Some Thermal Fragmentation Reactions of 3-Thiabicyclo[3.2.0]heptane 3,3-Dioxide Ring Systems

by

Caroline M. Buchan, B.Sc.

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Doctor of Philosophy

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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 the results of research carried out in the Department of Chemistry, University of Edinburgh, under the supervision of Dr. I. Gosney since 1st October 1980, the date of my admission as a research student.

Post-graduate Lecture Courses

The following is a statement of the courses attended during the period of research:

Organic Research Seminars (3 years attendance).

Current Topics in Organic Chemistry, various lecturers (15 lectures).

Homogeneous Catalysis, Dr. T.A. Stephenson (5 lectures).

Molecular Interactions in Industrial Food Research, Unilever Research (5 lectures).

Bio-organic Chemistry, various lecturers (5 lectures).

Synthesis and Mechanism of Action of the β-Lactam Antibiotics, Glaxo Group Research (5 lectures).

Radiochemical Techniques, various lecturers (5 lectures).

1,3-Dipoles in Organic Synthesis, Dr. J.T. Sharp and Dr. R.M. Paton (5 lectures).

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Abstract

The preparation and flash vacuum pyrolysis (FVP) of derivatives of 3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]-decane 9,9-dioxide have been studied. The cheletropic elimination of SO_2 from these sulphones leads to *cis*-1,2-divinyl compounds which, for acyclic analogues, undergo rearrangement to *cis*,*trans*-hexa-1,5-dienes by a Cope reaction. The stereochemistry of this highly stereospecific reaction has been validated by FVP of epimeric sulphones and by isomerisation to the *trans*,*trans*-1,5-dienes. Under basic conditions, the *cis*-1,2-divinyl compounds undergo rearrangement to the corresponding hexa-2,4-dienes.

Other synthetically useful reactions based on the extrusion of SO_2 from compounds having the 3-thiabicyclo[3.2.0]-heptane 3,3-dioxide ring system are also described. Under flash vacuum pyrolytic conditions, the bis(sulphone), 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4,9,9-tetroxide, is shown to give 4-vinylcyclohexene and 1,5-cyclo-octadiene. By using the novel technique of vacuum pyrolysis in the presence of palladium on charcoal, both the bis(sulphone) and 1,5-cyclo-octadiene are converted into styrene, the latter process being of some industrial importance.

The novel synthon, 6,7-dimethylene-3-thiabicyclo[3.2.0]-heptane 3,3-dioxide has also been prepared and its reactions investigated. Under FVP conditions, it loses SO_2 to form 3,4-dimethylene-1,5-hexadiene, a highly reactive dehydrodimer of butadiene. It also forms a variety of Diels-Alder adducts from which SO_2 can be extruded, whereupon a novel

tandem annulation procedure is effected. Diels-Alder reactions of 3,4-dimethylene-1,5-hexadiene have also been studied.

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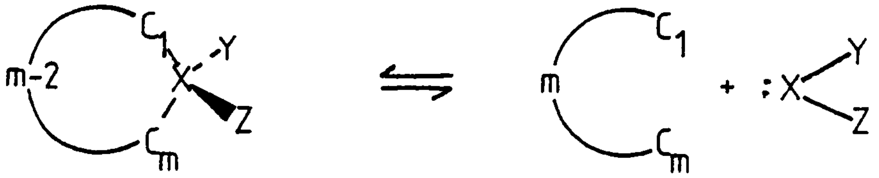
Cyclic sulphones containing aromatic rings, functional groups, heteroatoms and further SO_2-groups as ring members decompose on heating with loss of SO_2 and the formation of new C-C bonds. Pyrolysis of cyclic sulphones can lead to ring contraction, ring expansion and fragmentation of the ring system. The majority of these reactions are regarded as radical processes but in certain cases the thermal elimination of SO_2 from cyclic monosulphones is interpreted as a cheletropic reaction which follows the Woodward-Hoffmann rules.

A. Cheletropic Extrusion of SO_2 from Cyclic Sulphones

1. Cheletropic Reactions

Introduction

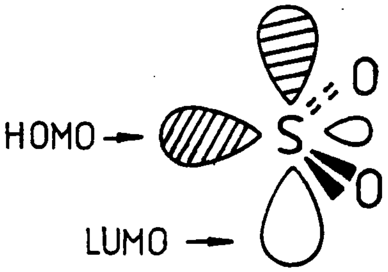
Cheletropic reactions have been defined by Woodward and Hoffmann[1] as those processes in which two σ bonds which terminate at a single atom are broken or made in concert (Scheme 1). As a subclass of cycloadditions, cheletropic reactions involve the reversible addition of small molecules such as SO_2, CO, N_2, N_2O and singlet carbenes to polyenes.



Scheme 1

Cheletropic reactions have been investigated from a theoretical viewpoint by several workers[1,2,3]. Using the frontier orbital approach[3], the course of bimolecular pericyclic processes such as cheletropic reactions is predicted from a consideration of the symmetry of the HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) of each component. This in turn is related to the number of electrons involved.

Sulphur dioxide (see 1) has a lone pair of electrons in the plane of the molecule and a vacant ρ orbital orthogonal to it. Thus the interaction of the HOMO (lone pair orbital) of sulphur dioxide with the LUMO of the alkene as well as the interaction of the LUMO (vacant ρ orbital) of SO_2 with the HOMO of the alkene have to be considered.



(1)

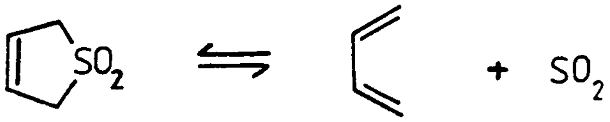
Analysis of the molecular orbital interactions shows that two reaction pathways are possible. Woodward and Hoffmann[1] have categorised the pathways as either linear (the least motion path) or non-linear (the non-least motion path). However, since the stereochemical orientation of SO_2 in the transition state is not imprinted upon the reaction products, there is no experimental evidence to distinguish which path is involved.

Several groups, of which particular mention should be made to Mock[4], have investigated the mechanism of the interaction of sulphur dioxide with unsaturated systems. The following family of cheletropic reactions have been studied, details of which will now be considered (Scheme 2).

a. The SO_2-alkene reaction

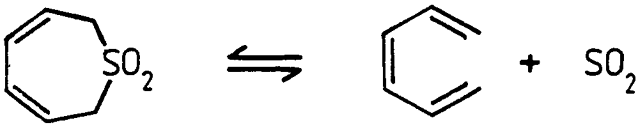
(2)

b. The SO_2-1,3-diene reaction



(3)

c. The SO_2-1,3,5-triene reaction



(4)

Scheme 2

a. The SO_2-alkene reaction

For cheletropic reactions in which a three-membered ring is produced or destroyed, a concerted suprafacial,suprafacial $\pi 2s + \omega 2s$ interaction is disallowed as shown in Fig.1. The SO_2 must depart or approach in an antarafacial manner following a non-linear reaction path (Fig.2). Formation of thiirane 1,1-dioxide (episulphone) (2) is thus described as a $\pi 2s + \omega 2a$ process and the reverse reaction, a $\sigma 2s + \sigma 2a$ fragmentation.

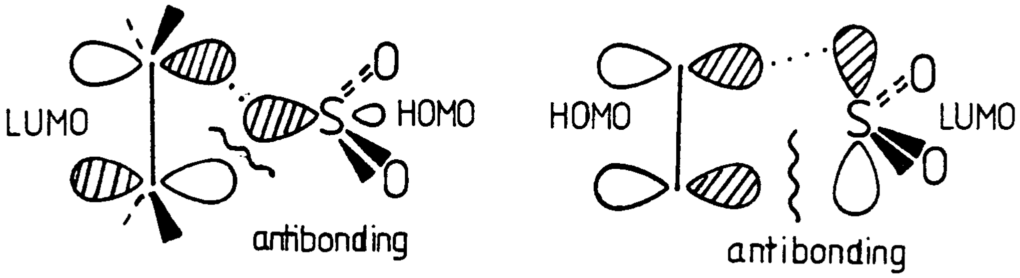


Fig.1 The linear approach of SO_2 to an alkene

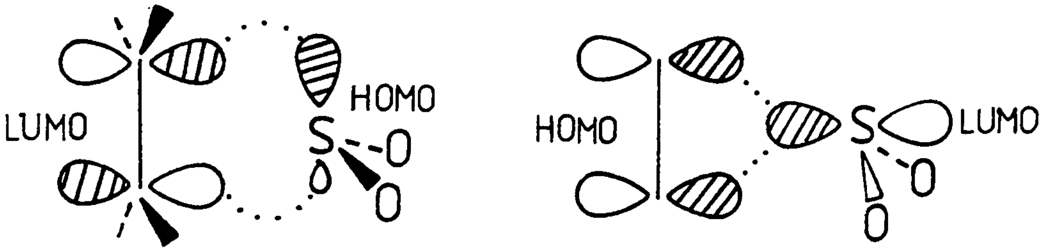
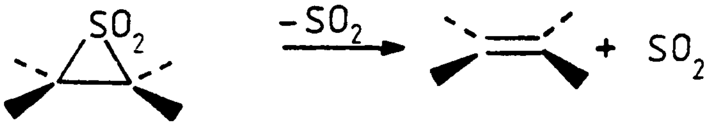


Fig.2 The non-linear approach of SO_2 to an alkene

The decomposition of episulphones has been found experimentally to be stereospecific and cleanly suprafacial with respect to the incipient olefin (Scheme 3)[4,5]. The observed stereospecificity can be accounted for if the non-linear reaction path is followed.

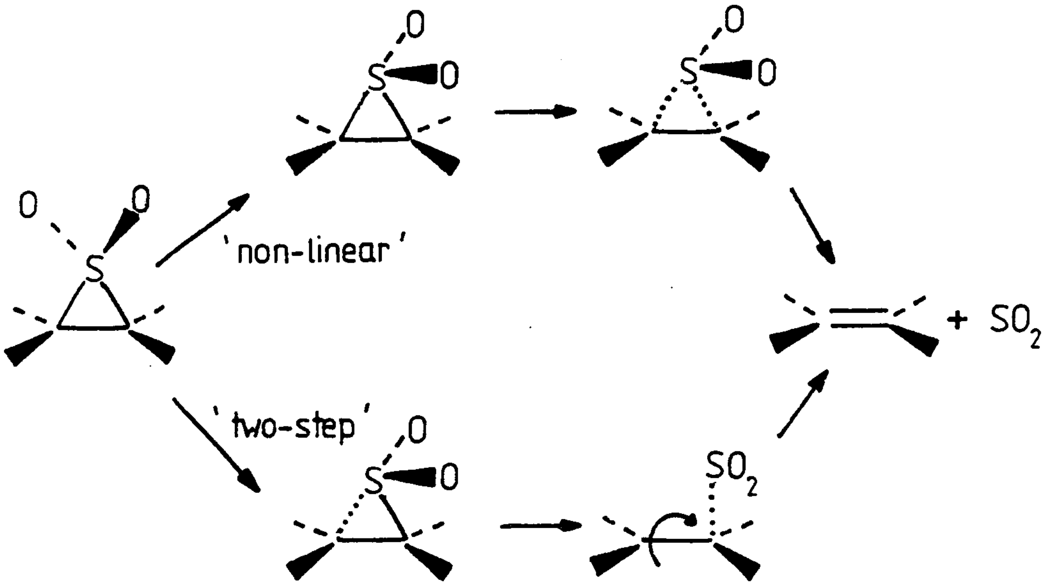


Scheme 3

However, kinetic studies of phenyl-substituted thiirane 1,1-dioxides[6] have provided evidence for a sequential bond cleavage mechanism as opposed to a concerted process (Scheme 4).

Since rate studies are ambiguous due to the effects of ring strain, the mechanism of episulphone fragmentation is still unclear[6,7,8].

The alternative mechanism, a two-step process[6,9], may involve dipolar or diradical intermediates but in order to explain the observed stereospecificity, dissociation of the intermediate must be more rapid than the internal rotation of the bond shown.



Scheme 4

b. The SO_2-1,3-diene reaction

The best studied cheletropic reaction is the reaction between 1,3-butadiene and SO_2 - the sulpholene reaction. The reaction proceeds by an allowed linear pathway described as a $\pi 4s + \omega 2s$ (or a $\pi 2s + \sigma 2s + \sigma 2s$ cycloreversion) (Fig.3). For good overlap of the interacting orbitals, the terminal carbons of butadiene must rotate in a disrotatory sense.

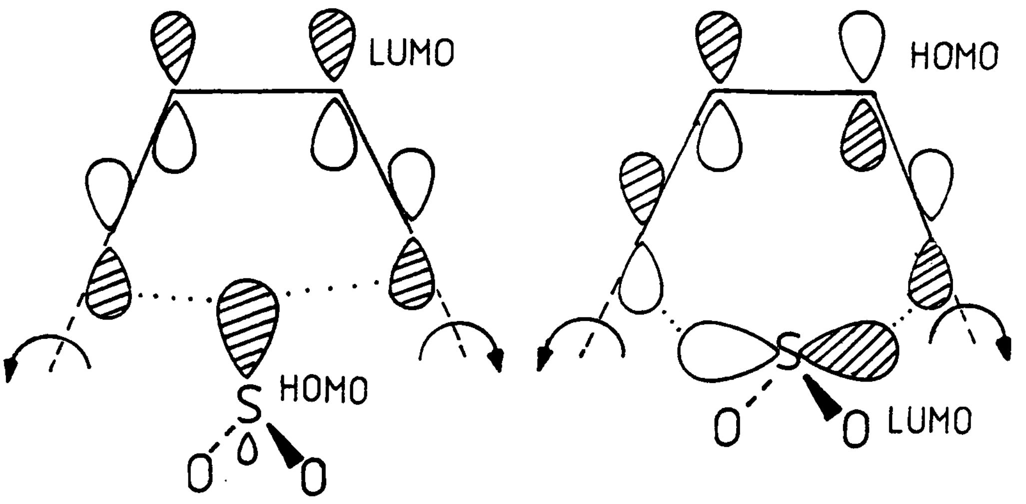
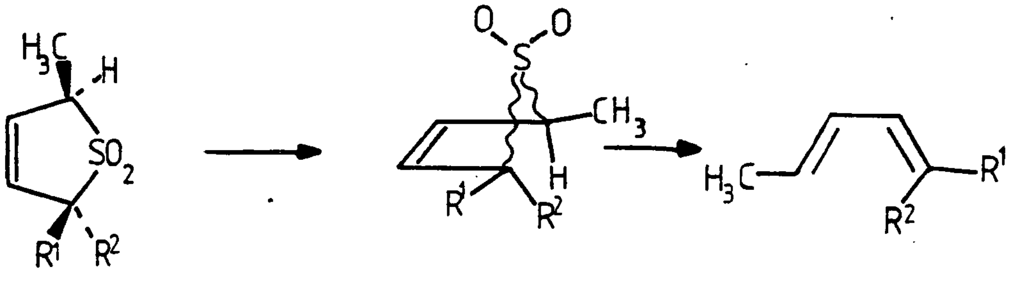


Fig.3 The linear approach of SO_2 to butadiene

The elimination of SO_2 from substituted 2,5-dihydrothiophen 1,1-dioxides (5) has been extensively studied and found to be cleanly suprafacial (99.9% *cis* elimination) with respect to the diene (Scheme 5).[4,10,11]



(5)

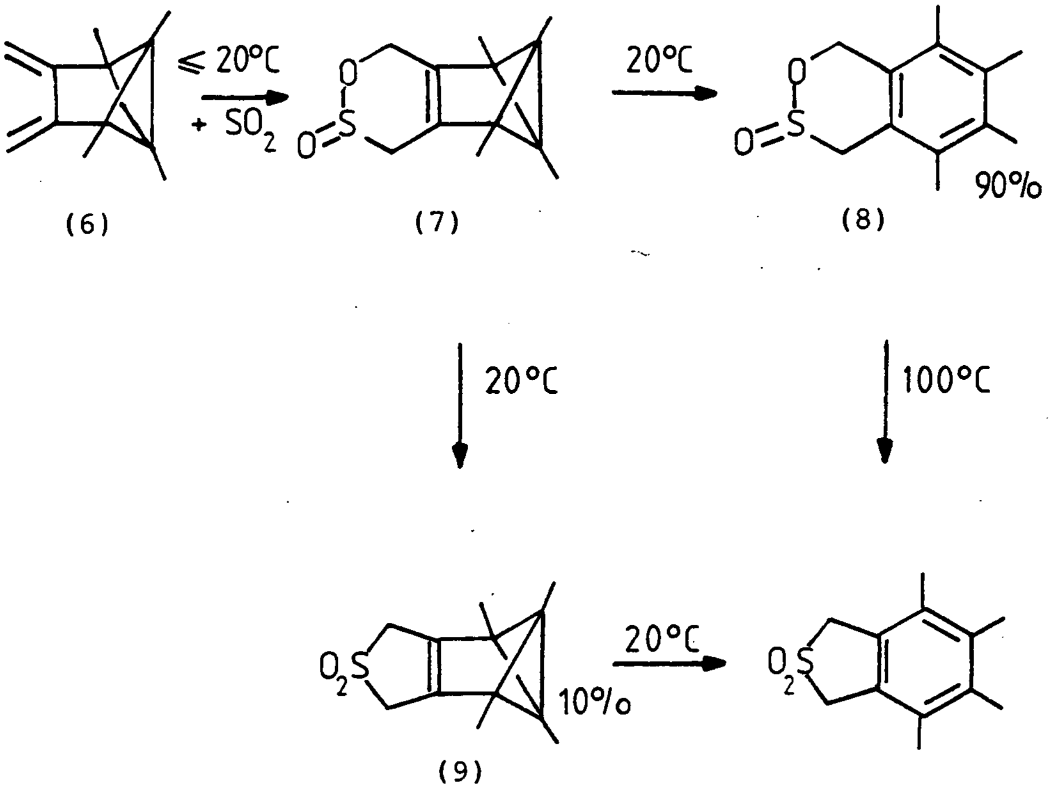
1) $R^1=CH_3$; $R^2=H$

2) $R^1=H$; $R^2=CH_3$

Scheme 5

Hogeveen *et al.*[12] have reported that the addition of SO_2 to the diene (6) at or below room temperature gives the sulphinic ester (7) which immediately rearranges to the aromatic ester (8) (90%) and to the sulphone (9) (10%)

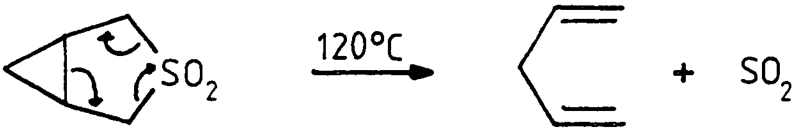
(Scheme 6). The thermal rearrangement of the sulphinic ester to the sulphone proceeds via a retro-Diels-Alder reaction followed by cheletropic addition[13]. The sulphinic ester thus represents the kinetically controlled product while the sulphone represents the thermodynamically controlled product.



Scheme 6

Mock[14] has also studied the fragmentation of sulpholanes (tetrahydrothiophen 1,1-dioxides). Thermolysis at elevated temperatures (>500°C) gives stereoisomeric mixtures of alkenes indicating that a multi-step mechanism is involved. Extrusion of SO_2 from the 3-thiabicyclo[3.1.0]hexane 3,3-dioxide ring system[15] (10) is however a concerted reaction (Scheme 7).

The pericyclic $\sigma 2s + \sigma 2s + \sigma 2s$ fragmentation gives rise to 1,4-dienes (11), the rate of decomposition being identical to that of 2,5-dihydrothiophen 1,1-dioxide (3) at 125°C. This implies coupling of the opening of the cyclopropane ring with the carbon-sulphur bond scission in the transition state with the attendant relief of ring strain.



(10) (11)

Scheme 7

c. The SO_2-1,3,5-triene reaction

The reversible formation of 2,7-dihydrothiepin 1,1-dioxide (4) from SO_2 and hexa-1,3,5-triene could formally be either a linear or non-linear cheletropic reaction. If the SO_2 is the suprafacial component, the addition is a $\pi 6a + \omega 2s$ linear cheletropic reaction and the terminal groups of the triene must rotate in a conrotatory way (Fig.4a). In the non-linear process, the SO_2 acts as the antarafacial component and the terminal groups must rotate in a disrotatory sense - a $\pi 6s + \omega 2a$ process (Fig.4b).

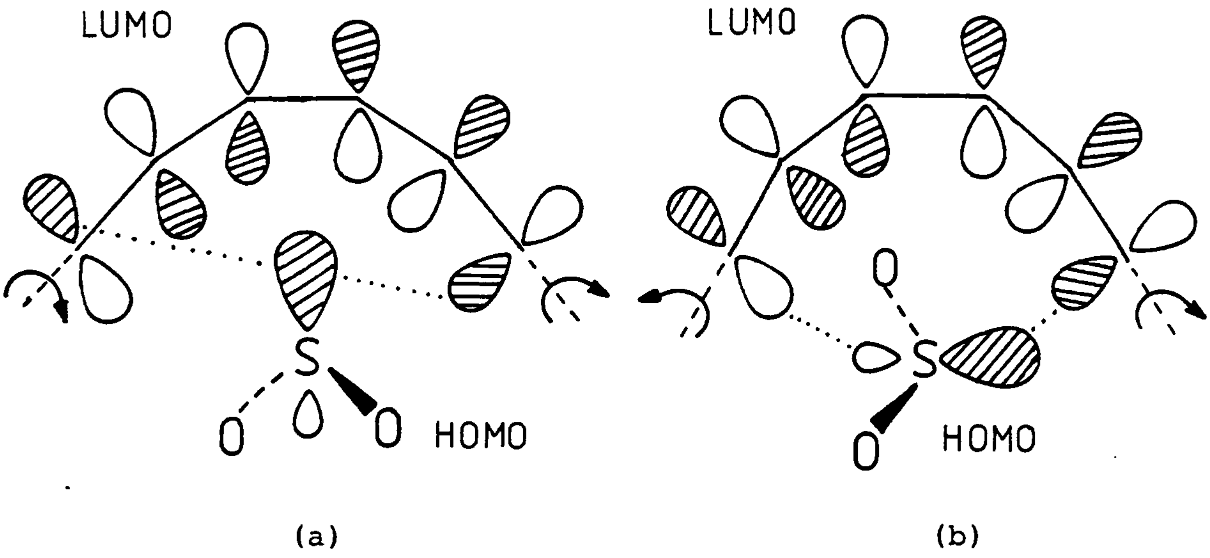
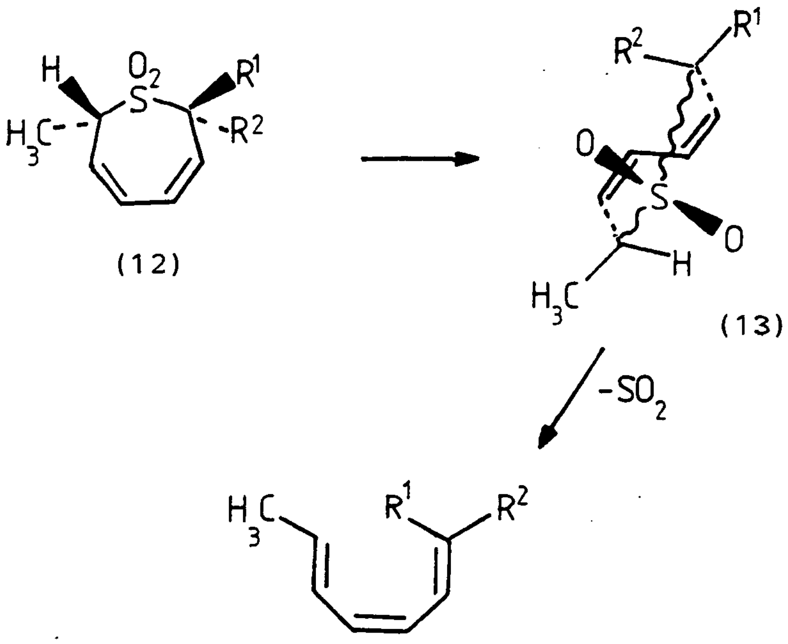


Fig.4 (a) Linear, antarafacial on the triene

(b) Non-linear, suprafacial on the triene

Mock established that fragmentation of the seven-membered sulphone (4) to SO_2 and *cis*-1,3,5-hexatriene proceeds antarafacially with respect to the triene. Thus from the observed stereochemistry of the decomposition of (12) to (14) (Scheme 8), the linear reaction path is favoured involving the transition state (13)[4,16-18].

The sulphones (12) could not however be prepared by the addition of SO_2 to the appropriately substituted triene[17]. The addition of SO_2 to 1,3,5-cyclooctatriene (15) is an example in which 1,4-addition competes effectively with 1,6-addition[9,19].



(12)

(13)

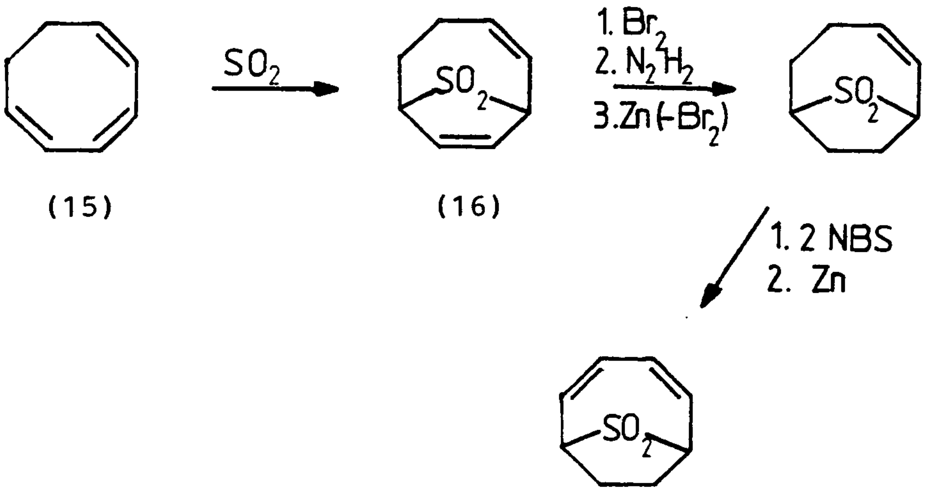
(14)

a) $R^1=CH_3$; $R^2=H$

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

>97% stereospecific

Scheme 8



(15)

(16)

(17)

Scheme 9

The antarafacial addition to the triene is geometrically impossible and the alternative $\pi 6s + \omega 2a$ non-linear addition does not compete with the $\pi 4s + \omega 2s$ linear cheletropic addition. Mock[9,19] converted the sulphone (16) into the formal 1,6-adduct of 1,3,5-cyclooctatriene and SO_2 (17) by the route shown (Scheme 9).

Fragmentation of (17), due to the steric constraints of the bicyclic system, may proceed only by a non-linear, retro [$\pi 6s + \omega 2a$] process. That this is unfavourable is reflected by its rate of decomposition which is 60,000 times slower than for (16). It is possible that the mechanism may involve a non-concerted sequential bond scission[9].

d. Selection Rules for Cheletropic reactions

Gilchrist and Storr[3a] have summarised the selection rules for cheletropic reactions as follows:

(a) Linear cheletropic reactions in which the polyene is a suprafacial component (involving disrotatory motion of the terminal carbons) are allowed for a total of (4n+2) electrons.

(b) Linear cheletropic reactions in which the polyene is an antarafacial component (involving conrotatory motion of the termini) are allowed for a total of 4n electrons.

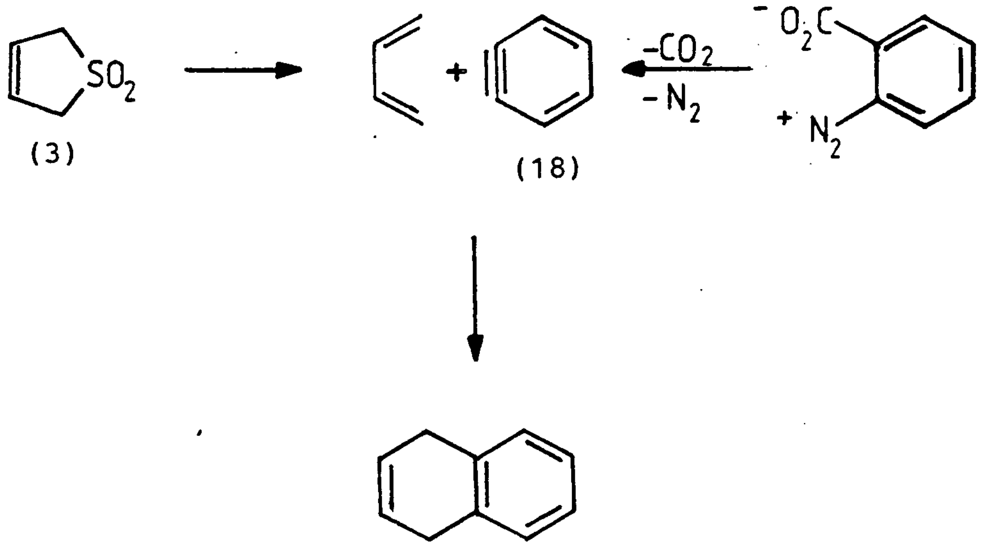
The rules are reversed for non-linear cheletropic reactions and the rules for photochemical extrusion are the reverse of those for thermal extrusion.

2. Synthetic Uses of the SO_2 Extrusion Reaction

a. The sulpholene reaction

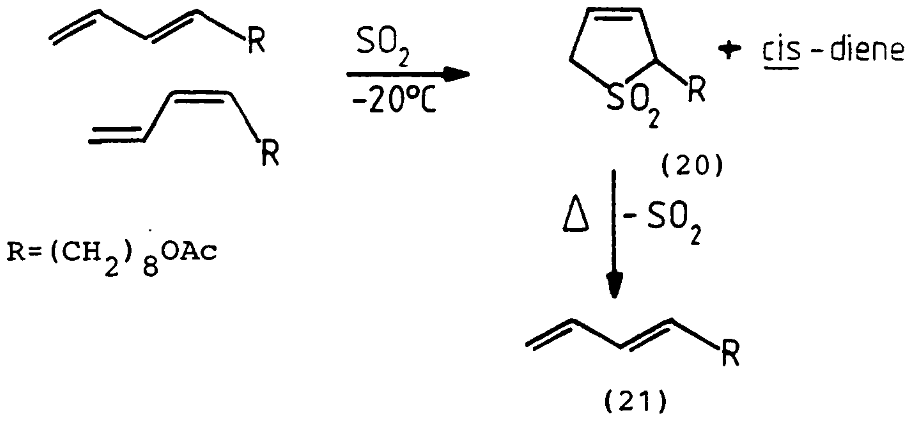
The reaction of 1,3-dienes with SO_2 was first reported in 1914 by de Bruin[20] who obtained the crystalline adduct of SO_2 and isoprene. Many synthetic reactions now employ this reversible reaction with a variety of conjugated dienes.

The thermal extrusion of SO_2 from sulpholenes has been used as a means to modify, purify and store dienes[21]. For example, 2,5-dihydrothiophen 1,1-dioxide (butadiene sulphone) (3) decomposes at 125°C and can be used as a convenient source of 1,3-butadiene[22]. Subsequent reaction with benzyne (18) gives 1,4-dihydronaphthalene (19) as the Diels-Alder cycloaddition product (Scheme 10)[23].



Scheme 10

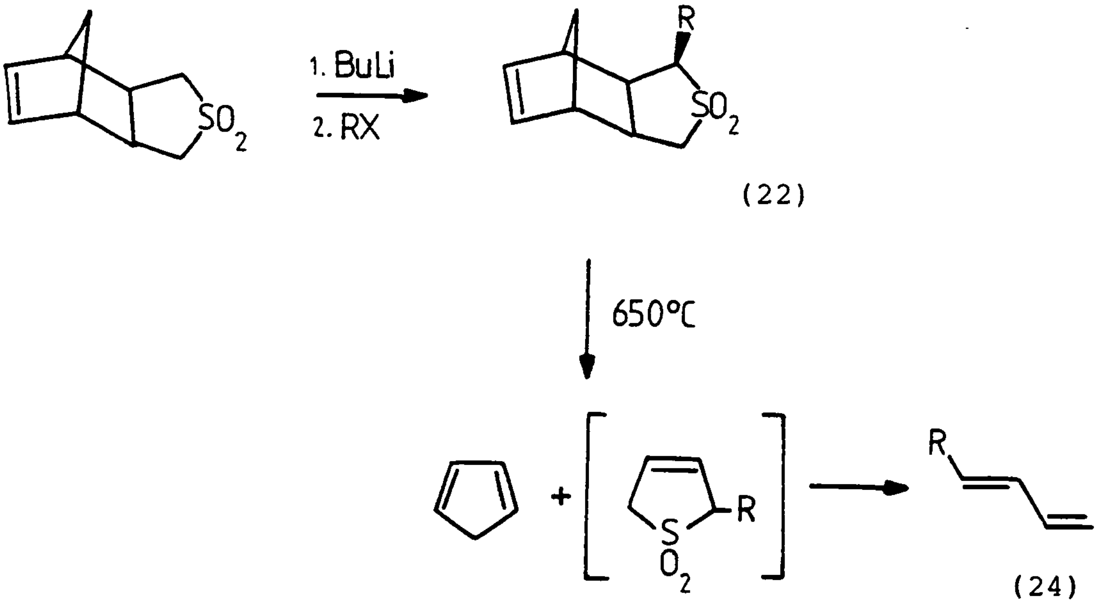
Nesbitt *et al.*[24] have used the sulpholene reaction to separate the *cis* and *trans* isomers of the red boll-worm moth sex pheromone. Reaction with SO_2 gives the *trans* adduct (20) which can be readily separated from the *cis*-diene which does not form the adduct. Thermal decomposition of the adduct (20) then provides the pure *trans*- isomer (21) (Scheme 11).



Scheme 11

The pheromone, 12-acetoxydodeca-1,3-diene (21), has also been prepared recently by Bloch and Abecassis[25]. Thermolysis of the alkylated sulphone (22) in the vapour phase at 650°C effects a retro-Diels-Alder reaction and SO_2 extrusion in one step to give a highly stereoselective synthesis of *trans*-1-substituted-1,3-dienes (24) (Scheme 12). The reaction proceeds via the 2-substituted-2,5-dihydrothiophen 1,1-dioxide (23), the synthesis of which from direct substitution of 2,5-dihydrothiophen 1,1-dioxide (3) is prevented by the opening of the five-membered ring in basic medium[26].

This procedure has been extended to the stereoselective synthesis of *trans*,*trans*-1,4-disubstituted 1,3-dienes (26) from thermolysis of the α,α'-dialkylated sulphone (25) (Scheme 13)[27].



(22)

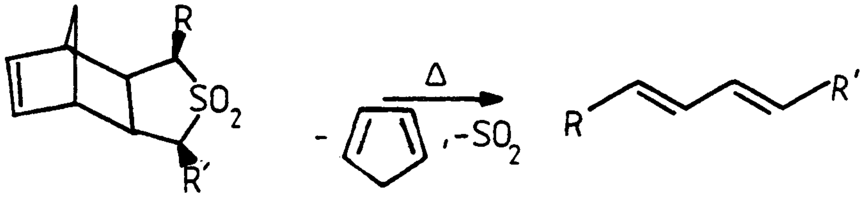
(23)

(24)

R=CH_3, nC_5H_{11}, $(CH_2)_8OAc$

Scheme 12

The synthetic potential of this method has been illustrated by the synthesis of two dienic insect sex pheromones.



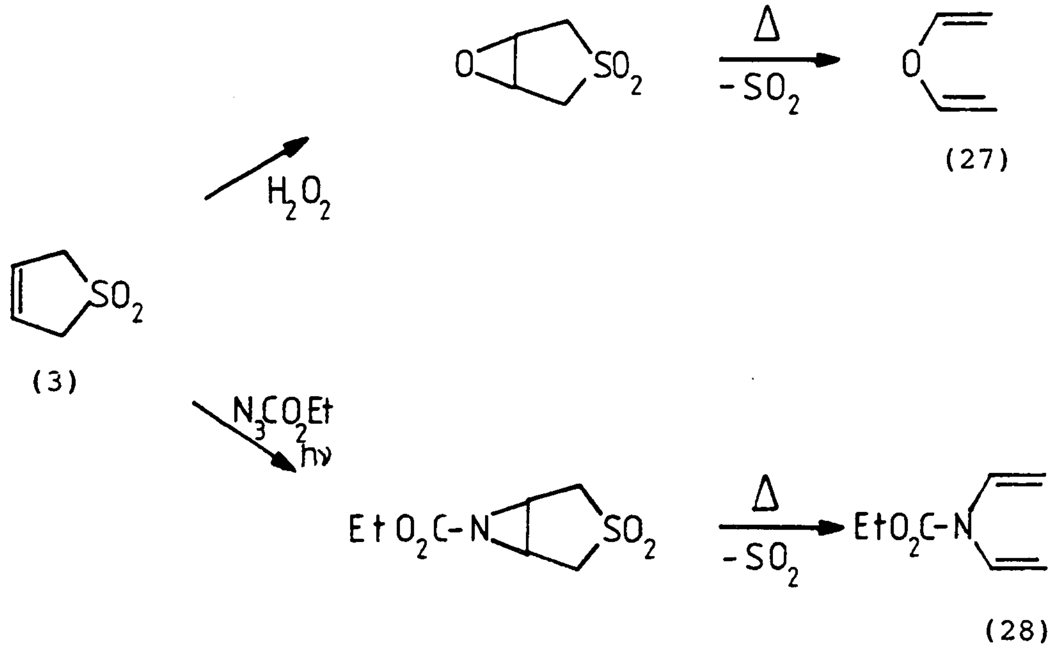
(25)

(26)

Scheme 13

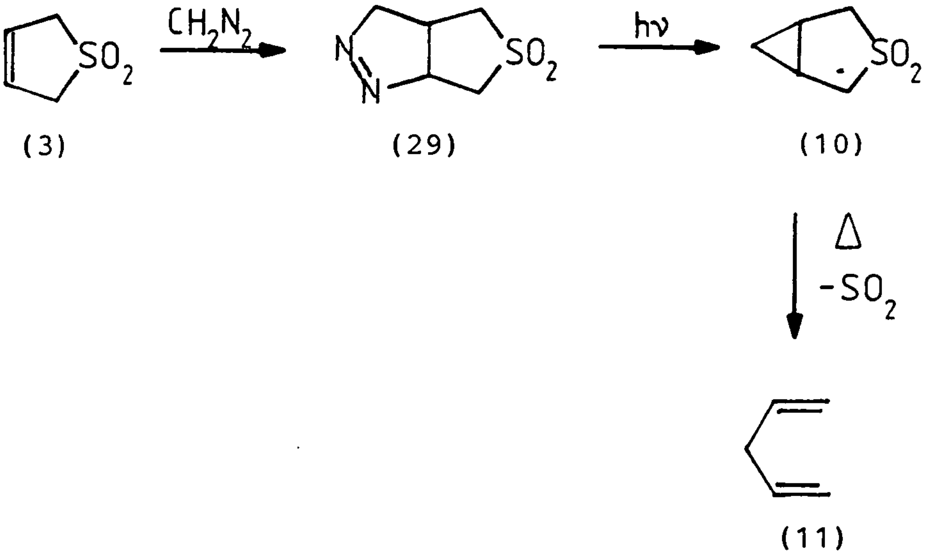
Both Zbiral[28] and Yamada[29] have prepared SO_2 adducts of vitamin D derivatives. Thermolysis of the mixture of adducts from the (5-*trans*)- and (5-*cis*)-vitamin D derivatives gave the 5,6-*trans*-isomer. Thus isomerisation of the 5,6-double bond could be achieved. Zbiral also found that elimination of SO_2 could be brought about by KOH/CH_3OH or on an alumina surface.

The sulpholene reaction can also be of use in the synthesis of divinyl ethers (27) and divinyl carbamates (28) as reported by Meyers *et al.*[30] (Scheme 14).



Scheme 14

By the 1,3-cycloaddition of diazomethane to (3) and photolytic extrusion of nitrogen from the adduct (29), Mock[15] has prepared the sulphone (10), pyrolysis of which yields 1,4-dienes (11) as previously discussed (p.8) (Scheme 15). This is therefore a useful method of inserting a methylene, nitrogen or oxide function between two double bonds.

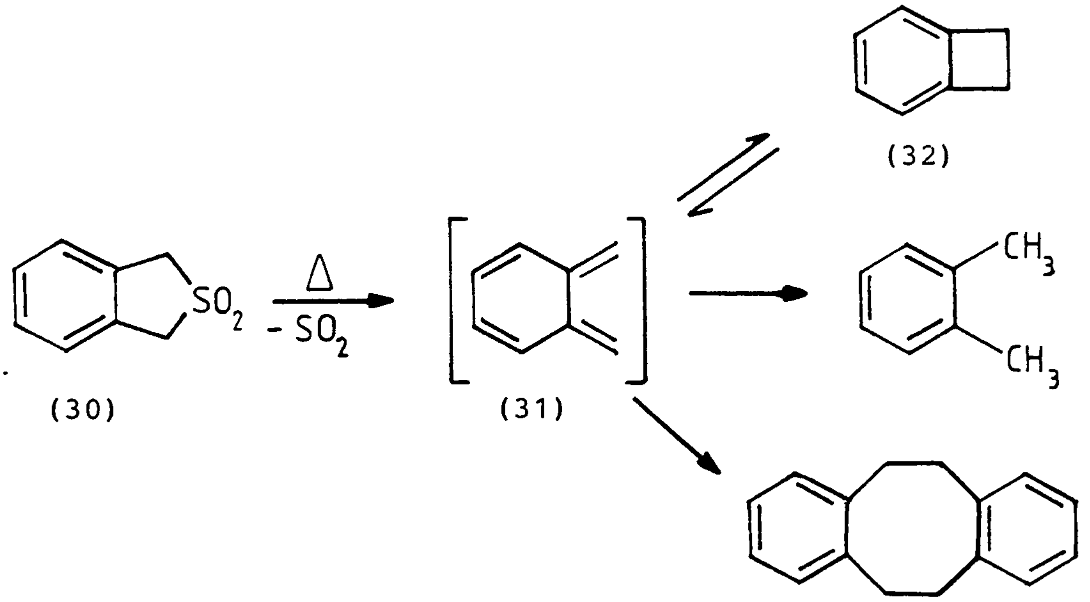


Scheme 15

b. The preparation of o-quinodimethanes, steroids and cyclophanes via loss of SO_2

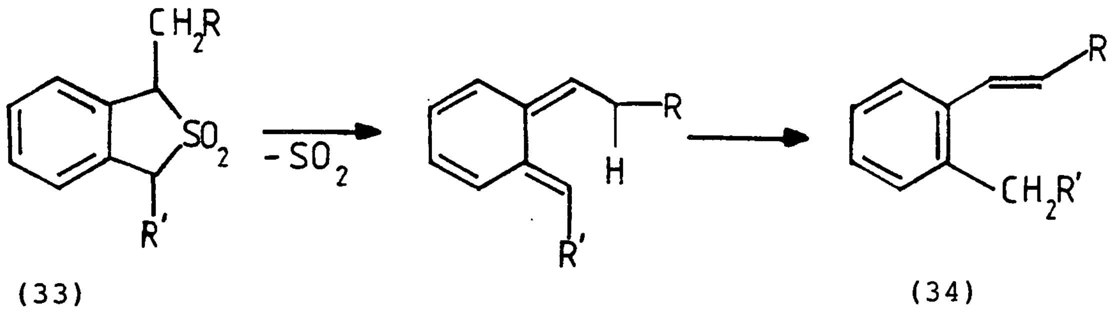
The elimination of SO_2 from 1,3-dihydrobenzo(c)thiophen 2,2-dioxide (30) was first investigated in 1959 by Cava and Deana[31]. King *et al.*[32] have since shown that the extrusion occurs in accordance with the Woodward and Hoffmann rules[1] by disrotatory loss of SO_2 followed by the conrotatory ring closure of the o-quinodimethane intermediate (31) to form benzocyclobutene (32). However the nature and yield of products depend markedly on the pyrolysis conditions (Scheme 16). Pyrolysis at 500°C gives the best yield of benzocyclobutene (63%)[31].

Recent studies on the extrusion of SO_2 from derivatives of the sulphone (33) have shown that benzocyclobutenes are the major products from pyrolysis at lower temperatures



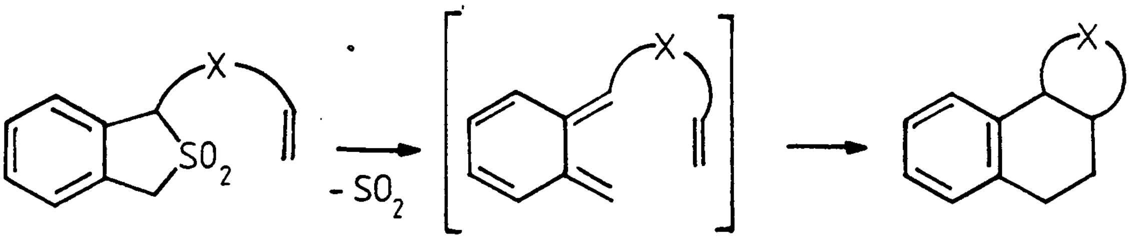
Scheme 16

whereas alkenes (34) derived from a [1,5] hydrogen shift predominate at higher temperatures and on photolysis (Scheme 17)[33].



Scheme 17

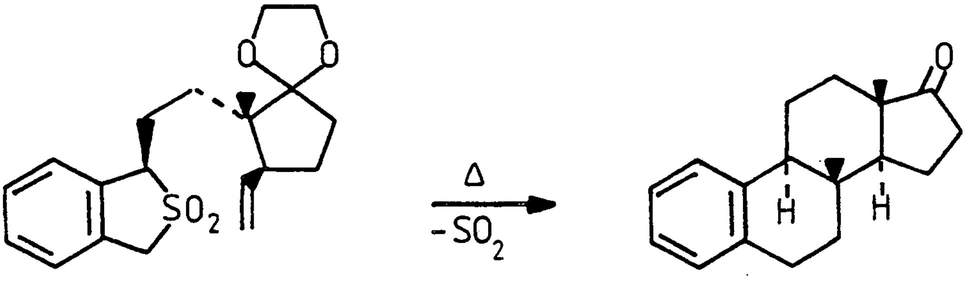
Nicolaou[34] and Oppolzer[35] have both used the sulphone (30) as the starting material in their syntheses of polycyclic systems (37). The general procedure involves alkylation of the sulphone to (35) and subsequent Diels-Alder reaction of the o-quinodimethane (36) generated by the cheletropic elimination of SO_2 (Scheme 18). For example, a simple and stereoselective synthesis of the steroid estra-1,3,5(10)-trien-17-one (38)



(35) (36) (37)

Scheme 18

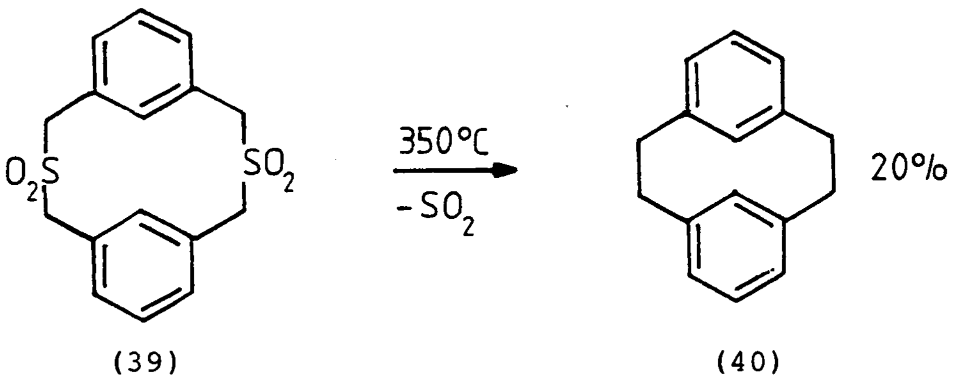
has been achieved by Nicolaou using such a reaction sequence (Scheme 19). (+)-Estradiol has been synthesised in the same way by Oppolzer *et al.*[36]



(38)

Scheme 19

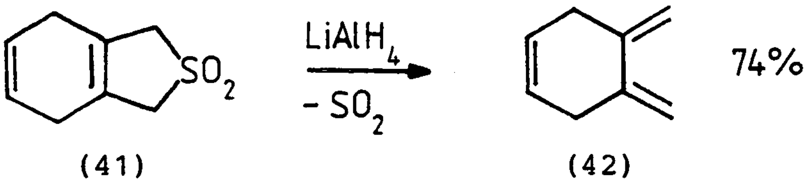
Sulphone pyrolysis has also been successful in the preparation of cyclophanes. Vögtle[37] was the first to prepare such a bridged aromatic compound by elimination of SO_2 when, in 1969, he obtained [2.2] metacyclophane (40) by thermolysis of the disulphone (39) at 350°C (Scheme 20). A radical mechanism is envisaged for this ring contraction. Vögtle[38] has also published a review on the pyrolysis of sulphones as a synthetic method.



Scheme 20

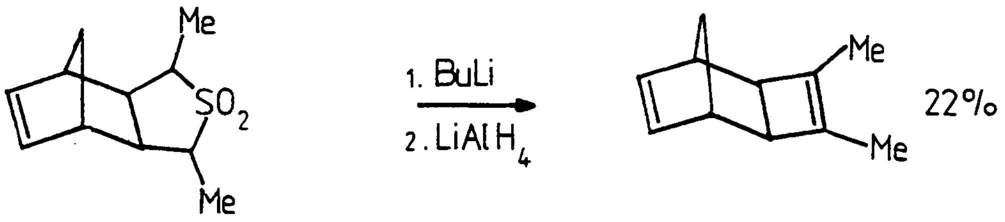
c. Other methods of SO_2 extrusion

Apart from the thermal extrusion of SO_2, loss of SO_2 from cyclic sulphones has also been achieved by chemical means. Gaoni[39] found that sulpholenes could undergo elimination of SO_2 by treatment with lithium aluminium hydride in ether. For example, the sulphone (41) yields the diene (42) (Scheme 21) but the reaction mechanism is not yet fully understood.



Scheme 21

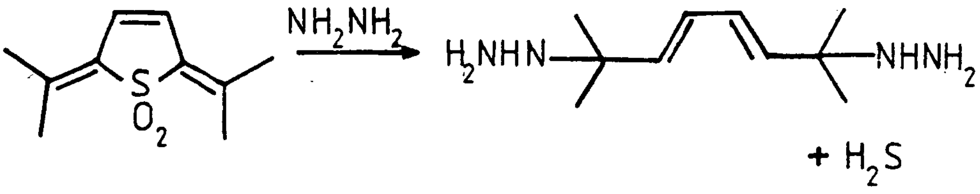
Lithium aluminium hydride has also been used to promote the ring contraction of α,α'-disubstituted cyclic five-membered sulphones to 1,2-dialkylcyclobutenes. Thus Paquette and Photis[40] have shown that the sulphone (43) gives the substituted cyclobutene (44) by a reaction similar to the Ramberg-Bäcklund rearrangement (Scheme 22).



(43) (44)

Scheme 22

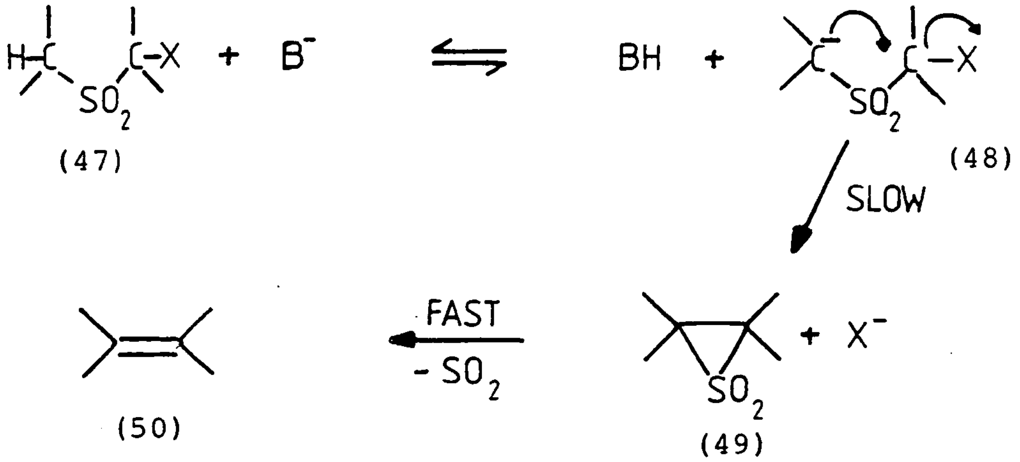
Another example of chemical extrusion is the reaction of 2,5-diisopropylidene sulpholene (45) with hydrazine hydrate[41]. The products are the addition compound (46) and H_2S which is formed by reduction of the extruded SO_2 (Scheme 23).



(45) (46)

Scheme 23

The Ramberg-Bäcklund rearrangement is an extrusion process in which an α-halosulphone (47) is treated with base to give an alkene (50) (Scheme 24)[42]. In the proposed mechanism the carbanion (48) undergoes intramolecular 1,3-elimination to give an episulphone intermediate (49). The episulphone is not isolated under the basic conditions and eliminates SO_2 stereospecifically to give the olefin (50). The stereochemistry of the alkene is thus determined at the ring-closure stage. A recent review by Paquette[43] covers



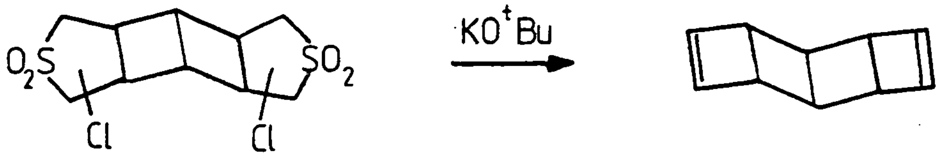
Scheme 24

the mechanistic aspects and summarises many examples of the reaction.

The reaction is particularly useful in the preparation of strained alkenes such as $\Delta^{1,5}$-bicyclo[3.3.0]octene (51) (Scheme 25)[44].

Scheme 25

More recently, Martin *et al.*[45] have prepared pterodactyladiene (tetracyclo[4.4.0.$0^{2,5}$$0^{7,10}$]deca-3,8-diene) (53) by a double Ramberg-Bäcklund ring contraction of the bis-chlorinated bis-sulphone (52) using potassium *tert*-butoxide in THF as base (Scheme 26).

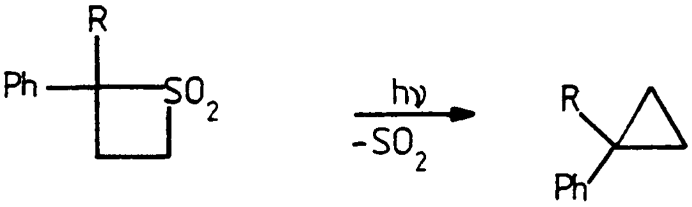


(52) (53)

Scheme 26

Saltiel and Metts[46] have studied the photochemical extrusion of SO_2 from sulpholenes. While not a totally stereospecific reaction, the major diene photoproduct was found to be in accordance with a concerted fragmentation.

It is of interest to note that the photolytic extrusion of SO_2 from cyclic four-membered sulphones, substituted thietan 1,1-dioxides (54) provides a synthetic route to substituted cyclopropanes (55) (Scheme 27)[47].



(54) (55)

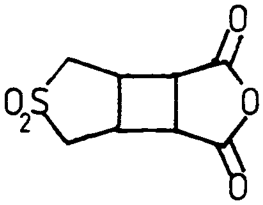
$R=CH_3, C_2H_5, C_6H_5CH_2, H_2C{=}CH{-}CH_2$

Scheme 27

The corresponding thermal extrusion is a non-concerted process, the stereochemistry of the four-membered ring exerting no pronounced influence on the configuration of the cyclopropane products. As a result a mixture of isomers is obtained[48].

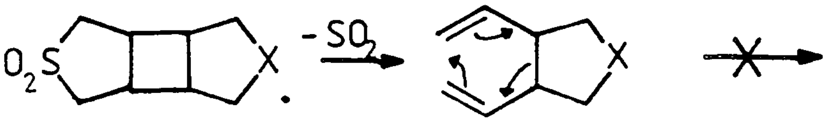
d. The preparation of *cis*-1,2-divinyl compounds

Work in these laboratories has concerned the preparation and pyrolysis of the anhydride (56) and its derivatives[49]. The extrusion of SO_2 from such compounds (57) leads to the



(56)

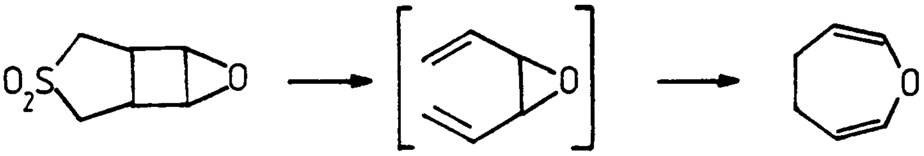
formation of novel *cis*-1,2-divinyl compounds (58) which are stable and do not undergo Cope rearrangement (Scheme 28).



(57) (58)

Scheme 28

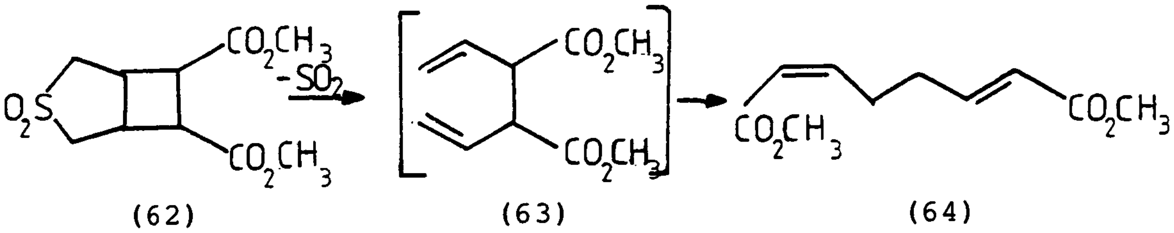
McLaughlin[50] has also shown that pyrolysis of the epoxide (59) gives a good yield of 4,5-dihydrooxepin (61) formed by Cope rearrangement of the intermediate divinyloxiran (60) (Scheme 29).



(59) (60) (61)

Scheme 29

Pyrolysis of the diester (62) yielded the *cis*,*trans*-hexa-1,5-diene (64) which also apparently results from the facile Cope rearrangement of the initially formed *meso*-1,2-divinyl compound (63) (Scheme 30). The mechanistic details of the Cope rearrangement is discussed in the next section.



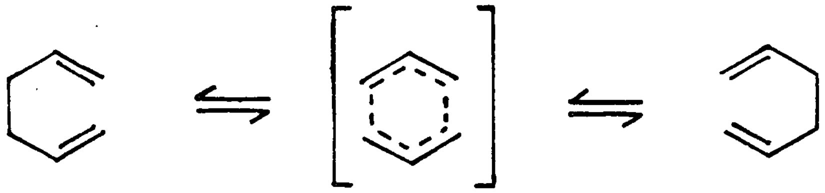
Scheme 30

B. The Cope Rearrangement

1. Mechanism of the Cope Rearrangement

Introduction

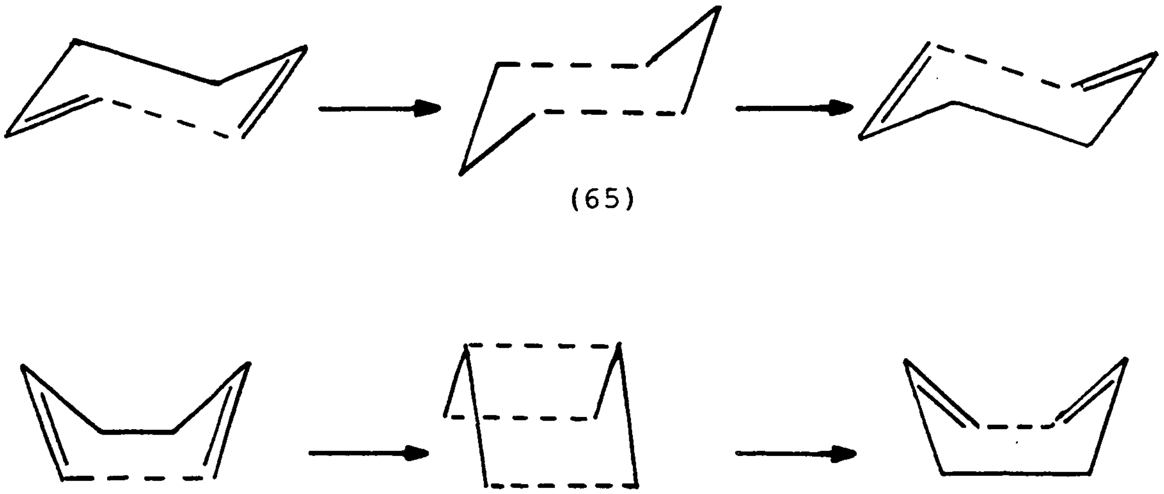
The thermal rearrangement of substituted 1,5-hexadienes was first recognised by Cope in 1940 [51,52]. Cope assumed that the reaction takes place in a single step via a cyclic transition state (Scheme 31)[53] and various theoretical interpretations of the rearrangement using molecular orbital approaches have since been put forward[1,54,55]. However, the mechanism still remains in some doubt.



Scheme 31

a. Mechanism and Stereochemistry

Woodward and Hoffmann[1] have classified the reaction as a [3,3] sigmatropic rearrangement. The various geometries possible for the transition state depend on whether each of the allyl systems interacts with the lobes of the other system on the same side (suprafacially) or on opposite sides (antarafacially). For a suprafacial-suprafacial transition state, there can be either a four-centre, chair overlap (65) or a six-centre, boat overlap (66) (Scheme 32). The chair



(65)

(66)

Scheme 32

arrangement is energetically favoured as the interaction of the central ρ lobes of the allyl systems in the boat form appears to have a destabilising effect.

Woodward and Hoffmann[1] regarded the intermediate in the Cope rearrangement to arise from the combination of a pair of allyl radicals. On considering the relevant orbital interactions (Fig.5) it can be noted that the non-bonding SOMO (singly occupied molecular orbital) - SOMO interaction has nothing to do with the boat-chair selectivity since these orbitals have a node at the central carbon.

In order to understand the preference for the chair-form transition state, the interaction between the NHO (next highest occupied) and NLU (next lowest unoccupied) orbitals have to be

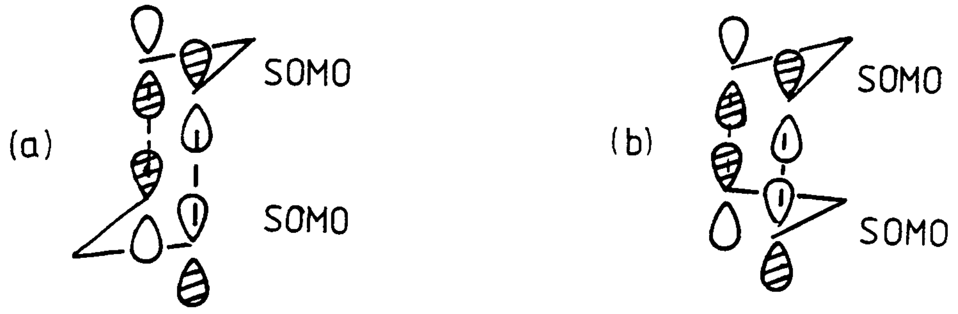


Fig.5 (a) Chair transition state (suprafacial-suprafacial)
(b) Boat transition state (suprafacial-suprafacial)

considered (Fig.6)[54]. In the boat-form, there is interaction between the central *p*-lobes of the two allyl systems but not in the chair-form.

