UNIVERSITY OF SOUTHAMPTON

SOME STUDIES ON THE ENE REACTIONS OF ALLENE SULPHOXIDES

A thesis submitted for the degree of

Doctor of Philosophy

by

Kevin Edward Burdon Parkes

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CONTENTS

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UNIVERSITY OF SOUTHAMPTON

FACULTY OF SCIENCE

CHEMISTRY

ABSTRACT

Doctor of Philosophy

SOME STUDIES ON THE ENE REACTIONS OF ALLENE SULPHOXIDES

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One example of an allene sulphoxide behaving as an enophile in an intramolecular ene reaction to give a cyclopentene was known at the beginning of the project. A series of substrates was prepared to assess the generality of the reaction and an attempt to realise the potential of the reaction for natural product synthesis was made.

Chapter Two describes attempts to form acyclic 1,4-dienes by the intermolecular ene reaction of 1-phenylsulphinyl-3-methylbuta-1,2-diene with a variety of alkenes under Lewis acid catalysis, or at high pressure or temperature. Some preliminary studies of the ene reactions of phenylsulphonylpropadiene are also described.

Chapter Three concerns the extension of the intramolecular ene reaction to the preparation of six membered rings, the use of enols as ene components to give acylcyclopentenes and the preparation of a potential intermediate for the Iridoid sesquiterpenes. An attempt to prepare the insect defence pheromone, Chrysomelidial, by Pummerer rearrangement and hydrolysis of this intermediate is described.

Chapter Four describes the use of the intramolecular ene reaction for the annelation of five membered rings and an attempt to take advantage of the functionality of the products obtained by this annelation to prepare medium ring compounds by means of a Grob fragmentation. An attempt to use the ene reaction for spiro-annelation, instead of giving the required spiro-[4,5]-decane gave a vinylsulphoxide containing the novel tricyclo [4,4,0,$0^{1,4}$] decane ring system.

CHAPTER 1

INTRODUCTION

1.1 Introduction

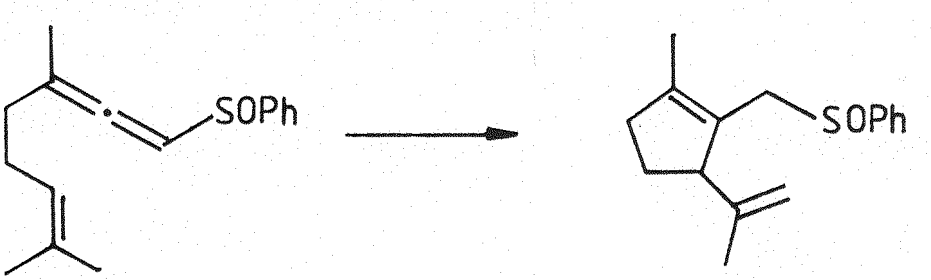
The synthesis of an organic molecule will generally involve both formation of carbon-carbon bonds and functional group interconversions. The elegance of the synthesis can depend on the degree of simplification obtained in the carbon-carbon bond forming reactions and the ease with which the functional groups involved can be removed or manipulated to give the desired target.

Recently, there has been a vast increase in the variety of carbon-carbon bond forming processes used in synthesis. A particularly exciting area is that of pericyclic reactions, which include: the Diels-Alder[1] reaction which is established as a highly facile method of preparing compounds with a six-membered ring; the 1,3-dipolar additions of compounds such as nitrones in the elegant synthesis of Elaeokanines A, B and C,[2] or nitrile oxides in a Biotin synthesis;[3] and the Cope and double Cope rearrangements which have recently been applied to the synthesis of a variety of macrocycles.[4]

The ene reaction is another example which was first studied by Alder[5] nearly forty years ago, but has only recently been much used in synthesis. It involves, in general, the reaction of an alkene containing an allylic hydrogen (ene) with an electron deficient double bond (enophile) to form a 1:1 adduct.

Scheme 1

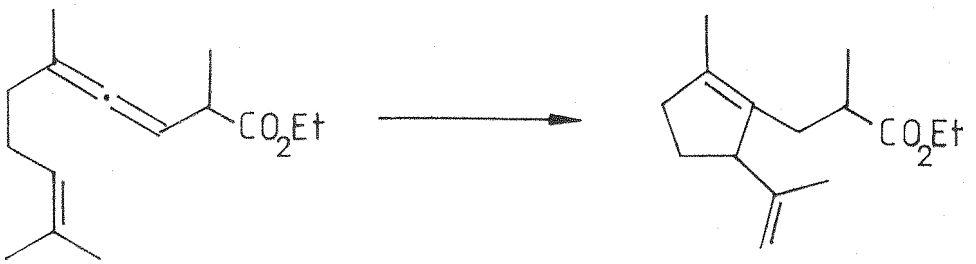
In some recent work, directed towards new syntheses of terpenes, Parsons observed the following ene reaction.[6]



(1) (2)

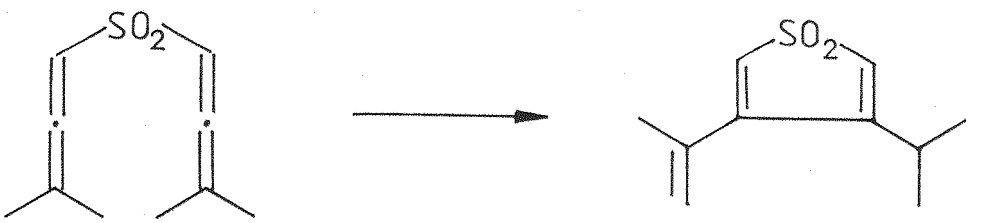
Scheme 2

Although there are analogies in the ene reaction of allenes such as (3),[7] the only published example of an allene-sulphur species under-



(3) Scheme 3

going an ene reaction is the transformation of (4) to (5), which has far less obvious synthetic utility.[8]



(4) Scheme 4 (5)

In view of the importance of carbon-carbon bond formation processes and the known versatility of the allylic sulphoxide for further elaboration of a target molecule, it was decided to prepare a variety of substrates to assess the scope and limitations of this reaction.

1.2 The Ene Reaction

The ene reaction is believed to be a concerted $[_{\pi}2_{s} + _{\pi}2_{s} + _{\sigma}2_{s}]$ electrocyclic reaction. This is supported by the following facts:-

(i) The rate has only a very slight dependence on solvent polarity,[9,10] which renders unlikely the involvement of ionic intermediates;

(ii) The rate is unaffected by the addition of radical inhibitors,[11] which eliminates mechanisms involving a radical chain;

(iii) Cyclobutanes have never been detected among the products of an intermolecular ene reaction,[11] thus rendering routes involving a diradical intermediate highly unlikely;

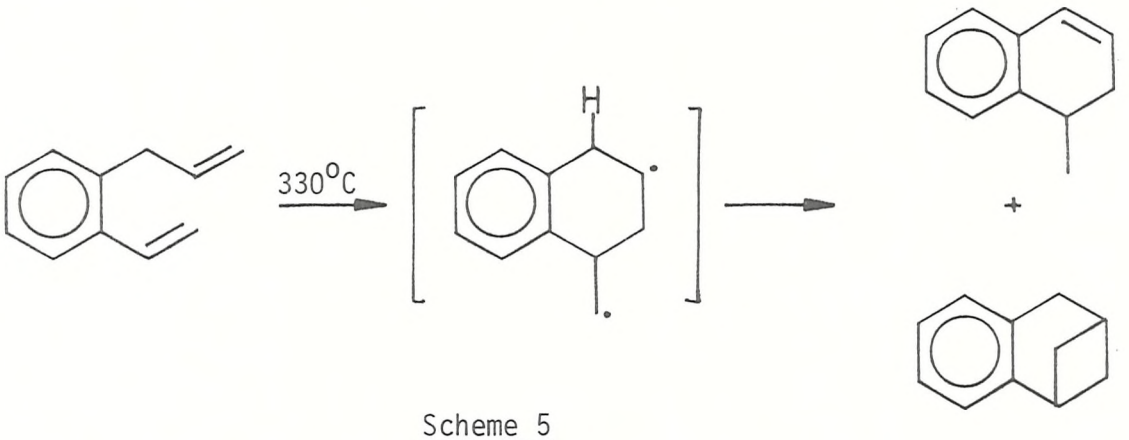
(iv) The reaction has been shown to be stereospecifically *cis* with respect

to the ene component.[10,12]

(v) High negative entropies of -30 to -40 eu are observed.[13] These values are similar to those measured for the Diels-Alder reaction for which a concerted mechanism is well established. Although the transition state geometries for the Diels-Alder and ene reactions are equally compact, they are actually quite different.[14]

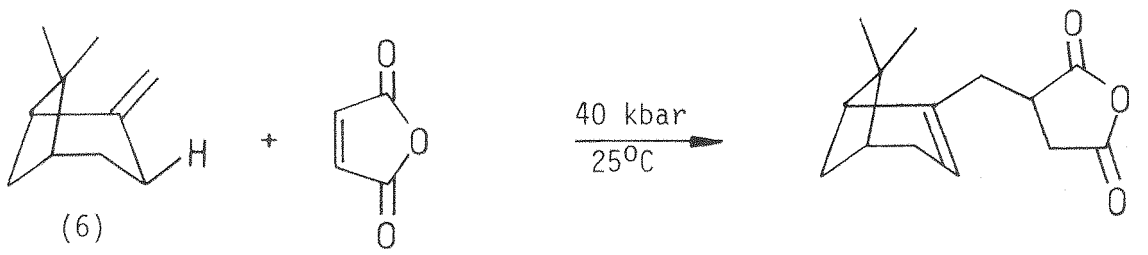
Diels Alder Figure 1 Ene

This evidence leaves little doubt that the ene reaction is normally concerted. However, ene type products have been observed along with radical products in the reaction of compounds in which the normal ene transition state would be highly strained.[15]



Scheme 5

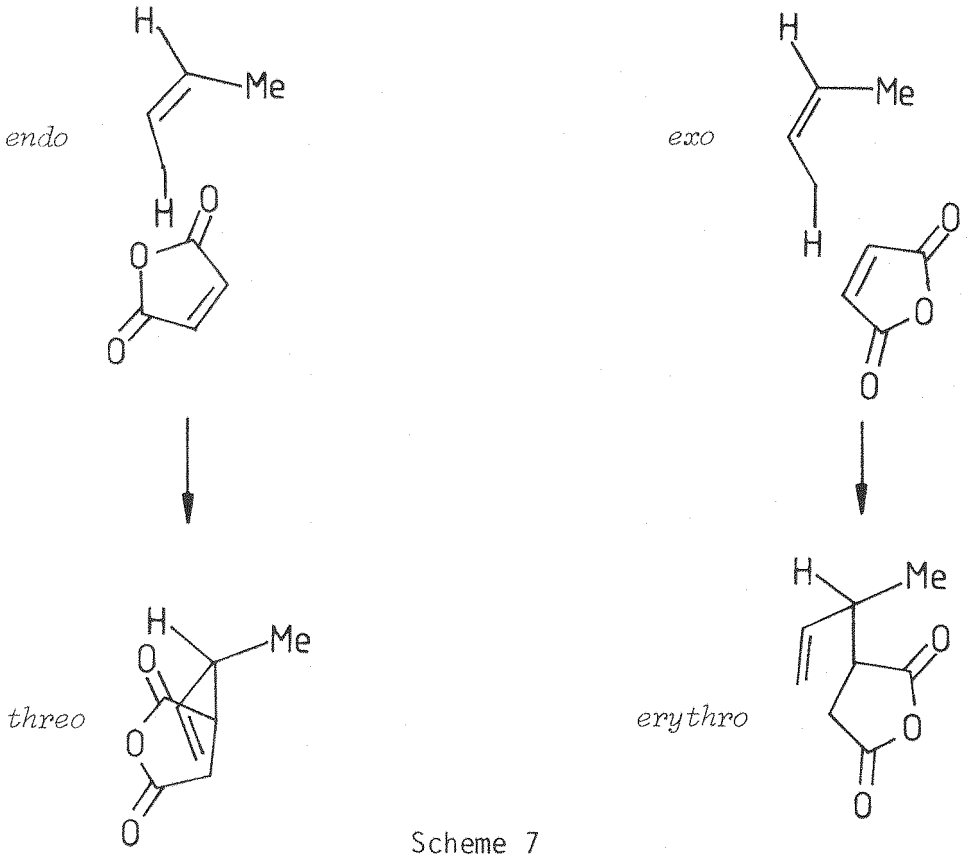
The fact that the ene reaction involves the combination of two molecules, as well as the compact transition state, would lead one to expect it to be favoured at high pressure. Almost no work has yet been done in this area although the reaction of β-pinene (6), itself a very reactive ene, with a variety of reactive enophiles has been observed under very high pressures.[16]



(6)

Scheme 6

The ene reaction is reversible at high temperatures and retro-ene reactions have their own place in synthesis; important examples include the decarboxylation of β-keto acids and the formation of alkenes by ester pyrolysis. The ene reaction shows a preference for *endo* adducts although very modest degrees of steric crowding are sufficient to make the *exo* adduct predominate.[10,14,17]



Scheme 7

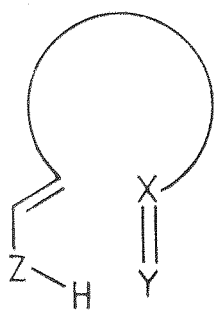
The intermolecular ene reaction can lead to a number of products depending on the hydrogen atom transferred and the orientation of addition. In general, electronic factors are far less important than in the Diels-Alder reaction and the product mixture may frequently be determined purely by steric effects. Thus, the allylic hydrogen transferred will be preferred in the order primary > secondary > tertiary as would be predicted from consideration of transition state crowding. The prediction of orientation is far more difficult, partly because so little work has been done in the area and partly because of the ease with which many ene products add a

further molecule of enophile to give 2:1 adducts. However, except in cases where there is significantly more steric crowding in one orientation than the other, the products reported are generally those expected on the basis of frontier orbital theory.[14,18]

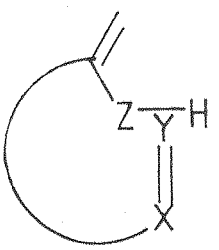
Also, for steric reasons the new double bond is generally *trans*, although there has been no systematic study.

Like the Diels-Alder reaction, and as frontier molecular theory predicts, the ene reaction proceeds more rapidly when the enophile is electron poor. Thus, the reaction is catalysed by Lewis acids which complex with the enophile and lower its LUMO. In the last few years Snider has made extensive studies of the Lewis acid catalysed ene reaction and favours the use of alkylaluminium halides as catalyst because of their ability to act simultaneously as Brönsted base and Lewis acid.[19] This is particularly desirable when the substrate is Brönsted acid labile, as in reactions where the enophile is an aldehyde and prone to polymerisation. The value of these new catalyst systems has been demonstrated by Snider's recent synthesis of (±)-Pseudomonic acid.[20]

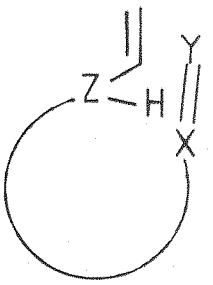
Probably, the most interesting uses of the ene reaction are those where the reaction is intramolecular and leads to cyclic products. Oppolzer and Snieckus[21] have classified the three modes of addition as Type I, Type II or Type III depending on whether the linking chain is attached to the central, allylic or vinylic terminus of the ene component.



Type I



Type II



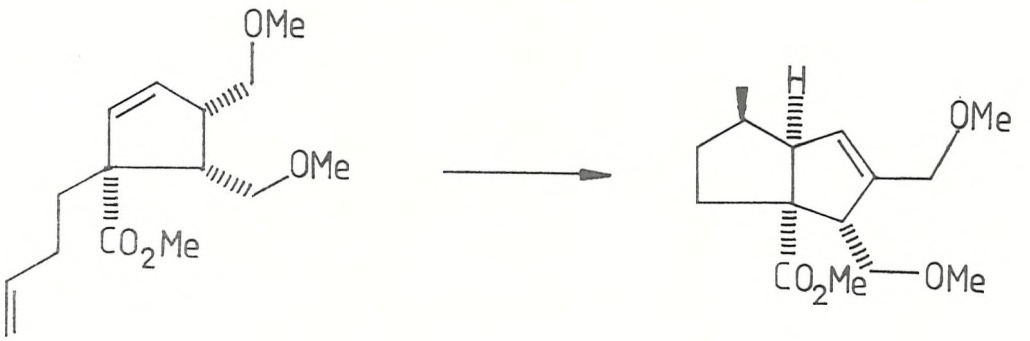
Type III

Figure 2

Many compounds have hydrogen atoms in two or three environments and then the preference for hydrogen transfer is in the order Type I > Type II > Type III. In Types I and II, carbon-carbon bond formation is generally between the two closest unsaturated centres.

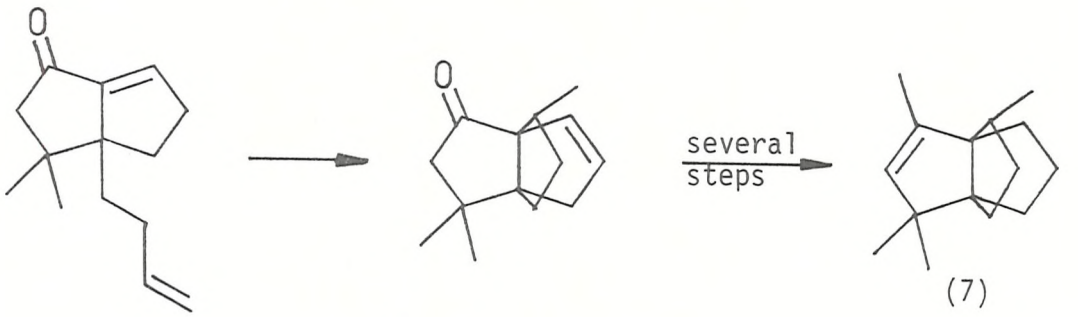
There are many good examples of the use of the intramolecular ene reaction in synthesis. In Heathcock's model study of Pentaleno-

lactone[22] use is made of the ene reaction both to annelate the second five-membered ring and form two of the required stereocentres.



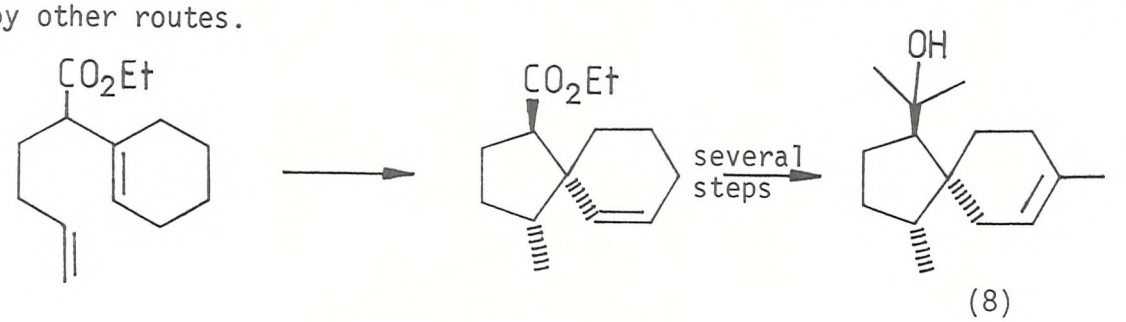
Scheme 8

An ene reaction is also used as the key step in Oppolzer's remarkably short synthesis of (±)-modhephene[23] (7).



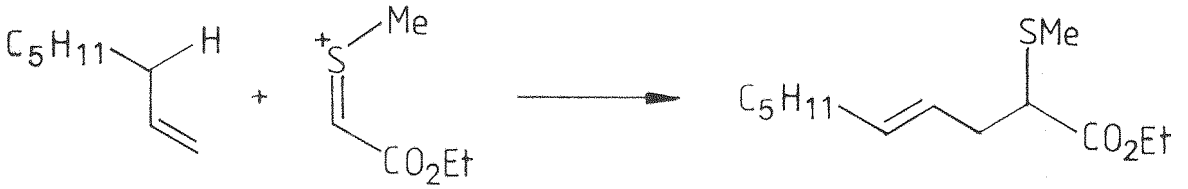
Scheme 9

The ene reaction has proved particularly useful for the synthesis of spirocycles, such as acorneol (8),[24] which are not readily accessible by other routes.



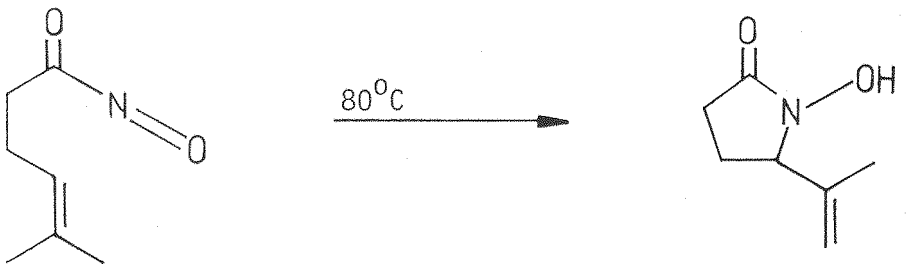
Scheme 10

While many of the published examples of the ene reaction involve hydrocarbon substrates, much greater variety is, in fact, possible. Reactions in which the enophile is an aldehyde have already been mentioned and analogous reactions involving sulphur ylids are known.[25]



Scheme 11

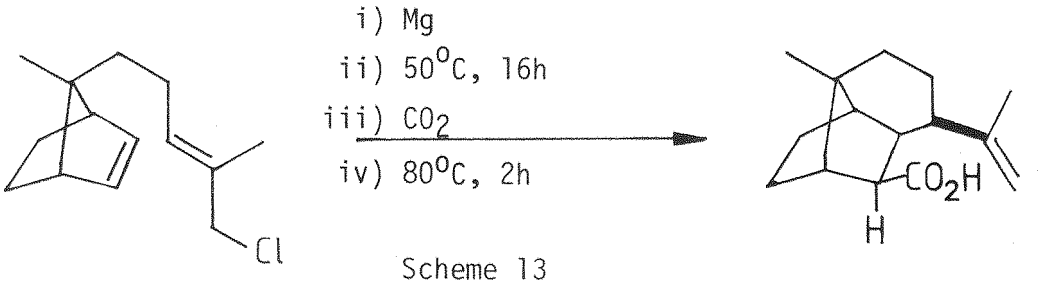
Both atoms of the enophile may be hetero-atoms, as in the following example:-[26]



Scheme 12

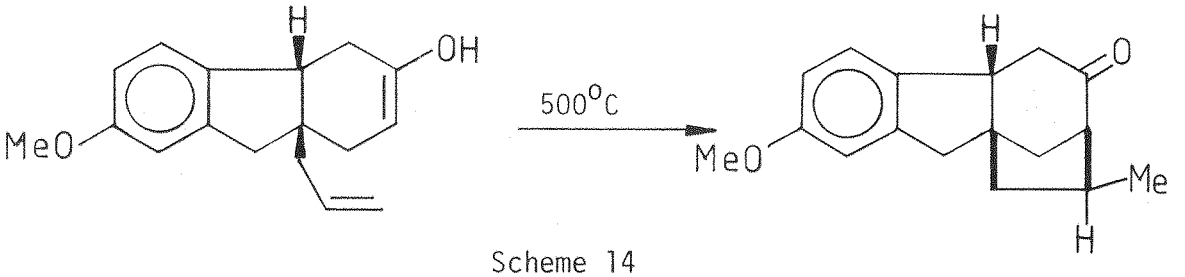
or in allylic oxidations with selenium dioxide[27] or the hydroperoxidation of alkenes with singlet oxygen.[28]

Oppolzer has recently published several very elegant syntheses in which the key steps involve the transfer of magnesium rather than hydrogen in what are structurally equivalent to ene reactions.[29]



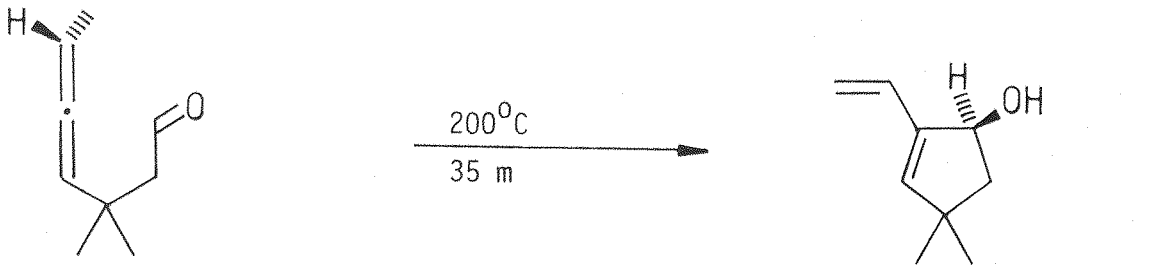
Scheme 13

Ketones in their enolic tautomers will also behave as ene components although fairly high temperatures may be required (>300°C).[30] This reaction has been used to annelate the D ring in the construction of the Gibbane system.[31]



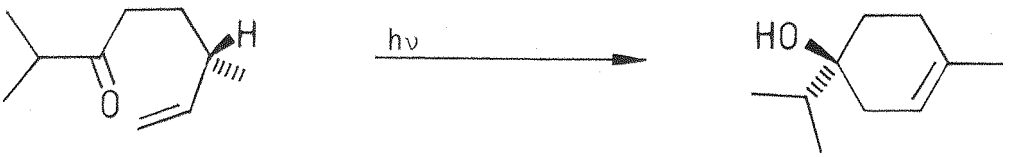
Scheme 14

An interesting feature of the ene reaction in general is that any chirality centred in the ene component may be transferred to the newly formed carbon centre.[14,32]



36% optical purity

Scheme 15



Scheme 16

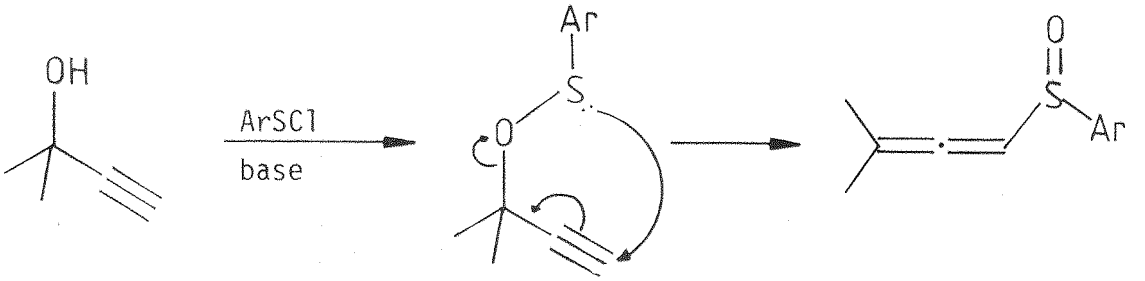
100% optical purity

High levels of asymmetric induction depend on the adoption of either a purely *exo* or a purely *endo* transition state and also on the adoption of a concerted mechanism.[33]

1.3 Allene Sulphoxides

1.3.1 Preparation of Allene Sulphoxides

Allene sulphoxides are readily prepared in good yield by the treatment of a propargylic alcohol with phenylsulphenyl chloride in the presence of triethylamine, or with n-butyllithium followed by phenylsulphenyl chloride.[34] The mechanism is normally presumed to involve the [2,3]-sigmatropic rearrangement of an intermediate sulphenate ester analogous to the better studied allylic sulphoxide-allylic sulphenate rearrangement.[35,36]



Scheme 17

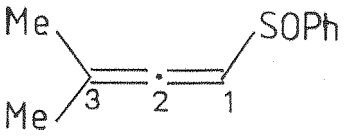
There seems to be little doubt that a sulphenate ester is involved as an intermediate in the reaction and in some cases, particularly when the aryl group bears electron withdrawing substituents, the sulphenate may be isolated. The most plausible mechanism for the conversion of this intermediate to the allene sulphoxide is a concerted [2,3]-sigmatropic rearrangement; any dissociative pathway would be expected to give an acetylene amongst the products and no such by-products have been observed in this or analogous reactions forming allenic sulphones[37] or allenic phosphonates.[38] These reactions are in strong contrast to many allene preparations which involve the displacement and/or equilibration of propargylic compounds and give a mixture of allene and acetylene.[39]

However, there are indications that the sulphenate is not formed by simple nucleophilic displacement, at least in reactions catalysed by triethylamine where it is found that diphenyl disulphide is formed as an invariable by-product. In addition, phenylsulphenyl chloride is known to react with triethylamine to give a colourless solution under the reaction conditions[6] and it may be that this 'complex' is an intermediate in the reaction. In the better studied methanesulphenyl chloride/methanol system, disulphides are known to be formed by the reaction of the sulphenate ester with further sulphenyl chloride,[40] and the presence of diphenyl disulphide and starting material amongst the products of the allene preparations suggests that analogous reactions are occurring.

1.3.2. Chemistry of Allene Sulphoxides

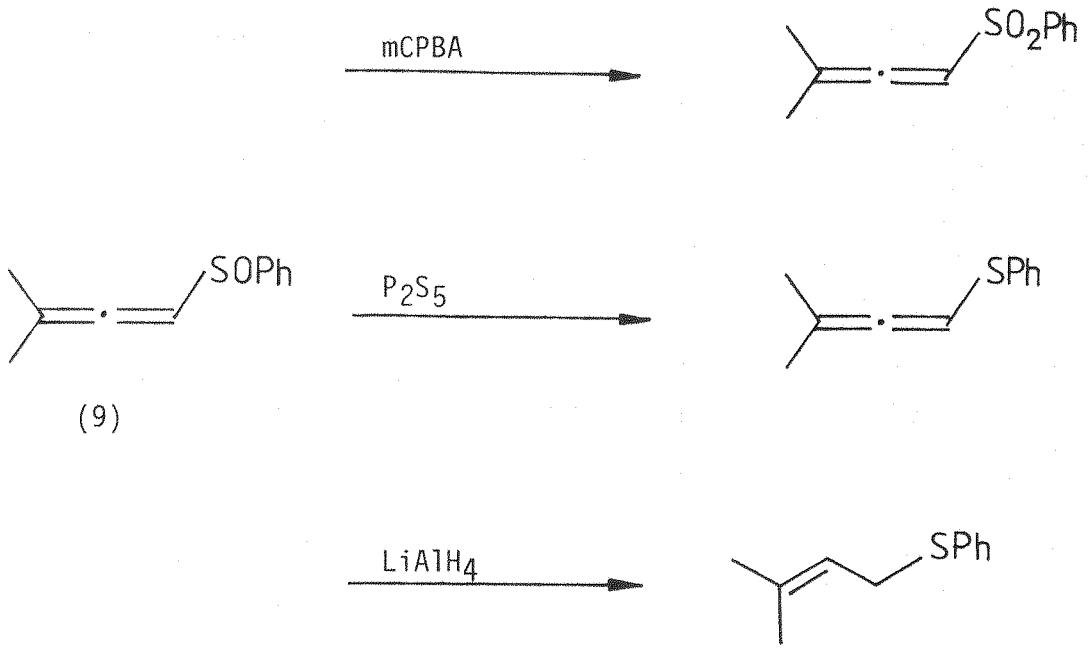
Allene sulphoxides are relatively stable compounds which may be stored almost indefinitely at $0^{o}C$, although at higher temperatures ($\sim 90^{o}C$) they readily rearrange to butadiene sulphoxides.[41] The nmr, uv and ir spectra have been discussed by Horner and Binder[34] and show no very remarkable features. However, because the sulphoxide is a chiral centre

the methyl protons in an allene such as (9) are diastereotopic and are quite strongly split in the proton nmr spectrum.



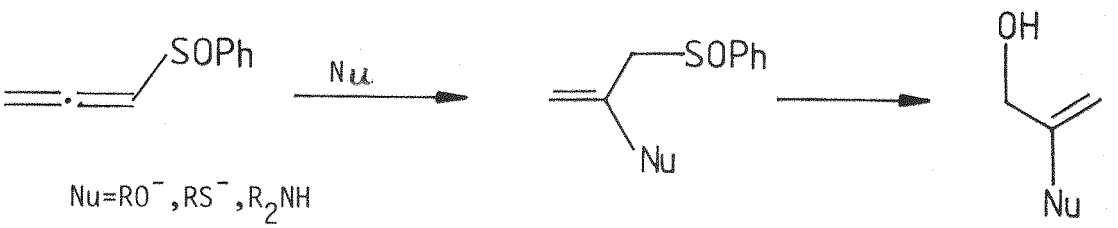
(9)

Allene sulphoxides may be oxidised with peracids to give sulphones or reduced with phosphorus pentasulphide to give the corresponding sulphide.[6] Treatment with lithium aluminium hydride leads to the more highly reduced allylic sulphide.[6]



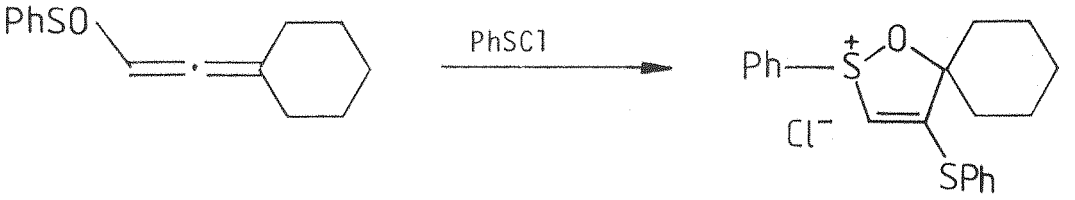
Scheme 18

Nucleophiles such as alkoxides, thioalkoxides or primary or secondary amines add to the 1,2-double bond to give vinyl ethers, vinyl thioethers, or enamines which may readily be desulphenated.[34]



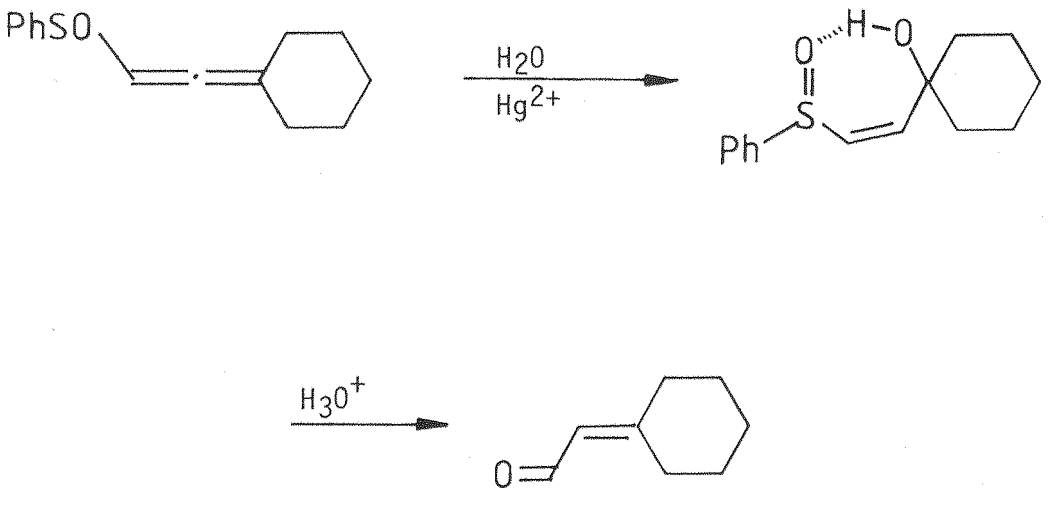
Scheme 19

Electrophiles add to the 2,3-double bond and generally the intermediate carbonium ion is intercepted by sulphoxide to give an alkoxysulphonium salt as the isolated product.[34]



Scheme 20

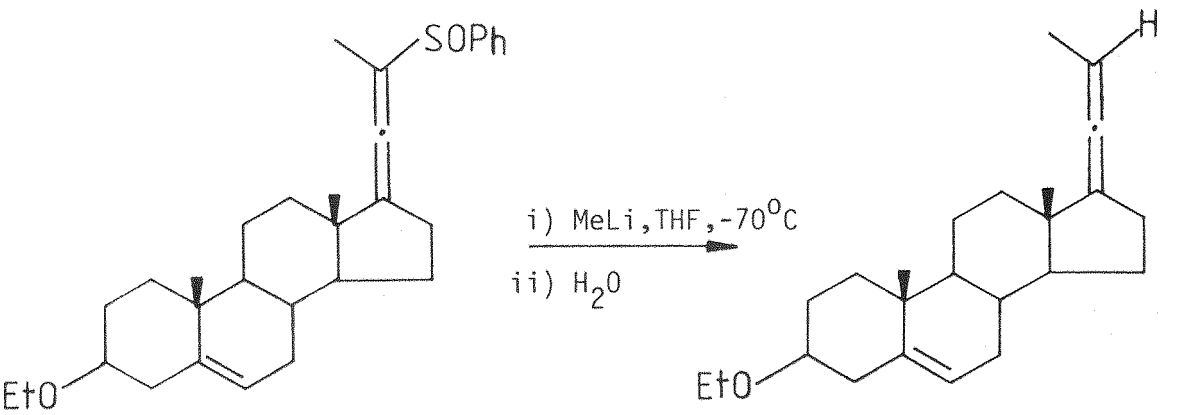
In the presence of mercury salts water may be added to the 2,3-double bond to give allylic alcohols which, on treatment with mineral acids, give α,β-unsaturated carbonyl compounds in modest yield.[6,34]



Scheme 21

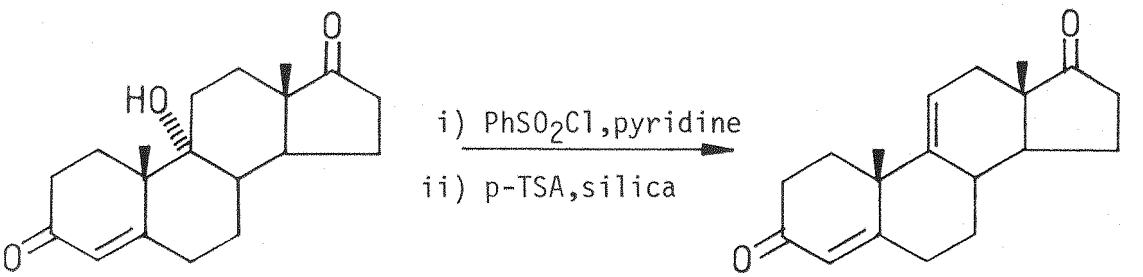
With strong bases the hydrogen adjacent to sulphoxide may be removed to give an ambident anion which can react at either the 1 or 3-positions. In general, hard electrophiles such as dialkylsulphates or trialkylsilyl halides will react predominantly at the 1 position and most soft electrophiles, such as alkyl halides at the 3-position.[6,42]

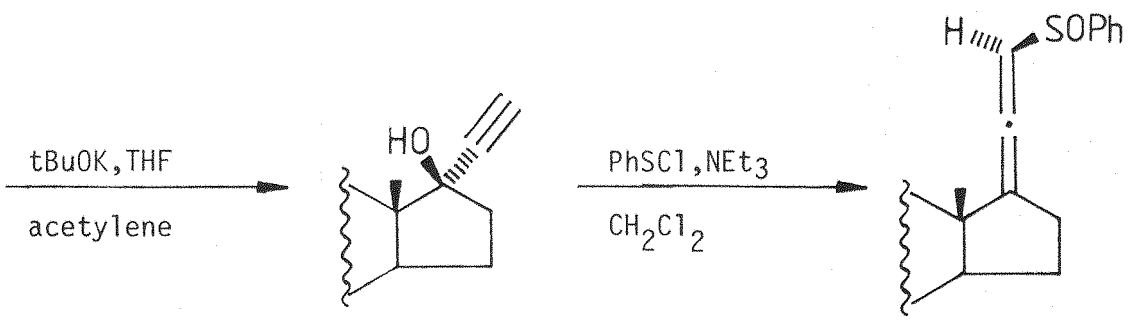
Treatment of allene sulphoxides in which the 1-position is substituted with alkyl lithium reagents leads, *via* nucleophilic attack on sulphur, to a desulphurised allene.[41]

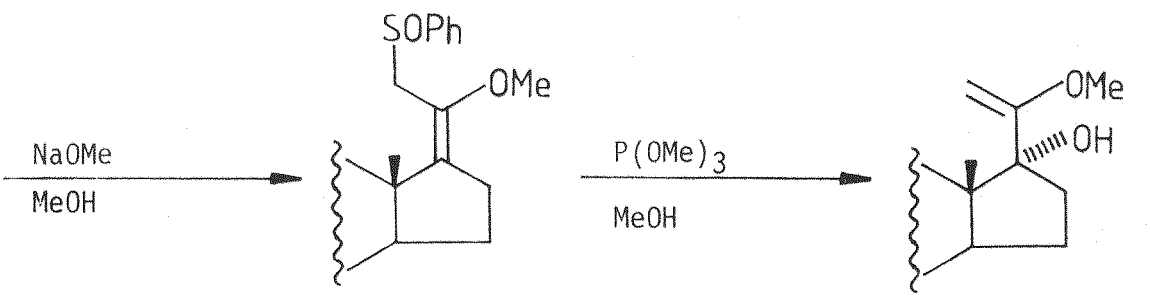


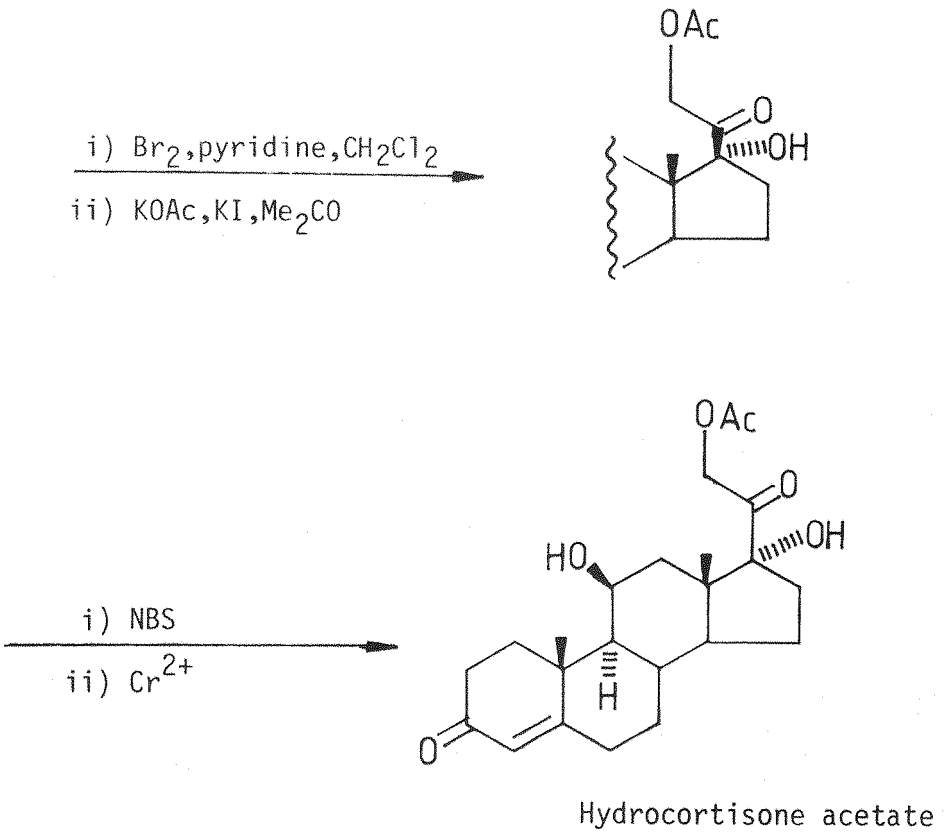
Scheme 22

Over the last few years there has been a considerable growth in the use of allene sulphoxides in synthesis and a particularly elegant example is the preparation of corticosteroids from 9α-androst-4-ene-3,17-dione (11) which is cheaply available by the degradation of soya beans.[43]







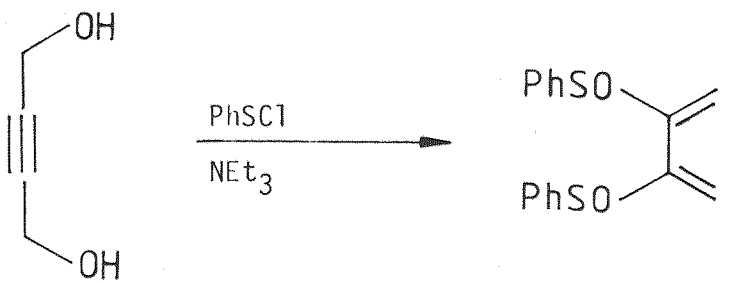


Hydrocortisone acetate

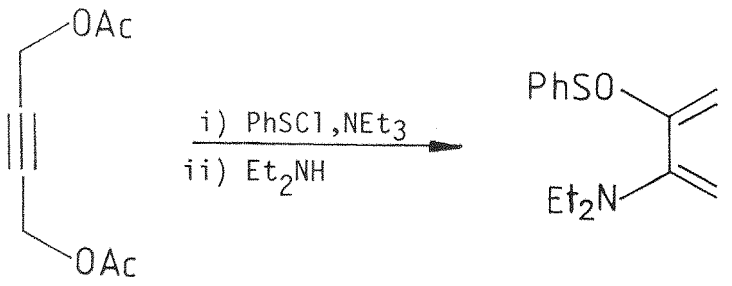
Scheme 23

The sulphoxide-sulphenate rearrangement is discussed more fully in the next Section.

