient step-by-step polyene synthesis, using this approach and extending the chain with four carbon atoms at a time, is shown in equation 62[191]. Further applications of the MIRB-synthesis in terpenoid[192], isoprenoid[193] and other linear polyene synthesis[194] have been published.

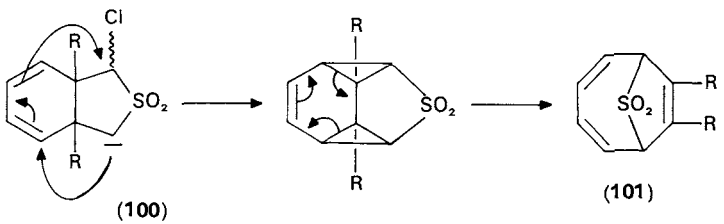


(61)

Finally, an electrochemical reduction of bis-α-bromobenzyl sulfone to stilbene[195] and a spectacular, so-called bis-homoconjugative, version of the Ramberg–Bäcklund reaction, which converts the α-chlorosulfone **100** into the bridged cyclooctatriene derivative **101** (equation 63)[196,197], have also been published.



(62)

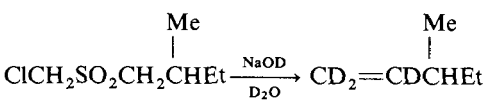


(63)

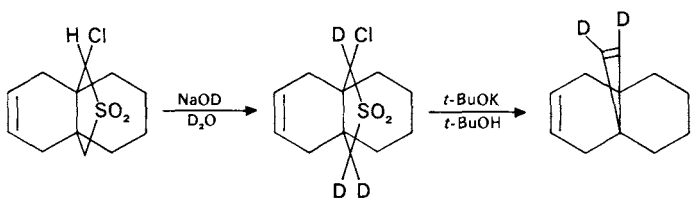
B. Synthetic Utility

The Ramberg–Bäcklund rearrangement represents one of the first alkene syntheses in which the position of the double bond is clearly defined. The synthetic potential of this reaction has been widely exploited in the past[15–18]. As pointed out by Paquette[18], the Ramberg–Bäcklund rearrangement of α-halosulfones can be advantageous in five broad chemical schemes. They involve (a) the coupling of two residues through a sulfide linkage with subsequent introduction of the double bond, (b) conversion of mercaptans into homologous terminal alkenes through chloromethylation, (c) homologation of olefins through H_2S addition to terminal mercaptans, (d) synthesis of olefins deuteriated exclusively at the vinyl position and (e) preparation of various strained cycloalkenes.

Two examples of this method for the synthesis of olefins deuteriated exclusively at the vinyl position by the simple use of deuteriated solvents are shown in equations 64[198] and 65[199]. Due to the alkaline reaction conditions no subsequent isomerization of the initially produced alkene is observed.

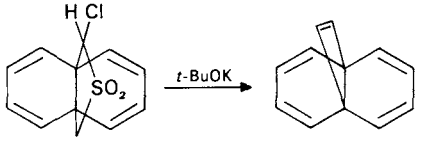


(64)

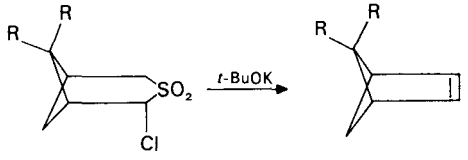


(65)

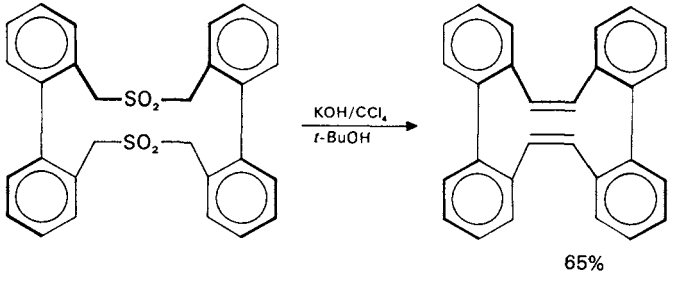
Two illustrations that show the power of this reaction for the preparation of strained cycloalkenes are the contractions of **102** to the propellane **103**[200], an application that has been reviewed[201,202], and of **104** to the bicyclo[2.1.1]hexene **105**[203]. The utility of the Ramberg–Bäcklund rearrangement in the preparation of various natural products such as steroids[204], terpenoids[192,193] and pheromones[182] has been demonstrated. In addition to the synthetic applications mentioned in the previous subsection, several selected examples taken from the recent literature[205–215] are given in equations 66–69. These examples further demonstrate the potential of this method for alkene synthesis in general.



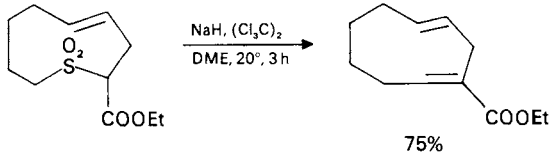
(**102**) (**103**)



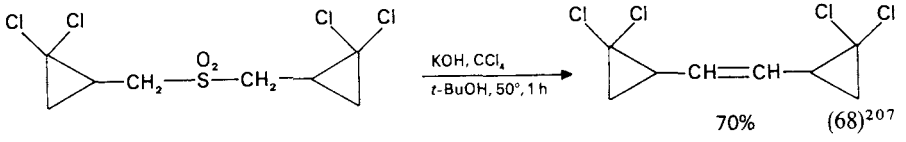
(**104**) R = H, Me (**105**)



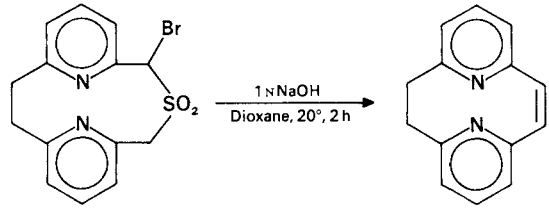
(66)[205]



(67)[206]



(68)[207]

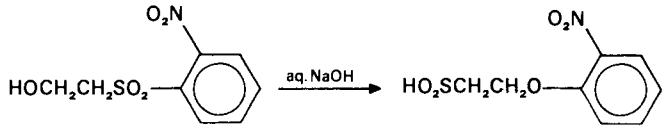


(69)[208]

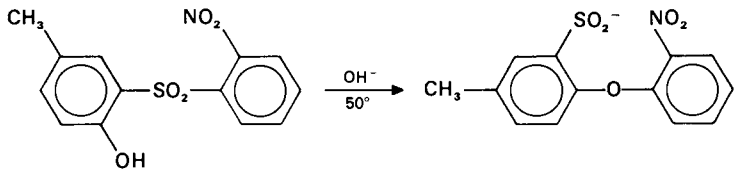
VI. THE SMILES AND RELATED REARRANGEMENTS

A. The Smiles Rearrangement

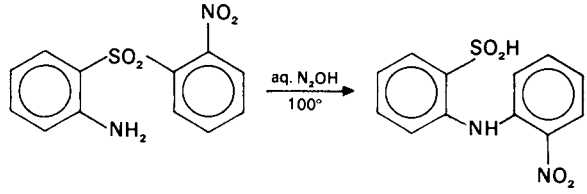
The Smiles rearrangement is one of the oldest and best studied rearrangements of sulfones. Although first reported by Henrique[216] and by Hinsberg[217–219], the rearrangement is named after Smiles[220–232], who has not only established the correct structures of the products, but also recognized the occurrence of a novel rearrangement and developed its chemistry. The rearrangement involves the isomerization of a sulfone to a sulfinic acid, and can be described as an intramolecular aromatic substitution of a sulfonyl group initiated by a nucleophilic group attached to the sulfonyl group through two atoms, which may also be part of an aromatic system. Several typical examples of this rearrangement, which is usually catalyzed by base, are given below (equations 70–73).



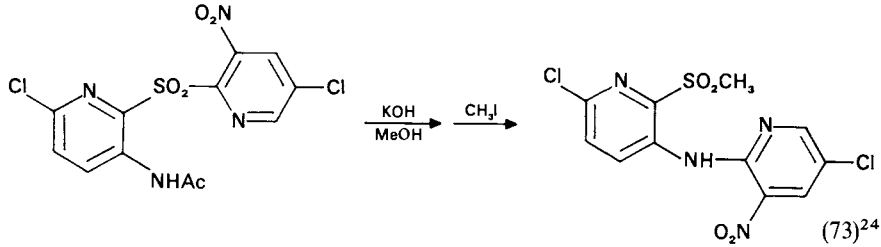
(70)[225]



(71)[231]



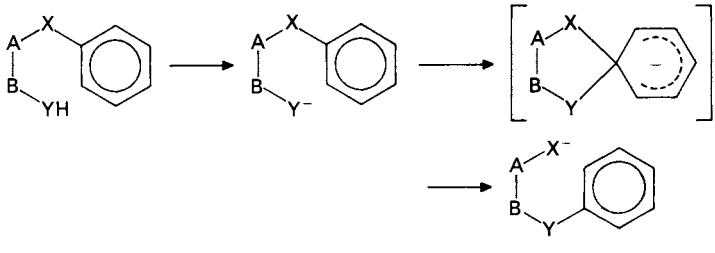
(72)[226]



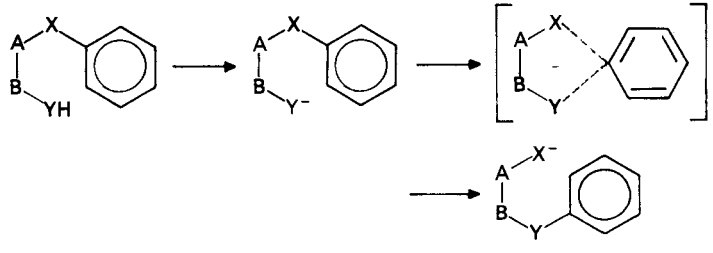
(73)[245]

Although diaryl and alkyl aryl sulfones are the most common types of compounds to undergo the Smiles rearrangement, several other substrates, such as sulfoxides[224,225], sulfides[226], ethers[233,234], sulfonamides[235], carboxylic and sulfonic esters[236], iodonium compounds[237] and phosphonium compounds[238] have also been found to undergo analogous rearrangements. The nucleophilic center in the Smiles rearrangement is usually a heteroatom such as oxygen, nitrogen or sulfur, while in the Truce–Smiles modification it may also be a carbanion. If one or both aromatic rings are pyridine, the rearrangement may also be catalyzed by acid[239]. Because of the considerable interest in the Smiles rearrangement, several excellent and comprehensive reviews have also been published in the past[19,240–242]. Therefore, a relatively brief survey of the main features of this rearrangement is presented below.

There are two mechanisms which have been suggested for this rearrangement (equations 74 and 75)[19,241].



(74)



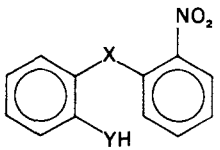
(75)

In the first mechanism (equation 74) the nucleophile function attacks the aromatic ring in an *ipso*-type displacement involving a Meisenheimer complex intermediate[243,244], and leads to the rearranged product after expulsion of sulfinate anion (X^-). This mechanism should be favoured by the presence of an electron-withdrawing substituent in conjugation with the anion. The second mechanism (equation 75) involves a direct displacement of sulfinate anion (X^-) by Y^-, without involvement of the aromatic π electrons.

The scope and limitations of the Smiles rearrangement are usually discussed in terms of several different factors: activation of the aromatic ring, nucleophilic strength of the entering group Y^-, acidity of the YH function and, in the case of diaryl sulfones, substitution in the ring connecting X and YH is also an important factor which influences this rearrangement.

The presence of an electron-withdrawing group in the migrating aromatic group is normally required for rearrangement to occur. An *o*- or *p*-nitro group is commonly used for activation, but a *p*-sulfonyl group may also be effective under more vigorous conditions[221]. Substituents which have not been successful in promoting rearrangement include *o*-hydroxyl[223], *o*-carboxyl[224] and *m*-nitro[225] groups. The only exception, where no activation of the migrating aromatic ring is necessary is when the nucleophile is a carbanion ($YH = CH_3$)[246].

An obvious relationship exists between the acidity of YH and the nucleophilicity of Y^-, which are also directly affected by the substitution pattern on the ring attached to them. Similarly the nature of YH and how substituents on Y (when Y = NH) can influence the acidity and nucleophilicity of this group have also been investigated[226,227,240]. Thus, when the series of N-substituted *o*-aminosulfones **106** was subjected to hot aqueous sodium hydroxide, the amino and acetamido derivatives rearranged rapidly, the benzenesulfonamido derivative rearranged slowly and the methylamino derivative required more concentrated alkali[226,227]. The low reactivity of the last two functions may be explained by the low nucleophilicity of the anion produced from the $NHSO_2Ph$ group, on the one hand, and the low acidity of the $NHCH_3$ group, on the other.



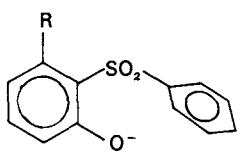
$X = SO_2$

$YH = NH_2$, $NHCH_3$, NHAc, $NHSO_2Ph$

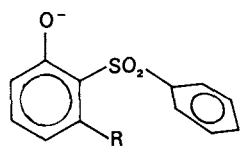
(106)

The electronic effects of substituents in the aromatic ring connecting X and YH (**106**) have also been investigated, but are more complex than those in the ring sustaining the nucleophilic attack[19,240]. An electron-withdrawing substituent will, by induction or resonance, stabilize the anion Y^-, therefore making YH more acidic. Similarly, it will also stabilize the developing negative charge on the sulfinate leaving group, thus promoting rearrangement. Obviously, the relative importance of these two effects will depend upon the nature of Y and the position of the substituent on the ring. For example, the following order of reactivity has been observed for the rearrangement of 2-hydroxy-2′-nitrodiphenyl sulfone: 5-chloro > 5-hydroxy > 5-methyl > 4-hydroxy[226].

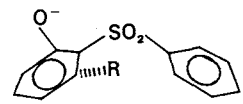
In addition to electronic effects, steric effects due to substituents may also be significant in the Smiles rearrangement. McClement and Smiles[247] first observed that 2-hydroxy-2′-nitrodiphenyl sulfones bearing a methyl group in the 6-position rearranged much faster than the corresponding unsubstituted compounds. Although originally attributed to an inductive effect, it was subsequently suggested[240] and clearly demonstrated[248,249] by Bunnett and coworkers that this is, in fact, a steric effect. According to these authors the steric acceleration can be explained in terms of a conformational equilibrium between the three extreme conformations **107**–**109**, the first of which is required for rearrangement. If R is hydrogen and an *o*′-substituent is also present, the preferred conformation will be **108**. However, if R is larger than hydrogen the relative amount of conformation **108** and **109** will be decreased, thus increasing the population of **107**. As a result the ground state of the system will be raised and the free energy barriers to rearrangement will be lowered.



(107)



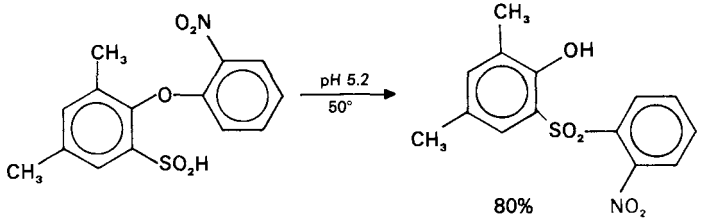
(108)



(109)

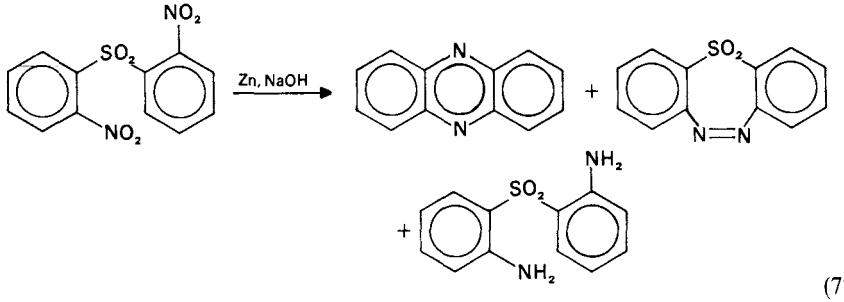
Coats and Gibson[250] have reported that sulfinic acids obtained from the rearrangement of *o*-hydroxy sulfones can be reconverted to the original sulfones. This reaction, which has been designated as the reverse Smiles rearrangement, took place readily when the sulfinic

acids were buffered in solution to a pH at which the sulfinic acid but not the product phenol was in the ionized form (equation 76).



(76)

In reducing media, a synthetically useful variation of the Smiles rearrangement, which leads to the formation of fused ring systems, has been observed (equation 77)[251]. In this reaction, rearrangement is followed by displacement of the sulfinate anion by a nucleophilic *o'*-substituent.



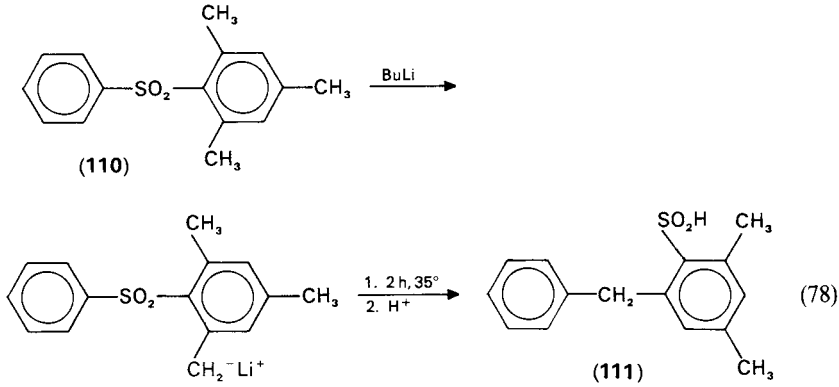
(77)

B. The Truce–Smiles Rearrangement

1. Diaryl sulfones

Directed lithiation of aromatic compounds is a reaction of broad scope and considerable synthetic utility[252]. The metalation of arenesulfonyl systems was first observed by Gilman and Webb[253] and by Truce and Amos[254], who reported that diphenyl sulfone is easily metalated at an *ortho*-position by butyllithium. Subsequently, in 1958, Truce and coworkers[246] discovered that metalation of mesityl phenyl sulfone (**110**) occurred entirely at an *ortho*-methyl group and not at a ring carbon, as expected. Furthermore, refluxing an ether solution of the lithiated species resulted in a novel and unusual variation of the Smiles rearrangement and formation of 2-benzyl-4, 6-dimethylbenzenesulfinic acid (**111**) in almost quatitative yield (equation 78). Several other *o*-methyl diaryl sulfones have also been shown to rearrange to *o*-benzylbenzenesulfinic acids when heated in ether solution with BuLi[255–257].

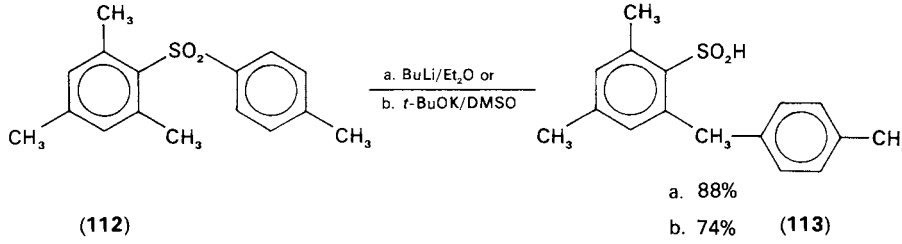
This rearrangement, commonly referred to as the Truce–Smiles rearrangement, is analogous to the Smiles rearrangement with two important differences: (a) while the nucleophilic center in the classical Smiles rearrangement is a heteroatom such as oxygen, nitrogen or sulfur, in the Truce–Smiles modification it is a carbanionoid unit; (b) in contrast with the Smiles rearrangement, no activating substituent such as *o*- or *p*-nitro in the migrating aryl group is needed in a metalated diaryl sulfone. This rearrangement has received considerable attention not only because of its mechanistic interest but also because of synthetic utility for the preparation of various substituted diarylmethanes. Two

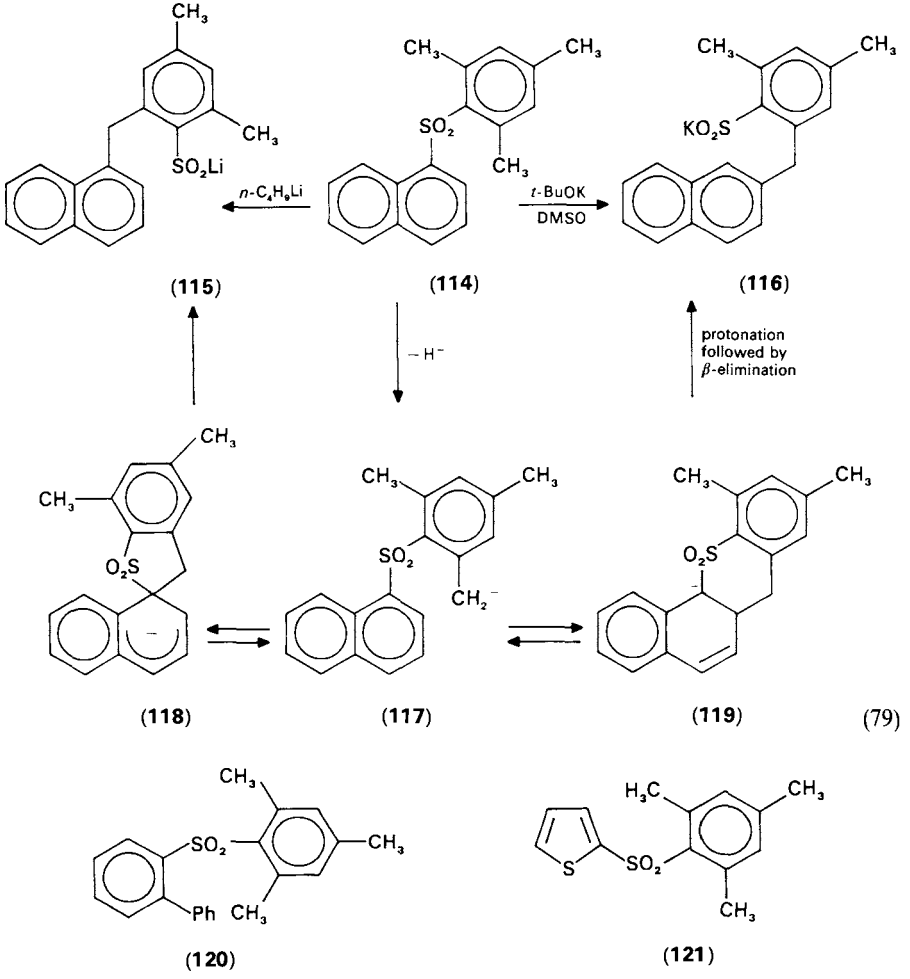


excellent and comprehensive reviews have been published by Truce[258] and by Drozd[20]. Therefore, only the fundamental principles and a selection of the latest developments is presented below.

One of the most investigated features is the influence of reaction conditions on the change in orientation of the migrating aryl group during rearrangement. For example, Truce and coworkers[259,260] have shown that treatment of mesityl *p*-tolyl sulfone (**112**) with either butyllithium in ether, or potassium *t*-butoxide in DMSO, gives the same product, the *o*-benzylbenzenesulfinic acid derivative **113**, in which the *p*-tolyl group has retained its original *p*-orientation. On the other hand, in the reaction of α-naphthyl mesityl sulfone (**114**) butyllithium in ether and potassium *t*-butoxide in DMSO lead to different products. The former gives the 'normal' Truce–Smiles product lithium 2-(1′-naphthylmethyl)-4, 6-dimethylbenzenesulfinate (**115**) but with the later, the product is the isomeric sulfinate **116**, wherein the migrating unit has undergone a change of orientation to β-naphthyl. Other aryl systems have also been shown to rearrange with a change in orientation. For example, mesityl 2-biphenylyl sulfone (**120**)[261] reacts in complete analogy with sulfone **114** to give a 'normal' Truce–Smiles product with BuLi in ether, and product of altered orientation (3-biphenyl) with potassium *t*-butoxide in DMSO, while mesityl 2-thienyl sulfone (**121**)[262] yields a product of altered orientation (3-thienyl), with both types of base/solvent systems employed.

Mechanistically, these results have been rationalized[20,258] by invoking two competing pathways, as shown in equation 79. The 'normal' Truce–Smiles rearrangement may involve intramolecular attack by the carbanion center in **117** at the *ipso*-position of the migrating aryl group with the formation of a Meisenheimer type intermediate **118**, or transition state of similar structure, followed by expulsion of sulfinate anion. This type of rearrangement with retained orientation for the migrating aryl group has also been referred to as 'direct displacement'[258]. On the other hand, an 'addition–elimination sequence' has been suggested for the rearrangement with a change of orientation. In

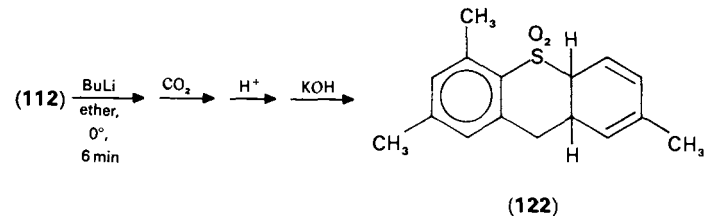




this route, rearrangement is initiated by internal Michael addition (**119**), followed by β-elimination to yield the product of altered orientation **116**.

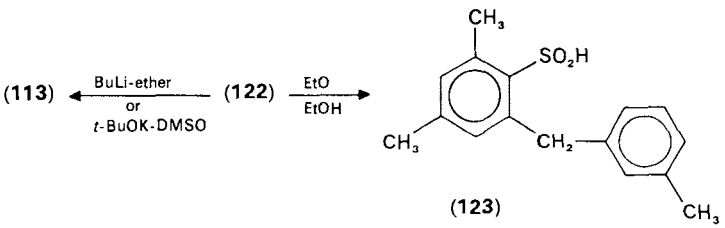
Of all cases studied, rearrangement through the direct displacement route is most common. The observation of the alternate rearrangement with certain aryl sulfones reflects their greater tendency to undergo reactions of addition as evidenced by the Michael addition of butyllithium to the α,β-bond of α-naphthyl *t*-butyl sulfone[263]. Interestingly, considerable evidence exists which indicates that the equilibria presented in equation 79 (i.e. **118**⇌**117**⇌**119**) are not limited to those substrates which react by both the normal and abnormal Truce–Smiles rearrangements, but may also include those substrates which react by the direct displacement mechanism only. This was originally postulated and observed by Drozd and coworkers[264–271] who have shown that it is possible to trap the internal Michael adducts with either carbon dioxide or protic acids. For example, treatment of mesityl *p*-tolyl sulfone (**112**) with butyllithium at 0 °C for a few minutes, followed by rapid quenching with CO_2 and subsequent decarboxylation with 10% KOH

solution, afforded the cyclized product 2, 5, 7-trimethyl-4a, 9a-dihydrothioxanthene 10, 10-dioxide (**122**, equation 80)[260,267,269]. Furthermore, this product could be caused to rearrange to **113** by treatment with butyllithium in ether, or to its *m*-isomer 2-(3′-methylbenzyl)-4, 6-dimethylbenzenesulfinic acid (**123**) by treatment with sodium ethoxide in ethanol (equation 81)[272]. Apparently metalation alpha to the sulfonyl group is followed by ring opening to metalated **112** which undergoes *ipso*-substitution and formation of the normal Truce–Smiles rearrangement product (**113**). On the other hand, in the alkoxide bases the cyclic sulfone **122** undergoes β-elimination to give the isomeric sulfinic acid **123**, which is formally the product of rearrangement via the addition–elimination sequence described above (equation 79). A facile conversion of the dihydrothioxanthene 10, 10-dioxides to the corresponding thioxanthene 10, 10-dioxides has also been reported[262].



(80)

(122)



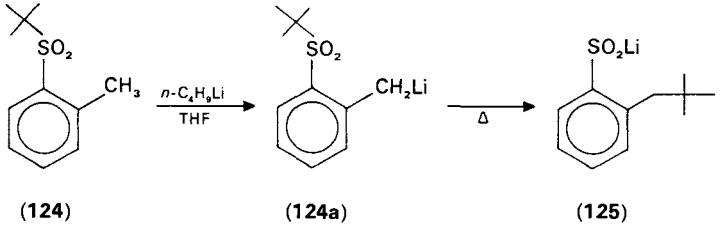
(81)

(123)

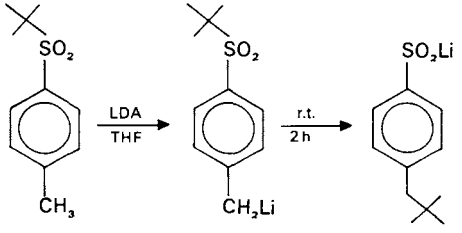
The groups of Truce and of Drozd have also investigated the factors affecting reactivity and orientation in the Truce–Smiles rearrangement. For example, a kinetic study for a variety of metalated sulfones has shown that the reaction was first-order in metalated sulfones, where the rate of initial metalation was very high. In addition, sulfones with a methyl substituent at the 6-position of the ring containing the *o*-lithiomethyl substituent were found to react one order of magnitude faster than those with an open 6-position[256–273]. The interpretation of this accelerating effect is similar to that suggested for the Smiles rearrangement (see the previous subsection)[249,250]. These authors have also observed an additional dependence of the rate of rearrangement by 'direct displacement' upon the proportion of cyclic (e.g. **119**) vs. noncyclic (e.g. **117**) carbanion. Thus, metalated sulfones which exist almost entirely in the cyclic form, such as α-naphthyl mesityl sulfone (**114**), rearrange slowly[259,270] under direct displacement conditions. On the other hand, *o*-benzyl diphenyl sulfone, for which a cyclic species is not observed, readily undergoes rearrangement to the expected Truce–Smiles product[274]. Other factors affecting reactivity in the Truce–Smiles rearrangement which have been studied include: (a) the effect of electron-withdrawing substituents in the migrating ring on competing metalation of the aromatic[254,275] ring or simple nucleophilic aromatic substitution at the position occupied by that substituent[276]; (b) the effect of substitution of the *ortho*-methyl hydrogens on their acidity relative to the ring hydrogens[277–279]. The effect of alkyl substitution on the migrating ring on the nature of the cyclic species formed by metalation and subsequent internal Michael addition has also been investigated[272,280,281].

2. Alkyl aryl sulfones

One of the most recent and interesting extensions of the Truce–Smiles rearrangement is the analogous rearrangement of aryl *t*-alkyl sulfones. For example, Snyder and Truce[282] reported facile metalation of *o*-tolyl *t*-butyl sulfone (**124**) with butyllithium in THF to yield the benzyllithium species **124a**, which was stable at room temperature or below. However, refluxing the solution for several hours resulted in the formation of the salt of *o*-neopentylbenzenesulfinic acid (**125**) in good yield (equation 82). This reaction, which constitutes a Truce–Smiles rearrangement with an alkyl group as the migrating unit, has also been observed with other *o*-methylaryl *t*-alkyl sulfones. Subsequently, and unexpectedly, Truce and coworkers[282–285] observed that this rearrangement can also be extended to *p*-tolyl *t*-alkyl sulfones. Thus, an attempt to metalate *p*-tolyl *t*-butyl sulfone (**126**) with butyllithium resulted in metalation at an *ortho*-position[283], but metalation with lithium diisopropylamide in THF resulted in benzylic metalation. Furthermore, the resulting metalated sulfone **126a** was found to rearrange readily to lithium *p*-neopentylbenzenesulfinate (**127**) even at room temperature (equation 83)[284].



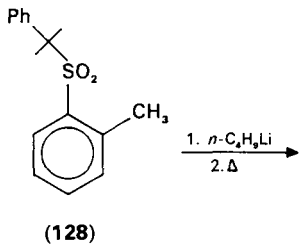
(124) (124a) (125) (82)



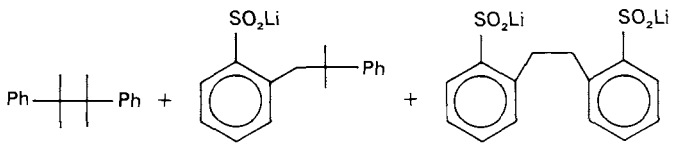
(126) (126a) (127) (83)

The facile rearrangement of **126** to sulfinate salt **127** is a strong argument against both a concerted pericyclic process as well as an intramolecular 'S_N2-like' displacement mechanism, as suggested for the classical Truce–Smiles rearrangement of *o*-methyl diaryl sulfones (see the previous subsection). Furthermore, rearrangement of *o*-tolyl *t*-butyl sulfone (**124**) via an intramolecular 'S_N2-like' attack at a tertiary carbon with displacement of sulfinate anion is also unlikely considering that sulfinates are relatively poor leaving groups in nucleophilic displacements and few documented examples exist of S_N2-type reactions at tertiary carbons, even with good leaving groups[286,287]. On the other hand, considerable evidence for a free radical mechanism was obtained[283–285]. For example, the rearrangement of *o*-tolyl cumyl sulfone (**128**) yielded equimolar quantities of radical coupling products **129** and **131**, in addition to the normal rearrangement product **130** (equation 84)[285]. Bicumyl (**129**) has been previously shown to arise by dimerization of cumyl radicals[288]. Consequently, an electron-transfer–radical-anion two-step mechanism was first suggested, as illustrated in equation 85[282]. In this mechanism, the first step involves fragmentation of the metalated sulfone **124a** to a *t*-butyl radical (**132**) and a benzyl

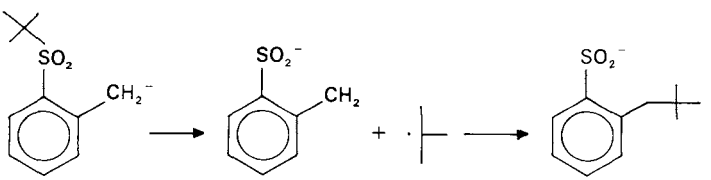
radical–sulfinate anion species (**133**), and the second step involves simple recombination of these radical species to give the observed product (**125**). This fragmentation–recombination mechanism shows considerable resemblance to the Wittig rearrangement[289] of benzyl alkyl sulfides or ethers which is believed[290,291] to proceed by similar routes.



(**128**)



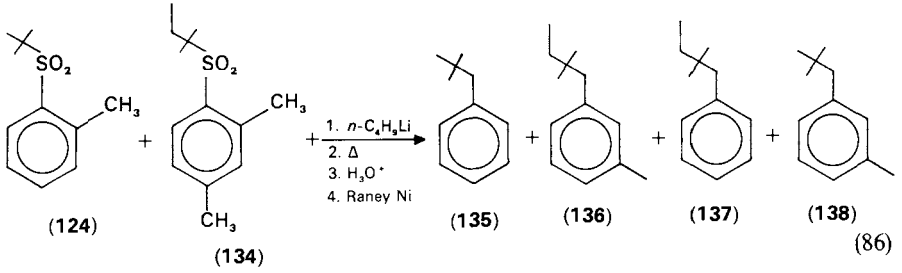
(**129**) (**130**) (**131**) (84)



(**124a**) (**133**) (**132**) (**125**) (85)

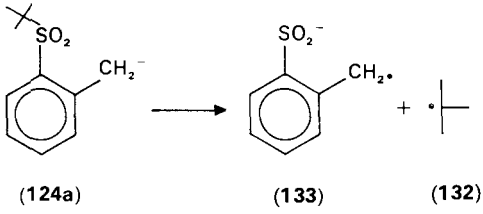
Further evidence supporting the mechanism shown in equation **85** was the practically complete lack of reactivity of both *o*- and *p*-tolyl 1-methylcyclopropyl sulfones under conditions where the corresponding *t*-butyl sulfones, **124** and **126** respectively, readily undergo rearrangement. Such a result is consistent with the reported difficulties in the generation of cyclopropyl free radicals and their reduced stability[292,293]. Another experiment supporting the intermediacy of free radicals involves a crossover study undertaken[282] on **124** and 2,4-dimethylphenyl *t*-amyl sulfone (**134**). When an equimolar mixture of these two sulfones was subjected to the normal rearrangement conditions and subsequently desulfurized over Raney nickel, four hydrocarbons were obtained in approximately equimolar quantities (equation 86). Two of these, **135** and **136**, correspond to the expected rearrangement products of **124** and **134**, respectively. The remaining two, **137** and **138**, are crossover products corresponding to an intermolecular process. However, the absence of bibenzylic coupling products from **124**, **134**, or their combination, argues against a simple fragmentation–recombination mechanism as the one depicted in equation 85. Therefore, a modified sequence involving a radical–radical anion chain process for this rearrangement has been suggested by the authors (equation 87)[285]. In this mechanism, initial fragmentation of the metalated sulfone **124a** is exactly like in the previous one. However, generation of the *t*-butyl free radical (**132**) is followed by its attack on a benzylic position of **124a** to give rise to radical anion **139**, which then fragments to give product **125** in addition to regenerating **132**. Similar radical–radical anion chain

mechanisms have been shown to operate in other systems including nucleophilic substitution at benzyl[294] as well as aryl[295] carbons.

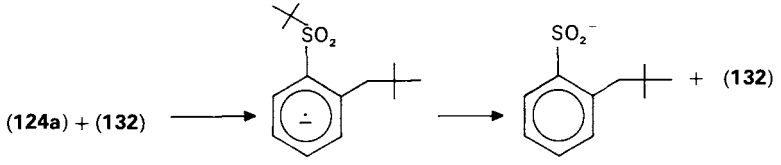


(124) (134) (135) (136) (137) (138)

(86)



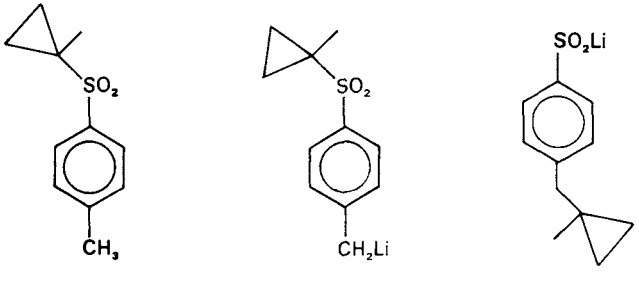
(124a) (133) (132)



(139) (125)

(87)

To distinguish between the nonchain and chain mechanisms (equations 85 and 87, respectively) advantage has been taken of the very different reactivities of *t*-butyl *p*-tolyl sulfone (**126**) and the corresponding 1-methylcyclopropyl sulfone (**140**), at room temperature. Assuming the lack of reactivity of **140a** to be due to the difficulty of generating a 1-methylcyclopropyl radical in the initation step, another radical source, such as **126a**, should facilitate the rearrangement of **140a**, if a chain process takes place. On the basis of this reasoning, a mixture of **126a** and **140a** should yield, at room temperature, both products **127** and **141**, even though **140a** alone does not react. Indeed, treatment of a



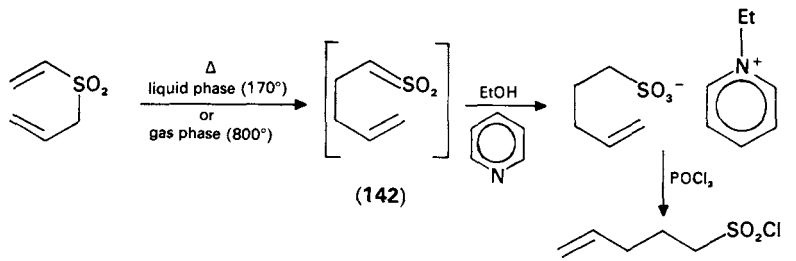
(140) (140a) (141)

mixture of **126** and **140** with LDA in THF at room temperature for 2h, followed by extraction with water and derivatization with benzyl chloride, afforded a mixture of the benzyl sulfones of **127** and **141** in a 2:1 molar ratio[285]. This result provides compelling evidence for the chain process shown in equation 87. On the other hand, an attempted similar crossover experiment using *t*-butyl and 1-methylcyclopropyl *o*-tolyl sulfones failed to provide conclusive results.

VII. MISCELLANEOUS REARRANGEMENTS

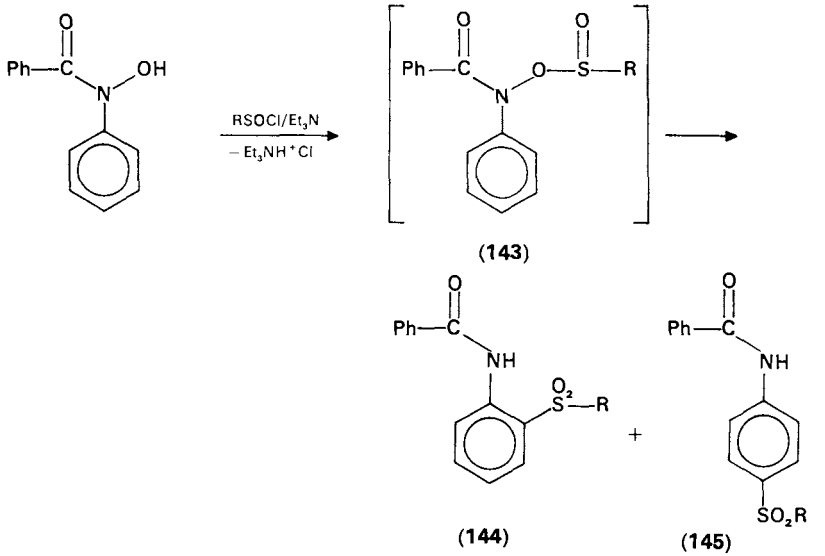
Several different rearrangements involving sulfones, which could not be classified according to the preceding section headings, are briefly described below.

King and Harding[296] have reported an interesting 'Sulfo-Cope' rearrangement, and have presented evidence for the formation of the unstable sulfene (**142**) during the gas or liquid phase thermal [3,3]sigmatropic rearrangement of allyl vinyl sulfone (equation 88).



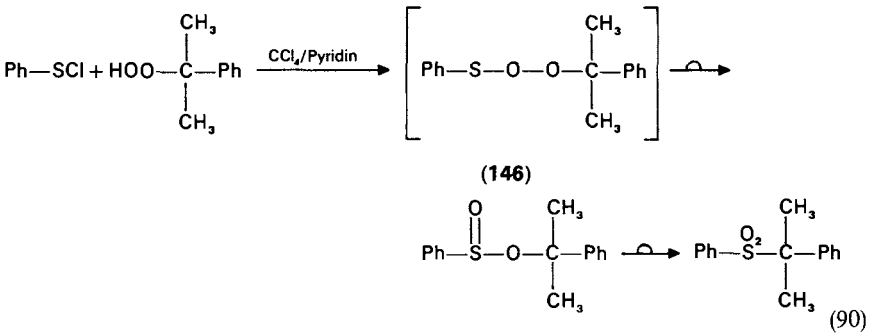
(88)

Heesing and coworkers[297] have reported the rearrangement of *O*-alkylsulfinyl-*N*-benzoyl-*N*-phenylhydroxylamine (**143**) at −70 °C to the corresponding sulfonamide together with the *o*- and *p*-alkylsulfonyl derivatives **144** and **145** (equation 89). The reaction has been suggested to proceed by an intramolecular radical pair mechanism, as evidenced by experiments with oxygen-18 labeling and ^{13}C-CIDNP effects.



(89)

The rearrangement of undetected cumyl benzenepersulfenate (**146**), during its preparation, to cumyl phenyl sulfone has been suggested to involve prior isomerization to cumyl benzenesulfinate (equation 90). The rearrangement proceeds in low yield due to competing oxidation of the sulfinate intermediate to sulfonate with excess hydroperoxide[304].

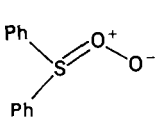


(146)

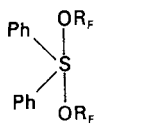
(90)

Another unstable species which rearranges to sulfone upon its formation is the so-called persulfoxide or sulfinyl oxide **147**, which can be obtained by hydrogen peroxide oxidation of dialkoxysulfuranes or alternatively by photooxygenation of sulfides with singlet oxygen[298–302]. Thus, diphenyl sulfone is obtained in high yield on treatment of the dialkoxysulfurane IV **148** with hydrogen peroxide at low temperature, through the intermediacy of persulfoxide **147**[298].

Schank[303] has reported a facile and quantitative isomerization of the β-keto sulfone **149** to **150** under base-catalyzed conditions.

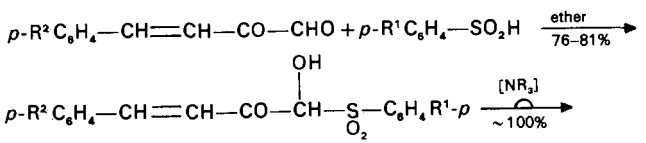


(147)



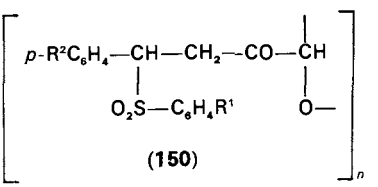
$[R_F = PhC(CF_3)_2]$

(148)



$R^1 = CH_3$

$R^2 = H, NO_2$ **(149)**



(150)

VIII. REFERENCES

1. C. M. Suter, *Organic Chemistry of Sulfur*, Chap. 7, Wiley, New York, 1944.
2. A. Schöberl and A. Wagner, in *Houben-Weyl, Methoden der Organischen Chemie* (Ed. E. Müller), Vol. 9, G. Thieme Verlag, Stuttgart, 1955, p. 223.
3. J. Strating, in *Organic Sulfur Compounds* (Ed. N. Kharasch), Vol. 1, Pergamon Press, Oxford, 1961, p. 146.
4. W. E. Truce, T. C. Klingler and W. W. Brand, in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, 1977, p. 527.
5. P. D. Magnus, *Tetrahedron*, **33**, 2019 (1977).
6. L. Field, *Synthesis*, 713 (1978).
7. T. Durst, in *Comprehensive Organic Chemistry* (Eds. D. H. R. Barton and W. D. Ollis), Vol. 3 (Ed. D. N. Jones), Pergamon Press, Oxford, 1979, p. 171.
8. *Specialist Periodical Reports: Organic Compounds of Sulfur, Selenium, and Tellurium*, Vols. 1–3 (D. H. Reid, Senior Reporter), Vols. 4–6 (D. R. Hogg, Senior Reporter), The Chemical Society, London, 1970–1981.
9. K. Schank, in *Houben-Weyl, Methoden der Organischen Chemie* (Ed. D. Klamann), E11, Part 2, G. Thieme Verlag, Stuttgart, 1985, p. 1129.
10. C. J. M. Stirling, *Int. J. Sulfur Chem. (B)*, **6**, 277 (1971).
11. S. Oae and N. Kumeda, in Ref. 4, Ch. 11.
12. K. K. Andersen, in Ref. 7, p. 317.
13. J. L. Kice, *Adv. Phys. Org. Chem.*, **17**, 65 (1980).
14. E. Krauthausen, in Ref. 9, E 11, Part 1, p. 64.
15. F. G. Bordwell, in *Organosulfur Chemistry* (Ed. M. J. Janssen), Chap. 16, Interscience, New York, 1967.
16. F. G. Bordwell, *Acc. Chem. Res.*, **3**, 281 (1970).
17. L. A. Paquette, *Acc. Chem. Res.*, **1**, 209 (1968).
18. L. A. Paquette, *Org. React.*, **25**, 1 (1977).
19. W. E. Truce, E. M. Kreider and W. W. Brand, *Org. React.*, **18**, 19 (1970).
20. V. N. Drozd, *Int. J. Sulfur Chem.*, **8**, 443 (1973).
21. R. Otto and A. Rossing, *Chem. Ber.*, **18**, 2493 (1885).
22. O. Hinsberg, *Chem. Ber.*, **50**, 468 (1917).
23. J. Kenyon and H. Phillips, *J. Chem. Soc.*, 1676 (1930).
24. C. L. Arcus, M. P. Balfe and J. Kenyon, *J. Chem. Soc.*, 485 (1938).
25. A. H. Wragg, J. S. McFadyen and T. S. Stevens, *J. Chem. Soc.*, 3603 (1958).
26. H. Mackle, *Tetrahedron*, **19**, 1159 (1963).
27. A. B. Burg in Ref. 3, pp. 35–37.
28. D. Darwish and R. A. McLaren, *Tetrahedron Letters*, 123 (1962).
29. R. A. McLaren, Ph.D. Thesis, University of Alberta, 1964.
30. J. Grover, Ph.D. Thesis, University of Alberta, 1969.
31. R. Mermelstein, Ph.D. Thesis, University of Alberta, 1966.
32. D. Darwish and E. A. L. Preston, *Tetrahedron Letters*, 113 (1964); E. A. L. Preston, M.Sc. Thesis, University of Alberta, 1963.
33. H. H. Persad, Ph.D. Thesis, University of Alberta, 1966.
34. O. T. Banfey, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 2488 (1952).
35. G. S. Hammond, C. E. Reeder, F. T. Fang and J. C. Kochi, *J. Amer. Chem. Soc.*, **80**, 568 (1958).
36. D. Darwish and R. A. McLaren, Abstracts, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964, p. 44S.
37. S. Winstein and G. C. Robinson, *J. Amer. Chem. Soc.*, **80**, 169 (1958); S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, *J. Amer. Chem. Soc.*, **78**, 328 (1956); **76**, 2597 (1954).
38. E. Ciuffarin, M. Isola and A. Fava, *J. Amer. Chem. Soc.*, **90**, 3594 (1968).
39. S. Braverman and S. Steiner, *Israel J. Chem.*, **5**, 267 (1967).
40. S. Braverman and T. Globerman, *Tetrahedron*, **30**, 3873 (1974).
41. (a) S. Braverman and Y. Duar, *Tetrahedron Letters*, 343 (1975).
    (b) Y. Duar, M.Sc. Thesis, Bar-Ilan University, 1975.
42. S. Braverman and H. Manor, *Phosphorus and Sulfur*, **2**, 213 (1976).
43. S. Winstein, E. Grunwald and H. W. Jones, *J. Amer. Chem. Soc.*, **73**, 2700 (1951).
44. J. B. Hendrickson and P. L. Skipper, *Tetrahedron*, **32**, 1627 (1976).

45. J. B. Hendrickson, D. D. Sternbach and K. W. Bair, *Acc. Chem. Res.*, **10**, 306 (1977).
46. F. Jung, M. Molin, R. Van Den Elzen and T. Durst, *J. Amer. Chem. Soc.*, **96**, 935 (1974).
47. R. F. Heldeweg and H. Hogeveen, *J. Amer. Chem. Soc.*, **98**, 2341 (1976).
48. A. C. Cope, D. E. Morrison and L. Field, *J. Amer. Chem. Soc.*, **72**, 59 (1950).
49. (a) J. Meisenheimer, *Chem. Ber.*, **52**, 1667 (1919).
(b) R. A. W. Johnstone, in *Mechanisms of Molecular Migrations* (Ed. B. S. Thyagarajan), Vol. 2, Interscience, New York, 1969, pp. 249–266.
50. (a) S. Braverman, Ph.D. Thesis, University of Alberta, 1963.
(b) D. Darwish and S. Braverman, 48th Chemical Institute of Canada Conference, Montreal, Canada, May 30–June 2, 1965.
51. (a) S. Braverman, 3rd Symposium on Mechanism and Structure in Sulfur Chemistry, Cork, Ireland, Sept. 29–Oct. 3, 1969.
(b) S. Braverman, *Int. J. Sulfur. Chem.* (*C*), **6**, 149 (1971).
52. R. W. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **18**, 563 (1979).
53. (a) M. Moriwaki, Y. Yamamoto, J. Oda and Y. Inouye, *J. Org. Chem.*, **41**, 300 (1976).
(b) K. Mislow, *Introduction to Stereochemistry*, Benjamin, New York, 1966, p. 131.
54. J. E. Baldwin and J. E. Patrick, *J. Amer. Chem. Soc.*, **93**, 3556 (1971).
55. U. Schollkopf, K. Fellenberger and M. Rizk, *Liebigs Ann. Chem.*, 734, 106 (1970).
56. K. K. Chan and G. Saucy, *J. Org. Chem.*, **42**, 3828 (1977).
57. Y. Yamamoto, J. Oda and Y. Ynouge, *J. Org. Chem.*, **41**, 303 (1976).
58. D. N. Jones, J. Blekinsopp, A. F. C. Edwards, E. Helms and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 2602 (1973).
59. C. A. Vernon, *J. Chem. Soc.*, 423 (1954).
60. (a) A. Iliceto, A. Fava and U. Mazzueato, *Tetrahedron Letters*, 27 (1960).
(b) A. Fava, in *Organic Sulfur Compounds* (Eds. N. Kharasch and C. Y. Meyers), Vol. 2, Pergamon Press, London, 1966, p. 86.
61. S. G. Smith, *J. Amer. Chem. Soc.*, **83**, 4285 (1961).
62. S. G. Smith, A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, **83**, 618 (1961).
63. A. Gagneaux, S. Winstein and W. G. Young, *J. Amer. Chem. Soc.*, **82**, 5956 (1960).
64. (a) A. Jefferson and F. Scheinmann, *Quart. Rev.*, **22**, 391; 420 (1968).
(b) J. E. Baldwin, R. E. Hackler and D. P. Kelly, *J. Chem. Soc., Chem. Commun.*, 538 (1968).
65. H. J. Reich, I. L. Reich and S. Wollowitz, *J. Amer. Chem. Soc.*, **100**, 5981 (1978).
66. (a) D. Darwish and A.-M. Armour, unpublished results.
(b) A.-M. Armour, Ph.D. Thesis, University of Alberta, 1970.
67. S. O. Myong, L. W. Linder, Jr., S. C. Seike and R. D. Little, *J. Org. Chem.*, **50**, 2244 (1985).
68. M. Mikolajczyk, J. Drabowicz and B. Bujnicki, *J. Chem. Soc., Chem. Commun.*, 568 (1974).
69. K. Hiroi, R. Kitayama and S. Sato, *Synthesis*, 1040 (1983).
70. K. Hiroi, R. Kitayama and S. Sato, *J. Chem. Soc., Chem. Commun.*, 1470 (1983); *Chem. Pharm. Bull.*, **32**, 2628 (1984).
71. D. Darwish and J. Noreyko, *Can. J. Chem.*, **43**, 1366 (1965).
72. P. A. Grieco and D. Boxler, *Synth. Commun.*, **5**, 315 (1975).
73. J. E. Baldwin, O. W. Lever, Jr. and N. R. Tzodikov, *J. Org. Chem.*, **41**, 2312 (1976).
74. J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962).
75. D. R. Taylor, *Chem. Rev.*, **67**, 317 (1967).
76. J. E. Baldwin and R. H. Fleming, *Fortschr. Chem. Forsch.*, **15**, 281 (1970).
77. W. D. Huntsman, in *The Chemistry of Ketenes, Allenes and Related Compounds* (Ed. S. Patai), Part 2, Wiley, Chichester, 1980, p. 521.
78. H. Hopf, in Ref. 77, p. 779.
79. (a) S. Braverman and H. Mechoulam, *Israel J. Chem.*, **4**, 17p (1966).
(b) S. Braverman and H. Mechoulam, *Israel J. Chem.*, **5**, 71 (1967).
(c) S. Braverman and H. Mechoulam, *Tetrahedron*, **30**, 3883 (1974).
80. (a) C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 131 (1967).
(b) G. Smith and C. J. M. Stirling, *J. Chem. Soc.* (*C*), 1530 (1971).
81. A. Burawoy and E. Spinner, *J. Chem. Soc.*, 3752 (1954).
82. S. Braverman and Y. Stabinsky, *J. Chem. Soc., Chem. Commun.*, 270 (1967); *Israel J. Chem.*, **5**, 71p (1967).
83. S. Braverman and Y. Stabinsky, *Israel J. Chem.*, **5**, 125 (1967).
84. S. Braverman and D. Segev, *J. Amer. Chem. Soc.*, **96**, 1245 (1974).

85. G. Büchi and R. M. Freidinger, *J. Amer. Chem. Soc.*, **96**, 3332 (1974).
86. Q. E. Thompson, *J. Org. Chem.*, **30**, 2703 (1965).
87. N. S. Zefirov and F. A. Abdulvaleeva, *Vestn. Mosk. Univ., Khim.*, **24**, 135 (1969); *Chem. Abstr.*, **71**, 112345 (1969).
88. J. E. Baldwin, G. Höfle and S. C. Choi, *J. Amer. Chem. Soc.*, **93**, 2810 (1971).
89. E. K. Fields and S. Meyerson, *J. Amer. Chem. Soc.*, **88**, 2836 (1966).
90. W. J. M. Tilborg, *Rec. Trav. Chim., Pays-Bas*, **96**, 282 (1977).
91. D. C. Dittmer, R. S. Henion and N. Takashina, *J. Org. Chem.*, **34**, 1310 (1969).
92. D. C. Dittmer and T. R. Nelsen, *J. Org. Chem.*, **41**, 3044 (1976).
93. R. W. Hoffmann and W. Sieben, *Justus Liebigs Ann. Chem.*, **703**, 96 (1967).
94. J. F. King, K. Piers, D. J. H. Smith, C. L. McIntosh and P. de Mayo, *J. Chem. Soc., Chem. Commun.*, 31 (1969).
95. J. F. King, P. de Mayo, C. L. McIntosh, K. Piers and D. J. H. Smith, *Can. J. Chem.*, **48**, 3704 (1970).
96. J. F. King, *Acc. Chem. Res.*, **8**, 10 (1975).
97. J. D. Finlay, C. R. Hall and D. J. Smith, *Tetrahedron Letters*, 1149 (1977).
98. H. Hogeveen and L. Zwart, *J. Amer. Chem. Soc.*, **104**, 4889 (1982).
99. M. Christl, E. Brunn and F. Lanzendörfer, *J. Amer. Chem. Soc.*, **106**, 373 (1984).
100. K. Schank and H.-G. Schmitt, *Chem. Ber.*, **107**, 3026 (1974).
101. G. W. Gokel and H. M. Gerdes, *Tetrahedron Letters*, 3375 (1979).
102. G. W. Gokel and H. M. Gerdes, *Tetrahedron Letters*, 3379 (1979).
103. K. Schank, H.-G. Schmitt, F. Schroeder and A. Weber, *Justus Liebigs Ann. Chem.*, 1116 (1977).
104. (a) T. Wickel, Ph.D. Thesis, University of Saarbrücken, 1979.
(b) K. Schank, *Ann. Univ. Sarav. Math-Naturwiss. Fak.*, **16**, 35 (1981); *Chem. Abstr.*, **96**, 5730 (1982).
105. R. M. Dodson, P. D. Hammen and R. A. Davis, *J. Chem. Soc., Chem. Commun.*, 9 (1968); *J. Org. Chem.*, **36**, 2693 (1971).
106. R. M. Dodson, P. D. Hammen and J. Y. Fan, *J. Org. Chem.*, **36**, 2703 (1971).
107. R. M. Dodson, P. D. Hammen, E. H. Jancis and G. Klose, *J. Org. Chem.*, **36**, 2698 (1971).
108. H. Kloostterziel, J. A. H. van Drunen and P. Galama, *J. Chem. Soc., Chem. Commun.*, 885 (1969).
109. E. V. Polanin, I. M. Zaks, A. M. Moisernkov and A. V. Semenovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 641 (1979); *Chem. Abstr.*, **91**, 5005 (1979).
110. R. L. Crumbie and D. D. Ridley, *Aust. J. Chem.*, **34**, 1017 (1981).
111. S. Braverman and D. Reisman, *J. Amer. Chem. Soc.*, **99**, 605 (1977).
112. S. Braverman and D. Reisman, *Tetrahedron Letters*, 1753 (1977).
113. S. Braverman and Y. Duar, *J. Amer. Chem. Soc.*, **105**, 1061 (1983).
114. S. Braverman, *Phosphorus and Sulfur*, **23**, 297 (1985).
115. M. Cinqui, S. Colonna and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 247 (1978).
116. G. Lowe, *J. Chem. Soc., Chem. Commun.*, 411 (1965); J. H. Brewster, *Topics in Stereochemistry*, **2**, 1 (1967); G. Krow, *Topics in Stereochemistry*, **5**, 31 (1970).
117. T. Durst and K.-C. Tin, *Tetrahedron Letters*, 2369 (1970).
118. D. F. Tavares, R. E. Estep and M. Blezard, *Tetrahedron Letters*, 2373 (1970).
119. J. R. Williams, G. M. Sarkisian, J. Quigley, A. Hasiuk and R. Vander Vennen, *J. Org. Chem.*, **39**, 1028 (1974).
120. T. Durst, K.-C. Tin, F. de Reinach-Hirtzbach, J. M. Decesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).
121. A. Jonczyk, K. Banko and M. Makosza, *J. Org. Chem.*, **40**, 266 (1975).
122. P. F. Vogt and D. F. Tavares, *Can. J. Chem.*, **47**, 2875 (1968).
123. A. Jonczyk and T. Radwan-Pytlewski, *Chem. Letters*, 1557 (1983).
124. A. A. M. Howen-Claassen, J. W. McFarland, B. H. M. Lammerink, L. Thijs and B. Zwanenburg, *Synthesis*, 628 (1983).
125. K. Schank and F. Werner, *Justus Liebigs Ann. Chem.*, 1739 (1983).
126. J. DeSales, R. Greenhouse and J. M. Muchowski, *J. Org. Chem.*, **47**, 3668 (1982).
127. A. R. Friedman and D. R. Graber, *J. Org. Chem.*, **37**, 1902 (1972).
128. (a) E. C. Leonard, *J. Org. Chem.*, **30**, 3258 (1965).
(b) M. I. Oftedahl, J. W. Baker and M. W. Dietrich, *J. Org. Chem.*, **30**, 296 (1965).
129. H. Stetter and K. Steinbeck, *Justus Liebigs Ann. Chem.*, 1315 (1974).

130. V. M. Neplyuev and I. M. Bazavova, *Zh. Org. Khim.*, **17**, 2231 (1981); *Chem. Abstr.*, **96**, 68494 (1982).
131. N. P. Petukhova, N. E. Dontsova, E. N. Prilizhaeva and V. S. Bogdanov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 474 (1984).
132. G. Melloni and G. Modena, *Int. J. Sulfur Chem. (A)*, **1**, 125 (1971).
133. D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974); Reference 23(b).
134. P. Bickart, F. W. Carson, J. Jacolens, E. G. Miller and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4869 (1968).
135. F. G. Bordwell and G. A. Pagani, *J. Amer. Chem. Soc.*, **97**, 118 (1975).
136. K. Ogura, T. Tihania, S. Kiuchi, T. Kajike, O. Koshikawa, K. Takahashi and H. Iida, *J. Org. Chem.*, **51**, 700 (1986).
137. P. S. Manchand, M. Rosenberger, G. Saucy, P. A. Wehrli, H. Wong, L. Chambers, M. P. Ferro and W. Jackson, *Helv. Chim. Acta*, **59**, 387 (1976).
138. R. D. Baechler, P. Bentley, L. Deuring and S. Fisk, *Tetrahedron Letters*, **23**, 2269 (1982).
139. S. O. Myong, L. W. Linder, Jr., S. C. Seike and R. D. Little, *J. Org. Chem.*, **50**, 2244 (1985).
140. B. Lythgoe, *Chem. Soc. Rev.*, **9**, 449 (1980); P. J. Kocienski, *Chem. Ind. (London)*., 648 (1981); *Tetrahedron Letters*, 441 (1979).
141. P. Kocienski, *J. Chem. Soc., Perkin Trans. 1*, 945 (1983).
142. P. Lin and G. H. Whitham, *J. Chem. Soc., Chem. Commun.*, 1102 (1983).
143. D. J. Knight, P. Lin and G. H. Whitham, unpublished results.
144. M. Julia, M. Nel, A. Righini and D. Uguen, *J. Organomet. Chem.*, **235**, 113 (1982).
145. T. A. K. Smith and G. H. Whitham, *J. Chem. Soc., Chem. Commun.*, 897 (1985).
146. (a) K. Inomato, T. Yamamoto and H. Kotake, *Chem. Letters*, 1357 (1981).
(b) K. Inomato, Y. Murato, H. Kato, Y. Tsukahava, H. Kinoshita and H. Kotake, *Chem. Letters*, 931 (1985).
147. B. M. Trost, N. R. Schmuff and M. J. Miller, *J. Amer. Chem. Soc.*, **102**, 5979 (1980).
148. B. Zwanenburg and A. Wagenaar, *Tetrahedron Letters*, 5009 (1973).
149. W. Jeblick and K. Schank, *Justus Liebigs Ann. Chem.*, 1727 (1976).
150. W. Jeblick and K. Schank, *Justus Liebigs Ann. Chem.*, 1096 (1977).
151. L. Ramberg and B. Bäcklund, *Arkiv. Kemi Mineral. Geol.*, **13A**, No. 27 (1940); *Chem. Abstr.*, **34**, 4725 (1940).
152. L. A. Paquette, in *Mechanism of Molecular Migrations* (Ed. B. S. Thyagarajan), Vol. 1, Interscience, New York, 1968, p. 121.
153. C. Y. Meyers, W. S. Matthews, L. L. Ho, V. M. Kolb and T. E. Parady, in *Catalysis in Organic Syntheses* (Ed. G. V. Smith), Academic Press, New York, 1977, p. 197.
154. C. Y. Meyers, in *Topics in Sulfur Chemistry* (Ed. M. Tisler), University Press, Ljubljana, 1978, p. 207.
155. F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **73**, 5184, 5187 (1951).
156. F. G. Bordwell and J. M. Williams, *J. Amer. Chem. Soc.*, **90**, 435 (1968).
157. L. A. Paquette and L. S. Wittenbrook, *J. Amer. Chem. Soc.*, **90**, 6783 (1968).
158. F. G. Bordwell and M. D. Wolfinger, *J. Org. Chem.*, **39**, 2521 (1974).
159. For a review, see N. H. Fischer, *Synthesis*, 393 (1970).
160. N. P. Neureiter, *J. Amer. Chem. Soc.*, **88**, 558 (1966).
161. F. G. Bordwell, J. M. Williams, Jr., E. B. Hoyt, Jr. and B. B. Jarvis, *J. Amer. Chem. Soc.*, **90**, 429 (1968).
162. N. Tokura, T. Nagai and S. Matsumara, *J. Org. Chem.*, **31**, 349 (1966).
163. L. A. Paquette and R. W. Houser, *J. Amer. Chem. Soc.*, **91**, 3870 (1969).
164. E. J. Corey and E. Block, *J. Org. Chem.*, **34**, 1233 (1969).
165. F. G. Bordwell, E. Doomes and P. W. R. Corfield, *J. Amer. Chem. Soc.*, **92**, 2581 (1970).
166. F. G. Bordwell and E. Doomes, *J. Org. Chem.*, **39**, 2526 (1974).
167. F. G. Bordwell and E. Doomes, *J. Org. Chem.*, **39**, 2531 (1974).
168. R. Hoffmann, C. C. Levin and R. A. Moss, *J. Amer. Chem. Soc.*, **95**, 629 (1973).
169. C. Y. Meyers, A. M. Malte and W. S. Matthews, *J. Amer. Chem. Soc.*, **91**, 7510 (1969); *Quart. Rep. Sulfur Chem.*, **5**, 229 (1970).
170. C. Y. Meyers, W. S. Matthews, G. J. McCollum and J. C. Branca, *Tetrahedron Letters*, 1105 (1974).
171. C. Y. Meyers and L. Litto, *Tetrahedron Letters*, 4319 (1972).

172. C. Y. Meyers and I. Sataty, *Tetrahedron Letters*, 4323 (1972).
173. C. Y. Meyers, L. L. Ho, G. J. McCollum and J. Branca, *Tetrahedron Letters*, 1843 (1973).
174. L. A. Carpino, L. V. McAdams, R. H. Rynbrandt and J. W. Spiewak, *J. Amer. Chem. Soc.*, **93**, 476 (1971).
175. U. Jacobsson, T. Kempe and T. Norin, *J. Org. Chem.*, **39**, 2722 (1974).
176. K. Dickoré, *Justus Liebigs Ann. Chem.*, **671**, 135 (1964).
177. J. C. Philips, J. V. Swisher, D. Haiducewych and O. Morales, *J. Chem. Soc., Chem. Commun.*, 22 (1971).
178. G. D. Hartman and R. D. Hartman, *Synthesis*, 504 (1982).
179. C. Y. Meyers, D. H. Hua and N. J. Peacock, *J. Org. Chem.*, **45**, 1721 (1980).
180. J. B. Hendrickson, G. J. Boudreaux and P. S. Palumbo, *Tetrahedron Letters*, **25**, 4617 (1984).
181. J. B. Hendrickson and P. S. Palumbo, *J. Org. Chem.*, **50**, 2110 (1985).
182. D. Scholtz, *Justus Liebigs Ann. Chem.*, 98 (1983).
183. D. Scholtz, *Justus Liebigs Ann. Chem.*, 264 (1984).
184. F. G. Bordwell, B. B. Jarvis and P. W. R. Corfield, *J. Amer. Chem. Soc.*, **90**, 5298 (1968).
185. F. G. Bordwell and B. B. Jarvis, *J. Amer. Chem. Soc.*, **95**, 3585 (1973).
186. L. A. Carpino and J. R. Williams, *J. Org. Chem.*, **39**, 2320 (1974).
187. R. B. Mitra, N. Y. Notekar and S. D. Virkar, *Indian J. Chem.*, **13**, 251 (1965).
188. E. Block and M. Aslam, *J. Amer. Chem. Soc.*, **105**, 6164 (1983).
189. E. Block, M. Aslam, V. Eswarakrishnan and A. Wall, *J. Amer. Chem. Soc.*, **105**, 6165 (1983).
190. C. Y. Meyers and D. H. Hua, *Phosphorus and Sulfur*, **6**, 197 (1979).
191. T. B. R. A. Chen, J. J. Burger and E. R. de Waard, *Tetrahedron Letters*, 4527 (1977).
192. E. R. de Waard, *Phosphorus and Sulfur*, **6**, 77 (1979).
193. J. J. Burger, T. B. R. A. Chen, E. R. de Waard and H. O. Huisman, *Tetrahedron*, **37**, 417 (1981).
194. F. Näf, R. Decorzant and S. D. Escher, *Tetrahedron Letters*, **23**, 5043 (1982).
195. A. J. Fry, K. Ankner and V. Handa, *Tetrahedron Letters*, **22**, 1791 (1981).
196. L. A. Paquette, R. E. Wingard Jr. and R. H. Meisinger, *J. Amer. Chem. Soc.*, **93**, 1047 (1971).
197. L. A. Paquette, R. H. Meisinger and R. E. Wingard Jr., *J. Amer. Chem. Soc.*, **95**, 2230 (1973).
198. N. P. Neureiter, *J. Org. Chem.*, **30**, 1313 (1965).
199. L. A. Paquette, R. E. Wingard Jr. and J. M. Photis, *J. Amer. Chem. Soc.*, **96**, 5801 (1974).
200. L. A. Paquette and J. C. Philips, *J. Amer. Chem. Soc.*, **91**, 3973 (1969).
201. L. A. Paquette, *Int. J. Sulfur Chem. (C)*, **7**, 73 (1972).
202. D. Ginsburg, *Acc. Chem. Res.*, **5**, 249 (1972).
203. R. G. Carlson and K. D. May, *Tetrahedron Letters*, 947 (1975).
204. J. Kattenberg, E. R. de Waard and H. O. Huisman, *Tetrahedron Letters*, 1173 (1977).
205. H. J. Bestman and W. Schapper, *Tetrahedron Letters*, 3511 (1975).
206. E. Vedejs and S. P. Singer, *J. Org. Chem.*, **43**, 4884 (1978).
207. I. V. Kazimirchik, K. A. Lukin, C. F. Bebikh and N. S. Zefirov, *Zh. Org. Khim.*, **19**, 2523 (1983); *Chem. Abstr.*, **100**, 174296 (1984).
208. M. P. Cooke Jr., *J. Org. Chem.*, **46**, 1747 (1981).
209. H. Böhme and H.-J. Wilke, *Lustus Liebigs Ann. Chem.*, 1123 (1978).
210. J. Nakayama, E. Oshima, A. Ishii and M. Hoshino, *J. Org. Chem.*, **48**, 60 (1983).
211. P. G. Gassman and S. M. Bonser, *J. Amer. Chem. Soc.*, **105**, 667 (1983).
212. P. G. Gassman and H. R. Drewes, *J. Amer. Chem. Soc.*, **100**, 7600 (1978).
213. E. Block, M. Aslam, R. Iyer and J. Hutchinson, *J. Org. Chem.*, **49**, 3664 (1984).
214. E. Block, V. Eswarakrishnan and K. Gebreyes, *Tetrahedron Letters*, **25**, 5469 (1984).
215. E. Block, M. Aslam, V. Eswarakrishnan, K. Gebreyes, J. Hutchinson, R. Iyer, J.-A. Lafitte and A. Wall, *J. Amer. Chem. Soc.*, **108**, 4568 (1986).
216. R. Henrique, *Ber.*, **27**, 2993 (1894).
217. O. Hinsberg, *J. Prakt. Chem.*, **90**, 345 (1914).
218. O. Hinsberg, *J. Prakt. Chem.*, **91**, 307 (1915).
219. O. Hinsberg, *J. Prakt. Chem.*, **93**, 277 (1918).
220. L. A. Warren and S. Smiles, *J. Chem. Soc.*, 956, 1327 (1930).
221. L. A. Warren and S. Smiles, *J. Chem. Soc.*, 1040 (1932).
222. L. A. Warren and S. Smiles, *J. Chem. Soc.*, 914 (1931).
223. L. A. Warren and S. Smiles, *J. Chem. Soc.*, 2207 (1931).
224. F. A. Galbraith and S. Smiles, *J. Chem. Soc.*, 1234 (1935).
225. B. A. Keat and S. Smiles, *J. Chem. Soc.*, 422 (1934).

226. W. J. Evans and S. Smiles, *J. Chem. Soc.*, 181 (1935).
227. L. A. Warren and S. Smiles, *J. Chem. Soc.*, 2774 (1932).
228. W. J. Evans and S. Smiles, *J. Chem. Soc.*, 329 (1936).
229. B. T. Tozer and S. Smiles, *J. Chem. Soc.*, 2052 (1938).
230. A. A. Levi and S. Smiles, *J. Chem. Soc.*, 1488 (1932).
231. A. A. Levi, H. C. Rains and S. Smiles, *J. Chem. Soc.*, 3264 (1931).
232. S. Smiles, *Ann. Reports*, **30**, 188 (1933).
233. J. D. London, J. R. Robertson, J. N. Watson and S. D. Aiton, *J. Chem. Soc.*, 55 (1950).
234. K. Florey and A. R. Restivo, *J. Org. Chem.*, **23**, 1018 (1958).
235. K. G. Kleb, *Angew. Chem.*, **80**, 284 (1968).
236. B. T. Tozer and S. Smiles, *J. Chem. Soc.*, 1897 (1938).
237. B. Karele and O. Neilands, *Zh. Org. Khim.*, **4**, 634 (1968); *Chem. Abstr.*, **69**, 2626 (1968).
238. E. Zbiral, *Monatsch. Chem.*, **95**, 1759 (1964).
239. O. R. Rodig, R. E. Collier and R. K. Schlatzer, *J. Org. Chem.*, **29**, 2652 (1964).
240. J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 362 (1951).
241. W. E. Truce, T. C. Klingler and W. W. Brand, in Ref. 4, p. 564.
242. S. W. Schneller, *Int. J. Sulfur Chem.*, **8**, 569 (1976).
243. M. R. Crampton, *Adv. Phys. Org. Chem.*, **7**, 211 (1969); *Org. React. Mech.*, 281 (1980).
244. C. F. Bernasconi, *Acc. Chem. Res.*, **11**, 147 (1978).
245. T. Takahashi and Y. Maki, *Chem. Pharm. Bull.* (Tokyo), **6**, 369 (1958); *Chem. Abstr.*, 53, 9228 (1959).
246. W. E. Truce, W. J. Ray, Jr., O. L. Norman and D. B. Eickemeyer, *J. Amer. Chem. Soc.*, **80**, 3625 (1958).
247. C. S. McClement and S. Smiles, *J. Chem. Soc.*, 1016 (1937).
248. T. Okamoto and J. F. Bunnett, *J. Amer. Chem. Soc.*, **78**, 5357 (1956).
249. J. F. Bunnett and T. Okamoto, *J. Amer. Chem. Soc.*, **78**, 5363 (1956).
250. R. R. Coats and D. T. Gibson, *J. Chem. Soc.*, 442 (1940).
251. M. F. Grundon and B. T. Johnston, *J. Chem. Soc.* (*B*), 255 (1966).
252. P. Beak and V. Snieckus, *Acc. Chem. Res.*, **15**, 306 (1982).
253. H. Gilman and F. J. Webb, *J. Amer. Chem. Soc.*, **71**, 4062 (1949).
254. W. E. Truce and F. M. Amos, *J. Amer. Chem. Soc.*, **73**, 3013 (1951).
255. W. E. Truce and W. J. Ray, Jr., *J. Amer. Chem. Soc.*, **81**, 481 (1959).
256. W. E. Truce and W. J. Ray, Jr., *J. Amer. Chem. Soc.*, **81**, 484 (1959).
257. W. E. Truce and M. M. Guy, *J. Org. Chem.*, **26**, 4331 (1961).
258. W. E. Truce and E. J. Madaj, Jr., *Sulfur Reports*, **3**, 259 (1983).
259. W. E. Truce, C. R. Robins and E. M. Krieder, *J. Amer. Chem. Soc.*, **88**, 4027 (1966).
260. W. E. Truce and W. W. Brand, *J. Org. Chem.*, **35**, 1828 (1970).
261. V. N. Drozd, Kh. A. Pak and B. B. Gumenyuk, *Zh. Org. Khim.*, **6**, 157 (1970).
262. W. E. Truce, B. VanGemert and W. W. Brand, *J. Org. Chem.*, **43**, 101 (1978).
263. F. M. Stoyanovich, R. G. Karpenko and Ya. L. Goldfarb, *Tetrahedron*, **27**, 433 (1971).
264. V. N. Drozd, V. A. Sazonova and A. N. Nesmeyanov, *Dokl. Akad. Nauk SSSR*, **159**, 591 (1964); *Chem. Abstr.*, **62**, 7794g (1965).
265. V. N. Drozd, *Dokl. Akad. Nauk SSSR*, **169**, 107 (1966); *Chem. Abstr.*, **65**, 13646a (1966).
266. V. N. Drozd, L. A. Nikonova and M. A. Tsel'eva, *Zh. Org. Khim.*, **6**, 825 (1970); *Chem. Abstr.*, 13893d (1970).
267. V. N. Drozd and T. Yu. Frid., *Zh. Org. Khim.*, **3**, 373 (1967); *Chem. Abstr.*, **67**, 2586c (1967).
268. V. N. Drozd and V. I. Scheichenko, *Zh. Org. Khim.*, **3**, 554 (1967); *Chem. Abstr.*, **67**, 10965r (1967).
269. V. N. Drozd, L. I. Zefirova and U. A. Ustynyuk, *Zh. Org. Khim.*, **4**, 1794 (1968).
270. V. N. Drozd, Kh. A. Pak, and U. A. Ustynyuk, *Zh. Org. Khim.*, **5**, 1267 (1969); *Chem. Abstr.*, **71**, 100960x (1969).
271. V. N. Drozd, L. I. Zefirova and U. A. Ustynyuk, *Zh. Org. Khim.*, **5**, 1248 (1969); *Chem. Abstr.*, **71**, 101657r (1969).
272. V. N. Drozd and O. I. Trifonova, *Zh. Org. Khim.*, **7**, 2388 (1971).
273. V. N. Drozd and O. I. Trifonova, *Zh. Org. Khim.*, **7**, 1926 (1971).
274. V. N. Drozd and L. A. Nikonova, *Zh. Org. Khim.*, **5**, 1453 (1969).
275. V. N. Drozd and T. R. Saks, *Zh. Org. Khim.*, **9**, 2544 (1973).
276. V. N. Drozd, L. I. Zefirova, Kh. A. Pak and U. A. Ustynyuk, *Zh. Org. Khim.*, **5**, 933 (1969).
277. V. N. Drozd and L. A. Nikonova, *Zh. Org. Khim.*, **5**, 325 (1969).

278. G. P. Crowther and C. R. Hauser, *J. Org. Chem.*, **33**, 2228 (1968).
279. J. Lu, Ph.D. Thesis, Purdue University, 1980.
280. V. N. Drozd and Kh. A. Pak, *Zh. Org. Khim.*, **6**, 818 (1970).
281. V. N. Drozd, O. I. Trifonova and V. V. Sergeichuk, *Zh. Org. Khim.*, **9**, 156 (1973).
282. D. M. Snyder and W. E. Truce, *J. Amer. Chem. Soc.*, **101**, 5432 (1979).
283. D. M. Snyder, Ph.D. Thesis, Purdue University, 1980.
284. E. J. Madaj, Ph.D. Thesis, Purdue University, 1983.
285. E. J. Madaj, Jr., D. M. Snyder and W. E. Truce, *J. Amer. Chem. Soc.*, **108**, 3466 (1986).
286. S. Winstein, S. Smith and D. Darwish, *Tetrahedron Letters*, 24 (1959).
287. F. G. Bordwell, P. F. Wiley and T. G. Mecca, *J. Amer. Chem. Soc.*, **97**, 132 (1975).
288. S. F. Nelsen and P. D. Bartlett, *J. Amer. Chem. Soc.*, **88**, 137 (1966).
289. G. Wittig and L. Löhmann, *Justus Liebigs Ann. Chem.*, **550**, 260 (1942).
290. J. F. Garst and C. D. Smith, *J. Amer. Chem. Soc.*, **98**, 1526 (1976).
291. J. F. Biellmann and J. L. Schmitt, *Tetrahedron Letters*, 4615 (1973).
292. H. M. Walborsky, *Tetrahedron*, **37**, 1625 (1981).
293. D. E. Applequist and J. H. Klung, *J. Org. Chem.*, **43**, 1729 (1978).
294. (a) N. Kornblum, in *The Chemistry of Functional Groups; Supplement F: The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives* (Ed. S. Patai), Wiley, New York, 1982, p. 361.
(b) N. Kornblum, *Angew. Chem., Int. Ed. Engl.*, **14**, 734 (1975).
295. J. F. Bunnett, *Acc. Chem. Res.*, **11**, 413 (1978).
296. J. F. King and D. R. K. Harding, *J. Chem. Soc., Chem. Commun.*, 959 (1971).
297. A. Heesing, W. Kleine-Homann and W. Müllers, *Chem. Ber.*, **113**, 152 (1980).
298. L. D. Martin and J. C. Martin, *J. Amer. Chem. Soc.*, **99**, 3511 (1977).
299. P. D. Bartlett, T. Aida, H.-K. Chu and T.-S. Fang, *J. Amer. Chem. Soc.*, **102**, 3515 (1980).
300. Y. Sawaki and Y. Ogata, *J. Amer. Chem. Soc.*, **103**, 5947 (1981).
301. C. Gu, C. S. Foote and M. L. Kacher, *J. Amer. Chem. Soc.*, **103**, 5949 (1981).
302. W. Ando, *Sulfur Rep.*, **1**, 147 (1981).
303. K. Schank, *Chem. Ber.*, **103**, 3087 (1970); Ref. 9, p. 1161.
304. H. Kropf, M. Ball and A. Gilberg, *Justus Liebigs Ann. Chem.*, 1013 (1974).

CHAPTER 14

Rearrangements involving sulfoxides

SAMUEL BRAVERMAN

Department of Chemistry, Bar-Ilan University, Ramat-Gan 52100, Israel

I. INTRODUCTION

Rearrangements involving sulfoxides have played an important role in the development of the chemistry of sulfoxides. It is therefore not surprising that all major literature surveys on sulfoxides[1–8], or their sulfenate precursors[9,10], also include a discussion of this subject. However, while excellent and detailed coverage exists for certain rearrangements of general mechanistic and synthetic interest, such as, for example, the Pummerer[8,11–14] or the related penicillin sulfoxide–cephalosporin[15–17] rearrangement, the treatment of all

other rearrangements is usually brief and partial. An attempt has therefore been made to provide the reader with a comprehensive and systematic survey of the literature dealing with rearrangements involving sulfoxides, most of which have never been reviewed before. An effort has also been made to scan the literature through 1986, as far as possible, and to cover the most significant aspects and most important advances, particularly work of the last two decades. At the same time, however, since the Pummerer reaction is not unanimously considered a rearrangement[8,11], and since the subject has been recently and extensively reviewed[8,11–14] and since there seems no merit in reiterating other authors' compilations, the review in hand does not include this reaction. The same applies for the related conversion of penicillin sulfoxides to cephalosporins[15–17].

Rearrangements have been included in which sulfoxides participate not only as reactants but also as products. Reactions have been classified according to mechanism, but although the main emphasis has been on mechanism and stereochemistry, special attention to synthetic applications has also been given wherever appropriate.

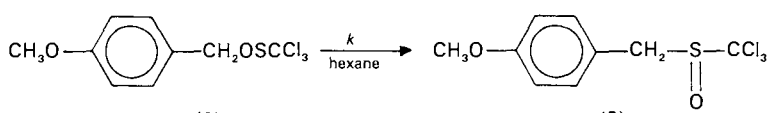
To a certain extent, the phenomenal expansion of organosulfur chemistry in recent years is also reflected in this review. It is hoped that this chapter, which is intended to serve all chemists, experts and students alike, will help them include its knowledge in their research programmes, and will stimulate further creative work in the area.

II. REARRANGEMENTS OF SULFENATES TO SULFOXIDES

A. The Rearrangement of Benzylic Sulfenates to Sulfoxides

In recent years considerable interest has been focused on the thermal sulfenate–sulfoxide interconversion, not only because of its mechanistic and stereochemical interest but also because of its remarkable synthetic utility. However, most of the work performed has centered around the rearrangement of allylic and propargylic sulfenates, which proceeds by an unusually facile concerted [2,3]-sigmatropic shift, as described in the following two subsections. When this mechanism is not available, the sulfenate–sulfoxide isomerization becomes much more difficult and has only been observed in certain selected systems. This phenomenon, which is in contrast with the relatively facile and well-studied sulfinate-to-sulfone rearrangement (see chapter on Rearrangements Involving Sulfones), may be attributed to the low acidity and general instability of sulfenic acids[18] as well as to the comparably reduced gain in energy in the analogous sulfenate-to-sulfoxide isomerization[19]. It therefore follows that if the sulfenate ester is derived from a particularly acidic sulfenic acid and it can generate a stable carbonium ion, then isomerization to the sulfoxide by an ionization mechanism should become possible.

Braverman and Sredni[20] have reported that *p*-methoxybenzyl trichloromethanesulfenate (**1**) undergoes a facile thermal rearrangement to the corresponding sulfoxide (**2**) on heating in highly nonpolar solvents (equation 1).

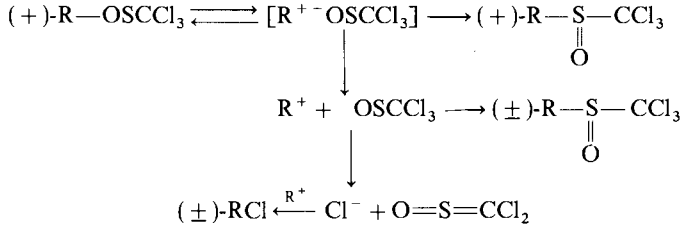


(1) (2) (1)

$[k = 3.4 \times 10^{-4} s^{-1}\ (77\,^{\circ}C);\ \Delta H^{\ddagger} = 28\,kcal\,mol^{-1};\ \Delta S^{\ddagger} = 5\,eu]$

Benzhydryl trichloromethanesulfenate rearranged to the corresponding sulfoxide after 10 min of reflux of a hexane solution, while the benzyl ester remained practically unchanged even after heating for 24 h at 120 °C in benzene. Isomerization of optically active (−)-α-phenylethyl trichloromethanesulfenate, $[\alpha]_D^{20} = -20.5^{\circ}$ on heating in

hexane yielded (−)-α-phenylethyl trichloromethyl sulfoxide, $[\alpha]_D^{20} = -17.8°$. The rate of disappearance of **1** is dramatically enhanced by an increase in the ionizing power of the solvent. For example, substitution of the hexane by chloroform, under similar conditions, leads to the formation of a mixture composed of *p*-methoxybenzyl chloride and the sulfine $Cl_2C{=}S{=}O$ (70%, each) and the sulfoxide **2** (30%), while the use of more polar solvents such as methylene chloride or acetonitrile leads to the almost exclusive formation of the first products. Reaction of the optically active α-phenylethyl ester in acetonitrile gave racemic chloride. To explain all these observations, the authors[20] have suggested the mechanism shown in equation 2.



(2)

Initial dissociation of the sulfenate ester yields an ion pair, which in highly nonpolar solvents like hexane undergoes rapid recombination to yield sulfoxide with retention of optical activity. While ion-pair mechanisms in nonpolar solvents are known in the literature[21] the observation of such a mechanism for the rearrangement of sulfenates to sulfoxides is apparently unprecedented and has only been observed with the solvolysis of the same ester as well[22]. Undoubtedly this may be attributed to the relatively high acid strength of Cl_3CSOH, and the consequent high leaving group ability of its anion as compared to sulfenate anions in general[18]. In more polar solvents, the rate of ionization of the sulfenate and the lifetime of the ion pair are increased to the point that further dissociation to dissociated ions, as well as decomposition of the Cl_3CSO^- ion to chloride ion and dichlorosulfine can occur[23,24]. Capture of R^+ by either Cl^- or Cl_3CSO^- gives racemic products.

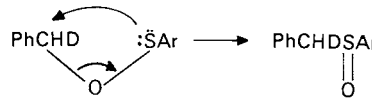
In continuation, Braverman and Manor[25] examined the reactivity of the analogous *p*-methoxybenzyl trifluoromethanesulfenate. Surprisingly, unlike ester **1**, this ester remained completely unchanged even after prolonged heating in hexane or acetonitrile (3 days at 100 °C), and failed to rearrange to the corresponding sulfoxide or fluoride, as expected. Similarly, in contrast to ester **1** which undergoes facile ethanolysis with complete C—O bond cleavage by an ion-pair mechanism[22], the ethanolysis of the trifluoro analog at 0° involves complete S—O bond fission by an S_N2-type mechanism. In view of the practical identity between the inductive effects of the trifluoro- and trichloromethyl groups, as reflected by their substituent constants and acid strengthening effects[26], and in view of the similarity in reactivity between benzyl trichloro- and trifluoromethanesulfinates[27,28] with regard to both rearrangement to sulfone and solvolysis, the lack of rearrangement of *p*-anisyl trifluoromethanesulfenate is at present difficult to explain.

The rearrangement of benzyl *p*-toluenesulfenate (**3**) to the corresponding sulfoxide (**4**, equation 3) has been reported by Mislow and coworkers[29,30] but it is much slower than the isomerization of **1** discussed above. However, in view of the complete inertness of the corresponding trichloromethanesulfenate under similar conditions, the operation of an ionization mechanism for this isomerization may be excluded. Although a radical-pair mechanism has also been considered for this rearrangement[29,31], it was rejected in favor of a concerted intramolecular mechanism (equation 4) on the basis of the negative entropy of activation and the partial (35%) retention of configuration at carbon observed in the rearrangement of (−)-(*R*)-benzyl-α-d *p*-toluenesulfenate to (+)-benzyl-α-d *p*-tolyl

sulfoxide[30].

$$\underset{(3)}{PhCH_2OS\text{-}Tol\text{-}p} \xrightarrow[PhH]{k_1} \underset{(4)}{PhCH_2S(=O)\text{-}Tol\text{-}p} \qquad (3)$$

$$[k = 8.7 \times 10^{-5}\,s^{-1}\,(120\,^{\circ}C);\ \Delta H^{\ddagger} = 29.7\,kcal\,mol^{-1};\ \Delta S^{\ddagger} = -2\,eu]$$



(4)

Besides the feeling that a process such as that shown in equation 4 should result in a considerably higher retention of configuration at carbon than 35%, our understanding is further complicated by the fact that while sulfenate **3** rearranges to sulfoxide, the corresponding methanesulfenate, $PhCH_2OSMe$, which should behave analogously, does not isomerize to the sulfoxide on heating but instead decomposes to a complex mixture of products by a free-radical mechanism initiated by homolytic fission of the C—O bond[30].

Interestingly, the somewhat analogous benzyl sulfoxylate (**5**) has been reported to readily undergo rearrangement in low yield to benzyl α-toluenesulfinate (**6**) during preparation (equation 5)[32].

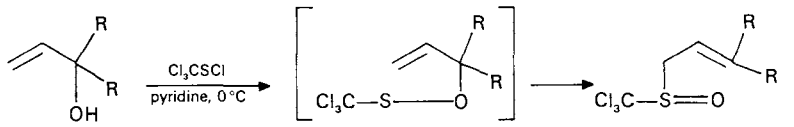
$$\underset{}{PhCH_2OH} \xrightarrow[Et_3N]{SCl_2,\ CH_2Cl_2} \underset{(5)}{[(PhCH_2O)_2S]} \longrightarrow \underset{(6)}{PhCH_2S(=O)\text{—}OCH_2Ph} \qquad (5)$$

B. The Reversible [2,3]-Sigmatropic Rearrangement of Allylic Sulfenates to Sulfoxides

Since its discovery two decades ago, the reversible interconversion of allylic sulfenates to sulfoxides has become one of the best known [2,3]-sigmatropic rearrangements. Certainly this is not only because of the considerable mechanistic and stereochemical interest involved, but also because of its remarkable synthetic utility as a key reaction in the stereospecific total synthesis of a variety of natural products such as steroids, prostaglandins, leukotrienes, etc.

1. Mechanism

As a continuation to the studies by Darwish and Braverman[33,34] on the [2,3]-sigmatropic rearrangement of allylic sulfinates to sulfones, and in view of its remarkable facility and stereospecificity (see Chapter 13), Braverman and Stabinsky[34–38] investigated the predictable analogous rearrangement of allylic sulfenates to sulfoxides, namely the reverse rearrangement of that attempted by Cope and coworkers[39]. These authors[35–38] initiated their studies by the preparation of the claimed 'allyl trichloromethanesulfenate' using the method of Sosnovsky[40]. This method involves the reaction between trichloromethanesulfenyl chloride and allyl alcohol in ether at 0 °C, in the presence of pyridine (equation 6).



(6)

(7) (a) R = H (8) a, b

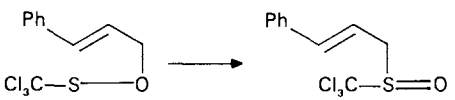
(b) R = Me

However, IR and NMR spectral data indicated beyond doubt that the product isolated by these authors, even on lowering the temperature of esterification to $-70°$, was allyl trichloromethyl sulfoxide (**8a**) and not allyl trichloromethanesulfenate (**7a**) as claimed[40]. This observation indicates that the initially formed ester undergoes spontaneous rearrangement to sulfoxide. Similarly, the attempted preparation of α,α-dimethylallyl trichloromethanesulfenate (**7b**) afforded γ,γ-dimethylallyl trichloromethyl sulfoxide (**8b**), thus proving the occurrence of a simultaneous 1,3-allylic shift.

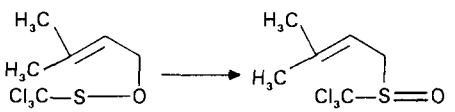
The enhanced rate of rearrangement of allyl trichloromethanesulfenate, which proceeds spontaneously at low temperature, as compared to allyl 2,6-dimethylbenzenesulfinate, which has a half-life of 23 days at 90 °C in THF, may be assigned to the greater nucleophilicity of the sulfur atom in the sulfenate ester. This observation, in connection with the evidence previously described for the rearrangement mechanism of allylic sulfinates, may be used as supporting evidence for a concerted [2,3]-sigmatropic cyclic intramolecular mechanism for the sulfenate–sulfoxide rearrangement.

The driving force for the sulfenate–sulfoxide as well as for the sulfinate–sulfone rearrangements is derived from the strong sulfur–oxygen bond formation in the products[14]. However, the formation of the second S=O bond in the sulfone is thermodynamically preferred by 22 kcal mol^{-1} over the S=O bond formation in the corresponding sulfoxide[19]. As a result, the driving force for the sulfenate–sulfoxide isomerization is considerably smaller than that for the sulfinate–sulfone isomerization. The following results show that the driving force is actually so small that interfering factors would cancel out its effect.

In contrast to the allylic sulfenates mentioned so far, cinnamyl trichloromethanesulfenate (**9**), prepared by the usual method, can be isolated and is relatively stable. Furthermore, its rearrangement to cinnamyl trichloromethyl sulfoxide (i.e., without allylic isomerization, equation 7), proceeds at a relatively slow rate (in CCl_4 at 80.0 °C, $k = 3.90 \times 10^{-5}\ s^{-1}$). This result also contrasts with the observation mentioned earlier that cinnamyl arenesulfinate rearranges to α-phenylallyl aryl sulfone[33,34]. Similar behavior has been detected for γ,γ-dimethylallyl ester **11** which undergoes thermal isomerization to sulfoxide **12** (equation 8)[36–38].



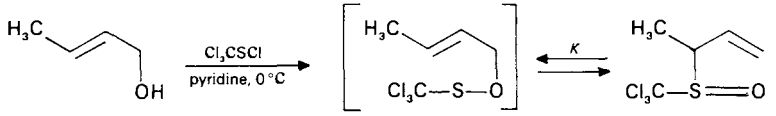
(9) (10) (7)



(11) (12) (8)

The authors have suggested[34] that the failure of the last two sulfenates to undergo allylic rearrangement has its source in thermodynamic rather than kinetic factors. Thus, the expected isomerization of cinnamyl sulfenate to α-phenylallyl sulfoxide would have resulted in a loss of conjugation energy as well as increased steric interactions between the phenyl group and the relatively large trichloromethyl group. Similarly, in the case of γ,γ-dimethylallyl sulfenate, rearrangement to α,α-dimethylallyl sulfoxide would result in even greater steric interactions and loss of hyperconjugation energy. The allylic rearrangement could thus be prevented by an increase in the free energy of the sulfoxide, exceeding the gain in free energy obtained by the sulfenate–sulfoxide rearrangement. On the other hand, the rearrangement to sulfoxide without allylic shift is practically unaffected by these conjugative and steric effects. In view of the similarity in reactivity between the cinnamyl and *p*-anisyl sulfenates **9** and **1** and the conversion of both to the corresponding chlorides and dichlorosulfine in polar solvents[20], it is not unlikely that the rearrangement of **9** to **10** also proceeds by an ion-pair mechanism.

Between these two extremes of spontaneous rearrangement and total failure to rearrange, Braverman and Stabinsky[36–38] have observed intermediate behavior. The reaction of crotyl alcohol with Cl_3CSCl afforded an equilibrium mixture of both crotyl trichlormethanesulfenate (**13**) and α-methylallyl trichloromethyl sulfoxide (**14**, equation 9).



(9)

(**13**) (**14**)

NMR measurements indicate that the equilibrium constant varies with the polarity of the solvent and temperature. The more polar the solvent, the greater the fraction of sulfoxide at equilibrium which is consistent with the greater dipole moment of the sulfoxide as compared with the sulfenate. Increasing temperature results in a reverse effect, due to the steric hindrance in the sulfoxide which becomes more marked at higher temperatures. These results are the first published evidence for the reversibility of the sulfenate–sulfoxide rearrangement and illustrate the occurrence of the rearrangement unsuccessfully attempted by Cope[39].

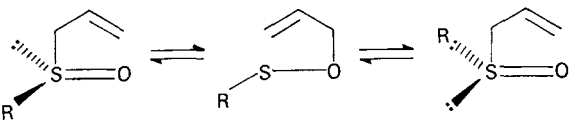
We have seen that allyl sulfenate **7a** undergoes spontaneous rearrangement to the corresponding sulfoxide, while substitution of a γ-hydrogen by a methyl group caused a decrease in the ΔG° of the reaction. This decrease could be attributed to a loss in hyperconjugation energy or to increased steric interactions in the sulfoxide. In order to determine which is the predominant effect, the preparation of α,γ-dimethylallyl trichloromethanesulfenate was undertaken[36,38]. The product obtained was an equilibrium mixture of sulfenate and sulfoxide which behaved as described above for the crotyl case. The fraction of sulfoxide at equilibrium was somewhat lower than that in the previous case, although the formation of the present sulfoxide is not accompanied by any loss of hyperconjugation energy. This fact indicates that the main factor responsible for the observed results with γ-substituted allylic sulfenates is a steric one rather than hyperconjugation. A relevant study has been reported by Fava[42,43] in connection with the rearrangement of allylic thiocyanates to isothiocyanates which has been suggested to proceed by a similar cyclic intramolecular mechanism.

In summary, the evidence described above demonstrates three main mechanistic features of the rearrangement of allylic sulfenates to sulfoxides: (1) spontaneous and wholly concerted [2,3]-sigmatropic shift of allyl or α-substituted allyl esters (**7** a, b) at one extreme; (2) complete stability of the γ-aryl and γ,γ-dialkyl substituted allyl sulfenates as well as

rearrangement *without* [2,3]-sigmatropic shift at the other extreme (equations 9 and 11); and (3) intermediate behavior of γ-alkylallyl sulfenates which rearrange by a facile reversible [2,3]-sigmatropic shift as illustrated in equation 9.

The observations of the interconversion of allylic sulfenates and sulfoxides made by Braverman and Stabinsky[34–38] are confirmed by the work of Mislow and coworkers[44–47] who approached the problem from a different angle, namely, enhanced racemization of optically active allylic sulfoxides.

In order to account for the unusually facile thermal racemization of optically active allyl *p*-tolyl sulfoxide (**15** R = *p*-Tol) whose rate of racemization is orders of magnitude faster than that of alkyl aryl or diaryl sulfoxides as a result of a comparably drastically reduced $\Delta H^{\ddagger}$ (22 kcal mol^{-1}), Mislow and coworkers[44] suggested a cyclic (intramolecular) mechanism in which the chiral sulfoxide is in mobile equilibrium with the corresponding achiral sulfenate (equation 10).



(*S*)-(**15**) (**16**) (*R*)-(**15**) (10)

In order to test the proposed mechanism, these authors[44] attempted the preparation of allyl *p*-toluenesulfenate (**16**) by reaction of *p*-toluenesulfenyl chloride with lithium alcoholate, but obtained instead the rearranged product **15**, directly. The authors concluded that the rearrangement proceeded by a concerted 1,3-allylic shift, since reaction of *p*-toluenesulfenyl chloride with lithium crotyl alcoholate and lithium α-methylallyl alcoholates afforded α-methylallyl and crotyl *p*-tolyl sulfoxides, respectively. Although this report[44] slightly preceded that by Braverman and Stabinsky[35], it only contained information with regard to the spontaneous rearrangement of sulfenates to sulfoxides, without mentioning the possible existence of *stable* sulfenates such as **9** or **11**, or a *detectable* equilibrium between sulfenates and sulfoxides such as shown in equation 9. Nevertheless, with just a few exceptions[8,52] the other group[44] is usually granted exclusive credit for the discovery of this [2,3]-sigmatropic rearrangement[60] and sometimes the process is also named the Mislow Rearrangement.[105]

Subsequently, these authors have also studied the effect of polar factors on the sulfenate–sulfoxide equilibrium and obtained similar results to those reported by Braverman and coworkers[34–38]. For example, reaction of 2,4-dinitrobenzenesulfenyl chloride with lithium allyl-α-d_2 alcoholate gives only[46] (or perhaps mainly[47]) allyl-α-d_2 2,4-dinitrobenzenesulfenate, whereas the corresponding reaction with 4-nitrobenzenesulfenyl chloride results in complete (> 99%) rearrangement to the sulfoxide. However, when a single nitro group is located in the *ortho* position, the ratio (*K*) of sulfenate to sulfoxide approaches unity. This ratio is also affected by the polarity of the solvent and changes from 1.43 in CCl_4 to 0.39 in chloroform, consistent with the results described above for the equilibrium shown in equation 9.

It thus appears that strongly electron-withdrawing substituents, attached to the sulfur, shift the equilibrium more toward the sulfenate[48], presumably by destabilizing the sulfoxide by their inductive effect, while an increase in the polarity of the solvent shifts the equilibrium back toward the sulfoxide. The remarkable sensitivity of the sulfenate-to-sulfoxide equilibrium to structure and solvent effects are easily explained by the rather low ΔG° value of 2.9 kcal mol^{-1} at 25 °C as calculated from the activation parameters of the allyl *p*-trifluoromethyl benzylsulfenate to allyl *p*-trifluoromethylphenyl sulfoxide rearrangement, $\Delta H^{\ddagger}$, 18.8 kcal mol^{-1}; $\Delta S^{\ddagger}$, −4.8 eu; and racemization of allyl *p*-trifluoromethylphenyl sulfoxide; $\Delta H^{\ddagger}$, 21.2 kcal mol^{-1}; $\Delta S^{\ddagger}$, −8.0 eu (benzene solvent)[47]. This of course means that, while the amount of sulfenate present at equilibrium is indeed

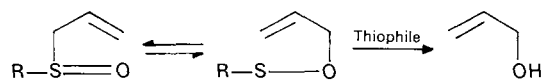
very small (< 1%), the free energy of the sulfenate is at the same time not much greater than that of the sulfoxide.

In conclusion, it may be noted that the pioneering investigations by both the Mislow and Braverman groups have contributed to the elucidation of the mechanism of this concerted [2,3]-sigmatropic rearrangement, and have thus laid the ground for the following stereochemical and synthetic studies.

2. *Stereochemistry and synthetic applications*

As previously mentioned, the remarkable popularity which the reversible [2,3]-sigmatropic rearrangement of allylic sulfenates to sulfoxides has enjoyed, is primarily a consequence of its high stereoselectivity. To cite Isobe[49], 'the synthetic utility of allylic alcohol-forming [2,3]-sigmatropic rearrangement of allylic aryl sulfoxides has recently been demonstrated by us and others as a key reaction for stereospecific total syntheses of natural products'. Because of the intensive activity on this subject, two excellent reviews have been published by Hoffmann[50,51] who has also made very significant contributions to the analysis and elucidation of the stereochemistry of this rearrangement. In addition, shorter presentations of the subject have appeared in general reviews on stereochemistry of organosulfur compounds[52–55] or sigmatropic rearrangements[56].

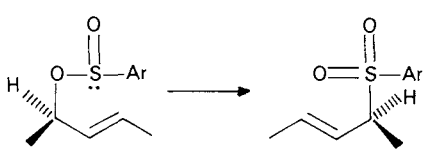
Owing to the reversible nature of the allylic sulfenate/allylic sulfoxide interconversion, the stereochemical outcome of both processes is treated below in an integrated manner. However, before beginning the discussion of this subject it is important to point out that although the allylic sulfoxide–sulfenate rearrangement is reversible, and although the sulfenate ester is usually in low equilibrium concentration with the isomeric sulfoxide, desulfurization of the sulfenate by thiophilic interception using various nucleophiles, such as thiophenoxide or secondary amines, removes it from equilibrium, and provides a useful route to allylic alcohols (equation 11).



(11)

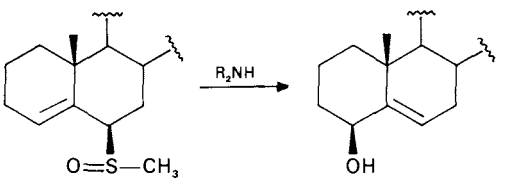
Although the interception of allylic sulfenates in the manner described by equation 11 was first observed by Abbott and Stirling[57], the general value of this transformation and its remarkable synthetic potential has been recognized by Evans and coworkers[58], who have also introduced the previously used[59] trimethyl phosphite as a preferable trapping agent. An early review of the synthetic utility of the reversible allylic sulfoxide–sulfenate rearrangement has also been published by Evans and Andrews[60].

a. 1 → 3 chirality transfer. The characteristic 1 → 3 chirality transfer accompanying the reversible allylic sulfenate–sulfoxide rearrangement could be predicted by the previously observed quantitative 1 → 3 chirality transfer in the analogous [2,3]-sigmatropic rearrangement of allylic sulfinates to sulfones (equation 12)[33,34], as required by the suprafacial course of rearrangement and observed with other [2,3]-sigmatropic shifts as well[61–63]. This prediction has been completely borne out by experiment in a variety of stereospecific transformations of allylic sulfoxides derived from natural products to corresponding alcohols, by thiophilic trapping and cleavage of intermediate sulfenates, as shown below.

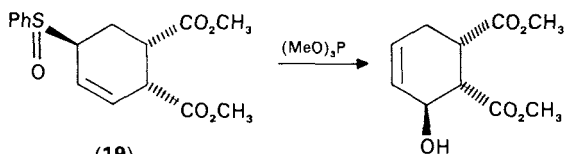


(12)

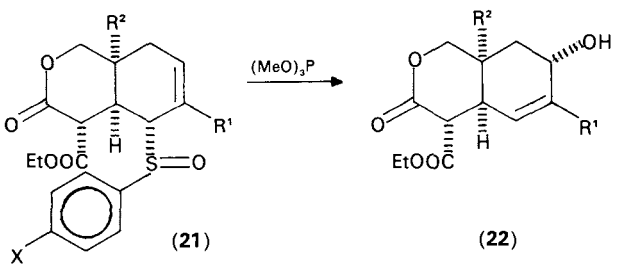
One of the first uses of the allylic sulfoxide–sulfenate interconversion was made by Jones and coworkers[64], who reported exclusive suprafacial rearrangement of the allyl group in the steroidal sulfoxide **17** shown in equation 13. Two other examples are shown in equations 14[65] and 15[66]. Evans and coworkers have demonstrated the utility of the suprafacial allylic sulfoxide–sulfenate rearrangement in a new synthesis of the tetracyclic alcohol **24** (equation 16)[67], as well as in a synthesis of prostaglandin intermediates as shown in equation 17[68]. The stereospecific rearrangement of the unstable sulfenate intermediate obtained from the *cis* diol **25** indicates the suprafacial nature of this process.



(17) (18) (13)

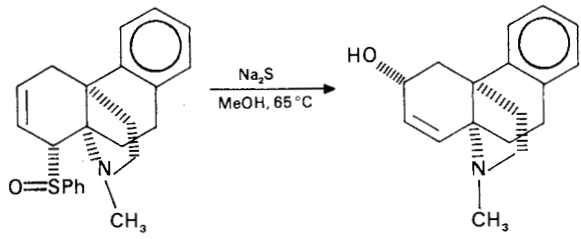


(19) (20) (14)



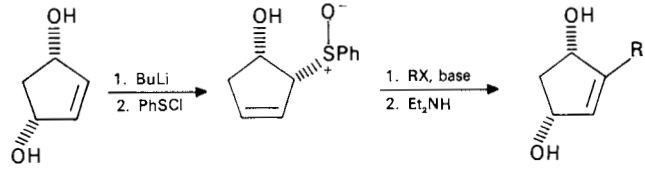
(21) (22) (15)

A number of investigators[69–72] have used the facile and stereospecific [2,3]-sigmatropic rearrangement of allylic sulfoxides, such as **27**, to construct the prostaglandin side-chain with the correct configuration (equation 18)[72]. These studies were preceded by a similar study by Untch, Stork and their coworkers[73], which represents one of the first and most remarkable uses of the reversible allylic sulfenate–sulfoxide interconversion. These authors have shown that the inversion of configuration of both the chiral and geometric centers in compound **29** could be accomplished concomitantly via the corresponding sulfenate ester which rearranges to sulfoxide **30**. Treatment of the latter with trimethyl phosphite provides the prostaglandin of natural configuration (**31**). The two-step sequence **29** → **30** → **31** proceeds with complete stereospecificity and in yields exceeding 85% (equation 19). The *E* preference in the **29** → **30** transformation results from the relative thermodynamic stabilities of the transition states, and is further explained below. More recently, the synthesis of some prostaglandin analogues[74] and other natural products[75–78] using the stereospecific sulfoxide–sulfenate rearrangement have also been published.



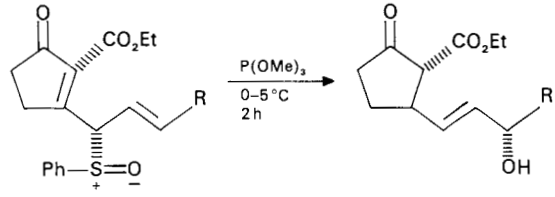
(16)

(23) (24)



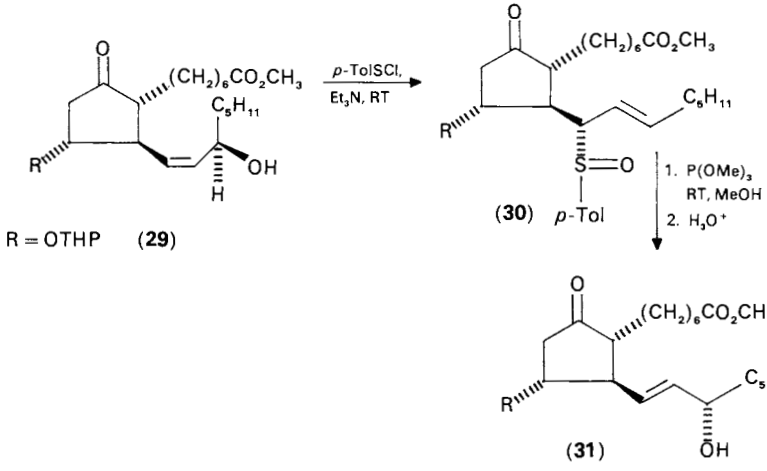
(17)

(25) (26)



(18)

(27) (28)

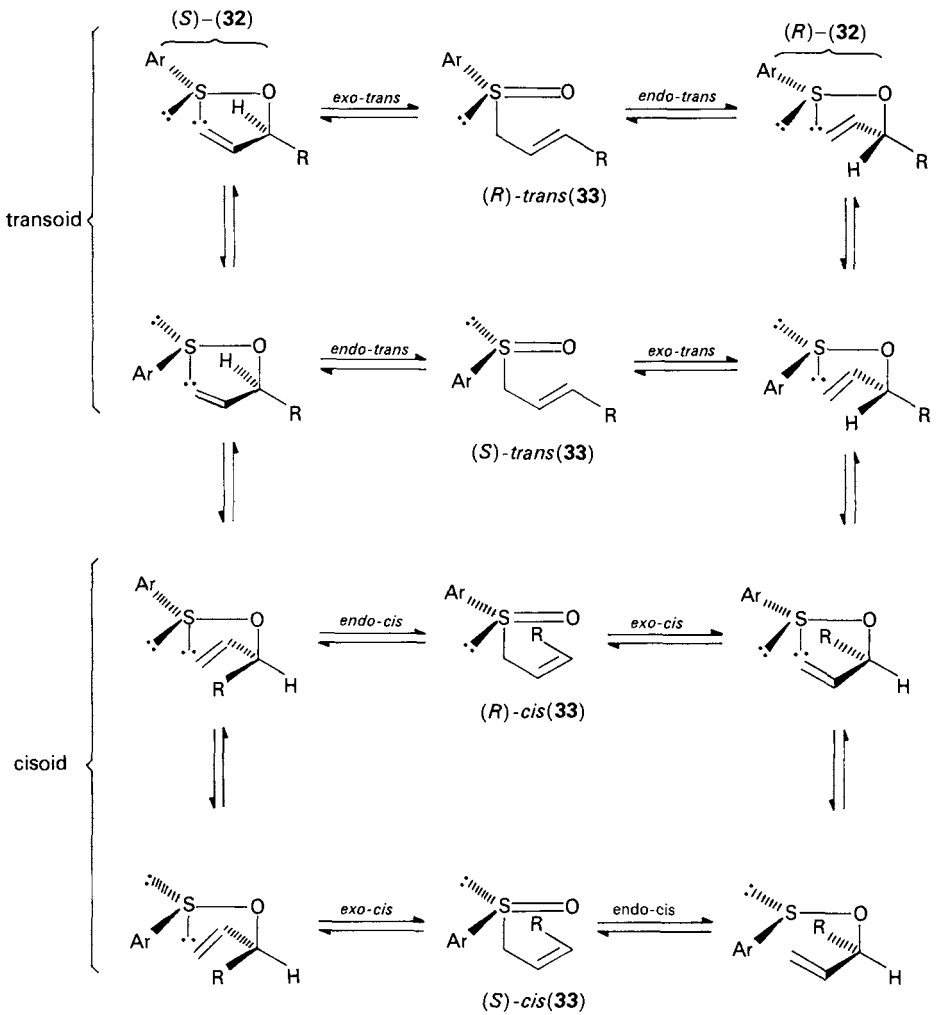


(19)

R = OTHP (29) (30) (31) R=OH

b. Transfer of chirality to and from a chiral sulfur. In addition to the 1→3 transfer of chirality discussed in the preceding subsection, the reversible [2,3]-sigmatropic rearrange-

ment of allylic sulfenates to sulfoxides also presents the opportunity for the transfer of chirality from carbon to sulfur, and vice-versa. Both phenomena have been described. For example, Mislow and coworkers[46] reported that rearrangement of (*S*)-α-methylallyl *p*-toluenesulfenate (**32**, R = Me) to (*S*)-(−)-*trans*-crotyl *p*-tolyl sulfoxide (**33**, R = Me) proceeds with at least 37% ee (Scheme 1). The relatively low stereospecificity observed in this case of transfer of chirality from carbon to sulfur has been explained by loss of configurational purity through leakage via competitive and readily interconvertible transition states, which differ only in conformation, as well as due to the reversibility of the sulfenate–sulfoxide rearrangement. These factors are also responsible for the rapid

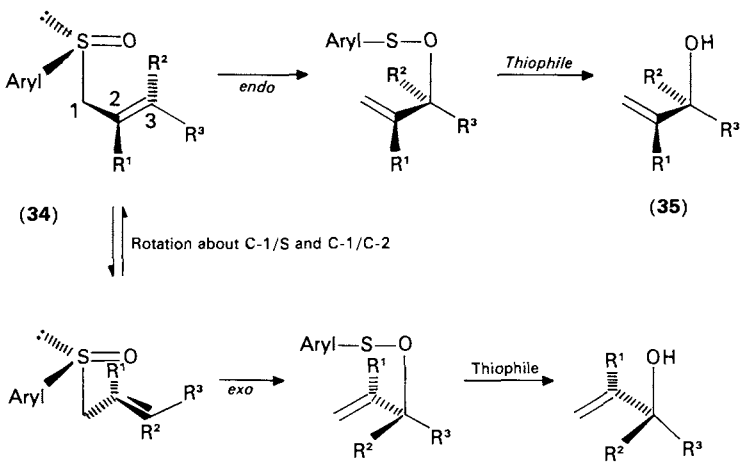


R = Me, Ar = *p*-Tolyl

SCHEME 1

racemization of the product (e.g. at 29 °C, $t_{1/2}$ = 51 min in toluene) and its equilibration to a mixture of racemic *trans*-(77%) and *cis*-(23%) crotyl *p*-tolyl sulfoxides, over a period of days. Using the concept of cisoid and transoid transition states introduced by Mislow[46] and that of *exo* and *endo* transition states suggested by Rautenstrauch[79], Hoffmann and coworkers[80] have presented a schematic interpretation of these results as depicted in Scheme 1.

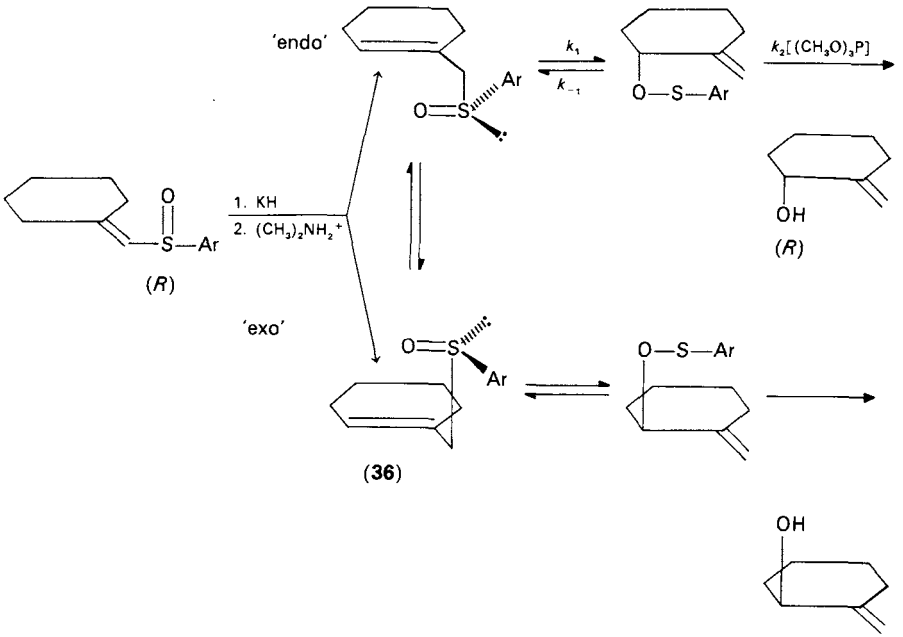
The transfer of chirality from sulfur to carbon in the rearrangement of optically active allylic sulfoxides has been thoroughly investigated and described in a series of papers by Hoffmann and coworkers[50,51,80–85] as a method for the asymmetric synthesis of allylic alcohols. Since previous studies have indicated that 1→3 chirality transfer usually dominates over sulfur-to-carbon chirality transfer, the latter can only be studied with allyl sulfoxides which are either unsubstituted, or bear identical substituents at the α-carbon of the allyl group. As pointed out by Hoffmann[51], the rearrangement of an allyl sulfoxide of a given configuration such as **34** can proceed through two diastereomeric transition states designated '*exo*' and '*endo*' and afford enantiomeric forms of allyl alcohol **35** (equation 20). The extent of S→C chirality transfer will be determined by the difference in energy between these two transition states. However, since allyl sulfoxides readily undergo racemization, often even at room temperature via the sequence shown in Scheme 1, both transition states are accessible.



(20)

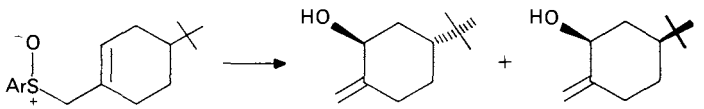
In a typical example, rearrangement of the (*R*)-(*E*)-sulfoxide **34** ($R^1 = R^2 = H$, $R^3 = C_5H_{11}$) gave (*R*)-(−)-1-octene-3-ol of only 29% optical purity, while rearrangement of (*R*)-(*Z*)-**34** ($R^1 = R^3 = H$, $R^2 = C_5H_{11}$) gave (*S*)-(+)-1-octene-3-ol with greater than 80% optical purity. These results indicate that the predominant transition state conformation in both cases is *endo*, and that the energy difference between *exo* and *endo* conformations for the (*E*)-sulfoxide is small (~ 0.5 kcal mol^{-1}) but considerably larger (~ 1.5 kcal mol^{-1}) for the (*Z*)-isomer[80], due to unfavorable steric interactions between the aryl group and the R^2 substituent in the *exo* conformation. Similar results were also obtained with γ,γ-dimethylallyl aryl sulfoxides[86].

In contrast to these results, a preference for rearrangement through an *exo*-transition state has been detected in the rearrangement of several cyclic allylic sulfoxides. For example, while sulfoxide **36** rearranged to alcohol **37** with 60% ee, introduction of bulky substituents at the β position of the ring enhanced the optical purity to 90%, as a result of further destabilization of the *endo* conformation (equation 21)[82,84].



(21)

Rearrangement of sulfoxides **38a, b** exhibited the interplay of several conformational factors. Both diastereomers afford predominant *axial* (*trans*) alcohol, but with opposite absolute configuration. The (*R*, *R*)-diastereomer strongly prefers the *exo*-transition state, whereas the (*R*, *S*)-isomer prefers the *endo* conformation. Hoffmann interprets these results in terms of an approximately 3-fold preference for the *exo*-transition state but a 6-fold preference for formation of an axial bond, these effects reinforcing each other in one isomer but opposing each other in the second.

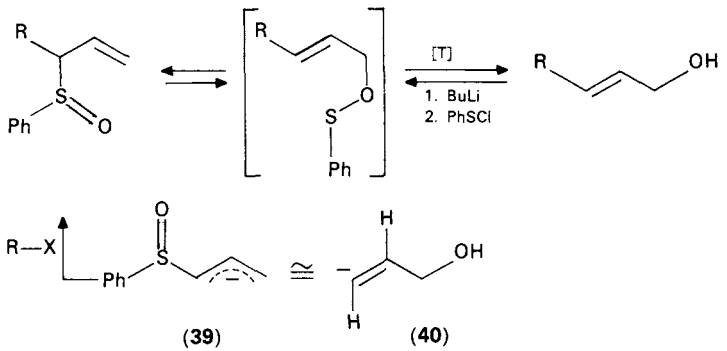


(**38a**) (*R*, *R*) ⟶ 95% (1*S*, 5*R*) + 5% (1*R*, 5*R*)

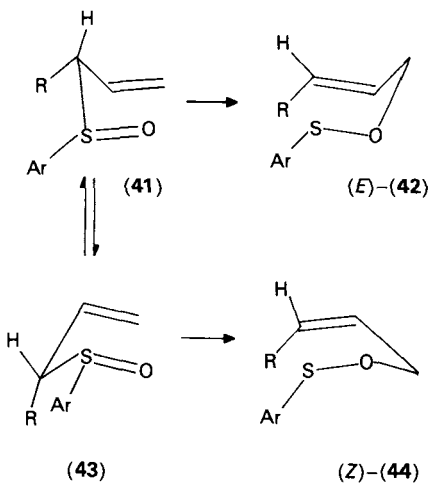
(**38b**) (*R*, *S*) ⟶ 65% (1*R*, 5*S*) + 35% (1*S*, 5*S*)

c. Configuration of the double bond. One of the first synthetic applications of the allylic sulfoxide–sulfenate interconversion has been a general stereoselective synthesis of allylic alcohols of defined double-bond geometry. For convenience, the discussion below will first deal with the stereoselectivity of 1,2-disubstituted, and next with trisubstituted olefins. Evans and coworkers[58,60,87] have first demonstrated the synthetic utility of the completely reversible allylic sulfoxide–sulfenate rearrangement as a potential new allylic alcohol synthesis, as illustrated in equation 22. This functional group transposition operation also demonstrates the utility of the relatively stable allylic sulfoxide anion **39** as a synthetic equivalent for the hypothetical vinyl anion **40**. In addition to its mildness and

efficiency this allylic alcohol synthesis also leads, with a high degree of selectivity (> 95%) via the transoid transition state (**41**), to products of the *E* configuration. The high degree of stereoselectivity observed is easily rationalized by examination of the envelope conformation for the five-membered cyclic transition state (equation 23) which indicates that an *R* substituent in the α-carbon atom in the sulfoxide should prefer the equatorial position, leading to the production of *E*-alkenes. This stereoselectivity, which is independent of stereochemistry at sulfur[50,51], has subsequently been confirmed by other investigators as well[77,88–90].



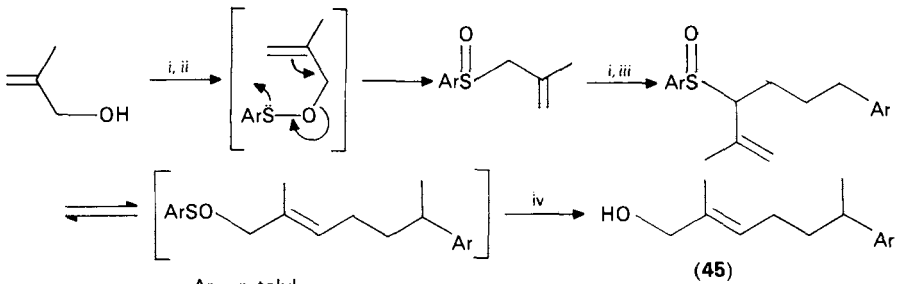
(22)



(23)

Although the introduction of a substituent at both C-α and C-β may be expected to destabilize the transoid state of rearrangement due to additional 1,2-allylic interactions, the tendency to form an *E*-double bond exclusively is retained in the synthesis of trisubstituted olefins as well. The first such report, shortly following the initial Evans report[58], was made by Grieco[91] who achieved a completely stereospecific general synthesis of (*E*)-γ-substituted methallyl alcohols, including the synthesis of racemic (*E*)-nuciferol (**45**, equation 24)[92]. Subsequently, other examples of nearly or completely stereospecific syntheses of (*E*)-β,γ-substituted allylic alcohols have also been published[87,93–106]. On the other hand, in the synthesis of γ,γ-disubstituted allylic alcohols a diminished stereoselectivity has been observed. In this case, the *E*/*Z* ratio depends on the

relative sizes of the substituents and values of 2[105] or 3[93] to 13[93] have been reported for the rearrangement of α,α-disubstituted allylic sulfoxides.

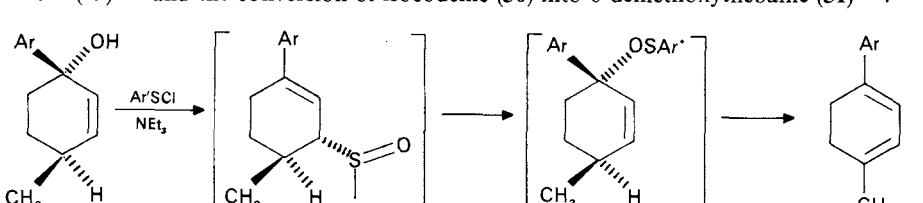


(24)

The data presented demonstrate that allylic sulfoxides can provide an easy and highly stereoselective route to allylic alcohols taking advantage of the facility of the allylic sulfoxide–sulfenate [2,3]-sigmatropic rearrangement. This is of considerable synthetic utility, since a number of stereoselective and useful transformations of allylic alcohols and their derivatives have become available in recent years[107–109].

3. *General synthetic utility*

In addition to the synthetic applications related to the stereoselective or stereospecific syntheses of various systems, especially natural products, described in the previous subsection, a number of general synthetic uses of the reversible [2,3]-sigmatropic rearrangement of allylic sulfoxides are presented below. Several investigators[110–113] have employed the allylic sulfenate-to-sulfoxide equilibrium in combination with the *syn* elimination of the latter as a method for the synthesis of conjugated dienes. For example, Reich and coworkers[110,111] have reported a detailed study on the conversion of allylic alcohols to 1,3-dienes by sequential sulfenate⇌sulfoxide rearrangement and *syn* elimination of the sulfoxide. This method of mild and efficient 1,4-dehydration of allylic alcohols has also been shown to proceed with overall *cis* stereochemistry in cyclic systems, as illustrated by equation 25. The reaction of *trans*-**46** proceeds almost instantaneously at room temperature, while that of the *cis*-alcohol is much slower. This method has been subsequently applied for the synthesis of several natural products, such as the stereoselective transformation of the allylic alcohol **48** into the sex pheromone of the Red Bollworm Moth (**49**)[112] and the conversion of isocodeine (**50**) into 6-demethoxythebaine (**51**)[113].

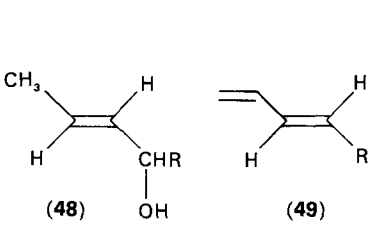


trans-(**46**)

(**47**)

Ar = 2, 5-$Cl_2C_6H_3$ Ar' = 2, 4-$(NO_2)_3C_6H_2$

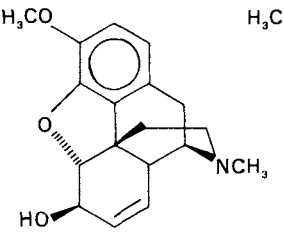
(25)



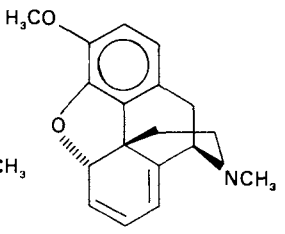
(48)

(49)

$R = (CH_2)_8OTHP$

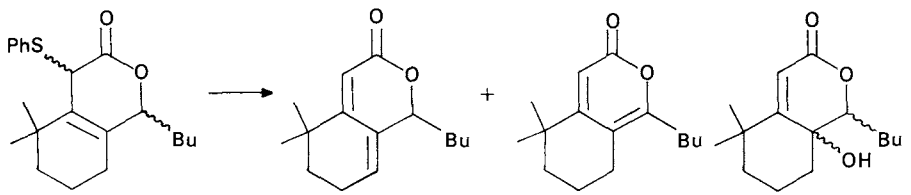


(50)



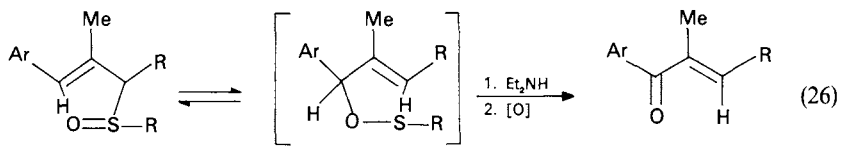
(51)

Another conjugated diene synthesis, usually involving carbonyl functions and allylic sulfoxides, has also been reported by several groups[114–117]. For example, de Groot and coworkers[114] reported that treatment of lactone **52** with excess periodate in refluxing aqueous methanol gave a mixture of products **53** (50%) and **54** (30%) directly. The mechanism of these eliminations was not studied but [2,3]-sigmatropic rearrangement of the allylic sulfoxide to sulfenate followed by thermal elimination of sulfenic acid may have occurred[114]. The isolation of allylic alcohol **55** as a minor product when oxidation of **52** is performed with *m*-chloroperbenzoic acid also points in this direction. However, an alternative or competing 1,3-allylic shift of the sulfinyl group, followed by *syn* elimination of sulfenic acid, is not unlikely. Isobe and coworkers[118] studied the effect of substituents in the arylsulfinyl moiety on the ratio of [2,3]-sigmatropic rearrangement vs. elimination of various allyl *p*-substituted aryl sulfoxides, which changes from more than 10 for *para*-methoxy to 1 for *para*-chloro, with *p*-nitro giving only elimination even at 0 °C. These results are consistent with the substituent effects reported for the pyrolysis of sulfoxides in general[119].



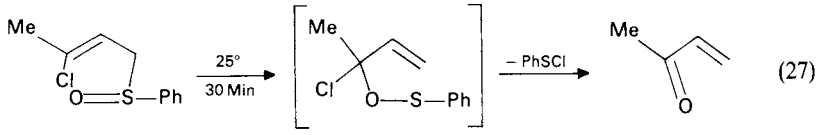
(52) (53) (54) (55)

The choice of the allylic sulfoxide–sulfenate rearrangement for a stereoselective synthesis of enones has also been reported by several workers[120–125]. The sequence depicted in equation 26 is *E* specific providing only one isomer of the desired enone[124]. In one of the early applications of this rearrangement Lansbury and Rhodes[120] have shown that γ-chloroallyl sulfoxides undergo a rapid [2,3]-sigmatropic isomerization at room temperature and 'self-immolative' fragmentation of the generated α-chloroallyl sulfenate, affording α,β-unsaturated carbonyl compounds (equation 27). A similar observation involving [2,3]-sigmatropic rearrangement of γ-chloroallyl thiocarbamate sulfoxides and



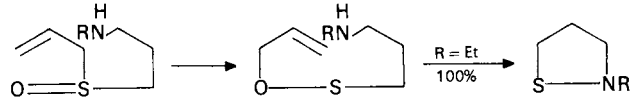
(56) (57) (26)

yielding α,β-unsaturated aldehydes was subsequently reported[122]. The latter compounds can also be obtained by treatment of γ-trimethylsilylallylic alcohols with PhSCl followed by rearrangement and hydrolysis of the unstable allylic sulfoxides obtained[123].



(27)

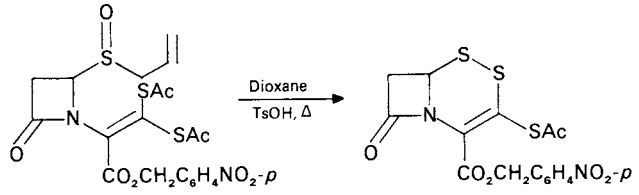
Recently, a simple and general synthetic method for the preparation of *N*-alkylisothioazolidines involving [2,3]-sigmatropic rearrangement of appropriately substituted allylic sulfoxides to corresponding sulfenates, followed by intramolecular substitution of the latter, has been described (equation 28)[126].



(28)

(58) (59) (60)

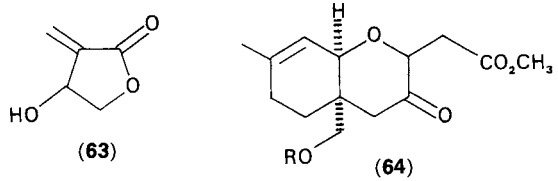
A similar intramolecular nucleophilic capture of an allylic sulfenate generated thermally from the corresponding sulfoxide was also reported for the facile transformation of the azetidinone **61** into a new 3-acetylthio-2-thiacephem ring system **62** (equation 29)[127].



(29)

(61) (62)

Further examples of the utility of the allylic sulfoxide–sulfenate interconversion in the construction of various biologically active natural products include intermediates such as the β-hydroxy-α-methylene-γ-butyrolactones (e.g. **63**)[128] and tetrahydrochromanone derivative **64**[129]. Interestingly, the facility and efficiency of this rearrangement has also attracted attention beyond the conventional boundaries of organic chemistry. Thus, a study on mechanism-based enzyme inactivation using an allyl sulfoxide–sulfenate rearrangement has also been published[130,131].

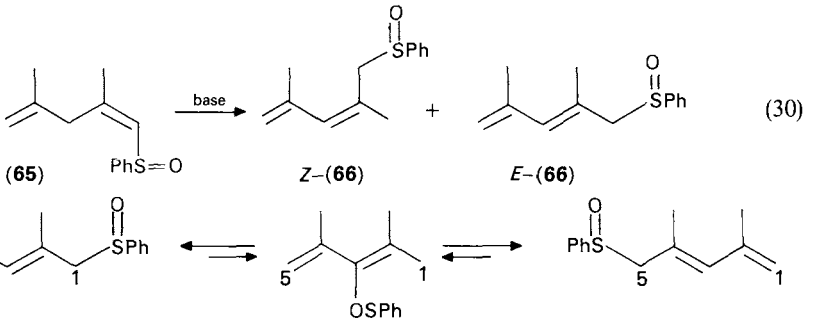


(63) (64)

4. Consecutive sulfoxide–sulfenate–sulfoxide rearrangements

Apparently, the first report of a double [2,3]-sigmatropic rearrangement of an allylic sulfoxide was published by Gaoni[132]. This author observed that the 1,4-pentadienyl

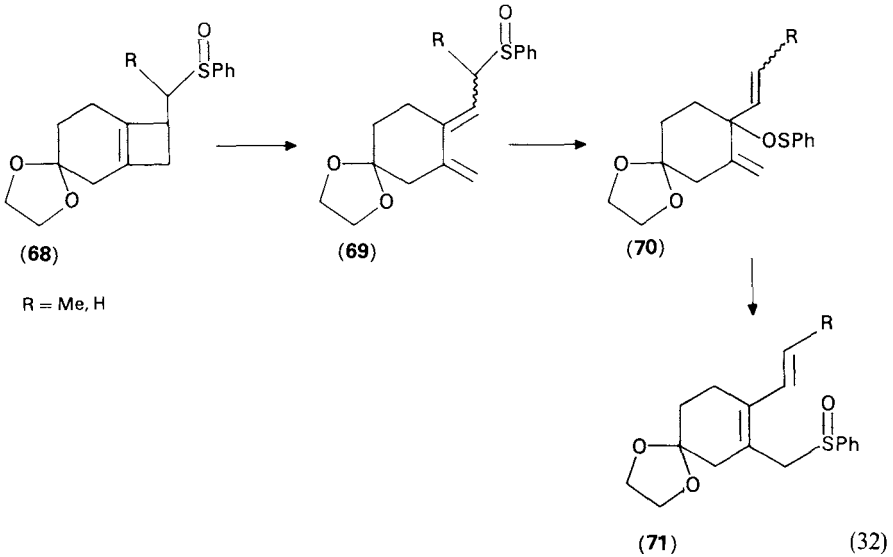
sulfoxide **65** underwent a facile rearrangement with base to the conjugated 2,4-dienylic sulfoxides *Z*- and *E*-**66** (equation 30)[132]. However, when separated, each of the two isomers **66** is found to thermally equilibrate to the same 2:1 mixture of *E*- and *Z*-**66**. This is believed to occur through a [2,3]-sigmatropic shift involving symmetrical intermediate **67**, which may yield a new sulfoxide by a degenerate rearrangement to the 5 position (equation 31). By using deuteriated *Z*-**66** the occurrence of such a process has been proven. With sulfoxides giving rise to an unsymmetrical sulfenate intermediate, the equilibrium shifts in the direction of the thermodynamically more stable isomer[132].



(30)

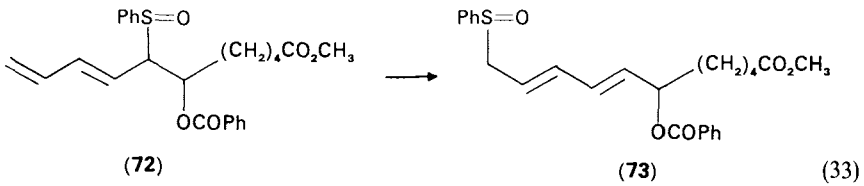
(31)

Subsequently, Kametani and coworkers[133] observed a similar allylic sulfoxide–sulfenate–sulfoxide rearrangement. These authors reported the exceptionally facile ring-opening reaction of condensed cyclobutenes facilitated by arylsulfinyl carbanion substituents. For example, treatment of sulfoxide **68** with butyllithium in tetrahydrofuran at −30 °C for 10 min, followed by normal workup, results in the formation of product **71**, which can be explained by the intervention of a double [2,3]-sigmatropic rearrangement of the initial product **69** via **70** (equation 32). A similar double [2,3]-sigmatropic rearrangement of 1,4-pentadienylic sulfoxides has also been reported by Sammes and coworkers[134].

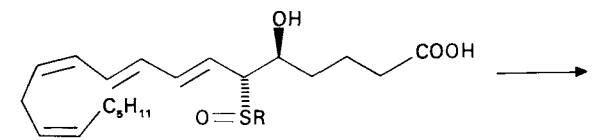


(32)

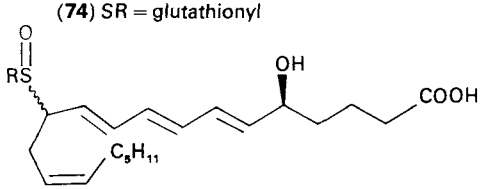
More recently, during their work on the synthesis of leukotrienes, Corey and coworkers[135] have noted the unusual facility of the double [2,3]-sigmatropic rearrangement of sulfoxide **72** to **73** and explained the ratio of **72**/**73** in excess of 20 by the stabilization achieved from the internalization of the diene unit (equation 33). The same authors[136] have also reported a remarkable facile 1,7-sulfinyl migration for the leukotriene sulfoxide (**74**) to its isomer (**75**), and tentatively considered a triple [2,3]-sigmatropic rearrangement of the starting material, followed by an ion-pair rearrangement of the intermediate sulfenate ester (equation 34).



(33)



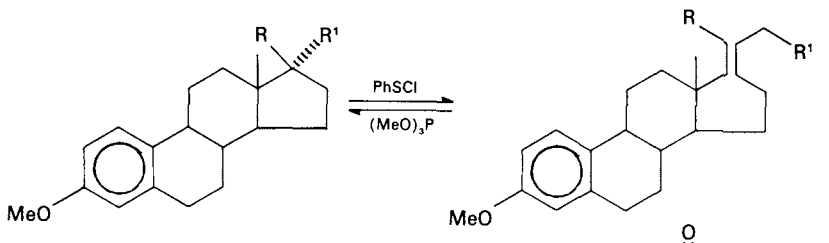
(**74**) SR = glutathionyl



(**75**) SR = glutathionyl

(34)

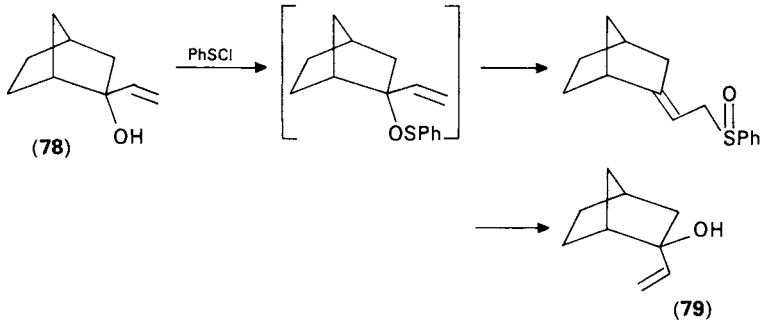
Another version of the double [2,3]-sigmatropic rearrangement, involving the sequence sulfenate → sulfoxide → sulfenate, has also been observed. For example, an effective 'one-pot' epimerization procedure of 17α-vinyl-17β-hydroxysteroids to the rather inaccessible 17-epimers has been achieved by the use of such a rearrangement (equation 35)[137]. Thus treatment of alcohol **76a** with benzenesulfenyl chloride afforded the sulfoxide **77** as a single isomer and *E*-geometry of the olefinic double bond. Exposure of **77** to trimethyl phosphite in refluxing methanol produced a mixture of **76b** and **76a** in a 73:27 ratio.



(**76**)(**a**) R = OH; R¹ = CH=CH₂
(**b**) R = CH=CH₂; R¹ = OH

(35)

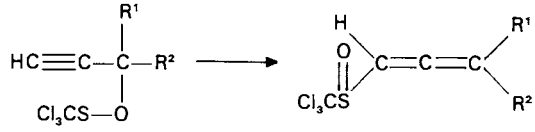
More recently, Brown and Fallis[138] have described a similar epimerization of bicyclic and allylic tertiary alcohols, such as, for example, the epimerization of the *endo* alcohol **78** to its *exo* epimer **79** (equation 36). An *exo*-to-*endo* ratio of 8 to 1 was obtained in this case.



(78) (79) (36)

C. [2,3]-Sigmatropic Rearrangements of Propargylic Sulfenates to Allenic Sulfoxides

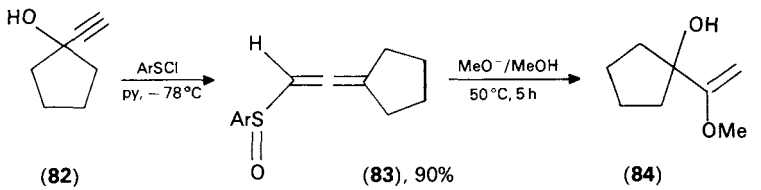
The [2, 3]-sigmatropic rearrangement of propargylic sulfenates to allenic sulfoxides, like the analogous rearrangements of propargylic sulfinates[34,139,140], has been discovered by the present author. Thus Braverman and Stabinsky[141] first observed that propargyl, α-phenylpropargyl and α,α-dimethylpropargyl trichloromethanesulfenates (**80a–c**) are transformed spontaneously at low temperatures to allenyl, γ-phenylallenyl and γ,γ-dimethylallenyl trichloromethyl sulfoxides (**81a–c**), respectively (equation 37). This observation is suggestive of a concerted mechanism for this [2, 3]-sigmatropic rearrangement as well. The great enhancement in rate of rearrangement of propargyl sulfenates as compared with the corresponding sulfinates[140] is reasonably ascribed to the greater nucleophilicity of the sulfur atom in the first compounds. In support of the postulated concerted mechanism, it was subsequently shown by Smith and Stirling[142] that treatment of (*R*)-(+)-α-methylpropargyl alcohol with *p*-toluenesulfenyl chloride in pyridine at −70 °C gave levorotatory α-methylallenyl *p*-tolyl sulfoxide directly. Oxidation of the product gave sulfone with the same sign of rotation as that obtained from the alcohol via rearrangement of the corresponding sulfinate ester[142]. Although the optical purities were not known in either system, this result indicates that the chirality of the allenyl group derived from both rearrangements is the same. An (*S*) absolute configuration was assigned for the allenic sulfoxide, as predicted for a stereospecific suprafacial [2, 3]-sigmatropic shift[142].



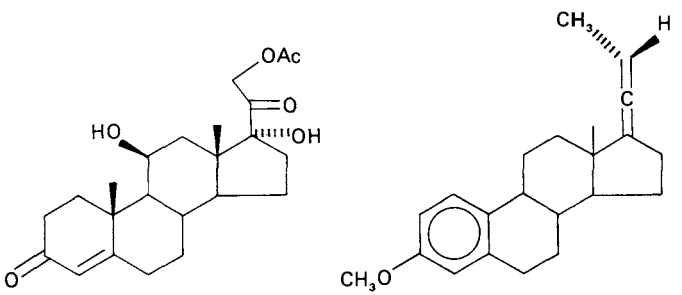
(80) (a) $R^1 = R^2 = H$ (81) a–c
(b) $R^1 = H$; $R^2 = Ph$
(c) $R^1 = R^2 = Me$ (37)

In one of its earliest applications, Horner and Binder[143] prepared a variety of allenyl aryl sulfoxides by the rearrangement of propargylic arenesulfenates, and noticed that accumulation of electron-withdrawing groups in the aromatic ring retard the rate of rearrangement. These authors have also performed a detailed study of the chemistry of

allenyl sulfoxides, and have reported a number of interesting and synthetically useful transformations, as illustrated in equation 38. The conversion of the allenyl sulfoxide (**83**) to the enol ether **84** involves α,β-addition of the solvent and sulfoxide–sulfenate rearrangement of the allylic sulfoxide thus generated. The sequence shown in equation 38 was subsequently used for an efficient and stereoselective introduction of the dihydroxyacetone side-chain at the C-17 position of 17-keto steroids, and a new synthesis of corticosteroids such as hydrocortisone acetate (**85**)[144]. A stereospecific synthesis of various steroidal allenes, such as **86**, has also been achieved by the use of the [2, 3]-sigmatropic rearrangement of the appropriate propargylic sulfenate in combination with methyllithium desulfurization of the allenyl sulfoxide intermediate[145,146].

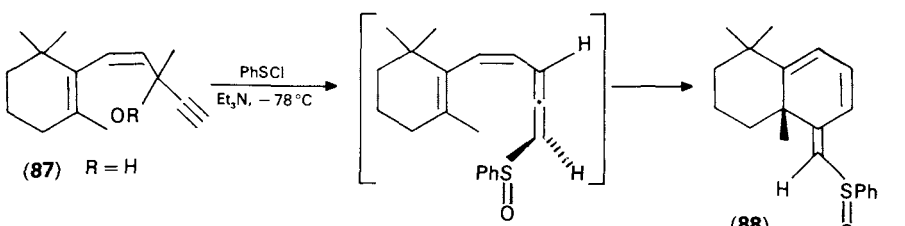


(**82**) (**83**), 90% (**84**) (38)

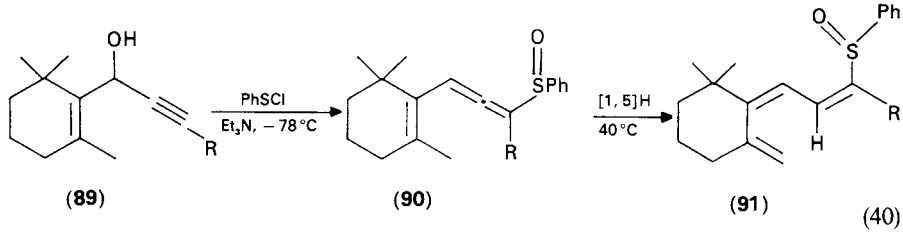


(**85**) (**86**)

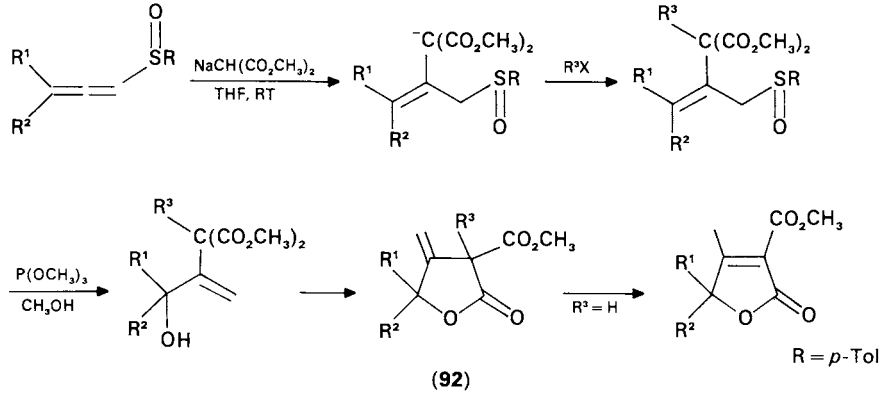
The synthetic utility of the remarkably facile and efficient [2, 3]-sigmatropic rearrangement of propargylic sulfenates has been further demonstrated in a variety of preparations and interesting reactions of allenyl sulfoxides[147–156], including the preparation of vinylallenes[153–156] which are useful intermediates in organic synthesis in general[157] and natural polyenes, such as Vitamins A and D, in particular[158]. Two typical examples, taken from the extensive studies by Okamura and coworkers[154–156], illustrating the formation of vinylallenes in tandem with a six-electron cyclization or a 1, 5 hydrogen shift, are shown in equations 39 and 40, respectively. An example of the use of allenyl sulfoxides for a simple synthesis of β-methylene-γ-butyrolactones, developed by Altenbach and Soicke[152], is shown in equation 41.



(**87**) R = H (**88**) (39)

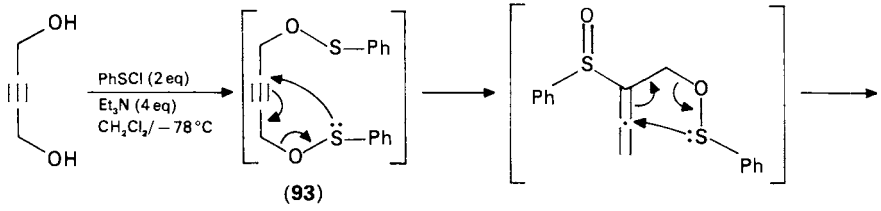


(89) (90) (91) (40)

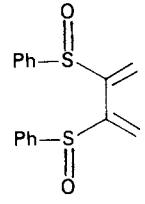


(92) (41)

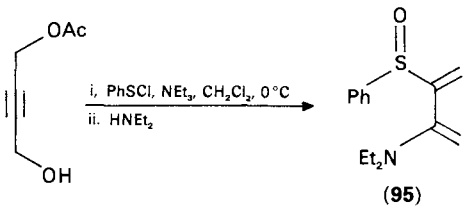
In another synthetic application, first reported by Smith and Stirling[142], the *bis*-2,3-(phenylsulfinyl)-1,3-butadiene **94** has been prepared in low yield by two spontaneous sequential [2,3]-sigmatropic rearrangements of the *bis*-sulfenate ester (**93**). More recently, the yield of this reaction (equation 42) has been improved[159], and a related dienyl sulfoxide **95** has been reported (equation 43)[160]. This type of sulfoxide is of considerable interest in view of recent studies on Diels–Alder reactions of polysubstituted butadienes[161–164].



(93)

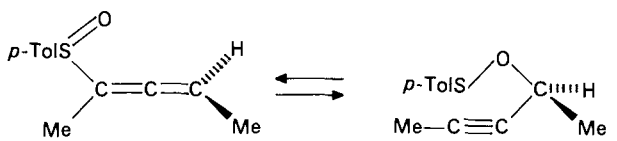


(94) (42)



(95) (43)

The rearrangement of allenic sulfoxides to propargylic sulfenates has received relatively little attention so far, although it was clearly established by Stirling and coworkers[165,166], over a decade ago. These workers have shown that (−)-α,γ-dimethylallenyl *p*-tolyl sulfoxide (**96**), which has been assigned an $(S)_S(R)_{allene}$ absolute configuration, undergoes mutarotation on standing at room temperature. Since the optical rotations of the two sulfones obtained by oxidation of (**96**) before and after mutarotation are practically the same, it has been concluded that the chirality of the allene is unaffected and that epimerization must occur at chiral sulfur only. Thus, mutarotation is believed to involve the stereospecific suprafacial equilibration of sulfoxide **96** with sulfenate **97**, as shown in equation 44. Further evidence in support of this mechanistic interpretation is found in the activation parameters, $\Delta H^{\ddagger}$ 22 kcal mol^{-1}, and $\Delta S^{\ddagger}$ − 6 eu, similar to those obtained for the racemization of optically active allylic sulfoxides[47], as well as by the interception of the sulfenate ester with secondary amines[166].

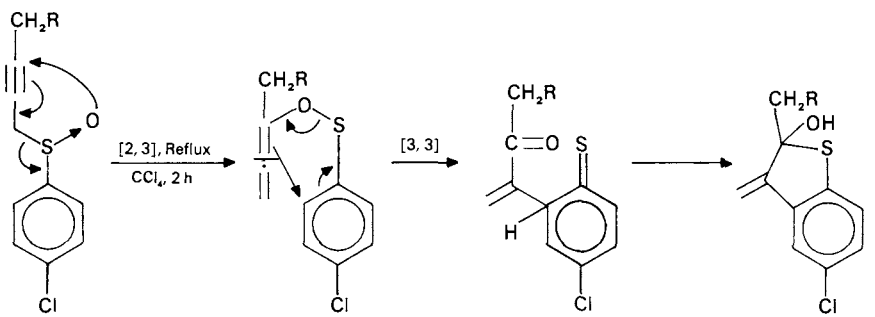


(96) $[\alpha]_D = 120°$ (97) (44)

III. REARRANGEMENTS OF SULFOXIDES TO SULFENATES

A. Thermal and Ionic Rearrangements

Analogous with the rearrangement of allylic sulfoxides is the [2,3]-sigmatropic rearrangement of propargylic sulfoxides to allenic sulfenates. This process, which has been relatively little studied so far, appears to be the first step in the facile and quantitative rearrangement of sulfoxide **98** to the hemithioacetal **101** (equation 45)[167]. This reaction,



(98) (99) (100) (101) (45)

which also involves a [3, 3]-sigmatropic rearrangement of the allenic sulfenate intermediate **100**, is the basis of a convenient synthesis of condensed thiophens[168]. Interestingly, the activation energy for the rearrangement of propargylic selenoxides is drastically reduced, and reaction at $-30\,^{\circ}C$ has been observed[169].

A somewhat unusual thermal rearrangement of α-alkoxy or α-dialkylaminomethyl aryl sulfoxides has also been reported[170,171]. Although the nucleophilic substitution of aryl halomethyl sulfoxides proceeds slowly[172], treatment of sulfoxide **102** with alkoxides is reported to give the expected α-alkoxymethyl aryl sulfoxides in good yields[170,173]. On the other hand, in the reaction of the same sulfoxide (**102**) with secondary amines (**103a–c**), the *p*-toluenesulfenamides (**104a–c**) were obtained quantitatively, instead of the expected α-aminomethyl *p*-tolyl sulfoxides (**106**) (equation 46)[170]. Based on the stoichiometry of the reaction the following reaction scheme has been suggested by the authors. This interpretation has also been supported by the observation that a substituted ethoxymethyl *p*-tolyl sulfenate was formed in the equilibrium when the corresponding sulfoxide, which has another effective electron releasing group at the α-position, was heated under high vacuum. Shortly following the publication of these results, another group[171] reported that methoxymethyl phenyl sulfoxide (**108**) rearranged completely to methoxymethyl benzenesulfenate (**109**) in two days at 36 °C. The sulfenate **109** is likewise unstable and reacts further in a manner that is unprecedented for sulfenate esters. After 4–5 days at 36 °C, **109** disproportionates to phenyl benzenethiosulfinate (**110**, 81%), bismethoxymethyl ether (**111**, 41%), as well as some phenyl disulfide and phenyl benzenethiolsulfonate (equation 47). While the latter reaction has been suggested to take place by a free radical chain mechanism, an intramolecular S → O 1, 2-shift has been proposed for the rearrangement of **108** to **109**. Such a mechanism, which is analogous to that suggested for the Meisenheimer rearrangement of benzyl dimethylamine *N*-oxides to *O*-benzyl-*N*, *N*-dimethylhydroxylamines[174], is rather unusual for saturated sulfoxides which generally prefer the reverse O → S 1, 2-shift (Section II.A).

$$\underset{\text{(102)}}{p\text{-Tol}-\overset{\overset{\text{O}}{\|}}{\text{S}}-\text{CH}_2\text{Br}} + \underset{\text{(103)a–c}}{4\text{RR'NH}} \xrightarrow[1-2\,\text{h}]{70\,^{\circ}\text{C}} \underset{\text{(104)a–c}}{p\text{-TolSNRR'}} + \underset{\text{(105)a–c}}{\text{RR'NCH}_2\text{NRR'}} + \text{RR'NH}\cdot\text{HBr} + \text{H}_2\text{O} \qquad (46)$$

(**a**) R, R′ = morpholino
(**b**) R, R′ = piperidino
(**c**) R = R′ = Et

$$\text{Ar}-\overset{\overset{\text{O}}{\|}}{\text{S}}-\text{CH}_2\text{X} \xrightarrow{2\text{RR'NH}} \underset{\text{(106)}}{\text{Ar}-\overset{\overset{\text{O}}{\|}}{\text{S}}-\text{CH}_2\text{NRR'}} + \text{RR'NH}\cdot\text{HX}$$

X = Cl, Br

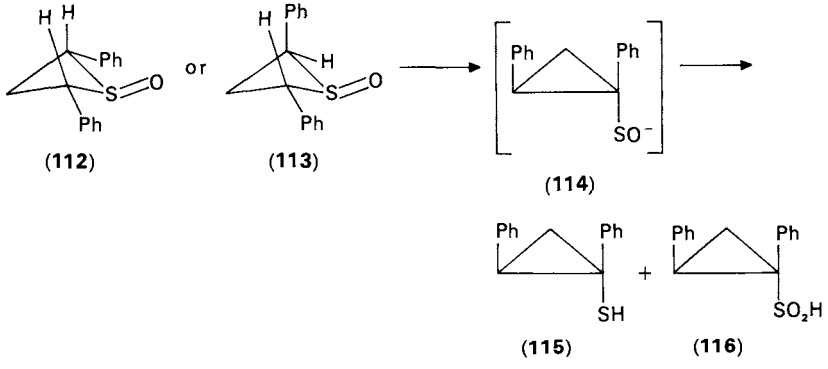
$$\text{Ar}-\overset{\overset{\text{O}}{\|}}{\text{S}}-\text{CH}_2\text{NRR'} \rightleftharpoons \underset{\text{(107)}}{\text{Ar}-\text{S}-\text{O}-\text{CH}_2\text{NRR'}}$$

$$\text{Ar}-\text{S}-\text{O}-\text{CH}_2\text{NRR'} \xrightarrow{\text{RR'NH}} \text{ArSNRR'} + \text{RR'NCH}_2\text{OH}$$

$$\text{RR'NCH}_2\text{OH} \xrightarrow{\text{RR'NH}} \text{RR'NCH}_2\text{NRR'} + \text{H}_2\text{O}$$

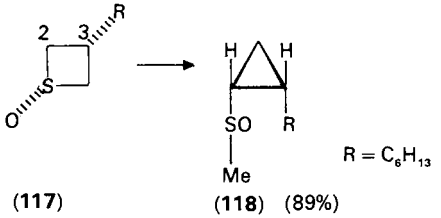
$$\underset{\textbf{(108)}}{PhS(O)CH_2OCH_3} \longrightarrow \underset{\textbf{(109)}}{PhS{-}OCH_2OCH_3} \longrightarrow \underset{\textbf{(110)}}{PhS(O)SPh} + \underset{\textbf{(111)}}{(CH_3OCH_2)_2O} \qquad (47)$$

A base-catalyzed rearrangement of a cyclic sulfoxide to sulfenate anion, accompanied by ring contraction, was first observed by Dodson and coworkers[175]. These authors reported that reaction of either *cis*- or *trans*-2,4-diphenylthietane-1-oxide (**112** or **113**) with potassium *t*-butoxide in dimethylformamide yielded a mixture of *cis*-1,2-diphenylcyclopropanethiol and *cis*-1,2-diphenylcyclopropanesulfinic acid by disproportionation of the sulfenate anion intermediate **114** (equation 48). Subsequently, Jones and coworkers[176] performed a detailed stereochemical study of this reaction and concluded that ring contraction of the lithio anions of 3-alkyl- and 2,3-dialkylthiethan 1-oxides occurred stereospecifically with retention of configuration at sulfur and the migrating residue, and inversion at the migration terminus. For example, treatment of *cis*- and *trans*-3-hexylthietan 1-oxides, (**117**) and (**119**), separately with lithium cyclohexylisopropylamide in tetrahydrofuran at $-20\,^{\circ}C$ for 15 min followed by addition of methyl iodide, gave respectively *cis*- and *trans*-2-hexyl-1-(methylsulfinyl)cyclopropane (**118**) and (**120**). The

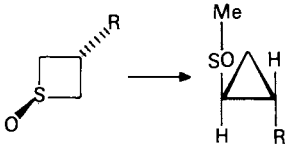


(112) (113) (114) (115) (116)

(48)

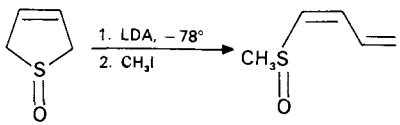


(117) (118) (89%)



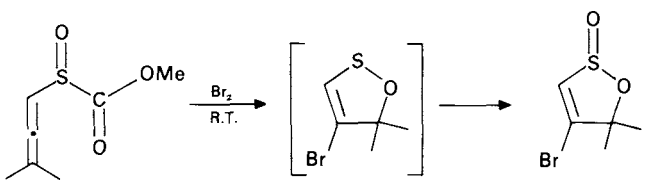
(119) (120) (68%)

mechanism of this process has also been discussed[176] and the authors point out that the stereochemical consequences accord with those expected for a concerted process[177], initiated by the preferential abstraction of an α-proton *cis* to the sulfinyl oxygen atom. In another base catalyzed isomerization of a cyclic sulfoxide to a sulfenate anion, 2,5-dithydrothiophen 1-oxide was found to undergo ring opening to (*Z*)-1-(methylsulfinyl)-buta-1,3-diene in 40% yield, upon treatment with lithium diisopropylamide at −78 °C followed by rapid quenching with a slight excess of methyl iodide (equation 49)[178].



(49)

Prompted by the observation of a facile electrophilic rearrangement of mono- and diallenic sulfones to α,β-unsaturated γ-sultines[179–181], Braverman and Reisman[182] have also investigated a similar rearrangement of allenic sulfoxides to the corresponding cyclic sulfenates. However, in order to avoid competing reactions through the sulfur nonbonding electron pair, its reactivity has been reduced by attachment of an electronegative carbomethoxyl group to the sulfinyl moiety. γ,γ-Dimethylallenyl sulfoxide **121** has thus been prepared by treatment of methoxycarbonyl sulfenyl chloride[183] with α,α-dimethyl-propargyl alcohol in the presence of a base. Although sulfoxide **121** is in mobile equilibrium with the corresponding α,α-dimethylpropargyl sulfenate, addition of bromine at room temperature took place immediately and resulted in fragmentation-cyclization of the starting material and formation of the β-bromo-α,β-unsaturated-γ,γ-dimethyl-γ-sultene (**122**). However, the latter could not be isolated due to its spontaneous transformation (equation 50) to the corresponding known γ-sultine (**123**)[179]. This behavior is in full accord with the known lack of stability of cyclic sulfenates in general[184,185], except for anhydrous conditions, and their rapid reaction with water or moist air to give the corresponding sulfinates[185].



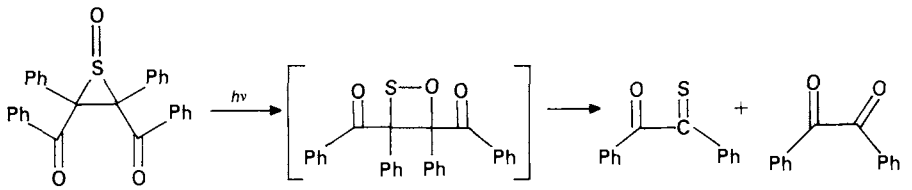
(50)

(**121**) (**122**) (**123**)

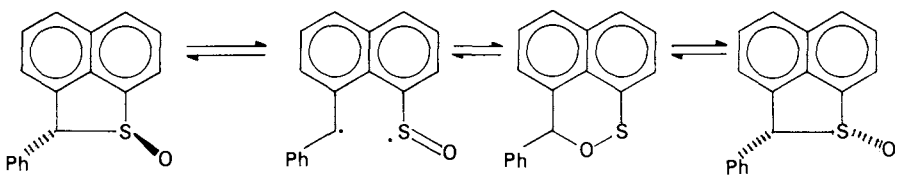
B. Photochemical Rearrangements

The photochemical behavior of compounds containing the sulfoxide chromophore attracted considerable attention in the past[186]. Two early reports described the photochemical conversion of dibutyl and dibenzyl sulfoxides into the corresponding disulfides[187,188] and Block[186] later proposed a sulfenate rearrangement pathway to explain the former rearrangement. Very interesting photochemical reactions observed for the sulfoxide group involve the conversion of a cyclic sulfoxide to a ring expanded sulfenate, which usually undergoes further transformation under the reaction conditions[189]. For example, ultraviolet irradiation of dibenzoylstilbene episulfoxide (**124**) in benzene afforded monothiobenzyl (**126**) and benzil, presumably by initial rearrangement

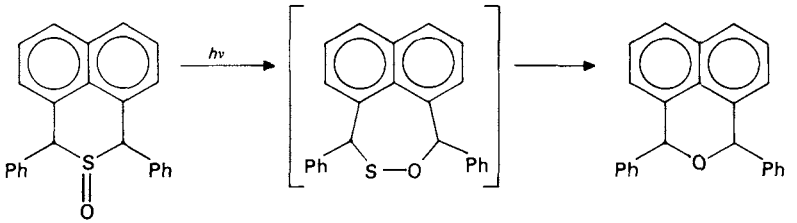
to a β-sultene intermediate (**125**) which undergoes fragmentation to observed products (equation 51)[189]. The photoinduced isomerization of sulfoxides (**127**) and (**129**) has been found to occur via both sulfur pyramidal inversion and reversible sulfenate ester formation (equation 52)[190]. It is interesting that no such sulfoxide–sulfenate interconversion could be detected even at 175 °C, while racemization of the sulfoxides was observed. Subsequently, the same authors[191] reported that on direct irradiation of *trans*-1,3-dihydro-2-thiaphenalene-2-oxide (**130**) in nonpolar solvents such as benzene, significant amounts of the unstable sulfenate **131** are produced. The latter is gradually converted into *cis*- and *trans*-pyrans **132** by fragmentation and desulfurization (equation 53).



