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INTRAMOLECULAR DIELS-ALDER REACTIONS OF CONFORMATIONALLY RESTRICTED SYSTEMS

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I declare that **'Intramolecular Diels-Alder Reactions of Conformationally Restricted Systems'** is my own work and that all sources that I have used or quoted have been indicated and acknowledged by means of complete references.

Signed by candidate

Richard S. Gordon

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Finally I wish to thank my wife, for putting up with me for the last three years. The stranger in the house is back.

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Summary

In the first phase of this investigation, the synthesis of triene systems, linked *via* a diester tether was investigated with the aim of studying the respective thermal Intramolecular Diels-Alder (IMDA) properties. It was envisaged that the diene and dienophile would be linked *via* a conformationally restricted spacer, *trans*-cyclohexane-1,2-dicarboxylic acid anhydride.

Nucleophilic opening of the anhydride with (2*E*,4*E*)-hexane-2,4-dien-1-ol afforded the diene tether, after which the resulting carboxylic acid was modified using a three-step sequence to afford the important primary alcohol – which was used as the precursor for all triene syntheses. This was coupled with a variety of carboxylic acid dienophiles to yield the desired trienes whose Intramolecular Diels-Alder properties were investigated. For example, heating of the triene derived from acryloyl chloride gave a mixture of both *endo*- and *exo*-cycloadducts. These were characterised as the corresponding lactones following removal of the spacer and lactonisation of the exposed functional groups.

IMDA reactions carried out on the remaining carbon based trienes displayed the expected rate enhancement, and selectivity variations, with the introduction of a dienophile activating group, and the expected attenuation of reactivity (and selectivity) with the introduction of additional substitution on the dienophile.

With the precedent of the foregoing results, attention was turned to the synthesis of oxygen and nitrogen containing dienophiles. Silyloxy protection of glycolic acid followed by coupling with the aforementioned alcohol yielded an advanced substrate for IMDA investigation. Desilylation of the alcohol followed by oxidation gave the desired *dienal*, which was subjected to thermal IMDA conditions. This gave a mixture of cycloadducts, the major component of which arose as a result of *endo* addition of the dienophile.

Reaction of the *dienal* with *p*-toluenesulfonylisocyanate, followed by thermal IMDA treament, gave the analogous nitrogen containing cycloadducts, which also comprised largely of *cis*-fused products arising from *endo*-addition of the dienophile.

The second phase of this investigation was targeted at the synthesis and reactivities of 1-phenylsulfonyl-1,2,(4+*n*),(6+*n*)-tetraenes (n = 2 – 4), with the objective of extending this investigation to the synthesis of these allenyl compounds in enantiomerically pure form. It was

envisaged that these axially chiral compounds would be suitable substrates for enantioselective IMDA investigations.

With this in mind, (8*E*) 1-phenylsulfonylundeca-1,2,8,10-tetraene was synthesised, however, its IMDA properties were disappointing, and involved reaction of the unactivated π-bond, to give a single cycloadduct in low yield. Synthesis of the three carbon tether analogue (7*E*) 1-phenylsulfonyldeca-1,2,7,9-tetraene was carried out and showed promising IMDA reactivity. The major cycloadduct arose from *exo*-addition of the activated π-bond. Chemoselective hydrogenation was carried out on the major cycloadduct.

Synthesis of (6*E*) 1-phenylsulfonylnona-1,2,6,8-tetraene was carried out and the resulting tetraene was highly reactive and complete reaction was achieved under exceptionally mild conditions. A similar result was observed with a furanyl derived analogue. In both cases, the major cycloadduct arose from *exo*-addition of the dienophile.

The above approach was extended to other two-carbon linker tetraenes possessing substitution at C-1 and C-6. In both cases, IMDA reactivity was observed, the former requiring mild temperatures to achieve reaction. As in the above examples, the major product arose from *exo*-addition of the dienophile.

This approach was extended further to the use of oxygen-terminated cyclohexadienyl systems. IMDA reaction followed by base mediated fragmentation of the cycloadducts gives rise to spiro-fused products. The same product is also synthesised *via* a base mediated intramolecular Michael reaction of the cycloadduct precursors.

In the last phase of this investigation, attempts were made to synthesise the allenyl compounds in high enantiomeric purity by prior isolation or synthesis of the respective alkynol precursors. This was first achieved by resolution of the respective alkynols and then later by asymmetric reduction of the achiral precursors.

The respective (*M*)- and (*P*)-phenylsulfonylallenes were subsequently synthesised for the unsubstituted aliphatic tetraenes and their IMDA reactivities were investigated. The results obtained demonstrated an effective route to the synthesis of cycloadduct diastereomers in high optical purity. This approach has been used to synthesise an (*M*)-phosphinylallenyl enantiomer, which, in turn gave rise to an *exo*-cycloadduct with high diastereoselectivity.

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CHAPTER 1

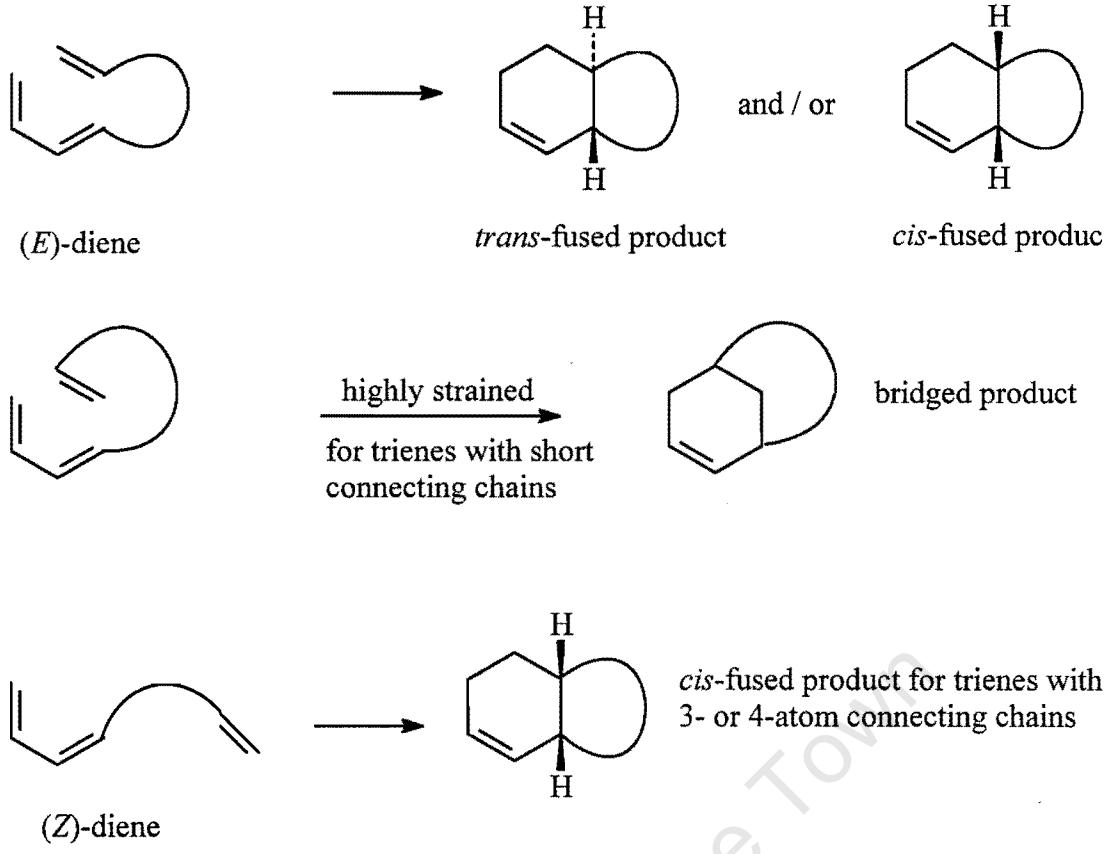
INTRODUCTION

Since its discovery in 1928,[1] the Diels-Alder reaction has enjoyed widespread use in organic synthesis. The ability to generate two bonds in a newly formed cyclohexenyl system, with simultaneous creation of up to four stereocenters, in a stereoselective and largely predictable fashion, has resulted in its applications to numerous synthetic challenges. The intramolecular version, in which the diene and dienophile are tethered *via* a connecting chain, was first reported in 1953 by Alder and Schumacher, [2] but it was not until the early 1960's that additional examples began to appear in the literature.[3]

Since the mid-1970's, a virtual explosion of interest in the IMDA reaction has occurred and its progress has been extensively reviewed.[4] The increase of reactivity generally observed with IMDA reactions is largely due to favourable entropy considerations, whereas, heightened regioselectivity is usually owing to constraints imposed by the connecting chain. The use of IMDA reactions also allows for the synthesis of stereochemically complex polycyclic ring systems. These features all account for the growth of applications of this reaction in organic synthesis particularly in regard of natural product synthesis.[5]

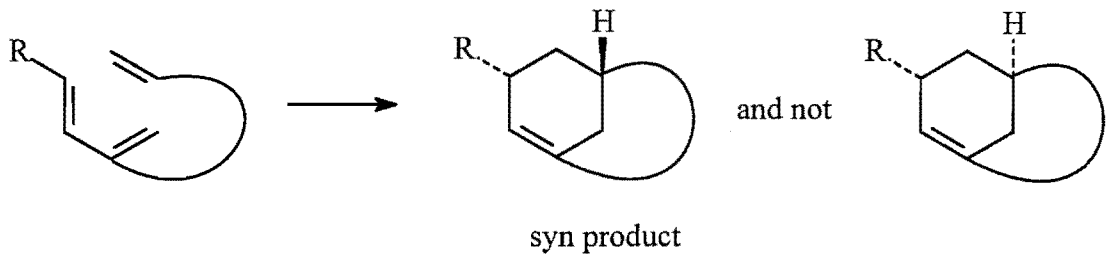
IMDA substrates may be divided into two classes depending on the point of attachment of the diene to the dienophile. Type I substrates involve trienes with the connecting chain attached to the diene terminus (be it (*E*) or (*Z*), Scheme 1), whereas type II substrates have the dienophile tethered *via* one of the internal diene positions (Scheme 2).

The ability to control the stereo- and regioselectivity of these cycloadditions is critical for their successful application in synthesis. Except for some specialised cases,[2,6] IMDA reactions involving type I trienes are only feasible if the connecting chain contains three or more atoms. In the vast majority of successful reactions, the fused rather than bridged product is obtained, even when (*Z*)-dienes are employed – the bridged product may be formed when the connecting chain comprises ten or more atoms.[7]



Scheme 1 Type I trienes

The most significant issue in reactions of type I trienes is that of stereoselectivity, as mixtures of *cis*- and *trans*-fused cycloadducts are accessible from (*E*)-dienes – the most frequently encountered class of substrates. The analogous problem does not arise in reactions of type I (*Z*) trienes with three or four atom connecting chains, as the transition states leading to *trans*-fused products are highly strained, and cis-fused cycloadducts usually predominate.[8]



Scheme 2 Type II trienes

Simple diastereoselection is often a potential concern for type II IMDA reactions. However, type II substrates with bridged chains comprising three or four members cyclise exclusively to the *syn*

cycloadduct, since the transition state leading to the *anti* diastereomer is more strained than the corresponding transition state for the *syn* diastereomer.[9] This class of trienes is restricted to substrates with connecting chains of at least three atoms – owing to the attendant strain encountered in the transition state.[10] Since the focus of this thesis will be the synthesis and reactions of type I (*E*-dienes), substrates of type II trienes will not be discussed further.

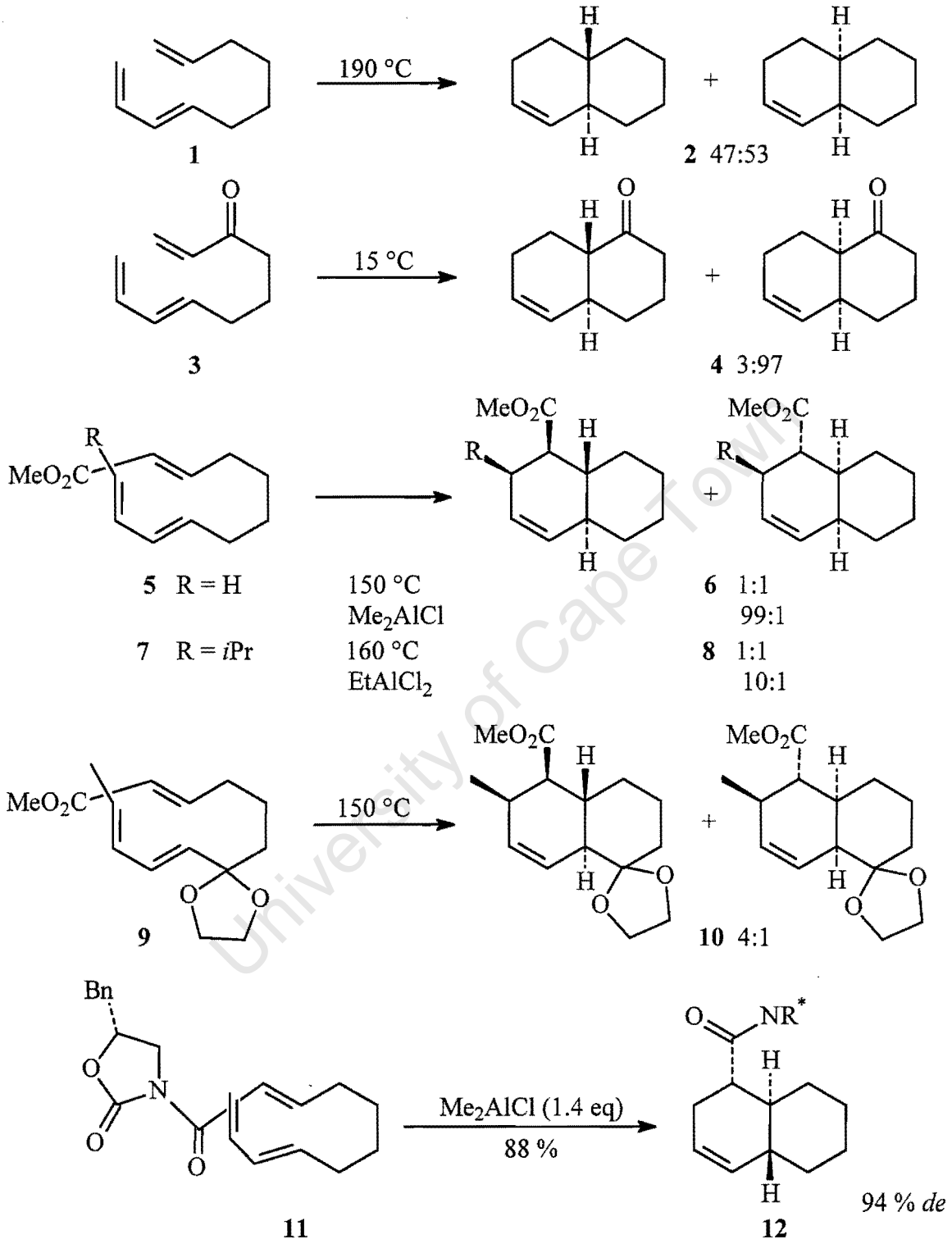
It has been shown that intramolecularity alone (see below), is often insufficient to ensure the best levels of stereoselectivity. Accordingly, as this concept evolved, it emerged that other diastereoselective elements can be introduced to influence the reaction outcome.

It has been known for many years that the introduction of a dienophile-activating group has a significant effect on the stereoselectivity of IMDA reactions (as well as rate enhancement). For example, reaction of **1** at 190 °C for 7 h gave both *cis*- and *trans*-octalins **2** in ~ 1:1 ratio (Scheme 3).[11] This ratio changes to 3:97 favouring the *cis*-product **4** when an internal oxo group is introduced (as for **3**).[12]

When an activating group is introduced in the terminal position on the dienophile (such as for ester **5**), little or no diastereoselection is obtained.[13] This is also observed when simple achiral substitution is introduced on the terminal position of the diene (as exemplified by compound **7**).[14] The introduction of substituents onto the tether markedly affects the diastereoselectivity of the IMDA reaction, and is dependent on factors such as the relative stereochemistry (and size) of the substituent and its position on the linker (as demonstrated by the IMDA reaction of **9**).[13] In general, steric effects are more important than electronic effects because the diastereoselectivity of reaction is greatly influenced by the introduction of substitution. Thus, in most IMDA reactions, the Alder *endo* rule fails because secondary orbital interactions are not of prime importance.[4b]

The use of Lewis acid catalysis in IMDA reactions has been used for some time, and is currently fulfilling an increasingly important role. This is exemplified by compounds **5** and **7** in which significant diastereoselection is achieved by the use of simple Lewis acids.[15,14] This approach has been extended to the use of chiral Lewis acids which may involve complexes with aluminium, titanium, boron, and lanthanide elements.[16] The use of these catalysts has introduced a new dimension into asymmetric Diels-Alder reactions due to the stereocontrol they impart on the substrate. For example, Evans *et al.*,[17] demonstrated the use of oxazolidinone chiral auxillaries, in

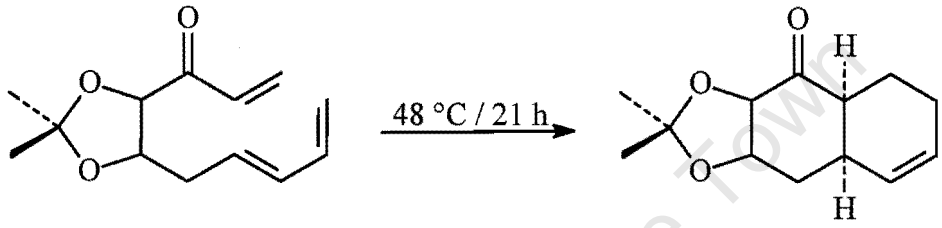
conjunction with C-2 symmetric Lewis acid catalysts, to achieve cycloadduct **12** in good yield and with excellent *diastereoselection.*[17] This approach has been extended further to enantioselective IMDA reactions.[18]



Scheme 3 Diastereoselection of decatrienes as a result of substituent effects and Lewis acid catalysis

Variation in reaction conditions may significantly influence the diastereoselection of IMDA reactions. The choice of solvent is often important as the diastereoselectivities may be influenced by solvent properties. For example, the effective use of liquid crystals as a reaction medium for IMDA reactions has recently been reported.[19] Other reaction variables may include: the use of reaction promoters[20] and activation of the reaction by other means – for example ultrasound.[21]

Other strategies to improve the level of stereochemical control in IMDA reactions have focussed on restricting the rotation of the linker molecule. For example, the use of cleavable control groups such as isopropylidene acetal **13** significantly alters diastereoselection (Scheme 4 *cf.* **3**).[22] Further demonstrations of this principle will be given in Chapters 2 and 4).



13 **14** (75 %, 10:1)

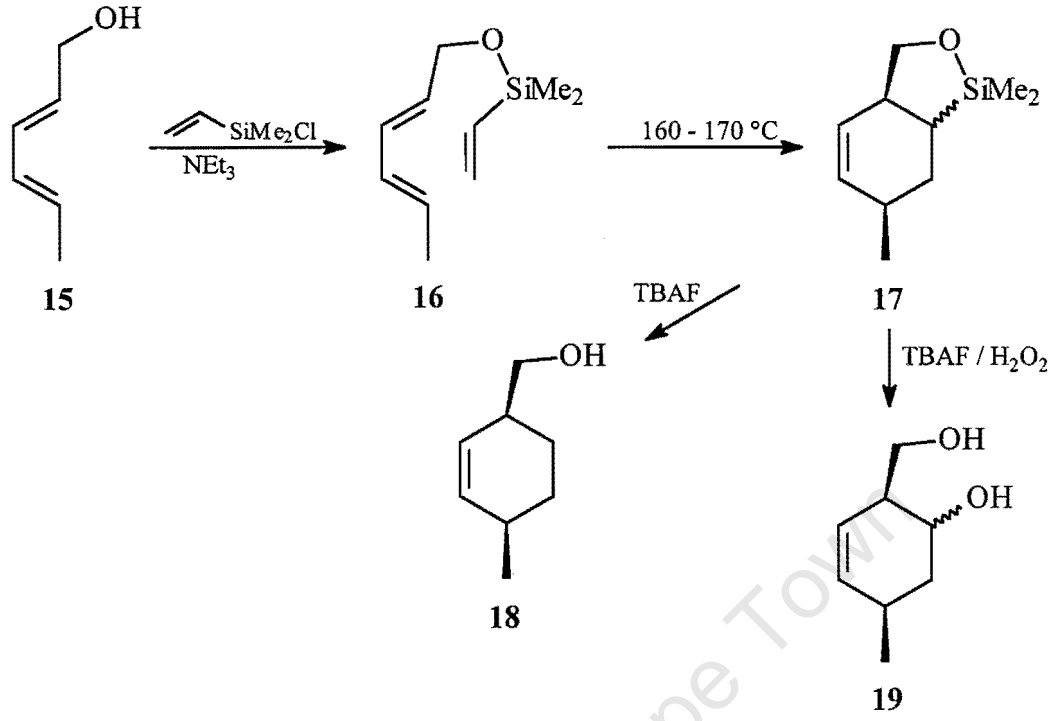
Scheme 4 Ispropylidene acetal substitution in the linker.

Synthesis of a temporary diene and dienophile linker allows for a powerful variation of the IMDA approach. Cleavage of the linker post-cycloaddition gives the products of overall *inter*molecular Diels-Alder reaction, but with the inherent regio- and stereochemical advantages of the *intra*molecular variant.

The best tether control groups should facilitate the achievement of a dominant transition state, induce required stereochemistry, and contain useful functionality that may be used in the product for subsequent synthetic manipulations. Several studies have been conducted involving temporary tethers, several of which will be discussed.

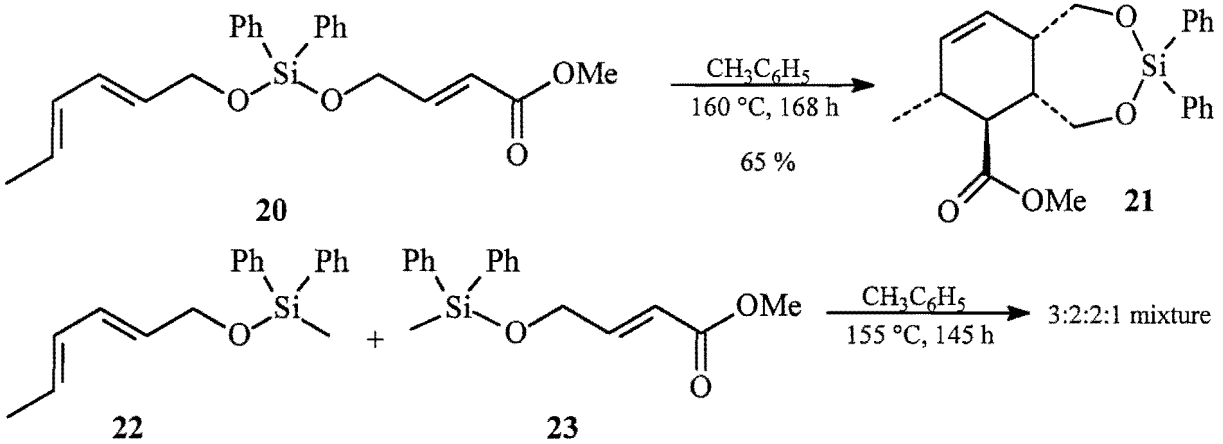
Silicon tethers have become increasingly popular as linkers in IMDA reactions.[23] The synthetic usefulness of these linkers is derived from their chemical properties as they are readily made, inert in most reactions, and are easily and selectively removed. Not only do the silicon derivatives serve as protecting groups, before and after the IMDA reaction, but may also be transformed into

other expressions of functionality, particularly in the case of the carbon-silicon bond – as exemplified by compound **16** in Scheme 5.



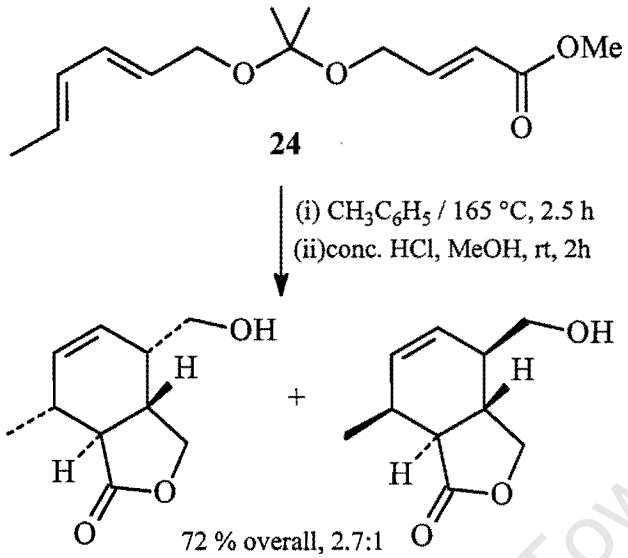
Scheme 5 An example of a silyl tethered IMDA reaction and subsequent functional group transformations

The above approach has been extended by Craig *et al.*,[24] to the use of silyl acetals in which the IMDA reaction was directly compared to the *inter*molecular variant of a closely-related system. The IMDA reaction of **20** gave **21** exclusively, whereas reaction of diene **22** and dienophile **23** gave a mixture of four products (stereo- and regioisomers) in a ratio of 3:2:2:1 (Scheme 6). Clearly the introduction of a tether has not only overcome the regiochemical dimension of the reaction, but also served to generate a stereodefined product.



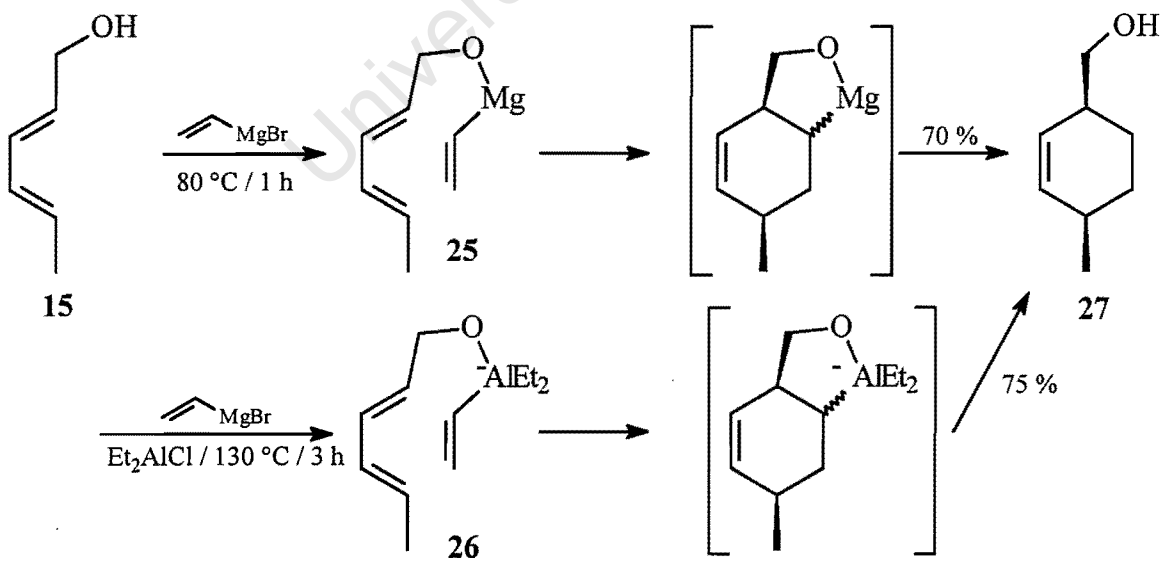
Scheme 7 Silyl acetal tethered IMDA reaction in relation to the intermolecular variant

Replacing the silicon atom with a carbon atom was also explored by Craig *et al.*,[25] and the IMDA reactivities/diastereoselectivities of these systems were investigated (for example **24** in Scheme 7). The stereoselectivities of the reactions were good in the presence of substitution on the intervening carbon atom.



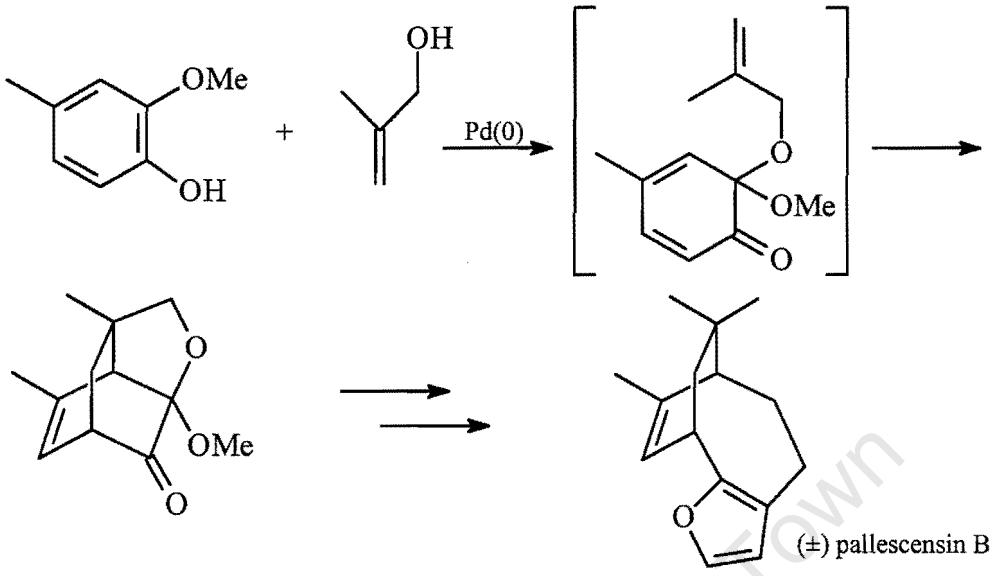
Scheme 7 Carbon acetal-tethered IMDA reaction followed by cleavage of the linker post-reaction

Stork *et al.*[26] introduced the concept of metal atoms as linkers for IMDA reactions with great success. Both magnesium and aluminum proved to be efficient linkers – as exemplified by trienes **25** and **26** in Scheme 8. Recently, the analogous reaction has been carried out using boron as an alternative linker.[27]



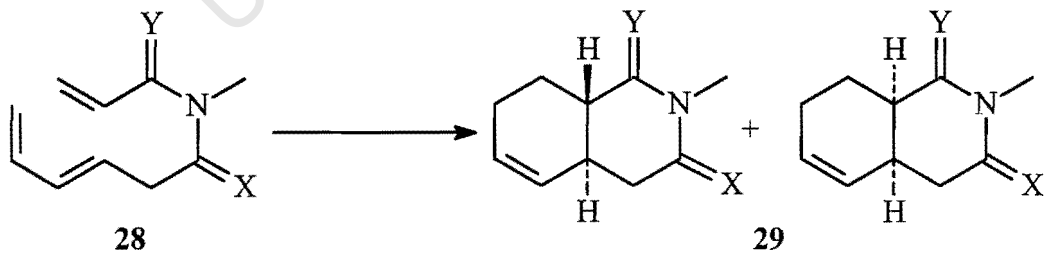
Scheme 8 Examples of IMDA reactions of metal tethered trienes

Ethers,[28] thioethers[29] and amines (see Scheme 10)[30] have also been used as tethers in IMDA reactions, with variable degrees of success. For example, Liao *et al.*,[31] used this approach for the total synthesis of (±)-pallescensin B (Scheme 9).



Scheme 9 IMDA reaction of a triene linked with an ether tether used for the synthesis of (±) pallescensin B

The presence of an amide in the tether has a significant effect on IMDA diastereoselection – as demonstrated by **28a-c** in Scheme 11. These effects were first observed by Oppolzer[30] and are related to conformational preferences exerted by the amide unit, and depend on the position of the amide in the linker and the direction of the amide. For example **28b** exhibits poor diastereoselectivity whilst activation of the dienophile (**28c**) results in *trans*-diastereoselectivity. Reversing the amide in the linker, results in a modest reversion of diastereoselectivity (as shown for **28a**).

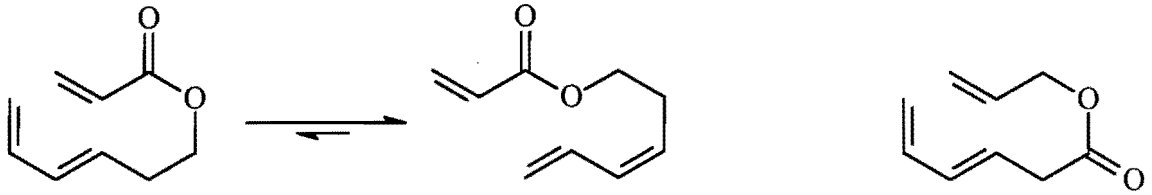


28 **29**

Triene	X	Y	Temp (°C)	*trans*:*cis*
a	O	H_2	185	33:67
b	H_2	H_2	140	48:52
c	H_2	O	80	89:11

Scheme 10 Diastereoselectivity variation due to amide variation in the tether

In contrast to the amide linker, trienes incorporating ester moieties (in short tethers) are unreactive as the ester prefers to adopt an s-*trans* orientation as opposed to an s-*cis* orientation required for reaction.[32] For example, compounds **30** and **31** fail to cyclise when heated at temperatures up to 275 °C (Scheme 11).[33] These systems will be discussed later. Combinations of ester and ether linkers[34] in the tether have also been investigated as well as the use of lactones.[35]

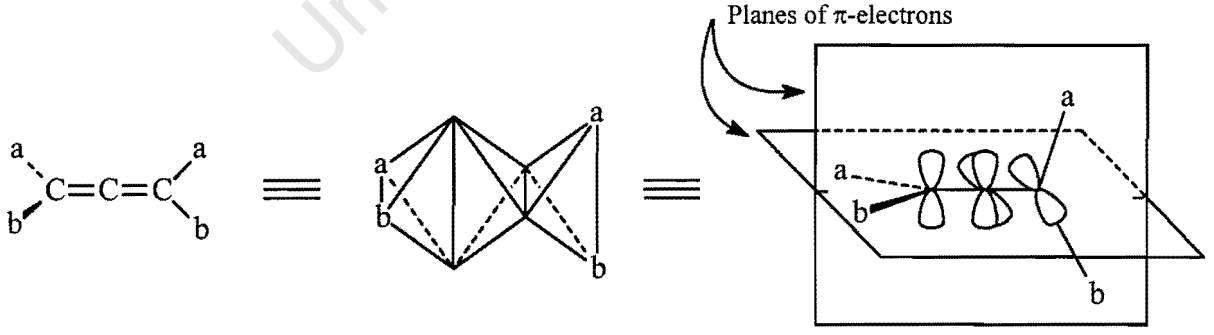


30 **31**

Scheme 11 Poor reaction of **29** and **30** due to preferred conformation of the ester in a *trans*-orientation

In 1887 Burton and Pechmann[36] prepared the first allenic compound, but it was only in 1954 that its structure was confirmed.[37] As a result of the mistaken belief that cumulated π-systems were unstable, allenes were initially regarded as curiosities.[38] This, as well as insufficient methodology available for their syntheses, hindered the earlier growth of allene chemistry.

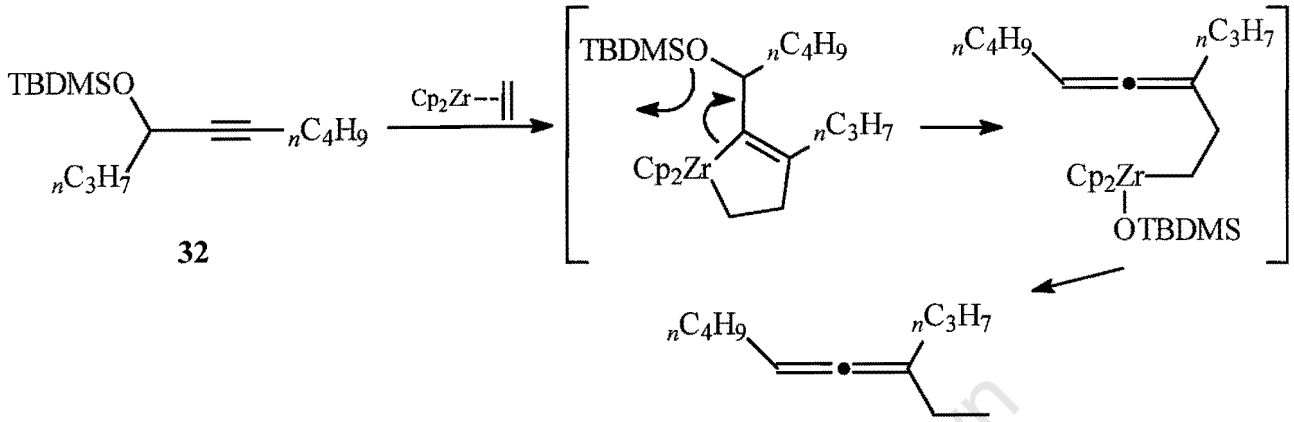
The physical properties of allenes have been reviewed.[39] A π-bond results from the overlapping of the two p-orbitals of each sp^2-hybridised carbon atom of the alkene. In the case of 1,2-diene systems, the central carbon is sp-hybridised with two sets of orthogonal p-orbitals available for bonding with the remaining p-orbitals of the two terminal sp^2-carbon atoms of the diene (Scheme 12).



Scheme 12 Orthogonal planes of allenyl orbitals

For maximum overlap to occur between these orbitals, the resulting π-bonds must be orthogonal to each other. As a consequence of this orthogonality, the diene is not conjugated, although an allenyl π-bond will conjugate with a π-system attached to it. (*viz.* C=C=CHC=C)

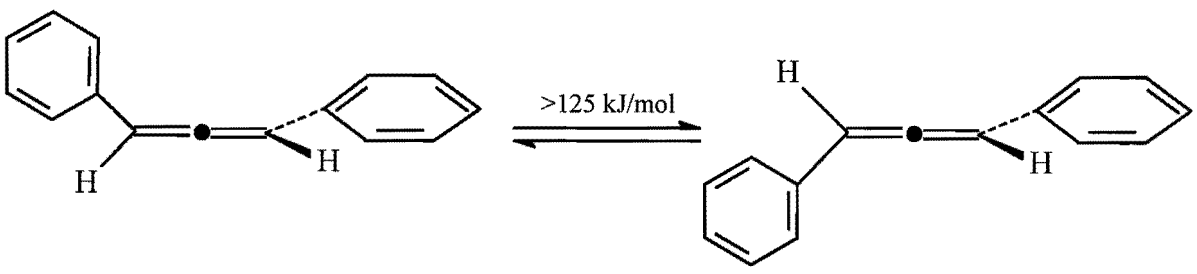
With the growth of interest in this field, allenes are routinely prepared using a variety of procedures[38 - 40] and several extensions of these approaches have been observed in recent literature.[41 - 44] For example, Takahashi *et al.*,[45] demonstrated the synthesis of trisubstituted allenes when reacting a variety of propargylic ethers with ethylene (or equivalents thereof) in the presence of zirconocene – as exemplified by compound **32** in Scheme 13.



Scheme 13 Zirconocene mediated synthesis of allenes exemplified for **31**

IMDA reactions involving allenes were first reported in the 1970's,[46] and have since experienced moderate coverage in the literature.[47] Of particular interest was the synthesis and use of optically pure allenes (for IMDA purposes) as the vast majority of reported IMDA investigations utilised achiral allenes (for exceptions see later). Hence the synthesis of chiral allenes will be discussed.

It was already pointed out in 1875 by van't Hoff that an appropriately substituted allene should exist in two enantiomeric forms. The experimental realization of van't Hoff's predictions proved to be difficult, and 60 years elapsed before the first optically enhanced allenic compound was obtained in the laboratory.[48] The lack of isomerisation of allenes is clearly demonstrated when one considers that the energy requirement for stereoisomerisation of chiral allenes amounts to 195 kJ/mol for 1,3-dialkylallenes and to >125 kJ/mol for diarylallenes (Scheme 14). Therefore chiral allenes generally maintain their stereochemical integrity.



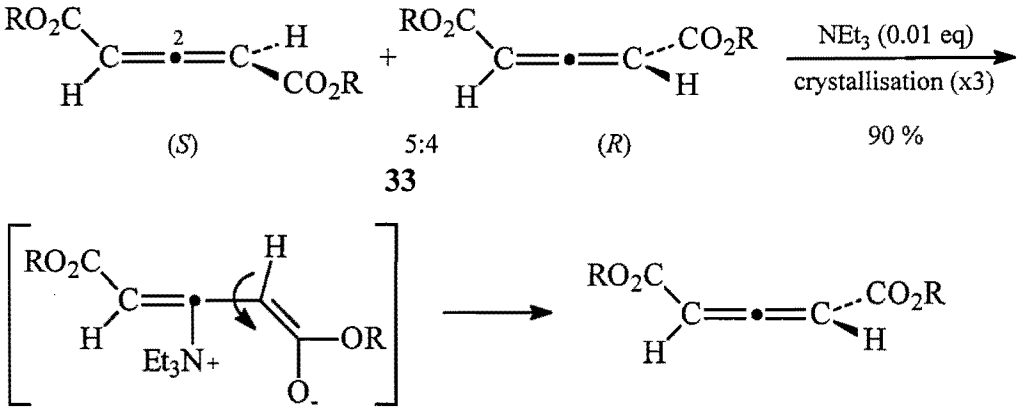
Scheme 14 Energy requirements for isomerisation of allenes

There are two possible approaches for obtaining chiral allenes. *viz.* resolution and asymmetric synthesis. Resolution of racemic allenes is a useful method to obtain optically enhanced entities; however, this methodology is often limited to the substrates bearing appropriate functionality (such as a carboxylic acid) and several methods are routinely used.[49]

Recent applications of chiral stationary phases for gas chromatography[50] and HPLC[51] allows for small-scale separation of simple racemates. Deracemisation (destruction of one enantiomer) of racemic allenyl compounds is an effective and direct method for obtaining chiral allenes. The only limitation of this approach is the use of stoichiometric amounts of chiral reagent. This reagent may take the form of a variety of nucleophiles – for example Lewis acids[52] or amine bases.[53]

A further extension of resolution methodology has involved the principle of chirality 'amplification', by complexation of the allenyl functionality with an organometallic reagent.[54] In this approach, the chirality of the allene is enhanced by coordination with a transition metal, and the resulting complexes are easily separated.

A relatively new approach, asymmetric transformation, has been used for obtaining allenes in high optical purity. This procedure involves isomerisation of the allene through a process of repeated epimerisation-recrystallisation experiments (exemplified by compound **33** in Scheme 15).[55] The thermodynamically driven epimerisation is based on the active equilibrium between Michael addition (of catalytic base) to the highly activated C-2 position followed by rotation around C-2 and then elimination. This process was derived from a procedure used by Pirkle,[56] in which the first successful enantiomeric epimerisation of allenyl amino acid derivatives (in high *ee*'s) was reported.



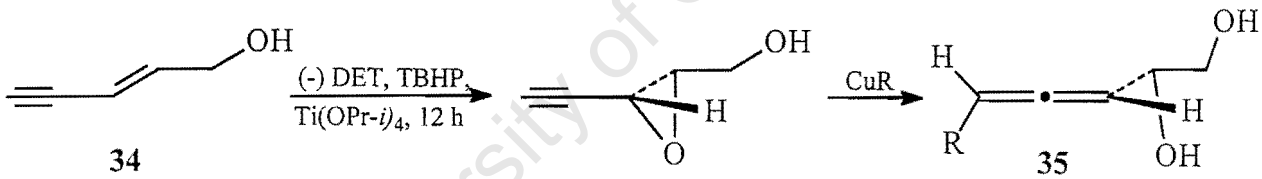
33

Scheme 15 An example of asymmetric transformation of allenes as demonstrated for R = (-)-(*L*)-Menthyl

Enantiomerically pure allenes may be obtained *via* asymmetric synthesis. This may be achieved by rearrangement/elimination reactions of chiral precursors or by direct enantiomeric synthesis of the allene. Many methods are known for the synthesis of these compounds [57] and only a few examples of recent applications will be mentioned.

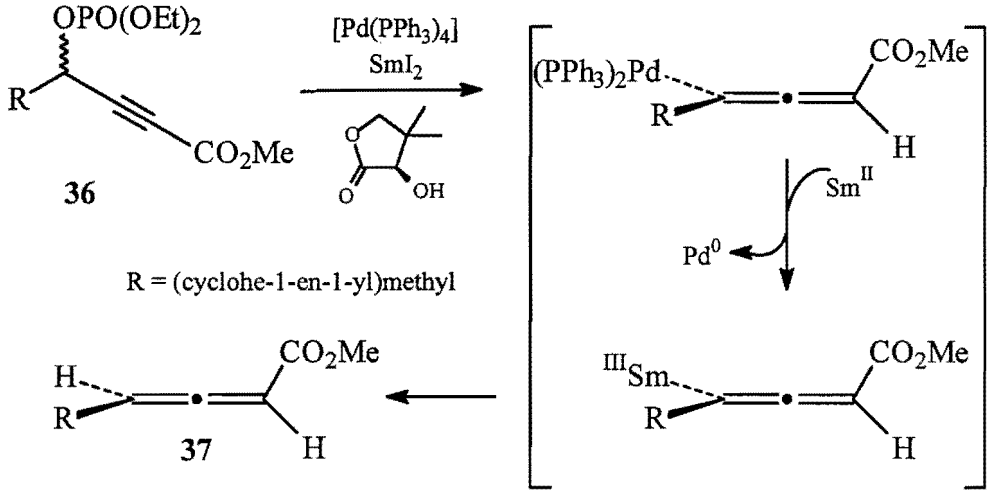
The synthesis of enantiomerically enriched propargyl alcohols is the most common approach for the subsequent synthesis of allenes. The synthesis of these moieties in high enantiomeric excess (*ee*) is essential and a variety of approaches are observed in the literature. These include asymmetric reduction (see later), direct synthesis from chiral pool starting materials[58] as well as enzymatic reductions of parent alkynes (or variations thereof).[59] Organometallic reagents have also been used for the synthesis of propargylic alcohols – these include alkyl zinc[60], titanium complexes[61] and cuprate reagents.[62]

Enantiomerically enriched allenes can be prepared directly using several approaches.[49,57] For example, stereoselective epoxidation (using Sharpless conditions) followed by cuprate mediated SN_2 rearrangement of the propargyl derivatives, gave allene **35** in high optical purity (Scheme 16). The respective *syn/anti* ratio was determined by the copper catalyst added.[63]



Scheme 16 Chiral epoxides as precursors of chiral allenes – exemplified for the *anti* product

Mikami and co-workers,[64] recently synthesised chiral allenes using dynamic kinetic protonation of allenylmetal species. For example, racemic compound **36** when treated with samarium iodide, catalytic palladiumtetrakistriphenylphosphine and a chiral proton source (as in (*R*)-(+)-pantolactone) gave the allene **37** in 68 % yield and an *ee* >95 % (Scheme 17). Several other syntheses have recently been reported.[65]



Scheme 17 Dynamic protonation using chiral proton source.

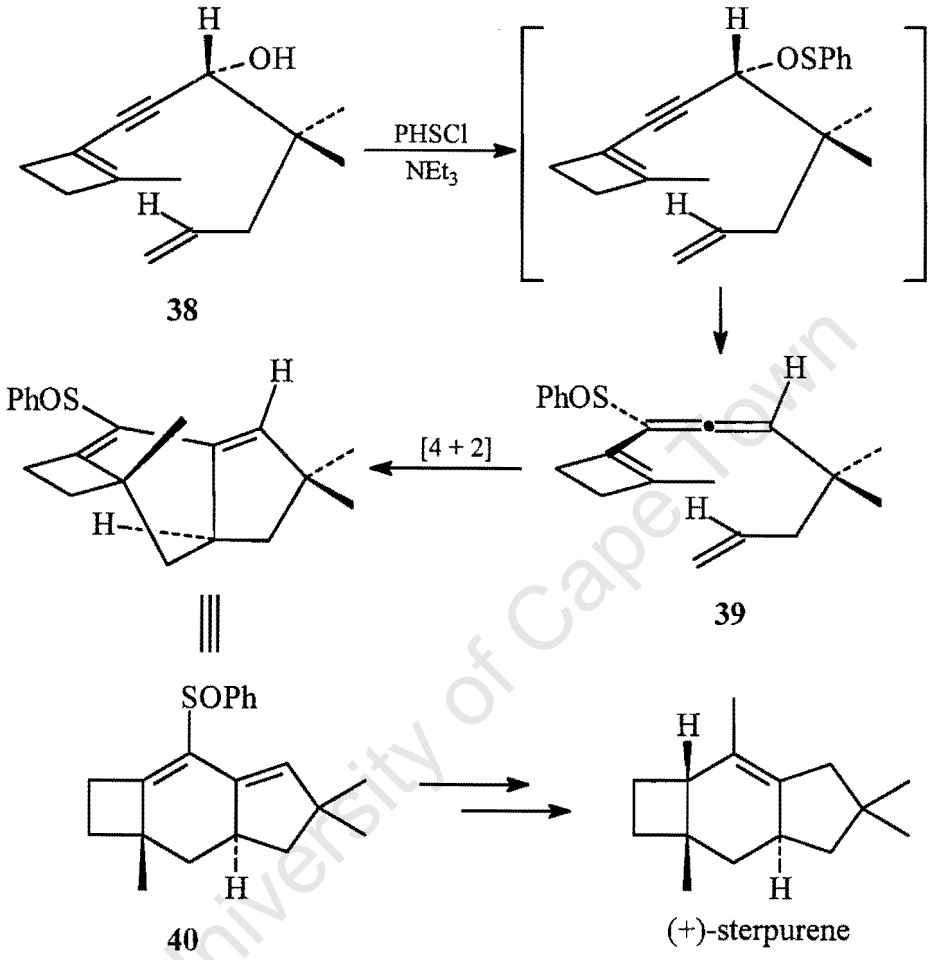
Examples of IMDA reactions in natural product synthesis involving monosubstituted allenyl termini have been described in the literature. Although the products of the reaction are chiral, this chirality is due to the inherent substituents on the tether, and are independent of the achiral allenes. Examples of these are given by Kanematsu *et al.*,[66] in his synthesis of furoscrobiculin, forskolin and dihydromevolin intermediates and Hiemstra *et al.*,[67] in his synthesis of (+)-gelsedine.

A similar feature is observed when transition metals are used to facilitate the IMDA reaction of monosubstituted achiral allenes as stereochemical control of these reactions is independent of the allenyl moiety. The choice of metal and subsequent catalyst loading were largely responsible for the stereoselectivities.[68]

Cycloaddition reactions of optically active allenes, which involves the transfer of the axial chirality of the allene to the cycloadducts, is a potentially powerful tool for enantioselective synthesis. Although chiral allenes have been synthesised routinely for several years, there are very few examples of their use in Diels-Alder reactions.

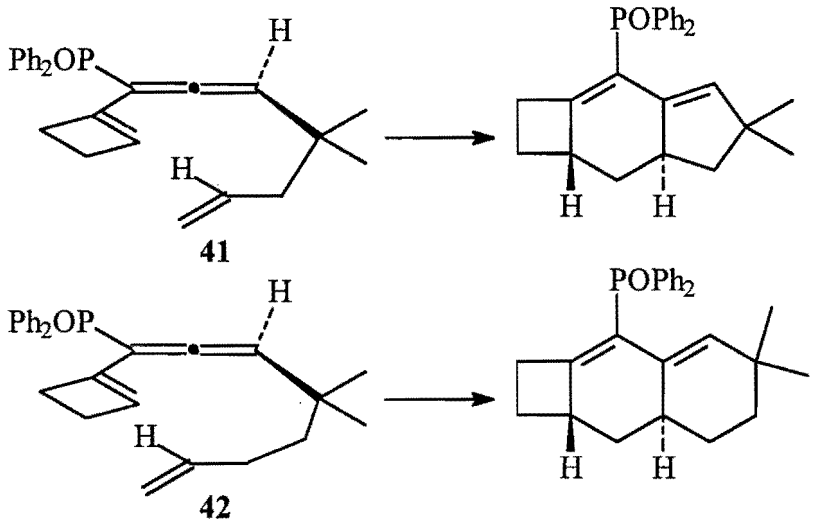
Kanematsu *et al.*,[69] only recently, reported the first example of enantiocontrolled *inter*molecular Diels-Alder reactions involving optically active allene-1,3-dicarboxyllates. Okamura *et al.*,[70] was first to demonstrate the transfer of chirality of the axially chiral element in IMDA reactions (Scheme 18). The study demonstrated the transfer of the propargyl chirality (when enantiomerically pure) to the axial chiral element of allene **39** and subsequently to the

cycloadduct **40**. This was demonstrated with the enantioselective synthesis of (+)-sterpurene in which the optical rotation of the cycloadduct was identical with that of the natural sterpurene, which was only possible if stereochemical retention of the intermediates was observed.[71] Analogous studies were carried out on phosphinyl allenes[72] and those containing carbon substituents (as opposed to the above heteroatom).[73]



Scheme 18 IMDA reaction of vinylallenyl sulfoxides demonstrating complete enantio- and diastereoselectivity

Tether length studies, carried out on the phosphinyl systems, showed that the three-carbon tethered allene **41** exhibited and 850-fold decrease in cyclisation rate versus the two carbon tethered derivatives **42** (Scheme 19) owing to the restricted rotation associated with the two-atom tether.



Scheme 19 Tether length influence on reaction rate.

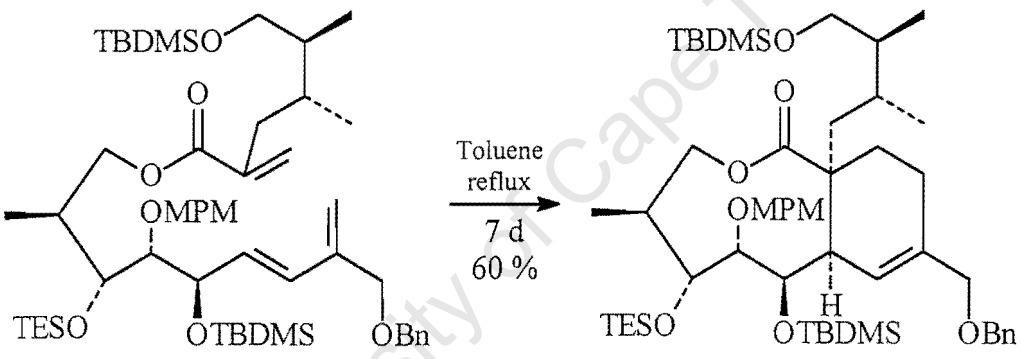
Apart from the research by Okamura *et al.*,[72,73] there are, to our knowledge, very few examples of IMDA reactions involving chiral 'terminal' allenyl moieties in which the axial chirality of the allene is transferred to the cycloadduct. Although the principle of chirality transfer has been studied for a variety of allenyl-olefin systems,[74] there is, to our knowledge, little studied in the field of enantiocontrolled IMDA reactions. Armed with this knowledge, it was hoped that the synthesis of 1-phenylsulfonyl-1,2-dienyl systems in optically pure form would facilitate enantioselective IMDA reactions. Synthesis or resolution of the respective alkynol precursors was expected to facilitate the synthesis of the corresponding phenylsulfonylallene enantiomers (as above) which, in turn, give rise to diastereomerically pure cycloadducts (see Chapter 5).