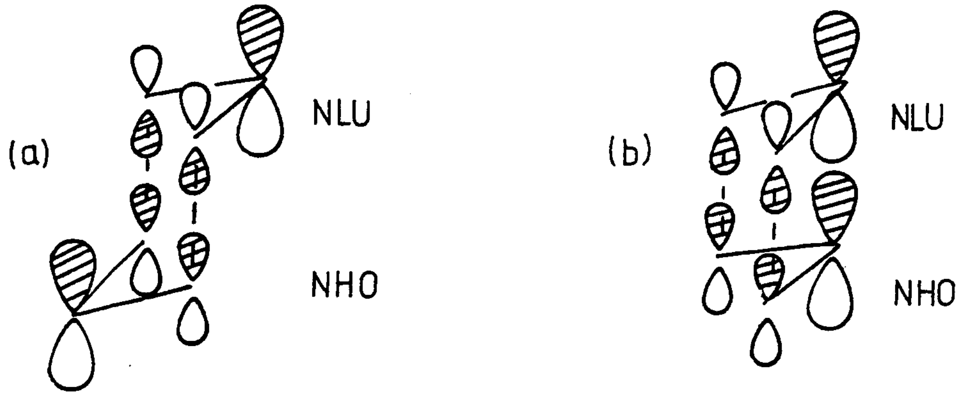
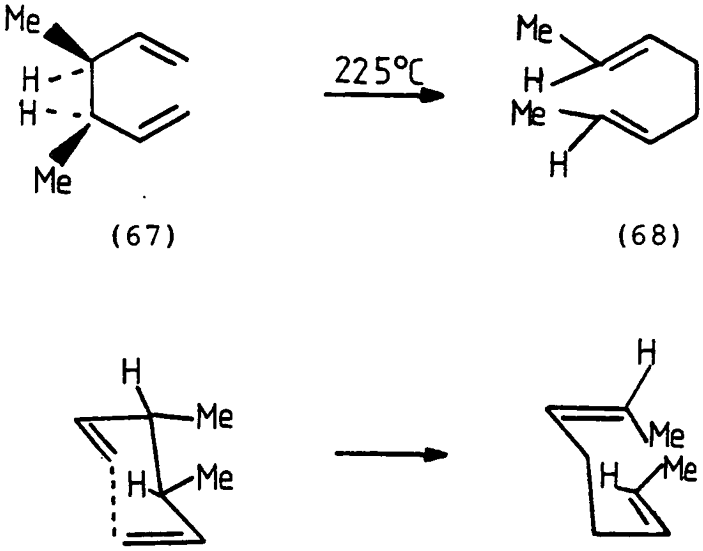


Fig.6 (a) NHO-NLU interaction in chair transition state
(b) NHO-NLU interactions in boat transition state

Evidence for the preference for the chair conformation in the transition state has been provided by Doering and Roth[56,57] in their study of the Cope rearrangement of *meso*-3,4-dimethyl-1,5-hexadiene (67). Rearrangement occurred to give almost exclusively (99.7%) *cis*,*trans*-octa-2,6-diene (68), the stereochemistry being consistent only with a chair conformation for the transition state (Scheme 33). A boat conformation would have given the *cis*,*cis*- or *trans*,*trans*-octadiene. It was also shown that *rac*-3,4-dimethyl-1,5-hexadiene rearranges at 180°C to a mixture of *trans*,*trans*-octa-2,6-diene (90%) and the *cis*,*cis*-isomer (10%) via a chair transition state.

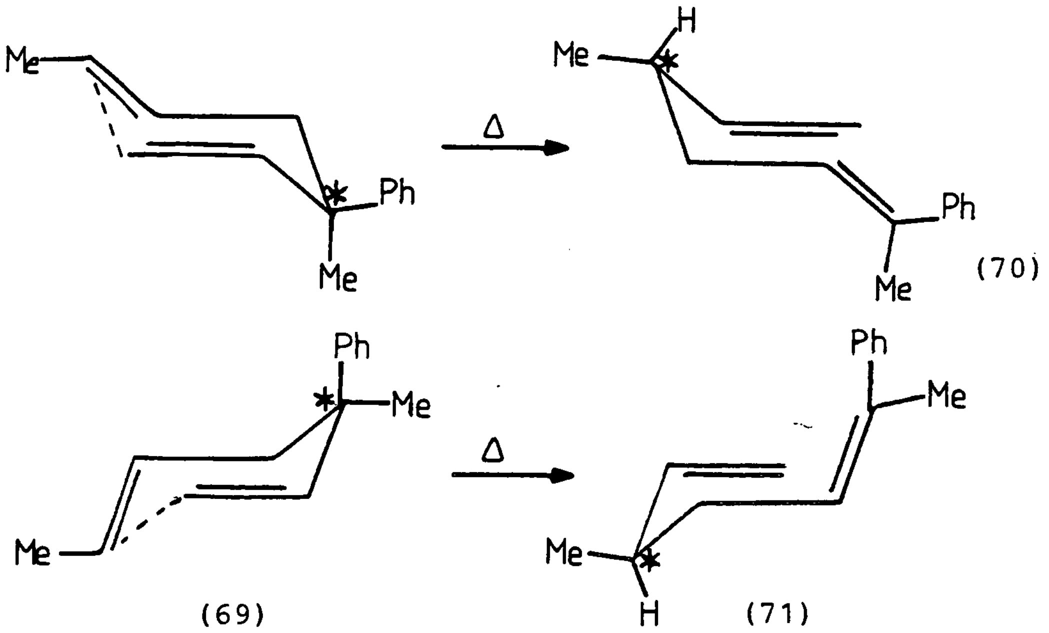


(67)

(68)

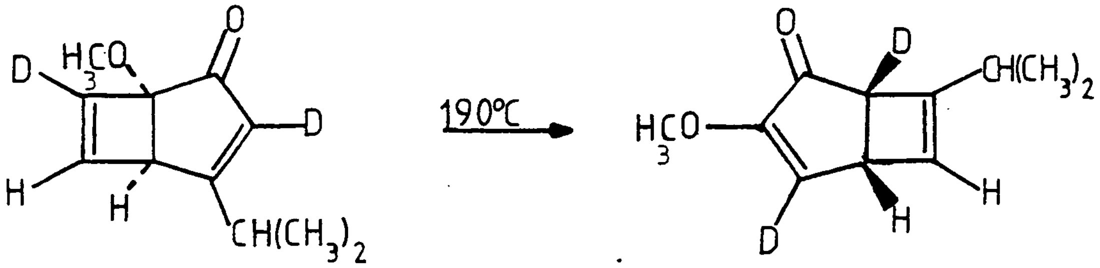
Scheme 33

In this connection Hill and Gilman[58] have shown that rearrangement of the optically active hepta-1,5-diene (69) gives a mixture of two other dienes (70) and (71) (Scheme 34). Thus *trans*-3-methyl-3-phenylhepta-1,5-diene (69) rearranges at 250°C to an 87:13 mixture of *cis*- and *trans*-3-methyl-6-phenylhepta-1,5-diene (70) and (71) respectively. The stereochemistry and absolute configurations of the products confirms the preference for the chair transition state.



Scheme 34

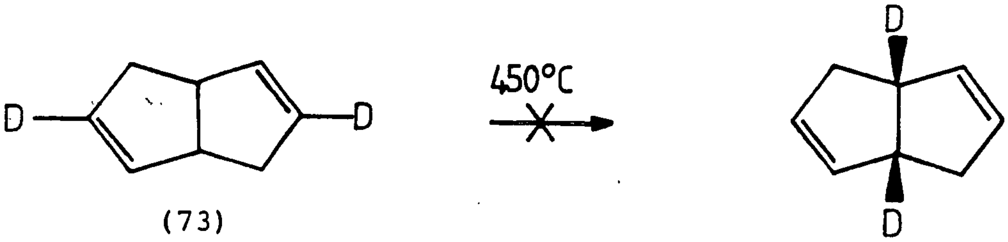
A third possible transition state for the Cope rearrangement involves an antarafacial-antarafacial interaction of the diallyl species. Although this is not usually in competition with the suprafacial-suprafacial chair or boat interactions, it explains the rearrangement of the bicyclic system (72) wherein steric restraints render the suprafacial-suprafacial interactions impossible (Scheme 35)[59].



(72)

Scheme 35

However a corresponding antarafacial-antarafacial [3,3] rearrangement was not observed for the rearrangement of 3,7-dideuteriobicyclo[3.3.0]octa-2,6-diene (73) (Scheme 36)[60].

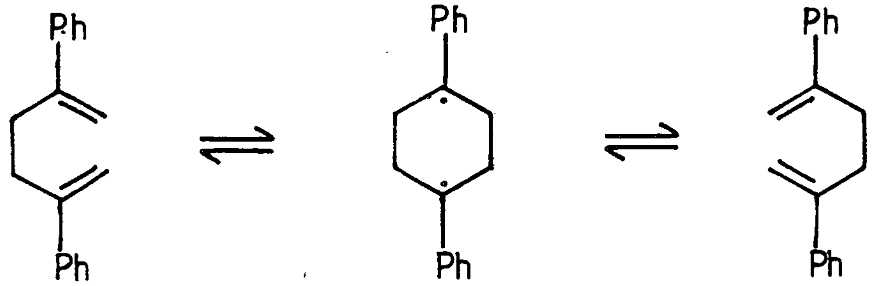


(73)

Scheme 36

b. Alternative Mechanism

The alternative to a concerted mechanism for the Cope rearrangement is a step-wise process, for which Doering *et al.*[61] have suggested that the intermediate may be a chair-like 1,4-cyclohexylene biradical. The results of Dewar *et al.*[62] from kinetic studies of the rearrangements of phenyl derivatives of 1,5-hexadiene, seem to support the work of Doering. Dewar established that phenyl substituents in 2 and/or 5 positions which could thus promote stabilisation of the radical centres, did lead to a significant rate enhancement of the reaction (Scheme 37). Wehrli and Schmid[63] have reported similar observations with 2,5-dicyano-1,5-hexadiene. Since singlet biradicals cannot be stable species, Dewar[64] has discussed a biradicaloid intermediate, derived from the corresponding biradical by some interaction between the radical centres which is sufficient to remove the orbital degeneracy.



Scheme 37

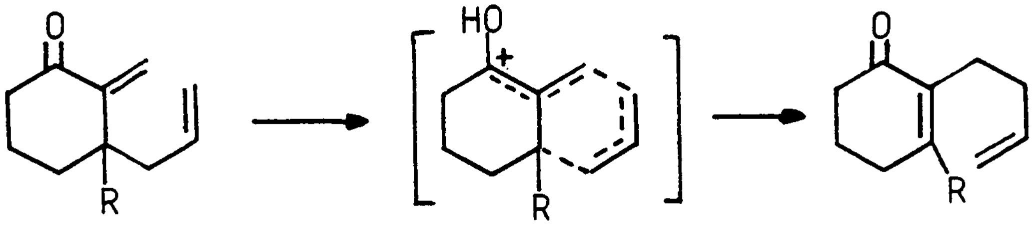
Studies by Lutz and Berg[65] have shown that the rate of the [3,3] shift is also accelerated with unsaturated substituents at positions 3 and/or 4 of hexa-1,5-diene. Furthermore, Kirmse[66] has recently reported that the pattern of substituent effects of hexa-1,5-dienes is more consistent with a diradicaloid mechanism than with a concerted sigmatropic rearrangement.

Another possibility is the dissociation of the 3,4-bond of the hexa-1,5-diene into a pair of allylic radicals followed by recombination. The failure to observe the predicted cross-over products of recombination invalidates this non-concerted mechanism. However, radical stabilising substituents at C_3 and C_4 should stabilise the transition state resembling two weakly coupled allyl radicals. Radical stabilising groups at C_2 and C_5 should stabilise the cyclohexane-1,4-diyl. As a result the Cope rearrangement transition state could be variable, depending on substitution[63,65,67].

c. Catalysed Cope Rearrangements

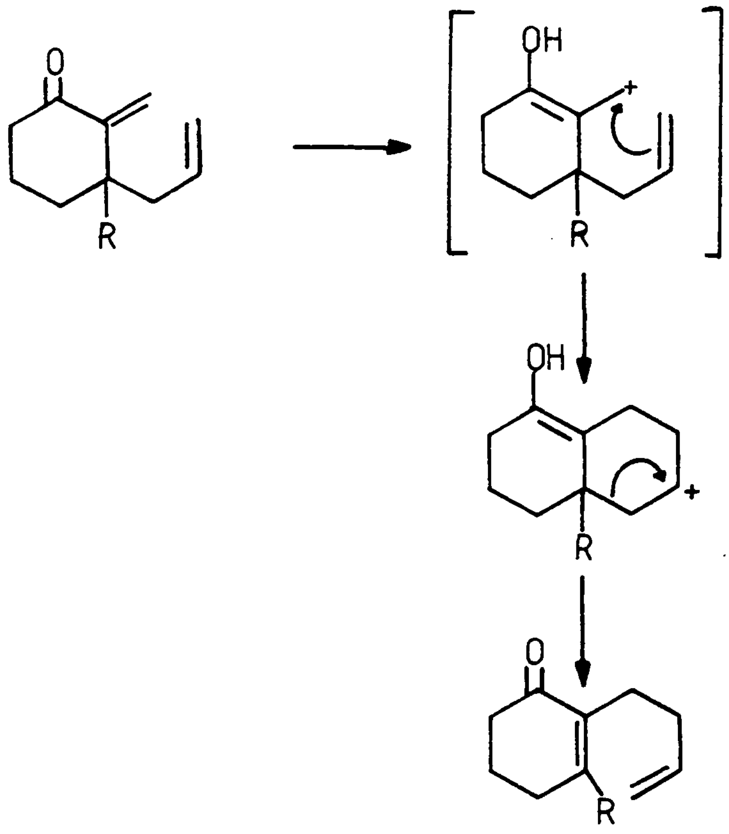
Lutz[68] has reported the alumina catalysed rearrangements of both *meso*- and dℓ -3,4-diphenyl-1,5-hexadiene. The Cope rearrangements of many acyclic 1,5-dienes have also been catalysed by palladium(II) chloride salts with the reactions occurring rapidly at room temperature[69].

Protic and Lewis acids have been found to strongly accelerate the Cope rearrangement of acyl-1,5-dienes and two different mechanisms have been suggested for this acid-catalysed rearrangement[70]. If a concerted mechanism is followed, the conjugated carbonium ion from protonation of the carbonyl group could facilitate the rearrangement by conjugation and stabilisation of the transition state (Scheme 38). Alternatively, a



Scheme 38

stepwise, carbocationic cyclisation-induced rearrangement may operate as shown in Scheme 39.

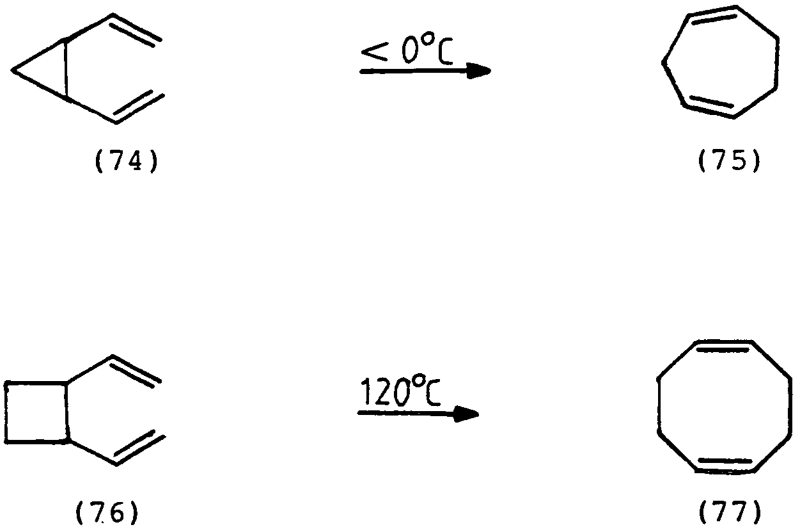


Scheme 39

2. Cope Rearrangement of *cis*-1,2-Divinylcycloalkanes

a. Three- and four-membered rings

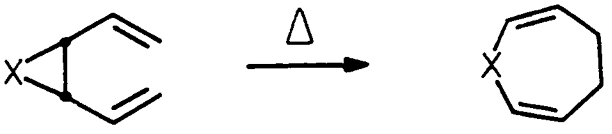
In the Cope rearrangement of some cyclic systems, the chair transition state is sterically impossible and the reaction must go by way of a boat transition state. This is the case in the rearrangements of *cis*-1,2-divinylcyclopropane (74) and *cis*-1,2-divinylcyclobutane (76) (Scheme 40).



Scheme 40

cis-1,2-Divinylcyclopropane (74) rearranges to give cyclohepta-1,4-diene (75) so readily that for many years attempts to isolate the compound were unsuccessful[71,72]. Its isolation was eventually achieved by Brown *et al.*[73] and more recently, by Schneider and Rau[74]. It is interesting to note that derivatives of (74) have been implied as possible precursors in the biosynthesis of natural products from marine brown algae[75].

The thermal rearrangements of analogues of *cis*-1,2-divinylcyclopropane in which the methylene group is replaced by a heteroatom have also been studied (Scheme 41). Thus, the rearrangement of *cis*-2,3-divinyloxirane[76], *cis*-2,3-divinylaziridines[77] and *cis*-2,3-divinylthiirane[78] have been investigated in detail. *cis*-2,3-Divinylthiirane 1,1-dioxide ($X=SO_2$) has not been isolated but it is the proposed intermediate in the synthesis of 4,5-dihydrothiepin 1,1-dioxide[79].



(78) (79)

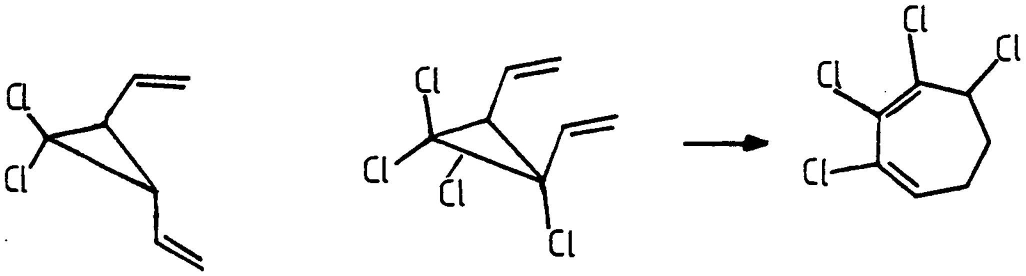
X=CH_2, O, NH, N-CH_3, N-C_2H_5, S, SO_2

Scheme 41

The temperatures necessary for ring expansion of (78) to (79) increase in the order C,N,O,S. However, competition between C-C and C-S bond cleavage has been reported to occur in the case of *cis*-2,3-divinylthiirane[78].

Rearrangement of the corresponding *trans*-divinyl compounds requires much higher temperatures and apparently involves either a diradical process or prior isomerisation to the more labile *cis*-isomer[76c,77b,80].

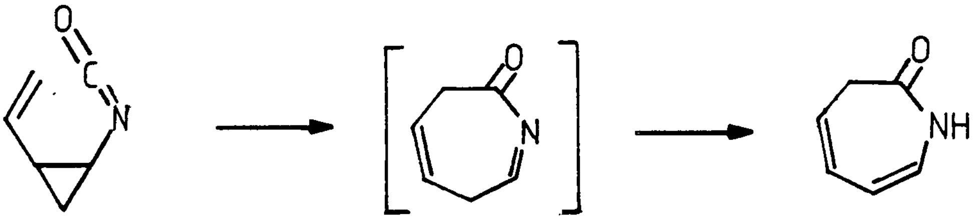
In a recent publication, the preparation of *trans*-1,1-dichloro-2,3-divinylcyclopropane (80) has been described[81]. The attempted preparation of the *cis*-divinyl compound (81) was found to give only the tetrachlorocycloheptadiene (82) from the Cope rearrangement of (81) followed by a [1,3] chlorine shift (Scheme 42).



(80) (81) (82)

Scheme 42

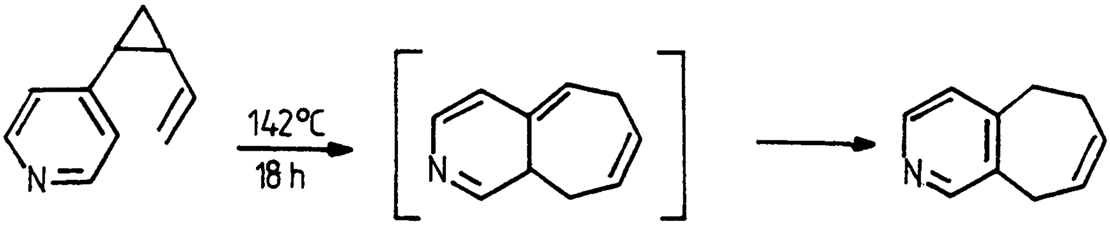
cis-2-Vinylcyclopropyl isocyanate (83) exhibits similar thermal behaviour to *cis*-1,2-divinylcyclopropane. Thus Cope rearrangement leads to the 2-azepinone (84) via a prototropic shift (Scheme 43)[80,82].



(83) (84)

Scheme 43

Recently Maas[83] has reported examples of a heteroaromatic Cope rearrangement. By heating 1-pyridyl-2-vinylcyclopropane (85) in an aromatic solvent, rearrangement occurs to give the cyclohepta[c]pyridine (86) (Scheme 44). The *cis*-vinylcyclopropanes were found to rearrange faster than their *trans*-isomers.



(85) (86)

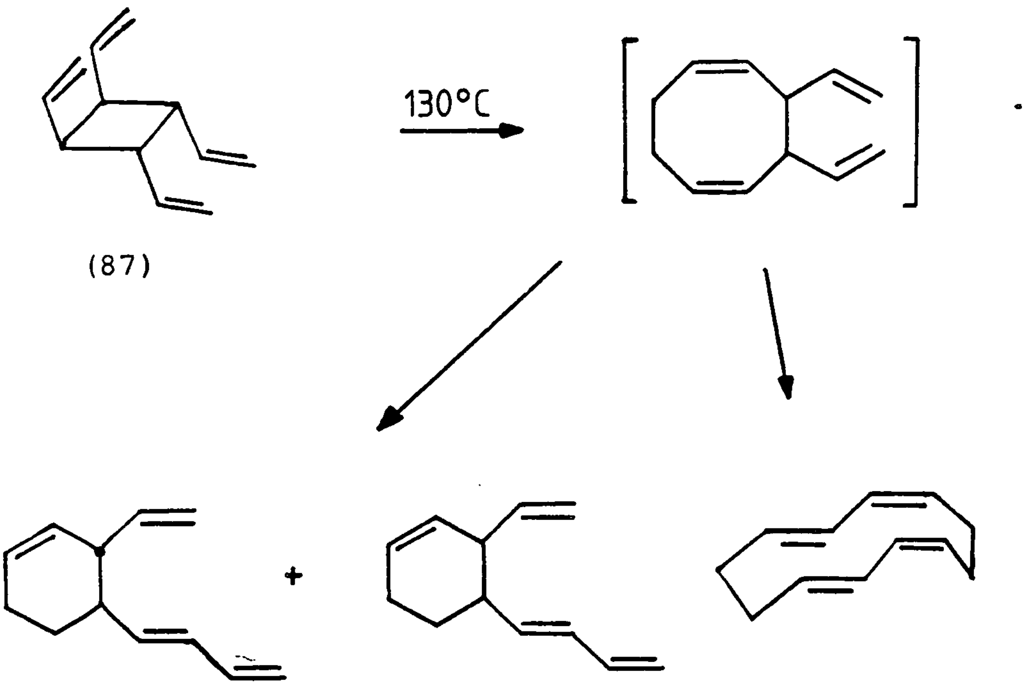
Scheme 44

The Cope rearrangement of *cis*-1,2-divinylcyclobutane (76) to *cis*,*cis*-1,5-cyclooctadiene (77) was first reported by Vogel in 1958 (Scheme 40)[84]. Like *cis*-1,2-divinylcyclopropane, rearrangement occurs via a boat transition state, the ease of these reactions being attributed to relief of ring strain in the three- and four-membered rings. The corresponding *trans*-1,2-divinylcyclobutane rearranges to 4-vinylcyclohexene and *cis*,*cis*-1,5-cyclooctadiene, the latter being formed by *cis*,*trans*-isomerisation of the divinylcyclobutane[80,85]. Hammond and DeBoer[85] have discussed a biradical mechanism for the reaction.

It has been found by Berson and Dervan[86] that methyl substitution at the terminal vinyl carbons of *cis*-1,2-divinylcyclobutane (76) retards the boat-like rearrangement. However, the high strain energy of *cis*,*trans*-1,5-cyclooctadiene precludes the formation of a chair conformation in the transition state.

With transition metal catalysis, rearrangement of (76) takes place at 24°C in contrast to the purely thermal process which requires temperatures of 80-120°C. This work by Heimbach and co-workers has involved nickel(II) and palladium(II) complexes[87].

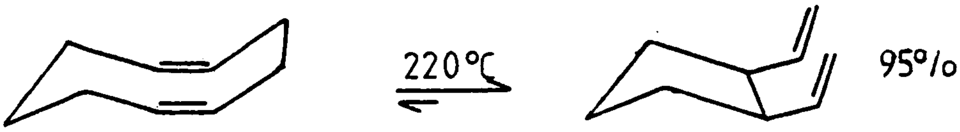
The rearrangement of *cis*,*trans*,*cis*-tetravinylcyclobutane (87) has recently been studied[88]. At temperatures above 120°C, (87) readily undergoes two consecutive Cope rearrangements to give cyclododeca-1,3,7,9-tetraene (88). Also formed in the reaction by a [1,3] shift, are *anti*- and *syn*-4-butadienyl-3-vinyl-1-cyclohexene (89) and (90) (Scheme 45).



Scheme 45

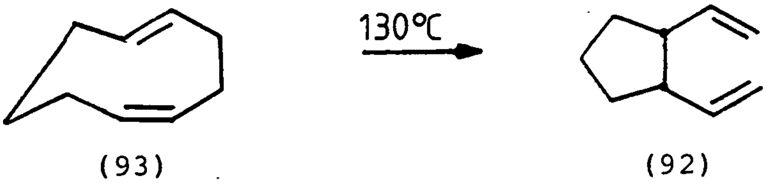
b. Five- and six-membered rings

In contrast to the *cis*-1,2-divinylcycloalkanes having three- and four-membered rings, the position of equilibrium for the medium ring systems is determined more by strain energy of the Cope rearranged product rather than the strain energy of the smaller rings. Thus in 1963 Vogel and co-workers[89] reported that *cis,cis*-1,5-cyclononadiene (91) and *cis*-1,2-divinylcyclopentane (92) equilibrate at 220° to a mixture that strongly favours the latter (Scheme 46). The more strained



Scheme 46

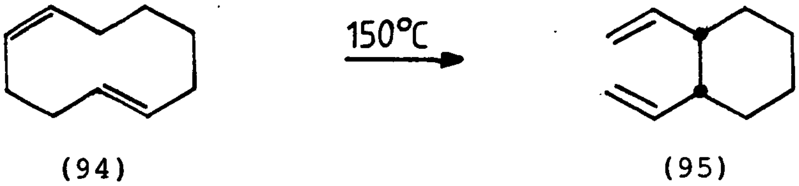
isomer, *cis,trans*-1,5-cyclononadiene (93) also isomerises to *cis*-1,2-divinylcyclopentane (92) (Scheme 47). This



Scheme 47

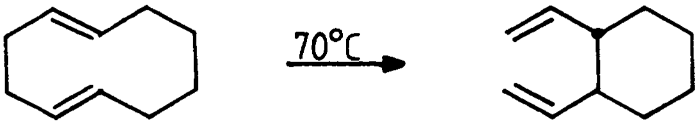
rearrangement proceeds via a chair-like transition state while a boat-like transition state must be involved in rearrangement of (91) to (92). At temperatures above 300°C (92) is known to undergo reversible *cis-trans* epimerisation[71,80].

Similarly, *cis,trans*-1,5-cyclodecadiene (94) isomerises quantitatively at 150°C to *cis*-1,2-divinylcyclohexane (95) (Scheme 48)[90]. The rearrangement involves the favoured chair



Scheme 48

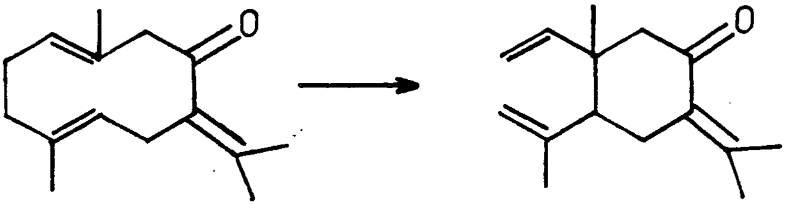
transition state which is also the case for the rearrangement of *trans,trans*-1,5-cyclodecadiene (96) to *trans*-1,2-divinylcyclohexane (97) (Scheme 49)[91].



(96) (97)

Scheme 49

These equilibria manifest themselves in the elemane-germacrane class of sesquiterpenes and are useful in structural assignment[92,93]. For example the isomerisation of germacrone (98) to β-elemenone (99) provides proof of the positions of



(98) (99)

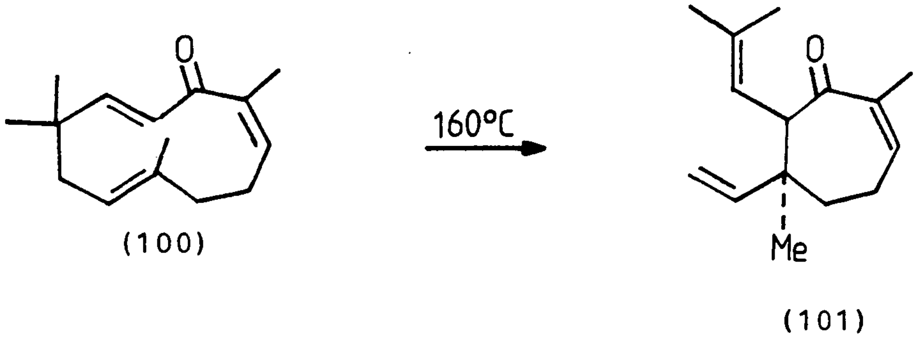
Scheme 50

the endocyclic double bonds in germacrone (Scheme 50)[94].

The transition-metal catalysed Cope rearrangement of *cis*,*trans*-1,5-cyclodecadiene (94) to (95) has also been studied and is thought to proceed through bis-π-allylic complexes of palladium(II) or platinum(II)[95].

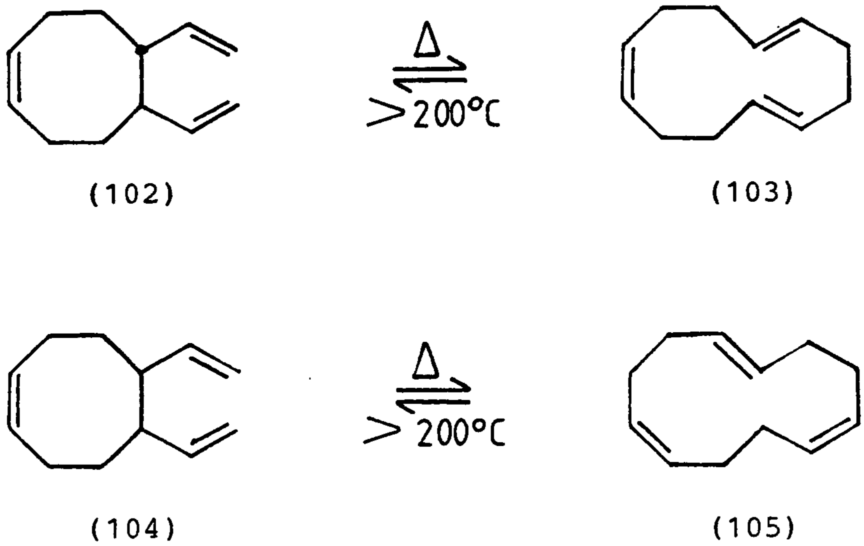
c. Seven- and eight-membered rings

The *trans*,*trans*-1,5-diene system in the eleven-membered ring compound zerumbone (100) readily isomerises to the *trans*-divinyl system (101) in the only example involving a seven membered cyclic divinyl compound (Scheme 51)[96].



Scheme 51

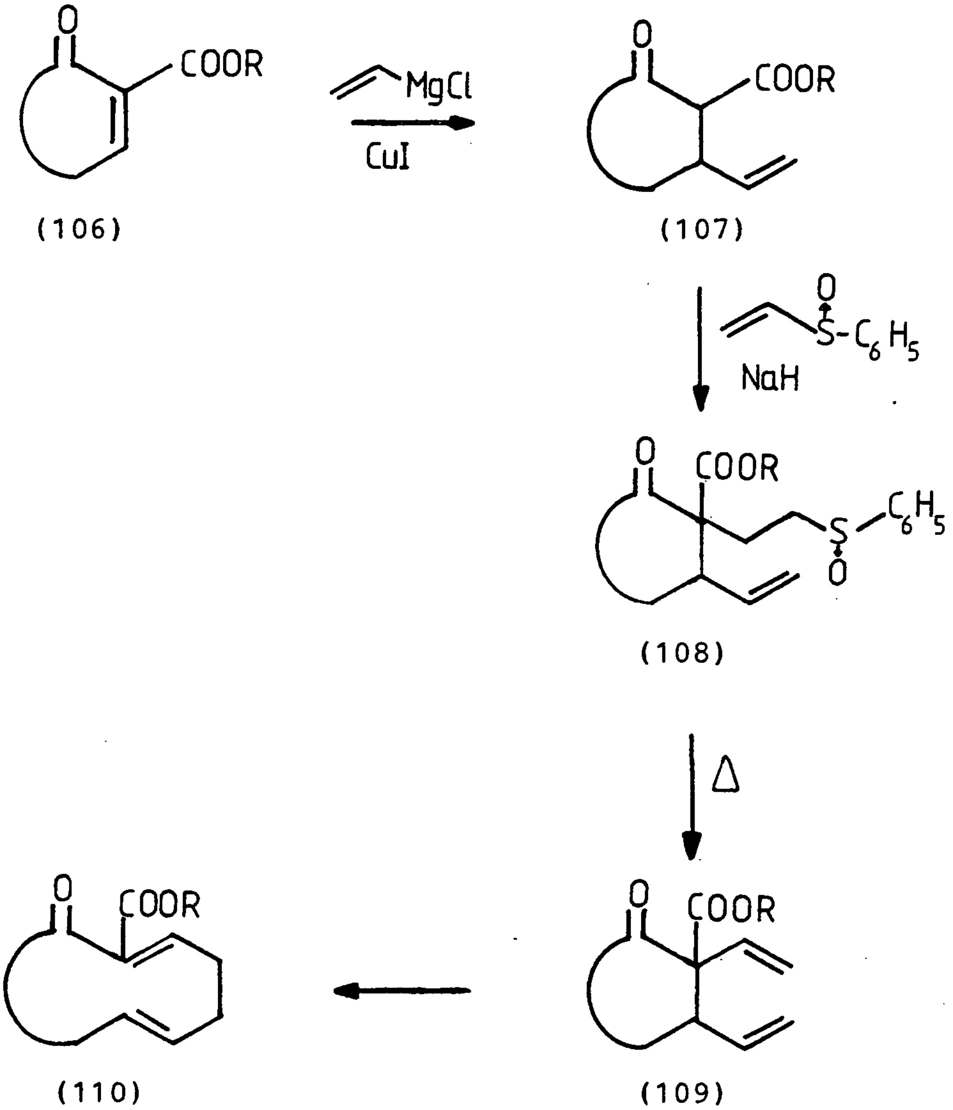
The rearrangement of divinyl compounds bearing eight-membered rings has also been studied[97]. Thus *trans*-5,6-divinyl-*cis*-cyclooctene (102) gives rise to *trans*-1,*trans*-5,*cis*-9-cyclododecatriene (103) while the *cis*-isomer (104) yields *trans*-1,*cis*-5,*cis*-9-cyclododecatriene (105) (Scheme 52). Both reactions are believed to involve a chair transition state. At temperatures above 200°C retro-rearrangements are observed.



Scheme 52

d. Further Examples

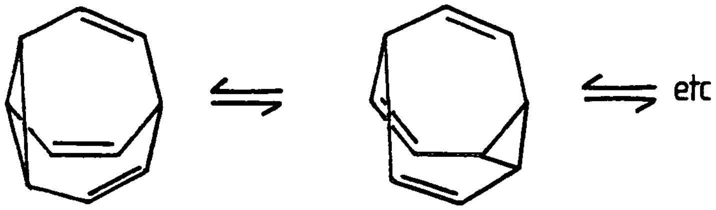
The Cope rearrangement has been described as a reaction for repeatable ring expansions by Heimgartner *et al.*[98]. The first step of their reaction sequence entails reacting the unsaturated β-keto-ester (106) with vinyl magnesium chloride. Subsequent treatment of (107) with phenyl vinyl sulphoxide followed by thermolysis of (108) leads to the α,β-divinyl ketoester (109) by elimination of a sulfinic acid. Cope



Scheme 53

rearrangement of (109) then gives (110) which being an unsaturated β-ketoester can undergo a further ring expansion sequence (Scheme 53). The reaction sequence was carried out with nine-, twelve- and fifteen-membered ketoesters, the ring size expanding by four carbons through the reaction scheme.

There are several systems which undergo Cope rearrangement very readily and in which the products have the same structure as the starting materials[57,72]. This multiple degeneracy is observed for tricyclo[3.3.2.$0^{4,6}$]deca-2,7,9-triene (111) commonly known as bullvalene for which there are 1,209,600 possible arrangements, the cyclopropane unit being at any three adjacent carbons (Scheme 54)[99].



(111)

Scheme 54

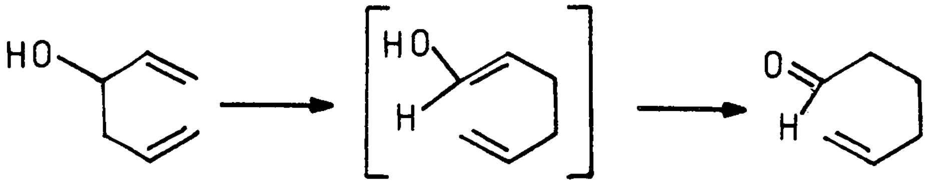
At temperatures above 100°C, the ^{1}H NMR spectrum of bullvalene becomes a sharp singlet indicating that the interconversion occurs too rapidly for the individual forms to be distinguished and an average structure, in which all the hydrogens are equivalent, is recorded.

In conclusion the driving force for shifting the equilibrium of a Cope rearrangement in a given direction may be an increase in conjugative interaction, the relief of ring strain or in more complex cyclic compounds, differences in conformational stabilities.

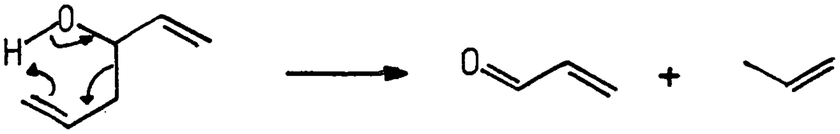
3. The oxy-Cope and Claisen rearrangements

a. The oxy-Cope rearrangement

When the 1,5-hexadiene system has a hydroxyl group at positions 3 and/or 4, thermal [3,3] sigmatropic rearrangement can occur to give an enolic or bis (enolic) product which tautomerises to the carbonyl or dicarbonyl derivative (Scheme 55)[52]. Products may also arise from a β-hydroxyolefin cleavage pathway (Scheme 56).

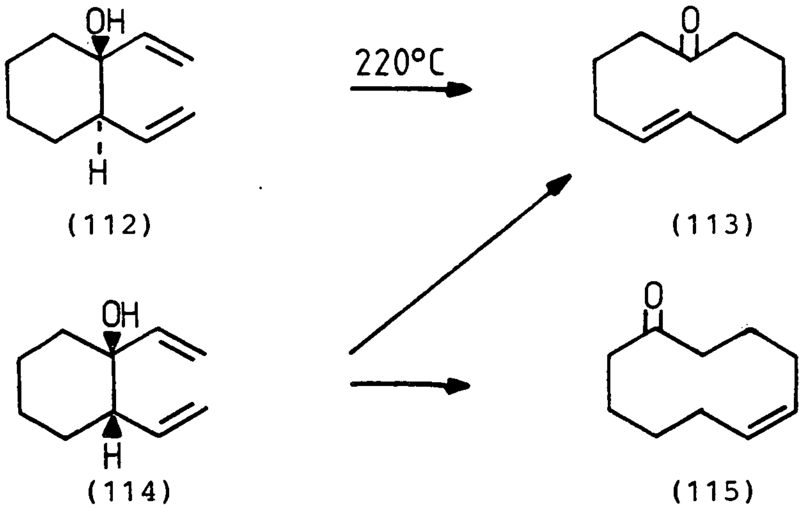


Scheme 55



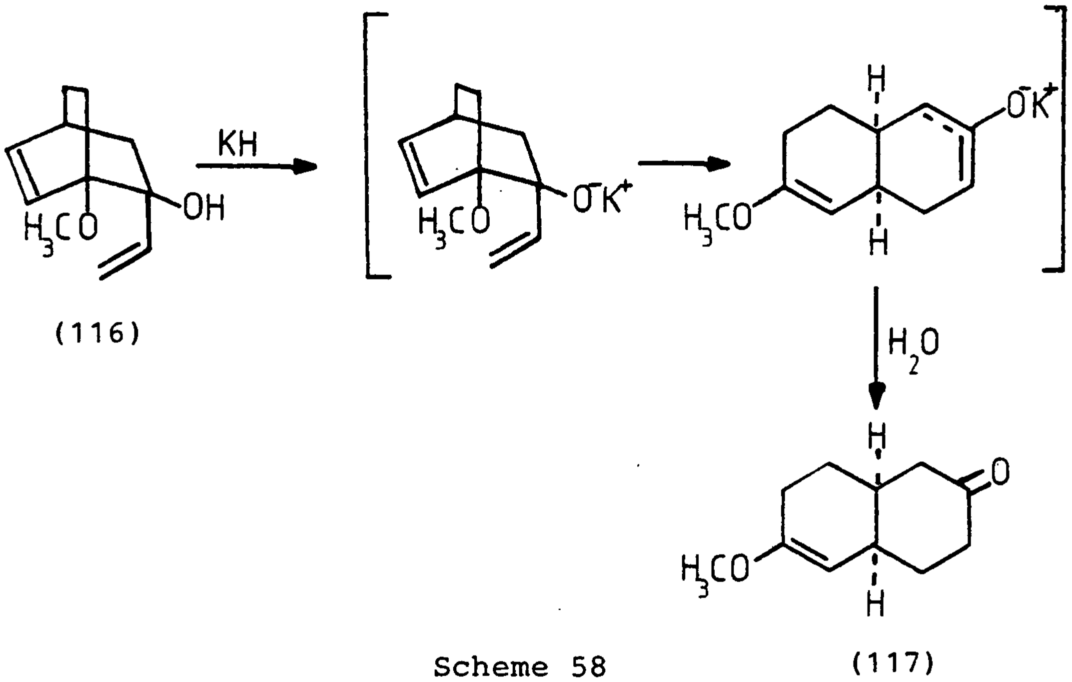
Scheme 56

Marwell and Whalley[100] have investigated the rearrangement of *trans*- and *cis*-1,2-divinylcyclohexanol. The *trans* isomer (112) rearranges to the single product, *trans*-5-cyclodecen-1-one (113) while the *cis* isomer (114) gives a mixture of *trans*- and *cis*-5-cyclodecen-1-one (113) and (115) (Scheme 57). Both rearrangements proceed via a chair transition state and provide a useful approach to functionalised ten-membered rings.



Scheme 57

Evans and Golob[101] have shown that the rearrangement is strongly accelerated by the presence of an alkoxide substituent. For example, the dienol (116) when treated with potassium hydride rearranges within several minutes at 66°. On quenching with water, the ketone (117), is obtained in high yield (Scheme 58).

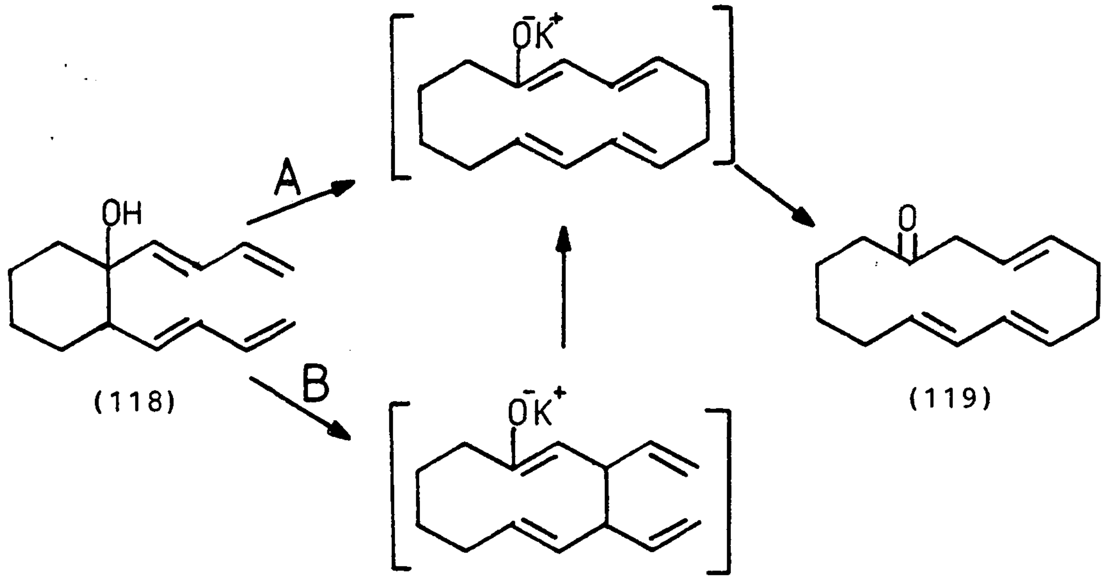


Scheme 58

Further acceleration of the reaction can be achieved by the addition of ionophores such as crown ethers which owing to ion pair dissociation results in maximal rate acceleration in the range of 10^{10}-10^{17}.

Evans[102] has also reported the application of these modified oxy-Cope rearrangements to the stereoselective synthesis of the sesquiterpene (±)-Juvabione.

In a recent publication, Wender *et al.*[103] have reported the synthesis of medium rings based on an eight-unit ring expansion process. Treatment of 1,2-*trans,trans*-di (1-buta-1,3-dienyl)cyclohexanol (118) with potassium hydride in THF at room temperature gave the 14-membered ring trienone (119) in 90% yield (Scheme 59). Studies of the mechanism of this macroexpansion are still in progress but the product is believed to arise from either a [5,5] sigmatropic shift, an unprecedented vinylogous oxy-Cope rearrangement (Path A), or by a consecutive [3,3] sigmatropic rearrangement (Path B). However, Pettit

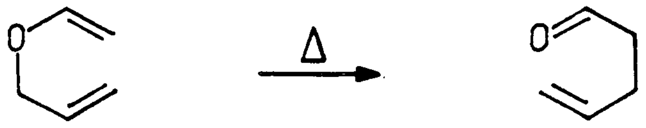


Scheme 59

and Gibson[104] have found that rearrangement of the all carbon acyclic analogue of (118) gives a mixture of products via a fragmentation-radical recombination process.

b. The Claisen rearrangement

Finally, mention should be made of the Claisen rearrangement, the thermal transformation of a vinyl allyl ether (120) to the corresponding homoallylic carbonyl compound (121) (Scheme 60)[52]. The reaction was first reported by Claisen[105] in 1912 and like the Cope, has been classified as a [3,3] sigmatropic rearrangement[1].

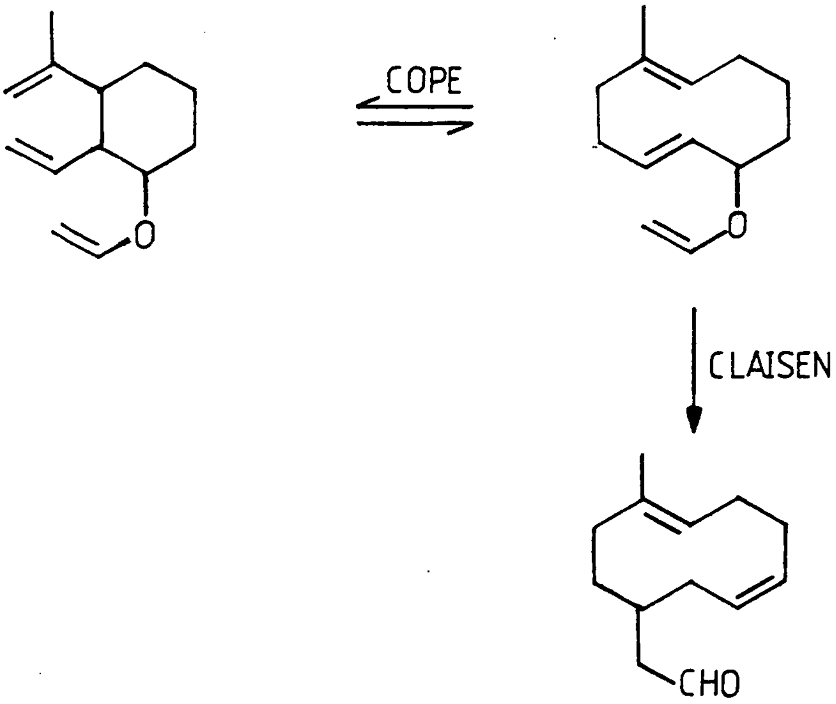


(120) (121)

Scheme 60

Ziegler and Piwinski[106] have recently reported on a tandem Cope-Claisen rearrangement. The initial Cope reaction triggers the irreversible Claisen rearrangement which can thus serve to shift the unfavourable Cope equilibrium (Scheme 61).

Ziegler[107] has applied the double rearrangement to a novel synthesis a (±)-estrone methyl ether. The tandem Cope-Claisen rearrangement has also been investigated by Raucher *et al.*[108] with the view of applying it towards the total synthesis of germacrane sesquiterpenes.

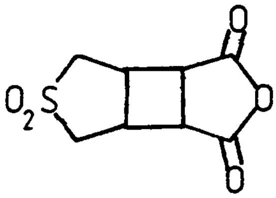


Scheme 61

Similarly, Thomas[109] and Cookson[110] have utilised a sequential Claisen-Cope rearrangement in the synthesis of terpenoid structures.

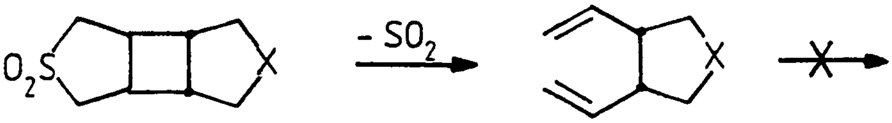
C. Programme of Research

Preparation of the tricyclic sulphone (56) was first reported in the literature in 1972 by Shaikhrazieva *et al.*[111] Its potential for divinyl synthesis by cheletropic extrusion of SO_2 was realised and previous work in these laboratories has succeeded in preparing a variety of novel *cis*-1,2-divinyl compounds via flash vacuum pyrolysis of the anhydride (56) and its derivatives[49]. Thus pyrolysis of derivatives of type (57)



(56)

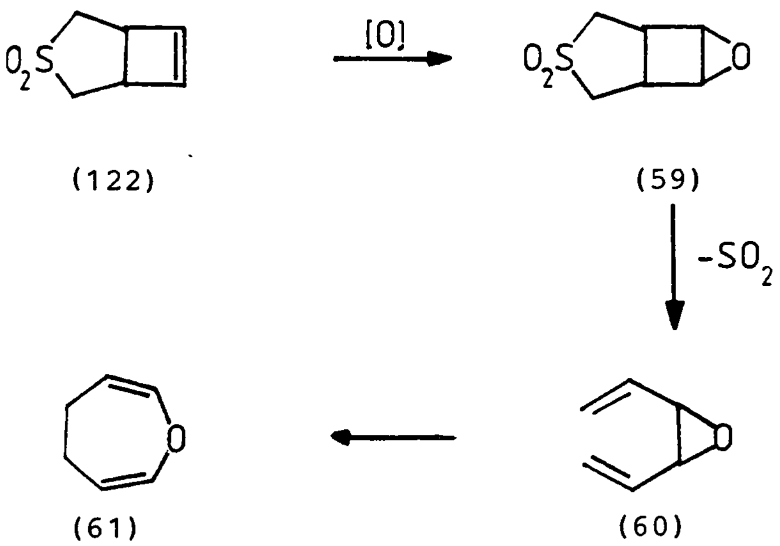
lead to the stereospecific formation of *cis*-1,2-divinylheterocycles (58) which having five-membered rings are not prone to Cope rearrangement (Scheme 28).



(57) (58)

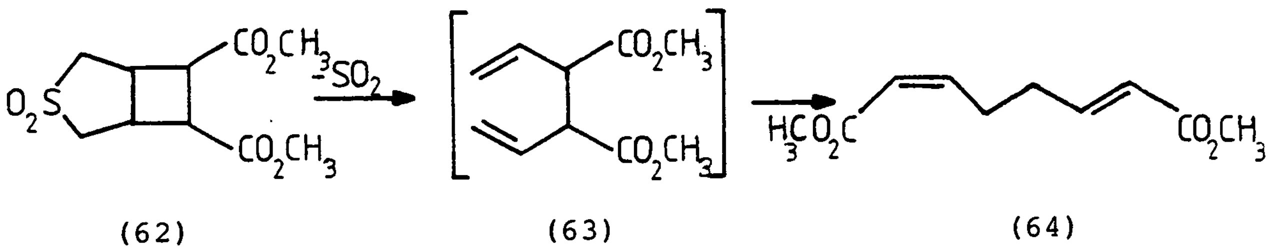
Scheme 28

Precursors to the divinyl system were also obtained by the addition of 1,3-dipoles and mononuclear electrophilic species to the alkene (122) formed from oxidative bis-decarboxylation of the diacid of (56)[151]. For example, epoxidation of the alkene (122) afforded (59) which on pyrolysis gave a good yield of 4,5-dihydrooxepin (61) by Cope rearrangement of the intermediate divinyloxiran (60) (Scheme 62)[50]. The alkene itself is a masked form of *cis*-1,3,5-hexatriene.



Scheme 62

As also mentioned in a previous section (p.23) pyrolysis of the diester (62) was found to yield the *cis,trans*-hexa-1,5-diene (64) formed by Cope rearrangement of the *meso*-diester (63) (Scheme 30). In an effort to extend this reaction to a general synthesis of *cis,trans*-1,5-dienes, it was



Scheme 30

decided to prepare and pyrolyse a variety of acyclic derivatives from the functionalisation of the anhydride (56) and to study the stereochemistry of the reaction in more detail. Furthermore, it was intended to prepare *cis*-1,2-divinylcyclic compounds of medium-sized rings and to study the effect of ring size on the Cope rearrangement of these compounds.

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EXPERIMENTAL

EXPERIMENTAL

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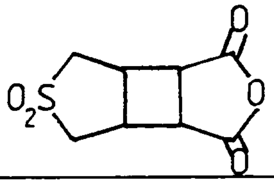
D. FVP of  and derivatives

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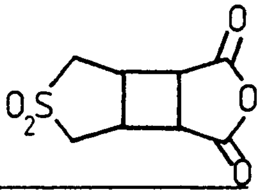
I. Preparation and FVP of methylated derivatives of 

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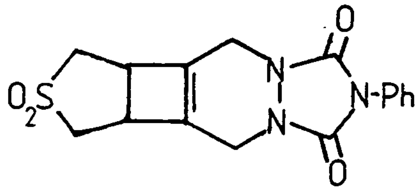
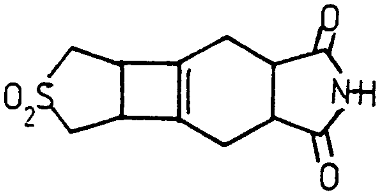
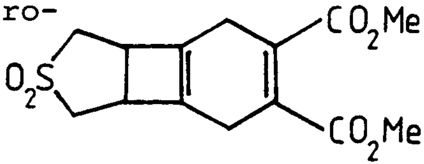
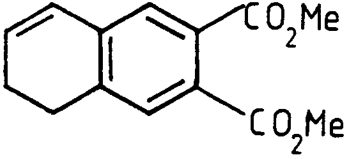
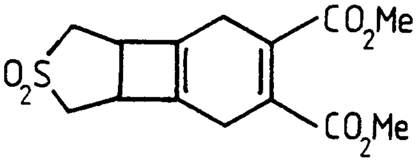
e. FVP of  125

f. FVP of  125

4. a. Attempted dehydrogenation of  125

b. Dehydrogenation of  126

c. Tandem FVP and dehydrogenation of  127

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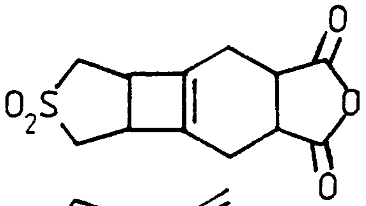
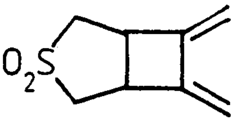
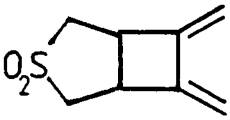
a. Reaction of EtOCN: with  128

b. Reaction of EtOCN: with  128

6. FVP of  129

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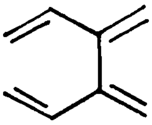
7. Reactions of 

A. Symbols and Abbreviations

m.p.	melting point
b.p.	boiling point
FVP	flash vacuum pyrolysis
i.r.	infrared
ν	wave number
n.m.r.	nuclear magnetic resonance
δ	chemical shift
s,d,t,q,	singlet, doublet, triplet, quartet,
m	multiplet
J	spin-spin coupling constant
MS	mass spectroscopy
m/z	mass to charge ratio
M^{+}	mass of molecular ion
t.l.c.	thin layer chromatography
GC	gas liquid chromatography
mmol	millimoles
h, min	hours, minutes

B. Instrumentation and General Techniques

1. N.m.r. Spectroscopy

a ^{1}H n.m.r.

Routine spectra were obtained on a Varian EM-360 (60 MHz) spectrometer. Spectra of new compounds were obtained using a Varian HA-100 (100 MHz) spectrometer operated by Mr. J.R.A. Millar unless otherwise stated when recorded on Bruker WP-80-SY (80 MHz) and Bruker WP-200-SY (200 MHz) spectrometers operated by Mr. J.R.A. Millar and Mr. L.H. Bell.

b ^{13}C n.m.r.

Routine spectra were obtained on a Varian CFT-20 (25 MHz) spectrometer operated by Mr. J.R.A. Millar. 90 MHz spectra were obtained using a Bruker WH-360 spectrometer operated by Dr. I.H. Sadler and Dr. D. Reed.

All spectra were obtained from solutions in deuteriochloroform unless otherwise stated. Chemical shifts were recorded in parts per million from tetramethylsilane.

2. Infrared Spectroscopy

Spectra were obtained on a Perkin-Elmer 157G grating spectrometer and later on a Perkin-Elmer 781 spectrometer. Liquids were examined as thin films and solids as nujol mulls, both on sodium chloride plates. Solution spectra were run in the solvent stated using matched sodium chloride cells of pathlength 0.1 mm. Spectra were calibrated with the polystyrene peak at 1603 cm^{-1}.

3. Mass Spectroscopy

Mass spectra and accurate mass measurements were obtained on an Associated Electrical Industries MS-902 instrument operated by Mr. D.J.A. Thomas.

4. Gas Chromatography-Mass Spectroscopy

GC-MS measurements were obtained on a Pye series 104 chromatograph coupled to a V.G. Micromass 12 spectrometer operated by Miss E. Stevenson.

5. Elemental Analysis

Microanalyses for carbon, hydrogen and nitrogen were carried out on a Perkin-Elmer 240 Elemental Analyser by Mr. J. Grunbaum, University of Edinburgh.

6. Melting Points

Routine melting points were determined using an Electrothermal melting point apparatus while melting points of new compounds were determined on a Reichert hot-stage microscope. All melting points are uncorrected.

7. Gas Liquid Chromatography

A Pye 104 chromatograph with a flame ionisation detector was used with nitrogen as carrier gas. The following columns were employed: 10% polyethyleneglycoladipate (PEGA), 1% dimethylsilicone gum (OV1), 2% carbowax 20m and 20% 1,2,3-Tris(2-cyanoethoxy)propane (Fractonitrile III, TCEP), all on Chromosorb W (80-100 mesh).

8. Preparative Gas Chromatography

Preparative GC was carried out using a Carlo Erba Strumentazione Fractovap 2450 instrument. The products were collected in traps cooled by dry ice/acetone.

9. Thin Layer Chromatography

This was carried out using 0.3 mm layers of alumina (Merck, neutral aluminium oxide 60G, Type E) or silica (Merck, Kieselgel 60G) containing 0.5% Woelm fluorescent green indicator, on glass plates. The components were observed under ultraviolet light or by their reaction with iodine vapour.

10. Preparative Thin Layer Chromatography

This was carried out using 1.0 mm layers of the supports mentioned above. After locating the components with iodine or UV light, the bands were scraped off and the products removed from the support by soaking with a suitable solvent.

11. Column Chromatography

The alumina used was Laporte Industries Alumina H (100-200 mesh), deactivated by addition of 6% water.

12. Photochemical Reactions

Photolysis was carried out using either 125W or 400W medium pressure water cooled mercury lamps supplied by Applied Photophysics Ltd., London . Large scale reactions were carried out by inserting the quartz or pyrex reactor well in a vessel containing the reaction mixture. For small scale reactions, a quartz tube containing the reaction mixture was attached to the side of the reactor well.

13. Drying and Evaporation of Organic Solutions

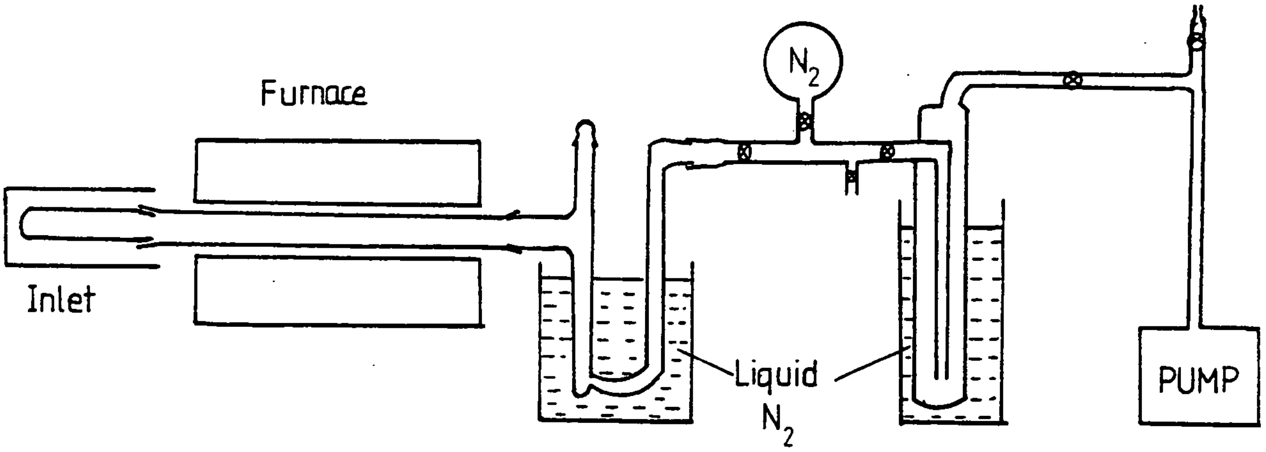
Organic solutions were dried by standing over anhydrous magnesium sulphate for several hours and were evaporated on a rotary evaporator under reduced pressure.