(**124**) (**125**) (**126**) (51)

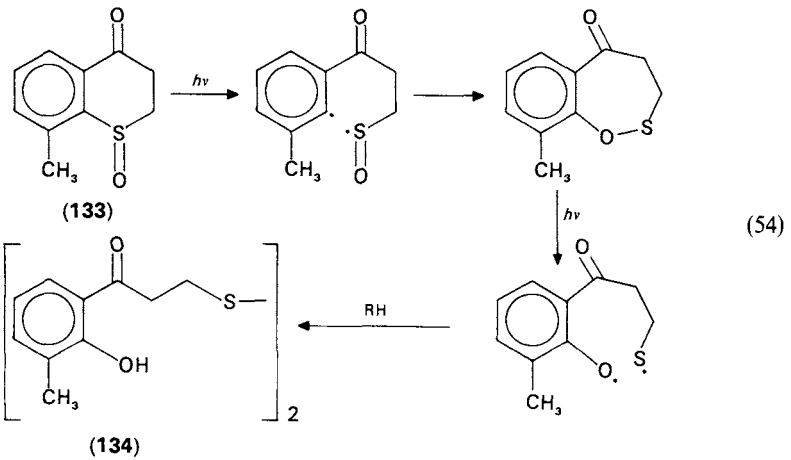


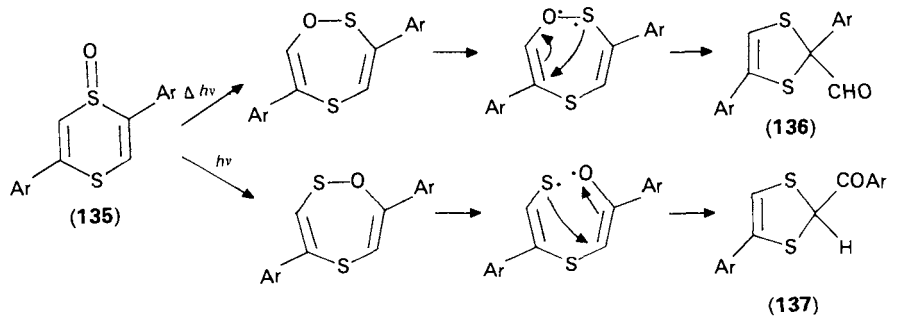
(**127**) (**128**) (**129**) (52)



(**130**) (**131**) (**132**) (53)

The photochemical behavior of a number of substituted derivatives of thiochroman-4-one 1-oxides has been examined by Still and coworkers[192–194]. These authors also report that rearrangement to cyclic sulfenates, with subsequent reaction by homolysis of the S—O bond, appears to be a particularly favorable process. For example, ultraviolet irradiation of a solution of 8-methylthiochroman-4-one 1-oxide (**133**) in benzene for 24 h afforded a single crystalline product which was assigned the disulfide structure **134** (equation 54). More recently, Kobayashi and Mutai[195] have also suggested a sulfoxide–sulfenate rearrangement for the photochemical conversion of 2,5-diphenyl-1,4-dithiin 1-oxide (**135**) to the 1,3-dithiole derivatives **136** and **137** (equation 55).

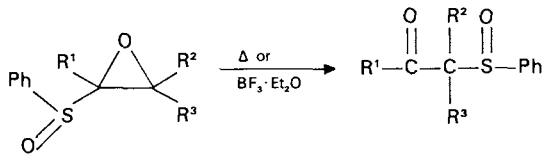




IV. 1,2- AND 1,3-REARRANGEMENTS OF SULFOXIDES

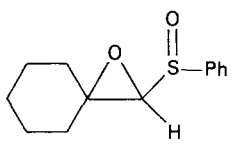
A. 1,2-Sulfinyl Migrations

The thermal and acid catalyzed rearrangements of α,β-epoxy sulfoxides **138** to β-carbonyl sulfoxides have been simultaneously reported by Durst[196] and Tavares[197] and their coworkers (equation 56). This 1,2-migration of the sulfinyl group is analogous to the migration of other electronegative groups such as, for example, the 1,2-acyl migration of α,β-epoxy ketones[198]. The α,β-epoxy sulfoxides are conveniently prepared by Darzens-type condensation between α-haloalkyl sulfoxides and carbonyl compounds[196,199]. The temperature required for thermal rearrangement varied from less than 25 °C for **138** ($R^2 = R^3 = Ph$) to more than 130 °C when $R^2 = R^3 =$ alkyl, as expected on the basis of relative stabilities of the intermediate carbonium ions. The rearrangement of sulfinyloxirane **139** was accompanied by desulfinylation to α,β-unsaturated aldehyde **140**, which may have arisen via elimination of benzenesulfenic acid from the expected product[200]. The thermolysis in refluxing toluene of a number of spiro epoxy sulfoxides, in which the carbocyclic ring varied in size from C_4 to C_8, has also been reported as a method for the synthesis of α,β-unsaturated aldehydes in 40–90% yield[201]. In a different 1,2-sulfinyl migration, 2-arylsulfinyl- and 2-alkylsulfinylpyrroles undergo a remarkably facile acid promoted rearrangement to the isomeric 3-sulfinylpyrrole at room temperature[202].

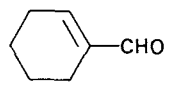


(56)

(138)



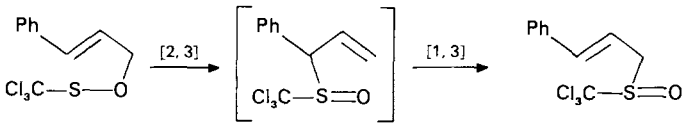
(139)



(140)

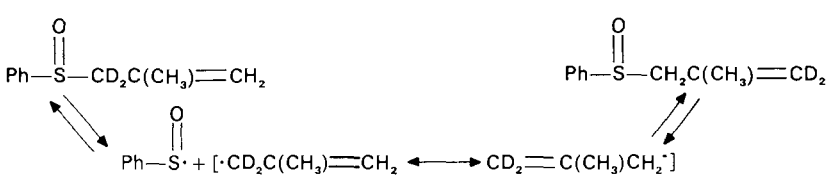
B. 1,3-Sulfinyl Migrations

The [1,3]-sigmatropic shift of allylic sulfoxides has initially escaped detection in the course of discovery of the considerably more mobile [2,3]-sigmatropic rearrangement described in Section II.B. The occurrence of such a rearrangement might have been first observed in the thermal rearrangement of cinnamyl trichloromethanesulfenate to cinnamyl trichloromethyl sulfoxide[35], assuming that this has been preceded by [2,3]-sigmatropic rearrangement to α-phenylallyl sulfoxide (equation 57)[60]. More recently, such an assumption has also been made by Baechler and coworkers[203] to explain the rapid rearrangement of cinnamyl benzenesulfenate to cinnamyl phenyl sulfoxide. However, in neither case is there compelling evidence for the correctness of this assumption[60], and alternative mechanisms are also likely.



(57)

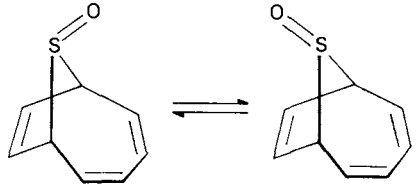
Baechler and coworkers[204] have also studied the kinetics of the thermal isomerization of allylic sulfoxides and suggested a dissociative free radical mechanism. This process, depicted in equation 58, would account for the positive activation entropy, dramatic rate acceleration upon substitution at the α-allylic position, and relative insensitivity to changes in solvent polarity. Such a homolytic dissociative recombination process is also compatible with a similar study by Kwart and Benko[204b] employing heavy-atom kinetic isotope effects.



(58)

The 1,3-allylic rearrangement has also been observed with several cyclic sulfoxides. For example, the interesting thermal interconversion of the bicyclic stereoisomeric pair **141**

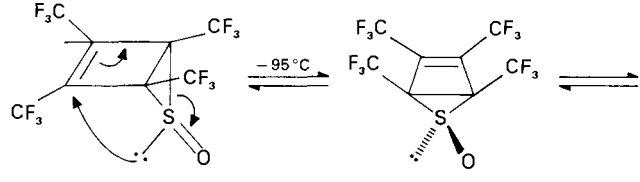
and **142** (equation 59) has been suggested to occur by a free radical dissociation–recombination mechanism, involving 1, 3-migration of the sulfoxide bridge, rather than by pyramidal inversion of the sulfinyl group. This mechanistic proposal is based on evidence accumulated from measurement of activation parameters as well as from the results obtained with specifically labeled 1, 6-dideuterio-**141** which indicates complete scrambling of the label[205].



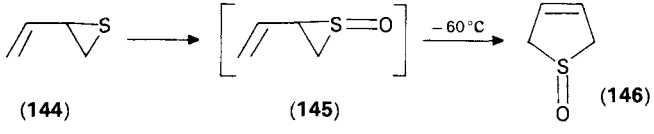
(**141**) (**142**)

$\Delta H^{\ddagger} = 27.8$ kcal mol^{-1}
$\Delta S^{\ddagger} = -4$ eu
at 110.7 °C (59)

Another, rather unusual [1, 3]-allylic sulfoxide rearrangement is that reported by Lemal and coworkers[206,207] for the remarkably facile automerization[208] of perfluorotetramethyl Dewar thiophen *exo*-*S*-oxide (**143**) (equation 60). The small barrier ($\Delta H^{\ddagger} = 6.6$ kcal mol^{-1})[207] has been interpreted by the authors to exclude both a four-electron pericyclic [1, 3]-sigmatropic shift and a biradical process as the reaction mechanism. A six-electron process was proposed instead in which the endocyclic lone pair on sulfur participates nucleophilicly with the result that bonding and nonbonding orbitals on sulfur interchange roles. The concept was generalized and the suggestion made that such transformation be designated as pseudopericyclic[206]. However, a subsequent theoretical study of this concept could not find supporting evidence for it[209]. A somewhat similar, but simpler and nondegenerate [1, 3]-sigmatropic rearrangement was observed earlier by Lautenschlaeger[210], upon hydrogen peroxide oxidation of vinylthiirane (**144**) at room temperature, which yielded directly 3-thiolene *S*-oxide (**146**). By carrying out the oxidation with peroxytrifluoroacetic acid, Lemal and coworkers[206] found that the presumed vinyl thiirane oxide intermediate (**145**) is short-lived even at temperatures below −60 °C (equation 61).



(**143**) (60)

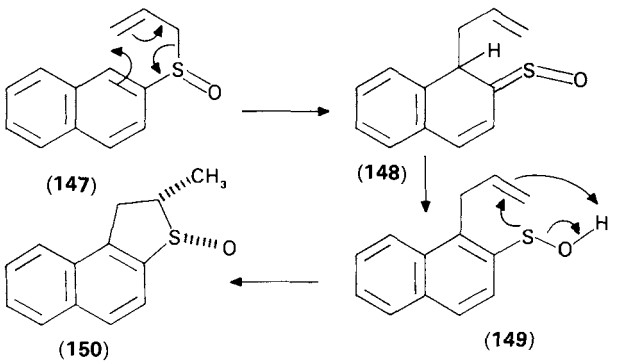


(**144**) (**145**) (**146**) (61)

V. MISCELLANEOUS REARRANGEMENTS

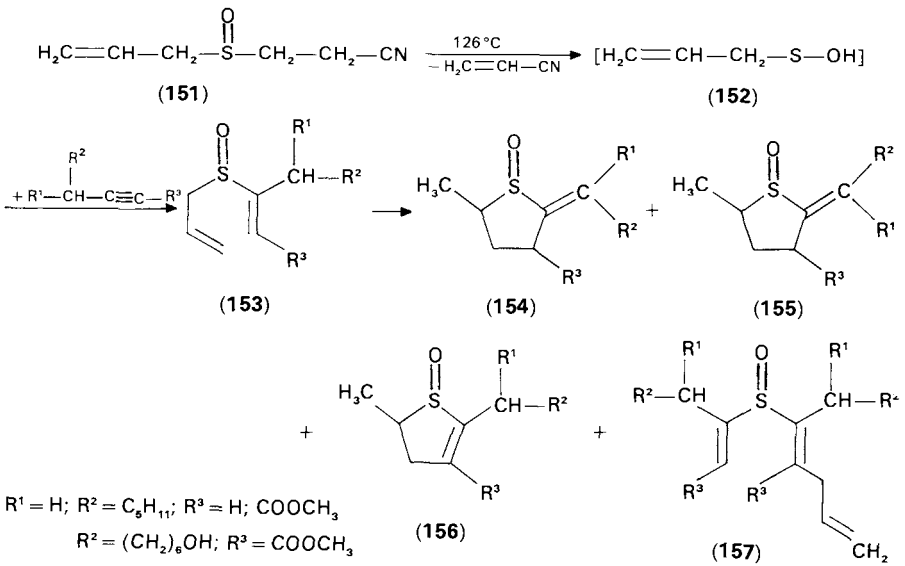
Similar to the well-known thio-Claisen rearrangement of allyl aryl sulfides[211] and sulfonium salts[212], the thio-Claisen rearrangement of allyl aryl sulfoxides has also been reported[213]. For example, heating of allyl 2-naphthyl sulfoxide (**147**) at 120 °C for 2 h in dimethylformamide resulted in quantitative isomerization to the dihydronaphthothio-

phen derivative **150**. A possible mechanism for the formation of the product involves initial [3,3]-sigmatropic rearrangement of sulfoxide **147** to sulfine **148**, followed by a [1,4]-sigmatropic rearrangement[214,215] to sulfenic acid intermediate **149** and intramolecular *cis*-addition of the latter (equation 62).



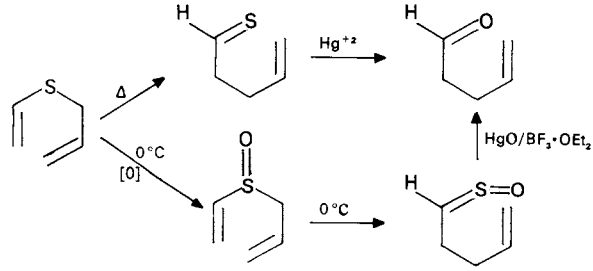
(62)

Subsequently, Jones and coworkers[215] observed a thio-Claisen rearrangement of allyl vinyl sulfoxides. These authors reported that thermolysis of 1-allylsulfinyl-2-cyanoethane (**151**) initiated five consecutive pericyclic reactions which led to the formation of thiolan 1-oxide derivatives (equation 63). The unstable allyl sulfenic acid (**152**) generated by thermolysis of **151** undergoes regiospecific addition to alkynes and affords the required allyl vinyl sulfoxides **153**. However, under the reaction conditions (126 °C), the latter is unstable but undergoes a double rearrangement to sulfine and sulfenic acid, followed by intramolecular cycloaddition, as described for the preceding sulfoxide thio-Claisen rearrangement. In some cases, cycloaddition of the intermediate sulfenic acid to starting alkyne and formation of products such as the acyclic sulfoxide **157** are also observed.



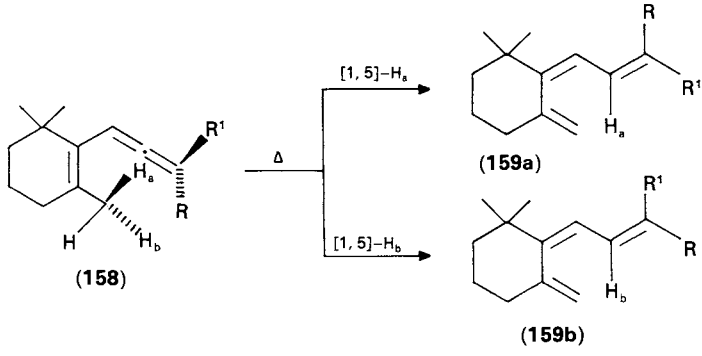
(63)

More recently, a direct observation of the unusually facile thio-Claisen rearrangement of various allyl vinyl sulfoxides was made by Block and Ahmad[216]. These authors discovered that oxidation of 1-alkenyl 2-alkenyl sulfides to the corresponding sulfoxides leads to a remarkable acceleration in the rate of the [3,3]-sigmatropic process, which in some cases occurs below 0 °C, affording isolable sulfines, which can be converted into carbonyl compounds[217] under mild conditions (equation 64). The use of elevated temperatures and the presence of mercuric salts, required in the rearrangement of allyl vinyl sulfides[218], are thus avoided. These results are also of interest in view of the elevated temperature required for the [3,3]-sigmatropic rearrangement of allyl vinyl sulfone to the nonisolable corresponding sulfene[219]. Another remarkable sulfoxide-induced acceleration and enhancement of geometric selectivity has been described by Okamura and coworkers[156] and involves the [1,5]-sigmatropic hydrogen shift isomerization of vinylallenes **158** to conjugated trienes **159a** and **159b** (equation 65). These reactions, which occur readily at room temperature, have been claimed to be 'the most facile examples of neutral, acyclic [1,5]-sigmatropic hydrogen shifts yet recorded'[156]. Equally significant is the unusual geometric selectivity observed which increases with the size of R, from 4:1 to 98:2 in favor of product **159b**, indicating that H favors migration *anti* to the sulfoxide. The origin of this effect, which controls π-facial stereoselection in these triene syntheses, is still uncertain.



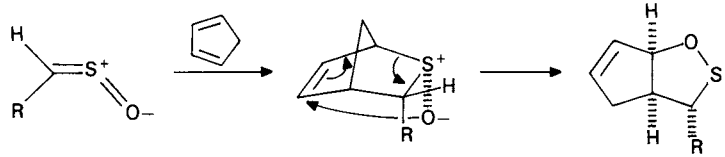
(64)

Recently, Block and coworkers[220] reported a striking difference between *exo* and *endo*-sulfoxide **160**. While the former remained unchanged even after refluxing in toluene for 20 h, the *endo*-sulfoxide **160**, rearranged at room temperature, presumably via a [2,3]-sigmatropic shift (Section II.B), to 4-ethyl-2-oxa-3-thiabicyclo[3,3,0]oct-7-ene (**161**), a rare example of an isolable sultene[185] (equation 66).



R	R¹
H	SOPh
Me	SOPh
Et	SOPh
i-Pr	SOPh
t-Bu	SOPh

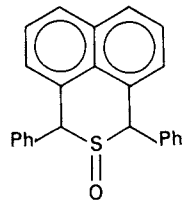
(65)



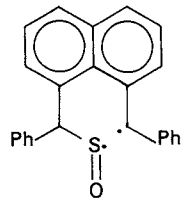
(66)

R = Et (160) (161)

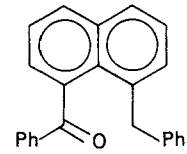
Several photochemical rearrangements also deserve attention. For example, Schlessinger and coworkers[221] first reported that benzophenone-sensitized irradiation of *cis*- or *trans*-1,3-dihydro-2-thiaphenalene 2-oxide (**162**) in benzene gave rise to 1-benzoyl-8-benzylnaphthalene (**166**, 80% yield) as the sole product. No photoepimerization between *cis*- and *trans*-**162** was observed, and no evidence could be obtained for any long-lived intermediates in this photodesulfurization reaction. However, it was subsequently shown[222] that irradiation of a mixture of **162** and Michler's ketone at 366 nm in purified degassed chloroform solution gave rise in high yield to a 1:3 mixture of sulfines **164** and **165**, respectively. Both the direct and sensitized irradiation of **164** and **165** at 366 nm were examined. This study has shown that while formation of ketone **166** from either of the sulfines occurs exclusively by a singlet-state reaction, only sulfine photoisomerization occurs under sensitized irradiation. These results show that the transformation of **162** to **166** proceeds from triplet-state sulfoxide through the diradical **163** to the isolable sulfine intermediates, which in turn undergo only singlet-state decomposition to product.



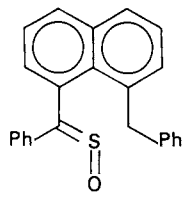
(162)



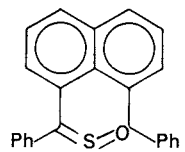
(163)



(166)



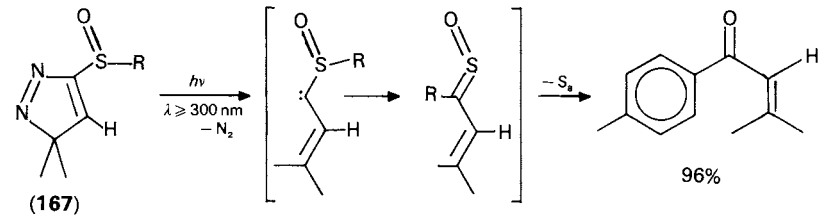
(165)



(164)

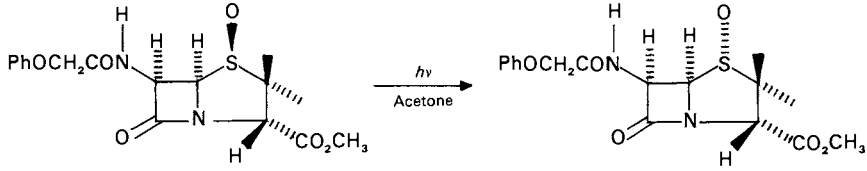
More recently, another sulfoxide→sulfine photoconversion has been reported by Franck-Neumann and Lohmann[223]. These authors have shown that the photolysis of allylsulfinylpyrazolenines (**167**) provides a novel route to vinyl sulfines **168**, presumably via ring-opening to α-diazosulfoxides and their α-sulfinylcarbene intermediates (equation 67).

Photochemical oxygen transfer reactions involving sulfoxides have also been documented. For example, a photochemical rearrangement of 2-nitrophenyl phenyl sulfoxide to 2-nitrosophenyl phenyl sulfone[224], and the inverse photoconversion of *o*-methylbenzoic acid[225] have been reported. Finally, photochemical epimerizations of the sulfoxide centers



(167) (168) (67)

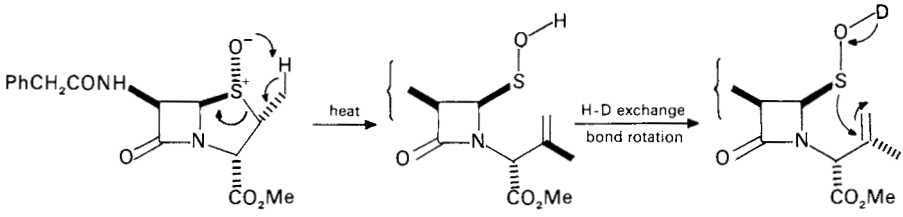
in penicillin sulfoxides on ultraviolet irradiation of acetone solutions have also been published[226,227], e.g. epimerization of phenoxymethylpencillin (*S*)-sulfoxide (**169**) to (*R*)-sulfoxide (**170**)[226].



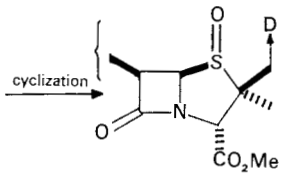
(*S*)-(**169**) (*R*)-(**170**)

Archer and De Marco[226], as well as Barton and coworkers[228], simultaneously reported a facile thermal isomerization of penicillin (*R*)-sulfoxides to the thermodynamically more stable *S* isomers. Evidence for the formation of a sulfenic acid intermediate in this reaction was first obtained by heating the (*R*)-sulfoxide **171** (80 °C, 3 h) in the presence of deuteriated *t*-butanol[229]. The product was the corresponding (*S*)-sulfoxide **173** in which only one atom was incorporated into the *β*-methyl group, *cis* to the resultant sulfoxide bond (equation 68). Under identical conditions, no deuterium incorporation was observed for the (*S*)-sulfoxide. Use of prolonged periods (24 h, 80 °C), however, showed that the (*S*)-sulfoxide **174** did undergo slow incorporation of deuterium specifically into the *cis*-disposed methyl group when heated in solution in the presence of deuterium oxide, thus demonstrating the reversibility of the sulfoxide–sulfenic acid equilibrium[230]. This stereospecific and reversible intramolecular cycloelimination is considered to proceed through a five-membered six-electron coplanar transition state (**175**), as first suggested by Kingsbury and Cram[231] for the thermal conversion of sulfoxides into sulfenic acids and olefins. Further proof for the suggested penicillin sulfoxide–sulfenic acid rearrangement mechanism depicted in equation 68 was derived from the observation of a variety of intermolecular trapping reactions of the intermediate sulfenic acid with olefins[232,233] or acetylenes[234,235], with azo compounds[236], with arenesulfinic acids[237], with silylated amides[238], with mercaptans[239–241] and with trimethyl phosphite[59,242]. Subsequently, Chou and coworkers[243] provided conclusive evidence for the intermediacy of the reactive sulfenic acid **177**, by its successful isolation from the thermal epimerization of the corresponding penicillin (*R*)-sulfoxide **176**. Sulfenic acid **177**, obtained as a crystalline solid by rapid cooling of a hot solution of sulfoxide **176**, was fully characterized and found to return to sulfoxide on standing at room temperature (equation 69)[243].

More recently, several similar thermal rearrangements of other cyclic sulfoxides involving reversible intramolecular cycloelimination of sulfenic acid have also been reported[244–247]. A detailed study of this rearrangement which, in certain cases, is accompanied by ring expansion or ring contraction has been performed by Jones and coworkers[244]. These authors found that at 140 °C in xylene, conditions under which acyclic sulfoxides readily decompose[248,249], thian 1-oxide (**180a**) was inert after 6 days,

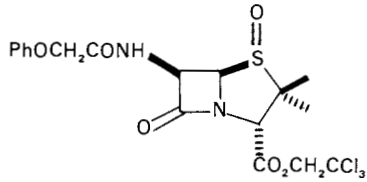


(*R*)-(**171**) (**172**)

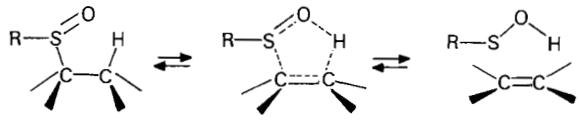


(68)

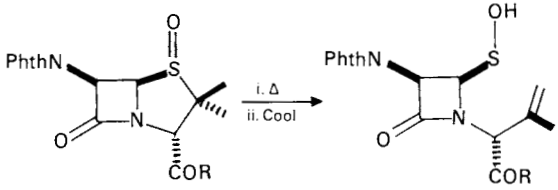
(*S*)-(**173**)



(**174**)



(**175**)



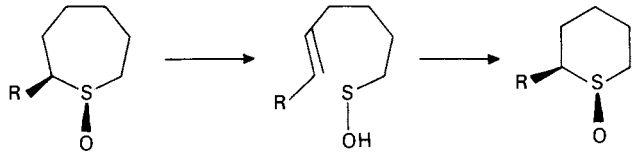
(**176**) (**177**)

(69)

R = $OCH_2C_6H_4NO_2$-*p*
PhthN = phthalimido

whereas thiepan 1-oxide (**178a**) decomposed with a half-life of ca. 28 h to give *cis*-2-methylthian 1-oxide (**180b**) (equation 70). The sharp contrast in reactivity between thian and thiepan 1-oxides is easily explained by steric control of the transition state, with the former unable to achieve required coplanarity of the relevant five-atom transition state[244].

Jones and Lewton[250] have also demonstrated the utility of the intramolecular addition of sulfenic acids to olefins as a stereospecific method for the synthesis of thiolan 1-oxides.



(70)

(**178**) (a) R = H (**179**) (**180**) (a) R = H (b) R = Me

VI. REFERENCES

1. H. H. Szmant, in *Organic Sulfur Compounds* (Ed. N. Kharasch), Vol. 1, Pergamon Press, Oxford, 1961, p. 154.
2. H. H. Szmant, in *Sulfur in Organic and Inorganic Chemistry* (Ed. A. Senning), Vol. 1, Marcel Dekker, New York, 1971, p. 107.
3. L. Field, *Synthesis*, 101 (1972).
4. P. A. Lowe, in *Rodd's Chemistry of Carbon Compounds*, 2nd edn. (Ed. M. F. Ansell), Elsevier, Amsterdam, 1975, Part 1A-B, Suppl. p. 109.
5. S. Oae, in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, 1977, p. 383.
6. E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, San Francisco, London, 1978, p. 53.
7. T. Durst, in *Comprehensive Organic Chemistry* (Eds. D. H. R. Barton and W. D. Ollis), Vol. 3 (Ed. D. N. Jones), Pergamon Press, Oxford, 1979, pp. 121, 157.
8. G. Kresze, in *Houben-Weyl, Methoden der Organischen Chemie* (Ed. D. Klamann), Ell, Part 1, G. Thieme Verlag, Stuttgart, 1985, p. 669.
9. D. R. Hogg, in *Comprehensive Organic Chemistry* (Eds. D. H. R. Barton and W. D. Ollis), Vol. 3 (Ed. D. N. Jones), Pergamon Press, Oxford, 1979, p. 261.
10. R. Schubart, in *Houben-Weyl, Methoden der Organischen Chemie* (Ed. D. Klamann), Ell, Part 1, G. Thieme Verlag, Stuttgart, 1985, p. 63.
11. G. A. Russell and G. J. Mikol, in *Mechanisms of Molecular Migrations* (Ed. B. S. Thyagarajan), Vol. 1, Interscience, New York, 1968, p. 157.
12. T. Durst, *Adv. Org. Chem.*, **6**, 356 (1969).
13. S. Oae and T. Numata, *Isot. Org. Chem.*, **5**, 45 (1980).
14. S. Oae, T. Numata and T. Yoshimura, in *The Chemistry of the Sulfonium Group* (Eds. C. J. M. Stirling and S. Patai) Part 2, Chap. 15, John Wiley and Sons, Chichester, 1981, pp. 624–644.
15. R. D. G. Cooper, L. D. Hatfield and D. O. Spry, *Acc. Chem. Res.*, **6**, 32 (1973).
16. R. J. Stoodley, *Tetrahedron*, **31**, 2321 (1975).
17. P. G. Sammes, *Chem. Rev.*, **76**, 113 (1976).
18. E. Kühle, *Synthesis*, 566 (1971).
19. H. Mackle, *Tetrahedron*, **19**, 1159 (1963).
20. S. Braverman and B. Sredni, *Tetrahedron*, **30**, 2379 (1974).
21. e.g. C. A. Grob and S. Winstein, *Helv. Chim. Acta*, **35**, 782 (1952).
22. S. Braverman and D. Reisman, *Tetrahedron*, **30**, 3891 (1974); *Tetrahedron Letters*, 3563 (1973).
23. J. Silhanek and M. Zbirovsky, *J. Chem. Soc., Chem. Commun.*, 878 (1969).
24. J. Strating, L. Thijs and B. Zwanenburg, *Tetrahedron Letters*, 4461 (1969).
25. S. Braverman and H. Manor, *Phosphorus and Sulfur*, **2**, 215 (1976).
26. G. B. Barlin and D. D. Perin, in *Elucidation of Organic Structure by Physical Methods*, 2nd edn. (Eds. K. W. Bentley and G. W. Kirby), Part I, Chap. IX., Wiley–Interscience, New York, 1972, pp. 165, 638, 653.
27. S. Braverman and Y. Duar, *Tetrahedron Letters*, 343 (1975).
28. S. Braverman and H. Manor, *Phosphorus and Sulfur*, **2**, 213 (1976).

29. D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon and K. Mislow, *J. Amer. Chem. Soc.*, **88**, 3138 (1966).
30. E. G. Miller, D. R. Rayner, H. J. Thomas and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4861 (1968).
31. J. Jacobus, *J. Chem. Soc., Chem. Commun.*, 709 (1970).
32. Q. E. Thompson, *J. Org. Chem.*, **30**, 2703 (1965).
33. (a) S. Braverman, Ph.D. Thesis, University of Alberta, 1963.
(b) D. Darwish and S. Braverman, 48th Chemical Institute of Canada Conference, Montreal, Canada, May 30–June 2, 1965.
34. (a) S. Braverman, *3rd Symposium on Mechanism and Structure in Sulfur Chemistry*, Cork, Ireland, Sept. 29–Oct. 3, 1969.
(b) S. Braverman, *Int. J. Sulfur Chem. (C)*, 149 (1971).
35. S. Braverman and Y. Stabinsky, *J. Chem. Soc., Chem. Commun.*, 270 (1967).
36. S. Braverman and Y. Stabinsky, *Israel J. Chem.*, **5**, 71p (1967).
37. S. Braverman and C. Simons, in *Mechanisms of Reactions of Sulfur Compounds* (Eds. N. Kharasch, B. S. Thyagarajan and A. I. Khodair), Vol. 2, Intra-Science Research Foundation, Santa-Monica, Calif., 1968, p. 102.
38. Y. Stabinsky, M.Sc. Thesis, Bar-Ilan University, 1968.
39. A. C. Cope, D. E. Morrison and L. Field, *J. Amer. Chem. Soc.*, **72**, 59 (1950).
40. G. Sosnovsky, *J. Chem. Soc.*, 3139 (1956).
41. A. B. Burg, in *Organic Sulfur Compounds* (Ed. N. Kharasch), Vol. 1, Pergamon, Oxford, 1961, pp. 35–37.
42. A. Iliceto, A. Fava and U. Mazzucato, *Tetrahedron Letters*, 27 (1960).
43. A. Fava, in *Organic Sulfur Compounds* (Eds. N. Kharasch and C. Y. Meyers), Vol. 2, Pergamon Press, London, 1966, p. 86.
44. E. G. Miller, D. R. Rayner and K. Mislow, *J. Amer. Chem. Soc.*, **88**, 3139 (1966).
45. K. Mislow, *Rec. Chem. Prog.*, **28**, 217 (1967).
46. P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4869 (1968).
47. R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, **92**, 2100 (1970).
48. N. S. Zefirov and F. A. Ablulvaleeva, *Zh. Org. Khim.*, **7**, 947 (1971).
49. M. Isobe, H. Iio, M. Kitamura and T. Goto, *Tetrahedron Letters*, 541 (1978).
50. R. W. Hoffmann, *Angew. Chem. (Int. Ed.)*, **18**, 563 (1979).
51. R. W. Hoffmann, in *IUPAC Organic Sulfur Chemistry* (Eds. R. K. Freidlina and A. E. Skorova), Pergamon Press, Oxford, 1981, p. 69.
52. P. H. Laur, in *Sulfur in Organic and Inorganic Chemistry* (Ed. A. Senning), Vol. 3, Marcel Dekker, New York, 1972, p. 91.
53. M. Mikolajczyk and J. Drabowicz, in *Topics in Stereochemistry* (Eds. N. L. Allinger, E. L. Eliel and S. H. Wilen), Vol. 13, Wiley–Interscience, New York, 1982, p. 333.
54. M. R. Barbachyn and C. R. Johnson, in *Asymmetric Synthesis* (Eds. J. D. Morrison and J. W. Scott), Vol. 4, Academic Press, New York, 1984, p. 227.
55. A. Nudelman, *The Chemistry of Optically Active Sulfur Compounds*, Gordon and Breach, New York, 1984.
56. R. K. Hill, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Vol. 3, Academic Press, 1984, p. 503.
57. D. J. Abbott and C. J. M. Stirling, *J. Chem. Soc. (C)*, 818 (1969).
58. D. A. Evans, G. C. Andrews and C. L. Sims, *J. Amer. Chem. Soc.*, **93**, 4956 (1971).
59. R. D. G. Cooper and F. L. José, *J. Amer. Chem. Soc.*, **92**, 2575 (1970).
60. D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974).
61. J. E. Baldwin and J. E. Patrick, *J. Amer. Chem. Soc.*, **93**, 3556 (1971).
62. U. Schöllkopf, K. Fellenberger and M. Rizk, *Justus Liebigs Ann. Chem.*, **734**, 106 (1970).
63. Y. Yamamoto, J. Oda and Y. Inouye, *J. Org. Chem.*, **41**, 303 (1976).
64. D. N. Jones, J. Blenkinsopp, A. C. F. Edmonds, E. Helmy and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 2602 (1973).
65. M. J. Carter and I. Fleming, *J. Chem. Soc., Chem. Commun.*, 679 (1976).
66. M. Isobe, H. Iio, T. Kawai and T. Goto, *J. Amer. Chem. Soc.*, **100**, 1940 (1978).
67. D. A. Evans, C. A. Bryan and C. L. Sims, *J. Amer. Chem. Soc.*, **94**, 2891 (1972).
68. D. A. Evans, T. C. Crawford, T. T. Fujimoto and R. C. Thomas, *J. Org. Chem.*, **39**, 3176 (1974).
69. D. F. Taber, *J. Amer. Chem. Soc.*, **99**, 3513 (1977).
70. D. Tunemoto, Y. Takahatake and K. Kondo, *Chem. Letters*, 189 (1978).

71. K. Kondo, T. Umemoto, K. Yako and D. Tunemoto, *Tetrahedron Letters*, 3927 (1978).
72. K. Kondo, T. Umemoto, Y. Takahatake and D. Tunemoto, *Tetrahedron Letters*, 113 (1977).
73. J. G. Miller, W. Kurz, K. G. Untch and G. Stork, *J. Amer. Chem. Soc.*, **96**, 6774 (1974).
74. K. Bannai, T. Toru, T. Oba, T. Tanaka, N. Okamura, K. Watanabe and S. Kurozumi, *Tetrahedron Letters*, **22**, 1417 (1981).
75. M. Kodama, K. Shimada, T. Takahashi, C. Kabuto and S. Ito, *Tetrahedron Letters*, **22**, 4271 (1981).
76. B. M. Trost and N. R. Schmuff, *J. Amer. Chem. Soc.*, **107**, 396 (1985).
77. M. Kodama, K. Shimada and S. Ito, *Tetrahedron Letters*, 2763 (1977).
78. J. K. Whitesell, D. James and J. F. Carpenter, *J. Chem. Soc., Chem. Commun.*, 1449 (1985).
79. V. Rautenstrauch, *J. Chem. Soc., Chem. Commun.*, 526 (1970).
80. S. Goldmann, R. W. Hoffmann, N. Maak and K. J. Geueke, *Chem. Ber.*, **113**, 831 (1980).
81. R. W. Hoffmann and N. Maak, *Tetrahedron Letters*, 2237 (1976).
82. R. W. Hoffmann and S. Goldmann, *Tetrahedron Letters*, 2599 (1978).
83. R. W. Hoffmann, S. Goldmann, N. Maak, R. Gerlach, F. Frickel and G. Steinbach, *Chem. Ber.*, **113**, 819 (1980).
84. R. W. Hoffmann, S. Goldmann, R. Gerlach and N. Maak, *Chem. Ber.*, **113**, 845 (1980).
85. R. W. Hoffmann, R. Gerlach and S. Goldmann, *Chem. Ber.*, **113**, 856 (1980).
86. H. J. Reich, K. E. Yelm and S. Wollowitz, *J. Amer. Chem. Soc.*, **105**, 2503 (1983).
87. D. A. Evans, G. C. Andrews, T. T. Fujimoto and D. Wells, *Tetrahedron Letters*, 1385 (1973).
88. J. Nokami, T. Mandai, Y. Imakura, M. Kawada and S. Wakabayashi, *Tetrahedron Letters*, 4489 (1981).
89. R. Annunziata, M. Cinquini, F. Cozzi and L. Raimondi, *J. Chem. Soc., Chem. Commun.*, 366 (1986).
90. R. S. Garigipati, A. J. Freyer, R. R. Whittle and S. M. Weinreb, *J. Amer. Chem. Soc.*, **106**, 7861 (1984).
91. P. A. Grieco, *J. Chem. Soc., Chem. Commun.*, 702 (1972).
92. P. A. Grieco and R. S. Finkelhor, *J. Org. Chem.*, **38**, 2245 (1973).
93. D. A. Evans, G. C. Andrews, T. T. Fujimoto and D. Wells, *Tetrahedron Letters*, 1389 (1973).
94. K. Kosugi, H. Uda and S. Yamagiwa, *J. Chem. Soc., Chem. Commun.*, 192 (1975).
95. P. R. Ortiz de Montellano and C. K. Hsu, *Tetrahedron Letters*, 4215 (1976).
96. P. Brownbridge and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1131 (1977).
97. S. Warren, *Acc. Chem. Res.*, **11**, 401 (1978).
98. Y. Masaki, K. Hashimoto and K. Kaji, *Tetrahedron Letters*, 4539, 5123 (1978).
99. Y. Masaki, K. Hashimoto and K. Kaji, *Tetrahedron*, **40**, 3481 (1984).
100. A. Ogiso, E. Kitazawa, M. Kurabayasho, A. Sato, S. Takahashi, H. Noguchi, H. Kuwano, S. Kobayashi and H. Mishima, *Chem. Pharm. Bull. Japan*, **26**, 3117 (1978).
101. S. Yamagiwa, H. Sato, N. Hoshi, H. Kosugi and H. Uda, *J. Chem. Soc., Perkin Trans 1*, 570 (1979).
102. P. Blatcher and S. Warren, *Tetrahedron Letters*, 1247 (1979).
103. P. Blatcher and S. Warren, *J. Chem. Soc., Perkin Trans 1*, 1055 (1985).
104. Y. Masaki, K. Hashimoto, K. Sakuma and K. Kaji, *Chem. Pharm. Bull.*, **32**, 3952 (1984).
105. Y. Masaki, K. Sakuma and K. Kaji, *Chem. Pharm. Bull.*, **33**, 2531 (1985).
106. P.-T. Ho, *Can. J. Chem.*, **58**, 861 (1980).
107. K. B. Sharpless, C. H. Beherens, T. Katsuki, A. W. M. Lee, V. S. Martin, M. Takatami, S. Mi Viti, F. J. Walker and S. S. Woodward, *Pure Appl. Chem.*, **55**, 589 (1983).
108. J. K. Cha, W. J. Christ and Y. Kishi, *Tetrahedron*, **40**, 2247 (1984).
109. W. C. Still and J. C. Barrish, *J. Amer. Chem. Soc.*, **105**, 2487 (1983).
110. H. J. Reich, I. L. Reich and S. Wollowitz, *J. Amer. Chem. Soc.*, **100**, 5981 (1978).
111. H. J. Reich and S. Wollowitz, *J. Amer. Chem. Soc.*, **104**, 7051 (1982).
112. J. H. Babler and B. J. Invergo, *J. Org. Chem.*, **44**, 3723 (1979).
113. C. W. Hutchins, G. K. Copper, S. Purro and H. Rapoport, *J. Med. Chem.*, **24**, 773 (1981).
114. Ae. de Groot, B. J. M. Jansen, J. T. A. Reuvers and E. M. Tedjo, *Tetrahedron Letters*, **22**, 4137 (1981).
115. E. Guittett and S. Julia, *Tetrahedron Letters*, 1155 (1978).
116. R. C. Cookson and P. J. Parson, *J. Chem. Soc., Chem. Commun.*, 821 (1978).
117. D. N. Jones, N. A. Meanwell and S. M. Mirza, *J. Chem. Soc., Perkin Trans 1*, 145 (1985).
118. M. Isobe, H. Iio, M. Kitamura and T. Goto, *Chem. Letters*, 541 (1978).

119. D. W. Emerson and T. J. Korniski, *J. Org. Chem.*, **34**, 4115 (1969).
120. P. T. Lansbury and J. E. Rhodes, *J. Chem. Soc., Chem. Commun.*, 21 (1974).
121. P. T. Lansbury and R. W. Britt, *J. Amer. Chem. Soc.*, **98**, 4577 (1976).
122. I. Schuphan and J. E. Casida, *Tetrahedron Letters*, 841 (1979).
123. I. Cutting and P. J. Parson, *Tetrahedron Letters*, **22**, 2021 (1981).
124. T. E. Goodwin, D. G. Ratcliff, C. M. Crowder and N. K. Seitzinger, *J. Org. Chem.*, **47**, 815 (1982).
125. B. M. Trost and J. L. Stanton, *J. Amer. Chem. Soc.*, **97**, 4018 (1975).
126. H. Matsuyama, A. Izuoka and M. Kobayashi, *Heterocycles*, **23**, 1897 (1985).
127. N. J. Daniels, G. Johnson, B. C. Ross and M. A. Yeomas, *J. Chem. Soc., Chem. Commun.*, 1119 (1982).
128. J.-P. Corbet and C. Benezra, *J. Org. Chem.*, **46**, 1141 (1981).
129. B. M. Trost and J. B. Rigby, *J. Org. Chem.*, **43**, 2938 (1978).
130. M. Johnstone, R. Raines, C. Walsh and R. A. Firestone, *J. Amer. Chem. Soc.*, **102**, 4241 (1980).
131. B. P. Branchand and C. T. Walsh, *J. Amer. Chem. Soc.*, **107**, 2153 (1985).
132. Y. Gaoni, *Phosphorus and Sulfur*, **6**, 101 (1979).
133. T. Kametani, M. Tsubuki, H. Nemoto and K. Suzuki, *J. Amer. Chem. Soc.*, **103**, 1256 (1981).
134. Q. B. Cass, A. A. Jaxa-Chamiec and P. G. Sammes, *J. Chem. Soc., Chem. Commun.*, 1248 (1981).
135. E. J. Corey and D. J. Hoover, *Tetrahedron Letters*, **23**, 3463 (1982).
136. E. J. Corey, H. Oh and A. E. Barton, *Tetrahedron Letters*, **23**, 3467 (1982).
137. E. Morera and G. Ortar, *J. Org. Chem.*, **48**, 119 (1983).
138. W. L. Brown and A. G. Fallis, *Tetrahedron Letters*, **26**, 607 (1985).
139. S. Braverman and H. Mechoulam, *Israel J. Chem.*, **5**, 71 (1967).
140. S. Braverman and H. Mechoulam, *Tetrahedron*, **30**, 3883 (1974).
141. S. Braverman and Y. Stabinsky, *Israel J. Chem.*, **5**, 125 (1967).
142. G. Smith and C. J. M. Stirling, *J. Chem. Soc. (C)*, 1530 (1971).
143. L. Horner and V. Binder, *Justus Liebigs Ann. Chem.*, **757**, 33 (1972).
144. V. Van Rheenen and K. P. Shephard, *J. Org. Chem.*, **44**, 1582 (1979).
145. G. Neef, U. Eder and A. Seeger, *Tetrahedron Letters*, **21**, 903 (1980).
146. A. Haces, E. M. G. A. Van Kruchten and W. H. Okamura, *Tetrahedron Letters*, **23**, 2707 (1982).
147. R. C. Cookson and R. Gopalan, *J. Chem. Soc., Chem. Commun.*, 608 (1978).
148. R. C. Cookson and P. J. Parsons, *J. Chem. Soc., Chem. Commun.*, 822 (1978).
149. H. J. Altenbach and H. Soicke, *Liebigs Ann. Chem.*, 1096 (1982).
150. I. Cutting and P. J. Parsons, *Tetrahedron Letters*, **24**, 4463 (1983).
151. I. Cutting and P. J. Parsons, *J. Chem. Soc., Chem. Commun.*, 1209 (1983).
152. H.-J. Altenbach and H. Soicke, *Tetrahedron Letters*, **27**, 1561 (1986).
153. E. M. G. A. Van Kruchten and W. H. Okamura, *Tetrahedron Letters*, **23**, 1019 (1982).
154. W. Reischl and W. H. Okamura, *J. Amer. Chem. Soc.*, **104**, 6115 (1982).
155. W. H. Okamura, R. Peter and W. Reischl, *J. Amer. Chem. Soc.*, **107**, 1034 (1985).
156. W. H. Okamura, G.-Y. Shen and R. Tapia, *J. Amer. Chem. Soc.*, **108**, 5018 (1986).
157. I. Z. Egenburg, *Russ. Chem. Rev.*, **47**, 900 (1978).
158. W. H. Okamura, *Acc. Chem. Res.*, **16**, 81 (1983).
159. S. Jeganathan and W. H. Okamura, *Tetrahedron Letters*, **23**, 4763 (1982).
160. A. J. Bridges and J. W. Fisher, *J. Chem. Soc., Chem. Commun.*, 665 (1982).
161. B. M. Trost, W. C. Vladuchiek and A. J. Bridges, *J. Amer. Chem. Soc.*, **102**, 3548, 3554 (1980).
162. L. E. Overman, L. A. Clizbe, R. L. Freerks and C. K. Marlowe, *J. Amer. Chem. Soc.*, **103**, 2807 (1977).
163. S. Danishefsky, C. F. Yan and P. M. McCurry, *J. Org. Chem.*, **42**, 1819 (1977).
164. G. H. Posner and W. Harrison, *J. Chem. Soc., Chem. Commun.*, 1786 (1985).
165. M. Cinquini, S. Colonna and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 256 (1975).
166. M. Cinquini, S. Colonna, F. Cozzi and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 1*, 2061 (1976).
167. K. C. Majumdar and B. S. Thyagarajan, *J. Chem. Soc., Chem. Commun.*, 83 (1972).
168. Y. Makisumi and S. Takada, *J. Chem. Soc., Chem. Commun.*, 848 (1974).
169. H. J. Reich and S. K. Shah, *J. Amer. Chem. Soc.*, **99**, 263 (1977).
170. T. Numata and S. Oae, *Int. J. Sulfur Chem. (A)*, **1**, 215 (1971).
171. T. J. Maricich and C. K. Harrington, *J. Amer. Chem. Soc.*, **94**, 5115 (1972).
172. F. G. Bordwell and W. T. Brannen, Jr., *J. Amer. Chem. Soc.*, **86**, 4645 (1964).
173. K. Ogura and G. Tsuchihashi, *J. Chem. Soc., Chem. Commun.*, 1689 (1970).

174. A. C. Cope and P. H. Towle, *J. Amer. Chem. Soc.*, **71**, 3423 (1949).
175. R. M. Dodson, P. D. Hammen and J. Y. Fan, *J. Org. Chem.*, **36**, 2703 (1971).
176. D. N. Jones, T. P. Kogan, R. F. Newton and S. Smith, *J. Chem. Soc., Chem. Commun.*, 589 (1982).
177. R. B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*, Verlag Chemie, Aschaffenburg, 1971, pp. 114, 131.
178. R. L. Crumbie and D. D. Ridley, *Aust. J. Chem.*, **34**, 1017 (1981).
179. S. Braverman and D. Reisman, *J. Amer. Chem. Soc.*, **99**, 605 (1977).
180. S. Braverman and Y. Duar, *J. Amer. Chem. Soc.*, **105**, 1061 (1983).
181. S. Braverman, Plenary Lecture, 11th International Symposium on the Organic Chemistry of Sulfur, Lindau (FRG), 10–14 Sept. 1984; *Phosphorus and Sulfur*, **23**, 297 (1985).
182. (a) S. Braverman and D. Reisman, unpublished results.
(b) D. Reisman, Ph.D. Thesis, Bar-Ilan University, 1985.
183. E. Kühle, *Synthesis*, 577 (1970).
184. J. S. Bradshaw and R. H. Hales, *J. Org. Chem.*, **36**, 318 (1971).
185. G. W. Astrologes and J. C. Martin, *J. Amer. Chem. Soc.*, **97**, 6910 (1975).
186. E. Block, *Quart. Rep. Sulfur Chem.*, **4**, 317 (1969).
187. R. G. Petrova and R. K. H. Freidlina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1797 (1966) (Engl. Transl.)
188. T. Sato, Y. Goto, T. Tohyama, S. Hayashi and K. Hata, *Bull. Chem. Soc. Japan*, **40**, 2975 (1967).
189. D. C. Dittmer, G. E. Kuhlman and G. C. Levy, *J. Org. Chem.*, **35**, 3676 (1970).
190. A. G. Schultz and R. H. Schlessinger, *J. Chem. Soc., Chem. Commun.*, 1294 (1970).
191. A. G. Schultz and R. H. Schlessinger, *Tetrahedron Letters*, 3605 (1973).
192. I. W. J. Still and M. T. Thomas, *Tetrahedron Letters*, 4225 (1970).
193. I. W. J. Still, N. S. Chauhan and M. T. Thomas, *Tetrahedron Letters*, 1311 (1973).
194. I. W. J. Still, P. C. Arora, M. S. Chauhan, M.-H. Kwan and M. T. Thomas, *Can. J. Chem.*, **54**, 455 (1976).
195. K. Kobayashi and K. Mutai, *Tetrahedron Letters*, **22**, 5201 (1981).
196. T. Durst and K.-C. Tin, *Tetrahedron Letters*, 2369 (1970).
197. D. F. Tavares, R. E. Estep and M. Blezard, *Tetrahedron Letters*, 2373 (1970).
198. J. R. Williams, G. M. Sarkisian, J. Quiglay, A. Hasiuk and R. Vander Vennen, *J. Org. Chem.*, **39**, 1028 (1974).
199. T. Durst, K.-C. Tin, F. de Reinach-Hirtzbach, J. M. Decesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).
200. B. M. Trost, T. N. Salzmann and K. Hiroi, *J. Amer. Chem. Soc.*, **98**, 4887 (1976).
201. V. Reutrakul and W. Kanghae, *Tetrahedron Letters*, 1377 (1977).
202. O. Carmona, R. Greenhouse, R. Landeros and J. M. Muchowski, *J. Org. Chem.*, **45**, 5336 (1980).
203. R. D. Baechler, L. J. San Filippo and A. Schroll, *Tetrahedron Letters*, **22**, 5247 (1981).
204. (a) R. D. Baechler, P. Bentley, L. Deuring and S. Fisk, *Tetrahedron Letters*, **23**, 2269 (1982).
(b) H. Kwart and D. A. Benko, *J. Amer. Chem. Soc.*, **101**, 1277 (1979).
205. A. G. Anastassiou, J. C. Wetzel and B. Y.-H. Chao, *J. Amer. Chem. Soc.*, **97**, 1124 (1975).
206. J. A. Ross, R. P. Seiders and D. M. Lemal, *J. Amer. Chem. Soc.*, **98**, 4325 (1976).
207. C. H. Bushweller, J. A. Ross and D. M. Lemal, *J. Amer. Chem. Soc.*, **99**, 629 (1977).
208. A. T. Balaban and L. D. Farcasiu, *J. Amer. Chem. Soc.*, **89**, 1958 (1967).
209. J. P. Snyder and T. A. Halgren, *J. Amer. Chem. Soc.*, **102**, 2861 (1980).
210. F. Lautenschlaeger, *J. Org. Chem.*, **34**, 3998 (1969).
211. H. Kwart and J. L. Schwartz, *J. Chem. Soc., Chem. Commun.*, 44 (1969), and references cited therein.
212. B. W. Bycroft and W. Landon, *J. Chem. Soc., Chem. Commun.*, 967 (1970).
213. Y. Makisumi, S. Takada and Y. Matsukura, *J. Chem. Soc., Chem. Commun.*, 850 (1974).
214. E. Block, R. E. Penn, and L. K. Revelle, *J. Amer. Chem. Soc.*, **101**, 2200 (1979).
215. R. Bell, P. D. Cottam, J. Davies, D. N. Jones and N. A. Meanwell, *Tetrahedron Letters*, **21**, 4379 (1980).
216. E. Block and S. Ahmad, *J. Amer. Chem. Soc.*, **107**, 6731 (1985).
217. E. Vedejs and P. L. Fuchs, *J. Org. Chem.*, **36**, 366 (1971).
218. E. J. Corey and I. J. Shulman, *J. Amer. Chem. Soc.*, **92**, 5522 (1970).
219. J. F. King and D. R. K. Harding, *J. Amer. Chem. Soc.*, **98**, 3312 (1976).
220. E. Block, A. Wall and J. Zubieta, *J. Amer. Chem. Soc.*, **107**, 1783 (1985).
221. A. G. Schultz, C. D. DeBoer and R. H. Schlessinger, *J. Amer. Chem. Soc.*, **90**, 5314 (1968).

222. A. G. Schultz and R. H. Schlessinger, *J. Chem. Soc., Chem. Commun.*, 1483 (1969).
223. M. Franck-Neumann and J. J. Lohmann, *Tetrahedron Letters*, 2397 (1979).
224. R. Tanikaga, Y. Higashio and A. Kaji, *Tetrahedron Letters*, 3273 (1970).
225. R. Lüdersdorf and K. Praefcke, *Z. Naturforsch.*, **31b**, 1658 (1976).
226. R. A. Archer and P. V. DeMarco, *J. Amer. Chem. Soc.*, **91**, 1530 (1969).
227. D. O. Spry, *J. Amer. Chem. Soc.*, **92**, 5006 (1970).
228. D. H. R. Barton, F. Comer and P. G. Sammes, *J. Amer. Chem. Soc.*, **91**. 1529 (1969).
229. D. H. R. Barton, F. Comer, D. G. T. Greig, G. Lucente, P. G. Sammes and W. G. E. Underwood, *J. Chem. Soc., Chem. Commun.*, 1059 (1970).
230. R. D. G. Cooper, *J. Amer. Chem. Soc.*, **92**, 5010 (1970).
231. C. A. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, **82**, 1810 (1960).
232. D. H. R. Barton, D. G. T. Greig, G. Lucente, P. G. Sammes, M. V. Taylor, C. M. Cooper, G. Hewitt and W. G. E. Underwood, *J. Chem. Soc., Chem. Commun.*, 1683 (1970).
233. I. Ager, D. H. R. Barton, G. Lucente and P. G. Sammes, *J. Chem. Soc., Chem. Commun.*, 601 (1972).
234. D. H. R. Barton, I. H. Coates, P. G. Sammes and C. M. Cooper, *J. Chem. Soc., Chem. Commun.*, 303 (1973).
235. I. Ager, D. H. R. Barton, D. G. T. Greig, G. Lucente, P. G. Sammes, M. V. Taylor, G. W. Hewitt, B. E. Looker, A. Mowatt, C. A. Robson and W. G. E. Underwood, *J. Chem. Soc., Perkin Trans. 1*, 1187 (1973).
236. S. Terao, T. Matsuo, S. Tsushima, N. Matsumoto, T. Miyawaki and M. Miyamoto, *J. Chem. Soc., Chem. Commun.*, 1304 (1972).
237. R. D. Allan, D. H. R. Barton, M. Girijavallabahn and P. G. Sammes, *J. Chem. Soc., Perkin Trans. 1*, 1456 (1974).
238. T. S. Chou, *Tetrahedron Letters*, 725 (1974).
239. D. H. R. Barton, P. G. Sammes, M. V. Taylor, C. M. Cooper, G. Hewitt, B. E. Looker and W. G. E. Underwood, *J. Chem. Soc., Chem. Commun.*, 1137 (1971).
240. R. D. Allan, D. H. R. Barton, M. Girijavallabahn, P. G. Sammes and M. V. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1182 (1973).
241. T. Kamiya, T. Teraji, Y. Saito, M. Hashimoto, O. Nakaguchi and T. Oku, *Tetrahedron Letters*, 3001 (1973).
242. R. D. G. Cooper, *J. Amer. Chem. Soc.*, **94**, 1018 (1974).
243. T. S. Chou, J. R. Burgtorf, A. L. Ellis, S. R. Lammert and S. P. Kukolja, *J. Amer. Chem. Soc.*, **96**, 1609 (1974).
244. D. N. Jones, D. R. Hill and D. A. Lewton, *Tetrahedron Letters*, 2235 (1975).
245. R. J. Bushby, *J. Chem. Soc., Perkin Trans. 1*, 2590 (1976).
246. H. Shimizu, N. Ueda, T. Kataoka and M. Hori, *Heterocycles*, **22**, 1025 (1984).
247. R. J. Stoodley and R. B. Wilkins, *J. Chem. Soc., Perkin Trans. 1*, 1572 (1974).
248. J. R. Shelton and K. E. Davis, *J. Amer. Chem. Soc.*, **89**, 718 (1967).
249. J. R. Shelton and K. E. Davis, *Int. J. Sulfur Chem.*, **8**, 197 (1973).
250. D. N. Jones and D. A. Lewton, *J. Chem. Soc., Chem. Commun.*, 457 (1974).

CHAPTER 15

Synthetic uses of sulfones

KAZUHIKO TANAKA and ARITSUNE KAJI

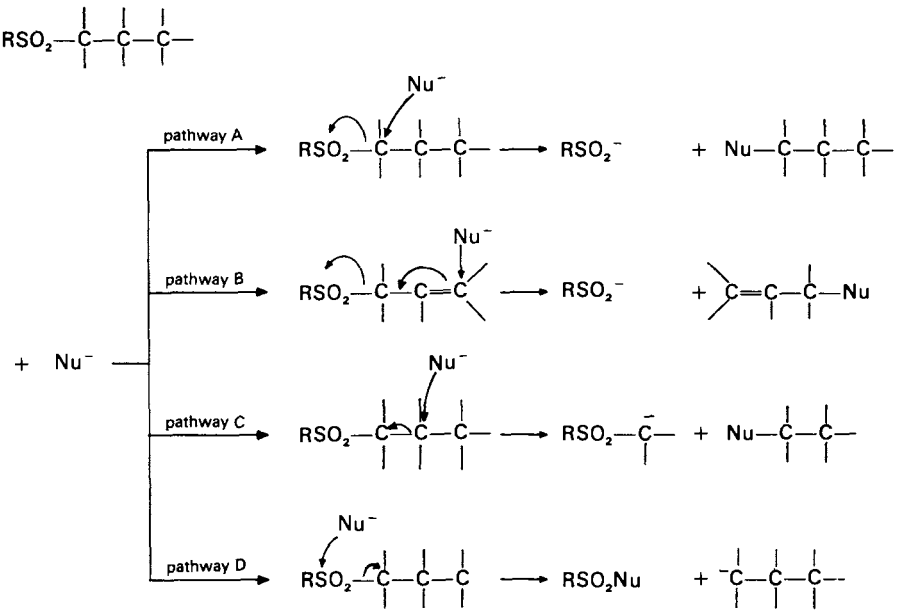
Department of Chemistry, Faculty of Science, Kyoto University, Sakyo, Kyoto 606, Japan

I. INTRODUCTION

This chapter deals with (1) the transformation of the sulfone functionality into other functional groups by nucleophilic substitution reaction, and (2) the addition and elimination reaction of α,β-unsaturated sulfones. Particular attention will be paid to recent uses of sulfones in organic syntheses[1].

II. SUBSTITUTION REACTIONS OF SULFONES

Reaction of sulfones with nucleophiles has been studied a great deal from both a preparative and a mechanistic standpoint[1,2]. The nucleophilic substitution reactions of sulfones may be categorized to four groups according to the sites attacked by the nucleophile (equation 1).



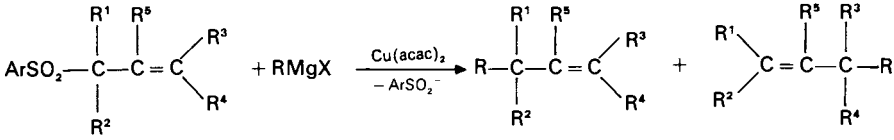
(1)

Pathway A shows the most common reaction where the nucleophilic substitution reaction occurs at the electron-deficient carbon atom due to the strong electron-attracting character of the sulfonyl group. Nucleophilic displacements at the allylic position (S_N2' reaction) are shown in pathway B. Pathway C is the formation of α-sulfonyl carbanion by nucleophilic attack on the carbon atom β to the sulfone moiety. There are relatively few reports on substitution reactions where nucleophiles attack the sulfone functionality and displace a carbanion as illustrated in pathway D[3].

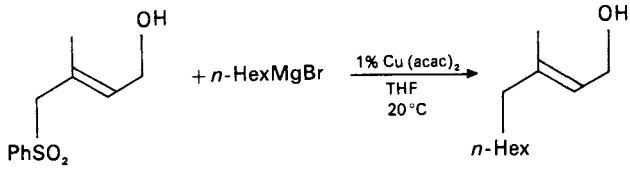
A. Nucleophilic Displacement of Sulfonyl Groups

1. Reaction of allylic sulfones

In the presence of copper(II) acetylacetonate, the reaction of Grignard reagents with allylic sulfones **1** occurs at the α-position (pathway A in equation 1) to give a substitution product **2**, or at the γ-position (pathway B) to give olefins **3** (equation 2). The highest α-regioselectivity has been observed in the cases of γ-alkyl-substituted allyl sulfones (Table 1)[4]. A similar reaction of the (*E*)-hydroxyallyl sulfone (**4**) with *n*-hexylmagnesium bromide produces the allyl alcohol **5** in 90% yield with high (*E*)-stereoselectivity (equation 3). However, reaction of the (*Z*)-isomer **6** affords a mixture of (*E*)- and (*Z*)-allyl



(1) **(2)** **(3)** (2)



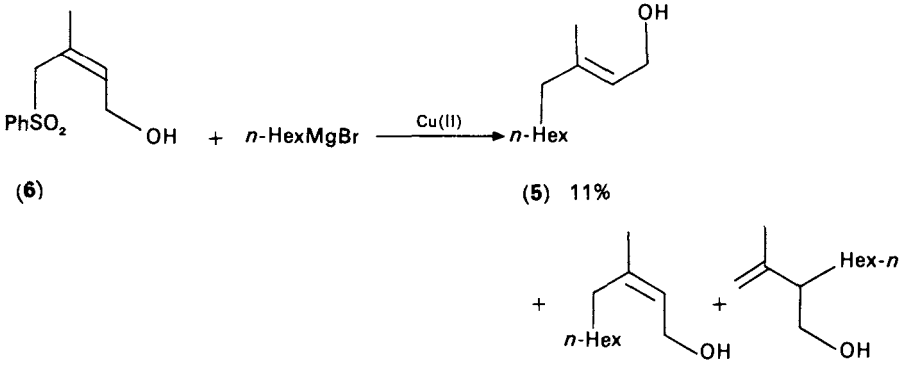
(4) **(5)** 90% (3)

TABLE 1. Reaction of allyl sulfones **1** with *n*-hexylmagnesium halides (*n*-HexMgX)[4]

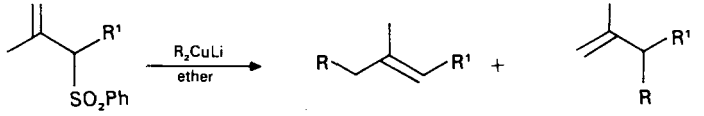
Allyl sulfone **1**	Yield of **2** + **3** (%)	**2**/**3** Ratio
$PhSO_2$	85	—
p-$TolSO_2$	91	100:0[a]
$PhSO_2$	65	16:84[b]
$PhSO_2$	2	100:0[a]
$PhSO_2$	30	100:0[a]

[a]Pure *E* isomer of **2** was obtained.
[b]40:60 of *E*/*Z* ratio of **3**.

alcohols **5** and **7** and the rearranged product **8** (equation 4)[5]. The reaction of allyl sulfones **9** with lithium dialkylcuprate yields predominantly the (*E*)-γ-adduct **10** together with some α-adduct **11** (equation 5). Olefins prepared by this method are listed in Table 2[6].



(4)



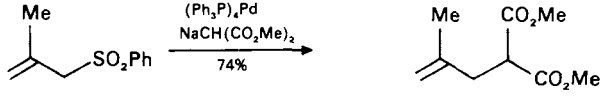
(9) (10) (11) (5)

Trost and coworkers[7] have reported the use of palladium(0) as a catalyst for displacement of the phenylsulfonyl group by soft nucleophiles. Thus, treatment of allyl sulfone **12** with the sodium salt of dimethyl malonate in the presence of 5 mol % of

TABLE 2. Product distribution for the displacement reaction of allyl sulfones **9** with lithium dialkyl cuprates[6]

Allyl sulfone R^1 in **9**	R in R_2CuLi	Yield of **10** + **11** (%)	**10**/**11** Ratio	*E*- **10**/*Z*- **10** Ratio
	Me	74	95:5	93:7
CH_3 $(CH_2)_2$—	*n*-Bu	73	98:2	92:8
$PhCH_2$—	Me	63	95:5	—
	n-Bu	89	92:8	86:14
$PhCH_2OCH_2CH{=}C(CH_2)_2$— Me	Me	85	95:5	85:15
	n-Bu	73	97:3	86:14

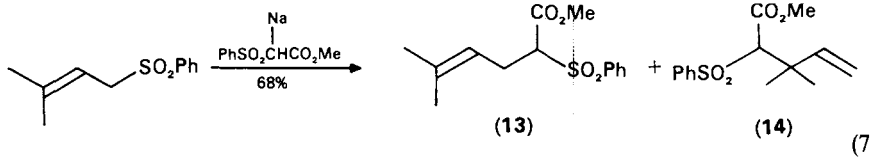
tetrakis(triphenylphosphine)palladium in THF yields the alkylation product (equation 6).



(6)

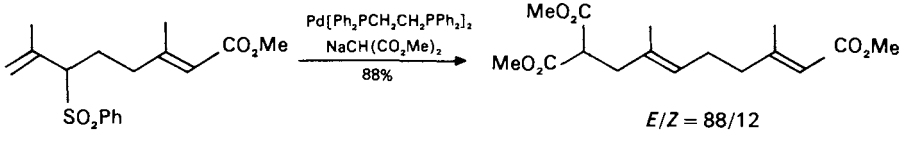
(12)

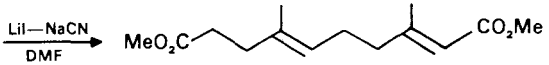
For trisubstituted olefins, the nucleophile attacks predominantly at the less substituted end of the allyl moiety, e.g. to afford a 78:22 mixture of **13** and **14** (equation 7). Both the oxidative addition of palladium(0) and the subsequent nucleophilic attack occur with inversion of configuration to give the product of net retention[7]. The synthesis of the sex pheromone **15** of the Monarch butterfly has been accomplished by using bis[bis(1,2-diphenylphosphinoethane)]palladium as a catalyst as outlined in equation 8[7]. A substitution of an allyl sulfone **16** by a stabilized carbon nucleophile, such as an alkynyl or vinyl system, proceeds regioselectively in the presence of a Lewis acid (equation 9)[8]. The



(13) (14)

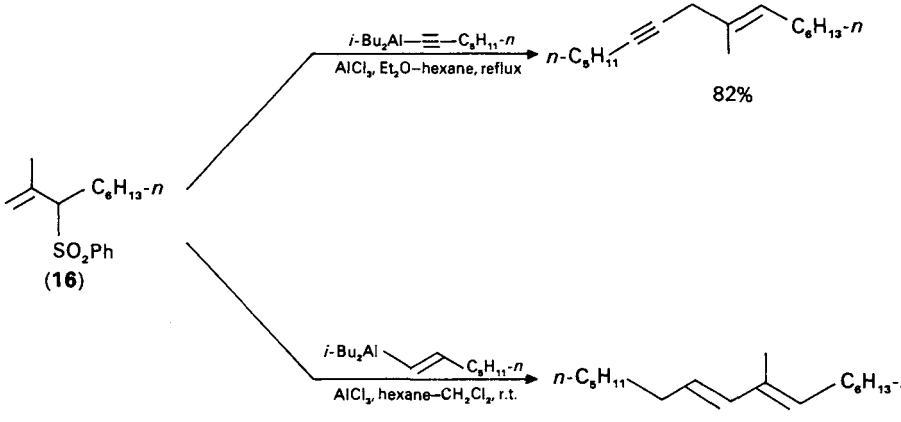
(7)





(15)

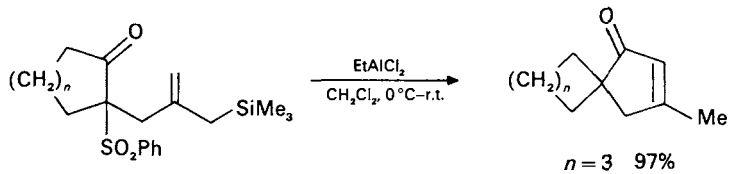
(8)



(9)

mechanism is reasonably explained by assuming an intermediate carbenium ion which is captured by the nucleophile. The transformation is compatible with a number of functional groups including esters, silyl ethers and hydroxyl groups[9].

A cyclization of β-keto sulfone **17** in the presence of a Lewis acid gives a spirocycles via a pinacol-type rearrangement in which the sulfone group serves as a leaving group (equation 10)[9].

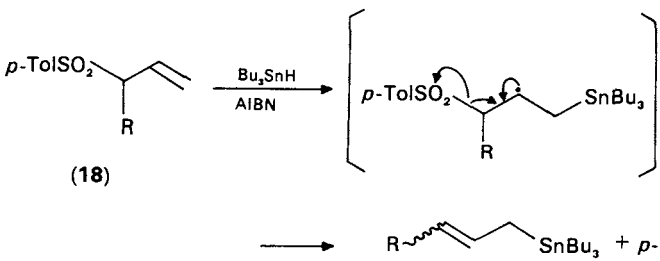


(17)

$n=3$ 97%
$n=4$ 95%
$n=5$ 97%

(10)

Ueno and coworkers[10] have found that the facile displacement of sulfonyl group from α-alkylated allyl *p*-tolyl sulfones **18** by tri-*n*-butyltin radical in the presence of 2,2′-azobis[2-methylpropanenitrile] (AIBN) occurs smoothly in refluxing benzene (equation 11). In contrast, vinyl sulfones undergo the radical substitution reaction to give vinylstannanes in the presence of AIBN at a higher temperature[11].



(18)

(11)

2. Reaction of α,β-unsaturated sulfones

The reaction of vinyl sulfones, e.g. **19**, with Grignard reagents in the presence of $Ni(acac)_2$ or $Fe(acac)_3$ leads to a stereoselective cross-coupling reaction (equation 12). Several examples of cross-coupling reaction are listed in Table 3[12]. In contrast, the cross-coupling reaction of alkynyl sulfones with alkyl Grignard or organolithium reagents proceeds smoothly without a catalyst to give substitution products (pathway A in

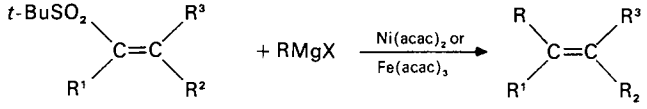
TABLE 3. Cross-coupling reaction of vinyl sulfones with Grignard reagents[12]

Vinyl sulfone (**19**)						
R^1	R^2	R^3	RMgX	Catalyst	Yield of **20** (%)	*E*:*Z* Ratio
H	Me	Me	PhMgBr	$Fe(acac)_3$	50	—
Me	Me	H	PhMgBr	$Ni(acac)_2$	68	100:0
n-Pr	*n*-Bu	H	MeMgCl	$Ni(acac)_2$	64	4:96
n-Hex	H	Me	MeMgBr	$Ni(acac)_2$	68	47:53

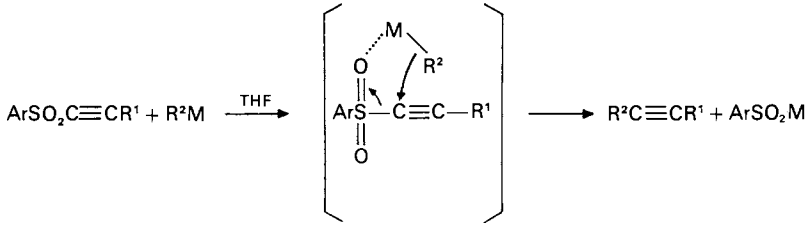
TABLE 4. Cross-coupling reaction of alkynyl sulfones $ArSO_2C{\equiv}CR^1$ with lithium reagents R^2Li[13]

Ar	R^1	R^2	Yield of alkyne (%)
Ph	Ph	*n*-Bu	98
Mesityl	Ph	Ph	81
p-Tol	*t*-Bu	*n*-Bu	84
p-Tol	*t*-Bu	*t*-Bu	95
Ph	H	Ph	61

equation 1) rather than Michael addition to the triple bond (equation 13)[13]. Alkynes prepared by this method are listed in Table 4.



(19) (20) (12)

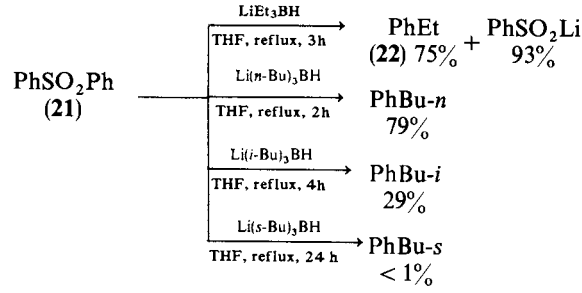


(13)

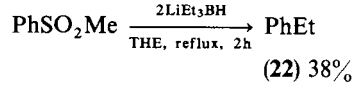
The reaction of organolithium reagents is rapid and complete in less than 1 min even at low temperature, while Grignard reagents require 12–24 h at room temperature to react completely. Treatment of (*E*)- or (*Z*)-1-methylsulfonyl-2-phenylethylene with trialkylboranes yields exclusively (*E*)-olefins via a vinyl radical intermediate[14].

3. *Reaction of aromatic sulfones*

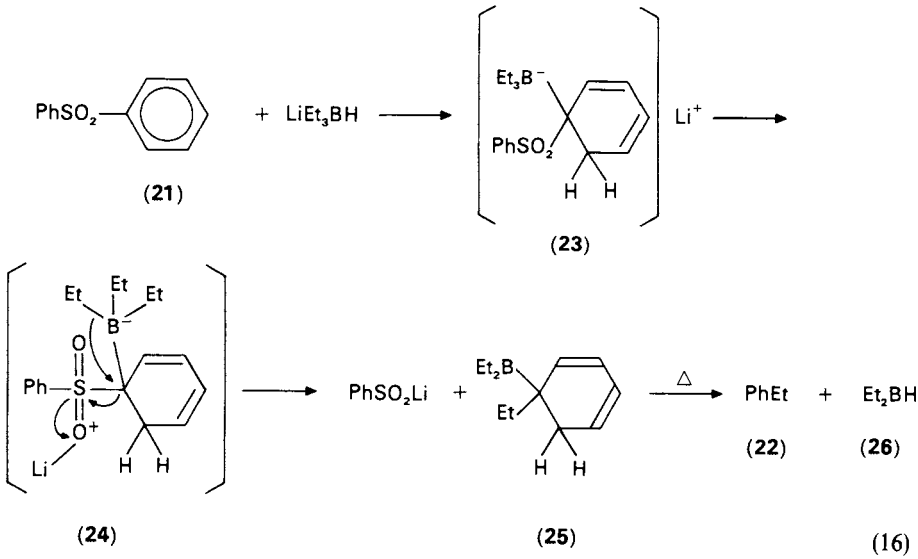
Aromatic and aliphatic sulfones are generally inert to metal hydride and complex metal hydride reducing agents. However, Brown and coworkers[15] have found recently that diaryl sulfones and alkyl aryl sulfones do react with lithium triethylborohydride in THF (equation 14). Alkyl aryl sulfones react more sluggishly, giving lower yields of the desired products (equation 15). Dialkyl sulfones are completely inert to this reagent. The suggested mechanistic pathway is given in equation 16. It has been concluded that the reaction proceeds by intramolecular migration of an ethyl group of **24** followed by elimination of diethylborane (**26**) to give ethylbenzene (**22**) in 71% yield. The presence of **26** is detrimental and lowers the yields of the product. When excess of 1-octene is added in order to trap the diethylborane produced, the yield of **22** can be increased to 92%[15].



(14)



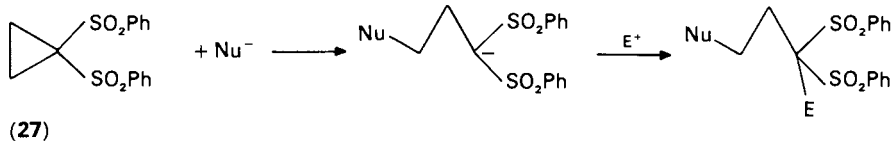
(15)



(16)

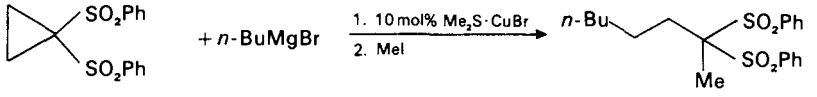
4. Reaction of cyclopropyl sulfones

Equations 17 and 18 illustrate the ring opening of 1, 1-bis(phenylsulfonyl)cyclopropane (**27**) leading to the formation of an α-sulfonyl carbanion via pathway C in equation 1[16].



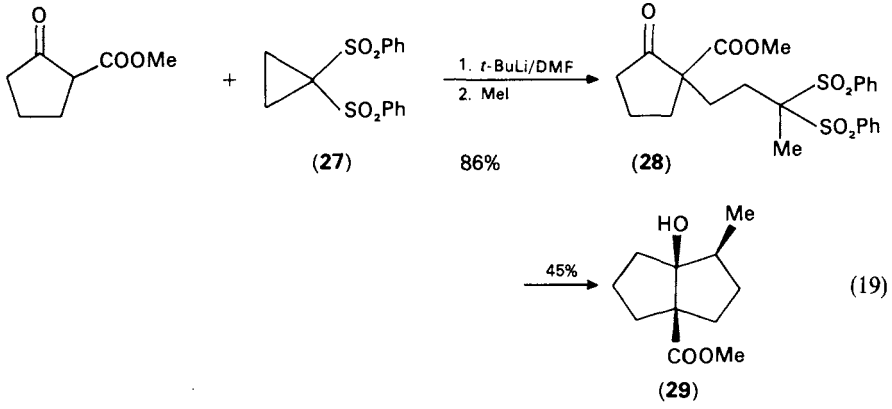
(27)

(17)



(27) 56% (18)

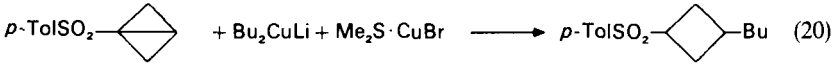
The α-sulfonyl carbanions can be trapped with a variety of electrophiles[19]. The method provides a synthetically useful synthon for a propylene 1,3-dipole. Reductive cleavage of the sulfone **28** thus prepared, with lithium phenanthrenide in THF, furnishes bicyclooctane **29** (equation 19)[16].



(27) 86% (28) (19)

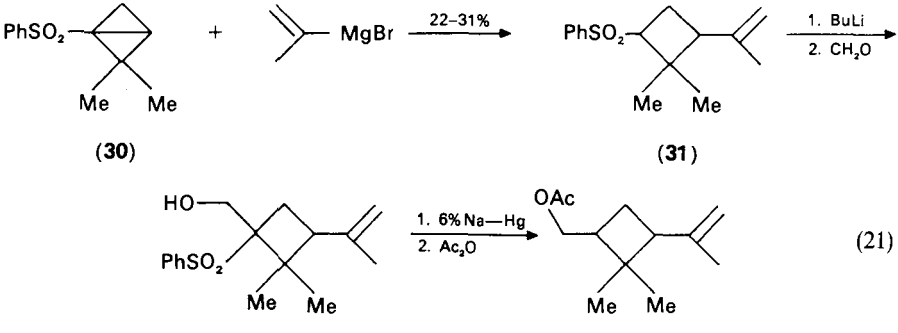
(29)

The central bond of the 1-(arylsulfonyl)bicyclo[1.1.0]butane system behaves like the double bond of α,β-unsaturated sulfones to give alkyl-substituted cyclobutyl aryl sulfones on treatment with organometallic reagents (equation 20)[17]. This method has been applied



(20)

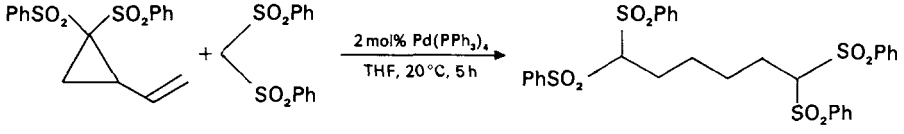
most elegantly in the synthesis of the sex pheromone **33** of the citrus mealybug *Planococcus citri* via hydroxymethylation of cyclobutyl sulfone **31** and subsequent reductive desulfonylation of **32** (equation 21).



(30) (31) (21)

(32) (33)

Palladium-catalyzed ring cleavage of 1,1-bis(phenylsulfonyl)-2-vinylcyclopropane has been reported (equation 22)[18].

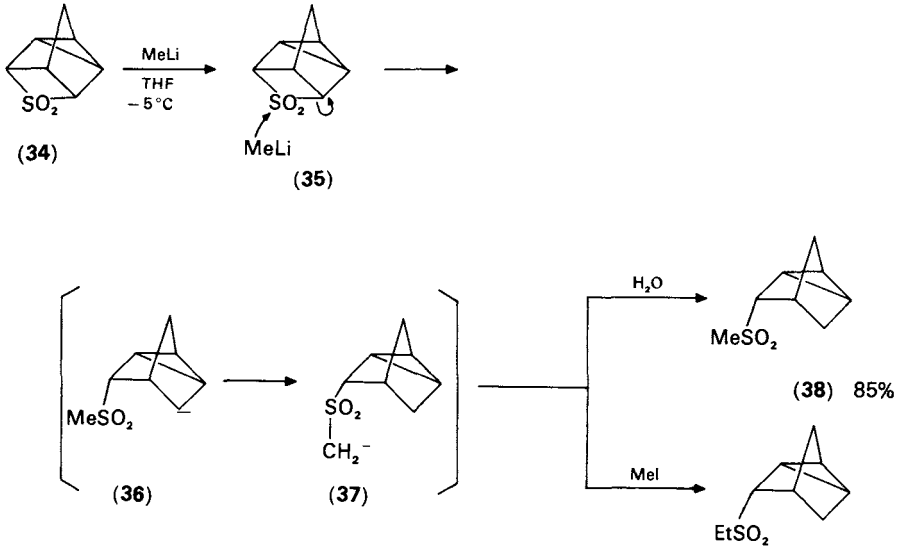


61% (22)

B. Nucleophilic Displacement on Sulfone Sulfur Atom

Whereas the reactions of sulfones with nucleophiles via pathways A and B of equation 1 are most frequently observed, the nucleophilic substitution reaction by pathway D has been observed only in the cases where the leaving carbanion can be stabilized, or in the highly strained molecules. Chou and Chang[3] has found recently that an organolithium reagent attacks the sulfur atom of the strained four-membered sulfone in **34**. When this sulfone is treated with 1 equivalent methyllithium, followed by workup with water or MeI, **38** or **39** are formed in high yield.

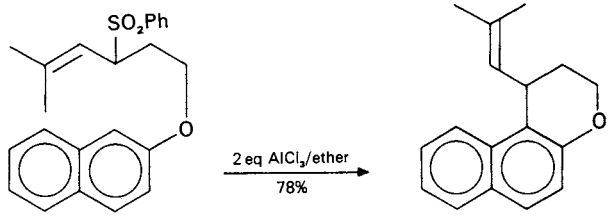
A reasonable mechanism is shown in equation 23: methyllithium attacks the sulfur atom, giving the secondary carbanion **36** by cleavage of the four-membered ring. A rapid proton transfer produces the sulfonyl-stabilized carbanion **37** which reacts with the added electrophile to give the product (equation 23)[3].



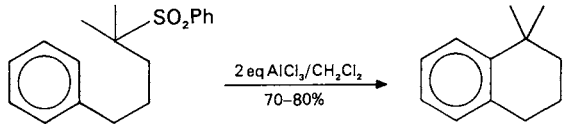
(23)

Trost and Ghadiri[19] have found a Lewis-acid-mediated intramolecular cyclization of allyl sulfones. When the allyl sulfone **40** is treated with $AlCl_3$, polycondensed aromatic system **41** can be obtained in good yield (equation 24). The mechanism probably involves

formation of a carbenium ion since a tertiary carbenium ion is about as stable as a simple allyl cation; the tertiary sulfone **42** gives **43** in good yield upon treatment with $AlCl_3$ in dichloromethane at low temperature (equation 25)[19].



(40) (41) (24)

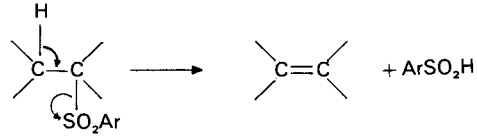


(42) (43) (25)

III. ELIMINATION REACTIONS OF SULFONES

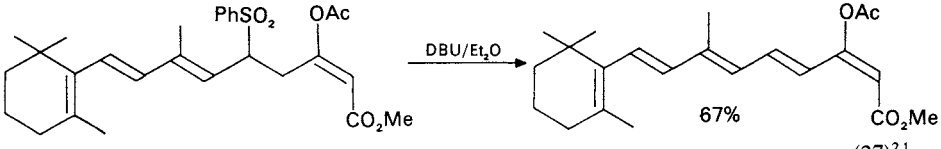
A. Synthesis of Alkenes by 1,2-Elimination Reactions

It is well known that elimination of a sulfonyl group from a system bearing acidic β-hydrogen atoms proceeds under relatively mild conditions to give olefins (equation 26)[2,20].

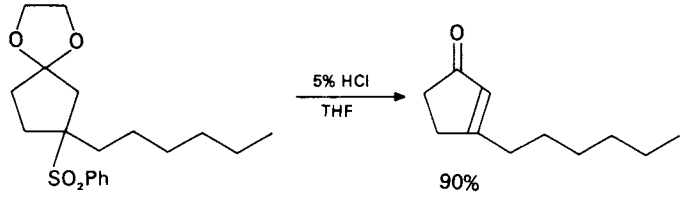


(26)

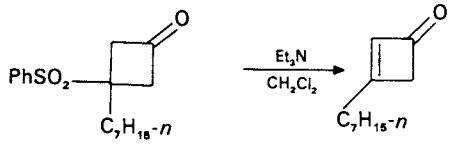
Examples of synthetically useful 1,2-eliminations under a variety of conditions are shown in equations 27–31. Sodium amalgam is the reagent of choice for the reductive elimination of sulfones involving leaving groups at the β-position. When the sulfone contains no such leaving groups, the sulfone moiety is replaced by hydrogen. Some representative examples of the reductive elimination of sulfones are given in equations 32–34. A reductive desulfonylation of 1,2-bis(arylsulfonyl)ethylenes is readily carried out by using sodium amalgam in methanol buffered with NaH_2PO_4, or magnesium in methanol (equations 35 and 36).



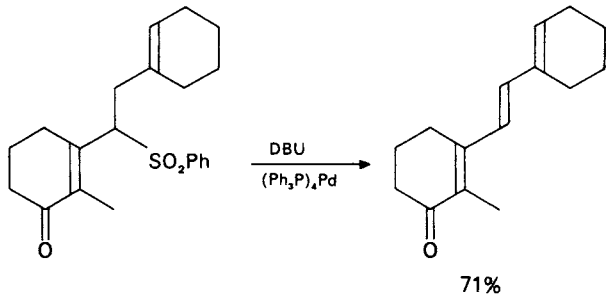
(27)[21]



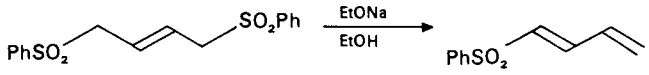
(28)[22]



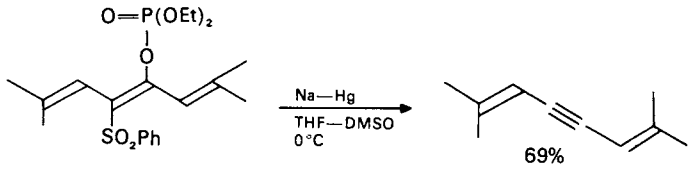
(29)[23]



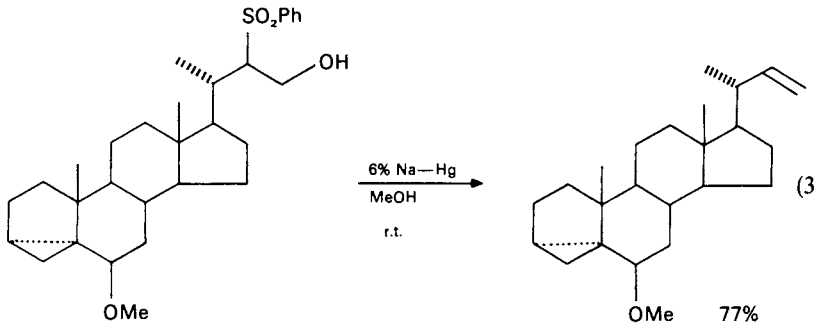
(30)[24]



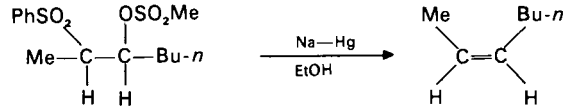
(31)[25]



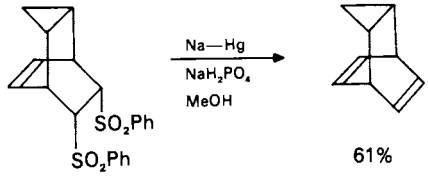
(32)[26]



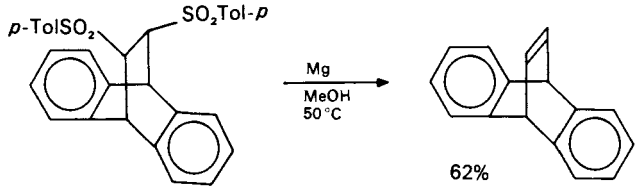
(33)[27]



(34)[28]

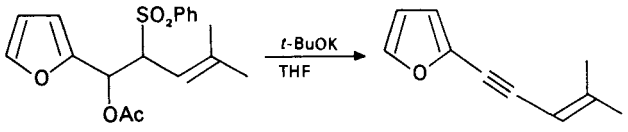


(35)[29]

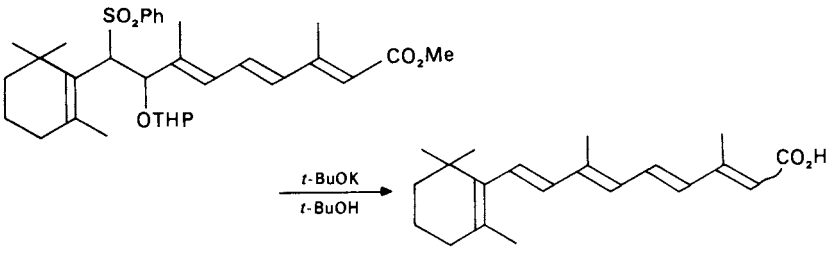


(36)[30]

Equations 37 and 38 show a convenient procedure for the preparation of acetylenes and polyenes which utilizes an excess of *t*-BuOK as a base in THF or THF–*t*-BuOH.

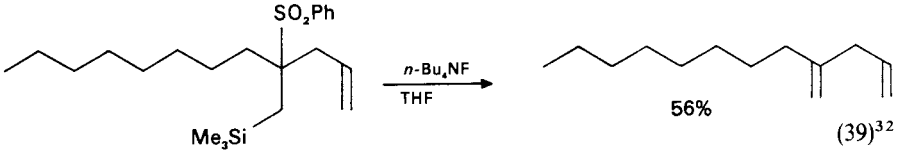


(37)[31]

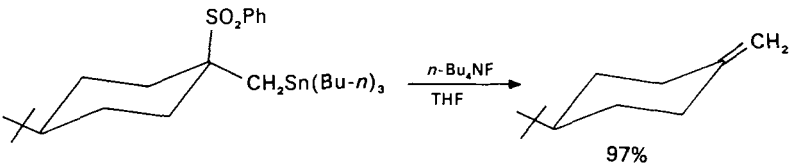


(38)[31]

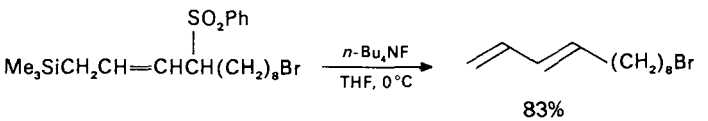
Sulfones with a trimethylsilyl or trialkylstannyl group at the δ-position or at the β-position are readily converted to olefins upon treatment with tetra-*n*-butylammonium fluoride in THF (equations 39–41). The method is compatible with the presence of a variety of functionalities.



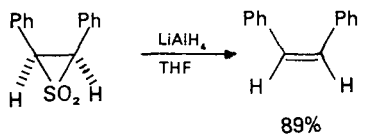
(39)[32]



(40)[33]

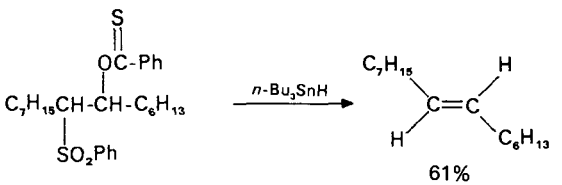


(41)[34]

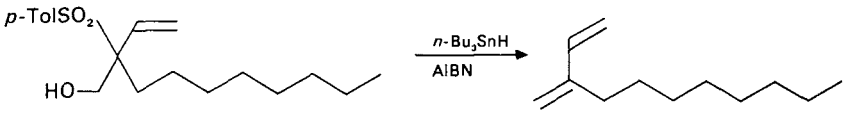


(42)[35]

Remarkable solvent effects on the selective bond cleavage are observed in the reductive elimination of *cis*-stilbene episulfone by complex metal hydrides. When diethyl ether or [bis(2-methoxyethyl)]ether is used as the solvent, dibenzyl sulfone is formed along with *cis*-stilbene. However, no dibenzyl sulfone is produced when *cis*-stilbene episulfone is treated with lithium aluminum hydride in tetrahydrofuran at room temperature (equation 42). Elimination of phenylsulfonyl group by tri-*n*-butyltin hydride proceeds by a radical chain mechanism (equations 43 and 44).



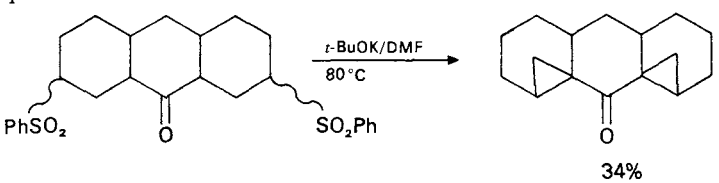
(43)[36]



(44)[37]

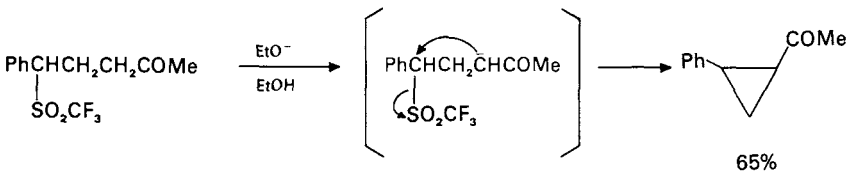
B. Synthesis of Cyclopropanes by 1,3-Elimination Reactions

The 1,3-elimination of γ-keto sulfones leads to the formation of cyclopropane rings as seen in equation 45[38].

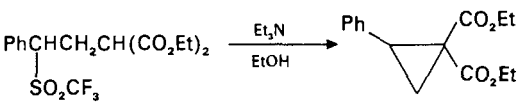


(45)

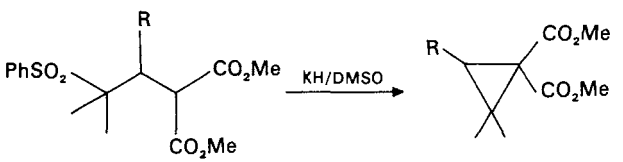
The cyclopropane cyclizations by elimination of triflinic acid (CF_3SO_2H) are readily effected by basic treatment of triflones (trifluoromethyl alkyl sulfones) with activated γ-protons (equations 46 and 47)[39]. The cyclopropane diesters **45** are formed on treatment of **44** with potassium hydride in DMSO or sodium methoxide in methanol (equation 48). In contrast, the monoester **46** failed to give the desired cyclopropane[40]. Addition of carbanions derived from β,γ-unsaturated phenyl sulfones to α,β-unsaturated carboxylic esters and subsequent elimination of benzenesulfinate ion give cyclopropanes possessing the unsaturated side chain and the ester function in *trans* positions (equation 49)[41].



(46)



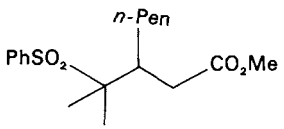
(47)



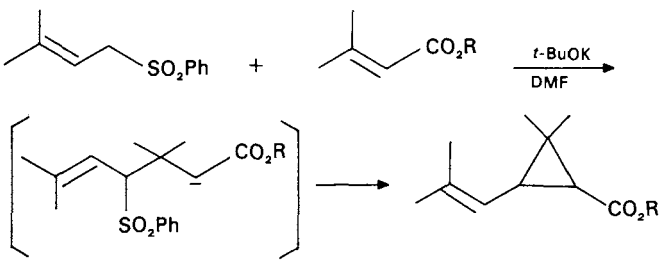
(48)

(44) **(45)**

R = Et 97%
R = *i*-Pr 76%



(46)



(49)

IV. ADDITION REACTIONS OF α,β-UNSATURATED SULFONES

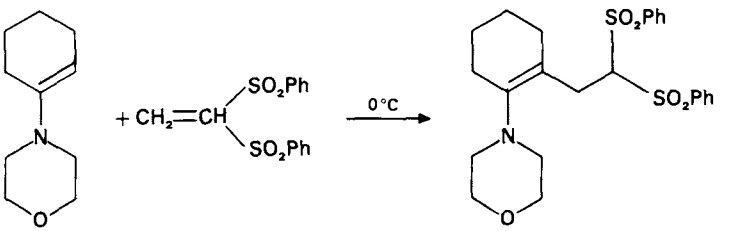
A. Addition of Nucleophiles to α,β-Unsaturated Sulfones

1. Reaction of alkenyl sulfones

a. Addition of amines, alcohols, thiols and enamines. Stirling and coworkers[42] have investigated nucleophilic addition reactions to α,β-unsaturated sulfones such as alkenyl, allenyl and alkynyl sulfones, with amines, alkoxides and thiolates. Reaction of 2-phenoxyethyl *p*-tolyl sulfone (**47**) with sodium ethoxide affords the sulfone **48** in 91% yield (equation 50). This reaction is not nucleophilic substitution reaction but a two-stage elimination–addition process. The reactions of α,β-unsaturated sulfones with enamines, amines and thiols are illustrated in equations 51[43], 52[44] and 53[45].

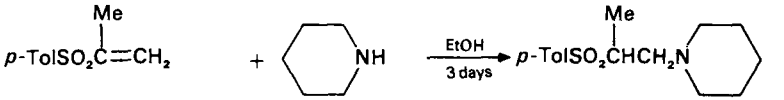
$$p\text{-TolSO}_2\text{CH}_2\text{CH}_2\text{OPh} \xrightarrow[\text{EtOH, 80°C}]{\text{NaOEt}} p\text{-TolSO}_2\text{CH}_2\text{CH}_2\text{OEt} + \text{PhOH} \qquad (50)$$

(**47**) (**48**)



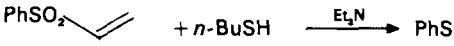
(51)

(**49**) (**50**) 100%



(52)

(**51**) (**52**) 88%

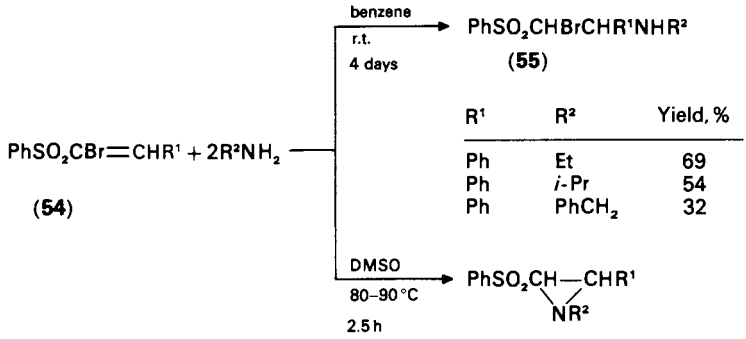


(53)

(**53**) 78%

The effect of the solvent on the product distribution is observed in the conjugate addition of amines to 1-bromo-1-(phenylsulfonyl)alkenes (**54**) (equation 54)[46]. When the reaction is conducted in benzene at room temperature for 4 days, the adduct **55** is formed in good yield. On the other hand, the reaction in DMSO at 80–90 °C for 2.5 h affords 2-(phenylsulfonyl)aziridines (**56**) and no adduct (**55**) is isolated.

The rate of the intramolecular displacement has been found to decrease in the order DMSO > DMF > HMPA > MeCN > benzenes ≃ 0.

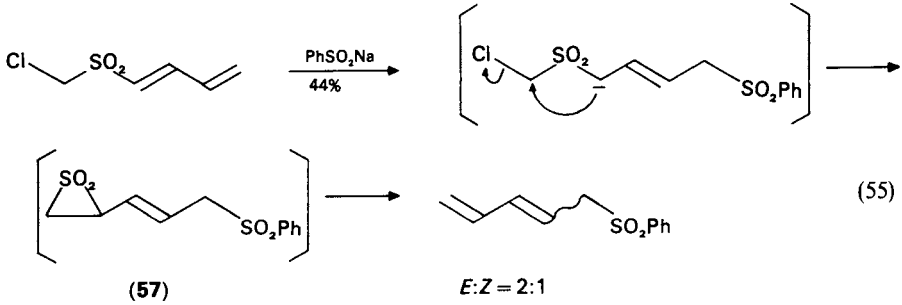


R^1	R^2	Yield,%
Ph	Et	69
Ph	*i*-Pr	54
Ph	$PhCH_2$	32

R^1	R^2	Yield,%
H	Me	25
Me	Et	38
Me	$PhCH_2$	66

(54)

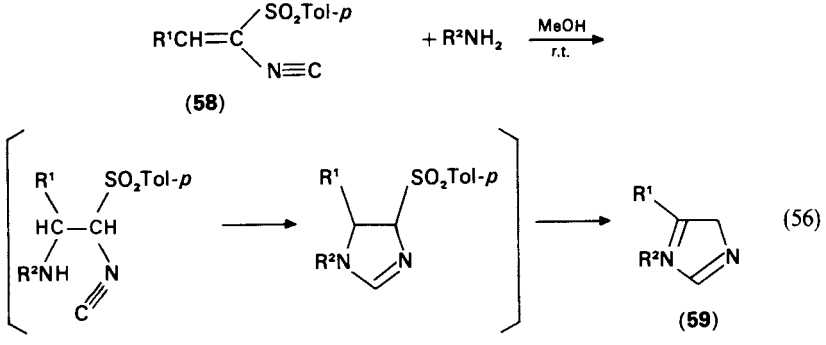
The Michael induced Ramberg–Bäcklund reactions gives a mixture of (*E*)- and (*Z*)-dienes via extrusion of SO_2 from the episulfone intermediate **57** (equation 55)[47].



(57) *E*:*Z* = 2:1

(55)

Reaction of α-isocyano-α,β-unsaturated sulfones with primary aliphatic amines affords 1,5-disubstituted imidazoles **59** (equation 56)[48]. The reaction of aromatic amines such as aniline is too slow to be of practical use. Results of the preparation of **59** are listed in Table 5.

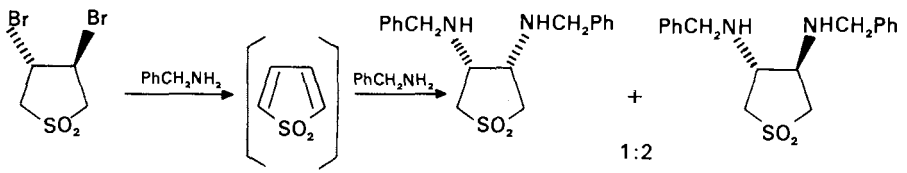


(56)

TABLE 5. Preparation of 1,5-disubstituted imidazoles (**59**)[48]

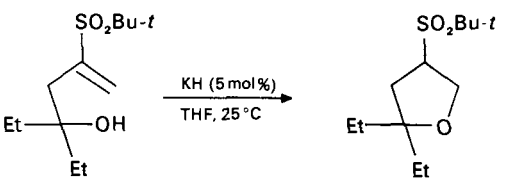
Sulfone (**58**) R^1	R^2	Reaction time, min	Yield of **59** (%)
Ph	H	180	65
Ph	Me	5	87
Ph	*t*-Bu	1440	82
Ph	*c*-C_6H_{11}	30	97
t-Bu	Me	10	46
H	Me	15	5

Addition of amines to α,β-unsaturated sulfones has been used in synthesis of key intermediates of biotin. In this reaction, benzylamine serves first as a base in the reaction with **60** to afford thiophene 1,1-dioxide (**61**) and also as a nucleophile to introduce two amino groups (equation 57)[49].

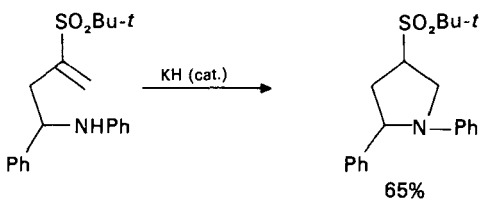


(**60**) (**61**) (57)

Normant and coworkers[50a] have recently studied the intramolecular addition of nucleophiles to vinyl sulfones. The presence of the sulfonyl group in equations 58 and 59 is essential for the disfavored 5-endo-trigonal closure[50b]. In contrast, the corresponding sulfoxide gives no cyclic product when treated with potassium hydride and only decomposition occurs.



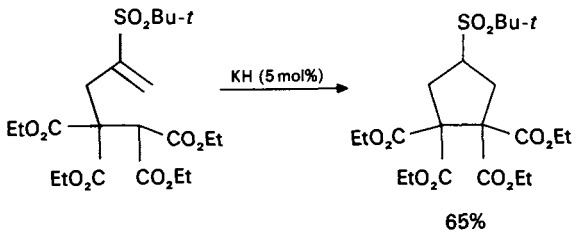
(58)



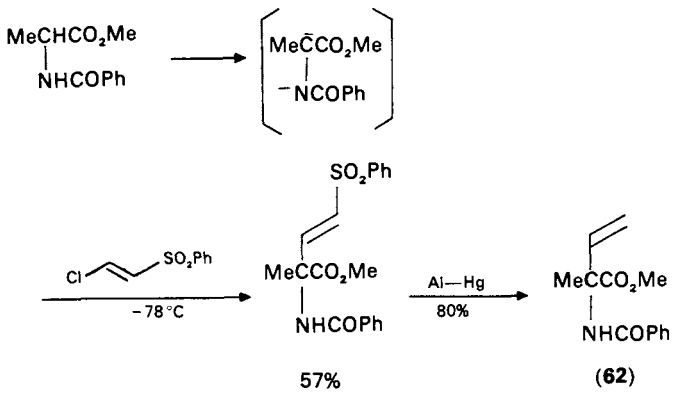
(59)

b. Addition of carbanions. Intramolecular addition of a carbanion to α,β-unsaturated sulfone is shown in equation 60[50]. (*E*)-2-Chlorovinyl phenyl sulfone can serve as a vinyl cation equivalent useful for the conversion of α-amino acids into α-vinyl α-amino acids[51].

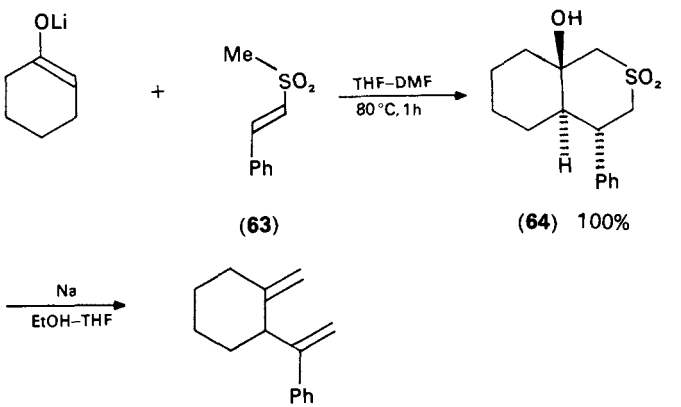
Thus, the dianion derived from α-amino acid substitutes the β-chloride to give the ester of 2-(phenylsulfonyl)ethenyl amino acid and subsequent desulfonylation provides *N*-(benzoyl)vinylalanine methyl ester (**62**) (equation 61). The conjugate addition of enolates to methyl styryl sulfone (**63**) and subsequent intramolecular addition to the carbonyl moiety provide a synthetically valuable method for the construction of bicyclic and tricyclic skeletons[52]. Desulfonylation of the cyclization product **64** with sodium in ethanol–THF gives the diene **65** in good yield (equation 62).



(60)

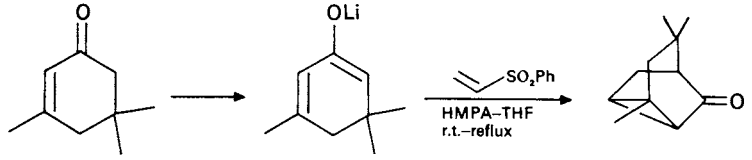


(61)



(62)

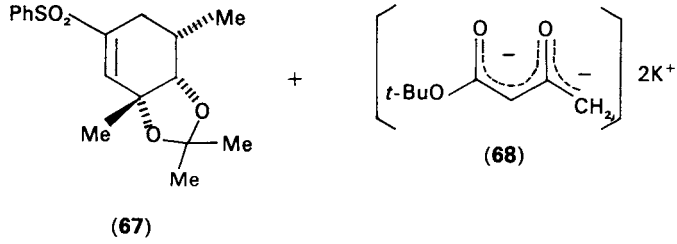
Cory and Renneboog[53] have devised an efficient bicycloannulation for the synthesis of tricyclo[3.2.1.$0^{2,7}$]octane-6-one (**66**) as shown in equation 63. The method involves three steps: (1) the enolate undergoes an initial conjugate addition to phenyl vinyl sulfone, (2) the resulting sulfone-stabilized carbanion undergoes an intramolecular Michael addition to the enone, and (3) the resulting enolate displaces phenylsulfinyl moiety from the tricyclooctanone. The amount of HMPA (3 mol equivalents) is critical for effective cyclization of the enolate.



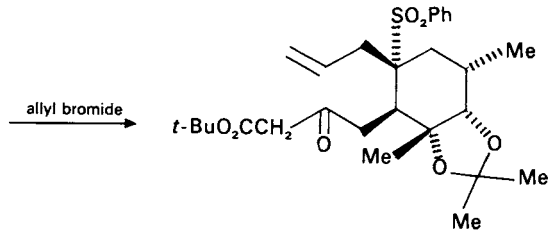
(63)

(**66**) 38%

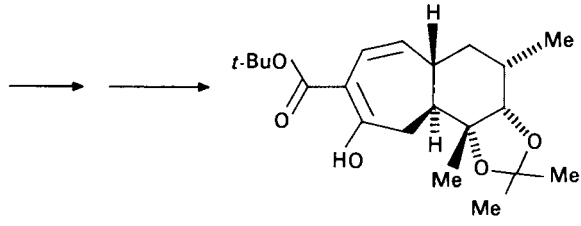
An example for synthesis of the chiral β-keto ester **69** is illustrated in equation 64. It involves conjugate addition of the dipotassium β-keto ester **68** to vinyl sulfone **67** followed by in situ quenching with allyl bromide[54]. The method provides a new procedure to seven-ring annulation product **70** that is a potential precursor for (1)-(−)-cytochalasin C.



(**67**) (**68**)



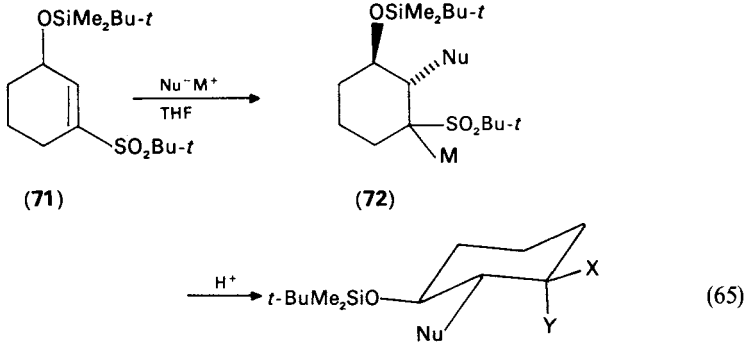
(**69**)



(64)

(**70**)

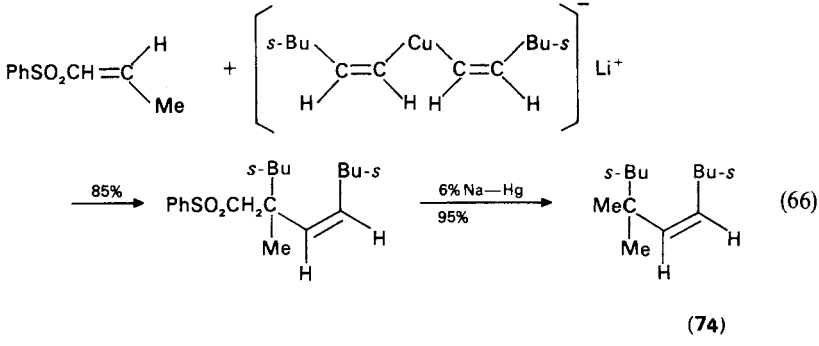
c. Addition of organometallic reagents. The reactivity of α,β-unsaturated sulfones with anionic nucleophiles is markedly dependent on the nature of the metal counterion (equation 65)[55]. Thus, the potassium salts are more reactive than the lithium salts and in several instances yield products **73** under conditions when the lithium counterion has failed completely. Table 6 shows the results of the addition of organometallic reagents.



(65)

(**73a**) X = SO_2Bu-*t*; Y = H
(**73b**) X = H; Y = SO_2Bu-*t*

The stereoselective conjugate addition of lithium (*Z*)-dialkenylcuprates to vinyl sulfones gives (*Z*)-olefins in the range of 70–80% overall yield and no (*E*)-isomer is detected (equation 66)[56]. The degree of stereoselectivity is higher than 90%.



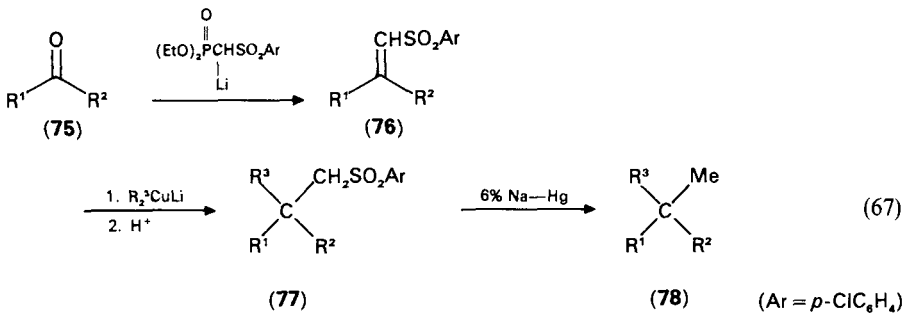
(66)

(**74**)

TABLE 6. Conjugate addition of organometallic reagents to vinyl sulfones[55]

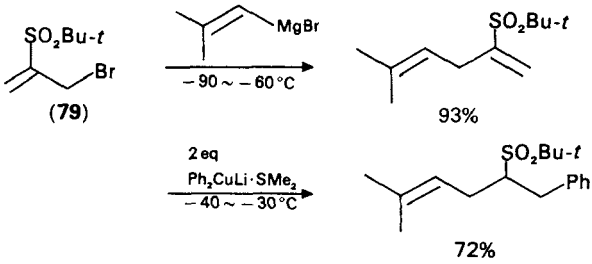
Organometallic nucleophile	Reaction conditions	Yield of **73a** + **73b** (%)	Ratio **73a:73b**
$LiCH_2CN$	−50 °C, 25 h	98	>99:1
$LiCH_2CO_2Et$	0 °C, 0.75 h	0	
KCH_2CO_2Et	0 °C, 0.75 h	88	>99:1
$LiCH_2COBu$-*t*	0 °C, 1 h	0	
KCH_2COBu-*t*	0 °C, 1 h	51	88:12

A synthetically useful conversion of the carbonyl group of **75** to a gem-dialkyl group has been investigated by Posner and Brunelle[57], who utilize diethyl arylsulfonyl phosphonate anion for the preparation of α,β-unsaturated aryl sulfones **76** (equation 67). Thus, conjugate addition of lithium dialkyl cuprate to **76** followed by desulfonylation yields alkanes **78**. The use of a *p*-chlorophenyl group in **76** is important since the *p*-chloro substituent would help in stabilizing the carbanion formed via the organocopper addition, thus apparently increasing the yield of the adduct **77**.



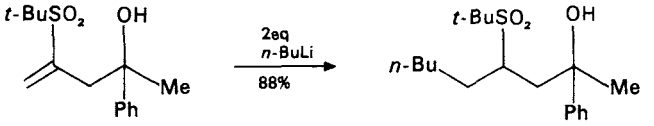
(67)

3-Bromo-2-(*t*-butylsulfonyl)propene (**79**) reacts with nucleophiles such as lithium benzenethiolate, lithium enolates and Grignard reagents to give α,β-unsaturated sulfones, which undergo nucleophilic addition of lithium cuprates (equation 68)[58].

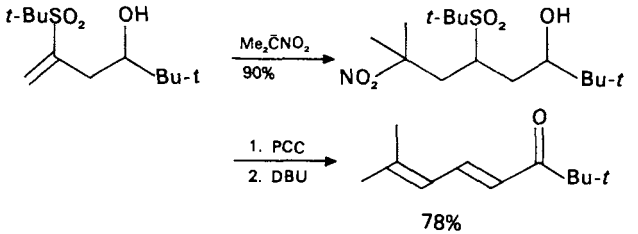


(68)

Nucleophiles such as alkyllithium, or the anion derived from 2-nitropropane, readily add to γ-hydroxy-α,β-unsaturated sulfones (equations 69 and 70)[59]. Oxidation followed by elimination of *t*-butylsulfinic acid leads to the formation of dienones (equation 70).

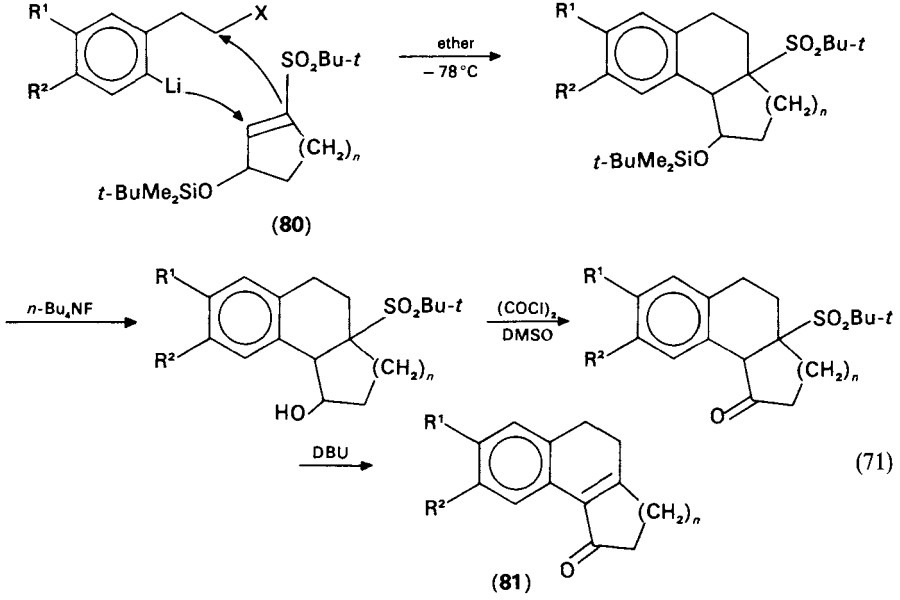


(69)



(70)

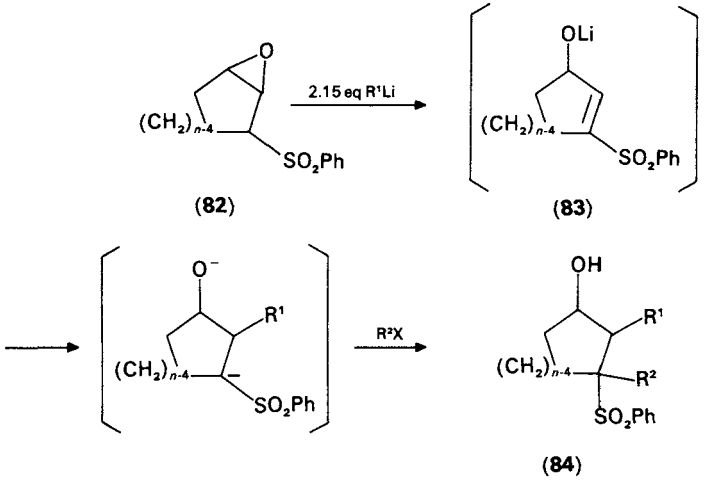
Helquist and coworkers[60] have developed a six-membered ring annulation via a conjugate addition of aryllithium generated by metal–halogen exchange and subsequent intramolecular alkylation. This is illustrated in equation 71.

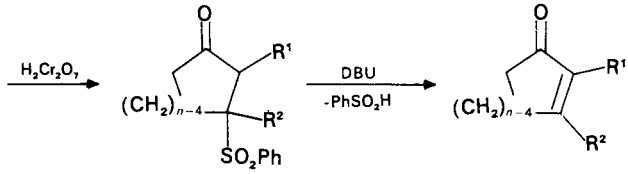


(71)

(81)

An interesting new method for the conversion of β,γ-epoxy sulfones (**82**) to cycloalkenones (**85**) has been developed[61]. It includes the addition of alkyllithium to γ-hydroxy-α,β-unsaturated sulfones generated from **82** and the alkylation of sulfonyl carbanion thus formed. Oxidation of the resulting γ-hydroxy sulfone to **84** followed by elimination of benzenesulfinic acid gives the desired product **85** in good yields (equation 72)[61].

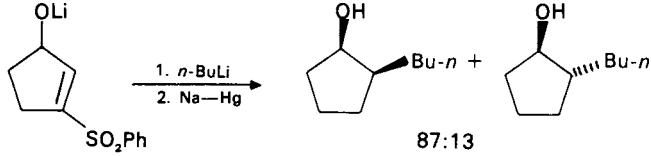




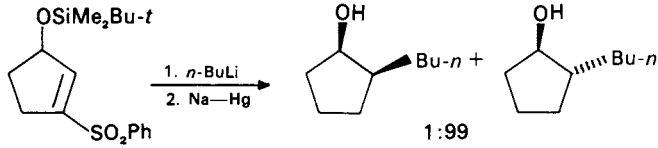
(85)

$n = 5, 6, 7$ (72)

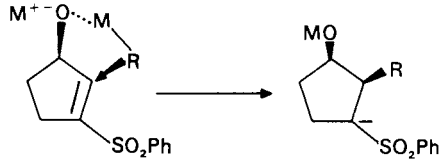
The reaction of the anion of γ-hydroxyvinyl sulfones **86** with organolithium or Grignard reagents gives mainly *cis* adducts in good yields after elimination of the phenylsulfinyl group (equation 73), while the reaction of γ-siloxyvinyl sulfones **87** affords almost exclusively *trans* adducts in moderate yields (equation 74)[62]. The *cis* addition to **86** can be explained by intramolecular assisted delivery of the alkyl group from the *cis* side via the alkoxide–organometallic complex **88** (equation 75). On the other hand, the alkyllithium attacks the least hindered face of the γ-siloxy sulfones (**87**) to give the *trans* adduct.



(86) (73)

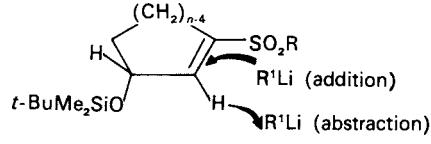


(87) (74)



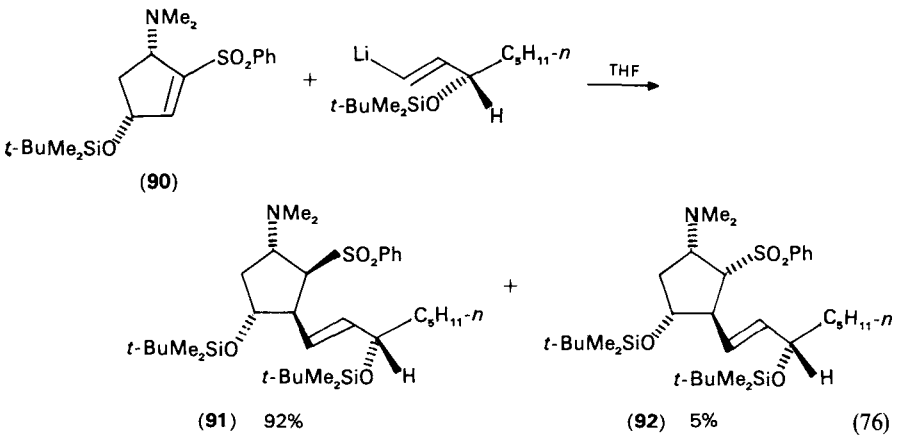
(88) (75)

Deprotonation of the vinylic proton is a serious side-reaction in the conjugate addition of organometallic reagents to γ-siloxy-α,β-unsaturated sulfones (**89**)[63b]. The use of the



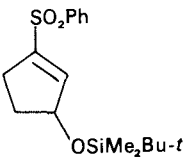
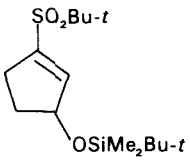
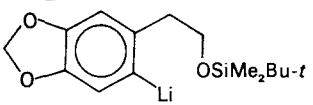
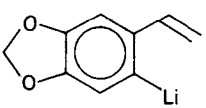
(89) R = Ph, t-Bu

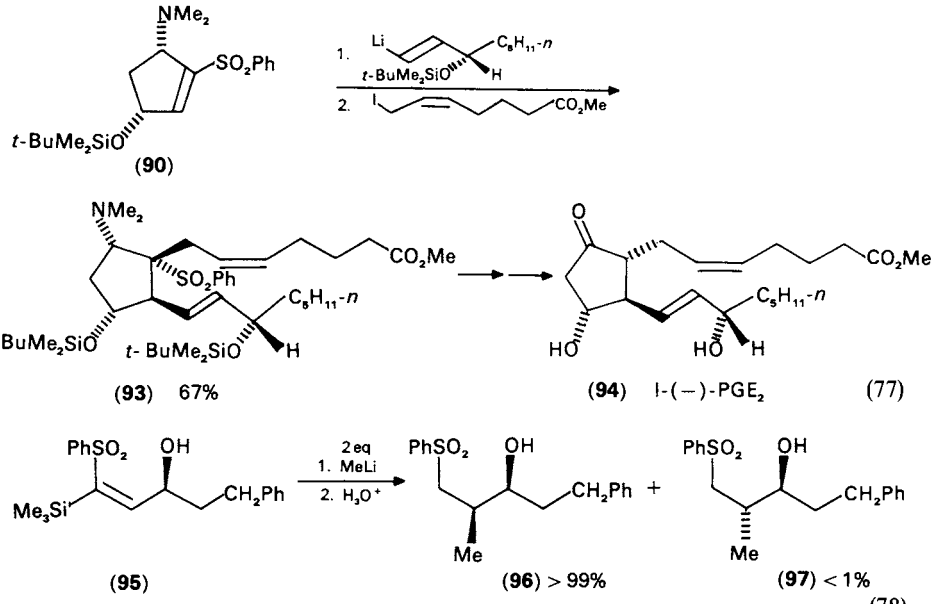
bulky *t*-butylsulfonyl group retards the deprotonation more strongly than it retards the conjugate addition reaction as judged from the yields of adducts (Table 7)[63]. Otherwise, this problem may be overcome by using the aminovinyl sulfone **90**. Treatment of **90** with methyl, phenyl, allyl, vinyl, *t*-butyl and (trimethylsilyl)ethynyllithium affords monoadducts **91** and **92** in excellent yields. A representative example is shown in equation 76[63]. A total synthesis of 1-(−)-prostaglandin E_2 (1-(−)-PGE_2 (**94**)) employing the chiral vinyl sulfone **90** has been reported (equation 77)[64]. The method involves an alkylation of the sulfone-stabilized carbanion derived from conjugate addition of optically active vinyllithium reagent. The overall yield of **94** from **90** is 36%. A stereoselective formation (>99%) of the syn γ-hydroxysulfone (**96**) has been achieved by conjugate addition of alkyllithium, which presumably coordinates with the oxygen atom of **95** (equation 78)[65]. The protection of the hydroxy group of **95** with *t*-butylchlorodimethylsilane reduces the stereoselectivity of the Michael addition **96**/**97** = 95/5). This high diastereoselective carbon–carbon bond formation can be used in the total synthesis of (±)-maytansinol[65e].



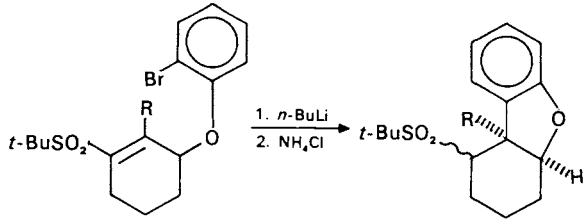
(76)

TABLE 7. Addition of organometallic reagents to sulfones[63b]

Organometallic reagents		
	Yield of adduct (%)	
	60	75
	26	95



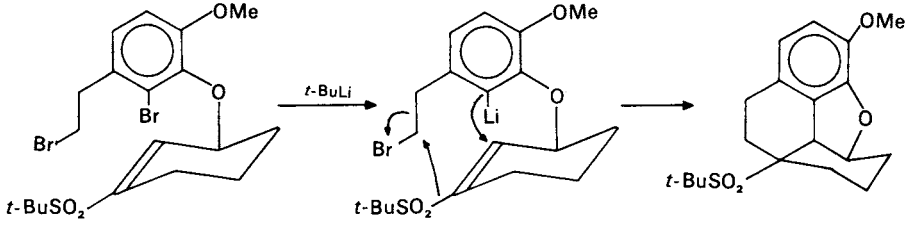
An example of intramolecular conjugate addition of aryllithium generated by halogen metal exchange reaction of **92** is illustrated in equation 79[66].



(79)

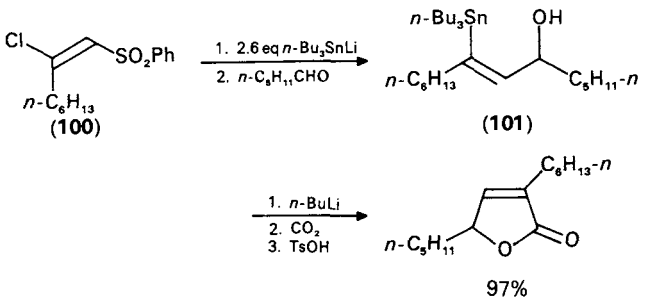
R = H	99%
R = Ph	83%
R = CH_2=CH	62%

The tandem intramolecular conjugate addition to **99** followed by an intramolecular alkylation reaction leads to a bis-cyclized product in good yield (equation 80)[66].



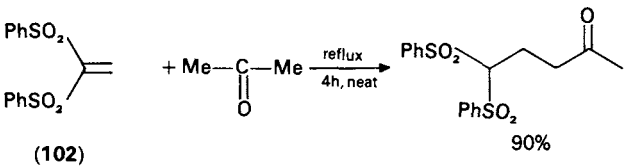
(80)

The conjugate addition of tributylstannylmethyllithium to unsaturated sulfones **100**, followed by trapping with an aldehyde, provides a route to the allyl alcohol **101** which may be transformed into 2(5*H*)-furanones (equation 81)[67].

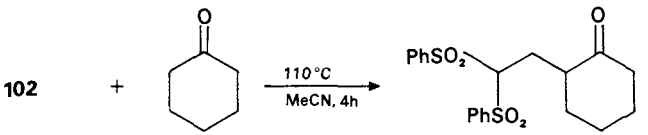


(81)

Lucchi and coworkers[68] have found a novel addition reaction of enolizable ketones to 1,1-bis(phenylsulfonyl)ethylene (**102**) under neutral conditions (equations 82 and 83).

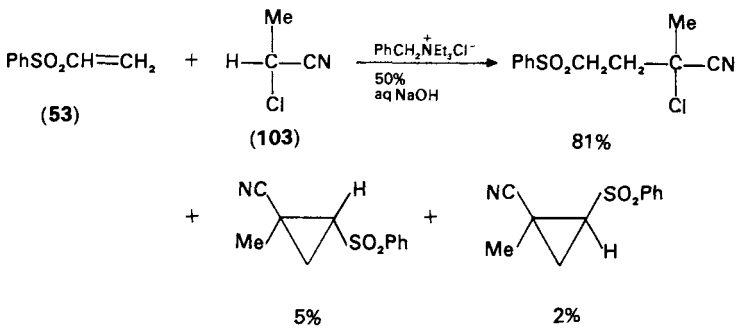


(82)



(83)

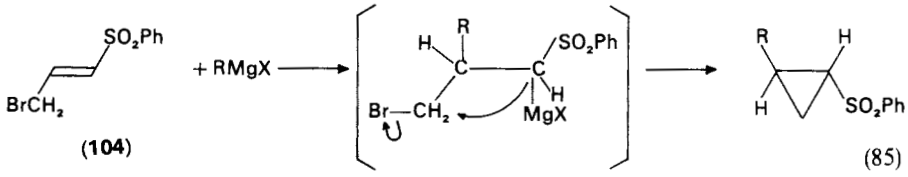
The conjugate addition of **103** to phenyl vinyl sulfone (**53**) proceeds under phase-transfer conditions. The yield of cyclopropanes in the following cyclization is low for synthetic purposes (equation 84)[69].



(84)

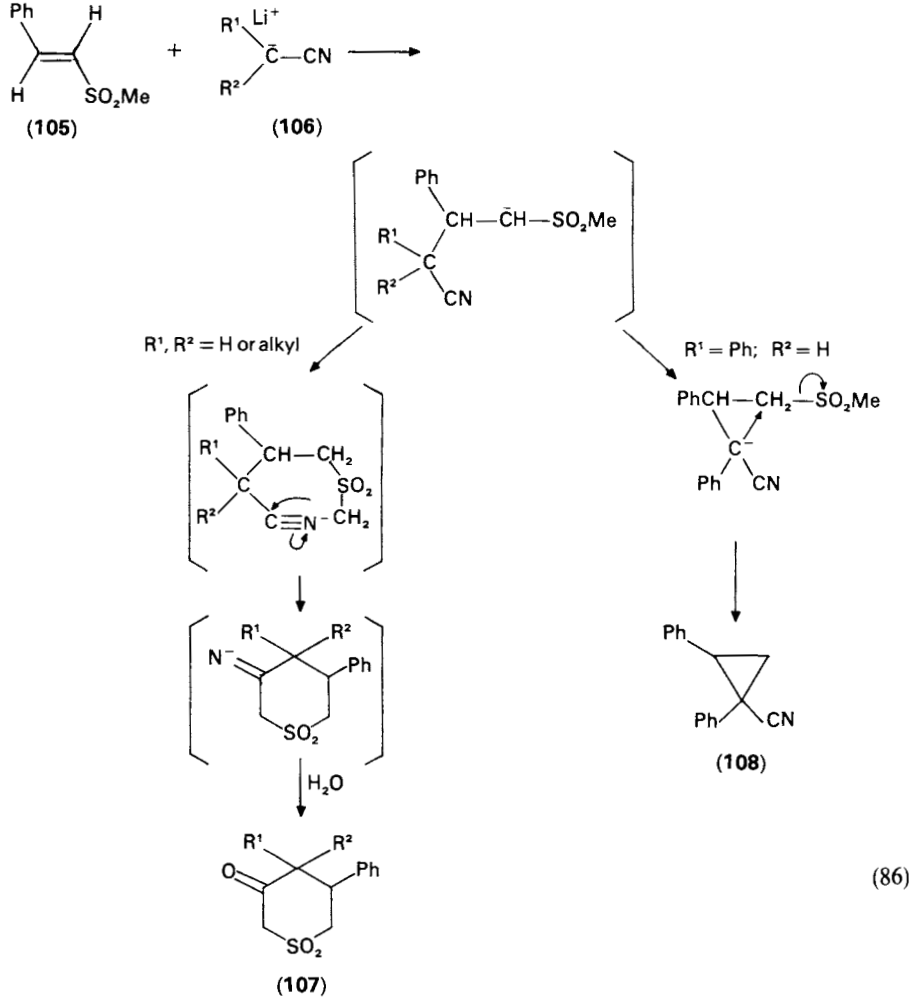
3-Bromo-1-propenyl phenyl sulfone (**104**) can serve as a Michael acceptor to Grignard reagents to give cyclopropyl phenyl sulfones in good yields. (equation 85)[70]. Cyclopropanes prepared by this method are listed in Table 8. However, with methyl, ethyl or *t*-butyl

Grignard reagents, no detectable amount of cyclopropyl sulfones is formed.



(104) (85)

When (*E*)-1-methylsulfonyl-2-phenylethylene (**105**) was allowed to react with α-lithionitriles (**106**) in THF at −60 to −70 °C and then under reflux, 3-oxothiane 1,1-dioxides (**107**) were obtained in good yield, and no cyclopropanes were formed (equation 86)[71]. On the other hand, α-lithiophenylacetonitrile (**106**, R^1 = Ph) reacted with **105** to give the cyclopropane **108** in good yield. Yields obtained in this cyclization are listed in Table 9 (equation 87)[71].



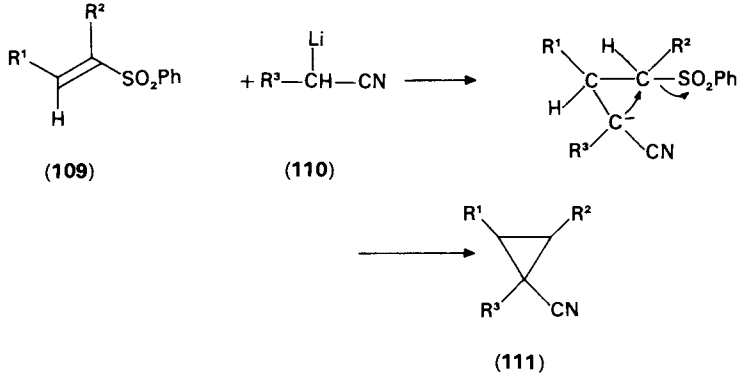
(105) (106) (107) (108) (86)

TABLE 8. Preparation of cyclopropyl sulfones from **104** and Grignard reagents[70]

RMgX	Yield (%)
CH_2=$CHCH_2MgBr$	76
CH≡CCH_2MgBr	50
CH_2=$CHCMe_2MgBr$	55
PhMgBr	40
$PhCH_2MgCl$	54

TABLE 9. Preparation of cyclopropanes **111** from α,β-unsaturated sulfones **109** and α-metallated nitriles **110**[71]

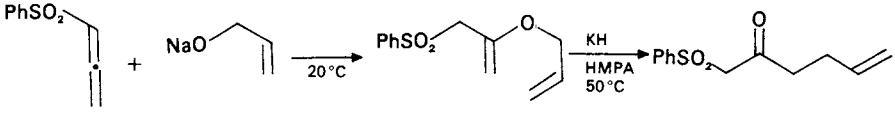
R^1	R^2	R^3	Yield of **111** (%)
Ph	H	Ph	83
—$(CH_2)_4$—		Ph	87
Ph	H	SPh	83
—$(CH_2)_3$—		SPh	69



(87)

2. Reaction of allenyl sulfones

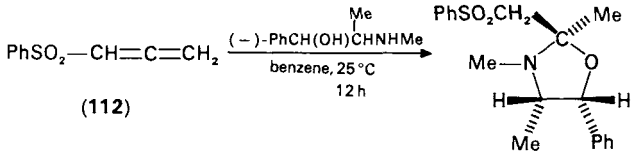
The base-catalyzed addition of allyl alcohol to (phenylsulfonyl)allene (**112**) gives the adduct which rearranges to β-keto sulfone (**113**) on the treatment with KH in HMPA (equation 88)[72].



(**112**) 65% (**113**) 78%

(88)

Conjugate addition of chiral amines to allenic and acetylenic sulfones has been reported[73]. The reaction **112** with (−)-ephedrine gives only one of the two possible diastereomeric oxazolines in high yield (equation 89).

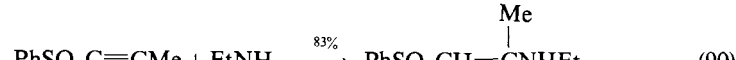


(89)

(114) 100%

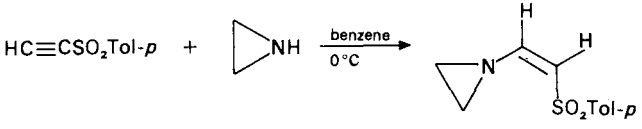
3. Reaction of alkynyl sulfones

The stereochemistry of the addition of amines to acetylenic sulfones has been investigated by Truce and coworkers[74]. Reaction of phenyl 1-propynyl sulfone with ethylamine gives a mixture of (*E*)- and (*Z*)-isomeric adducts (equation 90)[75].



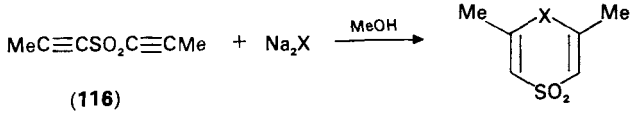
(90)

Ethyleneimine reacts with (*p*-tolylsulfonyl)acetylene to give only the (*Z*)-product **115** via *trans* addition (equation 91), while primary and secondary aliphatic amines afford (*E*)-products[76]. With nonterminal acetylenes such as 1-(ethylsulfonyl)-1-propyne, the reactions of ethyleneimine, *n*-propylamine and *t*-butylamine give mixtures of (*E*)- and (*Z*)-adducts. The double conjugate addition of sodium sulfide, selenide and telluride to bis(1-propynyl)sulfone (**116**) produces heterocycles (**117**) as illustrated in equation 92[77].



(91)

(115) 89%



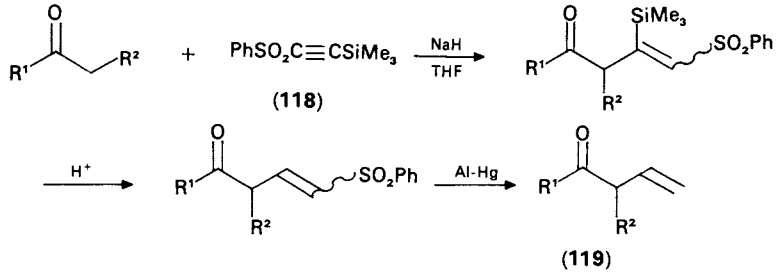
(92)

(116)

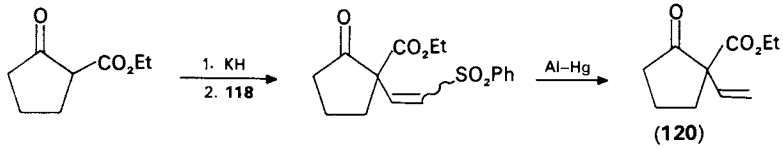
(117)

X = S 57%
X = Se 71%
X = Te 65%

Phenyl 2-(trimethylsilyl)ethynyl sulfone (**118**) can act as a vinyl cation synthon (equations 93 and 94)[78,79]. Thus, the reaction of enolates with **118** and subsequent desulfonylation of the adduct gives α-vinyl ketone, such as **119** and **120**.

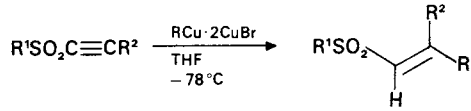


(93)



(94)

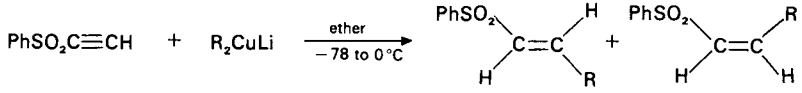
The reaction of acetylenic sulfones with Grignard reagents is slow in THF at 0 °C. The presence of copper(I) halide exhibits a strong accelerating effect upon the rate of the addition to give a mixture of the *E*- and *Z*-isomers[80]. In contrast, the use of RCu·2CuBr, prepared from Grignard reagents and CuBr, results in the formation of vinyl sulfones via *cis*-addition (equation 95).



(95)

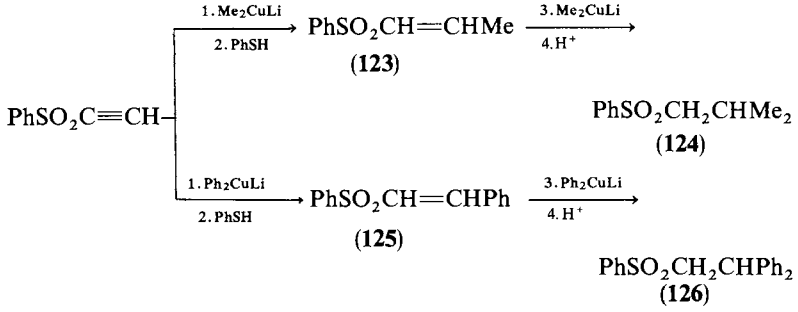
R = Me, Et, *i*-Pr, CH_2=CH, Ph

Lithium dimethyl and diphenylcuprates add to (phenylsulfonyl)acetylene with complete *syn*-stereoselectivity leading to *E*-olefins **121**. In the case of di-*n*-butyl and di-*s*-butylcuprates, 5–20% of *Z*-olefins **122** are also formed (equation 96)[80].



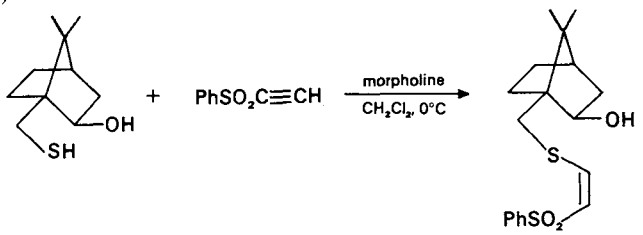
(96)

When benzenethiol is used as a quenching acid, and the resulting reaction mixture (containing **123** or **125**) is added into another cuprate solution, a bis-addition product (**124** or **126**) can be obtained, as illustrated in equation 97[81].



(97)

The addition of 10-mercaptoisoborneol to (phenylsulfonyl)acetylene proceeds smoothly in the presence of morpholine as a catalyst to give the (*Z*)-vinyl sulfone **127** (equation 98)[82].

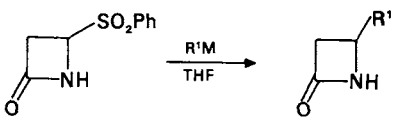


(98)

(127) 85%

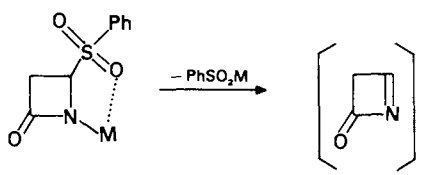
4. Reaction of carbon–nitrogen double bond

The reaction of 4-(phenylsulfonyl)azetidin-2-one (**128**) with nucleophiles such as dialkylcopper lithium and Grignard reagents gives 4-alkyl, 4-allyl, 4-vinyl or 4-ethynylazetidinon-2-one (**129**) in good yields (equation 99)[83]. The yields of several azetidin-2-ones obtained by this method are given in Table 10. The reaction apparently proceeds through an intermediate azetin-2-one **131** derived from the five-membered coordination complex (equation 100).



(99)

(128) **(129)**



(100)

(130) **(131)**

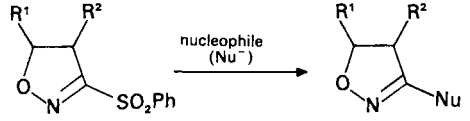
TABLE 10. Reaction of 4-phenylsulfonylazetidin-2-one **128** with organometallic reagents[83]

R^1M	Yield of **129** (%)
$LiCu(Bu\text{-}n)_2$	94
EtMgBr	74
$CH_2{=}CHMgBr$	66
$LiCu(CH_2CH{=}CH_2)_2$	100
$CH_2{=}CHCH_2MgCl$	55
$EtOC{\equiv}CMgBr$	95
$PhSC{\equiv}CMgBr$	69

TABLE 11. Substitution reaction of 3-(phenylsulfonyl)isoxazolines[84]

Isoxazoline (132) R^1	R^2	Nucleophile	Reaction conditions		Yield of 133 (%)
Ph	H	MeLi	−70 °C,	15 min	94
Ph	H	$NaOCH_2CH{=}CH_2$	97 °C,	30 min	78
—$(CH_2)_3$—		*n*-BuLi	−70 °C,	15 min	85
—$(CH_2)_3$—		KCN	38–41 °C,	48 h	87
—$(CH_2)_4$—		LiOMe	65 °C,	1 h	88
n-Bu	H	*s*-BuLi	−70 °C,	15 min	62

The phenylsulfonyl group attached at the 3-position of isoxazolines (**132**) is readily substituted by a variety of nucleophiles (equation 101), as summarized in Table 11[84].

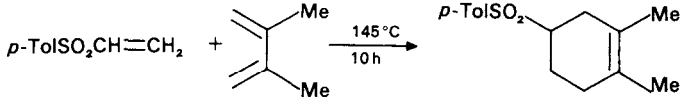


(132) (133) (101)

B. Cycloaddition Reactions of α, β-Unsaturated Sulfones

1. [4 + 2] Cycloaddition reactions with dienes

Since the first demonstration of a cycloaddition reaction of α, β-unsaturated sulfones in 1938 by Alder and coworkers[85], a variety of α, β-unsaturated sulfones have been prepared and used as dienophiles. For example, when a mixture of *p*-tolyl vinyl sulfone and 2, 3-dimethylbutadiene in benzene is heated at 145–150 °C for 10 h in a sealed tube, crystals of the cycloadduct (**134**) are obtained (equation 102). Other examples of this intermolecular cycloaddition reaction are given in Table 12.

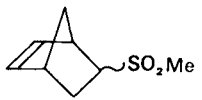
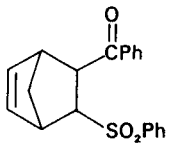
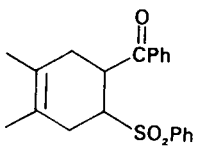
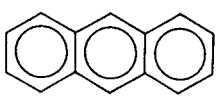
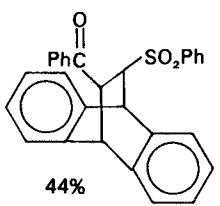


(134) (102)

While (*Z*)-1, 2-bis(phenylsulfonyl)ethylene (**140**) does not add to dienes such as furan, cyclopentadiene, cyclo-octatetraene, indene and β-naphthol, (*E*)-1, 2-bis(phenylsulfonyl)ethylene (**141**) is more reactive and the reaction with furan proceeds at room temperature for 2 h to give the adduct in 95% yield. The reactivity of dienophiles having sulfonyl group in the [4 + 2]cycloaddition is shown in equation 103[93,101].

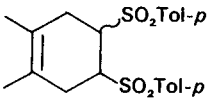
Due to the low reactivity of ethylene and acetylene as dienophiles, forcing conditions, such as high temperature and high pressure, are necessary for [4 + 2]cycloaddition. The hazards associated with handling acetylene under these conditions are well known and

TABLE 12. Cycloaddition of α,β-unsaturated sulfones to dienes

Dienophile	Diene	Conditions	Product	References
$MeSO_2$ (**135**)		r.t., 4 days	 83%	86 87
p-$TolSO_2$ (**136**)		r.t., 2 days	 **96%**	88
136		reflux, 18 h	 **96%**	88
$PhSO_2$ (**137**)		160 °C, 20 h	 **44%**	89

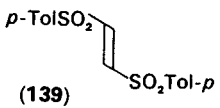
(**138**)

80 °C,
20 h



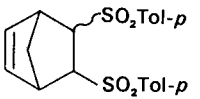
92%

89

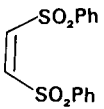


(**139**)

80 °C,
17 h

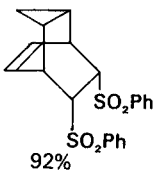


88



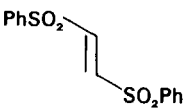
(**140**)

toluene, 111 °C,
14 h

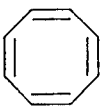


92%

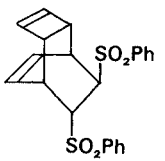
90
91



(**141**)

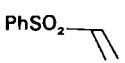
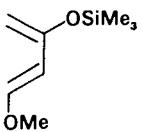
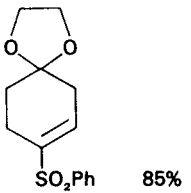
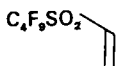
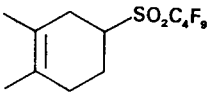
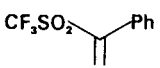
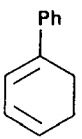
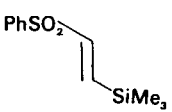
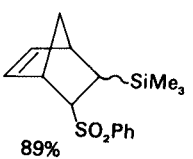


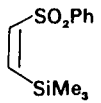
o-dichlorobenzene,
reflux, 4 h



91, 92
93, 94

TABLE 12. (*Contd.*)

Dienophile	Diene	Conditions	Product	References
 (53)		80 °C, 28 h, then $HOCH_2CH_2OH$	 85%	95, 96, 97, 98, 99
 (142)		r.t., 48 h	 100%	100
 (143)		r.t., several days	 75%	39
 (144)		20 °C, 3.5 days	 89%	97 101

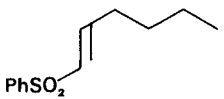


(145)

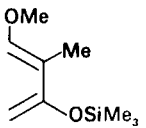
20 °C, 2.5 weeks

30%

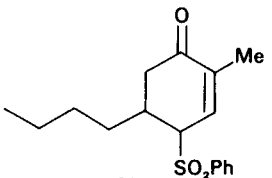
97
101



(146)

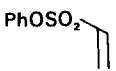


1. 130 °C, 28 h
2. H^+



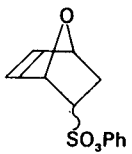
68%

98
102



(147)

r.t., 20 days

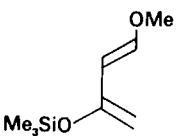


84%

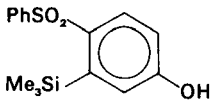
103

PhSO2C≡CSiMe3

(118)

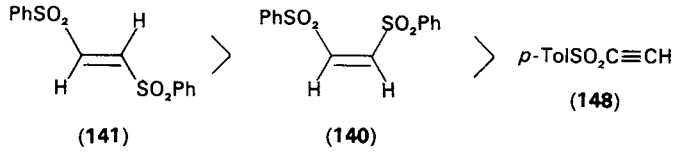


1. toluene, reflux
2. H^+



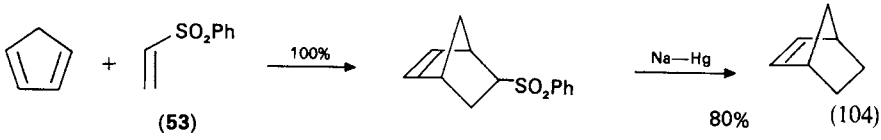
45%

104

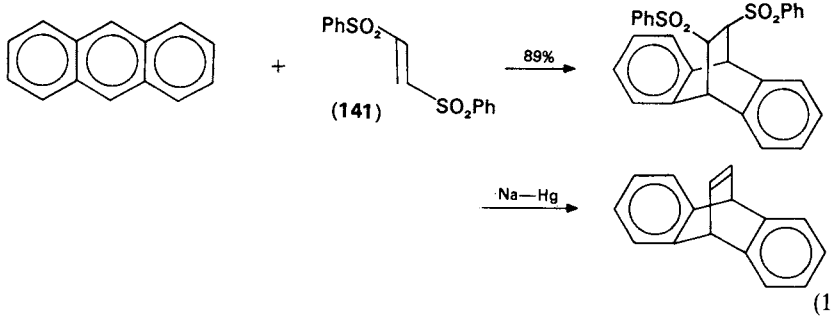


(103)

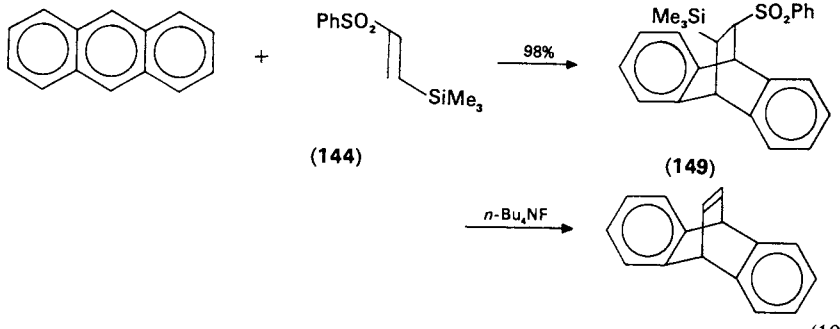
should be avoided. Since the sulfonyl group can be readily removed by sodium amalgam, the sulfone **50** can serve as an ethylene equivalent (equation 104)[99], and compounds **141**, **144** and **148** as acetylene equivalents (equations 105, 106 and 107)[91,97,97b]. The



(104)

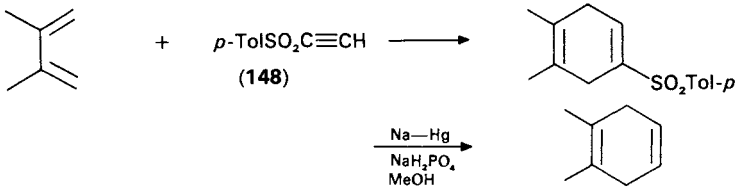


(105)

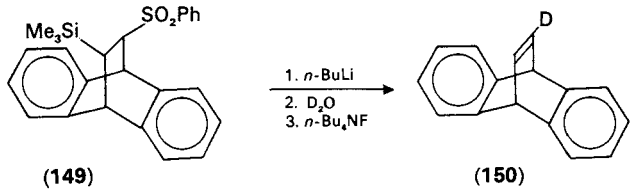


(106)

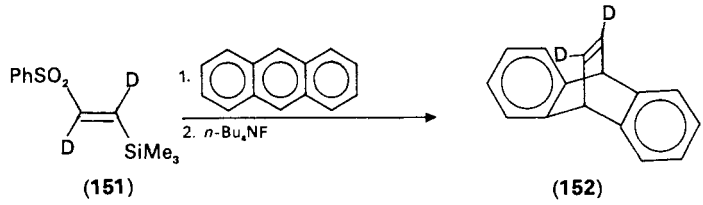
introduction of deuterium is readily carried out by quenching the α-sulfonyl carbanion derived from **149** with D_2O (equation 108)[97] or by using the deuteriated vinyl sulfone **151** as a dienophile (equation 109)[97].



(107)

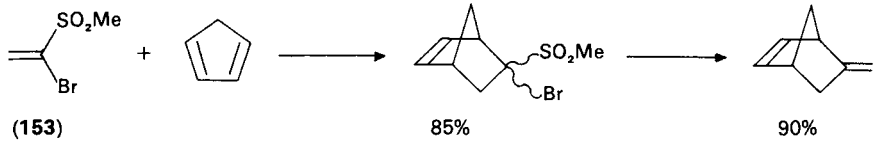


(108)

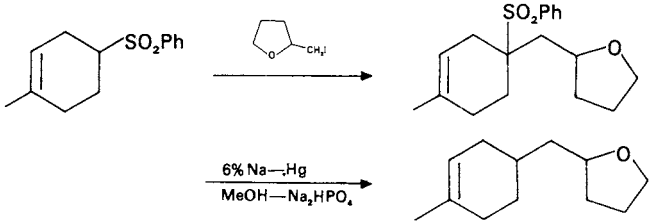


(109)

1-Bromo-1-(methylsulfonyl)ethylene (**153**) can also be employed as an allene equivalent since the Diels–Alder adduct with cyclopentadiene rearranges to 5-methylene-2-norbornene on treatment with sodium methoxide in DMSO (equation 110)[105]. The reactivity of 3-phenylsulfonylpropiolate is greater than that of dimethylacetylenedicarboxylate, and ethyl 3-(phenylthio)propiolate is found to be unreactive towards diene addition at room temperature and polymerizes at elevated temperature.[106] Alkylation and subsequent removal of the phenylsulfonyl residue provides cyclohexene derivatives possessing a wide variety of side chains (equation 111)[99].

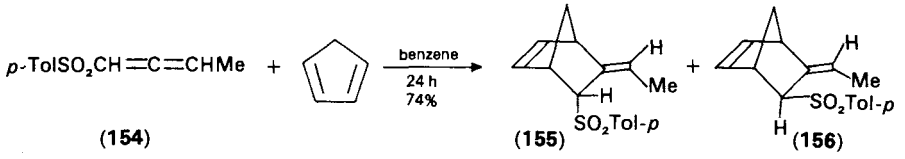


(110)



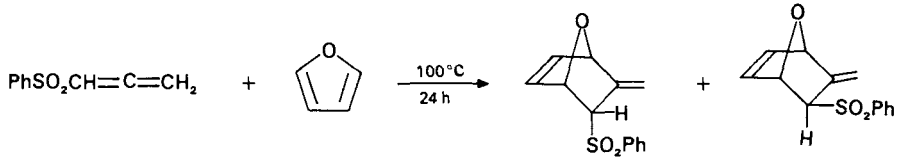
(111)

A chirality transfer from the allenic sulfone **154** to the Diels–Alder adducts is observed in the reaction of (+)-(*S*)-1-(*p*-tolylsulfonyl)buta-1,2-diene with cyclopentadiene (equation 112), in which the diastereomers **155** and **156** are formed predominantly[107].

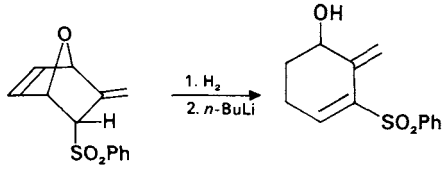


(**154**) (**155**) (**156**) (112)

A high endo selectivity is observed in the reaction of (phenylsulfonyl)allene (**112**) with furan (**157**)(equation 113)[108]. The endo adduct **158** can be readily transformed into highly substituted cyclohexenol **160** upon treatment with *n*-butyllithium after hydrogenation of the ring double bond (equation 114)[108].

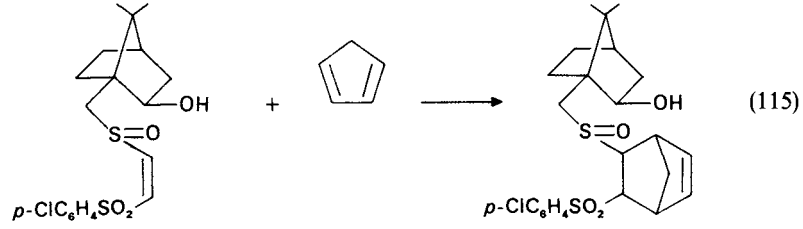


(**112**) (**157**) (**158**) 53% (**159**) 3% (113)



(**158**) (**160**) (114)

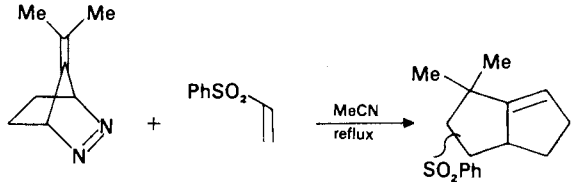
The reaction of chiral sulfones **161**, derived from (1*S*)-(+)-10-camphorsulfonyl chloride, with cyclopentadiene gives predominantly the endo adduct in a diastereomeric ratio of 91:9 from which one diastereomer **162** can be isolated in pure form by recrystallization (equation 115)[109].



(**161**) (**162**) (115)

A bicyclo[3.3.0]octane ring system **164** can be conveniently prepared by refluxing an acetonitrile solution of the azo compound **163** in the presence of excess of phenyl vinyl

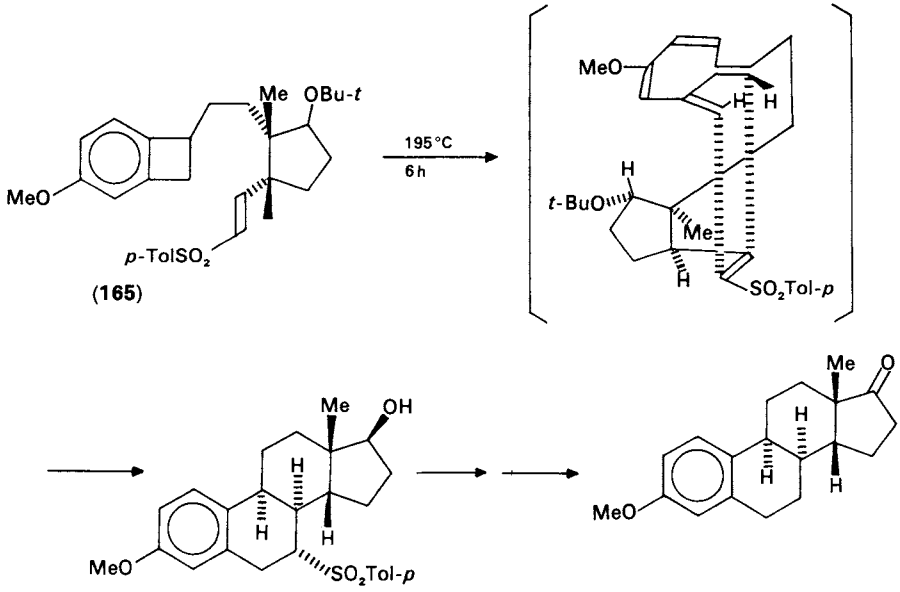
sulfone (**53**) (equation 116)[110]. The bicyclooctene **164** can be transformed into cyclopentadienone via ozonolysis and a subsequent Wittig reaction.



