GAS-PHASE PYROLYSES OF 3-THIABICYCLO[3.2.0]-

HEPTANE 3,3-DIOXIDE RING SYSTEMS

by

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Thesis presented for the degree of

Doctor of Philosophy

Dedication

To the memory of my parents, Patrick and

Margaret McLaughlin.

DECLARATION

I declare that this thesis is my own composition, that the work of which it is a record has been carried out by myself, and that it has not been submitted in any previous application for a Higher Degree.

The thesis describes results of research carried out in the Department of Chemistry, University of Edinburgh, under the supervision of Professor J. I. G. Cadogan since the 1st of October 1977, the date of my admission as a research student.

POST-GRADUATE COURSES

The following is a statement of post-graduate courses attended during the last three years.

Lab 29 Seminars	1977-1980
"Strategy of Organic Synthesis"	Dr. I. Gosney
"Chemistry at its most Colourful"	Staff of ICI Blackley
"Basic and Advanced Stereochemistry"	Dr. H. McNab
"Flash Vacuum Pyrolysis"	Dr. H. McNab
"The Bio-Organic Chemistry of Drugs, Toxins and other Xenobiotics"	Dr. A. G. Rowley

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ABSTRACT

The flash vacuum pyrolysis of 3, 5-dioxo-4-oxa-9-thiatricyclo-$[5.3.0.0^{2,6}]$decane 9,9-dioxide and its derivatives has been extensively investigated. Under these conditions, it is found that cheletropic elimination of SO_2 occurs leading to the formation of novel 1,2-divinylcyclopentane compounds. In all cases the reaction is stereo-specific and yielded only cis-isomers which are not prone to Cope rearrangement.

On oxidative bis-decarboxylation 3, 5-dioxo-4-oxa-9-thiatricyclo-$[5.3.0.0^{2,6}]$decane 9,9-dioxide is converted into the novel synthon 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide. It is shown that although the reaction is sluggish epoxidation of this alkene and subsequent pyrolysis provides a worthwhile synthesis to 4,5-dihydrooxepin in good yield. Attempts to obtain suitable precursors to the carbon and nitrogen analogues of 4,5-dihydrooxepin by addition of carbenes and nitrenes to 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide failed as the alkene did not react with these species.

3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide is also observed to undergo cycloaddition reactions with a variety 1,3-dipoles including nitrile oxides, nitrones and diazo compounds, to give precursors of other new cis-1,2-divinyl heterocycles, difficult to prepare by other methods. In the case of the less reactive diphenylnitrilimine no addition product could be detected. An attempt to prepare the precursor of 1,4-cycloheptadiene indirectly by addition of diazomethane to the

alkene was also unsuccessful; extrusion of nitrogen by photolysis

from the derived adduct gave unidentified products.

^{1}H n.m.r. and ^{13}C n.m.r. spectroscopy were used extensively

to determine the structure of the products and in two cases X-ray

analysis was used to confirm assigned structures.

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INTRODUCTION

Preamble

Elemental sulphur has been known since ancient times, yet research on the element and its compounds continues apace. The first organosulphur compound to be prepared was ethanethiol in 1834.[1] Sulphones, the major topic of this thesis, were first prepared in 1867.[2] 3, 5-Dioxo-4-oxa-9-thiatricyclo[5. 3. 0. 0^{2,6}]decane 9, 9-dioxide (1) was first reported in the literature in 1972.[3] The molecule was recognised to have potential for divinyl synthesis and considered to merit further investigation. This thesis describes the results of the study.

(1)
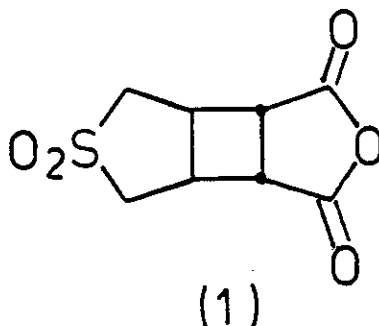
Sections A. 1, A. 2 and A. 3 focus attention on the properties, preparation and reactions of sulphones in general. Cheletropic reactions involving sulphur dioxide formed a major part of the study and will be considered separately in section B. Cope, and to a lesser extent the Claisen, rearrangements, featured in the study and so will be introduced in section C. Finally section D will focus on the programme of research.

A.   Sulphones

A.1   General properties of sulphones.

The sulphone group has been known for more than a century but it is only in the last few decades that a more diverse range of chemistry has been discovered.   The past fifteen years in particular have witnessed many publications both of a theoretical nature and involving synthetic applications of sulphones.   Both these aspects of sulphone chemistry have been reviewed.[4,5]

The sulphone group is represented by the general formula (2) in which the substituents R and R' can be any combination of alkyl, vinyl, alkynyl or aryl.

$$R-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-R' \qquad (2)$$
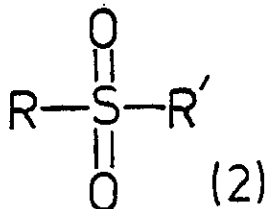
The sulphur-oxygen bonds are polar giving rise to a large dipole moment relative to the analogous ketones ($CH_3SO_2CH_3$, 3.22D; CH_3COCH_3 2.88D).[6]   This polarity manifests itself in the physical properties of sulphones.   They occur as either solids or high boiling point liquids.

The presence of a sulphone function in a molecule is most easily ascertained by infrared spectroscopy.   All sulphones show strong bands in the 1300-1320 and 1140-1160 cm^{-1} regions due to the asymmetric stretching modes of the SO_2 group.[7,8]   On the other hand proton n.m.r. spectroscopy is of lesser diagnostic value.   Aliphatic hydrogens α to a sulphone function are generally found in the range 2.5-3.1δ: typical examples being $CH_3SO_2CH_3$ 3.03 δ and $CH_2 = CHSO_2CH_3$ 2.62δ.[9]

Typically sulphones exhibit high chemical and thermal stability,

and this would tend to suggest a lack of ready manipulation.   That this

is   not the case is testified by recent reviews on sulphone

chemistry.[4, 5, 10-12]   The sulphone group is fully oxidised and is

reduced to the sulphide only with great difficulty.[13]   A sulphone group

can be removed and replaced by hydrogen using Raney Nickel,[14] Li

in diethylamine,[15] or 6% Na/Hg in methanol using Na_2HPO_4 as buffer.[16]

The chemistry of sulphones can be broadly classified into two areas:

(i) those reactions in which the sulphone functional group is a

particularly stable unit surviving a large number of transformations,

and (ii) those reactions which rely on the disruption and elimination

of the sulphone group.

This discussion will focus attention on the latter as these reactions

are central to the theme of the thesis.

A. 2   Preparation of sulphones.

a) Oxidation of sulphides and sulphoxides.

The most common method of sulphone preparation is the direct

oxidation of sulphides and sulphoxides.   A variety of oxidising agents

have been utilized to effect these transformations.   An extensive

tabulation of the experimental results for these processes is available.[17]

The most commonly used oxidant is hydrogen peroxide (30%) in

acetic acid (Scheme 1).   This method gives excellent yields.[18]

$$C_6H_5CH_2S\,C_2H_5 \xrightarrow[\text{HOAc}]{H_2O_2} C_6H_5CH_2SO_2\,C_2H_5$$

$$80^{\circ} \qquad\qquad 87\%$$
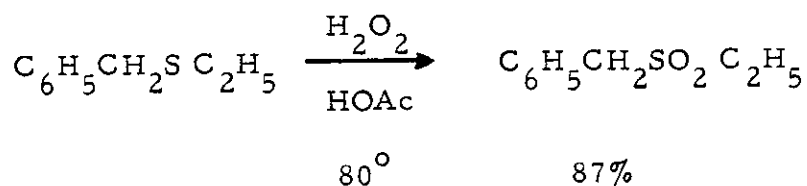
Scheme 1

m-Chloroperbenzoic acid in various organic solvents has also been

used and in general is a very effective reagent giving clean products in high yield.[9]

b) Aromatic sulphonylation.

The reaction between an arene and a sulphonyl halide in the presence of a suitable Lewis acid constitutes an excellent route to diaryl or alkyl-aryl sulphones (Scheme 2).[19] Sulphonyl chlorides are commonly employed although sulphonyl bromides and fluorides have also

$$RSO_2Cl + C_6H_6 \xrightarrow{AlCl_3} RSO_2C_6H_5$$

$$R = CH_3 \quad 80\%$$

$$R = C_6H_5 \quad 90\%$$
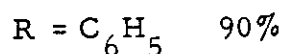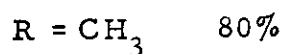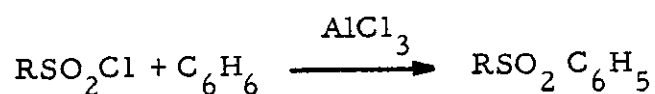
Scheme 2

been used. Generally, the reaction gives better yields in the case of arenesulphonyl chlorides.

c) Alkylation of sulphinic acids.

This method of preparing sulphones has been known for about eighty years,[20] but has gained importance only relatively recently mainly in connection with the alkylation of the more accessible and stable aromatic sulphinic acids with reactive halides.

d) Cycloaddition reactions of sulphur dioxide with polyenes.

The addition of sulphur dioxide to polyenes as a route to sulphones is only of moderate importance. However, since their classification[21] as $\pi 4_s + \pi 2_s$ cheletropic transformations, there has been a tremendous upsurge of interest in these reactions. For this reason and since these cycloadditions are central to the theme of this discussion they will be discussed at length in section B.

A.3 Reactions of sulphones.

a) The Ramberg-Bäcklund reaction

When a α-halosulphone (3) bearing an α'-hydrogen is treated with base the resultant carbanion (4) is capable of intramolecular 1,3-elimination to give an alkene (6) in which the position of the double bond is unambiguous (Scheme 3). This extrusion process is known as the Ramberg-Bäcklund reaction after its discoverers.[18] A recent review is available.[10]
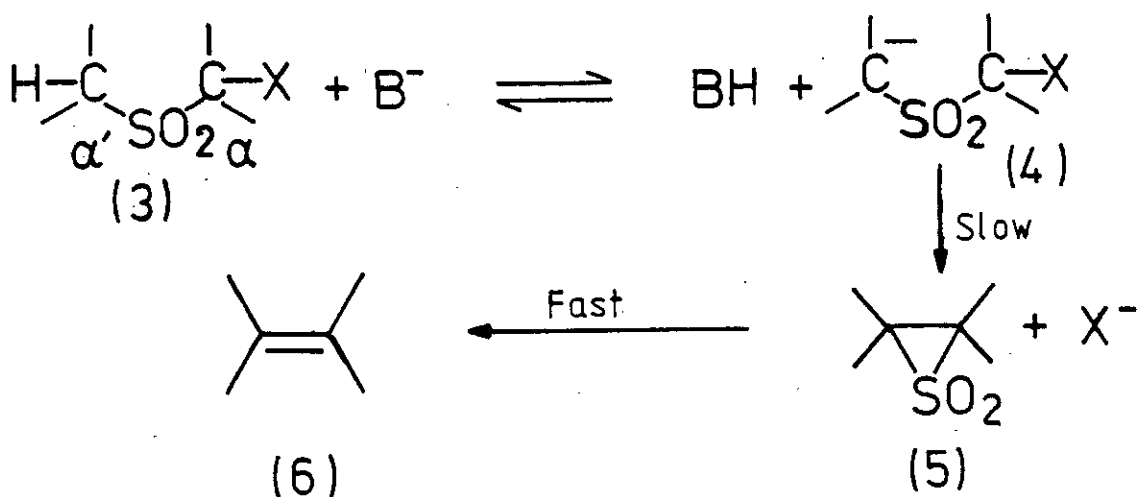
Scheme 3

To date the postulated episulphone intermediates (5) have not been isolated although they have been prepared by other routes.[23-25] When episulphones of the type (5) are treated with base the expected alkene is obtained. The sulphur dioxide loss is markedly stereo-specific. Consequently the stereochemistry of the alkene is determined at the ring-closure stage.

The formation of the anion (4) in the proposed reaction mechanism, has been intensively investigated by Paquette[26] and Bordwell[27] and their co-workers. Anion formation occurs at both the α and α' positions in a

reversible manner and does so more rapidly than episulphone formation. This has been demonstrated by the incorporation of deuterium in un-reacted starting material if the reaction is carried out in D_2O and by the isolation of deuterated alkenes under similar conditions.[28] This gives the Ramberg-Bäcklund reaction an advantage in alkene synthesis where one wishes to prepare alkenes in which the alkene hydrogens are replaced by deuterium.[29, 30] One simply has to conduct the reaction in deuterated solvents. A typical example is shown in Scheme 4.[31]
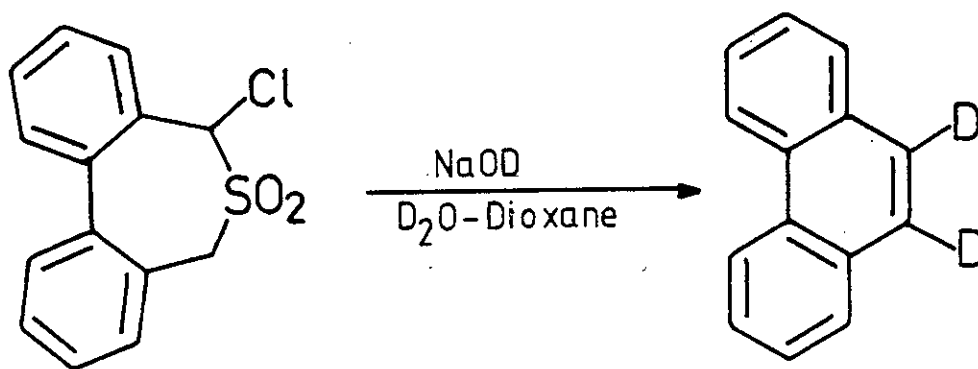
Scheme 4

As other methods of alkene synthesis are now available the importance of the reaction has declined, but it still retains usefulness as a route to stained carbocycles such as (7) (Scheme 5).[32]
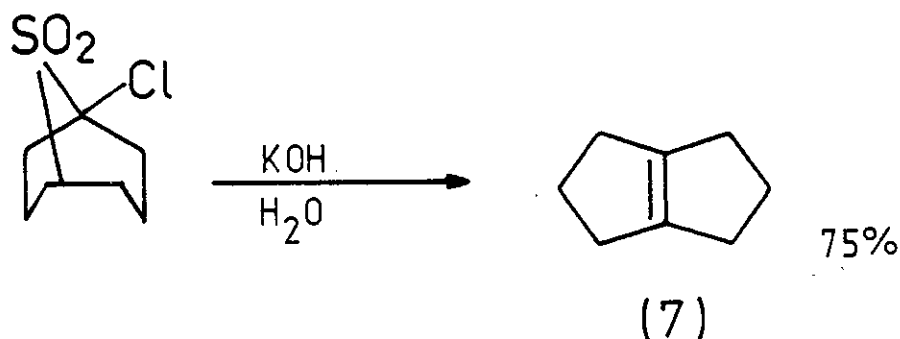
Scheme 5

Meyers et al.[33] have shown that the need to prepare α-halosulphones in a separate step can be circumvented by treating a sulphone (containing both α and α' hydrogens) with tetrachloromethane in t-butyl alcohol. This gives rise to in situ Ramberg-Bäcklund reactions. A typical example is shown (Scheme 6). A drawback to this reaction is that

$$(PhCH_2)_2\ SO_2 \xrightarrow[\underline{t}-C_4H_9OH]{KOH,\ CCl_4} \underline{trans} - PhCH{=}CHPh$$

$$100\%$$
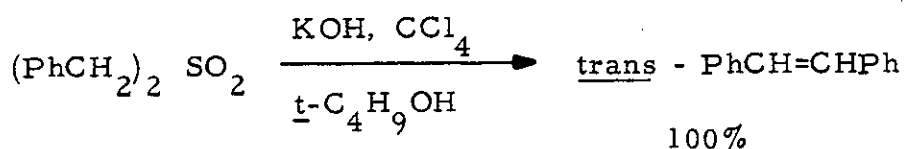
Scheme 6

dichlorocarbene is sometimes generated concomitantly and may react subsequently with the desired alkene to form a dichlorocyclopropane.

b) Reduction of sulphones.

Sulphones are resistant to most reducing agents. In attempts to reduce sulphones using $LiAlH_4$ Bordwell and McKellin[13] found that four or five membered ring species gave the corresponding sulphides whereas six-membered rings and acyclic sulphones were either inert or reduced to only a small extent. More recently Gardner and his co-workers[34] have shown that di-isobutylaluminium hydride (Dibal-H) in ether or THF is an effective reagent for the reduction of sulphones to sulphides. The general reaction is shown in Scheme 7.

$$R\ R'SO_2 + 2(C_4H_9)_2\ AlH \xrightarrow{PhCH_3} R\ R'S + 2(C_4H_9)_2\ AlOH$$
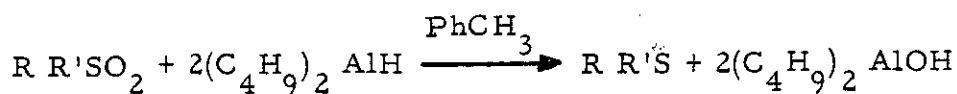
R=R'=	n-propyl	yield = 77%
R=R'=	n-butyl	yield = 68%
R=R'=	phenyl	yield = 57%
R=Me, R'=	phenyl	yield = 61%

Scheme 7

Paquette and Photis[35] have reported an interesting reductive elimination of cyclic sulphones (8) and (10) leading to the formation of substituted cyclobutenes (9) and (11) (Scheme 8). This conversion is formally similar to the Ramberg-Bäcklund reaction discussed in the previous section.

Scheme 8
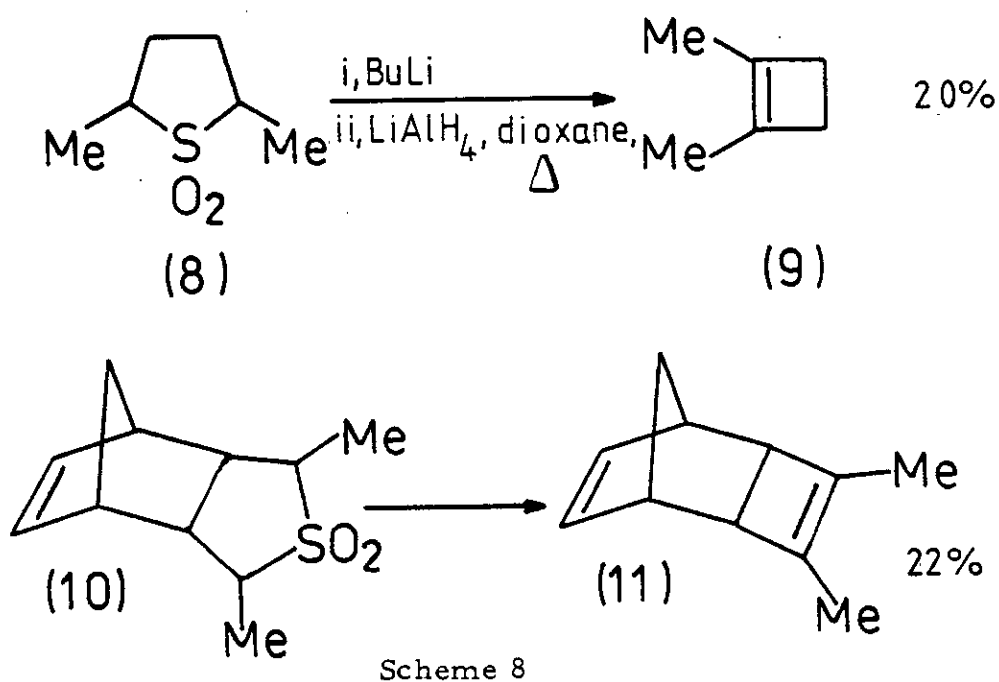
c) <u>Thermal and photochemical extrusion of sulphur dioxide</u>.

Cyclic sulphones containing structural elements such as aromatic rings, functional groups, heteroatoms and further SO_2-groups as ring members decompose on heating with loss of SO_2 and formation of new C-C bonds. The importance of this reaction as synthetic method has recently been reviewed.[12] Cheletropic extrustion of SO_2 from sulpholenes are discussed in more detail in section B.

Smith and co-workers have reported[36] that photolysis of the sulphones (12) give 1-substituted phenylcyclopropanes (13) in high yield (Scheme 9).

(12) $\xrightarrow[-SO_2]{h\nu}$ (13)
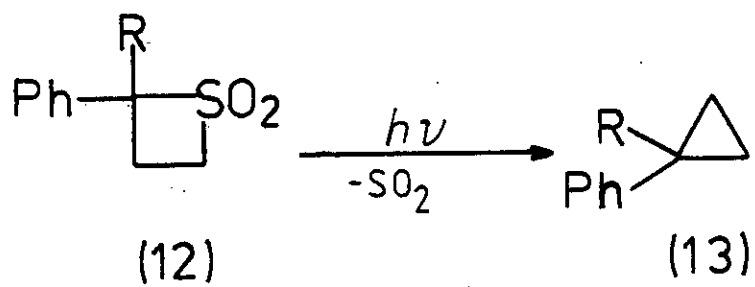
R=H, CH$_3$, C$_2$H$_5$, PhCH$_2$, or CH$_2$=CH-CH$_2$

Scheme 9

B. Cheletropic Reactions

B.1 Introduction

In 1969 Woodward and Hoffmann[21] defined a cheletropic reaction as a process in which two bonds which terminate at a single atom are made or broken in concert. Cheletropic reactions are really a sub-class of cycloadditions, the only difference being that on one of the components both new bonds are being made to the same atom.

The dissociation of (14) to give a molecule Xyz (16) and a polyene containing an $\underline{m}$-electron π system (15) is an example of a cheletropic reaction (Scheme 10). Xyz is usually a small inorganic molecule of high thermodynamic stability, e.g. CO, N_2, SO_2 or N_2O.
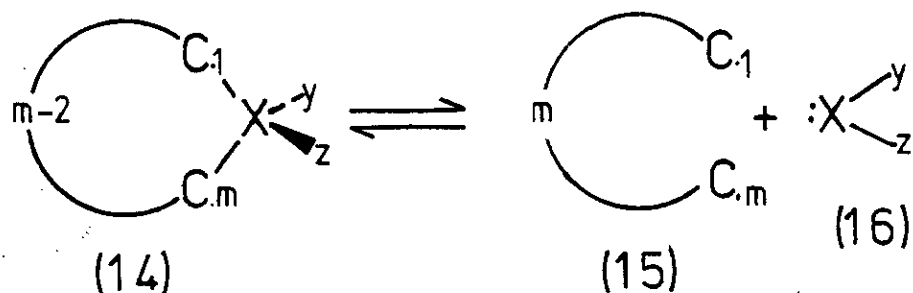
Scheme 10

In order to gain insight into the stereochemical features of the cheletropic reaction one must consider the general reaction in which the substrate (17) carries substituents $\underline{a}$ at the atoms C_1 and C_m (Scheme 11). The major stereochemical features of this process
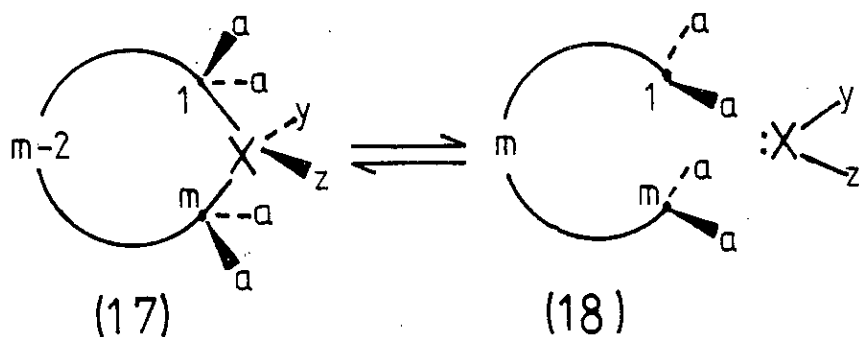
Scheme 11

which require consideration are:

(i)   The nature of the concerted rotations that must occur about C_1 and C_m in order to bring the substituents $\underline{a}$ into the 'plane' of the polyene molecule (18) as it is formed.

(ii)   The relative dispositions of the polyene (18) and Xyz when the bond breaking process is complete (forward reaction) or bond formation commences (reverse reaction).

(iii)   The nature of the orbitals utilized by Xyz.

In case (i) there are only two distinguishable rotation modes $\underline{viz}$. conrotation and disrotation.   Each mode has two formal possibilities and hence there are four possible polyenic products when the substituents $\underline{a}$ are all different.   However usually the steric constraints imposed by the substituents $\underline{a}$ dictate that one mode of disrotation or conrotation is preferred over the other and so only one mode operates.

In case (ii) analysis of the pertinent molecular orbital interactions show that two distinct reaction pathways are possible.   The pathways have been categorized[21] as either linear (the least motion path) or non-linear (non-least motion path).   In this respect Woodward and Hoffmann recognised that there is mechanistic ambiguity for cheletropic reactions, in that the scission (or formation) of a pair of bonds at one atom means that the stereochemical imprint of the transition state for that moiety will be absent in the product.   Thus there is no experimental procedure which allows distinction between linear and non-linear cheletropic reactions and so interpretations of this nature are purely theoretical.

In case (iii) the molecule Xzy $\underline{e.g.}$ SO_2, N_2, or CO can be

considered to utilize a filled sp^n orbital and an empty p-orbital for bonding purposes.

Finally since cheletropic reactions are pericyclic changes they are governed by the general orbital symmetry control rule for such processes which is:

A ground state pericyclic change is symmetry-allowed when the total number of $(4q+2)_s$ and $(4r)_a$ components is odd.

B. 2   Theory of cheletropic extrusion of SO_2 from sulpholenes.

The term sulpholene has been used[4] generically to describe sulphones which may be considered as cheletropic adducts of SO_2 and a (poly)alkene, e.g. butadiene and hexatriene.   Loss of SO_2 from sulpholenes has been analysed from a theoretical viewpoint by workers using a number of different approaches.[21, 37, 38]   The frontier orbital approach of Gilchrist and Storr[37] will be used in the present discussion.

According to frontier orbital theory, the overriding factor in determining the selection rules for polyene cycloaddition is the symmetry of the HOMO (highest occupied molecular orbital) and the LUMO (lowest unoccupied molecular orbital) of the reactants.   This is in turn related to the number of electrons involved in each of the reactants. Any component other than a neutral polyene which can supply the same number of electrons in an orbital of the same symmetry is potentially able to participate in a cycloaddition in place of a polyene.   Sulphur dioxide is just such a component.

(19)
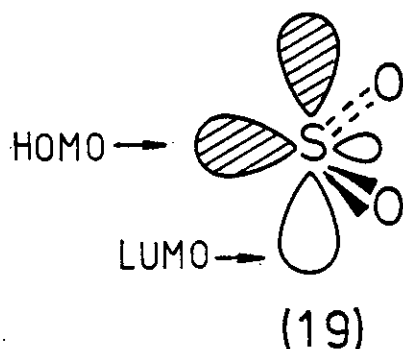
Sulphur dioxide (19) has a lone pair of electrons in the plane of the molecule and a vacant p orbital orthogonal to it. Thus when considering cheletropic extrusion reactions of sulpholenes one considers the interaction of the HOMO (lone pair orbital) of sulphur dioxide with the LUMO of the alkene as well as the LUMO (vacant p orbital) of sulphur dioxide with the HOMO of the alkene.

Mock[39] has extensively investigated the family of cheletropic extrusions which are now to be considered (Scheme 12).
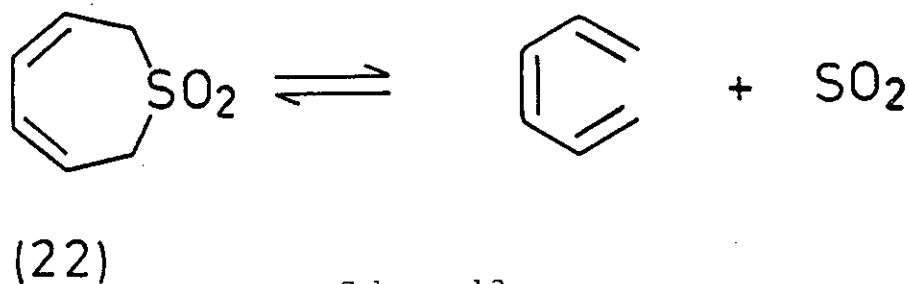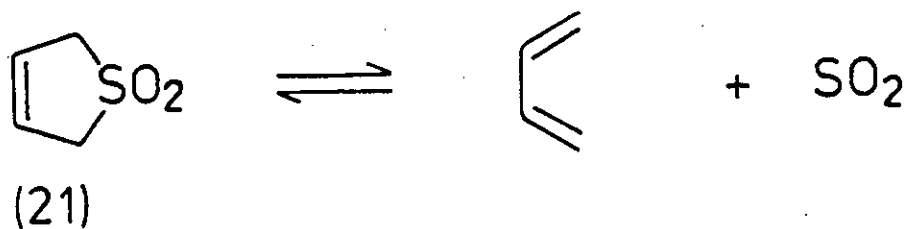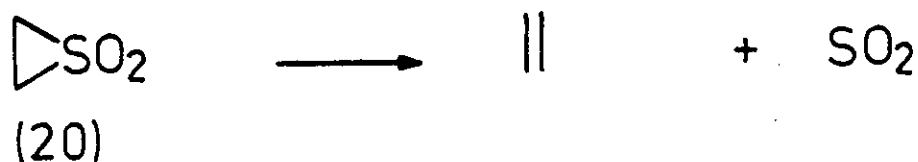
Scheme 12

First consider fragmentation of the episulphone (20), the orbital representations of which are shown in figure 1 and figure 2, for the linear and non-linear reaction pathways respectively.
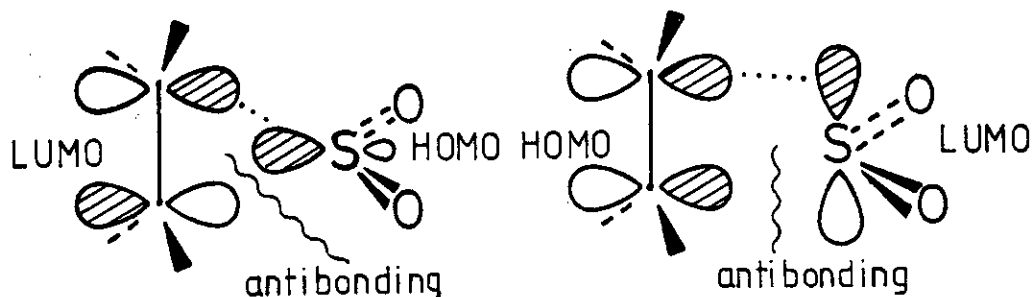
<u>Fig. 1.</u>   The linear approach of SO_2 to an alkene
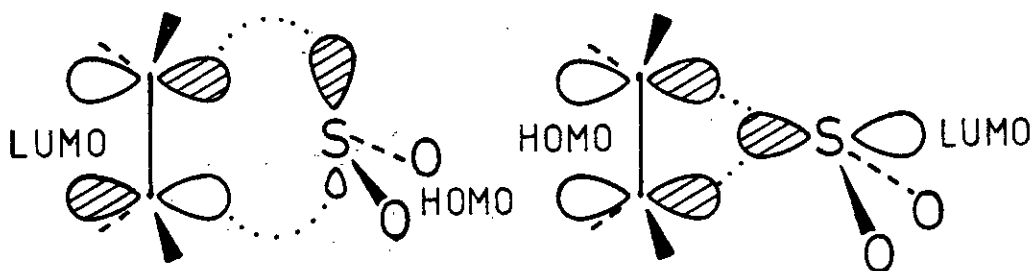
<u>Fig. 2.</u>   The non-linear approach of SO_2 to an alkene

Thus as shown in Figure 1 a concerted suprafacial, suprafacial $\pi 2_s + \omega 2_s$ interaction is a disallowed process.   For the reaction to be concerted the sulphur dioxide must depart (or approach) in an antarafacial manner as illustrated in Figure 2, an interaction described as a $\pi 2_s + \omega 2_a$ process.

The best known of this family of reactions is undoubtedly the reversible formation of butadiene sulphone (21) from butadiene and sulphur dioxide.   The relevant orbital representation of the reaction is shown in Figure 3.
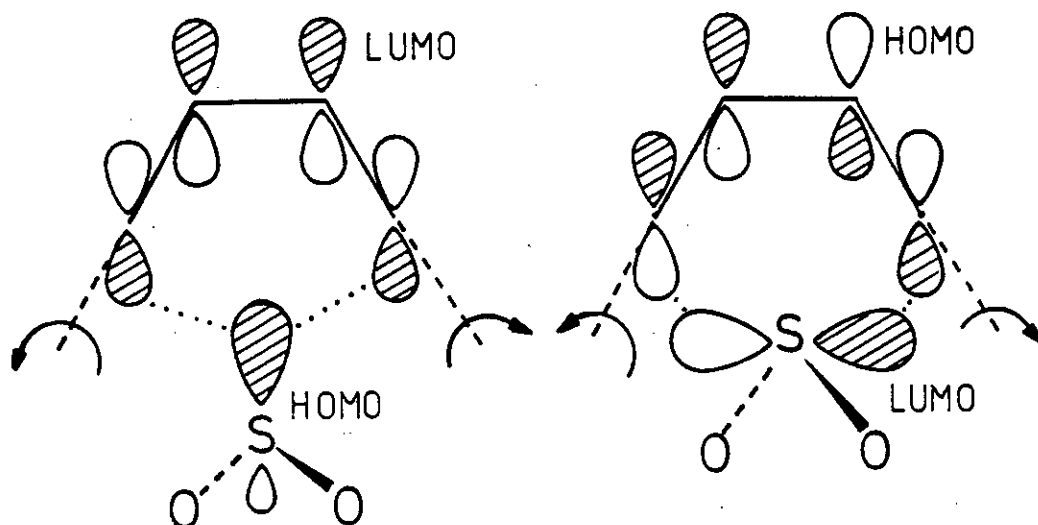
<u>Fig. 3.</u>   The linear approach of SO_2 to butadiene.

The reaction proceeds <u>via</u> an allowed linear pathway described as a $\pi4_s+\omega2_s$ process (or a $\pi2_s+\sigma2_s+\sigma2_s$ cycloreversion).   A point to note is that good overlap of the interacting orbitals requires the terminal carbons on butadiene to rotate in a disrotatory sense.

The concerted framentation of 2, 7-dihydrothiepin 1, 1-dioxide (22) could formally be either a linear or a non-linear cheletropic reaction.[37] Symmetry considerations require that the thermal $\pi6+\omega2$ process be suprafacial, antarafacial.   If the sulphur dioxide is the suprafacial component, it is a $\pi6_a+\omega2_s$ linear cheletropic reaction and the triene must rotate in a conrotatory sense as illustrated in Figure 4a; if the sulphur dioxide is the antarafacial component, it is a $\pi6_s+\omega2_a$ non-linear cheletropic process and the triene must rotate in a disrotatory sense as illustrated in Figure 4b.
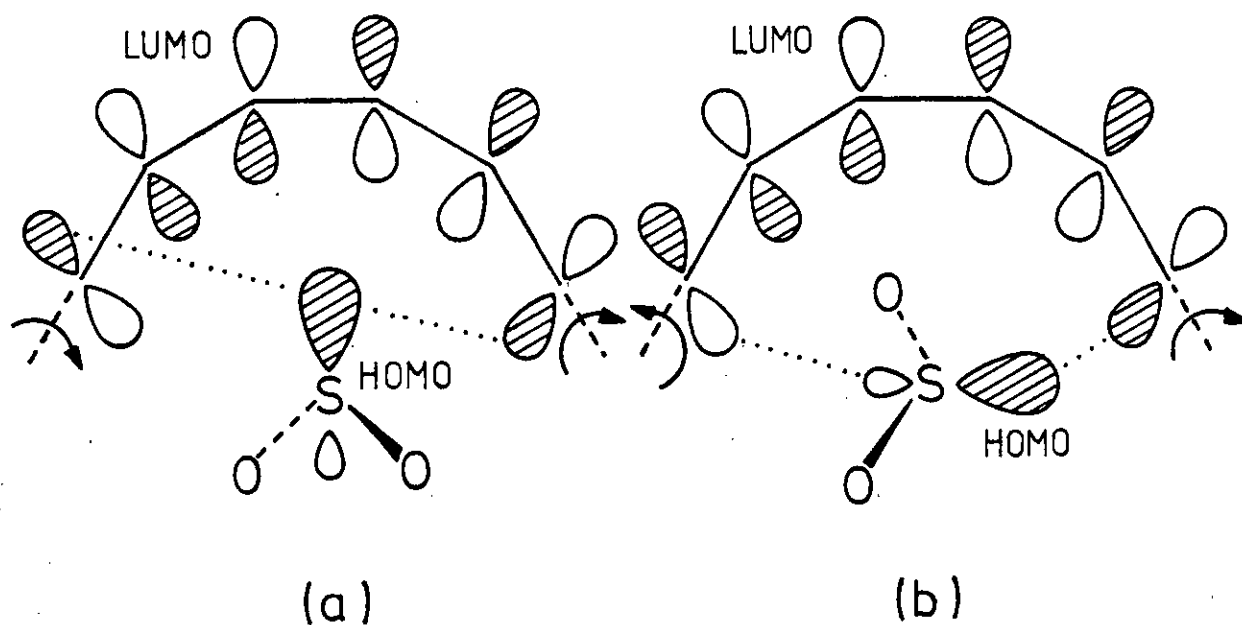
Fig. 4   a) Linear and antarafacial on the triene

b) Non-linear and suprafacial on the triene.

Gilchrist and Storr[37] have summarized the selection rules for

cheletropic reactions as follows:

(a)   Linear cheletropic reactions in which the polyene is a supra-

facial component (i. e. involving distrotatory motion of the terminal

carbons) are allowed for a total of (4n+2) electrons.

(b)   Linear cheletropic reactions in which the polyene is an antara-

facial component (i. e. conrotatory motion of the termini) are allowed

for a total of 4n electrons.   The rules for the non-linear cheletropic

reaction are the reverse of these.

The rules for photochemical extrusion are the reverse of those

for thermal extrusion.

B. 3 Stereochemistry, kinetics and mechanism of sulpholene and

sulpholane extrusion reactions.

This section details the experimental observations which fit the

theory discussed in section B. 2.

The decomposition of the substituted episulphone (23) is

stereospecific and cleanly suprafacial with respect to the alkene (24)

(Scheme 13).[39,40] However a $\pi 2_s + \omega 2_s$ process is disallowed (see
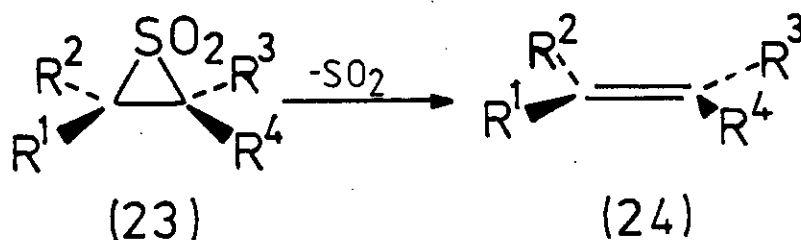
R^1=H, R^2, R^3, R^4= Ar, alkyl or H in various combinations.

Scheme 13

fig. 1) and so if the reaction is to be concerted the sulphur dioxide

must depart in an antarafacial manner (see fig. 2) to give a $\pi 2_s + \omega 2_a$

process. However this is only a rationalization of the observed

stereospecificity, not a proven mechanism.

Mock[39] has suggested that the non-linear reaction path for

episulphone fragmentation (Scheme 14a), can be readily accommodated

by sequential bond cleavage (Scheme 14b). In the two-step mechanism

in order to explain the observed stereospecificity it is necessary and

sufficient that dissociation of the dipolar intermediate be more rapid

than the internal rotation of a bond. It is pertinant to point out that,
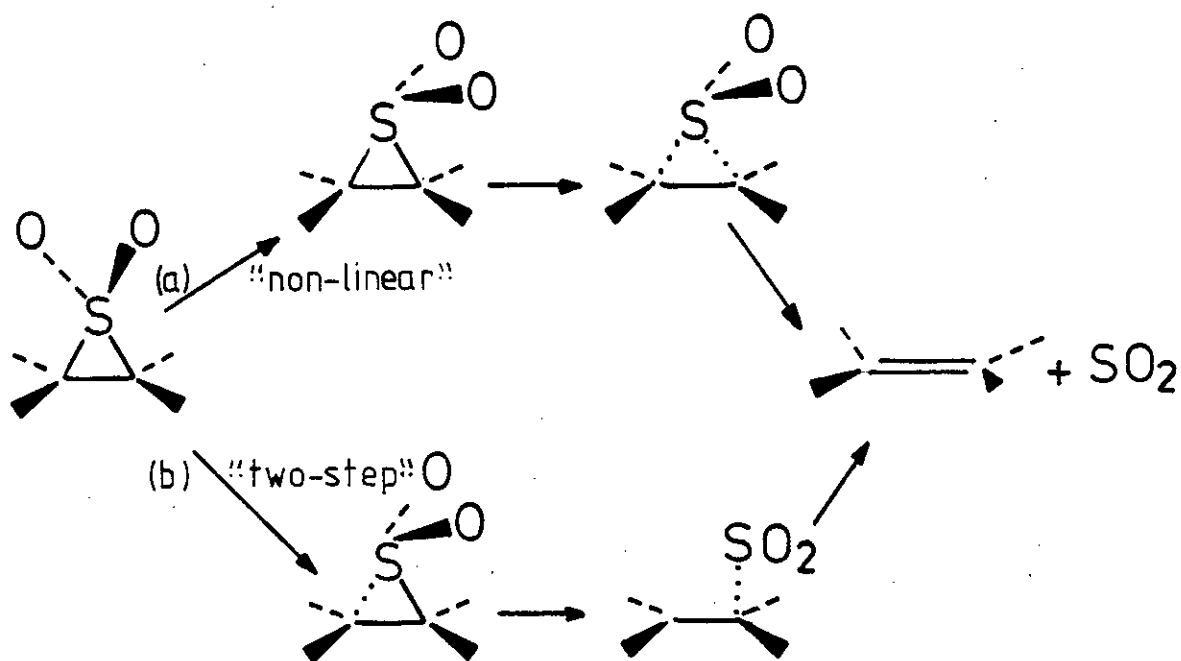
Scheme 14

on more than one occasion, doubts have been expressed[4,41] about

the applicability of the selection rules to episulphone fragmentations.

An alternative mechanism involving ring expansion to a four membered

ring isomer has also been suggested.[5]

Kinetic studies involving episulphone fragmentations are not very

informative since ring strain plays an important part in the rate of the

reaction and thus clouds the effect of orbital symmetry constraints.[4]

The mechanism of episulphone fragmentation is thus still open to question.

The thermal extrusion of sulphur dioxide from substituted 2, 5-

dihydrothiophene 1, 1-dioxides (25) has been extensively investigated[39,42-44]

and shown to be cleanly suprafacial with respect to the incipient diene

(26) (Scheme 15). The reaction has been suggested[39] to proceed via

the transition state (27), a linear concerted process, described as a

(25)　　　　$-SO_2$　　　　(26)
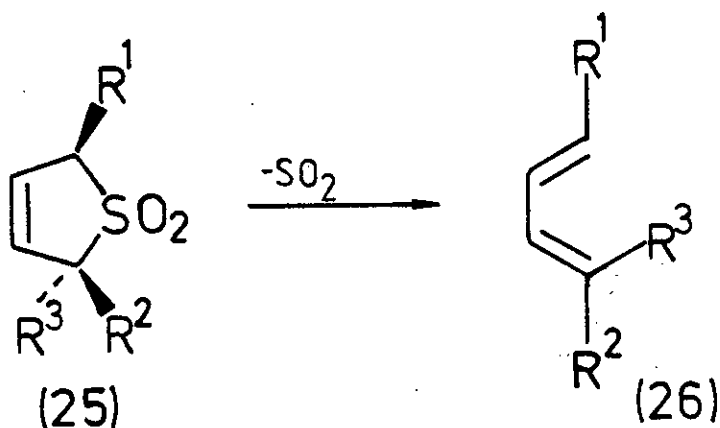
a)　　$R^1, R^2 = CH_3;$　$R^3 = H$　$> 99.9\%$ stereospecific

b)　　$R^1, R^3 = CH_3;$　$R^2 = H$　　　Scheme 15

retro-$[\pi 4_s + \omega 2_s]$ process in keeping with the orbital symmetry predictions

previously discussed in section B. 2.　However Mock[39] has alluded to

the fact that this is a "nonrisky orbital symmetry prediction" as other

(27)
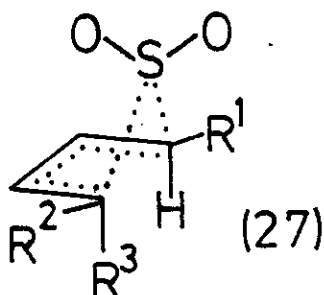
possible transition states which have been suggested suffer from un-

favourable ring strain considerations.　Thus once again the conclusion

that one is getting stereoelectronic control is somewhat tentative.

From kinetic studies[45-48] it has been concluded that substituents

in the parent sulphone do not affect the rate as much as might be

expected for ionic or radical mechanisms.　Ašperger et al.[46] have

examined secondary deuterium isotope effect and the primary [34]S

isotope effect on the kinetics of thermal decomposition of substituted

butadiene sulphones.　The results obtained give support to a concerted

mechanism.

Recently Hogeveen and co-workers[49] have reported that

addition of sulphur dioxide to the diene (28) at or below room temperature

led to the formation of the sulphinic ester (29) which immediately

rearranged preferentially to an aromatic ester (30) (90%) and to the

sulphone (31) (10%) (Scheme 16). The thermal rearrangement to the

sulphone was shown to proceed via a retro-Diels-Alder reaction. Thus

five-membered ring sulphones and six-membered ring sulphinate esters

from the cycloaddition of sulphur dioxide to 1,3-dienes may represent

the thermodynamically and kinetically controlled products respectively.

Mock et al.[39,50-52] have also investigated the reversible

formation of 2,7-dihydrothiepin 1,1-dioxide from SO_2 and cis-1,3,5-

hexatriene. In contrast to the five-membered ring analogue, decom-

position of (32) preferentially proceeded antarafacially with respect

to the triene fragment (33) (Scheme 17), the stereochemistry of which

is in accord with the reaction pathway being a linear concerted process;

this signifies a retro-$[\pi 6_a + \omega 2_s]$ process, involving a transition state

(34).[39]

SO₂ + (28) ≪20°C → (29)

(30) 90% 20°C

(28)

(31) 10% 20°C

Scheme 16

(32)   (33)
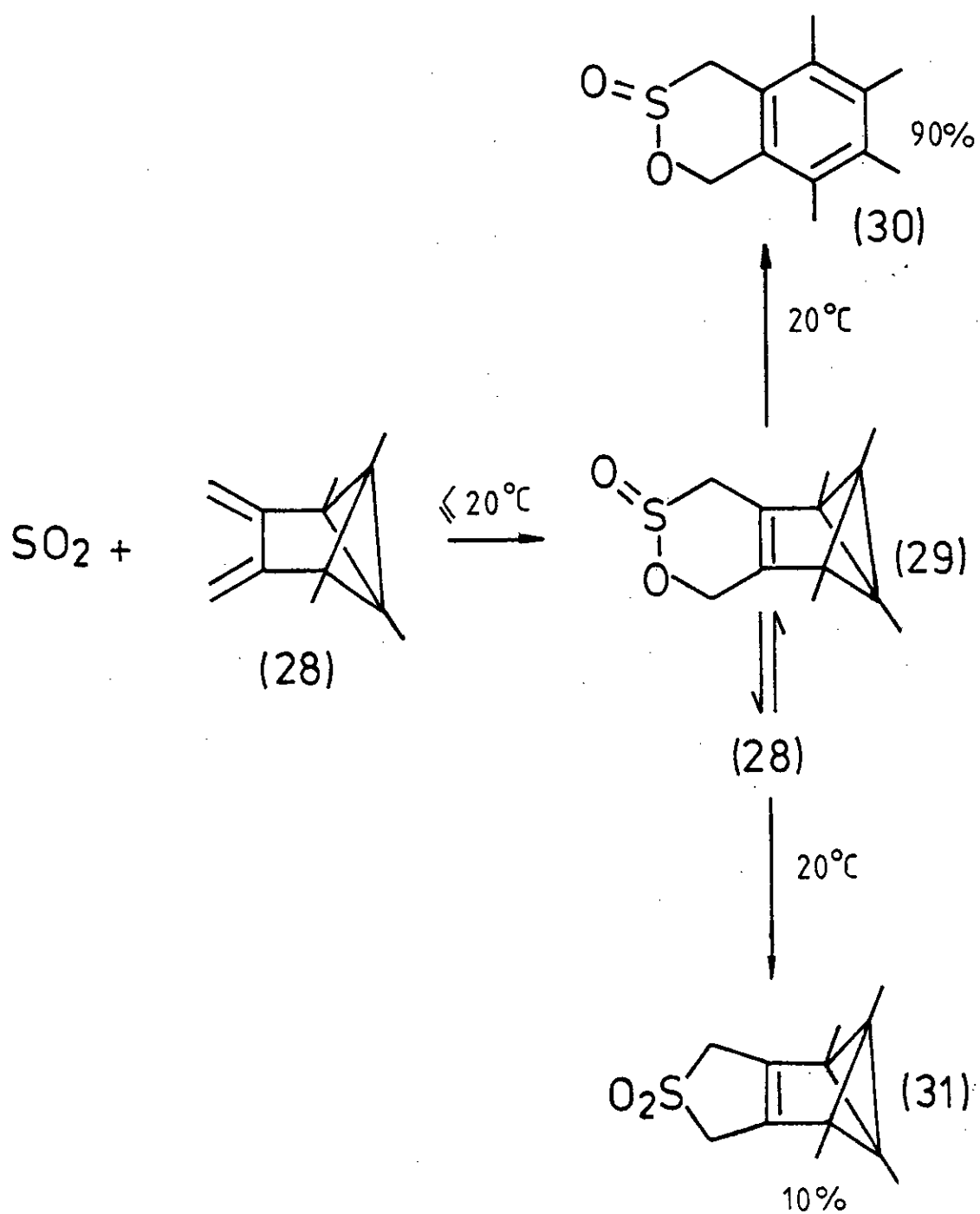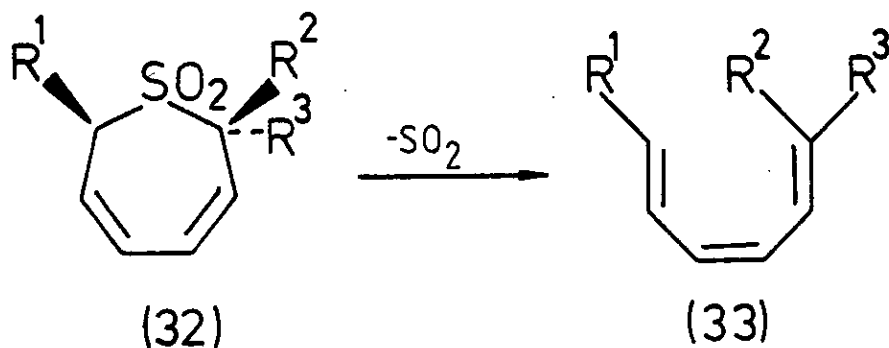
a) R^1, $R^2 = CH_3$; $R^3 = H$

> 97% stereospecific

b) R^1, $R^3 = CH_3$; $R^2 = H$

Scheme 17

Notwithstanding these conclusions it is of interest to note that an analysis of steric considerations[39,51] shows that bond-angle deformations

(34)
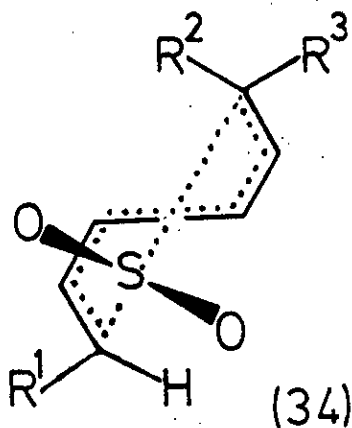
and non-bonded interactions are sufficient to explain the observed stereospecificities without the need to invoke orbital symmetry constraints.

Interestingly the sulpholenes (32) could not be prepared by addition of sulphur dioxide to the appropriately substituted triene.[51] A thorough investigation[52] of this reaction further established that in some cases 1,4-addition of sulphur dioxide could compete effectively with 1,6-addition, depending on the nature of the triene. A typical example is provided by the reaction of SO_2 with the hydrocarbon (35) to give the

sulphone (36) (Scheme 18).[52]

(35)   (36)
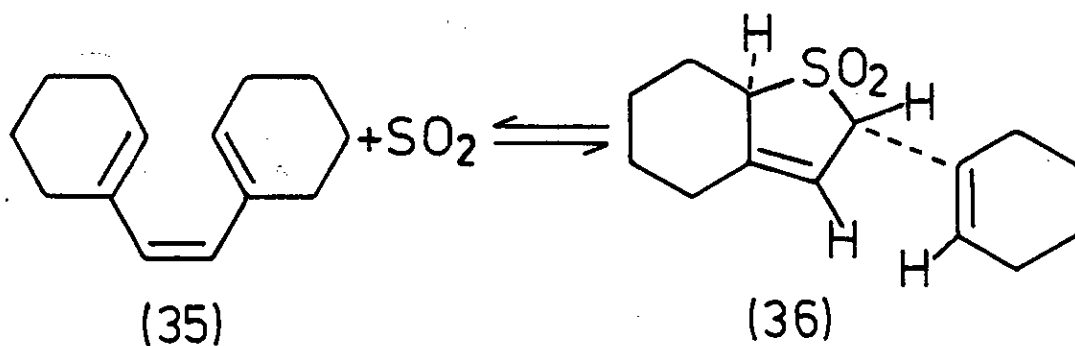
Scheme 18

Kinetic data for the extrusion of sulphur dioxide from the parent

compound *viz.* 2, 7-dihydrothiepin 1, 1-dioxide (32, $R^1 R^2, R^3 = H$)[45]

showed that the rate of decomposition was almost identical to that for

butadiene sulphone. This observation may offer an explanation as to

why the two modes of cycloaddition can effectively compete with each

other.

Another classic example of 1, 4-addition of sulphur dioxide is the

addition of SO_2 to 1, 3, 5-cyclooctatriene (37) to give the sulphone (38)

(Scheme 19).[45, 52, 53] In this case antarafacial addition to the triene

is geometrically impossible and the alternative $\pi 6_s + \omega 2_a$ non-linear

addition to the triene does not compete with concerted $\pi 4_s + \omega 2_s$ linear

cheletropic addition to the diene component. Mock[53] has converted

(38) into (40) the formal 1, 6-adduct of 1, 3, 5-cyclooctatriene and

sulphur dioxide by the indirect route shown in Scheme 19.

The geometry of (40) is such that the usual retro-$[\pi 6_a + \omega 2_s]$

fragmentation process is impossible. This means that the elimination

if concerted would have to be a non-linear cheletropic process *i. e.*

retro-$[\pi 6_s + \omega 2_a]$. The extreme unfavourability of the retro-$[\pi 6_s + \omega 2_a]$
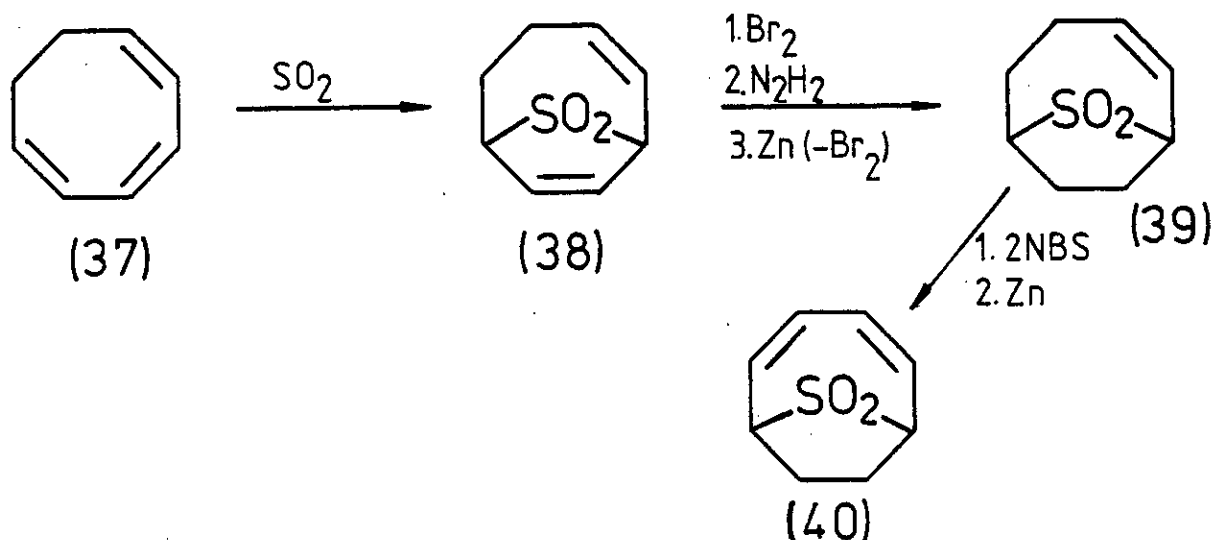
Scheme 19

process is illustrated by the fact that at $180°C$ (40) undergoes fragmentation

some 60,000 times more slowly than does (38) for which an allowed

retro-$[\pi 4_s + \omega 2_s]$ process is possible. However it has been suggested

that other paths could operate[45] and the mechanism of fragmentation

of (40) remains unclear.