CHAPTER 2

SYNTHESIS AND REACTIVITY OF TRIENES TETHERED *VIA* A DIESTER SPACER

Introduction As a contribution towards the design and synthetic application of temporary tethered substrates for IMDA reactions, this chapter outlines an investigation into the synthesis and reactivity of systems incorporating temporary diester tethers.

It has been shown that trienes tethered *via* a three of four atom tether containing an ester linker exhibit poor IMDA reactivity as a result of the ester adopting a s-*trans* orientation (see Scheme 12, Chapter 1). This feature can be overcome by making the tether sufficiently long enabling the ester to react in its preferred orientation. For example, Hirama *et al.*,[75] recently used this approach in a synthesis of the AG-ring of pinnatoxin A (compound **43** in Scheme 1).



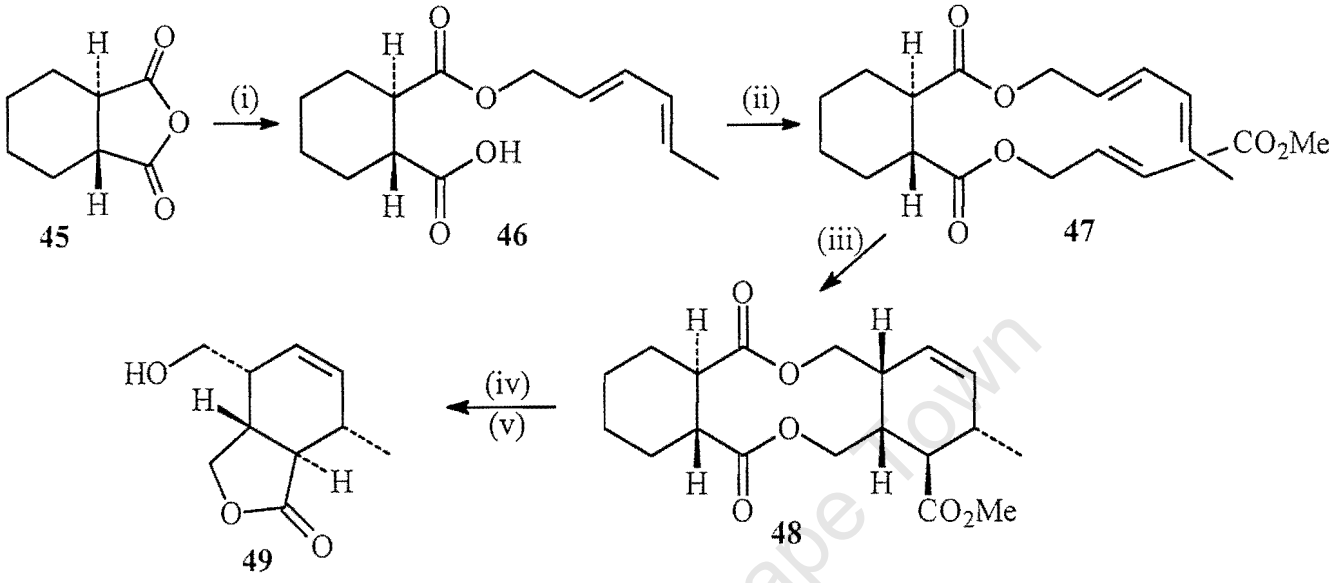
43 **44**

Scheme 1 IMDA approach to the AG-ring of pinnatoxin.

In research conducted by Craig *et al.*,[76] it was thought that a *diester* group would not prevent the diene and dienophile attaining the requisite close mutual proximity if the resultant heterocycle was sufficiently large to accommodate two s-*trans* ester linkages. In addition, it was thought that the medium-ring ester-containing products would not suffer from prohibitively destabilising transannular interactions. It was also believed that incorporation of a *conformationally restricted* diester spacer would offset the anticipated decrease in reactivity usually associated with the formation of a larger ring.

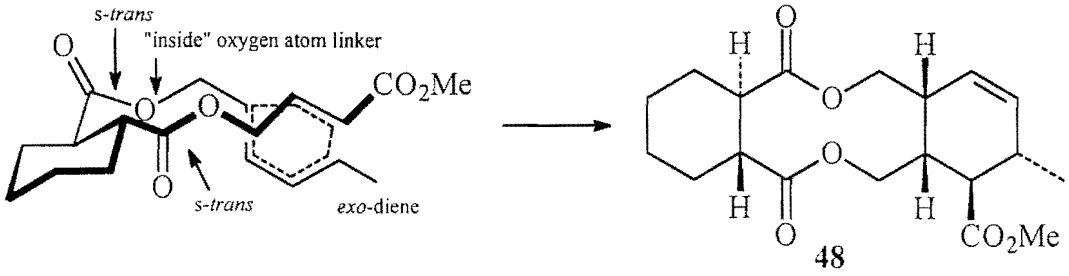
With this in mind, both *cis*- and *trans*-1,2-cyclohexane-dicarboxylic acid **45** were believed to be ideally suited as conformationally restricting spacers and were therefore used as starting points

for this investigation. For example, anhydride **45** was opened *via* nucleophilic attack with sorbyl alcohol, in the presence of DMAP and pyridine, to yield intermediate **46**, which was in turn coupled (using a variety of coupling techniques) with a suitable dienophile (for example (*E*)-methyl 4-hydroxybut-2-enoate, Scheme 2). Heating the triene **47** at 180 °C for 100 h, afforded major cycloadduct **48** in 65 % yield, which was transformed to the corresponding lactone **49** (85 %).



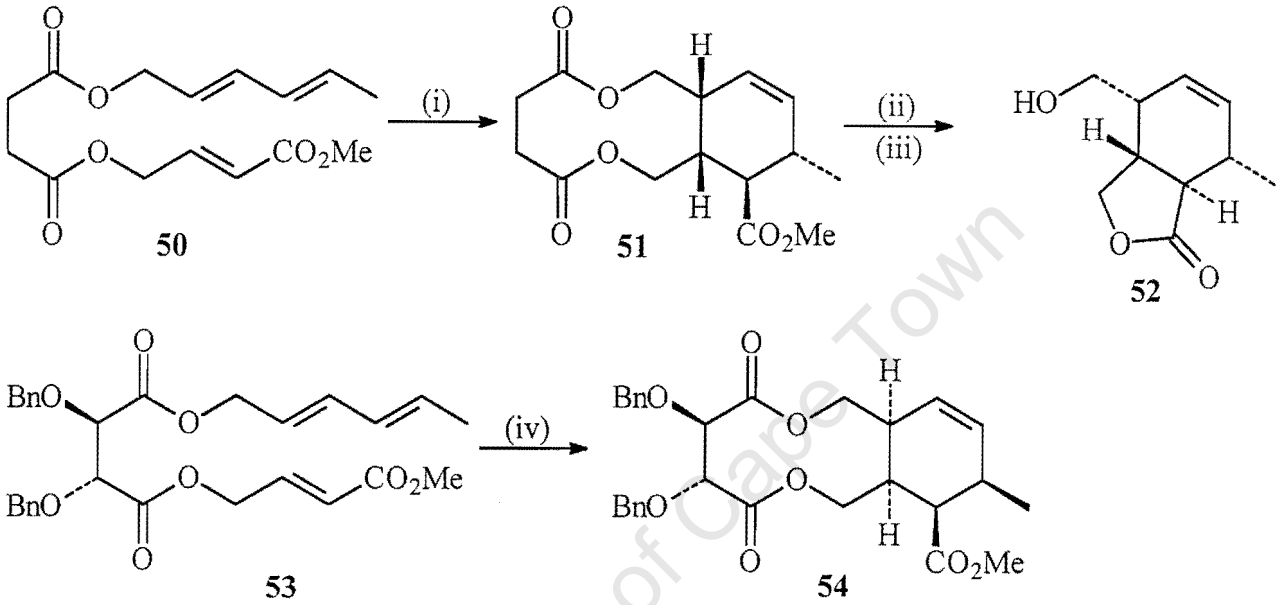
Scheme 2 *Reagents and Conditions*: (i) (2*E*,4*E*)-$CH_3(CH)_4CH_2OH$, DMAP, CH_2Cl_2, reflux, 75 %; (ii) 2,4,6-$Cl_3C_6H_2COCl$, NEt_3, DMF, 25 °C, then add $Me_2OC(CH)_2CH_2OH$, DMAP, DMF, 89 %; (iii) $CH_3C_6H_5$, 180 °C, 100 h, 65 %; (iv) LiOH, THF – MeOH – H_2O, 25 °C; (v) TFA, CH_2Cl_2, 25 °C

The observed stereoselectivity for this reaction arose from the transition state depicted in Scheme 3. The *trans*-diequatorial nature of the diene- and dieneophile-containing substituents on the cyclohexane spacer was such that only one transition state, having both esters in the favourable s-*trans* conformation, allowed for close mutual approach of the cycloaddition partners. Therefore, cycloadduct **48** arose from an *exo*-addition of the dienophile (in respect of the dienophile ester group) and with an "inside" orientation[77] of the alkyl C-O bond – a feature which had been observed previously in an earlier related study (see later).[24]



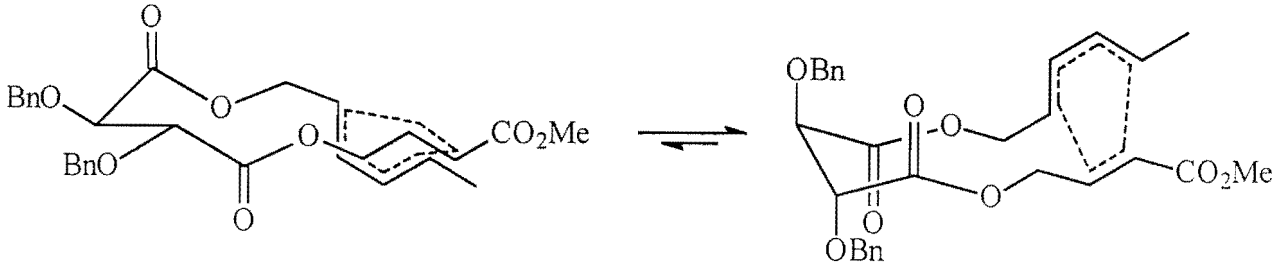
Scheme 3 Transition state for **47** giving rise to major cycloadduct **48**.

The advantage of using conformationally restricted molecules, such as compound **45**, as a spacer for IMDA reactions, was demonstrated by comparison with model studies carried out on related diester trienes (Schemes 4). Reaction of the succinate containing substrate **50** was markedly less reactive that that of substrate **47** undergoing a 50 % conversion to a 6:1 mixture of two products after prolonged heating. The major isomer **51** was assigned following its conversion into lactone **52** upon base mediated hydrolysis of the esters, followed by acid-catalysed cyclisation (as carried out before on cycloadduct **48**).



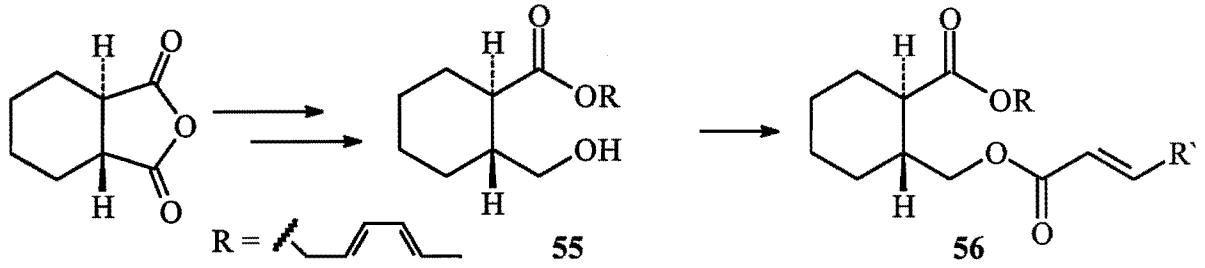
Scheme 4 *Reagents and Conditions*: (i) $CH_3C_6H_5$, 180 °C, 266 h; (ii) LiOH, THF – MeOH – H_2O, 25 °C; (iii) TFA, CH_2Cl_2, 25 °C; (iv) $CH_3C_6H_5$, 180 °C, 170 h, 80 % (+ minor 3:1)

Reaction of **53** was more rapid than **50**, and gave rise to a 3:1 mixture of cycloadducts – the major cycloadduct **54** was assigned by analogy to previous results. The increase in IMDA reaction rate of the succinate spacer with benzyloxy groups could be attributed to the increase population of reactive conformations, in which dipole-dipole repulsion between the alkoxy groups is minimised (Scheme 5).



Scheme 5 Equilibrium between reactive and non-reactive conformations of triene **53**.

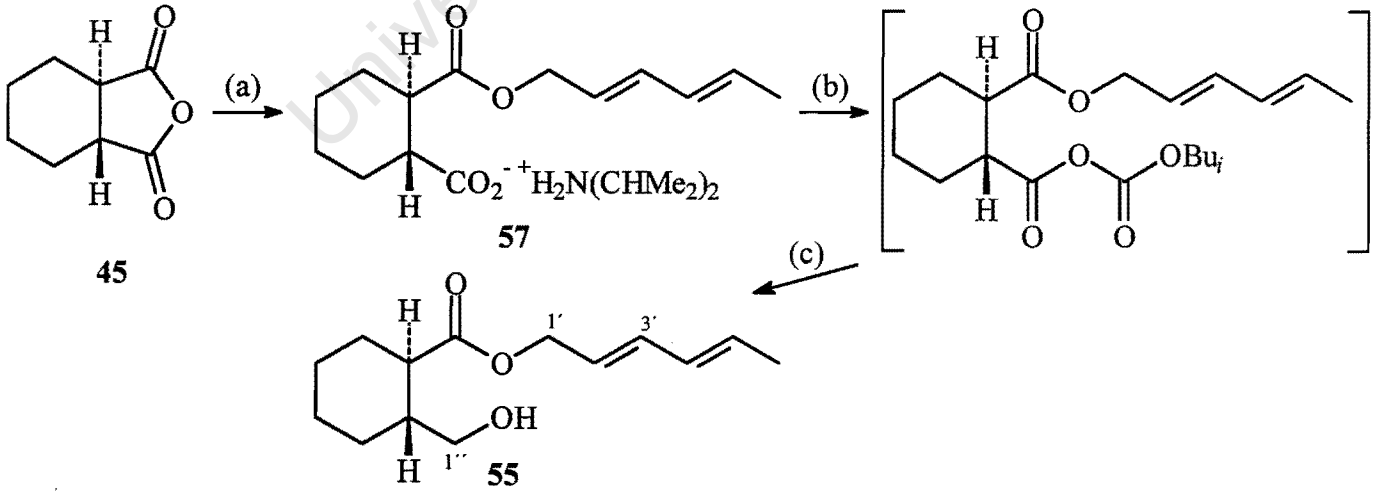
The main advantage of using this approach was the versatility of triene synthesis, as access to a wide variety of triene systems was possible by simple modification of the standard protocol. Reversing the ester on the dienophile tether would significantly enhance the reaction rate and, hopefully, the selectivity.[78] Synthesis of trienes, such as **56**, will be investigated for both carbocyclic and heterocyclic systems (Scheme 6).



Scheme 6 Proposed synthesis of the 'reversed' dienophilic ester tether

2.2 Carbocyclic systems

2.2.1 Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-pent-4-ene)cyclohexanecarboxylate An effective protocol was required to synthesise key compound **55**, as all subsequent trienes would be derived from it. This was achieved *via* a multi-step, 'one pot' experiment, based on a procedure by Zwanenburg *et al.*[79] Nucleophilic opening of **45** with sorbyl alcohol gave mono-ester **57** followed by *in situ* reaction with *t*-butyl chloroformate gave mixed carboxylic-carbonic anhydride. Filtration followed by reduction gave key intermediate **55** in 69 % overall yield (Scheme 7).



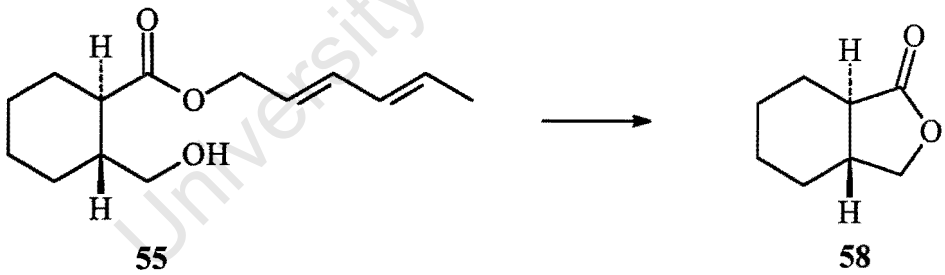
Scheme 7 *Reagents and Conditions:* (i) (a) HO , DMAP, $HN(CHMe_2)_2$, CH_2Cl_2; (b) $Me_3COCOCl$, -10 °C → 25 °C, then filter; (c) $NaBH_4$, CH_2Cl_2 - H_2O, -20 °C

The ^{1}H NMR spectrum of **55** displayed a two-proton multiplet at δ 3.50 for diastereotopic 1′′-H_2. The diene signals were in accordance with reported literature values, for previously synthesised compounds and are summarised in Table 1.[76] The infrared spectrum (IR) displayed absorption at ν_{max} 3485 (OH) and 1730 cm^{-1} (COOR). Accurate mass determination using CI techniques displayed a molecular ion at 256.1913, corresponding to the M+NH_4 molecular ion.

Table 1: Observed ^{1}H NMR dienyl signals

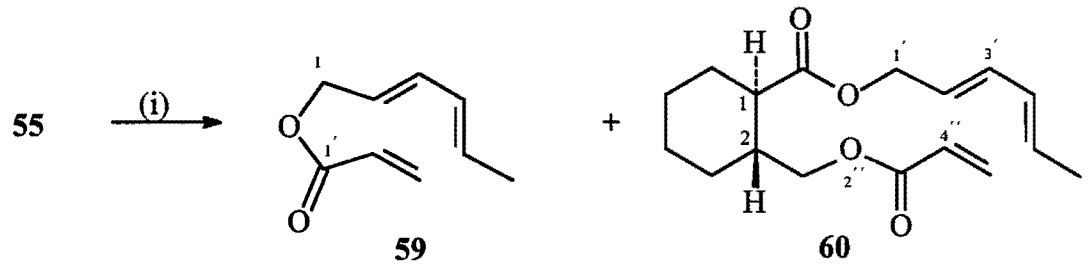
Signal	δ ppm	Multiplicity	*J* Hz
2′-H	5.56	dt	15.0 and 2 x 6.5
3′-H	6.26	dd	15.0 and 10.5
4′-H	6.05	ddd	15.0, 10.5 and 1.5
5′-H	5.75	dq	15.0 and 3 x 6.5

Alcohol **55** slowly underwent intramolecular reaction on standing to give *trans*-hexahydrophthalide **58**, with concomitant liberation of sorbyl alcohol (Scheme 8). This 'decomposition' complicated future coupling reactions, and best yields of the desired trienes were achieved when compound **55** was freshly prepared. All attempts to synthesis of **55** from lactone **58** failed.



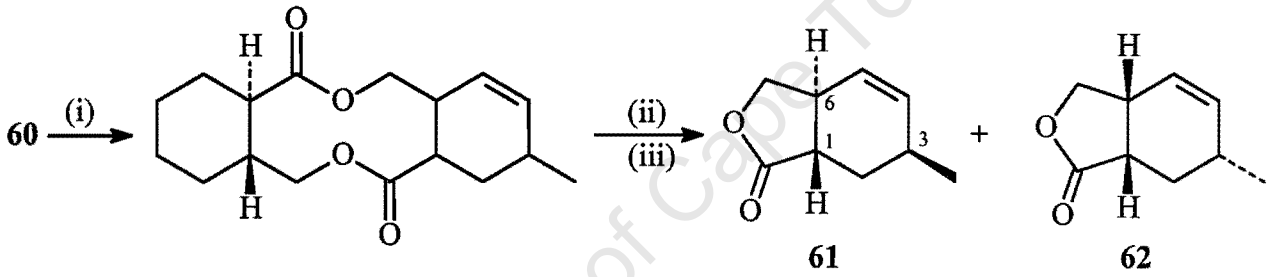
Scheme 8 The observed lactonisation of **55**

Treatment of alcohol **55** in dichloromethane with acryloyl chloride and triethylamine afforded the monoester **59** (11 %) and diester **60** (74 %, Scheme 9). The ^{1}H NMR of **60** displayed acryloyl signals at δ 5.80 (dd, *J* 10.5 and 1.5 Hz) for 5′′-H_{cis}, δ 6.10 (dd, *J* 17.5 and 10.5 Hz) for 4′′-H and δ 6.38 (dd, *J* 17.5 and 1.5 Hz) for 5′′-H_{trans} while the dienyl signals were in accordance with previous results. The IR spectrum displayed absorption at ν_{max} 1719 cm^{-1} (COOR). The corresponding signals for **59** were assigned *via* analogy to **60**.



Scheme 9 *Reagents and Conditions:* (i) $CH_2CHCOCl$, NEt_3, CH_2Cl_2, 20 °C

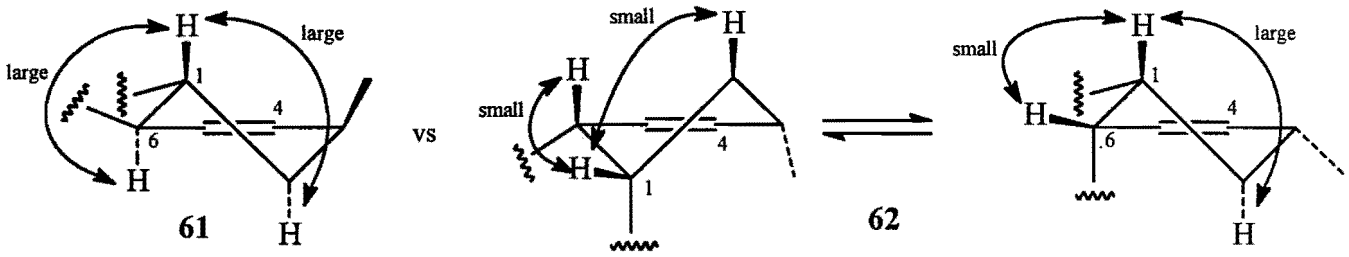
Triene **60** was dissolved in toluene and the resulting solution was heated at 170 °C for 16 h to give an inseparable mixture of two cycloadducts (2:1 by NMR) in 85 % yield. Severe signal overlap in the ^1H NMR spectrum prevented spectroscopic characterisation, however, treatment of the mixture with aqueous lithium hydroxide, followed by exposure to catalytic acid, gave lactones **61** (44 %) and **62** (Scheme 10).



Scheme 10 *Reagents and Conditions:* (i) $CH_3C_6H_5$, 170 °C, 16 h, 85 %; (ii) LiOH, THF – MeOH – H_2O, 25 °C; (iii) *p*-TosH, CH_2Cl_2, Δ, 1 h

The ^1H NMR spectrum for major lactone **61** displayed signals at δ 2.75 (m, *W* 28 Hz) for 1-H, δ 5.68 (dt, *J* 10.0 and 2 x 2.5 Hz) for 4-H and δ 5.75 (dt, *J* 10.0 and 2 x 1.5 Hz) for 5-H. Also seen in the spectrum were the diastereotopic 7-H protons at δ 3.87 (dd, *J* 11.5 and 7.0 Hz) and 4.46 (dd, *J* 11.5 and 8.0 Hz) in the expected range for these protons. The IR spectrum displayed absorption at ν_{max} 1778 cm^{-1} (COOR-lactone). Assignment of **62** was complicated by the co-elution of *trans*-hexahydrophthalide **58**, which made spectroscopic assignment difficult. Identifiable signals in the ^1H NMR spectrum were observed at δ 5.58 (ddd, *J* 10.0, 4.0 and 2.5 Hz) for 4-H and δ 5.75 (br d, *J* 10.0 Hz) for 5-H.

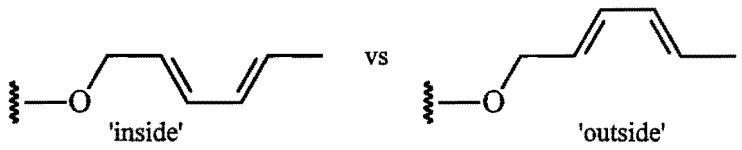
Assignment of **61** as a *trans*-fused lactone was based on the respective signal width for 1-H, as this is only possible if the1-H has a *anti*periplanar relationship with two neighbouring protons. (Scheme 11)



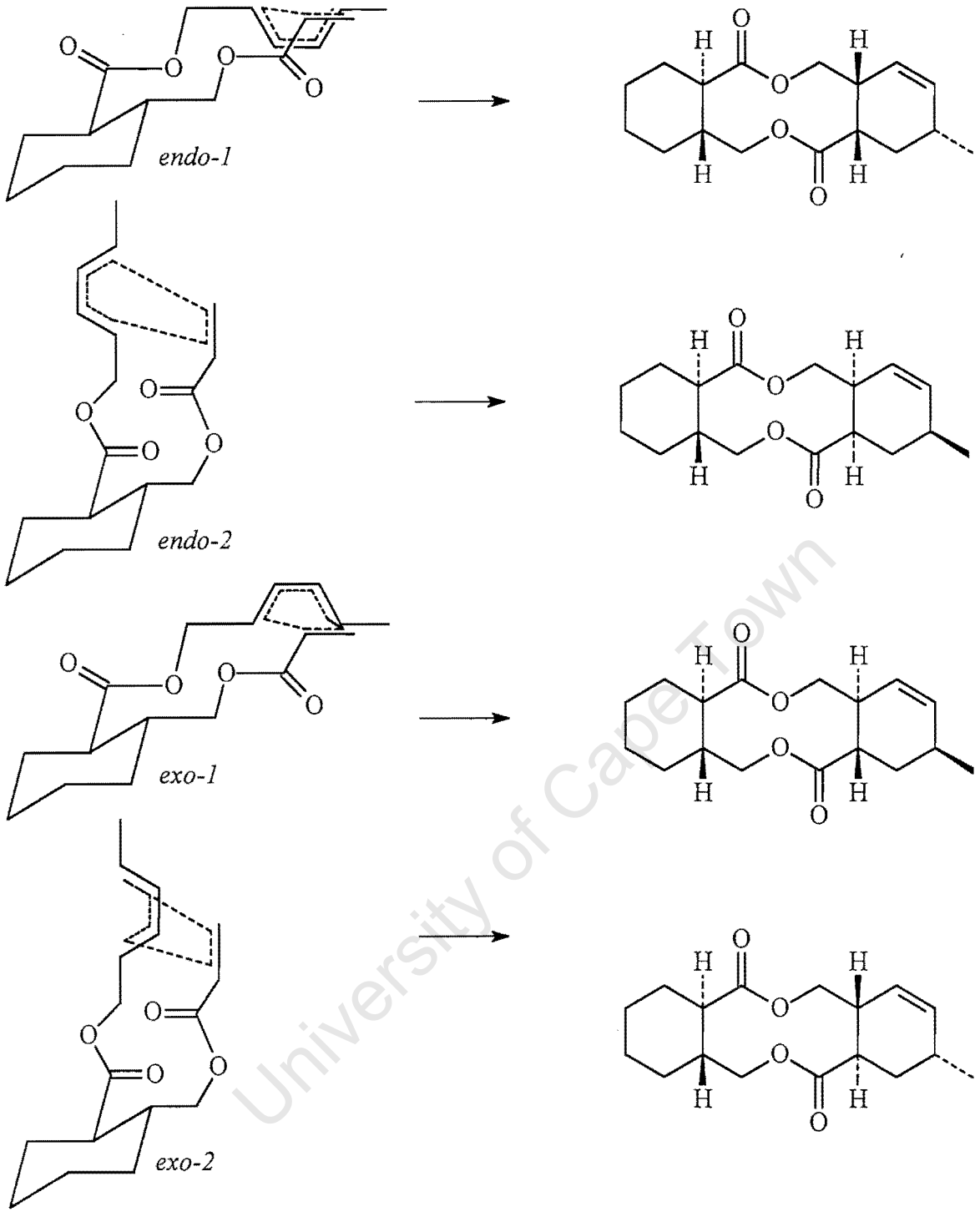
Scheme 11 Large couplings between 1-H, 2-H and 6-H for **61** when compared to possible couplings for lactone **62**

The relative stereochemistry of the lactones is assigned by comparison of the possible transition states of the IMDA reaction (Schemes 13). The transition states shown were derived from the assumption that both ester moieties were found in their thermodynamically preferred s-*trans* conformation, and that the spacer substituents were in a 1,2-*trans*-diequitorial relationship. The two possible conformations for *endo* addition give rise of *cis*-fused products, whilst the *exo* transition states (1 and 2) give rise to *trans*-fused products. From research conducted in earlier studies it was expected that *endo-1* and *exo-1* would be the thermodynamically favoured transition states.[76]

Houk *et al.*,[80] showed that during an electrophilic attack on an allylic double bond, an ether prefers the 'inside' conformation, as this stabilises the transition state to the greatest extent (Scheme 12). Craig *et al.*,[24] extended this argument to an allylic ether possessing an adjacent carbonyl (*i.e.* an ester) and subsequently demonstrated the importance of this feature.[74] With the result obtained from the above reaction, it was clear that this feature was not applicable for this (and subsequent) systems, as the major product obtained arose from *exo* addition to the diene in an 'outside' conformation.



Scheme 12 The inside/outside conformation for the 'allylic' ester

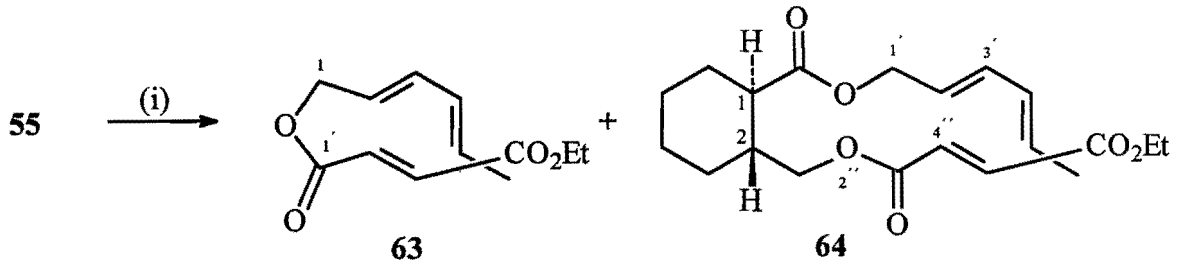


Scheme 13 *Endo* and *Exo* transition states for triene **60**

Epimerisation of the acidic protons, in the base mediated hydrolysis of the initial cycloadduct mixture, did not occur to a great extent as only two cycloadduct-derived lactones were obtained. If this were so, then all four possible lactones should have been observed. Conclusive proof of these structures could only be solved by x-ray analysis, however, as this was a pilot experiment, it was not deemed necessary. No reaction studies were conducted on the monoester triene **59**.

2.2.2 Hexa-2′,4′-dienyl-2-[2′′,7′′-dioxa-3′′,6′′-dioxo-non-4′′-ene]-cyclohexane-carboxylate

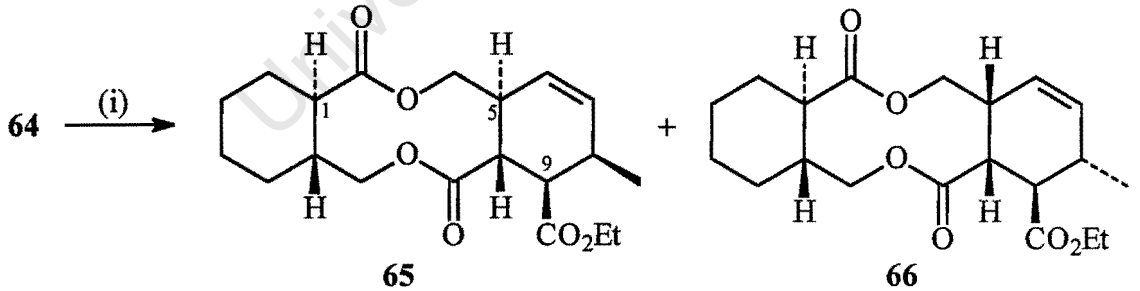
Treatment of freshly prepared **55** with ethyl fumarate, dicyclohexylcarbodiimide (DCC)[81] and DMAP gave the monoester **63** (9 %) followed by the desired diester **64** (81 %) (Scheme 14).



Scheme 14 *Reagents and Conditions:* (i) $CO_2HCHCHCO_2Et$, DCC, DMAP, CH_2Cl_2, 25 °C

The ^1H NMR spectrum of **64** displayed signals at δ 6.82 (2H, s) for 4′′-H and 5′′-H, δ 4.05 (dd, *J* 11.0 and 5.0 Hz) and δ 4.10 (dd, *J* 11.0 and 5.5 Hz) for 1′′-H_2 whereas the characteristic signals for the hexadienyl moiety were consistent with previously prepared compounds. It was not possible to achieve signal distinction for coincident 4′′-H and 5′′-H signals. The IR spectrum displayed absorption at ν_{max} 1719 cm^{-1} (CO) whilst accurate mass determination displayed the corresponding M+NH_4 molecular ion. Assignment of monoester **63** was based on analogy to **64**.

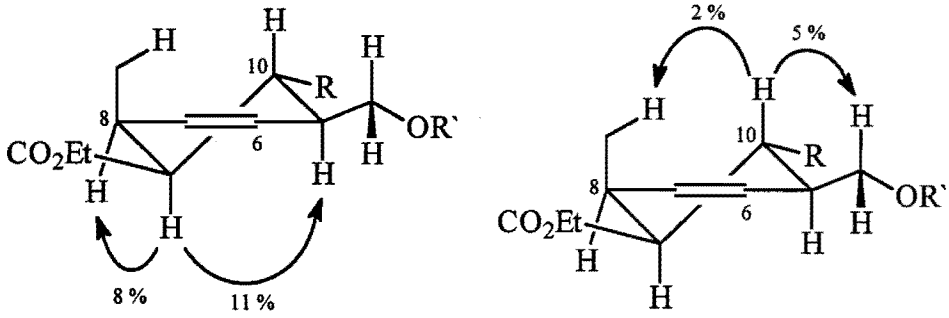
Triene **64** was dissolved in toluene and the resulting solution was heated at 80 °C for 24 h to give a mixture of two cycloadducts (2:1 by NMR) in 90 % yield. Preparative reverse-phase HPLC of the mixture gave the *trans-trans* cycloadduct **65** in 60 % followed by the *trans-cis* cycloadduct **66** in 27 % yield (Scheme 15).



Scheme 15 *Reagents and Conditions:* (i) $CH_3C_6H_5$, 80 °C, 90 %

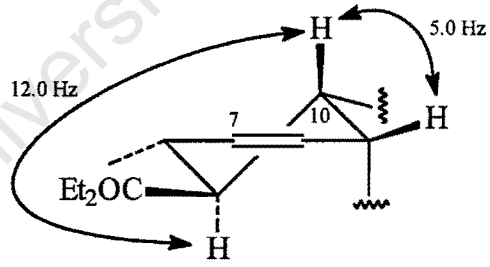
Structural assignment of **65** was based on 1D and 2D NMR experiments. The ^1H NMR spectrum displayed signals at δ 2.45 (dd, *J* 12.0 and 10.5 Hz) for 10-H, δ 5.56 (ddd, *J* 10.0, 5.0 and 2.5 Hz) for 7-H and at δ 5.61 (dt, *J* 10.0 and 2 x 1.5 Hz) for 6-H. The IR spectrum displayed absorption ν_{max} 1735 cm^{-1} (CO) whereas accurate mass determination displayed the corresponding M+NH_4 molecular ion.

The 10-H signal was indicative of a *trans*-fused ring junction as two large couplings are only possible for this configuration. This was supported by NOE difference NMR when 9-H and 10-H were irradiated (Scheme 16). Irradiation of 9-H displayed a significant enhancement of 5-H (~ 11 %).



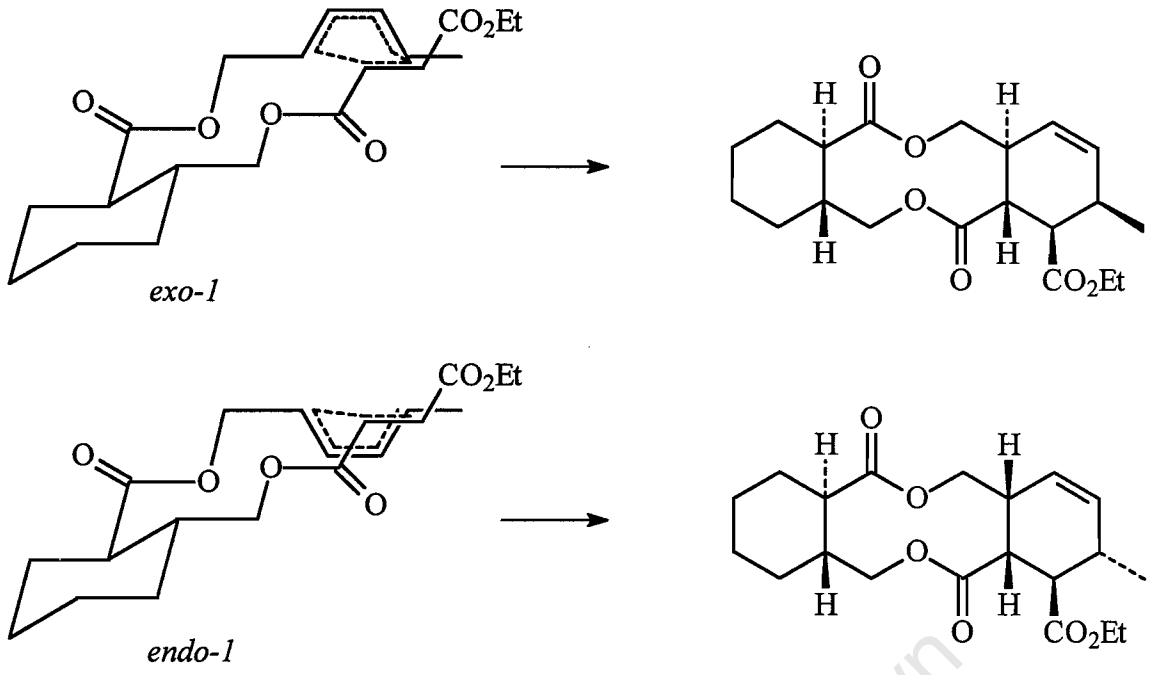
Scheme 16 NOE experiments of **65**

The ^{1}H NMR spectrum of the minor cycloadduct **66** displayed corresponding signals at δ 3.00 (dd, *J* 12.0 and 5.0 Hz) for 10-H, δ 5.56 (ddd, *J* 10.0, 5.0 and 2.5 Hz) for 7-H and at δ 5.61 (dt, *J* 10.0 and 2 x 1.5 Hz) for 6-H. The IR spectrum displayed absorption at ν_{max} 1736 cm^{-1} (CO) whilst accurate mass determination displayed the corresponding M+H molecular ion. The 10-H signal, in contrast with 10-H of **65**, is consistent with the expected coupling constants of a *cis*-fused ring junction, as only one large and one small coupling were observed (Scheme 17).



Scheme 17 Observed couplings with 10-H for **66**.

The relative stereochemistry (in relation to the spacer) of the cycloadducts was based on the analogous transition states as demonstrated for the acryloyl triene (Scheme 18). Therefore, major cycloadduct **65** arose from *exo-1* (*exo* in regard to the tether) whilst **66** arose from *endo-1* addition. The presence of an additional dienophile activating group (which was hence *endo* for **65**) exemplified the predicted rate enhancement, as the reaction was complete at 80 °C within 24 h (*cf.* 170 °C for 16 h for **60**).



Scheme 18 Transition states giving rise to **65** and **66**

In light of the importance of the relative stereochemistry of the newly formed ring in relation to the spacer, it was decided to submit **66** for an x-ray crystal structure determination (Figure 1). This was carried out and the result was indeed in accordance with our assignment – thus confirming our relative structural assignment, and hence also the transition state model.

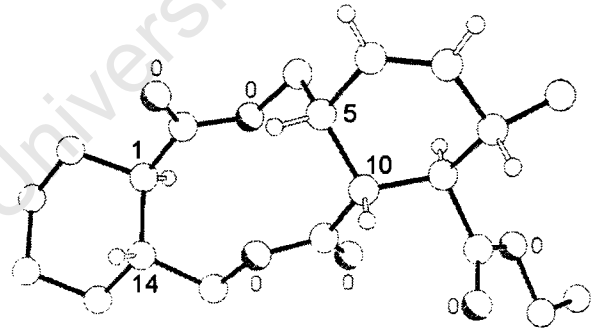
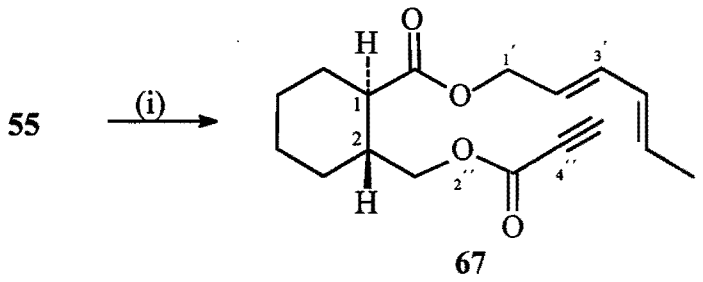


Figure 1 X-ray crystal structure of **66**

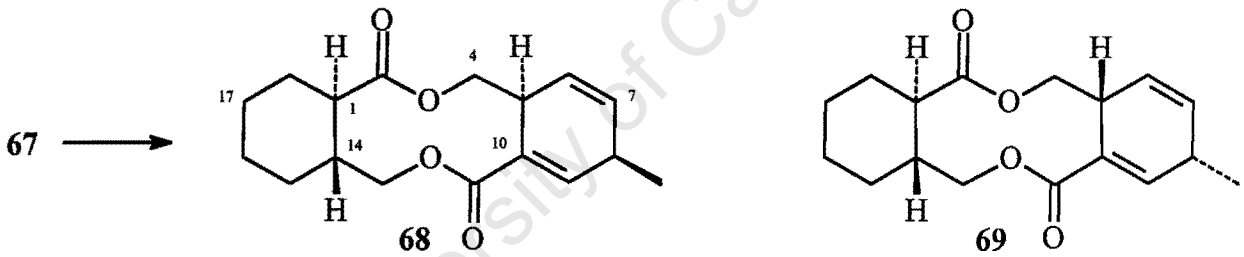
With the success of the above reactions, attention was turned to the synthesis of alternate IMDA substrates in an attempt to assess the scopes and limitations of this methodology for its potential use as an effective synthetic tool.

2.2.3 Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-pent-4-yne)-cyclohexanecarboxylate Treatment of alcohol **55** with propiolic acid, DCC and DMAP afforded the ynoate ester **67** in 60 % yield (Scheme 19). The ^{1}H NMR spectrum of **67** displayed a characteristic acetylenic signal at δ 2.87 (s) for 5′′-H while the spacer and dienyl signals were analogous to those of previously prepared compounds. The IR spectrum displayed absorption at ν_{max} 1719 (CO) and 3297 cm^{-1} (C≡CH).



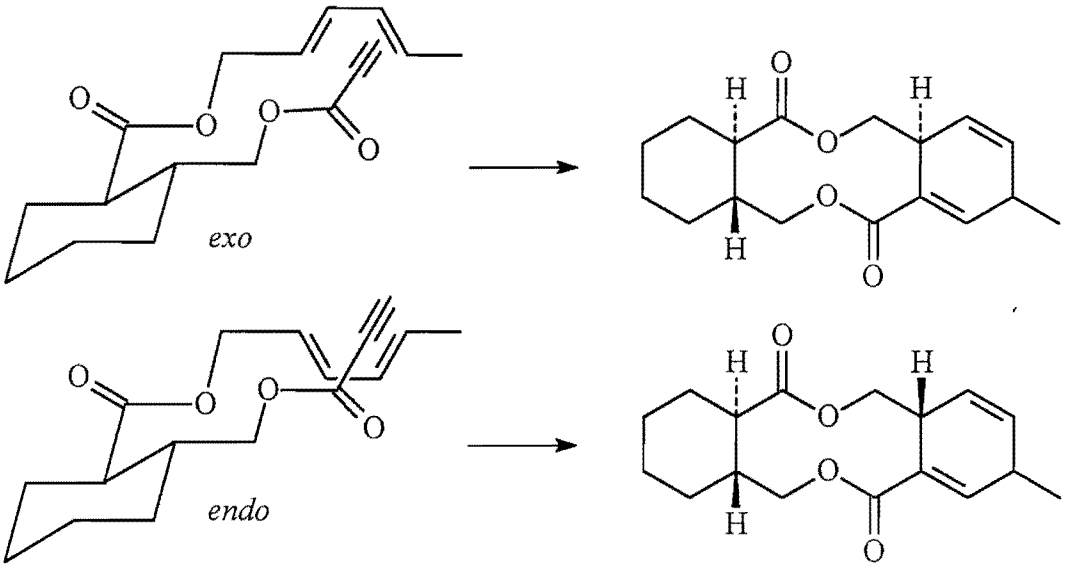
Scheme 19 *Reagents and Conditions:* (i) $CHCO_2H$, DCC, DMAP, CH_2Cl_2, 61 %

Heating the dienynone **67** at 150 °C for 24 h gave an inseparable mixture (1:1 by NMR) of cycloadducts **68** and **69** in 100 % yield (Scheme 20). ^{1}H and ^{13}C NMR were of limited use owing to signal overlap.



Scheme 20 *Reagents and Conditions:* (i) $CH_3C_6H_5$, 180 °C, 100 %

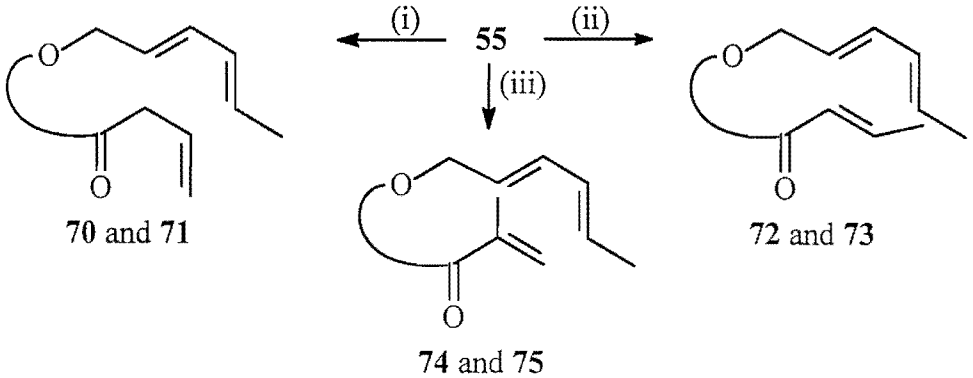
The poor selectivity of this reaction was rationalised in terms of the respective *trans*ition states (Scheme 21). As the acetylenic moiety is sp hybridised there could be little differentiation between the two possible transition states which was clearly demonstrated by the lack of selectivity of the cycloaddition reaction.



Scheme 21 Possible transition states for dienynone **67**.

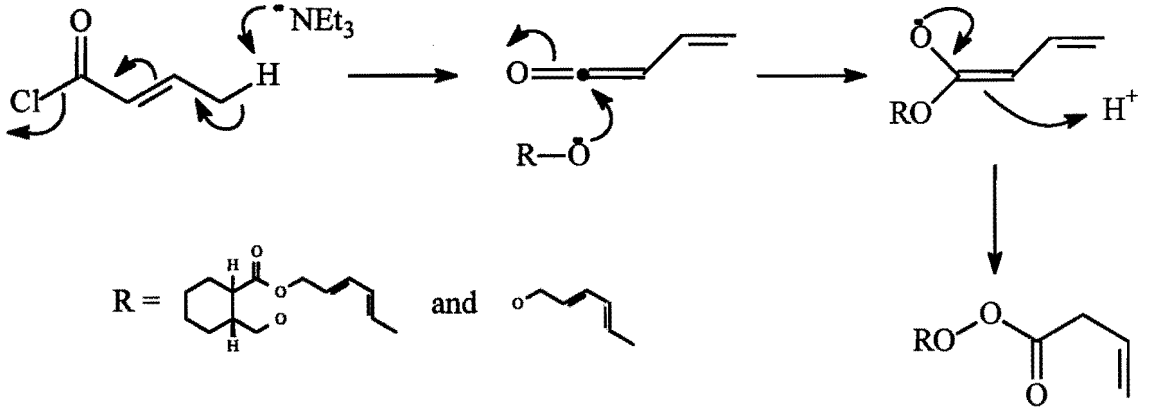
As a result of the poor selectivity of dienyne **67**, this reaction was not investigated further. Attention was now turned to the introduction of aliphatic substitution on the dienophile in an attempt to investigate the effect of substitution on reaction stereoselectivities.

2.2.4 Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-4′′*E*-hex-4′′-ene)cyclohexanecarboxylate and Hexa-2′,4′-dienyl-2-(4′′-methyl-2′′-oxa-3′′-oxo-hex-4′′-ene)cyclohexane-carboxylate With the above aim in mind, alcohol **55** was treated with *trans*-crotonyl chloride and triethylamine at room temperature to give the unexpected monoester triene **70** (24 %) and diester triene **71** (76 %, Scheme 22). When a softer base, such as pyridine was used, the desired trienes **72** (60 %) and **73** (31 %) were indeed formed. Treatment of alcohol **55** with methacryloyl chloride and triethylamine at room temperature gave the monoester **76** (36 %) and diester **77** (64 %) trienes respectively.



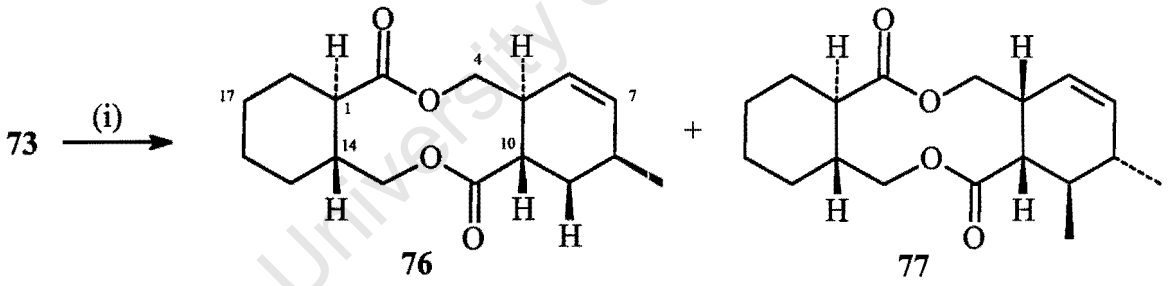
Scheme 22 *Reagents and Conditions:* (i) $CH_3CHCHCOCl$, NEt_3, CH_2Cl_2; (ii) $CH_3CHCHCOCl$, C_5H_6N, CH_2Cl_2, 91 %; (iii) $CH_2CH(CH_3)COCl$, NEt_3, CH_2Cl_2, 96 %

The formation of **70** and **71** was believed to be a result of an initial chloride elimination (facilitated by NEt_3) to form a ketene intermediate, which in turn reacts with alcohol (sorbyl alcohol or **55**, Scheme 23).



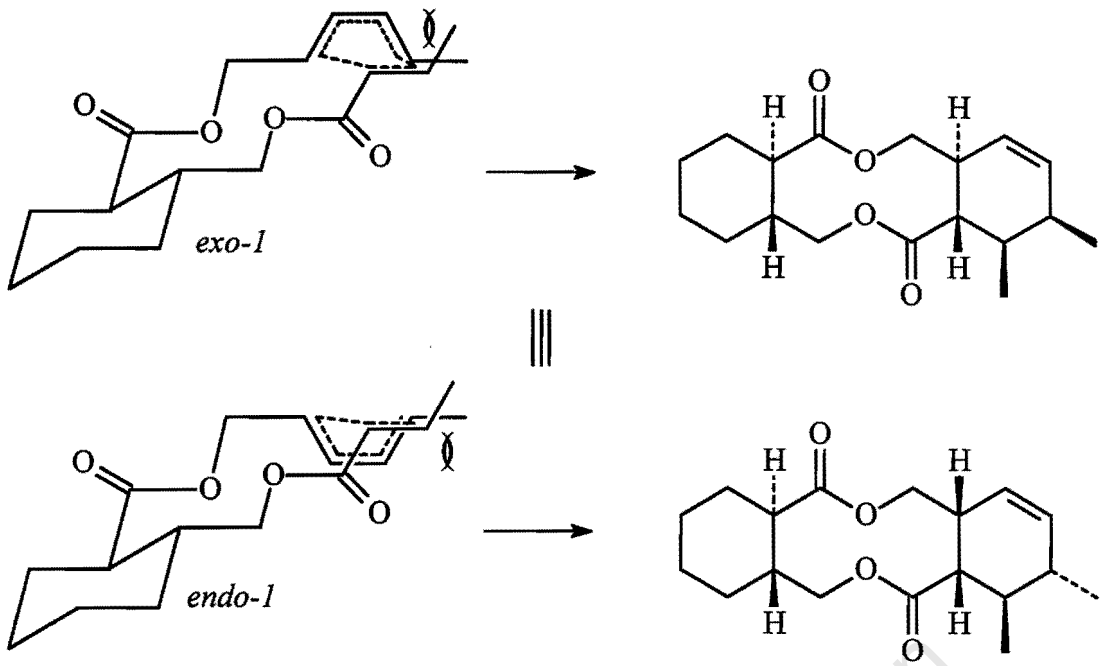
Scheme 23 Base mediated mechanism for formation of **70** and **71**

Characterisation of the desired trienes **73** and **75** was carried out as before and were consistent with the assigned structures. Triene **73** was dissolved in deuteriotoluene and the resulting solution was heated at 160 °C for 72 h to give an inseparable mixture of cycloadducts **76** and **77** (~1:1 by NMR) in 66 % yield (Scheme 24).