(116)

(**163**) (**53**) (**164**) 85%

A highly efficient construction of the steroidal skeleton **166** is reported by Kametani and coworkers[111] in the intramolecular Diels–Alder reaction of the α,β-unsaturated sulfone moiety of **165** (equation 117). Thus, when the sulfone **165** is heated in 1, 2-dichlorobenzene for 6 h, the steroidal compound **166** can be obtained in 62% yield. The compound **166** produces estrone (**167**) by elimination of benzenesulfinic acid and subsequent hydrogenation of the formed double bond. The stereoselectivity of the addition reflects a transition state in which the *p*-tosyl group occupies the exo position to minimize the steric repulsion between methyl and *t*-butoxy groups and the *o*-quinodimethane group as shown in equation 117.



(**165**)

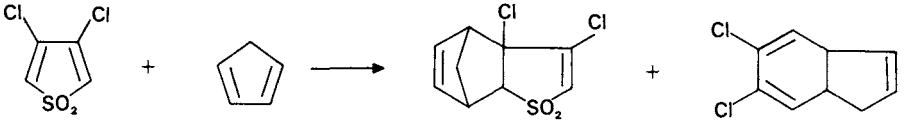
(**166**) (**167**)

(117)

2. [4 + 2]Cycloaddition reactions with olefins

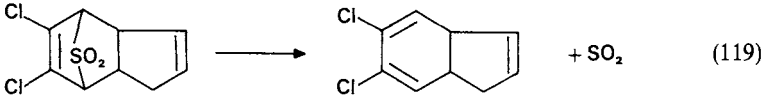
3, 4-Dichlorothiophene 1, 1-dioxide (**168**) is stable and of particular interest in the Diels–Alder reactions[112]. Thus, when **168** is treated with cyclopentadiene in acetone, adducts

169 and **170** can be obtained in 61% and 16% yields, respectively (equation 118). An adduct **169** would result if **168** behaved as a dienophile whereas **170** would be expected if **168** functioned as an enophile to give the adduct **171**. Extrusion of SO_2 from **171** gives **170** (equation 119).



(**168**) (**169**) 61% (**170**) 16%

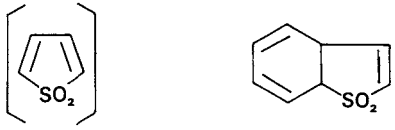
(118)



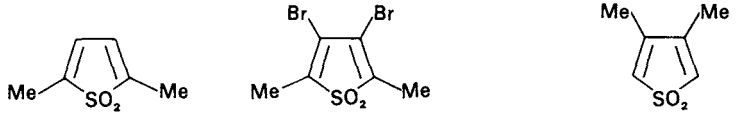
(**171**) (**170**)

(119)

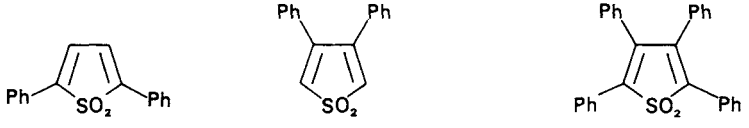
Thiophene 1, 1-dioxide (**61**) is too unstable to isolate and dimerizes with loss of SO_2 to give 3a, 7a-dihydrobenzothiophene 1, 1-dioxide (**172**) in 34%[113]. However, alkyl-substituted thiophene 1, 1-dioxides can serve as dienes in the Diels–Alder reaction, since the aromatic properties of the thiophene nucleus are lost completely and the π-electrons of the sulfur atom are used for forming the bond with oxygen. The sulfones **173–178** are found to react with two moles of maleic anhydride at elevated temperature to give bicyclic anhydrides[114]. Thus, at high reaction temperature, SO_2 is split off to give cyclohexadiene



(**61**) (**172**)

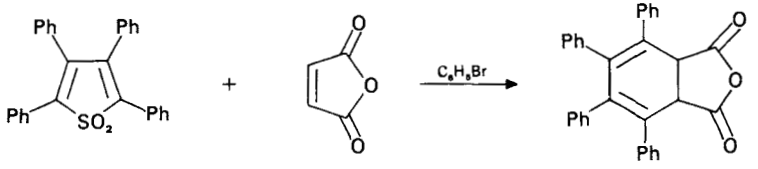


(**173**) (**174**) (**175**)



(**176**) (**177**) (**178**)

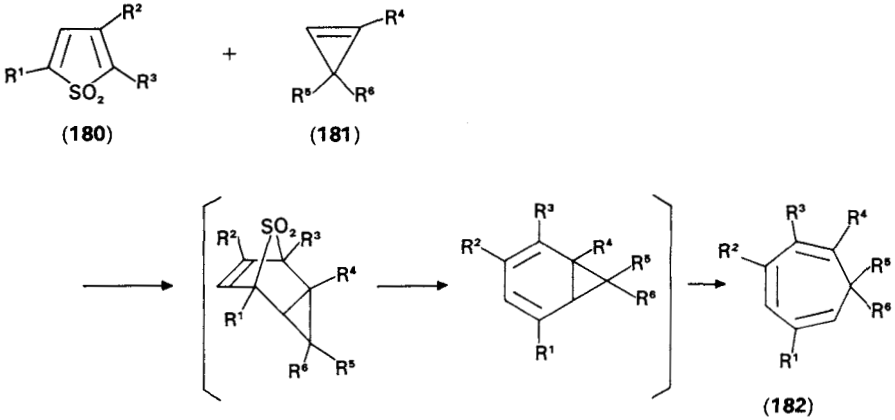
dicarboxylic anhydrides which again react with maleic anhydride. The diene thus formed is more reactive than the starting thiophene 1, 1-dioxides **173–177**. In contrast, the reaction of **178** with maleic anhydride gives tetraphenyldihydrophthalic anhydride (**179**) in high yield. In this case no further cycloaddition of maleic anhydride can be observed due to steric hindrance of the phenyl groups of **179** (equation 120)[114].



(120)

(178) **(179)**

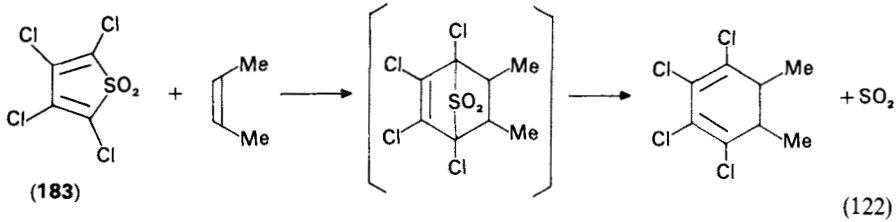
An interesting cycloheptatriene (**182**) synthesis has been described using thiophene 1, 1-dioxides (**180**) and cyclopropenes **181** (equation 121)[115]. Concerted [4 + 2]cycloaddition and subsequent cheletropic extrusion of sulfur dioxide are suggested by the second-order kinetics (first in each reactant), and by the large negative activation entropy.



(180) **(181)** **(182)**

(121)

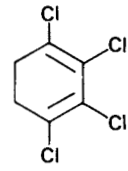
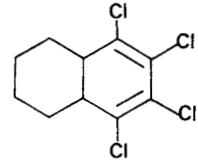
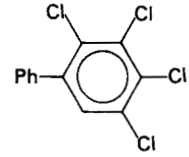
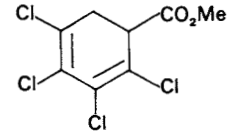
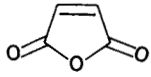
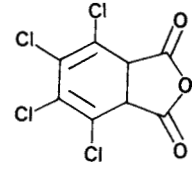
Tetrachlorothiophene 1, 1-dioxide (**183**) possesses high reactivity as a cheletropic Diels–Alder reagent. It undergoes a Diels–Alder addition to olefins to form an adduct which spontaneously loses sulfur dioxide to give a product in which the original double bond is annelated with a tetrachlorobutadienyl group (equation 122). Annelation of other olefins by this method is illustrated in Table 13[116]. The reaction of **183** with 1, 5-cyclooctadiene gives the tetracycle **185** in high yield via intramolecular cycloaddition of **184** (equation 123).

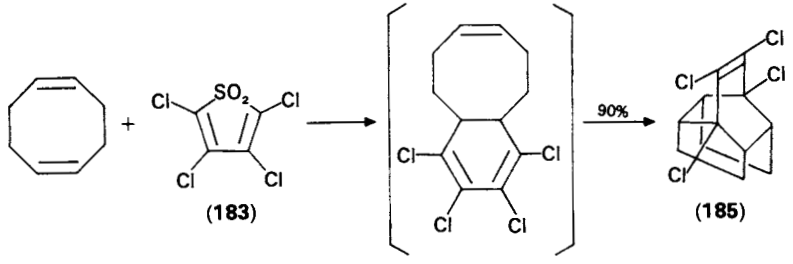


(183)

(122)

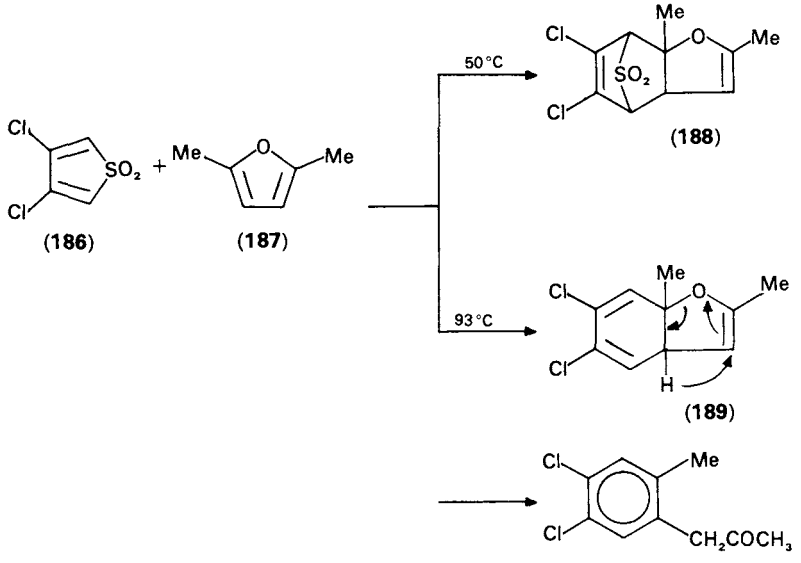
TABLE 13. Annelation of olefins and acetylenes with tetrachlorothiophene 1, 1-dioxide[116]

Olefin or acetylene	Reaction conditions	Product	Yield
$CH_2{=}CH_2$	80 °C (200 psi) 4 h		89%
	83 °C, 1 h		90%
PhC≡CH	0 °C,		86%
$CH_2{=}CHCO_2Me$	80 °C, 2 h		91%
	100 °C, 48 h		61%



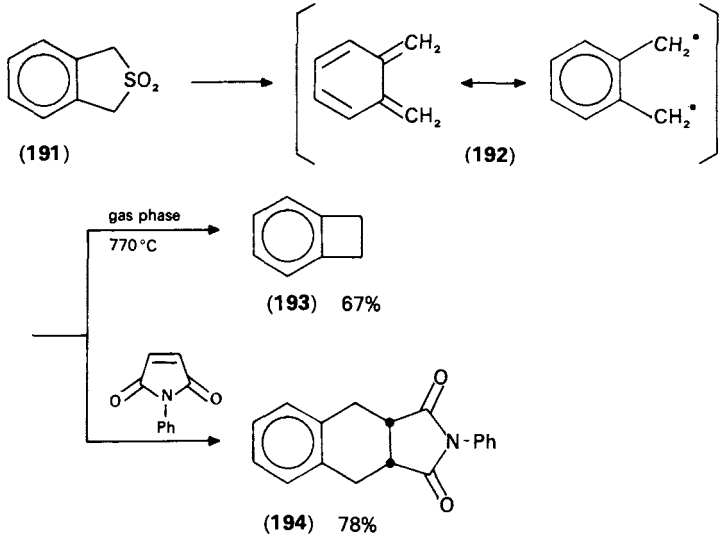
(123)

When 3,4-dichlorothiophene 1,1-dioxide (**186**) is treated with 2,5-dimethylfuran (**187**) at 50 °C, the adduct **188** can be obtained in 68% yield. Treatment of the reaction mixture at 93 °C gives the ketone **190** in 77% yield via extrusion of SO_2 from **188** and the rearrangement of **189** (equation 124)[117]. Other examples are listed in Table 14.



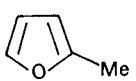
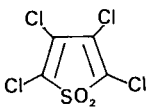
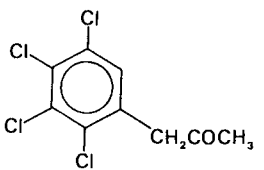
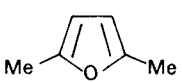
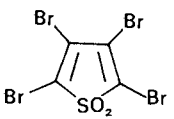
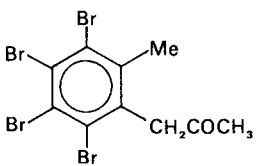
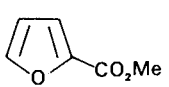
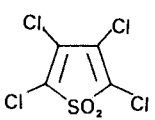
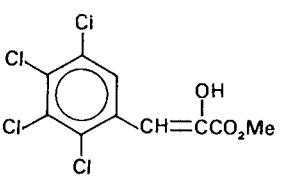
(124)

During investigation of the synthesis of benzocyclobutane **193**, Cava and coworkers[118] found that *o*-quinodimethane **192**, generated in the pyrolysis of 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (**191**), can be trapped by *N*-phenylmaleimide to give *N*-phenyl-1,2,3,4-tetrahydronaphthalene 2,3-dicarboimide (**194**) (equation 125).

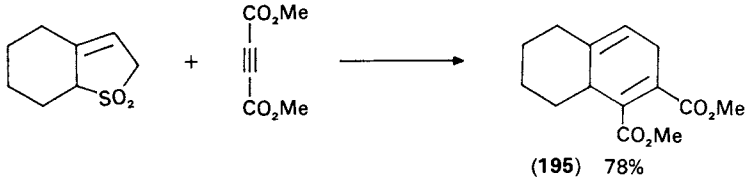


(125)

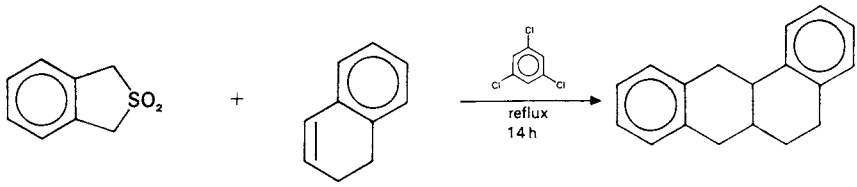
TABLE 14. Reaction of furans and halogenated thiophene 1,1-dioxides[117]

Furan	Halogenated thiophene dioxide	Reaction conditions	Product	Yield
		65 °C, 0.5 h		92%
		93 °C, 0.5 h		90%
		100 °C, 22 h		62%

Similarly, 1-vinylcyclohexane can be trapped with dimethyl acetylenedicarboxylate in refluxing xylene to afford **195** in 78% yield (equation 126)[119]. Benzo[*a*]anthracene can be obtained by the reaction of **196** and 1,2-dihydronaphthalene (equation 127) and oxidation of **197** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[120].

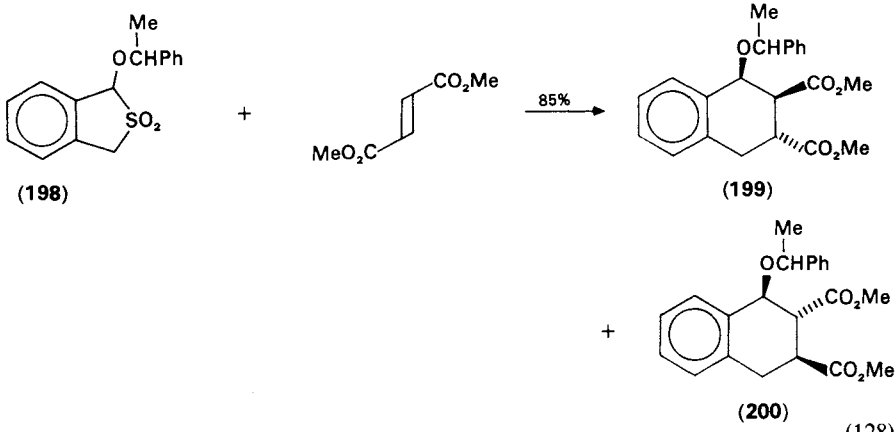


(195) 78% (126)



(196) (197) 73% (127)

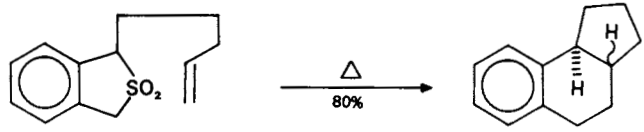
Charlton[121] has recently reported the asymmetric induction in the reaction of dimethyl fumarate and 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (**198**) containing a chiral α-alkoxy group at the 2-position (equation 128). A diastereomeric excess of 2.8:1 of **199** to **200** is achieved by using **198** derived from optically active α-methylbenzyl alcohol.



(198) (199) (200) (128)

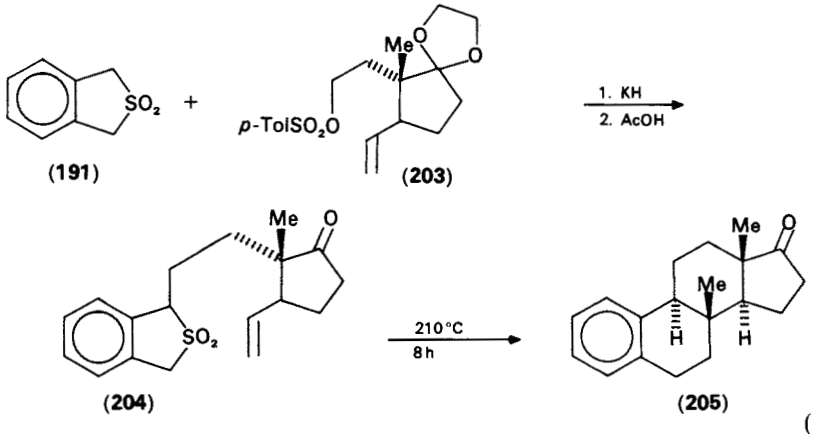
The synthetic utility of *o*-quinodimethane generated by cheletropic elimination of SO_2 has been amply demonstrated by Oppolzer and Nicolaou, who have conducted an intramolecular cycloaddition coupled with the alkylation of 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide[122]. When 1,3-dihydro-1-(4-pentenyl)benzo[*c*]thiophene 2,2-dioxide (**201**) prepared from 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide and 4-pentenyl bromide is heated in di-*n*-butyl

phthalate at 210 °C or in a quartz tube at 300 °C, a mixture of *cis*- and *trans*-2,3,3a,4,5,9b-hexahydro-1*H*-benzo[*c*]indenes (**202**) can be obtained in a ratio of 1:3 (equation 129)[123].

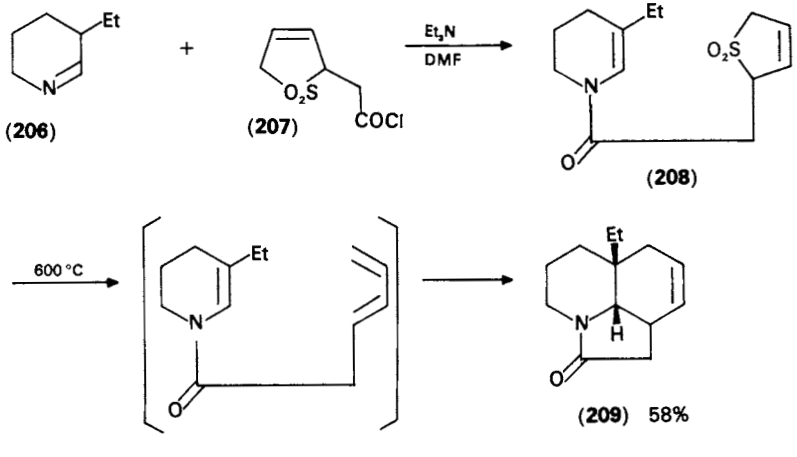


(**201**) (**202**) (129)

The intramolecular cycloaddition has proven to be the method of choice for the preparation of steroids. A diastereomeric mixture of **204**, prepared from **191** and tosylate **203** has been cleanly converted to dl-estra-1,3,5(10)-trien-17-one (**205**) in 85% yield (equation 130). A second example of the intramolecular cycloaddition reaction is the formation of the cycloadduct (**209**), the key intermediate in a synthesis of the Aspidosperma alkaloid aspidospermine, upon heating **208** at 600 °C (equation 131)[124]. The sulfone **208** can be prepared by reaction of 3-ethyl-3,4,5,6-tetrahydropyridine (**206**) with the acid chloride **207**.



(**191**) (**203**) (**204**) (**205**) (130)

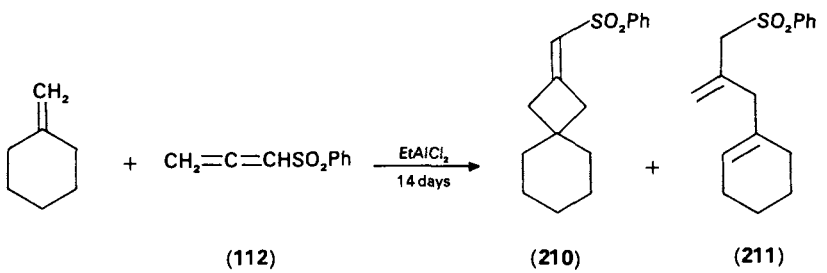


(**206**) (**207**) (**208**) (131)

(**209**) 58%

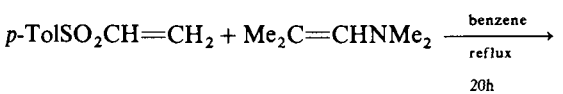
3. [2 + 2]Cycloaddition reactions

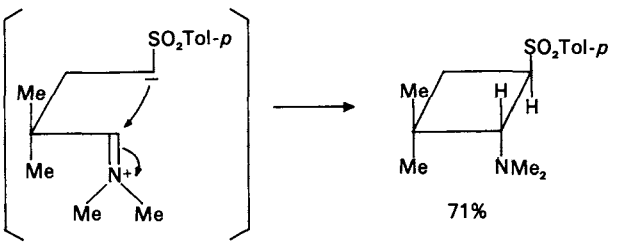
Snider and coworkers[125] have reported the Lewis acid catalyzed [2 + 2]cycloaddition of (phenylsulfonyl)allene **112**. The reaction with methylenecyclohexane in dichloromethane gives a 25% yield of an 8:1 mixture of **210** and **211** (equation 132). An addition reaction of 1-(*p*-tolylsulfonyl)ethylene with enamines gives aminocyanobutanes via the zwitterionic intermediate (**212**) as shown in equation 133[126].



(112) (210) (211)

(132)





(212)

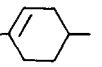
(133)

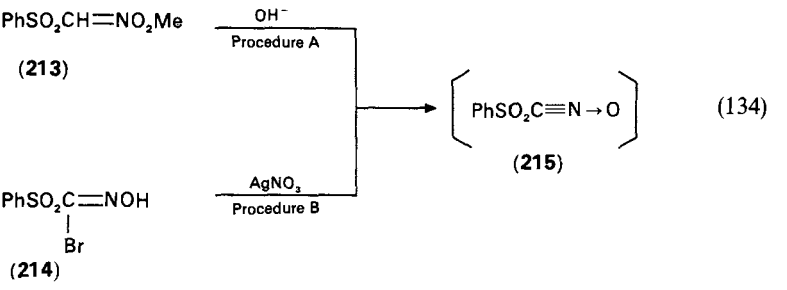
4. [3 + 2]Cycloaddition reactions

It is well recognized that nitrones and nitrile oxides behave as 1,3-dipoles and readily undergo thermal [3 + 2]cycloaddition reactions with olefins to give isoxazolidine and isoxazole derivatives, respectively[127]. The synthetically significant features of these reactions are introduction of nitrogen and oxygen functionality with concomitant high regioselective carbon–carbon bond formation which are utilized in the total synthesis of naturally occurring alkaloids.

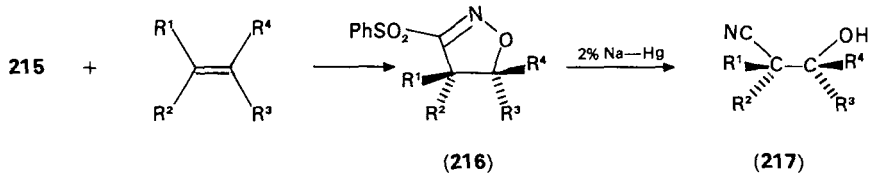
(Phenylsulfonyl)carbonitrile oxide (**215**) can be generated by treatment of **213** with hydroxide ion in a two-phase system, or of **214** with 2 equivalents of $AgNO_3$ in THF (equation 134)[128]. The reaction of **215** with olefins gives 3-(phenylsulfonyl)isoxazolines **216** which can be converted into the corresponding *β*-cyanohydrins **217** upon treatment with 2% sodium amalgam (equation 134). Table 15 indicates the yields of **216** and of **217** based on the starting alkene, without isolation of cycloadduct **216**. The reaction of **215** with (*S*)-vinylglycine **218** leads to the formation of a mixture of diastereomers **219** and **220** (equation 135)[129].

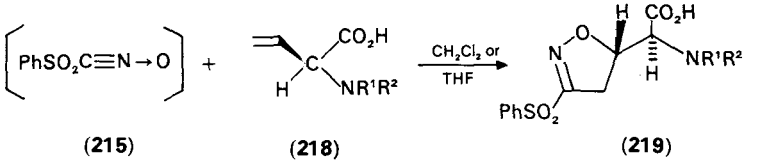
TABLE 15. Reaction of benzenesulfonylcarbonitrile oxide with olefins[128]

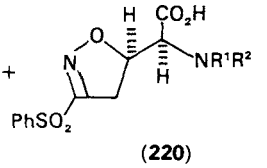
Olefin				Yield of **216** (%)		Yield of 217
R^1	R^2	R^3	R^4	Procedure A	Procedure B	(%)
H	H	H	*n*-Bu	72	81	69
H	H	Me	Me 	46	65	44
H	$-(CH_2)_4-$		Me	—	72	88
Me	Me	Me	Me	—	44	—



(134)





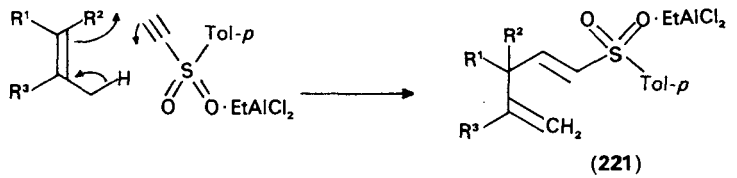


(135)

5. *Ene reactions*

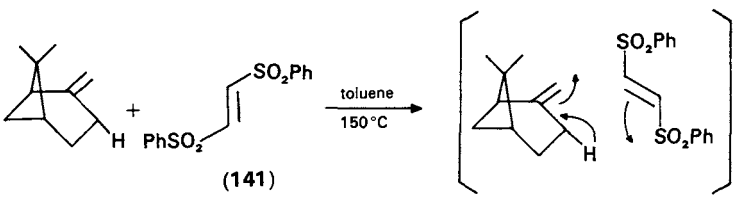
The ene reaction[130] of ethynyl *p*-tolyl sulfone with alkenes has been investigated by Snider and coworkers[131] using $EtAlCl_2$ as a Lewis acid catalyst (equation 136). The reaction is very sluggish requiring 4 to 18 days at room temperature to obtain a reasonable

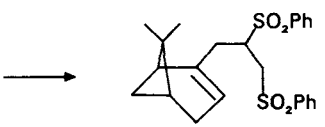
yield of the product **221**. In a study of the synthetic utility of (*E*)-1,2-bis(phenylsulfonyl)ethylene (**141**) as an acetylene equivalent, Lucchi and coworkers[91] found an ene reaction of **141** with β-pinene which leads to **222** (equation 137).



(136)

(221)





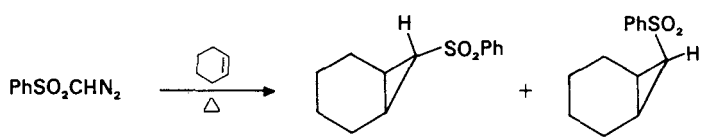
(137)

(222) 93%

V. ADDITION OF SULFONYL CARBENES AND SULFONYL NITRENES

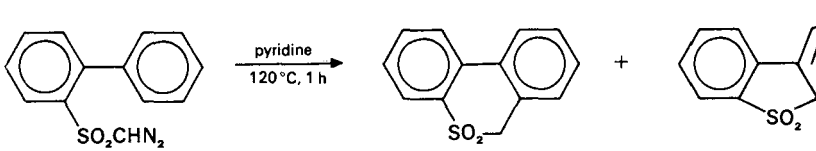
A. Sulfonyl Carbenes

The thermal decomposition of diazo(phenylsulfonyl)methane **223** under a nitrogen atmosphere generates phenylsulfonylcarbene which is trapped by olefin such as cyclohexene to give norcaranes **224** and **225** (equation 138)[132]. No cycloheptatriene derivative is isolated from the thermolysis of **223** in benzene[133]. In contrast, intramolecular insertion of sulfonylcarbenes into a benzene ring is observed in the thermolysis of **226** (equation 139)[134].



(138)

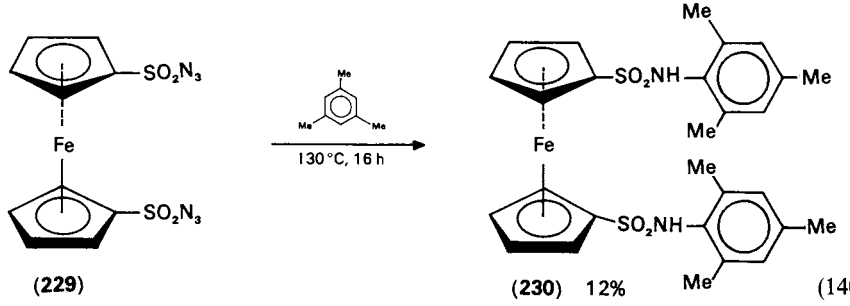
(223) (224) 36% (225) 17%



(226) (227) 8% (228) 23% (139)

B. Sulfonyl Nitrenes

Sulfonyl nitrenes react with benzene to produce appreciable yields of aromatic substitution products. The nitrene thermally generated in benzene from **229** gives a monosubstitution product. When the reaction is carried out in mesitylene as a solvent, the two sulfonylnitrenes react with mesitylene to afford **230** (equation 140)[135].

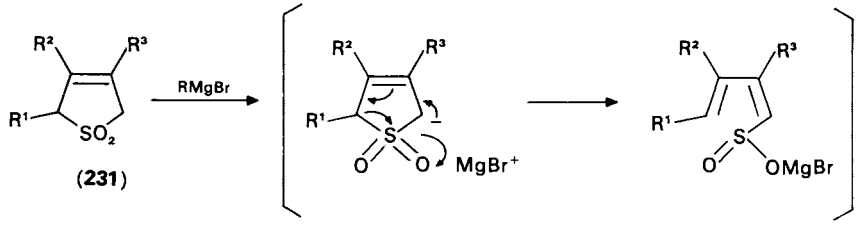


(229) **(230)** 12% (140)

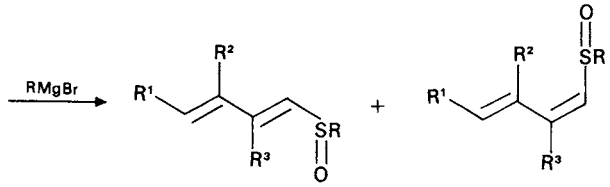
VI. MISCELLANEOUS SYNTHETIC USES OF SULFONES

A. Synthesis of Olefins

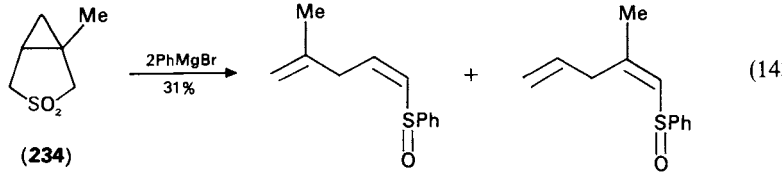
A procedure for a synthesis of dienyl sulfoxides (**232** and **233**) involves ring opening of dihydrothiophene 1,1-dioxide (**231**) by two molar equivalents of Grignard reagent (equation 141)[136]. The yields are usually in the 20–66% range. Similarly, treatment of the bicyclic sulfones **234**, with 2 equivalents of phenylmagnesium bromide, produced a mixture of 1,4-dienylic sulfoxides (equation 142)[136].



(231)



(232) **(233)** (141)



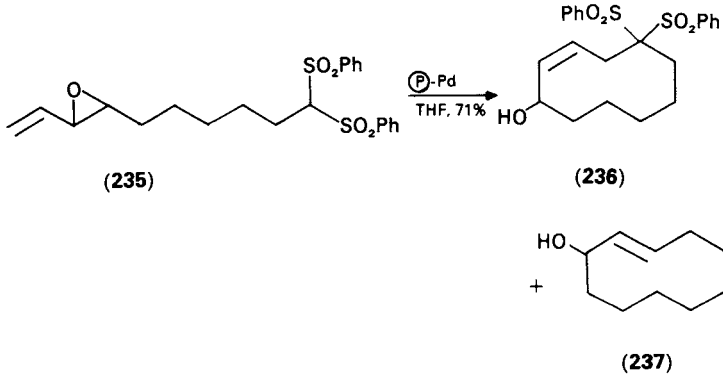
(234) (142)

TABLE 16. Preparation of allyl alcohols[138]

Epoxysulfone (**239**)				
R^1	R^2	R^3	Yield of **240** (%)	Ratio *E*:*Z* of **240**
Me	H	H	70	7:3
H	Me	H	62	4:1
H	Me	Me	89	*E* only

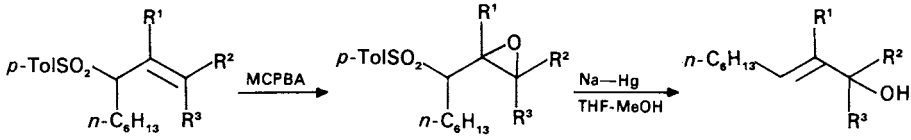
B. Synthesis of Allyl Alcohols

Trost and coworkers[137] have reported the polymer-supported palladium catalyzed cyclization of 1,1-bis(phenylsulfonyl)epoxyalkene **235** which gives cycloalkanes **236** and **237** in a 2:1 ratio (equation 143). This method has proven useful for the synthesis of macrocyclic compounds under neutral conditions without using high dilution technique. Temperature and concentrations are critical. The best results are achieved if a reaction mixture of 0.1–0.5 M is added to a preheated (at 65 °C) suspension of the catalyst.



(**235**) (**236**) (**237**) (143)

Desulfurization of β,α-epoxy sulfones **239** prepared from allylic sulfones **238** and *m*-chloroperbenzoic acid with sodium amalgam leads to the formation of allyl alcohols (**240**) in good yields (equation 144)[138]. Allyl alcohols prepared by this method are listed in Table 16.

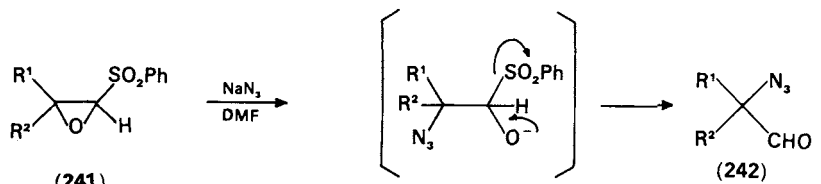


(**238**) (**239**) (**240**) (144)

C. Synthesis of Aldehydes and Ketones

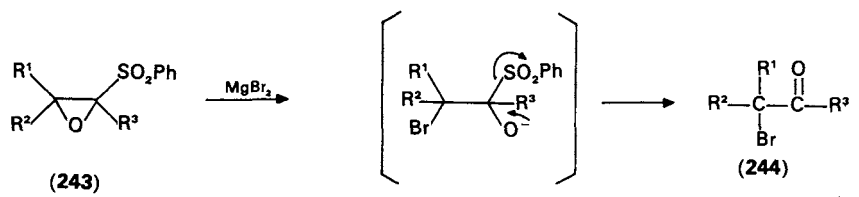
Watt and coworkers[139] prepared the α-azidoaldehydes (**242**) by nucleophilic ring opening with sulfinate ion expulsion of α,β-epoxy sulfones **241** with sodium azide in DMF

(equation 145)[139]. A similar route for the preparation of α-bromo carbonyl compounds **244** starting from α,β-epoxy sulfone **243** has been reported (equation 146 and Table 17)[140]. An interesting stereoselective synthesis of α,β-unsaturated aldehydes **248** has been recently described using 1-[(2-methoxyethoxy)methoxyl-2-(phenylsulfonyl)cyclopropanes **246** (equation 147)[141].



(241) (242) (145)

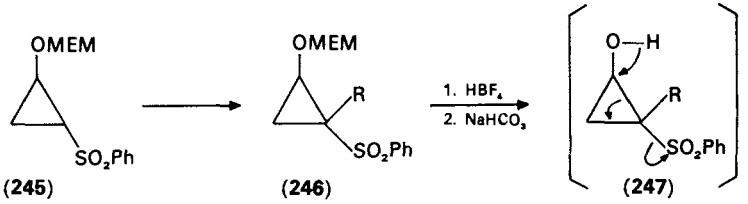
Epoxysulfone (**241**) R^1	R^2	Yield of **242** %
$-(CH_2)_5-$		52
$-(CH_2)_7-$		63
$-(CH_2)_{11}-$		100
Me	Ph	68
c-C_5H_9		86



(243) (244) (146)

TABLE 17. Preparation of α-bromo aldehydes and ketones[140]

Epoxysulfone (**243**) R^1	R^2	R^3	Yield of **244** (%)
Me	Me	H	85
Ph	H	H	78
$-(CH_2)_5-$		Me	89
Ph	H	Me	95
Me	*n*-C_6H_{13}	H	80



(147)

MEM = $MeOCH_2CH_2OCH_2O$

R in **246**	Yield of **246** (%)
n-C_7H_{15}	80
n-C_9H_{19}	65
n-$C_{11}H_{23}$	70
n-$C_{15}H_{31}$	90
n-$C_{16}H_{33}$	89

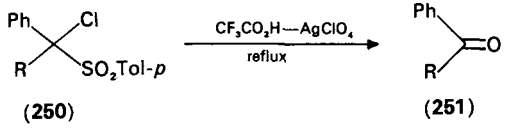
The procedure involves C-alkylation of an α-sulfonyl carbanion derived from **245** with alkyl halides or carbonyl compounds, followed by cleavage of the cyclopropanols **247** produced by deprotection of the hydroxy group of **246** to give (*E*)-substituted aldehydes[141].

Symmetrical 1,4-diketones (**249**) can be prepared by the reaction of phenyl vinyl sulfones (**53**) or divinyl sulfone with aldehydes in the presence of 3-benzyl-5-(2-hydroxymethyl)-4-methylthiazolium chloride as a catalyst (equations 148 and 149)[142].

$$n\text{-}C_5H_{11}CHO + \underset{(\mathbf{53})}{CH_2{=}CHSO_2Ph} \xrightarrow[CH_3CO_2Na]{EtOH} n\text{-}C_5H_{11}COCH_2CH_2COC_5H_{11}\text{-}n \quad \underset{(\mathbf{249})}{} \quad 49\% \tag{148}$$

$$n\text{-}C_5H_{11}CHO + CH_2{=}CHSO_2CH{=}CH_2 \longrightarrow \mathbf{249} \quad 53\% \tag{149}$$

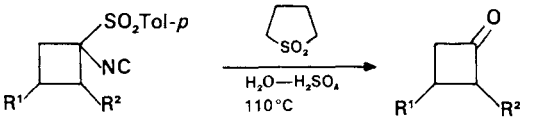
Treatment of α-chloro sulfones **250** with silver perchlorate in refluxing trifluoroacetic acid containing a small amount of water gives the corresponding aromatic ketones **251** in good yields (equation 150)[143].



(150)

R in **250**	Yield of **251** (%)
$PhCH_2$	85
$PhCH_2CH_2$	79
$CH_3(CH_2)_4$	88

An attractive synthesis of cyclobutanone (**253**) has been recently described using 1-isocyano-1-tosylcyclobutane (**252**) (equation 151)[144]. 1-Isocyano-1-tosylcyclobutanes **252** can be prepared from (tosylmethyl)isocyanide and alkyl-substituted 1, 3-dibromobutanes. This method appears to be superior to previously reported methods for the preparation of cyclobutanone because of high purity and high yields.

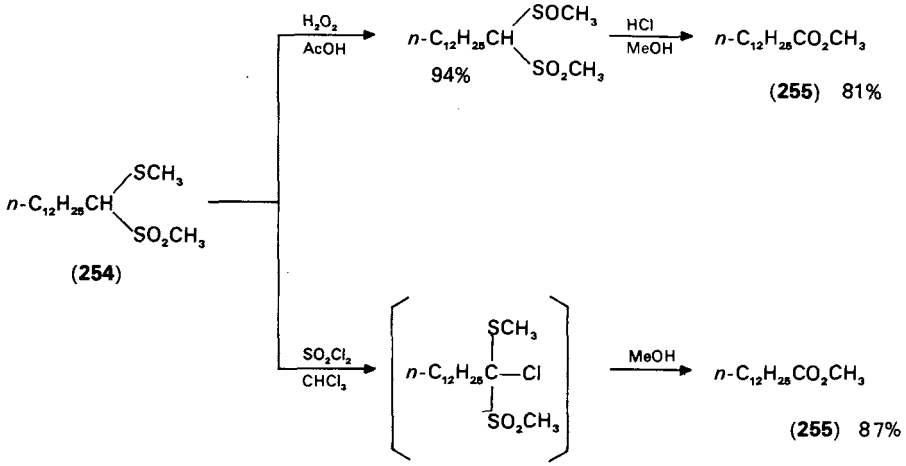


(**252**) (**253**) (151)

Cyclobutanones (**252**)		Yield of **253**
R^1	R^2	(%)
H	H	85
H	Me	88
Me	H	88

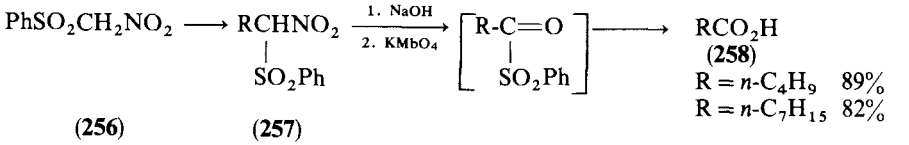
D. Synthesis of Esters, Acids and Lactones

The transformation of 1-methylthio-1-(methylsulfonyl)alkanes (**254**) to methyl esters can be efficiently carried out by oxidation or by α-chlorination followed by methanolysis (equation 152)[145]. The lithium or the sodium salt of (phenylsulfonyl)nitromethane (**256**) is a very useful reagent for the preparation of higher homologues of nitromethanes by alkylation since the salts are air insensitive, non-hygroscopic, and easily handled without decomposition. The oxidation of the resulting secondary α-nitro sulfone (**257**) gives

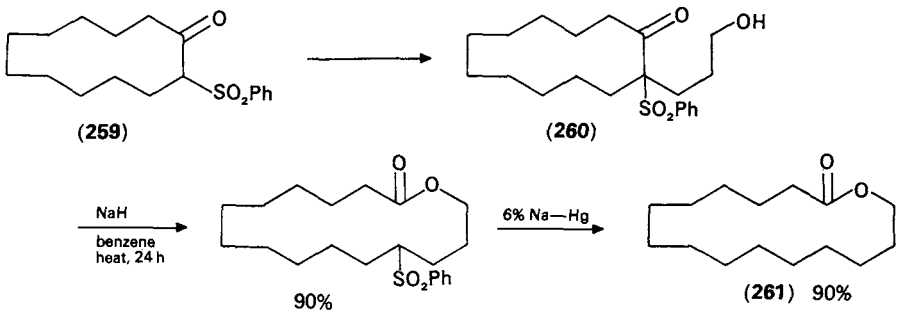


(152)

carboxylic acids (**258**) in high yields (equation 153)[146]. Bhat and Cookson[147] have developed a very efficient synthesis of sulfonyl lactones via ring expansion of δ-hydroxy ketones **260** (equation 154). The yield of this transformation is normally quite high. The sulfonyl group of **259** which facilitates alkylations may be removed to give **261** with excess of sodium amalgam in MeOH–DMF buffered with disodium hydrogen phosphates.



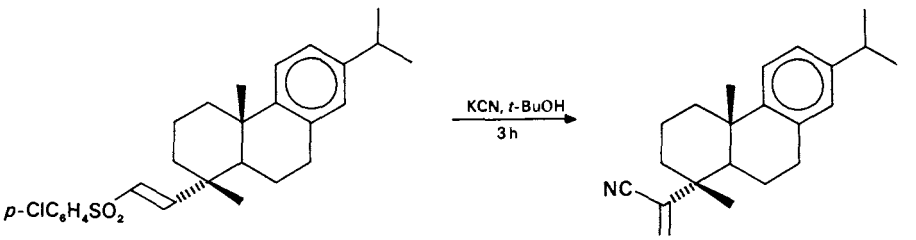
(153)



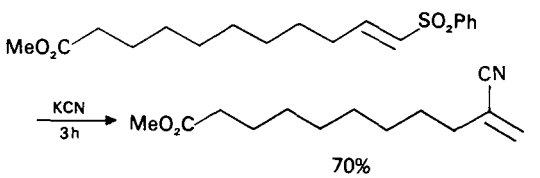
(154)

E. Synthesis of Nitriles

Vinyl sulfones such as **262** are smoothly converted to α,β-unsaturated nitriles such as **263** on treatment with KCN in the presence of dicyclohexyl-18-crown-6 in refluxing *t*-butyl alcohol (equation 155)[148]. The reaction conditions are compatible with base-labile functionalities such as a methoxycarbonyl group (equation 156)[148]. This method can be used in the preparation of the sesquiterpene aldehyde nuciferal from allyl phenyl sulfones.

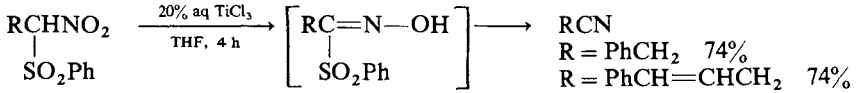


(155)



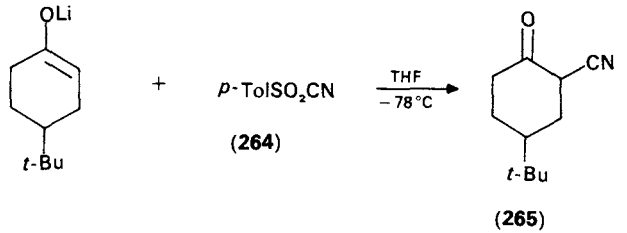
(156)

The conversion of secondary α-nitro sulfones (**257**) upon treatment with 20% aqueous titanium(III) chloride in THF to nitriles has been reported (equation 157)[146].



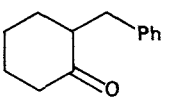
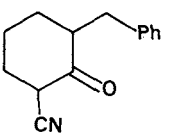
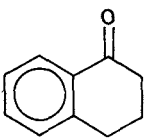
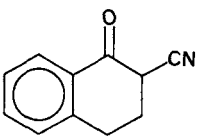
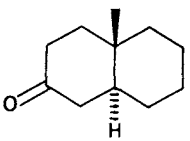
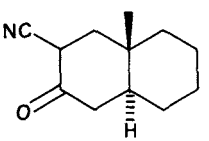
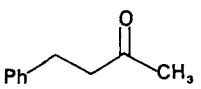
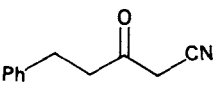
(**257**) (157)

A convenient preparation of α-cyano ketones via ketone enolates has been recently described[149]. The yields are consistently high when using *p*-tolylsulfonyl cyanide (**264**) in THF at − 78 °C. Thus, the addition of the lithium enolates of 4-*t*-butylcyclohexanone to 2 equivalents of **264** at − 78 °C gives α-cyano ketone **265** in 80% yield (equation 158). Use of



(**264**) (**265**) (158)

TABLE 18. Preparation of α-cyano ketones by using **264**[149]

Ketone	Product	Yield of nitrile (%)
		67
		78
		80
		< 5

other cyano compounds such as cyanogen bromide, cyanogen chloride or phenyl cyanate leads to the formation of the bromide or the nitrile with low yields. Other examples of the successful use of reagent **264** are listed in Table 18. With 4-phenyl-2-butanone, the yield is significantly lower due to polymerization of the nitrile under these basic conditions.

VII. REFERENCES

1. (a) P. D. Magnus, *Tetrahedron*, **33**, 2019 (1977).
   (b) L. Field, *Synthesis*, 101 (1972).
   (c) L. Field, *Synthesis*, 713 (1978).
   (d) W. E. Truce, T. C. Klingler and W. W. Brand, in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, 1977, pp. 527–602.
   (e) E. Block, *Aldrichimica Acta*, **11**, 51 (1978).
   (f) E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, 1978.
2. C. J. M. Stirling, *Int. J. Sulfur Chem., C* **6**, 41 (1971).
3. T. Chou and L.-J. Chang, *J. Org. Chem.*, **50**, 4998 (1985).
4. (a) M. Julia, A. Righini and J.-N. Verpeaux, *Tetrahedron Letters*., 2393 (1979).
   (b) M. Julia, A. Righini and J.-N. Verpeaux, *Tetrahedron*, **39**, 3283 (1983).
5. M. Julia and J.-N. Verpeaux, *Tetrahedron*, **39**, 3289 (1983).
6. Y. Masaki, K. Sakuma and K. Kaji, *J. Chem. Soc., Chem. Commun.*, 434 (1980).
7. (a) B. M. Trost, N. S. Schmuff and M. J. Miller, *J. Amer. Chem. Soc.*, **102**, 5979 (1980).
   (b) B. M. Trost, L. Weber, P. Strege, T. J. Fullerton and T. J. Dietsche, *J. Amer. Chem. Soc.*, **100**, 3426 (1978).
8. B. M. Trost and M. R. Ghadiri, *J. Amer. Chem. Soc.*, **108**, 1098 (1986).
9. B. M. Trost and B. R. Adams, *J. Amer. Chem. Soc.*, **105**, 4849 (1983).
10. (a) Y. Ueno, S. Aoki and M. Okawara, *J. Amer. Chem. Soc.*, **101**, 5414 (1979).
    (b) Y. Ueno, S. Aoki and M. Okawara, *J. Chem. Soc., Chem. Commun.*, 683 (1980).
11. Y. Watanabe, Y. Ueno, T. Araki, T. Endo and M. Okawara, *Tetrahedron Letters*, **27**, 215 (1986).
12. (a) J.-L. Fabre, M. Julia and J.-N. Verpeaux, *Tetrahedron Letters*, **23**, 2469 (1982).
    (b) M. Julia, A. Righini and D. Uguen, *J. Chem. Soc., Perkin Trans. 1*, 1646 (1978).
    (c) J.-L. Fabre and M. Julia, *Tetrahedron Letters*, **24**, 4311 (1983).
13. R. L. Smorada and W. E. Truce, *J. Org. Chem.*, **44**, 3444 (1979).
14. N. Miyamoto, D. Fukuoka, K. Utimoto and H. Nozaki, *Bull. Chem. Soc. Japan*, **47**, 503 (1974).
15. H. C. Brown, S.-C. Kim and S. Krishnamurthy, *Organometallics*, **2**, 779 (1983).
16. B. M. Trost, J. Cossy and J. Burks, *J. Amer. Chem. Soc.*, **105**, 1052 (1983).
17. (a) Y. Gaoni, *Tetrahedron Letters*, **22**, 4339 (1981).
    (b) Y. Gaoni, *Tetrahedron Letters*, **23**, 5215 (1982).
    (c) Y. Gaoni, *Tetrahedron Letters*, **23**, 5219 (1982).
    (d) Y. Gaoni, *J. Org. Chem.*, **47**, 2564 (1982).
18. K. Burges, *Tetrahedron Letters*, **26**, 3049 (1985).
19. B. M. Trost and M. R. Ghadiri, *J. Amer. Chem. Soc.*, **106**, 7260 (1984).
20. A. K. Colter and R. E. Miller, Jr., *J. Org. Chem.*, **36**, 1898 (1971).
21. (a) S. Welch and J. M. Gruber, *J. Org. Chem.*, **47**, 385 (1982).
    (b) D. Miller, M. Trammell, A. Kini and R. S. H. Liu, *Tetrahedron Letters*, **22**, 409 (1981).
    (c) T. Mandai, K. Hara, T. Nakajima, M. Kawada and J. Otera, *Tetrahedron Letters*, **24**, 4993 (1983).
    (d) P. S. Manchard, H. S. Wong and J. F. Blount, *J. Org. Chem.*, **43**, 4769 (1978).
    (e) T. Mandai, Y. Iuchi, K. Suxuki, M. Kawada and J. Otera, *Tetrahedron Letters*, **23**, 4721 (1982).
    (f) L. Berthon and D. Uguen, *Tetrahedron Letters*, **26**, 3975 (1985).
    (g) T. Mandai, K. Nishikawa, H. Yamaguchi, M. Kawada and J. Otera, *Chem. Letters*, 473 (1981).
22. T. Yoshida and S. Saito, *Chem. Letters*, 165 (1982).
23. (a) B. Corbel, J. M. Decesare and T. Durst, *Can. J. Chem.*, **56**, 505 (1978).
    (b) S. Torii, K. Uneyama and I. Kawahara, *Bull. Chem. Soc. Japan*, **51**, 949 (1978).
    (c) D. Orr, *Synthesis*, 139 (1979).

(d) T. Mandai, H. Yamaguchi, K. Nishikawa, M. Kawada and J. Otera, *Tetrahedron Letters*, **22**, 763 (1981).
24. B. M. Trost, N. R. Schmuff and M. J. Miller, *J. Amer. Chem. Soc.*, **102**, 5979 (1980).
25. (a) G. Griffiths, S. Hughes and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 236 (1982).
(b) T. Mandai, K. Hara, T. Nakajima, N. Kawada and J. Otera, *Tetrahedron Letters*, **24**, 4993 (1983).
(c) L. Berthon and D. Uguen, *Tetrahedron Letters*, **26**, 3975 (1985).
26. (a) B. Lythgoe and I. Waterhouse, *Tetrahedron Letters*, 2625 (1978).
(b) P. A. Bartlett, F. R. Green III and E. H. Rose, *J. Amer. Chem. Soc.*, **100**, 4852 (1978).
(c) B. Lythgoe and I. Waterhouse, *J. Chem. Soc., Perkin Trans. 1*, 2429 (1979).
27. B. M. Trost and Y. Matsumura, *J. Org. Chem.*, **42**, 4036 (1977).
28. (a) M. Julia and J.-M. Paris, *Tetrahedron Letters*, 4833 (1973).
(b) J. E. Burks, Jr. and J. K. Crandall, *J. Org. Chem.*, **49**, 4663 (1984).
(c) P. J. Kocienski, B. Lythgoe and S. Ruston, *J. Chem. Soc., Perkin Trans. 1*, 829 (1978).
(d) P. J. Kocienski, B. Lythgoe and I. Waterhouse, *J. Chem. Soc., Perkin Trans. 1*, 1045 (1986).
(e) P. J. Kocienski, *Chem. Ind.*, 548 (1981).
(f) P. J. Kocienski and M. Todd., *J. Chem. Soc., Chem. Commun.*, 1078 (1982).
(g) R. Baker, M. J. O'Mahony and C. J. Swain, *J. Chem. Soc., Chem. Commun.*, 1326 (1985).
(h) C.-N. Hsiao and H. Schechter, *Tetrahedron Letters*, **23**, 1963 (1982).
(i) S. D. A. Street, C. Yeates, P. J. Kocienski and S. F. Campbell, *J. Chem. Soc., Chem. Commun.*, 1386 (1985).
29. O. D. Lucchi, V. Lucchini, L. Pasquato and G. Modena, *J. Org. Chem.*, **49**, 596 (1984).
30. A. C. Brown and L. A. Carpino, *J. Org. Chem.*, **50**, 1749 (1985).
31. T. Mandai, T. Yanagi, K. Araki, Y. Morisaki, M. Kawada and J. Otera, *J. Amer. Chem. Soc.*, **106**, 3670 (1984).
32. (a) P. J. Kocienski, *Tetrahedron Letters*, 2649 (1979).
(b) P. J. Kocienski, *J. Org. Chem.*, **45**, 2037 (1980).
33. (a) B. A. Pearlman, S. R. Putt and J. A. Fleming, *J. Org. Chem.*, **50**, 3622 (1985).
(b) M. Ochiai, S. Tada, K. Sumi and E. Fujita, *Tetrahedron Letters*, **23**, 2205 (1982).
34. C.-N. Hsiao and H. Shechter, *Tetrahedron Letters*, **25**, 1219 (1984).
35. S. Matsumura, T. Nagai and N. Tokura, *Bull. Chem. Soc. Japan*, **41**, 635 (1968).
36. B. Lythgoe and I. Waterhouse, *Tetrahedron Letters*, 4223 (1977).
37. Y. Ueno, H. Sano, S. Aoki and M. Okawara, *Tetrahedron Letters*, **22**, 2675 (1981).
38. W. L. Parker and R. B. Woodward, *J. Org. Chem.*, **34**, 3085 (1969).
39. J. B. Hendrickson, A. Giga and J. Wareing, *J. Amer. Chem. Soc.*, **96**, 2275 (1974).
40. A. Krief and M. J. De Vos, *Tetrahedron Letters*, **26**, 6115 (1985).
41. (a) R. V. M. Campbell, L. Crombie, D. A. R. Findley, R. W. King, G. Pattenden and D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 897 (1975).
(b) J. Nartel and C. Hoynh, *Bull. Soc. Chem. Fr.*, 985 (1967).
(c) P. F. Schatz, *J. Chem. Ed.*, **55**, 468 (1978).
(d) D. Arlt, M. Jautelat and R. Lantzsch, *Angew. Chem., Int. Ed. Engl.*, **20**, 703 (1981).
42. (a) C. J. M. Stirling, *Chem. Ind. (London)*, 933 (1960).
(b) M. J. van der Sluijs and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 2*, 1268 (1974).
(c) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 343 (1967).
(d) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 351 (1967).
(e) C. J. M. Stirling, *J. Chem. Soc.*, 5856 (1964).
(f) C. J. M. Stirling, *J. Chem. Soc.*, 5863 (1964).
43. (a) S. Fatutta and A. Risaliti, *J. Chem. Soc., Perkin Trans. 1*, 2387 (1974).
(b) A. Risaliti, S. Fatutta and M. Forchiassin, *Tetrahedron*, **23**, 1451 (1967).
(c) O. D. Lucchi, L. Pasquato and G. Modena, *Tetrahedron Letters*, **25**, 3643 (1984).
(d) F. Benedetti, S. Fabrissin and A. Risaliti, *Tetrahedron*, **40**, 977 (1984).
44. (a) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 351 (1967).
(b) A. R. Friedman and D. R. Graber, *J. Org. Chem.*, **39**, 1432 (1974).
45. L. Horner and H. Lindel, *Liebigs Ann. Chem.*, 22 (1985).
46. P. Carlier, Y. Gelas-Mialhe and R. Vessiere, *Can. J. Chem.*, **55**, 3190 (1977).
47. (a) T. B. R. A. Chen, J. J. Burger and E. R. de Waard, *Tetrahedron Letters*, 4527 (1977).
(b) M. Julia, D. Lave, M. Mulhauser, M. Ramirez-Munoz and D. Uguen, *Tetrahedron Letters*, **24**, 1783 (1983).

48. A. M. van Leusen, F. J. Schaart and D. van Leusen, *Rec. Trav. Chim. Pays-Bas*, **98**, 258 (1979).
49. H. A. Bates, L. Smilowitz and J. Lin, *J. Org. Chem.*, **50**, 899 (1985).
50. (a) P. Auvray, P. Knochel and J. F. Normant, *Tetrahedron Letters*, **26**, 4455 (1985).
(b) J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 734 (1976).
51. B. W. Metcalf and E. Bonilavri, *J. Chem. Soc., Chem. Commun.*, 914 (1978).
52. K. Takagi, K. Nakagawa and K. Negoro, *J. Org. Chem.*, **45**, 4789 (1980).
53. (a) R. M. Cory and R. M. Renneboog, *J. Org. Chem.*, **49**, 3898 (1984).
(b) R. M. Cory and R. M. Renneboog, *J. Chem. Soc., Chem. Commun.*, 1081 (1980).
54. S. G. Pyne, D. C. Spellmeyer, S. Chen and P. L. Fuchs, *J. Amer. Chem. Soc.*, **104**, 5728 (1982).
55. P. R. Hamann and P. L. Fuchs, *J. Org. Chem.*, **48**, 914 (1983).
56. G. De Chirico, V. Fiandanese, G. Marchese, F. Naso and O. Sciacovelli, *J. Chem. Soc., Chem. Commun.*, 523 (1981).
57. (a) G. H. Posner and D. J. Brunelle, *Tetrahedron Letters*, 935 (1973).
(b) G. H. Posner and D. J. Brunelle, *J. Org. Chem.*, **37**, 3547 (1972).
(c) G. H. Posner and D. J. Brunelle, *J. Org. Chem.*, **38**, 2747 (1973).
58. P. Knochel and J. F. Normant, *Tetrahedron Letters*, **26**, 425 (1985).
59. P. Auvray, P. Knochel and J. F. Normant, *Tetrahedron Letters*, **26**, 2329 (1985).
60. J. Ponton, P. Helquist, P. C. Conrad and P. L. Fuchs, *J. Org. Chem.*, **46**, 118 (1981).
61. P. C. Conrad and P. L. Fuchs, *J. Amer. Chem. Soc.*, **100**, 346 (1978).
62. J. C. Saddler, P. C. Conrad and P. L. Fuchs, *Tetrahedron Letters*, 5079 (1978).
63. (a) V. E. Donaldwon and P. L. Fuchs, *J. Amer. Chem. Soc.*, **103**, 2108 (1981).
(b) D. L. Barton, P. C. Conrad and P. L. Fuchs, *Tetrahedron Letters*, **21**, 1811 (1980).
(c) D. K. Hutchinson and P. L. Fuchs, *J. Amer. Chem. Soc.*, **107**, 6137 (1985).
64. (a) J. C. Saddler, R. E. Donaldson and P. L. Fuchs, *J. Amer. Chem. Soc.*, **103**, 2110 (1981).
(b) J. C. Saddler and P. L. Fuchs, *J. Amer. Chem. Soc.*, **103**, 2112 (1981).
65. (a) M. Isobe, M. Kitamura and T. Goto, *Chem. Letters*, 331 (1980).
(b) M. Isobe, Y. Funabashi, Y. Ichikawa, S. Mio and T. Goto, *Tetrahedron Letters*, **25**, 2021 (1984).
(c) M. Isobe, M. Kitamura and T. Goto, *Tetrahedron Letters*, 3465 (1979).
(d) M. Isobe, M. Kitamura and T. Goto, *Tetrahedron Letters*, **21**, 4727 (1980).
(e) M. Isobe, M. Kitamura and T. Goto, *J. Amer. Chem. Soc.*, **104**, 4997 (1982).
66. P. R. Hamann, J. E. Toth and P. L. Fuchs, *J. Org. Chem.*, **49**, 3865 (1984).
67. (a) M. Ochiai, T. Ukita and E. Fujita, *Tetrahedron Letters*, **24**, 4025 (1983).
(b) M. Ochiai, T. Ukita and E. Fujita *J. Chem. Soc., Chem. Commun.*, 619 (1983).
68. O. De Lucchi, L. Pasquato and G. Modena, *Tetrahedron Letters*, **25**, 3647 (1984).
69. A. Jonczyk and M. Makosza, *Synthesis*, 387 (1976).
70. J. J. Eisch and J. E. Galle, *J. Org. Chem.*, **44**, 3277 (1979).
71. T. Agawa, Y. Yoshida, M. Komatsu and Y. Ohshiro, *J. Chem. Soc., Perkin Trans. 1*, 751 (1981).
72. S. E. Denmark and M. A. Harmata, *J. Amer. Chem. Soc.*, **104**, 4972 (1982).
73. (a) M. Cinquini, F. Cozzi and M. Pelosi, *J. Chem. Soc., Perkin Trans. 1*, 1430 (1979).
(b) M. Cinquini, S. Colonna and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 247 (1978).
74. W. E. Truce and D. G. Brady, *J. Org. Chem.*, **31**, 3543 (1966).
75. G. Pourcelot and P. Cadiot, *Bull. Soc. Chem. Fr.*, 3024 (1966).
76. W. E. Truce and L. P. Markley, *J. Org. Chem.*, **35**, 3275 (1970).
77. W. Verboom, M. Shoufs, J. Meijer, H. D. Verkruijsse and L. Brandsma, *Rec. Trav. Chim. Pays-Bas*, **97**, 244 (1978).
78. T. Ohnuma, N. Hata, H. Fujiwara and Y. Ban, *J. Org. Chem.*, **47**, 4713 (1982).
79. J. J. Eisch, M. Behrooz and S. K. Dua, *J. Organometal. Chem.*, **285**, 121 (1985).
80. J. Meijer and P. Vermeer, *Rec. Trav. Chim. Pays-Bas*, **94**, 14 (1975).
81. V. Fiandanese, G. Marchese and F. Naso, *Tetrahedron Letters*, 5131 (1978).
82. O. De Lucchi, V. Lucchini, C. Marchioro and G. Modena, *Tetrahedron Letters*, **26**, 4539 (1985).
83. T. Kobayashi, N. Ishida and T. Hiraoka, *J. Amer. Chem. Soc.*, 736 (1980).
84. P. A. Wade, H.-K. Yen, S. A. Hardinger, M. K. Pillay, N. V. Amin, P. D. Vail and S. D. Morrow, *J. Org. Chem.*, **48**, 1796 (1983).
85. K. Alder, H. F. Rickert and E. Windemuth, *Chem. Ber.*, **71**, 2451 (1938).
86. H. R. Snyder, H. V. Anderson and D. P. Hallada, *J. Amer. Chem. Soc.*, **73**, 3258 (1951).
87. J. C. Philips and M. Oku, *J. Org. Chem.*, **37**, 4479 (1972).
88. W. E. Truce and R. J. McManimie, *J. Amer. Chem. Soc.*, **75**, 1672 (1953).

89. H. R. Snyder and D. P. Hallada, *J. Amer. Chem. Soc.*, **74**, 5595 (1952).
90. O. De Lucchi and G. Modena, *J. Chem. Soc., Chem. Commun.*, 914 (1982).
91. O. De Lucchi, V. Lucchini, L. Pasquato and G. Modena, *J. Org. Chem.*, **49**, 596 (1984).
92. W. E. Parham and J. Heberling, *J. Amer. Chem. Soc.*, **77**, 1175 (1955).
93. O. De Lucchi, G. Licini and L. Pasquato, *J. Chem. Soc., Chem. Commun.*, 418 (1985).
94. O. De Lucchi and G. Modena, *Tetrahedron Letters*, **24**, 1653 (1983).
95. L. A. Paquette and W. A. Kinney, *Tetrahedron Letters*, **23**, 131 (1982).
96. G. R. Krow, J. T. Carey, K. C. Cannon and K. J. Henz, *Tetrahedron Letters*, **23**, 2527 (1982).
97. (a) R. V. C. Carr, R. V. Williams and L. A. Paquette, *J. Org. Chem.*, **48**, 4976 (1983).
(b) A. P. Davis and G. H. Whitham, *J. Chem. Soc., Chem. Commun.*, 639 (1980).
98. W. A. Kinney, G. D. Crouse and L. A. Paquette, *J. Org. Chem.*, **48**, 4986 (1983).
99. R. V. C. Carr and L. A. Paquette, *J. Amer. Chem. Soc.*, **102**, 853 (1980).
100. K. Laping and M. Hanack, *Tetrahedron Letters*, 1309 (1979).
101. L. A. Paquette and R. V. Williams, *Tetrahedron Letters*, **22**, 4643 (1981).
102. L. A. Paquette and G. D. Crouse, *J. Org. Chem.*, **48**, 141 (1983).
103. L. L. Klein and T. M. Deeb, *Tetrahedron Letters*, **26**, 3935 (1985).
104. J. A. Kloek, *J. Org. Chem.*, **46**, 1951 (1981).
105. J. C. Philips and M. Oku, *J. Amer. Chem. Soc.*, **94**, 1012 (1972).
106. M. Shen and A. G. Scultz, *Tetrahedron Letters*, **22**, 3347 (1981).
107. G. Barbarella, M. Cinquini and S. Colonna, *J. Chem. Soc., Perkin Trans. 1*, 1646 (1980).
108. A. G. Guildford and R. W. Turna, *J. Chem. Soc., Chem. Commun.*, 466 (1983).
109. O. De Lucchi, C. Marchioro, G. Valle and G. Modena, *J. Chem. Soc., Chem. Commun.*, 878 (1985).
110. R. D. Little and L. Brown, *Tetrahedron Letters*, **21**, 2203 (1980).
111. T. Kametani, M. Aizawa and H. Nemoto, *Tetrahedron*, **37**, 2547 (1981).
112. H. Bluestone, R. Bimber, R. Berkey and Z. Mandel, *J. Org. Chem.*, **26**, 346 (1961).
113. (a) W. J. Bailey and E. W. Cummins, *J. Amer. Chem. Soc.*, **76**, 1932 (1954).
(b) W. J. Bailey and E. W. Cummins, *J. Amer. Chem. Soc.*, **76**, 1936 (1954).
(c) W. J. Bailey and E. W. Cummins, *J. Amer. Chem. Soc.*, **76**, 1940 (1954).
114. J. L. Melles, *Rec. Trav. Chim. Pays-Bas*, **71**, 869 (1952).
115. W. J. M. van Tilborg, P. Smael, J. P. Visser, C. G. Kouwenhoven and D. N. Reinhoudt, *Rec. Trav. Chim. Pays-Bas*, **94**, 85 (1975).
116. M. S. Raasch, *J. Org. Chem.*, **45**, 856 (1980).
117. (a) M. S. Raasch, *J. Org. Chem.*, **45**, 867 (1980).
(b) R. M. Bimber, U. S. Patent 3,110,739 (1963); *Chem. Abstr.*, **60**, 2870b (1964).
118. M. P. Cava and A. A. Deana, *J. Amer. Chem. Soc.*, **81**, 4266 (1959).
119. J. M. McIntosh and H. B. Goodbrand, *Tetrahedron Letters*, 3157 (1973).
120. L. A. Levy and L. Pruitt, *J. Chem. Soc., Chem. Commun.*, 227 (1980).
121. J. L. Charlton, *Tetrahedron Letters*, **26**, 3413 (1985).
122. (a) W. Oppolzer, D. A. Roberts and T. G. C. Bird, *Helv. Chim. Acta*, **63**, 2017 (1979).
(b) W. Oppolzer and D. A. Roberts, *Helv. Chim. Acta*, **63**, 1703 (1980).
123. K. C. Nicolaou, W. E. Barnette and P. Ma, *J. Org. Chem.*, **45**, 1463 (1980).
124. (a) S. F. Martin, T. Chou and C. Tu, *Tetrahedron Letters*, 3823 (1979).
(b) S. F. Martin, S. R. Desai, W. Phillips and A. C. Miller, *J. Amer. Chem. Soc.*, **102**, 3294 (1980).
125. B. B. Snider and D. K. Spindell, *J. Org. Chem.*, **45**, 5017 (1980).
126. R. H. Rynbrandt and F. E. Dutton, *J. Org. Chem.*, **40**, 2282 (1975).
127. (a) B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, **25**, 1 (1986).
(b) W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977).
128. P. A. Wade and M. K. Pillary, *J. Org. Chem.*, **46**, 5425 (1981).
129. P. A. Wade, S. M. Singh and M. K. Pillay, *Tetrahedron*, **40**, 601 (1984).
130. W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, **23**, 876 (1984).
131. B. B. Snider, T. C. Kirk, D. M. Roush and D. Gonzalez, *J. Org. Chem.*, **45**, 5015 (1980).
132. A. M. van Leusen and J. Strating, *Quart. Reports on Sulfur Chem.*, **5**, 67 (1970).
133. (a) R. A. Abramovitch, V. Alexanian and J. Roy, *J. Chem. Soc., Perkin Trans. 1*, 1928 (1977).
(b) R. A. Abramovitch and J. Roy, *J. Chem. Soc., Chem. Commun.*, 542 (1965).
134. R. A. Abramovitch, V. Alkexanian and E. M. Smith, *J. Chem. Soc., Chem. Commun.*, 893 (1972).
135. (a) R. A. Abramovitch and W. D. Holcomb, *J. Org. Chem.*, **41**, 491 (1976).
(b) R. A. Abramovitch, C. I. Azogu and I. T. McMaster, *J. Amer. Chem. Soc.*, **91**, 1219 (1969).

136. Y. Gaoni, *Tetrahedron Letters*, 4521 (1977).
137. B. M. Trost and R. W. Warner, *J. Amer. Chem. Soc.*, **104**, 6112 (1982).
138. (a) P. J. Kocienski, *Tetrahedron Letters*, 441 (1979).
(b) P. J. Kocienski and J. Tideswell, *Synth. Commun.*, **9**, 411 (1979).
139. A. D. Barone, D. L. Snitman and P. S. Watt, *J. Org. Chem.*, **43**, 2066 (1978).
140. (a) F. de Reinarch-Hirtzbach and T. Durst, *Tetrahedron Letters*, 3677 (1976).
(b) T. Durst, K.-C. Tin, F. de Reinach-Hirtzbach, J. M. Decesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).
(c) C. G. M. Janssen, P. M. van Lier, H. M. Buck and E. F. Godefroi, *J. Org. Chem.*, **44**, 4199 (1979).
141. (a) K. Tanaka, H. Uneme, S. Matsui and A. Kaji, *Bull. Chem. Soc. Japan*, **55**, 2965 (1982).
(b) M. Pohmakotr and S. Pisutjaroenpong, *Tetrahedron Letters*, **26**, 3613 (1985).
142. (a) H. Stetter and H.-J. Bender, *Chem. Ber.*, **114**, 1226 (1981).
(b) H. Stetter and H.-J. Bender, *Angew. Chem., Int. Ed. Engl.*, **17**, 131 (1978).
143. H. Kotake, K. Inomata, H. Kinoshita, Y. Sakamoto and Y. Kaneto, *Bull. Chem. Soc. Japan*, **53** 3027 (1980).
144. D. van Leusen and A. M. van Leusen, *Synthesis*, 325 (1980).
145. K. Ogura, J. Watanabe and H. Iida, *Tetrahedron Letters*, **22**, 4499 (1981).
146. P. A. Wade, H. R. Hinney, N. V. Amin, P. D. Vail, S. D. Morrow, S. A. Hardinger and M. S. Saft, *J. Org. Chem.*, **46**, 765 (1981).
147. V. Bhat and R. C. Cookson, *J. Chem. Soc., Chem. Commun.*, 1123 (1981).
148. D. F. Taber and S. A. Saleh, *J. Org. Chem.*, **46**, 4817 (1981).
149. D. Kahne and D. B. Collum, *Tetrahedron Letters*, **22**, 5011 (1981).

CHAPTER **16**

Asymmetric synthesis using α-sulfinyl carbanions and β-unsaturated sulfoxides

GARY H. POSNER

Department of Chemistry, The Johns Hopkins University, Baltimore, MD 21218, USA

I. INTRODUCTION

Sulfoxides are used synthetically in many different ways. Pyrolytic β-elimination of sulfoxides leads to formation of carbon–carbon double bonds in a position-specific manner[1]. In this way vinylic sulfoxides used in Diels–Alder 2 + 4-cycloaddition reactions are the synthetic equivalents of acetylenes (i.e., cycloaddition, then pyrolysis)[2]. Nucleophilic addition to some vinylic sulfoxides (CH_2=CRSOAr) followed by sulfoxide pyrolysis is the synthetic equivalent of attaching a CH=CHR group to the nucleophile[3]. 2,3-Sigmatropic rearrangement of allylic sulfoxides leads to allylic alcohols often in a highly stereocontrolled fashion[4]. Pummerer rearrangement of sulfoxides leads usually to α-oxygenated sulfides[5], and special use of this procedure is prominent in the chemistry of penicillin sulfoxides forming cephalosporin derivatives of antibiotic value.

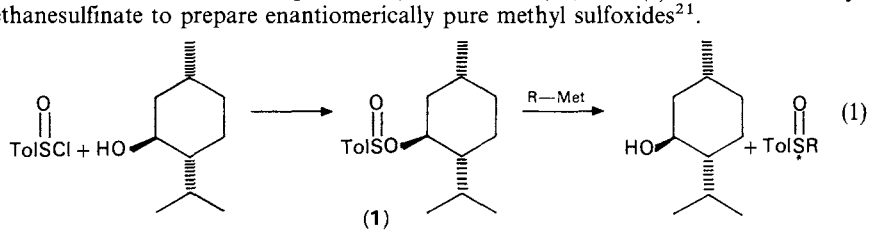
This chapter, however, does not deal with above-mentioned reactions of sulfoxides. Rather it is limited to asymmetric synthesis using α-sulfinyl carbanions and β-unsaturated sulfoxides, specifically in which the stereogenic sulfoxide sulfur atom is enantiomerically pure. Therefore reactions of *racemic* sulfoxides are for the most part excluded from this review. For more general discussions, the reader is referred to other chapters in this volume and to other reviews on the chemistry of sulfoxides. Especially useful are the reviews by Johnson and Sharp[6] and by Mislow[7] in the late 1960s and by Oae[8] and by Nudelman[9] as well as a book by Block[10]. A review by Cinquini, Cozzi and Montanari[11] through mid-1983 summarizes the chemistry and stereochemistry of optically active sulfoxides. This chapter emphasizes results reported from 1984 through mid-1986.

II. PREPARATION OF ENANTIOMERICALLY PURE SULFOXIDES

Three excellent reviews cover this subject through the early 1980s[12–14]. The second review summarizes through 1981 the methods used for determining the enantiomeric purity and the absolute configuration of sulfoxides[13], and the third review summarizes this area through 1983[14].

A. Nucleophilic Substitution at Sulfur

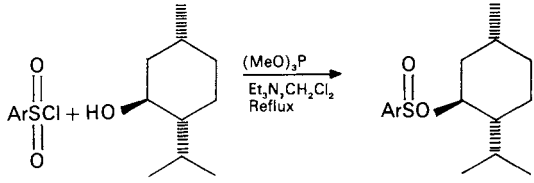
Although first resolved in 1925[15], diastereomerically pure menthyl *p*-toluenesulfinate (**1**) is still by far the most common source of enantiomerically pure sulfoxides. Now *p*-toluenesulfinates **1**, derived from both (+)- and (−)-menthol, are each commercially available and an *Organic Syntheses* procedure has appeared illustrating one application of sulfinate **1** to synthesis of some sulfoxides in enantiomerically pure form[16]. The seminal observation by Andersen in 1962, followed by the work of Mislow in 1968, showed unambiguously that nucleophilic attack by organometallic reagents on such menthyl sulfinates leads via complete inversion of stereochemistry at the sulfur atom to enantiomerically pure sulfoxides (equation 1)[17,18]. Refinements on this procedure include the following: (1) use of benzene as solvent to improve chemical and optical yields[19]; (2) use of organocopperlithium reagents rather than Grignard or simple organolithium reagents to afford cleaner substitution products (i.e., sulfoxides)[20]; and (3) use of cholesteryl methanesulfinate to prepare enantiomerically pure methyl sulfoxides[21].



(1)

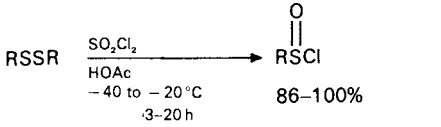
(1)

Sharpless and Klunder[22] are developing a new procedure for conversion of sulfonyl chlorides directly into menthyl sulfinate esters using trimethyl phosphite as a reducing agent (equation 2). This method, starting with sulfonyl chlorides rather than with the much less available sulfinyl chlorides, should allow access to an even wider range of sulfinate esters and, ultimately, to various chiral, non-racemic sulfoxides.

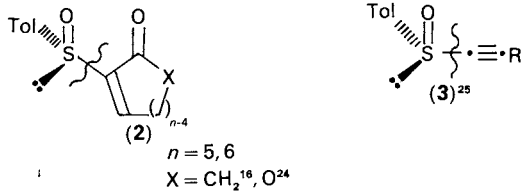


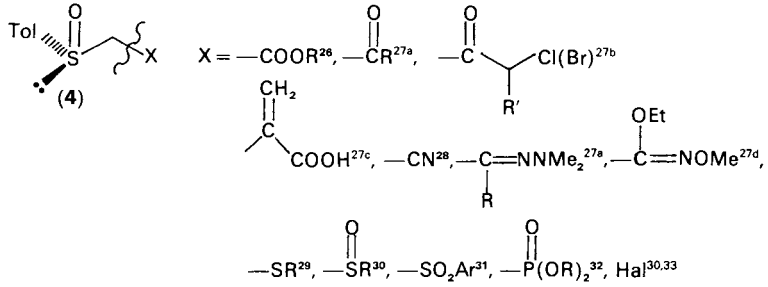
(2)

Also, sulfinyl chlorides (precursors to sulfinate esters) have recently been prepared directly from disulfides (equation 3)[23].

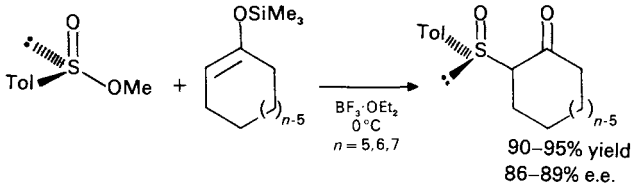


(3)



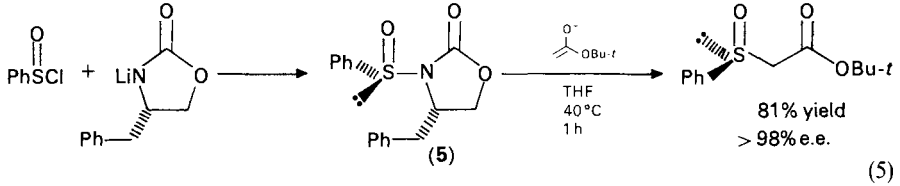


The nature of the organometallic nucleophile in equation 1 can be quite diverse and even highly functionalized, leading to a variety of differently substituted sulfoxides. For examples, the sulfoxides **2**–**4**[24–33] have been prepared in enantiomerically pure form by attack of the corresponding organometallic reagent on a menthyl *p*-toluenesulfinate with formation of the carbon–carbon bonds indicated by wavy lines in the structures. α-Phosphoryl sulfoxides **4**, $X = P(OR)_2$, are especially useful for Horner–Wittig type conversion of aldehydes into α,β-ethylenic sulfoxides of high enantiomeric purity[32]. In a complementary fashion, Lewis acid catalysis has been used successfully in reaction of some cycloalkanone enol silyl ethers with sulfinate esters to give β-ketosulfoxides in very good enantiomeric purity (equation 4)[34].



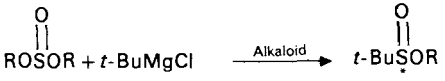
(4)

Evans and Colombo[35] are developing a different route to enantiomerically pure sulfoxides involving intermediate *N*-sulfinyl oxazolidinones **5**. Reaction of these diastereomerically pure species with organometallic reagents gives enantiomerically pure sulfoxides, as illustrated by equation 5 carried out on a multigram scale.



(5)

The Mikolajczyk group[36] has developed use of natural alkaloids as chiral catalysts in conversion of symmetrical dialkyl sulfites into alkyl *t*-butylsulfinate esters in 40–70% enantiomeric purity (equation 6).



(6)

B. Stereocontrolled Oxidation of Sulfides

1. *Enantioselective oxidation*

a. Chemical. The Sharpless asymmetric epoxidation of allylic alcohols using titanium isopropoxide, diethyl tartrate (DET) and *t*-butyl hydroperoxide is one of the most outstanding successes of asymmetric synthesis[37]. Separately, Kagan and Modena and their associates have found that a modified Sharpless procedure is useful also for enantioselective oxidation of sulfides into sulfoxides. The Kagan modification uses one mole equivalent of water[38], whereas the Modena modification involves a 1:4:2 ratio of $Ti(OPr\text{-}i)_4$:DET:*t*-BuOOH[39].

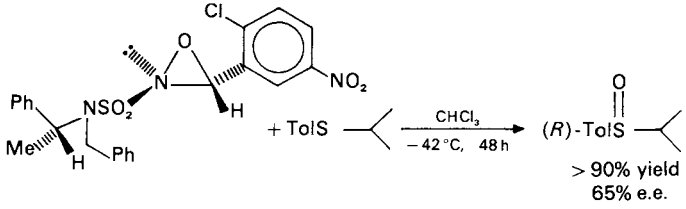
The Kagan group has reported on the scope and limitations of their procedure. The sulfoxides shown in Table 1, prepared by the Kagan procedure in the enantiomeric purities indicated, illustrate the following generalizations: (1) methyl aryl sulfides are the best substrates; (2) alkyl aryl sulfide oxidation is sensitive to the size of the alkyl group, with smaller alkyl groups producing higher enantioselectivities; (3) dialkyl and diaryl sulfides are oxidized with only low to moderate enantioselectivity; and (4) variously functionalized sulfides can be enantioselectively oxidized, with the most impressive asymmetric induction (95%) involving cyclopropyl phenyl sulfide.

Davis and coworkers[40] have developed use of diastereomerically pure 2-sulfonyl and 2-sulfamyloxaziridines for asymmetric oxidation of sulfides into sulfoxides (equation 7). The best results (using the sulfamyloxaziridines) range from 38 to 68% enantiomeric purity of the resultant sulfoxides. The structural diversity of such substituted oxaziridines, their

TABLE 1. Kagan preparation of sulfoxides (RS(=O)R')[38]

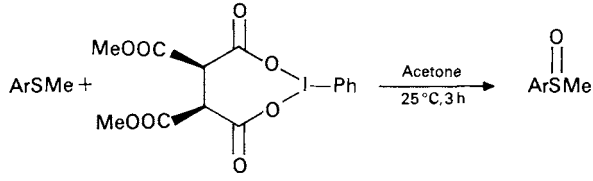
R	R'	%e.e.
Ph	Me	89
p-Tol	Me	93
o-Tol	Me	89
1-Naphthyl	Me	89
p-Tol	Et	74
p-Tol	Pr-*i*	63
p-Tol	Bu-*n*	20
p-Tol	CH_2Ph	7
n-Oct	Me	71
$Ph(CH_2)_3$	Me	50
Cyclohexyl	Me	54
s-Bu	Me	40
$EtOOCH_2$	Me	63
$EtOOCCH_2CH_2$	Me	64
$MeSCH_2$	Me	40
$ClCH_2$	Ph	47
$NCCH_2$	Ph	34
$MeOOCCH_2$	Ph	64
CH_3COCH_2	Ph	60
$CH_2=CH$	Ph	70
Cyclopropyl	Ph	95

thermal stability, and their rigid structures provide good prospects, especially for study of the mechanism and the structure–reactivity patterns in enantioselective chemical oxidations of sulfides.

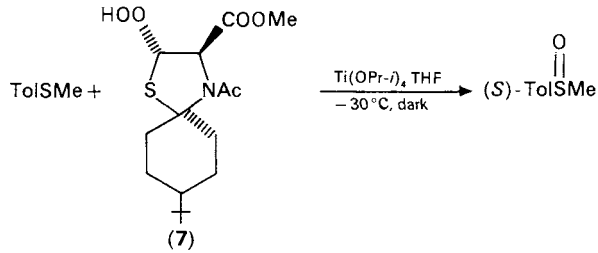


(7)

Some enantiomerically pure chemical oxidizing reagents have been used recently with moderate success for asymmetric oxidation of sulfides into sulfoxides. Trivalent iodine species **6**, derived from iodosylbenzene and L-tartaric anhydride, converts several methyl aryl sulfoxides in high chemical yields into the corresponding sulfoxides in 30–53% e.e. (equation 8)[41]; dialkyl sulfides and benzyl *t*-butyl sulfide were not oxidized with effective enantioselection using this procedure. Optically active hydroperoxide **7**, prepared *in situ* by photosensitized oxygenation of the parent thiazolidine, reacted with methyl *p*-tolyl sulfide in the presence of titanium isopropoxide to produce the corresponding sulfoxide in 37% e.e. (equation 9); other sulfides were oxidized with lower enantioselectivities[42]. Some enantioselective oxidations of alkyl phenyl sulfides have been reported also using sodium metaperiodate supported on chiral Montmorillonite clays at 25 °C; the best result of 78% e.e. involved cyclohexyl phenyl sulfide[43].



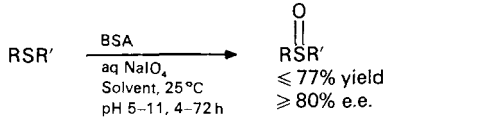
(6) (8)



(7) (9)

Several alkyl aryl sulfides were electrochemically oxidized into the corresponding chiral sulfoxides using poly(amino acid)-coated electrodes[44a]. Although the levels of enantioselection were quite variable, the best result involved *t*-butyl phenyl sulfoxide which was formed in 93% e.e. on a platinum electrode doubly coated with polypyrrole and poly(L-valine). Cyclodextrin-mediated *m*-chloroperbenzoic acid oxidation of sulfides proceeds with modest enantioselectivity[44b].

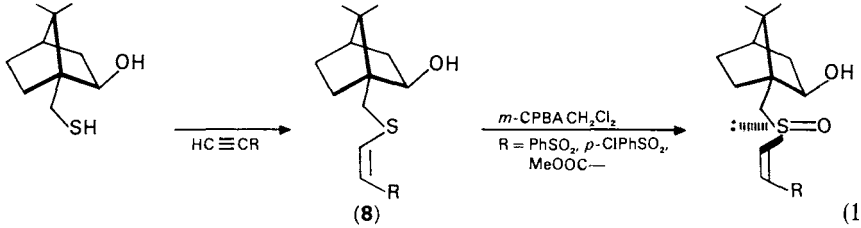
b. Enzymatic. Colonna and associates[45] have shown that bovine serum albumin (BSA) catalyzes asymmetric oxidation of aliphatic, aromatic and heterocyclic sulfides into the corresponding sulfoxides with enantiomeric excesses up to 80% (equation 10). Similarly alkyl aryl sulfoxides have been oxidized by *Corynebacteruim equi* with variable but in some cases excellent enantioselectivity[46].



(10)

2. Diastereoselective chemical oxidation

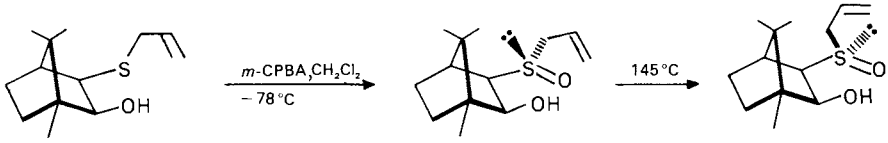
Modena and colleagues[47] have developed use of some chiral, non-racemic terpene alcohols as directing groups for highly diastereoselective *m*-chloroperbenzoic oxidation of sulfides into sulfoxides. Specifically the isobornyl vinylic sulfides **8** undergo hydroxyl-directed oxidation to give a ~9:1 ratio of diastereomeric sulfoxides (equation 11).



(8) (11)

Crystallization to obtain the major diastereomer in pure form is possible in some cases. These hydrogen-bonded vinylic sulfoxides undergo asymmetric 2 + 4-cycloaddition reactions with 1,3-cyclopentadiene (see p. 845).

In a conceptually similar fashion, camphor-derived hydroxysulfide **9** is oxidized diastereospecifically into hydroxysulfoxide **10** whose absolute configuration has been determined by X-ray crystallography[48]. Heating this diastereomer to 145 °C causes complete epimerization at sulfur to form diastereomer **11** in quantitative yield (equation 12). This type of allylic sulfoxide can be deprotonated and then added in a Michael fashion to cycloalkenones (see p. 834).



(**9**) (**10**) 55% (**11**) 100%

(12)

C. Enzymatic Kinetic Resolution

Enzyme-mediated hydrolysis of some racemic ω-arenesulfinylalkanoic methyl esters, $ArSO(CH_2)_nCOOMe$, using *Corynebacterium equi* has led to a kinetic resolution in which the unreacted sulfinyl esters are enriched in one enantiomer at the sulfoxide center[49]. The enantiomeric purity of unreacted sulfinyl acetates and propionate ranges from 90 to 97%.

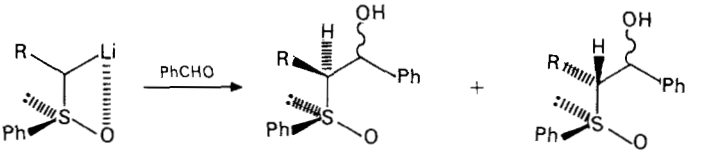
III. REACTIONS OF ELECTROPHILES WITH α-SULFINYL CARBANIONS

A. Carbanions from Alkyl Sulfoxides

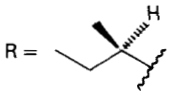
The conjugate bases of alkyl sulfoxides (i.e., α-sulfinyl carbanions) have been studied on theoretical grounds (i.e., is the carbanion planar or tetrahedral?) and for synthetic purposes (i.e., attachment of electrophiles adjacent to the sulfoxide sulfur atom). It is now clear that the stereochemical course by which an electrophile becomes attached to the α-carbon atom of such α-lithiosulfinyl carbanions depends in a complex way on the choice of solvent, the nature and origin of initial lithiating reagent, the presence of added lithium salts, the presence of complexing reagents, and the nature of the quenching reaction. Despite this complex situation, trapping α-sulfinyl carbanions in a stereocontrolled manner is often very useful synthetically and is one of the key features in asymmetric total synthesis of physiologically active biotin[50] and maytansine[51]. This topic has been reviewed extensively[11,52] and excellent reviews, specifically of aldol condensations using chiral α-sulfinyl carbanions, are also available[53,54]. Therefore, this section deals only with reactions of α-sulfinyl carbanions which carry also one or more additional stereogenic atoms[55].

The following discussion is based in large part on the work of Williams and coworkers[56]. For α-lithiosulfinyl species —SOCH(Li)R in which R has no heteroatom but may have a stereogenic atom, it is assumed that the carbanion is tetrahedral and that lithium is intramolecularly coordinated with (i.e., solvated by) the sulfoxide oxygen atom. The diastereomeric species **12** and **13** result from these assumptions. In **12** the bulky R and Ph substituents are eclipsed, whereas in **13** they are on opposite sides of the plane defined by the four-membered 'metallocycle'. Although diastereomer **13** may be more stable (and therefore more populated) than **12**, both diastereotopic faces of **13** are sterically hindered, one face by the R group and one by the Ph group; diastereomer **12** therefore, having one diastereotopic face bearing both small H and sulfoxide lone pair, should be more reactive toward aldehydes. Reaction with benzaldehyde proceeds in good yield to produce two diastereomeric aldol-type products **14** and **15** in which **14**, having the H and sulfoxide lone pair *syn*, predominates over **15** (H and lone pair *anti*) by a ratio of 6:1 (equation 13).

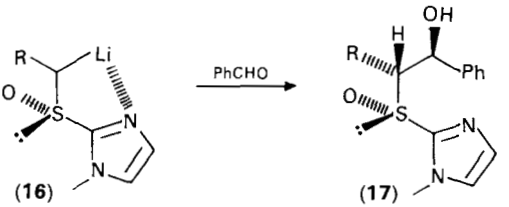
(12) (13)



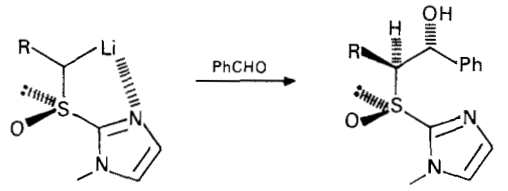
(13) (14) 6 : (15) 1 (13)



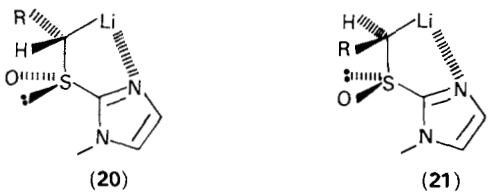
When the aromatic group of the sulfoxide is replaced by a heteroaromatic group (e.g., *N*-methylimidazole), the internal coordination between Li—N to form a five-membered 'metallocycle' apparently predominates over Li—O coordination to form a four-membered 'metallocycle'. Reaction of imidazole (*S*)-sulfoxide **16** with benzaldehyde produces aldol **17** as the major product in which the α-H and the sulfoxide lone pair are *syn* (equation 14); imidazole (*R*)-sulfoxide **18** reacts similarly (equation 15). The stereochemical outcome of these reactions is rationalized in terms of α-lithiosulfoxides in which the reactive diastereomer (i.e., **20** and **21**) is that having one diastereotopic face of the five-membered Li—N 'metallocycle' carrying *both* H and sulfoxide lone pair.



(16) (17) (14)

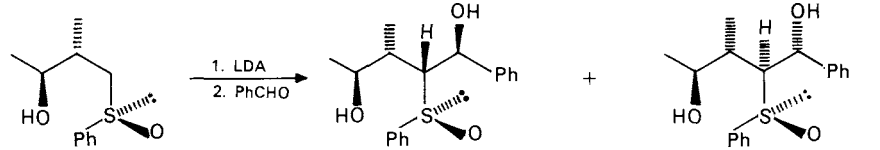


(18) (19) (15)

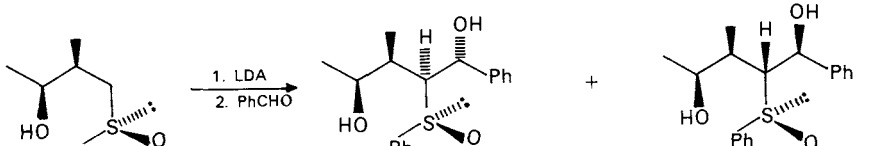


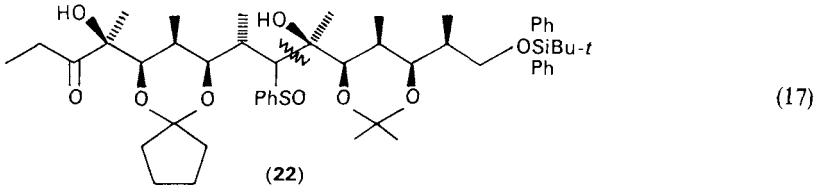
(20) (21)

Finally, when the R substituent bears both a stereogenic atom β to the sulfoxide group and also a potentially coordinating heteroatom γ to the sulfoxide, then analysis of the stereochemical course of aldol condensations becomes speculative and conclusions about mechanism become questionable. Nevertheless, one legitimate generalization seems to be that in such cases a methyl substituent at a stereogenic β-carbon atom induces asymmetry such that the newly formed aldol hydroxy group is usually *anti* to the original β-methyl group (equations 16 and 17). Stork and coworkers[57] have reported application of this type of α-lithiosulfinyl carbanion aldol condensation to synthesis of erythronolide intermediate **22**.



(16)

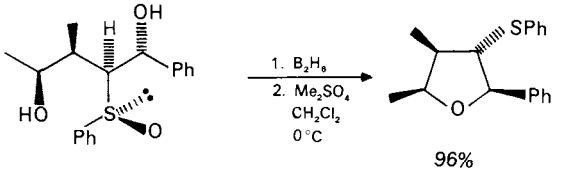




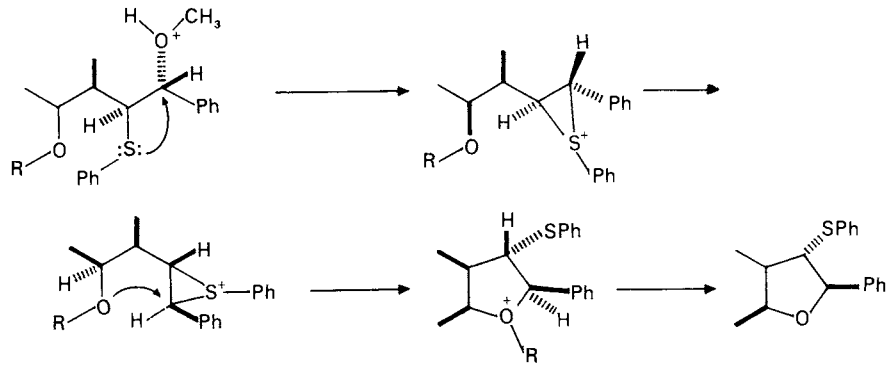
(17)

Williams[56] argues that these aldol-type condensations do *not* proceed via cyclic, chairlike six-membered transition states, in contrast to previous arguments to the contrary[58].

Williams and Phillips have developed this stereocontrolled aldol-type condensation of α-lithiosulfinyl carbanions into an efficient route to stereochemically complex tetrahydrofurans (e.g., equation 18)[56b]. Their procedure involves reduction of the sulfoxide group into a sulfide and then methylation (Me_2SO_4) of the hydroxyl group followed by solvolysis of the protonated methyl ether where the loss of methanol is assisted by backside participation of the neighboring sulfur atom, producing an intermediate sulfonium salt. Intramolecular attack by the hydroxy (alkoxy) group which was present in the original reactant sulfoxide proceeds through a five-membered transition state to form an oxonium ion which undergoes deprotonation (dealkylation) to give the observed tetrahydrofuran (Scheme 1).



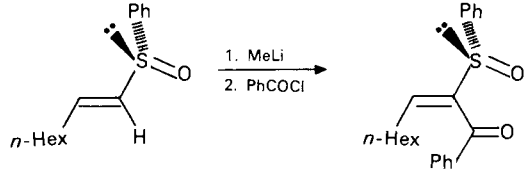
(18)



SCHEME 1

B. Carbanions from 1-Alkenyl Sulfoxides

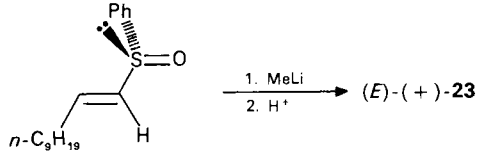
Kinetic deprotonation of 1-alkenyl sulfoxides produces the corresponding α-lithiosulfinyl carbanions[59] which have been deuterated, alkylated, acylated (e.g., equation 19)[60] and carboxylated.



44%
$[\alpha]_D^{25} + 97.6°$
(c. 2.4, acetone)

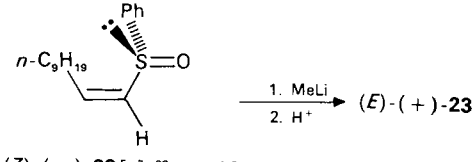
(19)

Deprotonation and then reprotonation of enantiomerically pure 1-alkenyl sulfoxide (*E*)-(+)-**23** produces no double bond isomerization and no racemization, whereas similar treatment of (*Z*)-(−)-**23** causes complete double bond isomerization and some racemization (equations 20 and 21)[59d].



(*E*)-(+)-**23** $[\alpha]_D^{22} = +95.7°$ $[\alpha]_D^{22} = +95.2°$

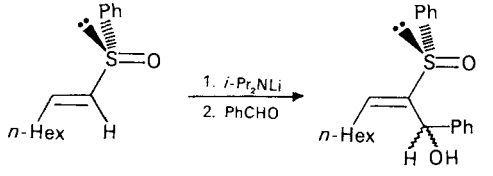
(20)



(*Z*)-(−)-**23** $[\alpha]_D^{22} = -199.9°$ $[\alpha]_D^{22} = +67.3°$

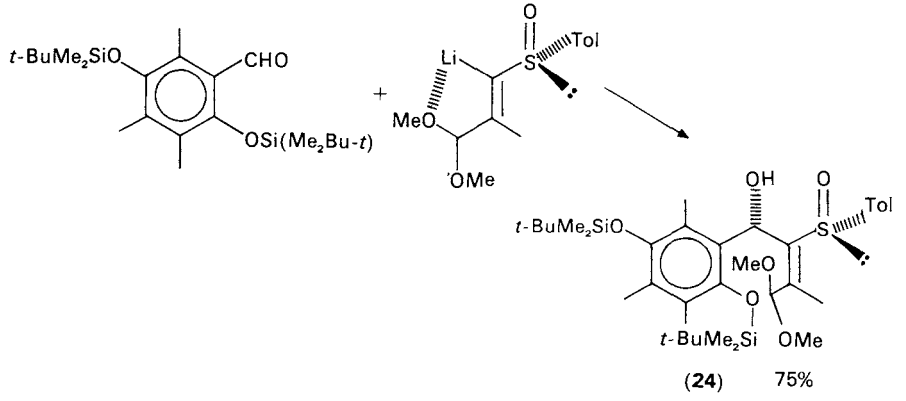
(21)

Addition of such α-lithiosulfinyl carbanions to aldehydes could proceed with asymmetric induction at the newly formed carbinol functionality. One study of this process, including variation of solvent, reaction temperature, base used for deprotonation, structure of aldehyde, and various metal salts additives (e.g., $MgBr_2$, $AlMe_3$, $ZnCl_2$, CuI), has shown only about 20–25% asymmetric induction (equation 22)[59d]. Another study, however, has been much more successful[53]. Solladié and Moine[61] obtain the highly diastereocontrolled aldol-type condensation as shown in equation 23, in which diastereomer **24** is the only observed product, isolated in 75% yield! This intermediate is then transformed stereospecifically via a sulfoxide-assisted intramolecular S_N2' process into formylchromene **25**, which is a valuable chiron precursor to enantiomerically pure α-Tocopherol (Vitamin E, **26**).



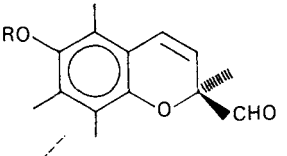
93%
Diastereomeric ratio 1.5:1.0

(22)

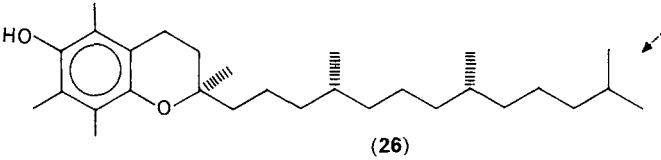


(24) 75%

(23)



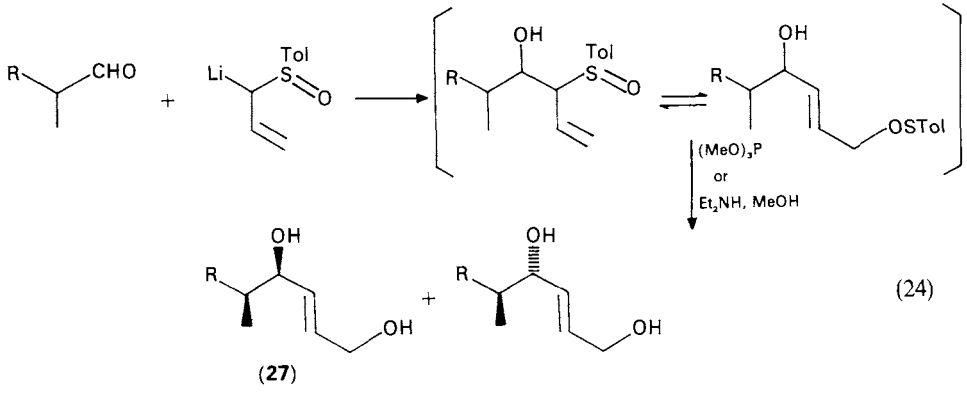
(25)



(26)

C. Carbanions from Allylic Sulfoxides

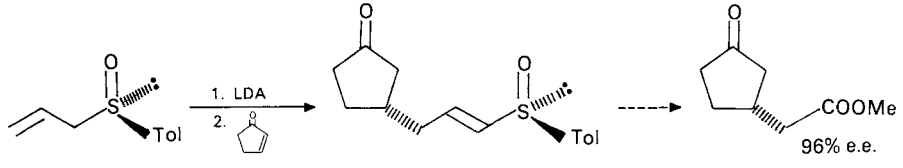
Deprotonation of allylic aryl sulfoxides leads to allylic carbanions which react with aldehyde electrophiles at the carbon atom α and also γ to sulfur[62]. With benzaldehyde at $-10\,^{\circ}C$ γ-alkylation predominates[63], whereas with aliphatic aldehydes at $-78\,^{\circ}C$ in the presence of HMPA α-alkylation predominates[64]. When the α-alkylated products, which themselves are allylic sulfoxides, undergo 2, 3-sigmatropic rearrangement, the rearranged compounds (i.e., allylic sulfenate esters) can be trapped with thiophiles to produce overall (*E*)-1, 4-dihydroxyalkenes (equation 24). When α-substituted aldehydes are used as electrophiles, formation of *syn*-diols **27** occurs in 40–67% yields with diastereoselectivities ranging from 2–28:1 (equation 24)[64].



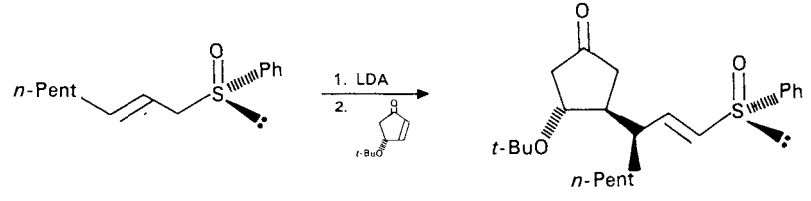
(24)

(**27**)

When enantiomerically pure allyl *p*-tolyl sulfoxide is deprotonated and then treated with electrophilic 2-cyclopentenone, a conjugate addition occurs forming a new carbon–carbon bond with very high control of absolute stereochemistry (equation 25)[65]. See also Reference 48. Similarly, using more substituted enantiomerically pure allylic sulfoxides leads to virtually complete diastereocontrol, as exemplified by equations 26 and 27; the double bond geometry in the initial allylic sulfoxide governs the stereochemistry at the newly allylic carbon atom (compare equations 26 vs. 27)[66]. Haynes and associates[67] rationalize this stereochemical result in terms of frontier molecular orbital considerations

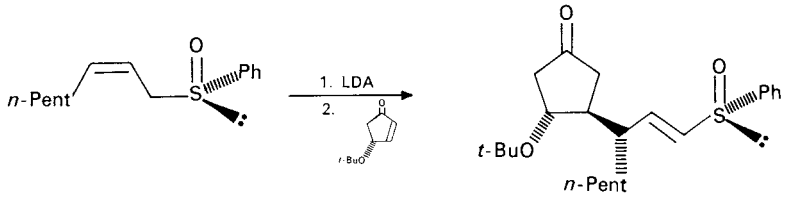


(25)

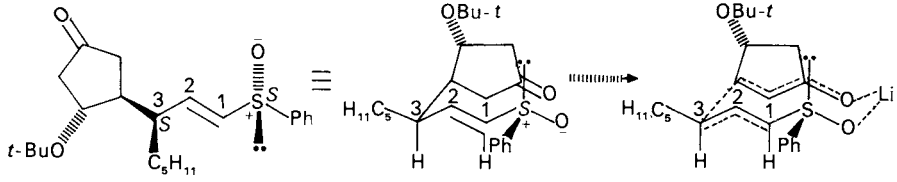


(26)

and in terms of a ten-membered cyclic transition state which is best described as '*trans*-fused chair-chair-' like or '*trans*-decalyl'-like (Scheme 2). These workers note that benzylic and propargylic sulfinyl carbanions, in contrast to allylic sulfinyl carbanions, add only 1,2 to the carbonyl group of cyclopentenone.

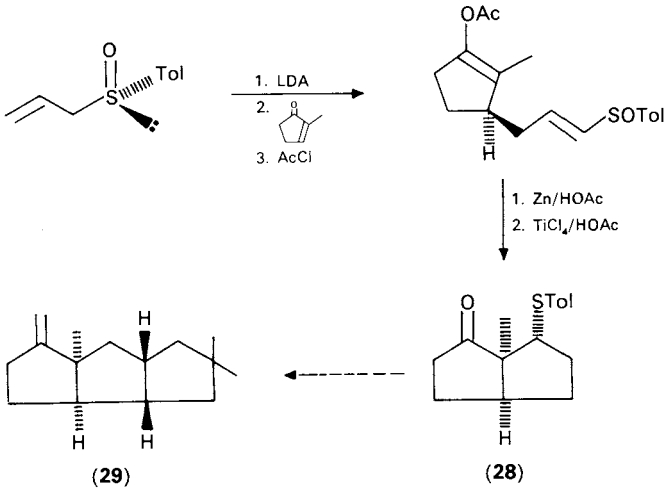


(27)

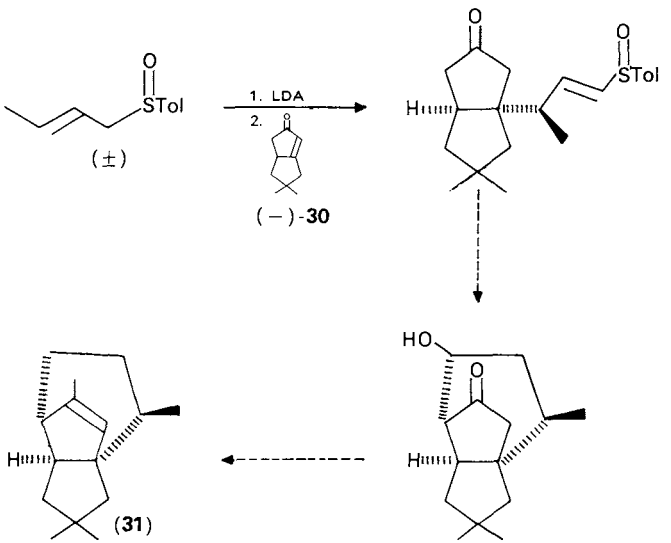


SCHEME 2

This type of asymmetric conjugate addition of allylic sulfinyl carbanions to cyclopentenones has been applied successfully to total synthesis of some natural products. For example, enantiomerically pure (+)-hirsutene (**29**) is prepared (via **28**) using as a key step conjugate addition of an allylic sulfinyl carbanion to 2-methyl-2-cyclopentenone (equation 28)[65], and (+)-pentalene (**31**) is prepared using as a key step kinetically controlled conjugate addition of racemic crotyl sulfinyl carbanion to enantiomerically pure cyclopentenone **30** (equation 29); this kinetic resolution of the crotyl sulfoxide is followed by several chemical transformations leading to (+)-pentalene (**31**)[68].



(28)



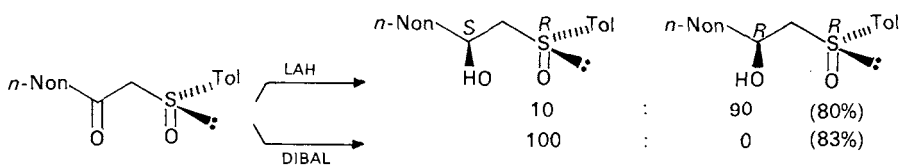
(29)

IV. ADDITION OF NUCLEOPHILES TO β-UNSATURATED SULFOXIDES

A. β-Keto sulfoxides

1. Hydride nucleophiles

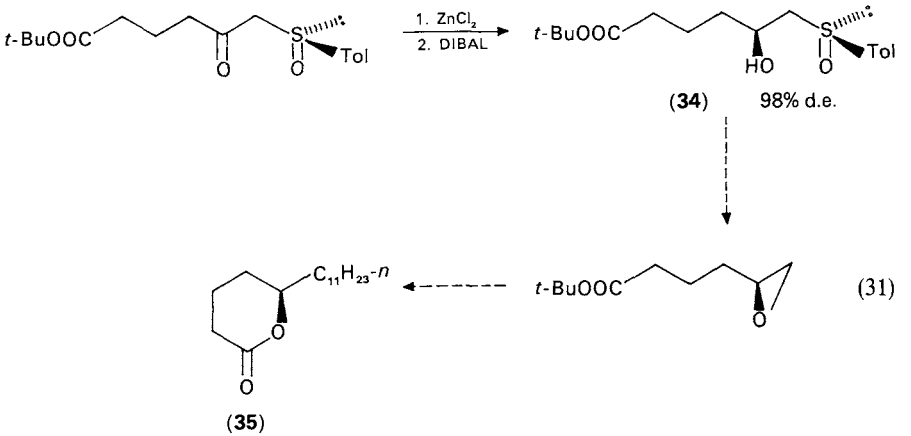
Enantiomerically pure β-keto sulfoxides are prepared easily via condensation of α-lithiosulfinyl carbanions with esters. Reduction of the carbonyl group in such β-keto sulfoxides leads to diastereomeric β-hydroxysulfoxides. The major recent advance in this area has been the discovery that non-chelating hydride donors (e.g., diisobutylaluminium hydride, DIBAL) tend to form one β-hydroxysulfoxide while chelating hydride donors [e.g., lithium aluminium hydride (LAH), or DIBAL in the presence of divalent zinc ions] tend to produce the diastereomeric β-hydroxysulfoxide. The level of diastereoselectivity is often very high. For example, enantiomerically pure β-ketosulfoxide **32** is reduced by LAH in diethyl ether to give mainly the (*RR*)-diastereomer whereas DIBAL produces exclusively the (*SR*)-diastereomer (equation 30)[53,69]. A second example is shown in



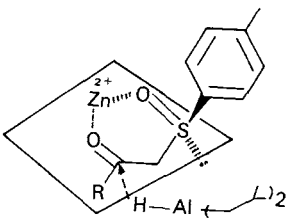
(30)

equation 31 in which zinc dichloride-mediated DIBAL reduction proceeds with a 99:1 diastereoselectivity (98% diastereomeric excess, d.e.), presumably via zinc chelate **33**, to form β-hydroxysulfoxide **34**; hydride delivery apparently is directed via chelate **33** to that diastereotopic face of the planar system carrying the sulfoxide lone pair (i.e., away from the bulky aromatic group)[70]. Several subsequent steps not involving the stereogenic oxygen-

bearing carbon atom lead to a highly stereocontrolled total synthesis of the Oriental hornet pheromone **35** (equation 31).

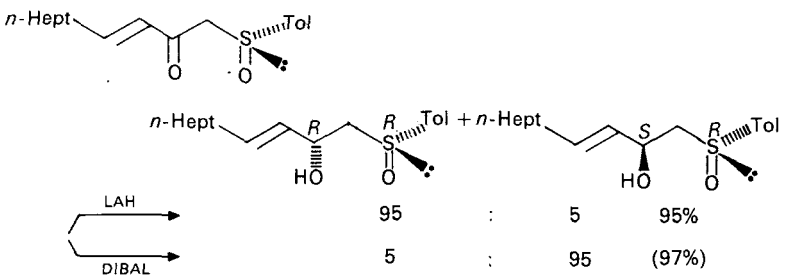


(31)



(**33**)

A similar complementarity has been observed in LAH vs. DIBAL reduction of β-ketosulfoxides in which the keto group is also part of a conjugated enone system (equation 32)[69]. After reductive cleavage (Li, $EtNH_2$) of the alkyl–sulfur bond, 3-alken-2-ols of high enantiomeric purity are produced[69].

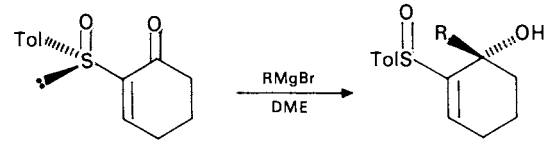


(32)

2. Carbon nucleophiles

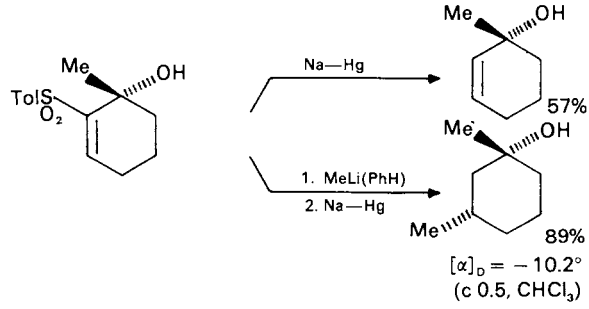
When *both* the carbonyl group *and* the sulfinyl group of a β-ketosulfoxide are attached to the same carbon atom of a carbon–carbon double bond, then addition of nucleophiles can occur at the electrophilic β-carbon atom (i.e., 1,4-addition, conjugate addition) and/or

at the electrophilic carbonyl carbon atom (i.e., 1,2 addition). Whereas 1,4 nucleophilic addition is the more common path (which is discussed in detail in the following section)[59e,71a], 1,2 addition of methyl and *n*-butyl Grignard reagents (vinyl, phenyl and alkyl Grignards give mainly 1,4 addition) proceed with good diastereoselectivities (equation 33)[71b]. Facile chromatographic separation of diastereomers and subsequent chemical manipulation lead to some stereospecifically functionalized tertiary cyclohexanols in virtually complete enantiomeric purity (equation 34)[71b].



(33)

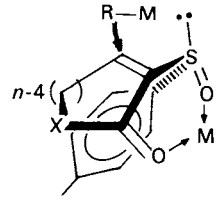
R	Yield	d.e.
Me	65%	82%
n-Bu	55%	92%



(34a)

(34b)

$[\alpha]_D = -10.2°$
(c 0.5, $CHCl_3$)

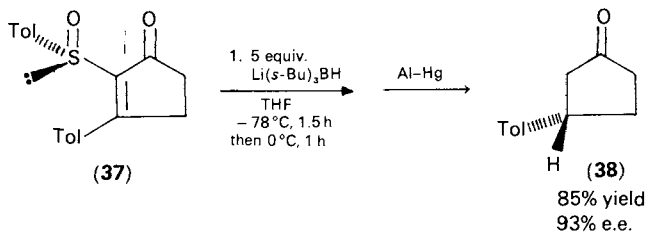


(36) $X = CH_2, O$
$n = 5, 6$

B. α,β-Ethylenic Sulfoxides

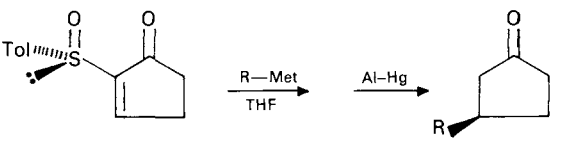
In contrast to α,β-ethylenic ketones or even α,β-ethylenic sulfones, α,β-ethylenic sulfoxides generally are not sufficiently electrophilic to undergo successful nucleophilic β-addition[59e,72]. α-Carbonyl-α,β-ethylenic sulfoxides, however, are potent, doubly activated alkenes which undergo rapid and complete β-addition of various types of nucleophiles even at −78 °C. A brief account summarizing this area is available[73]. The stereochemical outcome of such asymmetric conjugate additions to enantiomerically pure 2-sulfinyl 2-cycloalkenones and 2-sulfinyl-2-alkenolides has been rationalized in terms of a metal-chelated intermediate in which a metal ion locks the β-carbonyl sulfoxide into a rigid conformation (**36**; cf. **33**). In this fixed conformation, one diastereoface of the cyclic π

system is blocked by an aromatic group, and therefore nucleophilic conjugate addition occurs selectively from the other diastereoface[74]. An alternative explanation based on chemical reactivity modeling techniques has recently been offered to account for the stereochemistry of conjugate addition[75]. Both ^{1}H and ^{13}C NMR evidence has been reported supporting chelate intermediate **36**, and several factors have been noted in some cases to increase the levels of diastereoselectivity: (1) use of poorly coordinating solvents (e.g., 2, 5-dimethyltetrahydrofuran instead of tetrahydrofuran)[76]; (2) use of electron-donating aromatic groups (e.g., *p*-anisyl in place of *p*-tolyl) to increase the stability of the chelate[77]; and (3) use of bulky organometallic reagents such as alkyltitanium trialkoxides to allow greater distinction between approach to each of the diastereopic faces of chelate **36**[76]. Examples of these effects are discussed in the following paragraphs.



(37) (38)
85% yield
93% e.e.

(35)



(36)

R	Yield (%)	e.e. (%)
MeMgCl	Me	91	> 98
$ZnBr_2$/EtMgCl	Et	84	80
EtTi(OPr-*i*)$_3$	Et	67	> 98
$ZnBr_2$/*t*-BuMgCl	*t*-Bu	98	86
$ZnBr_2$/CH_2=CHMgBr	CH_2=CH	75	98.7
$ZnBr_2$/PhMgCl	Ph	70	92
6-MeONaphMgBr	6-MeONaph	90	> 98

1. *Hydride nucleophiles*

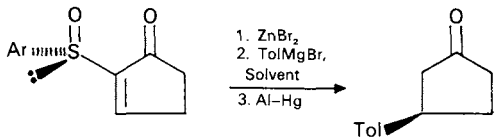
Enantiomerically pure 3-tolyl-2-sulfinyl-2-cyclopentenone **37** undergoes smooth, mild and diastereoselective conjugate hydride addition with lithium tri(sec-butyl)borohydride to afford ultimately 3-tolylcyclopentanone **38** in 93% enantiomeric purity (equation 35)[78]. The absolute stereochemistry of product **38** is consistent with a chelated intermediate directing hydride addition from that diastereoface containing the sulfoxide lone pair.

2. *Carbon nucleophiles*

a. Hydrocarbon groups. The best results using hydrocarbon nucleophiles in the form of organometallic reagents are summarized in equation 36. In some cases, zinc dibromide is used to preform a zinc chelate, followed by conjugate addition of a Grignard reagent. Among the most impressive results using this procedure is the preparation of (*R*)-3-

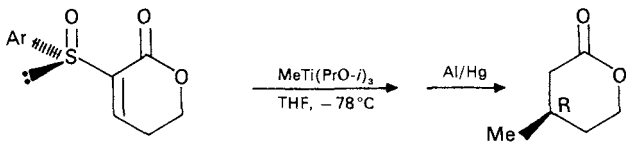
vinylcyclopentanone in 98.7% e.e. (> 150:1 *R*:*S*) as assayed by chiral capillary gas chromatography[59e,79]. 3-Vinylcyclopentanone derivatives are valuable synthons in many elegant Diels–Alder *o*-quinodimethane syntheses of estrone steroids; (*R*)-3-vinylcyclopentanone derivatives therefore are valuable chirons in asymmetric steroid syntheses. A survey of metal dibromides (M = Ni, Co, Pd, Mg) shows $ZnBr_2$ to be the most effective in promoting high stereochemical control in the conjugate addition step. Because the metal-chelated cyclopentanone sulfoxide is so electrophilic even ethyltitanium triisopropoxide, which normally adds directly to the carbonyl group of an enone, adds in a conjugate and highly (> 98%) diastereoselective fashion. Note that the bulky ethyltitanium reagent produces substantially higher asymmetric induction than ethylmagnesium chloride.

If indeed chelation is required before diastereoselective conjugate addition, then making the aryl group in the arylsulfinyl function more electron-releasing and making the solvent less coordinating should increase the stability of the chelate and thereby increase the diastereofacial bias. As shown in equation 37, replacing a *p*-tolyl by a *p*-anisyl group in the arylsulfinyl functionality causes a noticeable increase (58 → 69%) in diastereoselectivity[77]. This effect is even more substantial (60 → 94%) in the corresponding lactone series (equation 38)[80]. Replacing THF by the less-coordinating (±)-2,5-dimethyltetrahydrofuran (DMTHF, mixture of *cis* and *trans* isomers) causes a dramatic increase in diastereoselectivity, as observed for conjugate methyl (87 → 96%) and conjugate phenyl (43 → 93%) addition (equation 39)[76]. In most cases, the *p*-anisylsulfoxides are not soluble in DMTHF (or in ether) and, therefore, a combined benefit of the anisyl group *and* the less polar solvent cannot be realized.



(37)

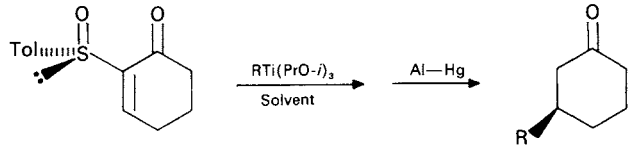
Ar	Solvent	e.e. (%)	*R*:*S*
p-Tol	THF	58	4:1
p-An	THF	69	6:1
p-Tol	DMTHF	86	13:1



(38)

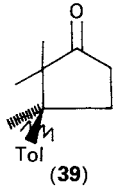
Ar	%e.e.	*R*:*S*
p-Tol	60	4:1
p-An	94	32:1

Successful applications of these stereocontrolled conjugate additions have led to asymmetric syntheses of several natural products such as (+)-cuparenone (**39**) which involves formation of a quaternary carbon center[81], (−)-β-vetivone (**40**)[80] and steroidal equilenin **41**[82]; the wavy lines in these structures indicate that C—C bond formed stereoselectively under the influence of a temporarily-attached stereogenic sulfoxide auxiliary group.

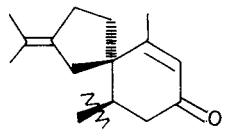


(39)

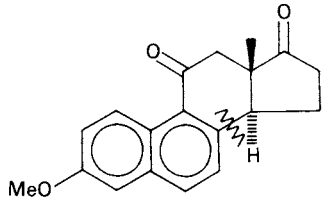
R	Solvent	e.e. (%)	R:S
Me	THF	87	13:1
Me	DMTHF	96	49:1
Ph	THF	43	2:1
Ph	DMTHF	93	28:1



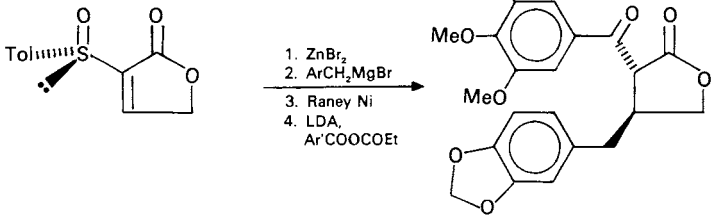
(39)



(40)



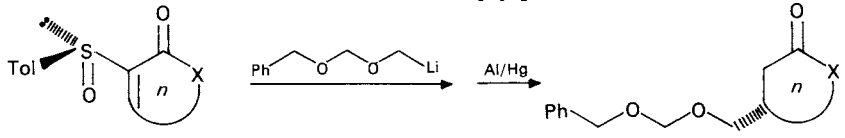
(41)



(40)

Ar = 3, 4-$(CH_2O_2)C_6H_3$

Ar' = 3, 4, 5-$(MeO)_3C_6H_2$

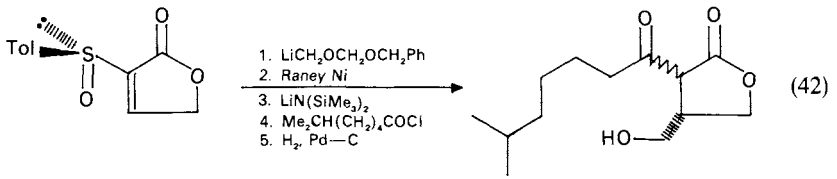


n	X	%e.e.
5	CH_2	78
6	CH_2	93
5	O	87

(41)

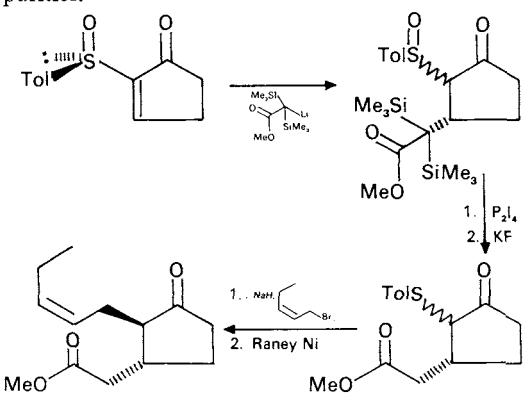
sp^3-Carbon nucleophiles carrying one or more oxygen substituents have also been used successfully in stereocontrolled β-addition to some enantiomerically pure 2-sulfinyl-2-cycloalkenones and 2-sulfinyl-2-alkenolides. For example, zinc-promoted chelate-mode conjugate addition of an oxygen-bearing benzylic Grignard reagent leads ultimately via equation 40 to (−)-podorhizon, a member of the anticancer podophyllotoxin family, in 95% enantiomeric purity[83]. In contrast, asymmetric conjugate addition of a $^-CH_2OH$ synthetic equivalent (derived from n-$Bu_3SnCH_2OCH_2OCH_2Ph$)[84] leads presum-

ably via the ground-state non-chelated form of the β-ketosulfoxide (with the polar sulfinyl and carbonyl groups oriented *anti* to each other)[85] to protected 3-hydroxymethyl conjugate adducts in 78–93% e.e. (equation 41)[84]; application of this procedure via equation 42 produces (+)-A Factor, a potent autoregulating factor essential for streptomycin biosynthesis[84,86].

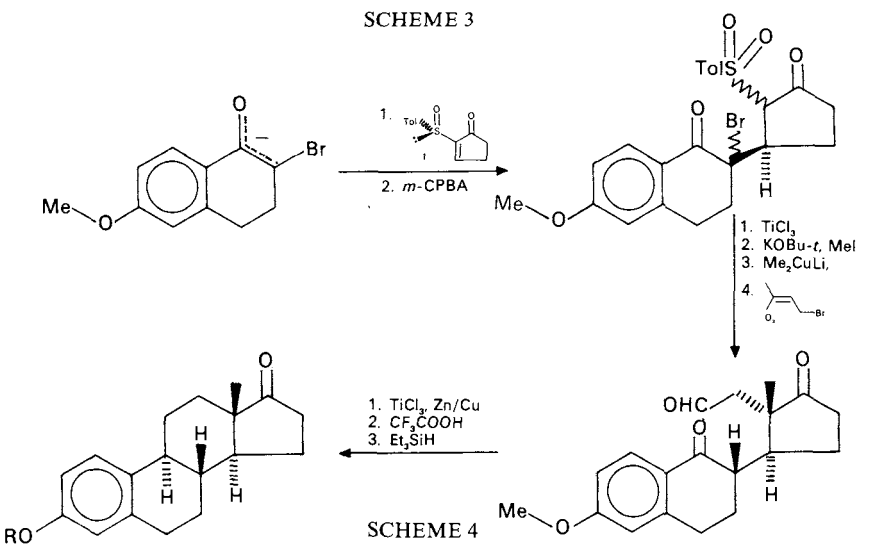


(42)

b. Enolates. Michael addition of α, α-*di*substituted lithium enolates proceed apparently via the chelated form of the β-keto sulfoxides with almost complete π-facial diastereoselectivity[87]; such asymmetric Michael additions are the key steps in preparation of natural (−)-methyl jasmonate (Scheme 3)[88] and of natural (−)-estrone (Scheme 4)[89] in extremely high enantiomeric purities.

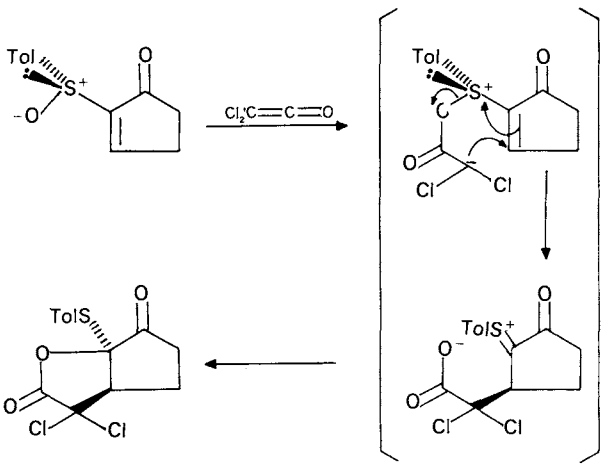


SCHEME 3

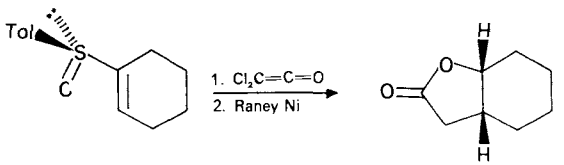


SCHEME 4

An intramolecular version of enolate Michael addition to enantiomerically pure vinylic sulfoxides is represented by reaction of a cyclopentenone sulfoxide with dichloroketene (Scheme 5)[90]; this type of additive Pummerer rearrangement has been developed by Marino and coworkers[91] into a highly effective way of constructing variously substituted lactones in very high enantiomeric purity (equation 43).



SCHEME 5

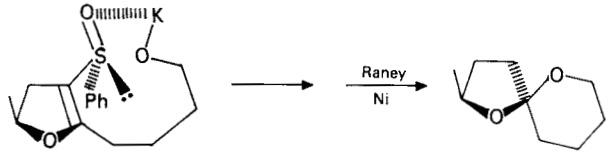


(43)

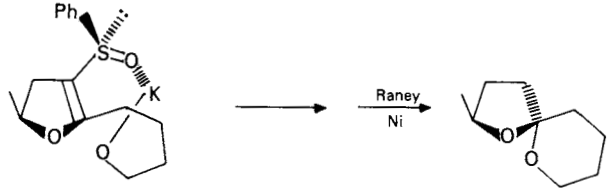
3. *Heteroatom nucleophiles*

The first pioneering report in 1971 of asymmetric heteroatom conjugate addition to an enantiomerically pure 1-alkenyl sulfoxide[92] has been followed by only a few studies. Potassium alkoxides **42** and **43**, which differ only in their absolute configuration at the sulfoxide sulfur atom, undergo intramolecular addition of the alkoxy oxygen atom to the electrophilic unsaturated carbon β to sulfur; it is proposed that chelation of the potassium counterion by both the sulfoxide and the alkoxide oxygen atoms directs the spirocyclization so that alkoxysulfoxides **42** and **43** produce ultimately and exclusively epimeric products as shown in equations 44 and 45[93]. Whereas the stereochemistry of this intramolecular cyclization seems to be governed by the stereogenic sulfoxide sulfur atom, a related case (equations 46 and 47) appears to be governed not by the sulfoxide sulfur atom but rather by a stereogenic allylic hydroxylated carbon atom; each diastereomer **44** and **45**, having the same stereochemistry at the sulfoxide center but differing only at the carbinol center, gives a *different* cyclized product (see stereochemistry at C-2) presumably via an S_N2' mechanism[53].

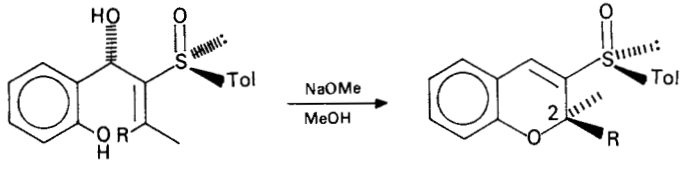
For a related study of intramolecular nucleophilic addition by an alkoxy group without generation of any new stereogenic center, see Reference 94.



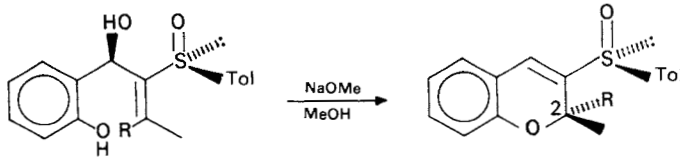
(42) (44)



(43) (45)



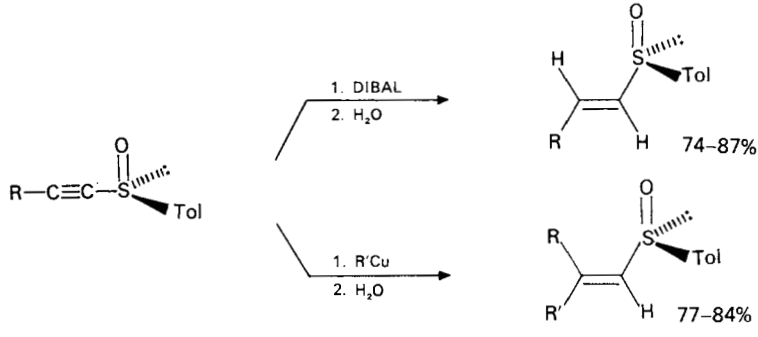
(44) (46)



(45) (47)

C. α,β-Acetylenic Sulfoxides

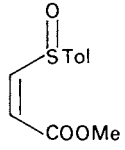
1-Alkynyl Grignard reagents react with menthyl sulfinate esters in *toluene* to produce enantiomerically pure α,β-acetylenic sulfoxides in over 80% yields[25]. Conjugate hydride addition (DIBAL) and conjugate hydrocarbon group addition (organocopper reagents) lead in good yields to various enantiomerically pure β-mono- and β,β-di-substituted vinylic sulfoxides (equation 48)[25].



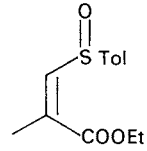
(48)

V. 2 + 4-CYCLOADDITIONS

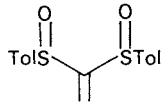
The enantiomerically pure, doubly activated α,β-olefinic sulfoxides **46–50**[95–98] undergo highly diastereoselective Diels–Alder cycloadditions with cyclopentadiene, and pyridyl vinylic sulfoxide **51**[99] reacts diastereoselectively with furan. It is noteworthy that olefins singly-activated by only a sulfinyl group are not effective partners in Diels–Alder cycloadditions, as we have found after many attempts and as has been reported recently[98].



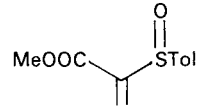
(46)[95]



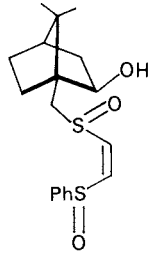
(47)[96]



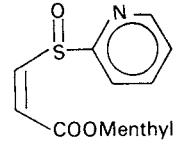
(48)[97]



(49)[98]

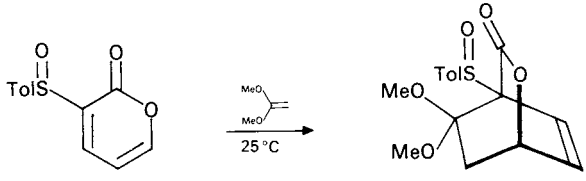


(50)[47]



(51)[99]

Racemic pyrone sulfoxide **52** undergoes a diastereoselective inverse-electron-demand 2 + 4-cycloaddition with 1,1-dimethoxyethylene to afford adduct **53** in > 95% yield (equation 49)[100]; this is the first example of an asymmetric Diels–Alder cycloaddition using a sulfinyldiene as an electron-deficient enophile[101].

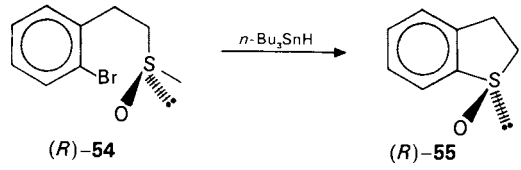


(52) **(53)** (49)

2 + 3-Cycloaddition of nitrones and of nitrile oxides to α,β-ethylenic sulfoxides have been recorded[102].

VI. MISCELLANEOUS

Formation of cyclic sulfoxide (*R*)-**55** by treatment of bromoarene (*R*)-**54** with tributylstannane apparently proves that intramolecular homolytic substitution at the sulfur atom of the sulfoxide group proceeds with strict inversion of configuration (equation 50)[103].



(*R*)-**54** (*R*)-**55** (50)

The absolute stereochemistry at the sulfoxide sulfur atom in some β-phenylsulfinyl radicals (prepared *in situ* by treating 2-bromo-3-phenylsulfinylbutanes with tributylstannane) controls the stereochemistry (i.e., *cis* vs. *trans*) of the olefinic products which are formed[104]. Implicit in this result is that loss of the sulfinyl group occurs more rapidly than rotation about C-2–C-3 of the intermediate radical[105].

Anionic (*n*-BuLi, *n*-BuMgBr) polymerization of enantiomerically pure tolyl vinyl sulfoxide occurs with asymmetric induction[106].

Phenylmagnesium bromide reacts with pyridyl and quinolyl sulfoxides to form pyridyl and quinolyl Grignard reagents and phenyl sulfoxides[107].

Recently, enantiomerically pure vinylic *sulfoximines* have been shown to undergo effective and highly stereocontrolled conjugate addition of hydrocarbon groups using organocopper reagents[108].

VII. REFERENCES

1. B. M. Trost, T. N. Salzmann and K. Hiroi, *J. Amer. Chem. Soc.*, **98**, 4887 (1976) and references therein.
2. For previous examples see O. DeLucchi, C. Marchioro, G. Valle and G. Modena, *J. Chem. Soc., Chem. Commun.*, 878 (1985); T. Koizumi, I. Hakamada and E. Yoshii, *Tetrahedron Letters*, **25**, 87 (1984); C. Maignan and R. Raphael, *Tetrahedron*, **39**, 3425 (1983); T. Koizumi, E. Hirai and E. Yoshii, *J. Org. Chem.*, **47**, 4004 (1982); L. A. Paquette R. E. Moerck, B. Harichian and P. D. Magnus, *J. Amer. Chem. Soc.*, **100**, 1597 (1978).
3. P. J. Brown, D. N. Jones, M. A. Khan, N. A. Meanwell and P. J. Richards, *J. Chem. Soc., Perkin Trans. 1*, 2049 (1984) and references therein.
4. (a) D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974).
(b) R. W. Hoffmann, in *Organic Sulfur Chemistry* (Eds. R. K. Friedlina and A. E. Skorova), Pergamon, England, 1981, p. 69.
(c) See also H. Kosugi, M. Kitaoka, A. Takahashi and H. Uda, *J. Chem. Soc., Chem. Commun.*, 1268 (1986).
5. For asymmetric Pummerer rearrangements (sulfoxide → α-heterosubstituted sulfide), see S. Glue, I. T. Kay and M. R. Kipps, *J. Chem. Soc., Chem. Commun.*, 1158 (1970); T. Numata, O. Itoh and S. Oae, *Tetrahedron Letters*, 1869 (1979); O. Itoh, T. Numata, T. Yoshimura and S. Oae, *Bull. Chem. Soc. Japan*, **56**, 266 (1983) and references therein; J. P. Marino and A. D. Perez, *J. Amer. Chem. Soc.*, **106**, 7643 (1984); and G. H. Posner and E. Asirvatham, *J. Chem. Soc., Chem. Commun.*, 542 (1985).
6. C. R. Johnson and J. C. Sharp, *Q. Rev. Sulfur Chem.*, **4**, 1 (1969).
7. K. Mislow, *Rec. Chem. Prog.*, **28**, 217 (1967).
8. S. Oae (Ed.), *Organic Chemistry of Sulfur*, Plenum Press, New York, 1977.
9. A. Nudelman, *The Chemistry of Optically Active Sulfur Compounds*, Gordon and Breach, New York, 1984.
10. E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, 1978.
11. M. Cinquini, F. Cozzi and F. Montanari, in *Organic Sulfur Chemistry, Theoretical and*

Experimental Advances (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Elsevier, 1985; cf. M. Cinquini, *Phosphorus Sulfur*, **24**, 39 (1985).
12. G. Solladié, *Synthesis*, 185 (1981).
13. M. Mikolajczyk and J. Drabowicz, *Top. Stereochem.*, **13**, 333 (1982).
14. M. R. Barbashyn and C. R. Johnson, in *Asymmetric Synthesis* (Eds. J. D. Morrison and J. W. Scott), Academic Press, New York, 1984, p. 230.
15. H. Phillips, *J. Chem. Soc.*, **127**, 2552 (1925).
16. M. Hulce, J. P. Mallamo, L. L. Frye, T. P. Kogan and G. H. Posner, *Org. Synth.*, **64**, 196 (1985).
17. K. K. Andersen, *Tetrahedron Letters*, 93 (1962).
18. M. Axelrod, P. Bickart, J. Jacobus, M. M. Green and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4835 (1968).
19. J. Drabowicz, B. Bujnicki and M. Mikolajczyk, *J. Org. Chem.*, **47**, 3325 (1982).
20. D. N. Harpp, S. M. Vines, J. P. Montillier and T. H. Chan, *J. Org. Chem.*, **41**, 3987 (1976).
21. K. K. Andersen, B. Bujnicki, J. Drabowicz, M. Mikolajczyk and J. B. O'Brien, *J. Org. Chem.*, **49**, 4070 (1984).
22. K. B. Sharpless and J. Klunder, (M.I.T.) personal communication; J. M. Klunder and K. B. Sharpless, *J. Org. Chem.*, **52**, 2598 (1987).
23. J.-H. Youn and R. Hermann, *Tetrahedron Letters*, **27**, 1493 (1986).
24. G. H. Posner, T. P. Kogan, S. R. Haines and L. L. Frye, *Tetrahedron Letters*, **25**, 2627 (1984).
25. H. Kosugi, M. Kitoaka, K. Tagami and H. Uda, *Chem. Letters*, 805 (1985).
26. (a) C. Mioskowski and G. Solladié, *Tetrahedron*, **36**, 227 (1980).
    (b) G. Solladié, F. Matlouki-Moghadam, C. Luttmann and C. Mioskowski, *Helv. Chim. Acta*, **65**, 1602 (1982).
27. (a) L. Banfi, L. Colombo, C. Gennari, R. Annunziata and F. Cozzi, *Synthesis*, 829 (1982); cf. F. Schneider and R. Simon, *Synthesis*, 582 (1986).
    (b) P. Bravo and G. Resnati, *Tetrahedron Letters*, **26**, 5601 (1985).
    (c) P. Bravo, G. Resnati and F. Viani, *Tetrahedron Letters*, **26**, 2913 (1985).
    (d) A. Bernardi, L. Colombo, C. Gennari and L. Prati, *Tetrahedron*, **40**, 3769 (1984).
28. R. Annunziata, M. Cinquini, S. Colonna and F. Cozzi, *J. Chem. Soc., Perkin Trans. 1*, 614 (1981).
29. (a) L. Colombo, C. Gennari and E. Narisano, *Tetrahedron Letters*, 3861 (1978).
    (b) See also A. R. Chamberlin and H. Nguyen, *J. Org. Chem.*, **51**, 940 (1986).
30. N. Kunieda, J. Nokami and M. Kinoshita, *Bull. Chem. Soc. Japan*, **49**, 256 (1976).
31. R. Annunziata, M. Cinquini and F. Cozzi, *Synthesis*, 535 (1979).
32. (a) M. Mikolajczyk, W. Midura, S. Grzejszczak, A. Zatorski and A. Chefczynska, *J. Org. Chem.*, **43**, 473 (1978).
    (b) R. W. Hoffmann and N. Maak, *Tetrahedron Letters*, 2237 (1976).
    (c) T. Koizumi, M. Iwata, N. Tanaka and E. Yoshii, *Chem. Pharm. Bull.*, **31**, 4198 (1986).
33. (a) M. Cinquini, S. Colonna, R. Fornasier and F. Montanari, *J. Chem. Soc. Perkin Trans. 1*, 1886 (1972).
    (b) M. Cinquinni, S. Colonna, D. Landini and A. M. Maia, *J. Chem. Soc. Perkin Trans. 1*, 996 (1976).
34. K. Hiroi and N. Matsuyama, *Chem. Letters*, 65 (1986) and references therein.
35. D. Evans and L. Colombo, personal communication (Harvard University).
36. J. Drabowicz, S. Legedz and M. Mikolajczyk, *J. Chem. Soc., Chem. Commun.*, 1670 (1985); for preparation of alkanesulfinic acids from 2-(alkylsulfonyl)benzothiazoles, see Y. Ueno, A. Kojima and M. Okawara, *Chem. Letters*, 2125 (1984).
37. M. G. Finn and K. B. Sharpless, in *Asymmetric Synthesis* (Eds. J. D. Morrison and J. W. Scott), Academic Press, New York, 1985, p. 247.
38. (a) P. Pitchen, E. Dunach, M. N. Deshmukh and H. Kagan, *J. Amer. Chem. Soc.*, **106**, 8188 (1984).
    (b) E. Dunach and H. Kagan, *Nouv. J. Chim.*, 1 (1985).
39. F. Di Furia, G. Modena and R. Seraglia, *Synthesis*, 325 (1984).
40. F. A. Davis, J. P. McCauley, Jr. and M. E. Harakal, *J. Org. Chem.*, **49**, 1465 (1984) and references therein.
41. T. Iwamoto, and H. Koto, *Chem. Letters*, 967 (1986).
42. (a) T. Takata and W. Ando, *Bull. Chem. Soc. Japan*, **59**, 1275 (1986).
    (b) T. Takata and W. Ando, *Tetrahedron Letters*, **27**, 1591 (1986); cf. W. Ando and L. Huang, *Tetrahedron Letters*, **27**, 3391 (1986).

43. A. Yamagishi, *J. Chem. Soc., Chem. Commun.*, 290 (1986).
44. (a) T. Komori and T. Nonaka, *J. Amer. Chem. Soc.*, **106**, 2656 (1984) and reference therein.
(b) A. W. Czarnik, *J. Org. Chem.*, **49**, 924 (1984).
45. S. Colonna, S. Banfi, R. Annunziata and L. Casella, *J. Org. Chem.*, **51**, 891 (1986) and references therein.
46. (a) H. Ohta, Y. Okamoto and G. Tsuchihashi, *Agric. Biol. Chem.*, **49**, 671 (1985).
(b) H. Ohta, Y. Okamoto and G. Tsuchihashi, *Chem. Letters*, 205 (1984).
47. O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle and G. Modena, *J. Org. Chem.*, **51**, 1457 (1986) and references therein; see F. Vögtle, J. Struck, H. Puff, P. Woller and H. Reuter, *J. Chem. Soc., Chem. Commun.*, 1298 (1986) for diastereoselective oxidation of cyclophane sulfide.
48. M. R. Binns, R. J. Goodridge, R. K. Haynes and D. D. Ridley, *Tetrahedron Letters*, **26**, 6381 (1985).
49. H. Ohta, Y. Kato and G. Tsuchihashi, *Chem. Letters*, 271 (1986); for other examples of resolution procedures, see N. Furukawa, T. Kawai, S. Oae and F. Iwasaki, *Synthesis*, 746 (1984) and F. Toda, K. Tanska and S. Nagamatsu, *Tetrahedron Letters*, **25**, 4929 (1984).
50. S. Lavielle, S. Bory, B. Moreau, M. J. Luche and A. Marquet, *J. Amer. Chem. Soc.*, **100**, 1558 (1978).
51. E. J. Corey, L. O. Weigel, A. R. Chamberlin, H. Cho and H. C. Hua, *J. Amer. Chem. Soc.*, **102**, 6613 (1980).
52. For leading references see S. Wolfe, L. A. LaJohn and D. F. Weaver, *Tetrahedron Letters*, **25**, 2863 (1984); for study of α-lithiosulfinyl carbanion initiated oligomerization, see M. Buese and T. E. Hogan-Esch, *J. Amer. Chem. Soc.*, **107**, 4509 (1985); for a study of α-lithiosulfinyl carbanion alkylation in a cyclic system, see Y. Tamura, J. Uenishi and H. Ishibashi, *Chem. Pharm. Bull.*, **32**, 891 and 898 (1984).
53. G. Solladié, *Chimia*, **38**, 233 (1984).
54. G. Solladié in *Asymmetric Synthesis* (Ed. J. D. Morrison), Vol. 2, Academic Press, New York, 1983, p. 184; for a recent application, see C. Papageorgiou and C. Benezra, *Tetrahedron Letters*, **25**, 1303 (1984).
55. For introduction to and discussion of this term, see K. Mislow and J. Siegel, *J. Amer. Chem. Soc.*, **106**, 3319 (1984).
56. (a) D. R. Williams, J. G. Phillips, F. H. White, and J. C. Huffman, *Tetrahedron*, **42**, 3003 (1986) and references therein.
(b) D. R. Williams and J. G. Phillips, *Tetrahedron*, **42**, 3013 (1986).
57. G. Stork, I. Patterson and K. C. Lee, *J. Amer. Chem. Soc.*, **104**, 4686 (1982); see also S. Masamune, P. Ma, H. Okamoto, J. W. Ellingboe and Y. Ito, *J. Org. Chem.*, **49**, 2834 (1984).
58. L. Colombo, C. Gennari, C. Scolastico, G. Guanti and E. Narisano, *J. Chem. Soc. Perkin Trans. 1*, 1278 (1981).
59. (a) H. Okamura, Y. Mitsuhira, M. Miura and H. Takei, *Chem. Letters*, 517 (1978).
(b) G. H. Posner, P. W. Tang and J. P. Mallamo, *Tetrahedron Letters*, 3995 (1978).
(c) R. R. Schmidt, H. Speer and B. Schmid, *Tetrahedron Letters*, 4277 (1979).
(d) G. H. Posner, J. P. Mallamo, K. Miura and M. Hulce, *Pure Appl. Chem.*, **53**, 2307 (1981).
(e) G. H. Posner, in *Asymmetric Synthesis* (Ed. J. D. Morrison), Academic Press, New York, 1983, p. 225.
(f) R. R. Schmidt and J. Kast, *Tetrahedron Letters*, **27**, 4007 (1986).
(g) R. A. Holton and H.-B. Kim, *Tetrahedron Letters*, **27**, 2191 (1986).
60. G. H. Posner and K. Miura, unpublished results.
61. G. Solladié and G. Moine, *J. Amer. Chem. Soc.*, **106**, 6097 (1984).
62. For a review of α vs. γ selectivity in related systems, see J. F. Bielmann and J. B. Ducep, *Org. React.*, **27**, 1 (1982).
63. D. J. Antonjuk, D. D. Ridley and M. A. Smal, *Aust. J. Chem.*, **33**, 2635 (1980).
64. R. Annunziata, M. Cinquini, F. Cozzi and L. Raimondi, *J. Chem. Soc., Chem. Commun.*, 366 (1986).
65. D. H. Hua, G. Sinai-Zingde and S. Venkataraman, *J. Amer. Chem. Soc.*, **107**, 4088 (1985); D. H. Hua, S. Venkataraman, M. J. Coulter and G. Sinai-Zingde, *J. Org. Chem.*, **52**, 719 (1987).
66. M. R. Binns, R. K. Haynes, A. A. Katsifis, P. A. Schober and S. C. Volwiller, *Tetrahedron Letters*, **26**, 1565 (1985).
67. M. R. Binns, O. L. Chai, R. K. Haynes, A. A. Katsifis, P. A. Schober and S. C. Volwiller, *Tetrahedron Letters*, **26**, 1569 (1985).
68. D. H. Hua, *J. Amer. Chem. Soc.*, **108**, 3835 (1986).

69. (a) G. Solladié, G. Damailly and C. Greck, *J. Org. Chem.*, **50**, 1552 (1985);
(b) G. Solladié, L. Fréchou, G. Demailly and C. Greck, *J. Org. Chem.*, **51**, 1912 (1986).
70. H. Kosugi, H. Konta and H. Uda, *J. Chem. Soc., Chem. Commun.*, 211 (1985) and references therein.
71. (a) G. H. Posner, J. P. Mallamo, K. Miura and M. Hulce, *Pure Appl. Chem.*, **53**, 2307 (1981).
(b) G. H. Posner and C. S. Switzer, unpublished results.
72. For three exceptions to this statement, see:
(a) H. Sugihara, R. Tamikaga, K. Tanaka and A. Kaji, *Bull. Chem. Soc. Japan*, **52**, 655 (1978).
(b) A. Pelter and L. Hughes, *J. Chem. Soc., Chem. Commun.*, 913 (1977).
(c) N. Ono, A. Kamimura, H. Miyake, I. Hamamoto and A. Kaji, *J. Org. Chem.*, **50**, 3692 (1985).
73. For a review, see G. H. Posner, *Acc. Chem. Res.*, **20**, 72 (1987).
74. G. H. Posner, *Chem. Scripta*, **25**, 157 (1985).
75. W. J. Hehre, personal communication; cf. S. D. Kahn and W. J. Hehre, *J. Amer. Chem. Soc.*, **108**, 7399 (1986).
76. G. H. Posner and L. L. Frye, *Isr. J. Chem.*, **24**, 88 (1984).
77. G. H. Posner, L. L. Frye and M. Hulce, *Tetrahedron*, **40**, 1401 (1986).
78. G. H. Posner and M. Hulce, unpublished results.
79. G. H. Posner, M. Hulce, J. P. Mallamo, S. Drexler and J. Clardy, *J. Org. Chem.*, **46**, 5244 (1981).
80. G. H. Posner and T. G. Hamill, unpublished results.
81. G. H. Posner, T. P. Kogan and M. Hulce, *Tetrahedron Letters*, **25**, 383 (1984).
82. G. H. Posner, J. P. Mallamo, M. Hulce and L. L. Frye, *J. Amer. Chem. Soc.*, **104**, 4180 (1982).
83. G. H. Posner, T. P. Kogan, S. R. Haines and L. L. Frye, *Tetrahedron Letters*, **25**, 2627 (1984).
84. G. H. Posner and M. Weitzberg, *Synth. Commun.*, **17**, 611 (1987).
85. G. H. Posner and M. Hulce, *Tetrahedron Letters*, **25**, 379 (1984).
86. Biological evaluation of our synthetic A-Factor confirmed its activity; we thank Dr. Richard Monaghan and his group at Merck Sharp and Dohme Research Labs for performing these tests.
87. G. H. Posner, M. Weitzberg, T. G. Hamill, E. Asirvatham, H. Cun-Heng and J. Clardy, *Tetrahedron*, **42**, 2919 (1986).
88. G. H. Posner and E. Asirvatham, *J. Org. Chem.*, **50**, 2589 (1985).
89. G. H. Posner and C. S. Switzer, *J. Amer. Chem. Soc.*, **108**, 1239 (1986).
90. G. H. Posner, E. Asirvatham and S. Ali, *J. Chem. Soc., Chem. Commun.*, 542 (1984).
91. J. P. Marino and R. F. de la Pradella, *Tetrahedron Letters*, **26**, 5381 (1985).
92. D. J. Abbot, S. Colonna and C. J. M. Stirling, *Chem. Commun.*, 471 (1971).
93. C. Iwata, K. Hattori, S. Uchida and T. Imanishi, *Tetrahedron Letters*, **25**, 2995 (1984).
94. J. C. Carretero, J. L. Garcia Ruano and J. H. Rodriguez, *Tetrahedron Letters*, 3029 (1984).
95. C. Maignan, A. Guessous and F. Rouessac, *Tetrahedron Letters*, **25**, 1727 (1984); cf. K. Picker, S. M. Proust and D. R. Ridley, *Aust. J. Chem.*, **39**, 575 (1986).
96. Y. Arai, M. Yamamoto and T. Koizumi, *Chem. Letters*, 1225 (1986).
97. Y. Arai, S. Kuwayama, Y. Takeuchi and T. Koizumi, *Synth. Commun.*, **16**, 233 (1986).
98. Y. Arai, S. Kuwayama, Y. Takeuchi and T. Koizumi, *Tetrahedron Letters*, **26**, 6205 (1985); cf. C. Maignan, A. Guessous and F. Rouessac, *Tetrahedron Letters*, **27**, 2603 (1986).
99. H. Takayama, A. Iyobe and T. Koizumi, *J. Chem. Soc., Chem. Commun.*, 771 (1986).
100. G. H. Posner and W. Harrison, *J. Chem. Soc., Chem. Commun.*, 1786 (1985).
101. For a 2 + 4-cycloaddition using an electron-rich sulfinyldiene as an enophile, see L. E. Overman, C. B. Petty, T. Ban and G. T. Huang, *J. Amer. Chem. Soc.*, **105**, 6335 (1983).
102. (a) T. Koizumi, H. Hirai and E. Yoshii, *J. Org. Chem.*, **47**, 4005 (1982).
(b) P. Caramella, E. Albini, T. Bandiera, A. C. Coda, P. Grumanger and F. M. Albini, *Tetrahedron*, **39**, 689 (1983).
103. A. L. J. Beckwith and D. R. Boate, *J. Chem. Soc., Chem. Commun.*, 189 (1985).
104. T. E. Boothe, J. L. Greene, Jr., P. B. Shevlin, M. R. Wilcott, III., R. Inners and A. Cornelius, *J. Amer. Chem. Soc.*, **100**, 3874 (1978).
105. Cf. G. A. Russell and P. Ngoviwatchai, *Tetrahedron Letters*, **26**, 4975 (1985).
106. F. Toda and K. Mori, *J. Chem. Soc., Chem. Commun.*, 1059 (1986); cf. J. E. Mulvaney and R. A. Ottaviani, *J. Polym. Sci., Part A-1*, **8**, 2293 (1970).
107. N. Furakawa, T. Shibutani, K. Matsumura, H. Fujihara and S. Oae, *Tetrahedron Letters*, **27**, 3899 (1986).
108. S. G. Pyne, *Tetrahedron Letters*, **27**, 1691 (1986) and references therein.

CHAPTER **17**

Methionine sulfoxide: chemistry and biochemistry

NATHAN BROT AND HERBERT WEISSBACH

Roche Institute of Molecular Biology, Roche Research Center, Nutley, NJ 07110, USA

ABBREVIATIONS

ACTH, adrenocorticotrophic hormone; Met, methionine; Met(O), methionine sulfoxide; DTT, dithiothreitol; L7, L12, *Escherichia coli* ribosomal proteins; Met(O)-L12, L12 containing Met(O) residues; α-1-PI, α-1-proteinase inhibitor; Met(O)-α-1-PI, α-1-PI

Editorial Note

Unfortunately, the chapter on biochemistry, pharmacology and toxicology of sulfones and sulfoxides planned for this volume did not materialize. In view of the importance and interest of methionine sulfoxide, we decided to include this chapter although, unlike the other chapters, it does not deal with the title groups *in toto* but only with a single representative of them.

—*The Editors*

containing Met(O) residues; PMN, polymorphonuclear leukocytes; HL-60, promyelocytic leukemia cell line; 70S, sedimentation coefficient of *Escherichia coli* ribosome; poly(U), polyuridylic acid; Met(O) peptide reductase, enzyme that reduces Met(O) containing peptides.

I. INTRODUCTION

It is now well recognized that the biological reduction of molecular oxygen results in the synthesis of free radical intermediates and other oxidizing agents. The ability of these reagents to react in a deleterious fashion with many different biological molecules makes them a constant threat to the viability of the organism. This threat, however, is counterbalanced by a large array of enzymes that function to neutralize the oxidizing agents. Although this defense mechanism is very efficient, one can envision situations in which it is overwhelmed, resulting in the consequent oxidation of macromolecules such as nucleic acids and proteins. In the case of proteins, this would result in a post-translational modification of the protein that in many instances can affect biological activity. If an organism is to survive this oxidative insult, it requires the presence of a mechanism to reverse the modification.

In spite of the fact that there are a large number of covalent post-translational modifications of proteins[1], only a few are thought to be reversible. These enzymatically catalysed modifications reactions include acetylation[2], adenylylation[3], methylation[4], phosphorylation[5] and uridylylation[6]. There are, however, modifications of proteins that occur non-enzymatically and although reactions such as deamidation of asparaginyl and glutaminyl residues[6] and racemization of amino acids[6] may proceed too slowly to have significant biological importance, the non-enzymatic oxidation of various amino acids occurs rapidly[7]. It is well established that the non-enzymatic oxidation of several amino acids including tryptophan, histidine, tyrosine, cysteine and methionine can occur in proteins. Amongst these reactions, attention has focused recently on the oxidation of methionine (Met) residues to methionine sulfoxide [Met(O)]. There are now numerous examples in which the non-enzymatic conversion of Met residues to Met(O) in proteins and peptides occurs during their isolation from biological material[8-11], solid phase peptide synthesis[12], and isoelectric focusing in sucrose gradients and polyacrylamide gels[13,14]. In addition, Met(O) is formed as a side-reaction during the oxidative cleavage of tryptophan residues in proteins[15,16] as well as during the reaction of cyanogen bromide with proteins[17]. Met(O) has also been used as a protecting group doing solid phase peptide synthesis[18]. Although the above reactions are artifacts of the procedures, it is now apparent that the oxidation of Met to Met(O) in proteins occurs both under physiological conditions *in vivo* and *in vitro* and that this conversion is associated with the loss of biological activity in a wide variety of proteins as well as peptides. This chapter will describe both the chemistry and biochemistry of Met(O), both free and in peptide linkage including the enzymatic systems involved in the reduction of Met(O) to Met. In addition, the clinical significance of the presence of Met(O) in specific proteins will be discussed.

II. CHEMICAL OXIDATION OF METHIONINE

Of the twenty amino acids that are normally found in proteins, only two contain sulfur, cysteine and methionine. Cysteine has long been recognized as being easily oxidized and this oxidation is associated with the loss of biological activity of many proteins. In recent years, it has been shown that methionine also shares these characteristics. Methionine was first isolated by Mueller[19] and was one of the last amino acids discovered. Its structure was later proven to be γ-methylthio-α-aminobutyric acid by Barger and Coyne[20] who named the amino acid methionine as a contraction for its chemical name.