Upon thermolysis (41a) yields sulphur dioxide and 1,4-pentadiene

(42a) in a rapid and clean reaction, similarly (41b) gave only sulphur

dioxide and trans, trans-2,5-heptadiene (Scheme 20).[54] Thus the

reaction is entirely stereospecific and can be classified as a $\sigma 2_s + \sigma 2_s + \sigma 2_s$

process. The rate of dissociation of (41a) at $125°C$ is identical to the

rate of dissociation of butadiene sulphone under the same conditions

implying a coupling of the C-S bond scission with opening of the cyclo-

propane ring.

(41) Δ, -SO₂ (42)
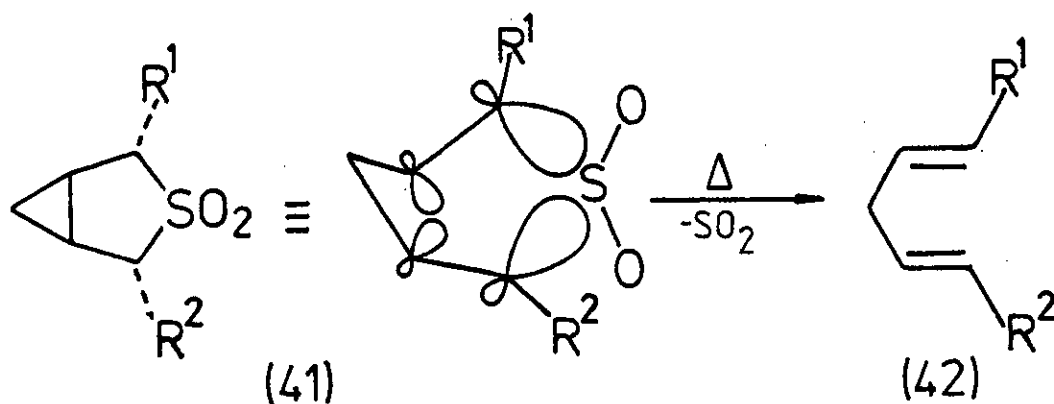
a) $R^1, R^2 = H$

b) $R^1, R^2 = CH_3$

c) $R^1, R^2 = -CH_2CH_2CH_2-$

Scheme 20

This conclusion is supported by the stability of the tricyclic

sulphone (41c) under similar conditions.   This inertness can be

readily understood when one considers that fragmentation of (41c) in

a manner directly analogous to (41a) or (41b) would produce the

impossibly strained trans, trans-1,4-cycloheptadiene.

Finally it is of interest to note that fragmentation of sulpholanes

(tetrahydrothiophene 1,1-dioxides)[55] give rise to stereoisomeric

mixtures of alkenes indicating that multistep mechanisms are operating

in these cases.

B.4   Synthetic utility of the sulpholene reaction.

The reaction of 1,3-dienes with sulphur dioxide was first

reported in 1914 by de Bruin,[56] who reacted isoprene (43) with liquid

sulphur dioxide at room temperature and obtained a pure crystalline

monoadduct to which he assigned the structure (44) (Scheme 21).

Today a wide variety of synthetic processes employ the reaction and

(43)   +SO₂ ⟶   (44)
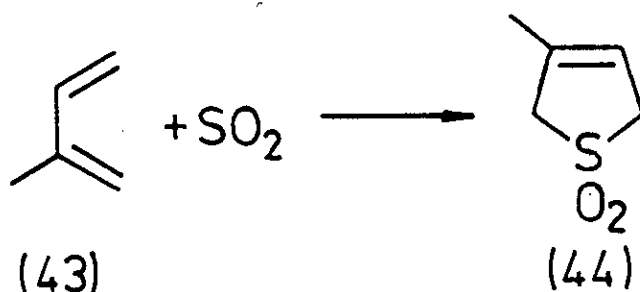
<u>Scheme 21</u>

its reverse.

B utadiene sulphone (21) rapidly decomposes on heating above
125°C and can serve as an excellent small scale laboratory source of
buta-1, 3-diene.[57]   For example it reacts with benzyne (45) to form
1, 4-dihydronaphthalene (46) (Scheme 22).[58]

(21)   (45)

(46)
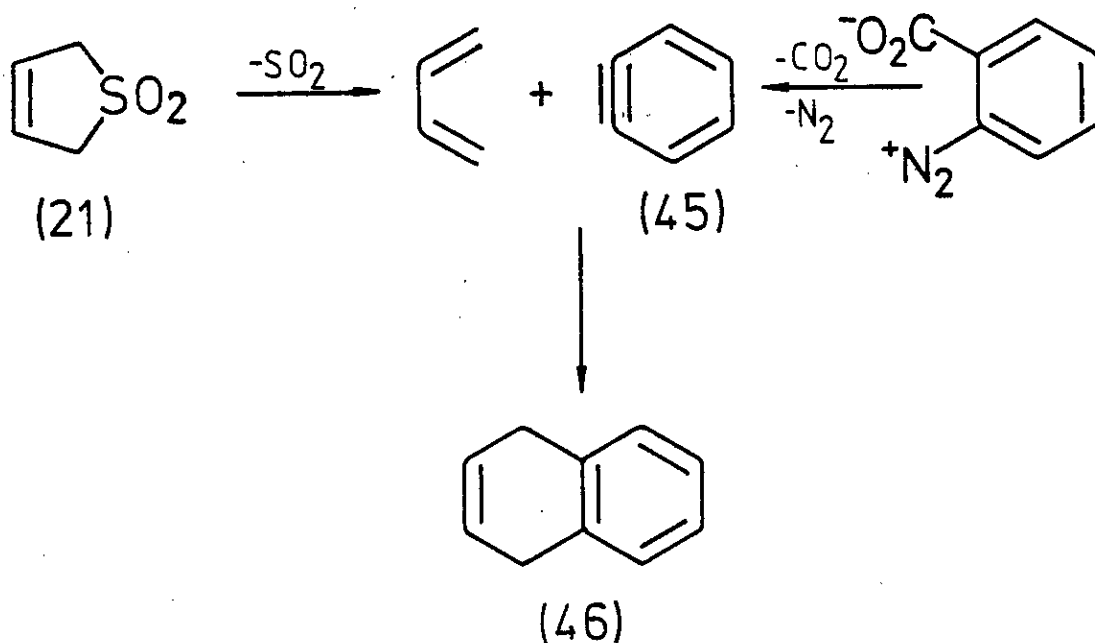
<u>Scheme 22</u>

Since the "sulpholene reaction" is almost always reversible
sulpholenes are useful intermediates for the modification, purification
and storage of dienes.[59]   In general addition of sulphur dioxide to
1, 3-dienes substituted in the 1-position is inhibited.   By comparison
the addition to 2-substituted dienes is enhanced and it is this difference
in reactivity which is exploited in using the reaction as a method of
separating diene mixtures.

The main limitation of using sulpholenes as a general synthesis

of dienes is that sulpholenes are usually prepared by the reverse of this

reaction. This limitation has been largely overcome by the alternative

synthesis of 2, 5-dihydrothiephenes (50) by McIntosh et al.[60] from the

reaction of α-mercapto ketones (47) with vinyl phosphonium salts (48)

the reaction proceeding via the intermediate (49) (Scheme 23). Com-

pounds of the type (50) can be readily oxidized to sulphones (51) which

can readily be thermolysed to give dienes (52).

An elegant example of the synthetic utility of the sulpholene

reaction has been provided by Nesbitt et al.,[61] who separated cis and

trans isomers of the red bullworm moth sex pheromone by selective

reaction with sulphur dioxide below $0°C$ (Scheme 24). Since only the

trans-isomer reacted, the adduct (53) could be readily separated from

the cis-isomer. Subsequent thermolysis of (53) then gave pure trans-

diene (54).

$R = (CH_2)_8 OAc$
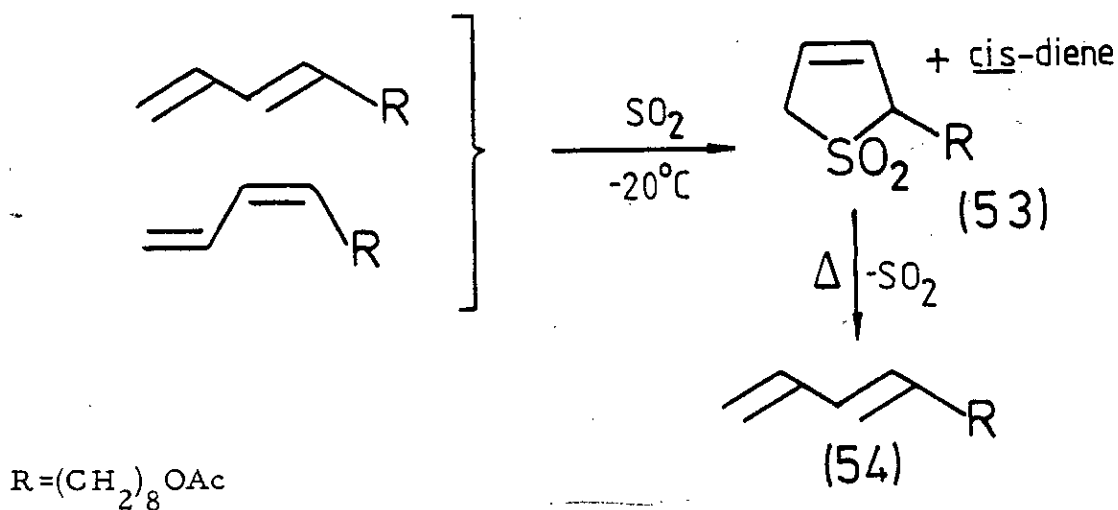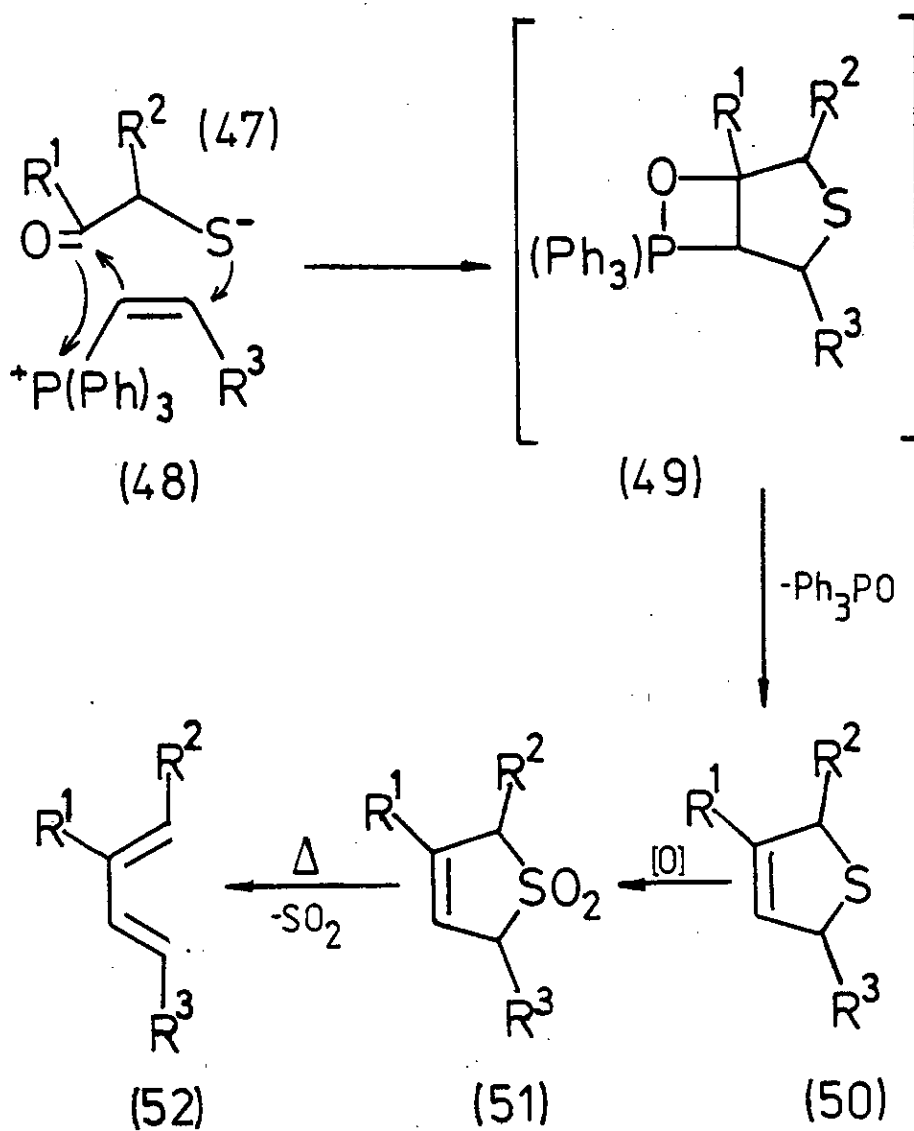
Scheme 24

$R^1 = Me$

$R^2, R^3, = H$ or Me

Scheme 23

A synthesis which takes advantage of the ability of sulphones to
readily exchange their α-hydrogens for deuterium atoms is the
preparation of deuteriobutadienes (55) (Scheme 25).[62]
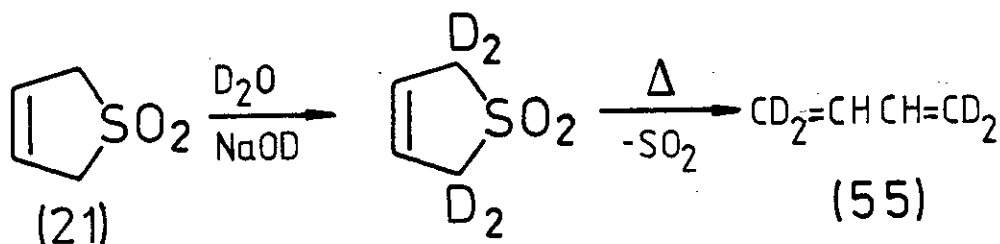
Scheme 25

A synthesis which takes advantage of the unreactivity of the
α-position of sulphones in free radical halogenations is the preparation
of 2-bromomethyl-1,3-butadiene (57) as shown in Scheme 26. Bromina-
tion of the methyl group of the sulpholene derivative (44) by N-bromo-
succinimide gave (56) thermolysis of which gave the modified diene
(57) in good yield (Scheme 26).[63] The complex mixture of bromo
derivatives expected from direct bromination of isoprene (43) was
thus avoided.
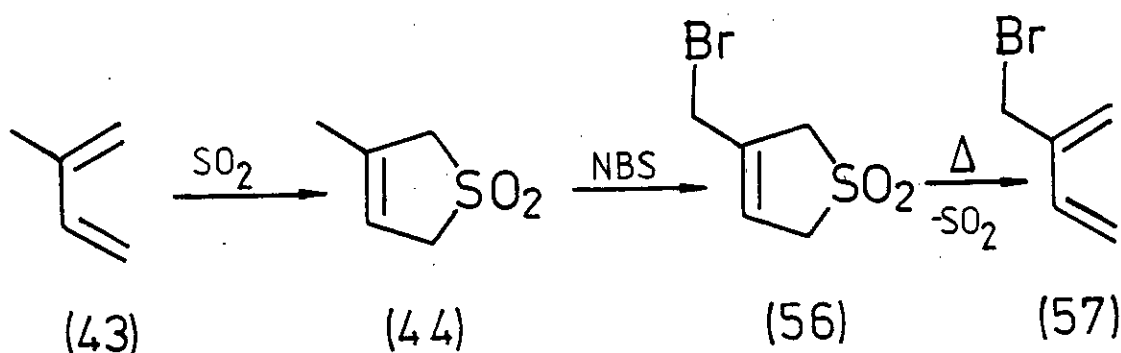
Scheme 26

Meyers et al.[64] have reported that the method used for the
synthesis of homoconjugated dienes (42) is capable of extension to the
preparation of divinyl ethers (59) and divinyl carbamates (61) via the

heterocyclic intermediates (58) and (60) (Scheme 27).
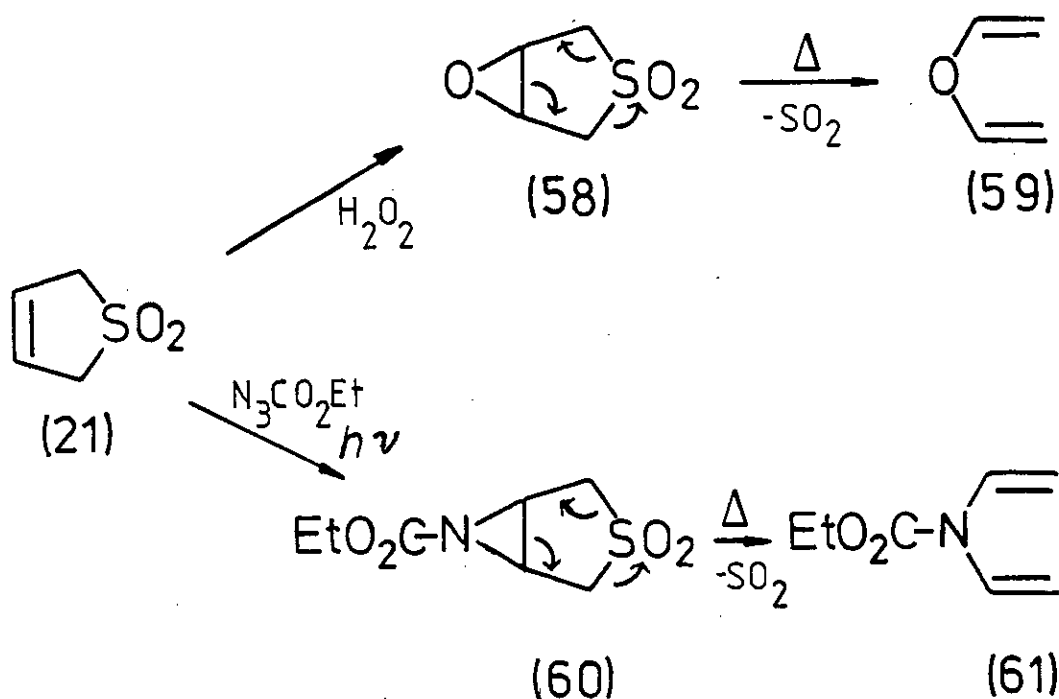
Scheme 27

The sulpholene reaction is usually carried out in the 80-150°C

temperature range. However in the case of mono or bicyclic sulphones

the temperature required may be higher and this can lead to a rearrange-

ment of the products.[34,65] This problem has been circumvented by Gaoni

who has reported,[66] that sulphones undergo elimination of sulphur

dioxide when treated with lithium aluminium hydride in ether to give

dienes in good yields. The mechanism of this reaction has not yet

been fully investigated.

B.5 Photochemistry.

The photochemical extrusion of sulphur dioxide from sulpholenes

is much less well studied than is the thermal reaction. Bordwell[67] has

reported that ultraviolet light induces decomposition of phenyl-substituted

episulphones, however the experiments were not rigorous.

Saltiel and Metts[68] have studied the photolysis of <u>cis</u> and <u>trans</u> dimethylsulpholene (25a and b) and whilst the reaction was not totally stereospecific, a preference for the antarafacial mode with respect to the diene was observed.

C.   The Cope and Claisen Rearrangements.

C. 1   Introduction.

The Cope and Claisen rearrangements both named after their

discoverers[69, 70] have been extensively studied and exploited for their

synthetic value.   The former, although less valuable than the latter

in general is more relevant to the present discussion.   Excellent

reviews of both reactions are available[71, 72] and thus attention will

focus on example of direct relevance to the present discussion.

The Cope rearrangement is typified by the thermal rearrangement

of biallyl compounds (62) to isomeric biallyl compounds (64) via the

transition state (63) (Scheme 28).[73]   Similarly an example of a typical

(62)   (63)   (64)

$X=C_6H_5$; CN; CO_2CH_3
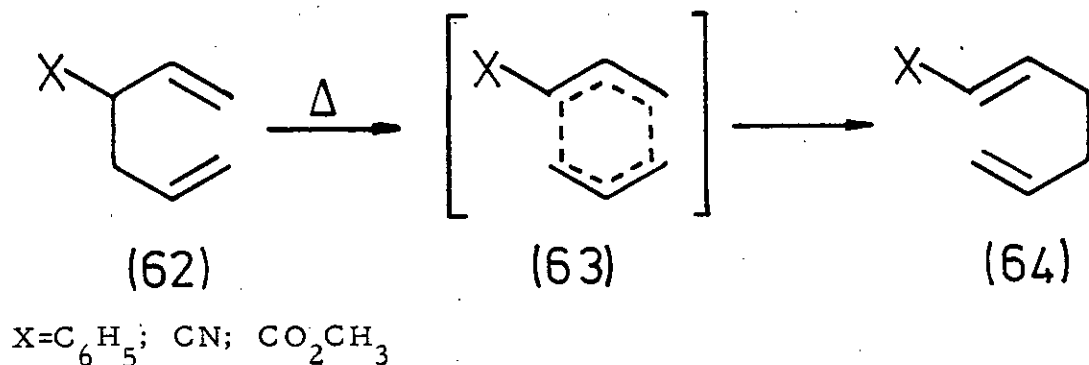
Scheme 28

Claisen rearrangement is the thermal rearrangement of a vinyl allyl

ether (65) to the corresponding homoallylic carbonyl compound (66)

(Scheme 29).

(65)   (66)
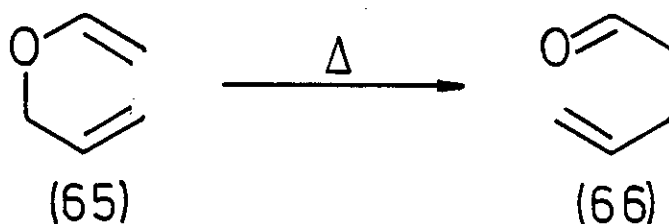
Scheme 29

These transformations have been classified as [3, 3] sigmatropic rearrangements by Woodward and Hoffmann.[21]

C. 2 Mechanism and stereochemistry of the Cope reaction.

Various geometries are possible for the transition state (63), which can be classified according to whether each of the allyl systems interacts with the lobes of the other system on the same side (suprafacially) or on opposite sides (antarafacially).   There are two possible geometries for the suprafacial, suprafacial transition states viz. the four-centre "chair-like" overlap (67) or the six centre "boat-like" overlap (68) typified by the 'degenerate' Cope rearrangement of hexa-1, 5-diene as shown (Scheme 30).[74]

(67)

(68)
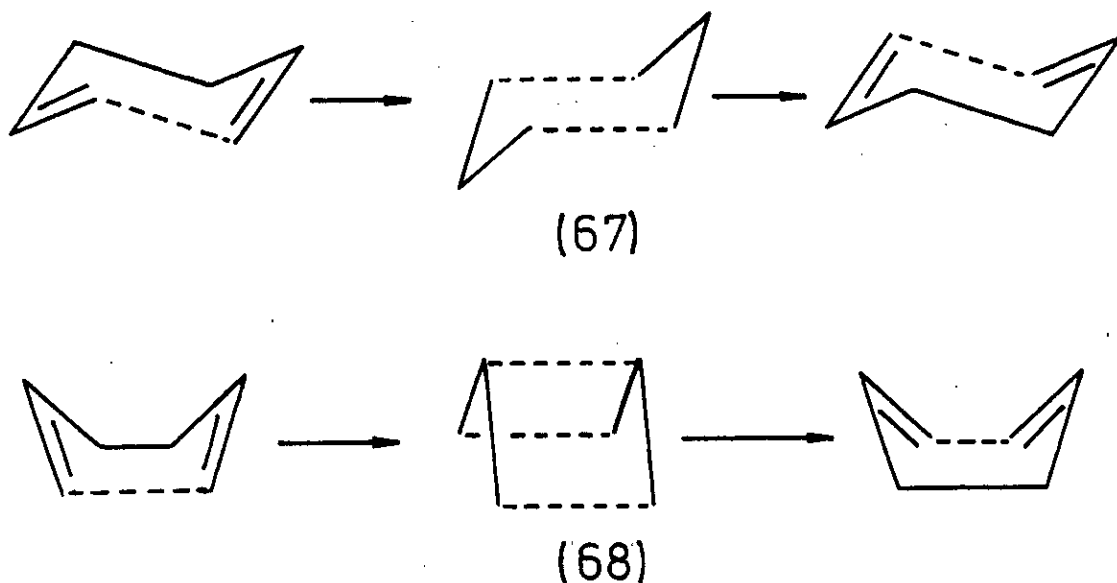
Scheme 30

The chair-like arrangement (67) has been deduced to be more favourable than the "boat-like" arrangement (68) by about 25 kJ mol^{-1}. This deduction came from the work of Doering and Roth[75] in which they observed that meso-3, 4-dimethyl-1, 5-hexadiene (69) rearranged

almost exclusively (99.7%) to <u>cis, trans</u>-2,4-octadiene (70) (Scheme 31).

This stereochemistry is consistent only with a chair conformation for

the transition state: as a boat conformation would give either <u>cis, cis</u>

or <u>trans, trans</u>-octadiene.
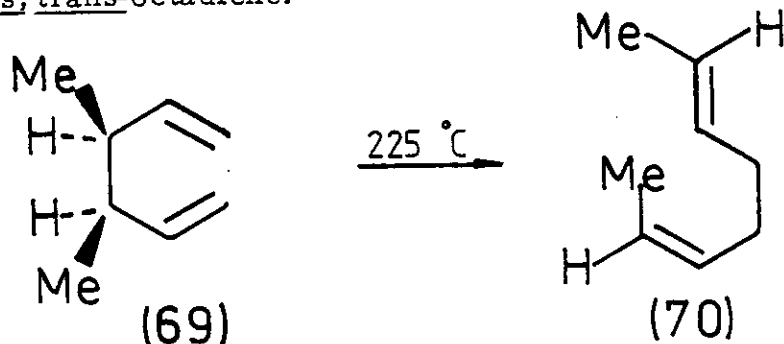
Scheme 31

The high stereospecificity and the stereopreference for the

"chair-like" transition state has been further confirmed by the work

of Hill and Gilman.[76] They reported that the optically active hepta-

1,5-diene (71) Cope rearranged to give a mixture of two other hepta-

1,5-dienes (72) and (73) (Scheme 32). In this case the products
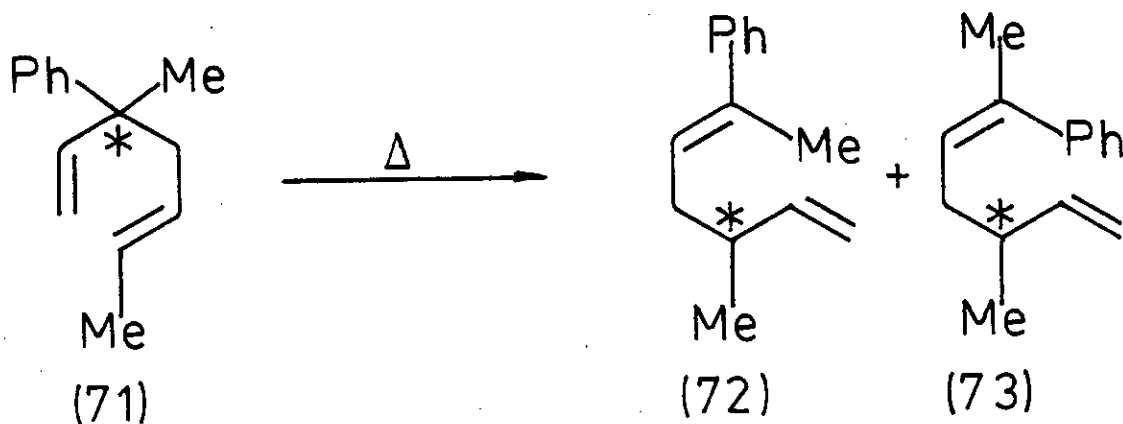
Scheme 32

possess opposite configurations not only at the double bonds but also

at the centres of asymmetry.

Various theoretical interpretations of the rearrangements based

on a variety of molecular orbital approaches have been advanced.[21,77-79]

These approaches vary in elegance and complexity but they do predict

that there should be a stereopreference for the "chair-like" transition

state.

One of the simpler ways of arriving at this conclusion is to

consider the transition states (67) and (68) as arising from the hypothetical

processes in which two allyl radicals approach each other from infinity,

in parallel planes, orientated with respect to each other in a "chair-like"

or in a "boat-like" fashion.

The relevant orbital interactions for the allowed "chair-like"

and "boat" transition states are illustrated in Fig. 5a and Fig. 5b

respectively.   As will be noted the non-bonding SOMO (singly occupied
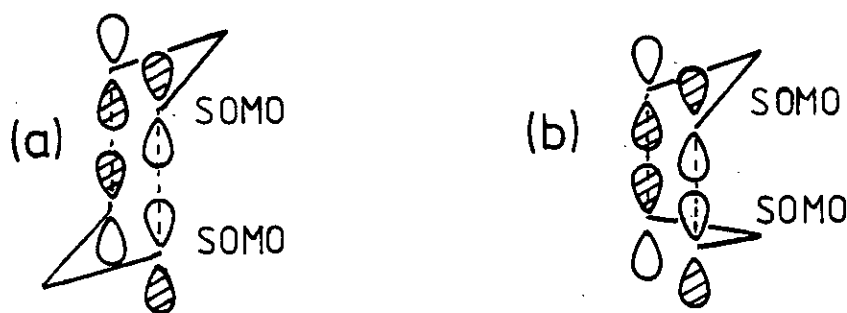
Fig. 5   a)   Chair transition state (suprafacial, suprafacial)

b)   Boat transition state (suprafacial, suprafacial)

molecular orbital)-SOMO interaction has nothing to do with this

selectivity since these MO's have a node at the central carbon atom.

In order to explain the preference for the "chair-form" transition

state one has to consider the NHO (next highest occupied) and NLU

(next lowest unoccupied) orbitals, which have interactions between

the central p-lobes of the two allyl systems in the "boat-form" (see

fig. 6b) but not in the "chair-form" (see fig 6a).[77]   It should be

emphasised that the interaction is not all that great and as examples will

show the "boat" transition state is often encountered in practice.
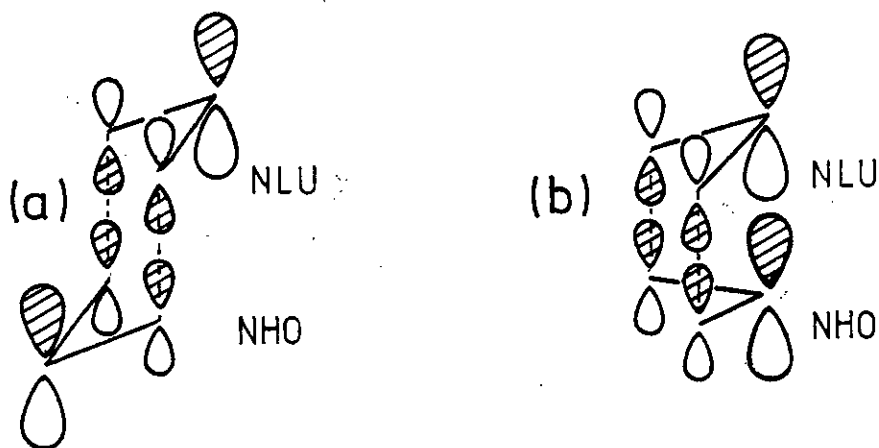
F ig. 6 a) N HO-NLU interactions in chair transition state

b) NHO-NLU interaction in boat transition state

It is pertinent to point out that the full details of the mechanism

of the Cope rearrangement have not yet been fully resolved as is

testified by fairly recent publications.[80-82]

Finally it should be mentioned that there is a third possible

allowed transition state viz. an antarafacial-antarafacial interaction

of the diallyl species. Although this is not usually competitive with

the other transition states one example does exist viz. the conversion

of (74) to (75) (Scheme 33).[83] However attempts to observe the same

(74)   (75)
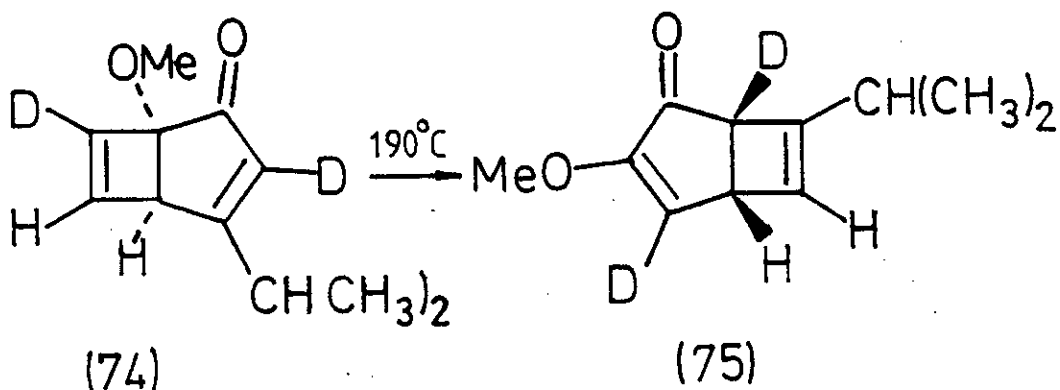
Scheme 33

mechanism operating for the rearrangement of the hydrocarbon (76)

failed (Scheme 34).[84]
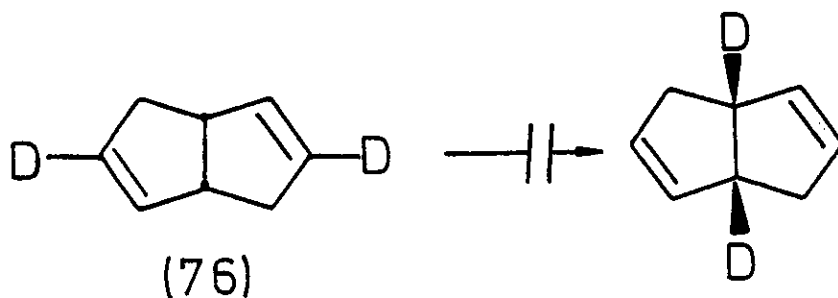
Scheme 34

C.3 Cope rearrangement of cis-1,2-divinylcycloalkenes and their

analogues.

The general Cope rearrangement for cis-1,2-divinylcycloalkanes

can be represented by the conversion of (77) to (79) via the transition

state (78) (Scheme 35). It should be noted that in this case the chair

(77)   (78)   (79)
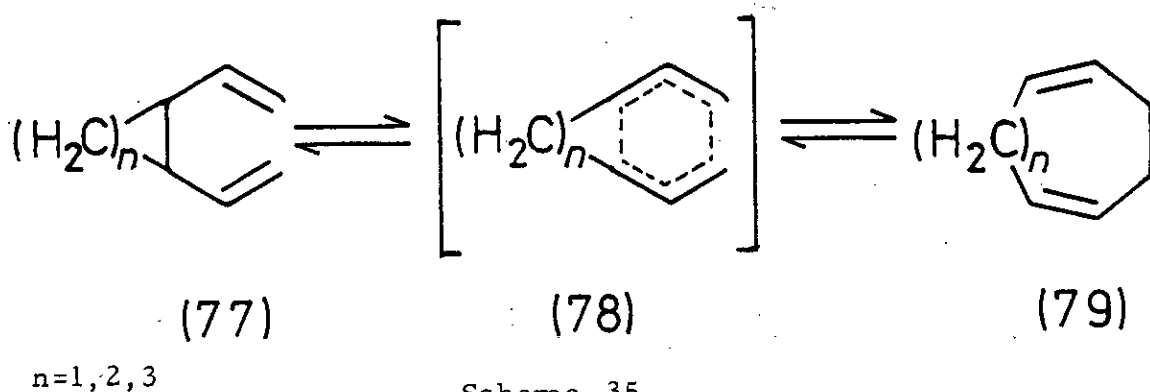
n=1,2,3   Scheme 35

transition state is sterically impossible and so the reaction must go

via a boat transition state.

The first member of this series cis-1,2-divinylcyclopropane (80)

(n=1) is interesting in that it undergoes the Cope rearrangement to give

cyclohepta-1,4-diene (81) so readily that for many years this precluded

its preparation (Scheme 36).[85,86] Success was finally achieved by

Brown et al.[87] and more recently Schneider and Rau[88] have reported
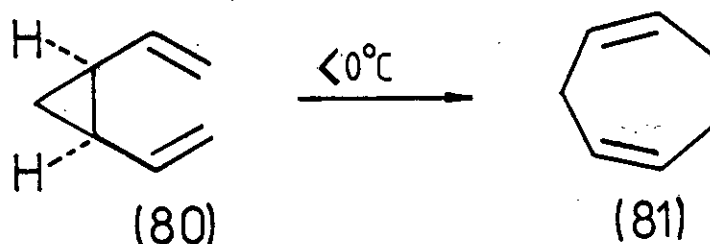
Scheme 36

a general and convenient synthesis for cis-1, 2-dialkenylcyclopropanes.

The ease with which (80) undergoes the Cope reaction has been attributed to release of ring strain in the cyclopropane ring. However Schneider and Rau[88] have reported that methyl substituents on terminal carbons of the vinyl groups have a dramatic effect on the rate of the isomerization. Indeed in the case of the hydrocarbon (82) there was no Cope rearrangement only cis-trans isomerization.

The thermal rearrangements of the heteroanalogues of divinyl-cyclopropane (83) to give 4, 5-dihydroheteroepins (84) have also been studied (Scheme 37). The Cope rearrangements of cis-2, 3-divinyl-
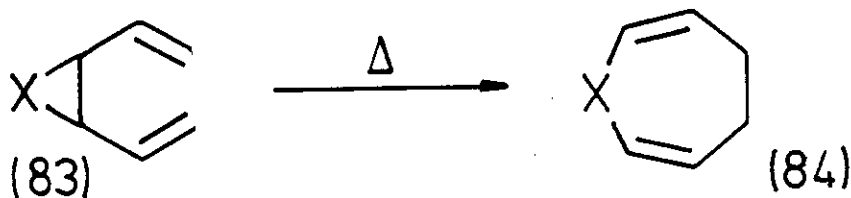
X= O, NH, S, SO$_2$

Scheme 37

oxirane (X=O),[89] cis-2, 3-divinylaziridine (X=NH)[90] and cis-2, 3-divinyl-thiirane (X=S)[91] have been investigated in detail. The intermediacy of cis-2, 3-divinylthiirane 1, 1-dioxides (X=SO$_2$)[92] in the synthesis of 4, 5-dihydrothiepin 1, 1-dioxides has also been reported but they have not been isolated or characterized.

The temperature necessary to induce the ring expansion of (83) to (84) increases in the order carbon, nitrogen, oxygen and sulphur. In the case of cis-2, 3-divinylthiirane[91] sulphur extrusion, to give hexatrienes, competes with the Cope rearrangement.

Rearrangement of the corresponding trans-divinyl derivatives has also been studied[89c, 90b, 91] and they require more vigorous conditions to rearrange apparently via diradical processes or by isomerization to the more labile cis-isomers.

Additional interest in the rearrangement of divinylcyclopropanes has arisen from the suggestion that they are possible precursors in the biosynthesis of natural products from brown algae.[93]

The second member of the series viz. cis-1, 2-divinylcyclobutane (85) rearranges similarly to give cis, cis-cycloocta-1, 5-diene (86) (Scheme 38), first reported by Vogel[94] and later more fully investigated

Scheme 38
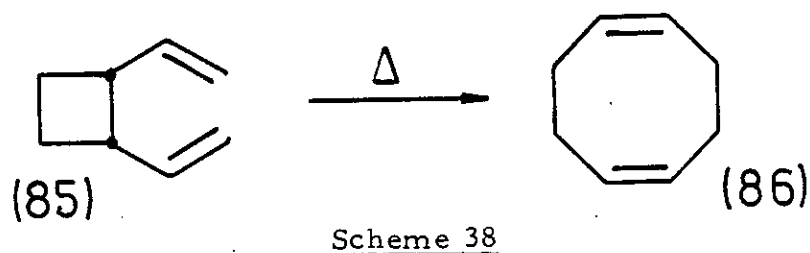
by others.[95, 96] The fact that the rearrangement (85) to (86) requires more vigorous conditions than for cis-1, 2-divinylcyclopropane has been suggested to be due to the lesser ring strain in the cyclobutane ring.[97] Also it has been found by Berson and Dervan[96] that substituents on the terminal carbons of the vinyl groups retard the rearrangement.

In contrast to the small strained ring (n=1, 2) cis-1, 2-divinylcycloalkanes the position of the equilibrium for the medium ring systems (n=3, 4, 5) is determined more by the strain energy of the Cope

rearranged product <u>viz.</u> the cyclic 1,5-hexadiene systems (79)

(Scheme 35), than by the strain energy of the smaller rings.

Vogel and co-workers[98] have reported that <u>cis, cis</u>-1,5-cyclo-

nonadiene (87) and <u>cis</u>-1,2-divinyl cyclopentane (88) equilibrate at $220^{\circ}C$

to form a mixture in which (88) is strongly favoured (Scheme 39).

5%   (87)   95%

$220^{\circ}C$

(88)
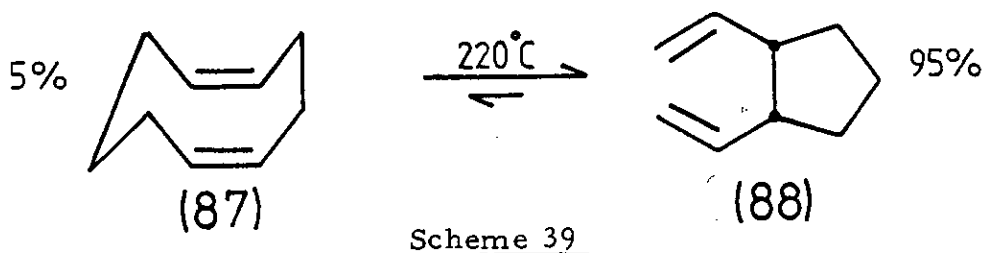
Scheme 39

Similarly, <u>cis, trans</u>-1,5-cyclononadiene (89), which is more strained

than (87), isomerizes to (88) when heated in the gas phase at $130^{\circ}C$

(Scheme 40).   The first of these reactions, <u>i.e.</u> (87) to (88), proceeds

<u>via</u> the "boat" transition state while the latter goes <u>via</u> the "chair"

(89)   130°C   (88)

Scheme 40
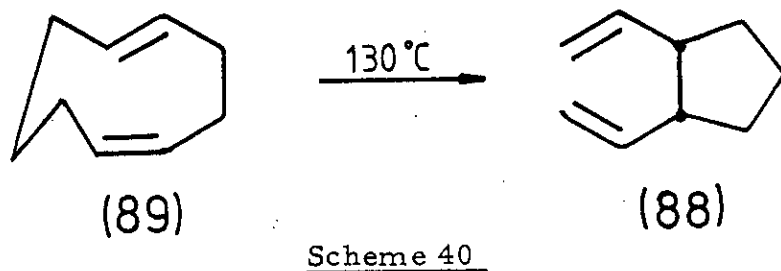
transition state.   It is known[97] that at temperatures above $300^{\circ}C$ (88)

undergoes reversible <u>cis-trans</u>-isomerization.

The situation for the next higher homolog (n=4) <u>viz.</u> 1,5-cyclo-

decadienes is similar to that just described for the 1,5-cyclononadienes.

Thus <u>cis, trans</u>-1,5-cyclodecadiene (90) isomerizes quantitatively at

$150^{\circ}C$ to <u>cis</u>-1,2-divinylcyclohexane (91) (Scheme 41) <u>via</u> a "chair"

transition state.[99]   Similarly <u>trans, trans</u>-1,5-cyclodecadiene (92)

(90)   150°C→   (91)
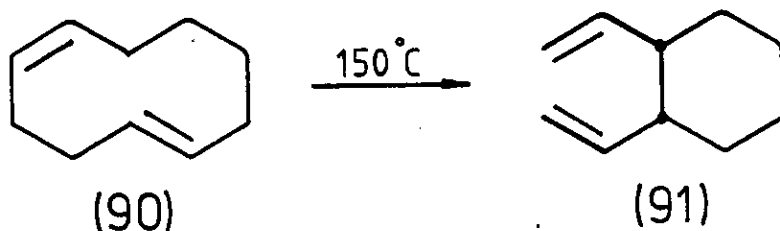
Scheme 41

isomerizes completely, _via_ a "chair" transition state to give _trans_-1,2-divinylcyclohexane (93) (Scheme 42).[100]   This reaction has importance

(92)   70°C→   (93)

Scheme 42

in the field of natural products.[71]

An example of the rearrangement of a yet higher homolog (n=5) is provided by Subba Rao _et al._[101]   Thus (94) is readily converted into (95) (Scheme 43) which as will be noted contains the _trans_-divinyl system.

(94)   160°C→   (95)
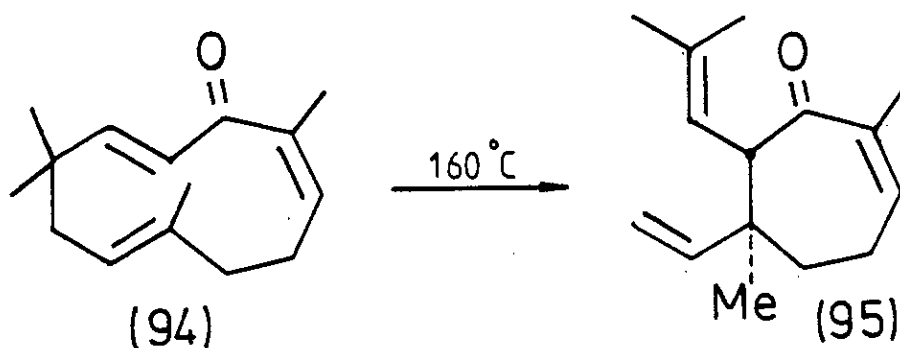
Scheme 43

The thermal rearrangement of _trans_ and _cis_-5,6-divinyl-_cis_-cyclooctenes (96) and (98) has also been studied.[102]   It has been found that the _trans_-isomer (96) gives rise to _trans_-1, _trans_-5, _cis_-9-cyclo-dodecatriene (97) whereas the _cis_-isomer (98) yields _trans_-1, _cis_-5, -_cis_-9-cyclododecatriene (99) (Scheme 44).   Both these processes have been attributed to Cope rearrangements involving "chair" transition states.
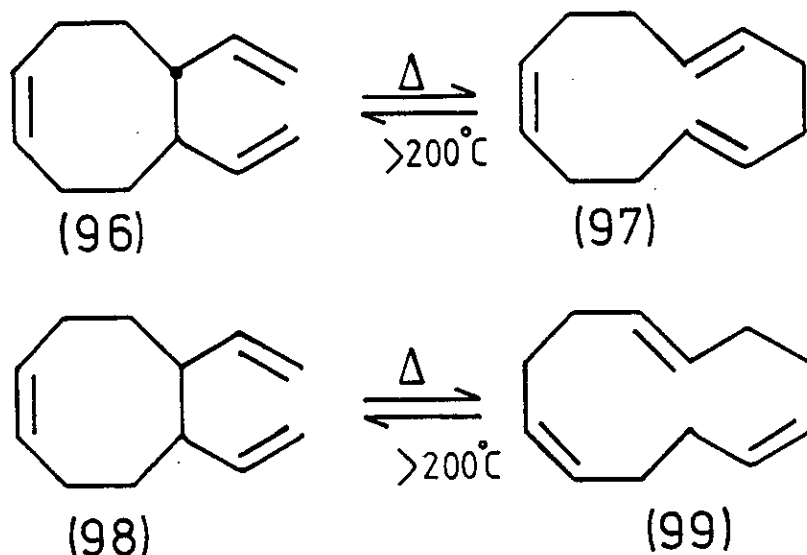
Scheme 44

Thus it would appear that a cross-over point has been reached (n=6) where the strain energy incurred by incorporation of the 1, 5-hexadiene system in a cyclic product does not preclude the reaction taking place.

Finally it should be mentioned that there are several systems which undergo Cope rearrangement very readily and in which the products have the same structure as the starting material. The best example of multiple degeneracy is the molecule tricyclo[3. 3. 2. 0$^{4, 6}$]-deca-2, 7, 9-triene (100) better known as bullvalene. Doering and Roth[103] predicted that this system to be capable of a 1 209 600-fold degenerate rearrangement, the cyclopropane unit being at any three adjacent carbons (Scheme 45).

(100)
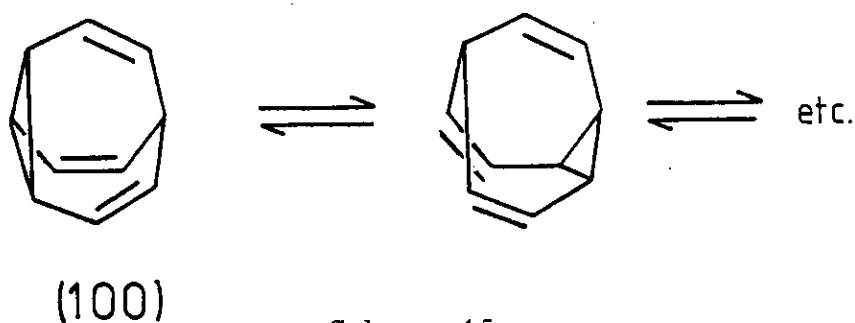
Scheme 45

This system was first synthesized by Schröder[104] and it was found that its [1]H n. m. r. spectrum collapses to a sharp singlet above 100°C, indicating that under these conditions the degenerate rearrangement is sufficiently rapid for all of the C-H units in the $(CH)_{10}$ system to be essentially equivalent, and they may be considered to move independently on the surface of a sphere.

C.4 Tandem Cope-Claisen rearrangement.

The only example of a Claisen rearrangement relevant to the present discussion is the recently reported[105] first example of a tandem Cope-Claisen rearrangement. As shown in Scheme 46 (101) rearranges to (102). Here the Cope rearrangement triggers the Claisen and as the Claisen rearrangement is irreversible this serves to shift the unfavourable Cope equilibrium.

(101)   (102)
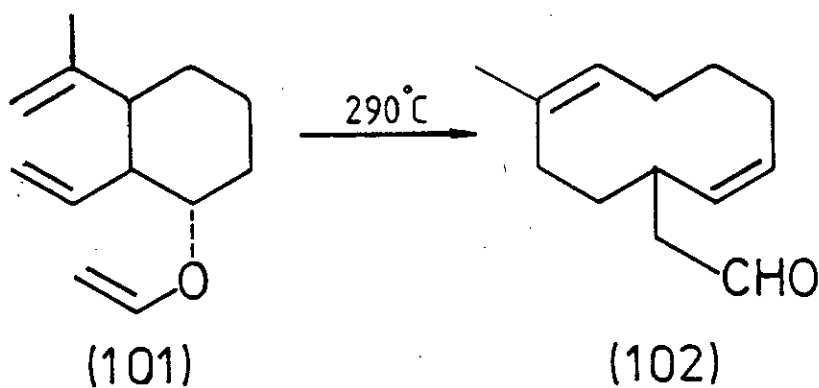
Scheme 46

D.   Programme of Research.

The preparation of 3, 5-dioxo-4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]-

decane 9, 9-dioxide (1) was first reported by Shaikrazieva et al. [3]

It should be noted that Scharf and Korte[106] had briefly reported the

preparation of a very similar type of compound much earlier.

(1)
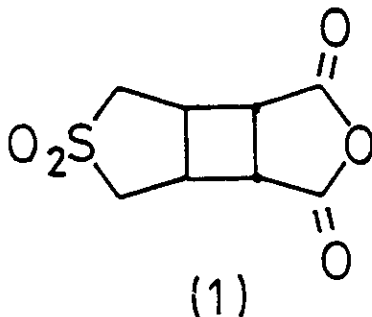
The initial publication gave details of a few chemical transformations

of (1) but a notable failure was their attempt to desulphurize it.

It was against this background that the present work began.   It

was recognised that if the sulphur dioxide was extruded from (1) and

its derivatives then this would provide a vehicle for the synthesis of

various divinyl compounds.   Flash vacuum pyrolysis was the technique

chosen for the extrusion and as will be described this proved to be

very effective and also general.

A further object of the research was to transform the anhydride

moiety into a variety of heterocyclic rings and study the pyrolysis of

the products.   It was also recognised that conversion of (1) to its

dicarboxylic acid derivative, followed by oxidative bis-decarboxylation

of this diacid would give the highly interesting molecule 3-thiabicyclo-

[3. 2. 0]hept-6-ene 3, 3-dioxide.   A programme designed to investigate

the reactions of this alkene with various reactive intermediate species

was considered worthwhile as this was a potential route to further hetero-

cycles.

EXPERIMENTAL

CONTENTS

A. Symbols and Abbreviations.

b. p.	boiling point
m. p.	melting point
I. R.	infra-red
n. m. r.	nuclear magnetic resonance
s; d; t;	singlet; doublet; triplet;
q; m; c	quartet; multiplet; complex
br.	broad
J	spin-spin coupling constant
δ	chemical shift
T. M. S.	tetramethylsilane
M^+	mass of molecular ion
m/e	mass to charge ratio
t. l. c.	thin layer chromatography
w/v	weight per unit volume
w/w	weight per unit weight
p. s. i.	pounds per square inch
u. v.	ultra violet
T. H. F.	tetrahydrofuran
F. V. P.	Flash vacuum pyrolysis
h; min; s;	hours; minutes; seconds
mmol	millimoles

B. Instrumentation and General Techniques.

Nuclear Magnetic Resonance Spectroscopy (n.m.r.).

a) Proton ^{1}H n.m.r. spectra of routine samples were obtained on a Varian EM-360 (60MHz) n.m.r. spectrometer at a probe temperature of 33°C. Spectra of new compounds and decoupling studies were obtained using a Varian HA 100 (100 MHz) n.m.r. spectrometer at a probe temperature of 28°C. The HA 100 instrument was operated by Mr. J.R.A. Millar. High resolution spectra were obtained on a Varian XL-100 (100 MHz) spectrometer equipped with pulse and Fourier transform accessory and was operated by Dr. A.S.F. Boyd. 360 MHz spectra were obtained on a Bruker WH-360 n.m.r. spectrometer which was operated by Mr. L.H. Bell. Chemical shifts were recorded as delta (δ) values in parts per million from tetramethylsilane ($\delta = 0.00$) which was used as internal reference. In a few cases where deuterated dimethyl sulphoxide was used as the n.m.r. solvent an external capillary lock of tetramethylsilane was used.

b) Carbon thirteen ^{13}C n.m.r. spectra were obtained on a Varian CFT 20 n.m.r. spectrometer which was operated by Mr. J.R.A. Millar. The operating frequency was 25.2 MHz. The deuterium signal from the solvent was used for frequency lock, and chemical shift values were recorded in parts per million from tetramethylsilane.

For all types of n.m.r. spectroscopy used, positive δ values are to low field relative to the reference.

Mass Spectrometry

Mass spectra and accurate mass measurements were obtained using an Associated Electrical Industries MS902 double focussing instrument (70eV) using a direct insertion probe. This instrument was operated by Mr. D. J. A. Thomas.

Infrared spectroscopy (i. r.)