14. Drying and Purification of Solvents

Dry benzene and toluene were prepared by addition of sodium wire to the Analytical Reagent (A.R.) grade solvent. Dry ether was also prepared by the addition of sodium wire. Dry methylene chloride and dimethylformamide were distilled from phosphorus pentoxide and stored over molecular sieves. Tetrahydrofuran and dimethoxyethane were dried by heating the solvent under reflux with calcium hydride under nitrogen for 3 h and distilling onto pre-dried molecular sieves. Dry dimethylsulphoxide was distilled and stored over molecular sieves.

15. Flash Vacuum Pyrolysis

The apparatus used is illustrated in Scheme 63.



Scheme 63

The sample was volatilised from a horizontal inlet tube heated in a Buchi Kugelrohr oven, through a silica tube (30 x 2.5 cm). This was heated at temperatures ranging from 350-800°C by a Stanton Redcroft laboratory tube furnace LM8 100, the temperature being measured by a Pt/Pt-13% Rh thermocouple situated at the centre of the furnace. The system was maintained at a pressure of 10^{-2}-10^{-3} mmHg by an Edwards Model ED100 high capacity rotary oil pump, the pressure being measured by a Pirani gauge. Under these conditions the contact time in the hot zone was estimated to be within 1-10 milliseconds. In some experiments, the contact time was increased by packing the furnace tube with 5 cm lengths of silica rods or a plug of silica wool. The products were collected in a U-shaped trap cooled in liquid nitrogen.

Small scale pyrolyses were carried out using 25-100 mg of material. After the pyrolysis was complete, the system was isolated from the pump and filled with nitrogen gas.

The product was then dissolved out of the trap by adding deuteriochloroform and analysed directly by n.m.r. By adding the solvent while the trap was still frozen, volatile or unstable products could be obtained in good yields. Yields were estimated by adding 5-10 mg of a solvent such as cyclohexane or benzene and comparing the ^{1}H n.m.r. integrals. If a residue remained in the inlet after pyrolysis, this was taken into account when calculating the yield.

In all pyrolyses the optimum conditions were quoted, the pressure being the pressure in the system before the pre-heated Kugelrohr oven was brought to surround the inlet to start the pyrolysis.

In FVP under dehydrogenating conditions, a furnace tube with a sinter halfway along its length was packed with a catalyst (Alfa 12686 Palladium on activated carbon, 5.2% Pd, 10 g), an even packing of the catalyst being ensured by using a quartz wool plug.

C. Preparation of 3,5-Dioxo-4-oxa-9-thiatricyclo $[5.3.0.0^{2,6}]$decane 9,9-dioxide and derivatives

1. 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 Shaikhrazieva *et al.*[111] A solution of butadiene sulphone (38 g, 0.33 mol) and maleic anhydride (39 g, 0.398 mol) in acetone (600 ml) was irradiated at 400W for 24 h. The crystals were filtered off and washed with acetone. By partial evaporation of the filtrate further crystals were obtained to give 3,5-dioxo-4-oxa-9-thiatricyclo-$[5.3.0.0^{2,6}]$decane 9,9-dioxide (35.2 g, 50%) as colourless crystals, m.p. 292-293°C (lit.,[111] 292-293°C).

2. Preparation of the Diacid and Diesters of 3,5-Dioxo-4-oxa-9-thiatricyclo$[5.3.0.0^{2,6}]$decane 9,9-dioxide

a. Preparation of 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 (15 g, 69.4 mmol) was suspended in water (120 ml). The mixture was boiled until a clear solution was obtained. The water was removed *in vacuo* to leave a colourless solid which was dried under vacuum to give 3-thiabicyclo[3.2.0]-heptane-6,7-dicarboxylic acid 3,3-dioxide (15.6 g, 96%) as a colourless crystalline solid, m.p. 191-193°C (lit.,[111] 194-195°C).

b. Preparation of Diesters

(i) 6,7-Dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A mixture of 3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.$0^{2,6}$] decane 9,9-dioxide (20 g, 92.5 mmol) and AR methanol (200 ml) to which a few drops of sulphuric acid had been added was heated under reflux for 3 h. On cooling, the solution gave a crystalline precipitate which was filtered off to give 6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (21.3 g, 88%) as colourless needles, m.p. 126-127°C (lit.,[111] 126-127°C).

(ii) 6,7-Diethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A mixture of 3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.$0^{2,6}$] decane 9,9-dioxide (1 g, 4.63 mmol) and ethanol (20 ml) to which a few drops of sulphuric acid had been added was heated under reflux for 3 h. On cooling, the solution gave a crystalline precipitate which was filtered off to give 6,7-diethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1.24 g, 92%) as colourless crystals, m.p. 139-140°C (Found: C, 49.4; H, 6.2. $C_{12}H_{18}O_6S$ requires C, 49.65; H, 6.2%); ν_{max} 1740, 1302, 1282, 1220, 1185, 1144, 1030, 893, and 720 cm^{-1}; δ_H 4.15 (4H, q, J7Hz), 3.60 (4H, m), 3.25-3.15 (4H, m), and 1.24 (6H, t, J7Hz); m/z 290 (M^+, 3%), 245 (32), 217 (19), 198 (11), 180 (18), 152 (27), 113 (23), 79 (52), and 29 (100).

(iii) 6,7-Dibenzyloxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A mixture of 3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.$0^{2,6}$]

decane 9,9-dioxide (1 g, 4.63 mmol) and benzyl alcohol (10 ml) to which a few drops of sulphuric acid had been added was heated under reflux for 2.5 h. Ether (50 ml) was added and the resulting precipitate was filtered off, washed with ether and dried to give 6,7-dibenzyloxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (0.82 g, 43%) as colourless crystals, m.p. 91.5-92.5°C (Found: C, 63.5; H, 5.45. $C_{22}H_{22}O_6S$ requires C, 63.75; H, 5.35%); ν_{max} 1733, 1210, 1137, 1021, 757, and 702 cm^{-1}; δ_H 7.40-7.24 (10H, m), 5.12-4.82 (4H, AB, J12Hz), 3.70-3.58 (4H, m), and 3.20-3.12 (4H, m); m/z 414 (M^+, <1%), 323 (2), 217 (14), 107 (100), and 91 (99).

3. Preparation of 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0] heptane 3,3-dioxide and derivatives

a. Preparation of 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0] heptane 3,3-dioxide

6,7-Dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (18 g, 68.7 mmol) was added in portions to a suspension of lithium aluminium hydride (10 g, 26.4 mmol) in dry tetrahydrofuran (500 ml) with stirring under nitrogen. The mixture was heated under reflux for 1 h, allowed to cool and the lithium aluminium hydride destroyed by addition of wet tetrahydrofuran (10 ml water in 100 ml THF) followed by 15% NaOH (10 ml) and finally water (10 ml). The inorganic salts were filtered off, washed with acetone and the solvent evaporated from the filtrate to give a brown oil which crystallised on standing. The solid was recrystallised from tetrahydrofuran to give 6,7-dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (9.22 g, 65%) as colourless crystals, m.p. 97-98°C (lit.,[50] 98-100°C).

b. Preparation of Diethers

(i) 6,7-Dimethoxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

This was prepared by the method of Johnstone and Rose[112]. Powdered potassium hydroxide (2.04 g, 0.04 mol) was added to dry dimethylsulphoxide (10 ml). After stirring for 5 min, 6,7-dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1.05 g, 0.005 mol) was added, followed immediately by methyl iodide (2.84 g, 0.02 mol). Stirring was continued for 30 min, after which time the mixture was poured into water (20 ml) and extracted with methylene chloride (3x20 ml). The combined organic extracts were washed with water (5x10 ml) and dried. Evaporation of solvent gave a colourless solid (1.06 g) which was recrystallised from petroleum ether to give 6,7-dimethoxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (0.68 g, 58%) as colourless plates, m.p. 80.5-81.5°C (Found: C, 51.2; H, 7.55. $C_{10}H_{18}O_4S$ requires C, 51.25; H, 7.75%); ν_{max} 1300, 1250, 1203, 1132, 1095, 954, 881, 776 and 697 cm^{-1}; δ_H 3.56-3.48 (4H, m), 3.29 (6H, s), 3.2-2.9 (6H, m) and 2.80-2.65 (2H, m); δ_C 71.88, 58.70, 55.19, 39.76, and 3.10; m/z 235 ($M+1^+$, <1%), 202 (5), 84 (100), and 45 (62).

(ii) Attempted Vinylation of 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (Preparation of 5-Methyl-4,6-dioxa-11-thiatricyclo[7.3.0.0^{2,8}]dodecane 11,11-dioxide)

Based on the method of Adelman[113], a mixture of 6,7-

dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1 g, 4.85 mmol) and vinyl acetate (120 ml) to which a few drops of sulphuric acid and a few crystals of mercuric acetate had been added, was heated under reflux for 3 h, with stirring under nitrogen. The excess vinyl acetate was removed under vacuum and the residue dissolved in methylene chloride, washed with water and dried. Evaporation of solvent and recrystallisation of the resulting solid from ethanol gave 5-methyl-4,6-dioxa-11-thiatricyclo[7.3.0.0^{2,8}]dodecane 11,11-dioxide (0.87 g, 77%) as colourless crystals, m.p.155-156^{o}C. (Found: C, 51.95; H, 6.8. $C_{10}H_{16}SO_4$ requires C, 51.7; H, 6.9%); ν_{max} 1399, 1310, 1249, 1186, 1145, 1092, 1044, 1020, 955, 852, 724, 735, 665, and 647 cm^{-1}; δ_H 4.66 (1H, q, J5Hz), 4.1-3.66 (4H, AB, J13Hz), 3.5-2.8 (8H, m), and 1.42 (3H, d, J5Hz) (also trace at 1.31, d, J5Hz); δ_C 106.25, 70.04, 54.51, 42.49, 37.71, and 21.55 (major isomer, 82%), 105.58, 69.69, 54.37, 40.81, 31.12, and 20.79 (minor isomer, 18%); m/z 232 (M$^+$, 3%), 231 (2), 217 (69), 187 (34), and 79 (100).

Attempts to prepare the divinyl ether using ethyl vinyl ether and *n*-butyl vinyl ether according to the method of Watanabe and Conlon[114] were unsuccessful. Due to the poor solubility of the diol, these experiments were carried out using soxhlet extraction.

c. Preparation of Diesters

(i) 6,7-Bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide

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

dioxide (1.76 g, 8.54 mmol) was added in portions to a solution of *p*-toluenesulphonyl chloride (6 g, 31.5 mmol) in pyridine (20 ml) stirred at 0°C. The mixture was stirred for a further 3 h at 0°C and then poured into water (75 ml) to precipitate a colourless solid. The solid was filtered off, washed with water and dried *in vacuo* to give 6,7-bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (3.7 g, 85%) as a colourless crystalline solid, m.p. 131-132°C (lit.,[50] 127-128°C).

(ii) 6,7-Diacetoxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

This was prepared in the intention of preparing the dibromide. 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (2.07 g, 10 mmol) was dissolved in warm glacial acetic acid (15 ml). After raising the temperature of the solution to 65°C, hydrogen bromide solution (48%, 4.16 g, 51.4 mmol) was added and the temperature maintained at 65°C for 10 min. After cooling, the mixture was poured into water and extracted with methylene chloride. After thorough washing with water, the solution was dried and evaporation of solvent gave a brown oil which crystallised on standing. The solid was recrystallised from toluene to give 6,7-diacetoxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1.82 g, 63%) as colourless crystals, m.p.85-86°C (Found: C, 49.5; H, 6.2. $C_{12}H_{18}O_6S$ requires C, 49.65; H, 6.2%); ν_{max} 1730, 1290, 1128, and 1030 cm^{-1}; δ_H 3.2-2.8 (8H, m), 4.24-4.19 (4H, m), and 2.05 (6H, s), m/z 290 (M^+, <1%), 170 (5), 167 (3), 113 (32), 106 (28), 91 (19), 79 (17), 54 (15), and 43 (100).

4. Preparation of the Dihalides and Dinitrile from 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

a. Preparation of Dihalides

(i) 6,7-Dichloromethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (2.0 g, 9.71 mmol) was added in portions to a solution of thionyl chloride (3.45 g, 0.029 mol) in dry benzene (25 ml) containing a few drops of pyridine. The mixture was heated under reflux for 1 h before adding to iced water (50 ml). The benzene layer was separated and the solvent removed *in vacuo* to leave a brown solid (1.88 g, 80%). The solid was recrystallised from toluene and decolourised by boiling with charcoal to give 6,7-dichloromethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide as a colourless crystalline solid, m.p. 120-121°C (Found: C, 39.35; H, 5.0. $C_8H_{12}C_{12}O_2S$ requires C, 39.5; H, 4.95%); ν_{max} 1300, 1240, 1144, 887, 870, and 715 cm^{-1}; δ_H 3.76-3.65 (4H, m), 3.15-3.1 (4H, m), and 3.05-3.0 (4H, m), δ_C 54.54, 43.60, 41.96, and 34.78; m/z (M^+, not apparent), 129 (13%), 106 (18), 89 (24), and 54 (100).

(ii) 6,7-Dibromomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

This was prepared by the method of Buchman *et al.*[115] A mixture of 6,7-bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide (1.26 g, 2.45 mmol) and sodium bromide (0.61 g, 5.93 mmol) in ethylene glycol (15 ml) was heated at 140°C for 4 h with stirring. The mixture was poured into water and extracted with methylene chloride. The organic extracts were washed with water, dried and solvent evaporated to give a brown solid. Recrystallisation of the solid from ethyl acetate gave 6,7-dibromomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (0.28 g, 35%) as colourless crystals, m.p. 117-119°C (Found: C, 29.2; H, 3.75. $C_8H_{12}Br_2O_2S$ requires C, 28.9; H, 3.6%); ν_{max} 1300, 1145, 924, 760, and 718 cm^{-1}; δ_H 3.7-2.75 (m); m/z 332 (M^+, <1%), 253/251 (20), 171 (100), 135/133 (38), 107 (55), and 105 (30).

(iii) 6,7-Di-iodomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

This was prepared by the method of Baer[116]. A mixture of 6,7-bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo[3.2.0] heptane 3,3-dioxide (4.05 g, 7.88 mmol) and sodium iodide (3.54 g, 0.0236 mol) was heated under reflux in methyl ethyl ketone for 18 h with stirring. After removal of the sodium *p*-toluenesulphonate by filtration, the solvent was removed *in vacuo* and the residue dissolved in methylene chloride. The solution was decolourised with sodium thiosulphate solution, washed with water, dried and the solvent evaporated to give a pale yellow solid. Recrystallisation from ethyl acetate gave 6,7-di-iodomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (2.63 g, 78%) as colourless needles, m.p. 173-174°C (Found: C, 22.75; H, 2.8. $C_8H_{12}I_2O_2S$ requires C, 22.55; H, 2.85%); ν_{max} 1292, 1280, 1180, 1118, 868, 725, and 646 cm^{-1}; δ_H (CD_3SOCD_3) 3.6-3.1 (8H, m), and 2.85-2.6 (4H, m); m/z 427 ($M+1^+$, 8%), 299 (83), 233 (53), 181 (77), 171 (60), 107 (83), 105 (100), 91 (40), and 79 (60).

b. Preparation of 6,7-Dicyanomethyl-3-thiobicyclo[3.2.0]heptane 3,3-dioxide

(i) A mixture of 6,7-bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (3.4 g, 6.6 mmol) and potassium cyanide (1.55 g, 0.024 mol) in ethanol (40 ml) was heated under reflux for 60 h. After removal of solvent *in vacuo*, the residue was dissolved in a 50:50 mixture of water and methylene chloride. The organic extract was washed with water, dried and the solvent evaporated to give an orange solid which on recrystallisation from methanol gave 6,7-dicyanomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (0.8 g, 54%) as colourless crystals, m.p. 153-156°C (Found: C, 53.35; H, 5.55; N, 12.2. $C_{10}H_{12}N_2O_2S$ requires C, 53.55; H, 5.4; N, 12.5%); ν_{max} 2245, 1295, 1260, 1138, 1105, 892, 720, and 685 cm^{-1}; δ_H (CD_3SOCD_3) 3.3-3.15 (4H, m), and 3.0-2.75 (8H, m); m/z 224 (M^+, <1%), 184 (7), 159 (4), 145 (3), 120 (14), 106 (91), and 80 (100).

(ii) Alternative Method

A mixture of 6,7-bis(*p*-toluenesulphonyloxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (2 g, 3.89 mmol) and potassium cyanide (0.572 g, 11.67 mmol) was stirred at room temperature for 24 h in dry dimethyl sulphoxide (25 ml). The solution was extracted with methylene chloride, washed thoroughly with water, dried and the solvent evaporated to give 6,7-dicyanomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (0.55 g, 63%) as a colourless crystalline solid.

5. Preparation of the Cyclic Hydrazide and Imide of 3-Thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide

a. Preparation and attempted oxidation of 8,11-Dioxo-9,10-perhydrodiazine-4-thiatricyclo[5.2.0.$0^{2,6}$]-undecane 4,4-dioxide

(i) 6,7-Dihydrazidocarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

This was prepared by the method of Shaikhrazieva *et al.*[111] A solution of 6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1.3 g, 4.96 mmol) and hydrazine hydrate (4 ml) in AR methanol (20 ml) was heated under reflux for 2 h. On cooling, the solution gave a colourless precipitate which was filtered off, washed with methanol and dried under vacuum to give 6,7-dihydrazidocarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1.25 g, 79%) as a colourless crystalline solid, m.p. 239-241°C (lit.,[111] 220-222°C).

(ii) 8,11-Dioxo-9,10-perhydrodiazine-4-thiatricyclo[5.4.0.$0^{2,6}$]-undecane 4,4-dioxide

Again using the method of Shaikhrazieva *et al.*[111] 6,7-dihydrazidocarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (530 mg, 1.98 mmol) was heated at 220°C at 7×10^{-3}mmHg. Sublimation with loss of hydrazine hydrate gave 8,11-dioxo-9,10-perhydrodiazine-4-thiatricyclo[5.4.0.$0^{2,6}$]undecane 4,4-dioxide (470 mg, 49%) as pale yellow crystals, m.p. 226-232°C (lit.,[111] 228-230°C).

(iii) Attempted oxidation of 8,11-Dioxo-9,10-perhydrodiazine-4-thiatricyclo[5.4.0.$0^{2,6}$]undecane 4,4-dioxide

Attempts to oxidise 8,11-dioxo-9,10-perhydrodiazine-4-thiatricyclo[5.4.0.$0^{2,6}$]undecane 4,4-dioxide using lead tetra-acetate in methylene chloride (method of Chapman and Dominianni[117]) and mercuric oxide in methylene chloride (method of Carpino *et al*[118]) and in dimethylsulphoxide resulted in the recovery of unreacted starting material.

Using the method of Fetizon *et al.*[119], the cyclic hydrazide was heated under reflux with 12 equivalents of silver carbonate on celite in benzene. After 17 h, the mixture was filtered and the solvent evaporated from the filtrate to give back unreacted starting material.

b. Preparation of 8,10-Dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$]-decane 4,4-dioxide

(i) This was prepared by the method of Shaikhrazieva *et al.*[111] A solution of butadiene sulphone (1.25 g, 10.6 mmol) and maleimide (1 g, 10.3 mmol) in acetone (12 ml) containing acetophenone (0.5 ml) was irradiated at 400W for 18 h. The precipitate that had deposited was filtered off, washed with acetone and dried to give 8,10-dioxo-4-thia-9-azatricyclo-[5.3.0.$0^{2,6}$]decane 4,4-dioxide, (1.01 g, 46%) as colourless crystals, m.p. >300°C [lit.,[111] 345°C (decomp.)].

(ii) The second method involved the preparation of 3-thiabicyclo-[3.2.0]heptane-6,7-dicarboxylic acid monoamide 3,3-dioxide and the subsequent sublimation with loss of water to give the imide.

3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.$0^{2,6}$]decane 9,9-

dioxide (1 g, 4.63 mmol) was added to 0.88 ammonia solution (10 ml). After stirring for 30 min, the solution was evaporated to give a white solid (1.14 g). Recrystallisation from aqueous methanol with precipitation by ether gave a colourless crystalline solid which consisted of a mixture of the monamide and the diamide from elemental analysis.

Sublimation of the product with loss of water or ammonia at 220-250°C and at 0.01 mmHg gave 8,10-dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$]decane 4,4-dioxide.

c. Preparation and attempted oxidation of 9-Amino-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$]decane 4,4-dioxide

(i) 9-Amino-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$] decane 4,4-dioxide

This was prepared by the method of Drew and Hatt[120]. A mixture of 8,10-dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$]decane 4,4-dioxide (360 mg, 1.67 mmol) and hydrazine hydrate (101 mg, 2.01 mmol) in methanol (10 ml) was heated under reflux for 18 h. The solid was filtered off (0.27 g, 70%) but contained impurities of the starting imide by comparison of i.r. Recrystallisation from methanol gave 9-amino-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$]decane 4,4-dioxide as a colourless crystalline solid, m.p. 230-232°C (Found: C, 4.55; H, 4.5; N, 12.45. $C_8H_{10}N_2O_4S$ requires C, 41.75; H, 4.35; N, 12.2%); ν_{max} 3460, 3260, 1780, 1660, 1614, 1535, 1300, 1141, 1095, 1030, 938, 922, and 720 cm^{-1}; δ_H (CD_3SOCD_3) 4.95 (2H, s, NH) and 3.6-3.05 (8H, m); m/z 230 (M^+, 50%), 112 (100), 32 (60), and 79 (35).

(ii) Attempted oxidation of 9-Amino-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.$0^{2,6}$]decane 4,4-dioxide

A mixture of 9-amino-8,10-dioxo-3-thia-9-azatricyclo-[5.3.0.$0^{6,10}$]decane 3,3-dioxide (400 mg, 1.73 mmol) and yellow mercuric oxide (750 mg, 3.5 mmol) in dry chloroform (10 ml) was heated under reflux for 16 h. The brown residue was washed with ethylacetate and the organic extracts evaporated to give a white solid which was not identified (111 mg), m.p. 198°C (decomp.).

6. Attempted Oxidation of 6,7-Dihydroxymethyl-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide

Preparation of 3-Oxo-4-oxa-9-thiabicyclo[5.3.0.$0^{2,6}$]decane 9,9-dioxide

To a solution of 6,7-dihydroxymethyl-3-thiabicyclo[3.2.0]-heptane 3,3-dioxide (500 mg, 2.5 mmol) in acetone (10 ml) was added Jones reagent (2 ml of standard solution, 3.34 g, of CrO_3 in 3 ml conc.H_2SO_4 diluted to 12 ml [121]). The organic layer was separated after 10 min and the acetone evaporated to give a colourless oil which on trituration with ether gave <u>3-oxo-4-oxa-9-thiabicyclo[5.3.0.$0^{2,6}$]decane 9,9-dioxide</u> as a colourless crystalline solid, m.p. 156-158°C (lit.,[49] 157-158°C).

Attempts to oxidise the diol using sodium dichromate in dimethyl sulphoxide and concentrated sulphuric acid[122], pyridinium chlorochromate[123], oxalyl chloride and dimethyl sulphoxide[124] and barium manganate[125] were unsuccessful. In the case of the latter oxidising reagent, the lactone was again obtained but in all cases, no trace of the desired dialdehyde was observed.

7. Epimerisation of 3-Thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide and its dimethyl ester

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

This was achieved using the method of Perkin, Jr.[126] A solution of 3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide (1 g, 5.24 mmol) in conc. hydrochloric acid (20 ml) was heated in a sealed tube for 16 h at 190°C. The resulting black liquid was decolourised by heating with charcoal and gave a colourless solid (810 mg, 81%) consisting of 82% *trans*-epimer by ^{13}C n.m.r. Heating the diacid in HCl for 4 h at 190°C afforded 80% *trans*-epimer. δ_C (CD_3SOCD_3) 174.14, 172.69 (C=O, other peaks under solvent) [δ_C (CD_3SOCD_3) *cis*-epimer 173.50 (C=O)].

b. Epimerisation of 6,7-Dimethoxycarbonyl-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide

(i) A solution of 6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]-heptane 3,3-dioxide (750 mg, 2.86 mmol) and 1,8-diazobicyclo-[5.4.0]undec-7-ene (870 mg, 5.73 mmol) in dry methylene chloride (30 ml) was heated under reflux for 5 h. The mixture was washed with dilute hydrochloric acid (0.1N), saturated sodium chloride solution and water. After drying, the solvent was evaporated to give a colourless oil which crystallised. The solid was recrystallised from methanol to give colourless needles (600 mg, 80%). The product was examined by GC (2% carbowax at 195°C) and the ratio of *trans* to *cis*-epimers estimated at 73:27. By ^{13}C n.m.r. the extent of epimerisation was 76%. Extending the reaction time to 84 h, 85% of the *cis*-epimer had been converted into *trans*; δ_C (90MHz) 172.03, 170.47, 53.65, 51.88, 51.84, 49.85, 43.85, 39.59, 33.03, and 32.99. [δ_C (90MHz) of *cis*-epimer 171.56, 53.78, 52.01, 42.80, and 33.35].

(ii) A solution of the *trans* epimer of 3-thiabicyclo[3.2.0]-heptane-6,7-dicarboxylic acid 3,3-dioxide (700 mg, 2.14 mmol, 82% *trans*) in AR methanol (50 ml) containing a few drops of sulphuric acid was heated under reflux for 4 h. On concentration of the solution (to 5 ml), the product crystallised to give a mixture of the dimethyl ester epimers (470 mg, 84%) as colourless needles.

An attempt to separate the dimethyl ester epimers by HPLC (UV 215 nm, silica, 70:30 ether : hexane-50% water saturated) was unsuccessful.

D. Flash Vacuum Pyrolysis of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide and derivatives

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

FVP of the title compound (19.8 g, 630°C, 4×10^{-3}mmHg, inlet 220°C) gave a yellow liquid which was distilled by Kugelrohr (130°C at 0.8 mmHg) to give 2,5-dioxo-*cis*-3,4-divinyltetrahydrofuran (11.24 g, 80%) as a colourless liquid (lit.,[49] b.p.65°C at 10 mmHg).

2. FVP of the Diacid and Diesters of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

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

FVP of the title compound (470 mg, 575°C, 7×10^{-3}mmHg, inlet 190°C, gave *meso*-1,5-hexadiene-3,4-dicarboxylic acid as a pale brown solid, m.p. 179-182°C (lit.,[50] 183-185°C).

b. FVP of 6,7-Dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

FVP of the title compound (3.6 g, 560°C, 4×10^{-3}mmHg, inlet 190°C) gave *cis,trans*-dimethyl octa-2,6-diene-1,8-dioate (2.36 g, 88%) as a colourless liquid; ν_{max} 1780, 1730, 1662, 1438, 1195, 980 and 810 cm^{-1}; δ_H 7.1-6.8 (1H, m), 6.25-6.05 (1H, m), 5.85-5.71 (2H, m), 3.66 (3H, s), 3.67 (3H, s), 2.85-2.65 (2H, m), and 2.45-2.2 (2H, m). (lit.,[127,128] δ_H (CCl_4)

6.90 (1H, d of t, J15.5Hz, 7Hz *trans* *CH*=$CHCO_2Me$), 6.19 (1H, d of t, J11.2Hz, 7Hz, *cis* *CH*=$CHCO_2Me$), 5.81 (1H, d, J15.5Hz, *trans* CH=*CH*CO_2Me), 5.77 (1H, d, J11.2Hz, *cis* CH=*CH*CO_2Me), 3.68 (6H, s, CO_2Me), 2.80 (2H, m, *cis* allylic CH_2), and 2.40 (2H, m, *trans* allylic CH_2)). GC analysis of the pyrolysate (10% PEGA, 180°C) showed that 25% of the *trans,trans*-isomer was present.

FVP of the title compound at slightly higher temperature (600°C) gave aldehydic impurities and distillation also resulted in decomposition of the diester. Using the same reaction conditions as stated by Williams and Lin[129] (500°C at 0.5 mmHg), pyrolysis of the sulphone gave *cis,trans*-dimethyl octa-2,6-diene-1,8-dioate with no trace of the *trans,trans*-isomer by ^1H n.m.r.[130]

c. FVP of Epimer of 6,7-Dimethoxycarbonyl-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide

FVP of the titled compound (82% *trans*-epimer, 97 mg, 560°C + silica rods, $4x10^{-3}$mmHg, inlet 180°C) gave a colourless liquid (46.4 mg, 63%, by calibration of ^1H n.m.r. with cyclohexane). ^1H n.m.r. showed the presence of *trans,trans*-dimethyl octa-2,6-diene-1,8-dioate and GC (10% PEGA, 180°C) showed the presence of the *trans,trans*-isomer (73%), the *cis,trans*-isomer (15%) and the *cis,cis*-isomer (12%). 18% of the *cis*-epimer present in the sulphone mixture before pyrolysis should give 13.5% of the *cis,trans*-isomer (assuming 75% stereospecificity). GC-MS confirmed the presence of these 3 isomers and identified the other minor components in the pyrolysate as breakdown products from the diesters.

3. Flash Vacuum Pyrolysis of 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide and derivatives

a. FVP of 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

FVP of the title compound (1.3 g, 530°C, 1×10^{-3}mmHg, inlet 180°C) gave a pale yellow liquid which was distilled by Kugelrohr (210°C at 0.9 mmHg) to give a colourless, viscous liquid. By comparison of ^{1}H n.m.r. with an authentic sample, the product was identified as *meso*-3,4-dihydroxymethyl-1,5-hexadiene (190 mg, 21%).

Pyrolysis of the title compound at a higher furnace temperature (136 mg, 600°C + silica rods, 6×10^{-3}mmHg, inlet 180°C) gave a clear liquid and much polymer. ^{1}H n.m.r. which was calibrated with benzene, showed the product to be *cis,trans*-octa-2,6-diene-1,8-diol (22 mg, 24%) (comparison of ^{1}H n.m.r. with authentic sample, see p.94).

b. FVP of 6,7-Dimethoxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

FVP of the title compound (665 mg, 530°C, 1×10^{-3}mmHg, inlet 140°C) gave *meso*-3,4-dimethoxymethyl-1,5-hexadiene (0.290 mg, 60%) as a colourless liquid (^{1}H n.m.r. identical with authentic sample, see p.82).

c. FVP of 6,7-Diacetoxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

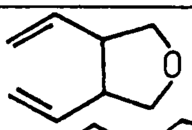
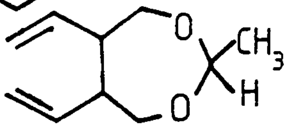
FVP of the title compound (111 mg, 530°C, 1×10^{-3}mmHg, inlet 150°C) gave *meso*-3,4-diacetoxymethyl-1,5-hexadiene as a colourless liquid. Traces of impurity in the ^{1}H n.m.r. were identified as being the Cope rearranged product.

Pyrolysis at a higher furnace temperature (41 mg, 650^{o}C, 5x10^{-3}mmHg, inlet 140^{o}C) gave *cis,trans*-1,8-diacetoxyocta-2,6-diene (8.7 mg, 27%) as a colourless liquid. Polymer was also formed in the pyrolysis (calibration of ^{1}H n.m.r. with benzene).

4. FVP of 5-Methyl-4,6-dioxa-11-thiatricyclo[7.3.0.0^{2,8}] dodecane 11,11-dioxide

FVP of the title compound (137.5 mg, 550^{o}C, 5x10^{-3}mmHg, inlet 160^{o}C) gave unreacted starting material and a colourless liquid. GC (10% PEGA, 150^{o}C) showed the presence of four components, the major (74%) thought to be *cis*-1,7-divinyl-4-methyl-3,5-dioxaheptane, δ_H 6.2-4.75 (7H, m), 3.9-3.6 (4H, m), 2.74-2.35 (2H, m), and 1.3 (3H, d, J6Hz).

The pyrolysis was repeated at a higher furnace temperature (314 mg, 650^{o}C, 3x10^{-3}mmHg, inlet 125^{o}C) to give a pale yellow liquid and dark brown polymer. ^{1}H n.m.r. was complex but showed the presence of *cis*-3,4-divinyltetrahydrofuran which was confirmed by GC on comparison with an authentic sample. The pyrolysate was also examined by GC-MS. The major peaks common to both pyrolysates in GC (10% PEGA, 150^{o}C) were:

	Furnace Temperature		
	500^{o}C	650^{o}C	
Retention time ↓	2%	58%	
	4%	21%	
	74%	21%	
	20%	-	

5. FVP of 6,7-Dibromomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

FVP of the title compound (50 mg, 550°C, 8×10^{-3}mmHg, inlet 140°C) gave unreacted starting material and a *ca.* 1:1 mixture of *meso*-3,4-dibromomethyl-1,5-hexadiene and *cis,trans*-1,8-dibromomethyl-1,5-hexadiene by ^{1}H n.m.r. On repeating the pyrolysis at 620°C, only polymeric material was recovered.

6. FVP of the Cyclic Hydrazide, Mono- and Di-amide Imide and N-aminoimide of 3-Thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide

a. FVP of 3,6-Dioxo-4,5-perhydrodiazine-10-thiatricyclo-$[6.3.0.0^{2,7}]$undecane 10,10-dioxide

FVP of the title compound (476 mg, 600°C, 5×10^{-3}mmHg, inlet 250°C) gave a yellow solid at the entrance to the trap (280 mg, 68%). The solid was sublimed under vacuum to give 4,5-divinyl-3,6-dioxoperhydrodiazine as colourless plates, m.p. 65-67°C. (Found: C, 57.6; H, 6.0; N, 16.7. $C_8H_{10}N_2O_2$ requires C, 57.8; H, 6.0; N, 16.9%); ν_{max} 3350-3180, 3090, 1790, 1710, 1640, 1205, 992, 925, 879, and 802 cm^{-1}; δ_H (CD_3SOCD_3) 5.85-5.5 (2H, m), 5.34-5.15 (4H, m), 4.8-4.6 (1H, br s, NH), and 3.74-3.68 (2H, dd, J5Hz and 2Hz); δ_C (CD_3SOCD_3) 174.76, 174.31, 132.89, 131.57, 120.84, 119.55, 48.19, and 47.13; m/z 166 (M$^+$, 96%), 150 (10), 137 (10), 107 (22), 80 (77), 79 (100), and 70 (53).

b. FVP of the mono- and diamide of 3-Thiabicyclo[3.2.0]-heptane-6,7-dicarboxylic acid

FVP of a mixture of the title compounds (1.44 g, 650°C,

5×10^{-3}mmHg, inlet 230°C) gave polymer and white solid. The solid was purified by column chromatography (alumina, ether) to give 3,4-diethylidenesuccinimide (67 mg, 7%) as a colourless crystalline solid, m.p. 160-162°C. (Found: C, 63.5; H, 6.0; N, 9.0. $C_8H_9NO_2$ requires C, 63.55; H, 6.0; N, 9.25%), ν_{max} 3033, 3193, 1763, 1728, 1651, 1191, 1161, 1130, 1034, 920, and 853 cm^{-1}; δ_H (CD_3SOCD_3) 7.05-6.65 (2H, overlapping quartets), 2.30 (2H, d), and 2.03 (2H, d); m/z 151 (M^+, 100%) and 79 (59).

c. FVP of 8,10-Dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide

FVP of the title compound (353 mg, 650°C, 8×10^{-3}mmHg, inlet 230°C) gave a colourless solid (237 mg, 95%). The solid was recrystallised from chloroform and petroleum ether to give *cis*-3,4-divinylsuccinimide (157 mg, 63%) as colourless crystals, m.p. 108-110°C. (Found: C, 63.6; H, 5.9; N, 9.0. $C_8H_9NO_2$ requires C, 63.55; H, 6.0; N, 9.25%); ν_{max} 3195, 1781, 1700, 1640, 1275, 1192, 1151, 990 and 944 cm^{-1}; δ_H 8.65-8.35 (1H, br s, NH), 5.92-5.26 (6H, divinyl) and 3.74-3.65 (2H, dd, J5 and 2Hz); m/z 151 (M^+, 4%), 123 (1.4), 108 (8), 80 (100), 79 (91), and 27 (18).

d. FVP of 9-Amino-8,10-dioxo-4-thia-9-azatricyclo[5.3.0.0^{2,6}] decane 4,4-dioxide

FVP of the title compound (112 mg, 575°C, 9×10^{-3}mmHg, inlet 240°C) gave a colourless gum (576 mg, 72%). δ_H 5.85-5.2 (6H, m), 4.65-4.45 (2H, br s) and 3.7-3.65 (2H, dd, J5 and 2Hz).

On evaporation of the $CDCl_3$ solution, an orange gum was obtained, t.l.c. of which showed the presence of several compounds.

On repeating the pyrolysis at various temperatures (500°C-625°C), various mixtures of products were obtained. At 500°C + silica rods, loss of sulphur dioxide did not occur to a large extent and a colourless crystalline solid, m.p. 222°C was obtained. I.r. of this solid was similar to that of 3,6-dioxo-4,5-perhydrodiazine-10-thiatricyclo[6.3.0.0^{2,7}]undecane 10,10-dioxide indicating that rearrangement to the 6-membered ring isomer may have occurred.

E. Preparation of *cis*-1,2-Divinyl Compounds

1. Preparation of the Diacid and Dimethyl ester of 2,5-Dioxo-*cis*-3,4-divinyltetrahydrofuran

a. Preparation of *meso*-1,5-Hexadiene-3,4-dicarboxylic acid

2,5-Dioxo-*cis*-3,4-divinyltetrahydrofuran (11 g, 72 mmol) was suspended in water (50 ml). The mixture was heated under reflux until a clear solution was obtained. On cooling, the resulting precipitate was filtered off to give meso-1,5-hexadiene-3,4-dicarboxylic acid (9 g, 74%) as colourless crystals, m.p. 182-185°C (lit.,[50] 183-185°C).

b. Preparation of *meso*-3,4-Dimethoxycarbonyl-1,5-hexadiene

A solution of 2,5-dioxo-*cis*-3,4-divinyltetrahydrofuran (14.3 g, 93 mmol) in methanol (130 ml) containing a few drops of sulphuric acid was heated under reflux for 24 h. The solvent was removed *in vacuo* to leave an orange oil which crystallised to give a colourless solid. Recrystallisation of the solid from petroleum ether (40-60) gave meso-3,4-dimethoxycarbonyl-1,5-hexadiene (13.78 g, 75%) as colourless crystals, m.p. 35-36°C (lit.,[50] 36-37°C).

2. Preparation of *meso*-3,4-Dihydroxymethyl-1,5-hexadiene and derivatives

a. Preparation of *meso*-3,4-Dihydroxymethyl-1,5-hexadiene

A solution of 2,5-dioxo-*cis*-3,4-divinyltetrahydrofuran (11 g, 73 mmol) in dry tetrahydrofuran (50 ml) was added dropwise to a suspension of lithium aluminium hydride (5.5 g, 145 mmol) in dry THF (200 ml) with stirring under nitrogen. The mixture was heated under reflux for 1 h, allowed to cool and the lithium aluminium hydride destroyed by addition of wet THF (10 ml water in 100 ml THF), 15% sodium hydroxide solution (10 ml) and finally water (10 ml). The inorganic salts were filtered off and the solvent evaporated from the filtrate to leave a colourless oil which was distilled by Kugelrohr (110°C at 0.6 mmHg) to give *meso*-3,4-dihydroxymethyl-1,5-hexadiene (8.47 g, 82%) as a colourless viscous liquid, (lit.,[50] b.p. 100°C at 0.8 mmHg).

b. Preparation of *meso*-3,4-Dimethoxymethyl-1,5-hexadiene

This was prepared by the method of Johnstone and Rose[112]. Powdered potassium hydroxide (4.42 g, 87 mmol) was added to dry dimethyl sulphoxide (10 ml). After stirring for 5 min, *meso*-3,4-dihydroxymethyl-1,5-hexadiene (1.54 g, 11 mmol) was added, followed by methyliodide (6.25 g, 44 mmol). Stirring was continued for 30 min, after which time the mixture was poured into water and extracted with methylene chloride. After thorough washing with water, the organic extract was dried and the solvent evaporated to give a pale yellow liquid. Kugelrohr distillation (70°C at 0.5 mmHg) gave *meso*-3,4-dimethoxymethyl-1,5-hexadiene (95 mg, 51%) as a colourless liquid. (Found: M^+ 170.130290. $C_{10}H_{18}O_2$ requires 170.130672); ν_{max} 1643, 1462, 1115, 915, and 695 cm^{-1}; δ_H 5.85-5.55 (2H, m), 5.13-5.0 (4H, m), 3.5-3.2 (10H, m), and 2.45-2.25 (2H, m); δ_C 138.20, 116.29, 74.04, 58.45, and 45.04; m/z 170 (M^+, <1%), 138 (5), 125 (7), 106 (16), 93 (38), and 45 (100).

c. Preparation of Diesters

(i) *meso*-3,4-Diacetoxymethyl-1,5-hexadiene

A solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (910 mg, 6.4 mmol) in glacial acetic acid (20 ml) containing a few drops of sulphuric acid was heated under reflux for 10 min. After cooling, the mixture was poured into water, extracted with methylene chloride and the organic extract washed with water and dried. The solvent was removed *in vacuo* to leave a brown oil which was distilled by Kugelrohr (160°C at 1.3 mmHg) to give meso-3,4-diacetoxymethyl-1,5-hexadiene (1.21 g, 83%) as colourless liquid; (Found: C, 63.45, H, 7.7; $C_{12}H_{18}O_4$ requires C, 63.7; H, 7.95%); ν_{max} 1737, 1645, 1220, 1045, and 920 cm^{-1}; δ_H 5.88-5.45 (2H, m), 5.2-4.95 (4H, m), 4.15-4.0 (4H, m), 2.55-2.4 (2H, m), and 2.01 (6H, s); δ_C 170.45, 136.30, 117.75, 65.09, 43.99, and 20.51; m/z 226 (M^+, <1%), 167 (3), 153 (1), 124 (5), 113 (22), 106 (16), 79 (31), 54 (34), and 43 (100).

(ii) *meso*-3,4-Bis(*p*-toluene sulphonyloxymethyl)-1,5-hexadiene

A solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (1.52 g, 11 mmol) in pyridine (10 ml) was added dropwise to a solution of *p*-toluenesulphonyl chloride (6.3 g, 33 mmol) in pyridine (20 ml) at 0°C. After stirring for a further 3 h the mixture was poured into water and the solid precipitated, filtered off, washed with water and dried to give meso-3,4-bis(p-toluenesulphonyloxymethyl)-1,5-hexadiene (4.39 g, 59%) as a colourless crystalline solid, m.p. 151-152°C; ν_{max} 1642, 1600, 1352, 1177, 948, 842, and 668 cm^{-1}; δ_H 7.78-7.25 (8H, AB J8Hz), 5.7-4.85 (6H, m), 4.06-3.85 (4H, m), and 2.44-2.3

(8H, m); m/z 450 (M^+, <1%), 225 (16), 224 (16), 172 (7), 155 (100), 106 (98), and 91 (100).

3.a Attempted preparation of *cis*-1,7-Divinyl-4-methyl-3,5-dioxaheptane

The method used was based on that of Adelman[113]. A solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (400 mg, 2.82 mmol) in vinylacetate (40 ml) containing a few crystals of mercuric acetate was heated under reflux for 18 h under nitrogen. The vinyl acetate was removed *in vacuo* and the residue dissolved in methylene chloride, washed with water and dried. Evaporation of solvent gave a brown oil which was distilled by Kugelrohr (100°C at 0.5 mmHg) to give a colourless liquid (124.4 mg, 70%). ^{1}H n.m.r. showed the presence of the desired product and GC trace was identical to that obtained on pyrolysis of the corresponding sulphone(p.77). The product decomposed to a black oil before further characterisation.

b. Preparation of *cis*-3,4-Divinyltetrahydrofuran

This was prepared by a modification of the method of Corfield *et al.*[131] A solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (500 mg, 3.52 mmol) and *p*-toluenesulphonic acid monohydrate (50 mg) in dry benzene (25 ml) was heated under reflux for 84 h in a flask containing some molecular sieves. (On a larger scale, the flask should be equipped with a Dean and Stark apparatus). The benzene was removed *in vacuo* at room temperature and the residue distilled by Kugelrohr (85-90°C at 760 mmHg) to give <u>*meso*-3,4-divinyltetrahydrofuran</u> as a volatile colourless liquid (50 mg, 12%), (lit.,[50] b.p. 41°C at 41 mmHg); δ_H 5.96-4.97 (6H, m), 4.56-4.02 (4H, m), and 3.11-2.76 (2H, m).

4. Preparation of the Dihalides and Dinitrile of *meso*-3,4-Dihydroxymethyl-1,5-hexadiene

a. Preparation of Dihalides

(i) *meso*-3,4-Dichloromethyl-1,5-hexadiene

A solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (920 mg, 6.48 mmol) in dry benzene (10 ml) was added dropwise to a solution of thionyl chloride (1.4 ml, 19.4 mmol) in dry benzene (15 ml) containing a few drops of pyridine. The solution was heated under reflux for 1 h. The mixture was poured onto iced water and the benzene layer separated, washed with water and dried. The benzene was removed *in vacuo* to give a black liquid. Distillation by Kugelrohr (63°C at 1.4 mmHg) gave meso-3,4-dichloromethyl-1,5-hexadiene (817.5 mg, 71%) as a colourless liquid or low melting solid, m.p. 20-23°C (Found: M^+ 129.047192. $C_7H_{10}{}^{35}Cl$ requires 129.047100); ν_{max} 1647, 1439, 1425, 1305, 1216, 1000, 931, 742 and 695 cm^{-1}; δ_H 5.9-5.13 (6H, m), 3.65-3.52 (4H, m) and 2.65-2.48 (2H, m); m/z 131 (8%), 129 (21), 79 (52), and 54 (100).

(ii) *meso*-3,4-Dibromomethyl-1,5-hexadiene

A solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (640 mg, 4.5 mmol) and phosphorus tribromide (1.83 g, 6.76 mmol) was heated under reflux for 30 min. The mixture was poured into water, extracted with methylene chloride and the organic extract washed with water and dried. Evaporation of solvent gave an orange oil which crystallised to give meso-

3,4-dibromomethyl-1,5-hexadiene (20 mg, 17%) as colourless needles, m.p. 54.5-55°C (Found: C, 35.75; H, 4.55. $C_8H_{12}Br_2$ requires C, 35.8; H, 4.5%); ν_{max} 1637, 983, 914, and 622 cm^{-1}; δ_H 5.90-5.55 (2H, m), 5.37-5.17 (4H, m), 3.60-3.35 (4H, m), and 2.58-2.44 (2H, m); m/z 189 (41%), 187 (41), 135 (57), 133 (57), 107 (61), 54 (100), and 53 (100).

(iii) *meso*-3,4-Di-iodomethyl-1,5-hexadiene

This was prepared by the method of Baer.[116] A mixture of *meso*-3,4-bis(*p*-toluene sulphonyloxymethyl)-1,5-hexadiene (6.87 g, 15.3 mmol) and sodium iodide (6.86 g, 45.8 mmol) in acetone (60 ml) was heated under reflux for 18 h with stirring. After removal of sodium *p*-toluenesulphonate by filtration, the acetone was evaporated and the residue dissolved in methylene chloride, washed with sodium thiosulphate solution, water and dried. The solvent was removed *in vacuo* to leave a pale yellow solid (5.1 g, 92%) which was recrystallised from petroleum ether to give *meso*-3,4-di-iodomethyl-1,5-hexodiene (3.86 g, 70%) as colourless needles, m.p. 72.5-73.5°C. (Found: C, 26.35; H, 3.2. $C_8H_{12}I_2$ requires C, 26.55; H, 3.35%; ν_{max} 1644, 1301, 1200, 1129, 994, 925, 793, and 704 cm^{-1}; δ_H 5.85-5.15 (6H, m), 3.45-3.05 (4H, m), and 2.2-2.0 (2H, m); m/z 362 (M^+, 3%), 308 (4), 254 (1), 235 (16), 181 (100), 128 (11), 127 (8), 108 (29), 107 (44), and 54 (96).

b. Preparation of *meso*-3,4-Dicyanomethyl-1,5-hexadiene

A mixture of *meso*-3,4-bis(*p*-toluenesulphonyloxymethyl)-1,5-hexadiene (3.1 g, 6.9 mmol) and potassium cyanide (1.54 g, 24 mmol) in ethanol (40 ml) was heated under reflux for 60 h. After removal of ethanol *in vacuo*, the residue was dissolved in water and methylene chloride. The organic phase was separated, washed with water and dried. Evaporation of solvent gave a pale brown solid which was recrystallised from chloroform to give *meso*-3,4-dicyanomethyl-1,5-hexadiene (840 g, 76%) as colourless crystals, m.p. 92-93°C (Found: C, 74.85; H, 7.55; N, 17.6. $C_{10}H_{12}N_2$ requires C, 74.95; H, 7.55; N, 17.5%); ν_{max} 2250, 1641, 1418, 1000, 931, and 720 cm^{-1}; δ_H 5.9-5.26 (6H, m) and 2.55-2.36 (6H, m); m/z 159 ($M-1^+$, 4%), 120 (14), 80 (100), 54 (41), and 53 (42).

5. Rearrangement of *cis*-1,2-Divinyl compounds to 3,4-Disubstituted-2,4-hexadienes

a. Preparation of 3,4-Dimethoxycarbonyl-2,4-hexadiene and the corresponding Diacid

(i) 3,4-Dimethoxycarbonyl-2,4-hexadiene

A mixture of *meso*-3,4-dimethoxycarbonyl-1,5-hexadiene (380 mg, 1.9 mmol) and sodium methoxide (43.7 mg, 1.9 mmol Na in 10 ml AR methanol) was stirred at room temperature for 48 h. The solution was acidified with 0.1 N HCl and extracted with methylene chloride. After washing with saturated sodium chloride solution and water, the organic extract was dried and the solvent evaporated to give a yellow liquid (370 mg, 97%). Distillation by Kugelrohr (150°C at 0.3 mmHg) gave 3,4-dimethoxycarbonyl-2,4-hexadiene (330 mg, 86%) as a colourless liquid (Found: C, 60.4; H, 7.35. $C_{10}H_{14}O_4$ requires C, 60.6; H, 7.1%); ν_{max} 1715, 1635, 1435, 1250, 1062, 1045, 800, 775, and 738 cm^{-1}; δ_H 7.15-6.95 (2H, q, J7Hz), 3.65 (6H, s), and 1.7-1.62 (6H, d, J7Hz); δ_C 165.89, 140.74, 127.76, 51.07 and

14.58; m/z 198 (M^+, 15%), 166 (100), 79 (54), and 59 (54).

Alternative Synthesis

meso-3,4-Dimethoxycarbonyl-1,5-hexadiene (400 mg, 2 mmol) was added to a solution of 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU, 615 mg, 4 mmol) in dry methylene chloride (10 ml). After stirring at room temperature for 60 h, the solution was acidified (0.1N HCl) and washed with saturated sodium chloride solution, water and dried. Removal of solvent *in vacuo* gave a yellow liquid which was distilled by Kugelrohr (145°C at 0.2 mmHg) to give 3,4-dimethoxycarbonyl-2,4-hexadiene (343 mg, 85%) as a colourless liquid.

(ii) 2,4-Hexadiene-3,4-dicarboxylic acid

Treatment of *meso*-1,5-hexadiene-3,4-dicarboxylic acid with sodium methoxide resulted in recovery of starting diacid.

A solution of *meso*-1,5-hexadiene-3,4-dicarboxylic acid (1 g, 5.88 mmol) and DBU (1.79 g, 12 mmol) in dry benzene (30 ml) was heated under reflux for 16 h. After removal of the benzene *in vacuo*, the residue was dissolved in water, acidified (0.1N HCl) and extracted with ethyl acetate (3X). The organic extract was washed with saturated sodium chloride solution, water and dried. Evaporation of solvent gave a colourless solid (790 mg, 79%) which was recrystallised from acetone, with addition of ether to precipitate the product, to give 2,4-hexadiene-3,4-dicarboxylic acid (510 mg, 51%) as a colourless crystalline solid, m.p. 248-252°C (subl.) (Found: C, 56.55; H, 5.85. $C_8H_{10}O_4$ requires C, 56.5; H, 5.9%); ν_{max} 1670, 1650, 1620, 1300, 945, 770 and 725 cm^{-1}; δ_H (CF_3COOH) 7.7-7.48 (2H, q, J7Hz) and 1.9-1.84 (6H, d, J7Hz); δ_C (CD_3COCD_3), 167.33, 139.96, 129.665, and 15.27; m/z 170 (M^+, <1%), 162 (81), 137 (19), 96 (24), 79 (100), and 43 (100).

b. Preparation of 2,4-Hexadiene-3,4-dicarbaldehyde

(i) The method used was that of Swern *et al.*[132] Dry methylene chloride (10 ml) and dry dimethylsulphoxide (1.69 g, 21.1 mmol) were placed in a 100 ml 3-necked flask equipped with magnetic stirrer. The flask was cooled to -50°C and a solution of trifluoroacetic anhydride (3.55 g, 16.9 mmol) in methylene chloride (10 ml) added dropwise to the solution over a period of 10 min under nitrogen. During the addition a white precipitate of trifluoroacetoxydimethylsulphonium trifluoroacetate formed. After 10 min at -50°C, a solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (600 mg, 4.22 mmol) in methylene chloride (10 ml) was added dropwise over 10 min. The mixture was stirred at -50°C for 2 h, followed by the dropwise addition of triethylamine (6 ml).

On warming to room temperature, water was added and the organic layer separated. After washing with dilute hydrochloric acid, sodium carbonate solution and water, the organic extract was dried and the solvent evaporated to leave a dark brown liquid.

The product was purified by prep.t.l.c. (silica, 25% ether/petroleum ether) to give 2,4-hexadiene-3,4-dicarbaldehyde as a pale yellow liquid (111.7 mg, 19%). (Found: M^+ 138.068198. $C_8H_{10}O_2$ requires 138.068075); ν_{max} 1695, 1683, 1639, 1420, 1378, 1225, 1185, 967, 920, and 845 cm^{-1}; δ_H 9.46 (2H, s), 7.05 (2H, q, J7Hz), and 1.85 (6H, d, J7Hz);

δ_c 191.396, 153.389, 137.443, and 15.658; m/z 138 (M^+, 100%), 136 (25), 123 (57), 95 (54), 79 (77), and 67 (75).

Previous attempts to distil the dialdehyde resulted in decomposition of the sample.

(ii) Attempted oxidation using oxalyl chloride and dimethyl sulphoxide

The method used was that of Swern *et al.*[124] A solution of oxalyl chloride (1.4 g, 11 mmol) in dry methylene chloride (25 ml) was placed in a 3-necked flask equipped with magnetic stirrer, nitrogen bubbler and 2 pressure equalising addition funnels. After cooling to -60°C, a solution of dry dimethyl sulphoxide (1.9 g, 24 mmol) in methylene chloride (5 ml) was added dropwise over 5 min. Stirring was continued for 10 min, followed by the addition of a solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (730 mg, 5.14 mmol) in methylene chloride (10 ml). The mixture was stirred for 40 min and then triethylamine (5.1 g, 50 mmol) added over 5 min.

The cooling bath was removed and water (30 ml) added at room temperature. After a further 10 min, the organic layer was separated and washed with water (5x). The solution was then dried and the solvent removed *in vacuo* to give a brown oil (400 mg, 66%). ^1H n.m.r. showed the presence of aldehydes and t.l.c. confirmed the presence of a mixture of products.

(iii) Attempted oxidation using $BaMnO_4$

The method used was that of Firouzabadi and Ghaderi[125]. A mixture of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (200 mg, 1.4 mmol) and barium manganate (2 g) in dry methylene chloride were stirred at room temperature for 2 weeks. After filtration, the solvent was evaporated to give a clear oil which was identified as starting material.

(iv) Attempted oxidation using $[Ag(C_5H_5N)_2]MnO_4$

Using the method of Firouzabadi *et al.*[133] bispyridine silver manganate was added to a solution of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (300 mg, 2.1 mmol) in dry benzene (25 ml). After refluxing for 3 h, the mixture was filtered and the organic phase washed with dilute hydrochloric acid (0.1N), water and dried. Evaporation of solvent gave a yellow oil. ^1H n.m.r. and t.l.c. showed the presence of a mixture of compounds, including unreacted starting material.

c. Attempted Diels-Alder reaction of 3,4-Dimethoxycarbonyl-2,4-hexadiene

A solution of 3,4-dimethoxycarbonyl-2,4-hexadiene (157 mg, 0.793 mmol) and dimethyl acetylenedicarboxylate (113 mg, 0.793 mmol) in mesitylene was heated under reflux for 12 days, during which time the red solution was monitored by t.l.c. and then GC (2% carbowax, 190°C). After removal of solvent *in vacuo* the remaining oil was found (n.m.r., t.l.c.) to contain a mixture of many products.

Previous attempts using benzene and toluene as solvents, resulted in no reaction and recovery of starting materials.

6. Attempted preparation of *meso*-3,4-divinylhexa-1,6-dial

a. Attempted preparation of *meso*-1,5-Hexadiene-3,4-bis-(methylmagnesium chloride) and reaction with Dimethylformamide

A solution of *meso*-3,4-dichloromethyl-1,5-hexadiene

(800 mg, 4.47 mmol) in dry tetrahydrofuran (10 ml) was added dropwise to a stirred suspension of magnesium (240 mg, 10 mmol) in dry THF (10 ml) under nitrogen, dibromoethane (0.05 ml) being added to initiate the reaction.

After the addition of the dichloride (1.5 h), the mixture was heated under reflux for 23 h but little magnesium had reacted. On cooling, dimethylformamide (700 mg, 9.8 mmol) was added at 0^{o}C. The mixture was heated under reflux for 3 h, cooled and water added. After extraction with ether, the organic phase was dried and the solvent evaporated to give a colourless liquid (800 mg). ^{1}H n.m.r., t.l.c. confirmed the product to be recovered starting material.

b. Attempted Lithiation of *meso*-3,4-Di-iodo-1,5-hexadiene and reaction with Dimethylformamide

n-Butyl-lithium (0.79 ml, 1.1 mmol) was added to a solution of *meso*-3,4-di-iodo-1,5-hexadiene (200 mg, 0.65 mmol) in dry tetrahydrofuran (20 ml) under nitrogen at -78^{o}C. After stirring for 30 min, an excess of dimethylformamide was added (201 mg, 2.75 mmol) and the solution stirred for 3 h. There was no colour change indicating the presence of the dianion. The solution was hydrolysed and after extraction with ether, washing with water and drying, evaporation of solvent gave an oil (^{1}H n.m.r. of butyl residues).

Similarly with 6,7-di-iodomethyl-3-thiabicyclo[3.2.0] heptane 3,3-dioxide, no reaction occurred and in this case, starting material was recovered.

c. Attempted Reduction of *meso*-3,4-Dicyanomethyl-1,5-hexadiene to the Dialdehyde

The method used was that of Trofimenko[134]. Di-isobutylaluminium hydride (1.04 ml, 1.56 mmol, 25% solution in toluene) was added to a solution of *meso*-3,4-dicyanomethyl-1,5-hexadiene (100 mg, 0.625 mmol) in dry benzene (15 ml) with stirring under nitrogen. The mixture was then stirred at 50°C for 9 h and heated under reflux for 4 h. The reaction complex was decomposed by addition of methanol at room temperature followed by water. The solid aluminium salts were filtered off, washed with ether and the filtrate evaporated. The residue was dissolved in ether and washed with water. Evaporation of solvent from the organic extract gave a brown oil. On further extraction after acidification more product was obtained but ^{1}H n.m.r. indicated the absence of aldehyde groups in the product.

Similarly, on treatment of 6,7-dicyanomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide with DIBAl.H, only starting material was recovered.

F. Cope Rearrangement of *cis*-1,2-Divinyl Compounds

1. Preparation of *cis,trans*-Octa-2,6-diene-1,8-dioic acid and its Dimethyl ester

a. Preparation of *cis,trans*-Octa-2,6-diene-1,8-dioic acid

FVP of *meso*-3,4-dicarboxylic acid-1,5-hexadiene (678 mg, 625°C + silica rods, 7×10^{-3}mmHg, inlet 150°C) gave cis,trans-octa-2,6-diene-1,8-dioic acid (230 mg, 34%) as a colourless solid, m.p.111-113°C (lit.,[135] 113-114°C); ν_{max} 1695, 1639, 986, 921, 827, 719, 705, and 680 cm^{-1}; δ_H (CF_3COOH) 7.50-7.23 (1H, m), 6.69-6.43 (1H, m), 6.11-5.90 (2H, m), 3.10-2.88 (2H, m), and 2.64-2.45 (2H, m); δ_C (CD_3SOCD_3) 167.09, 147.94, 147.75, 122.51, 121.34, 30.67, and 26.84.

b. Preparation of *cis,trans*-Dimethyl octa-2,6-diene-1,8-dioate

FVP of *meso*-3,4-dimethoxycarbonyl-1,5-hexadiene (56.5 mg, 580°C + silica rods, 1×10^{-2}mmHg, inlet 90°C) gave cis,trans-dimethyl octa-2,6-diene-1,8-dioate as a colourless liquid. Calibration of ^1H n.m.r. with cyclohexane gave the yield as 28.6 mg, 51% (n.m.r. identical to that obtained on pyrolysis of 6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide).

2. Preparation of *cis,trans*-Octa-2,6-diene-1,8-diol and Derivatives

a. Preparation of *cis,trans*-Octa-2,6-diene-1,8-diol

FVP of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (400 mg, 550°C + silica rods, 9×10^{-3} mmHg, inlet 110°C) gave *cis,trans*-octa-2,6-diene-1,8-diol as a pale yellow liquid. After filtration to remove some polymer, calibration of the ^{1}H n.m.r. with benzene gave the yield as 156 mg, 39%. Kugelrohr distillation gave the diol as a colourless viscous liquid (195°C at 0.9 mmHg); ν_{max} 3700-3100, 1675, 1435, 1087, 969, and 917 cm^{-1}; δ_H 5.76-5.58 (4H, m), 4.25-4.11 (4H, m), 2.90 (2H, br s), and 2.18 (4H, m). δ_C 131.18, 130.69, 129.57, 128.95, 62.63, 57.64, 31.38, and 26.61; m/z (M^+ not apparent), 106 (15%), 93 (13), 80 (24), 70 (63), and 54 (100).