Methionine contains a thioether group that is weakly nucleophilic. However, in contrast to other nucleophilic amino acids in proteins, it is not protonated at low pH and therefore can be selectively oxidized at pH 2–3. Thus, the primary reaction of H_2O_2 with proteins under acidic conditions is the oxidation of Met to Met(O)[21,22] while at pH 7.5 to 8.5 H_2O_2 can also oxidize indole, sulfhydryl, disulfide, imidazole, phenol and thioether groups. A number of other oxidizing agents have also been used to oxidize Met to Met(O) in proteins. Although the periodate ion is commonly used in the oxidation of carbohydrate moieties of glycoproteins, it has also been found to attack cysteine, cystine, methionine, tryptophan, tyrosine and histidine residues as well as *N*-terminal serine and threonine[23–25]. However, under very specific conditions of temperature and pH periodate has been shown to specifically oxidize Met to Met(O) in α-chymotrypsin[26] and apomyoglobin[27]. Other reagents that have been used to oxidize methionine include iodine, dimethyl sulfoxide, rose bengal (a dye sensitized photooxidation), chloramine-T and *N*-chlorosuccinimide. At both low and neutral pH *N*-chlorosuccinimide oxidizes only methionine, cysteine and tryptophan residues[28] while at pH 7.0–8.5 chloramine-T only oxidizes cysteine and Met residues to cystine and Met(O) respectively[28]. The use of these reagents have made it possible to distinguish between exposed, partially exposed and buried Met residues in proteins[28]. Although methionine sulfoximine is produced after treatment of Met with nitrogen tetroxide[29,30] or hydrazoic acid[30,31], the products of Met oxidation are usually Met(O) and methionine sulfone. Figure 1 shows the reactions by which Met is converted into Met(O) and methionine sulfone by some commonly used oxidizing agents. Under appropriate conditions oxidizing agents such as H_2O_2, $NaIO_4$, iodine and *N*-chlorosuccinimide oxidize Met only to the sulfoxide level, whereas a stronger reagent such as performic acid is required to oxidize Met to methionine sulfone. The conversion of Met to Met(O) leads to the formation of an asymmetric centre around the sulfur atom and consequently two diastereoisomers of Met(O) are formed. The ratio in which these diastereoisomers are formed depends upon the oxidant employed[32]. The two diastereoisomers can be resolved from each other by taking advantage of the differences in solubility of their picrate salts[33].

Although the oxidation to the sulfone stage is essentially an irreversible reaction, Met(O) can be chemically reduced back to methionine by a number of sulfhydryl and non-sulfhydryl reagents. The time required for the reduction, however, can be very long and often requires high temperatures (for a review see Houghten and Li[34]). For example, in order to reduce chemically formed Met(O) in ACTH, Dedman and coworkers[35] employed cysteine·HCl and mercaptoacetic acid. Complete reduction required either long reaction times (90 h, 37 °C) or high temperatures (18 h, 75 °C). Dithiothreitol has also been used for

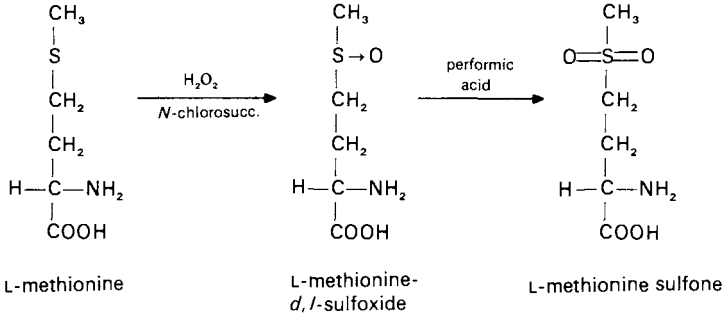


FIGURE 1. The chemical oxidation of the methionine to methionine sulfoxide and methionine sulfone.

the reduction of Met(O) but long reaction times and elevated temperatures were again required[36]. On the other hand it has been shown that Met(O) residues in *Escherichia coli* ribosomal protein L12 can be reduced back to Met at the more physiological temperature of 37 °C when the oxidized protein was incubated with 0.8 M 2-mercaptoethanol[37]. This reaction, however, also required a long period of incubation (48 h). In addition to the sulfhydryl reagents a number of other reagents such as tripotassium nonachloroditungstate, sodium dithionite and sodium thiosulfate have been used to reduce Met(O) to Met[34].

III. BIOLOGICAL OXIDATION OF METHIONINE

One of the principal functions of polymorphonuclear leukocytes (PMN) and mononuclear phagocytes is the destruction of invading infectious microorganisms. The mechanism by which this is achieved involves the stimulation of the phagocyte membrane either by phagocytosis, chemotactic factors released by bacteria or by compounds such as phorbol myristate acetate. All of these stimuli ultimately result in the partial reduction of oxygen leading to the synthesis of a number of oxidizing agents[38–40] including superoxide (O_2^-) and hydroxyl (OH·) radicals, H_2O_2 and the hypochlorite ion (OCl^-), all potentially bactericidal.

It was at first thought that only the H_2O_2 produced during the respiratory burst was the antimicrobial agent[39]; however, Babior and coworkers[40] later suggested that the superoxide anion was also bactericidal. Superoxide is the one-electron reduced product of oxygen and is unstable in aqueous media. Although it spontaneously decomposes to H_2O_2 and O_2 ($k = 4 \times 10^5\,M^{-1}s^{-1}$), this reaction is greatly increased by superoxide dismutase ($k = 2.4 \times 10^9\,M^{-1}s^{-1}$) an enzyme that is found in large amounts in neutrophils. Although H_2O_2 is bactericidal and can also convert Met to Met(O), there is evidence that the hypochlorite ion is the major bactericidal oxidant. This oxidizing agent is synthesized by the action of the enzyme myeloperoxidase on H_2O_2 but only in the presence of an oxidizable cofactor such as chloride ions[41]. It is interesting to note that this enzyme accounts for about 5% of the dry weight of neutrophils[42]. Thus, it has been shown that all three components (myeloperoxidase, H_2O_2 and Cl^-) are required for the inactivation [due to Met(O) formation] of α-1-proteinase inhibitor (α-1-PI) and the chemotactic peptide *N*-formylMet-Leu-Phe. A summary of various reactions leading to the formation of these oxidants is shown in Figure 2. Briefly, when the phagocytic membrane is stimulated as described above, a membrane bound oxidase[43–46] catalyzes the univalent reduction of

$$2O_2 + NADPH \xrightarrow[\text{Oxidase}]{\text{NADPH}} NADP^+ + 2O_2^- + H^+ \qquad (1)$$

$$2O_2^- + 2H^+ \xrightarrow[\text{Dismutase}]{\text{Superoxide}} H_2O_2 + O_2 \qquad (2)$$

$$H_2O_2 + Cl^- \xrightarrow{\text{Myeloperoxidase}} H_2O + OCl^- \qquad (3)$$

$$H_2O_2 + O_2^- \xrightarrow{Fe^{3+}} O_2 + OH^- + OH^{\cdot} \qquad (4)$$

FIGURE 2. Reactions leading to the synthesis of biological oxidants.

oxygen to superoxide. NADPH that is synthesized in the hexose monophosphate shunt is used as substrate in this reaction (reaction 1). Two moles of O_2^- then react in the presence of superoxide dismutase to form H_2O_2 and O_2 (reaction 2). The H_2O_2 formed is then converted to the highly toxic hypochlorite ion by myeloperoxidase (reaction 3). The cofactor requirement for the above reaction can be satisfied by chloride, iodide or bromide but not fluoride[32,47,48]. Although iodide is the most effective, physiological levels of this halide are quite low. On the other hand the Cl^- ion is very active at concentrations found in the PMN[49] and is probably the cofactor that is used in this reaction. Lastly, the formation of hydroxyl radicals, one of the most potent oxidizing agents, is thought to be produced by the Haber–Weiss reaction (reaction 4). This reaction involves the nonenzymatic conversion of H_2O_2 and O_2^- in the presence of Fe^{3+} to form the $OH\cdot$ radical. The presence of this radical in PMNs during phagocytosis has been shown by electron spin spectroscopy[50].

IV. ASSAY FOR MET(O) IN PROTEINS

The presence of Met(O) in proteins would go undetected in studies which use the usual method of amino acid analysis (6 M HCl, anaerobic). Under these conditions Met(O) is unstable[51] and is reduced, largely back to Met[52] with some methionine methyl sulfonium salt, homocysteine, and homocysteic acid being formed as well[53]. The conversion to Met can be made quantitative by the addition of a sulfhydryl reagent during the hydrolysis. There are, however, a number of methods that can be used to quantitate the amount of Met(O) residues in proteins. Met(O) residues are stable to base and the amount present in a protein can be determined in an amino acid analyzer after hydrolyzing the protein with 4 N NaOH. An indirect method involves assaying for methionine sulfone. This method employs first the exhaustive and selective alkylation of Met residues [Met(O) is resistant to alkylation] followed by performic acid oxidation of the Met(O) residues to methionine sulfone. Since the latter is stable to acid hydrolysis, it can be detected by amino acid analysis under standard conditions[54]. A third method involves treatment of the protein with cyanogen bromide. This reagent specifically cleaves proteins at Met residues [Met(O) residues again are resistant] resulting in the formation of methylthiocyanate and peptides containing homoserine lactone and Met(O). The peptides are then subjected to acid hydrolysis in the presence of a sulfhydryl reagent which reduces any Met(O) to Met. The amount of Met found after hydrolysis represents the level of Met(O) originally present in the protein while the amount of homoserine corresponds to the quantity of methionine in the protein.

Finally, a simple and sensitive assay for Met(O) using a modification of the CNBr assay has been described[55]. This assay is only valid for growing cells since it requires the prelabelling of cellular proteins with ^{35}[S]methionine. As noted above treatment of the proteins with cyanogen bromide results in the formation of homoserine lactone and methylthiocyanate, which is volatile. Thus, after the [^{35}S]methionine labelled cells are treated with cyanogen bromide, the incubation mixture is taken to dryness to evaporate the volatile methyl^{35}[S]thiocyanate. Because ^{35}[S]Met(O) residues are stable to cyanogen bromide, any non-volatile ^{35}[S] remaining after the cyanogen bromide treatment represents ^{35}[S]Met(O) residues. The validity of the assay was determined by assaying a protein preparation from HL-60 cells that had been uniformly labelled with ^{35}[S]methionine and subsequently oxidized with H_2O_2. Table 1 shows that the amount of ^{35}[S]Met(O) found by the above method is in excellent agreement with the total amount of Met(O) found by amino acid analysis after cyanogen bromide treatment and acid hydrolysis. It is important to note that the accuracy and reproducibility of the assays using the cyanogen bromide and alkylation methods require that the reaction of the Met residues with the respective reagents goes to completion.

TABLE 1. Chemical oxidation of methionine in HL-60 cell proteins previously uniformly labeled with [^{35}S]methionine[a]

Condition	CNBr assay, % [^{35}S]Met(O)	Amino acid analysis % Met(O)
Without H_2O_2	15	16
With H_2O_2	86	87

[a] HL-60 cellular proteins were labeled uniformly with [^{35}S]methionine and then oxidized with H_2O_2. The proteins were then assayed for the presence of Met(O) using either the CNBr assay or amino acid analysis. Reproduced with permission from Fliss and coworkers[55].

V. PRESENCE OF MET(O) IN PROTEINS

As noted above, the presence of Met(O) in proteins would go undetected after acid hydrolysis and subsequent amino acid analysis. Thus, since this method of hydrolysis is most commonly used, it is impossible to ascertain from the literature the abundance of Met(O) residues normally present in proteins. However, a number of studies have reported the presence of Met(O) residues in various proteins using one of the appropriate procedures described above. It has been found that Met(O) residues comprise 30% of the total Met in proteins isolated from bovine glomerular basement membranes and anterior lens[56]. Other investigators have reported that the levels of Met(O) in proteins of the trabecular meshwork of human eyes increased with the age of the donor[57]. The amount of Met(O) detected ranged from 15% (10 years old) to 55% (79 years old) of the total methionine content found in the tissue samples. Other studies have shown that in certain species of clams the proteins of the hinge ligament contain only Met(O) residues and no Met[58,59]. In addition, it has also been reported that as much as 18% of the Met residues in pea seed proteins is in the form of Met(O)[60]. Lastly, Met(O) residues have been found in

TABLE 2. Proteins and peptides whose biological activity is affected by oxidation of methionine residues[a]

Protein or peptide	Reference
E. coli ribosomal protein L12	37, 61
Lysozyme	62
Pepsin	63
Ribonuclease	64
α-Chymotrypsin	65, 66
Phosphoglucomutase	65
α-1-Proteinase inhibitor	67–69
Calmodulin	70
ACTH	66
Snake venom cardiotoxin	71
Parathyroid hormone	72
Calcitonin	73, 74
Lipoxygenase	75
Plasmimogen activator inhibitor	76
Chemotactic factors	
fMet-Leu-Phe	77
Complement C5A	77

[a] Taken in part from Brot and Weissbach[78].

proteins extracted from human cataractous lens and in α-I-PI that has been isolated from patients suffering from a variety of diseases. This clinical aspect of the presence of Met(O) in these proteins will be discussed below.

In recent years a number of *in vitro* studies have shown that the presence of Met(O) residues in a wide variety of proteins causes loss of biological activity. Table 2 lists some proteins which have been demonstrated to lose activity when specific Met residues are oxidized *in vitro*. Two of these proteins, *E. coli* ribosomal protein L12 and mammalian α-1-PI, have been studied extensively and will be discussed in detail.

VI. OXIDIZED *E. COLI* RIBOSOMAL PROTEIN L12

The 70S *E. coli* ribosome contains 52 proteins and one of these ribosomal proteins, L12 (and its acetylated congener L7), is present as 4 copies per ribosome and has been shown to be required for the initiation, elongation and termination reactions of protein synthesis[79]. During the course of studying the mechanism of action of ribosomal protein L12, the protein was treated with H_2O_2. As indicated above, oxidation of proteins with H_2O_2 affects several amino acids including methionine, tryptophan, tyrosine, cysteine and histidine. Since the latter four amino acids are absent in L12[80], H_2O_2 oxidation should result in the conversion of the three Met residues in L12 to Met(O). Table 3 shows that the methionine content of L12 decreases after oxidation with H_2O_2 and can be restored when the oxidized protein is incubated with mercaptoethanol. In addition, it was shown that this decrease in methionine content was paralleled by an increase in the amount of Met(O) residues in the protein[37]. These studies demonstrated that all of the Met residues of L12 could be oxidized to Met(O) which then could be quantitatively reduced back to Met.

It was of interest to study how the presence of Met(O) residues in L12 affected its biological activity. These studies were facilitated by the fact that L12 can readily be removed from the ribosome and the resulting ribosome is then no longer capable of carrying out protein synthesis. Since this L12-depleted ribosome can be subsequently reactivated by incubation with additional L12, it was possible to investigate the effect of the presence of Met(O) residues in L12 on its biological activity. Table 4 (column 1) shows that oxidized L12 is incapable of binding to L12-depleted ribosome but that this binding is restored after treatment of the protein with mercaptoethanol. Since oxidized L12

TABLE 3. Oxidation of L12 with H_2O_2 decreases its methionine content[a]

L12 treatment	Methionine (mol/mol L12)
None	2.5
$+H_2O_2$	0.2
$-H_2O_2$[b]	2.5
$+H_2O_2$, +2-mercaptoethanol	2.1
$-H_2O_2$, +2-mercaptoethanol	2.4

[a] Ribosomal protein L12 was oxidized with 0.3 M H_2O_2 at 30 °C for 1 h. After dialysis, the protein was incubated in the presence of 0.8 M 2-mercaptoethanol for 48 min at 37 °C and dialyzed. The amount of methionine residues was quantitated by exhaustive alkylation of the protein with [^{14}C]iodoacetic acid.

[b] These L12 samples were subjected to the oxidation conditions but H_2O_2 was not added.

Taken from Caldwell and coworkers[37].

TABLE 4. Peroxidation of L12 blocks various biological reactions[a]

L12 treatment	Ribosome binding (pmol/pmol ribosome)	Polyphenylalanine synthesis (pmol)	Acetylation (pmol)
None	2.3	2.4	14.5
$+H_2O_2$	0.3	0.2	3.0
$-H_2O_2$	2.2	2.6	14.7
$+H_2O_2$, +2-mercaptoethanol	2.0	2.1	11.2
$-H_2O_2$, +2-mercaptoethanol	2.3	2.8	15.8

[a]The protein was oxidized and reduced as described in Table 3. This table and the assays for binding of L12 to depleted ribosomes, poly(U)-directed polyphenylalanine synthesis, and enzymatic acetylation of L12 to form L7 are from Caldwell and coworkers[37].

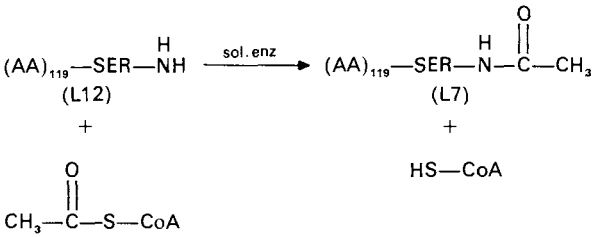


FIGURE 3. Enzymatic acetylation of L12 to L7.

[Met(O)–L12] does not bind to the ribosome and the presence of L12 on the ribosome is required for protein synthesis, Met(O)–L12 does not restore the ability of L12-depleted ribosome to support polyphenylalanine synthesis (Table 4, Column 2). Again, the oxidized protein after reduction is as active as native L12. Finally, Met(O)–L12 has a decreased ability to serve as a substrate for the enzymatic acetylation of L12 to yield L7 (Table 4, column 3). This acetylation reaction (Figure 3) is catalyzed by an enzyme that has been purified and shown to use acetyl-CoA as the acetyl donor and to have high specificity for L12. This specificity was used to develop an assay for an enzyme capable of reducing Met(O) residues in proteins. The assay involved the reduction of Met(O)–L12 to L12 followed by its enzymatic acetylation to form L7 (see below). It is of interest to note that although both L12 and L7 are found on the ribosome in varying proportions, no difference in the ability of ribosomes containing either only L12 or only L7 to function in protein synthesis has been found[81–84].

The mechanism for the decreased biological activity of Met(O)–L12 was clarified by studies in which the molecular weight of the oxidized protein was determined. It was shown that, although L12 contains 120 amino acids and has a molecular weight of 12,200, it exists in solution as a dimer[85–87]. It was found, by ultracentrifugal analysis, that the molecular weight of the oxidized protein was about 11,500 whereas both native L12 and Met(O)–L12 after reduction yielded molecular weights of about 22,000[37]. These results suggest that the dimer form of L12 is the biologically active species and that oxidation of one or more Met residues prevents the formation of L12 dimers.

VII. OXIDATION OF α-1-PI

α-1-PI is the major serum inhibitor of elastase activity and is a protein that is of both biochemical and clinical interest. Oxidative inactivation of this protein has been

implicated in the pathology of both rheumatoid arthritis and emphysema (see below). α-1-PI contains nine Met residues; however, four of these residues are found as Met(O) in α-1-PI purified from the bronchoaveolar lavage fluid of smokers and in the synovial fluid of patients with rheumatoid arthritis[88,89]. It was found that the oxidized α-1-PI had lost its ability to inhibit elastase[89,90]. *In vitro* studies have correlated well with that seen *in vivo*. Chemical oxidation of α-1-PI results in a loss of biological activity that can be related to the oxidation of two methionine residues[68]. It has also been shown that there is a loss of elastase inhibitory activity when this protein is exposed *in vitro* to cigarette smoke condensate[90–92].

VIII. ENZYMATIC REDUCTION OF Met(O) RESIDUES

A. Free Met(O)

It is well documented from growth studies that Met(O) can be used to satisfy the Met requirement of animals[93–96] and microorganisms[92–99] whereas methionine sulfone is inactive. These observations lead to the prediction that these organisms possess mechanisms for first transporting Met(O) into cells followed by the subsequent reduction of Met(O) to Met. The latter reaction is essential since Met(O) cannot be acylated to tRNA[100] and therefore lacks the ability of being directly incorporated into proteins. It has been shown in *Salmonella typhimurium* that Met(O) can be taken up by two transport systems. One of these is a high affinity Met transport system (metP) and the second is involved in transporting glutamine (gluP)[101]. This study showed that: (1) a methionine auxotroph carrying mutations affecting both of these transport systems was unable to use Met(O) as a source of Met; (2) a Met auxotroph with a mutation in the metP system could not grow on Met(O) in the presence of glutamine because glutamine inhibited the transport of Met(O) by the gluP system; and (3) the transport of Met(O) was inhibited by both Met and glutamine in wild type *Salmonella*.

In eukaryotes there is also evidence that Met(O) is actively transported. It has been reported that Met(O) is transported into purified rabbit intestinal and renal brush border membrane vesicles by a Met-dependent mechanism and accumulates inside the vesicles against a concentration gradient[102]. In both types of vesicles the rate of transport is increased with increasing concentrations of Na^+ in the incubation medium. The effect of the Na^+ is to increase the affinity of Met(O) for the carrier. Similar to that found in the bacterial system, the presence of Met and other amino acids in the incubation medium decreased the transport of Met(O). These results suggest that Met(O) is not transported by a unique carrier.

As mentioned above, Met(O) must be converted to Met before it can be incorporated into proteins. There are a wide variety of organisms that have been shown to be capable of enzymatically reducing Met(O) residues. The enzymatic reduction of free Met(O) to Met has been observed in yeast[103], *E. coli*[98,99,104,105], *Pseudomonas*[106], plants[107] and animal tissues[102,108,109]. The enzyme from *E. coli* has been purified about 1100-fold using a newly developed very sensitive assay[100]. The assay involves first the conversion of [^{35}S]Met(O) to [^{35}S]Met by the Met(O) reductase followed by the measurement of [^{35}S]Met-tRNA after enzymatic acylation of $tRNA^{Met}$. Since Met(O) is not a substrate for the acylation reaction[100], the amount of [^{35}S]Met-tRNA formed is proportional to the amount of [^{35}S]Met(O) converted to [^{35}S]Met. The assay is sensitive to Met levels of less than 1 pmol.

The purified enzyme has a molecular weight of about 21,000, and although the enzyme can use dithiothreitol as a reducing agent, the physiological reducing agent appears to be thioredoxin and NADPH. The yeast enzyme has been reported to have the same characteristics[103,110]. Figure 4 summarizes the overall reaction based on these studies.

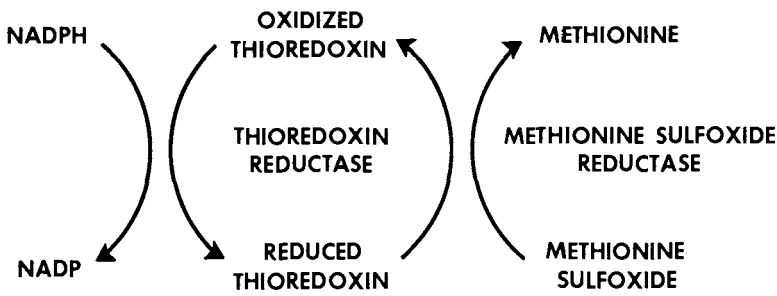


FIGURE 4. Proposed pathway for the physiological reduction of Met(O).

B. Met(O)–L12

It was initially thought that the enzyme that reduces free Met(O) might also have the ability to reduce peptide bound Met(O) residues. To study this possibility, an assay was developed to measure the enzymatic reduction of peptide-bound Met(O) residues[111]. The assay utilized the observation that the oxidation of Met residues in *E. coli* ribosomal protein L12 results in the loss of the ability of the protein to be enzymatically acetylated at the amino-terminal serine (Table 4). Figure 5 shows the scheme of the assay which is carried out in two steps. It became clear during the purification that a separate enzyme catalyzes the reduction of Met(O)–L12, and this enzyme was purified to homogeneity from *E. coli* extracts[112]. Because it reduces Met(O) in any peptide, it will be referred to as Met(O)–peptide reductase. The purified enzyme migrates with a molecular weight of about 23,000–24,000 when electrophoresed under denaturing conditions (Figure 6A). One major band was also observed when the electrophoresis was carried out under non-denaturing conditions (Figure 6B), and it was found that the protein extracted from the single band in the non-denaturing gel contained Met(O)–peptide reductase activity. It was also demonstrated that the purified enzyme could not use free Met(O) as substrate and since an earlier report showed that the purified *E. coli* enzyme that reduces free Met(O) residues was unable to reduce peptide bond Met(O)[101], it is clear that there are two

TABLE 5. Requirements for enzymatic reduction of Met(O)–L12[a]

System	Acetyl-L12 formed (pmol)
Complete	16.6
Enzyme	1.3
Met(O)–L12	0
Dithiothreitol	3.7
Dithiothreitol plus 2-mercaptoethanol	1.0
Dithiothreitol plus NADPH, thioredoxin, and thioredoxin reductase	52.7

[a] Ribosomal protein L12 was oxidized with *N*-chlorosuccinimide as described by Schechter and coworkers[28] and dialyzed. The complete system contained 33 mM Tris-HCl (pH 7.4), 13 mM $MgCl_2$, 275 pmol Met(O)–L12, 13 mM dithiothreitol (or 2-mercaptoethanol where indicated), and enzyme. See the legend to Figure 5 for further details of the assay.
Reproduced by permission of Academic Press from Brot and coworkers[111].

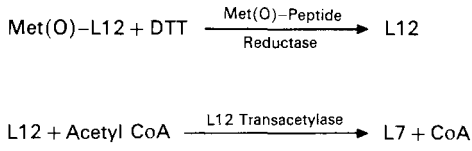


FIGURE 5. Assay for Met(O)–peptide reductase. The assay for Met(O)–peptide reductase is carried out in a two-step incubation. The first incubation mixture contains Met(O)–L12, DTT and the Met(O)–peptide reductase. At the end of this incubation, purified L12 transacetylase and [^{3}H]acetylCoA are added and the amount of radioactivity incorporated into L7 is determined by its ability to be retained on a nitrocellulose filter. The latter represents the amount of Met(O)–L12 reduced since the oxidized protein is not a substrate for the transacetylase.

separate enzyme systems for converting Met(O) residues to Met. One employs Met(O) as substrate while the other reduces Met(O) either in peptide linkage or as *N*-substituted Met(O) derivatives. Table 5 shows some of the requirements for the enzymatic reduction of Met(O)–L12. The reaction requires the presence of the enzyme [Met(O)–peptide reductase] and dithiothreitol. The latter cannot be replaced by 2-mercaptoethanol, although the dithiothreitol can be very efficiently replaced by NADPH, thioredoxin and thioredoxin reductase. This suggests that reduced thioredoxin is very likely the physiological reducing agent.

A wide spectrum of various organisms and animal tissues were assayed for the presence of Met(O) peptide reductase, and it was found to be a very ubiquitous protein. The enzyme was found to be present in *Euglena gracilis*[111], *Tetrahymena pyriformis*[111], plants[60,111], rat tissues[111], Hela cells[111], bovine and human lens[113] and human neutrophils[114]. The observation that Met(O)–peptide reductase is widely distributed in nature and that the *E. coli* enzyme can reduce Met(O) peptides from both prokaryotes and eukaryotes suggests that this enzyme may have an important physiological function. It is known that many different types of cells synthesize a wide variety of oxidizing agents that have the potential to oxidize Met residues in proteins. Although the toxicity of many of these oxidizing agents may be minimized by a number of various cellular enzymes such as superoxide dismutase, peroxidase and catalase, it is possible that under specific conditions these enzymes are not capable of completely destroying the accumulated oxidants. In addition, for agents such as the hypochlorite ion and hydroxyl radical, there are no enzymatic mechanisms to neutralize these potent oxidants. Therefore, there is a good possibility that the oxidation of Met residues in proteins could occur physiologically. Indeed, in some cells the synthesis of large amounts of oxidants is part of their normal function. As noted above, neutrophils and macrophages produce oxidizing agents that function to inactivate microorganisms[115]. Another example is doing the fertilization of sea urchin eggs[116]. During the process of fertilization, the ovum rapidly synthesizes large quantities of H_2O_2 which is used by the enzyme ovoperoxidase to oxidize and crosslink tyrosine residues between membrane proteins. This reaction results in the 'hardening' of the fertilization membrane around the ovum and thereby acts to prevent polyspermy. In addition, the synthesized H_2O_2 is also secreted from the cell and acts as a spermicide thereby killing supernumerary sperm. Although it is clear that the oxidants produced in the above systems have a positive biological role, at the same time these oxidants could cause damage to the proteins in these

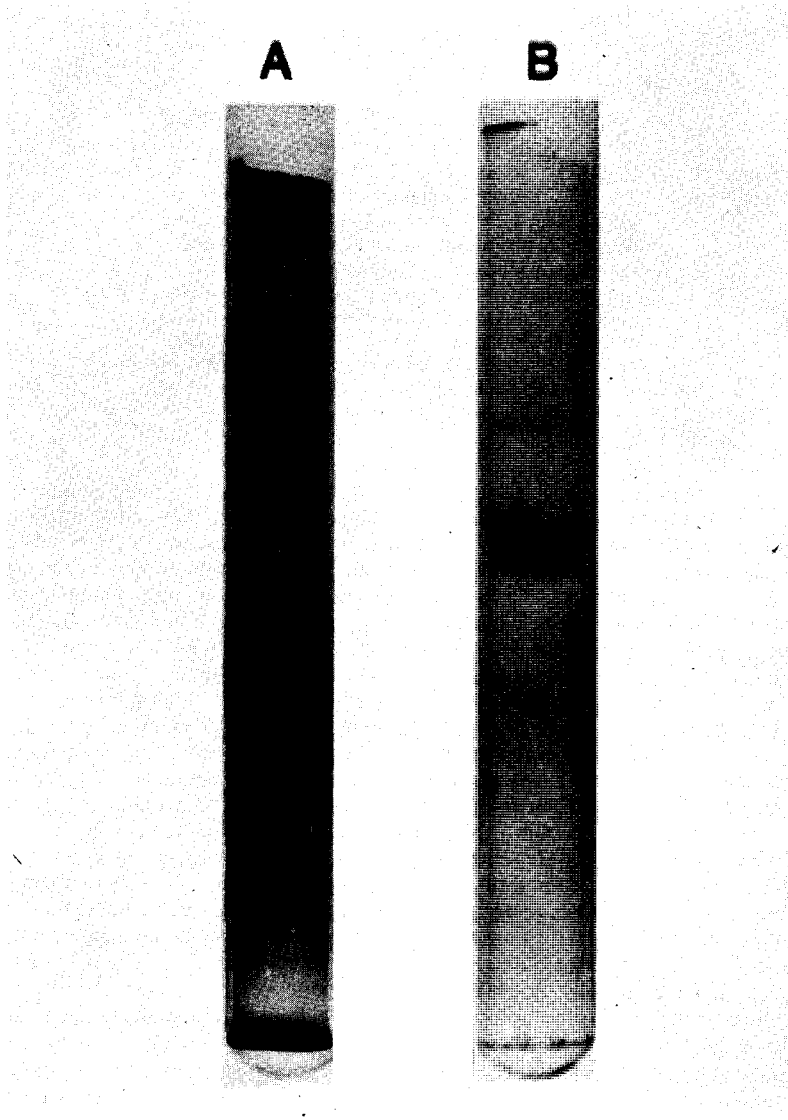


FIGURE 6. Gel electrophoresis of purified *E. coli* Met(O)–peptide reductase. (A) 15% polyacrylamide containing 0.1% $NaDodSO_4$. (B) 13% polyacrylamide (pH 8.8) non-denaturing. Reproduced by permission of Academic Press from Brot and coworkers[112].

cells and in the surrounding tissues. It is of interest to speculate that Met(O)–peptide reductase may function as a repair enzyme and have an important role to prevent the accumulation of Met(O) residues in proteins, especially in those cells that produce large amounts of oxidants. In that regard, neutrophils appear to have the highest level of Met(O) peptide reductase of all the sources so far studied (unpublished observations).

TABLE 6. Requirements for the reduction of Met(O)–α-1-PI[a]

System	Elastase inhibition (%)
Complete	28
Without Met(O)–peptide reductase	3
Without dithiothreitol	0
Without oxidized α-1-PI	0

[a] The incubation mixture is described in the legend to Table 5 and contained partially purified *E. coli* Met(O)–peptide reductase and 10.2 pmol oxidized α-1-PI. The inhibition of elastase, due to reactivation of oxidized α-1-PI, was assayed after a 60-min incubation.
Reproduced with permission from Abrams and coworkers[119].

C. Met(O)–α-1-PI

There are other substrates for the *E. coli* Met(O)–peptide reductase, one of which is Met(O)–α-1-PI. The native protein is the major serum elastase inhibitor that functions by forming a binary complex with elastase which inhibits its activity. Met(O)–α-1-PI, on the other hand, which can be formed by treatment of the protein with *N*-chlorosuccinimide, cannot form a complex with elastase and therefore is not able to inhibit elastase activity[117,118]. Table 6 shows, however, that when Met(O)–α-1-PI is incubated in the presence of Met(O)–peptide reductase and dithiothreitol the protein regains its ability to form a complex with elastase and inhibit elastase activity[119]. Similar to results found with Met(O)–L12 reduced thioredoxin could replace the dithiothreitol as reductant in the enzymatic reaction.

D. Calcitonin

Human calcitonin is a polypeptide hormone containing 32 amino acids and is normally secreted by the thyroid gland. This hormone causes hypocalcemia by inhibition of the release of calcium from bone[120]. When extracts from human thyroid glands, pituitaries, hypothalami and plasma were subjected to high performance liquid chromatography, a biologically inert calcitonin peak containing a Met(O) residue (amino acid 8 of the peptide) was observed[73,74]. When the oxidized form was incubated in the presence of Met(O)–peptide reductase and dithiothreitol, it was converted to a form that coeluted with authentic calcitonin and in addition regained biological activity[74].

E. Plasminogen Activator Inhibitor

Plasminogen activator inhibitors have been shown to be present in a large variety of different cells and tissues. These inhibitors are thought to play an important role in regulating tissue fibrinolysis. One of these inhibitors has been purified from cultured bovine aortic epithelial cells[121]. This inhibitor has been shown to be a serine protease inhibitor and inhibits the function of two proteolytic enzymes urokinase and tissue plasminogen activator[121], both of which cleave and activate plasminogen. The mechanism by which this inhibitor functions is very similar to that described above with α-1-PI. Thus, the inhibitor forms a binary complex with the proteolytic enzyme and thereby inhibits its activity. Again in a situation comparable to that with α-1-PI, it was found that when the purified bovine aortic epithelial inhibitor was exposed to *N*-chlorosuccinimide,

chloramine-T or H_2O_2, the inhibitor lost its ability to bind to tissue plasminogen activator[76]. However, when the oxidized protein was incubated with Met(O)–peptide reductase and dithiothreitol greater than 90% of the activity could be recovered[76]. The observation that the plasminogen activator inhibitor was oxidized under conditions that selectively oxidize Met residues and its biological activity could be restored by the Met(O)–peptide reductase suggests that the loss of inhibitor activity is due to oxidation of one or more Met residues.

F. Peptides

Further studies using low molecular weight peptides were carried out in an attempt to investigate the substrate specificity of the enzyme. It was found that the enzyme has a broad substrate specificity and can reduce Met(O) residues not only in proteins but also in small peptides. Thus, the Met(O) in oxidized [Met]enkephalin [Tyr-Gly-Gly-Phe-Met(O)] could be reduced by the enzyme[111] which showed that the carboxyl group of Met(O) does not have to be in peptide linkage in order to serve as a substrate for the enzyme. As shown in Table 2, the oxidized chemotactic peptide fMet(O)-Leu-Phe is biologically inactive; however, incubation of this peptide with either the purified Met(O)–peptide reductase or with a crude neutrophil extract in the presence of DTT, resulted in the reduction of the Met(O) residue (Figure 8), and the concomitant restoration of the chemotactic activity of the peptide[114]. Although the activity of Met(O)–peptide reductase could be assayed using Met(O)–L12 or Met(O)–α-1-PI as substrate, the assays were long and tedious. Since the experiments with oxidized chemotactic peptide and enkephalin demonstrated that a small peptide could be utilized as a substrate, a rapid and sensitive assay was developed using radiolabelled *N*-acetylMet(O) as substrate[112,122]. The labelled substrate is very easily synthesized and purified[112]. Briefly, L-methyl-[^{3}H]methionine is first incubated with H_2O_2 for 1 h at 23 °C which oxidizes about 90% of the Met to Met(O). The incubation mixture is then treated with glacial acetic acid and acetic anhydride and the *N*-acetyl[^{3}H]Met(O) is purified by thin layer chromatography. This simple Met(O) derivative is an excellent substrate for the enzyme and its enzymatic conversion to *N*-acetylMet provides a simple assay for the reaction (Figure 7). The reduction can easily be followed using a procedure in which about 50% of the product *N*-acetyl-[^{3}H]Met is extracted into ethyl acetate while only about 1–2% of the substrate is extracted[112,122]. Figure 8 shows that the rate of reduction of *N*-acetylMet(O) by Met(O)–peptide reductase

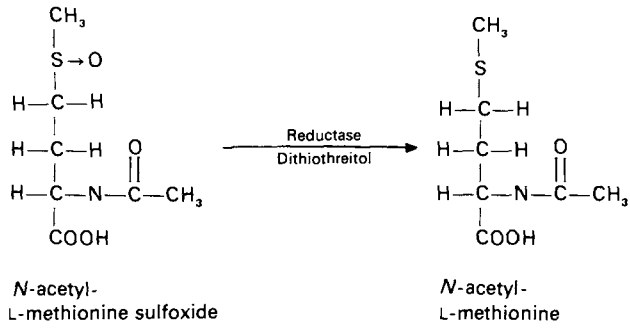


FIGURE 7. The enzymatic reduction of *N*-acetyl-L-methionine sulfoxide.

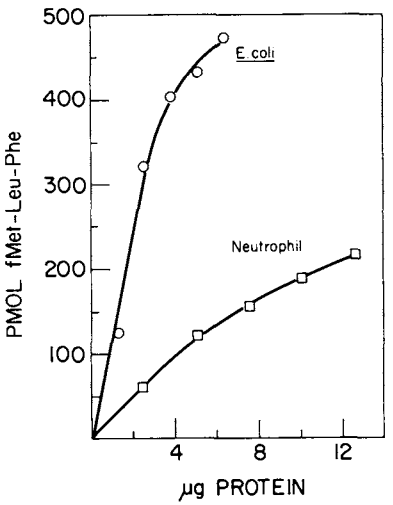


FIGURE 8. The reduction of fMet(O)-Leu-Phe by a human neutrophil and purified *E. coli* Met(O) peptide reductase. Each assay contained in a final volume of 30 μl 25 mM Tris-HCl (pH 7.4), 10 mM $MgCl_2$, 15 mM dithiothreitol 540 pmole fMet(O)–[^{3}H]Phe-Leu and Met(O)–peptide reductase. After incubating at 37 °C for 60 min, the incubation mixture is acidified and extracted with ethyl acetate. After centrifugation, an aliquot of the organic phase is removed and assayed for radioactivity. Reproduced by permission of Academic Press from Fliss and coworkers[114].

TABLE 7. Requirements for the enzymatic reduction of *N*-acetylMet(O)[a]

System	*N*-AcetylMet pmol
Complete (15 mM dithiothreitol)	420
Enzyme	0
Dithiothreitol	0
Dithiothreitol plus 2-mercaptoethanol	23
Dithiothreitol plus NADPH, thioredoxin, and thioredoxin reductase	927
Complete (1 mM dithiothreitol)	5
Complete plus thioredoxin	787

[a] Details of the incubation and assay are described in the legend to Figure 8. Reproduced by permission of Raven Press, New York from Brot and coworkers in Holmgren (ed.) *Thioredoxin and Glutaredoxin Systems.* © 1986.

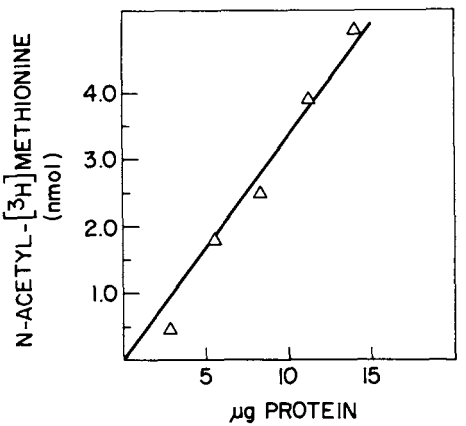


FIGURE 9. The effect of protein concentration of purified *E. coli* Met(O)–peptide reductase on the reduction of *N*-acetylMet(O). Each incubation contained 5×10^{-4} M *N*-acetyl[^{3}H]Met(O). The conditions and assay are described in the legend to Figure 8. Reproduced by permission of Academic Press from Brot and coworkers[112].

increases linearly with protein concentrations up to about 15 μg per incubation. Table 7 shows that the characteristics of this reduction are essentially identical to that found using either Met(O)–L12 or Met(O)–α-1-PI as substrate. Thus, the reaction requires the presence of dithiothreitol which cannot be replaced by 2-mercaptoethanol. On the other hand, NADPH, thioredoxin and thioredoxin reductase not only can substitute for dithiothreitol but are about twice as efficient as a reducing system[123]. It can also be seen that dithiothreitol at low levels (1 mM) is unable to support the enzymatic reduction of *N*-acetylMet(O). However, excellent reduction of *N*-acetylMet(O) occurs when thioredoxin is added to these incubations. These results suggest that the low concentrations of dithiothreitol are chemically reducing the thioredoxin which then serves as the reductant in the presence of Met(O)–peptide reductase. The results of these experiments demonstrate that Met(O)–peptide reductase utilizes a wide range of substrates. The enzyme is capable of reducing Met(O) residues in proteins, peptides and even in as simple a substrate as *N*-acetylMet(O). It appears that the enzyme can utilize any substrate that contains Met(O) with the amino group in a peptide bond.

IX. CLINICAL RELATIONSHIP

In the past number of years a number of studies have shown that in a variety of diseases there is a significant oxidation of Met residues to Met(O) in specific proteins that results in a loss of biological activity. These diseases include cataracts, rheumatoid arthritis, adult respiratory distress syndrome and emphysema. The most convincing evidence that Met(O) in proteins may be involved in the etiology of a pathological condition comes from studies with α-1-PI. It is well accepted that α-1-PI is inactivated upon oxidation of its Met residues. A decreased activity of α-1-PI in lung tissue that would result in an increased elastase activity has been associated with pulmonary emphysema. In patients who have a

low level of serum α-1-PI due to a genetic deficiency in which the newly synthesized protein in the liver cannot be glycosylated and secreted into the serum, there is precocious development of emphysema[124]. This relationship has led to the idea that pulmonary emphysema may be due to an imbalance between elastase and α-1-PI in the lungs[125]. This hypothesis is strengthened by the evidence that the oxidation of Met residues in α-1-PI *in vivo* may be involved in smoking related emphysema. Thus, it has been demonstrated that there is a large decrease of α-1-PI activity in the bronchoaveolar lavage fluid of rats after exposure to cigarette smoke[126]. Similarly in a study in which the α-1-PI in the lavage fluids obtained from smokers and non-smokers were compared, it was found that the specific activity of the α-1-PI from smokers is about 50% of that of non-smokers (Table 8, column 5), although the total amount of antigenically reactive α-1-PI is about the same for both groups[88,127] (Table 8, column 6). This inactivation of α-1-PI in smokers' lavage fluid is thought to arise as a result of the oxidation of essential Met residues in the protein. This conclusion comes from the observation that α-1-PI purified from smokers' lavage fluid contains four Met(O) residues while no Met(O) is found in α-1-PI from non-smokers (Table 8, column 7). A very comparable situation appears to be present in patients with adult respiratory distress syndrome[128], and in monkeys in whom inflammatory pulmonary injury was induced[129]. Cochrane and coworkers[128] have reported that α-1-PI isolated from lung lavage fluid from these patients contained inactive α-1-PI. Although a direct assay for the presence of Met(O) residues could not be performed due to the small amount of material available, it was found that incubation of the inactive α-1-PI with purified *E. coli* Met(O)–peptide reductase and dithiothreitol restored the biological activity of the inactive α-1-PI[128]. In an attempt to investigate the relationship between lung disease and α-1-PI inactivation, an animal model was used[129]. In these studies the intrabronchial installation of phorbol myristate or the formylated peptide fnorleu-leu-phe was used to induce inflammatory pulmonary damage. Both of these compounds have been shown to cause aggregation of neutrophils, release of oxidants and proteases, and to cause lung damage when administered *in vivo*[130–138]. Similar to that found in the case of the human diseases, the bronchial lavage fluid from the treated monkeys contained inactive α-1-PI whose activity could be restored upon incubation with Met(O)–peptide reductase and dithiothreitol. These observations demonstrate the first example of an *in vivo* oxidized protein containing Met(O) that could be reduced and whose activity could be restored by the Met(O)–peptide reductase. All previously used proteins and peptide substrates that could be enzymatically reduced were prepared by oxidation *in vitro*.

TABLE 8. Activity and Met(O) content of α-1-PI in smokers' and non-smokers' bronchoaveolar lavage fluid

Category	No.	Age	Smoking history (pack-years)[a]	Elastase inhibitory capacity[b] (per μg α-1-PI)	α-1-PI (μg/mg albumin)	Met(O) (mol/mol inactive α-1-PI)
Non-smokers	24	25 ± 6.8	0	0.59 ± 0.08	57 ± 12	0
Smokers	26	28 ± 3.2	18.1 ± 3.5	0.34 ± 0.10	65 ± 20	3.8 + 0.2

[a]Mean ± SD. A pack-year is 1 pack per day for a year.
[b]Micrograms of elastase inhibited after incubation for 10 min at 37 °C per microgram of α-1-PI (measured immunologically) in concentrated BAL fluid; mean of at least three measurements ± 1 SD.
Reproduced with permission from Carp and coworkers[88].

Emphysema that is found in smokers is probably related to the oxidants known to be present in cigarette smoke as well as oxidants release by neutrophils that accumulate in the lung. Chronic cigarette smoking not only increases the number of neutrophils in bronchoaveolar fluid[139] but also metabolically activates these cells to produce oxidizing agents[140]. The latter are the most likely source of the oxidants found to be present in adult respiratory distress syndrome. In both cases the inactivation of α-1-PI would result in an increase in the amount of free elastase. This would cause an increased susceptibility of the lung tissue to proteolysis and an increase in the destruction of lung tissue.

In rheumatoid arthritis the damage that is found in joints may also be a result of the inactivation of α-1-PI due to the oxidation of an essential methionine(s) residue in this protein. It has been found that α-1-PI purified from the synovial fluid of patients with rheumatoid arthritis contained four Met(O) residues and was not able to form a binary complex with elastase[89]. It is probable that the presence of the Met(O) residues in α-1-PI from these patients results from a high level of oxidants produced by neutrophils in the inflammed joint.

In addition to α-1-PI, there are other examples of the presence of Met(O) residues in proteins isolated from biological material. Proteins found in lens tissue are particularly susceptible to photooxidation and because of the long half-lives of these proteins, any oxidation could be especially detrimental. In this tissue, protein synthesis is localized to the outer region of the tissue and most proteins are stable for the life of the tissue[141,142]. It is thus somewhat surprising that not only is there no Met(O) residues in the young normal human lens but even in the old normal human lens only a small amount of Met(O) residues is found[143,144]. However, in the cataractous lens as much as 65% of the Met residues of the lens proteins are found in the form of Met(O)[143,144]. Whether this increase in Met(O) content in these proteins is a cause or a result of the cataracts is not known. In order to determine whether the high content of Met(O) in the cataractous lens is related to a decreased activity of Met(O)–peptide reductase, the level of this enzyme was determined in normal and cataractous lenses. It can be seen from Table 9 that there are no significant differences between the levels of Met(O)–peptide reductase in normal and cataractous lenses. In spite of these results, however, it is still possible that the Met(O)–peptide

TABLE 9. Comparison of Met(O)–peptide reductase activity in normal and cataractous lens

Age	Normal (units/lens)[a]	Age	Cataract (units/lens)[a]
54	456	64	614
57	596	64	260
62	1303	66	382
62	273	67	125
62	408	69	697
69	565	69	341
70	164	78	415
81	560	88	947
Mean	541[b]	Mean	472[b]
SE	121	SE	94

[a]pmol *N*-acetyl[^{3}H]Met(O) reduced/h/lens.

[b]Comparison of the difference of the mean indicates no significant difference ($P > 0.05$).

Reproduced by permission of Academic Press from Spector and coworkers[113].

reductase in the cataractous lenses is non-functional because the reducing system is inoperative. It is known that in cataractous lenses almost all of the thiol groups of the lens proteins as well as glutathione are oxidized. There is evidence that NADPH synthesis in the cataractous lens is decreased[145] and since this pyridine nucleotide is a component of the reducing system for both the glutathione reductase and Met(O)–peptide reductase, a decrease in reducing potential might be the reason for the accumulation of Met(O) residues in cataractous lenses.

Finally, a number of studies[146–149] have demonstrated that a variety of enzymes purified from tissues of older animals have a decreased specific activity when compared to the enzyme purified from younger animals. These proteins, however, appear to be identical as measured by a variety of physical and chemical parameters. It is possible that one of the differences is due to the accumulation of Met(O) residues in the proteins of the older animals.

The findings discussed above suggest that the presence of Met(O) residues in α-1-PI and lens proteins might account for some of the observed clinical manifestations. It is of interest to speculate that Met(O)–peptide reductase may function as a repair enzyme to prevent the accumulation of Met(O) residues in most proteins. Whether in those examples as discussed above, the accumulation of Met(O) in proteins is a result of an overwhelming increase in the synthesis of biological oxidants and/or a decrease in the ability to either destroy the biological oxidants or reduce the Met(O) residues in the proteins is not known. If it is the latter, this could be due to a decrease in the reductase itself or to some impairment in the reducing system that the enzyme requires.

X. REFERENCES

1. R. Uy and F. Wold, *Science*, **198**, 890 (1977).
2. E. L. Gershey, G. Vidali and V. G. Allfrey, *J. Biol. Chem.*, **243**, 5018 (1968).
3. P. B. Chuck, S. G. Rhee and E. R. Stadtman, *Annu. Rev. Biochem.*, **49**, 813 (1980).
4. E. N. Kort, M. F. Goy, S. H. Larsen and J. Adler, *Proc. Natl. Acad. Sci. USA*, **72**, 3939 (1975).
5. E. G. Krebs, and J. Beavo, *Annu. Rev. Biochem.*, **48**, 923 (1979).
6. J. H. McKerrow, *Mech. Ageing Dev.*, **10**, 371 (1979).
7. R. K. Root and S. M. Cohen, *Rev. Infect. Dis.*, **3**, 565 (1981).
8. H. B. Dixon, S. Moore, M. P. Stack-Dunne and F. G. Young, *Nature (London)*, **168**, 1044 (1951).
9. T. Lo, J. J. Dixon and C. H. Li, *Biochim. Biophys. Acta*, **53**, 584 (1961).
10. W. Vale, J. Spiess, C. Riviev and J. Riviev, *Science*, **213**, 1394 (1981).
11. P. H. Tobler, F. A. Tschopp, M. A. Dambacher, W. Born and J. A. Fischer, *J. Clin. Endocrinol. Metab.*, **57**, 749 (1983).
12. K. Norris, J. Halmstrom and K. Brunfeldt, *Acta Chim. Scand.*, **25**, 945 (1971).
13. M. L. Dedman, T. H. Farmer and C. Morris, *Biochim. J.*, **66**, 166 (1957).
14. B. Iselin, *Helv. Chim. Acta*, **44**, 61 (1961).
15. G. J. Omena, A. Fontana and C. B. Anfinsen, *J. Biol. Chem.*, **245**, 1895 (1969).
16. A. Patchornik and Y. Burstein, *Biochem.*, **11**, 4641 (1972).
17. R. Joppich-Kuhn, J. A. Corkill and R. W. Giese, *Anal. Biochem.*, **119**, 73 (1982).
18. B. Gutte and R. B. Merrifield, *J. Amer. Chem. Soc.*, **91**, 501 (1969).
19. J. H. Mueller, *J. Biol. Chem.*, **56**, 157 (1923).
20. G. Barger and F. P. Coyne, *Biochem. J.*, **22**, 1417 (1928).
21. G. Toennies and T. P. Callan, *J. Biol. Chem.*, **139**, 481 (1939).
22. K. A. Caldwell and A. L. Tappel, *Biochemistry*, **3**, 1643 (1964).
23. J. R. Clamp and L. Hough, *Biochem. J.*, **94**, 17 (1965).
24. T. Y. Liu, in *The Proteins* (Eds. H. Neurath and R. L. Hill), 3rd ed., Academic Press, New York, 1977, pp. 239–402.
25. P. de la Llosa, A. E. Abed and M. Roy, *Canad. J. Biochem.*, **58**, 745 (1980).
26. J. R. Knowles, *Biochem. J.*, **95**, 180 (1965).
27. M. Z. Atassi, *Biochem. J.*, **102**, 478 (1967).

28. Y. Shechter, Y. Burstein and A. Patchornik, *Biochemistry*, **14**, 4497 (1975).
29. H. R. Bentley, E. E. McDermott and J. K. Whitehead, *Nature*, **165**, 735 (1950).
30. J. K. Whitehead and H. R. Bentley, *J. Chem. Soc. (London)*, **2**, 1572 (1952).
31. A. S. Brill and I. Weinryb, *Biochemistry*, **6**, 3528 (1967).
32. J. P. Greenstein and M. Winitz, *Chemistry of the Amino Acids*, Vol. 3, Wiley, New York, 1961, pp. 2125–2155.
33. T. F. Lavine, *J. Biol. Chem.*, **169**, 477 (1947).
34. R. A. Houghten and C. H. Li, *Methods in Enzymology*, Vol. 91, Academic Press, 1983, pp. 549–559.
35. M. L. Dedman, T. H. Farmer and C. Morris, *Biochem. J.*, **66**, 166 (1957).
36. K. P. Polzhofer and K. H. Ney, *Tetrahedron*, **27**, 1997 (1971).
37. P. Caldwell, D. C. Luk, H. Weissbach and N. Brot, *Proc. Natl. Acad. Sci. USA*, **75**, 5349 (1978).
38. C. W. Balridge and R. W. Gerald, *Amer. J. Physiol.*, **103**, 235 (1933).
39. G. Y. N. Iyer, M. F. Islem and J. H. Quaslel, *Nature*, **192**, 535 (1961).
40. B. M. Babior, R. S. Kipnes and J. Carnutte, *J. Clin. Invest.*, **52**, 741 (1973).
41. J. E. Harrison and J. Schultz, *J. Biol. Chem.*, **251**, 1371 (1976).
42. J. Schultz and K. Kaminker, *Arch. Biochem. Biophys.*, **96**, 465 (1962).
43. I. M. Goldstein, M. Cerquiera, S. Lund and H. B. Kaplan, *J. Clin. Invest.*, **59**, 249 (1977).
44. B. M. Babior, J. J. Carnutte and B. J. McMurrich, *J. Clin. Invest.*, **58**, 989 (1976).
45. B. M. Babior, *N. Engl. J. Med.*, **298**, 659 (1978).
46. S. J. Klebanoff, *Ann. Inter. Med.*, **93**, 480 (1980).
47. S. J. Klebanoff, *J. Exp. Med.*, **126**, 1063 (1967).
48. S. J. Klebanoff, *J. Bact.*, **95**, 2131 (1968).
49. D. N. Baron and S. A. Ahmed, *Clin. Sci.*, **37**, 205 (1969).
50. H. Rosen and S. J. Klebanoff, *J. Clin. Invest.*, **64**, 1725 (1979).
51. W. J. Ray, Jr. and D. E. Koshland, Jr., *Brookhaven Symp. Biol.*, **13**, 135 (1960).
52. W. E. Savige and A. Fontana, in *Methods in Enzymology*, Vol. 47 (Eds. C. H. W. Hirs and S. N. Timasheff), Academic Press, New York, 1977, pp. 453–459.
53. N. F. Floyd, M. C. Cammaroti and T. F. Lavine, *Arch. Biochem. Biophys.*, **102**, 343 (1963).
54. N. P. Neumann, in *Methods in Enzymology*, Vol. 25 (Eds. C. H. W. Hirs and S. N. Timasheff), Academic Press, New York, 1972, pp. 393–405.
55. H. Fliss, H. Weissbach and N. Brot, *Proc. Natl. Acad. Sci. USA*, **80**, 7160 (1983).
56. B. G. Hudson and R. G. Spiro, *J. Biol. Chem.*, **247**, 4229 (1972).
57. H. J. Horstmann, K. James and J. W. Rohen, *Eur. J. Cell Biol.*, **20**, 122 (1979).
58. Y. Kikuchi and N. Tamiya, *J. Biochem.*, **89**, 1975 (1981).
59. Y. Kikuchi, N. Tamiya, T. Nozawa and M. Hatano, *Eur. J. Biochem.*, **125**, 575 (1982).
60. J. Sanchez, B. J. Nikolau and P. K. Stumpf, *Plant Physiol.*, **73**, 619 (1983).
61. V. E. Koteliansky, S. P. Domogatsky and A. T. Gudkov, *Eur. J. Biochem.*, **90**, 319 (1978).
62. G. Jori, G. Galiazzo, A. Marzotto and E. Scoffone, *J. Biol. Chem.*, **243**, 4272 (1968).
63. K. Kido and B. Kassell, *Biochemistry*, **14**, 631 (1975).
64. N. P. Neumann, S. Moore and W. H. Stein, *Biochemistry*, **1**, 68 (1962).
65. W. J. Ray, Jr., H. G. Latham, Jr., M. Katsoulis and D. E. Koshland, Jr., *J. Amer. Chem. Soc.*, **82**, 4743 (1960).
66. H. Schachter and G. H. Dixon, *Biochem. Biophys. Res. Commun.*, **9**, 132 (1962).
67. H. Carp and A. Janoff, *Amer. Rev. Resp. Dis.*, **118**, 617 (1978).
68. D. Johnson and J. Travis, *J. Biol. Chem.*, **254**, 4022 (1979).
69. W. R. Abrams, A. Eliraz, P. Kimbel and G. Weinbaum, *Exp. Lung Res.*, **1**, 211 (1980).
70. J. Wolff, G. H. Cook, A. R. Goldhammer and S. A. Berkowitz, *Proc. Natl. Acad. Sci. USA*, **77**, 3841 (1980).
71. F. H. H. Carlsson and A. I. Louw, *Biochim. Biophys. Acta*, **534**, 322 (1978).
72. A. L. Frelinger and J. E. Zull, *Arch. Biochem. Biophys.*, **244**, 641 (1986).
73. P. H. Tobler, A. Jöhl, W. Burn, R. Maier and J. A. Fischer, *Biochim. Biophys. Acta*, **707**, 59 (1982).
74. P. H. Tobler, F. A. Tschopp, M. A. Dambacher, W. Born and J. A. Fischer, *J. Clin. Endocrinol. Metab.*, **57**, 749 (1983).
75. S. Rapoport, B. Hertel and G. Hausdorf, *Eur. J. Biochem.*, **139**, 573 (1984).
76. D. A. Lawrence and D. J. Loskutoff, *Biochem.*, **25**, 6351 (1986).
77. R. A. Clark, in *Advances in Inflammation Res.*, Vol. 5 (Ed. G. Weissman), Raven Press, New York, 1983, pp. 127–146.

78. N. Brot and H. Weissbach, *Trends Biochem. Sci.*, **7**, 137 (1982).
79. N. Brot and H. Weissbach, *Mol. Cell. Biochem.*, **36**, 47 (1981).
80. C. Terhorst, B. Wittmann-Liebold and W. Möller, *Eur. J. Biochem.*, **23**, 13 (1972).
81. H. F. Kung, J. E. Fox, C. Spears, N. Brot and H. Weissbach, *J. Biol. Chem.*, **248**, 5012 (1973).
82. N. Brot, R. Marcel, E. Yamasaki and H. Weissbach, *J. Biol. Chem.*, **248**, 6952 (1973).
83. A. H. Lockwood, U. Maitra, N. Brot and H. Weissbach, *J. Biol. Chem.*, **249**, 1213 (1974).
84. N. Brot, W. P. Tate, C. T. Caskey and H. Weissbach, *Proc. Natl. Acad. Sci. USA*, **71**, 89 (1974).
85. W. Möller, A. Groene, C. Terhorst and R. Amons, *Eur. J. Biochem.*, **25**, 5 (1972).
86. K.-P. Wong and H. H. Paradies, *Biochem. Biophys. Res. Commun.*, **61**, 178 (1974).
87. R. Osterberg, B. Sjoberg, A. Lilas and I. Pettersson, *FEBS Letters*, **66**, 48 (1976).
88. H. Carp, F. Miller, J. R. Hoidal and A. Janoff, *Proc. Natl. Acad. Sci. USA*, **79**, 2041 (1982).
89. P. S. Wong and J. Travis, *Biochim. Biophys. Res. Commun.*, **96**, 1449 (1980).
90. H. Carp and A. Janoff, *Amer. Rev. Resp. Dis.*, **118**, 617 (1978).
91. H. Carp and A. Janoff, *J. Clin. Invest.*, **66**, 987 (1980).
92. W. R. Abrams, A. Eliraz, P. Kimbel and G. Weinbaum, *Exp. Lung Res.*, **1**, 211 (1980).
93. D. S. Miller and P. D. Samuel, *J. Sci. Food Agric.*, **21**, 616 (1970).
94. G. H. Anderson, D. V. M. Ashley and J. D. Jones, *J. Nutr.*, **106**, 1108 (1976).
95. J. L. Cug, P. Besancon, L. Chartier and C. Cleftel, *Food Chem.*, **3**, 85 (1978).
96. L. R. Niaz, *Br. J. Nutr.*, **16**, 571 (1962).
97. G. D. Shockman and G. Toennies, *Arch. Biochem. Biophys.*, **50**, 1 (1954).
98. S.-I. Ejiri, H. Weissbach and N. Brot, *J. Bacteriol.*, **139**, 161 (1979).
99. J. M. Tuffnell and J. W. Payne, *FEMS Microbiol. Letters*, **12**, 273 (1981).
100. S.-I. Ejiri, H. Weissbach and N. Brot, *Anal. Biochem.*, **102**, 393 (1980).
101. P. D. Ayling, *J. Bact.*, **148**, 514 (1981).
102. V. Ganapathy and F. H. Leibach, *Biochem. Biophys. Acta*, **693**, 305 (1982).
103. S. Black, E. M. Harte, B. Hudson and L. Wartofsky, *J. Biol. Chem.*, **235**, 2910 (1960).
104. J. O. Lampen, M. J. Jones and A. B. Perkins, *Arch. Biochem. Biophys.*, **13**, 33 (1947).
105. T. L. Sourkes and Y. Trano, *Arch. Biochem. Biophys.*, **42**, 321 (1952).
106. R. M. Wagner and M. F. Mallette, *Fed. Proc.*, **41**, 638 (1982).
107. R. C. Doney and J. F. Thompson, *Biochim. Biophys. Acta*, **124**, 39 (1966).
108. S.-I. Ejiri, H. Weissbach and N. Brot, *Fed. Proc.*, **38**, 829 (1979).
109. C. Aymard, L. Seyer and J.-C. Cheftel, *Agr. Biol. Chem.*, **43**, 1869 (1979).
110. P. G. Porque, A. Baldesten and P. Reichard, *J. Biol. Chem.*, **245**, 2371 (1970).
111. N. Brot, L. Weissbach, J. Werth and H. Weissbach, *Proc. Natl. Acad. Sci. USA*, **78**, 2155 (1981).
112. N. Brot, H. Fliss, T. Coleman and H. Weissbach, in *Methods in Enzymology*, Vol. 107B, (Eds. F. Wold and K. Moldave), Academic Press, New York, 1984, pp. 352–360.
113. A. Spector, R. Scotto, H. Weissbach and N. Brot, *Biochem. Biophys. Res. Commun.*, **108**, 429 (1982).
114. H. Fliss, G. Vasanthakumar, E. Schiffmann, H. Weissbach and N. Brot, *Biochem. Biophys. Res. Commun.*, **109**, 194 (1982).
115. J. A. Badwey and M. L. Karnovsky, *Annu. Rev. Biochem.*, **49**, 695 (1980).
116. B. M. Shapiro, R. W. Schackmann and C. A. Gabel, *Annu. Rev. Biochem.*, **50**, 815 (1981).
117. S. Satoh, T. Kurecki, L. F. Kress and M. Laskowski, Sr., *Biochem. Biophys. Res. Commun.*, **86**, 130 (1979).
118. D. Johnson and J. Travis, *J. Biol. Chem.*, **254**, 4022 (1979).
119. W. R. Abrams, G. Weinbaum, L. Weissbach, H. Weissbach and N. Brot, *Proc. Natl. Acad. Sci. USA*, **78**, 7483 (1981).
120. L. A. Austin and H. Heath III, *N. Engl. J. Med.*, **304**, 269 (1981).
121. J. A. Van Mourik, D. A. Lawrence and D. J. Loskutoff, *J. Biol. Chem.*, **259**, 14914 (1984).
122. N. Brot, J. Werth, D. Koster and H. Weissbach, *Anal. Biochem.*, **122**, 291 (1982).
123. N. Brot, H. Fliss and H. Weissbach, in *Thioredoxin and Glutaredoxin Systems: Structure and Function* (Ed. A. Holmgren, C.-I. Brändén, H. Jörnvall and B.-M. Sjöberg), Raven Press, New York, 1986, pp. 141–153.
124. C. B. Laurell and S. Eriksson, *Scand. J. Clin. Invest.*, **15**, 132 (1963).
125. J. Bignon and G. L. Scarpa (Eds.), *Biochemistry, Pathology and Genetics of Pulmonary Emphysema: Proceedings of a Meeting held at Porto Conte, Sassari, April 27–30, 1981*, Pergamon, New York, 1981.
126. A. Janoff, H. Carp, D. K. Lee and R. T. Drew, *Science*, **206**, 1313 (1979).
127. J. E. Gadek, G. A. Fells and R. G. Crystal, *Science*, **206**, 1315 (1979).

128. C. G. Cochrane, R. Spragg and S. B. Revak, *J. Clin. Invest.*, **71**, 754 (1983).
129. S. D. Revak, C. L. Rice, I. U. Schraufstatter, W. A. Halsey, Jr., B. P. Bohl, R. M. Clancy and C. G. Cochrane, *J. Clin. Invest.*, **76**, 1182 (1985).
130. D. M. Shasby, K. M. Vanbenthuysen, R. M. Tate, S. S. Shasby, I. McMurtry and J. E. Repine, *Ann. Rev. Respir. Dis.*, **125**, 443 (1982).
131. I. U. Schraufstatter, S. D. Revak and C. G. Cochrane, *J. Clin. Invest.*, **73**, 1175 (1984).
132. H. J. Showell, R. J. Freer, S. H. Zigmond, E. Schiffmann, S. Aswanikumar, B. Corcoran and E. L. Becker, *J. Exp. Med.*, **143**, 1154 (1976).
133. J. T. O'Flaherty, H. J. Showell, E. L. Becker and P. A. Ward, *Amer. J. Pathol.*, **92**, 155 (1978).
134. S. H. Zigmond, *J. Cell. Biol.*, **77**, 269 (1978).
135. R. J. Freer, A. R. Day, J. A. Radding, E. Schiffmann, S. Aswanikumar, H. J. Showell and E. L. Becker, *Biochemistry*, **19**, 2404 (1980).
136. J. T. O'Flaherty, S. Cousart, A. S. Lineberger, E. Bond, D. A. Bass, D. Phil, L. R. De Chatelet, E. S. Leake and C. G. McCall, *Amer. J. Pathol.*, **101**, 79 (1980).
137. G. Weissmann, J. E. Smolen and H. M. Korchak, *N. Engl. J. Med.*, **303**, 27 (1980).
138. K. J. Johnson and P. A. Ward, *Amer. J. Pathol.*, **107**, 29 (1982).
139. G. W. Hunninghake, J. Gadek and R. Crystal, *Chest*, **77**, 273 (1980).
140. W. G. Hocking and D. W. Golde, *N. Engl. J. Med.*, **301**, 639 (1979).
141. C. F. Wannemacher and A. Spector, *Exp. Eye Res.*, **7**, 623 (1968).
142. J. J. Harding and K. J. Dilley, *Exp. Eye Res.*, **22**, 1 (1976).
143. M. H. Garner and A. Spector, *Proc. Natl. Acad. Sci. USA*, **77**, 1274 (1980).
144. R. J. W. Truscott and R. C. Augusteyn, *Biochim. Biophys. Acta*, **492**, 43 (1977).
145. R. C. Augusteyn, in *Mechanisms of Cataract Formation in the Human Lens*, Academic Press, New York, 1981, pp. 104–106.
146. H. Gershon and D. Gershon, *Proc. Natl. Acad. Sci. USA*, **70**, 909 (1973).
147. U. Reiss and M. Rothstein, *Biochem. Biophys. Res. Commun.*, **61**, 909 (1973).
148. U. Reiss and M. Rothstein, *J. Biol. Chem.*, **250**, 826 (1975).
149. U. Reiss and D. Gershon, *Eur. J. Biochem.*, **63**, 617 (1976).

CHAPTER **18**

Photochemistry of sulfoxides and sulfones

I. W. J. STILL

Department of Chemistry, University of Toronto, Erindale Campus, Mississauga, Ontario, Canada, L5L 1C6

I. INTRODUCTION

The photochemistry of sulfoxides and sulfones, which was first comprehensively reviewed in 1969[1], continues to be an area of active research interest. In this early review some 30 to 40 primary publications on the photochemistry of sulfoxides and sulfones were described. Since that date, interest in this field has continued at a steady, rather than accelerated, pace but further reviews of the general area of photochemistry of organic sulfur compounds have appeared[2,3]. The present review will focus on the main areas of interest for both sulfoxides and sulfones which, in spite of their apparent similarity, exhibit quite different photochemical behavior.

II. SULFOXIDES

A. Photolysis of Acyclic Sulfoxides

The photolysis of dimethyl sulfoxide (DMSO), as befits the parent compound in the series, has received considerable attention, both neat and in solvents like water or

acetonitrile, primarily as the result of the pioneering studies of Gollnick and Stracke[4]. These authors concluded that the primary photochemical reactions of DMSO resulted from excitation to the singlet state ($E_s = 105\,kcal\,mol^{-1}$), the nature of the electronic excitation involved, e.g. $n_S \rightarrow \pi^*$ or $n_O \rightarrow \pi^*$, remaining ambiguous. The major primary photochemical reactions resulting from this excitation were photofragmentation (equation 1) and disproportionation (equation 2). *Direct* photodissociation of DMSO into dimethyl sulfide and [O] was essentially ruled out.

$$CH_3SOCH_3 + \xrightarrow{h\nu} [CH_3SO]^{\cdot} + CH_3^{\cdot} \tag{1}$$

$$[CH_3SOCH_3]^* + CH_3SOCH_3 \longrightarrow CH_3SCH_3 + CH_3SO_2CH_3 \tag{2}$$

The formation of dimethyl sulfide, dimethyl sulfone, and methane (by H-abstraction) observed in these photolyses is thus accounted for. Hydrogen abstraction by the methylsulfinyl radical affords methanesulfenic acid, CH_3SOH, a very reactive molecule, which rapidly undergoes a series of secondary reactions to produce the methanesulfonic acid, methyl methanethiolsulfonate ($CH_3SO_2SCH_3$), and dimethyl disulfide which were also observed during these photolyses.

Two more recent studies of the nature of the sulfur–carbon bond cleavage in sulfoxide photolyses have been conducted, using ESR[5] and CIDNP[6] detection methods, respectively. In the latter case there is some evidence for a triplet process being involved in the photocleavage of aryl methyl sulfoxides.

The sulfur–carbon bond homolysis in sulfoxide photolyses is reversible by way of a cage recombination process. Recombination may to some extent involve carbon–oxygen bond formation to give a sulfenate ester[7]. Not surprisingly, several applications of this process to the racemization or configurational inversion of sulfoxides have been reported[8,9]. Interestingly, Kagan and coworkers[10] have reported the photochemical conversion of a racemic sulfoxide into an optically active mixture of sulfoxides of low optical purity, using a chiral naphthalene compound as photosensitizer.

Majeti[11] has studied the photochemistry of simple β-ketosulfoxides, $PhCOCH_2SOCH_3$, and found cleavage of the sulfur–carbon bond, especially in polar solvents, and the Norrish Type II process to be the predominant pathways, leading to both 1,2-dibenzoylethane and methyl methanethiolsulfonate by radical dimerization, as well as acetophenone (equation 3). Nozaki and coworkers[12] independently revealed similar results and reported in addition a pH-dependent distribution of products. Miyamoto and Nozaki[13] have shown the incorporation of protic solvents into methyl styryl sulfoxide, by a polar addition mechanism.

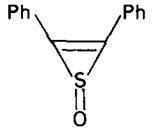
$$\begin{array}{l} PhCOCH_2SOCH_3 \xrightarrow[MeOH]{h\nu} PhCOCH_3 + PhCO\dot{C}H_2 + \dot{S}OCH_3 \\ \qquad\qquad\qquad\qquad\qquad\qquad\quad \downarrow \qquad\quad \downarrow \\ \qquad\qquad\qquad\qquad\qquad\qquad PhCOCH_2CH_2COPh \quad CH_3SO_2SCH_3 \end{array} \tag{3}$$

B. Photolysis of Cyclic Sulfoxides

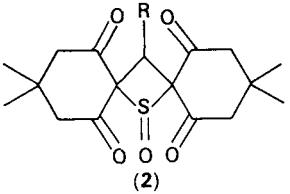
One of the major areas of interest in the photochemistry of cyclic sulfoxides has been photochemical extrusion (photodesulfurization). The general area of photoextrusion of small molecules has been comprehensively reviewed by Givens[14]. Although it is probably fair to point out that more photochemical studies of this type have been carried out for sulfones (*q.v.*) than for sulfoxides, there are now several examples in the literature of photochemical desulfinylation and these will be reviewed here.

Small (three- and four-membered) cyclic sulfoxides, or strained bicyclic sulfoxides, appear to be particularly good candidates for the photoextrusion process. For example,

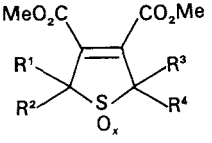
the photolysis of 2, 3-diphenylthiirene 1-oxide (**1**) in benzene has been shown by Carpino and Chen[15] to lead rapidly and almost quantitatively to the formation of diphenylacetylene (equation 4). Likewise, the irradiation of a series of thietane oxides (**2**) in benzene[16] leads to the corresponding cyclopropanes, although in some cases products resulting from ring-expansion to a cyclic sulfenate (see below) were observed. Successful photochemical desulfinylation of bridged bicyclo[2.2.1]sulfoxides has been reported by Kato and coworkers[17]. Kellogg and Prins[18] have studied the photolysis of sulfides, sulfoxides and sulfones (**3**) in the 2, 5-dihydrothiophene series. Good yields of the dienes derived by formal



(**1**)



(**2**)
R = H, alkyl



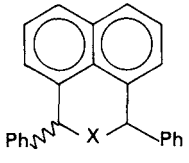
(**3**)
R^1–R^4 = H, alkyl
(x = 0, 1, 2,)

loss of sulfur monoxide were obtained but, in contrast to the analogous sulfones, the reactions are not stereospecific, suggesting the intervention of biradical intermediates. The formation of sulfur monoxide could not be demonstrated.

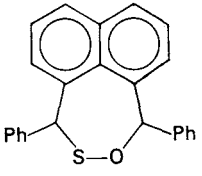
$$1 \xrightarrow[C_6H_6]{h\nu} PhC{\equiv}CPh \qquad (4)$$

The course of the photolysis of a number of cyclic sulfoxides, however, has been shown not to involve simple photoextrusion processes. In fact, the work of Schultz and Schlessinger[19,20] and Still and coworkers[21] has shown the existence of a novel desulfurization pathway leading to cyclic ethers or to carbonyl compounds by formal loss of the sulfur atom only, by certain cyclic sulfoxides.

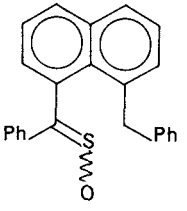
Schultz and Schlessinger[19] have postulated that the formation of the analogous pyran derivatives (**4**, X = O) on *direct* irradiation of the *cis*- and *trans*-thiopyran oxides (**4**, X = SO) proceeds by way of initial conversion to a cyclic sulfenate (**5**), for which some spectroscopic evidence was obtained. Whether the formation of the sulfenate involves a stepwise pathway via α-cleavage of the sulfoxide, or a concerted sigmatropic rearrangement, is not clear. The system has an interesting analogy with the well-known oxacarbene pathway observed in the photochemistry of cyclic ketones. In contrast, Schultz and Schlessinger[20] have also shown that the benzophenone-sensitized irradiation of the same *cis*-/*trans*-sulfoxide (**4**, X = SO) leads to the ketone (**7**), via the isomeric sulfines (**6**), both of which could be isolated. The sulfines presumably arise by photochemical α-cleavage of the sulfoxide and (intramolecular) hydrogen transfer, and are converted by loss of sulfur, in a



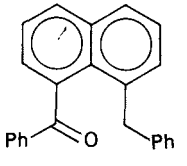
(**4**)
X = SO, O



(**5**)



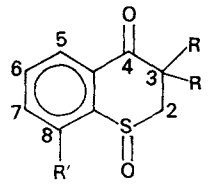
(**6**)



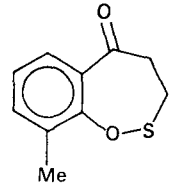
(**7**)

second photochemical step, into the corresponding carbonyl compound. (Photochemical reactions of sulfines will be reviewed later in this chapter.)

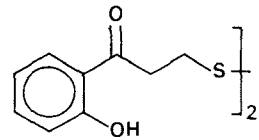
Still and coworkers[21] have studied the photolysis of a series of sulfoxides in the 4-thiochromanone series (**8a, b**) and have identified three distinct reaction pathways. Two of these, like the results discussed above, call for the initial formation of a cyclic sulfenate. The presence of an alkyl substituent on the aryl moiety (**8a**) appears to favor the initial α-cleavage of the sulfoxide preferentially on the aryl side leading, via intermediates such as **9**, to the eventual phenolic disulfide product (**10**) observed. With alkyl substituents in the hetero-ring, e.g. at C-3 (**8b**), however, the alternative sulfenate (**11**) is formed and the major product observed is the dicarbonyl compound, $PhCOCMe_2CHO$. This may be explained by further (photochemical) cleavage of the sulfenate, loss of sulfur and a hydrogen transfer which has been shown by labelling experiments to be intramolecular. Alternatively, a pathway involving α-cleavage of the aryl–sulfinyl bond and hydrogen transfer from C-2 could lead to a sulfine intermediate. Loss of sulfur in a fashion analogous to that proposed by Schultz and Schlessinger would lead to the aldehyde observed. The third type of product observed, on irradiation of 2,2-dimethylthiochroman-4-one 1-oxide (**12**), is the ring contraction product (**13**). One possible route to this product is via β-hydrogen abstraction from C-3 by the initially formed sulfinyl radical, leading to the unsaturated sulfenic acid (**14**). Photochemically initiated radical addition of the thiyl radical derived from **14** to the double bond, followed by loss of a hydrogen atom, would lead to **13**. Interestingly, when methanol was used as the solvent for the irradiation instead of benzene, the unsaturated thiol (**15**) was obtained. It is interesting to speculate that hydrogen abstraction by the sulfinyl radical from one of the C-2 methyl groups, rather



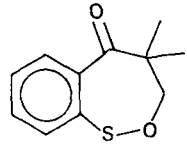
(**8**)
(**a**) R = H; R′ = Me
(**b**) R = Me; R′ = H



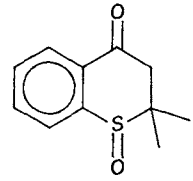
(**9**)



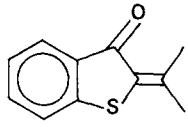
(**10**)



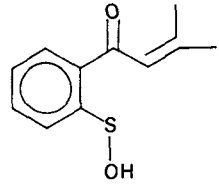
(**11**)



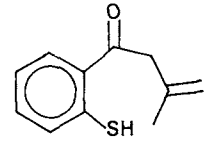
(**12**)



(**13**)



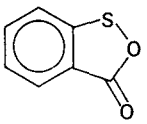
(**14**)



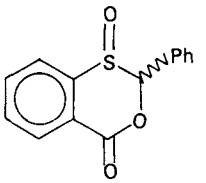
(**15**)

than from C-3, followed by reduction of the thiyl radical by methanol, could account for this result. The role of α-cleavage and/or cyclic sulfenate formation appears to be fairly well established by these results and thus some justification for comparing the photochemical behavior of cyclic sulfoxides with their far better known cyclic ketone counterparts appears to exist.

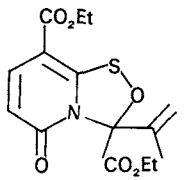
Other examples of the photochemical α-cleavage of cyclic sulfoxides have been noted. Lawesson and coworkers[22] have proposed that the mixed sulfenic-carboxylic anhydride (**16**) is formed on photolysis of **17**, by α-cleavage followed by the loss of benzaldehyde. The



(**16**)



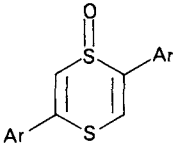
(**17**)



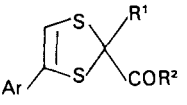
(**18**)

same type of process appears to be responsible for the formation of fused 2,1,4-oxathiazolidines such as **18**, observed by Young and coworkers[23]. Praefcke and Weichsel[24] have proposed that α-cleavage in certain cyclic sulfoxides, followed by intramolecular hydrogen transfer, leads, via sulfine intermediates, to carbonyl compounds and have suggested future synthetic applications for this reaction as a four-carbon homologation of carbonyl compounds. Again, the analogy with the formation of ketenes during the photolysis of some cyclic ketones is striking. The photochemical rearrangement of 1,4-dithiin sulfoxides (**19**) to the two 1,3-dithioles[25] (**20, b**) is believed to involve the isomeric sulfenate ring-expansion products as intermediates.

Minor amounts of the corresponding deoxygenated 1,4-dithiins were also found in the above reactions—a result noted independently for highly substituted 4-thiochromanone and naphtho-fused 4-thiopyranone sulfoxides by Still and coworkers[21,26,27]. While the mechanism of such photochemical deoxygenation reactions is not clear, it does not appear to involve disproportionation, in that the corresponding sulfone has never been isolated in these reactions. It also appears likely that photochemical deoxygenation occurs only when other pathways, e.g. α-cleavage or hydrogen abstraction, are disfavoured. A few examples are known where intramolecular oxygen transfer from sulfoxide groups occurs under photochemical conditions, for example in the conversion of 2-sulfinylbenzaldehyde derivatives (**21**) into the corresponding 2-alkyl- (or 2-aryl-)thiobenzoic acids[28]. The

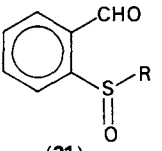


(**19**)



(**20**)

(**a**) $R^1 = H$; $R^2 = Ar$
(**b**) $R^1 = Ar$; $R^2 = H$



(**21**)

intramolecular photochemical *oxidation* of a sulfoxide by the neighboring nitro groups in 2-nitrophenyl phenyl sulfoxides, interestingly, has also been reported by Tanikaga and Kaji[29].

While the photochemical [2 + 2] cycloaddition and dimerization reactions of α,β-

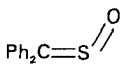
unsaturated sulfoxides have not been nearly as widely studied as for the analogous sulfones (*q.v.*), a few examples have been reported[30].

C. Photolysis of Sulfines (Thiocarbonyl S-Oxides)

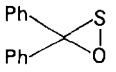
While not strictly speaking sulfoxides, sulfines (thiocarbonyl S-oxides) have attracted a considerable amount of interest from the standpoint of their photochemistry, since an early example was reported by Schlessinger and Schultz[31]. The subject has been reviewed recently by Carlsen[32]. Matrix-isolated diphenyl sulfine (**22**) is photochemically converted to the unstable oxathiirane (**23**) which, after breaking of the weak S—O bond, loses a sulfur atom to afford benzophenone[33] (equation 5). The dye-sensitized photooxygenation of sulfines is believed to proceed via an unstable 1, 2, 3-dioxathietane 3-oxide intermediate (**24**) to produce SO_2 and the corresponding ketone[34]. Very recently, *ab initio* calculations have been carried out on both the photochemical formation and the photochemical decomposition of oxathiirane[35], leading to the conclusion that S—O bond cleavage gives a singlet biradical.

$$Ph_2CSO \xrightarrow{h\nu} \mathbf{23} \longrightarrow Ph_2C\begin{matrix} S\cdot \\ O\cdot \end{matrix} \xrightarrow{-\frac{1}{8}S_8} Ph_2CO \qquad (5)$$

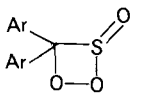
In an interesting contrast to the photochemical behavior of the simpler sulfine system, the photolysis of thioketene S-oxides such as **25** in carbon tetrachloride leads to the corresponding thioketenes in excellent yield[36]. This photochemical deoxygenation is



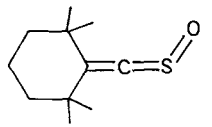
(**22**)



(**23**)



(**24**)



(**25**)

attributed to an interaction between the excited S-oxide and the solvent. In support of this suggestion, phenol has been detected as a by-product when the photolysis was conducted in benzene.

D. Miscellaneous Photolyses

The photolysis of the sulfimide group, isoelectronic with the sulfoxides, has been studied by Oae and coworkers[37,38], using a series of *N*-acyl-*S*, *S*-diphenylsulfimides, $Ph_2S{=}NCOR$. The primary photolytic process observed, in contrast to the sulfoxide series, is S—N bond cleavage, to afford diphenyl sulfide and the acyl nitrene (equation 6). Further experiments with sensitizers and intra- and intermolecular trapping have confirmed that the acyl nitrene is formed in the singlet state, in contrast to the analogous thermal decompositions, which appear to yield isocyanates directly. The concomitant formation of significant amount of diphenyl disulfide in some of these photolyses is not explained.

$$Ph_2S{=}NCOR \xrightarrow{h\nu} Ph_2S + {}^1[RCON]^* \qquad (6)$$

Similar results were reported independently by Shingaki and coworkers[39] for the *S*, *S*-dimethyl-*N*-ethoxycarbonyl sulfimide analogs. The photolysis of the higher valent sulfoximide derivatives, $ArSO_2N{=}S(O)Me_2$, had earlier been reported by Abramovitch and Takaya[40] not to yield the expected sulfonylnitrene but instead to give products arising

mainly from initial photocleavage of the Ar—SO_2 bond, producing aryl radicals. The photochemical cleavage of two quite different types of *S,S*-dimethyloxosulfonium ylide, $Me_2\dot{S}(O)\bar{C}HR$, has been reported independently by Kunieda and Witkop[41] and by Ide and coworkers[42] to afford primarily products arising from carbene intermediates, resulting from a similar photocleavage to that reported above for sulfimides.

III. SULFONES

A. Photolysis of Acyclic Sulfones

Some of the earliest studies of the photolysis of acyclic sulfones have been carried out in the diaryl sulfone series. The work of Oae and coworkers[43], using ^{14}C-labelled diphenyl sulfone in benzene, has established that the initial cleavage into $C_6H_5^{\cdot}$ and $C_6H_5\dot{S}O_2$ is followed by attack of the phenyl radical on benzene to produce an intermediate cyclohexadienyl radical. Hydrogen abstraction from this intermediate by the phenylsulfonyl radical leads to the biphenyl and benzenesulfinic acid observed (equation 7). The phenylsulfonyl radical does not react with solvent benzene to any significant extent. The arylation of pyridine by the photolysis of pyridine solutions of diaryl sulfones has also been reported[44], while Kobayashi and coworkers[45] have obtained a series of products from the photolysis of diaryl α-disulfones which are consistent with the initial formation of two arylsulfonyl radicals. Novi and coworkers[46] have adapted this photolysis to effect the nucleophilic displacement of —SO_2Me groups using sodium benzenethiolate in DMSO, possibly via a chain mechanism. The work of Matsuda and coworkers[47] has established by flash photolysis that the odd electron in the arylsulfonyl radical remains localized on the SO_2 group. Rettig and Chandross[48] have studied and proposed a mechanism for the multiple fluorescence of 4,4′-dimethylamino- and 4,4′-diaminophenyl sulfone in polar solvents.

$$C_6H_5SO_2C_6H_5 \xrightarrow{h\nu} C_6H_5\dot{S}O_2 + C_6H_5^{\cdot} \xrightarrow{C_6H_6}$$

$$[C_6H_5{-}C_6H_6]^{\cdot} \xrightarrow{C_6H_5\dot{S}O_2} Ph{-}Ph + PhSO_2H \qquad (7)$$

Among the related aryl sulfone systems studied photochemically have been the azosulfones[49] and azoxysulfones[50]. Since no N_2O could be detected during the photolysis of the aryl arylazoxysulfones, Kobayashi and coworkers[50] propose an initial rearrangement to the arenediazonium arenesulfonate, followed by homolysis to produce aryl radicals. Synthetic applications of the facile photochemical generation of phenylsulfonyl radicals have been reported. Photolysis of *p*-toluenesulfonyl cyanide, for example, in the presence of alkenes, leads to the expected free-radical addition products[51], while the photolysis of phenyl(arylsulfonyl)acetylenes, $PhC{\equiv}CSO_2Ar$, in the presence of alkenes leads stereospecifically to the *trans* adducts, such as **26** from indene, in good yields[52].

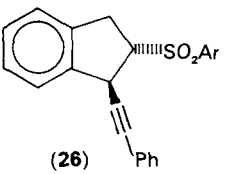
The photolytic behavior of benzylic sulfones has also been studied extensively, since the first report of this reaction by Cava and coworkers[53] in 1964 and the subject has been reviewed quite recently by Givens[14]. There is still considerable speculation as to the details of the bond homolysis, as evidenced by recent mechanistic papers by Wylie and coworkers[54], and by Givens and Turro[55,56]. The work of the latter authors shows that both singlet and triplet processes are possible and that extrusion of SO_2 involves two successive homolytic bond cleavages, with no evidence for charged intermediates. Stereochemical and CIDNP studies of these reactions have shown that radical recombination is significant for the singlet radical pair. The CIDNP study also revealed that a triplet pathway was preferred for the 1-naphthylmethyl sulfone analogs only. In an interesting

synthetic application of the photolysis of benzylic sulfones, Langler and Pincock[57] have shown that the photolysis of a series of sulfones, $ArCH_2SO_2R$, in methanol leads to the corresponding sulfinic acids, RSO_2H (accompanied by the bibenzyl derivative), in 26–63% yield (equation 8).

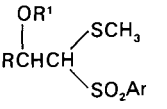
$$ArCH_2SO_2R \xrightarrow[CH_3OH]{h\nu} Ar\dot{C}H_2 + R\dot{S}O_2 \longrightarrow ArCH_2CH_2Ar + RSO_2H \qquad (8)$$

Collins and Whitton[58] have irradiated 1-phenylsulfonyl derivatives of tetra-*O*-acetyl-D-glucose, in both the α- and β-furanosyl and pyranosyl forms, and obtained some of the corresponding (dimeric) dodecitols by radical coupling, accompanied by the product of hydrogen abstraction by the C-1 radical. Ogura and coworkers[59] have successfully employed photolysis under neutral or basic aqueous conditions for the conversion of the protected carbonyl compounds (**27**) into the free α-hydroxyaldehydes and ketones. While no mechanism is postulated, presumably an initial C—SO_2Ar cleavage is again involved.

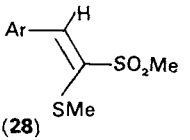
The photochemical extrusion of SO_2 from α-phenylsulfonyl-substituted enone systems, to give the analogous β-phenylenones in modest yield, has also been reported[60]. Where *Z*, *E*-photoisomerization is possible, however, for example in compounds such as **28** or **29**, photoequilibration of the two isomeric sulfones is the dominant process observed[61,62].



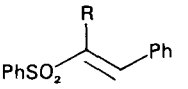
(**26**)



(**27**)
R^1 = Ac or THP



(**28**)



(**29**)
R = H, Me

Wegener and coworkers[63] have reported the detailed investigation of a series of styryl methyl sulfones.

B. Photolysis of Cyclic Sulfones

One of the most extensively investigated topics in the photochemistry of sulfones is the photochemical extrusion of SO_2 from cyclic sulfones. This topic has been reviewed recently by Givens[14] as part of a general review of the photoextrusion of small molecules. Not unexpectedly, the loss of SO_2 from such systems has been observed in many cases and, in general, the photolysis of cyclic sulfones is considerably less complex than for the analogous sulfoxides. For example, straightforward photochemical extrusion of SO_2 is not confined to simple three- and four-membered ring compounds only. Some representative examples of SO_2 extrusion will be presented below, along with some reports of photochemical reactions of sulfones which do not appear to follow the general pattern. The topic of photoextrusion of SO_2 has also been reviewed briefly by Reid[64] as part of a more general review of the photochemistry of oxygen- and sulfur-containing heterocycles.

A few studies have been carried out on the parent four- and five-membered cyclic sulfones—for thietane 1, 1-dioxide (**30**) by Scala and Colon[65] and for thiolane 1, 1-dioxide (sulfolane) (**31**) by Honda and coworkers[66] and, later, by Schuchmann and von Sonntag[67]. In the former compound, the major photochemical process, in the vacuum UV range, is the initial production of a trimethylene (C_3H_6) biradical and SO_2 (equation 9). In both the solid- (77 K) and gas-phase photolyses, formation of a triplet biradical appears to be favored. As well as the expected cyclopropane and propylene, ethylene is also obtained during these photolyses, presumably by a cycloreversion process (equation 10).

$$C_3H_6SO_2 \xrightarrow{h\nu} \cdot CH_2CH_2CH_2 \cdot + SO_2 \tag{9}$$

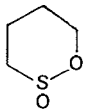
$$C_3H_6SO_2 \xrightarrow{h\nu} C_2H_4 + CH_2{=}SO_2 \tag{10}$$

In the analogous studies of the photolysis of sulfolane (**31**), the work of Honda and coworkers[66] was carried out in the gas phase at 70–130 °C and established the formation of SO_2, ethylene, cyclobutane and acetylene as the major products, on mercury-sensitized photolysis. In considerable contrast, photolysis of sulfolane at 185 nm in the liquid phase[67] produced ethylene($\phi = 0.22$), the sultine (**32**) ($\phi = 0.10$), and "acid" ($\phi = 0.30$). The "acid" is believed to be mainly SO_2, although in parallel experiments on aqueous solutions of sulfolane, a sulfinic acid is also believed to be formed. The authors believe that both four-membered (**33**) and six-membered (**32**) sultines may be formed during these photolyses. Further work in this area would appear to be necessary to unravel the full mechanistic details.

Several studies of the application of the photoextrusion of SO_2 have been conducted in substituted analogs of the parent compounds above. For example, the photolysis of 2-phenylthietane 1, 1-dioxides (**34**), in *dichloromethane or methanol*, at 254 nm affords the expected phenylcyclopropanes in almost quantitative yields[68]. The 2-phenyl substituent

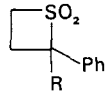
(**30**)

(**31**)



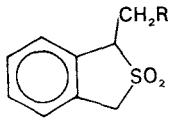
(**32**)

(**33**)

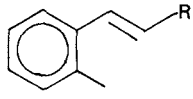


(**34**)

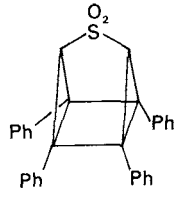
allows the photolysis of these saturated sulfones to be conducted in the normal UV range and may also play an important role in stabilizing the intermediate biradicals. In some contrast, the photolysis of the dihydrobenzo[*c*]thiophene dioxides (**35**) afforded none of the expected benzocyclobutanes, but only the *trans*-alkenes (**36**), arising from a 1, 5-hydride shift (internal disproportionation)[69]. Other examples of the successful photoextrusion of SO_2 in five-membered rings appear in the work of Kellogg and Prins[18] on 2, 5-dihydrothiophenes, discussed earlier in the sulfoxide section, and in the study of a presumed thiaquadricyclane dioxide system (**37**) by Weiss and coworkers[70]. Harpp and



(**35**)

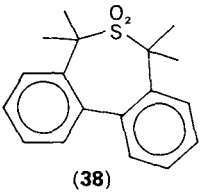


(**36**)

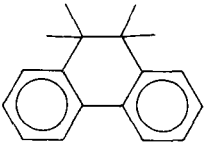


(**37**)

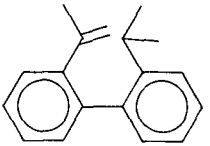
Mullins[71] have shown that the seven-membered cyclic sulfone (**38**) can be converted photochemically at 254 nm, as well as by thermolysis, into a mixture of **39** and **40**. Interestingly, in this series, compound **40**, the result of hydrogen transfer (disproportionation) in the presumed intermediate biradical, remained the major product when different solvents and different wavelengths were employed for the irradiation.



(38)

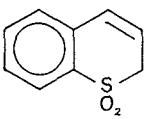


(39)

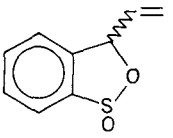


(40)

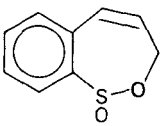
When the ring system containing the sulfone moiety is unsaturated, a quite different set of products has been observed on photolysis, apparently arising from an initial cycloreversion to a short-lived sulfene intermediate. For example, irradiation of 2*H*-1-benzothiopyran 1, 1-dioxide (**41**) in dichloromethane or methanol gave the *cis*- and *trans*-sultines (**42**) and the ring-expanded sultine (**43**) in roughly equal amounts, accompanied by minor amounts ($\sim 5\%$) of the products of formal loss of SO_2, i.e. indene, and SO, i.e. **44**[72]



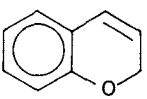
(41)



(42)



(43)

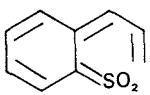


(44)

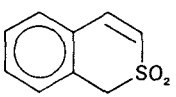
(equation 11). The authors believe that the absence of products arising from trapping by methanol may be rationalized by the very rapid cyclization of the intermediate sulfene (**45**) on either sulfur (to reform the starting compound) or oxygen (to form the sultines).

$$\mathbf{41} \xrightarrow[CH_2Cl_2 \text{ or MeOH}]{h\nu} \mathbf{42}\ (55\%) + \mathbf{43}\ (25\%) + \mathbf{44}\ (5\%) + \text{indene}\ (5\%) \qquad (11)$$

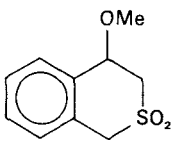
Photolysis of the isomeric sulfone (**46**) in methanol, interestingly, gave mainly the simple methanol adduct (**47**), accompanied by the ring-expansion product (**48**) in only 10% yield.



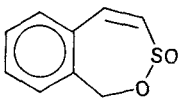
(45)



(46)

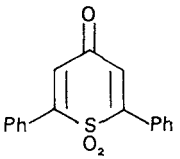


(47)

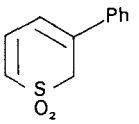


(48)

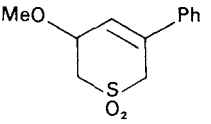
The methanol adduct may arise by photoprotonation of the double bond. A similar photoaddition of methanol has been reported on photolysis of **49**[73]. In a closely related study, King and coworkers[74] have shown that photolysis in methanol of the monocyclic unsaturated sulfone (**50**) gives the methanol adduct (**51**) and the acyclic sulfonate, $CH_2{=}C(Ph)CH{=}CHCH_2SO_2OMe$, in 43 and 30% yield, respectively. Formation of the sulfonate ester in this case strongly supports the intermediacy of the sulfene (**52**) produced on cycloreversion.



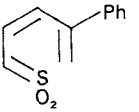
(49)



(50)



(51)

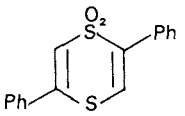


(52)

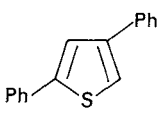
Kobayashi and Mutai[75] have recently reported an interesting rearrangement of the 1,4-dithiin sulfone (**53**) to the thiophenes (**54**) and (**55**) (equation 12). While **54** presumably arises as a result of simple photoextrusion, the rearranged thiophene (**55**) is postulated to arise via the valence isomer (**56**), followed by cyclization to the thiophene, concomitant with, or preceded by, loss of SO_2. Some support for the intermediacy of the thioketone (**56**) was revealed by the isolation of the pyrrole (**57**), when the photolysis was conducted in *n*-butylamine. Compound **57** presumably arises by cyclization of the *N*-butylimine analog of **56** initially formed.

$$\mathbf{53} \xrightarrow[\text{MeOH}]{h\nu} \mathbf{54}\ (1\%) + \mathbf{55}\ (4\%) \tag{12}$$

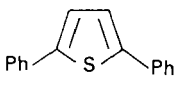
Ried and Bopp[76] have shown that the photolysis of 3,5-diphenyl-4*H*-thiopyran-4-one 1,1-dioxide (**58**) in chloroform very rapidly leads to a trimer, or to photoadducts with



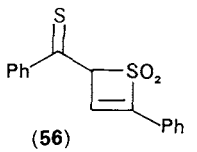
(53)



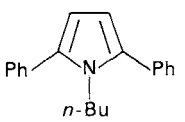
(54)



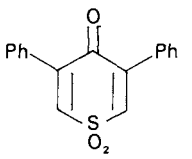
(55)



(56)



(57)



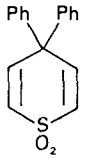
(58)

added dienophiles, arising from the cyclopentadienone formed on photoextrusion of SO_2. This is in remarkable contrast to the results obtained by Sugiyama and coworkers[73] for the isomeric 2,6-diphenyl derivative (**49**), which appears to be quite resistant to photoextrusion. The importance of the substitution pattern in this series has been noted previously[76].

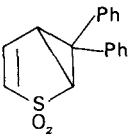
Gravel and Leboeuf[77] have conducted an extensive photochemical investigation of the thiopyran sulfone (**59**) and the analogous sulfide. In addition to the isolation of starting material and the product of simple methanol addition (see above), the rearranged sulfone (**60**) was formed in 15% yield on either direct or sensitized irradiation of **59** in methanol. The authors therefore propose that a di-π-methane type rearrangement occurs in this system, via the lowest (π,π^*) triplet state and vinyl–vinyl bonding in the intermediate (**61**), rather than the phenyl–vinyl bonding observed for the sulfide analog.

Still and coworkers[78] have been able to convert the α-azidosulfone (**62**) into the 1,2-thiazepinone (**63**) in good yield, on photolysis in benzene. The reaction is postulated to

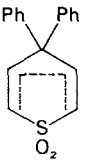
occur via a triplet nitrene, followed by a 1,2-shift of the sulfonyl unit and double bond migration. A later attempt[79] by these workers to extend this photochemical ring-expansion to the α-azidosulfone (**64**) led largely to recovered starting



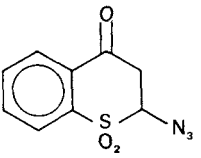
(**59**)



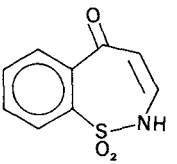
(**60**)



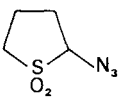
(**61**)



(**62**)



(**63**)



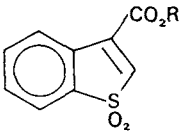
(**64**)

compound, accompanied by a small amount of the acyclic α-disulfone, $NC(CH_2)_3SO_2 \cdot SO_2(CH_2)_3CN$.

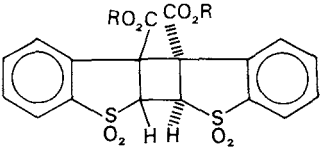
C. [2 + 2] Photodimerization and Photoaddition Reactions of Unsaturated Sulfones

The [2 + 2] photodimerization of α,β-unsaturated sulfones is correctly viewed as a photoreaction of alkenes, rather than the sulfone group, and this aspect has been reviewed recently by Reid[64], as part of a wider survey of the photoreaction of O- and S-heterocycles. The topic continues to attract considerable interest and a few recent examples, as well as some synthetic applications, will be discussed here. Much of the photodimerization work has been carried out on the benzo[*b*]thiophene (thianaphthene) 1,1-dioxide system. For example, Porter and coworkers[80] have shown that both 3-carboxybenzo[*b*]thiophene 1,1-dioxide (**65**) and its methyl ester give only the *head-to-head* (*hth*), *anti* dimer (**66**) on irradiation in ethanol. In a rather unusual finding for such systems, the same dimer was obtained on thermal dimerization of **65**. Similar findings for a much wider variety of 3-substituted benzo[*b*]thiophene 1,1-dioxides have been reported more recently by Geneste and coworkers[81]. In the 2-substituted analogs, the *hth* dimer is accompanied by some of the *head-to-tail* (*htt*), *anti* dimer. The formation of the major dimer appears to proceed by way of an excited triplet and the regiochemistry observed is in accord with frontier MO theory.

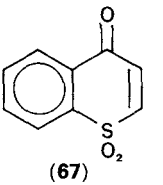
The photodimerization of thiochromone 1,1-dioxide (**67**) has also been studied. In



(**65**)
R = H, Me

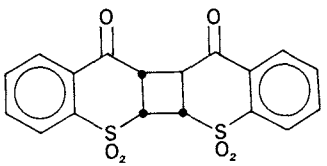


(**66**)

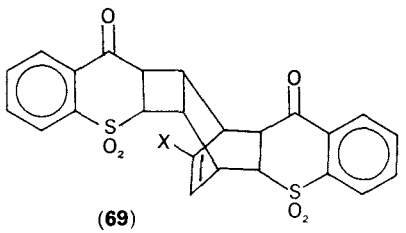


(**67**)

contrast to the simpler thianaphthene sulfone series, four photodimers were obtained in this series, three of which have been shown conclusively to be *hth* type dimers[82]. One of these (**68**) has been found, surprisingly, to possess a *trans*-fused cyclobutane ring junction. This may be accounted for by prior *cis/trans*-isomerization of the double bond in the excited state and concerted [2 + 2] addition to a second (ground-state) molecule or, of course, by addition in nonconcerted fashion via a 1,4-biradical intermediate, as suggested earlier by Geneste and coworkers[81]. Thiochromone 1,1-dioxide was shown earlier[27] to undergo photoaddition with benzene and simple monosubstituted benzenes to give 2:1 adducts, such as **69**. Support for the proposed mechanism in this case comes from the



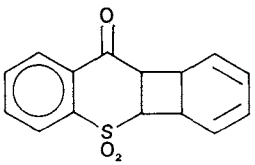
(**68**)



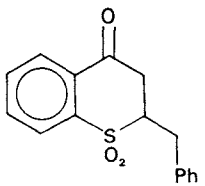
(**69**)

X = H, Cl, CF_3

isolation of a simple Diels–Alder (1:1:1) adduct of the proposed intermediate [2 + 2] photoadduct (**70**) when the photolysis of **67** in benzene was conducted in the presence of the dienophile, *N*-phenylmaleimide. It is noteworthy that this photoaddition failed with electron-rich benzene derivatives, although with toluene as the solvent the benzyl derivative (**71**), as well as bibenzyl, was formed in low yield. The formation of (**71**) clearly



(**70**)



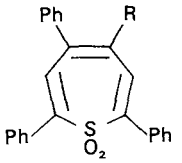
(**71**)

involves a hydrogen transfer, perhaps via an initially formed exciplex. Ishibe and coworkers[83] found that simple[2 + 2] photoadducts were *not* obtained on photolysis of the related 2,6-diphenyl-4*H*-thiopyran-4-one 1,1-dioxide (**49**) in benzene, in the presence of simple acetylenic compounds (equation 13). Instead, the thiepin 1,1-dioxides (**72**), arising by an unexplained photodecarbonylation, were obtained in moderate yields.

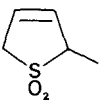
$$\mathbf{49} + \mathrm{PhC{\equiv}CR} \xrightarrow[C_6H_6]{h\nu} \mathbf{72}\ (20\text{–}60\%) \qquad (13)$$

Recent synthetic applications of the photochemical [2 + 2] cycloaddition of unsaturated sulfones have been noted. Musser and Fuchs[84] have effected an intramolecular [2 + 2] addition of a 6-membered ring vinyl sulfone and a five-membered ring vinylogous ester in excellent yield, as part of a synthetic approach to the synthesis of the mould metabolite, cytochalasin C. The stereospecificity of the addition was only moderate, however, and later problems with this synthetic approach led to its abandonment. Williams and coworkers[85] have used the facile [2 + 2] photoaddition of **73** and

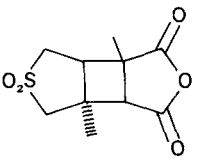
methylmaleic anhydride to produce the adduct (**74**), in 80% yield, in a novel approach to the synthesis of the monoterpene, 10-hydroxygeraniol.



(**72**)
R = H, Me, Ph



(**73**)



(**74**)

IV. REFERENCES

1. E. Block, *Quart. Rep. Sulfur Chem.*, **4**, 237, pp. 315–326 (1969).
2. J. D. Coyle, *Chem. Soc. Rev.*, **4**, 523 (1975).
3. I. W. J. Still, in *Organic Sulfur Chemistry—Theoretical and Experimental Advances*, Elsevier, Amsterdam, 1985, Chap. 11, pp. 596–659.
4. K. Gollnick and H.-U. Stracke, *Pure Appl. Chem.*, **33**, 217 (1973)
5. B. C. Gilbert, B. Gill and M. D. Sexton, *J. Chem. Soc., Chem. Commun.*, 78 (1978).
6. I. Khait, R. Lüdersdorf, K. A. Muszkat and K. Praefcke, *J. Chem. Soc., Perkin Trans. 2*, 1417 (1981).
7. A. G. Schultz and R. H. Schlessinger, *J. Chem. Soc., Chem. Commun.*, 1294 (1970).
8. C. Ganter and J.-F. Moser, *Helv. Chim. Acta*, **54**, 2228 (1971).
9. M. Kishi and T. Komeno, *Tetrahedron Letters*, 2641 (1971).
10. G. Balavoine, S. Jugé and H. B. Kagan, *Tetrahedron Letters*, 4159 (1973).
11. S. Majeti, *Tetrahedron Letters*, 2523 (1971).
12. H. Nozaki, T. Shirafuji, K. Kuno and Y. Yamomoto, *Bull. Chem. Soc. Japan*, **45**, 856 (1972).
13. N. Miyamoto and H. Nozaki, *Tetrahedron*, **29**, 3819 (1973).
14. R. S. Givens, in *Organic Photochemistry*, Volume 5 (Ed. A. Padwa), Marcel Dekker, New York, 1981, Chap. 3, pp. 317–328.
15. L. A. Carpino and H.-W. Chen, *J. Amer. Chem. Soc.*, **101**, 390 (1979).
16. S. Ito and J. Mori, *Bull. Chem. Soc. Japan*, **51**, 3403 (1978).
17. H. Kato, Y. Arikawa, M. Hashimoto and M. Masuzawa, *J. Chem. Soc., Chem. Commun.*, 938 (1983).
18. R. M. Kellogg and W. L. Prins, *J. Org. Chem.*, **39**, 2366 (1974).
19. A. G. Schultz and R. H. Schlessinger, *Tetrahedron Letters*, 3605 (1973).
20. A. G. Schultz and R. H. Schlessinger, *J. Chem. Soc., Chem. Commun.*, 1051 (1970).
21. I. W. J. Still, P. C. Arora, M. S. Chauhan, M.-H. Kwan and M. T. Thomas, *Can. J. Chem.*, **54**, 455 (1976).
22. B. S. Larsen, J. Kolc and S.-O. Lawesson, *Tetrahedron*, **27**, 5163 (1971).
23. N. K. Capps, G. M. Davies, P. B. Hitchcock, R. W. McCabe and D. W. Young, *J. Chem. Soc., Chem. Commun.*, 199 (1983).
24. K. Praefcke and C. Weichsel, *Ann. Chem.*, 333 (1980).
25. K. Kobayashi and K. Mutai, *Tetrahedron Letters*, **22**, 5201 (1981).
26. I. W. J. Still, P. C. Arora, S. K. Hasan, G. W. Kutney, L. Y. T. Lo and K. Turnbull, *Can. J. Chem.*, **59**, 199 (1981).
27. I. W. J. Still and T. S. Leong, *Tetrahedron Letters*, 1097 (1979).
28. R. Lüdersdorf and K. Praefcke, *Z. Naturforsch.*, **31B**, 1658 (1976).
29. R. Tanikaga and A. Kaji, *Bull. Chem. Soc. Japan*, **46**, 3814 (1973).
30. M. S. El Faghi El Amoudi, P. Geneste and J.-L. Olivé, *J. Org. Chem.*, **46**, 4258 (1981).
31. R. H. Schlessinger and A. G. Schultz, *Tetrahedron Letters*, 4513 (1969).
32. L. Carlsen, *Sulfur Rep.*, **3**, 217 (1983).
33. L. Carlsen, N. Harrit and A. Holm, *J. Chem. Soc., Perkin Trans. 1*, 1404 (1976).
34. B. Zwanenburg, A. Wagenaar and J. Strating, *Tetrahedron Letters*, 4683 (1970).
35. G. Karlstrom, B. O. Roos and L. Carlsen, *J. Amer. Chem. Soc.*, **106**, 1557 (1984).

36. L. Carlsen and E. Schaumann, *J. Chem. Soc., Faraday Trans. 1*, 2624 (1979).
37. N. Furukawa, M. Fukumura, T. Nishio and S. Oae, *Phosphorus and Sulfur*, **5**, 231 (1978).
38. N. Furukawa, M. Fukumura and S. Oae, *Chem. Letters*, 209 (1978).
39. N. Torimoto, T. Shingaki and T. Nagai, *Bull. Chem. Soc. Japan*, **51**, 1200 (1978).
40. R. A. Abramovitch and T. Takaya, *J. Chem. Soc., Chem. Commun.*, 1369 (1969).
41. T. Kunieda and B. Witkop, *J. Amer. Chem. Soc.*, **91**, 7752 (1969).
42. Y. Kishida, T. Hiraoka and J. Ide, *Chem. Pharm. Bull.*, **17**, 1591 (1969).
43. M. Nakai, N. Furukawa, S. Oae and T. Nakabayashi, *Bull. Chem. Soc. Japan*, **45**, 1117 (1972).
44. T. Nakabayashi, T. Horii, S. Kawamura and M. Hamada, *Bull. Chem. Soc. Japan*, **50**, 2491 (1977).
45. M. Kobayashi, K. Tanaka and H. Minato, *Bull. Chem. Soc. Japan*, **45**, 2906 (1972).
46. M. Novi, G. Garbarino and C. Dell'Erba, *J. Org. Chem.*, **49**, 2799 (1984).
47. H. H. Thoi, O. Ito, M. Iino and M. Matsuda, *J. Phys. Chem.*, **82**, 314 (1978).
48. W. Rettig and E. A. Chandross, *J. Amer. Chem. Soc.*, **107**, 5617 (1985).
49. T. Yamase, H. Hisada, S. Suzuki and T. Ikawa, *Bull. Chem. Soc. Japan*, **49**, 351 (1976).
50. M. Kobayashi, K. Ochiai and H. Minato, *Chem. Letters*, 433 (1976).
51. R. G. Pews and T. E. Evans, *J. Chem. Soc., Chem. Commun.*, 1397 (1971).
52. O. DeLucchi, G. Licini, L. Pasquato and M. Senta, *J. Chem. Soc., Chem. Commun.*, 1597 (1985).
53. M. P. Cava, R. H. Schlessinger and J. P. VanMeter, *J. Amer. Chem. Soc.*, **86**, 3173 (1964).
54. P. L. Wylie, K. S. Prowse and M. A. Belill, *J. Org. Chem.*, **48**, 4022 (1983).
55. R. S. Givens, B. Hrinczenko, J. H.-S. Liu, B. Matuszewski and J. Tholen-Collison, *J. Amer. Chem. Soc.*, **106**, 1779 (1984).
56. I. R. Gould, C. Tung, N. J. Turro, R. S. Givens and B. Matuszewski, *J. Amer. Chem. Soc.*, **106**, 1789 (1984).
57. R. F. Langler, Z. A. Marini and J. A. Pincock, *Can. J. Chem.*, **56**, 903 (1978).
58. P. M. Collins and B. R. Whitton, *J. Carbohydr. Res.*, **36**, 293 (1974).
59. K. Ogura, T. Tsuruda, K. Takahashi and H. Iida, *Tetrahedron Letters*, **27**, 3665 (1986).
60. Y. Tamura, H. Kiyokawa and Y. Kita, *Chem. Pharm. Bull.*, **27**, 676 (1979).
61. H. A. Selling, *Tetrahedron*, **31**, 2387 (1975).
62. M. A. A. M. El Tabei, N. V. Kirby and S. T. Reid, *Tetrahedron Letters*, **21**, 565 (1980).
63. W. Wegener, D. Palm, G. Michael and K.-D. Schleinitz, *Z. Chem.*, **23**, 59 (1983).
64. S. T. Reid, in *Advances in Photochemistry*, Volume 33, Academic Press, New York, 1983, pp. 1–93.
65. A. A. Scala and I. Colon, *J. Phys. Chem.*, **83**, 2025 (1979).
66. K. Honda, H. Mikuni, M. Takahasi and Y. Morii, *J. Photochem.*, **3**, 199 (1974).
67. H.-P. Schuchmann and C. von Sonntag, *J. Photochem.*, **22**, 55 (1983).
68. J. D. Finlay, D. J. H. Smith and T. Durst, *Synthesis*, 579 (1978).
69. T. Durst, M. Lancaster and D. J. H. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1846 (1981).
70. R. Weiss, C. Schlierf and H. Kolbl, *Tetrahedron Letters*, 4827 (1973).
71. D. N. Harpp and D. F. Mullins, *Can. J. Chem.*, **61**, 757 (1983).
72. C. R. Hall and D. J. H. Smith, *Tetrahedron Letters*, 3633 (1974).
73. H. Aoyama, Y. Sato, T. Nishio and N. Sugiyama, *Bull. Chem. Soc. Japan*, **46**, 1007 (1973).
74. J. F. King, E. G. Lewars, D. R. K. Harding and R. M. Enanoza, *Can. J. Chem.*, **53**, 3656 (1975).
75. K. Kobayashi and K. Mutai, *Chem. Letters*, 1641 (1983).
76. W. Ried and H. Bopp, *Angew. Chem., Int. Ed. Engl.*, **16**, 653 (1977).
77. D. Gravel and C. Leboeuf, *Can. J. Chem.*, **60**, 574 (1982).
78. I. W. J. Still and T. S. Leong, *Can. J. Chem.*, **58**, 369 (1980).
79. I. W. J. Still, W. L. Brown, R. J. Colville and G. W. Kutney, *Can. J. Chem.*, **62**, 586 (1984).
80. W. Davies, B. C. Ennis, C. Mahavera and Q. N. Porter, *Aust. J. Chem.*, **30**, 173 (1977).
81. M. S. El Faghi El Amoudi, P. Geneste and J. L. Olivé, *Nouv. J. Chim.*, **5**, 251 (1981).
82. S. C. Nyburg, L. Prasad, T. S. Leong and I. W. J. Still, *Acta Cryst. [C]*, **42**, 816 (1986).
83. N. Ishibe, K. Hashimoto and M. Sunami, *J. Org. Chem.*, **39**, 103 (1974).
84. A. K. Musser and P. L. Fuchs, *J. Org. Chem.* **47**, 3121 (1982).
85. J. R. Williams, C. Lin and D. F. Chodosh, *J. Org. Chem.*, **50**, 5815 (1985).

CHAPTER 19

Radiation chemistry of sulfoxides and sulfones

ZEEV B. ALFASSI

Department of Nuclear Engineering, Ben-Gurion University of the Negev, Beer Sheva 84102, Israel

I. INTRODUCTION

Radiation chemistry is the study of the chemical effects produced in a system by the absorption of ionizing radiation. This definition includes the chemical effects due to radiation from radioactive sources, high-energy charged particles and short-wavelength (less than about 400 Å)[1] electromagnetic radiation from accelerators. The principal characteristic of high-energy radiation is that it causes ionization in all materials. This makes a distinction between radiation chemistry and photochemistry[2,3]. Photochemistry deals with longer-wavelength electromagnetic radiations which have lower energy (less

than about 30 eV). This relatively low energy leads in many cases only to the excitation of the molecules and does not produce ions. Usually, the energy of the particles and photons applied in radiation chemistry is much higher. The whole energy is not absorbed by a single molecule, as in photochemistry, but rather distributed over several molecules, along the track of the ionizing particle or photon. The high-energy photons and particles are not selective and may ionize, excite or dissociate any molecule lying in their path, while in photochemistry only some compounds may interact with the radiation, in accordance with the energy of the photons.

The high-energy photons or particles lose energy in successive events and produce primary electrons which in turn produce several secondary electrons with lower energies[4]. The chemical effects of ionizing radiation occur almost exclusively through the secondary electrons most of which have less than 100 eV. These electrons will cause ionization and excitation of the surrounding molecules and will lose energy until they reach thermal energies. In many solvents these thermal electrons polarize the solvent and are bound in a stable quantum state to it; these electrons are called solvated electrons.

The study of radiation chemistry might be divided, from the experimental point of view, into two parts. The first is the study of unstable intermediates which have short lifetimes and thus cannot be studied by the usual methods of chemistry. The second part is the study of the final products of the radiolysis which are measured by common chemical techniques.

One way to make the short-lived intermediates amenable to study is to increase their lifetime, usually by irradiating in the solid state and at very low temperatures. Then, the intermediates can be measured at the end of the irradiation by optical absorption spectroscopy or ESR.

Another method of making the lifetime longer in the liquid phase is by adding compounds which, upon addition of radicals, produce long-lived radicals; this method is called spin trapping[5].

More common in the liquid phase is pulse radiolysis[6]. In this technique, electron accelerators which can deliver intense pulses of electrons lasting a very short time (ns up to μs) are used. Each single pulse can produce concentrations of intermediates which are high enough to be studied by methods such as light absorption spectroscopy or electrical conductivity.

The yields of radiolysis products are always expressed by the G value, which is defined as the number of particles (molecules, radicals, ions) produced or consumed per 100 eV of energy absorbed in the system.

The units for the absorbed energy (dose) are the rad, defined by 1 rad = 100 erg/g = 6.243×10^{13} eV/g, and the Gray (Gy) defined by 1 Gy = 100 rad.

II. PRIMARY SPECIES IN THE RADIOLYSIS OF SULFOXIDES

A. Crystalline Sulfoxides

Nishikida and Williams[7] studied the ESR spectra of a gamma-irradiated single crystal of dimethyl sulfoxide (DMSO). The irradiation was done at 77 K and then the samples were annealed for 10 min at 253 K. The ESR spectra were taken at various temperatures and it was found that the spectrum is temperature dependent. At 183 K the main spectrum consists of two 1:3:3:1 quartets, the hfs being 11.6 G in each case. In addition, two groups of weak lines displaying the same quartet structures are found and their integrated absorption intensities are 500 times less than those of the corresponding lines in the main spectrum. These satellites can be assigned to the outer $m_I = \pm\frac{3}{2}$ components of the ^{33}S spectrum present in natural abundance. Additional proof of the ^{33}S interaction was obtained from the observation of both $m_I = -\frac{1}{2}$ and $m_I = +\frac{3}{2}$ components in a single crystal of perdeuterated dimethyl sulfoxide (DMSO-d_6) where the main spectrum is

narrowed considerably. These observations show that the radical contains sulfur and three equivalent hydrogens, indicating that the spectrum is due to the $\cdot CH_3SO$ radical. This assignment is further supported by the similarity of ^{33}S hyperfine splitting tensors of this radical and the isoelectronic SO_2.

Chung and coworkers[8] studied the ESR and absorption of γ-irradiated crystalline dimethyl sulfoxide-d_6 at 77 K. They found that the ESR spectrum is composed of an isotropic well-resolved multiplet and an unisotropic broad overlapping resonance at low field. The narrow multiplet consists of a septet pattern with intensity ratios (1:3:6:7:6:3:1) characteristic of coupling to three equivalent ^2H nuclei. The isotropic ^2H hfs was found to be 2.99 ∓ 0.05 *G*, appreciably smaller than the corresponding hfs of 3.576 G for the free $\cdot CD_3$ radical[9]. The ESR results are consistent with a radical spin density of about 0.84. The absorption spectrum recorded immediately after γ irradiation at 77 K consists of a strong band centered at 540 nm. Both this absorption band and the ESR spectrum can be eliminated either by photobleaching with a visible light from a tungsten lamp or by heating to 82 K and waiting for one hour. The annealing and photobleaching studies provide independent proof that the septet ESR spectrum and the 540-nm absorption belong to the same intermediate species. The possibility that this species is the $\cdot CD_3$ radical can be ruled out as the absorption band of methyl radicals is located near 215 nm[10] and as the septet ESR spectrum indicates a spin density of less than unity.

The intermediate species cannot either be a methylsulfinyl radical ($CD_3SO\cdot$), as the $CD_3SO\cdot$ radical which was found after annealing at 253 K[7] was found to have ^2H hfs for the freely rotating $\cdot CD_3$ group in this radical of only 1.80 *G*. The possibility that this species is the methylsulfinyl radical pair can be rejected in view of the absence of ESR anisotropy. Consequently Chung and coworkers[8] suggested that this species is the methyl radical-methanesulfenate pair $\cdot CD_3 \cdots CD_3SO^-$, similarly to the formation of weakly interacting alkyl radical-anion pairs formed by the process of dissociative electron capture in γ-irradiated crystalline alkyl halides and pseudohalides. Chung and coworkers said that while an assignment of this species to the undissociated $(CD_3)_2SO^-$ radical anion cannot be completely ruled out, it seems highly unprobable due to the spin density of 0.84 concentrated at the axial methyl group.

In the case of the $(CD_3)_2SO^-$ radical anion it is expected that a larger part of the spin will be on the O-group (see Figure 1).

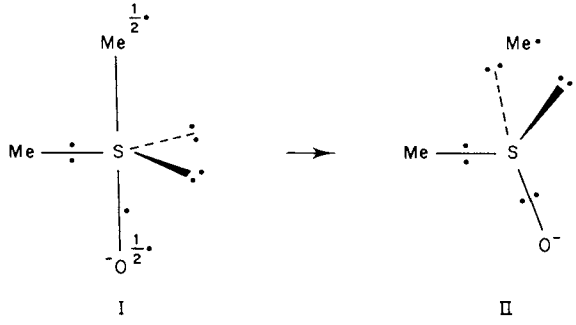


FIGURE 1. Structures for Me_2SO^-(I) and $MeSO^- \cdots Me$(II). The assignment of 0.5 spin density to each of the two axial ligands in I is only applicable to equivalent ligands in the Rundle formulation. Qualitatively, more spin density is expected to reside on the axial methyl than on the O^- group. Reproduced by permission of the authors from Reference 8.

Chung and coworkers tried to observe similar species in γ-irradiated DMSO-h_6 at 77 K, however, repeated attempts were unsuccessful. Besides no free $\cdot CH_3$ radicals were detected in the γ-irradiated DMSO-h_6. They suggested that this remarkable difference of an 'all-or-nothing' deuterium effect might be connected with the very much larger reactivity of the methyl radical in a subsequent reaction of hydrogen abstraction due to the greater reactivity of the C—H over the C—D bond.

$$\cdot CH_3—CH_3SO^- \longrightarrow CH_4 + \cdot CH_2SO^- \quad (1)$$

This explanation was substantiated by the ESR detection of the $\cdot CH_3—CH_3SO^-$ species below 50 K following gamma irradiation of $(CH_3)_2SO$ at 4 K[11]. Irradiation at 77 K of CH_3SOCD_3 leads to detection of only $\cdot CH_3—CD_3SO^-$ but not $\cdot CD_3—CH_3SO^-$ and the decay of $\cdot CH_3—CD_3SO^-$ species parallels exactly that of the $\cdot CD_3—CD_3SO^-$ species at the same temperature. Symons[12] repeated the ESR study for $(CH_3)_2SO$ at 77 K and he also did not find any methyl radicals; however, he found methyl radicals in dilute solutions of $(CH_3)_2SO$ in $(CD_3)_2SO$, due probably to the fact that the $CH_3\cdot$ radicals abstract hydrogen atom not from the other CH_3 group in the adduct pair (reaction 1) but from another molecule (reaction 2). In the case of a dilute solution of $(CH_3)_2SO_4$ in $(CD_3)_2SO_4$ the CH_3 radicals cannot abstract a deuterium atom.

$$\cdot CH_3 + (CH_3)_2SO \longrightarrow CH_4 + \cdot CH_2S(O)CH_3 \quad (2)$$

Symons[12] also found that in the case of irradiated $(CD_3)_2SO$ at 77 K during the annealing process the hfs is changed from the value of the adduct (2.95 *G*) to that of the free $\cdot CD_3$ radicals (3.5 *G*).

Shislov and coworkers[13] studied the photochemical transformation of the paramagnetic particles of irradiated polycrystalline DMSO-d_6 in order to evaluate the energy of the electrons involved in the formation of the anion-radical pair.

$$CD_3SOCD_3 + e^- \longrightarrow \cdot CD_3—CD_3SO^- \quad (3)$$

That 'hot' (non-thermal) electrons are involved in the formation of this species is clear, due to the observation that its ESR intensity does not decrease when acceptors of thermal electrons, e.g. CCl_4 and Cd^{+1}, were introduced. However, these electron scavengers reduce sharply the ESR signal due to the anion radicals of DMSO which are a minor part of the spectrum. The action of light with $\lambda = 540$ nm on γ-irradiated DMSO-d_6 at 77 K leads to the disappearance of the septet ESR spectrum and to increase in the anisotropic signal, keeping the total number of paramagnetic particles almost unchanged. Shislov and coworkers[13] suggested that the anisotropic signal is due to the anion radical of DMSO-d_6. The photochemical reaction is the transformation of the anion-radical pair (the adduct) to the anion radical:

$$\cdot CD_3—CD_3SO^- \xrightarrow{\lambda = 540\,nm} (CD_3SOCD_3)^{\cdot -} \quad (4)$$

The violet color of the anion radical pair is changed to the yellow color of the anion radical. The replacement of the septet of the adduct by an anisotropic spectrum and the change of the color from violet to yellow occurs also on prolonged standing of a freshly irradiated sample of DMSO-d_6 at 77 K (~ 15 h[8,13]).

The irradiation of the yellow sample by light with $\lambda = 363$ or 400 nm leads to the restoration of the violet color and the septet ESR spectrum.

$$[CD_3SOCD_3]^{\cdot -} \xrightarrow{\lambda = 380\,nm} \cdot CD_3—CD_3SO^- \quad (5)$$

If we assume[13] that both photochemical reactions 4 and 5 proceed through the same

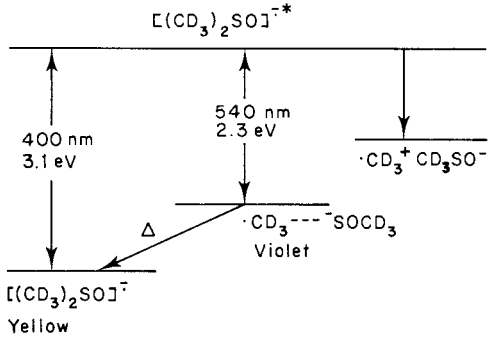


FIGURE 2. Energy diagram of photochemical reactions in γ-irradiated DMSO-d_6 at 77K.

excited state and that same excited state is responsible also for the partial formation of free radicals (very little in the case of the radical anion pair but 30–50% in the case of the radical anion)

$$(CD_3)_2SO^{-} \longrightarrow \cdot CD_3 + CD_3SO^{-} \tag{6}$$

then the photochemical reactions can be presented by an energy diagram given in Figure 2.

Assuming that reaction 3 leads also to the same excited state $[(CD_3)_2SO]^{-}*$, Shislov and coworkers[13] calculated that the energy of the 'hot' electrons in reaction 3, E_e is given by

$$E_e = h\nu_{400}\text{-EA} \tag{7}$$

where EA is the electronic affinity of a DMSO molecule. Assuming $EA_{DMSO} \sim EA_{SO} =$ 1.1 eV they got $E_e \sim 2$ eV. This result agrees with their findings that the maximum of yields of negative ions of DMSO-d_6 and DMSO-h_6 in mass spectra is for an electron energy of 2.1 eV.

Shislov and coworkers[14] studied the formation of radical-anion pairs in γ-irradiated diethyl sulfoxide (DESO) in order to test whether the higher stability of $\cdot CD_3 — {}^{-}S(O)CD_3$ relative to $\cdot CH_3 — {}^{-}SOCH_3$ is due to the larger mass of $\cdot CD_3$ compared to $\cdot CH_3$. They found ESR spectra hfs of 21 *G* as compared to 26 *G* usually. The decrease in the hfs is one of the characteristic signs of a radical anion pair[15]. At the temperature of liquid nitrogen the radical-anion pair in DESO exists for weeks, as compared to 15 h for DMSO-d_6 and none at all for DMSO-h_6. Shislov and coworkers[14] explained qualitatively the dependence of the stability of the pairs on the mass of the particles forming them, by consideration of the main vibrational states of the pairs in the potential energy well. The main vibrational states of two associated quasi-particles A and B^{-} will be deeper in the potential well, the larger their masses.

Shislov and coworkers[14] found that the radical-anion pair irradiated in DESO behaved similarly to that in γ-irradiated DMSO-d_6: (a) it is formed by 'hot' electrons since its formation is not inhibited by thermal electron scavengers; (b) its ESR spectra and visible color (red) can be changed either by photochemical reaction with light of $\lambda = 500$–540 nm or by thermal annealing. The photobleaching of the red sample leads to two products, a species with ESR spectra of a free ethyl radical together with a five-component signal assigned to the molecular radical anion of DESO while thermal annealing leads only to the

second product.

$$\cdot C_2H_5—SOC_2H_5^- \xrightarrow{\lambda=500-540\text{nm}} \begin{cases} \longrightarrow \cdot C_2H_5 + C_2H_5SO^- \\ \longrightarrow [(C_2H_5)_2SO]^{\cdot-} \end{cases} \quad (8)$$

Irradiation of the molecular radical anion of DESO, which has a yellow color, with light of $\lambda = 350$–400 nm partially restores the red color and the ESR spectrum of the radical-anion pair. Similarly to the case of DMSO-d_6 a comparison of the energetics of the photodissociation of the radical anion and dissociative capture of an electron by a DESO molecule permits an estimation of the energy of the 'hot' electrons which form the radical-anion pair of DESO. This energy is equal to ~ 2 eV, similarly to DMSO-d_6. The spin density on the ethyl radical in the radical-anion pair of DESO can be estimated from the decrease in hfs in comparison with the free radical to be 0.81, smaller than DMSO-d_6.

Shislov[14,16] observed radiothermoluminescence associated with the recombination of radical-anion pairs in γ-irradiated DMSO-d_6 (peak at 105 K) and DESO (peak at 153 K). The equation of the reaction giving the indicated luminescence can be written in general as follows:

$$\cdot A—B^- \longrightarrow [AB]^{\cdot-*} \longrightarrow [AB]^{\cdot-} + h\nu \quad (9)$$

In the case of DESO it was found that the radiothermoluminescence spectrum at 153 K lies in the region of 400–700 nm. Shislov and colleagues[16] proposed an energy model of radical-anion pairs to explain the observed radiothermoluminescence. In this model the minimum energy corresponding to the pair is coupled not with the ground state of the radical anion, but with the electronically excited state. During radiolysis there is a resonance dissociative capture of low-energy electrons by the sulfoxide molecules and the formation of electronically excited states of the radical anions, which are stabilized in the form of a radical-anion pair at 77 K. Thermal activation of the pairs may lead both to complete dissociation and to recombination of the pair into a radical anion. From the ground state of the radical anion we can obtain again a radical-anion pair photochemically (see Figure 3).

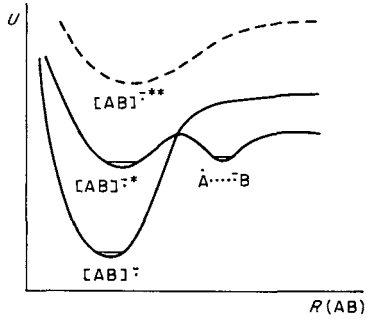


FIGURE 3. Qualitative energy model of a radical-anion pair in sulfoxides where A = CH_3, C_2H_5; B = $^-SOCH_3$, $^-SOC_2H_5$; u is the potential energy; R(AB) is the distance between A and B. Reproduced by permission of the authors from Reference 16.

In certain cases the radical-anion pairs are considered as an example of a 'covalent bond, close to zero'[15] and an isolated pair outside a crystal was depicted[17], however Shislov and coworkers[16] proposed that more likely the entire potential well for the radical-anion pairs is completely the result of the action of the crystal lattice[18]. As a proof they used their observation that radical-anion pairs are not formed in irradiated frozen aqueous-sulfoxide glasses.

Trofimov and coworkers[19] studied the yields of the radicals by ESR in the radiolysis at 100–110 K of diphenyl sulfoxide and tetramethylene sulfoxide. They found for tetramethylene sulfoxide a higher yield of radicals ($G = 1.8$) than for tetramethylene sulfide ($G = 0.45$).

Introduction of a sulfur atom into saturated hydrocarbons leads to a considerable decrease, by an order of magnitude, in the yield of radicals [G(radicals) for hydrocarbons ~ 4[20]]. This was explained as due to the existence of low-lying d-orbitals at the sulfur atom. This explanation agrees with the observation that this decrease is smaller in the case of insertion of a SO group, as there are four p electrons of the S atoms which may be excited at the d-orbital for sulfide and only two p electrons in the case of sulfoxides. Additional proof is that for sulfones, where there is no available p electron, the yield of the radicals [G(radicals) = 3.7 for tetramethylene sulfone] is about the same as for hydrocarbons.

For the case of diphenyl sulfoxide the yield of the radicals is very low ($G = 0.1$), not much different than for diphenyl sulfide.

B. Liquid Sulfoxides

Kemp and coworkers[21] employed the pulse radiolysis technique to study the radiolysis of liquid dimethyl sulfoxide (DMSO) with several amines as solutes [triphenylamine, and N, N, N', N'-tetramethyl-p-phenylenediamine (TMPD)]. The radiolysis led to the formation of transient, intense absorptions closely resembling those of the corresponding amine radical cations. Pulse radiolysis studies determine only the product $G\varepsilon$, where G is the radiolytic yield and ε is the molar absorption. Michaelis and coworkers[22] measured ε for $TMPD^+$ as $1.19 \times 10^4\ M^{-1}\ s^{-1}$ and from this a G value of 1.7 is obtained for $TMPD^+$ in DMSO. The insensitivity of the yield to the addition of electron scavenger (N_2O) and excited triplet state scavenger (naphthalene) proved that this absorption spectrum belonged to the cation.

Hayon[23] studied the yields of ions and excited states in pulse radiolysis of liquid DMSO using anthracene as a solute to determine the yield of free ions and naphthalene as a solute to measure the yield of triplet excited states. Anthracene is known to react with solvated electrons to give the anthracene radical anion, $A^{\cdot-}$

$$A + e_{sol}^- \longrightarrow A^{\cdot-} \tag{10}$$

which has a visible absorption spectra with a maximum at $\lambda \sim 720$ nm. Assuming that for DMSO $\varepsilon A^{\cdot-max} = 9.9 \times 10^3\ M^{-1}\ cm^{-1}$ as was found in tetrahydrofuran[24], it was found that the radiolytic yield of solvated electrons in DMSO is $G = 1.62$. The yield of $A^{\cdot-}$ is considered to be equal to the yield of the free electrons, in other words it is the yield of electrons which escape the Coulombic attraction of their counter-ions and become thermalized in DMSO.

Kira and coworkers[25] found that in deaerated DMSO solution of *trans*-stilbene both the solute cation and anion are produced and the anions are eliminated by aeration. Since they found[26] that the absorption spectra of the anthracene cation and anion are quite similar, they suggested[25] that the absorption spectrum observed by Hayon for anthracene solution in DMSO is a superposition of the spectra of the solute cation and anion. This observation casts a serious question on the yield of solvated electrons found by Hayon[23].

Another disadvantage of the work of Hayon is that he did not substract the absorption of the initial products in the radiolysis of DMSO itself[27–29], as was done in later works[30].

Koulkes-Pujo and colleagues[27] measured the yield of anthracene anion radicals in DMSO solution 10^{-1} M in Br^- and 5×10^{-3} M in anthracene (the same concentration as Hayon[23]) and obtained $G(A^{\cdot-}) = 0.64$. No explanation for the difference between the two results can be given. Cooper and coworkers[30] measured $G(A^{\cdot-})$ for DMSO solutions containing varying concentrations of anthracene and found that from 5 mM to 20 mM anthracene there is not much increase in $G(A^{\cdot-})$ and they obtain for 5 mM anthracene $G(A^{\cdot-}) = 1.2$ after correction for the absorption of the other species in DMSO. This value agrees better with Hayon's result of 1.62[23] before correction, but does not agree with Koulkes-Pujo and coworkers' result[27] of 0.64 although the difference might be due to an absorbed dose higher by two orders of magnitude in the latter study. Cooper and coworkers[31] found that there are two steps in the formation of $A^{\cdot-}$. This suggests that anthracene scavenges the anionic product resulting from reaction of the solvated electron with the solvent, as well as either the solvated electron or its precursor or both.

Bensasson and Land[29] used biphenyl as electron scavenger and obtained $G(e^-) \sim 1.4$ for 10^{-2} M and 1.8 for 10^{-1} M. Neglecting the result of Koulkes-Pujo and coworkers[27] it can be concluded that the yield of the free ion is 1.4 ∓ 0.2.

Koulkes-Pujo and colleagues[27] and Cooper and colleagues[30] measured the yield of $Br_2^{\cdot-}$ in irradiated DMSO containing Br^- at concentration of $5.10^{-3} < [Br^-] < 0.1$ M and obtained $G\varepsilon = 1.5 \times 10^4$. Assuming $\varepsilon(Br_2^{\cdot-})$ in DMSO is the same as in aqueous solution (1.0×10^4 M^{-1} cm^{-1} [33]) lead to G for the oxiding species, probably the positive ion, of 1.5.

From the pulse radiolysis of DMSO solutions of naphthalene and the absorption of the naphthalene triplets ($\varepsilon = 2.26 \times 10^4$ M^{-1} cm^{-1}) Hayon[23] found that the yield of triplet excited states in irradiated DMSO is $G = 0.57$ and $G = 0.36$ for DMSO saturated with argon gas or N_2O gas, respectively.

The presence of N_2O reduces the yield of triplet excited molecules since at least part of these are due to reaction of electrons with either the solvent molecules (S) or solute molecules (D).

$$\begin{aligned} S &\longrightarrow S^+ + e^- \text{ or } {}^1S \text{ or } {}^3S \\ S^+ + e^- &\longrightarrow {}^1S \text{ and/or } {}^3S \\ e^- + S/D &\longrightarrow S^{\cdot-}/D^{\cdot-} \\ S^+ + D &\longrightarrow S + D^+ \\ S^{\cdot-}/D^{\cdot-} + S^+/D^+ &\longrightarrow S + {}^1D/{}^3D \text{ or } D + {}^1S/{}^3S \end{aligned} \tag{11}$$

Cooper and Walker[31] measured the yield of the gaseous products obtained in γ-radiolysis of pure liquid DMSO and DMSO with several additives. The gaseous products in γ-radiolysis of pure liquid DMSO are hydrogen, methane and ethane. The addition of nitrous oxide (N_2O) leaves the yields of hydrogen and ethane almost unchanged; the yield of methane decreased and nitrogen is also formed. $G(N_2)$ is increasing with the concentration of N_2O up to 0.09 M, which is the largest attainable concentration. No simple plateau is evident and $G(N_2)$ increases from 1.4 to 1.8 over the range 0.03 to 0.09 M. N_2 can be formed in irradiated DMSO by one of the following reactions:

$$e_S^- + N_2O \longrightarrow N_2 + O^{\cdot-} \tag{12}$$

$$H^{\cdot} + N_2O \longrightarrow N_2 + OH^{\cdot} \tag{13}$$

$$R^{\cdot} + N_2O \longrightarrow N_2 + RO^{\cdot} \tag{14}$$

$$DMSO^{\cdot-} + N_2O \longrightarrow N_2 + DMSO_2^{\cdot-} \tag{15}$$

In this scheme $DMSO^{\cdot-}$ is to be regarded as a solvent anion formed by an electron attachment or solvent decomposition from free or solvated electrons. Reaction 13 can be

disregarded as hydrogen atom scavengers (methanol or isopropanol) did not change $G(N_2)$, and as $G(H_2)$ is almost the same in the radiolysis of DMSO in the presence or absence of N_2O. Reaction 14 can also be disregarded on the basis of competition of N_2O with I_2. Iodine is known in other systems to be a much better radical scavenger than N_2O, yet the competition of iodine and nitrous oxide in the case of nitrogen formation in DMSO shows almost equal reactivity towards the precursor of nitrogen. Thus the yield of N_2 is equal to the yield of the free anions e_S^- and $DMSO^-$ ($G = 1.4$ to 1.8). However the curvature of $G(N_2)$ at $[N_2O] > 0.03$ M is not understood yet. It might be due to reactions of $DMSO^-$, the fate of which in the absence of N_2O is not known. Cooper and Walker[27] believe that any solvated electrons formed in DMSO do not resemble in reactivity the strongly-solvated electrons found in other highly polar solvents, such as water, due to the following observations: (1) While some electron scavengers, e.g. H^+, Ag^+ and CCl_4, reduce the yield of N_2 in the radiolysis of DMSO + N_2O, acetone which is a good electron scavenger in aqueous solution does not reduce $G(N_2)$. (2) Analyzing the reduction of $G(N_2)$ through normal competition kinetics yields different values for k_S/k_{N_2O} in DMSO and water, where k_S and k_{N_2O} are the rate of the reaction of the precursor of nitrogen with the scavenger and with nitrous oxide, respectively. Cooper and Walker argued finally that most of N_2, at least at high N_2O concentration, is formed by reaction 15.

The pulse radiolysis of pure liquid dimethyl sulfoxide was measured by three groups[27–30]. The absorption spectrum of transient species produced in the radiolysis of pure liquid DMSO at room temperature consists of at least four principal bands (Figure 4). The bands can be attributed to different species according to their different behavior towards scavengers and their different decay time. The fastest decaying species decay by a first-order kinetics with half-life of 14 ns and have a broad absorption stretching into the IR with $\lambda_{max} > 1500$ nm.This band is assigned to the solvated electron in DMSO due to the following reasons: (a) It is reduced or eliminated by known electron scavengers

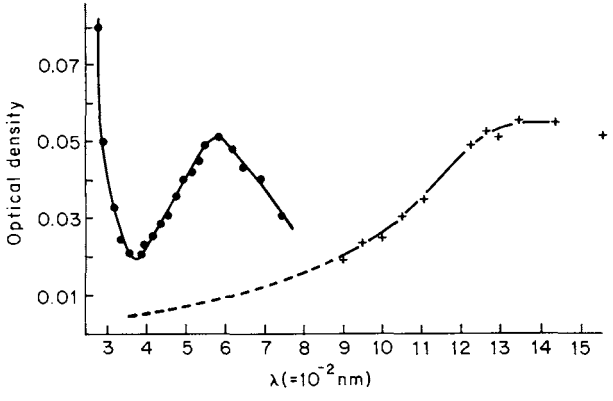


FIGURE 4. Transient absorption spectrum immediately after pulse radiolysis of dimethyl sulphoxide alone. Pulse length 50 ns, dose 1000–2000 rad; •, path length 2.5 m, time resolution 3 ns; +, path length 5 cm, time resolution 10 ns. The dashed line represents the spectrum of the short-lived component ($t_{1/2}$, 14 ns), subtracted from the overlapping longer-lived component which is unaffected by N_2O. Reproduced by permission of the authors from Reference 29.

such as O_2, N_2O, Ag^+, H^+, naphthalene and CCl_4. (b) It is unaffected by the addition of Br^- which is known to react with oxidizing agents. (c) Its shape, intensity and position resemble that found in irradiated glassy hydrocarbon compounds where it is attributed to trapped electrons.

A second band which is centered at 600[28,29]–625[27] nm was found to decay by second-order kinetics with $k/\varepsilon = 2 \times 10^7 M^{-1}s^{-1}$ and its first half-life is 6 μs[27] or 0.8 μs[28,30]. This band is attributed to an oxidizing species, either solvent cations or their decomposition products. This assignment is based on the following observations: (a) In the presence of Br^- this band is eliminated and replaced by a band at 375 nm which is the Br_2^- absorption band. (b) The absorption is not diminished by the addition of electron scavengers such as N_2O, anthracene, H^+ and Ag^+. (c) High concentrations of efficient electron scavengers, which may inhibit neutralization of geminate ions, increased the absorption of this band (e.g. 0.5 M Ag^+ increased it by 90%).

There are at least two longer-lived absorption bands which lie at shorter wavelengths than 600 nm. Koulkes-Pujo and coworkers[27] observed a > 300 nm band which decays by first-order kinetics with a half-life of 1.35 μs and another band in this region with longer half-life. Walker and colleagues[28] found that the UV absorption has at least two components with decay half-lives of $\sim 12\,\mu$s and > 1 ms while Cooper and coworkers[30] gave the half-lives as $\sim 10\,\mu$s and $> 100\,\mu$s. No assignment was given for these relatively long-lived bands.

Cooper and coworkers[30] measured also the absorption spectrum of transient species produced in the radiolysis of pure liquid DMSO-d_6 and found the same absorption of the first two bands, however, the intensity of the absorption is about $\sim 30\%$ larger in the case of the deuterated compound for both of the absorption bands. The intensity of the absorption is given by $G\varepsilon$, but as the same change was found for both bands it seems most reasonable that the 30% difference arises from a change in G rather than in ε. This is similar to water, where the fraction of ions which become free ions is substantially larger for the deuterated compound[32].

Different yields, mainly of the oxidizing species, were found by Koulkes-Pujo and Berthou[34] who studied the system Fe^{+2}/DMSO in the presence of high concentration of H_2SO_4. They found that the yields of the primary species in acidic media are $G_H = 2.1 \pm 0.3$ and G_{OX} (for the oxidizing species) $= 3.8 \pm 0.4$. These results are supported by studies of the system Ce^{4+}/DMSO in the presence of H_2SO_4[35]. Assuming that the radicals have stoichiometric equivalence to those found in water–DMSO mixtures, we may write the observed $G(-Ce^{4+}) = 13.9 + 0.4$ as equal to $= 3G_{OX} + G_H = 13.5$. The difference between the yields in acidic media and for pure DMSO is due to reaction of H^+ with the precursors of these species.

C. Aqueous Solutions of Sulfoxides

Irradiation of dilute aqueous solutions results in the interaction of the ionizing radiation with water molecules. The radiolysis of water produces hydrated electrons (e_{aq}^-, $G = 2.8$), hydrogen atoms ($G = 0.6$) and hydroxyl radicals ($G = 2.8$) which react with the molecules of the solutes. The use of special scavengers can convert one species to another, e.g.

$$e_{aq}^- + H^+ \longrightarrow H^\cdot \tag{16}$$

$$e_{aq}^- + N_2O + H_2O \longrightarrow N_2 + OH^\cdot + OH^- \tag{17}$$

or eliminate one of the species, e.g., *t*-butyl alcohol is used to scavange only OH radicals, and isopropanol to scavange both $H^\cdot$ and $OH^\cdot$ radicals.

Meissner and coworkers[36] studied the pulse radiolysis of aqueous solutions of dimethyl sulfoxide. It was found that hydrated electrons react with DMSO with a rate constant of

$2.0 \times 10^7\ M^{-1}\ s^{-1}$ to give an anion which absorbs at 350 nm.

$$e_{aq}^- + (CH_3)_2SO \longrightarrow (CH_3)_2SO^{\cdot -} \tag{18}$$

In the presence of H^+ this gives the acidic form $(CH_3)_2SOH$, a species which is formed also by the reaction of $OH^\cdot$ with dimethyl thioether.

$$(CH_3)_2SO^{\cdot -} + H^+ \longrightarrow CH_3\overset{\displaystyle OH}{\overset{|}{\dot{S}}}CH_3 \tag{19}$$

The pK_a value of the equilibrium was found to be equal to 10.2. Meissner and coworkers[36] studied also the reaction of OH radicals with DMSO, however, the product of this reaction has no optical absorption in the range 270–800 nm and they measured only the rate of this reaction by a competition method and obtained $k = 4.2 \times 10^9\ M^{-1}\ s^{-1}$.

The reaction of $OH^\cdot$ radicals with dimethyl sulfoxide in aqueous solution was studied already in 1964 by Norman and coworkers[37,38]. They used the system T_1^{III}–H_2O_2 to produce $OH^\cdot$ radicals and using ESR/rapid mixing techniques they were able to demonstrate elimination of a methyl radical during the $OH^\cdot$ induced oxidation. Further studies showed the formation of sulfinic radicals in this reaction either directly or by spin trapping experiments[39–44].

Due to the high rate of reaction observed by Meissner and coworkers[36] it is unlikely that the reaction of $OH^\cdot$ with DMSO is a direct abstraction of a hydrogen atom. Gilbert and colleagues[41] proposed a sequence of four reactions (equations 20–23) to explain the formation of both $CH_3^\cdot$ and $CH_3SO_2^\cdot$ radicals in the reaction of $OH^\cdot$ radicals with aqueous DMSO. The reaction mechanism started with addition of $OH^\cdot$ radical to the sulfur atom [they revised the rate constant of Meissner and coworkers[36] to $7 \times 10^9\ M^{-1}\ s^{-1}$ according to a revision in the hexacyanoferrate(II) standard]. The S atom in sulfoxides is known to be at the center of a pyramidal structure with the free electron pair pointing toward one of the corners which provides an easy access for the electrophilic $OH^\cdot$ radical.

$$(CH_3)_2SO + OH^\cdot \longrightarrow (CH_3)_2S(O)OH^\cdot \tag{20}$$

$$(CH_3)_2S(O)OH^\cdot \longrightarrow {}^\cdot CH_3 + CH_3SO_2H \tag{21}$$

$${}^\cdot CH_3 + CH_3SOOH \longrightarrow CH_3SO_2^\cdot + CH_4 \tag{22}$$

$${}^\cdot CH_3 + CH_3SO_2^\cdot \longrightarrow (CH_3)_2SO_2 \tag{23}$$

Gilbert and coworkers[42] found the same behavior of $OH^\cdot$ radicals with other aliphatic sulfoxides. In many of these cases the $OH^\cdot$ adduct is decomposed to the sulfonyl radical.

Veltwisch and colleagues[45] studied the reaction of $OH^\cdot$ with several sulfoxides by pulse radiolysis using electrical conductivity for the detection of formation or disappearance of ions. Pulse radiolysis of N_2O-saturated aqueous solution of DMSO (10^{-3} M) leads to a decrease in conductivity at basic pH (pH = 9.0) and an increase in conductivity at acidic pH (pH = 4.4). This is explained by the reactions

$$(CH_3)_2SO + OH^\cdot \longrightarrow CH_3^\cdot + CH_3SO_2^- + H^+ \quad \text{acidic pH} \tag{24}$$

$$(CH_3)_2SO + OH^\cdot + OH^- \longrightarrow CH_3^\cdot + CH_3SO_2^- + H_2O \quad \text{basic pH} \tag{25}$$

Thus at acidic pH the formation of ions increases the conductivity, while at basic pH the higher specific conductivity anion OH^- is replaced by the less-conducting $(CH_3)_2SO_2^-$ anion. The yield of the sulfinic anion can be measured from the decrease in conductivity at basic pH and the increase at acidic pH (equation 26–27).

$$G(CH_3SO_2^-) \times [l(OH^-) - l(CH_3SO_2^-)] = \Delta_{OH^-} \tag{26}$$

$$G(CH_3SO_2^-) \times [l(H_{aq}^+) + l(CH_3SO_2^-)] = \Delta_{H^+} \tag{27}$$

$G(CH_3SO_2^-)$ is the yield of $CH_3SO_2^-$ radicals, Δ_{OH^-} and Δ_{H^+} are the decrease and increase of the conductivity in basic and acidic solutions respectively, l is the specific conductivity and $l(H_{aq}^+)$ and $l(OH^-)$ are known to be 315 and 178 Ω^{-1} cm^2, respectively. For dimethyl sulfoxide $G(RSO_2^-)$ was found to be 5.46; comparing this to $G(OH) = 6.0$ for N_2O^--saturated aqueous solution leads to the conclusion that 91% of the OH radicals were added to the sulfoxide bond. There is no proof for the fate of the other 9%; it is probable that they abstract hydrogen atoms from the methyl groups.

Veltwisch and coworkers[45] also measured $G(RSO_2^-)$ for other sulfoxides and their results are summarized in Table 1. They explained the lower yield of OH$^\bullet$ reacting with the sulfur atom of other sulfoxides as due to their higher reactivities in hydrogen abstraction. However, it is not clear why, for example, the yield for diisopropyl sulfoxide is higher than for di-*n*-propyl sulfoxide, or the yield of the cyclic tetramethylene sulfoxide is higher than that of diethyl sulfoxide. For aromatic sulfoxides a low yield of addition of OH$^\bullet$ to the S atom was found. However, at least in the case of diphenyl sulfoxide the competing reaction cannot be hydrogen atom abstraction and it seems reasonable that for both diphenyl and dibenzyl sulfoxides the main reaction of the OH$^\bullet$ radical is addition to the π system of the aromatic ring to form hydroxycyclohexadienyl-type radicals.

A proof for the sulfinic acids in these reactions is found in the study of the pH dependence of the conductivity signal. This study can give in some cases the pK_a of the acid formed (this is true only for some cases, since the conductivity measurements are limited to pH < 2). It was found, for example, that for DMSO, pK_a is 2.35 compared to the literature value of 2.28.

TABLE 1. Yields of RSO_2^- in the radiolysis of N_2O-saturated aqueous solutions of symmetrical sulfoxides (R_2SO), the percent of OH forming RSO_2^- [$G(OH) = 6.0$] and the rate constants for ion formation (equation 30)

A. Symmetric sulfoxides

R_2SO	$G(RSO_2^-)$	%OH	$k_1(M^{-1}s^{-1}) \times 10^{-9}$	$k_2(s^{-1}) \times 10^{-6}$
$(CH_3)_2SO$	5.5	92	7.0	15
$(C_2H_5)_2SO$	4.8	80	6.5	~23
$(C_3H_7)_2SO$	3.3	55	6.3	7.7
$(i\text{-}C_3H_7)_2SO$	4.75	79	6.8	10
$(C_4H_9)_2SO$	2.9	48	8.0	14
$(t\text{-}C_4H_9)_2SO$	4.75	79	5.3	11
$[HO(CH_2)_2]_2SO$	3.9	65	5.3	9.5
$(C_6H_5)_2SO$	1.85	31	10.0	>15
$(C_6H_5CH_2)_2SO$	0.9	15		
$(CH_2)_3\text{-}SO\text{-}(CH_2)$	5.4	90	7.0	7.3

B. Phenyl alkyl sulfoxides ($R—\overset{\overset{O}{\|}}{S}—C_6H_5$)

R	$G(RSO_2^- + C_6H_5SO_2^-)$	%OH	$\%(RSO_2^-)$	$k_1(M^{-1}s^{-1}) \times 10^{-9}$	$k_2(s^{-1}) \times 10^{-6}$
CH_3	2.8	47	0.25	9.7	6.5
C_2H_5	2.6	43	~0.04	8.4	8.0
C_2H_4Cl	2.6	43	0	—	—
$i\text{-}C_3H_7$	2.6	43	0	10.0	8.5

A proof for the formation of alkyl radicals was found by their addition to the aci-nitromethane anion ($CH_2{=}NO_2^-$) and by their reaction with *p*-benzoquinone to give the optically active nitroalkane radical-anion and the semiquinone radicals, respectively. In the case of di-*t*-butyl sulfoxide the *t*-butyl radical was observed directly by its absorption spectra.

In the case of diaryl sulfoxides the formation of both the aryl radical and the hydroxycyclohexadienyl radical was observed optically. Veltwisch and coworkers[45] studied also the reaction of $OH^\bullet$ radicals from radiolysis of aqueous solutions of mixed (alkyl phenyl) sulfoxides (PhSOR). They found the formation of both alkylsulfinic and phenylsulfinic acids.

$$\mathrm{PhSOR} + \mathrm{OH}^\bullet \longrightarrow \mathrm{PhRSO_2H}^\bullet \longrightarrow \begin{cases} \mathrm{PhSO_2^-/H^+ + R^\bullet} & (28a) \\ \mathrm{Ph^\bullet + RSO_2^-/H^+} & (28b) \end{cases}$$

The branching of the adduct decomposition was studied by measuring the pK_a of the mixtures. Thus for pulse radiolysis of N_2O-saturated methyl phenyl sulfoxide the results yield a $pK_{a,obs}$ value of 1.50 while the values for methane sulfinic and benzene sulfinic acids are 2.28 and 1.29, respectively. The fraction of each branch can be calculated from the equation,

$$\frac{1}{1+10^{pK_{obs}-pH}} = \frac{X_a}{1+10^{pK_{a1}-pH}} + \frac{1-X_a}{1+10^{pK_{a2}-pH}} \qquad (29)$$

where X_a is the fraction of the adduct going by route 28a and pK_{a1} and pK_{a2} are the dissociation constants of the benzene sulfinic and the alkane sulfinic acids, respectively. The results are summarized in Table 1.

For methyl phenyl sulfoxide it was found that 25% of the adduct decomposes to give phenyl radical and methane sulfinic acid, while 75% of the adduct leads to methyl radical and benzene sulfinic acid. For heavier alkyl groups the formation of the benzene sulfinic acid is even more dominant, 96% for R = Et and 100% for R = C_2H_4Cl or *i*-Pr.

The total yield of sulfinic acid from the mixed sulfoxides is higher than that from diphenyl sulfoxides (31%) but lower than that from the corresponding dialkyl sulfoxides, and accounts for about 45% of the $OH^\bullet$ radicals (Table 1).

The build-up of the conductivity signal occurs exponentially for all the studied sulfoxides and at all concentrations. At low sulfoxide concentrations the observed pseudo-first-order rate constants are proportional to the concentration of the sulfoxides indicating that these are second-order reactions which behave as first order due to [sulfoxide] > [$OH^\bullet$]. However, at higher solute concentrations the half-lives of the exponential build-up are no longer inversely proportional to the concentration and for the largest solute concentration the half-lives level off to a constant value, e.g. 73 + 8 ns for $(HOCH_2CH_2)_2SO$. This result indicates that there is also a pure first-order reaction in the process of the formation of the RSO_2^-/H_{aq}^+ ion pair. At low solute concentration the bimolecular reaction is slower one and hence the rate-determining step, whereas at high solute concentration the higher rate of the bimolecular step causes the first-order process to be the slower one.

The suggested model is similar to that suggested by Gilbert and coworkers[41].

$$\mathrm{R_2SO} + \mathrm{OH}^\bullet \xrightarrow{k_1} \mathrm{R_2SO(OH)}^\bullet \xrightarrow{k_2} \mathrm{R}^\bullet + \mathrm{RSO_2^-/H_{aq}^+} \qquad (30)$$

Table 1 shows values of k_1 and k_2 for various sulfoxides[45]. In the case of the mixed

phenyl alkyl sulfoxides the rates of the reaction of $OH^{\cdot}$ with the sulfoxides can be measured in two ways: (a) optically by measuring the formation of the hydroxycyclohexadienyl radicals, (b) conductivity measurement of the formation of the sulfinic acids. The rate of formation of the hydroxycyclohexadienyl radicals was found to be of pseudo-first-order (half-life inversely proportional to concentration) over the entire solute concentration. Identical rate constants were obtained for the build-up kinetics of the conductivity signal at low concentration. At higher concentration the results were similar to those obtained for symmetrical sulfoxides, i.e., the pseudo-first-order changes to pure first-order and the half-life is independent of solute concentration.

This indicates that there is a bimolecular-type first step in which the hydroxycyclohexadienyl radicals are formed.

In a consecutive step, a first-order process, the hydroxycyclohexadienyl radicals decompose to give the sulfinic acids as is given in reaction 30. The rate constants k_1 and k_2 are also given in Table 1. In this case k_1 was calculated from the build-up of the hydroxycyclohexadienyl radicals.

Chaudhri and colleagues[46] studied the pulse radiolysis of very acidic aqueous solutions of DMSO (10^{-1} M DMSO and 3 M $HClO_4$) and obtained an optically absorbing transient with a pronounced maximum of the spectrum at 285 nm. The formation of this absorption requires high concentration of the perchloric acid and was not observed in solutions containing less than 10^{-2} M $HClO_4$. A curve of the yield of this absorption as a function of the concentration of $HClO_4$ at 0.1 M DMSO is of a saturation shape, however a plateau was not reached even at 2–3 M although the curve starts to level off. A similar absorption was found in the pulse radiolysis of 3 M $H_2SO_4 + 10^{-1}$ M DMSO. Addition of 10^{-3} M O_2 (oxygen-saturated solutions) or 10^{-2} M $Fe(CN)_6^{3-}$, both of which are good $H^{\cdot}$ atom scavengers, results in complete disappearance of the 285 nm absorption. Addition of *t*-butyl alcohol, which is an efficient $OH^{\cdot}$ scavenger but moderate $H^{\cdot}$ atom scavenger, reduces only little the absorption at 285 nm. The primary reactive radicals in acidic aqueous solution are only $H^{\cdot}$ atoms and $OH^{\cdot}$ radicals formed with about equal yields. Thus these results indicate that the reaction of $OH^{\cdot}$ radicals with DMSO lead to a nonabsorbing species whereas the reaction of $H^{\cdot}$ atoms with DMSO yields a product which absorbs at 285 nm. Chaudhri and colleagues[46] assigned the 285 nm absorption to $(CH_3)_2S^{\ddagger}$, radical cation which is formed via atom addition to the oxygen atom followed by acid-assisted dehydration.

$$(CH_3)_2SO + H^{\cdot} \longrightarrow (CH_3)_2SOH^{\cdot} \tag{31}$$

$$(CH_3)_2SOH^{\cdot} + H^{+} \longrightarrow (CH_3)_2S^{\ddagger} + H_2O \tag{32}$$

Protonation of the sulfoxide prior to $H^{\cdot}$ atom addition can be probably excluded, at least at lower $HClO_4$ concentrations due to a pK_b of the DMSO of -1.54.

Addition of small amounts of $(CH_3)_2S$ ($5 \times 10^{-5} - 5 \times 10^{-4}$ M) to deoxygenated solutions of 3 M $HClO_4$ and 0.5 M DMSO leads to replacement of the 285 nm absorption by 465 nm absorption which is known to belong to the complexed three-electron-bonded radical cation of the disulfide[47].

$$(CH_3)_2S^{\ddagger} + (CH_3)_2S \longrightarrow [(CH_3)_2S \therefore S(CH_3)_2]^{+} \tag{33}$$

k_{33} was measured to be $(3.0 + 0.3) \times 10^9$ M^{-1} s^{-1}; the back reaction was found to be very slow compared to the forward reaction. Chaudhri and colleagues[46] studied also the radiolysis of aqueous $(CH_3)_2SO/HClO_4$ in the presence of various solutes, e.g. $(CH_3)_2S_2$, $(t\text{-Bu})_2S$ and Cl^{-}, to study their reaction with $(CH_3)_2S^{\ddagger}$. All these chemical reactions also support the conclusion that $(CH_3)_2S^{\ddagger}$ radical cations are formed in the reduction of $(CH_3)_2SO$ by hydrogen atoms in $HClO_4$ containing solutions.

It should be pointed out that Symons[12] suggested for the solid state another

pathway of the hydrogen atom and proposed that it leads to the formation of a CH_3SO radical.

$$(CH_3)_2SO + H^{\cdot} \longrightarrow (CH_3)_2SOH^{\cdot} \longrightarrow CH_4 + CH_3SO^{\cdot} \tag{34}$$

Chaudhri and colleagues[46] calculated the rate of reaction 31 assuming that the final product $(CH_3)_2S$ is due only to reaction of $H^{\cdot}$ atoms. From the inhibition of formation of $(CH_3)_2S$ by $Fe(CN)_6^{3-}$ and from the known rate constant for $H^{\cdot} + Fe(CN)_6^{3-}$ they found $k_{31} = 3.3 \times 10^6\ M^{-1}\,s^{-1}$. They said that error associated with this value is probably high but it should be correct within the order of magnitude.