Liquid samples were examined as thin films and solid samples as nujol mulls, both on polished sodium chloride plates, using a Perkin-Elmer 157G grating spectrometer.

Elemental Analyses

Microanalyses were carried out on a Perkin Elmer 240 Elemental Analyser by Mr. J. Grunbaum, University of Edinburgh.

Melting Points

The melting points of all new compounds were determined using a Kofler hot stage instrument and are uncorrected.

Medium Pressure Liquid Absorption Chromatography

This is a relatively new technique and a full description has been given.[107]

The pump used was a series II micrometering pump with a mechanically activated diaphragm head, supplied by Metering Pumps Ltd., Ealing. The diaphragm was constructed of nitrile rubber faced with Teflon. The pressure was monitored using a Budenburg guage equipped with a Nupro pressure relief valve set to open at about 80

pounds per square inch. Glass high performance liquid chromatography columns and Teflon tubing and connections were supplied by Jobling. For small separations (1 g) 1000 x 15 mm columns and 250 x 15 mm pre-columns were used and for longer separations (ca 10 g) 1000 x 25 mm columns and 250 x 25 mm pre-columns were used. Teflon to metal connections at the pump, pressure gauge and detector were made using Swagelok fittings. Columns were packed with Merck aluminium oxide ("90 active, neutral for column chromatography") or silica gel ("60, 40-60mm for column chromatography").

In most cases detection of the products was by t.l.c. but in a few cases use of a u.v. detector was possible.

A model 1521 LUV monitor, Model II detector and chart recorder, manufactured by Laboratory Data Control, Florida U.S.A., was used, the u.v. absorbance of the effluent being observed at 280 nm. The effluent was collected using a central automatic fraction collector equippped with 25 or 50 ml syphons.

Flow rates were generally adjusted to about 5 ml min^{-1}. When the alumina columns were used the solvents were 50% water saturated. This was achieved by saturating a given amount of solvent with water and then mixing this with an equivalent amount of dry solvent.

Column Chromatography

The alumina used was Laporte industries, Grade H, 100/200 mesh. B.D.H. silica gel for chromatography, 80-200 mesh was also used.

Thin-layer Chromatography (t.l.c.)

Thin layer chromatograms were obtained on 0.3 mm layers of alumina (Merck, aluminium oxide G, type 60/E) or silica gel

(Merck, silica gel G, type 60) containing fluorescent indicator. Components in the developed chromatograms were detected by observing the plate under u.v. light, or by reaction with iodine.

Gas Liquid Chromatography

A Pye 104 chromatograph with flame ionisation detector was used; all columns were 2m x 2.2mm in diameter. The carrier gas was nitrogen and the flow rates were those recommended by the manufacturer. The following stationary phases, supported on 80-100 mesh celite were employed: silicone elastomer (SE 30) and polyethyleneglycoladipate. '80-100 Chromosorb W' was used to support 30% β, β'-oxydipropionitrile.

Flash Vacuum Pyrolysis (F.V.P.)

The type of apparatus used was the conventional horizontal flow reactor a diagram of which is shown in Figure 7.

The inlet consisted of a pyrex tube (30 cm long x 25 mm) closed at one end and a B-24 ground glass joint at the other. The inlet tube was attached <u>via</u> the ground glass joint to a silica tube (30 cm x 25 mm) which was surrounded by a furnace. The products were trapped in a 'U'-tube which was surrounded by liquid nitrogen and was connected to the silica tube at the exit point of the furnace. The pressure was measured by either a McLeod or a Pirani gauge situated between the trap and the pump.

The heat required for the inlet was supplied by either a metal or glass Buchi Kugelrohr. The furnace and control box were supplied

Thermolysis tube containing silica rods

Product trap

Release tap

To guage

Release tap

Furnace

Liquid
N₂

Pump

Inlet tube
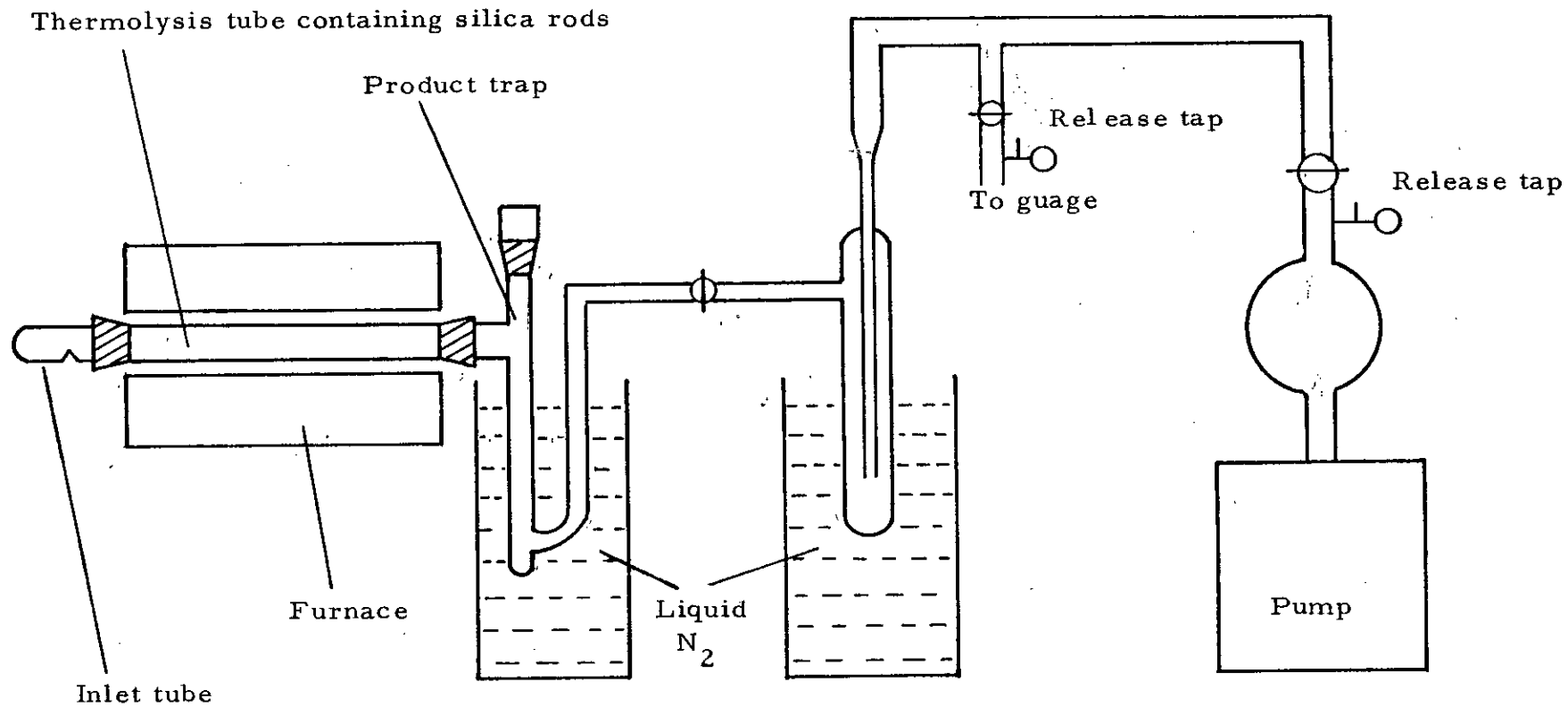
Fig. 7 Flash vacuum pyrolysis apparatus

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by Stanton Redcroft London. The high vacuum pump and vacuum gauge were supplied by Edwards of Crawley.

Photolysis

Photolysis were carried out using either 100 or 400W medium pressure mercury lamps supplied by Applied Photophysics Ltd. London. The filters used were either quartz or pyrex insertion wells also supplied by Applied Photophysics. Similarly power was supplied by an Applied Photophysics power pack of the appropriate rating depending on the lamp being used.

The reactions were carried out under dry nitrogen and the reaction mixture was stirred continuously.

Solvents

Anhydrous acetone was prepared by standing analar acetone (2.5 litres) over anhydrous magnesium sulphate (30 g) for a minimum of three hours. The acetone was filtered through a glass sinter and used directly. Benzene was distilled, dried and stored over sodium wire. Toluene was washed with sulphuric acid, sodium carbonate solution and water, dried over magnesium sulphate, then distilled and dried and stored over sodium wire. Pyridine was heated under reflux over potassium hydroxide pellets for 5 h and then distilled onto molecular sieve.

Tetrahydrofuran was dried over sodium wire, then boiled under reflux for 5 h over calcium hydride and distilled onto molecular sieve. The whole process was carried out under dry nitrogen.

X-Ray Crystallography

X-Ray studies were carried out by G. W. Smith, X-ray analytical laboratory B. P. Research Centre, Sunbury.

C. Nomenclature

All compounds are named in accordance with the principles laid down in the "I. U. P. A. C. 1957 and 1965 Rules." All compounds of the type (103) are named as derivatives of tricyclo$[5.3.0.0^{2,6}]$decane. The locant 1 is assigned to the bridge-head which allows the hetero

W=O, N, C
X=O, S, N

(103)
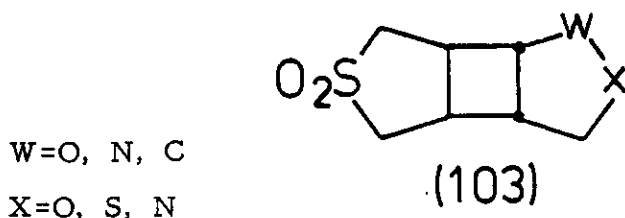
atom of highest priority to be assigned the lowest number, while adhering to the principal that numbering must begin at the point which gives the longest path between bridge-heads the lowest numbers. The order of priority of the heteroatoms is O>S>N.

According to the same rules (104) and (105) are named as derivatives of bicyclo[3, 2. 0]heptanes and divinylcyclopentanes respectively.

(104)

(105)
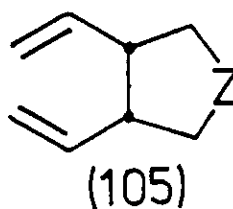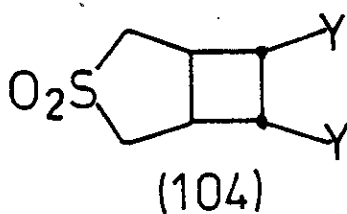
Y = COOH, CO_2Me, CH_2OH etc.   Z = O, S, N

D. Preparation of 3, 5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]-

decane 9, 9-dioxide.

This was prepared by the method of Shaikrazieva et al.[3]

Irradiation of butadiene sulphone (19.0 g, 160 mmol) and maleic

anhydride (20.0 g, 200 mmol) in anhydrous acetone (360 ml), at 20-

25°C for 24 h, with a 400 W medium pressure mercury lamp, in a

cylindrical water cooled quartz reactor gave a colourless crystalline

precipitate.   The precipitate was filtered off, washed with anhydrous

acetone and dried in vacuo to yield 3, 5-dioxo-4-oxa-9-thiatricyclo-

[5.3.0.0^{2,6}]decane 9, 9-dioxide (17.7 g, 51%) m.p. 292-293°C

(lit.,[3] 292-293°C).

^{1}H n.m.r. δ [CD$_3$)$_2$SO] 3.49-3.26 (8H, cm, 1-H, 2-H, 6-H,

7-H, 8 and 8'-H, 10 and 10'-H);

^{13}C n.m.r.δ [(CD$_3$)$_2$SO] 172.98 (C=O), 52.67 (C$_8$ and C$_{10}$),

43.35 (C$_2$ and C$_6$),   35.03 (C$_1$ and C$_7$);

Mass spectrum m/e 216 (0.6%), 198 (2), 172 (6), 108 (50),

80 (100).

E.   Preparation of Precursors of 3,4-Divinylcyclopentane Analogues.

E.1   4-Oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide.

a)   Dimethyl-3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylate

3,3-dioxide.

3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

(15.0 g, 69 mmol) in analar methanol (150 ml) to which a few drops of

concentrated sulphuric acid had been added, was boiled for 3 h.   When

cooled this solution gave a colourless crystalline product.   The

precipitate was filtered off and dried in vacuo to yield dimethyl-3-thia-

bicyclo[3.2.0]heptane-6,7-dicarboxylate 3,3-dioxide (16.4 g, 90%)

m.p. 126-127°C (lit.,[3] 126-127°C).

^{1}H n.m.r. δ (CDCl$_3$) 3.7 (6H, s, -Me), 3.6 (4H, m, 1-H, 5-H,

6-H, 7-H), 3.2-3.1 (4H, m, 2 and 2'-H, 4 and 4'-H);

^{13}C n.m.r. δ [(CD$_3$)$_2$SO] 171.92 (C=O), 53.17 (C$_2$ and C$_4$),

51.88 (-OMe), 43.00 (C$_6$ and C$_7$), 33.29 (C$_1$ and C$_5$);

Mass spectrum m/e 262 (1.4%), 231 (62), 138 (66), 99 (100).

b) 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide.

To a suspension of lithium aluminium hydride (5.8 g, 150 mmol)

in anhydrous T.H.F. (120 ml) was added dimethyl-3-thiabicyclo[3.2.0]-

heptane-6,7-dicarboxylate 3,3-dioxide (10 g, 38 mmol) over a period

of ½ h with stirring (mechanical).   The mixture was stirred for a further

1 h at room temperature, then heated under reflux for 1 h and cooled to

room temperature.   The excess lithium aluminium hydride was destroyed

by dropwise addition of water (7 ml), 15% sodium hydroxide solution

(7 ml) and then water (21 ml).   The mixture was stirred for ¼ h and was

then filtered to remove the inorganic salts.   Removal of solvent from

the filtrate gave a yellow oil (4 g) which crystallised. The solid

inorganic residue was extracted using T. H. F. (500 ml) in a Soxlet

apparatus over a period of 48 h. Removal of solvent in vacuo gave a

further amount of yellow oil (3. 3 g) which crystallised. The two solid

fractions were combined and recrystallised from T. H. F. to give a

colourless crystalline solid (5.4 g, 69%) m. p. 98-100°C (lit.,[3] 75-

82°C). In view of the discrepancy with the literature value the compound

was characterized and shown to be the title compound.

I. r. ν_{max} (nujol) 3500-3100 (associated-OH), 1310 (SO$_2$), 1255,

1150, 1050 (-OH) cm^{-1};

^{1}H n. m. r. δ (TFA) 4. 75-4. 65 (2H, m, -OH), 4. 14-4. 04 (4H, m,

-C$\underline{H}_2$O-), 3. 5-2. 9 (8H, m, 1-H, 2 and 2'-H, 4 and 4'-H, 5-H, 6-H, 7-H);

^{13}C n. m. r. δ [(CD$_3$)$_2$SO] 60. 50 (-C$\underline{H}_2$O-), 54. 66 (C$_2$ and C$_4$),

41. 56 (C$_6$ and C$_7$), 33. 29 (C$_1$ and C$_5$);

Mass spectrum m/e 170 (6. 8%), 79 (79), 70 (100); (Found:

C, 46.6; H, 6.8; calc. for C$_8$H$_{14}$O$_4$S: C, 46.6; H, 6.8%).

c) 4-Oxa-9-thiatricyclo[5. 3. 0. 0^{2,6}]decane 9, 9-dioxide.

Method (i)

This was prepared by the method of Culberson et al.[108] p-

Toluenesulphonyl chloride (1. 5 g, 8 mmol) and 6, 7-dihydroxymethyl-3-

thiabicyclo[3. 2. 0]heptane 3, 3-dioxide (1. 5 g, 7 mmol) were dissolved

in anhydrous pyridine (12 ml) and the mixture was stirred for 19 h.

The mixture was then heated on a steam bath for 1 h and then poured onto

crushed ice (50 g). The resultant mixture was neutralized with 10%

hydrochloric acid. This mixture was extracted with dichloromethane

(3 x 100 ml) and the extract was dried over magnesium sulphate. The

solvent was removed under reduced pressure to leave an oily liquid (5

g) which smelt strongly of pyridine.   The pyridine was removed under

high vacuum to leave the crude product (0.79 g).   The product was

purified by use of medium pressure chromatography with alumina as the

packing material and dichloromethane as the eluent .   A colourless

crystalline compound (0.39 g) was eluted and recrystallized from

dichloromethane/hexane to yield 4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane

9,9-dioxide (0.34 g, 26%) m.p. 129-130°C.

I.R. ν_{max} (nujol) 1302, 1287, 1179, 1134 (SO$_2$), 1107, 1073

(C-O-C), 690 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 3.9 (2H, d J 9.5 Hz, 3-H, 5-H),   3.45 (2H,

diffuse d of d J 9.5 Hz, 4.5 Hz, 3'-H, 5'-H), 3.1 (4H, m, 1-H, 2-H, 6-H,

7-H), 2.9 (2H, m, 8-H, 10-H), 2.8 (2H, m, 8'-H, 10'-H);

^{13}C n.m.r. δ (CDCl$_3$) 73.24 (C$_3$ and C$_5$), 54.59 (C$_8$ and C$_{10}$)

43.05 (C$_2$ and C$_6$), 36.20 (C$_1$ and C$_7$);

Mass spectrum m/e 188 (8%), 94 (60), 79 (100), 54 (78);

(Found: C, 50.80; H, 6.2; C$_8$H$_{12}$O$_3$S requires C, 51.05; H, 6.4%).

Method (ii)

This alternative method[109] gave a high yield on one occasion but

subsequent attempts to repeat the preparation failed.

6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

(1g, 4.9 mmol) was dissolved in dimethyl sulphoxide (10 g) and the

mixture was heated at 156-166°C for 16 h.   The mixture was allowed to

cool, water (30 ml) was added to it, and then was extracted with dichloro-

methane (2 x 70 ml).   The extract was washed with water (2 x 70 ml)

to remove any remaining dimethyl sulphoxide and then dried over magnesium sulphate. The solvent was removed under reduced pressure to give a colourless solid. Purification by chromatography on alumina with dichloromethane as eluent gave 4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]-decane 9,9-dioxide (0.62 g, 71%) m.p. 130°C (benzene).

Method (iii)

6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1 g, 4.9 mmol) was dissolved in acetone and a few drops of concentrated sulphuric acid added. The mixture was boiled under reflux for 48 h during which time it became reddish brown in colour, solvent was removed in vacuo to leave a dark brown oil which was swirled with ether to remove soluble material. The dark brown oil was then chromatographed on silica with dichloromethane:acetone 5:1 as eluent gave 4-oxa-9-thia-tricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide (0.5 g, 55%) m.p. 129-130°C.

E.2 4,9-Dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

a) 6,7-Dimesylmethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide.

This was made by the method described in Organic Synthesis.[110]
A solution of 6,7-dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (6.54 g, 31.7 mmol) in pyridine (25 ml) was introduced to a solution of methanesulphonyl chloride (11.1 g, 97 mmol) in dry pyridine (120 ml) at such a rate that the temperature did not exceed 0°C. The mixture was stirred (mechanical) throughout the addition and then for a further 2 h during which time the temperature was kept at -5 -0°C. Then, cold, 10% hydrochloric acid (200 ml), was introduced at such a rate that the temperature of the mixture remained below 20°C. The

solid which separated was recovered by filtration and washed sequentially with dilute hydrochloric acid (100 ml), water (200 ml) and was then dried in vacuo to give a colourless crystalline solid (11.09 g). This solid was recrystallized from water:ethanol 1:10 to yield 6,7-dimesyl-methyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (8.65 g, 75%) m.p. 190-191.5°C.

I.R. ν_{max} (nujol) 1333, 1295, 1175, 1141, 1105, 980, 858, 833 750 cm^{-1};

^{1}H n.m.r. δ [(CD$_3$)$_2$SO] 4.4-4.3 (4H, m -CH$_2$O-) 3.2-2.8 (14H, m, 1-H, 2 and 2'-H, 4 and 4'-H, 5-H, 6-H, 7-H, -Me);

^{13}C n.m.r. δ [(CD$_3$)$_2$SO] 69.14 (-CH$_2$O-), 53.68 (C$_2$ and C$_4$), 37.82 (C$_6$ and C$_7$), 36.75 (C$_1$ and C$_5$), 32.99 (-Me);

Mass spectrum m/e M$^+$ not observed;

(Found: C, 33.24; H, 5.07; C$_{10}$H$_{18}$O$_8$S$_3$ requires C, 33.14; H, 5.01%).

b) 4,9-Dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

This was prepared by a modification of the method of Auret et al.[111]

6,7-Dimesylmethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (5 g, 13.8 mmol) and sodium sulphide nonahydrate (9.92 g, 41.4 mmol) were dissolved in 1:1 aqueous ethanol (150 ml) and heated under reflux for 4 h. The ethanol was removed under reduced pressure and the aqueous residue was extracted with dichloromethane (2 x 100 ml) and the extract was dried over anhydrous magnesium sulphate. The solvent was removed under vacuum to give a colourless crystalline solid (2.25 g). This was recrystallized from trichloromethane (precipitated with petrol) to yield 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (1.73 g, 62%) m.p. 195-196°C.

I.R. ν_{max} (nujol) 1290 (SO$_2$), 1235, 1190, 1130 (SO$_2$), 1090, 905, 687 cm^{-1}; ^{1}H n.m.r. δ (CDCl$_3$) 3.2-2.9 (6H, m, 2-H, 2 and 3'-H, 5 and 5'-H, 6-H), 2.9-2.54 (6H, m, 1-H, 7-H, 8 and 8'-H, 10 and 10'H); ^{13}C n.m.r. δ (CDCl$_3$) 54.64 (C$_3$ and C$_5$), 45.96 (C$_1$ and C$_7$), 38.29 (C$_8$ and C$_{10}$), 35.97 (C$_2$ and C$_6$);

Mass spectrum m/e 204 (47%), 86 (100), 85 (94);

(Found: C, 47.29; H, 6.02; C$_8$H$_{12}$O$_2$S$_2$ requires C, 47.03; H, 5.92%).

E.3 9-Benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

a) 6,7-Ditosylmethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide.

This was prepared by the method of Mundy et al.[112] 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (5 g, 24.3 mmol) was dissolved in pyridine (38 ml) and the solution added dropwise to a suspension of p-toluenesulphonyl chloride (29.7 g, 156 mmol) in pyridine (38 ml) stirred at 0°C. The mixture was stirred for a further 3 h at 0°C and then it was poured into water (300 ml) and the product crystallised as a colourless solid. This was filtered off (11.61 g), washed with water and dried in vacuo. The solid was recrystallised from ethanol to yield colourless needles of 6,7-ditosylmethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (6.39 g, 51%) m.p. 127-128°C.

I.R. ν_{max} (nujol) 1600, 1315, 1175, 1097, 956, 899, 858, 812, 696, 668 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 7.8-7.3 (8H, AB system, aromatic H), 4.15-4.05 (4H, m -CH$_2$O-), 3.1-2.8 (8H, m, 1-H, 2 and 2'-H, 4 and 4'-H, 5-H, 6-H, 7-H), 2.46 (6H, s, -Me);

^{13}C n.m.r. δ (CDCl$_3$) 145.27 (Ar), 132.24 (Ar), 130.02 (Ar), 127.71 (Ar), 68.74 (-$\underline{C}$H$_2$O-), 54.14 (C$_2$ and C$_4$), 38.00 (C$_6$ and C$_7$), 33.35 (C$_1$ and C$_5$), 21.54 (-Me);

Mass spectrum m/e 514 (0.2%), 343 (14.2), 172 (35.7), 155 (100), 124 (3.6), 91 (100);

(Found: C, 51.13; H, 5.0. C$_{22}$H$_{26}$O$_8$S$_3$ requires C, 51.34; H, 5.09%).

b) <u>9-Benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.</u>

A solution of 6,7-ditosylmethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (5 g, 3.88 mmol) and benzylamine (3.1 g, 29 mmol) in ethanol (50 ml) was heated under reflux for 48 h. The solvent was removed <u>in vacuo</u> to leave a colourless solid which was leached with dichloromethane (100 ml). The mixture was filtered and solvent removed under reduced pressure to give a clear oil (3.0 g) which crystallised to give a colourless solid. This was purified by recrystallisation from ethanol to give <u>9-benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide</u> (1.5 g, 55.7%) m.p. 132-135°C.

I.R. ν$_{max}$ (nujol) 2780, 1603, 1300 (SO$_2$), 1247, 1140 (SO$_2$), 740, 700 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 7.4-7.2 (5H, m, PhH), 3.65 (2H, s, -C$\underline{H}_2$Ph), 3.1-2.6 (10H, m, 2-H, 3 and 3'-H, 5 and 5'-H, 6-H, 8 and 8'-H, 10 and 10'H), 2.2-2.0 (2H, m, 1-H, 7-H);

^{13}C n.m.r. δ (CDCl$_3$) 139.11 (Ph), 128.34 (Ph), 128.04 (Ph), 125.76 (Ph), 59.09 (C$_8$, C$_{10}$ and -C$\underline{H}_2$Ph) 54.98 (C$_3$ and C$_5$), 41.80 (C$_1$ and C$_7$), 36.71 (C$_2$ and C$_6$);

Mass spectrum m/e 277 (47.4%), 200 (26.3), 186 (47.4), 91 (100);

(Found: C, 64.84; H, 6.63; N, 4.97; $C_{15}H_{19}NO_2S$ requires C, 64.95;

H, 6.90; N, 5.05%).

E.4   9-Phenyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

This preparation of the title compound proved to be largely

unsuccessful.

a)   7-Phenylcarbamoyl-3-thiabicyclo[3.2.0]heptane-6-carboxylic

acid 3,3-dioxide.

This was prepared by the method of Shaikrazieva et al.[3]

3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide (20 g,

93 mmol) was stirred (mechanical) with absolute methanol (250 ml).

Aniline (8 ml) was added and the mixture stirred for a further 3 h.

The colourless solid which formed was filtered off and dried to yield

7-phenylcarbamoyl-3-thiabicyclo[3.2.0]heptane-6-carboxylic acid 3,3-

dioxide (20.2 g, 58%) m.p. 217-220°C (lit.[3], 220°C).

b)   9-Phenyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane

4,4-dioxide.

This was prepared by the method of Shaikrazieva et al.[3]   A mixture

of 7-phenylcarbamoyl-3-thiabicyclo[3.2.0]heptane-6-carboxylic acid

3,3-dioxide (6.3 g, 20.3 mmol), acetic anhydride (28 ml) and sodium

acetate (0.6 g) was heated and stirred vigorously for 4 h.   The precipitate

was filtered off, washed with methanol and dried in vacuo to give 9-

phenyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide

(5.0 g, 84%) m.p. 308-314°C (lit.[3] 310-315°C) as a colourless crystal-

line solid.

^{1}H n.m.r.δ (T.F.A.) 7.6-7.5 (3H, $\underline{m}$, $\underline{m}$ and $\underline{p}$-PhH), 7.3-7.15 (2H, $\underline{m}$, $\underline{o}$-PhH), 3.9-3.5 (8H, $\underline{m}$, 1-H, 2-H, 3 and 3'-H, 5 and 5'-H, 6-H, 7-H).

^{13}C n.m.r. δ [(CD$_3$)$_2$SO] 176.93 (C=O), 132.64 (Ph), 128.76 (Ph), 128.36 (Ph), 127.28 (Ph), 53.01 (C$_3$ and C$_5$), 42.62 (C$_1$ and C$_7$), 35.22 (C$_2$ and C$_6$);

Mass spectrum m/e 291 (69.4%), 119 (11.1), 80 (100).

c) 9-Phenyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

The method used for this reduction is that of Otzenberger et al.[113]

To a suspension of lithium aluminium hydride (1.4 g, 36.2 mmol) in dry tetrahydrofuran (100 ml) was added 9-phenyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (4.5 g, 15.5 mmol) over a period of fifteen minutes. The mixture was boiled under reflux for 5 h and then left to stir for a further hour. The excess lithium aluminium hydride was destroyed by the dropwise addition of water (2 ml) in tetrahydrofuran (20 ml), followed by 4M sodium hydroxide (2 ml) and then water (6 ml). The mixture was stirred for fifteen minutes and then was filtered to remove inorganic salts to give a yellow filtrate. The solvent was removed under reduced pressure to give a brown oil which was taken up in dichloromethane (100 ml) and dried over anhydrous magnesium sulphate. The solvent was removed under reduced pressure to give a brown gum which was chromatographed on silica with dichloromethane as eluent. The eluent polarity was gradually increased by using first ether then ethanol and finally methanol as the eluent. Four fractions were obtained but all proved to be intractable gums except

the second which on trituration with ether gave brown crystals (0.587

g). Recrystallisation from ethanol gave <u>9-phenyl-4-thia-9-azatricyclo-</u>

<u>[5.3.0.0^{2,6}]decane 4,4-dioxide</u> (0.129 g, 3.2%) m.p. 200-204°C as

reddish crystals.

I.R. ν_{max} (nujol) 1602, 1302, 1141, 760, 795 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 7.5-7.25 (2H, m, o-PhH), 6.94-6.7 (3H,

m, m and p-PhH), 3.8-3.5 (4H, m, 8 and 8'-H, 10 and 10'-H), 3.25-2.9

(8H, m, 1-H, 2-H, 3 and 3'-H, 5 and 5'-H, 6-H, 7-H);

Mass spectrum m/e 263 (100%), 144 (14), 119 (33), 91 (57),

(Found: C, 63.64; H, 6.65; N, 5.15. C$_{14}$H$_{17}$NO$_2$S requires C,

63.88; H, 6.51; N, 5.32%).

E.5   <u>Attempted preparation of 9-methyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]-</u>

   <u>decane 4,4-dioxide.</u>

The following route to 9-methyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]-

decane 4,4-dioxide proved unsuccessful owing to the failure of the final

step.

a)   <u>7-Methylcarbamoyl-3-thiabicyclo[3.2.0]heptane-6-carboxylic</u>

   <u>acid 3,3-dioxide.</u>

This was prepared by the method of Shaikrazieva et al.[3]

3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide (50 g,

230 mmol) was suspended in methanol (300 ml) and a 25% w/v solution

of methylamine [135 ml   31.38 g of CH$_3$NH$_2$ (338 mmol)] in water was

added to this suspension.   The mixture became warm and a pale yellow

solution formed.   This solution was stirred for 3 h and then the solvent

was removed   <u>in vacuo</u> to give a gummy yellow solid (68.31 g).   This

was recrystallised from 10:1 ethanol:water to yield 7-methylcarbamoyl-3-thiabicyclo[3.2.0]heptane-6-carboxylic acid 3,3-dioxide (44.09 g, 77%) m.p. 121-123°C as a colourless crystalline solid.

I.R. ν_{max} (nujol) 1640, 1570, 1140 cm^{-1};

^{1}H n.m.r. 8.1-7.9 (1H, m, -CO$_2$H), 3.4-2.9 (8H, m, 1-H, 2 and 2'-H, 4 and 4'-H, 5-H, 6-H, 7-H), 3.15 (3H, s, -Me);

^{13}C n.m.r. 175.68 (CON), 172.70 (C=O), 54.63 (C$_2$), 54.10 (C$_4$), 46.38 (C$_7$), 45.26 (C$_6$), 34.41 (C$_1$), 32.40 (C$_5$), 24.44 (-Me) (Found: M$^+$, 247. C$_9$H$_{13}$NO$_5$S requires 247).

b) 9-Methyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

The method used is that of Shaikrazieva et al.[3] A mixture of 7-methylcarbamoyl-3-thiabicyclo[3.2.0]heptane-6-carboxylic acid 3,3-dioxide (30 g, 120 mmol), acetic anhydride (107 ml) and anhydrous sodium acetate was heated and stirred on a water bath for 4 h. The solution was left to stand overnight and a white solid precipitated. This was recovered by filtration and washed with methanol (50 ml) and ether (50 ml) and dried in vacuo to yield 9-methyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]-decane 4,4-dioxide (26.8 g, 96%) m.p. 235-237°C as a colourless crystalline solid.

I.R. ν_{max} (nujol), 1694, 1433, 1390 (SO$_2$), 1283, 1160, 1137, 1100, 959, 753, 745 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 3.4 (2H, s, 1-H, 7-H), 3.26 (6H, s, 2-H, 3 and 3'-H, 5 and 5'-H, 6-H), 3.04 (3H, s, -Me);

^{13}C n.m.r. δ [(CD$_3$)$_2$SO] 177.79 (C=O), 53.05 (C$_3$ and C$_5$), 42.35

$(C_1$ and $C_7)$, 35.04 $(C_2$ and $C_6)$, 24.90 (-Me);

Mass spectrum m/e 229 (35%), 165 (57.5), 98 (20), 80 (100), 79 (100);

(Found: C, 47.38; H, 4.81; N, 6.08; $C_9H_{11}NO_4S$ requires C, 47.15;

H, 4.84; N, 6.11%).

c) <u>Attempted lithium aluminium hydride reduction of 9-methyl-</u>
<u>8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.</u>

The method that was used was that of Otzenberger et al.[113] To a

suspension of lithium aluminium hydride (2 g, 5.24 mmol) in dry tetra-

hydrofuran (500 ml) was added 9-methyl-8,10-dioxo-4-thia-9-aza-

tricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (6 g, 26.2 mmol) over a period

of five minutes. The mixture was stirred and boiled under reflux for

3 h and left to stir for a further hour. The excess lithium aluminium

hydride was destroyed by the dropwise addition of water (2 ml) in

tetrahydrofuran (20 ml), followed by 4M sodium hydroxide (2 ml) and

then water (6 ml). The mixture was stirred for fifteen minutes and

then was filtered to remove inorganic salts and gave a pale yellow

filtrate. The solvent was removed under reduced pressure to give a

yellow oil which was kept under high vacuum for 5 h. A sample of

the oil (1.63 g) was distilled in a glass Kugelrohr at 100°C/0.01mmHg

and gave a semi-crystalline pale yellow oil (0.45 g) which was un-

identified.

F.   Preparation and Reactions of   3-Thiabicyclo[3.2.0]hept-6-

ene 3,3-dioxide.

F.1   3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

a) 3-Thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide.

3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

(50 g, 230 mmol) was suspended in water (450 ml) and the mixture was

heated under reflux for $\frac{1}{2}$ h and gave a clear solution.   The water was

removed under reduced pressure to give a colourless solid residue (57.68 g).

This was dissolved in the minimum amount of wet acetone (acetone:water

50:1) and the product was precipitated using ether.   The precipitate was

recovered by filtration and dried in vacuo to yield 3-thiabicyclo[3.2.0]-

heptane-6,7-dicarboxylic acid 3,3-dioxide (42.3 g, 78%) m.p. 188-191°C

(lit.^{3} 194-195°C) as a colourless crystalline solid.

I.R. ν_{max} 1700 (CO_2H), 1125 (SO_2) cm^{-1};

^{1}H n.m.r. δ [$(CD_3)_2CO$] 9-7 (2H, V.br., $-CO_2\underline{H}$), 3.6-3.4 (4H,

m, 1-H, 5-H, 6-H, 7-H), 3.3-3.2 (4H, m, 2 and 2'-H, 4 and 4'-H);

^{13}C n.m.r. δ [$(CD_3)_2SO$] 173.66 ($-\underline{C}O_2H$), 54.00 (C_2 and C_4),

43.87 (C_6 and C_7), 33.79 (C_1 and C_5);

Mass spectrum m/e 234 (-), 216 (2.3%), 198 (2.5), 172 (8),

108 (65), 108 (65), 80 (100), 79 (100).

b) 3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

This was prepared by the method of Jefford et al.[114]

3-Thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide (9.9 g,

42 mmol) and lead tetraacetate (37.3 g, 84 mmol) were intimately mixed

and dissolved in dry dioxane (130 ml).   The mixture was purged with

dry nitrogen for fifteen minutes and then placed in a water bath at

12-15°C. The mixture was vigorously stirred (mechanical) while nitrogen continued to be passed through it and dry pyridine (250 ml) was next admixed. The mixture was placed in a water bath at 60°C for twenty minutes during which time there was rapid evolution of carbon dioxide. The mixture was rapidly cooled and poured into 2N nitric acid (800 ml). This mixture was extracted using dichloromethane (8 x 100 ml) and the extract was washed in turn with water (1 x 100 ml), saturated sodium hydrogen carbonate solution (2 x 100 ml) and saturated sodium chloride solution (1 x 100 ml). The extract was dried over anhydrous magnesium sulphate and the solvent removed _in vacuo_ to leave the crude product (3.92 g). This was purified by medium pressure chromatography on silica with ether as the eluent. 3-Thia-bicyclo[3.2.0]hept-6-ene 3,3-dioxide was eluted as a colourless crystalline solid (1.14 g, 18.8%) m.p. 71-75°C.

I.R. ν_{max} (nujol) 1410, 1287, 1229, 1167, 1110, 942, 852, 728 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 6.18 (2H, s, alkenyl), 3.7-3.6 (2H, m, 1-H, 4-H), 3.2-2.9 (4H, m, 2 and 2'-H, 4 and 4'-H),

^{13}C n.m.r. δ (CDCl$_3$) 139.00 (olefinic), 51.96 (C$_2$ and C$_4$), 41.04 (C$_1$ and C$_5$);

Mass spectrum m/e 144 (3%), 81 (5), 80 (55), 79 (100), 77 (30); (Found: C, 50.10; H, 5.35; C$_6$H$_8$O$_2$S requires C, 50.0; H, 5.5%).

F.2   8-Oxa-4-thiatricyclo[5.1.0.0^{2,6}]octane 4,4-dioxide

Method (i)

The method that was used is that of Bianchi et al.[115] To a stirred mixture of hydrogen peroxide 30% (10 ml) and formic acid 90% (40 ml)

was added 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (0.6 g, 4.2 mmol) in small portions over a period of twenty minutes at room temperature. The mixture was stirred for 48 h at $50^{\circ}C$ and for a further 48 h at room temperature. The solvent was removed in vacuo and the oil which remained was taken up in a small amount of ethanol and 8-oxa-4-thia-tricyclo[5.1.0.0^{2,6}]octane 4,4-dioxide was precipitated as a courless crystalline solid (0.26 g, 39%) m.p. $118-119^{\circ}C$.

I.R. ν_{max} (nujol) 3080, 1325, 1290, 1240, 1130, 855, 835, 715 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 4.0-3.9 (2H, d J 1.5Hz, 1-H, 7-H), 3.3-3.1 (4H, m, 3 and 3'-H, 5 and 5'-H), 3.05-2.9 (2H, m, 2-H, 6-H).

^{13}C n.m.r. δ (CDCl$_3$) 56.51 (C$_1$ and C$_7$), 49.69 (C$_3$ and C$_5$), 40.85 (C$_2$ and C$_6$);

Mass spectrum m/e 160 (0.13%), 131 (0.35), 104 (2.9), 95 (44), 94 (100); (Found: C, 45.15, H, 5.00; C$_6$H$_8$O$_3$S requires C, 45.0; H, 5.00%).

Method (ii) via 6-chloro-7-hydroxy-3-Thiabicyclo[3.2.0]heptane 3,3-dioxide.

a) 6-Chloro-7-hydroxy-3-thiabicyclo[3.2.0]heptane 3,3-dioxide.

This was prepared by the method of Sorenson.[116] To a stirred ice-cooled solution of 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (360 mg, 2.5 mmol) in water (2.5 ml) was added a solution of HOCl, as prepared in Organic Synthesis,[117] until no more HOCl was taken up (KI-HCl test). Water (100 ml) was added to the reaction mixture to increase its volume and this mixture was then extracted with dichloromethane (4 x 50 ml). The extract was dried over magnesium sulphate and solvent was removed under vacuum to leave a solid (223 mg).

Recrystallisation of the solid from ethanol gave 6-chloro-7-hydroxy-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (141 mg, 29%) m.p. 146-148°C as colourless crystals.

I.R. ν_{max} (nujol) 3440 (-OH), 1275, 1118, 857, 802 cm^{-1};

Mass spectrum m/e M^{+} not observed;

(Found: C, 36.19; H, 4.53; $C_6H_9ClO_3S$ requires C, 36.65; H, 4.61%).

b) Attempted dehydrohalogenation of 6-chloro-7-hydroxy-3-thia-bicyclo[3.2.0]heptane 3,3-dioxide.

The method used was that of McClure[118]. 6-Chloro-7-hydroxy-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (165 mg, 0.84 mmol) was dissolved in dimethoxyethane (25 ml) with silver (1) oxide (195 mg, 1.68 mmol) and the mixture was boiled under reflux for 24 h. The solids were removed by filtration and extensively washed with hot acetone. The filtrate was dried over magnesium sulphate and solvent removed under reduced pressure to give an oil (260 mg). This was triturated with ether and cooled in an acetone carbon dioxide (-70°C) bath and the product crystallised and was recovered by filtration. However I.R. showed that this solid was unchanged starting material.

F.3 Attempted addition of carbenes to 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

a) Ethoxycarbonyl carbene.

Method (i)

3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (105 mg, 0.73 mmol) was stirred in dry benzene (10 ml) with 3-diazo-2-oxopropionate (105 mg, 0.73 mmol)[119] in the presence of a pinch (1 mg) of rhodium (IV) acetate

as catalyst. After a short induction period (5 minutes) nitrogen gas was evolved. The mixture was stirred for 21 h and the benzene was removed under vacuum and gave a clear oil. On examination by n. m. r. it was apparent that this oil was a mixture of unchanged alkene, diethyl-maleate, diethyl fumarate and 1-ethoxycarbonylcycloheptatrienyladiene. The mixture was analysed by gas chromatography using a $2\frac{1}{2}\%$ SE30 column three peaks were observed and the presence of diethyl fumarate and diethyl maleate confirmed by peak enhancement experiments using authentic samples. Thus the experiment was a failure as the carbenes preferred to dimerize or add to benzene rather than add to the alkene.

Method (ii)

The experiment was repeated as before with the modification that this time the 3-diazo-2-oxo-propionate (105 mg, 0.73 mmol) in benzene (5 ml) was added slowly to 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (105 mg, 0.73 mmol) dissolved in benzene (5 ml) to which rhodium (IV) acetate (1 mg) had been added. The addition took place over a period of $\frac{1}{2}$ h and nitrogen was slowly evolved. However work up as before revealed that the products were exactly the same and none of the desired carbene addition compound to the alkene had been formed.

Control experiment

A control experiment was carried out in which the experiment was carried out exactly as in method (ii) except that this time no 3-thiabicyclo[3.2.0]hep-6-ene 3,3-dioxide was added. On removal of the benzene in vacuo the residue was distilled in a glass Kugelrohr (100°C/16 mmHg) and gave a clear liquid. Spectral analysis showed

that this liquid was a mixture of diethylmaleate, diethyl fumarate
and 1-ethoxycarbonylcycloheptatrienyladiene as before.

Method (iii)

3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide   (140 mg, 6.97 mmol)
was intimately mixed with copper bronze and placed in a Dreschel
tube and a flow of nitrogen passed over it.   The tube was placed in
an oil bath at $110^{o}C$ and 3-diazo-2-oxo-propionate (100 mg, 0.70 mmol)
added to it.   There followed a vigorous   reaction and after 10 minutes
the Dreschel tube was   removed from the oil bath and trichloromethane
(200ml) was added to the reaction mixture.   The copper bronze was
removed by filtration and removal of solvent   in vacuo gave a clear
oil.   Spectroscopic analysis (n.m.r.) show that this consisted of
diethyl maleate, diethyl fumarate and unchanged alkene.   Thus 3-
thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide is very unreactive toward
carbenes.

F.4   Attempted addition of nitrenes to 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

a) Ethoxycarbonylnitrene.

The   method used to generate ethoxycarbonyl nitrene was that of
Cadogan et al.[120]   3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (240 mg,
1.6 mmol) and p-nitrophenylsulphonyloxyurethane (500 mg, 1.7 mmol)
were dissolved in anhydrous dichloromethane (25 ml) and a solution
of triethylamine (200 mg, 1.98 mmol) in dichloromethane (15 ml) was
added dropwise to the reaction mixture over a period of ten minutes.
The mixture was stirred for 3 h, the reaction being monitored by the

disappearance of nitrene precursor by t. l. c. (alumina, ether).

Dichloromethane (75 ml) was added to the reaction mixture and this

mixture was washed with water (3 x 25 ml) to remove excess amine.

The solution was dried over anhydrous magnesium sulphate and solvent

removed in vacuo to leave an oil (310 mg). It was shown spectroscopi-

cally (n. m. r.) that the alkene was unchanged and that the only other

species present was the ethoxycarbonyl nitrene dimer. The mixture

was chromatographed on alumina. Elution with dichloromethane and

the dichloromethane:ether 9:1 gave recovered alkene (0. 2 g).

b) N-Phthalimidonitrene.

The method used was that of Anderson et al.[121] To a stirred

mixture of N-aminophthalimide[122] (263 mg, 1. 62 mmol) and 3-thia-

bicyclo[3. 2. 0]hept-6-ene 3, 3-dioxide (900 mg, 6. 25 mmol) in dichloro-

methane (20 ml), was added lead tetraacetate (690 mg, 1. 56 mmol) in

small portions, over a period of ten minutes. The mixture was stirred

for an additional thirty minutes and then the precipitated inorganic

salts were removed by filtration. The solvent was removed under

reduced pressure to leave a yellow oil (1. 21 g) which crystallised.

This was purified by medium pressure chromatography on silica.

Elution with petroleum ether (40-60): acetone 3:1 gave a colourless

crystalline compound (29. 9 mg) m. p. 180-181°C which was probably

the nitrene addition product but this was not confirmed.

I. R. ν_{max} (nujol) 1775, 1719, 1310, 1247, 1179, 1107, 708,

658 cm^{-1};

Mass spectrum m/e 304 (16. 7%), 240 (13. 9), 225 (100), 160 (9. 3),

132 (16. 7).

F. 5   Addition of 1, 3-dipoles   to 3-thiabicyclo[3. 2. 0]hept-6-ene

3, 3-dioxide.

a) Preparation of 1, 3-dipole   precursors.

    i) C, N-Diphenylnitrone.

This was prepared by the method of Wheeler et al.[123] Equimolar

amounts of phenylhydroxylamine and benzaldehyde were condensed in

ethanol and the product crystallized as a colourless solid.   Recrystalli-

zation from ethanol gave C, N-diphenylnitrone (88%) as a colourless

solid m. p. 109-111°C (lit 114°C).

    ii) Anisohydroxamic chloride

    Stage (i) Anisaldehyde bisulphate.

This was prepared by the method outlined in Vogel's handbook.[124]

Equimolar amounts of sodium metabisulphite and anisaldehyde were

condensed in aqueous ethanol and the product was precipitated immediately,

and was recovered by filtration (99% yield).   It was dried in vacuo

and used in the next stage without purification.

    Stage (ii) Anisaldoxime

    This was prepared by a modification of the method given in Vogel's

handbook.[125] Anisaldehyde bisulphite (160 g, 0. 67 mol) was dissolved

in water (900 ml) and to this was added a solution of sodium hydroxide

(100 g of NaOH in 300 ml of water).   Hydroxylamine hydrochloride

(48 g, 0. 7 mol) was added in small portions, the mixture being stirred

continuously.   Solid carbon dioxide was added to the resulting pale

yellow solution and a colourless solid precipitated.   The solid was re-

covered by filtration and dissolved in dichloromethane (600 ml).   This

solution was washed with water (2 x 200 ml) and then dried over magnesium

sulphate. Removal of solvent under reduced pressure gave an oil (84.8 g) which crystallised. This solid was recrystallised from toluene/pentane to give anisaldoxime (75 g, 73%).

Stage (iii) Anisohydroxamic Chloride.

This was prepared by the method of Rheinboldt et al.[126]

Anisaldehyde oxime (18.6 g, 0.12 mol) was dissolved in dry ether (160 ml) and the solution was cooled to between -10 -0°C. An ether solution of nitrosyl chloride (20% w/v 81 ml, 16.2 g, 0.25 mol)[127] was added carefully with constant stirring. The solution was stirred for a further hour at room temperature. The solvent was removed in vacuo to leave a brown oil which was taken up in trichloromethane. Addition of petroleum ether (40-60) gave a colourless precipitate. This was recovered by filtration and dried in vacuo to yield anisohydroxamic chloride (14.06 g, 61%) m.p. 74-75°C (lit.,[126] 88-89°C).

iii) Benzhydroxamic chloride.

Stage (i) and (ii)

The preparation of benzaldoxime was achieved in two stages by procedures analogous to those used for anisaldoxime. The bisulphite addition compound was obtained in 97% yield and the oxime in 94% yield.

Stage (iii) Benzhydroxamic Chloride

This was prepared by the method of Perold et al.[128] Benzaldoxime (20 ml) was added to 8.3N hydrochloric acid (120 ml) and the reaction vessel was placed in an ice salt bath and when the temperature of the mixture had dropped to 0°C chlorine was passed through it for 20 minutes. The mixture was extracted with dichloromethane (5 x 200 ml) to give a green solution which was washed with water (8 x 100 ml) to

remove any residual chlorine. The solution was dried over magnesium

sulphate and solvent was removed in vacuo to give an oily residue.

This was taken up in trichloromethane (20 ml) and the product was

precipitated by addition of petroleum ether (40-60). The colourless

solid was recovered by filtration and dried in vacuo to yield benzhydrox-

amic chloride (6.12 g) m.p. 44-48°C (Lit.[128] 42-48°C).

iv) *a-Chlorobenzoylphenylhydrazone.*

Stage (i) β-Benzoylphenylhydrazine.

This was prepared by the method of Tinley.[129] Phenylhydrazine

(10 g, 93 mmol) in pyridine (50 ml) was stirred in an ice-water bath

during the addition of benzoyl chloride (108 ml 13 g; 93 mmol). This

mixture was shaken for fifteen minutes before being poured into water

(350 ml). An orange coloured solid was washed with water and re-

crystallized from ethanol to yield β-benzoylphenylhydrazine as colourless

crystals (11.82 g, 60%) m.p. 165-167°C (lit.[130] 168°C).

Stage (ii) *a-Chlorobenzoylphenylhydrazone.*

This was prepared by the method of Huisgen et al.[131] Finely

divided β-benzoylphenylhydrazine (5 g, 21.7 mmol) and phosphorous

pentachloride (6 g) were suspended in dry ether (15 ml) and boiled

under reflux in dry conditions for 16 h. The solution was cooled and

filtered. Then phenol (10 g) dissolved in ether (8 ml) and methanol (10

ml) was added with cooling. The ether was removed in vacuo and the

resultant suspension was cooled in fridge. The solid was filtered off,

washed with ice-cold methanol and dried in vacuo to give a-chlorobenzoyl-

phenylhydrazone (1.37 g, 25%) m.p. 127-129°C (lit.[131] 129.5-130.5°C)

as pale green crystals.

b) **4, 5-Diphenyl-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0^{2,6}]decane**

   9, 9-dioxide.

A solution of 3-thiabicyclo[3. 2. 0]hept-6-ene 3, 3-dioxide (150 mg, 1. 04 mmol) and C, N-diphenylnitrone (205 mg, 1. 04 mmol) in dry toluene was heated under reflux for 72 h. The reaction progress was monitored by t. l. c. (alumina, petroleum ether (40-60) : trichloromethane 1:1). The solvent was removed under reduced pressure and gave a brown solid (0. 5 g). Recrystallization of this solid from ethanol gave 4, 5-diphenyl-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0^{2,6}]decane-9, 9-dioxide (0. 1 g, 28%) m. p. 185-186°C as a light brown crystalline solid.

I. R. ν_{max} (nujol) 1598, 1490, 1309, 1132, 768, 742, 709, 701 cm^{-1};

^{1}H n. m. r. δ (CDCl$_3$) 7. 5-7. 0 (10H, m, Ph), 4. 8 (1H, d of d, J 7Hz, 2Hz, 2-H), 4. 5 (1H, d J 7Hz, 5-H), 3. 5-2. 6 (7H, cm, 1-H, 6-H, 7-H, 8 and 8'-H, 10 and 10'-H);

Mass spectrum m/e 341 (50%), 180 (17), 91 (100), 77 (36);

(Found: C, 66.60; H, 5.65; N, 3.95; C$_{19}$H$_{19}$NO$_3$S requires C, 66.85; H, 5.60; N, 4.10%).

c) **5-(p-Methoxyphenyl)-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0^{2,6}]-**

   dec-4-ene 9, 9-dioxide.

A solution of 3-thiabicyclo[3. 2. 0]hept-6-ene 3, 3-dioxide (260 mg, 1. 8 mmol) and anisohydroxamic chloride (310 mg, 1. 8 mmol) in dry toluene (20 ml) was boiled under reflux for 48 h. The reaction progress was monitored by evolution of hydrogen chloride gas. When the mixture was cooled to room temperature a brown solid precipitated which was recovered by filtration (0. 39 g). This solid was recrystallized from ethanol to give colourless crystals of 5-(p-methoxyphenyl)-3-oxa-9-

thia-4-azatricyclo[5. 3. 0. 0$^{2, 6}$]dec-4-ene 9,9-dioxide (0. 24 g, 45%)

m. p. 182-184°C

I.R. ν_{max} (nujol) 1302, 1246, 1125, 872, 835 cm^{-1}.

^{1}H n.m.r. δ (CDCl$_3$) 7. 2 (4H, AB pattern, aromatic), 5. 2 (1H, d of d, J 8Hz, 4Hz, 2-H), 4. 3 (1H, d, J 8Hz, 6-H), 3. 8 (3H, s, -OMe), 3. 6-3. 1 (6H, c m, 1-H, 7-H, 8 and 8'-H, 10 and 10'-H).

^{13}C n.m.r. δ(CDCl$_3$) 161. 34 (aromatic carbon adjacent to -OMe), 157. 61 (C$_5$), 128. 36 (Ar), 119. 76 (Ar), 114. 44 (Ar), 81. 91 (C$_2$), 55. 28 (-OMe), 53. 46 (C$_{10}$), 53. 10 (C$_8$), 41. 54 (C$_6$), 37. 30 (C$_1$ and C$_7$);

Mass spectrum m/e 293 (30%), 175 (100);

(Found: C, 57. 10; H, 5. 15; N, 4. 70; C$_{14}$H$_{15}$NO$_3$S requires C, 57. 30; H, 5. 15; N, 4. 80%).

d) 5-Phenyl-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0$^{2, 6}$]dec-4-ene 9, 9-dioxide.

A solution of 3-thiabicyclo[3. 2. 0]hept-6-ene 3, 3-dioxide (1. 1 g, 7. 6 mmol) and benzhydroxamic chloride (1. 19 g, 7. 6 mmol) in dry toluene (100 ml) was boiled under reflux for 64 h. The reaction progress was monitored by the evolution of hydrogen chloride gas. The solvent was removed in vacuo to leave a brown oil (0. 93 g). This was purified by medium pressure chromatography on an alumina column. Elution with at first petroleum ether (40-60) and later with dichloromethane gave a colourless crystalline solid (0. 74 g). Recrystallization from ethanol gave 5-phenyl-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0$^{2, 6}$]dec-4-ene 9, 9-dioxide (0. 37 g, 18. 5%) m. p. 175-176°C as colourless crystals.

I.R. ν_{max} (nujol) 1308, 1128, 878, 768, 691, 666 cm^{-1}.

^{1}H n.m.r. δ (CDCl$_3$) 7.6-7.4 (5H, m, Ph), 5.3-5.1 (1H, d of d

J 7.5Hz 2.5Hz, 2-H), 4.4-4.2 (1H, m, 6-H), 3.5-3.2 (6H, c m,

1-H, 7-H, 8 and 8'-H, 10 and 10'-H);

^{13}C n.m.r. δ [(CD$_3$)$_2$ SO] 158.43 (C$_5$), 130.36 (Ph), 129.06 (Ph),

127.66 (Ph), 127.01 (Ph), 82.11 (C$_2$), 52.49 (C$_{10}$), 52.28 (C$_8$),

41.54 (C$_6$), 37.40 (C$_1$ and C$_7$);

Mass spectrum m/e 263 (8.7%), 145 (100), 144 (57), 117 (13), 77 (22);

(Found: C, 59.15; H, 5.00; N, 5.10; C$_{13}$H$_{13}$NO$_3$S requires C, 59.30;

H, 5.00; N, 5.30%).

e) 4-Thia-9,10-diazatricyclo[5.3.0.0^{2,6}]dec-9-ene 4,4-dioxide.

The diazomethane was prepared by the method outlined in Vogel's

handbook.[132] Diazald [CH$_3$C$_6$H$_4$SO$_2$N(CH$_3$)NO] (4.3 g, 20 mmol)

was dissolved in dry ether (60 ml) and an alcoholic solution of potassium

hydroxide (0.8 g in 20 ml of 96% aqueous ethanol). This solution was

stood in an ice bath for fifteen minutes and then the resultant ethanol

solution of diazomethane was distilled off into cold dry ether (50 ml).