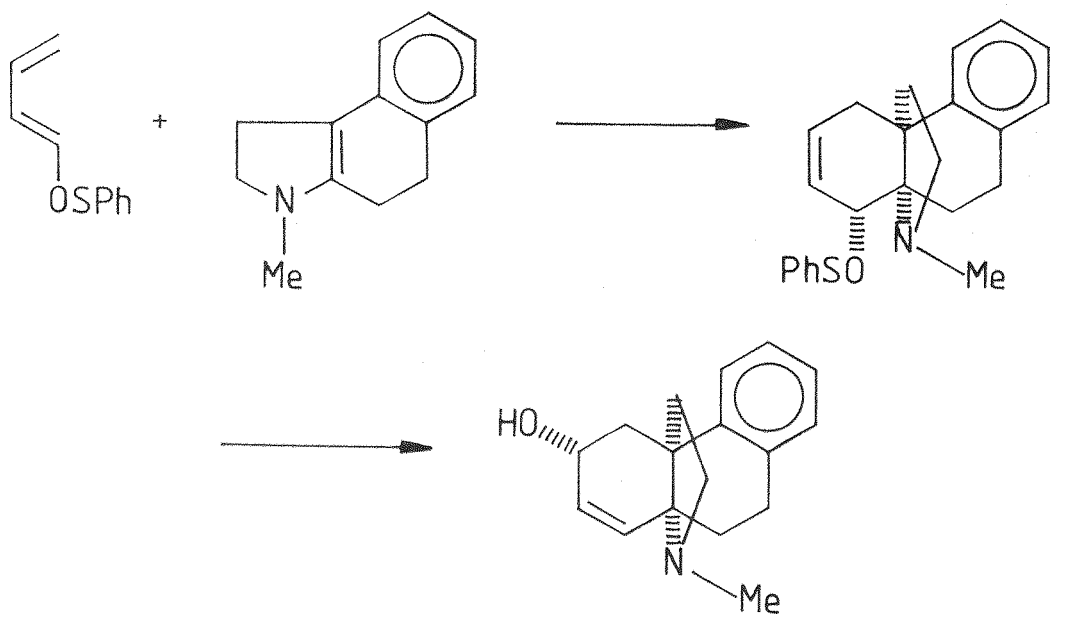
Several interesting sulphur substituted dienes have been synthesised by routes involving allene sulphoxide intermediates;[44,45] however, their usefulness in synthesis has yet to be demonstrated, although a related diene (12) has been used to prepare the hasubanan alkaloid skeleton.[46]



Scheme 24



Scheme 25



Scheme 26

The Diels-Alder reactions of allene sulphoxides with furan and cyclopentadiene have been reported under thermal, high pressure and Lewis acid catalysed conditions. However, allene sulphoxides do not appear to be sufficiently reactive to add to acyclic dienes such as isoprene or 2,3-dimethylbutadiene.[47] Allene sulphones show rather greater reactivity although the range of adducts reported is small.[48]

1.4 Chemistry of Allylic Sulphoxides

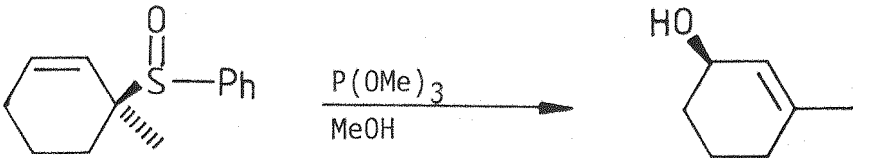
The expected product from the ene reaction of an allenic sulphoxide is an allylic sulphoxide and much of the synthetic value of the reaction rests on the considerable synthetic versatility of this unit.

The hydrogens next to sulphoxide are fairly acidic and allow the formation of an anion which may be quenched with a variety of electro-

philes. If the sulphoxide is first oxidised to sulphone, anion formation will occur more readily and give a more highly stabilised anion. With both sulphoxide and sulphone both α and γ alkylation can occur. However, if the phenyl sulphoxide is replaced by an α-pyridyl or N-methyimidazoyl sulphoxide, very high α selectivities are observed with a wide variety of electrophiles. This effect is probably due to the ability of these groups to chelate the counter-ion.[36]

Pummerer[49] rearrangement induced by carboxylic anhydrides, followed by hydrolysis should give α,β-unsaturated aldehydes. The same products could be obtained less directly by oxygenation,[50] boration[51] or stannation[52] of the sulphur stabilised anion to give an α-hydroxy-sulphoxide which should readily lose benzenesulphenic acid.

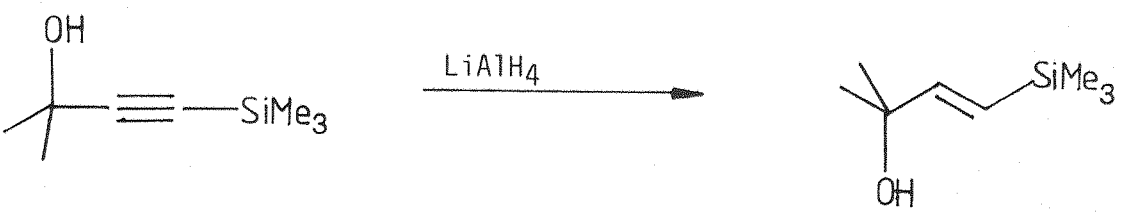
Allylic sulphoxides will undergo a suprafacial [2,3]-sigmatropic rearrangement with trimethylphosphite in boiling methanol to give the transposed allylic alcohol.[35,36,43]

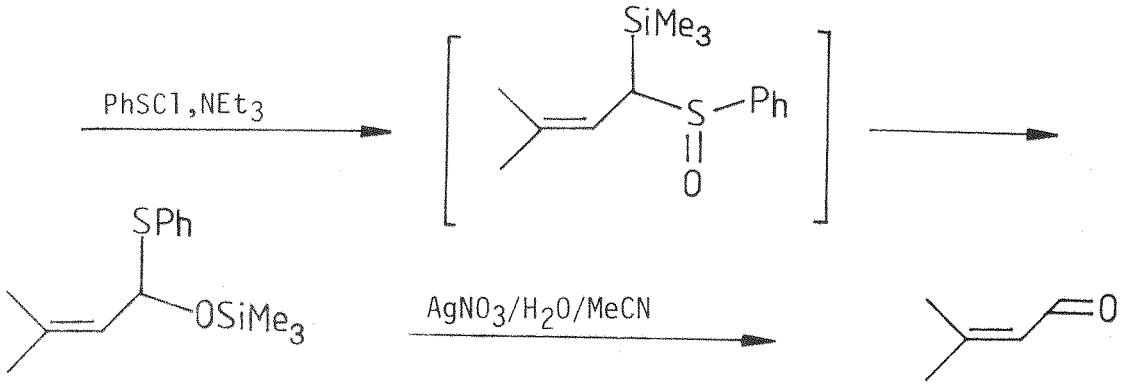


Scheme 27

The transition state adopted is that which involves least steric crowding, thus accounting for the high stereospecificity of the rearrangement in the synthesis of hydrocortisone acetate described above.

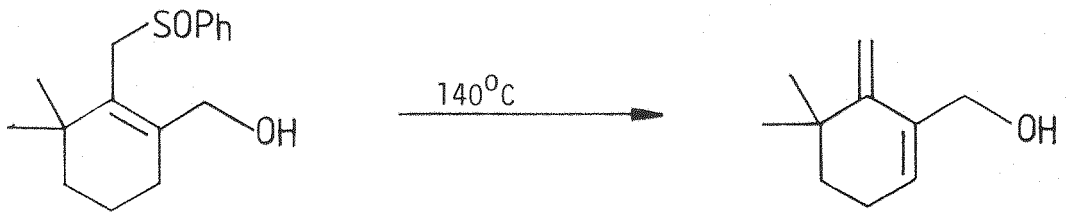
In conjunction with silicon chemistry this rearrangement has been used in a new synthesis of α,β-unsaturated aldehydes.[53]





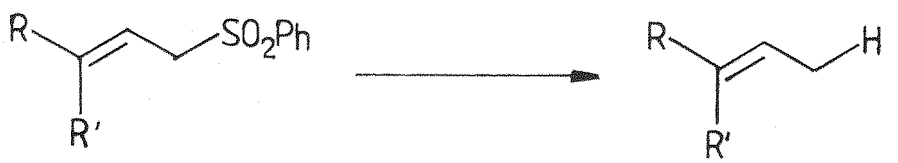
Scheme 28

On thermolysis, allylic sulphoxides lose phenylsulphenic acid to give 1,3-dienes.[54]



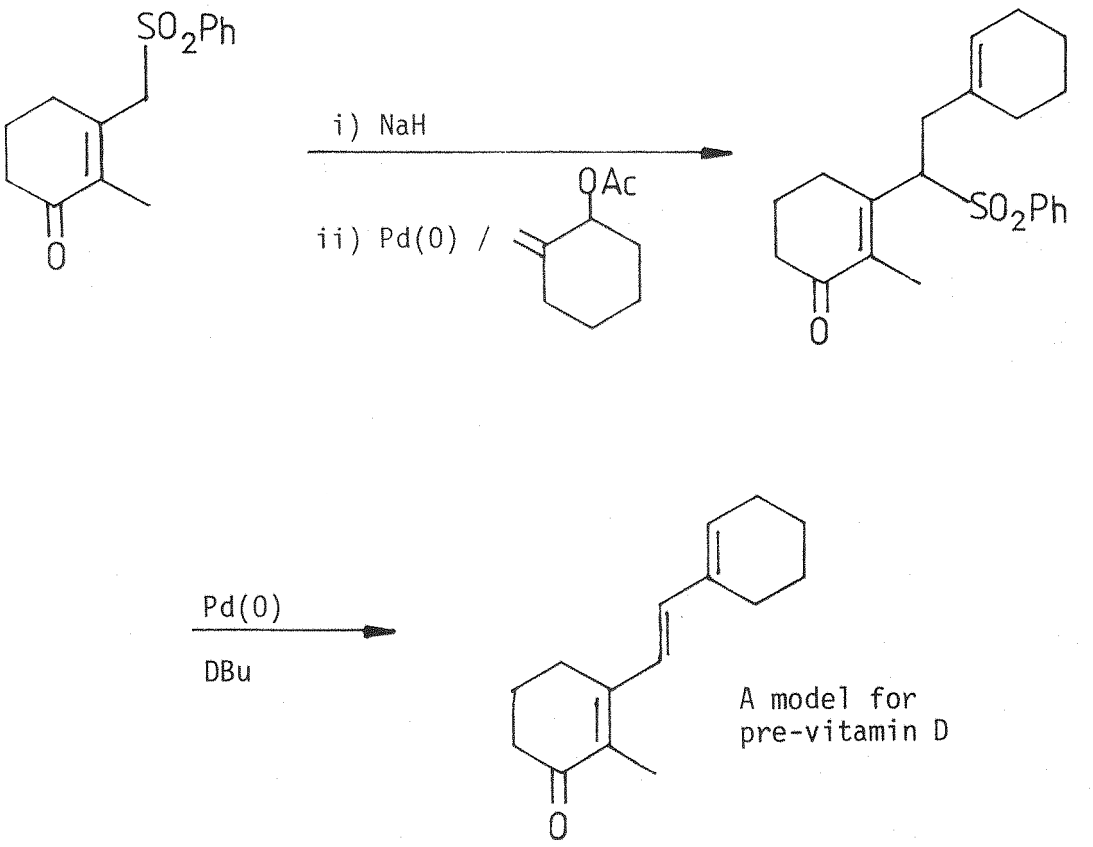
Scheme 29

The allylic sulphoxide is readily oxidised with peracids to give an allylic sulphone which besides its anion chemistry may be reductively cleaved with a wide variety of reagents including sodium or aluminium amalgams, sodium dithionate,[55] lithium aluminium hydride/Raney nickel/ triphenylphosphine and also by cathodic reduction.[56]

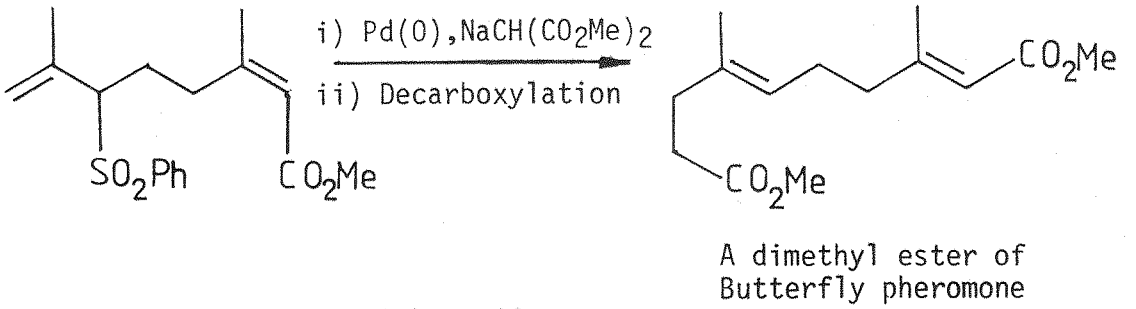


Scheme 30

Allylic sulphones may also be used to prepare π-allyl palladium complexes[57] which, by displacement with nucleophiles or base catalysed elimination allows the elaboration of a wide variety of structures.[58]



Scheme 31



Scheme 32

1.5 Objectives of Work

While the general aim of the project was to explore the scope and limitations of the ene reaction of allene sulphoxides, there was a number of more specific questions which presented themselves: 'Will allene sulphoxides give intramolecular ene reactions?';'Can six-membered or larger rings be formed?'; 'Can further functionality be introduced into the molecule?' and 'May the reaction be used for ring annelation?' Our attempts to answer these questions are described in the following Chapters.

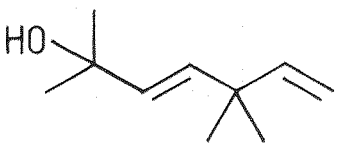
CHAPTER 2

APPLICATION TO THE PREPARATION OF ACYCLIC SYSTEMS

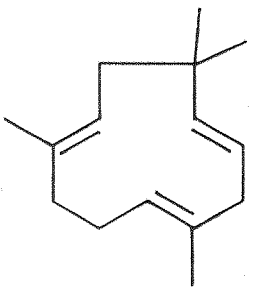
2.1 Introduction

The ene reaction of an allene sulphoxide observed by Parsons[7] was a novel transformation and very little information was available to assess the reactivity of allene sulphoxides in ene reactions. In particular, it was not known whether, despite the far less favourable entropy of activation, an intermolecular ene reaction leading to an acyclic 1,4-diene would occur. The reaction was also expected to provide a good model system for investigating high pressure ene reactions, which have previously only been studied with highly reactive enes and enophiles.[16]

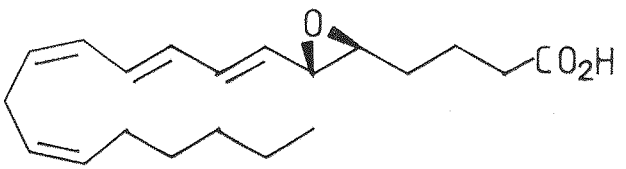
1,4-dienes, although less common than either 1,3- or 1,5-dienes, do occur widely in nature in compounds of both terpenoid and fatty acid origin, and include several commercially important insect sex pheromones and the leucotrienes which have potential applications in the treatment of allergic and inflammatory conditions.



Yomogi alcohol[59]

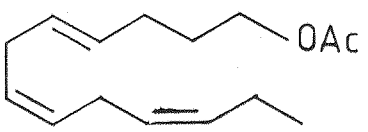


α-Humulene[60]

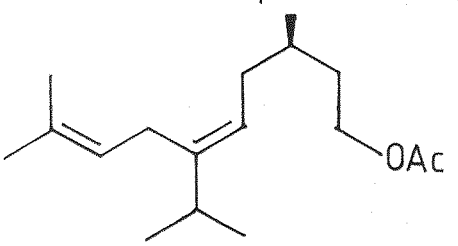


Leucotriene A[61]

Almond moth and Indian meal moth sex pheromone[62]



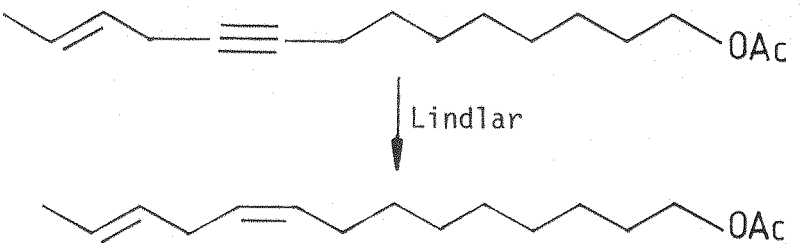
Potato tuberworm moth moth sex pheromone[63]



Yellow scale sex pheromone[64]

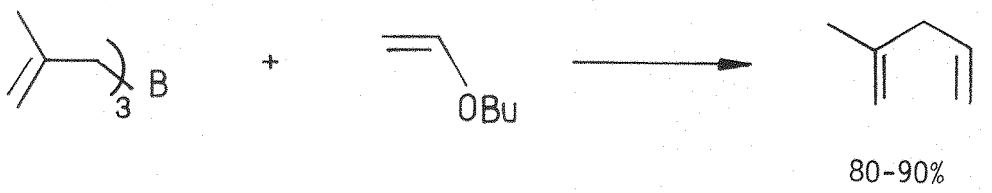
Despite the importance of 1,4-dienes there are relatively few reliable methods for their preparation. The most widely used method is by the reduction of ene-ynes or di-ynes with hydride reagents, alkali

metals in liquid ammonia or Lindlar's catalyst. By appropriate choice of substrate and reducing agent either (E,E), (Z,E) or (Z,Z) 1,4-dienes may be prepared.[63,65] This method is limited to the preparation of compounds with at least one disubstituted double bond and by the accessibility of the appropriate acetylenic precursors.



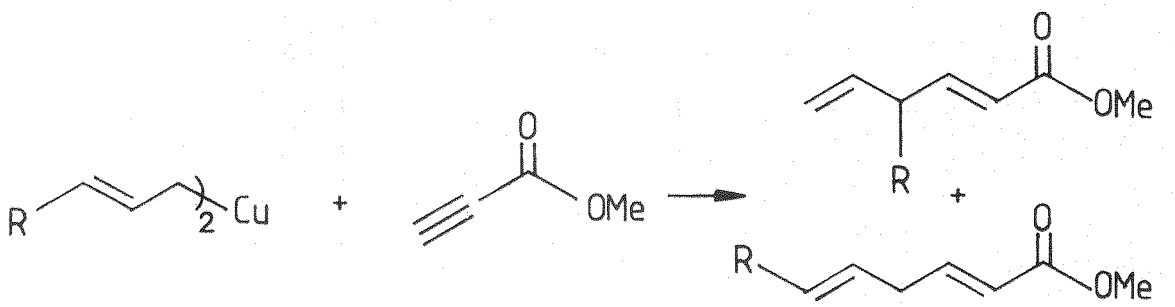
Scheme 33

More recently, several routes have been developed which involve the conjugate addition of allyl-metal intermediates, such as the reaction of tri-*iso*-propenylborane with vinyl ethers,[66]



Scheme 34

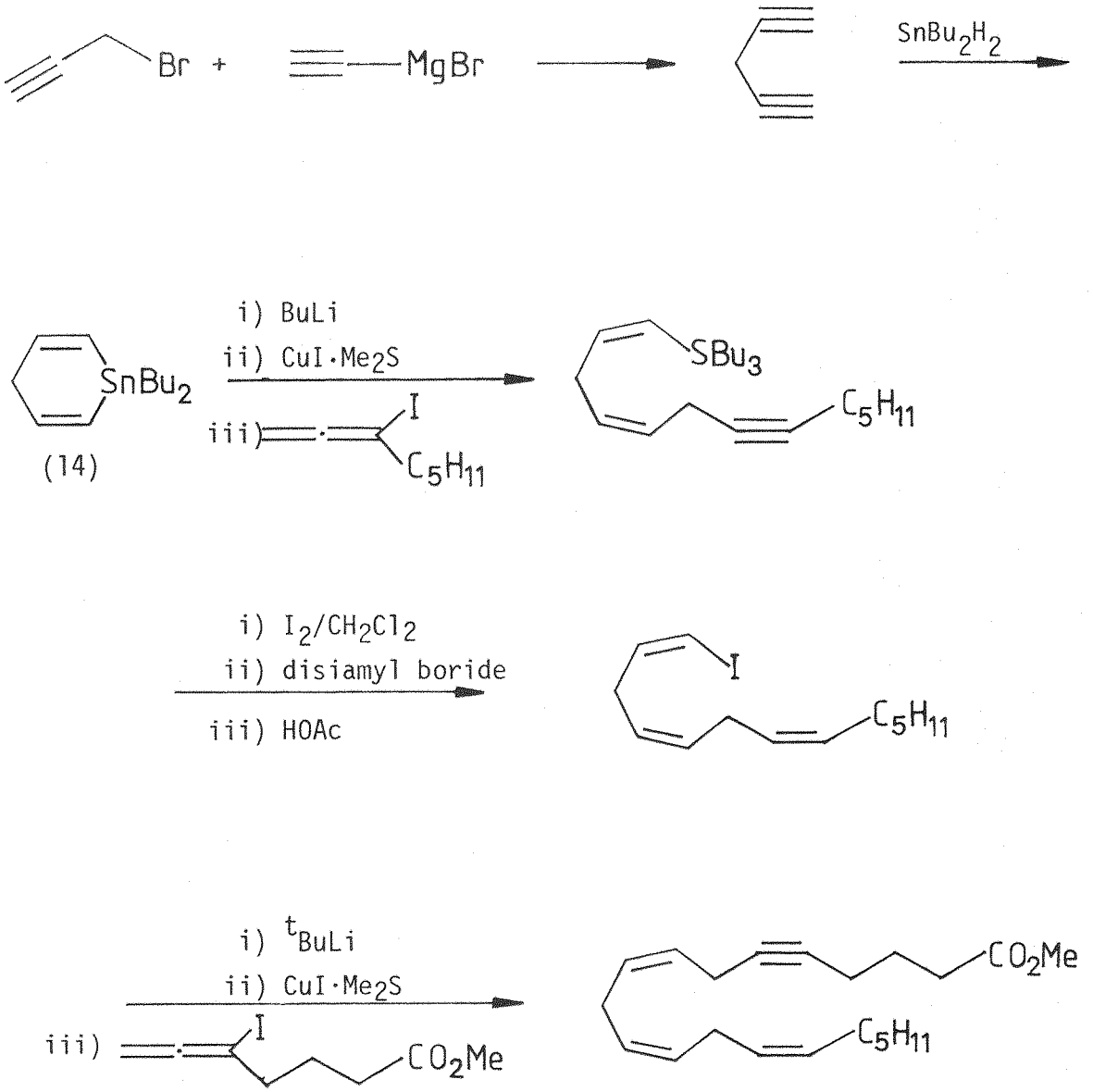
or of allyl coppers with methyl propargylate.[67]



Scheme 35

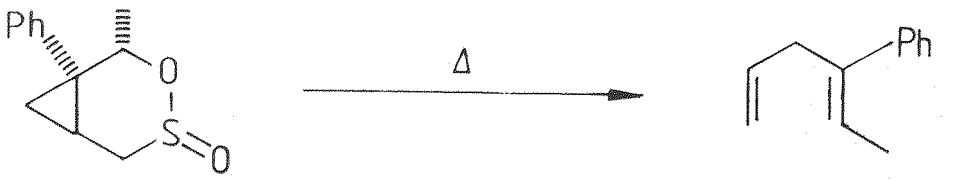
This latter reaction suffers from the major draw-back that, although if carried out at low temperatures it gives stereospecific addition, there is no regiochemical control.

Corey has developed the use of the organostannane (14) as a 1,4-diene synthon in the synthesis of some dehydrodarachidonic acids which were required for biological studies.[68] Unfortunately, (14) is available only in 8% overall yield from 3-bromopropyne.[69]

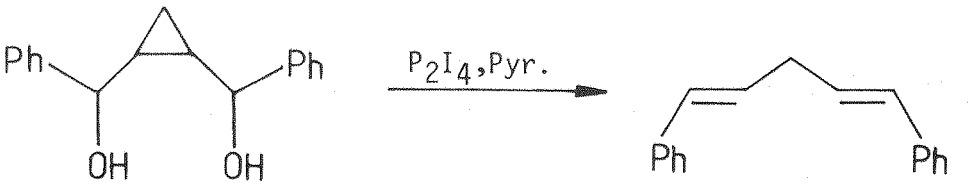


Scheme 36

Other routes, such as those involving eliminations from substituted cyclopropanes, cannot easily be generalised to the preparation of other examples. Indeed, the precursors for these reactions are not sufficiently readily available to make them very attractive syntheses of any 1,4-dienes although the high stereospecificity is a point in their favour.[70,71]

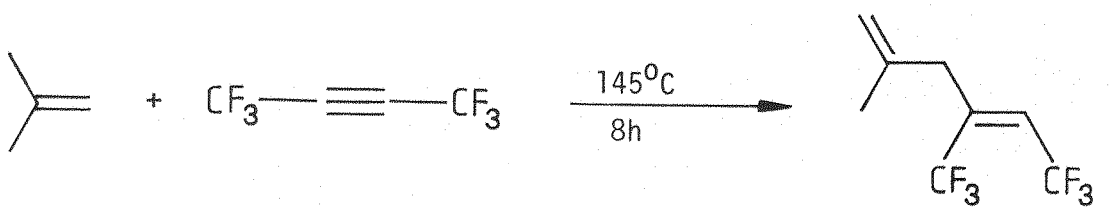


Scheme 37



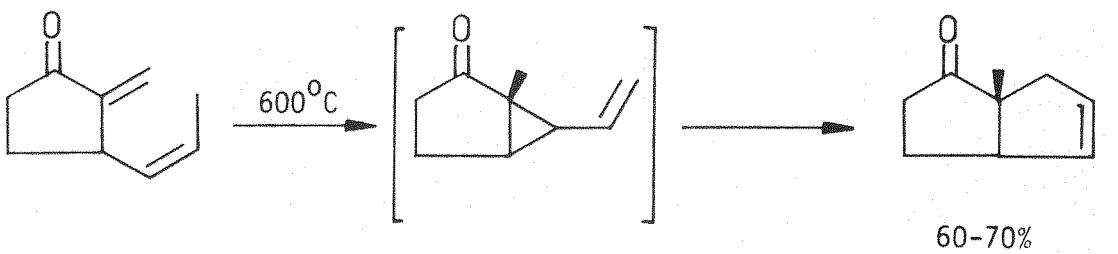
Scheme 38

In the present context of ene reactions the preparation of a 1,4-diene by the reaction of methylpropene with a perfluoroacetylene is of interest, although of little general synthetic use.[72]



Scheme 39

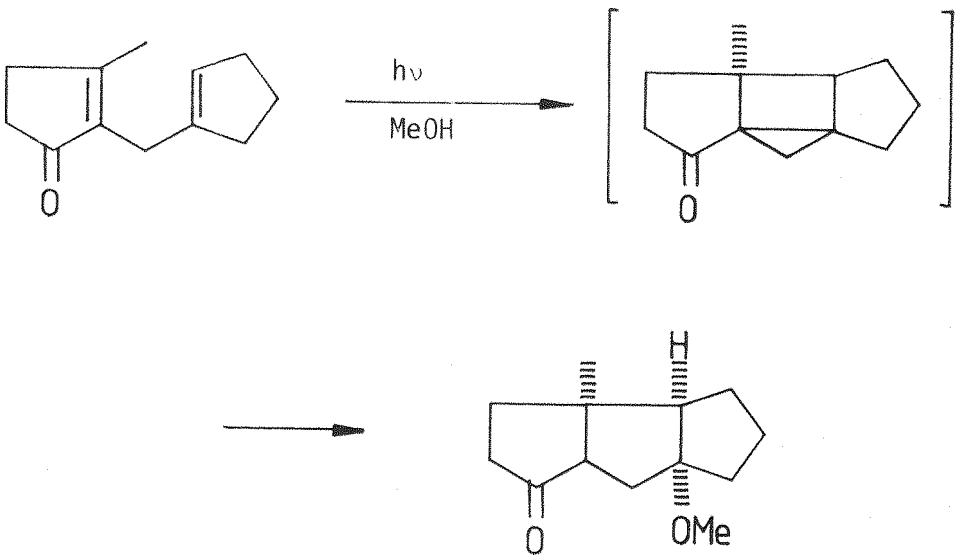
Very recently there has been a renewed interest in the use of 1,4-dienes as intermediates in synthesis, in particular for cyclopentene preparation and annelation. One method involves the flash pyrolysis of suitably substituted 1,4-dienes which form cyclopentenes *via* a vinyl-cyclopropane as presumed intermediate.[73]



Scheme 40

Alternatively, the conversion may be achieved by a photochemical

[2+2] addition with the housane intermediate being trapped by a nucleophile such as methanol. This chemistry has been successfully applied to the synthesis of tricycles analogous but of the opposite stereochemistry to those found in the hirsutane and coriolin natural products.[74]

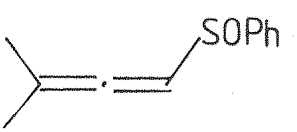


Scheme 41

Thus, setting aside reasons of curiosity, it would appear that both the variety of natural products and the potential chemistry of 1,4-dienes would justify work on the intermolecular ene reactions of allene sulphoxides.

2.2 Studies on 3-Methyl-1-phenylsulphinylbuta-1,2-diene (9)

The reaction of 3-methyl-1-phenylsulphinylbuta-1,2-diene (9), prepared from 2-methylbut-3-yn-2-ol,[34] with methylpropene in dichloromethane catalysed by aluminum chloride, was tried first but only starting material was recovered in good yield.



(9)

It seemed likely that during the reaction period (24h) the vapourisation of methylpropene might be considerable and also that there might be sufficient ingress of water to have hydrolysed and deactivated the catalyst. Therefore, the reaction of (9) with oct-2-ene catalysed by aluminium chloride in the presence of triethylaluminium was tried, but again only starting material was recovered. At the temperature of the reaction (20°C), the triethylaluminium and aluminium trichloride would not be expected to exchange to form any of the alkylaluminium halide catalysts used by Snider.[19] These catalysts, which can be prepared by heating appropriate quantities of aluminium chloride and trialkylaluminium to 180°C for about ½h,[75] are weaker Lewis acids than aluminium chloride and would not, therefore, be expected to catalyse this reaction.[19]

It is conceivable that other strong Lewis acids, such as titanium (IV) chloride, might catalyse the reaction but in view of the total lack of success with aluminium chloride, and also with the use of the high pressure and thermal conditions described below, it was felt that this was unlikely.

Before leaving the area of Lewis acid catalysis, the effect of heating a mixture of allene (9) with oct-2-ene in the presence of traces of iron pentacarbonyl was tried. This could complex both reactants and bring them into an orientation favourable to reaction. However, a complex mixture of products was formed which was not fully resolved by tlc. In addition, the spectra of the crude material did not suggest that any of the desired ene product had been formed, but rather that carbonyl addition products involving both the allene and octene were present.

Treatment of allene (9) with methylpropene under high pressure (10kbar) at both rt and 60°C led to the recovery of the allene in high yield and purity.

In view of these discouraging results and also the following considerations, high pressure work was discontinued:-

1) The only high pressure ene reactions reported are between β-pinene and a small number of highly reactive enophiles and pressures as great as 40kbar were used.[16] This suggests that the rate enhancement of an ene reaction by pressure may be small.

2) The rate constant of a chemical reaction has an approximately logarithmic dependence on pressure.[76]

3) Our apparatus was not suitable for use at higher temperatures or pressures, or performing high pressure reactions in the presence of Lewis acids.

Heating a mixture of allene (9) and oct-2-ene without solvent in a Carius tube at 120°C left the material unchanged but at 160°C an extremely complex mixture of products was obtained. No attempt was made to analyse the mixture which was probably derived from the highly reactive 1,3-diene. This would be expected to form readily under these conditions by rearrangement of the allene.[41]

2.3 Studies on Phenylsulphonylpropadiene (15)

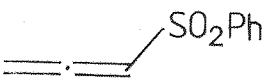
It appeared from the above results that allene sulphoxides had only very low, if any, reactivity in the intermolecular ene reaction. There did, however, appear to be three ways in which the reactivity of the system could be increased:-

1) by removing the methyl groups which may be causing some steric crowding in the transition state;

2) by using the sulphone rather than the sulphoxide to make the allene more electron poor and;

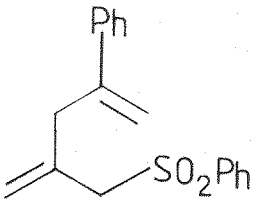
3) by using electron rich ene components such as 2-phenylpropene or 2-methoxypropene.

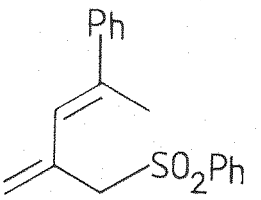
Phenylsulphonylpropadiene (15) was prepared from 3-bromopropyne and sodium benzenesulphinate[47] and its thermal reaction with both 2-phenylpropene and 2-methoxypropene studied. In neither case did heating at 80°C lead to any reaction but after 7h at 160°C no starting allene remained and a number of new products could be seen on tlc.

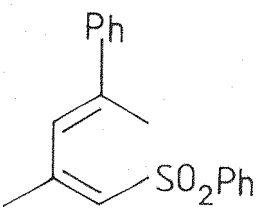


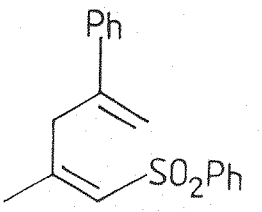
(15)

Preparative tlc allowed the separation of two bands of compounds from the 2-phenylpropene reaction. Integration of the nmr spectra of the two fractions showed the slower moving material to be derived from two molecules of allene sulphone and one of phenylpropene whereas the fast moving material was derived from one molecule of each. Both nmr spectra show singlets at δ1.50 which integrate at less than three protons, strongly suggesting that methyl on a double bond is present in some of the components of each fraction. These results could be explained by the product being a mixture of the following compounds.

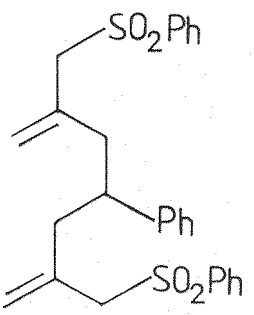


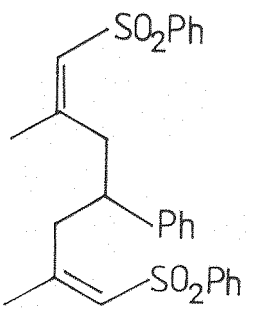


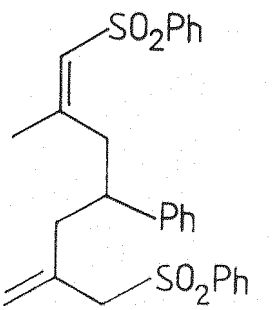




Fast Fraction







Slow Fraction

These compounds are all either ene products or compounds that could be formed from them by double bond migration.