Sumiyoshi and coworkers[48] studied the radiolysis of aqueous solution of methyl methylthiomethyl sulfoxide [$CH_3S(O)CH_2SCH_3$; MTMSO] at various pH by pulse radiolysis. They found that the reaction of e_{aq}^- with MTMSO (in the presence of 1 M *t*-butyl alcohol to scavenge $OH^{\cdot}$ radicals) leads to formation of a transient with a broad absorption band of $\lambda_{max} = 375$ nm. The absorbance at 375 nm as a function of pH are of S shape, indicating an equilibrium due to reaction with H^+. Similar to the finding in dimethyl sulfoxide they suggested the scheme.

$$CH_3S(O)CH_2SCH_3 + e_{aq}^- \longrightarrow CH_3S(O)CH_2SCH_3^{\cdot-}$$

$$\xrightarrow[pK_a = 10]{H^+} CH_3S(OH)CH_2SCH_3 \tag{35}$$

The absorption at 375 nm is assigned to the radical anion. $OH^{\cdot}$ radicals were found to give an optically active transient which absorbs at 360 nm and which is assigned by the authors to the radical anion formed by the reaction of $OH^{\cdot}$ with the sulfur atom of the thiomethyl bond of MTMSO,

$$CH_3S(O)CH_2SCH_3 + OH^{\cdot} \longrightarrow CH_3S(O)CH_2\overset{\displaystyle OH}{\overset{|}{\dot{S}}}CH_3$$

$$\xrightarrow[pK_a = 9]{-H^+} CH_3S(O)CH_2\overset{\displaystyle O^-}{\overset{|}{\dot{S}}}CH_3 \tag{36}$$

Sumiyoshi and coworkers[48] suggested that the reaction of $OH^{\cdot}$ radical with the sulfoxides S—C bond can be studied by looking for the sulfinic acid which is expected from the reaction of OH radical and a sulfoxide[37,45] (reaction 24).

They measured the formation of ionic species in the pulse radiolysis of a 10^{-3} M MTMSO aqueous solution saturated by N_2O gas at pH 5.6 by conductivity detection and found an increase in conductivity. Assuming the molar conductivity of $CH_3SCH_2SO_2^-$ to be the same as that measured for $CH_3SO_2^-$ [45], it is found that $G(CH_3SCH_2SO_2^-) = 2.7$.

$$CH_3S(O)CH_2SCH_3 + OH^{\cdot} \longrightarrow CH_3^{\cdot} + CH_3SCH_2SO_2^- + H^+ \tag{37}$$

The total yield of $OH^{\cdot}$ radicals is 6.0 and hence the yield of sulfinic acid of $G = 2.7$ indicates that 45% of the OH radical produced in the radiolysis attack the sulfinyl group of MTMSO. The authors[48] said that the residual 55% attack the sulfide S—C bond, but this claim ignores completely other routes, such as hydrogen abstraction, which was found for other sulfoxides[45].

They[48] measured also the rate constant for the $OH^{\cdot}$ + MTMSO reaction both by the build-up of the conductivity signal and by optical absorption of $(SCN)_2^-$ in competition with KSCN, and obtained $4.8 \times 10^9\ M^{-1}\,s^{-1}$.

D. Organic Solutions of Sulfoxides

Rao and Symons[49] studied the formation of radicals in γ-radiolysis of dilute solutions of dimethyl sulfoxide in fluorotrichloromethane. By ESR studies they found the radical cation $(CH_3)_2SO^{\ddagger}$ whose ESR spectrum show considerable g anisotropy and small methyl proton hyperfine coupling.

E. Mixtures of Water–DMSO

While aqueous solutions mean only dilute solutions, 'mixtures' can be any proportion of H_2O and DMSO. Cooper and coworkers[30] found in the pulse radiolysis of H_2O/DMSO mixtures two easily resolvable absorption bands at wavelengths >400 nm. One band corresponds to the oxidizing species with a maximum at ~ 600 nm and a relatively long half-life (1 to 4 μs). The second band with higher wavelength (720–1500 nm) and shorter half-life is attributed to the solvated electrons.

The wavelength of the oxidizing species band is almost unaltered by changing the composition from 1.0 to 0.2 mole fraction DMSO. Only the magnitude of the absorbance changes monotonously with the composition; $G\varepsilon$ is increasing with the increase in DMSO mole fraction (Figure 5). The decay rate of the oxidizing species absorption is largely unaffected by the composition. If the oxidizing species is formed only from direct reaction of the radiation with DMSO, the yield $G\varepsilon$ should be linear with electron fraction of the DMSO (Figure 6) which give the fractional dose absorbed by DMSO. For solutions of >0.72 mole fraction DMSO the yield was found to be almost proportional to the dose deposited in DMSO molecules. For lower concentrations there is deviation from linearity, but it is not clear if this deviation is real or an artifact due to the changing of the width of the absorption band. An important conclusion from this is that there is no important charge transfer, proton exchange or radical interaction between water molecules and the DMSO oxidizing species or its precursor ions. This is in contrast to non-polar aprotic solvents

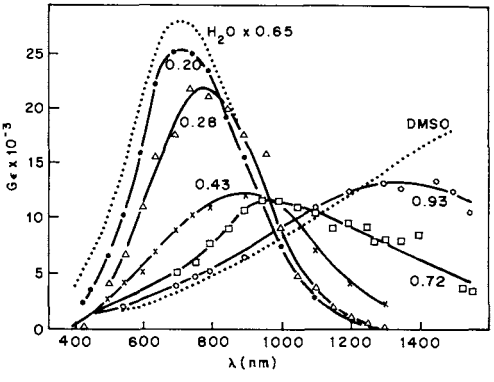


FIGURE 5. Absorption spectra of solvated electrons in DMSO/H_2O mixtures; 0, 0.20, 0.28, 0.43, 0.72, 0.93 and 1.0 mole fraction DMSO. To fit into the Figure, the data for pure water have been multiplied by a factor of 0.65 relative to the others. These spectra represent the short-lived solvated electron band only, the longer-lived 600 nm band and UV bands having been substracted from the observed absorbances. Reproduced by permission of the authors from Reference 30.

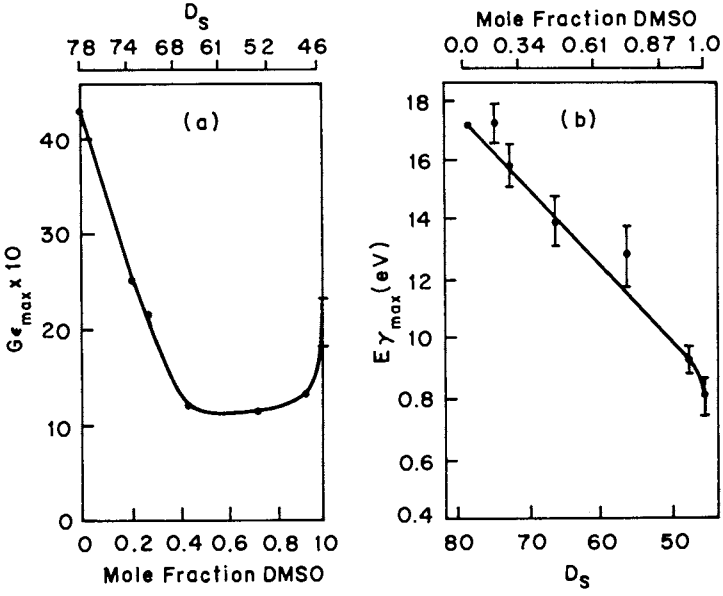


FIGURE 6. (a) Values of $G\varepsilon_{max}$ for the solvated electron absorption bands plotted against the mole fraction DMSO for DMSO/H_2O mixtures. (b) Photon energy of the absorption band maxima for the solvated electron in DMSO/H_2O mixtures plotted against the bulk static dielectric constant (25 °C) of the mixture. Non-linear axes showing dielectric constant and mole fraction for (a) and (b) respectively are given as top abscissae. Reproduced by permission of the authors from Reference 30.

where the positive ions will undergo proton transfer to water. This difference is probably a reflection of the strongly dipolar character of DMSO and its strong solvation of the cations.

The wavelength of the solvated electron in H_2O/DMSO mixtures was found to be inversely linearly dependent on the mole fraction (up to 0.9 mole fraction) of DMSO (Figure 6). The photon energy at the absorption band maxima is linearly dependent. This means also a linear dependence on the dielectric constant although the λ_{max} of e_{sol}^- in pure DMSO occurs at much longer wavelengths than it does in many solvents with lower dielectric constants, such as alcohols. This suggests a monotonous increasing cavity radius and charge delocalization with increasing DMSO content in the mixture. Besides, the absorption band full width half maximum (FWHM) in energy units, is fairly constant. These results are surprising, since water solvates negative ions by strong hydrogen bonding while DMSO is known to solvate negative ions quite weakly through ion–dipole interactions. However, the linearity of $1/\lambda_{max}$ with the mole fraction of DMSO indicates that the optical properties of e_{sol}^- in these mixtures are not dominated by the water.

The decay of the absorption of e_{sol}^- was followed at 1000 nm[30] or 900 nm[50] where the oxidizing species do not absorb. It was found[30] that e_{sol}^- decays by first-order kinetics. A second-order rate constant was calculated assuming that the decay is only by reaction with DMSO. These second-order rate constants appear to go through a maximum between 0.20 and 0.43 mole fraction of DMSO where $k = 5.6 \times 10^6$ M^{-1} s^{-1}, however, there is not a large difference between the different concentrations as the lowest value is 2.9×10^6

$M^{-1} s^{-1}$ for 0.017 mole fraction DMSO. The $t_{1/2}$ for the decay of e_{sol}^- is almost constant in the range 0.28–1.0 mole fraction DMSO ($t_{1/2} = 13 \mp 2$ ns).

The plot of the optical yield, $G\varepsilon_{max}$, of the e_{sol}^- when plotted vs. the DMSO molar fraction has a broad minimum between 0.43 and 0.93 mole fraction DMSO. It is unlikely that the minimum in $G\varepsilon_{max}$ arises from a minimum in ε_{max} alone (especially as ΔW was found to be nearly constant over the full range) and it seems more reasonable that the main reason is a minimum in the radiation yield, G. Cooper and coworkers[30] suggested that the minimum in $G(e_{sol}^-)$ is the result of a decreased fraction of the free electron which become solvated.

Koulkes-Pujo and colleagues[50] studied the rate of the reaction of solvated electrons in mixtures of H_2O/DMSO with nitrous oxide and found that the plot of the rate constant vs. DMSO molar fraction has a minimum around 0.5 mole fraction. Up to 0.21 mole fraction DMSO (50% volume DMSO) the decrease in k with the concentration of DMSO fits with the change of the viscosity. Between 0.21 and 0.68 mole fraction of DMSO the observed rate constants are lower than expected according to the viscosity. The authors suggested that, as in this range the mixture is known to be strongly structured by hydrogen bonding, it can be expected that the electron solvated by such bonded molecules would be less reactive than the simple hydrated electrons in the same medium. Above 0.68 mole fraction DMSO (90% volume DMSO) the rate constant was found to be too fast to be measured and the authors suggested that in this range the electrons are not solvated but are 'dry' electrons. It should be mentioned that in hydrocarbons the rate constant of quasi-free electrons with N_2O is smaller than that of solvated ones.

Koulkes-Pujo and coworkers[51] studied also the reaction of the radiolysis-produced electrons in H_2O/DMSO mixtures with NO_3^- and H^+. In the case of NO_3^- they found that the observed rate constants are always lower than those calculated from pure water taking into consideration the change of the viscosity. For concentrations of DMSO equal to or larger than 0.33 mole fraction, the rate of disappearance of the solvated electron in the presence of NO_3^- is the same as in its absence. For the case of reaction of $e_{sol}^- + H^+$ in H_2O/DMSO, experiments were conducted only at relatively low concentrations of DMSO ($\leqslant 0.1$ mole fraction) and the experimental results show increase in the rate constant with increase in the concentration of DMSO, although the viscosity dependence will predict the opposite trend. The authors suggested that this effect is due to structure breaking of water either by DMSO or by ClO_4^- (the H^+ is added as $HClO_4$).

Koulkes-Pujo and coworkers[35] studied the radiolytic reduction of Ce^{4+} in water–DMSO mixtures and found that while in water $G(Ce^{4+})$ is 2.5, the addition of DMSO increases the yield very much and leads to $G(Ce^{4+}) = 18.1$ for 1.4 M DMSO. At higher concentrations of DMSO the yields decrease down to 14.4 for pure DMSO. The high value of $G(Ce^{4+})$ was explained on the basis that all species created by ionization of the medium, including H, OH, H_2O_2 and HO_2, are rendered reducing in the presence of DMSO. It is not necessary to increase the DMSO concentration beyond 0.5 M to increase significantly the reduction yield. In aqueous solution without DMSO the Ce^{4+} reduction is accompanied by O_2 formation with a yield near 0.8, however in the presence of DMSO, O_2 is never formed. The increased yield of reduction and the absence of O_2 formation might have implications in radiobiochemistry[52].

III. THE FINAL PRODUCTS IN THE RADIOLYSIS OF SULFOXIDES

A. Dimethyl Sulfoxide

Machado and coworkers[53] studied the products produced in the radiolysis of DMSO and found the formation of a product which absorbs at 252–262 nm, absorption which is known to be that of dimethyl disulfide. Gas chromatographic studies show the formation

of dimethyl disulfide, dimethyl sulfide, methanethiol, methane, ethane and propane. There is no quantitative information on the yields, except that the last product was formed only in trace amounts. Also Koulkes-Pujo and Berthou[34] found qualitatively the formation of dimethyl sulfide (by NMR measurements) and dimethyl sulfone (by IR spectrophotometry). Cooper and Walker[31] and Koulkes-Pujo and Berthou[34] studied the yield of the volatile products in the γ-radiolysis of pure DMSO. The yields of hydrogen and ethane were found to be proportional to the absorbed radiation energy, $G(H_2) = 0.20 \mp 0.01$ or 0.19 ∓ 0.006[34] and $G(C_2H_6) = 0.49 \mp 0.03$[31] at least up to 1.3 Mrad[31]. Koulkes-Pujo and Berthou found that the yield of CH_4 is proportional to the dose and independent of the dose rate (1.36–4.68 krad min^{-1}), $G(CH_4) = 3.4 \pm 0.3$. On the other hand, Cooper and Walker[31] found that only up to 180 krad is the yield of CH_4 proportional to the absorbed dose, while for higher doses the increase in the yield is less than linear. The radiolytic yield of methane varies in the range 3.3 ± 0.1 to 2.1 ± 0.1 when the absorbed energy is increased to 1.6 Mrad. The data suggest that some non-volatile radiation product, the concentration of which is increasing with the absorbed dose, reacts with the precursor or one of the precursors of methane.

The addition of N_2O to DMSO before irradiation[31] leads to a decrease in the yield of CH_4 (from 3.3 to 2.6) while hydrogen and ethane were unaffected. The addition of H^+ to DMSO does not change the yield of any of the gaseous products[31,34] while addition of I_2 decreases the yield of CH_4 and C_2H_6 but leaves the yield of H_2 almost unchanged (a small increase). The effect of I_2 on the yield of CH_4 is much stronger than on the yield of C_2H_6.

B. Aqueous Solutions of Dimethyl Sulfoxide

Nelson[54] studied the products of radiolysis of aqueous solution by variable-field CIDNP pulse radiolysis. On the basis of the chemical shifts the following products were identified: methyl methanesulfinate, methanol, 1,2-bis(methylsulfinylethane) [$CH_3S(O)CH_2CH_2S(O)CH_3$], dimethyl sulfone, dimethyl sulfide, methane and ethane. The high field polarization was used to study the mechanism of formation of polarized products.

Methanol is a very minor product and the observation that its polarization is more intense in N_2O-saturated solution than in He-saturated solution suggests that it is formed by reaction of $OH^\cdot$ radical, probably by a degradation of the radical formed by the addition of $OH^\cdot$ to DMSO other than the main one given in reaction 21.

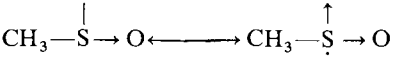
$$(CH_3)_2SO(OH)^\cdot \longrightarrow CH_3O^\cdot + CH_3SOH \tag{38}$$

$$CH_3O^\cdot + H_2O \longrightarrow CH_3OH + OH^\cdot \tag{39}$$

Methyl methanesulfinate, $CH_3OS(O)CH_3$, is formed by combination of methyl and methylsulfinyl radicals:

$$CH_3^\cdot + CH_3SO_2^\cdot \longrightarrow CH_3OS(O)CH_3 \tag{40}$$

The methylsulfinyl radical has several resonance structures



which can lead in a combination reaction with methyl radical either to $CH_3OS(O)CH_3$ (reaction 40) or to $(CH_3)_2SO_2$ (reaction 23). Norman and his colleagues[41] suggested the formation of dimethyl sulfone (reaction 29), however Nelson claims that reaction 40 is the main combination reaction.

At low pH, where e_{aq}^- is transformed to $H^\cdot$ atoms, an increase in the signal of

$(CH_3S(O)CH_2)_2$ is observed indicating that H$^\cdot$ atoms abstract hydrogen from DMSO to form $CH_3S(O)CH_2^\cdot$ which dimerizes to $(CH_3S(O)CH_2)_2$. The radical $CH_3S(O)CH_2^\cdot$ is not found in the reaction of OH$^\cdot$ with DMSO[41].

The pH dependences of methane and ethane signals suggest that their formation by H$^\cdot$ atom reaction (addition to the SO bond) is at best a very minor pathway. The intensity of the C_2H_6 signal is larger for He-saturated solutions than for N_2O-saturated solution indicating that at least part of C_2H_6 is formed from e_{aq}^-. However, H^+ addition does not reduce the C_2H_6 signal. The addition of nitromethane, a spur scavenger of e_{aq}^-, dramatically decreases the observed intensity of the ethane CIDNP signal. These data indicate that e_{aq}^- in the spur is the precursor of ethane, the first step being ion recombination.

$$(CH_3)_2SO^+ + e^- \longrightarrow [(CH_3)_2SO]^* \longrightarrow CH_3SO^\cdot + CH_3^\cdot \tag{41}$$

$$CH_3SO^\cdot + CH_3^\cdot \longrightarrow C_2H_6 + SO \tag{42}$$

This mechanism is further proved by the observation that addition of 0.05 M Br^- to aqueous DMSO results in reduced intensity of the ethane signal. Bromide ion at this concentration does not effectively compete with DMSO for OH$^\cdot$ ($k_{OH+DMSO} = 7 \times 10^9$ $M^{-1}s^{-1}$, [DMSO] = 0.23 M, $k_{OH+Br^-} = 1.1 \times 10^{10}\,M^{-1}s^{-1}$) and the effect of Br^- can be due to its reaction with the cation of DMSO[30,34] found also in pure DMSO, $(CH_3)_2SO^+$ is reduced by Br^- and consequently cannot react with the spur electrons.

Another pathway of ethane formation is the disproportionation equivalent to reactions 23 and 40.

$$CH_3^\cdot + CH_3SO_2^\cdot \longrightarrow C_2H_6 + SO_2 \tag{43}$$

Koulkes-Pujo and coworkers[55] studied the formation of methane in the reaction of OH$^\cdot$ radicals and H$^\cdot$ atoms with aqueous DMSO in acidic media. In the radiolysis of deaerated acidic aqueous solution of DMSO they found that $G(CH_4)$ increases monotonously with CH_4 concentration up to 0.8 M DMSO. Similar results were obtained for C_2H_6 but the yields of C_2H_6 are much lower than that of CH_4.

The yields at the high concentration are slightly lower than the values obtained for neutral media, $G(CH_4) = 2.25$; $G(C_2H_6) = 0.45$[56]. The formation of CH_4 by H$^\cdot$ atoms was studied by competition with ethanol which reacts with hydrogen atoms to give molecular hydrogen.

$$H^\cdot + (CH_3)_2SO \longrightarrow \text{products } (CH_4 \text{ and others}) \tag{44}$$

$$H^\cdot + C_2H_5OH \longrightarrow H_2 + {}^\cdot C_2H_4OH \tag{45}$$

$$H_2O \rightsquigarrow \text{molecular } H_2 + H_2O_2 + \text{radicals} \tag{46}$$

These reactions lead to the equation

$$\Delta G(H_2)^{-1} = G_H^{-1}\left(1 + \frac{k_{44}[\text{DMSO}]}{k_{45}[C_2H_5OH]}\right) \tag{47}$$

where $\Delta G(H_2) = G(H_2) - G_{H_2}$, G_{H_2} and G_H are the radiolytic yields of molecular H_2 and hydrogen atoms in the radiolysis of water. It was found[55] that $\Delta G(H_2)^{-1}$ is quite linear with the concentration ratio [DMSO]/[C_2H_5OH]. G_H was found to be 3.65, in agreement with the literature value of G_H in acid solution. The ratio of the rate constants is $k_{44}/k_{45} = 0.57$ and from the known value of k_{45} ($4.6 \times 10^7\,M^{-1}s^{-1}$)$k_{44}$ is found to be $2.6 \pm 0.3 \times 10^7\,M^{-1}s^{-1}$. As the highest yield of CH_4 was found to be 1.8 while $G_H = 3.65$, it is clear that not all the hydrogen atoms give CH_4 with DMSO. The plot of $G(CH_4)^{-1}$ vs. [DMSO]/[C_2H_5OH] is not linear, showing that methane formation is more complex than simple reaction of H$^\cdot$ atoms with DMSO.

Another source for CH_4 is by the reaction of $OH^{\bullet}$ radicals, as can be proved by the reduction of the yield by the addition of Br^- to the solution. In the presence of 7×10^{-2} M KBr the methane yield has been reduced to 0.85, independently of DMSO concentration in the range 1.5×10^{-3} M–6×10^{-2} M, which represents the contribution of the $H^{\bullet}$/DMSO reaction to CH_4 production. Defining $\Delta G(CH_4) = G(CH_4) - 0.85$ as the contribution of $OH^{\bullet}$ radicals to CH_4 formation, leads to a linear plot of $\Delta G(CH_4)^{-1}$ vs. [KBr]/[DMSO], from which $G(OH^{\bullet}) = 0.69$ and a rate constant of $2.0 \mp 0.2 \times 10^{10}$ for $OH^{\bullet}$ + DMSO were obtained. This rate constant in acid media is three times higher than that found in neutral pH. These results show that only 23% of the $H^{\bullet}$ atoms (0.85/3.65) and of the $OH^{\bullet}$ radicals (0.69/2.95) lead to CH_4 formation, probably due to the various pathways of decomposition of the adducts $(CH_3)_2S(O)OH^{\bullet}$ and $(CH_3)_2SOH^{\bullet}$. The sum of the yields of methane from $H^{\bullet}$ atoms and $OH^{\bullet}$ radicals is 1.54 (0.85 + 0.69), significantly less than the experimental 1.8 value, suggesting the existence of another, as yet unidentified source of methane.

C. Other Sulfoxides and their Aqueous Solutions

Nishimura and coworkers[57–59] studied the γ-radiolysis of aqueous solutions of sulfoxide amino acids. Sulfoxide amino acids are the precursors of the flavors of onions (*S*-propyl-L-cysteine sulfoxide, *S*-methyl-L-cysteine sulfoxide and *S*-(1-propenyl)-L-cysteine sulfoxide) and garlic (*S*-allyl-L-cysteine sulfoxide). In studies on sprout inhibition of onion by γ-irradiation it was found that the characteristic flavor of onions became milder. In the γ-radiolysis of an aqueous solution of *S*-propyl-L-cysteine sulfoxide (PCSO)[57,58] they identified as the main products alanine, cysteic acid, dipropyl disulfide and dipropyl sulfide. In the radiolysis of *S*-allyl-L-cysteine sulfoxide (ACSO) they found that the main products are *S*-allyl-L-cysteine, cysteic acid, cystine, allyl alcohol, propyl allyl sulfide and diallyl sulfide. The mechanisms of formation of the products were partly elucidated by the study of the radiolysis in the presence of N_2O and Br^- as e_{aq}^- and $OH^{\bullet}$ radicals scavengers, respectively.

In the case of PCSO the addition of N_2O leads to increased formation of cysteic acid, alanine and dipropyl sulfide and to a decrease in the yield of dipropyl disulfide. The addition of KBr decreases the yield of all the four products. These findings indicate that cysteic acid and alanine are formed by the reaction of $OH^{\bullet}$ radicals in parallel reactions as given in Figure 7.

The authors suggested that di-*n*-propyl disulfide is formed by the reaction of both hydrated electrons and $OH^{\bullet}$ radicals, however it should be mentioned that the yield from hydrated electrons should be higher than from $OH^{\bullet}$ radicals as otherwise N_2O will not reduce the yield of dipropyl disulfide as N_2O merely converts e_{aq}^- to $OH^{\bullet}$ radicals. The yield from each radical could be calculated from the yields in the presence of the various scavengers, but unfortunately these data were not given by the authors.

In the case of ACSO it was found also that N_2O addition reduces the yield of *S*-allyl-L-cysteine (ACS), indicating that this product is formed by e_{aq}^- but not by $OH^{\bullet}$ radicals. As a result it can be expected that KBr addition will not reduce the ACS yield. It was found that KBr not only does not reduce the yield of ACS, but it rather increases its formation. This is explained as due to ACS formation by reaction of e_{aq}^- with ACSO, and its disappearance by reaction with $OH^{\bullet}$ radicals to give back ACSO as it is known for the reaction with sulfides. The authors suggest the same reactions for PCSO and PCS (propyl-L-cysteine) although the yield of PCS was not determined.

The authors did not give much quantitative information in their papers. The *G* values for decomposition are almost twice as large in ACSO (8.5) as compared to PCSO (4.6). The value in ACSO is higher than the yield of the radicals in aqueous solution and should be attributed to reactions of radicals produced from ASCO with other ASCO molecules, for

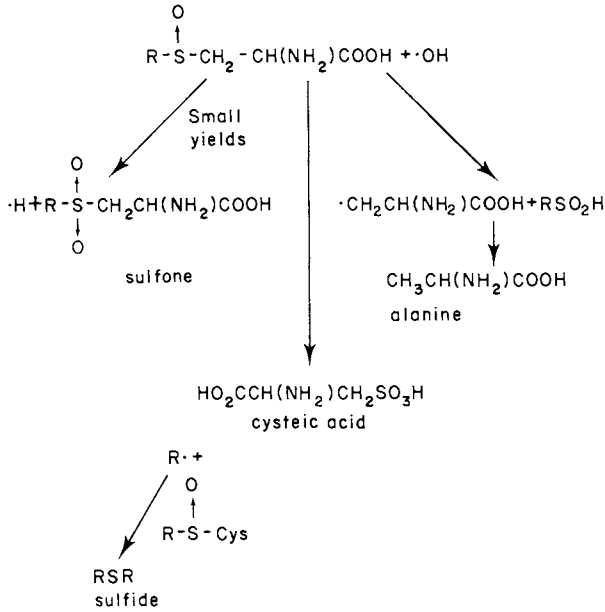


FIGURE 7. The reactions of OH· radical with alkyl-L-cysteine sulfoxide.

example

$$R^{\cdot} + R{-}S(O){-}Cys \longrightarrow RSR + \text{radicals} \tag{48}$$

or

$$^{\cdot}CH_2CH(NH_2)COOH + R{-}S(O){-}Cys \longrightarrow CH_3CH(NH_2)COOH + \text{radicals} \tag{49}$$

If reaction 49 is responsible for the high decomposition yield of ASCO, it can be understood why it does not occur for PSCO, since the C—H bond strength in the allyl compound is weaker than in the propyl derivative due to the resonance stabilization of the radical[60]. However, the yield of alanine was found to be 1.97 in the case of radiolysis of PCSO and almost zero for ACSO. Thus reaction 49 does not occur for the case of ACSO. Since only the yields of cysteine (0.98 for ACSO and 0 for PCSO) are given, no explanation can be proposed for the high decomposition yield of ACSO.

The observation that in the case of PCSO there is no formation of propanol while allyl alcohol is formed from ACSO agrees with the resonance stabilization of the allyl radical[60] and hence weaker bond for *S*-allyl than for *S*-propyl. The yield of allyl alcohol from irradiation of ACSO is considerably greater than that from *S*-allyl-L-cysteine, probably due to energy delocalization by the four p electrons of the S atom.

In contrast with irradiation of ACSO and PCSO, where volatile products were formed (sulfides, disulfides and alcohols), no volatile products were formed in the radiolysis of aqueous solutions of *S*-(*cis*-1-propenyl)-L-cysteine. Here the authors found that reactions of OH· radicals are responsible for the formation of propyl-1-propenyl sulfides (*cis* and *trans*).

Korobeinikova and coworkers[61] studied the extractability of petroleum sulfides (PSO) and their closest analog, tetramethylene sulfoxide (TMSO) upon gamma irradiation. The

PSO are products of the oxidation of mono- and bithiocyclanes contained in kerosene/gas–oil fractions and are of great practical utility as extractants for a large number of transition metals and actinides. They found that irradiation of up to a dose of 5.6 Mrad failed to change the extraction capability of PSO and TMSO with regard to extraction of UO_2^{+} from aqueous solution. However, the acidity in the aqueous phase increased. The radiation yield of sulfoxide group decomposition product for neat PSO was 7.2, the value of G for sulfidic sulfur is 3.6 and for acidic H^+ it was 0.48. In the presence of aqueous phase of 0.1 M $UO_2(NO_3)$ and 1 M HNO_3 the yield of decomposition of sulfoxide groups decreased to 2.6 and sulfide formation to 2.7, probably due to scavenging by UO_2^{+2} and NO_3^{-}.

After irradiation of deoxygenated TMSO it changed from colorless to amber, and the color intensified with increasing doses. The liquid became viscous and no longer dissolved in hexane. In addition, a small amount of a dark brown oily fraction was observed to separate upon dissolving the irradiated TMSO in water. According to the IR spectrum the fraction retained the sulfoxide groups. The authors postulated that the structure of this fraction is similar to dimeric TMSO molecules. A small amount of mercaptans formed by irradiation can be detected by their characteristic odor but their yield was too small to be identified chemically; $G(RSH) \leqslant 5 \times 10^{-3}$. The radiation yield for TMSO sulfoxide-group decomposition was found to be similar to that for PSO (~ 7) over the dose range 5.4–132 Mrad. Increasing the dose to 315 Mrad increased $G(-SO)$ to a value of 8. Of the TMSO radiolysis products a large fraction consisted of sulfides and acids with yields of 3.3 and 0.9, respectively. IR spectra do not show formation of sulfones, similar to PSO. Addition of about 10 wt% water to the TMSO had no effect on the yield of the sulfoxide group decomposition but decreased slightly the yield of the sulfides ($G = 2.3$) and caused the formation of mercaptans ($G = 3 \times 10^{-2}$).

The effect of irradiation on the extractability of sulfoxides towards plutonium, uranium and some fission products were studied by Subramanian and coworkers[62,63]. They studied mainly the effect of irradiation on dihexyl sulfoxide (DHSO) and found that irradiation did not change the distribution coefficient for Ru, Eu and Ce but increases the distribution coefficient for Zr and Pu. When comparing DHSO and tributyl phosphate (TBP), the usual solvent for the recovery and purification of plutonium and uranium from spent nuclear fuels, the effect of irradiation to deteriorate the extraction capability is much larger in TBP. Lan and coworkers[64] studied diphenyl sulfoxides as protectors for the gamma radiolysis of TBP. It was found that diphenyl sulfoxide can accept energy from two different kinds of excited TBP and thus inhibits the decomposition of the latter.

IV. THE PRIMARY SPECIES IN THE RADIOLYSIS OF SULFONES

A. Sulfones

Ayscough and coworkers[65] studied the ESR spectra of γ-irradiated sulfones and polysulfones. Irradiation at 77 K leads mainly to alkyl radicals R$^{\bullet}$ formed by rupture of the C—S bonds. Small amounts of $RSO_2^{\bullet}$ were also observed in some cases as well as radicals formed by loss of an α-hydrogen from the parent molecule—R''. On warming the irradiated samples the simple alkyl radicals disappear first. At room temperature only the $RSO_2^{\bullet}$ radicals have any appreciable stability. In some cases the yield of $RSO_2^{\bullet}$ radicals increases on warming of the sample.

Dimethyl sulfone irradiated at 77 K gives an initial spectrum of quartet known to be due to the methyl radical. After warming the sample to 193 K for 2 min the spectrum is replaced by an asymmetric singlet that is attributed to $CH_3SO_2^{\bullet}$ together with a weak triplet which probably belongs to $CH_3SO_2CH_2^{\bullet}$. The heights of the peaks are such that it can be positively stated that $CH_3SO_2^{\bullet}$ was not present in the initial spectrum, while

$CH_3SO_2CH_2^{\cdot}$ may have been present but with its spectrum obscured by the dominant $CH_3^{\cdot}$. The assignment of the asymmetric singlet to $CH_3SO_2^{\cdot}$ is justified by obtaining the same spectrum from glow discharge in hydrogen on methanesulfonyl chloride at 77 K.

Diethyl sulfone gives, on irradiation at 77 K, a complex spectrum which consists of that of the ethyl radical spectrum and a quintet with a superimposed asymmetric singlet which belongs to $CH_3\dot{C}HSO_2C_2H_5$. On warming to 193 K the ethyl radical disappears while the $CH_3\dot{C}HSO_2C_2H_5$ signal intensity increases. At room temperature $CH_3\dot{C}HSO_2C_2H_5$ slowly disappears, leaving a spectrum ascribed to $C_2H_5SO_2^{\cdot}$. Similar results were obtained for dipropyl sulfone and dibutyl sulfone except that the proportion of the R'' radical (parent molecule minus α-hydrogen atom) increased. This trend is in agreement with the expectation that with weaker α C—H bonds higher yields of R'' radicals will be formed. Thus for dimethyl sulfone only the C—S bond is cleaved while for the other dialkyl sulfones where the C—H bond is weaker than in the methyl group, although stronger than the C—S bond, there is also cleavage of the C—H bond. It is interesting to note that dissociation of one C—S bond occurs very little, if at all, and usually both C—S bonds in the molecule are broken. This might be due to the fact that the energy of the lowest excited electronic level in sulfones is well in excess of the sum of the two C—S bond dissociation energies.

Other alkyl sulfones studied are di-isopropyl, methyl isopropyl and di-*t*-butyl sulfones.

The total yield of radicals produced by irradiation of alkyl sulfones at 77 K was estimated[65] by comparison of the areas of the absorption peaks with that of a known amount of diphenylpicrylhydrazine to be G(radicals) ~ 2.0.

Ayscough[65] studied also the ESR spectrum of irradiated aromatic sulfones and stated that the spectrum is a very weak structureless one due to the well-known radiation protection of the aromatic rings. Lyons and coworkers[66] studied the ESR spectra of 77 K γ-irradiated diphenyl sulfone and found a superposition of a mixture of various cyclohexadienyl radicals formed by the addition of hydrogen atoms to the phenyl groups. Geoffroy and Lucken[67] studied the ESR spectra of X-irradiated single crystals of dibenzyl, phenyl methyl, diphenyl and phenyl acetic acid sulfones at room temperature. Irradiation of dibenzyl sulfone yields the radical $C_6H_5\dot{C}H_2SO_2^{\cdot}$ while irradiation of the other compounds yields the $C_6H_5SO_2^{\cdot}$ radical. In the case of $C_6H_5SO_2CH_2COOH$ an extra radical was observed at 77 K and the author suggested that it is a trapped electron. At room temperature the ESR lines are too broad to be detected but reappear as the temperature is lowered. The ESR spectrum disappears when the crystal is illuminated with UV light.

Ito and Matsuda[68] studied the γ-radiolysis of 2-methyltetrahydrofuran (MTHF) solutions of diphenyl sulfone and dibenzothiophene-*S*,*S*-dioxide (DBTSD) at 77 K. They found that the radical anions of these sulfone compounds are formed and have intense absorption bands at 1030 nm and 850 nm, respectively. The blue glassy solution of γ-irradiated diphenyl sulfone has absorption bands at both 1030 nm and 360 nm[68] while the absorption spectrum of the benzenesulfonyl radical formed by UV irradiation of diphenyl sulfone solution at 77 K showed only a peak at 382 nm. Gamma-irradiated phenyl methyl sulfone solution showed an absorption band only at 385 nm. Consequently the appearance of the absorption bands in 800–1030 nm of diphenyl sulfone and DBTSD may suggest that the unpaired electron is delocalized on two phenyl rings. The same authors[69] studied the radiolysis of MTHF solutions of disulfones (diphenyl and dihexyl disulfones). They found a blue coloring of the solution by the γ-radiolysis of diphenyl disulfone and dihexyl disulfone due to absorption peaks at 695 nm and 690 nm respectively, besides smaller absorptions at 300–400 nm. Comparing these results to the previous observation, that phenyl methyl sulfone solution absorbs only at 398 nm, results in the conclusion that the absorption band at 690 nm is due to the linked two sulfone moieties. The authors found[68] that substituents on the phenyl ring lead to shifts in the absorption maxima of the

disulfone radical anions. When electron-donating substituents such as CH_3— and CH_3O— are introduced to *para* positions, the absorption peaks shift towards shorter wavelengths.

B. Polysulfones

Ayscough and coworkers[65] studied also the ESR of 77 K γ-irradiated polysulfones $[—CR^1R^2CR^3R^4SO_2—]_n$.

In contrast with simple sulfones the spectra obtained from the irradiated polysulfones are generally not well-resolved and consequently more difficult to interpret. Polysulfones of straight chain 1-alkenes (2, 3, 4, 5, 6, 8 and 10 carbon atoms) exhibit two main spectral features immediately after irradiation at 77 K, belonging to hydrocarbon radicals and to $RSO_2^{\cdot}$ radicals. On warming to 193 K, the spectrum of the hydrocarbon radical is reduced while the $RSO_2^{\cdot}$ spectrum gains intensity and after a few minutes only a considerably strengthened $RSO_2^{\cdot}$ spectrum remains; this is fairly stable at 20 °C. Similar results were obtained for the following polyalkene sulfones: 2-butene, isobutene, 3-methyl-1-butene, cyclopentene, 2-methyl-1-pentene and 4,4-dimethyl-1-pentene.

Lyons and coworkers[66] studied the ESR spectra of bakelite polysulfone $[—C_6H_4—O—C_6H_4—SO_2—C_6H_4—O—C_6H_4—C(CH_3)_2—]_n$ γ-irradiated at 77 K and found features characteristic of at least four radicals, the cyclohexadienyl radical, formed from addition to the aromatic ring, methylene groups ($—^{\cdot}CH_2$) formed from H abstraction from the methyl group, phenoxy radicals and peroxy radicals.

V. THE FINAL PRODUCTS IN THE RADIOLYSIS OF SULFONES

A. Sulfones

Ayscough and coworkers[65] studied the amount of gaseous products from radiolysis of dimethyl, diethyl and dipropyl sulfones at 77 K and found that their yields were an order of magnitude lower than expected from G(radicals) [G(radicals) ~ 2.0]. Due to the small amounts of gas only approximate analyses were made. A little hydrogen was formed, the yield increasing with the length of the hydrocarbon chain. Only a trace of methane was recovered from irradiated dimethyl sulfone and only a trace of ethane was found in irradiated diethyl sulfone, which indicates that methyl and ethyl radicals disappear by combination and not by abstraction reaction. The authors found also formation of some SO_2, indicating simultaneous cleavage of both S—C bonds.

Kevan and colleagues[69] studied the products of the radiolysis of solid diaryl sulfones at room temperature, such as *p,p'*-ditolyl, diphenyl sulfone and dibenzothiophene-*S,S*-dioxide. The products found for the first two were SO_2 and the diaryl hydrocarbon. For *p,p'*-ditolyl sulfone the SO_2 yield is linear with dose upto about 13 Mrad, above which it falls off considerably from linearity. The initial yields give $G(SO_2) = 0.05$, which is equal within experimental error to the yield of *p,p'*-bitolyl. The only another organic product observed had a smaller yield by a factor of 7, and could not be identified. The authors pointed out that no polymeric product was found in contrast to what is known on benzene radiolysis. The mass balance suggests that a simple decomposition as shown by equation 50 is the net consequence of radiolysis.

$$Ar—SO_2—Ar \longrightarrow SO_2 + Ar—Ar \tag{50}$$

In the radiolysis of diphenyl sulfone, the yield of SO_2 shows marked deviation from linearity as a function of the dose. For higher doses it appears that SO_2 yield is 2–3 times less than the biphenyl yield of 0.05. The authors suggested that not all of the SO_2 was detected and that a significant amount was trapped in the irradiated crystals. After

radiolysis, several irradiated diphenyl sulfone samples were heated to 100 °C for 1 h. This treatment increased the SO_2 yields but did not give very reproducible results. The authors suggested that radiolysis of diphenyl sulfone also occurs by reaction 50 and since the yield of Ar—Ar is the same for diphenyl and *p,p'*-ditolyl sulfones, both sulfones appear to have about the same stability toward radiolytic decomposition.

In dibenzothiophene-*S,S*-dioxide the S atom is in a ring, and hence more constrained. The yield of SO_2 in the radiolysis is linear with the dose to about 13 Mrad after which it levels off as in *p,p'*-ditolyl sulfone. However, the yield of SO_2 in this case is much lower (a factor of 25) than in the case of *p,p'*-ditolyl sulfone ($G = 0.002$ compared to $G = 0.05$). This stability of the dibenzothiophene sulfone could be partially due to back reaction to reform the parent sulfone and partially due to more efficient energy delocalization. The expected biphenylene product was not detected due to limitations of the analytical method. Bowmer and O'Donnell[70] studied the volatile products in γ-radiolysis of dialkyl, alkyl aryl and diaryl sulfones. Table 2 gives the radiolytic yields of SO_2 and of the hydrocarbon products of the alkyl or aryl radicals. The hydrocarbon products are those obtained either by H atom abstraction or by radical combination. The authors[69] suggested the mechanism

$$RSO_2R' \rightsquigarrow R^{\bullet} + {}^{*}SO_2R' \tag{51}$$

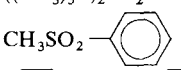
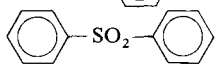
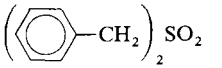
$$^{*}SO_2R' \longrightarrow R'^{\bullet} + SO_2 \tag{52}$$

$$R^{\bullet} + RSO_2R' \longrightarrow RH + {}^{\bullet}R''SO_2R' \tag{53}$$

$$R^{\bullet} + R''^{\bullet} \longrightarrow RR' \tag{54}$$

Besides the products given in Table 2 the authors also observed hydrogen, but they did not report their results. The table shows that the yield of alkane (RH + R'H) resulting

TABLE 2. Yields of major radiolysis products from dialkyl/aryl sulfones (after Reference 70 with permission of the authors)[a]

Sulfone (RSO_2R')	Products[b]				
	($G(SO_2)$	G(RH)	G(R'H)	G(R–R')	X[d]
$CH_3SO_2CH_3$	0.26	0.6	0.6	0.13	4.6
$C_2H_5SO_2C_2H_5$	0.15	0.24	0.24	0.05	3.2
$(CH_3CH_2CH_2)_2SO_2$	0.5	0.3	0.3	0.05–0.1	1.2
$CH_3SO_2C_2H_5$	0.1	0.3	0.3–0.35	0.07	6.2
$((CH_3)_2CH)_2SO_2$	0.8	0.9	0.9	0.1	2.2
$((CH_3)_3C)_2SO_2$	1.5	2.2[c]	2.2[c]		2.9
	0.04	0.045	0.01–0.02	0.01	1.5
	0.035	0.005	0.005		0.29
	0.14	0.015	0.015		0.21

[a] Irradiation at 25 °C; *G* values constant to 10 Mrad.
[b] If R = R', *G*(RH) in table = $G(R'H) = \frac{1}{2}$(total alkane yield), e.g. $G(CH_4) = 1.2$ from dimethyl sulfone.
[c] *G*(isobutane) = 1.2, *G*(isobutene) = 3.2.
[d] $X = [G(RH) + G(R'H)]/G(SO_2)$

from the hydrogen abstraction reaction 53 is an order of magnitude larger than the yield of the alkane (R—R′) formed in the combination reaction 54. This indicates that RH is mainly due to hydrogen abstraction and not to disproportionation reaction as the ratio disproportionation/combination is less than one for these radicals[71]. Scission of the two adjacent C—S bonds in a dialkyl sulfone is a prerequisite for SO_2 formation. Therefore a minimum yield for alkyl radical production in pairs can be estimated as $2G(SO_2)$, assuming that SO_2 is not lost in other reactions. Comparing the yields of SO_2 and R—R′ in Table 2 shows that only at most 50% and in most cases considerably less of the alkyl radicals formed in pairs combine to form R—R′. These are upper limits of combination as it is reasonable that some of the formed SO_2 is lost in reaction with radicals to give sulfinic acids and disulfones.

The apparent efficiency of combination of the alkyl radicals decreases as the size of the alkyl radical increases; $G(R—R')/G(SO_2)$ is a decreasing linear function of the number of carbon atoms of the alkyl radical[69]. This effect of the radical size presumably reflects the decreasing mobility of the alkyl radical with increasing size.

The yield of the alkane RH (and R′H) is much larger than the yield of SO_2, as shown in Table 2, indicating that reaction 53 does not always follow reaction 52. A substantial proportion of the RH is produced as a consequence of a single C—S scission. The ESR studies of Ayscough and coworkers[65] have shown that the main radical species produced by irradiation at 77 K, and hence presumably the initial radical produced during irradiation at 25 °C, is the alkyl radical resulting from C—S scission. The relatively low concentration of $RSO_2^{\cdot}$ radicals indicates that either reaction 52 follows rapidly reaction 51, or the $RSO_2^{\cdot}$ species resulting from a single C—S scission in the molecule is not a radical. As the yields of RH and R′H are larger than the yield of SO_2, Bowmer and O'Donnell[70] propose that the first explanation cannot be the sole cause for the low concentration of $RSO_2^{\cdot}$ radicals and suggest that the second is also an important one and consequently suggest that the intial radiolysis reactions are

$$RSO_2R' \rightsquigarrow [RSO_2R']^{\ddagger} + e^- \tag{55}$$

$$[RSO_2R']^{\ddagger} \longrightarrow RSO_2^{+} + R^{\cdot} \tag{56}$$

This sequence of formation of radical cation which is followed by a C—S bond scission into alkyl radical and alkyl sulfonyl cation was previously suggested by the same authors for the radiolysis of poly(olefin sulfone)s in the solid state[72] and was confirmed by scavenger studies[73]. Scavengers are ineffective in crystalline solids such as dialkyl sulfones and hence could not be used in this study.

The dialkyl sulfones with branched alkyl radicals, viz. di-isopropyl sulfone and di-*t*-butyl sulfone, gave considerably higher yields of SO_2 and RH compared to linear alkyl sulfones. The increased steric constraint at the C—S bond for the branched alkyl sulfones results evidently in increased C—S scission and hydrogen abstraction. Comparison of alkyl-aryl sulfones and diaryl sulfones with dialkyl sulfones shows a strong decrease in the yield of volatile product, the well-known protection effect of the aromatic groups. This is in accord with the ESR results of Ayscough and coworkers[65] on the ESR spectra of sulfones irradiated at 77 K, however this study was only a qualitative one. The yield of SO_2 is four times higher in the case of *p,p*′-ditolyl sulfone than in radiolysis of dibenzyl sulfone, which is the same trend observed previously by Kevan and coworkers[69]. However, the yield of SO_2 observed by Bowmer and O'Donnell[71] is higher than that measured by Kevan and coworkers ($G = 0.14$ and 0.05 respectively for *p,p*′-ditolyl sulfone). Thus the phenyl substituent is far more efficient in radiation protection of the sulfones. One phenyl group is sufficient for protection concerning the SO_2 yield, as the radiolytic yields of methyl phenyl sulfone and di-phenyl sulfone are about the same. However, a large difference exists between methyl phenyl sulfone and diphenyl sulfone concerning the yields of hydrocar-

bons. For most dialkyl sulfones $G(RH + R'H)/G(SO_2) > 2$ and a very similar value is obtained for methyl phenyl sulfone. However, for the two diaryl sulfones this ratio is only 0.2–0.3. This observation can be due to a competing reaction removing aryl radicals by another mechanism than hydrogen abstraction, or to a high efficiency of combination of $R^\bullet$ and $R'^\bullet$. The second explanation is supported by the results of Kevan and coworkers[69] on the yields of the diaryl hydrocarbon.

Di-*t*-butyl sulfone is different from the other dialkyl sulfones in that RH is mainly alkene and not alkane [G(isobutene) = 3.2 and G(isobutane) = 1.2]. The preference for isobutene over isobutane means that the formation of the alkene cannot be due to disproportionation of two *t*-butyl radicals but is due to a hydrogen atom expulsion as suggested by Bowmer and O'Donnell[70]

$$CH_3-\overset{\displaystyle CH_3}{\overset{|}{\dot{C}}}-CH_3 \longrightarrow CH_2{=}\overset{\displaystyle CH_3}{\overset{|}{C}}-CH_3 + H^\bullet \qquad (57)$$

or may be due to disproportionation with $RSO_2^\bullet$ radicals to give isobutene and sulfinic acid.

$$R^\bullet + RSO_2^\bullet \longrightarrow R(-H) + RSO_2H \qquad (58)$$

Although SO_2, RH and RR are the major products, they are not the only ones and for radiolysis of dimethyl sulfone Bowmer and O'Donnell[70] identified another twenty products.

B. Poly(olefin sulfone)s: Volatile Products

Most of the radiolysis studies with polysulfones were done on poly(olefin sulfone)s due to their application in the field of microelectronics, where their high radiation sensitivity is used to produce lithographic masks, for the manufacture of integrated circuits on silicon wafers, by electron beam writing on poly(olefin sulfone) films. Poly(olefin sulfone)s are copolymers containing sulfur dioxide and two carbon–atom units in the chain, i.e. $-SO_2-CHR-CH_2-$, or more generally $-SO_2-CR_2-CR_2-$. They are usually prepared by the free radical copolymerization of SO_2 and an olefin. Bowmer and O'Donnell[74] studied the volatile products of radiolysis of several poly(olefin sulfone)s, and the yield of the main products, SO_2, olefin and H_2, are given in Table 3. Other products with lower yields are also formed[74]. The general features of the formation of volatile products can be summarized as follows: (a) the G value for the total yield of volatile products from all poly(olefin sulfone)s studied is large compared to the values from hydrocarbon polymers; (b) the major products are sulfur dioxide and olefin, i.e., the two monomers; (c) $G(\text{olefin})/G(SO_2)$ increases with the irradiation temperatures towards unity, the value in the initial polymer; (d) at 0 °C $G(\text{olefin})/G(SO_2)$ is considerably lower than unity (0.1–0.5); (e) the yield of volatile products rises rapidly as the irradiation temperature is increased; and (f) depolymerization, which produces the two monomers, dominates the irradiation process with side-chain fracture and fragmentation reactions and secondary reactions being of minor importance.

The observation that G(volatile products) is very high, 10–200 at 0 °C and 10,000–15,000 at 150 °C, indicates that a chain reaction has been initiated, as the yields of the products is much higher than the yield of primary species. The chain reaction leads mainly to depolymerization to the monomers. The depolymerization to monomers is thermodynamically favored at high temperatures (above the ceiling temperatures), resulting in a rapid increase in the radiolytic yields of SO_2 and olefin. The yield of hydrogen increases very little with temperature in the range 75 °C to 150 °C, but the trend is unclear in the range 0 °C to 75 °C where for some poly(olefin sulfone)s the yield increases while for others there is a decrease in $G(H_2)$.

TABLE 3. *G* values of volatile products from poly(olefin sulfone)s

	Yields											
	0 °C				75 °C				150 °C			
	SO_2	Olefin[a]	Olefin	H_2	SO_2	Olefin[a]	Olefin	H_2	SO_2	Olefin[a]	Olefin	H_2
Olefin			SO_2				SO_2				SO_2	
Ethylene	2.4–3.0	0.3–0.4	0.1	0.13	9.8	3.3	0.29	0.19	57	56	1.0	0.84
Propene	13.2	1.7	0.13	0.36	110	58	0.53	0.1	3500	3500	1.0	0.51
1-Butene	13.2	1.99	0.15	0.4	475	405	0.85	0.53	4110	4700	1.1	0.7
Isobutene	80	40.2	0.5	0.54	1625	1300	0.8	0.27	4900	4400	0.9	1.0
1-Hexene	21.1	23.1	1.1	0.94	1610	1225	0.8	0.80	4500	3775	0.85	1.5
4,4-Di-methyl-1-pentene	115	53	0.5	0.52	1200	860	0.7	0.57	6500	5950	0.9	1.0
3-Methyl-1-butene	310	6.15	0.2	0.63	550	131.4	0.24	0.2	2350	595	0.25	50
2-Butene	80.6	40.4	0.5	0.41	1800	1610	0.90	0.55	8125	8300	1.0	1.0
Cyclohexene	210	36.5	0.17	0.06	2000	1400	0.70	0.63	9000	7400	0.82	1.1

[a]The sum of the parent olefin and its isomer.

The lower yield for olefin than for SO_2 was explained by scavenging of the formed free olefin on the cationic sites of the irradiated polymer in a homopolymerization reaction, thus reducing G(olefin). Adding cation scavengers it was found that the overall product yield was reduced with concurrent reduction of the SO_2/olefin ratio towards unity[73]. Thus it can be concluded that the homopolymerization of the olefin is occurring by a cationic mechanism.

Bowmer and Bowden[75] studied the radiation degradation of poly-2-methyl-1-pentene sulfone and found that at low radiation doses the SO_2/olefin ratio is $\sim 2:1$, however at high doses this ratio is decreased and is close to unity. Thus the oligomerization of the olefin, which is the cause for the discrepancy between $G(SO_2)$ and G(olefin), appears to be reversible.

The missing olefin is not due to free olefin being physically trapped in the polymer, as was proved by dissolving the polymer in an appropriate solvent, a process which should free any trapped olefin. The G(olefin)/$G(SO_2)$ ratio is determined by competition of the cation in the polymer undergoing (a) depropagation or (b) olefin oligomerization, a competition which depends on the cation lifetime. At higher temperatures depropagation is favored.

The dose dependence of the major products is linear for low doses but for doses of about 1 Mrad there is deviation from linearity and the yield levels off. This deviation from linearity was explained by Bowmer and O'Donnell as due to several factors: (a) Substantial degradation of the polymer leads to a noticeable weight loss. However if this was the main factor it could be expected that the leveling-off will be more prominent, the higher the irradiation temperature, due to the higher G value, while Bowmer and O'Donnell's results show the opposite trend. (b) The occurrence of the secondary reactions between the volatile products and the polymer, although SO_2 may also react with the polymer to form sulfinic or sulfonic acids. (c) The influence of the monomer–polymer equilibrium at high monomer vapor pressures. The effect of the equilibrium will become more important at high irradiation temperatures and high radiation doses.

The most radiation-stable poly(olefin sulfone) is poly(ethylene sulfone) and the most radiation-sensitive is poly(cyclohexene sulfone). In the case of poly(3-methyl-1-butene sulfone) there is very much isomerization of the olefin formed by radiolysis and only 58.5% of the olefin formed is 3-methyl-1-butene. The main isomerization product is 2-methyl-2-butene (37.3% of the olefin). Similar isomerization, though to a smaller extent, occurs in poly(1-butene sulfone) where about 10% of 2-butene is formed. The formation of the olefin isomer may occur partly by radiation-induced isomerization of the initial olefin, but studies with added scavengers[73] do not support this as the major source of the isomers. The presence of a cation scavenger, triethylamine, eliminates the formation of the isomer of the parent olefin in both cases of poly(1-butene sulfone) and poly(3-methyl-1-butene sulfone)[73] indicating that the isomerization of the olefin occurred mainly by a cationic mechanism, as suggested previously[72].

The minor products are generally 1–3% of the total yield and arose from: (a) side-chain fragmentation producing hydrogen and low-molecular-weight hydrocarbons; (b) addition of these fragments to the free olefin; (c) dimerization and trimerization of the free olefin; (d) fragmentation of the alkyl radical and cation intermediates.

Hydrogen, which is a major product in the radiolysis of most hydrocarbon polymers, is only a minor product in the radiolysis of poly(olefin sulfone)s, although it is of the largest yield between the minor products. Hydrogen is formed by H$^\cdot$ atoms combination or by an H$^\cdot$ atom abstracting hydrogen

$$H^\cdot + RH \longrightarrow R^\cdot + H_2 \tag{59}$$

The effect of the temperature is an exponential increase in the radiolytic yield of the volatile products for each poly(olefin sulfone). If the logarithm of G(volatile products) is

plotted versus a reduced temperature scale (T/T_c), where T and T_c are the irradiation and ceiling temperatures, similar plots are obtained for most poly(olefin sulfone)s[76], although they did not form a master curve. Some of the variation may be attributed to the inadequacy of the chosen T_c. The G value increased by about 3 orders of magnitude from $T = 0.7T_c$ to $T = 1.3T_c$ for all of the poly(olefin sulfone)s.

The main reaction in the radiation degradation of all the poly(olefin sulfone)s is the depropagation step

$$-(MS)_n- \longrightarrow -(MS)_{n-x}- + xM + xS \tag{60}$$

One way to measure the thermodynamics of the reaction is by the ceiling temperatures, T_c (the temperature at which the free energy of reaction 56 is zero). Bowmer and O'Donnell[74] found that $G(SO_2)$ increases with decreasing T_c showing the importance of the thermodynamic factor. Although kinetic factors can explain also the increase in $G(SO_2)$ with temperature, they do not explain the observed correlation with T_c.

Bowmer and O'Donnell suggested a general mechanism (Figure 8) for the degradation

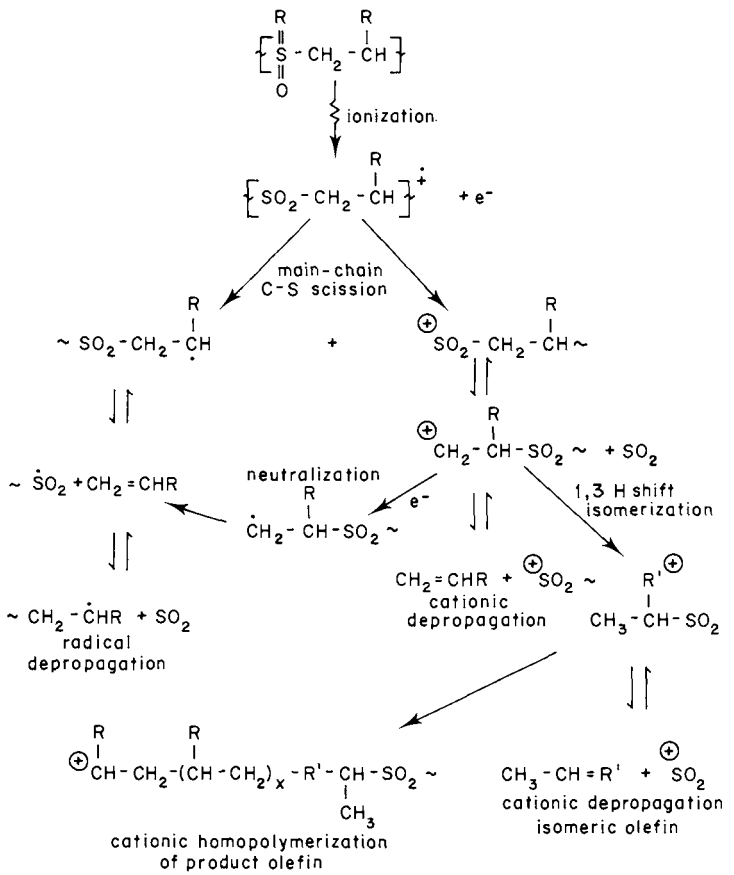


FIGURE 8. Overall reactions scheme for radiation degradation of poly(olefin sulfone)s. Reproduced by permission of the authors from Reference 74.

of poly(olefin sulfone)s which involved initial C—S bond scission producing free radicals and cationic fragments followed by: (a) depropagation via both radical and cationic species; (b) oligomerization of free olefin initiated by cationic species on the residual polymer; (c) isomerization of the olefin via the cationic species.

However, Pacansky and his coworkers[77] studied the degradation of poly(2-methyl-1-pentene sulfone) by electron beams and from infrared studies of the products suggest another mechanism. They claim that SO_2 was exclusively produced at low doses with no concomitant formation of the olefin. The residual polymer was considered to be essentially pure poly(2-methyl-1-pentene) and this polyolefin underwent depolymerization after further irradiation. However, the high yield of SO_2 requires the assumption of a chain reaction and it is difficult to think of a chain reaction which will form SO_2 and no olefin.

Kaplan[78] studied the X-ray radiolysis of poly(ω-chloroolefin sulfone)s and found that the chlorine-containing polymers are less sensitive to radiation than the non-chlorine containing species. He found that dehydrochlorination is a significant reaction in the radiolysis of poly(ω-chloroolefin sulfone)s, but it is not a necessary one in order to lose SO_2.

C. Poly(olefin sulfone)s: Molecular Weight Changes

The molecular-weight changes in radiolysis of polymers are due to two reactions of opposite trends: (a) scission of the backbone chains which leads to a decrease in the molecular weight; (b) intermolecular crosslinking of the polymer molecules leading to increasing molecular weight. The changes in molecular weight are usually determined from measurement of solution properties, e.g. viscosity, osmotic pressure, light scattering and gel permeation chromatography.

The high sensitivity of poly(olefin sulfone)s to chain scission by radiation was first discovered for poly(1-butene sulfone) and poly(1-hexene sulfone) by Brown and O'Donnell[79,80].

Brown and O'Donnell[80] measured the changes in the molecular weights of these polymers after various radiation doses at different temperatures in air and in vacuum by viscometry (yielding viscosity-average molecular weight, M_v) and by osmometry (yielding number-average molecular weight, M_n). The osmometric method is advantageous as it gives absolute values but suffers from experimental difficulties. The molecular weights can be derived from the K and a parameters of the relation for the $[\eta]$, limiting viscosity number, $[\eta] = K\bar{M}^{a}$[85] for the unirradiated polymer. However branching, cross-linking and mainly intramolecular cross-linking caused also by the irradiation can alter the hydrodynamic behavior and hence the values of the parameters K and a. Thus, the calculated molecular weights might possess a slight error. In any case the rapid decrease in limiting viscosity number on irradiation shows that main-chain scission is predominant and that it occurs more rapidly in air than in vacuum.

The ratio M_v/M_n was not changed considerably with the dose; it remained in the range of 5.2–7.0 for one case where M_v itself changes by more than one order of magnitude (from 2.75×10^6 to 1.78×10^5), indicating that the molecular-weight distribution remains broad despite the substantial decrease in the molecular weight. The value of M_n after irradiation by dose D, namely function $M_n(D)$, is related to the initial value of M_n, $M_n(0)$, by the relation[81]

$$M_n^{-1}(D) = M_n^{-1}(0) + D[G(S)\text{-}G(x)]/(9.65 \times 10^5) \tag{61}$$

where $G(S)$ and $G(x)$ are the radiolytic yields of scission and cross-linking, respectively. Brown and O'Donnell[80] found for both poly(sulfones) of 1-butene and 1-hexene $G(S)\text{-}G(x) \sim 10$ in vacuum at 30 °C. These values are essentially equal to $G(S)$, since it is usually

considered that cross-linking is negligible in the radiation degradation of poly(olefin sulfone)s of the lower olefins. However, for higher olefins considerable cross-linking does occur. Gray[82] observed that γ-irradiation of poly(hexadecene-1-sulfone) to a dose of 2.5 Mrad produced a substantial increase in density, tensile strength and tensile modulus, indicative of cross-linking and not of scission. It is reasonable to assume that cross-linking does occur in polysulfones containing large proportions of CH_2 groups, since such polymers will resemble polyethylene, in which cross-linking occurs readily.

Bowden and Thompson[83] studied the degradation of thin films of various poly(olefin sulfone)s of low olefins due to radiolysis by electron beams at 20 °C. All samples decreased in thickness, indicating scission and depropagation.

VI. THE RADIOLYSIS OF SOLUTIONS OF POLY(OLEFIN SULFONE)S

Horie and Schnabel[84] studied the radiolysis of dilute solutions of poly(1-butene sulfone), PBS, and poly(1-hexene sulfone), PHS, in various solvents, mainly 1,4-dioxane. The radiolyses were done with single 100 ns pulses of 16 MeV electrons from a linear acceletator. Molecular-size changes were followed by light-scattering measurements at a scattering angle of 90°. The scattered-light intensity was found to decay with firsr-order kinetics. A measure of the final degradation of the polymer due to the absorbed dose D is given by

$$R^{D} = \frac{U_0 - U_f}{U_f - U_L} \tag{62}$$

where U is the measured signal of the scattered light, which is proportional to the intensity of the scattered light. The subscripts 0, f and L refer to the system before irradiation and after irradiation, and to the pure solvent, respectively.

The quantity R^{D} is proportional to the number of chain scissions per original macromolecule. For both PBS and PHS, for all solvents studied (1,4-dioxane, acetonitrile, chloroform, tetrahydrofuran, toluene and 2-butanone) the scattered light intensity decreases after irradiation. The amount of degradation R^{D} for the same polysulfone is higher for solvents with larger yield of radicals. R^{D} is larger for PHS than for PBS in the case of the solvents 1,4-dioxane and acetonitrile, which have the highest yield of radicals; R^{D} for PHS and PBS are about the same in the case of chloroform and tetrahydrofuran as solvents. The half-life of the degradation process (30–100 μs) increases with increasing viscosity of the solvent which indicates that the rate-determining step is the diffusion of the fragments. The half-life is about the same as for poly(phenyl vinyl ketone) in the same solvents and there the rate-determining step is clearly the diffusion of the fragments, since the chemical-bond rupture occurs much more rapidly.

Increasing the dose of the electron pulse leads to initial increase in R^{D}. In the case of PBS in argon-saturated dioxane the increase in R^{D} is not linear with the dose and for high doses ($D > 40$ krad) R^{D} is almost independent of the dose. On the other hand, in the case of PBS in aerated dioxane solution, where R^{D} is higher than in argon-saturated solution, R^{D} is linear with the absorbed dose. In the case of PHS there is no difference between aerated and argon-saturated dioxane. For PHS, R^{D} is not linearly dependent on dose but the levelling off is much smaller than in the case of PBS/Ar-saturated dioxane. The non-linear dependence of R^{D} on the absorbed dose, as observed with PHS both in the presence and absence of oxygen and with PBS in the absence of oxygen, can be interpreted in terms of recombinations of fragments, at times much shorter than the diffusion time of the fragments(F).

$$\text{Polymer} \rightsquigarrow F_1^{\cdot} + F_2^{\cdot} + F_3^{\cdot} + \text{etc.} \tag{63}$$

Each macromolecule is fragmented several times at high doses and the relatively high local concentration of macroradicals favors recombination of the fragments, e.g.

$$F_1^{\cdot} + F_2^{\cdot} \longrightarrow F_1F_2 \tag{64}$$

The recombination of fragments stemming from one macromolecule, at times shorter than the diffusion time, prevents the linear increase in R^D with the absorbed dose per pulse, as not all main-chain scissions result in the formation of fragments. The effect of molecular oxygen on R^D in the case of PBS can be interpreted by formation of peroxyl radicals, e.g.

$$F_1^{\cdot} + O_2 \longrightarrow F_1O_2^{\cdot} \tag{65}$$

which are incapable of forming stable combination products between two of them. Thus oxygen acts as a fixing agent for the main-chain scission. The different behavior of PBS and PHS is not explained by the authors[84] except for a general statement that it might be due to steric hindrance which retarded the reaction between the fragments (and consequently the leveling-off with dose is not as strong as in PBS) and also the reaction between the fragments and oxygen, so that the presence of oxygen does not increase R^D. This explanation can be questioned, since the steric hindrance only retards the combination but does not prevent it completely, so it should be expected that the fragments will still react with oxygen. The reduced reactivity of the PHS radical can be explained as due to the six-membered ring of the radicals[84] which will result in a longer lifetime of the radical.

An alternative explanation suggested by the authors for the non-linearity of R^D with dose is the formation of reactive solvent species capable of intercepting the scission reaction, with a yield which becomes greater the higher the absorbed dose per pulse. However, this mechanism does not explain the effect of oxygen.

An interesting finding is a slow increase ($t_{1/2} \sim 0.5$ ms), observed in PBS in tetrahydrofuran solution, after the faster decrease ($t_{1/2} \sim 30\,\mu$s). This indicates that some of the fragments diffuse while still carrying reactive sites and can combine in the bulk.

Transient absorption spectra were measured with PBS in dioxane solution. In aerated solution the absorption decayed by two processes, a rapid one with $t_{1/2} \sim 50\,\mu$s and a slow one with $t_{1/2} \sim 20$ ms. In argon-saturated solution, a relatively weak absorption which decayed with $t_{1/2} \sim 20$ ms was observed. The rate of the rapid decrease in the optical density agrees with that of the decrease in the intensity of the scattered light.

As no long-lasting absorption was detected with pure dioxane, the transient absorptions found with PBS solutions are due to macroradicals or macroions.

The molecular-weight change due to irradiation of PBS in dioxane solution was measured by gel chromatography. The initially rather broad molecular-weight distribution becomes narrower with radiation-induced main-chain scission. However, the change is much less than that expected from statistical main-chain scission as a sole process. This observation, and the finding that at intermediate dose range there is a binodal distribution, indicate that another process also occurs, namely cross-linking. The number of scissions per initial macromolecule, Z_s, can be calculated from the distribution curves by the equation

$$Z_s = [M_n(0)/M_n(D)] - 1 \tag{66}$$

It was found that Z_s levels off at dose > 20 krad. The cross-linking process in dioxane occurs at times longer than several milliseconds. Similar results were obtained for PHS in dioxane, however the radiolytic yield of scission, $G(S)$, measured from the initial slope of the plot of Z_s vs. D, is different for the two polymers; $G(S)$ is about 12 for PBS and about 4 for PHS, in contrast to irradiation of the pure polymers, where for both at 30° $G(S) \sim 10$[80].

VII. REFERENCES

1. J. H. O'Donnell and D. F. Sangster, *Principles of Radiation Chemistry*, Edward Arnold, London, 1970.
2. J. W. T. Spinks and R. J. Wood, *An Introduction to Radiation Chemistry*, 2nd edn, Wiley, Chichester, 1976.
3. A. J. Swallow, *Radiation Chemistry—An Introduction*, Longman, London, 1973.
4. A. Mozumder, *Adv. Radiat. Chem.*, **1**, 1 (1969).
5. E. G. Janzen, *Acc. Chem. Res.*, **4**, 31 (1971).
6. P. K. Ludwig, *Adv. Radiat. Chem.*, **3**, 1 (1972).
7. K. Nishikida and F. Williams, *J. Amer. Chem. Soc.*, **96**, 4781 (1974).
8. Y. T. Chung, K. Nishikida and F. Williams, *J. Phys. Chem.*, **78**, 1882 (1974).
9. R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, **39**, 2147 (1963).
10. G. Herzberg, *The Spectra and Structure of Simple Free Radicals*, Cornell University Press, New York, 1971, p. 173.
11. F. Williams and E. D. Sprague, *Acc. Chem. Res.*, **15**, 408 (1982).
12. M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 908 (1976).
13. N. M. Shislov, R. A. Sadykov, V. A. Mazunov and A. A. Panasenko, *Khim. Vys. Energ.*, **16**, 523 (1982).
14. N. M. Shislov, V. N. Korobeinikova, V. A. Mazunov, A. A. Panasenko and R. A. Sadykov, *Khim. Vys. Energ.*, **17**, 179 (1983).
15. M. C. R. Symons, *Radiat. Phys. Chem.*, **15**, 453 (1980).
16. N. M. Shislov, A. I. Ivanov, R. A. Sadykov, A. A. Panasenko and V. N. Korobeinikova, *Khim. Vys. Energ.*, **17**, 554 (1983).
17. E. D. Sprague, K. Takeda, J. T. Wang and F. Williams, *Can. J. Chem.*, **52**, 2840 (1974).
18. E. D. Sprague and F. Williams, *J. Chem. Phys.*, **54**, 5425 (1971).
19. V. I. Trofimov, I. I. Chkheidze and L. I. Belenkii, *Theor, Exp. Khim.*, **5**, 406 (1969).
20. V. I. Trofimov, I. I. Chkheidze, L. I. Belenkii and N. Y. Buden, *Theor. Exp. Khim.*, **4**, 82 (1968).
21. T. J. Kemp, J. P. Roberts, G. A. Salmon and G. F. Thompson, *J. Phys. Chem.*, **72**, 1464 (1968).
22. L. Michaelis, M. P. Schubert and S. Granick, *J. Amer. Chem. Soc.*, **61**, 1981 (1939).
23. E. Hayon, *J. Chem. Phys.*, **53**, 2353 (1970).
24. D. Gill, J. Jagur-Grodzinski and M. Szwarc, *Trans. Faraday Soc.*, **60**, 1424 (1964).
25. A. Kira, S. Arai and M. Imamura, *Int. J. Radiat. Phys. Chem.*, **5**, 127 (1973).
26. S. Arai, A. Kira and M. Imamura, *J. Chem. Phys.*, **54**, 5073 (1971).
27. A. M. Koulkes-Pujo, L. Giles, B. Lesigne and J. Sutton, *Chem. Commun.*, 749 (1971).
28. D. C. Walker, N. V. Klassen and H. A. Gillis, *Chem. Phys. Letters*, **10**, 636 (1971).
29. R. Bensasson and E. J. Land, *Chem. Phys. Letters*, **15**, 195 (1972).
30. T. K. Cooker, D. C. Walker, H. A. Gillis and N. V. Klassen, *Can. J. Chem.*, **51**, 2195 (1973).
31. T. K. Cooper and D. C. Walker, *Can. J. Chem.*, **49**, 2248 (1971).
32. E. M. Fielden and E. J. Hart, *Radiat. Res.*, **33**, 426 (1968).
33. G. L. Hug, *Optical Spectra of Nonmetallic Inorganic Transient Species in Aqueous Solution, NSRDS–NBS*, **69**, 1981, p. 52.
34. A. M. Koulkes-Pujo and M. Berthou, *J. Chim. Phys.*, **66**, 1178 (1969).
35. A. M. Koulkes-Pujo, M. Moreau and J. Sutton, *J. Phys. Chem.*, **86**, 1421 (1982).
36. G. Meissner, A. Henglein and G. Beck, *Z. Naturforsch.*, **22b**, 13 (1967).
37. W. T. Dixon, R. O. C. Norman and A. J. Buley, *J. Chem. Soc.*, 3625 (1964).
38. R. O. C. Norman and B. C. Gilbert, *Adv. Phys. Org. Chem.*, **5**, 53 (1967).
39. W. Dameru, G. Lassman and K. Lohs, *Z. Chem.* (Leipzig), **9**, 343 (1969).
40. H. Taniguchi, H. Tagaki and H. Hatano, *J. Phys. Chem.*, **76**, 135 (1972).
41. B. C. Gilbert, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 303 (1975).
42. B. C. Gilbert, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 308 (1975).
43. C. Lagercrantz, *J. Phys. Chem.*, **75**, 3466 (1971).
44. W. B. Gara and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 1708 (1977).
45. D. Veltwisch, E. Janata and K.-D. Asmus, *J. Chem. Soc., Perkin Trans. 2*, 146 (1980).
46. S. A. Chaudhri, M. Gobl, T. Freyholdt and K.-D. Asmus, *J. Amer. Chem. Soc.*, **106**, 5988 (1984).
47. K.-D. Asmus, *Acc. Chem. Res.*, **12**, 436 (1979).
48. T. Sumiyoshi, N. Miura, M. Aikawa and M. Katayama, *Bull. Chem. Soc. Japan*, **55**, 2347 (1982).
49. D. N. R. Rao and M. C. R. Symons, *Chem. Phys. Letters*, **93**, 495 (1982).

50. A. M. Koulkes-Pujo, L. Gilles and J. Sutton, *J. Chem. Soc., Chem. Commun.*, 912 (1974).
51. A. M. Koulkes-Pujo, L. Gilles and J. Sutton, *J. Phys. Chem.*, **79**, 3038 (1975).
52. A. M. Koulkes-Pujo, L. Gilles and J. Sutton, *Nature*, **281**, 128 (1979).
53. J. C. Machado, C. Roneau, J. Cara, D. J. Apers and P. C. Capron, *Radiochem. Radioanal. Letters*, **8**, 33 (1971).
54. D. J. Nelson, *J. Phys. Chem.*, **82**, 1400 (1978).
55. A. M. Koulkes-Pujo, M. Moreau and J. Sutton, *FEBS Letters*, **129**, 52 (1981).
56. E. Hart, private communication cited in Reference 55.
57. H. Nishimura, S. Kawakishi and M. Namiki, *Agric. Biol. Chem.*, **34**, 609 (1970).
58. H. Nishimura, J. Mizutani, Y. Obata and M. Namiki, *Tetrahedron*, **27**, 307 (1971).
59. H. Nishimura and J. Mizutani, *Agric. Biol. Chem.*, **37**, 213 (1973).
60. Z. B. Alfassi, D. M. Golden and S. W. Benson, *Int. J. Chem. Kinet.*, **5**, 157 (1973).
61. V. N. Korobeinikova, G. G. Bikbaeva, Y. I. Morinov, Y. E. Nikitin and V. P. Kagakov, *Radiokhimiya*, **25**, 281 (1982).
62. S. A. Pai, J. P. Shukla and M. S. Subramanian, *J. Radioanal. Chem.*, **42**, 323 (1978).
63. S. A. Pai, J. P. Shukla and M. S. Subramanian, *Abstracts of papers presented at the Nuclear Chemistry and Radiochemical Symposium*, Waltair, 1980, p. 89.
64. W. J. Lan, F. Y. Xian and W. W. Qing, *Rad. Phys. Chem.*, **23**, 601 (1984).
65. P. B. Ayscough, K. J. Ivin and J. H. O'Donnell, *Trans. Faraday Soc.*, **61**, 1110 (1965).
66. A. R. Lyons, M. C. R. Symons and J. K. Yandell, *Macromol. Chem.*, **157**, 103 (1972).
67. M. Geoffroy and E. A. C. Lucken, *J. Chem. Phys.*, **55**, 271 (1971).
68. O. Ito and M. Matsuda, *Chem. Letters*, 909 (1974); O. Ito and M. Matsuda, *Bull. Chem. Soc. Japan*, **48**, 3389 (1975).
69. L. Kevan, P. L. Hall and E. T. Kaiser, *J. Phys. Chem.*, **70**, 853 (1966).
70. T. N. Bowmer and J. H. O'Donnell, *Rad. Phys. Chem.*, **17**, 177 (1981).
71. Z. B. Alfassi, in *Chemical Kinetics of Small Organic Radicals* (Ed. Z. B. Alfassi), CRC Press, Boca Raton, in press.
72. T. N. Bowmer, J. H. O'Donnell and P. R. Wells, *Polym. Bull.*, **2**, 103 (1980).
73. T. N. Bowmer, J. H. O'Donnell and P. R. Wells, *Makromol. Chem., Rapid Commun.*, **1**, 1 (1980).
74. T. N. Bowmer and J. H. O'Donnell, *J. Macromol. Sci., Chem.*, **A17**, 243 (263).
75. T. N. Bowmer and M. J. Bowden, in *Polymers in Electronics*, ACS Symposium No. 242, 1984, p. 153.
76. T. N. Bowmer and J. H. O'Donnell, *J. Polym. Sci., Polym. Chem. Ed.*, **19**, 45 (1981).
77. A. Gutierrez, J. Pacansky and R. Kroker, *Org. Coatings and Appl. Polym. Sci. Proceedings*, **46**, 520 (1982).
78. M. Kaplan, *Polym. Eng. Sci.*, **23**, 957 (1983).
79. J. R. Brown and J. H. O'Donnell, *Macromolecules*, **3**, 265 (1970).
80. J. R. Brown and J. H. O'Donnell, *Macromolecules*, **5**, 109 (1972).
81. A. Charlesby, *Atomic Radiation and Polymers*, Pergamon, London, 1960.
82. D. N. Gray, *Polym. Eng. Sci.*, **17**, 719 (1977).
83. M. J. Bowden and L. F. Thompson, *J. Appl. Polym. Sci.*, **15**, 1881 (1971).
84. K. Horie and W. Schnabel, *Polymer Deg. Ste.*, **8**, 145 (1984).
85. F. W. Billmeyer Jr., *Textbook of Polymer Science*, 2nd edn, John Wiley, New York, 1971, p. 87.

CHAPTER **20**

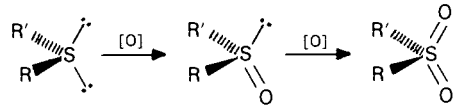
Reduction of sulphoxides and sulphones

J. STUART GROSSERT

Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada, B3H 4J3

I. INTRODUCTION

Sulphur, the sixteenth element in the Periodic Table, possesses filled K and L electron shells and has an M shell that is only two electrons short of being filled. It is thus an electronegative element that regularly forms two covalent bonds to other atoms in order to satisfy its valency requirements. However, the remaining lone electron pairs on a dicoordinate sulphur atom are available for further polar covalent bonding with certain very electronegative atoms; the nature of this bonding has been the subject of much research and discussion[1,2]. For example, the oxidation of a sulphide, first to a sulphoxide and then to a sulphone, is a well-explored and facile reaction that constitutes the prime example of the ability of sulphur to enter into this type of bonding; the process is depicted in equation (1):



(1)

This chapter deals with the reverse of these reactions. Since this is not a simple process, a brief discussion of the nature of the S—O bonds in sulphoxides and sulphones will be of assistance in understanding the requirements for reduction of these functional groups.

The polar covalent S—O bonds in sulphoxides and sulphones are of special interest to chemists. They are different from 'regular' S—O bonds, which, like all single bonds between atoms possessing lone pairs of electrons, are relatively weak and occur in relatively less-stable compounds. 'Regular' S—O bonds can be found in sulphenic acids and their esters, two of the lesser-known functional groups in organic sulphur chemistry[3]. These 'regular' S—O bonds are significantly longer than polar covalent S—O bonds and follow the general trend that longer bonds are weaker bonds. The typical S—O bond length in a sulphoxide is 149 pm whereas the S—O bond in a sulphenate ester is about 166 pm; both types of bond are found in the sulphite functional group and the structural properties of a number of sulphites are known in detail. For example, the crystal structure of 4, 4, 6-trimethyl-1, 3, 2-dioxathian-2-oxide has been determined[4] and relevant details are shown in Figure 1; this illustrates effectively the differences between the two types of S—O bonds.

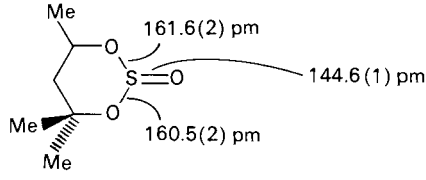


FIGURE 1

These arguments can be carried one step further; the S—O bonds in sulphones are both shorter (143 pm vs. 149 pm)[5,6] and stronger (bond dissociation energy of 469 vs. 368 kJ mol^{-1})[7] than those of sulphoxides. Typically, the S—O stretching frequencies in a sulphone are around 1290 (asymmetric stretch) and 1130 cm^{-1} (symmetric stretch), whereas in sulphoxides the frequencies are about 1040 cm^{-1}[6]. These frequencies can also be related to bond strengths. In fact, the S—O bond in a sulphone is one of the strongest bonds known, which is reflected in the chemistry of this functional group. Sulphones are normally quite unreactive and are a chemically inert species[2], especially with regard to oxidation or reduction reactions.

It is almost impossible to find a reducing agent that will *directly* deoxygenate a sulphone and convert it into a sulphoxide; apparently only one unusual example is known to date. By contrast, the sulphur atom in sulphoxides can be readily reduced (or oxidized) and numerous methods are available for either process. Thus, any reducing agent powerful enough to deoxygenate a sulphone to a sulphoxide would also readily reduce the latter group and sulphides would normally be expected from the *direct* reduction of a sulphone. However, as will be described, reductions of the S—C bonds in sulphones are more facile than are reductions of the S—O bonds, because reducing agents that are electron donors of sufficient power readily convert sulphones into radical anions. Addition of a second electron to these radical anions leads to a facile carbon–sulphur bond cleavage. Reduction reactions of these two types, together with other approaches, are discussed in this chapter.

II. REDUCTION OF SULPHOXIDES

The sulphur–oxygen bond in the sulphoxide functional group has a bond dissociation energy (~ 368 kJ mol^{-1})[7] of less than either the silicon–oxygen bond (~ 467 kJ mol^{-1})[8,9] in siloxanes, the boron–oxygen bond in borates (~ 510 kJ mol^{-1})[10], or the phosphorus–oxygen bond in phosphates or phosphonates (~ 540 kJ mol^{-1})[11]. It is thus to be expected that sulphoxides could be reduced by reacting them with the appropriate silane or trivalent phosphorus derivatives so that oxygen exchange can occur; indeed, this approach has been used effectively and it constitutes a major portion of the plethora of methods that have been devised for the reduction of sulphoxides. The other obvious approach to the reduction of sulphoxides is to use low-valent metals which can be either used directly or generated *in situ*.

This area of organosulphur chemistry has been fortunate to have been well and regularly reviewed in recent years[12], the reviews by a team of Polish and Japanese workers in 1977[13] and 1984[14] meriting special mention. This review will concentrate on recent developments in the reduction of sulphoxides.

A. Reduction by Oxygen-exchange Reactions

1. *Trivalent phosphorus reagents*

Phosphorous compounds that have been used as reducing agents for sulphoxides include triphenylphosphine, PCl_3, PBr_3 and triphenyl phosphite. However, the reaction with triphenylphosphine is sluggish although it has been found to be accelerated by the addition of iodine and sodium iodide in boiling acetonitrile as solvent[15]. The difficulty with reactions in which triphenylphosphine is converted to its oxide, is that this substance is often not readily separated from the reaction products without the use of procedures that on a large scale are expensive or cumbersome, such as chromatography. Three alternate procedures that claim simple workup procedures have been published. The first, due to Olah[15], equation (2), uses tris(dimethylamino)phosphine(HMPT)–iodine–sodium iodide and effectively reduces a useful range of sulphoxides to sulphides in a reasonable

time, with yields ranging from 68 to 96%. The phosphorus-containing end product is hexamethylphosphoric triamide (HMPA), which is water soluble, albeit toxic. Since the other products are also water soluble, extraction and workup of most sulphides prepared with this reaction is a simple procedure. The second reagent type, viz. P_2I_4 or PI_3, was proposed independently by Denis and Krief[16,17] and by Suzuki[18], see equation (3). Both reagents are commercially available, or can be prepared from readily available starting materials (either from $P_4 + I_2$ in CS_2[19], or from $KI + PCl_3$ in ether[18]), are easy to use and the reactions are complete in minutes. Workup is straightforward, giving 'practically pure sulphides' from a useful range of aryl and alkyl sulphoxides, in 70 to > 90% yields. The third reagent in this series, proposed by Amos[20], is a polymer-supported diphenylphosphine. Numerous polymer-supported reagents have been developed in recent years and they offer the great advantage of normally being removable from the reaction solution simply by filtration. This reaction is summarized in equation (4):

$$RS(O)R' \xrightarrow{(Me_2N)_3P-I_2-NaI/MeCN} RSR' \quad (2)$$

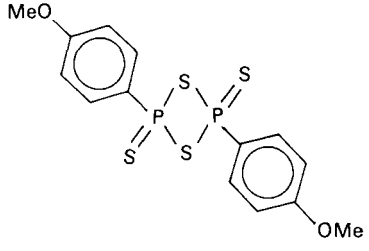
$$RS(O)R' \xrightarrow{P_2I_4 \text{ or } PI_3/CH_2Cl_2} RSR' \quad (3)$$

$$3\text{Ⓟ—}PPh_2 + CCl_4 + 2\,RS(O)R' \longrightarrow 2\,RSR' + 2\text{Ⓟ—}PPh_2O + \text{Ⓟ—}\overset{+}{P}Ph_2CCl_3Cl^- \quad (4)$$

Amos prepared his polymer-supported reagent in two steps from commercially available polystyrene beads (bromination, then condensation with lithium diphenylphosphide). He found that a useful range of sulphoxides could be reduced effectively, in good yields and in a few hours, to give clean samples of sulphides.

2. *Pentavalent phosphorus reagents*

There have apparently been no recent developments in reagents for desulphurizing sulphoxides that use pentavalent phosphorus compounds. Reagents that were reviewed in 1984[14] include phosphorus pentasulphide[21], thiophosphoryl bromide[22], Lawesson's reagent (**1**)[23], and phosphorus pentachloride in the presence of a trap for Cl^+ ions[24]. The traps used included an enamine or an *N*, *N*-dialkylaniline. Presumably, the net effect of this reaction is to generate phosphorus trichloride *in situ*. The three thiophosphorus reagents obviously function because the P=S bond is some 150 kJ mol^{-1} weaker than the P=O bond[11].



(**1**)

3. *Boron-containing reagents*

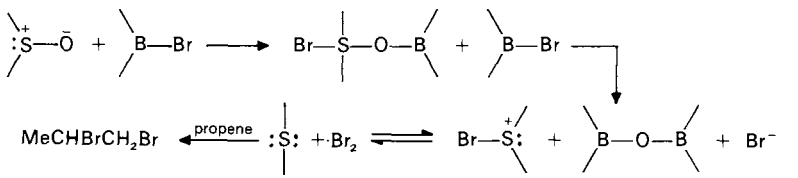
Sulphoxides are reduced by the more powerful metal hydride reducing agents[14], but the less reactive reagents such as sodium borohydride are ineffective. Recently, Yoon[25] has

developed a more potent reducing system in the form of sodium borohydride allied with triphenyl borate in dry THF solutions. Yields, determined by glc, ranged from 77 to > 95% for a useful range of sulphoxides after reaction periods of up to 28 h and a straightforward workup procedure.

Although dichloroborane has been successfully used to reduce dialkyl sulphoxides, it was less useful for the reduction of diaryl sulphoxides and recent work[26] has found that fully substituted bromoboranes can fill this gap. Three reagents were introduced, viz. bromodimethylborane, 9-bromo-9-borabicyclo[3.3.1]nonane (9-BBN-Br) and tribromoborane, the reactions being shown in equation (5):

$$RS(O)R' \xrightarrow{BBr_3 \text{ or } Me_2BBr \text{ or } 9\text{-BBN-Br}} RSR' \qquad (5)$$

The reactions were carried out in dichloromethane solvent in the presence of propene which serves as a bromine trap. In the cases of the two simpler boranes workup was quite simple with no chromatography being needed. Isolated yields ranged from 87 to > 95% for a useful range of sulphoxides and the reaction is selective in the presence of a range of other functional groups such as hydroxyls, acetals, esters, certain ethers and isolated alkenes. A reasonable pathway for the reaction is given in equation (6). Trapping of the liberated bromine by the propene displaces the equilibrium towards the formation of sulphides and precludes the intervention of Pummerer-type rearrangements or halogenation reactions that can readily divert sulphoxides or sulphides to unwanted products. The third boron-based deoxygenation reaction[27] uses a mixture of boron trifluoride etherate and sodium iodide in anhydrous acetone (equation 7). A very similar procedure in which acetonitrile was used as the solvent has recently been published by Vankar and Rao[28]. In both studies, nearly all the substrates were aryl sulphoxides, but the reactions were facile, isolated yields were generally about 90% and the workup was straightforward. The reaction pathway is probably similar to that outlined in equation (6).



(6)

$$RS(O)R' \xrightarrow{BF_3\text{–NaI/dry acetone or MeCN}} RSR' \qquad (7)$$

4. Silicon-containing reagents

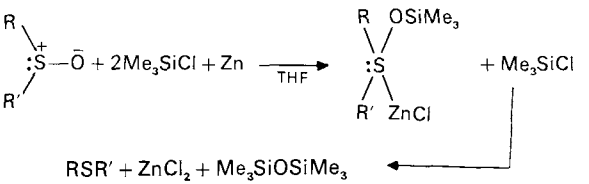
The structurally simplest silicon reagent that has been used to reduce sulphoxides is the carbene analog, dimethylsilylene (Me_2Si:)[29]. This molecule was used as a mechanistic probe and did not appear to be useful synthetically. Other silanes that have been used to reduce sulphoxides include iodotrimethylsilane, which is selective but unstable, and chlorotrimethylsilane in the presence of sodium iodide, which is easy to use, but is unselective since it cleaves esters, lactones and ethers; it also converts alcohols into iodides. To circumvent these complications, Olah[30] has developed the use of methyltrichlorosilane, again in the presence of sodium iodide, in dry acetonitrile (equation 8). A standard range of sulphoxides was reduced under mild conditions, with yields between 80 and 95% and with a simple workup process. The mechanism for the reaction is probably very similar to that given in equation (6), if the tricoordinate boron atoms in this reaction scheme are replaced

by tetracoordinate silicon atoms and the bromine atoms by iodine atoms.

$$RS(O)R' + MeSiCl_3 + NaI \xrightarrow[MeCN]{} RSR' + I_2 + (MeSiX_2)_2O \qquad (8)$$

$$X = Cl \text{ or } I$$

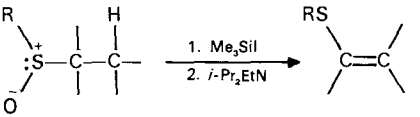
A related reaction process involves the use of chlorotrimethylsilane in the presence of zinc dust in anhydrous THF[31], in which the zinc functions as both an electron donor and a chlorine scavenger. The stoichiometry and a plausible mechanism for the reaction are given in equation (9):



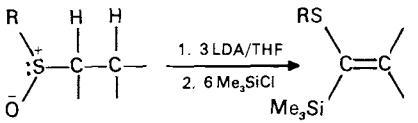
(9)

The reaction is easy to carry out and workup was effected simply by the addition of dichloromethane and cyclohexane to the reaction mixture, filtration and evaporation of the solvents. Yields ranged from 77 to 96%, although in the case of tetramethylene sulfoxide, the product was contaminated with hexamethyldisiloxane.

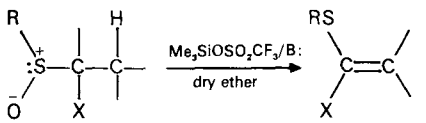
Silicon reagents have also been used by Miller and coworkers in a series of deoxygenation reactions (equation 10–12), that convert sulphoxides into vinyl sulphides[32–35]. The reactions required careful control of conditions, but then gave good yields (generally $> 75\%$) of the vinyl sulphides after isolation and purification (the stoichiometry given in (11) was required for optimum yield). In most cases this required chromatography. The mechanisms of these reactions are undoubtedly similar, both with respect to each other, and to those discussed previously. The sulphoxides will become silylated which makes them readily susceptible to elimination, and in the cases described in equation (12), this is so facile that only a weak, non-nucleophilic base is required. Vinyl sulphides are important synthetic intermediates[36], and these reactions open up a useful route to this functionality, using mild conditions and reasonably accessible reagents.



(10)[32]



(11)[33]



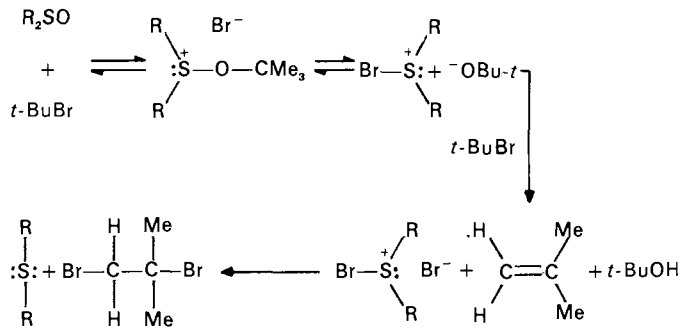
(12)[34,35]

(**a**) X = Cl; B: = Et_3N

(**b**) X = CN or COOR'; B: = $Me_3SiN^-SiMe_3$

5. Miscellaneous reduction reagents

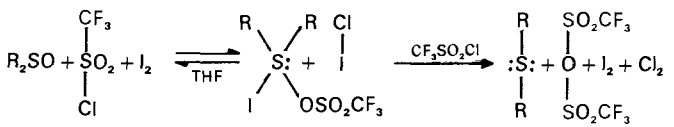
A number of other sulphoxide reduction reactions bear mentioning. The first, due to Marchelli and coworkers[37], is a very simple procedure whereby the sulphoxide is refluxed with *t*-butyl bromide and chloroform. A useful range of sulphoxides was studied and distillation of the reaction mixture (or percolation through a column of silica gel) gave pure sulphides in yields of > 90%. The procedure is appealing because of its experimental simplicity, and its use of a relatively inexpensive reagent. It may not be very successful with sterically hindered sulphoxides and the authors do not comment on this possibility. The mechanism of this reduction reaction is akin to that of BBr_3 (cf. Section II.A.3), except that the bromine trap is provided by a second mole of *t*-butyl bromide, as shown in equation (13):



(13)

The authors actually detected the dibromomethylpropane and the *t*-butyl alcohol, but found no evidence for α-bromosulphides in their reaction products, which can be rationalized by the pathway outlined in equation (13).

In a mechanistically related process, Fukamiya, Okano and Aratani have shown[38] that the reaction of a sulphoxide with 3 mole equivalents of trifluoromethanesulphonyl chloride and iodine in cold, dry THF gives the corresponding sulphide in yields ranging from 52 to 96%. When compared to *t*-butyl bromide, this reagent is more expensive, and the products were isolated after chromatographic separation. The reaction pathway can most probably be described as depicted in equation (14):



(14)

It is conceivable that the reaction could be improved if it were run in the presence of a chlorine trap such as propene (cf. Section II.A.3).

In a similar vein, large excesses of chlorosulphonyl isocyanate and sodium iodide in dry acetonitrile were used to deoxygenate the usual range of sulphoxides in yields of 82 to > 95%[39] (equation 15). Although the reported yields are high, this reaction required relatively large quantities of reagents and the products needed purification by chromatography. The reaction mechanism probably passes through a tetracoordinate sulphur(IV) intermediate similar to that in equation (14), but the fate of the remaining atoms is not described in the paper.

$$R_2SO + ClSO_2N{=}C{=}O \xrightarrow[MeCN]{I^-} R{-}S{-}R \qquad (15)$$

Sulphoxides may be reduced by heating in weakly basic ethanol with one of a range of hydrazine or hydroxylamine derivatives[40]. The process has been patented both for simple sulphoxides and for more complex molecules such as α-methylsulphinylacetophenone, $PhCOCH_2SOMe$, although the yield for this reduction was only 48%.

Finally, sulphoxides may be reduced to sulphides with $AlCl_3$ in MeCN[217].

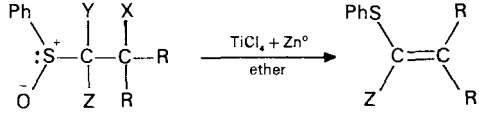
B. Reductions by Hydrides, Metal and Single-Electron-Transfer (SET) Processes

1. Sodium borohydride in the presence of activating reagents

Although sodium borohydride does not reduce sulphoxides, addition of cobaltous chloride to an ethanolic reaction medium produces a much more potent reducing agent that even reduces alkenes and alkynes[41]. The reactions are easy to carry out and to work up, a useful range of sulphoxides being reduced in reasonable yields. In a similar vein, a combination of sodium borohydride, titanium tetrachloride and dry dimethoxyethane was shown[42] to be a powerful reducing agent with similar properties to lithium aluminium hydride. The combination readily reduces carboxylic acids, acid chlorides, oximes and amides, but, of significance to the present discussion, it also readily reduces sulphoxides to sulphides, in isolated yields of 85 to 93%.

2. Reductions by metals under various conditions

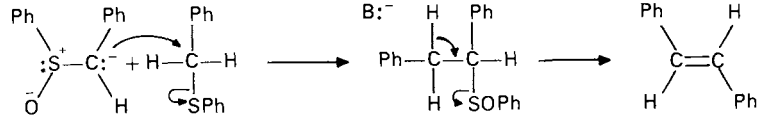
This series of reagents is characterized by the use of metals under the appropriate conditions. In this regard, a mixture of zinc dust and titanium tetrachloride in ether provided a useful synthesis of vinyl sulphides[43], with the possibility of further substitution alpha to the sulphur atom, as outlined in equation (16). The reaction is easy to carry out and gave yields of 49 to 87%, although the authors do not provide much detail of their experimental procedure and of the purity (chemical or stereochemical) of their products.



(16)

X = H, OH; Y = H, Cl, Br; Z = H, Cl

Rajanikanth and Ravindranath[44] have recently published a deoxygenation reaction for sulphoxides that uses metallic lithium in refluxing dimethoxyethane. Dialkyl and alkyl phenyl sulphoxides were reduced cleanly in yields around 70%, even if sterically hindered, but benzyl sulphoxides gave mixtures of products. For example, benzyl phenyl sulphoxide gave *trans*-stilbene (33%), benzyl phenyl sulphide (20%) and diphenyl disulphide (47%). These products can be rationalized by reaction pathways such as in equation (17):



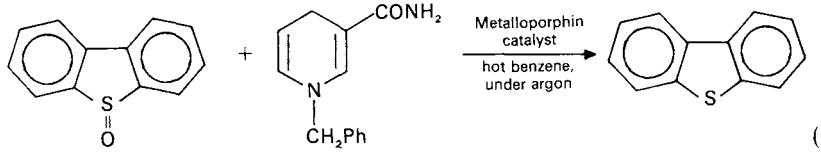
(17)

It is appropriate to conclude this section with a brief mention of the procedure published over 20 years ago by Corey and Chaykovsky[45], with which β-ketosulphoxides are desulphinylated with Al/Hg in wet THF to give ketones. Such reactions are very important synthetically and formally constitute a reduction at both sulphur and carbon. For their

efficacy they depend on the appropriate proximity to the sulphoxide of an electron-accepting group.

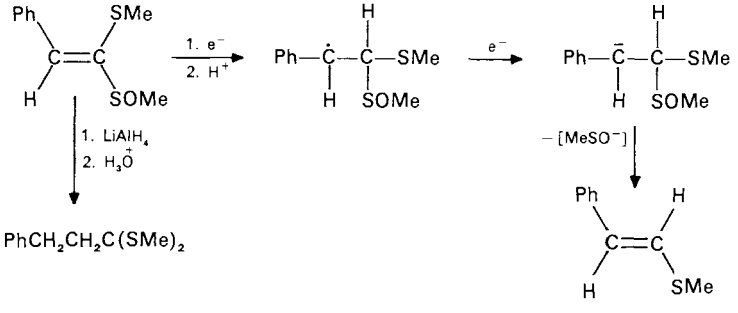
3. *Reactions involving SET processes*

Although single-electron-transfer (SET) processes would be expected to be important in reactions that use metals as reagents, this type of process has also been recognized in the reduction of carbonyl groups that involve 1,4-dihydronicotinamide derivatives[46]. Recent work by Oae and coworkers[47] has shown that an SET process is operative in the reduction of dibenzothiophene S-oxide by 1-benzyl-1,4-dihydronicotinamide when the reaction is catalyzed by metalloporphins. The reaction is outlined in equation (18), but the study gave results of much more mechanistic than synthetic value. This type of study is relevant to understanding biochemical mechanisms since it is known that methionine sulphoxide is reduced to methionine by NADPH when the reaction is catalyzed by an enzyme isolated from certain yeasts[47].



(18)

Few electrochemical reductions of sulphoxides have been reported recently, although such reductions have been known for many years[48]. A note[49] and a full paper[50] describe work on the electrochemical reduction of (*E*)-1-methylsulphinyl-1-methylthio-2-phenylethene. This gives a quite different product on electrochemical reduction, as compared to reduction by lithium aluminium hydride[51] (equation 19). The reductive elimination outlined in equation (19) occurred in the presence of a weak proton source such as phenol and could be carried out on a one-mmole scale using a stirred mercury pool cathode to give yields of over 80%. The authors suggest the mechanism outlined in equation (19) on the basis that the electrode process taking place at the first reduction wave is coupled to a protonation reaction, which is then followed by charge transfer. They propose further reduction of the eliminated methanesulfinate anion since they detected the characteristic odour of methanethiol during the electrolysis.



(19)

III. REDUCTION OF SULPHONES

Reduction of the sulphur–oxygen bonds in a sulphone is especially difficult and there are few methods available to effect this; by contrast, it is easier to reduce the sulphur–carbon

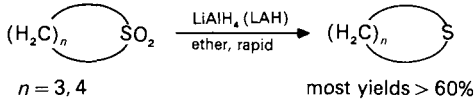
bonds and many procedures have been found to be effective for this type of reaction. The reduction of sulphones has been most comprehensively reviewed by Truce, Klinger and Brand[52], but this work only covered the literature up to 1970 and there have been many developments since then. The most recent review on the reduction of sulphones in the English language is by Durst[2,53] although there is a fairly recent review in Japanese[54], as one of a series of articles[54–60] that reviewed the reduction of organosulphur compounds comprehensively. There is also an excellent and recent review by Schank (in German) of the chemistry of sulphones, as part of the Houben–Weyl series[61].

A. Reduction of the S—O Bonds in Sulphones

1. Reduction to sulphides with nucleophilic hydride reagents

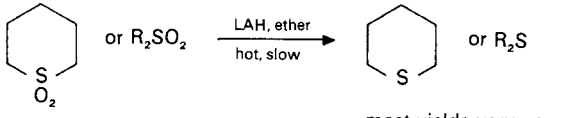
The first apparent reduction of sulphones was reported by Krafft and Vorster over ninety years ago, in which they treated diphenyl sulphone with hot elemental sulphur and isolated diphenyl sulphide[62]. The reaction is, however, not a direct reduction of the sulphonyl group because the corresponding reaction with elemental selenium gave diphenyl selenide, which shows that carbon–sulphur rather than sulphur–oxygen bond cleavage had occurred. Other reducing agents available at that time were not generally effective.

Hydride reducing agents became available some forty years ago and, given that lithium aluminium hydride (LAH) showed powerful reducing properties, it was an obvious experiment to test these on the reduction of sulphones. Bordwell was the first to report his results in this area[63], which may be summarized by stating that four- or five-membered cyclic sulphones in boiling diethyl or ethyl butyl ether were reduced readily to the corresponding sulphides (equation 20). For example, tetramethylene sulphone was reduced in 30 min at 35°, the yield of sulphide being 75%, but ethyl phenyl sulphone was only reduced to a 60% yield of sulphide after 8 h at 92°. Dibutyl sulphone required 18 h at 92° for a 73% yield of sulphide whereas diphenyl sulphone required only 2 h at the same temperature for a comparable yield of sulphide. The smaller dialkyl sulphones were essentially inert as was pentamethylene sulphone (equation 21). Bordwell and McKellin[63] observed gas evolution in the reduction of 2,3-dihydrobenzothiophene-1,1-dioxide, and although they did not make an accurate determination of the gas, they proposed the stoichiometry given in equation (22), the reduction being essentially quantitative in 30 min at 35°.



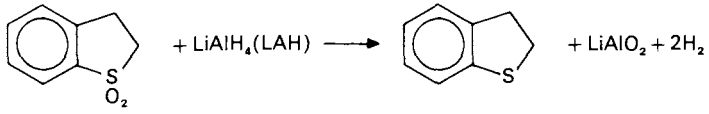
(20)

$n = 3, 4$ most yields > 60%



(21)

most yields very poor

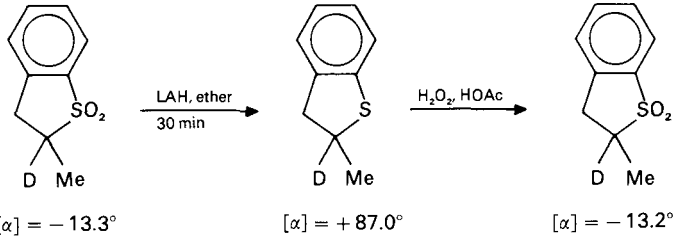


(22)

Dittmer and Christy[64] studied the reactions of thiete sulphone. Included in these was an attempt to synthesize thiete itself, a highly strained olefin of theoretical interest, by the LAH reduction of thiete sulphone. The reduction was expected to be feasible since Bordwell and McKellin[63] had found that thietane sulphone was readily reduced, but the only product that Dittmer and Christy isolated was 1-propanethiol (equation 23). Reduction of the thiete sulphone with sodium borohydride in basic aqueous methanol gave a 61% yield of the saturated ring, thietane sulphone.

$$\begin{array}{l} HC{=}CH \\ | \quad | \\ H_2C{-}SO_2 \end{array} \xrightarrow[40^\circ,\ 45\ min]{\text{LAH, dibutyl ether}} \underset{36\%}{CH_3CH_2CH_2SH} \qquad (23)$$

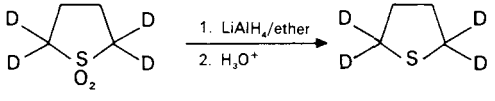
Subsequently, Paquette[65,66] and Johnson[67,68] used LAH reductions to convert strained thietane or thiolane derivatives to their respective sulphides, generally in good yields. Whitney and Cram[69] described the LAH reduction of a chiral derivative of benzothiophene sulphone, as outlined in equation (24). The authors also noted the formation of hydrogen gas and suggested that their results were consistent with those of Bordwell[63] as outlined in equation (22), namely that reduction takes place by the formation of an aluminium oxide and hydrogen gas. In this case, the reduction clearly cannot involve the formation of an α-sulphonyl carbanion and it is unlikely that any C—S bond cleavage and reformation could have occurred.



(24)

$[\alpha] = -13.3^\circ$ $[\alpha] = +87.0^\circ$ $[\alpha] = -13.2^\circ$

Weber and coworkers[70] have studied LAH reduction of a number of acyclic and cyclic sulphones, by the incorporation of deuterium atoms α to the sulphonyl function. By means of the reaction shown in equation (25) they confirmed Cram's finding[69] that reduction of a sulphone in a five-membered ring does not involve carbanion formation. The reaction proceeds in 'virtually quantitative yield', and, from previous accounts, rapidly. By contrast, the reduction of acyclic sulphones, or of pentamethylene sulphone, is extremely sluggish. Weber advances evidence[70] that these reductions are so slow that carbanion formation in fact occurs first, and suggests that reduction may be occurring on the anion rather than on the neutral sulphone. Part of the authors' evidence for their arguments is outlined in the following equations (26)–(28). Thus, not only is carbanion formation important in the sluggish LAH reductions of sulphones, but in fact α,α′-dianions are formed and these presumably can eject a hydride anion to form the alkenes described in equation (28).



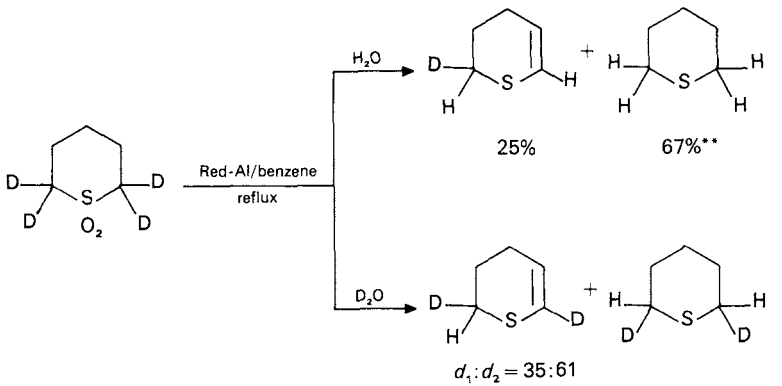
(25)

$$BuSO_2Bu \xrightarrow[2.\ D_3O^+]{\text{1. Red-Al*/benzene, 25}^\circ} PrCHDSO_2CHDPr \qquad (26)$$

*Red-Al = $[(MeOCH_2CH_2O)_2AlH_2]Na$

$$(MeCH_2CH_2CD_2)_2SO_2 \xrightarrow[2.\ H_3O^+]{1.\ \text{LAH/refluxing dioxane}} \text{dibutyl sulphide*} \qquad (27)$$

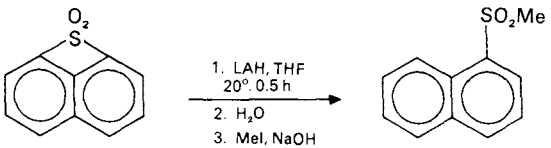
*Partially deuteriated, $d_1 = 8\%$, $d_2 = 50\%$ and $d_3 = 42\%$, by m.s.



(28)

**The deuteriation level for this compound was not given

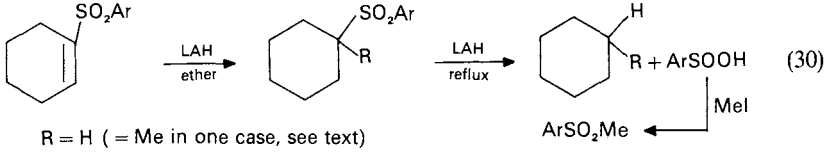
Meinwald and coworkers[71] studied the chemistry of naphtho[1,8-*bc*]thiete and its S-oxides. The reaction of the sulphone **2** with LAH (equation 29) is of particular and direct relevance to this section since it is different from the reductions that have been discussed thus far, because the major reaction pathway is now cleavage of an S—C bond, rather than a deoxygenation of the sulphur atom. The major product (equation 29) was isolated in 65% yield; two minor products accounted for a further 15% yield. One of the minor products is 1-methylthionaphthalene and this was most probably produced by an initial reduction of the strained 1,8-naphthosulphone, **2**, to the thiete, which was then cleaved to the thiol and subsequently methylated. Meinwald also showed[71] that the thiete was subject to cleavage by LAH as well as that both molecules were susceptible to attack and cleavage by other nucleophiles, notably methyllithium. These reactions are in fact very useful in attempts to assess a probable mechanism for the reduction of sulphones by LAH and this will be discussed at the end of this section.



(**2**) (29)

Dufort and Jodoin[72] report on LAH reductions of cycloalkyl *p*-tolyl sulphones. Various types of cycloalkyl rings were investigated with the ring carbon atom bound to the sulphone sulphur being vinyl, tertiary or quaternary. Reduction of the unsaturated sulphones with LAH in ether for an hour gave excellent yields of the corresponding saturated sulphone that results from a Michael reaction by hydride anion. When any of the sulphones were refluxed with LAH in ether for 144 h, or in THF for 40 h, the products were saturated sulphones (recovered starting materials when a saturated cycloalkyl *p*-tolyl sulphone was the starting material), hydrocarbons and *p*-toluenesulphinic acid, which was isolated as methyl *p*-tolyl sulphone. These reactions are outlined in equation (30). The conjugate addition reactions were facile and gave good yields of the saturated sulphones.

The authors comment that this specific reduction reaction is superior to the use of catalytic hydrogenation for reducing vinyl sulphones. Yields of the cleavage reaction were variable, but were generally below 50%. Dufort and Jodoin reported[72] one case in which they attempted the reduction on a sulphone bound to a quaternary carbon atom, namely on the first product of equation (30), R = Me. Reductive cleavage was observed, *p*-toluenesulphinic acid, and methylcyclohexane being isolated in about 33% yield. This reaction rules out the possibility that the cleavage reaction occurs via the carbanion that would be an intermediate in the Michael reactions, or could be an intermediate when R = H (equation 30)[72]. It is noteworthy that both these authors and Bordwell and McKellin[63] recovered diphenyl sulphone intact after attempting its reduction in boiling diethyl ether; the latter authors were however able to reduce this sulphone in ethyl butyl ether at 92°[63].



(30)

The mechanism by which LAH is able to effect deoxygenation of sulphones to sulphides has apparently not as yet been delineated. Some sulphones are reduced with remarkable ease, yields of sulphide exceeding 80% after reaction for less than an hour at room temperature, or below. By contrast, the conditions required for reduction of acyclic sulphones or unstrained cyclic sulphones are so vigorous that little reduction takes place but rather other reaction pathways become available. Thus, there was a rapid evolution of two equivalents of hydrogen (or deuterium) in the reactions outlined in equations (26) to (28), leading to the formation of a dianion, even apparently at room temperature. Since the pK_a values of all regular, acyclic and cyclic sulphones are not appreciably different[2,73-77], including, for example, the chiral sulphone used for the reaction in equation (24), there has to be a reaction pathway at a lower activation energy that leads to the reduction of sulphones in four- and five-membered rings, rather than to a deprotonation reaction.

When proposing a mechanism for such a reduction reaction, it should be recognized that the sulphone is a functionality that is characterized by highly polar S—O bonds, so that any attack by a nucleophile at the sulphur atom would have to take place in a way that minimizes interactions with the oxygen atoms. It is unlikely that the reduction process would involve a direct nucleophilic displacement at sulphur, since the oxide anion is not a likely leaving group. Furthermore, it is not possible to find hard evidence to support a significant variation in the S—O bond strengths between, for example, tetramethylene sulphone or pentamethylene sulphone. A search of the chemical literature for infrared stretching frequencies associated with the sulphonyl groups of these and many other sulphones is frustrated by the fact that the spectra are often recorded in different phases, or that the peaks are rather broad or are complicated by several bands appearing in the region normally associated with the symmetric or asymmetric stretching frequencies of sulphones.

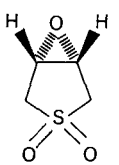
However, an examination of the bonding geometries in a range of sulphones has produced some differences between those sulphones that are readily reduced and those that are not. These are summarized in Table 1.

Measurements of the bond angles and lengths for typical acyclic and unstrained cyclic sulphones show that the OSO angle is in the range of 116 to 120° (mean, 118°)[5], the CSC angle is in the range of 103 to 105°[78], and the C—S bond length depends on whether it is to a terminal (i.e., methyl) carbon or to a carbon in a chain. The nature of the substituents on the carbon is also relevant, but if these are nonpolar or not especially bulky, the C—S

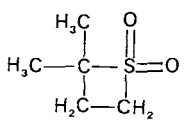
TABLE 1. Structural features of sulphones in relation to their reduction by lithium aluminium hydride

Compound	OSO angle (deg.)	CSC angle (deg.)	C—S length (pm)	Reduction conditions and yield of sulphide
Dimethyl sulphone[a]	117	103	177	35°, 12 h, trace
Diphenyl sulphone[b]	119.2(1)	104.1(1)	176.9(2) 176.6(2)	35°, 12 h, none or, 92°, 2 h, 71%
2[c]	117.5(3)	74.6(3)	182.1(4) 181.7(4)	20°, 0.5 h, see text
Dihydrobenzothiophene[d]	117.8(4)	92.2(4)	182(1) 180(1)	35°, 1 h, 83%
3[e]	117.7(2)	97.7(2)	179.7(3) 179.3(3)	—[f]
Tetramethylene sulphone[g]	115(3)	101(2)	179.8(8)	35°, 0.5 h, 75%
Trimethylene sulphone	—	—	—	35°, 0.5 h, 61%
4[h]	117.6(3)	80.2(3)	177.7(6) 180.7(6)	—[f]

[a]D. A. Langs, J. V. Silverton and W. M. Bright, *J. Chem. Soc., Chem. Commun.*, 1653 (1970).
[b]J. G. Sime and D. I. Woodhouse, *J. Cryst. Mol. Struct.*, **4**, 269 (1974).
[c]Reference 71.
[d]R. L. R. Towns and S. H. Simonsen, *Cryst. Struct. Commun.*, **3**, 373 (1974).
[e]D. E. Sands, *Acta Cryst.*, **B28**, 2463 (1972).
[f]The reduction of this compound has not been reported.
[g]Determined by electron diffraction; results from Hargittai, Ref. 5, p. 80.
[h]M. L. Ziegler, J. Weiss, H. Schildknecht, N. Grund and H.-E. Sasse, *Liebigs Ann. Chem.*, 1702 (1973).

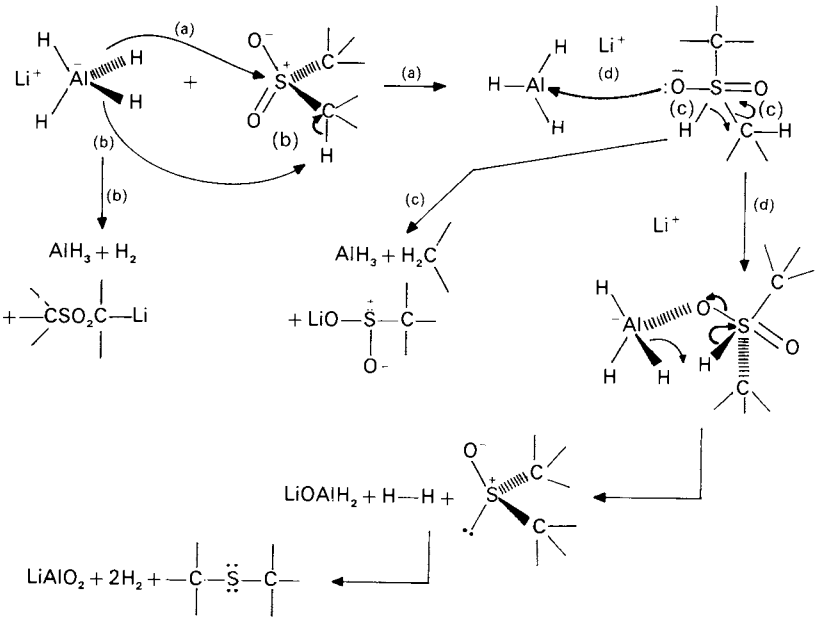


(**3**)



(**4**)

bonds typically have lengths in the range of 176 to 178 pm[78,79]. Granted, the data that are presented in Table 1 cover a limited range of compounds, but a trend does seem to emerge in that those sulphones with smaller CSC bond angles and longer C—S bonds are easier to reduce with LAH. This trend can be related to the orbitals around the sulphur atom. Longer C—S bonds with a concomitant smaller CSC bond angle reflect a greater p character in the orbitals used for bonding in the sulphone. Since p orbitals are larger than s orbitals, the greater p character of the C—S bond would also provide a greater orbital back lobe, which would be available for accepting electrons from the incoming hydride nucleophile. In addition, the energies of the orbitals must be taken into account, although this is a complex matter. However, if this hypothesis is accepted, it is then possible to write a reasonable mechanism for the reduction of sulphones to sulphides with LAH, while at the same time recognizing that there are three reaction pathways open for reaction, namely (1) attack by hydride at the sulphonyl sulphur atom to form a sulphide [paths (a) and (d) in Scheme 1] or (2) attack at the sulphonyl sulphur atom followed by displacement of a partially stabilized carbanion, that is, C—S bond cleavage [paths (a) and (c) in Scheme 1] or (3) if either of these possibilities is too energetically unfavourable, the carbon atom α to the sulphone can be deprotonated [path (b) in Scheme 1]. In any consideration of the type



SCHEME 1

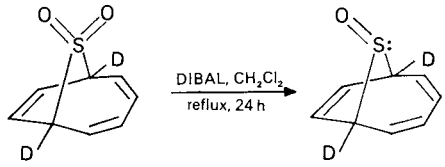
of reaction, the role of the lithium counterion must be taken into account. Since sulphones are extremely weak Lewis bases, the lithium cation is probably largely complexed by the solvent molecules (ethers) and is unlikely therefore to play a major role in any 'activation' of a sulphone towards nucleophilic attack. This is in contrast to its role in the reduction of certain carbonyl groups. Possibilities (1) to (3) are outlined in Scheme 1.

It is intriguing to note that this reaction scheme for the reduction of a sulphone to a sulphide leads to the same reaction stoichiometry as proposed originally by Bordwell in 1951[63]. Which of the three reaction pathways predominates will depend on the relative activation barriers for each process in any given molecule. All are known. Process (1) is preferred in somewhat strained cyclic sulphones (equations 22 and 24), process (2) occurs in the strained naphtho[1, 8-*bc*]thiete 1, 1-dioxide, **2**, cleavage of which leads to a reasonably stabilized aryl carbanion (equation 29) and process (3) occurs in unstrained sulphones, as outlined in equations (26) to (28). Examples of other nucleophiles attacking strained sulphones are in fact known. For instance, the very strained sulphone, **2**, is cleaved by hydride from LAH, by methyllithium in ether at 20°, by sodium hydroxide in refluxing aqueous dioxane, and by lithium anilide in ether/THF at room temperature[71]. In each case, the product resulted from a nucleophilic attack at the sulphonyl sulphur atom. Other examples of this process include the attack of hydroxide ion on highly strained thiirene *S*, *S*-dioxides[80,81], and an attack on norbornadienyl sulphone by methyllithium in ice-cold THF[82].

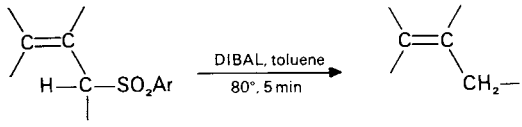
At this stage, it is not possible to decide whether what little reduction that does occur on unstrained, acyclic or cyclic sulphones is occurring directly on the sulphone or whether reduction is indeed occurring on the α,α'-dianion as was proposed by Weber[70]. Further work on the mechanisms of the LAH reactions with sulphones is thus needed to clarify the above proposals.

2. Reduction to sulphides with electrophilic hydride reagents

The use of electrophilic hydride reagents was first described in a U.S. Patent in 1972[83]. Details of the reductions with DIBAL (diisobutylaluminium hydride) were subsequently published[84]. A range of alkyl and aryl sulphones was reduced to sulphides, generally in boiling toluene for 18 to 72 h, in yields that ranged from 57 to 77%. This reaction has not found wide use as, apparently, only three other reports using DIBAL to reduce sulphones have been published. Anastassiou and coworkers[85] found that this reagent was effective in reducing the bicyclic sulphone given in equation (31), but, quite remarkably, the reduction was selective and produced a 36% yield of one sulphoxide diastereomer, together with a small quantity of sulphide. Janssen and Godefroi[86] have used DIBAL for the detosylation of allylic *p*-toluenesulphonyl groups (equation 32). The reaction sequences described by these authors used the sulphone as a directing group for alkylations, followed by acid-catalyzed polyene cyclizations, to generate tricyclic ring systems. The sulphur was then reductively removed as outlined in equation (32).

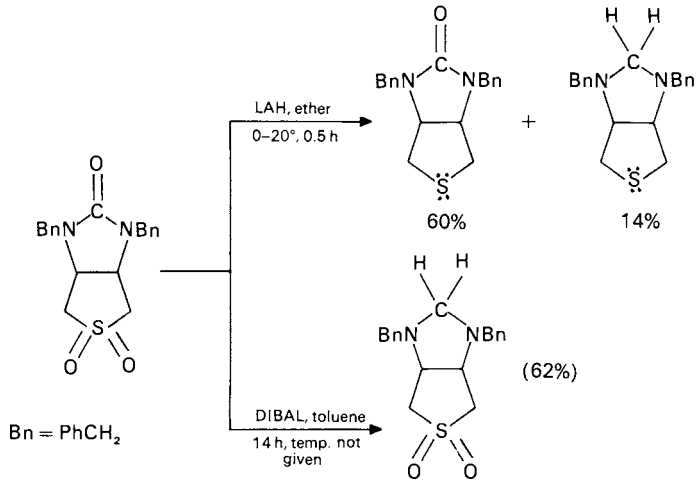


(31)



(32)

One of the more interesting reactions involving the reduction of a sulphone was recently described in a paper[87] that reported on a synthetic approach to biotin. The molecule in question contains a sulphone as part of a thiolane ring that is fused to a cyclic urea. As outlined in equation (33), either functionality can be reduced depending on the selection of

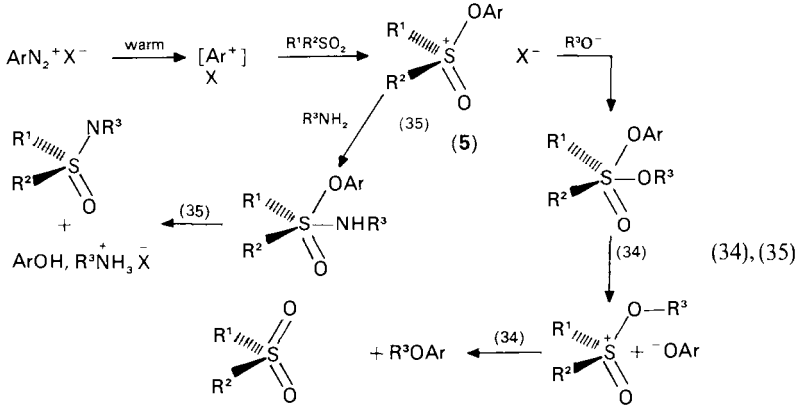


(33)

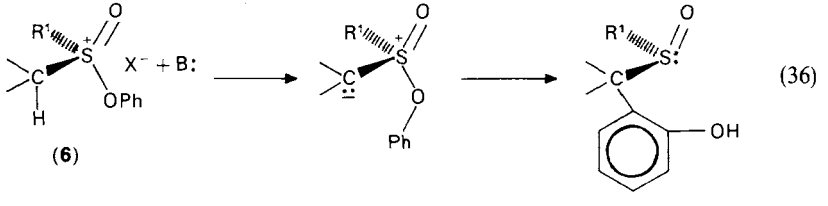
reagent. Furthermore, this reaction provides evidence that if sulphones are to be reduced by LAH, a source of nucleophilic hydride, they will be reduced more readily by this hydride than by DIBAL an electrophilic reagent. The same conclusion can be drawn by comparing reaction times and temperatures for the reduction of sulphones done by Bordwell (LAH)[63] and by Gardner and coworkers (DIBAL)[84]. The inference that can be drawn from these reactions is consistent with known properties of sulphones, namely that they are very weakly nucleophilic, and hence are not likely to be efficient substrates for electrophilic reagents. However, it should be noted that DIBAL can be used for the reduction of sulphones devoid of other reducible groups, and although the reaction is slow, it probably does not suffer from the complications of dianion formation, as does reduction with LAH.

3. The interaction of sulphones with other electrophiles—formation of sulphoxides and sulphinates

The reactions that have been described above have indicated that sulphones interact poorly with electrophiles. However, in 1970, Whiting and coworkers announced the synthesis of aryloxysulphoxonium salts[88], by the reaction of sulphones with the potent electrophile produced in the thermolysis of aryldiazonium tetrafluoroborates or hexafluorophosphates. Fluorobenzenes are by-products of the reaction. In a subsequent paper[89], Whiting described the reactions of the aryloxysulphoxonium salts, **5**, with oxygen and nitrogen nucleophiles. The fundamentals of these are outlined in equations (34) (oxygen nucleophile) and (35) (nitrogen nucleophile).



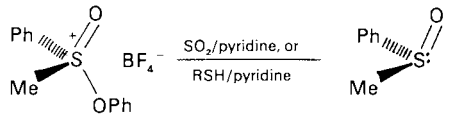
The reactions with nitrogen nucleophiles, equation (35), were most useful synthetically, leading to a range of sulphoximines in yields that were generally over 70%. They do not, however, constitute a reduction process at sulphur; this was achieved by treating the sulphoxonium salt, **6**, with sodium phenoxide or trimethylamine, as outlined in equation (36). Whiting and his coworkers also found[89] that other aryloxysulphoxonium



(36)

salts could be converted into a range of products with other nucleophiles, but the reactions did not proceed in high yields to any one particular product. Likewise, Okuma and coworkers found[90] that the ylids from aryloxysulphoxonium salts reacted with aldehydes to give vinyl sulphones in yields of 35 to 60%, but the reactions do not constitute a reduction at sulphur and are thus not considered further in this chapter.

Another group of Japanese workers[91] found that the sulphoxonium salt, **7**, was reducible to sulphoxides with either alkyllithiums or lithium dialkylcuprates, the exact reaction pathway being complicated by halide ions originating from the preparation of the metal alkyls. However, good yields of methyl phenyl sulphoxide were obtained by reduction of **7** with sulphur dioxide or a thiol in pyridine (equation 37).



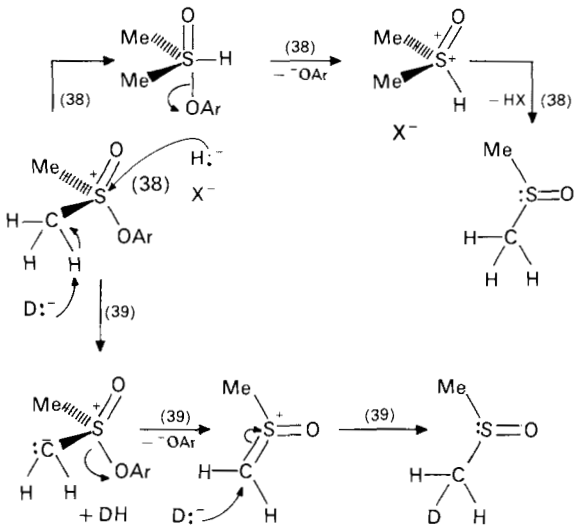
(37)

(**7**)

An interesting set of reactions has been carried out by Still and coworkers[92,93], who found that aryloxysulphoxonium salts could be reduced by stirring with a dichloromethane slurry of sodium borohydride adsorbed on alumina. The intriguing part about this reaction sequence is that the products are sulphoxides, which makes the reaction essentially unique, since there appears to be only one other case known of such a reduction (discussed in Section III.A.2)[85]. Still carried out experiments to optimize the formation of the aryloxysulphoxonium salts and found that the *p*-chlorophenyl group was the most useful. Following the same procedure as used by Whiting, Still and coworkers prepared the salts by mixing 4-chlorobenzenediazonium tetrafluoroborate with 3 mole equivalents of sulphone[92] and added small portions of this mixture to a flask that was immersed in an oil bath heated to about 140° and was equipped with a stirrer. Reduction of the salts was accomplished by adding dichloromethane plus an excess of sodium borohydride adsorbed on alumina and stirring for 12 h. The method suffers from an inherent limitation in that the decomposition of the aryldiazonium salt generates a very reactive intermediate, which will attack any functional group more reactive than a sulphone; this includes most other functionalities, which limits the success of the method to relatively simple sulphones. Given that a large excess of sulphone was used in the reaction, and part of this could be recovered, the yields of sulphoxides are rather modest. For example, methyl phenyl sulphone gave a 43% yield of *p*-chlorophenoxysulphoxonium salt (based on the amount of diazonium salt used) and from this 43% yield, a 45% yield of methyl phenyl sulphoxide was isolated. The yields from a range of other dialkyl and aralkyl sulphones were somewhat better than this specific example.

Still has also carried out mechanistic experiments[93] from which he could deduce that the major reduction pathway is by attack of hydride ion at the sulphur atom. This conclusion was deduced from the fact that reduction with sodium borodeuteride-aluminium oxide gave a sulphoxide that had only incorporated about 25% mole equivalent of deuterium on to a methyl carbon atom bound to the sulphur atom. The mechanistic pathway for direct reduction is outlined in equation (38), whereas the pathway whereby deuterium could be incorporated is portrayed in equation (39). These reactions support the proposed mechanism for the hydride reduction of sulphones as outlined in Section III.A.1, namely that attack at sulphur by hydride ions may occur, but will be competitive with proton abstraction in cases when the attack at sulphur is not facilitated.

The conclusion that can be drawn from this discussion of the reduction of sulphones is that reactions involving either nucleophilic or electrophilic attack are relatively difficult to

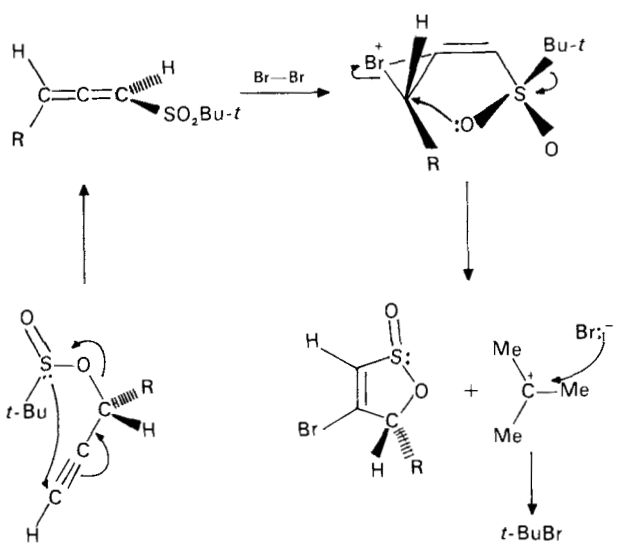


(38)

(39)

carry out, and, if these reactions are attempted in the presence of most other functional groups, these will invariably be attacked more readily.

Despite the aversion of the sulphonyl group to function as a nucleophile, there are a limited number of literature reports that describe such a process[94,95]. The first of these does not lead to a reduction at sulphur and is thus not directly relevant, but the report by Braverman and Duar[95] describes reactions in which an acetylenic sulphinate ester can undergo a [2, 3] sigmatropic rearrangement to an allenic *t*-butyl sulphone. Reaction of this sulphone with the appropriate electrophile, for example bromine, gave a γ-sultine, formation of which requires the participation of the sulphonyl group in an intramolecular cyclization process. The reactions are outlined in equation (40).



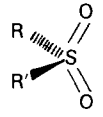
(40)

The driving force behind this remarkable reaction in which the sulphone participates intramolecularly in a 5-*exo*-tet ring closure process[96] is that the geometry of the intermediate bromonium ion is nicely set up for the attack by the sulphone oxygen. Probably, the process is assisted by the ready cleavage of the sulphur to the *t*-butyl bond, with the concomitant formation of *t*-butyl bromide.

B. Reduction of the C—S Bonds in Sulphones — Desulphonylation Reactions

1. The use of Group I metals as a source of electrons

As discussed earlier, the C—S bonds in a sulphone are weaker than the S—O bonds. A large number of methods have been developed to take advantage of this fact which has made it possible for sulphones to be used extensively as control groups in synthetic sequences, after which they are removed when no longer needed. Most of the removal methods are reductive cleavages. One of these methods, pioneered by Truce and coworkers[97], is a reductive cleavage of sulphones with sodium and lithium metal in ammonia or low-molecular-weight amines. These reagents were already known to cleave ethers and sulphides, or to reduce aromatic hydrocarbons, so it was a logical extension to apply them to the reduction of sulphones. In two papers[97,98], Truce examined the breadth and limitations of the reactions, focussing on the use of lithium in methylamine, and showing that the cleavage probably proceeded via intermediate carbanionic and sulfinate species, as summarized in equation (41).



$$\xrightarrow{2Li^{\circ}\text{ in }MeNH_2} R{:}^{-} + R'SO_2Li \xrightarrow{H_2O} RH + R'SO_2H \qquad (41)$$

Truce also examined a few examples of the cleavage of sulphones with sodium in liquid ammonia[97] and found essentially similar results except that diaryl sulphones were reduced to sulphinate salts instead of to arylthiolates as with the lithium reductions. Dialkyl sulphones were unreactive towards sodium in liquid ammonia.

Relatively few reports have been published subsequently on the use of these reagents. Hope and coworkers[99] have used sodium in liquid ammonia to cleave the benzyl sulphonyl derivatives of cysteamine, L-cysteine and L-homocysteine to prepare the corresponding sulphinic acids, as in equation (42).

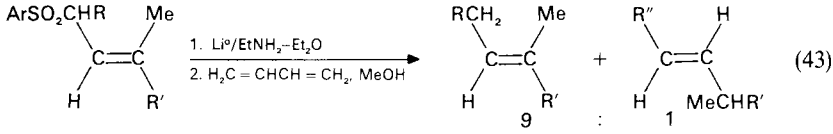
$$PhCH_2SO_2R \xrightarrow[2.\ HOAc]{1.\ 2Na^{\circ}/liq.\ NH_3} RSO_2H(70\text{–}80\%) \qquad (42)$$

In a variation of these reactions, Grieco and Masaki[100,101] used *p*-toluenesulfonyl groups to direct alkylation reactions in the formation of carbon chains and then cleaved the sulphones with lithium in ethylamine. This type of synthetic construction involving the use of sulphur-containing molecules has become a typical sequence in organic syntheses. In this case, the reactions formed part of successful syntheses of squalene[100] and sesquifenchene[101] and were carried out without any migration or loss of stereochemical integrity of the double bonds. Similar sequences have been reported by Trost[102] (prenylation reactions) and Marshall[103] (synthesis of a cembranoid precursor).

Subsequently, Julia, Uguen and Callipolitis[104,105] used both lithium metal in ethylamine and sodium amalgam in ethanol to effect reductive cleavages of β-hydroxysulphones or of allylic sulphones. The latter reaction is part of a synthetic sequence for the construction of alkenes that has been used with some considerable success

and has been named after Professor Julia, the senior author[106]. These reactions will be discussed in detail in Section III.B.3., and the cleavage of β-ketosulphones will be discussed in Section III.B.4.

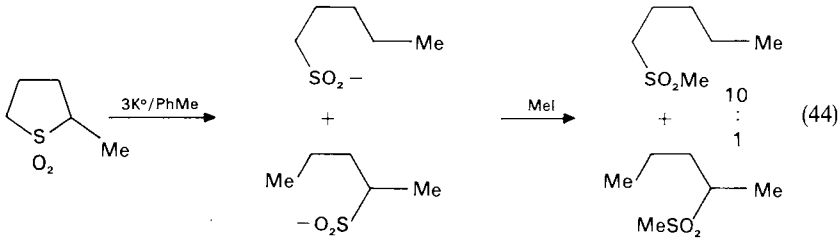
Solanesol and other prenyl alcohols are important as metabolites in mulberry and tobacco leaves and in the synthesis of isoprenoid quinones. Hence, Sato and collaborators[107] have developed a stereoselective synthesis of all-*trans*-polyprenol alcohols up to C_{50}. Construction of the requisite skeletons was accomplished by the alkylation of a *p*-toluenesulphonyl-stabilized carbanion, followed by reductive desulphonylation of the resulting allylic sulphonyl group. This was achieved most efficiently by the use of a large excess of lithium metal in ethylamine (equation (43)), although all reaction conditions led to mixtures. The minor product results from double bond rearrangement.



(43)

Similar work[108] on the desulphonylation of allylic aryl sulphones showed that although it was often possible to isolate the alkene products in yields of 60 to 80%, the reaction was not stereoselective. Lithium in methylamine at $-110°$ gave the greatest retention of configuration of the alkene ($Z:E$ ratio = 13:7), the use of potassium intercalcated in graphite gave a comparable yield with $Z:E$ ratio = 2:3. Interestingly, none of the above reports makes reference to the earlier work by Truce's group[97,98].

Most of the above reactions are used for the cleavage of aryl sulphones. Recently, a note has appeared[109] in which the use of potassium metal dispersed ultrasonically in toluene to cleave saturated cyclic sulphones is described. Addition of iodomethane permits the isolation of acyclic alkyl methyl sulphones (as outlined in equation (44)).

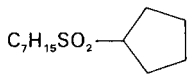
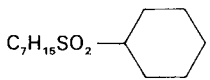
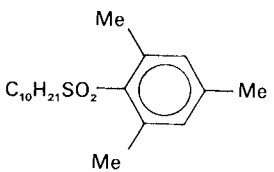
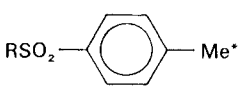


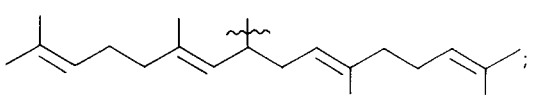
(44)

Some details of the mechanism of these reductive cleavage reactions can be gleaned from the regioselectivity of the process. Some examples selected from the results outlined above are collected in Table 2. There is no evidence that reduction of the sulphonyl S—O bonds occurs, and it appears that the cleavage process normally takes place only after the second electron has been added to the molecule. In some cases, the reaction pathway is consistent with the sequence outlined in equation (41). In other cases, for example the last entry in Table 2, cleavage has taken place towards the allylic carbon (the other fragment presumably being lithium *p*-toluenesulphinate). However, an allylic C—H bond is at least 10^3 times weaker an acid than is an aryl C—H bond[110]. Also, the direction of fragmentation reported on by Chou and You[109] in equation (44) is opposite to the sense reported on by Truce[97,98], which suggests that the mechanisms involved are not fully understood at this point.

Extrusion of SO_2 from unsaturated cyclic sulphones, promoted by ultrasonically dispersed potassium, is described in Reference 218.

TABLE 2. Reductive cleavage reactions of sulphones induced by lithium in methylamine or ethylamine

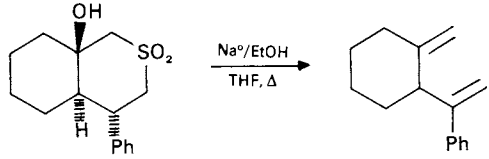
Sulphone structure RSO_2R'	Sulphinates Yield %	Ratio RSO_2Li : $R'SO_2Li$		Hydrocarbon Yield %	Ratio RH : R'H		Ref.
	—	—	—	78	70	30	98
	—	—	—	56	30	70	98
$C_{10}H_{21}SO_2Ph$	95	100	—	PhH not isolated			97
	80	100	—	55	—	100	97
	—	—	—	77	100*	—	100

*R =  ;

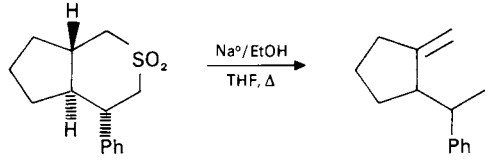
RH = all-*trans*-bisgeranyl

2. The use of Group I and Group II metals in alcoholic solutions

Classical reducing agents are known generally to be ineffective in the reduction of sulphones[2,52]. Thus, although the procedure of Bouveault and Blanc[111,112] has been used in the reduction of esters, the first mention of a modified Bouveault–Blanc reduction of sulphones was only published recently. Two papers are relevant. Takaki and coworkers showed[113] that refluxing a range of substituted, β-hydroxythiane-*S*,*S*-dioxides with sodium in THF, containing one mole equivalent of absolute ethanol, led to the extrusion of the sulphonyl group and the formation of either an alkene or an unconjugated diene. Examples of reactions are illustrated in equations (45) and (46), but the reasons for the apparently different courses of the reaction are not clear.



(45)



(46)

Shortly thereafter, Kuo, Aoyama and Shioiri described essentially the same procedure[114] for the desulphonylation of α-benzylsulphonylacetate esters. They acknowledged their procedure as being due to Tsuchihashi, who had described it previously in conference proceedings and in a Japanese patent. The reactions are structure- and reagent-dependent, as illustrated in equations (47) and (48). Yields ranged from 49 to 78%. The sulphone used in equation (47) also gave some dibenzyl sulphone with sodium and ethanol in THF.

$$\underset{\underset{\displaystyle SO_2CH_2Ph}{|}}{PhCHCOOCH_2Ph} \xrightarrow[MeOH,\ dry]{Na-Hg/Na_2HPO_4} (PhCH_2)_2SO_2 \quad (71\%) \tag{47}$$

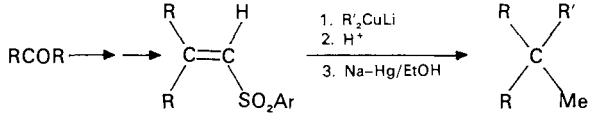
$$\underset{\underset{\displaystyle SO_2CH_2Ph}{|}}{i\text{-}PrCHCOOCH_2Ph} \xrightarrow[MeOH,\ dry]{Na-Hg/Na_2HPO_4} \underset{\underset{\displaystyle SO_2CH_2Ph}{|}}{i\text{-}PrCHCOOMe} \xrightarrow[THF,\ \Delta]{Na°/EtOH} i\text{-}PrCH_2COOH \tag{48}$$

Brown and Carpino[115] used acid-washed magnesium turnings in dry methanol at 50° as an efficient reagent for the reductive elimination of sulphones. Examples given included a *trans*-1,2-bis(sulphone), a pair of 1,1-bis(sulphones) and *i*-$PrCH_2CH_2SO_2Ph$, and yields of the reduced products were in the range of 60 to 80%. The procedure is offered as a practical alternative to the use of sodium amalgam. This has been widely used (see next section), but on a large scale requires the handling of substantial quantities of mercury, which is toxic and relatively expensive.

3. Desulphonylation by amalgams of Group I metals

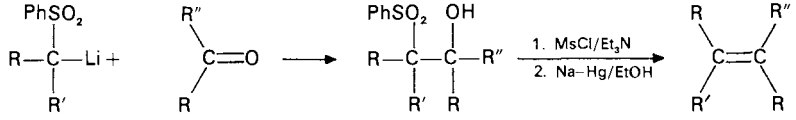
The first study into the use of 6% sodium amalgam in refluxing ethanol for the reductive desulphurization of sulphones was reported[116] in 1952. Methyl phenyl sulphone gave an

82% yield of benzenesulphinic acid, whereas benzyl phenyl sulphone gave benzenesulphinic acid in what seems to be greater than 100% yield, together with 'C_7H_7', presumably toluene, which was isolated in low yield as benzoic acid. The authors showed that the cleavage of aryl sulphones was general, whereas dialkyl sulphones were not cleaved by the sodium amalgam. The method then apparently lay dormant for 20 years until it was used by Posner and Brunelle[117] in the final step of a sequence that converts aldehydes and ketones into more-substituted alkanes as outlined in equation (49). Yields for the sequence varied, with the best being exemplified by the conversion of heptanal into 2-methyloctane in 82% overall yield. The reagent has also been used[118,119] for the desulphonylation of phenyl sulphones as part of syntheses of aldehydes and ketones.



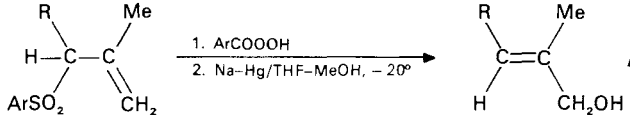
(49)

Julia and Paris[120] described an olefin synthesis, based on the use of a sulphonyl group which directs the formation of a carbon–carbon bond. Subsequent reductive elimination with sodium amalgam leads to the alkene, as outlined in equation (50). The reaction sequence is similar in principle to an olefin synthesis first developed by Cornforth[121]. The yields of all steps are generally above 80%.



(50)

This synthetic sequence for an olefin synthesis has been further developed by Kocienski who has shown that eliminative desulphonylations carried out on β-acyloxysulphones are remarkably stereoselective for the synthesis of *trans*-disubstituted-olefins[122]. The method has wide applicability in that α-lithio phenyl sulphones are readily generated, and are readily coupled to aldehydes or ketones, to give β-hydroxysulphones. The hydroxyl function of these is then esterified and the synthesis is completed by the reductive elimination with sodium amalgam. Kocienski has prepared two reviews that summarize his syntheses of a range of natural products[106,123] one of which is diumycinol[124], obtained from the antibiotic diumycin, and previously synthesized by Grieco in a reaction sequence[125] that depended on the use of 3% sodium amalgam for the desulphonylation of a β-keto aryl sulphone. A variation on the above theme consists of carrying out the desulphonylation on β,γ-epoxysulphones as outlined in equation (51).



(51)

The yields of the desulphonylation step are generally in the range of 70 to 80%. A related alkene synthesis is described in Section III.C.1.

Trost published a desulphonylation procedure for aryl alkyl sulphones using an excess of sodium amalgam in buffered ethanol[126] (equation 52). Trost claimed that this is superior to earlier reactions using sodium amalgam in ethanol because of a couple of factors: the use of the acid phosphate buffer to prevent formation of significant amounts of sodium methoxide is particularly important, since this can cause isomerizations in base-sensitive substrates, and the temperature should be kept low, but optimized for each substrate.

$$RR'CHSO_2Ar\ (1\ eq.) \xrightarrow[MeOH,\ -20^\circ\ to\ 0^\circ]{excess\ 6\%\ Na\text{-}Hg,\ 4eq.\ Na_2HPO_4} RR'CH_2 \qquad (52)$$

Trost found[126] that aryl sulphones containing a range of other functionalities could be successfully desulphonylated without attack at alkenes, esters or nitriles, and without any detectable degree of alkene migration.

The process has been successfully used in a range of syntheses, among which are those of mokupalide[127], of medium-ring compounds[128], and the constructions of functionalized six-membered rings[129]. The synthesis of 2-phenylthioaziridines[130] apparently used the same procedure but the authors do not provide full details. Not all applications have been without complications. Work of Kuo, Aoyama and Shioiri[114] has already been referred to in Section III.B.2, equations (47) and (48). In a subsequent paper[131], these authors showed that in other similar cases of α-substituted, α-benzylsulphonylacetic acid esters the optimum desulphonylation reagent was *unbuffered* sodium amalgam in methanol. Another example[132] of the use of alkali-metal amalgams will be discussed in Section III.E. Recent work of Paquette, De Lucchi and coworkers[133] showed that desulphonylations of vicinal phenylsulphonyl groups, leading to highly reactive sesquinorbornatrienes, were only successful when carried out with 1 to 2% sodium amalgam in buffered methanol, with rigorous exclusion of oxygen. This latter requirement is due to the air-sensitivity of the trienes.

4. *Desulphonylation by amalgams of Group III metals*

Pioneering work on the desulphonylation of β-ketosulphones was carried out by Corey and Chaykovsky[45,134]. This reaction was part of a sequence which could be used in the synthesis of ketones, as shown in equation (53). The main thrust of this work was in the use of sulphoxides, but Corey did stress the merits of both sulphones and sulphonamides for different applications of this type of reaction. The method soon found application by Stetter and Hesse for the synthesis of 3-methyl-2,4-dioxa-adamantane[135], and by House and Larson in an ingenious synthesis of intermediates directed towards the gibberellin skeleton, and also for more standard applications[136]. Other applications of the method have also been made[137–140], although it does suffer from certain limitations in that further alkylation of an α-alkyl-β-ketosulphone is a very sluggish, inefficient process. Kurth and O'Brien[139] have proposed an alternative, one-pot sequence of reactions (equation 54), carried out at −78 to −50°, with yields better than 50%. The major difference between the two routes is that the one-pot process uses the desulphonylation step to generate the enolate anion, whereas in the Corey–House procedure, the desulphonylation with aluminium amalgam is a separate, non-productive step.

$$RCOOR' \xrightarrow[2.\ H_2O]{1.\ {}^-CH_2SO_2Me} RCOCH_2SO_2Me \xrightarrow[3.\ Al\ Hg/THF\text{-}H_2O]{1.\ B:\ \ 2.6''X} RCOCH_2R'' \qquad (53)$$

$$RCOCHR'SO_2Me \xrightarrow[3.\ R''X\ in\ HMPA]{1.\ Li^\circ/NH_3\ \ THF\ \ 2.(n\text{-}Bu)_3SnCl} RCOCHR'R'' \qquad (54)$$

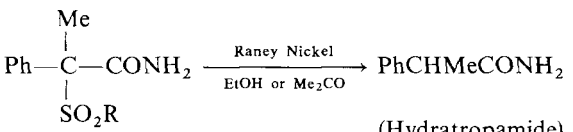
The reagent has also been used to desulphonylate vinyl sulphones to give alkenes[141–143]. The solvent was refluxing 10% aqueous THF and the yields reported were over 80%.

The desulphonylation of *E*-homoallylic sulphones is described in Reference 219.

5. *Transition-metal-mediated desulphonylations*

The use of Raney nickel for desulphurization reactions has been well known for a considerable time[144]. Some work has been carried out on sulphones, the most notable

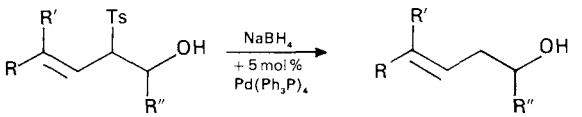
being a paper by Grimm and Bonner[145], in which more questions are raised than are answered. The work was focussed on the desulphurization reaction outlined in equation (55). The starting sulphones were prepared with either the above chirality (Fischer projection), or its enantiomer. Refluxing in ethanol for five hours produced hydratropamide with approximately 2:1 inversion of configuration, whereas acetone produced the opposite result. However, the results did depend significantly on the pretreatment of the Raney nickel, the benzylsulphonyl compound was more reactive than the phenylsulphonyl compound and the phenylsulphenyl compound gave only racemic hydratropamide. Desulphurization using Raney nickel has traditionally been thought of as a radical process, but these experiments suggest that an understanding of the actual mechanism will require further work.



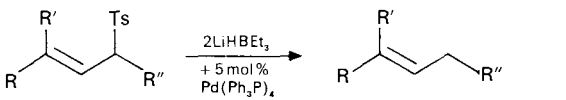
(55)

(R = Ph or $PhCH_2$)

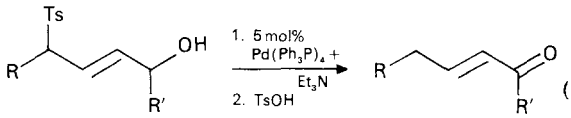
Modern organic chemistry is increasingly intertwined with the use of new organometallic reagents, and desulphonylation processes are no exception. Four recent communications[146–149] offer different aspects of the use of palladium complexes in desulphonylation reactions. One note[146] describes a synthesis of homoallylic alcohols in which the final step is a palladium-assisted desulphonylation, whereas a second[147] describes a similar process leading from allylic sulphones to alkenes and a third[148] describes the formation of α,β-unsaturated ketones from allylic sulphone alcohols (equations 56–58). The authors discuss difficulties that they experienced with the migration of double bonds when they attempted to use some of the traditional desulphonylation reactions described in Sections III.B.1, 3 and 4; these difficulties were minimized by using the above palladium-assisted reactions. Hutchins and Learn have also reported regio- and stereoselective reductions of allylic functional groups[149], one of which was a sulphone, using $LiHBEt_3$ in the presence of $Pd(Ph_3P)_4$.



(56)[146]



(57)[147]

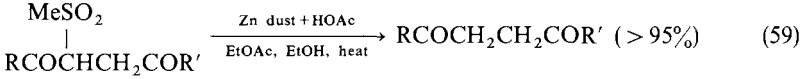


(58)[148]

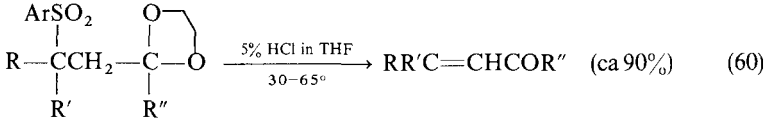
6. *Desulphonylation reactions in acidic media*

There are only a few examples of reductions of sulphones in acidic media. One of the earliest was a mention by Bordwell and McKellin[63] (see Section III.A.1) that

benzothiophene-*S*,*S*-dioxide could be reduced to benzothiophene by heating with zinc in hot acetic–hydrochloric acid. More recently, Czech workers described[150] the reduction of β-ketosulphones with zinc and acetic acid, as shown in equation (59). A somewhat different approach was taken by Yoshida and Saito[151] who found that β-sulphonyl acetals could be converted into α,β-unsaturated ketones by warming with dilute hydrochloric acid, as given in equation (60).



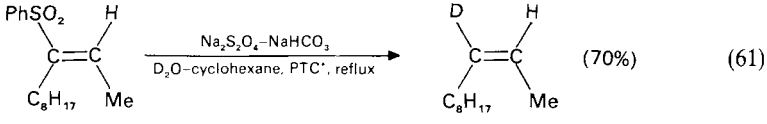
(59)



(60)

7. *Reductions with sodium dithionite*

Although sodium dithionite (sodium hydrosulphite, $Na_2S_2O_4$) is a useful reducing agent[152], especially for multiply bonded nitrogen compounds and quinones[153], it has only recently been applied to the reduction of carbonyl compounds[154]. In an extension of the Julia olefin synthesis (Section III.B.3), Julia has shown[155–157] that α-tosyloxy- and acetoxysulphones can undergo elimination reactions to yield vinyl sulphones of either configuration. These vinyl sulphones are in turn readily reduced to alkenes by the action of sodium dithionite using a range of weakly basic reaction conditions. The chemical yields of the alkenes were fair to good (50 to 80%), but the process is stereochemically very clean, with excellent retention of the configuration of the original vinyl sulphone. Of even greater interest is the fact that carrying out the reaction in D_2O in the presence of $NaHCO_3$ gave monodeuteriated alkenes in yields of 31 to 85%, but with >97.5% incorporation of deuterium[157]. The reaction is illustrated by equation (61).

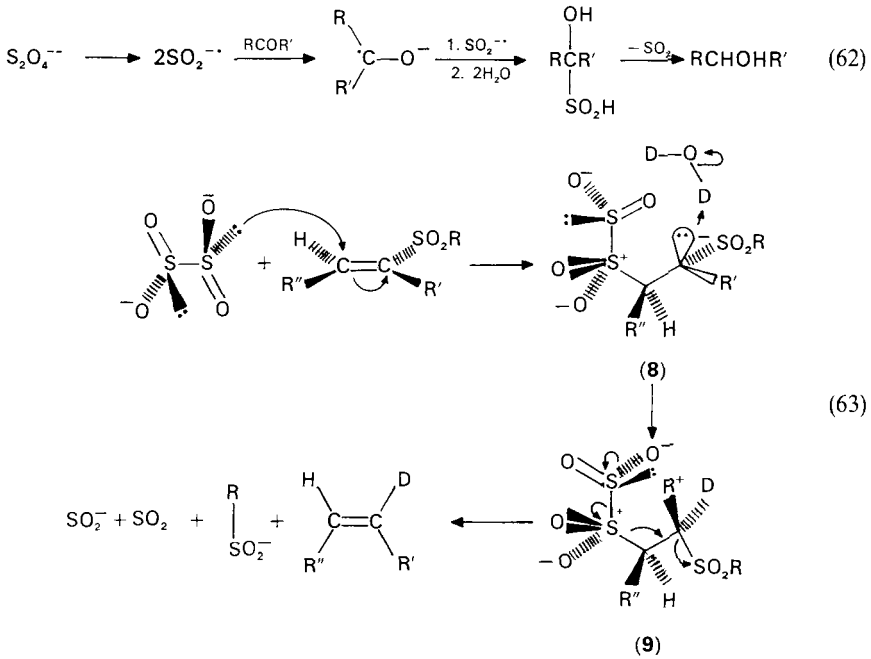


(61)

*PTC = phase-transfer catalyst

It is, of course, intriguing to speculate on the pathway of such a reduction, given the difficulties normally encountered in the reduction of sulphones. The reduction of carbonyl groups has been suggested[154] to proceed as outlined in equation (62), although this must be interpreted with caution since no pinacolic products were found. The reduction of a vinyl sulfone must proceed quite differently, since the dithionite is not a powerful reductant[158] and it is unlikely to have adequate energy to attack the sulphur atom of a sulphone. Furthermore, the involvement of radical anions is unlikely, given the very high degree of stereoselectivity of the reduction process. A possible reaction pathway is presented in equation (63), in which the tendency of sulphinyl sulphur, a relatively soft nucleophile, to undergo a Michael reaction is used. The reaction mechanism outlined in equation (63) is plausible because the α-sulfonyl carbanion in **8** would be configurationally stable[79] and the barrier to rotation in **9** could be sufficiently high that elimination of sulphinate would occur preferentially. The driving force behind the dithionite reduction of a vinyl sulphone is most likely the elimination of sulphur dioxide, which would be largely

removed from the reaction medium at the temperatures used for these reductions.



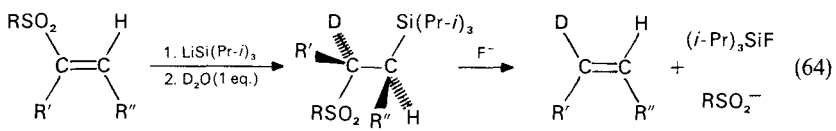
(62)

(63)

(8)

(9)

Given the above possible reaction mechanism, it is then intriguing to speculate that another approach to the same stereoselective reduction of a vinyl sulphone could be achieved by the use of a suitably sterically hindered organosilane, as outlined in equation (64). Such a reaction would provide an interesting test for the stereoelectronics of a conjugate addition reaction by a second-row heteroatom to a vinyl sulphone.



(64)

Further examples of reductions with sodium dithionate are given in References 220–222. The stereoselective syntheses of 1, 3- and 1, 4-dienes and pheromones are described in Reference 223.

C. Desulphonylations by Elimination or Substitution Reactions

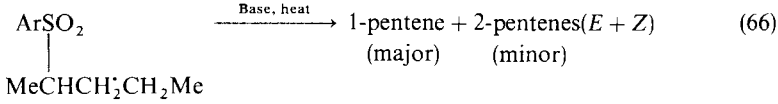
1. Eliminations under basic conditions

Normally, the influence of base on a sulphonyl compound simply removes the α proton, giving a carbanion that can be alkylated, as in equation (65).

$$RSO_2CH_2R' + B:^- \rightleftharpoons RSO_2^-CHR' + BH \qquad (65)$$
$$RSO_2^-CHR' + R''X \longrightarrow RSO_2CHR'R'' + X:^-$$

However, in some circumstances, an arylsulphonyl group is a sufficiently good nucleofuge that an elimination reaction is possible. This has actually been known for some 60 years,

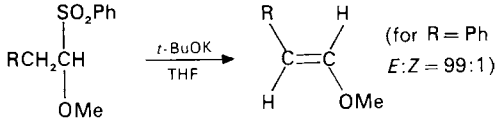
with the most recent paper being by Colter and Miller[159]. These workers studied the reaction outlined in equation (66) using both sodium ethylene glycolate in refluxing ethylene glycol (ca. 197°) and potassium *t*-butoxide in refluxing pyridine (ca. 114°). The conditions were thus vigorous.



(66)

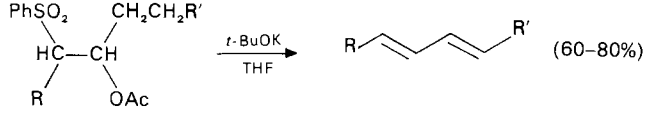
As would be expected in a substrate with a poor leaving group the predominant elimination process is of the Hofmann type. However, the authors did find some unexpected reactions. For example, the *p*-nitrophenyl sulphone was completely consumed within six hours of heating with the glycolate system, yet alkenes formed only a minor part of the products, the major part not being clearly identified. The *p*-dimethylaminophenyl sulphone was three to six times more reactive than the other sulphones, but it also underwent elimination at a significant rate with either solvent, even in the absence of alkoxides. The reasons for this are obscure.

Otera and coworkers have published several reaction sequences[160–163] that effect eliminations of phenylsulphonyl groups under basic conditions. In one sequence[160], α-methoxy phenyl sulphones are treated with potassium *t*-butoxide in THF to give fairly good yields of vinyl ethers, by the elimination of phenylsulphinate anion, as shown in equation (67).



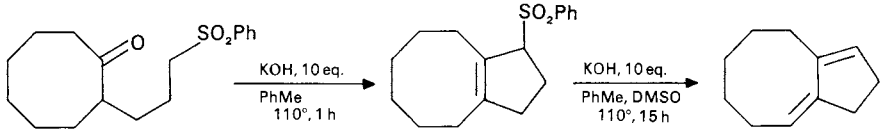
(67)

A second paper[161] describes the use of the same base in either THF or *t*-butanol for the elimination of α-acetoxy phenyl sulphones as outlined in equation (68), in essence a reaction sequence very similar to the Julia olefin synthesis (Section III.B.3) except in the method by which the sulphonyl group is finally removed.



(68)

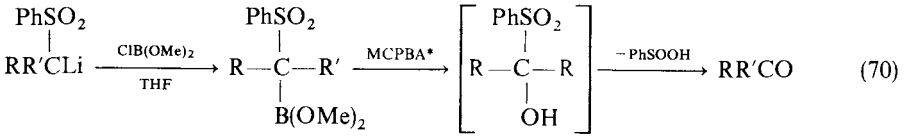
Base-induced elimination of sulphinate from homoallylic sulphones[162,164,165], from γ-ketosulphones[163,166,167], and from 1,2-bissulphones[168] has been used in synthetic sequences ranging from the preparation of retinoic acid[165] and of its methyl ester[162], to a novel pentannulation sequence that leads to a range of cross-conjugated dienes[169], as exemplified by equation (69). The overall yield for the two steps was 63%.



(69)

An unusual desulphonylation process has been developed by Julia's group[170] in which a masked α-hydroxysulphone spontaneously loses the elements of phenylsulphinic acid

when unmasked, this reaction being part of a new, high-yield synthesis of aldehydes and ketones as shown in equation (70).



(70)

*MCPBA = *meta*-chloroperoxybenzoic acid in CH_2Cl_2, at low temperature.

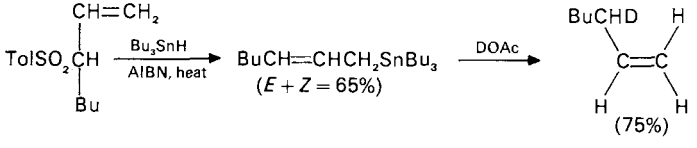
A further series of reactions involving strong bases and sulphones is the rearrangement that occurs when aryl sulphones containing an α-methyl group are induced to give substituted arylsulphinic acids[171,172]. This reaction is now known as the Truce rearrangement.

Stereoselective preparations of 1,3-dienes are described in References 219 and 224 and the preparation of (+)-aspicillin in Reference 225.

2. *Reductions involving stannanes or silanes*

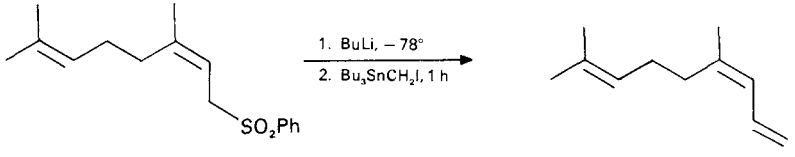
Modern organic chemistry is characterized by the many reactions that have been developed in which 'new' heteroatoms are involved—'new', as distinct from the traditional heteroatoms of oxygen, nitrogen, sulphur and perhaps even phosphorus. Especially prominent in this 'new' chemistry are tin and silicon, and it is not surprising to find these have been allied with sulphur in novel approaches to syntheses. These novel reactions are often characterized by the mild conditions under which they occur.