3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (500 mg, 3.5 mmol) was

added to this solution and stood in a cold room for 42 days during which

time there precipitated a pale yellow solid. The excess diazomethane

was destroyed by addition of glacial acetic acid and the solid was

recovered by filtration and dried in vacuo to yield 4-thia-9,10-diaza-

tricyclo[5.3.0.0^{2,6}]dec-9-ene-4,4-dioxide (500 mg, 82%) m.p. 157-

158°C as pale yellow needles.

I.R. ν$_{max}$ (nujol) 1535, 1295, 1137, 888, 686 cm^{-1};

^{1}H n.m.r. δ(CDCl$_3$) 5.36-5.2 (1H, m, 1-H), 4.64-4.56 (2H, d of d

J 2.5Hz 1Hz, 8 and 8'-H), 3.46-2.97 (5H, c m, 2-H, 3 and 3'-H,

5 and 5'-H) 2.82-2.5 (2H, c m, 6-H, 7-H);

^{13}C n.m.r. δ(CDCl$_3$) 90.05 (C$_1$), 84.03 (C$_8$), 54.10 (C$_3$), 53.18 (C$_5$),

38.09 (C$_7$), 37.95 (C$_2$), 32.72 (C$_6$);

Mass spectrum m/e 187 (0.8%), 186 (0.04), 93 (16.6), 91 (21),

79 (100), 77 (50);

(Found: C, 45.26; H, 5.38; N, 14.87; C$_7$H$_{10}$N$_2$O$_2$S requires

C, 45.15; H, 5.4; N, 15.04%).

f) <u>Attempts to add diphenylnitrilimine to 3-thiabicyclo[3.2.0]-</u>
   <u>hept-6-ene 3,3-dioxide.</u>

3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (250 mg, 1.7 mmol)

and α-chlorobenzoylphenylhydrazone (400 mg, 1.7 mmol) in dry toluene

(30 ml) was boiled under reflux for 90 h the reaction progress was

monitored by the evolution of hydrogen chloride gas. The solvent was

removed under reduced pressure and gave a brown crystalline solid.

This was shown by n.m.r. to consist of unreacted 3-thiabicyclo[3.2.0]hept-6-

ene 3,3-dioxide and nitrilimine decomposition products. The unreacted

3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide was recovered by chromato-

graphy of the brown solid on silica with ether as the eluent. The

recovery was virtually quantitative showing that the nitrilimine had

not reacted with the alkene.

<u>Method (ii)</u>

This method is that of Huisgen.[131] To a solution of 3-thiabicyclo-

[3,2,0]hept-6-ene 3,3-dioxide (120 mg, 0.83 mmol) and α-chlorobenzoyl-

phenylhydrazone (200 mg, 0.83 mmol) in dry benzene (15 ml) was added

a solution of triethylamine (200 mg, 2 mmol) in benzene (5 ml) over a

period of 1 h. during which time the solution became fluorescent.

The benzene was removed under reduced pressure and gave an almost

colourless crystalline solid. This was shown by n.m.r. to be almost

identical to the product obtained by method (i) and once again the

nitrilimine had failed to react with the alkene.

G.   Preparation of Divinylcyclopentane Analogues by Flash Vacuum Pyrolysis (F. V. P.).

G. 1   General procedure.

The pyrolyses were carried out using the apparatus described in section B.   The following procedure is typical.

A sample of the substrate was placed in the inlet of the F. V. P. apparatus and the inlet was then attached to the pyrolysis tube.   The 'U' shaped trap was attached to the pyrolysis tube exit and the system was sealed by connecting the other end of the trap to the pump.   The joints which were subject to high temperatures were sealed with high vacuum silicone grease and the others with L Apiezon grease.   When the furnace temperature had reached the required temperature and the system pressure had fallen to approximately 10^{-3} mmHg the trap was surrounded by a liquid nitrogen trap and the inlet was surrounded by a Kugelrohr already heated to the required temperature.   The substrate was then sublimed into the furnace over a period of between $\frac{1}{2}$ h and 5 h, and the products were trapped in the cold trap.   When all of the substrate had sublimed the heat sources were switched off and the system allowed to cool.   When the apparatus had cooled it was flooded with dry nitrogen taken apart and the product recovered from the cold trap and purified by standard procedures.

In general each new pyrolysis required a series of small scale (50 mg) experiments in order to find optimum conditions.   The two parameters which were of particular importance were (i) the inlet temperature, and (ii) the furnace temperature.   The correct inlet temperature was determined by carrying out a pyrolysis in which the

inlet temperature was gradually increased in 10°C intervals from room temperature until a reasonable rate of sublimation was attained. It was desirable to avoid melting the substrate in the inlet and also either very low or very high rates of sublimation. Sometimes however it was impossible to avoid melting the substrate as in these cases inlet temperatures below the melting point of the substrate gave negligible rates of sublimation. The correct furnace temperature had to be found such that the substrate was completely pyrolysed to give the desired products without the products themselves being decomposed. In general furnace temperature was in the range 500-625°C.

Another feature worthy of note is that on some occasions a residue remained in the inlet at the end of the pyrolysis. On these occasions the amount of residue was determined by weighing and taken into account when the yields of the pyrolysis was calculated. One feature which was also of interest was that if one changed the scale of an experiment from small (50 mg) to medium (1 g) scale then one had to increase the furnace temperature by 20-50°C to get the same results as in the lower scale experiment.

In small scale experiments the crude pyrolysate was dissolved in $CDCl_3$ (0.3 ml) and this solution was analysed directly by n.m.r. [after addition of cyclohexane (5μl) as an integral calibrant]. Absolute yields in these small scale experiments were obtained from the n.m.r. spectra by relating the integral of the various protons to that of cyclohexane. This procedure is estimated to be accurate to $\pm 5\%$.

In all the pyrolyses optimum conditions are quoted.

G. 2 Pyrolysis of 3, 5-dioxo-4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]decane

  9, 9-dioxide.

A sample of 3, 5-dioxo-4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]decane

9, 9-dioxide (15 g, 69 mmol) was pyrolysed at 630°C. The inlet temperature

was 180°C, the pressure 6 x 10^{-3} mmHg and time taken was 5 h. At the

end of the pyrolysis the pyrolysate was transferred to a Kugelrohr bulb

and distilled bulb-to-bulb (65°C 10. 0 mmHg) and gave 2, 5-dioxo-cis-3, 4-

divinyltetrahydrofuran as a clear liquid (8. 43 g, 80%) n$_D^{25}$ 1.4835.

I. R. ν $_{max}$ (liquid film) 1900-1700, 1642, 1417, 1206, 1072, 945, 783

cm^{-1}.

^{1}H n. m. r. δ (CDCl$_3$) 5. 9-5. 5 (2H, m, 6-H, 8-H), 5. 4-5. 3 (4H, c d of d,

7 and 7'-H, 9 and 9'-H), 3. 9-3. 4 (2H, d of d J 4. 5 Hz 2Hz, 3-H, 4-H)

^{13}C n. m. r. δ (CDCl$_3$) 170. 44 (C=O), 127. 34 (C$_6$ and C$_8$), 122. 11 (C$_7$

and C$_9$) 48. 88 (C$_3$ and C$_4$);

Mass spectrum m/e 152 (11. 3%), 108 (6. 8), 80 (100), 79 (100);

(Found: C, 62. 90; H, 5. 45; C$_8$H$_8$O$_3$ requires C, 63. 15; H, 5. 30%).

G. 3 Pyrolysis of 4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]decane 9, 9-dioxide

  and an alternative synthesis of product.

a) Pyrolysis

A sample of 4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]decane 9, 9-dioxide

(486 mg, 2. 59 mmol) was pyrolysed at 625°C. The inlet temperature

was 110°C, the pressure 10^{-3}mmHg and the time taken was 5 h. The

pyrolysate was recovered with a dropping pipette and distilled in a

micro distillation apparatus to give cis-3, 4-divinyltetrahedrofuran (197

mg, 61. 5%) b. p. 41°C/41 mmHg, n$_D^{18}$ 1. 465 as a clear liquid.

I. R. ν $_{max}$ (liquid film) 3325, 1638, 1423, 1047, 991, 910 cm^{-1}.

^{1}H n. m. r. δ (CDCl$_3$) 5.9-5.6 (2H, m, 6-H, 8-H), 5.1-5.0 (4H, c d of

d J 5.3Hz 2.3Hz, 7 and 7'-H, 9 and 9'-H), 4.0-3.9 (2H, d of d J 8.5Hz,

7 Hz, 2-H, 5-H), 3.7-3.6 (2H, d of d J 8.5Hz, 6Hz, 2'-H, 5'-H),

3.1-2.8 (2H, m, 3-H, 4-H);

^{13}C n. m. r. δ (CDCl$_3$) 135.78 (C$_6$ and C$_8$), 116.15 (C$_7$ and C$_9$), 7.192

(C$_2$ and C$_3$), 47.54 (C$_3$ and C$_4$).

Mass spectrum m/e 124 (1.3%), 94 (45), 79 (100), 77 (38), 54 (43);

(Found: C, 41.00; H, 4.3. C$_8$H$_{12}$O requires C, 41.1; H, 4.6%).

  b) Alternative synthesis of cis-3,4-divinyltetrahydrofuran.

  i) meso-Dimethyl-1,5-hexadiene-3,4-dicarboxylate.

  2,5-Dioxo-cis-3,4-divinyltetrahydrofuran (8.43 g, 55 mmol) and

a few drops of concentrated sulphuric acid were added to methanol (130

ml) and the mixture was boiled under reflux for 24 h. The reaction

mixture was filtered and the solvent was removed in vacuo to leave a

clear oil (10.76 g) which crystallized and gave a colourless translucent

solid. Recrystallization of this solid from petroleum ether (40-60) gave meso-

dimethyl-1,5-hexadiene-3,4-dicarboxylate (5.6 g, 51%) m.p. 36-37°C

as colourless crystals.

I.R. ν_{max} (nujol) 1743, 1640, 1315, 1235, 1088, 1000, 892, 787,

695 cm^{-1};

^{1}H n. m. r. δ (CDCl$_3$), 5.9-5.6 (2H, d of d of d of d J 17Hz, 10Hz, 6Hz,

2.5Hz, 2-H, 5-H), 5.3-5.1 (4H, overlapping d of d J 17Hz, 1.5Hz,

10Hz, 1.5Hz, 1 and 1'-H, 6 and 6'-H) 3.62 (6H, s, -Me) 3.5-3.4 (2H,

d of d J 6Hz, 2.5Hz, 3-H, 4-H);

^{13}C n. m. r. δ (CDCl$_3$) 171.38 (C=O), 132.61 (C$_2$ and C$_5$), 119.04 (C$_1$

and C$_6$), 52.49 (-OMe), 51.51 (C$_3$ and C$_4$);

Mass spectrum m/e 198 (1%), 167 (18), 139 (23), 138 (27), 99 (100);

(Found: C, 60.45; H, 6.90. $C_{10}H_{14}O_4$ requires C, 60.60; H, 7.10%).

ii)   meso-3,4-Dihydroxymethyl-1,5-hexadiene.

To a stirred (mechanical) suspension of lithium aluminium hydride

(8.26 g, 220 mmol) in dry tetrahydrofuran (170 ml) was added dropwise a

solution of meso-dimethyl-1,5-hexadiene-3,4-dicarboxylate (10.76 g, 54 mmol)

in dry tetrahydrofuran (50 ml) over a period of ½ h.   The mixture was stirred

for 1 h at room temperature and then boiled under reflux for a further

1 h.   On cooling the excess lithium aluminium hydride was destroyed

by dropwise addition of water (8 ml), 4M sodium hydroxide solution

(8 ml) and water (24 ml).   The inorganic salts were removed by

filtration and the solvent removed from the filtrate in vacuo and gave

a clear oil (9.45 g).   This oil was dissolved in trichloromethane (60

ml) and this solution was washed with water (10 ml) to remove any

residual tetrahydrofuran.   The trichloromethane solution was dried

over magnesium sulphate and solvent was removed in vacuo to give a

clear oil (7.16 g).   This oil was distilled in a Kugelrohr (100°C/0.8

mmHg) to give meso-3,4-dihydroxymethyl-1,5-hexadiene (6.7 g, 87%)

as a clear oil n_D^{18} 1.4865.

I.R. ν_{max} (liquid film) 3700-3100 (-OH), 1640 (C=C), 1425, 1055, 995,

917 cm^{-1};

^{1}H n.m.r. δ(CDCl$_3$) 5.9-5.5 (2H, d of d of d J 16Hz, 11Hz, 8.3Hz,

2-H, 5-H), 5.2-5.0 (4H, overlapping d of d J 16 Hz, 2.5Hz, 11Hz, 2.5Hz,

1 and 1'-H, 6 and 6'-H), 3.8-3.4 (4H, two sets of d of d J 10.5Hz, 4.5Hz,

10.5Hz, 6.5Hz, 7 and 7'-H, 8 and 8'-H), 2.5-2.1 [4H, (2H, when sample

shaken with D_2O) br. m, 3-H, 4-H, -OH].

[13]C n.m.r. δ ($CDCl_3$) 137.46 (C_2 and C_5), 117.69 (C_1 and C_4) 63.51

(C_7 and C_8), 47.84 (C_3 and C_4);

Mass spectrum m/e 142 (0.3%), 124 (1), 94 (45), 79 (75), 54 (100);

(Found: C, 67.45; H, 10.10. $C_8H_{14}O_2$ requires C, 67.55; H, 9.90%).

iii) cis-3,4-Divinyltetrahydrofuran.

This was prepared by the method of Corfield et al.[133] A solution of me-

so-3,4-dihydroxymethyl-1,5-hexadiene (3.8 g, 27 mmol) and toluene-p-

sulphonic acid monohydrate (300 mg, 1.58 mmol) in dry benzene (60 ml)

was boiled under reflux for 40 h in a flask equipped with a Dean and

Stark apparatus. At the end of this period about ½ ml of water had

collected below the benzene in the Dean and Stark trap. The benzene

was removed from the reaction mixture under reduced pressure at

room temperature. The residue was distilled and gave cis-3,4-divinyl-

tetrahydrofuran (2.03 g, 62%) b.p. 41°C/41 mmHg as a clear liquid.

Analytical and spectroscopic data showed that it was identical in every

way to the compound prepared by the pyrolysis of 4-oxa-9-thiatricyclo-

[5.3.0.0^{2,6}]decane 9,9-dioxide.

G.4 Pyrolysis of 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

A sample of 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide

(320 mg, 1.55 mmol) was pyrolysed at 620°C. The inlet temperature

was 106°C, the pressure was 3 x 10^{-3} mmHg and the time taken for the

pyrolysis was 2 h. The pyrolysate a pale yellow liquid was transferred

to a microdistillation apparatus and distillation yielded cis-3,4-divinyl-

tetrahydrothiophene (27 mg, 24.6%) b.p. 140°C/16 mmHg as a clear

liquid. As in this case a solid residue (162 mg) remained in the inlet this was taken into account when estimating the yield of the reaction.

ν_{max} (liquid film) 1640 (C=C), 1450, 1425, 980, 917 cm^{-1};

^{1}H n. m. r. δ (CDCl$_3$) 6.0-5.0 (6H, divinyl system, 6-H, 7 and 7'-H, 8-H, 9 and 9'-H), 3.1-2.6 (6H, br. m, 2 and 2'-H, 3-H, 4-H, 5 and 5'-H);

^{13}C n. m. r. δ (CDCl$_3$) 136.32 (C$_6$ and C$_8$), 116.29 (C$_7$ and C$_9$), 51.09 (C$_3$ and C$_4$), 34.77 (C$_2$ and C$_5$);

Mass spectrum m/e 140 (30.3%), 86 (100), 85 (75.8);

(Found: C, 68.67; H, 8.59; C$_8$H$_{12}$S requires C, 68.52; H, 8.62%).

G. 5 Pyrolysis of 9-benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

A sample of 9-benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (90 mg, 0.32 mmol) was pyrolysed at 525°C. The inlet temperature was 160°C, the pressure was 1 x 10^{-3} mmHg and the time taken was 1 h. The pyrolysate which was a brown oil was dissolved in trichloromethane (2 ml) and this solution was transferred to a micro distillation apparatus. The trichloromethane was blown off in a stream of dry nitrogen and then distillation of the pyrolysate gave 1-benzyl-cis-3,4-divinylpyrrolidine (40 mg, 58%) b. p. 100°C/10^{-3} mmHg as a light brown oil.

I. R. ν_{max} (liquid film) 1642, 1454, 912, 802, 742, 700 cm^{-1};

^{1}H n. m. r. δ (CDCl$_3$) 7.4-7.2 (5H, m, Ph), 6.1-5.8 (6H, divinyl system, 6-H, 7 and 7'-H, 8-H, 9 and 9'-H), 3.6 (2H, s, -CH$_2$Ph) 3.1-2.9 (4H,

$\underline{m}$, 2 and 2'-H, 5 and 5'-H), 2.4-2.1 (2H, $\underline{m}$, 3-H, 4-H).

Mass spectrum m/e 213 (33%), 133 (28.6), 91 (86), 42 (100);

(Found: C, 84.61; H, 9.08; N, 6.66. $C_{15}H_{19}N$ requires C, 84.46;

H, 8.98; N, 6.57%; M^+, 213.1516. $C_{15}H_{19}N$ requires 213.1517).

G.6 Pyrolysis of 9-phenyl-8,10-dioxo-4-thia-9-azatricyclo- $[5.3.0.0^{2,6}]$decane 4,4-dioxide.

A sample of 9-phenyl-8,10-dioxo-4-thia-9-azatricyclo$[5.3.0.0^{2,6}]$-

decane 4,4-dioxide (283 mg, 6.97 mmol) was pyrolysed at 625°C. The

inlet temperature was 186°C, the pressure 2×10^{-3} mmHg and the

time taken was 53 minutes. The pyrolysate collected as a colourless

solid at the entrance to the cold trap. The pyrolysate was dissolved

in trichloromethane (20 ml) and the solution was filtered. The

solvent was removed to leave a colourless crystalline solid (210 mg).

Recrystallisation of this solid from ethanol gave 1-phenyl-cis-3,4-divinyl-

succinimide (120 mg, 52%) m.p. 134-136°C as colourless needles.

ν_{max} (nujol) 1767, 1598, 1496, 1459, 1382, 1264, 1188, 933, 753,

692 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 7.5-7.2 (5H, $\underline{m}$, Ph) 5.95-5.28 (6H, $\underline{c}$ divinyl

system, 6-H, 7 and 7'-H, 8-H, 9 and 9'-H), 3.8-3.7 (2H, $\underline{d}$ of $\underline{d}$

$\underline{J}$ 7Hz, 2Hz, 3-H, 4-H);

^{13}C n.m.r. δ (CDCl$_3$) 175.37 (C=O), 131.72 (Ph), 129.58 (Ph), 128.92

(Ph), 128.41 (Ph), 126.17 (C$_6$ and C$_8$), 121.31 (C$_7$ and C$_9$), 48.88

(C$_3$ and C$_4$);

Mass spectrum m/e 227 (62.5%), 157 (5), 119 (7.5), 108 (7.5), 91

(7.5), 80 (100), 79 (60):

(Found: C, 73.70; H, 5.82; N, 6.11. $C_{14}H_{13}NO_2$ requires C, 73.99; H, 5.77; N, 6.16%).

G. 7 Pyrolysis of 9-Phenyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]-

decane 4,4-dioxide.

A sample of 9-phenyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (60 mg, 0.23 mmol) was pyrolysed at 625°C. The inlet temp was 148°C, the pressure was 4 x 10^{-3} mmHg and the time taken was 1.25 h. The pyrolysate was examined by n.m.r. and this was consistent with the product being 1-phenyl-cis-3,4-divinylpyrrolidine. However attempts to pyrolyse larger amounts led to failure on account of the fact that substrate decomposed badly in the inlet. Also since the substrate itself was prepared somewhat fortuitously on only one occasion it was not possible to confirm the pyrolysis result.

^{1}H n.m.r. (60MHz) δ (CDCl$_3$) 7.45-7.24 (2H, m, o-PhH) 6.82-6.5 (3H, m, m and p-PhH), 6.2-4.9 (6H, c divinyl system, 6-H, 7-H, 8 and 8'-H, 9 and 9'-H), 3.5-2.9 (6H, c m, 2 and 2'-H, 3-H, 4-H, 5 and 5'-H).

G. 8 Pyrolysis of 9-methyl-8,10-dioxo-4-thia-9-azatricyclo-

[5.3.0.0^{2,6}]decane 4,4-dioxide.

A sample of 9-methyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]-decane 4,4-dioxide (1 g, 4.4 mmol) was pyrolysed at 625°C. The inlet temperature was 180°C, the pressure was 3 x 10^{-3} mmHg and the time taken was 7 h. There was a solid residue (0.24 g) left in the inlet at the end of the pyrolysis. The pyrolysate was a light brown oil and

this was distilled in a microdistillation apparatus to yield <u>1-methyl-</u> cis-

<u>3,4-divinyl succinimide</u> (0.32 g, 58%) b.p. $100^{\circ}/10^{-3}$ mmHg.

n_D^{19} 1.486 as a pale yellow oil.

I.R. ν_{max} (liquid film) 1690, 1435, 1380, 1290, 980, 930 cm^{-1};

^{1}H n.m.r. δ(CDCl$_3$) 6.1-5.22 (6H, <u>c</u> divinyl system, 6-H, 7 and 7'-H,

8-H, 9 and 9'-H), 3.8-3.6 (2H, <u>m</u>, 3-H, 4-H), 3.05 (3H, <u>s</u>, -Me);

^{13}C n.m.r. 176.59 (C=O), 129.64 (C$_6$ and C$_8$), 121.15 (C$_7$ and C$_9$),

49.75 (C$_3$ and C$_4$), 25.00 (-Me);

Mass spectrum m/e 165 (78%), 80 (100), 79 (100), 64 (88), 60 (55).

(Found: M$^+$, 165.0778. C$_9$H$_{11}$NO$_2$ requires 165.0790; C, 65.26;

H, 6.83, N, 8.65; C$_9$H$_{11}$NO$_2$ requires C, 65.44; H, 6.71; N,

8.48%).

H.   Pyrolysis of 3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide and its

Adducts.

H.1   Pyrolysis of 3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

A sample of 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (50 mg,

0.35 mmol) was pyrolysed at 500°C.   The inlet temperature was 70°C,

the pressure 5 x 10⁻³ mmHg and the time taken was 1.5 h.   Analysis

of the pyrolysate by n.m.r. showed that the product was entirely 1,3-

cyclohexadiene.   This indicates that the first formed product was

hexa-1,3,5-triene but the conditions of the pyrolysis were such that

it had undergone an electrocyclic reaction to give 1,3-cyclohexadiene.

In an attempt to prevent the hexa-1,3,5-triene isomerizing to

1,3-cyclohexadiene milder conditions for the pyrolysis were employed.

It was found that, if the furnace temperature was below 400°C, then

unchanged starting material was the "product!"   At a temperature

of 400°C the product consisted of 1,3-cyclohexadiene, cis-hexa-1,3,5-

triene and unchanged 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

The presence of cis-hexa-1,3,5-triene was confirmed by comparing

the ¹H n.m.r. of the pyrolysate to that of the published[134] spectra

for cis-hexa-1,3,5-triene.   Thus it was found impossible to get

cis-hexa-1,3,5-triene as the sole product of the pyrolysis.

H.2   Lithium aluminium hydride extrusion of sulphur dioxide from

3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.

This method used is that of Gaoni.[66]   3-Thiabicyclo[3,2.0]hept-

6-ene 3,3-dioxide (200 mg, 1.4 mmol) was added portionwise to a

suspension of lithium aluminium hydride (200 mg, 5.2 mmol) in boiling

ether (50 ml). The mixture was boiled under reflux for 1 h and then samples of the ether solution were withdrawn and analysed by gas chromatography. The column used was 30% β,β'-oxydipropionitrile on '80-100 Chromsorb W' at an oven temperature of 50°C. Two product peaks were observed and these were shown to be due to cis and trans-hexa-1,3,5-triene by peak enhancement experiments using an etheral solution containing authentic samples of cis and trans-hexa-1,3,5-triene prepared as described by Hwa et al.[135] Thus the importance of this result is that in this case the extrusion is non-stereospecific.

Control experiment

In order to check that the reaction conditions could not cause isomerization of cis to trans-hexa-1,3,5-triene a sample of the authentic mixture of cis and trans hexa-1,3,5-triene was dissolved in ether (25 ml). This solution was analysed by gas chromatography and then lithium aluminium hydride (200 mg, 5.2 mmol) was added and the mixture was boiled under reflux for 1 h. The mixture was then analysed again by gas chromatography under the same conditions as before and the traces obtained were identical to those obtained before the reflux period. Thus this confirms that the extrusion of sulphur dioxide by lithium aluminium hydride in this case is non-stereospecific.

H.3 Pyrolysis of 8-oxa-4-thiatricyclo[5.1.0.0^{2,6}]octane 4,4-dioxide.

A sample of 8-oxa-4-thiatricyclo[5.1.0.0^{2,6}]octane 4,4-dioxide (50 mg, 0.31 mmol) was pyrolysed at 580°C. The inlet temperature was 106°C, the pressure 3×10^{-3} mmHg and the time taken was fifteen minutes. The pyrolysate was dissolved in CDCl$_3$ (0.3 ml) and analysed

by ^{1}H and ^{13}C n.m.r. spectroscopy and comparison of the data with

known literature values$^{89d, 136}$ showed that the product was 4, 5-

dihydrooxepin (30 mg, 55%).

^{1}H n.m.r. δ (CDCl$_3$) 6.1 (2H, d J 7.5Hz, 2-H, 7-H), 5.2 (2H,

m, 3-H, 6-H), 2.3 (4H, m, 4 and 4'-H, 5 and 5'-H);

^{13}C n.m.r. δ (CDCl$_3$) 142.76 (C$_2$ and C$_7$), 108.5 (C$_3$ and C$_6$),

26.91 (C$_4$ and C$_5$),

H.4 **Pyrolysis of 5-(p-Methoxyphenyl)-3-oxa-9-thia-4-azatricyclo-**

[5.3.0.0^{2,6}]dec-4-ene 9,9-dioxide.

A sample 5-(p-methoxyphenyl)-3-oxa-9-thia-4-azatricyclo-

[5.3.0.0^{2,6}]dec-4-ene 9,9-dioxide (50 mg, 0.17 mmol) was pyrolysed

at 500°C. The inlet temperature was 148°C, the pressure was 7 x 10^{-3}

mmHg and the time taken was 3 h. The pyrolysate was dissolved in

trichloromethane (2 ml) and transferred to a sublimation apparatus.

The solvent was blown off in a stream of dry nitrogen and the residue

sublimed (100°C/5 x 10^{-3} mmHg) to yield colourless translucent crystals

of 4, 5-dihydro-3-(p-methoxyphenyl)-cis-4, 5-divinylisoxazole (13 mg, 33%)

m.p. 58-60°C.

I.R. ν$_{max}$ (nujol) 1607, 1512, 1245, 1177, 1043, 837, 810 cm^{-1};

^{1}H n.m.r. δ (CDCl$_3$) 7.8-6.8 (4H, AB pattern, aromatic H) 6.1-4.9

(6H, c, divinyl system, 6-H, 7 and 7'-H, 8-H, 9 and 9'-H), 4.1 (1H,

t, J Hz, 5-H), 3.66 (3H, s, -OMe), 3.2 (1H, br.s, 4-H);

^{13}C n.m.r. δ(CDCl$_3$) 160.86 (aromatic carbon ajacent to -OMe),

158.52 (C$_3$), 132.05 (C$_6$), 131.83 (C$_8$). 128.53 (Ar), 121.52 (C$_7$),

120.21 (C$_9$), 119.94 (Ar), 113.91 (Ar), 86.09 (C$_5$), 55.30 (-OMe),

55.16 (C_4).

Mass spectrum m/e 229 (100%), 173 (92);

(Found: C, 73.20; H, 6.50; N, 6.00; $C_{14}H_{15}O_2N$ requires

C, 73.35; H, 6.60; N, 6.10%).

H.5   High temperature Pyrolysis of 5-(p-methoxyphenyl)-3-oxa-9-

thia-4-azatricyclo[5.3.0.0^{2,6}]dec-4-ene-9,9-dioxide.

A sample of 5-(p-methoxyphenyl)-3-oxa-9-thia-4-azatricyclo-

[5.3.0.0^{2,6}]dec-4-ene 9,9-dioxide (79 mg, 0.26 mmol) was pyrolysed

at a furnace temperature of 625°C.   The inlet temperature was 144°C,

the pressure was 8 x 10^{-3} mmHg and the time taken for the pyrolysis

was 3 h.   The pyrolysate was dissolved in $CDCl_3$ (0.3 ml) and analysed

by ^{1}H n.m.r. and then by gas chromatography (2½% SE30 on 80-100

chromsorb) at an oven temperature of 180°C for four minutes and then

an increase of 6°C per minute to 240°C over a period of ten minutes.

The gas chromatograph showed 9 product peaks.   Thus due to prolifer-

ation of products this investigation was discontinued.

^{1}H n.m.r. δ ($CDCl_3$) 8-6.7 (aromatic peaks), 3.8 (various types

of -OMe).

H.6   Pyrolysis of 5-Phenyl-3-oxa-9-thia-4-azatricyclo[5.3.0.0^{2,6}]-

dec-4-ene-9,9-dioxide.

A sample of 5-phenyl-3-oxa-8-thia-4-azatricyclo[5.3.0.0^{2,6}]-

dec-4-ene 9,9-dioxide (50 mg, 0.19 mmol) was pyrolysed at 500°C.

The inlet temperature was 142°C, the pressure was 12 x 10^{-3} mmHg

and the time taken for the pyrolysis was 2 h.   Pyrolysate was dissolved

in $CDCl_3$ (0.3 ml) and transferred to a microdistillation apparatus.
The solvent was blown off in a stream of dry nitrogen and the residue
was distilled and gave <u>4,5-dihydro-3-phenyl-</u>cis-<u>4,5-divinylisoxazole</u>
(7 mg, 19%) b.p. $100^{\circ}C/0.1$ mmHg as a clear liquid.

I.R. ν_{max} (liquid film) 1447, 1346, 987, 926, 767, 693 cm^{-1};

^{1}H n.m.r. $\delta(CDCl_3)$ 7.74-7.64 (2H, <u>m</u>, <u>o</u>-ArH), 7.4-7.2 (3H, <u>m</u>,

<u>m</u> and <u>p</u>-ArH), 6.1-4.95 (7H, <u>c m</u>, 5-H, 6-H, 7 and 7'-H, 8-H, 9 and

9'-H), 4.14 (1H, <u>t J</u> 10Hz, 4-H);

Mass spectrum m/e 199 (15%), 143 (100), 117 (70), 115 (25);

(Found: C, 78.07; H, 6.42; N, 7.33; $C_{13}H_{13}NO$ requires C, 78.36;

H, 6.58; N, 7.03%).

H.7   <u>4-Thia-9,10-diazatricyclo[5.3.0.0^{2,6}]dec-9-ene-4,4-dioxide.</u>

a)   <u>Pyrolysis</u>

A sample of 4-thia-9,10-diazatricyclo[5.3.0.0^{2,6}]dec-9-ene-
4,4-dioxide (75 mg, 0.47 mmol) was pyrolysed at $450^{\circ}C$. The inlet
temperature was $118^{\circ}C$, the pressure was 5×10^{-3} mmHg and the
time taken for the pyrolysis was 2 h. The pyrolysate was dissolved
in $CDCl_3$ (0.3 ml) and examined by ^{1}H n.m.r. and by gas chromatography
(30% β,β'-oxydipropionitrile on 80-100 Chromsorb W) at a column
temperature of $90^{\circ}C$. Five product peaks were observed. The
products were not positively identified.

b)   <u>Photolysis</u>

4-Thia-9,10-diazatricyclo[5.3.0.0^{2,6}]dec-9-ene 4,4-dioxide
(50 mg, 0.3 mmol) was dissolved in deuterated acetonitrile and placed
in an n.m.r. tube. The tube was then irradiated with a 100W medium

pressure mercury lamp through a pyrex filter for 58 h.   The reaction

was monitored by ^{1}H n. m. r.   The resonances in the region 4-6 δ almost

disappeared while new resonances appeared in the region 0-2δ.   Other

more subtle changes took place in the main body of the spectrum.   The

solvent was removed in vacuo to leave a yellow oil which on trituration

with ether gave a brown solid (8 mg).   However attempts to identify

this solid were unsuccessful.

I.   Miscellaneous Preparations and Pyrolyses

I. 1   meso-1, 5-Hexadiene-3, 4-dicarboxylic acid.

2, 5-Dioxo-cis-3, 4-divinyltetrahydrofuran (11.6 g, 76 mmol) was suspended in water (50 ml) and boiled for a few minutes.   The mixture became homogeneous and when cooled gave a colourless crystalline precipitate.   The precipitate was recovered by filtration and dried in vacuo to yield meso-1, 5-hexadiene-3, 4-dicarboxylic acid (9.06 g, 70%) m. p. 183-185°C.

I. R. ν_{max} (nujol) 1697 (C=O), 987, 927, 767, 667 cm^{-1};

^{1}H n. m. r. δ [(CD$_3$)$_2$CO] 6. 1-5. 7 (4H, $\underline{d}$ of $\underline{d}$ of $\underline{d}$ of $\underline{d}$ and broad signal overlapping $\underline{J}$ 16. 5Hz, 10Hz, 6Hz, 2. 5Hz, 2-H, 5-H), 5. 3-5. 1 (4H, overlapping $\underline{d}$ of $\underline{d}$ $\underline{J}$16. 5 Hz, 2Hz, 10Hz, 2Hz, 1 and 1'-H, 6 and 6'-H), 3. 4-3. 3 (2H, $\underline{d}$ of $\underline{d}$ $\underline{J}$ 6Hz, 2. 5Hz, 3-H, 4-H);

^{13}C n. m. r. δ [(CD$_3$)$_2$CO] 172. 16 (C=O), 134. 06 (C$_2$ and C$_5$), 118. 59 (C$_1$ and C$_6$), .52. 82 (C$_3$ and C$_4$);

Mass spectrum m/e 157 (28%), 134 (40), 124 (100);

(Found: C, 56. 25; H, 5. 9.   C$_8$H$_{10}$O$_4$ requires C, 56. 5; H, 5. 9%).

I. 2   7-Ethoxycarbonyl-3-thiabicyclo[3. 2. 0]heptane-6-carboxylic acid 3, 3-dioxide.

3-Thiabicyclo[3. 2. 0]heptane-6, 7-dicarboxylic acid 3, 3-dioxide (34 g, 145 mmol) was taken up in boiling ethanol.   When the solution cooled a white crystalline solid was obtained.   Recovery of the solid by filtration gave 7-ethoxycarbonyl-3-thiabicyclo[3. 2. 0]heptane-6-carboxylic acid 3, 3-dioxide (33.85 g, 89%) m. p. 152-154°C as colourless crystals.

I. R. 1735 (C=O), 1300 (SO$_2$), 1188, 1142 cm^{-1};

^{1}H n. m. r. δ [(CD$_3$)$_2$CO] 6. 5-5. 3 (1H, br. s, -COOH), 3. 7-3. 3 (2H,

q, -CH$_2$-), 3. 0-2. 5 (8H, m, 1-H, 2 and 2'-H, 4 and 4'-H, 5-H, 6-H,

7-H), 0. 75-0. 55 (3H, t, -Me);

Mass spectrum m/e M$^+$ not observed;

(Found: C, 46.14; H, 5.46; C$_{10}$H$_{14}$O$_6$S requires C, 46.17; H, 5. 38%).

I. 3   Attempted Vinylation of 6, 7-dihydroxymethyl-3-thiabicyclo-
        [3. 2. 0]heptane 3, 3-dioxide.[137]

        The general method used in the attempts was that of Watanabe
et al.[138]

Method (i)

        6, 7-Dihydroxymethyl-3-thiabicyclo[3. 2. 0]heptane 3, 3-dioxide

(1 g, 4. 9 mmol) mercuric acetate (0. 2 g, 0. 6 mmol) and one drop of

concentrated sulphuric acid was added to ethyl vinyl ether (3. 0 g) and

the resultant mixture was boiled under reflux for 2 h and then a further

portion of ether (1. 5 g) was added.   The mixture was boiled under

reflux for a further seven days and the solid residue was removed by

filtration.   The solvent was removed from the filtrate under reduced

pressure to give a colourless solid (193 mg).   The solid residue was

shown to be a mixture of mercuric acetate and starting material by

examination of its I. R. spectrum.   Although the colourless solid was

not positively identified ^{1}H n. m. r. showed that it did not contain any

vinyl groups and thus was not the desired product.

Method (ii)

Since the main difficulty in the vinylation experiment is the insolubility of the substrate the experiment was carried out using a Soxlet apparatus. This time the diol was placed in the Soxlet and the ether (100 ml) used to extract it. However this also proved unsuccessful.

I.4 Attempted preparation of 5,6-divinyl-3,8-dioxadeca-1,9-diene.[137]

meso-3,4-Dihydroxymethyl-1,5-hexadiene (1.02 g, 7.2 mmol), mercuric acetate (0.5 g, 1.6 mmol) and one drop of concentrated sulphuric acid were added to ethyl vinyl ether (25 ml). This mixture was boiled under reflux for 48 h and then mercuric acetate (0.5 g) was added again and this was repeated 24 h later. After 96 h the mixture was filtered and the solvent removed in vacuo to leave an oil. This was distilled bulb-to-bulb in a Kugelrohr and the clear oil (210 mg) distils b. to b. $110^{\circ}C$ 10^{-2} mmHg was obtained. Although the spectral properties of this oil were consistent with it being the desired compound this was not confirmed by analysis.

^{1}H n.m.r. 6.6-6.2 (2H, d of d J 14.6Hz 7.3Hz, 2-H, 9-H), 5.9-5.5 (2H, m, 11-H, 13-H), (4H, m, 12 and 12'-H, 13 and 13'-H), 4.2-3.9 (4H, m, 1 and 1'-H, 10 and 10'-H), 3.7 (4H, d J 4Hz, 4 and 4'-H, 7 and 7'-H), 2.6-2.3 (2H, m, 5-H, 6-H);

^{13}C n.m.r. 151.70 (C_2 and C_9), 137.27 (C_{11} and C_{13}), 117.37 (C_{12} and C_{14}), 80.30 (C_1 and C_{10}), 69.12 (C_4 and C_7), 44.41 (C_5 and C_6).

I. 5   Pyrolysis of the product from the attempted preparation of

5, 6-divinyl-3, 8-dioxadecan-1, 9-diene. [137]

Method (i)

A sample of the clear oil (56. 5 mg, 0. 29 mmol), obtained as

described in I.4, was pyrolysed at a furnace temperature of 500°C.

The inlet was at room temperature, the pressure was 6×10^{-3} mmHg,

and the pyrolysis was five minutes.   The pyrolysate was examined by

^{1}H n. m. r. but the product was not positively identified.

^{1}H n. m. r. δ (CDCl$_3$) 9. 6 (br. s), 6. 5-6. 3 (d of d J 14Hz 7Hz),

5. 9-5. 4 (c m), 5. 3-4. 9 (c m), 4. 22 (d J 2. 5Hz), 4. 15-3. 9 (c m),

3. 72 (d J 5Hz), 2. 6-2. 3 (c m), 2. 14 (s), 1. 4 (c m).

Method (ii)

A sample of the oil was dissolved in [^{2}H$_8$] toluene and sealed

in an n. m. r. tube.   The tube was then placed in a bath of boiling

xylene (150°C) for 5 days but during this time no change in the n. m. r.

spectrum of the substrate was observed.

I. 6   Pyrolysis of Dimethyl-3-thiabicyclo[3, 2. 0]heptane-6, 7-dicarboxylate

3, 3-dioxide.

A sample of dimethyl-3-thiabicyclo[3. 2. 0]heptane-6, 7-dicar-

boxylate 3, 3-dioxide (1 g, 3. 8 mmol) was pyrolysed at 625°C.   The

inlet temperature was 180°C, the pressure was 1×10^{-3} mmHg, and

the time taken for the pyrolysis was 1. 5 h.   The pyrolysate, a very

volatile pale yellow liquid, was distilled in a micro distillation apparatus

at atmospheric pressure and gave cis, trans-octa-2, 6-diene-1, 8-

dicarboxylic acid dimethyl ester (0.574 g, 76%) as a clear liquid.

Owing to the very volatile nature of the compound elemental analysis

failed but exact mass measurement of the parent peak in the mass

spectrum was consistent with the assigned structure. Also the ^{1}H

n.m.r. and I.R. data were in agreement with published values.^{139}

I.R. ν_{max} (liquid film) 1725 (C=O), 1660 (C=C) 1440, 1200 cm^{-1};

^{1}H n.m.r. (360 MHz) δ(CDCl$_3$) 7.010-6.928 (1H, $\underline{d}$ of $\underline{t}$ $\underline{J}$ 16Hz 7Hz,

3-H), 6.233-6.160 (1H, $\underline{d}$ of $\underline{t}$ $\underline{J}$ 12Hz 7.5Hz, 6-H), 5.895-5.809 (2H

$\underline{m}$, 2-H, 7-H), 3.727 (3H, $\underline{s}$ -OMe), 3.715 (3H, $\underline{s}$, -OMe), 2.874-2.808

(2H, $\underline{m}$, 4 and 4'-H) 2.403-2.339 (2H, $\underline{m}$, 5 and 5'-H);

^{13}C n.m.r. δ (CDCl$_3$) 166.58 (C=O), 166.28 (C=O), 147.91 (C$_2$ or C$_7$)

147.54 (C$_2$ or C$_7$), 121.53 (C$_3$ or C$_6$), 120.29 (C$_3$ or C$_6$), 51.15 (C$_4$),

50.81 (C$_5$), 31.13 (-OMe), 26.98 (-OMe).

Mass spectrum m/e 198 (1%), 167 (43), 166 (33), 138 (100).

(Found: M$^+$, 198.090244 C$_{10}$H$_{14}$O$_4$ requires 198.089202 error

less than 6 ppm).

I.7   Pyrolysis of meso-dimethyl-1,5-hexadiene-3,4-dicarboxylate.

Method (i)

A sample of meso-dimethyl-1,5-hexadiene-3,4-dicarboxylate (100 mg,

0.5 mmol) was pyrolysed at a furnace temperature of 625°C. The inlet

temperature was 50°C, the pressure 1 x 10^{-3} mmHg and the time taken

was $\frac{1}{2}$ h. The pyrolysate was dissolved in CDCl$_3$ (0.3 ml) and examined

^{1}H n.m.r. This showed the presence of cis, trans-octa-2,6-diene-

1,8-dicarboxylic acid dimethyl ester which had been prepared in the

previous pyrolysis.

Method (ii)

A sample of meso-dimethyl-1, 5-hexadiene-3, 4-dicarboxylate was dissolved in $[^2H_8]$toluene and placed in an n. m. r. tube. The tube was placed in a bath of boiling toluene and the reaction progress was monitored over a period of 5 days by ^1H n. m. r. At the end of this period all the substrate signals had disappeared to be replaced by those of cis, trans-octa-2, 6-diene-1, 8-dicarboxylic acid dimethyl ester.

J.   X-Ray Structures and other Structural Evidence.

J. 1   Structure of 1,5-hexadiene-3,4-dicarboxylic acid.

The assigned stereochemistry of 1,5-hexadiene-3,4-dicar-boxylic acid (106) was validated,[140] by its essentially quantitative chemical transformation to meso-2,3-diethylsuccinic acid (107) m. p. 190-191°C (dec.) (lit.,[141] 192°C; cf. racemic acid, m. p. 129°C), by hydrogenation over 10% palladium-charcoal at room temperature (Scheme 47).
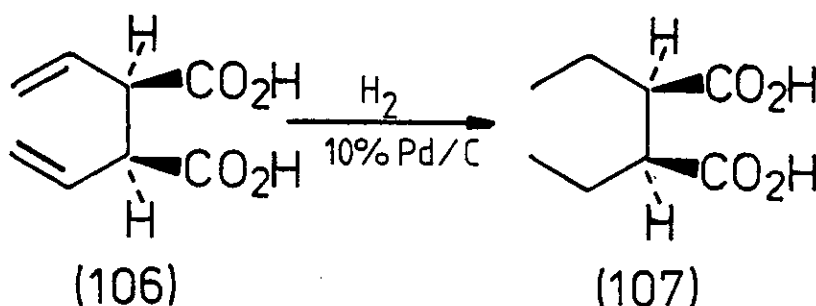
Scheme 47

J. 2   X-Ray structure of 9-phenyl-8,10-dioxo-4-thia-9-azatri-cyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

9-Phenyl-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (108) was recrystallized from glacial acetic acid.   The solution was left to stand overnight in a thermos containing hot water, allowing slow crystallization and giving large colourless crystals m. p. 310-315°C.

Crystal data $C_{14}H_{13}NO_4S$, M = 291, orthorhombic, a = 9.664± 0.001, b = 10.510±0.001, c = 25.407±0.003Å, V = 2581 Å^3, Z = 8, D_c = 1.498 g cm^{-3}. Space group Pbca. Structure was refined to an R factor of 0.072.
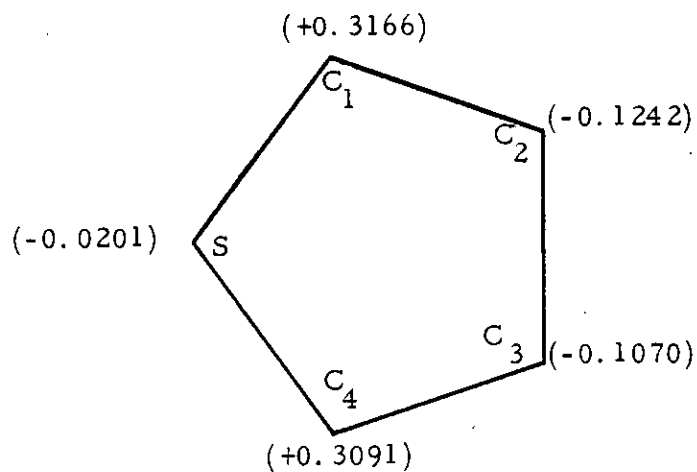
The molecular geometry of (108) is shown in Figure 8. The bond lengths (Å) given in Figure 8 have standard de viations ±0. 003- 0. 005Å. Bond angles (°) and standard deviations are given in Table 1. The numbering used for (108) is arbitrary.
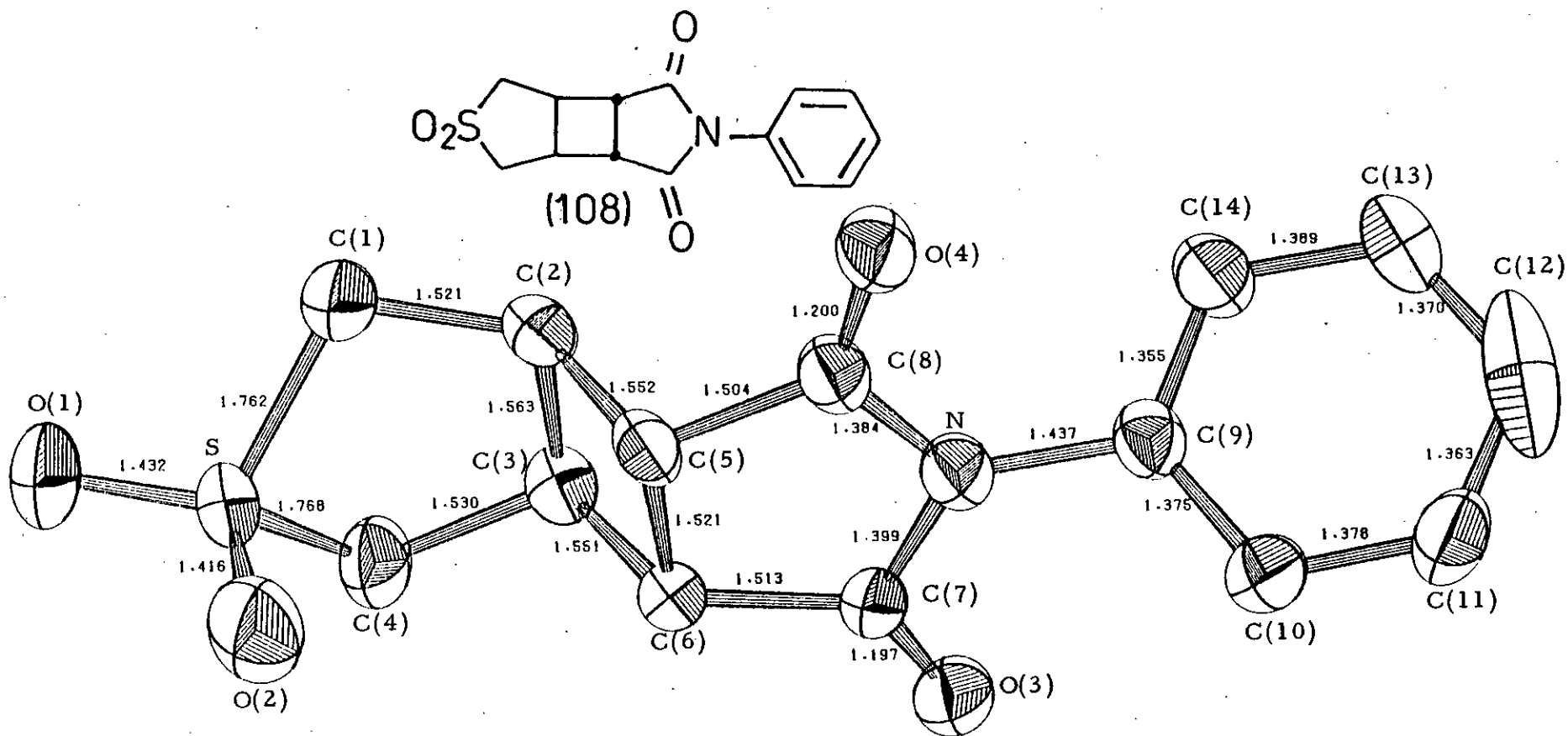
Mean plane displacement s

Cyclobutane ring is nearly planar but slightly saddle shaped:- Perpendicular displacements from least squares plane in Å.
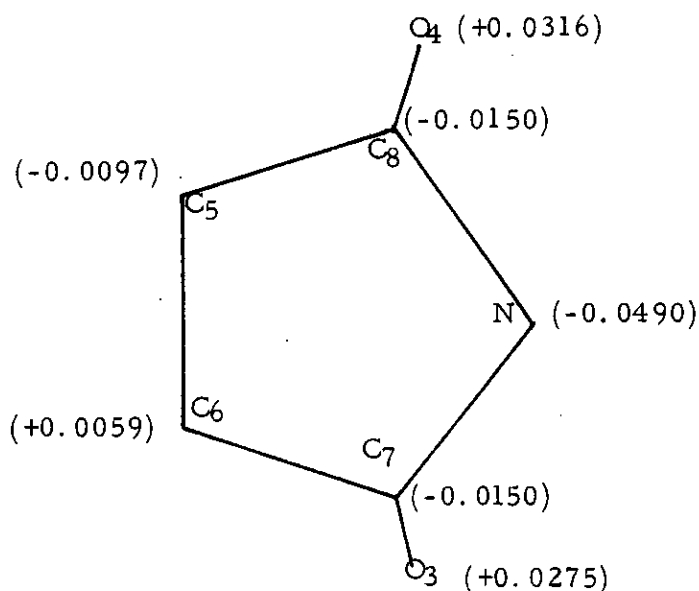
(+0. 0093) C_3 C_2 (-0. 0093)

(-0. 0085) C_6 C_5 (+0. 0084)

sulphone ring:-

(+0. 3166)

C_1

C_2 (-0. 1242)

(-0. 0201) S

C_3 (-0. 1070)

C_4

(+0. 3091)
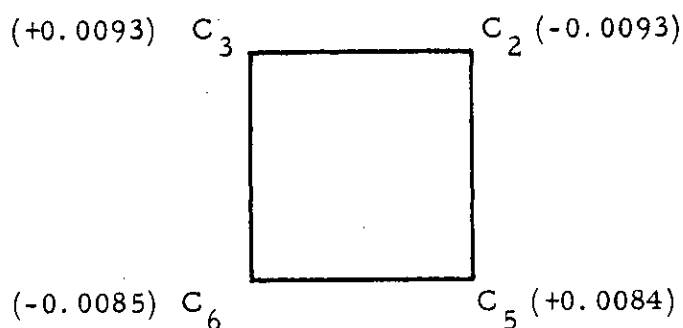
Fig. 8. A computer generated perspective drawing of 9-phenyl-8,10-dioxo-4-thia-9-aza-tricyclo-[5.3.0.0^{2,6}]decane 4,4-dioxide (108) with bond lengths in Å. Hydrogens have been omitted for clarity.

TABLE 1

Bond angles (°) in (108). The e. s. d. 's are given in parenthesis

O(1)-S-O(2)	118.0(2)	C(3)-C(6)-C(5)	90.7(3)
O(1)-S-C(1)	108.7(2)	C(3)-C(6)-C(7)	114.0(3)
O(1)-S-C(4)	108.9(2)	C(3)-C(6)-H(6)	114.6(24)
O(2)-S-C(1)	111.6(2)	C(5)-C(6)-C(7)	105.5(3)
O(2)-S-C(4)	111.7(2)	C(5)-C(6)-H(6)	116.0(24)
C(1)-S-C(4)	95.7(2)	C(7)-C(6)-H(6)	113.8(24)
C(7)-N-C(8)	113.4(3)	O(3)-C(7)-N	124.5(3)
C(7)-N-C(9)	123.0(3)	O(3)-C(7)-C(6)	128.1(3)
C(8)-N-C(9)	.123.6(3)	N - C(7)-C(6)	107.4(3)
S-C(1)-C(2)	105.5(3)	O(4)-C(8)-N	124.3(3)
S-C(1)-H(101)	107.0(29)	O(4)-C(8)-C(5)	127.5(3)
S-C(1)-H(201)	101.9(37)	N - C(8)- C(5)	108.2(3)
C(2)-C(1)-H(101)	110.0(29)		
C(2)-C(1)-H(201)	117.4(37)	N - C(9)- C(10)	119.4(3)
H(101)-C(1)-H(201)	113.8(47)	N - C(9)- C(14)	118.6(3)
		C(10)-C(9)-C(14)	122.0(4)
C(1)-C(2)-C(3)	110.0(3)		
C(1)-C(2)-C(5)	116.5(3)	C(9)-C(10)-C(11)	118.1(4)
C(1)-C(2)-H(102)	109.5(23)	C(9)-C(10)-H(10)	118.5(26)
C(3)-C(2)-C(5)	89.1(3)	C(11)-C(10)-H(10)	123.4(26)
C(3)-C(2)-H(102)	116.6(23)		
C(5)-C(2)-H(102)	114.1(23)	C(10)-C(11)-C(12)	121.6(4)
		C(10)-C(11)-H(11)	116.8(30)
C(2)-C(3)-C(4)	110.5(3)	C(12)-C(11)-H(11)	121.6(30)
C(2)-C(3)-C(6)	89.4(3)		
C(2)-C(3)-H(103)	114.8(2)	C(11)-C(12)-C(13)	118.9(4)
C(4)-C(3)-C(6)	116.1(3)	C(11)-C(12)-H(12)	122.7(29)
C(4)-C(3)-H(103)	112.1(21)	C(13)-C(12)-H(12)	118.3(29)
C(6)-C(3)-H(103)	112.2(21)		
		C(12)-C(13)-C(14)	121.0(4)
S-C(4)-C(3)	105.5(3)	C(12)-C(13)-H(13)	123.6(29)
S-C(4)-H(104)	107.1(22)	C(14)-C(13)-H(13)	115.4(29)
S-C(4)-H(204)	112.3(31)		
C(3)-C(4)-H(104)	105.9(22)	C(9)-C(14)-C(13)	118.5(4)
C(3)-C(4)-H(204)	113.2(31)	C(9)-C(14)-H(14)	121.3(32)
H(104)-C(4)-H(204)	112.4(38)	C(13)-C(14)-H(14)	120.3(33)
C(2)-C(5)-C(6)	90.9(3)		
C(2)-C(5)-C(8)	111.8(3)		
C(2)-C(5)-H(5)	117.7(26)		
C(6)-C(5)-C(8)	105.5(3)		
C(6)-C(5)-H(5)	119.7(26)		
C(8)-C(5)-H(5)	109.7(26)		

nitrogen ring:-

O₄ (+0.0316)

(-0.0150)
C₈

(-0.0097)

C₅

N (-0.0490)

(+0.0059)
C₆

C₇

(-0.0150)

O₃ (+0.0275)

Angle between sulphone ring and cyclobutane ring = 100.4°

Angle between cyclobutane ring and nitrogen ring = 113.5°

Angle between nitrogen ring and benzene ring   = 64.0°.