Scheme 24 *Reagents and Conditions:* (i) $C_6D_5CD_3$, 160 °C, 72 h

The structures were assigned by analogy to previous results as signal overlap made assignment of key stereochemical signals difficult. The sluggish reaction demonstrated the expected attenuation of IMDA reactivity as a result of additional substitution on the dieneophile. Examination of *exo-1* and *endo-1 trans*ition states for triene **73** displays little difference (in respect of steric interactions) and hence the above result is not surprising.



Scheme 25 *Exo-1* and *endo-1* transition states for **73**, depicting steric clash between the methyl groups

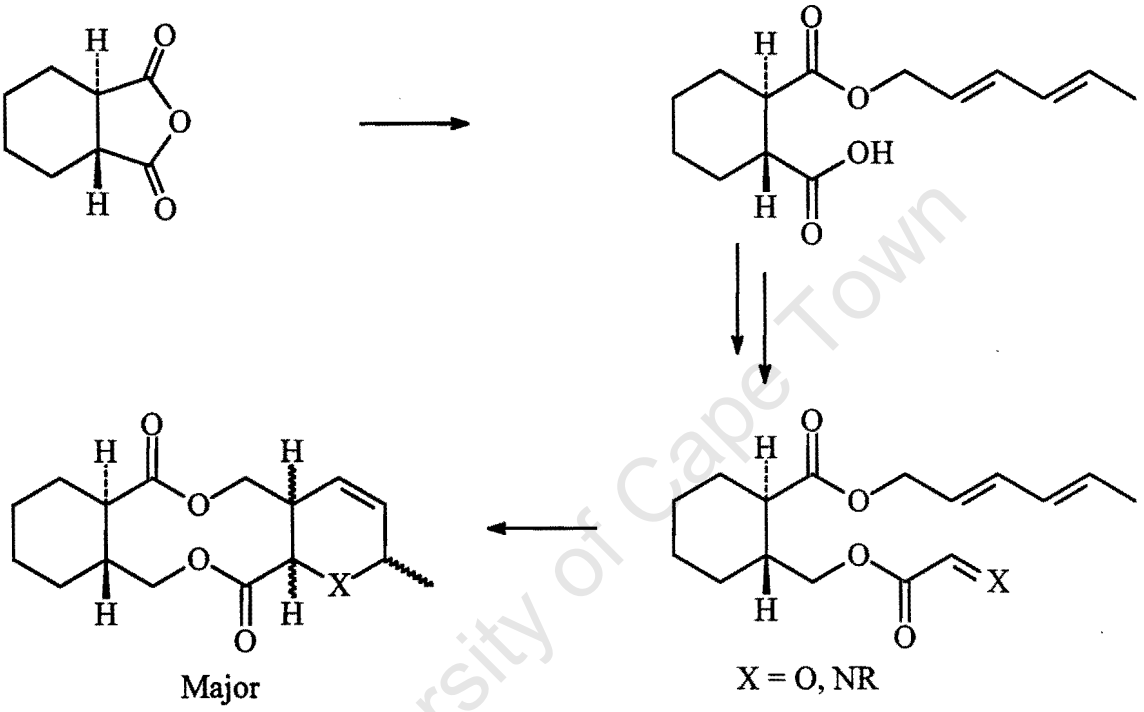
The poor selectivity afforded by the triene **73** limits the synthetic utility of this approach and was therefore not investigated further. Heating triene **75** for extended periods at 180 °C failed to yield any reaction whatsoever. Therefore further investigation into the synthesis of carbocyclic products was terminated.

2.2.5 Conclusions The synthesis of a series of diester trienes was carried out and their cycloaddition properties were investigated. As expected, IMDA reactions required relatively mild reaction conditions (*cf.* reversed ester **47**). The trienes, with one exception, were reactive and gave cyclohexanoid products in good yields in all cases. Where selectivity was observed, the reactions were *exo* (with respect to the tether) selective.

No cyclisation studies were conducted on the isolated monoester trienes.

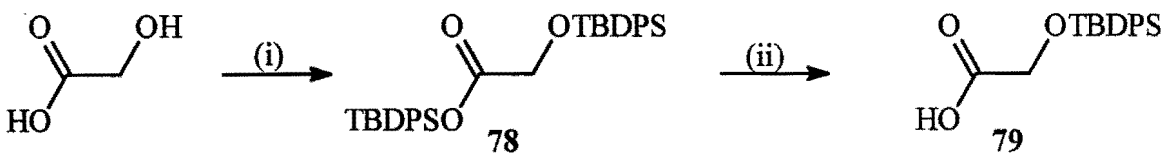
2.3 Heterocyclic synthesis

2.3.1 Introduction. Armed with the above results, we proceeded in designing alternate substrates in an attempt to synthesise products containing a heteroatom in the newly formed ring. This objective stems form the substantial number of natural product substructures containing a heteroatom embedded in a six-membered ring. It was hoped that successful implementation of this hetero-Diels-Alder approach may offer an alternate approach for the synthesis of these classes of compounds. The proposed synthetic route is described in Scheme 26.



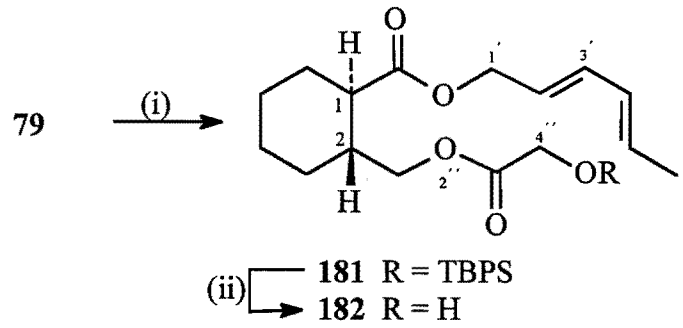
Scheme 26 Proposed synthesis of heteroatom containing diester system

2.3.2 (1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-butan-4′′-ol)cyclohexane-carboxylate.** Treatment of glycolic acid with *t*-butyldiphenylsilyl chloride in the presence of triethylamine afforded the bis-silylated compound **79** (Scheme 27). The crude product was treated with aqueous potassium carbonate to yield silyl ether **80** in 85 % yield over the two steps. Spectroscopic properties were in agreement with literature values.[82] Compound **79** was also prepared by using alternate literature methods.[83]



Scheme 27 *Reagents and Conditions:* (i) TBDPSCl, CH_2Cl_2, reflux; (ii) K_2CO_3, THF – H_2O, 20 °C.

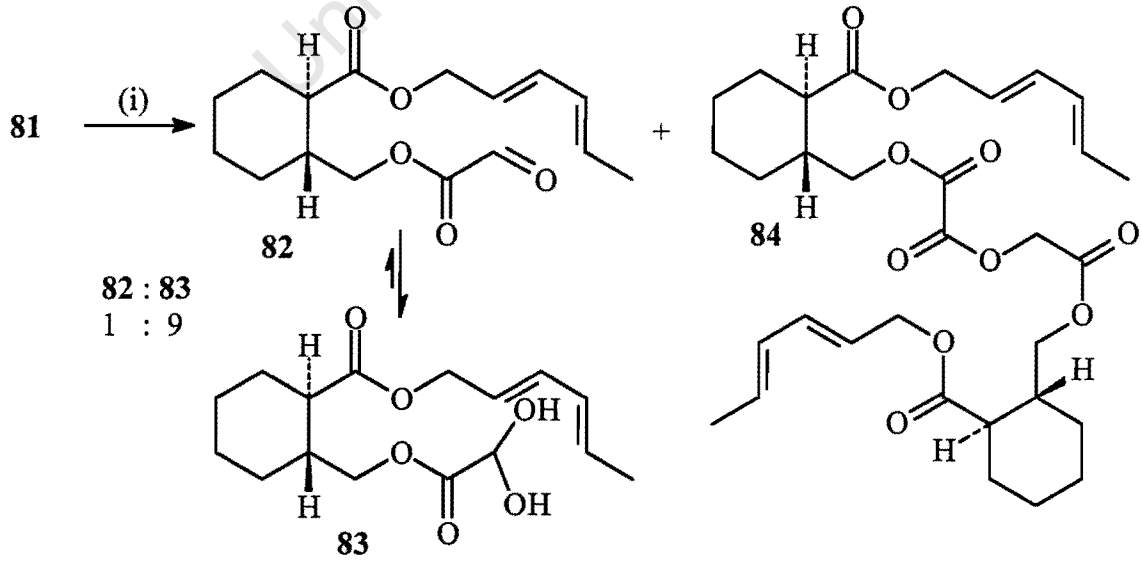
Treatment of compound **79** with alcohol **55** in the presence of DCC and DMAP at room temperature gave the desired diester **80** in 83 % yield (Scheme 28). Reaction of compound **80** with tetrabutylammonium fluoride (TBAF) gave primary alcohol **81** in 80 % yield.



Scheme 28 *Reagents and Conditions:* (i) **55**, DCC, DMAP, CH_2Cl_2, (ii) TBAF, THF, 20 °C

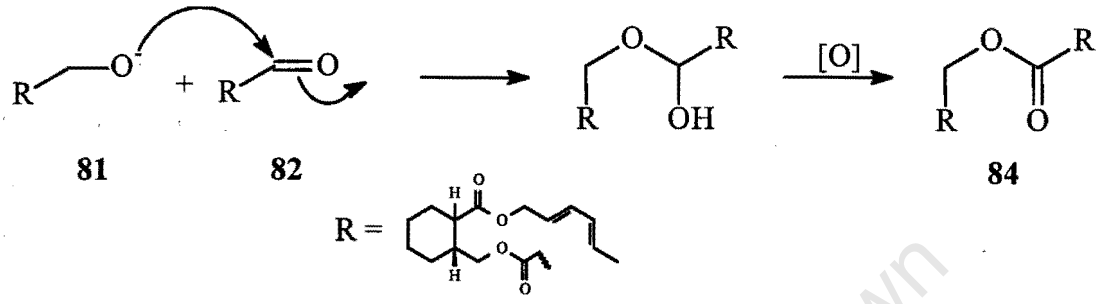
The ^{1}H NMR spectrum of **81** displayed a two-proton singlet at δ 4.12 for diastereotopic 4′′-H_2 whereas diastereotopic signals for 1′′-H were observed at δ 4.00 (dd, *J* 11.0 and 5.5 Hz) and δ 4.14 (dd, *J* 11.0 and 6.0 Hz). Spectroscopic signals for the spacer and hexadienyl moieties were in close agreement with previously synthesised compounds.

Oxidation of alcohol **81** with Dess-Martin Periodinane [84] in refluxing dichloromethane for 16 h gave the aldehyde **82** (which existed as an equilibrium mixture containing predominantly the hydrate **83**, ~1:9, Scheme 29) in 68 % yield and oxalate **84** in 21 % yield. Spectroscopic characterisation of the **82** / **83** mixture was difficult due to signal overlap and duplication as a result of the active equilibrium. The ^{1}H NMR spectrum of the mixture displayed the diagnostic signals at δ 9.35 (s) for CHO for **83** and at δ 5.20 (s) for 4′′-H of **82**.



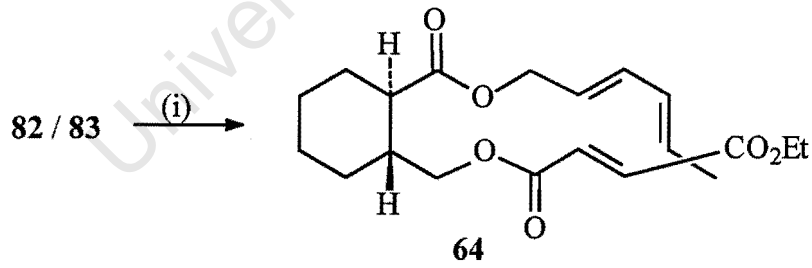
Scheme 29 *Reagents and Conditions:* (i) Periodinane, CH_2Cl_2, reflux

The modest yield achieved in this oxidation was largely a result of competitive formation of the oxalate **84**, whose formation was attributed to the nucleophilic interception of **82** by unconsumed starting material, followed by oxidation (Scheme 30). In attempts to minimise this side reaction various other oxidation reagents were investigated.[85,86] One such approach involved attempted oxidation with TPAP. This was unsuccessful as a result of chelation of the ruthenium metal to the α-oxygenated alcohol, thus preventing catalyst turnover.



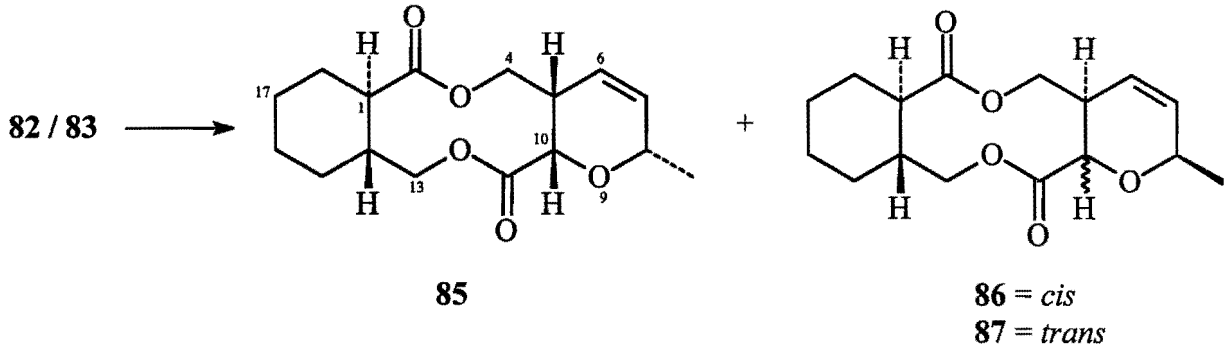
Scheme 30 Probable mechanism for the formation of **84**

Confirmation of the **82** ↔ **83** equilibrium was achieved by reacting the aldehyde/hydrate **82** + **83** mixture with (carbethoxymethylene)triphenylphosphine to give diester **64** in 64 % yield (Scheme 31). This therefore, was proof of the active equilibrium, and the aldehyde/hydrate mixture was used directly in future reactions. Attempts to obtain crystalline derivatives of **82** + **83** revolved around treatment of the mixture with tosylhydrazine or dinitrotosylhydrazine. However, the resultant products were not crystalline, and this approach was not investigated further.



Scheme 31 *Reagents and Conditions:* (i) $EtO_2CCHPPh_3$, CH_2Cl_2, 25 °C

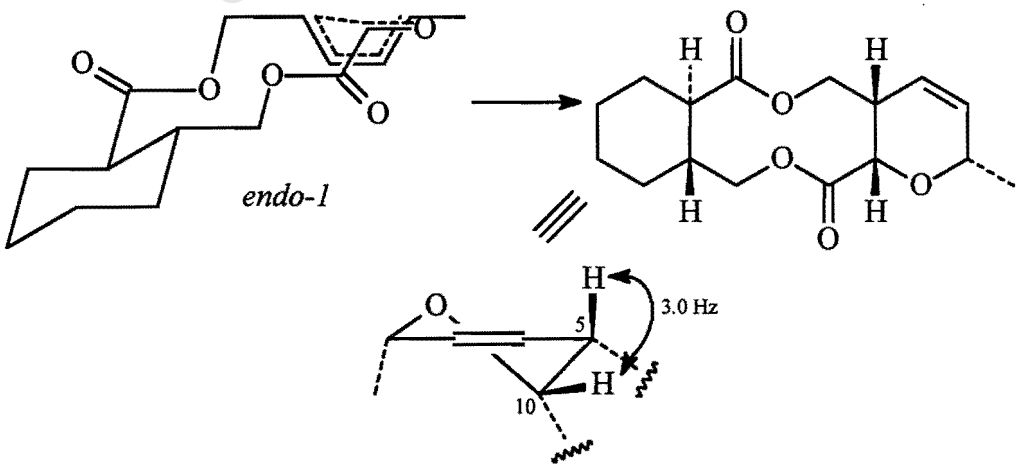
The aldehyde / hydrate mixture was azeotropically dried with the repeated evaporation of anhydrous toluene. The resulting aldehyde **82** was dissolved in toluene and the solution was heated at 150 °C for 24 h to give a mixture of three cycloadducts (4:2:1 by NMR, Scheme 32). This was subjected to reverse-phase HPLC to afford major cycloadduct **85** followed by an inseparable mixture of **86** and **87**.



Scheme 32 *Reagents and Conditions:* (i) $CH_3C_6H_5$, 150 °C, 24 h, 64 % overall

The ^{1}H NMR spectrum of **85** displayed a signal at δ 4.22 (d, *J* 3.0 Hz) for 10-H while diastereotopic 4-H_2 and 13-H_2 signals were in accordance with previously prepared cycloadducts. The IR spectrum displayed absorption at ν_{max} 1732 cm^{-1} (CO), whereas the accurate mass spectrum displayed the corresponding M+NH_4 molecular ion.

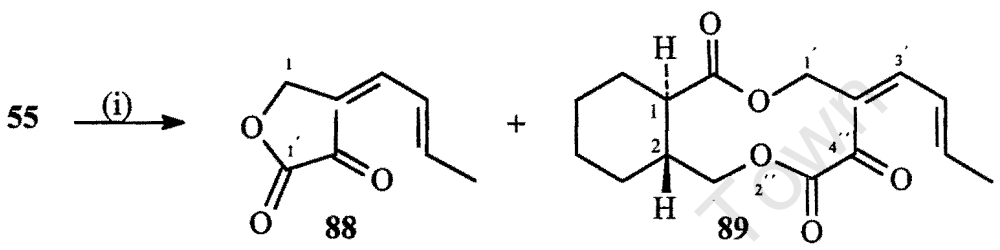
The assignment of **85** as a *cis*-fused cycloadduct was based of the small coupling observed between 10-H and 5-H (*viz.* 3.0 Hz). The relative stereochemistry (in relation to the spacer) was assigned by analogy to the preceding results and arose as a result of the *endo-1* transition state (Scheme 33).



Scheme 33 Transition state for major cycloadduct

The structural assignment of the minor cycloadducts were based on the ^{1}H NMR signals for the 10-H signals observed at δ 4.20 (d, *J* 3.0 Hz) for **86** and δ 3.95 (d, *J* 9.5 Hz) for **87**. These are indicative of the relationship at the newly formed ring junction and are assigned accordingly as *trans-cis* **86** and *trans-trans* **87** cycloadducts accordingly. With the success of this reaction outcome, attention was turned to the methyl analogue.

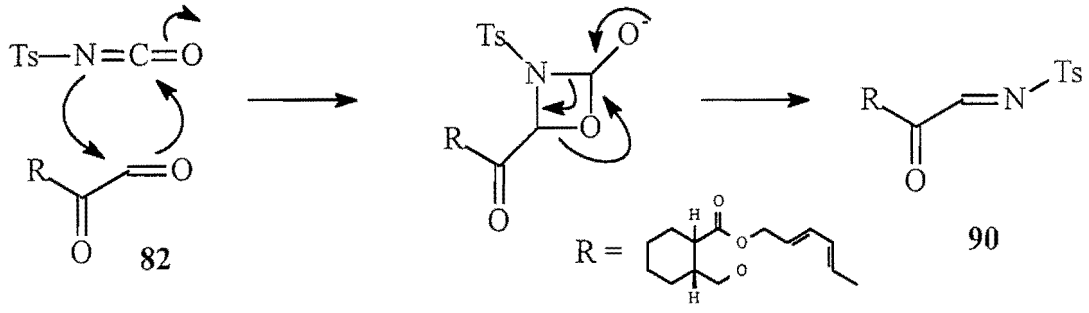
Treatment of alcohol **55** with pyruvic acid in the presence of DCC and DMAP afforded ester **88** (12 %) and the diester **89** in 49 % yield (Scheme 34). The diester **89** did not afford any cycloaddition when heated at elevated temperatures for extended periods.



Scheme 35 *Reagents and Conditions:* (i) CO_2HCOCH_3, DCC, DMAP, CH_2Cl_2, 61 % overall

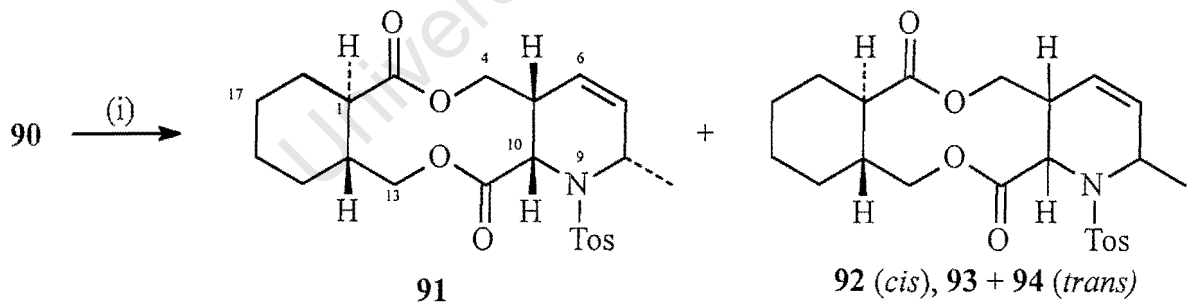
With the success of the above approach, attention was turned to the synthesis of nitrogen containing heterocycles.

2.3.3 8-Methyl-9-*p*-toluenesulfonyl-9-aza-3,12-dioxa-2,11-dioxo-[12.4.0.0^{5,10}]-tricyclo-octadec-6-ene Using a procedure by Holmes *et al.*,[87] aldehyde/hydrate was heated with tosylisocyanate which gave, at first, an *in situ* bimolecular [2 + 2] cycloaddition (with loss of CO_2) to give intermediate **90** (Scheme 35). The geometry of **90** was assigned (*Z*) from first principles, as formation of an (*E*)-imine seems improbable based on postulated mechanism.



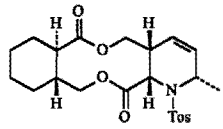
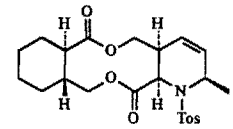
Scheme 35 Intermolecular [2 + 2] Diels-Alder reaction to form **90**

Intermediate **90** undergoes a facile IMDA reaction to give piperidine **91** in 42 % yield (Scheme 36) followed by a mixture of cycloadducts **92** – **94** (5:1:1 by NMR, key spectroscopic data for the two major *cis*-products are summarised in Table 2). It was not possible to isolate intermediate **90** as the initial [2 + 2] reaction was the rate limiting one. It was also not possible to monitor the reaction by NMR as the release of CO_2 made this experiment hazardous.



Scheme 36 *Reagents and Conditions:* (i) TsNCO, $C_6H_5CH_3$, 125 °C, 16 h

Table 2: Key coupling data and chemical shift for **91** and **92**.

				
	δ ppm	*J* (Hz)	δ (ppm)	*J* (Hz)
10-H	4.58	5.5	4.62	5.5
13α-H	4.52	2 x 11.5	3.60	11.5 and 4.5
13β-H	3.60	11.5 and 4.5	3.45	2 x 11.5

As in previous cases, the major cycloadduct arose as a result of *endo* addition of the dienophile (*exo* with respect to tosyl group) to give the major cycloadduct **91**. This was confirmed by x-ray structure analysis (Figure 2).

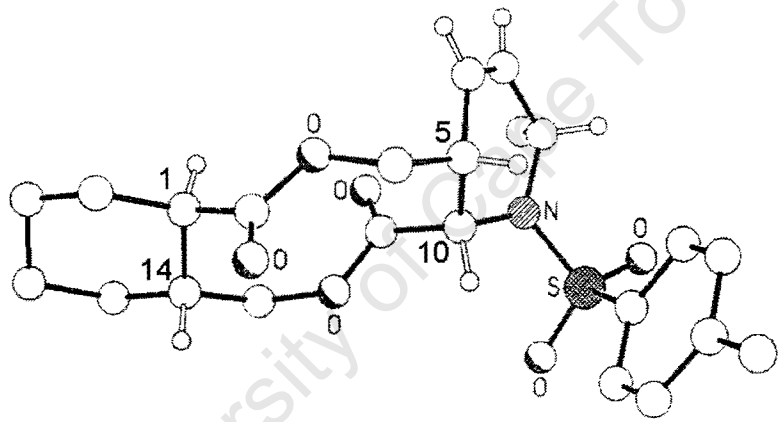
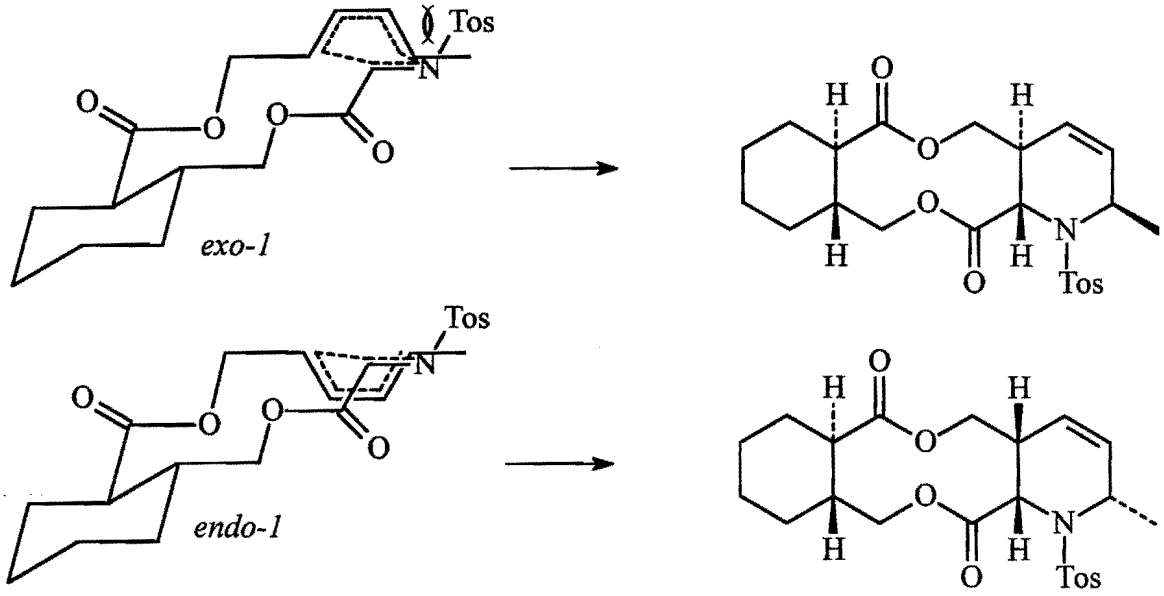


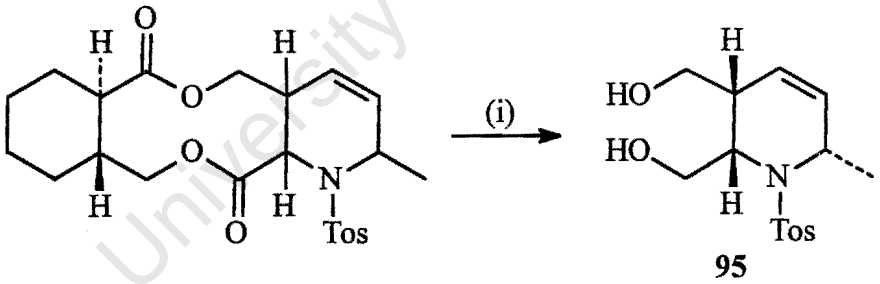
Figure 2 X-ray crystal structure of major cycloadduct **91**.

IMDA reaction of the *N*-tosylimine derivative **90** displayed not only enhanced *cis*-selectivity (~ 8:1) with respect to the parent oxygen analogue **82**, but a preference (2:1) for one of the *cis*-fused products over the other. The increased predominance for the *cis*-fused isomers, may reflect the steric bulk of the tosyl substituent on the imine – as these interactions with the diene are such that the latter approaches the dienophile *endo* (with respect to the ester, Scheme 37).



Scheme 37 Steric interactions between Tosyl group and diene for *exo* transition state (shown as *exo-1* for example) versus the *endo* variant (shown as *endo-1* for example) leading to the preferred *cis*-fused products

Due to the possibility of epimerisation of 10-H using base-mediated hydrolysis of the esters, it was decided to reduce the crude mixture of cycloadducts with excess lithium aluminum hydride. Reduction of the crude mixture gave diol **95** in 60 % yield (Scheme 38). The crude mixture of the remaining cycloadducts was not isolated or characterised.



Scheme 38 *Reagents and Conditions:* (i) $LiAlH_4$, THF, 25 °C, 60 %

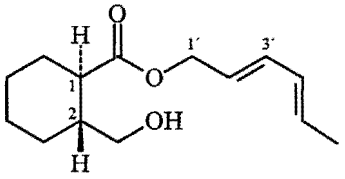
2.2.5 Conclusions. The above results have demonstrated that the synthesis of pyran and piperidine heterocyclic systems was possible using the above methodology. The IMDA reactions were *endo*-selective in both cases. The results of this investigation carried out at Imperial College have been published.[78] With the conclusion of this investigation, attention was turned to the synthesis and reactions of 1-phenylsulfonylallenyl systems.

CHAPTER 3

EXPERIMENTAL

General Procedures All reactions, where necessary, were carried out under an atmosphere of either argon or nitrogen. Air and moisture sensitive reagents were *trans*ferred via syringe or cannula, and reactions involving these materials were carried out in oven-dried flasks. NMR spectra were recorded on either Bruker Am-500, Bruker DRX-300, Jeol GX 270Q spectrometers using residual isotopic solvent ($CHCl_3$, δ_H = 7.26, toluene, δ_H = 2.03 ppm) as internal reference. ^1H NMR spectra were recorded in $CDCl_3$ on the 270 MHz spectrometer and ^{13}C were recorded at 50 MHz unless otherwise stated. Infrared spectra were recorded on a Matson 500 FTIR spectrometer as films, unless otherwise stated. Mass spectra were recorded using Jeol SX-102, VG-7070B, VG 12-253, VG ZAB-E or Jeol DX 303 using chemical ionisation techniques. Microanalyses were performed in the Imperial College Chemistry Department Microanalytical Laboratory. Melting points were determined on a Stuart Scientific Melting Point SMPL and are uncorrected. Sonication was carried out using a Semat 80 W, 50 kHz ultrasonic cleaning bath. X-ray crystal data were measured on a Nicolet R3m diffractometer with Cu-K_α radiation. Column chromatography was performed with Merck Kieselgel 60 (230 – 300 mesh) under pressure unless otherwise stated. Tlc referes to analytical thin layer chromatography performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F_{254}) and visualised with ultraviolet light, iodine and acidic ammonium molybdate (IV), anisaldehyde or potassium permanganate solutions as appropriate. Petrol refers to redistilled 40 – 60 °C petroleum ether, and ether to diethyl ether. Ether and tetrahydrofuran (THF) were distilled from sodium-benzophenone ketyl, dichloromethane from phosphorus pentoxide and toluene from sodium. Other reagents and solvents were purified according to standard procedures.[88]

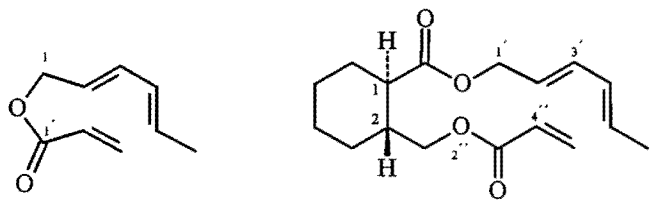
(1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(hydoxymethyl)cyclohexanecarboxylate 55**



Diisopropylamine (0.92 ml, 7.1 mmol) was added to a solution of anhydride **45** (1 g, 6.52 mmol) and dienol **2** (640 mg, 6.52 mmol) dichloromethane (10 ml) and the resulting solution was heated to reflux for 2 h. This was cooled to -10 °C upon which isobutylchloroformate (0.94 ml, 7.2 mmol) was added. The solution was allowed to warm to room temperature over 1 h. The ammonium salt was evaporated by filtration through a sintered glass funnel whilst washing with tetrahydrofuran.

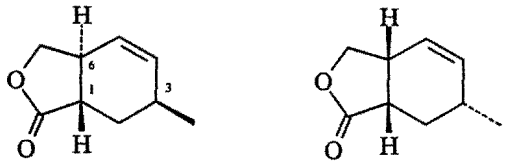
Sodium borohydride (360 mg, 9 mmol in 1 ml water) was added dropwise to the vigorously stirred filtrate at -20 °C. The reaction was allowed to warm to room temperature over 1 h and was then stirred for a further 1 h. The solution was filtered through $MgSO_4$ whilst washing with ether and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate-hexane (1:4) as eluent to yield *dienol* **55** (1.066 g, 69 %) as an oil; ν_{max}/cm^{-1} 3485 (OH) and 1730 (CO); δ_H (300 MHz) 1.77 (3H, d, *J* 6.5, 6′-Me), 3.50 (2H, m, CH_2OH), 4.58 (2H, d, *J* 6.6, 1′-H_2), 5.56 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.75 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 6.05 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.26 (1H, dd, *J* 15.0 and 10.5, 3′-H); δ_C 18.1 (C-6′), 25.2 (C-5), 25.3 (C-4), 29.7 (C-3), 32.0 (C-6), 39.5 (C-2), 46.5 (C-1), 64.8 (C-1′), 66.5 (CH_2OH), 123.6 (C-2′), 130.4 (C-4′), 131.3 (C-5′), 135.0 (C-3′) and 176.1 (CO); (Found: $M+NH_4^+$, 256.1913. $C_{14}H_{26}NO_3$ requires M, 256.1902).

(2*E*,4*E*)-Hexa-2,4-dienyl-acrylate 59 and (1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-pent-4-ene)cyclohexanecarboxylate 60**



Acryloyl chloride (0.9 ml, 1.1 mmol) and triethylamine (0.12 ml, 0.86 mmol) were added to a solution of alcohol **55** (204 mg, 0.86 mmol) in dichloromethane (2 ml). The mixture was stirred at 20 °C for 30 min, after which it was filtered through a sintered glass funnel whilst washing with ether. The solvent was evaporated under reduced pressure and the residue chromatographed on silica gel with ether-petrol (1:9) as eluent to afford the triene **59** (15 mg, 11 %) as a pungent volatile oil; ν_{max}/cm^{-1} 1725 (CO); δ_H 1.75 (3H, d, *J* 7.1, 6-H_3), 4.65 (2H, d, *J* 6.5, 1-H_2), 5.55 (1H, dt, *J* 15.0 and 2 x 6.5, 2-H), 5.67 (1H, m, 5-H), 5.80 (1H, dd, *J* 10.5 and 1.5, 3′-H_{cis}), 6.04 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4-H), 6.10 (1H, dd, *J* 17.5 and 10.5, 2′-H), 6.22 (1H, dd, *J* 15.0 and 10.5, 3-H) and 6.43 (1H, dd, *J* 17.5 and 1.5, 3′-H_{trans}); (Found: $M+NH_4^+$, 170. $C_9H_{16}NO_2$ requires M, 170). This was followed by *triene* **60** (185 mg, 74 %) as an oil; ν_{max}/cm^{-1} 1728 (CO); δ_H (400 MHz) 1.77 (3H, d, *J* 7.0, 6′-H_3), 2.20 (1H, td, *J* 2 x 11.5 and 3.5, 1-H), 4.02 (1H, dd, *J* 11.0 and 5.0, 1′′-H), 4.05 (1H, dd, *J* 11.0 and 5.5, 1′′-H), 4.56 (2H, m, 1′-H_2), 5.55 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.74 (1H, dq, *J* 15.0 and 3 x 7.0, 5′-H), 5.80 (1H, dd, *J* 10.5 and 1.5, 5′′-H_{cis}), 6.04 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H), 6.10 (1H, dd, *J* 17.5 and 10.5, 4′′-H), 6.22 (1H, dd, *J* 15.0 and 10.5, 3′-H) and 6.38 (1H, dd, *J* 17.5 and 1.5, 5′′-H_{trans}); δ_C (100 MHz) 18.1 (C-6′), 25.0 (C-5), 25.2 (C-4), 28.5 (C-3), 29.8 (C-6), 38.3 (C-2), 46.4 (C-1), 64.8 (C-1′), 67.6 (C-1′′), 123.6 (C-5′), 128.4 (C-2′), 130.4 (C-4′), 130.7 (C-3), 131.2 (C-4′′), 134.8 (C-5′′), 166.1 (C-3′′) and 175.2 (CO_2); (Found: $M+NH_4^+$, 310.2175. $C_{17}H_{28}NO_4$ requires M, 310.2167).

(1*S,3*S**,6*R**)- and (1*S**,3*R**,6*S**)-3-Methyl-8-oxa-9-oxo-[4.3.0]-bicyclonon-4-ene 61 and 62**

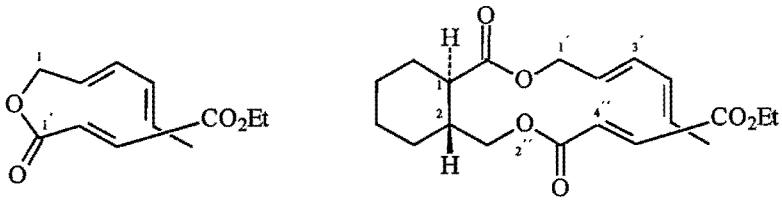


The triene **60** (150 mg, 0.5 mmol) was dissolved in toluene (5 ml) and the solution sealed under an atmosphere of nitrogen. The resulting solution was heated at 170 °C for 24 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with ether-petrol (3:10) as eluent to yield an inseparable mixture of cycloadducts (130 mg, 85 %, 2:1 by NMR) which was used without further purification.

These were dissolved in methanol (3.2 ml) and tetrahydrofuran (2ml). A solution of $LiOH.H_2O$ (2.8 ml, 2.5 M, 7 mmol) was added and the reaction was stirred at 20 °C for 1 h. The reaction was acidified (2M HCl) and the mixture partitioned between brine (10 ml) and ether (10 ml).The mixture was extracted (Et_2O) and the combined organic extract was dried ($MgSO_4$) and evaporated.

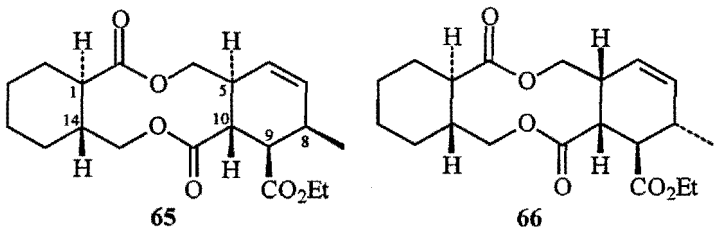
The residue was redissolved in dichloromethane (5 ml). *p*-Toluene sulfonic acid (70 mg, 0.26 mmol) was then added, and the mixture was refluxed for 1 h. The solvent was evaporated under reduced pressure and the residue chromatographed on silica gel using ether-petrol (3:10) as eluent to give the major *trans*-lactone **61** (30 mg, 44 %), mp 66 – 68 °C (from hexane); ν_{max}/cm^{-1} 1778 (CO); δ_H (500 MHz) 1.08 (3H, d, *J* 7.5, Me), 1.83 (1H, dd, *J* 12.5 and 3.0, 2-H), 1.95 (1H, td, *J* 2 x 12.5 and 3.0, 2-H), 2.23 (1H, dt, *J* 12.5 and 2 x 2.5, 3-H), 2.56 (1H, m, 6-H), 2.75 (1H, m, *W* 28, 1-H), 3.87 (1H, dd, *J* 11.5 and 8.0, 7-H), 4.46 (1H, dd, *J* 11.5 and 7.0, 7-H), 5.68 (1H, dt, *J* 10.0 and 2 x 2.5, 4-H) and 5.75 (1H, dt, *J* 10.0 and 2 x 1.5, 5-H); (Found: $M+NH_4^+$, 170.1185. $C_9H_{16}NO_2$ requires M, 170.1181) followed by a mixture of *trans*-hexahydrophthalide **58** and the *cis* lactone **62** (2:1 by NMR, 90 mg) (compound **62**); ν_{max}/cm^{-1} 1779 (CO); δ_H (500 MHz) 1.08 (3H, d, *J* 7.3, Me), 1.95 (1H, m, 2-H), 2.25 (1H, m, 3-H), 2.56 (1H, m, 6-H), 2.68 (1H, m, 1-H), 3.87 (1H, t, *J* 8.5, 7-H), 4.46 (1H, t, *J* 8.5, 7-H), 5.56 (1H, ddd, *J* 10.0, 4.0 and 2.5, 4-H), 5.75 (1H, br d, *J* 10.0, 5-H).

(2′*E*,2*E*,4*E*)-Hexa-2,4-dienyl-5′-oxa-1′,4′-dioxo-hept-2′-en-carboxylate 63 and (1*R,2*R**,2′*E*, 4′*E*,4′′*E*)-hexa-2′,4′-dienyl-2-[2′′,7′′-dioxa-3′′,6′′-dioxo-non-4′′-ene]cyclohexane-carboxylate 64**



The alcohol **55** (452 mg, 1.9 mmol) and monoethylesterfumaric acid (274 mg, 1.9 mmol) were dissolved in dichloromethane (5 ml) at room temperature. Dicyclohexyldicarbodiimide (DCC)(440 mg, 2.1 mmol) and DMAP (40 mg, 0.2 mmol) were added and the reaction was stirred for 2 h at 20 °C. The resulting slurry was filtered through a sintered glass funnel whilst washing with ether and the solvent evaporated under reduced pressure. The residue was chromatographed on silica gel with ether-petrol (1:9) as eluent to yield the monoester **63** (41 mg, 9 %); ν_{max}/cm^{-1} 1715 (CO); δ_H 1.32 (3H, t, *J* 6.9, OCH_2CH_3), 1.75 (3H, d, *J* 6.5, 6-H_3), 4.25 (2H, q, *J* 6.9, OCH_2CH_3), 4.68 (2H, d, *J* 6.8, 1-H_2), 5.64 (1H, dt, *J* 15.0 and 2 x 6.5, 2-H), 5.54 (1H, m, 5-H), 6.07 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4-H), 6.28 (1H, dd, *J* 15.0 and 10.5, 3-H) and 6.84 (2H, s, 2′-H and 3′-H); (Found: $M+NH_4^+$, 242. $C_{12}H_{20}NO_4$ requires M, 242). This was followed by the *triene* **64** (563 mg, 81 %) as an oil; ν_{max}/cm^{-1} 1719 (CO); δ_H (500 MHz) 1.13 (1H, qd, *J* 3 x 11.0 and 3.5, 3α-H_x), 1.30 (2H, m, 5-H_2), 1.32 (3H, t, *J* 7.0, 9′′-H_3), 1.50 (1H, qd, *J* 3 x 11.0 and 3.5, 6β-H), 1.75 (3H, d, *J* 6.5, 6′-H_3), 1.83 (3H, m, 3- and 4-H_2), 1.95 (1H, m, 6-H), 2.01 (1H, m, 2-H), 2.21 (1H, td, *J* 2 x 11.6 and 3.5, 1-H), 4.05 (1H, dd, *J* 11.5 and 5.0, 1′′-H), 4.10 (1H, dd, *J* 11.0 and 5.5, 1′′-H), 4.25 (2H, q, *J* 7.0, 8′′-H_2), 4.60 (2H, m, 1′-H_2), 5.56 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.75 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 6.03 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H), 6.23 (1H, dd, *J* 15.0 and 10.5, 3′-H) and 6.82 (2H, s, 4′′-H and 5′′-H); δ_C (100 MHz) 14.1 (q, C-9′′), 18.1 (q, C-6′), 25.1 (t, C-5), 25.2 (t, C-4), 28.6 (t, C-3), 29.8 (t, C-6), 38.3 (d, C-2), 46.2 (d, C-1), 61.3 (t, C-1′′), 64.9 (t, C-1′), 68.3 (t, C-8′′), 123.6 (d, C-5′), 130.5 (d, C-2′), 131.2 (d, C-4′), 133.3 (d, C-3′), 133.8, 135.0 (d, C-4′′ and C-5′′), 164.8 and 165.0 (s, 2x CO_2) and 175.2 (s, CO_2); (Found: $M+NH_4^+$, 382.2226. $C_{20}H_{32}NO_6$ requires M, 382.2230).

Ethyl ($1R^*,5R^*,8S^*,9R^*,10R^*,14R^*$)- and ($1R^*,5S^*,8R^*,9R^*,10R^*,14R^*$)-8-Methyl-3,12-dioxa-2,11-dioxo-[12.4.0.0^{5,10}]-tricyclo-octadec-6-en-9-carboxylate 65 and 66

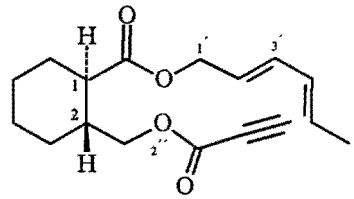


65 66

The triene **64** (560 mg, 1.5 mmol), once repeatedly sonicated in toluene (2 ml), was heated in a sealed tube at 80 °C for 24 h. The solution was cooled and the solvent was evaporated under reduced pressure to yield a mixture (2:1) of cyclocloadducts (520 mg, 90 %). A portion (150 mg, 0.41 mmol) of this residue was chromatographed and was subjected to reverse-phase HPLC (Vydac C_{18} 25 cm x 20 mm column, UV detection @ 230 nm, mobile phase: 0.1 % TFA in water (solvent A) and 0.1 % TFA in acetonitrile (solvent B); gradient elution, using 3:10 solvent A:solvent B→ pure solvent B; flow rate 5 ml min^{-1}) to give the major *trans-trans* adduct **65** (89 mg, 60 %); ν_{max}/cm^{-1} 1735 (CO); δ_H (400 MHz) 1.10 (3H, d, *J* 6.5, Me), 1.30 (3H, t, *J* 7.0, CH_2CH_3), 2.05 (1H, td, *J* 2 x 11.0 and 3.5, 1-H), 2.42 (1H, m, 8-H), 2.45 (1H, dd, *J* 12.0 and 10.5, 10-H), 3.05 (1H, dd, *J* 12.0 and 5.0, 9-H), 3.42 (1H, m, 5-H), 3.45 (1H, t, *J* 11.5, 13α-H), 3.54 (1H, t, *J* 11.5, 4β-H), 4.16 – 4.26 (2H, m, CH_2CH_3), 4.42 (1H, dd, *J* 11.5 and 3.5, 13β-H), 4.46 (1H, dd, *J* 11.5 and 3.4, 4α-H), 5.56 (1H, ddd, *J* 10.0, 5.0 and 2.5, 7-H), 5.61 (1H, dt, *J* 10.0 and 2 x 1.5, 6-H); δ_C (100 MHz) 14.2 (q, CH_2CH_3), 19.6 (q, 8-Me), 24.8 (t, C-17), 25.5 (t, C-16), 27.2 (t, C-15), 29.9 (t, C-18), 33.7 (d, C-5), 35.3 (d, C-8), 35.7 (d, C-14), 43.2 (d, C-10), 44.3 (d, C-9), 49.7 (d, C-1), 60.6 (t, CH_2CH_3), 63.8 (t, C-4), 69.8 (t, C-13), 123.2 (d, C-6), 135.0 (d, C-7), 173.0, 175.5 and 176.1 (s, 3x CO_2); (Found; C, 65.8; H, 7.8 %: Calc. for $C_{20}H_{28}O_6$; C, 65.9; H, 7.7 %); (Found: $M+NH_4^+$, 382.2203. $C_{20}H_{32}NO_6$ requires M, 382.2203) and the minor *trans-cis* cycloadduct **66** (48 mg, 27 %), mp 118 – 120°C (from dichloromethane-ether); ν_{max}/cm^{-1} 1736 (CO); δ_H (500 MHz) 1.08 (3H, d, *J* 6.5, 8-Me), 1.28 (3H, t, *J* 7.0, CH_2CH_3), 2.38 (1H, m, 8-H), 2.50 (1H, dd, *J* 12.0 and 11.5, 9-H), 3.00 (1H, dd, *J* 12.0 and 5.0, 10-H), 3.45 (1H, m, 5-H), 3.55 (1H, t, *J* 11.0, 4α-H_{ax}), 3.60 (1H, dd, *J* 11.1 and 3.0, 13β-H), 4.06 – 4.17 (2H, m, CH_2CH_3), 4.38 (1H, dd, *J* 11.0 and 3.0, 4β-H), 4.67 (1H, t, *J* 11.1, 13α-H), 5.56 (1H, ddd, *J* 10.0, 5.0 and 2.5, 7-H), 5.60 (1H, dt, *J* 10.0 and 2 x 1.5, 6-H); δ_C (100 MHz) 14.2 (q, CH_2CH_3), 19.6 (q, C-8), 24.6 (t, C-17), 24.8 (t, C-16), 28.3 (t, C-15), 29.7 (t, C-18), 33.7 (d, C-5), 35.2 (d, C-8), 39.8 (d, C-14), 43.4 (d, C-10), 44.3 (d, C-9), 47.7 (d, C-1), 60.6 (t, CH_2CH_3), 63.7 (t, C-4), 67.9 (t, C-13), 123.2

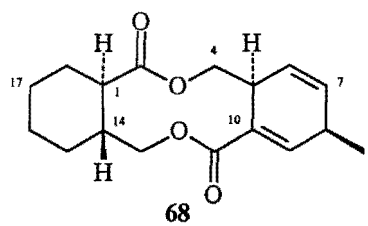
(d, C-6), 135.0 (d, C-7), 173.0, 175.5 and 175.9 (s, 3x CO_2); (Found: $M+H^+$, 365.1964. $C_{20}H_{29}O_6$ requires M, 365.1953).

(1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-pent-4-yne)-cyclohexanecarboxylate 67**

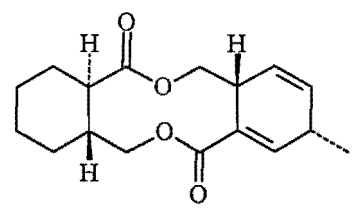


Propiolic acid (0.05 ml, 0.59 mmol) was added dropwise to a solution of the alcohol **55** (130 mg, 0.54 mmol), DCC (150 mg, 0.73 mmol) and DMAP (10 mg, 0.05 mmol) in dichloromethane (4 ml) at room temperature. The reaction was stirred for 1 h, after which it was filtered through a sintered glass funnel whilst washing with ether. The solvent was evaporated under reduced pressure and the residue chromatographed on silica gel with ethyl acetate-hexane (1:19) as eluent to yield the *dienyne* **67** (97 mg, 61 %); ν_{max}/cm^{-1} 3297 (C≡C), 1719 (CO); δ_H 1.77 (3H, d, *J* 7.0, 6′-H_3), 2.20 (1H, td, *J* 11.5 and 3.5, 1-H), 2.87 (1H, s, 5′′-H), 4.01 (1H, dd, *J* 11.0 and 5.0, 1′′-H), 4.10 (1H, dd, *J* 11.0 and 5.5, 1′′-H), 4.59 (2H, d, *J* 6.5, 1′-H_2), 5.62 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.74 (1H, dq, *J* 15.0 and 3 x 7.0, 5′-H), 6.04 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.25 (1H, dd, *J* 15.0 and 10.5, 3′-H); δ_C (100 MHz) 18.0 (C-Me), 25.0 (C-5), 25.2 (C-4), 28.4 (C-3), 29.7 (C-6), 38.2 (C-2), 46.2 (C-1), 65.0 (C-1′), 69.2 (C-1′′), 74.6 and 74.7 (C-4′′ and C-5′′), 123.7 (C-5′), 130.5 (C-2′), 131.1 (C-4′), 135.0 (C-3′), 152.6 (C-3′′) and 174.9 (CO_2); (Found: $M+NH_4^+$, 308.1857. $C_{16}H_{26}NO_4$ requires M, 308.1861).

(1*R,5*R**,8*R**,14*R**)- and (1*R**,5*S**,8*S**,14*R**)-8-Methyl-3,12-dioxa-2,11-dioxo-[12.4.0.0^{5,10}]-tricyclo-octadeca-6,9-diene 68 and 69**



68

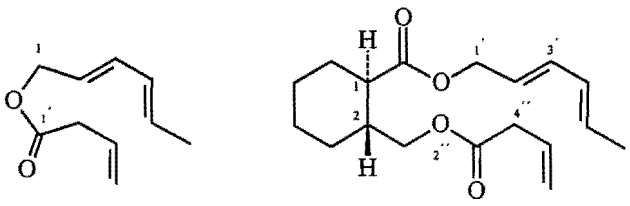


69

The triene **67** (61 mg, 0.2 mmol) dissolved in toluene (2 ml) was subjected to alternate sonication and flushing with nitrogen. The solution was heated in a sealed tube at 150 °C for 24 h when the solvent was evaporated under reduced pressure. This gave an inseparable mixture of cycloadducts

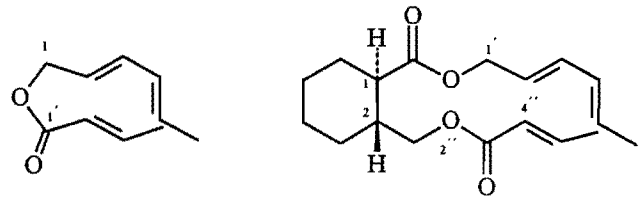
(1:1 by NMR, 61mg, 100 %); ν_{max}/cm^{-1} 1722 (CO); δ_H (**68**) 6.95 (1H, dd, *J* 4.5 and 1.5, 9-H); (**69**) 6.90 (1H, dd, *J* 4.5 and 1.5, 9-H), 0.86 (3H, d, *J* 6.5, Me); (**68** and **69**) 2.70 – 3.00 (2H, m, 5-H) 3.70 – 3.80 (2H, m, 8-H), 5.60 – 6.00 (4H, m, 6- and 7-H); (Found: $M+NH_4^+$, 308. $C_{17}H_{28}NO_4$ requires M, 308).