The reaction products with 2-methoxypropene appear to be entirely derived from the 2:1 adduct and again the spectra suggest that a large number of double bond isomers are formed.

Because of the preponderance of a 2:1 adduct, and the apparent ease with which double bond migration occurred during the reaction and the synthetically rather restricted range of possibilities allowed by the combination of unsubstituted allene sulphone and highly electron rich ene component, no further studies were carried out on the intermolecular reaction.

CHAPTER 3

APPLICATION TO THE PREPARATION OF MONOCYCLIC SYSTEMS

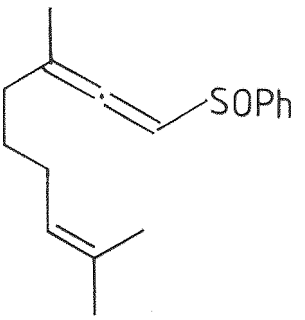
3.1 Introduction

Although a wide variety of conditions were studied, no intermolecular examples of the ene reaction of allene sulphoxides were found, and it became clear that any application of the reaction would have to be as a ring forming reaction in the synthesis of alicyclic compounds. The questions then posed were:-

i) What sizes of ring can be prepared? and

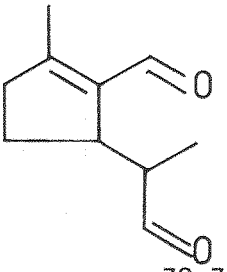
ii) What other functionality can be tolerated in the molecule during the ene reaction?

It is known that the intramolecular ene reaction proceeds most readily in reactions leading to normal ring compounds. Reactions giving five-membered rings are most favoured, and relatively few examples are known of ene reactions leading to the formation of small or large rings.[21] Because the synthesis of five-membered rings by this reaction had already been reported,[6] question i) becomes 'can six-membered rings be prepared?'. The allene (16) was chosen for studies of cyclohexene synthesis; these are described in Section 3.4.

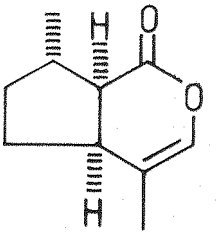


(16)

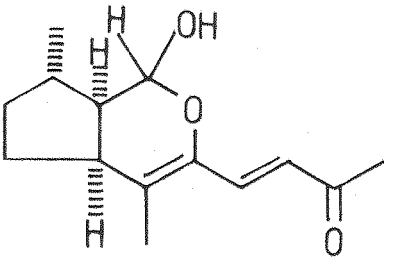
The second question, 'what other functionality can be tolerated in the molecule during the ene reaction?', is very wide ranging, and is probably best considered in the context of the substituents required for the synthesis of natural products. Because, when this work was initiated, it was not known whether six-membered rings could be formed, only cyclopentanoid natural products were considered. These compounds, which show considerable structural variation, are widely distributed in nature and may be derived from either fatty acid or terpenoid precursors.[77]



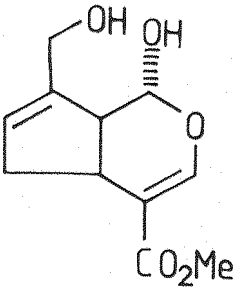
Chrysomelidial (17)[78,79]



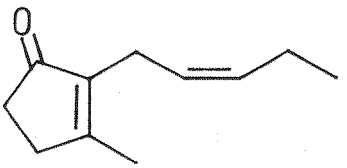
Nepetalactone[80]



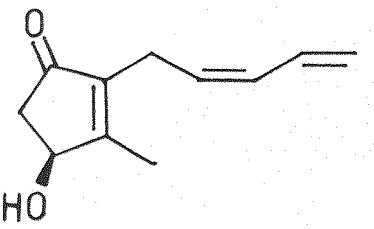
Gyrinidone[81]



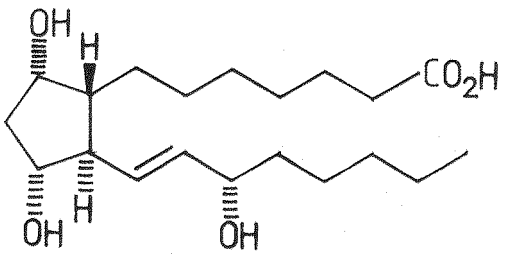
Genepin[82]



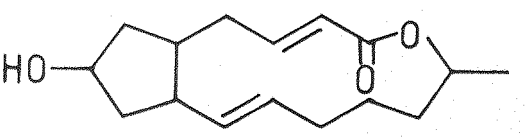
cis-Jasmone[83]



Pyrethrolone[84]

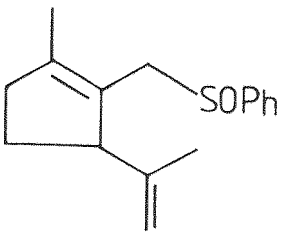


$PGF_{1\alpha}$ (18)[85]



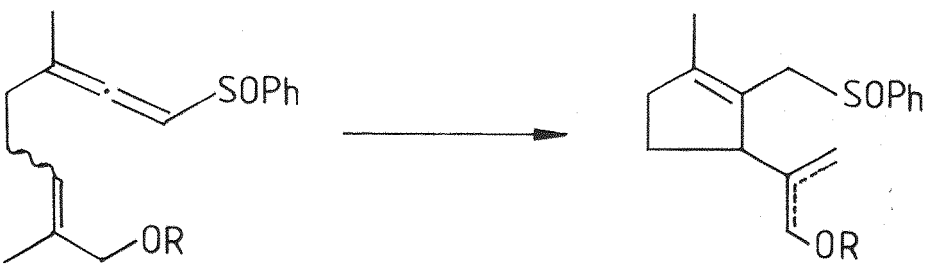
Brefeldin A[86]

Many of these compounds would be easily accessible if the ene reaction could be used to prepare difunctionalised cyclopentanes. Such intermediates would allow the preparation of compounds such as Nepetalactone by functional group manipulation, or Brefeldin A by the attachment of suitable side-chains. In particular, analogues of (2) with an oxygen containing side-chain rather than the propen-2-yl radical were expected to be versatile synthetic intermediates.



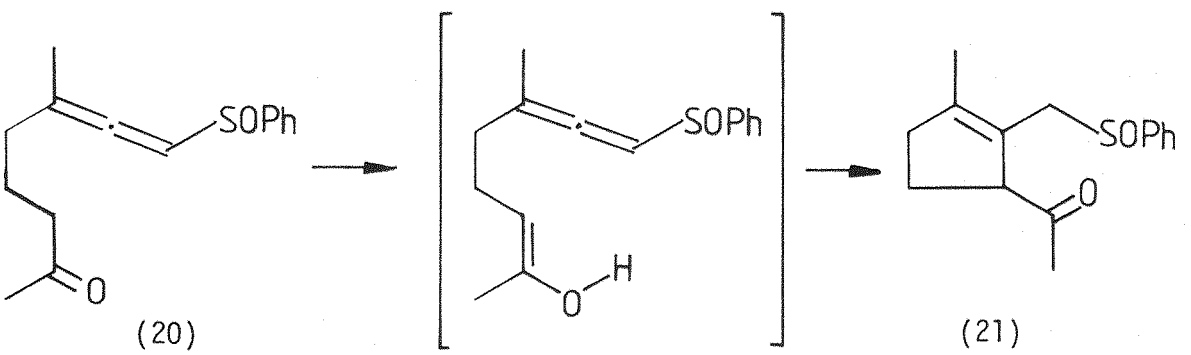
(2)

Two such systems have been studied (i) the protected allylic alcohols (19) which, depending on the stereochemistry of the double bond, will give allyl alcohol or vinyl ether side chains after cyclisation, and (ii) the ketone (20) which could react in its enol form to give products containing a methyl ketone side-chain.



(19)

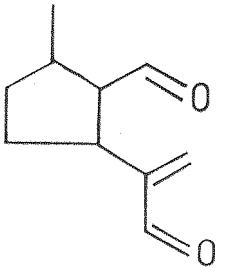
Scheme 42



(20) (21)

Scheme 43

It should also be possible to prepare compounds with suitable functionality from the cyclopentene (2). For instance, Pummer rearrangement[87] followed by reduction and allylic oxidation[88] would give the natural product (22).[77] However, such transformations were not studied.

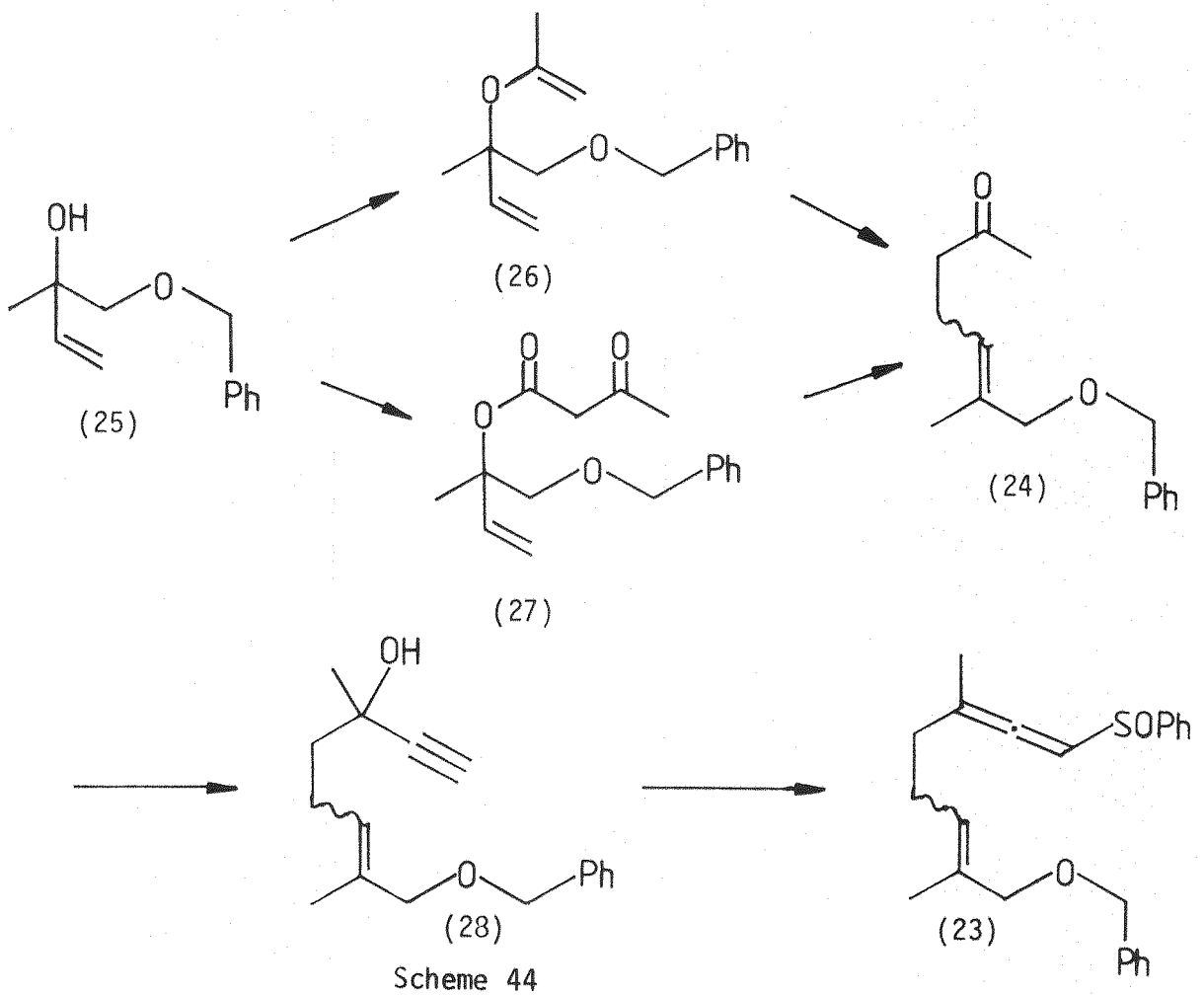


(22)

3.2 Synthesis and Reactions of 8-Hydroxy-3,7-dimethyl-1-phenylsulphinyl-octa-1,2,6-triene Derivatives

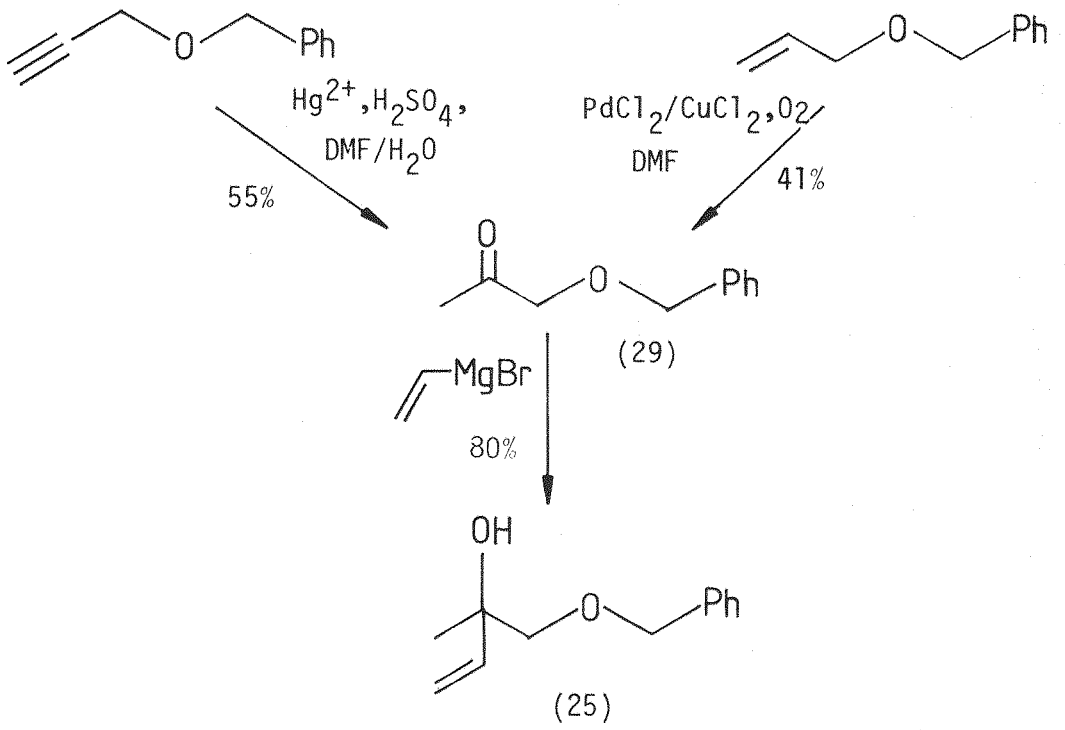
3.2.1 Synthetic Routes involving [3,3]-Sigmatropic Rearrangements

The allene (23) was expected to be easily available from the ketone (24) by addition of acetylene followed by treatment with phenylsulphenyl chloride in the presence of triethylamine.[34] The synthesis of allene (23) thus depends on the preparation of ketone (24) which was envisaged as being accessible by Carroll[89] or Claisen[90] rearrangement of appropriate derivatives of the alcohol (25).



Scheme 44

The alcohol (25) thus becomes the key intermediate and was easily prepared in 80% yield by the addition of vinyl magnesium bromide to benzyloxypropanone which is available either by the hydration[91] of propynyl benzyl ether or by the Waker oxidation[92] of propenyl benzyl ether.



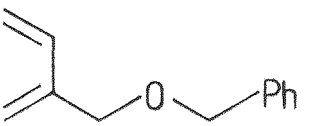
Scheme 45

Treatment of the alcohol (25) with diketene in the presence of a catalytic quantity of sodium methoxide gave a 60% yield of the acetoacetate (27).

Heating the acetoacetate (27) with aluminium *iso*propoxide at 170°C[89] gave only polymeric products and experiments performed at lower temperatures did not show any loss of starting material or appearance of products as judged from tlc.

Recently, Tsuji[93] has claimed that the Carroll reaction is strongly catalysed by palladium acetate or sodium hydride/palladium acetate both in the presence of triphenylphosphine and may be performed at relatively low temperatures. In tetrahydrofuran at room temperature palladium acetate failed to catalyse the desired Carroll reaction and heating the mixture to reflux led, over 3h, to some loss of starting material, and the formation of a wide variety of decomposition products which were

not characterised. Applying the sodium hydride/palladium acetate conditions,specifically recommended for the acetoacetates of tertiary alcohols,to our system did not lead to the isolation of any involatile products, strongly suggesting that an alternative elimination pathway to give diene (30) has been followed.[94]

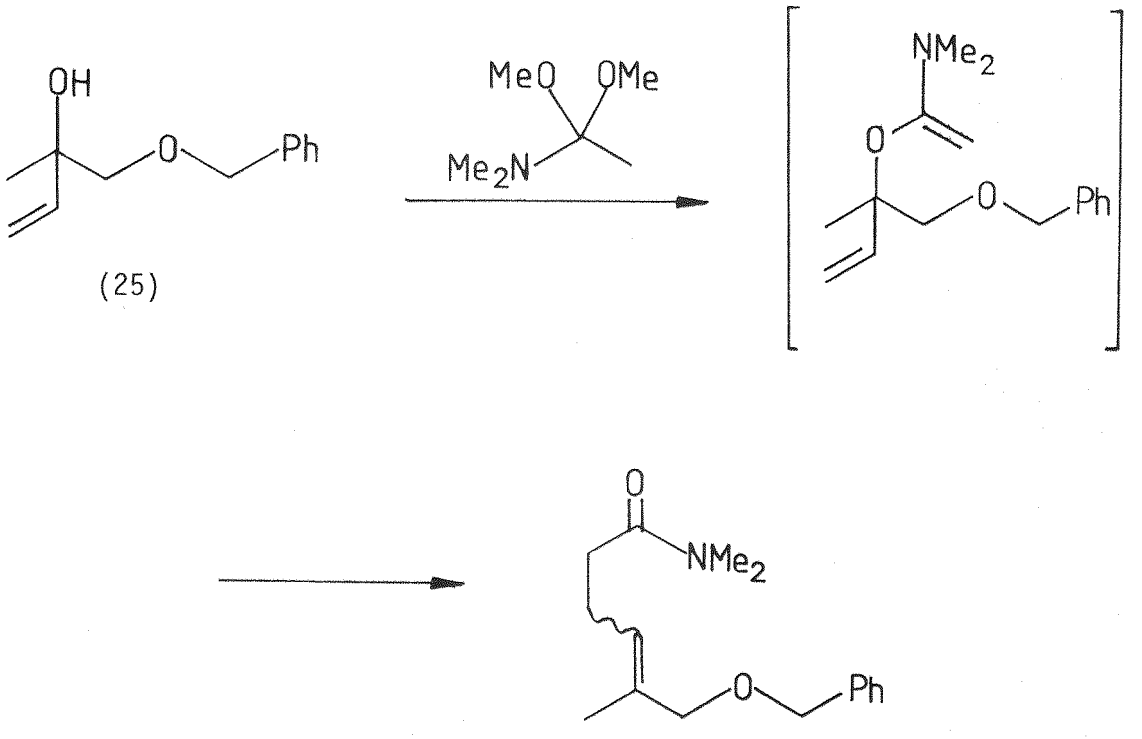


(30)

A number of analogous experiments using tetrakis(triphenylphosphine palladium(0) or palladium (II) chloride as catalyst in refluxing tetrahydrofuran all led to the recovery of unchanged acetoacetate (27).

The preparation and rearrangement of the vinyl ether (26) was attempted by refluxing the alcohol (25) with 2-methoxypropene in xylene in the presence of a catalytic quantity of toluenesulphonic acid.[90] Loss of starting material was monitored by tlc and was virtually complete after 20h. However, work-up and attempted purification by high vacuum distillation gave material whose nmr spectrum showed chiefly aromatic absorption and no signs of the desired ketone.

In an attempt to discover whether Claisen-type rearrangements were unduly disfavoured in this system, the allylic alcohol (25) was refluxed in xylene with the dimethyl acetal of N,N-dimethyl acetamide.[95] These conditions normally give amides by a very ready rearrangement of an intermediate vinyl amine species. However, (25) was recovered substantially unchanged even after 8h reflux.

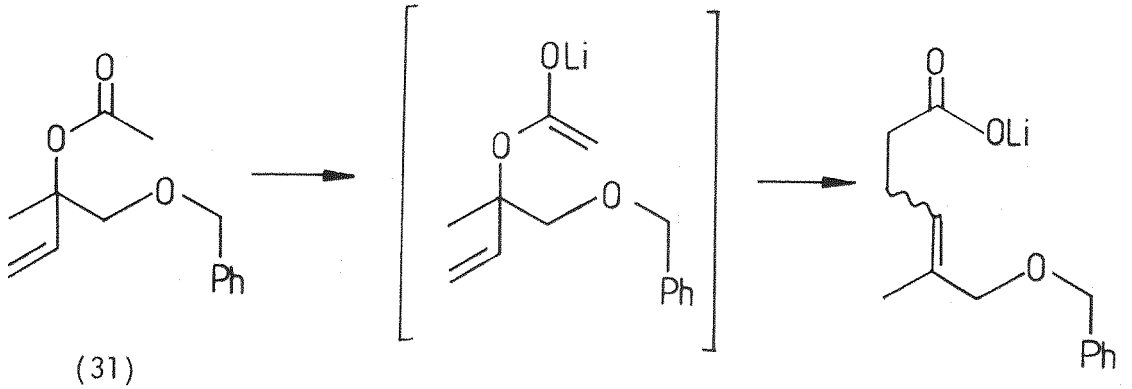


(25)

Scheme 46

The work described in the next section on the synthesis of ketone (24) using selenium dioxide oxidation and the work described in this section were performed in parallel, and at this point the required ketone (24) became available by allylic oxidation. Although the yield of material in this route was low, it seemed sufficient to prepare a sample of the allene (23) for study of the ene reaction, and work on rearrangement routes was discontinued. However, the [3,3]-rearrangement route would permit the preparation of a greater variety of compounds than would be easily accessible by allylic oxidation and might justify further work in the area.

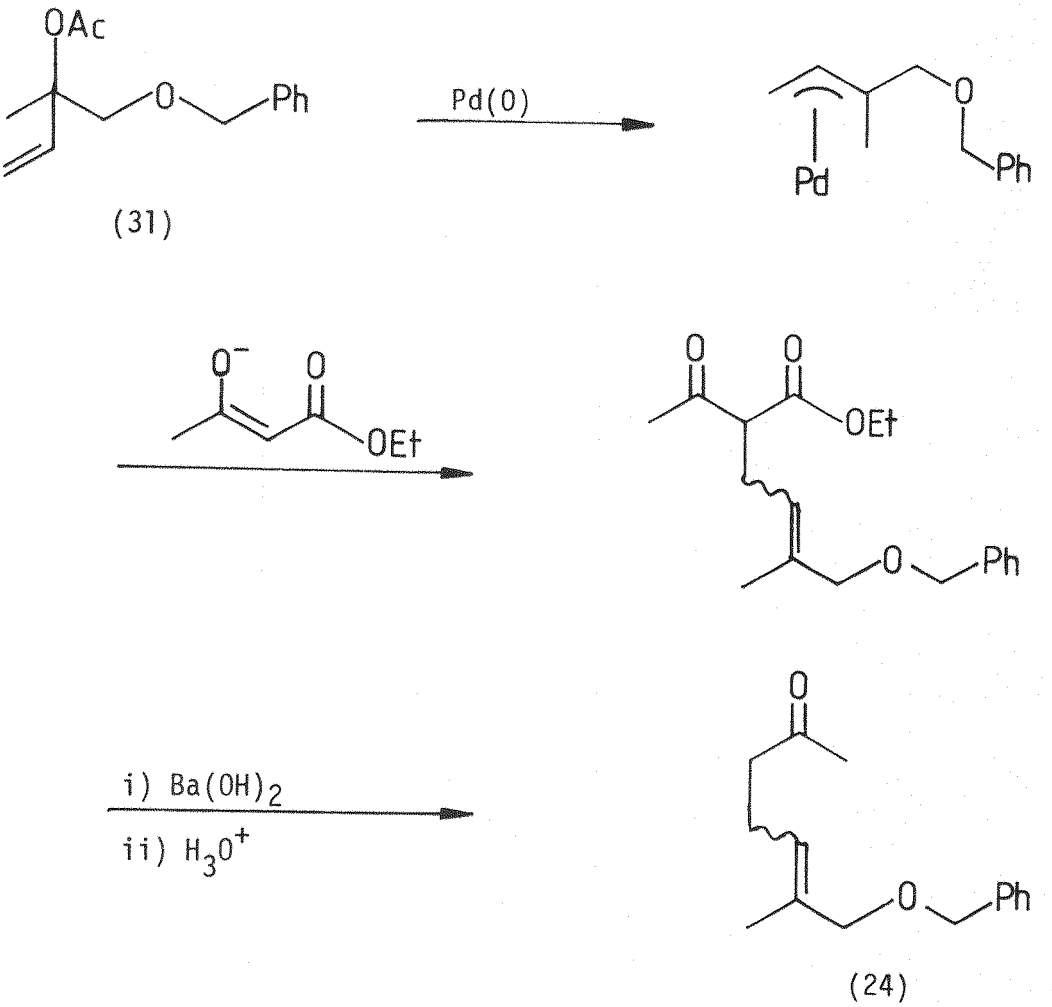
One possibility would be the preparation of the acetate (31) and the Claisen rearrangement of its enolate[90] - a reaction which is generally more favoured than the Claisen rearrangement of an allyl vinyl ether.



(31)

Scheme 47

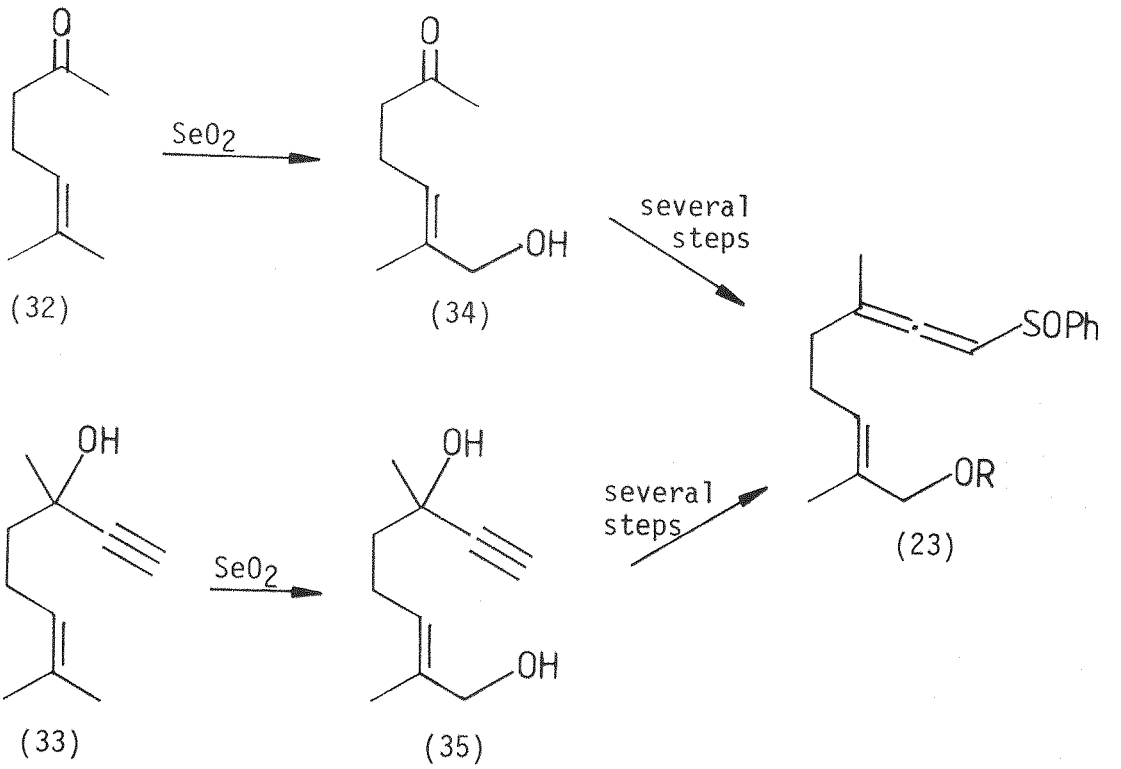
Although preliminary attempts to prepare the acetate (31) with acetyl chloride in triethylamine or with acetic anhydride/toluene-sulphonic acid were unsuccessful, more forcing basic conditions using 4-dimethylaminopyridine as catalyst should allow its preparation.[96] Possession of this acetate would also allow the preparation of a palladium π-allyl derivative which, after treatment with the anion of ethyl acetoacetate and decarboxylation, would give the required ketone (24).[58]



Scheme 48

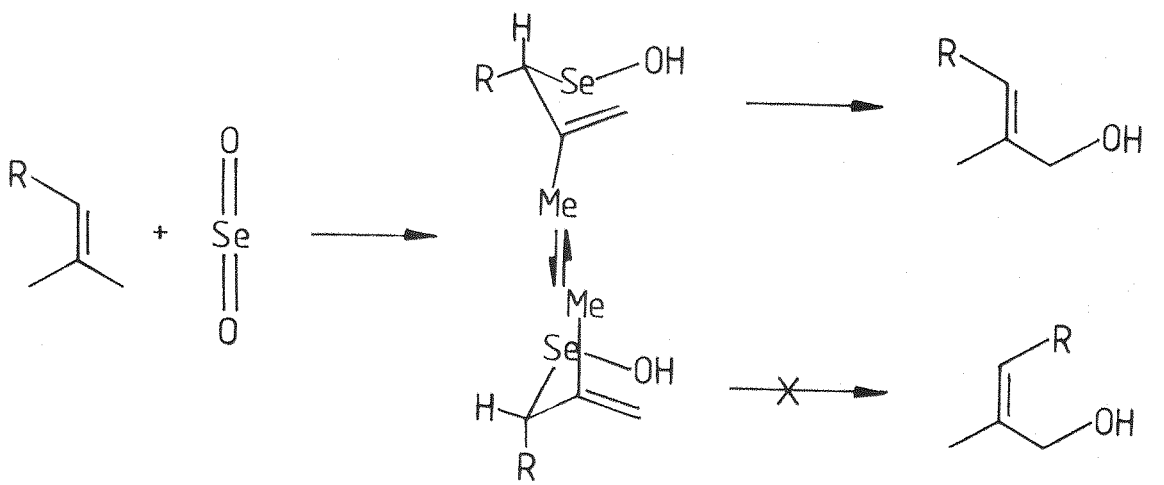
3.2.2 Synthetic Routes Involving Allylic Oxidation

Because both the ketone (32) and the acetylenic alcohol (33) are commercially available the idea of preparing compounds (34) and (35) as precursors to the desired allene (23) by allylic oxidation with selenium dioxide appears very attractive.



Scheme 49

This route contrasts with those described in Section 3.2.1 in that the product allylic alcohol would be expected to be E whereas the products from the rearrangement reactions will be E/Z mixtures. This stereospecificity is normally observed with *gem*-dimethyl alkenes[97] and is probably due to the mechanism of the selenium dioxide oxidation in which the transition state with R equatorial is preferred.[98]

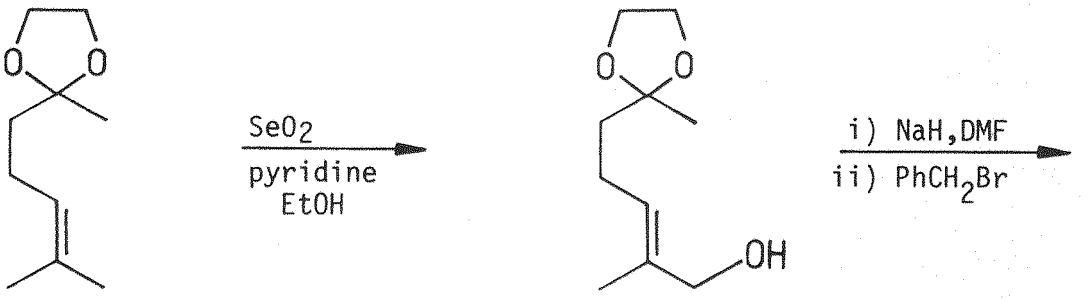


Scheme 50

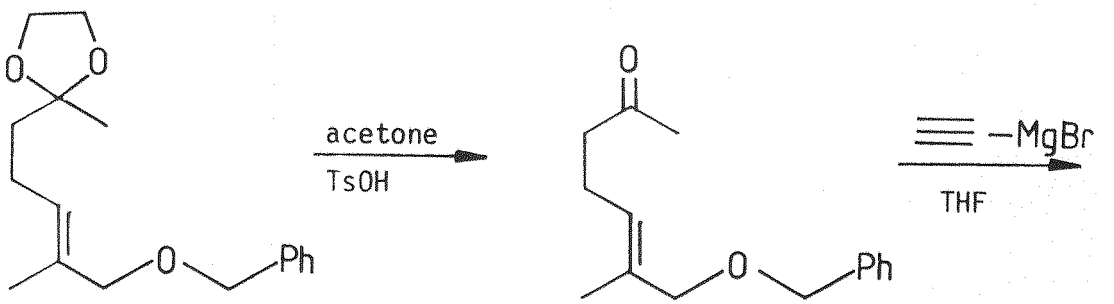
Treatment of either (32) or (33) with selenium dioxide in refluxing ethanol did give allylic oxidation, but unfortunately, the products were heavily contaminated with selenium and the red colour and unpleasant odour of the products persisted after flash chromatography, treatment with mercury or with reducing agents. Distillation only gave tars and more highly oxidised material.

Sharpless has developed conditions using catalytic quantities of selenium dioxide which is re-oxidised *in situ* with t-butylhydroperoxide, thus avoiding problems of product purification.[99,100] However, when applied to either (32) or (33) these conditions gave back unchanged starting material or, after protracted reaction times, products containing t-butyl groups. These are probably either ethers or per-ethers which have been reported as byproducts in some of these reactions.[100]

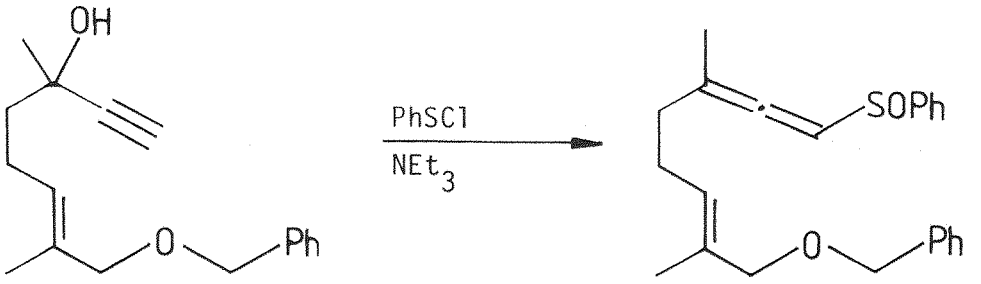
The preparation of acetal (36) by allylic oxidation of (37) in the presence of pyridine has been reported.[101] Although the yield of this reaction is poor (40% not allowing for a little recovered starting material) it did allow the preparation of the required allene (23) without any further difficulties.



(37) (36)



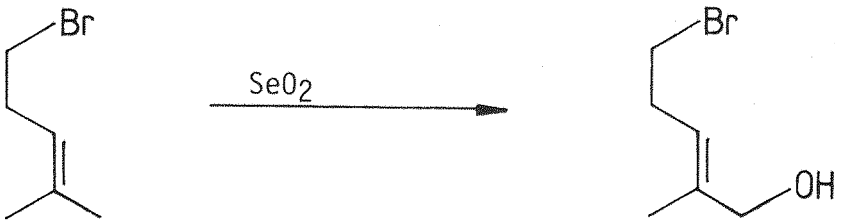
(38) (24)



(28) (23)

Scheme 51

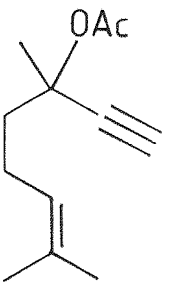
The oxidation of (32) and (33) using the same conditions was tried, but again products inseparable from selenium were obtained. Attempts to prepare (39), a possible precursor of (23), from (40) were also unsuccessful and gave a mixture of ethoxy compounds which were not fully characterised.



(40) (39)

Scheme 52

Now that sufficient allene (23) for the purposes of our study could be prepared, work on the synthesis was discontinued. However, precedents for the allylic oxidation of compounds containing alcohol or ketone functionality are uncommon[88] and, should the allene (23) prove synthetically useful, the oxidation of acetate (41) might well be worth studying. In addition, the use of methyl rather than benzyl ethers would reduce the difficulty of separating the ether (24) from excess halide particularly in larger scale reactions.



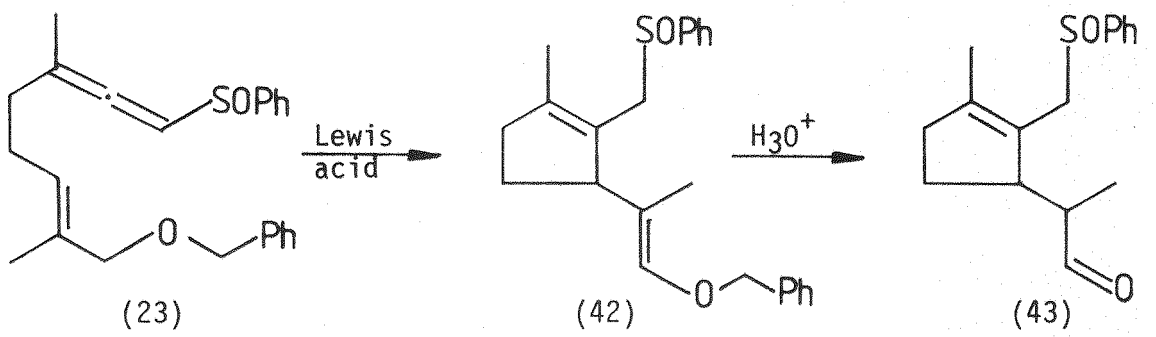
(41)

The oxidative conditions tried are summarised in Table 1.

3.2.3 Ene Reactions of 8-Benzyloxy-3,7-dimethyl-1-phenylsulphinylocta-1,2,6-triene (23)

Treatment of allene (23) with a variety of Lewis acids in either dichloromethane or aromatic solvents gave chiefly polymeric tars, although hydrolysis of the product from the tin (IV) chloride reaction with dilute hydrochloric acid in tetrahydrofuran did give some of the desired aldehyde which was isolated as its 2,4-dinitrophenylhydrazone.

These results suggested that the ene reaction is occurring but that either the vinyl ether (42) or aldehyde (43), both of which are acid sensitive, is polymerising. Formation of the aldehyde would require the presence of some water. Unfortunately, weaker Lewis acids such as zinc bromide, which were not expected to catalyse the polymerisation, gave no reaction.



Scheme 53

The best results were obtained when acetonitrile was used as solvent with either tin (IV) chloride or boron trifluoride etherate as catalyst and the crude product hydrolysed directly with oxalic acid in aqueous tetrahydrofuran to give the desired aldehyde (43) in a modest 29% yield.

The studies described in this Section are summarised in Table 2.