J.3   X-Ray structure of 1-phenyl-3,4-divinylsuccinimide.

1-Phenyl-3,4-divinylsuccinimide (109) was recrystallized

from ethyl acetate.   The solution was left to stand overnight in a

thermos containing hot water, allowing slow crystallization and giving

large colourless crystals m.p. 134-136°C.

The structure was refined to an R factor of 0.081.

The molecular geometry of (109) is shown in Figure 9.   The bond

lengths (Å) given in Figure 9 have standard deviations ±0.015Å.   The

numbering used for (109) is arbitrary.
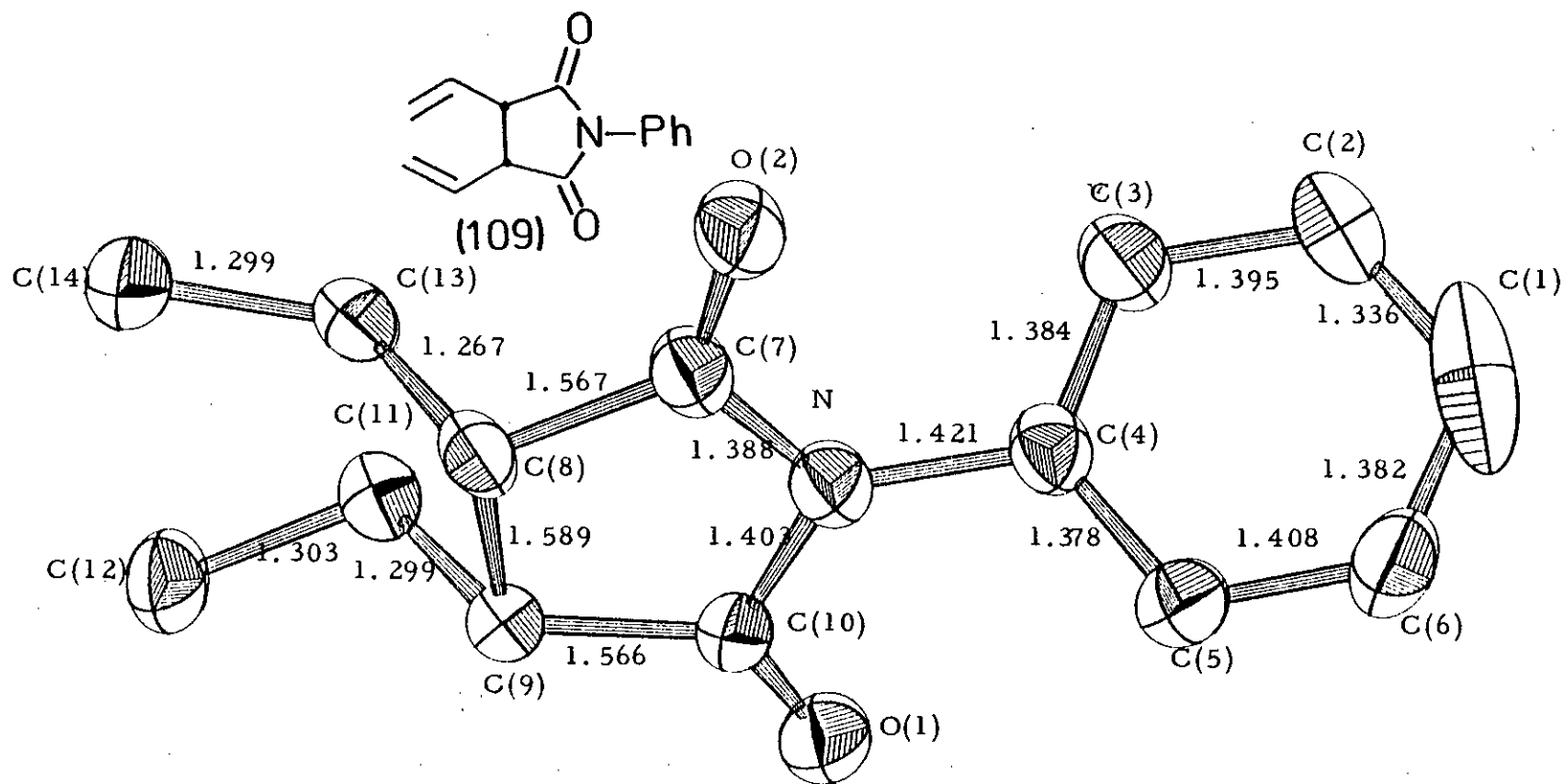
Fig. 9   A perspective drawing of 1-Phenyl-cis-3,4-divinylsuccinimide (109) with bond lengths in Å.

DISCUSSION

CONTENTS

A.   3, 5-Dioxo-4-oxa-9-thiatricyclo$[5.3.0.0^{2,6}]$decane 9, 9-dioxide.

A. 1   Preparation and stereochemistry of 3, 5-dioxo-4-oxa-9- thiatricyclo$[5.3.0.0^{2,6}]$decane 9, 9-dioxide.

As mentioned in the introduction, the title compound (1), which possesses some activity as a plant growth inhibitor,[142] has been prepared in 51% yield by photolysis of butadiene sulphone (21) and maleic anhydride for 24 h in anhydrous acetone[3] (Scheme 48).
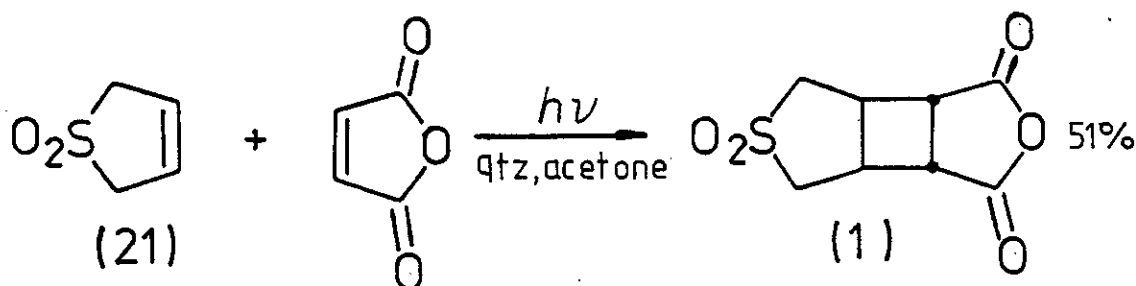
Scheme 48

No details of the absolute stereochemistry of compound (1) were reported at the time, but this is not surprising, since as shown in Figure 10 the 100 MHz proton n.m.r. spectrum is of little use in this respect because the various resonances overlap and preclude unambiguous assignment.   Little information can also be obtained from [13]C n.m.r. spectroscopy (see figure 11) other than that the spectrum is consistent with either a syn or an anti-structure for which a four line spectrum is expected.

The only absolute way to determine the configuration of (1) is by X-ray analysis but the lack of suitable crystals prevented this approach.   However, as shown in scheme 49 the anhydride (1) could
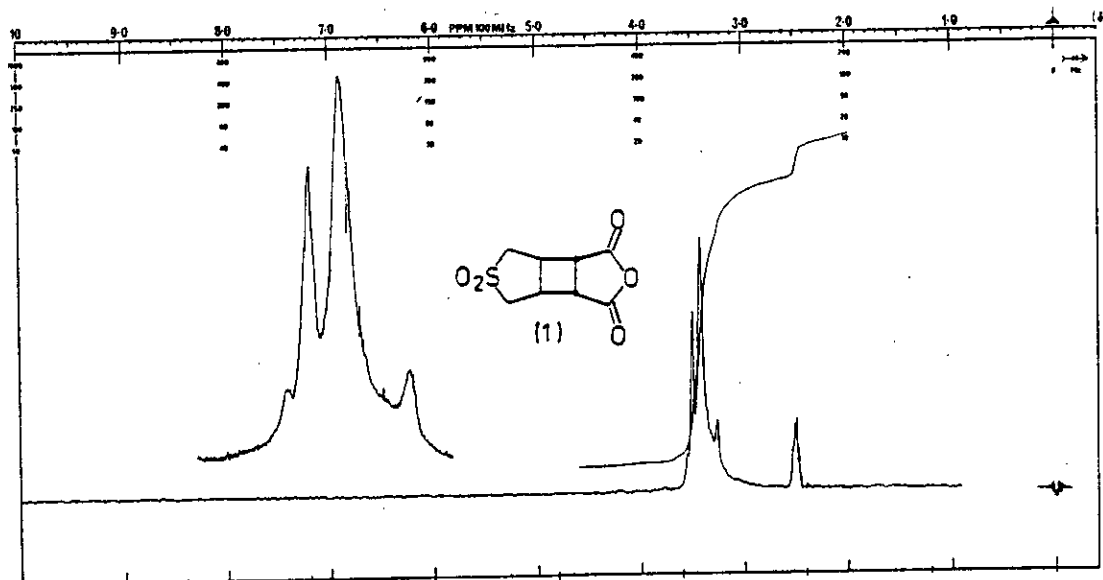
Fig. 10. 100MHz ^{1}H n. m. r. spectrum of 3, 5-dioxo-4-oxa-9-thiatricyclo-
[3. 5. 0. 0$^{2, 6}$]decane 9, 9-dioxide (1). Inset is an expansion of
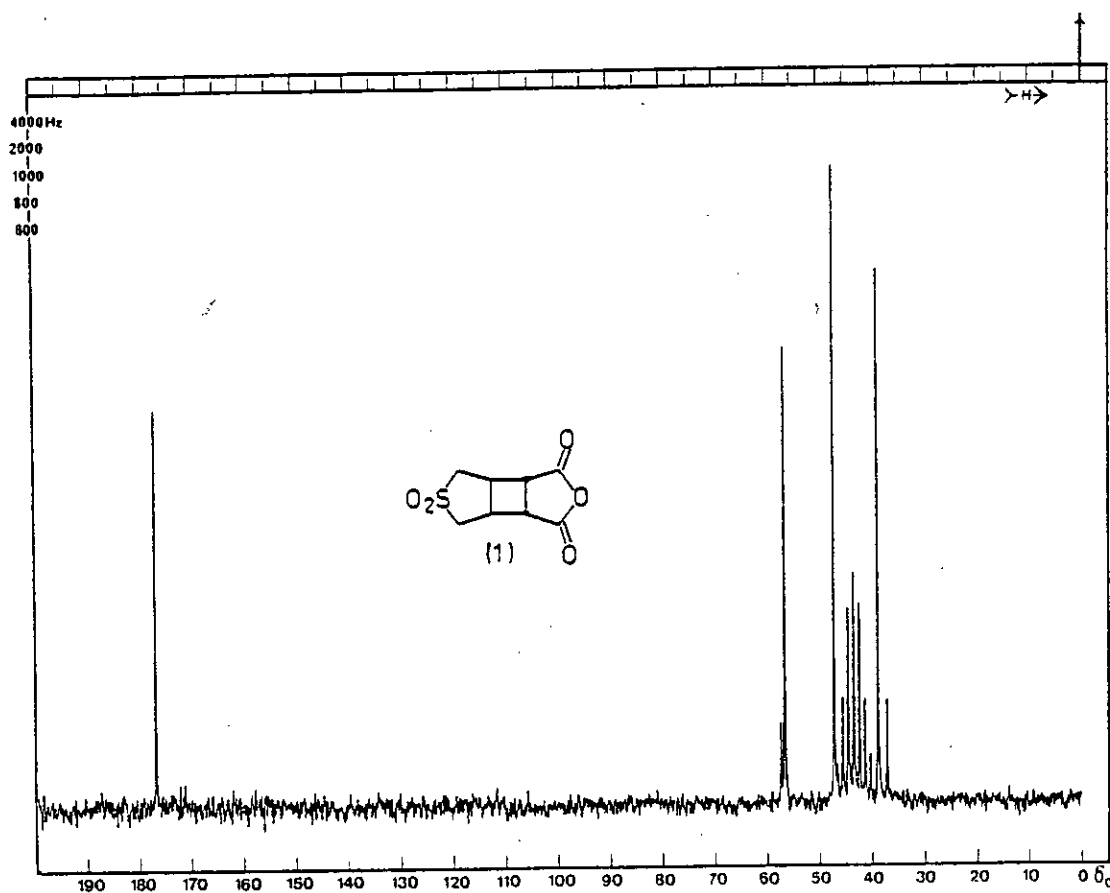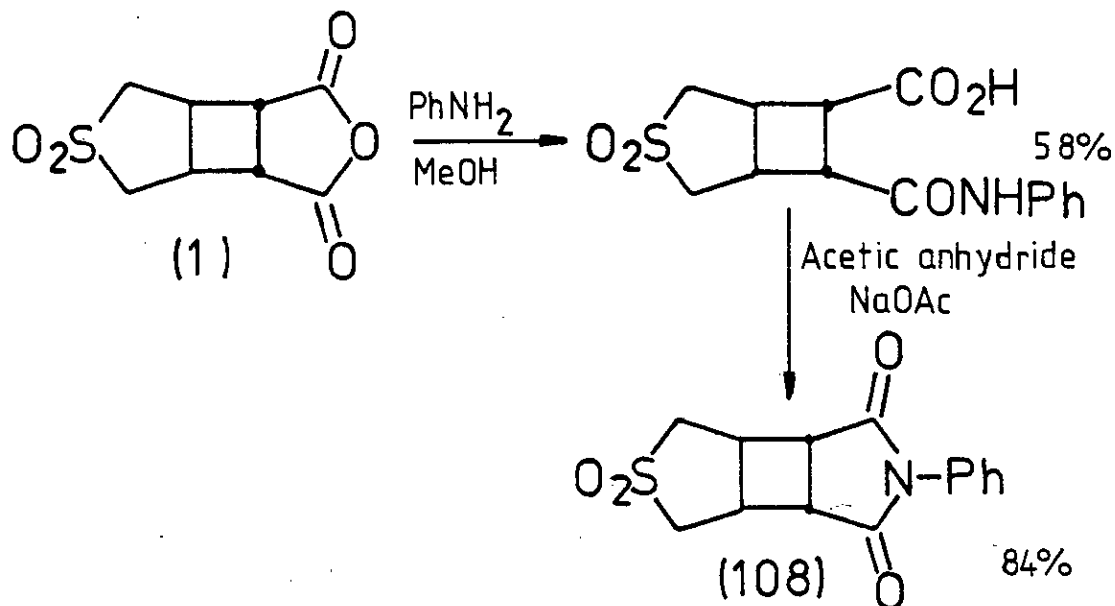the complex multiplet in the 3. 0-3. 5 δ region.

Fig. 11. 25. 2MHz ^{13}C n. m. r. spectrum of 3, 5-dioxo-4-oxa-9-thiatricyclo-
[5. 3. 0. 0$^{2, 6}$]decane 9, 9-dioxide (1).

be converted into its imide derivative (108) which on careful recrystal-

lization from glacial acetic acid gave colourless crystals ideal for

X-ray analysis.   This showed that the compound possessed an _anti_-

Scheme 49

structure, details of which are shown in Figure 8 (p. 112).   As can

be seen, the cyclobutane ring is essentially square planar, whereas

the sulphone ring is puckered and the imide ring is essentially planar

presumably because of the sp^2 hybridised carbons at C7 and C8.

The sulphone and the imide rings form dihedral angles of 100.4 and

113.5°, respectively with the mean cyclobutane plane.   The bond

lengths and bond angles are within expected limits.

Since it is likely that no change occurs in the stereochemistry

about the C2-C6 bond in the conversion of (1) into (108), it seems

reasonable to assume that the _anti_-configuration can also be assigned

to (1) and to the variety of compounds subsequently derived from it.

A. 2 Pyrolysis of 3, 5-dioxo-4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]decane

9, 9-dioxide.

Evidence presented in the introduction shows that pyrolysis of

sulpholenes provides a useful synthesis of dienes. The present

investigation sought to use pyrolysis of compounds of the general type

(110) as a preparative route to cis-1, 2-divinyl compounds, e.g. (110)->

(111) (Scheme 50). It was decided to use the flash vacuum pyrolysis

(F. V. P.) technique to achieve this objective.

(110)   (111)
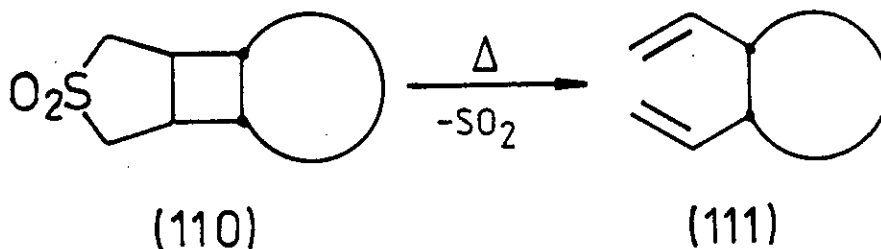
Scheme 50

Whilst pyrolysis has long been of great preparative utility in

organic chemistry it is only recently that flash vacuum pyrolysis has

found widespread application.[143] The principle of this technique is

that the substrate is sublimed under high vacuum into a hot zone where

it resides for only a short time (10^{-3}-1s), whereupon the products

are swept into a trap cooled to very low temperatures (-196°C).

Its main advantage over conventional pyrolyses is that the dilute

conditions and rapid separation of the primary products from the

reaction zone help prevent secondary reactions taking place. As a

result it is usually clean, convenient and efficient, and frequently has

advantages over other synthetic methods for the preparation of

sensitive or strained compounds.

In this connection it is noteworthy that flash vacuum pyrolysis has been used to great advantage in the field of cyclophane chemistry,[144] cumulating in the recent synthesis of superphane (112) which was once described by Vögtle[145] as the ultimate achievement of work in this area.

(112)
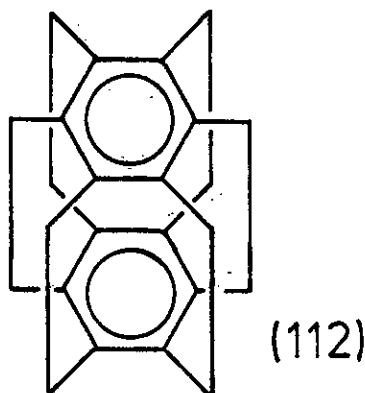
Recently Seybold[143] has reviewed the technique in general, while Vögtle and Rossa[12] have focused on its application to sulphones in particular. A very recent monograph by Brown[146] has emphasized that preparative pyrolysis of organic compounds are best run in flow systems.

Upon pyrolysis at 630°C under f.v.p. conditions, the anhydride (1) gave a pale yellow oil which hydrolysed readily on exposure to the atmosphere. Nevertheless, the product could be purified by bulb-to-bulb distillation at 65°C/0.1mmHg to give a clear liquid which on the basis of analytical, spectral and chemical evidence was characterized as 2,5-dioxo-cis-3,4-divinyltetrahydrofuran (113) (Scheme 51). Elemental analysis gave percentage composition for carbon and
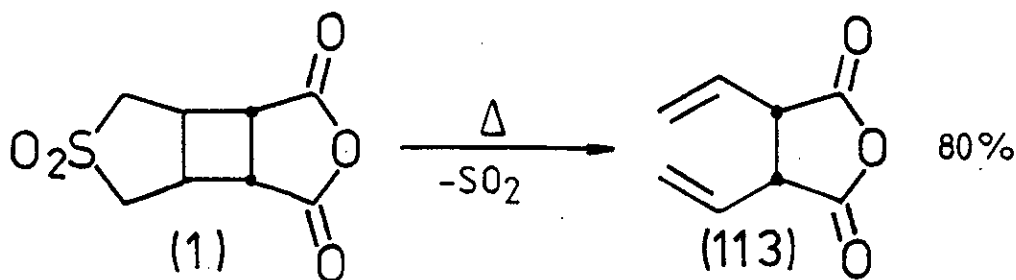
Scheme 51

hydrogen consistent with an empirical formula $C_8H_8O_3$. This was

confirmed by observation in the mass spectrum of a peak at m/e 152.

The 100 MHz ^{1}H n.m.r. spectrum of the product is shown in

figure 12 and corroborates the structure as 2, 5-dioxo-cis-3, 4-divinyl-

tetrahydrofuran (113). Thus, the complex multiplet at 5.9-5.3 δ is

ascribed to the cis-divinyl system in (113) and an examination of the

fine detail shows that this resonance is very similar to that reported

by Brown[87] for cis-divinylcyclopropane. The doublet of doublets

(J 4.5Hz, 2Hz) can be assigned to the protons 3-H and 4-H. The ^{13}C

n.m.r. spectrum reproduced in Figure 13 is also consistent with the

assigned structure. The anhydride moiety in (113) gives rise to a

very broad band at 1900-1700 cm^{-1} in the I.R. spectrum, while the

band at 1642 cm^{-1} is due to an olefinic stretch.

The cis-stereochemistry of (113) was validated by its essentially

quantitative transformation to meso-2, 3-diethylsuccinic acid (107)

m.p. 190-191°C (decomp.) (lit.[141] 192°C) (Scheme 52). Thus the

possibility of trans-stereochemistry could be ruled out as the trans-

isomer would have given a racemic mixture of (±)-2, 3-diethylsuccinic

acid (m.p. 129°C[141]).
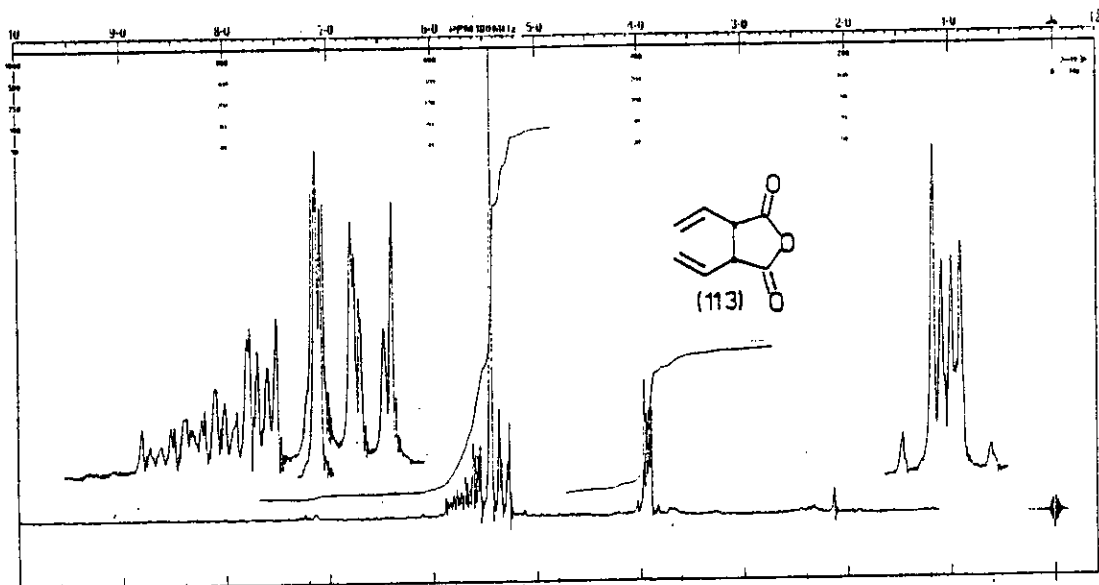
Fig. 12. 100MHz ^{1}H n. m. r. spectrum of 2, 5-dioxo-cis-3, 4-divinyl-
tetrahydrofuran (113). Insets are expansions of the olefinic
and 3. 8-4. 0δ regions respectively.
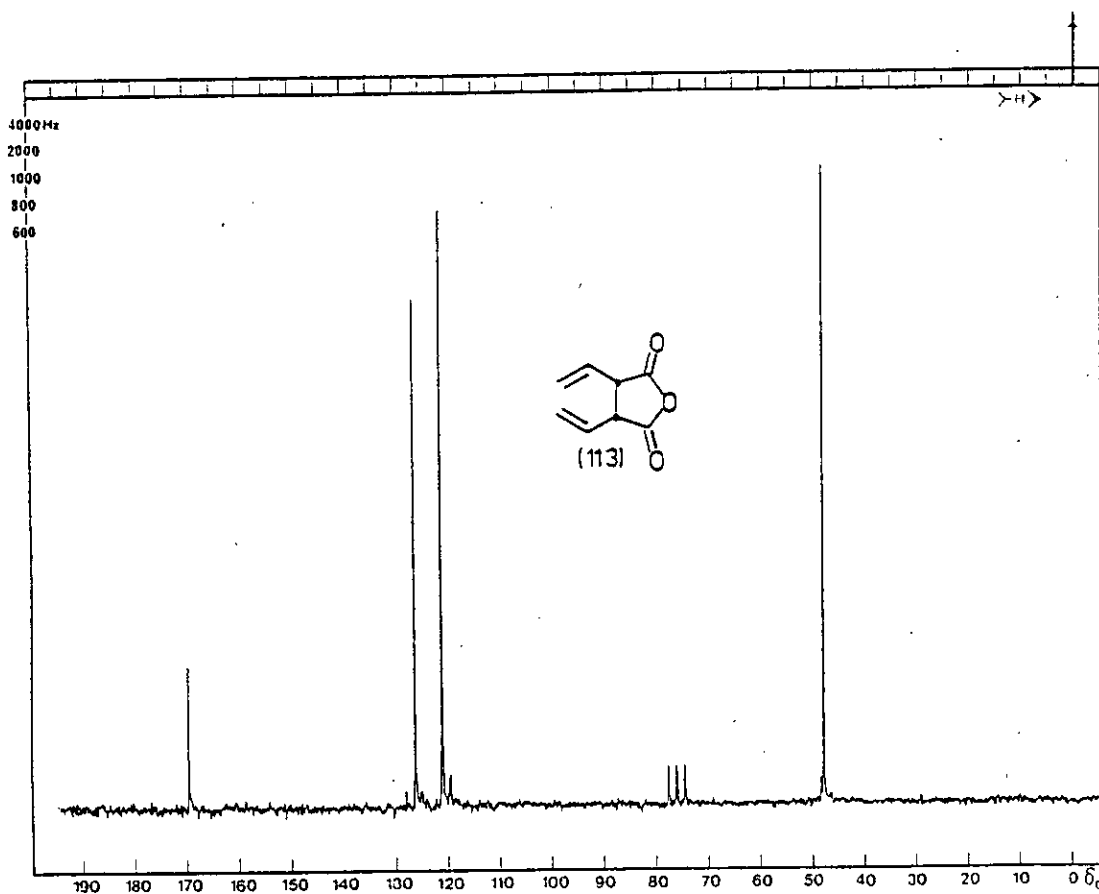
Fig. 13. 25. 2MHz ^{13}C n. m. r. spectrum of 2, 5-dioxo-cis-3, 4-divinyl-
tetrahydrofuran (113).
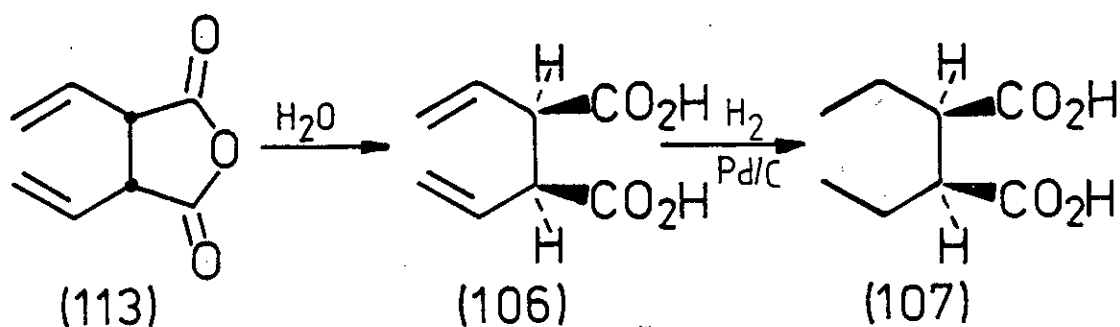
Scheme 52

A plausible mechanism for formation of the cis-divinyl

compound (113) from the anhydride (1) is a $_\sigma 2s$ + $_\sigma 2s$ + $_\sigma 2s$ cheletropic

process similar to that postulated for the extrusion of sulphur dioxide

from 3-thiabicyclo[3.1.0]hexanes 3,3-dioxides (41a and 41b) (see

scheme 20, p. 25). However, one cannot discount the possibility

that the fragmentation goes via a radical process or polar mechanism.

Distinction between these possibilities would require a stereochemical

investigation involving pyrolysis of an appropriately substituted 3,5-

dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide similar

to the studies carried out by Mock[54] with 3-thiabicyclo[3.1.0]hexanes

(see p. 24). Such a study has not been carried out to date.

In view of the successful preparation of the cis-divinyl compound

(113) it was decided to prepare a variety of derivatives of (1) and

investigate their pyrolysis as a general route to cis-1,2-di vinyl

systems. To date, synthetic access to these systems has been

difficult and existing methods usually give mixtures of cis and trans

isomers which can only be separated by preparative gas chromatography.

A typical approach which illustrates some of the problems involved is

the preparation of cis-divinylcyclopropane (80) reported by Brown[87]

in which addition of ethoxycarbonyl carbene to butadiene yielded a

mixture of <u>cis</u> and <u>trans</u>-vinylcyclopropanecarboxylic esters (Scheme 53).
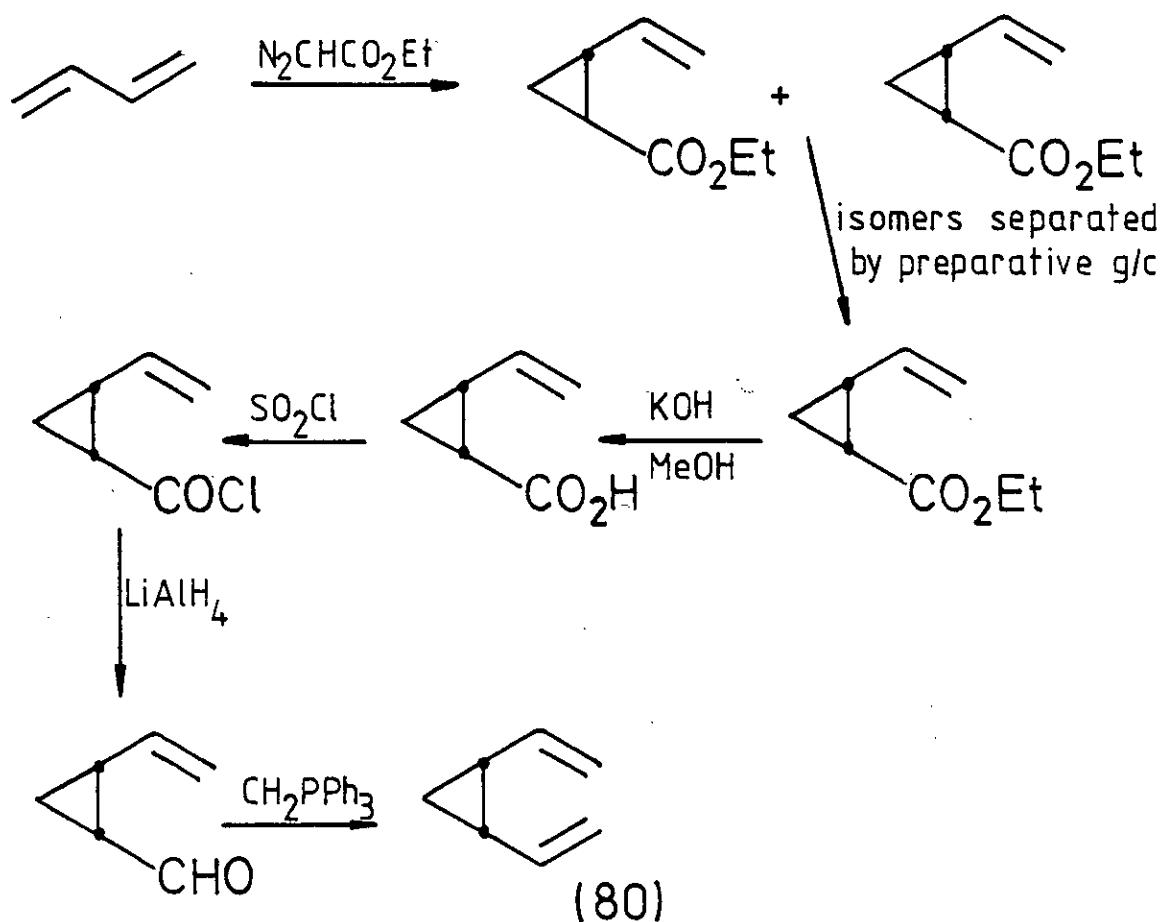
Scheme 53

This mixture was separated by preparative gas chromatography and

the <u>cis</u>-isomer then used in the remaining steps of the sequence.

It is of interest to note that the final product was still contaminated

with 10% of <u>trans</u>-divinylcyclopropane, perhaps due to some epi-

merisation in the Wittig step.

Other attempts at the preparation of <u>cis</u>-1, 2-divinyl compounds

have also led to isomeric mixtures. For example, Stogryn[89a] prepared

2, 3-divinyloxiranes by the route shown in Scheme 54.   Once again

isolation of the pure _cis_ and _trans_ isomers required preparative

gas chromatography.
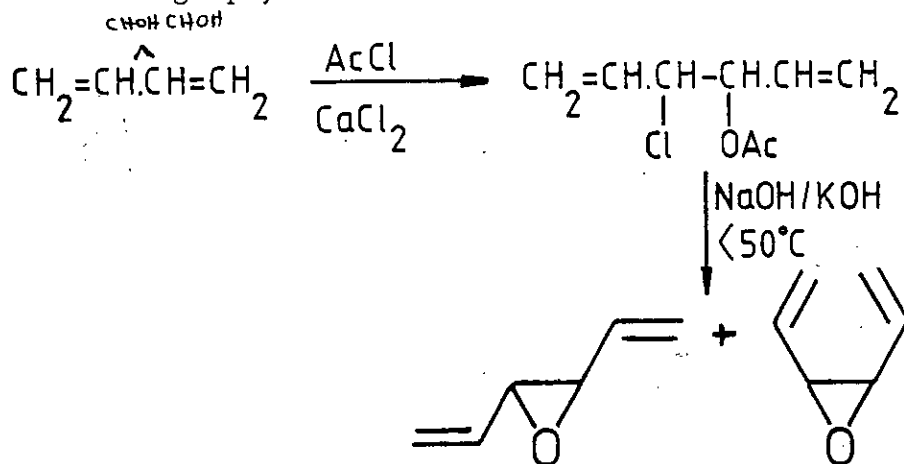
<u>Scheme 54</u>

A further example is the recently reported preparation of

cis-2, 3-divinylthiirane in which treatment of a mixture of _cis_ and

trans-divinyloxiranes with a saturated aqueous solution of KSCN

gave a mixture of _cis_ and _trans_-divinylthiirane (Scheme 55).[91b] The

pure isomers were obtained by preparative gas chromatography.
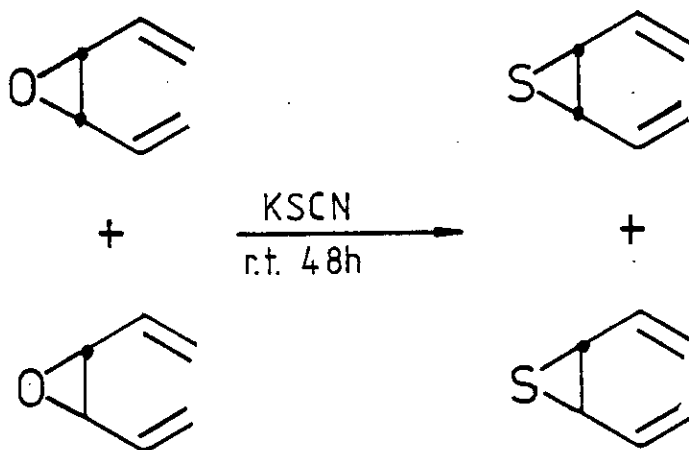
<u>Scheme 55</u>

Finally it is of interest to note that Hammond[147] has reported

that photosensitized dimerization of butadiene leads to a mixture

of <u>cis</u> and <u>trans</u>-1, 2-divinylcyclobutane and 4-vinylcyclohexene with

the <u>cis</u>-isomer being the minor product (Scheme 56).

52%

7%

(85)

41%

Scheme 56

One example of a stereospecific synthesis in this area has

been reported by Heimbach[99] who utilized a reverse Cope-reaction

to prepare <u>cis</u>-1, 2-divinylcyclohexane from <u>cis</u>, <u>trans</u>-1, 5-cyclo-

decadiene (90) (see Scheme 41, p. 41).   The latter was easily prepared

from butadiene and ethylene using nickel-based π-complex catalysts.[148]
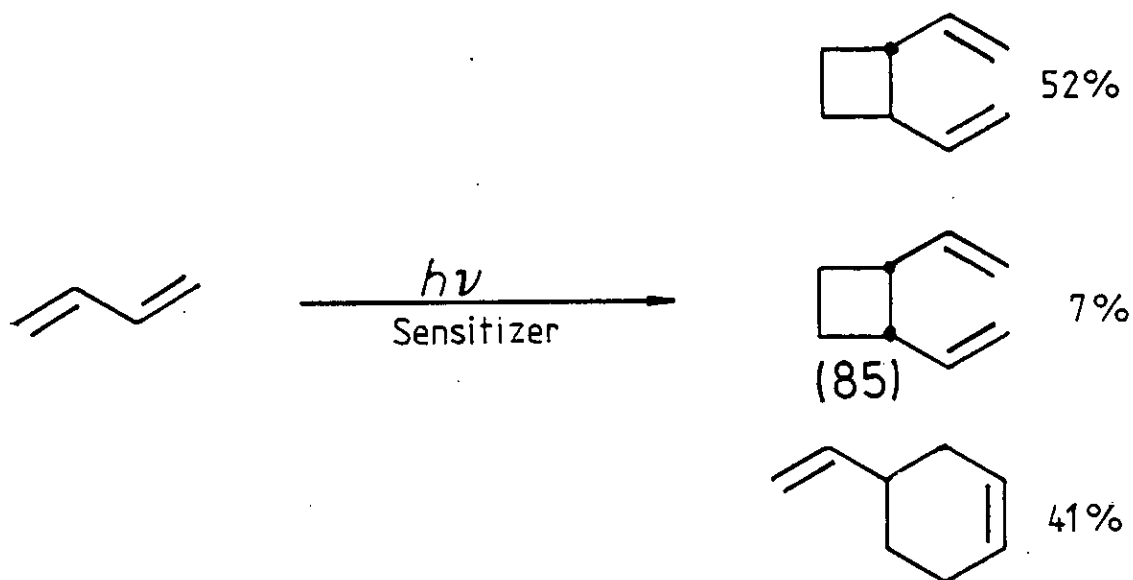
To date the only method which gives entirely <u>cis</u>-divinyl com-

pounds is that due to Vogel[94] but this lengthy route suffers from the

fact that it requires different starting materials for each preparation.

Scheme 57 shows the typical preparation of <u>cis</u>-1, 2-divinylcyclobutane

(85) from <u>cis</u>-1, 2, 3, 6-tetrahydrophthalic anhydride (114) by the

methods indicated.
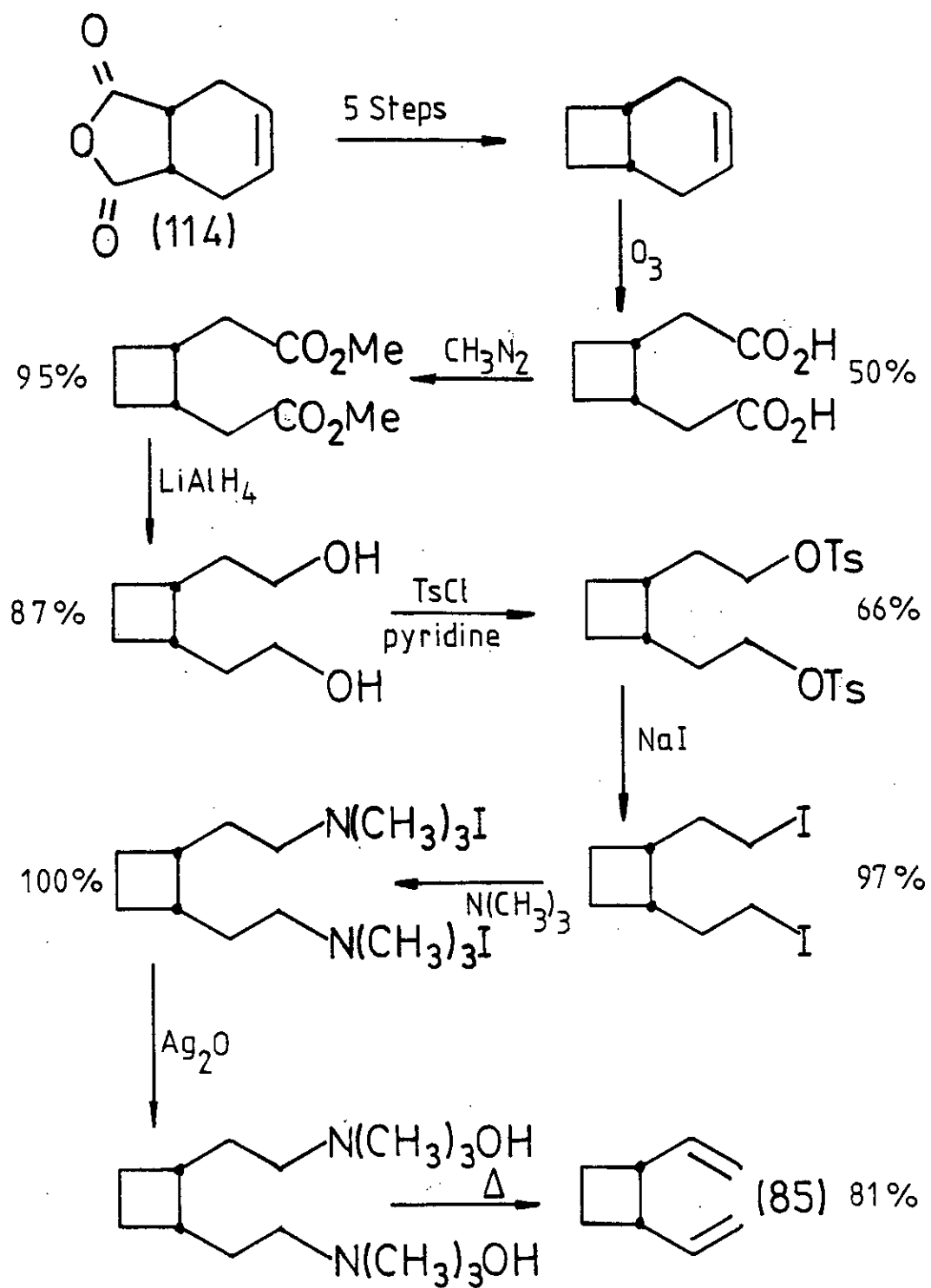
Scheme 57

B.   Preparation of Precursors of 3,4-Divinylcyclopentane Analogues.

B.1   4-Oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide.

The preparation of the title compound (117) was carried out in three steps starting from (1) as outlined in Scheme 58.   When boiled with a few drops of concentrated sulphuric acid in methanol the anhydride (1) gave a 90% yield of the diester (115) as a white crystalline solid m.p. 126-127°C (lit.[3] 126-127°C).
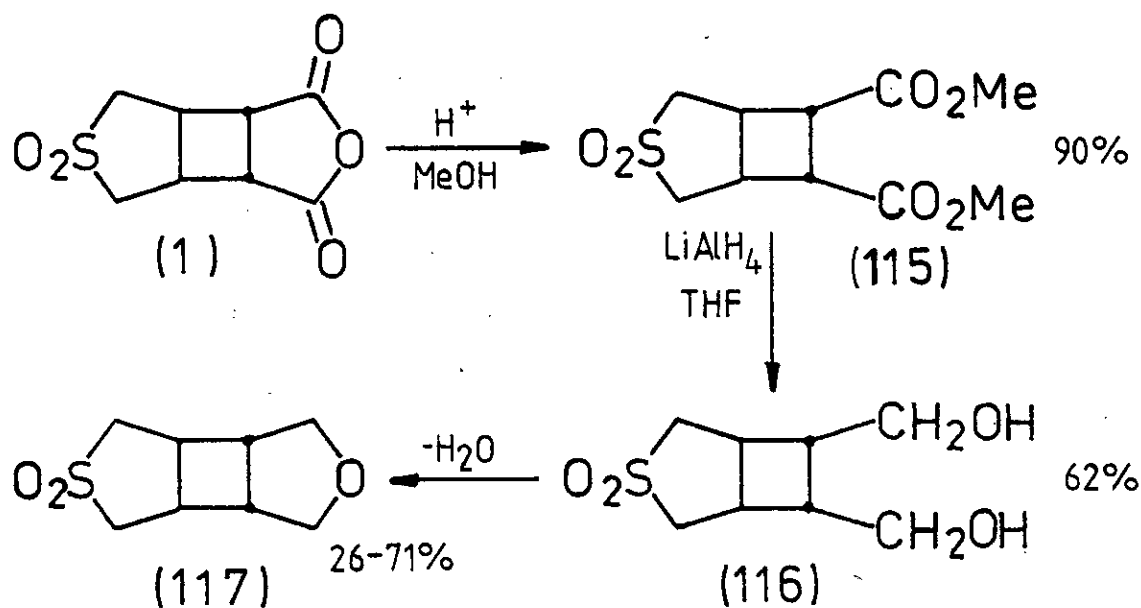
Scheme 58

In the case of the diol (116) reduction of the diester (115) with lithium aluminium hydride in THF gave a colourless crystalline compound which had a m.p. 98-100°C compared to the literature value of 75-82°C.[3]   Nevertheless on the basis of analytical, spectral and chemical evidence the structure of the colourless compound was established as 6,7-dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (116).   Elemental analysis gave percentage composition for carbon and hydrogen consistent with an empirical formula $C_8H_{14}O_4S$.

Despite its insolubility in most solvents, the diol (116) could be recovered from the inorganic salts after reduction by continuous extraction with THF in a Soxhlet apparatus over a period of 48 h.

Some difficulty was encountered in the third step, viz. the conversion of the diol (116) into 4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]-decane 9,9-dioxide (117). Initial attempts to dehydrate the diol (116) using dimethyl sulphoxide as the dehydrating agent[109] gave, in one instance, a 71% yield of a colourless crystalline solid m.p. 129-130°C which on the basis of its analytical and spectral data was identified as the desired tetrahydrofuran (117). However when the method was repeated, the extraction step using dichloromethane did not give any product, presumably because the diol (116) had not reacted. Whilst there is no obvious explanation for this failure it is clear that the dimethyl sulphoxide needs to be super dry and the reaction temperature carefully controlled for this procedure to be successful.

To circumvent this problem an alternative procedure[108] was adopted involving conversion of the diol (116) into its tosylate and cyclisation in pyridine. This procedure proved successful but the work-up required chromatography and gave the cyclic ether (117) in only 26% yield.

In another procedure concentrated sulphuric acid was employed as the dehydrating agent and whilst this method was successful, giving yields of 55%, it suffered from the drawback that the acid tended to char the reaction mixture.

The n.m.r. data for the ether (117) will be fully discussed in Section B.6.

B. 2   <u>4, 9-Dithiatricyclo[5. 3. 0. 0^{2,6}]decane 4, 4-dioxide.</u>

Conversion of the diol (116) into the title compound (119) was achieved in two steps as shown in Scheme 59.

(116)   (118)   75%   (119)   62%
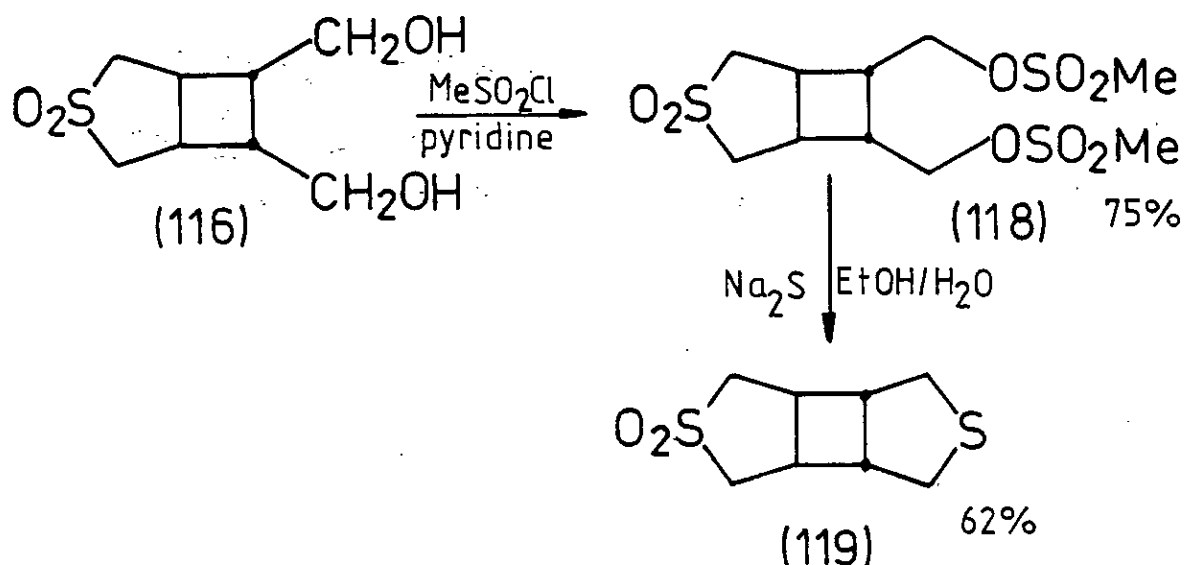
<u>Scheme 59</u>

In the first step, reaction of the diol (116) with methanesulphonyl chloride in pyridine gave the dimesyl ester (118) in 75% yield. When boiled under reflux with sodium sulphide nonahydrate in aqueous ethanol the latter gave a colourless crystalline solid in 62% yield. This was identified as 4, 9-dithiatricyclo[5. 3. 0. 0^{2,6}]decane 4, 4-dioxide (119) on the basis of analytical and spectral evidence. Elemental analysis gave percentage composition for carbon and hydrogen consistent with an empirical formula $C_8H_{12}O_2S_2$. This was verified by observation in the mass spectrum of a parent ion peak at m/e 204.

B.3   Attempted preparation of 9-phenyl and 9-methyl-4-thia-9-

azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxides by lithium aluminium

hydride reduction of the cyclic imides.

Attempts to prepare the 9-phenyl amine (120) by reduction of

the cyclic imide (108), as shown in Scheme 60 were largely unsuccessful.
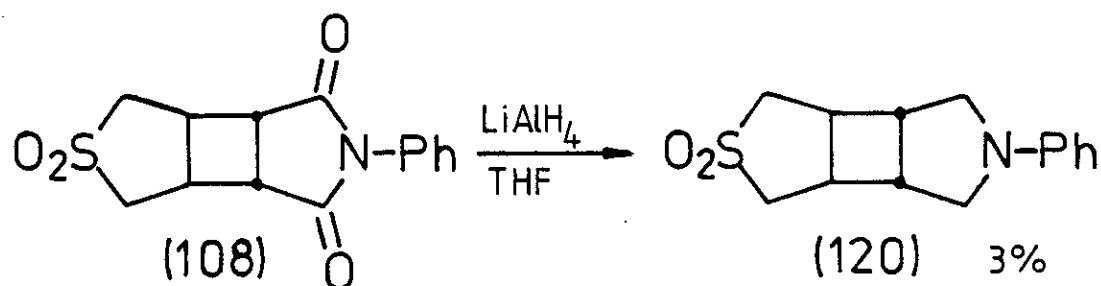
Scheme 60

On one occasion a 3% yield of (120) was obtained but it could not be

obtained in a pure state due to decomposition on standing.   All

attempts to work-up the products from the reduction of (108) by

chromatography inevitably led to the formation of intractable tarry

residues.   This is not surprising since (120) is a tertiary aromatic

amine which are very susceptible to aerial oxidation.[149]

As tertiary alkyl amines are less susceptible to aerial oxidation

than are their aromatic counterparts, it was decided to try to prepare

the methyl analogue of (120).   The 9-methyl analogue of (108) was

prepared by a route similar to that used for the preparation of (108)

(see Scheme 49, p.121), using methylamine instead of aniline.

Reduction of this imide with lithium aluminium hydride in THF gave

a pale yellow oil whose [13]C n.m.r. spectrum identified it as the

desired amine but showed the presence of large amounts of unidentified

impurities. Attempts to purify this oil, by bulb-to-bulb distillation and by chromatography failed and so a pure sample for elemental analysis could not be obtained. However the mass spectrum of the yellow oil did have a peak at 201 consistent with an empirical formula $C_9H_{15}NO_2S$.

B.4 9-Benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide.

In view of the failure to prepare amines by the reduction of imides it was decided to adopt a procedure similar to that used for the preparation of the cyclic sulphide (119). Thus treatment of the diol (116) with tosyl chloride in pyridine gave a 51% yield of the ditosylate (121), which on boiling with benzylamine under reflux in ethanol for 48 h gave a 56% yield of a colourless solid (Scheme 61).
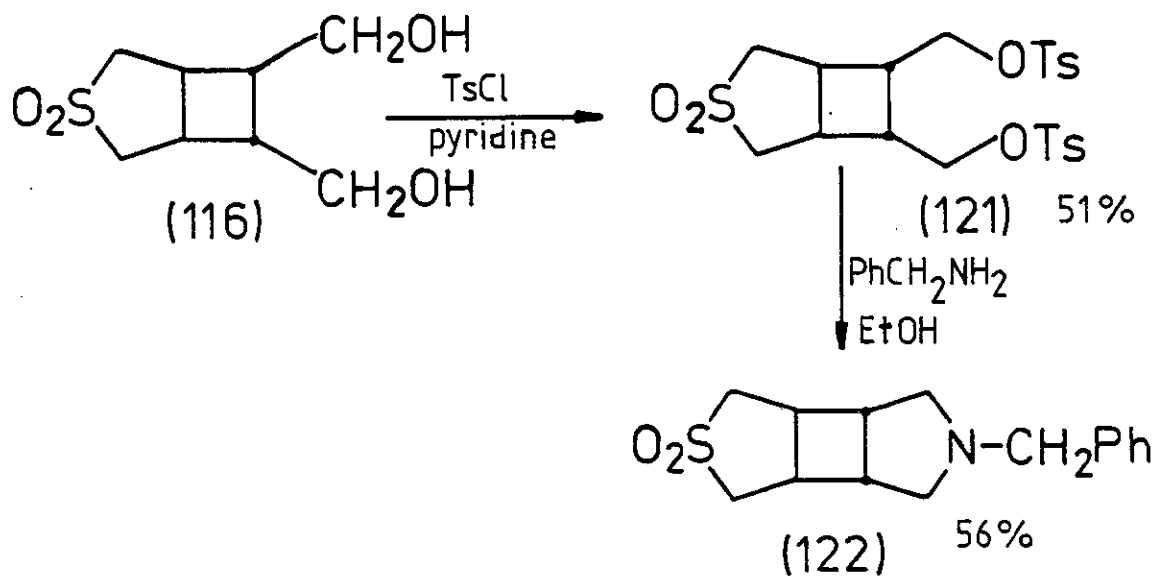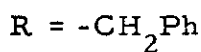

Scheme 61

Analytical and spectral evidence established the structure of the colourless solid as 9-benzyl-4-thia-9-azatricyclo[5.3.0.0^{2,6}]-decane 4,4-dioxide (122). Elemental analysis gave percentage

composition for carbon, hydrogen and nitrogen consistent with an empirical formula $C_{15}H_{19}NO_2S$. This was verified by observation in the mass spectrum of a parent ion peak at m/e 277.

B.5 Mechanism of formation of l-heterocyclopentane rings.