(2*E*,4*E*)-Hexa-2,4-dienyl 1′-oxo-but-3′-en-carboxylate 70 and (1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-hex-5′′-ene)-cyclohexanecarboxylate 71**



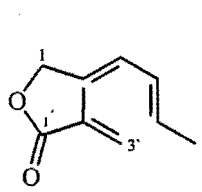
Trans-crotonyl chloride (44 µl, 0.46 mmol) and triethylamine (64 µl, 0.46 mmol) were added sequentially to a solution of dienol **55** (100 mg, 0.42 mmol) dissolved in dichloromethane (1 ml) and the mixture was stirred at room temperature for 1 h. The resulting slurry was filtered through a sintered glass funnel whilst washing with ether. The solvent was evaporated under reduced pressure and the residue chromatographed on silica gel with ether-petrol (1:5) as eluent to afford the monoester triene **70** (17 mg, 24 %); ν_{max}/cm^{-1} 1736 (CO); δ_H 1.77 (3H, d, *J* 6.5, 6-H_3), 3.10 (2H, dt, *J* 6.9 and 1.5, 2′-H_2), 4.60 (2H, m, 1-H_2), 5.15 (1H, dq, *J* 6.5 and 3 x 1.5, 4′-H_{trans}), 5.19 (1H, t, *J* 1.5, 4′-H_{cis}), 5.62 (1H, dt, *J* 15.0 and 2 x 6.5, 2-H), 5.76 (1H, m, 5-H), 5.95 (1H, m, 3′-H), 6.07 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4-H) and 6.28 (1H, dd, *J* 15.0 and 10.5, 3-H); (Found: $M+NH_4^+$, 184. $C_{10}H_{18}NO_2$ requires M, 184). This was followed by the *triene* **71** (100 mg, 76 %); ν_{max}/cm^{-1} 1736 (CO); δ_H (400 MHz) 1.10 (1H, qd, *J* 3 x 11.0 and 3.5, 3-H_{ax}), 1.57 (1H, qd, *J* 3 x 11.0 and 3.5, 6-H_{ax}), 1.77 (3H, d, *J* 6.5, 6′-H_3), 2.20 (1H, td, *J* 11.5 and 3.5, 1-H), 3.07 (2H, dt, *J* 6.9 and 2 x 1.5, 4′′-H_2), 3.92 (1H, dd, *J* 11.0 and 5.0, 1′′-H), 4.00 (1H, dd, *J* 11.0 and 5.8, 1′′-H), 4.56 (2H, d, *J* 6.5, 1′-H_2), 5.12 (1H, dq, *J* 6.5 and 3 x 1.5, 6′′-H_{trans}), 5.17 (1H, t, *J* 1.5, 6′′-H_{cis}), 5.60 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.74 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 5.90 (1H, m, 5′′-H), 6.05 (1H, ddd, *J* 15.1, 10.5 and 1.5, 4′-H) and 6.24 (1H, dd, *J* 15.0 and 10.5, 3′-H); δ_C (100 MHz) 18.1 (C-Me), 25.0 (C-5), 25.2 (C-4), 28.5 (C-3), 29.8 (C-6), 38.3 (C-2), 39.0 (C-4′′), 46.2 (C-1), 64.9 (C-1′), 67.7 (C-1), 118.5 (C-6′′), 123.5 (C-5′), 130.2 (C-5′′), 130.4 (C-2′), 131.3 (C-4′), 134.9 (C-3′), 171.5 (C-3′′) and 175.2 (CO_2); (Found: $M+NH_4^+$, 324.2172. $C_{18}H_{30}NO_4$ requires M, 324.2174).

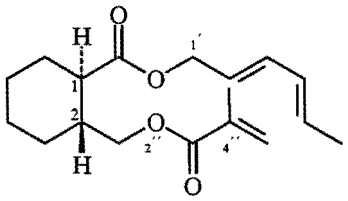
(2*E*,4*E*)-Hexa-2,4-dienyl 1′-oxo-but-2′-en-carboxylate 72 and (1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-4′′*E*-hex-4′′-ene)-cyclohexanecarboxylate 73**



Reaction was carried out, as before, on dienol **55** (100 mg, 0.42 mmol) with *trans*-crotonyl chloride (44 μl, 0.46 mmol) and pyridine (37 μl, 0.46 mmol). Filtration and chromatography [silica gel, ether-petrol (1:5)] gave sorbyl triene **72** (42 mg, 60 %); ν_{max}/cm^{-1} 1722 (CO); δ_H 1.77 (3H, d, *J* 6.5, 6-H_3), 1.87 (3H, dd, *J* 7.0 and 1.5, 4′-H_3), 4.62 (2H, d, *J* 6.5, 1-H_2), 5.65 (1H, td, *J* 15.0 and 2 x 6.5, 2-H), 5.76 (1H, m, 5-H), 5.85 (1H, dq, *J* 15.4 and 3 x 1.5, 2′-H), 6.05 (1H, ddd, *J* 15.1, 10.5 and 1.5, 4-H), 6.25 (1H, dd, *J* 15.0 and 10.5, 3-H) and 7.00 (1H, dq, J 15.4 and 3 x 7.0, 3′-H); (Found: $M+NH_4^+$, 184. $C_{10}H_{18}NO_2$ requires M, 184). This was followed by the *triene* **73** (40 mg, 31 %); ν_{max}/cm^{-1} 1730 (CO); δ_H (400 MHz) 1.10 (1H, qd, *J* 3 x 11.0 and 3.5, 3-H_{ax}), 1.45 (1H, qd, *J* 3 x 11.0 and 3.5, 6-H_{ax}), 1.77 (3H, d, *J* 6.5, 6′-H_3), 1.85 (3H, dd, *J* 7.0 and 1.5, 6′′-H_3), 2.20 (1H, td, *J* 2 x 11.5 and 3.5, 1-H), 3.98 (1H, dd, *J* 11.0 and 5.0, 1′′-H), 4.02 (1H, dd, *J* 11.0 and 6.0, 1′′-H), 4.55 (2H, m, 1′-H_2), 5.57 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.74 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 5.82 (1H, dq, *J* 15.5 and 3 x 1.5, 4′′-H), 6.03 (1H, ddd, *J* 15.1, 10.5 and 1.5, 4′-H), 6.22 (1H, dd, *J* 15.0 and 10.5, 3′-H) and 7.05 (1H, dq, *J* 15.6 and 3 x 7.0, 5′′-H); δ_C 18.0 (C-6′′), 18.1 (C-6′), 25.0 (C-5), 25.2 (C-4), 28.5 (C-6), 29.8 (C-3), 38.4 (C-2), 46.4 (C-1), 64.8 (C-1′), 67.2 (C-1′′), 122.5 (C-4′′), 123.6 (C-5′), 130.4 (C-2′), 131.1 (C-4′), 134.8 (C-3′), 144.7 (C-5′′), 166.4 (C-3′′) and 175.2 (CO_2); (Found: $M+NH_4^+$, 324.2166. $C_{18}H_{30}NO_4$ requires M, 324.2174).

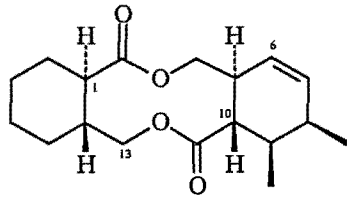
(2*E*,4*E*) Hexa-2,4-dienyl methacrylate 74 and (1*R,2*R**,2′*E*,4′*E*)-hexa-2′,4′-dienyl-2-(4′′-methyl-2′′-oxa-3′′-oxo-hex-4′′-ene)cyclohexanecarboxylate 75**



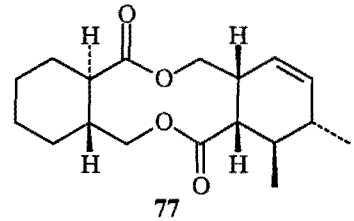


Methacryloyl chloride (44 μl, 0.46 mmol) was added to a stirred solution of dienol **55** (100 mg, 0.42 mmol) and triethylamine (64 μl, 0.46 mmol) and the resulting solution was stirred for 1 h. The solvent was removed and the residue was chromatographed directly [silica gel, ether-petrol (1:5] to give sorbyl triene **74** (25 mg, 36 %); ν_{max}/cm^{-1} 1718 (CO); δ_H (300 MHz) 1.77 (3H, d, *J* 6.7, 6-H_3), 2.00 (3H, t, *J* 1.3, 2′-H_3), 4.70 (2H, d, *J* 6.7, 1-H_2), 5.57 (1H, dq, *J* 2.6 and 3 x 1.3, 3′-H), 5.62 (1H, dt, *J* 15.0 and 2 x 6.5, 2-H), 5.72 (1H, m, 5-H), 5.85 (1H, dq, *J* 2.6 and 3 x 1.3, 3′-H), 6.10 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4-H) and 6.28 (1H, dd, *J* 15.0 and 10.5, 3-H); (Found: $M+NH_4^+$, 184. $C_{10}H_{18}NO_2$ requires M, 184). This was followed by the *diester* **75** (80 mg, 62 %); ν_{max}/cm^{-1} 1729 (CO); δ_H (400 MHz) 1.12 (1H, qd, *J* 3 x 11.1 and 3.7, 3-H_{ax}), 1.50 (1H, qd, *J* 3 x 11.0 and 3.5, 6-H_{ax}), 1.77 (3H, d, *J* 6.5, 6′-H_3), 1.93 (3H, t, *J* 1.5, 5′′-H_3), 2.22 (1H, td, *J* 11.5 and 3.5, 1-H), 4.02 (2H, d, *J* 5.5, 1′′-H_2), 4.56 (2H, m, 1′-H_2), 5.60 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.72 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 5.82 (1H, dq, *J* 2.5 and 3 x 1.5, 5′′-H), 6.05 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H), 6.24 (1H, dd, *J* 15.0 and 10.5, 3′-H), 6.26 (1H, dq, *J* 2.6 and 3 x 1.0, 5′′-H); δ_C (100 MHz) 18.0 (C-6′), 18.3 (C-4′′-*Me*), 25.2 (C-5), 25.9 (C-4), 28.7 (C-6), 29.8 (C-3), 38.4 (C-2), 46.4 (C-1), 64.8 (C-1′), 67.7 (C-1′′), 123.6 (C-5′), 125.5, 129.0 (C-4′ and C-2′′), 130.4 (C-3′), 131.1 (C-4′′), 134.8 (C-5′′), 163.0 (C-3′′) and 175.2 (CO_2); (Found: $M+NH_4^+$, 324. $C_{18}H_{30}NO_4$ requires M, 324).

($1R^*,5R^*,8S^*,9R^*,10S^*,14R^*$)- and ($1R^*,5S^*,8R^*,9R^*,10S^*,14R^*$)-8,9-Dimethyl-3,12-dioxa-2,11-dioxo-[12.4.0.0$^{5.10}$]-tricyclooctadec-6-ene 76 and 77



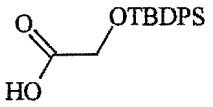
76



77

The triene **73** (30 mg, 0.1 mmol) in toluene-d_8 (1 ml) was heated to 160 °C for 72 h, whilst the reaction was monitored by NMR over 72 h, after which the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel with ether-petrol (3:7) as eluent. This afforded the starting triene (10 mg, 33 %) followed by an inseparable mixture of cycloadducts **76** and **77** (~ 1:1 by NMR, 20 mg, 66 %); ν_{max}/cm^{-1} 1730 (CO); δ_H (400 MHz)(**76**) 1.10 (3H, d, *J* 6.5, 8-Me), 1.12 (3H, d, *J* 7.0, 9-Me), 3.20 (1H, m, 5-H), 3.95 – 4.25 (4H, m, 4- and 13-H_2), 5.55 (1H, ddd, *J* 10.0, 5.0 and 2.5, 6-H), 5.65 (1H, br d, *J* 10.0, 7-H); (**77**) 0.90 (3H, d, *J* 7.0, 8-Me), 0.92 (3H, d, *J* 7.0, 9-Me), 2.03 (1H, m, 9-H), 2.05 (1H, dd, *J* 11.0 and 5.9, 10β-H), 2.20 (1H, m, 8-H), 2.90 (1H, m, 5-H), 3.63 (1H, t, *J* 11.3, 13α-H), 3.82 (1H, dd, *J* 11.0 and 4.1, 4β-H), 4.43 (1H, dd, *J* 11.3 and 4.0, 13β-H), 4.53 (1H, t, *J* 11.1, 4α-H), 5.26 (1H, dq, *J* 10.0 and 3 x 2.5, 6-H), 5.82 (1H, ddd, *J* 10.0, 5.0 and 2.5, 7-H); (Found: $M+NH_4^+$, 324. $C_{18}H_{30}NO_4$ requires M, 324).

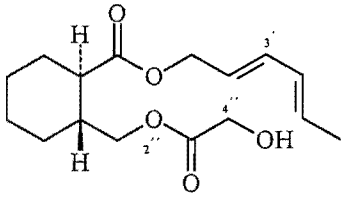
2-*t*-Butyldiphenylsilyoxylacetic acid 79



t-Butyldiphenylsilyl chloride (1.8 mmol, 17 mmol), triethylamine (0.94 ml, 17 mmol) and DMAP (60 mg, 0.3 mmol) were sequentially added to a solution of glycolic acid (500 mg, 6.7 mmol) in dichloromethane (3 ml). The solution was stirred at room temperature for 1 h, following which the solvent was evaporated under reduced pressure. The residue was filtered through a sintered glass funnel whilst washing with ether. The solvent was evaporated and the process was repeated. This gave the diprotected glycolic acid **78** (3.1 g).

The residue was dissolved in tetrahydrofuran (30 ml) and water (15 ml). Potassium carbonate (2 g, 62 mmol) was added and the resulting homogenous solution was stirred at room temperature for 1 h. The tetrahydrofuran was evaporated under reduced pressure and the resulting aqueous solution was cooled to 0 °C and the pH adjusted to 4 using 1M HCl. The aqueous phase was extracted with ether and the combined organic phase was washed with brine. This was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The residue was chromatographed on silica gel with ether-petrol (1:1) as eluent to yield the silyl ether **79** (1.76 g, 85 %). Mass spectrometry results and ^{1}H NMR were identical to those reported in the literature.[82]

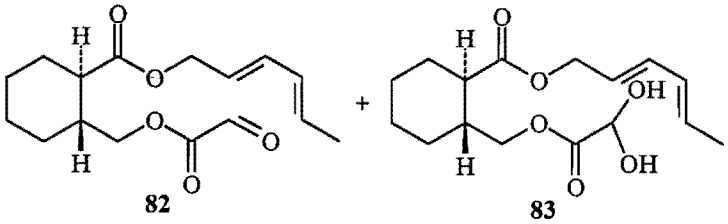
(1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-butan-4′′-ol)cyclohexane-carboxylate 81**



t-Butyldiphenylsilyloxyacetic acid (300 mg, 0.95 mmol), DCC (210 mg, 1.0 mmol) and DMAP (20 mg, 0.1 mmol) were sequentially added to a solution of dienol **55** (200 mg, 0.84 mmol) in dichloromethane (2 ml) and the resulting slurry was stirred at room temperature for 2 h. This was filtered through a sintered glass funnel whilst washing repeatedly with dichloromethane. The solvent was evaporated under reduced pressure and the residue chromatographed on silica gel using ether-petrol (1:19) as eluent to yield the monosilylated *diene* **80** (386 mg, 83 %); ν_{max}/cm^{-1} 1732 and 1704 (CO); δ_H 1.08 (9H, s, CMe_3), 1.77 (3H, d, *J* 7.0, 6′-H_3), 2.20 (1H, td, *J* 2 x 11.5 and 3.5, 1-H), 4.05 (2H, m, 1′′-H_2), 4.20 (2H, s, 4′′-H_2), 4.50 (2H, d, *J* 6.5, 1′-H_2), 5.56 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.73 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 6.00 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H), 6.20 (1H, dd, *J* 15.0 and 10.5, 3′-H) and 7.40 – 7.70 (10H, m, Ph); (Found: $M+NH_4^+$, 552.3149. $C_{32}H_{46}NO_5Si$ requires M, 552.3145).

Tetrabutylammonium fluoride (1.0 ml of 95 % tetrahydrofuran solution, 3.5 mmol) was added to a solution of the TBDPS ether **80** (1.6 g, 3 mmol) in tetrahydrofuran (25 ml) and at 0 °C, and the solution was allowed to warm to room temperature. After 30 min, the reaction was quenched with brine and the alcohol was extracted (Et_2O). The combined organic phase was washed (brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with ether-petrol (3:7) as eluent to yield the *alcohol* **81** (710 mg, 80 %); ν_{max}/cm^{-1} 1734 (CO); δ_H 1.75 (3H, d, *J* 7.0, 6′-H_3), 2.18 (1H, td, *J* 2 x 11.0 and 3.5, 1-H), 4.00 (1H, dd, *J* 11.0 and 5.5, 1′′-H), 4.12 (2H, s, 4′′-H_2), 4.14 (1H, dd, *J* 11.0 and 6.0, 1′′-H), 4.55 (2H, d, *J* 6.7, 1′-H_2), 5.57 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.75 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 6.04 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.26 (1H, dd, *J* 15.0 and 10.5, 3′-H); δ_C 18.2 (C-6′), 25.0 (C-5), 25.2 (C-4), 28.5 (C-3), 29.8 (C-6), 38.3 (C-2), 46.3 (C-1), 60.6 (C-4′′), 65.0 (C-1′), 68.6 (C-1′′), 123.5 (C-2′), 130.4 (C-4′), 131.4 (C-5′), 135.0 (C-3′), 170.9 (C-3′′), 175.1 (CO_2); (Found: $M+NH_4^+$, 314.1957. $C_{16}H_{28}NO_5$ requires M, 314.1967).

(1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-(2′′-oxa-3′′-oxo-butan-4′′-al)cyclohexane-carboxylate 82 and (1*R**,2*R**,2′*E*, 4′*E*)-hexa-2′,4′-dienyl-2-(4′′- dihydroxy-2′′-oxa-3′′-oxo-butyl)cyclohexanecarboxylate 83**



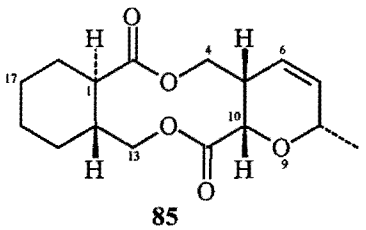
82 **83**

The alcohol **81** (570 mg, 1.97 mmol) dissolved in dichloromethane (1 ml) was added to a solution of Dess-Martin periodinane (triacetoxyperiodinane)(2 g, 4.8 mmol) in dichloromethane (5 ml) and the heterogeneous solution was heated to reflux for 16 h. The reaction was cooled and diluted with ether. The slurry was poured into saturated $NaHCO_3$, containing $Na_2S_2O_3$ (1g), and the mixture was stirred until the solution became homogenous. The organic phase was washed ($NaHCO_3$, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel using ether-petrol (3:2) as eluent to afford the *oxalate* **84** (120 mg, 21 %); ν_{max}/cm^{-1} 1778, 1749 and 1731 (CO); δ_H 1.77 (6H, d, *J* 6.5, 6′-H_3), 2.20 (2H, td, *J* 2 x 11.1 and 3.5, 1-H), 4.00 (2H, m, 1′′-H_2), 4.20 (2H, m, 1′′-H_2), 4.60 (4H, m, 1′-H_2), 4.75 (2H, s, 4′′-H_2), 5.60 (2H, m, 2′-H), 5.72 (2H, m, 5′-H), 6.05 (2H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.25 (2H, m, 3′-H); (Found: $M+NH_4^+$, 606. $C_{32}H_{48}NO_{10}$ requires M, 606) followed by an equilibrium mixture of *aldehyde* **82** and *hydrate* **83** (1:9 by NMR, 390 mg, 68 %); ν_{max}/cm^{-1} 3465 (OH) and 1732 (CO); δ_H (400 MHz) (**82** and **83**) 1.77 (3H, d, *J* 6.5, 6′-H_3), 2.20 (1H, td, *J* 2 x 11.0 and 3.5, 1-H), 4.00 – 4.20 (2H, m, 1′′-H_2), 4.60 (2H, m, 1′-H_2), 5.60 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.76 (1H, m, 5′-H), 6.05 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.24 (1H, dd, *J* 15.0 and 10.5, 3′-H); (**82**) 9.35 (1H, s, 4′′-H); (**83**) 5.20 (1H, s, 4′′-*H*$(OH)_2$); (Found: $M+NH_4^+$, 312.1830. $C_{16}H_{26}NO_5$ requires M, 312.1837).

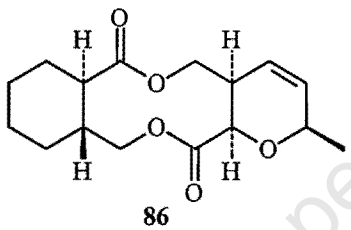
(1*R,2*R**,2′*E*,4′*E*)-Hexa-2′,4′-dienyl-2-[4′′*E*,2′′,7′′-dioxa-3′′,6′′-dioxo-non-4′′-ene]-cyclohexanecarboxylate 64**

Hydrate/aldehyde **82** + **83** (40 mg, 0.1 mmol) was added to a solution of (carbethoxymethylene)triphenylphosphine (50 mg, 0.1 mmol) in dichloromethane (1 ml). The solution was stirred at room temperature for 1 h and the solvent evaporated under reduced pressure. The residue was chromatographed directly on silica gel with ether-petrol (1:5) as eluent to yield the *trans* ethyl ester **64** (30 mg, 64 %).

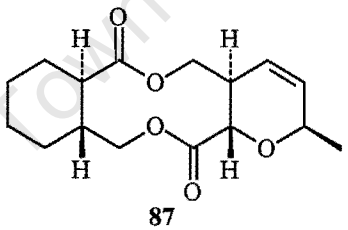
(1*R,5*S**,8*S**,10*S**,14*R**)- (1*R**,5*R**,8*R**,10*R**,14*R**)- and (1*R**,5*R**,8*R**,10*S**,14*R**)-8-Methyl-3,9,12-trioxa-2,11-dioxo-[12.4.0.0^{5,10}]-tricyclo-octadec-6-ene 85, 86 and 87**



85



86

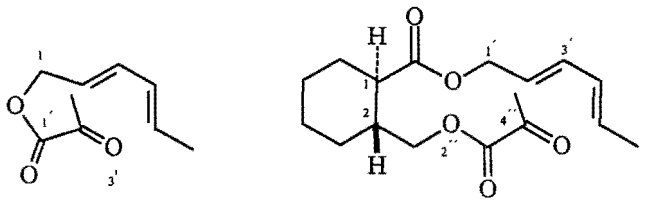


87

Azeotropically dried aldehyde **82** (200 mg, 0.64 mmol) in toluene (3 ml) was heated at 150 °C for 24 h in a sealed tube. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with ether-petrol (1:1) as eluent to afford a mixture of cycloadducts (120 mg, 64 %). This was subjected to reverse-phase HPLC (Vydac C_{18} 25 cm x 20 mm column, UV detection @ 230 nm, mobile phase: 0.1 % TFA in water (solvent A) and 0.1 % TFA in acetonitrile (solvent B); gradient elution, using 3:10 solvent A:solvent B→ pure solvent B; flow rate 5 ml min^{-1}) to give the *trans-cis* adduct **85** (50 % by peak integration); ν_{max}/cm^{-1} 1732 (CO); δ_H (400 MHz) 0.80 (1H, dq, *J* 3 x 11.5 and 3.6, 15α-H), 1.35 (3H, d, *J* 6.5, CH_3), 2.00 (1H, td, *J* 2 x 11.5 and 3.5, 1-H), 2.45 (1H, tq, *J* 3 x 11.5 and 3.5, 14-H), 3.20 (1H, m, 5-H), 3.50 (1H, t, *J* 11.5, 13α-H), 3.84 (1H, t, *J* 11.5, 4α-H), 4.22 (1H, d, *J* 3.0, 10-H), 4.34 (1H, m, 8-H), 4.40 (1H, ddd, *J* 11.5, 3.5 and 1.0, 4β-H), 4.58 (1H, dd, *J* 11.5 and 3.5, 13β-H) and 5.75 (2H, m, 6-H and 7-H); δ_C (100 MHz) 21.2 (q, Me), 24.9 (t, C-17), 25.6 (t, C-16), 27.3 (t, C-15), 29.7 (t, C-18), 29.9 (d, C-8), 34.5 (d, C-14), 36.0 (d, C-5), 50.1 (d, C-1), 62.6 (t, C-4), 69.8 (t, C-13), 72.9 (d, C-10), 122.7 (d, C-6), 134.4 (d, C-7), 172.9 and 176.2 (s, CO_2); (Found: $M+NH_4^+$, 312.1811. $C_{16}H_{26}NO_5$ requires M, 312.1811) followed by an inseparable mixture of *trans-cis* (**86**) and *trans-trans* (**87**) cycloadducts (2:1 by NMR); ν_{max}/cm^{-1} 1736 (CO); δ_H (300 MHz)(**86**) 1.27

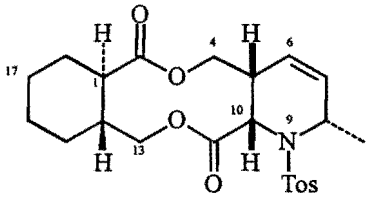
(3H, d, *J* 7.0, Me), 3.20 (1H, m, 5-H), 3.60 and 3.85 (2H, m, 4-H and 13-H), 4.20 (1H, d, *J* 3.0, 10-H), 4.38 and 4.85 (2H, m, 4-H and 13-H), 5.75 (2H, m, 6-H and 7-H); (**86**), 1.30 (3H, d, *J* 6.5, Me), 3.76 and 3.80 (2H, m, 4-H and 13-H), 3.95 (1H, d, *J* 9.5, 10-H), 4.50 and 4.75 (2H, m, 4-H and 13-H), 5.45 (1H, dt, *J* 10.0 and 2 x 1.0, 6-H), 5.90 (1H, dt, *J* 10.0 and 2 x 2.5, 7-H); (Found: $M+NH_4^+$, 312. $C_{16}H_{26}NO_5$ requires M, 312).

(2*E*,4*E*)-Hexa-2,4-dienyl pyruvate 88 and (1*R,2*R**,2′*E*, 4′*E*)-hexa-2′,4′-dienyl-2-(2′′-oxa-3′′,4′′-dioxo-pentan)cyclohexanecarboxylate 89**

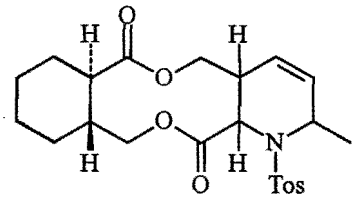


DCC (200 mg, 1.2 mmol) and DMAP (20 mg, 0.1 mmol) and pyruvic acid (0.06 ml, 0.86 mmol) were sequentially added to a solution of dienol **55** (200 mg, 0.86 mmol) in dichloromethane (2 ml) at 20 °C, and the resulting slurry was stirred for 2 h. This was filtered through a sintered glass funnel whilst washing with ether. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel and ether-petrol (1:5) as eluent to give the monoester triene **88** (17 mg, 12 %); ν_{max}/cm^{-1} 1724 (CO); δ_H 1.77 (3H, d, *J* 7.0, 6′-H_3), 2.46 (3H, s, COMe), 4.74 (2H, d, *J* 6.5, 1′-H_2), 5.67 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.81 (1H, m, 5′-H), 6.04 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.30 (1H, dd, *J* 15.0 and 10.5, 3′-H); (Found: $M+NH_4^+$, 186. $C_9H_{16}NO_3$ requires M, 186) and the diester *triene* **89** (89 mg, 49 %); ν_{max}/cm^{-1} 1732 (CO); δ_H 1.77 (3H, d, *J* 7.0, 6′-H_3), 2.20 (1H, td, *J* 2 x 11.5 and 3.5, 1-H), 2.45 (3H, s, 3′′-H_3), 4.05 (1H, dd, *J* 11.0 and 5.5, 1′′-H), 4.16 (1H, dd, *J* 11.0 and 6.0, 1′′-H), 4.56 (2H, d, *J* 6.7, 1′-H_2), 5.69 (1H, dt, *J* 15.0 and 2 x 6.5, 2′-H), 5.72 (1H, dq, *J* 15.0 and 3 x 6.5, 5′-H), 6.04 (1H, ddd, *J* 15.0, 10.5 and 1.5, 4′-H) and 6.26 (1H, dd, *J* 15.0 and 10.5, 3′-H); δ_C 18.1 (C-6′), 24.9 (C-5), 25.1 (C-4), 26.7 (C-5′′), 28.4 (C-3), 29.8 (C-6), 37.9 (C-2), 46.2 (C-1), 65.0 (C-1′), 69.3 (C-1′′), 123.5 (C-5′), 130.4 (C-4′), 131.3 (C-2′), 135.0 (C-3′), 160.7 (C-3′′) and 175.0 (CO_2), 191.6 (C-4′′); (Found: $M+NH_4^+$, 326.1965. $C_{17}H_{28}NO_5$ requires M, 326.1967).

($1R^*,5R^*,8S^*,10S^*,14R^*$)-, ($1R^*,5S^*,8R^*,10R^*,14R^*$)-, ($1R^*,5S^*,8R^*,10S^*,14R^*$)- and ($1R^*,5R^*,8S^*,10R^*,14R^*$)-8-Methyl-9-*p*-toluenesulfonyl-9-aza-3,12-dioxa-2,11-dioxo-[12.4.0.0^{5,10}]-tricyclo-octadec-6-ene 91, 92, 93 and 94.



91

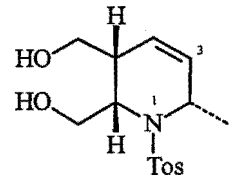


92 (*cis*), **93** + **94** (*trans*)

The aldehyde/hydrate **82/83** (130 mg, 0.41 mmol) was dissolved in toluene. The solution was repeatedly sonicated and flushed with nitrogen. *p*-Toluene isocyanate (200 mg, 1 mmol) was added, the reaction was heated in a sealed tube at 120 °C for 16 h. The reaction was cooled and the solvent evaporated under reduced pressure. The residue was chromatographed on silica gel with ether-petrol (1:1) as eluent to yield partial separation of the *trans-cis* cycloadduct **91** (42 mg, 33 %); ν_{max}/cm^{-1} 1736 (CO); δ_H (500 MHz) 1.60 (3H, d, *J* 6.5, 8-Me), 2.00 (1H, td, *J* 2 x 11.0 and 3.5, 1-H), 2.10 (1H, m, 14-H), 2.35 (1H, m, *W* 10.9, 5-H), 2.40 (3H, s, PhMe), 3.60 (1H, dd, *J* 11.5 and 4.5, 13β-H), 3.85 (1H, dd, *J* 12.0 and 2.5, 4-H), 4.44 (1H, m, 8-H), 4.52 (1H, t, *J* 11.5, 13α-H), 4.58 (1H, d, *J* 5.6, 10-H), 4.97 (1H, dd, *J* 12.1 and 2.8, 4-H), 5.70 (1H, dt, *J* 10.5 and 2 x 2.5, 6-H), 5.76 (1H, dt, *J* 10.5 and 2 x 2.5, 7-H), 7.29 (2H, d, *J* 8.3, H_o) and 7.68 (2H, d, *J* 8.3, H_m); δ_C 21.6 (8-Me), 22.4 (PhMe), 24.8 (C-16 and C-17), 27.9 (C-15), 28.5 (C-18), 37.4 (C-8), 39.7 (C-14), 46.5 (C-5), 50.2 (C-1), 54.4 (C-10), 63.4 (C-4), 68.0 (C-13), 117.0 (Ph), 122.5 (C-6), 127.0 (Ph), 129.8 (Ph), 131.5 (C-7), 143.7 (Ph), 173.0 and 179.2 (CO_2); (Found: $M+NH_4^+$, 465.2059. $C_{23}H_{29}N_2O_6S$ requires M, 465.2059). The remaining mixture (87 mg, 68 %) was subjected to reverse-phase HPLC (Vydac C_{18} 25 cm x 20 mm column, UV detection @ 230 nm, mobile phase: 0.1 % TFA in water (solvent A) and 0.1 % TFA in acetonitrile (solvent B); gradient elution, using 3:10 solvent A:solvent B→ pure solvent B; flow rate 5 ml min^{-1}) to give further major *trans-cis* adduct **91** (40 % of 68 % by integration). This was followed by an inseparable mixture of 3 cycloadducts (5:1:1 by NMR); ν_{max}/cm^{-1} 1722 (CO); δ_H (400 MHz)(**92**) 1.65 (3H, d, *J* 6.5, 8-Me), 2.50 (3H, s, PhMe), 3.45 (1H, t, *J* 11.5, 13α-H), 3.82 (1H, dd, *J* 12.0 and 2.5, 4-H), 4.37 (1H, dd, *J* 11.4 and 2.6, 13β-H), 4.42 (1H, m, 8-H), 4.62 (1H, d, *J* 5.5, 10-H), 4.93 (1H, dd, *J* 12.0 and 5.0, 4-H), 5.70 – 5.90 (2H, m, 6-H and 7-H) and 7.20 – 7.70 (4H, m, Ph); (**93**) 1.32 (3H, d, *J* 6.5, 8-Me), 2.40 (3H, s, PhMe), 3.86 (1H, d, *J* 10.5, 10-H), 5.20 (1H, t, *J* 11.4, 13α-H), 5.70 – 5.80 (2H, m, 6-H and 7-H) and 7.20 – 7.70 (4H, m, Ph); (**94**) 1.36 (3H, d, *J*

6.5, 8-Me), 2.50 (3H, s, PhMe), 3.90 (1H, d, *J* 10.5, 10-H), 5.20 (1H, t, *J* 11.4, 13α-H), 5.70 – 5.90 (2H, m, 6-H and 7-H) and 7.20 – 7.70 (4H, m, Ph); (Found: $M+NH_4^+$, 465. $C_{23}H_{29}N_2SO_6$ requires M, 465).

(2*S,5*S**,6*S**)-*p*-Toluenesulfonyl-5,6-dihydroxymethyl-2-methyl-5,6-dihydropyridine 95**



The cycloadducts (20 mg, 0.04 mmol) were dissolved in tetrahydrofuran (1 ml). Lithium aluminium hydride (15 µl, 0.2 mmol of 1M solution in tetrahydrofuran) was added and the reaction was stirred for 1 h. The reaction was quenched with ethyl acetate and the solution was poured into a sat. $NaHCO_3$. The aqueous phase was extracted with chloroform. The combined organic phase was washed (1M HCl, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-hexane (7:3) as eluent to afford *diol* **95** (9 mg, 60 %); ν_{max}/cm^{-1} 3477 (OH); δ_H (400 MHz) 1.38 (3H, d, *J* 7.0, 2-Me), 2.40 (3H, s, PhMe), 3.55 – 3.65 (4H, m, CH_2OH), 3.80 (1H, m, 5-H), 4.20 (1H, q, *J* 3 x 7.0, 6-H), 4.40 (1H, m, 2-H), 5.40 (1H, br d, *J* 10.5, 4-H), 5.65 (1H, dt, *J* 10.5 and 2 x 3.0, 3-H), 7.27 (2H, d, *J* 8.5, Ph) and 7.70 (2H, d, *J* 8.5, Ph); (Found: $M+NH_4^+$, 312.1295. $C_{15}H_{22}NSO_4$ requires M, 312.1294).

CHAPTER 4

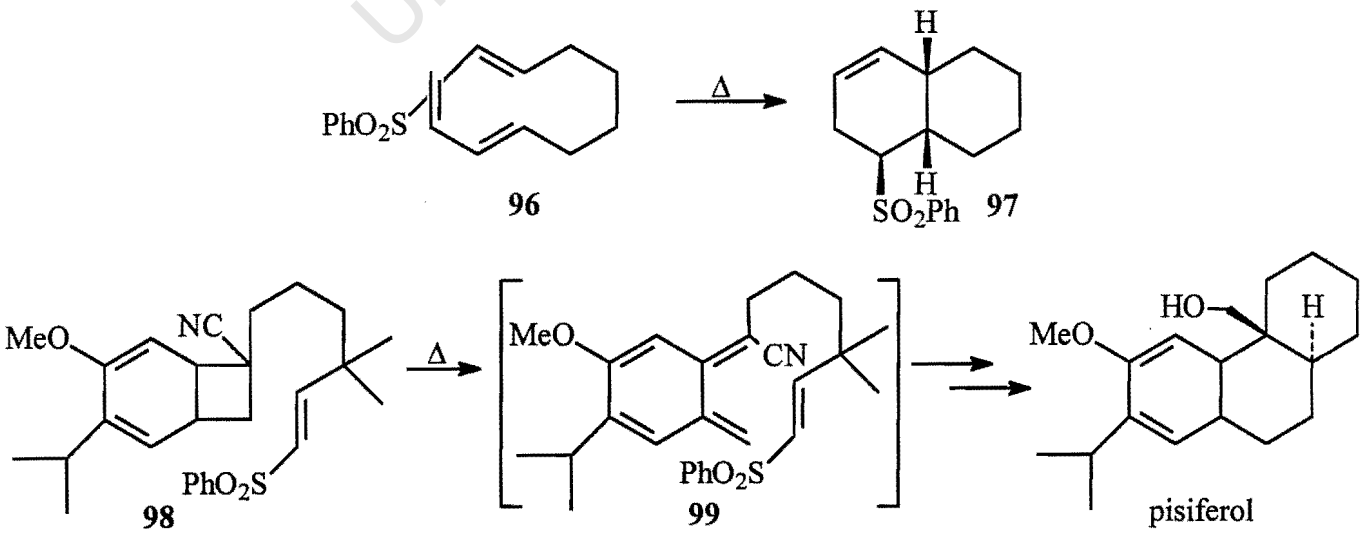
SYNTHESIS AND REACTIONS OF 1-PHENYL SULFONYLTETRAENES

4.1 Unbranched aliphatic 1-phenylsulfonylalka-1,2,(*n* + 4),(*n* + 6)-tetraenes

4.1.1 Introduction Vinyl sulfones are well known as excellent dienophiles and undergo a range of pericyclic reactions, including [2 + 2], [3 + 2] and [4 + 2] cycloadditions.[89,90] The first systematic examination of phenyl vinyl sulfone in Diels-Alder reactions was carried out by Paquette and co-workers[91] who showed that cycloaddition reactions with phenyl vinyl sulfones are best performed under thermal conditions as no evidence of rate acceleration was found when performing the reaction under Lewis acid catalysis.

The sulfonyl group has also been used as a handle for further manipulation of the cycloadducts and it has been demonstrated that site-specific functionalisation can be achieved by condensation of the derived α-sulfonyl carbanion with electrophiles,[91] and the adducts could be desulfonylated by a number of methods.[92]

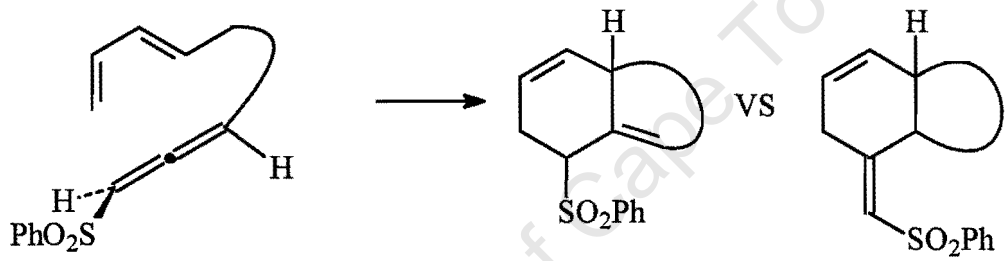
The use of phenyl vinyl sulfones in IMDA reactions was investigated by Craig *et al.*,[93] in approaches to synthesis of hydrindane and decalin structures. For example, the terminally substituted vinyl sulfone **96** gave a single diastereomer **97** when heated at 140 °C for 44 h (Scheme 1).[94]



Scheme 1 IMDA reaction of terminally substituted vinyl sulfones

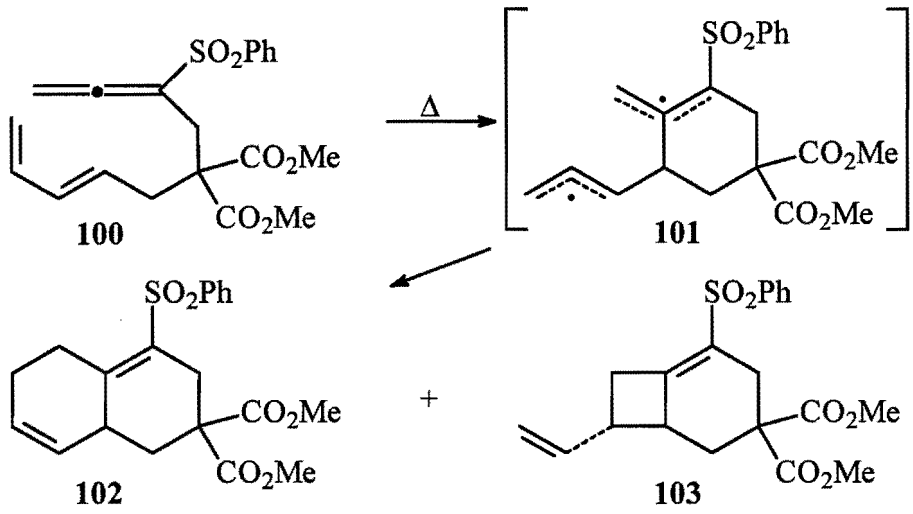
The stereoselectivity of the reaction is due to the preferred *exo*-orientation for the dienophile, induced by the bulky phenylsulfonyl group. This *exo*-selective characteristic of the phenylsulfonyl group in IMDA reactions, has been advantageously used in several syntheses. For example, Craig *et al.*, in Vitamin D_3 studies,[95a] whereas Kametani *et al.*,[95b] and Bush *et al.*,[95c] both used this substructure in their analogous syntheses of pisiferol (for example compound **98**). IMDA reactions involving internally substituted vinyl sulfones have also been reported,[96] and several examples of their use in synthesis have been reported.[97]

Arising from research conducted in our group on bis(phenylsulfonyl)allenes,[98] the synthesis of IMDA substrates incorporating a phenylsulfonylallenyl terminus as the dienophilic element, was considered an interesting extension of the aforementioned methodology. The reactivity and periselectivity of the allene coupled with its potential use of axial chirality transfer make this an exciting prospect (Scheme 2).



Scheme 2 The proposed investigation of phenylsulfonylallenes

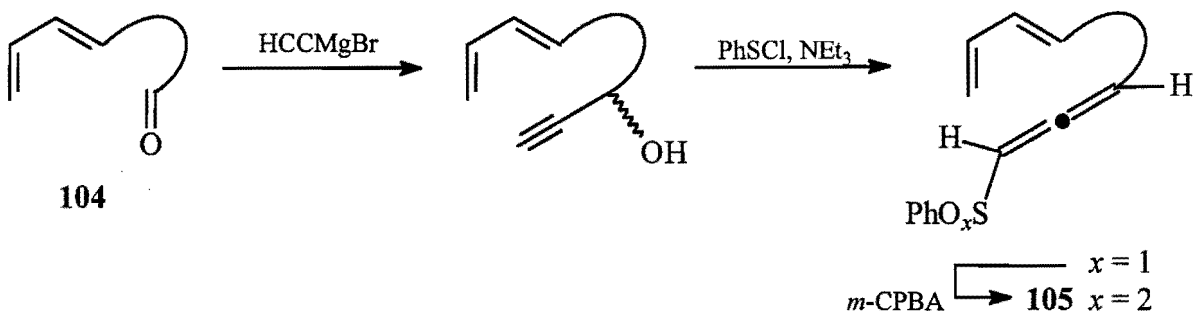
Padwa *et al.*[99] synthesised a series of internally substituted phenylsulfonylallenes and examined their thermal behavior. For example, when the tetraene **100** was heated in refluxing benzene, cycloadducts **102** and **103** (2:1) were formed in 96 % yield (Scheme 3). The assigned products arose from competing [4 + 2] and [2 + 2] addition pathways. The latter pathway was considered a 'topic of much study and debate' as most prior studies could not unequivocally establish whether such cyclisations were concerted or not. According to Padwa *et al.*,[99] the most widely accepted theory was that the initial reaction involves a fast radical cyclisation to give intermediate **101**, whilst the second, 'product determining step', would determine the reaction outcome. Although several phenylsulfonylallenyl compounds were synthesised only two examples of IMDA reactivity were investigated (for other example, see later).[99]



Scheme 3 Background study involving 'diradical' mechanism

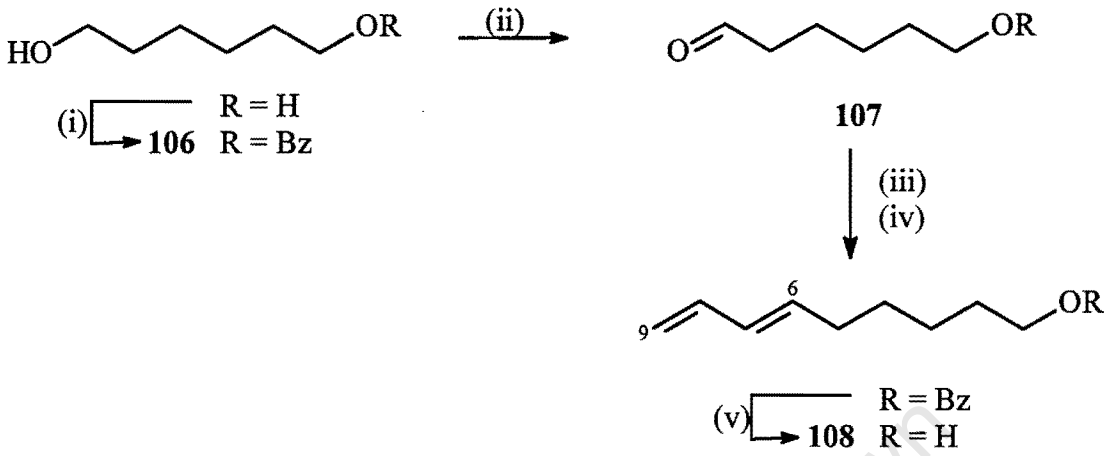
The radical nature of these allenyl cyclisation reactions was first observed by Solomon *et al.*,[100] who showed that the thermal reaction of a variety of vinyl allenes underwent thermally induced radical cyclisations. Although a study conducted by Houk and coworkers[101] was based on strained cyclic allenes, *ab initio* calculations predicted the diradical pathways to be preferred (in certain cases).

The foregoing literature precedent reveals much scope for synthetic exploration of structure-reactivity trends associated with the use of the reactive phenylsulfonylallenyl substructures in IMDA reactions. The first phase of this investigation addresses the question of the role of the 1-phenylsulfonyl substitution, and of tether length, on reactivity and periselectivity. Synthesis of the key intermediates **104** was based on literature precedent (or variations thereof). Ethynylation of appropriate dienals, followed by [2,3]sigmatropic rearrangement of the derived dienynyl sulfenate esters, was expected to provide access to the corresponding sulfinyl allene (Scheme 4). Oxidation of the sulfoxide would give the desired sulfonyl tetraene **105**.



Scheme 4 Proposed synthesis of 1-phenylsulfonylallenes **105**.

4.1.2 1-Phenylsulfonylundeca-1,2,8,10-tetraene Hexane-1,6-diol was treated with benzoyl chloride, using an excess of diol, to give the monoprotected compound **106**. Swern oxidation of **106** gave aldehyde **107** in 67 % overall yield (Scheme 5).[102, 103]



Scheme 5 *Reagents and conditions*: (i) BzCl, C_5H_6N, 0 °C, 69 %; (ii) $(COCl)_2$, DMSO, NEt_3, -78 °C, 98 %; (iii) $Ph_3P^+CH_2CH{=}CH_2\ Br^-$, *n*-BuLi, 0 °C, 59 %; (iv) I_2, *hv*, 0 °C, 2 h, 84 %; (v) KOH, THF/ H_2O/ MeOH, 82 %

Treatment of the aldehyde **107** with allyltriphenylphosphorane [104] gave an inseparable mixture of dienes (~*E*/*Z* 1:1 by NMR) in 59 % yield. The composition of the mixture was evident from the diagnostic NMR signals for the central π-bond protons (for example see Figure 1). Thus a signal at δ 5.65 (dt, *J* 15.2 and 2 x 6.6 Hz) was assigned to 6-H for the (*E*)-component, whereas a signal at δ 5.41 (br dt, *J* 10.4 and 2 x 6.5 Hz) was assigned as 6-H for the (*Z*)-component, demonstrating the expected difference in magnitude of ^3J_E and ^3J_Z.

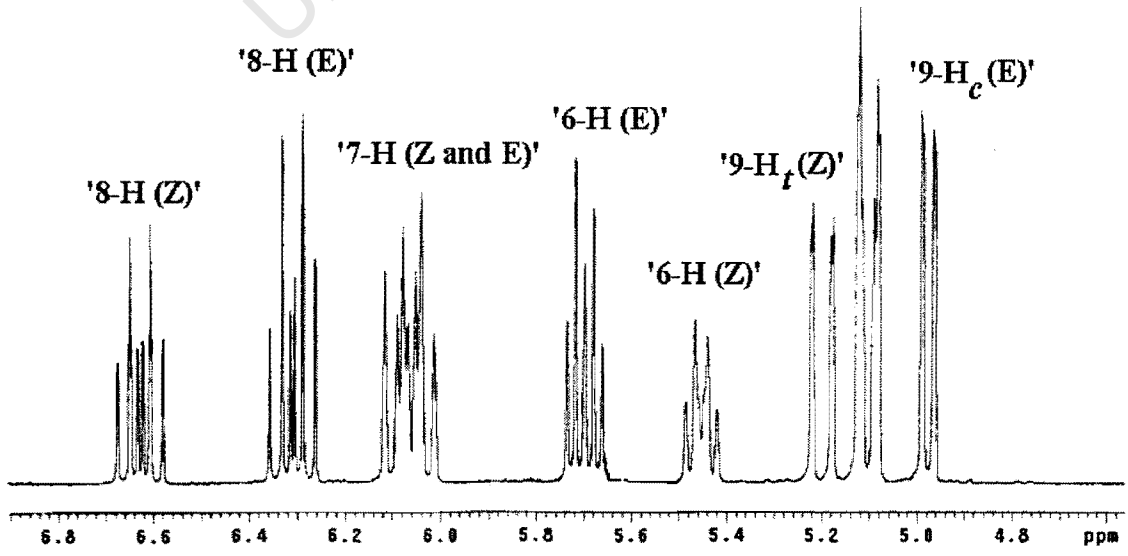
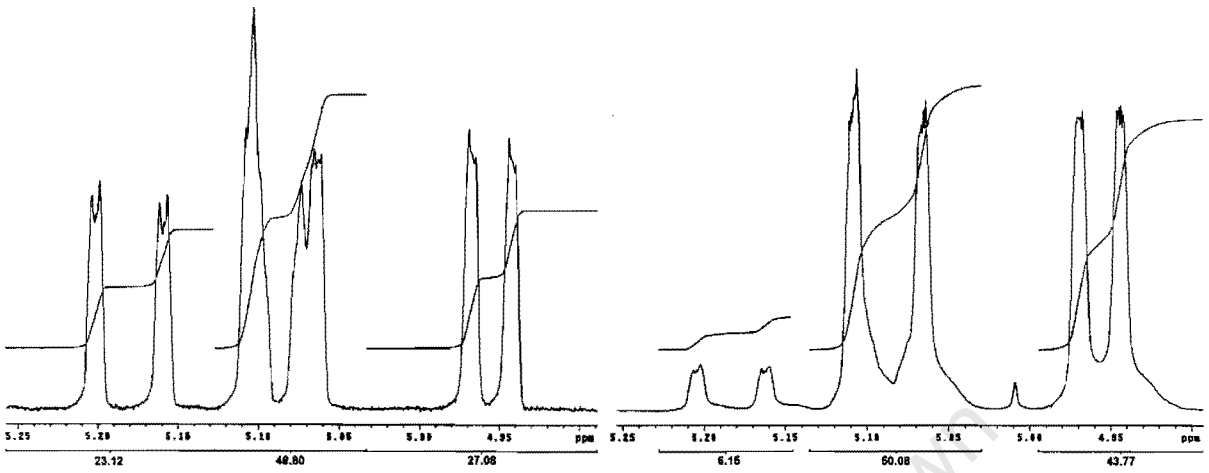


Figure 1 A typical spectrum of the *E*- and *Z*-dienes (as shown for a related compound from model studies)

The mixture was subjected to irradiation for 16 h,[105] in the presence of catalytic iodine (~ 4 mol %), to give a product in 84 % yield enriched in the (*E*)-diene (~ 88 % (*E*) by NMR). Further irradiation (24 h) failed to increase the (*E*/*Z*) ratio.

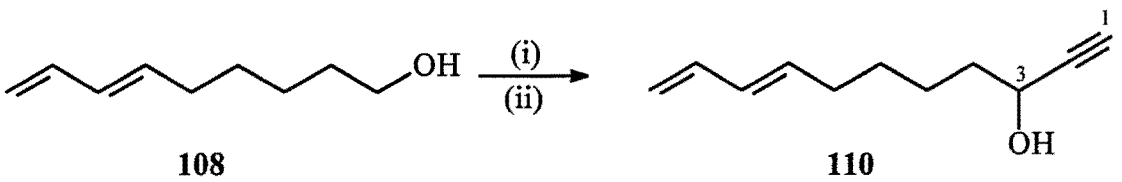


Prior to isomerisation | Irradiation of diene in the presence iodine for 16 h

Figure 2 ^{1}H NMR monitoring of the iodine catalysed isomeristion of the dienes **108**

The reaction progress was monitored by ^{1}H NMR (Figure 2) by comparative integration of the signals for 9-H_{trans} (at δ 5.17 for (*Z*)-isomer) and the 9-H_{cis} (δ 4.95 for (*E*)-isomer). These signals were chosen as they were sharp and free from overlap – which allowed for the most accurate (*E*/*Z*) ratio determination. Hydrolysis of the ester with aqueous potassium hydroxide gave dienol **108** in 82 % yield.

Swern oxidation of the alcohol **108** proceeded efficiently to give aldehyde **109** in 83 % yield. The aldehyde was subjected to ethynylation, using a preparative experimental procedure described by Holmes.[106] Thus, aldehyde **109** was treated with ethynylmagnesium bromide, generated *in situ*, to give propargyl alcohol **110** in 87 % yield (Scheme 6). Best results were achieved when excess Grignard reagent was used and when the aldehyde was freshly prepared.