Stereospecifity by ^{13}C n.m.r. was 94% - only 6% of the *trans,trans* isomer was present in the sample.

b. Preparation of *cis,trans*-1,8-Dimethoxyocta-2,6-diene

(i) By rearrangement in solution

By heating *meso*-3,4-dimethoxymethyl-1,5-hexadiene in a n.m.r. tube in a bath of refluxing benzyl alcohol (b.p.205°C) for 65 h, rearrangement occurred to give *cis,trans*-1,8-dimethoxyocta-2,6-diene; ν_{max} 1670, 1450, 1193, 1113, 970, and 910 cm^{-1}; δ_H 5.75-5.54 (4H, m), 4.0-3.83 (4H, m), 3.30 (6H, s), and 2.19-2.17 (4H, m); δ_C 133.04, 132.08, 126.54, 126.21, 79.69, 67.68, 57.43, 57.26, 31.75, and 26.75; m/z (M^+ not apparent), 138 (17%), 106 (46), 84 (100), 71 (69), 55 (72), and 45 (97).

(ii) By O-Methylation of *cis,trans*-Octa-2,6-diene-1,8-diol

cis,trans-Octa-2,6-diene-1,8-diol (530 mg, 3.73 mmol) was added to a mixture of powdered potassium hydroxide (1.52 g, 29.8 mmol) in dry dimethyl sulphoxide (10 ml). After addition of methyl iodide (2.12 g, 14.9 mmol) the mixture was stirred for 30 min before pouring into water and extracted with methylene chloride. The organic extract was washed several times with water, dried and the solvent evaporated to give a yellow oil. Kugelrohr distillation (130°C at 0.4 mmHg) gave *cis,trans*-1,8-dimethoxyocta-2,6-diene (410 mg, 65%) as a colourless liquid.

(iii) By rearrangement under FVP conditions

FVP of *meso*-3,4-dimethoxymethyl-1,5-hexadiene (32 mg, 580°C + silica rods, 7×10^{-3}mmHg, no inlet heating) gave *cis, trans*-1,8-dimethoxyocta-2,6-diene (15 mg, 47%) as a colourless liquid. (Yield by calibration of ^{1}H n.m.r. with benzene).

c. Preparation of *cis,trans*-1,8-Diacetoxy-2,6-octadiene

(i) By rearrangement in solution

A sample of *meso*-3,4-diacetoxymethyl-1,5-hexadiene was placed in a n.m.r. tube and heated in a bath of refluxing benzyl alcohol (b.p. 205°C) for 45 h. The resulting black liquid was distilled by Kugelrohr (175°C at 0.7 mmHg) to give *cis,trans*-1,8-diacetoxy-2,6-octadiene as a colourless liquid; ν_{max} 1730, 1650, 1220, 1018, and 600 cm^{-1}; δ_H 5.74-5.57 (4H, m), 4.64-4.49 (4H, m), 2.19-2.12 (4H, m), and 2.06 (6H, s); δ_C 170.63, 170.54, 134.68, 133.68, 123.89, 124.54, 64.77, 60.01, 31.65, 26.63, and 20.73; m/z 226 (M^+, <1%), 167 (11), 112 (31), 106 (36), 91 (10), 70 (44), 54 (33), and 43 (100).

(ii) By rearrangement under FVP conditions

FVP of *meso*-3,4-diacetoxymethyl-1,5-hexadiene (580°C, 6×10^{-3}mmHg, inlet 80°C) gave a mixture of starting material and *cis,trans*-1,8-diacetoxy-2,6-octadiene. On pyrolysis at a higher furnace temperature (625°C + silica rods, 1×10^{-2} mmHg, inlet 90°C) another mixture of compounds was obtained. Loss of acetic acid was thought to have occurred to give 3,4-dimethylene-1,5-hexadiene[136].

3a. Attempted preparation of *cis,trans*-Octa-2,6-diene-1,8-dialdehyde

To a solution of *cis,trans*-octa-2,6-diene-1,8-diol (293 mg, 2 mmol) in acetone (10 ml) was added a standard solution of Jones Reagent (1 ml). The acetone layer was separated, filtered and evaporated to leave an orange liquid which was distilled by Kugelrohr (150°C at 3 mmHg) to give a colourless liquid (156 mg). ^{1}H n.m.r. and t.l.c. showed the presence of several products; ν_{max} 1773, 1690, 1638, 1302, 975, 920, and 733 cm^{-1}; δ_H (aldehyde peaks only listed) 9.53 and 9.46.

b. Attempted Vinylation of *cis,trans*-Octa-2,6-diene-1,8-diol

A solution of *cis,trans*-octa-2,6-diene-1,8-diol (20 mg, 0.14 mmol) in ethyl vinyl ether (15 ml) containing a few crystals of mercuric acetate was heated under reflux for 6 days. Evaporation of solvent gave a pale yellow sweet smelling liquid, ^{1}H n.m.r. spectrum of which was complicated and t.l.c. indicated at least 2 compounds present in the mixture.

4. Isomerisation of *cis,trans*-Octa-2,6-diene-1,8-dioic acid and its Dimethyl ester

a. Preparation of *trans,trans*-Octa-2,6-diene-1,8-dioic acid

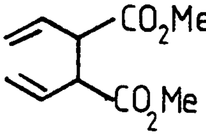
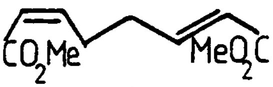
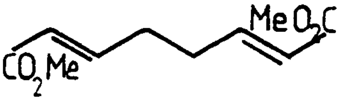
Heating *cis,trans*-octa-2,6-diene-1,8-dioic acid in methanol resulted in isomerisation to give trans,trans-octa-2,6-diene-1,8-dioic acid as a pale brown solid, m.p.257°C (decomp.) (lit.,[130] 256°C (decomp.)); ν_{max} 1698, 1645, 991, 875, and 711 cm^{-1}; δ_H (CF_3COOH) 7.42-7.15 (2H, m), 6.09-6.89 (2H, d, J16Hz), and 2.6-2.5 (4H, m); δ_C (CD_3SOCD_3) 167.23, 147.51, 122.68, and 29.78.

b. Preparation of *trans,trans*-Dimethyl octa-2,6-diene-1,8-dioate

A solution of *cis,trans*-dimethyl octa-2,6-diene-1,8-dioate (2.3 g, 11.6 mmol) in *n*-heptane (70 ml) containing a few crystals of iodine was heated under reflux, the composition of the solution being monitored by GC (10% PEGA, 180°C). After 304 h, the solution contained 75% of trans,trans-dimethyl octa-2,6-diene-1,8-dioate. The solvent was removed *in vacuo* and the residue dissolved in methylene chloride, washed with an aqueous solution of sodium thiosulphate (5%), water and dried. Evaporation of solvent gave an orange liquid which was distilled by Kugelrohr (180°C at 3 mmHg). Distillation gave partial separation of the isomers, the *trans,trans*-isomer distilling at the slightly higher temperature (lit.,[130] b.p.78°C at 0.05 mmHg). Further purification of the *trans,trans*-isomer was achieved by preparative GC (carbowax, 180°C). ν_{max} 1725, 1661, 1440, 1275, 1040, and 980 cm^{-1}; δ_H 7.08-6.83 (2H, m), 5.91-5.78 (2H, d, J15.5Hz), 3.69 (6H, s), and 2.42-2.32 (4H, m); δ_C 166.25, 146.77, 121.57, 50.98, and 30.02 (lit.,[130] δ_H (CCl_4) 6.90 (2H, m, C(2)H, C(5)H), 5.80 (2H, perturbed d, J15.5Hz, C(1)H, C(7)H), 3.67 (6H, s), and 2.37 (4H, m, C(3)H, C(4)H)].

c. Rearrangement and Isomerisation Reactions on GC Column

The Cope rearrangement of *meso*-3,4-dimethoxycarbonyl-1,5-hexadiene on a GC column was studied. Under the reaction conditions (10% PEGA, 180-196°C), *cis-trans* isomerisation also occurred. The Cope rearrangement at 180°C with full gas flow was found to be highly stereospecific but on turning off the gas flow significant isomerisation to the *trans*-isomer was observed.

Time with no gas flow secs	Column temp. °C	% Products		
			 *cis*, *trans*	 *trans*, *trans*
-	180	45.7%	53.4%	0.88%
30	180	8.47	78.96	12.56
45	180	10.56	77.69	11.75
75	196	6.38	73.27	20.35

G. Flash Vacuum Pyrolysis under Dehydrogenating Conditions

1. Preparation and FVP of 4,9-Dithiatricyclo[5.3.0.0^{2,6}]decane 4,4,9,9-tetroxide

a. Preparation of 4,9-Dithiatricyclo[5.3.0.0^{2,6}]decane 4,4,9,9-tetroxide

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

A solution of 6,7-bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (3.4 g, 6.6 mmol) in ethanol (50 ml) was added to a solution of sodium sulphide nonahydrate (4.77 g, 19.8 mmol) in water (50 ml) and heated under reflux for 15 h. After removal of the ethanol *in vacuo* the aqueous residue was extracted with methylene chloride and the organic extract dried. Evaporation of solvent gave 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (1.08 g, 80%) as a pale yellow solid, m.p. 203-204°C (lit.,[50] 195-196°C).

(ii) 4,9-Dithiatricyclo[5.3.0.0^{2,6}]decane 4,4,9,9-tetroxide

To a stirred solution of 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4-dioxide (1.08 g, 5.3 mmol) in dry methylene chloride (30 ml) at 0°C was added dropwise a cold solution of *m*-chloroperoxybenzoic acid (85%, 1.92 g, 11 mmol) in dry methylene chloride (70 ml). After the addition, the mixture was stirred at room temperature for 4.5 days. After washing with an aqueous solution of sodium carbonate, the solid which was insoluble in both the aqueous and organic phases, was filtered off and dried *in vacuo* to give 4,9-dithiatricyclo[5.3.0.0^{2,6}]decane 4,4,9,9-tetroxide (1.02 g, 82%) as a colourless solid, m.p. >320°C (Found: C, 40.45, H, 4.95. $C_8H_{12}O_4S_2$ requires C, 40.7; H, 5.1%; ν_{max} 1278, 1232, 1121, 1081, 958, 911, 883, 728, 716, and 665 cm^{-1}; δ_H (CD_3SOCD_3) 3.35 (m); m/z (Electron Impact) 107 (24%), 93 (67), 91 (77), 79 (100), and 64 (15); m/z (Chemical Ionisation)* 237 ($M+1^+$, 100%), 221 (33), 205 (9), 173 (3), 107 (6), 79 (6), and 69 (5).

b. FVP of 4,9-Dithiatricyclo[5.3.0.$0^{2,6}$]decane 4,4,9,9-tetroxide

FVP of the title compound (153.8 mg, 650°C, $4x10^{-3}$mmHg, inlet 250°C) gave a yellow oil and polymer. The pyrolysate was analysed by ^1H n.m.r. and GC (1% OV1, 80°C) to be a mixture of 4-vinylcyclohexene and 1,5-cyclooctadiene in the ratio of 4:1. Two trace components were unidentified.

2. FVP of 1,5-Cyclooctadiene

FVP of the title compound (4.45 mg, 650°C, $4x10^{-3}$mmHg, no inlet heating) gave a colourless liquid pyrolysate which was analysed by ^1H n.m.r. and GC (1% OV1, 80°C) to be a mixture of unreacted starting material and 4-vinylcyclohexene in the ratio of 1:1.6. 1,3-Butadiene was also detected by ^1H n.m.r.

4-Vinylcyclohexene was found to pass unchanged through the furnace at 650°C at $12x10^{-3}$mmHg.

* Chemical ionisation mass spectra were recorded by VG Analytical.

3. Tandem FVP and Dehydrogenation

a. FVP of 1,5-Cyclo-octadiene over dehydrogenation catalyst

The titled compound (250 mg) was pyrolysed at temperatures ranging from 350° to 750°C through a sintered furnace tube packed with a catalyst of Palladium on activated carbon (5.2% Pd, 10 g) and a quartz wool plug. The average vacuum was 10×10^{-3}mmHg and the inlet was cooled in an ice bath. The liquid pyrolysates were analysed by ^{1}H n.m.r., GC (10% PEGA, 55°C) and by GC-MS (for 550°C pyrolysate).

Pyrolysis Temp. °C	Styrene	Xylene	Toluene	Benzene	Ethyl Benzene	1,5-cyclo-octadiene	C_8H_{12}
750°	-	-	15%	85%	-	-	-
650°	62%	3%	9%	26%	-	-	-
550°	38%	15%	4%	14%	22%	-	7%
450°	42%	4%	2%	14%	35%	2%	-
350°	3%	15%	7%	8%	26%	31%	9%

Ratios of Products (from GC)

The proportion of 1,3-butadiene was not quantified. The 750°C pyrolysate contained a large proportion of gaseous material and at 350°C, there were several unidentified components.

By comparison of the areas of the peaks in the GC with a standard solution of styrene in ether, the yield of styrene at 650°C was 28% while at 550°C, the yield obtained was 25%. At 450°C, the yield of styrene decreased to 12%. At 650°C, there was 45% conversion to liquid pyrolysate, 55% being gaseous or highly volatile material including 1,3-butadiene.

b. FVP of 4,9-Dithiatricyclo[5.3.0.0^{2,6}]decane 4,4,9,9-tetroxide over Dehydrogenation Catalyst

FVP of the titled compound (104 mg, 650°C, 10x10^{-3}mmHg, inlet 250°C) over a catalyst of Palladium on activated carbon (5.2% Pd, 10 g) gave a large amount of polymer, butadiene and benzene. Similar results were obtained on FVP at 450°C and on FVP at 650°C with only a 2 cm bed of catalyst (^{1}H n.m.r. and GC analysis -10% PEGA, 55°C).

The pyrolysis was repeated on a larger scale by S.F. Newlands as part of a summer research project. On pyrolysis at 600°C over the catalyst, styrene was obtained as the major product (12%) together with benzene (4%), toluene (2%), xylenes (2%) and ethyl benzene (2%).

H. Preparation and Attempted Bis-Wittig reactions of some Bis-phosphonium salts

1. Preparation of 6-Triphenylphosphoniumiodomethyl-7-iodomethyl-3-thiabicyclo[3.2.0]heptane 3.3-dioxide

A solution of 6,7-di-iodomethyl-3-thiabicyclo[3.2.0] heptane 3,3-dioxide (195 mg, 0.458 mmol) and triphenylphosphine (240 mg, 0.92 mmol) in dry toluene (10 ml) was heated under reflux for 60 h. The resulting solid was recrystallised from methanol to give 6-triphenylphosphoniumiodomethyl-7-iodomethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (283.6 mg, 90%) as a colourless crystalline solid, m.p. 167°C (decomp.) (Found: C, 45.7; H, 4.0. $C_{26}H_{27}I_2PSO_2$ requires C, 45.35; H, 3.95%); δ_H (CD_3SOCD_3) 8.0-7.5 (15H, m), 4.75 and 4.55 (1H, broad d, J19Hz), 3.95 and 3.85 (1H, broad d, J19Hz), and 3.3-2.6 (10H, m); m/z 262 (86%, PPh_3) and 183 (100).

Attempts to prepare the phosphonium salts of the corresponding dibromo and dichloro sulphones were unsuccessful.

2. Preparation of *meso*-3,4-Bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene

A solution of *meso*-3,4-di-iodomethyl-1,5-hexadiene (2.52 g, 6.96 mmol) and triphenylphosphine (3.65 g, 13.9 mmol) in dry benzene (25 ml) was heated under reflux for 40 h. The resulting solid was filtered off (5.99 g, 97%) and recrystallised from methanol to give *meso*-3,4-bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene (4.01 g, 65%) as a pale yellow crystalline solid, m.p. 254-257°C (Found: C, 59.35; H, 4.85. $C_{44}H_{42}P_2I_2$ requires C, 59.6; H, 4.8%); δ_H 8.0-7.55 (30H, m), 5.75-4.53 (6H, m), 4.1-3.5 (4H, m), and 2.6-2.5 (2H, m); ^{31}P single peak at 23.236; m/z 262 (100%, PPh_3), 204 (26), 183 (64), 128 (48), 127 (27), and 108 (33).

Attempts to prepare the bisphosphonium salt of *meso*-3,4-dibromomethyl-1,5-hexadiene were unsuccessful - after 66 h under reflux in toluene, little reaction had occurred.

3. Attempted Bis-Wittig Reactions of *meso*-3,4-Bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene

a. Attempted reaction with Benzil

(i) *n*-Butyl-lithium (0.76 ml, 1.13 mmol) was added to a stirred solution of *meso*-3,4-bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene (500 mg, 0.566 mmol) in dry tetrahydrofuran (50 ml) under nitrogen. After stirring for 1 h, a solution of benzil (119 mg, 0.566 mmol) in dry THF (15 ml) was added dropwise and the solution heated under reflux for 6 h. On cooling, water and ether were added to the yellow solution and the organic phase separated. T.l.c. indicated unreacted benzil as the major component in the mixture.

(ii) Using the method of Sondheimer *et al.*[137], lithium ethoxide (8.95 mg lithium in 5 ml dry ethanol) was added dropwise over 4 h to a solution of *meso*-3,4-bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene (570 mg, 0.645 mmol) and benzil (0.136 g, 0.646 mmol) in dry dimethylformamide (60 ml) at 90°C with stirring under nitrogen. The dark red solution was monitored by t.l.c. (silica, 20% ether/pet.ether) but after 22 h, there still remained starting material.

b. Attempted reaction with o-Phthalicdicarboxaldehyde

(i) *n*-Butyl-lithium (0.76 ml, 1.13 mmol) was added to a solution of *meso*-3,4-bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene (500 mg, 0.56 mmol) in dry dimethoxyethane (50 ml). The solution was heated under reflux for 1 h before the addition of a solution of o-phthalicdicarboxaldehyde (76 mg, 0.56 mmol) in dry dimethoxyethane (15 ml). After refluxing for a further 8 h, the solution was left stirring under nitrogen for 12 h.

After the addition of water and ether, the organic phase was separated, washed with water and dried. Evaporation of solvent gave a brown oil (480 mg) which by n.m.r., t.l.c. contained a complex mixture of compounds and polymer.

(ii) The method used was that of Sondheimer *et al.*[137] Lithium ethoxide (15.8 mg Li in 7 ml dry ethanol) was added dropwise over 3 h to a solution of *meso*-3,4-bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene (1.01 g, 1.139 mmol) and o-phthalicdicarboxaldehyde (152 mg, 1.13 mmol) in dry dimethylformamide (60 ml) at 90°C under nitrogen. The resulting deep red solution was stirred for 2 h, allowed to cool and hydrolysed by the addition of water. Extraction with ether followed by drying and evaporation of solvent gave a red oil (470 mg). After preparative t.l.c. (silica, petroleum ether 40-60) a colourless oil was obtained (57.8 mg, 24%), ^{1}H n.m.r. of which was consistent with the desired product but ^{13}C n.m.r. indicated the probable presence of at least two compounds; δ_H 7.25-7.05 (4H, m), 6.65-4.75 (10H, m), and 2.7-2.15 (2H, m); δ_C 46.36, 40.59, 36.83, and 29.13 (aromatic and olefinic carbons not listed).

c. Attempted reaction with Isophthaldehyde

The reaction conditions used were again based on those of Sondheimer *et al.*[137] Lithium ethoxide (9.5 mg lithium in 4 ml dry ethanol) was added dropwise over 2 h to a solution of *meso*-3,4-bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene (500 mg, 0.56 mmol) and isophthaldehyde (75.6 mg, 0.56 mmol) in dry dimethylformamide (50 ml) under nitrogen at room temperature. After stirring for 12 h, the orange solution was hydrolysed and extracted with ether. The organic extract was washed with water, dried and the solvent evaporated to give a yellow oil (170 mg) which was purified by preparative t.l.c. (silica, petroleum ether (40-60)). ^1H n.m.r. showed the presence of aromatic, vinyl and aldehyde groups in the product (not starting materials). The reaction was repeated at 90^o for 5 h to give a more complex mixture of products.

I. Preparation and Flash Vacuum Pyrolysis of Methylated Derivatives of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}] decane 9,9-dioxide

1. Preparation and FVP of 1-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

a. Preparation of 1-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo-[5.3.0.0^{2,6}]decane 9,9-dioxide

(i) 3-Methyl-2,5-dihydrothiophen 1,1-dioxide

This was prepared by the method of Frank and Seven[138]. To a precooled glass vessel (MeOH, dry ice) was added liquid sulphur dioxide (22.7 ml, 0.5 mol), 2-methyl-1,3-butadiene (50 ml, 0.5 mol), methanol (25 ml) and hydroquinone (1 g). The glass vessel was placed in an autoclave and heated at 85°C for 4 h. The resulting crystalline solid was filtered off (64.27 g, 97%) and recrystallised from methanol to give 3-methyl-2,5-dihydrothiophen 1,1-dioxide (36.7 g, 56%) as colourless plates, m.p. 62.5-63°C (lit.,[138] 63-64°C).

(ii) 1-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]-decane 9,9-dioxide

A solution of 3-methyl-2,5-dihydrothiophen 1,1-dioxide (15 g, 0.114 mol) and maleic anhydride (13.7 g, 0.14 mol) in acetone (450 ml) was irradiated at 400W for 24 h. Evaporation of acetone left a brown oil which on trituration with chloroform, gave 1-methyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}] decane 9,9-dioxide (9.42 g, 36%) as a colourless crystalline solid, m.p. 157-159°C. (Found: C, 46.8; H, 4.5. $C_9H_{10}SO_5$

requires C, 46.95; H, 4.4%); ν_{max} 1860, 1777, 1308, 1153, 1118, 1059, 905, and 723 cm^{-1}; δ_H (CD_3COCD_3) (80MHz) 3.85-3.10 (7H, m), and 1.4776 (3H, s); m/z 231 ($M+1^+$, 4%), 230 (M^+, 6), 138 (31), 99 (90), and 93 (100).

b. FVP of 1-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo-[$5.3.0.0^{2,6}$]decane 9,9-dioxide

FVP of the title compound (1.285 g, 580°C, 0.005 mmHg, inlet 170°C) gave a pale yellow liquid. This was distilled by Kugelrohr (110°C at 0.3 mmHg) to give *cis*-2-methyl-1,5-hexadiene-3,4-dicarboxylic anhydride (0.639 g, 69%) as a colourless liquid. (Found: M^+ 166.064145. $C_9H_{10}O_3$ requires 166.062989); ν_{max} 1865, 1785, 1650, 1455, 1445, 1423, 1386, 1033, and 977 cm^{-1}; δ_H (200MHz) 5.81-5.63 (1H, m), 5.52-5.39 (2H, m), 5.16, 5.04 (2H, br d), 4.0-3.87 (2H, m), and 1.73 (3H, s); δ_C 170.76, 170.19, 135.86, 126.73, 122.13, 118.04, 52.44, 47.72, and 21.12; m/z 166 (M^+, 14%), 122 (17), 94 (36), and 79 (100),

2. Preparation and FVP of 2-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo[$5.3.0.0^{2,6}$]decane 9,9-dioxide

a. Preparation of 2-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo-[$5.3.0.0^{2,6}$]decane 9,9-dioxide

This was prepared by the method of Shaikhrazieva *et al.*[111] A solution of butadiene sulphone (15 g, 0.127 mol) and citraconic anhydride (17.1 g, 0.152 mol) in acetone (300 ml) was irradiated at 400W for 24 h. The precipitate was filtered off, washed with acetone and dried to give 2-methyl-3,5-dioxo-

4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide (13 g, 45%) as colourless crystals, m.p. 249-250°C (Found: C, 47.1; H, 4.35. $C_9H_{10}SO_5$ requires C, 46.95; H, 4.4%); ν_{max} 1858, 1776, 1303, 1141, 1006, 920, 771, 721, and 680 cm^{-1}; δ_H (200MHz, CD_3COCD_3) 3.76-3.30 (7H, m), and 1.57 (3H, s); δ_C (CD_3COCD_3) 51.78, 48,28, 47.05, 38.47, 33.68, and 13.63; m/z 231 ($M+1^+$, <1%), 158 (29), 110 (10), 94 (41), 79 (100), and 77 (38).

b. FVP of 2-Methyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}] decane 9,9-dioxide

FVP of the title compound (1.398 g, 580°C, $8x10^{-3}$mmHg, inlet 200°C) gave a yellow liquid which was distilled by Kugelrohr (110-115°C at 0.8 mmHg) to give *cis*-3-methyl-1,5-hexadiene-3,4-dicarboxylic anhydride (872 mg, 86%) as a colourless liquid (Found: M^+ 166.062849. $C_9H_{10}O_3$ requires 166.062989), ν_{max} 1850, 1790, 1674, 1642, 1454, 1416, 1380, 1235, and 939 cm^{-1}; δ_H (80MHz) 5.89-5.10 (6H, m), 3.55, 3.47, (1H, d, J6.7Hz), and 1.49 (3H, s); δ_C 172.47, 169.59, 133.77, 126.50, 123.03, 117.61, 56.07, 52.91, and 20.00; m/z 166 (M^+, <1%), 122 (0.1), 94 (73), 79 (100), and 77 (41).

3. Preparation and FVP of 1,6-Dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide and its 1,2-Dimethyl Isomer

a. Photochemical Addition of 3-Methyl-2,5-dihydrothiophen 1,1-Dioxide and Citraconic Anhydride

A solution of 3-methyl-2,5-dihydrothiophen 1,1-dioxide

(15 g, 0.113 mol) and citraconic anhydride (15.26 g, 0.136 mol) in acetone (300 ml) was irradiated at 400W for 24 h. The resulting yellow solution was partially evaporated to precipitate an isomeric mixture of 1,6-dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide and 1,2-dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide (6.26 g, 23%) as a colourless powder. (Found: C, 49.45; H, 4.7. $C_{10}H_{12}O_5S$ requires C, 49.15; H, 4.95%); ν_{max} 1855, 1770, 1310, 1141, 1020, and 914 cm^{-1}; δ_H (CD_3SOCD_3) mixture of anhydrides and diacids obtained due to hydrolysis by water in solvent; m/z 244 (M^+, <1%), 172 (16), 136 (5), 132 (9), 108 (49), 93 (100), and 68 (48).

b. FVP of 1,6-Dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide and its 1,2-Dimethyl Isomer

FVP of an isomeric mixture of the titled compounds (356 mg, 600°C, 8x10^{-3}mmHg, inlet 220°C) gave a colourless liquid which was distilled by Kugelrohr (100°C at 0.1 mmHg) to give an isomeric mixture of *cis*-2,4-dimethyl-1,5-hexadiene-3,4-dicarboxylic anhydride and *cis*-2,3-dimethyl-1,5-hexadiene-3,4-dicarboxylic anhydride (152 mg, 59%) as a colourless liquid; δ_H (200MHz) (equal ratio of isomers) 5.85-5.58 (2H m), 5.48-5.28 (4H, m), 5.19-4.99 (4H, m), 3.63 (1H, s), 3.58-3.54 (1H, d, J8Hz), 1.77 (3H, s), 1.73 (3H, s), 1.58 (3H, s), and 1.57 (3H, s); δ_C 173.57, 173.05, 170.04, 169.28, 139.64, 135.46, 133.48, 126.79, 123.00, 119.04, 117.72, 116.14, 59.83, 55.88, 55.16, 51.89, 23.53, 21.56, 20.94, and 20.68.

4. Preparation and FVP of 2,6-Dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

a. Photochemical Addition of Butadiene Sulphone and Dimethylmaleic Anhydride

The method used was that of Shaikhrazieva *et al.*[111] A solution of butadiene sulphone (3.9 g, 33 mmol) and dimethylmaleic anhydride (5 g, 39.6 mmol) in acetone (400 ml) was irradiated at 400W for 24 h under nitrogen. The solid which had deposited was filtered off (2.28 g) and on evaporation of solvent and trituration of the resulting brown oil with chloroform a further 1.27 g of colourless crystalline solid was obtained. However, the first crop of crystals was found to be the dimer of dimethylmaleic anhydride and the latter crop found by i.r., ^{1}H n.m.r. and MS to be a mixture of 2,6-dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide and the dimer.

b. FVP of 2,6-Dimethyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

FVP of the title compound (431 mg, 580°C, 7x10^{-3}mmHg, inlet 200°C) gave a yellow liquid which was distilled by Kugelrohr (105°C at 0.4 mmHg) to give *cis*-3,4-dimethyl-1,5-hexadiene-3,4-dicarboxylic anhydride as a colourless viscous liquid (131 mg, 41%). However, ^{1}H n.m.r. showed that the dimer of dimethylmaleic anhydride was present in the pyrolysate even after distillation and separation by t.l.c. proved to be unsuccessful. δ_H (200MHz) 5.84-5.70 (2H, m), 5.39-5.26 (4H, m), 2.05 (dimethylmaleic anhydride dimer), and 1.37 (6H, d, J2Hz).

5. Preparation of Dimethyl esters

a. Preparation of 1-Methyl-6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A mixture of 1-methyl-3,5-dioxo-4-oxa-9-thiatricyclo [5.3.0.0^{2,6}]decane 9,9-dioxide (1 g, 4.35 mmol) in AR methanol (40 ml) containing a few drops of sulphuric acid was heated under reflux for 18 h. On cooling the solution gave a precipitate which was filtered off and dried to give 1-methyl-6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (970 mg, 81%) as colourless needles, m.p. 118-119°C (Found: C, 47.85; H, 5.8. $C_{11}H_{16}SO_6$ requires C, 47.8; H, 5.85%); ν_{max} 1729, 1741, 1309, 1300, 1181, 1130, 1120, 1108, 1029, and 727 cm^{-1}; δ_H 3.67 (3H, s), 3.65 (3H, s), 3.55-2.96 (7H, m), and 1.38 (3H, s); δ_C 171.78, 169.86, 61.00, 55.07, 51.65, 51.39, 47.42, 41.28, 39.84, 39.72, and 22.24; m/z (M^+ not apparent) 180 (18%), 152 (30), 113 (100), and 93 (50).

b. Preparation of 6-Methyl-6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A mixture of 2-methyl-3,5-dioxo-4-oxa-9-thiatricyclo-[5.3.0.0^{2,6}]decane 9,9-dioxide (2 g, 8.69 mmol) in AR methanol (30 ml) containing a few drops of sulphuric acid was heated under reflux for 6 h. The excess methanol was partially evaporated and on cooling, a colourless solid crystallised from the solution to give 6-methyl-6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (1.65 g, 78%) as colourless crystals, m.p. 72.5-73.5°C (Found: C, 47.9; H, 5.7. $C_{11}H_{16}O_6S$ requires C, 47.8; H, 5.85%); ν_{max} 1735, 1718, 1295, 1206, 1139, 1114, 1091, 1060, and 901 cm^{-1}; δ_H (200MHz) 3.699 (3H, s), 3.65 (3H, s), 3.42-3.06 (7H, m), and 1.47 (3H, s); δ_C 174.28, 171.37, 53.47, 52.20, 51.63, 49.65, 49.47, 47.57, 37.76, 32.32, and 18.46; m/z 276 (M^+, 5%), 245 (37), 185 (44), 180 (42), 152 (100), 127 (38), 113 (54), 93 (79), and 59 (66).

c. Preparation of *meso*-2-Methyl-3,4-dimethoxycarbonyl-1,5-hexadiene

A mixture of *cis*-2-methyl-1,5-hexadiene-3,4-dicarboxylic-anhydride (630 mg, 38 mmol) in AR methanol (20 ml) containing a few drops of sulphuric acid was heated under reflux for 16 h. The solution was evaporated to leave a yellow liquid which crystallised on standing. Recrystallisation of the solid from petroleum ether (40-60) gave meso-2-methyl-3,4-dimethoxycarbonyl-1,5-hexadiene (430 mg, 54%) as colourless plates, m.p. 34-36°C (Found: M^+ 212.105767. $C_{11}H_{16}O_4$ requires 212.104851); ν_{max} 1743, 1646, 1155, 1003, 930, 907, and 726 cm^{-1}; δ_H (200MHz) 5.76-5.58 (1H, m), 5.21-5.02 (2H, m), 4.83 (2H, m), 3.55 (1H, m), 3.52 (6H, s), 3.33 (1H, d, J11.5 Hz), and 1.69 (3H, s); δ_C 171.74, 171.19, 140.18, 133.06, 119.14, 115.10, 54.89, 51.63, 51.16, and 20.65; m/z 212 (M^+, <1%), 181 (17), 113 (93), 99 (68), and 93 (100).

d. Preparation of *meso*-3-Methyl-3,4-dimethoxycarbonyl-1,5-hexadiene

A solution of *cis*-3-methyl-1,5-hexadiene-3,4-dicarboxylic-anhydride (668 mg, 4.0 mmol) in AR methanol (20 ml) containing a few drops of sulphuric acid was heated under reflux for 24 h.

The solvent was evaporated and the remaining oil dissolved in ether and washed with water. After drying and removal of ether *in vacuo*, the oil was distilled by Kugelrohr (150°C at 0.2mmHg) to give *meso*-3-methyl-3,4-dimethoxycarbonyl-1,5-hexadiene (407 mg, 48%) as a colourless, viscous liquid; ν_{max} 1778, 1748, 1639, 1436, 1244, 1200, 1165, and 930 cm^{-1}; δ_H (80MHz) 6.36-4.95 (6H, m), 3.60 (3H, s), 3.62 (3H, s), 3.57-3.45 (1H, d, J9Hz), and 1.30 (3H, s); m/z 212 (M^+, 9%), 181 (38), 180 (59), 152 (45), 148 (60), 120 (66), 113 (97), 100 (90), and 93 (100).

J. Preparation and Reactions of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

1. Preparation of 6,7-Dimethylene-3-thiabicyclo[3.2.0] heptane 3,3-dioxide

A solution of 6,7-di-iodomethyl-3-thiabicyclo[3.2.0] heptane 3,3-dioxide (1 g, 2.35 mmol) in dry tetrahydrofuran (25 ml) was added dropwise over 1 h to a stirred suspension of sodium hydride (60%, 3 equiv, 282 mg, 11.75 mmol) in dry THF (15 ml) under nitrogen. The reaction mixture was stirred at room temperature for 18 h. Water (40 ml) was then added cautiously and the solvent removed *in vacuo*. The remaining aqueous solution was extracted with methylene chloride and the organic extract washed with water and dried. Evaporation of solvent gave a colourless oil which crystallised (356 mg, 89%). Recrystallisation of the solid from methanol gave some polymer (66 mg) and 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (209 mg, 52%) as a colourless crystalline solid, m.p. gradual decomp. (Found: C, 56.55; H, 5.9. $C_8H_{10}O_2S$ requires C, 56.45; H, 5.9%); ν_{max} 1649, 1313, 1291, 1219, 1121, 1068, 918, 901, and 711 cm^{-1}; δ_H 5.39 (2H, s), 4.96 (2H, s), 3.83-3.65 (2H, m), and 3.50-2.98 (4H, m); δ_C sample decomposed in probe of ^{13}C spectrometer; m/z 170 (M^+, 31%), 105 (41), and 91 (100).

Alternative Synthesis

Following the method of Butler and Snow[139], powdered potassium *t*-butoxide (262 mg, 2.33 mmol) was added to a solution of 6,7-bis(*p*-toluenesulphonyloxymethyl)-3-thiabicyclo-

[3.2.0]heptane 3,3-dioxide (400 mg, 0.78 mmol) in dry dimethylsulphoxide (10 ml). The mixture darkened to a dark brown colour. After stirring for 5 h under nitrogen, water was added and the mixture extracted with methylene chloride, washed with saturated sodium chloride solution and water several times and dried. Evaporation of solvent gave an oil which crystallised (105 mg, 78%). Recrystallisation of the solid from methanol removed traces of *t*-butanol to give 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (57 mg, 43%).

Treatment of the bis(*p*-toluenesulphonate) ester with sodium hydride gave back unreacted starting material (71% recovery).

2. Diels-Alder Reactions of 6,7-Dimethylene-3-thiabicyclo [3.2.0]heptane 3,3-dioxide

a. Preparation of 1,9-Dehydro-4,6-Dioxo-5-oxa-12-thiatetracyclo[7.5.0.0^{3,7}0^{10,14}]tetradecene 12,12-dioxide

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (115 mg, 0.676 mmol) and maleic anhydride (66 mg, 0.676 mmol) in dry benzene (10 ml) was heated under reflux for 5 h. The resulting solid was filtered off to give 1,9-dehydro-4,6-dioxo-5-oxa-12-thiatetracyclo[7.5.0.0^{3,7}0^{10,14}] tetradecene 12,12-dioxide (139 mg, 77%) as a colourless crystalline solid, m.p. 223-225°C (Found: C, 53.5; H, 4.35. $C_{12}H_{12}O_5S$ requires C, 53.7; H, 4.5%), ν_{max} 1850, 1775, 1294, 1129, 950, and 915 cm^{-1}; δ_H (CD_3SOCD_3) 3.75-2.97 (8H, m), and 2.62-2.05 (4H, m); m/z 268 (M^+, 13%), 176 (10), 131 (100), and 91 (100).

b. Preparation of 1,7-Dehydro-9,10-dimethoxycarbonyl-4-thiatricyclo[5.3.0.$0^{2,6}$]undecene 4,4-dioxide

A solution of 1,9-dehydro-4,6-dioxo-5-oxa-12-thiatetracyclo[7.5.0.$0^{3,7}0^{10,14}$]tetradecene 12,12-dioxide (131 mg, 0.49 mmol) in AR methanol (20 ml) containing a few drops sulphuric acid was heated under reflux for 5 h. The methanol was partially evaporated and a solid crystallised from the remaining solution to give <u>1,7-dehydro-9,10-dimethoxycarbonyl-4-thiatricyclo[5.4.0.$0^{2,6}$]undecene 4,4-dioxide</u> (87 mg, 57%) as colourless crystals, m.p.141-142°C (Found: C, 53.75; H, 5.7. $C_{14}H_{18}O_6S$ requires C, 53.5; H, 5.75%); ν_{max} 1745, 1728, 1290, 1231, 1129, 1043, 1028, 903, 851, 726, and 711 cm^{-1}; δ_H 3.75-3.60 (2H, m), 3.67 (6H, s), 3.29-2.69 (6H, m), and 2.49-2.32 (4H, m); δ_C 173.19, 141.88, 51.85, 50.04, 41.60, 40.13, and 23.91; m/z 314 (M^+, 8%), 283 (19), 254 (49), 195 (9), 190 (19), 131 (100), 115 (23), and 91 (59).

c. Preparation of 1,7:9,10-Tetradehydro-9,10-dimethoxycarbonyl-4-thiatricyclo[5.4.0.$0^{2,6}$]undeca-1,9-diene 4,4-dioxide

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0] heptane 3,3-dioxide (68 mg, 0.4 mmol) and dimethyl acetylenedicarboxylate (56.8 mg, 0.4 mmol) in dry toluene (10 ml) was heated under reflux for 17 h. On cooling a white solid precipitated from the solution to give <u>1,7:9,10-tetradehydro-9,10-dimethoxycarbonyl-4-thiatricyclo[5.4.0.$0^{2,6}$]undeca-1,9-diene 4,4-dioxide</u> (66 mg, 53%) as colourless crystals, m.p. 160-161.5°C (Found: C, 53.95; H, 5.1. $C_{14}H_{16}O_6S$ requires C, 53.85; H, 5.15%); ν_{max} 1734, 1710, 1629, 1316, 1300, 1238, 1130, and 1061 cm^{-1}; δ_H (200MHz) 3.78 (8H, m, OMe and C(2)H, C(6)H) and 3.12-2.94 (8H, m, C(3)H, C(5)H and C(8)H, C(11)H); δ_C 167.98 (C=O), 139.55 (C-9, C-10), 132.88 (C-1, C-7), 52.25 (OMe), 50.15 (C-3, C-5), 41.72 (C-2, C-6), and 26.04 (C-8, C-11); m/z 312 (M$^+$, 2%), 310 (1), 281 (30), 216 (70), 215 (87), 189 (76), 157 (67), 129 (100), 128 (81), 115 (49), and 59 (66).

d. Preparation of 1,7-Dehydro-9,10-tetracyano-4-thiatricyclo [5.4.0.0^{2,6}]undecene 4,4-dioxide

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (205 mg, 1.2 mmol) and tetracyanoethylene (155 mg, 1.2 mmol) in dry benzene (20 ml) was heated under reflux for 2 h. The resulting solid was filtered off to give 1,7-dehydro-9,10-tetracyano-4-thiatricyclo[5.4.0.0^{2,6}]undecene 4,4-dioxide (327 mg, 91%) as a pale brown crystalline solid. The solid was purified by vacuum sublimation to give colourless crystals, m.p. 260°C (decomp.) (Found: C, 56.55; H, 3.35; N, 18.65. $C_{14}H_{10}N_4SO_2$ requires C, 56.35; H, 3.4; N, 18.8%); ν_{max} 1298, 1238, 1121, 895, 720, and 711 cm^{-1}; δ_H (200MHz; CD_3SOCD_3) 3.73 (2H, br s) and 3.62-3.08 (8H, m); m/z 298 (M$^+$, 16%), 234 (36), 106 (99), 105 (89), and 91 (100).

e. Preparation of 1,7-Dehydro-11-phenyl-9,11,13-triazolidine-10,12-dione-4-thiatetracyclo[7.5.0.0^{2,6}0^{9,13}]tetradecene 4,4-dioxide

A mixture of 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (137 mg, 0.806 mmol) and 4-phenyl-3H-1,2,4-triazoline-3,5-dione (141 mg, 0.806 mmol) in dry ether (10 ml) was stirred at room temperature for 1 h. The resulting solid was filtered off, washed with chloroform to give *1,7-dehydro-11-phenyl-9,11,13-triazolidine-10,12-dione-4-thiatetracyclo-$[7.5.0.0^{2,6}0^{9,13}]$tetradecene 4,4-dioxide* (252 mg, 91%) as a colourless crystalline solid, m.p. 235-236°C (Found: C, 55.6; H, 4.3; N, 11.95. $C_{16}H_{15}N_3SO_4$ requires C, 55.65; H, 4.4; H, 12.15%); ν_{max} 1777, 1705, 1600, 1500, 1305, 1235, 1123, and 893 cm^{-1}; δ_H (80MHz; CD_3SOCD_3) 7.49-7.36 (5H, m), 4.25-4.07 (4H, m), 3.83-3.80 (2H, m), and 3.37-3.11 (4H, m); m/z 345 (M^+, 33%), 281 (66), 161 (9), 134 (18), 119 (101), 105 (47), and 91 (100).

f. *Preparation of 1,7-Dehydro-10,12-dioxo-4-thia-11-azatetracyclo$[7.5.0.0^{2,6}0^{9,13}]$tetradecene 4,4-dioxide*

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (163 mg, 0.96 mmol) and maleimide (93 mg, 0.96 mmol) in dry benzene (10 ml) was heated under reflux for 3 h. The resulting solid was filtered off and recrystallised from methanol to give *1,7-dehydro-10,12-dioxo-4-thia-11-azatetracyclo$[7.5.0.0^{2,6}0^{9,13}]$tetradecene 4,4-dioxide* (199 mg, 78%) as a colourless crystalline solid, m.p. 264-265°C (Found: C, 53.8; H, 4.85; N, 5.2. $C_{12}H_{13}NO_4S$ requires C, 53.9, H, 4.9; N, 5.25%); ν_{max} 3160, 1778, 1699, 1302, 1129 and 724 cm^{-1}; δ_H (80MHz; CD_3SOCD_3) 3.6-3.0 (9H, m), and 2.3-2.2 (4H, m); m/z 267 (M^+, 11%), 203 (47), 202 (73), 132 (99), 131 (97), 117 (74), 105 (78), and 91 (100).

g. (i) Attempted Lewis Acid catalysed Diels-Alder reaction with Methyl Vinyl Ketone

The method used was that of Bridges and Fischer[140]. 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (99 mg, 0.582 mmol) was added to an excess of methyl vinyl ketone (489.5 mg, 6.98 mmol) containing hydroquinone as stabiliser under nitrogen. Boron trifluoride etherate (20μℓ) was added and the mixture stirred for 3 days at room temperature. The volatile compounds were removed under reduced pressure and the residue dissolved in ether and vacuum filtered through g.l.c. grade silica gel to give a yellow oil. Preparative t.l.c. (silica, ether) gave a colourless oil (40 mg) which on trituration with ether yielded a colourless solid. Attempted recrystallisation of this solid from methanol resulted in decomposition. m/z 240 (M^+, 12%), 133 (51), 117 (20), 105 (26), 91 (58), and 43 (100).

(ii) Attempted reaction with Sulphur Dioxide

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0] heptane 3,3-dioxide (47 mg, 0.28 mmol) in AR methanol (5 ml) to which a few crystals of hydroquinone had been added, was cooled in solid CO_2. An excess of liquid sulphur dioxide was added and the flask stoppered and allowed to stand at room temperature for several days. Evaporation of solvent gave back starting material.

(iii) Attempted reaction with Sulphur Monoxide

The method used was that of Dodson and Sauers[141]. A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane

3,3-dioxide (83 mg, 0.488 mmol) and thiiran-1-oxide (excess used, 110 mg) was heated under reflux in dry toluene (5 ml). After 1 h, removal of solvent *in vacuo* gave a brown oil. Trituration with methanol afforded a yellow solid (102 mg) which was not identified, m/z 262 (M^+ of desired product 218).

Diels-Alder reactions of 6,7-dimethylene-3-thiabicyclo [3.2.0]heptane 3,3-dioxide with diethyl azodicarboxylate and with 1,4-naphthoquinone were also unsuccessful.

h. Attempted Photocyclisation of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0] heptane 3,3-dioxide (5 mg) in deuteriochloroform was irradiated at 125W in a quartz tube for 5 h during which time a yellow solid precipitated from the solution. The product was identified as polymeric material by ^{1}H n.m.r. and by MS.

3. FVP of Diels-Alder Adducts

a. FVP of 1,9-Dehydro-4,6-dioxo-5-oxa-12-thiatetracyclo [7.5.0.0^{3,7}0^{10,14}]tetradecene 12,12-dioxide

FVP of the title compound (107 mg, 550°C, 7×10^{-3}mmHg, inlet 210°C) gave a colourless solid (65 mg, 80%). The product decomposed in solution ($CDCl_3$) to give an orange gum. The MS was however consistent for the desired product from loss of SO_2 from the title compound; m/z 204 (M^+, 40%), 131 (77), 130 (100), and 91 (94).

b. FVP of 1,7-Dehydro-9,10-dimethoxycarbonyl-4-thiatricyclo $[5.4.0.0^{2,6}]$undecene 4,4-dioxide

FVP of the title compound (39 mg, 580°C, 5×10^{-3}mmHg, inlet 140°C) gave 2,3-dimethoxycarbonyl-1,2,3,4,6,7-hexahydronaphthalene (20 mg, 65%) as a colourless oil, ν_{max} ($CHCl_3$) 3025, 2958, 1732, and 1439 cm^{-1}; δ_H (200MHz) 5.69 (2H, s, C(5)H, C(8)H), 3.68 (6H, s, OMe), 3.12-3.0 (2H, m, C(2)H, C(3)H), and 2.65-1.95 (8H, m, C(1)H, C(4)H and C(6)H, C(7)H); m/z 250 (M^+, 20%), 248 (11), 190 (43), 188 (34), 131 (100), 129 (99), and 91 (31).

c. FVP of 1,7:9,10-Tetradehydro-9,10-dimethoxycarbonyl-4-thiatricyclo$[5.4.0.0^{2,6}]$undec-1,9-diene 4,4-dioxide

(i) FVP at 550°C

FVP of the title compound (64 mg, 550°C, 7×10^{-3}mmHg, inlet 180°C) gave a pale yellow liquid ^{1}H n.m.r. of which was consistent with 2,3-dimethoxycarbonyl-1,4,6,7-tetrahydronaphthalene (27 mg, 54% by calibration of ^{1}H n.m.r. with cyclohexane). The impurity in the n.m.r. spectrum was later identified as being 2,3-dimethoxycarbonyl-5,6-dihydronaphthalene. δ_H (80 MHz) 5.8-5.73 (2H, m, C(5)H, C(8)H), 3.8 (6H, s, OMe), 3.03 (4H, s, C(1)H, C(4)H), and 2.28-2.02 (4H, m, C(6)H, C(7)H).

On repeating the pyrolysis at 500°C, a similar ^{1}H n.m.r. spectrum was obtained.

(ii) FVP at 700°C

FVP of the title compound (32 mg, 700°C, 6×10^{-3}mmHg, inlet 180°C) gave 2,3-dimethoxycarbonyl-5,6-dihydronaphthalene (25 mg, 88% by calibration of ^{1}H n.m.r. with methylene chloride) as a pale yellow liquid; (Found: M^+ 246.087574. $C_{14}H_{14}O_4$ requires 246.089202); δ_H (200MHz) 7.44 (1H, s, C(1)H), 7.32 (1H, s, C(4)H), 6.49-6.43 (1H, d of t, C(8)H, $J_{7,8}$ 9.65Hz, $J_{6,8}$ 1.73Hz), 6.20-6.11 (1H, overlapping triplets, C(7)H, $J_{7,8}$ 9.65Hz, $J_{6,7}$ 4.37Hz), 3.67 (6H, s, OMe), 2.87-2.78 (2H, t, C(5)H, J 8.27Hz), and 2.28-2.39 (2H, m, C(6)H); m/z 246 (M^+, 66%), 215 (83), 188 (71), 129 (100), and 128 (89).

(iii) FVP at 550° + silica wool in furnace tube

FVP of the title compound (28 mg, 550°C + silica wool, 7×10^{-3}mmHg, inlet 180°C) gave a colourless liquid, ^{1}H n.m.r. (80MHz) of which showed the presence of a mixture of the diesters 2,3-dimethoxycarbonyl-1,4,6,7-tetrahydronaphthalene, 2,3-dimethoxycarbonyl-5,6-dihydronaphthalene and 2,3-dimethoxycarbonyl-1,4-dihydronaphthalene[142].

d. FVP of 1,7-Dehydro-9,10-tetracyano-4-thiatricyclo [5.4.0.0^{2,6}]undecene 4,4-dioxide

FVP of the title compound (44 mg, 550°C. 6×10^{-3}mmHg, inlet 220°C) gave a pale brown solid and some polymer. Purification by preparative t.l.c. (alumina, ether) gave a pale yellow crystalline solid (21 mg, 61%), MS of which was consistent with 2,3-tetracyano-1,2,3,4,6,7-hexahydronaphthalene but ^{1}H n.m.r. indicated a possible mixture of isomers; δ_H (200MHz) 6.02-5.89 and 5.71-5.62 (2H, m), 3.21 and 3.1 (4H, both br.s), and 2.35-2.13 (4H, m); m/z 234 (M^+, 44%), 106 (70), and 91 (100).

e. FVP of 1,7-Dehydro-11-phenyl-9,11,13-triazolidine-10,12-dione-4-thiatetracyclo[7.5.0.0^{2,6}0^{9,13}]tetradecene 4,4-dioxide

FVP of the title compound (88 mg, 500°C, 8x10^{-3}mmHg, inlet 225°C) gave 5-phenyl-3,5,7-triazolidine-4,6-dione-5-azatricyclo[7.4.0.0^{3,7}]trideca-9,13-diene (40 mg, 56%) as a pale brown crystalline solid, m.p.141-142°C (Found: C, 68.35; H, 5.2; N, 14.7. $C_{16}H_{15}N_3O_2$ requires C, 68.3; H, 5.35; N, 14.95%); ν_{max} 1764, 1710, 1596, 1299, 1251, 1136, 796, 769, 738, 724, 693, and 643 cm^{-1}; δ_H (200MHz) 7.53-7.34 (5H, m), 5.83 (2H, br.s), 4.32 (4H, br.s, J1.2Hz), and 2.19 (4H, br.s, J2Hz), m/z 281 (M$^+$, 100%), 134 (16), 121 (27), 119 (19), 105 (24), and 91 (53).

f. FVP of 1,7-Dehydro-10,12-dioxo-4-thia-11-aza-tetracyclo [7.5.0.0^{2,6}0^{9,13}]tetradecene 4,4-dioxide

FVP of the title compound (47 mg, 500°C, 8x10^{-3}mmHg, inlet 230°C) gave a colourless solid MS of which was consistent with 4,6-dioxo-5-azatricyclo[7.4.0.0^{3,7}]trideca-1,9-diene but ^{1}H n.m.r. indicated a mixture of isomers; ν_{max} 3160, 1780, 1703, 1168, and 1024 cm^{-1}; δ_H (80MHz) 8.85-8.55 (1H, br.s), 5.87-5.5 (2H, m) and 3.4-2.0 (10H, m); m/z 203 (M$^+$, 100%), 202 (75), 131 (47), and 91 (62).

4. Dehydrogenation - in solution and in gas phase

a. Attempted Dehydrogenation of 1,7:9,10-Tetradehydro-9,10-Dimethoxycarbonyl-4-thiatricyclo[5.4.0.0^{2,6}] undeca-1,9-diene 4,4-dioxide

Using the reaction conditions of Butler and Snow[142], a solution of 1,7:9,10-tetradehydro-9,10-dimethoxycarbonyl-4-thiatricyclo[5.4.0.$0^{2,6}$]undeca-1,9-diene 4,4-dioxide (63 mg, 0.2 mmol) and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ, 55 mg, 0.24 mmol) in dry benzene (5 ml) was stirred at room temperature for 24 h. On filtration and evaporation of solvent from the filtrate, the product recovered was identified as starting material. Refluxing the diester with DDQ in solvents such as benzene and toluene for reaction times up to 30 h were also unsuccessful.

A further attempt was made by heating a solution of the diester in dry benzene with an excess of palladium on charcoal catalyst under reflux with stirring under nitrogen. After 24 h, a pale yellow solid was obtained but was found to be mainly starting material by ^{1}H n.m.r.

b. <u>Dehydrogenation of 2,3-Dimethoxycarbonyl-5,6-dihydronaphthalene</u>

A mixture of 2,3-dimethoxycarbonyl-5,6-dihydronaphthalene (22 mg) and an excess of palladium on charcoal (10%, 20 mg) in dry benzene (10 ml) was heated under reflux with stirring under nitrogen for 24 h. ^{1}H n.m.r. showed that the dihydro-ester had been completely dehydrogenated to <u>2,3-dimethoxycarbonylnaphthalene</u>; δ_H (80MHz) 8.25 (2H, s), 7.99-7.55 (4H, m) and 3.95 (6H, s). (lit.,[142] δ_H (CCl_4) 8.18 (2H, s), 7.95-7.44 (4H, m) and 3.88 (6H, s)).

c. Tandem FVP and Dehydrogenation

(i) FVP of 1,7:9,10-Tetradehydro-9,10-dimethoxycarbonyl-4-thiatricyclo[5.4.0.0^{2,6}]undeca-1,9-diene 4,4-dioxide over dehydrogenation catalyst

FVP of the title compound (50 mg, 500°C, 9x10^{-3}mmHg, inlet 180°C) over a catalyst bed of palladium on activated carbon (5.2%Pd, 10g) gave a colourless solid. ^{1}H n.m.r. showed the absence of the methyl ester groups and i.r. and MS indicated the product to be 2,3-naphthalenedicarboxylic anhydride. ^{1}H n.m.r. also indicated the presence of naphthalene as the major product; δ_H (80MHz) 8.54 (2H, s), 8.20-8.08 (2H, m), 7.94-7.73 (21H, m), and 7.57-7.39 (19H, m); m/z 198 (M^+, 82%), 154 (50) and 126 (100) (lit.,[143] m/z (900°C) 198, 178, 154, 142, 128 (100%), 126, 116, 102, 92, and 78).

(ii) FVP of 2,3-Dimethoxycarbonylnaphthalene over dehydrogenation catalyst

FVP of the title compound (50 mg, 500°C, 7x10^{-3}mmHg, inlet 180°C) over palladium on activated carbon (5.2% Pd, 10 g) gave a colourless solid. Again ^{1}H n.m.r. showed that the methyl ester groups had been eliminated on pyrolysis. The major product was 2,3-naphthalenedicarboxylic anhydride, the other aromatic product was not identified; δ_H (80Hz) 8.53 (2H, s), 8.23-8.08 (2H, m), 7.89-7.73 (4H, m), and 7.51-7.28 (5H, m).

Attempts to examine the pyrolysate by GC using a variety of columns were unsuccessful. FVP of the title compound at 500°C and at 800°C without the catalyst gave unchanged diester.

5. Attempted Nitrene Addition

a. Reaction of Ethoxycarbonylnitrene with 1,9-dehydro-4,6-dioxo-5-oxa-12-thiatetracyclo$[7.5.0.0^{3,7}0^{10,14}]$ tetradecene 12,12-dioxide

The method used was based on that of Senó *et al.*[144]

A solution of 1,9-dehydro-4,6-dioxo-5-oxa-12-thiatetracyclo$[7.5.0.0^{3,7}0^{10,14}]$tetradecene 12,12-dioxide (92 mg, 0.54 mmol), ethyl *p*-nitrobenzenesulphonoxycarbamate (157 mg, 0.54 mmol) and benzyl triethyl-ammonium chloride (13 mg, 0.054 mmol) in methylene chloride (10 ml) was stirred vigorously with 1M aqueous sodium bicarbonate solution (2 ml) for 28 h. After adding water (25 ml), the organic layer was separated, washed with water and dried. Evaporation of solvent gave a yellow oil. ^{1}H n.m.r. and t.l.c. (silica, ether) showed the presence of nitrene byproducts with none of the expected aziridine.

b. Reaction of Ethoxycarbonyl nitrene with 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

A solution of 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide (85 mg, 0.5 mmol), ethyl *p*-nitrobenzenesulphonoxycarbamate (145 mg, 0.5 mmol) and benzyl triethylammonium chloride (12 mg, 0.05 mmol) in methylene chloride (10 ml) was stirred vigorously with 1M aqueous sodium bicarbonate solution (2 ml) for 23 h. Water was added and the organic layer separated and washed with water. After drying, the solvent was evaporated to give a yellow oil. ^{1}H n.m.r. and t.l.c. (silica, ether) showed the presence of unreacted starting material (26 mg) and nitrene byproducts. (Yield estimated from ^1H n.m.r.).

6. FVP of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

FVP of the titled compound (95 mg, 500°C, $9x10^{-3}$mmHg, inlet 180°C) gave a white solid and an orange oil. This was dissolved in deuteriochloroform and analysed by n.m.r. to be a mixture of unreacted starting material (18 mg) and <u>3,4-dimethylene-1,5-hexadiene</u> (24.6 mg, 82%). (Yield from ^1H n.m.r., taking into account recovered starting material and polymer left in inlet).

Pyrolysis at 550°C gave 3,4-dimethylene-1,5-hexadiene without any unreacted starting material. However, low yields were obtained (22%) due to most of the starting sulphone polymerising in the inlet with only 25-56% subliming. To try to overcome this problem, the vertical dropping furnace was used but with no success. δ_H (200MHz) 6.52-6.38 (2H, dd, vinyl) and 5.26-4.95 (8H, 3m, methylene). [lit.,[136] δ_H 6.40 (2H, q) and 5.33-4.94 (8H, 3m)].

7. Reactions of 3,4-Dimethylene-1,5-hexadiene

a. Attempted Dimerisation

A solution of 3,4-dimethylene-1,5-hexadiene (5 mg) in d^6 benzene in a sealed n.m.r. tube was heated in a bath of refluxing benzene. After 1 week, the sample was unchanged by ^1H n.m.r. although some black polymer had formed.

b. Diels-Alder Reactions of 3,4-Dimethylene-1,5-hexadiene

(i) Reaction with Maleic Anhydride

To a solution of 3,4-dimethylene-1,5-hexadiene (3 mg, 0.028 mmol) in d^6 benzene (0.4 ml) in a n.m.r. tube was added an equivalent amount of maleic anhydride (2.8 mg, 0.028 mmol). The tube was sealed and heated in a bath of refluxing benzene for 2 h. The precipitate which had formed was filtered off to give a mixture of the bis- and tris-adduct as a pale brown crystalline solid (4 mg); ν_{max} 1840, 1770, 1705; δ_H (200MHz; CD_3SOCD_3) 6.45 (s), and 4.0-2.2 (m); m/z 302 (M^+ for the addition of two dienophiles, 34%), 274 (19), 230 (60), 201 (55), 157 (61), 155 (60), and 90 (100), presence of m/z 400, 372, and 354 due to the addition of three dienophiles.

(ii) Reaction with 4-Phenyl-3H-1,2,4-triazoline-3,5-dione

To a solution of 3,4-dimethylene-1,5-hexadiene (4 mg, 0.035 mmol) in d^6 benzene (0.4 ml) in a n.m.r. tube was added an excess of 4-phenyl-3H-1,2,4-triazoline-3,5-dione. A yellow precipitate formed immediately and the resulting solid was filtered and washed with chloroform to remove the unreacted red triazoline. The resulting colourless solid, 8,8-bis(3-phenyl-2,4-dioxo-1,3,5-triazolidine-3-azabicyclo[5.4.0]non-7-ene (4 mg, 10%) was insoluble in most solvents, m.p. 280°C (decomp.); ν_{max} 1764, 1695, 1290, 1140, 767, and 722 cm^{-1}; m/z 456 (M^+, 91%), 309 (11), 279 (24), 267 (16), 190 (13), 161 (19), 120 (48), 119 (71), and 91 (100).

(iii) Reaction with Dimethyl Acetylenedicarboxylate

To a solution of 3,4-dimethylene-1,5-hexadiene (4 mg, 0.038 mmol) in $\underline{d}^6$ benzene (0.4 ml) in a n.m.r. tube was added an equimolar amount of dimethyl acetylenedicarboxylate (5.6 mg, 0.039 mmol). The tube was sealed and heated in a bath of refluxing benzene for 6 h, reaction being monitored by ^{1}H n.m.r. Evaporation of solvent left a yellow oil which on trituration with ether gave <u>5,5-bis(2,3-dimethoxycarbonyl-1,4-dihydrobenzene)</u> (7.2 mg, 94%) as a colourless solid, m.p. 142-145°C; δ_H (80MHz) 5.77 (2H, br.s), 3.79 and 3.78 (12H, s) and 3.16 (8H, br.s); m/z 390 (M^+, 19%), 359 (49), 358 (73), 299 (35), 240 (32), 163 (100), and 59 (46).

DISCUSSION

DISCUSSION

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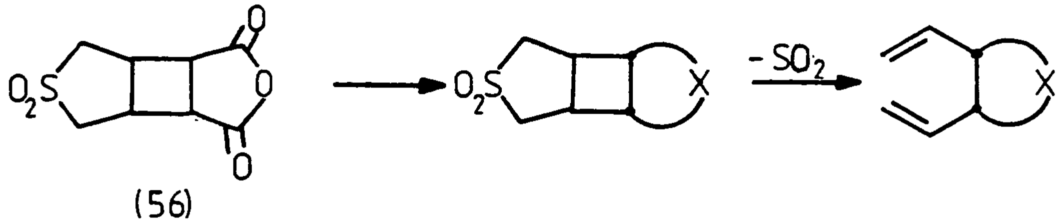
A. Preparation of 3,5-Dioxo-4-oxa-9-thiatricyclo-$[5.3.0.0^{2,6}]$decane 9,9-dioxide and derivatives

B. Flash vacuum pyrolysis of 3,5-Dioxo-4-oxa-9-thiatricyclo$[5.3.0.0^{2,6}]$decane 9,9-dioxide and derivatives

C. Preparation of *cis*-1,2-Divinyl compounds

In 1980, McLaughlin[49,50] showed in these laboratories that flash vacuum pyrolysis (FVP) of the 3-thiabicyclo[3.2.0]-heptane 3,3-dioxide ring system led to extrusion of SO_2 and the formation of *cis*-1,2-divinyl compounds (Scheme 64).