The mechanism for the formation of the l-heterocyclopentane rings in compounds (116), (119) and (122) is presumably similar in each case. Scheme 62 illustrates the typical conversion of the ditosylate (121) into the cyclic amine (122). Thus nucleophilic attack on one of the -CH$_2$OTs groups by the amine followed by loss of a proton gives an amine which is ideally suited to repeat the process intramolecularly and thus give the observed cyclic amine (122).

$R = -CH_2Ph$
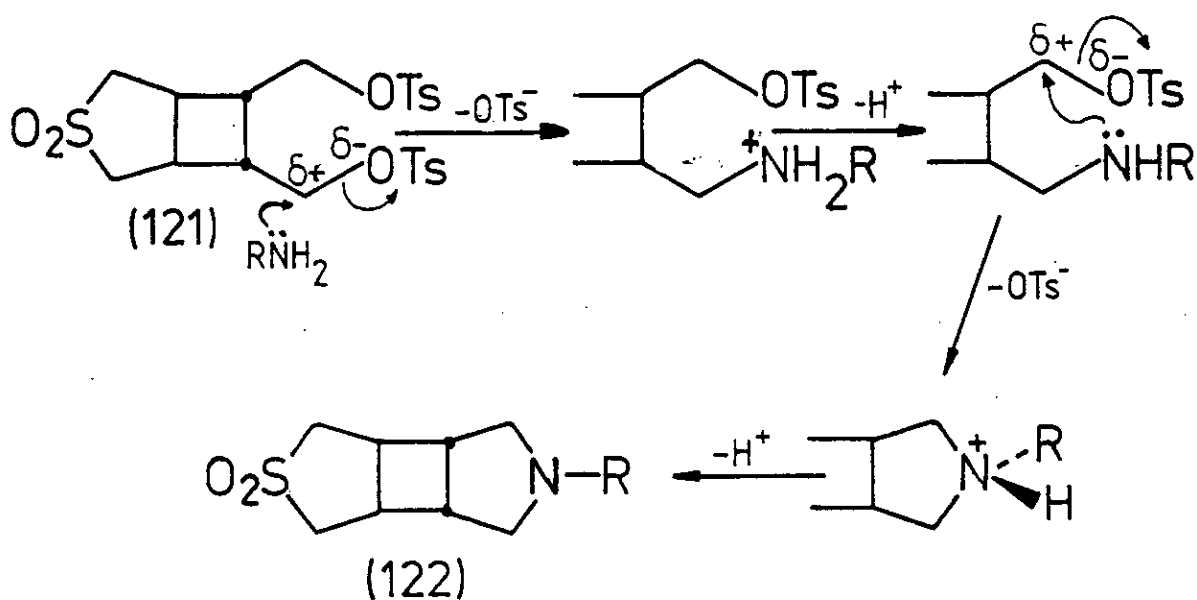
Scheme 62

The mechanism for the dehydration of the diol (116) using dimethyl sulphoxide is more difficult to rationalize but it is thought[109] that a cyclic transition state ensues as depicted in Figure 14.
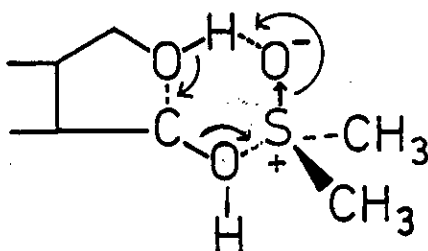
Fig. 14 Transition state for dehydration of 1,4-diols by DMSO.

B. 6 Spectroscopic properties of precursors of 3,4-divinylcyclo-

pentane analogues.

The main evidence for the structural assignments given to (116),

(119) and (122) comes from their ^{1}H and ^{13}C n. m. r. spectra which

show strong similarities for each compound.

These compounds could possibly exist in either syn or anti-

configurations but were assigned the anti-structure on the grounds

that they are all derived from (1), presumably with retention of

configuration.

As can be seen from figure 15 the most striking feature of the

^{1}H n. m. r. spectrum of 4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]decane 9, 9-

dioxide (117) is the pair of doublets centred at 3. 9 and 3. 5 δ These

signals are due to the methylenes adjacent to the ether linkage and

since they are pro-chiral centres, the protons are non-equivalent.

This is confirmed by the differences in chemical shift and by the fact

that they show geminal coupling (9. 5Hz). The ^{13}C n. m. r. spectrum

of (117) shown in figure 16 further confirms this assignment as it

shows only four resonances.
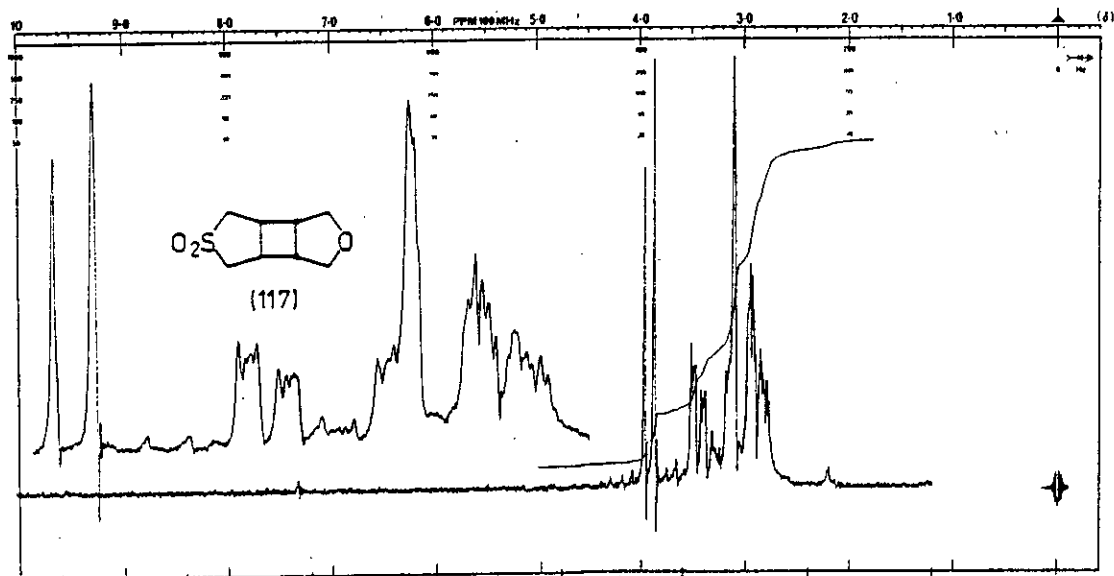
Fig. 15.   100MHz ^{1}H n. m. r. spectrum of 4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]-
decane 9, 9-dioxide (117).   Inset is an expansion of the signals
in 2. 5-4. 0δ region.
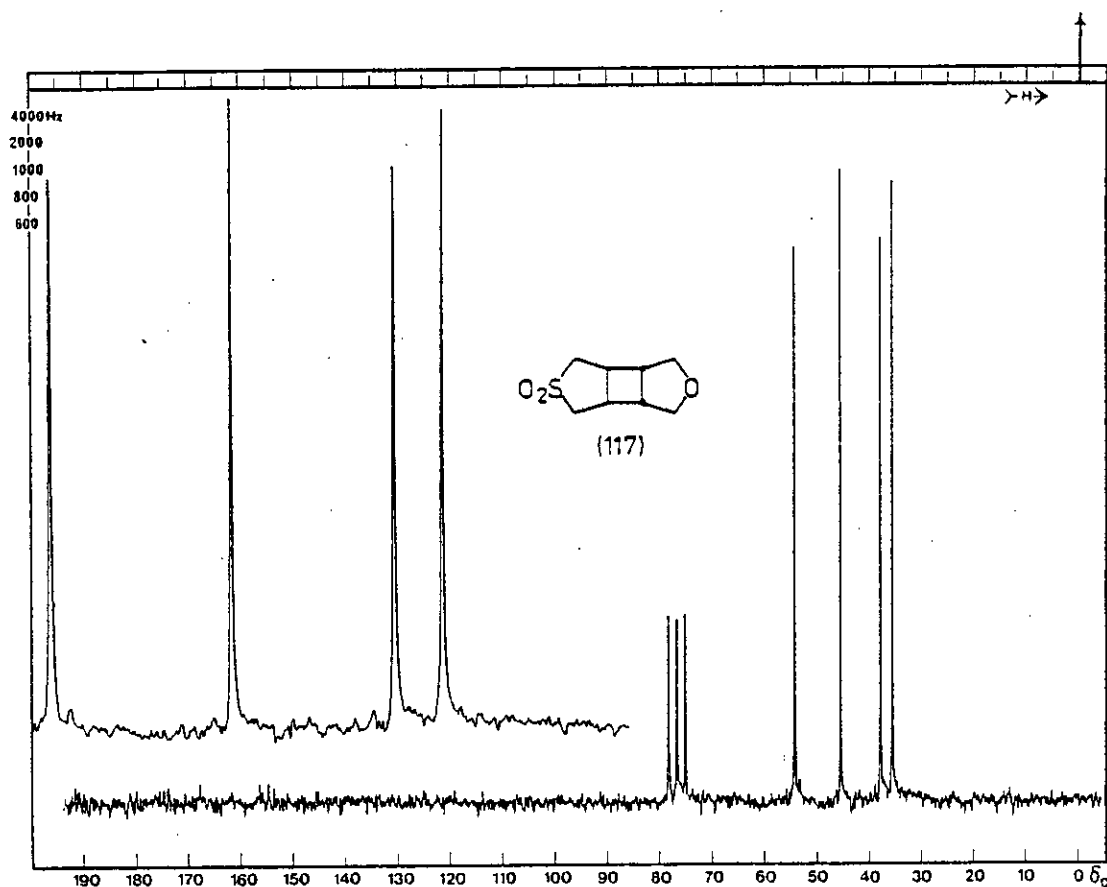
Fig. 16.   25. 2MHz ^{13}C n. m. r. spectrum of 4-oxa-9-thiatricyclo[5. 3. 0. 0$^{2, 6}$]-
decane 9, 9-dioxide (117).   Inset is an expansion of the signals in
30-60 δ region.

The ^{1}H and ^{13}C n. m. r. spectra of compounds (119) and (122) are similarly consistent with the assigned structures. However in these cases there is more overlap of resonances in the ^{1}H n. m. r. spectra and the individual peaks are less easy to assign unambiguously.

C   <u>Preparation and Reactions of 3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.</u>

C.1   <u>Preparation of 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide.</u>

The bicyclic compound, 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide (123) offers considerable scope as a synthon for the preparation of other <u>cis</u>-divinyl derivatives, which might be difficult to obtain by existing methods. A methodology can be envisioned, as illustrated in scheme 63, involving annelation of the strained cyclobutene ring to give (110) which under flash vacuum pyrolytic conditions, might be expected to lose SO_2 and form <u>cis</u>-1,2-divinyl compounds (111). It is pertinent to point out that when the ring in (111) is of suitable size,

$$O_2S \quad (123) \longrightarrow O_2S \quad (110) \xrightarrow[-SO_2]{\Delta} \quad (111)$$
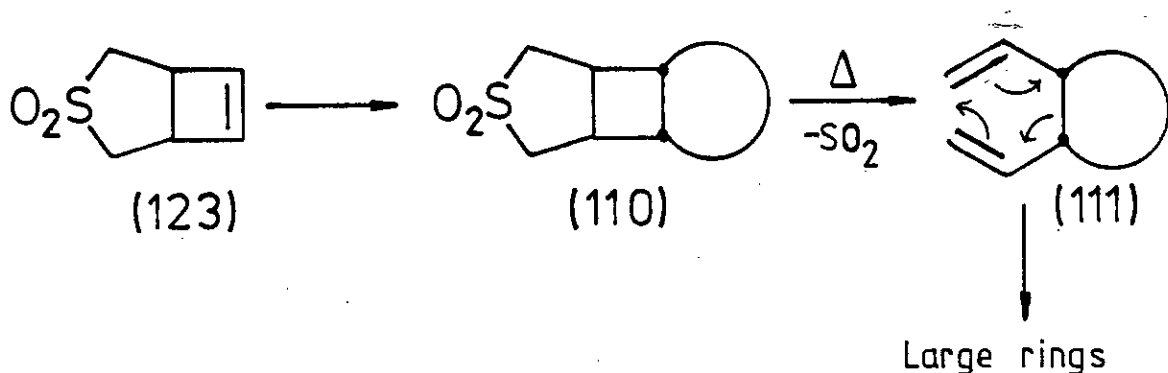
Large rings

<u>Scheme 63</u>

such compounds can readily undergo a Cope rearrangement to give larger rings (see Section C in Introduction).

Several well-documented procedures exist for functionalising the alkene moiety in compounds of type (123). For example Meyers[64] has used a variety of epoxidation and nitrene addition reactions to prepare precursors to divinyl ethers (59) and divinyl carbamates (61) (see Scheme 27, p. 30).

In an extension of these procedures, Meyers and his co-workers[150] have reported an efficient synthesis of 1,4-dihydropyridines (124) as outlined in Scheme 64.

R=PhSO$_2$, p-MeOPh,
EtO$_2$C etc,
yields = 80-90%
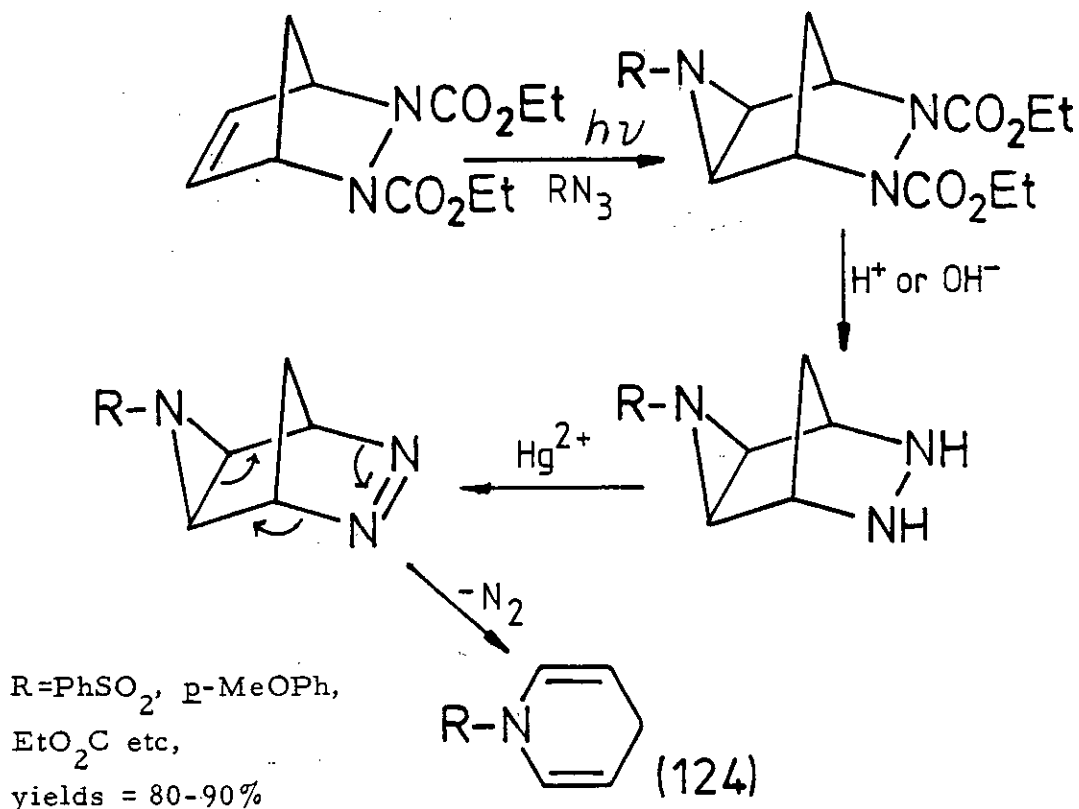
Scheme 64

Other workers have reported the application of similar ring-forming reactions involving cyclobutene and its derivatives. For example, Anderson et al.[121,151] found that reaction of N-phthalimidonitrene, generated by treatment of N-aminophthalimide with lead tetraacetate, with cyclobutene (125) or cis-3,4-dichlorocyclobutene (127) gave adducts (126) or (128) in 18-22% and 9-12% yields, respectively (Scheme 65).

Scheme 65
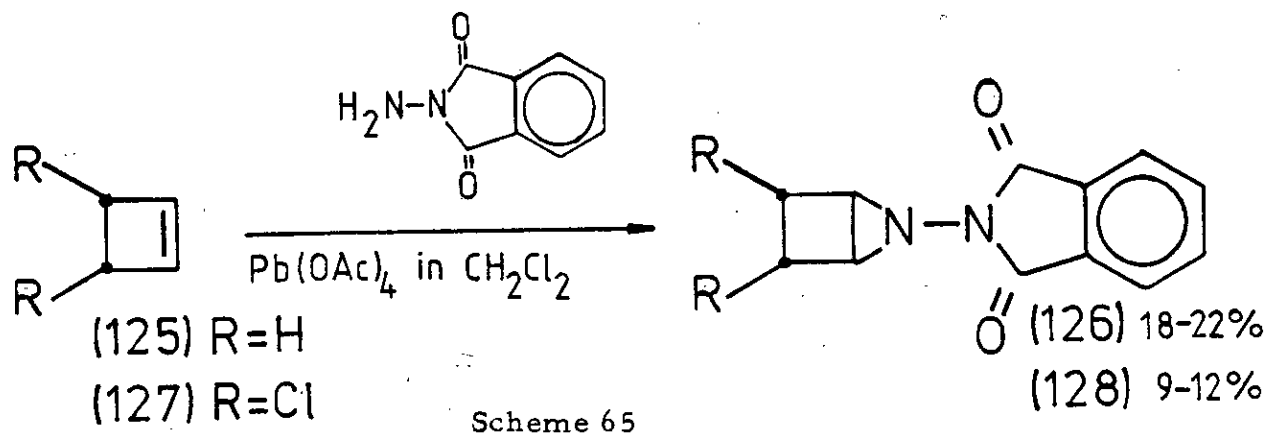
The facile addition of 1,3-dipoles to alkenes including cyclobutenes

has also found extensive application in the synthesis of five-membered

heterocycles.   In these circumstances the 1,3-dipole (129), which can

only be represented by zwitterionic octet resonance structures, combines

in a concerted fashion with a multiple bond system (130) (the dipolaro-

phile) to form an unchanged five-membered ring (131) (Scheme 66).
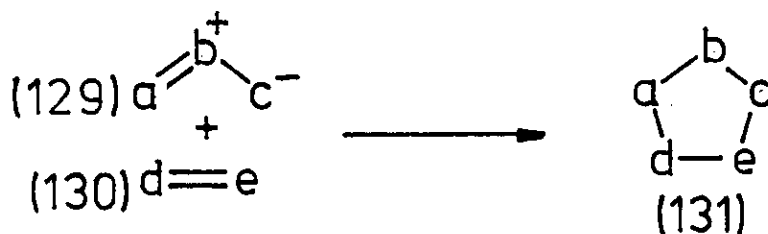
Scheme 66

Thus, benzonitrile oxide affords an 82% yield of the adduct (132)

when added to cis-3,4-dichlorocyclobutene (127) (Scheme 67).[152]
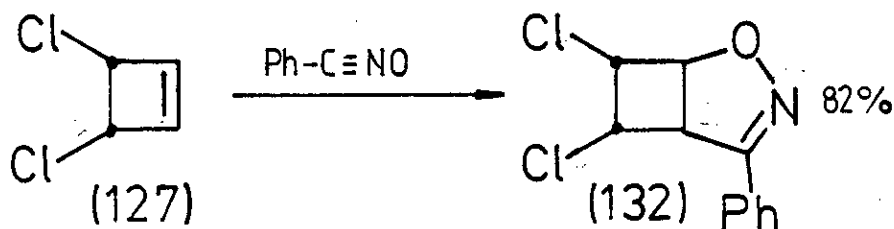
Scheme 67

Diazoalkanes and cyclic nitrones have also been reported to react

readily with cis-3,4-dichlorocyclobutene (127) to give the corresponding

adducts in 90% and 70% yields, respectively.[153,154] More recently

nitrilimines have been successfully reacted with cyclobutenes.[155]

The synthetic strategy adopted for the preparation of the bicyclic

alkene (123) was to convert the readily available anhydride (1) into its

diacid (133) then bis-decarboxylate the latter with either lead tetra-

acetate[114] or by electrolysis[156] (Kolbe reaction) (Scheme 68). The
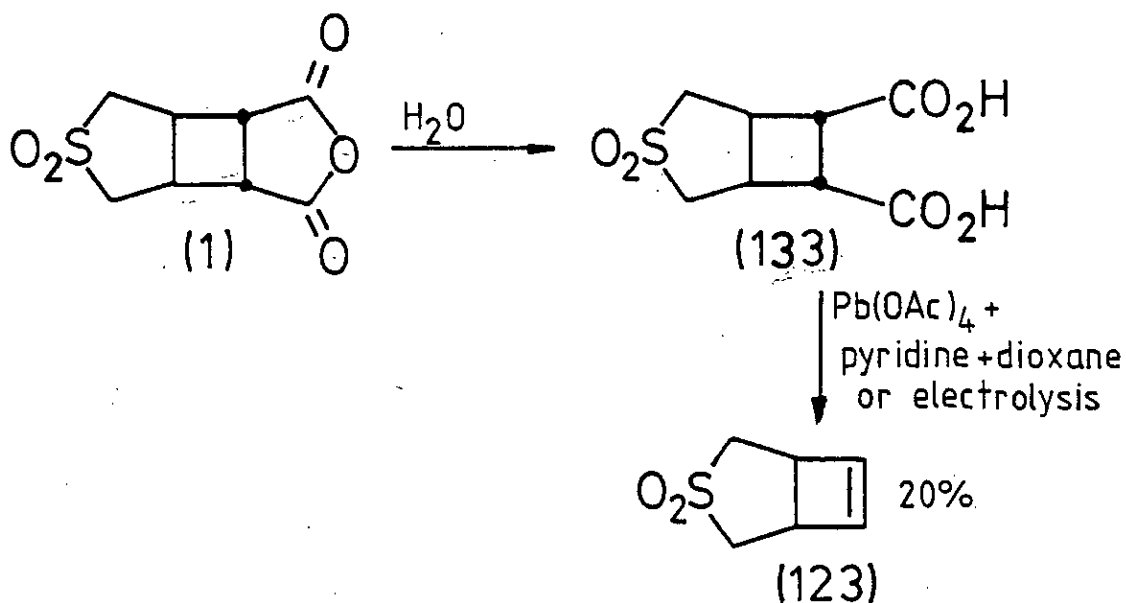
Scheme 68

oxidative bis-decarboxylation step (133) -> (123) has adequate precedent

in that similar decarboxylations have been used with considerable

success to prepare cyclobutene derivatives.

For example, treatment of the dibasic acid (134) with lead tetra-

acetate gave bicyclo[2.2.0]hex-2-ene (135) in 30-38% yield as shown

in Scheme 69.[157] Under similar conditions the anhydride (136) afforded
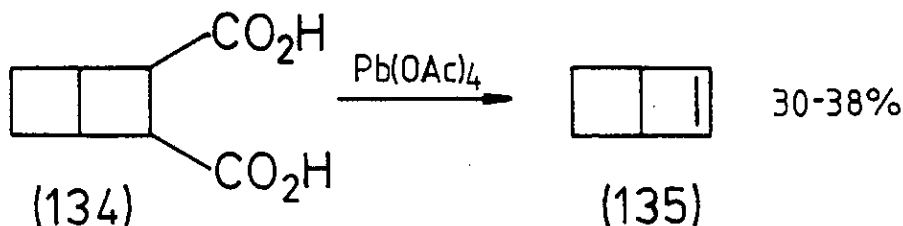
Scheme 69

bicyclo[2. 2. 0]hex-2, 5-diene (Dewar benzene) in 20% yield,[158]

which could be raised 35-40% by carrying out the decarboxylation

using electrolysis[156, 159] (Scheme 70). However, in general the
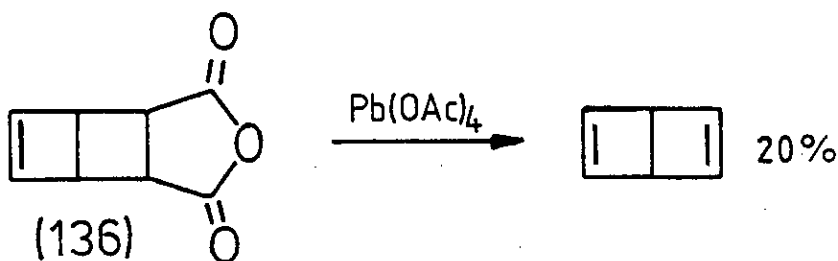
Scheme 70

electrolytic technique is limited to small scales and is not very

convenient.

Hydrolysis of the anhydride (1) was first carried out by treatment

with 3M sodium hydroxide solution.[160] This method gave the diacid

(133) as a colourless crystalline solid, m. p. 188-191°C (lit,[3] 194-195°C)

in 70% yield but subsequent experiments showed that the diacid could

be obtained quantitatively simply by boiling the anhydride with water

for ½ h.

Traditionally oxidative bis-decarboxylation reactions give low

yields[156] and the conversion of (133) into (123) was no exception. Thus

treatment of the diacid (133) with lead tetraacetate according to the

procedure of Jefford et al.[114] produced a brown oil, purification of

which by medium pressure chromatography gave only 19% yield of a

colourless crystalline solid, m. p. 71-75°C. This was identified as

the alkene (123) on the basis of its spectral and analytical properties.

Thus elemental analysis of (123) gave a percentage composition

for carbon and hydrogen consistent with the empirical formula $C_6H_8O_2S$.

This was corroborated by observation in the mass spectrum of a parent

ion peak at m/e 144.

The i. r. spectrum of the alkene (123) shows very weak absorptions at 3120 cm^{-1} and 1553 cm^{-1} characteristic of the cyclobutene ring.[161]

The ^{1}H n. m. r. spectrum of (123) is reproduced in Figure 17 and shows that the two olefinic protons in the cyclobutene ring resonate as a singlet at 6. 18 δ Presumably the lack of coupling between the olefinic and bridgehead protons is due to the fact that the dihedral angle between these protons is approximately 90° and thus give zero coupling constants. The multiplet at 3. 7-3. 6δ is due to the bridgehead protons (1-H and 5-H), while the remaining methylene groups give rise to a multiplet at 3. 2-2. 9δ In keeping with the assigned structure, the ^{13}C n. m. r. spectrum of the alkene (123) exhibited only three resonances as shown in figure 18.

Attempts to improve the yield of alkene (123) by adopting other methods for the decarboxylation of the diacid (133) gave only mediocre results. Thus use of the alternative procedure of Cimarusti and Wolinsky[162] whereby oxygen instead of nitrogen is bubbled through the reaction mixture gave only a 16% yield of the alkene (123). Likewise electrolysis (60-100V dc 0. 5-0. 8 amp) of the diacid (133) in a mixture of 10% pyridine and triethylamine at room temperature gave only a 20% yield of the alkene (123).

In another approach, use was made of bis-triphenylphosphinenickel dicarbonyl as a decarboxylating agent.[163] This reagent is relatively new but its synthetic utility has been clearly demonstrated by Dauben[164] who used it with spectacular success in the preparation of barralene (138) as shown in Scheme 71. Its main drawback appears to be the high
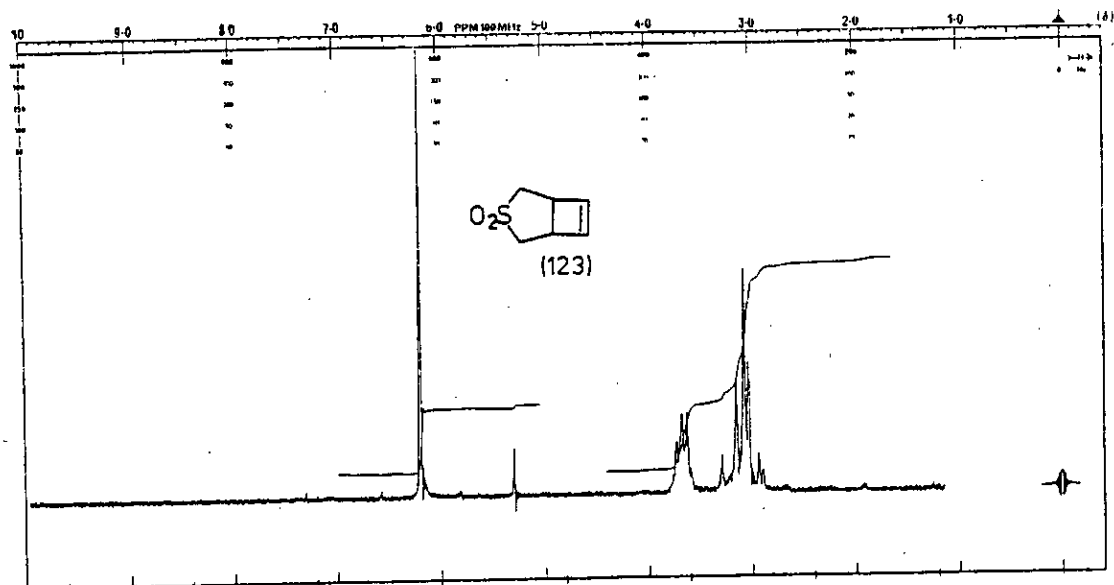
Fig. 17.   100MHz ^{1}H n. m. r. spectrum of 3-thiabicyclo[3. 2. 0]hept-6-
ene 3, 3-dioxide (123).
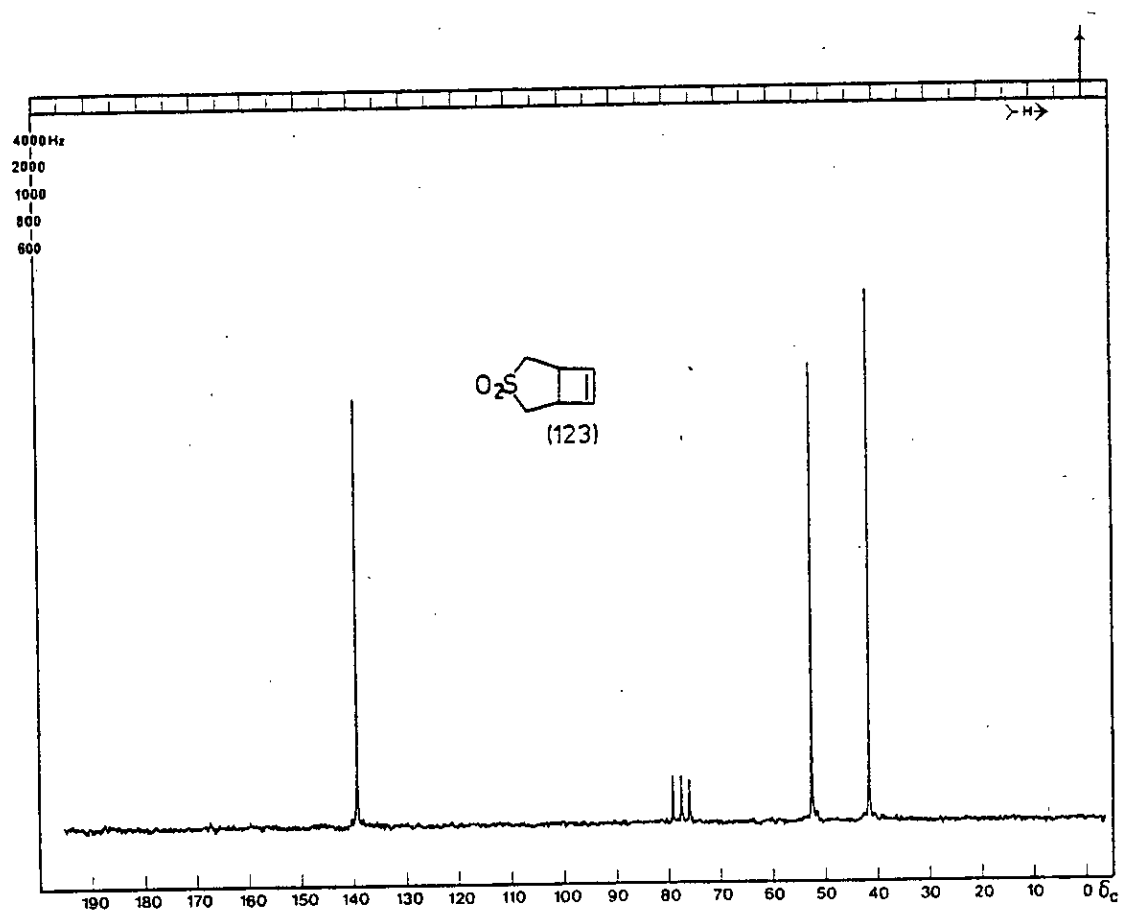
Fig. 18.   25. 2MHz ^{13}C n. m. r. spectrum of 3-thiabicyclo[3. 2. 0]hept-6-
ene 3, 3-dioxide (123).
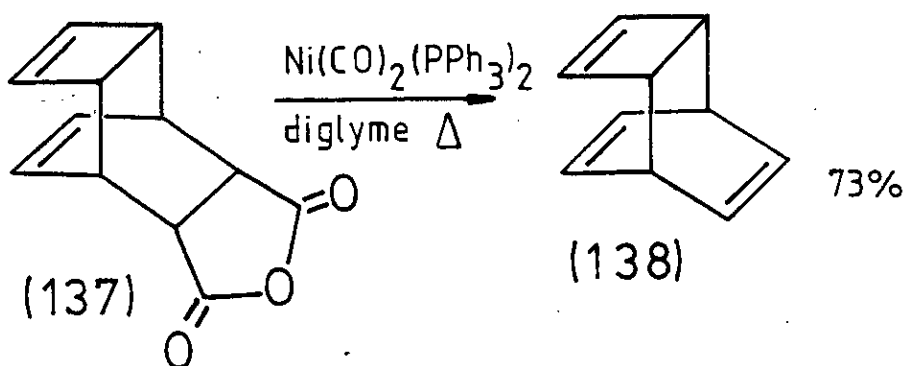
Scheme 71

temperature required for decarboxylation making it unsuitable for products that are thermally labile. Since the alkene (123) decomposes at temperatures above 140°C [vide infra] it was decided to modify the procedure by using dimethoxyethane (b. p. 81°C) instead of diglyme (b. p. 165°C) as the solvent. However, even after several days under reflux, the reaction mixture showed no apparent change in colour and examination by t. l. c. showed the absence of any alkene. When the reaction was repeated with diglyme as solvent decomposition ensued within three hours.

In order to corroborate the structure of the alkene (123) it was also synthesised by the alternative route outlined in Scheme 72. Thus
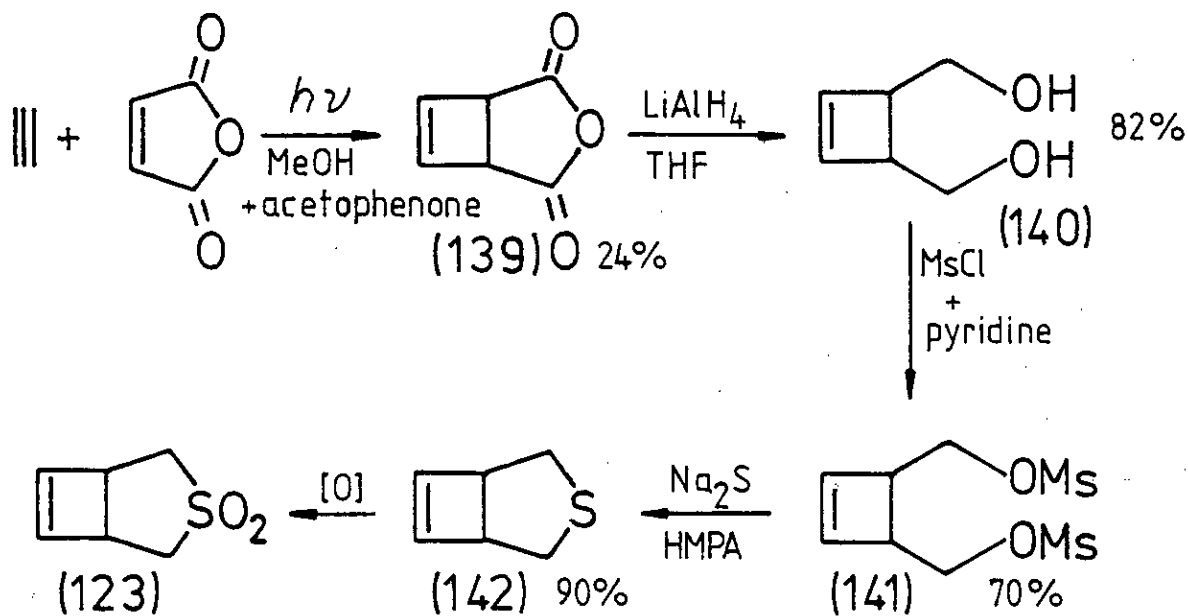
Scheme 72

cyclobutene anhydride (139) was obtained as a colourless crystalline

solid in 24% yield by photochemical cycloaddition of acetylene to maleic

anhydride in methanol.[165]   Reduction of this anhydride with lithium

aluminium hydride in tetrahydrofuran gave an 82% yield of the diol (140)

as a pale yellow oil which was converted into its dimesylate (141) in

70% yield by treatment with methanesulphonyl chloride in pyridine.

Treatment of this diester with sodium sulphide in hexamethylphosphor-

amide (HMPA) at 50°C according to the procedure of Paquette[166] gave

the cyclic sulphide (142) as a yellow oil in 90% yield.   Oxidation of this

oil with m-chloroperbenzoic acid in dichloromethane gave the alkene

(123) together with another compound which was subsequently shown to

be the epoxide of (123) (see section C. 2).

C. 2   8-Oxa-4-thiatricyclo[5. 1. 0. 0$^{2, 6}$]octane 4, 4-dioxide.

The title compound (143) was recognised as a potential precursor

to cis-2, 3-divinyloxirane (83,   X=O) which is known to undergo a facile

Cope rearrangement to give 4, 5-dihydrooxepin (84, X=O)[89] as outlined

in Scheme 73.   A potential drawback to this strategy is the possible
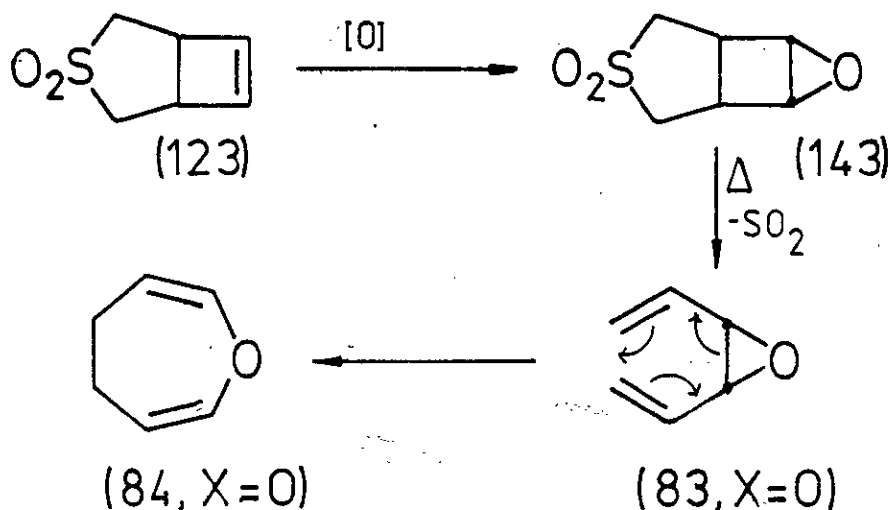
Scheme 73

isomerization of the highly strained (143) to (144) prior to cheletropic

extrusion of SO_2. This would lead eventually to the formation of

cyclohex-1-ene-3-one (145) as depicted in Scheme 74.
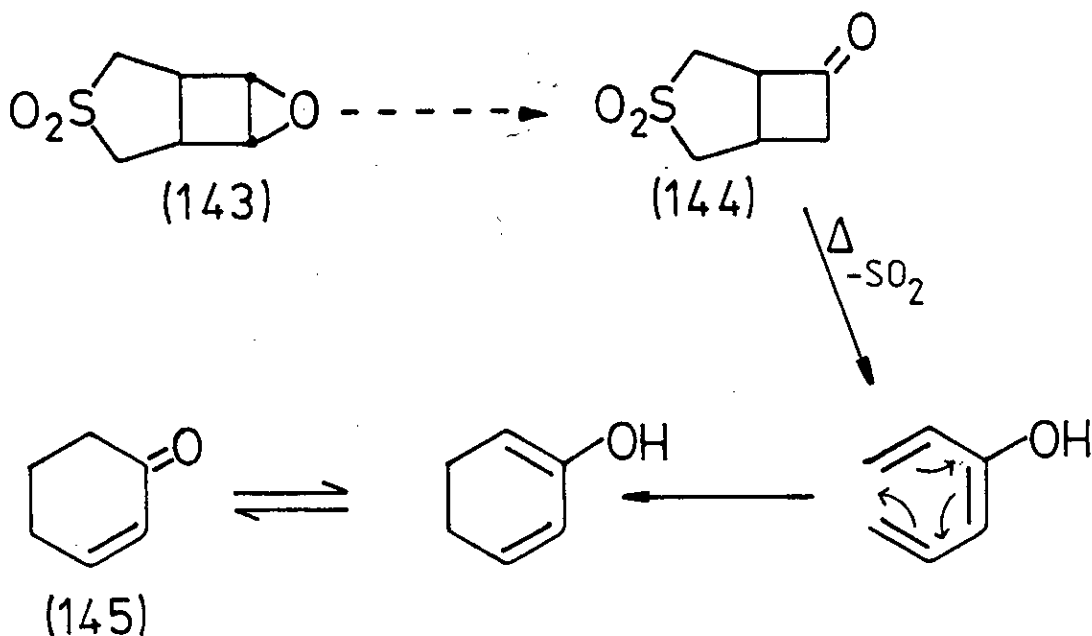
Scheme 74

Initial attempts to convert the alkene (123) into the epoxide (143)

were carried out using m-chloroperbenzoic acid as the oxidant.   How-

ever the reaction proved to be very slow, an observation consistent

with the observation by Cope et al.[167] that epoxidation of the cyclobutene

ring in compound (146) with m-chloroperbenzoic acid required a reaction

time of 400 h.   Work-up of the reaction after several days gave 12%
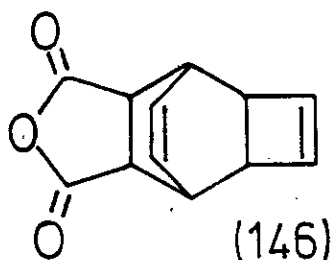
yield of a colourless crystalline solid which on the basis of analytical

data was established as the desired epoxide (143).

In view of the poor yield of epoxide (143) obtained by direct

oxidation of the alkene (123) it was decided to seek a different synthetic

approach.   One possibility involved the dehydrohalogenation of the

appropriate chlorohydrin using silver oxide.   This method had been

reported[118] to give an efficient synthesis of the epoxide (148) from

(147) in 90% yield (Scheme 75).
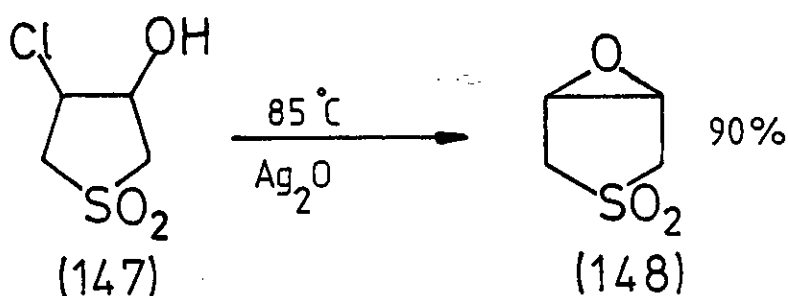
Scheme 75

The preparation of the desired chlorohydrin (149) was carried

out as shown in Scheme 76 by addition of hypochlorous acid to the alkene

(123) according to the procedure of Sorenson.[116]   However, subsequent

attempts to dehydrohalogenate compound (149) with silver (1) oxide in

dimethoxyethane[118] led to the recovery of starting material.   Apparently,
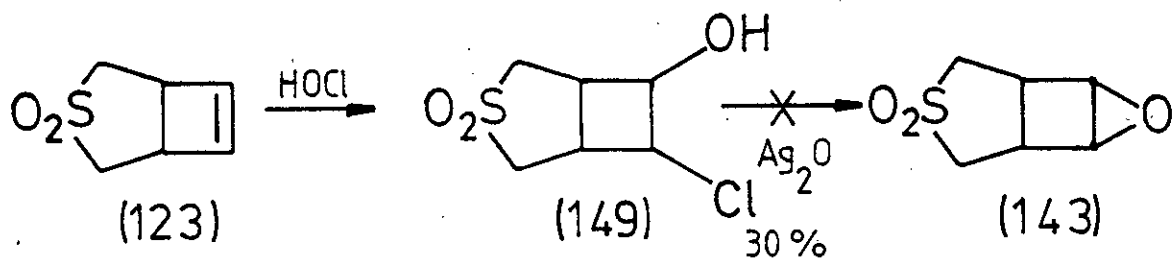
Scheme 76

in this case, the strain energy incurred in the formation of the epoxide

(143) is too high and cyclization is disfavoured.

In a final attempt to obtain (143) by direct oxidation of the alkene

(123) performic acid was employed as the oxidising agent.[115]   As a rule

performic acid is not considered to be a good epoxidation reagent

because the high acidity of formic acid (employed either as solvent or

formed in the oxidation) usually leads to epoxide ring opening.[168]

Nonetheless its use was prompted by a report by Bianchi et al.[115]

describing the successful epoxidation of the alkene (150).

(150) Ph
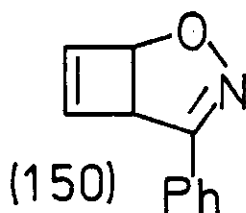
Treatment of (123) with performic acid did give a 40% yield of the

epoxide (143) but the reaction was still slow and required a 96 h

reaction period.

As shown below the epoxide (143) can exist in two geometric

forms, viz. in either a syn or an anti-configuration. Only one isomer

(143) anti

(143) syn
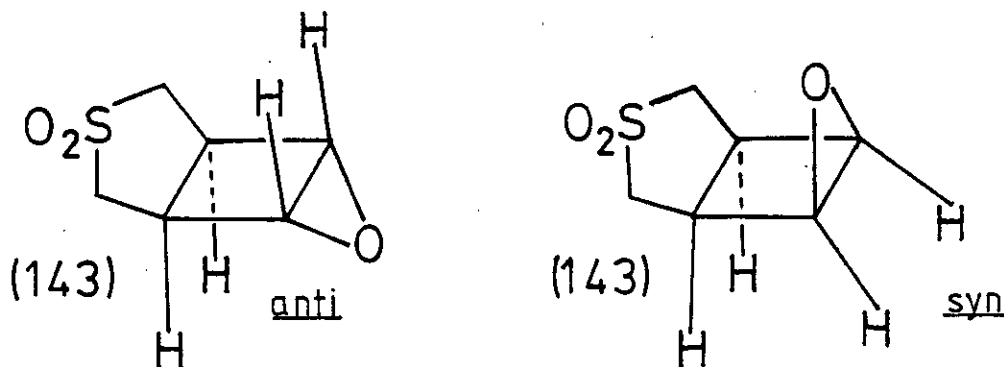
was detected by t.l.c. and by ^{13}C n.m.r. spectroscopy and this was

tentatively assigned the anti-configuration as it has been reported[115]

that epoxidation of formally similar cyclobutenes such as (150) give

an anti-epoxide as the predominant product (anti:syn 20:1) upon treat-

ment with performic acid.   The latter assignments were made from

evidence that treatment of the major product with HCl gave a chloro-

hydrin whose stereochemistry was confirmed by ^{1}H n.m.r. spectro-

scopy[169] and shown to arise from an anti-epoxide.

The stereochemistry of (143) could not be determined by

[1]H n. m. r. spectroscopy since assignment of cis and trans orientations

of protons on four-membered rings from vicinal coupling constants

gives results that are ambiguous.[170]

The only type of [1]H n. m. r. analysis which might resolve this

stereochemical problem is to utilize the approach adopted by Gamba and

Mondelli[169] who reported that the sign of four bond couplings in cyclo-

butanes is highly stereospecific and much more sensitive to cis-trans

orientation of the two interacting protons than to the effects of sub-

stituents or to distortions of the ring. However the authors did not

elaborate on the details of the experimental methods employed.

C.3   Attempted addition of carbenes and nitrenes to 3-thiabicyclo-

[3.2.0]hept-6-ene 3,3-dioxide.

a) Attempted addition of carbenes.

The addition of carbenes to the alkene (123) was investigated as

a possible route to the carbon analogue of the epoxide (143). It was

recognised that pyrolysis of this compound (151) should lead to cis-1,2-

divinylcyclopropanes (152) which are known[85,86] to undergo Cope

rearrangement and thus give cyclohepta-1,4-dienes (153) (Scheme 77).

$R = CO_2Et$
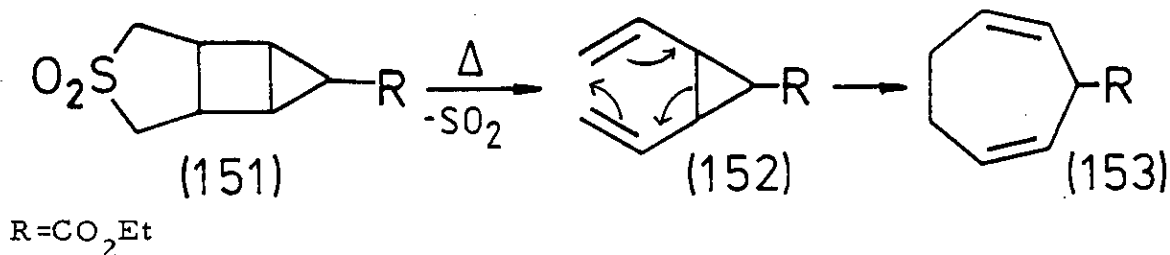
Scheme 77

All attempts to prepare compound (151) by addition of ethoxy-carbonyl carbene to the alkene (123) failed completely. It was found that reaction occurred preferentially with benzene which was used as solvent or the carbenes dimerized rather than add to the alkene (123).

b) Attempted addition of nitrenes

The addition of nitrenes to the alkene (123) was investigated as a possible route to the nitrogen analogue of the epoxide (143) viz. the aziridine (154) (Scheme 78).

$$O_2S \overset{R-\underset{\cdot\cdot}{\overset{\cdot\cdot}{N}}:}{\longrightarrow} O_2S \quad N-R$$

(123)   (154)
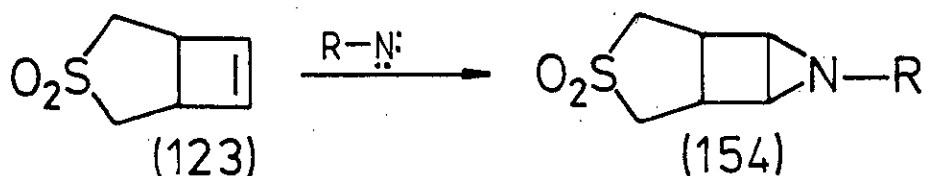
Scheme 78

The first attempt at nitrene addition involved the use of ethoxy-carbonylnitrene generated by treatment of p-nitrophenylsulphonyloxy-urethane[120] with triethylamine and gave only nitrene dimers and unchanged alkene (123) as the product. This failure is hardly surprising in that it has been reported[121] that addition of the same nitrene to cyclobutene (125) gave only a 1.5% yield of the aziridine product (155)

(125)   (155)   1.5%
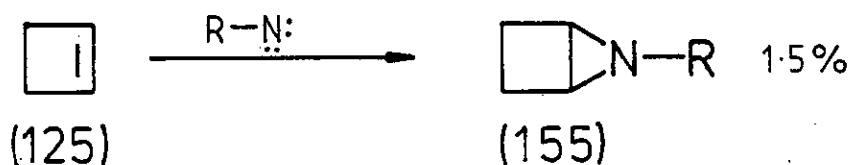
$R = CO_2Et$

Scheme 79

(Scheme 79). However it has been reported[171] that photolysis of a dichloromethane solution of ethylazidoformate and 1,2-dimethylcyclo-

butane gave a 65% yield of the desired aziridine product which proved stable.*

In view of the failure of ethoxycarbonylnitrene to add to the alkene (123) it was decided to try the same reaction using the more nucleophilic nitrene N-phthalimidonitrene, generated by treatment of N-aminophthalimide with lead tetraacetate.[121] Work-up of the reaction mixture gave a 6% yield of a colourless crystalline compound which exhibited a parent ion peak at m/e 304 indicative of the expected structure
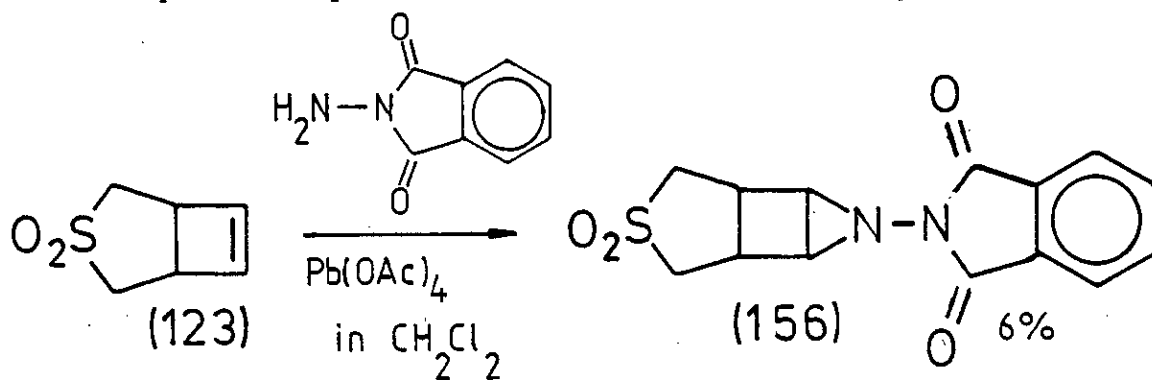
Scheme 80

(156) (Scheme 80). Unfortunately, correct analytical data could not be obtained due to the unstability of the compound. In this connection it is worth noting that the corresponding adducts obtained by addition of N-phthalimidonitrene to cyclobutene tend to decompose fairly readily. In these instances also the yields of adducts were low (ca. 10-20%).[121, 151]

The lack of reactivity of the strained alkene (123) toward reactive species is only one of several examples in a much wider study presently

---

* Photolysis of the alkene (123) with neat ethyl azidoformate, gave the desired aziridine in 31% yield. The mode of formation is assumed to proceed by way of electronically excited azide with the intermediacy of ethoxycarbonylnitrene.

being carried out by other workers at Edinburgh.[172] They have found

that alkenes of the same general type as (123) show a pronounced lack

of reactivity toward addition of reactive species such as carbenes and

nitrenes.

In an attempt to explain this phenomenon, Simpson[173] has carried

out both theoretical and photoelectron spectroscopic studies on (123)

and several related compounds. The results showed that the energetic

availability of the alkene π electrons was determined by a combination

of through space delocalization, inductive and hyperconjugative effects

which lead to the stabilization of the π level; this is evidenced by a

relatively high ionization potential of the olefinic π electrons as shown

in Table 2.