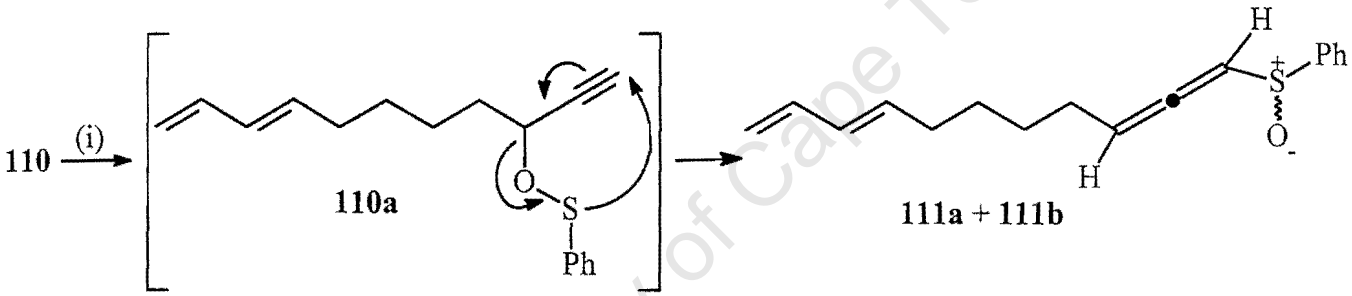


108 **110**

Scheme 6 *Reagents and conditions*: (i) $(COCl)_2$, DMSO, NEt_3, -78 °C, 83 %; (ii) HC≡CMgBr, 25 °C, 87 %

The dienynol **110** was readily characterised with the use of spectroscopic data. ^{1}H NMR signals were observed at δ 2.47 (dd, *J* 2.3 and 0.8 Hz) for 1-H and δ 4.40 (td, *J* 2 x 6.3 and 2.3 Hz) for 3-H, and ^{13}C signals of the acetylenic C-1 and C-2 (*viz.* 72.8 and 84.9 respectively) were diagnostic.[107] The infrared spectrum displayed absorption at ν_{max} 3305 cm^{-1} (for C≡C-H stretching vibration for *terminal* alkyne) and 3684 cm^{-1} (OH). Mass spectrometry of the dienynol **110** failed to display a molecular ion peak under high resolution. However, complete characterisation of derived products, including accurate mass determination of molecular ion peaks, confirmed the structural assignment of **110**.

Reaction of propargyl alcohol **110** with benzenesulfenyl chloride[108] and triethylamine at –78 °C, gave a mixture of diastereomeric phenylsulfinylallenes **111a** and **111b** in 77 % yield, arising from the formation of the intermediate sulfenate ester **110a** and subsequent [2,3]sigmatropic rearrangement (Scheme 7).[109] Optimisation of the yields of this, and related reactions, through variations of reaction conditions will be discussed later.



Scheme 7 *Reagents and conditions*: (i) PhSCl, NEt_3, -78 °C, 77 %

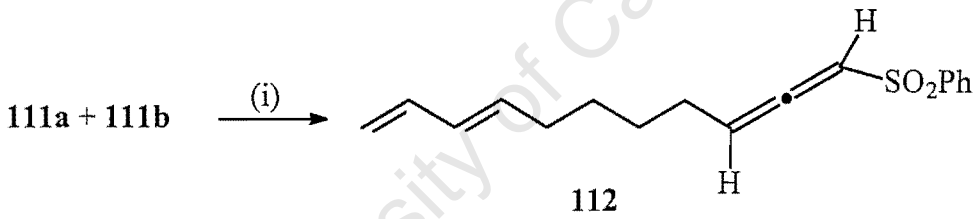
Column chromatography of the reaction product gave partial separation of the diastereomisomeric allenylsulfoxides **111a** and **111b**. The only difference in the ^{1}H NMR spectra of the sulfoxides was the relative chemical shift of the signal for 3-H (td, *J* 2 x 7.0 and 6.2 Hz) which appeared at δ 5.68 for compound **111a** and δ 5.73 for **111b** . The reason for this difference is not obvious. The signal for 1-H was obscured owing to overlap with the signal for 9-H. A detailed NMR discussion will be given of the oxidised product – *i.e.* the allenylsulfone (see below).

The mixture of **111a** and **111b** was also characterised. The overall structural assignment of the mixture was based on characteristic ^{13}C NMR signals at δ 99.1 (C-1), 203.7 (C-2) and 102.7 (C-3). [107] Signal ^{13}C NMR signals were duplicated for this and other sulfinyl compounds and are

reported accordingly. IR analysis was also noteworthy and displayed absorption at ν_{max} 1950 cm^{-1} (C=C=C).

The final step in preparing the target substrate entailed conversion of the sulfoxide into the corresponding sulfone. Numerous methods are available for this well documented oxidation.[92] Reagents and conditions were sought to achieve chemoselective reaction and to ensure that the primary reaction product could be isolated without interference from possible cyclisation reactions. It was hoped that the conjugated dienyl moiety would be relatively resistant towards competing epoxidation reactions.

Attempts to oxidize a mixture of sulfoxide **111a** + **111b** using oxone[99] and sodium perborate[110] were unsatisfactory, but treatment with *m*-CPBA at 0 °C gave sulfone **112** in 66 % yield (Scheme 8). This was chosen as the method of choice for all future oxidations. Attempts to increase the yield of the sulfone **112**, by sequential additions of small amounts of excess reagent only resulted in a rapid decrease of yield accompanied by the presumed formation of epoxide(s) (TLC).



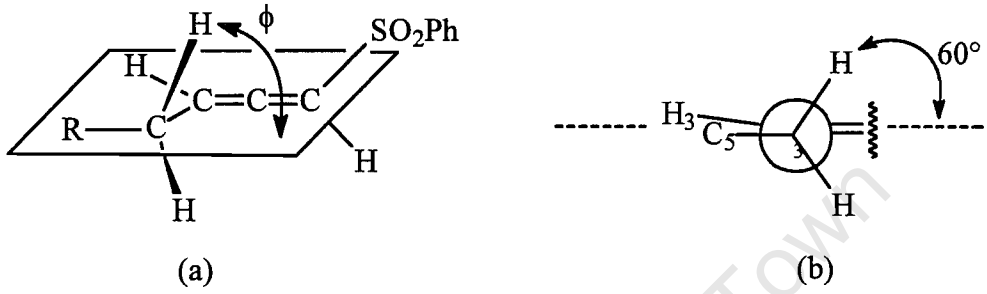
Scheme 8 *Reagents and conditions*: (i) *m*-CPBA, 0 °C, 66 %

The IR spectrum of **112** displayed absorption at ν_{max} 1955 cm^{-1} (C=C=C), 1319 and 1148 cm^{-1} (S=O).The ^1H NMR spectrum displayed signals at δ 5.83 (td, *J* 2 x 7.0 and 6.2 Hz) for 3-H and δ 6.30 (dt, *J* 6.2 and 2 x 3.1 Hz) for 1-H whose chemical shift was in close agreement with the expected calculated values (Table 1).[111]

Table 1 Observed and calculated chemical shifts for 1-H and 3-H for compound **112**

δ (ppm)	1-H	3-H
Observed	6.30	5.83
Calculated	6.18	5.72

In general, long range proton-proton coupling constants in allenes are very useful for structural investigations.[111] Vicinal couplings in allenes, as ^3J in general, depend upon the dihedral angle ϕ, defining the *anti* (*trans*) arrangement (Scheme 9a) by $\phi = 0°$ and the *syn* (*cis*) arrangement by $\phi = 180°$. Standard values for the *trans* vicinal coupling ^3J_t (HH) are ~11 Hz, whilst that for a *gauche* arrangement ^3J_g (HH) are ~4.3 Hz. Since our observed value corresponds to two equal couplings of 7 Hz, we can conclude that the vicinal protons prefer to adopt a *gauche* arrangement with respect to 3-H. *i.e.* $\phi = 60°$ (as seen by Newman projection along C(3) – C(4), Scheme 9b).



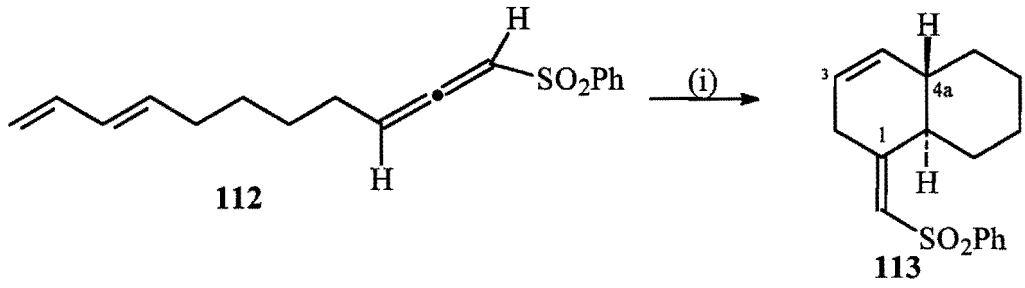
Scheme 9 Definition of alkyl group dihedral angle ϕ.

^5J couplings are not uncommon between the terminal allenic proton and the protons on C-4.[107,111] A quantitative calculation using the dihedral angle may be carried out to confirm the magnitude of ^5J couplings between 1-H and 4-H_2. This is related to ϕ according to Equation 1 (Scheme 10).[112] Hence with $\phi = 60°$ the value for ^5J (1,4) is ~2.9 Hz which is in close agreement with the observed value (*viz.* 3.1 Hz). Since there are two protons found at the same angle, a triplet is observed. The corresponding ^{13}C signals for C-1, C-2 and C-3 were at 101.0, 205.5 and 101.2 respectively, and correspond closely to expected values.[111]

$$^5J\,(HH) = 2.25\sin^2\phi + 1.18 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Scheme 10 Calculation of long range coupling between 1-H and 4-H

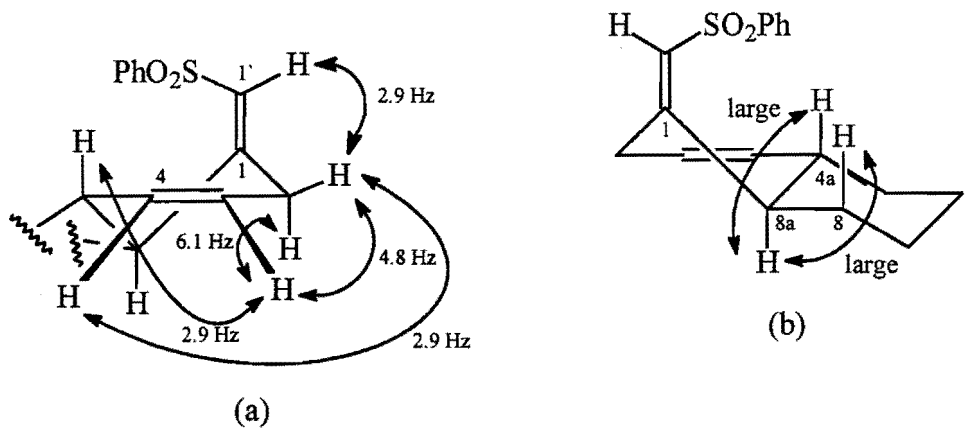
With the first of the model substrates in hand, experiments were conducted to determine IMDA reactivity. It was observed that heating the phenylsulfonylallene **112** at temperatures of 120 and 150 °C resulted only in progressive decomposition without any formation of discrete products. However, in an experiment conducted at 180 °C for 20 h, it was possible to isolate a single product **113** in 30 % yield (Scheme 11).



Scheme 11 *Reagents and conditions*: (i) PhMe, 180 °C, 30 %

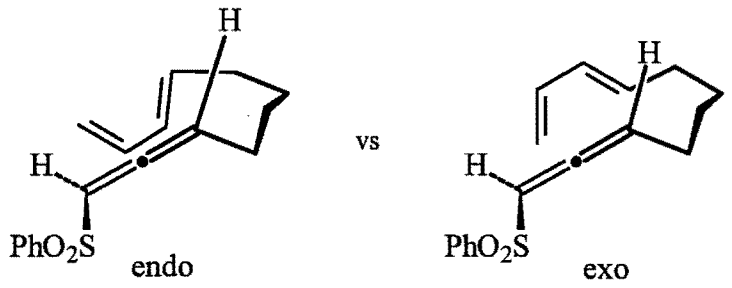
1D and 2D NMR spectroscopy displayed several important features, used to assign the structure of **113**. The signals at δ 5.52 (dt, *J* 8.8 and 2 x 2.9 Hz) and δ 5.43 (dddd, *J* 8.8, 6.1, 4.8 and 2.9 Hz) were identified as 4-H and 3-H respectively with the aid of a COSY NMR. Thus signals at δ 2.12 (dd, *J* 15.1 and 6.1 Hz) and δ 2.27 (ddt, *J* 15.1, 4.8 and 2 x 2.9 Hz) were identified as 2α-H and 2β-H respectively – the latter exhibiting an allylic coupling with 4-H and 1′-H of 2.9 Hz (Scheme 12a). These results support the assignment of an exocyclic π-bond, as no large coupling was observed with either 2-H proton. Had the π-bond been endocyclic (arising from reaction of the activated π-bond of the allene) a relatively larger coupling (~ 6 – 8 Hz) would have been observed.

Identification of 8a-H was based on COSY cross-peaks arising from an allylic coupling with 1′-H. This signal had a width of 29 Hz which is consistent with the expected magnitude for a *trans* fused ring junction. This is only possible if two large couplings of 8a-H with neighboring antiperiplanar protons are found (Scheme 12b), which is only possible in a *trans*-fused ring system. The structure of **113** is consistent with spectroscopic evidence.



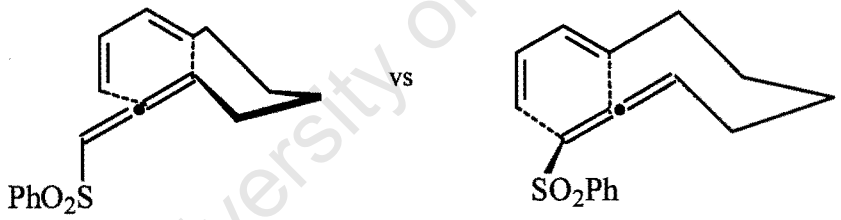
Scheme 12 Coupling information of cycloadduct **113** and the large couplings responsible for the assignment of the ring junction as *trans*.

It was therefore inferred that the *exo* transition state is favoured (*exo* with respect to the tether), leading to *trans* ring junction formation in the products, with *Z*-orientation of the phenylsulfonylmethylene group (Scheme 13).



Scheme 13 *Endo-* and *exo-* transition states for IMDA reaction of unactivated π-bond

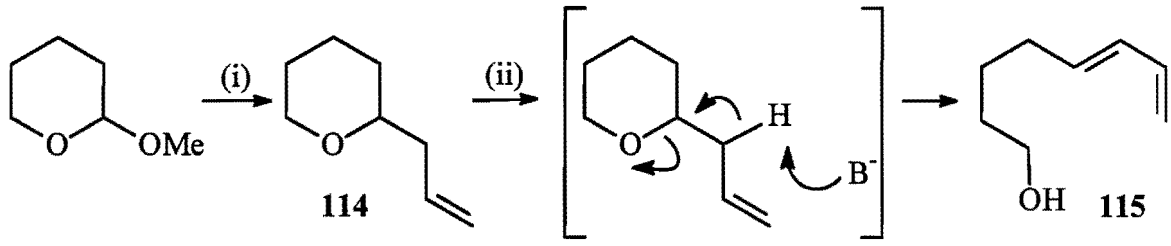
The inefficiency of this reaction was disappointing; however, it did set a starting point from which to proceed. The reaction is evidently influenced by tether length, as only the unactivated π-bond of the allene was engaged in reaction. This suggests that the tether is too long, as demonstrated by the tetraene preference to adopt a six-membered transition state, as opposed to the seven-membered transition state required for reaction of the activated π-bond (Scheme 14).



Scheme 14 Transition state for (8*E*) 1-phenylsulfonylundeca-1,2,8,10-tetraene **113**

With the precedent of the above finding, it was decided to investigate the synthesis of tetraenes linked *via* a three-carbon tether.

4.1.3 1-Phenylsulfonyldeca-1,2,6,8-tetraene Following a procedure of Noyori *et al.*,[113] treatment of the 2-methoxytetrahydropyran with allyltrimethylsilane and trimethylsilyltrifluro-methanesulfonate at –50 °C, gave allyltetrahydropyran **114** in 62 % yield (Scheme 15). Using a procedure of Schlosser *et al.*,[114] treatment of **114** with superbase LIDAKOR gave dienol **115** in 66 % yield and a high (*E*/*Z*) ratio (97 % (*E*) by NMR).



Scheme 15 *Reagents and conditions*: (i) TMSOTf, $CH_2CHCH_2Si(CH_3)_3$, -50 °C, 62 %; (ii) $HN(CH(CH_3)_2)$, *n*-BuLi, *t*-BuOK, -78 °C, 66 %

The favourable outcome arises from the stereo-electronically preferred *anti*-elimination of the ether functionality resulting in high *trans*-selectivity which is clearly demonstrated by the observed *E*/*Z* ratio. The ^{1}H NMR of dienol **115** was analogous to that of the previously prepared homologue **108** and the olefinic proton region is shown in Figure 3.

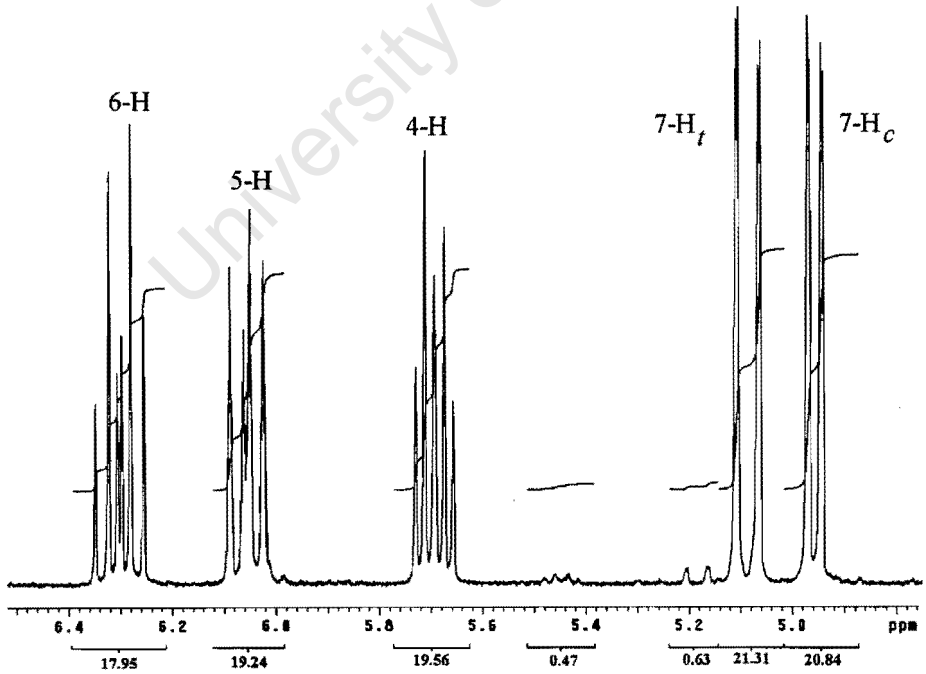
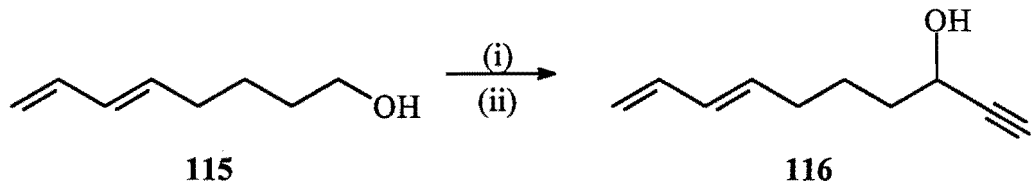


Figure 3 ^{1}H NMR expansion of olefinic region of dienol **115** with relative integration.

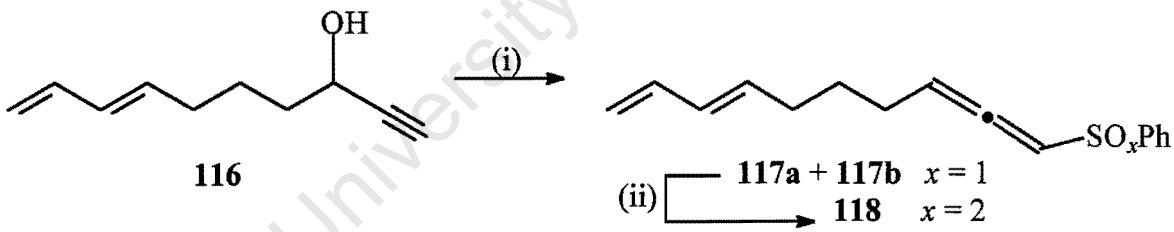
Oxidation of dienol **115** with pyridinium chlorochromate (PCC) followed by ethynylation of the derived crude aldehyde with ethynylmagnesium bromide, prepared *in situ*, gave dienynol **116** in 67 % yield over two steps (Scheme 16). The ^{1}H NMR spectrum of **116** displayed signals at δ 2.47 (d, *J* 2.3 Hz) for 1-H and δ 4.38 (td, *J* 6.3 and 2.3 Hz) for 3-H in close correlation with the previously prepared dienynol **110**. The infrared spectrum of **116** displayed absorption at ν_{max} 3305 (C≡C-H) and 3684 cm^{-1} (OH). The choice of PCC as oxidant was based the availability of the reagent.



115 **116**

Scheme 16 *Reagents and conditions*: (i) PCC, CH_2Cl_2, 25 °C; (ii) HC≡CMgBr, THF, 67 %

Low temperature treatment of alcohol **116** with benzenesulfenyl chloride in the presence of triethylamine, gave a mixture of diastereomeric phenylsulfinylallenes **117a** + **117b** in 65 % yield. Signal overlap in the ^{1}H NMR made characterisation difficult, however the IR spectrum displayed absorption ν_{max} 1950 (C=C=C) and 1037 cm^{-1} (SO). Oxidation of the sulfoxide was performed with *m*-CPBA at 0 °C to give phenylsulfonylallene **118** in 53 % yield (Scheme 17).

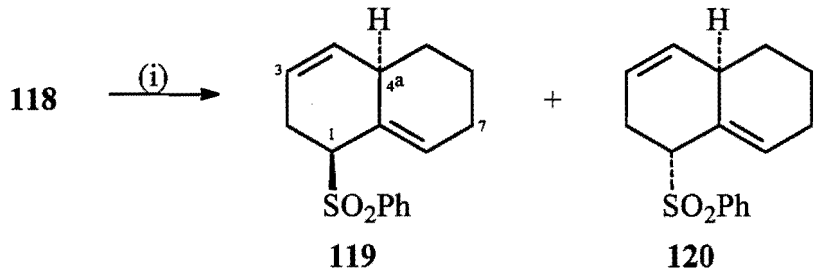


116

Scheme 17 *Reagents and conditions:* (i) PhSCl, NEt_3, -78 °C, 65 %; (ii) *m*-CPBA, 0 °C, 53 %

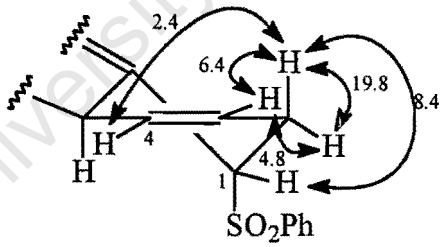
Spectroscopic data for **118** were consistent with the assigned structure, and diagnostic signals for the key structural elements were similar to those of the analogous compound **112**. Thus the ^{1}H NMR spectrum displayed signals at δ 5.85 (td, *J* 2 x 7.0 and 6.2 Hz) for 3-H and δ 6.20 (dt, *J* 6.2 and 2 x 3.1 Hz) for 1-H accompanied by the familiar pattern of signals for the dienyl moiety. Furthermore, the ^{13}C NMR signals for C-1, C-2 and C-3 were diagnostic (see Appendix 2, page ix). In addition, the IR spectrum of **118** displayed absorption at ν_{max} 1956 cm^{-1} (C=C=C), 1307 and 1149 cm^{-1} (S=O) in close correlation with **112**. The mass spectrum displayed an M+H molecular ion, a feature not uncommon for this class of compound.[115]

With the desired triene in hand, reactions were conducted to investigate its IMDA properties. Complete consumption of starting material was observed when the tetraene **118** was heated at 80 °C for 20 h. This gave a two-component mixture, chromatography of which furnished the *endo* cycloadduct **119** (18 %) and the *exo* cycloadduct **120** (54 %, Scheme 18).



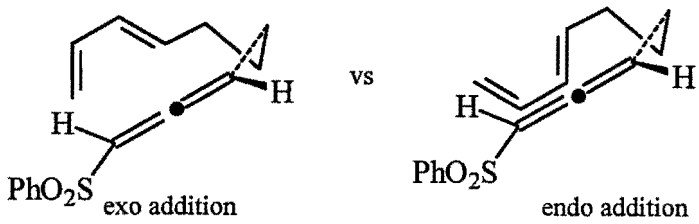
Scheme 18 *Reagents and conditions*: (i) PhMe, 80 °C, 20 h, 72 %

The structures of **119** and **120** were assigned with the aid of 1D and 2D NMR spectra. The ^{1}H NMR of **120** displayed signals at δ 5.57 (br d, *J* 10.4 Hz) for 4-H and δ 5.65 (dddd, *J* 10.4, 6.4, 4.8 and 2.4 Hz) for 3-H – the latter showing allylic coupling with 4a-H (Scheme 19). COSY NMR allowed for the identification of both 2-H signals (Figure 4). These appeared at δ 2.55 (dddd, *J* 19.8, 8.4, 6.4 and 2.4 Hz) for 2β-H and at δ 3.00 (dd, *J* 19.8 and 4.8 Hz) for 2α-H. The signal for 1-H appeared at δ 3.72 (d, *J* 8.4 Hz).



Scheme 19 Couplings found in the major cycloadduct **120**

In view of the importance of this reaction outcome, an X-ray crystal structure determination was carried out on compound **120** for confirmatory purposes, and to provide confirmation of the NMR based conclusions. Of particular importance was the absence of coupling between 1-H and 2α-H which is only possible if the relevant torsion angle is ~ 90°. This was indeed the case as the H – C(1) – C(2) – α-H torsion angle was observed as 88.9 ° (Figure 5, Appendix 1, page v), thus confirming the spectroscopic observations. This result confirms the major reaction pathway entailed *exo* addition of the activated π-bond of **118** to give **120** (Scheme 20) as predicted from the literature precedent of the vinyl phenylsulfonyl analogue.[94]



Scheme 20 *Exo-* and *endo-* transition states for (7*E*) 1-phenylsulfonyldeca-1,2,7,9-tetraene **118**

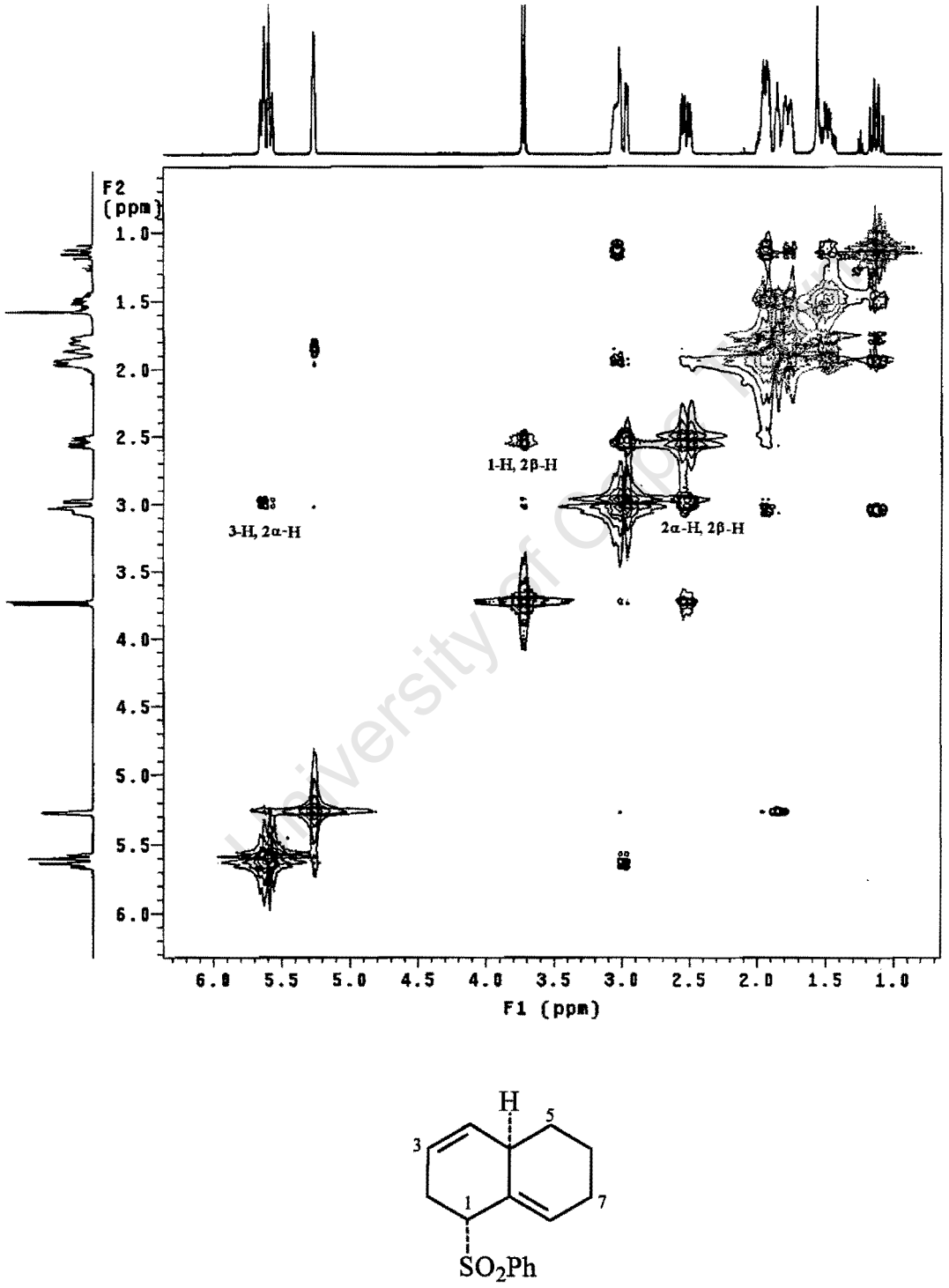


Figure 4 COSY NMR plot of cycloadduct **120** – SO_2Ph excluded

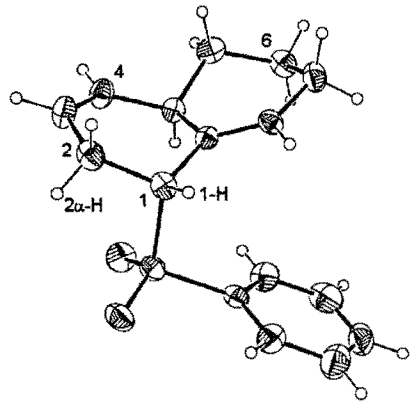
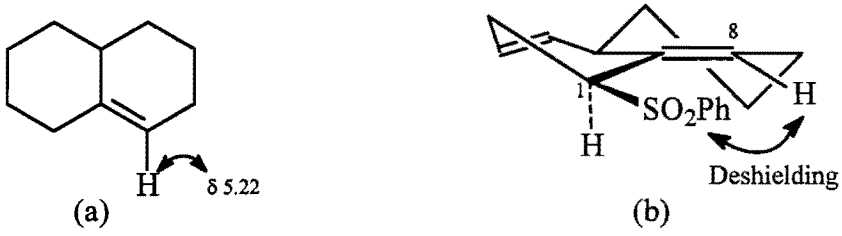


Figure 5 X-Ray crystal structure of (1*R**,4a*R**)-1-phenylsulfonyl-1,2,4a,5,6,7-hexahydronaphthalene **120**.

Assignment of the minor cycloadduct was carried out as in the case of the major cycloadduct. The ^{1}H NMR spectrum of **119** displayed signals at δ 5.43 (br d, *J* 9.9 Hz) for 4-H, δ 5.52 (ddt, *J* 9.9, 7.7 and 2 x 2.4 Hz) for 3-H and δ 3.82 (ddd, *J* 9.9. 3.5 and 1.3 Hz) for 1-H. The respective 2-H signals were complex (and were partially obscured by one 1-H signal). The above findings were consistent with assignment of structure **119** – which conversely arose as a result of *endo* addition of the activated π-bond. It was difficult to distinguish between ^{13}C signals of C-8a and the quaternary benzene signal for both cycloadducts (and subsequent cycloadducts), and assignments are tentative.

It was interesting to note the ^{1}H NMR chemical shift of 8-H for the cycloadducts – *viz.* **120** displayed a multiplet at δ 5.25 whilst **119** displayed the corresponding signal at δ 6.55. When this was compared with 2,3,4,4a,5,6,7,8-octahydronaphthalene (Scheme 21a), the corresponding shift of this was proton was 5.22 ppm.[116] Clearly, the phenylsulfonyl group of the *endo* cycloadduct was exerting a significant anisotropic deshielding effect on 8-H (Scheme 21b). This pattern of relative chemical shifts was observed in all the analogous cycloadducts prepared in subsequent experiments.

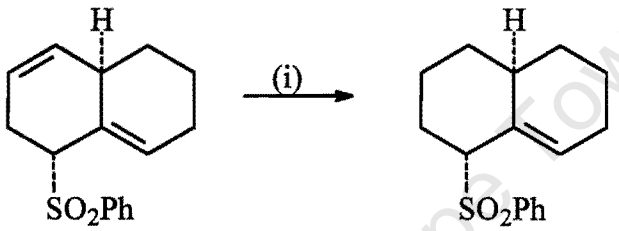


Scheme 21 Anisotropic deshielding (b) of 8-H found in the *endo* cycloadduct **119** when compared to (a)

A noteworthy aspect of the reaction of **118** was the significant rate enhancement arising from the one-carbon truncation of the tether (*viz.* a 30 % yield at 180 °C for 24 h for **113** → 72 % yield at

80 °C for 20 h for **118**). Clearly the shorter tether is advantageous as it places the activated olefin in an orientation facilitating cycloaddition. No trace of reaction with the inner allenic π-bond was seen. This observation could be attributed to: (a) The differences in activities of the π-bonds, and (b) the preference of the tetraene to adopt a six-membered transition state as opposed to a five-membered one (if reaction occurred on the inner π-bond).

Chemoselective hydrogenation was carried out on cycloadduct **120** using 10 % palladium on carbon to give **121** in 89 % yield (Scheme 22). The structure was assigned using both 1D and 2D NMR. A signal in the ^{1}H NMR spectrum for **121** at δ 5.00 (br s) for 8-H confirmined the retention of the hindered π-bond. Signal identification and further spectroscopic characterisation was hindered by signal overlap.

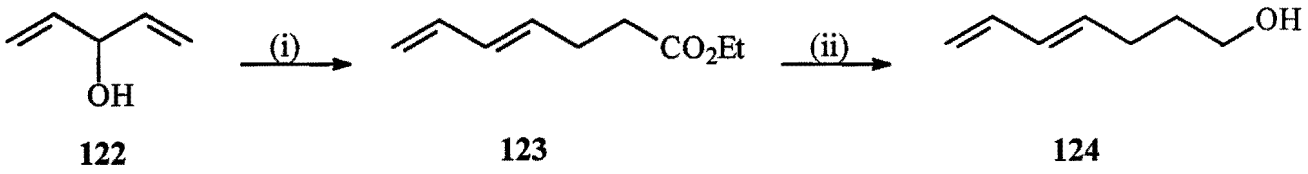


120 **121**

Scheme 22 *Reagents and conditions*: (i) Pd on carbon, 20 °C, 1 h, 89 %

The increase IMDA reaction rate associated with the truncation of the tether by one-carbon unit, suggests that the trend should be further pursued *via* synthesis of an analogous compound linked with a two-carbon tether.

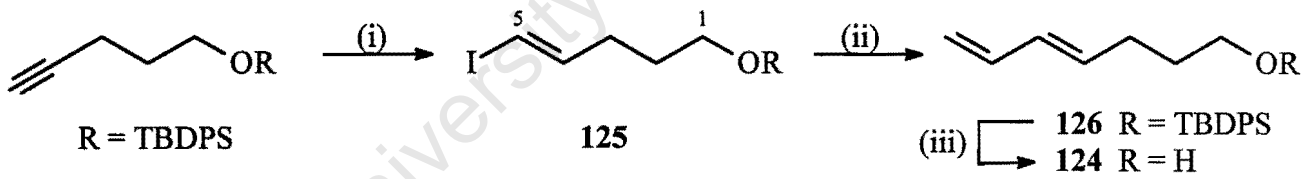
4.1.4 1-Phenylsulfonylnona-1,2,6,8-tetraene Treatment of penta-1,4-dien-3-ol **122** with triethyl orthoacetate and propionic acid (~ 20 mol %) in refluxing toluene for 16 h, proceeded *via* Claisen rearrangement,[117] to give the expected dienoate ester **123** in 98 % yield (Scheme 23). The product displayed the high (*E*)-selectivity (95% (*E*) by NMR) associated with the process, and the spectroscopic properties of the product were identical to those reported.[117] Reduction of ethyl ester **123** with DIBAH gave dienol **124** in 86 % yield.



122 **123** **124**

Scheme 23 *Reagents and conditions*: (i) $(EtO)_3CCH_3$, $CH_3CH_2CO_2H$, Δ, 16 h, 98 %; (ii) DIBAH, 0 °C, 86 %

An alternative approach was also examined for the synthesis of **124**. Schwartz's reagent[118] was added to a solution of (*t*-butyldiphenysiloxy)pent-4-yne. Quenching the reaction with iodine gave the (*E*)-vinyl iodide **125** (Scheme 24). ^{1}H NMR of **125** displayed signals at δ 5.97 (br d, *J* 14.3 Hz) for 5-H and δ 6.50 (dt, *J* 14.3 and 2 x 7.1 Hz) for 4-H which are consistent with the expected couplings of an (*E*)-substituted diene.

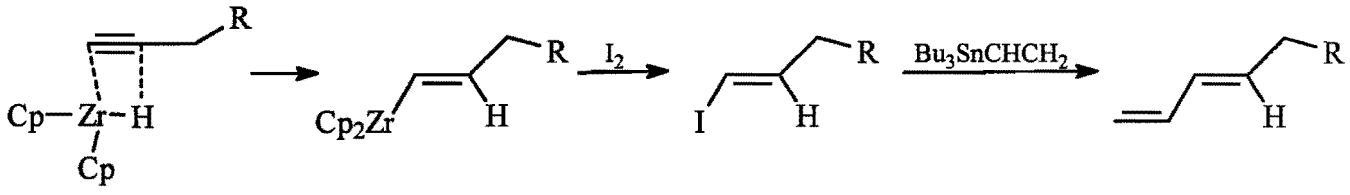


R = TBDPS **125**

126 R = TBDPS
124 R = H

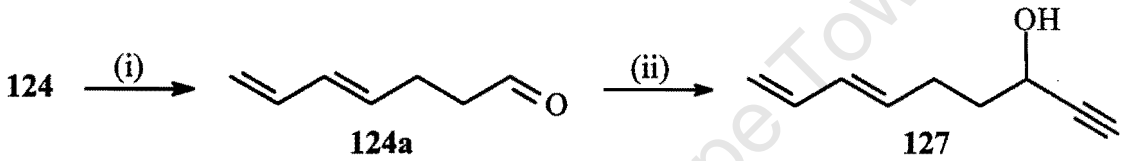
Scheme 24 *Reagents and conditions*: (i) Cp_2ZrHCl, CH_2Cl_2, I_2; (ii) $(PPh_3)_2Pd(Cl)_2$, DMF, $CH_2CHSnBu_3$, 70 % over 2 steps; (iii) TBAF, THF, 42 %

Stille coupling[119] of the iodide with vinyltributyltin and bis(triphenylphoshpine)palladium (II) chloride[120] in DMF gave (on deprotection) the dienol **124** (100 % (*E*) by NMR) in 28 % yield from the starting alkyne. These reaction yields are unoptimised. The overall mechanism of the Negeshi coupling,[121] followed by the Stille coupling, is shown in Scheme 25. Addition of the Zr-H across the alkyne, followed by iodine insertion gave the (*E*)-vinyl iodide. Stille coupling with vinyltributyltin completes the synthesis of the (*E*)-diene. This method provided a useful alternative approach to the synthesis of other diene-substituted substrates (see later)



Scheme 25 Mechanism for synthesis of *E*-diene involving Negeshi and Stille coupling reactions

Dess-Martin oxidation of the dienol **124** gave the aldehyde in 92 % yield (Scheme 26). This was adopted as the reagent of choice for all further oxidations, owing to the mild reaction conditions and ease of work-up, which facilitated the isolation of volatile aldehyde intermediates. A slight excess of freshly prepared periodinane gave best results for oxidation reactions. Ethynylation was carried out on the crude aldehyde **124a** using ethynylmagnesium bromide, generated *in situ*, to give dienynol **127** in 91 % yield.



Scheme 26 *Reagents and conditions*: (i) Periodinane, CH_2Cl_2, 25 °C, 92 %; (ii) HC≡CMgBr, THF, 25 °C, 91 %

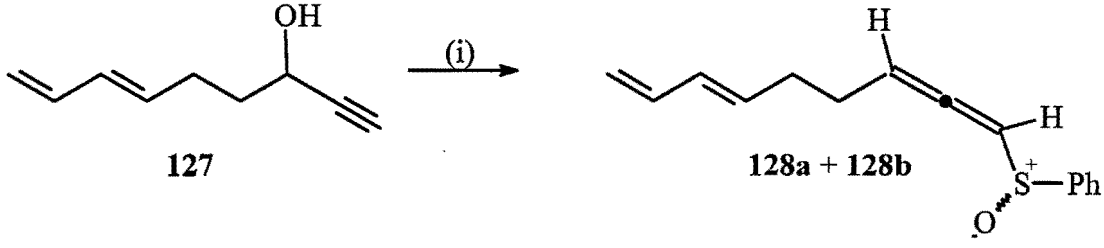
Spectroscopic assignment of **127** displayed analogous spectroscopic features observed for previously prepared compounds **110** and **116**. A comparison of key signals is shown in Table 2. Coupling constants were identical and are omitted.

Table 2 ^{1}H NMR summary of key signals for acetylenic alcohols

Number	δ (ppm)						
	1-H	3-H	H_2CR_c	H_2CR_t	C*H*CH_2	CHCHCH	CH_2CH
127	2.48	4.40	4.98	5.10	5.70	6.10	6.32
116	2.47	4.38	4.95	5.10	5.70	6.05	6.32
110	2.47	4.40	4.95	5.10	5.70	6.05	6.32

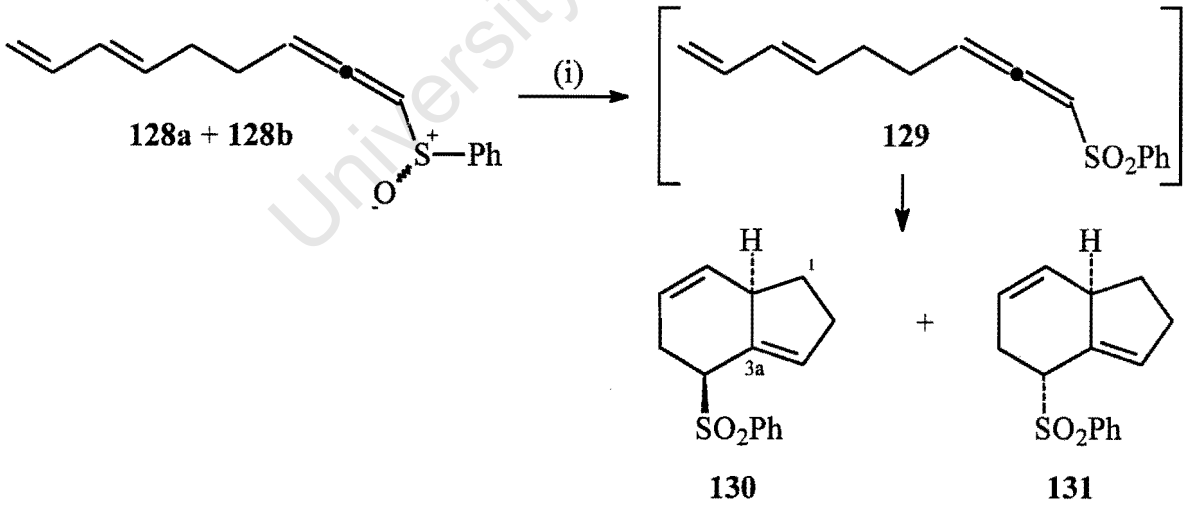
Treatment of dienynol **127** with benzenesulfenyl chloride in the presence of triethylamine at –78 °C, gave a mixture of phenylsulfinylallenyl diastereomers **128a** + **128b** in 69 % yield (Scheme 27). The ^{1}H NMR of **128a** + **128b** was complicated by signal overlap, particularly the signals of

1-H and 3-H whereas ^{13}C NMR displayed signals at δ 98.5 (C-1), 203.6 (C-2) and 103.1 (C-3). The IR spectrum displayed absorption at ν_{max} 1950 (C=C=C) and 1037 cm^{-1} (SO). The mass spectrum displayed an M+H ion, as previously observed for the analogous phenylsulfinyl compound **117a** + **117b**.



Scheme 27 *Reagents and conditions*: (i) PhSCl, NEt_3, -78 °C, 69 %

In an attempt to prepare the corresponding phenylsulfonyl tetraene, treatment of sulfoxide **128a** + **128b** with *m*-CPBA in dichloromethane at 0 °C proceeded to completion (TLC) within 30 min. After the addition of sodium hydrogen carbonate, and subsequent work-up at 25 °C, significant amounts of secondary products were present (TLC). Maintaining this material at 30 °C resulted in rapid accumulation of these products and, after 20 min, the cycloadducts **130** and **131** were isolated in 68 % overall yield, thus confirming their partial formation during the oxidation work-up (Scheme 28). Attempts to isolate the phenylsulfonyl tetraene intermediate **129** failed.



Scheme 28 *Reagents and conditions:* (i) (a) *m*-CPBA, 0 °C, 0.5 h; (ii) 30 °C, 20 min, 68 %

The structure of major cycloadduct **131** was assigned by analogy to previously prepared cycloadducts. Signals in the ^1H NMR spectrum were observed at δ 4.04 (d, *J* 8.4 Hz) for 4-H (*cf.* 1-H of **120**), δ 5.37 (br d, 2.4 Hz) for 3-H (*cf.* 8-H of **120**). Also observed were signals at δ 2.53

(ddq, *J* 19.5, 8.4 and 3 x 2.7 Hz) for 5β-H and δ 3.00 (ddq, *J* 19.5, 4.4 and 3 x 2.3 Hz) for 5α-H, which both exhibited allylic coupling (with 7-H) and homoallylic coupling with 7a-H (see below). COSY crosspeaks (Figure 6) allowed for the identification of 6-H (ddt, *J* 10.0, 4.4 and 2 x 2.7 Hz) at δ 5.57. These values were in agreement with the signal at δ 5.73 (dq, *J* 10.0 and 3 x 2.4 Hz) for 7-H (Scheme 29). The apparent difference in coupling magnitude of 5-H protons (*viz.* 2.4 vs 2.7 Hz) with 7-H (which was seen as an apparent quartet) could be attributed to lack of adequate resolution.

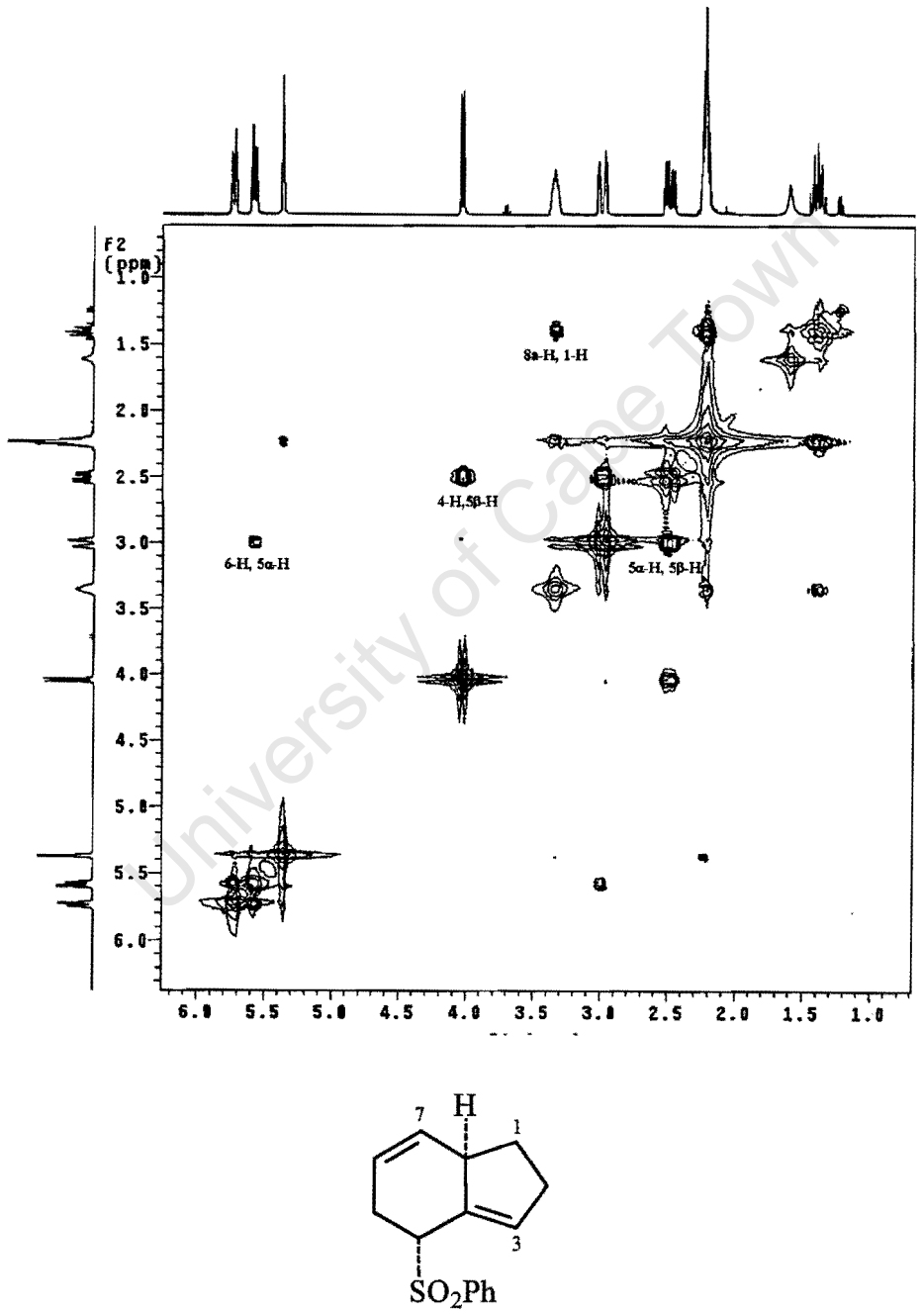
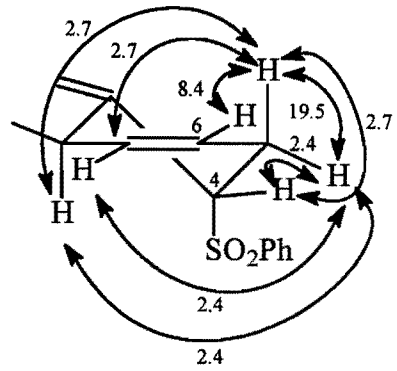


Figure 6 COSY crosspeaks for cycloadduct **131** – Phenyl group excluded



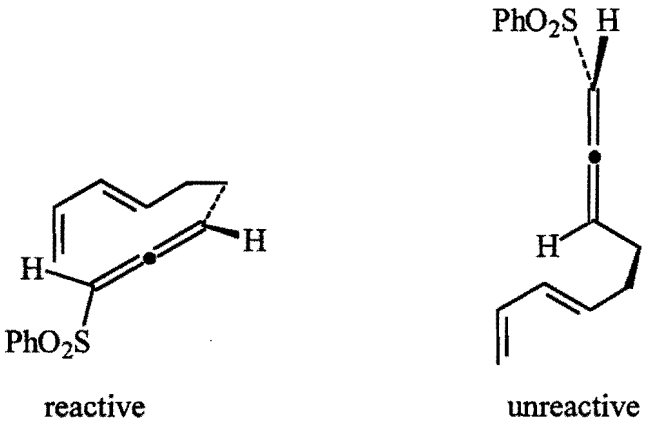
Scheme 29 Coupling information observed for major cycloadduct **131**.

The structure of minor cycloadduct **130** was assigned by analogy to cycloadduct **119**. The most striking feature was the similarity of the signal at δ 6.42 (t, *J* 2.3 Hz) for 3-H to that of 8-H for **119**. The signals for δ 5.18 (ddt, *J* 9.8, 5.0 and 2 x 2.4 Hz) for 6-H and δ 5.45 (br d, *J* 9.8.0 Hz) for 7-H allowed for identification of both 5-H signals (COSY). These signals were complex and overlapped with both 2-H signals, thus preventing complete signal assignment.

The reaction conditions under which the obligatory, but unisolable sulfone **129** underwent IMDA reaction (*viz*. 20 min at 30 °C) revealed a remarkable increase in reactivity by comparison with the substrates **112** and **118**. It is inferred that the tether length in this instance [... $(CH_2)_2$...] facilitates highly favourable alignment of the interacting centres in the transition state leading to the respective products.

The influence of the phenylsulfonylallenyl terminus on the reactivity of the tetraene was also highlighted by comparison with the IMDA reaction of (6*E*) 1-phenysulfonylnona-1,6,8-triene which requires 140 °C for 44 h for complete reaction (80 % yield of a 1:1 mixture of *exo* diastereomers).[95]

The stereoselectivity of the reaction was analogous to that observed for **118** as the major product arose from *exo*-addition of the dienophile. There are two possible *exo*-transition states available for reaction of **129**. However, only one of these is feasible as the tether is too short to facilitate reaction on the opposite face (Scheme 30 for the indicated allene).



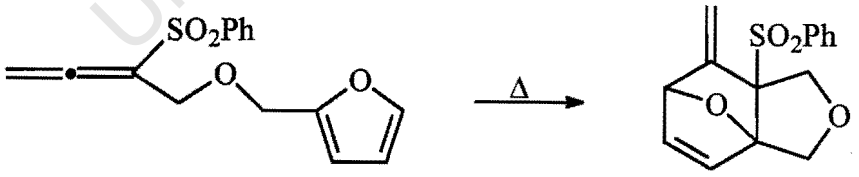
reactive unreactive

Scheme 30 *Exo* transition state for (6*E*) 1-phenylsulfonylnona-1,2,6,8-tetraene **129**.

Armed with the success of the above results, we proceeded in designing additional two-carbon tethered systems in order to ascertain the scope and limitations of this approach for the synthesis of a variety of hydrindane systems.