Scheme 64

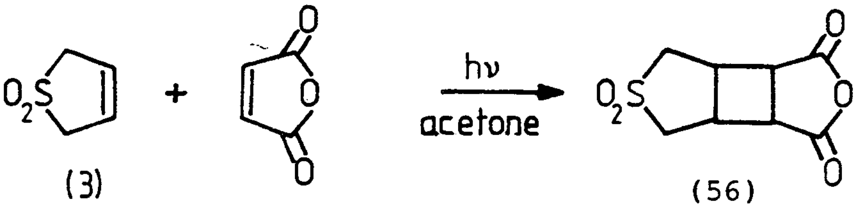
The reaction was stereospecific with no evidence for the formation of *trans*-isomers. As part of these studies, he found that the dimethyl ester (62) gave rise to the *cis,trans*-diene (64) apparently via a Cope rearrangement of the *cis*-1,2-divinyl intermediate (63) (see Scheme 30, p.24). This reaction represented a novel approach to the *cis,trans*-divinylethane grouping which occurs in a number of natural products. The method was particularly noteworthy in that it allowed the stereospecific construction of the carbon-carbon double bonds in a single step from a readily available precursor, e.g. (56).

This thesis describes the extension of these preliminary studies and gives an account of a more detailed investigation into the pyrolysis of 3-thiabicyclo[3.2.0]heptane 3,3-dioxide ring systems under flash vacuum conditions.

A. Preparation of 3,5-Dioxo-4-oxa-9-thiatricyclo$[5,3,0.0^{2,6}]$decane 9,9-dioxide and derivatives

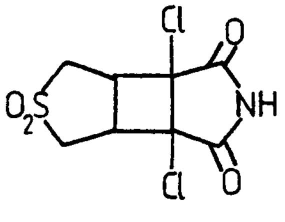
1. 3,5-Dioxo-4-oxa-9-thiatricyclo$[5,3,0,0^{2,6}]$decane 9,9-dioxide

The title compound (56), first reported in 1972 by Shaikhrazieva *et al*,[111] is readily available in 50% yield by the photolysis of 2,5-dihydrothiophen 1,1-dioxide (3) and maleic anhydride for 24 h in acetone (Scheme 65). It is interesting to note that (56) possesses activity as a plant growth inhibitor.[145]

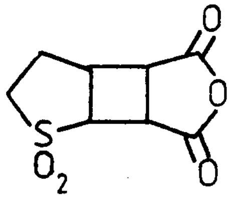


Scheme 65

Earlier reports of the preparation of similar photoadducts such as (123) were made by Scharf and Korte[146] in 1965. The isomeric sulphone (124) has also been prepared recently in these laboratories from the cycloaddition of 2,3-dihydrothiophen 1,1-dioxide and maleic anhydride, albeit in low yield.[147]



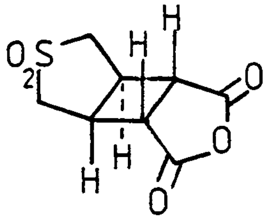
(123)



(124)

^{1}H and ^{13}C N.m.r. spectroscopy provided little information about the stereochemistry of (56), although its four line carbon spectrum indicated that there is either a *syn* or *anti* structure.

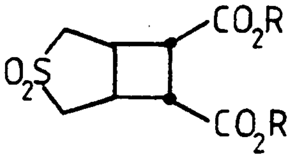
From X-ray analysis of the *N*-phenylimide derivative, McLaughlin[50] established an *anti*-configuration and it is presumed that derivatives from the anhydride (56) are formed with retention of configuration.



(56)

2. Preparation of the diacid, diesters (and epimers) of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

The diacid (62; R=H) was prepared in 96% yield by boiling the anhydride (56) in water. The diesters (62; R=CH_3, C_2H_5, CH_2Ph) were obtained by heating the anhydride (56) in an excess of alcohol containing a trace of sulphuric acid. However, attempts to prepare the diacid chloride with thionyl chloride from either the diacid (62; R=H) or anhydride (56) resulted in recovery of the anhydride.

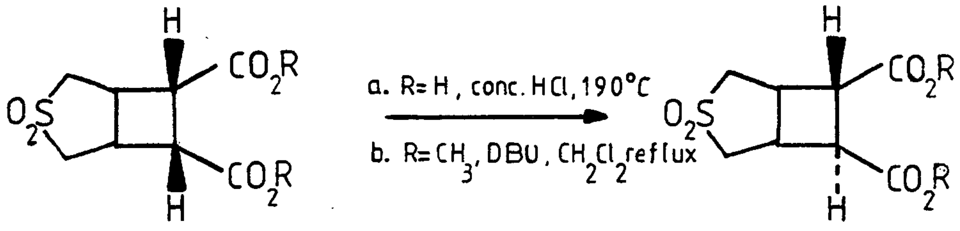


(62)

The diacid and diesters (62) all have *cis* stereochemistry at the 6,7-bond as a consequence of the symmetrical nature of the anhydride ring. The preferred method for epimerisation of the 6,7-bond of the diacid (62; R=H) was to heat a solution of

(62; R=H) in conc. hydrochloric acid in a sealed tube at 190°C.[126] From a comparison of the ^{13}C n.m.r. spectrum with that of the *cis*-epimer, the extent of epimerisation to the *trans*-form was calculated as 82%.

Similar epimerisation of the dimethyl ester (62; $R=CH_3$) by boiling in methylene chloride with DBU gave 85% *trans*-epimer (125; $R=CH_3$) by ^{13}C n.m.r. spectroscopy (Scheme 66). A comparison of the ^{13}C n.m.r. spectra of the *cis*- and *trans*-epimers, (62; $R=CH_3$) and (125; $R=CH_3$), are shown in Figure 7. An expansion of the signals in the 20-60δ region of the δ_C spectrum of (125; $R=CH_3$) is included. The epimers could not be separated by chromatography nor could complete epimerisation be achieved by this method. However, it has been previously reported that base catalysed equilibrations of cyclic esters yield an equilibrium mixture which reflects the relative stabilities of the *cis*- and *trans*-compounds.[148]

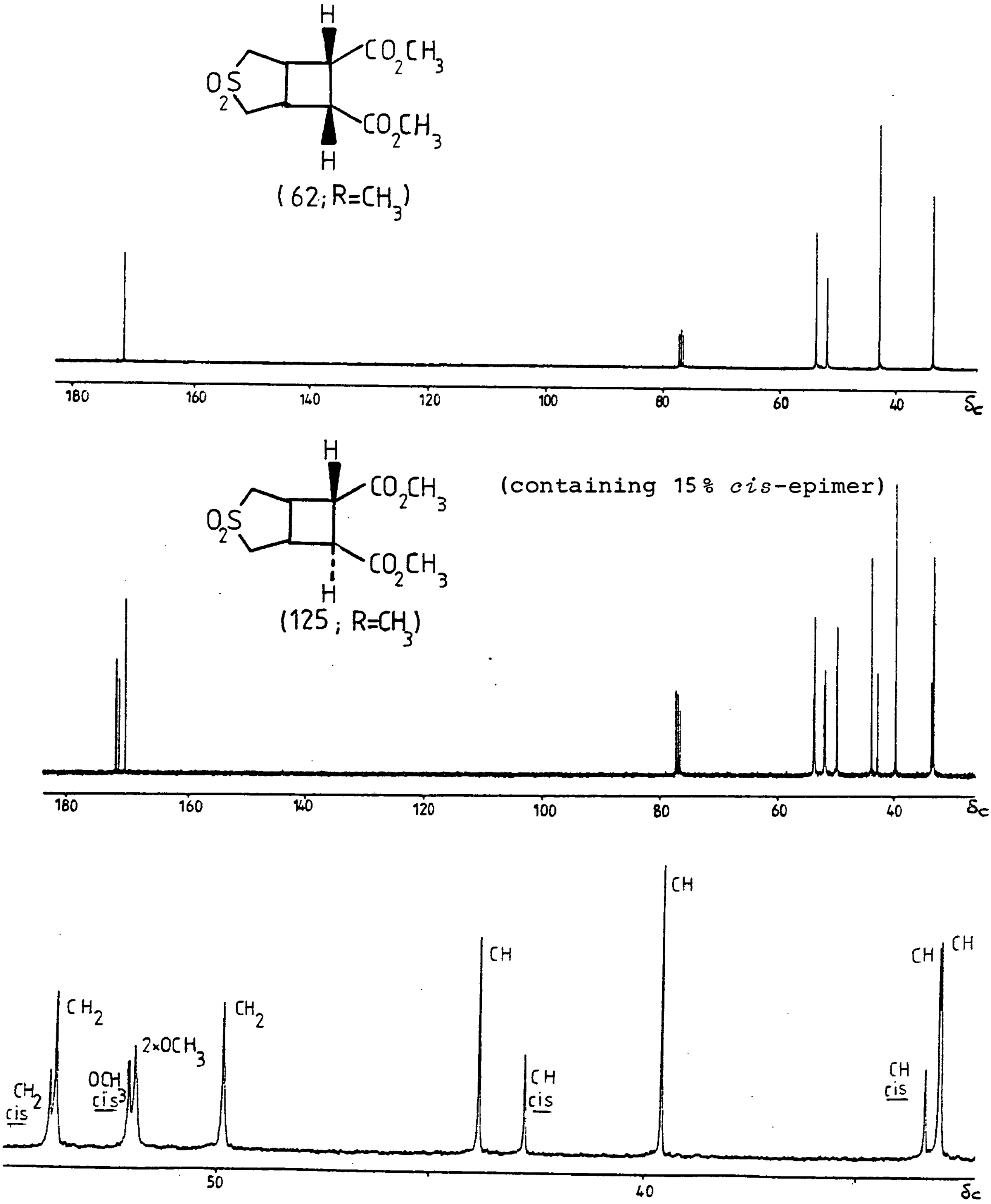


(62) (125)

$R=CH_3$		$R=CH_3$		
δ_C ($CDCl_3$)	171.56	δ_C ($CDCl_3$)	172.03	
	53.78		170.47	
	52.01		53.65	43.85
	42.80		51.88	39.59
	33.35		51.84	33.03
			49.85	32.99

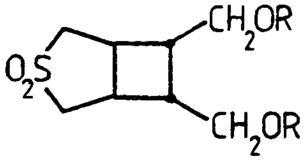
Scheme 66

Fig.7 90MHz ^{13}C N.m.r. spectra of the *cis*- and *trans*-epimers of 6,7-dimethoxycarbonyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide



3. Preparation of 6,7-Dihydroxymethyl-3-thiabicyclo [3.2.0]heptane 3,3-dioxide and its derivatives

Reduction of the dimethyl ester (62; R=CH_3) with lithium aluminium hydride in THF gave a 65% yield of the diol (126; R=H) as a colourless crystalline solid with m.p.97-98°C. This differed from the m.p.75-82°C reported by Shaikhrazieva *et al*[111] but agreed with the data of McLaughlin.[50]

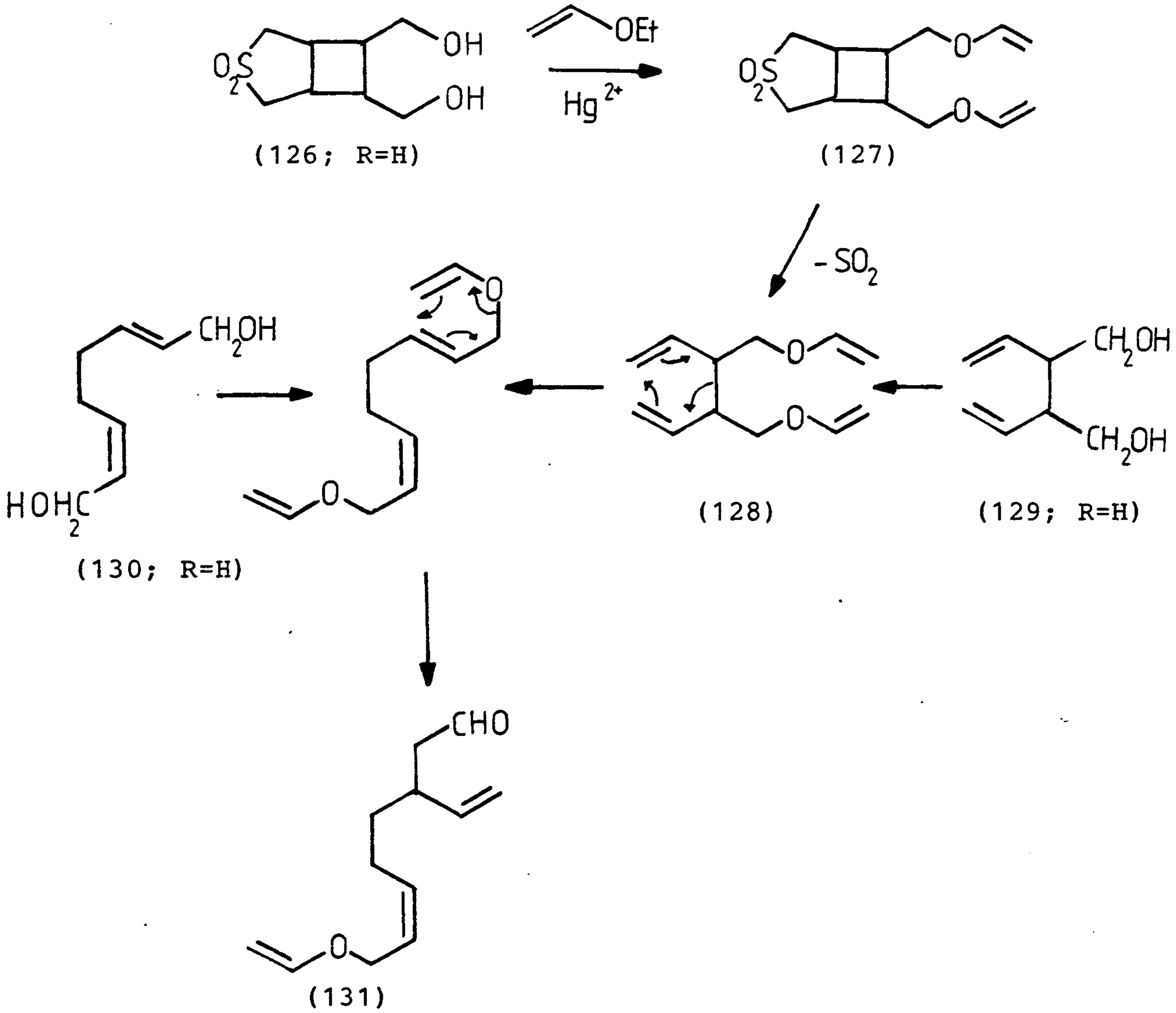


(126)

The corresponding dimethyl ether (126; R=CH_3) was prepared from the diol (126; R=H) by treatment with methyl iodide in the presence of potassium hydroxide in dimethyl sulphoxide.

In accord with McLaughlin's findings,[50] attempted vinylation of the diol (126; R=H) by heating the diol in ethyl or *n*-butyl vinyl ether in the presence of a trace of mercuric acetate and sulphuric acid proved unsuccessful. It was hoped that SO_2 extrusion from the expected product (127) would afford the *cis*-1,2-divinyl compound (128) which could then undergo a Cope-Claisen rearrangement to give the aldehyde (131) as shown in Scheme 67. Such rearrangements are of current interest largely through the work of Ziegler as mentioned in the Introduction (p.47).

McLaughlin[50] also attempted to prepare (128) by vinylation of *meso*-3,4-dihydroxymethyl-1,5-hexadiene (129) using the same method. ^1H and ^{13}C n.m.r. spectra of the product were consistent with the structure of (128) but analytical data was not



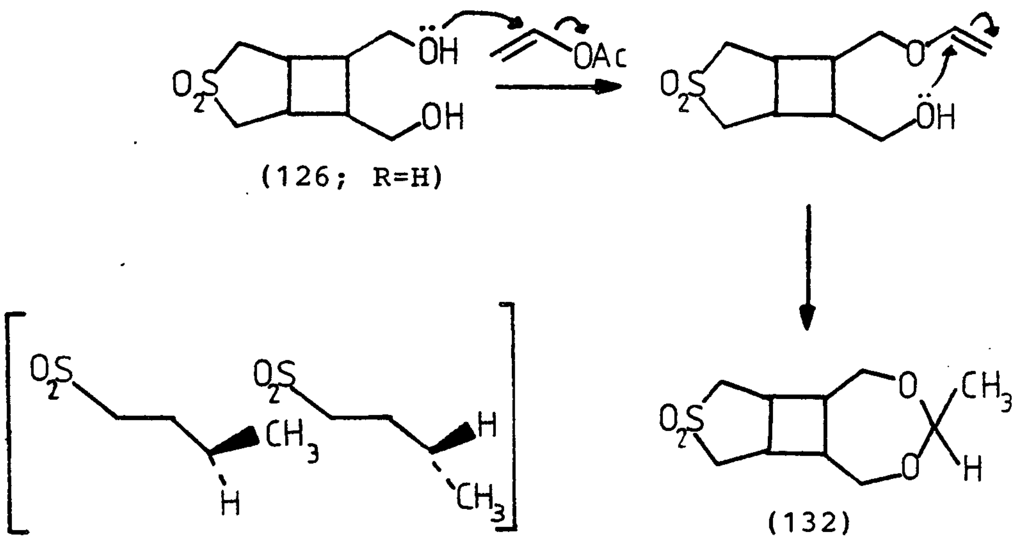
Scheme 67

obtained owing to the volatile nature of the compound. On pyrolysis of this product at 500°C, the pyrolysate contained an aldehyde function by ^{1}H n.m.r. spectroscopy thus indicating that (128) may have undergone a tandem Cope-Claisen rearrangement. However, the product was not positively identified.

Vinylation of *cis,trans*-octa-2,6-diene-1,8-diol (130) was also attempted. After boiling in ethyl vinyl ether for 6 days, the product was isolated as a sweet smelling oil and gave a complicated ^{1}H n.m.r. spectrum (no aldehyde resonances). T.l.c.

indicated the presence of at least two compounds.

When the solvent was changed to vinyl acetate, the product obtained from the sulphone (126; R=H) after heating under reflux for 3 h was identified as 5-methyl-4,6-dioxa-11-thiatricyclo-$[7.3.0.0^{2,8}]$dodecane 11,11-dioxide (132) (Scheme 68). This cyclic acetal (132), formed in 77% yield, was shown by ^{1}H and ^{13}C n.m.r. spectroscopy to consist of a mixture of two isomers with different configurations of the methyl groups. The formation of acetals by the acid catalysed addition of an alcohol to a vinyl ether is a common competing reaction to the formation of the vinyl ether of the alcohol.[149]



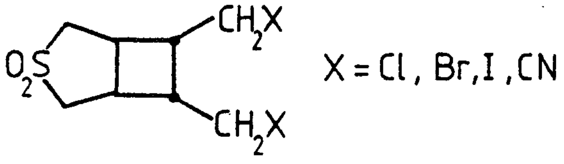
Scheme 68

The diol (126; R=H) was also converted into the bis(*p*-toluenesulphonate) (126; R=SO_2PhCH_3) by treatment with *p*-toluenesulphonyl chloride in pyridine at 0°C. Occasionally, dehydration of the diol occurred to give the cyclic ether as a by-product but the use of an excess of *p*-toluenesulphonyl chloride led to a repression of the undesired ether formation.[150]

With the intention of preparing the dibromide (133; X=Br), the diol was reacted with hydrogen bromide in glacial acetic acid but the product, by spectroscopic and analytical data, was found to be the diacetate (126; $R=COCH_3$), formed in 63% yield.

4. Preparation of the dihalides and dinitrile from 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

The dibromide (133; X=Br) was successfully obtained from the bis(*p*-toluenesulphonate) (126; $R=SO_2PhCH_3$) in 35% yield by treatment with sodium bromide in ethylene glycol at 140°C. A much better yield of 80% was obtained in the case of the dichloride (133; X=Cl) which was prepared from the diol (126; R=H) by treatment with thionyl chloride. The di-iodide (133; X=I) was also prepared from the bis(*p*-toluenesulphonate) (126; $R=SO_2PhCH_3$) in 78% yield by reaction with sodium iodide in boiling methyl ethyl ketone.

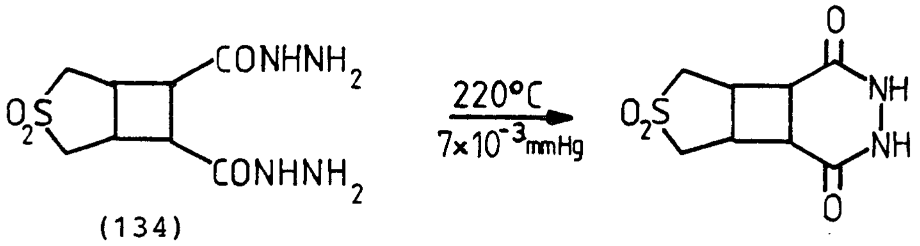


(133)

Treatment of the bis(*p*-toluenesulphonate) (126; $R=SO_2PhCH_3$) with potassium cyanide in boiling ethanol or in dimethyl sulphoxide at room temperature gave the dinitrile (133; X=CN) in good yield.

5. Preparation of the dihydrazide, cyclic hydrazide imide and *N*-aminoimide of 3-Thiabicyclo[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide

The dihydrazide (134) was prepared from the dimethyl ester in accordance with the method of Shaikhrazieva *et al*[111] who reported a m.p. of 220-222°C which was much lower than the value of 239-241°C obtained. By heating the dihydrazide (134) at 220°C at 7×10^{-3} mmHg, loss of hydrazine hydrate occurred to give the cyclic hydrazide (135), whose i.r. and m.p. were in good agreement with literature values[111] (Scheme 69).



(134)

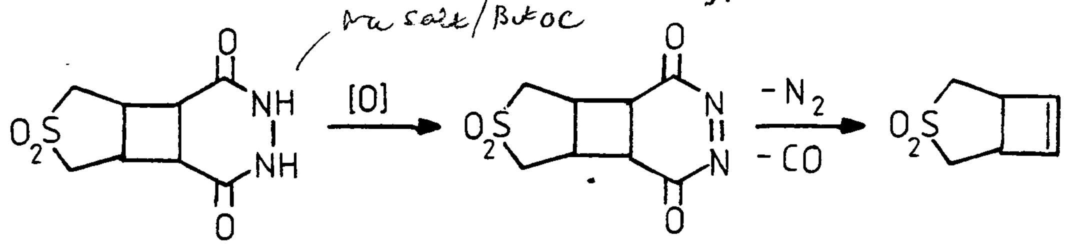
(135)

Scheme 69

Attempts to oxidise (135) using either lead tetraacetate, mercuric oxide or silver carbonate failed, in all cases unchanged starting material was recovered. The aim was to prepare the alkene (122) via loss of nitrogen and carbon monoxide from the α,α-dicarbonylazo intermediate (136) (Scheme 70). The alkene (122) has previously been prepared in these laboratories by the oxidative bis-decarboxylation of the diacid (62; R=H) and, by functionalisation of the double bond followed by FVP, has provided access to a range of *cis*-1,2-divinyl compounds and their Cope-derived products (see Scheme 62, p.50).[151]

It is worth noting that cyclic α-carbonyl azo compounds are known to be highly reactive species which polymerise readily on attempted isolation but may add to conjugated dienes.[152]

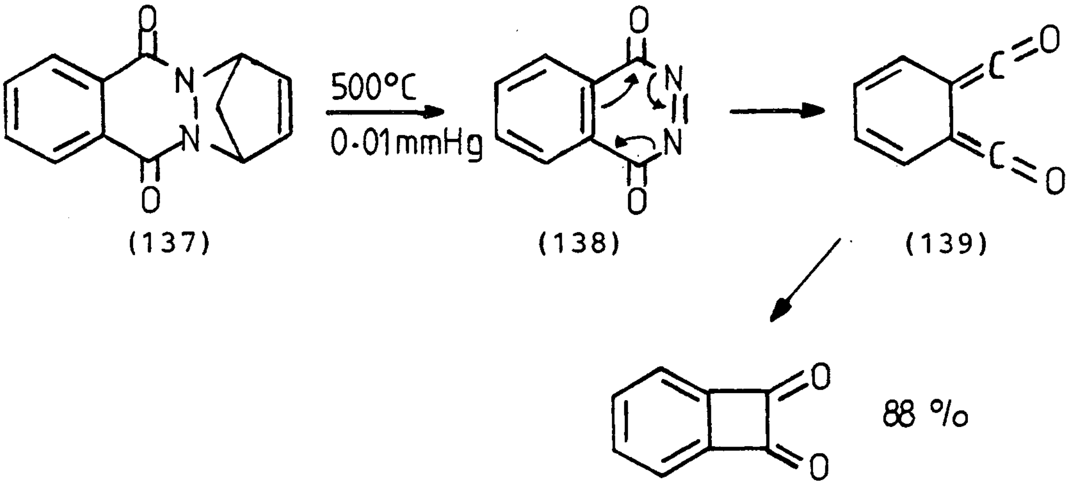
C.T. Moody.



(135) (136) (122)

Scheme 70

Gilchrist and Rees[153] have generated α-carbonyl azo compounds by FVP of their Diels-Alder adducts with a conjugated diene. For example, pyrolysis of the cyclopentadiene adduct (137) of phthalazine-1,4-dione (138) yielded benzocyclobutenedione (140) by nitrogen extrusion and ring closure of the bis-keten (139) as shown in Scheme 71.

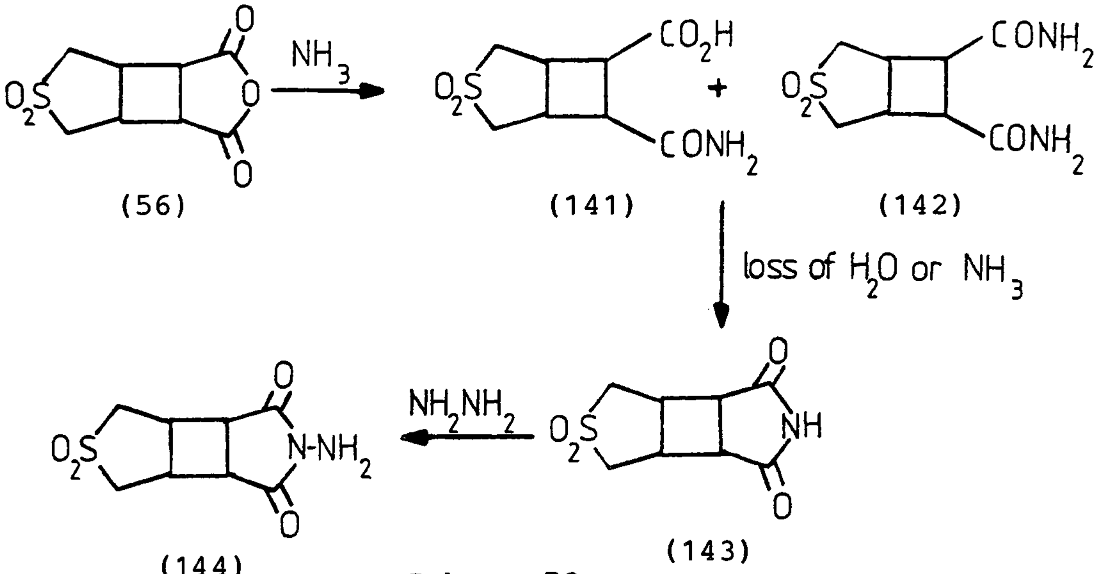


(137) (138) (139)

(140)

Scheme 71

The imide (143) was prepared according to the method of Shaikhrazieva *et al*[111] by the photolysis of butadiene sulphone (3) and maleimide in acetone containing acetophenone as sensitiser. An alternative method of preparation involved treatment of the anhydride (56) with 0.88 ammonia solution although the procedure gave a mixture of the mono- and diamide on the basis of elemental analysis. Chromatographic separation of these highly polar amides was not possible whilst sublimation resulted in loss of water or ammonia to give the imide (143) which was identified by comparison of its i.r. spectrum with literature data[111] (Scheme 72).

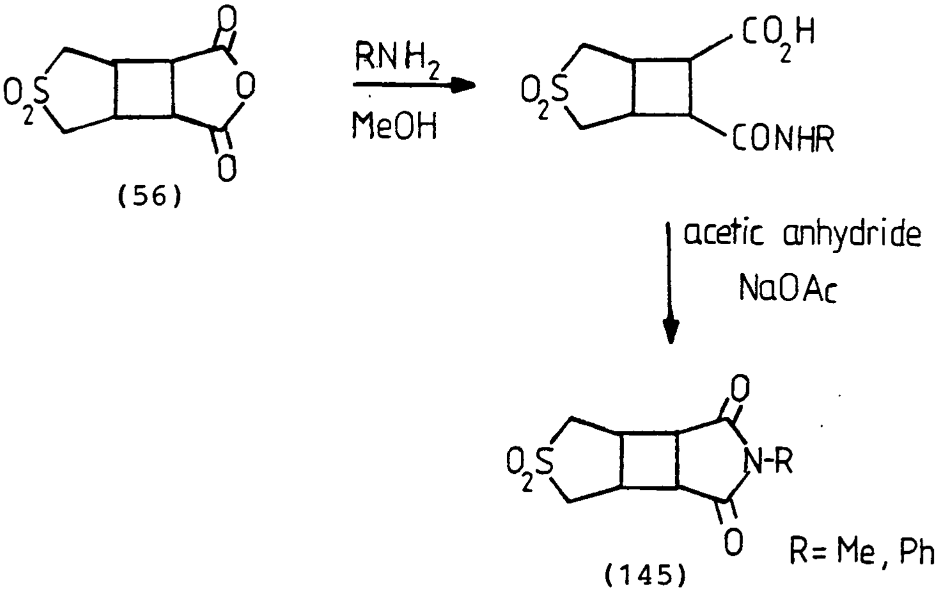


Scheme 72

The *N*-amino compound (144) was prepared from the imide (143) by reaction with an equimolar amount of hydrazine hydrate. Although the m.p. 230-232°C was identical to that obtained for the aforementioned six-membered ring isomer (135), its i.r. spectrum was consistent with the proposed structure. Thus its i.r. spectrum showed absorptions at 1780, 1660, and 1614 cm^{-1} whereas the cyclic hydrazide (135) absorbed at 1783, 1710, and 1613 cm^{-1}. Both compounds showed strong bands in the region of 1300-1320 and 1140-1160 cm^{-1} which are typical of the sulphone grouping.

Oxidation of (144) with mercuric oxide gave a colourless solid which was not identified.

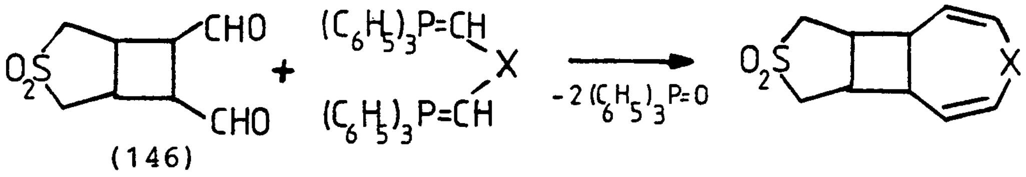
Hitherto, adducts of butadiene sulphone (3) with *N*-substituted maleimides have not been prepared due to preferential self-dimerisation of the imides. This problem was overcome by the reaction of the anhydride (56) with the respective amine, for example, aniline and methylamine, followed by dehydration to the cyclic imide (145) (Scheme 73).[50,111]



Scheme 73

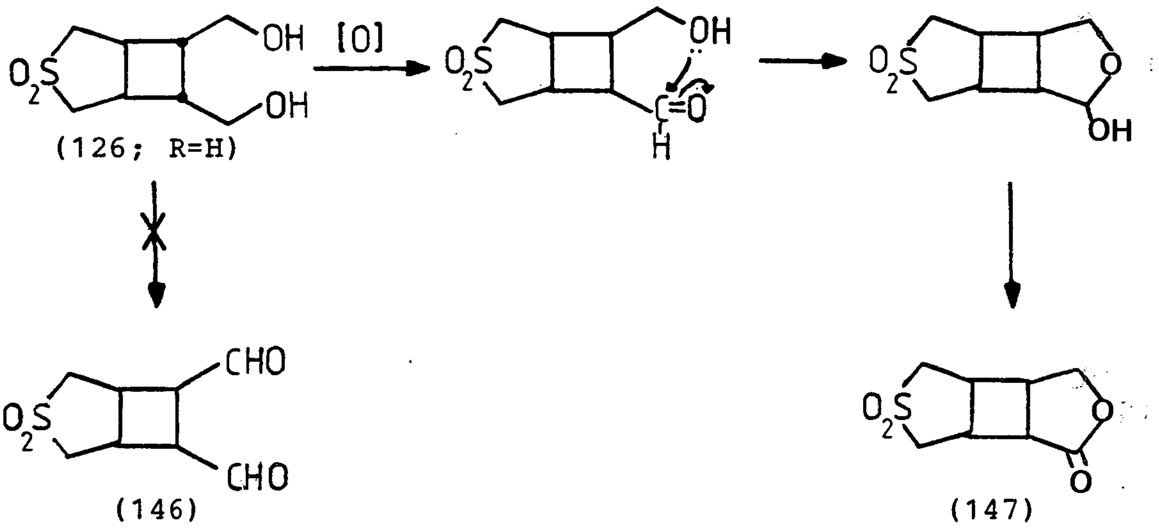
6. Attempted oxidation of 6,7-Dihydroxymethyl-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide

The dialdehyde (146) was considered to be a useful starting material for the preparation of large rings by the bis-Wittig reaction as shown in Scheme 74 (see Section F, p.188). However, all attempts to prepare (146) by oxidation of the diol (126; R=H) proved unsuccessful.



Scheme 74

A variety of oxidising reagents were employed in the oxidation of the *cis*-diol (126; R=H). Thus treatment of the diol with Jones Reagent[121] (CrO_3 in conc. H_2SO_4) gave the lactone (147) which had previously been prepared in these laboratories[49] by sodium borohydride reduction of the anhydride (56) (Scheme 75). The lactone was also formed from the treatment of (126; R=H) with barium manganate[125] but in this instance the reaction was very slow.



Scheme 75

In retrospect, it is not uncommon for the oxidation of 1,4-diols to give good yields of γ-lactones when no stereochemical barrier to cyclisation is present. However, when the configuration of the 1,4-diol is *trans*, cyclisation is inhibited and the corresponding dialdehyde is the favoured product.[154]

The following section describes the behaviour of the 3-thiabicyclo[3.2.0]heptane 3,3-dioxide ring systems so far prepared under FVP extrusion of SO_2.

B. Flash vacuum pyrolysis of 3,5-Dioxo-4-oxa-9-thiatricyclo-[5.3.0.0^{2,6}]decane 9,9-dioxide and derivatives

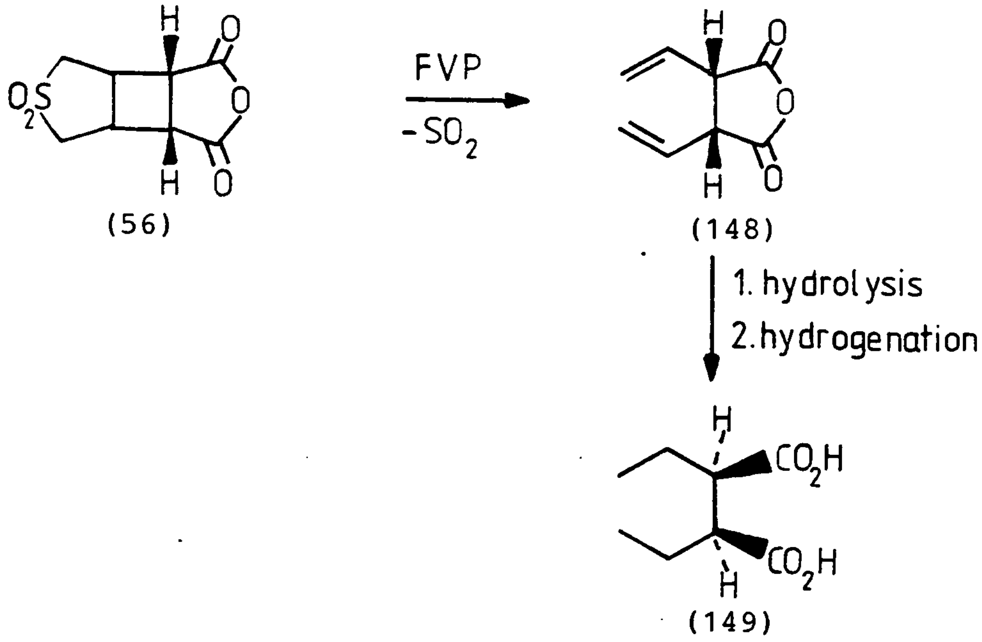
1. FVP of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

Although the anhydride (56) and some derivatives had been prepared previously by Russian workers,[111] no attempt had been made to extrude SO_2 under thermal conditions. Previous work in these laboratories had shown that SO_2 elimination from such sulphones could be achieved and provided a short and stereospecific route to *cis*-1,2-divinyl compounds.[49] As described in the following section (p.157), other methods of generating 1,2-divinyl compounds usually gave rise to mixtures of *cis*- and *trans*-isomers and hitherto no general and stereoselective method for their preparation has been reported.

In order to effect the thermal extrusion of SO_2 cleanly, the technique of flash vacuum pyrolysis (FVP) was the preferred method. FVP has found widespread utility in the production and isolation of thermolabile reaction products and its main advantage over thermolysis in solution or in a melt is that the short contact time involved precludes complicating secondary reactions.[155] Details of the technique are given on p.57.

FVP of the title compound (56) at 630°C gave 2,5-dioxo-*cis*-3,4-divinyltetrahydrofuran (148) in 80% yield in agreement with the findings of McLaughlin[49,50] who validated the *cis* stereochemistry by hydrolysis and hydrogenation of (148) over 10% palladium on charcoal at room temperature (Scheme 76). This resulted in the formation of only *meso*-2,3-diethylsuccinic acid (149) (m.p. 190-191°C (decomp.)) with no evidence for

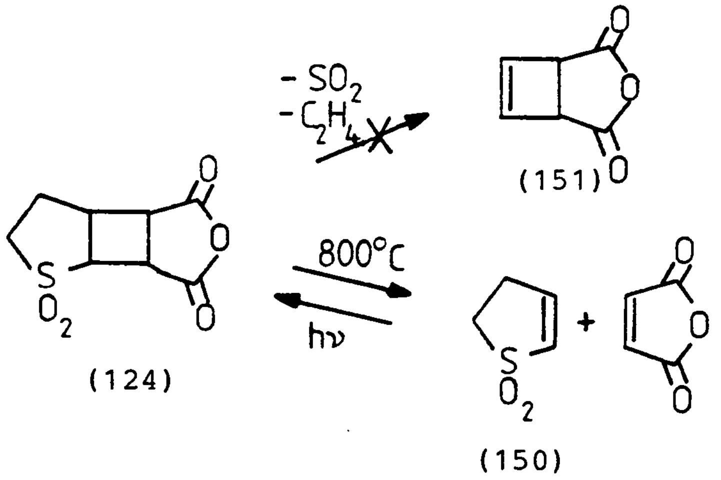
(±)-2,3-diethylsuccinic acid (m.p.129°C)[156] which might have been expected from the corresponding *trans*-1,2-divinyl compound.



Scheme 76

The SO$_2$ elimination from (56) is analogous to the conversion of 3-thiabicyclo[3.1.0]hexane 3,3-dioxide (10) into 1,4-dienes (11)[15], details of which have been given in the Introduction (p.8).

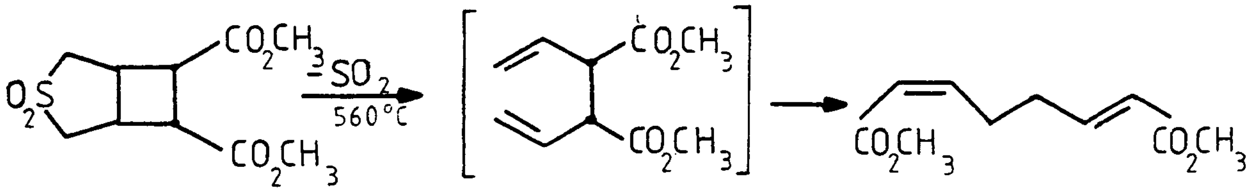
By way of contrast, it is of interest to note that other work in these laboratories has shown that the isomeric sulphone, 3,5-dioxo-4-oxa-8-thiatricyclo[5.3.0.0^{2,6}]decane 8,8-dioxide (124) undergoes a retro [2+2] cycloaddition under FVP conditions to give the reactants from which it is formed by photolysis (Scheme 77).[147] The conjugative effect of SO$_2$ with the double bond in (150) apparently makes this pathway more likely than the alternative extrusion of SO$_2$ with loss of ethylene to the bicyclic anhydride (151).



Scheme 77

2. FVP of the diacid, dimethyl ester (and its epimer) of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.$0^{2,6}$]decane 9,9-dioxide

Like its anhydride, FVP of the diacid (62; R=H) at 575°C gave a *meso*-derivative which was identified as *meso*-1,5-hexadiene-3,4-dicarboxylic acid (63; R=H). This behaviour contrasted markedly with the pyrolysis of its dimethyl ester (62; $R=CH_3$) which resulted in the formation of the straight-chain *cis*,*trans*-dimethyl octa-2,6-diene-1,8-dioate (64) as a colourless liquid in 88% yield (Scheme 30). The structure of the *cis*, *trans*-dienoate (64; $R=CH_3$) was assigned on the basis of spectroscopic data (see Fig.11, p.178), especially by comparison with ^1H n.m.r. literature values[127,128] [δ_H 7.1-6.8 (1H, m), 6.25-6.05 (1H, m), 5.85-5.71 (2H, m), 3.66 (3H, s), 3.67 (3H, s), 2.85-2.65 (2H, m) and 2.45-2.2 (2H, m)]. Further verification of the stereochemistry was provided by isomerisation of (64) to its *trans*,*trans*-isomer (153) by boiling in heptane with iodine (see Scheme 110, p.176).



(62; R=CH_3) (63; R=CH_3) (64; R=CH_3)

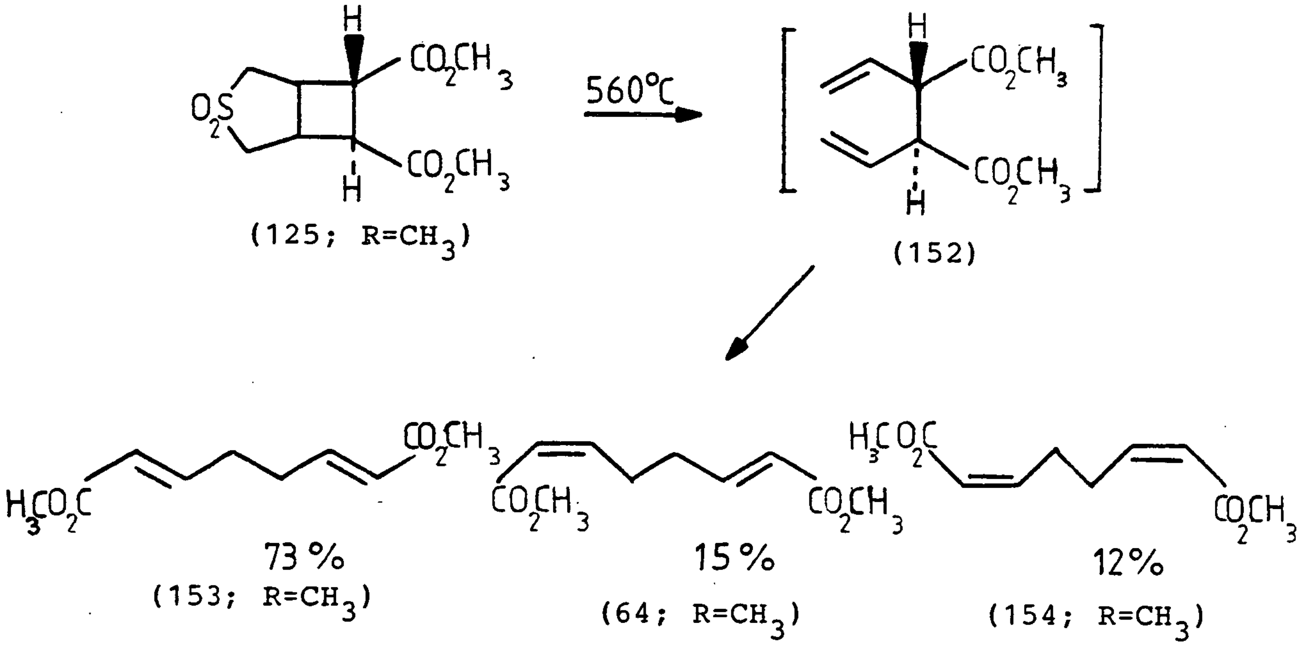
Scheme 30

The formation of (64) can be rationalised by proposing cheletropic loss of SO_2 from the diester (62) to give the intermediate *meso*-3,4-dimethoxycarbonyl-1,5-hexadiene (63) which readily undergoes Cope rearrangement to (64) under the pyrolysis conditions. The *cis*,*trans*-1,5-diene is formed from the *meso*-compound via a chair-like transition state, details of which are discussed in the Introduction (p.28).

Pyrolysis at higher temperatures (600°C) resulted in the formation of minor amounts of aldehyde impurities which were detected by ^{1}H n.m.r. spectroscopy. These are presumably formed by loss of formaldehyde[157] which also occurred during purification of (64) by distillation.

Analysis of the pyrolysate at 560°C by GC (10% PEGA, 180°C) showed that it consisted of 75% *cis*,*trans*-isomer (64) and 25% *trans*,*trans*-isomer (153) but it is quite possible that some isomerisation to the *trans*,*trans*-isomer occurred on the GC column under the conditions of analysis.

Whilst these studies were being undertaken, a report appeared by Williams and Lin[129] who also found that pyrolysis of derivatives of the 3-thiabicyclo[3.2.0]heptane 3,3-dioxide ring system gave *cis*-1,2-divinyl compounds but went on to claim that heating of these compounds, e.g. (63; R=CH_3) caused a Cope rearrangement leading cleanly to *trans*,*trans*-1,5-dienes in high yields. This is at variance with the results obtained above and those of others[52,128] which show that *cis*-1,2-divinyl compounds rearrange, upon heating, with a high degree of stereoselectivity to *cis,trans*-1,5-dienes. In actuality *trans,trans*-1,5-dienes are the major products from the thermal rearrangement of (*dl*)-1,2-divinyl intermediates. Unequivocal evidence on this point, which is discussed in greater detail in Section D.1, was obtained by FVP of the epimer of the dimethyl ester (125; R=CH_3) to give a colourless liquid. This was shown by GC analysis to consist of a mixture of predominantly *trans,trans*-(153) (73%) together with *cis,trans*-(64) (15%) and the *cis,cis*-isomer (154) (12%) (Scheme 78). Since the sulphone (125) consisted of 18% of the *cis*-epimer, this accounts for most of the 15% *cis,trans*-isomer (64) found in the pyrolysate.



(125; R=CH_3)

(152)

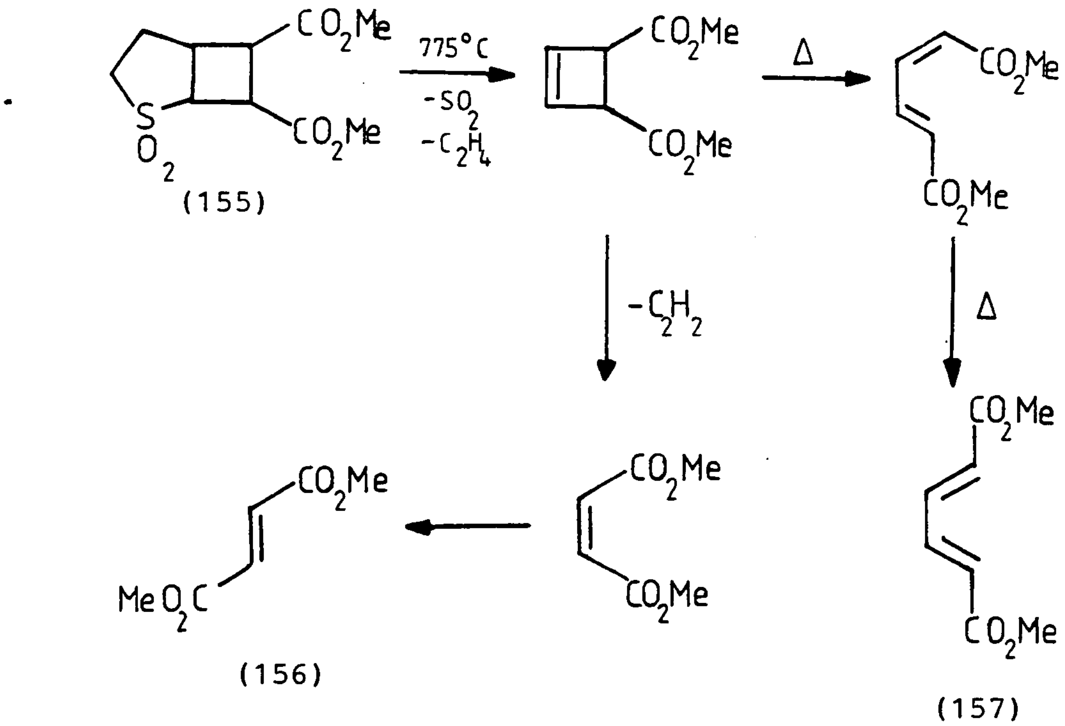
(153; R=CH_3)

(64; R=CH_3)

(154; R=CH_3)

Scheme 78

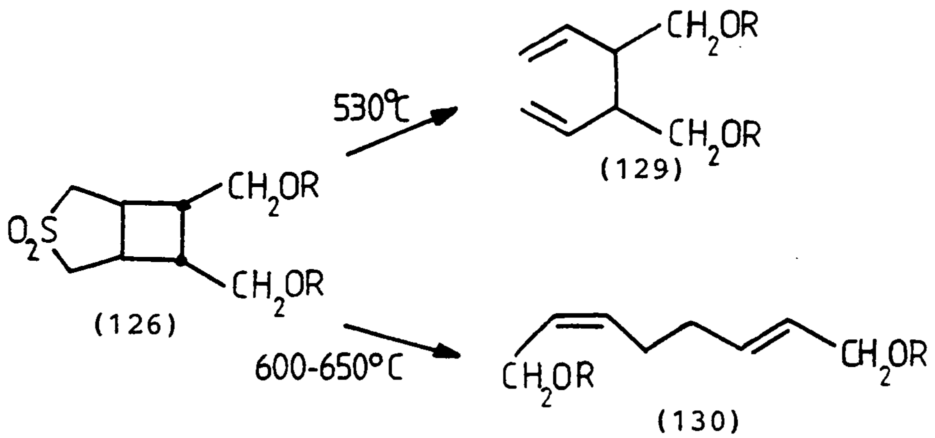
In passing it is of interest to note that pyrolysis of the dimethyl ester of the isomeric sulphone (155) gave a complex mixture of products. From the pyrolysate, Aitken[147] identified both the *trans*-diesters (156) and (157) which were formed from the sulphone (155) by loss of SO_2 and ethylene followed by loss of acetylene (Scheme 79).



Scheme 79

3. FVP of 6,7-Dihydroxymethyl-3-thiabicyclo[3.2.0]heptane 3,3-dioxide and its derivatives

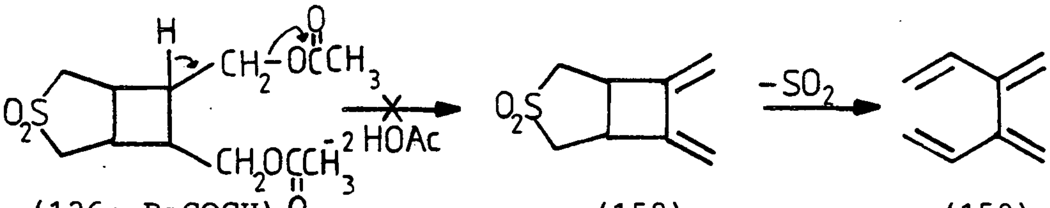
In contrast to the dimethyl ester (62; R=CH_3) just discussed, FVP of the titled diol (126; R=H) at 530°C gave *meso*-3,4-dihydroxymethyl-1,5-hexadiene (129; R=H) in 21% yield. By increasing the contact time in the furnace by pyrolysis over silica rods at 600°C, a Cope rearrangement did occur and the *cis*,*trans*-diene(130; R=H) was obtained in 24% yield (Scheme 80).



Scheme 80

Similar pyrolysis of the dimethyl ether (126; R=CH_3) at 530°C gave the *meso*-derivative (129; R=CH_3) in 60% yield. The *meso*-diacetate (129; R=$COCH_3$) was also obtained from the corresponding sulphone (126; R=$COCH_3$) at 530°C but traces of an impurity, which was identified as the Cope rearrangement product, were also obtained. As an end to identification, the *meso*-compounds (129) were all prepared from the anhydride (148) by conventional synthetic methods as described in the following section.

The diacetate (126; R=$COCH_3$) was also pyrolysed at 650°C with the aim of eliminating acetic acid to give the dimethylene compound (158) (Scheme 81). Instead, pyrolysis resulted in the formation of the straight-chain diacetate (130; R=$COCH_3$) in 27% yield.



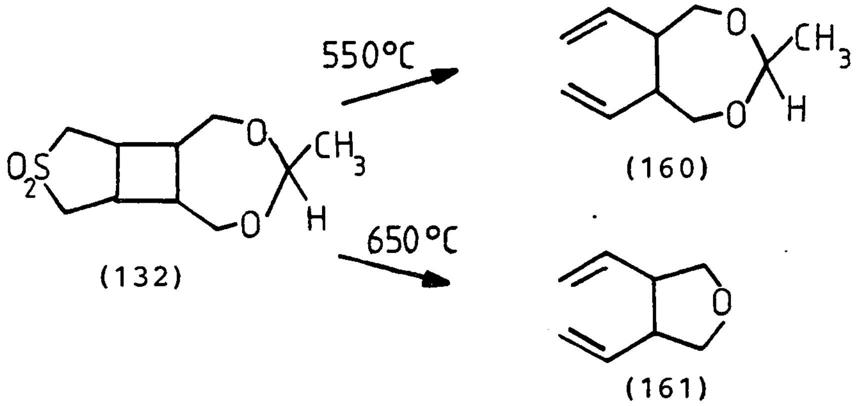
(126; R=$COCH_3$) (158) (159)

Scheme 81

Compound (158) was considered to be of interest not only as a masked form of 3,4-dimethylene-1,5-hexadiene (159) but as a precursor to a variety of cyclic systems via the Diels-Alder reaction. Details of the preparation and chemistry of (158) are given in Section H, p.201.

Pyrolysis of the cyclic acetal (132) was also investigated. GC analysis of the liquid pyrolysate obtained at 550°C showed the presence of four compounds, the major product (74%) of which was tentatively identified by n.m.r. spectroscopy as *cis*-1,7-

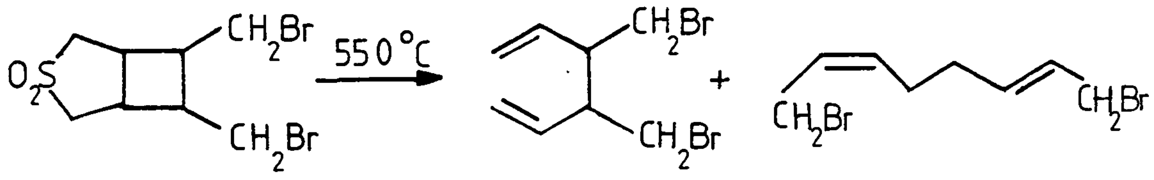
divinyl-3,5-dioxa-4-methylheptane (160) (Scheme 82). Attempts were made to prepare this compound by an independent route (see p.162) and although the product obtained by this route compared favourably with the pyrolysate from (132), it readily decomposed on handling. Comparison of (160) with the only other seven-membered 1,2-divinyl cyclic compound to have been prepared to date (Scheme 51, p.41) indicates a reluctance for such compounds to undergo the Cope rearrangement.



Scheme 82

Pyrolysis of (132) at the higher furnace temperature of 650°C gave *cis*-3,4-divinyltetrahydrofuran (161) as indicated by n.m.r. spectroscopy and GC comparison with an authentic sample. This result verifies that (160) is unstable and at high temperatures readily eliminates acetaldehyde.

FVP of the dibromide (133) at 550°C yielded a *ca* 1:1 mixture of *meso*-(162) and *cis,trans*-(163) by ^{1}H n.m.r. spectroscopy (Scheme 83). On repeating the pyrolysis at 620°C, only polymeric material was obtained.

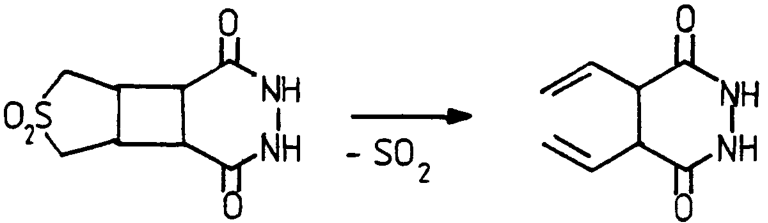


(133; X=Br) (162; X=Br) (163; X=Br)

Scheme 83

4. FVP of the cyclic hydrazide and imide of 3-Thiabicyclo-[3.2.0]heptane-6,7-dicarboxylic acid 3,3-dioxide

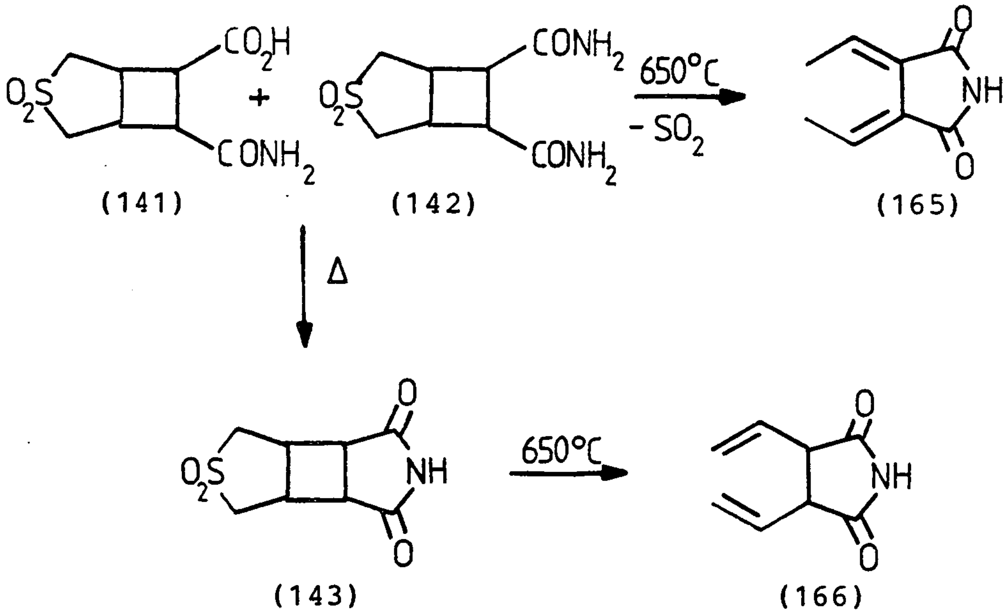
Pyrolysis of the cyclic hydrazide (135) at 600°C gave a 68% yield of the corresponding *cis*-1,2-divinyl compound (164) having the expected analytical and spectroscopic properties (Scheme 84). Its ^{13}C n.m.r. spectrum consisted of 8 lines due to the non-planarity of the six-membered ring whilst careful examination of its ^1H n.m.r. spectrum showed no indication of any product arising from a Cope rearrangement. This is not surprising since to date no six-membered 1,2-divinyl cyclic compounds have been reported to undergo the Cope rearrangement.[52] For example, as noted in the Introduction (p.39), *cis,trans*-1,5-cyclodecadiene isomerises quantitatively at 150°C to *cis*-1,2-divinylcyclohexane.[90]



(135) (164)

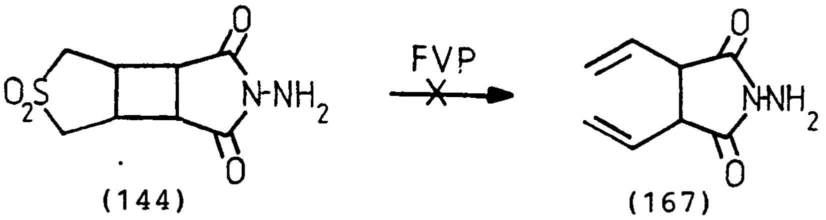
Scheme 84

It was envisaged that pyrolysis of the mixture of the mono- and diamides (141) and (142), prepared by reaction of the anhydride (56) with ammonia solution, might result in the simultaneous loss of SO_2 and water or ammonia to give the divinylimide (166). Analysis of the pyrolysate revealed a mixture of several compounds which were separated by column chromatography over alumina to give 3,4-diethylidene succinimide (165) in 7% yield (Scheme 85). It seems likely that (166) is formed during the pyrolysis but may have rearranged to (165) during column chromatography. Details of the rearrangement of *cis*-1,2-divinyl compounds to 2,4-hexadiene derivatives are given in the next section (p.163).



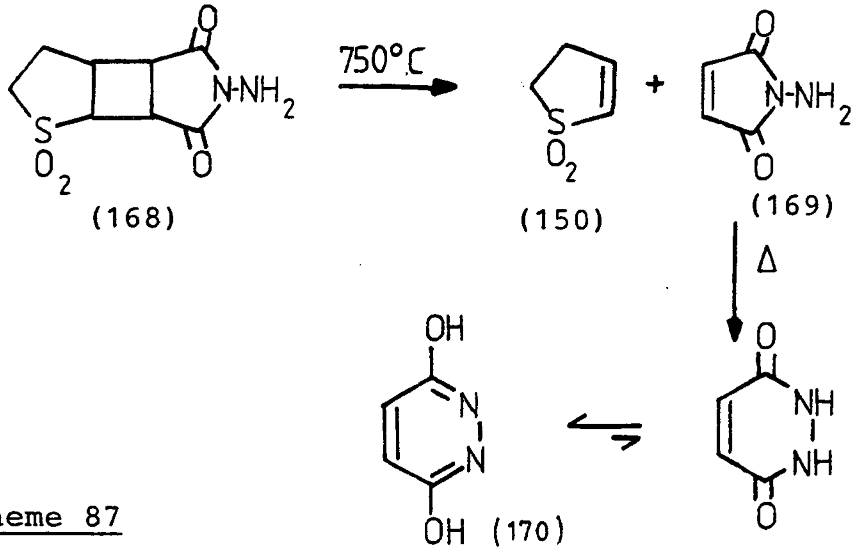
Scheme 85

The desired *cis*-3,4-divinylsuccinimide (166) was eventually prepared in 63% yield by FVP of the imide (143) at 650°C. Under these conditions, the *N*-amino derivative (144) gave a colourless gum whose ^{1}H n.m.r. spectrum was consistent with the corresponding divinyl compound (167) (Scheme 86). However, the sample decomposed on work-up and when the pyrolysis was repeated at different temperatures, various mixtures of products were obtained.