C.4   The addition of 1, 3-dipoles to 3-thiabicyclo[3. 2. 0]hept-6-ene

      3, 3-dioxide.
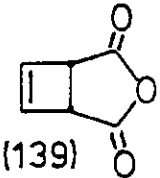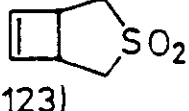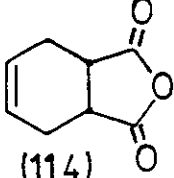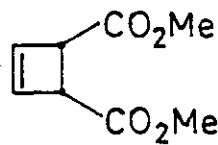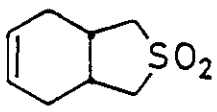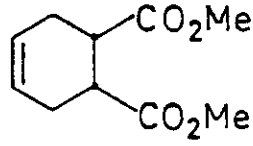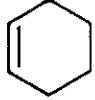
The addition of 1, 3-dipoles of general formula (129) was studied

as a possible general route to precursors of cis-divinyl-5-membered

heterocycles (158) as depicted in Scheme 81.
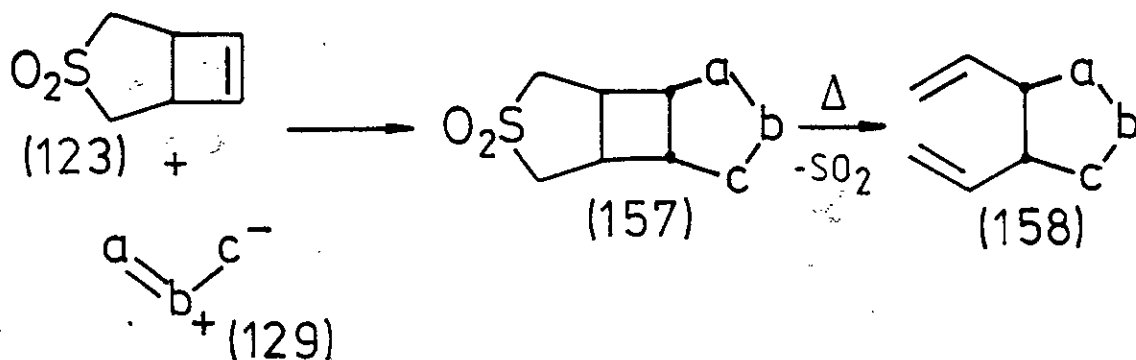
Scheme 81

TABLE 2

Magnitude of 1st ionization potential (eV) of unsaturated level.

Structure	IP (eV)
(139) bicyclic anhydride with C=C	10.49
(123) bicyclic SO₂ with C=C	10.25
(114) cyclohexene-fused anhydride	10.00
cyclobutene-1,2-dicarboxylate (CO₂Me, CO₂Me)	9.76
bicyclic SO₂ with cyclohexene	9.69
(125) cyclobutene	9.43
cyclohexene-dicarboxylate (CO₂Me, CO₂Me)	9.25
cyclohexene	8.94

* Data reproduced from ref. 173.

a) <u>Addition of C, N-diphenylnitrone</u>

The reaction of <u>C</u>, <u>N</u>-diphenylnitrone (159) with the alkene (123)

in boiling toluene gave a 28% yield of a light brown solid which on the

basis of analytical and spectral evidence was assigned the structure (160)

.(Scheme 82).
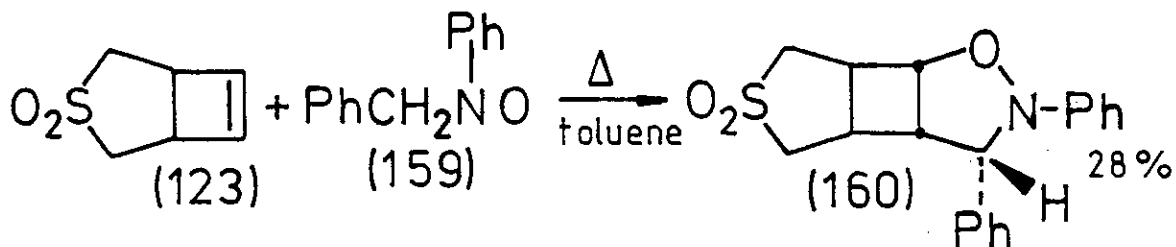
Scheme 82

Elemental analysis of the solid gave percentage composition for

carbon, hydrogen, and nitrogen consistent with an empirical formula

$C_{19}H_{19}NO_3S$.   This was corroborated by observation in the mass

spectrum of a parent ion peak at m/e 341.

As indicated in Scheme 83 the structure of (160) is of interest
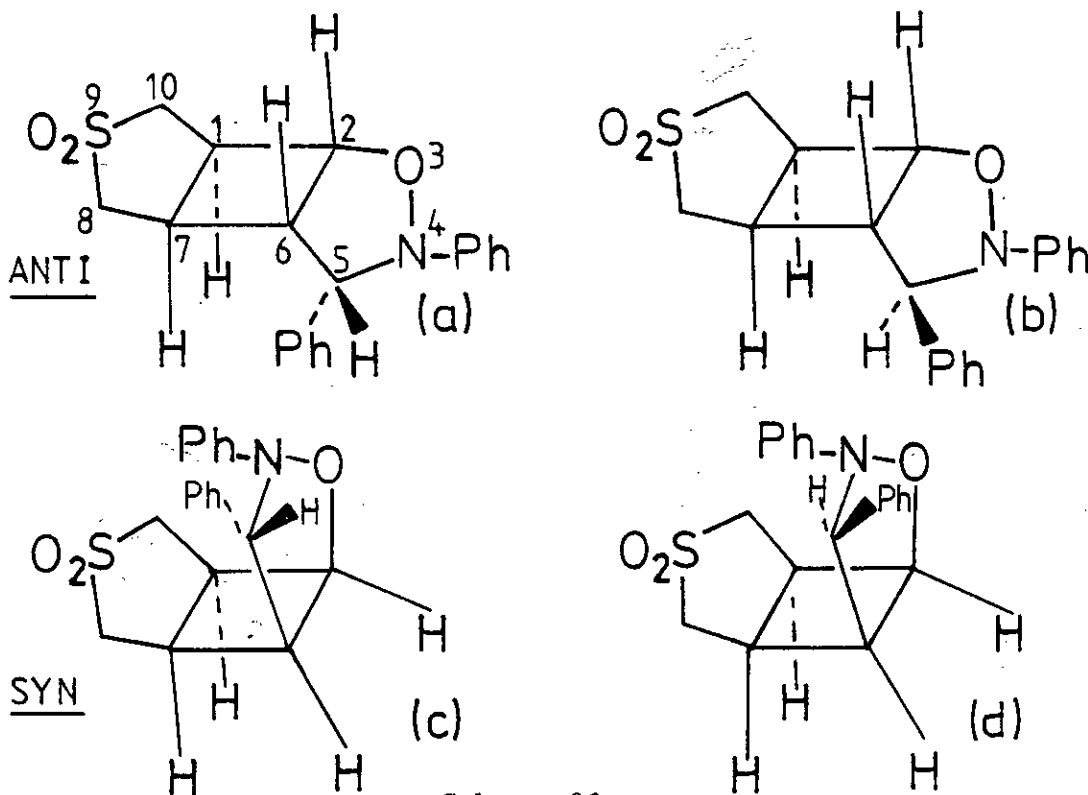
Scheme 83

not only from the point of view of a syn or anti-configuration, but also

with regard to the stereochemistry about the C_5 atom.   Only one

isomer could be detected by t.l.c. and this was tentatively assigned

the anti-structure (a) or (b) from consideration of the steric interactions

involved.   Further evidence in support of the assigned stereochemistry

of (160) was obtained by ^{1}H n.m.r. spectroscopy using the technique

of double irradiation.   An examination of the ^{1}H n.m.r. spectrum of

(160) (Fig. 19) shows that two of the protons viz. 2-H and 5-H, can

easily be assigned to the resonances at 4.8δ and 4.5δ, respectively

due to the deshielding effects of the oxygen and nitrogen atoms.   Upon

irradiation of the large multiplet at 3.6δ both these signals collapsed

to broad singlets (figure 20) presumably as a result of decoupling of the

6-H proton leading to the disappearance of both 7Hz couplings.   This

suggests that there is a cis-relationship between the 5-H and 6-H protons

because of the large $\underline{J}_{5,6}$ = 7Hz, compared to the value of <0.5Hz for

the coupling between trans orientated protons in the adduct formed by

addition of 3,4-dihydroisoquinoline-$\underline{N}$-oxide to the alkene (139).   The

smaller coupling constant of 2Hz found in the resonance at 4.8δ is most

likely to be $\underline{J}_{1,2}$.   This supports the assignment of (160) as an anti-

structure since as already reported[154] for cyclobutane rings, values of

coupling constants lower than 5Hz cannot arise from cis-interactions

of adjacent protons.

b) Addition of anisonitrile oxide and benzonitrile oxide.

The nitrile oxides used in these experiments were generated in

situ by thermal dehydrohalogenation of the appropriate hydroxamic
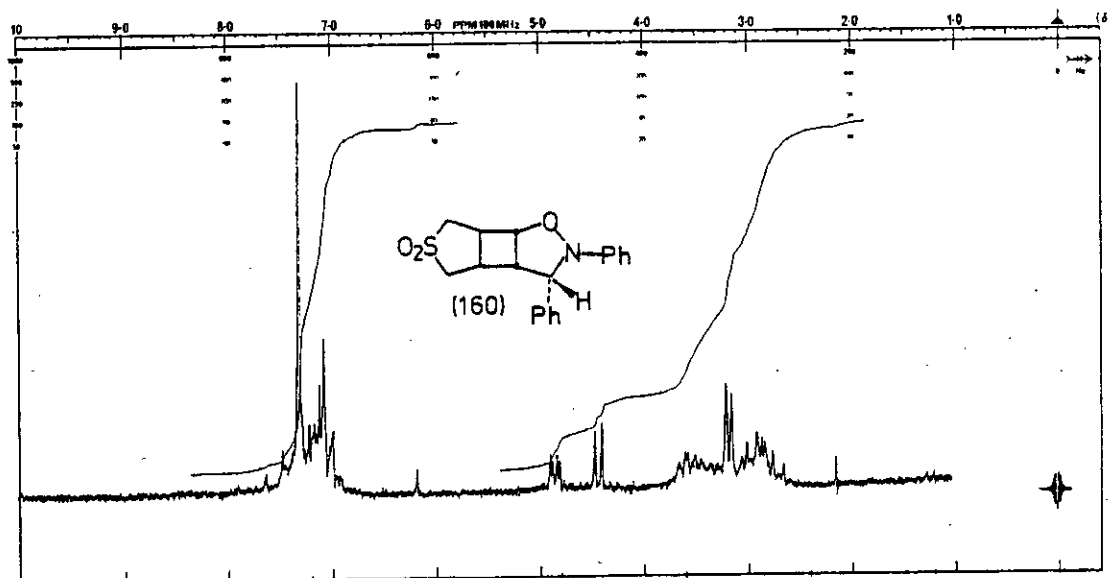
Fig. 19. 100MHz [1]H n. m. r. spectrum of 4, 5-diphenyl-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0^{2,6}]decane 9, 9-dioxide (160).
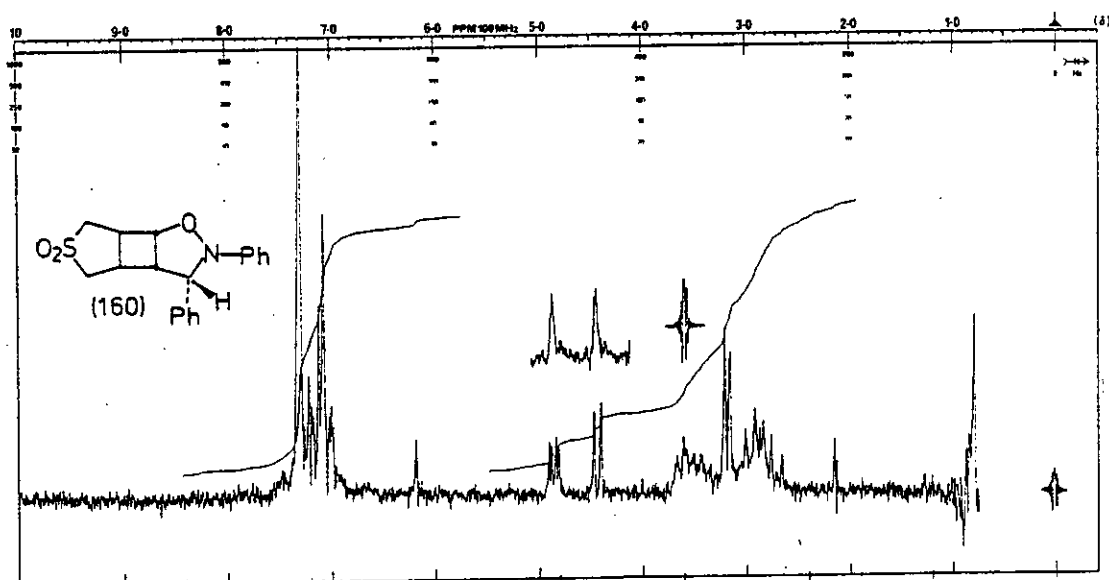
Fig. 20. 100MHz [1]H n. m. r. spectrum of 4, 5-diphenyl-3-oxa-9-thia-4-azatricyclo[5. 3. 0. 0^{2,6}]decane 9, 9-dioxide (160) with inset showing effect of irradiating multiplet at 3. 6δ.

chloride. Thus when the alkene (123) was boiled in toluene with anisohydroxamic chloride (161) for 48 h the reaction gave a 45% yield of a colourless solid which on the basis of analytical and spectral evidence was characterized as compound (162) (Scheme 84). Similarly reaction of the alkene (123) with benzonitrile oxide (163) gave a 19% yield of an adduct whose structure was established as compound (164).

(123)   (161) X=OMe   (162) 45%

(163) X=H   (164) 19%
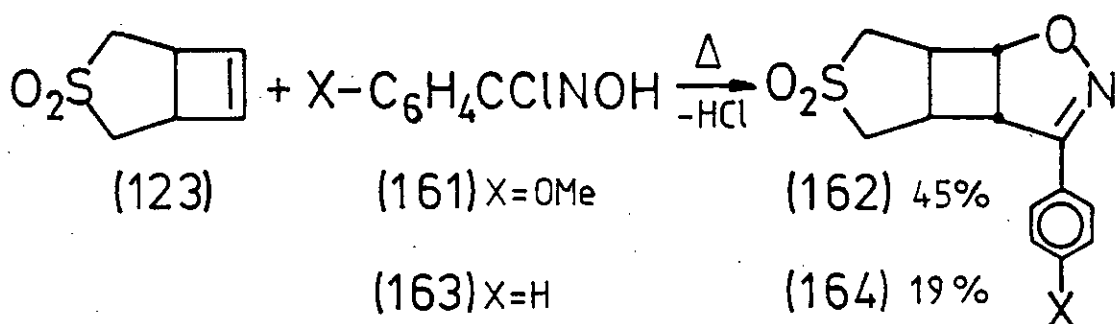
Scheme 84

The structural assignments of compound (162) and (164) were mainly based on their ^{1}H n.m.r. spectra which showed strong similarities to the ^{1}H n.m.r. spectrum of the nitrone adduct (160). As shown in Figure 21 the ^{1}H n.m.r. spectrum of compound (162) displays resonances at 5.2 δ and 4.3δ which are assigned to the 2-H and 6-H protons, respectively. These chemical shift values compare favourably with those reported for the corresponding protons in the adducts obtained from the cycloaddition of nitrile oxides to cis-3,4-dichlorocyclobutene.[152] The large coupling constant (8Hz) observed for these two signals is probably $J_{2,6}$ since these protons are cis-orientated.

The small coupling constant (2Hz) in the resonance at 5.2δ is presumably $J_{1,2}$ in keeping with the assignment of the stereochemistry
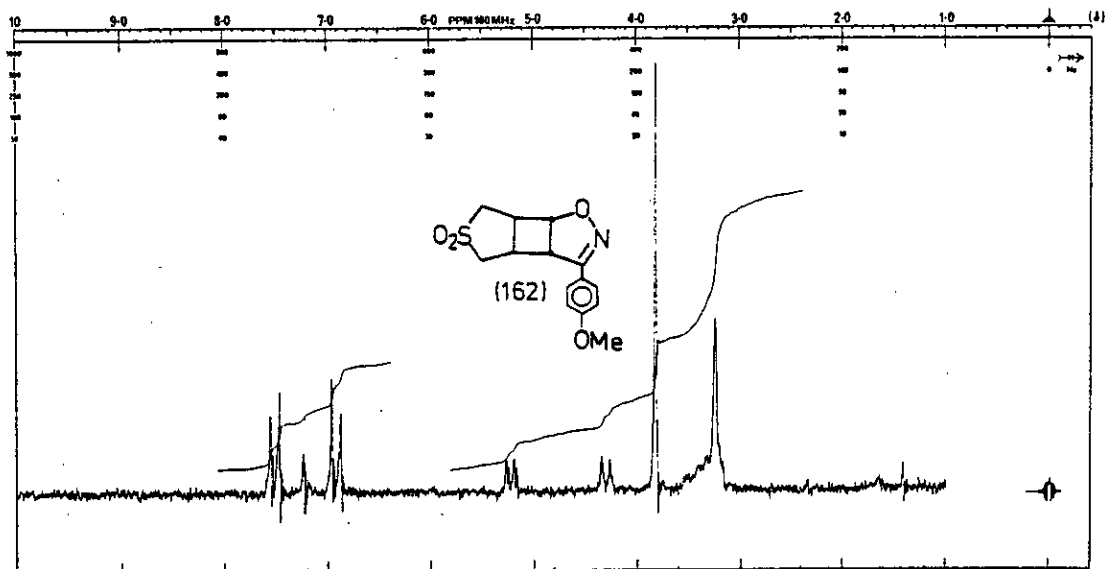
Fig. 21. 100MHz ^{1}H n.m.r. spectrum of 5-(p-methoxyphenyl)-3-oxa-9-thia-4-azatricyclo[5.3.0.0^{2,6}]dec-4-ene 9,9-dioxide (162).
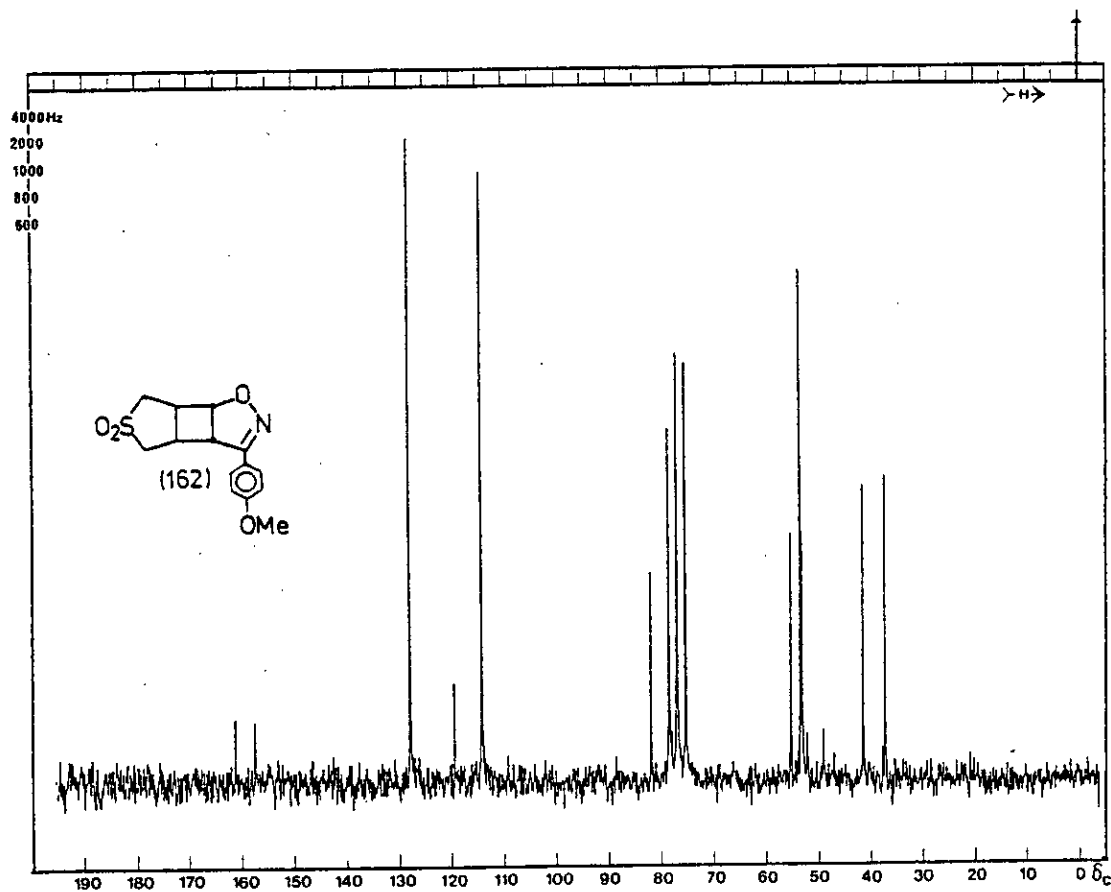
Fig. 22. 25.2MHz ^{13}C n.m.r. spectrum of 5-(p-methoxyphenyl)-3-oxa-9-thia-4-azatricyclo[5.3.0.0^{2,6}]dec-4-ene 9,9-dioxide (162).

as an _anti_-structure.   This is further supported by the secondary

splitting of the doublet at 4.3δ which is just visible and is presumably

$\underline{J}_{6,7}$.

Figure 22 shows the ^{13}C n.m.r. spectrum of (162) and contains

eleven lines which is consistent with the assigned structure.

The ^{1}H n.m.r. and ^{13}C n.m.r. spectra of adduct (164) shows

strong similarities to the spectra of adduct (162) and a similar analysis

to that described above confirms the assigned structure.

c) Addition of diazomethane

The reaction was carried out by standing an etheral solution of

the alkene (123) and diazomethane in a cold room (0-5°C) for several

weeks during which time a colourless crystalline solid gradually

precipitated out of solution in 80% yield.   Analytical and spectral

evidence established the structure of the compound as the pyrazoline

(165) shown in Scheme 85.   The slow rate of formation of the adduct
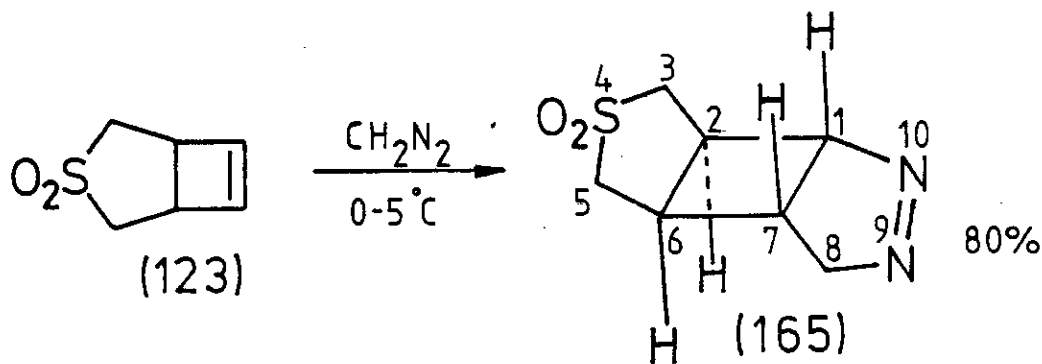
Scheme 85

(165) accords with a report by Mock[54] who observed that diazomethane

only adds to butadiene sulphone in 35% yield over a period of several

weeks.

Elemental analysis for (165) gave percentage composition for

carbon, hydrogen and nitrogen consistent with an empirical formula $C_7H_{10}N_2O_2S$. This was verified by observation in the mass spectrum of a peak at m/e 186.

The i.r. spectrum of (165) showed a band at 1535 cm^{-1} which is characteristic of Δ^1-pyrazolines.[174]

The assigned stereochemistry of (165) is based on its [1]H n.m.r. and [13]C n.m.r. spectra and on the results of selective [1]H n.m.r. decoupling experiments. The 360MHz [1]H n.m.r. spectrum of (165) is shown in Figures 23 and 23a and contains five multiplets. Due to the strong deshielding effect of the diazo group on adjacent protons the multiplet at 5.3-5.2δ is considered to be due to the bridgehead methine proton 1-H. Similarly the multiplet centred at 4.6δ is due to the methylene protons 8-H and 8'-H. The α-sulphone methylenes are considered to give rise to the multiplet from 3.4-3.1δ whilst the bridgehead methine protons 2-H, 7-H, 6-H are assigned to the multiplets at 3.05δ, 2.7δ and 2.6δ respectively.

Double resonance experiments helped to confirm these assignments as well as the anti-structure. Thus irradiation of the multiplet at 5.2δ leads to a simplification in the resonance at 4.6δ (Fig. 23b). This shows that there is coupling between 1-H and the methylene at C-8, an effect which has been noted for similar compounds.[174] Of the three cyclobutane protons the resonance due to 7-H simplifies to a much greater extent than the other two suggesting the removal of a fairly large coupling constant in this case. This is in keeping with the anti-orientation of the sulphone and pyrazoline rings.
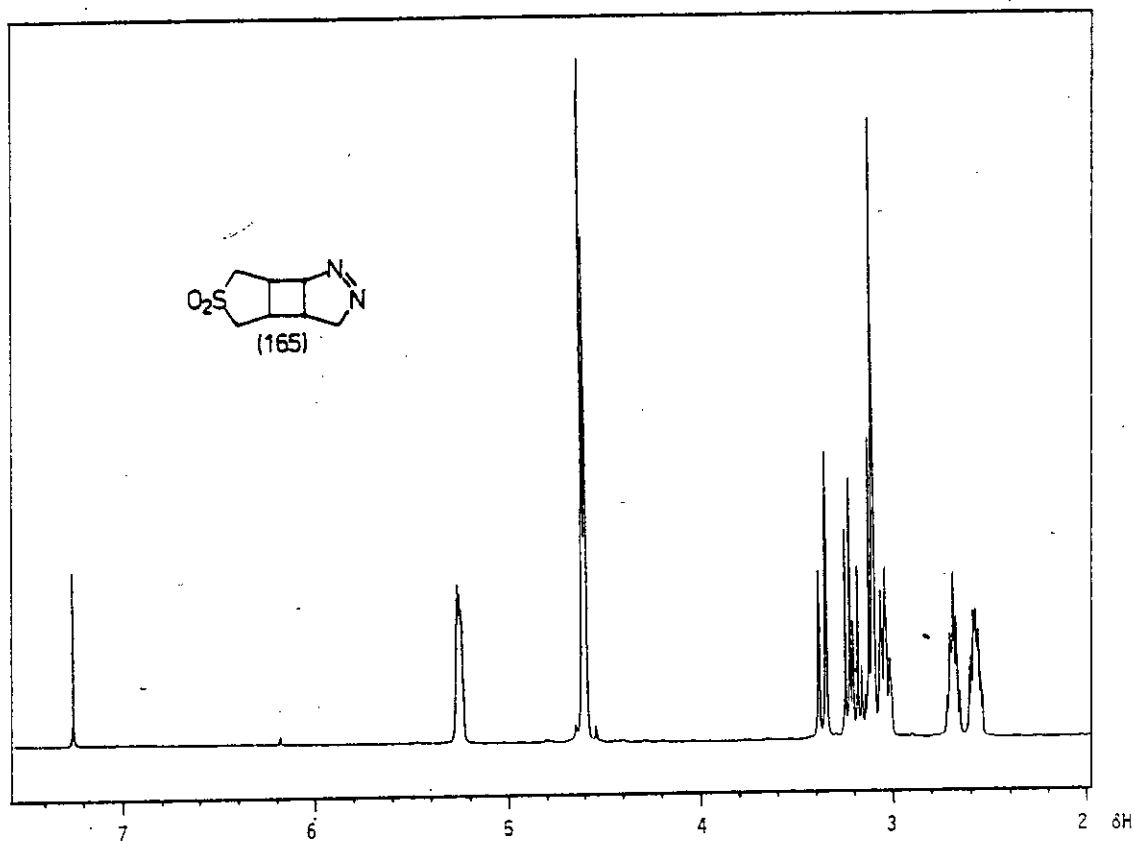
Fig. 23. 360MHz $^1_2$H n. m. r. spectrum of 4-thia-9, 10-diazatricyclo-[5. 3. 0. 0^{2,6}]dec-9-ene 4, 4-dioxide (165).
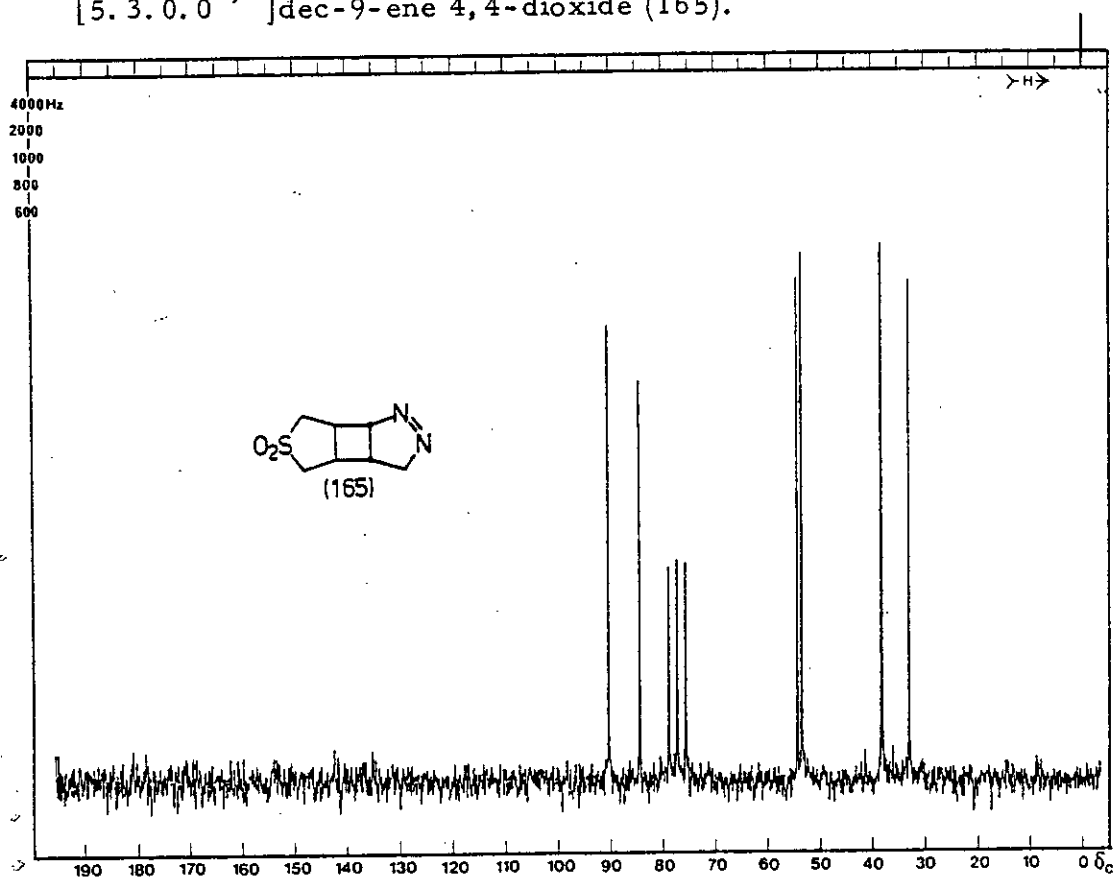
Fig. 24. 25. 2MHz ^{13}C n. m. r. spectrum of 4-thia-9, 10-diazatricyclo-[5. 3. 0. 0^{2,6}]dec-9-ene 4, 4-dioxide (165).
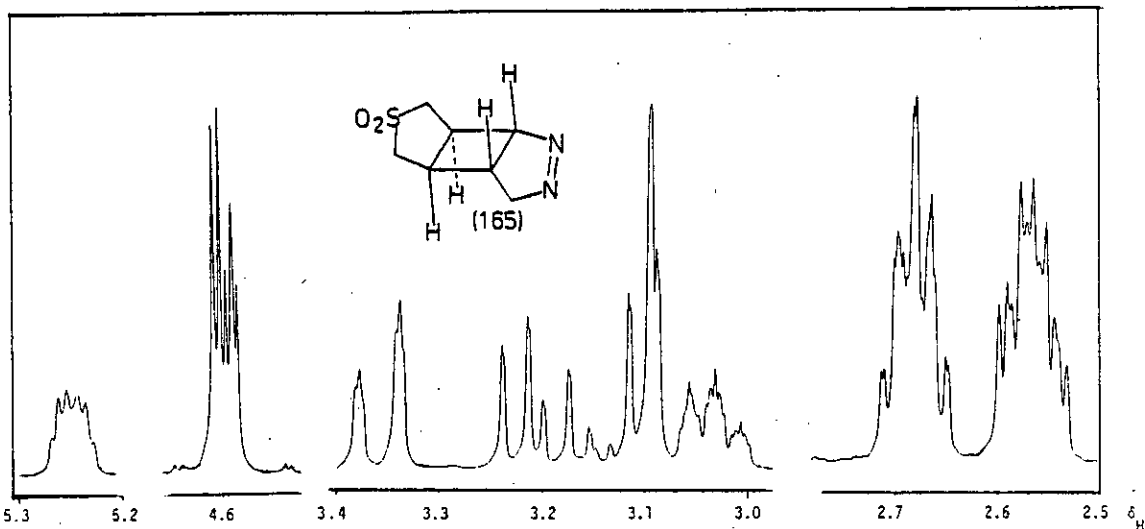
Fig. 23a. Expansion of 360MHz ^{1}H n.m.r. spectrum of 4-thia-9,10-diaza-tricyclo[5.3.0.0^{2,6}]dec-9-ene 4,4-dioxide (165).
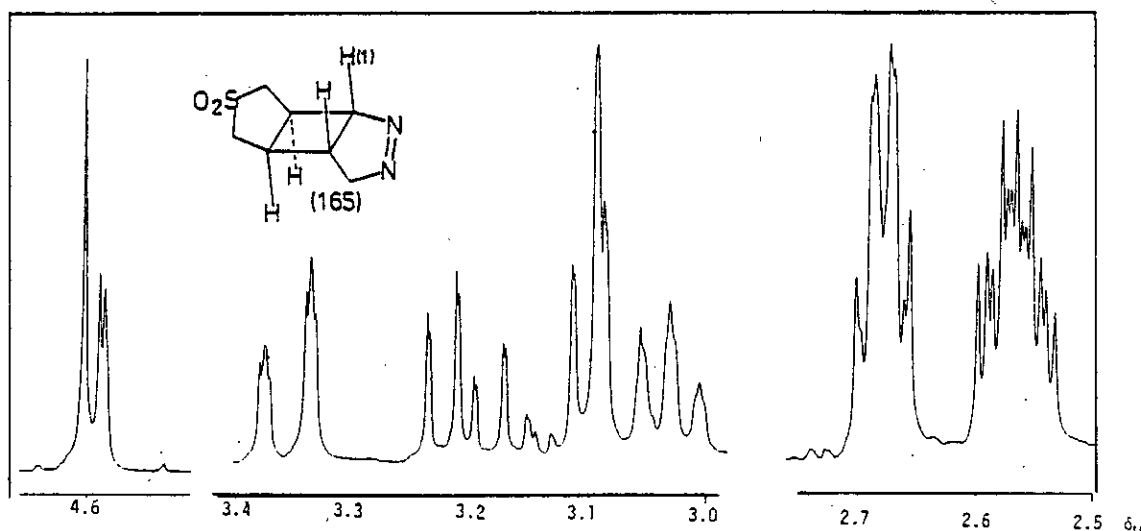
Fig. 23b. 360MHz ^{1}H n.m.r. spectrum of 4-thia-9,10-diazatricyclo[5.3.0.0^{2,6}]-dec-9-ene 4,4-dioxide (165) with decoupling of the 1-H proton by irradiation at 5.2δ.
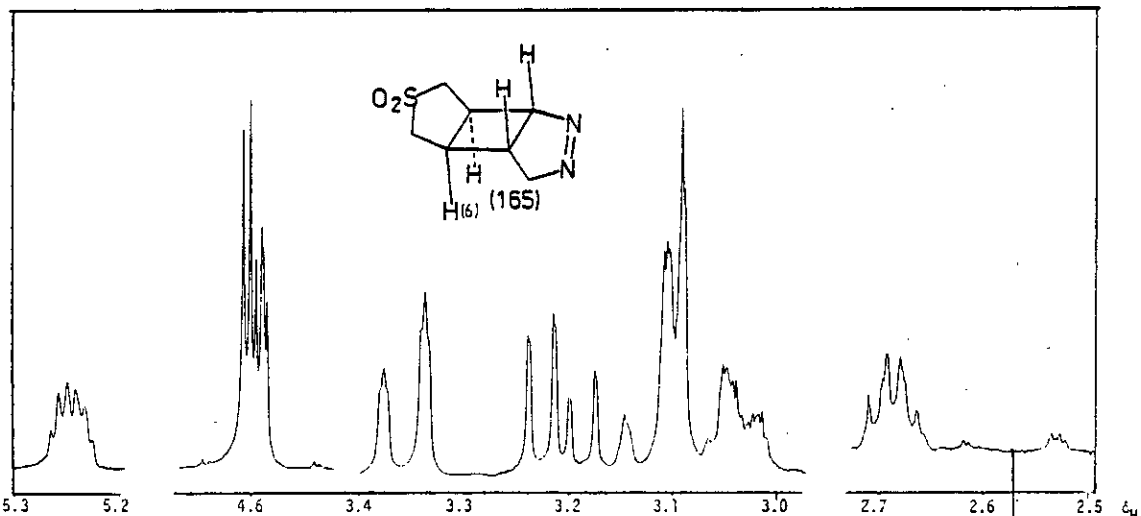
Fig. 23c. 360MHz ^{1}H n.m.r. spectrum of 4-thia-9,10-diazatricyclo-[5.3.0.0^{2,6}]dec-9-ene 4,4-dioxide (165) with decoupling of the 6-H proton by irradiation at 2.6δ.
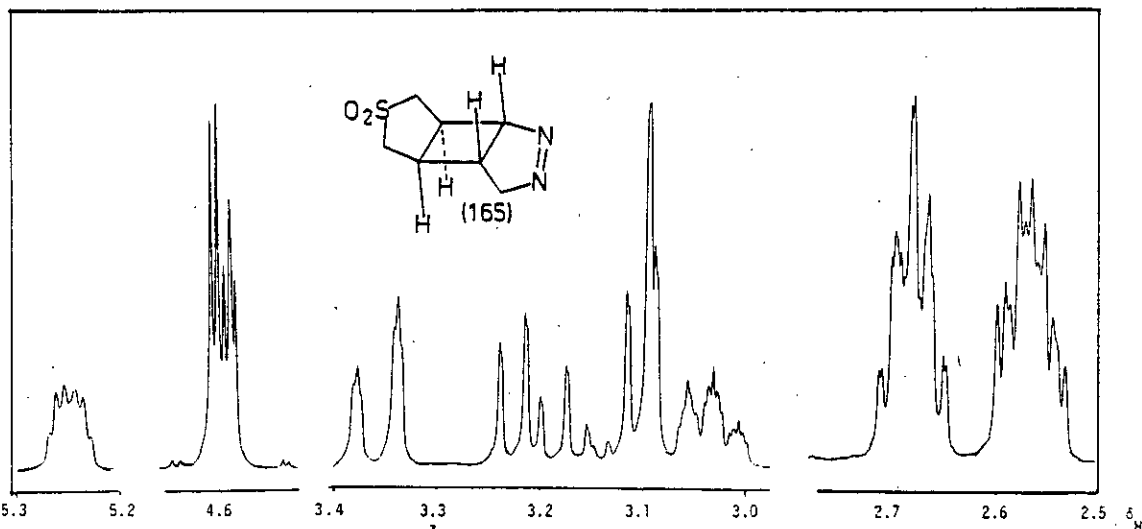
Fig. 23a. Expansion of 360MHz ^{1}H n. m. r. spectrum of 4-thia-9, 10-diazatricyclo[5. 3. 0. 0^{2,6}]dec-9-ene 4,4-dioxide (165).
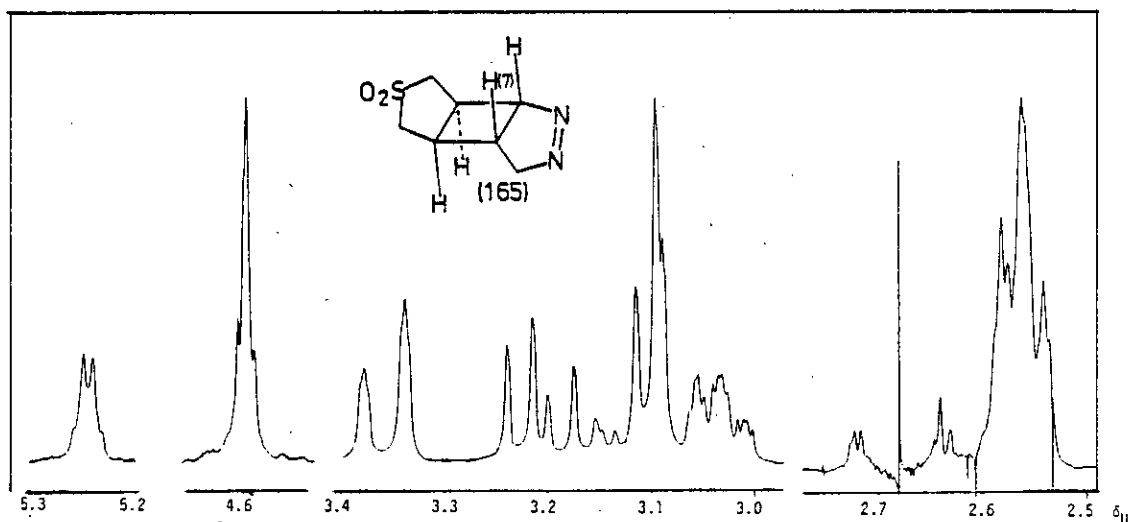
Fig. 23d. 360MHz ^{1}H n. m. r. spectrum of 4-thia-9, 10-diazatricyclo-[5. 3. 0. 0^{2,6}]dec-9-ene 4,4-dioxide (165) with decoupling of the 7-H proton by irradiation at 2. 7δ.
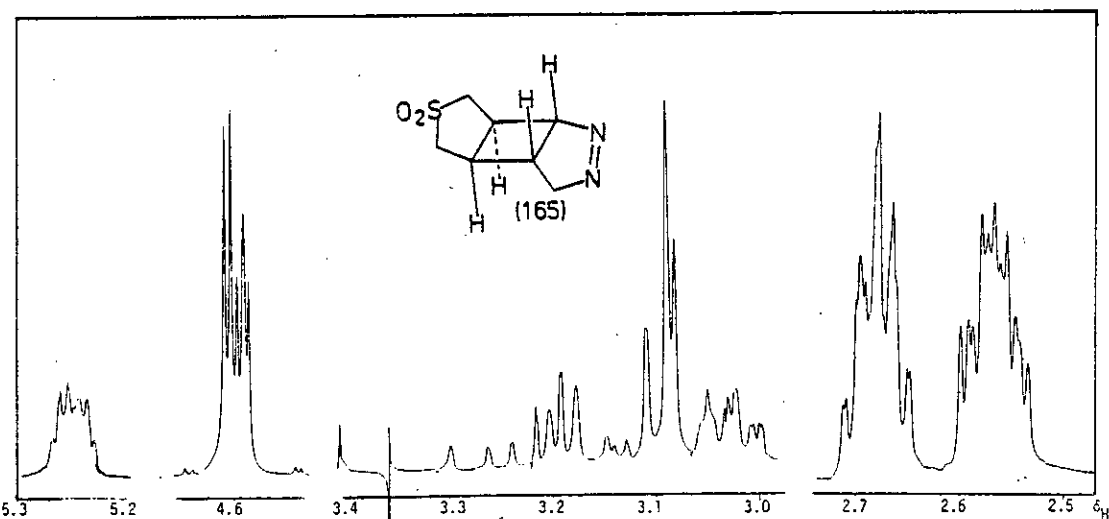
Fig. 23e. 360MHz ^{1}H n. m. r. spectrum of 4-thia-9, 10-diazatricyclo[5. 3. 0. 0^{2,6}]-dec-9-ene 4,4-dioxide (165) with decoupling of the C-3 methylene by irradiation at 3.4 δ.

Similarly, irradiation at 2.6 δ, 2.7δ and 3.4δ, respectively

gave results which corroborated these assignments (see figures 23c-e).

Notably irradiation at 2.7δ (7-H) produces major simplification in the

resonances at 5.25δ (1-H) and at 4.6δ (8 and 8'-H) (Figure 23d).

Little simplification is observed in the resonances due to 2-H and 6-H

as would be expected for the removal of a four-bond and a trans-coupling

constant, respectively.

The ^{13}C n.m.r. spectrum of (165) shown in figure 24 has only

seven lines (2, overlap) and confirms that there is only one isomer present.

d) Attempted addition of diphenylnitrilimine.

Attempts to add diphenylnitrilimine to the alkene (123) led to

failure.   The diphenylnitrilimine was generated by two different routes,

one involving thermal elimination of HCl from α-chlorophenylhydrazone

in boiling toluene, and the other by addition of triethylamine to the

substrate in benzene.   In both cases work-up of the reaction mixtures

by chromatography gave an almost quantitative recovery of unreacted

alkene.   This lack of reactivity is presumably due to the lower reactivity

of nitrilimines compared to the nitrile oxides which were investigated

earlier.   In this connection it is noteworthy that Tinley[129] has observed

that the same dipole also failed to react with the structurally similar

cyclobutene anhydride (139).

D.   Synthesis of cis-Divinyl Compounds by Flash Vacuum Pyrolysis

of Tricyclic Sulphones.

D.1   Preparation of 1-phenyl and 1-methyl-cis-3,4-divinylsuccinimides.

As mentioned in section A.2 of the discussion pyrolysis of the

anhydride (1) provides a clean and efficient synthesis of the hitherto

unknown 2,5-dioxo-cis-3,4-divinyltetrahydrofuran (113).   This initial

success prompted a more detailed investigation aimed at evaluating

the usefulness of this approach as a general route to cis-divinyl

compounds.   Since X-ray structure determination of 9-phenyl-8,10-

dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (108)

provided key evidence as to the stereochemistry of the anhydride (1)

it was decided to pyrolyse compound (108) in an attempt to prepare

the previously unknown 1-phenyl-cis-3,4-divinylsuccinimide (109)

as shown in Scheme 86.

(108) X = Ph   (109) X = Ph   52%

(166) X = CH$_3$ (167) X = CH$_3$ 58%
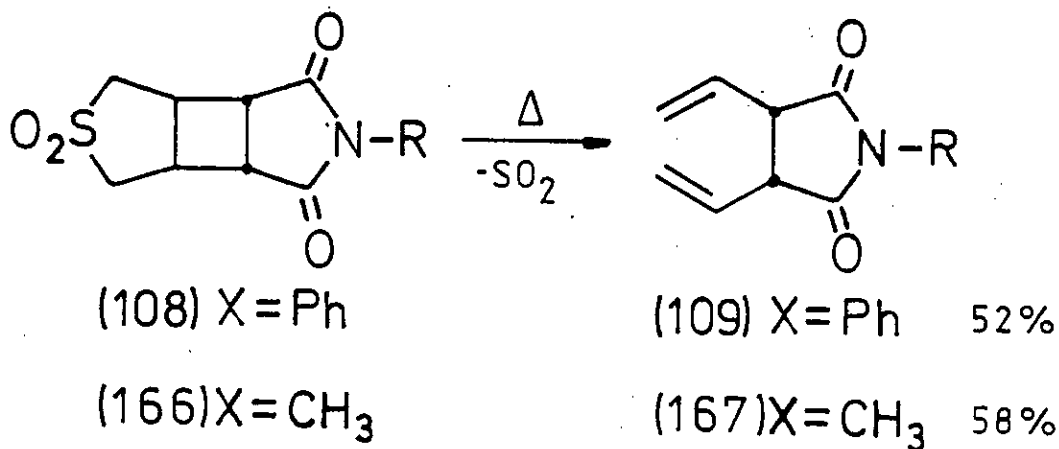
Scheme 86

Pyrolysis of the imide (108) at 625°C in a flow system gave a

52% yield of a colourless crystalline solid whose analytical and

spectroscopic data established its structure as the desired succinimide

(109).   Thus elemental analysis gave percentage composition for

carbon, hydrogen and nitrogen consistent with an empirical formula $C_{14}H_{13}NO_2$. This was verified by observation in the mass spectrum of a parent ion peak at m/e 227.

The ^1H n.m.r. spectrum of (109) is reproduced in figure 25 and is consistent with the assigned structure. Thus the multiplet centred at 7.35δ is attributed to the phenyl protons whilst the complex multiplet at 5.9-5.3δ is typical of a cis-divinyl system. The doublet of doublets centred at 3.75δ is assigned to the 3-H and 4-H protons.

The ^{13}C n.m.r. spectrum of (109) is shown in figure 26 and as expected consists of eight resonances. The carbonyl carbons give rise to the signal at 175δ whilst the signals due to the aromatic carbons occur in the 132-128δ region. The signals at 126δ and 121δ are due to the secondary (C_6 and C_8) and terminal vinyl carbons, respectively. Finally the C_3 and C_4 carbons are represented by the signal at 49δ.

Since compound (109) is a crystalline solid it was decided to carry out an X-ray study to further confirm the assigned stereochemistry. Careful recrystallization of (109) from ethyl acetate gave colourless crystals ideal for X-ray studies. This showed that the compound possessed cis-orientated vinyl groups at the 3 and 4 positions (see figure 9, p.115). However the quality of the X-ray data was not very high presumably because there is some disorder in the crystal lattice. As a consequence the bond geometry obtained from the analysis was unsatisfactory and no comment can be made on the bond lengths or bond angles obtained.

Similar pyrolysis of the methyl analogue of (108) viz. compound
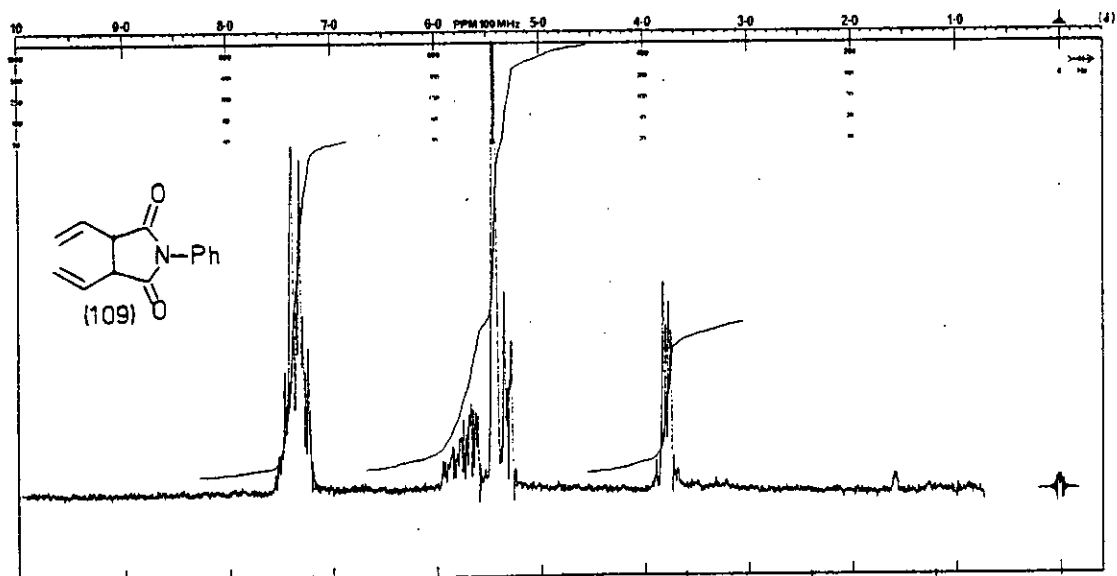
Fig. 25. 100MHz ^{1}H n. m. r. spectrum of 1-phenyl-cis-3,4-divinyl-
succinimide (109).
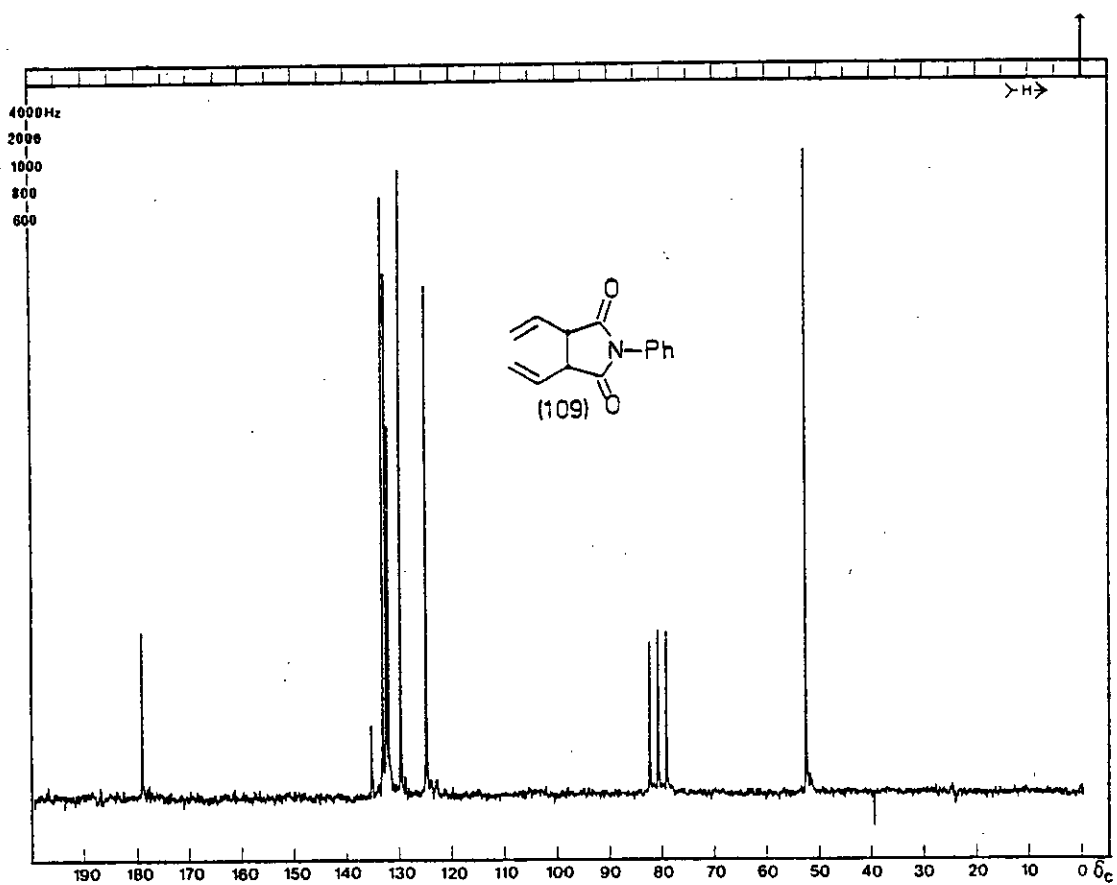
Fig. 26. 25.2MHz ^{13}C n. m. r. spectrum of 1-phenyl-cis-3,4-divinyl-
succinimide (109).

(166) gave a 58% yield of a light brown oil which was characterized

as 1-methyl-cis-3,4-divinylsuccinimide (167) on the basis of its

elemental composition and spectral properties which showed strong

similarities to those described above for compound (109).

D. 2   Preparation of cis-3,4-divinyl-1-heterocyclopentanes.

Prior to the present study, the heterocyclic analogues of cis-

1,2-divinylcyclopentane (88) were unknown although the latter had been

the subject of several studies concerned with its Cope rearrangement to

cis, cis-1,5-cyclononadiene (87) (see Scheme 39, p.40).   Consequently

it was of considerable interest to examine the utility of compounds of

type (168) previously obtained by chemical modification of the anhydride

(1) as precursors to cis-3,4-divinyl-1-heterocyclopentanes (169) under

flash vacuum pyrolysis conditions (Scheme 87).
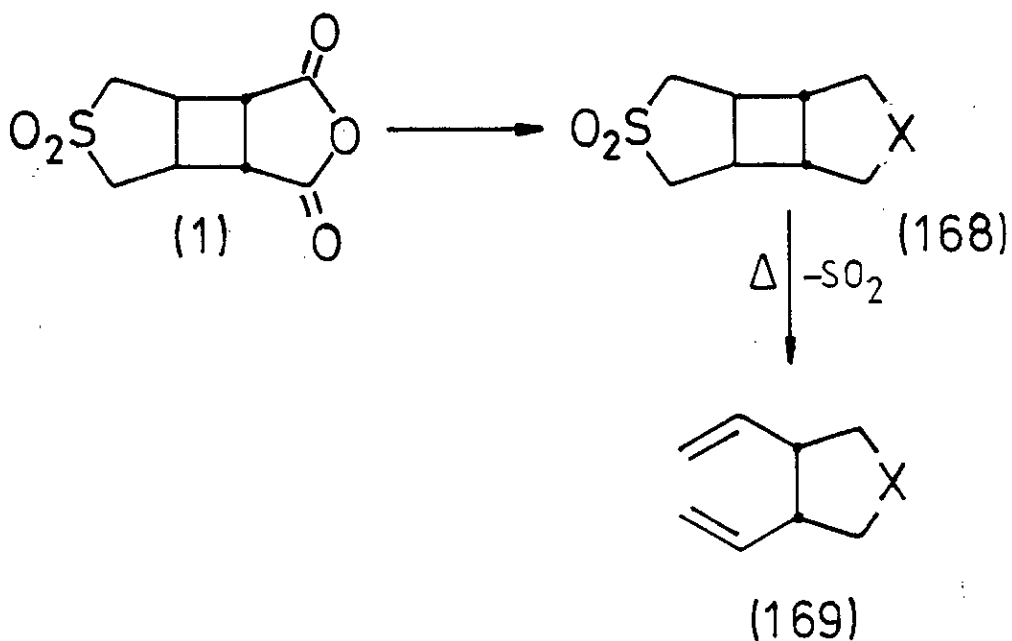
Scheme 87

a) cis-3, 4-Divinyltetrahydrofuran.