4.2 Furanyl terminated 1-phenylsulfonyl 1,2-dienes

4.2.1 Introduction Several examples of intramolecular Diels-Alder reactions containing furanyl dienes (IMDAF) and allenyl moieties as dienophilic elements are found in the literature.[122] For example, Padwa *et al.*,[99] have shown that 3-phenylsulfonylallenyl substructures linked to a furanyl diene moiety *via* a three-atom tether readily undergo IMDAF reaction. This is illustrated by compound **132** (Scheme 31).

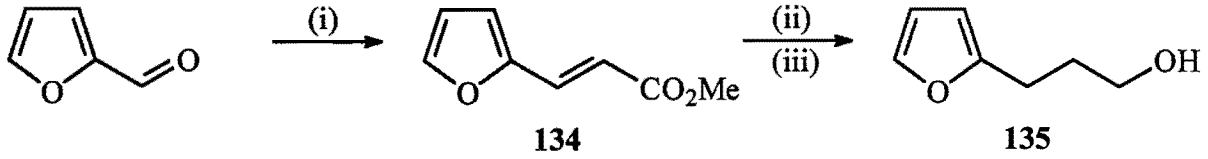


132 **133**

Scheme 31 IMDA reaction of internally substituted sulfonyl allene with furanyl diene

An extension of this methodology to the 1-phenylsulfonylallenyl series would provide an interesting analogy to these and foregoing results.

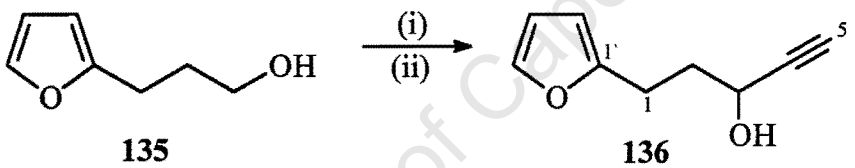
4.2.2 5-(2-Furyl)-1-phenylsulfonylpenta-1,2-diene. Furfural was treated with (methoxycarbonylmethylene)triphenylphosphorane to give ester **134** in good yield (98 % *E*) (Scheme 32). Reduction of the ester **134** with DIBAH followed by hydrogenation with Pd on carbon, under atmospheric hydrogen pressure, gave the known [123] alcohol **135** in 80 % overall yield.



134 **135**

Scheme 32 *Reagents and conditions*: (i) Ph_3PCHCO_2Me, CH_2Cl_2, 20 °C, 100 %; (ii) DIBAH, THF, 0 °C, 89 %; (iii) Pd on carbon, EtOAc, 20 °C, 90 %

Dess-Martin oxidation of alcohol **135** gave the aldehyde in 93 % yield. Treatment of the aldehyde with ethynylmagnesium bromide, generated *in situ*, was carried out as before to give the propargyl alcohol **136** in 88 % yield (Scheme 33).

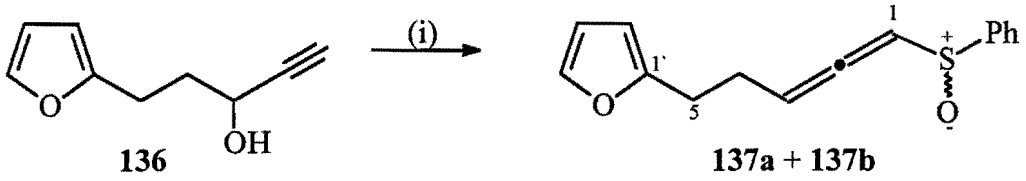


135 **136**

Scheme 33 *Reagents and conditions*: (i) Periodinane, 20 °C, 93 %; (ii) HC≡CMgBr, THF, 20 °C, 88 %

The ^{1}H NMR spectrum of **136** displayed furfuryl signals at δ 6.00 (dd, *J* 3.1 and 0.9 Hz) for 3′-H, δ 6.28 (dd, *J* 3.1 and 3 x 1.8 Hz) for 4′-H and δ 7.31 (dd, *J* 31.8 and 0.9 Hz) for 5′-H whereas the acetylenic signals were analogous to those of previously prepared alkynols. The IR spectrum of **136** displayed absorption ν_{max} 3305 (for C≡C-H) and 3687 cm^{-1} (OH).

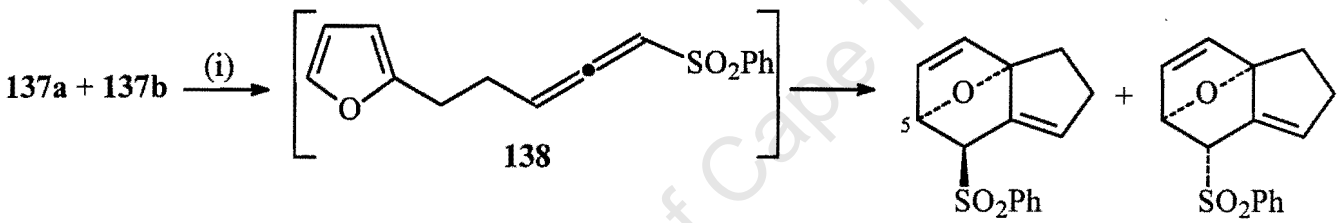
Low temperature treatment of dienynol **136** with benzenesulfenyl chloride in the presence of triethylamine was carried out as before, to give a mixture of phenylsulfinylallenyl diastereomers **137a** + **137b** in 49 % yield (Scheme 34). ^{13}C NMR of this mixture displayed signals at δ 98.1 (C-1), 203.6 (C-2) and 103.2 (C-3) respectively which were diagnostic for an allenyl moiety. The IR spectrum displayed absorption at ν_{max} 1951 cm^{-1} (C=C=C) and 1036 cm^{-1} (SO). ^{1}H NMR was of limited use arising from signal duplication and/or overlap.



136 **137a + 137b**

Scheme 34 *Reagents and conditions*: (i) PhSCl, NEt_3, -78 °C, 49 %

Treatment of the sulfoxides **137a** + **137b** with *m*-CPBA at -10 °C for 30 min was followed by the addition of aqueous sodium hydrogen carbonate containing ice. The reaction product was worked-up while maintaining the temperature at ~0 °C. A ^{1}H NMR spectrum of the crude product material revealed a three-component mixture (10:2:1by NMR) containing cycloadducts **139** and **140** and the allenyl sulfone intermediate **138**. Diagnostic signals for **138** were observed at δ 5.87 (td, *J* 2 x 7.0 and 6.2 Hz) for 3-H and at δ 6.20 (dt, *J* 6.2 and 2 x 3.1 Hz) for 1-H (Scheme 35).

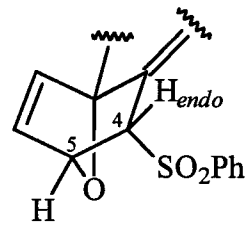


139 **140**

Scheme 35 *Reagents and conditions*: (i) *m*-CPBA, CH_2Cl_2, -10 °C; work-uo at 0 °C, 63 %

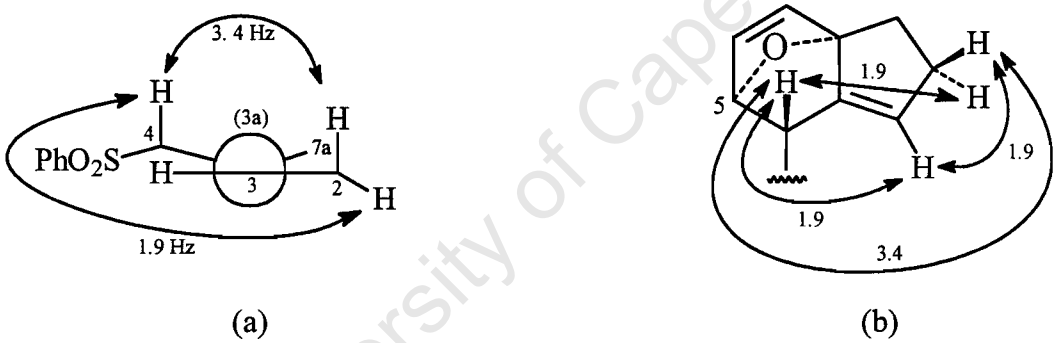
Observed in the same spectrum were signals for the minor cycloadduct **139** which were identified at δ 4.42 (d, *J* 3.6 Hz) for 4-H, δ 5.30 (dd, *J* 3.6 and 1.7 Hz) for 5-H, δ 6.54 (d, *J* 5.6 Hz) for 7-H and at δ 6.57 (dd, *J* 5.6 and 1.7 Hz) for 6-H. Chromatography of this crude material gave the *exo* cycloadduct **140** in 63 % overall yield whereas the minor cycloadduct **139** could not be isolated. Lability of these systems is well documented,[124] and hence cycloadduct was handled with caution.

The ^{1}H NMR spectrum of **140** displayed signals at δ 6.50 (d, *J* 5.7 Hz) for 7-H and δ 6.41 (dd, *J* 5.7 and 2.1 Hz) for 6-H. The COSY spectrum of **140** allowed for the identification of 5-H at δ 5.38 (d, *J* 2.1 Hz) and 4-H at δ 3.65 (dt, *J* 3.4 and 2 x 1.9 Hz). The absence of coupling between 4-H and 5-H supports the above structure as *endo* protons, in norbornane type structures, exhibit zero coupling with bridgehead protons (Scheme 36).



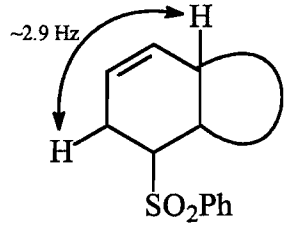
Scheme 36 Zero coupling between *endo* 4-H and bridgehead 5-H, consistent with norbornane-type structures

The signal for 4-H was more complex than expected and displayed long range coupling with both 2-H protons and 3-H (dt, J 3.4 and 2 x 1.9 Hz) at δ 5.75. This was ascribed to homoallylic coupling $^5J_{4,2}$, which is known to occur between protons separated by a π-bond flanked on either side by two single bonds, *i.e.* for the system H-C-C=C-C-H.[107] Orthogonality of both coupling partners to the olefinic plane maximises the coupling magnitude, which typically ranges between 1.9 and 3.5 Hz for cyclic systems. From a molecular model, this orientation was compatible with 2-H_2 as visualised by the Newman projection along C(3a) - C(3) (Scheme 37a).



Scheme 37 (a) Homo-allylic coupling between 2-H_2 and 4-H, projected along C-3 - C-3a for **140** and (b) Observed long range and allylic couplings of the major cycloadduct **140.**

Thus observed are two ^5J couplings – *viz.* $^5J_{2\beta,4}$ 3.4 Hz and $^5J_{2\alpha,4}$ 1.9 Hz which are shown in Scheme 37b. Also observed is an allylic coupling $^4J_{3,4}$ 1.9 Hz. The same principle is also observed in previous cycloadduct systems as ^5J coupling is observed (in some cases) between the bridgehead proton and the allylic protons in the cyclohexane ring (Scheme 38).

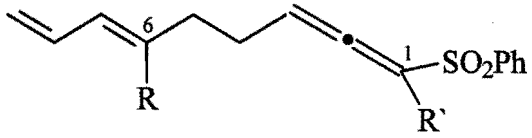


Scheme 38 Long-range coupling observed between bridgehead proton and vinylic protons

This exploratory result also demonstrates the enhanced reactivity of tetraenes linked *via* a two-carbon tether and offers encouraging scope for future investigations.

4.3 1- and 6-Substituted 1-phenylsulfonyl 1,2,6,8-tetraenes

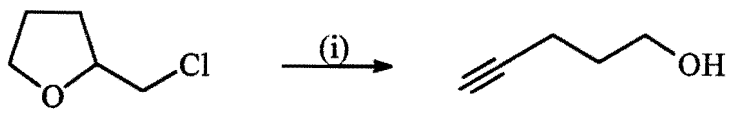
4.3.1 Introduction The foregoing results revealed that two unrelated types of substrate, in which the 4π and 2π participants are linked *via* a two-carbon tether, display exceptional IMDA reactivity. In order to extend and explore this reactivity, attention was turned to introduction of structural elements at C(1) or C(6) of the parent system (Scheme 39).



Scheme 39 Proposed introduction of substitution at C-1 and C-6

It was expected that substitution at either of these positions would introduce a degree of steric impediment to IMDA reactivity and would allow for the isolation of the precursor substrates and the application of controlled reaction conditions. Furthermore, successful IMDA reaction would allow for the synthesis of products containing substructures often encountered in natural products, and hence may be of synthetic value.

4.3.2 6-Methyl-1-phenylsulfonylnona-1,2,6,8-tetraene and 1-(*t*-Butyldiphenylsilyloxy)-4-phenylsulfonyldodeca-4,5,9,11-tetraene Tetrahydrofurfuryl chloride was treated with sodium amide, generated *in situ*, in refluxing ammonia, to give ynol **141** in 93 % yield (Scheme 40).[125] The product contained ~ 5 % (by NMR) of pent-4-en-1-ol.

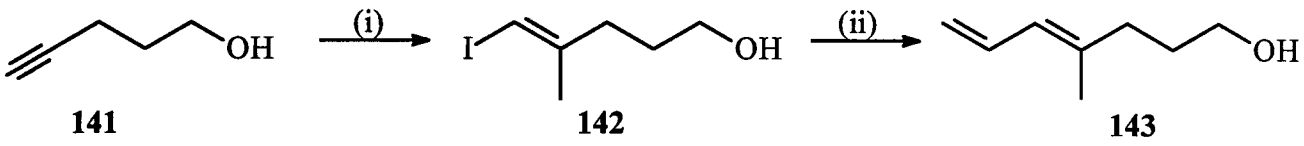


141

Scheme 40 *Reagents and conditions*: (i) Na, NH_3, $FeCl_3$, 93 %

Using the procedure of Wender *et al.*,[126] trimethylaluminium was added to a solution of zirconocene chloride[121] followed by alcohol **141**. The reaction was quenched with iodine to yield

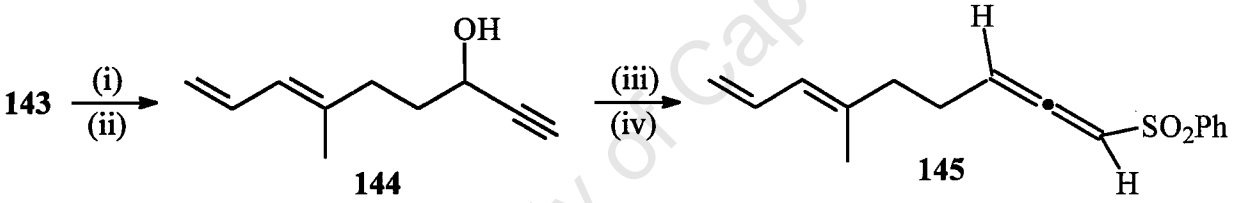
the vinyl iodide **142** in 75 % yield (Scheme 41). Stille coupling of the iodide with vinyltributyltin and freshly prepared Pd(0) catalyst gave the (*E*)-diene **143** in 91 % yield.



141 **142** **143**

Scheme 41 *Reagents and conditions*: (i) Cp_2ZrCl_2, Me_3Al, CH_2Cl_2, I_2; (ii) $(PPh_3)_2Pd(Cl)_2$, DMF, $CH_2CHSnBu_3$

Dess-Martin oxidation of alcohol **143**, followed by ethynylation gave the acetylenic alcohol **144** in 74 % overall yield (Scheme 42). In addition to the diagnostic signals associated with the dienynol functionality, a signal was observed at δ 1.78 (3H, br s) for the 6-Me group. Treatment of alcohol **144** with benzenesulfenyl chloride in the presence of triethylamine at low temperature afforded a mixture of phenylsulfinylallenyl diastereomers in 57 % yield which was oxidized with *m*-CPBA to afford the phenylsulfonylallene **145** in 50 % yield. The spectroscopic properties of **145** closely resembled those of previously synthesised tetraenes.



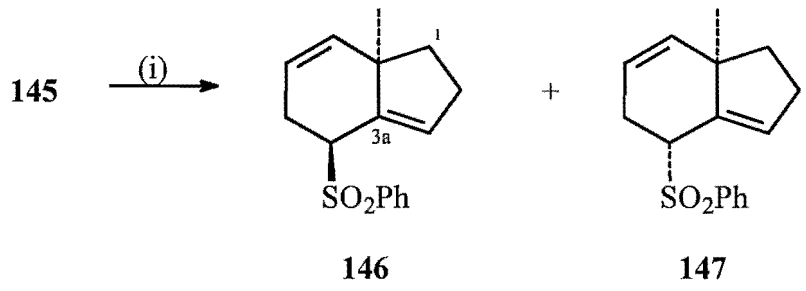
144 **145**

Scheme 42 *Reagents and conditions*: (i) Periodinane, CH_2Cl_2, 25 °C: (ii) HC≡CMgBr, THF, 25 °C, 75 %; (iii) PhSCl, NEt_3, -78 °C, 57 %; (iv) *m*-CPBA, CH_2Cl_2, 50 %

The modest yield of **145** was clearly associated with competing epoxidation of the diene which was probably attributed to the enhanced reactivity of the trisubstituted Δ^6-bond. Conducting the reaction at –78 °C did not improve chemoselectivity nor did reverse addition of reagent. Recycling the sulfoxide, isolated after oxidation work-up, was the only effective method for increasing the sulfone yield. It was evident however, that the 6-methyl substitution resulted in diminished IMDA reactivity, since there was no evidence of cycloadducts during the oxidation step.

The cycloaddition reaction was monitored by NMR to ascertain the minimum conditions required for reaction to occur. It was observed that heating the phenylsulfonylallene **145** at temperatures of 80 and 120 °C for 2 h respectively had no effect. However, in an experiment conducted at 150 °C, complete reaction was observed within 2 h, to yield a two component mixture (Scheme 43).

Chromatography gave the *endo* cycloadduct **146** in 13 % yield, followed by the *exo* cycloadduct **147** in 45 % yield.

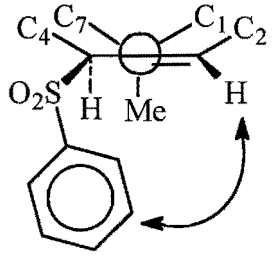


146 **147**

Scheme 43 *Reagents and conditions*: (i) PhMe, 150 °C, 2 h, 66 % overall

Structural assignment of **147** as the *exo* adduct was based on comparative signals observed in the ^{1}H NMR spectrum at δ 5.55 (dt, *J* 10.0 and 2 x 3.7 Hz) for 6-H, δ 5.60 (m, $W_{½}$ 1.7 Hz) for 3-H and δ 5.82 (br d, *J* 10.0 Hz) for 7-H. These signals compare favourably with those of previously observed *exo* cycloadducts **120** and **131**. The signals for 4-H and 5-H_2 were complex and could not be fully assigned.

The structure of minor cycloadduct **146** was also assigned by analogy to previous results as signals observed in the ^{1}H NMR spectrum at δ 5.38 (ddd, *J* 9.9, 5.3 and 2.3 Hz) for 6-H, δ 5.65 (dd, *J* 9.9 and 2.7 Hz) for 7-H and δ 6.10 (br d, *J* 1.8 Hz) for 3-H compare favourably with those of previous examples. The decisive distinguishing feature between **146** and **147** was the relative chemical shift of 3-H of **146**, which was significantly deshielded by the phenylsulfonyl group and is consistent with findings of previously prepared *endo* cycloadducts (Scheme 44). The results observed thus far have been published.[127]

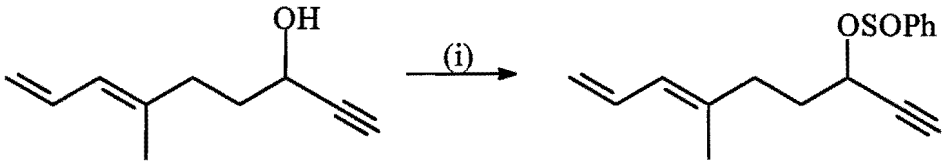


Scheme 44 Anisotropic interaction between 3-H and the phenylsulfonyl group for *endo* cycloadduct **146**

In an attempt to overcome the inherently difficult sulfoxide → sulfone conversion in this sequence, it was decided to synthesise the benzenesulfinate ester **148** as it is known[128] that thermal [2,3]sigmatropic rearrangement of a sulfinate ester, after heating at elevated

temperatures, affords the corresponding allenyl sulfone. The relatively slow IMDA reaction of sulfonylallene **146** made its isolation, after rearrangement, feasible.

Therefore, treatment of alcohol **144** with benzenesulfinyl chloride[129] in the presence of pyridine at low temperature gave a mixture of diastereomeric esters **148** in 78 % yield (Scheme 45), whose spectroscopic features were in an close agreement with those of previously synthesised compounds.

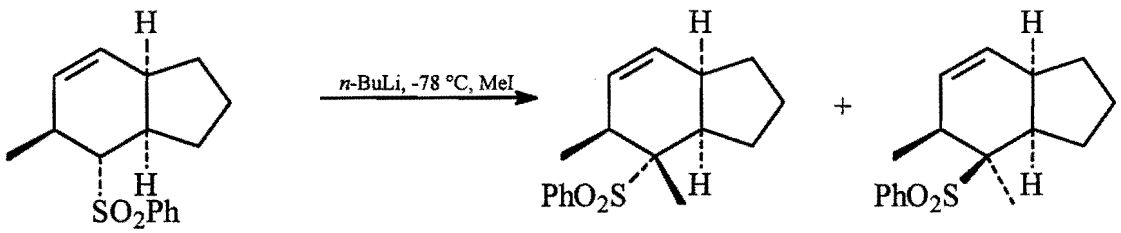


144 **148**

Scheme 45 *Reagents and conditions*: (i) PhOSCl, NEt_3, -78 °C, 75 %

Unfortunately, heating the ester **148** at 130 °C for 2 h afforded a complex mixture of products. ^1H NMR spectrum of the crude reaction mixture revealed the presence of cycloadducts **146** and **147** (major) in addition to several minor products. This trial experiment demonstrated the feasibility of this process; however, the complexity of the product make-up discouraged further investigation

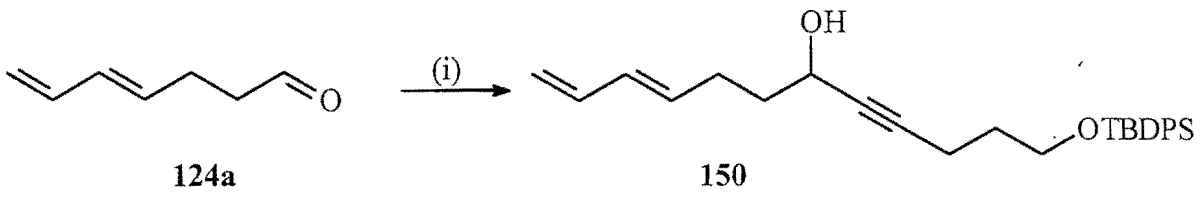
The introduction of substitution at C-1 (of the parent compound) would facilitate the generation of a quaternary centre, thereby bypassing the unsatisfactory alkylation of the unsubstituted cycloadducts. Craig *et al.*, [96] observed that methylation of the analogous position for a series of related compounds (*e.g.* compound **149**, Scheme 46) resulted in significant scrambling of the chiral centre. This was indeed observed for several attempted ethylation reactions carried out on cycloadduct **120**



149 ~ 1:1

Scheme 46 Alkylation of cycloadducts in a study preformed by Craig *et al* (one example shown)

Following a procedure of Djuric *et al.*,[130] aldehyde **124a** was added to a solution of 1-(*t*-butyldiphenylsiloxy)-pent-4-yne in the presence of *n*-BuLi. This gave the acetylenic alcohol **150** in 14 % yield (Scheme 47, unoptimised). This procedure has since been superseded (see later).

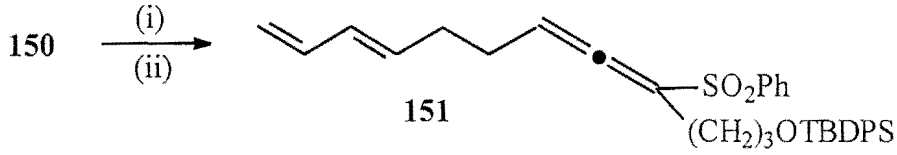


124a **150**

Scheme 47 *Reagents and conditions*: (i) TBDPSO$(CH_2)_3$C≡CH, *n*-BuLi, THF, 25 °C, 14 %

The ^{1}H NMR spectrum of **150** displayed a signal at δ 4.36 (br m) for 6-H and the ^{13}C NMR displayed signals at δ 81.1 (C-4) and 85.3 (C-5) respectively, which were in the expected range for internal acetylenic carbons. The IR spectrum displayed absorption ν_{max} 3674 (OH) and 2228 cm^{-1} (C≡CR). The mass spectrum displayed a molecular fragment ion which corresponded to the loss of the *tert* butyl group of the protecting group – a feature not uncommon for this protecting group.[107]

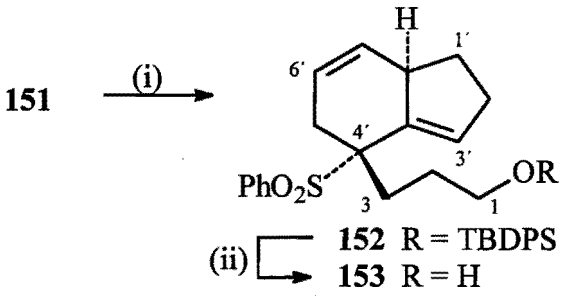
Treatment of **150** with benzenesulfenyl chloride, followed by oxidation with *m*-CPBA gave the phenylsulfonyltetraene **151** in 48 % yield over the two steps (Scheme 48). The ^{1}H NMR spectrum displayed a signal at δ 5.70 (m) for 6-H, while allenic signals were observed in the ^{13}C NMR at δ 113.7 (C-4), 203.8 (C-5) and 100.7 (C-6). The IR spectrum displayed the characteristic allenic absorption at 1960 cm^{-1}. Mass spectrometry of these and related trisubstituted allenes, were particularly difficult as both (EI) and (FAB) techniques gave complex fragmentation patterns, which were not decipherable. Chemical ionisation (CI) techniques were unavailable. Only electron spray (ES) techniques allowed for the identification of the parent molecular ion, which was observed as the corresponding M+Na ion.



151

Scheme 48 *Reagents and conditions*: (i) PhSCl, NEt_3, -78 °C, 68 %; (ii) m-CPBA, 0 °C, 70 %

The tetraene **151** was dissolved in deuteriochloroform and the resulting solution was sealed in an NMR tube. This was heated at 50 °C for 2 h to yield a single product **152** in 75 % yield (Scheme 49) which desilylated with TBAF to give alcohol **153** in 44 % yield.

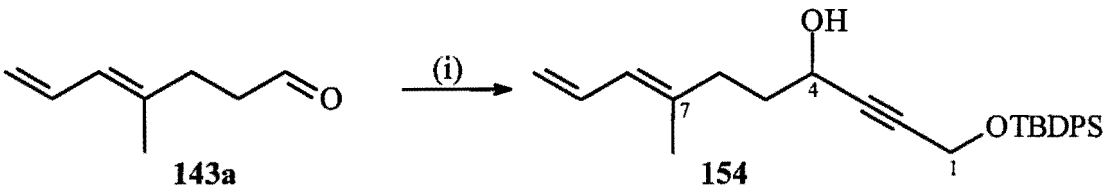


Scheme 49 *Reagents and conditions*: (i) $CDCl_3$, 50 °C, 2 h min, 75 %, (ii) TBAF, THF, 0.5 h, 44 %

The cycloadduct was assigned using both 1D and 2D NMR, although signal overlap and non first-order behavior made assignments difficult. The ^{1}H NMR spectrum of **152** displayed signals at δ 5.40 (br s) for 3′-H, δ 5.63 (ddd, *J* 9.9, 7.4 and 2.5 Hz) for 6′-H and at δ 5.70 (br d, *J* 9.9 Hz) for 7′-H – as observed in previous examples. The signal for 3′-H was consistent with the assignment of **152** as a product arising from *exo* addition, based on analogy to previous results.

The high diastereoselectivity accompanying formation of **152** demonstrates this approach, to generate 4-alkylhydrindane systems, is superior to that in which cycloadducts such as **120** are subjected to base-mediated alkylation experiments.

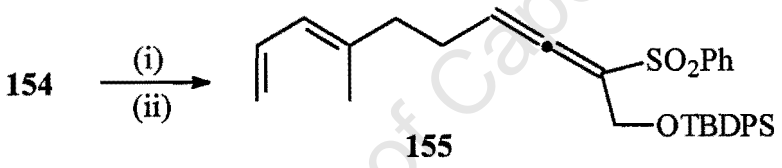
4.3.3 1-(*t*-Butyldiphenylsilyloxy)-2-phenylsulfonyl-7-methyldeca-2,3,7,9-tetraene It was decided to investigate tetraenes containing substitution at *both* C-1 and C-6 positions, with the intention of obtaining hydrindane cycloadducts containing two quaternary carbon centres. Therefore, aldehyde **143a** was treated with 1-(*t*-butyldiphenylsilyloxy)prop-2-yne in the presence of *n*-BuLi to give alkynol **154** in 42 % yield (Scheme 51).



Scheme 51 *Reagents and conditions*: (i) $TBDPSOCH_2C{\equiv}CH$, *n*-BuLi, THF, 25 °C, 42 %

Characterisation was carried out as before. The ^{1}H NMR spectrum for **154** displayed signals at δ 1.74 (3H, s) for 7-Me, δ 4.27 (br m, *W* 10 Hz) for 4-H and δ 4.38 (2H, d, *J* 1.6 Hz) for 1-H_2 – the latter corresponding to the diastereotopic 1-H_2 and exhibit ^{5}J coupling with 4-H. The ^{13}C NMR spectrum displayed signals at δ 83.6 (C-2) and 86.0 (C-3) respectively which was consistent with previously observed results. The IR spectrum displayed absorption at ν_{max} 2252 (C≡CR) and 3603 cm^{-1} (OH).

Treatment of alkynol **154** with benzenesulfenyl chloride, followed by oxidation with *m*-CPBA gave the phenylsulfonyl tetraene **155** in 13 % yield over the two steps (Scheme 52). The spectroscopic data are in close agreement with previously prepared compounds (See Appendix 2 pp viii). As a result of the poor overall yield of the target substrate, it was not possible to conduct experiments on a preparative scale. However, sufficient material was isolated to perform a preliminary trial. Thus tetraene **155**, in toluene (sealed tube), was heated at 155 °C for 2 h when the starting material was consumed (TLC).



Scheme 52 *Reagents and conditions*: (i) PhSCl, NEt_3, -78 °C, 28 %; (ii) m-CPBA, 0 °C, 48 %

An NMR spectrum of the reaction product revealed the presence of a complex mixture of products (including cycladduct-like signals). Further work will be necessary to optimise the sythetic route to **155**, and investigation of the potential of this IMDA process. As a result of time constraints, this investigation was discontinued.

4.4. Cyclohexandienyl terminated 1-phenylsulfonylpenta-1,2-dienes

4.4.1 Introduction The use of cycloaddition-fragmentation methodology has been used extensively in several studies of our research group.[131] It was decided to explore the scope of the extending the foregoing IMDA studies to substrates designed for subsequent fragmentation of the derived cycloadducts. For example, an IMDA reaction of a phenylsulfonylallene terminus with an oxygen terminated cyclohexadiene **156**, followed by base mediated retrograde cleavage[132] would lead to the synthesis of spiro fused ring systems **157** (Figure 53). A large number of natural products possess spiro-fused ring junctions, and successful application of the above methodology may offer an alternative route to the synthesis of these compounds.

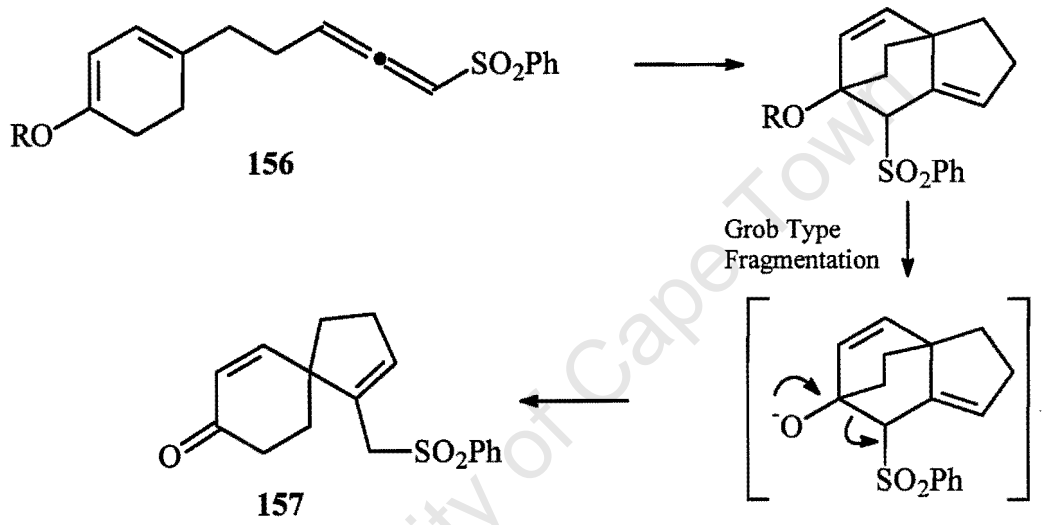
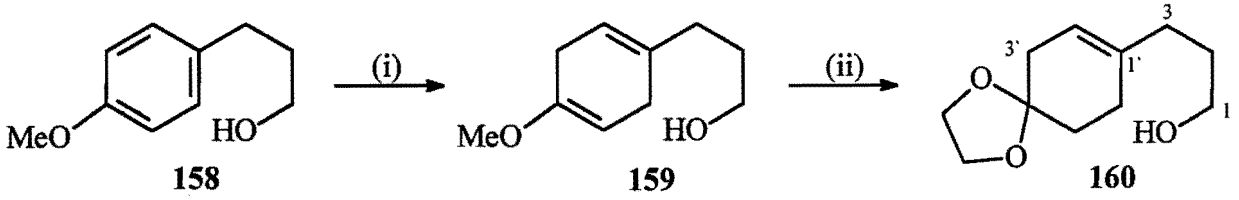


Figure 53 Proposed synthesis of spiro [5,4] ring system

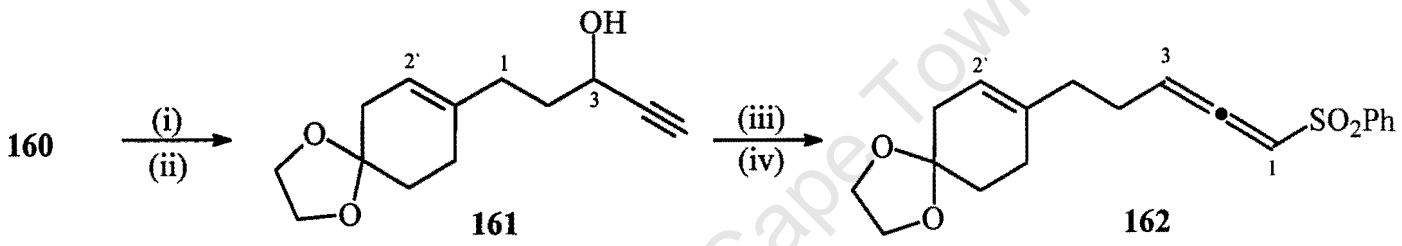
4.4.2 4-(5-Phenylsulfonylpenta-3,4-dienyl)cyclohex-3-en-1-one 3-(4-Anisyl)propan-1-ol **158** (prepared by hydroboration of 4-allylanisole) was subjected to Birch reduction, followed by functional group modification of enol ether **159** with $BF_3.OEt_2$ and ethylene glycol to give ketal **160** in 57 % overall yield (Scheme 54).



Scheme 54 *Reagents and conditions*: (i) Na, NH_3, EtOH, 93 %; (ii) $BF_3.OEt_2$, $HO(CH_2)_2OH$, THF, 61 %

The ^{1}H NMR spectrum of **160** displayed signals at δ 5.35 (br s) for 2′-H and δ 3.95 (4H, s) for the acetal methylene groups. The Birch reduction was also successful if carried out with lithium. In both cases, best results were achieved when a large excess of the metal was used.

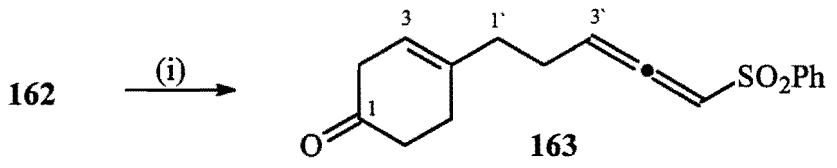
Dess-Martin oxidation of alcohol **160**, followed by ethynylation with ethynylmagnesium bromide, prepared *in situ*, gave the propargylic alcohol **161** in 53 % overall yield (Scheme 55). Spectroscopic data were in agreement with previously prepared compounds. Low temperature treatment of dienynol **161** with benzenesulfenyl chloride, followed by oxidation of the resulting sulfoxides with *m*-CPBA gave phenylsulfonyl tetraene **162** in 41 % yield. Spectroscopic characterisation was analogous to previously prepared compounds. The modest yield of sulfone **162** is due to the familiar problem of competing epoxidation reaction with the trisubstituted $\Delta^{1'}$-bond.



Scheme 55 *Reagents and conditions*: (i) Periodinane, CH_2Cl_2, 25 °C, 89 %; (ii) HC≡CMgBr, THF, 25 °C, 59 %; (iii) PhSCl, NEt_3, CH_2Cl_2, -78 °C, 80 %; (iv) *m*-CPBA, CH_2Cl_2, 25 °C, 41 %

The improved yield for the [2.3]sigmatropic rearrangement was due to an increased amount of base in the reaction mixture. Our approach was based on findings observed for the synthesis of phospinyl allenes,[133] where the authors found that trace amounts of HCl, whether neutralised or not, gave rise to unwanted propargylic and allenic chlorides. Their approach involved bubbling nitrogen through the reaction mixture, containing excess base, for the duration of the experiment. This approach was followed resulting in improved yields, however, similar yields were achieved using *only* excess base. The latter variant was then adopted as the method of choice.

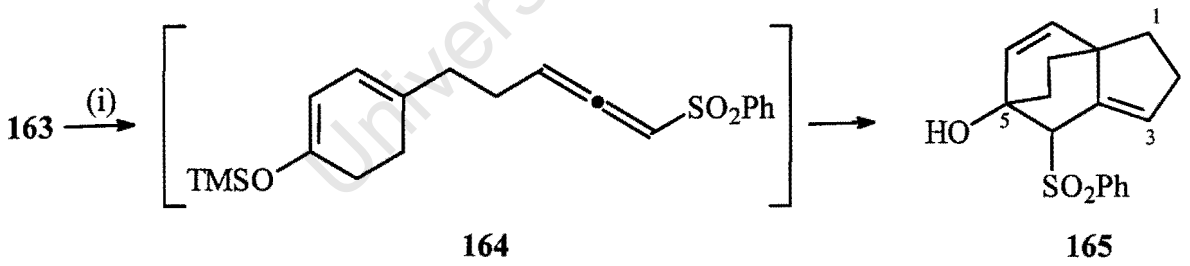
Treatment of the **162** with trifluoroacetic acid, followed by neutralisation with aqueous sodium hydrogen carbonate, gave the enone **163** in 92 % yield (Scheme 56).



Scheme 56 *Reagents and conditions*: (i) (a) TFA, 25 °C; (b) $NaHCO_3$, 0 °C, 92 %

The ^{13}C NMR spectrum of **163** displayed signals at δ 205.6 (C-4′) and 210.4 (C-1), thus confirming the presence of both the allenyl and carbonyl functionalities. This was supported by the IR spectrum which displayed absorption ν_{max} 1956 (C=C=C) and 1713 cm^{-1} (CO). No isomerisation of the allenyl or isolated π-bond was seen.

Based on research by Rubottom *et al.*,[134] enone **163** was treated with lithium diisopropylamide at -78 °C, followed by trapping with trimethylsilyl chloride. Thin layer chromatography of the reaction mixture revealed complete consumption of starting material and the reaction was subsequently quenched. Chromatography of the residue afforded the desilylated cycloadducts **165** in poor yield (12 %, Scheme 57).

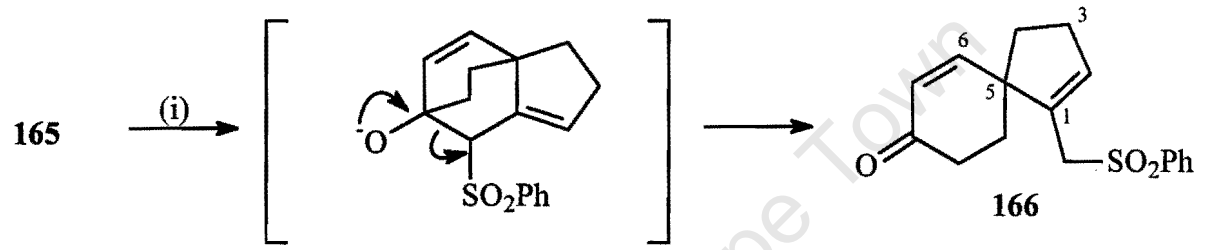


Scheme 57 *Reagents and conditions*: (i) LDA, TMSCl, -78 °C → 25 °C, 12 %

The ^1H NMR spectrum of the trapping experiment product revealed a mixture of cycloadducts **165** in ~5:1 ratio. Diagnostic signals were identified for the major cycloadduct δ 4.05 (br s) for 4-H, δ 4.90 (q, *J* 3 x 2.0 Hz) for 3-H, δ 6.10 (d, *J* 8.6 Hz) for 7-H and δ 6.12 (d, *J* 8.6 Hz) for 6-H and for the minor cycloadduct δ 4.15 (br s) for 4-H, δ 5.60 (d, *J* 8.6 Hz) for 7-H, δ 5.65 (q, *J* 3 x 2.0 Hz) for 3-H, and δ 6.12 (d, *J* 8.6 Hz) for 6-H.

It is evident from the poor yield of the described cycloaddition that several factors may militate against efficient IMDA reactivity. In the first place, deprotonation of the enone **163** may not be adequately regiocontrolled, and may lead to isomerisation in competition with the trapping. Secondly, the intermediate silyl dienyl ether **164** may not be able to withstand the temperature increase associated with *in situ* IMDA reaction. In an attempt to overcome the latter problem, alternative methods of trapping and the use of more hindered silicon reagents were investigated, but without success.

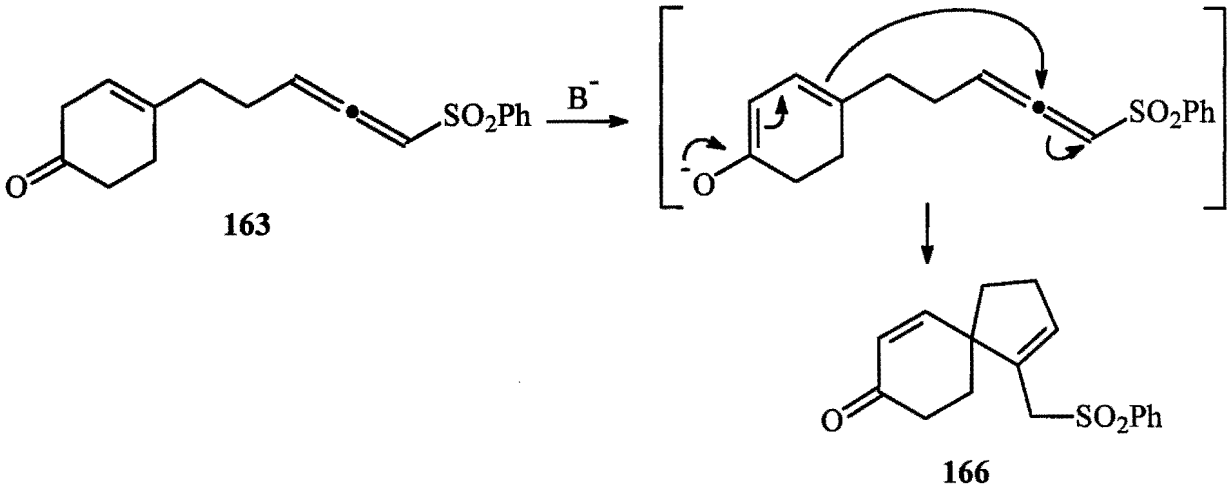
As predicted, treatment of the cycloadduct **165** with potassium hydroxide gave spiro compound **166** in 70 % yield. (Scheme 58).



Scheme 58 *Reagents and conditions*: (i) KOH, THF – H_2O, 25 °C, 70 %

Spectroscopic evidence supports the structural assignment of **166**. The ^1H NMR spectrum displayed signals for the three olefinic protons at δ 6.50 (dd, *J* 10.0 and 1.6 Hz) for 6-H, δ 6.19 (1H, m) for 2-H and δ 5.91 (dd, *J* 10.0 and 0.8 Hz) for 7-H and two protons α- to the phenylsulfonyl group δ 3.68 (dd, *J* 14.4 and 1.2 Hz) and δ 3.77 (dd, *J* 14.4 and 1.6 Hz). IR absorption ν_{max} 1674 cm^{-1} (CO) demonstrated the presence of a conjugated cyclohexenone substructure.

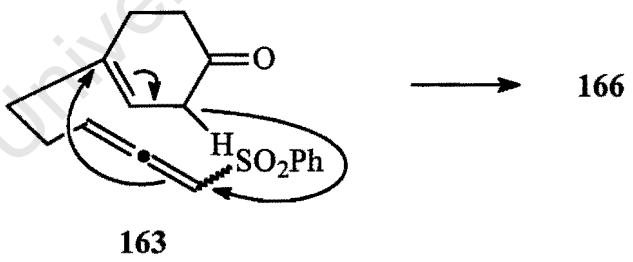
Although the foregoing reaction sequence demonstrated the feasibility of using this reaction pathway to spiro[4,5]decadienyl systems, a minor by-product was detected during the reaction work-up leading to **163**, was identified as **166**. This suggested the synthetic route to **166** could be greatly simplified. Indeed, treatment of **162** in TFA, followed by treatment with aqueous alkali for 1 h gave spiro compound **166** in 85 % yield. The mechanism for this reaction is believed to involve the initial formation of the a dienolate intermediate followed by an intramolecular Michael reaction (Scheme 59).



Scheme 59 Intramolecular Michael reaction resulting in spiro **166**

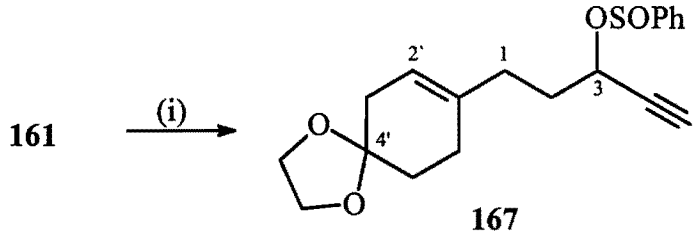
This approach allowed for the synthesis of the spiro compound **166** in high yield, thereby avoiding the troublesome dienolate trapping experiments.

Research conducted, on closely related substructures, by Uguen *et al.*,[135] suggests that an alternative mechanism could be responsible for the formation of **166** owing to an intramolecular *ene* reaction (Scheme 60). This principle was demonstrated was for both phenylsulfonylallenyl and its phenylsulfinylalkynyl ester precursor (with similar results) and was based on the assumption that the [2,3]sigmatropic rearrangement affording the allenyl product preceded the intramolecular ene reaction.



Scheme 60 Proposed ene reaction to form spiro fused ring system

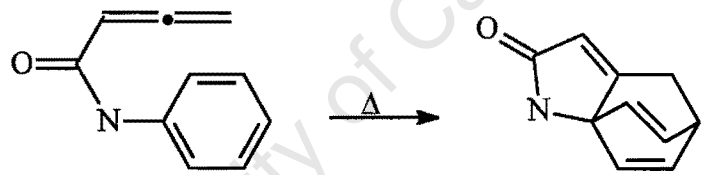
Treatment of alcohol **161** with benzenesulfinyl chloride and triethylamine at low temperature gave a mixture esters **167** in quantitative yield (Scheme 61). The ^{1}H NMR spectrum was of limited used arising from signal duplication, however, both 3-H and 5-H appeared at the expected ranges. Infrared spectroscopy displayed the diagnostic absorption at ν_{max} 3306 (C≡CH) and 1116 cm^{-1} (S=O) in agreement with previously the prepared ester **148**.



Scheme 61 *Reagents and conditions*: (i) PhSOCl, NEt_3, CH_2Cl_2, -78 °C, 99 %

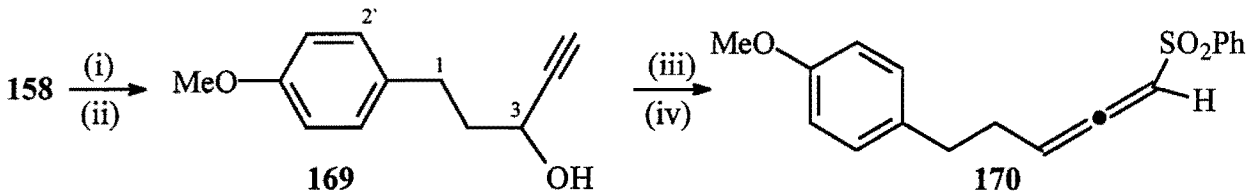
Pilot experiments have proved disappointing as several products are obtained when heating the ester **167** in chlorobenzene. Owing to the success of the intramolecular Michael reaction, this approach was not investigated further. It was interesting that three different reaction pathways could potentially give rise to the desired spiro compound.

4.4.3 4-(5-Phenylsulfonylpenta-3,4-dienyl)anisole Research conducted by Himbert *et al.*,[136] displayed that an IMDA reaction between an aromatic ring (as diene) and an allene , tethered *via* an amide was possible (Scheme 62). This raises the question whether a phenylsulfonylallenyl dienophile can be induced to participate in an IMDA reaction with an aromatic ring.



Scheme 62 Reaction between a terminal allene and an aromatic ring

Dess-Martin oxidation of 3-(4-anisyl)propanol **158** followed by ethynylation, gave alkynol **169** in 49 % yield overall yield (Scheme 63). Standard benzenesulfenyl chloride treatment and subsequent oxidation, gave the corresponding phenylsulfonylallene **170** in 51 % overall yield whose spectroscopic data was as expected. However, compound **170** failed to react at all, even when heated at 200 °C for 24 h.



Scheme 63 *Reagents and conditions*: (i) Periodinane, CH_2Cl_2, 25 °C; (ii) HC≡CMgBr, THF, 25 °C; (iii) PhSCl, NEt_3, -78 °C, 51 %; (iv) *m*-CPBA, CH_2Cl_2, 100 %

4.4.4 Conclusions The synthesis of a series of 1-phenylsulfonyl-1,2,(4+*n*),(6+*n*)-tetraenes has been carried out and their IMDA reactivities have been investigated and the following conclusions can be drawn. The IMDA reaction is dependent on tether length as reaction of **112** (*n* = 4) is slow, and engages the unactivated π-bond, whilst reaction of **129** (*n* = 2) is facile and the reaction is complete under exceptionally mild conditions. Lewis acid catalysis was not investigated.

IMDA reaction of tetraenes **118** (*n* = 3) and **129** (*n* = 2) afforded two cycloadducts in which the major cycloadduct arose from *exo* addition of the dienophile, of which the former was confirmed by x-ray crystal structure. Incorporation of a furanyl ring, as the dienyl moiety, had little effect on IMDA reactivity as reaction was complete within 30 min at 0 °C. IMDA reaction was also observed when substitution was introduced on the dienophile (C-1) or diene (C-6) and displayed the expected attenuation of reactivity. In all systems studied products arising from *exo* addition dominated.

The above findings were extended to the synthesis of spiro-fused compounds *via* an IMDA reaction of oxygen terminated cyclohexadienyl phenysulfonylallene elements followed by Grob fragmentation. This was successfully performed, however, an intramolecular Michael reaction of the allenyl precursor has been shown to be a preferred route.

The foregoing studies have demonstrated the synthetic utility of cycloaddition mediated by a terminal phenylsulfonylallenyl dienophile element, particularly when linked to the diene moiety by a two-carbon tether. It was envisaged that exploitation of an axially chiral dienophilic element would realise the full potential of this method leading to enantiocontrolled synthesis of cycloadducts.

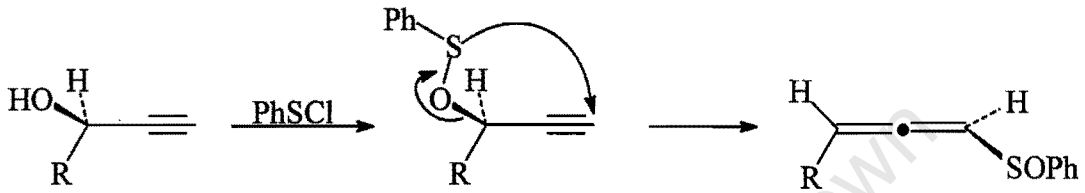
Accordingly, the next strategic objective of this study was to synthesise enantiopure 1-phenylsulfonylallenyl substrates, in order to investigate chirality transfer during cycloaddition. The general methodology for synthesising cycloaddition precursors suggests the obvious expedient of introducing the key stereogenic element at the alkynyl alcohol stage. The alternative approach of resolving the immediate cycloaddition precursors was deemed impractical. The first phase of this investigation was to resolve the respective alkynyl alcohol precursors.