TABLE 1

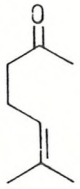
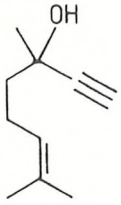
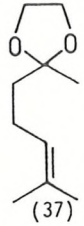
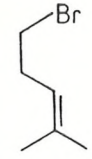
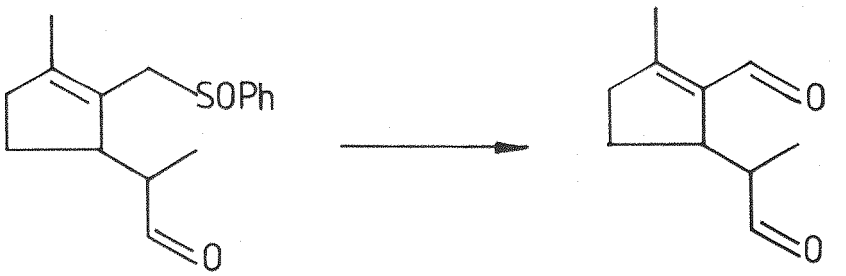
Substrate	Mole Equivalents of Reactants and Conditions						Remarks
	SeO_2	Pyridine	$^tBuO_2H$	Solvent	Temp.	Time	
 (32)	0.5			EtOH	Reflux	4h	Products were not separable from selenium
	0.5	0.55		EtOH	Reflux	3d	
	0.02		2.0	CH_2Cl_2	rt	4d	No reaction
	0.02		3.0	CH_2Cl_2	Reflux	2d	^{t}Butyl ethers?
 (33)	0.5			EtOH	Reflux	4h	No characterised products
	0.02		3.0	CH_2Cl_2	Reflux	2d	^{t}Butyl ethers?
	0.5	0.55		EtOH	Reflux	6h	Products inseparable from Selenium
	0.1		2.0	CH_2Cl_2	rt	4d	No reaction
 (37)	1.0	1.2		EtOH	Reflux	5h	Desired Product
 (40)	0.5			EtOH	Reflux	3h	Mixture of ethoxide containing materials

TABLE 2

Lewis Acid	Solvent	Temperature °C	Remarks
$SnCl_4$	CH_2Cl_2	rt	Some product isolated
$BF_3.Et_2O$	CH_2Cl_2	rt	Polymer
$ZnBr_2$	PhMe	rt	sm recovered
$EtAlCl_2$	PhMe	rt	Polymer
$SnCl_4$	MeCN	-30^o	sm recovered
$SnCl_4$	MeCN	0^o-rt	Modest yield of the desired product
$BF_3.Et_2O$	MeCN	0^o-rt	

3.2.4 Attempted Synthesis of Chrysomelidial (17)

Chrysomelidial (17) has been isolated from the larvae of several species of Chrysomelid beetle,[78,79] and has been shown to be a component of the defence secretion of the larvae of the Chrysomelid beetle *Plagiodera versicolora*.[78]



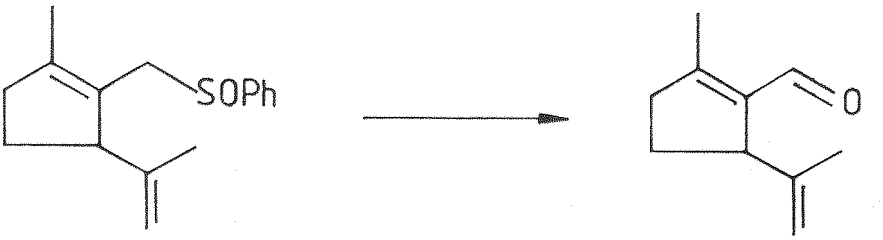
(43) (17)

Scheme 54

This natural product could formally be derived by the oxidation of the aldehyde sulphoxide (43) and would thus provide an attractive demonstration of the value of such an intermediate.

The most widely used method of effecting the sulphoxide to carbonyl transformation is the Pummerer rearrangement which is generally performed with acid anhydrides, although a wide variety of acidic reagents may be used.[87] In his discussion of the reaction, Durst[102] states that the reaction is particularly favourable for allylic-, benzylic-, β-keto- and β-alkoxycarbonylsulphoxides and indeed the majority of Pummerer rearrangements reported are of one of the latter three cases. However, although a complete search of the literature is difficult, exceedingly few examples of the rearrangement of allylic sulphoxides could be found and it is difficult to see where Durst found sufficient experimental evidence to justify the generalisation.

Because the preparation of (43) is somewhat tedious, the sulphoxide (2), which can be prepared in only two steps, was used as a model compound for the optimisation of the reaction conditions.



(2) (44)

Scheme 55

Treatment of (2) with dilute inorganic acids failed to induce any reaction and the starting material was recovered.[103,104] Strong solutions of hydrochloric acid or iodine in methanol[105] do induce the Pummerer rearrangement but addition of the reagents to the double bonds also occurred giving a mixture of products.

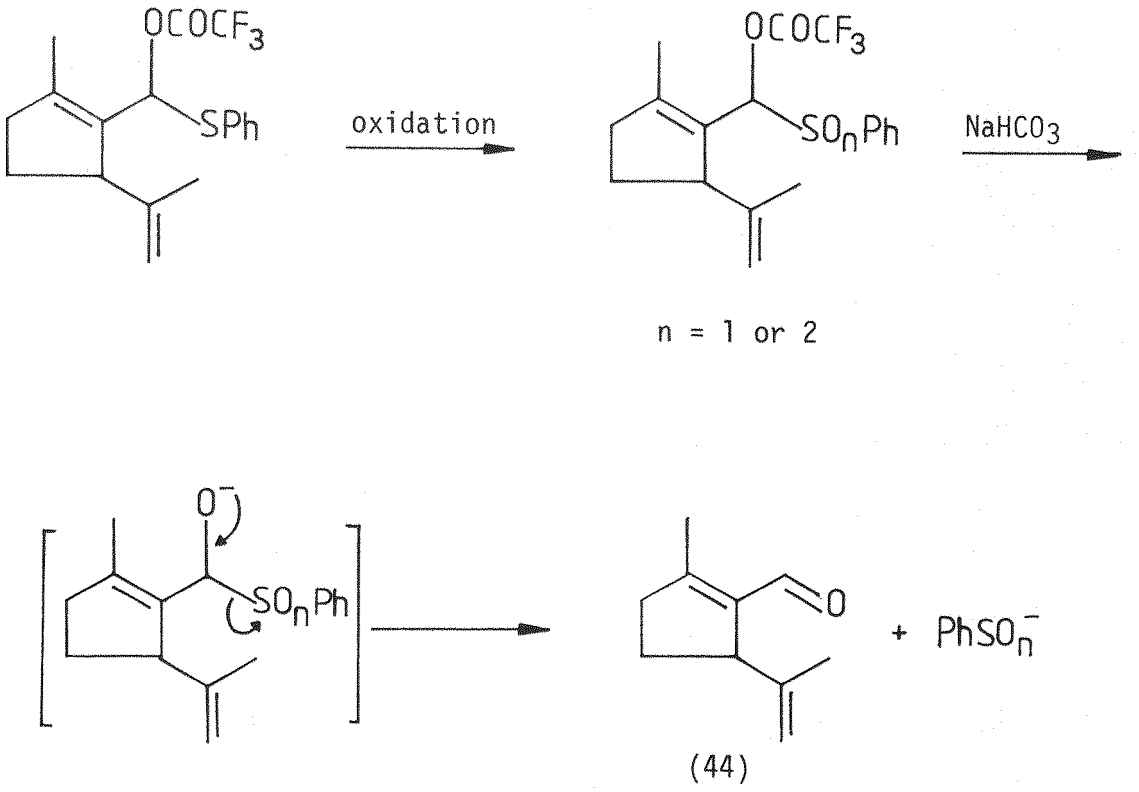
Acetic anhydride in the presence of sodium acetate or toluene-4-sulphonic acid or the mixed acetic trifluoroacetic anhydride.[49] gave a very complex mixture of products which could not be separated. At 0°C trifluoroacetic anhydride appeared to give a mixture of the sulphides (45) and (46) from the nmr spectrum of the crude product which showed multiplets at δ5.70 and δ6.00.

(45) (46)

Unfortunately, this material was unstable at room temperature and could not be properly characterised, nor were attempts to hydrolyse it to the required aldehyde successful. In one experiment, in which the hydrolysis was performed with silver nitrate in wet acetonitrile, a partial separation of the products suggested that they were derived from oxidation or Michael readdition to the required aldehyde and some of its double bond isomers.

Attempts were then made to effect the hydrolysis by sequential oxidation and treatment with mild base. Both sulphinate and sulphenate ions are less nucleophilic than thiolates and would not be expected to

re-add to the unsaturated aldehyde. In addition, none of the steps involves a potentially oxidising metal-ion species. Thus it was hoped that the problems experienced with the hydrolysis of the sulphide might be avoided.



(44)

Scheme 56

Experiments with m-chloroperbenzoic acid, peracetic acid, or hydrogen peroxide as oxidant in a variety of solvents were tried, but complex mixtures were obtained in all cases.

When one equivalent of oxidant was used this may be due to the ease with which sulphenic acids disproportionate. The equilibria involved are complex and the eventual products seem to depend on the pH of the medium. In basic solution the principal products are thiolates and sulphinates, whereas in neutral or acid media significant quantities of disulphide are formed. In both cases radical intermediates are likely to be involved and either these or the thiolate produced could react with the aldehyde (44).[106]

$$ArSOH + OH^- \rightleftharpoons ArSO^- + H_2O$$

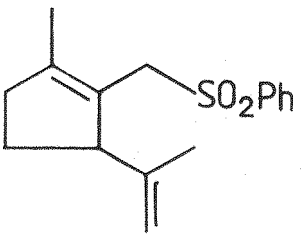
$$2ArSO^- + H_2O \rightleftharpoons ArSO{\cdot}SAr + 2OH^-$$

$$ArSO{\cdot}SAr + 2OH^- \longrightarrow ArSO_2^- + ArS^- + H_2O$$

$$ArS^- + ArSO{\cdot}SAr \rightleftharpoons ArSO^- + ArSSAr$$

Scheme 57

Why the experiments using two equivalents of oxidant also gave complex mixtures is more obscure but the observation of an epoxide among the products suggests that the selectivity of the oxidants used might not be sufficient, despite the fact that sulphone (47) may be prepared quite easily by oxidation of (2) with m-chloroperbenzoic acid.



(47)

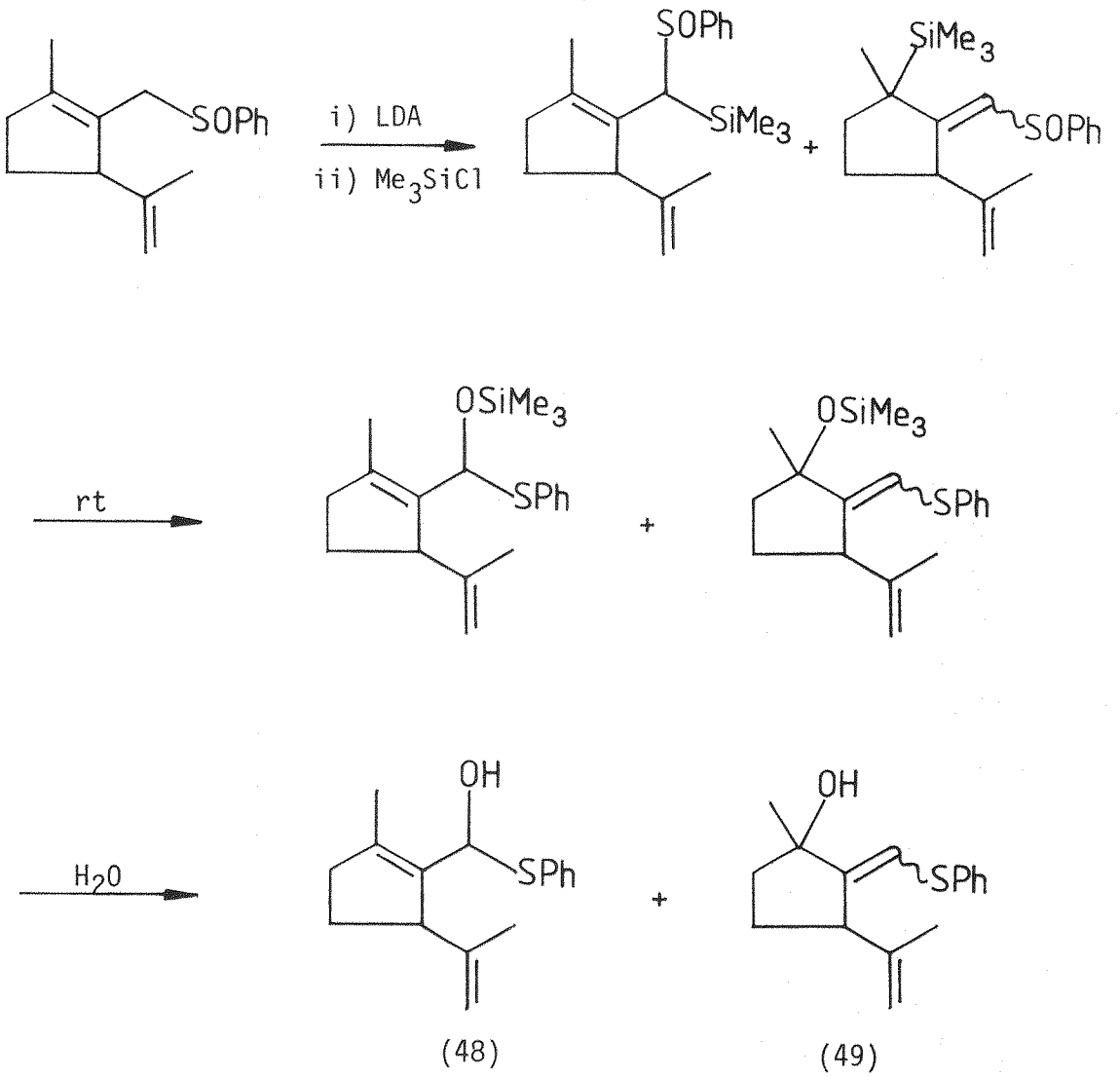
In all nearly fifty variants on the Pummerer rearrangement of (2) and hydrolysis of the product were tried and a small selection is summarised in Table 3.

There are several other possible methods for preparing carbonyl compounds from sulphoxides. One possibility is the sila-Pummerer rearrangement.[107] In this, the sulphoxide anion was quenched with chlorotrimethylsilane to give a trimethylsilylsulphoxide which, after warming and aqueous work-up, gave a mixture of the two hydroxy-sulphides (48) and (49) which could be observed by nmr spectroscopy. However, these compounds, like the trifluoroacetates prepared previously, are unstable and give a similar mixture of products on hydrolysis with silver nitrate.

TABLE 3

Selection of Conditions for Pummerer Rearrangement

Reagents	Solvent	Temp.	Time	Remarks
i) Ac_2O/NaOAc	-	reflux	3h	Product is a mixture of sulphides which were unchanged by treatment with Cu^{2+}.
ii) $Cu(OAc)_2 \cdot H_2O$	$CHCl_3$	rt	3h	
TsOH	THF/H_2O	rt	48h	sm recovered
TFAA/Ac_2O/lutidine	-	rt	0.5h	One major product which decomposes rapidly at rt to complex mixture
i) TFAA	Et_2O	-5^oC	5m	Complex mixture of PhSAg readdition products and oxidised materials
ii) $AgNO_3$	$MeCN/H_2O$	rt	2d	
i) TFAA	Et_2O	-5^oC	5m	Black polymeric tars
ii) $HgCl_2$	$MeCN/H_2O$	rt	2.5h	
i) TFAA	Et_2O	-5^oC	5m	Products is mixture including sulphone (47) and desired aldehyde (<20%)
ii) MCPBA (1 equiv.)	Et_2O	-5 to rt	2h	
iii) $NaHCO_3$	MeOH	rt	2h	
i) TFAA	Et_2O	-40^o	30m	Mixture which includes aldehyde, epoxide and various sulphides
ii) MCPBA (2 equiv.)	Et_2O	-80 to -10^o	1h	
iii) $NaHCO_3$	MeOH	rt	2h	
i) TFAA	Et_2O	-20	1h	Complex mixture of products
ii) $MeCO_3H$	Et_2O	-80	0.5h	
iii) $NaHCO_3$	MeOH	rt	2h	

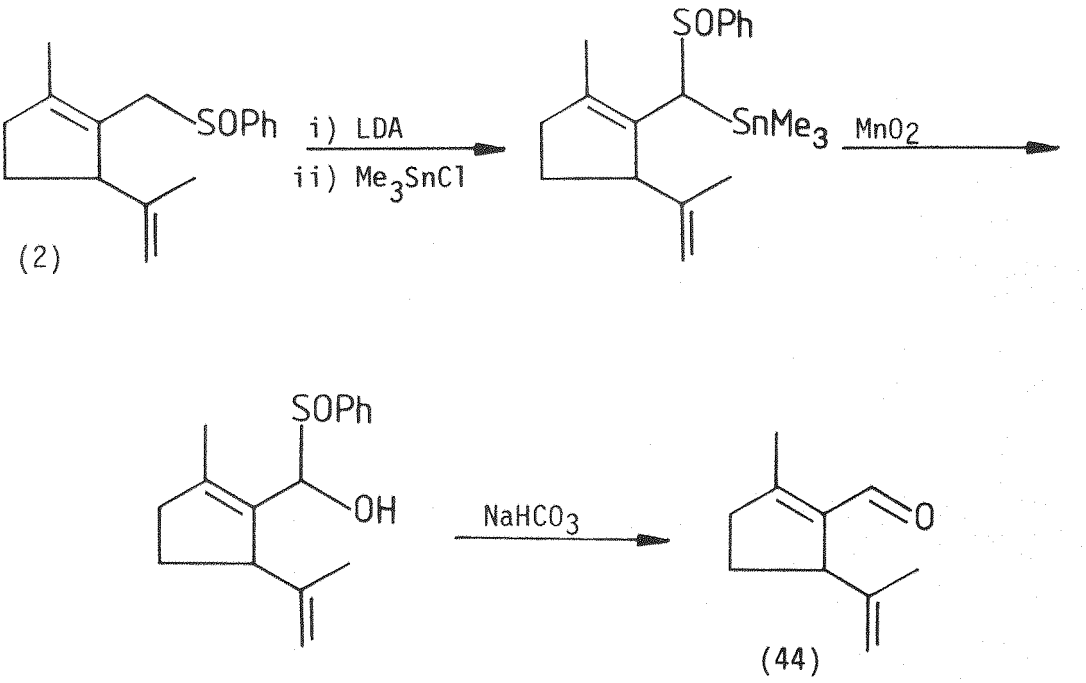


(48) (49)

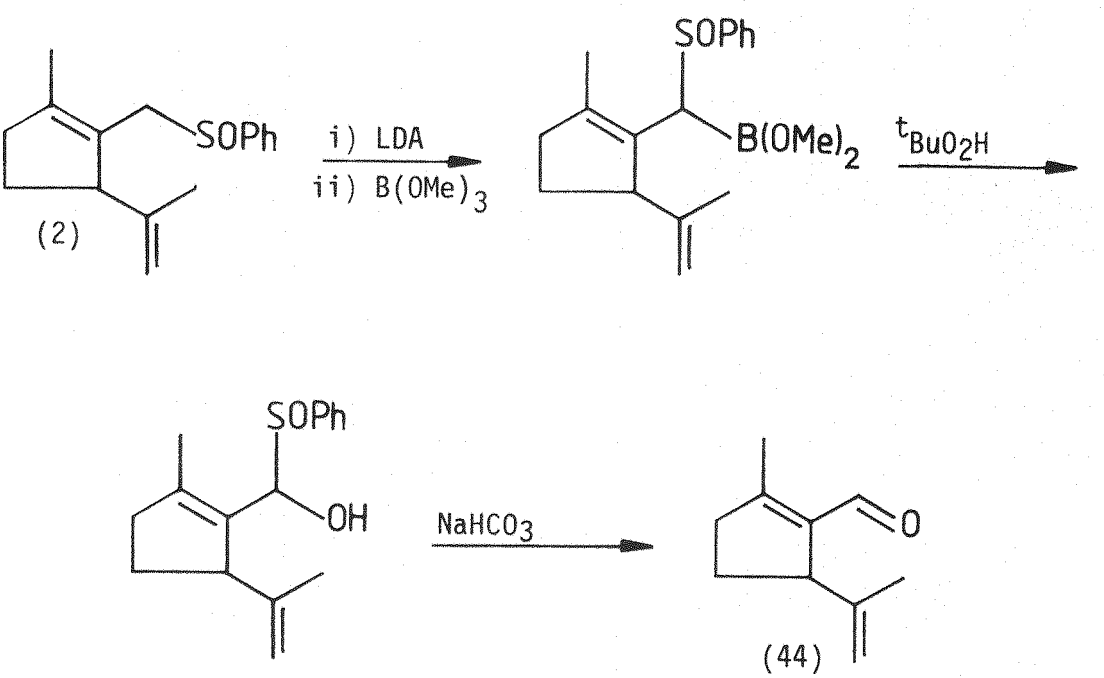
Scheme 58

Vedejs' reagent[108] has been used to hydroxylate a wide variety of anions[109] including those derived from sulphones.[110] However, no hydroxylated material was derived from the anions of either (2) or (47) and a mixture of double bond isomers was recovered.

The reactions of the anion of (2) with trimethyl borate[51] or chlorotrimethyltin[52] have been less exhaustively studied but the product mixtures chiefly contain starting material alongwith a variety of uncharacterised minor components.



Scheme 59



Scheme 60

A selection of the anion reactions tried are summarised in Table 4.

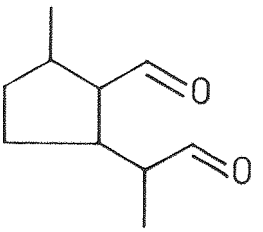
At this point shortage of time forced the discontinuance of practical work, although it is difficult to see what conditions might

TABLE 4

Selection of Anion Reactions of (2)

Reagents	Solvent	Temp.	Time	Remarks
i) LDA	THF/HMPA	-80	1h	
ii) $B(OMe)_3$	"	-80	1h	sm recovered
iii) $NEt_3/{}^tBuO_2H$	"	rt	3h	
i) LDA	THF	-70	15m	nmr after quenching anion
ii) Me_3SiCl	THF	-70	30m	similar to TFAA product but
iii) $AgNO_3$	$MeCN/H_2O$	rt	12h	treatment Ag^+ gives mixture of sulphide products
i) LDA	THF	-78	30m	Chiefly sm along with traces
ii) Me_3SnCl	THF	-78	20m	of many other products
i) LDA	THF	-70	15m	Mixture of products close
ii) MOC_5·HMPA·Pyr.	THF	-80	1h	in Rf to sm.
i) LDA	THF	-80	15m	Mixture of products close
ii) MOO_5·HMPA·Pyr.	CH_2Cl_2	-80	1h	in Rf to sm.

give the required unsaturated aldehyde. If the conversion cannot be achieved it has quite severe consequences for the usefulness of the products obtained in the ene reactions of allene sulphoxides, although alkylation and elimination reactions would allow the elaboration of quite a variety of compounds.[36] However, it would appear that some of the problems found with these reactions are due to the presence of a double bond β,γ to sulphoxide and it is possible that if the substrate could be first hydrogenated, Pummerer[87] or sila-Pummerer[107] rearrangement might occur quite easily; the product in this case would be the natural product Iridodial (50).[77]

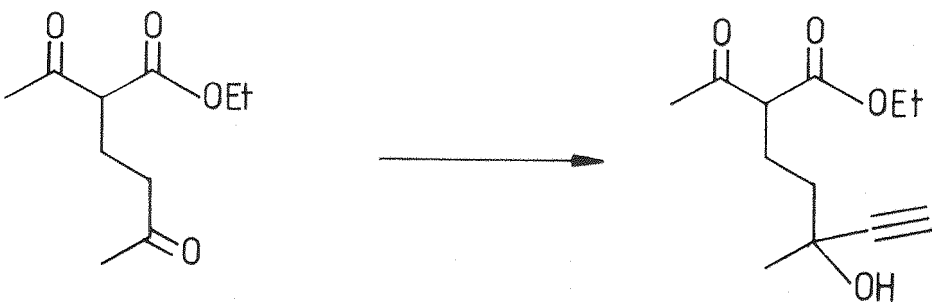


(50)

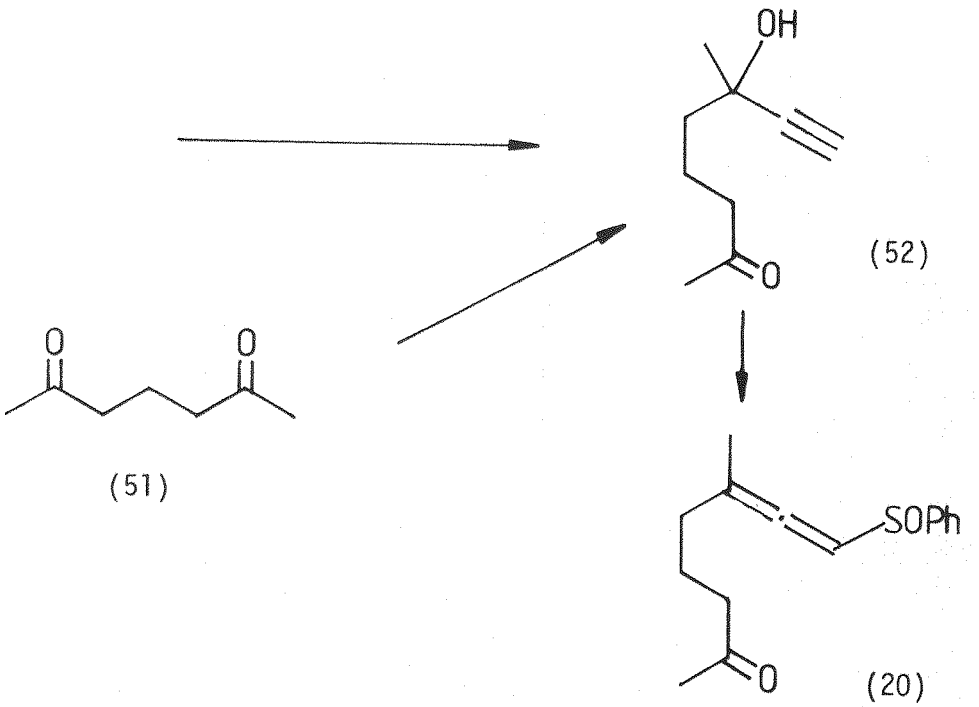
3.3 Synthesis and Reactions of 6-Methyl-8-phenylsulphinylocta-6,7-dien-2-one (20)

3.3.1 Synthetic Routes Involving Selective Protection

Both heptane-2,6-dione (51) and ethyl 2-acetyl-5-oxohexanoate (53) are easily accessible from readily available starting materials,[111,112] and would allow short syntheses of allene (20) if acetylene could be added selectively to one carbonyl group.



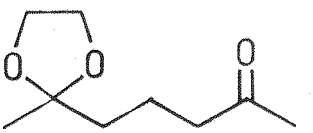
(53) (54)



Scheme 61

Unfortunately, ethynylmagnesium bromide was found not to add to heptane-2,6-dione (51) and starting material was recovered. With sodium acetylide in liquid ammonia a modest yield (38%) of 3-methylcyclohex-2-enone was obtained as the only recovered material. This suggests that enolization of the diketone is occurring rather than addition in both experiments, although only the more reactive sodium enolate cyclizes.

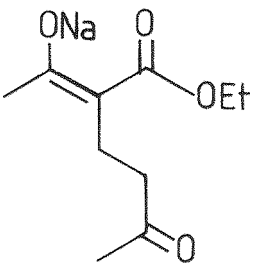
An attempt to prepare the mono-ethylene acetal (55) by refluxing the ketone (51) with ethane-1,2-diol and a few crystals of toluene-4-sulphonic acid in benzene under Dean and Stark conditions was unsuccessful and gave a mixture of starting diketone (51), 3-methylcyclohex-2-enone and several other unidentified products.



(55)

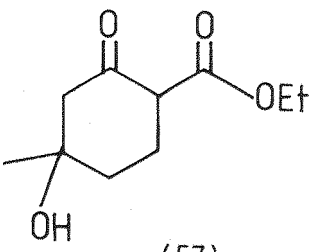
The three carbonyl groups in ethyl 2-acetyl-5-oxohexanoate (53) are quite different and selective addition to the terminal carbonyl should be possible.

To prevent reaction of the acetoacetate moiety, (53) was first treated with one equivalent of sodium hydride to form the anion (56), which was then treated with ethynylmagnesium bromide; however, only starting material was recovered.

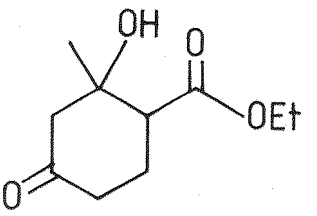


(56)

Treatment of the same anion (56) with sodium acetylide in liquid ammonia gave a 1:1 mixture of the two condensation products (57) and (58) which were not separated.

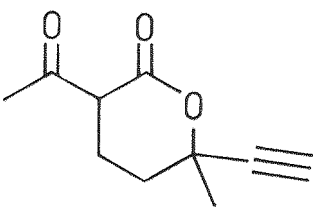


(57)



(58)

Treatment of the anion (56) in tetrahydrofuran with a slurry of sodium acetylide in hexamethylphosphoramide (used because of the very high insolubility of sodium acetylide in most organic solvents) gave a very small yield of acetylene (59) (10%).



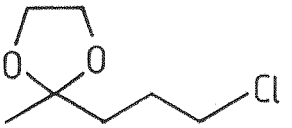
(59)

Although this acetylenic ester would give the required keto-alcohol (52) on hydrolysis the yield was far too low to make such a route viable, and no further studies of the reaction were made.

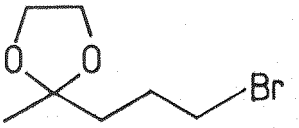
An attempt to mono-acetalise one carbonyl group of (53), using conventional Dean and Stark conditions, was totally unsuccessful and gave a complex mixture of acetals and transesterification products.

3.3.2 Synthetic Routes Involving Grignard Reagents

5-Chloro and 5-bromopentan-2-one are both readily available and may be acetalised in good yield to give (60) and (61) respectively.[113]

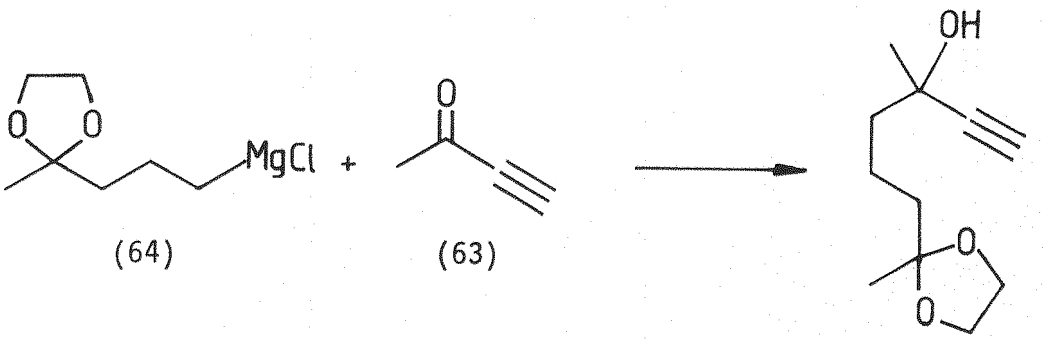


(60)



(61)

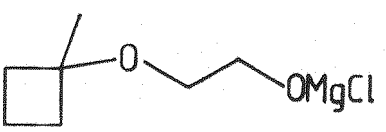
The Grignard reagent derived from these halides was expected to add readily to but-3-yn-2-one (63) thus providing a short synthesis of the required acetylenic alcohol (65).



(64) (63) (65)

Scheme 62

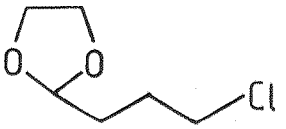
There have been several conflicting reports of the preparation of this Grignard reagent. In the first, Feugeas[114] claimed that the treatment of the chloride (60) with magnesium in tetrahydrofuran at less than 60°C gave high yields of (64) whereas in ether the cyclobutane ether (66) was the chief product.



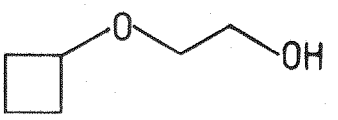
(66)

Later, authors have been unable to duplicate these results and have claimed that prolonged reflux (12h) of the halide with magnesium were required to obtain reasonable yields of the Grignard reagent.[115]

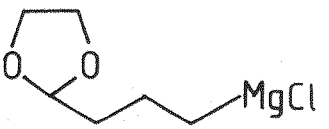
Forbers *et al.*,[116] working on the related acetal (67), although unable to duplicate the work of Feugeas,[114] found that reflux conditions led to a cyclobutane like that reported for the ether reaction (68) and polymeric material, but none of the required Grignard reagent. However, by adding the chloroacetal with 1,2-dibromoethane in a small quantity of tetrahydrofuran to excess magnesium, and initiating the reaction by gentle warming, good yields of the Grignard reagent (69) were obtained providing the reaction temperature did not rise above 30°C, when ring opening reactions were found to occur. Stetter and Mertens[117] found that this method also gave good yields of Grignard reagent (64).



(67)



(68)

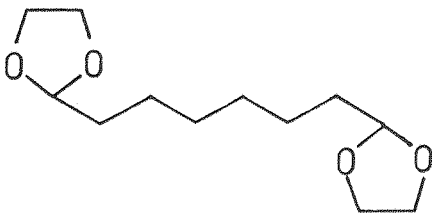


(69)

In our hands the best yields of the Grignard reagent (64) were obtained by using the method of Forbes[116] with the chloride (60) at high concentration. Neither chloride (60) nor bromide (61) gave any observable reaction with magnesium under the conditions of Feugeas,[114] although some Grignard reagent was obtained when the reaction was induced by the addition of iodomethane/magnesium. No reaction was observed when small quantities of iodine or 1,2-dibromoethane were added or if the highly active magnesium powder prepared by the reduction of magnesium chloride with potassium[118] was used.

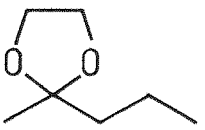
A study of Grignard reagent (69) published after this work was completed[119] also reports difficulty in preparing the reagent and eventually conditions similar to those described here were adopted. However, in contrast to the present work on (60), active magnesium prepared from potassium and magnesium chloride[118] was effective.

In addition, the Wurtz coupled product (70) was found to be a major impurity (up to 30%) when the reagent was prepared by the usual methods.

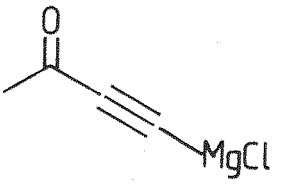


(70)

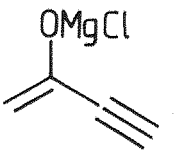
Attempts to prepare the acetylenic alcohol (65) by reaction of this Grignard reagent with but-3-yn-2-one (63) gave a complex mixture of products which appeared to contain small amounts of the desired product, 2-methyl-2-propyl-1,3-dioxolan (71), and other unidentified material. This suggested that either the acetylenic Grignard reagent (72) or magnesium enolate (73) are forming in preference to the desired addition product.



(71)

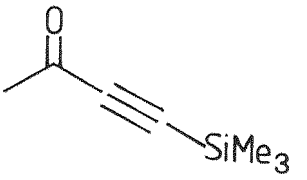


(72)



(73)

The first of these side reactions could be avoided by using a suitable protected acetylene such as 4-trimethylsilylbut-3-yn-2-one (74).

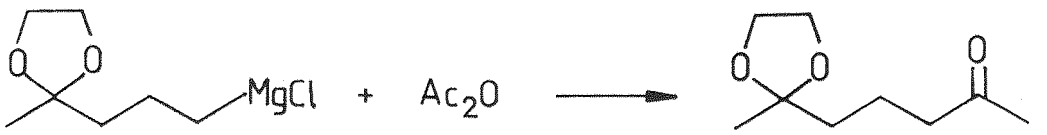


(74)

However, treatment of Grignard reagent (64) with ketone (74) also gave a mixture of products, including, in one reaction, what appears on the basis of its nmr spectrum, to be a silicon polymer. The formation of the silicon polymer is very puzzling, but probably involves the nucleophilic attack of the Grignard reagent at silicon as a first step. If this is so, the trimethylsilyl group does not protect the acetylene as had been hoped.

Because of the discouraging results obtained in these trial reactions and the rather poor yields in the preparation of butynones (63) and (74) work on this reaction was discontinued.

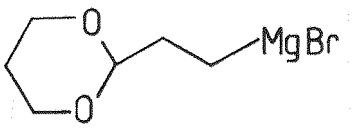
Feugeas,[114] in his original paper on acetal Grignard reagents, describes the preparation of ketone (75) in fair yield by reaction of Grignard reagent (64) with acetic anhydride at -65°C.



(64) (75)

Scheme 63

Although the reaction of Grignard reagents with acid derivatives is normally regarded as proceeding to the tertiary alcohol there are many literature precedents for the preparation of ketones from such reagents, although there is some disagreement between authors as to the generality of the reaction. Sato *et al.*[120] and Newman *et al.*[121] claim that the inverse addition of Grignard reagents to acid chlorides or anhydrides respectively provide general syntheses of ketones. Stowell,[122] working with the Grignard reagent (76) suggests that the reaction with acid chlorides is a special property of such Grignard reagents and incidentally also observes that the Grignard reagent derived from the six-membered cyclic acetal shows greater thermal stability than that derived from the five.



(76)

The preparation of a keto-acetal from Grignard reagent (69) and acetic anhydride has also been reported.[123]

The ketone (75) was made by the reaction of Grignard reagent (64) with either acetic anhydride or acetyl chloride, with the best yields being obtained when freshly purified acetic anhydride was used along with a basic work-up to prevent deprotection of the acetal, which

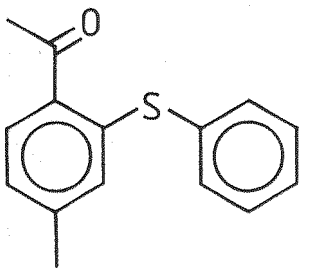
occurs readily even on washing the organic phase with ammonium chloride solution.

The synthesis was then completed by addition of acetylene,[124] Horner rearrangement[34] and hydrolysis of the acetal to give the required allene (20) in 43% yield from the ketone (75).

Because the preparation of this Grignard reagent is tricky and requires practice, it is possible that some of the early results with butynone are misleading and would merit repetition.

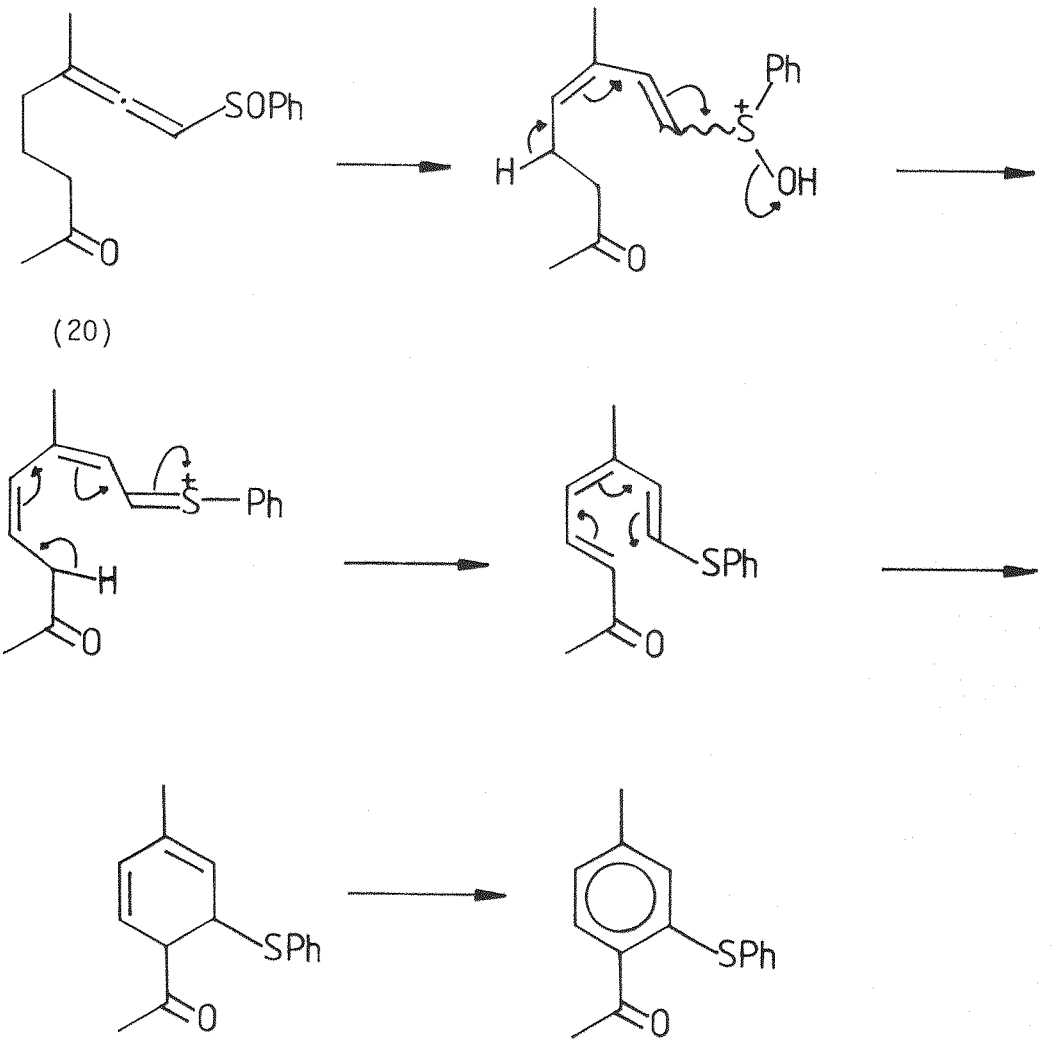
3.3.3. Studies on 6-methyl-8-phenylsulphinylocta-6,7-dien-2-one (20)

Because few ene reactions with enols as enophile have been reported much below 300°C,[30] the effect of heating the allene at 275°C was tried first. After ½h no starting material remained and two new spots were observable by tlc as well as much background material. The more rapidly moving of these was shown to be diphenyl disulphide. The exact structure of the slower moving product, which is present in far smaller quantities, is uncertain. However, the spectral data are compatible with an acetophenone structure such as (77), although other isomers cannot be ruled out.