In what is apparently the first of such papers, Ueno, Aoki and Okawara[173] have shown that allylic sulphones undergo ready allylic substitution by tributyltin hydride, in a reaction that is facilitated either thermally or photochemically and undoubtedly involves the tributyltin radical in a radical chain process. Protonolysis of the resulting terminal allylstannanes gives high yields of terminal alkenes, although the authors point out that electrophiles other than the proton (or deuteron) can be used in the destannylation step. A typical example is given in equation (71). The appeal of this procedure is that it does not appear to give any rearranged products, but rather the contrathermodynamic, terminal alkenes. The reaction has been used by Jones and Peel as a key step in a recent, elegantly simple, stereoselective steroid synthesis[174].



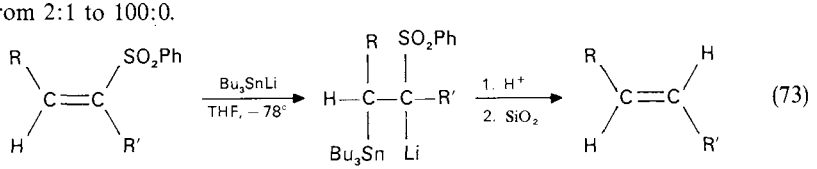
(71)

Three reaction sequences, all of a similar nature, have been published by Fujita and coworkers. The first[175] is an alkene synthesis in which only three examples that involve sulphones are given. The most useful of these is a conversion of nerly phenyl sulphone (from neryl chloride) into a C_{11} triene (75%), with the extra carbon atom being supplied by the iodomethylstannane reagent. The reaction proceeds spontaneously, with apparent retention of configuration at the Z alkene, as in equation (72).

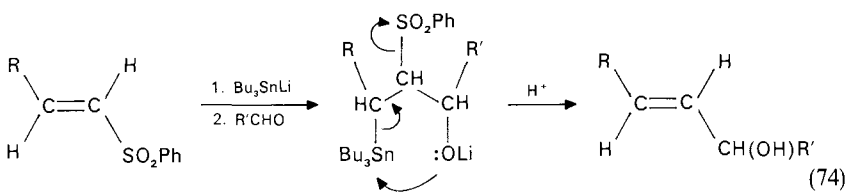


(72)

The second sequence has been published in English as a note[176] and in Japanese as a full paper[177], in which vinyl sulphones are desulphonylated by an addition–elimination sequence, illustrated in equation (73). Overall yields in the sequence are good (mostly better than 80%), although the stereoselectivity does not appear to be outstanding, and this method should be compared to Julia's reduction of vinyl sulphones with sodium dithionite (Section III.B.7). The third reaction sequence from this research group is ingenious[178], in that it effects the desulphonylation of a vinyl sulphone, and also permits the introduction of an alkylcarbinol group to give a synthesis of allylic alcohols while retaining a high degree of control on the configuration of the original vinyl sulphone. The reaction is displayed in equation (74). Yields are generally over 80% and the *E*:*Z* ratio varies from 2:1 to 100:0.



(73)



(74)

A similar elimination in which the tin is attacked by fluoride anions (cf. the reaction of silanes with F^-) has been used[179] to synthesize terminal methylene compounds as in equation (75). An analogous reaction sequence using a trimethylsilyl group in place of the trialkyltin group has been published by Hsiao and Shechter[180] as part of a synthesis of substituted 1,3-butadienes.

$$RR'CHSO_2Ph \xrightarrow[2.\,R''_3SnCH_2I]{1.\,LDA} RR'C(SO_2Ph)CH_2SnR''_3 \xrightarrow{F^-} RR'C{=}CH_2 \quad (75)$$

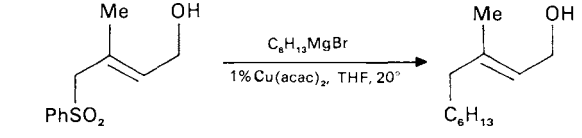
3. *The use of Grignard and related reagents*

This section will be divided arbitrarily into two portions, the first dealing with the reactions of allyl sulphones and the second with those of vinyl sulphones. Posner and Brunelle had shown[117] (Section III.B.3) that organocuprates will give conjugate addition reactions with vinyl sulphones. Julia and coworkers then showed[181,182] that the same reaction could be achieved by the use of a Grignard reagent in the presence of the copper(II) complex, $Cu(acac)_2$ in catalytic quantities, following which they proceeded to explore the analogous reactions with allylic sulphones. The main feature is that the reaction permits the conversion of an allyl sulphone into an alkylated alkene, in one step, often in good yield and often with a high degree of stereoselectivity (equation 76). However, the actual success of any given reaction is dependent on a range of factors. For example, if R′ is a methyl group, the reaction proceeds exactly as given in equation (76), except that the yield is low, although this can be boosted dramatically with 10 mol% of the cupric-complex catalyst and an increase in the reaction time to 3 days. If, however, R′ is a proton, the alkylation takes place mostly at the terminal vinyl carbon which results in an allylic transposition. In the case of 1,2-disubstitution of the double bond in allylic sulphones, the alkylation is highly favoured to be α to the sulphonyl group if the alkene

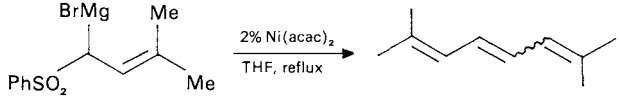
stereochemistry is *E*, but less so if it is *Z*. The use of a Grignard reagent derived from an alkyl chloride was found to be distinctly more efficacious than that from an alkyl bromide and, especially relevant to this review, allylic chlorides or acetates were less effective substrates than were allylic sulphones! Julia and coworkers also compared their copper-catalyzed reaction with a comparable reaction developed by Masaki and coworkers[183] using fully formed organocuprates. It appears that the catalyzed process with an alkylmagnesium chloride is superior to the cuprate in the case of a 1,2-disubstituted alkene, but the two processes are very comparable in the case of a terminal vinyl group.

$$RMgX + PhSO_2CH_2CH{=}CR'_2 \xrightarrow[THF,\,18h,\,20^\circ]{1\ mol\%\ Cu(acac)_2} RCH_2CH{=}CR'_2 \qquad (76)$$

A development of these reactions is the synthesis of allylic alcohols developed by Julia and Verpeaux[184], a representative example of which is given in equation (77), the yield in this case being 90%. The analogous *Z* allylic alcohol only gave a 62% yield of the desired product, plus 11% of the stereoisomer and 5% of the regioisomer. Julia has noted[182] that these coupling reactions suffer from competition in that the allylic protons, α to the sulphonyl group, are sufficiently acidic that they can be deprotonated by the Grignard reagent. He also found[185] that treatment of the preformed sulphonyl 'anion' with a catalytic amount of nickel acetoacetate complex results in a dimerization of the allyl entities, presumably with the concomitant formation of Ni^0 and diphenyl disulphone. The process is outlined in equation (78) and constitutes a potentially useful synthesis of trienes, or even polyenes, that is formally somewhat reminiscent of the McMurray synthesis of alkenes from carbonyl compounds and low-valent titanium species[186].



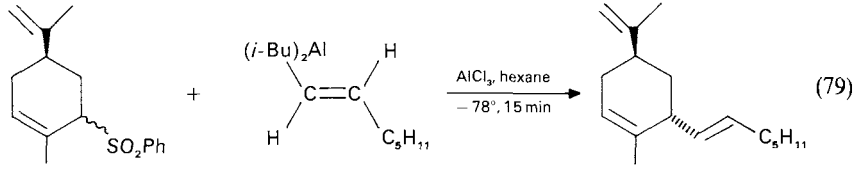
(77)



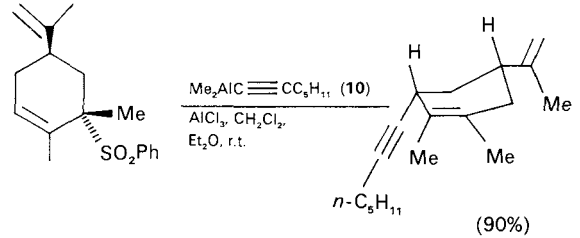
(78)

In recent work by Trost and Ghadiri[187] allyl sulphones are treated with vinylic or acetylenic alanes, which leads to a wide range of dienes and enynes in moderate to very good yields, even in the presence of functional groups like esters and alcohols. Three examples will be examined here. In equation (79), a stereoisomeric mixture of carvyl phenyl sulphone is reacted with a *trans*-vinylalane to give a *trans*-3,5-dialkylcyclohexene in 46% yield. Methylation of the carvyl ring at the position of the sulphonyl group and reaction with an acetylenic alane, **10**, reverses the regiochemistry of the process, increases the yield by more than half as compared to the unmethylated product, but retains the interesting stereochemistry of the process so that the incoming alkynyl group ends up in a pseudoaxial orientation (equation 80). When a β-hydroxysulphone is first complexed with trimethylaluminium and then reacted with the alkynylalane **10**, the incoming alkynyl group apparently 'displaces' the sulphonyl group directly, as outlined in equation (81). Trost and Ghadiri suggest[187] that the mechanism of the reaction 'most likely involves ionization to a carbonium ion followed by capture by the nucleophile' and that 'organosulfones are a new general class of substrates as electrophilic conjunctive reagents in the presence of Lewis acids as mild as alkylaluminium halides'. It is difficult to reconcile the involvement of carbonium ions in a reaction such as that outlined in equation (81),

since it would be reasonable to expect anchimeric assistance by the complexed hydroxyl group that would be α to any cation formed by a departing phenylsulphonyl group. Such involvement by the hydroxyl group would lead to a mixture of products, owing to attack by the nucleophilic alane, **10**, at either electrophilic centre. Trost and Ghadiri[187] make no suggestion that any significant quantities of another product were detected. Given the previous discussions on the interactions of electrophilic reagents with sulphones (Sections III.A.2 and 3), it is difficult to envisage that there will be much interaction of a Lewis acid–base nature with the sulphonyl group in the compounds studied by these authors. Such an interaction would most likely be a prerequisite for any significant nucleofugal character on the part of the phenylsulphonyl group.

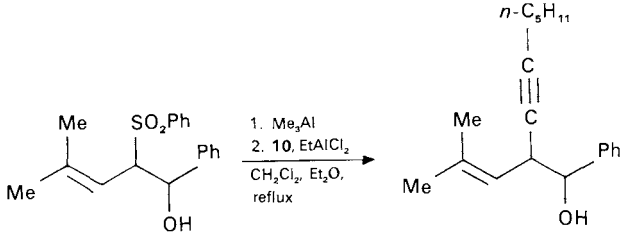


(79)



(80)

(90%)



(81)

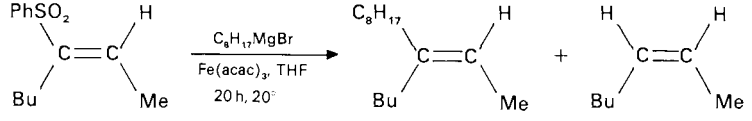
(71%)

However, there is evidence that reactions of aluminium hydride produced *in situ* involve single-electron-transfer (SET) processes[188,189]. The reactions described by Trost and Ghadiri[187] have most likely not been studied in sufficient detail to permit an adequate description of the reaction mechanism to be given at this stage. It is, however, quite likely that the Grignard reactions catalyzed by copper(II) and nickel(II) complexes[190], as developed by Julia[181,182,184,185] and by Masaki[183], do involve SET processes, although, if this is so, the preservation of stereochemistry in some of the examples described by these workers is quite remarkable. (In this context, the reader's attention is drawn to Reference 196, end of this section.)

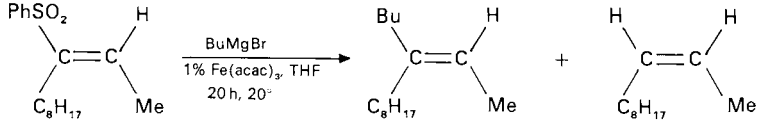
The work on vinyl sulphones and their reactions with Grignard reagents, in the presence of transition metal catalysts, all emanates from Julia's laboratory[191–195], with the exception of a note[196] that presents evidence for SET processes in the alkylation of vinyl sulphones by organometallic reagents.

The stereoselective hydrogenolysis of vinyl sulphones using sodium dithionite was described in Section III.B.7. Fabre and Julia have also described the hydrogenolysis of vinylic sulphones by butylmagnesium chloride[191] in the presence of nickel(II) or palladium(II) complexes, such as acetylacetonate, and often in the presence of auxiliary ligands such as DABCO or tributylphosphine. The reaction is complicated by the coupling product between the alkene and the Grignard reagent, or in one case by dimerization of the desulphonylated alkene itself. The yields vary from modest to good, and although the authors give a more varied set of examples, it would appear from the data presented that the dithionite desulphonylation is much simpler to carry out and is at least as effective, even with respect to the stereochemical integrity of the reduction process. However, the reaction has been used as one step in a synthesis of 9*Z*, 11*E*-tetradecadienyl acetate, the pheromone of the Egyptian cotton-leaf worm[192].

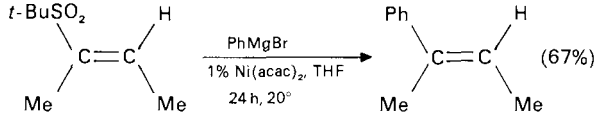
Of greater potential practical significance, however, are the note[193] and full papers[194,195] in which Fabre, Julia and Verpeaux describe a new stereoselective synthesis of trisubstituted alkenes in which vinyl sulphones are attacked by Grignard reagents in the presence of iron or nickel catalysts (equations 82–84).



Yield (ratio *E*/*Z*): 63% 63% (97/3) 18% (13/87) (82)



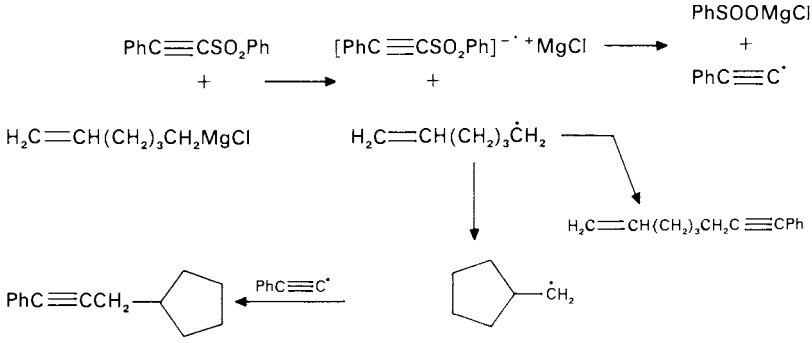
Yield (ratio *E*/*Z*): 65% (3/97) 15% (13/87) (83)



(67%) (84)

It is not possible to give complete details of the ninety-odd runs described in these papers. Suffice it to say that not all results are as good as those given and some mixtures were encountered. The optimum solvent in most cases appears to be tetrahydrofuran; chloride is the best counterion in the case of the methyl Grignard reagent and stereoselectivity depends on the degree of substitution of the vinyl sulphone, or sometimes also on its stereochemistry, *E* being higher than *Z*. Omission of the catalyst led in some cases to the Michael adduct, or even to dimeric products. However, incomplete removal of the catalyst when it is used can lead to isomerization of certain alkenes, which indicates a need for very careful experimental technique. The authors acknowledge the complexity of the reactions and suggest the need for further work to gain a better mechanistic understanding.

Eisch, Behrooz and Galle[196] give compelling evidence for the intervention of radical species in the desulphonylation of certain acetylenic or aryl sulphones with metal alkyls having a lower oxidation potential at the anionic carbon. The primary evidence presented by these workers is that the reaction of 5-hexenylmagnesium chloride outlined in equation (85) gives a mixture of desulphonylation products, in accord with the known behaviour of the 5-hexenyl radical, in which the cyclopentylmethyl radical is also formed.

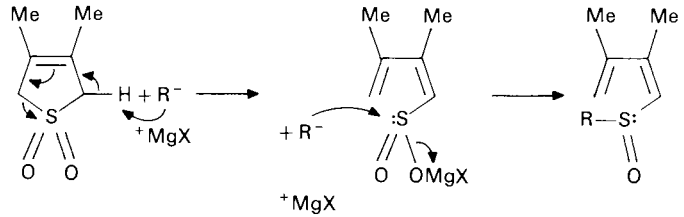


(85)

This evidence is undoubtedly directly relevant to all of the reactions described in this section and should be valuable in guiding further studies into an interesting and potentially useful area of desulphonylation reactions.

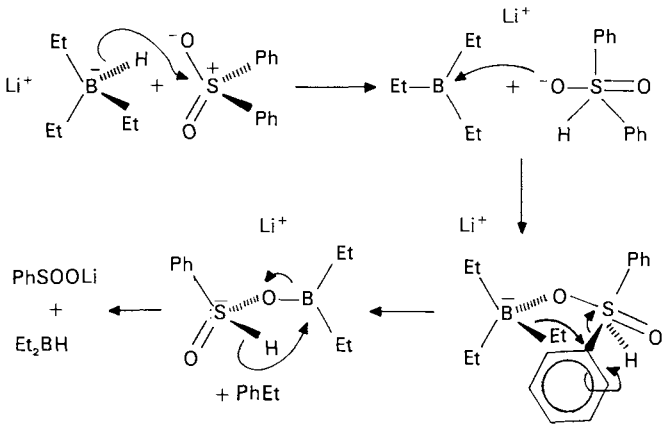
4. Miscellaneous desulphonylation reactions

Gaoni has published[197] a novel preparation of 1,3- and 1,4-dienylic sulphoxides in which certain sulpholenes or sulpholanes can be cleaved with two equivalents of a Grignard reagent. The reactions outlined in equation (86) can be classified formally as a double reduction at the sulphur atom. The 1,4-dienylic sulphoxides can be obtained by the same type of reactions, via bicyclo[3.1.0] sulphones, that are accessible from the sulpholenes and dichlorocarbene, followed by dechlorination with $LiAlH_4$[197]. Yields for all the reactions are poor to modest (26 to 66%).



(86)

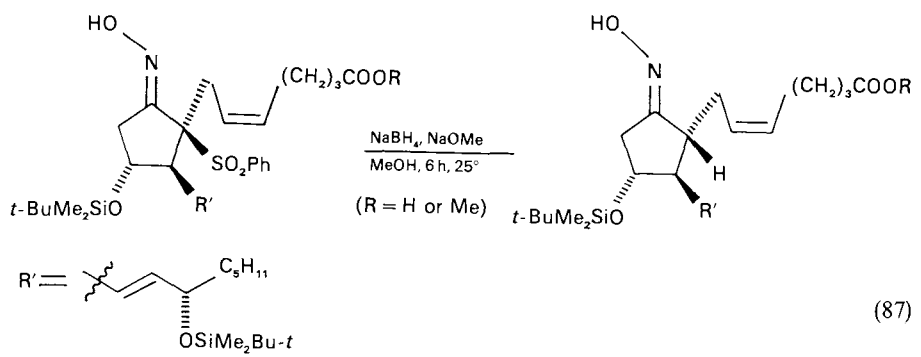
Another reaction in which the sulphonyl group shows nucleofugal properties has been described by Brown and coworkers[198]. The simplest example is between diphenyl sulphone and lithium triethylborohydride which gives a mixture of ethylbenzene and lithium benzenesulphinate after refluxing for a few hours in THF solution. Phenyl *p*-tolyl sulphone gives a mixture of ethylbenzene (66%) and *p*-ethyltoluene (8%), whereas methyl phenyl sulphone gives only a 38% yield of ethylbenzene and aliphatic sulphones do not react. Brown proposes a mechanism in which the triethylborohydride anion acts as a hydroborating agent for the benzene ring with the lower electron density, but this



SCHEME 2

mechanism does not account adequately for the observed regiochemistry of the reaction. He does give experimental evidence for the presence of diethylborane in the reaction mixture, since this can be trapped by carrying out the reaction in the presence of 1-octene. Normally, lithium triethylborohydride is a powerful hydride nucleophile, and so far as this reviewer is aware, it is not a formal source of the ethyl carbanion. It is conceivable that the reaction pathway is actually similar to that proposed in Section III.A.1 (Scheme 1) for the reduction of sulphones with lithium aluminium hydride, and that the reaction would also be successful on strained cyclic sulphones with smaller than normal CSC bond angles. Brown and coworkers[198] do not mention if they have tried these as possible substrates. A plausible reaction pathway for this interesting conversion is proposed in Scheme 2, which would predict ethane as a by-product from a minor pathway of the reaction.

Examples of a desulphonylation procedure on complex molecules are provided by Fuchs and coworkers[199] who reported on a triply convergent synthesis of L-(−)-prostaglandin E_2. The molecules can be classified as homoallylic sulphones and reductive desulphonylation was best achieved with a mixture of sodium methoxide and sodium borohydride in methanol, with yields being better than 90%, despite the complexity of the molecules involved (equation 87).

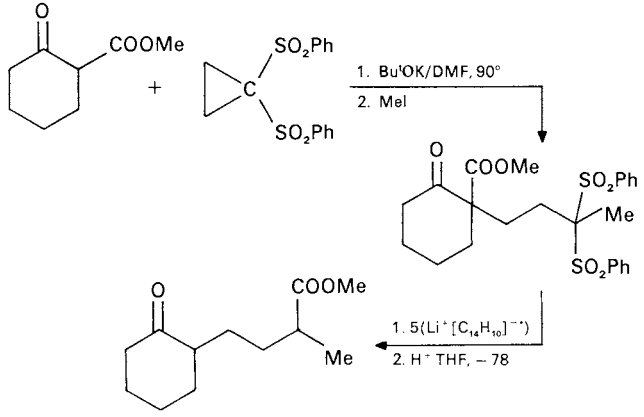


(87)

A novel reduction of a 'vinyl sulphone' has been published by Ueno, Kojima and Okawara[200] who have found that 2-(alkylsulphonyl)benzothiazoles can be reduced by aqueous sodium borohydride to form the sodium salts of alkylsulphinic acids, in good

yields. Alkylsulphinic acids are not readily accessible and this reaction sequence should improve this situation.

Finally, an ingenious synthetic sequence by Trost, Cossy and Burks[201] includes a unique desulphonylation reaction that involves an electron-transfer process. The synthetic sequence uses 1, 1-bis(phenylsulphonyl)cyclopropane as a source of three carbon atoms, since this species is readily alkylated even by weakly nucleophilic species. Given an appropriate structure for the nucleophile, Trost found that desulphonylation with lithium phenanthrenide in an aprotic solvent allowed for an efficient intramolecular trapping of the resultant carbanion (equation 88). This desulphonylation process occurs under very mild conditions and in high yields; it will undoubtedly attract further interest.



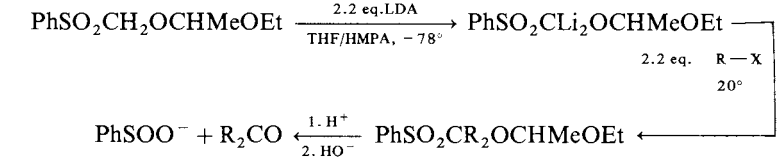
(88)

The desulphonylation of β-ketosulphones with the Hantzsch ester is described in Reference 226.

D. Oxidative Desulphonylation Reactions

In all the desulphonylation reactions discussed in Sections III.B and III.C the sulphur is lost from the starting sulphone and is reduced in the process; simultaneously, the former carbon–sulphur bond is either reduced to a C—H bond or is converted into a C=C bond. The reactions described in this section have the common thread that the sulphur atom is lost with reduction at sulphur, but the carbon atom is converted directly into a carbonyl group. Formally, these reactions offer a route from alkyl halides to aldehydes or ketones.

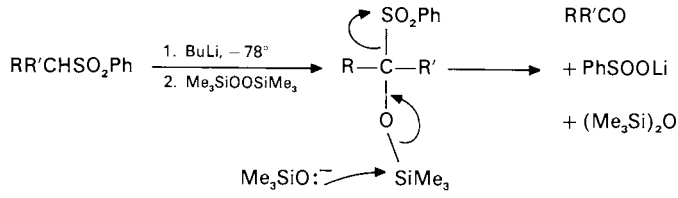
In a reaction sequence[202] protected α-hydroxy sulphones were alkylated, after which acid hydrolysis followed by mild basic hydrolysis gave ketones. The protecting group used was the 1-ethoxyethyl ether, and overall yields for the sequence were generally modest (equation 89).



(89)

Another approach to an oxidative desulphonylation reaction is to oxidize an α-sulphonyl carbanion with an oxidizing agent that is also nucleofugal. An example of this was presented by Little and Sun Ok Myong[203] who used a molybdenum peroxide complex (MoO_5.Pyridine.HMPA) as the oxidant. However, this reagent is expensive and

somewhat inaccessible. More recently, Jih Ru Hwu has proposed[204] the use of bis(trimethylsilyl) peroxide for the same purpose (equation 90). Yields are in the range of 66 to 91% and the reaction has the added bonus that it can be used for the preparation of ketones labelled with oxygen-18.



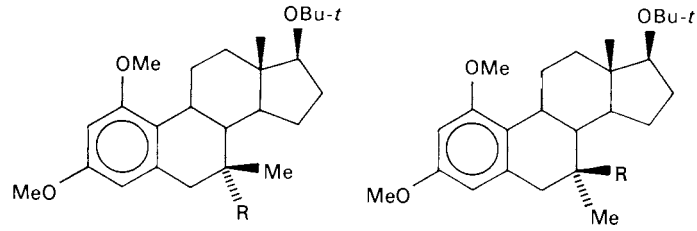
(90)

E. Reductions of Sulphones Using Thermolyses, Photolyses or Electrochemical Processes

These topics are discussed in more detail in other chapters of this text. Formally, the pyrolytic elimination of sulphur dioxide from a sulphone, with the concomitant formation of a new carbon–carbon bond, constitutes a reduction at sulphur. These reductions have been valuable in the formation of new molecules, especially macrocycles and cyclophanes, and have been reviewed by Vögtle and Rossa[205]. Pyrolytic elimination of sulphur dioxide has been used by Julia and coworkers in the formation of mixtures of isoprenoids[206], and by Takayama and collaborators in the stereoselective synthesis of vitamin D_3 19-alkanoic acids[207].

The photoextrusion of sulphur dioxide to form cyclophanes or other novel aromatic molecules has been reviewed and studied by Givens[208–210], while the photodecomposition of aromatic sulphones to form products of radical coupling reactions has recently also received attention[211].

Electrochemical reductions of sulphones have been reviewed[212], and have been discussed at intervals[213–215]. There is evidence that the cathodic reduction reaction proceeds via a radical anion, followed by a cleavage reaction, as outlined in equation (91)[212,213].



(11) R = SO_2Ph
(13) R = H

(12) R = SO_2Ph
(14) R = H

11 —(Hg cathode, undivided cell; MeOH solvent + $LiClO_4$)→ 14 + 13 (yield 75%, ratio 9.2:1)

12 —(Pt cathode, divided cell; DMF solvent + Me_4NBr)→ 14 + 13 (yield 35%, ratio 1:2.5)

SCHEME 3

$$RSO_2R \xrightarrow{e^-} [RSO_2R]^{-\cdot} \xrightarrow{e^-} R^- + RSOO^- \xrightarrow{2H^+} RH + RSOOH \qquad (91)$$

Of some relevance in this connection is a study[216] on the structure of the anion radicals formed when diaryl sulphones react with *n*-butyllithium in hexane–HMPA solution under an argon atmosphere. Apparently, a dehydrogenative cyclization and a further one-electron reduction occurs to produce the anion radicals of substituted dibenzothiophene-*S*,*S*-dioxides. These anion radicals were studied by ESR spectroscopy.

Perhaps of more significance is a detailed study[132] into the reductive desulphonylation of 7-methyl-7-phenylsulphonylestratrienes. The goal was stereoselective removal of the sulphonyl group, and hydride reductions, alkali-metal-amalgam reductions and electrochemical reductions were explored. The latter proved to be the most effective and the best results are illustrated in Scheme 3.

Details of the conditions used in these reductions are discussed, especially the fact that this is apparently the first example in which the stereochemical aspects of an electrochemical desulphonylation reaction on a complex molecule have been examined. It is likely that further work will be profitable, given suitable substituents on a molecule, since sulphones (especially vinyl and aryl sulphones) should be good candidates for this type of reduction.

IV. ACKNOWLEDGEMENTS

I thank Miss Patricia Lutley of the Macdonald Science Library, Dalhousie University, for her generous help, as well as Alan Grossert and NSERC (Canada) Summer Scholars Matthew Morgan and Cheryl Wallace for their assistance with the references.

V. REFERENCES

1. H. H. Szmant in *Sulfur in Organic and Inorganic Chemistry*, Vol. 1 (Ed. A. Senning), Dekker, New York, 1971, pp. 107–152.
2. T. Durst in *Comprehensive Organic Chemistry*, Vol. 3 (Ed. D. N. Jones), Pergamon Press, Oxford, 1979, pp. 171–195.
3. R. Schubart in *Methoden der organischen Chemie* (*Houben-Weyl*) Vol. E11—Organische Schwefel-Verbindungen (Ed. D. Klamann), G. Thieme Verlag, Stuttgart, 1985, pp. 63–107.
4. G. H. Petit, A. T. H. Lenstra and H. J. Geise, *Bull. Soc. Chim. Belg.*, **90**, 23 (1981).
5. I. Hargittai, *Sulphone Molecular Structures*, Lecture Notes in Chemistry No. 6, Springer-Verlag, Berlin, 1978.
6. E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, 1978, p. 294.
7. S. W. Benson, *Chem. Rev.*, **78**, 23 (1978).
8. C. T. Mortimer, *Reaction Heats and Bond Strengths*, Pergamon Press, Oxford, 1962, p. 185.
9. R. Walsh, *Acc. Chem. Res.*, **14**, 246 (1981).
10. R. T. Sanderson *Polar Covalence*, Academic Press, New York, 1983, p. 82.
11. C. T. Mortimer, *Reaction Heats and Bond Strengths*, Pergamon Press, Oxford, 1962, p. 189.
12. S. Oae in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, 1977, pp. 383–471.
13. J. Drabowicz, T. Numata and S. Oae, *Org. Prep. Proc. Int.*, **9**, 63 (1977).
14. J. Drabowicz, H. Togo, M. Mikolajczyk and S. Oae, *Org. Prep. Proc. Int.*, **16**, 171 (1984).
15. G. A. Olah, B. G. B. Gupta and S. C. Narang, *J. Org. Chem.*, **43**, 4503 (1978).
16. J. N. Denis and A. Krief, *Tetrahedron Letters*, 3995 (1979).
17. J. N. Denis and A. Krief, *J. Chem. Soc., Chem. Commun.*, 544 (1980).
18. H. Suzuki, N. Sato and A. Osuka, *Chem. Letters*, 143 (1980).
19. M. Lauwers, B. Regnier, M. van Eenoo, J. N. Denis and A. Krief, *Tetrahedron Letters*, 1801 (1979).
20. R. A. Amos, *J. Org. Chem.*, **50**, 1311 (1985).
21. I. W. J. Still, S. K. Hasan and K. Turnbull, *Synthesis*, 468 (1977); *Can. J. Chem.* **56**, 1423 (1978); *Phosphorus and Sulfur*, **6**, 293 (1979).
22. I. W. J. Still, J. N. Reed and K. Turnbull, *Tetrahedron Letters*, 1481 (1979).

23. J. B. Rasmussen, K. A. Jørgensen and S.-O. Lawesson, *Bull. Soc. Chim. Belg.*, **87**, 307 (1978).
24. M. Wakisaka, M. Hatanaka, H. Nitta, M. Hatamura and T. Ishimaru, *Synthesis*, 67 (1980).
25. Nung Min Yoon, Byung Tae Cho, Ji Uk Yoo and Gun Poong Kim, *Taehan Hwahakhoe Chi (J. Korean Chem. Soc.)*, **27**, 434 (1983); *Chem. Abstr.*, **100**, 138 654f (1984).
26. Y. Guindon, J. G. Atkinson and H. E. Morton, *J. Org. Chem.*, **49**, 4538 (1984).
27. G. Palumbo, C. Ferreri and R. Caputo, *Phosphorus and Sulfur*, **15**, 19 (1983).
28. Y. D. Vankar and C. T. Rao, *Tetrahedron Letters*, **26**, 2717 (1985).
29. I. S. Alnaimi and W. P. Weber, *J. Organomet. Chem.*, **241**, 171 (1983).
30. G. A. Olah, A. Husain, B. P. Singh and A. K. Mehrotra, *J. Org. Chem.*, **48**, 3667 (1983).
31. A. H. Schmidt and M. Russ, *Chem. Ber.*, **114**, 822 (1981).
32. R. D. Miller and D. R. McKean, *Tetrahedron Letters*, **24**, 2619 (1983).
33. R. D. Miller and R. Hässig, *Tetrahedron Letters*, **25**, 5351 (1984).
34. R. D. Miller and R. Hässig, *Synth. Commun.*, **14**, 1285 (1984).
35. R. D. Miller and R. Hässig, *Tetrahedron Letters*, **26**, 2395 (1985).
36. D. N. Harpp, T. Aida and T. H. Chan, *Tetrahedron Letters*, **26**, 1795 (1985).
37. C. Tenca, A. Dossena, R. Marchelli and G. Casnati, *Synthesis*, 141 (1981).
38. N. Fukamiya, M. Okano and T. Aratani, *Chem. Ind. (London)*, 199 (1982).
39. K. S. Keshavamurthy, Y. D. Vankar and D. N. Dhar, *Indian J. Chem.*, **22B**, 504 (1983).
40. H. Lardon and G. Seybold, *Eur. Pat. Appl.*, EP 68 371; *Chem. Abstr.*, **98**, 215 313p (1983).
41. Sung-Kee Chung and Guangdian Han, *Synth. Commun.*, **12**, 903 (1982).
42. S. Kano, Y. Tanaka, E. Sugino and S. Hibino, *Synthesis*, 695 (1980).
43. V. Reutrakul and P. Poochaivatananon, *Tetrahedron Letters*, **24**, 531 (1983).
44. B. Rajanikanth and B. Ravindranath, *Indian J. Chem.*, **24B** 296 (1985).
45. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **86**, 1639 (1964).
46. A. Ohno, H. Yamamoto and S. Oka, *J. Amer. Chem. Soc.*, **103**, 2041 (1981).
47. T. Nagata, T. Yoshimura, K. Fujimori and S. Oae, *Tetrahedron Letters*, **25**, 341 (1984).
48. J. Q. Chambers in *Encyclopedia of Electrochemistry of the Elements*, Vol. XII (Eds. A. J. Bard and H. Lund), Dekker, New York, 1978, pp. 389–393.
49. A. Kunugi and K. Abe, *Chem. Letters*, 159 (1984).
50. A. Kunugi, T. Hagi, T. Hirai and K. Abe, *Electrochim. Acta*, **30**, 1049 (1985).
51. K. Ogura and G. Tsuchihashi, *Tetrahedron Letters*, 1383 (1972).
52. W. E. Truce, T. C. Klinger and W. W. Brand in *Organic Chemistry of Sulfur* (Ed. S. Oae), Plenum Press, New York, 1977, pp. 527–602.
53. T. Durst in *Comprehensive Organic Chemistry*, Vol. 3 (Ed. D. N. Jones), Pergamon Press, Oxford, 1979, pp. 197–213.
54. S. Oae and H. Togo, *Kagaku (Kyoto)*, **37**, 909 (1982); *Chem. Abstr.*, **98**, 160 185r (1983).
55. S. Oae and H. Togo, *Kagaku (Kyoto)*, **37**, 812 (1982); *Chem. Abstr.*, **98**, 16 023n (1983).
56. S. Oae and H. Togo, *Kagaku (Kyoto)*, **38**, 48 (1983); *Chem. Abstr.*, **98**, 197 543g (1983).
57. S. Oae and H. Togo, *Kagaku (Kyoto)*, **38**, 201 (1983); *Chem. Abstr.*, **98**, 215 134f (1983).
58. S. Oae and H. Togo, *Kagaku (Kyoto)*, **38**, 280 (1983); *Chem. Abstr.*, **99** 69 677n (1983).
59. S. Oae and H. Togo, *Kagaku (Kyoto)*, **38**, 341 (1983); *Chem. Abstr.*, **99**, 52 580c (1983).
60. S. Oae and H. Togo, *Kagaku (Kyoto)*, **38**, 506 (1983); *Chem. Abstr.*, **99**, 157 366r (1983).
61. K. Schank in *Methoden der organischen Chemie (Houben-Weyl)*, Vol. E11—Organische Schwefel-Verbindungen (Ed. D. Klamann), G. Thieme Verlag, Stuttgart, 1985, pp. 1132–1298.
62. F. Krafft and W. Vorster, *Ber. Deutsch. Chem. Gesell.*, **26**, 2813 (1893).
63. F. G. Bordwell and W. H. McKellin, *J. Amer. Chem. Soc.*, **73**, 2251 (1951).
64. D. C. Dittmer and M. E. Christy, *J. Amer. Chem. Soc.*, **84**, 399 (1962).
65. L. A. Paquette, R. E. Wingard, Jr., J. C. Philips, G. L. Thompson, L. K. Read and J. Clardy, *J. Amer. Chem. Soc.*, **93**, 4508 (1971).
66. L. A. Paquette and R. W. Houser, *J. Amer. Chem. Soc.*, **93**, 4522 (1971).
67. C. R. Johnson, J. E. Keiser and J. C. Sharp, *J. Org. Chem.*, **34**, 860 (1969).
68. W. O. Siegl and C. R. Johnson, *J. Org. Chem.*, **35**, 3657 (1970).
69. T. A. Whitney and D. J. Cram, *J. Org. Chem.*, **35**, 3964 (1970).
70. W. P. Weber, P. Stromquist and T. I. Ito, *Tetrahedron Letters*, 2595 (1974).
71. J. Meinwald, S. Knapp, S. K. Obendorf and R. E. Hughes, *J. Amer. Chem. Soc.*, **98**, 6643 (1976).
72. N. Dufort and B. Jodoin, *Can. J. Chem.*, **56**, 1779 (1978).
73. F. G. Bordwell, R. H. Imes and E. C. Steiner, *J. Amer. Chem. Soc.*, **89**, 3905 (1967).

74. F. G. Bordwell, M. Van Der Puy and N. R. Vanier, *J. Org. Chem.*, **41**, 1883 (1976).
75. F. G. Bordwell, M. Van Der Puy and N. R. Vanier, *J. Org. Chem.*, **41**, 1885 (1976).
76. F. G. Bordwell, *Pure Appl. Chem.*, **49**, 963 (1977).
77. F. G. Bordwell, J. C. Branca, C. R. Johnson and N. R. Vanier, *J. Org. Chem.*, **45**, 3884 (1980).
78. F. Mo, B. C. Hauback and S. Winther, *Acta Cryst.*, **B40**, 288 (1984).
79. J. S. Grossert, J. Hoyle, T. S. Cameron, S. P. Roe and B. R. Vincent, *Can. J. Chem.*, **65**, 1407 (1987).
80. L. A. Paquette and L. S. Wittenbrook, *J. Amer. Chem. Soc.*, **89**, 4483 (1967).
81. L. A. Paquette, L. S. Wittenbrook and V. V. Kane, *J. Amer. Chem. Soc.*, **89**, 4487 (1967).
82. Ta-shue Chou and Lee-Jean Chang, *J. Org. Chem.*, **50**, 4998 (1985).
83. J. N. Gardner, U. S. Patent 3 819 652 (1972); *Chem. Abstr.*, **81**, 120 444s (1974).
84. J. N. Gardner, S. Kaiser, A. Krubiner and H. Lucas, *Can. J. Chem.*, **51**, 1419 (1973).
85. A. G. Anastassiou, J. C. Wetzel and B. Y.-H. Chao, *J. Amer. Chem. Soc.*, **97**, 1124 (1975).
86. C. G. M. Janssen and E. F. Godefroi, *J. Org. Chem.*, **47**, 3274 (1982).
87. H. A. Bates, L. Smilowitz and J. Lin, *J. Org. Chem.*, **50**, 899 (1985).
88. G. R. Chalkley, D. J. Snodin, G. Stevens and M. C. Whiting, *J. Chem. Soc. (C)*, 682 (1970).
89. G. R. Chalkley, D. J. Snodin, G. Stevens and M. C. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 1580 (1978).
90. K. Okuma, K. Nakanishi and H. Ohta, *J. Org. Chem.*, **49**, 1402 (1984).
91. M. Shimagaki, H. Tsuchiya, Y. Ban and T. Oishi, *Tetrahedron Letters*, 3435 (1978).
92. I. W. J. Still and S. Szilagyi, *Synth. Commun.*, **9**, 923 (1979).
93. I. W. J. Still and F. J. Ablenas, *J. Org. Chem.*, **48**, 1617 (1983).
94. J. I. G. Cadogan, D. K. Cameron, I. Gosney, R. M. Highcock and S. F. Newlands, *J. Chem. Soc., Chem. Commun.*, 766 (1986).
95. S. Braverman and Y. Duar, *J. Amer. Chem. Soc.*, **105**, 1061 (1983).
96. P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, Oxford, 1983, p. 171; J. E. Baldwin, *J. Chem. Soc. Chem. Commun.*, 734 (1976).
97. W. E. Truce, D. P. Tate and D. N. Burdge, *J. Amer. Chem. Soc.*, **82**, 2872 (1960).
98. W. E. Truce and F. J. Frank, *J. Org. Chem.*, **32**, 1918 (1967).
99. D. B. Hope, C. D. Morgan and M. Wälti, *J. Chem. Soc. (C)*, 270 (1970).
100. P. A. Grieco and Y. Masaki, *J. Org. Chem.*, **39**, 2135 (1974).
101. P. A. Grieco and Y. Masaki, *J. Org. Chem.*, **40**, 150 (1975).
102. B. M. Trost, L. Weber, P. Strege, T. J. Fullerton and T. J. Dietsche, *J. Amer. Chem. Soc.*, **100**, 3426 (1978).
103. J. A. Marshall and D. G. Cleary, *J. Org. Chem.*, **51**, 858 (1986).
104. M. Julia and D. Uguen, *Bull. Soc. Chim. Fr.*, 513 (1976).
105. M. Julia, D. Uguen and A. Callipolitis, *Bull. Soc. Chim. Fr.*, 519 (1976).
106. P. Kocienski, *Phosphorus and Sulfur*, **24**, 97 (1985).
107. K. Sato, S. Inoue, A. Onishi, N. Uchida and N. Minowa, *J. Chem. Soc., Perkin Trans. 1*, 761 (1981).
108. D. Savoia, C. Trombini and A. Umani-Ronchi, *J. Chem. Soc., Perkin Trans. 1*, 123 (1977).
109. Ta-shue Chou and Mei-Li You, *Tetrahedron Letters*, **26**, 4495 (1985).
110. T. H. Lowry and K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, 2nd ed., Chap. 3, Harper and Row, New York, 1981.
111. J. March, *Advanced Organic Chemistry*, 3rd ed., Wiley, New York, 1985, p. 1101.
112. H. O. House, *Modern Synthetic Reactions*, 2nd ed., Benjamin, Menlo Park, Ca., 1972, p. 150.
113. K. Takaki, N. Nakagawa and K. Negoro, *J. Org. Chem.*, **45**, 4789 (1980).
114. Ying-Che Kuo, T. Aoyama and T. Shioiri, *Chem. Pharm. Bull.*, **30**, 2787 (1982).
115. A. C. Brown and L. A. Carpino, *J. Org. Chem.*, **50**, 1749 (1985).
116. R. E. Dabby, J. Kenyon and R. F. Mason, *J. Chem. Soc.*, 4881 (1952).
117. G. H. Posner and D. J. Brunelle, *J. Org. Chem.*, **38**, 2747 (1973).
118. M. Julia and B. Badet, *Bull. Soc. Chim. Fr.*, 1363 (1975).
119. K. Kondo, E. Saito and D. Tunemoto, *Tetrahedron Letters*, 2275 (1975).
120. M. Julia and J.-M. Paris, *Tetrahedron Letters*, 4833 (1973).
121. J. W. Cornforth, Mrs R. H. Cornforth and K. K. Mathew, *J. Chem. Soc.*, 112 (1959).
122. P. J. Kocienski, B. Lythgoe and S. Ruston, *J. Chem. Soc., Perkin Trans. 1*, 829 (1978).
123. P. J. Kocienski, *Chem. Ind. (London)*, 548 (1981).

124. P. Kocienski and M. Todd, *J. Chem. Soc., Chem. Commun.*, 1078 (1982).
125. P. A. Grieco, Y. Masaki and D. Boxler, *J. Org. Chem.*, **40**, 2261 (1975).
126. B. M. Trost, H. C. Arndt, P. E. Strege and T. R. Verhoeven, *Tetrahedron Letters*, 3477 (1976).
127. F. W. Sum and L. Weiler, *J. Amer. Chem. Soc.*, **101**, 4401 (1979).
128. B. M. Trost and T. R. Verhoeven, *J. Amer. Chem. Soc.*, **101**, 1595 (1979).
129. R. V. C. Carr and L. A. Paquette, *J. Amer. Chem. Soc.*, **102**, 853 (1980).
130. J.-M. Gaillot, Y. Gelas-Mialhe and R. Vessière, *Chem. Letters*, 1137 (1983).
131. Ying-Che Kuo, T. Aoyama and T. Shioiri, *Chem. Pharm. Bull.*, **31**, 883 (1983).
132. G. Sauer, K. Junghans, U. Eder, G. Haffer, G. Neef, R. Wiechert, G. Cleve and G.-A. Hoyer, *Liebigs Ann. Chem.*, 431 (1982).
133. L. A. Paquette, H. Kuenzer, K. E. Green, O. De Lucchi, G. Licini, L. Pasquato and G. Valle, *J. Amer. Chem. Soc.*, **108**, 3453 (1986).
134. E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).
135. H. Stetter and R. Hesse, *Monatsh. Chem.*, **98**, 755 (1967).
136. H. O. House and J. K. Larsen, *J. Org. Chem.*, **33**, 61 (1968).
137. K. Kondo and D. Tunemoto, *Tetrahedron Letters*, 1397 (1975).
138. S. Cavicchioli, D. Savoia, C. Trombini and A. Umani-Ronchi, *J. Org. Chem.*, **49**, 1246 (1984).
139. M. J. Kurth and M. J. O'Brien, *J. Org. Chem.*, **50**, 3846 (1985).
140. S. N. Suryawanshi and P. L. Fuchs, *J. Org. Chem.*, **51**, 902 (1986).
141. V. Pascali and A. Umani-Ronchi, *J. Chem. Soc., Chem. Commun.*, 351 (1973).
142. B. W. Metcalf and E. Bonilavri, *J. Chem. Soc., Chem. Commun.*, 914 (1978).
143. M. Inbasekaran, N. P. Peet, J. R. McCarthy and M. E. LeTourneau, *J. Chem. Soc., Chem. Commun.*, 678 (1985).
144. J. March, *Advanced Organic Chemistry*, 3rd ed., Wiley, New York, 1985, pp. 652, 653.
145. R. A. Grimm and W. A. Bonner, *J. Org. Chem.*, **32**, 3470 (1967).
146. H. Kotake, T. Yamamoto and H. Kinoshita, *Chem. Letters*, 1331 (1982).
147. M. Mohri, H. Kinoshita, K. Inomata and H. Kotake, *Chem. Letters*, 451 (1985).
148. K. Inomata, Y. Murata, H. Kato, Y. Tsukahara, H. Kinoshita and H. Kotake, *Chem. Letters*, 931 (1985).
149. R. O. Hutchins and K. Learn, *J. Org. Chem.*, **47**, 4380 (1982).
150. B. Koutek, L. Pavlíčková and M. Souček, *Coll. Czech. Chem. Commun.*, **39**, 192 (1974).
151. T. Yoshida and S. Saito, *Chem. Letters*, 165 (1982).
152. Ref. 144, p. 391.
153. Ref. 144, pp. 810, 1110.
154. J. G. de Vries and R. M. Kellogg, *J. Org. Chem.*, **45**, 4126 (1980).
155. M. Julia, M. Launay, J.-P. Stacino and J.-N. Verpeaux, *Tetrahedron Letters*, **23**, 2465 (1982).
156. J. Bremner, M. Julia, M. Launay and J.-P. Stacino, *Tetrahedron Letters*, **23**, 3265 (1982).
157. M. Julia and J.-P. Stacino, *Bull. Soc. Chim. Fr.*, 831 (1985).
158. A. Teder, *Acta Chem. Scand.*, **27**, 705 (1973).
159. A. K. Colter and R. E. Miller, Jr., *J. Org. Chem.*, **36**, 1898 (1971).
160. T. Mandai, K. Hara, T. Nakajima, M. Kawada and J. Otera, *Tetrahedron Letters*, **24**, 4993 (1983).
161. T. Mandai, T. Yanagi, K. Araki, Y. Morisaki, M. Kawada and J. Otera, *J. Amer. Chem. Soc.*, **106**, 3670 (1984).
162. T. Mandai, Y. Iuchi, K. Suzuki, M. Kawada and J. Otera, *Tetrahedron Letters*, **23**, 4721 (1982).
163. T. Mandai, K. Nishikawa, H. Yamaguchi, M. Kawada and J. Otera, *Chem. Letters*, 473 (1981).
164. P. R. Hamann and P. L. Fuchs, *J. Org. Chem.*, **48**, 914 (1983).
165. D. Arnould, P. Chabardes, G. Farge and M. Julia, *Bull. Soc. Chim. Fr.*, 130 (1985).
166. J. Otera, T. Mandai, M. Shiba, T. Saito, K. Shimohata, K. Takemori and Y. Kawasaki, *Organometallics*, **2**, 332 (1983).
167. P. Auvray, P. Knochel and J. F. Normant, *Tetrahedron Letters*, **26**, 2329 (1985).
168. O. de Lucchi and L. Pasquato, *Gazz. Chim. Ital.*, **114**, 349 (1984).
169. C. Fehr, *Helv. Chim. Acta*, **66**, 2519 (1983).
170. J.-B. Baudin, M. Julia and C. Rolando, *Tetrahedron Letters*, **26**, 2333 (1985).
171. W. E. Truce and W. W. Brand, *J. Org. Chem.*, **35**, 1828 (1970).
172. E. J. Madaj, Jr., D. M. Snyder and W. E. Truce, *J. Amer. Chem. Soc.*, **108**, 3466 (1986).

173. Y. Ueno, S. Aoki and M. Okawara, *J. Amer. Chem. Soc.*, **101**, 5414 (1979).
174. D. Neville Jones and M. R. Peel, *J. Chem. Soc., Chem. Commun.*, 216 (1986).
175. M. Ochiai, Shin-ichi Tada, K. Sumi and E. Fujita, *Tetrahedron Letters*, **23**, 2205 (1982).
176. M. Ochiai, T. Ukita and E. Fujita, *Tetrahedron Letters*, **24**, 4025 (1983).
177. M. Ochiai, T. Ukita, Y. Nagao and E. Fujita, *Nippon Kagaku Kaishi*, 339 (1985); *Chem. Abstr.*, **104**, 168 039j (1986).
178. M. Ochiai, T. Ukita and E. Fujita, *J. Chem. Soc., Chem. Commun.*, 619 (1983).
179. B. A. Pearlman, S. R. Putt and J. A. Fleming, *J. Org. Chem.*, **50**, 3625 (1985).
180. C.-N. Hsiao and H. Shechter, *Tetrahedron Letters*, **25**, 1219 (1984).
181. M. Julia, A. Righini and J.-N. Verpeaux, *Tetrahedron Letters*, 2393 (1979).
182. M. Julia, A. Righini-Tapie and J.-N. Verpeaux, *Tetrahedron*, **39**, 3283 (1983).
183. Y. Masaki, K. Sakuma and K. Kaji, *J. Chem. Soc., Perkin Trans. 1*, 1171 (1985).
184. M. Julia and J.-N. Verpeaux, *Tetrahedron*, **39**, 3289 (1983).
185. M. Julia and J.-N. Verpeaux, *Tetrahedron Letters*, **23**, 2457 (1982).
186. Ref. 144, p. 1112.
187. B. M. Trost and M. R. Ghadiri, *J. Amer. Chem. Soc.*, **108**, 1098 (1986).
188. E. C. Ashby, R. N. DePriest and T. N. Pham, *Tetrahedron Letters*, **24**, 2825 (1983).
189. A. Pross, *Acc. Chem. Res.*, **18**, 212 (1985).
190. Ref. 144, pp. 820, 821.
191. J.-L. Fabre and M. Julia, *Tetrahedron Letters*, **24**, 4311 (1983).
192. T. Cuvigny, J. L. Fabre, C. Hervé du Penhoat and M. Julia, *Tetrahedron Letters*, **24**, 4319 (1983).
193. J.-L. Fabre, M. Julia and J.-N. Verpeaux, *Tetrahedron Letters*, **23**, 2469 (1982).
194. J.-L. Fabre, M. Julia and J.-N. Verpeaux, *Bull. Soc. Chim. Fr.*, 762 (1985).
195. J.-L. Fabre, M. Julia and J.-N. Verpeaux, *Bull. Soc. Chim. Fr.*, 772 (1985).
196. J. J. Eisch, M. Behrooz and J. E. Galle, *Tetrahedron Letters*, **25**, 4851 (1984).
197. Y. Gaoni, *Tetrahedron Letters*, 4521 (1977).
198. H. C. Brown, Suk-Choong Kim and S. Krishnamurthy, *Organometallics*, **2**, 779 (1983).
199. R. E. Donaldson, J. C. Saddler, S. Byrn, A. T. McKenzie and P. L. Fuchs, *J. Org. Chem.*, **48**, 2167 (1983).
200. Y. Ueno, A. Kojima and M. Okawara, *Chem. Letters*, 2125 (1984).
201. B. M. Trost, J. Cossy and J. Burks, *J. Amer. Chem. Soc.*, **105**, 1052 (1983).
202. K. Tanaka, S. Matsui and A. Kaji, *Bull. Chem. Soc. Japan*, **53**, 3619 (1980).
203. R. D. Little and Sun Ok Myong, *Tetrahedron Letters*, **21**, 3339 (1980).
204. Jih Ru Hwu, *J. Org. Chem.*, **48**, 4432 (1983).
205. F. Vögtle and L. Rossa, *Angew. Chem., Int. Ed. Engl.*, **18**, 515 (1979).
206. M. Julia, D. Lavé, M. Mulhauser, M. Ramirez-Muñoz and D. Uguen, *Tetrahedron Letters*, **24**, 1783 (1983).
207. S. Yamada, T. Suzuki, H. Takayama, K. Miyamoto, I. Matsunaga and Y. Nawata, *J. Org. Chem.*, **48**, 3483 (1983).
208. R. S. Givens in *Organic Photochemistry*, Vol. 5 (Ed. A. Padwa), Dekker, New York, 1981, pp. 227–346.
209. R. S. Givens, R. J. Olsen and P. L. Wylie, *J. Org. Chem.*, **44**, 1608 (1979).
210. R. S. Givens, B. Hrinczenko, J. H.-S. Liu, B. Matuszewski and J. Tholen-Collison, *J. Amer. Chem. Soc.*, **106**, 1779 (1984).
211. I. R. Gould, Chen-ho Tung, N. J. Turro, R. S. Givens and B. Matuszewski, *J. Amer. Chem. Soc.*, **106**, 1789 (1984).
212. Ref. 48, pp. 330–389.
213. L. Horner and H. Neumann, *Chem. Ber.*, **98**, 1715 (1965).
214. F. Pragst and B. Kaltofen, *Electrochim. Acta*, **27**, 1181 (1982).
215. R. Kossai, *Electrochim. Acta*, **30**, 75 (1985).
216. A. Staško, L. Malik, A. Tkač and P. Pelikán, *Z. Phys. Chem. (Leipzig)*, **261**, 1205 (1980).
217. J. R. Babu and M. V. Bhatt, *Tetrahedron Letters*, **27**, 1073 (1986).
218. Ta-Shue Chou and Mei-Li You, *J. Org. Chem.*, **52**, 2224 (1987).
219. C. Hervé du Penhoat and M. Julia, *Tetrahedron*, **42**, 4807 (1986).
220. O. Louis-André and G. Gelbard, *Bull. Soc. Chim. Fr.*, 565 (1986).
221. M. Julia, H. Lauron, J.-P. Stacino, J.-N. Verpeaux, Y. Jeannin and Y. Dromzee, *Tetrahedron*, **42**, 2475 (1986).

222. T. Cuvigny, C. Hervé adu Penhoat and M. Julia, *Rec. Trav. Chim. Pays-Bas*, **105**, 409 (1986).
223. T. Cuvigny, C. Hervé du Penhoat and M. Julia, *Tetrahedron*, **43**, 859 (1987).
224. T. Cuvigny, C. Hervé du Penhoat and M. Julia, *Tetrahedron*, **42**, 5321 (1986).
225. G. Quinkert, N. Heim, J. Glenneberg, U.-M. Billhardt, V. Autze, J. W. Bats and G. Dürner, *Angew. Chem. Int. Ed. Engl.*, **26**, 362 (1987).
226. N. Nakamura, M. Fujii, H. Mekata, S. Oka and A. Ohno, *Chem. Letters*, **87** (1986).

CHAPTER **21**

Oxidation of sulphoxides and sulphones

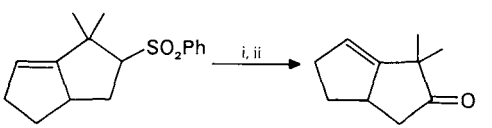
JEFFREY HOYLE

Chemistry-Soils Department, Nova Scotia Agricultural College, PO Box 550, Truro, Nova Scotia, Canada, B2N5E3

I. INTRODUCTION

The oxidation of organosulphur compounds containing a single sulphur atom attached directly to two carbon atoms has been studied by many workers for at least the last one hundred years. Such reactions may start from the sulphide functionality and proceed through the various stages to sulphate as shown in equation(1). The first step in this sequence has been covered in an earlier volume of this series[1] whilst the second, third and fourth steps, namely the oxidation of sulphoxides to sulphones, the oxidation of sulphones to sulphonic acids and the oxidation of sulphones to sulphate, will be covered in the present work. A few other oxidation reactions of sulphoxides and sulphones will also be covered, however these will not include the oxidative removal of the sulphur-containing functionality to produce carbonyl-containing compounds. These latter reactions may be carried out using a wide range of reaction conditions using rather expensive and exotic oxidizing reagents such as a molybdenum peroxide complex[2] (equation 2) and bis(trimethylsilyl)peroxide[3] (equation 3).

$$RSR' \xrightarrow{ox} R\overset{\overset{O}{\|}}{S}R' \xrightarrow{ox} R\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}R' \xrightarrow{ox} RSO_3H \xrightarrow{ox} SO_4^{2-} \qquad (1)$$



(2)

(i) LDA, THF (ii) $MoO_5 \cdot py \cdot HMPA$, $-78\,^{\circ}C$

$$RR'CHSO_2Ph \xrightarrow{i,\,ii} RR'C{=}O + PhSO_2Li \qquad (3)$$

(i) BuLi, THF (ii) $Me_3SiOOSiMe_3$

The oxidation of disulphide species with at least one sulphur atom at the sulphoxide oxidation level will also be covered briefly.

The chapter covers material presented in the literature up to the end of December 1985.

II. OXIDATION OF SULPHOXIDES

The oxidation of sulphoxides usually leads to the formation of sulphones, although under vigorous conditions the sulphonic acid or sulphate may result (see equation 1). Procedures involving a wide range of oxidizing agents are well established and these will be discussed in the present work together with the extensive kinetic data available for these reactions. In addition the oxidation of sulphoxides to sulphoximines will be covered briefly.

A. General Methods of Preparation of Sulphones from Sulphoxides

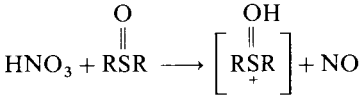
1. Nitrogen oxides and nitric acid

Nitric acid is one of the most common, and cheaper, oxidants used in organic chemistry. It will oxidize sulphoxides to sulphones in good yields if heated under reflux for several

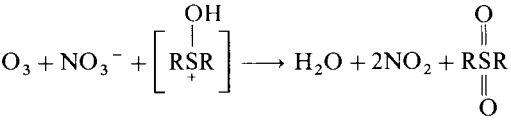
hours which should be contrasted with the mild conditions required with this reagent to oxidize a sulphide to the corresponding sulphoxide[1].

The earliest reported, successful use of nitric acid for this purpose was in the oxidation of dimethyl sulphoxide to dimethyl sulphone[4]. This was followed much later by the conversion of dibutyl sulphoxide to the corresponding sulphone. The latter reaction was performed under reflux using a large excess of fuming nitric acid, giving the product in about 60% yield[5]. The same workers reported a very low yield if nitrogen dioxide was used in place of the acid. Previous workers[6–8] had reported only failure when attempting to use these two reagents.

Goheen and Bennett[9] showed that regular nitric acid could be used, in about two molar excess, for the oxidation of dimethyl sulphoxide to dimethyl sulphone in 86% yield. The reaction temperature was 120–150 °C with a reaction time of about 4 hours. The mechanism for this reaction was postulated to involve initially a protonated sulphoxide species (which has been shown to be present in other strongly acidic systems[10,11]) followed by nucleophilic attack by nitrate, and the loss of nitrogen dioxide as shown in equations (4) and (5).

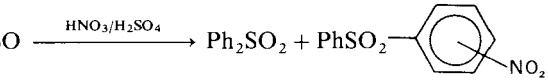


(4)



(5)

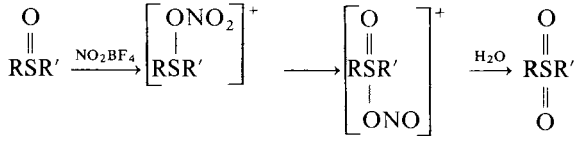
The oxidation of sulphoxides containing aromatic groups such as methyl phenyl sulphoxide and diphenyl sulphoxide proceeds at 20–30 °C in low yields in the presence of sulphuric acid as solvent[12]. However the product is usually contaminated with compounds containing nitro groups in the aromatic nucleus, as indicated in equation (6).



(6)

If acetic anhydride is employed in place of the sulphuric acid, only the sulphone is formed[12,13] whilst if nitroethane or acetic acid are employed, no oxidation at sulphur occurs. A patent has been secured for the industrial oxidation of dimethyl sulphoxide to the sulphone with nitric acid[14]. This procedure yielded 84% of the sulphone in a continuous process which was prone to detonation at water concentrations below 14%.

Oxidation of either alkyl or aryl sulphoxides to sulphones in 65–90% yields may be accomplished by treatment with a nitronium salt[15]. In the case of aryl sulphoxides no nitration is observed (which is in contrast to the results of nitric acid oxidation). The reaction was shown to proceed through intermediate nitratosulphonium and nitritosulphoxonium ions, as depicted in equation (7), which were studied by nmr spectroscopy.



(7)

Tertiary amine N-oxides may also be used to convert sulphoxides to sulphones[16]. The reaction proceeds by initial attack by the N-oxide oxygen atom on the sulphoxide moiety, followed by subsequent elimination of the amine. In order to obtain good yields, the reaction must be carried out at 190 °C for 20 hours with a 20-fold excess of N-oxide in the presence of acid catalysts. The sulphone must then be separated by chromatography, thus making the method less attractive than other procedures and so it has not been employed synthetically.

2. *Oxygen and ozone*

Oxygen, in the air, is probably the cheapest, most readily available oxidant and so it is not suprising that industrial processes using this reagent for the oxidation of sulphoxides has been patented. These procedures involve the use of transition metal ion catalysts[17–20] in solvents containing acetic acid[17], acetone[18,19,21] and carboxylic acids[18,19].

A more elegant, but expensive, approach[22] has been the use of soluble iridium and rhodium catalysts which contain coordinated dimethyl sulphoxide (e.g. $IrHCl_2(Me_2SO)_3$) which promote the oxidation of sulphoxides in aqueous media, equation (8). The ease of oxidation depends on the substituents and this decreases in the order Me > Ph > $PhCH_2$. This reaction is especially useful since sulphides are not oxidized under the reaction conditions due to the formation of strong complexes with the catalyst.

$$R_2SO + \tfrac{1}{2}O_2 \xrightarrow{IrHCl_2(MeSO)_3} R_2SO_2 \qquad (8)$$

R = Me, Ph, $PhCH_2$

Photochemical irradiation of dimethyl and diethyl sulphoxides yields the corresponding sulphone in the presence of air and a photosensitizer such as methylene blue in yields up to 99%[23]. Sulphoxides are also oxidized when they act as traps for persulphoxides, the intermediate formed on reaction of a sulphide with photochemically generated singlet oxygen[24,25,26], equation (9). Isotope studies have shown that such reactions proceed through a linear sulphurane intermediate[26]. Persulphones also react with sulphoxides in a similar manner[25], equation (10).

$$R_2S + {}^1O_2 \longrightarrow R_2\overset{+}{S}OO^- \xrightarrow{Ph_2SO} \left[R_2\overset{+}{S}OOS(O^-)Ph_2\right] \longrightarrow R_2SO + Ph_2SO_2 \qquad (9)$$

$$R_2\overset{+}{S}OO^- + R'_2SO \longrightarrow \left[R_2\overset{+}{S}(=O)OSR'_2(=O)\right] \longrightarrow R_2SO_2 + R'_2SO_2 \qquad (10)$$

Little work has been reported on the oxidation of sulphoxides using ozone, one notable exception being the nearly quantitative reaction producing the sulphone in chloroform solution at 0 °C[27].

3. *Hydrogen peroxide*

As an oxidant, hydrogen peroxide may be used either alone or in the presence of a catalyst. Such reactions are often carried out using acetic acid as a solvent. These latter reactions strictly involve oxidation by peracetic acid and will be dealt with in the next section.

Hydrogen peroxide was used to oxidize sulphoxides to sulphones at an early stage in the development of organosulphur chemistry[28] and has remained the reagent of choice for everyday laboratory oxidations of this type. Typically, an excess of 30% hydrogen peroxide in water is employed at room temperature, often with a co-solvent such as an alcohol or acetone.

Slight variations of this method using reflux temperatures[29–31] and a foam-emulsion system[30] have been used industrially since the oxidant is cheap and readily available and yields are usually above 70%.

Sulphilimines (the nitrogen analogues of sulphoxides) may also be oxidized using hydrogen peroxide. In this case a sulphoximine (a nitrogen analogue of a sulphone) is produced in good yields[32], as shown in equation (11).

$$\begin{array}{c} \text{NTs} \\ \| \\ \text{RSR}' \end{array} \xrightarrow{H_2O_2} \begin{array}{c} \text{NTs} \\ \| \\ \text{RSR}' \\ \| \\ \text{O} \end{array} \qquad (11)$$

In the presence of metal catalysts, hydrogen peroxide oxidations proceed in improved yields. The most common catalyst is an iron(II) salt which produces the well-known Fenton system or reagent. Dimethyl sulphoxide is oxidized to the sulphone using this system although a range of unwanted side-products such as methanol and methane are produced[33]. Diphenyl sulphoxide does not react using this reagent due to its insolubility and in all cases some iron(III) is formed by other side-reactions.

If a dilute solution of hydrogen peroxide in dry acetonitrile is added to a solution of a sulphoxide and an iron(II) salt in dry acetonitrile then the sulphone is produced in quantitative yield[34]. This latter reaction works equally well for aliphatic and aromatic sulphoxides and is thought to involve oxygen transfer by the reaction of a ferryl ion with the sulphoxide, as shown in equation (12).

$$\begin{aligned} Fe^{2+} + H_2O_2 &\longrightarrow FeO^{2+} + H_2O \\ FeO^{2+} + R_2SO &\longrightarrow R_2SO_2 + Fe^{2+} \end{aligned} \qquad (12)$$

Iron(III) salts also activate the oxidation of sulphoxides by hydrogen peroxide in dry acetonitrile although the yields are typically lower than for the iron(II) system[35]. With iron(III) salts the hydrogen peroxide seems to be activated by direct complexation between the metal ion and the peroxide moiety.

Sodium tungstate has also been used as a catalyst in the oxidation of dimethyl sulphoxide to the sulphone[36]. The kinetics of this reaction have been studied in great detail and it has been shown that oxygen transfer to the sulphoxide takes place via two peroxytungstic acid species (HWO_5^- and HWO_8^-).

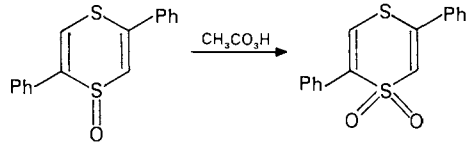
4. Hydroperoxides and peroxy acids

The great utility of hydrogen peroxide as a reagent for the conversion of sulphoxides to sulphones spurred the investigation of other peroxy-containing compounds. Probably the most commonly used species is peracetic acid which is formed by the reaction of acetic acid with hydrogen peroxide. In addition, other peroxy acids such as pertrifluoroacetic acid and *m*-chloroperbenzoic acid and hydroperoxides and hydrotrioxides are often used to convert sulphoxides to sulphones.

An early study of the oxidation of diphenyl sulphoxide to the sulphone[37] compared the rate for this reaction with that of the oxidation of the corresponding sulphide to the sulphoxide. The former reaction was shown to proceed approximately 200 times slower

than the latter. This evidence showed that the peracid was acting as an electrophile and that the reduced nucleophilicity of the sulphoxide moiety, compared to that of the sulphide, caused the observed rate phenomenon. A further study of this reaction[38] showed that the reaction was second order and acid catalysed. In the presence of metal ions and metal ion complexes such as $Mn(acac)_3$, peracid oxidations proceed in nearly quantitative yield[39].

Peracetic acid oxidation of 2,5-diphenyl-1,4-dithiadiene-1-oxide produces 2,5-diphenyl-1,4-dithiadiene-1,1-dioxide in 72% yield without reaction with the sulphide sulphur atom[40] (equation 13). This is rather surprising given the earlier evidence concerning relative rates[37].

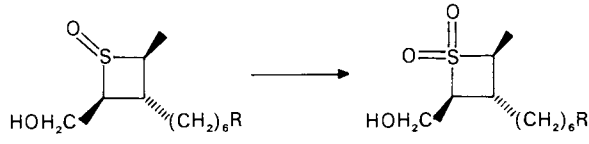


(13)

Peracetic acid can be used to preferentially oxidize sulphoxides to sulphones in the presence of hydroxyl groups[41], whilst attempted peracid oxidation of 2,6-diiodoaryl sulphoxides was not successful[42].

Pertrifluoroacetic acid has also been used for the oxidation of sulphoxides[43,44]. Typically the reactions are more rapid at lower temperatures compared to other peroxy acids and so this reagent is often the one chosen when other sensitive functional groups are present. For example, if the oxidation of a sulphoxide, with an amino group, to the corresponding sulphone is required then neat pertrifluoroacetic acid is used. In this case the amine group is protected by protonation by the extremely acidic medium and is easily deprotected after the oxidation is complete. Another advantage of the use of pertrifluoroacetic acid is the ease with which the by-product, trifluoroacetic acid, can be removed. Simple evaporation is all that is required, although it is imperative that all peroxides are first removed in order to avoid the possibility of explosions. Olefinic groups are also unaffected by this reagent[44].

In a synthetic sequence involving thietanoprostanoids[45], peroxydodecanoic acid was successfully used to oxidize a hydroxysulphoxide to the corresponding hydroxysulphone (equation 14). The use of pertrifluoroacetic acid in this case apparently produced unidentifiable products.



(14)

Peracetic acid specifically labelled with oxygen-18 has been used for the oxidation of (+)-benzyl-*p*-tolyl sulphoxide to the (−)-[$^{16}O^{18}O$]sulphone[46] (equation 15). The reaction gives the required enantiomer in no less than 80% yield.

$$CH_3C^{16}O^{18}O_2H + RR^1S^{16}O \longrightarrow RR^1S^{16}O^{18}O \qquad (15)$$

Optically active peracids such as percamphoric acid have been used to oxidize selectively one sulphoxide enantiomer in a racemic mixture. These reactions involve the use of 0.5 molar equivalents of the peracid in either ether[47] or chloroform[48] as solvent. The presence of nitro groups causes the oxidant to be consumed without oxidation of the sulphoxide functionality. This method is usually used to obtain an optically active sulphoxide by recovery of the unreacted material after oxidation.

Aromatic peracids are frequently used for the oxidation of sulphoxides to sulphones. The most common peracids of this type are perbenzoic acid and *meta*-chloroperbenzoic acid, although many others have been employed.

Peroxybenzoic acid readily oxidizes aryl and alkyl sulphoxides in acetone, methylene chloride or chloroform solutions, to the sulphone in high yield[38,49]. The reaction is second order and acid catalysed as is the reaction with peracetic acid[38]. The rate of oxidation is about five times faster than when peracetic acid is used. Other work considering the oxidation of sulphoxides with peracids[50] gathered kinetic evidence and showed that the reaction was indeed second order and that the reaction involved nucleophilic attack by the sulphoxide sulphur atom on the peracid moiety. A further study by the same authors[51] showed that with benzyl and phenyl alkyl sulphoxides the rate of reaction was very sensitive to the inductive effect of the alkyl group. Support for the nucleophilic attack by the sulphur atom on the peracid in acidic solution was forthcoming from other sources[52,53].

In contrast, the reaction mechanism in alkaline solution was shown to occur by nucleophilic attack by the anion of the peracid on the sulphoxide group[53]. Thus two different mechanisms seem to operate for the oxidation of sulphoxides to sulphones with peracids. At pH < 7 the sulphoxide acts as the nucleophile whilst at pH > 10 the peracid anion is the nucleophilic species. Presumably at intermediate pH values both mechanisms are operable.

It is interesting to note that the oxidation of sulphoxides by peracids is faster in alkaline than in acidic solution. This is in contrast to the oxidation of sulphides and amines with the same reagents[54,55]. The oxidation rate of *ortho*-substituted aryl alkyl sulphoxides with aromatic peracids is less than the corresponding *meta*- and *para*-substituted species due to steric hindrance of the incoming peracid anion nucleophiles[56]. Steric bulk in the alkyl group also has some effect[57]. Such hindrance is not nearly so important in the oxidation reaction carried out under acidic conditions[58].

Electron-donating groups in the *para* position of the perbenzoic acid tend to decrease the rate of reaction[59]. The reverse seems to be true when these groups are present in a 4,4′-disubstituted diaryl sulphoxide. The effect of ring size on the oxidation of cyclic sulphoxides is apparently very small in dioxane–water solution under either acidic or basic conditions[60]. This suggests that no major hybridisation change occurs for the sulphur atom in going to the transition state.

The reaction for the oxidation of sulphoxides by peracids in an alkaline medium is probably best described as shown in equation (16). Here the addition step is usually much slower than the latter step due to the low O—O bond energy which allows easy bond fission. For the reaction in acidic media, equation (17) is probably a good representation.

$$RCO_3^- + R'R''SO \rightleftharpoons \left[RCO_2OSO^- \begin{matrix} R' \\ | \\ R'' \end{matrix} \right] \longrightarrow RCO_2^- + R'R''SO_2 \qquad (16)$$

$$RCO_3^- + R'R''SO \rightleftharpoons RCO_2^- + \left[R'R''SO_2H \right] \qquad (17)$$

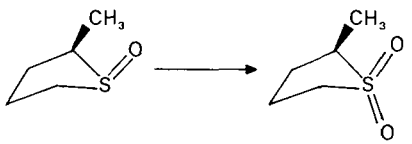
$$\downarrow$$

$$RCO_2H + R'R''SO_2$$

Solvents have also been shown to play a role in the reaction mechanism in acidic solution, although there is no marked effect related to the dielectric constant of the solvent.

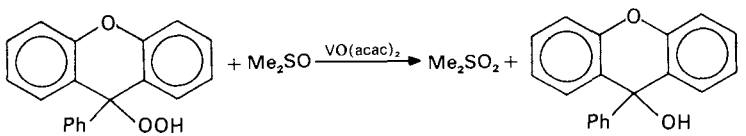
Instead, particular solvents interact rather specifically with the reactants and the transition state by intra- and intermolecular hydrogen bonding[61,62].

It has been noted[63] that in competitive reactions of thiolane-1-oxides, the *cis* sulphoxide, is oxidized somewhat quicker by peracids than the *trans* isomer (equation 18). This observation is presumably due to the greater accessibility of the electron pair for electrophilic attack in the *cis* species.



(18)

Organic hydroperoxides have also been used for the oxidation of sulphoxides to sulphones. The reaction in neutral solution occurs at a reasonable rate in the presence of transition metal ion catalysts such as vanadium, molybdenum and titanium[64,65], but does not occur in aqueous media[57,58,66,67]. The usual reaction conditions involve dissolution of the sulphoxide in alcohols, ethers or benzene followed by dropwise addition of the hydroperoxide at temperatures of 50–80 °C. By this method dimethyl sulphoxide and methyl phenyl sulphoxide have been oxidized to the corresponding sulphone in greater than 90% yields[64]. A similar method for the oxidation of sulphoxides has been patented[68]. Unsaturated sulphoxides are oxidized to the sulphone without affecting the carbon–carbon double bonds. A further patent has also been obtained for the reaction of dimethyl sulphoxide with an organic hydroperoxide[69] as shown in equation (19).



(19)

Anions of hydroperoxides may be used to successfully obtain sulphones by the oxidation of sulphoxides in non-aqueous media, without the use of transition metal catalysts. This is in contrast to oxidations with peracids where aqueous media are invariably used. Thus, dimethyl sulphoxide was oxidized by the anion of cumene hydroperoxide in ethanol or benzene solution at room temperature in 90% yield[66]. The yield is very much dependent on the base used and decreases along the series:

$$t\text{-BuONa} > \text{NaOH} \gg \text{Na}_2\text{CO}_3,\ \text{MeCO}_2\text{Na}$$

Under acidic conditions, no oxidation occurs but the hydroperoxide is decomposed by an acid catalysed mechanism.

A mechanistic study[65] of the reaction of sulphoxides with the sodium salt of 1-methyl-1-phenylethyl hydroperoxide in benzene-alcohol solutions at room temperature showed that the reaction is first order with respect to sulphoxide and the hydroperoxide salt. The rate was also shown to be inversely proportional to the alcohol concentration in the solvent and this dependence was shown to increase with increasing pH. Also, more sterically crowded alcohols caused a decreased rate of reaction.

The pH dependence of the rate suggests that nucleophilic attack by the sulphur atom of the sulphoxide on the undissociated hydroperoxide is unimportant while nucleophilic attack by the hydroperoxide anion on the sulphoxide is the preferred reaction under these conditions. Changing the alkyl substituent of the sulphoxide had little effect on the rate and thus the reaction probably proceeds in a similar manner as for oxidation by peracids

in alkaline media as described above. Equation (20) shows the mechanism for oxidation of sulphoxides by hydroperoxide anions. In this case the second step, the cleavage of the O—O bond, is probably the rate-determining step, in contrast to the reaction involving peracids. The hydroperoxide anion is a much better nucleophile than the peroxy acid anion and the alkoxide ion is not as good a leaving group as the benzoate or acetate ions.

$$ROO^- + R'R''SO \rightleftharpoons \left[ROO-\underset{\displaystyle R''}{\overset{\displaystyle R'}{\overset{|}{\underset{|}{S}}}}=O \right] \longrightarrow RO^- + R'R''SO_2 \qquad (20)$$

A similar study of the oxidation of sulphoxides by potassium *tert*-butyl hydroperoxide found similar results[70].

Organic hydrotrioxides (formed by the low temperature ozonization of aldehydes, ethers and alcohols[71,72]), in 3–5 molar excess, have been used to convert dialkyl sulphoxides into the corresponding sulphones in good yield at -78 to $-50\,^{\circ}C$[73]. The yield of sulphone decreases with increasing temperature.

Carbonyl oxides (formed by the reaction of diazo compounds with singlet oxygen) may also be used to oxidize sulphoxides[74]. The corresponding sulphone is formed in reasonable yields and the reaction may be carried out in the presence of the sulphide functionality. The reaction proceeds as shown in equation (21) and involves initial nucleophilic attack by the carbonyl oxide on the sulphoxide sulphur atom followed by the facile departure of the carbonyl compound yielding the required sulphone.

$$R_2\overset{+}{C}OO^- + \begin{matrix} R' \\ \diagdown \\ R'' \diagup \end{matrix} S=O \longrightarrow R_2\overset{+}{C}OO-\underset{\displaystyle R''}{\overset{\displaystyle R'}{\overset{|}{\underset{|}{S}}}}-O^- \longrightarrow R_2C=O + R'R''SO_2 \qquad (21)$$

Solutions of potassium superoxide–crown ether in dimethyl sulphoxide have been shown to cause oxidation of the solvent to the sulphone[75]; such a reaction could possibly be used synthetically. In the presence of water the reaction probably proceeds as shown:

$$\begin{aligned} 2O_2^- + H_2O &\longrightarrow HO_2^- + OH^- + O_2 \\ HO_2^- + Me_2SO &\longrightarrow OH^- + Me_2SO_2 \end{aligned} \qquad (22)$$

The phosphorus-containing peroxy species obtained on reaction of potassium superoxide with diethylchlorophosphate, as shown in equation (23), has also been used to prepare sulphones from sulphoxides[76] at 20 °C in reasonable yields.

$$(EtO)_2\overset{\displaystyle O}{\overset{\|}{P}}Cl + KO_2 \xrightarrow[MeCN]{\text{18-crown-6}} (EtO)_2\overset{\displaystyle O}{\overset{\|}{P}}OO^- \qquad (23)$$

5. Inorganic phosphorus- and sulphur-containing peroxy species

Peroxomonophosphoric acid and peroxodiphosphoric acid have both been used to oxidize sulphoxides to sulphones.

Peroxomonophosphoric acid (PMPA) oxidizes dimethyl sulphoxide in high yield in water[77,78] and aqueous ethanol[79]. In neutral solution the reaction mechanism was thought to be very complex but actually occurs by two different mechanisms that are very similar to those for sulphoxide oxidation by peracids in acidic and basic media. In an alkaline medium the mechanism involves nucleophilic attack by a phosphorus-containing species (probably PO_5^{3-}) on the sulphur atom of the sulphoxide, followed by O—O bond scission yielding the sulphone (equation 24). In acidic solution, on the other hand, the sulphoxide is the nucleophilic species as detailed in equation (25). It should be noted however that there is some evidence that these mechanisms are oversimplified since there are other nucleophilic species (such as $H_2PO_5^-$ and HPO_5^{2-}) present in aqueous solutions of PMPA over a wide pH range[78].

$$PO_5^{3-} + Me_2SO \longrightarrow \left[O_3POO-\underset{\displaystyle Me}{\overset{\displaystyle Me}{\overset{|}{\underset{|}{S}}}}=O \right]^{3-} \longrightarrow PO_4^{3-} + Me_2SO_2 \qquad (24)$$

$$H_2O_3POOH + Me_2SO \longrightarrow H_2O_3PO^- + \left[HO-\underset{\displaystyle Me}{\overset{\displaystyle Me}{\overset{|}{\underset{|}{S}}}}=O \right]^{+} \longrightarrow H_3PO_4 + Me_2SO_2 \qquad (25)$$

Peroxodiphosphoric acid (PDPA) may also be used to convert sulphoxides to sulphones in good yields. An initial study of this reaction[80] concluded that the mechanism was a free radical process, involving the reaction of a hydroxyl radical with the sulphoxide as shown in equation (26). This was later claimed to be incorrect; the reaction actually occurs by the initial decomposition of PDPA to PMPA which then reacts as described above[81].

$$\begin{aligned} H_3P_2O_8^- &\longrightarrow H_2PO_4^{\bullet} + HPO_4^{\bullet} \\ H_2PO_4^{\bullet} + H_2O &\longrightarrow H_3PO_4 + HO^{\bullet} \\ HO^{\bullet} + Me_2SO &\longrightarrow Me_2SO^{+\bullet} + OH^- \\ H_2PO_4^{\bullet} + Me_2SO &\longrightarrow Me_2SO^{+\bullet} + H_2PO_4^- \\ Me_2SO^{+\bullet} + OH^{\bullet} &\longrightarrow Me_2SO_2 + H^+ \end{aligned} \qquad (26)$$

Peroxomonosulphate and peroxodisulphate have also been used to oxidize sulphoxides to sulphones in good yields at room temperature. Potassium persulphate ($KHSO_5$) readily oxidizes a range of sulphoxides to sulphones at 0 °C in yields greater than 90%, in the presence of hydroxy, keto and alkene groups[82–84]. The mechanism is similar to that observed for other peroxy species, as discussed above. Peroxomonosulphate oxidation has been used as an analytical procedure for the estimation of dimethyl sulphoxide[84].

Potassium peroxodisulphate ($K_2S_2O_8$) also oxidizes sulphoxides to sulphones in high yield, either by catalysis with silver(I) or copper(II) salts at room temperature[85] or in pH 8 buffer at 60–80 °C[86–88]. The latter conditions have been the subject of a kinetic study, and of the five mechanisms suggested, one has been shown to fit the experimental data best. Thus, the reaction involves the heterolytic cleavage of the peroxodisulphate to 'sulphur

tetroxide' which then further reacts, as shown in equation (27).

$$S_2O_8^{2-} \rightleftharpoons SO_4^{2-} + \left[\overset{+}{O}—SO_3^-\right] \xrightarrow{R_2SO} \left[R_2\overset{+}{S}(=O)—O—SO_3^-\right] \xrightarrow{H_2O} R_2SO_2 + HSO_4^- + H_3O^+ \quad (27)$$

6. Chlorine-containing reagents

A wide range of chlorine-containing oxidants have been used for the preparation of sulphones from sulphoxides. These reagents include chlorine, hypochlorites, sulphuryl chloride and *N*-chloro compounds.

The use of chlorine as an oxidizing agent for the conversion of sulphoxides into sulphones is completely unsuccessful under anhydrous conditions. In aqueous solutions, the sulphone is formed but this is usually part of a complex mixture of chlorinated sulphoxides, chlorinated sulphones and sulphonyl chlorides[89], so that the reaction is usually not very useful as a preparative method for alkyl sulphones. Dimethyl sulphone has however been obtained in 70% yield in one isolated case[90]. In methanol solution dibenzyl sulphoxide is cleanly oxidized to dibenzyl sulphone and benzyl sulphonyl chloride in reasonable overall yield[91].

A study of the chlorine oxidation of 2-hydroxyethyl octyl sulphoxide[92] (equation 28) showed that a cyclic intermediate is probably involved in the process which gives the sulphone in good yield. Labelling studies have shown that the hydroxyl group is replaced by a chlorine atom whilst the hydroxyl oxygen atom is transferred to the sulphur atom. A similar result was obtained for 3-hydroxypropyl and 4-hydroxybutyl alkyl sulphoxides[93].

$$C_8H_{17}SOCH_2CH_2OH \xrightarrow{Cl_2/H_2O} C_8H_{17}SO_2CH_2CH_2Cl \quad (28)$$

Oxidative chlorination of diaryl sulphoxides with chlorine is generally much more useful than for alkyl-containing substrates. The sulphone is obtained cleanly, with no (or little) halogenation[94]. The rate of reaction is first-order with respect to both the sulphoxide and chlorine and has an order of minus one with respect to chloride ion. This is consistent with the mechanism given in equation (29).

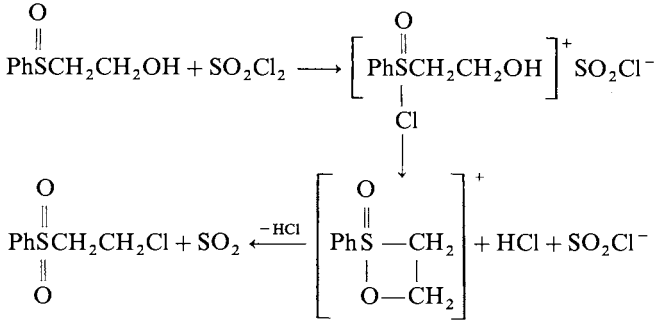
$$R_2SO + Cl_2 \rightleftharpoons Cl^- + \left[R_2SOCl\right]^+ \xrightarrow{H_2O} R_2SO_2 + Cl^- + 2H^+ \quad (29)$$

Both inorganic and organic hypochlorites may be used for the oxidation of sulphoxides. The cheapest method involves the use of a commercial bleach, such as Chlorox®. Such a method is indeed successful for unsaturated sulphoxides[95] such as allyl methyl sulphoxide although the yields are generally low. Other sulphoxides may also be oxidized by this method, for example, dimethyl sulphoxide gave bis(trichloromethyl) sulphone in low yield[96,97]. In some cases bis(dichloromethyl) sulphone was also isolated in very low yield. This oxidation procedure is also commonly used by organosulphur chemists for the removal of unwanted odours, caused by sulphoxides (and sulphides), from dirty glassware.

The reaction of dimethyl sulphoxide with *t*-butyl hypochlorite initially yields trichloromethyl methyl sulphone but further reactions, involving C—S bond cleavage, occur on prolonged contact of the two reagents[98,99].

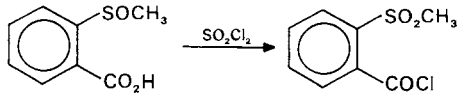
Sulphoxides containing a β, γ, or δ-hydroxyl group are readily converted to the

sulphone by reaction with sulphuryl chloride in methylene chloride at 0 °C. The reaction also involves concomitant replacement of the hydroxyl group with a chlorine atom[100,101]. The reaction proceeds via a cyclic alkoxyoxosulphonium ion as exemplified in equation (30). With α-, ε- and further removed hydroxyl groups no oxidation of the sulphoxide moiety was evident[101].



(30)

Sulphoxides with β-carboxylic acid or amide groups are converted, in nearly quantitative yields, to the sulphone whilst other acids and amides did not show oxidation. In the cases where oxidation did occur, the acid group was converted to the acid chloride (equation 31) whilst the amide was converted to the nitrile (equation 32). These results indicate that neighbouring-group participation in the case of carboxylic acids and amides occurs only when a five-membered intermediate is formed. In the case of hydroxyl groups, four-, five- or six-membered intermediates are favourable.



(31)

$$PhSOCH_2CH_2CONH_2 \xrightarrow{SO_2Cl_2} PhSO_2CH_2CH_2CN \qquad (32)$$

Sulphoxides with β-carboxylic acid groups are also converted to the corresponding sulphone by oxidation with (dichloroiodo)benzene (DCIB), which is a source of electrophilic chlorine[102]. In this reaction the free acid group remains in the product.

In aqueous pyridine solution, most diaryl sulphoxides may be oxidized to the corresponding sulphones with (dichloroiodo)benzene in reasonable yields[103]. The reaction involves nucleophilic attack by the sulphoxide on the electrophilic chlorine-containing species, yielding an intermediate chlorosulphonium ion which then reacts with water producing the sulphone. If the sulphoxide is optically active, then an optically active sulphone is produced in excellent optical yield when the reaction is carried out in oxygen-18 labelled water[104], as indicated in equation (33).

$$ArAr'SO + H_2O^* \xrightarrow{DCIB} ArAr'SOO^* \qquad (33)$$

N-chloro compounds have also been used for the preparation of sulphones from sulphoxides. *N*-chlorosuccinimide(NCS) oxidizes sulphoxides in aqueous acetic acid and acetic acid–perchloric acid mixtures. In purely aqueous media, the reaction is very slow and marked decomposition of the NCS occurs with no oxidation being evident[105].

Oxidation of racemic sulphoxides with an optically active *N*-chloro caprolactam derivative produces a good yield of the corresponding sulphone. The utility of this reaction, however, is that one enantiomer of the sulphoxide is left unreacted and so can be isolated in pure form[106].

Chloramine-B (CAB, $PhSO_2NClNa$) and chloramine-T (CAT, *p*-Me-$C_6H_4SO_2NClNa$) have also been used for the oxidation of sulphoxides[107–115]. The required sulphone is produced after initial attack by the sulphoxide sulphur atom on the electrophilic chlorine-containing species, forming a chlorosulphonium intermediate as shown in equation (34). These reactions take place at room temperature, in water and aqueous polar solvents such as alcohols and dioxane, in both acidic and basic media. In alkaline solution the reaction is slow and the rate is considerably enhanced by the use of osmium tetroxide as a catalyst[115].

$$\begin{array}{l} R_2SO + R'NHCl \longrightarrow R_2SO^+ + R'NH^- \\ \quad (CAB, CAT) \qquad\quad | \qquad\quad | \\ \qquad\qquad\quad\ Cl \qquad\quad \downarrow_{H_2O} \\ \qquad\qquad\quad\ R_2SO_2 + R'NH_3Cl \end{array} \tag{34}$$

7. Bromine-containing reagents

Oxidation of sulphoxides to sulphones may be brought about by the use of several different bromine-containing reagents which act as a source of electrophilic bromine. To date, these reagents have not received the same attention as their chlorine analogues.

The first report of the use of bromine for the oxidation of sulphoxides appeared in 1966[116]. Diphenyl sulphone was isolated in 0.5–1% yield when the sulphoxide was treated with bromine in aqueous acetic acid for several hours. The yield was increased to about 5% by quenching the reaction with sodium carbonate. A kinetic study[117] of a similar reaction involving dimethyl sulphoxide showed no significant yield improvement but postulated that the mechanism proceeds via an equilibrium step forming a bromosulphonium type intermediate which reacted slowly with water giving dimethyl sulphone as indicated in equation (35).

$$Br_2 + Me_2SO \rightleftharpoons Br^- + Me_2\overset{+}{S}(O)Br \xrightarrow{H_2O} Me_2SO_2 + 2H^+ + 2Br^- \tag{35}$$

A synthetically useful reaction has been reported between alkaline bromine water and dimethyl sulphoxide[118], the product being the perbromosulphone (equation 36). A kinetic study of the oxidation of dimethyl sulphoxide by bromate ions, catalysed by ruthenium(III) salts, has also been published but no yield data are available[119].

$$CH_3SOCH_3 \xrightarrow[NaOH]{Br_2} CBr_3SO_2CBr_3 \tag{36}$$

Hypobromite has also been used as a sulphoxide oxidant. In this case, as with hypochlorite, multi-halogenated species are usually found. Thus, treatment of ethyl methyl sulphone with a basic aqueous hypobromite solution at 45 °C yielded the product shown in equation (37) in high yield[97]. In the presence of α-carboxylate groups, C—C bond cleavage occurs[96] (equation 38).

$$CH_3CH_2SOCH_3 + OBr^- \xrightarrow{OH^-} CH_3CBr_2SO_2CBr_3 \tag{37}$$

$$RSOCH_2CO_2Na \xrightarrow[base]{NaOBr} RSO_2CBr_3 \tag{38}$$

As with chlorine-containing oxidants, *N*-bromo species have been used to oxidize sulphoxides to sulphones (with no bromine incorporation) through the initial formation of a bromosulphonium ion, by nucleophilic attack of the sulphoxide sulphur atom on the electrophilic halogen atom. Such reactions involve *N*-bromosuccinimide[120,121], bromamine-T[122], *N*-bromoacetamide[105] and *N*-bromobenzenesulphonamide[123]. All reported studies were of a kinetic nature and yields were not quoted. In acid solution all oxidations occurred at or around room temperature with the nucleophilic attack on the electrophilic bromine atom being the rate-limiting step. In alkaline solution a catalyst such as osmium tetroxide is required for the reaction to proceed[122,123].

8. *Iodine-containing reagents*

These oxidants have been used rarely. The kinetics of periodate oxidation of sulphoxides have been studied[119,124]. In an acid medium the reaction proceeds without catalysis but in alkali a catalyst such as an osmium(VIII) or ruthenium(III) salt is required[124]. Iodosylbenzene derivatives have also been used for the oxidation of sulphoxides to the sulphone level[94,125] (equation 39). In order to use this reaction for the synthesis of sulphones, a ruthenium(III) complex should be used as a catalyst; thus quantitative yields are obtained at room temperature in a few minutes. However, column chromatography is required to separate the sulphone from the other products of the reaction.

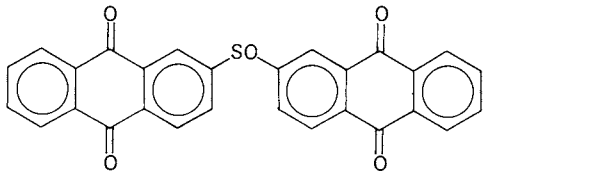
$$\mathrm{PhSOMe + PhIO} \xrightarrow{\mathrm{RuCl_3(PPh_3)_3}} \mathrm{PhSO_2Me} \tag{39}$$

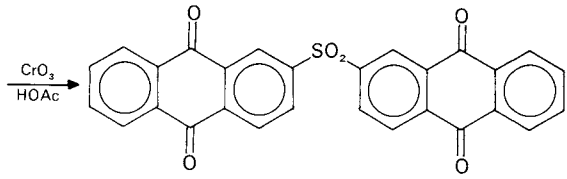
9. *Transition metal ion oxidants*

There are many transition metal ion oxidants used in organic chemistry for the interconversion of functional groups. Those which have been used for the preparation of sulphones from sulphoxides will be discussed below. It is very interesting to note that this type of oxidant often reacts more rapidly with sulphoxides than with sulphides and so sulphoxides may be selectively oxidized with transition metal ion oxidants in the presence of sulphides. This is in direct contrast to the oxidation of sulphides and sulphoxides with peracids and periodate, for example, where the rate of reaction of the sulphide is more than 100 times that for the corresponding sulphoxide.

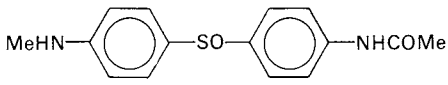
a. Chromium. Early work showed that sulphoxides containing β-chlorine atoms could be quantitatively converted to the corresponding sulphone with a hot aqueous 5–10% chromium trioxide solution containing 15–18% sulphuric acid, as shown in equation (40)[126]. The chromium trioxide may also be replaced by potassium dichromate[127]. A similar reaction in which the sulphuric acid is replaced by acetic acid has also been reported to yield a nearly quantitative yield of 2, 2′-dianthraquinonyl sulphone from the sulphoxide as shown in equation (41)[128]. The latter type of reaction has been patented for the preparation of aromatic sulphones containing acetyl-protected amino groups and *N*-alkylamino groups from the corresponding sulphoxides[129] as shown, for example, in equation (42). Chromium trioxide in water is a more powerful oxidizing agent than many other oxidants. For example, it can be used successfully to prepare diaryl sulphones containing one or more nitro, hydroxyl, amino or hydrazino group(s) from the corresponding sulphoxide when other reagents fail (equation 43)[130].

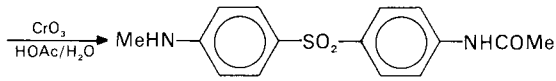
$$(\mathrm{ClCH_2CH_2})_2\mathrm{SO} \xrightarrow[\mathrm{H_2O/H_2SO_4}]{\mathrm{CrO_3}} (\mathrm{ClCH_2CH_2})_2\mathrm{SO_2} \tag{40}$$



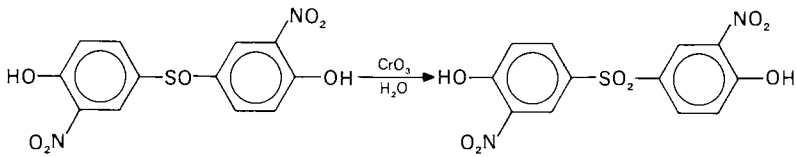


(41)





(42)



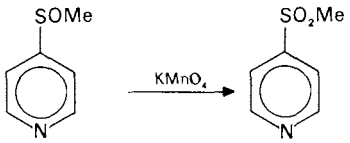
(43)

Kinetic studies of the oxidation of sulphoxides to sulphones by chromium(VI) species have been carried out[131–133]. The reaction has been found to be first order with respect to the chromium(VI) species and the sulphoxide and second order with respect to acid. At high sulphoxide concentrations the order with respect to sulphoxide is two. The proposed mechanism involves an electron transfer from the sulphoxide to the active chromium(VI) species ($HCrO_3^+$ in strong acidic media) in the rate-determining step producing a sulphoxide radical cation which further reacts to give the sulphone.

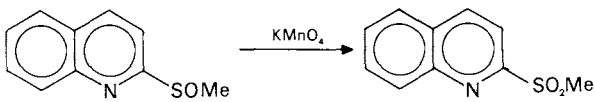
b. Manganese. Potassium permanganate can also be used to prepare sulphones by oxidation of sulphoxides in aqueous acid media[126,134–138]. Yields are usually good but are generally lower than similar reactions where chromium trioxide is used. If primary or secondary hydroxyl groups are present in the sulphoxide, they are converted quantitatively to the corresponding carbonyl compound[134], as indicated in equation (44). Zinc permanganate has been recommended in place of the potassium salt[139]. Sulphoxides containing six-membered heterocyclic rings with nitrogen are converted to the corresponding sulphone in good yields with no *N*-oxide formation[137] (equations 45 and 46). Potassium permanganate is used to oxidize dimethyl sulphoxide to the sulphone as part of a method for the quantitative determination of dimethyl sulphoxide[135,138]. This quantitative reaction has also been exploited in the preparation of perdeuterio dimethyl sulphone by the reaction of potassium permanganate with d_6-DMSO in D_2O at 90 °C for

three and a half hours[136].

$$PhSOCH_2CH(OH)Ph \xrightarrow{KMnO_4} PhSO_2CH_2COPh \tag{44}$$



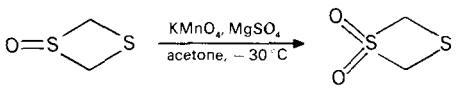
(45)



(46)

In the presence of magnesium sulphate, potassium permanganate in acetone (at room temperature or below) becomes a highly selective oxidant reacting faster with sulphoxides than with sulphides. This reaction pattern is also evident if sodium permanganate is employed as oxidant, in aqueous dioxane at room temperature[140]. The selective reaction of potassium permanganate in acetone with $MgSO_4$ has been utilised in an elegant series of reactions of 1,3-dithietane and its derivatives[141]. In this sequence 1,3-dithietane-1-oxide was selectively and quantitatively converted to 1,3-dithietane-1,1-dioxide (equation 47).

Benzyltriethylammonium permanganate has also been used for the mild oxidation of sulphoxides to sulphones at $-10\,^{\circ}C$ in methylene chloride in the presence of keto, amino and ester groups in $> 65\%$ yields[142].



(47)

A single report concerning the kinetics of the oxidation of dimethyl sulphoxide by tervalent manganese has been published[143]. This reaction proceeds by one-electron transfer forming the sulphoxide radical cation which, in the presence of a monomer such as acrylonitrile, may be used to initiate polymerization. Equation (48) has been proposed to describe the reaction.

$$\begin{aligned} Mn^{3+} + Me_2SO &\rightleftharpoons Mn^{2+} + Me_2SO^{+\cdot} \\ Me_2SO^{+\cdot} + H_2O &\rightleftharpoons Me_2SO + H^+ + OH^{\cdot} \\ Me_2SO^{+\cdot} + OH^{\cdot} &\longrightarrow Me_2SO_2 + H^+ \end{aligned} \tag{48}$$

c. Other transition metals. Cerium(IV) may be used to oxidize sulphoxides to sulphones in aqueous acid[131,144,145]. The reaction appears to proceed by initial complexation of the sulphoxide to the metal ion species followed by electron transfer to form a sulphoxide radical cation, which then transfers a further electron and is attacked by water forming the sulphone[131]. Silver(I)-dimethyl sulphoxide adducts are oxidized in a similar fashion by aqueous cerium(IV) sulphate[144]. In this case silver(I) acts as a catalyst.

Osmium(VIII) will also oxidize sulphoxides to sulphones[146] although this is usually accomplished in alkaline media in contrast to other transition-metal oxidations described above. The reaction may also be carried out in the presence of potassium

hexacyanoferrate(III)[147]. During both reactions black osmium trioxide precipitates out of solution.

If a mixture of diphenyl sulphide and the corresponding sulphoxide are treated with osmium tetroxide in boiling ether for 48 hours the sulphide is unchanged whilst the sulphoxide is converted into the sulphone in 96% yield with concomitant production of osmium trioxide[140]. It thus seems that this method would be useful synthetically for the preparation of sulphones from sulphoxides containing sulphide functionalities. Ruthenium tetroxide may be used in place of osmium(VIII) oxide[148].

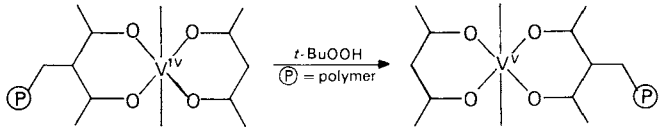
Nickel(IV) complexes react with dimethyl sulphoxide in acidic solution to give the sulphone and nickel(II) ions. The kinetics of this reaction have been studied and found to be very complex in nature. The reaction probably proceeds by initial complexation of the dimethyl sulphoxide to the nickel(IV) species followed by electron transfer and oxygen atom transfer producing the observed products[149].

10. Polymer-supported oxidations

Polymer-supported reactions are a relatively recent development in synthetic organic chemistry. In an ideal case a reagent is prepared as part of a polymer which is then poured onto a column. The reactant is then passed through the column in a suitable solvent and the product is obtained free of both starting material and other reagents and is simply isolated by evaporation of the solvent. Ideally the polymer should be easily recyclable.

Two polymer-supported reagents have been developed for the oxidation of sulphoxides to sulphones; these involve peracid groups[150], and bound hypervalent metals activated by *t*-butyl hydroperoxide[151,152].

The oxidation of sulphoxides with peracid resins occurs rapidly and quantitatively at 20 °C using dioxane as solvent[150]. Vanadium(V), generated on a polymer support by treatment of vanadium(IV) with a hydroperoxide (equation 49) may be used to oxidize successfully sulphoxides to sulphones in very good yields[151].



(49)

If molybdenum(VI) is generated by treatment of a polymer-supported complex containing molybdenum(V) with a hydroperoxide, then this polymer-supported oxidant may also be used to prepare sulphones from sulphoxides. In this case the yield is not good unless the sulphoxide is repeatedly passed through a column containing the oxidant or the reaction is performed by stirring the polymer and the sulphoxide together at 56 °C for 16 hours[152].

11. Phase-transfer catalysed oxidations

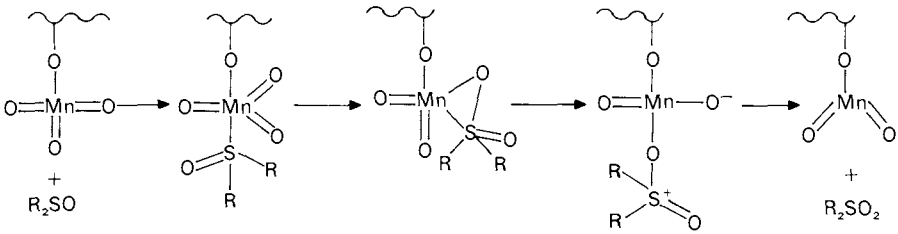
Phase-transfer catalysis is another modern synthetic method that is currently receiving much attention. This method tends to have several advantages over traditional methods, such as higher yields, the requirement of milder reaction conditions, simplicity and the use of relatively inexpensive reagents.

An early study[153] of the attempted phase-transfer catalysed oxidation of dibenzyl sulphoxide to the sulphone using a variety of conditions and oxygen, periodate, hypochlorate and permanganate as oxidants showed that only potassium permanganate gave any of the required product, albeit in low yields. A further study, using Adogen 464 as

the catalyst, showed that sulphones may be formed in yields exceeding 80% in 2 hours at room temperature[154] (equation 50). If this reaction is carried out as described and is irradiated with ultrasound, then there is a 5–10% increase in yield and reaction times are usually shorter[155].

$$R_2SO \xrightarrow[NR_4{}^+X^-/CH_2Cl_2]{KMnO_4/H_2O} R_2SO_2 \tag{50}$$

Phase-transfer catalysed oxidation of sulphoxides to sulphones using copper(II) permanganate or a mixture of potassium permanganate and copper(II) sulphate is also possible[156]. In this case hexane is used as the solvent for the organic phase and the reaction is carried out under reflux for 24 hours. Sulphones are prepared by this method in quantitative yields and the mechanism proposed is given in equation (51).



(51)

12. Electrochemical oxidation

Surprisingly few studies of the electrochemical oxidation of sulphoxides have been performed considering the importance of sulphoxides as antioxidants and as biological intermediates.

The first electrochemical oxidation of an organic sulphur-containing compound with oxidation number above two was reported as late as 1974[157]. In this study the oxidation of diphenyl sulphoxide at a platinum electrode was investigated in acetonitrile and in benzene using cyclic voltametry and controlled-potential electrolysis. A single anodic process occurred at + 1.83 volts which involved the oxidation of the sulphoxide causing the formation of a radical cation. Further reactions then occurred forming diphenyl sulphone in 50% yield as shown in equation (52). In benzene solution the sulphide radical cation, generated when diphenyl sulphone was formed, reacted with solvent molecules forming triphenyl sulphonium ions (equation 53). Chromatographic separation of the sulphone from the remainder of the reaction mixture could easily be carried out, thus providing an excellent method of preparation for some sulphones.

$$Ph_2SO \xrightarrow{-e} Ph_2SO^{+\cdot} \xrightarrow{Ph_2SO} [Ph_2SO{-}S(Ph)_2O]^{+\cdot} \longrightarrow Ph_2S^{+\cdot} + Ph_2SO_2 \tag{52}$$

$$Ph_2S^{+\cdot} \xrightarrow{PhH} Ph_3S^+ \tag{53}$$

Dimethyl sulphoxide has also been oxidized electrochemically, using either a platinum anode or a dimensionally stable anode containing iridium and selenium in 1 *M* sulphuric acid solution[158]. The former electrode requires a potential close to that required for oxygen evolution whilst the latter needed a potential 0.5 volts lower. Thus the dimension-

ally stable anode would be the one favoured in this case although it was noted that the overvoltage was high.

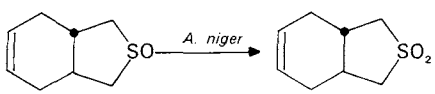
It is rather surprising that more studies in this area have not been reported, especially since the yield in the case of diphenyl sulphoxide oxidation is good and the product is easily separable from other materials formed in the electrochemical cell. Presumably more reports will be forthcoming in the next few years, especially for the oxidation of aryl sulphoxides.

13. Biological oxidations

Sulphones occur relatively rarely as natural products. Thus there is no reported *specific* enzymatic system for the formation of sulphones. However, there are several well-understood pathways for the oxidation of sulphides to sulphoxides and these do lead to sulphones in some cases.

Studies concerning sulphide oxidations by *Aspergillus niger* have shown that sulphoxides are slowly oxidized to the corresponding sulphone[159,160]. This same reaction may also be carried out using a crude acetone extract of *Aspergillus niger*[161]. These oxidations have been shown to be stereospecific[162] and yields have been optimised to about 30% at best. A fairly wide range of sulphoxides may be oxidized by this method (equations 54 and 55).

$$PhCH_2SOBu\text{-}t \xrightarrow{A.\,niger} PhCH_2SO_2Bu\text{-}t \tag{54}$$



(55)

Other species such as *Rhizopus arrhizus* and *Rhizopus stolonifer* also produce some sulphone by oxidation of a sulphoxide, albeit in low yields (less than 10%)[163].

The stereospecificity of the biological oxidation reactions has been exploited in the preparation of optically active sulphoxides. One enantiomer of the sulphoxide is oxidized to the sulphone faster than the other and so there is an excess of one enantiomeric sulphoxide after partial reaction has occurred[164].

A more detailed study of the biological oxidation of sulphoxides to sulphones has been reported[165]. In this study cytochrome P-450 was obtained in a purified form from rabbit cells and was found to promote the oxidation of a series of sulphoxides to sulphones by NADPH and oxygen (equation 56). Kinetic measurements showed that the process proceeds by a one-electron transfer to the activated enzymatic intermediate [an oxenoid represented by $(FeO)^{3+}$] according to equation (57).

$$ArSOCH_2R \xrightarrow[O_2/NADPH]{\text{cyt P-450}} ArSO_2CH_2R \tag{56}$$

$$\begin{aligned} ArSOCH_2R + (FeO)^{3+} &\longrightarrow [ArSOCH_2R]^{+\cdot} + (FeO)^{2+} \\ &\downarrow \\ &ArSO_2CH_2R + Fe^{3+} \end{aligned} \tag{57}$$

It should also be noted in this section that studies of the metabolism of dimethyl sulphoxide in calves[166], rabbits[167,168], guinea pigs[168], rats[169] and man[169–172] have shown that one metabolic pathway involves its oxidation to the sulphone.

A similar study of the metabolism of tetrahydrofurfuryl sulphoxide, a drug metabolite

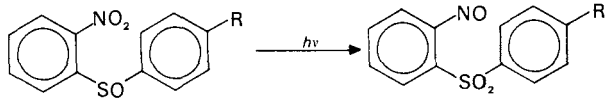
(and the corresponding sulphide), by rats involves partial oxidation to the sulphone (equation 58)[173].

(58)

14. Photochemical and thermal oxidations

Photochemical oxidation reactions involving the conversion of sulphoxides to sulphones have not been widely studied. However, there are several interesting examples in the literature that merit mention.

When a diaryl sulphoxide containing a 2-nitro group is irradiated in benzene solution at 30 °C for 2 hours with a high-pressure mercury lamp, the corresponding nitrososulphone is formed in 20–35% yield (equation 59)[174]. It should be noted that this reaction does not occur in the absence of light even under refluxing conditions. The mechanism proposed consists of the initial formation of an excited ($\pi \rightarrow \pi^*$) singlet state followed by nucleophilic attack by the 'oxyanion' of the nitro group on the sulphoxide sulphur atom allowing oxygen atom transfer to occur[174,175].



(59)

The photolysis of dimethyl sulphoxide (at 253.7 nm) in a wide range of solvents has been studied in detail[176]. Three primary reactions occur, namely (i) fragmentation into methyl radicals and methanesulphinyl radicals, equation (60), (ii) disproportionation into dimethyl sulphone and dimethyl sulphide, equation (61) and (iii) deactivation of the excited state to ground state dimethyl sulphoxide. All chemical processes occur through the singlet state. Further chemical reactions of the initial photochemical products produce species that have been oxidized relative to dimethyl sulphoxide.

$$CH_3SOCH_3 \xrightarrow{h\nu} CH_3SO^{\cdot} + CH_3^{\cdot} \tag{60}$$

$$CH_3SOCH_3{}^* + CH_3SOCH_3 \longrightarrow CH_3SO_2CH_3 + CH_3SCH_3 \tag{61}$$

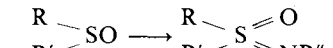
Gollnick and Stracke[176] investigated the very complex mechanism involved in the photolysis of dimethyl sulphoxide and concluded that disproportionation is probably the route for the major sulphone-producing reaction. Other oxidized species such as methanesulphonic acid are also produced and are also probably formed by a series of disproportionation reactions, for example equation (62). Thus photolysis of dimethyl sulphoxide is not a synthetically useful reaction due to the large number of compounds produced.

$$CH_3SO^{\cdot} \underset{-X^{\cdot}}{\overset{HX}{\longrightarrow}} CH_3SOH \xrightarrow[-CH_3SCH_3]{CH_3SOCH_3} CH_3SO_2H \xrightarrow[-CH_3SCH_3]{CH_3SOCH_3} CH_3SO_3H \tag{62}$$

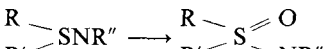
B. Oxidation of Sulphoxides and Sulphilimines to Sulphoximines

In this section the oxidation of sulphoxides to sulphoximines (equation 63) will be briefly covered together with the related reaction, the oxidation of sulphilimines to

sulphoximines (equation 64). The product of both reactions, a sulphoximine, is a nitrogen analogue of a sulphone, whilst the precursors in reactions as shown in equation (64) are nitrogen analogues of sulphoxides.



(63)



(64)

An excellent review of the preparation and chemistry of sulphoximines (also known as sulphoximides) has been published[177]. Here, some of the more interesting and important reactions amounting to oxidation at sulphur will be considered.

1. Oxidation of sulphoxides producing sulphoximines

The most general reaction for the preparation of sulphoximines from sulphoxides is simply by reaction with hydrazoic acid (equation 65)[178]. Highly substituted sulphoxides, such as diethyl sulphoxide with more than two chlorine substituents, do not undergo reaction to form the sulphoximine in this way.

$$RR'SO + HN_3 \longrightarrow RR'S(O)NH + N_2 \tag{65}$$

Sulphoximines may also be obtained from sulphoxides by reaction with benzene- and toluenesulphonyl azides[179,180]. Yields are often nearly quantitative and the reaction is usually carried out in the presence of copper. This reaction shows a high degree of stereospecificity[181], for example, if (*R*)-methyl *p*-tolyl sulphoxide is the reactant then (*S*)-methyl-*S*-*p*-tolyl-*N*-*p*-toluenesulphonylsulphoximine is the product (equation 66). It has been suggested that this reaction involves the intermediacy of a nitrene species[182].

$$(R)\text{-MeSOAr} \xrightarrow[\text{Cu, MeOH}]{PhSO_2N_3} (S)\text{-MeSO(NSO}_2\text{Ph)Ar} \tag{66}$$

A high yield synthesis involving formal oxidation of a sulphoxide to a sulphoximine has been reported[183] using *O*-mesitylenesulphonyl hydroxylamine (NH_2OMes) (equation 67). The reaction is successful for a wide range of sulphoxides including dialkyl, diaryl and cyclic species.

(67)

High yields of sulphoximines are also obtained from the reaction of sulphoxides with chloramine-T in the presence of copper(II) salts or copper metal (equation 68)[180,184].

$$Me_2SO + TsNClNa \xrightarrow{Cu^{2+} \text{ or } Cu^{\circ}} Me_2S(O)NTs \tag{68}$$

2. Oxidation of sulphilimines to sulphoximines

The S=N bond in sulphilimines is relatively sensitive to hydrolysis and so the oxidation of these compounds to sulphoximines must be carried out under mild conditions. For example, attempted oxidation of many sulphilimines with potassium permanganate usually leads to decomposition without formation of the required product[178]. It should be noted, however, that once the sulphoximine is formed the S=N bond is much more stable and hence less readily available for reaction.

Low-temperature oxidation of sulphilimines with potassium permanganate in dioxane

is successful but usually proceeds in low overall yields[185]. The use of potassium permanganate is more successful if it is used in conjuction with magnesium sulphate[186] (equation 69). Other common oxidizing agents for the sulphoxide to sulphone transformation, such as periodate or peracids, are also usually ineffective (as with potassium permanganate) or produce only low yields for the analogous reaction of sulphilimines producing sulphoximines[187].

$$Ph_2S{=}NH \xrightarrow[MgSO_4]{KMnO_4} Ph_2S(O)NH \tag{69}$$

A novel oxidation of sulphilimines using ruthenium tetroxide (generated *in situ* from ruthenium dioxide in a two-phase system) for the preparation of sulphoximines has been reported and proceeds in yields greater than 85%[185].

Another two-phase system using phase-transfer catalysis for the oxidation of diaryl-*N*-arylsulphonyl sulphilimines to sulphoximines has also been described[188]. In this reaction the oxidizing reagent is sodium hypochlorite and yields are in excess of 90% in most cases (equation 70). This reaction presumably occurs by initial attack by the nucleophilic hypochlorite ion on the sulphur atom followed by chloride ion elimination.

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!S{=}NTs \xrightarrow[P.T.C.]{NaOCl} \begin{matrix} R \\ R' \end{matrix}\!\!>\!S\!\!<\!\!\begin{matrix} O \\ NTs \end{matrix} \tag{70}$$

C. Oxidation of Sulphoxides to Higher Oxidation Levels

A few studies are reported which describe the direct oxidation of sulphoxides to sulphonic acids, sulphonyl halides, thiosulphonates and sulphate. These reactions will be considered in this section but it should be noted that they are rarely of synthetic utility.

The base catalysed autoxidation of dimethyl sulphoxide and methyl phenyl sulphoxide at 80 °C produces low quantities of methanesulphonic acid in both cases and benzenesulphonic acid in the latter case[189] (equation 71 and 72). There is no evidence of sulphone formation in either reaction. Dimethyl sulphoxide oxidation to methanesulphonic acid also occurs in the presence of trace quantities of acid and oxygen. Again the reaction would not be synthetically useful[190].

$$Me_2SO \xrightarrow{base} MeSO_3H \tag{71}$$

$$PhSOMe \xrightarrow{base} MeSO_3H + PhSO_3H \tag{72}$$

Photolysis[191] and flash vacuum pyrolysis[192] of diaryl sulphoxides both lead to the formation of thiosulphonates as shown in equation (73). This reaction presumably occurs by initial S—C bond scission followed by combination of two arylsulphinyl radicals as depicted in equation (74).

$$Ar_2SO \xrightarrow{h\nu \text{ or } \Delta} ArSO_2SAr \tag{73}$$

$$2ArSO^{\bullet} \longrightarrow \left[ArS(O)OSAr \right] \longrightarrow \left[ArS(O)^{\bullet} + {}^{\bullet}SAr \right] \longrightarrow ArSO_2SAr \tag{74}$$

In the case of flash vacuum pyrolysis, the reaction may be of some synthetic utility. For example, at 700 °C diphenyl sulphoxide produces diphenyl thiosulphonate in 40% yield, however, several other products are also formed.

As has been mentioned in an earlier section, aqueous chlorination of sulphoxides leads to sulphones. If excess reagents are used, sulphonyl chlorides may be formed directly from sulphoxides in good yields (equation 75)[89,90,193]. In order for this reaction to be synthetically useful, the sulphoxide used should be symmetrical. The product is presumably formed in a stepwise manner via the sulphinyl chloride [RS(O)Cl] and the sulphinic acid [RS(O)OH]. In the case of chloromethyl dichloromethyl sulphoxide, the only sulphonyl chloride formed is chloromethanesulphonyl chloride (equation 76) and this may be readily separated from the other products by distillation[90,193]. Similarly, oxidation of dichloromethyl methyl sulphoxide and methyl trichloromethyl sulphoxide with chlorine in aqueous acetic acid leads to the formation of methanesulphonyl chloride in 75% and 86% yields respectively. Other species are also produced but these are much more volatile and thus easily removed (equations 77 and 78). In the absence of acetic acid the yields are somewhat reduced.

$$\begin{matrix} R \\ R \end{matrix}\!\!>\!S{=}O + Cl_2 \xrightarrow{H_2O} RSO_2Cl \tag{75}$$

$$ClCH_2SOCH_2Cl \xrightarrow[H_2O]{Cl_2} ClCH_2SO_2Cl + CHCl_3 + CCl_4 + CO_2 \tag{76}$$

$$65\% \qquad 6\% \qquad 10\% \quad 67\%$$

$$CH_3SOCHCl_2 \xrightarrow[H_2O/HOAc]{Cl_2} CH_3SO_2Cl + CCl_4 + CH_3COCl \tag{77}$$

$$CH_3SOCCl_3 \xrightarrow[H_2O/HOAc]{Cl_2} CH_3SO_2Cl + CCl_4 + CH_3COCl \tag{78}$$

Drastic oxidations of sulphoxides are used when analytical measurements of sulphur content are required. These methods usually lead to the formation of sulphate and occur via the formation of sulphones. These reactions will be discussed in Section III.

D. Oxidation of Thiosulphinates to Thiosulphonates

Thiosulphinates are derivatives of disulphides with one of the sulphur atoms at the sulphoxide oxidation level. In theory, oxidation of a thiosulphinate could produce two products, a disulphoxide and a thiosulphonate (equation 79). Discussions of this topic have been very polarised over the years but now it is fairly well established that the thiosulphonate is the major product formed in most cases, although the intermediacy of a α-disulphoxides is indicated from some data.

$$RSOSOR' \longleftarrow RSOSR' \longrightarrow RSO_2SR' \tag{79}$$

Hydroperoxides or peracids may be used for the oxidation of thiosulphinates producing good yields of the thiosulphonate[194–198]. Early arguments that the initial product was the disulphoxide, which was unstable and decomposed producing the thiosulphonate, were discounted because it was claimed that this intermediacy could not explain certain experimental results. For example, when a reaction was halted before the product was realised in high yield, there was a substantial quantity of the disulphide present in the reaction mixture. It was also found that in the initial stages of the reaction, the thiosulphinate was consumed more rapidly than the oxidant. These data suggest that the

major pathway by which the thiosulphinate is produced does not involve direct oxidation but rather disproportionation occurs and the oxidizing agent oxidizes the disulphide produced back to the thiosulphinate.

If 30% hydrogen peroxide is used as the oxidant then stepwise oxidation occurs leading to the α-disulphone (equation 80)[195]. In this study the trioxide, RSO_2SOR, was not found but was assumed to be produced.

$$RSOSR \xrightarrow{H_2O_2} RSO_2SR \xrightarrow{H_2O_2} RSO_2SOR \longrightarrow RSO_2SO_2R \qquad (80)$$

The reaction mechanism for the peracid oxidation of thiosulphinates is perhaps more complex than described above. A study of the low-temperature (− 40 °C) peracetic acid oxidation of 2-methyl-2-propyl 2-methyl-2-propanethiosulphinate gave two products as shown in equation (81)[196]. During the reaction the α-disulphoxide was apparently detected by NMR spectroscopy.

$$Me_3CSOSCMe_3 \xrightarrow{CH_3CO_3H} Me_3CSO_2SCMe_3 + Me_3CSO_2SSCMe_3 \qquad (81)$$

Sodium periodate oxidation of (2,2-dimethylpropyl)benzenethiosulphinate produces the thiosulphonate in quantitative yield (equation 82) whilst attempted oxidation of phenyl 2,2-dimethylpropanethiosulphinate with the same reagent was unsuccessful after 48 hours (equation 83)[197]. It has been found that for most unsymmetrical thiosulphinates the thiosulphonate is produced in good yield by this method and is catalysed by iodine or acid[199]. Oxidation of the two above-mentioned thiosulphinates with mCPBA yielded a complex mixture including di(2,2-dimethylpropyl) thiosulphonate (t-$BuCH_2SO_2SCH_2Bu$-t), phenyl 2,2-dimethylpropanethiosulphonate (t-$BuCH_2SO_2$-SPh), 2,2-dimethylpropanesulphinic acid (t-$BuCH_2SO_2H$) and the corresponding sulphonic acid[197,198].

$$PhSOSCH_2Bu\text{-}t \xrightarrow{NaIO_4} PhSO_2SCH_2Bu\text{-}t \qquad (82)$$

$$t\text{-}BuCH_2SOSPh \xrightarrow{NaIO_4} \text{no reaction} \qquad (83)$$

Unsymmetrical thiosulphinates and thiosulphonates are both oxidized by potassium superoxide in pyridine in the presence of 18-crown-6 ether to produce sulphinic and sulphonic acids and a disulphide, under mild conditions (equation 84)[200,201]. Sulphinic and sulphonic acids were produced from both the R and R′ substituents whilst the disulphide was derived only from the sulphenyl side of the reactant. Thus, the reaction mixture contained five products, making the reaction not synthetically useful. Pyrolysis of thiosulphinates also produces mixtures of products, one being the thiosulphonate; again this is not a synthetically useful reaction[202].

$$RSOSR' \xrightarrow[18\text{-crown-6}]{KO_2} RSO_2^- + R'SO_2^- + RSO_3^- + R'SO_3^- + R'SSR' \qquad (84)$$

Electrochemical oxidation of thiosulphinates leads cleanly to the corresponding thiosulphonate in reasonable yields with no observed side-products[203].

III. OXIDATION OF SULPHONES

Sulphones are blessed with high thermal and chemical stability and so the oxidation of these species requires extreme, forcing conditions in most cases.

The oxidation of sulphones leads to either a sulphonic acid (or a sulphonic acid derivative) or to sulphate. Such reactions have rarely been used for the preparation of sulphonic acids since these are usually readily available by other well-established routes. However, polyhalogenated sulphones can be oxidized relatively easily to sulphonic acids and these reactions will be discussed here.

Notwithstanding the forcing conditions required, organic sulphides, sulphoxides and sulphones are analysed quantitatively by their conversion to sulphate. These methods will also be briefly covered in this section.

A. Oxidation of Sulphones to Sulphonic Acids and Derivatives

Sulphones containing multiple fluorine and chlorine atoms are very susceptible to hydrolytic cleavage forming sulphonic acids. These reactions may thus be considered as oxidations of sulphones[204]. For example, methyl heptafluoropropyl sulphone is readily cleaved as shown in equation (85) at 100 °C with dilute aqueous sodium hydroxide solution, followed by acid work-up. The reaction occurs by initial nucleophilic attack by hydroxide ion on the sulphone sulphur atom followed by elimination of the more stable $C_3F_7^-$ group. At lower temperatures the sulphone was recovered unchanged whilst prolonged heating at 140 °C (7 days) produced sulphur dioxide and a mixture of organic compounds which did not contain sulphur.

$$CH_3SO_2C_3F_7 \xrightarrow[2.\ H_3O^+]{1.\ OH^-} CH_3SO_3H + C_3F_7H \tag{85}$$

Oxidation of methyl perfluoroalkyl sulphones with refluxing aqueous potassium permanganate produced the perfluorinated alkanesulphonic acid in 85% yield as the potassium salt (equation 86). On the other hand, attempted oxidation with sodium hypochlorite caused only chlorine substitution (equation 87). Reaction of the new sulphone with aqueous hydroxide gave the same perfluoroalkane sulphonic acid salt (equation 88).

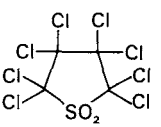
$$C_2F_5SO_2CH_3 \xrightarrow{KMnO_4} C_2F_5SO_3^-K^+ \tag{86}$$

$$C_2F_5SO_2CH_3 \xrightarrow{NaOCl} C_2F_5SO_2CCl_3 \tag{87}$$

$$C_2F_5SO_2CCl_3 \xrightarrow{OH^-} C_2F_5SO_3^- \tag{88}$$

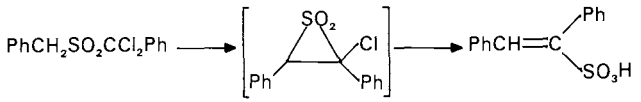
The permanganate oxidation of bis(alkylsulphonyl)perfluoroalkanes yielding perfluoroalkanedisulphonic acids (equation 89) has been patented using a similar procedure to that outlined above[205]. The reaction occurs in 80–90% yield. Cyclic sulphones containing α,α'-chlorine substituents are also susceptible to easy hydrolysis yielding sulphonic acid salts in good yields (equation 90)[206]. The above-described behaviour should be contrasted with simple dialkyl sulphones which do not normally undergo such reactions[207].

$$RSO_2(CF_2)_nSO_2R \xrightarrow{KMnO_4} K^+{}^-O_3S(CF_2)_nSO_3^-K^+ \tag{89}$$



$$\xrightarrow{KOH} CCl_2{=}CCl_2CCl_2CCl_3SO_3^-K^+ \tag{90}$$

Acyclic sulphones with α-chlorine substituents also produce sulphonic acid derivatives in good yields, although in these cases rearrangement occurs via a thiiren dioxide intermediate (equation 91)[208].



(91)

Dialkyl sulphones may be converted to sulphonic acids by reaction with carbon tetrachloride and base at 80 °C[209]. This reaction proceeds by initial formation of α-chloro sulphones which are then converted to a thiiren intermediate which decomposes to give a sulphonic acid (equation 92).

$$RCH_2SO_2CH_2R \xrightarrow[t\text{-BuOH}]{CCl_4-KOH} RCH{=}C\begin{matrix}R\\ SO_3^-K^+\end{matrix} \qquad (92)$$

The direct fluorination of sulphones has also been studied[210] and this leads to oxidation. At room temperature dimethyl sulphone produced bis(trifluoromethyl)-sulphone and trifluoromethylsulphonyl fluoride in 34% and 15% yields respectively (equation 93).

$$CH_3SO_2CH_3 \xrightarrow{F_2} \underset{34\%}{CF_3SO_2CF_3} + \underset{15\%}{CF_3SO_2F} \qquad (93)$$

A much improved synthesis of perfluoroalkanesulphonyl fluorides from sulphones has been published. This involves the electrolysis of cyclic unsaturated sulphones in anhydrous HF at 8–10 °C using a potential of 5–7 volts. Thus, butadiene sulphone was oxidized to perfluorobutanesulphonyl fluoride in quantitative yield[211] (equation 94).

(94)

The oxidation of disulphones with iodine in aqueous perchloric acid apparently produces the corresponding sulphonic acid (equation 95)[212].

$$RSO_2SO_2R + I_2 \xrightarrow[HClO_4]{H_2O} 2RSO_3H + 2I^- \qquad (95)$$

B. Oxidation of Sulphones to Sulphate

The reactions described in this section are used for the quantitative analysis of sulphones. Extreme, forcing, oxidizing conditions are used for these procedures. Sulphoxides and sulphides may also be analysed in the same way and so the discussion also applies to these types of compounds.

There are several methods of exhaustive oxidation of sulphones to sulphate used in quantitative analytical chemistry. These have been discussed at length elsewhere[213] and will thus only be described briefly here. Various oxidizing agents have been recommended for these procedures.

The lamp method involves combustion of a sample of sulphone in a closed system with an atmosphere of 30% oxygen and 70% carbon dioxide[214]. The mixture of sulphur dioxide and sulphur trioxide formed is converted *in situ* to sulphate by oxidation with hydrogen

peroxide. A variation of this method is the flask combustion of sulphones[215] which occurs rapidly, but there are problems associated with multi-halogenated compounds which cause incomplete conversion to sulphate[216]. Another variation of the oxidation procedure using oxygen involves the combustion of the sulphone in a bomb containing oxygen at 30–40 atmospheres pressure[217].

A procedure involving catalytic oxidation of sulphones has also been developed[218]. In this case the sulphone is mixed with sodium carbonate and cobalt(II) oxide and the mixture is burned in a stream of oxygen. This method works very well for nitrogen-containing sulphones and requires no expensive equipment.

Simple combustion at 700 °C in a stream of oxygen over platinum or silver has also been used for the sulphone–sulphate oxidation[219]. However, this method does not work well for halogen- and nitrogen-containing sulphones.

Exhaustive oxidation of sulphones to sulphate using a mixture of potassium chlorate, sodium peroxide and sugar in a bomb has also been recommended[220]. This procedure is known as the Parr method and produces a mixture of soluble alkali sulphates.

Nitric acid is also useful as an oxidant for the formation of sulphate from sulphones. Two such methods have been developed, firstly the established AOAC method which involves oxidation with a mixture of nitric acid and bromine[221], and secondly the Carius method[222]. The latter is probably the oldest method used for the determination of sulphones as sulphate. This oxidation procedure involves heating the sulphone with concentrated nitric acid and sodium chloride at 280–300 °C in a sealed tube. The traditional method as described is prone to explosions. This problem may be alleviated by using less nitric acid whilst employing an oxygen atmosphere[223,224]. The Carius method is slower than the other oxidation methods described above but it usually yields the best results.

IV. ACKNOWLEDGEMENTS

I wish to express my sincere thanks to all those friends and colleagues who gave suggestions and encouragement during the preparation of this manuscript. I especially wish to thank my wife Niki Hoyle for her skillful assistance and dedication.

V. REFERENCES

1. E. Block, in *The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and Their Sulphur Analogues* (Ed. S. Patai), Part I, Chap. 13, Wiley, New York, 1980.
2. R. D. Little and S. O. Myong, *Tetrahedron Letters*, **21**, 3339 (1980).
3. J. R. Hwu, *J. Org. Chem.*, **48**, 4432 (1983).
4. A. Saytzeff, *Ann. Chem.*, **144**, 148 (1867).
5. H. L. Gray and G. O. Gutekunst, *J. Amer. Chem. Soc.*, **42**, 856 (1920).
6. O. Beckmann, *J. Prakt. Chem.*, (2), **17**, 471 (1878).
7. F. Beilstein and A. Kurbatow, *Ann.*, **197**, 75 (1879).
8. G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 3127 (1928).
9. D. W. Goheen and C. F. Bennett, *J. Org. Chem.*, **26**, 1331 (1961).
10. N. C. Marziano, G. Cimino, U. Romano and R. C. Passerini, *Tetrahedron Letters*, 2833 (1969).
11. N. C. Marziano, G. Cimino, R. C. Passerini and P. Fiandaca, *Boll. Accad. Gioenia Sci. Nat. (Catania), IV*, **9**, 589 (1969).
12. N. Marziano, P. Fiandaca, E. Maccarone, U. Romano and R. Passerini, *Tetrahedron Letters*, 4785 (1967).
13. B. Ciocca and L. Canonica, *Gazz. Chim. Ital.*, **76**, 113 (1946); G. Leandri and M. Pallotti, *Boll. Sci. Fac. Chim. Ind. (Bologna)*, **13**, 48 (1955).
14. J. Fiala, J. Klanduch and R. Borisek, *Czech*, **170**, 679 (1977); *Chem. Abstr.*, **88**, 169595a (1978).
15. G. A. Olah and B. G. B. Gupta, *J. Org. Chem.*, **48**, 3585 (1983).

16. M. E. C. Biffin, J. Miller and D. B. Paul, *Tetrahedron Letters*, 1015 (1969); M. E. C. Biffin, G. Boksteiner, J. Miller and D. B. Paul, *Aust. J. Chem.*, **27**, 789 (1974).
17. A. D. Mallievskii, V. V. Vints, V. N. Parfenov and N. M. Emanuel, USSR Pat. 323, 966 (1979); *Chem. Abstr.*, **90**, 167390x (1979).
18. G. V. Varnakova, A. V. Mashkina, L. M. Zagryatskaya, Z. A. Suleimanova, R. M. Masagutov and A. K. Sharipov, USSR Pat. 650, 999 (1979); *Chem. Abstr.*, **90**, 203010j (1979).
19. G. V. Varnakova, A. V. Mashkina and L. D. Vidergol'd, USSR Pat. 676, 588 (1979); *Chem. Abstr.*, **91**, 156829s (1979).
20. L. V. Vlasova, G. N. Sem'ekhin, V. M. Mastikhin and A. V. Mashkina, *Zh. Khim.*, abstract 17N188 (1979); *Chem. Abstr.*, **92**, 22002d (1980).
21. G. V. Varnakova, L. M. Zagryatskaya, Z. A. Suleimanova, R. M. Masagutov, A. K. Sharipov, V. N. Yakovleva, L. V. Vlasova, N. N. Kirik and A. V. Mashkina, *Katal. Sint. Org. Soedin. Sery.*, 66 (1979); *Chem. Abstr.*, **94**, 15468y (1981).
22. J. Trocha-Grimshaw and H. B. Henbest, *J. Chem. Soc., Chem. Commun.*, 1035 (1968); H. B. Henbest and J. Trocha-Grimshaw, *J. Chem. Soc., Perkin Trans. 1*, 607 (1974).
23. G. O. Schenck and C. H. Krauch, *Chem. Ber.*, **96**, 517 (1963).
24. C. Gu, C. S. Foote and M. L. Kacher, *J. Amer. Chem. Soc.*, **103**, 5949 (1981).
25. Y. Sawaki and Y. Ogata, *J. Amer. Chem. Soc.*, **103**, 5947 (1981).
26. T. Akasaka and W. Ando, *J. Chem. Soc., Chem. Commun.*, 1203 (1983).
27. H. Böehme and H. Fischer, *Ber.*, **75B**, 1310 (1942).
28. A. Saizew, *Ann. Phys. (Leipzig)*, **139**, 354 (1866); O. Hinsberg, *Chem. Ber.*, **41**, 2828 (1908).
29. I. Tashlick, US Pat. 3,069, 471 (1962).
30. T. P. Burmistrova, A. A. Khitrik, G. D. Gal'pern, E. N. Karaulova, G. S. Latypov, N. N. Terpilovskii, N. Z. Gil'menshina and A. K. Sharipov, USSR Pat. 469,326 (1976); *Chem. Abstr.*, **85**, 191592g (1976).
31. A. Morimoto, N. Nanbu and T. Nanbu, Jpn. Kokai Tokkyo Koho 7944, 611 (1979); *Chem. Abstr.*, **91**, 91170y (1979).
32. C. R. Johnson and R. A. Kirchoff, *J. Org. Chem.*, **44**, 2280 (1979).
33. B. C. Gilbert, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 303 (1975).
34. H. Sugimoto and D. T. Sawyer, *J. Amer. Chem. Soc.*, **106**, 4283 (1984).
35. H. Sugimoto and D. T. Sawyer, *J. Org. Chem.*, **50**, 1784 (1985).
36. Y. Ogata and K. Tanaka, *Can. J. Chem.*, **59**, 718 (1981).
37. M. J. Boeseken and E. Arrias, *Rec. Trav. Chim. Pays Bas.*, **54**, 711 (1935).
38. H. H. Szmant, H. F. Harnsberger and F. Krahe, *J. Amer. Chem. Soc.*, **76**, 2185 (1954).
39. A. R. Doumaux, J. E. McKeon and D. J. Trecker, *J. Amer. Chem. Soc.*, **91**, 3992 (1969).
40. H. H. Szmant and L. M. Alfonso, *J. Amer. Chem. Soc.*, **79**, 205 (1957).
41. H. Fillion and A. Boucherle, *Bull. Soc. Chim. Fr.*, 3674 (1971).
42. P. Block and J. L. Balmat, *J. Amer. Chem. Soc.*, **72**, 5638 (1950).
43. N. P. Petukhova, N. E. Dontsova and E. N. Prilezhaeva, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 2327 (1982); *Chem. Abstr.*, **98**, 71447k (1983).
44. C. G. Venier, T. G. Squires, Y.-Y. Chen, G. P. Hussmann, J. C. Shei and B. F. Smith, *J. Org. Chem.*, **47**, 3773 (1982).
45. D. N. Jones, T. P. Kogan and R. F. Newton, *J. Chem. Soc., Perkin Trans. 1*, 1333 (1982).
46. C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963).
47. M. Kobayashi and A. Yabe, *Bull. Chem. Soc. Japan*, **40**, 224 (1967).
48. U. Folli, D. Iarossi and F. Montanari, *J. Chem. Soc. (C)*, 1372 (1968).
49. T. Durst, R. Viau, R. Van Den Elzen and C. H. Nguyen, *J. Chem. Soc., Chem. Commun.*, 1334 (1971).
50. A. Cerniàni and G. Modena, *Gazz. Chim. Ital.*, **89**, 843 (1959); *Chem. Abstr.*, **54**, 22446i (1960).
51. A. Cerniàni, G. Modena and P. E. Todesco, *Gazz. Chim. Ital.*, **90**, 3 (1960); *Chem. Abstr.*, **55**, 9322c (1961).
52. G. Kresze, W. Schramm and G. Cleve, *Chem. Ber.*, **94**, 2060 (1961).
53. R. Curci and G. Modena, *Tetrahedron Letters*, 1749 (1963).
54. R. Curci and G. Modena, *Tetrahedron Letters*, 863 (1965).
55. R. Curci and G. Modena, *Gazz. Chim. Ital.*, **94**, 1257 (1964); *Chem. Abstr.*, **62**, 7604g (1965).
56. D. Carnimeo and R. Curci, *Boll. Sci. Fac. Chim. Ind. (Bologna)*, **23**, 293 (1965); *Chem. Abstr.*, **64**, 17401b (1966).
57. R. Curci and G. Modena, *Tetrahedron*, **22**, 1227 (1966).

58. R. Curci, A. Giovini and G. Modena, *Tetrahedron*, **22**, 1235 (1966).
59. S. A. Khan, M. Ashraf and A. B. Chughtai, *Sci. Res. (Dacca, Pakistan)*, **4**, 135 (1967).
60. R. Curci, F. DiFuria, A. Levi and G. Scorrano, *J. Chem. Soc., Perkin Trans. 2*, 408 (1975).
61. G. Modena and P. E. Todesco, *Boll. Sci. Fac. Chim. Ind. (Bologna)*, **23**, 31 (1965).
62. R. Curci, R. A. DiPrete, J. O. Edwards and G. Modena, *J. Org. Chem.*, **35**, 740 (1970).
63. J. J. Rigau, C. C. Bacon and C. R. Johnson, *J. Org. Chem.*, **35**, 3655 (1970).
64. L. Kuhnen, *Angew. Chem., Int. Ed. Engl.*, **5**, 893 (1966).
65. Y. Ogata and S. Suyama, *J. Chem. Soc., Perkin Trans. 2*, 755 (1973).
66. Y. Ogata and S. Suyama, *Chem. Ind. (London)*, 707 (1971).
67. M. J. Gibian and T. Ungermann, *J. Org. Chem.*, **41**, 2500 (1976).
68. I. S. de Roch and P. Menguy, Fr 1,540,284 (1968); *Chem. Abstr.*, **71**, 80944q (1969).
69. A. Goosen, S. African ZA82 06,827 (1983); *Chem. Abstr.*, **100**, 138954d (1984).
70. R. Curci, F. DiFuria and G. Modena, *J. Chem. Soc., Perkin Trans. 2*, 603 (1978).
71. F. Kovac and V. Plesnicar, *J. Chem. Soc., Chem. Commun.*, 122 (1978).
72. W. A. Pryor, N. Ohto and D. F. Church, *J. Amer. Chem. Soc.*, **104**, 5813 (1982).
73. V. V. Shereshovets, L. A. Bachanova, V. D. Komissarov and G. A. Tolstikov, *J. Org. Chem. USSR*, **21**(3), 437 (1985).
74. Y. Sawaki, H. Kato and T. Ogata, *J. Amer. Chem. Soc.*, **103**, 3832 (1981).
75. H. Gampp and S. J. Lippard, *Inorg. Chem.*, **22**, 357 (1983).
76. M. Miura, M. Nojima and S. Kusabayashi, *J. Chem. Soc., Chem. Commun.*, 1352 (1982).
77. G. P. Panigrahi and R. Panda, *Int. J. Chem. Kinet.*, **12**, 491 (1980).
78. R. Viswamurthy and P. Maruthamuthu, *Oxidat. Commun.*, **2**, 37 (1981).
79. Y. Ogata, Y. Sawaki and Y. Tsukamoto, *Bull. Chem. Soc. Japan*, **54**, 2061 (1981).
80. P. Maruthamuthu and M. Santappa, *Ind. J. Chem.*, **16A**, 43 (1978).
81. S. N. Mahapatro, R. Panda and G. P. Panigrahy, *Ind. J. Chem.*, **19A**, 905 (1980).
82. E. Howard and L. S. Levitt, *J. Amer. Chem. Soc.*, **75**, 6170 (1953).
83. B. M. Trost and D. P. Curran, *Tetrahedron Letters*, **22**, 1287 (1981).
84. T. Pandurengan and P. Maruthamuthu, *Bull. Chem. Soc. Japan*, **54**, 3551 (1981).
85. A. S. Reddy and J. N. Reddy, *Ind. J. Chem.*, **20A**, 608 (1981).
86. L. S. Levitt, *J. Phys. Chem.*, **88**, 1177 (1984).
87. E. J. Behrman, *J. Phys. Chem.*, **89**, 2964 (1985).
88. L. S. Levitt, *J. Chem. Phys.*, **89**, 2965 (1985).
89. C. F. Bennett, D. W. Goheen and W. S. MacGregor, *J. Org. Chem.*, **28**, 2485 (1963).
90. J. S. Grossert and R. F. Langler, *Can. J. Chem.*, **55**, 407 (1977).
91. V. I. Dronov, A. U. Baisheva, A. E. Pototskaya and L. M. Soskova, *Khim. Seraorg. Soedin., Soderzh. Neftyakh. Nefteprod., Akad. Nauk SSSR, Bashkirsk. Filial*, **7**, 40 (1964).
92. A. R. Derzhinskii, O. S. Chizhov and E. N. Prilezhaeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 850 (1977); *Chem. Abstr.*, **87**, 38791t (1977).
93. A. R. Derzhinskii, L. D. Konyushkin and E. N. Prilezhaeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2070 (1978); *Chem. Abstr.*, **90**, 38501k (1979).
94. A. A. Humffray and H. E. Imberger, *J. Chem. Soc., Perkin Trans. 2*, 382 (1981).
95. D. E. O'Connor and W. I. Lyness, *J. Amer. Chem. Soc.*, **86**, 3840 (1964).
96. W. V. Farrar, *J. Chem. Soc.*, 508 (1956).
97. H. Liebig and H. Pfetzing, Ger 1,256,216 (1967); *Chem. Abstr.*, **69**, 18609q (1968).
98. C. Walling and M. J. Mintz, *J. Org. Chem.*, **32**, 1286 (1967).
99. K. Kikukawa, W. Tagaki, N. Kunieda and S. Oae, *Bull. Chem. Soc. Japan*, **42**, 831 (1969).
100. T. Durst and K.-C. Tin, *Can. J. Chem.*, **49**, 2374 (1971).
101. T. Durst, K.-C. Tin and M. J. V. Marcil, *Can. J. Chem.*, **51**, 1704 (1973).
102. R. Annunziata, M. Cinquini and S. Colonna, *J. Chem. Soc., Perkin Trans. 1*, 282 (1975).
103. G. Barbiere, M. Cinquini, S. Colonna and F. Montanari, *J. Chem. Soc. (C)*, 659 (1968).
104. R. Annunziata, M. Cinquini and S. Colonna, *J. Chem. Soc., Perkin Trans. 1*, 2057 (1972).
105. P. S. Radhakrishnamurti and N. C. Sahu, *Ind. J. Chem.*, **20A**, 269 (1981).
106. Y. Sato, N. Kunieda and M. Kinoshita, *Mem. Fac. Eng. Osaka City Univ.*, **18**, 135 (1977).
107. Rangaswamy [sic] and H. S. Yathirajan, *Curr. Sci.*, **50**, 757 (1981).
108. D. K. Padma, R. A. Shaw, A. R. Vasudeva Murthy and M. Woods, *Int. J. Sulfur Chem.*, **A1**, 243 (1971).
109. P. S. Radhakrishnamurti and S. C. Padhi, *Curr. Sci.*, **46**, 517 (1977).
110. K. Ganapathy and P. Jayagandhi, *J. Ind. Chem. Soc.*, **56**, 1036 (1979).

111. D. S. Mahadevappa, M. B. Jadhav and H. M. K. Naidu, *Int. J. Chem. Kinet.*, **11**, 261 (1979).
112. M. B. Jadhav, H. M. K. Naidu and D. S. Mahadevappa, *J. Ind. Chem. Soc.*, **57**, 693 (1980).
113. D. S. Mahadevappa, M. B. Jadhav and H. M. K. Naidu, *React. Kinet. Catal. Letters*, **14**, 15 (1980).
114. K. Ganapathy and P. Jayagandhi, *Int. J. Chem. Kinet.*, **15**, 129 (1983).
115. D. S. Mahadevappa, M. B. Jadhav and H. M. K. Naidu, *Ind. J. Chem.*, **20A**, 665 (1981).
116. W. Tagaki, K. Kikukawa, N. Kumeda and S. Oae, *Bull. Chem. Soc. Japan*, **39**, 614 (1966).
117. B. G. Cox and A. Gibson, *J. Chem. Soc., Perkin Trans. 2*, 1355 (1973).
118. L. A. Carpino and J. R. Williams, *J. Org. Chem.*, **39**, 2320 (1974).
119. P. S. Radhakrishnamurti and N. S. Sahu, *Kinet. Katal.*, **22**, 627 (1981); *Chem. Abstr.*, **95**, 68656k (1981).
120. C. Srinivasan, S. Rajagopal and N. Thirunavukarasu, *Oxidat. Commun.*, **4**, 403 (1983).
121. S. M. Pandey, J. Sharma, O. Prakash and S. P. Mushran, *Ind. J. Chem.*, **20A**, 1021 (1981).
122. D. S. Mahadevappa, M. B. Madegowda, S. Ananda and K. S. Rangappa, *Ind. J. Chem.*, **23A**, 325 (1984).
123. D. S. Mahadevappa, S. Ananda, A. S. A. Murthy and K. S. Rangappa, *Tetrahedron*, **40**, 1673 (1984).
124. P. S. Radhakrishnamurti and S. C. Padhi, *Ind. J. Chem.*, **17A**, 57 (1979).
125. P. Müller and J. Godoy, *Helv. Chim. Acta*, **66**, 1790 (1983).
126. O. B. Helfrich and E. E. Reid, *J. Amer. Chem. Soc.*, **42**, 1208 (1920).
127. K. Stelmach, *Chem. Anal.*, **11**, 627 (1966).
128. A. G. Perkin and W. G. Sewell, *J. Chem. Soc.*, 3023 (1923).
129. R. Tschesche, US Pat. 2,382,924 (1945); *Chem. Abstr.*, **40**, 361^2 (1946).
130. T. Matsukawa, B. Ohta and T. Imada, *J. Pharm. Soc. Japan*, **70**, 77 (1950).
131. P. S. Radhakrishnamurti and S. C. Padhi, *Curr. Sci.*, **43**, 715 (1974).
132. C. Srivasan, R. Venkatasamy and S. Rajagopal, *Ind. J. Chem.*, **20A**, 505 (1981).
133. V. Balaiah and P. V. V. Satyanarayana, *Curr. Sci.*, **54**, 384 (1985).
134. H. Bredereck, A. Wagner and A. Kottenhahn, *Chem. Ber.*, **93**, 2415 (1960).
135. L. H. Krull and M. Friedman, *J. Chrom.*, **26**, 336 (1967).
136. G. Malewski and L. Mitzinger, *Monatsber. Deut. Akad. Wiss. Berlin*, **10**, 74 (1968); *Chem. Abstr.*, **70**, 77239n (1969).
137. G. B. Barlin and W. V. Brown, *J. Chem. Soc.* (*C*), 921 (1969); D. J. Brown and P. W. Ford, *J. Chem. Soc.* (*C*), 568 (1967).
138. L. A. de Oliveira, H. E. Toma and E. Giesbrecht, *Inorg. Nucl. Chem. Letters*, **12**, 195 (1976).
139. S. Wolfe and C. F. Ingold, *J. Amer. Chem. Soc.*, **105**, 7755 (1983).
140. H. B. Henbest and S. A. Khan, *J. Chem. Soc., Chem. Commun.*, 1036 (1968).
141. E. Block, E. R. Corey, R. E. Penn, T. L. Renken and P. F. Sherwin, *J. Amer. Chem. Soc.*, **98**, 5715 (1976).
142. D. Scholz, *Monatsch. Chem.*, **112**, 241 (1981).
143. N. G. Devi and V. Mahadevan, *J. Chem. Soc., Chem. Commun.*, 797 (1970).
144. Y. R. Rao and P. K. Saiprakash, *Acta Ciencia Indica*, **5C**, 92 (1972).
145. H. K. Pratihari, A. K. Roy and P. L. Nayak, *J. Ind. Chem. Soc.*, **53**, 4 (1976).
146. G. Neogi, S. Acharya, R. K. Panda and D. Ramaswamy, *Int. J. Chem. Kin.*, **15**, 881 (1983).
147. P. S. Radhakrishnamurti and S. C. Padhi, *J. Ind. Chem. Soc.*, **54**, 1097 (1977).
148. C. Djerassi and R. R. Engle, *J. Amer. Chem. Soc.*, **75**, 3838 (1953).
149. G. Neogi, S. Acharya, R. K. Panda and D. Ramaswamy, *Int. J. Chem. Kinet.*, **15**, 945 (1983).
150. T. Takagi, *Yukagaku*, **24**, 319 (1975); *Chem. Abstr.*, **83**, 164782w (1975).
151. S. Bhaduri, A. Ghosh and H. Khwaja, *J. Chem. Soc., Dalton Trans.*, 447 (1981).
152. S. Bhaduri and H. Khwaja, *J. Chem. Soc., Dalton Trans.*, 415 (1983).
153. H. J.-M. Dou, H. K. Zadeh and M. Crozet, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **284**, 685 (1977).
154. D. G. Lee and N. S. Srinivasan, *Sulfur Letters*, **1**, 1 (1982).
155. J. Hoyle, unpublished results.
156. N. A. Noureldin, W. B. McConnell and D. G. Lee, *Can. J. Chem.*, **62**, 2113 (1984).
157. G. Bontempelli, F. Magno, G. A. Mazzocchin and R. Seeber, *Electroanal. Chem. Interface Electrochem.*, **55**, 109 (1974).
158. D. Cipris and D. Pouli, *J. Electroanal. Chem.*, **69**, 423 (1976).
159. R. M. Dodson, N. Newman and H. M. Tsuchiya, *J. Org. Chem.*, **27**, 2707 (1962).

160. B. J. Auret, D. R. Boyd and H. B. Henbest, *J. Chem. Soc., Chem. Commun.*, 66 (1966).
161. B. J. Auret, D. R. Boyd, H. B. Henbest and S. Ross, *J. Chem. Soc.* (*C*), 2371 (1968).
162. B. J. Auret, D. R. Boyd and H. B. Henbest, *J. Chem. Soc.* (*C*), 2374 (1968).
163. T. Sugimoto, T. Kokubo, J. Miyazaki, S. Tanimoto and M. Okano, *J. Chem. Soc., Chem. Commun.*, 1052 (1979).
164. B. J. Auret, D. R. Boyd, H. B. Henbest, C. G. Watson, K. Balenovic, V. Polok, V. Johanides and S. Divjak, *Phytochemistry*, **13**, 65 (1974).
165. Y. Watanabe, T. Iyanagi and S. Oae, *Tetrahedron Letters*, **23**, 533 (1982).
166. J. Tiews, L. Floegel, E. Scharrer and N. Harre, *Berl. Muench. Tieraerztl. Wochenschr.*, **85**, 161 (1972); *Chem. Abstr.*, 77, 96734f (1972).
167. K. I. H. Williams, K. S. Whittemore, T. N. Mellin and D. S. Layne, *Science*, **149**, 203 (1965).
168. H. B. Hucker, P. M. Ahmad and E. A. Miller, *J. Pharmacol. Exp. Ther.*, **154**, 176 (1966).
169. H. B. Hucker, P. M. Ahmad, E. A. Miller and R. Brobyn, *Nature*, **209**, 619 (1966).
170. E. Gerhards and H. Gibian, *Ann. N.Y. Acad. Sci.*, **141**, 65 (1967).
171. H. B. Hucker, J. K. Miller, A. Hochberg, R. D. Brobyn, F. H. Riordan and B. Calesnick, *J. Pharmacol. Exp. Ther.*, **155**, 309 (1967).
172. K. I. H. Williams, S. H. Burstein and D. S. Layne, *Arch. Biochem. Biophys.*, **113**, 251 (1966).
173. K. Nishikawa, S. Kikuchi and Z. Suzuoki, *Eur. J. Pharmacol.*, **9**, 111 (1970) and references cited therein.
174. R. Tanikaga, Y. Higashio and A. Kaji, *Tetrahedron Letters*, 3273 (1970).
175. R. Tanikaga and A. Kaji, *Bull. Chem. Soc. Japan*, **46**, 3814 (1973).
176. K. Gollnick and H. U. Stracke, *Pure Appl. Chem.*, **33**, 217 (1973).
177. P. D. Kennewell, *Chem. Soc. Rev.*, **9**, 477 (1980).
178. J. K. Whitehead and H. R. Bentley, *J. Chem. Soc.*, 1572 (1952).
179. H. Kwart and A. A. Khan, *J. Amer. Chem. Soc.*, **89**, 1950 (1967).
180. C. R. Johnson, R. A. Kirchhoff, R. J. Reischer and G. F. Katekar, *J. Amer. Chem. Soc.*, **95**, 4287 (1973).
181. M. A. Sabol, R. W. Davenport and K. K. Andersen, *Tetrahedron Letters*, 2159 (1968).
182. D. Carr, T. P. Seden and R. W. Turner, *Tetrahedron Letters*, 477 (1969).
183. Y. Tamura, K. Sumoto, J. Minamikawa and M. Ikeda, *Tetrahedron Letters*, 4137 (1972).
184. M. Moriyama, T. Numata and S. Oae, *Org. Prep. Proced. Int.*, **6**, 207 (1974).
185. H. S. Veale, J. Levin and D. Swern, *Tetrahedron Letters*, 503 (1978).
186. P. Stross and G. Satzinger, *Tetrahedron Letters*, 1973 (1974); D. J. Cram, J. Day, D. R. Rayner, D. M. Schriltz, D. J. Duchamp and D. C. Garwood, *J. Amer. Chem. Soc.*, **92**, 7369 (1970).
187. M. Moriyama, T. Yoshimura, N. Furukawa, T. Numata and S. Oae, *Tetrahedron*, **32**, 3003 (1976).
188. K. Akutagawa and N. Furukawa, *J. Org. Chem.*, **49**, 2282 (1984).
189. T. J. Wallace, *J. Org. Chem.*, **30**, 4017 (1965); A. N. Shapovalova, R. N. Sivakova, M. A. Komova, Y. G. Urman and V. I. Lyubomilov, *Osnovn. Org. Sint. Neftekhim.*, **13**, 49 (1980); *Chem. Abstr.*, **97**, 144291w (1982).
190. T. M. Santosusso and D. Swern, *J. Org. Chem.*, **41**, 2762 (1976).
191. C. Chatgilialoglu, B. C. Gilbert, B. Gill and M. D. Sexton, *J. Chem. Soc., Perkin Trans. 2*, 1141 (1980).
192. F. A. Davis, T. W. Panunto, S. B. Awad, R. L. Billmers and T. G. Squires, *J. Org. Chem.*, **49**, 1228 (1984).
193. J. S. Grossert, W. R. Hardstaff and R. F. Langler, *J. Chem. Soc., Chem. Commun.*, 50 (1973).
194. D. Barnard and E. J. Percy, *Chem. Ind.* (*London*), 1332 (1960).
195. P. Allen and J. W. Brook, *J. Org. Chem.*, **27**, 1019 (1962).
196. F. Freeman and C. N. Angeletakis, *J. Amer. Chem. Soc.*, **103**, 6232 (1981).
197. F. Freeman, C. N. Angeletakis and T. J. Maricich, *J. Org. Chem.*, **47**, 3403 (1982).
198. F. Freeman and C. N. Angeletakis, *J. Amer. Chem. Soc.*, **104**, 5766 (1982).
199. Y. H. Kim, T. Takata and S. Oae, *Tetrahedron Letters*, 2305 (1978).
200. S. Oae, T. Takata and Y. H. Kim, *Tetrahedron*, **37**, 37 (1981).
201. S. Oae, T. Takata and Y. H. Kim, *Bull. Chem. Soc. Japan*, **54**, 2712 (1981).
202. A. J. Bridgewater and M. D. Sexton, *J. Chem. Soc., Perkin Trans. 2*, 530 (1978).
203. H. Viertler, P. D. Nachion, J. F. Ganzerli, V. L. Pardini and P. R. Schumacher, *An. Simp. Bras. Electroquim, Electroanal. 3rd.*, **1**, 173 (1982); *Chem. Abstr.*, **98**, 4279r (1983).
204. R. N. Haszeldine, R. B. Rigby and A. E. Tipping, *J. Chem. Soc., Perkin Trans. 1*, 676 (1973).

205. R. B. Ward, US Pat. 3,346,606 (1967).
206. M. S. Raasch, *J. Org. Chem.*, **45**, 2151 (1980).
207. L. A. Paquette, *J. Amer. Chem. Soc.*, **86**, 4089 (1964).
208. L. A. Paquette and L. S. Wittenbrook, *J. Chem. Soc., Chem. Commun.*, 471 (1966).
209. C. Y. Meyers, L. L. Ho, G. J. McCollum and J. Branca, *Tetrahedron Letters*, 1843 (1973); C. Y. Meyers and L. L. Ho, US Pat. 3,876,689 (1975).
210. L. A. Harmon and R. J. Lagow, *J. Chem. Soc., Perkin Trans. 1*, 2675 (1979).
211. M. Wechsberg, Ger. Offen., 2,725,211 (1978); *Chem. Abstr.*, **90**, 84603t (1979).
212. G. Toennies and T. F. Lavine, *J. Biol. Chem.*, **105**, 107 (1934).
213. C. S. Allbright and C. J. Thompson, in *The Analytical Chemistry of Sulfur and its Compounds* (Ed. J. H. Karchner), Part I, Chap. 2, Wiley–Interscience, New York, 1970.
214. ASTM Standards, D1266-64T, Part 17, Amer. Soc. for Testing and Materials, Philadelphia, PA, 1966, p. 456.
215. W. Hempel, *Z. Angew. Chem.*, **5**, 393 (1892).
216. J. M. Corliss and E. J. W. Rhodes, *Anal. Chem.*, **36**, 394 (1964).
217. ASTM Standards, D129-64, Part 17, Amer. Soc. for Testing and Materials, Philadelphia, PA, 1966, p. 67.
218. O. Brunck, *Z. Angew. Chem.*, **18**, 1560 (1905); G. H. Young, *Ind. Eng. Chem. Anal. Ed.*, **10**, 686 (1938).
219. F. Pregl, *Die quantitaive organische Mikroanalyse*, 3rd ed., Springer, Berlin, 1930, pp. 131–165; E. W. D. Huffman, *Ind. Eng. Chem., Anal. Ed.*, **12**, 53 (1940).
220. S. W. Parr, W. F. Wheeler and R. Berolzheimer, *J. Ind. Engl. Chem.*, **1**, 689 (1909).
221. *Official Methods of Analysis of the Association of Official Analytical Chemists*, 11th ed., 1970, p. 31.
222. L. Carius, *Ann.*, **116**, 1 (1860); L. Carius, *Ann.*, **136**, 129 (1865); L. Carius, *Ber.*, **3**, 697 (1870).
223. W. Kirsten, *Anal. Chem.*, **25**, 74 (1953).
224. J. B. Niederi, H. Baum, J. S. McCoy and J. A. Kuck, *Ind. Eng. Chem., Anal. Ed.*, **12**, 428 (1940).

CHAPTER **22**

The electrochemical reactivity of sulphones and sulphoxides

JACQUES SIMONET

Laboratoire d'Electrochimie, CNRS, Université de Rennes 1, France

I. INTRODUCTION

Most sulphones are known to react with chemical reducing reagents like dissolved metals or amalgams. However, electron transfers may be produced also directly from metallic or conducting carbon cathodes maintained at a certain potential depending on the desired reducing power. We will discuss the reactivity of sulphones towards electrons issued from cathodes, especially in the light of recent results.

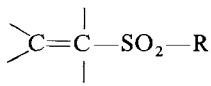
All aromatic sulphones $ArSO_2R$ react with electrons. The nature of the $ArSO_2$ group is sufficiently electroactive so as to allow electron transfer to the sulphone itself, which in most of the cases may trigger off an overall two-electron process leading to a cleavage reaction. In other words, electron transfer is favoured by the combination of the strongly electron-withdrawing —SO_2— group and the electron-rich aromatic moiety. This means that the corresponding energy level of the LUMO of the unsaturated group is notably decreased and allows a much faster charge (or electron) transfer. On the other hand, sulphones RSO_2R' (possessing no aromatic group adjacent to the sulphonyl group) may undergo cathodic reduction only in certain cases including, e.g., olefins activated by an SO_2 group in a vicinal position.

In most cases, the behaviour of sulphones at the cathodic interface (obviously rendered basic when insufficiently buffered due to the accumulation of electrogenerated bases) may be strongly modified by the presence of vicinal CH groups in the α position to the SO_2 group. These acidic groups may transfer protons and are often responsible for low yields of the cleavage processes or for undesirable isomerization reactions.

In contrast, sulphoxides appear to possess a more 'classical' behaviour in electrochemistry, due to their intermediate oxidation state which allows, in most of the cases, their reduction to sulphides but also their oxidation to sulphones with no cleavage process. Moreover, the increase of the sulphur atom basicity may also produce catalytic hydrogen evolution in acidic solution.

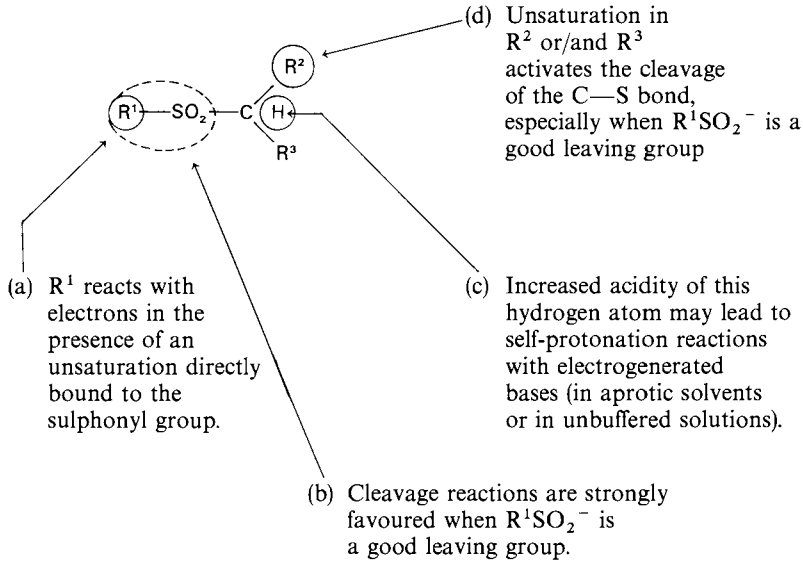
II. ELECTROCHEMICAL BEHAVIOUR OF SULPHONES

The structural requirements of sulphones to react cathodically and to possess specific electrochemical properties are summarized in Scheme 1. In other words, condition (a) means that aromatic sulphones and α unsaturated sulphones are electroactive, i.e., electron transfer to the LUMO leads to the anion radical, but a cleavage reaction (see b) is mainly observed when $R^1SO_2^-$ is a fairly good leaving group. Consequently, the two main classes of electroactive sulphones may react differently: with aromatic sulphones, $ArSO_2$—R, cleavage is strongly favoured, while with unsaturated sulphones:



cathodic saturation of the activated unsaturated bond is generally observed. In addition, conditions (c) and (d) could be considered as minor points influencing the selectivity or/and the yield of the cathodic reaction. Thus, the transfer of a proton from the acidic substrate to the electrogenerated bases formed at the cathodic interface should lead to the formation of the conjugated base of the starting sulphone, which is obviously less electroactive than the starting material. However, it is worth noting that the intermediacy of basic species may promote base-catalyzed rearrangements often affording more easily reducible species. The presence of an unsaturated group β to the —SO_2— group (d in Scheme 1) can activate the C—S bond cleavage even if R^1 is saturated, when the unsaturated R^2 or R^3 would play the role of electron acceptors.