Scheme 86

Other work in these laboratories has shown that pyrolysis of the isomeric *N*-amino sulphone (168) results in a facile retro[2+2]cycloaddition reaction with the formation of *N*-aminomaleimide (169) which rearranges to the more stable dihydroxypyridazine (170) (Scheme 87).[147]



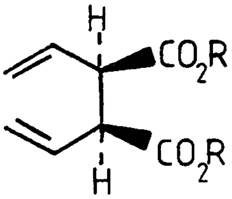
Scheme 87

The results from the pyrolysis of the 3-thiabicyclo-[3.2.0]heptane 3,3-dioxide ring system have shown that *cis*-1,2-divinyl compounds can be generated by loss of SO_2 but only in the case of acyclic (or small ring[151]) analogues does a Cope rearrangement take place.

C. Preparation of *cis*-1,2-Divinyl Compounds

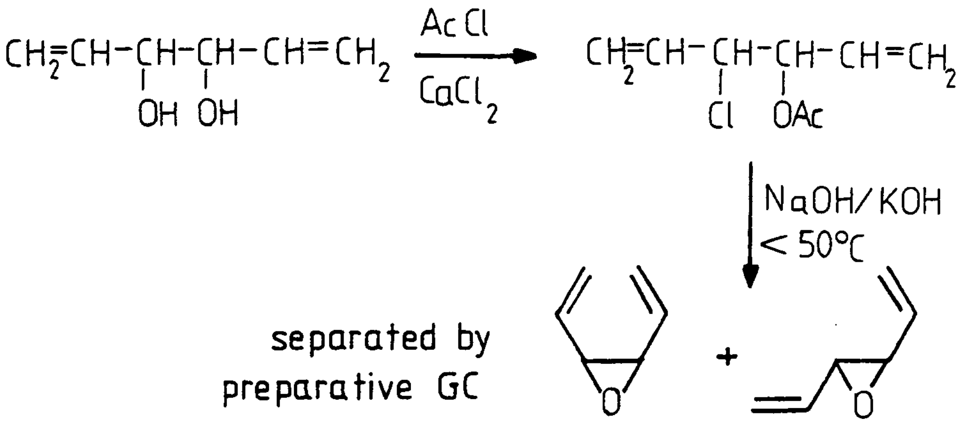
1. Preparation of the diacid and dimethyl ester of 2,5-Dioxo-*cis*-3,4-divinyltetrahydrofuran

The diacid (63; R=H) and its dimethyl ester (63; $R=CH_3$) were prepared by boiling the anhydride (148) in water and an excess of methanol containing a trace of sulphuric acid, respectively. Their analytical and spectroscopic data were in agreement with those obtained by McLaughlin who proposed a *meso* configuration.[50]



(63)

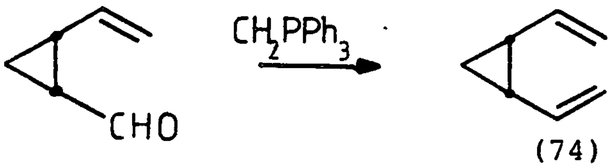
The diester (63; $R=CH_3$) has been previously prepared, albeit in very small yield, from the allylic coupling of methyl-4-bromobut-2-enoate but only as a mixture of its *meso*- and *dl*-diastereoisomers.[130] In comparison to this route the preparation of *cis*-1,2-divinyl systems such as (63) from 3-thiabicyclo-[3.2.0]heptane 3,3-dioxide ring systems by thermal extrusion of SO_2 is short and stereospecific. Indeed, synthetic routes to *cis*-1,2-divinyl systems have hitherto usually led to isomeric mixtures which have been separated often with great difficulty by preparative GC. For example, the *cis*- and *trans*-2,3-divinyloxiranes (171) and (172) respectively, were prepared as a mixture (1:2) by Stogryn[76b] using the route outlined in Scheme 88.



(171) (172)

Scheme 88

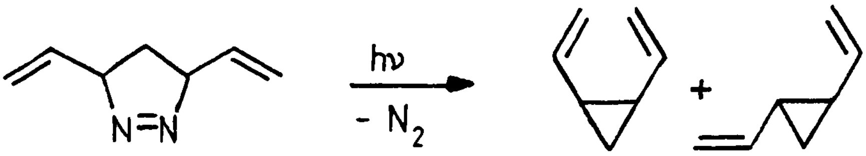
The approach to *cis*-divinylcyclopropane (74) by Brown *et al*[73] has also involved preparative GC to separate isomers. The last step in this synthesis involved the Wittig reaction of *cis*-2-vinylcyclopropane carbaldehyde with methylenetriphenylphosphorane (Scheme 89).



(74)

Scheme 89

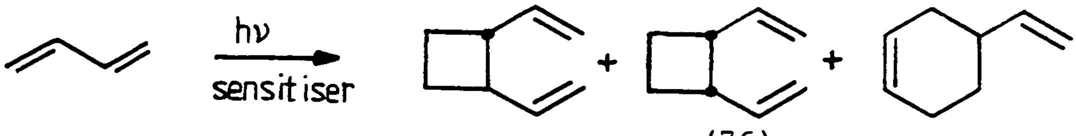
(74) has also been prepared (in an equal mixture with its *trans* isomer) by low temperature photolysis of 3,5-divinylpyrazoline (Scheme 90).[74]



(74)

Scheme 90

Hammond[158] has also reported that photosensitised dimerisation of butadiene gives *trans*-1,2-divinylcyclobutane as the major product along with 4-vinylcyclohexene and a small amount of *cis*-1,2-divinylcyclobutane (Scheme 91).

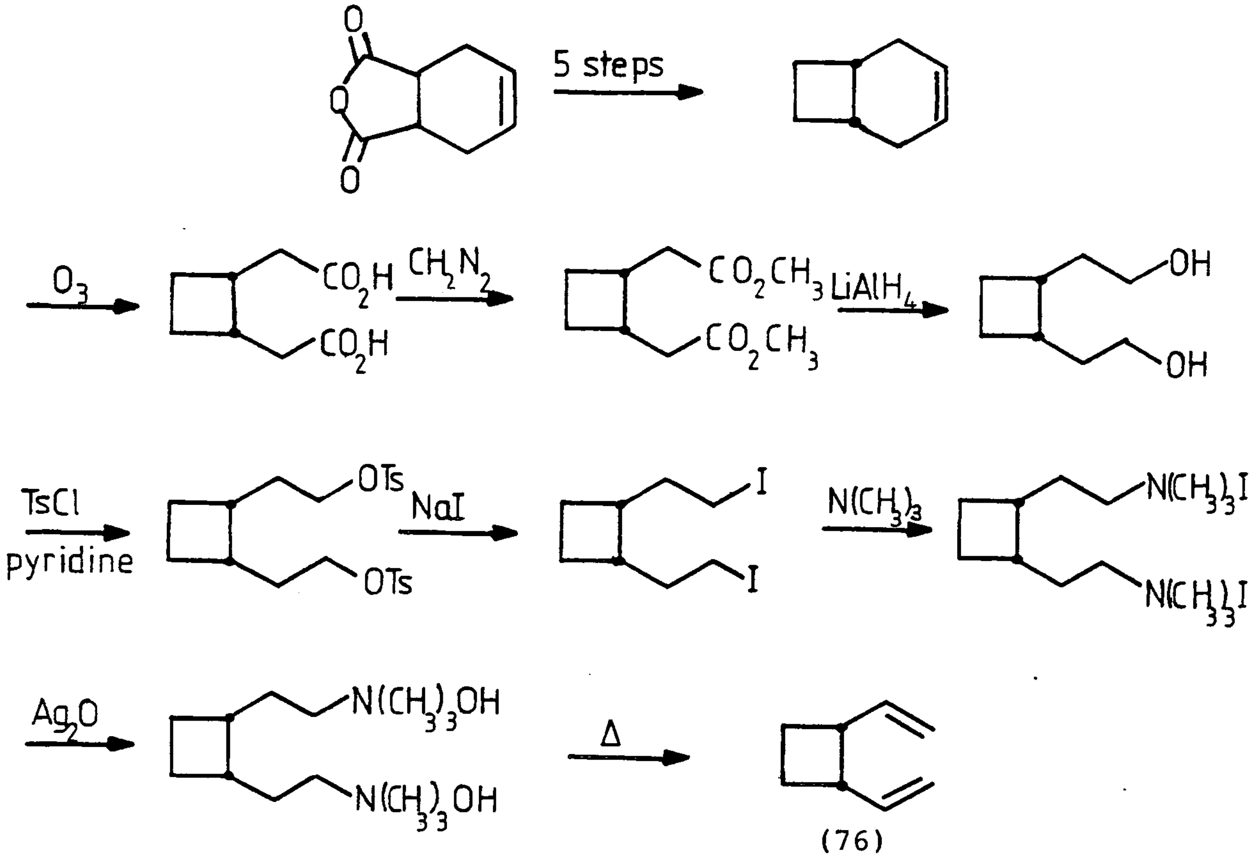


(76)

Scheme 91

One stereospecific synthesis that has been reported is the preparation of *cis*-1,2-divinylcyclohexane (95) by the thermal rearrangement of *cis*,*trans*-cyclodeca-1,5-diene (94) (Scheme 48, p.39).[90] (94) itself can be easily prepared from butadiene and ethylene using nickel-based π-complex catalysis.[159]

Another stereospecific route to *cis*-divinyl compounds is that described by Vogel.[84] Thus, *cis*-1,2-divinylcyclobutane (76) was prepared from *cis*-1,2,3,6-tetrahydrophthalic anhydride by a rather lengthy reaction sequence as shown in Scheme 92.

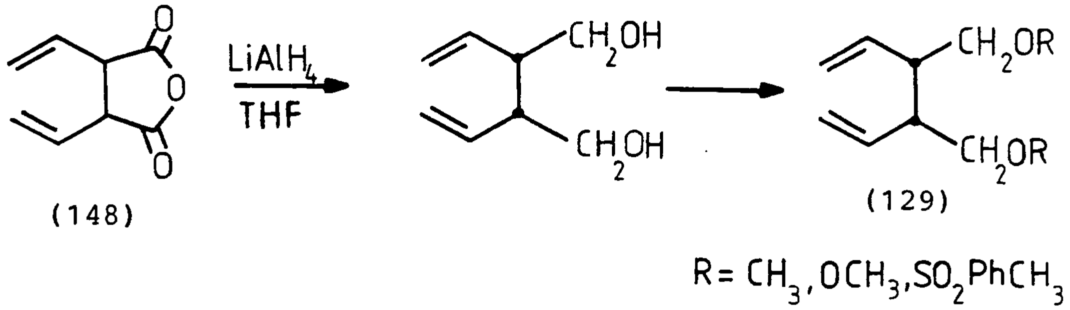


(76)

Scheme 92

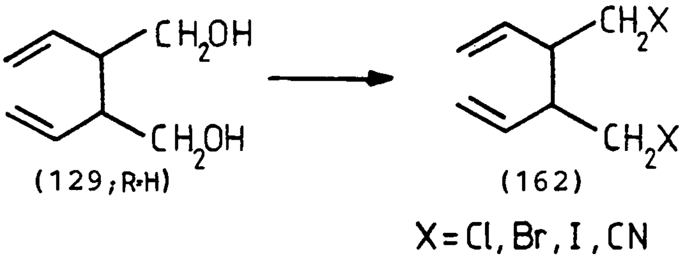
2. Preparation of *meso*-3,4-Dihydroxymethyl-1,5-hexadiene and its derivatives

Reduction of the anhydride (148) with lithium aluminium hydride in THF gave an 82% yield of the diol (129; R=H) which could be easily transformed into a variety of derivatives by conventional methods. Thus the dimethyl ether (129; R=CH_3), the diacetate (129; R=OCH_3) and the bis(*p*-toluenesulphonate) (129; R=SO_2PhCH_3) were readily accessible by the route outlined in Scheme 93. Figure 8 (p.165) shows the 100MHz ^1H n.m.r. spectrum of *meso*-3,4-dimethoxymethyl-1,5-hexadiene (129; R=CH_3) with the multiplet at δ5.85-5.0 being typical of the *cis*-1,2-divinyl system.



Scheme 93

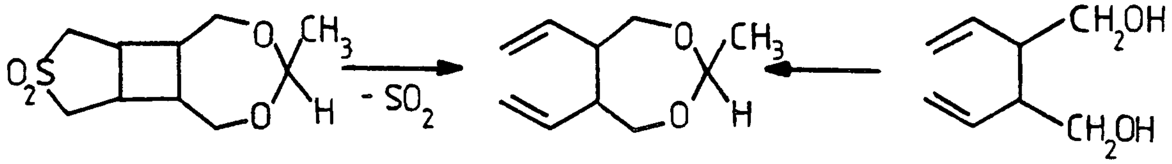
The diol (129) also gave access to other derivatives. Thus, on treatment with thionyl chloride in benzene, it gave a good yield of the dichloride (162; X=Cl) which existed as a low melting solid, m.p.20-23°C. The corresponding dibromide (162; X=Br), m.p.54.5-55.5°C, was obtained in only 17% yield by reaction of the diol (129) with phosphorus tribromide. The di-iodide (162; X=I) and dinitrile (162; X=CN) were both prepared from the bis(*p*-toluenesulphonate) (129; $R=SO_2PhCH_3$) in good yields (Scheme 94).



Scheme 94

As discussed in the previous Section (p.151) the diol (129; R=H), dimethyl ether (129; $R=CH_3$), and diacetate (129; $R=OCH_3$) were also obtained by FVP of the corresponding sulphones (Scheme 80, p.151). However, the route to *cis*-1,2-divinyl compounds from the divinyl anhydride (148) resulted in better yields in general and could be carried out on a larger scale.

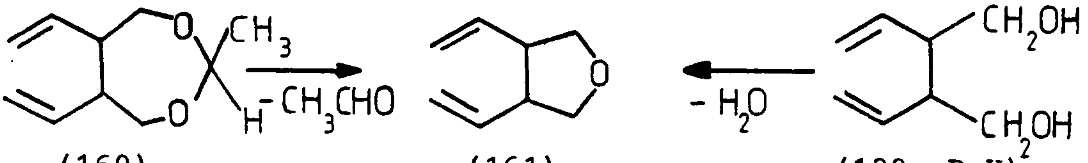
Since FVP of the cyclic acetal (132) was thought to give the corresponding *cis*-1,2-divinyl compound (160) its preparation was attempted by reaction of the diol (129) with vinyl acetate in the presence of mercuric acetate (Scheme 95). Examination of the product by ^{1}H n.m.r. spectroscopy indicated the presence of a compound with the desired structure. Moreover GC analysis showed the product was identical to that obtained by pyrolysis of (132) at 550°C but further attempts at characterisation were frustrated by its ready tendency to decompose into a black oil.



(132) (160) (129; R=H)

Scheme 95

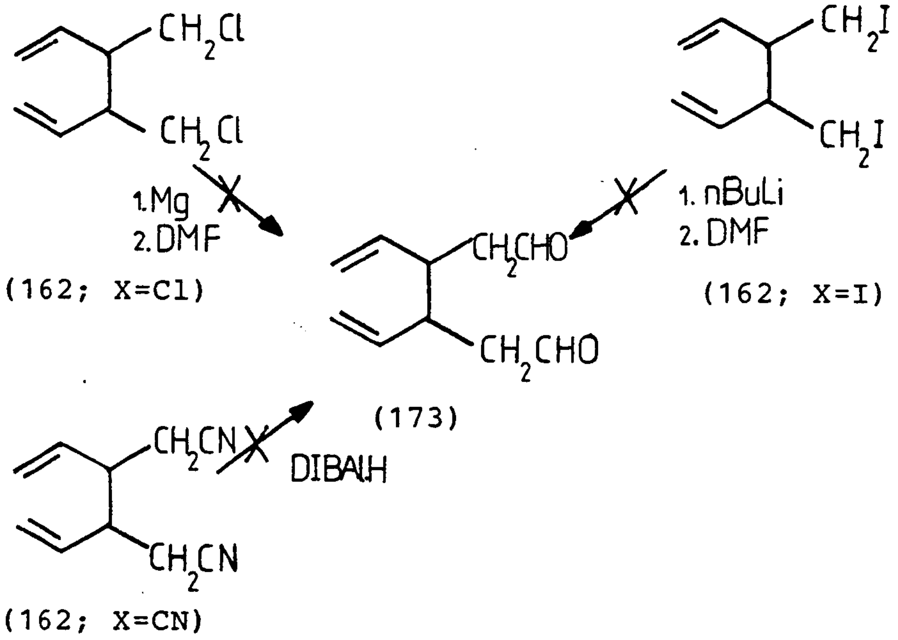
Since previous experiments (p. 153) had shown that pyrolysis of (132) at the higher furnace temperature of 650°C was suspected of giving *cis*-3,4-divinyltetrahydrofuran (161) by loss of acetaldehyde, an authentic sample was prepared by dehydration of the diol (129) with *p*-toluenesulphonic acid monohydrate over molecular sieves (Scheme 96). GC analysis and ^{1}H n.m.r. spectroscopy of (161) confirmed that the elements of acetaldehyde had indeed been eliminated in the pyrolysis of (132) to give (161).



(160) (161) (129; R=H)

Scheme 96

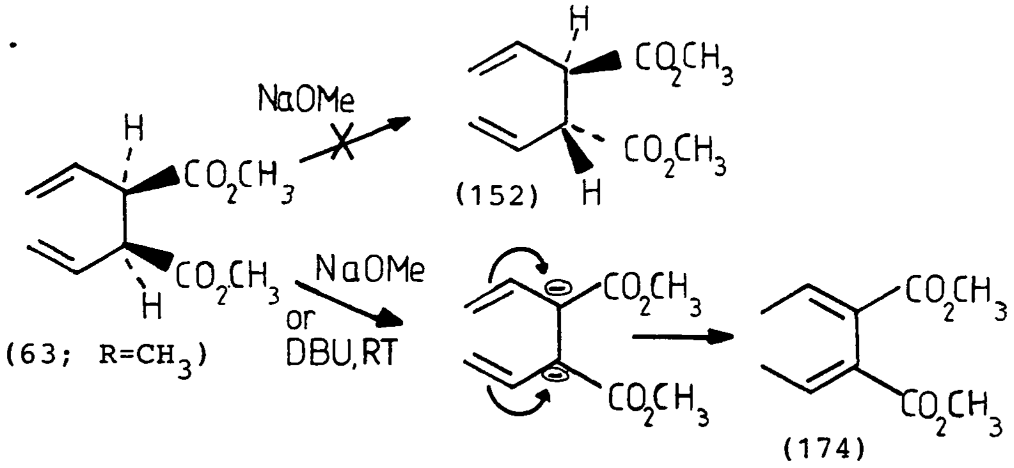
Several attempts were made to prepare *meso*-3,4-divinylhexa-1,6-dial (173) which could serve as a valuable precursor to large ring *cis*-1,2-divinyl compounds (see Section F). Thus treatment of the di-Grignard reagent of (162; X=Cl) with DMF as outlined in Scheme 97 resulted in the recovery of only unreacted dichloride (162; X=Cl). Reaction of the di-iodide (162; X=I) with *n*BuLi followed by treatment with DMF also failed as did the reduction of the dinitrile (162; X=CN) with DIBAlH.



Scheme 97

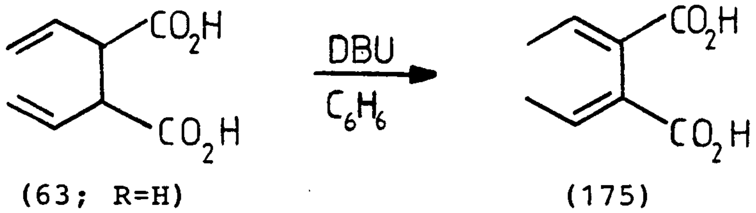
3. Preparation of 3,4-Disubstituted-2,4-hexadienes

In an attempt to convert the *meso*-diester (63; R=CH_3) into its *dl* diastereoisomer (152), the diester (63) was treated with sodium methoxide (Scheme 98). This reaction gave a colourless liquid in 86% yield which was identified as the rearranged diester, 3,4-dimethoxycarbonyl-2,4-hexadiene (174), in which the double bonds were now in conjugation with each other and with the carbonyl groups of the ester functions. This base-catalysed rearrangement was also effected by DBU. Figure 9 shows the 100MHz ^1H n.m.r. spectrum of the dimethyl ester (174).



Scheme 98

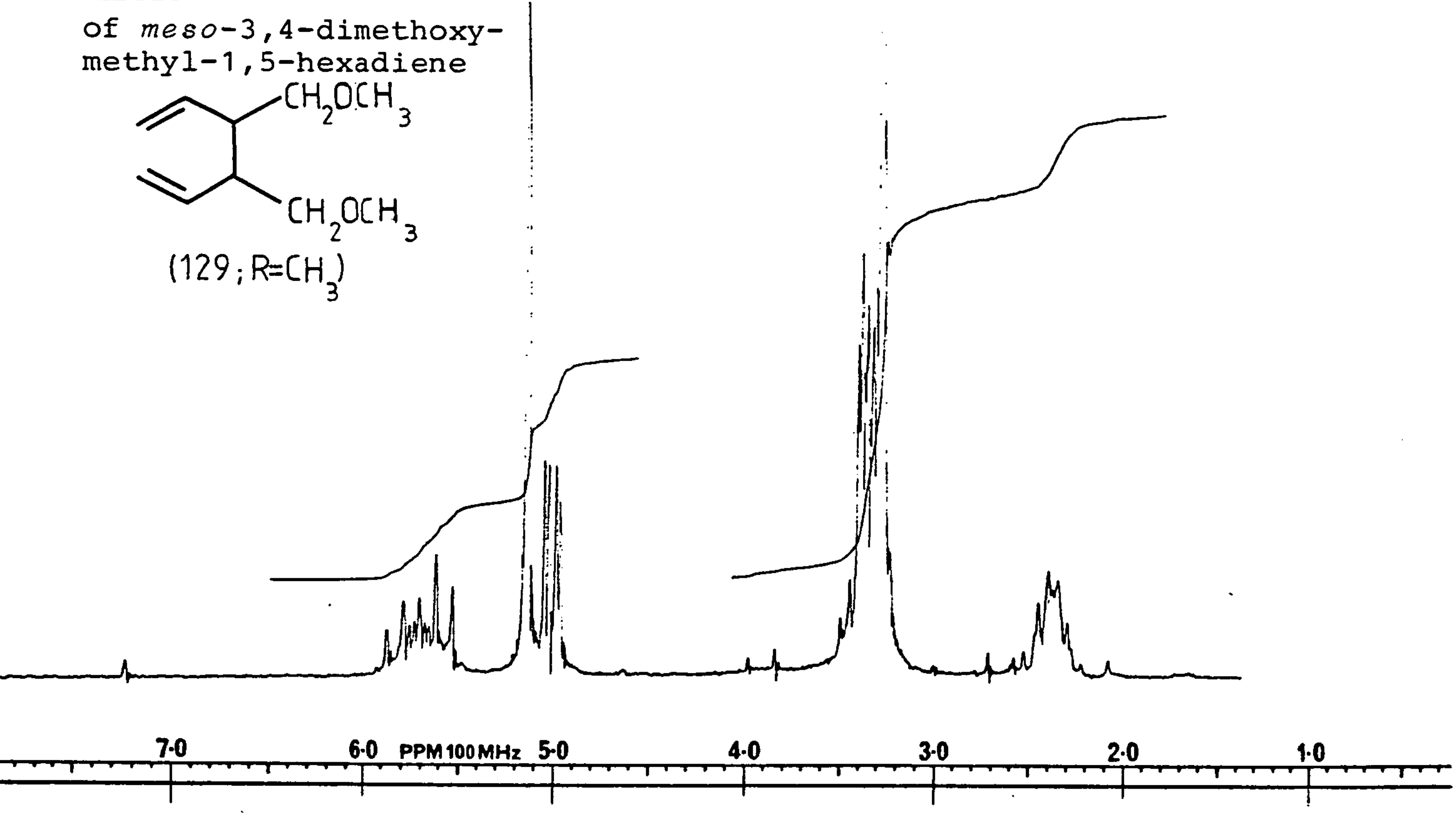
Similar reaction of the diacid (63; R=H) with sodium methoxide gave unchanged starting material but on boiling with DBU in benzene for 16 h, the rearranged product (175) was obtained with the expected analytical and spectroscopic properties (Scheme 99).



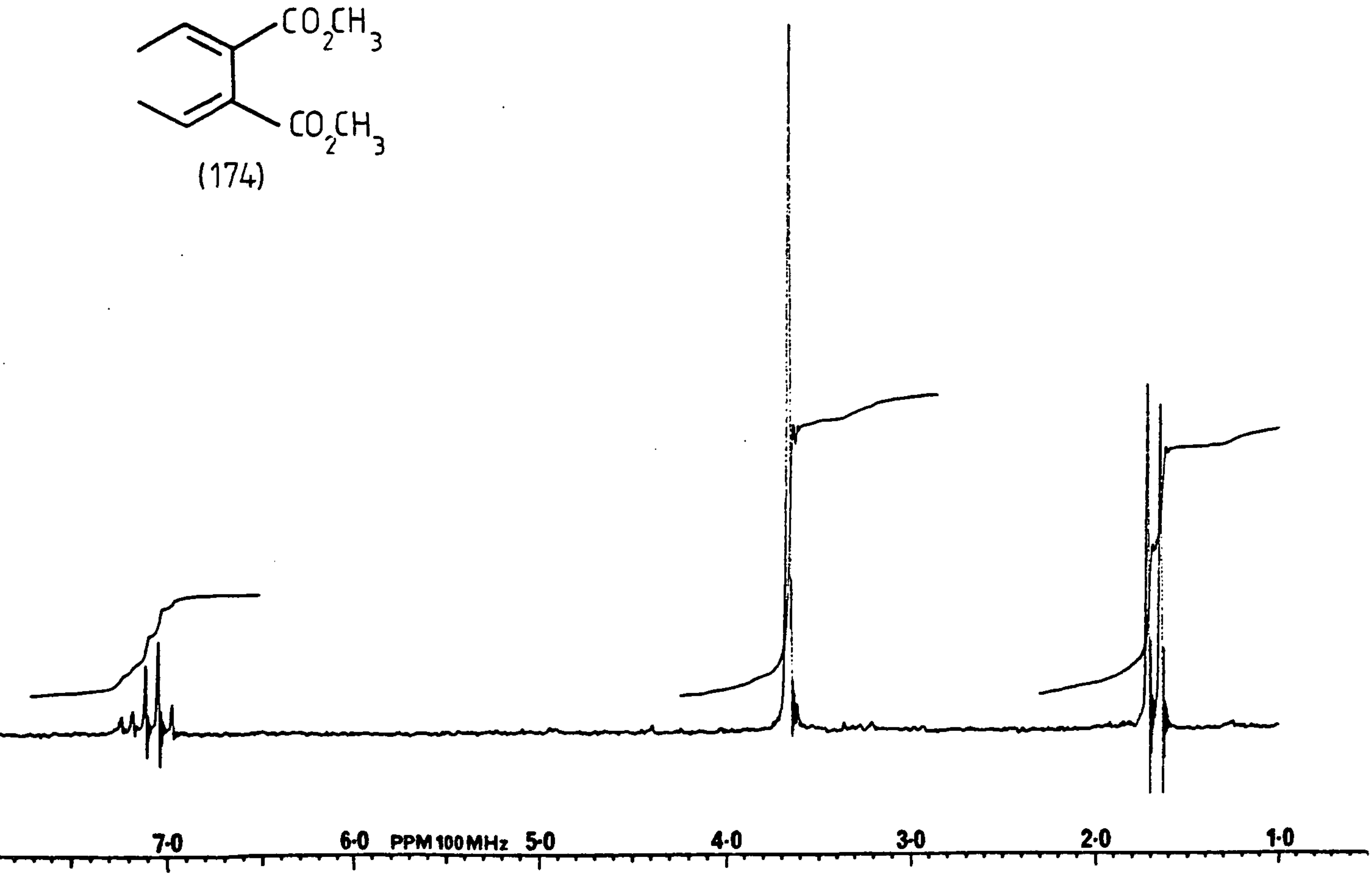
Scheme 99

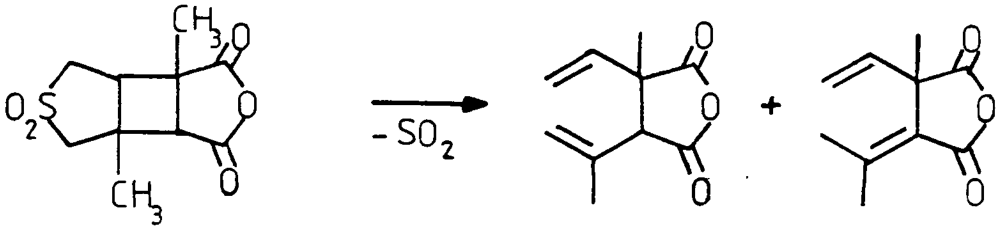
Williams and Lin[129] observed a similar rearrangement of (177) to (178) during the thermolysis of the sulphone (176) in a sealed tube at 290°C. It was proposed that the SO_2 liberated during the reaction was responsible for promoting the isomerisation of the double bond. Under FVP conditions, a mixture of the *cis*-3,4-divinyl anhydride (177) and its conjugated isomer (178) was formed (Scheme 100).

<u>Fig.8</u> ^{1}H N.m.r. spectrum of *meso*-3,4-dimethoxymethyl-1,5-hexadiene



<u>Fig.9</u> ^{1}H N.m.r. spectrum of 3,4-dimethoxycarbonyl-2,4-hexadiene

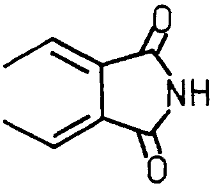




(176) (177) (178)

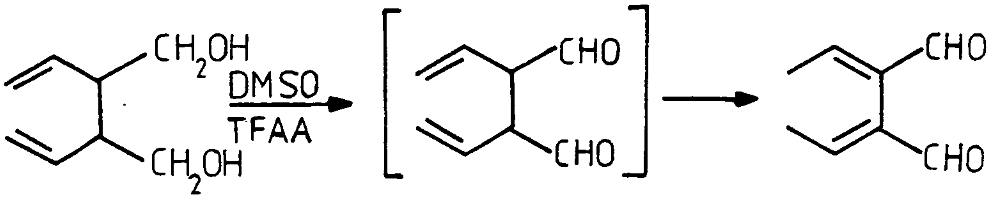
Scheme 100

The imide (165) was also obtained from pyrolysis of the sulphones (141) and (142), but, in this instance, the rearrangement was thought to have occurred during purification by chromatography on alumina (see p.155).



(165)

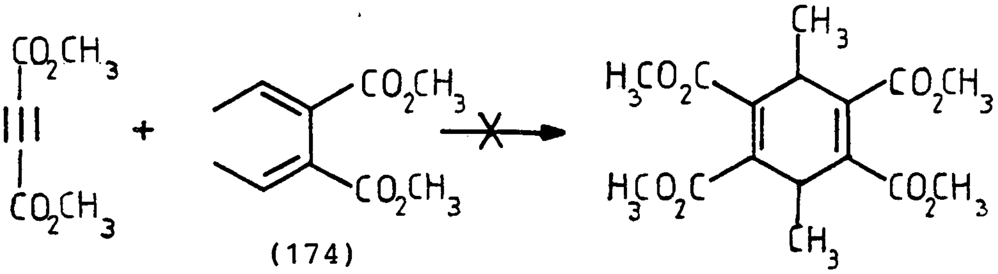
A similar rearrangement was also observed during the oxidation of the diol (129) using the method of Swern *et al*[132] which involves reaction with DMSO and trifluoroacetic anhydride at -50°C in the presence of base. Under these conditions 2,4-hexadiene-3,4-dicarboxaldehyde (179) was obtained in 19% yield after purification by preparative t.l.c. (Scheme 101). The base, triethylamine, was added at the final stage of the reaction and so rearrangement to (179) may have occurred at this step. Oxidation of the diol (129) was also attempted by various other methods. Thus the use of oxalyl chloride and DMSO[124] resulted in the formation of a mixture of dialdehydes while barium manganate[125] and bispyridine-silver manganate[133] gave mainly unchanged starting material.



(129; R=H) (179)

Scheme 101

An attempt was made to prepare a Diels-Alder cycloadduct of (174) with dimethyl acetylene dicarboxylate (Scheme 102) but in benzene and toluene as the reaction solvent, only starting materials were recovered. With the higher boiling solvent mesitylene, decomposition resulted to give a complex mixture of products.



(174)

Scheme 102

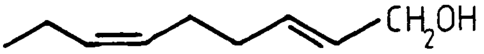
D. Cope Rearrangement of *cis*-1,2-Divinyl Compounds

As discussed in Section B.2 (p.148), pyrolysis of the diacid (62; R=H) gave exclusively the *meso*-1,2-divinyl derivative (63; R=H) whereas pyrolysis of its diester (62; R=CH_3) led to the stereoselective formation of the *cis*,*trans*-1,5-diene (64; R=CH_3) via Cope rearrangement of the 1,2-divinyl intermediate (63; R=CH_3). This synthesis of (64) is an important finding since it allows, in a single step, the stereospecific construction of the *cis*,*trans*-divinylethane grouping which is found in certain natural products.[160] For example, gossyplure, the sex pheromone of the female pink bollworm moth, is a *ca* 1:1 mixture of (7-*cis*, 11-*trans*)- and (7-*cis*, 11-*cis*)-hexadeca-7,11-dien-1-yl acetate, (180) and (181) respectively.[161] For maximum effect, stereochemically pure alkenes are of critical importance for synthetic sex pheromones. To date the *cis*, *trans*-isomer (180) has been synthesised in only *ca* 84% purity owing to loss of selectivity in the preparation of starting materials.[161]

(180)

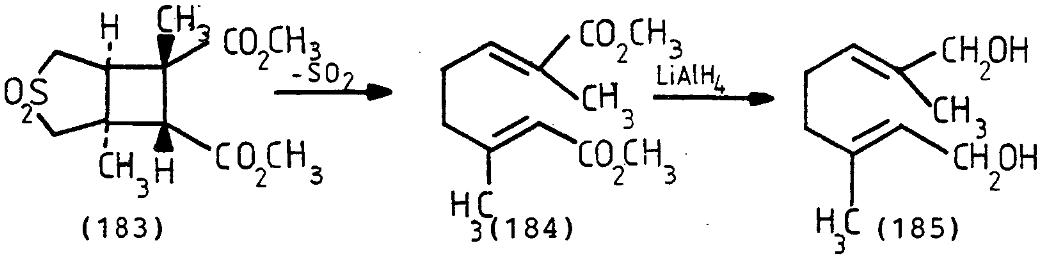
(181)

Generally a combination of *cis*- and *trans*-stereoselective Wittig reactions are employed to construct the *cis*,*trans*-divinylethane group as has been used in the preparation of *trans*,*cis*-nona-2,6-dien-1-ol (182), a constituent of the odiferous principle of violets.[162]



(182)

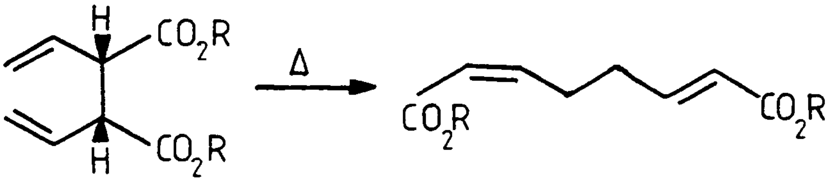
Stereoselective olefin syntheses have thus become an area of growing interest and the stereocontrolled synthesis of *cis,trans*-1,5-dienes by FVP of suitable precursors may provide a useful approach to such syntheses. Bloch and Abecassis[27] have already applied the technique of FVP of sulphones to the synthesis of insect sex pheromones containing a conjugated *trans,trans*-diene group (see Scheme 13, p.14). In addition, the synthesis of 10-hydroxygeraniol (185) has been reported;[129] the diester (184) being obtained from FVP of the sulphone (183) as shown in Scheme 103.



Scheme 103

1. Preparation of *cis,trans*-Octa-2,6-diene-1,8- dioic acid and its dimethyl ester

The Cope rearrangement of *meso*-3,4-dicarboxylic acid-1,5-hexadiene (63; R=H) was effected by sublimation through the FVP apparatus at 625°C. This gave *cis,trans*-octa-2,6-diene-1,8-dioic acid (64; R=H) as a colourless crystalline solid (m.p. 111-113°C) in 34% yield (Scheme 104). The crystal structure of (64; R=H) has been reported previously in the literature together with its melting point (113-114°C) but no other information was given.[135]



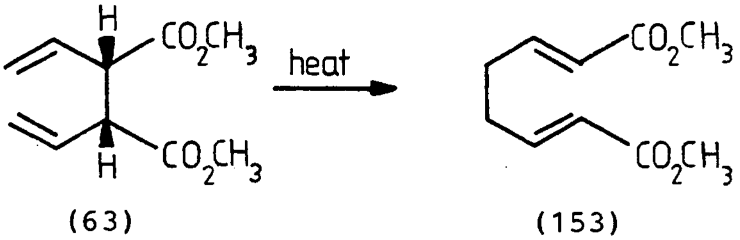
(63) (64)

Scheme 104

Similar rearrangement of the dimethyl ester (63; $R=CH_3$) at 580°C gave a 51% yield of the *cis,trans*-diester (64; $R=CH_3$) which was identical according to ^1H n.m.r. spectroscopy with the product obtained by pyrolysis of the sulphone (62; $R=CH_3$) (Scheme 30, p.149). In earlier work in these laboratories McLaughlin[50] also effected rearrangement of (63; $R=CH_3$) by heating a sample in d_8-toluene in a bath of boiling toluene. Monitoring of the reaction by ^1H n.m.r. spectroscopy showed that complete rearrangement of (63; $R=CH_3$) to (64; $R=CH_3$) occurred after a period of 5 days.

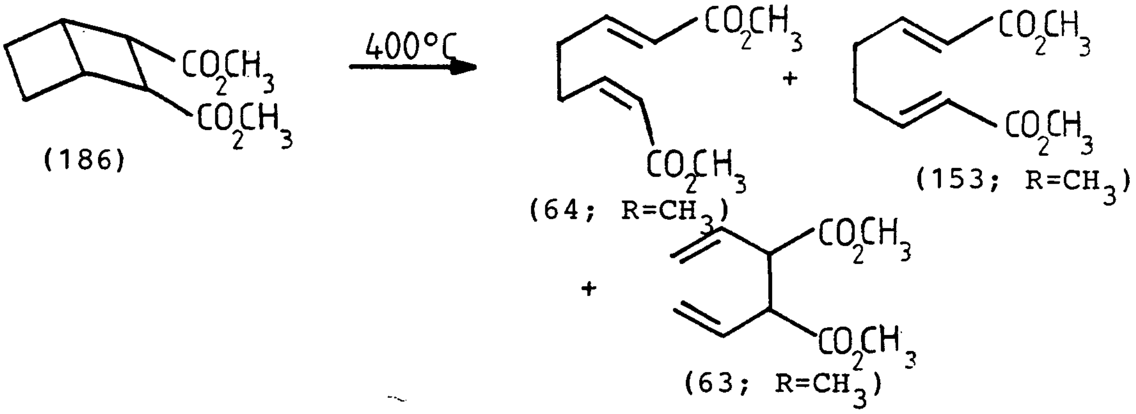
^1H and ^{13}C n.m.r. spectra of the diacid and diester (63) were consistent with the assigned stereochemistry which was also validated by isomerisation to their *trans,trans*-isomers (see p.175). Figures 11 and 12 (p.178) show the 100MHz ^1H n.m.r. spectra of the *cis,trans*-diester (64; $R=CH_3$) and its *trans,trans*-isomer (153; $R=CH_3$). Further confirmation of the stereochemistry of these compounds was obtained from their ^{13}C n.m.r. spectra, details of which are given on p.176.

As discussed in the Introduction (p.28), the Cope rearrangement of *cis*-1,2-divinyl compounds is considered to involve a chair-like transition state giving rise to *cis,trans*-1,5-dienes exclusively. The stereoselective formation of (64; R=H) and (64; R=CH_3) is consistent with this observation but is at odds with the work of Williams and Lin[129] who reported that thermolysis of (63; R=CH_3) at 290°C gave only the *trans,trans*-diester (153; R=CH_3) in 78% yield (Scheme 105). No supporting evidence was given for this conclusion which also conflicts with the results of Paquette and Schwartz[128] which showed that pyrolysis of the *endo,cis*-isomer of dimethyl bicyclo[2.2.0]hexane-2,3-dicarboxylate (186) at 400°C gave mainly the *cis,trans*-diester (64; R=CH_3) together with minor amounts of the *trans,trans*-diester (153; R=CH_3) and the *meso*-isomer (63; R=CH_3). The product composition for this pyrolysis is shown in Scheme 106 along with the results for the pyrolysis of the corresponding *trans*-dimethyl bicyclo[2.2.0]-hexane-2,3-dicarboxylate (187) which gave the expected *trans,trans*-isomer (153; R=CH_3) as the major product.



Scheme 105

To verify that *meso*- (63; R=CH_3) and its *dℓ*-diastereoisomer (152) were intermediates in the rearrangement, the products from their pyrolyses at 410°C were analysed and found to be in agreement with the results obtained for pyrolysis of (186) and its *trans*-isomer (187) respectively. From these results, it is clear that the *cis,trans*-diene (64; R=CH_3) is formed by Cope rearrangement of *meso*- (63; R=CH_3) whilst the *trans,trans*-diene (153; R=CH_3) is derived from the *dl*-diastereoisomer (152).



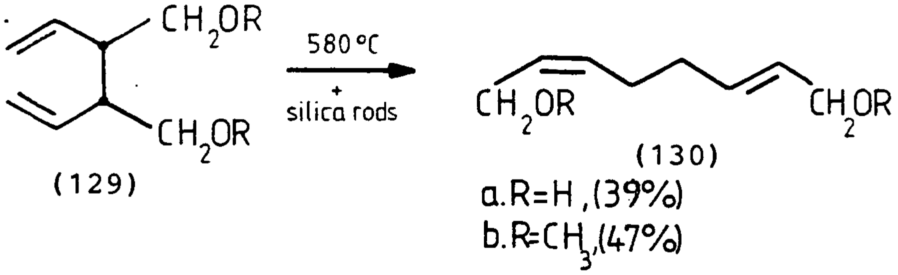
	cis,trans (64; R=CH_3)	*trans,trans* (153; R=CH_3)	*cis,cis* (154; R=CH_3)	
endo,cis-(186)	79%	9%		12% *meso*- (63; R=CH_3)
trans-(187)	6%	75%	18%	1%, *dl*-(152)

Scheme 106

2. Preparation of *cis,trans*-Octa-2,6-diene-1,8-diol and its derivatives

As in the case of the diacid and diester (63), the *meso*-diol (129; R=H) and its derivatives (129; R=CH_3, $COCH_3$) rearranged to the *cis,trans*-dienes (130) with a high degree of stereospecificity when pyrolysed under flash vacuum conditions (580°C at 0.001 mmHg) (Scheme 107). In the case of the diol (130;

R=H) the stereospecificity was found to be 94%, the stereochemistry being validated by ^{13}C n.m.r. spectroscopy which showed the expected 8-line spectrum as shown in Figure 10. The spectrum also exhibited trace amounts of the *trans,trans*-isomer.



Scheme 107

For the dimethyl ether (129; R=CH_3) the rearrangement could also be effected by heating a neat sample in a bath of boiling benzyl alcohol (b.p. 205°C) for 65 h. The product (130; R=CH_3) was also prepared in 65% yield by *O*-methylation of the *cis,trans*-diol (130; R=H) with methyl iodide in dimethyl sulphoxide using potassium hydroxide as base.

Heating of the diacetate (129; R=$COCH_3$) under similar conditions also resulted in a ready Cope rearrangement whereas FVP at 580°C gave a mixture of the rearranged product (130; R=$COCH_3$) and starting material. At higher furnace temperatures, e.g. 625°C, loss of acetic acid occurred giving rise to a mixture of unidentifiable products. In this connection it is worth noting that the pyrolytic decomposition of acetates is a common method of preparing alkenes. For example, isobenzofulvene (190) is formed by loss of acetic acid from either of the acetates (188) or (189) under flash vacuum pyrolytic conditions (Scheme 108).[163] A similar loss of acetic acid from

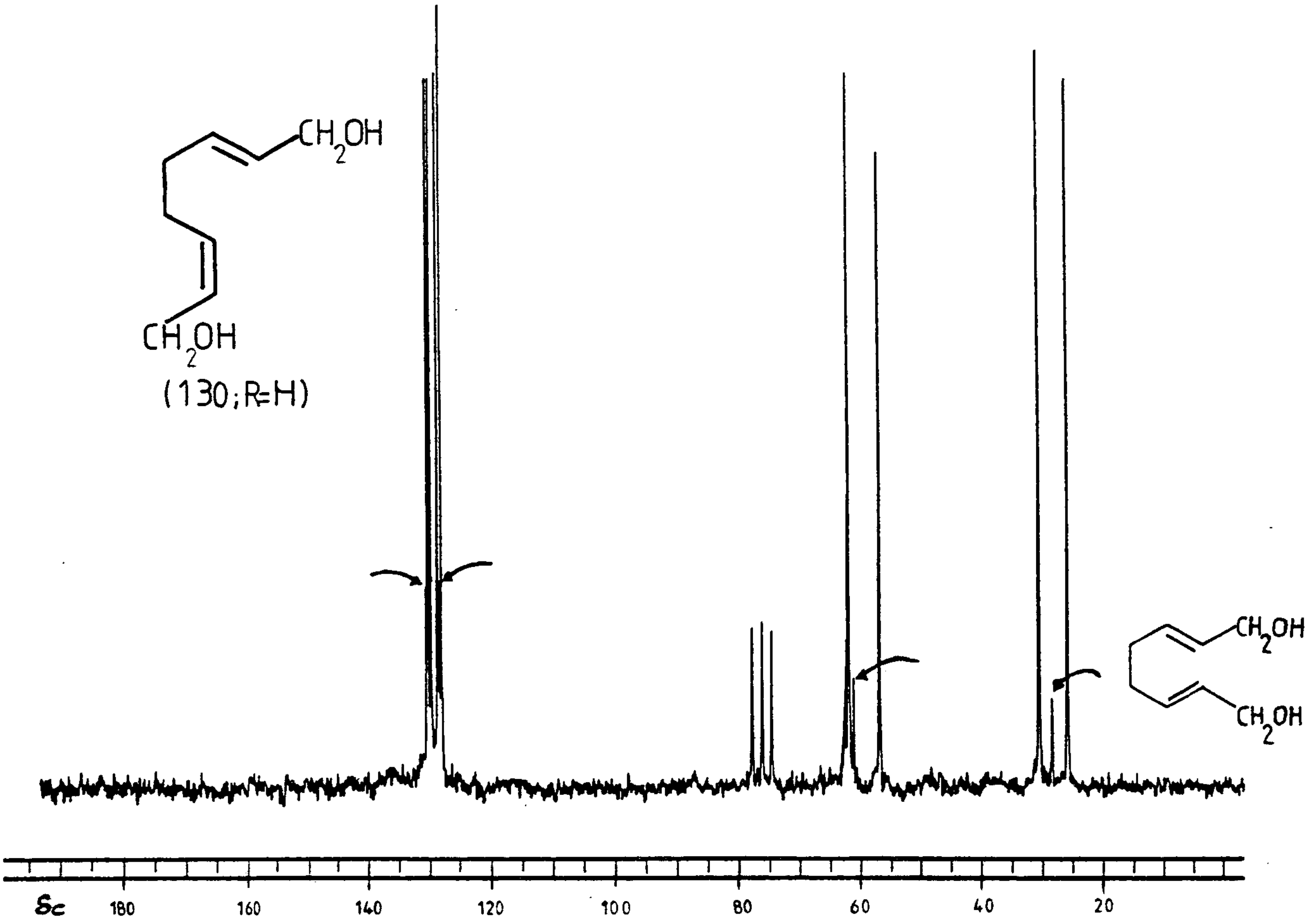
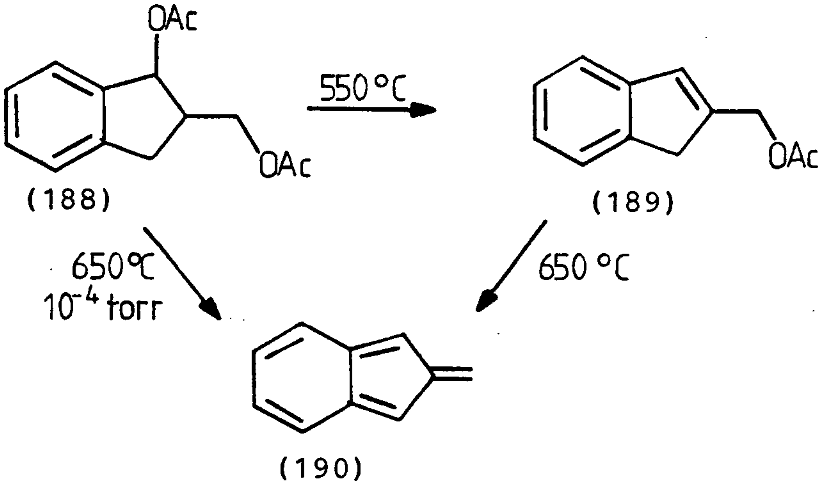
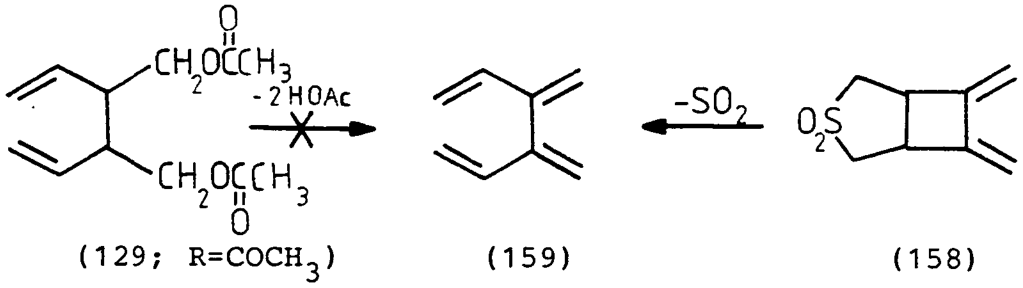


Fig.10. ^{13}C n.m.r. spectrum of *cis*,*trans*-Octa-2,6-diene-1,8-diol



Scheme 108

the *meso*-diacetate (129; R=$COCH_3$) would give rise to 3,4-dimethylene-1,5-hexadiene (159) but this compound could not be detected in the reaction mixture. (Scheme 109). As will be discussed in Section H.2, p.204, (159) can be formed by extrusion of SO_2 from the compound (158).



(129; R=$COCH_3$) (159) (158)

Scheme 109

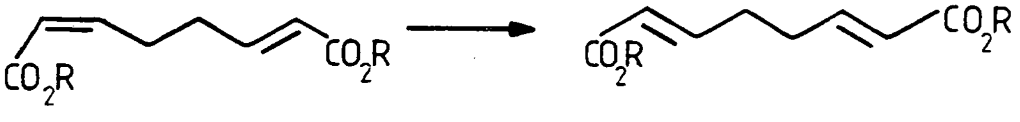
In contrast to the thermal rearrangement of the divinyl acetate (129; R=$COCH_3$), pyrolysis of the sulphone (126; R=$COCH_3$) at 650°C gave the *cis,trans*-diacetate (130; R=$COCH_3$) as a pure compound. Similarly, the *cis,trans*-diol (130; R=H) was formed by FVP of the sulphone (126; R=H) at 600°C (see Section B.3, p.151).

3. Isomerisation of *cis,trans*-Octa-2,6-diene-1,8-dioic acid and its dimethyl ester

To provide further evidence for the stereochemical course of the Cope rearrangement of the *meso*-divinyl compounds (63), the isomerisation of the *cis,trans*-dienes (64) to their *trans,trans*-isomers (153) was examined (Scheme 110). Thus, thermally induced isomerisation of the *cis,trans*-diacid (64; R=H) (m.p. 111-113°C) in boiling methanol resulted in a quantitative yield of the *trans,trans*-diacid (153; R=H) with m.p. 257°C (decomp.). This compared favourably with the literature value of 256°C (decomp.).[130] The isomerisation to the *trans,trans*-form was supported by ^{13}C n.m.r. spectroscopy which showed a conversion from an 8-line spectrum to one with only 4 lines.

Isomerisation of the dimethyl ester (64; R=CH_3) was achieved by boiling in heptane in the presence of iodine. After several days, 75% of the *cis,trans*-form (64; R=CH_3) had isomerised to its *trans,trans*-isomer (153; R=CH_3) which could be separated by bulb-to-bulb distillation then isolated in pure form by preparative GC.

Scheme 110 gives details of the ^{13}C n.m.r. spectra of both isomeric forms while Figure 12 shows the 100MHz ^1H n.m.r. spectrum of the *trans,trans*-isomer (153; R=CH_3) which agrees well with that reported by Della and Kendal.[130] The spectrum also compared well with that obtained for the product from FVP of the *trans*-epimer of the sulphone (125; R=CH_3) (see p,150).



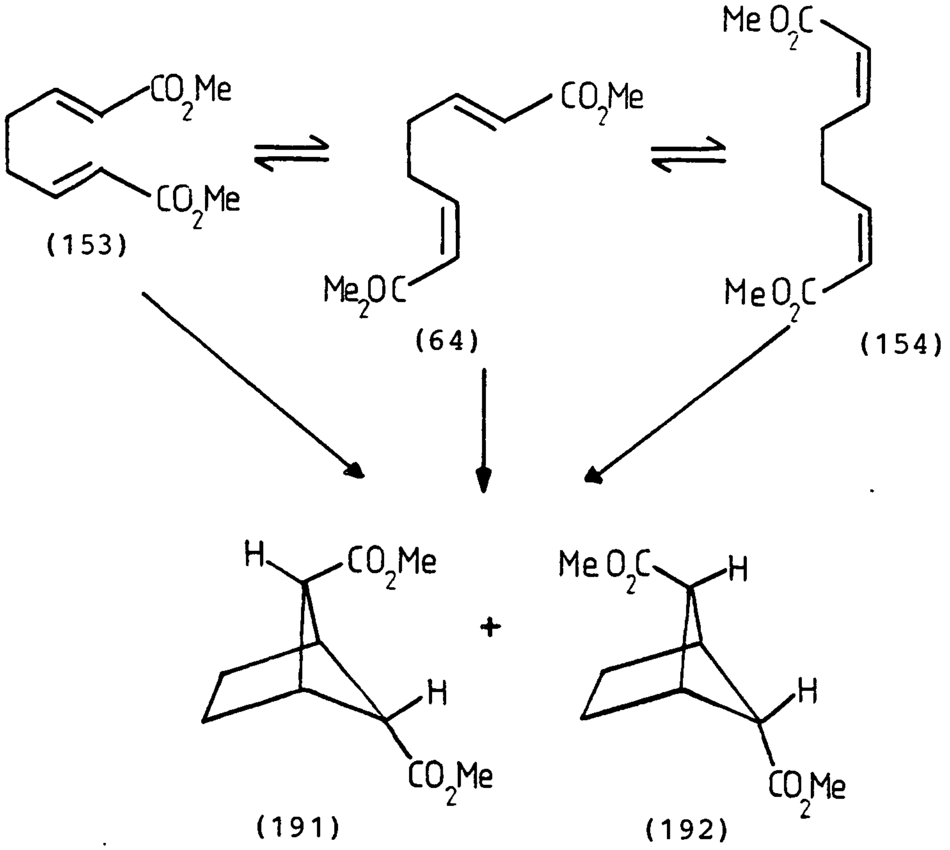
(64) (153)

For R=CH_3, ^{13}C nmr ($CDCl_3$):

δ_C 166.58	δ_C 166.25
166.28	146.77
147.91	121.57
147.54	50.98
121.53	30.02 ppm
120.29	
51.15	
50.81	
31.13	
26.13 ppm	

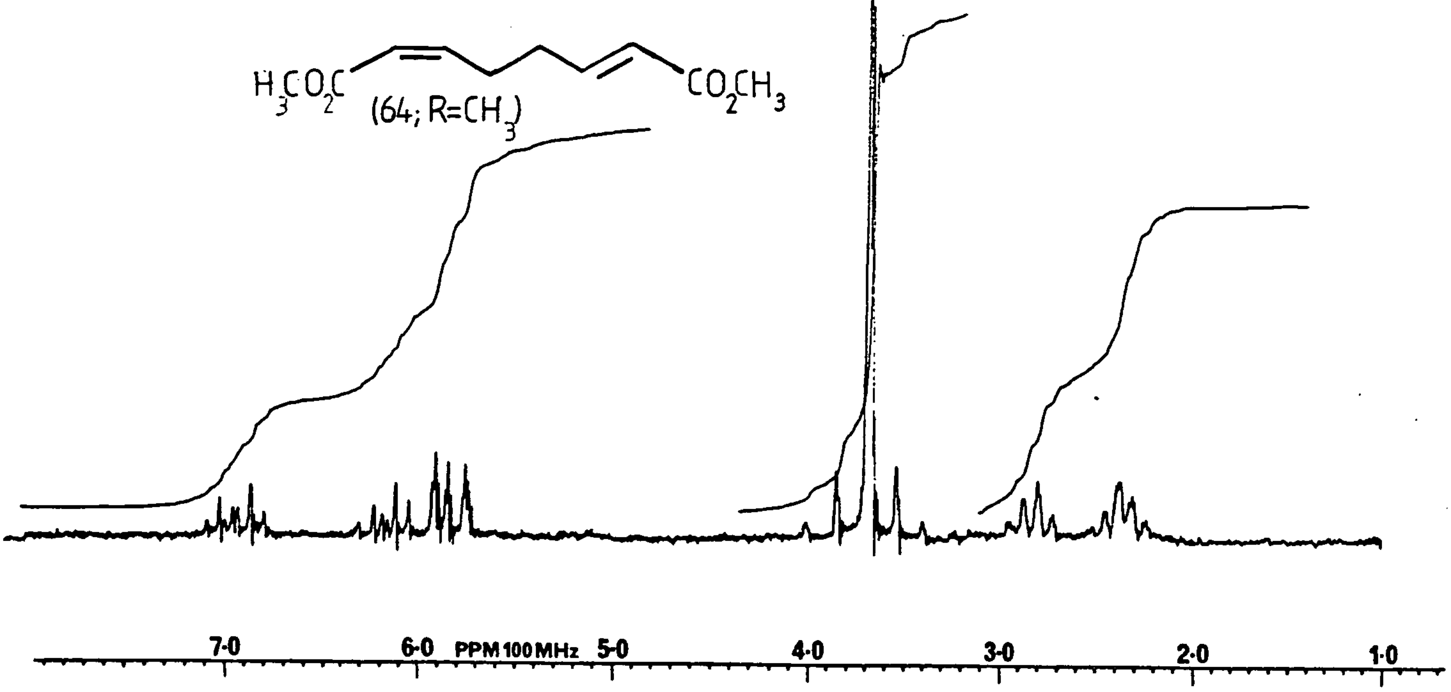
Scheme 110

In passing, it is of interest to note that Scheffer and Wostradowski[127] have reported the acetone-sensitised photoisomerisation of the same dienes but also observed an internal "crossed" [2+2] cycloaddition to give adducts (191) and (192) (Scheme 111).



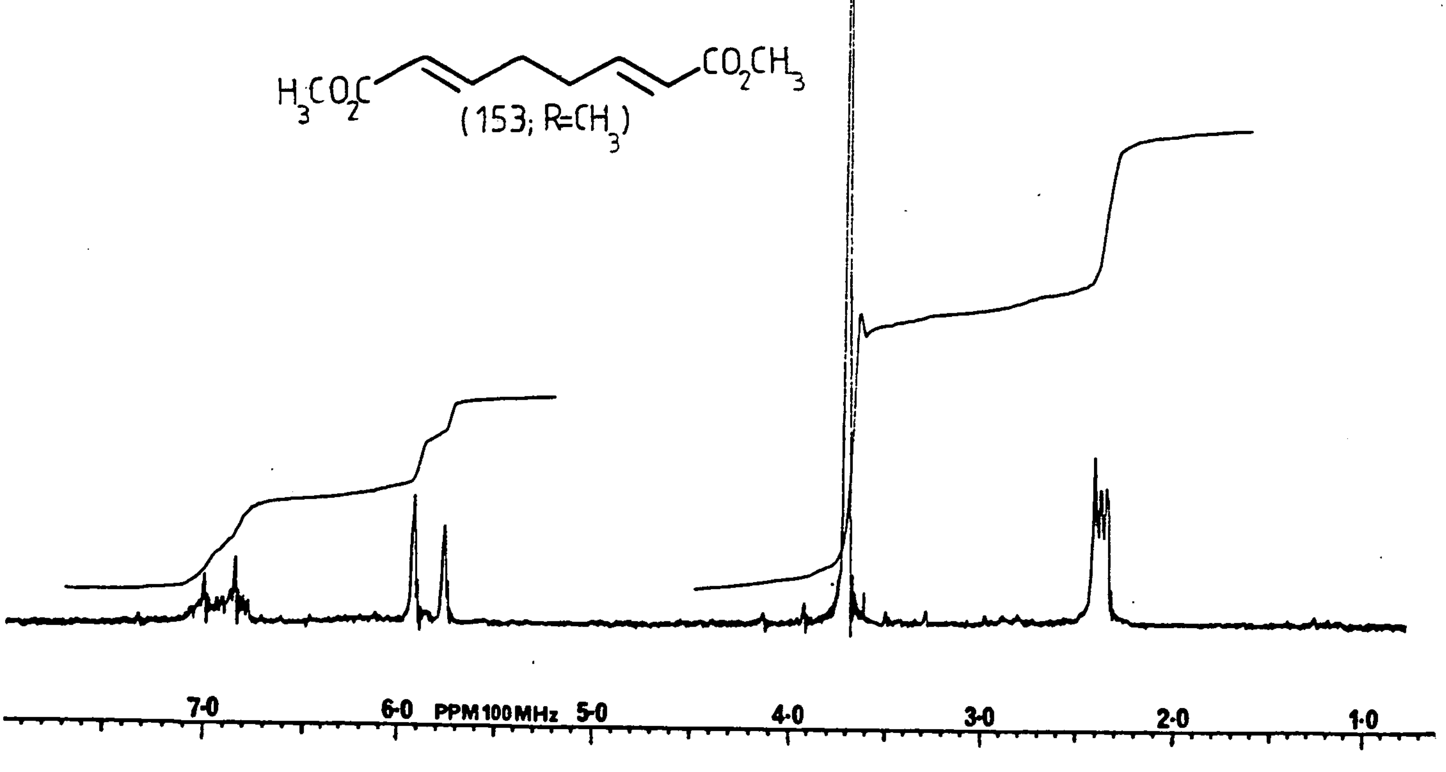
Scheme 111

Fig.11 ^{1}H n.m.r. spectrum of *cis*, *trans*-dimethyl octa-2,6-diene-1,8-dioate.