(77)

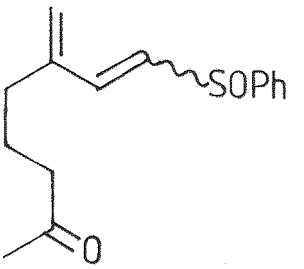
The mechanism by which such a compound might be formed is obscure but may involve rearrangement and acid catalysed dehydration to form a triene which undergoes a Cope rearrangement[125] which in the presence of diphenyl disulphide, which is also found in the reaction mixture, would rapidly aromatise.[126]



Scheme 64

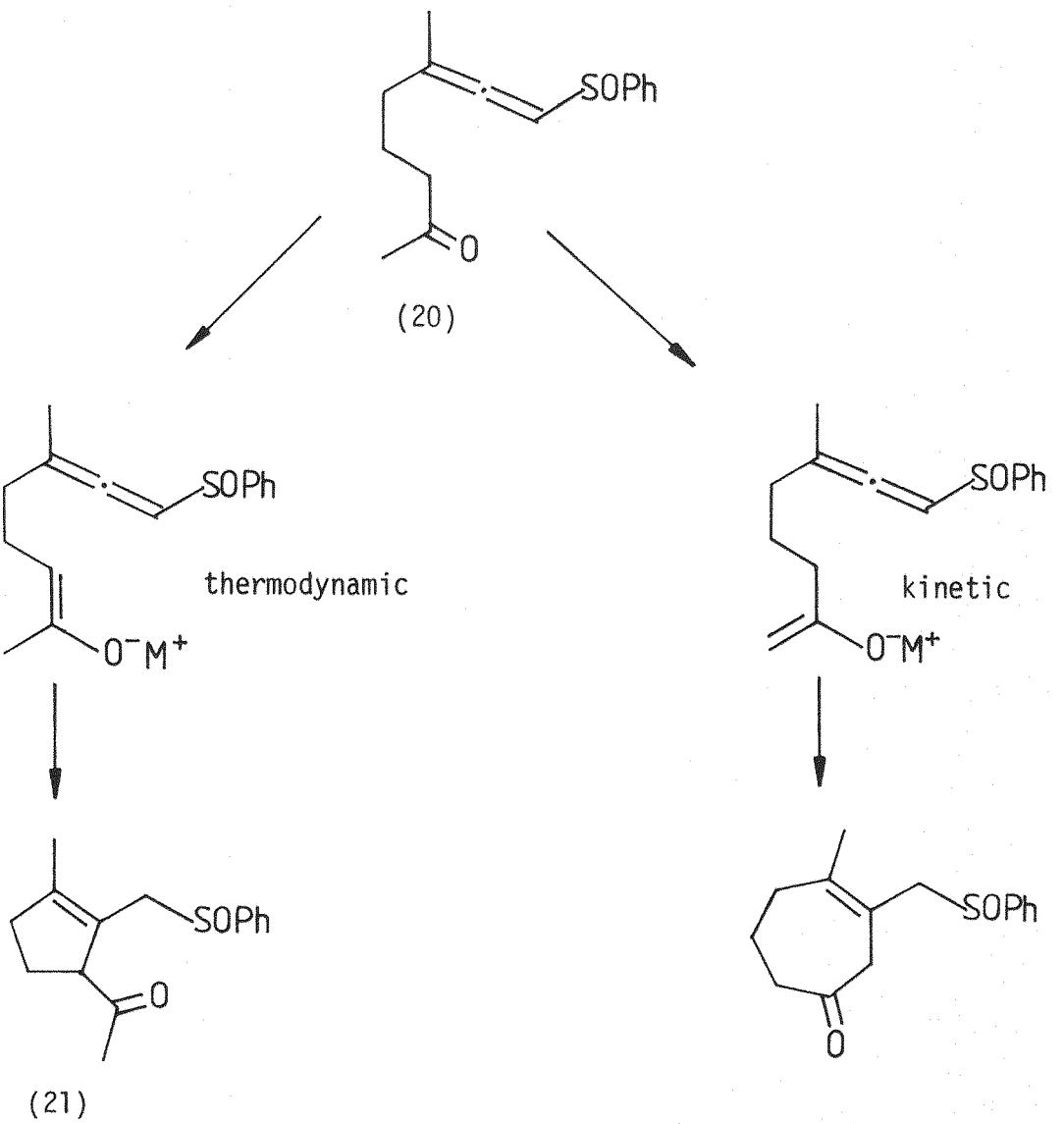
Only diphenyl disulphide could be identified from the complex mixture of products obtained by heating the keto-allene (20) at 185°C for 15 m.

Because both the sulphoxide and carbonyl groups would complex a Lewis acid it is not possible to catalyse enol ene reactions with Lewis acids. However, enolization of the ketone is believed to be the rate determining step and would be catalysed by Brönsted acids.[30] The effect of warming the ketoallene (20) with an acidic resin (Amberlyst-15) was tried, but gave only the 1,3-dienes (78) after several hours reflux in toluene. Only starting material was recovered from experiments performed at lower temperatures in tetrahydrofuran. The fact that some allene sulphoxides rearrange to 1,3-diene in refluxing toluene[41] suggests that this rearrangement does not require the presence of acid.



(78)

Although it would not be an ene reaction, it should also be possible to obtain the desired product by an intramolecular Michael addition of the thermodynamic enolate, although cyclisation of the kinetic enolate to give a cycloheptenone could compete.



Scheme 65

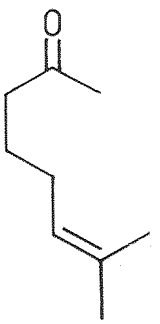
Treatment of the keto-allene (20) with lithium di*iso*propylamide at -78°C and quenching either at -78°C or after warming to room temperature gave complex mixtures of products none of which could be visualised on tlc with 2,4-dinitrophenylhydrazine. No reaction was observed when (20) was treated with tetrabutylammonium fluoride supported on silica.[127]

If sufficient effort was made it seemed likely that suitable conditions for the base catalysed cyclisation could be found. However, because of the total failure of the ene-type conditions and the shortage of time, work in this area was discontinued.

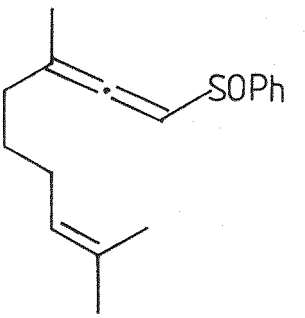
3.4 Synthesis and Reactions of 3,8-dimethyl-1-phenylsulphinylnona-1,2,7-triene (16)

3.4.1 Syntheses Involving Claisen Rearrangement

Although 7-methyloct-6-en-2-one(79), an obvious precursor to allene (16), is known[128] its synthesis is fairly lengthy (five steps) and a shorter approach was sought.

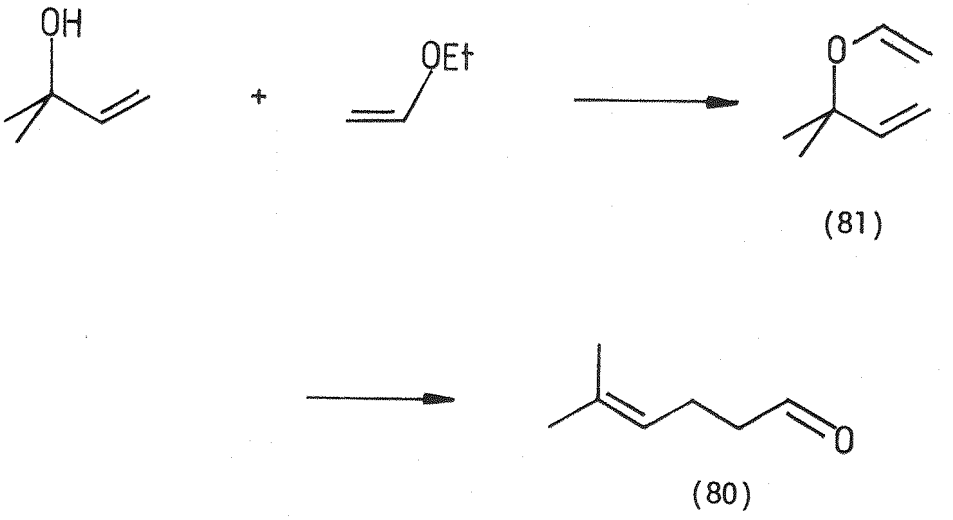


(79)



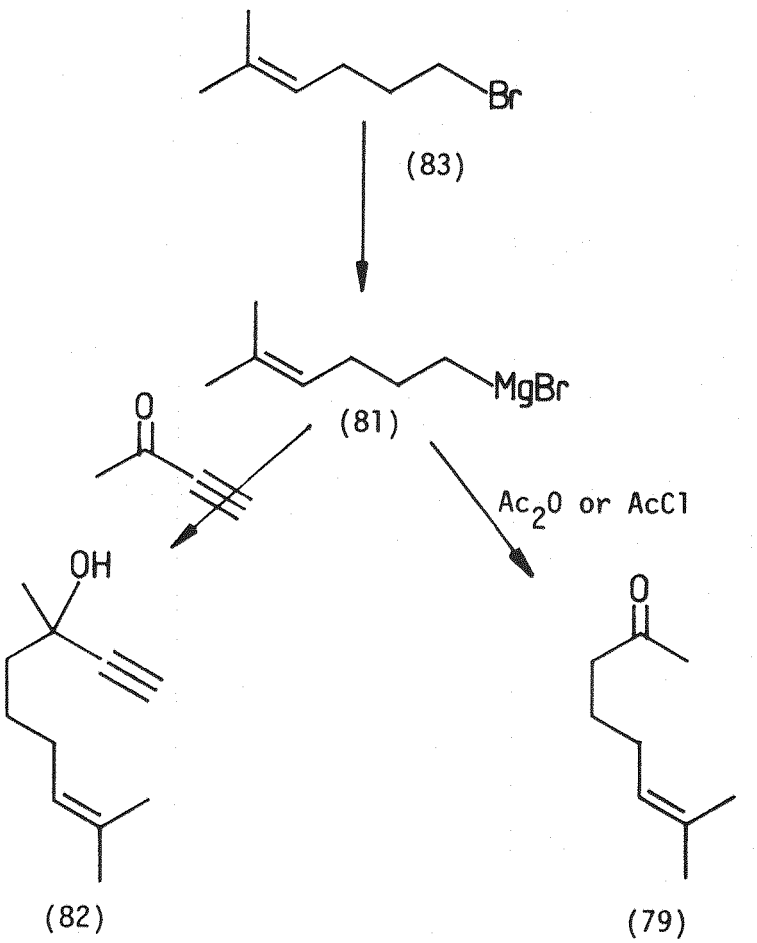
(16)

The aldehyde (80) has been prepared by Claisen rearrangement of allyl vinyl ether (81) at 150°C which is formed *in situ* from 2-methylbut-3-en-2-ol and ethoxyethene with acid catalysts.[129]



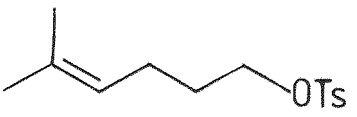
Scheme 66

This after reduction and bromination would allow the preparation of the Grignard reagent (81) which could be treated with butynone, acetic anhydride or acetyl chloride to give the acetylenic alcohol (82) or ketone (79).

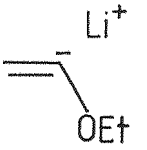


Scheme 67

Alternatively, it may be possible to displace either the halide (83) or tosylate (84) with 1-lithio-1-ethoxyethene (85)[130] which, after hydrolysis, would also give the ketone (79).



(84)

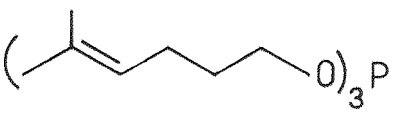


(85)

Although the preparation of aldehyde (80) could be performed quite satisfactorily on a small scale preparation of larger quantities proved difficult. The published procedure required 2.1 mole equivalents of ethoxyethene which, because of its low density, requires a large Carius tube even for reactions of a quite modest scale. The equipment available did not permit the use of Carius tubes containing more than about 20ml of reactants nor could access to suitable autoclave equipment be obtained.

Several attempts were made to preform the vinyl ether using mercuric acetate catalysis.[90] Unfortunately, only mixtures of products heavily contaminated with mercury were obtained. The difficulties experienced in preparing reasonable quantities of aldehyde (80) eventually led to the abandonment of this route in favour of the longer but more certain preparation of methyloctenone (79).

The small quantities of aldehyde available by the phosphoric acid catalysed rearrangement, were reduced with sodium borohydride and the tosylate (84) prepared by treatment with toluene-4-sulphonyl chloride in pyridine. An attempt to displace the toluenesulphonate with anion (85) prepared from ethoxyethene and t-butyllithium[130] in tetrahydrofuran, gave back unchanged starting material. An attempt was also made to prepare the bromide (83) from the alcohol with phosphorus tribromide/pyridine, but only phosphite (86) was isolated.

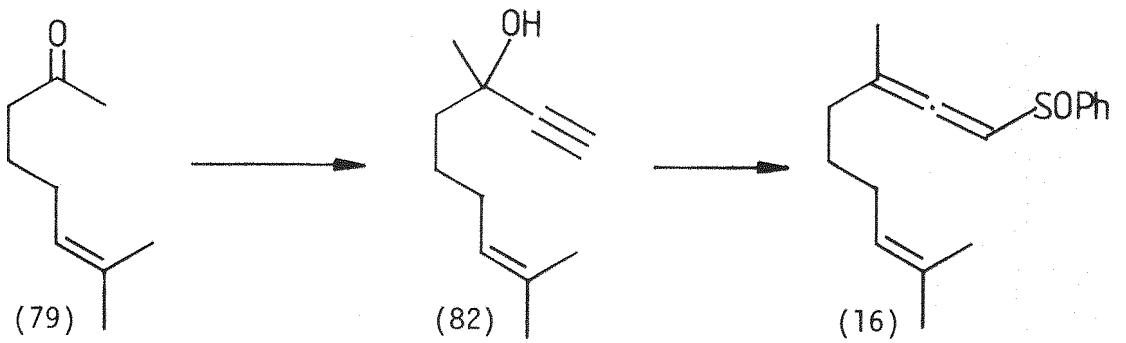


(86)

While doubtless suitable conditions for the preparation of this bromide could be found, the difficulties encountered in preparing useful quantities of the aldehyde discouraged further work in the area, particularly as a more certain, if longer, route was available.

3.4.2. Synthesis from 7-Methyloct-6-en-2-one

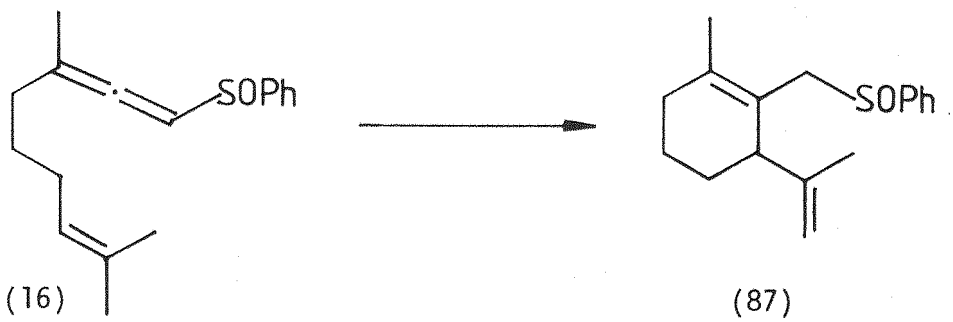
7-Methyloct-6-en-2-one (79) prepared by the method of Favre,[128] was ethynylated[124] and treated with phenylsulphenyl chloride[34] to give the required allene (16) in 40% unoptimised yield.



Scheme 68

3.4.3 Ene Reactions

A variety of Lewis acid-solvent combinations was tried to effect the conversion (16) to (87).

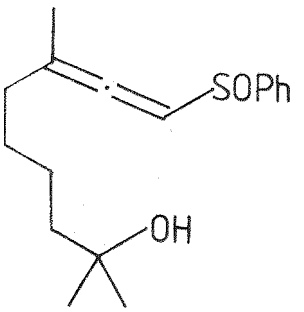


Scheme 69

With boron trifluoride etherate in dichloromethane or tin (IV) chloride in benzene no reaction was observed and starting material was recovered. In tetrachloromethane catalytic quantities of tin (IV) chloride again gave no reaction although when excess Lewis acid was added the

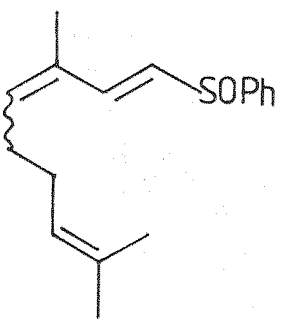
allene decomposed to give intractable polymeric material.

One experiment using tin (IV) chloride in dichloromethane lead to loss of starting material. However, the presence of hydroxyl and allene bands in the infrared spectrum as well as the lack of $=CH_2$ or CH_2-SO in the nmr spectrum suggest that the expected product (87) is not formed, nor does the data support (88) as the correct structure.



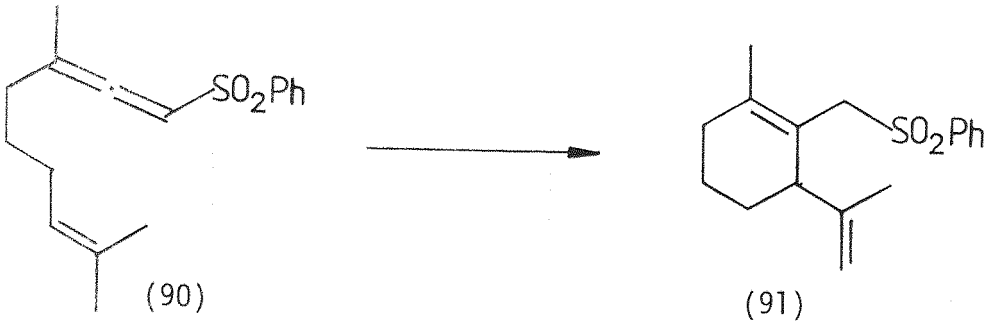
(88)

Heating the allene (16) either neat or in acetonitrile or benzene at 140°C gave a mixture of the 1,3-diene (89), diphenyl disulphide and the acetylene (82) as well as a number of minor decomposition products.



(89)

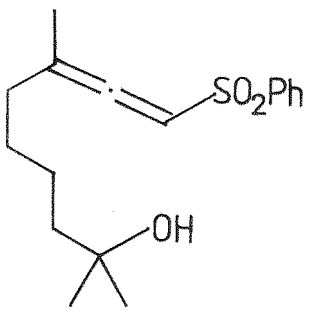
It would thus appear that the allene sulphoxide is insufficiently electron poor to undergo an intramolecular ene reaction when the less favoured six-membered ring would be formed. However, it was felt that the allene sulphone (90) might well undergo the desired cyclisation to (91) more readily, and it was also expected to be less prone to rearrangement to the 1,3-diene.[41]



(90) (91)

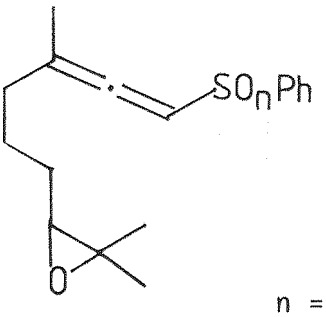
Scheme 70

Several attempts were made to prepare the allene sulphone (90) from the sulphoxide (16). Treatment of (16) with oxone ($KHSO_4 + K_2SO_4 + KHSO_5$) in aqueous methanol[131] gave material in which the trisubsituted double bond had hydrated to give the sulphone (92). Attempts to prepare unhydrated material by reducing the reaction time gave a mixture of sulphone and starting material. This problem is probably due to the considerable acidity of the oxone solution (~pH5),[132] which cannot be buffered due to the instability of persulphate in neutral solutions.[132]



(92)

The oxidation with m-chloroperbenzoic acid in dichloromethane at room temperature was a little more satisfactory although starting material and compounds containing a trisubstituted epoxide (93) invariably accompanied the desired sulphone.



n = 1 or 2

(93)

Lewis acid catalysed cyclisation was tried on some small samples of sulphone. However, on a scale of about 0.2mmol total exclusion of water was not possible and only allene-alcohol (92) was isolated.

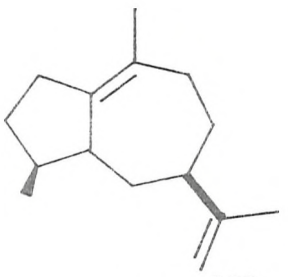
It seems likely that by careful control of the temperature, good yields of sulphone should be obtainable by the oxidation of allene (16) with m-chloroperbenzoic acid. Then, given the larger quantities of material and the fact that in general the six-membered ene cyclisation is not greatly less favoured than the five-membered, it should be possible to obtain the desired cyclohexene (91). Unfortunately, in the time available further work in this area was impossible.

CHAPTER 4

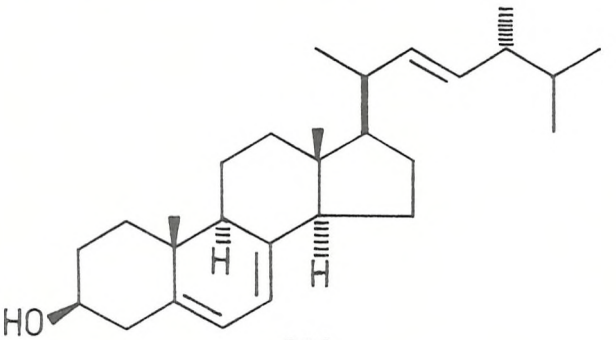
APPLICATION TO THE PREPARATION OF BICYCLIC SYSTEMS

4.1 Introduction

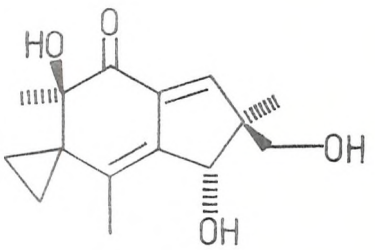
Polycyclic cyclopentanoid natural products are a very large and varied class of compound as a few examples will illustrate



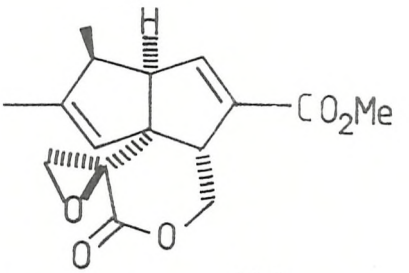
α-Bulnesene[133]



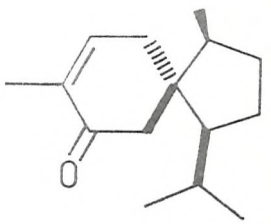
Ergosterol[134]



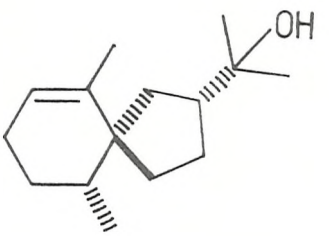
Illudin-S[135]



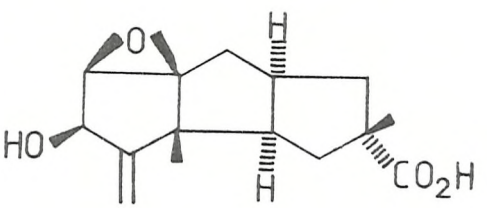
Pentalenolactone[136]



Acorenone[137]



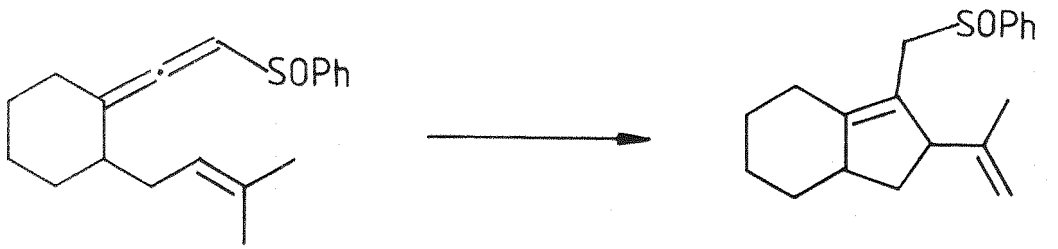
Agarospitol[138]



Hirsutic acid (94)[139]

Although the polycyclopentanoids, such as hirsutic acid (94), are of great medical and chemical interest and might be accessible from cyclopentanone or by a repetition of the ene reaction after suitable refunctionalisation, the cyclohexanone derived allene (95) was chosen for a model study for cyclopentane annelation and was expected to give

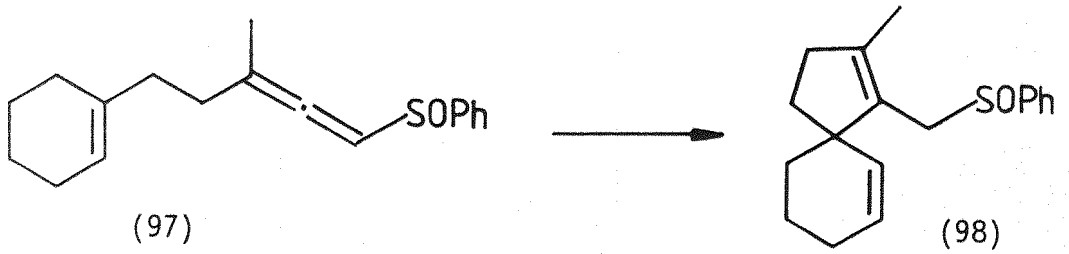
access to the bicyclo[4,3,0]nonane system.



(95) (96)

Scheme 71

Probably the largest class of naturally occurring spirocycles is the spiro-[4,5]-decane sesquiterpenes[140] and as a model study for their preparation the reactions of allene (97) were studied.



(97) (98)

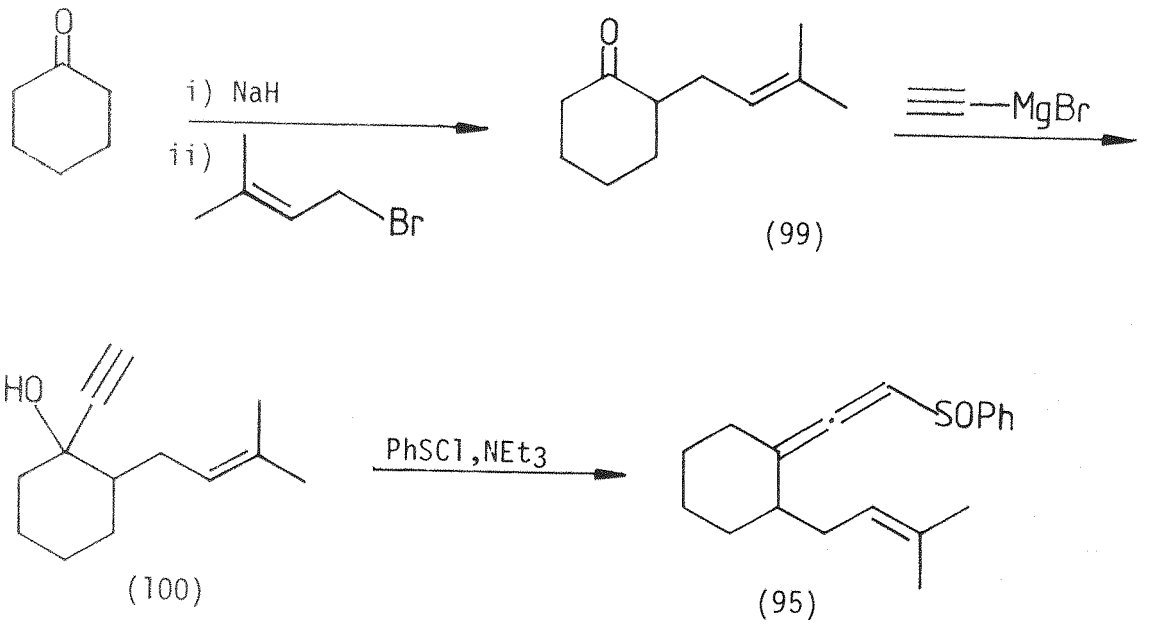
Scheme 72

Large ring compounds are of great importance to the perfumery industry and are also acquiring importance as antibiotics.[141] The synthesis of these compounds is often difficult because of the unfavourable entropy for ring closure and ring expansion is frequently preferred.[141,142] In one form these reactions involved the annelation of a normal ring onto a readily available medium ring precursor such as cyclododecanone followed by the rupture of the bond common to both rings.[142,143] An attempt to take advantage of the functionality present after cyclopentane annelation by the ene reaction to obtain a three carbon ring expansion is described in Section 4.3.

4.2 Synthesis and Reactions of 3,3-[1-(3-methylbut-2-en-1-yl)pentanylene]-1-phenylsulphinylpropadiene (95)

4.2.1 Synthesis

Allene (95) was synthesised in three steps from cyclohexanone in 21% unoptimised yield.



Scheme 73

An attempt to prepare ketone (99) by the reaction of 1-bromo-3-methylbut-2-ene with the pyrrolidine enamine of cyclohexanone proceeded in far lower yield and the reaction of the sodium enolate was therefore preferred.

4.2.2 Ene Reactions

Treatment of (95) with either boron trifluoride etherate in dichloromethane or tin (IV) chloride in benzene gave a single product. Because the former reagent gave a cleaner reaction and higher yield (77%), it was used for the remainder of the study.

The ms and ir data observed are consistent with the expected product (96). However, both the ^{1}H and ^{13}C nmr spectra are complex and a satisfactory assignment of resonances and couplings was not possible

Because (96) contains three chiral centres, four diastereomers are possible, and although all four are unlikely to be present in exactly equal proportions there is no very obvious reason why any should predominate. It therefore seems likely that the confusion of resonances and couplings observed is due to the presence of all four diastereomers.

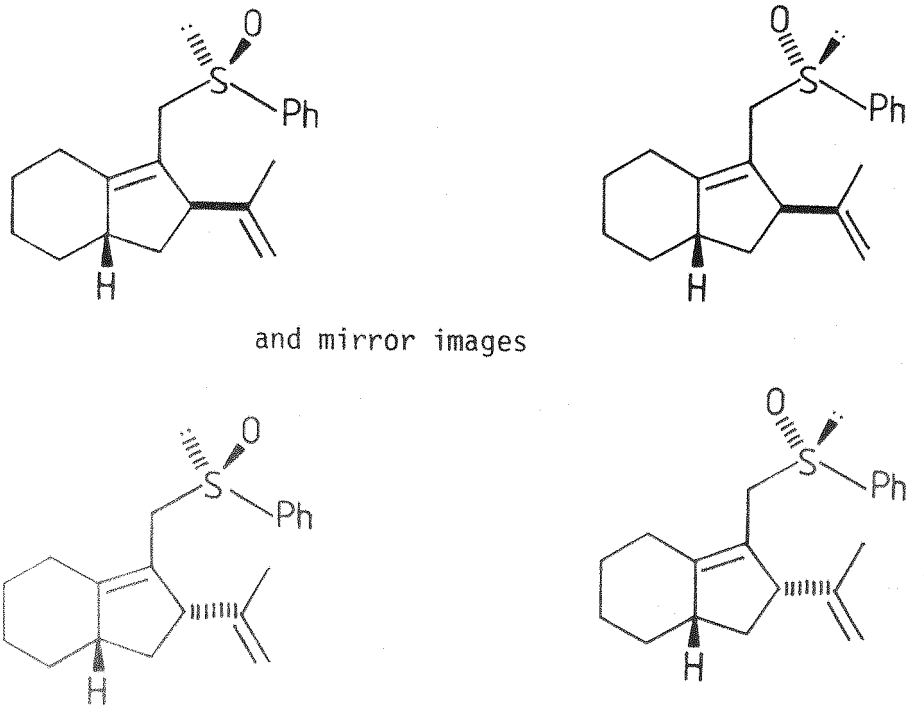
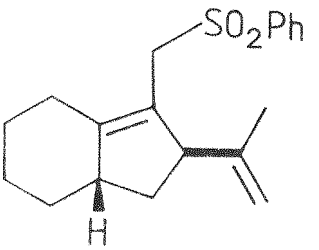


Figure 4

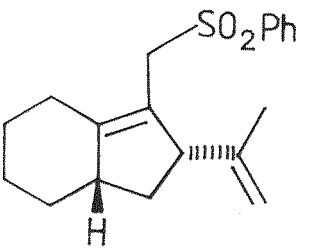
In the hope of obtaining single diastereomers which could be characterised by nmr, and in view of the fact that no separation was observed by tlc, the behaviour of the product on hplc was studied.

With an analytical phase ODS-2 column no separation was obtained although a very minor impurity was resolved and could be removed by the use of a semi-preparative ODS-2 column. On a normal phase analytical Partisil-10 column the product was resolved into two peaks with nearly complete separation when 0.5% 2-propanol in n-heptane was used as elutant. However, the preparative Partisil-10 column did not give quite as good a resolution and only a partial separation of the two fractions was obtained. ^{1}H nmr spectra of both fractions were recorded but several diastereomers were present in each fraction and confident assignment of the spectra was still impossible.

Removal of the sulphoxide chiral centre by oxidation or reduction will halve the number of diastereomers present and may aid the full characterisation of the product. Treatment of the presumed sulphoxide (96) with oxone[131] in aqueous methanol gave a reasonable yield of a new product which gave the ms, ir, ^{1}H and ^{13}C nmr expected for the sulphone (101). By integration of the ^{13}C nmr peak areas the diastereomers were found to be in the ratio 4:1, no assignment of which diastereomer preponderates was made.



(101a)



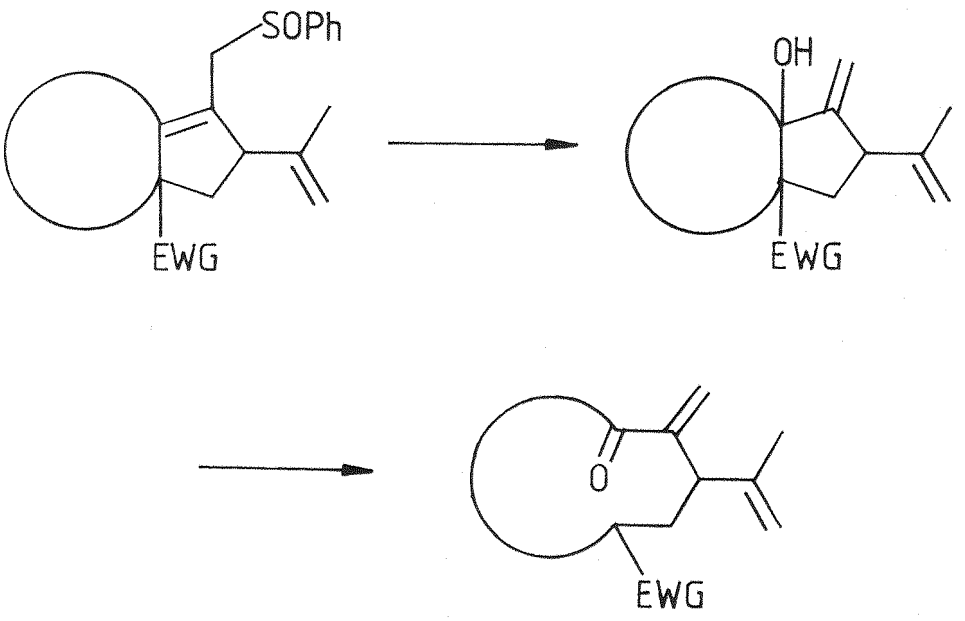
(101b)

The ene reaction of allene sulphoxides is thus suitable for cyclopentene annelation.

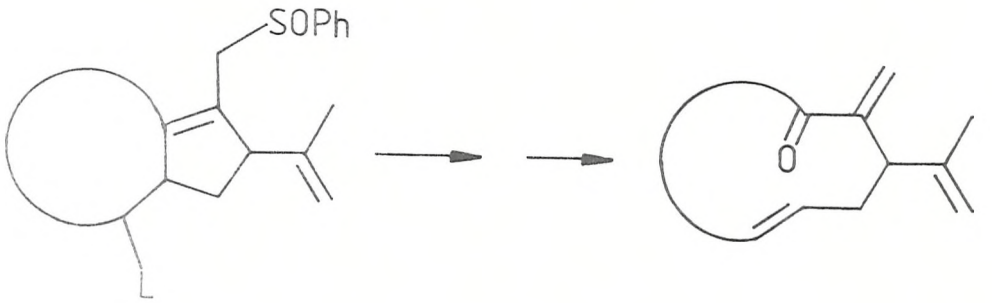
4.3 Application to Macrolide Synthesis

4.3.1 Introduction

Normally, one of two basic methods is used to break the bridging carbon-carbon bond of a bicyclic system so as to give a large ring compound, a retro-aldol reaction[144] or Grob fragmentation.[145] Both of these require that the molecule has bridgehead functionality, and for preference alcohol functionality. Because compounds such as (96) can be converted to a bridgehead alcohol by a sulphoxide - sulphenate rearrangement the ene products appear to be attractive precursors for macrolide preparation.



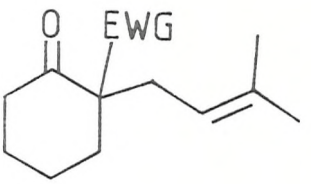
Scheme 74



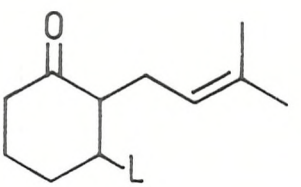
Scheme 75

This would constitute a three carbon ring expansion - a potentially useful reaction for preparing muscone and exaltone derivatives from the readily available cyclododecanone, although as a trial the expansion of a cyclohexanone to a cyclononane derivative was chosen.

An *exo*-cyclic allene with either an electron withdrawing group in the 2-position or a leaving group in the 3-position of the ring was therefore required, and possible precursors would be the ketones (102) or (103).