Sulphones are not electroactive anodically. This is probably related to the fact that the



SCHEME 1

—SO_2— group decreases dramatically the energy level of the HOMO. This low reactivity can be overcome since the conjugated base of the sulphone, which is obviously richer in reactive electrons, can produce the corresponding free neutral radical which is able to dimerize.

A. Cathodic Cleavage of Aromatic Sulphones

1. General aspects

All diaryl sulphones $ArSO_2Ar$ and mixed aromatic, aliphatic sulphones $ArSO_2R$ are cleaved by cathodic reduction at fairly reducing potentials (from about -2.1 to -2.4 volts vs. a saturated calomel electrode) at a mercury cathode. The necessity of a rather high energy in order to achieve the preliminary electron transfer and the cleavage (see equations 1 and 2) excludes for most aromatic sulphones the possibility to conduct their electrolyses in acidic solvents or even in protic media, since hydrogen evolution by cathodic reduction of a proton occurring at less reducing potentials may occur. For the same reasons, electrode materials like mercury or cathodically unreactive glassy carbon should be preferred since they need a higher overvoltage for the proton reduction, so that hydrogen evolution is inhibited. However, when mercury is chosen as cathode material, it is necessary to avoid the use of alkali or alkaline earth metal salts as electrolytes because those metallic cations are reduced and form amalgams in the same potential range as that necessary for the cleavage of sulphones.

Thus, under suitable experimental conditions, all aromatic sulphones are cleaved, in most cases by a two-electron process summarized by equations 1 and 2. Such reactions have been established[1–5] by means of coulometric titration, isolation of cleavage residues ArH and RH and chemical identification of the anion $ArSO_2^-$ (e.g. by treatment of the

product mixture with an electrophile such as methyl iodide or benzyl chloride and further identification of the corresponding sulphone).

$$ArSO_2R \xrightarrow[\text{HS solvent}]{2e^-} RH + ArSO_2^- + S^- \quad (1)$$

$$ArSO_2Ar \xrightarrow[\text{HS solvent}]{2e^-} ArH + ArSO_2^- + S^- \quad (2)$$

The overall two-electron mechanism has been generally reported to obey an ECE (Electrochemical–Chemical–Electrochemical) process where the chemical reaction is the generally fast chemical scission of the C—S bond of the sulphone anion radical.

$$ArSO_2R + e^- \longrightarrow [ArSO_2R]^{\cdot -} \quad (3)$$

$$[ArSO_2R]^{\cdot -} \xrightarrow{k} ArSO_2^- + R^{\cdot} \quad (4)$$

$$R^{\cdot} + e^- \xrightarrow{\text{fast}} R^- \quad (5)$$

$$R^- \xrightarrow[\text{such as solvent}]{\text{proton source}} RH \quad (6)$$

The location of reactions 3–6 is quite important for the mechanistic terminology. Reaction 3 in the absence of electrogenerated reducing species occurs only at the conducting interface. Its electrochemical standard potential E°_3 depends principally on the intrinsic structure of the reduced substance (here a sulphone) and its solvation energy. This electron transfer reaction is the elementary stage of the cathodic process. The first electrochemical step may be followed (depending on temperature) by a more or less fast chemical decomposition of the sulphone anion radical. For most aromatic sulphones, this step may be considered as rather fast at room temperature. However, the rate of reaction 4 determines the location of the formation of $R^{\cdot}$. In the case of *very* fast reactions (cleavage of strongly activated C—S bonds) the radical $R^{\cdot}$ appears in the vicinity of the reducing interface itself and reaction 5 may occur (the second electron being *also* provided directly by the cathode). For slower cleavage reactions $R^{\cdot}$ is formed in the diffusion layer, or for very low reaction rates in the solution itself. Thus, the second electron transfer on $R^{\cdot}$ occurs via the transient $ArSO_2R^{\cdot -}$ which plays the role of an electron carrier due to its relative stability. In this case the reduction occurs via a solution electron transfer (SET) reaction

$$R^{\cdot} + [ArSO_2R]^{\cdot -} \rightleftharpoons R^- + ArSO_2R \quad (5')$$

Thus, in the latter case, the term ECE has to be abandoned and replaced by 'disp'. (the SET occurs obviously via a disproportionation process). Finally, the strong base R^- formed after an overall two-electron reaction is protonated by the solvent or by any acidic impurity. Alternative mechanisms could be proposed taking into account that $R^{\cdot}$ or $Ar^{\cdot}$ may abstract hydrogen atoms from the solvent:

$$R^{\cdot} + SH \longrightarrow RH + S^{\cdot} \quad (7)$$

or

$$Ar^{\cdot} + SH \longrightarrow ArH + S^{\cdot} \quad (7')$$

$$S^{\cdot} + e^- \longrightarrow S^- \quad (8)$$

The occurrence of such a mechanism is also subordinated to the value of kinetic constant k (high values of k strongly favour an ECE process, the reduction rate of $R^{\cdot}$ or $Ar^{\cdot}$ being in most cases faster than any other chemical reaction). Electrochemical potential values

necessary for the reduction of neutral free radicals R$^{\bullet}$, Ar$^{\bullet}$ and S$^{\bullet}$ [namely, potential for $R^-/R^{\bullet}$ (E°_5), $Ar^-/Ar^{\bullet}$ ($E^\circ_{5'}$, for R = Ar), $S^-/S^{\bullet}$ (E°_8) redox couples] are easily predicted[67] to be low (E°_5 or E°_8 less cathodic than E°_3) and the two-electron process may finally take place without any large-scale side-reaction.

The electroactivity of aromatic sulphones can be easily visualized by means of current–potential curves like polarography or cyclic voltammetry. When the potential of the working electrode (where in the present case the reduction process occurs) is made more and more reducing, it reaches the energy range where the electron transfer is fast enough and the reduction process may start. For example, in voltammetry (Figure 1) the peak potential (depending for irreversible systems on the potential variation, the concentration and the electrode material) is however well representative of the cathodic reactivity of the substance. For more negative potential values, a decay is noted and is provoked by the fact that the substrate concentration at the interface becomes null. A diffusion process of the sulphone from the bulk to the interface has to take place and the observed limiting current no longer depends on the interfacial electron-transfer kinetics but on the diffusion rate of the electroactive substance in the electrolysis medium. By means of the reverse sweep, one might obtain complementary information on the nature of the electrochemical process.

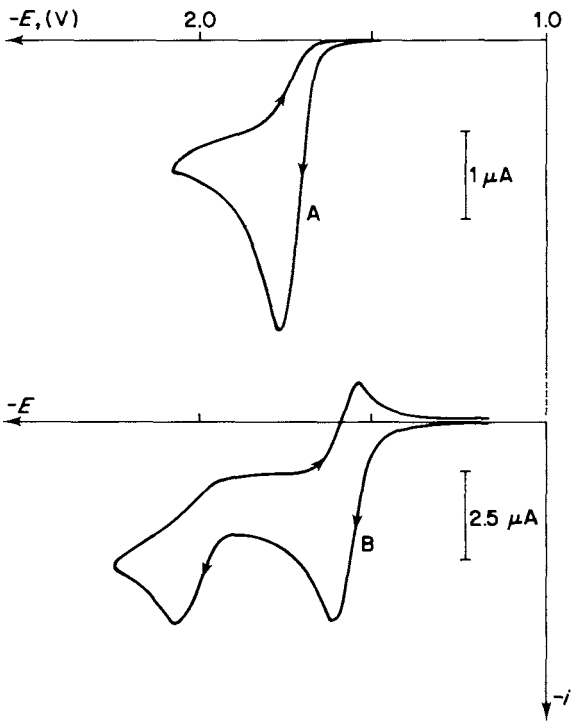


FIGURE 1. Voltammetric curves in DMF in the presence of Bu_4NBF_4 (0.1 M), reference electrode Ag/AgI/I^- (0.1 M), mercury stationary microelectrode: (A) $PhSO_2Me$ (10^{-3} M), sweep rate 500 mV s^{-1}. (B) $PhSO_2Ph$ (10^{-3} M), sweep rate 500 mV s^{-1}.

Thus, in Figure 1A, in the case of phenyl methyl sulphone, the current increases with potential continuously to reach the zero current axis. The process is said to be irreversible because no reducing species is oxidized within this potential range. On the other hand, in Figure 1B diphenyl sulphone shows during the forward sweep (reduction) two peaks, whereas an additional peak, associated with the first reduction peak, is clearly seen during the backward sweep (progressive decay of the reducing power of the electrode). Thus, cyclic voltammetry features a certain stability of the anion radical formed in the first step. The second cathodic step is therefore the reduction of the anion radical into a dianion capable of being cleaved or protonated at that stage. During the reverse sweep, the rather stable anion radical which accumulated in the neighbourhood of the cathode is oxidized. Fully reversible systems (in which the cathodic current is strictly equal to the anodic one) may be observed when the sweep rate is made fast enough to totally overcome the chemical degradation (cleavage, disproportionation, protonation, etc.) of the anion radical. It seems also important to note that the cathodic intensity (for a given sweep rate, when the electrode and the concentration of the substrate are maintained unchanged and when the diffusion coefficients of the electroactive species are fairly constant) is directly proportional to the number of electrons exchanged in the course of the overall process.

Consequently, in conducting aprotic media, most of the diaryl sulphones follow the scheme written below for diphenyl sulphone:

$$PhSO_2Ph \underset{-e^-}{\overset{e^-}{\rightleftharpoons}} [PhSO_2Ph]^{\cdot -} \qquad (9)$$

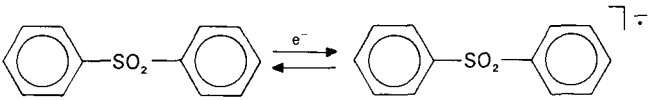
reversible first step (Figure 1B)

$$[PhSO_2Ph]^{\cdot -} \xrightarrow{e^-} [PhSO_2Ph]^{=} \xrightarrow{H^+} \text{Cleavage products} \qquad (10)$$

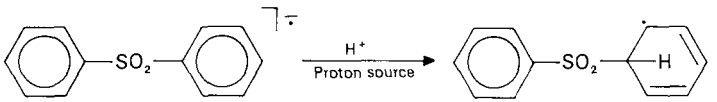
irreversible second step (Figure 1B)

Here, the relative stability of the anion radical confers to the cleavage process a special character. Thus, at a mercury cathode and in organic solvents in the presence of tetraalkylammonium salts, the mechanism is expected[16] to be an ECE one in protic media or in the presence of an efficient proton donor, but of EEC type in aprotic solvents. In such a case, simple electron-transfer reactions 9 and 10 have to be associated chemical reactions and other electron transfers (*at the level* of the first step). Those reactions are shown below in detail:

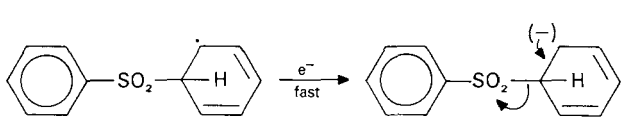
ECE mechanism (the chemical reaction is a protonation)

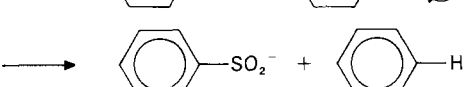


(9)



(11)





(12)

In the case of a slow protonation rate (with inefficient proton donors and/or low concentrations of the proton source), the alternative could be an EECC mechanism through a disproportionation process, still at the potential of the first step.

$$PhSO_2Ph \overset{e^-}{\rightleftharpoons} [PhSO_2Ph]^{\cdot -} \tag{9}$$

$$2[PhSO_2Ph]^{\cdot -} \overset{(K)}{\rightleftharpoons} PhSO_2Ph + [PhSO_2Ph]^{=} \tag{13}$$

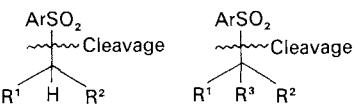
$$[PhSO_2Ph]^{=} \xrightarrow[\text{proton source}]{H^+} [PhSO_2PhH]^{-} \longrightarrow PhSO_2^{-} + PhH \tag{14}$$

The relative importance of the disproportionation process (SET between two anion radicals) depends principally on the thermodynamic constant (K). It can be easily determined more or less accurately from the potential difference existing between the first cathodic peak and the second one. (An exact calculation would be possible from the *thermodynamic* potentials of the two reversible transfers in the absence of proton sources and at reasonable sweep rates so as to inhibit any undesirable chemical reaction.)

2. *Preparative cleavage of aromatic sulphones*

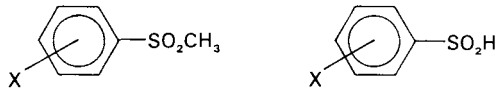
The high preparative interest in a selective removal of *one* arenesulfonyl group connected to an aliphatic chain prompted several chemists to study new modes of reductive cleavage. Thus, it has been found that many sulphones are cleaved under rather mild conditions by classical chemical reductors such as Raney nickel[6], sodium amalgam[7] and alkali metals in amines[8–10]. In addition, preparative electrochemistry may furthermore present an efficient alternative for the cleavage of aryl alkyl sulphones. The reduction of diaryl sulphones (also useful for the removal of strongly electron-withdrawing groups used for orienting a substitution on the ring) is complex, since the regioselectivity of the C—S bond cleavage appears to be strongly dependent on the nature of the substituents on the aromatic rings and therefore will be discussed separately.

a. Aryl alkyl sulphones. In most cases, the regioselectivity of reaction 1 is fully observed and the cleavage gives a fair yield of RH. The cleavage occurs on the S—C linkage so that the formation of the aryl sulphinate anion is nearly always strongly favoured[12,13]. Thus, the cathodic reduction of phenyl methyl sulphone can be performed[12] with a yield of 85% in RH (although traces of R—R are also formed). These preliminary results have been fully confirmed[13] with secondary and tertiary alkyl aryl sulphones.



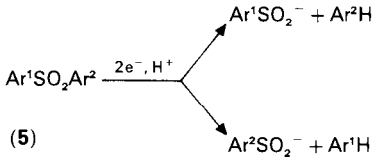
(1) Ar = Ph or *p*-Tol **(2)**

Other data relating to aryl alkyl sulphones with more complex substituents (either electron withdrawing or donating) on the phenyl ring are available[14,15]. However, the nature of substituents [supposed here to be electron unreactive, e.g. 4-NH_2, 4-OCH_3, 4-F, 3,4-$(OCH_3)_2$, 4-CN] may bring large discrepancies in terms of selectivity. Comparisons of reduction potentials between sulphones **3** and the corresponding sulphinic acids **4** are also available[14]. The observed cathodic step in case of **4** should be hydrogen evolution.



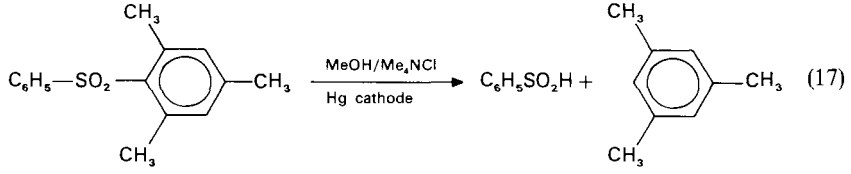
(3) (4)

b. Diaryl sulphones. An extensive study on diaryl sulphones has been published by Horner and Meyer[16]. As already mentioned, the nature of the cleavage may be monitored by means of the introduction of substituents onto the phenyl rings. As shown in Table 1 the cleavage is not always highly selective. However, the ratio Ar^2H/Ar^1H may to a significant extent depend on the cathode material (see, for example, Table 1) but the more efficient donor substituent remains attached in most cases to the sulphinic acid moiety.



(5) (15) (16)

c. Reversal of selectivity and ortho effect. The cleavage may occur differently with liberation of the *more* hindered ArH when a choice exists[16] (equation 17). The introduction of an *ortho* alkyl substituent, which might influence the electronic structure of the C—SO_2—C linkage, may lead also to anomalies in the mode of cleavage and consequently in the selectivity of the bond scission.



(6) (17)

TABLE 1. Macroelectrolytes of (4-aminophenyl) phenyl sulphone (I) and (2-aminophenyl) phenyl sulphone (II) showing the effect of the electrode material and the influence of the *ortho* substituent[a]

Cathode material	Electroactive substance	Reaction potential $-E$ (V)	Electrical yield (%)	benzene (molar yield) (%)	aniline (molar yield) (%)	1,4-cyclohexadiene (molar yield) (%)
Hg		2.24	95	84	9	7
Sn		2.24	48	82	13	5
Pb	I	2.29	64	75	15	10
Cd		2.27	64	76	16	8
Hg		2.14	95	32	68	traces
Sn		2.15	50	32	68	traces
Pb	II	2.21	67	42	58	traces
Cd		2.18	67	35	65	traces

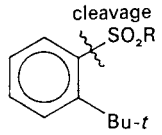
[a]Solvent-electrolyte: tetramethylammonium chloride 0.1 M in methanol; current density (start of the experiment): 22 mA/cm^2; reference electrode: Ag/AgCl/KCl sat. (after Reference 16).

TABLE 2 (after Reference 19)

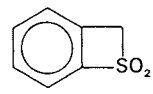
Cyclic sulphone	Solvent	Supporting electrolyte	Alkylation agent after cleavage reaction	Products	Isolated yield
8	MeOH	Me_4NCl	$PhCH_2Cl$	$PhCH_2SO_2CH_2Ph$	35[a]
				o-$TolSO_2CH_2Ph$	9[a]
9	MeOH	Me_4NCl	$PhCH_2Cl$	$Ph(CH_2)_2SO_2CH_2Ph$	30
9	DMF	Et_4NClO_4	$PhCH_2Cl$	$Ph(CH_2)_2SO_2CH_2Ph$	80
10	DMF	Et_4NClO_4	$PhCH_2Cl$	$Ph(CH_2)_3SO_2CH_2Ph$	97
11	DMF	Et_4NClO_4	$PhCH_2Cl$	$Ph(CH_2)_4SO_2CH_2Ph$	68[b]

[a] As mixture.
[b] Possibly also containing benzyl *o*-butyl phenyl sulphone.

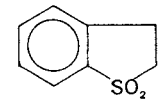
Several studies confirm an '*ortho*' effect leading to a dominating aryl sulphur bond cleavage. For example, the introduction of a bulky *ortho* substituent[17] will provide the formation of the aliphatic sulphinic acid. A series of cyclic sulphones was studied[18,19] at the mercury cathode and the results (see Table 2) appear to be fully in agreement with those expected when considering the preliminary works presented above.



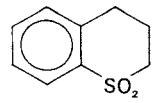
(7)



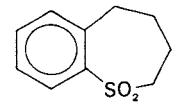
(8)



(9)



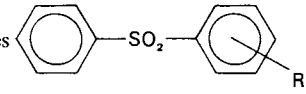
(10)



(11)

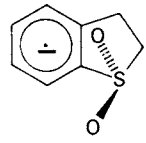
The difference in reactivity could reasonably come from the change in resonance interaction between the sulphonyl group and the aromatic π system as a function of the orientation of the sulphonyl group. Performing MO calculations of the interaction between the sulphur 3d orbitals and the aromatic π system, the symmetry property of the d orbitals must be considered. It could be argued from works[20] taking into account the bulkiness of the $-SO_2^-$ group that, since different d orbitals combine with the π system, according to the orientation of the S—O bonds, the energy levels of the MOs are also different and, in particular, the energy of the LUMO is lowered on going from a bulky cyclic sulphone (e.g. **10**) to the methyl phenyl sulphone conjugation. However, in the light of recent studies on cathodic cleavage in general, it seems more reasonable to consider the structure of the anion radical *before* cleavage and not that of the substrate *before* electron transfer.

Here, a change in the aromatic $-SO_2$ conjugation at the anion radical stage should destabilise differently the C—S bonds. Unfortunately, no kinetic data on the rate of cleavage of the different sulphonic (hindered or not) anion radicals are available for the moment.

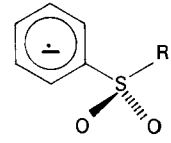
TABLE 3. Reduction of several diaryl sulphones  at a mercury pool cathode[a]

R	Reduction potential (V)	Electro-chemical yield (%)	Benzene (Mol. %)	Other products (Mol. %)
H	−2.07	94	100	
4-CH_3	−2.10	94	65	Toluene: 35
2-CH_3	—	96	20	Toluene: 80
3-CH_3	—	96	55	Toluene: 45
2,4-$(CH_3)_2$	—	95	31	*m*-Xylene: 69
3,4-$(CH_3)_2$	—	96	63	*o*-Xylene: 37
2,4,6-$(CH_3)_3$	—	95	2	Mesitylene: 98
4-NH_2	−2.24	95	84	Aniline: 9 1,4-Cyclohexadiene: 7 1,3-Cyclohexadiene: (traces)
2-NH_2	−2.14	95	32	Aniline: 68 1,4-Cyclohexadiene: (traces)
4-HO	—	83	84	Phenol: 16
2-HO	—	96	24	Phenol: 76
4-CH_3O	−2.16	96	76	Anisole: 24
2-CH_3O	−2.11	96	18	Anisole: 82
4-$(CH_3)_2N$	—	82	86	*N*,*N*-Dimethylaniline: 14
4-HOOC	—	90	0	Benzoic acid: 100
4-CH_3O_2C	−1.57	91	0	Methyl benzoate: 94 Benzyl alcohol: ca. 5 Methyl 1,2,3,4-tetrahydro-benzoate: (traces)
4-CN	−1.58	90	traces	Benzonitrile: 97 Benzylamine: 1 1,2,3,4-Tetrahydrobenzo-nitrile: ca. 1 1,4-Dihydrobenzonitrile: ca. 1

[a] Electrolyte: methanol containing tetramethylammonium chloride and tetramethylammonium hydroxide; current density: 22 mA/cm^2; reference system: Ag/AgCl/KCl sat. (after Reference 16).



(12)

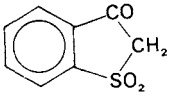


(13)

The influence of the steric effect in the *ortho* position is particularly well demonstrated in Table 3, giving, among others, data for two amino diaryl sulphones.

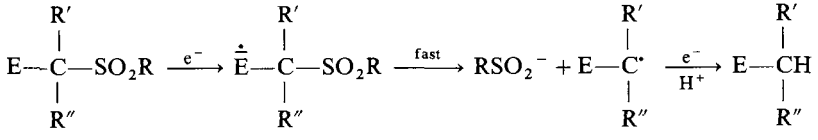
d. Electrophoric groups attached to the sulphonyl moiety. Groups which decrease the energy level of the LUMO and thus activate electron transfer are now usually

TABLE 4. Cathodic cleavage of some β-ketosulphones by fixed potential electrolysis in DMF (after Reference 48)[a]

	Entries	Electrolysis potential E (V)	Coulometry n(F mol^{-1})	Products (yield of conversion %)	
a	$PhCOCH_2SO_2Me$	−1.20	1.98	PhCOMe	(98)
				$MeSO_2Me$	(92)
b	$PhCOCH_2SO_2Et$	−1.20	1.90	PhCOMe	(95)
				$MeSO_2Et$	(91)
c	$PhCOCHMeSO_2Et$	−1.20	2.10	PhCOEt	(98)
				$MeSO_2Et$	(95)
d	$PhCOCH_2SO_2Ph$	−1.10	2.15	PhCOMe	(95)
				$MeSO_2Ph$	(90)
e	$PhCOCH_2Ts$	−1.10	2.00	PhCOMe	(93)
				MeTs	(95)
f	$PhCOCHMeSO_2Ph$	−1.20	1.80	PhCOEt	(97)
				$MeSO_2Ph$	(90)
g	$PhCOCHPhSO_2Ph$	−1.00	1.87	$PhCOCH_2Ph$	(93)
				$MeSO_2Ph$	(88)
14		−0.90	2.10	$CH_3SO_2C_6H_4COCH_3$	(80)

[a]Reference electrode: Ag/AgI/I$^-$ 0.1 M in DMF; working electrode: stirred Hg pool of 10 cm^2 area: mass of substrate cleaved: 1–2 g. In all cases the produced sulfinate anion is methylated by CH_3I at the end of the electrolysis. Ts = p-$MeC_6H_4SO_2^-$.

called 'electrophores' (E). Any such group attached to the carbon bearing the sulphonyl

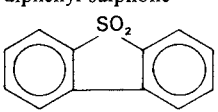


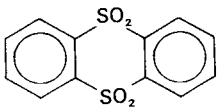
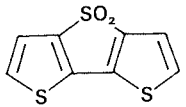
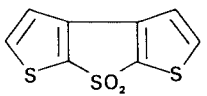
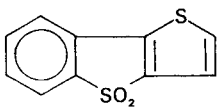
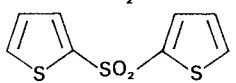
group will strongly favour the C—S cleavage. Thus, electrophores such as styryl or naphthyl groups should help the cleavage reaction especially if the sulphonyl moiety is in an allylic or benzylic position. Similarly, benzoyl groups may strongly activate[47] the C—S scission.

Under different conditions (in aqueous electrolyte) the selectivity of the cleavage reaction may be perturbed by the occurrence[51–53] of a dimerization process. Thus, while the major process remains the two-electron reductive pathway, 20% of a dimer (γ diketone) may be isolated from the cathodic reduction of $PhCOCH_2SO_2CH_3$. The absence of cross-coupling products when pairs of β-ketosulphones with different reduction potentials are reduced in a mixture may indicate that the dimerization is mainly a simple radical–radical coupling[53] and not a nucleophilic substitution.

However, in strongly acidic media, the cleavage may be overcome due to formation of

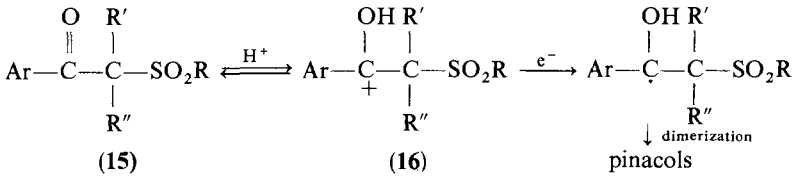
TABLE 5. Analytical and coulometric data concerning some diaryl sulphones and related compounds in aprotic conditions

Substance[a]	Electrolysis product when isolated and coulometric amount at the level of the 1st step ($F\,mol^{-1}$)	Reduction potentials and (experimental conditions)	Ref.
$PhSO_2Ph$	C_6H_6 and $C_6H_5SO_2^-$ at the level of the *second* step (1.99)[b]	1st step: −2.063 V *vs.* Ag/AgCl/KCl sat. 2nd step: −2.498 V (DMF + 0.15 M TBAP)[f] Mercury cathode	1,2
$PhSO_2Ph$	— (3)[c]	1st step: −2.16 V *vs.* SCE 2nd: −2.41 V (DMF + TEAB)[f]	3
$PhSO_2Ph$	— (2.02)	−1.57 V *vs.* Hg pool (DMF + 0.15 M TBAI)[f]	4
2,2′-Dimethyl[e] diphenyl sulphone	— (3.40)	1st step: −2.099 V *vs.* Ag/AgCl/KCl sat. (DMF + 0.15 M TBAP)[f]	2
4,4′-Dimethyl[e] diphenyl sulphone	$C_6H_5CH_3$ + arylsulphinate — (2.46)	1st step: −2.181 V *vs.* Ag/AgCl/KCl sat. 2nd step: −2.612 V (DMF + 0.15 M TBAP)[f]	2
2,6-Dimethyl[e] diphenyl sulphone	Arylsulphinate (2.07)	1st step: −1.779 V *vs.* Ag/AgCl/KCl sat. 2nd step: −2.360 V (DMF + 0.15 M TBAP)[f]	2
2,7-Dimethyl[e] diphenyl sulphone	— (1.67)	−1.400 V *vs.* Ag/AgCl/KCl sat. (DMF + 0.15 M TBAP)[f]	2
	— (1.90)	−1.732 V *vs.* Ag/AgCl/KCl sat. (DMF + 0.15 M TBAP)[f]	2

	$PhSO_2^-$ [d] (1.77)	1st step: −1.311 V *vs.* Ag/AgCl/KCl sat. 2nd step: −1.878 V 3rd step: −2.25 V (DMF + 0.15 M TBAP)[f]	2
	— (1.81)	−1.00 V *vs.* Hg pool (DMF, 0.15 M TBAI)[f]	4
	— (1.95)	−1.02 V *vs.* Hg pool (DMF, 0.15 M TBAI)[f]	4
	— (1.89)	−1.89 V *vs.* Hg pool −0.55 V *vs.* SCE (DMF, 0.15 M TBAI)[f]	4
	— (2.34)	−1.38 V *vs.* Hg pool (DMF, 0.15 M TBAI)[f]	4

[a] The formation of a fairly stable anion radical was reported[5] in all cases at room temperature except on electrolysis in aqueous dioxane.
[b] Coulometric measurement at the level of the first step.
[c] Under protic conditions.
[d] Formation of $PhSO_2^-$ on electrolysis at the level of the second step.
[e] Data on other dimethyl sulphones are available from Reference 2.
[f] TBAP, tetrabutylammonium perchlorate; TEAB, tetraethylammonium bromide; TBAI, tetrabutylammonium iodide.

the protonated form, which on reduction does not cleave but dimerizes:



3. Indirect cathodic reduction of sulphones. Redox catalysis

It is well known[21,22] that organic species RX containing a leaving group X^- which can be irreversibly and rapidly cleaved by cathodic means are, in general, good candidates to undergo *indirect* reductions in solution via an electron carrier. Evidence exists for this, both in analytical and preparative scales in the reactivity of aromatic sulphones toward the rather stable reduced forms of conjugated organic π systems. Thus Figure 2 shows that pyrene in dry DMF, in the presence of a quaternary ammonium salt within a potential range consistent with the solvent/electrolyte electroactivity, leads to two successive single electronic transfers (appearance of two peaks on curve **a**, Figure 2). The first electron transfer on pyrene is reversible—as shown by an anodic peak during the reverse sweep of which the current is about equal to that of the cathodic peak—whereas a second electron transfer (further reduction of the anion radical of pyrene into dianion) is not. The two reduction steps for pyrene correspond to the electrochemical reactions 18 and 19.

$$\textit{First step}\quad \text{Pyrene} \overset{e^-}{\rightleftharpoons} [\text{Pyrene}]^{\cdot} \qquad E^\circ_1 = -155\,\text{V} \tag{18}$$

$$\textit{Second step}\quad [\text{Pyrene}]^{\cdot -} \rightleftharpoons [\text{Pyrene}]^{=} \qquad E^\circ_2 = -185\,\text{V} \tag{19}$$

$$\xrightarrow[\text{as proton donors}]{\text{acidic impurities}} \text{dihydropyrenes}$$

Let us now consider another organic species, such as a sulphone $ArSO_2R$ known to be irreversibly reduced *less* easily than pyrene. The basic mechanism for its cathodic reduction has already been presented (reactions 3–6). It is necessary, however, to assume here that the chemical degradation of the anion radical when produced in solution is at least reasonably fast.

The reactivity of pyrene anion radical toward $ArSO_2R$ may be demonstrated as follows: adding some $ArSO_2R$ to the pyrene solution leads to an *increase* of the peak current corresponding to reduction of the pyrene, while this step becomes progressively irreversible. It may also be noted that for small amounts of $ArSO_2R$, the specific step for the sulphone more or less vanishes. This corresponds to the following scheme:
At the cathode/solution interface:

$$\text{Pyrene} \overset{e^-}{\rightleftharpoons} [\text{Pyrene}]^{\cdot} \tag{18}$$

Electron transfer in solution:

$$[\text{Pyrene}]^{\cdot} + \text{ArSO}_2\text{R} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{Pyrene} + [\text{ArSO}_2\text{R}]^{\cdot} \tag{20}$$

Fast chemical reaction subsequent to the electron transfer in solution:

$$[\text{ArSO}_2\text{R}]^{\cdot} \xrightarrow{k} \text{ArSO}_2^{\cdot -} + \text{R}^{\cdot} \tag{4}$$

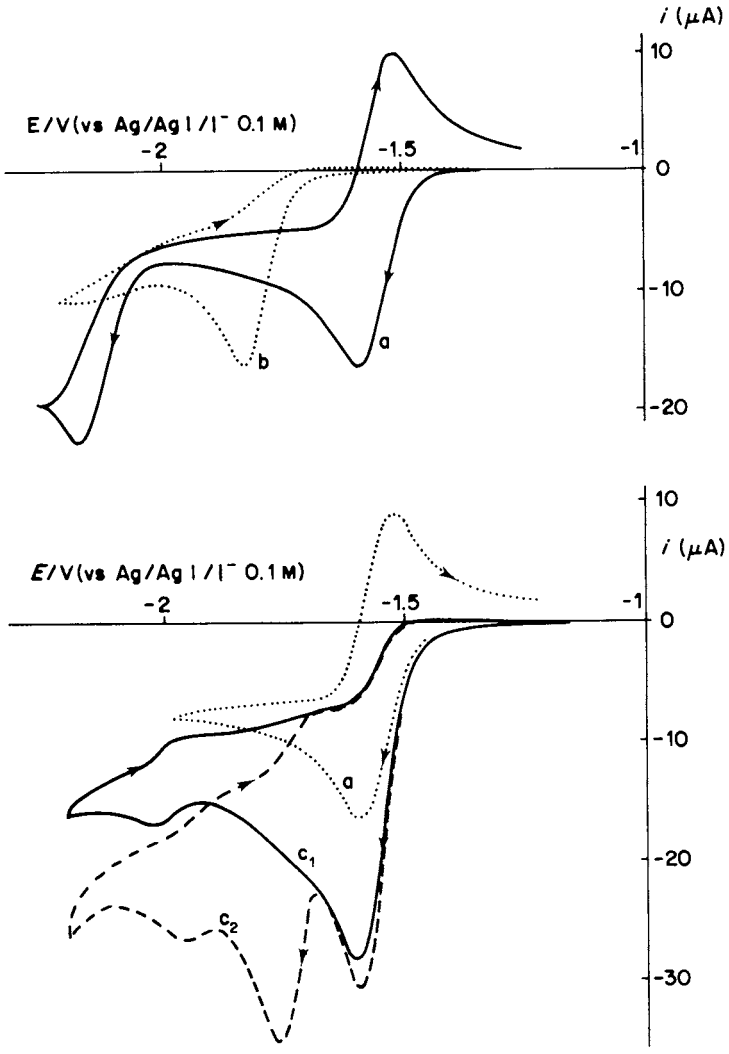


FIGURE 2. Voltammetries in DMF/Bu_4NBF_4 0.1 M, mercury stationary microcathode, sweep rate 100mVs^{-1}: (a) pyrene 2.10^{-3} M; (b) $PhSO_2Bu$-*t* 2.10^{-3} M; (c1) solution (a) with $PhSO_2Bu$-*t* 2.10^{-3} M; (c2) solution (a) with $PhSO_2Bu$-*t* 4.10^{-3} M.

This first single electron transfer (SET) is followed, due to the chemical and electrochemical instability of $R^{\cdot}$, by at least one of the following reactions:

Second SET $$R^{\cdot} + [ArSO_2R]^{\cdot -} \xrightarrow{\text{fast}} R^{-} + ArSO_2R \qquad (21)$$

Reaction with the solvent

$$R^{\cdot} + HS \longrightarrow RH + S^{\cdot} \tag{7}$$

Dimerization

$$R^{\cdot} + R^{\cdot} \longrightarrow R{-}R \tag{22}$$

Disproportionation

$$R^{\cdot} + R^{\cdot} \longrightarrow R^{+} + R^{-} \tag{23}$$

In most cases, when reactions 22 and 23 occur, they do not take place to a major extent. Moreover, the standard potential for the redox couple $R^{-}/R^{\cdot}$ is located, on the potential range, at not very reducing values, often with $E_{R^{-}/R^{\cdot}} \gg E^{\circ}_{1}$. Therefore reaction 21 is expected to be very fast and the redox catalysis process appears to correspond principally to reaction 18 followed by an overall two-electron process *in solution*. In the case of Figure 2, pyrene is the electron carrier and is completely regenerated in the whole process till the total disappearance of the aryl sulphone in solution, thus showing a case of a pure catalysis. It is worth remarking that redox catalysis allows one to reduce sulphones at *less* reducing potentials with an energy gain which may reach 0.5 eV. This is possible for thermodynamic reasons[21] summarized (in a general case where the solvation changes provoked by charge transfer reactions can be neglected) by the potential inequalities.

$$E^{\circ}_{ArSO_2R \rightarrow R^{-}} > E^{\circ}_{ArSO_2R \rightarrow R^{\cdot}} > E^{\circ}_{1} > E^{\circ}_{ArSO_2R} > E^{\circ}_{ArSO_2R/ArSO_2R^{-}}$$

Moreover, redox catalysis may provide valuable information concerning thermodynamics and kinetics. Thus, let us recall that the value of $E^{\circ}_{ArSO_2R/ArSO_2R^{-}}$ and of the kinetic constant k can no longer be obtained (when k is large) from conventional voltammetric techniques, since there is an absolute necessity to reach, when one increases potential sweep rates, the *reversible* one-electron step for $ArSO_2R$. For evident technical reasons (ohmic drop compensation, capacitive current effect) this method unfortunately suffers limitations. While recent work on the theory of redox catalysis by Saveant and his group[23] has contributed much to enlarge the potentialities of voltammetry as a most valuable tool, for the moment, there are practically no data to enable the determination of $E^{\circ}_{ArSO_2R}$ and k by means of the theory of redox catalysis. Below we briefly develop the case for methyl phenyl sulphone.

In this example[24] redox catalysis kinetics is governed partly by chemical reaction, i.e., the scission of $C_6H_5SO_2CH_3^{\cdot-}$. For given concentrations of pyrene and sulphone at sweep rate v one can find values of k_1k/k_2 from published graphs[23] in the case of EC processes.

Pyrene (M)	2.10^{-4}	10^{-3}	2.10^{-3}
$MeSO_2Ph$ (M)	8.10^{-4}	4.10^{-3}	8.10^{-3}
i_p/i_{p_0}	0.37	0.39	0.41
k_1k/k_2	0.6	0.6	1.5

The value of k_1/k_2 may then be obtained from the following relation, which is a thermodynamic consequence of the equilibrium 20:

$$E^{\circ}_{MeSO_2Ph} - E^{\circ}_{pyrene} = 0.06 \log k_1/k_2 \tag{24}$$

Thus in order to obtain the value of k it is absolutely necessary to know the standard cathodic redox potential. In the case of $MeSO_2Ph$, very fast voltammetric measurements at high sweep rates ($1000\ V\ s^{-1}$) permit one to reach the reversible step of the sulphone and give $E^{\circ}_{MeSO_2Ph} = -1.85$ V. Hence, the value $k = 0.9 \times 10^5\ s^{-1}$ may be estimated for the

cleavage reaction. Additional experiments are however necessary to obtain more precise data on k values of other aromatic sulphones.

In many other cases (by a change in experimental conditions, faster chemical reaction) the value of the catalytic current may be governed by the SET rate (see reaction 20). The value of k_1 may be found and its variation as a function of the nature of the mediator (with several values for E°_1) leads by extrapolation (when k_2 can be assumed to be diffusion-controlled) to the thermodynamical potential $E^\circ_{RSO_2Ar}$ which is somewhat different from the 'reduction' potentials of overall ECE processes observed in voltammetry.

However, in all cases it appears important to check that the increase of current for the mediator is determined by the SET (catalytic current) and not by the protonation of the mediator anion radical e.g., in cases of acidic sulphones acting as proton donors.

Large-scale indirect electrolyses have both advantages and disadvantages compared to direct electrolyses. Among the advantages is the relative independence of the cell design. A wrong current distribution at the working electrode (leading to discrepancies of the potential values on its whole area) can be overcome utilizing macroredox catalysis and this permits one to achieve a certain selectivity. Thus, for example to carry out the cleavage of *one* C—S bond of the disulphone **17** is very difficult either by conventional reducing reagents or by direct electrochemical means. The voltammetric data[25] give a very slight energy difference (of about 0.15 V) between the reduction potential of the allylic sulphonyl function (α arrow) and that of the non-activated one (β arrow). This voltammetric behaviour is shown in Figure 3, curve e with two peaks, where the favoured ECE process is obviously the one with the faster chemical reaction. In the presence of anthracene (A), the

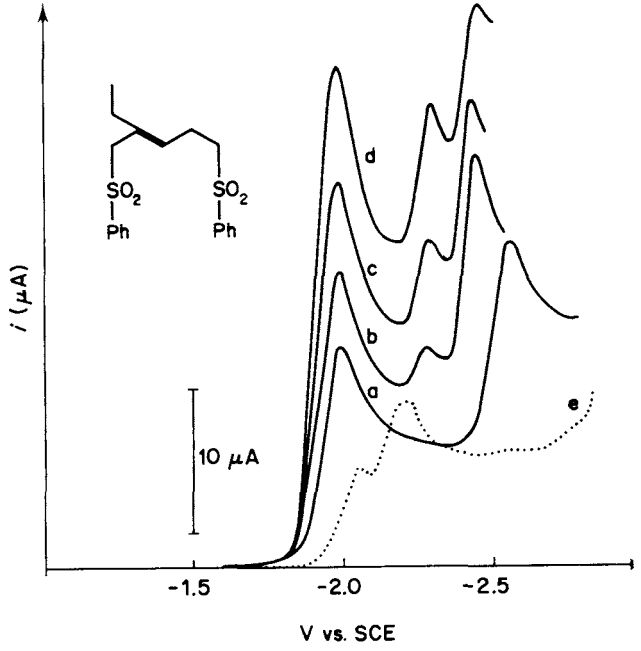
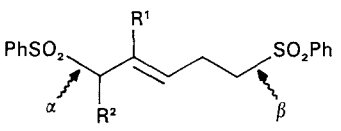


FIGURE 3. Voltammetric curves at a stationary mercury microelectrode for anthracene in the presence of **17b**: (a) anthracene alone, 6.5×10^{-3} M; (b, c, d) previous solution with 2.3, 5.1 and 7.6×10^{-3} M of **17b**; (e) disulphone **17b** without anthracene. Medium, DMF–Bu_4NClO_4 0.14 M; sweep rate, 10 mV s^{-1} (after Reference 25).

homogeneous reduction of a disulphone (YRX) may be schematized as in reactions 25–28. Since the allylic benzenesulphonyl groups (X) are cleaved[25] preferentially to the unactivated ones (Y), it follows that $K_X k_x \gg K_Y k_y$. The mediator A should be chosen in such a way that it has a suitable reduction potential with $K_X k_x$ of an appropriate magnitude, while $K_Y k_y$ should be negligible. Since the X and Y groups are practically isolated, the mediators A can be screened in order to test their cathodic selectivity by using suitable allylic and unactivated aromatic sulphones RX and RY as mixtures.



(17)

(**a**) $R^1 = CH_3$, $R^2 = H$
(**b**) $R^1 = C_2H_5$, $R^2 = H$
(**c**) $R^1 = CH_3$ $R^2 = CH_2CH{=}C(CH_3)_2$

$$A + e \rightleftharpoons A^{\cdot-} \tag{25}$$

$$A^{\cdot-} + YRX \overset{K_X(K_Y)}{\rightleftharpoons} A + YRX^{\cdot-}(XRY^{\cdot-}) \tag{26}$$

$$YRX^{\cdot-}(XRY^{\cdot-}) \xrightarrow{k_x(k_y)} YR^{\cdot} + X^-(XR^{\cdot} + Y^-) \tag{27}$$

$$A^{\cdot-} + YR^{\cdot}(XR^{\cdot}) \xrightarrow{\text{fast}} A + YR^-(XR^-) \tag{28}$$

Thus, 9, 10-diphenylanthracene ($E_p = -1.83$ V vs. SCE) is reduced at too positive a potential and hence its rate of reaction with the sulphonyl moieties is too low. On the other hand, pyrene ($E_p = -2.04$ V) has a too negative reduction potential and exchanges electrons rapidly both with allylic and unactivated benzenesulphonyl moieties. Finally, anthracene ($E_p = -1.92$ V) appears to be a suitable choice, as illustrated in Figure 3 (curves a–d). Using increasing concentrations of the disulphone **17b**, the *second* reduction peak of XRY behaves normally and gives no indication of a fast electron transfer from A.

The selectivity can be further checked by preparative experiments. *Direct* electrolyses on **17a,b** and **c** (at -2.10 V vs. SCE) were reported to consume 3.4–3.8 F mol^{-1}. Analytical determination of $PhSO_2^-$ by anodic polarography (by the anodic wave of the sulphinate) showed that both benzenesulphonyl groups had been cleaved. In contrast, preparative electrolyses on **17a, 17b** and **17c** using anthracene as electron transfer reagent permitted a *selective* cleavage of the allylic $PhSO_2$ group. Thus, in the reduction of **17a** and **17b**, the electrolysis product was shown to possess only *one* unactivated benzenesulphonyl group and no vinylic or allylic benzenesulphonyl group. The indirect reduction of **17a** gave 2-methyl-5-benzenesulphonyl-2-pentene as the major product and a small amount of 2-methyl-5-benzenesulphonyl-1-pentene. These two isomers would be expected by protonation of the allylic anion formed by cleavage of the activated C—S bond.

Redox catalysis appears also to be an elegant way to conduct alkylations. In this case the RX compound has to produce a free radical R which is sufficiently reactive toward the electron carrier A or its reduced form. Generally the mechanism, developed mainly for the case of alkyl halides, may be summarized as in reactions 25, 29–36.

$$A + e^- \rightleftharpoons A^{\cdot-} \tag{25}$$

$$A^{\cdot-} + RX \rightleftharpoons A + RX^{\cdot-} \tag{29}$$

$$RX^{\cdot} \xrightarrow{\text{fast}} R^{\cdot} + X^- \tag{30}$$

coupling with the reduced form of the mediator

$$A^{\cdot -} + R^{\cdot} \longrightarrow AR^{-} \quad (31)$$

$$AR^{-} + RX \longrightarrow \underset{\text{electrophile}}{} AR_2 + X^{+} \quad (32)$$
dialkylation

$$AR^{-} + H^{+} \longrightarrow \underset{\text{proton source}}{} ARH \quad (33)$$
monoalkylation

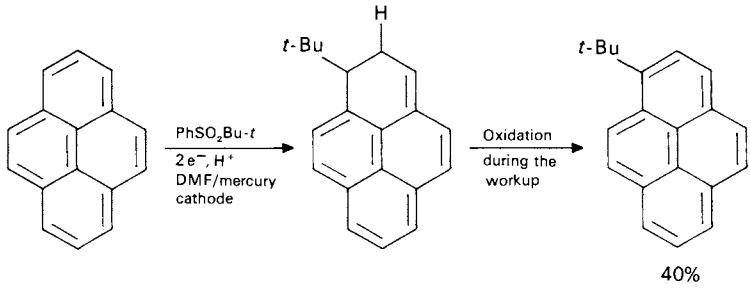
radical addition to the mediator

$$A + R^{\cdot} \longrightarrow AR^{\cdot} \quad (34)$$

$$AR^{\cdot} + A^{\cdot} \longrightarrow AR^{-} + A \quad (35)$$

$$AR^{-} \xrightarrow{RH \text{ or } H} \underset{\text{dialkylated product}}{\text{monoalkylated or}} \quad (36)$$

The ratio ARH/AR_2 (monoalkylation/dialkylation) should depend principally on the electrophilic capability of RX. Thus it has been shown[27,28] that in the case of *t*-butyl halides (due to the chemical and electrochemical stability of *t*-butyl free radical) the yield of *mono* alkylation is often good. Naturally, aryl sulphones may also be employed in the role of RX-type compounds. Indeed, the *t*-butylation of pyrene can be performed[24] when reduced cathodically in the presence of $C_6H_5SO_2Bu$-*t*. Other alkylation reactions are also possible with sulphones possessing an $ArSO_2$ moiety bound to a *tertiary* carbon. In contrast, coupling reactions via redox catalysis do not occur in a good yield with primary and secondary sulphones. This is probably due to the disappearance of the mediator anion radical due to proton transfer from the acidic sulphone.



B. Cathodic Activation of Unsaturated Systems by Sulphonyl Groups

It is well known that the presence of an electron-withdrawing group on a single unsaturated bond leads to a spectacular shift of the electroactivity of the molecule. Thus, mono unsaturated aliphatic chains do not react fast with electrons while the corresponding conjugated enone is easily reduced electrochemically. Similarly vinylic sulphones[29,30,46] can be easily reduced at the mercury cathode. In contrast to most activated olefins[30] (e.g. unsaturated ketones or nitriles), aliphatic sulphones are reported to exhibit reduction potentials which are not dependent on the acidity of the medium within a large range of moderate pH. Moreover, there is scarcely any evidence for dimer formation. Consequently, the behaviour of unsaturated sulphones is quite exceptional within the class of activated olefins. Many alkyl vinyl sulphones[31] are reduced in aqueous alcoholic solutions in two-electron processes, and yield (Table 6) the corresponding alkyl ethyl

TABLE 6. Cathodic reduction of unsaturated sulphones[a]

Unsaturated sulphone	Reduction potential (Electrolyte)[c]	Product	Coulometry ($F\,mol^{-1}$)	Ref.
$CH_3SO_2CH{=}CH_2$	−1.08 V *vs.* SCE (10% EtOH. buffered media)	$CH_3SO_2C_2H_5$	—	29
$CH_3SO_2CH{=}CH_2$	−1.8 V *vs.* SCE (aqueous TEAOTs)[c]	?	—	30
$CH_3SO_2CH{=}CH_2$	−1.76 V *vs.* SCE (aqueous MeOH/LiCl)	?	3.10	32
$C_2H_5SO_2CH{=}CH_2$	−1.735 V *vs.* SCE (aq. EtOH/TEAI)[c]	$C_2H_5SO_2C_2H_5$	4.06[b]	31
Other $RSO_2CH{=}CH_2$ (R: complex alkyl groups)	between −1.8 to −2.065 V (aq. EtOH/TEAI)[c]	$RSO_2C_2H_5$	3.6 to 6.3[b]	31
$C_2H_5SO_2CH{=}CHSO_2C_2H_5$				
trans	−0.88 V *vs.* SCE			
cis	−0.73 V *vs.* SCE (10% EtOH/KCl)	$(C_2H_5SO_2CH_2)_2$	—	33
$C_6H_5CH_2SO_2CH{=}CH_2$	−1.67 V *vs.* SCE (aqueous MeOH/LiCl)	$C_6H_5CH_2SO_2C_2H_5$	2.98	32
$C_6H_5CH_2SO_2CH{=}CHCH{=}CH_2$				
trans	−1.50 V *vs.* SCE			
cis	−1.50 V *vs.* SCE (aq. MeOH, pH 9.2)	$C_6H_5CH_2SO_2C_2H_5$	—	34
$CH_3SO_2C{\equiv}CH$	−1.110 V *vs.* SCE (aq. EtOH/LiCl) second wave	$CH_3SO_2CH{=}CH_2$	—	35
	−1.790 V *vs.* SCE	$CH_3SO_2C_2H_5$	—	35
$RSO_2C{\equiv}CH$ (R: C_2 to C_4 alkyl substituents)	from −1.120 V to −1.175 V *vs.* SCE (aq. EtOH + LiCl)	$RSO_2C_2H_5$	—	35

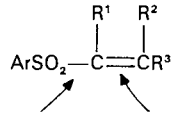
[a] The $-SO_2^-$ group is linked to an aliphatic carbon.
[b] Low current yields could be due to hydrogen evolution.
[c] TEAOT, Et_4N^+ tosylate; TEAI, Et_4NI.

sulphones.

$$\underset{\textbf{(18)}}{RSO_2CH{=}CH_2} \xrightarrow[\substack{H_2O/EtOH\,50\% \\ Et_4NCl \\ -1.7\text{ to }-2.0\text{ V} \\ \text{vs. SCE}}]{2e^-,2H^+} \underset{\textbf{(19)}}{RSO_2CH_2CH_3}$$

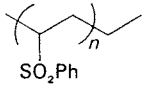
A surprising exception has been reported with evidence for a cleavage reaction in the case of divinyl sulphone[32]. In non-aqueous and slightly acidic media, the behaviour of α,β-unsaturated aromatic sulphones is also complex (see Table 7) since the cleavage and the saturation may compete[24]. Strongly electrophilic double bonds undergo Michael additions in aprotic solvents by slowly protonated anions. Transfer of labile hydrogen may also lead to unactivated bases[26]. It is noteworthy that in numerous cases (Table 6) the saturation is the preferred route.

$$\underset{\textbf{(20)}}{CH_2{=}CHSO_2CH{=}CH_2} \xrightarrow[\substack{6.5<pH<11 \\ 10\text{-}50\%\ MeOH \\ LiCl \\ -1.55\text{ V vs. SCE}}]{2e^-,H^+} CH_2{=}CHSO_2^- + CH_2{=}CH_2$$



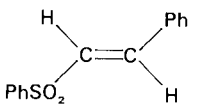
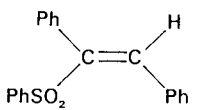
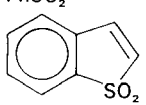
(21)

In dry dimethylformamide, phenyl vinyl sulphone (Figure 4) is reduced[24] in two steps: surprisingly, the first peak usually has a larger current than the second, and the ratio between these two currents (depending on concentration) is not strongly affected by the presence of an efficient proton donor. Thus, phenol or dilute perchloric acid have only a small effect. In aprotic solvents, coulometric measurements carried out at the level of the first step demonstrate that the reaction involves one electron whereas it involves two electrons in the presence of an efficient proton donor such as perchloric acid. The potential of the second peak (and comparison with authentic samples) could be in agreement with either the partial formation of a dimer (in aprotic media) or a saturation process (in protic media). However, cleavage of the anion radical of phenyl vinyl sulphone seems to agree more with the experimental facts. The overall reaction would remain monoelectronic since the vinyl radical is not electroactive. Under other experimental conditions (higher concentrations of substrate, adding small amounts of a proton donor), polymerisation should be favoured: in the latter case, the coulometric measurement of 2 faradays per mole of substrate has to take into account the fact that all the electroactive moieties have totally disappeared from the electrolysis solution. On the other hand, soluble phenyl alkyl sulphones (such as phenyl ethyl sulphone) are *indirectly* reduced at the first step by presumed redox catalysis involving the phenyl vinyl sulphone anion radical. Consequently, a similar indirect cathodic process could be expected for the polysulphone **(22)** continuously produced in the reduction process by means of a radical polymerization process. In the presence of acetic acid dimer formation is observed accompanied by a small amount of the saturated compound.



(22)

TABLE 7. Cathodic reduction of unsaturated sulphones[a]

Aromatic unsaturated sulphones	Reduction potentials (electrolyte)[b]	Main product	Coulometry ($F\,mol^{-1}$)	Ref.
$C_6H_5SO_2CH{=}CH_2$	-1.47 V *vs.* SCE (aq. ethanol—basic pH)	$C_6H_5SO_2C_2H_5$	—	36
$C_6H_5SO_2CH{=}CH_2$	-1.55 V *vs.* SCE (aq. MeOH, LiCl; $6.5 < pH < 11$	$C_6H_5SO_2C_2H_5$	2.98	32
$C_6H_5SO_2CH{=}CH_2$	1st step: -1.53 V *vs.* Ag/AgI/I^- 0.1 M 2nd step: -1.83 V (DMF, TBAP 0.1 M with acetic acid)[b]	Dimeric disulphone	0.9	24
$C_6H_5SO_2CH{=}CH_2$	1st step: -1.54 V *vs.* Ag/AgI/I^- 0.1 M 2nd step: -1.8 V (DMF, TBAP + 10^{-2} M $HClO_4$)[b]	$C_6H_5SO_2C_2H_5$	1.6	24
	1st step: -1.15 V *vs.* Ag/AgI/I^- 0.1 M 2nd step: -1.63 V (DMF/TEAP)[b]	Polystyrene	1.87	37
	1st step: -1.20 V *vs.* Ag/AgI/I^- 0.1 M (DMF/TEAP)[b]	*trans*-stilbene 25% *cis*-stilbene 5% Bibenzyl 20%	1.63	37
	1st step: -1.07 V *vs.* Ag/AgI/I^- 0.1 M 2nd step: -1.59 V (DMF/TEAP 0.1 M)[b]	Hydrodimer in aprotic medium Dihydro derivative (phenol as proton donor)	1.0 2.2	37 37
$(C_6H_5SO_2CH{=}CH{\rightarrow}_2$	-0.96 V *vs.* SCE (aq. MeOH—pH 9.2)	?	—	34
p-$TolSO_2CH{=}CH_2$	-1.61 V *vs.* SCE (aq. MeOH—pH 9.2)	Saturation	—	34
p-$TolSO_2CH{=}C{=}CH_2$	1st step: -1.36 V *vs.* SCE 2nd step: -2.09 V (aq. MeOH—pH 9.2)	*p*-$TolSO_2CH_2CH{=}CH_2$	—	34
p-$TolSO_2C{\equiv}CCH_3$	1st step: -1.46 V *vs.* SCE (aq. MeOH—pH 9.2)	*p*-$TolSO_2CH{=}CHCH_3$	—	34

[a] The $-SO_2^-$ moiety in linked to an aromatic group
[b] TBAP, Bu_4NClO_4; TEAP, Et_4NClO_4.

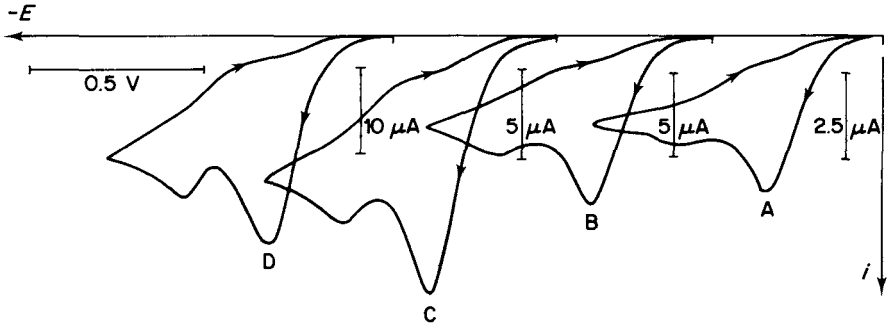
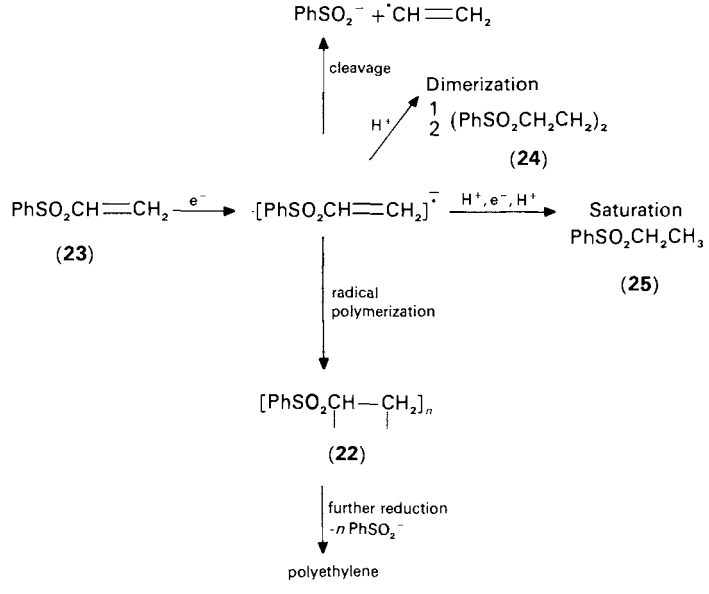


FIGURE 4. Cyclic voltammetries of $PhSO_2CH{=}CH_2$ in dry DMF/Bu_4NBF_4 0.1 M, working microelectrode of mercury, starting potentials -1.2 V. vs. Ag/AgI/I^- (0.1 M) system, sweep rate 100 mV s^{-1}, Sulphone concentration: (A) 2×10^{-3} M; (B) 4×10^{-3} M; (C) 6×10^{-3} M; (D) 10^{-2} M.

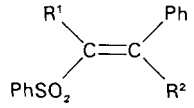
More data are obviously necessary to elucidate carefully the cathodic behaviour of the model molecule **23**. The complexity of the many chemical pathways shown in Scheme 2 may illustrate the electrochemical reactivity of unsaturated sulphones in general.

At this point, special mention[37] should be made of the behaviour of highly conjugated ethylenic sulphones in weakly acidic media. For example, in the case when $R^1 = Ph$ (*Z* isomer), a fairly stable anion radical was obtained in dry DMF. However, either in aprotic (consecutive two one-electron transfer) or in protic media (ECE process, occurrence of the protonation step on anion radical), C—S bond cleavage is observed. The formation of the corresponding olefins by C—S bond cleavage may occur in high yield, and is nearly quantitative when $R^1 = H$ and $R^2 = Ph$ for an electrolysis conducted in



SCHEME 2

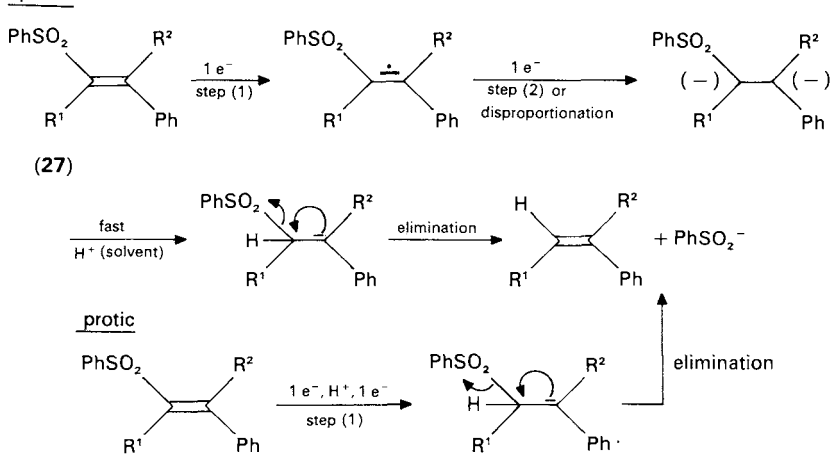
protic medium at -1.4V vs. Ag/AgI/I$^-$ 0.1 M electrode.



(**26**)

The cleavage mechanism can be clarified by cyclic voltammetries as shown in Figure 5. In aprotic solution (curves a) steps (1) and (2) correspond to the successive electron transfers leading finally to the dianion. On the other hand, in protic solution (curve c), step (2) has disappeared while step (1) has grown and then obviously corresponds to an ECE process. Anyhow, and whatever the medium, step (3) is identified as that in which the produced olefin (here 1, 1-diphenylethylene) is reduced in all cases.

The same overall cleavage process may occur via one of two main pathways (see Scheme 3) according to proton availability in the electrolysis solution.



SCHEME 3

The cleavage of some more complex aryl methyl sulphones may occur in a similar way. This is actually the case[38] with α and β naphthyl methyl sulphones for which the cleavage does not occur directly via the radical anion but through a scheme involving protonation. A similar process is probably available[45,47] for most sulphonyl groups (aryl or alkyl) attached to a π system. The cleavage of such sulphones is exemplified[38] by the behaviour of methyl β-naphthyl sulphone **28** (see Scheme 4). It can be easily seen from Scheme 4 that α acetylenic aromatic sulphones may be reduced[24] through three steps, although the use of aqueous electrolytes makes the observation of the third one difficult due to the cathodic limit of the solvent:

$$\underset{\textbf{(29)}}{ArSO_2{-}C{\equiv}CR} \xrightarrow[2H^+]{2e^-} \underset{\textbf{(30)}}{ArSO_2{-}CH{=}CHR} \xrightarrow[2H^+]{2e^-} \underset{\textbf{(31)}}{ArSO_2{-}CH_2{-}CH_2R}$$

$$\xrightarrow[H^+]{2e^-} ArSO_2^- + CH_3CH_2R$$

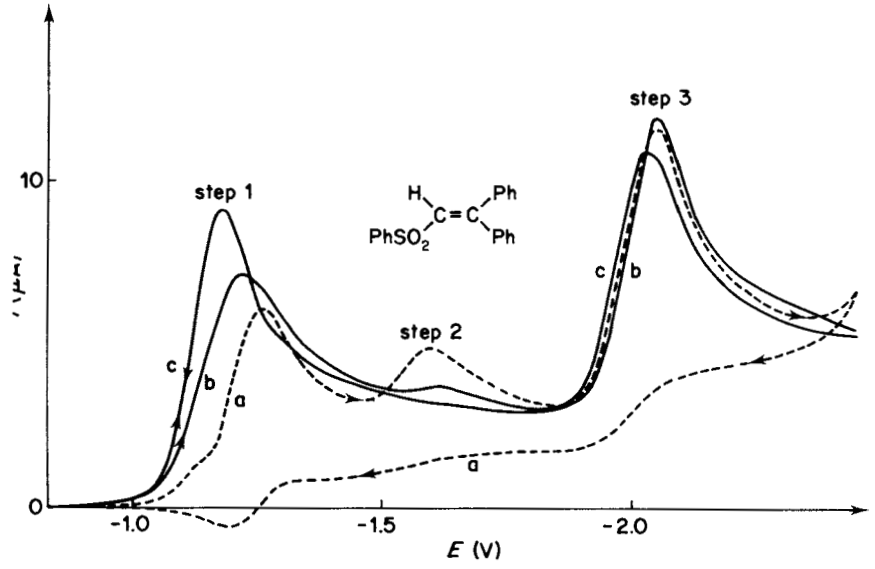
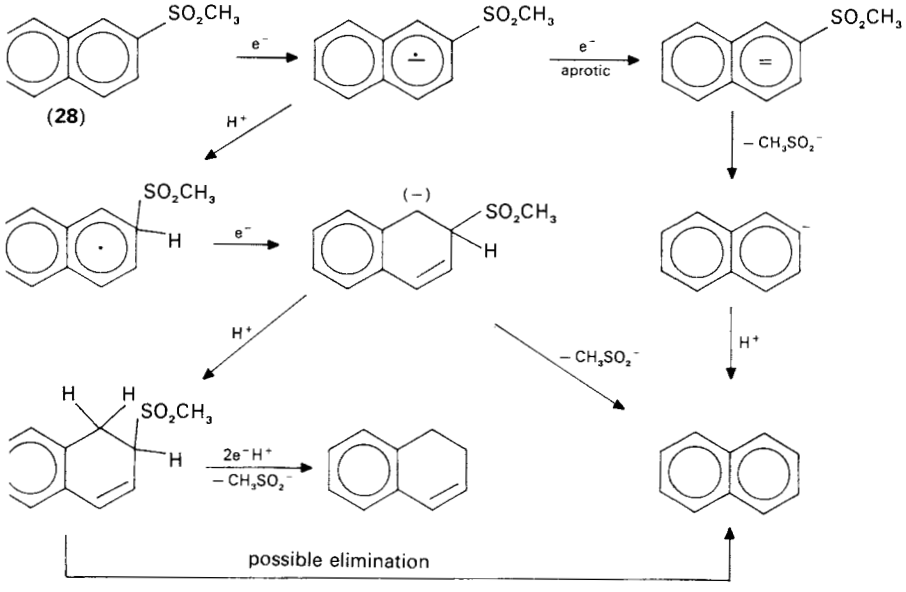
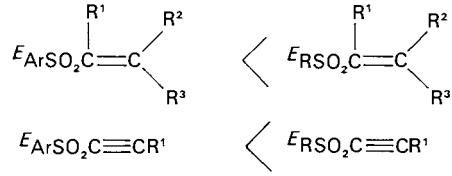


FIGURE 5. Voltammograms at a microelectrode of mercury of 2,2-diphenylvinyl phenyl sulphone in DMF, sweep rate 600 mV s^{-1}, substrate concentration 10^{-3} M: broken line curve (a) without proton donor present, full line curves (b) and (c) with phenol at concentration 0.5 and 4×10^{-3} M, respectively, reference electrode Ag/AgI/I^- 0.1 M in DMF (after Reference 37).



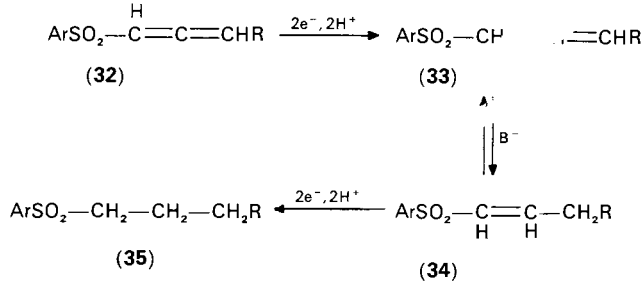
SCHEME 4

Data are also available with α-acetylenic aliphatic sulphones, which involve only two steps i.e., saturation of the triple bond *without* subsequent cleavage of the $C_{aliphatic}$—S bond, since it is not reactive. However, the introduction of an aromatic ring to the SO_2 group does not lead, contrary to what is observed with enones, to a potential shift toward less reducing potential values. Thus, the aromatic moiety introduced apparently does not bring any additional conjugation effect but even seems to decrease the activation of the unsaturated bond, as shown by data in Tables 6 and 7 where most of the potentials refer to the same saturated calomel electrode under similar experimental conditions.



α-Allenic sulphones were also studied in aqueous electrolyte solutions. Logically, the saturation occurs[34] first at the double bond directly attached to the —SO_2— group. The formation of a fully saturated sulphone (4e reduction) seems to be subordinated to isomerisation of the β, γ isomer into the α, β one, (especially in basic media or in the absence of buffers in slightly protic solvents.

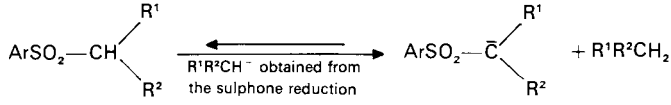
The obtaining of *two* steps (with an overall four-electron proc vas shown to be a function of the efficiency and concentration of the proton donc heme 5).



SCHEME 5

C. Influence of the Acidity of Sulphones on their Cathodic Behaviour

From the electrochemical point of view, the presence of a mobile hydrogen in β position to the sulphonyl group has *two* main effects: a fast proton transfer in weakly protic media from the non-reduced substrate to the so-called electrogenerated bases (i.e. the organic anions produced by cleavage of the sulphone C—S bond). This leads to the formation of a fairly stable conjugate base of the sulphone, which is unactive, although its reduction may occur at much more reducing potentials.



(36)

Moreover, under well-defined experimental conditions, the organic anion produced may be unstable and undergo isomerisation or/and elimination. Several examples of side-reactions or unexpected formation of new electroactive species at the cathodic interface are listed in the following subsections.

1. Deactivation in the presence of electrogenerated bases

The use of *aprotic* (and therefore totally *unbuffered*) media in analytical studies of sulphones may lead to wrong conclusions. The voltammetric determination of the benzyl phenyl sulphone[26] was aimed to clearly exemplify the deactivation process in dry dimethylformamide. So, in aprotic or low acidity solvents, two main steps (equivalent to the transfer of one electron each) can be seen (Figure 6, curve 1). These two steps were shown at the potential of the cleavage (-1.7 volt) to correspond, for acidic sulphones, to the following processes:

$$PhSO_2CH_2Ph \xrightarrow{1\,e^-} PhSO_2CH_2Ph^{\cdot -}$$

$$PhSO_2CH_2Ph^{\cdot -} \xrightarrow[\text{fast}]{} PhSO_2^- + {}^{\cdot}CH_2Ph$$

$${}^{\cdot}CH_2Ph \xrightarrow{1\,e^-} {}^-CH_2Ph$$

$${}^{(-)}CH_2Ph + PhSO_2CH_2Ph \rightleftharpoons CH_3Ph + PhSO_2\overset{(-)}{C}HPh$$

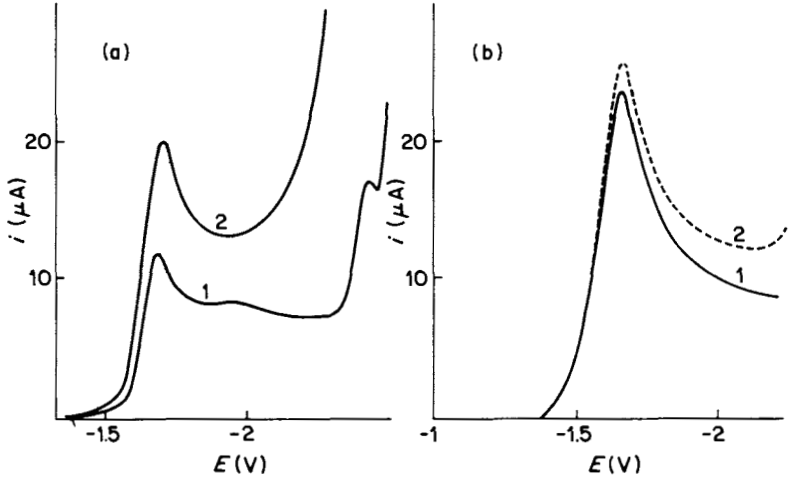


FIGURE 6. Voltammetric curves in DMF–TBAP 0.1 M, stationary mercury micro-electrode, sweep rate $10\,mV\,s^{-1}$: (1) without phenol, (2) 10^{-2} M phenol added; (a) $PhSO_2CH_2Ph$, (b) $PhSO_2C(Et)(Me)Ph$.

with an overall balance of *one* electron per electroactive species:

$$2PhSO_2CH_2Ph \xrightarrow{2e^-} PhSO_2^- + CH_3Ph + PhSO_2\bar{C}HPh$$

Of course, such a reaction implies a very slow rate of protonation of the anionic deactivated form.

At more highly reductive potentials a specific step may occur for the highly conjugated anion:

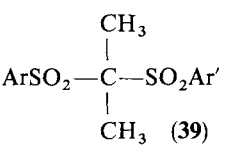
$$PhSO_2\bar{C}HPh \xrightarrow[\text{solvent contribution}]{2e^-} \text{further cleavage}$$

The slow protonation rate of the conjugated anion of the sulphone (1st step) leads to the obtainment of a *pseudo* one-electron process. However, no self-protonation process exists in the presence of an excess of a proton donor of lower pK_a than that of the electroactive substrate and Figure 6a, curve 2 shows evidence for a two-electron step. Full substitution on the α carbon, as in the case of phenyl 2-phenylbut-2-yl sulphone, does not allow one to observe any deactivation (Figure 6b, curve 1). It is worth mentioning that cathodic deactivations of acidic substrates in aprotic solvents are rather general in electrochemistry, e.g. aromatic ketones behave rather similarly, showing deprotonation of the substrate by the dianion of the carbonyl compound[39].

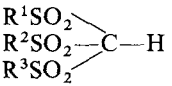
2. *Cathodic behaviour of gem di- and tri-sulphones*

Aromatic sulphones **36** in which R^1 and/or R^2 are electron-withdrawing substituents should behave as mentioned above. This is the case[40,41] for β disulphones **37** and **38**, for which the first cleavage in aprotic solvent also leads to deactivation phenomena. The electricity consumption should be one electron per mole with recovery of half of the starting material after electrolysis and work up. In contrast, **39** exhibits two steps for each C—S bond cleavage whatever the nature of the medium. However, the behaviour of *gem* trisulphones **40** appears to be quite unexpected. Thus, in the case of triarylsulfonyl methanes ($R^1 = R^2 = R^3 =$ aryl), one step is observed in the potential range -1.4 to -1.5 V *vs.* SCE and the complex reduction process corresponds to hydrogen evolution concomitant with a partial cleavage of one C—S bond (see Scheme 6). The addition of an excess of base (such as Et_4NOH) to the trisulphone allows only *one* main step to be observed at about -2.5 V (Figure 7, curve b). The reduction of the anion is discussed below.

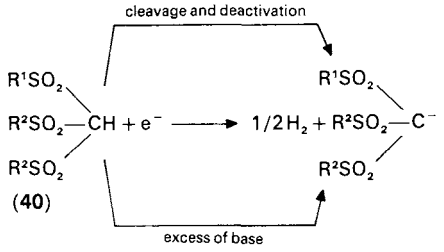
$ArSO_2CH_2SO_2Ar$ (**37**) $\qquad$ $ArSO_2CH_2SO_2CH_3$ (**38**)



(**39**)



(**40**) (R^1, R^2, R^3 aromatic or/and aliphatic)



SCHEME 6

3. A specific cathodic reduction step for sulphonyl anions

A reduction step specific to the cleavage of *gem* trisulphonyl anions has been described[43]. Such a step may correspond to the selective cleavage of *one* C—S bond due to the fact that the strong electron-withdrawing effect of the sulphonyl groups can balance the coulombic repulsion of the anionic charge located formally on the central carbon atom. Two main kinds of cleavage may occur in cases when X is *p*-Me, *m*-Me, *p*-F or *p*-CH_3O in Scheme 7. The selectivity of the cleavage is determined by the facts that the $XC_6H_4SO_2^-$ group is a much better leaving group and that no significant protonation of the produced anion occurs within the duration of the electrolysis. This mode of cleavage of conjugated anions may be proposed as a good synthetic route to obtain non-symmetric sulphones.

Ar^1SO_2, Ar^2SO_2—C^-, Ar^3SO_2 and Ar^1SO_2, Ar^2SO_2—C^-, R^1SO_2

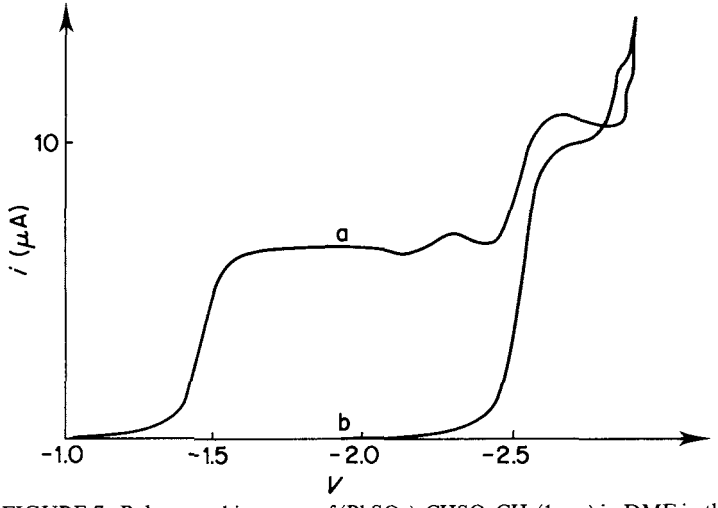


FIGURE 7. Polarographic curves of $(PhSO_2)_2CHSO_2CH_3$(1 mM) in DMF in the presence of Et_4NBr 0.1 M: curve a, response in neutral DMF; curve b, obtained in the presence of an excess of Et_4NOH (after Reference 42).

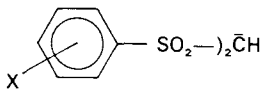
$$(XC_6H_4SO_2)_3C^- \xrightarrow[H^+(\text{solvent})]{2e^-} (XC_6H_4SO_2)_2\bar{C}H + XC_6H_4SO_2^-$$

$$(XC_6H_4SO_2)_2\bar{C}SO_2CH_3 \xrightarrow[H^+(\text{solvent})]{2e^-} XC_6H_4SO_2^- + XC_6H_4SO_2\bar{C}HSO_2CH_3$$

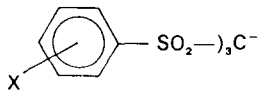
$$XC_6H_4SO_2\bar{C}HSO_2CH_3 \xrightarrow{\text{protonation during the work-up}} XC_6H_4SO_2CH_2SO_2CH_3 \quad (100\%\ \text{selectivity})$$

SCHEME 7

In contrast, it was shown[42,44] that organic anions possessing several intrinsic possibilities of cleavage such as haloaryl di- and trisulphones favour always the prior scission of the C—X bond owing to specific deactivation of the central —SO_2—C—SO_2— linkages, whereas the protonated form (especially in the first case above) may behave in a totally different way: here a selective cleavage of the C—S bond is observed representing an easy synthesis of halogenated sulphinic acids.

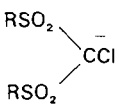


X = Br, Cl, F

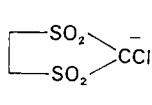


Similarly[44] the presence of a good leaving group (other than a sulphonyl group) on the central atom may shift in certain cases the potential of the specific step for the anion. However, the potential appears to be strongly dependent on the structure of the β-disulphone. Thus, gem chloro disulphonyl anion possessing an open chain such as **41** does not exhibit a specific cathodic step, whereas **42** and **43** are reduced at -2.04 V and -2.65 V *vs.* ECS, respectively. The surprising large difference in the case of electroreduction seems to depend on the structural effect which would favour the cleavage of the C—Cl bond. The reduction mechanism probably implies the formation of a transient radical dianion cleaved very fast with expulsion of the halide anion exclusively. Due to the low basicity of the anion, its protonation before the electron transfer appears to be excluded. The intermediate formation of a carbon anion radical (route 1, Scheme 8) was postulated, but there is no clear evidence of its existence.

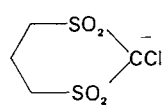
Other similar cyclic structures may present quite unexpected behaviour. Let us give the example of **46**, where X is Cl or Br. Such structures are very easily reduced[44] (polished platinum microelectrodes are preferred owing to the reaction of mercury with C—X linkages), and the presence of an anion radical of some stability can be demonstrated in the



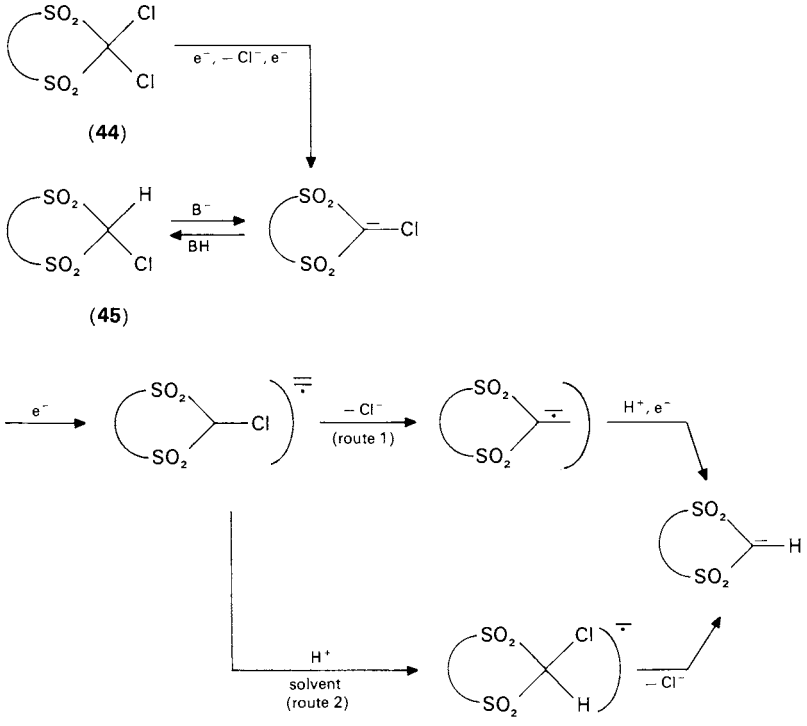
(41)



(42)



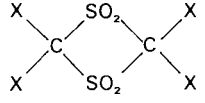
(43)



(44)

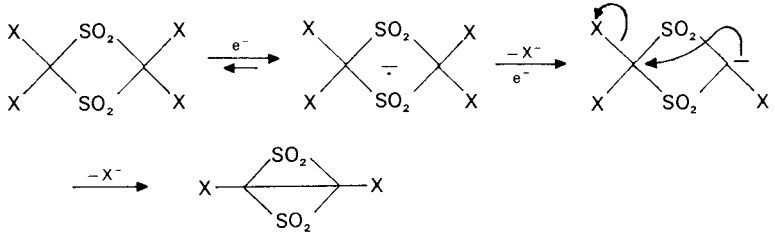
(45)

SCHEME 8



(46)

case where X = Cl. In aprotic media, cathodic reaction occurs with the transfer of two electrons and loss of no more than two X^- ions, suggesting the formation of an intramolecular carbon–carbon bond (47):



(47)

4. Cathodic behaviour of allylic and propargylic sulphones in low-acidity solvents

Benzylic, allylic and propargylic positions enhance the cathodic cleavage rate of C—heteroatom bonds as, for example, in the reduction of benzylic and allylic halides or alcohols[56]. Similar activated sulphones, due to their acidity, are in a class apart. Figure 8 shows the similitude between the cathodic behaviour of an allylic sulphone and its isomer, i.e., the corresponding vinylic sulphone when the electrolyses are run in an aprotic solvent. However, in the presence of an excess of proton donor, discrepancies appear.

Figure 8 exhibits two simultaneous phenomena, i.e., an isomerization process concomitant with the deactivation. Hence both sulphones show a decay of 50% in the main step and the appearance of a new step at very reducing potentials (curves a_1 and b_1). This behaviour is very similar to that of benzylic sulphones. The deprotonation process by the electrogenerated bases (EGB) formed in the first step, involving a cleavage for the allylic or saturation for the vinylic sulphone, is accompanied by isomerization which implies that the two isomers behave identically. A slight difference can be seen at the foot of the voltammetric step of the vinylic sulphone. This early step could be considered as an intermediate stage between the a_1 and a_2 curves at low concentration of the EGBs. Thus the behaviour of allylic and vinylic sulphones may be very similar and discrepancies are *only* noticeable in protic solvents. Under the experimental conditions given above, the

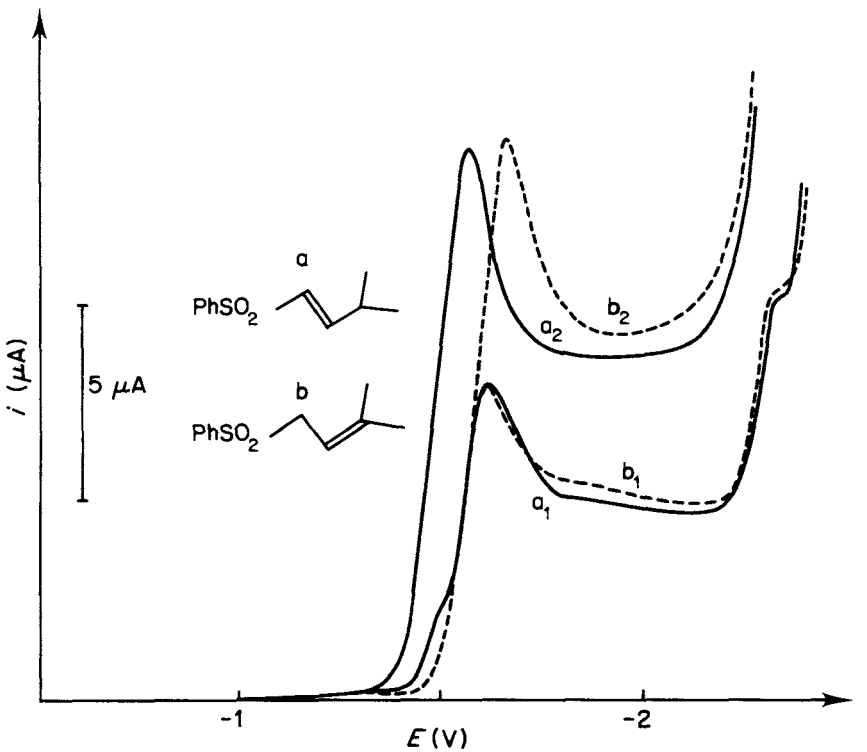
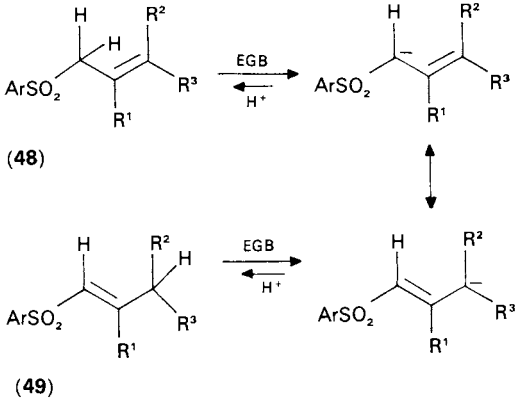
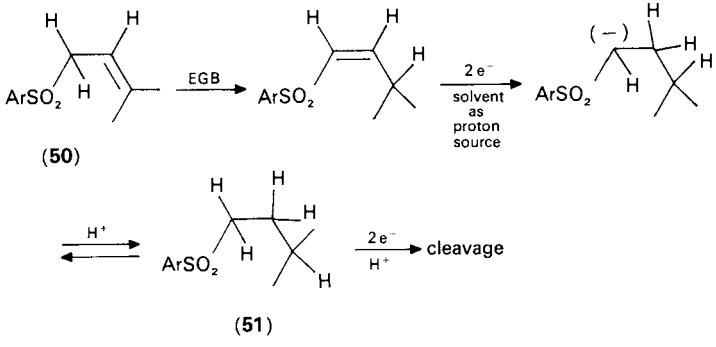
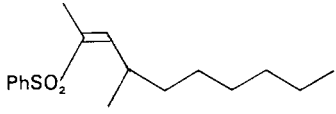


FIGURE 8. Voltammetries in DMF–TBAP 0.1 M, stationary mercury electrode, sweep rate $10\,mV\,s^{-1}$, concentration of sulphones 5×10^{-3} M: (1) in aprotic DMF, (2) DMF with phenol (10^{-2} M) (after Reference 26).

isomerization b → a is observed and allows the saturation of the moving double bond as shown below. Thus allylic aromatic sulphones are reduced in aprotic solvents according to an overall two-electron process.[26] This means that the electrolysis solution becomes more and more basic in the course of the reduction and finally, due to the high pH value, the conjugated base of the resulting saturated sulphone is totally stable and therefore deactivated. Hence further electrochemical reaction (i.e. cathodic cleavage) *does not* occur. Such a selectivity caused by the basicity of the solvent is also observed with vinylic sulphones. For example, **52** gives only a two-electron reaction in dry DMF (1.8 F mol^{-1} coulometry) but a four-electron overall process in the presence of an efficient proton donor-like phenol (found, 3.2 F mol^{-1}).







(52)

However, a very unexpected situation is found[24] for the phenyl allyl sulphone (**53**), for which a *one*-electron cleavage occurs in aprotic non-aqueous solvents. The allyl radical is apparently not electroactive at the cleavage potential, and forms the dimer. Therefore, in this one-electron bond scission no strong base is formed and the isomerization into the vinylic isomer is not observed (Figure 9). Similarly, the cleavage of phenyl propargyl

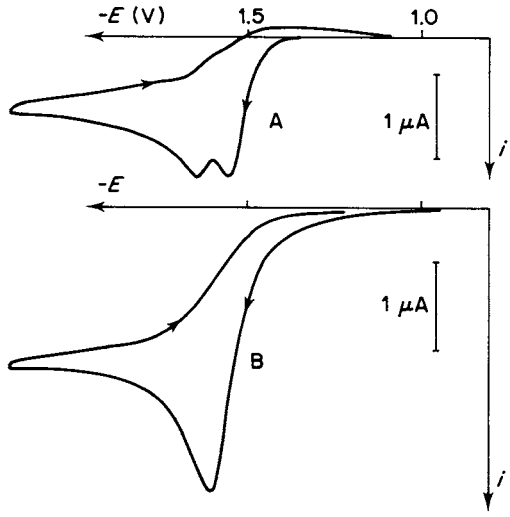
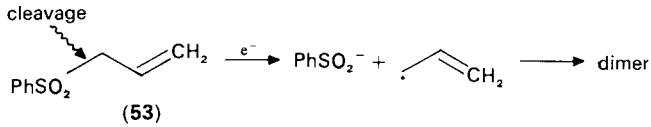


FIGURE 9. $PhSO_2CH_2—CH=CH_2$ (10^{-3} M) voltammetries in dry DMF/Bu_4NBF_4 0.1 M, sweep rate 50 mV s^{-1}, working microelectrode of mercury, reference Ag/AgI/I^- 0.1 M: (A) voltammetry without proton donor added; (B) solution (A) in the presence of 2×10^{-3} M phenol.

sulphone also leads to the formation of a dimer[49]. Radical coupling can explain the dimer formation, but other mechanisms taking into account the transient formation of the conjugated base (acting as a nucleophile towards the substrate) could also be proposed. In the presence of a proton donor *at moderate concentration*, six-electron process is found which implies the isomerization of the phenyl propargyl sulphone (**54**) into its allenic isomer (**55**).



$$PhSO_2—CH_2C{\equiv}CH \xrightarrow{e^-} PhSO_2^- + \tfrac{1}{2}\,\begin{matrix}CH_2C{\equiv}CH\\ |\\ CH_2C{\equiv}CH\end{matrix}$$

(54)

$$PhSO_2—CH_2C{\equiv}CH \xrightarrow[(EGB)]{B^-} PhSO_2—CH{=}C{=}CH_2$$

(54) (55)

$$\xrightarrow[2H^+]{2e^-} PhSO_2CH_2—CH{=}CH_2$$

(53)

$$\xrightarrow[EGB]{B^-} PhSO_2CH{=}CH—CH_3 \xrightarrow[2H^+]{2e^-} PhSO_2—CH_2CH_2CH_3$$

(56) (57)

$$\xrightarrow[H^+]{2e^-} PhSO_2^- + CH_3CH_2CH_3$$

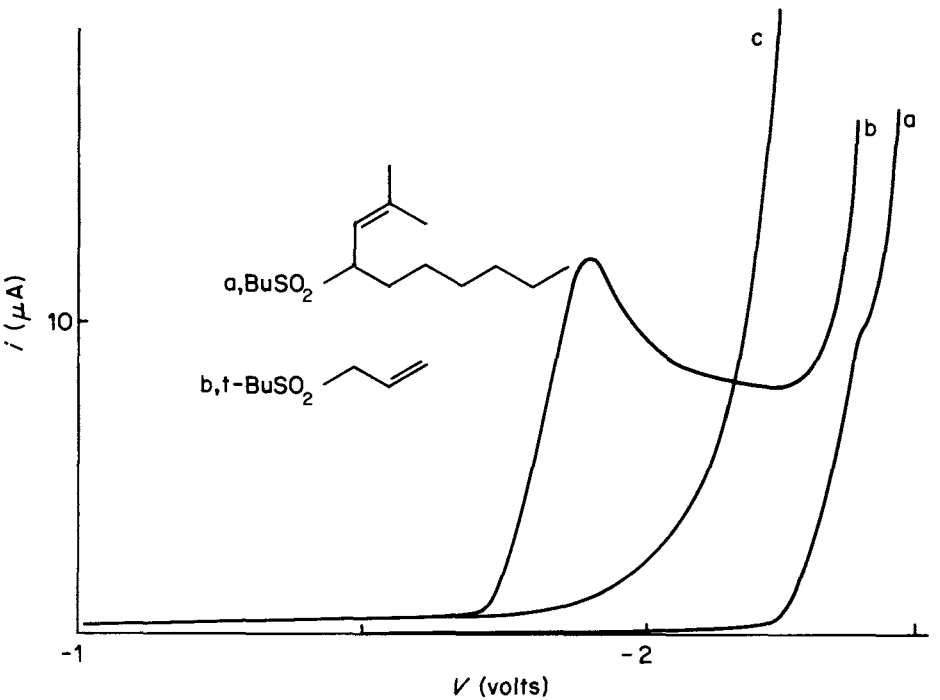
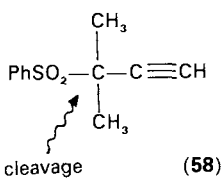
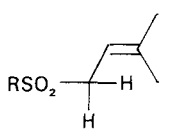


FIGURE 10. Voltammetric curves of fully aliphatic allylic sulphones ($c = 3 \times 10^{-3}$ M) in DMF/TBAP 0.1 M electrolyte, stationary mercury electrode, sweep rate 10 mV s^{-1}: (a) and (b) curves in aprotic DMF; (c) response of the sulphone, (b) with phenol 10^{-2} M (after Reference 26).

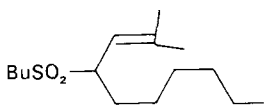
It has been found[50] that such a multielectron step does not exist with **58**, which exhibits a classical two-electron scission. In general, allylic sulphones (**59**) without an unsaturated system in a suitable position are not reducible. Thus, they do not exhibit a cathodic step in protic solutions. However, in aprotic media the isomerization may be base catalyzed, since small amounts of electrogenerated bases from electroactive impurities, even at low concentration, may contribute to start the isomerization. Figure 10 shows the behaviour of *t*-butyl allylic sulphone which is readily transformed in the absence of proton donor. On the other hand, **60** is not isomerized but exhibits a specific step (Figure 10, curve a) at very negative potentials.



(**58**)



(**59**)

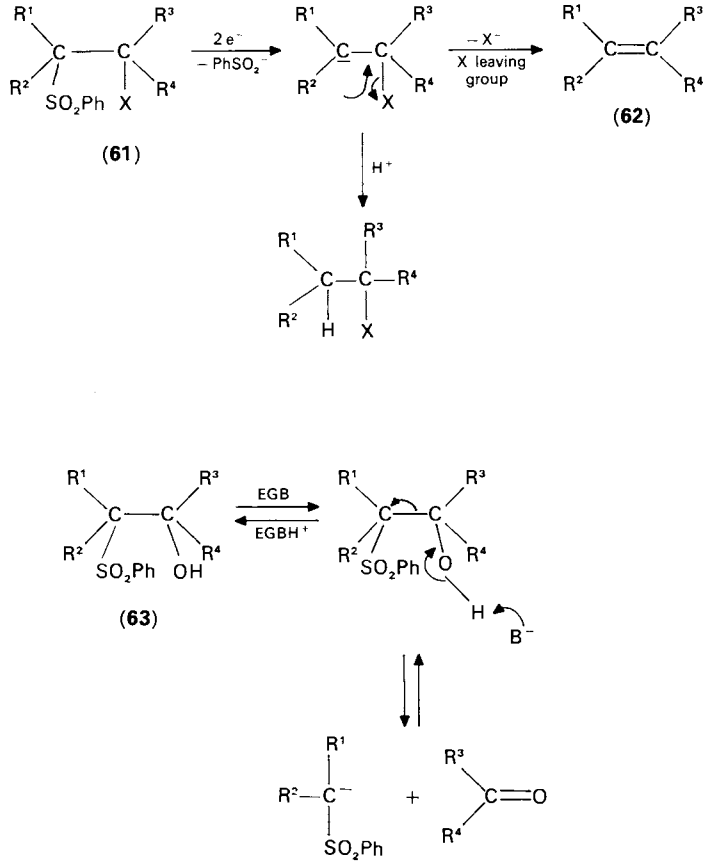


(**60**)

5. The sulphonyl group involved in cathodic and anionic eliminations

Eliminations can be promoted by arene sulphonyl groups simultaneously acting as electroactivated systems leaving groups and strongly withdrawing moieties.

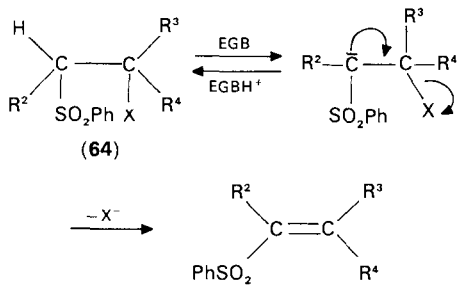
a. Cathodic eliminations. The electrochemical reduction of vicinal disubstituted compounds with at least one electrophore may lead to unsaturation by elimination. For example[54], the β-acetoxy sulphone **61** eliminates in a two-electron reaction to yield 85% of styrene in an acetic acid/DMF medium. The stereochemistry of the elimination, both from erythro or threo β-acetoxy sulphones, leads always to a large excess of the *trans* (~ 80%) and a minor amount of the *cis* (5–15%) olefin. Considering the possibility of deprotonation by the electrogenerated bases (followed by anionic elimination) it follows that cathodic eliminations should always be run in a protic solution. In the case of β-hydroxy sulphones, retro-condensation may occur in aprotic solutions by means of the EGBs. Hence, in such conditions, conclusions on the stereochemistry of the cathodic elimination appear to be problematical. Reduction products from ketones (mainly pinacols) are often isolated.



(**61**) (**62**) (**63**)

b. Anionic elimination by means of electrogenerated bases. The electron-withdrawing effect of the sulphonyl moiety permits [54], in unbuffered media, the formation of a negative

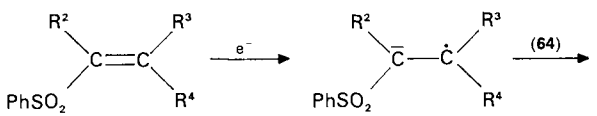
charge and, further, the elimination of a leaving group (AcO^-, MeO^-) located at a suitable position. The charge displacement leads to the formation of an ethylenic sulphone which is more reducible than the starting substrate:



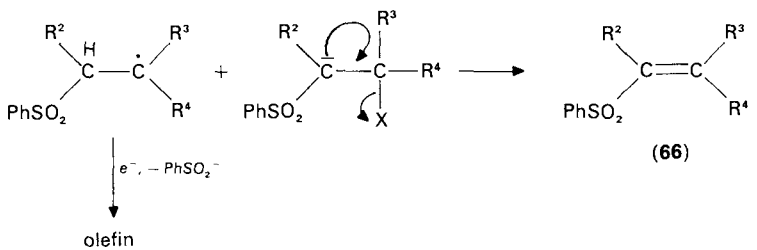
(64)

(65)

This formation of an ethylenic sulphone at the cathodic interface when reducing β-acetoxysulphones leads to a peculiar feature in cyclic voltammetry. The activated olefin, itself a source of new electrogenerated bases, contributes to render[54] the overall process autocatalyzed.

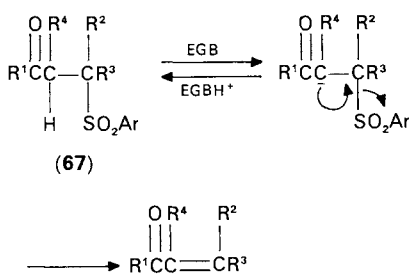


(66)



(66)

Quite similarly, γ-ketosulphones may give elimination in aprotic solution[48]. A multisweep voltammetric experiment (Figure 11) shows the formation, already from the second sweep, of the activated olefine. Here, the sulphonyl group leaves:



(67)

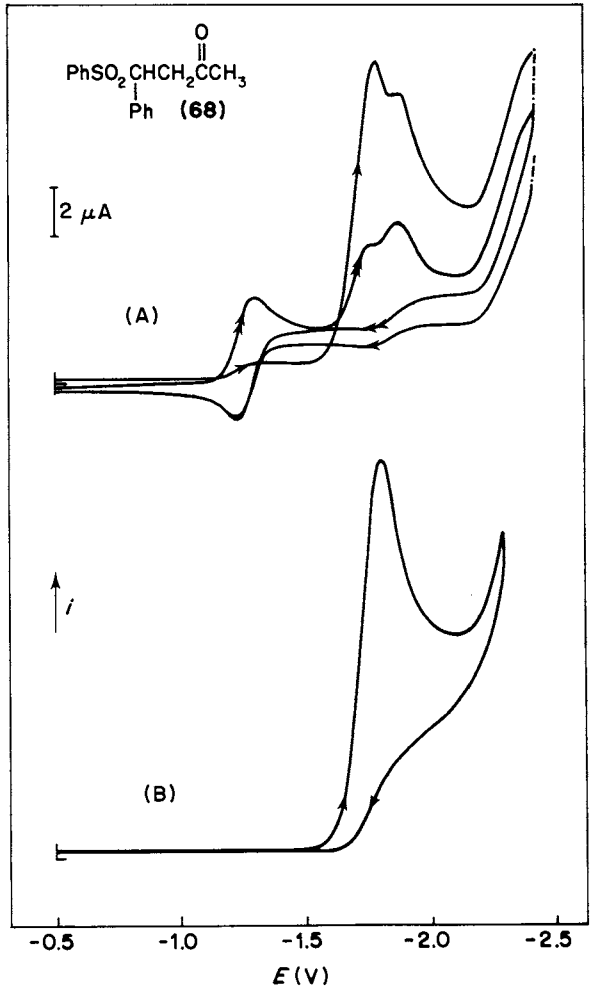
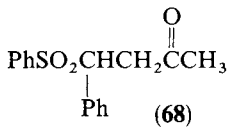
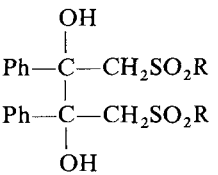


FIGURE 11. Cyclic voltammetries of **68** at a mercury microelectrode, concentration 2×10^{-3} M, electrolyte DMF/Bu_4NI 0.1 M, reference electrode Ag/AgI/I^- 0.1 M, sweep rate 300 mV s^{-1}: (A) voltammetries corresponding to two successive sweeps; (B) same as A, but with added phenol (2×10^{-3} M).

This behaviour is shown in the voltammetry of **68** which leads under suitable conditions to the formation of benzylidene acetone at the cathodic interface. The latter structure exhibits a reversible step, i.e., formation at -1.25 V of a fairly stable anion radical.



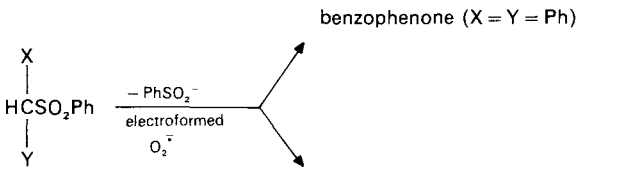
Other complex sulphones, e.g., **69** with several labile hydrogens, were studied[54]. Thus disulphonyl pinacols can be reduced (by four-electron cleavage) into pinacols in protic solution or decomposed by means of EGBs into benzil and methyl phenyl sulphone (R = Ph). With R = alkyl, other modes of cleavage by EGBs were found[55-57], especially the scission of the central C—C bond when 50% of the β-ketosulphone could be isolated.



(**69**)

6. Other reactions of acidic sulphones with electrogenerated bases

There are many possibilities for acidic sulphones to react with electrogenerated bases, and give specific functionalization on the α carbon. The first significant example was reported by Baizer[58] when reducing sulphone **70** in the presence of oxygen.

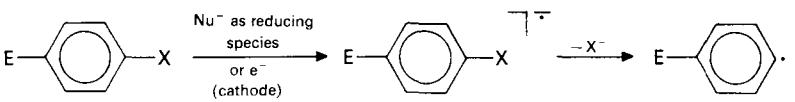


(**70**)

7. The sulphonyl group as activating factor in $S_{RN}1$ reactions

It has been well known since the pioneering work of Bunnett[59] that some nucleophilic aromatic substitutions can be catalyzed by single electron transfer. Electrochemistry was shown[60,61] to be an efficient technique both for inducing reactions and for determining mechanisms and thermodynamic data concerning equilibria in the overall process.

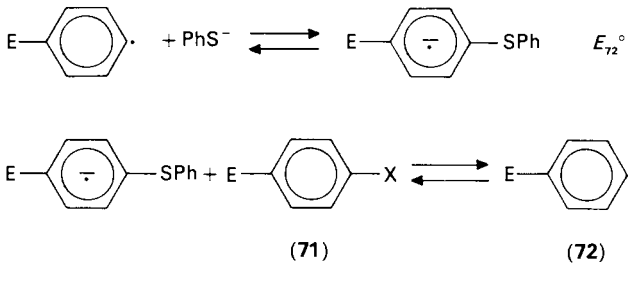
In most known examples of catalyzed aromatic nucleophilic substitution ($S_{RN}1$), the preliminary step aims at producing an aromatic electrophilic radical. Such electrophilicity is obtained, in general[59-62], by substitution on the phenyl ring with a strongly electron-withdrawing substituent (E) which also activates the leaving of the other group (X) and the creation of a transient σ radical.



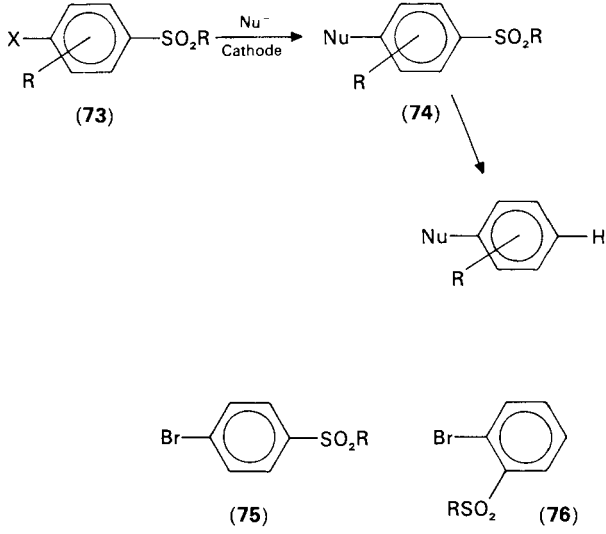
In the presence of an excess of non-reducible soft nucleophile (for example PhS^- or $PhSe^-$), a new reducing species may be formed which allows in certain cases a propagation cycle (electron chain catalysis).

The two main conditions (besides the stability of the σ radical towards the solvent to observe such an electron catalysis are a sufficient high rate of addition of the nucleophile and the thermodynamic inequality $E^\circ_{71} > E^\circ_{72}$ implying a fast displacement of the latter equilibrium to the direction of the formation of the anion radical of **71**.

In general the reaction is studied with electron-withdrawing groups (—CN,—COAr)



groups attached to the aromatic ring. However, sulphonyl groups may play a more versatile role, since they can efficiently induce the $S_{RN}1$ reaction and be cleaved afterwards by cathodic means. The process may be written as presented in the Scheme below, in the case of the presence of *two* leaving groups on the aromatic ring, one being the leaving group X and the other the inducing $—SO_2R$ group, which in turn can also be removed after the final formation of the C—Na bond. Such $S_{RN}1$ reactions were shown[63] to occur with aromatic bromosulphones (R = Me or Ph), with which the C—Br bond cleaves first and the attack by the phenylthio (PhS^-) anion on the σ radical is fast even in DMF which is known to be a good hydrogen atom donor.



It is also interesting to note that sulphoxide groups may play[64] a similar inductive role in such reactions.

8. Anodic coupling of conjugated bases of sulphones

As in the case of enolates and organic anions in general[65] it may be expected that the oxidation of —C—H systems strongly activated by sulphonyl groups in basic solvents may produce C—C dimer bonds. A very recent[66] first example concerns the oxidation of

1, 3-disulphones:

$$2EtSO_2CH_2SO_2Et \xrightarrow[MeOH/MeONa]{-2e^-} \begin{matrix} EtSO_2CHSO_2Et \\ | \\ EtSO_2CHSO_2Et \end{matrix}$$

III. ELECTROCHEMICAL BEHAVIOUR OF SULPHOXIDES

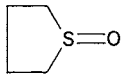
Surprisingly there are relatively few data on the cathodic or anodic behaviour of sulfoxides **77**. It is quite interesting to consider that the sulphoxide function is intermediate between the corresponding thioether and sulphone. Thus data concerning the cathodic properties of sulphoxides derive both from the basicity of the S=O group and from their capability to allow the formation of the corresponding thioether, while cleavage reactions on the C—S bond are quite unusual. On the other hand, oxidation may provide sulphones.

$$R^1—\underset{\underset{O}{\|}}{S}—R^2$$

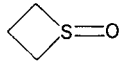
(77)

A. Cathodic Reactions of Sulphoxides

Aliphatic sulphoxides give[68–71] usually catalytic hydrogen waves in strongly acidic solutions (e.g., 1 N H_2SO_4). This points to electron transfer to the protonated form of the sulphoxide. However, surprisingly, some aliphatic sulphoxides are electroinactive: in some cases, the bulkiness of R^1 and R^2 (e.g. di-*t*-butyl sulphoxide) may be related to the absence of a polarographic step but this is far from being general; $(CH_3)_2CHCH_2SOCH(CH_3)C_2H_5$ exhibits a wave whereas $(CH_3)_3CSO(CH_2)_3CH_3$ does not. The available data[68] seem to show that if R^1 and/or R^2 are long primary chains, the occurrence of a catalytic wave is favoured. Cyclic sulphoxides (**78, 79**) have no specific cathodic behaviour.



(78)

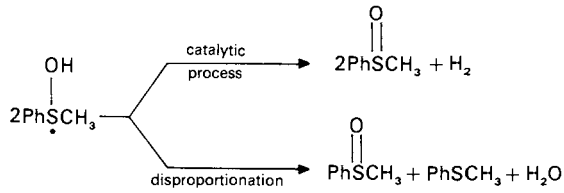


(79)

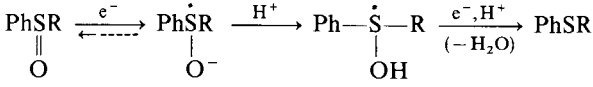
In contrast, aromatic sulphoxides do not need extreme experimental conditions to give a well-defined step in polarography and voltammetry. Thus methyl phenyl sulphoxide (**80**) exhibits[69] a well-defined wave in strongly acidic media at very moderate potential values. The reduction scheme assumes the transient formation of a protonated form prior to the electron transfer:

$$\underset{\underset{(80)}{}}{\begin{matrix} O \\ \| \\ PhSCH_3 \end{matrix}} + H^+ \rightleftharpoons \begin{matrix} OH \\ | \\ PhSCH_3 \end{matrix}$$

$$\begin{matrix} OH \\ | \\ PhS^{+}CH_3 \end{matrix} + e^- \longrightarrow \begin{matrix} OH \\ | \\ PhS^{\cdot}CH_3 \end{matrix}$$



The reduction of aromatic sulphoxides into the corresponding thioethers appears to be general; it occurs at a lead cathode[72], in alcoholic sulphuric acid solution[72] and also in the presence of tetraalkylammonium salts[73,74]. Data in DMF are also available, when phenol is used as a proton donor.



In aprotic solvents (e.g. in DMF), the reduction does not take place by an ECE-type mechanism. In the case of diphenyl sulphoxide[75] it can be shown that a fast disproportionation process occurs at the stage of the substrate anion radical:

$$\underset{(\mathbf{81})}{\text{PhSOPh}} \xrightarrow{e^-} [\text{PhSOPh}]^{\cdot-}$$

$$2\text{PhSOPh}^{\cdot-} \longrightarrow [\text{PhSPh} + \text{PhSO}_2\text{Ph}]^{\cdot-} \xrightarrow[e^-,H^+]{} \text{PhSO}_2^- + \text{PhH} + \text{PhSPh}$$

Coulometric measurements demonstrated the formation of the thioether with an electricity consumption of *one* Faraday per mole. However, the thioether yield was only of the order of 50% and, in addition, the presence of sulphinate ion in the electrolysis solutions was shown by methylation with CH_3I, when methyl phenyl sulphone was formed and determined.

Data on the behaviour of α-ethylenic (**82**) and α,α-diethylenic (**83**) sulphoxides in aqueous-methanolic solutions are also available[76]. The sulphoxide function, when activated both by benzylic and propargylic moieties (as in **84**), gives[76] a reduction wave ($E = -1.44$ V *vs.* SCE) in basic aqueous methanolic media. However, no results are available for cathodical reduction of activated sulphoxides.

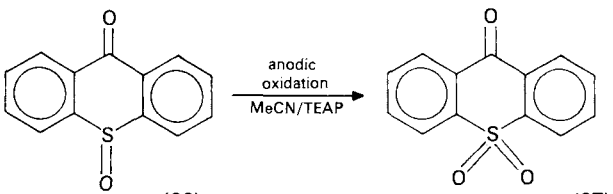
$ArCH_2SOCH{=}CH_2$	$(CH_2{=}CH_2)_2SO$	$PhCH_2SOCH_2C{\equiv}CH$
(**82**)	(**83**)	(**84**)

β-Ketosulphoxides undergo cleavage reactions when reduced in aqueous DMF solutions. Thus, methyl cyclohexyl ketone (54% yield) may be obtained[77] from the cathodic reduction of **85** (R = cyclohexyl) (fixed potential: −1.74 V *vs.* SCE, pH 11, KNO_3 electrolyte). Similar results[77] were observed in the case when the sulphoxide group was attached to an aromatic ketone moiety (**85**, R = *p*-$CH_3OC_6H_4$). However, the cleavage reaction seems to occur not at the sulphoxide group but at the intermediate thioether.

$$\underset{(\mathbf{85})}{RCCH_2SCH_3} \longrightarrow RCCH_3$$

B. Oxidation of the Sulphoxide Group

The anodic oxidation reaction of sulphoxides was not much studied, and just a few reports are available so far. The conversion into the corresponding sulphones of some phenyl alkyl and diaryl sulphoxides[79] (oxidation potential for **86**: + 2.07 V *vs.* SCE in acetonitrile/$NaClO_4$ electrolyte, Pt anode) has been reported. Similarly, diphenyl sulphoxide was long known[72] to be transformed in a quantitative yield into the sulphone (Pt anode, solvent: glacial acetic acid). Additional examples of the oxidation of a sulphoxide function attached to aryl groups are available[78].



(**86**) (**87**)

IV. ACKNOWLEDGEMENT

The author of the present review wishes to express his warmest gratitude to Dr. Georges Jeminet, Université de Clermont (France) who has strongly contributed to promote interest in sulphur compounds in this Laboratory and initiated a long collaboration and friendship.

V. REFERENCES

1. L. Horner and H. Nickel, *Chem. Ber.*, **86**, 1681 (1956).
2. R. Gerdil and E. A. C. Lucken, *Mol. Phys.*, **9**, 529 (1965).
3. R. Gerdil, *Helv. Chim. Acta*, **56**, 196 (1973).
4. G. Jeminet and J. Simonet, *C. R. Acad. Sci., Paris, Ser. C*, **272**, 661 (1971).
5. F. de Jong and M. Janssen, *J. Chem. Soc., Perkin Trans. 2*, 572 (1972).
6. R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, *J. Amer. Chem. Soc.*, **65**, 1013 (1943).
7. R. E. Dabby, J. Kenyon and R. F. Mason, *J. Chem. Soc.*, 4881 (1952).
8. W. E. Truce, D. P. Tate and D. N. Burdge, *J. Amer. Chem. Soc.*, **82**, 2872 (1960).
9. Anon., *Angew. Chem.*, **66**, 654 (1954).
10. L. Reggel, R. A. Friedel and J. Wender, *J. Org. Chem.*, **22**, 891 (1957).
11. L. Horner and E. Meyer, *Ber. Bunsenges Phys. Chem.*, **79**, 186 (1975).
12. L. Horner and H. Neumann, *Chem. Ber.*, **98**, 1715 (1965).
13. J. Simonet, unpublished observations concerning many aryl/alkyl sulphones provided by Prof. Marc Julia, Paris.
14. O. Manousek, O. Exner and P. Zuman, *Coll. Czech. Chem. Commun.*, **33**, 3988, 4000 (1958).
15. J. Simonet and G. Jeminet, *Bull. Soc. Chim.*, 2754 (1971).
16. L. Horner and E. Meyer, *Liebigs Ann. Chem.*, 2053 (1975).
17. B. Lamm and K. Ankner, *Acta Chem. Scand.*, **B31**, 375 (1977).
18. B. Lamm, *Tetrahedron Letters*, 1469 (1972).
19. B. Lamm and J. Simonet, *Acta Chem. Scand.*, **B28**, 147 (1974).
20. R. Gerdil and E. A. C. Lucken, *Mol. Phys.*, **9**, 529 (1965).
21. J. Simonet and G. Le Guillanton, *Bull. Soc. Chim.*, 180 (1985) and references cited therein.
22. J. Simonet, in *Organic Electrochemistry, An Introduction and a Guide* (Eds. M. M. Baizer and H. Lund), Chap. 26, Dekker, New York, 1983.
23. C. P. Andrieux, J. M. Dumas-Bouchiat and J. M. Saveant, *J. Electroanal. Chem.*, **87**, 39, 43, 55 (1978).
24. N. Djeghidjegh and J. Simonet, to appear.

25. J. Simonet and H. Lund, *Acta Chem. Scand.*, **B31**, 909 (1977).
26. J. Y. Pape and J. Simonet, *Electrochim. Acta*, **23**, 445 (1978).
27. H. Lund, *Denki Kagatu*, **45**, 2 (1977).
28. H. Lund and J. Simonet, *J. Electroanal. Chem.*, **65**, 205 (1975).
29. C. W. Johnson, C. G. Overberger and W. J. Seagers, *J. Amer. Chem. Soc.*, **75**, 1495 (1953).
30. M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 3138 (1965).
31. A. A. Pozdeeva, S. G. Mairanovskii and L. K. Gladkova, *Sov. Electrochem.*, **3**, 1005 (1967); *Elektrokhimiya*, **3**, 1127 (1967).
32. B. A. Arbuzov and E. A. Berdnikov, *Dokl. Akad. Nauk SSSR*, **171**, 860 (1966).
33. S. G. Mairanovskii, E. N. Prilezhaeva, L. L. Skopina, V. I. Snegotskii, N. V. Surikova and V. I. Laba, *Bull. Acad. Sci. USSR, Ser. Chem.*, 137 (1971); *Izv. Akad. Nauk SSSR*, 1546 (1971).
34. R. W. Howsam and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 2*, 847 (1972).
35. M. K. Polievktov, S. G. Mairanovskii, V. I. Laba, V. I. Snegotskii and E. N. Prilezhaeva, *Izv. Akad. Nauk SSSR., Ser. Khim.*, 687 (1968); V. I. Laba, M. K. Polievktov, E. N. Prilezhaeva and S. G. Mairanovskii, *Bull. Div. Chem. Sci. USSR*, 2004 (1969).
36. J. Sestakava, P. Zuman and V. Horak, *Coll. Czech. Chem. Commun.*, **31**, 827 (1965).
37. K. Ankner, B. Lamm and J. Simonet, *Acta Chem. Scand.*, **B31**, 742 (1977).
38. B. Lamm and K. Ankner, *Acta Chem. Scand.*, **B32**, 264 (1978).
39. M. A. Michel, G. Mousset and J. Simonet, *J. Electroanal. Chem.*, **98**, 319 (1979).
40. G. Jeminet and J. Simonet, *C. R. Acad. Sci.*, **272C**, 661 (1971).
41. J. G. Gourcy, G. Jeminet and J. Simonet, *Bull. Soc. Chim. Fr.*, 2982 (1972).
42. G. Jeminet, J. G. Gourcy and J. Simonet, *Tetrahedron Letters*, 2975 (1972).
43. J. G. Gourcy, *These D.I.*, University of Clermont, 1981.
44. J. G. Gourcy, G. Jeminet and J. Simonet, *Bull. Soc. Chim. Fr.*, 1713 (1975).
45. E. A. Berdnikov, S. B. Fedorov, Yu. M. Kargin, *Dokl. Akad. Nauk SSSR* **232(4)**, 832 (1977).
46. E. A. Berdnikov, Yu. M. Kargin and F. R. Tantasheva, *Zh. Obshch. Khim., SSSR*, **44**, 1366 (1974).
47. E. A. Berdnikov, V. S. Savel'ev and Yu. M. Kargin, *Dokl. Akad. Nauk SSSR*, **244(4)**, 909 (1979).
48. R. Kossai and J. Simonet, *Electrochim. Acta*, **26**, 189 (1981).
49. R. Rozas and J. Simonet, to appear.
50. G. Mabon, N. Djeghidjegh and J. Simonet, to appear.
51. B. Lamm and B. Samuelson, *Acta Chem. Scand.*, **24**, 561 (1970).
52. B. Samuelson and B. Lamm, *Acta Chem. Scand.*, **24**, 3070 (1970).
53. B. Lamm and B. Samuelson, *J. Chem. Soc., Chem. Commun.*, 1010 (1970).
54. S. Gambino, P. Martigny, G. Mousset and J. Simonet, *J. Electroanal. Chem.*, **90**, 105 (1978).
55. R. Kossai, *Electrochim. Acta*, **30**, 75 (1985).
56. J. Simonet, unpublished observations.
57. R. Kossai, *These d'Etat*, University of Clermont, 1981.
58. M. Sugawara, M. M. Baizer, W. T. Monte, R. D. Little and U. Hess, *Acta Chem. Scand.*, **B37**, 509 (1983).
59. J. F. Bunnett, *Acc. Chem. Res.*, **11**, 413 (1978).
60. J. Pinson and J. M. Saveant, *J. Chem. Soc., Commun.*, 933 (1974); *J. Amer. Chem. Soc.*, **100**, 1506 (1978).
61. J. M. Saveant, *Acc. Chem. Res.*, **13**, 323 (1980).
62. C. Degrand, *J. Chem. Soc., Chem. Commun.*, 1113 (1986).
63. J. Simonet and N. Djeghidjegh, *J. Electroanal. Chem.*, **218**, 367 (1987).
64. N. Djeghidjegh and J. Simonet, to appear.
65. See for example, J. T. Anderson and J. H. Stocker, in *Organic Electrochemistry* (Eds. M. M. Baizer and H. Lund), Chap. 21, Dekker, New York, 1983, pp. 707–713.
66. G. Le Guillanton and J. Simonet, unpublished observation.
67. L. Horner and H. Lund (Chap. 22) and R. Dietz (Chap. 6), in *Organic Electrochemistry* (Eds. M. M. Baizer and H. Lund), Dekker, New York, 1983.
68. L. Suchomelova, J. Zyka and P. Zuman, *J. Electroanal. Chem.*, **12**, 194 (1966).
69. G. Gavioli, G. Davolio and E. S. Guidetti, *J. Electroanal. Chem.*, **27**, 135 (1970).
70. V. G. Luk'yanista, *Sov. Electrochem.*, **5**, 822 (1969).
71. I. C. Rodacanu and W. J. Lorenz, *Electrochim. Acta*, **16**, 995 (1971).
72. F. Fichter and F. Braun, *Chem. Ber.*, **47**, 1526 (1914); F. Fichter and W. Wenk, *Chem. Ber.*, **45**, 1373 (1912); F. Fichter and P. Sjastedt, *Chem. Ber.*, **43**, 3422 (1910).

73. R. C. Bowers and H. D. Russel, *Anal. Chem.*, **32**, 1271 (1960).
74. P. Chiorboli, G. Davolio, G. Gavioli and M. Salvaterra, *Electrochim. Acta*, **12**, 767 (1967).
75. J. Simonet and N. Djeghidjegh, unpublished observations.
76. R. W. Howsan and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 2*, 847 (1972).
77. B. Lamm and B. Samuelsson, *Acta Chem. Scand.*, **23**, 691 (1969).
78. P. T. Kissinger, P. T. Holt and C. N. Reilley, *J. Electroanal. Chem.*, **33**, 1 (1971).
79. S. Torii and K. Uneyama, *Tetrahedron Letters*, 4513 (1972).

CHAPTER **23**

Electron transfer reactions of sulfoxides and sulfones

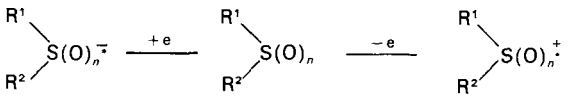
MICHEL CHANON AND ANDRE SAMAT

Université d'Aix-Marseille III, Laboratoire de Chimie Inorganique Moléculaire, UA 126-CNRS, 13397 Marseille, Cédex 13, France

I. INTRODUCTION

This review is concerned with the formation of cation radicals and anion radicals from sulfoxides and sulfones. First the clear-cut evidence for this formation is summarized (ESR spectroscopy, pulse radiolysis in particular) followed by a discussion of the mechanisms of reactions with chemical oxidants and reductants in which such intermediates are proposed. In this section, the reactions of α-sulfonyl and α-sulfinyl carbanions in which the electron transfer process has been proposed are also dealt with. The last section describes photochemical reactions involving anion and cation radicals of sulfoxides and sulfones. The electrochemistry of this class of compounds is covered in the chapter written by Simonet[1] and is not discussed here; some electrochemical data will however be used during the discussion of mechanisms (some reduction potential values are given in Table 1).

Cation and anion radicals form from sulfoxides or sulfones by either chemical or electrochemical oxidation and reduction, respectively. The ability of compounds to accept

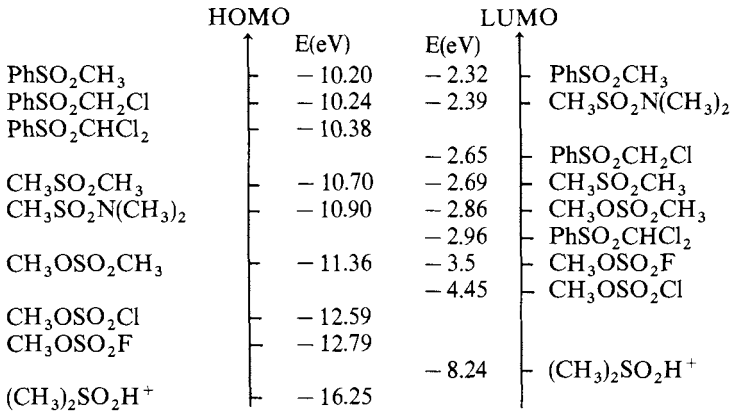


$n = 1, 2$

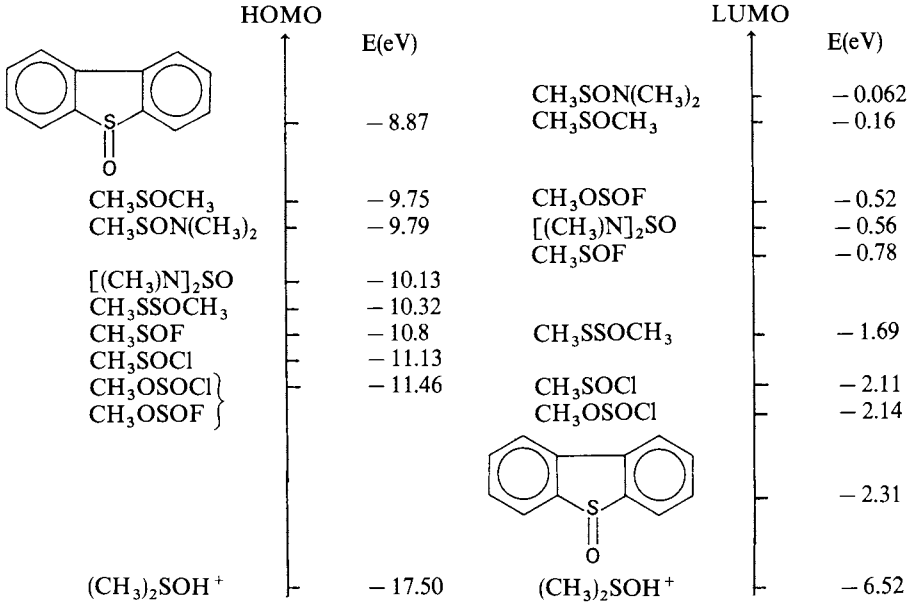
TABLE 1. Reduction potentials (*vs* SCE)[4] of some sulfones and sulfoxides

Compound	$E_{1/2}(V)$	Compound	$E_{1/2}(V)$
$C_6H_5SO_2CH_3$	-2.295^a	$4\text{-}O_2NC_6H_4SO_2CH_3$	-0.93^a
	-2.14^b	$(C_6H_5)_2SO_2$	-2.04^b
$4\text{-}CH_3OC_6H_4SO_2CH_3$	-2.48^a	$(C_6H_5)_2SO$	-2.07^b
$4\text{-}CH_3C_6H_4SO_2CH_3$	-2.42^a	$C_6H_5SOCH_3$	-2.295^a
$4\text{-}ClC_6H_4SO_2CH_3$	-1.94^a		-2.18^b

[a]In DMF, with 0.1 M tetraethylammonium bromide.
[b]In 50% ethanol, with 0.1 M tetraethylammonium bromide.



SCHEME 1. Energy levels (eV) of the HOMO and LUMO obtained from MNDO calculations of some sulfones and sulfonyl-like compounds.



SCHEME 2. Energy levels (eV) of the HOMO and LUMO obtained from MNDO calculations of some sulfoxides and sulfinyl-like compounds.

one electron is measured by their electron affinity or their reduction potential. Similarly, the ability to loose one electron is measured by the ionization potential or the oxidation potential. Theoretical calculations allow the comparison of these properties in homogeneous series of compounds, through the values of the highest occupied molecular orbital (HOMO) or the lowest unoccupied molecular orbital (LUMO) levels[2]. Schemes 1 and 2 display the HOMO and LUMO energies for sulfone- and sulfoxide-like compounds (MNDO calculations[3]). Substituents of various electronegativity are attached to the sulfur atom. In the sulfonyl series, replacement of a methyl group by a phenyl group leads to a higher HOMO (better donor) and LUMO (weaker acceptor); the opposite result follows a halogen substitution in agreement with experimental results: only phenyl (or benzo)sulfones or alkyl sulfones are electrochemically reduced[1,4]. These theoretical calculations must be considered with caution, however, because 3d orbitals of the S atom are not taken into account and could interact with the aromatic π system[5a]. The protonation of the sulfonyl group results in a great stabilization of both the HOMO and LUMO. These results imply increased electronic affinity for the protonated species. For the sulfoxides, the HOMO is about 1 eV more (greater donor ability) and the LUMO is about 2 eV higher (weaker acceptor ability) than those of the corresponding sulfones; the experimental reduction potentials are, however, approximately the same[4]. The gap between HOMO and LUMO is small for dibenzothiophene *S*-oxide. For the calculated sulfones and sulfoxides, the LUMO is a σ^* orbital essentially localized on the S, O and adjacent C atoms. For the protonated form of the dimethyl sulfoxide, the LUMO retains the same σ^* character with a participation of the n* orbitals of the S atom.

II. ESR SPECTROMETRY OF RADICAL ANIONS AND RADICAL CATIONS OF SULFOXIDES AND SULFONES

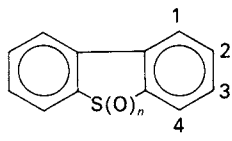
A. Radical Anions of Sulfoxide- and Sulfone-containing Aromatic Compounds

The spectroscopic data available for sulfoxide- and sulfone-containing aromatic compounds may be divided into two categories according to the position of the functional groups. When the SO or SO_2 may be considered as substituents, their presence involves only small perturbations of the characteristics of the aromatic systems. The SO or SO_2 group may be also a direct component of the conjugated system and so it contributes directly to these characteristics. These two cases are called respectively the 'perturbation case' and 'direct conjugation case' by Urberg and Kaiser in their review[6a]. This section deals only with the second situation.

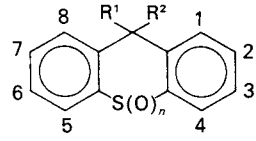
A number of radical anions of sulfur-containing aromatic compounds have been studied essentially by means of ESR spectroscopy and sometimes by electronic spectroscopy. The studied compounds include aromatic rings separated by the oxidized sulfur functionality. The effects caused by the latter depend on the geometry and topology of the aromatic systems as well as on the electron-withdrawing ability of the other substituents.

The radical anion of diphenyl sulfone is prepared by metallic reduction, and its ESR spectrum has been studied by Kaiser and coworkers[7] and Gerdil and coworkers[8]. The ESR parameters are rather similar to those of the biphenyl radical anion[9] (Table 2), suggesting a good conjugation through the sulfonyl group. **A** d orbital model for conjugation through the sulfone group was proposed[7,8] and gave good agreement with experiment.

Table 3 presents the hyperfine splitting constants of some sulfur-containing aromatic radical anions. The series studied included the monoxides and dioxides of dibenzothiophene **1**, thioxanthene **2**, thioxanthone **3**, dibenzo[*b*, *f*] thiepin **4** and dithienothiophene dioxide **5**.

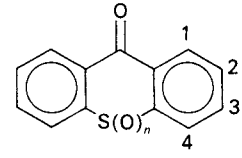


(1)

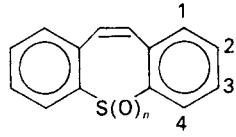


R = H, CH_3, C_6H_5

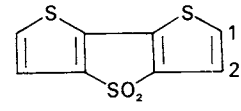
(2)



(3)



(4)



(5)

TABLE 2. ESR results for diphenyl sulfone radical anion

a_{ortho}	a_{meta}	a_{para}	Ref.
2.41	0.65	4.64	8b
2.37	0.70	4.74	7

[a]Splittings are in gauss.

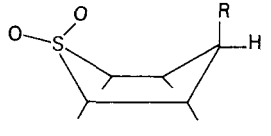
TABLE 3. Hyperfine splitting constants (gauss) of some sulfur-containing aromatic radical anions obtained in 1,2-dimethoxyethane with K metal as the reductant at −80 °C

Radical anion	a_1	a_2	a_3	a_4	Ref.
Dibenzothiophene[a]	4.48	0.86	5.16	1.46	8a
Dibenzothiophene[a]	4.60	1.05	5.04	1.45	6c
Dibenzothiophene *S*-oxide	?	> 2.4	< 2.4	0.20	6b
Dibenzothiophene *S,S*-dioxide	< 0.2	2.50	2.16	< 0.4	8b
Dibenzothiophene *S,S*-dioxide	0.12	2.36	1.84	0.24	6b
9,9-Dimethylthioxanthene *S*-oxide	0.75	4.33	1.95	?	10
9,9-Dimethylthioxanthene *S,S*-dioxide	0.30	4.54	0.64	2.00	11
Thioxanthone[b]	3.33	0.29	3.90	0.89	14
Thioxanthone *S*-oxide[c]	1.87	0.17	2.93	0.70	14
Thioxanthone *S,S*-dioxide[c]	2.05	0.38	3.08	0.80	14
Dibenz[*b,f*]thiepin	1.48	< 0.12	3.65	1.33	15
Dibenz[*b,f*]thiepin *S*-oxide	0.95	0.14	3.52	0.71	15
Dibenz[*b,f*]thiepin *S,S*-dioxide	1.85	0.20	4.15	1.50	15
Dithienothiophene 7,7-dioxide	0.73	2.89	—	—	16

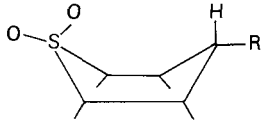
[a]The a_2 and a_3 assignments may be reversed.
[b]HMPA as solvent, K, room temperature.
[c]THF as solvent, K, −50 °C.

The conjugative effect of the sulfur group may be evaluated from the spin densities on the *ortho*, *meta* and *para* position of the rings. In the dibenzothiophene derivative **1** ($n = 1,2$)[6b,8b] the spin densities *para* to SO_2 are large while those at the *meta* position are smaller. A greater conjugation through the sulfoxide and sulfone groups appears to be involved in comparison with that observed for the parent dibenzothiophene **1** ($n = 0$) (the greater splitting constant being here in the *meta* position). In the case of thioxanthene *S*-oxide (**2**, $n = 1$)[10] and thioxanthene *S,S*-dioxide (**2**, $n = 2$)[11], the conjugation between the two aromatic rings is possible only through the sulfur functionality and the assignments have been made on the basis of the results for diphenyl sulfone where the spin density is in the order *para* > *ortho* > *meta*. For these compounds conformational information is gained from the splitting constants. For example, 9-monosubstituted derivatives of thioxanthene *S,S*-dioxides (**2**, $n = 2$, $R^1 = H$, $R^2 \neq H$) adopt the conformation **I**[12,13].

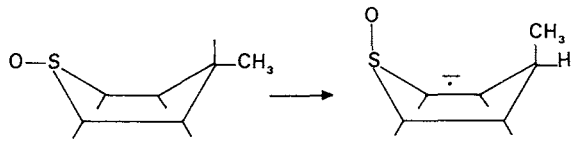
The ESR spectrum of the thioxanthene *S,S*-dioxide radical anion itself shows that the two possible conformers coexist, since the two methylene protons are not equivalent. In the case of the 9-monoalkyl derivatives, the large coupling constant observed for the 9-proton leads to the conclusion that the 9-substituent is in the boat equatorial position as in **II**[11]. Thus the radical anions and the neutral molecule display different conformations. The protons in the 9-position of the radical anions of *cis*-9-methylthioxanthene *S*-oxides (**2**, $n = 1$, $R^1 = H$, $R^2 = CH_3$) have an appreciable coupling constant[10] which suggests that these radical anions have the substituent in the pseudo-axial position. Furthermore, in the radical anions the S—O bond is pseudo-axial. These situations are exactly the opposite of that observed for the neutral compound.



(I)



(II)



cis

The same inversion occurs in the case of the *trans* isomer[10]. Changes in conformational properties when passing from the neutral to the corresponding radical anion is a recent and well-documented topic in conformational analysis[17–21].

The ESR spectra of thioxanthone *S,S*-dioxide radical anion were first described by Vincow[22] in basic ethanol and then by Kaiser and coworkers[23] in dimethyl ether and potassium. The high spin density in the position *para* to the carbonyl group indicates that the conjugation between the aromatic rings occurs essentially through this group. More recently, the data on electronic absorption and ESR spectra have been discussed in terms of the oxidation number of the sulfur atom in the thioxanthone series[14]. ESR spectra of free thioxanthone radical anions $[(TOSO_n)^{\cdot-}]$ in HMPA and contact ion pairs $[(TOSO_n)^{\cdot-}(M^+)]$ in ethereal solution depend critically on the size of the counterion M^+. When this counterion is lithium, the electrostatic interaction increases, leading to large splitting constants of aromatic ring hydrogens. Table 4 gives the most extreme values obtained, respectively, for the free radical anion and for the tight contact ion pair. The hyperfine splitting constants are very similar for $(TOSO)^{\cdot-}(M^+)$ and $(TOSO_2)^{\cdot-}(M^+)$ and both are much like the radical anion of fluorenone. Thus $(TOSO^{\cdot-})(M^+)$ and the equivalent sulfonyl species may exist as the ketyls. A large conjugative ability is displayed both by the sulfone and the sulfoxide groups in the ketyls whereas there is no evidence for a conjugation through the sulfide. The reduction potentials (Table 5) of thioxanthone-*S*-oxides, thioxanthone itself and fluorenone confirm this ability. The conjugative properties of sulfur when the oxidation states of sulfur change have been studied also in the dibenzo[*b,f*]thiepin series **4**[15]. The small density at the position *para* to the heteroatom indicates that the conjugation through the S, SO or SO_2 bridge is much weaker than conjugation through the vinyl unit. In general, the total width of the ESR spectra of SO- and SO_2-containing aromatic radical anions is smaller than the one observed for the sulfide analogue[25]. This observation suggests that the localizing ability of sulfoxide and sulfone groups is larger than that of sulfur. In the dibenzothiepin series, this proposition is verified for sulfoxides but for sulfones the total width is larger than that measured for the sulfide and the sulfoxide (20.45, 17.65 and 23.70 G respectively for increasing oxidation states of S). This fits a nonplanar molecule: the sulfonyl group would then be removed from

TABLE 4. Hyperfine splitting constants (gauss) of thioxanthone *S*-(mono or di)oxide radical anions as free or tight contact ion-pair[a]

Radical anion	a_{H_1}	a_{H_2}	a_{H_3}	a_{H_4}
$(TOSO_2)^{\cdot-}$[b]	1.75	0.19	2.93	0.76
$(TOSO_2)^{\cdot-}(Li^+)$[c]	2.34	0.54	3.20	0.85
$(TOSO)^{\cdot-}$[b]	1.67	0.09	2.83	0.68
$(TOSO)^{\cdot-}(Li^+)$[c]	2.28	0.48	3.20	0.81

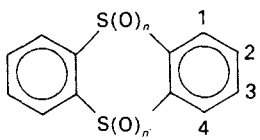
[a]TOS = thioxanthone.
[b]HMPA as solvent, room temperature.
[c]THF as solvent at −50 °C.

TABLE 5. Reduction potentials (volt) of thioxanthone (TOS) and its oxides (TOSO, $TOSO_2$) compared with that of fluorenone (FlO)

Compound	$-E_{1/2}$	Ref.
TOS	1.62	14
TOSO	1.14	14
$TOSO_2$	1.04	14
FlO	1.35	24

[a]Solvent: DMF; ref. electrode: SCE; electrolyte: tetrabutylammonium perchlorate.

conjugation and the unpaired electron would be delocalized mainly in the double bond. The radical anions derived from all possible sulfur oxides of the thianthrene ring system (**6**) have been studied[6d]. *Cis* and *trans* thianthrene rings have very different ESR spectral parameters[26] because the interaction between a pseudo-axial S—O bond and a phenyl ring differs considerably from that observed for a pseudo-equatorial S—O bond. The radical anions derived from the dithienothiophene 7,7-dioxide (**5**) have been studied by ESR spectroscopy and the hyperfine splitting constants were related to computed spin densities[16].



(**6**)

B. Radical Anions of Dialkyl Sulfoxides and Dialkyl Sulfones

The radical anions of dialkyl sulfoxides (or sulfones) may be obtained by direct capture of electron during γ-irradiation. It was shown that electron capture by several electron acceptors in the solid state gave 'anion adducts'[27]. It was concluded[27d] that these species are not properly described as radical anions but are genuine radicals which, formed in a solid state cavity, are unable to leave the site of the anions and exhibit a weak charge-transfer interaction which does not modify their conformation or reactivity appreciably, but only their ESR spectra. For hexadeuteriodimethyl sulfoxide in the solid state, electron capture gave this kind of 'adduct'[27g,28] (^2H isotopic coupling 2.97 G is less than 3.58 G normally found for $^{\bullet}CD_3$).

$$(CD_3)_2SO + e \longrightarrow D_3\dot{C}\cdots S(O)\bar{C}D_3$$

Curiously, this phenomenon is not observed for $(CH_3)_2SO$ under the same conditions[28]. On the other hand, solutions of $(CH_3)_2SO$ or $(CD_3)_2SO$ in CD_3OD gave 'normal' $^{\bullet}CH_3$ and $^{\bullet}CD_3$ radicals[28] corresponding to a C—S bond cleavage following electron capture.

$$(CH_3)_2SO \xrightarrow{+e} (CH_3)_2SO^{\bullet-} \longrightarrow \dot{C}H_3 + CH_3SO^-$$

TABLE 6. ESR parameters for radical cations arising from sulfoxides or sulfones

Species	g values (G)	Hyperfine coupling (G)
$(CD_3)_2SO^{+a,b}$	2.007	(^{2}H): ca 2.0
$(CH_3)_2SO^{+a,c}$	2.008	(^{1}H): ca 12.0; (^{33}S): $a_1 = 83$,
	2.008	$a_2 = 38$, $a_3 = 38$, $a_4 = 53$
	2.002	
$((CH_3)_2N)_2SO^{+d}$	2.004	(^{1}H): 12.4; (N): 13.0

[a] Reference 28.
[b] Pure compound, ^{60}Co γ-ray source, 77 K.
[c] Solution in D_2SO_4, ^{60}Co γ-ray source, 77 K.
[d] Reference 33; electrochemical oxidation in CH_2Cl_2, 268 K.

Among the other radicals detected in irradiated pure DMSO or in solution are $(CH_3)_2SO^{+}$ and the dimer cation $(CH_3)_2S(O)$–$S(O)(CH_3)_2^{+}$. Pulse radiolysis optical studies in aqueous solution[29], reveal that the solvated electrons react slowly with DMSO leading to an absorption attributed to $(CH_3)_2SO^{-}$. Transient species corresponding to the radical cation $(CH_3)_2SO^{+}$ were also reported[30]. Irradiated pure glasses of dimethyl sulfone gave evidence for methyl adduct formation (Table 6), whereas in methanolic solution both the 'adduct' and the 'normal' methyl radical were observed[28]. The adducts of this type were primarily interpreted, as a result of hard stretching which is halted by repulsive environmental forces prior to complete separation[28]. In a more general manner, these results have been explained by the formation of radical anion pair intermediates RAP[31]. The detection of radioluminescence associated with recombination of radical anion pairs in γ-irradiated DMSO-D_6 and diethyl sulfoxide suggests a general reaction as in the following equation:

$$AB \xrightarrow{+e} \dot{A} \ldots \bar{B} \xrightarrow{\Delta} [AB^{-}]^{*} \longrightarrow [AB^{-}] + h\nu$$

An energy model of the RAP is proposed by Shishlov and coworkers[31] in which the minimum energy corresponding to the pair is coupled, not with the ground state of the radical anion but with an electronically excited state. This model can be summarized as follows. 'During the radiolysis there is a resonance dissociative caputre of low energy electrons by sulfoxide molecules[32] and then formation of electronically excited states of the radical anions which are stabilized under the form of the RAP at 77 K. Thermal activation of the pairs may lead either to complete dissociation or to recombination of the pair into a radical anion; transition to the ground state of the radical anion occurs either from an electronically excited state with emission of light or emissionlessly along the potential energy curve of the ground state with vibrational relaxation'. In the case of sulfoxides, dissociation of the radical anions would occur through their electronically excited state and not through vibrational excitation.

C. Radical Cations from Sulfoxides and Sulfones

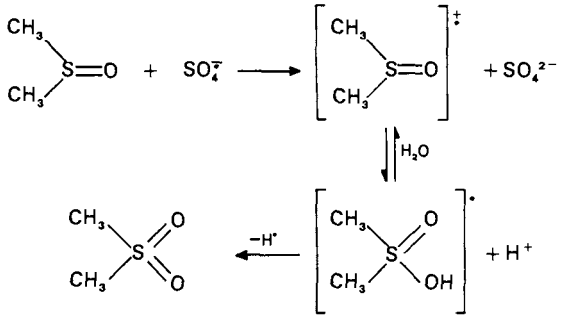
As seen before, the radical cation of dimethyl sulfoxide $(CH_3)_2SO^{+}$ has been detected by ESR spectroscopy among other radicals when DMSO glasses at 77 K are submitted to γ-irradiation[28]. It has also been reported in pulse radiolysis experiments[30] (Table 6). Constant current electrochemical oxidation of bis(dialkylamino)sulfoxides $(R_2N)_2SO$ gives rise to radical cations which have been detected by ESR spectroscopy[33].

$$(R_2N)_2SO \xrightarrow{-e} [(R_2N)_2SO]^{+}$$

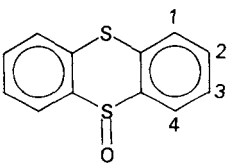
$$R_2\ddot{N}—\overset{+}{\dot{S}}(O)—\ddot{N}R_2 \leftrightarrow R_2\overset{+}{\dot{N}}—\ddot{S}(O)—\ddot{N}R_2 \leftrightarrow R_2\ddot{N}—\ddot{S}(O)—\overset{+}{N}R_2$$
(a) (b) (c)

The majority of the spin density is on nitrogen due to the high electronegativity of the sulfoxide sulfur. This is shown by the low 'g' factor and high proton and nitrogen splitting compared to the bis(dimethylamino)sulfide cation.

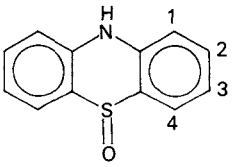
ESR experiments employing *in situ* photolytic decomposition of the peroxydisulfate anion ($S_2O_8^{2-}$) have been carried out to study the reaction of $SO_4^{\cdot-}$ with aliphatic sulfoxides[34]. In the case of dimethyl sulfoxide three radicals are detected: ($^{\cdot}CH_3$, $CH_3{}^{\cdot}SO_2$, $CH_2{}^{\cdot}S(O)CH_3$), the proportion being pH-dependent. The reaction is assumed to proceed via an initially formed radical cation (not detected) which would be rapidly hydrated to give an intermediate identical with that generated by $^{\cdot}OH$ addition on the sulfoxide. Such a process parallels the rapid hydration of radical cations formed from thiophene in their reactions with $SO_4^{\cdot-}$ and $^{\cdot}OH$[35].



The formation of adduct is followed by fragmentation and subsequent H-atom abstraction reaction from the sulfinic acid produced. Strong acid solutions of aromatic sulfoxides like thianthrene 5-oxide (**7**) or phenothiazine 5-oxide (**8**) gives rise to ESR signals, which



(**7**)



(**8**)

correspond to the radical cation of the reduced form of sulfur[36]. The cation radical is probably formed from the protonated sulfoxide followed by homolysis of the S—O bond.

$$R_2S{=}O \underset{-H^+}{\overset{H^+}{\rightleftharpoons}} R_2\overset{+}{S}{-}OH \xrightarrow{-(\dot{O}H)} R_2S^{\cdot+}$$

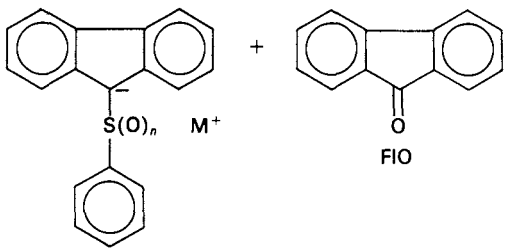
III. REACTIONS WITH CHEMICAL OXIDANTS AND REDUCTANTS

A. SET Involving α-Sulfonyl and α-Sulfinyl Carbanions

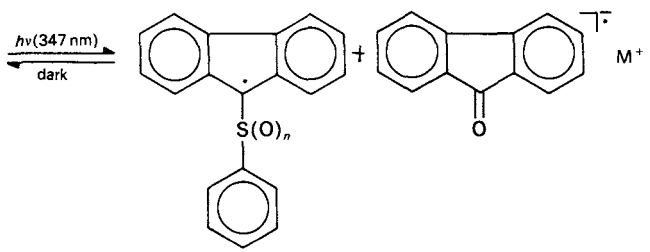
1. SET from α-sulfonyl and α-sulfinyl carbanions to fluorenone

The electron transfer reaction from fluorenyl carbanions adjacent to sulfoxide or sulfone (**9**) to fluorenone (FlO) has been studied by means of flash photolysis[37]. For $n = 1$ as well as $n = 2$ the transient $FlO^{\cdot-}$, M^+ (contact ion pair) appeared in THF and $FlO^{\cdot-}$ (free ion)

in HMPA. The $FlO^{\bullet}$ (free ion) was also generated from the α-sulfonyl carbanion in THF. Special interaction between the sulfone moiety and the counter cation in the excited state results in the formation of the $FlO^{\bullet}$.

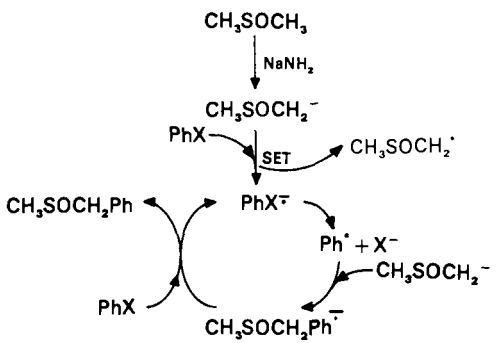


(9)
$PhS(O)_nFl^-(M^+)$
$n = 0, 1, 2$; $M^+ = Li^+, Na^+, K^+$



2. SET from α-sulfinyl carbanion to phenyl halides

The anion of DMSO undergoes a phenylation reaction with aryl halides under sunlight stimulation[38]. The presence of benzhydryl methyl sulfoxide (maximum yield 5%) in all runs, the sunlight activation, the order of reactivity of halobenzenes (I > Br > Cl), the inhibition of the reaction with oxygen, all hint at the $S_{RN}1$[39–44] mechanism (Scheme 3).



SCHEME 3

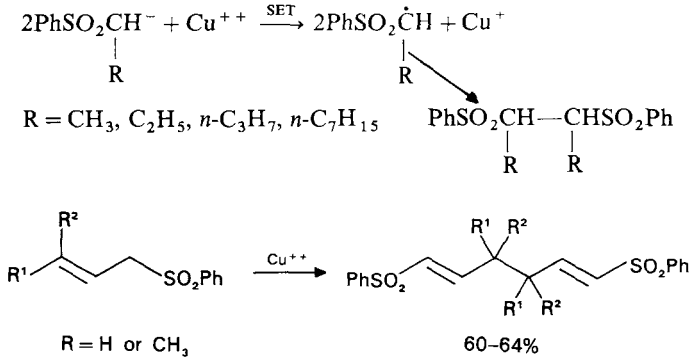
3. SET from DMSO carbanion to inert free radicals

Perchlorotriphenyl methyl radicals are particularly persistent[45]. Among the factors contributing to the exceptional persistency[46] of this kind of radicals the steric shielding of the α-(tricovalent) carbon is predominant. Only hydrogen or electron can reach the carbon radical. Thus, when perchloro radicals are formed in a DMSO–alkaline hydroxide solution an electron transfer occurs, leading to the perchlorocarbanions. It is assumed that the donor is the DMSO carbanion.

$$(C_6Cl_5)_3\dot{C} + {}^{-}CH_2\underset{\underset{O}{\|}}{S}CH_3 \longrightarrow (C_6Cl_5)_3C^{-} + \dot{C}H_2\underset{\underset{O}{\|}}{S}CH_3$$

4. SET from α-sulfonyl carbanions to cupric salts

The oxidative dimerization of the anion of methyl phenyl sulfone (from a Grignard reagent) in ethereal solution in the presence of cupric chloride in 5% yield has been reported[47]. Despite the reported[48] poor stability of the α-sulfonyl C-centered radicals, Julia and coworkers[49] provoked the dimerization (in 13 to 56% yields) of the lithiated carbanion of alkyl phenyl sulfones using cupric salts as oxidants. The best results are obtained with cupric triflates in THF-isobutyronitrile medium (56% yield for R = H). For allyl phenyl sulfones the coupling in the 3-3′ mode is predominant.

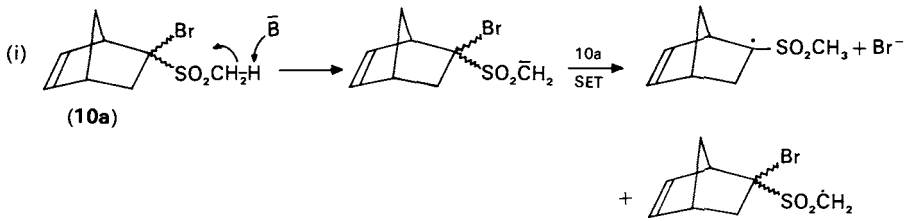


5. The Ramberg–Bäcklund reaction

This extensively studied reaction involving sulfones[50] is of general synthetic utility. It converts an α-halosulfone into an alkene via the α′-carbanion and SO_2 extrusion. A dipolar mechanism has been proposed[51]. However, some observations suggest that paramagnetic species are involved[52,53]. Thus, when the bromosulfones **10** are treated in an aqueous sodium hydroxide solution, **11** is formed in competition with the normal Ramberg–Bäcklund rearrangement when $R = CH_3$. In the case of **10a** Philips[53] proposed that the initial formation of the α-sulfonyl carbanion was followed by a SET from this carbanion to **10a** [Scheme 4, reaction (i)]. Such a type of carbanion cannot be formed from **10b**, and **10b** rearranges nevertheless. It is possible, as suggested elsewhere[52], that a homoallylic anion generated by nucleophilic attack on bromine may serve as an electron transfer agent initiating the radical chain reaction [Scheme 4, reaction (ii)]. This chain is inhibited when small amounts of iodine (10% mol) are added to the medium.

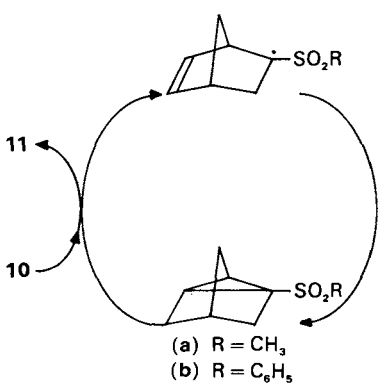
$$R^1CH_2SO_2CHR^2X \xrightarrow{B^-} R^1CH{=}CHR^2$$

Possible initiation reactions:

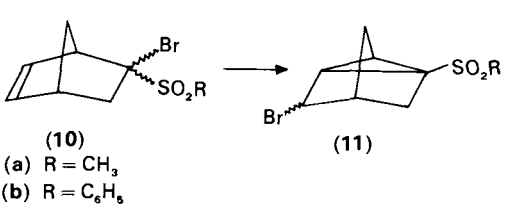


(10b)

Chain reaction:



SCHEME 4



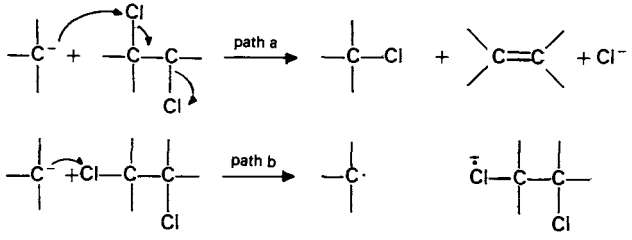
(10)
(a) R = CH_3
(b) R = C_6H_5

(11)

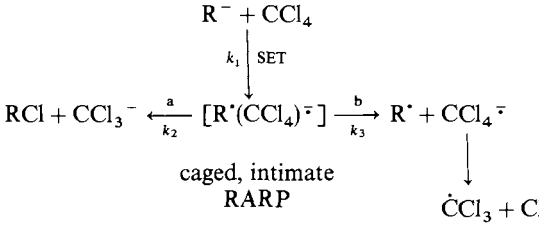
6. α-Halogenation of sulfones with perhaloalkanes

Kattenberg and coworkers[54] studied the chlorination of α-lithiated sulfones with hexachloroethane. These compounds may react as nucleophiles in a nucleophilic substitution on halogen (path a, Scheme 5) or in an electron transfer reaction (path b, Scheme 5) leading to the radical anions. The absence of proof for radical intermediates (in particular, no sulfone dimers detected) is interpreted by these authors in favour of a S_N substitution on X.

In 1977, Meyers and coworkers[55] proposed a unified crossroad of ionic and radical



SCHEME 5



SCHEME 6. Suggested radical/anion-radical pair mechanism for the reaction of α-sulfonyl carbanions with perhaloalkanes (CCl_4 as the example)[55a], $R^- = R^3SO_2\bar{C}R^1R^2$, $k_2 >> k_3$.

channels for rationalizing the experimental results of halogenation of α-sulfonyl carbanions with perhaloalkanes (CX_4) in *t*-BuOH-powdered KOH medium. In this proposition (Scheme 6) a solvent caged radical/anion-radical pair (RARP) plays a central role[55a]. In this cage $—SO_2C^{\bullet}<$ abstracts a halogen atom from $CX_4^{\bullet-}$, the halogenation of the radical proceeding with retention of configuration. This route enables one to account for the observed retention of configuration in α-halogenation of sulfones via their corresponding anions[55b,56]. Such a stereochemical result would usually lead to the conclusion[57] that the reaction of CX_4 with α-sulfonyl carbanions involves a simple ionic-type displacement on positive halogen[58] viewed as a generalized electrophilic center. However, Meyers and colleagues found it necessary to introduce the RARP concept for explaining other experimental observations, such as leaving group effects, observed selectivity when using mixed perhaloalkanes, correlation of rates with redox potentials and trapping of $^{\bullet}CCl_3$ in the medium[55c]. The only radicals trapped in the medium are $^{\bullet}CCl_3$ and they could originate from escape of $CCl_4^{\bullet-}$ from the RARP (path b, Scheme 6 for CCl_4) or from the reaction between CCl_3^- and CCl_4. On the other hand, if the $^{\bullet}CCl_3$ radical may originate from these two different sources, the strength of the $^{\bullet}CCl_3$ trapping

$$CCl_3^- + CCl_4 \xrightarrow{SET} 2\dot{C}Cl_3 + Cl^-$$

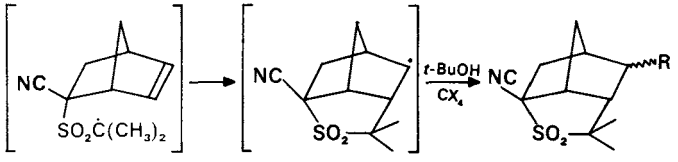
experiments as an argument for backing the RARP hypothesis decreases. The other data which supported the RARP hypothesis may be rationalized within a classical approach[59] mainly centered on the Edwards equation[60] dealing with rates of reactions between generalized nucleophiles and generalized electrophiles. In order to design less ambiguous experiments 5-cyano-5-(*endo*)isopropylsulfonyl-2-norbornene, a highly efficient radical clock[59,61], was halogenated in a *t*-BuOH–KOH–CX_4 medium. If a one-electron process is involved in the reaction, the radical **12** would be formed by an intramolecular addition to the double bond and would then give the tricyclic compounds **13**. The absence of trapping product during the experiment shows that no radical species (free radical or caged radical) having a lifetime $> 10^{-10}$ s occur during the reaction. But then, why should CCl_3^- be a

TABLE 7. pK_a (DMSO) of sulfones and standard oxidation potentials of the corresponding carbanions in DMSO

Sulfone	pK_a[63b]	E^0_{ox} (V/SCE) of the corresponding carbanion[59]
$PhSO_2CHPh_2$	22.3	−0.31
$PhSO_2CH_2Ph$	23.4	−0.27
$PhCH_2SO_2CH_2Ph$	23.5	−0.33
$PhSO_2CH_2CH{=}CH_2$	24.5	−0.43
$PhCH_2SO_2CH_3$	25.5	−0.37
$PhSO_2CH_3$	29.0	−0.19[a]
$PhSO_2CH_2CH_3$	31.0	−0.25[a]
$PhSO_2CH_2CH_2OCH_2CH{=}CH_2$	30[b]	−0.09[a]

[a] Slow systems: the determined $E_{1/2}$ does not correspond to the standard potential.
[b] Estimated value.

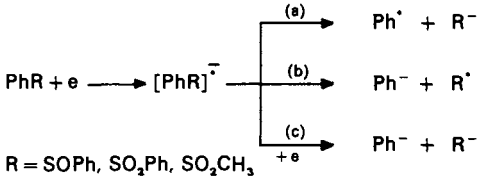
better reducing agent than $-SO_2\bar{C}H$? Standard oxidation potentials of α-sulfonyl carbanions (Table 7) have been measured[59]. The direct measure of the oxidation potential of CCl_3^- is precluded because of its short lifetime: a thermodynamic cycle approach has been used to evaluate the oxidation potential $[(E^\circ_{CCl_3\cdot/CCl_3^-})_{DMSO} = -0.83\ V]$[59]. The results suggest that, thermodynamically, the electron transfer is easier from CCl_3^- than from α-sulfonyl carbanion. Marcus' theory[62] suggests also that the rate of SET to tetrachloromethane is faster from CCl_3^- than from α-sulfonyl carbanion[59]. Therefore at this point, the whole set of results concerning the halogenation reaction of α-sulfonyl carbanions with perhaloalkanes may be rationalized within the 'classical' S_NCl^+ mechanism[63a].



(12) (13) R = H or X

B. Reductive Cleavage of Sulfones and Sulfoxides

Rossi and Bunnett[64] studied the chemical reductive cleavage of diphenyl sulfoxide, diphenyl sulfone and methyl phenyl sulfone under the action of potassium metal in liquid ammonia in the presence of acetone. The enolate ion is used to trap phenyl radicals formed eventually during the process, in order to determine whether one or two electrons are required for the mechanism of cleavage (Scheme 7). In all the runs, phenyl anion is



SCHEME 7

indicated to be the immediate product of cleavage, but there is little to indicate whether cleavage occurs according to reaction (b) or (c) of Scheme 7. The by-product of scission for the sulfoxide (probably $PhSO^-$) is further reduced to PhS^- in good yield. The by-product of diphenyl sulfone cleavage (probably $PhSO_2^-$) is further cleaved to form phenyl anions without the intermediacy of phenyl radicals. For the cleavage of methyl phenyl sulfone, an initial methyl–sulfur bond scission and subsequent cleavage of the sulfur-containing fragment, as in the second stage of the diphenyl sulfone reaction, could explain the reported results.

The experimental results described in this work[64] concerning the sulfoxide and the sulfones can also be explained by a two-electron process in agreement with electrochemical evidence and photosensitized reactions (see the previous section), using the successive reactions[1]:

$$PhSO_{(n)}R + e \longrightarrow [PhSO_{(n)}R]^{\cdot}$$

$$[PhSO_{(n)}R]^{\cdot} \longrightarrow PhSO_{(n)}^- + R^{\cdot}$$

$$R^{\cdot} + e \xrightarrow{\text{fast}} R^-$$

$$R^- \xrightarrow[\text{(solvent)}]{SH} RH + S^-$$

The reduction rate of $R^{\cdot}$ (low reduction potential)[1] is faster than any chemical reaction such as trapping by enolate ion. The difference from the electrochemical results is that, in the latter, the secondary reduction of the sulfinate anion does not occur.

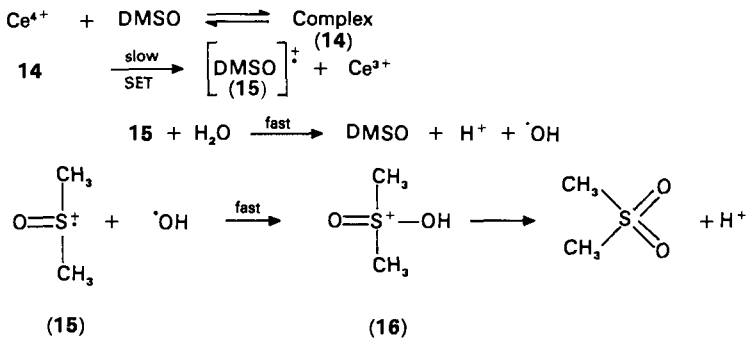
The cleavage of alkyl aryl sulfones by sodium amalgam and alcohols[65] probably proceeds also through the intermediacy of a radical anion, followed by splitting to the arylsulfinate anion and an alkyl radical. Both the sulfinate anion and the disproportionation products of the radical have been observed.