(64; R=CH_3)

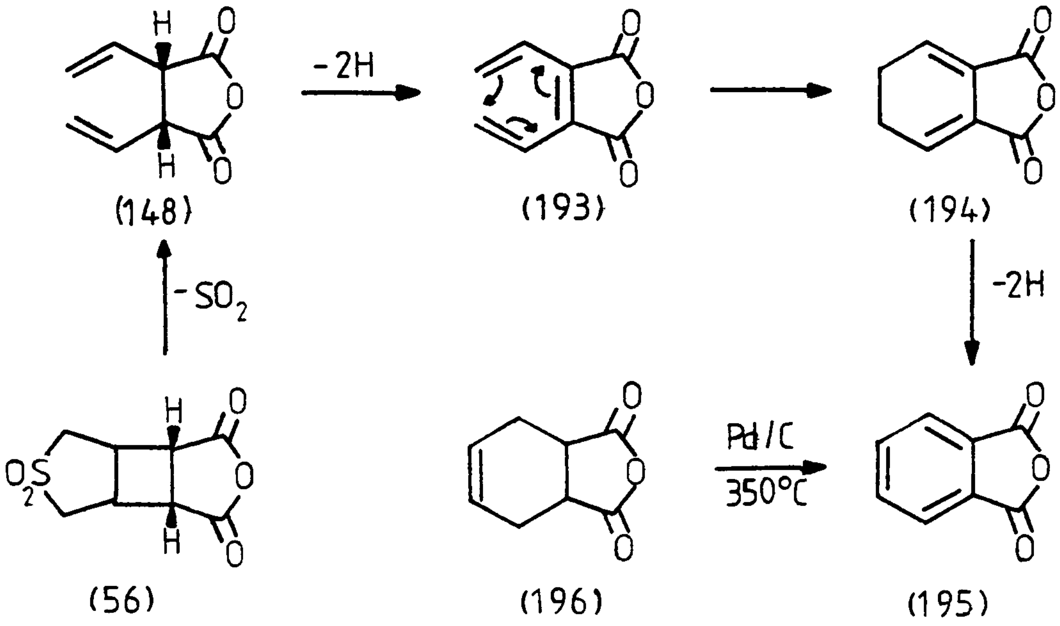
Fig.12 ^{1}H n.m.r. spectrum of *trans*, *trans*-dimethyl octa-2,6-diene-1,8-dioate



(153; R=CH_3)

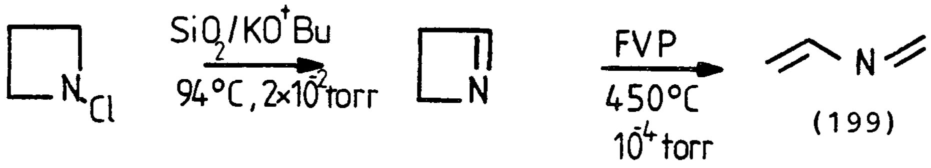
E. Flash vacuum pyrolysis under dehydrogenating conditions

As discussed earlier (p.146), when the anhydride (56) was subjected to FVP at 630°C, the *cis*-1,2-divinyl compound (148) was obtained in 80% yield. It was reasoned by Hamill[164] during post-doctoral studies in these laboratories that removal of the ring-junction hydrogens from (148) should lead to electrocyclisation of the resulting (193) to (194) which would afford phthalic anhydride (195) under dehydrogenating conditions (Scheme 112). This was readily accomplished in a single step in 51% yield by FVP of (56) at 400°C through a catalyst bed of 5% palladium on activated charcoal. Similar pyrolyses of 2,5-dioxo-*cis*-3,4-divinyltetrahydrofuran (148) at 425°C and of *cis*-1,2,3,6-tetrahydrophthalic anhydride (196) at 350°C also gave phthalic anhydride (195) (48-52%). It is noteworthy that in none of these pyrolyses did significant, undesirable disproportionation to hydrogenated products take place as found, for example, when the dehydrogenation of (196) is carried out in solution.[165]



Scheme 112

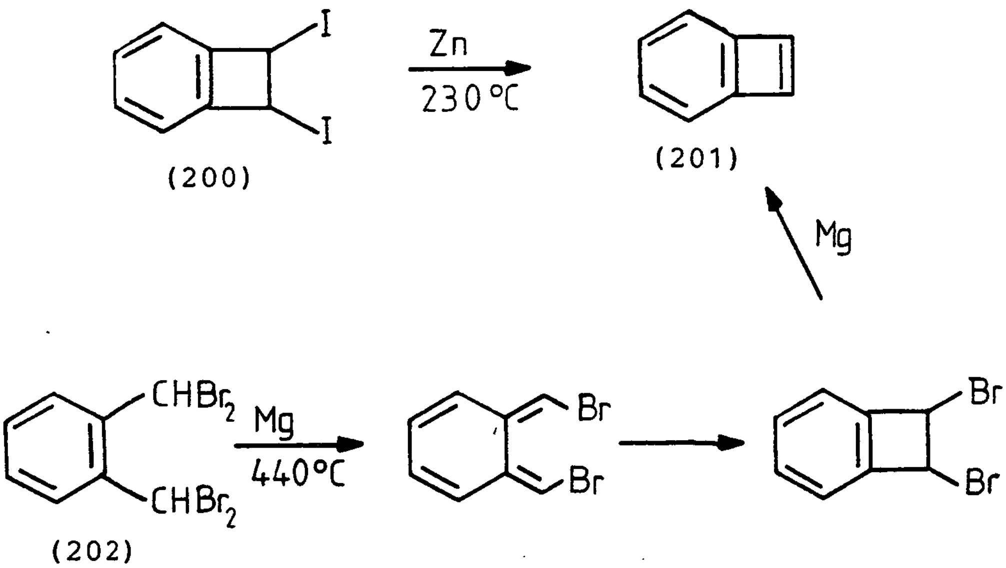
Dehydrogenative flash vacuum pyrolysis is a novel synthetic technique. Indeed, the preparative possibilities of FVP under catalytic conditions has been relatively little studied. French workers have recently demonstrated the direct synthesis of highly strained olefins by vacuum gas phase elimination of the halogenated precursors over silica supported potassium *tert*-butoxide.[166] For example, 1-azetine (198) was obtained from its *N*-chloro derivative (197) as shown in Scheme 113.[167] The thermal ring opening of (198) to 2-azabutadiene (199) was also investigated.



(197) (198) (199)

Scheme 113

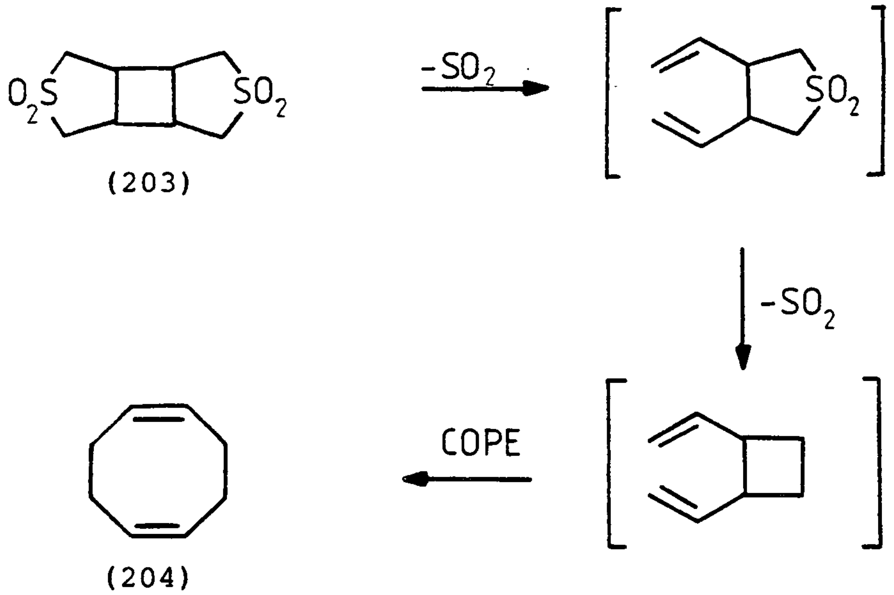
Further examples of pyrolysis under catalytic conditions have involved zinc and magnesium in dehalogenation reactions. Thus sublimation of *cis*-1,2-di-iodobenzocyclobutene (200) over zinc powder at 230°C afforded benzocyclobutadiene (201) (Scheme 114).[168] Benzocyclobutadiene (201) was also generated by pyrolysis of α,α,α',α'-tetrabromo-σ-xylene (202) at 440-470°C over sublimed magnesium.[169]



Scheme 114

1. Preparation and FVP of 4,9-Dithiatricyclo[5.3.0.0^{2,6}]-decane 4,4,9,9-tetroxide

As part of earlier work described in Section B (p.146) dealing with the generation of *cis*-1,2-divinyl compounds by flash vacuum pyrolysis of the 3-thiabicyclo[3.2.0]heptane 3,3-dioxide ring system, a study of the thermal decomposition of the bis(sulphone) (203) was undertaken. It was envisaged that the stepwise loss of SO_2 from the bis(sulphone) (203) would give rise to *cis*-1,2-divinylcyclobutane which is known to undergo a Cope rearrangement[52] to 1,5-cyclo-octadiene (204) (Scheme 115).

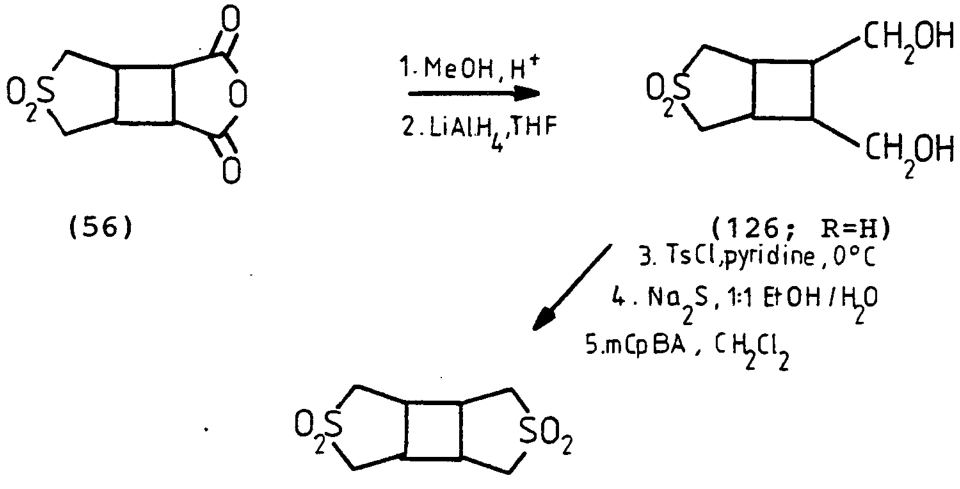


(203)

(204)

Scheme 115

The bis(sulphone) (203) was prepared from the anhydride (56) by successive esterification, reduction to the diol (126; R=H), conversion into the bis(*p*-toluenesulphonate), treatment with Na_2S and oxidation of the sulphide with *m*-chloroperoxybenzoic acid in methylene chloride (Scheme 116).



(56)

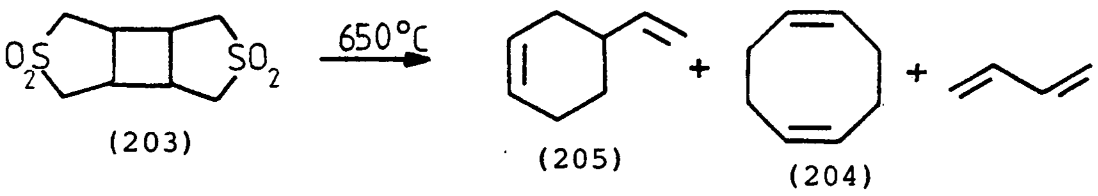
(126; R=H)

(203)

Scheme 116

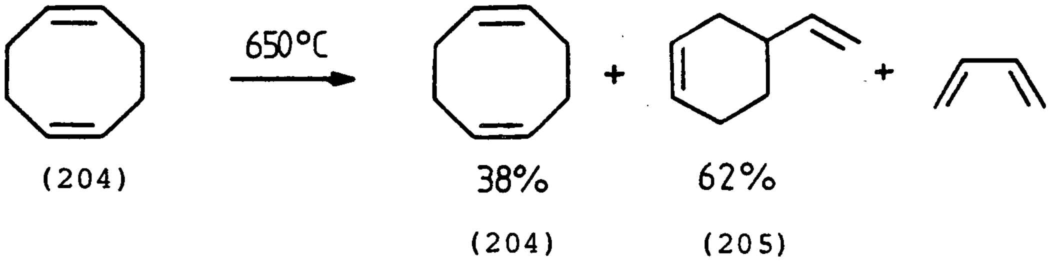
N.m.r. spectroscopy afforded little information as to the structure of the crystalline, high-melting (>320°C) product. Owing to its insolubility, insufficient of the compound dissolved in n.m.r. solvents to allow its ^{13}C n.m.r. spectrum to be recorded while the ^{1}H n.m.r. spectrum consisted of a complex multiplet at δ3.35. However, the proposed structure was supported by elemental analysis whilst its i.r. spectrum showed the characteristic sulphone absorptions at 1278 and 1121 cm^{-1}. Mass spectra were recorded using both electron impact and chemical ionisation techniques. The advantage of chemical ionisation over the conventional technique is the increased ion abundance in the molecular ion region. Thus (203) showed an ion peak at m/e 237 (100%) for $M+1^{+}$ while with electron impact, the highest peak in the spectrum was m/e 107 (24%) due to loss of two moieties of SO_2.

When subjected to flash vacuum pyrolysis at 650°C, the sparingly volatile bis(sulphone) (203) gave a mixture of the expected 1,5-cyclo-octadiene (204) and 4-vinylcyclohexene (205) in the ratio of 1:4 as determined by GC analysis (Scheme 117). Butadiene was also detected but not quantified.



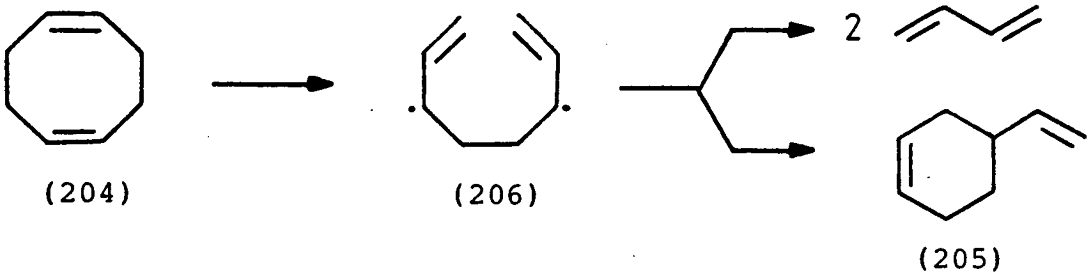
Scheme 117

Since Srinivasan and Levi[170] have shown that 1,5-cyclooctadiene (204) rearranges to 4-vinylcyclohexene (205) at temperatures around 300°C and at low pressures, it seemed reasonable to conclude that 1,5-cyclo-octadiene is the primary product in the thermal decomposition of the bis(sulphone) (203) but that under the reaction conditions, it undergoes rearrangement to 4-vinylcyclohexene (205). In keeping with these results, pyrolysis of 1,5-cyclo-octadiene (204) at 650°C gave a mixture of unreacted starting material (204) and 4-vinylcyclohexene (205) in the ratio of 1:1·6 (Scheme 118). 1,3-Butadiene was also detected by ^{1}H n.m.r. spectroscopy.



Scheme 118

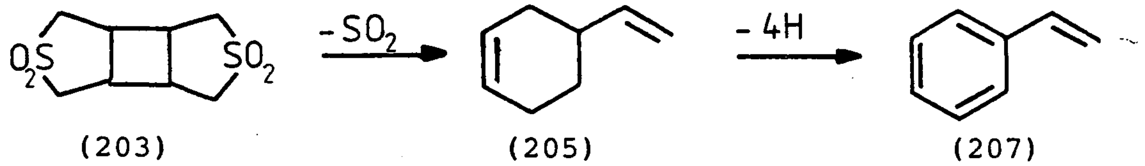
Under the same conditions, 4-vinylcyclohexene (205) was found to pass through the furnace unchanged indicating that the butadiene is formed solely from the decomposition of 1,5-cyclo-octadiene (204). From this observation it seems clear that the reaction must involve two parallel pathways as outlined in Scheme 119 with both products arising from a common precursor, namely the *cis,cis*-octadiene-1,7-diyl-3,6-biradical (206).[171]



Scheme 119

2. Pyrolytic conversion of 1,5-Cyclo-octadiene into Styrene under dehydrogenating conditions

In the light of Hamill's[164] successful preparation of phthalic anhydride by FVP of 3,5-dioxo-4-oxa-9-thiatricyclo-[5.3.0.0^{2,6}]decane 9,9-dioxide (56) under dehydrogenating conditions (vide supra), it was foreseen that similar pyrolysis of the bis(sulphone) (203) might lead to the formation of styrene (207) via loss of SO_2 in tandem with loss of hydrogen as outlined in Scheme 120.



Scheme 120

In practice, this was achieved in a single step by FVP over 5% palladium on activated carbon catalyst at 650°C whereupon both rearrangement and dehydrogenation occurred to give styrene (12%) together with benzene (4%), toluene (2%), xylenes (2%) and ethyl benzene (2%).

Better yields of styrene (207) at 45% conversion were obtained by direct FVP of 1,5-cyclo-octadiene (204) under the same dehydrogenating conditions. At the optimum temperature of 650°C, the crude pyrolysate consisted of styrene (62%), xylenes (3%), toluene (9%) and benzene (26%). No ethylbenzene was detected. The results of pyrolysis of (204) at different temperatures over 5% Pd/C are summarised in Table 1.

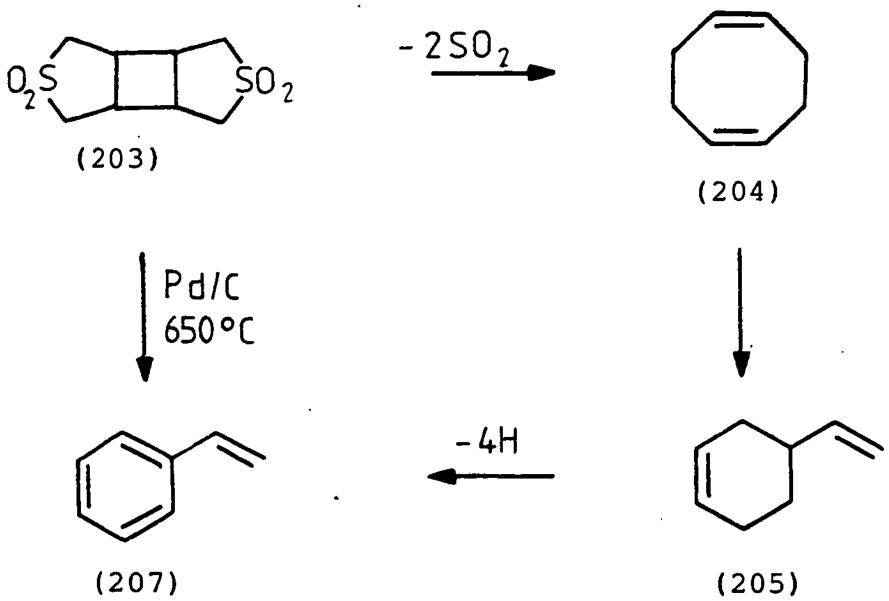
Pyrolysis Temp. °C	Styrene	Xylenes	Toluene	Benzene	Ethyl Benzene	1,5-cyclo-octa-diene	C_8H_{12}
750°	-	-	15%	85%	-	-	-
650°	62%	3%	9%	26%	-	-	-
550°	38%	15%	4%	14%	22%	-	7%
450°	42%	4%	2%	14%	35%	2%	-
350°	3%	15%	7%	8%	26%	31%	9%

Table 1

The pyrolysates were analysed by ^{1}H n.m.r. spectroscopy, GC (10% PEGA, 55°C) and by GC-MS. The butadiene also formed was not quantified but with increasing temperature, it was apparent that the proportion of gaseous products also increased.

The results in Table 1 give comparative ratios of the products. On comparison with a standard solution of styrene, its yield from pyrolysis of 1,5-cyclo-octadiene (204) at 650°C was 28% (by GC analysis) and 25% from pyrolysis at 550°C. At 450°C, the yield of styrene (207) decreased to 12%. The reaction sequence is summarised in Scheme 121.

On an industrial scale, styrene (207) is usually manufactured by direct dehydrogenation of ethylbenzene formed in turn by the alkylation of benzene with ethylene. An economic drawback to this process is the difficulty in separating styrene from unreacted ethylbenzene. By comparison, 1,5-cyclo-octadiene is readily obtained from the cyclic dimerisation of butadiene,[84] and, as the above results show, can be converted into styrene with no contamination by ethyl benzene.

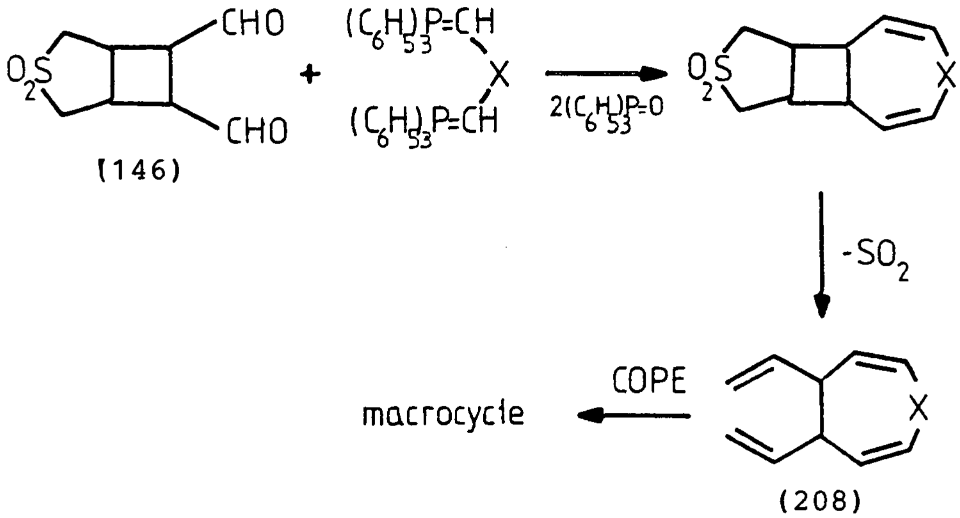


Scheme 121

Consequently this novel vapour phase catalytic dehydrogenation of 1,5-cyclo-octadiene has formed the basis of a patent application by British Petroleum[172] for the production of styrene. The only other known direct route to styrene from 1,5-cyclo-octadiene has been patented by Shell and involves oxygen and iodine in a molten medium containing a metal compound.[173]

F. Attempted preparation of Macrocycles via Cope rearrangement of *cis*-1,2-Divinyl cyclic compounds

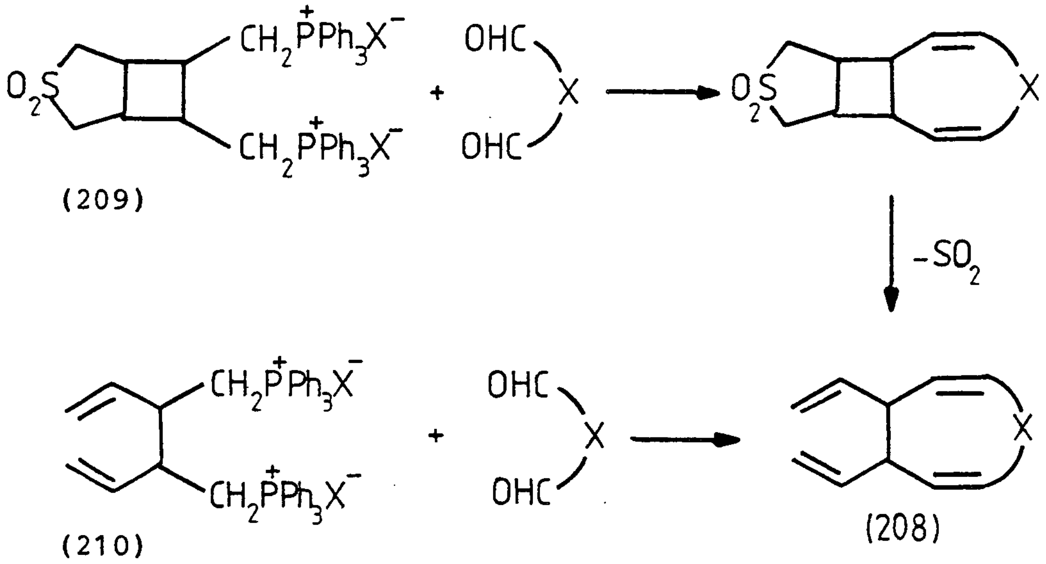
In Section A6 (p.144), the sulphone dialdehyde (146) was discussed as a possible starting material for a route to large rings via a bis-Wittig reaction. As outlined in Scheme 122 it was envisaged that, following thermal elimination of SO_2, the resulting cyclic 1,2-divinyl compound (208) could undergo a Cope rearrangement provided the ring was sufficiently large. The effect of ring size on the ease of Cope rearrangement of these cyclic compounds could thus be studied.



Scheme 122

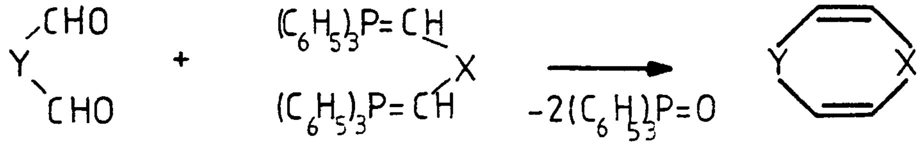
As discussed in the Introduction (p.33), *cis*-1,2-divinyl cyclic systems of three- and four-membered rings rearrange very readily while those with five- and six-membered rings are inert to the ring expansion. The largest ring size to have been studied so far, an eight-membered ring, is however susceptible to Cope rearrangement.

Unfortunately, all attempts to prepare the dialdehyde (146) and its *cis*-1,2-divinyl derivative were unsuccessful because of lactone formation and double bond shifts, respectively (see p.145 and p.166). In an attempt to circumvent these problems, it was decided to adopt an alternative approach whereby a bis(aldehyde) was condensed with a bis(phosphonium) salt as shown in Scheme 123.



Scheme 123

The Wittig reaction has been used as a general route to the formation of a carbon-carbon double bond since its discovery in 1953 by Wittig and Geissler.[174] The bis-Wittig reaction, between a bis-alkylidenetriphenylphosphorane and a dicarbonyl compound, leads to the formation of unsaturated cyclic compounds (Scheme 124). A review by Vollhardt[175] covers the synthesis

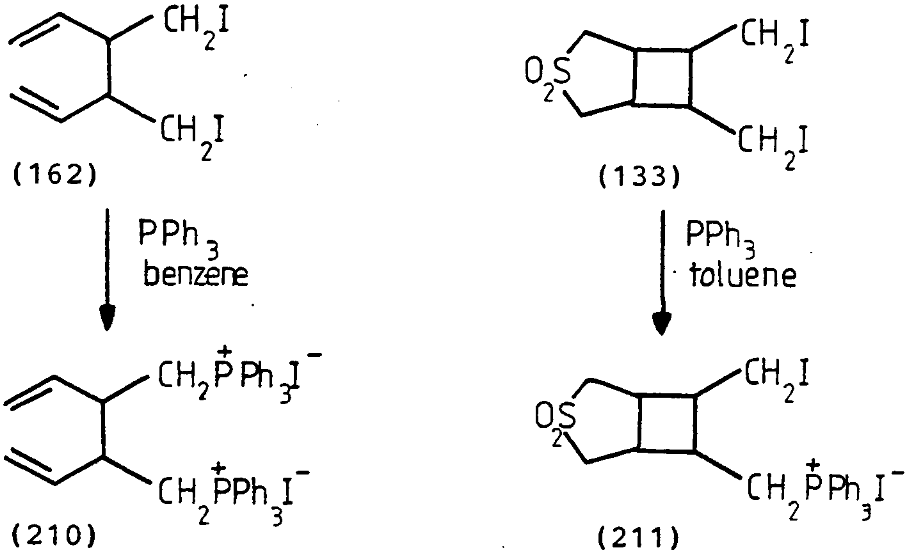


Scheme 124

of cyclic systems ranging in size from five to thirty-six members by this method.

1. Preparation of bis(phosphonium) salts

The phosphonium salts (210) and (211) were prepared by boiling a solution of the di-iodide (162; X=I) or (133; X=I) and triphenylphosphine in an aromatic solvent (Scheme 125). Thus the bis(phosphonium) salt (210) was obtained analytically pure in 65% yield after recrystallisation from methanol. ^{31}P n.m.r. spectroscopy indicated a single peak at 23.2 ppm which is characteristic for phosphonium salts.[176]



Scheme 125

When the sulphone di-iodide (133; X=I) was heated with triphenylphosphine under similar conditions, a colourless crystalline product was obtained which was identified as the mono-phosphonium salt (211) by elemental analysis (90% yield) (Scheme 125). Longer reaction times and higher temperatures failed to produce the corresponding bis(phosphonium) salt.

Attempts to prepare the same phosphonium salts from the corresponding dibromo- and dichloro-compounds were unsuccessful.

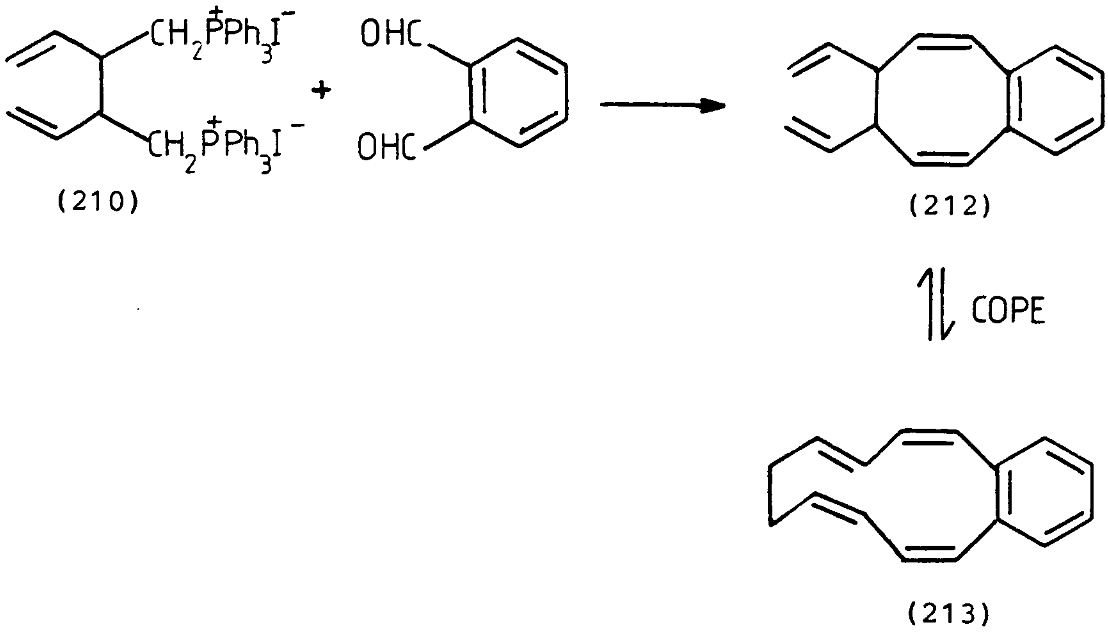
2. Attempted bis-Wittig reactions of *meso*-3,4-Bis(triphenylphosphoniumiodomethyl)-1,5-hexadiene

Since the bis(phosphonium) salt of the sulphone (133; X=I) could not be obtained, the *cis*-1,2-divinyl bis(phosphonium) salt (210) was used in the attempts to prepare macrocycles by the Cope rearrangement.

Using *n*BuLi in dry THF under reflux, no reaction occurred between the bis(phosphonium) salt (210) and benzil. Upon changing the reaction conditions to lithium ethoxide in dimethylformamide at 90°C, the dark red reaction mixture, monitored by t.l.c., showed the presence of only starting material even after 22 h.

The corresponding reaction with *o*-phthalicdicarboxaldehyde was more successful. The best result was obtained using lithium ethoxide in DMF when, after preparative t.l.c., a colourless oil was isolated in 24% yield. Although its ^1H n.m.r. spectrum was consistent with the expected structure (212), ^{13}C n.m.r. spectroscopy indicated the presence of more than one compound. [δ_C 46.36, 40.59, 36.83, and 29.13 (aromatic and olefinic carbons not listed)]. Positive identification was not achieved due to the small amount obtained but it is conceivable that the initially formed (212) might exist in equilibrium with its Cope-derived isomer (213) (Scheme 126).

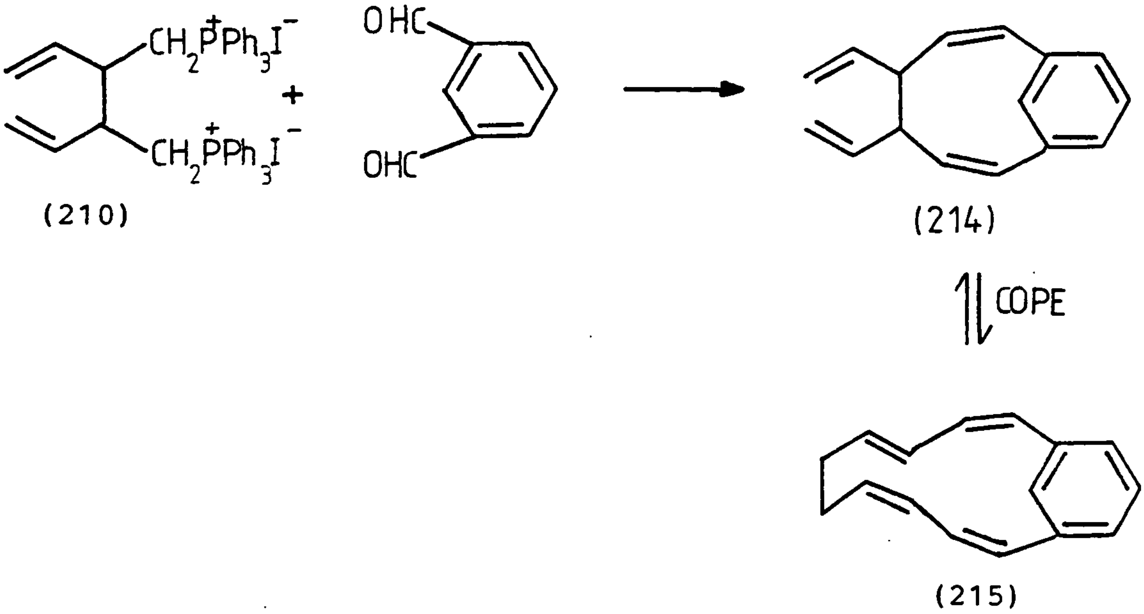
The reaction between (210) and isophthaldehyde was also studied using the conditions of Sondheimer *et al*[177] (LiOEt, DMF).



(210) (212) (213)

Scheme 126

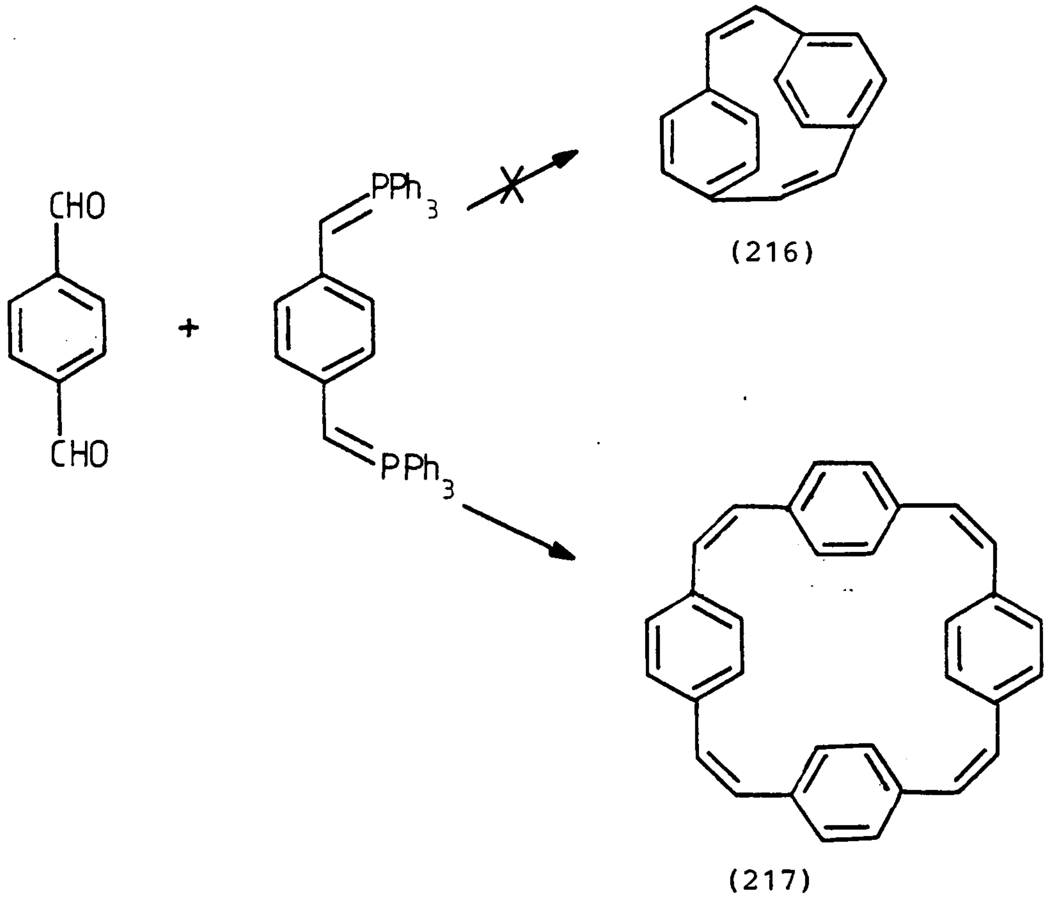
The product was isolated in low yield by preparative t.l.c. and was found from ^{1}H n.m.r. spectroscopy to consist of aromatic, vinyl and aldehyde groups. Due to the small amount of material obtained, further purification was not attempted but, if formed, the product (214) would have contained a nine-membered ring. According to molecular models, such a system is highly strained and might be expected to undergo a ready ring-expansion to the thirteen-membered ring compound (215) (Scheme 127).



(210) (214) (215)

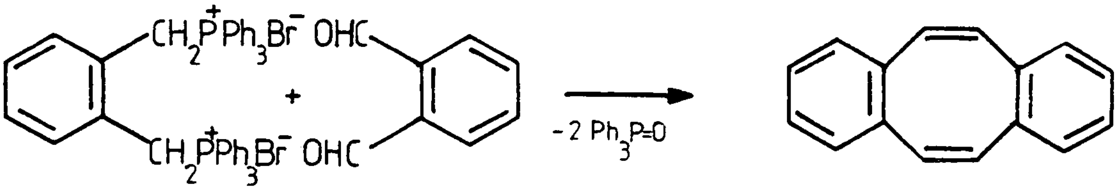
Scheme 127

Clearly more work is required to determine the structure of these low-yield products. It is possible that polycondensation may have occurred instead since it is observed that if the product from a bis-Wittig reaction is too strained, four-fold Wittig reactions may occur.[178] For example, condensation of terephthaldehyde and *p*-xylene bisylidenetriphenylphosphorane leads to [2.2.2.2]paracyclophane-1,9,17,25-tetraene (217) in 15% yield rather than (216) (Scheme 128).[179]



Scheme 128

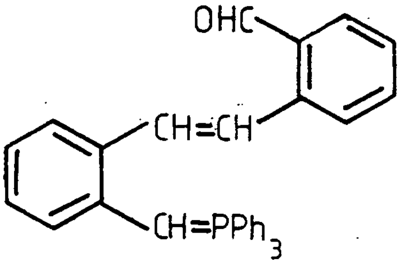
Another problem with the approach to macrocycles outlined in Scheme 124, is that, in general, the yields of cyclic compounds from bis-Wittig reactions are low and often very dependent on the reaction conditions. A major difficulty is that the new double bonds can be formed in the *cis* and/or *trans* configuration. An example by Griffin and Peters[180] illustrates the effect of reaction conditions on the formation of 1,2,5,6-dibenzocyclooctatetraene (218) (Scheme 129).



(218)

Scheme 129

Using lithium ethoxide in dimethylformamide, (218) was obtained in 18% yield. However, using sodium ethoxide in absolute ethanol which are conditions known to give *trans*-alkenes, mainly polymeric side-products were obtained. In this case, the initial product (219) has a *trans* double bond and



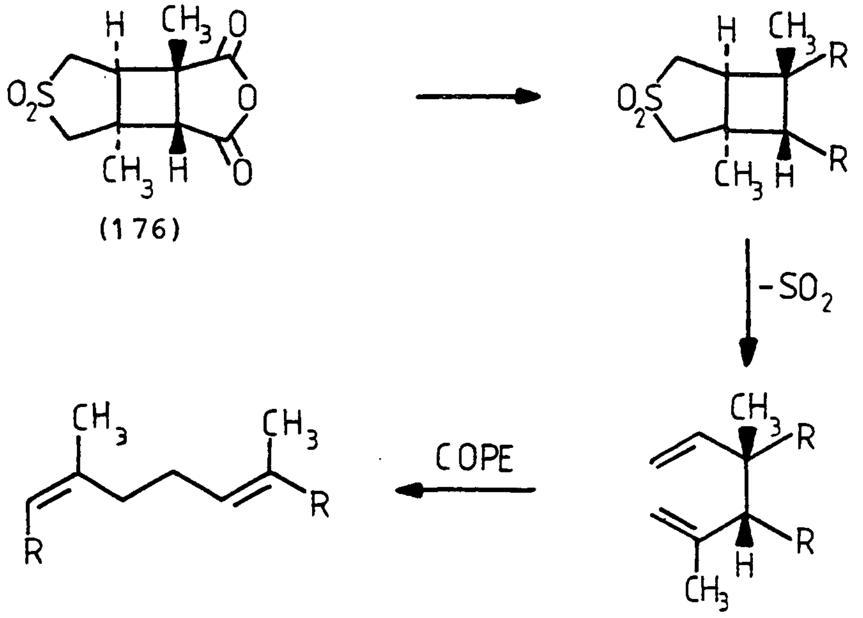
(219)

undergoes intermolecular reaction to form polymer instead of intramolecular ring closure which requires a *cis* stereochemistry.

G. Preparation and flash vacuum pyrolysis of methylated derivatives of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]-decane 9,9-dioxide

1. Preparation of methylated derivatives of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

It was envisaged that by preparing the methylated sulphone anhydride (176), it would be possible to extend the stereospecific synthesis of *cis*,*trans*-1,5-dienes to isoprenoid systems. The strategy to be adopted would involve the conversion of (176) into suitable derivatives followed by extrusion of SO_2 under flash vacuum conditions. It was hoped that the stereospecific formation of the *cis*-1,2-divinyl intermediate (220) would lead to isoprenoids via a Cope rearrangement as shown in Scheme 130.



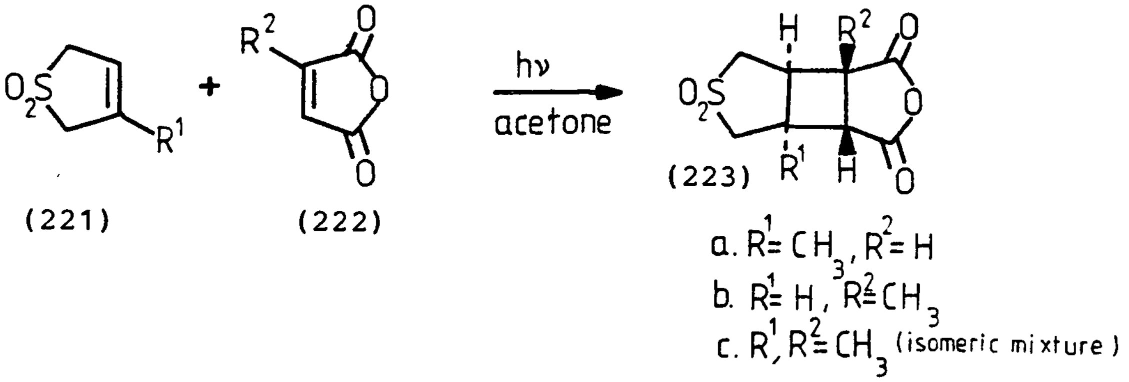
(176)

(220)

Scheme 130

It is to be emphasised that the following studies are of a preliminary nature and future work is necessary to achieve the aims described above. However, initial results obtained are encouraging especially in view of independent work by Williams and Lin[129] with similar systems.

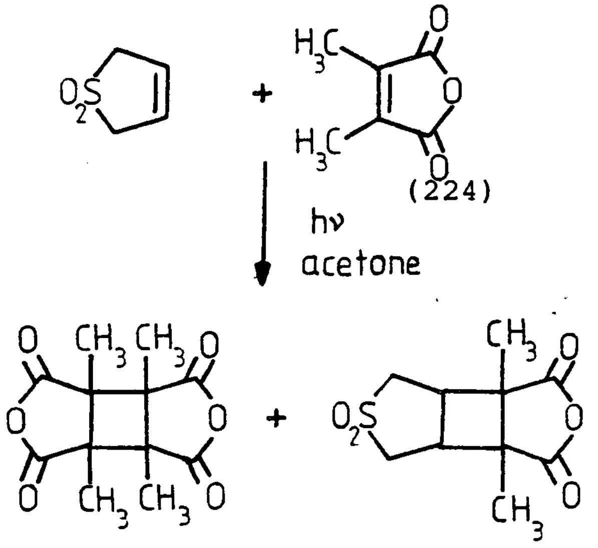
As part of model studies, it was necessary to first prepare 3-methyl-2,5-dihydrothiophen 1,1-dioxide (221; R=CH_3). This involved the reaction of isoprene with liquid sulphur dioxide in an autoclave at 85°C for 4 h. Subsequent photolysis of (221; R^1=CH_3) and maleic anhydride gave the adduct, 1-methyl-3,5-dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide (223a) in 36% yield (Scheme 131). The 2-methyl derivative (223b) was similarly obtained from the photolysis of a solution of butadiene sulphone and citraconic anhydride (222; R^2=CH_3) in acetone. Despite their extreme sensitivity towards hydrolysis, both anhydrides (223a) and (223b) showed expected analytical and spectroscopic properties.



Scheme 131

Photocycloaddition of (221; R^1=CH_3) and (222; R^2=CH_3) following the reaction conditions of Shaikhrazieva *et al* [111] gave an isomeric mixture of the 1,6-dimethyl and 1,2-dimethyl compounds (223c). In independent studies, Williams and Lin[129] reacted (221; R^1=CH_3) and (222; R^2=CH_3) by photolysis in methylene chloride under nitrogen at -78°C for 30 h. Under these conditions, they reported isolation of the 1,6-dimethyl compound (176) in 80% yield but stated that their product crystallised in two forms which they presumably separated by fractional crystallisation.

Attempts to prepare the dimethyl analogue (226) by photolysis of dimethylmaleic anhydride (224) and butadiene sulphone failed to give a useful yield due to preferential dimerisation of (224) (Scheme 132). Similar findings have been reported by Shaikhrazieva *et al.*[111] From i.r., MS and ^{1}H n.m.r. spectroscopy it was apparent that there was a trace of the desired adduct (226) but chromatographic separation could not be achieved.

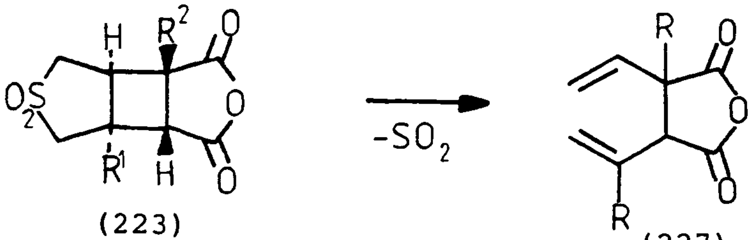


(225) (226)

Scheme 132

2. FVP of methylated derivatives of 3,5-Dioxo-4-oxa-9-thiatricyclo[5.3.0.0^{2,6}]decane 9,9-dioxide

Pyrolysis of the 1-methyl sulphone (223a) at 580°C gave *cis*-2-methyl-1,5-hexadiene-3,4-dicarboxylic anhydride (227a) as a colourless liquid in 69% yield. Similarly, the 2-methyl sulphone (223b) gave an 86% yield of the corresponding divinyl anhydride (227b) (Scheme 133).



(223)

(227)

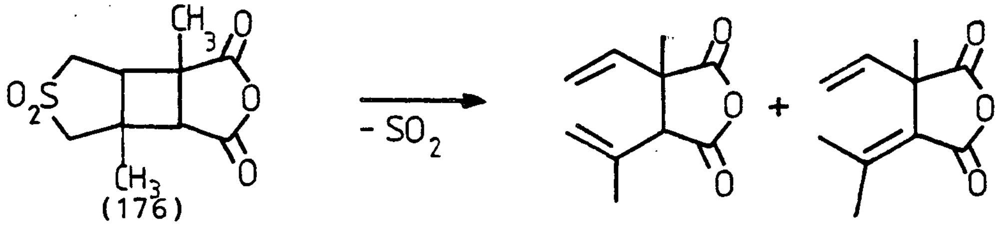
a. $R^1=CH_3$, $R^2=H$

b. $R^1=H$, $R^2=CH_3$

c. $R^1,R^2=CH_3$ (isomeric mixture)

Scheme 133

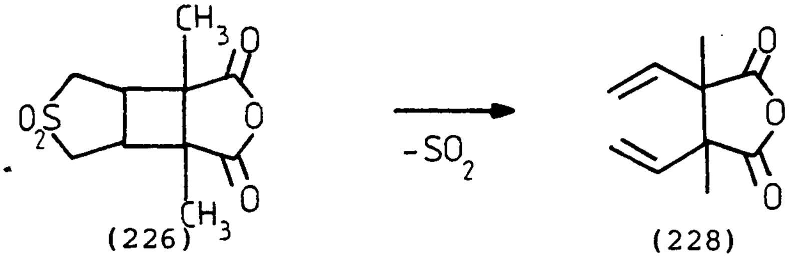
In the case of the mixture of 1,6-dimethyl- and 1,2-dimethyl-isomers (223c), FVP gave a 59% yield of the 2,4- and 2,3-dimethyl divinyl anhydrides (227c) in equal ratios from both ^1H and ^{13}C n.m.r. spectroscopy. In contrast, Williams and Lin[129] have reported that FVP of the 1,6-dimethyl sulphone (176) afforded a mixture of the *cis*-3,4-divinyl anhydride (177) and its conjugated isomer (178).



(176) (177) (178)

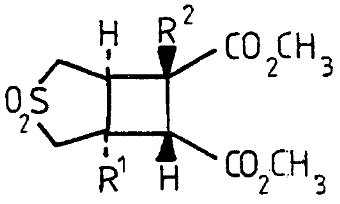
Scheme 100

Similar pyrolysis of the 2,6-dimethyl sulphone (226) at 580°C gave *cis*-3,4-dimethyl-1,5-hexadiene-3,4-dicarboxylic anhydride (228) (Scheme 134). The presence of a singlet at δ2.05 in the ^1H n.m.r. spectrum was attributed to impurities of the dimer (225) which could not be separated from the dimethyl anhydride (228) either by distillation or by preparative t.l.c.

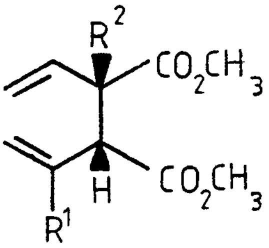


Scheme 134

The dimethyl esters (229a) and (229b) were easily obtained by boiling the corresponding sulphone anhydrides in an excess of methanol containing a trace of sulphuric acid. *meso*-2-Methyl- and *meso*-3-methyl-3,4-dimethoxycarbonyl-1,5-hexadiene, (230a) and (230b) respectively, were also prepared from the corresponding 1,2-divinyl anhydrides by the same method. The 2-methyl compound (230a) was obtained as colourless plates, m.p. 34-36°C, while the 3-methyl diester (230b) was isolated as a colourless, viscous liquid.



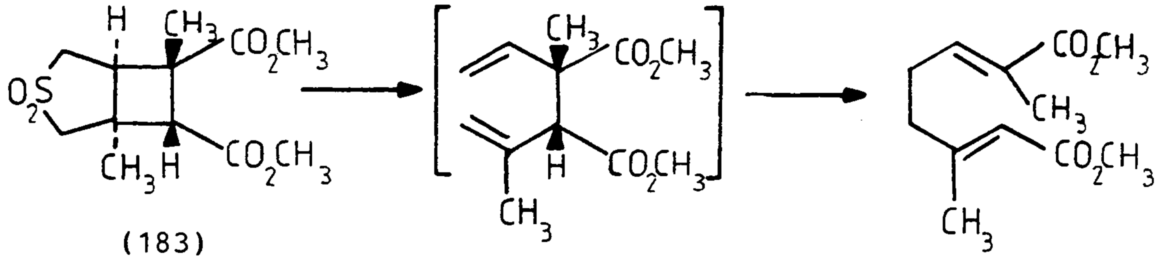
(229)



(230)

a. $R^1 = CH_3, R^2 = H$
b. $R^1 = H, R^2 = CH_3$

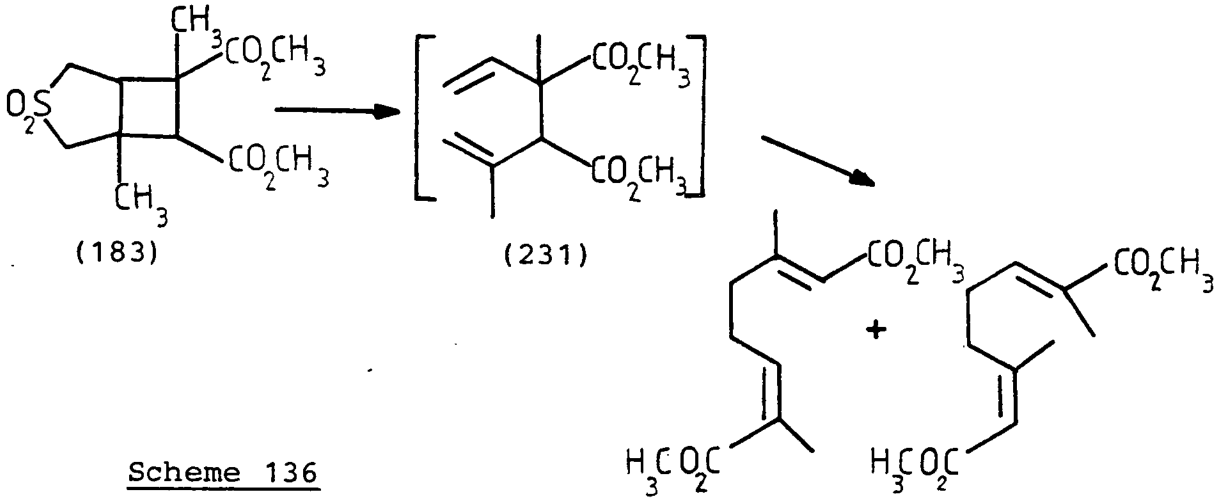
Limitations of time prevented an investigation of the pyrolyses of these diesters but related work by Williams and Lin[129] reported that FVP of the 1,6-dimethyl sulphone (183) at 500°C gave *trans,trans*-dimethyl 2,6-dimethylocta-2,6-diene-1,8-dicarboxylate (184) in 87% yield (Scheme 135). This result is surprising because if the reaction proceeds via a chair-like Cope rearrangement of the intermediate *cis*-1,2-



(183) (231) (184)

Scheme 135

divinyl compound (231), the product might be expected to consist of two isomers having *cis,trans*-stereochemistry as shown in Scheme 136.



(183) (231)

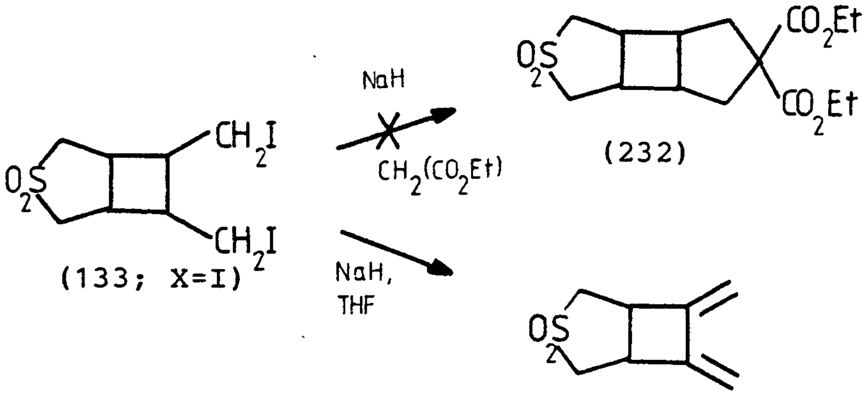
Scheme 136

The ^{13}C n.m.r. spectrum of (184) is reported by Williams and Lin[129] to consist of 12 signals. This attests to the stereoisomeric purity of (184) but does not provide proof of its stereochemistry since the *cis,trans*-isomer would also give 12 signals by ^{13}C n.m.r. spectroscopy. Nonetheless, some evidence for *trans,trans*- (184) was obtained by conversion of (184) into 10-hydroxygeraniol (185) (see Scheme 103, p.169).

H. Preparation and reactions of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

1. Preparation of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

While attempting to prepare the tricyclic compound (232) by cycloalkylation of the di-iodide (133; X=I) with diethylmalonate in the presence of sodium hydroxide,[181] a colourless crystalline compound was isolated and identified as the dimethylene derivative (158) (Scheme 137). Elemental analysis agreed with the proposed structure of (158) but the major confirmatory evidence came from its ^{1}H n.m.r. spectrum (Fig.13) consisting of two broad singlets at δ5.39 and δ4.96 which are typical of the exocyclic methylenes.[139] Definitive proof of the structure of (158) was obtained from subsequent reactions, especially its pyrolysis which gave 3,4-dimethylene-1,5-hexadiene (159).



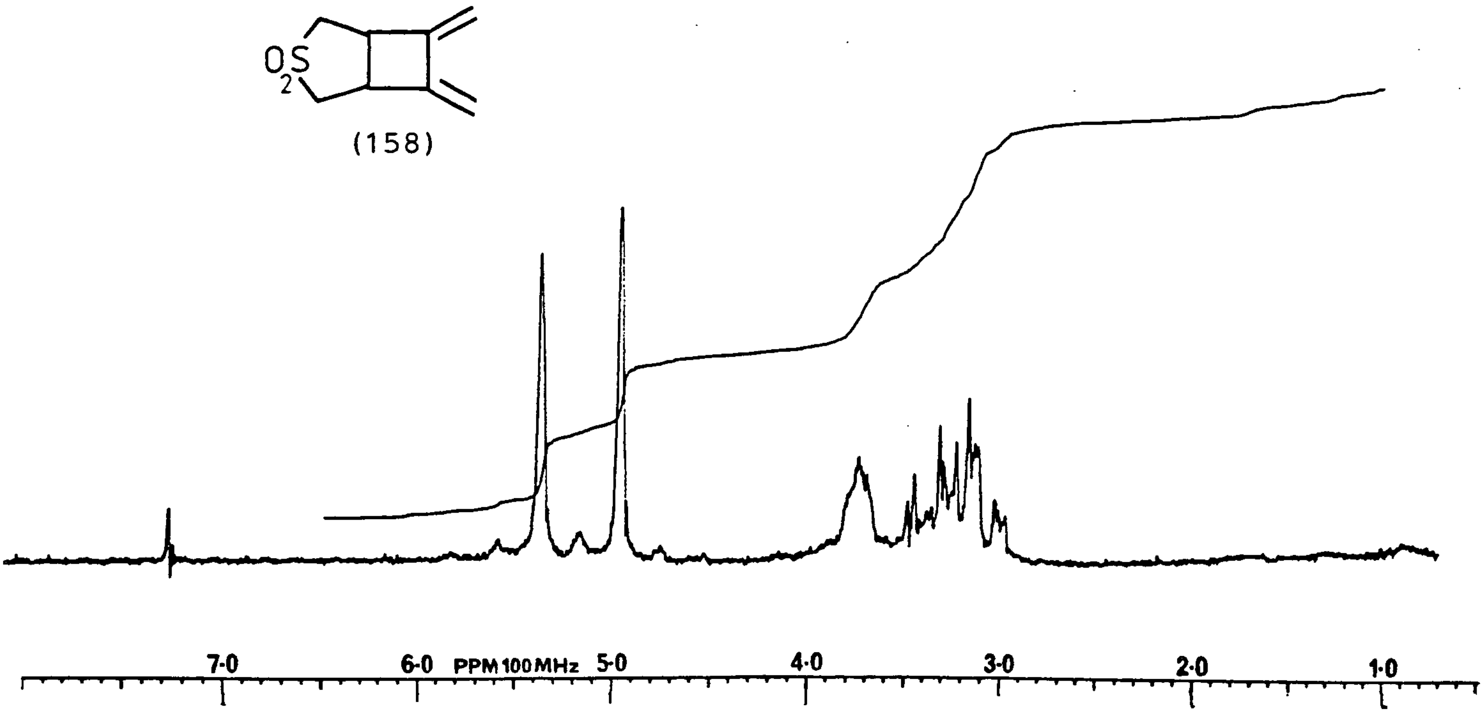
(133; X=I)

(232)

(158)

Scheme 137

That the dimethylene sulphone (158) arose from the di-iodide (133; X=I) was shown by the direct treatment of the latter with sodium hydride in THF at room temperature to give (158) in 89% yield. The compound (158) exhibited some



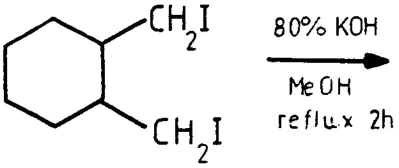
(158)

Fig. 13 ^{1}H n.m.r. spectrum of 6,7-Dimethylene-3-thiabicyclo-[3.2.0]heptane 3,3-dioxide

instability as a consequence of which partial polymerisation occurred during recrystallisation. It also underwent decomposition when exposed to the atmosphere for long periods thus precluding the determination of its ^{13}C n.m.r. spectrum.