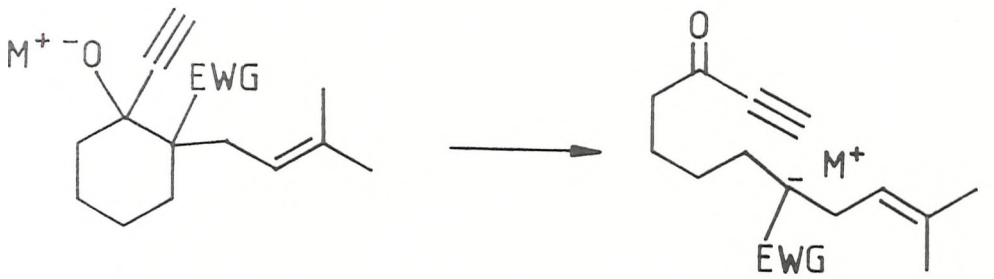


(102)

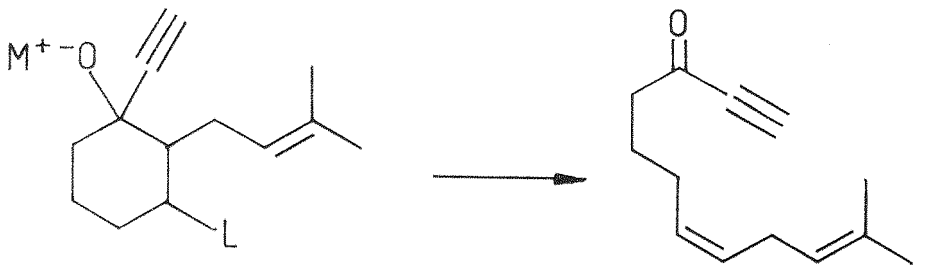


(103)

Unfortunately, addition of acetylene to either of these compounds would lead to a ring opened product by fragmentation of the propargylic anion as shown in Schemes 76 and 77.

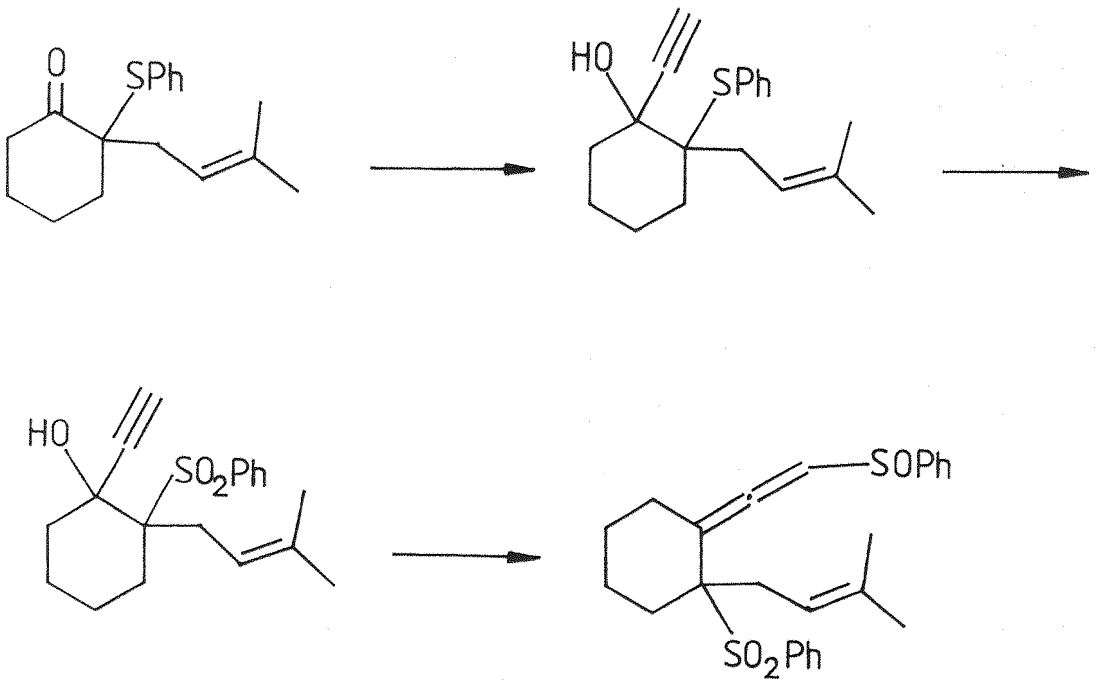


Scheme 76



Scheme 77

Thus, to allow the preparation of the allene the electron withdrawing or leaving group must be either latent or protected. Only sulphone or nitro groups would be sufficiently anion stabilizing to make the ring opened form favoured in the aldol-retroaldol equilibrium,[144] and of these only sulphone can be readily disguised.

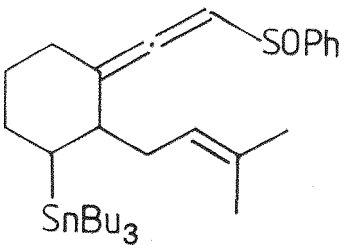


Scheme 78

However, this route requires the oxidation of a sulphide to sulphone in the presence of a reactive, and less hindered, double bond. This step, although probably achievable, is likely to present some difficulty and this approach was therefore not tried.

The other alternative is to use a disguised leaving group, and because the group chosen must have almost no leaving group ability whatsoever if formation of the propargylic alcohol is to occur

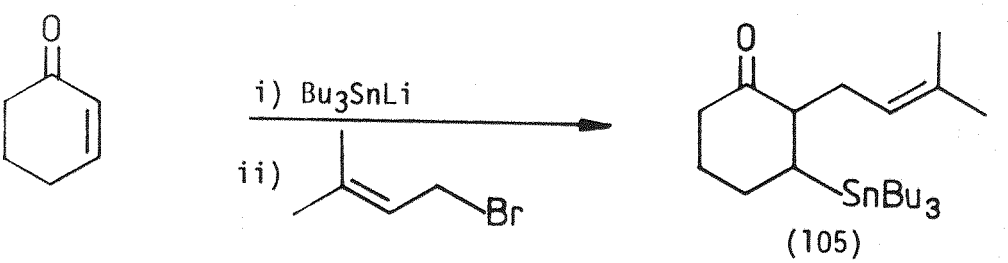
without fragmentation, the choice of substituent is very restricted. Both organoboron and organotin compounds may be cleaved oxidatively to give alcohols,[51,52] and neither show leaving group ability, and would therefore be suitable. However, organoboranes are compounds of limited stability and high reactivity, and organoboronates hydrolyse rapidly to the parent acids which are insoluble in organic media,[146] making neither of these species very convenient for our purposes. Organostannanes show neither of these drawbacks and allene (104) was thus selected for study.



(104)

4.3.2 Attempted Synthesis of (104)

Ketone (105) was prepared in 44% yield by the conjugate addition of tributyltinlithium to cyclohex-2-enone and quenching the resulting enolate with 1-bromo-3-methylbut-2-ene by a procedure derived from that of Still.[147]



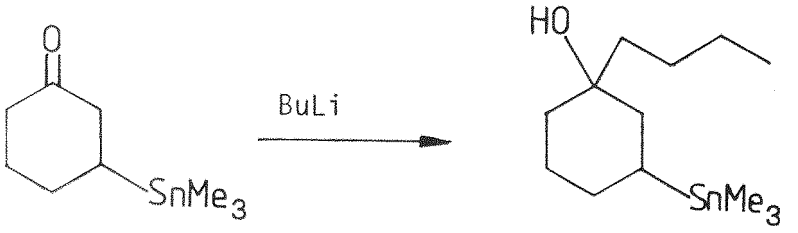
(105)

Scheme 79

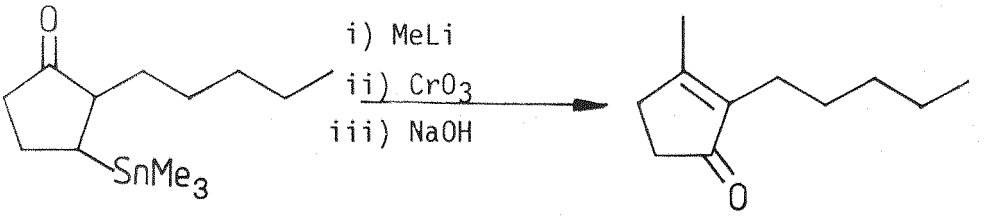
Several unsuccessful attempts were made to add acetylene to this ketone (105). Ethynylmagnesium bromide failed to add either after being stirred overnight at room temperature in tetrahydrofuran at various concentration or in 10% hexamethylphosphoramide in tetrahydrofuran, nor did the addition of a catalytic quantity of boron trifluoride etherate[148] aid reaction. An attempt to add ethynylsodium in liquid ammonia was also unsuccessful. In none of

the experiments did the ir spectrum of the crude products show any acetylenic absorption.

Surprisingly, despite the interest several authors have shown in β-stannyl ketones,[52,147,149,150] only Still has reported any examples of the addition of nucleophiles. These additions are all of primary alkyllithium reagents and, although experimental detail is scanty, appear to have been done at low temperature in ether.[147]



Scheme 80



Scheme 81

Ethynylmetal reagents are more highly ionic than are alkylmetal compounds and are consequently more prone to act as a base when both anion formation or nucleophilic attack is possible. This effect is accentuated by the fact that ethynylmetal reagents can only be prepared in fairly highly solvating solvents.[124] It would thus be expected that if tin stabilized an anion in the β-position, enolization reactions would be a far greater problem with the ethynyl reagents than with the alkyl reagents. In support of this suggestion, that the problem may be due to the basicity of the ethynyl species, it was found that n-butyllithium in ether would add to (105) and the ir spectrum shows a carbonyl absorption of less than 50% that observed in the starting material judged by the C-H stretch as internal reference. A second treatment with butyllithium gave a carbonyl-free product from which the expected alcohol and some tetrabutyltin were isolated.

No reports suggesting that the β-hydrogen atoms in an alkyltin show significant acidity could be found, and a consideration of possible inductive or hyperconjunctive effects would suggest that such

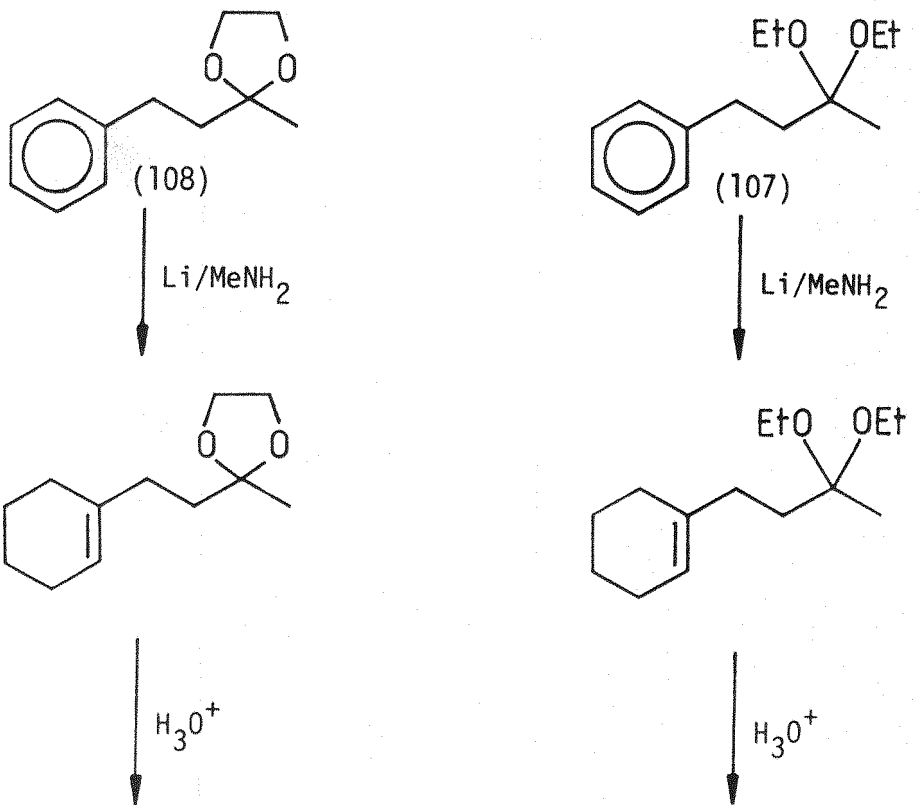
protons might be less acidic than in the corresponding hydrocarbon. However, 3-trimethylstannylcyclohexanone is known to occur significantly in the axial conformer (40%)[149] and stabilization of the oxygen anion by complexation with the more electropositive tin may be possible, although until more work has been done this can be only regarded as a tentative speculation.

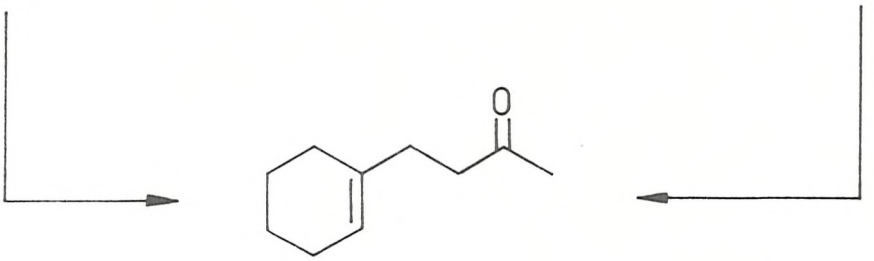
In view of these considerations there seemed little point in trying such reagents as ethynyllithium N,N,N',N',-tetramethyl-1,2-diaminoethane complex or sodium acetylide solubilised with 15-crown-5, because these are also likely to show strongly basic behaviour, and work in this area was therefore discontinued.

4.4 Synthesis and Reactions of 5-(cyclohex-1-enyl)-3-methyl-1-phenylsulphinylpenta-1,2-diene (97)

4.4.1 Synthetic Routes using the Benkeser Reduction[151]

The cyclohexenyl ketone (106) has been reported both by Benkeser,[152] who made it by reduction of the acetal (107) with lithium in methylamine and, more recently, by Polish workers who made it for some studies of insect juvenile hormone by reduction of the ethylene acetal (108) with lithium in methylamine.[153]





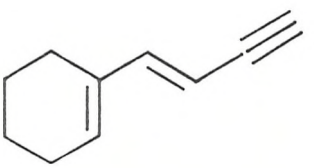
51% (106) (77%)

Scheme 82

Benkeser also found that acetals nearer than two carbon atoms from the aromatic ring were reductively cleaved. Thus, 1-ethylcyclohexene was obtained from acetophenone acetals.[152] Later work suggests that the double bond purity of the products from Benkeser reductions is lower than was originally thought and significant quantities of the 3- and 4-substituted cyclohexenes are also formed.[154,151]

However, in our hands this reduction proved highly unsatisfactory and the individual results obtained could not readily be repeated despite the care that was taken to ensure the purity and dryness of all reagents. Several experiments were performed which are summarised in Table 5. All reactions were run overnight.

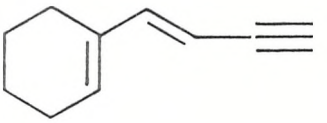
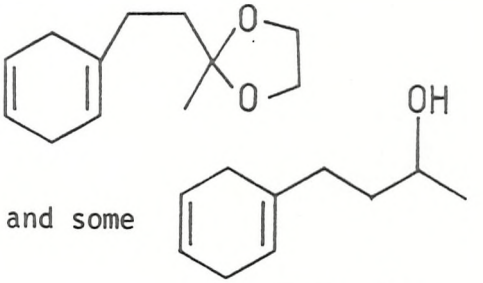
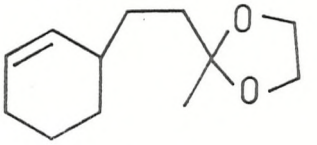
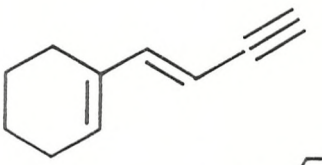
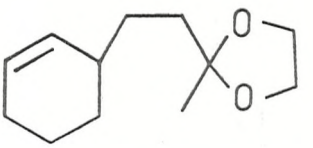
The most surprising observation is the formation in two reactions of the acetylene (109).

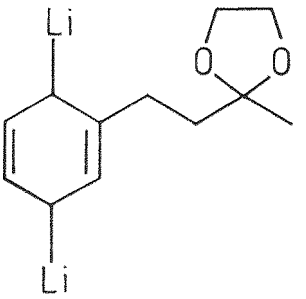


(109)

Although this product can formally be derived by base catalysed elimination of the acetal followed by rearrangement of the double bonds in a dihydrobenzene, such a mechanism seems decidedly unlikely. In the absence of either Brönsted or Lewis acids, alkoxides are very poor leaving groups and the only literature examples of acetal elimination that could be found were of compounds that had additional substituents which promoted the acidity of the α hydrogen atoms.[155] However, the first product of reduction of the benzene ring will be a dilithiobenzene, and on thermodynamic grounds probably (110).

TABLE 5

Solvent	Temperature	Products
$EtNH_2$	-10 to -15°C	Starting material
$EtNH_2$	-10 to 15°C	
$EtNH_2$	-20 to +5°C	Starting material
$MeNH_2$	Reflux	60% starting material + various cyclohexenes
$EtNH_2$/EtOH	-5°C	Starting material  and some
$MeNH_2$	Reflux	Chiefly 
$EtNH_2$	-10 to +5°C	 +  + small quantities of starting material



(110)

Two processes might then lead to acetal elimination:-

1) The lithium is sufficiently strongly co-ordinated to the acetal to make alkoxide a powerful enough leaving group to permit elimination by any lithium methylamide present.

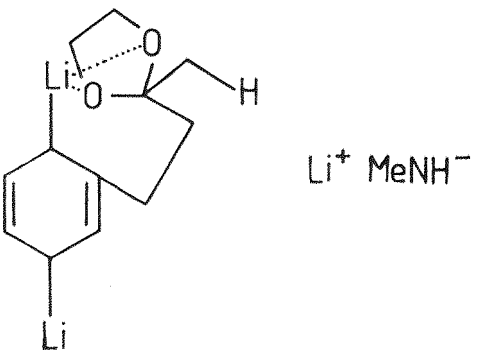
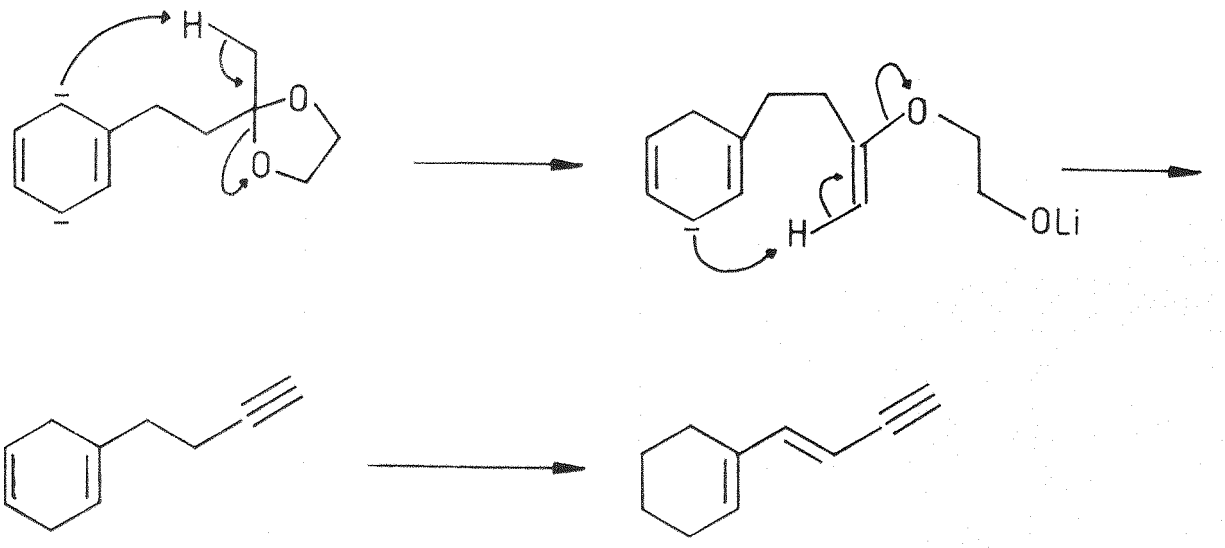


Figure 5

Two moles of amide are required to complete this elimination and these can only be formed if the amine protonates the dilithio-benzene. Although the intermediate vinyl ether is more reactive and might react without 'activation', this must be regarded as a rather unlikely mechanism.

2) The dilithio-benzene might act as an internal base and the elimination might occur because of the favourable geometry of the transition state.



(109)

Scheme 83

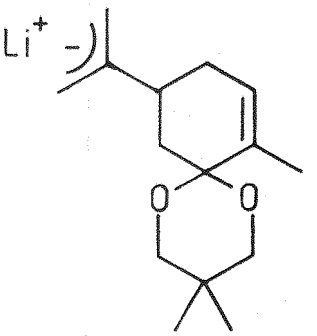
In both cases the presence of catalytic quantities of strong base should be sufficient to isomerise the double bonds into the most stable conjugated form observed.

Due to the problems of reproducibility, and the fact that even the most satisfactory reactions appeared to give mixtures in which the 3- rather than the 1-isomer predominates, work on this route was discontinued. It is, however, a disturbing fact that when ketone (106) was eventually prepared the physical and spectral data quoted in the two papers[152,153] proved to be correct.

4.4.2 Synthetic Routes Involving Lithium Reagents

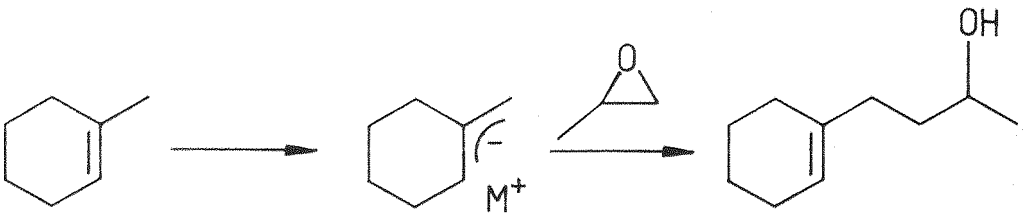
There are several reports in the literature that very strong bases, such as n-butyllithium/potassium t-butoxide or n-butyllithium/ N,N,N',N'-tetramethyl-1,2-diaminoethane, will abstract allylic hydrogen atoms to give allylically stabilised anions such as (111)[156] or (112).[157]

(111)



(112)

Most known examples are derived from 2-substituted propenes in which both of the major valence-bond isomers bear the negative charge at a primary centre. Nevertheless, it might be possible to form the anion of 1-methylcyclohexene which should react with epoxypropane at the primary end to give alcohol (114), which on oxidation would give the required ketone.



(113) (114)

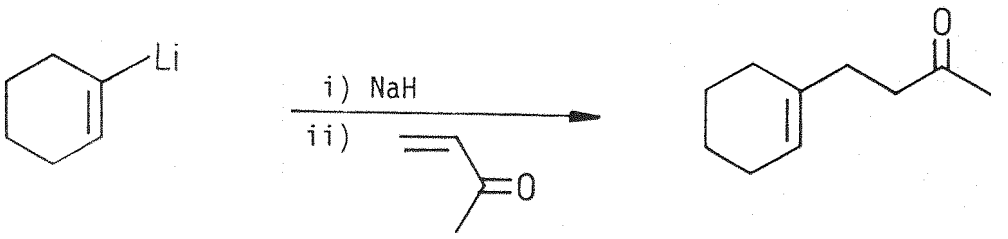
Scheme 84

Attempts to prepare the anion (113) from methylcyclohexene and n-butyllithium/N,N,N',N'-tetramethyl-1,2-diaminoethane n-butyllithium/potassium t-butoxide, t-butyllithium and t-butyllithium/N,N,N',N'-tetramethyl-1,2-diaminoethane were made and the reactions quenched with epoxypropane. In all cases the only isolated products were derived from the lithium reagent and epoxypropane. Sequential treatment of methylcyclohexene with n-butyllithium/potassium t-butoxide in ether, lithium bromide in tetrahydrofuran/ether, and epoxypropane, gave a complex mixture of products. In all these reactions low recoveries of organic materials were obtained and no products derived from methylcyclohexene were observed.

Because the anion may be inducing base catalysed rearrangement of the epoxypropane to propenol, attempts were made to trap the presumed anion obtained with n-butyllithium/N,N,N',N'-tetramethyl-1,2-diaminoethane with ethanal or chlorotrimethylsilane. However, in neither case was the expected product isolated.

These results strongly suggest that the required allylic anion is not being formed. This may be due to the fact that the alkene involved is trisubstituted and would give a less stable anion than reported examples such as (111); indeed if such anions cannot be formed the selectivity observed in the formation of (112) becomes far less surprising.

An alternative approach to the required ketone (106) could be by the conjugate addition of cyclohexenyl cuprate to but-3-en-2-one.

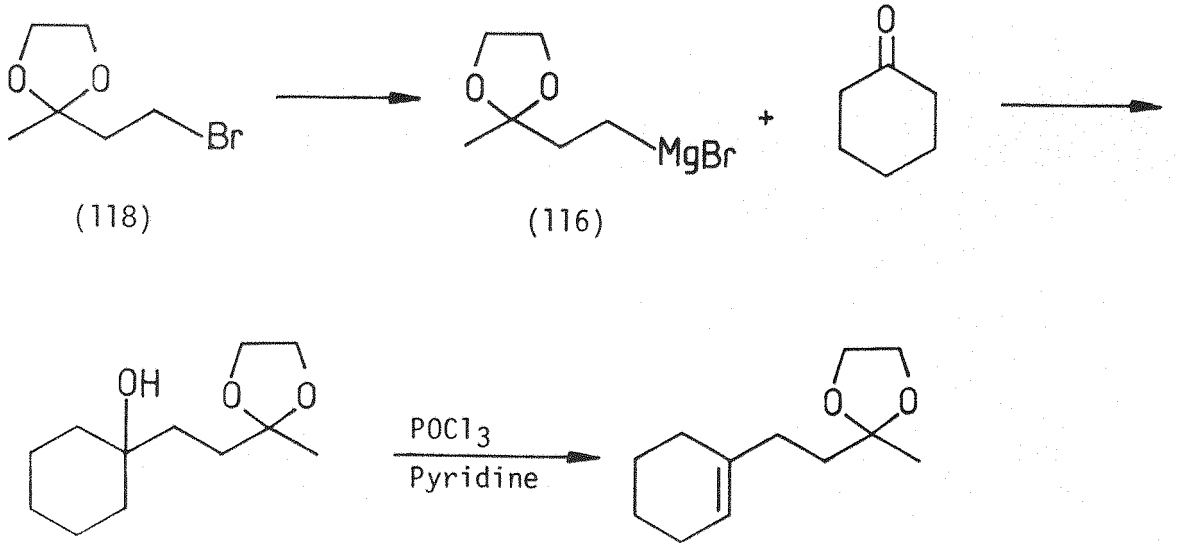


Scheme 85

Although cyclohexenyllithium, which would be required for the preparation of the cuprate, has been reported,[158] the yield claimed is only modest (60%), so attention was concentrated on the route described in the next Section.

4.4.3 Synthetic Routes involving Grignard Reagents

Ponaras[159] has reported the preparation of the ketal (115) by the route shown in Scheme 86, but has not published any experimental details, and no citations giving further details could be found.



(118) (116) (117) (115)

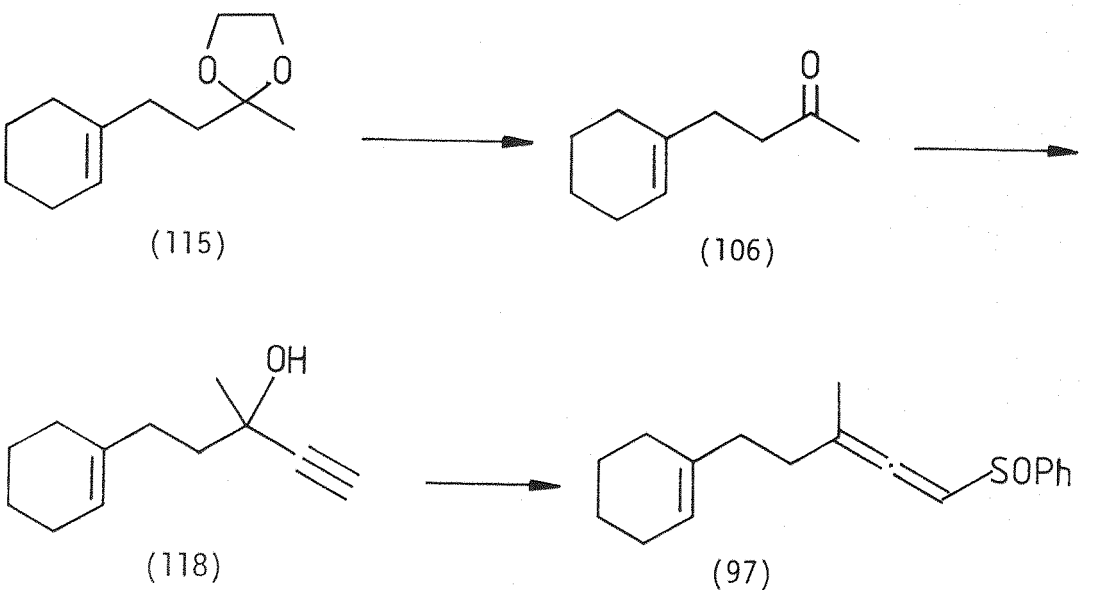
Scheme 86

Although Feugeas[114] was unable to prepare the Grignard reagent (116), coaddition of (118) with 1,2-dibromoethane to an excess of magnesium in tetrahydrofuran and careful cooling to prevent the temperature rising above 25°C gave the required Grignard reagent (116) which reacted with cyclohexanone to give alcohol (117) in 98% crude yield.

Purification was not normally necessary.

Many completely unsuccessful attempts were made to dehydrate alcohol (117) with phosphorus oxychloride/pyridine. Various other conditions were then tried and these results along with the results of the phosphorus oxychloride/pyridine experiments are summarised in Table 6. Although the Dean and Stark conditions and acetic acid/tosic acid conditions[160] did appear to give some of the required material the neutral conditions of the dehydration with inner salt (118)[161] were found to give the best yields. The inner salt, prepared in solution from chlorosulphonyl isocyanate,[162] was used in excess without isolation.

The acetal was hydrolysed in refluxing methanolic hydrochloric acid,[153] acetylene added and the allene formed in the usual manner.



(115) (106) (118) (97)

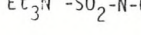
Scheme 87

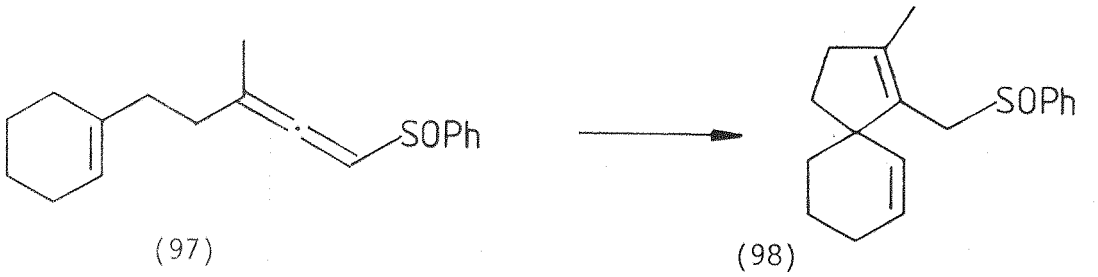
4.4.4 Reactions of (97)

An attempt to prepare (98) by thermolysis of the allene (97) at 185°C for ½h lead to a mixture of products in which most of the aromatic material was present as diphenyl disulphide. In view of this failure, subsequent attempts to prepare (98) were all by acid catalysis.

TABLE 6

Attempted Dehydration of (117)

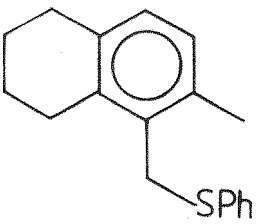
Reagents	Temp.	Time	Results
$POCl_3$/pyridine	rt	24h	Became very hot during work-up. Complex mixture with no acetal by nmr.
$POCl_3$/pyridine	rt	10d	Complex mixture of >9 products - little acetal or methyl ketone observable by nmr.
$POCl_3$/pyr/benzene	reflux	4h	Complex mixture containing no acetal or methyl ketone by nmr.
$POCl_3$/pyridine	70-80° then reflux	7h 3h	No change by tlc. Complex mixture, no acetal or methyl ketone by nmr.
$POCl_3$/pyridine	reflux	24h	Mixture - no DNP active products, no acetal or methyl ketone by nmr.
Me_2CO/TsOH	reflux	24h	Much polymerisation, very small yield of desired product in one trial reaction.
MsCl/pyridine	rt	7d	Starting material.
$SOCl_2$/pyridine	rt	1h	Mixture, >7 products by tlc. No acetal or methyl ketone by nmr.
DMSO	reflux	12h	Deprotected alcohol.
AcOH/TsOH	reflux	6h	After chromatography a small fraction containing some olefinic material obtained.
 OH/PhH/TsOH	reflux Dean and Stark	2d	Product mixture contains about 60% desired acetal, remainder starting material.
	rt	24h	Desired acetal.



(97) (98)

Scheme 88

Diethylaluminium chloride was found to be too weak a Lewis acid to induce any reaction of allene (97) and starting material was recovered unchanged. Treatment of the allene (97) with a mixture of diethylaluminium chloride and aluminium chloride in benzene also lead to the recovery of starting material but when dichloromethane was used as solvent the benzylic sulphide (119) was isolated in modest yield along with diphenyl disulphide and a mixture of hydrocarbons.

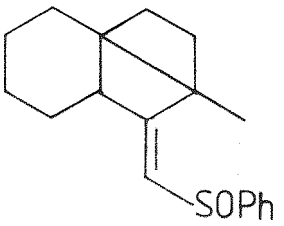


(119)

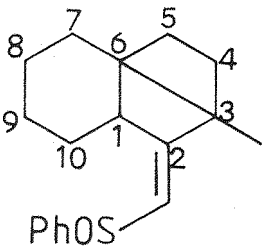
This dramatic change on using dichloromethane as solvent instead of benzene is probably due to the relative insolubility of aluminium chloride in benzene.

A similar mixture of benzylic sulphide, diphenyl disulphide and hydrocarbons was obtained when the allene was treated with tin (IV) chloride in benzene.

When the experiment was performed with tin (IV) chloride in acetonitrile or boron trifluoride etherate in dichloromethane a mixture of the two bicyclohexanes (120a) and (120b) was obtained.



(120a)



(120b)

These experiments are summarised in Table 7.

The formation of these compounds was quite unexpected, but is probably due to the fact that unlike in previous examples it is the 6-position rather than the 7 which is trisubstituted and thus the regiochemistry of the addition of the double bond to allene is reversed.

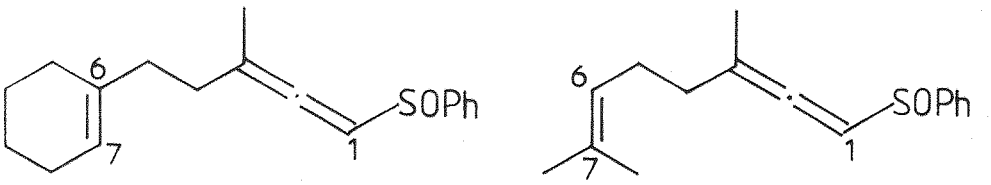
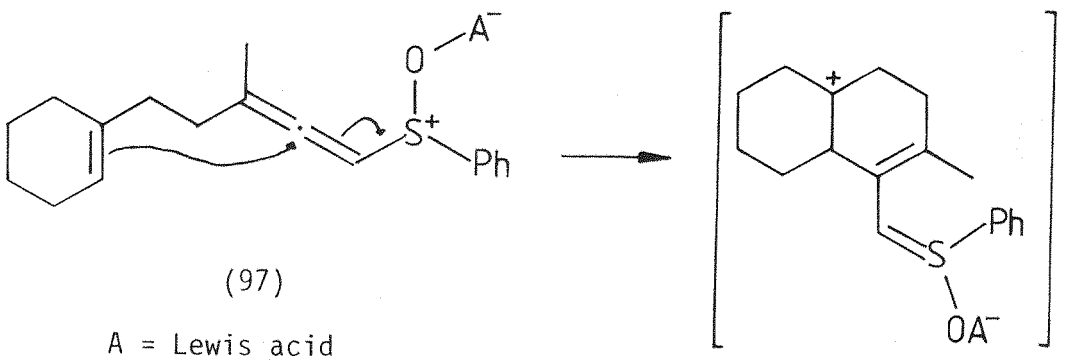


Figure 6

After the initial cyclization the dipolar intermediate (121) can either collapse directly to the bicyclohexane, or to a diene which can undergo Lewis acid catlysed Pummerer rearrangement[87] to give, after a proton shift, the benzylic sulphide.



(97)

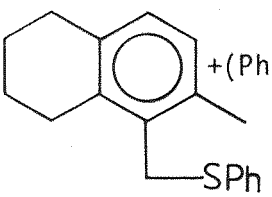
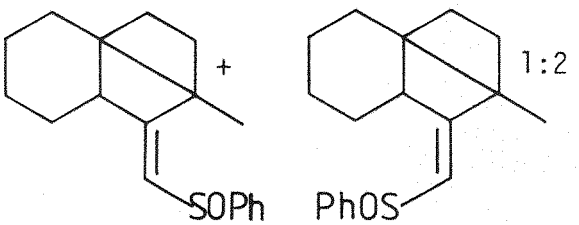
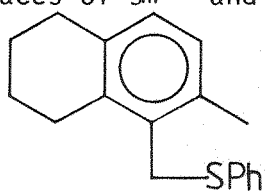
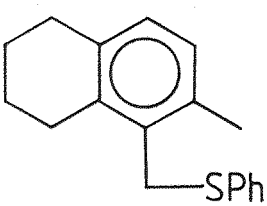
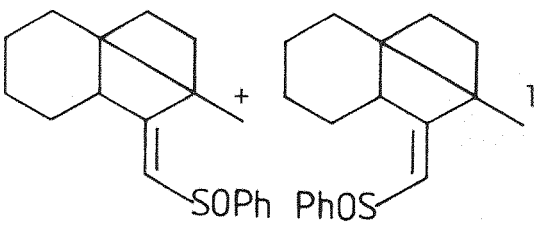
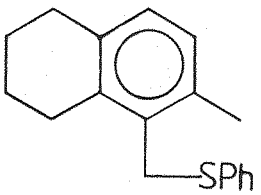
A = Lewis acid

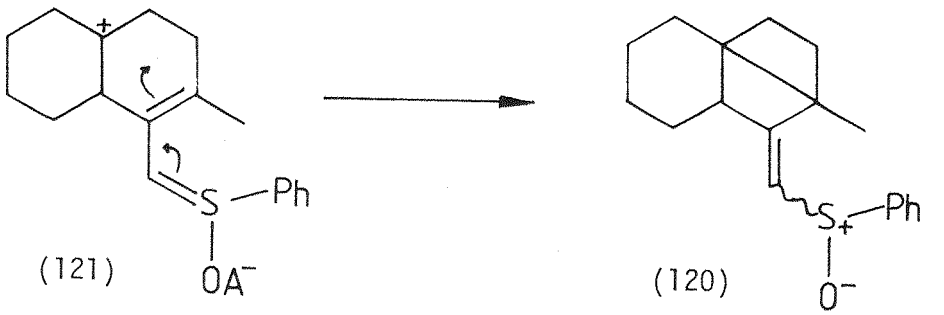
(121)

Scheme 89

TABLE 7

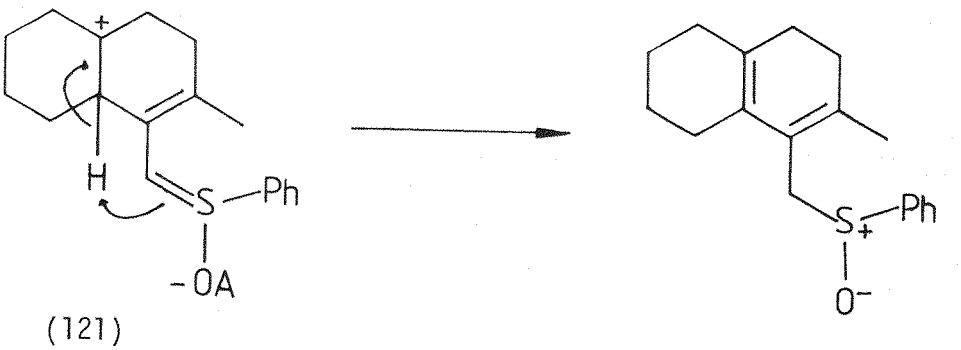
Reactions of (97) Catalysed by Lewis Acids

Lewis Acid	Solvent	Products
Et_2AlCl	Benzene	sm recovered
$Et_2AlCl/AlCl_3$	Benzene	sm recovered
$SnCl_4$	Benzene	 +$(PhS)_2$ + hydrocarbons (?
$SnCl_4$	MeCN	 1:2 + traces of sm and 
$Et_2AlCl/AlCl_3$	CH_2Cl_2	 + $(PhS)_2$ + hydrocarbons (?)
$BF_3 \cdot Et_2O$	CH_2Cl_2	 1:2 + traces of 

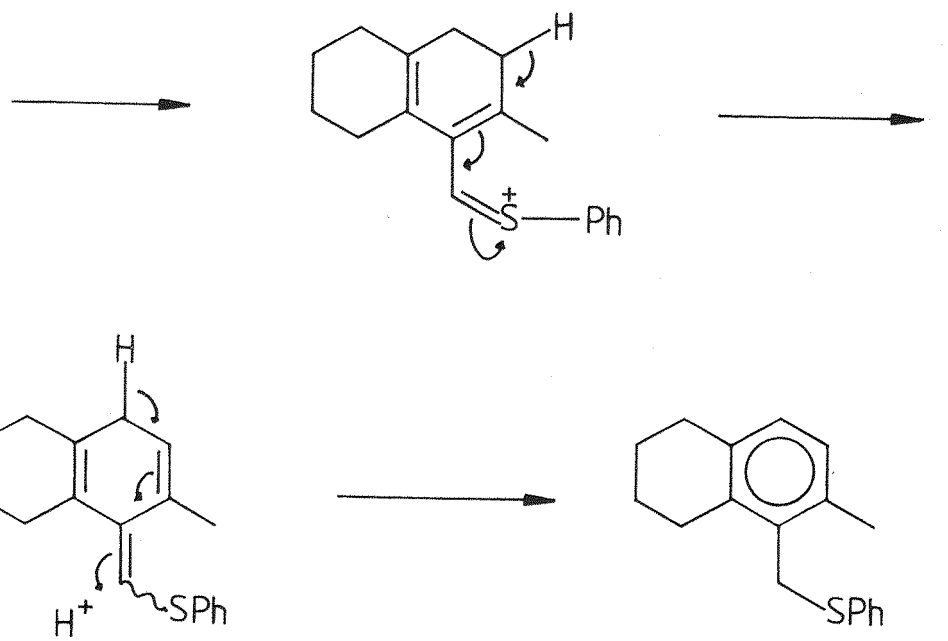


(121) (120)

Scheme 90



(121)



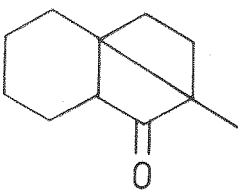
(119)

Scheme 91

The reason why the pathway forming the benzylic sulphide is favoured with the stronger Lewis acids is obscure as is the mechanism by which diphenyl disulphide is formed in these reactions.