CHAPTER 5

ENANTIOSELECTIVE METHODOLOGY

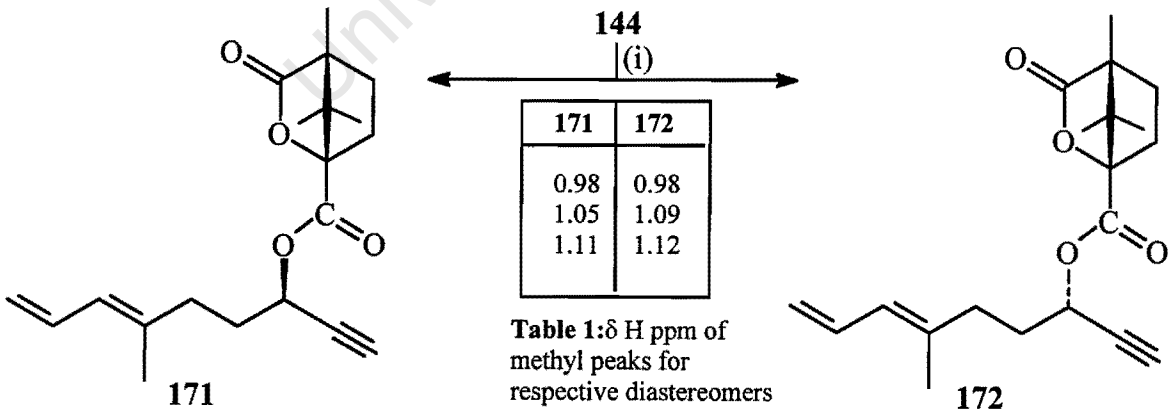
5.1 Resolution of propargylic alcohols

5.1.1 Introduction Resolution of the propargylic precursors would allow for the synthesis of the respective allene enantiomers, as several researchers have demonstrated that the [2,3]sigmatropic rearrangement of phenylsulfenyl esters proceeds with complete retention of configuration (Scheme 1).[70 – 73, 109]



Scheme 1 Transfer of stereochemistry for [2,3]sigmatropic rearrangement

5.1.2 (*R*)- and (*S*)-6-Methylnona-6,8-dien-1-yn-3-ol Treatment of racemic dienyol **144** with (*S*)-camphanic acid, DMAP (catalytic) and DCC gave the expected mixture of diastereomeric esters (see below for configuration assignment). Careful gravity chromatography conducted on silica gel (silica, 200:1) gave partial separation of **171** (41 %) and **172** (39 %) diastereomers, each ~ 95 % pure (Scheme 2) based on the relative integration of the camphanoyl methyl peaks in the respective ^{1}H NMR spectra (see Table 1).

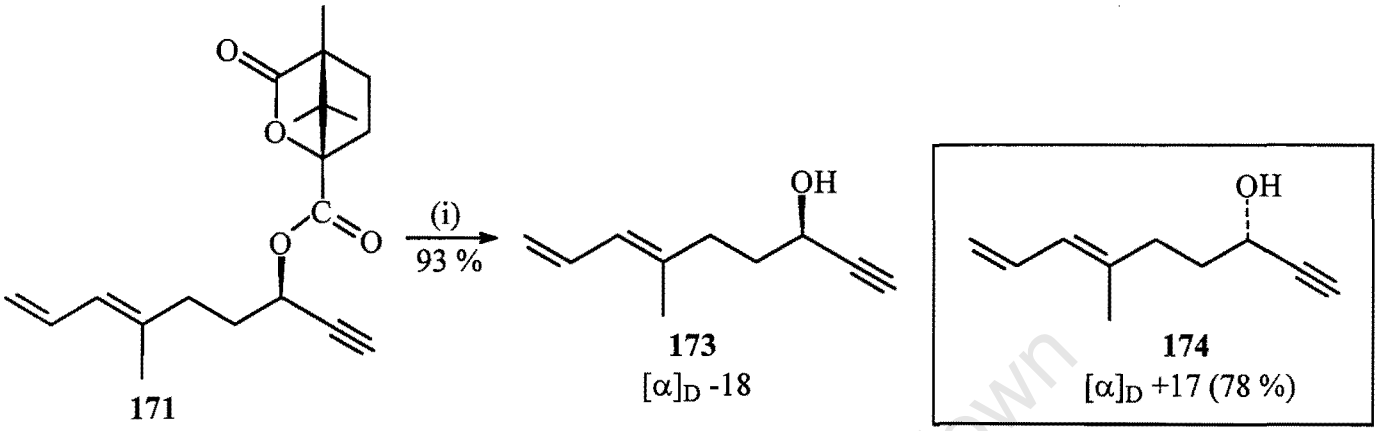


171	172
0.98	0.98
1.05	1.09
1.11	1.12

Table 1: δ H ppm of methyl peaks for respective diastereomers

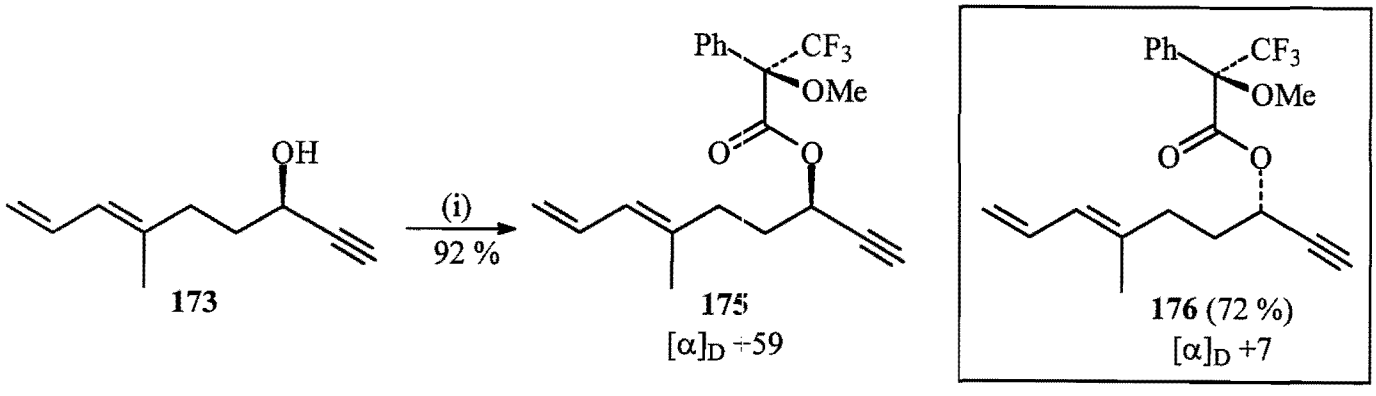
Scheme 2 *Reaction conditions*: (i) (*S*)-Camphanic acid, DCC, DMAP, CH_2Cl_2, 25 °C, 80 %

Comparative reactions were performed using (*R*)-mandelic acid and (+)-camphorsulfonic acid, but the derived esters were inseparable. Accordingly (*S*)-camphanic acid was used for all future resolution experiments. Hydrolysis of the respective diastereomers with aqueous potassium hydroxide gave the corresponding (*R*)- and (*S*)-alcohols **173** and **174** in high optical purity. These were analytically and spectroscopically indistinguishable, but displayed the expected antipodal specific rotations. (Scheme 3).



Scheme 3 *Reaction conditions*: (i) KOH, MeOH – THF – H_2O, 25 °C.

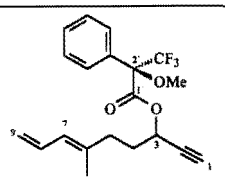
The stereocentre at C-3 was assigned by comparison of the derived Mosher's esters spectroscopic data in conjunction with reported literature.[137, 138] The (*R*)-dienynol **173** was treated with (*R*)-(2-methoxy-2-trifluoromethyl)phenylacetyl chloride (MPTACl) to give the ester **175** in 92 % yield with an *ee* of 95 % (Scheme 4). The identical reaction was carried out with the (*S*)-enantiomer **174** to give the Mosher's ester **176** in 72 % yield, and with an *ee* of 91 %. The reported *ee*'s are inferred from the observed *de*'s from reaction of dienynols **173** and **174** with enantiomerically pure Moshers acid. Hence, the observed *de* is a true reflection of *ee* and is reported as such for all subsequent compounds synthesised.



Scheme 4 *Reaction conditions*: (i) $Ph(F_3C)(MeO)CCOCl$, NEt_3, 25 °C

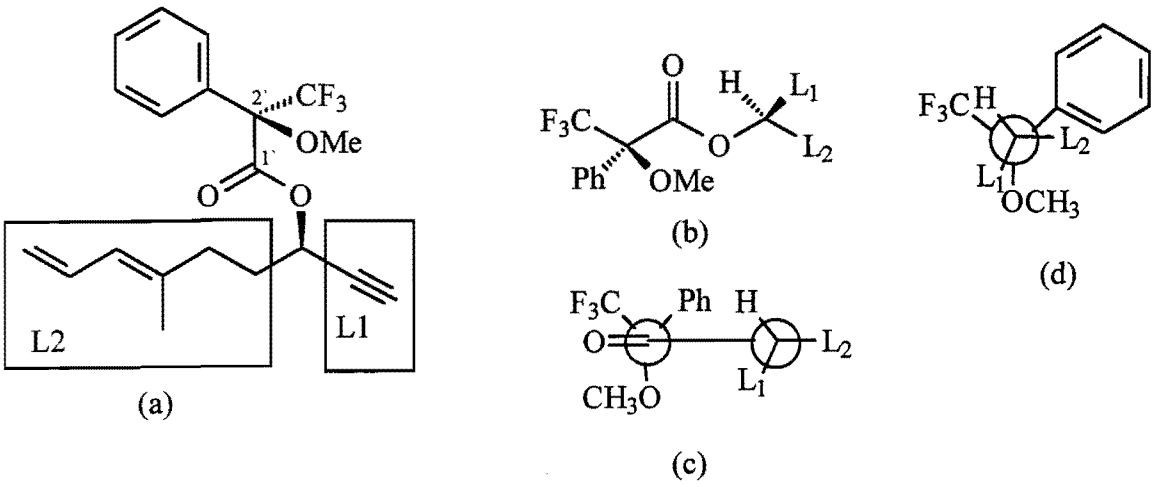
The easiest manner to assign the configuration of C-3 was to compare the relative chemical shifts of the ^1H spectra of the respective Mosher's esters **175** and **176**. These are shown in Table 2, and summarises the chemical shifts of all protons, as well as, the relative difference.

Table 2: Spectroscopic summary of diastereomeric Mosher esters **175** and **176** (Ph excluded)

	**175** δ (ppm)	**176** δ (ppm)	Δδ = δ**175-176**
H-8	6.54	6.57	-0.04
H-7	5.78	5.86	-0.08
H-3	5.52	5.50	0.02
H-9_{trans}	5.10	5.12	-0.02
H-9_{cis}	5.02	5.05	-0.03
Ome	3.60	3.55	0.05
H-1	2.57	2.52	0.05
H-5_2	2.10	2.22	-0.12
H-4_2	1.95	2.03	-0.08
6-Me	1.71	1.76	-0.05

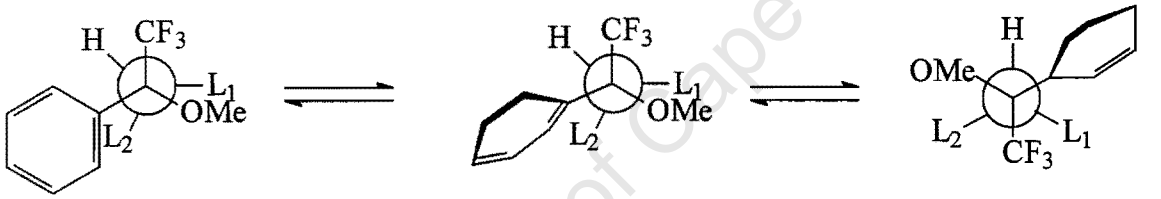
The interpretation of the relationship between the configuration at C-3 and the relative chemical shifts of the diastereomers is based on the assumption that the preferred conformer of each diastereomer locates ligand 3-H gauche to C-1′ (Scheme 5b).[137] Consequently, ligands L_1 (-C≡CH) and L_2 $(CH_2)_2C(CH_3)$=CHCH=CH_2) adopt complementary orientations in the respective diastereomers- *viz.* L_2 is antiperiplanar to CF_3.

The preferred orientation of the C-2′ ligands in the MPTA moiety are assumed to correspond to the lowest energy rotamer, in which the phenyl substituent is spatially proximal to the L_2 in the (3*R*,6*E*) diastereomer **175** and to L_1 in the (3*S*,6*E*) diastereomer **176**. Since this locates the respective ligand in a region perpendicular to the relevant ring plane, it is expected that attached protons should experience relative shielding



Scheme 5 Stereochemical projections of the (3*R*,6*E*) diastereomer **175**.

Some unexpected ^{1}H NMR results for the Mosher ester of alcohols have been reported. A recent computational study [138] displayed that, contrary to the conformational model applied above, three low energy conformations of the esters may exist, each of which having a different shielding effect on L1 or L2. (Scheme 6)



(a) Shielding on L2 (b) Deshielding on L2 (c) Deshielding on L

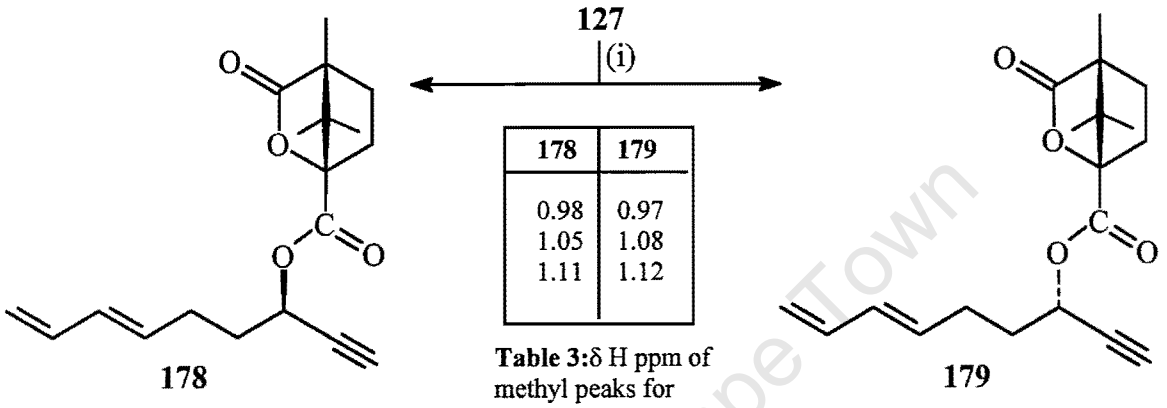
Scheme 6 Low energy rotamers of (*R*)-MTPA esters

The relative populations of each conformer, as well as the degree of shielding or deshielding contribution of each, would have to have been calculated for the ester concerned, before the absolute configuration could be quoted with certainty. It was shown in the same study that (in the case of methoxyphenylactetic acid esters) one conformer was dominant and therefore allowed for a more reliable determination of absolute configuration. Further support of the above was demonstrated by equivalent modeling studies on Mosher amides[138] in which rotamer (6a) was shown to be the lowest in energy, thus also allowing reliable predictions.

The observed small $\Delta\delta$ values could thus be explained by the mutual cancellation of the anisotropic effects on L2 in 6(a) and 6(b) and the fact that the magnitude of deshielding, as provided by 6(c), was usually less than shielding. Therefore, this allowed of the assignment of

(*R*)- and (*S*)-dienynols **173** and **174**. Further discussion and comparison with related alcohols lend further support to these assignments (see later).

5.1.3 (*R*)- and (*S*)-Nona-6,8-dien-1-yn-3-ol Treatment of racemic dienyol **127** with (*S*)-camphanic acid, DMAP (catalytic) and DCC gave the expected mixture of (3*R*,6*E*) **178** and (3*S*,6*E*) **179** diastereomers (see below for configuration assignment). Careful gravity chromatography conducted on silica gel (silica, 200:1) gave partial separation of **178** (26 %) and **179** (12 %) diastereomers each with high optical purity (Scheme 7).



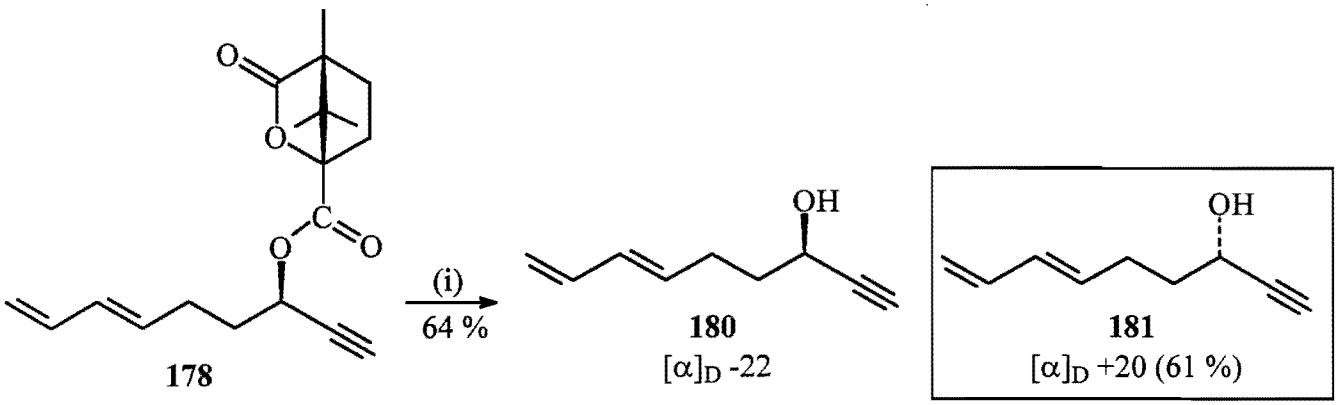
178	179
0.98	0.97
1.05	1.08
1.11	1.12

Table 3: δ H ppm of methyl peaks for respective diastereomers

Scheme 7 *Reaction conditions*: (i) DCC, DMAP, CH_2Cl_2, 25 °C, 90 overall %

The low yields were attributed to the cautious pooling of column fractions in which significant overlap of diastereomers existed. Therefore, only fractions deemed pure were combined and the remaining fractions were pooled and were used separately. Enantiomeric excesses were again based on the integration of the camphanoyl methyl peaks (Table 3).

Hydrolysis of the respective diastereomers with aqueous potassium hydroxide gave the corresponding (*R*)- and (*S*)-dienynols **180** and **181** in high optical purity, which were analytically and spectroscopically indistinguishable, but displayed the expected antipodal specific rotations. (Scheme 8). These dienynols will be discussed later (see below).



Scheme 8 *Reaction conditions*: (i) KOH, MeOH/THF/H_2O, 25 °C; [In this and subsequent Schemes, the enantiomer is illustrated for comparative reference purposes and is supplied without reaction conditions]

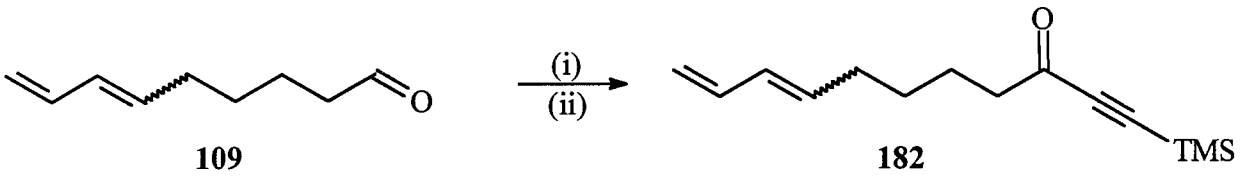
Resolution of alkyl tetraenes containing three- and four-atom tethers failed, as the resulting camphanoyl diastereomers were inseparable. Due to the limited success of the aforementioned results, attention was turned to the asymmetric synthesis of the respective (*R*)- and (*S*)-alkynol precursors.

5.2 Asymmetric synthesis of unbranched aliphatic 1-phenylsulfonylalka-1,2,(*n* + 4),(*n* + 6)-tetraenes

5.2.1 Introduction An alternative approach to securing enantiopure dienynol precursors for the synthesis of the corresponding enantiopure 1-phenylsulfonylallenyl IMDA precursors, entail reaction of prochiral dienynones with chiral reducing reagents. This was reasoned to be the most practical method of obtaining the alkynols in high optical purity.

Several reagents are known to perform such a transformation. Examples include Brown's β-chlorodiisopinocamphenylborane,[139] Corey's oxazaborolidene (CBS) reagents,[140] Noyori's transfer hydrogenation catalysts [141] and binapthol-modified lithium aluminum hydride reagents.[142] In this investigation, Midland's Alpine-Borane®,[143] was chosen as it is readily prepared in both enantiomeric forms.

5.2.2 (*M*)- and (*P*)-1-Phenylsulfonylundeca-1,2,8,10-tetraene Treatment of aldehyde **109** (*E*/*Z* 3:1 by NMR[1]) with the trimethylsilylacetylene anion [generated by adding *n*-BuLi to a THF solution of TMS-acetylene at room temperature] gave the corresponding dienynol, which was oxidised with Dess-Martin periodinane to yield the dienynone **182** in 54 % yield over the two steps (Scheme 9).

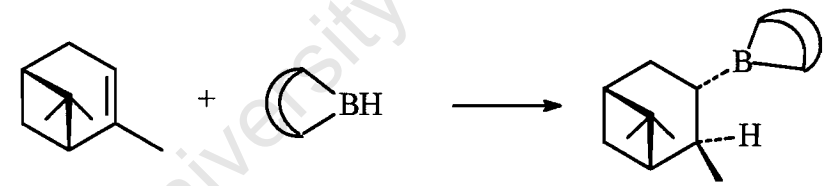


109 **182**

Scheme 9 *Reaction conditions*: (i) TMSC≡CH, *n*-BuLi, THF, 25 °C; (ii) Periodinane, CH_2Cl_2, 25 °C, 54 %

The ^{1}H NMR spectrum of **182** displayed a signal at δ 0.24 (9H,s) for $SiMe_3$ whereas the IR spectrum displayed absorption ν_{max} 2150 (C≡CR) and 1669 (CO) cm^{-1}. It was important to use controlled equivalents of ethereal HCl to quench the reaction, as desilylation occurred if a significant excess of acid (or aqueous ammonium chloride) was present.

Reduction of the ynone **182** with (*R*)-Alpine-Borane, prepared *in situ* (Scheme 10), gave the (*R*)-ynol **183** in 69 % yield (Scheme 11). The analogous reduction was carried out with (*S*)-Alpine-Borane, prepared *in situ*, to give the (*S*)-ynol **185** in 63 % yield.

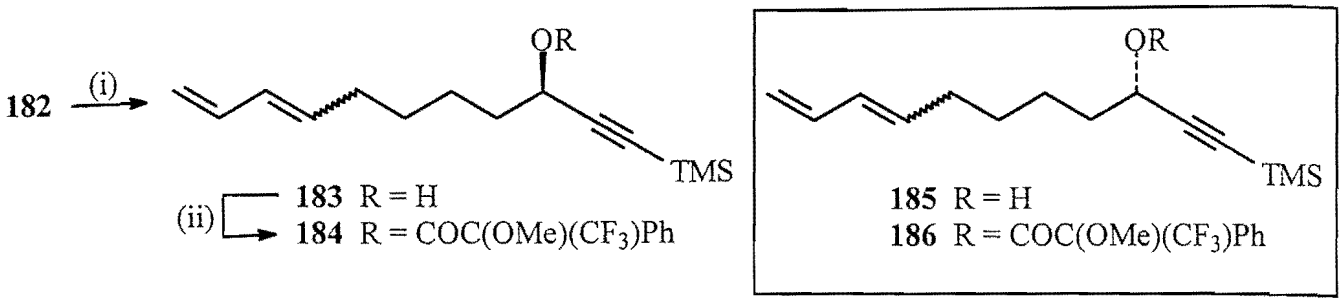


(+)-α-pinene

Scheme 10 Formation of (*R*)-Alpine-Borane

Treatment of ynol **182** with Mosher's acid, DCC, DMAP gave the corresponding ester **184** in 87 % yield and an *ee* of 96 % based of ^{19}F NMR. This method of *ee* determination was the method of choice as no signal overlap or intensity stealing was encountered - a feature often encoutered with ^{1}H NMR spectroscopy which makes this method of accurate *ee* determination unreliable.

[1] For the purpose of this model study, the *E*/*Z* ratio was not considered important since it was not planned to demonstrate enantiocontrolled IMDA reactivity with this substrate.



Scheme 11 *Reaction conditions*: (i) 9-BBN, (+)-α-Pinene, THF, 25 °C, 69 %; (ii) $Ph(F_3C)(MeO)CCO_2H$, DCC, DMAP, CH_2Cl_2, 25 °C, 87 %

The high *ee*'s for the reduction were largely due to statistical reasons as a twofold excess of reagent (which itself had an *ee* of ~ 91 %) was used. Best *ee*'s were achieved when stirring the ketone in neat solutions of reagent which generally required 16 h for complete reaction.[143] Commercially available Alpine-Borane® (available as a 0.5M solution in THF) was too dilute and resulted in significantly longer reaction times being required (*viz.* 72 h).

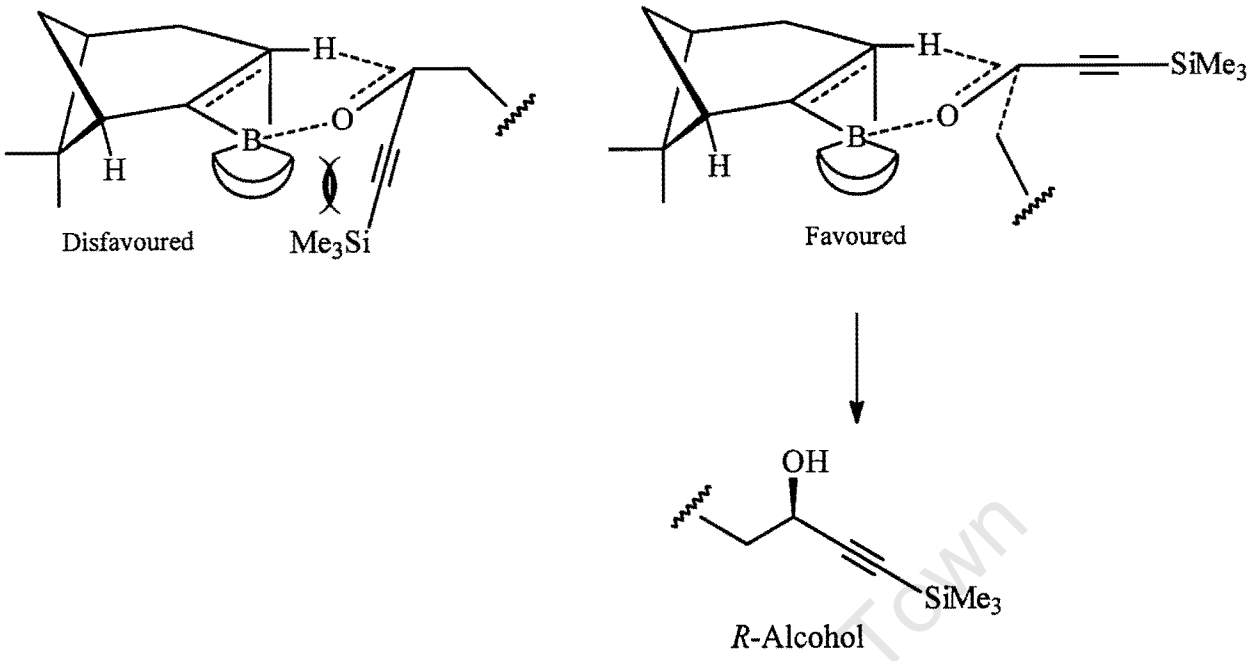
Mosher ester formation was carried out on compound **185** to give diastereomer **186** in 93 % yield and an *ee* of 96 % (^{19}F NMR, δ 80.3) whose results are summarised in Table 4. The choice of TMS protected acetylene was based on literature precedent[144, 145] - pilot experiments carried out on unsubstituted acetylenic ketones gave low *ee*'s (see later for example).

Table 4: Summary of reaction yields, optical rotations and ^{19}F NMR of (*R*)- and (*S*)-dienynols and their corresponding Mosher ester derivatives

Compound	Yield %	$[\alpha]_D$	ΔF^{19}	*ee/de* %
183	69	-3.4°		
185	63	+3.8°		
184	87	+46.4°	80.7	96
186	93	-4.9°	80.3	96

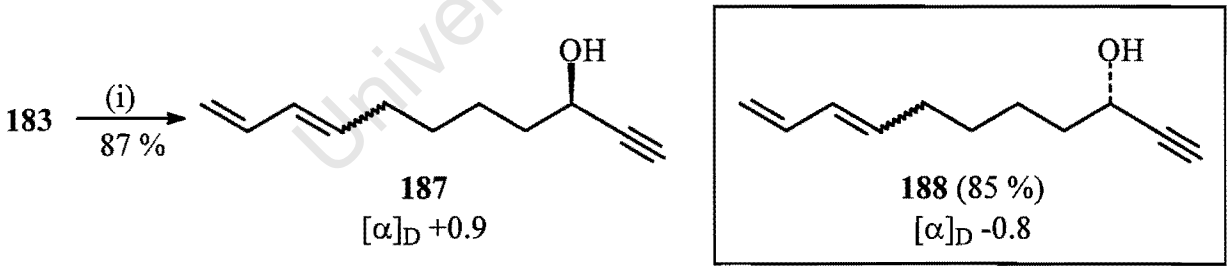
Midland[143] has postulated that the transition state responsible for the stereocontrol resembles a boat-like cyclohexane structure, in which the largest substituent faces away from the methyl group (β to the BBN moiety) and the BBN moiety (Scheme 12). This mechanism was based on experimental observations and was further supported by *ab initio* calculations.[143] Therefore reduction of the ketone **181** with (*R*)-Alpine-Borane gave the (*R*)-alcohol **182** in accordance with

literature precedent.[143,144] (and subsequently confirmed by comparison to known compounds– see later)



Scheme 12 Boat-like transition state of (*R*)-Alpine-Borane reduction to give (*R*)-dienynol

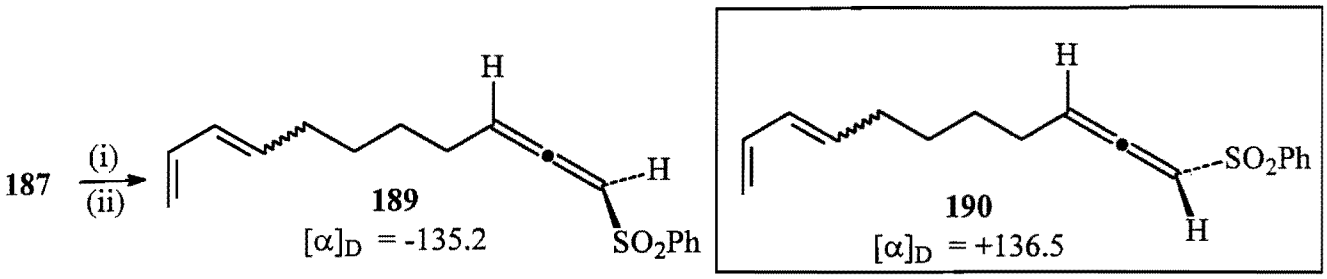
Desilylation of acetylenic compound **183** with methanolic potassium carbonate gave the (*R*)-dienynol **187** in 87 % yield (Scheme 13). The analogous reaction was carried out on the other enantiomer to give the (*S*)-ynol **188** in 85 % yield.



Scheme 13 *Reaction conditions*: (i) K_2CO_3, MeOH, 25 °C, 87 %;

Treatment of the (*R*)-dienynol **187** with benzenesulfenyl chloride in the presence of triethylamine, at low temperature, followed by oxidation with *m*-CPBA gave the (*M*)-phenylsulfonylallene **189** in 34 % overall yield (Scheme 14) whose spectroscopic properties was identical to tetraene **112**. The analogous reactions were carried out for the (*S*)- enantiomer to give (*P*)-phenylsulfonylallene **190** in 27 % overall yield. The alcohol – sulfenate ester rearrangement of the enantiopure alcohols proceeds without stereocontrol at the S-O bond, to give a

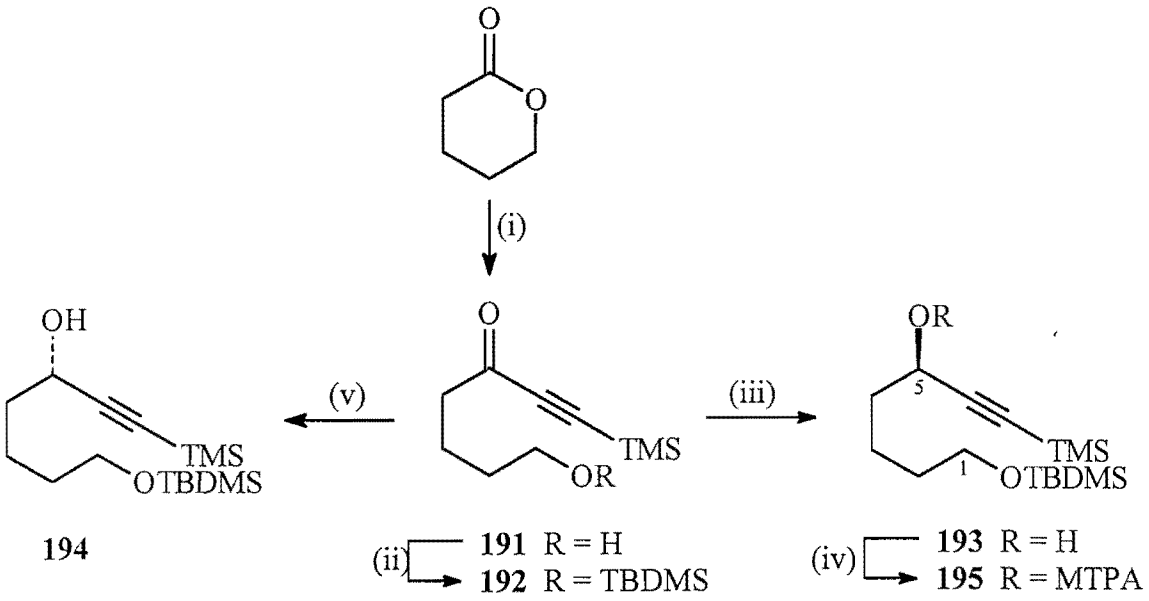
diastereomeric mixture (~3:2) of sulfoxides, however, subsequent oxidation to the sulfone is convergent.



Scheme 14 *Reaction conditions*: (i) PhSCl, NEt_3, CH_2Cl_2 , -78 °C; (ii) *m*-CPBA, CH_2Cl_2 , 25 °C, 34 %

These experiments have demonstrated the synthesis of (*M*)- and (*P*)-phenylsulfonylallene enantiomers **189** and **190**. With the asymmetric methodology in place, attention was turned to the synthesis of the analogous tetraenes linked *via* three- and two-carbon tethers.

5.2.3 (*M*)- and (*P*)-1-Phenylsulfonyldeca-1,2,7,9-tetraene Overman *et al.*,[145] has reported the synthesis of **194** *via* treatment of δ-valerolactone with TMS acetylene and *n*-BuLi at low temperature to give hydroxy-ynone **191**, which was protected as a *t*-butyldimethylsilyl ether. The resulting silyloxyketone **192** was reduced with (*S*)-Alpine Borane, prepared *in situ*, to give the (*S*)-alcohol **194**. We repeated this sequence and applied the procedure to synthesise the opposite (*R*)-enantiomer **193** (Table 5). Mosher ester formation of the alkynol **193** was carried out, to give the (5*R*)- diastereomer **195** in 79 % (*ee* 95 % by ^{19}F NMR, δ 80.8), whose enantiomeric purity compared favourably with that reported by Overman.[145]

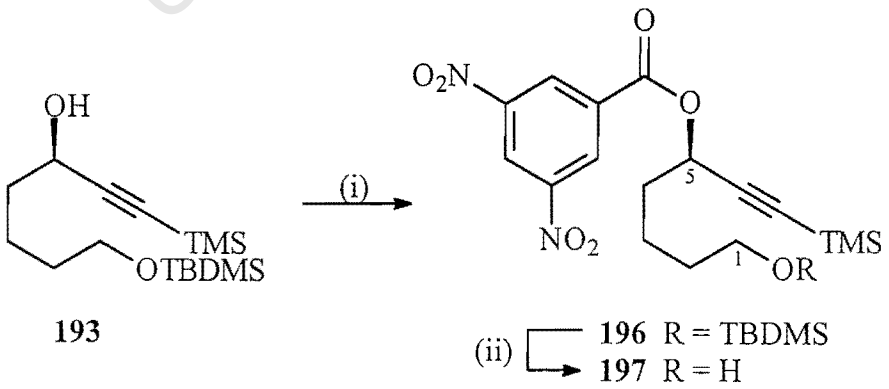


Scheme 15 *Reaction conditions*: (i) TMSCCH, *n*-BuLi, THF , -78 °C; (ii) TBDMSCl, imidazole, CH_2Cl_2 , 25 °C; (iii) 9-BBN, (+)-α-Pinene, 87 %; (iv) $Ph(F_3C)(MeO)CCO_2H$, DCC, DMAP, 79 %; (v) 9-BBN, (-)-α-Pinene, 87 %;

Table 5: Specific rotations of (*R*)- and (*S*)-alkynols **193** and **194**

	193	**194**
$[\alpha]_D$	-0.5	+0.6
ee %	95 (based on ^{19}F of **195**)	95 (by analogy to ref)[145]

Protection of the (*R*)-alcohol **193** as a 3,5-dinitrobenzoyl ester **196** in 80 % was achieved *via* a coupling reaction of the alcohol **193** and 3,5-dinitrobenzoic acid, facilitated by DCC (Scheme 16). Deprotection of the primary hydroxy group with pyridinium *p*-toluenesulfonate (PPTS)[146] gave the alcohol **197** in good yield.

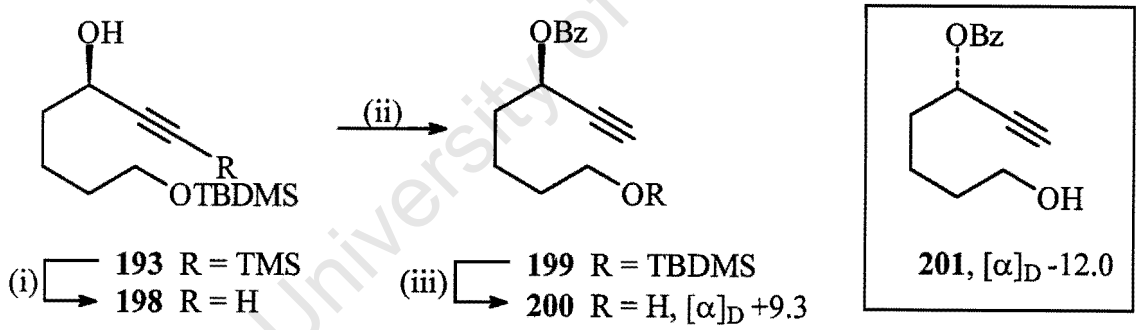


Scheme 16 *Reaction conditions*: (i) $(NO_2)_2C_6H_3CO_2H$, DCC, DMAP , 25 °C, 80 %; (ii) PPTS, MeOH , 25 °C, 90 %

Compound **197** was crystalline (hence the choice of protecting group) and repeated recrystallisation gave the enantiopure alcohol. The ^{1}H NMR spectrum displayed a signal at δ 5.72 (t, *J* 2 x 6.6 Hz) for 5-H whereas the IR spectrum displayed absorption at ν_{max} 3619 (OH), 2178 (C≡CR), 1734 (CO), 1549 and 1345 (NO) cm^{-1}. The mass spectrum of **197** was obtained using FAB techniques, and required the addition of RbI to visualise the molecular ion. Hence, a molecular ion at 479 was observed corresponding to a M+Rb.

Dess-Martin oxidation of **197** gave the corresponding aldehyde, which failed to undergo Wittig reaction with allytriphenylphosphonate. The possibility that the nitro groups were reagent incompatible was explored and confirmed by the unsuccessful reaction of the corresponding *p*-nirtobenzoyl ester. In addition, it was thought that the silyl group was too unstable to withstand the relatively aggressive Wittig reaction conditions.

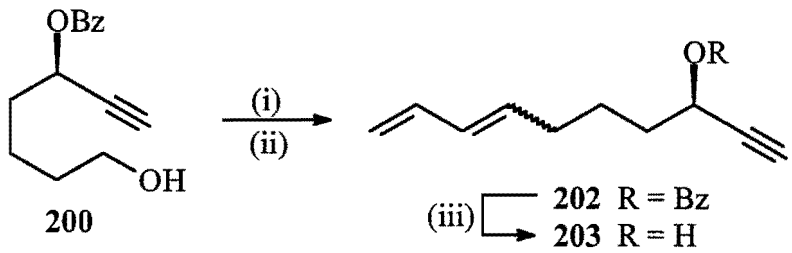
Therefore, (*R*)-ynol **193** was desilylated with aqueous potassium carbonate to yield the terminal acetylene moiety **198** (Scheme 17) which was confirmed by the ^{1}H NMR spectrum which displayed the appearance of the characteristic acetylenic signal at δ 2.44 (d, *J* 2.0 Hz). The IR spectrum displayed absorption ν_{max} 3306 (C≡CH) and 3617 cm^{-1} (OH).



Scheme 17 *Reaction conditions*: (i) K_2CO_3, MeOH; (ii) BzCl, pyridine, 25 °C; (iii) PPTS, MeOH , 25 °C, 68 %

Protection of the secondary alcohol as a benzoyl ester (to give compound **199**), followed by deprotection of the primary alcohol with PPTS, gave the ynol **200** in 68 % overall yield. The ^{1}H NMR spectrum displayed signals at δ 2.50 (d, *J* 2.1 Hz) for 7-H and δ 5.60 (td, *J* 6.6 and 2.1Hz) for 5-H. while the IR spectrum displayed absorption at ν_{max} 1718 (CO), 3306 (C≡CH) and 3625 (OH) cm^{-1}. The series of reactions was also carried out on the (*S*)-enantiomer to give the (*S*)-ynol **201** in 74 % overall yield.

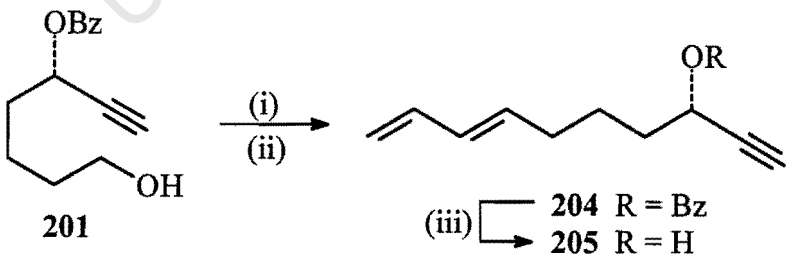
Dess-Martin oxidation of alcohol **200** afforded the aldehyde in 97 % (Scheme 18) which was treated directly with allyltriphenylphosphonate to give a mixture of (*E*/*Z*) dienes **202** (3:2 by NMR) in 40 % yield. Hydrolysis of the ester with sodium hydoxide gave the (*R*)-dienol **203** in 100 % yield, whose spectroscopic properties were analogous to compound **116**.



Scheme 18 *Reaction conditions*: (i) Periodinane, CH_2Cl_2, 25 °C, 97 %; (ii) $Ph_3P^-CH_2CH{=}CH_2\ Br^+$, *n*-BuLi, 25 °C, 40 %; (iii) NaOH, THF/MeOH/H_2O , 25 °C, 100 %

In view of the limited material available, it was decided not to attempt to improve the (*E*/*Z*) ratio through isomerisation, since it was expected that the derived (*Z*)-dienyl substrate would remain unreactive under thermal IMDA conditions

Similarly, the (*S*)-enantiomer **201** was subjected to Dess-Martin oxidation to afford the corresponding aldehyde in 93 % yield (Scheme 19) which was in turn subjected to a Horner-Wittig reaction with allyldiphenylphospine oxide,[147] in the presence of *n*-BuLi and freshly distilled HMPA at low temperature. Hydrolysis of the ester with NaOH gave the (*S*)-dienol **205** in 63 % overall yield (86 % *E* by NMR). Spectroscopic and analytical data were identical to compound **116**.

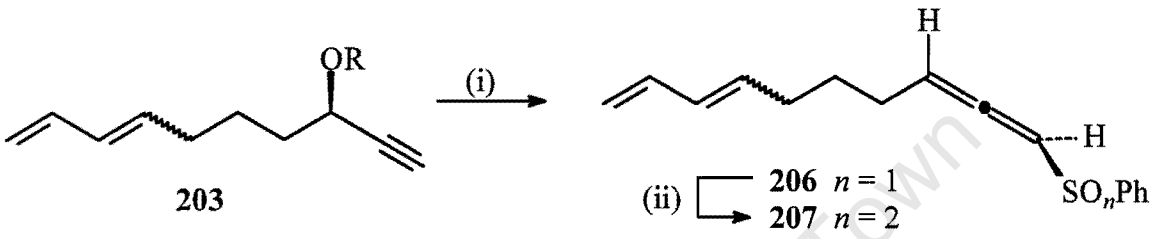


Scheme 19 *Reaction conditions*: (i) Periodinane, CH_2Cl_2, 25 °C, 93 %; (ii) $Ph_2POCH_2CH{=}CH_2$, *n*-BuLi, HMPA, -78 → 25 °C; (iii) NaOH, THF/MeOH/H_2O , 25 °C, 63 %

The Horner-Wittig reaction was extremely useful as the diene could be directly synthesised in a high (*E*/*Z*) ratio, without the need for subsequent isomerisation. Although the use of HMPA was

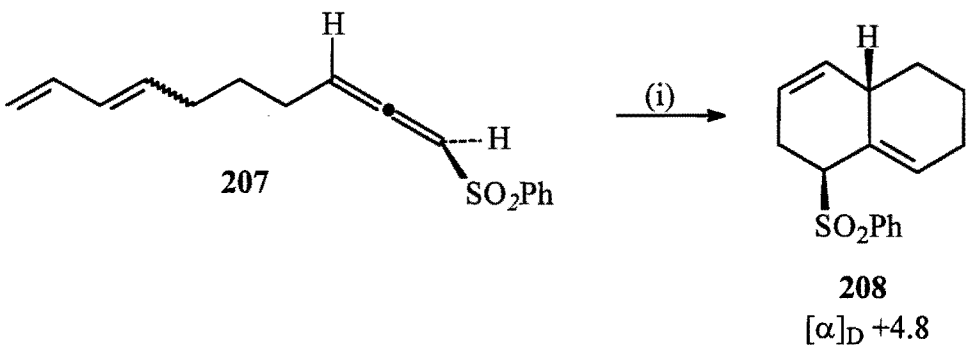
undesirable, it was unavoidable for reactions of this type, as it facilitated the final elimination of the phosphinate by-product

Low temperature treatment of (*R*)-dienynol **203** with benzenesulfenyl chloride gave a mixture of (*M*)-phenylsulfinyl allenes **206** (47 %) which was oxidised with *m*-CPBA to give the (*M*)-phenylsulfonylallene **207** (40 %) (the *ee* of the allene is assumed to be 95 % based on the *ee* of dienynol precursor **203**, Scheme 20). Spectroscopic and analytical properties were identical to tetraene **118**. The relatively low yields of these reactions are due to lack of material (only conducted once), and are hence, unoptimised.



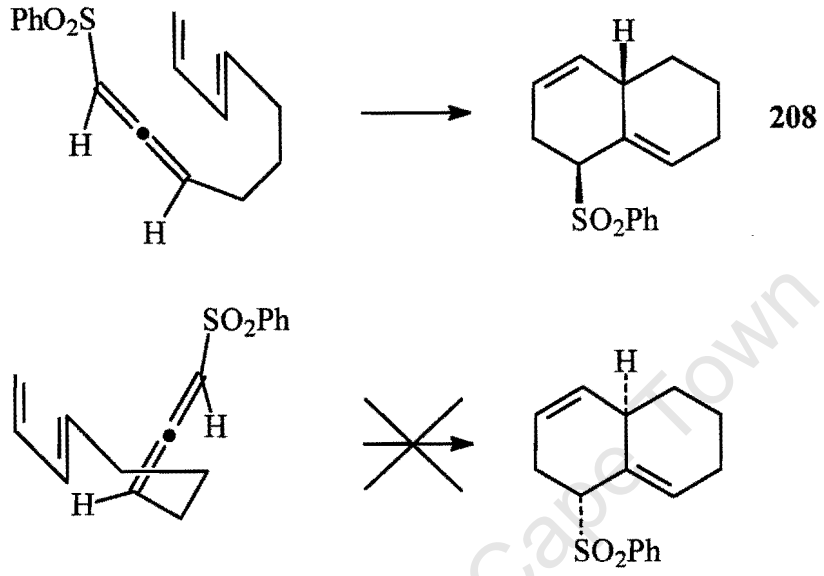
Scheme 20 *Reaction conditions*: (i) PhSCl, NEt_3, CH_2Cl_2, -78 °C, 47 %; (ii) *m*-CPBA, CH_2Cl_2, 25 °C, 40 %

The (*M*)-phenylsulfonylallene compound **207** was heated at 110 °C for 16 h to give the *exo* cycloadduct **208** in 25 % yield (*i.e.* ~45 % based on original 3:2 (*E*/*Z*) diene mixture, Scheme 21) in favourable comparison with the results observed for the racemic tetraene. Also isolated was the unreacted (*Z*)-diene in 31 % yield (~ 75 %). Coloration of the reaction mixture indicated that polymerisation/decomposition of the tetraene was occurring and may account for the relatively low yield obtained. There was insufficient material to isolate the minor cycloadduct.



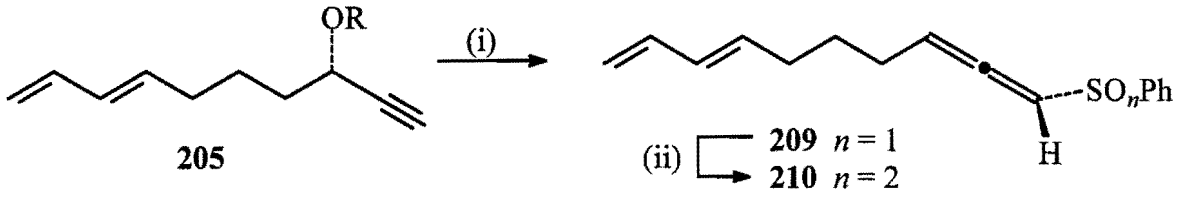
Scheme 21 *Reaction conditions*: (i) $CH_3C_6H_5$, 110 °C, 15 %

Assignment of stereochemistry of the cycloadduct was determined from first principles. When the two possible *exo* transition states (Scheme 22) are examined, only one can allow for close interaction of the reacting orbitals, as the tether is too short to facilitate *exo*-addition on the opposite face. Therefore, it can be concluded that the IMDA reaction mediated by an *exo* transition state of (*M*)-allenyldiene **207** gave rise to cycloadduct **208**, as examination of the corresponding transition state suggests a high degree of chirality transfer (see below).



Scheme 22 *Exo* transition states of (*M*)-phenylsulfonylallene tetraene **207**.

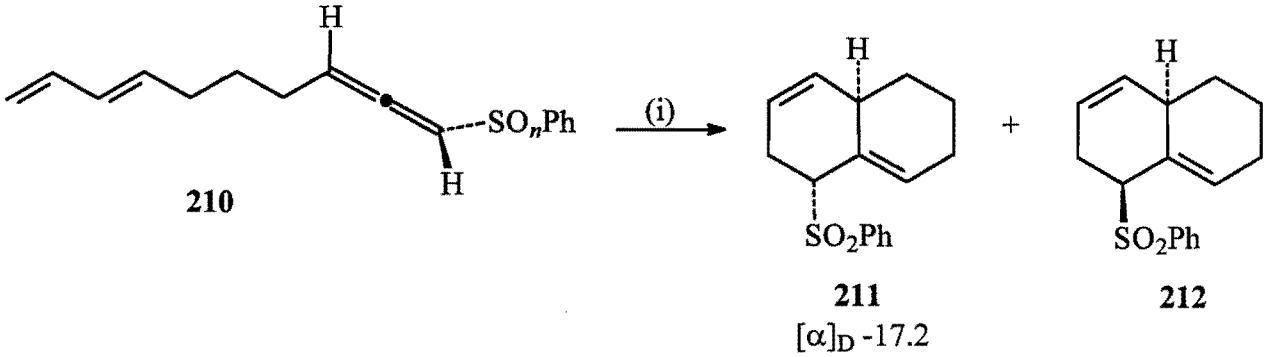
Treatment of the (*S*)-dienol **205** with benzenesulfenyl chloride at low temperature gave a mixture of (*P*)-phenylsulfinylallenyl diastereomers **209** in 44 % yield (Scheme 23) which was oxidised with *m*-CPBA to give the (*P*)-phenylsulfonylallenene **210** in 58 % yield. As in the case of the (*M*)-enantiomer, there was insufficient material to optimise these reactions.



Scheme 23 *Reaction conditions*: (i) PhSCl, NEt_3, CH_2Cl_2, -78 °C, 44 %; (ii) *m*-CPBA, CH_2Cl_2, 25 °C, 58 %

The allene **210** was dissolved in toluene and the solution was heated at 110 °C for 16 h to give a mixture of two cycloadducts. Chromatography gave the *exo* cycloadduct **211** in 52 % yield (Scheme 24) which was assigned *via* analogy to previous results. Recrystallisation allowed for

the isolation of **211** in high optical purity. This was followed by a mixture of the *endo* cycloadduct **212** and **211** (~20% by NMR). Analytical and spectroscopic data of **211** were identical to **120**.

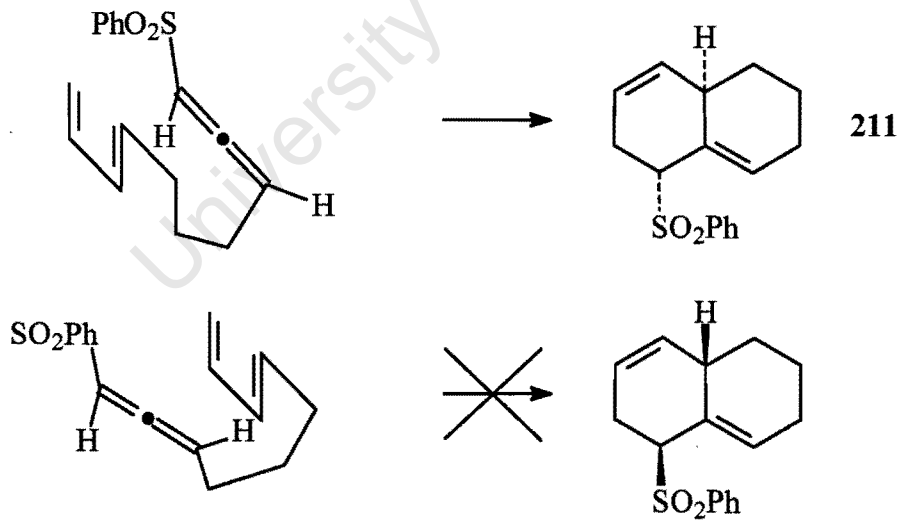


210 **211** **212**

$[\alpha]_D$ -17.2

Scheme 24 *Reaction conditions*: (i) $CH_3C_6H_5$, 110 °C, 93 %

(*P*)-Phenylsulfonylallenyl compound **210** gave rise to cycloadduct **211** *via exo* addition of the dienophile. By analogy to the previous example, this result is rationalised by examining the corresponding transition states of which only one is able to achieve orbital alignment owing to the rotational constraint imposed by the allene (Scheme 25). This therefore suggests a high degree of chirality transfer. Experiments involving gas chromatographic separation, on chiral stationary phases, of cycloadducts **208** and **211** is currently in progress and will allow for a quantitative evaluation of the above findings

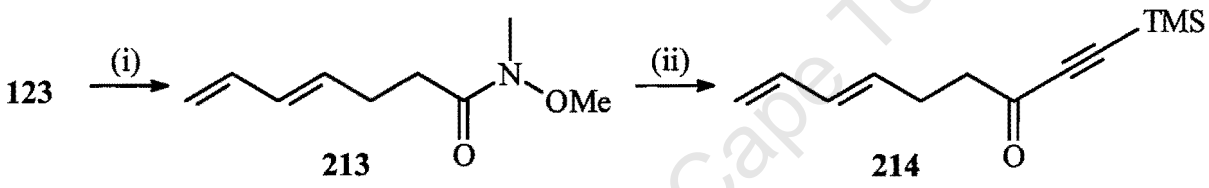


Scheme 25 *Exo*-transition states for the (*P*)-phenylsulfonylallenyl **210** leading to enantiomer **211**.