Pyrolysis of the tetrahydrofuran (117) under f. v. p. conditions

at $625°C$ gave a 62% yield of a clear volatile liquid with a sickly odour

and spectroscopic properties typical of the desired cis-3, 4- divinyl-

tetrahydrofuran (170) (Scheme 88).

(117) $-SO_2$ (170)   62%
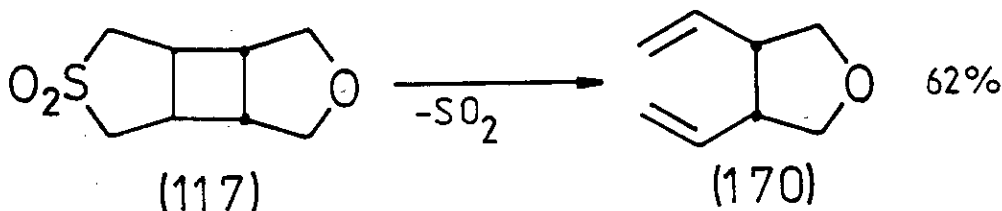
Scheme 88

Elemental analysis of the liquid gave percentage composition

for carbon and hydrogen consistent with an empirical formula $C_8H_{12}O$

which was corroborated by observation in the mass spectrum of a

parent ion peak at m/e 124.

The ^1H n. m. r. spectrum of (170) was recorded in $[^2H_6]$-acetone

at a frequency of 360MHz and this spectrum is reproduced in figure 27.

The high frequency used allows a full analysis of this spectrum.

The multiplet centred at 5.75δ is assigned to the 6-H and 8-H

protons and can be considered as a doublet of doublet of doublets

$(J_{6, 7-trans} = 17.5Hz,$ $J_{6, 7-cis} = 10.5Hz,$ $J_{3, 6} = 9.5Hz).$ The protons

7, 7', 9 and 9'-H give rise to the multiplet centred at ca. 5.05δ which may

be interpreted as overlapping sets of doublets of doublets with fine

splitting due to the allylic couplings to the 3-H proton. The coupling

constants for the proton trans to 6-H are $(J_{6, 7-trans} = 17.5Hz,$

$J_{7, 7'} = 2.5Hz,$ $J_{3, 7'} = 1Hz)$ and those due to the proton cis to 6-H are
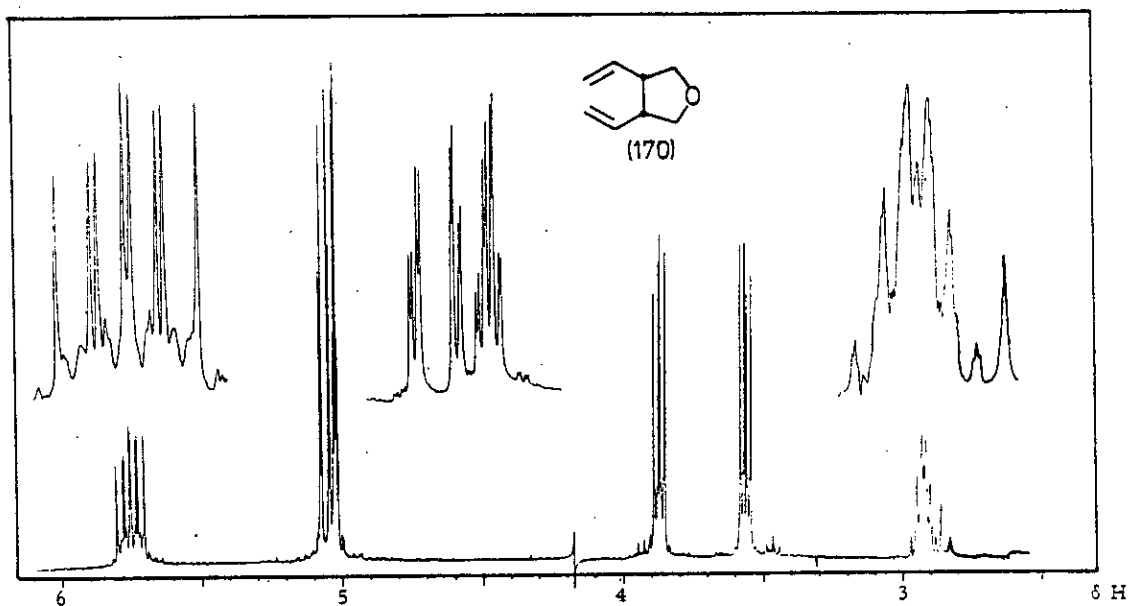
Fig. 27. 360MHz ^{1}H n.m.r. spectrum of cis-3,4-divinyltetrahydrofuran (170).
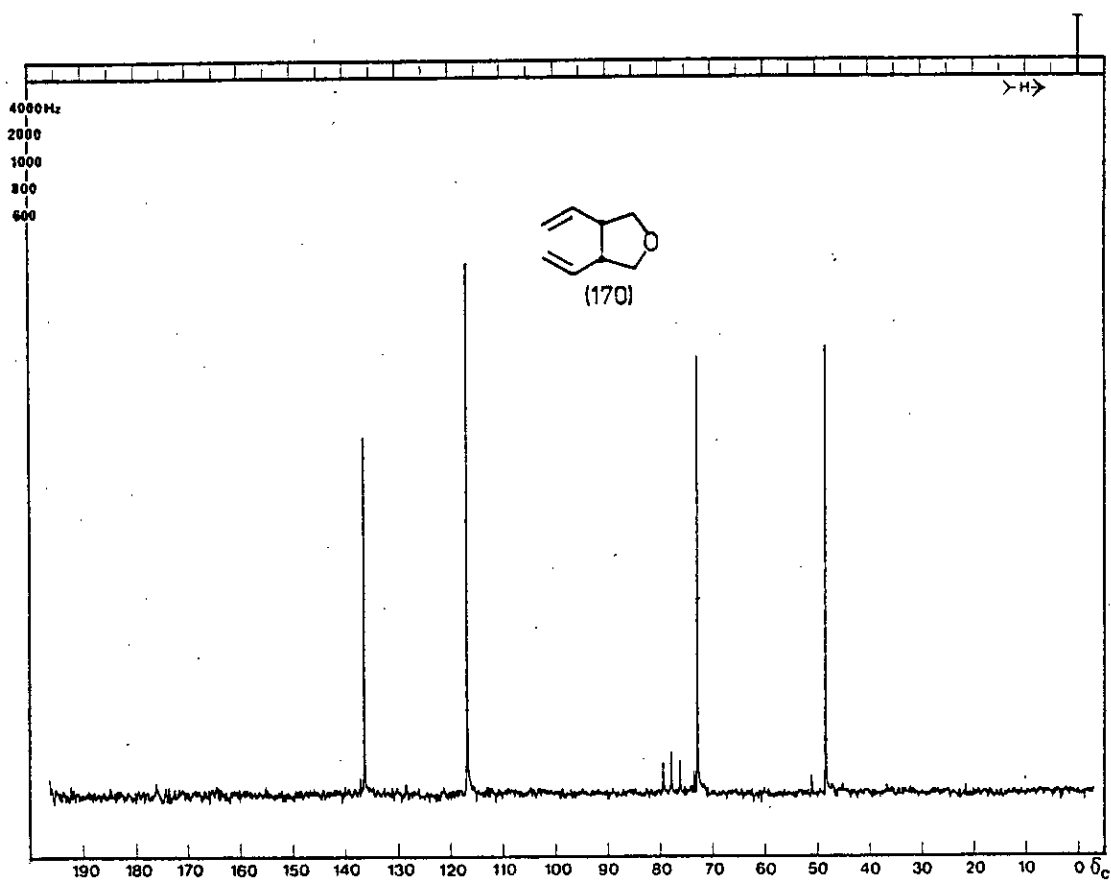
Fig. 28. 25.2MHz ^{13}C n.m.r. spectrum of cis-3,4-divinyltetrahydrofuran (170).

$(\underline{J}_{6,\,7\text{-}\underline{cis}} = 10.5\text{Hz},\ \underline{J}_{7,\,7'} = 2.5\text{Hz},\ \underline{J}_{3,\,7} = 0.5\text{Hz}).$

The 2 and 5'-H and 2' and 5'-H give rise to the doublet of doublets centred at 3.87δ and 3.5δ respectively with coupling constants $(\underline{J}_{2,\,2'} = 9.5\text{Hz},\ \underline{J}_{2,\,3} = 7.5\text{Hz})$ and $(\underline{J}_{2,\,2'} = 9.5\text{Hz},\ \underline{J}_{2',\,3} = 6\text{Hz})$. The multiplet centred at 2.93δ is due to the 3-H and 4-H protons. The shifts and coupling constants for the divinyl system compare very well with those reported for cis-divinylcyclopropane.[87]

The ^{13}C n.m.r. spectrum of (170) is shown in figure 28 and as expected consists of four lines.

The structure of (170) was unambiguously confirmed by its alternative synthesis via the route shown in Scheme 89. Thus pyrolysis of the anhydride (1) gave the cis-3,4-divinyl derivative (113) (see Scheme 51, p.124), which could be converted into the dimethyl ester (171) in 50% yield by boiling in methanol with a few drops of concentrated

Scheme 89
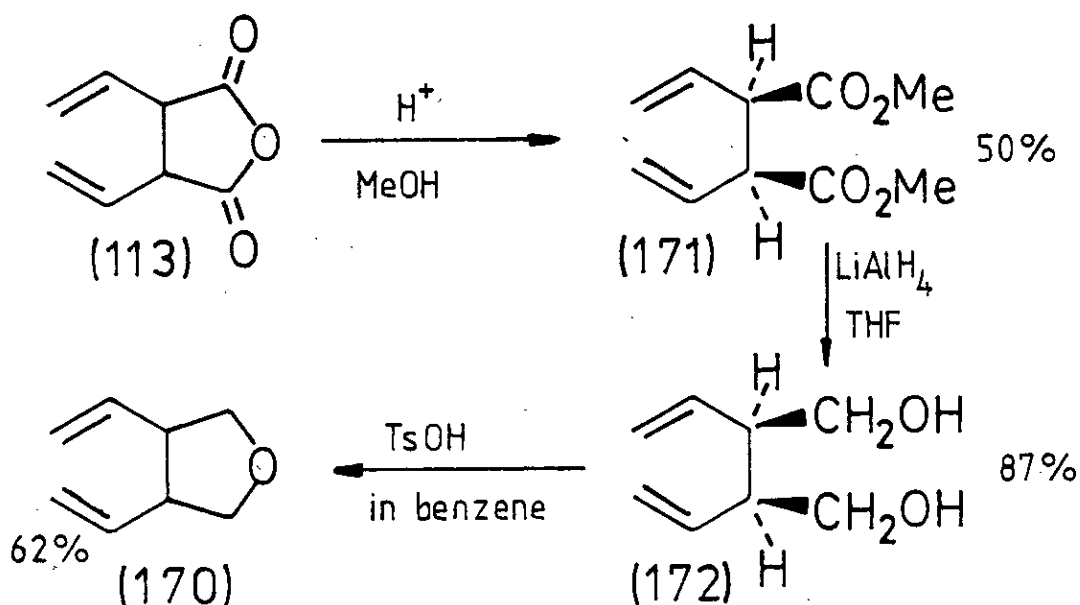
sulphuric acid. Reduction of this diester with lithium aluminium hydride in tetrahydrofuran followed by dehydration[133] of the resulting

diol (172) yielded the desired product in 62% yield.

In passing it is of interest to note that the diester (171) has been reported[175] but only as a mixture of the meso form and its diastereomers. The proton n. m. r. of (171) compared well with that reported by these workers, whilst the ^{13}C n. m. r. supported the assigned structure and confirmed the presence of only one isomer.

The fact that cis-3, 4-divinyltetrahydrofuran (170) is stable under the pyrolysis conditions indicates that it has little tendency to undergo a Cope rearrangement to the unknown heterocycle 1-oxa-cis, cis-3, 7-cyclononadiene (173) as depicted in Scheme 90. This contrasts strongly

(170)

(173)

Scheme 90
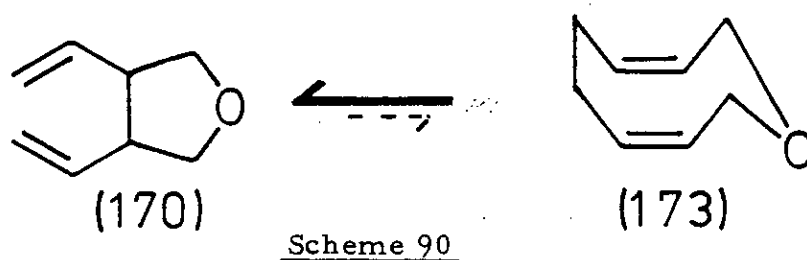
with cis-1, 2-divinyloxirane (83, X=O) which is known to undergo a facile Cope rearrangement[89] but is in keeping with the report by Vogel[98] that the Cope equilibrium of cis-1, 2-divinylcyclopentane with its hydrocarbon counterpart strongly favours the former.

b) cis-3, 4-Divinyltetrahydrothiophene

The appropriate precursor (119) for the synthesis of the title compound was successfully prepared as discussed in Section B. 2. Pyrolysis of (119) under f. v. p. conditions at 620°C gave a 25% yield of a pale yellow liquid which was identified as cis-3, 4-divinyltetra-hydrothiophene (174) on the basis of analytical and spectral data after

purification by bulb-to-bulb distillation (Scheme 91).
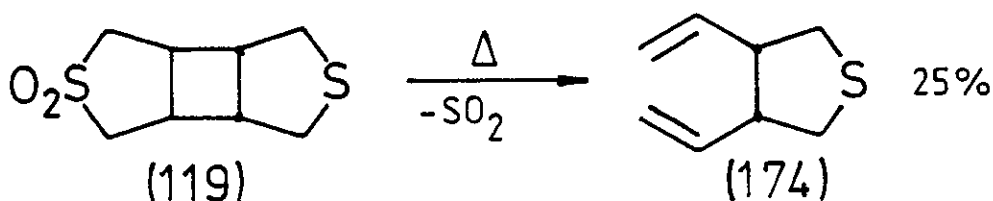
<p style="text-align: center;">Scheme 91</p>

A gummy residue remained in the inlet system after pyrolysis indicating that some decomposition of (119) had occurred during sublimation into the furnace. The spectra of the crude product also contained peaks due to unidentified impurities probably formed by extrusion of sulphur. This decomposition might also explain the low yield of (174) obtained.

Elemental analysis of the clear liquid obtained by microdistillation gave percentage composition for carbon and hydrogen consistent with an empirical formula $C_8H_{12}S$. This was confirmed by observation in the mass spectrum of a parent ion peak at m/e 140. A very strong peak at m/e 86 corresponds to the loss of the two vinyl groups (140-2x27 =86).

The ^1H n.m.r. and ^{13}C n.m.r. spectra of (175) were entirely consistent with the assigned structure and showed strong similarities to those described in detail for cis-3,4-divinyltetrahydrofuran (170).

It would seem that compound (174) like compound (170) has little tendency to undergo a Cope rearrangement as no Cope rearranged products were detected.

c) 1-Benzyl-cis-3,4-divinylpyrollidine

In an attempt to prepare a nitrogen analogue of (170) and (174),

the precursor (122) was prepared as described in Section B.2.

Pyrolysis of (122) at $525^{\circ}C$ under f.v.p. conditions gave a 58% yield

of light brown oil which was purified by microdistillation and charac-

terized as the title compound (175) (Scheme 92).

$$O_2S \underset{(122)}{\text{}} N-CH_2Ph \xrightarrow[-SO_2]{\Delta} \underset{(175)}{\text{}} N-CH_2Ph \quad 58\%$$
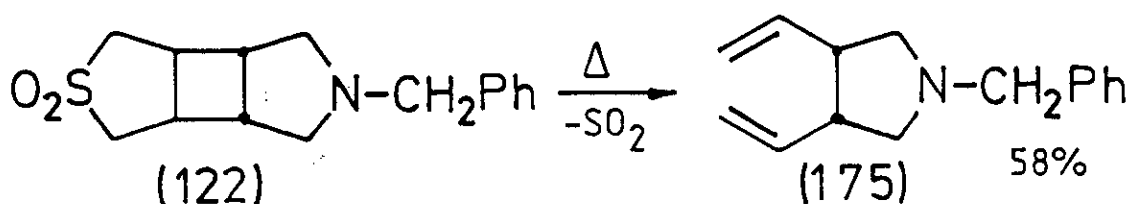
Scheme 92

Elemental analysis of the oil obtained by microdistillation gave

percentage composition for carbon, hydrogen and nitrogen consistent

with an empirical formula $C_{15}H_{19}N$. This was confirmed by observation

in the mass spectrum of a parent ion peak at m/e 213.

The ^{1}H n.m.r. spectrum of (175) was entirely consistent with

the assigned structure and showed strong similarities to that just

described for cis-3,4-divinyltetrahydrofuran (170).

Also as with the oxygen and sulphur analogues there was no

evidence to indicate any Cope rearrangement. However when the

pyrolysis was carried out above $550^{\circ}C$ total breakdown of the product

occurred to give unidentified aromatic compounds as indicated by

^{1}H n.m.r. spectroscopy.

E.   Pyrolysis of 3-Thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide
     and its Adducts

E.1 Pyrolysis of 3-thiabicyclo[3.2.0]hept-6-ene 3,3-dioxide

The preparation of the title compound (123) has already been
described in Section C as well as its reactions with carbenes, nitrenes
and 1,3-dipoles in an effort to prepare a wider range of potential cis-
divinyl precursors.   The pyrolysis of the alkene (123) itself provided
a convenient starting point for the investigation.

Thus when the alkene (123) was pyrolysed in a flow system at
500°C the product obtained was identified by [1]H n.m.r. spectroscopy
as 1,3-cyclohexadiene (176).   The formation of the latter can be
explained in terms of a cheletropic extrusion of sulphur dioxide to
give cis-1,3,5-hexatriene which under the pyrolytic conditions under-
goes an electrocyclic ring closure reaction as indicated in Scheme 93.
Support for this pathway was obtained by lowering the temperature of
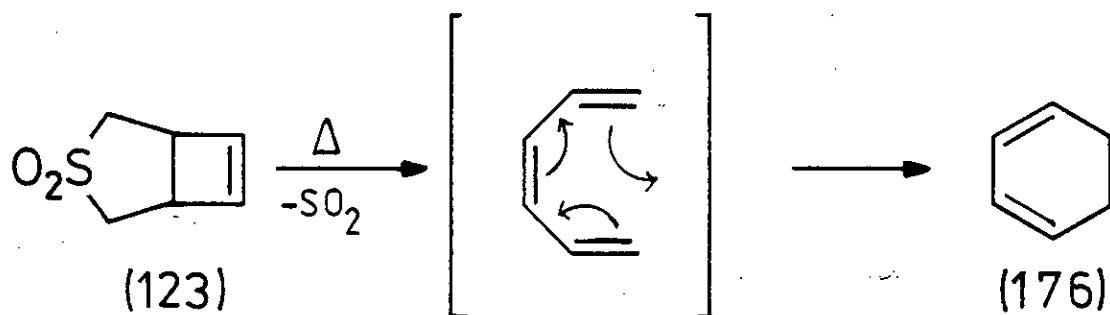
Scheme 93

the pyrolysis to 400°C whereupon cis-1,3,5-hexatriene, 1,3-cyclo-
hexadiene (176) together with unchanged alkene were detected in the
pyrolysate in approximately equal amounts.   At temperatures below
400°C, the starting alkene sublimed through the furnace unchanged.

The formation of cis-1, 3, 5-hexatriene can be envisaged to occur by two different routes. Firstly compound (123) could extrude SO_2 in the normal linear disrotatory manner and give cis-1, 3, 5-hexatriene directly. Alternatively (123) could undergo an initial ring opening reaction, in a manner analogous to that reported for bicyclo[3, 2. 0]hept-6-ene,[176] to afford 2, 7-dihydrothiepin 1, 1-dioxide (22) which is known to lose SO_2 under the pyrolytic conditions[50, 51] to give cis-1, 3, 5-hexatriene (Scheme 94). No evidence is available to
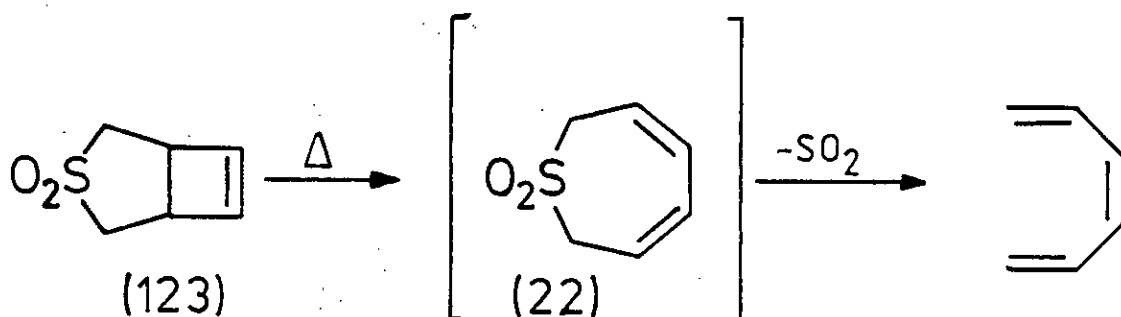
Scheme 94

differentiate between these two pathways but the former is preferred on the grounds that it is an allowed process whereas the isomerization of (123) into (22) is disfavoured by orbital symmetry considerations.

Following the report by Gaoni[66] that sulphones such as (177) are smoothly converted to the corresponding diene (178) by reaction with lithium aluminium hydride as outlined in Scheme 95, the alkene (123) was treated in a similar manner and the resultant mixture
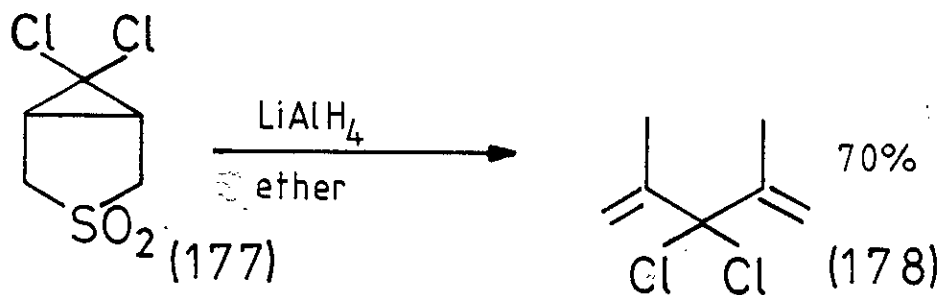
Scheme 95

analysed by gas chromatography. This showed the presence of only two products which were identified as cis and trans-hexa-1, 3, 5-trienes by peak enhancement experiments using authentic samples prepared by the method of Hwa et al.[135] The lack of stereospecificity indicates that loss of SO_2 presumably occurs via a radical or polar mechanism rather than a cheletropic elimination.

In order to rule out the possibility that the reaction conditions had caused isomerization of the resultant trienes a control experiment was carried out using an authentic mixture of cis and trans-hexa-1, 3, 5-trienes. However after boiling the mixture for 1 h, gas chromatographic analysis showed no change in the ratio of cis to trans isomers.

E. 2   **Pyrolysis of 8-oxa-4-thiatricyclo[5. 1. 0. 0$^{2, 6}$]octane 4, 4-dioxide.**

The title compound (143) was prepared by the method outlined in Section C. 2 as a potential precursor of cis-2, 3-divinyloxirane (83, X=O) which upon Cope rearrangement is known[89] to give 4, 5-dihydrooxepine (84, X=O). When the epoxide (143) was pyrolysed under f. v. p. conditions at 580°C a clear liquid was obtained in 55% yield. This was identified as 4, 5-dihydrooxepin (84, X=O) by comparison of the ^{1}H n. m. r. and ^{13}C n. m. r. spectroscopy data with known literature values.[89d, 136]

The formation of (84, X=O) is easily explained in terms of a cheletropic extrusion of sulphur dioxide from (143) in the normal manner

leading to cis-2, 3-divinyloxirane (83, X=O) which subsequently under-

goes a Cope rearrangement to form 4, 5-dihydrooxepin (84, X=O) as

shown in Scheme 96.
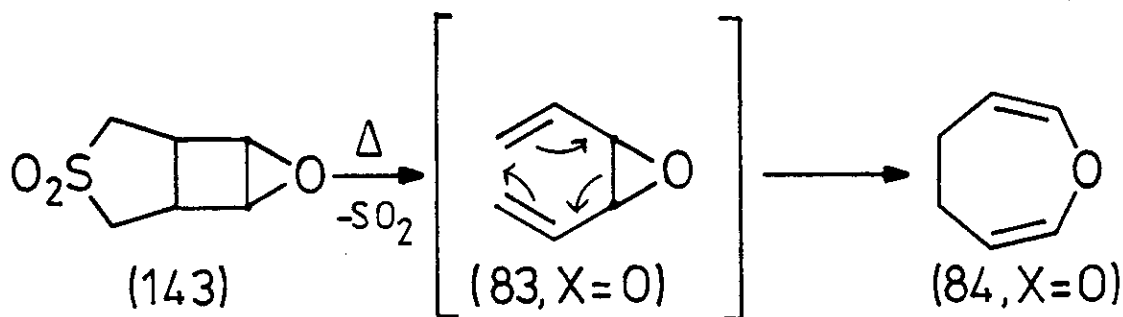
Scheme 96

E. 3   Pyrolysis of adducts obtained by nitrile oxide addition to 3-
       thiabicyclo[3. 2. 0]hept-6-ene 3, 3-dioxide.

The adduct (162) from the addition of anisonitrile oxide to 3-

thiabicyclo[3. 2. 0]hept-6-ene 3, 3-dioxide (123) was pyrolysed in the

usual way at 500°C in a flow system and the pyrolysate obtained

sublimed to give a 33% yield of a colourless translucent solid, m. p.

$58-60^{\circ}$C.   Analytical and spectral data established the structure of

this solid to be 4, 5-dihydro-3-(p-methoxyphenyl)-cis-4, 5-divinyliso-

xazole (179) (Scheme 97).   Thus elemental analysis gave percentage

(162) X=OMe   (179) X=OMe 33%
(164) X=H   (180) X=H   19%
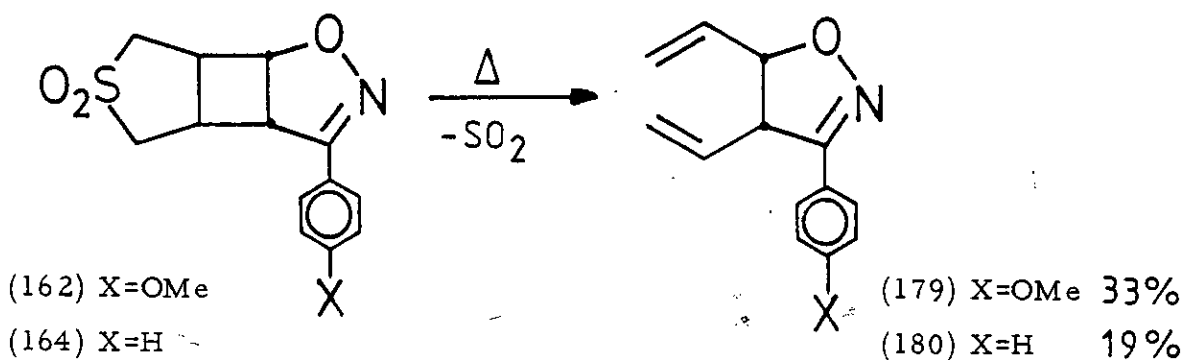
Scheme 97

composition for carbon, hydrogen and nitrogen consistent with an empirical formula $C_{14}H_{15}O_2N$. This was confirmed by observation in the mass spectrum of a parent ion peak at m/e 229.

The ^{1}H n. m. r. spectrum (179) was exceptionally complicated in the olefinic region due to overlapping signals of the non-equivalent vinyl groups. The ^{13}C n. m. r. spectrum contained twelve lines in keeping with the assigned structure.

Similar pyrolysis of compound (164) at 500°C yielded a brown-coloured pyrolysate which after distillation at 100°C/0.1mmHg provided a 19% yield of a colourless oil. This compound was identified as 4,5-dihydro-3-phenyl-cis-4, 5-divinylisoxazole (180) on the basis of analytical and spectral data (Scheme 97). As expected the spectral data for compound (180) showed strong similarities to the data for compound (179).

E.4 Pyrolysis and photolysis of 4-thia-9, 10-diazatricyclo[5. 3. 0. 0$^{2, 6}$]-dec-9-ene 4, 4-dioxide.

The title compound (165) was of some interest as it provided the first example in the present study of a molecule which could extrude either sulphur dioxide or nitrogen or both under pyrolytic conditions. In particular the loss of nitrogen might be expected to lead to the formation of the potential cis-divinylcyclopropane precursor (181) (Scheme 98).

Slow sublimation of compound (165) through a furnace at 450°C under f. v. p. conditions gave a pyrolysate which according to g. c.
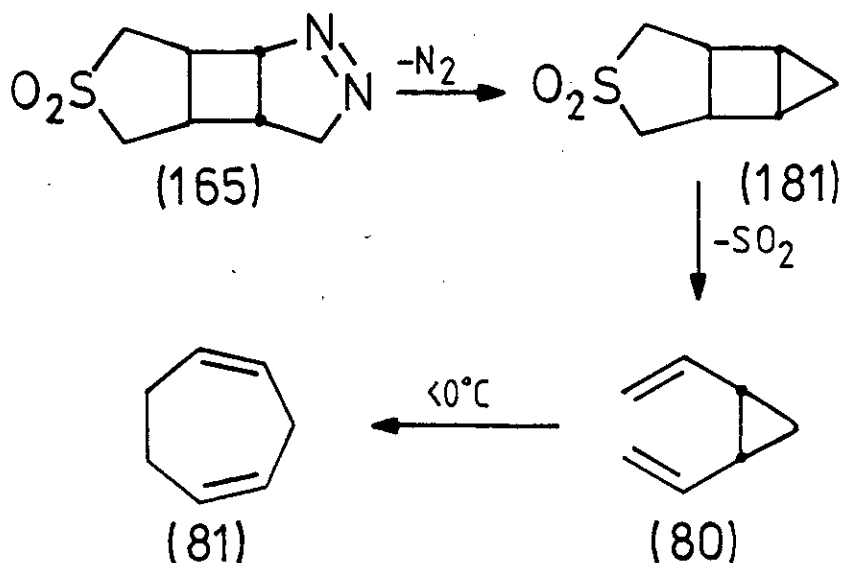
Scheme 98

analysis contained five components, none of which could be positively

identified.   The proton n. m. r. spectrum of the pyrolysate suggested

the presence of cyclohepta-1,4-diene (81) but this was not confirmed.

Apparently under these conditions loss of both nitrogen and sulphur

dioxide occurred simultaneously giving rise to the plethora of products

observed.

In certain circumstances nitrogen can be selectively removed in

the presence of a sulphone moiety by photolysis in acetonitrile.   For

example Mock[54] has shown that irradiation of the pyrazolines (182a-d),

prepared by addition of diazomethane to the appropriate sulpholene,

gave the cyclopropanes (183a-d) in 25-55% yield (Scheme 99).

Similar photolysis of compound (165) on an n. m. r. scale using

a 100w medium pressure lamp resulted in a gradual evolution of gas

which ceased after 3 days.   Examination of the resulting solution

by [1]H n. m. r. spectroscopy revealed a spectrum profile which suggested

that the sulphone moiety had been retained intact.   However removal
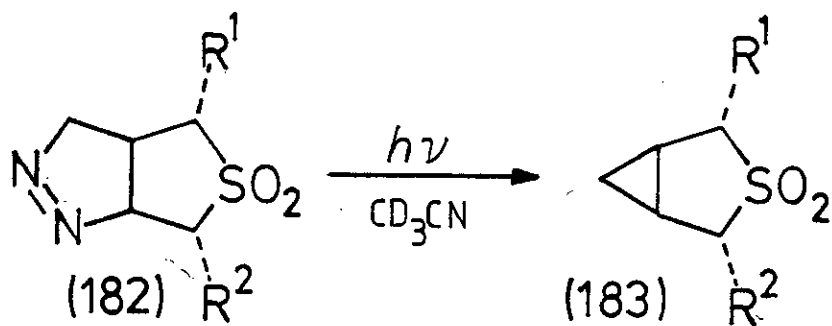
(a) $R^1, R^2 = H$

(b) $R^1, =CH_3; R^2=H$

(c) $R^1, R^2=CH_3$

(d) $R^1, R^2 = -CH_2CJ_2CH_2-$

Scheme 99

of the solvent gave a small amount of a brown solid which on the basis

of specteoscopic evidence, appeared to be polymeric in nature.   No

evidence could be obtained to indicate the formation of the desired

cyclopropane derivative (181).

F.   Miscellaneous Preparations and Pyrolyses.

F. 1   Attempted preparation of 5, 6-divinyl-3, 8-dioxadeca-1, 9-diene.

As discussed in the introduction Ziegler[105] has recently reported

the first example of a tandem Cope-Claisen rearrangement (see Scheme

46, p.43) and this prompted an effort to seek further examples using

the f. v. p. technique.   The conversion of the diol (116) to the vinyl

ether (184) followed by SO_2 extrusion offered the possibility of another

example of a tandem Cope-Claisen rearrangement leading to the aldehyde

(187) as outlined in Scheme 100.

The usual method for preparing vinyl ethers from an alcohol is

to boil the latter in ethyl vinyl ether in the presence of mercuric acetate

and one drop of sulphuric acid[138].   However in the case of the diol

(116) this procedure failed due to its extreme insolubility in ethyl vinyl

ether.   Attempts to overcome this problem by using Soxhlet extraction

also failed.

In order to circumvent this problem it was decided to try to

prepare compound (185) by vinylation of meso-3, 4-dihydroxymethyl-

1, 5-hexadiene (172), prepared as described previously (see Scheme 89,

p.174), as shown in Scheme 101.   On heating the diol (172) in boiling

ethyl vinyl ether with mercuric acetate and one drop of sulphuric acid

followed by careful removal of solvent at low temperature, a colourless

oil was obtained which was purified by bulb-to-bulb distillation.

(116)

(184)

(185)

(186)

(187)
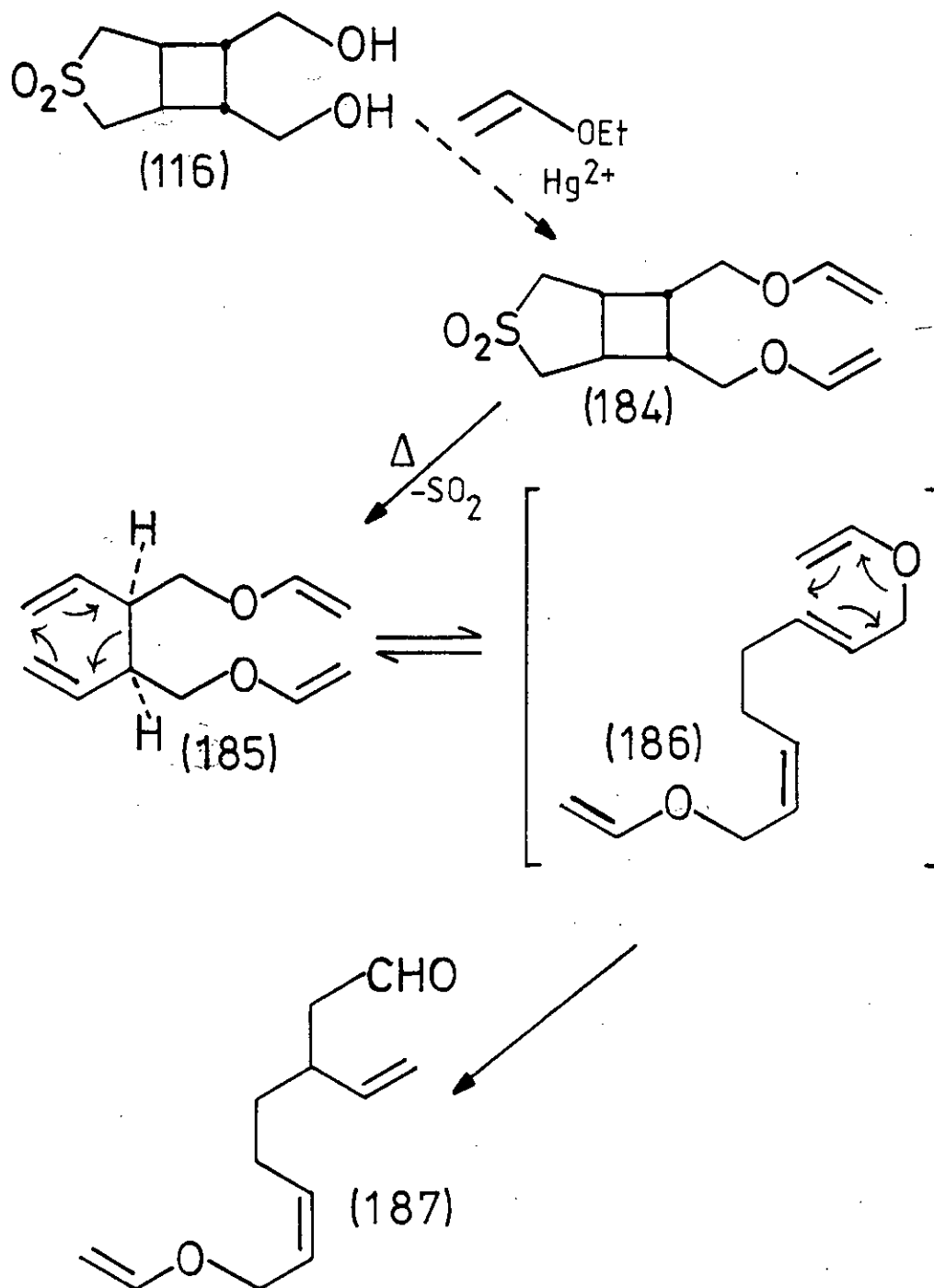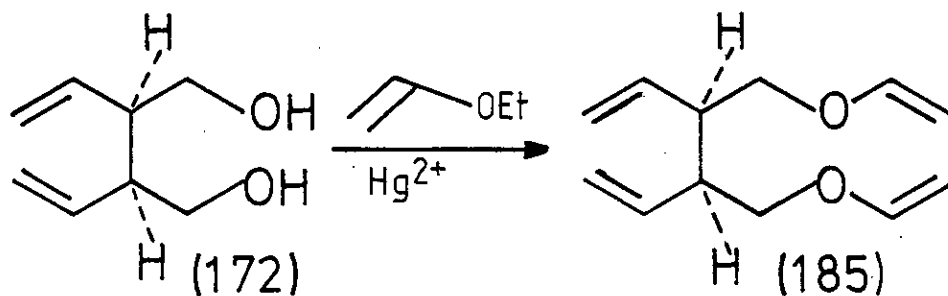
Scheme 100

Scheme 101

The ^{1}H n. m. r. spectrum of this oil was consistent with the

assigned structure (185). Likewise the ^{13}C n. m. r. spectrum contained

six lines and so supported the assigned structure. However correct

analytical data could not be obtained due to the extreme volatility of

the oil.

A sample of the oil was pyrolysed in a flow system at 500°C and

the pyrolysate was analysed by ^{1}H n. m. r. spectroscopy. The most

characteristic feature of the spectrum obtained was a peak at 9.6 δ

indicative of an aldehyde function. The presence of an aldehyde can

be rationalized in terms of a tandem Cope-Claisen rearrangement of

compound (185) as indicated in Scheme 100. Thus this provides further

evidence that the oil was indeed compound (185).

An attempt to achieve the rearrangement by heating the same oil

in $[^2H_8]$toluene in a sealed n. m. r. tube at 150°C resulting in no change

even after five days.

F. 2   Pyrolysis of Dimethyl-3-thiabicyclo[3. 2. 0]heptane-6, 7-dicarb-

oxylate 3, 3-dioxide.

On pyrolysis at 625°C under f. v. p. conditions dimethyl-3-

thiabicyclo[3. 2. 0]heptane-6, 7-dicarboxylate 3, 3-dioxide (115) gave a

76% yield of cis, trans-octa-2, 6-diene-1, 8-dicarboxylic acid dimethyl

ester (188) the structure of which was assigned on the basis of ^{1}H n. m. r.

and ^{13}C n. m. r. spectroscopic evidence comparison with known

literature values.[139]

The proton n. m. r. spectrum of (188) was recorded at a frequency of

360MHz and this spectrum is reproduced in figure 29.   The signal at

6. 9δ is a doublet of triplets due to the proton (3-H) cis to the carbo-

methoxy group ($J_{2, 3}$=16Hz, $J_{3, 4}$=7Hz).   Similarly the proton (6-H)

which is trans to a carbomethoxy group gives rise to the doublet of

triplets at 6. 2δ ($J_{6, 7}$=12Hz, $J_{5, 6}$=8Hz).

The multiplet at 5. 85δ can be interpreted as an overlapping pair

of doublets due to the remaining olefinic protons (2-H, 7-H) ($J_{2, 3}$=16Hz,

$J_{6, 7}$=12Hz).   The signals due to the carbomethoxy groups occur as

singlets at 3. 73 and 3. 72δ The allylic CH_2 cis to the carbomethoxy

group give rise to the multiplet at 2. 8δ, while the multiplet due to the

remaining CH_2 group occurs at 2. 4 δ All these assignments agree

well with data[139, 177] for compounds similar to (188).

The ^{13}C n. m. r. spectrum of (188), shown in figure 30, exhibits

five pairs of resonances.   The pair of signals at 166δ are due to the

carbonyl carbons.   The signals due to C_2 and C_7 occur at 148δ and

those due to C_3 and C_6 at ca. 121δ .   The signal due to the methylene

groups occur at ca. 51δ .

The formation of (188) can be rationalized in terms of an initial

extrusion of SO_2 to give meso-dimethyl-1, 5-hexadiene-3, 4-dicarboxylate

(171) which under the conditions of the pyrolysis undergoes a Cope

rearrangement as outlined in Scheme 102.   The observed cis, trans
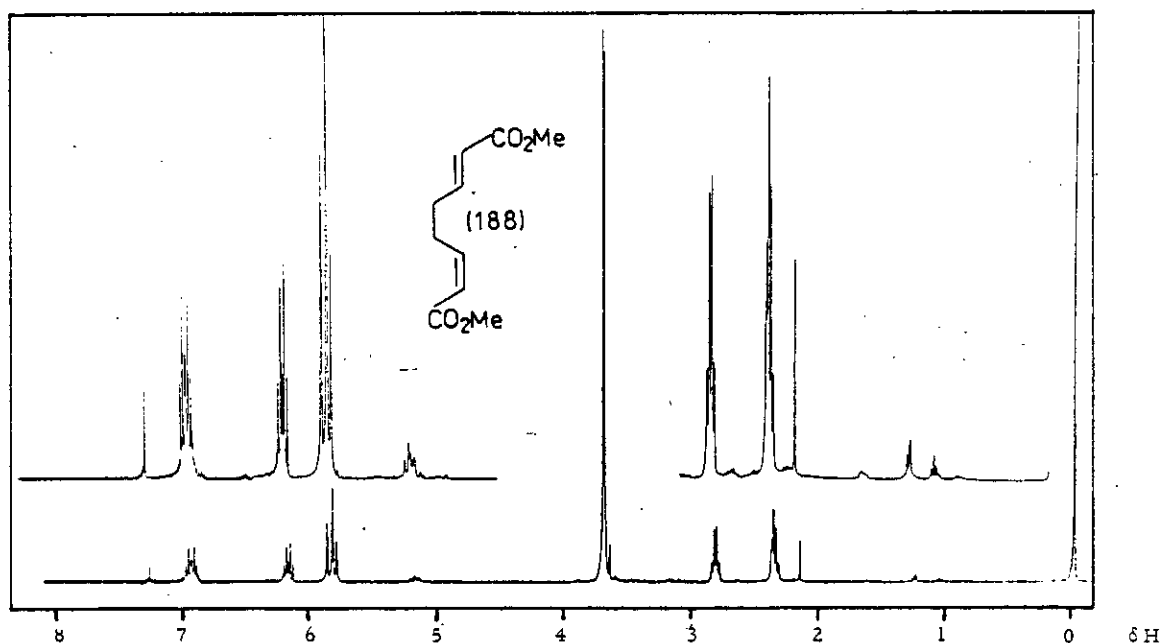
Fig. 29. 360MHz ^{1}H n. m. r. spectrum of cis, trans-octa-2, 6-diene-1, 8-dicarboxylic acid dimethyl ester (188).
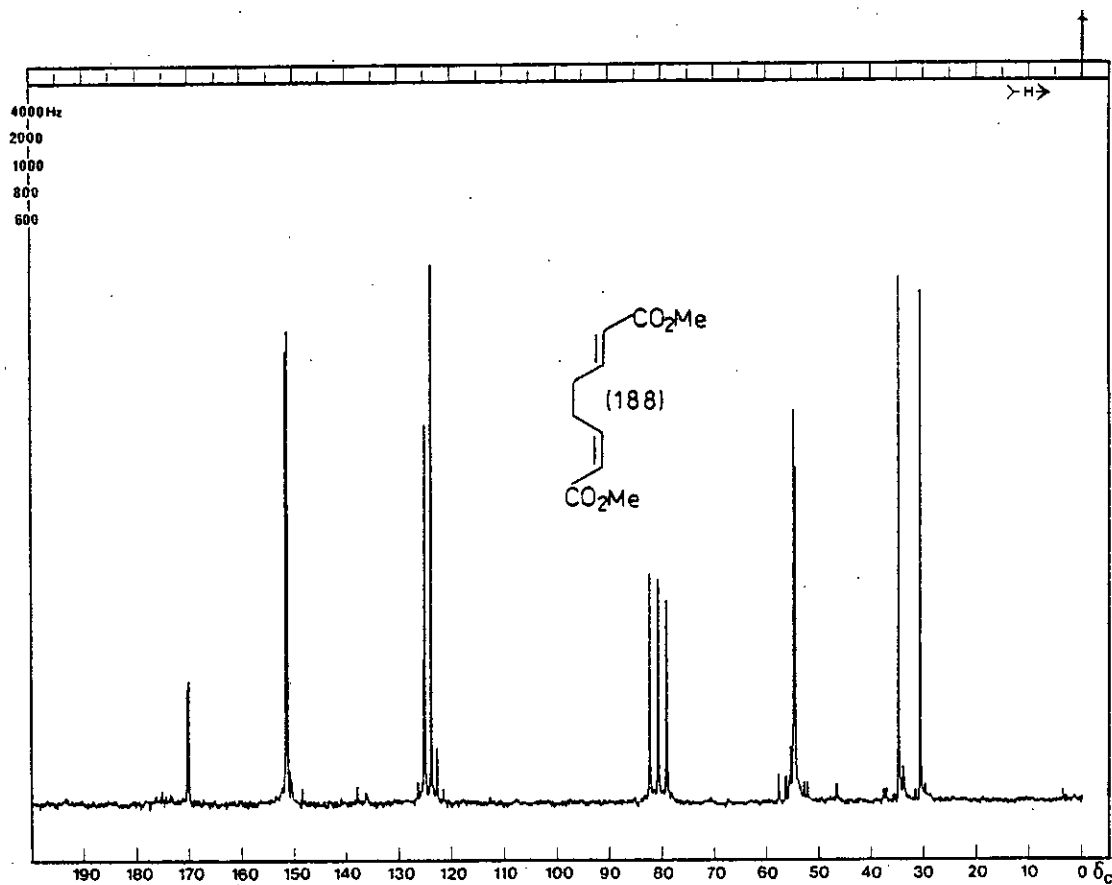
Fig. 30. 25. 2MHz ^{13}C n. m. r. specteum of cis, trans-octa-2, 6-diene-1, 8-dicarboxylic acid dimethyl ester (188).

stereochemistry of (188) can be rationalized in terms of the usual

chair-like Cope transition state as discussed in the introduction (see

Scheme 31, p. 34) whereas dl (171) would give rise to trans, trans (188)

and cis, cis (188) diesters.
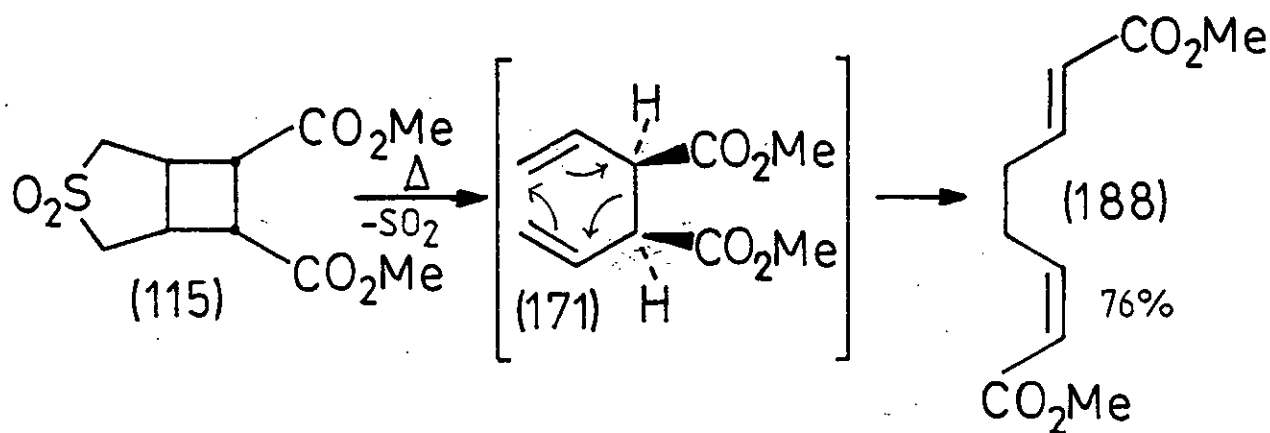
Scheme 102

The stereochemistry of (188) is interesting in that it is the

same stereochemistry as that in compound (189) which is a component

of gossyplure, the sex attractant of the female pink vollworm moth

Pectinphora gossypiella.   For maximum potency synthetic sex

(189)
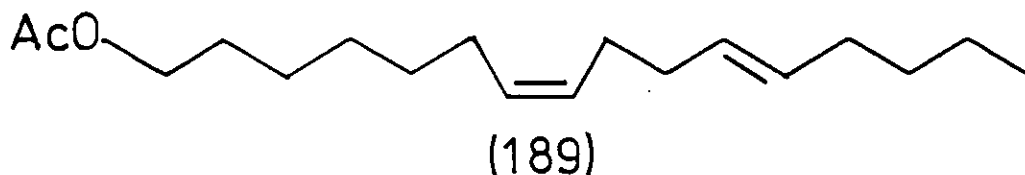
pheromones require stereochemically pure alkenes.[178]   However

(189) can only be prepared in ca. 84% purity and since (188) is obtained

in virtually 100% purity it could possibly be used as a key intermediate

in the preparation of (189).   This approach is currently under inves-

tigation but appears to suffer from the drawback that one requires to

selectively protect one terminus of the molecule with retention of

stereochemical purity.   However as yet this problem has not been

overcome.

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Flash Vacuum Pyrolysis of the 3-Thiabicyclo[3.2.0]heptane 3,3-Dioxide Ring System: a New Stereospecific Synthesis of cis-1,2-Divinyl Derivatives

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Summary A short and stereospecific route to cis-1,2-divinyl compounds from derivatives of the readily available 3,3-dioxide (1) of 3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic anhydride by cheleotropic elimination of SO_2 is reported.

THE considerable interest in cis-1,2-divinyl systems now current[1] is tempered by difficulties in synthetic access through existing methods[2] which usually give mixtures of cis- and trans-isomers. We now report a simple, stereo-specific, and general route to novel cis-1,2-divinyl systems by thermal extrusion of SO_2 from derivatives of the 3,3-dioxide (1) of 3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic anhydride, easily prepared by photolysis of 2,5-dihydro-thiophen 1,1-dioxide and maleic anhydride for 24 h in anhydrous acetone.[3]

Thus, esterification of (1) followed by reduction with $LiAlH_4$ and subsequent cyclisation[4] of the resulting diol (2) afforded 4-oxa-9-thiatricyclo[5.3.0.0²,⁶]decane 9,9-dioxide (3, X=O; m.p. 129—130 °C)† which on pyrolysis under

† All new compounds were fully characterised by ¹H and ¹³C n.m.r., i.r. and mass spectral and microanalytical data.

(2)   ←   (1)   →   (5)

(3)   (7)   (6)

(4)

X = O, S, NCH₂Ph
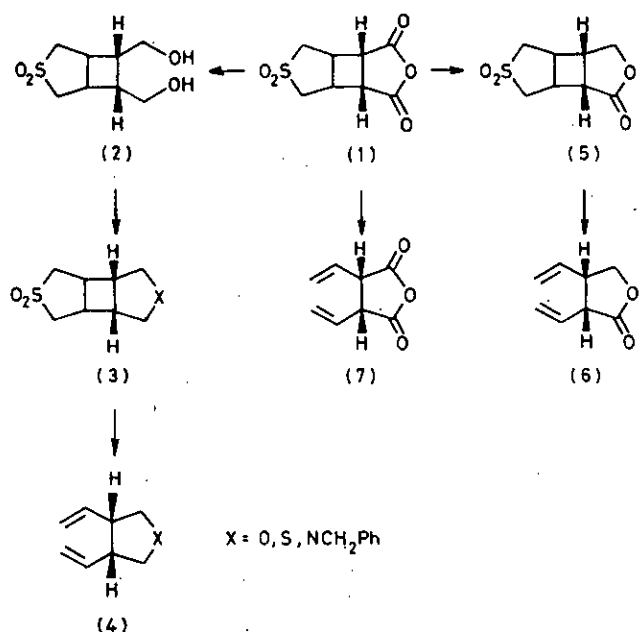
flash vacuum conditions (625 °C at 10⁻³ mmHg) gave exclusively cis-3,4-divinyltetrahydrofuran (4, X=O; b.p. 40 °C at 41 mmHg; 62%). Similar pyrolysis of the lactone

(5); m.p. 157—158 °C, prepared by reduction of (1) with NaBH₄ in dimethylformamide, afforded the corresponding cis-1,2-divinyl derivative (6; b.p. 75 °C at 0·1 mmHg) in 31% overall yield from (1). Further transformations of (1), which serve to illustrate the potential of our procedure, have been effected leading to (4, X=S; b.p. 140 °C at 16 mmHg; 25%) and (4, X=NCH₂Ph; b.p. 100 °C at 0·01 mmHg; 67%) by pyrolysis of (3, X=S; m.p. 195—196 °C) [conversion of (2) into its dimethanesulphonate and treatment with Na₂S-aq.EtOH; 82%] and (3, X=NCH₂-Ph; m.p. 132—135 °C) [reaction of the ditosylate of (2) with benzylamine; 56%] respectively. We have also shown that flash vacuum pyrolysis of (1) gave cis-hexa-1,5-diene-3,4-dicarboxylic anhydride (7; b.p. 65 °C at 0·1 mmHg; 80%) from which cis-1,2-divinyl systems of type (4) could be obtained by conventional synthetic methods.

Stereospecificity in all cases exceeded 99·9% and the cis-stereochemistry, which is a consequence of the symmetrical structure of the starting anhydride (1), was validated by the essentially quantitative chemical transformation of (7) into meso-2,3-diethylsuccinic acid, m.p. 190—191 °C (decomp.) (lit.⁵ 192 °C; cf. racemic acid, m.p. 129 °C) by hydrolysis with boiling water and subsequent hydrogenation over 10% palladium–charcoal at room temperature.

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