Although the spectral data obtained are in full support for (120) as the structure of the major product from the treatment of allene (97) with boron trifluoride etherate in dichloromethane or tin (IV) chloride in acetonitrile it would be desirable if chemical support for such an unusual structure could also be obtained.

Perhaps the most conclusive degradation would be the oxidative cleavage of the double bond to give a bicyclohexanone (122) which should give an infrared carbonyl absorption chracteristic of a cyclobutanone at about 1780cm^{-1}.



(122)

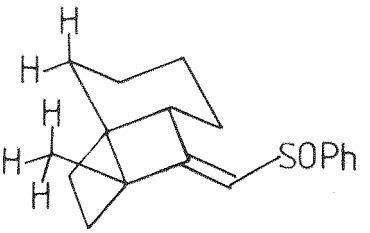
Unfortunately, work on preparation of the parent system, bicyclo-[2,2,0]-hexanone, shows that these systems are highly unstable and could only be observed as a presumed transitory species at low temperatures.[163] While there is no *a priori* reason why stable degradation products should be used to characterise an organic compound, in this case the degradation would have to involve either ozonolysis and work-up or an osmium tetroxide/periodate cleavage,[164] neither of which reactions could be done entirely at a sufficiently low temperature to allow the isolation and characterisation of ketone (122).

Small membered ring compounds may frequently be hydrogenolytically opened under relatively mild conditions.[165] Normally cyclobutanes can be hydrogenlysed only under fairly extreme conditions. However, the 3,6-bond is quite highly strained and should hydrogenolyse under fairly mild conditions.

The sulphoxide (120) was treated with Adam's catalyst in acetic acid under an atmosphere of hydrogen at 15psi or 70psi, but the starting material was recovered in both instances.

The failure of this reaction may be because the presence of sulphur in the molecule led to poisoning of the catalyst despite the fact that

it is present as sulphoxide and that a relatively large amount of catalyst was used. Another possibility is that the high level of substitution around the central bond prevents its complexation with the catalyst. An examination of models supports this idea and suggests that the methyl group and methylene of the cyclohexane ring would be forced close together effectively shielding the central (3,6) bond.

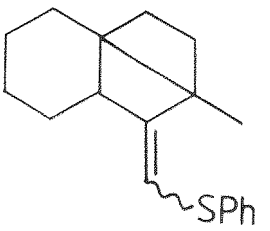


(120)

Attempts were then made to aromatise the tricyclic ring system in the hope of obtaining a known tetralin or naphthalene derivative.[166] However, treatment of (120) with palladium on charcoal in acetic acid at room temperature (4h) or under reflux (6h) gave back unchanged starting material. In benzene in a Carius tube at 200°C for 6h extensive decomposition occurred to give diphenyl disulphide among other chiefly nonaromatic products. Because these materials were evidently not derived from dehydrogenation processes, time was not spent purifying or characterising them.

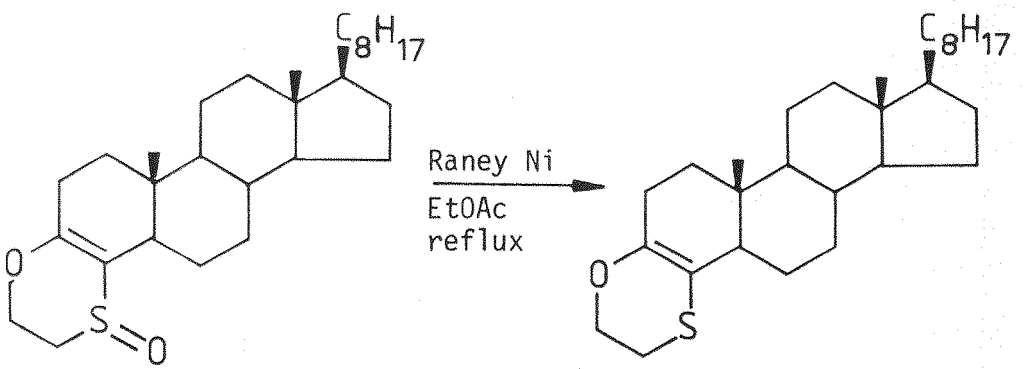
The catalyst used in these experiments was known to be of high activity and was being used successfully by others. It would, therefore, appear that the presence of sulphoxide in the molecule does poison the catalysts used in both the attempted hydrogenolysis and dehydrogenation.

There are several reports of sulphoxides being desulphurized by Raney nickel.[167] However, refluxing the sulphoxide (120) with Raney nickel in ethanol gave a material which has an unchanged nmr from the starting material except that the aromatic absorption at δ7.47 and the vinylic absorption at δ5.70 are both shifted upfield to δ7.08 and δ5.47 respectively.These results very strongly suggest that the sulphoxide has been deoxygenated to give vinyl sulphide (123).



(123)

It is very surprising that Raney nickel should remove oxygen under conditions where sulphur is unaffected, although there is a precedent in the deoxygenation of the steroidal vinyl sulphoxide (124) with deactivated Raney nickel.[168]



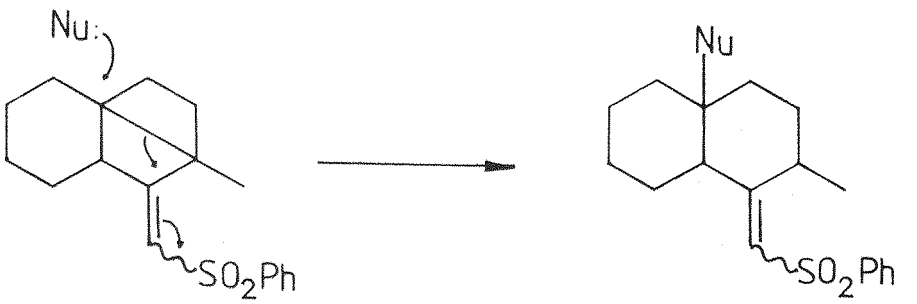
(124)

Scheme 92

Because sulphones are generally crystalline solids[169] and might allow X-ray crystallographic analysis, the sulphone (125) was prepared by the oxidation of sulphoxide (120) with m-chloroperbenzoic acid in dichloromethane, and a nearly quantitative yield was obtained.

After double recrystallisation from ether/pentane the sulphone (125) gave satisfactory analytical data and a sample is awaiting X-ray crystallographic analysis.

Examination of models of (125) and (122) suggests that the approach of a nucleophile for 1,4-addition to the sulphoxide would be very hindered, although 1,6-addition might be possible.

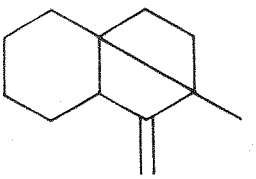


(125) Nu = nucleophile

Scheme 93

However, attempts to add sodium thiophenoxide or nucleophilic oxidants such as alkaline hydrogen peroxide or sodium hypochlorite to the sulphone (125) were all totally unsuccessful and led to the recovery of starting material.

Attempts to prepare the exocyclic alkene (126) by treatment of the sulphone with either sodium dithionate[55] or sodium amalgam[56] left the starting material unaffected. Treatment of (125) with lithium in liquid ammonia/ether gave a very low yield (14%) of the alkene (126).[170]



(126)

Because of the low yield of its preparation, no work was done on the chemistry of alkene (126) although it might be possible to aromatise it by treatment with palladium in benzene.[166] However, aromatisation would not provide direct evidence for the presence of the bicyclohexane system and, in view of the shortage of time, it was decided to discontinue chemical studies and allow the final proof of structure to rest on X-ray crystallography.

CHAPTER 5

EXPERIMENTAL

5.1 Purification of Reagents

The following drying agents were used to obtain the listed anhydrous solvents:-

Calcium Hydride	Triethylamine
	Pyridine
	Di-*iso*-propylamine
	Hexamethylphosphoric triamide (HMPA)
	Dimethyl formamide (DMF)
	Dimethyl sulphoxide
	Acetonitrile
	Dioxan
Phosphorus Pentoxide	Dichloromethane
Lithium aluminium hydride	Tetrahydrofuran (THF)
Magnesium	Ethanol
	Methanol
	Acetic anhydride
Sodium	Ether
	Benzene

Ether refers to diethylether and chloroform contained 2% ethanol. Light petroleum refers to that fraction with bp 40-60^{o}C and was distilled prior to use.

5.2 General Procedures

All starting materials were distilled or recrystallised prior to use.

Organic extracts were dried over anhydrous magnesium sulphate unless stated otherwise and solvent evaporation was carried out at reduced pressure using a rotary evaporator.

n-Butyllithium was used as a 15% solution in hexane as supplied by Pfizer Ltd. and was standardised before use.

Analytical tlc was carried out using precoated silica gel or alumina plates (Macherey-Nagel Kieselgel G25 UV_{254} or Alox-25 UV_{254}

respectively) and visualisation was by uv fluorescence, exposure to iodine vapour or by spraying with dilute aqueous solutions of potassium permanganate or 2,4-dinitrophenylhydrazine as appropriate.

Flash column chromatography[171] was performed with columns packed with Macherey-Nagel Kieselgel-60 (230-400 mesh) with 5-10 $Lbin^{-2}$ applied pressure.

Preparative tlc was carried out either on uncut 20cm x 20cm analytical tlc plates or on 1mm plates prepared from Merck Kieselgel-60 $HF_{254+366}$.

The yields quoted are of isolated materials and have not been optimised. All data quoted are from measurements on pure products unless otherwise stated.

5.3 Instrumentation

Infra-red (ir) spectra were recorded either on a Perkin-Elmer model 157G or 298 spectrometer. A polystyrene film was used as standard. The following abbreviations are used: s - strong; m - medium; w - weak.

Ultra-violet (uv) spectra were recorded on a Perkin Elmer model 402 spectrometer. Values are quoted in nm followed by their extinction coefficient in parentheses.

^{1}H nuclear magnetic resonance spectra were recorded on a Perkin Elmer model R12 or R24B operating at 60MHz or a Varian Associates model XL100/30 operating at 100MHz. Tetramethylsilane was used as an external standard for organosilicon compounds and as an internal standard for all others. Chemical shifts are quoted on the δ scale and the following abbreviations are used for peak multiplicity: s - singlet; d - doublet; t - triplet; q - quartet; m - multiplet and in combination with the above b - broad. Coupling constants, J, are expressed in Hertz.

^{13}C nuclear magnetic resonance spectra were recorded on a Varian Associates XL100/30 instrument operating at 25.15MHz. Tetramethylsilane was used as internal standard. Chemical shifts are quoted on the δ scale from broad band decoupled spectra and multiplicities are those of the off-resonance decoupled spectra.

Mass spectra were recorded on a Kratos MS30 instrument with a DS 55 Data System. Spectra were obtained using a 70eV ionizing beam unless otherwise stated, and values are quoted as m/z ratios. The major ion fragmentations, together with those of structural significance, are reported followed by their percentage intensity relative to the base peak in parentheses.

Melting points were recorded on either an electrothermal melting point apparatus or a Koffler block.

Gas chromatography was performed on a Pye Series 105 chromatograph equipped with a flame ionization detector.

Elemental analyses were carried out at the Microanalytical Laboratory, University College, London.

High performance liquid chromatography was performed on a Waters Associates instrument fitted with a two head pump and differential uv and differential refractometer (R401) detectors. ODS2 and Partisil-10 prepacked analytical and semi-preparative columns were used and sample injection was by means of a loop system.

5.4 Experimental Procedures

Preparation of Allene Sulphoxides

All allene sulphoxides were prepared using the method of Horner and Binder[34] by the addition of phenylsulphenyl chloride[172] to the appropriate propargylic alcohol, in the presence of triethylamine (3-6 equivalents), in ether solution at -30 to -40°C. The products were purified by flash chromatography.

3-Methyl-1-phenylsulphinylbuta-1,2-diene (9) was prepared from 2-methylbut-3-yn-2-ol and gave data in agreement with that published.[6,34]

3,7-Dimethyl-1-phenylsulphinylocta-1,2,6-triene (1) was prepared from 3,7-dimethyloct-6-en-1-yn-3-ol and gave data in agreement with that published.[6]

3,8-Dimethyl-1-phenylsulphinylnona-1,2,7-triene (16) was prepared from 3,8-dimethylnon-7-en-1-yn-3-ol (82) in 60% yield.

nmr $\delta(CDCl_3)$: 1.15-2.05(15H,m,CH_3 and CH_2), 5.06(1H,m,C=CH), 5.98(1H,m,C=C=CH), 7.55(5H,m,aromatic).

ir ν_{max} (film): 2960(s,CH stretch), 1952(w, allene), 1442(s), 1375(m), 1082(m), 1048(s), 745(m, benzene ring)cm^{-1}.

ms m/z: 257(30), 149(15), 126(30), 125(12), 110(11), 109(13), 107(27), 93(29), 79(38), 77(42), 69(66), 67(32), 55(51), 43(40), 41(100), 39(40).

8-Benzyloxy-3,7-dimethyl-1-phenylsulphinylocta-1,2,6-triene (23) was prepared from 8-benzyloxy-3,7-dimethyloct-6-en-1-yn-3-ol (28) in 42% yield.

nmr $\delta(CDCl_3)$: 1.65(3H,s,Me-C=C=C), 1.84(3H,d,J=2Hz,Me-C=C), 2.11(4H,m,CH_2), 3.88(2H,m,=C-CH_2-O), 4.24(2H, s,Ph-CH_2-O), 5.40(1H,m,C=CH), 5.98(1H,m, C=C=CH), 7.20(10H,m,aromatic).

ir ν_{max} (film): 2900(m), 1955(w,allene), 1440(m), 1050(s), 770(s)cm^{-1}.

ms m/z (25eV): 366(M^+,0.1), 349(1.1), 275(0.2), 259(0.3), 258(1.3), 257(0.7), 256(0.7), 241(8), 125(21), 124(17), 121(16), 109(17), 107(21), 105(30), 93(25), 91(100), 79(25), 78(34), 77(47), 65(34).

3,3 -[1-(3-Methylbut-2-en-1-yl)pentanylene]-1-phenylsulphinyl-propadiene (95) was prepared from 1-ethynyl-2-(3-methylbut-3-en-1-yl) cyclohexan-1-ol (100) in 47% yield.

nmr $\delta(CDCl_3)$: 1.1-2.2(17H,m,CH_3 and CH_2), 5.00(1H,m,C=CH), 5.95(1H,m,C=C=CH), 7.50(5H,m,aromatic).

ir ν_{max}(film): 2960(s), 1950(w,allene), 1445(s,C=C), 1050(s), 790(s), 750(s), 690(s)cm^{-1}.

ms m/z: 285(0.2), 175(30), 133(12), 91(22), 77(16), 69(100), 41(24).

5-(Cyclohexen-1-yl)-3-methyl-1-phenylsulphinylpenta-1,2-diene (97) was prepared in 54% yield from 5-(cyclohexen-1-yl)-3-methylpent-1-yn-3-ol (118).

tlc: R_f = 0.53 (silica,ether).

nmr $\delta(CDCl_3)$: 1.58(4H,m,CH_2), 1.83(3H,d,J=3Hz,Me), 1.8-2.2 (8H,m,CH_2), 5.41(1H,m,C=CH), 5.97(1H,m,C=C=C), 7.50(5H,m,aromatic).

ir ν_{max} (film): 2920(s), 1950(w,allene), 1443(m,C=C), 1048(m, S=O), 740(m), 690(m)cm^{-1}.

ms m/z: 286(M^+,0.1), 271(1.4), 270(2.4), 269(11), 161(16), 126(30), 119(14), 105(18), 95(100), 93(20), 91(20), 79(22), 77(24), 67(32), 55(23), 41(31).

An accurate mass measurement on M^+ gave m/z 286.1502, $C_{18}H_{22}SO$ requires m/z 286.1391.

6-Methyl-8-phenylsulphinylocta-6,7-dien-2-one ethylene acetal (126) was prepared from 2-methyl-2-(4-methylhex-5-yn-4-ol)-1,3-dioxolan (65) in 50% yield.

tlc: R_f = 0.36 (silica,ether).

nmr $\delta(CDCl_3)$: 1.20(3H,s,Me-acetal), 1.54(4H,m,CH_2), 1.82(3H, d,J=4Hz,Me-allene), 2.03(2H,m,CH_2C=C), 3.84 (4H,s,O-CH_2-CH_2-O), 5.83(1H,m,allene), 7.50 (5H,m,aromatic).

ir ν_{max} (film): 2950(m,CH), 1950(w,allene), 1445(m), 1380(m), 1045(s), 740(m), 690(m)cm^{-1}.

ms m/z: 291(0.1), 204(0.1), 125(3), 109(4), 99(3), 87(20), 79(11), 77(10), 45(11), 43(100).

Phenylsulphonylpropadiene (15)[47] - 1-Bromoprop-2-yne (1.46g, 12mmol) was added dropwise to a solution of sodium benzenesulphinate (2.0g,12mmol) in dimethylsulphoxide (30ml) at 20°C, stirred for ½h, poured into water and extracted with ether (3x15ml). The combined organic phases were washed with water (4x15ml), dried and the solvent

evaporated to give a mixture of phenylsulphonylpropadiene (15) and 1-phenylsulphonylprop-2-yne. Equilibration of this mixture in ether with triethylamine at rt gave phenylsulphonylpropadiene containing only traces of 1-phenylsulphonylprop-2-yne, which could be removed by careful flash chromatography to give an uncontaminated sample of phenylsulphonyl propadiene (15) (0.5g,25%). Spectral data was in agreement with that published.[47,48]

Ethynylation reactions - The propargylic alcohols required for the preparation of the allene sulphoxides were prepared by the addition of ethynylmagnesium bromide to the appropriate ketone according to the following general method.

Ethylmagnesium bromide, prepared by the addition of bromoethane (20mmol) in THF (5ml) to dry magnesium turnings (20mmol) was added dropwise to THF (50ml) saturated with dry, acetone free, ethyne to give a grey-pink solution of ethynylmagnesium bromide. The ketone (17mmol) was then added, the reaction mixture stirred at rt for 1½h, poured into saturated ammonium chloride and the product extracted with ether (3x30ml). The combined extracts were washed with brine (30ml), dried and the solvent evaporated. The products were purified by either distillation or flash chromatography.

8-Benzyloxy-3,7-dimethyloct-6-en-1-yn-3-ol (28) was prepared from 7-benzyloxy-6-methylhept-5-en-2-one (24) in 61% yield.
bp 130-140°C at 0.2mm Hg.

nmr $\delta(CDCl_3)$: 1.50(3H,s,Me), 1.74(4H,m,CH_2), 2.14(1H,s,C≡CH), 2.46(3H,s,Me), 3.90(2H,s,CH_2-O), 4.96(2H,s, CH_2-Ph), 5.50(1H,bt,C=CH), 7.32(5H,m,aromatic).

ir ν_{max} (film): 3350(bs,OH), 2900(s), 2085(w), 1485(m), 1450(s), 1355(s), 1060(s), 730(s), 690(s)cm^{-1}.

ms m/z (25eV): 108(22), 107(21), 92(69), 91(100), 81(24), 80(25), 79(28), 69(57), 43(90).

3,8-Dimethylnon-7-en-1-yn-3-ol (82) was prepared in 67% yield from 7-methyloct-6-en-2-one (79)[128] and was purified by distillation.
bp 108-10°C under water pump.

nmr $\delta(CDCl_3)$: 1.50(3H,s,Me), 1.62(6H,m,C=CMe), 1.71(4H,m, CH_2), 2.00(2H,m,C=C-CH_2), 2.35(1H,bs,OH), 2.43(1H,s,C≡CH), 5.13(1H,m,=CH).

ir ν_{max} (film): 3380(bs), 3300(s), 2930(s), 1448(m), 1372(s), 1113(m) cm^{-1}.

ms m/z: 165(1.2), 149(2.3), 147(2.8), 95(14), 82(30), 69(39), 55(25), 43(100).

6-Methyl-6-hydroxyoct-7-yn-2-one ethylene acetal (65) was prepared from heptan-2,6-dione monoethylene acetal (75) in 94% yield after purification by flash chromatography.

tlc: R_f = 0.54 (silica,ether).

nmr $\delta(CCl_4)$: 1.28(3H,s,Me-CO_2), 1.44(3H,s,MeCO), 1.62(6H, s,CH_2), 2.35(1H,s,C≡CH), 2.63(1H,bs,OH), 3.92(4H,s,acetal).

ir ν_{max} (film): 3410(bs), 3280(s), 2980(s), 2100(w), 1370(s), 1170(s), 1115(s), 1050(s), 785(s)cm^{-1}.

ms m/z: 183(5), 165(3), 87(100), 43(35).

1-Ethynyl-2-(3-methylbut-2-en-1-yl)cyclohexan-1-ol (100) was prepared in 45% yield from 2-(3-methylbut-2-en-1-yl)cyclohexanone (99).

gc: Retention time 60s on an SE-30 column at 130°C. No other peaks were observed.

nmr $\delta(CDCl_3)$: 1.70(17H,m,CH_2 and CH_3), 2.44(1H,s,C≡CH), 2.51(1H,s,OH), 5.20(1H,m,C=CH).

ir ν_{max} (film): 3450(OH,s), 3330(s), 2930(s), 2100(w), 1450(s), 1375(m), 1055(m), 970(m), 950(m), 840(w), 640(s)cm^{-1}.

ms m/z: 191(5), 95(31), 91(36), 81(39), 69(100), 55(66), 43(81), 41(100).

5-(Cyclohex-1-en-1-yl)-3-methylpent-1-yn-3-ol (118) was prepared from 5-(cyclohex-1-en-1-yl)butan-2-one (106) in 78% yield.

tlc: R_f = 0.51 (silica, 1:1, ether:light petroleum).

nmr $\delta(CDCl_3)$: 1.50(3H,s,Me), 1.50-2.20(12H,m,CH_2), 2.41(1H, s,-OH), 2.47(1H,s,C≡CH), 5.50(1H,m,C=CH).

ir ν_{max} (film): 3400(s,OH), 3300(s,≡-H), 2920(s,C-H), 2100(w,≡), 1440(s), 1365(s), 1120(s), 915(s), 635(s)cm^{-1}.

ms m/z: 163(8), 160(20), 145(100), 135(15), 131(55), 117(56), 109(30), 95(32), 91(66), 81(60), 79(96), 69(52), 67(93), 55(43), 53(32), 43(62), 41(64).

Attempts to observe ene reactions of 3-methyl-1-phenylsulphinylbut-1,2-diene (9)

(i) With Lewis acid catalysis - 3-Methyl-1-phenylsulphinylbuta-1,2-diene (9) (0.25g,1.3mmol) was dissolved in dichloromethane (5ml) and methylpropene (1ml) and tin (IV) chloride (2 drops) added. The mixture was stirred under nitrogen for 48h, poured into saturated sodium hydrogen carbonate solution and extracted with ether (2x10ml). The combined organic phases were washed with brine (10ml), dried and the solvent evaporated to give a colourless oil (0.2g) which was pure by tlc and had identical spectral properties to the starting material.

A similar experiment was performed using oct-2-ene as the ene component and with aluminium chloride/triethylaluminium as catalyst but unchanged starting material was again recovered.

Heating (9) (0.5g) and oct-2-ene (0.5g) together at 80°C in a Carius tube for 16h with a few drops of iron pentacarbonyl lead to near complete loss of starting materials and a complex mixture of products which could not be fully resolved by tlc.

The residual starting allene and catalyst were separated by flash chromatography and oct-2-ene removed by drying under high vacuum. The ir spectrum of the residual material shows a strong broad absorption at 1720cm^{-1} suggesting carbonyl incorporation and the ms is dominated by a series of peaks at 14amu intervals suggesting that octene is also

incorporated. However, the lack of any signal in the nmr spectrum assignable to methyl on a double bond, as well as the almost total absence of olefinic absorption, rules out the possibility of significant quantities of ene products having been formed.

(ii) Under high pressure - A solution of allene sulphoxide (9) (0.25g,1.3mmol) and methylpropene (1ml) in dichloromethane (3ml) were maintained at rt and 10.5kbar for 68h. Removal of solvent and methylpropene under reduced pressure gave complete recovery of starting material.

A similar experiment run for 8 days at 60°C and at a pressure of 9.5kbar again led to recovery of starting material.

(iii) Thermally - Allene (9) (0.5g) and oct-2-ene (0.5g) were heated in a Carius tube at 120°C. After 1h no reaction was observed by tlc so heating was continued at 160°C. After 5½h tlc showed that no starting material remained but a very large number of products had formed with R_f in the range 0.0-0.65 (silica, 2:1, light petroleuem:ether). The nmr spectrum did not suggest that there were significant quantities of the desired ene product present in the mixture.

Attempts to observe ene reactions of phenylsulphonylpropadiene (15) - Phenylsulphonylpropadiene (15) (120mg) and 2-phenylpropene (120mg) or 2-methoxypropene (120mg) were dissolved in toluene and heated in a Carius tube at 160°C for 7h. The solvent was then removed under reduced pressure and the products partially purified by preparative tlc (1mm, silica, 1:1 light petroleum:ether). The products from both reactions appear to be mixtures of double bond isomers and the integration of the nmr absorptions are therefore quoted as an approximate ratio.

(i) 2-Methoxypropene - Only one band of products was isolated and has $\delta(CCl_4)$ 1.30(2,s), 2.85(1,bm), 3.12(3,s), 5.40(2,d), 6.18(2,t), 7.40-8.00(10,m).

(ii) 2-Phenylpropene - Two product bands were isolated from this reaction, the more rapidly moving has $\delta(CCl_4)$ 1.50(2,s), 3.0(2,m), 3.43(2,bs), 6.10(1,m), 7.20-7.90(10,m). The slower product has $\delta(CCl_4)$ 1.45(2,s), 3.0(1,m), 3.45(2,m), 5.40(2,d), 6.20(2,t), 7.20-8.00 (15,m).

7-Benzyloxy-6-methylhept-5-en-2-one ethylene acetal (38) - Sodium hydride (50% dispersion in oil, 4.92g, 0.103mol) was washed thrice with light petroleum, cooled in an ice bath under nitrogen , and covered with DMF (20ml). 7-Hydroxy-6-methylhept-5-en-2-one ethylene acetal (36), prepared by the method of Camps *et al*,[101] (18.6g,0.10mol) was added in DMF (20ml) and the mixture stirred for 2h or until all effervescence had ceased. Benzyl bromide (16.0g,0.094mol) was then added and the reaction mixture stirred overnight, poured into water (150ml) and extracted with ether (3x50ml). The combined extracts were washed with water (3x50ml), dried and the solvent evaporated to give 7-benzyloxy-6-methylhept-5-en-2-one ethylene acetal (38) 24.0g (84%)which was used without purification.

nmr $\delta(CCl_4)$: 1.25(3H,s,Me), 1.65(3H,s,Me-C=C), 2.0(4H,m, CH_2), 3.82(6H,s,CH_2-O), 4.35(2H,s,$PhCH_2$), 5.35(1H,m,C=CH), 7.20(5H,s,aromatic).

ms m/z (25eV): 91(30), 87(84), 43(100).

7-Benzyloxy-6-methylhept-5-en-2-one (24) - The ketal (38) (8.53g, 31mmol) was refluxed overnight in acetone (300ml) with a few crystals of toluene sulphonic acid. The reaction mixture was then allowed to cool to rt and poured into water (1 litre) and the product extracted with ether (3x100ml). The combined extracts were washed with brine (2x100ml), dried, the solvent evaporated, and the resulting material distilled under high vacuum to give 7-benzyloxy-6-methylhept-5-en-2-one (24) 5.68g (80%) b.p. 105-20°C 0.2mm Hg.

nmr $\delta(CDCl_3)$: 1.68(3H,s,Me), 2.51(3H,s,MeCO), 2.20-2.60 (4H,m,CH_2), 3.88(2H,s,=-CH_2-O), 4.24(2H,s, CH_2-Ph), 5.38(1H,m,=CH), 7.29(5H,s,aromatic protons).

ir ν_{max} (film): 2900(m), 1715(s), 1455(m), 1360(m), 1080(m), 745(m), 705(m)cm^{-1}.

ms m/z: 232(0.1), 174(2.9), 124(10), 91(100), 43(86).

1-Methyl-2- phenylsulphinylmethyl -3-(propanal-2-yl)cyclopentene (43) - 8-Benzyloxy-3,7-dimethyl-1-phenylsulphinylocta-1,2,6-triene (23) (500mg) was dissolved in dry acetonitrile (6ml) and cooled under argon

in an ice bath, boron trifluoride etherate (0.25ml) added, and the mixture allowed to warm to rt. After 24h, the mixture was poured into saturated sodium hydrogen carbonate, solution extracted with ether (3x10ml) and the combined extracts washed with water (10ml), dried and evaporated.

The crude product was dissolved in THF (10ml) and stirred with aqueous oxalic acid (10% solution, 10ml) at rt for 3h. The mixture was poured into excess water, extracted with ether (4x10ml), the combined extracts washed with both sodium hydrogen carbonate solution (2x10ml) and water (10ml), dried and the solvent evaporated to give after flash chromatography (Et_2O) 1-methyl-2- phenylsulphinylmethyl -3-(propanal-2-yl) cyclopentene (43) (130mg) (29%) as a mixture of four diastereomers.

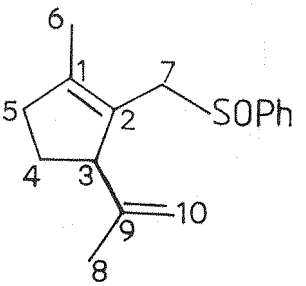
tlc	Rf = 0.30 (silica, ether).
nmr $\delta(CDCl_3)$:	0.95(3H,d,Me), 1.30(2H,m,CH_2), 1.52(3H,s,Me), 2.25(3H,m,allylic CH_2), 2.72(1H,m,CH-aldehyde), 3.60(2H,m,CH_2-S), 7.56(5H,m,aromatic), 9.65 (1H,s,CHO).
ir ν_{max} (film):	2920(s), 1718(s), 1430(s), 1082(s), 1037(s), 785(s), 750(s),cm^{-1}.
ms m/z:	151(21), 126(34), 125(55), 123(75), 121(20), 109(36), 107(41), 95(88), 94(27), 93(75), 92(25), 91(74), 81(46), 79(65), 78(54), 77(100), 67(23), 65(25), 55(25), 53(26), 51(49), 43(46), 41(40), 39(35).
uv λ_{max} (EtOH):	216(20,000), 248(16,000)nm.

A 2,4-dinitrophenylhydrazone was prepared and had m.p. 160-161°C.

1-Methyl-2-phenylsulphinylmethyl-3-(propen-2-yl)cyclopentene (2) was prepared as a mixture of diastereomers from allene (1) as described by Parsons.[6]

^{13}C nmr:	The chemical shifts given are the weighted mean of the shifts due to the different diastereomers.
$\delta(CDCl_3)$:	14.1 and 18.5(q,C6 and C8), 27.3(t,C4), 37.5(t,C5), 56.4(t,C7), 56.4(d,C3),

112.0(t,C10), 124.1, 128.8 and 130.9(d, aromatic ring), 125.5(s,C9), 143.5 and 146.6 (s,C1 and C2).



Other data were in agreement with that previously recorded.[6]

Attempted Pummerer Rearrangement of (2) - A typical experiment was as follows:-

Trifluoroacetic anhydride (2ml) was added to a solution of (2) (260mg,1mmol) in dry ether (2ml) cooled in an ice/salt bath. After 5m, m-chloroperbenzoic acid (1mmol) was added as a solution in ether and the reaction allowed to warm to room temperature. The mixture was stirred for 2h, poured into sodium hydrogen carbonate solution and extracted with ether (3x10ml). The combined extracts were dried (Na_2SO_4) and the solvent evaporated. The residue was taken up in methanol and stirred with sodium hydrogen carbonate at room temperature for 3h, poured into water, extracted with ether (2x10ml), dried and the solvent evaporated. Flash chromatography allowed the isolation of 1-methyl-2-phenylsulphonylmethyl-3-propen-2-ylcyclopentene (47) 20mg (7%) and 2-formyl-1-methyl-3-propen-2-ylcyclopentene (44) 30mg (20%), although the latter was of only modest purity.

The data for (47) was in agreement with an authentic sample and that for (44) as follows:-

tlc: Rf = 0.40 (silica, ether).

nmr $\delta(CCl_4)$: 1.70(3H,s,Me), 2.20(3H,s,Me), 1.30-2.30(4H, m,CH_2), 3.50(1H,m,CH), 4.70(2H,m,CH_2), 9.90 (1H,s,CHO).

1-Methyl-2-phenylsulphonylmethyl-3-propen-2-ylcyclopentene (47) - A solution of m-chloroperbenzoic acid (2mmol) in dichloromethane (5ml) was added to a solution of the sulphoxide (2) (520mg,2mmol) in dichloromethane at -20°C. After ¾h the reaction mixture was allowed to warm to rt, poured into sodium metabisulphite solution, and extracted with ether (2x15ml). The combined extracts were washed with saturated sodium carbonate solution (2x15ml), dried, the solvent evaporated and the residue purified by flash chromatography to give 1-methyl-2-phenylsulphonylmethyl-3-propen-2-ylcyclopentene (47) 220mg (42%).

tlc: R_f = 0.61 (silica, 1:1, ether:light petroleum).

nmr $\delta(CCl_4)$: 1.40(3H,s,Me), 1.56(3H,s,Me), 1.60-2.4(4H,m, CH_2), 3.40(1H,m,CH), 3.55 and 3.90(2H, AB quartet J = 14Hz, CH_2-SO_2), 4.70(2H,bd,=CH_2), 7.60(3H,m,aromatic), 7.85(2H,m,aromatic).

Benzyloxypropanone (29) - was prepared from 1-benzyloxyprop-2-yne[173] using a method analogous to that of Newman.[91] Yellow mercuric oxide (1.43g,6.6mmol) was dissolved in sulphuric acid (3.2ml) and water (13.2ml) and warmed to 40°C in an oil bath, and 1-benzyloxyprop-2-yne[173] (14.6g, 0.1mol) added slowly with vigorous stirring. When the addition was complete the reaction mixture was heated to 70°C for 1h, filtered through celite and extracted with ether (3x10ml). The combined extracts were washed with water (3x10ml), dried, and the solvent evaporated. Distillation under reduced pressure gave benzyloxypropanone (8.96g, 55%), b.p. 70-80°C at 0.1mm Hg.

Alternatively, benzyloxypropanone (29) was prepared by the Wacker oxidation of 1-benzyloxyprop-2-ene[174] using a method based on that of Tsuji.[92] Copper (I) chloride (1.0g, 10mmol) and palladium (II) chloride (0.36g,2mmol) were suspended in DMF (10ml) and water (1.2ml) and stirred vigorously under oxygen for 1h. 1-Benzyloxyprop-2-ene[174] (1.48g,10mmol) was then added and the reaction mixture stirred under oxygen for 16h, poured into dilute hydrochloric acid (20ml) and extracted with dichloromethane (3x10ml). The combined extracts were washed with both water (10ml) and copper (II) sulphate solution, dried, and the solvent evaporated. The residue was distilled under reduced pressure to give benzyloxypropanone 0.40g (41%), b.p. 85°C at 0.9mm Hg.

nmr $\delta(CCl_4)$: 2.0(3H,s,Me), 3.80(2H,s,O-CH_2-C(=O)), 4.45(2H,s, CH_2-Ph), 7.25(5H,s,aromatic).

ir ν_{max} (film): 2860(w), 1728(s), 1452(m), 1356(m), 1120(s), 738(s), 700(s)cm^{-1}.

ms m/z: 121(0.1), 108(14), 107(51), 91(100), 79(11), 77(8), 65(9), 58(9), 43(13).

Other data was in agreement with that published.[175]

1-Benzyloxy-2-methylbut-3-en-2-ol (25) - Magnesium turnings (1.44g,60mmol) and THF (15ml) were placed in a flask fitted with a cold finger condenser filled with acetone slush. Bromoethane (6.36g,60mmol) in THF (15ml) was added slowly and the reaction initiated by warming. On completion of the addition the mixture was warmed gently until all the magnesium dissolved. Benzyloxypropanone (29) (8.96g,55mmol) was added dropwise and the mixture refluxed under a water-cooled condensor for 40m, allowed to cool, poured into saturated ammonium chloride solution and extracted with ether (3x20ml). The combined extracts were washed with water (3x20ml), dried and the solvent evaporated to give 1-benzyloxy-2-methylbut-3-en-2-ol (25) 8.42g (80%).

nmr $\delta(CCl_4)$: 1.10(3H,s,Me), 3.15(2H,s,OCH_2), 4.35(2H,s,Ph-CH_2), 4.80-6.05(3H.A_2B,CH_2=CH-), 7.15(5H,s,Ph).

ir ν_{max} (film): 3420(s,b), 2860(s), 1495(m), 1450(s), 1365(s), 1205(m), 1100(s), 730(s), 695(s)cm^{-1}.

ms m/z: 121(1.4), 108(14), 107(23), 92(26), 91(100), 85(5), 79(11), 71(45).