C. SET During Oxidation and Reduction of Sulfoxides

The electrochemical or polarographical reduction of sulfoxides leads to sulfides and the electrochemical oxidation, less frequently, produces the corresponding sulfone[4]. The oxidation of sulfoxide to sulfones has been proved to involve a SET when a powerful oxidative metallic cation is used. A single electron transfer has been proposed for some reductions of sulfoxides but the mechanism is not unambiguously settled. During the chemical reduction of the sulfonyl group, no clear-cut example of the electron transfer process is reported. For a sulfonyl radical anion, as described above, the normal course is not a cleavage of the S—O bond but a cleavage of the C—S bond[1,4].

1. Oxidation reactions of sulfoxides

Ce^{4+} is a versatile one-electron oxidizing agent ($E^\circ = -1.71$ eV in $HClO_4$[66] capable of oxidizing sulfoxides. Rao and coworkers[66] have described the oxidation of dimethyl sulfoxide to dimethyl sulfone by Ce^{4+} cation in perchloric acid and proposed a SET mechanism. In the first step DMSO rapidly replaces a molecule of water in the coordination sphere of the metal (Ce^{IV} has a coordination number of 8). An intramolecular electron transfer leads to the production of a cation which is subsequently converted into sulfone by reaction with water. The formation of radicals was confirmed by polymerization of acrylonitrile added to the medium. We have written a plausible mechanism for the process (Scheme 8), but there is no compelling experimental data concerning the inner versus outer sphere character of the reaction between H_2O and the radical cation of DMSO.



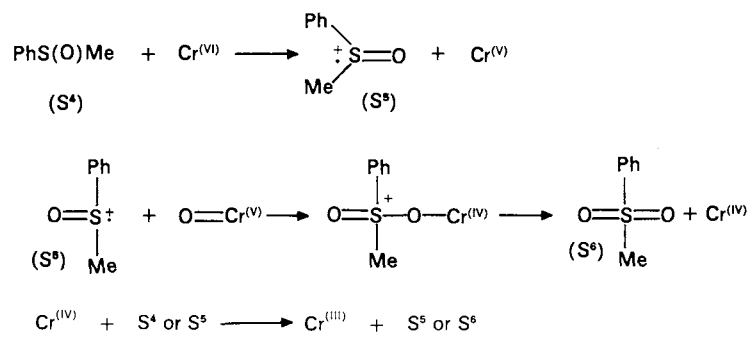
SCHEME 8

This oxidation of DMSO is catalyzed by Ag^+ cations. Kinetic and infrared spectrometric evidence fits a mechanism where DMSO coordinates rapidly with Ag^+ through its oxygen atom. The oxidation of this complex by Ce^{4+} then constitutes the slow step. The Ag^{2+} adduct would then undergo an intramolecular electron transfer in a fast step resulting in the oxidation of DMSO.

Kinetic studies of the oxidation of diaryl sulfoxides by Cr^{VI} led to the proposition of a single electron transfer[67] as in the case of aryl methyl sulfoxides[68]. These reactions were performed in aqueous acetic acid/perchloric acid medium, $HCrO_3^+$ being the active

$$3R_2SO + 2HCrO_3^+ + 4H^+ \longrightarrow 3R_2SO_2 + 2Cr^{3+} + 3H_2O$$

oxidant. In the mechanism proposed by Baliah and Satyanarayana[68] (Scheme 9), an electron transfer from the sulfoxide to Cr^{VI} occurs in the rate-determining step. These authors supported their proposition by the observation that electron-releasing *para*-substituents in the aryl moiety accelerate the reaction. The sulfoxide radical cation would then react with the Cr=O bond (Cr^V or Cr^{VI}) and the solvolysis of the Cr—O bond would give the sulfone. A reaction between an oxo-bond Cr^V center and S^5 as radical (radical anion $SO_3^{\cdot-}$) was postulated for the reduction of carboxylato-Cr^V bond by bisulfite[69]. It was proved that oxygen transfer takes place during the oxidation of diphenyl sulfide to diphenyl sulfone with chromyl acetate[70], probably via the sulfoxide. Comparison of this



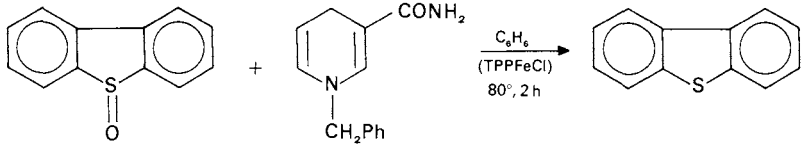
SCHEME 9

oxidation of diphenyl sulfide with experimental results observed during the oxidation of aromatic aldehydes under the same conditions (and in particular the ESR signals arising from Cr^V species)[69] suggests that both oxidations proceed by SET. Oxygen transfer after complexation of the substrate with the oxidant was also proposed for the oxidation of sulfide[71] or sulfoxide[5b] by permanganate anions. Similarly, a facile oxygen transfer from Cr^VO complexes to olefins and phosphines was postulated[72].

2. Reduction reactions of sulfoxides

Among the chemical reductions of sulfoxides, only those where the reducing agent is a low valent metal may involve a single electron process. For example, $MoCl_3$–Zn, VCl_2[73], $K_3W_2Cl_9$, $(NH_4)_4Mo_2Cl_8 \cdot NH_4Cl$, $Cs_3Mo_2Cl_8H$, K_3MoCCl_6[74], $SnCl_2$[75], and $Rh^{III}H_2$[76], $CrCl_2$[77], reduce the sulfonyl group under mild conditions. Oae[78] proposed that, initially, the reaction proceeds via the coordination of oxygen of the sulfoxide to the central metal atom followed by electron transfer from metal to sulfur.

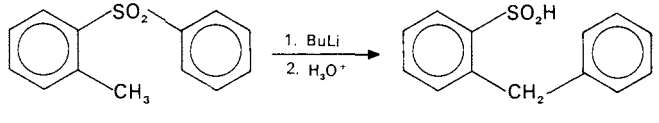
Biologically, the reduction of methionine sulfoxide to methionine with NADPH is catalyzed by an enzyme[79]. Recently, the mechanism of reduction of sulfoxides by treatment with an NADPH model has been studied[80].



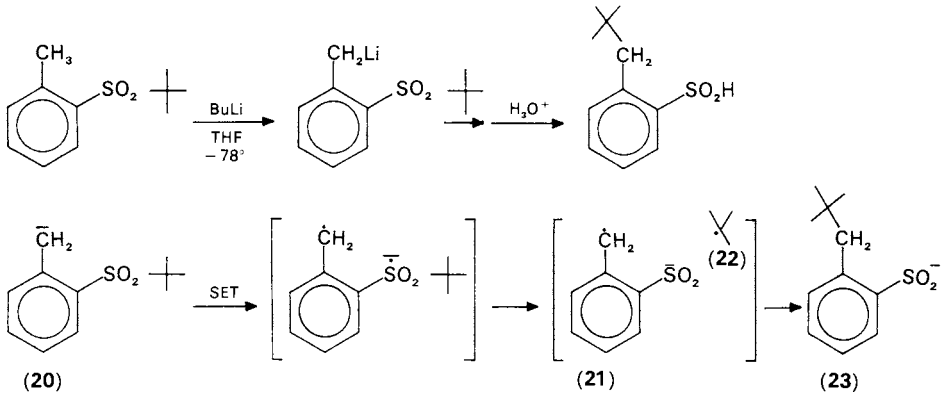
It was shown that dibenzothiophene oxide **17** is inert to 1-benzyl-1,4-dihydro nicotinamide (BNAH) but that, in the presence of catalytic amounts of metalloporphyrin, **17** is reduced quantitatively by BNAH. From experimental results with different catalysts [*meso*-tetraphenylporphinato iron(III) chloride (TPPFeCl) being the best] and a series of substituted sulfoxides, Oae and coworkers[80] suggest an initial SET from BNAH to Fe^{III} followed by a second SET from the catalyst to the sulfoxide. The results are also consistent with an initial coordination of the substrate to Fe^{III}, thus weakening the sulfur–oxygen bond in a way reminiscent of the reduction of sulfoxides with sodium borohydride in the presence of catalytic amounts of cobalt chloride[81].

D. The Truce–Smiles Rearrangement of Sulfones

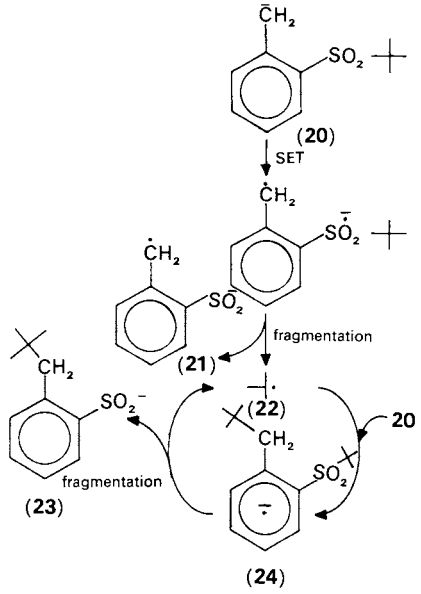
The Truce–Smiles rearrangement involves the formation of *O*-benzyl benzenesulfinic acid from diaryl sulfones[82]. When the migrating group is alkyl rather than aryl, an electron-transfer/radical-anion reaction pathway has been proposed[82]. The benzylic carbanion transfers one electron to the sulfonyl group leading to an intramolecular radical/radical-anion pair (Scheme 10). The homolytic cleavage of the *t*-Bu–SO_2 bond followed by a radical coupling then gives rise to the observed product. Beside the simple fragmentation–recombination sequence, another route (Scheme 11) could involve a radical chain process[84]. The *t*-butyl radical **22** would attack the benzylic position of a



(18) **(19)**



SCHEME 10



SCHEME 11

metalated sulfone **20** and give the radical anion **24**, which would fragment to give product **23** and a *t*-butyl radical able to initiate a new chain. Experimental evidence[85] (such as dimerization of benzylic radicals) shows unambiguously the radical nature of the mechanism and complementary data[86] support a radical chain process. To confirm this hypothesis, it would be interesting to carry out this kind of rearrangement in the presence of a catalytic amount of strong oxidants (inhibition of the initial SET) or radical traps (inhibition of the chain).

E. Reduction of Halomethyl Phenyl Sulfones and Chloromethyl Phenyl Sulfoxide by Fluorenide Anions

Bordwell and coworkers[63a,87] have studied the reaction of 9-fluorenyl carbanions (9-RFl$^-$) with a series of electron acceptors and in particular α-halosulfones and sulfoxides, in dimethyl sulfoxide solution. The overall reaction is characterized by the formation of the 9,9′-bis-fluorenyl derivative and the reduction of the halogenated acceptor. A family of 9-substituted fluorenyl carbanions covering a basicity range of 9.1 pK_a units was used and

$$9\text{-RFl}^- + \text{PhSO}_2\text{CR}^1\text{R}^2\text{X} \longrightarrow (9\text{-RFl})_2 + \text{PhSO}_2\text{CHR}^1\text{R}^2 + \text{X}^-$$

$$\text{R} = \text{Ar, CH}_3$$
$$\text{R}^1 = \text{H, CH}_3\text{, Ph}$$
$$\text{R}^2 = \text{H, Ph}$$
$$\text{X} = \text{Cl, Br, I}$$

the acceptors were selected in order to monitor a systematic increase in their acceptor ability. Kinetic and electrochemical data indicate that electron transfer from 9-RFl$^-$ to the electron acceptor is the rate-limiting step. The produced 9-RFl$^\bullet$ radicals then dimerize

$$9\text{-RFl}^- + \text{PhSO}_2\text{CR}^1\text{R}^2\text{X} \xrightarrow{\text{SET}} 9\text{-RFl}^\bullet + \text{PhSO}_2\text{CR}^1\text{R}^2\text{X}^{\bullet-} \xrightarrow[\text{(solvent)}]{\text{H}} \text{PhSO}_2\text{CHR}^1\text{R}^2 + \text{X}^-$$

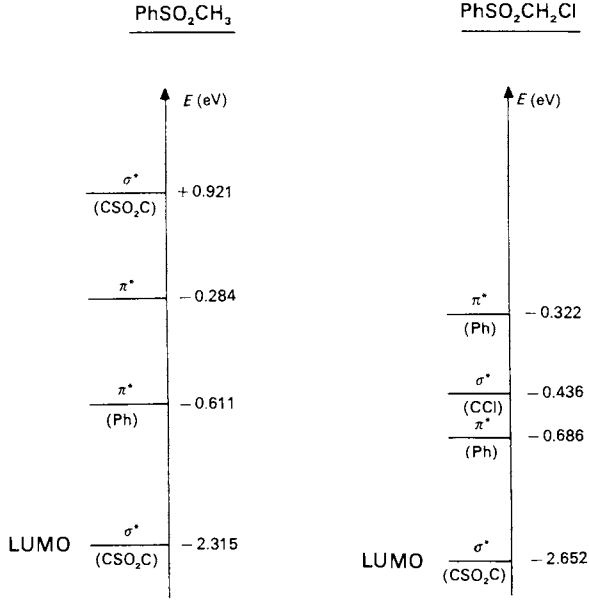
to $(9\text{-RFl})_2$ in a non-chain process. The rate differences are correlated with the electron accepting ability of sulfoxides and sulfones (Table 8). Plots of log k *versus* pK_a of the 9-RFlH give Brönsted β values near unity; therefore, the higher the basicity of a carbanion the more it should give electron transfer in preference to alternative pathways. It is interesting to note that the electron accepting ability of 2, 2-bis(phenylsulfonyl) propane, $(\text{PhSO}_2)_2\text{C(CH}_3)_2$, is smaller than those of α-halosulfones since it fails to react with 9-RFl$^-$ carbanions. Only the reaction of the strongly basic 9-arylxanthenide ion family (26.6

TABLE 8. Second-order rate constants for reactions of 9-R-fluorenyl carbanions with α-halosulfones and sulfoxides in Me_2SO solution at 25 °C[63a,87]

R	pK_{HA}[a]	Electron acceptor[b]	$E_{1/2}$[c] (V)	$10k$ ($M^{-1}s^{-1}$)
9-(*p*-MeC_6H_4)	18.3	$PhSO_2CH_2Br$	−0.60	8.1
9-C_6H_5	17.9	$PhSO_2CH_2Br$	—	3.0
9-(*m*-ClC_6H_4)	16.8	$PhSO_2CH_2Br$	—	0.16
9-(C_6H_5S)	15.4	$PhSO_2CH(Ph)Br$	—	133
9-(*p*-BrC_6H_4S)	14.8	$PhSO_2CH(Ph)Br$		58
9-(*m*-ClC_6H_4)	16.8	$PhSO_2C(Me)(Ph)Br$		103
9-(*p*-BrC_6H_4S)	14.8	$PhSO_2C(Me)(Ph)Br$		0.2
9-Me	22.3	$PhSO_2CH_2Cl$	−1.5	0.14
9-Me	22.3	$PhS(O)CH_2Cl$		1.8
9-C_6H_5	17.9	$PhSO_2CH_2I$	−0.50	2.8

[a] pK_a of the conjugate acid of the anions in the Me_2SO at 25 °C.
[b] Used in excess.
[c] Irreversible potentials obtained with a hanging mercury drop working electrode a Ag/AgI/Me_2SO reference electrode, and 0.1 M $Et_4N^+BF_4^-$ in Me_2SO as a supporting electrolyte at a scan rate of 25 V/s.

$< pK_a < 28.4$) with this acceptor is possible. Nevertheless, the reduction potential of this acceptor (-1.6 eV) is rather close to that of chloromethyl phenyl sulfone (-1.5 eV)[87] and this latter sulfone reacts with 9-RFl$^-$ carbanions. If we consider the Marcus approach of electron transfer rates[62,88] the thermodynamic parameters being approximately the same, the relative rates should be governed by the parameters λ measuring the reorganization energies. These energies are (1) the energy needed to convert the initial geometry of the acceptor to the geometry where the electron transfer can take place, and (2) the energy required for reorganization of the solvent molecules. The foregoing results therefore suggest that the reorganization energies are somewhat different for these two acceptors. In order to estimate the influence of the chloro substituent on the energy and localization of the unoccupied molecular orbitals we have performed MNDO-3 calculations on the methyl phenyl sulfone and chloromethyl phenyl sulfone (Scheme 12). The results show that: (i) as expected the LUMO of the halogeno compound is the lowest, hinting at a greater electron affinity; (ii) in both cases this LUMO is mainly described in terms of σ^* C_{sp^3}—S, C_{sp^2}—S, S—O, and to a smaller extent in terms of n* of O and S; and (iii) in the case of the halogeno derivative the σ^* C—Cl appears immediately after the first phenyl π^* S—O, contrary to what is generally assumed[87] for this type of electron acceptor. These theoretical data suggest that the added electron could be first transferred from the donor into the antibonding orbitals of the C—SO_2—C group and not into the antibonding σ^* of the C—Cl bond. The cleavage of the C—Cl bond would result only when an intramolecular electron transfer from SO_2 to σ^* C—Cl has taken place. If such a description is correct, α-halosulfones would behave as 'hidden' ambident electrophilic centers. The term hidden[89] indicates that the structure of the formed product suggests a reactivity involving mainly the C—Cl bond (apparent electrophilic center) whereas the theoretical calculations hint at a participation of the SO_2 center (hidden electrophilic center) in the reactivity.



SCHEME 12

F. Desulfonylation of Acetylenic and Vinylic Sulfones by Organometallic Reagents

The properties of carbanions as single electron donor reagents have been recently reviewed by Guthrie[90] and Eberson[88]. Eisch and Behrooz[91] recently described electron transfer processes in the alkylation of α,β-unsaturated sulfones by organometallic reagents. The starting point was the alkyldesulfonylation (Truce reaction) observed when some acetylenic sulfones react with particular organometallic:

$$R{-}C{\equiv}C{-}SO_2Ph + R'M \longrightarrow R{-}C{\equiv}C{-}R'$$

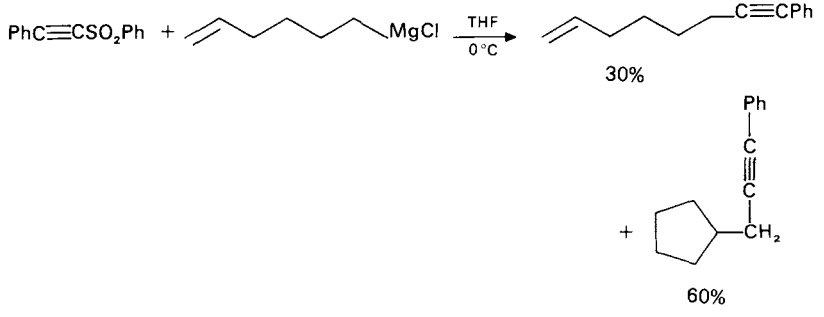
$$R = \text{aryl, alkyl without } \alpha\text{-hydrogen, } Me_3Si$$

$$R'M = R'Li \text{ or } R'MgX$$

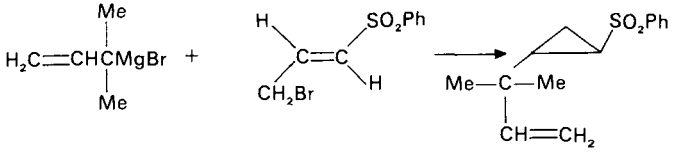
Three possible mechanisms may be envisioned for this reaction. The first two i.e.: 1) Michael addition of R'M to the acetylenic sulfone followed by α-elimination of LiO_2SPh to yield a vinyl carbene which undergoes a 1, 2 aryl shift and 2) carbometallation of the acetylenic sulfone by R'M followed by a straightforward β-elimination, where discarded by the authors. The third mechanism in which the organometallic reagent acts as an electron donor and the central intermediates is the radical anion:

$$[Ph{-}\dot{C}{=}\bar{C}{-}SO_2Ph]Mg^{+}Cl$$

is strongly supported by the observation that, when the organometallic reagent contains a built in trap for paramagnetic species, the products anticipated for a radical mechanism are isolated:

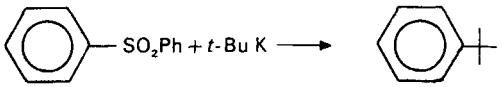


Vinylic sulfones undergo the same reaction especially when allylic, benzylic or t-alkylithium reagents are employed. One case of a vinyl sulfone deserves special mention[65,92]. When phenyl *trans*-3-bromopropenyl sulfone is treated with certain Grignard reagents it undergoes an alkylating cyclization:



The dimethylallyl group is attached to the cyclopropyl ring at the more hindered terminus of the allyl group. Such an astonishing regioselectivity in terms of steric effects can be reconciled if one admits that the intermediate dimethylallyl radical (with the highest spin density on the tertiary carbon) is involved in the reaction. The observation that these alkyldesulfonylations occur most readily with those RM reagents whose anionic R groups have the lower electron affinities fits also with the SET process. Finally, diphenyl sulfone

reacts with *t*-butylpotassium to form alkyldesulfonylation products in fair yields:

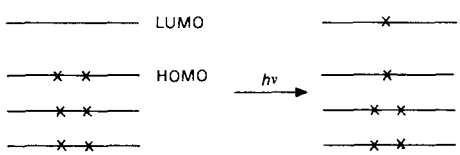


In contrast, *n*-butyllithium reacts with this sulfone principally by lithiation *ortho* to the sulfonyl group and the lithio compound is then converted into dibenzothiophene. This observation which shows the difference in behavior of *n*-alkyl and *t*-alkyl carbanions is taken as additional hint for the electron transfer pathway. Stasko and coworkers results[93–95] diminish however the weight of this evidence. They observed the ESR signal due to the corresponding radical anion when diphenyl sulfone reacts with *n*-butyllithium; this radical anion is then converted into a dibenzothiophene sulfone anion radical. When the reaction proceeds in HMPA the dibenzothiophene is obtained in yields up to 50%. On addition of non polar solvents such as benzene or hexane, the radical anion of the original diphenyl sulfone is observed and its transformation to that of dibenzothiophene sulfone is accelerated by addition of HMPA. These authors propose, in contrast with Eisch, that *n*-butyllithium first transfers its electron to yield the radical anion of diphenyl sulfone. The reactive butyl radical then abstract hydrogen from the phenyl group, opening the way to the formation of dibenzothiophene. This set of observations shows that even if electron transfer plays a role in these reactions, the mechanistic details are far from being settled. One open question concerns the possible participation of chain reactions in these transformations.

IV. DONOR–ACCEPTOR PROPERTIES OF SULFONES AND SULFOXIDES IN PHOTOCHEMISTRY

Using correspondence principles[96] between photochemistry, electrochemistry and ordinary chemistry tells us that the redox properties of sulfones and sulfoxides could photochemically manifest themselves in two main directions.

The first direction has to do with the fact that redox properties of excited states are usually strongly enhanced in comparison with redox properties of the ground state of the same compound[97]. This may be approximately justified by the simple diagram in Scheme 13[98], where one sees that electronic excitation creates a hole in a low-lying molecular orbital. This molecular orbital will therefore behave as a potential well far better able to welcome an electron than the LUMO in the ground state. The enhancement in accepting ability is approximately given by the difference in LUMO–HOMO energy. The electronic excitation also stocks the LUMO where the electron is less efficiently held than it was in the ground state when it occupied the HOMO. Here again, the enhancement of reducing properties is given by the LUMO–HOMO energy difference. For example, in the ground state dimethyl sulfoxide displays an oxidizing ability approximately measured by a potential -2.18 V ($E_{1/2}$ versus SCE). If one takes 0.242 for the difference between SCE and NHE values, this provides a potential versus NHE of about -2.0 V.



SCHEME 13

The LUMO–HOMO gap is approximately given by the spectroscopic properties of the SO group. Since DMSO absorbs in the region of 2380 and 2560 Å, we obtain[96] $1.24 \times 10^4/2560 = 4.8$ eV. This measures the drastic enhancement in redox properties anticipated for this compound. Indeed the 4.8 V value for the ground-state potential covers the whole range of usual redox potentials. The same principle applies to the sulfones because their electrode potential and absorption properties differ little from their sulfoxide analogues.

This considerable enhancement in redox properties may however remain chemically hidden. Several causes may converge to mask these properties. First of all electron transfer is an intermolecular act of reactivity: even when thermodynamically feasible it may have to compete with very rapid *intramolecular* acts of deactivation (fluorescence, phosphorescence, internal conversion)[99]. The rate of electron transfer is given by the Rehm–Weller equation[96,100]

$$\Delta G = 23.06[E(\mathrm{D/D^+}) - E(\mathrm{A^-/A}) - \varepsilon_0{}^2/\varepsilon_a] - F_{00}$$

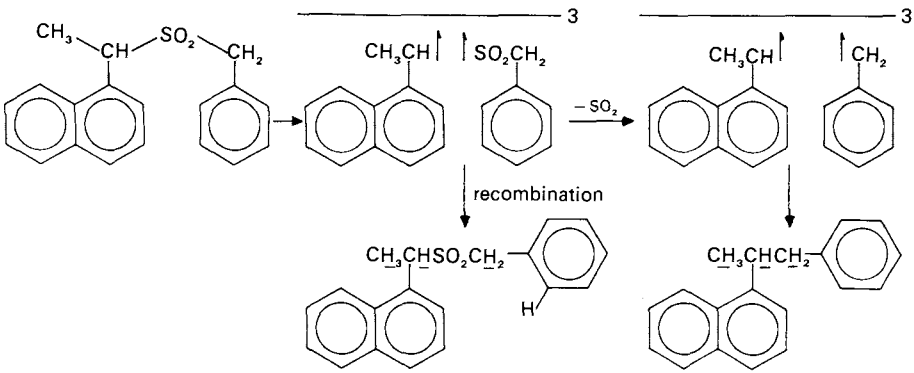
where ΔG is in kcal mol^{-1}, $E(\mathrm{D/D^+})$ is the oxidation potential of the donor in its ground state, $E(\mathrm{A^-/A})$ is the reduction potential of the acceptor A in its ground state and $\varepsilon_0{}^2/\varepsilon_a$ is the free enthalpy associated with the coulombic interaction of $\mathrm{D^+}$ and $\mathrm{A^-}$. For highly polar solvents this term can be neglected since, for example in acetonitrile, it amounts to only 0.06 kcal mol^{-1}; F_{00} is the electronic excitation energy expressed in eV. If $F_{00} = n$ Å its value in eV is $1.24 \times 10^4/n$. If $F_{00} = n$ cm^{-1}, its eV value will be $124 \times 10^{-6} \times n$. When ΔG is more negative than -5 kcal mol^{-1}, the reaction should be diffusion controlled. However, even when the competition between intermolecular electron transfer and intramolecular modes of deactivation is won by the intermolecular term, redox chemistry is still not necessarily displayed by the compound. Indeed if we consider the acceptor, a very fast back electron transfer[101] is highly favored as soon as the excited state A* with the excess electron returns to the ground state. $\mathrm{A^-}$ becomes a strong reductant in the vicinity of the oxidant constituted by $\mathrm{D^+}$ which was formed when D was willing to give its electron to A*. It is now rather eager to recuperate it. The rate of this back electron transfer may be decreased by using different techniques, such as charge separation at solid-aqueous interfaces[102], micelles[103], liposomes[104], microemulsions[105], polyelectrolytes[106] and β-cyclodextrin[107]. Sometimes, such tricks are not needed because the transfer of an electron strongly activates the substrates towards a given reaction[96,108]. If this activation is sufficient, the substrate which has received or given up an electron is transformed into products at a rate which may be competitive with a rapid back electron transfer. In the foregoing sections we have seen that the radical anions of sulfoxides and sulfones are highly prone to undergo the cleavage reactions:

$$[\mathrm{RSO}_n\mathrm{R'}]^{\cdot} \longrightarrow \mathrm{RSO}_n{}^- + \mathrm{R'^{\cdot}}$$
$$n = 1, 2$$

provided that R and R′ are not both alkyl substituents[109]. The radical cations of sulfoxides and sulfones seem to be activated mainly toward association.

A third factor to be considered in this triangular competition (internal deactivation, back electron transfer, chemical reaction) is the possibility of an unfavored chemical reaction followed by the initiation of a long chain[39,40].

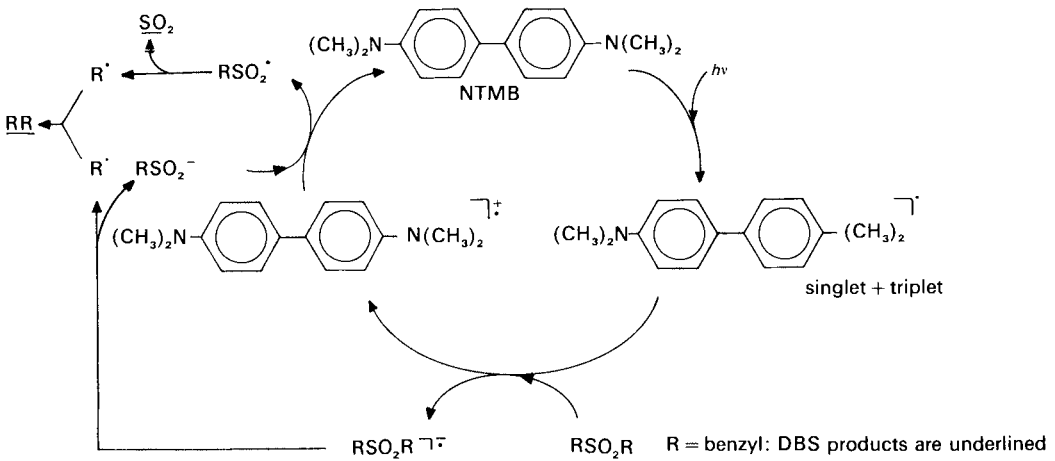
The second direction in which redox properties of sulfones and sulfoxides could manifest themselves in photochemistry is redox photosensitization[108,110–114]. In such a photosensitization the photosensitizer is transformed by light into a short-lived oxidant or reductant able to react with the substrate to be activated. Tazuke and Kitamura[115] have discussed the parameters to play with when one



(underlined protons are those for which CIDNP effects were observed)

SCHEME 14

wants to improve the efficiency of electron transfer sensitization (see also Reference 116 for an original way). Givens and coworkers[117–120] and Tung[121] have performed exhaustive mechanistic studies on the photoreactivity of aryl sulfones. Upon irradiation these compounds lose molecular sulfur dioxide and give products typical of radical coupling reactions. Both the singlet and triplet states of these compounds are photolabile[117,118] and the intermediates involved in these reactions are radicals[117]. However, in the absence of specific donors or acceptors in the medium no electron transfer seems to be reported in this photoreactivity. A weak hint at such an involvement could be taken from photo-CIDNP NMR experiments on α-naphthylmethyl benzyl sulfone (Scheme 14). Indeed, Hrinczenko[122] irradiated this sulfone in benzene-d_6 under four different conditions: (1) without added sensitizer, (2) with benzophenone (E_T = 69 kcal mol^{-1}) added as triplet sensitizer, (3) with tri-*n*-butyltin hydride added as free radical trap and (4) with benzophenone and tri-*n*-butyltin hydride. Condition (4) surprisingly yielded the strongest CIDNP effects. This effect of added tri-*n*-butyltin hydride, not explained in the foregoing report, could possibly originate from an electron transfer induced cleavage by added tri-*n*-butyltin hydride. This hydride is indeed a radical trap but also an electron donor[123]. Turro's group specifically designed photochemical systems in which the cleavage of S—C bonds in sulfones is induced by electron transfer[110,121]. The simplified principle of this cleavage is shown in Scheme 15 (in CH_3CN solvent). A few comments concerning Scheme 15 are in order. The fact that 10^{-4} M of the sensitizer (NTMB) is sufficient to convert 10^{-2} M of the sulfone clearly indicates a catalytic process as displayed in the scheme. However, no evidence for an increased yield of NTMB cation radical transient absorption could be found when dibenzyl sulfone (DBS) was added in the time-resolved experiments, therefore the report[121] describing the nature of the photosensitization is somewhat ambiguous. On the other hand, a rather thorough mechanistic analysis was performed and provided a complex picture of elementary steps, summarized in Scheme 16. α and β represent the limiting efficiency of diphenylethane production through the successive steps proposed in the simplified scheme. Based on the consumed DBS, the yield of diphenylethane (DPE) is 100% and NTMB is recovered quantitatively. A plot of $1/\Phi_{DPE}$ (Φ_{DPE} denotes quantum yield of DPE formation) versus 1/[DBS] at a given concentration of NTMB yields a curve rather than a straight line. This curvature is observed because the triplet lifetime of NTMB is significantly longer than that of the singlet; therefore at low DBS concentrations, quenching of the singlet is negligible


SO2
R·
RSO2·
RR
R·
RSO2−
(CH3)2N
N(CH3)2
NTMB
hν
(CH3)2N
N(CH3)2
(CH3)2N
(CH3)2
singlet + triplet
RSO2R
RSO2R
R = benzyl: DBS products are underlined

SCHEME 15

$$\text{NTMB} \xrightarrow{3130\,\text{Å}} {}^1\text{NTMB}^*$$

$${}^1\text{NTMB}^* \xrightarrow{k_F = 3 \times 10^7 s^{-1}} \text{NTMB} + h\nu$$

$${}^1\text{NTMB}^* + \text{DBS} \xrightarrow{{}^1k_q = 10^{10}\,M^{-1}s^{-1}} {}^1[\text{DBS}\cdots\text{NTMB}]^{+-}$$

$${}^1\text{NTMB}^* \xrightarrow{k_{ISC} = 6.3 \times 10^7 s^{-1}} {}^3\text{NTMB}^*$$

$${}^3\text{NTMB}^* \xrightarrow{k_T = 2 \times 10^5 s^{-1}} \text{NTMB}$$

$${}^3\text{NTMB}^* + \text{DBS} \xrightarrow{{}^3k_q = 2 \times 10^7\,M^{-1}s^{-1}} {}^3[\text{DBS}\cdots\text{NTMB}]^{+-}$$

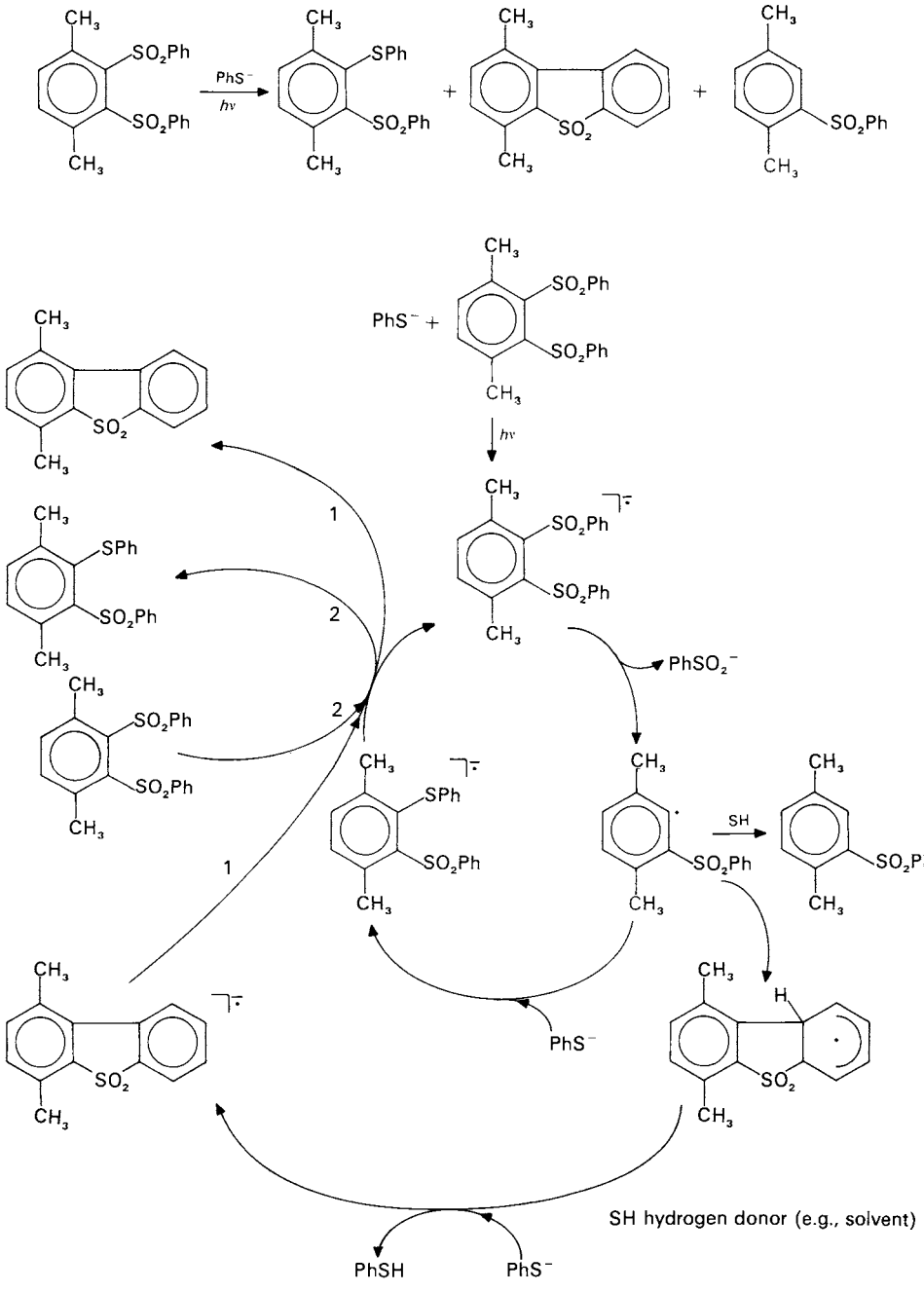
$${}^1[\text{DBS}\cdots\text{NTMB}]^{+-} \xrightarrow{\alpha} \text{products} + \text{NTMB}$$

$${}^3[\text{DBS}\cdots\text{NTMB}]^{+-} \xrightarrow{\beta} \text{products} + \text{NTMB}$$

SCHEME 16

while the triplet is quenched. Increasing concentration of DBS quencher obviously increases the overall quantum yield for reaction but, beyond a certain threshold of DBS concentration, quenching of singlet NTMB becomes possible. Therefore less NTMB triplets are formed by the intersystem crossing process. Since α (0.04), efficiency of DPE formation from quenching NTMB singlet, is one-tenth the value of β (escape favored in a triplet cage), a continuing increase in DBS concentration leads to a decrease in Φ_{DPE}. This type of redox photosensitization has been extended with success to α- and β-naphthyl benzyl sulfone, the irradiation being performed in these cases at 3500 Å. This redox photosensitization may be extended to the other sulfones provided that their radical anions are sufficiently short lived to prevent back electron transfer to the photosensitizer. If one views the activation act as a result of charge transfer complex formation[110] rather than free ion formation, one reaches a rather comparable picture for the practical limitation of the method, the parameter to consider in this case being the localization and the antibonding character of the MO mainly populated in the electron donor–acceptor interaction.

Novi and coworkers[124] have shown that the reaction of 2,3-bis(phenylsulfonyl)-1,4-dimethylbenzene with sodium benzenethiolate in dimethyl sulfoxide yields a mixture of substitution, cyclization and reduction products when subjected at room temperature to photostimulation by a sunlamp. These authors proposed a double chain mechanism (Scheme 17) to explain the observed products. This mechanism is supported by a set of carefully designed experiments[125]. The addition of PhSH, a good hydrogen atom donor, increases the percent of reduction products. When the substitution process can effectively compete with the two other processes, the increase in the relative yield of substitution (e.g., with five molar equivalents of benzenethiolate) parallels the decrease in those of both cyclization and reduction products. This suggests a common intermediate leading to the three different products. This intermediate could either be the radical anion formed by electron transfer to 2,3-bis(phenylsulfonyl)-1,4-dimethylbenzene or the σ radical formed

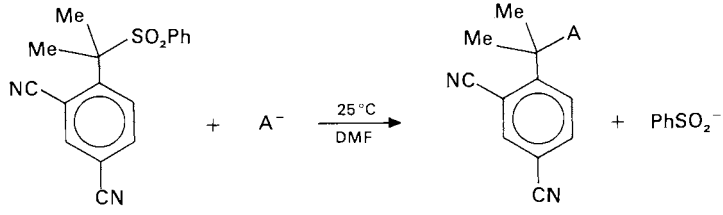


SCHEME 17

by the cleavage[126] of this radical anion. The first possibility was discarded because the addition of 2.5 molar equivalents of phenol (a good proton donor) does not change the product distribution. The intermediate is therefore the σ radical. This conclusion is strengthened by the increase in the relative concentrations of products when the quantity of added PhSH increases. Interestingly, the addition of PhSH slows down the overall rate of formation for both the substitution and cyclization products. This observation, totally expected for the substitution product (classical $S_{RN}1$ test), is more puzzling for the cyclization product and explains why the authors begin to think about a double chain mechanism. The chain forming cyclization products was further supported by (1) study of the pattern of reactivity for 2,3-bis(phenylsulfonyl)-1,4,5,6-tetramethylbenzene which gives minimum amounts of substitution products, (2) measurement of quantum yields for formation of the cyclization product ($\phi = 4$) in this case, and (3) cyclic voltammetry and controlled-potential electrolysis[127] of 2,3-bis(phenylsulfonyl)-1,4-dimethylbenzene in the presence of increasing quantities of a base. The addition of base considerably reduces the charge consumption in the controlled-potential electrolysis of this product.

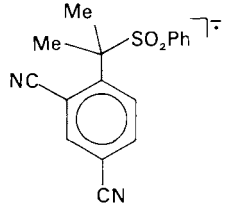
The foregoing mechanistic scheme displays two original features beyond the double chain overall representation. The first one is the step in the second chain where an aryl radical rather than losing a hydrogen as it usually does, gives up a proton in a reaction which may be viewed as a substitution reaction where the nucleophile is a base, the electrophilic center is a proton and the leaving group is a radical anion. The second one is the fast and regioselective cleavage of the C—S bond in the radical anion formed in the initial electron transfer to the substrate. Indeed, several diaryl sulfones have been shown to stand rather well the addition of an electron[128–130]. The rapid cleavage of this radical anion could be the result of steric strain release associated with the cleavage in *ortho*-substituted diaryl sulfones[131]; electronic effects[132] may also play a role in this easy cleavage.

The cleavage of C—S bonds in $C—SO_2R$ anion radicals plays an important role in $S_{RN}1$ type processes[39–44]. Kornblum and coworkers[41,126] described a photostimulated electron transfer chain substitution at a saturated carbon where the leaving group is $PhSO_2$:

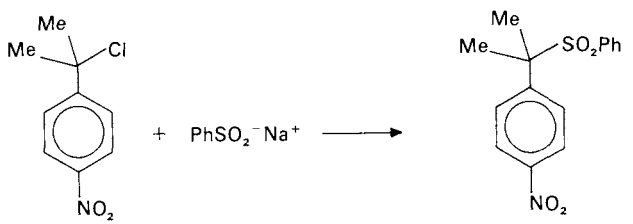


$A^- = CH_3\bar{C}(CO_2Et)_2$, and $(CH_3)_2\bar{C}NO_2$ (in HMPA), PhS^- (in DMF)

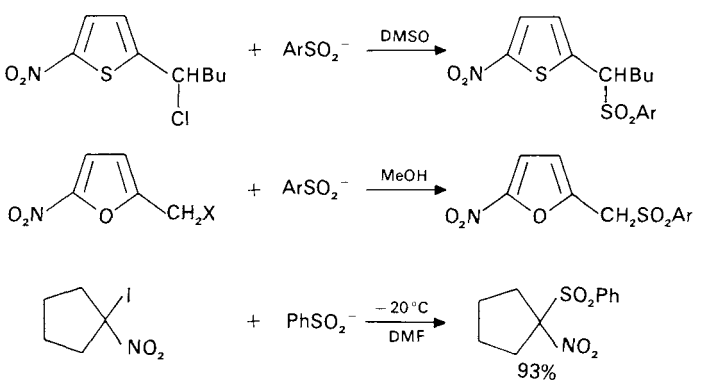
The mechanism involves the radical anion:



and a similar intermediate is formed when the two cyano groups are replaced by a NO_2 group[41]. However, the reaction [with $A^- = (CH_3)_2CNO_2^-$] does not occur when the CN groups are absent. A possible explanation of this observation, which is consistent with the hidden ambident reactivity approach[89], could be that the LUMO accepting the electron is lowered by the CN groups making both initiating and propagating electron transfer easier in the chain reaction. The complete regioselectivity of cleavage (sp^3-C—SO_2 bond exclusively broken) could result (1) from the main localization of the LUMO in the cumylic system, (2) from the far poorer overlap between the empty orbital of π symmetry and the antibonding orbital in the sp^2-C—SO_2 fragment in the SO_2Ph moiety in comparison with the overlap between the LUMO of π symmetry and the antibonding orbital in the sp^3-C—SO_2 fragment in the part 2,4-$(NC)_2C_6H_3C(Me)_2SO_2$ moiety. It would be interesting to check if the introduction of a NO_2 substituent in the phenyl part of $PhSO_2$ which is also disubstituted in the *ortho* positions to the SO_2 group may revert the foregoing regioselectivity. Such problems of regioselectivity of cleavage have been considered in detail by Rossi and coworkers[134–136] and more recently by Guthrie[137]. Another possible fate for the sulfonyl radical anion is electron transfer where it plays the role of the donor in an $S_{RN}1$ propagation step. Thus, treatment of *p*-nitrocumyl chloride with sodium benzenesulfinate in DMSO at room temperature and under photostimulation yields 95% of the sulfone[41].



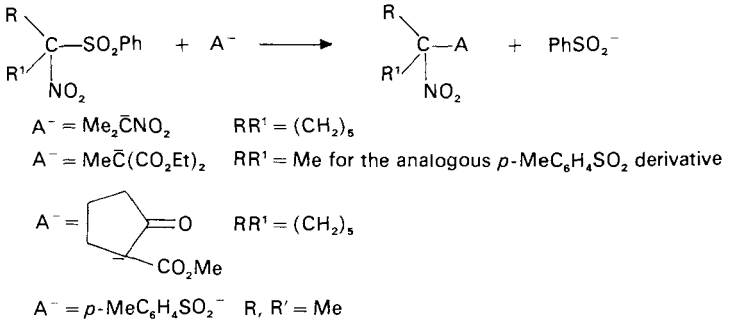
This type of substitution is also feasible with heteroaromatic substrates[138]. Curiously, the analogous reaction performed on furans in MeOH apparently follows a classical S_N2 mechanism although a non-chain electron transfer mechanism[139] cannot be totally dismissed[140] (Scheme 18). Tertiary α-nitrosulfones are obtained according to this principle of reactivity[41] (Scheme 18) and the reaction still works when an azido group[141] or a thiocyanato group[142] are used in place of the halogen as leaving group.



SCHEME 18

At room temperature under photostimulation α-nitrosulfones react with a variety of nucleophiles via radical anion chain reactions[41]; interestingly, in none of the cases where the $PhSO_2^-$ group is involved in $S_{RN}1$ type of substitution does the O end of the ambident anion[143] play a role. This strong regioselectivity is reminiscent of the one reported for other ambident anions involved in these radical chain substitutions[144].

Bowman and Symons[145] probed the stability of a series of radical anions involved in the $S_{RN}1$ substitution for α-substituted aliphatic nitro-compounds $[Me_2C(X)NO_2]$ by studying with ESR at 77 K the succession of events following electron capture by $Me_2C(X)NO_2$. The radical anions were more concentrated in an ether matrix than in an



alcohol matrix. Among the studied X (Br, Cl, SCN, NO_2, CN, PO_2Et_2, CO_2Et, COMe, SO_2Me, SO_2Ar, Me), COMe, SO_2Me, SO_2Ar and CN provided the highest concentrations of anion radicals. On this wide range of X and at this temperature, there is a trichotomy of reactions following electron capture: loss of NO_2^-, loss of X^- or radical-anion formation. The highest concentration of anion radical does not necessarily indicate a greater intrinsic stability of the anion radical because at this temperature the equilibrium

$$Me_2C(NO_2)X^{\cdot-} \underset{2}{\overset{1}{\rightleftharpoons}} Me_2CNO_2^{\cdot-} + X^-$$

may play an important role[146a]. The results suggest that when $X^- = PhSO_2^-$ the reverse reaction 2 is faster than the forward reaction 1. The bond cleaved in the radical anion varies with $X—X^-$ leaves where X = Br, Cl, SCN, SO_2R but NO_2^- leaves when X = COR, CO_2R, CN and NO_2. (See also the review by Bowman[146b]).

α-Cleavage of the S=O unit on irradiation can account for the photoracemization of sulfoxides[147]. For their breakdown[148] and for reactions of sulfinate esters[149], Muszkat, Praefcke and coworkers[150] performed a detailed mechanistic study of these carbon–sulfur bond cleavages. The photo-CIDNP investigation of sulfoxides revealed a great variety of photocleavage reactivity both by reaction from directly excited triplet and singlet states and by sensitization with triplet ketones. None of the reported experiments hints at electron transfer photoinduced chemistry. (When benzophenone was used as sensitizer during the irradiation of *p*-tolyl methyl sulfoxide, limited polarization was evidenced in benzophenone *ortho* protons. This could hint at an electron transfer from excited benzophenone to sulfoxide followed by back electron transfer.) The field of redox sensitization of S=O remains therefore open to investigation.

V. ACKNOWLEDGEMENTS

The authors would like to thank Mr. Rajzmann for performing theoretical MNDO calculations and M. Meyer for her help in the preparation of the manuscript. Drs Petrillo and Marino read the manuscript at the proof stage and we thank them for useful suggestions and comments.

VI. REFERENCES

1. J. Simonet, Chapter 22 in the present volume.
2. T. Koopmans, *Physica*, **1**, 104 (1933).
3. (a) M. J. S. Dewar and W. Thiel, *J. Amer. Chem. Soc.*, **99**, 4899 (1977).
   (b) M. J. S. Dewar and M. L. McKee, *J. Comput. Chem.*, **1**, 84 (1983).
   (c) M. J. S. Dewar and H. S. Rzepa, *J. Comput. Chem.*, **2**, 158 (1984).
   (d) L. M. Molino, J. M. Poblel and E. Canadell, *J. Chem. Soc., Perkin Trans. 2*, 1217 (1982).
   (e) C. Glidewell, *J. Chem. Soc., Perkin Trans. 2*, 551 (1985).
4. J. O. Chambers, *Encyclopedia of Electrochemistry of The Elements*, Organic Section Vol. XIII (Ed. A. J. Bard), Dekker, New York, 1978.
5. E. Block, *Reactions of Organosulfur Compounds, Organic Chemistry*, Vol. 37 (Eds. A. T. Blomquist and H. H. Wasserman), Academic Press, New York, 1978: (a) p. 15, (b) pp. 18–21.
6. M. M. Urberg and E. T. Kaiser, in *Radical Ions* (Eds. E. T. Kaiser and L. Kevan), Chap. 8, Interscience, New York, 1968; (a) pp. 301–320; (b) p. 307; (c) p. 306; (d) p. 311.
7. E. T. Kaiser, M. M. Urberg and D. H. Eargle, Jr., *J. Amer. Chem. Soc.*, **88**, 1037 (1966).
8. (a) R. Gerdil and E. A. C. Lucken, *Proc. Chem. Soc.*, 144 (1963).
   (b) R. Gerdil and E. A. C. Lucken, *Mol. Phys.*, **9**, 529 (1965).
9. A. D. McLachlan, *Mol. Phys.*, **3**, 233 (1960).
10. P. Lambelet and E. A. C. Lucken, *J. Chem. Soc., Perkin Trans. 2*, 617 (1978).
11. P. Lambelet and E. A. C. Lucken, *J. Chem. Soc., Perkin Trans. 2*, 164 (1976).
12. A. L. Ternay, Jr., L. Ens, J. Herrmann and S. Evans, *J. Org. Chem.*, **34**, 940 (1969).
13. S. S. Chu and B. Chung, *Acta Cryst.*, **B29**, 2253 (1973).
14. T. Aruga, O. Ito and M. Matsuda, *J. Amer. Chem. Soc.*, **101**, 785 (1979).
15. R. Leardini and G. Placucci, *J. Heterocycl. Chem.*, **13**, 277 (1976).
16. P. B. Koster and M. J. Janssen, *J. Chem. Soc., Perkin Trans. 2*, 803 (1974).
17. B. A. Olsen and D. H. Evans, *J. Amer. Chem. Soc.*, **103**, 839 (1981).
18. P. Neta and D. H. Evans, *J. Amer. Chem. Soc.*, **103**, 7041 (1981).
19. D. H. Evans and N. Xie, *J. Amer. Chem. Soc.*, **105**, 315 (1983).
20. E. Ahlberg, O. Hammerich and V. D. Parker, *J. Amer. Chem. Soc.*, **103**, 844 (1981).
21. O. Hammerich and V. D. Parker, *Acta Chem. Scand., Ser. B*, **35**, 395 (1981).
22. G. Vincow, *J. Chem. Phys.*, **37**, 2484 (1982).
23. M. M. Urberg and E. T. Kaiser, *J. Amer. Chem. Soc.*, **89**, 5179 (1967).
24. M. K. Kalinowski, *Chem. Phys. Letters*, **7**, 55 (1970).
25. D. H. Eargle, Jr. and E. T. Kaiser, *Proc. Chem. Soc.*, 22 (1964).
26. (a) E. T. Kaiser and D. H. Eargle, Jr., *J. Chem. Phys.*, **39**, 1353 (1963).
   (b) E. T. Kaiser and D. H. Eargle, Jr., *J. Amer. Chem. Soc.*, **85**, 1821 (1963).
27. (a) E. D. Sprague and F. Williams, *J. Chem. Phys.*, **54**, 5425 (1971).
   (b) Y. J. Chung and F. Williams, *J. Phys. Chem.*, **76**, 1792 (1972).
   (c) M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 797 (1973).
   (d) S. P. Mishra and M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 391 (1973).
   (e) A. R. Lyons, M. C. R. Symons and S. P. Mishra, *Nature*, **249**, 341 (1974).
   (f) E. D. Sprague, K. Takeda, J. T. Wang and F. Williams, *Can. J. Chem.*, **52**, 2840 (1974).
   (g) Y. J. Chung, K. Nishikida and F. Williams, *J. Phys. Chem.*, **78**, 1882 (1974).
28. M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 908 (1976).
29. G. Meissner, A. Henglein and G. Beck, *Z. Naturforsch.*, **22b**, 13 (1967).
30. A. M. Koulkes-Pujo, L. Gilles, B. Lesigne and J. Sutton, *J. Chem. Soc., Chem. Commun.*, 749 (1971).
31. N. M. Shishlov, A. I. Ivanov, R. A. Sadykov, A. A. Panasenko and V. N. Korobeinikova, *Khim. Vys. Energ.*, **17**, 554 (1983).
32. (a) N. M. Shishlov, V. K. Korobeinikora, V. A. Mazunov, A. A. Panasenko and R. A. Sadykov, *Khim. Vys. Energ.*, **17**, 179 (1983).
   (b) N. M. Shishlov, R. A. Sadykov, V. A. Mazunov and A. A. Panasenko, *ibid.*, **16**, 523 (1982).
33. W. B. Gara, J. R. M. Giles and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 1444 (1979).
34. M. J. Davies, B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 503 (1984).
35. B. C. Gilbert, R. O. C. Norman and P. S. Williams, *J. Chem. Soc., Perkin Trans. 2*, 207 (1981).
36. H. J. Shine, *Organo Sulfur Chemistry* (Ed. M. J. Janssen), Chap. 6, Interscience, New York, 1967, pp. 93–117.

37. S. Nish and M. Matsuda, *Kotagaku Toronkai Koen Yoshishu* (Jap), **52** (1979); C.A. **93**, 94472 (1980).
38. S. Rajan and K. Muralimohan, *Tetrahedron Letters*, 483 (1978).
39. M. Chanon and M. L. Tobe, *Angew. Chem., Int. Ed. Engl.*, **21**, 1 (1982).
40. J. F. Bunnett, *Acc. Chem. Res.*, **11**, 413 (1978).
41. N. Kornblum, in *The Chemistry of Amino, Nitroso and Nitro Compounds and their Derivatives* (Ed. S. Patai), Suppl. F, Wiley, New York, 1982, p. 361.
42. G. A. Russell, *Adv. Phys. Org. Chem.*, **23**, 271 (1987).
43. R. A. Rossi and R. H. de Rossi, *Aromatic Substitution by the $S_{RN}1$ Mechanism*, ACS Monograph 178, American Chemical Society, Washington DC, 1983.
44. R. K. Norris, in *The Chemistry of Functional Groups* (Eds. S. Patai and Z. Rappoport), Suppl. D, Wiley, New York, 1983, pp. 681–702.
45. M. Ballester, J. Riera, J. Castañer, C. Badia and J. M. Monso, *J. Amer. Chem. Soc.*, **93**, 2215 (1971).
46. (a) D. Griller and K. U. Ingold, *Acc. Chem. Res.*, **9**, 13 (1976).
(b) L. Stella, Z. Janousek, R. Merényi and H. G. Viehe, *Angew. Chem., Int. Ed. Engl.*, **17**, 691 (1978).
47. L. Field, J. R. Holsten and R. D. Clark, *J. Amer. Chem. Soc.*, **81**, 2572 (1959).
48. G. A. Russell, in *Free Radicals* (Ed. J. K. Kochi), Vol. 1, Wiley, New York, 1973, p. 299.
49. M. Julia, G. Le Thuillier, C. Rolando and L. Saussine, *Tetrahedron Letters*, **23**, 2453 (1982).
50. (a) L. A. Paquette, *Acc. Chem. Res.*, **1**, 209 (1968).
(b) F. G. Bordwell, *Acc. Chem. Res.*, **3**, 281 (1970).
51. F. G. Bordwell, J. M. Williams, Jr., F. B. Hoyt, Jr and B. B. Jarvis, *J. Amer. Chem. Soc.*, **90**, 429 (1968).
52. M. Oku, and J. C. Philips, *J. Amer. Chem. Soc.*, **95**, 6495 (1973).
53. J. C. Philips and M. Oku, *J. Amer. Chem. Soc.*, **94**, 1012 (1972).
54. J. Kattenberg, E. R. de Ward and H. O. Huisman, *Tetrahedron*, **29**, 4149 (1973).
55. C. Y. Meyers, W. S. Matthews, L. L. Ho, V. M. Kolb and T. E. Parady, *Catalysis in Organic Synthesis*, Academic Press, New York, 1977, pp. 197–278: (a) p. 270, (b) p. 267, (c) p. 262–267.
56. C. Y. Meyers and T. W. Sam, abstracts, *Conference on Conformational Analysis*, Durham, NH, 1981.
57. F. G. Bordwell and B. B. Jarvis, *J. Amer. Chem. Soc.*, **95**, 7708 (1973).
58. N. S. Zefirov and D. I. Makhon'kov, *Chem. Rev.*, **82**, 615 (1982).
59. (a) B. Vacher, A. Samat and M. Chanon, *J. Amer. Chem. Soc.*, submitted.
(b) B. Vacher, Thesis, Marseilles, France, 1987.
60. (a) J. O. Edwards, *J. Amer. Chem. Soc.*, **76**, 1540 (1954).
(b) C. D. Ritchie, *J. Amer. Chem. Soc.*, **105**, 7313 (1983).
61. B. Vacher, A. Samat and M. Chanon, *Tetrahedron Letters*, **26**, 5129 (1985).
62. R. A. Marcus, *Ann. Rev. Phys. Chem.*, **15**, 155 (1964).
63. (a) F. G. Bordwell, A. H. Clemens, D. E. Smith and J. Begeman, *J. Org. Chem.*, **50**, 1151 (1985).
(b) F. G. Bordwell, personal communication.
64. R. A. Rossi and J. F. Bunnett, *J. Amer. Chem. Soc.*, **96**, 112 (1974).
65. J. J. Eish, *Pure Appl. Chem.*, **56**, 35 (1984).
66. K. N. Rao, B. Sethuram and T. N. Rao, *Oxidation Commun.*, **7** (1–2), 199 (1984).
67. C. Srinivasan, R. Venkatamy and S. Rajagopal, *Indian J. Chem.*, **20A**, 505 (1981).
68. V. Baliah and P. V. V. Satyanarayana, *Indian J. Chem.*, **16A**, 966 (1978).
69. R. N. Bose, N. Rajasekar, D. M. Thompson and E. S. Gould, *Inorg. Chem.*, **25**, 3349 (1986).
70. K. B. Wiberg and P. A. Lepse, *J. Amer. Chem. Soc.*, **86**, 2612 (1964).
71. N. A. Noureddin, W. B. McConnell and D. G. Lee, *Can. J. Chem.*, **62**, 2113 (1984).
72. T. L. Siddal, N. Miyaura, J. C. Huffmann and J. K. Kochi, *J. Chem. Soc., Chem. Commun.*, 1185 (1983).
73. G. A. Olah, G. K. S. Prakash and T. L. Ho, *Synthesis*, 810 (1976).
74. R. G. Nozzo, H. J. Simon and J. S. Filippo, *J. Org. Chem.*, **42**, 568 (1977).
75. T. L. Ho and C. M. Wong, *Synthesis*, 206 (1973).
76. B. R. James, F. T. T. Ng and G. L. Empel, *Can. J. Chem.*, **47**, 4521 (1969).
77. Y. Akita, M. Inaba, H. Uchida and A. Ohta, *Synthesis*, 792 (1977).
78. J. Drabowicz, H. Togo, M. Milolajczyk and S. Oae, *Org. Prep. Proc. Int.*, **16**, 171 (1984).
79. S. Black, E. M. Harte, B. Hudson and L. Wartosfsky, *J. Biol. Chem.*, **235**, 2910 (1960).
80. T. Nagata, T. Yoshimura, K. Fujimori and S. Oae, *Tetrahedron Letters*, **25**, 341 (1984).
81. D. W. Chasar, *J. Org. Chem.*, **36**, 613 (1971).

82. W. E. Truce, W. J. Ray, O. L. Norman and D. B. Eichemyer, *J. Amer. Chem. Soc.*, **80**, 2635 (1958).
83. D. M. Snyder and W. E. Truce, *J. Amer. Chem. Soc.*, **101**, 5432 (1979).
84. W. E. Truce and K. V. Madaj, *Sulfur Rep.*, **3**, 259 (1983).
85. D. M. Snyder, Ph.D. Thesis, Purdue University, 1980.
86. E. J. Madaj, Ph.D. Thesis, Purdue University, 1983.
87. F. G. Bordwell and A. H. Clemens, *J. Org. Chem.*, **47**, 2510 (1982).
88. L. Eberson, *Acta Chem. Scand.*, **B38**, 439 (1984).
89. M. Julliard, J. P. Scagliarini, M. Rajzmann and M. Chanon, *Chimia*, **40**, 16 (1986) and references therein.
90. R. D. Guthrie, in *Comprehensive Carbanion Chemistry* (Eds. E. Buncel and D. Durst), Part A, Chapter 5. Elsevier, New York, 1980.
91. J. J. Eish and M. Behrooz, *Tetrahedron Letters*, **25**, 4851 (1984).
92. J. J. Eish and J. E. Galle, *J. Org. Chem.*, **44**, 3277 (1979).
93. A. Stasko, *Chem. Zvesti*, **37**, 95 (1983).
94. A. Stasko, L. Malik, A. Tkac and E. Matasova, *Zh. Fiz. Khim.*, **53**, 486 (1979).
95. A. Stasko, L. Malik, A. Tkac and P. Pelikan, *Z. Phys. Chem.*, **261**, 1205 (1980).
96. M. Chanon, *Bull. Soc. Chim. Fr. II*, 209 (1985).
97. M. Julliard and M. Chanon, *Chem. Brit.*, **18**, 558 (1982).
98. V. Balzani, F. Bolletta, M. Gandolfi and M. Maestri, *Top. Curr. Chem.*, **75**, 1 (1978).
99. N. J. Turro, *Modern Molecular Photochemistry*, Addison-Wesley/Benjamin-Cummings, London, 1978.
100. D. Rehm and A. Weller, *Israel J. Chem.*, **8**, 259 (1970).
101. D. Mauzerall and S. G. Ballard, *Ann. Rev. Phys. Chem.*, **33**, 377 (1982).
102. I. Willner, J. W. Otvos and M. Calvin, *J. Amer. Chem. Soc.*, **103**, 3203 (1981).
103. N. J. Turro, M. Grätzel and A. Brown, *Angew. Chem., Int. Ed. Engl.*, **19**, 675 (1980).
104. P. P. Infelta, M. Grätzel and J. H. Fendler, *J. Amer. Chem. Soc.*, **102**, 1479 (1980).
105. C. A. Jones, L. E. Weaner and R. A. Mackay, *J. Phys. Chem.*, **84**, 1495 (1980).
106. D. Meisel, M. S. Matheson and J. Rabani, *J. Amer. Chem. Soc.*, **100**, 117 (1978).
107. E. Adar, Y. Degani, Z. Goren and I. Willner, *J. Amer. Chem. Soc.*, **108**, 4696 (1986).
108. M. Julliard and M. Chanon, *Chem. Rev.*, **83**, 425 (1983).
109. L. Horner and H. Lund, in *Organic Electrochemistry* (Ed. M. Baizer), Dekker, New York, 1973, p. 747.
110. G. J. Kavarnos and N. J. Turro, *Chem. Rev.*, **86**, 401 (1986).
111. A. Albini, *Synthesis*, 249 (1981).
112. S. L. Mattes and S. Farid, in *Organic Photochemistry* (Ed. A. Padwa), Vol. 6, M. Dekker, New York, 1983, p. 233.
113. L. W. Reichel, G. W. Griffin, A. J. Muller, P. K. Das and S. N. Ege, *Can. J. Chem.*, **62**, 424 (1984).
114. P. J. Kropp, in *Organic Photochemistry* (Ed. A. Padwa), Vol. 4, Dekker, New York, 1979, p. 1.
115. S. Tazuke and N. Kitamura, *Pure Appl. Chem.*, **56**, 1269 (1984).
116. A. P. Schaap, S. Siddiqui, G. Prasad, E. Palomino and L. Lopez, *J. Photochem.*, **25**, 167 (1984).
117. R. S. Givens, *Org. Photochem.*, **5**, 227 (1981).
118. R. S. Givens and B. Matuszewski, *Tetrahedron Letters*, 861 (1978).
119. R. S. Givens and R. J. Olsen, *J. Org. Chem.*, **44**, 1608 (1979).
120. R. S. Givens, B. Hrinczenko, J. H. S. Liu, B. Matuszewski and J. Tholen-Collison, *J. Amer. Chem. Soc.*, **106**, 1779 (1984).
121. (a) C. H. Tung, Ph.D. Thesis, Columbia University, 1983.
(b) P. K. Das, A. J. Muller, G. W. Griffin, I. R. Gould, C. H. Tung and N. J. Turro, *Photochem. Photobiol.*, **39**, 281 (1984).
122. B. W. Hrinczenko, Ph.D. Thesis, University of Kansas, Lawrence, 1983.
123. R. J. Klinger, K. Mochida and J. K. Kochi, *J. Amer. Chem. Soc.*, **101**, 6626 (1979).
124. M. Novi, C. Dell'Erba, G. Garbarino and F. Sancassan, *J. Org. Chem.*, **47**, 2292 (1982).
125. M. Novi, G. Garbarino and C. Dell'Erba, *J. Org. Chem.*, **49**, 2799 (1984).
126. M. Novi, C. Dell'Erba, G. Garbarino, G. Scarponi and G. Capodaglio, *J. Chem. Soc., Perkin Trans. 2*, 951 (1984).
127. M. Novi, G. Garbarino, C. Dell'Erba and G. Petrillo, *J. Chem. Soc., Chem. Commun.*, 1205 (1984).
128. F. De Jong and M. Janssen, *J. Chem. Soc., Perkin Trans. 2*, 572 (1972).
129. R. Gerdil, *Helv. Chim. Acta*, **56**, 196 (1973).
130. L. Horner and E. Meyer, *Ber. Bunsen. Phys. Chem.*, **79**, 136 (1975) and references cited therein.
131. J. Grimshaw and J. Trocha-Grimshaw, *J. Chem. Soc., Perkin Trans. 1*, 799 (1979).

132. C. P. Andrieux, J. M. Saveant and D. Zann, *Nouv. J. Chim.*, **8**, 107 (1984).
133. N. Kornblum and M. J. Fifolt, *J. Org. Chem.*, **45**, 360 (1980).
134. H. O. Villar, E. A. Castro and R. A. Rossi, *Z. Naturforsh.*, **39a**, 49 (1984).
135. R. A. Rossi, *Acc. Chem. Res.*, **15**, 164 (1982).
136. H. O. Villar, E. A. Castro and R. A. Rossi, *Can. J. Chem.*, **60**, 2525 (1982).
137. P. Maslak and R. D. Guthrie, *J. Amer. Chem. Soc.*, **108**, 2637 (1986).
138. P. J. Newcombe and R. K. Norris, unpublished data cited in Ref. 122, p. 694.
139. G. A. Russell, M. Jawdosiuk and M. Makosza, *J. Amer. Chem. Soc.*, **101**, 2355 (1979).
140. C. D. Beadle, W. R. Bowman and J. Prousek, *Tetrahedron Letters*, **25**, 4979 (1984).
141. S. I. Al-Khalil and W. R. Bowman, *Tetrahedron Letters*, **23**, 4513 (1982).
142. S. I. Al-Khalil and W. R. Bowman, *Tetrahedron Letters*, **24**, 2517 (1983).
143. N. Kornblum and A. P. Lurie, *J. Amer. Chem. Soc.*, **81**, 2705 (1959).
144. M. Meyer, A. Samat and M. Chanon, *Heterocycles*, **24**, 1013 (1986) and references cited therein.
145. W. R. Bowman and M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 25 (1983).
146. (a) W. R. Bowman and M. C. R. Symons, *J. Chem. Res. (S)*, 162 (1984).
(b) W. R. Bowman, *Photoinduced Electron Transfer* (Eds. M. A. Fox and M. Chanon), Elsevier, Amsterdam, 1988.
147. R. S. Cooke and G. S. Hammond, *J. Amer. Chem. Soc.*, **90**, 2958 (1968).
148. H. Nozaki, T. Shirafugi, K. Kuno and Y. Yamamoto, *Bull. Chem. Soc. Japan*, **45**, 856 (1972).
149. M. Kobayashi, H. Minato, Y. Miyaji, T. Yoshioka, K. Tanaka and K. Honda, *Bull. Chem. Soc. Japan*, **45**, 2817 (1972).
150. I. Khait, R. Lüdersdorf, K. A. Muszkat and K. Praefcke, *J. Chem. Soc., Perkin Trans. 2*, 1417 (1981).

CHAPTER **24**

Sulfinyl radicals

C. CHATGILIALOGLU

Istituto dei composti del carbonio contenenti eteroatomi e loro applicazioni, CNR, Ozzano Emilia, Bologna, Italy

I. INTRODUCTION

Sulfinyl radicals have the general structure **1** in which X may be a hydrogen, alkyl, aryl, amino or alkoxy group. Sulfinyl radicals are formal analogues of peroxyl (ROO$^{\bullet}$) and perthiyl (RSS$^{\bullet}$) radicals and play important roles in organosulfur chemistry as well as in biological systems. Until the mid-seventies, this class of radicals was elusive and was invoked in a wide variety of chemical reactions; however, spectroscopic techniques in the last years have been successfully used to elucidate these transient species. A number of extensive review articles have recently appeared on sulfur-containing radicals which also treat in part this subject[1]. Therefore, this chapter will necessarily be a selective résumé dealing mainly with recent literature.

(1)

II. STRUCTURAL PROPERTIES

The hydrosulfinyl radical (HṠO), which is believed to be one of the important intermediates in the oxidation reactions of sulfur-containing compounds, has been studied in detail in the last decade. Becker and coworkers[2] assigned a chemiluminescence spectrum in the range 520–960 nm to the $n \rightarrow \pi^*$ transition in HṠO, thereby providing the first spectroscopic evidence for the existence of this radical in the gas phase. High-resolution spectroscopic studies on HṠO and DṠO radicals have also been reported and molecular constants have been determined[3]. The hyperfine coupling constants of the hydrogen

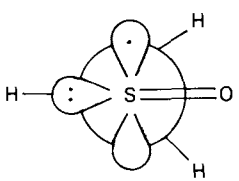
TABLE 1. ESR data and bond dissociation energies of some sulfinyl radicals

Radical	g-value	Hyperfine splittings[a] (gauss)	Rotational barrier (kcal mol^{-1})	$2k_t$(M^{-1}s^{-1}) at 173 K	BDE[X—ṠO] (kcal mol^{-1})
CH_3—ṠO	2.0100	11.5(3H)	2.6		50 ± 2
$CH_3CH_2CH_2$—ṠO	2.0111	9.1(2H)	4.3		48
$(CH_3)_3C$—ṠO	2.0106	singlet		6.0×10^7	
C_6H_5—ṠO	2.0090	2.4(3H), 0.7(2H)			67 ± 2
$(CH_3CH_2)_2N$—ṠO	2.0060	6.1(1N), 2.3(4H)		1.1×10^9	59
CH_3CH_2O—ṠO	2.0049	0.4(2H)			60

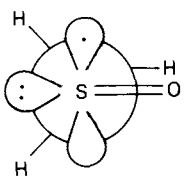
[a]Number of nuclei coupling given in parentheses.

nucleus have been determined by means of microwave spectroscopy[4] and suggest that the unpaired electron occupies a p-type molecular orbital perpendicular to the molecular plane in the ground electronic state and that the unpaired electron spin-density at the sulfur atom is about two thirds (in the isoelectronic HOO• radical the unpaired electron resides two thirds and one third on terminal and central oxygen, respectively). The radiative lifetime for this transition[5] as well as the electric dipole moment[6] of both ground and excited states of HṠO have also been obtained. Furthermore, the properties of both ground and first excited state have been calculated using *ab initio* SCF and CI methods[7].

The ESR spectrum of methanesulfinyl radical (CH_3ṠO), identified in a γ-irradiated single crystal of dimethyl sulfoxide[8], indicates that the unpaired electron resides essentially (72%) on the sulfur 3p orbital with modest population on the sulfur 3s (0.65%)†. A detailed analysis of the temperature dependence leads to 2.6 kcal mol^{-1} barrier height for the hindered internal rotation of the methyl group. At low temperature (88 K) the radical adopts a fixed conformation in which one proton lies in the nodal plane of the sulfur 3p orbital; however, it was not possible to distinguish either experimentally[8] or by *ab initio* SCF-MO calculations[9] between the two possible conformations, that is, **2** and **3**.



(**2**)



(**3**)

ESR studies of a variety of substituted sulfinyl radicals in the liquid phase have been reported[10–14]; some spectroscopic parameters are shown in Table 1, which also includes some kinetic and thermodynamic data. Typical aliphatic sulfinyl radicals have g-values of ca. 2.010, hyperfine splittings of β-H in the range 8.0–11.0 gauss and usually large linewidths which increase with increasing temperature[10]. The ESR parameters of the aromatic derivatives show an extensive delocalization of the unpaired electron on to the aromatic ring, confirming the π-nature of these species[10,12]. Table 1 contains also some estimated values for the X—ṠO bond dissociation energies (BDE) taken from Benson's

† The percentage of the spin-density on the 3s and 3p orbitals of the sulfur has been recalculated using the atomic parameters given by J. R. Morton and K. F. Preston, *J. Magn. Reson.*, **30**, 577 (1978).

review[15]; these relatively high values suggest that the α-scission process is not a feature of sulfinyl radicals.

III. CHEMICAL PROPERTIES

A. Methods of Formation

Sulfinyl radicals studied by ESR spectroscopy have been generated photolytically either from the appropriate sulfoxide or from the corresponding chlorides, namely[10,12–14,16]

$$XS(O)—Y \xrightarrow{h\nu} X\dot{S}O \xleftarrow{h\nu} XS(O)—Cl$$

where X and/or Y = alkyl, aryl, amino, alkoxy

However, in most cases photolysis of XS(O)Y alone produced much weaker signals from the radical $X\dot{S}O$ than when mixtures of the compounds with peroxides were irradiated. A mechanism has been proposed which involves hydrogen abstraction to form species **4**, the fragmentation of which gives the sulfinyl radical, namely[13,14,16]

$$(CH_3)_3CO—OC(CH_3)_3 \xrightarrow{h\nu} 2(CH_3)_3CO^{\bullet}$$

$$(CH_3)_3CO^{\bullet} + XS(O)—ZCH_2R \longrightarrow (CH_3)_3COH + XS(O)—\dot{Z}CHR \quad \textbf{(4)}$$

$$XS(O)—\dot{Z}CHR \longrightarrow X\dot{S}O + RCH{=}Z$$
(4)

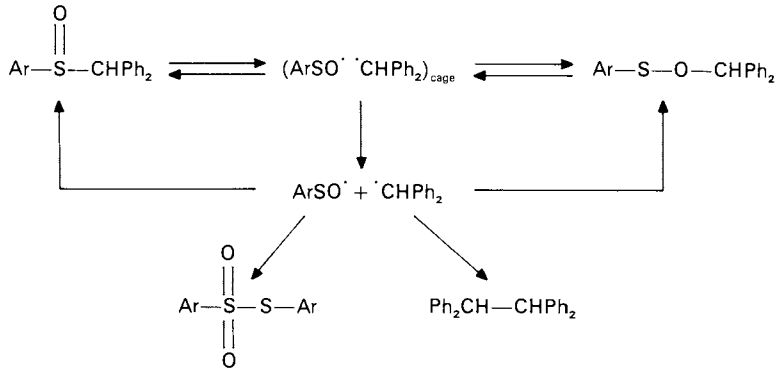
where Z = CR_2, NR, O

The sulfenic acids have been found to be extremely active radical scavengers showing rate constants of at least $10^7\ M^{-1}\ s^{-1}$ for the reactions with peroxyl radicals at 333 K[17]. It has also been suggested that the main inhibiting action of dialkyl sulfoxides or related compounds in the autoxidation of hydrocarbon derives from their ability to form the transient sulfenic acids on thermal decomposition, i.e.[17]

$$R—\overset{\overset{O}{\|}}{S}—C(CH_3)_3 \longrightarrow RSOH + H_2C{=}C(CH_3)_2$$

Gilbert and coworkers[18] were able to detect ESR spectra of sulfinyl radicals together with other sulfur-centered radicals during the oxidation of disulfides and thiols with a titanium(III)–peroxide couple; reaction mechanisms involving sulfenic acids as intermediates have been discussed.

The thermal and/or photolytic homolysis of thiosulfinates, *vic*-disulfoxides, sulfinyl sulfones and sulfenyl nitrates leads to the formation of a sulfinyl radical as one of the members of the initial radical pair[19]. From early studies it is known that arenesulfinyl radicals are involved in the thermal racemizations of aryl benzyl sulfoxides and arene sulfinamides[19]. However, Iino and coworkers[20] have lately shown from product analysis, ESR and CIDNP results that both benzhydryl *p*-tolyl sulfoxides [$ArS(O)CHPh_2$] and benzhydryl methyl sulfoxide give the corresponding sulfinyl radical by scission of the C—S bond at 373–403 K. The mechanism of $CH_3S(O)CHPh_2$ shows a simple behavior contrary to the decomposition of $ArS(O)CHPh_2$ where the presence of equilibrium between sulfoxide and sulfenate increases the complexity of the system. The overall mechanism of the latter is given in Scheme 1, although a non-radical path for the



SCHEME 1

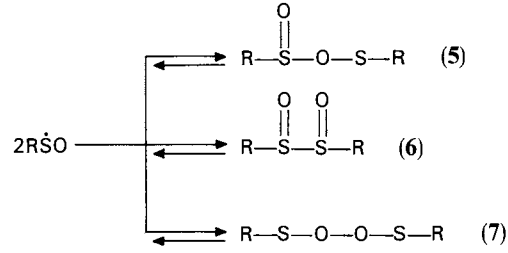
sulfoxide–sulfenate rearrangement cannot be ruled out. However, the fact that, at least in part, the rearrangement occurs through a radical pair indicates that the cross-termination reaction of sulfinyl radicals can take place with either sulfur or oxygen atoms.

Sulfinyl radicals have also been invoked in the synthetically useful reaction of alkane- and arenesulfinyl chlorides with activated zero-valent metals (Ag, Cu, Zn) to give the corresponding symmetrical thiosulfonates[21].

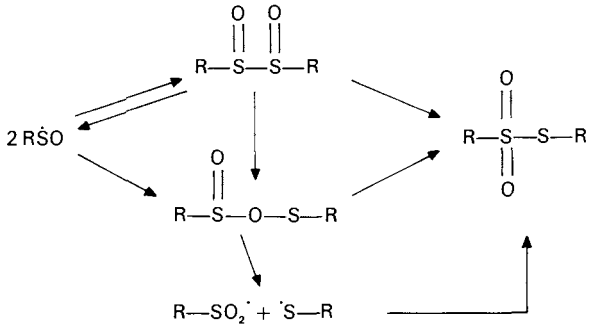
B. Self-termination Reaction

A characteristic reaction of free radicals is the bimolecular self-reaction which, in many cases, proceeds at the diffusion-controlled limit or close to it, although the reversible coupling of free radicals in solution to yield diamagnetic dimers has been found to be a common feature of several classes of relatively stable organic radicals. Unfortunatly, only the rate constants for self-termination of $(CH_3)_3C\dot{S}O$ ($6 \times 10^7\,M^{-1}\,s^{-1}$ at 173 K)[11] and $(CH_3CH_2)_2N\dot{S}O$ ($1.1 \times 10^9\,M^{-1}\,s^{-1}$ at 163 K)[13] have been measured up to date by kinetic ESR spectroscopy and consequently not many mechanistic conclusions can be reached.

On the other hand, it seems to be generally agreed that combination of two sulfinyl radicals leads to thiosulfonate (RSO_2SR) as the final product[22]; the usual suggestion has been that it takes place via an initial head-to-tail combination of the radicals to give a O, S-sulfenyl sulfinate (**5**) which then rearranges to the thiosulfonate.



According to the distribution of the unpaired electron spin-density in the sulfinyl radicals, two other possibilities of coupling products exist, that is, the formation of dimers involving oxygen-to-oxygen (**7**) or sulfur-to-sulfur (**6**) coupling. Thermodynamic arguments based on some rather gross assumptions suggest that the dimer **7** has very weak (or



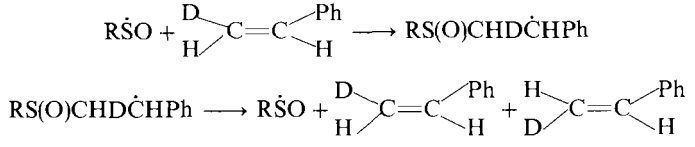
SCHEME 2

even negative) O—O bond strength, while *vic*-disulfoxides (**6**) have recently been detected as intermediates in the *m*-chloroperoxybenzoic acid oxidation of S-alkyl alkanethiosulfinates[23]. ESR studies also indicate that aromatic sulfinyl radicals (ArṠO) to some extent undergo irreversible disproportionation to yield the appropriate sulfonyl ($ArSO_2^{\cdot}$) and thiyl ($ArS^{\cdot}$) radicals[12].

Scheme 2 summarizes the mechanism for the formation of thiosulfonate from sulfinyl radicals: it is shown that the sulfinyl radicals combine to give both *vic*-disulfoxides and O, S-sulfenyl sulfinates, although they may rearrange to thiosulfonates either via a free radical route or via a concerted mechanism. The reader is referred to the recent review of Freeman[22], who has collected and discussed the vast amount of information published on *vic*-disulfoxides and O, S-sulfenyl sulfinates.

C. Addition Reactions

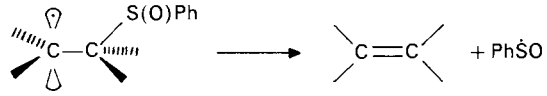
Early investigations have indicated that sulfinyl radicals apparently do not add, at least in the usual way, to olefinic double bonds[24]. However, some recent results by Iino and Matsuda[25] obtained by studying the thermal decomposition of benzhydryl *p*-tolyl and benzhydryl methyl sulfoxides in the presence of *cis*-*β*-deuteriostyrene lead one to believe that sulfinyl radicals add reversibly to CH_2=CHPh. The molar ratio of *trans* to *cis* *β*-deuteriostyrene that they observed at nearly 50% conversion was explained by addition–elimination reaction of sulfinyl radicals.



where R = methyl or *p*-tolyl

These results are in accordance with the findings of Boothe and coworkers[26], who found that the reactions of four diastereomeric 2-bromo-3-phenylsulfinylbutanes with tributyltin radicals generate *β*-phenylsulfinyl *sec*-butyl radicals (**8**) which eliminate PhṠO radicals to form the 2-butenes in a stereoselective manner. The stereoselectivities observed in this free radical elimination must result from the fact that the rate constant for elimination is greater than that for rotation about the C—C bond. Furthermore, a neighboring phenyl group on the radical center seems to stabilize the radical enough so that the internal rotation can compete with the *β*-elimination reaction. It is also noteworthy that the small

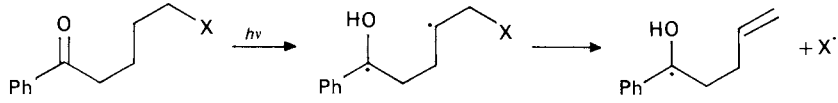
differences observed in the relative rates of reaction of the diastereomeric bromo sulfoxides towards tributyltin radicals are inconsistent with oxygen participation in the radical formation and may be consistent with a modest interaction between sulfur and the developing p orbital of the radical[26].



(8)

It seems to the author that another possible pathway can coexist with the above-mentioned reversible addition of sulfinyl radicals to olefinic double bonds, that is, the reversible addition by the sulfinyl oxygen, since a substantial amount of the unpaired electron spin-density resides on the oxygen atom.

Wagner and coworkers[27] have reported that the relative rates of cleavage of BuṠO and PhṠO are in a ratio of 1:8.3 when the 1,4-biradicals **9** are generated via the Norrish type II photoreaction as shown in Scheme 3 (X represents the appropriate sulfur-containing moiety). The relative β-cleavage rates of BuS$^{\cdot}$, BuṠO and BuSO$_2^{\cdot}$ are in the ratio of 1:475:2.9, confirming Kice's suggestion[19] that sulfinyl radicals have the greatest relative kinetic stability of the three.



(9)

SCHEME 3

IV. REFERENCES

1. F. Freeman and M. C. Keindl, *Sulfur Rep.*, **4**, 231 (1985); L. Lunazzi and G. F. Pedulli, in *Organic Sulfur Chemistry* (Ed. F. Bernardi, I. G. Csizmadia and A. Mangini), Chap. 9, Elsevier, Amsterdam, 1985, pp. 484–567.
2. K. H. Becker, M. A. Inocêncio and U. Schurath, *Int. J. Chem. Kinet. Symp., 1*, 205 (1979); U. Schurath, M. Weber and K. H. Becker, *J. Chem. Phys.*, **67**, 110 (1977).
3. N. Ohashi, M. Kakimoto, S. Saito and E. Hirota, *J. Mol. Spectrosc.*, **84**, 204 (1980); M. Kakimoto, S. Saito and E. Hirota, *J. Mol. Spectrosc.*, **80**, 334 (1980).
4. Y. Endo, S. Saito and E. Hirota, *J. Chem. Phys.*, **75**, 4379 (1981).
5. M. Kawasaki, K. Kasatani and H. Sato, *Chem. Phys. Letters*, **75**, 128 (1980).
6. C. R. Webster, P. J. Brucat and R. N. Zare, *J. Mol. Spectrosc.*, **92**, 184 (1982).
7. A. B. Sannigrahi, K. H. Thunemann, S. D. Peyerimhoff and R. J. Buenker, *Chem. Phys.*, **20**, 25 (1977); A. Hinchliffe, *J. Mol. Struct.*, **66**, 235 (1980).
8. K. Nishikida and F. Williams, *J. Amer. Chem. Soc.*, **96**, 4781 (1974).
9. A. Hinchliffe, *J. Mol. Struct.*, **88**, 213 (1982).
10. B. C. Gilbert, C. M. Kirk, R. O. C. Norman and H. A. H. Laue, *J. Chem. Soc., Perkin Trans. 2*, 497 (1977).
11. J. A. Howard and E. Furimsky, *Can. J. Chem.*, **52**, 555 (1974).
12. C. Chatgilialoglu, B. C. Gilbert, B. Gill and M. D. Sexton, *J. Chem. Soc., Perkin Trans. 2*, 1141 (1980).
13. J. A. Baban and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 678 (1978).
14. B. C. Gilbert, C. M. Kirk and R. O. C. Norman, *J. Chem. Res.*, (*S*) 173, (*M*) 1974 (1977).

15. S. W. Benson, *Chem. Rev.*, **78**, 23 (1978).
16. (a) C. Chatgilialoglu, B. C. Gilbert, C. M. Kirk and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 1084 (1979).
(b) On the photochemistry of sulfoxides see: I. Khait, R. Lüdersdozf, K. A. Muszkat and K. Praefcke, *J. Chem. Soc., Perkin Trans. 2*, 1417 (1981) and references cited therein.
17. P. Koelewijn and H. Berger, *Recl. Trav. Chim. Pays-Bas.*, **91**, 1275 (1972).
18. B. C. Gilbert, H. A. H. Laue, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 892 (1975).
19. For a recent review see: J. L. Kice, *Adv. Phys. Org. Chem.*, **17**, 65 (1980).
20. H. Mizuno, M. Matsuda and M. Iino, *J. Org. Chem.*, **46**, 520 (1981).
21. F. Freeman, C. N. Angeletakis and M. C. Keindl, *J. Org. Chem.*, **49**, 454 (1984) and references cited therein.
22. F. Freeman, *Chem. Rev.*, **84**, 117 (1984).
23. F. Freeman and C. N. Angeletakis, *J. Amer. Chem. Soc.*, **103**, 6232 (1981); *J. Amer. Chem. Soc.*, **104**, 5766 (1982); *J. Amer. Chem. Soc.*, **105**, 4039 (1983).
24. See, for example: P. Koch, E. Ciuffarin and A. Fava, *J. Amer. Chem. Soc.*, **92**, 5971 (1970).
25. M. Iino and M. Matsuda, *J. Org. Chem.*, **48**, 3108 (1983).
26. T. E. Boothe, J. L. Greene, Jr., P. B. Shevlin, M. R. Willcott, III, R. R. Inners and A. Cornelis, *J. Amer. Chem. Soc.*, **100**, 3874 (1978).
27. P. J. Wagner, J. H. Sedon and M. J. Lindstrom, *J. Amer. Chem. Soc.*, **100**, 2579 (1978).

CHAPTER **25**

Sulfonyl radicals

C. CHATGILIALOGLU

Istituto dei composti del carbonio contenenti eteroatomi e loro applicazioni, CNR, Ozzano Emilia, Bologna, Italy

I. INTRODUCTION

Sulfonyl radicals are often represented simply as $XSO_2^{\bullet}$ where the sulfur atom is understood to be bonded to two oxygens as well as to X; the moiety X may be an alkyl, aryl, amino or alkoxy group. The unpaired electron does not reside on one particular atom but rather it extends over all atoms of the SO_2 group. It should be noted that in recent literature some authors refer to alkanethiyl peroxyl radicals, the adduct of alkanethiyl ($RS^{\bullet}$) to molecular oxygen, as $RSO_2^{\bullet}$ rather than $RSOO^{\bullet}$ and the fact has already caused some inconvenience.

Sulfonyl radicals are highly reactive transient species; despite their short lifetime, they figure in a wide variety of organosulfur reactions, some of which are of great synthetic

utility as we will see. Sulfonyl radicals have also important roles in polymer chemistry, in air pollution and in some biological systems. Many papers deal with sulfonyl radicals starting back in the twenties; from time to time review articles appeared on sulfur-containing radicals describing some of their structural and/or chemical properties[1]. The subject being quite extensive, this survey is not meant to be exhaustive but rather to reflect the scientific interests of the author.

A few words about the pattern of organization of this chapter. The theoretical studies are included in Section II. In Section VII some interesting chain reactions involving sulfonyl radicals are discussed, although often one of the propagation steps is treated earlier in Section IV or V. Finally, some general concepts of free radical chemistry are introduced at appropriate points throughout the review without any reference.

II. STRUCTURAL CHARACTERISTICS

A. Electron Spin Resonance (ESR) Data

The ^{33}S hyperfine splitting constants have been obtained for a variety of sulfonyl radicals in the solid state[2,3]. The anisotropic and isotropic components of the ^{33}S interaction in these radicals have been analyzed to obtain the percent occupancy of the sulfur 3s and 3p orbitals by the unpaired electron. Using appropriate parameters from Reference 4, details of the analysis are contained in Table 1. The replacement of the O^- by an amino or an alkyl group has the consequence of reducing the total spin density on the sulfur atom from 48.2% to 42.9% or to 31.8%, and increasing the 3p/3s ratio, indicating that the radical takes up a much flatter configuration. In other words, Table 1 shows that as the electronegativity of the substituent in $X—SO_2^{\cdot}$ increases, the radical becomes more pyramidal.

The ESR spectra of hydrosulfonyl and fluorosulfonyl radicals have been obtained by the reaction of sulfur dioxide with hydrogen and fluorine atoms respectively in inert gas matrices at 4.2 K[5]. The large isotropic splittings of 112 and 142 gauss indicate the σ-nature of these species. For $HSO_2^{\cdot}$ the optimum geometry, obtained by *ab initio* calculations using very large basis sets, is as follows: $r_{S—H} = 133.6$ pm, $r_{S—O} = 145.8$ pm, $\widehat{OSO} = 132°$ and the out-of-plane angle is 50.5°, the molecule having C_s symmetry[6].

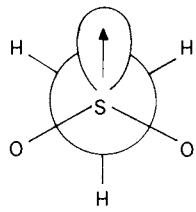
The ESR spectra of a large variety of sulfonyl radicals have been obtained photolytically in liquid phase over a wide range of temperature. Some selected data are summarized in Table 2. The magnitudes of hyperfine splittings and the observations of line broadening resulting from restricted rotation about the C—S bond have been used successfully in conjunction with INDO SCF MO calculations to elucidate both structure and conformational properties. Thus the spin distribution in these species is typical of σ-radicals with a pyramidal center at sulfur and in accord with the solid-state ESR data.

A conformational analysis of the methanesulfonyl radical indicates the staggered structure **1** as the most stable, with a barrier of rotation of ca. 3.8 kcal mol^{-1}[7]. The

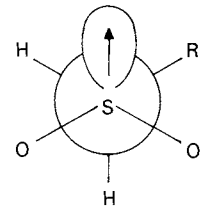
TABLE 1. Characteristics of the orbital containing the unpaired electron in sulfonyl radicals calculated from ^{33}S splittings

	$CH_3SO_2^{\cdot}$	$H_2NSO_2^{\cdot}$	$^-OSO_2^{\cdot}$
%3s	5.8	7.5	10.2
%3p	26.0	35.4	38.0
3s + 3p	31.8	42.9	48.2
3p/3s	4.5	4.7	3.7

replacement of an α-H by an alkyl group increases the activation energy for this process and indicates that the most stable conformation is the one close to rotamer **2**. The spectra of some alkenesulfonyl radicals have also been described (cf. entries 5 and 6 in Table 2) and their conformational characteristics have been discussed[7].

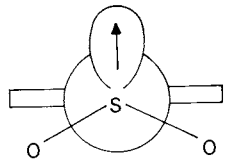


(1)

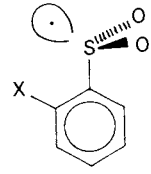


(2)

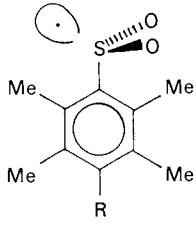
Arenesulfonyl radicals without *ortho*-substituents undergo relatively rapid rotation about the C—S bond at all accessible temperatures in the ESR experiments (cf. entries 7 and 8 in Table 2)[8]. However, *ab initio* and INDO molecular orbital calculations on the benzenesulfonyl radical suggest that the preferred conformation is a structure of type **3** in which the singly occupied orbital is perpendicular to the aromatic ring and that the barrier of rotation is 1.4 kcal mol^{-1} [9]. Some mono-*ortho*-substituted radicals demonstrate a marked preference, in ESR time scale, for a conformation in which the unpaired electron mainly resides in a sulfur orbital in the plane of the aryl ring, the sulfonyl oxygens lying *anti* to the *ortho*-substituent (**4**). For some di-*ortho*-substituted radicals, rotation around the C—S bond is slow at low temperature and barriers to rotation have been determined in a few instances, e.g. the activation energy for the interconversion process **5** ⇆ **6**, where R = H or Me, is 5.3 kcal mol^{-1} [8].



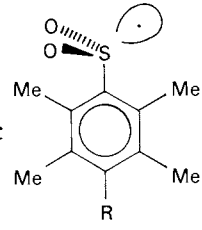
(3)



(4)



(5)



(6)

The thiophene-2-sulfonyl radicals without substituents at position 3 exhibit rapid rotation about the C—S bond in the ESR time scale, while the 3-bromo-substituted ones demonstrate a marked conformational preference which has been interpreted in terms of a π-type conjugated structure similar to **3** (cf. entries 10 and 11 in Table 2)[10]. Calculations

TABLE 2. ESR spectra of a selected number of sulfonyl radicals at temperatures between 170 and 200 K

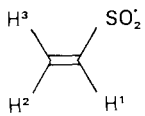
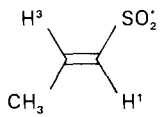
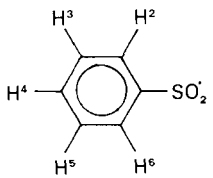
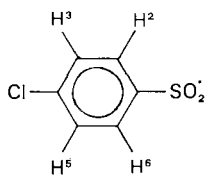
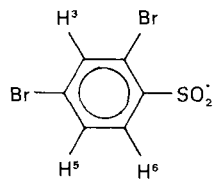
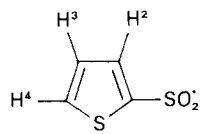
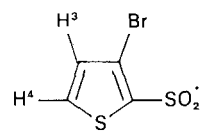
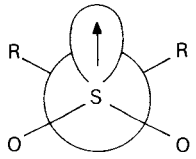
Entry	Radical	g-value	Hyperfine splittings	Ref.
1.	$H—SO_2^{\bullet}$	2.0061	111.9(1H)	5
2	$CH_3—SO_2^{\bullet}$	2.0049	0.7(3H)	7
3	$CH_3CH_2—SO_2^{\bullet}$	2.0050	1.0(2H), 1.7(3H)	7
4	$(CH_3)_2CH—SO_2^{\bullet}$	2.0052	0.4(1H), 1.9(6H)	7
5		2.0045	$0.4_5(H^1)$, 5.2_5 (H^2), 0.8_5 (H^3)	7
6		2.0045	$0.1_5(H^1)$, $0.2_5(H^3)$, $1.8_5(3H)$	7
7		2.0045	$0.3(H^2,H^6)$, $1.1(H^3, H^5)$, $0.5(H^4)$	8
8		2.0045	$0.3(H^2, H^6)$, 1.0 (H^3, H^5)	8
9		2.0068	$1.8(H^5)$	8
10		2.0042	$0.5(H^2)$, $0.7(H^3, H^4)$	10
11		2.0054	$0.6_5(H^3)$	10

TABLE 2. (*Contd.*)

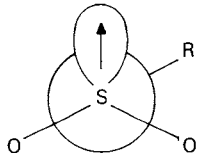
Entry	Radical	*g*-value	Hyperfine splittings	Ref.
12	$NH_2—SO_2^•$	2.0036	5.0(1N), 5.0(2H)	3
13	$CH_3NH—SO_2^•$	2.0036	5.8(1N), 5.8(1H), 4.5(3H)	3
14	$(CH_3)_2N—SO_2^•$	2.0036	6.9(1N), 5.2(6H)	3
15	$HO—SO_2^•$	2.0033		11
16	$CH_3O—SO_2^•$	2.0032	1.6_5(3H)	11
17	$CH_3(CH_2)_3O—SO_2^•$	2.0032	1.4_5(2H), 0.4(2H)	11
18	$FSO_2^•$	2.0026	141.1(1F)	5

carried out for the unsubstituted thiophene-2-sulfonyl radical confirm the preference for this conformation and indicate the values of 3.4 and 4.9 kcal mol^{-1} for the asymmetric barrier of rotation[9].

In the aminosulfonyl radicals the similarity of the splittings from nitrogen, the α-protons (N—H) and the β-protons (N—CH_3) suggest a small but significant π spin-density on nitrogen and that a formally-conjugated structure, i.e. **7**, rather than a twisted conformation, is preferred (cf. entries 12, 13 and 14 in Table 2)[3]. The magnitude of the splittings in alkoxysulfonyl radicals, which are temperature independent, indicates that these species prefer the asymmetrical rotamer **8** to either of the two possible symmetrical conformations[11]. Further support that the staggered structure **7** and the asymmetrical conformation **8** are the most stable ones for $H_2NSO_2^•$ and $HOSO_2^•$ comes from theoretical studies; barriers, only referred to rigid rotation, of 4.6 and 4.4 kcal mol^{-1} respectively, have been calculated[12].



(**7**)



(**8**)

Typical values of *g* for some sulfonyl radicals are also listed in Table 2. Two main features stand out from these data. First, there is a decrease in the *g*-value as the electronegativity of the substituents increases, that is, $MeSO_2^•$ (2.0049), $Me_2NSO_2^•$ (2.0036), $MeOSO_2^•$ (2.0032) and $FSO_2^•$ (2.0026), and second, there is an increase in the *g*-value when introducing atoms characterized by large spin–orbit couplings in positions of significant spin density of the radical (cf., for example, entries 7 and 9 as well as 10 and 11 in Table 2).

B. Optical and Infrared Absorption Spectra

The optical absorption spectra of sulfonyl radicals have been measured by using modulation spectroscopy[13], flash photolysis[14] and pulse radiolysis[15] techniques. These spectra show broad absorption bands in the 280–600 nm region, with well-defined maxima at ca. 340 nm. All the available data are summarized in Table 3. Multiple Scattering X_α calculations[13] successfully reproduce the experimental UV–visible spectra of $MeSO_2^•$ and $PhSO_2^•$ radicals, indicating that the most important transition observed in this region is due to transfer of electrons from the lone pair orbitals of the oxygen atoms to

TABLE 3. Electronic spectral parameters of sulfonyl radicals

Radical	Solvent	λ_{max}(nm)	$\varepsilon_{max}(M^{-1}\,cm^{-1})$	Ref.
$RSO_2^{\bullet}$	Hydrocarbon	350	~1000	13
	H_2O	332		13, 15
$ArSO_2^{\bullet}$	Hydrocarbon	330	~1000	13, 14
	H_2O	315		14
$R_2NSO_2^{\bullet}$	Hydrocarbon	352		13
$ROSO_2^{\bullet}$	Hydrocarbon	347		13

the Single Occupied Molecular Orbital (SOMO). Furthermore, the X_α calculations show that the SOMO is efficiently localized on the SO_2 moiety; thus, for the methanesulfonyl radical, the distribution is predicted to be 42% on sulfur (6% in 3s, 29% in 3p and 7% in 3d) and 44% in the p orbital of the oxygen atoms, in excellent agreement with the ESR data (cf. Table 1).

Four IR absorption bands have been identified in the spectrum of the hydroxysulfonyl radical ($HOSO_2^{\bullet}$) which has been obtained by the reaction of hydroxyl radicals with sulfur dioxide in argon matrix at 11 K[16]. The observed bands at 3539.9 and 759.5 cm^{-1} have been assigned to O—H and S—OH stretching modes while the bands at 1309.2 and 1097.3 cm^{-1} have been assigned to the asymmetric and symmetric stretching modes of the double bonded SO_2 moiety. These data are consistent with the theoretical prediction on the geometry of the hydroxysulfonyl radical[12].

III. THERMODYNAMIC DATA

Benson[17] has tried to collect some thermodynamic data based on a number of empirical rules for this class of radicals. He estimated heats of formation for $HSO_2^{\bullet}$, $MeSO_2^{\bullet}$, $PhSO_2^{\bullet}$ and $HOSO_2^{\bullet}$ as −42, −55, −37 and −98 kcal mol^{-1}, respectively. He also estimated a stabilization energy for the benzenesulfonyl radical of 14 kcal mol^{-1}, which is very similar to that of the benzyl radical. However, recent kinetic studies[18] (*vide infra*) have shown that arenesulfonyls are not appreciably stabilized relative to alkanesulfonyl radicals, in accord with the ESR studies.

The bond dissociation energies in the gas phase for $Me—SO_2^{\bullet}$, $Et—SO_2^{\bullet}$ and $Ph—SO_2^{\bullet}$ have been evaluated to be 18, 16 and 44 kcal mol^{-1} respectively[17], although Horowitz, from complex kinetic studies of the radiolysis of $MeSO_2Cl$ in cyclohexane, has obtained the values of 15 and 12 kcal mol^{-1} for $D(Me—SO_2^{\bullet})$ and $D(c\text{-}C_6H_{11}—SO_2^{\bullet})$, respectively; these bond dissociation energies are considerably lower than the gas-phase values, and it has been suggested that the possible cause of this difference is due to the heat of vaporization of sulfur dioxide[19].

IV. METHODS OF FORMATION

Sulfones are thermally very stable compounds, diaryl derivatives being more stable than alkyl aryl sulfones which, in turn, are more stable than dialkyl sulfones; allyl and benzyl substituents facilitate the homolysis by lowering the C—S bond dissociation energy[17]. Arylazo aryl sulfones, on heating in neutral or weakly basic media at 100 °C, yield an aryl and arenesulfonyl radical pair via a reversible one-bond fission followed by dediazoniation of the aryldiazenyl radical (see Scheme 2 below)[20]. However, photolysis provides a relatively easy method for generating sulfonyl radicals from compounds containing the SO_2 moiety.

Norman and coworkers[21–23] used ESR spectroscopy to study in detail the reaction of several organic compounds containing the sulfinyl moiety with the Ti(III)–H_2O_2 system; in particular, dimethyl sulfoxide yields the methyl and methanesulfonyl radicals as shown in reactions 1–3[21].

$$Ti(III) + H_2O_2 \longrightarrow Ti(IV) + {}^{\bullet}OH + OH^- \quad (1)$$

$$Me_2SO + {}^{\bullet}OH \longrightarrow Me_2\dot{S}(O)OH \longrightarrow Me^{\bullet} + MeSO_2H \quad (2)$$

$$MeSO_2H + Me^{\bullet} \longrightarrow MeSO_2^{\bullet} + MeH \quad (3)$$

Rate constants for the reaction between $HO^{\bullet}$ and Me_2SO and for that between $Me^{\bullet}$ and $MeSO_2H$ have been estimated to be 5×10^9 and ca. $10^6\ M^{-1}\ s^{-1}$, respectively. Alkanesulfinic acids react with *t*-butoxyl radicals even at 232 K to give the corresponding sulfonyl radicals via a hydrogen abstraction reaction[24]; also, aromatic sulfonyl radicals in aqueous solution have been generated from arenesulfinic acids either by oxidation with ceric sulfate[25] or by direct photolysis[14].

The most common way to generate sulfonyl radicals for spectroscopic studies has been the photolysis of solutions containing di-*t*-butyl peroxide, triethylsilane and the corresponding sulfonyl chloride in a variety of solvents (equations 4–6). The slowest step in this sequence is the reaction between *t*-butoxyl radicals and triethylsilane ($k_5 = 5.3 \times 10^6\ M^{-1}\ s^{-1}$)[26] since that for chlorine abstraction (equation 6) is extremely efficient (cf. Table 4).

$$Me_3COOCMe_3 \xrightarrow{h\nu} 2\,Me_3CO^{\bullet} \quad (4)$$

$$Me_3CO^{\bullet} + Et_3SiH \longrightarrow Me_3COH + Et_3Si^{\bullet} \quad (5)$$

$$Et_3Si^{\bullet} + RSO_2Cl \longrightarrow Et_3SiCl + RSO_2^{\bullet} \quad (6)$$

Although reaction 6 is essentially a diffusion-controlled process for all kinds of substituents, the small differences observed in the rate constants through the series alkane-, amino- and alkoxy-sulfonyl chlorides have been attributed to the increased importance of polar effects to the transition state[11].

In pulse radiolysis studies, sulfonyl radicals have normally been generated by dissociative electron capture using sulfonyl chlorides as substrates, namely[15].

$$RSO_2Cl + e_{aq}^- \longrightarrow [RSO_2Cl]^{-\bullet} \longrightarrow RSO_2^{\bullet} + Cl^- \quad (7)$$

The key step in the radical chain decomposition of alkanesulfonyl halides as well as in the adduct formation of sulfonyl halides with alkenes (*vide infra*) is equation 8 in which the $R^{\bullet}$ radical abstracts an X atom from the sulfonyl halide to regenerate a sulfonyl radical.

$$R'SO_2X + R^{\bullet} \longrightarrow R'SO_2^{\bullet} + RX \quad (8)$$

The rate constants for the reaction of some carbon-centered radicals with sulfonyl chlorides have been measured in solution and are collected in Table 4. Horowitz[19,27] has determined rate constants for the reaction of cyclohexyl radicals with CH_3SO_2Cl, $CH_3(CH_2)_2SO_2Cl$ and $CH_3(CH_2)_3SO_2Cl$ at 393 K, relative to the reaction with tetrachloroethylene, as well as relative Arrhenius parameters in the case of CH_3SO_2Cl, while Chatgilialoglu[28], using laser flash photolysis, has measured absolute data for the Cl-transfer reaction between $PhCH_2SO_2Cl$ and *n*-butyl, *sec*-butyl and phenyl radicals (see Table 4). The abnormally high preexponential factor† observed for reaction 8 has been

†A 'normal' preexponential factor for free-radical abstraction is considered to be $10^{8.5 \pm 0.5}\ M^{-1}\ s^{-1}$.

TABLE 4. Absolute kinetic data for halogen abstraction by some radicals from sulfonyl halides

Substrate	Radical	log A/M^{-1} s^{-1}	E_a(kcal mol^{-1})	k(M^{-1} s^{-1}) at 298 K	Ref.
$MeSO_2F$	$Et_3Si^{\bullet}$			1.3×10^7	18
p-$TolSO_2F$	$Et_3Si^{\bullet}$			8.9×10^6	18
$MeSO_2Cl$	c-$C_6H_{11}^{\bullet}$	9.1	4.9	2.9×10^5	19
	$Et_3Si^{\bullet}$			3.2×10^9	18
$PrSO_2Cl$	c-$C_6H_{11}^{\bullet}$			1.5×10^6	27
$PhCH_2SO_2Cl$	$CH_3CH_2CH_2CH_2^{\bullet}$	10.1	5.5	1.3×10^6	28
	$CH_3CH_2\dot{C}HCH_3$	9.6	4.8	1.2×10^6	28
	$C_6H_5^{\bullet}$			1.0×10^8	28
	$Et_3Si^{\bullet}$			5.7×10^9	18
$PhSO_2Cl$	$CH_2{=}CH(CH_2)_3CH_2^{\bullet}$			1.9×10^{5a}	35
	$Et_3Si^{\bullet}$			4.6×10^9	18
$(CH_3)_2NSO_2Cl$	$Et_3Si^{\bullet}$			5.4×10^9	11
CH_3OSO_2Cl	$Et_3Si^{\bullet}$			5.1×10^9	11
$CH_3CH_2OSO_2Cl$	$Et_3Si^{\bullet}$			7.5×10^9	11

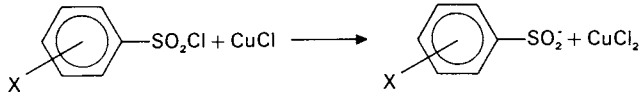
[a] Based on a unimolecular cyclization rate constant of 5×10^5 s^{-1} for Δ^5-hexenyl radical at 318 K (cf. Reference 34).

attributed to the great importance of the polar contribution to the transition state, namely[28,29]

$$R'SO_2Cl \cdot R \leftrightarrow R'SO_2^{\bullet}Cl^- {}^+R \leftrightarrow R'SO_2^- Cl^{\bullet +} R \longrightarrow R'SO_2^{\bullet} + RCl \qquad (9)$$

and an explanation has also been advanced for such a phenomenon[29]. Relative rate constants have also been obtained for the reaction of a variety of substituted benzenesulfonyl halides with phenyl, 1-cyano-1-methylethyl and benzyl radicals[30], the relative reactivities of the phenyl radical toward *p*-toluenesulfonyl iodide, bromide and chloride being 602:192:1. Matsuda and coworkers[31] have determined chain-transfer constants of arene- and alkanesulfonyl chlorides at 333 K in styrene and methyl methacrylate polymerization; a Hammett plot for substituted benzenesulfonyl chlorides gave $\rho = 0.86$, which supports the involvement of charge-transfer interactions in the transition state (cf. equation 9).

Asscher and coworkers[32] have measured the oxidation rates of cuprous chloride by substituted aromatic sulfonyl chlorides covering a wide range of Hammett σ-values, namely



This is one of the steps in the copper-catalyzed redox-transfer chain addition of arenesulfonyl chlorides to styrenes (*vide infra*). The ρ-value of $+0.56$ indicates the involvement of a simple atom transfer as well as a polar contribution to the transition state.

One of the steps in the radical chain 'selenosulfonation' of multiple bonds (*vide infra*) is equation 10, in which the R$^{\bullet}$ radical attacks via a S_H2 reaction the Se-aryl areneselenosulfonates to regenerate a sulfonyl radical, namely.

$$ArSO_2SeAr' + R^{\bullet} \longrightarrow RSeAr' + ArSO_2^{\bullet} \qquad (10)$$

Based on a unimolecular cyclization rate constant of $5 \times 10^5\ s^{-1}$ for the Δ^5-hexenyl radical[34], the rate constant for the attack of the Δ^5-hexenyl radical on *p*-TolSO_2SePh has been found to be $1.5 \times 10^7\ M^{-1}\ s^{-1}$ at 45 °C[35]. Although the structurally analogous thiosulfonates, $ArSO_2SAr'$, are not cleaved by the attack of carbon-centered radicals, Kobayashi and coworkers[33] have shown by ^{13}C CIDNP and products analysis that they undergo a S_H2 reaction with triethylgermyl radicals. Se-Aryl areneselenosulfonates react with germyl radicals in a similar way[33].

An important route to sulfonyl radicals is the reaction of a radical with sulfur dioxide:

$$R^{\bullet} + SO_2 \longrightarrow RSO_2^{\bullet} \qquad (11)$$

This type of reaction is involved as an intermediate step in few synthetically useful reactions, in the formation of polysulfones by copolymerization of an olefin with SO_2, as well as in aerosol formation in polluted atmospheres. We will discuss later in some detail the most important chain reactions involving step 11. However, Good and Thynne[36a] determined the Arrhenius parameters for the addition of methyl and ethyl radicals to SO_2 in gas phase, the rate constants being 5×10^6 and $4 \times 10^5\ M^{-1}\ s^{-1}$ respectively at ambient temperature. Subsequent studies of Calvert and coworkers[36b] have shown that the system investigated by Good and Thynne was more complex than originally suggested. Later, the rate of addition of the methyl radical to SO_2 was directly determined to be $1.8 \times 10^8\ M^{-1}\ s^{-1}$ by James and colleagues[36c]. All the data obtained in the gas-phase kinetic studies, however, indicate that the addition of alkyl radicals to sulfur dioxide is a fast process. Gilbert and colleagues[22] have obtained the ESR spectra of a variety of sulfonyl

radicals by the reaction of substituted alkyl radicals with SO_2 in aqueous solution. Hydroxyl and alkoxyl radicals add also to sulfur dioxide; Davies and coworkers[24] estimated a rate constant between 10^7 and $10^8\,M^{-1}\,s^{-1}$ at 232 K for the addition of *t*-butoxyl to SO_2.

V. UNIMOLECULAR RADICAL REACTIONS

One of the peculiar features of sulfonyl radicals is the α-scission process, namely

$$RSO_2^{\bullet} \longrightarrow R^{\bullet} + SO_2 \qquad (12)$$

For comparison purposes activation energies for reaction 12, in both gas and liquid phase, are collected in Table 5. The value for the α-toluenesulfonyl radical is in line with the activation energies of the other $RSO_2^{\bullet}$ desulfonylations, provided allowance is made for differences in the stabilization energies of the organic radicals that are produced. However, electrostatic repulsions within the radical molecule and phase effect may considerably influence activation energies.

The rapid desulfonylation of $PhCH_2SO_2^{\bullet}$ has been used successfully as a probe for laser flash photolytic investigations of various reactions generating sulfonyl radicals from sulfonyl halides[26,28].

The decomposition of alkanesulfonyl halides, namely

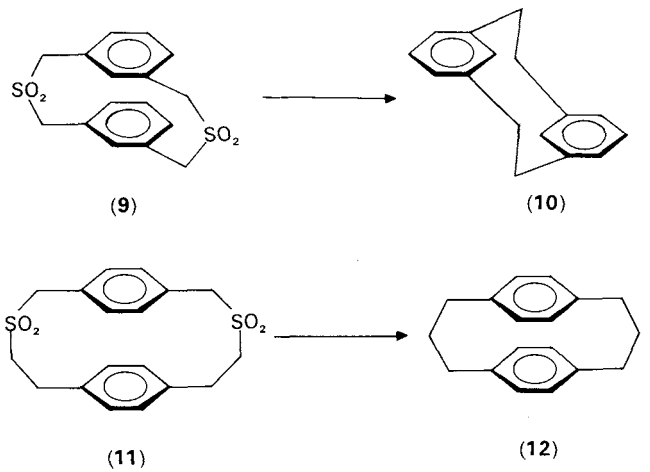
$$RSO_2X \longrightarrow RX + SO_2 \qquad (13)$$

promoted by radical initiators, ultraviolet light or, under certain conditions, thermally, proceeds by a radical chain mechanism[38]. Reactions 12 and 8 represent the propagation steps in these radical chain decompositions. Perfluoroalkanesulfonyl halides behave similarly[39].

Extrusion of sulfur dioxide as a route to carbon–carbon single bonds is a well-known reaction and represents a particularly valuable and versatile synthetic approach to cyclophanes[40], benzocyclobutenes[41] and steroids[42]. Thus both thermally and photochemically initiated SO_2 extrusion reactions have been employed and it is thought that in many cases equation 12 is the key step of the overall reaction. However, each method has particular advantages and limitations; for example, irradiation of sulfone **9** gives [2.2] cyclophane **10** in quantitative yield[43] while pyrolysis of **9** affords **10** in only about 20% yield[44]. In contrast, sulfone **11** undergoes smooth pyrolytic extrusion of SO_2 to give a 94% yield[45] of [3.3] cyclophane **12** while irradiation of **11** does not produce cyclophane **12** at all[43]. The reaction in all cases occurs stepwise going through the monosulfone by loss of the first SO_2, followed by loss of the second molecule of SO_2. The above results suggest that initial homolytic benzyl carbon–sulfur bond cleavage occurs and that loss of SO_2 from the resultant biradical intermediate requires different activation energies, depending on the stability of forming alkyl radicals. These conclusions are in accord with the data in Table 5. Recently, detailed mechanistic studies on the photoextrusion of SO_2 from arylmethyl sulfones have been carried out by Givens and coworkers[46].

TABLE 5. Activation energies for the decomposition of some sulfonyl radicals

Radical	E_a (kcal mol^{-1})	Phase	Ref.
$CH_3SO_2^{\bullet}$	22.4	gas	36a
$CH_3CH_2SO_2^{\bullet}$	19.9	gas	36a
$CH_3CH(Cl)SO_2^{\bullet}$	13.4	liquid	37
$C_6H_5CH_2SO_2^{\bullet}$	< 5	liquid	18



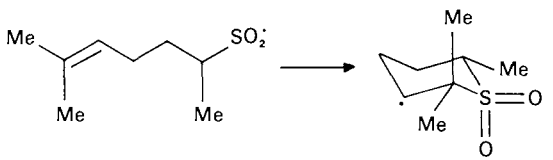
SCHEME 1

In an early work Kandror and Freidlina[47a] suggested the occurrence of 1, 3 migration of the chlorine atom from sulfur to carbon, *viz.*,

$$PhSCH_2\dot{C}HSO_2Cl \longrightarrow PhSCH_2CH(Cl)SO_2^{\cdot} \qquad (14)$$

followed by loss of sulfur dioxide, as key steps in the reaction of benzenethiol and ethenesulfonyl chloride to give 2-(phenylthio)ethyl chloride; however, King and Khemani[47b] have recently presented strong evidence indicating that the above rearrangement simply does not take place, as the same reaction proceeds *via* an ionic addition followed by a thermal rearrangement with the formation of the episulfonium ion as intermediate.

Intramolecular cyclization of sulfonyl radicals is almost absent from literature. The fact that free radical cyclization has been the subject of a large number of studies and applications in the last decade in organic chemistry[48] and that sulfonyl radicals add quickly to multiple bonds (*vide infra*) makes cyclization of sulfonyl radicals a rather attractive area. Recently, Johnson and Derenne[49] studied the reaction of 6-methylhept-5-en-2-ylcobaloxime(III) with sulfur dioxide and, based on the product analysis, they suggested reaction 15 to be an intermediate step.



(15)

VI. RADICAL–RADICAL REACTIONS

A characteristic of free radicals is the bimolecular radical–radical reaction which in many cases proceeds at the diffusion-controlled limit. These radical–radical reactions can occur either between two identical radicals or between unlike radicals, the two processes being known as self-termination and cross-termination reactions, respectively.

A. Self-termination

Kinetic ESR spectroscopy has been used to determine the rate constants for self-termination of $MeSO_2^{\bullet}$, $EtSO_2^{\bullet}$, $PhSO_2^{\bullet}$ and $2,5\text{-}Cl_2C_6H_3SO_2^{\bullet}$ radicals[18]. At 233 K and in cyclopropane as a solvent the values found for $2k_t$ were in the range $(4.5 \pm 1.5) \times 10^9\ M^{-1}\ s^{-1}$ for all $RSO_2^{\bullet}$ radicals.

$$2RSO_2^{\bullet} \xrightarrow{2k_t} \text{products} \tag{16}$$

Time-resolved optical absorption spectroscopy experiments have shown that arenesulfonyl radicals decay with 'clean' second-order kinetics[14]; the values of $2k_t/\varepsilon_\lambda$, where ε_λ is the extinction coefficient at the monitoring wavelength, increased linearly with decreasing viscosity of the solvent, further indicating that reaction 16 is clearly a diffusion-controlled process.

Corrêa and Waters[50] have shown that *p*-toluenesulfonyl radicals ($ArSO_2^{\bullet}$), produced by thermolysis or photolysis of the corresponding sulfonyl iodide, tend to disproportionate according to equation 17 in carbon tetrachloride.

$$6ArSO_2^{\bullet} \longrightarrow 2(ArSO_2)_2O + ArSO_2SAr \tag{17}$$

Corrêa and Waters[50] also proposed a mechanistic scheme where the key step of the overall reaction involves the recombination of sulfonyl radicals to form an intermediate with an O—S bond, the decomposition of which yields a sulfinyl radical ($ArSO^{\bullet}$) and an oxygen-centered radical $ArSO_2O^{\bullet}$. Later this suggestion was further strengthened on the basis of ESR studies[51] and thanks to the elucidation of the electronic structure of sulfonyl radicals. However, it seems to the author that the available literature data point to an overall mechanism for equation 17 more complex that the one suggested[50] (cf., for

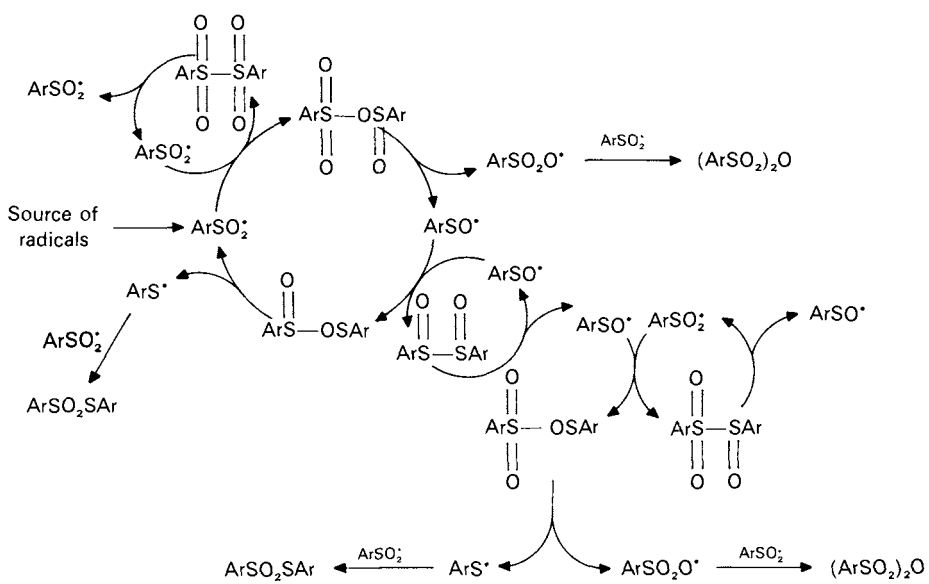


FIGURE 1. Proposed mechanism for the disproportionation reaction of the arenesulfonyl radicals.

example, References 51 and 52). A proposed mechanistic scheme for the overall disproportionation reaction of the arenesulfonyl radicals is given in Figure 1. Although some reactions in Figure 1 are potentially reversible, they have not been indicated as such in the absence of data. The reader is referred to the chapter on the reactions involving sulfinyl radicals for more details.

It should be noted that the oxygen-to-oxygen or sulfur-to-sulfur coupling products are less favorable than the oxygen-to-sulfur ones in the self-termination of sulfonyl radicals; the reason for this behavior is probably due to the electrostatic repulsion between atoms bearing a charge of the same sign. Furthermore, the oxygen-to-oxygen dimers probably have very weak or even negative O—O bond strengths in contrast to the observed activation energy of ~ 41 kcal mol^{-1} for the sulfur–sulfur bond fission in aryl α-disulfones[52].

The product distribution derived from the disproportionation of sulfonyl radicals is expected to be dependent on the conditions under which the reaction is being carried out; thus, in hydrogen donor solvents, the formation of $ArSO_2OH$ should be important while at higher temperatures the formation of an aryl radical, namely

$$ArSO_2^{\bullet} \longrightarrow Ar^{\bullet} + SO_2 \tag{18}$$

should increase the variety of resulting products.

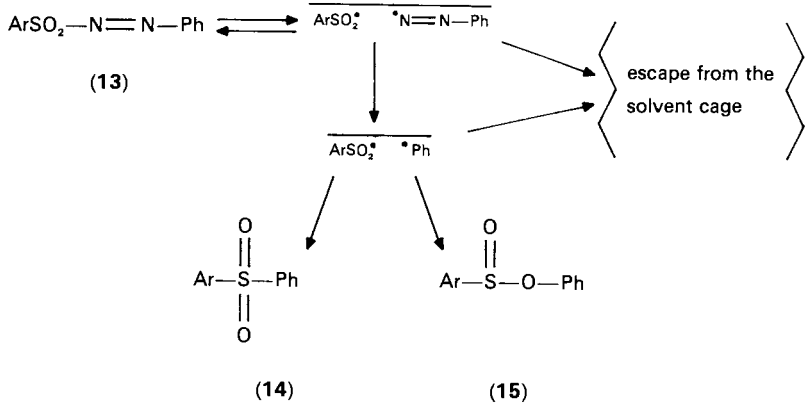
B. Cross-termination

From complex kinetic studies the rate constants for the cross-termination reaction:

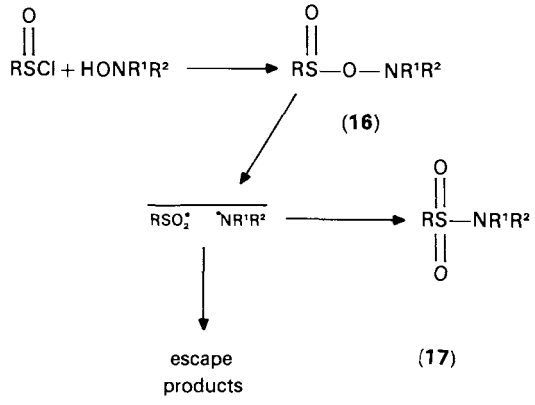
$$c\text{-}C_6H_{11}SO_2^{\bullet} + ROO^{\bullet} \longrightarrow \text{products} \tag{19}$$

have been evaluated and found to be 1.5×10^8 and $3.0 \times 10^8\ M^{-1}\ s^{-1}$ for cyclohexylperoxyl and tridecylperoxyl radicals respectively at 293 K[53].

The ^1H and ^{13}C CIDNP studies have shown that not only the sulfone **14**, but also the sulfinic ester **15**, is generated as cage products from the phenyl/*p*-toluenesulfonyl radical pair during the thermal decomposition of phenylazo aryl sulfone (**13**)[54] (Scheme 2). The cross-termination of arenesulfonyl and triethylgermyl radicals was found to occur exclusively via the formation of germyl sulfinate, $ArS(O)OGeEt_3$[33].



SCHEME 2



SCHEME 3

Alkane- and arenesulfinyl chlorides have been found to react with several types of *N*-hydroxy compounds, including *N*-hydroxysulfonamides[55], *N*-phenylhydroxamic acid[56], oximes[57], *N*-hydroxycarbamates[58] and hydroxylamines[59] in the presence of a base to give the corresponding sulfonamides **17**. Evidence for a radical pathway has been found for these reactions by means of ESR, ^1H and ^{13}C CIDNP and kinetic studies[55–59]. These reactions predominantly occur via the formation of O-sulfinylated intermediates **16** which subsequently undergo thermal rearrangement at room temperature or below, involving a radical cage process (Scheme 3). A similar mechanistic pathway has also been suggested for the reaction of *t*-butylsulfinyl chloride with *t*-butylhydroperoxide in the presence of pyridine[60].

VII. RADICAL–MOLECULE REACTIONS

A. Abstraction

The abstraction reaction, generally, is not a common feature of sulfonyl radicals,

$$R'Y + RSO_2^{\bullet} \longrightarrow RSO_2Y + R'^{\bullet} \qquad (20)$$

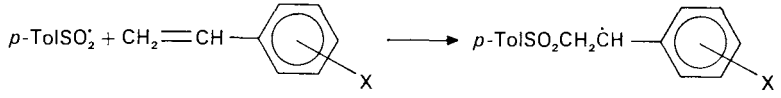
the reason probably being the relative weakness of the newly formed bonds. Hydrogen abstraction from alkanes by $RSO_2^{\bullet}$ radicals has often been invoked as a possible step in the mechanism of the gas-phase photochemical reaction between paraffin hydrocarbons and sulfur dioxide, where the sulfinic acids appear to be among the main products. However, the liquid-phase rate constants for hydrogen abstraction by $RSO_2^{\bullet}$ radicals (R = methyl, *n*-propyl, *n*-butyl) from cyclohexane have been estimated to be about $2 \times 10^2\ M^{-1}\ s^{-1}$ at 393 K[27].

Evidence that *p*-toluenesulfonyl radicals abstract a chlorine atom from CCl_4 under certain conditions has also been given[50]; from available thermodynamic data this reaction should be nearly thermoneutral.

B. Addition

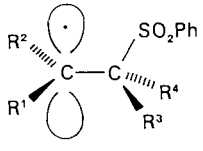
Absolute rate constants for the addition of a sulfonyl radical to multiple bonds are absent from the literature. However, there are some relative kinetic data. Corrêa and

Waters[61] have measured relative rates of *p*-toluenesulfonyl radical addition to substituted styrenes, deducing from the value of $\rho^+ = -0.50$ in the Hammett plot that the sulfonyl radical has an electrophilic character (equation 21). Further indications that sulfonyl radicals are strongly electrophilic have been obtained by Takahara and coworkers[62], who measured relative reactivities for the addition reactions of benzenesulfonyl radicals to various vinyl monomers and plotted rate constants versus Hammett's σ_p and Alfrey–Price's *e* values; these relative rates are spread over a wide range, for example, acrylonitrile (0.006), methyl methacrylate (0.08), styrene (1.00) and α-methylstyrene (3.21). The relative rates for the addition reaction of *p*-methylstyrene to styrene towards methane- and *p*-substituted benzenesulfonyl radicals are almost the same in accord with their σ-type structure discussed earlier in this chapter.



(21)

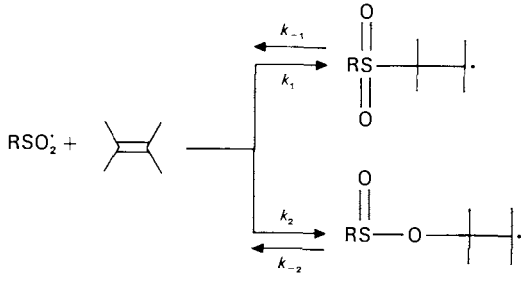
There is clear evidence that the addition of a sulfonyl radical to an olefin is a reversible reaction. This has been demonstrated for the case of but-2-ene, where *cis-trans isomerization of the olefin accompanies addition*[63,64]. Furthermore, **18a** and **18b** radicals generated by the reaction of $Bu_3Sn^\cdot$ with *erythro-* and *threo*-2-bromo-3-(phenylsulfonyl)butane, respectively, eliminate benzenesulfonyl radicals to some extent, even at −67 °C, to form 2-butenes in a non-stereospecific manner, providing also indication that the rotation about the central C—C bond is faster than the β-cleavage process[65].

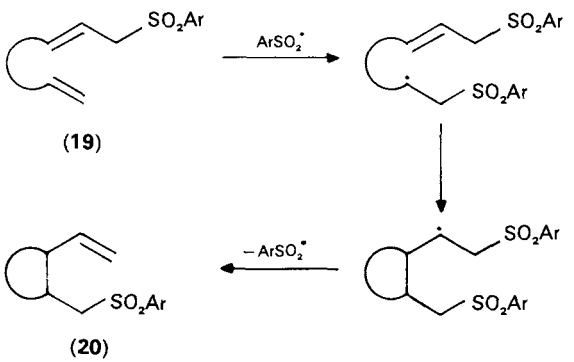


(18a) $R^1 = R^4 = H$; $R^2 = R^3 = Me$
(18b) $R^1 = R^4 = Me$; $R^2 = R^3 = H$

Under particular conditions the 1,3-rearrangement of certain allylic sulfones occurs via a chain mechanism involving addition–elimination of $ArSO_2^\cdot$ radicals[66]. Smith and Whitham[67] have recently taken advantage of the concept of the reversible homolytic addition of sulfonyl radicals to olefinic double bonds to design an elegant route to the construction of rings. By choosing the appropriate olefinic allylic sulfone **19** they obtained **20** in good yields through a chain process involving addition, cyclization and elimination (see Scheme 4).

In principle two possible pathways may exist for the addition of sulfonyl radicals to olefinic double bonds, that is, attack by either the sulfur or an oxygen atom, as in sulfonyl radicals the spin density is almost equally divided between sulfur and the two oxygens, namely





SCHEME 4

All studies on this class of reactions show that they occur exclusively through path 22. However, evidence that reaction 23 may also be involved comes from ESR studies[68]; notably, radical **21** itself has not been detected even at low temperatures, but a strong signal from $MeSO_2^{\bullet}$ has been observed, in agreement with the fast occurrence of reaction 25.

$$Et_3Si^{\bullet} + BrCH_2CH_2OSMe \longrightarrow \underset{\textbf{(21)}}{\dot{C}H_2CH_2OSMe} + Et_3SiBr \qquad (24)$$

$$\underset{\textbf{(21)}}{\dot{C}H_2CH_2OSMe} \longrightarrow CH_2{=}CH_2 + MeSO_2^{\bullet} \qquad (25)$$

These results imply that $k_{-2} \gg k_{-1}$.

1. Addition of sulfonyl halides to olefins, allenes and acetylenes

The free radical additions of sulfonyl halides to alkenes, catalyzed by light or typical chemical radical initiators (In), were first investigated in the 1950s[69]. The products which are β-halo sulfones (**22**) were obtained via a chain reaction in which $RSO_2^{\bullet}$ acts as the chain carrier, namely[61,62,70,71]

$$RSO_2X + In^{\bullet} \longrightarrow RSO_2^{\bullet} + InX \qquad (26)$$

$$RSO_2^{\bullet} + R'CH{=}CH_2 \rightleftharpoons RSO_2CH_2\dot{C}HR' \qquad (27)$$

$$RSO_2CH_2\dot{C}HR' + RSO_2X \longrightarrow \underset{\textbf{(22)}}{RSO_2CH_2CHR'(X)} + RSO_2^{\bullet} \qquad (28)$$

Although sulfonyl chlorides add readily to unactivated olefins, with vinylic monomers telomeric and/or polymeric products were observed. This difficulty has been overcome by carrying out the addition in the presence of catalytic amounts of $CuCl_2$, so as to provide a general and convenient synthesis of β-chlorosulfones (Asscher–Vofsi reaction)[63]. For the copper-catalyzed system a redox-transfer mechanism has been suggested in which the

transfer step 28 is completely replaced by reactions 29 and 30[63,72]:

$$RSO_2CH_2\dot{C}HR' + CuCl_2 \longrightarrow RSO_2CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HR' + CuCl \quad (29)$$

$$CuCl + RSO_2Cl \longrightarrow CuCl_2 + RSO_2^{\bullet} \quad (30)$$

Reaction 29 is very fast and apparently capable of shifting the equilibrium 27 more to the right.

The copper-catalyzed additions of sulfonyl chlorides to conjugated dienes and trienes[73] as well as to aryl-substituted cyclic olefins[74] and substituted styrenes have been described[75]; for example, arenesulfonyl chlorides add to vinylarenes providing good to excellent yields[75] of β-chlorosulfones:

$$ArCH{=}CH_2 + Ar'SO_2Cl \xrightarrow[CH_3CN]{CuCl_2/Et_3N\cdot HCl} \underset{\displaystyle Cl}{\underset{|}{Ar}}CH{-}CH_2SO_2Ar' \quad (31)$$

Reaction 31 appears to be little affected by substituent electronic effects or by steric effects of either sulfonyl chloride or styrenes. Treatment of β-chlorosulfones with triethylamine in benzene affords the corresponding α, β-unsaturated sulfones in excellent yield. The copper-catalyzed addition of sulfonyl iodides to simple and cyclic alkenes has also been exploited[76].

Arenesulfonyl chlorides[77] as well as alkenesulfonyl chlorides[78] react with vinylarenes in the presence of $RuCl_2(PPh_3)_3$ and 1 molar equiv. of Et_3N to form α, β-unsaturated sulfones in 70–90% yields. The reaction mechanism for the ruthenium(II) catalyzed reaction involves a free-radical redox-transfer chain process as outlined below[77]:

$$Ar'SO_2Cl + Ru^{II} \rightleftharpoons Ar'SO_2^{\bullet} + Ru^{III}Cl \quad (32)$$

$$Ar'SO_2^{\bullet} + ArCH{=}CH_2 \rightleftharpoons Ar'SO_2CH_2\dot{C}HAr \quad (33)$$

$$Ar'SO_2CH_2\dot{C}HAr + Ru^{III}Cl \rightleftharpoons Ar'SO_2CH_2CHClAr + Ru^{II} \quad (34)$$

(**23**)

$$Ar'SO_2CH_2CHClAr + Et_3N \longrightarrow Ar'SO_2CH{=}CHAr + Et_3N\cdot HCl \quad (35)$$

The three steps 32–34 have been suggested[77] to be equilibria, and the overall equilibrium must lie far to the left because no adduct **23** is found in the reaction mixture when the reaction of sulfonyl chloride with olefin is carried out in the absence of a tertiary amine. A second possible mechanism involving oxidative addition of the arenesulfonyl halide to form a ruthenium(IV) complex and subsequent reductive elimination of the ruthenium complex hydrochloride, $[HRu^{IV}Cl]$, was considered to be much less likely.

The addition of sulfonyl iodides to allenes to give 1:1 adducts has also been investigated[79]; the addition to phenylallene and 3-methyl-1,2-butadiene proceeds regioselectively and in excellent yields to give only the products arising from central attack by the sulfonyl radical. In contrast, the addition of sulfonyl iodides to 1,2-propadiene yields a mixture of products including the two 1:1 adducts resulting from attack by the sulfonyl radical on both the central and terminal positions of the allenic unit. The strong preference for the sulfonyl radicals[79,80] to become bonded to the central carbon is in contrast to the regioselectivity more commonly observed in free radical additions to allene. However, the results[79,80] have been rationalized by reference to the idea developed by Heiba[81] as shown in Figure 2.

Since the π bonds of allenes are orthogonal, the rates of formation of radicals resulting

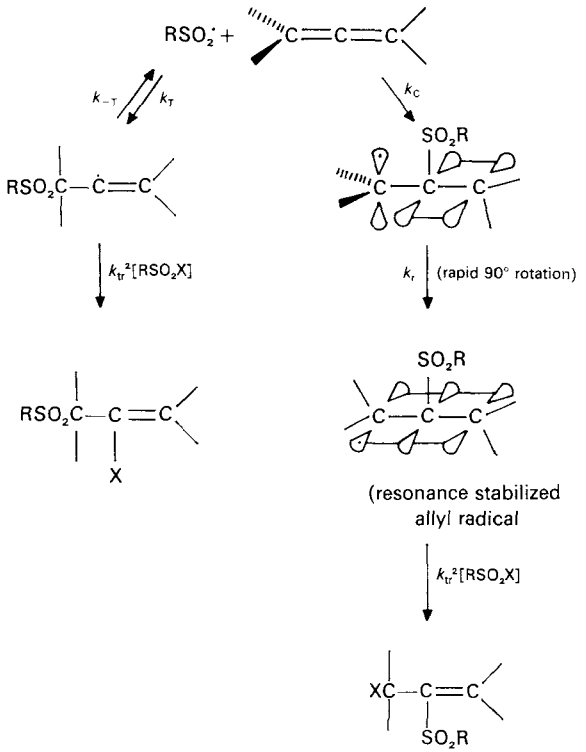
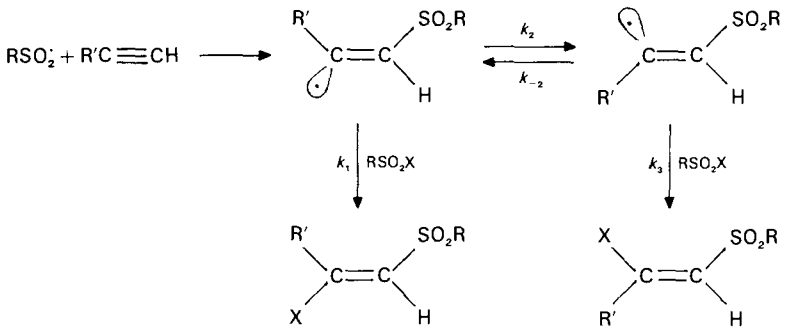


FIGURE 2. Proposed mechanism for radical addition of some sulfonyl iodides[79] (X = I) and Se-phenyl areneselenosulfonates[80] (X = SePh) to allenes.

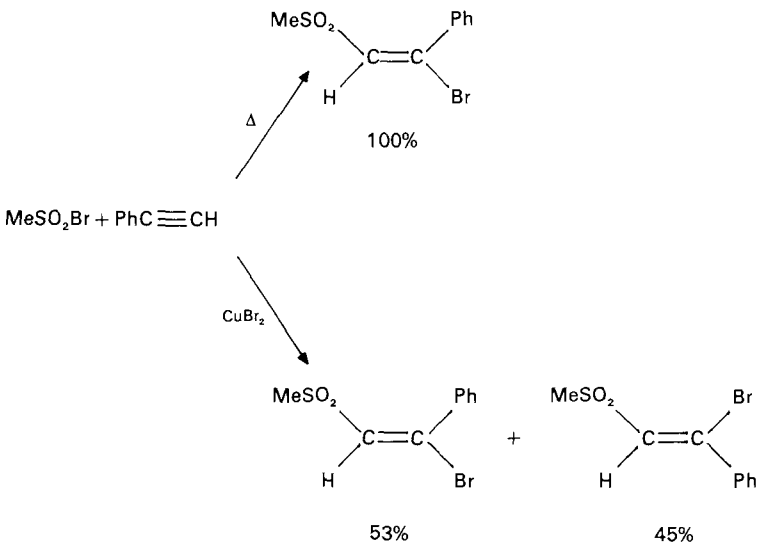
either from central or from terminal addition should be similar, i.e. $k_T \simeq k_C$. However, the central carbon adduct formation is not reversible because the formed radical undergoes a rapid 90° rotation to give a resonance-stabilized allyl radical; thus, the distribution of the final products will depend on the magnitude of the rate constants of the reversible reaction (k_T) and of the transfer reaction (k_{tr}^1).

In the thermal reaction of aliphatic and aromatic sulfonyl chlorides with acetylenes no adduct has been observed[82]. However, the light-catalyzed additions of sulfonyl iodides to acetylenes[83] as well as the thermal addition of sulfonyl bromides to phenylacetylene[84] to form 1:1 adducts have been shown to be stereoselective and to occur in good to excellent yields. The fact that the addition occurs in a *trans* manner forced the authors[83,84] to suggest that chain transfer by the sulfonyl halide (k_1) is much faster than isomerization of the intermediate vinyl radical (k_2) (see Scheme 5).

The copper-catalyzed 1:1 additions of aliphatic and aromatic sulfonyl chlorides[82,85] or bromides[84] to acetylenes yielding mixtures of *trans*- and *cis*-β-halovinyl sulfones have also been described. Highly polar solvents favored *trans* addition, while *cis* addition predominated in low polarity media[84,85]. A comparison between the thermal and the copper-catalyzed addition of sulfonyl bromides to phenylacetylene (cf. Scheme 6) enabled Amiel[84] to suggest that the two stereoisomers do not have a common intermediate. That is, the *trans* addition product is a result of a normal radical chain, while the *cis* addition



SCHEME 5

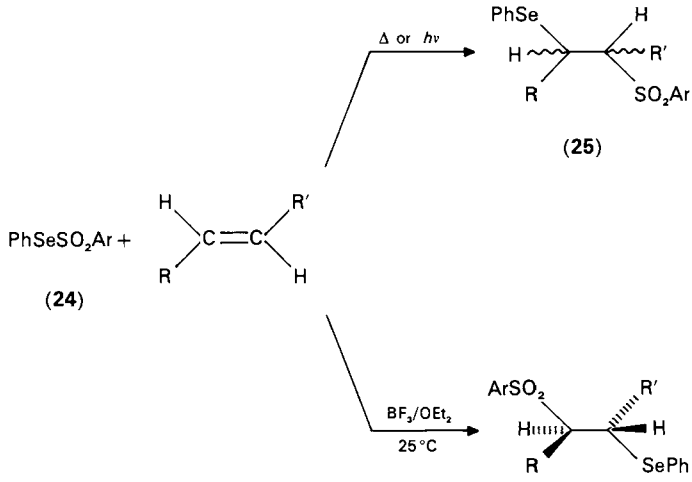


SCHEME 6

product, which is formed concurrently in the copper-catalyzed reaction, arises presumably from a concerted reaction.

2. Selenosulfonation of olefins, allenes and acetylenes

Se-phenyl areneselenosulfonates (**24**) undergo facile free-radical addition to alkenes to produce β-phenylseleno sulfones (**25**) in excellent yield[86,87] (see Scheme 7). The addition occurs regiospecifically and affords anti-Markovnikov products contrary to the analogous boron trifluoride catalyzed reaction which produces exclusively Markovnikov and highly stereospecific products[86] (equation 37). Reaction 36 has been shown to have the radical



SCHEME 7

chain mechanism outlined below:

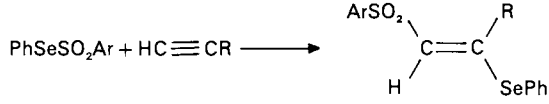
$$PhSeSO_2Ar \xrightarrow{\Delta \text{ or } h\nu} PhSe^{\bullet} + ArSO_2^{\bullet} \tag{38}$$

$$ArSO_2^{\bullet} + CH_2{=}CHR \longrightarrow ArSO_2CH_2{-}\dot{C}HR \tag{39}$$

$$ArSO_2CH_2{-}\dot{C}HR + PhSeSO_2Ar \longrightarrow ArSO_2CH_2{-}\underset{\displaystyle SePh}{\underset{|}{C}}HR + ArSO_2^{\bullet} \tag{40}$$

Se-phenyl areneselenosulfonate also undergoes highly regioselective free-radical addition to allenes ($R^1CH{=}C{=}CR^2R^3$) to afford the regioisomer $R^1CH(SePh)C(SO_2Ar){=}CR^2R^3$, arising from addition of the sulfonyl radical to the central carbon of the allene and transfer of the phenylseleno group to the less highly substituted of the two terminal carbons[80]. This regioselectivity has been explained by reference to concepts proposed by Heiba[81] as shown in Figure 2 (*vide supra*).

Free-radical addition of Se-phenyl areneselenosulfonates to acetylenes is also a facile process, occurring regiospecifically and stereoselectively to afford the *E*-isomer of a *β*-(phenylseleno) vinyl sulfone (**26**) in high yield[88].

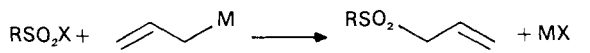


The reaction proceeds by a radical chain mechanism analogous to that outlined in equations 38–40. The observed stereoselectivity in the above addition indicates that reaction between the intermediate vinyl radical, $ArSO_2CH{=}\dot{C}R$, and $PhSeSO_2Ar$ must

be faster than radical inversion. Since inversion of vinyl radicals is normally a fast process, this is evidence of the high reactivity of $PhSeSO_2Ar$ as a chain-transfer agent.

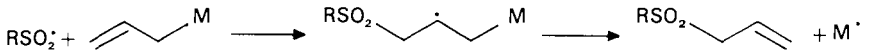
3. S_H2' reactions

Allyl- and substituted allylstannanes[89] as well as allylcobaloximes[90–92] undergo substitution with sulfonyl halides:



(42)

This 'allyl transfer' reaction, which is a valuable synthetic method, has been shown to be a free-radical chain substitution (S_H2'), namely



(43)

$$M^{\bullet} + RSO_2X \longrightarrow MX + RSO_2^{\bullet} \tag{44}$$

It is worth mentioning that the displacement of $Bu_3Sn^{\bullet}$ by $RSO_2^{\bullet}$ radicals has been shown to be reversible[93], so that the equilibrium 45 can be driven to the left by the reaction of $RSO_2^{\bullet}$ with Bu_3SnH or to the right by the reaction of $Bu_3Sn^{\bullet}$ with RSO_2Cl. Propargylstannanes[89] (equation 46) and allenylcobaloximes[91,94] (equation 47) undergo similar types of reaction, i.e. S_H2',

(45)

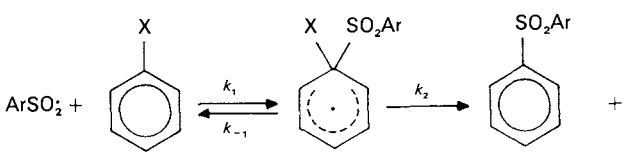
$$RSO_2^{\bullet} + R'C{\equiv}CCH_2SnBu_3 \longrightarrow RSO_2(R')C{=}C{=}CH_2 + Bu_3Sn^{\bullet} \tag{46}$$

$$ArSO_2^{\bullet} + R^1R^2C{=}C{=}CHCo^{III}(dmgH)_2py \longrightarrow ArSO_2{-}\underset{\displaystyle R^2}{\overset{\displaystyle R^1}{\overset{|}{\underset{|}{C}}}}{-}C{\equiv}CH + Co^{\bullet II}(dmgH)_2py \tag{47}$$

where (dmgH) = monoanion of dimethylglyoxime.

C. Homolytic Aromatic Substitution

When arenesulfonyl radicals are generated in benzene the only reported products are those of disproportionation[50,95] (*vide supra*). However, Camaggi and coworkers[95] have found that arenesulfonyl radicals in halobenzene replace the halogen atom at 150–190 °C, the relative reactivities being for Cl:Br:I, 1:5.9:18.6. These authors[95] proposed that the reaction proceeds via a reversible *ipso*-substitution,



(48)

Thus the products are determined by the strength of the C—X bond: for X = Cl, Br, or I the rate of aromatization (k_2) appears to be sufficiently high to compete with the reverse reaction (k_{-1}).

D. S_H2 and S_Hi Reactions

The photostimulated reaction of alkylmercury halides with $ArSO_2Y$ yields RY, where Y = Cl or SePh, according to the mechanism given in equations 49–50[35]. In the case of the

$$ArSO_2^{\bullet} + RHgX \xrightarrow{S_H2} ArSO_2HgX + R^{\bullet} \quad (49)$$

$$R^{\bullet} + ArSO_2Y \longrightarrow RY + ArSO_2^{\bullet} \quad (50)$$

Δ^5-hexenyl substituent, extensive cyclization occurs to yield the cyclopentylcarbinyl product; from the yields of uncyclized and cyclized products for Δ^5-hexenylmercury chloride, the rate constants for equation 50 have been estimated (*vide supra*). The S_H2 reaction 49 has also been invoked to be the key step in the alkylation of β-substituted styrenes by a free-radical addition–elimination sequence, namely[96]

$$ArSO_2^{\bullet} + RHgCl \xrightarrow{S_H2} ArSO_2HgCl + R^{\bullet} \quad (51)$$

$$R^{\bullet} + PhCH{=}CHSO_2Ar \longrightarrow Ph\dot{C}HCH(R)SO_2Ar \quad (52)$$

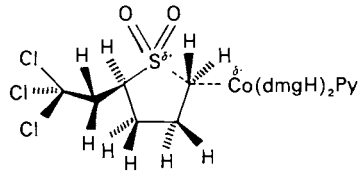
$$Ph\dot{C}HCH(R)SO_2Ar \longrightarrow PhCH{=}CHR + ArSO_2^{\bullet} \quad (53)$$

Toluenesulfonyl iodide reacts with benzylcobaloximes to give good yields of the benzyl *p*-tolyl sulfones, the key step being the homolytic attack of the sulfonyl radical at the α-carbon of the benzyl ligand[90,91]:

$$ArSO_2^{\bullet} + Ar'CH_2Co^{III}(dmgH)_2py \xrightarrow{S_H2} Ar'CH_2SO_2Ar + Co^{II}(dmgH)_2py \quad (54)$$

The yield of sulfone was found to be dependent on the nature of substituents in the benzene ring, being high ($\geqslant 85\%$) in the case of methyl substituents but low ($\leqslant 50\%$) in the case of nitro substituents.

The thermal and photochemical reactions of a number of substituted pent-4-enylcobaloximes with trichloromethanesulfonyl chloride give good yields of the corresponding 2-(β,β,β-trichloroethyl)sulfolanes. The process is thought to occur by initial attack of $^{\bullet}CCl_3$ at the terminal olefinic carbon of the pent-4-enyl moiety[97]; in the presence of SO_2 a sulfonyl radical is then formed that can undergo an S_Hi reaction on the α-carbon of the organic ligand (**27** represents the transition state), thereby displacing cobaloxime(II).



(**27**)

Although the free-radical chemistry of organocobaloximes is an interesting and useful reaction of some potential in organic synthesis, the validity of the label S_H2 and S_Hi for

some of these reactions, as also pointed out by Johnson[90], will remain in doubt until the redox characteristics of the radicals and substrates have been determined, accurate kinetic studies have been carried out and a careful search has been made for the intermediates.

VIII. REFERENCES

1. See, for example: F. Freeman and M. C. Keindl, *Sulfur Rep.*, **4**, 231 (1985); L. Lunazzi and G. F. Pedulli, in *Organic Sulfur Chemistry* (Eds. F. Bernardi, I. G. Csizmadia and A. Mangini), Chap. 9, Elsevier, Amsterdam, 1985, pp. 484–567; E. Block, *Reactions of Organosulfur Compounds*, Chap. 5, Academic Press, New York, 1978, pp. 176–220; J. L. Kice, *Free Radicals* (Ed. J. K. Kochi), Vol. 2, Chap. 24, Wiley, New York, 1973, pp. 711–740.
2. R. S. Andersen, *J. Chem. Phys.*, **66**, 5610 (1977); M. Geoffroy and E. A. C. Lucken, *J. Chem. Phys.*, **55**, 2719 (1971); G. M. Chantry, A. Horsfield, J. R. Morton and D. H. Whiffen, *Mol. Phys.*, **5**, 233 (1962).
3. C. Chatgilialoglu, B. C. Gilbert, R. O. C., Norman and M. C. R. Symons, *J. Chem. Res.*, (*S*) 185 (*M*) 2610 (1980).
4. J. R. Morton and K. F. Preston, *J. Magn. Reson.*, **30**, 577 (1978).
5. C. A. McDowell, F. G. Herring and J. C. Tait, *J. Chem. Phys.*, **63**, 3278 (1975).
6. A. Hinchliffe, *J. Mol. Struct.*, **71**, 349 (1981).
7. C. Chatgilialoglu, B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 1429 (1980).
8. C. Chatgilialoglu, B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 770 (1979).
9. C. Chatgilialoglu and M. Guerra, unpublished data.
10. A. Alberti, C. Chatgilialoglu and M. Guerra, *J. Chem. Soc., Perkin Trans. 2*, 1179 (1986).
11. C. Chatgilialoglu and S. Rossini, manuscript in preparation.
12. R. J. Boyd, A. Gupta, R. F. Langler, S. P. Lownie and J. A. Pincock, *Can. J. Chem.*, **58**, 331 (1980).
13. C. Chatgilialoglu, D. Griller and M. Guerra, *J. Phys. Chem.*, **91**, 3747 (1987).
14. H. H. Thoi, O. Ito, M. Iino and M. Matsuda, *J. Phys. Chem.*, **82**, 314 (1978).
15. T. E. Eriksen and L. Lind, *Radiochem. Radioanal. Letters*, **25**, 11 (1976).
16. S. Hashimoto, G. Inoue and H. Akimoto, *Chem. Phys. Letters*, **107**, 198 (1984).
17. S. W. Benson, *Chem. Rev.*, **78**, 23 (1978).
18. C. Chatgilialoglu, L. Lunazzi and K. U. Ingold, *J. Org. Chem.*, **48**, 3588 (1983).
19. A. Horowitz, *Int. J. Chem. Kinet.*, **8**, 709 (1976).
20. M. Yoshida, N. Furuta and M. Kobayashi, *Bull. Chem. Soc. Japan*, **54**, 2356 (1981).
21. B. C. Gilbert, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 303 (1975).
22. B. C. Gilbert, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 308 (1975).
23. B. C. Gilbert, H. A. H. Laue, R. O. C. Norman and R. C. Sealy, *J. Chem. Soc., Perkin Trans. 2*, 1040 (1976).
24. A. G. Davies, B. P. Roberts and B. R. Sanderson, *J. Chem. Soc., Perkin Trans. 2*, 626 (1973).
25. M. McMillian and W. A. Waters, *J. Chem. Soc.* (*B*), 422 (1966).
26. C. Chatgilialoglu, *Gazz. Chim. Ital.*, **116**, 511 (1986).
27. A. Horowitz and L. A. Rajbenbach, *J. Amer. Chem. Soc.*, **97**, 10 (1975).
28. C. Chatgilialoglu, *J. Org. Chem.*, **51**, 2871 (1986).
29. C. Chatgilialoglu, *Advances in Chemical Reaction Dynamics*, NATO ASI (Eds. P. M. Rentzepis and C. Capellos), Reidel, Amsterdam, 1986, pp. 571–579.
30. C. M. M. da Silva Corrêa and M. A. B. C. S. Oliveira, *J. Chem. Soc., Perkin Trans. 2*, 711 (1983).
31. M. Iino, M. Igarashi and M. Matsuda, *Macromolecules*, **12**, 697 (1979).
32. A. Orochov, M. Asscher and D. Vofsi, *J. Chem. Soc.* (*B*), 255 (1969).
33. M. Kobayashi and M. Yoshida, *Bull. Chem. Soc. Japan*, **58**, 473 (1985).
34. C. Chatgilialoglu, K. U. Ingold and J. C. Scaiano, *J. Amer. Chem. Soc.*, **103**, 7739 (1981).
35. G. A. Russell and H. Tashtoush, *J. Amer. Chem. Soc.*, **105**, 1399 (1983).
36. (a) J. A. Good and J. C. Thynne, *Trans. Faraday Soc.*, **63**, 2708 (1967); *Trans. Faraday Soc.*, **63**, 2720 (1967).
    (b) J. G. Calvert, D. H. Slater and J. W. Gall, in *Chemical Reactions in Urban Atmospheres* (Ed. C. S. Tuesday), Elsevier, New York, 1971.
    (c) F. C. James, J. A. Kerr and J. P. Simons, *J. Chem. Soc., Faraday Trans. 2*, 2124 (1973).
37. H. H. Thoi, M. Iino and M. Matsuda, *Macromolecules*, **12**, 338 (1979).

38. H. H. Thoi, M. Iino and M. Matsuda, *J. Org. Chem.*, **45**, 3626 (1980) and references cited therein.
39. M. Oudrhiri-Hassani, D. Brunel, A. Germain and A. Commeyras, *J. Fluorine Chem.*, **25**, 491 (1984).
40. V. Boekelheide, *Acc. Chem. Res.*, **13**, 65 (1980).
41. R. P. Thummel, *Acc. Chem. Res.*, **13**, 70 (1980).
42. K. C. Nicolaou, W. E. Barnette and P. Ma, *J. Org. Chem.*, **45**, 1463 (1980).
43. R. S. Givens, R. J. Olsen and P. L. Wylie, *J. Org. Chem.*, **44**, 1608 (1979).
44. F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, **8**, 274 (1969).
45. D. T. Longone, S. H. Kusefoglu and J. A. Gladysz, *J. Org. Chem.*, **42**, 2787 (1977).
46. R. S. Givens, B. Hrinczenko, J. H. S. Lin, B. Matuszewski and J. Tholen-Collison, *J. Amer. Chem. Soc.*, **106**, 1779 (1984); J. G. Gould, C. Tung, N. J. Turro, R. S. Givens and B. Matuszewski, *J. Amer. Chem. Soc.*, **106**, 1789 (1984).
47. (a) I. I. Kandror and R. Kh. Freidlina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1890 (1974).
(b) J. F. King and K. C. Khemani, *Can. J. Chem.*, **63**, 619 (1985).
48. See, for example: A. Alberti and C. Chatgilialoglu, *Org. React. Mech.*, 73 (1984); 83 (1985); 87 (1986); 85 (1987).
49. M. D. Johnson and S. Derenne, *J. Organomet. Chem.*, **286**, C47 (1985).
50. C. M. M. da Silva Corrêa and W. A. Waters, *J. Chem. Soc. (C)*, 1874 (1968); C. M. M. da Silva Corrêa, *J. Chem. Soc., Perkin Trans. 1*, 1519 (1979).
51. C. Chatgilialoglu, B. C. Gilbert, B. Gill and M. D. Sexton, *J. Chem. Soc., Perkin Trans. 2*, 1141 (1980).
52. J. L. Kice, *Adv. Phys. Org. Chem.*, **17**, 65 (1980).
53. A. I. Nikolaev, R. L. Safiullin and V. D. Komissarov, *Khim. Fiz.*, **3**, 257 (1984).
54. M. Yoshida, N. Futura and M. Kobayashi, *Bull. Chem. Soc. Japan*, **54**, 2356 (1981).
55. I. P. Bleeker and J. B. F. N. Engberts, *J. Org. Chem.*, **46**, 1012 (1981).
56. A. Heesing, W. K. Homann and W. Müllers, *Chem. Ber.*, **113**, 152 (1980).
57. C. Brown, R. F. Hudson and K. A. F. Record, *J. Chem. Soc., Perkin Trans. 2*, 822 (1978).
58. W. J. Bouma and J. B. F. N. Engberts, *J. Org. Chem.*, **41**, 143 (1976).
59. K. Hovious and J. B. F. N. Engberts, *Tetrahedron Letters*, 181 (1972).
60. I. P. Bleeker and J. B. F. N. Engberts, *Recl., J.R. Neth. Chem. Soc.*, **100**, 459 (1981).
61. C. M. M. da Silva Corrêa and W. A. Waters, *J. Chem. Soc., Perkin Trans. 2*, 1575 (1972).
62. Y. Takahara, M. Iino and M. Matsuda, *Bull. Chem. Soc. Japan*, **49**, 2268 (1976).
63. M. Asscher and D. Vofsi, *J. Chem. Soc.*, 4962 (1964).
64. J. Sinneich and M. Asscher, *J. Chem. Soc., Perkin Trans. 1*, 1543 (1972).
65. T. E. Boothe, J. L. Greene, Jr. and P. B. Shevlin, *J. Org. Chem.*, **45**, 794 (1980).
66. P. Lin and G. H. Whitham, *J. Chem. Soc., Chem. Commun.*, 1102 (1983).
67. T. A. K. Smith and G. H. Whitham, *J. Chem. Soc., Chem. Commun.*, 897 (1985).
68. C. Chatgilialoglu, B. C. Gilbert, C. M. Kirk and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 1084 (1979).
69. M. S. Kharasch and A. F. Zavist, *J. Amer. Chem. Soc.*, **73**, 964 (1951); P. S. Skell, R. C. Woodworth and J. H. McNamara, *J. Amer. Chem. Soc.*, **79**, 1253 (1957).
70. S. J. Cristol and J. A. Reeder, *J. Org. Chem.*, **26**, 2182 (1961); S. J. Cristol and D. I. Davies, *J. Org. Chem.*, **29**, 1282 (1964).
71. E. Block, M. Aslam, V. Eswarakrishnan, K. Gebreyes, J. Hutchinson, R. Iyer, J.-A. Laffitte and A. Wall, *J. Amer. Chem. Soc.*, **108**, 4568 (1986); E. Block and M. Aslam, *J. Amer. Chem. Soc.*, **105**, 6164 (1983); E. Block, M. Aslam, V. Eswarakrishnan and A. Wall, *J. Amer. Chem. Soc.*, **105**, 6165 (1983).
72. A. Or, M. Asscher and D. Vofsi, *J. Chem. Soc., Perkin Trans. 2*, 1000 (1973).
73. W. E. Truce, C. T. Goralski, L. W. Christensen and R. H. Bavry, *J. Org. Chem.*, **35**, 4217 (1970).
74. W. E. Truce and C. T. Goralski, *J. Org. Chem.*, **35**, 4220 (1970).
75. W. E. Truce and C. T. Goralski, *J. Org. Chem.*, **36**, 2536 (1971).
76. L. K. Lin, Y. Chi and K.-Y. Jen, *J. Org. Chem.*, **45**, 406 (1980).
77. N. Kamigata, H. Sawada and M. Kobayashi, *J. Org. Chem.*, **48**, 3793 (1983); N. Kamigata, T. Narushima, H. Sawada and M. Kobayashi, *Bull. Chem. Soc. Japan*, **57**, 1421 (1984).
78. N. Kamigata, J. Ozaki and M. Kobayashi, *J. Org. Chem.*, **50**, 5045 (1985).
79. W. E. Truce, D. L. Heuring and G. C. Wolf, *J. Org. Chem.*, **39**, 238 (1974).
80. J. L. Kice and Y.-H. Kang, *Tetrahedron*, **41**, 4739 (1985).
81. E.-A. I. Heiba, *J. Org. Chem.*, **31**, 776 (1966).
82. Y. Amiel, *J. Org. Chem.*, **36**, 3691 (1971).

83. W. E. Truce and G. C. Wolf, *J. Org. Chem.*, **36**, 1727 (1971).
84. Y. Amiel, *J. Org. Chem.*, **39**, 3867 (1974).
85. Y. Amiel, *J. Org. Chem.*, **36**, 3697 (1971).
86. T. G. Back and S. Collins, *J. Org. Chem.*, **46**, 3249 (1981).
87. R. A. Gancarz and J. L. Kice, *J. Org. Chem.*, **46**, 4899 (1981).
88. T. G. Back, S. Collins and R. G. Kerr, *J. Org. Chem.*, **48**, 3077 (1983) and references cited therein.
89. G. A. Russell and L. L. Herold, *J. Org. Chem.*, **50**, 1037 (1985).
90. M. D. Johnson, *Acc. Chem. Res.*, **16**, 343 (1983) and references cited therein.
91. M. R. Ashcroft, P. Bougeard, A. Bury, C. J. Cooksey and M. D. Johnson, *J. Organomet. Chem.*, **289**, 403 (1985).
92. S. Roy, B. D. Gupta and S. Chaklanobis, *J. Organomet. Chem.*, **269**, 201 (1984).
93. Y. Ueko and M. Okawara, *J. Amer. Chem. Soc.*, **101**, 1893 (1979); Y. Ueko, S. Aoki and M. Okawara, *J. Amer. Chem. Soc.*, **101**, 5414 (1979).
94. B. D. Gupta and S. Roy, *Tetrahedron Letters*, **27**, 4905 (1986).
95. L. Benati, C. M. Camaggi and G. Zanardi, *J. Chem. Soc., Perkin Trans. 1*, 2817 (1972).
96. G. A. Russell, H. Tashtoush and P. Ngoviwatchai, *J. Amer. Chem. Soc.*, **106**, 4622 (1984).
97. M. R. Ashcroft, P. Bougeard, A. Bury, C. J. Cooksey and M. D. Johnson, *J. Org. Chem.*, **49**, 1751 (1984).

Author Index

This author index is designed to enable the reader to locate an author's name and work with the aid of the reference numbers appearing in the text. The page numbers are printed in normal type in ascending numerical order, followed by the reference numbers in parentheses. The numbers in *italics* refer to the pages on which the references are actually listed.

Subject Index