With hindsight, the dehydrohalogenation of (133; X=I) to (158) is not unexpected. The patented method for the preparation of 1,2-dimethylenecyclohexane (233) (useful in the preparation of resinous polymers) involves treatment of the corresponding di-iodide with basic methanol (Scheme 138).[182]

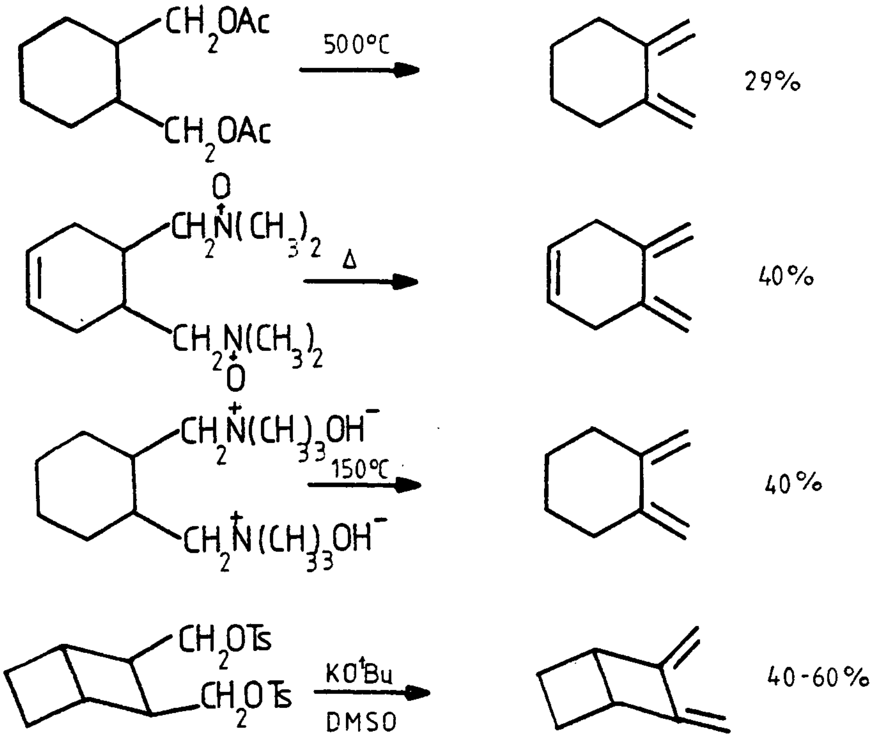
Other methods for the formation of exocyclic double bonds are known and include acetate[183] or amine oxide pyrolysis,[184] Hofmann degradation of a bisquaternary ammonium hydroxide,[183] and elimination from a bis(*p*-toluenesulphonate)derivative.[139]



(233)

Scheme 138

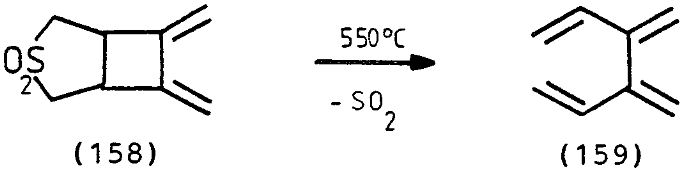
Some examples are shown in Scheme 139. Apart from the latter, all these methods involve high temperatures which might encourage polymerisation of the diene product. Use of the bis(*p*-toluenesulphonate) elimination method did prove successful for the preparation of (158) but it involved a more difficult work-up in order to completely remove traces of DMSO and *t* butanol.



Scheme 139

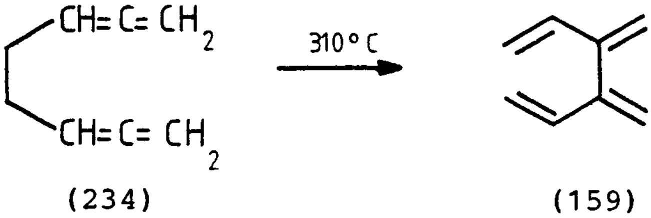
2. FVP of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide: Preparation of 3,4-Dimethylene-1,5-hexadiene

Thermal extrusion of SO_2 from (158) at 550°C and at 0.001 mmHg resulted in the formation of 3,4-dimethylene-1,5-hexadiene (159) in yields that varied from 22-82% depending on the extent of polymerisation of (158) in the inlet of the FVP apparatus (Scheme 140). By comparison of the ^{1}H n.m.r. spectrum of the pyrolysate (Fig.14) with literature data,[136] it was clear that FVP of (158) had given rise to (159) without the formation of any of the isomeric forms which usually accompany its preparation by other routes.



Scheme 140

The preparation of (159) was first reported by Skattebøl and Solomon[136] in 1965 by heating the bisallene (234) at 310°C (Scheme 141). Under these conditions they obtained a mixture of (159) and another unstable, unidentified compound. Since (159) was very unstable and tended to polymerise very readily, structural proof was provided only by spectroscopic data.



Scheme 141

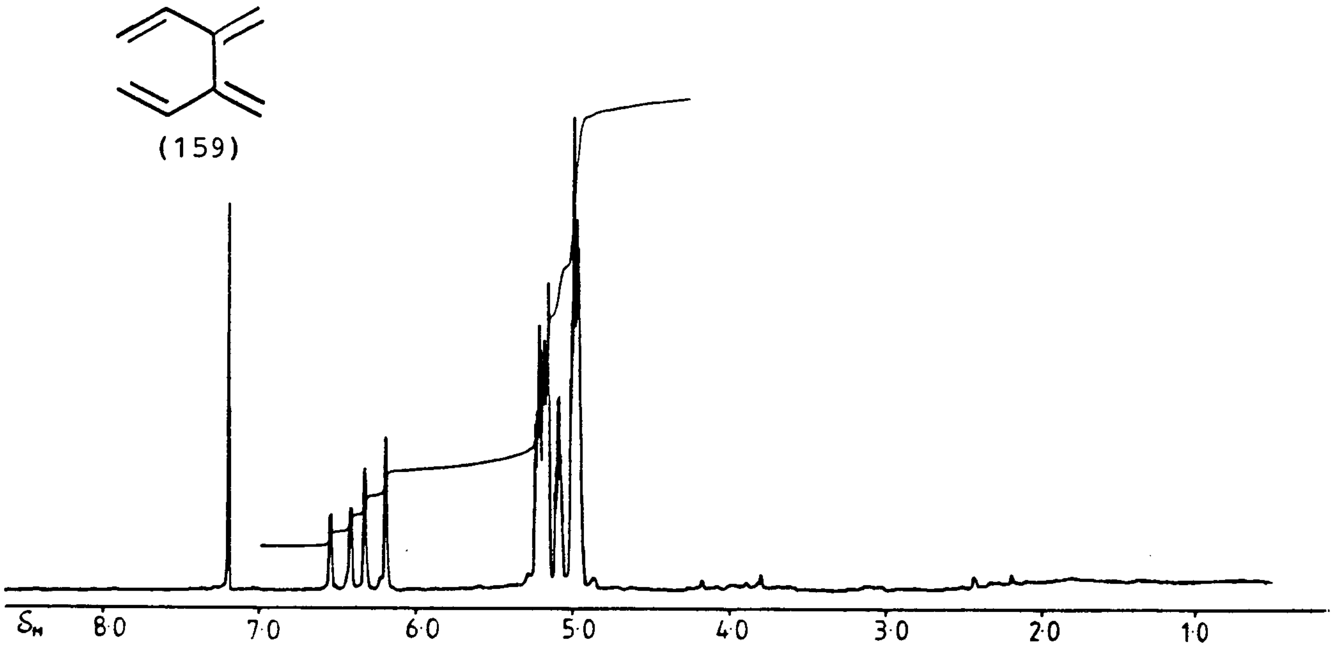
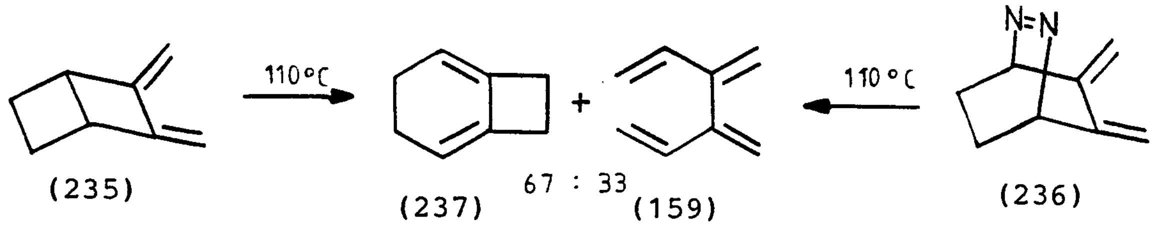
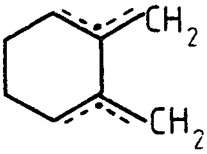

(159)

Fig.14 ^{1}H n.m.r. spectrum of 3,4-Dimethylene-1,5-hexadiene

Following these observations, the preparation of (159) was studied in detail by Roth *et al.* In 1973, these workers[185] obtained (159) together with bicyclo[4.2.0]octa-1,5-diene (237) from the gas-phase thermolysis of both (235) and (236) at 110°C (Scheme 142). The formation of (237) and (159) in the same ratio of 67:33 from either (235) or (236) indicated the occurrence of a common intermediate to which Roth *et al*[185] ascribed the structure of the diradical, 2,3-dimethylene-1,4-cyclohexadiyl (238).

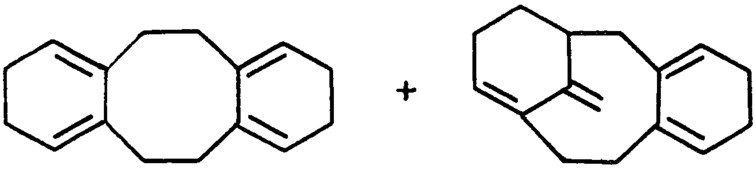

(235) (237) (159) (236)

Scheme 142



(238)

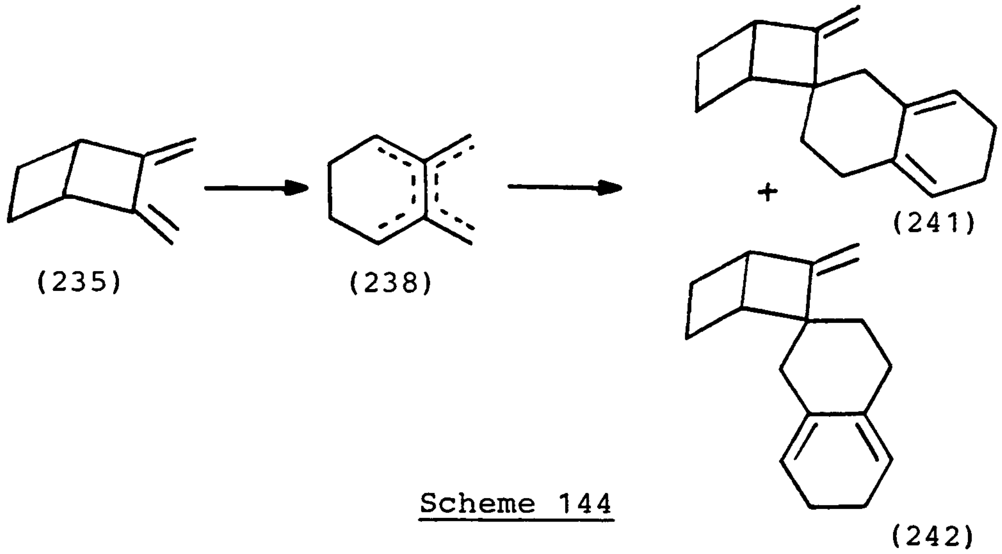
This intermediate is also implicated in the formation of the dimers (239) and (240) from the thermolysis of (235) or (236) at 110°C in cyclohexane (Scheme 143).[185]



(239) (240)

Scheme 143

Bauld and Chang[186] have also investigated the reactions of 2,3-dimethylenebicyclo[2.2.0]hexane (235). They found that decomposition of (235) in tetrachloroethylene at 40-60°C gave different dimers, (241) and (242), corresponding to *exo*- and *endo*-addition of the tetramethylene-ethane derivative (238) to (235) (Scheme 144). The spectroscopic properties for Roth's dimers are different from those reported by Bauld and Chang for their dimers but no explanation has been given for this dichotomy. In passing it is worth noting that no evidence for dimer formation could be obtained in the present study by heating a solution of (159) in d^6 benzene at 80°C for one week. This is not really surprising since the aforementioned dimers presumably arise from the 2,3-dimethylene-1,4-cyclohexadiyl (238) which is not involved in the formation of (159) from

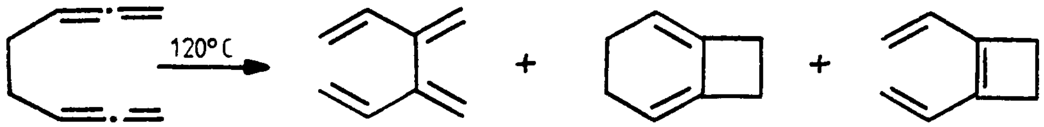


(235) (238) (241) (242)

Scheme 144

pyrolysis of the sulphone (158).

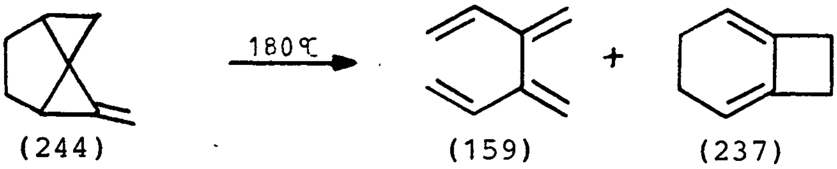
Roth *et al*[187] have also investigated the rearrangement of the bisallene, 1,2,6,7-octatetraene (234), and discovered that its thermolysis besides affording (159) and (237) also led to the formation of 1,2-divinyl-1-cyclobutene (243) (Scheme 145). It was also shown that at 170°C (243) rearranged to (159) and (237) while at 250°C, (237) passed irreversibly to (159) which was also reported to be favoured at low pressure.



(234) (159) (237) (243)

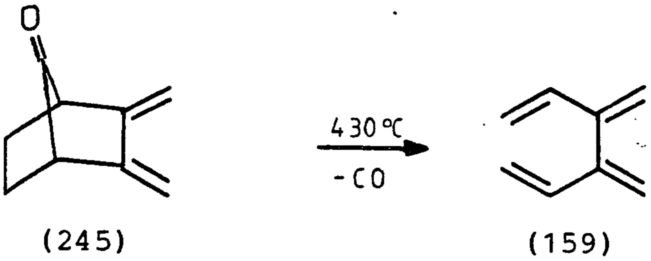
Scheme 145

A mixture of (159) and (237) was also obtained from the thermolysis of 2-methylenetricyclo[4.1.0.0^{1,3}]heptane (244) in the gas phase at 180°C (Scheme 146).[188]



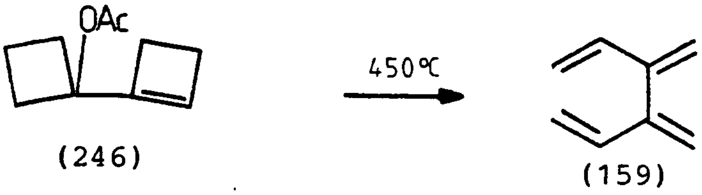
Scheme 146

In contrast to the methods cited above, thermal fragmentation of 2,3-dimethylene-7-norbornanone (245) at 430°C gave only (159) (Scheme 147).[189] It seems likely that (237) is also formed in the thermolysis but is converted into (159) at the higher reaction temperature.



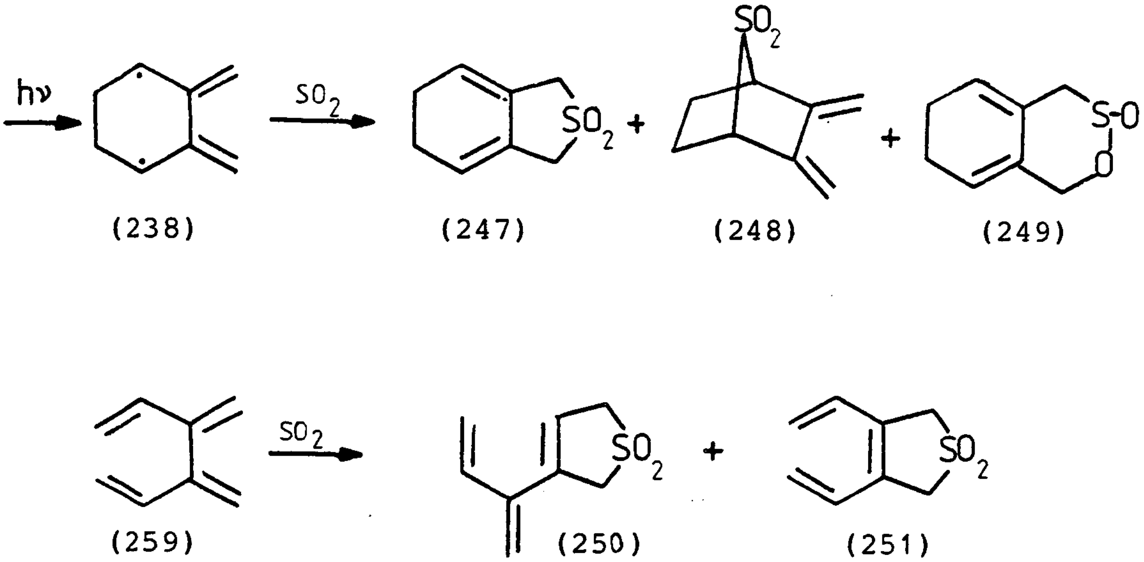
Scheme 147

Garratt *et al*[190] have also reported the preparation of (159) in 23% yield by a method involving the flow pyrolysis of the acetate (246) at 450°C and at 0.1 mmHg (Scheme 148).



Scheme 148

In a more recent publication, Roth *et al*[191] have made further kinetic studies on the thermal rearrangement of the bisallene (234). They have also demonstrated the competition between the concerted and non-concerted reaction paths for the Cope rearrangement of (234) to (159) by trapping experiments. The products from the reactions of the diradical (238), (159) and of the bisallene (234) with SO_2 are compared in Scheme 149. This shows the preference for the non-concerted reaction path for the rearrangement (234) to (159) via the diradical intermediate (238).



(238) (247) (248) (249)

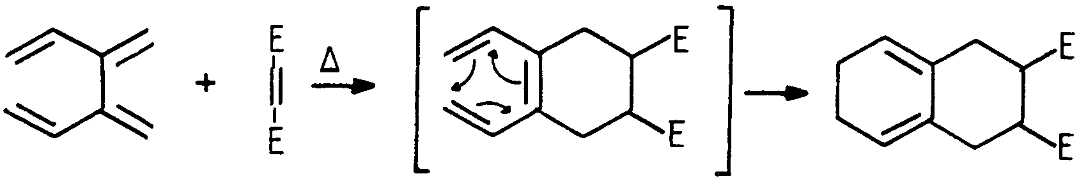
(259) (250) (251)

	% (247)	% (248)	% (249)	% (250)	% (251)
(238)	85	4	11		
(159)				80	20
(234)	68	5	8	16	3

Scheme 149

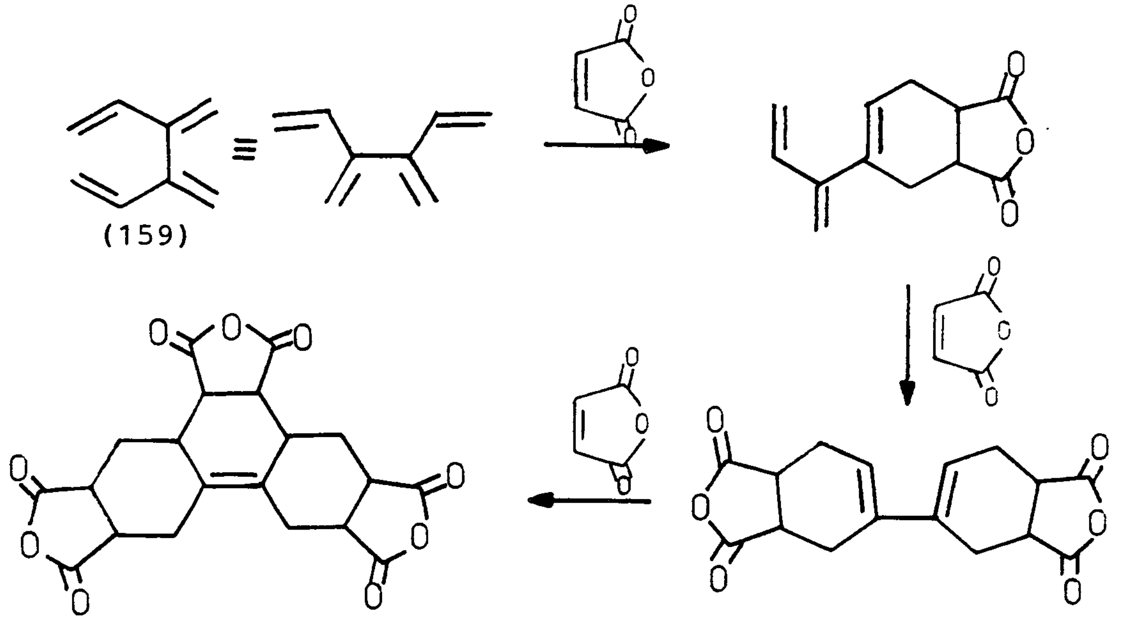
3. Reactions of 3,4-Dimethylene-1,5-hexadiene

In principle, 3,4-dimethylene-1,5-hexadiene (159) has the potential to serve as a tandem annulating reagent as outlined in Scheme 150. Unfortunately, this prospect is marred by a lack of regiospecificity in reactions with dienophiles. Thus, Roth and his co-workers[191] have already shown that cycloaddition with SO_2 affords the adduct (250) and the isomeric *cis*-hexatriene (251) which surprisingly failed to undergo electrocyclisation. Further difficulties were experienced in the present work with other dienophiles due to the formation of bis- and sometimes tris-adducts. For example, in the reaction of (159) with maleic anhydride, a crystalline solid was obtained which from mass spectroscopy consisted of a mixture of the bis- and tris-adducts, (254) and (255) respectively (Scheme 151). This is also in keeping with the results of Skattebøl and Solomon[136] who obtained a mixture of the bis- and tris-adducts from the reaction of 2,3-divinyl-



(159) (252) (253)

Scheme 150

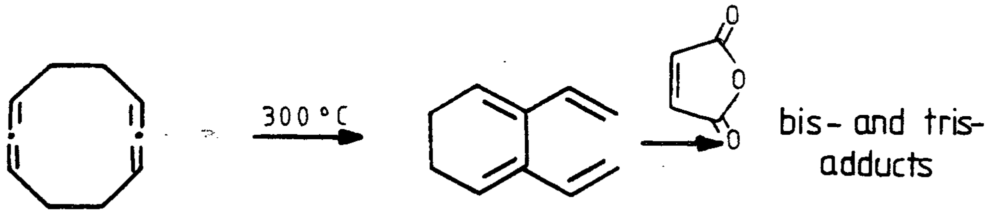


(255)

(254)

Scheme 151

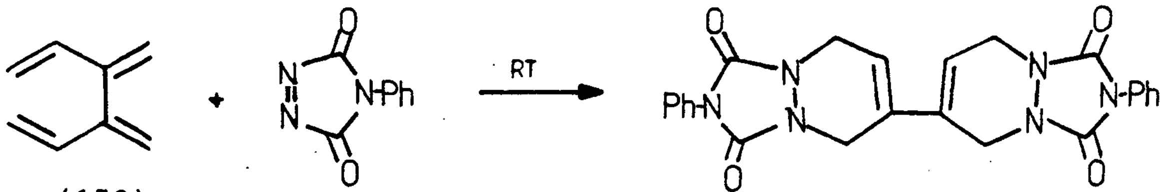
1,3-cyclohexadiene (256) with maleic anhydride (Scheme 152).



(256)

Scheme 152

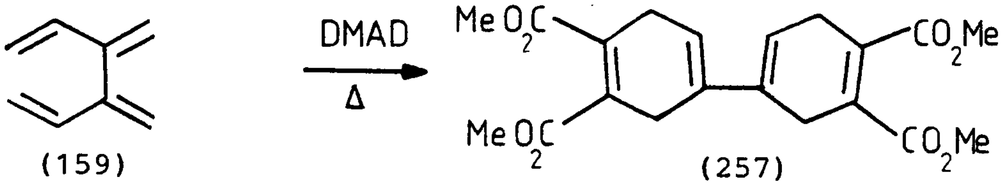
Similar reaction of (159) with 4-phenyl-3H-1,2,4-triazoline-3,5-dione yielded an insoluble, colourless solid, m.p. 280°C (decomp.) whose mass spectrum was consistent with the addition of 2 moles of dienophiles (Scheme 153).



(159)

Scheme 153

In the same way, reaction of (159) with an equivalent amount of dimethyl acetylenedicarboxylate failed to give a 1:1 adduct as was observed by Roth *et al*[191] in the foregoing reaction with SO_2 (Scheme 149). Instead, the bis-adduct (257) was obtained in 94% yield as shown in Scheme 154. MS and ^1H n.m.r. spectroscopy were consistent with the proposed structure [δ_H 5.77 (2H, br s), 3.79 and 3.78 (12H, s), and 3.16 (8H, br s)].

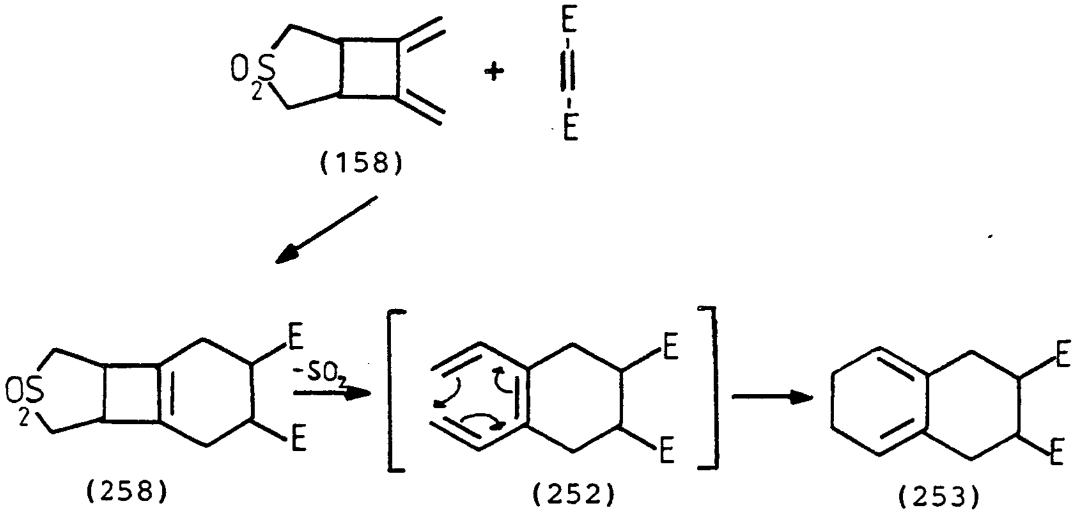


Scheme 154

4. Preparation and FVP of Diels-Alder adducts of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide

It was envisaged that the lack of regiospecificity in the reaction of 3,4-dimethylene-1,5-hexadiene (159) with dienophiles could be circumvented by use of the dimethylene sulphone (158) which in actuality is its synthetic equivalent. Although (158) polymerises readily on heating, it was found to undergo [4+2] cycloaddition reactions with a variety of dienophiles. The adducts (259)-(264) were formed in good yields (53-91%) by heating a solution of the diene (158) with the dienophile in benzene or toluene for several hours whereas the more reactive dienophile, 4-phenyl-3H-1,2,4-triazoline-3,5-dione, yielded the adduct (263) in ether at room temperature (Table 2). The adducts all exhibited the expected analytical and spectroscopic properties.

When subjected to FVP, the adducts, e.g. (258) extruded SO_2 cleanly to give good-to-fair yields of the hexahydronaphthalene derivative (253). The formation of the latter presumably occurs via the hexatriene (252), a transient intermediate which subsequently undergoes an electrocyclic ring closure as shown in Scheme 155. In the overall transformation to (253), it is apparent that the dimethylene sulphone (158) serves as a tandem annulation reagent. Such reagents are rare and of current interest.



Scheme 155

Thus Trost *et al*[192] have recently described the use of 2-bromomethyl-3-(trimethylsilylmethyl)buta-1,3-diene (273) whereupon alkylation of the enolate (272) with (273) followed by cyclisation of the allysilane moiety onto the carbonyl group resulted in the first annulation step. In the second step, the resultant 2,3-dimethylenecyclohexane (274) was reacted

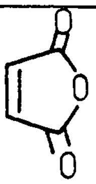
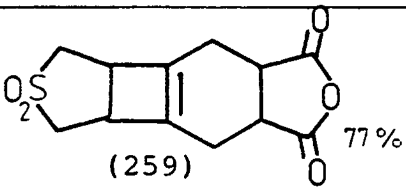
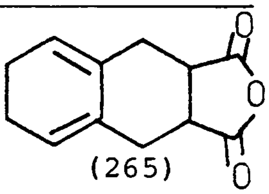
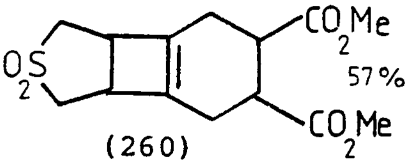
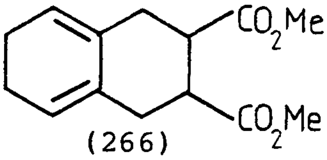
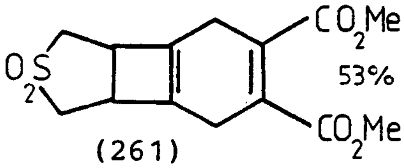
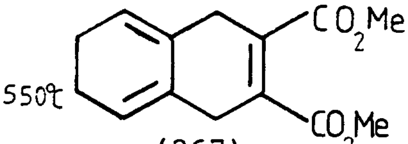
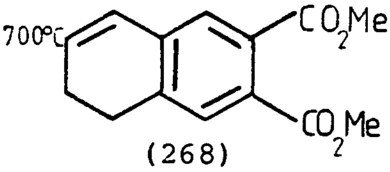
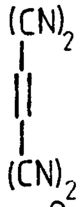
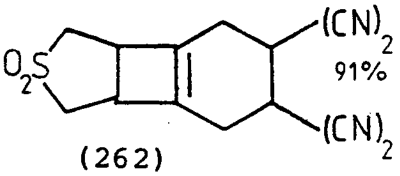
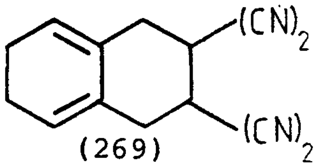
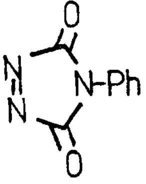
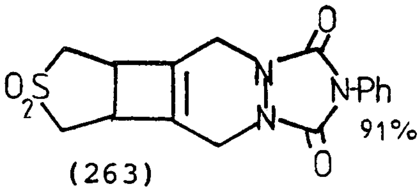
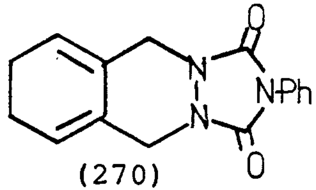
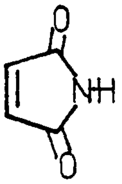
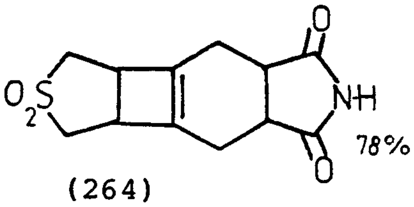
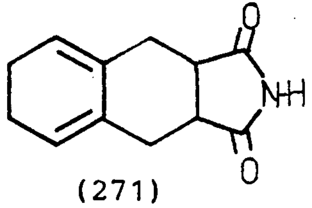
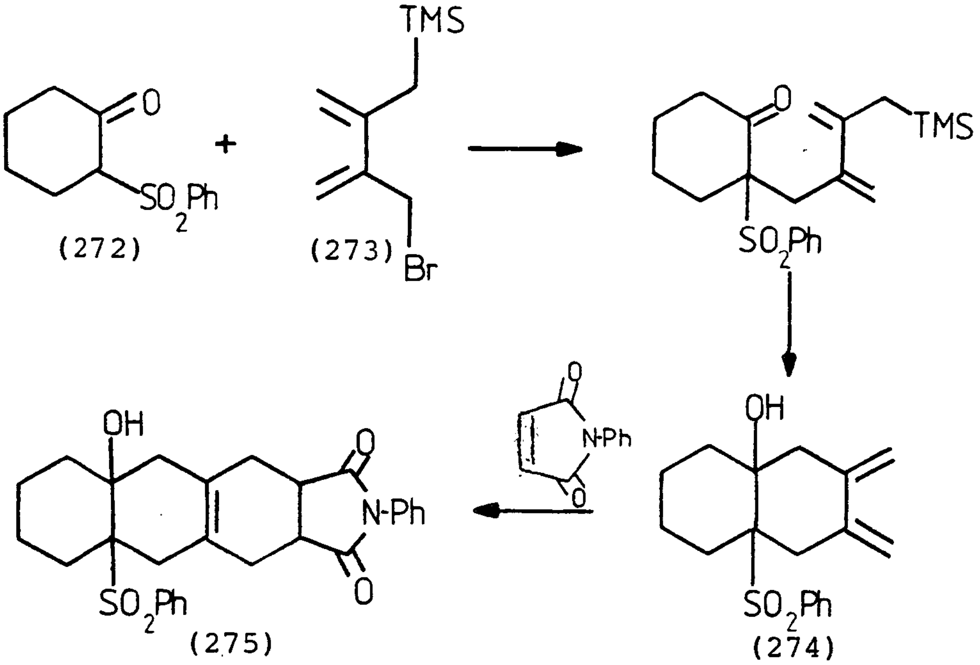
Dienophile	Adduct	Product on FVP
	 (259)	 (265)
	 (260)	 (266)
	 (261)	 (267)  (268)
	 (262)	 (269)
	 (263)	 (270)
	 (264)	 (271)

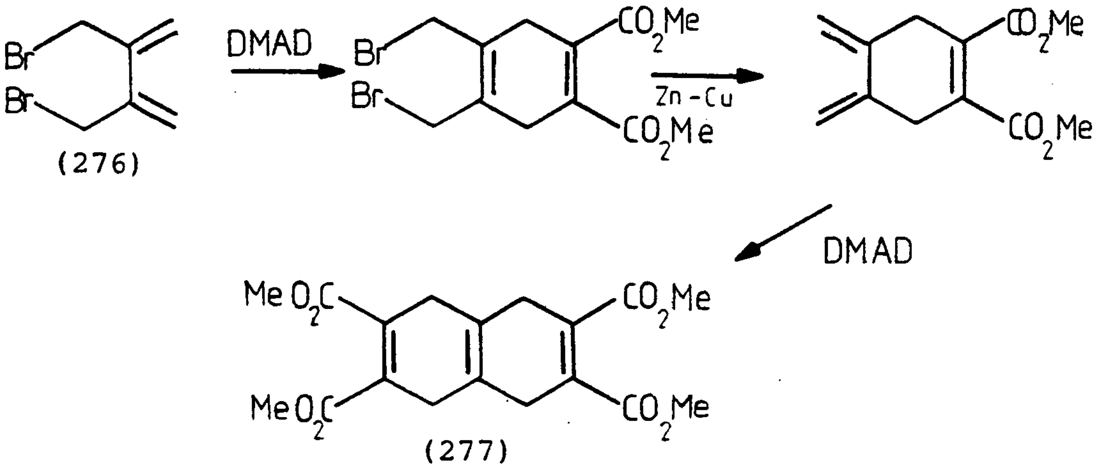
Table 2: Diels-Alder adducts of 6,7-Dimethylene-3-thiabicyclo[3.2.0]heptane 3,3-dioxide and their products on FVP.

with a dienophile to give the annulated product (275) (Scheme 136).



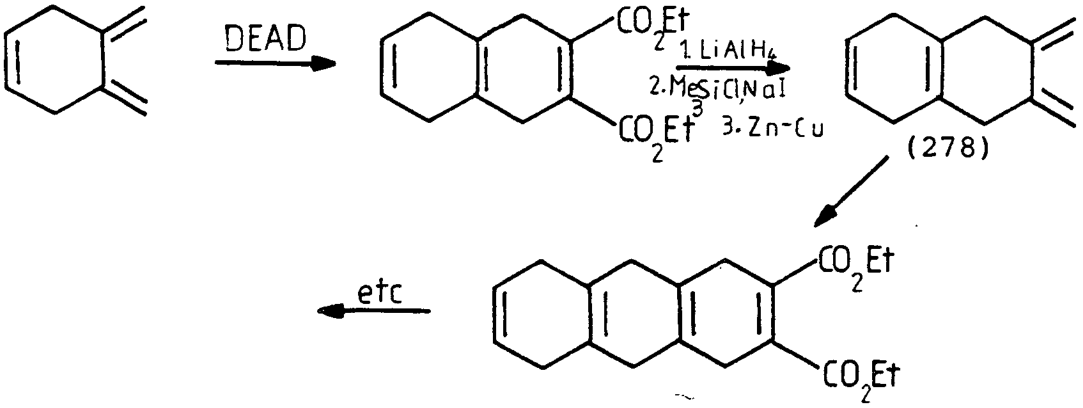
Scheme 156

In another case, Gaoni[193] has applied the versatile reagent, 2,3-bis(bromomethyl)-1,3-butadiene (276), to the formation of carbocyclic systems (277) by successive Diels-Alder reactions (Scheme 157).



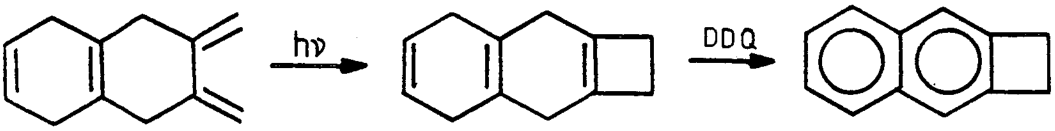
Scheme 157

The multiple linear homologation of six-membered rings using diethyl acetylenedicarboxylate (DEAD) as a butatriene cycloaddition equivalent has also been recently reported (Scheme 158).[194] This homologation procedure also provides



Scheme 158

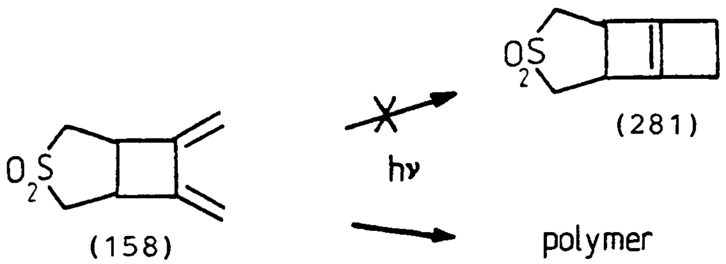
a route to benzocyclobutenes (280) by photocyclisation of (278) followed by oxidation of the polydehydro compound (279) (Scheme 159).



(278) (279) (280)

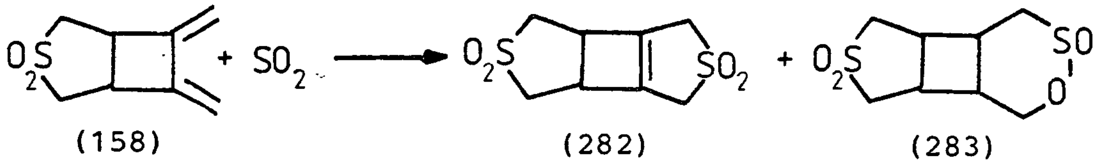
Scheme 159

The photocyclisation of dimethylene compounds such as (278) has been reported by several workers.[184,194,195] However when (158) was photolysed only polymeric material could be isolated (Scheme 160). If formed, it is probable that the desired cyclobutene (281) would have been highly strained.



Scheme 160

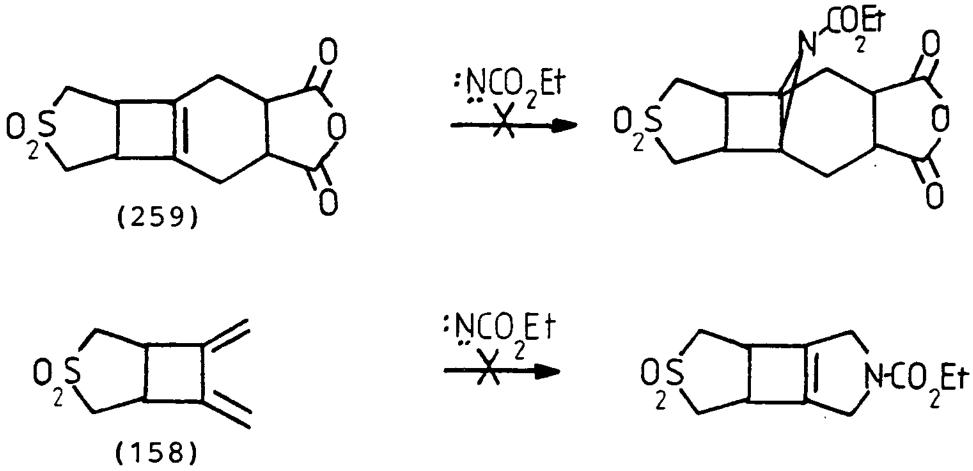
The diene (158) also failed to give adducts with SO_2 and SO. Reaction with SO_2 could have yielded either or both of the adducts (282) and (283) by competing $\pi+\pi\pi$ and $n+\pi\pi$ cycloadditions (Scheme 161).[196]



Scheme 161

Attempts were also made to prepare the nitrene adducts of (259) and (158) (Scheme 162). The method used was based on that of Senó *et al*[144] and involved phase transfer catalysis, the nitrene being generated by base-induced α-elimination from Lwowski's salt.[197] However, the only products obtained were nitrene byproducts and, in the case of (158), unreacted starting material.

The products from the FVP of the adducts of (158) are summarised in Table 2. Mass spectroscopic data of the products was consistent with loss of SO_2 from the corresponding adduct but the ^1H n.m.r. spectra often consisted of the desired compound plus an unidentifiable isomeric form.

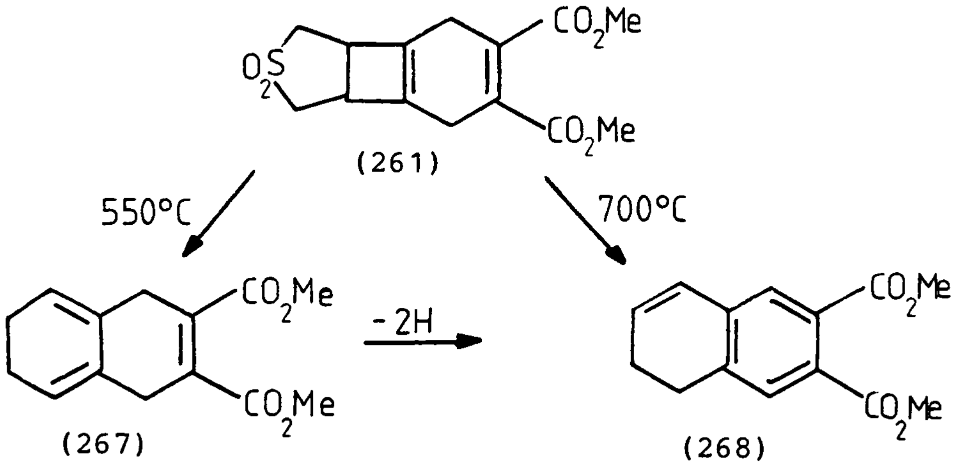


(259)

(158)

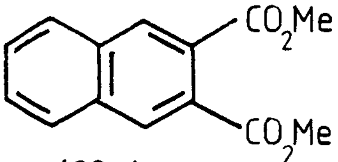
Scheme 162

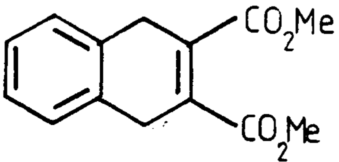
Pyrolysis of the DMAD adduct (261) gave interesting results. At 550^{o}C, the major product was 2,3-dimethoxycarbonyl-1,4,6,7-tetrahydronaphthalene (267) which was isolated in 54% yield. At 700^{o}C, a different product was obtained in 88% yield and was identified by ^{1}H n.m.r. spectroscopy and exact MS as 2,3-dimethoxycarbonyl-5,6-dihydronaphthalene (268) which was readily dehydrogenated to 2,3-dimethoxycarbonylnaphthalene (284) by treatment with excess of palladium on charcoal in boiling benzene. The 5,6-dihydronaphthalene (268) is presumably formed from (267) by a 1,5-hydrogen shift and subsequent loss of hydrogen (Scheme 163). (268) is also formed as a minor product by FVP of (261) at 550^{o}C. When the pyrolysis was carried out at 550^{o}C over silica wool to increase the contact time in the furnace, a complex mixture of dimethyl esters resulted. From spectroscopic data, the mixture was



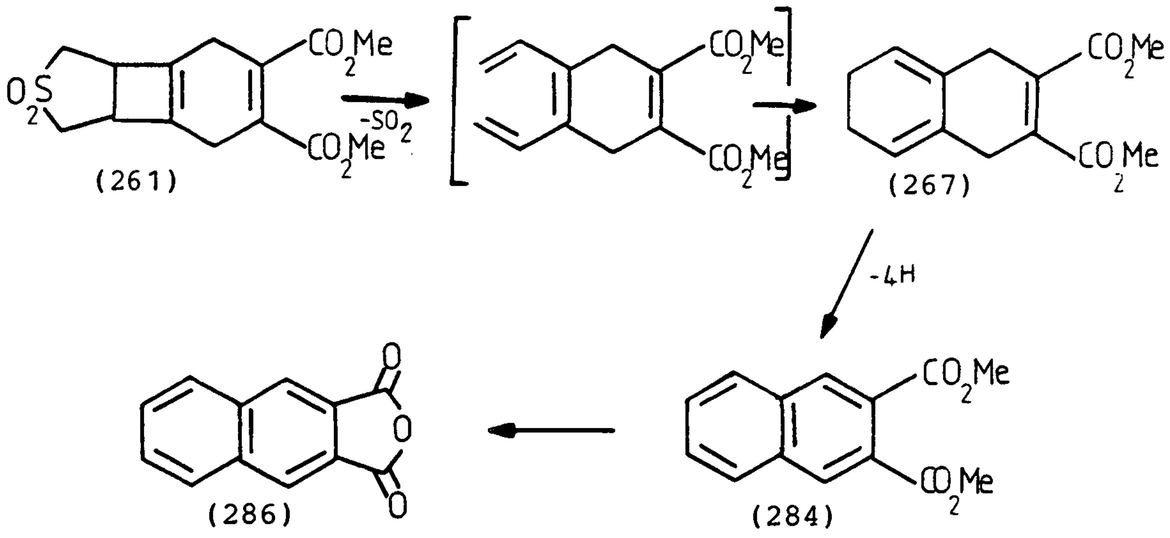
Scheme 163

shown to consist of the tetrahydronaphthalene (267), the dihydro-compound (268) and its isomer, 2,3-dimethoxycarbonyl-1,4-dihydronaphthalene (285).


(284)

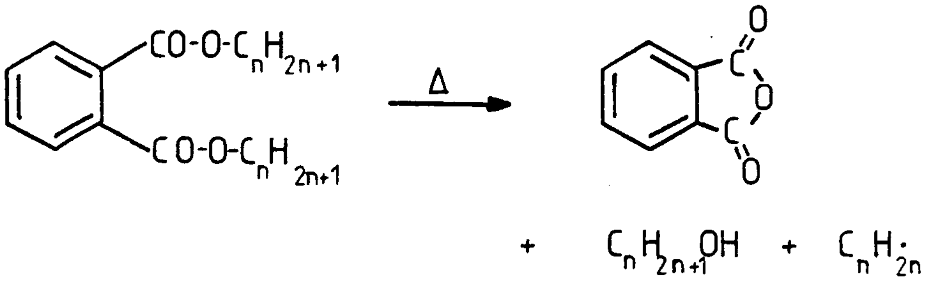

(285)

Pyrolysis of (261) over a catalyst bed of palladium on charcoal as described in Section E (p.179), resulted in the unexpected formation of 2,3-naphthalenedicarboxylic anhydride (286), the structure of which was confirmed by ^{1}H n.m.r. and mass spectroscopy. T.l.c. analysis of the pyrolysate also showed the presence of another product which was identified as naphthalene. The origin of (286) is best accounted for by the pathway outlined in Scheme 164. Proof for the intermediacy of the naphthalene diester (284) was obtained by its pyrolysis over Pd/C under similar conditions. This gave the anhydride (286) contaminated to a minor extent by an unidentified, aromatic compound. The conversion of the



Scheme 164

diester (284) into its anhydride has not been reported previously but the reaction has an analogy in the decomposition of alkyl phthalates at their boiling points.[198] The general equation of pyrolysis is shown in Scheme 165, although it should be noted that dimethyl phthalate is an exception.



Scheme 165

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A Simple, Stereocontrolled Synthesis of *E,Z*-1,5-Dienes†

J. I. G. Cadogan,*[a] Caroline M. Buchan,[b] Ian Gosney,*[b] Brendan J. Hamill,[b] and Leo M. McLaughlin[b]

[a] *B.P. Research Centre, Chertsey Road, Sunbury-on-Thames, Middlesex TW16 7LN, U.K.*
[b] *Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, U.K.*

The readily available 3,3-dioxide (**1**) of 3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic anhydride acts as a general synthetic precursor for *E,Z*-1,5-dienes such as (**4a**—**e**) *via* functionalisation followed by thermal extrusion of SO_2.

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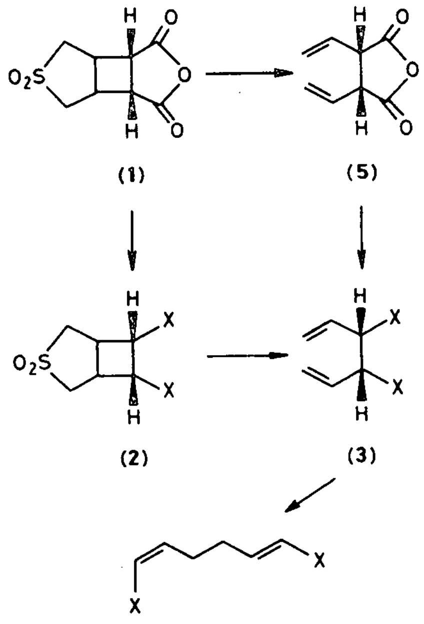
[a] *B.P. Research Centre, Chertsey Road, Sunbury-on-Thames, Middlesex TW16 7LN, U.K.*
[b] *Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, U.K.*

The readily available 3,3-dioxide (1) of 3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic anhydride acts as a general synthetic precursor for *E*,*Z*-1,5-dienes such as (**4a**—**e**) *via* functionalisation followed by thermal extrusion of SO_2.

Of the methods currently available for the synthesis of compounds with the *E*,*Z*-divinylethane grouping,[1] none allows the stereospecific construction of the carbon–carbon double bonds in a single step from a readily available precursor. We now report the realisation of this goal, exemplified by the preparation of the *E*,*Z*-1,5-dienes (**4a**—**e**)‡ in yields ranging from 30 to 87%.

The stereochemical course of our procedure, outlined in Scheme 1, relies on the usual chair-like transition state in the Cope rearrangement[2] of *meso*-1,2-divinyl compounds (3), generated by thermal extrusion of SO_2 from derivatives of the 3,3-dioxide (**1**) of *exo*-3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic anhydride.§[3] In a typical synthetic sequence, hydrolysis of (**1**) with boiling water, followed by esterification of the resulting diacid [(**2a**); 89%; m.p. 189—190 °C; ^{13}C n.m.r. (CD_3SOCD_3) δ 173.66, 54.00, 43.87, and 33.79 p.p.m.] afforded the *cis*-diester [(**2e**); 91%; m.p. 126.5—127.5 °C; ^{13}C n.m.r. (CD_3SOCD_3) δ 171.92, 53.17, 51.88, 43.00, and 33.29 p.p.m.] which on flash vacuum pyrolysis (550 °C at 10^{-3} mm Hg) gave the known *E*,*Z*-diene [(**4e**); 87%] in a purity of 85—90% (containing *ca.* 10% of the *E*,*E*-isomer)¶ as confirmed by ^1H n.m.r. spectral comparison with literature data[4] and ^{13}C n.m.r. spectroscopy [10 signals at $\delta(CDCl_3)$ 166.58, 166.28, 147.91, 147.54, 121.53, 120.29, 51.15, 50.81, 31.13, and 26.98 p.p.m.; *cf.* *E*,*E*-isomer, 5 signals at $\delta(CDCl_3)$ 166.25, 146.77, 121.57, 50.98, and 30.02 p.p.m.]. Alternatively, (**4e**) could be prepared by pyrolytic conversion of (**1**) into (**5**),[3] esterification to give *meso*-dimethyl 2,3-divinylsuccinate [(**3e**); m.p. 36—37 °C; ^{13}C n.m.r. ($CDCl_3$) δ 171.38, 132.61, 119.04, 52.49, and 51.51 p.p.m.], and subsequent



(4) a; X = CO_2H (34%)
b; X = CH_2OH (39%)
c; X = CH_2OMe (47%)
d; X = CH_2OAc (30%)
e; X = CO_2Me (87%)

Scheme 1

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† Delivered at the Annual Congress of the Chemical Society, Durham, 9—11 April 1980 (*Chem. Br.*, 1980, **16**, 385).

‡ All new compounds gave satisfactory microanalytical and spectral data.

§ The *exo*-configuration in this case is the one in which the two 5-membered rings are on opposite sides of the central cyclobutane ring.

¶ The product composition was quantitatively analysed by g.l.c. (10% Pega at 180 °C). Preparative g.l.c. under similar conditions allowed the isolation of the individual dienes in pure form for unequivocal identification.

thermal rearrangement either under flash vacuum conditions (580 °C; 51%), or by heating at elevated temperatures for a short period of time.[5]

Similar pyrolyses of other derivatives obtained from (**1**) or (**5**) by conventional synthetic methods produced the dienes (**4a**—**d**) with a high degree of stereospecificity (>90%) in 30—47% yield. The stereochemistry of these products was validated by ^{13}C n.m.r. spectroscopy, and in the case of the diacid [(**4a**); m.p. 111—113 °C; lit.[6] 113—114 °C], by thermally induced isomerization to the *E,E*-form, m.p. 257 °C (decomp.) (lit.[7] 256 °C). Subsequent conversion of the latter into its dimethyl ester gave a sample identical to that obtained by isomerization of (**4e**) in boiling heptane in the presence of iodine.

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Addendum (Received, 19th January 1982). After this work had been completed and following the submission of this communication, Williams and Lin[8] confirmed our previously reported[3] synthesis of *cis*-1,2-divinyl derivatives from the 3-thiabicyclo[3.2.0]heptane 3,3-dioxide ring system, and went on to claim that heating of these compounds, *e.g.* (**3e**), causes a Cope rearrangement leading cleanly to *E,E*-1,5-dienes in high yields. This is at variance with our results described above and those of others,[2,5] which show that *meso*-1,2-divinyl compounds rearrange, upon thermolysis, with a remarkably high degree of stereoselectivity to *E,Z*-1,5-dienes. In actuality, *E,E*-1,5-dienes are the major products from the thermal rearrangement of (±)-1,2-divinyl intermediates. Evidence on this point, which also invalidates the claim of Williams and Lin, derives from our observation that conversion of (**2e**) with 1,5-diazabicyclo[5.4.0]undec-5-ene into its epimer [two ^{13}C carbonyl resonances in $CDCl_3$ (δ 172.00 and 170.44 p.p.m.)], followed by pyrolysis in the usual way, gives a mixture of dimethyl octa-2,6-dienedioates containing 83% of the *E,E*-isomer (*cf.* ref. 5).

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1 For existing methods of preparing *E,Z*-divinylethane systems, see different approaches to the sex pheromone, gossyplure: K. Mori, in 'The Total Synthesis of Natural Products,' ed. J. ApSimon, Wiley-Interscience, New York, 1981, vol. 4, p. 46, and references therein.

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Dehydrogenative Vacuum Pyrolysis: a Novel Synthetic Technique. Conversion of Cyclo-octa-1,5-diene into Styrene and Related Reactions

Caroline M. Buchan,[a] **J. I. G. Cadogan,***[b] **Ian Gosney,***[a] **Brendan J. Hamill,**[a] **Stephen F. Newlands,**[a] **and David A. Whan**[a]

[a] *Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, U.K.*
[b] *B.P. Research Centre, Chertsey Road, Sunbury-on-Thames, Middlesex TW16 7LN, U.K*

Vacuum pyrolysis in the presence of palladium on charcoal of the 3,3-dioxide (**1**) of 3-thiabicyclo[3.2.0]-heptane-6,7-dicarboxylic anhydride gave, without undesirable disproportionation, phthalic anhydride, also obtained from *cis*-2,3-divinylsuccinic anhydride (**2**) and *cis*-1,2,3,6-tetrahydrophthalic anhydride (**5**), while cyclo-octa-1,5-diene (**7**) and the disulphone (**6**) each gave styrene.

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Dehydrogenative Vacuum Pyrolysis: a Novel Synthetic Technique. Conversion of Cyclo-octa-1,5-diene into Styrene and Related Reactions

Caroline M. Buchan,[a] J. I. G. Cadogan,*[b] Ian Gosney,*[a] Brendan J. Hamill,[a] Stephen F. Newlands,[a] and David A. Whan[a]

[a] *Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, U.K.*
[b] *B.P. Research Centre, Chertsey Road, Sunbury-on-Thames, Middlesex TW16 7LN, U.K*

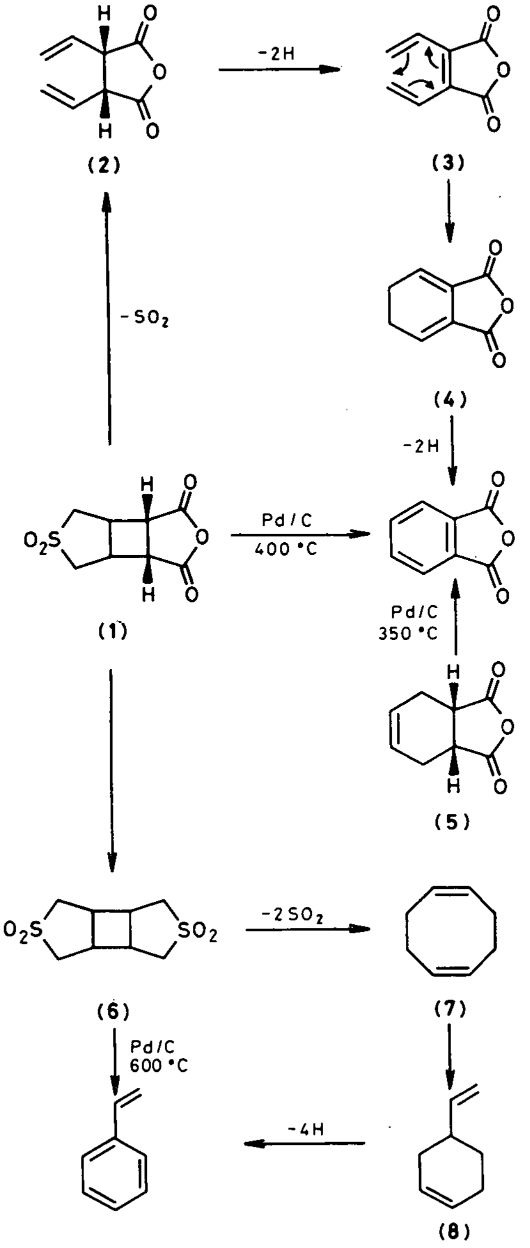
Vacuum pyrolysis in the presence of palladium on charcoal of the 3,3-dioxide (1) of 3-thiabicyclo[3.2.0]-heptane-6,7-dicarboxylic anhydride gave, without undesirable disproportionation, phthalic anhydride, also obtained from *cis*-2,3-divinylsuccinic anhydride (2) and *cis*-1,2,3,6-tetrahydrophthalic anhydride (5), while cyclo-octa-1,5-diene (7) and the disulphone (6) each gave styrene.

Over the past decade flash vacuum pyrolysis (F.V.P.) has played an increasingly important role in preparative organic chemistry.[1] We now report an extension of this technique of potentially wide application based on the simultaneous use of a dehydrogenation catalyst.

The origin of our procedure lies in our earlier observation[2] that F.V.P. of the 3,3-dioxide (1) of 3-thiabicyclo[3.2.0]heptane-6,7-dicarboxylic anhydride, easily prepared by photolysis of equimolar amounts of butadiene sulphone and maleic anhydride, gave *cis*-2,3-divinylsuccinic anhydride (2) in 80% yield. We reasoned that removal of the ring-junction hydrogens from (2) should lead to electrocyclisation of the resulting (3) to (4) which would afford phthalic anhydride under dehydrogenating conditions (Scheme 1). This was readily accomplished *in a single step* with the same apparatus[3] by subliming (1) at 10^{-3} mmHg and 400 °C through a catalyst bed of 5% palladium on activated carbon.† In accord with this, similar pyrolyses of *cis*-2,3-divinylsuccinic anhydride (2) at 425 °C and of *cis*-1,2,3,6-tetrahydrophthalic anhydride (5) at 350 °C, also gave phthalic anhydride (48—52%). It is noteworthy that in none of these pyrolyses did significant and undesirable disproportionation to hydrogenated products take place. The method is therefore superior to the corresponding dehydrogenation in solution wherein, for example, *cis*-1,2,3,6-tetrahydrophthalic acid is converted into a 2 : 1 mixture of phthalic acid and cyclohexane-1,2-dicarboxylic acid, respectively, by palladium black in boiling tetrahydrofuran.[4]

We also pyrolysed the crystalline, high-melting (>320 °C) disulphone (6), prepared from (1) by successive esterification, reduction to the diol, conversion into the bistoluene-*p*-sulphonate, treatment with Na_2S, and essentially quantitative oxidation of the resulting sulphide with *m*-chloroperoxybenzoic acid in methylene chloride.‡ The sparingly volatile (6) at 650 °C gave a mixture of 4-vinylcyclohexene (8) and cyclo-octa-1,5-diene (7) in the ratio *ca.* 4 : 1 as determined by g.l.c. (10% Pega at 100 °C). Butadiene was also detected by n.m.r., but was not quantified. Since heating of cyclo-octa-1,5-diene in the gas phase causes a rearrangement to 4-vinylcyclohexene as well as giving minor amounts of butadiene,[5] it is reasonable to conclude that this compound is an intermediate in the thermal decomposition of (6), although its mode of formation is not certain.

When we subjected (6) to pyrolysis over 5% palladium on activated carbon catalyst at 600 °C, both rearrangement and dehydrogenation occurred simultaneously. As a result, styrene was obtained as the major product, albeit in low yield (12%), together with benzene (4%), toluene (2%), xylenes (2%), and ethylbenzene (2%). Much better yields of styrene at 45%



Scheme 1

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† The catalyst, available from Alpha Division in 6—8 mesh pellets, is packed into the horizontal pyrolysis tube (35 × 2.3 cm, i.d.) between a coarse silica frit 12 cm from the exit end and a loose plug of quartz wool. Prior to each pyrolysis, it is conditioned by baking at 700 °C until a pressure of 10^{-3} mmHg is obtained.

‡ Satisfactory elemental analytical data were obtained for compound (6).

conversion were obtained by direct pyrolysis of cyclo-octa-1,5-diene (7) under dehydrogenating conditions. At 650 °C with 5% palladium on activated carbon catalyst, the crude pyrolysis product consisted of styrene (62%), xylenes (3%), toluene (9%), and benzene (26%). No ethylbenzene was detected.

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References

1 For a review explaining the technique of F.V.P. with a description of apparatus and a survey of applications, see: R. F. C. Brown, 'Pyrolytic Methods in Organic Chemistry,' Academic Press, London, 1980.

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