1-Benzyloxy-2-methylbut-3-en-2-yl 3-oxobutanoate (27) - The allylic alcohol (25) (1.0g,5.2mmol) and sodium methoxide (~2mg) were dissolved in ether (3ml) and diketene (0.96g,11.4mmol) added. After 48h the mixture was poured into saturated sodium hydrogen carbonate solution (10ml) and the layers separated. The organic phase was washed with water (10ml), dried and the solvent evaporated to give 1-benzyloxy-2-methylbut-3-en-2-yl 3-oxobutanoate (27) 1.16g (59%).

nmr $\delta(CCl_4)$: 1.55(3H,s,Me), 2.10(3H,s,MeCO), 3.25(2H,s, CH_2-O), 3.60(2H,s,CO -CH_2- CO), 4.50(2H,s, Ph-CH_2), 5.0-6.3(3H,A_2B,CH_2=CH-), 7.25(5H, s,aromatic).

ir ν_{max} (film): 3500(w,enolic-OH), 1720(s,MeCO), 1745(s,ester), 1650(w,C=C), 1460(m), 1420(m), 1370(m), 1325(m), 1275(m), 1110(s), 1035(m), 740(m), 700(m)cm^{-1}.

ms m/z: 192(0.8), 164(3), 121(0.1), 107(27), 91(100), 85(8), 79(6), 77(5), 71(41), 65(11), 43(21).

Reactions of Ethyl-2-acetyl-5-oxohexanoate (53) with Sodium Acetylide - Sodium hydride dispersion (50%,360mg,7.5mmol) was washed twice with light petroleum and covered with THF (10ml) and the diketo ester (53) (1.36g,6.8mmol) added in THF (5ml). When the evolution of gas had ceased, sodium acetylide (360mg,7.5mmol) was added as a slurry in HMPA (10ml). After stirring at rt for 3d, the reaction mixture was poured into saturated ammonium chloride solution and extracted with ether (3x15ml). The extracts were combined, washed with water, dried and evaporated to give a material with no acetylenic absorption in the ir and which appears to be a mixture of starting material and HMPA by nmr.

The aqueous phase was then acidified with dilute hydrochloric acid and the extraction repeated to give after purification by flash chromatography 2-acetyl-5-methylhept-6-yn-5-olide (59) 130mg (10%). m.p. = 59-61°C.

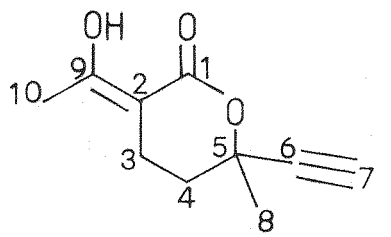
tlc: R_f = 0.60 (silica, 1:1, ether:light petroleum).

nmr $\delta(CCl_4)$: 1.67(5H,s,Me and CH_2), 2.0(5H,s,Me and CH_2), 2.48(2H,s,enolic OH and -H).

ir ν_{max} (film): 3310(s), 2975(s), 2140(m), 1750(s), 1660(s), 1420(s), 1350(s), 1160(s), 1100(s), 985(s) cm^{-1}.

ms m/z: 180(1.1), 138(18), 66(95), 43(100). An accurate mass measurement for M^+ gave m/z 180.0722, $C_{10}H_{12}O_3$ requires 180.0763.

^{13}C nmr $\delta(CDCl_3)$: 19.0(q,C8), 20.0(t,C4), 28.9(q,C10), 33.8(t,C3), 74.1(s,C5), 75.3(d,C7), 82.7(s,C6), 92.0(s,C2), 171.9(s,C9), 176.6(s,C1).



In another experiment the diketoester (53) (1.50g,7.5mmol) was treated with sodium hydride (200mg,8.25mmol) in ether. After 1h, when all evolution of gas had ceased, the ether was evaporated under reduced pressure, the sodium salt redissolved in liquid ammonia, and added to a solution of sodium acetylide (400mg, 8.25mmol) in liquid ammonia. After 2h the solvent was allowed to evaporate, the residue taken up in aqueous ammonium chloride and extracted with ether (3x15ml). After drying and evaporation of solvent a yellow oil (1.0g) was obtained which gave the following data.

tlc: R_f = 0.43 and a minor component.
R_f = 0.29 (silica,ether).

ir ν_{max} (film): 3450(s), 2960(s), 1720(s), 1670(s), 1385(s), 1300(s), 1230(s), 1123(s) cm^{-1}.

nmr $\delta(CCl_4)$: 1.03(s), 1.14(s), 1.25(m), 1.45(bs), 2.25(bm), 3.35(bq), 4.20(bq).

ms m/z: 200(0.03), 182(0.4), 136(2.3), 130(1.6), 121(1.7), 69(10), 55(18), 43(100). An accurate mass measurement for m/z 200 gave m/z 200.1166, $C_{10}H_{16}O_4$ requires 200.1048.

These data strongly suggest that the product is a mixture of 2-ethoxycarbonyl-5-hydroxy-5-methylcyclohexanone (57) and 4-ethoxycarbonyl-3-hydroxy-3-methylcyclohexanone (58). No attempts to separate these components were made.

Heptan-2,6-dione monoethylene acetal (75) - 5-Chloropentan-2-one ethylene acetal (60)[113] (5.0g,30.5mmol) and 1,2-dibromoethane (1.08g,6mmol) were added in an equal volume of THF, to anhydrous magnesium turnings (0.85g,36.5mmol) under argon, with cooling to prevent the temperature rising above 35°C. After stirring at rt for 16h the resulting Grignard reagent was diluted with further THF, to give a total volume of approximately 20ml and added dropwise to a solution of acetic anhydride (acid free, 10ml) in THF (100ml) at -80°C. The reaction mixture was stirred for ½h, allowed to warm to rt and poured into saturated sodium hydrogen carbonate solution. When all effervescence had ceased the layers were separated and the aqueous phase extracted with ether (3x50ml), the organic layers were combined, washed with both water (50ml) and brine (50ml), dried and the solvent evaporated. The resulting material was distilled (b.p. 96-98°C at 10mm) to give heptan-2,6-dione monoethylene acetal (75) 2.67g (51%).

nmr $\delta(CCl_4)$: 1.23(3H,s,Me), 1.56(4H,m,CH_2), 2.04(3H,s,Me), 2.38(2H,m,CH_2), 3.83(4H,s,acetal).

ir ν_{max} (film): 2930(s), 1710(s), 1370(m), 1230(m), 1050(m)cm^{-1}.

ms m/z: 157(4.2), 99(21), 87(100), 43(57).

6-Methyl-8-phenylsulphinylocta-6,7-dien-2-one (20) - 6-Methyl-8-phenylsulphinylocta-6,7-dien-2-one ethylene acetal (126) (1.16g) in THF (25ml), was stirred overnight with 2M hydrochloric acid (5ml). The reaction mixture was poured into saturated sodium hydrogen carbonate solution, the product extracted with ether (3x25ml) and the combined extracts were washed with sodium hydrogen carbonate solution, dried and the solvent evaporated to give 6-methyl-8-phenylsulphinyloct-6,7-dien-2-one 0.91g (91%). After purification by flash chromatography, the following data were obtained.

tlc: R_f = 0.25 (silica,ether).

nmr $\delta(CDCl_3)$: 1.80(7H,m,CH_2 and CH_3), 1.16(3H,d,Me), 5.98(1H,m,C=CH), 7.54(5H,m,aromatic).

ir ν_{max} (film): 2930(m), 1950(w), 1710(s), 1442(m), 1368(m), 1160(w), 1080(m), 1040(s), 918(m), 734(s), 688(w)cm^{-1}.

ms m/z: 263(M+1,2.3), 187(2.4), 137(10), 126(5), 125(4.8), 109(16), 95(11), 79(12), 77(11), 43(100).

Thermolysis of 6-Methyl-8-phenylsulphinylocta-6,7-dien-2-one (20) - 6-Methyl-8-phenylsulphinylocta-6,7-dien-2-one (20) (80mg) was sealed into a Carius tube under argon and heated to 275°C for 30m by immersion in refluxing tetraglyme. After cooling and opening the Carius tube the tlc (silica,ether) showed two major products R_f 0.73 and 0.64 as well as a range of minor products. Both spots are uv active but only the slower moving could be visualised with 2,4-dinitrophenylhydrazine solution. The two major products were isolated by flash chromatography and nmr, ir and ms spectra recorded. The data for the faster moving component were found to be identical to those found for diphenyldisulphide.

The slower moving compound gave the following data:-

ir ν_{max} (CCl_4): 2920(w), 1690(s), 1268(m), 750(bw)cm^{-1}.

nmr δ(CCl_4): 2.40(bs), 2.46(bs), 7.22(m), 7.65(m). The aromatic and aliphatic integrals are approximately equal.

ms m/z: 242(100), 227(77), 199(9), 197(11), 184(75), 165(13), 121(11), 109(12), 89(12), 77(16), 69(11), 65 (16), 63(17), 51(25), 43(74).

An accurate mass measurement for M^+ gave m/z 242.0773, $C_{15}H_{14}SO$ requires m/z 242.0765.

Reactions of (20) Catalysed by Amberlyst-15 - The allene (20) (100mg) was refluxed in toluene (3ml) with a few beads of Amberlyst-15 for 3h, after which time the tlc showed no starting material and a single product with R_f 0.63 (silica,ether), and nmr δ(CCl_4) 1.25-1.80 (2H,m), 2.05(3H,s), 2.40(4H,s), 5.70-6.80(2H,m), 7.10(2H,m), 7.42(5H,m) which strongly suggests that thermal rearrangement to 6-methylene-8-phenylsulphinylocta-7-en-2-one (78) has occurred.

5-Methylhex-4-en-1-ol - Crude 5-methylhex-4-enal prepared by the method of Market and Saucey[129] from 2-methylbut-3-en-2-ol (10g) was stirred with sodium borohydride (1.0g) in ethanol (10ml) for 2h. The reaction mixture was poured into saturated ammonium chloride solution and extracted with ether (3x30ml), the extracts combined and washed with water (30ml), dried and the solvent evaporated. Distillation gave 5-methylhex-4-en-1-ol 1.78g (14% overall from 2-methylbut-3-en-2-ol). b.p. 40-50°C at 0.03mm Hg.

nmr $\delta(CCl_4)$: 1.65(6H,m,Me), 1.30-2.10(4H,m,CH_2), 2.90(1H,bs, OH), 3.55(2H,t,CH_2-O), 5.10(1H,m,C=CH).

ir ν_{max} (film): 3480(bs), 2920(s), 1450(m), 1375(m), 1058(s).

ms m/z: 114(21), 96(46), 81(100), 71(24), 69(92), 67(30), 59(24), 57(20), 55(60), 41(75). An accurate mass measurement for M^+ gave m/z 114.1077,$C_7H_{14}O$ requires m/z 114.1045.

5-Methylhex-4-en-1-yl toluene-4-sulphonate (84) - 5-Methylhex-4-en-1-ol (0.5g,4.4mmol) was dissolved in pyridine (5ml), cooled to 0°C and toluene-4-sulphonyl chloride (1.25g,6.5mmol) in pyridine (5ml) added. The reaction mixture was allowed to warm to rt and stand for 4h, a few drops of water were then added and the reaction mixture allowed to stand for a further ½h before pouring into excess water and extracting with ether (3x5ml). The combined extracts were washed with dilute hydrochloric acid (5ml), copper (II) chloride solution (5ml) and water (5ml), dried and the solvent evaporated to give without further purification 5-methylhex-4-en-1-yl toluene-4-sulphonate (84) in quantitative yield.

nmr $\delta(CCl_4)$: 1.50-2.00(10H,m,CH_3CH_2), 2.40(3H,s,Me), 3.90(2H,t,CH_2-O), 4.90(1H,bt,=CH), 7.45(4H, bq,aromatic)

Attempted Preparation of 1-bromo-5-methylhex-4-ene (83) - Pyridine (0.5g,6.6mmol) and phosphorus tribromide (0.65g,2.4mmol) were added successively to a solution of 5-methylhex-4-en-1-ol (0.25g,2.2mmol) in ether (3ml). The mixture was stirred at room temperature for 12h, poured into water and extracted with ether (3x10ml). The combined organic

extracts were washed with dilute hydrochloric acid, aqueous copper (II) chloride and water, dried and the solvent evaporated. Purification by flash chromatography gave tri(5-methylhex-4-en-1-yl)phosphite (86) 120mg (44%) for which the following data was recorded:-

tlc: R_f = 0.47 (silica,ether).

nmr $\delta(CCl_4)$: 1.63(9H,s,Me), 1.70(9H,s,Me), 1.90(12H,m,CH_2), 4.00(6H,d of t,J=6,10Hz,CH_2-OP), 5.08(3H,m, C=CH).

A Lassaigne sodium fusion test was positive for phosphorus and negative for bromine.

Thermolysis of 3,8-Dimethyl-1-phenylsulphinylnona-1,2,7-triene (16) - 3,8-Dimethyl-1-phenylsulphinylnona-1,2,7-triene (16) (0.5g) in acetonitrile (20ml) was sealed into a Carius tube and heated at 140°C for 1½h. When the reaction mixture had cooled the tube was opened and the solvent removed under reduced pressure. Flash chromatography gave two fractions: the first was a mixture of diphenyldisulphide and 3,8-dimethylnon-7-en-1-yn-3-ol (82); and the second 3,8-dimethyl-1-phenylsulphinylnona-1,3,7-triene (89) which gave the following data:-

nmr $\delta(CDCl_3)$: 1.61(3H,s,Me), 1.69(3H,s,Me), 2.06(3H,s,Me), 2.16(4H,m,CH_2), 5.12(1H,m,CH=CMe_2), 6.09(1H,t, CH=CMe), 6.57(1H,d,J=10Hz,CH=CH), 6.82(1H,d, J=10Hz,CH=CH), 7.55(5H,m,aromatic). A small number of impurity peaks are also present but could not be assigned.

ms m/z: 274(1.7), 257(100), 189(60), 163(22), 147(63), 109(46), 95(35), 79(86), 77(44), 69(72), 55(26), 41(50).

Reactions of 3,8-Dimethyl-1-phenylsulphinylnona-1,2,7-triene (16) catalysed by Lewis Acids - Several attempts were made to prepare (87) by treating allene (16) with Lewis acids but in only one experiment was the starting material not recovered. In this experiment a solution of the allene (16) (200mg) in dichloromethane (3ml) was stirred with tin (IV) chloride (2 drops) under nitrogen for 12h. The reaction mixture

was poured into water and extracted with ether (3x5ml). The combined extracts were washed with water, dried, the solvent evaporated and the product purified by preparative tlc. The following data was collected:-

nmr $\delta(CDCl_3)$: 0.86(6H,dd), 1.10(3H,d), 1.40-1.80(6H,m), 2.50(2H,m), 3.28(1H,bs), 6.04(1H,m), 7.50 (5H,m).

ir ν_{max} (film): 3500(s), 2970(s), 1900(w), 1445(m), 1375(w), 1090(m), 1050(s), 775(s)cm^{-1}.

^{13}C nmr $\delta(CDCl_3)$: 18.17(q), 24.36(t), 25.12(t), 32.92(t), 35.49(t), 51.66(s), 104.58(d), 122.0(s), 124.51(d), 129.14(d), 130.82(d), 145.4(s). Many of these resonances show slight splitting suggesting that two diastereomers may be present.

ms m/z: 274(2.0), 258(2.8), 250(3.5), 231(3.4), 218(5), 216(6), 215(4.1), 149(77), 126(80), 107(100), 105(43), 93(72), 91(72), 79(71), 78(57), 77(77), 69(64), 55(51), 51(37), 43(88), 41(75).

3,8-Dimethyl-1-phenylsulphonylnona-1,2,7-triene (90) was prepared by treating a solution of the sulphoxide (16) (0.50g,1.83mmol) in methanol (7ml) with a solution of oxone (1.83mmol) in water (7ml). The mixture was stirred at room temperature for 4h, poured into water and extracted with ether (3x10ml). The combined organic extracts were washed with water, dried and the solvent evaporated. Purification of the residue by flash chromatography gave starting material (40mg) and 3,8-dimethyl-1-phenylsulphonylnona-1,2,7-triene (90) 30mg (6%) for which the following data was recorded:-

tlc: R_f = 0.47 (silica,ether).

nmr $\delta(CDCl_3)$: 1.35(2H,m,CH_2), 1.58(3H,s,Me), 1.68(3H,s,Me), 1.77(3H,d,J=3Hz,Me), 2.00(4H,m,CH_2), 5.05(1H, m,CH=), 6.07(1H,m,HC=C=C), 7.48 and 7.90(5H, m,aromatic).

ir ν_{max} (film): 2920(m), 1925(w), 1450(m), 1330(m), 1310(m), 1150(s), 1085(m), 730(s),cm^{-1}.

ms m/z: 290(1.0), 234(15), 149(71), 133(35), 107(35), 93(72), 91(36), 82(100), 81(29), 77(60), 69(48), 67(32), 55(34).

An accurate mass measurement for M^+ gave m/z 290.1268, $C_{17}H_{22}SO_2$ requires 290.1340.

In another experiment which was performed in an identical manner except that the sulphoxide was stirred with oxone for 12h, only 2,7-dimethyl-9-phenylsulphonylnona-7,8-dien-2-ol (92) was isolated.

nmr $\delta(CCl_4)$: 1.00(6H,s,Me), 1.20-2.00(8H,m,CH_2), 1.65(3H, s,Me), 5.90(1H,m,C=C=CH), 7.50 and 7.80(5H,m, aromatic).

2-(3-Methylbut-2-en-1-yl)cyclohexanone (99) - Sodium hydride dispersion (50% in oil, 3.36g, 70mmol) was washed with light petroleum (2x10ml), covered with THF (20ml) and cyclohexanone (6.85g,70mmol) added cautiously. After the reaction had subsided the mixture was refluxed for 1h, allowed to cool and 1-bromo-3-methylbut-2-ene (10.40g, 70mmol) added dropwise. The mixture was then stirred for 1h without further heating, poured into water and extracted with ether (3x30ml). The combined extracts were washed with water (3x20ml), dried and the solvent evaporated to give 2-(3-methylbut-2-en-1-yl)cyclohexanone[176] (99), 11.70g (100%) which did not require purification.

nmr $\delta(CDCl_3)$: 1.75(6H,m,Me), 2.20(11H,m,CH_2), 5.10(1H,m,C=CH).

gc - retention time 20s on SE-30 at 150°C. In addition, an impurity with retention time 95s and of approximately 4% of the area of the main peak is observed, suggesting the presence of some dialkylated material.

ir ν_{max} (film): 2920(s), 1710(C=O,s), 1450(m), 1028(m)cm^{-1}.

ms m/z: 166(M^+,35), 165(100), 151(33), 147(40), 141(48), 129(33), 117(38), 111(44), 98(78), 91(33), 81(45), 69(81), 55(19), 41(90).

Late scans during the ms run also show a few ions up to m/z 234

which are assignable to di-alkylated material.

Benkeser Reductions - A typical experiment was as follows. To ethylamine (15ml), freshly distilled from sodium, was added successively finely chopped lithium wire (0.49g, 70mmol) and 4-phenylbutan-2-one ethylene acetal (3.0g, 15.6mmol) and the reaction mixture was then maintained between -10°C and 5°C for 12h. Water was then added, the ethylamine removed under reduced pressure and the residue extracted with ether (4x10ml). The combined organic extracts were washed with brine (10ml), water (10ml), dried and the solvent evaporated.

The product mixture was separated by flash chromatography to give 4-cyclohexen-1-ylbut-3-en-1-yne (109) 0.30g (15%) and 4-cyclohexen-3-ylbutan-2-one ethylene acetal 0.96g (31%), the latter being slightly contaminated with starting material.

The following data was recorded for (109):

tlc: R_f = 0.67 (silica, 1:1 light petroleum:ether).

nmr $\delta(CDCl_3)$: 1.67(4H,m,CH_2), 2.15(4H,m,CH_2), 2.9(1H,d,J=3Hz, C≡C-H), 5.46(1H,dd,J=15 and 3Hz,=CH-C≡),5.89 (1H,m,=CH-CH_2), 6.69(1H,d,J=5Hz,=C-CH=).

ir ν_{max} (film): 3300(s,≡-H), 2930(s), 2090(m,C≡C), 1.650(s,C=C), 1590(m), 1445(m), 1432(m), 1188(m), 954(s), 790(m)cm^{-1}.

ms m/z: 132(47), 120(15), 115(19), 104(91), 91(100), 79(62), 78(43), 77(35), 65(35), 51(54), 39(60).

An accurate mass measurement for M^+ gives 132.0971, $C_{10}H_{12}$ requires 132.0939.

The following data was recorded for 4-cyclohexen-3-ylbutan-2-one ethylene acetal.

tlc: R_f = 0.53 (silica, 1:1 ether:light petroleum).

nmr $\delta(CCl_4)$: 1.23(3H,s,Me), 1.30-2.00(11H,m,CH,CH_2), 3.82(4H, s,acetal), 5.35(1H,m,=CH), 5.57(1H,m,CH=).

7-Phenylsulphinylmethyl-8-(propen-2-yl)[4,3,0]bicyclonon-6-ene (96) - The allene (95) (4.5g,1.5mmol) was stirred in dichloromethane (100ml) with boron trifluoride etherate (0.5ml) under argon for 24h. The solution was poured into water, the layers separated and the aqueous phase extracted with ether (3x30ml). The combined organic phases were washed with sodium hydrogen carbonate solution, dried, and the solvent evaporated. The residual oil was purified by flash chromatography (1:1 petrol:ether) to give 7-phenylsulphinylmethyl-8-(propen-2-yl)[4,3,0]bicyclonon-6-ene (96) 3.45g (77%) as a mixture of diastereomers.

nmr $\delta(CDCl_3)$: 0.80-1.10(8H,m,CH_2), 1.55(3H,several peaks, CH_3), 1.40(3H,m,CH_2-C=C), 3.10-3.80(3H,m, CH_2SO_2 and CH). 4.68(2H,m,=CH_2), 7.50(5H,m, aromatic).

ir ν_{max} (film): 3060(m), 2920(s), 1640(s), 1478(m), 1442(s), 1410(m), 1370(s), 1085(s), 1040(s), 900(s), 784(m), 747(s), 690(s)cm^{-1}.

ms m/z: 175(100), 159(14), 133(23), 119(18), 105(20), 91(28), 81(22), 77(18).

tlc: R_f = 0.52 (silica,ether).

^{13}C nmr $\delta(CDCl_3)$: 18.6, 25.6, 25.7, 26.0, 26.5, 35.5, 35.9, 46.1, 46.2, 54.9, 55.2, 56.1, 111.2, 122.3, 124.3, 124.5, 128.9, 129.0, 131.0.

Attempts to separate the four diastereomers by HPLC using ODS-2 and Partisil 10 columns were unsuccessful.

2-Phenylsulphonylmethyl-3-(propen-2-yl) [4,3,0] bicyclonon-1-ene (101) - To a solution of the sulphoxide (96) (0.90g,3mmol) in methanol (12ml) was added oxone[131] (1.38g,4.5mmol) in water (12ml), the resulting mixture stirred at rt for 3½h, poured into water and extracted with ether (3x15ml). The combined organic extracts were washed with brine (15ml), dried, the solvent evaporated and the residue purified by flash chromatography (1:1 ether:petrol) to give 2-phenylsulphonylmethyl-3-(propen-2-yl)[4,3,0]bicyclonon-1-ene (101) 0.50g (53%) as a mixture of two diastereomers which were not separated.

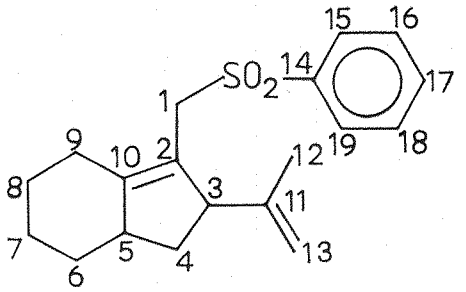
tlc: R_f = 0.66 (silica,ether).

nmr $\delta(CDCl_3)$: 1.0-2.0(8H,m,CH_2), 1.53(3H,s,CH_3), 2.0-2.5 (3H,m,allylic C-H), 3.35(1H,bd,CH), 3.62 and 3.96 (2H,broadened AB,J=13Hz,CH_2-SO_2), 4.68(2H,m,C=CH_2), 7.58 and 7.85(5H,m,aromatic).

ir ν_{max} (film): 2930(s), 1642(w,C=C), 1450(s), 1310(s), 1320(s), 1145(s), 1088(s), 900(m), 740(m), 690(m)cm^{-1}.

ms m/z: 316(M^+,4.7), 175(100), 174(69), 133(34), 119(22), 105(23), 91(35), 81(24), 77(25).

^{13}C nmr $\delta(CDCl_3)$: The product is a mixture of two diastereomers and many peaks are observed as a 1:4 doublet. The values quoted are for the major isomer. 18.8(q,C12), 26.3(t,C6), 25.7 and 25.5 (t,C7 and C8), 35.6 and 35.3(t,C4 and C9), 45.9(d,C5), 53.5(d,C3), 53.8(t,C1), 111.3(t, C13), 120.9(s,C11), 128.9, 128.4, 135.5 and 139.2(s,C14,15,16,17,18,19), 146.7 and 150.6(s,C10 and C2).



2-(3-Methylbut-2-en-1-yl)-3-tributylstannylcyclohexanone (104) -

To cyclohex-2-enone (0.48g,5mmol) in THF at -78°C was added tributyltinlithium (6mmol) prepared from tributyltin hydride by the method of Still,[147] followed after 15m by 1-bromo-3-methylbut-2-ene (0.89g,6mmol). The reaction mixture was allowed to warm to rt, poured into aqueous ammonium chloride, the layers separated and the aqueous phase extracted with ether (3x10ml). The organic phases were

combined, washed with both brine (10ml) and water, and dried. The solvent was evaporated and the crude material purified by flash chromatography to give 2(3-methylbut-2-en-1-yl)-3-tributylstannylcyclohexanone (104) 1.21g(44%).

tlc: R_f = 0.54 (silica, 3:1 light petroleum:ether).

nmr $\delta(CDCl_3)$: 0.92(6H,m,CH_2-Sn), 1.1-2.5(36H,m,CH_2 and CH_3), 5.06(1H,m,=CH).

ir ν_{max} (film): 2920(s,C-H), 1710(s), 1460(m), 1325(m), 1070(w), 660(w)cm^{-1}.

ms m/z: 399(100), 291(28), 235(37), 179(50), 121(27), 69(25).

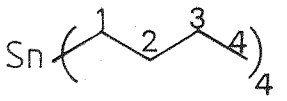
Reaction of 2-(3-methylbut-2-en-1-yl)-3-tributylstannylcyclohexanone (104) with n-Butyl lithium - A solution of the stannyl ketone (104) (0.46g,1mmol) in ether (3ml) was cooled under nitrogen to -80°C and n-butyllithium (1.2mmol) added slowly. After 30m the reaction mixture was allowed to warm to 0°C, poured into ammonium chloride solution, the layers separated and the aqueous phase extracted with ether (10ml). The organic phases were combined, dried, and the solvent evaporated. The ir spectrum of this product showed a carbonyl absorption at 1710cm^{-1} of approximately 45% of the intensity observed in the starting material (relative to the CH band at 2920cm^{-1}) and also an -OH absorption at 3520cm^{-1}. Repetition of the n-butyllithium treatment gave a product with a strong OH absorption and no carbonyl absorption in the ir. The tlc of this material shows two compounds R_f = 0.70 and 0.77 (silica, 3:1 light petroleum:ether) which were partially separated by flash chromatography.

The faster moving fraction is tetrabutyltin (60mg) and gave the following data.

ir ν_{max} (film): 2930(s), 1460(m), 1375(m), 783(m)cm^{-1}.

nmr $\delta(CCl_4)$: 0.90(8H,m,$SnCH_2$), 1.10 to 1.70(21H,m,CH_2 & CH_3).

^{13}C nmr $\delta(CDCl_3)$: 8.79(t,C1), 13.73(q,C4), 27.44 and 29.33(t, C2 and C3).



The slower fraction appears to be 1-butyl-2-(3-methylbut-2-en-1-yl)-3-tributylstannylcyclohexanol and gave the following data.

ir ν_{max} (film): 2930(s), 1460(m), 1375(m), 783(s)cm^{-1}.

nmr $\delta(CCl_4)$: 0.90(7H,m,CH-Sn and CH_2-Sn), 1.10 to 1.60 (37H,m,CH_2 and CH), 1.75(8H,m,allylic CH), 5.25(1H,m,C=CH).

^{13}C nmr: Due to the small amount of sample available and the possibility of four diastereomers the spectrum is very complex and could not be fully assigned. However, the particularly strong resonances at $\delta(CDCl_3)$ 9.00, 13.72, 27.66 and 29.42 are probably due to tributyltin, weaker signals at 74.75, 71.32 and 70.98 are probably C-OH and the signals at 134.60, 132.45 and 122.31 indicate the presence of at least one carbon-carbon double bond.

These observations are all consistent with the proposed structure.

1-(Butan-3-on-1-yl)-cyclohexanol ethylene acetal (117) - was prepared as follows using the method of Ponaras.[159] 1-Bromobutan-3-one ethylene acetal (118)[177] in THF (40ml) was added dropwise to magnesium turnings (7.2g,0.3mol) and THF (50ml) under argon. The reaction was initiated by adding a few small crystals of iodine. As soon as the reaction starts it was cooled in an ice bath and the rate of addition of halide adjusted so as to keep the temperature at about 15-20°C, great care being taken not to allow the temperature to exceed 25°C even for short periods. When the addition was complete the reaction mixture was stirred for ½h at rt and then cyclohexanone (9.8g,0.1mmol) added dropwise with cooling as before and the stirring continued for a further 16h. The reaction mixture was poured into saturated ammonium chloride and extracted with ether (3x50ml). The combined extracts were washed with brine (2x50ml), dried and the solvent

evaporated to give 1-(butan-3-on-1-yl)-cyclohexanol ethylene acetal (117) 20g (98%) which was used without further purification and gave the following data:-

nmr $\delta(CDCl_3)$:	1.27(3H,s,Me), 1.30 to 1.70(14H,m,CH_2), 1.90(1H,bs,OH), 3.92(4H,s,acetal).
ms m/z:	214(0.4), 199(2.1), 181(4.2), 171(6.3), 153(2.3), 127(8), 99(9), 87(100), 81(7), 73(10), 71(10), 55(12), 43(45).
ir ν_{max} (film):	3450(bs), 2930(s), 1448(s), 1373(s), 1220(s), 1065(s), 850(s)cm^{-1}.
tlc:	R_f = 0.12 (silica, 1:1 ether:light petroleum).

1-(Butan-3-on-1-yl)cyclohexene ethylene acetal (115) - Chlorosulphonyl isocyanate (4.5g,32mmol) was dissolved in dry benzene (20ml) and ethanol (1.45g,32mmol) and triethylamine (6.40g,64mmol) added successively with cooling. After stirring for ½h at room temperature, the triethylamine hydrochloride was filtered off under nitrogen and 1-(butan-3-on-1-yl)cyclohexanol ethylene acetal (117) (4.5g,21mmol) added to the filtrate. The reaction mixture was stirred for 16h at rt under nitrogen, washed with water (3x20ml), dried, and the solvent evaporated to give after purification by flash chromatography, 1-(butan-3-on-1-yl) cyclohexene ethylene acetal (115) 2.56g (64%). Spectral data obtained were in agreement with those published.[153,159]

1-(Butan-3-on-1-yl)cyclohexene (106) - was prepared from 1-(Butan-3-on-1-yl)cyclohexene ethylene ketal (115) by the method of Borowiecki *et al.*[153] and gave the expected spectral data.[153]

Reactions of 5-cyclohexen-1-yl-3-methyl-1-phenylsulphinylpenta-1,2-diene (97) catalysed by Lewis acids - A typical experiment was as follows. The allene (0.75g,2.62mmol) in acetonitrile (30ml) was stirred with tin (IV) chloride (330mg,0.78mmol) under an atmosphere of argon for 12h. The mixture was then poured into water and extracted with ether (3x15ml). The combined extracts were washed with sodium hydrogen carbonate solution (15ml), dried, and the solvent evaporated. The product was purified by flash chromatography and gave the following

materials.

1) 6-Methyl-5-phenylthiomethyl-1,2,3,4-tetrahydronaphthalene (119) (10mg) (1.6%).

tlc: R_f = 0.76 (silica,ether).

nmr $\delta(CCl_4)$: 1.75(4H,m,CH_2), 2.30(3H,s,Me), 2.75(4H,m,CH_2), 4.06(2H,s,CH_2-S), 6.85(2H,s,aromatic), 7.28 (5H,m,aromatic).

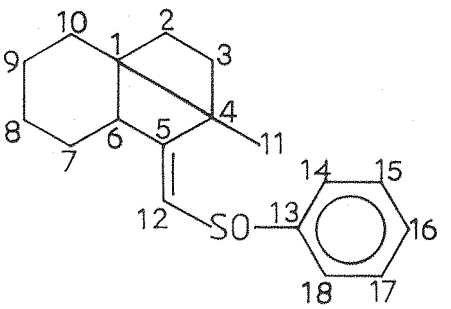
ms m/z: 268(2.8), 159(100), 158(76).

2) Z 4-Methyl-5-phenylsulphinylmethylenetricyclo-[4,4,0,$0^{1,4}$] decane (120a) 320mg (43%).

tlc: R_f = 0.43 (silica,ether).

nmr $\delta(CDCl_3)$: 1.53(3H,s,Me), 1.40-1.90(13H,m,CH,CH_2), 5.86 (1H,s,=CH), 7.53(5H,m,aromatic).

^{13}C nmr $\delta(CDCl_3)$: 15.03(q,C11), 21.44, 23.14, 23.21, 24.82(t,C7, C8, C9 and C10), 31.75, 32.92(t,C2 and C3), 46.59(d,C6), 53.76(s,C1), 57.33(s,C4), 119.12(d,C12),123.92, 128.99(t,C14,C15,C17 and C18) 130.04(t,C16), 145.84(s,C5), 166.28(s,C13).



ms m/z: 286(M^+,0.4), 271(27), 270(23), 269(100), 177(15), 159(62), 119(35), 117(30), 105(47), 95(81), 93(34), 79(47), 77(59), 67(51), 55(40), 41(56).

An accurate mass measurement for M^+ gave m/z 286.1347, $C_{18}H_{22}SO$ requires m/z 286.1391.

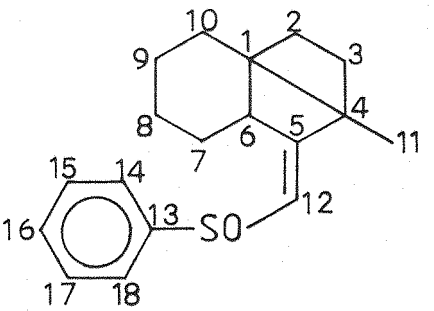
ir ν_{max} (film): 2930(s), 1660(m), 1448(s), 1088(m), 1045(s), 795(s), 760(s), 700(s),cm^{-1}.

3) E 4-Methyl-5-phenylsulphinylmethylenetricyclo-[4,4,0,$0^{1,4}$] decane (120b) 240mg (32%).

tlc: R_f = 0.52 (silica,ether).

nmr δ($CDCl_3$): 1.03(3H,s,Me), 1.40-1.90(13H,m,CH_2 and CH), 5.91(1H,s,=CH), 7.60(5H,m,aromatic).

^{13}C nmr δ($CDCl_3$): 11.70(q,C11), 21.77, 22.66, 23.21 and 23.73 (t,C7,C8,C9 and C10), 31.68 and 32.46(t,C2 and C3), 46.88(d,C6), 54.62(s,C1), 55.97(s,C4), 117.10(d,C12), 124.22, 129.14(d,C14,C15,C17 and C18), 130.32(d,C16), 146.13(s,C5), 169.79(s,C13).



ms m/z: 286(7), 271(32), 270(22), 269(100), 177(15), 161(24), 159(55), 119(34), 105(48), 95(54), 91(63), 77(51), 67(33), 55(20), 41(22).

ir ν_{max} (film): 2920(s), 1655(m), 1442(s), 1080(m), 1040(s), 790(s), 755(s), 695(s)cm^{-1}.

The stereochemistry of the double bond in the two isomers was determined by adding the shift reagent tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium portionwise to a mixture of the two isomers when final downfield shifts of 53Hz and 42Hz were observed for the methyl group of fractions 2 and 3 respectively thus confirming their assignment as Z and E resepctively.

Reaction of 4-Methyl-5-phenylsulphinylmethylenetricyclo-[4,4,0,$0^{1,4}$]decane (120) with Raney Nickel - 4-Methyl-5-phenylsulphinylmethylenentricyclo-[4,4,0,$0^{1,4}$]decane (120) (100mg) was mixed with an approximately equal volume of Raney nickel suspension, diluted with ethanol (5ml) and refluxed under argon for 12h. After allowing to cool to rt the mixture was filtered through celite to remove the nickel and the solvent evaporated to give 4-methyl-5-phenylthiomethylenetricyclo-[4,4,0,$0^{1,4}$]decane (123)

tlc: R_f = 0.73 (silica,ether).

nmr $\delta(CCl_4)$: 1.10(3H,s,Me), 1.60(13H,m,CH_2,CH), 5.48(1H,s, C=CH), 7.10(5H,m,aromatic).

4-Methyl-5-phenylsulphonylmethylenetricyclo-[4,4,0,$0^{1,4}$]decane (125) - To 4-methyl-5-phenylsulphinylmethylenetricyclo-[4,4,0,$0^{1,4}$] decane (120) (200mg, 0.7mmol) in dichloromethane (5ml) was added at 0°C m-chloroperbenzoic acid (80%,250mg,1.1mmol) in dichloromethane (5ml). After stirring for 1h the solution was poured into aqueous sodium hydrogen carbonate solution, the layers separated, the organic phase dried and the solvent evaporated to give, after purification by flash chromatography, 4-methyl-5-phenylsulphonylmethylenetricyclo[4,4,0,$0^{1,4}$] decane (125) 200mg (95%).

tlc: R_f = 0.68 (silica,ether).

m.p.: 76-78°C (recrystallised from ether/pentane).

Chemical analysis: Calculated for $C_{18}H_{22}SO_2$: C,71.49; H,7.33; S,10.60: found C,71.38; H,7.32; S,10.43.

nmr $\delta(CCl_4)$: 1.00(3H,s,Me), 1.60(13H,m,CH_2 and CH), 5.72 and 5.80(1H,s,C=CH), 7.50(3H,m,meta and para aromatic), 7.80(2H,m,ortho aromatic).

ir ν_{max} (film): 2920(s), 1650(m), 1443(m), 1300(s), 1140(s), 1083(m), 715(m), 686(m)cm^{-1}.

ms m/z: 302(M^+,2.3), 285(23), 237(23), 181(19), 161(100), 160(49), 145(47), 132(29), 131(36), 119(52), 117(38), 105(51), 91(77), 79(54), 77(84), 67(47), 55(37), 51(41) 41(57).

A doubly recrystallised sample has been submitted for X-ray crystallographic analysis.

Reduction of 4-methyl-5-phenylsulphonylmethylenetricyclo [4,4,0,$0^{1,4}$]decane (125) with lithium in liquid ammonia - To the sulphone (130mg) in dry ether (1ml) and liquid ammonia (10ml) were added small pieces of lithium wire until the blue colour persisted for 30m (approximately 300mg lithium). The reaction was then quenched by the addition of ethanol (1ml) and the ammonia allowed to evaporated. The residue was taken up in water, extracted with ether (3x10ml), the combined extracts dried and the solvent evaporated to give, after flash chromatography, 4-methyl-5-methylenetricyclo[4,4,0,$0^{1,4}$]decane (126) (10mg (14%).

tlc: R_f = 0.64 (silica,light petroleum).

nmr $\delta(CCl_4)$: 1.00(3H,s,Me), 1.23(5H,m,CH_2,CH), 1.50(6H,m, CH_2), 4.25 and 4.35(2H,s,C=CH_2).

ir ν_{max} (film): 2925(s), 1687(w), 1455(w), 1378(w).

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