A comparison of the results obtained for the above IMDA reactions involving optically active allenes **207** and **210**, demonstrates the synthetic power of this approach. It now remains to conduct an analogous study of tetraenes possessing a two-carbon tether.

5.2.4 (*M*)- and (*P*)-1-Phenylsulfonylnona-1,2,6,8-tetraene The synthesis of the (*R*)- and (*S*)-dienynol precursors was initially based on the previously investigated approach involving a capricious Claisen-rearrangement – reduction – oxidation sequence. It was believed that formation of an amide, directly from the ester **123**, followed by ethynylation would offer a significant advantage over the previous route. The removal of one reaction step in the sequence and the prevention of handling volatile aldehyde **124a** was significant reason to investigate this alternate approach.

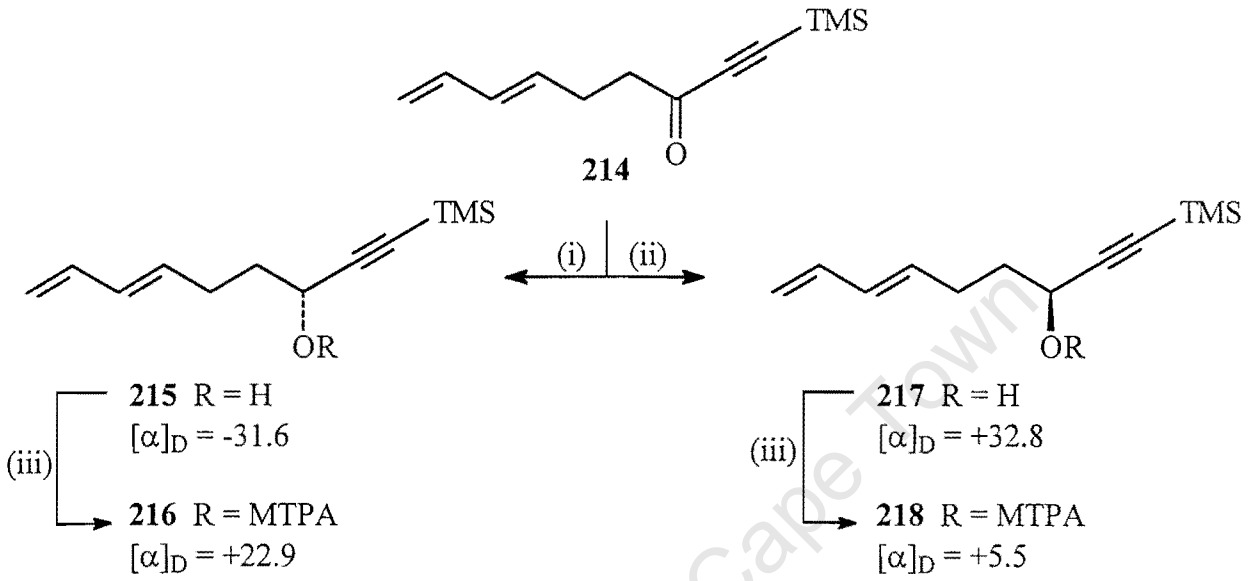
With this in mind, dimethylaluminum chloride was added to a solution of *N*-methyl-*N*-methoxy-ammonium chloride at 0 °C, followed by dienoate ester **123** to give Weinreb amide **213** in 78 % yield (Scheme 26).[148] The use of dimethylaluminium chloride was based on the modified approach of Nakata *et al.*,[149] who observed that the original Weinreb conditions (Me_3Al-MeONH.HCl) often gave unsatisfactory results.



Scheme 26 *Reaction conditions*: (i) (MeO)(Me)NH.HCl, Me_2AlCl, 0 °C, 78 %; (ii) $Me_3SiC{\equiv}CH$, *n*-BuLi, THF , 0 °C, 61 %

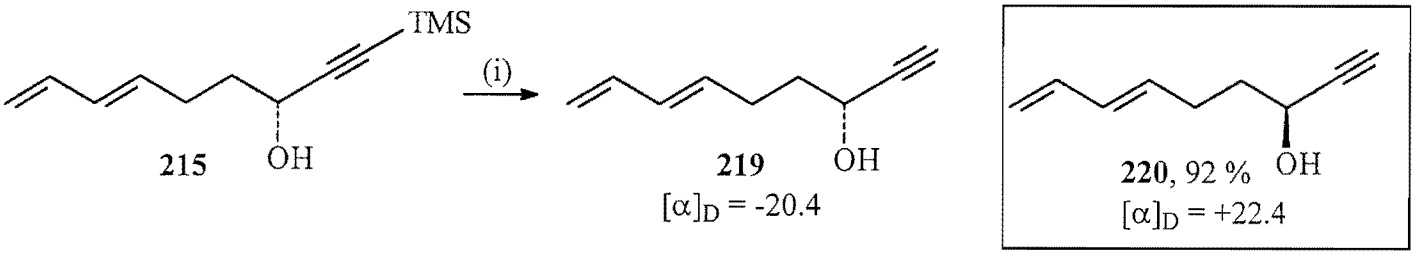
The ^1H NMR spectrum of **213** displayed singlets at δ 3.17 and 3.67 for Me and OMe respectively whereas the IR spectrum displayed absorption at ν_{max} 1648 cm^{-1} (CO).[150] Treatment of amide **213** with the anion generated from TMS-acetylene [generated using *n*-BuLi] at 0 °C gave the ynone **214** in 61 %. Spectroscopic properties were in accordance with previously prepared compounds.

Reduction of the ynone **214** with (*R*)-Alpine-Borane, prepared *in situ*, gave the (*R*)-ynol **215** in 83 % yield (Scheme 27). Treatment of the ynol **215** with Moshers' acid, DMAP and DCC gave the corresponding Moshers' ester **216** in 99 % yield and an *ee* of 94 % (by ^{19}F NMR, δ 80.7). Reduction of the ynone **214** with (*S*)-Alpine-Borane, prepared *in situ*, gave the (*S*)-alkynol **217** in 86 % yield. Formation of the Moshers' ester was carried out as before to yield **218** in 93 % yield and an *ee* of 93 % (^{19}F NMR, δ 80.3). Spectroscopic data were in accordance with those of previously synthesised alkynols.



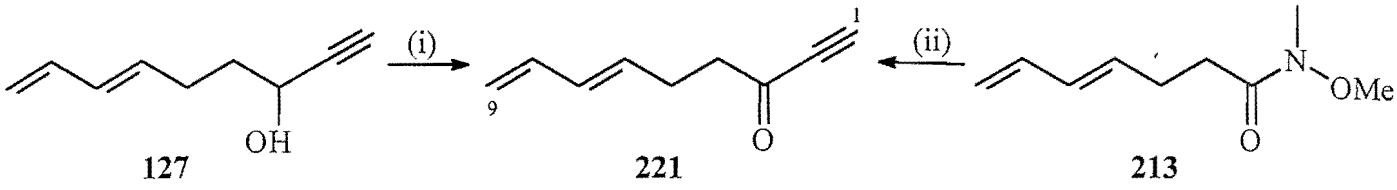
Scheme 27 *Reaction conditions*: (i) 9-BBN, (+)-α-Pinene, 25 °C, 89 %; (ii) 9-BBN, (-)-α-Pinene, 25 °C, 86 %; (iii) $Ph(F_3C)(MeO)CCO_2H$, DCC, DMAP, 25 °C, 99 %

Desilylation of (*R*)-alcohol **215** with methanolic potassium carbonate, as carried out before, gave the dienynol **219** in 91 % yield (Scheme 28). The identical reaction was carried out for the opposite enantiomer to give the (*S*)-dienynol **220** in 92 % yield. Spectroscopic and analytical data were identical to those observed previously. These findings were in agreement with the results of resolution experiments on racemic compound **127**, as the corresponding specific rotations were in close agreement.



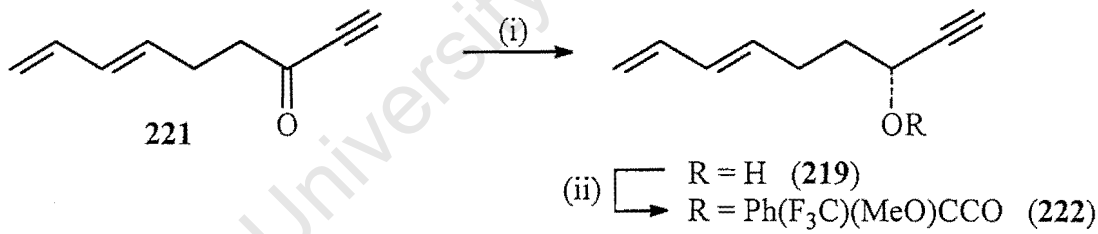
Scheme 28 *Reaction conditions*: (i) K_2CO_3, MeOH, 25 °C, 93 %;

The foregoing procedure could correspondingly be shortened by avoiding the use of the trimethylsilyl terminated intermediates. Accordingly, the dienynone **221** was prepared by Dess-Martin oxidation of racemic ynol **128**, or by ethynylation of Weinreb amide **213** (Scheme 29, unoptimised). Spectroscopic data were in accordance with expected values



Scheme 29 *Reaction conditions*: (i) Periodinane, CH_2Cl_2, 25 °C, 71 %; (ii) HCCMgBr, THF, 25 °C, 29 %

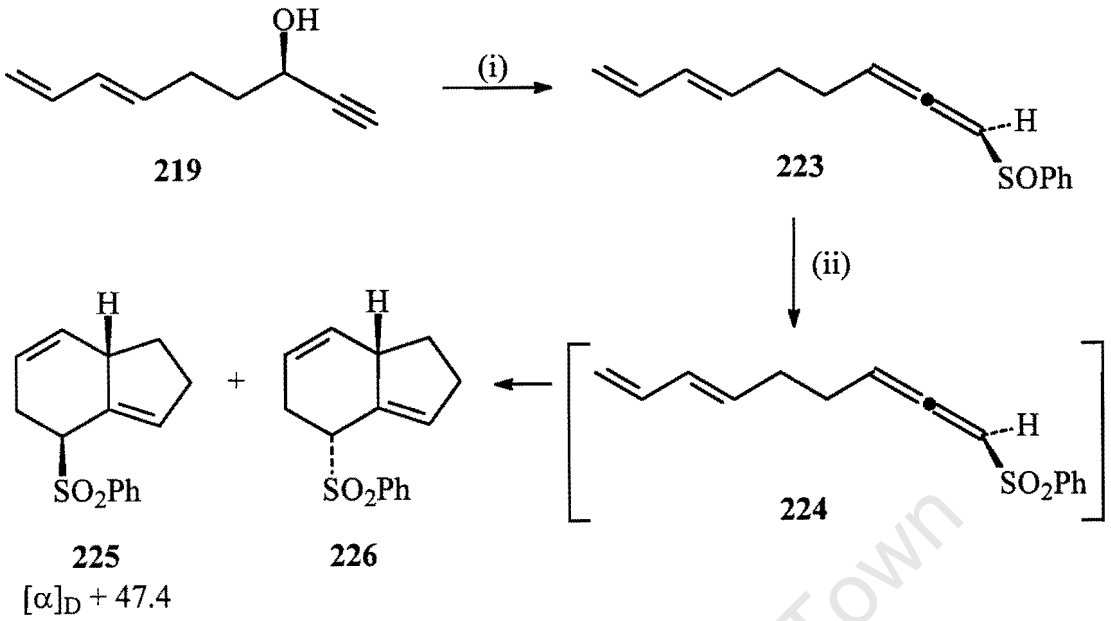
Reduction of dienynone **221** with (*R*)-Alpine-Borane, prepared *in situ*, gave the (*R*)-dienynol **215** in 88 % yield (Scheme 30). This was converted to the corresponding Moshers' ester **216** in 39 % yield and a low *ee* (~33 % by ^{19}F NMR). These results clearly illustrate the influence of the TMS group, as reductions carried out in its presence typically display *ee*'s greater than 90 %. As a result of this finding, all asymmetric reductions carried out involved the incorporation of the TMS group. The analogous reduction of **221** was also carried out with binaphthol-modified lithium aluminum hydride, previously resolved using *N*-benzylcinchonidinium chloride, with similar results.[142,151]



Scheme 30 *Reaction conditions*: (i) 9-BBN, (+)-α-Pinene, 25 °C, 88 %; (ii) $Ph(F_3C)(MeO)CCO_2H$, DCC, DMAP, 25 °C, 39 %

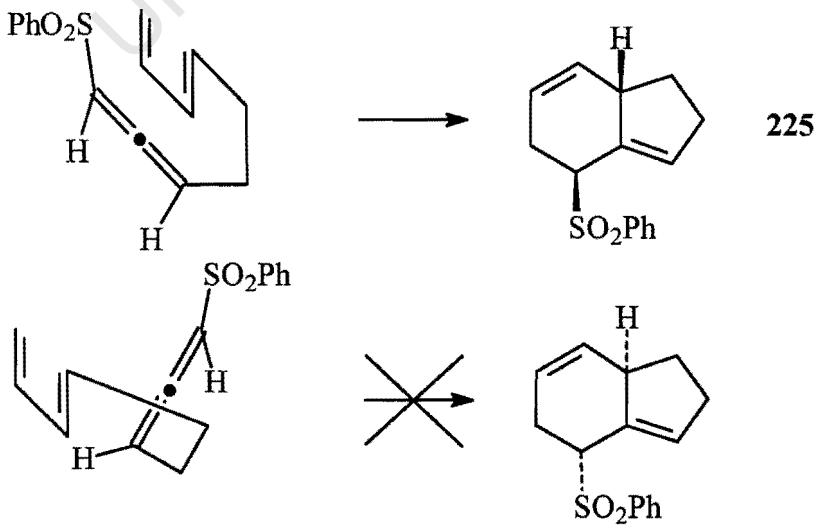
Low temperature treatment of (*R*)-ynol **219** with triethylamine and benzenesulfenyl chloride gave a mixture of (*M*)-phenylsulfinylallenyl diastereomers **223** in 67 % yield (Scheme 31). Oxidation of the sulfoxides **223** with *m*-CPBA (and subsequent quenching with $NaHCO_3$), followed by stirring the solution at 30 °C for 20 min, gave a mixture of cycloaddition products. Chromatography furnished the pure (1*S*,4a*S*) cycloadduct **225** in 24 % yield accompanied by mixed fractions (15 %) which comprised a mixture of **225** and the minor cycloadduct **226** (1:1 by NMR). This research was conducted in the closing stages of this investigation, and insufficient

material prevented optimisation of reaction yields. Spectroscopic and analytical data were identical to cycloadduct **131**.



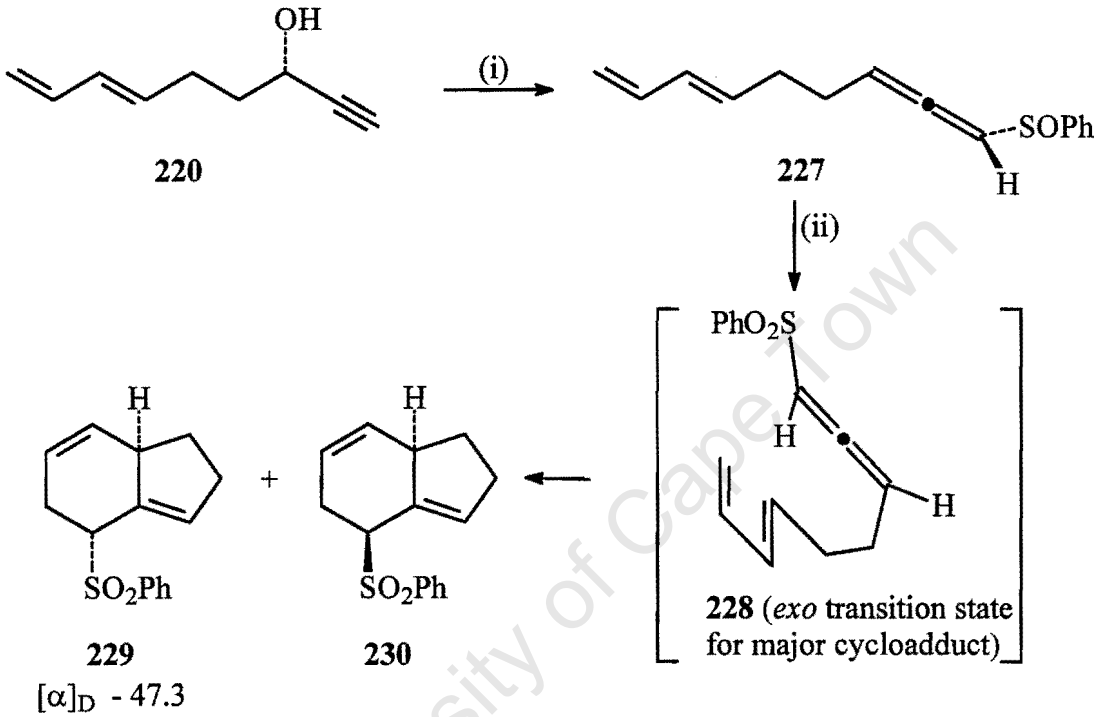
Scheme 31 *Reaction conditions*: (i) PhSCl, NEt_3, CH_2Cl_2, -78 °C, 67 %; (ii)(a) *m*-CPBA, CH_2Cl_2, 25 °C; (b) $NaHCO_3$, 30 °C, 20 min, 40 % overall

As observed for the three-carbon tether cycloaddition studies, there are two potential *exo* transition states for the two-carbon tetraene; however, only one is feasible as the tether is too short to facilitate orbital alignment of the opposite face of the molecule. As in the previous examples, results and mechanistic interpretation indicate that reaction of (*M*)-phenylsulfonylallenyl compound **224** (once formed) gave major cycloadduct **225** exclusively.



Scheme 32 *Exo* transition states of (*M*)-phenylsulfonylallene **224** leading to cycloadduct **225**.

Treatment of alkynol **220** with benzenesulfinyl chloride at low temperature followed by oxidation with *m*-CPBA gave a mixture of cycloadducts. Chromatography gave the pure (1*R*,4a*R*) cycloadduct **229** in 25 % (from the sulfoxide, Scheme 33) which was followed by a mixture of minor cycloadduct **230** and **229** in 23 % yield (1:1 by NMR). As in the case of the (*M*)-enantiomer, insufficient material and time constraints prevented the optimisation of reaction yields. Therefore the (*P*)-phenylsulfonylallenyl compound **228** (once formed) gave cycloadduct **229** in accordance with previously prepared systems.

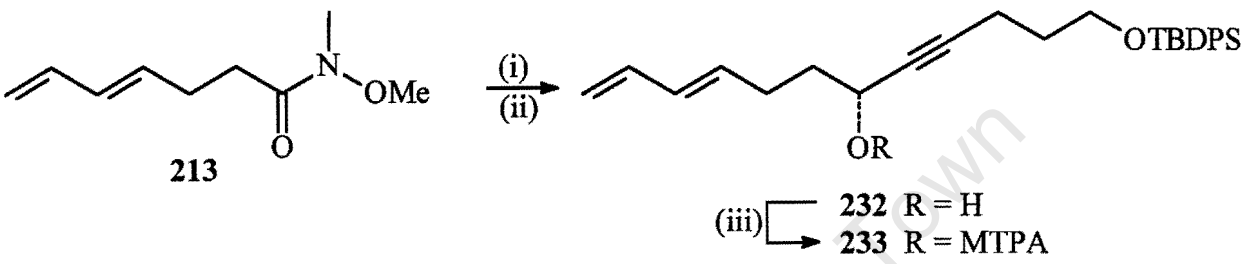


Scheme 33 *Reaction conditions*: (i) PhSCl, NEt_3, CH_2Cl_2, -78 °C, 69 %; (ii)(a) *m*-CPBA, CH_2Cl_2, 25 °C; (b) $NaHCO_3$, 30 °C, 20 min, 48 % overall

The foregoing results have demonstrated the practicality of using the enantioselective reduction of alkynones to furnish dienynols in high optical purity. Stereocontrolled rearrangement of the resulting phenylsulfenyl esters gives the corresponding allenes in high purity, which in turn impart their chirality on the cycloadduct. A question arising from these findings is the scope for achieving enantiocontrol in 1-alkyldien-1-yn-3-ones, since the ensuing cycloaddition reaction has been shown to proceed readily – as shown by examples of derived tetraenes for the racemic series.

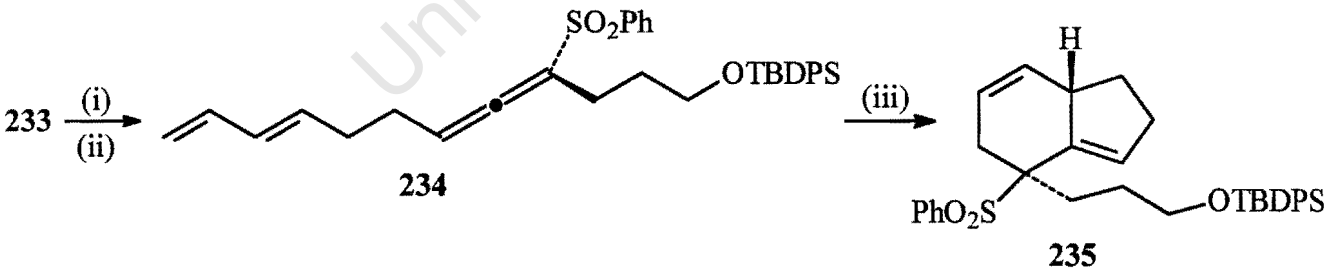
5.2.5 (6*R*)- 1-(*t*-Butyldiphenylsilyloxy)-dodeca-9,11-dien-4-yn-6-ol Weinreb amide **213** was added to a solution of 1-(*t*-butyldiphenysiloxy)-pent-4-yne (previously treated with *n*-BuLi) to give ynone **231** in 72 % yield (Scheme 34). The ^{1}H NMR spectrum displayed signals at δ 3.74 (t, *J* 6.0 Hz) for 1-H_2 and δ 1.82 (quint, *J* 4 x 6.0 Hz) for 2-H_2 whereas the IR spectrum displayed absorption at ν_{max} 2213 (C≡CR) and 1668 cm^{-1}(CO).

Reduction of the dienynone **231** with (*R*)-Alpine-Borane gave the (*R*)-dienol **232** in 85 % yield, whose spectroscopic properties were identical to that of racemic analogue **150**. Formation of the Mosher ester **233** was carried out in 99 % yield and revealed an *ee* of 85 % by ^{19}F NMR.



Scheme 34 *Reaction conditions*: (i) TBDPSO$(CH_2)_3$C≡CH, *n*-BuLi, THF, 0 °C, 72 % (ii) 9-BBN, (+)-α-Pinene, 25 °C; (iii) Ph(F_3C)(MeO)CCO_2H, DCC, DMAP, 25 °C

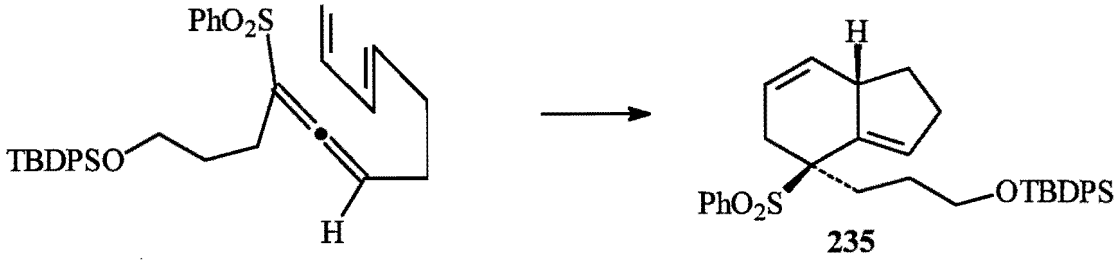
Treatment of (*R*)-dienynol **232** with benzenesulfenyl chloride and triethylamine at low temperature gave a mixture of (*M*)-phenylsulfinylallenyl diastereomers (63 %) which was oxidised with *m*-CPBA to give the (*M*)-phenylsulfonylallene **234** in 38 % yield.



Scheme 35 *Reaction conditions*: (i) PhSCl, NEt_3, -78 °C, 63 %; (ii) *m*-CPBA, CH_2Cl_2 25 °C, 38 %, (iii) CH_2Cl_2 40 °C, 19 %

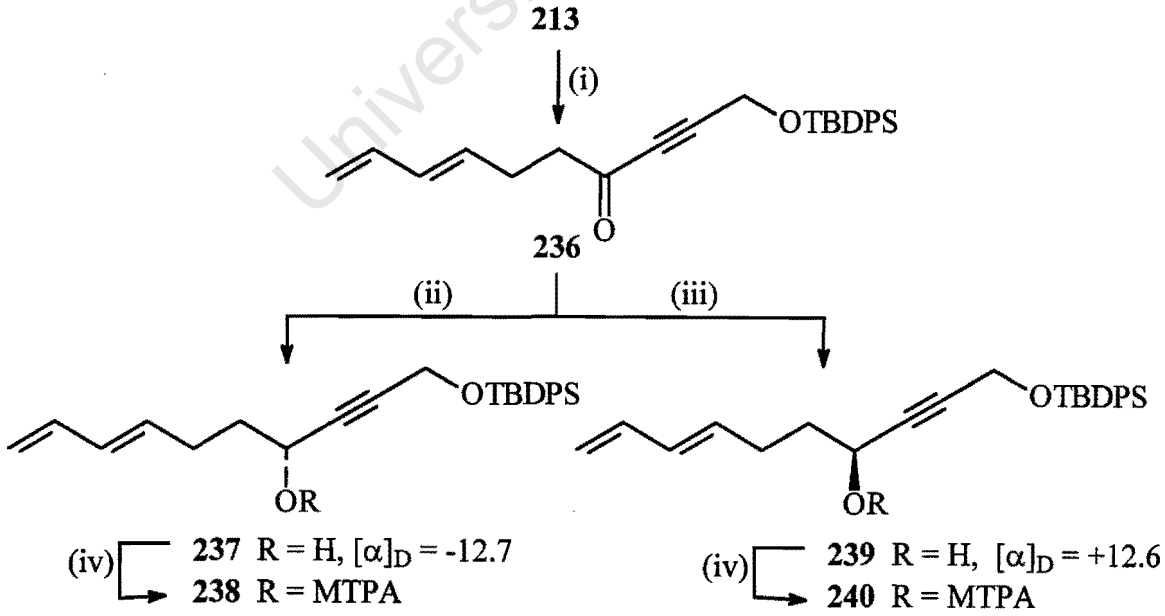
Preliminary IMDA reactions were disappointing as heating the tetraene at 40 °C for 3 h gave low yields of cycloadduct **235** (~19 %). Heating the tetraene for extended periods only afforded decomposition (*cf.* heating **151** 50 °C for 2 h to give **152** in 75 % yield) which is now believed to be attributed to an inappropriate choice of solvent. Insufficient material and time constraints

prevented this reaction being optimised. A reliable $[\alpha]_D$ value could not be obtained for cycloadduct **235**. Spectroscopic characterisation of **235** was consistent with that of the racemic cycloadduct **151** and arose as a result of *exo* addition of the dienophile (Scheme 36) in which the silyl ether terminated chain is located away from the reaction centre. Therefore IMDA reaction of (*M*)-phenylsulfonylallene **234** gave cycloadduct **235** as observed for IMDA reaction of other (*M*)-phenylsulfonyl tetraenes.



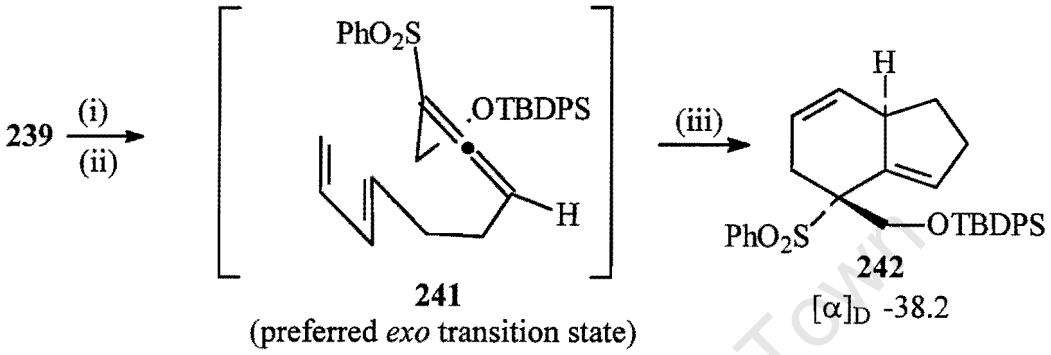
Scheme 36 Transition states for the preferred *exo* adduct

The analogous series of reactions were carried out on the analogous tetraene in which the silyl terminated chain contained one-carbon unit. Reduction of alyknone **236** with (*R*)- and (*S*)-Alpine-Borane, generated *in situ*, gave the corresponding (*R*)- and (*S*)-dienyols **235** and **237** (Scheme 37) whose spectroscopic properties were as expected, although it was not possible to achieve resolution of the coincident diasterotopic 1-H signals. Subsequent conversion of the dienynols to the corresponding Moshers' esters revealed *ee*'s of 92 and 93 % respectively.



Scheme 37 *Reaction conditions*: (i) $TBDPSOCH_2C{\equiv}CH$, *n*-BuLi, THF, 0 °C, 72 % (ii) 9-BBN, (+)-α-pinene, 25 °C; (iii) 9-BBN, (-)-α-pinene, 25 °C; (iv) $Ph(F_3C)(MeO)CCO_2H$, DCC, DMAP, 25 °C

Treatment of (*S*)-alcohol **239** with benzenesulfenyl chloride gave the corresponding mixture of (*P*)-phenylsulfinylallene diastereomers (47 %) which was oxidised with *m*-CPBA. As previously observed for the unsubstituted aliphatic series, a ^{1}H NMR spectrum of the crude reaction product revealed significant evidence of IMDA reactivity as tetraene **241** existed in a 1:1 ratio with cycloadduct **242**. The crude product was subsequently dissolved in ethyl acetate and the resulting solution was heated at 50 °C for 30 min. Chromatography afforded cycloadduct **242** in 85 % yield (Scheme 38), which was assigned by analogy to previous results as spectroscopic and optical data were in accordance with expected values.

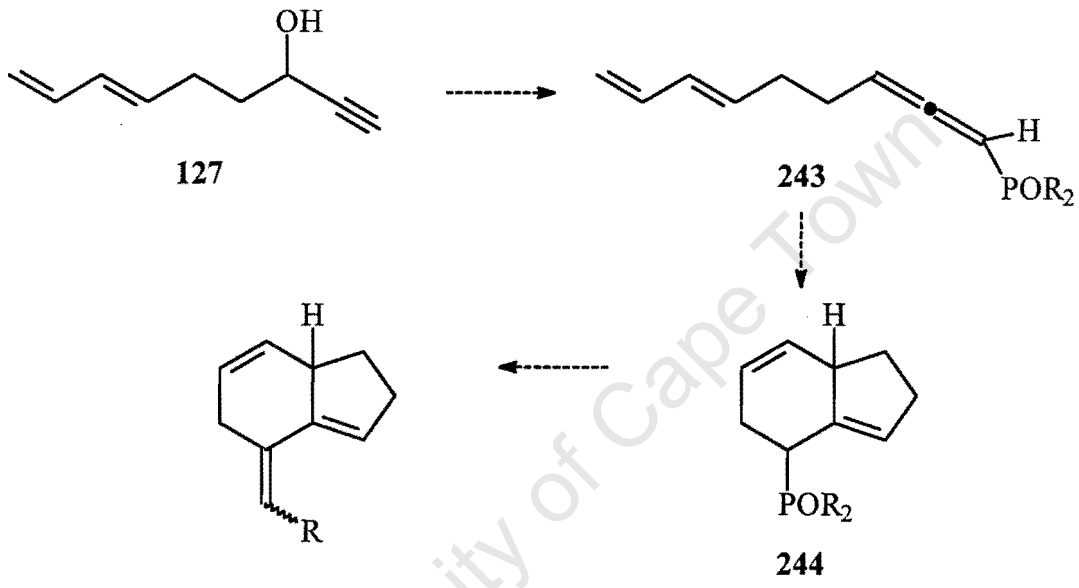


Scheme 38 Competing transition states for IMDA reaction of **241**

Following on from the findings of the racemic sereis, the synthesis of enantiopure trisubstituted (*M*)-phenylsulfonylallene **234** was successfully completed and pilot IMDA reactions appear promising. This approach was successfully extended to the one-carbon analogue to synthesise (*P*)-phenylsulfonylallene **241**, which underwent a facile IMDA reaction with a high degree of chirality transfer.

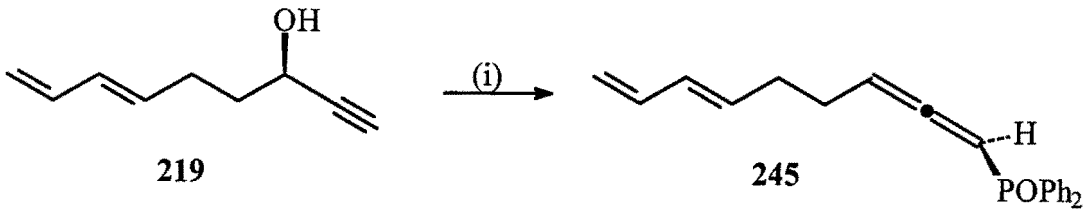
5.3 Aliphatic phosphinyl allenes

5.3.1 Introduction In the late stages of the investigation, it was considered appropriate to explore other terminal activating groups, with the aim of expanding the above findings to a broader class of '1-functionalised'-nona-1,2,6,8-tetraenes substrates which may also demonstrate high reactivity. It was envisaged that a phospinyl allene may provide a suitable analogy to the aforementioned investigation, and may provide a useful substructure for subsequent manipulations (Scheme 39). For example, a Horner-Wittig reaction on substrates such as **243** could be used for the synthesis of Vitamin D_3 precursors.[152]



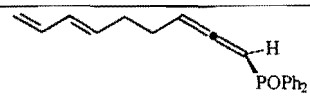
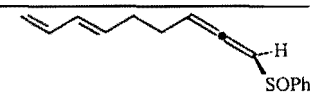
Scheme 39 The proposed synthesis and reactivity of phosphinyl allene

5.3.2 (*M*,6*E*)-1-Diphenylphosphinylnona-1,2,6,8-tetraene Using a procedure of Okamura *et al*,[73] reaction of (*R*)-dienol **219** with diphenylphosphinyl chloride and DMAP gave a mixture (*M*)-phosphinylallenes **245** in 40 % yield (Scheme 40) whose key spectroscopic data are summarised in Table 6. The yield of this reaction is unoptimised owing to insufficient material and time constraints.

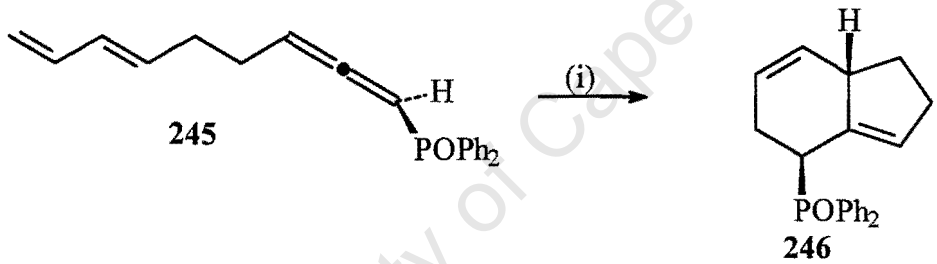


Scheme 40 *Reaction conditions*: (i) Ph_2PCl, DMAP, Et_2O, 25 °C, 16 h, 40 %

Table 6: Summary of key spectroscopic features of **245** in comparison with **223**

		
^{13}C NMR ppm	84.6, 86.1 (C-1), 91..9, 92.2 (C-3) and 211.5 (C-2)	98.5 (C-1), 103.1 (C-3) and 203.6 (C-2)
ν_{max} cm^{-1}	1952 (C=C=C), 1121 (PO)	1950 (C=C=C), 1037 (SO)
$[\alpha]_D$	-72.7	-45.0

The tetraene **245** was dissolved in toluene and the solution was heated at 90 °C for 2 h. Chromatography afforded a single *exo* cycloadduct **246** in 64 % yield (Scheme 41) which was identified using 1D and 2D NMR. The ^{1}H NMR displayed signals at δ 5.58 (ddd, *J* 9.9, 7.2 and 2.8 Hz) for 6-H, δ 5.73 (dq, *J* 9.9 and 3 x 2.2 Hz) for 7-H and δ 3.61 (d, *J* 8.4 Hz) for 4-H while the ^{13}C NMR spectrum displayed a signal at δ 37.0 (d, *J* 129.6 Hz) for C-4. ^{31}P NMR displayed a signal at δ 31.7.



Scheme 41 *Reaction conditions:* (i) PhMe, 90 °C, 2 h, 64 %

The cycloadduct was assigned *via* analogy to previous results as key ^{1}H NMR signals are in close agreement with corresponding signals of related *exo* cycloadducts. Of particular importance was the signal for 4-H which displayed a zero coupling with 5β-H proton – a feature observed in all previous cases for the product arising from *exo* addition. The IMDA reaction was slower than that of the phenylsulfonyl analogue **223** owing to the sterically larger phosphinyl moiety.

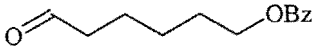
5.4 Conclusions The synthesis of the (*M*)- and (*P*)-phenylsulfonylallenyl enantiomers, through asymmetric reduction of the alkynone precursors, has been carried out and their IMDA properties investigated. The results, in all cases, are encouraging and examination of the respective transition states suggest a high degree of axial chirality transfer. Asymmetric reductions using Alpine-Borane reagents gave high *ee*'s in most cases. Preliminary investigation into phospinyl terminated systems has been carried out and the results obtained appear promising.

CHAPTER 6

EXPERIMENTAL

General procedures. Reactions were monitored by thin layer chromatography using Merck F_{254} aluminum-backed precoated silica gel plates and were visualised with a combination of ultraviolet, iodine vapour and either anisaldehyde or ceric ammonium sulfate solutions as appropriate. Column chromatography was performed using Merck Kieselgel 60: 70 – 230 mesh for gravity columns and 230 – 400 mesh for flash chromatography. Melting points were determined using a Reichert-Jung Thermovar hot-stage microscope and are uncorrected. Specific rotations were measured on a Perkin-Elmer 141 Polarimeter using chloroform solutions unless otherwise stated. Infrared spectra were recorded as chloroform solutions on a Perkin-Elmer Paragon 1000 FT-IR spectrometer. ^{1}H and ^{13}C NMR were recorded on a Varian VXR-200 instrument at 200 MHz, Varian Mercury 300 MHz or a Varian Unity spectrometer at 400 MHz. All spectra were recorded in deuteriochloroform, unless otherwise stated, using $CHCl_3$, δ 7.26 as internal standard. ^{1}H NMR were recorded as 200 MHz spectra and ^{13}C as 50 MHz unless otherwise stated. All chemical shifts are reported in ppm. Elemental analyses were performed using a Fison's Instruments Elemental Analyser EA1108. Mass spectra were recorded on a VG micromass 16F spectrometer and accurate mass determinations were performed on a Kratos Limited MS9/50 spectrometer. All mass spectra data were performed using Electron Impact techniques unless otherwise stated. Ether and tetrahydrofuran (THF) were distilled from sodium-benzophenone ketyl, dichloromethane from phosphorus pentoxide and toluene from sodium. Other reagents and solvents were purified according to standard procedures.[88]

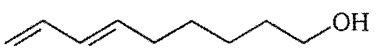
6-Oxohexan-1-yl benzoate 107



Benzoyl chloride (2.86 ml, 25 mmol) was added dropwise, over 30 min, to a solution of hexane-1,6-diol (3.5 g, 29 mmol) and pyridine (2 ml, 25 mmol) in dichloromethane (25 ml) at 0 °C. The solution was stirred at room temperature for 1 h, after which water was added. The mixture was extracted (CH_2Cl_2), and the organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-hexane (2:3) as eluent. This afforded the 1,6-dibenzoate (1.8 g, 22 %) which was not characterised, followed by the monobenzoate **106** (3.81 g, 69 %) as a colourless oil. Spectroscopic data were in agreement with previously reported data.[102]

The following is a typical procedure for Swern oxidations carried out in this investigation. Oxalyl chloride (1.1 ml, 13 mmol) and dimethyl sulfoxide (1.85 ml, 26 mmol) were stirred in dichloromethane (15 ml) for 30 min at -78 °C. The alcohol **106** (2.4 g, 10.8 mmol) was added, followed 30 min later with triethylamine (6.5 ml, 50 mmol). The solution was warmed to room temperature, water was added and the mixture was extracted (CH_2Cl_2). The organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was flash chromatographed on silica gel with ethyl acetate-hexane (1:9) as eluent to yield aldehyde **107** (2.33 g, 98 %) as an oil, whose identity was confirmed by ^{1}H NMR. δ_H (400 MHz) 1.50 – 1.80 (6H, m, 2-, 3- and 4-H_2), 2.48 (1H, td, *J* 2 x 7.3 and 1.7, 5-H_2), 4.32 (1H, t, *J* 6.5, 1-H_2), 7.40 – 8.10 (5H, m, C_6H_5) and 9.77 (1H, t, *J* 1.7, CHO).

(6*E*)-Nona-6,8-dien-1-ol 108



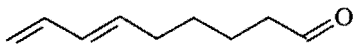
The following is a typical procedure for Wittig reactions carried out in this investigation. *n*-BuLi (3.9 ml, 9.7 mmol, 2.5M solution in hexanes) was added to a stirred suspension of allyltriphenylphosphonium bromide (3.7 g, 9.7 mmol) in THF (40 ml) at 0 °C. This was stirred at 0 °C for 30 min, after which the aldehyde **107** (2.1 g, 9.7 mmol) in THF (20 ml) was added, and the reaction mixture was allowed to warm to room temperature. After a further 2 h, water

was added and the mixture was extracted (Et_2O). The organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. Flash chromatography of the residue on silica gel with ethyl acetate-hexane (1:19) as eluent afforded a mixture (*ca* 5:4 *E/Z* by NMR) of dienes (1.4 g, 59 %); δ_H (400 MHz)(*E*- isomer) 4.95 (1H, dd, *J* 10.3 and 1.9, 9-H_{cis}), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 6-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H); (*Z*-isomer) 5.18 (1H, dd, *J* 17.0 and 1.9, 9-H_{trans}), 5.41 (1H, br dt, *J* 10.4 and 2 x 6.5, 6-H), 6.60 (1H, dtd, *J* 16.9, 2 x 11.0 and 1.1, 8-H); (Coincident) 4.30 (2H, t, *J* 6.4, 1-H_2), 5.20 (1H, m, 9-H), 6.05 (1H, m, 7-H) and 7.40 – 8.00 (5H, m, Ph).

Iodine was added (50 mg, 0.2 mmol) to the diene mixture (1.4 g, 59 %) dissolved in hexane (20 ml) and the resulting solution was irradiated for 2 h at 0 °C (Hg radiation, 400 W OSRAM, HQI-T). The solution was sequentially washed (thiosulfate, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude (*E*)-diene (1.18 g, 84 %, 88 % *E* by NMR); δ_H (400 MHz) 4.95 (1H, dd, *J* 10.3 and 1.9, 9-H_{cis}), 5.08 (1H, dd, *J* 17.0 and 1.9, 9-H_{trans}), 5.68 (1H, dt, *J* 15.2 and 2 x 6.6, 6-H), 6.05 (1H, br dd, *J* 15.2 and 10.3, 7-H) and 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H).

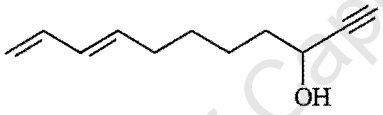
The crude ester (700 mg, 2.86 mmol) in THF – H_2O – MeOH (100 ml, 2:2:1) was treated with potassium hydroxide (1 g, 25 mmol) for 3 h at 20 °C, after which the reaction was acidified with dil. HCl (1M). The mixture was extracted (Et_2O) and the combined extract was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was flash chromatographed on silica gel with ether-hexane (2:3) as eluent to yield the (*E*)-dienol **108** (330 mg, 82 %); δ_H 1.40 – 1.60 (6H, m, 2-, 3-, and 4-H_2), 2.10 (2H, q, *J* 6.6, 5-H_2), 3.63 (2H, t, *J* 6.4, 1-H_2), 4.95 (1H, dd, *J* 10.3 and 1.9, 9-H_{cis}), 5.08 (1H, dd, *J* 17.0 and 1.9, 9-H_{trans}), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 6-H), 6.05 (1H, br dd, *J* 15.2 and 10.3, 7-H) and 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H) as a colourless oil. Spectroscopic data were in agreement with previously reported data.[13]

(6*E*)-Nona-6,8-dienal 109



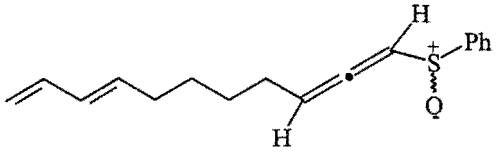
A Swern oxidation was carried out on alcohol **108** (250 mg, 1.78 mmol) using oxalyl chloride (0.2 ml, 1 mmol), dimethyl sulfoxide (0.15 ml, 2 mmol) and triethylamine (1.5 ml, 10 mmol). Work-up followed by flash chromatography [silica gel, ethyl acetate-hexane (3:10)] gave *aldehyde* **109** (206 mg, 83 %) as a pungent oil; δ_H (400 MHz) 1.40 – 1.65 (4H, m, 3- and 4-H_2), 2.10 (2H, q, *J* 6.6, 5-H_2), 2.43 (2H, t, *J* 7.2, 2-H_2), 4.95 (1H, dd, *J* 10.3 and 1.9, 9-H_{cis}), 5.08 (1H, dd, *J* 17.0 and 1.9, 9-H_{trans}), 5.68 (1H, dt, *J* 15.2 and 2 x 6.6, 6-H), 6.05 (1H, br dd, *J* 15.2 and 10.3, 7-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H) and 9.76 (1H, s, CHO). Spectroscopic data were in agreement with previously reported data.[13]

(8*E*)-Undeca-8,10-dien-1-yn-3-ol 110



The following is a typical procedure for a series of ethynylations carried out in this investigation. Dry acetylene was bubbled vigorously through THF (40 ml). After 30 min, a solution of hot ethylmagnesium bromide [prepared by refluxing a mixture of magnesium (166 mg, 7.2 mmol), bromoethane (0.53 ml, 7.2 mmol) and iodine (cat.) in THF (40 ml) for 2 h] was added, whilst maintaining the passage of acetylene. After 30 min, the aldehyde **109** (520 mg, 3.77 mmol) was added and the mixture was stirred at room temperature for 2 h, then quenched by addition of sat. NH_4Cl. The mixture was extracted (Et_2O) and the organic phase was washed (dil. HCl, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield the *dienynol* **110** (540 mg, 87 %, TLC pure); ν_{max}/cm^{-1} 3684 (OH) and 3305 (C≡C); δ_H (400 MHz) 1.60 – 1.80 (6H, m, 4-, 5- and 6-H_2), 2.15 (2H, m, 7-H_2), 2.47 (1H, dd, *J* 2.3 and 0.8, 1-H), 4.40 (1H, td, *J* 2 x 6.3 and 2.3, 3-H), 4.95 (1H, dd, *J* 10.2 and 2.7, 11-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 11-H_{trans}), 5.70 (1H, dt, *J* 15.1 and 2 x 6.8, 8-H), 6.05 (1H, br dd, *J* 15.1 and 10.3, 9-H) and 6.32 (1H, dt, *J* 17.0 and 2 x 10.3, 10-H); δ_C (100 MHz) 24.5 and 28.7 (C-5 and C-6), 32.3 (C-7), 37.4 (C-4), 62.1 (C-3), 72.8 (C-1), 84.9 (C-2), 114.7 (C-11), 131.1 (C-9), 134.9 (C-8) and 137.2 (C-10); (Found: M^+, 164. $C_{11}H_{16}O$ requires M, 164).

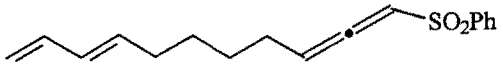
(8*E*,*S*-*R)- and (8*E*,*S*-*S**)-1-Phenylsulfinylundeca-1,2,8,10-tetraene 111a and 111b**



a) The following is a typical procedure for the synthesis of allenes *via* [2,3] sigmatropic rearrangement from proparglic alcohols. Triethylamine (0.28 ml, 0.79 mmol) was added to a stirred solution of alcohol **110** (130 mg, 0.79 mmol) in THF (5 ml) at -78 °C, followed by benzenesulfenyl chloride (0.82 µl, 0.79 mmol). After 1 h at -78 °C and was allowed to warm to room temperature when aq. NH_4Cl was added and the products were extracted (EtOAc). The combined extract was washed (brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-hexane (1:9) as eluent to yield *sulfinyl tetraene* **111a** (20 mg, 9 %) as a colourless oil; δ_H (400 MHz) 1.60 – 1.90 (4H, m, 5- and 6-H_2), 2.15 – 2 .25 (4H, m, 4- and 7-H_2), 4.98 (1H, dd, *J* 10.2 and 2.7, 11-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 11-H_{trans}), 5.67 (1H, dt, *J* 15.1 and 2 x 6.7, 8-H), 5.68 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.05 (2H, m, 1-, and 9-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.2, 10-H) and 7.52 – 7.90 (5H, m, SOPh); δ_C (100 MHz) 27.9 and 28.1 (C-5 and C-6), 28.4 (C-4), 32.0 (C-7), 99.1 (C-1), 102.7 (C-3), 114.8 (C-11), 124.2 (SOPh), 129.1 (SOPh), 130.9 (SOPh), 131.2 (C-9), 134.7 (C-8), 137.1 (C-10), 144.8 (SOPh) and 203.7 (C-2). This was followed by mixed fractions (34 mg, 16 %); ν_{max}/cm^{-1} 1948 (C=C=C) and 1042 (SO); (Found: M^+, 272.1140. $C_{17}H_{20}OS$ requires M, 272.1130), which was in turn followed by the other *sulfinyl tetraene* **111b** (15 mg, 7 %); δ_H (400 MHz) 1.60 – 1.90 (4H, m, 5- and 6-H_2), 2.15 – 2.25 (4H, m, 4- and 7-H_2), 4.98 (1H, dd, *J* 10.2 and 2.7, 11-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 11-H_{trans}), 5.66 (1H, dt, *J* 15.1 and 2 x 6.7, 8-H), 5.73 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.05 (2H, m, 1-, and 9-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.2, 10-H) and 7.52 – 7.90 (5H, m, SOPh); δ_C (100 MHz) 27.9 and 28.1 (C-5 and C-6), 28.4 (C-4), 32.1 (C-7), 99.0 (C-1), 102.7 (C-3), 114.9 (C-11), 124.2 (SOPh), 129.1 (SOPh), 130.9 (SOPh), 131.2 (C-9), 134.6 (C-8), 137.1 (C-10), 144.8 (SOPh) and 203.7 (C-2).

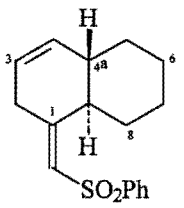
b) The analogous reaction was carried out on alcohol **110** (540 mg, 3.29 mmol) with triethylamine (0.52 ml, 3.74 mmol) and benzenesulfenyl chloride (0.41 ml, 3.74 mmol). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)] gave a mixture of phenylsulfinylallenyl diastereomers **111** (685 mg, 77 %).

(8*E*)-1-Phenylsulfonylundeca-1,2,8,10-tetraene 112



The following is a typical procedure for all subsequent oxidations of sulfoxides carried out in this investigation. *m*-CPBA (370 mg, 67 %, 1.1 mmol) was added to a solution of the tetraenes **111** (300 mg, 1.1 mmol) in dichloromethane (15 ml) at 0 °C. After 1 h at room temperature, aq. NH_4Cl was added and the mixture was extracted (EtOAc). The organic phase was washed (dil. HCl, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield an oil which was flash chromatographed on silica gel with ethyl acetate-hexane (1:4) as eluent to yield *allenylsulfone* **112** (210 mg, 66 %) as a colourless oil; ν_{max}/cm^{-1} 1955 (C=C=C), 1319 and 1148 (SO); δ_H (400 MHz) 1.38 – 1.43 (4H, m, 5- and 6-H_2), 2.15 – 2 .25 (4H, m, 4- and 7-H_2), 4.96 (1H, dd, *J* 10.2 and 2.7, 11-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 11-H_{trans}), 5.66 (1H, dt, *J* 15.1 and 2 x 6.7, 8-H), 5.83 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.05 (1H, br dd, *J* 15.1 and 10.2, 9-H), 6.19 (1H, dt, *J* 6.2 and 2 x 3.1, 1-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.2, 10-H) and 7.50 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 27.5 and 27.8 (C-5 and C-6), 28.3 (C-4), 32.0 (C-7), 101.0 (C-1), 101.2 (C-3), 114.9 (C-11), 127.2 (SO_2Ph), 129.1 (SO_2Ph), 131.2 (C-9), 133.3 (SO_2Ph), 134.6 (C-8), 137.1 (C-10), 141.3 (SO_2Ph) and 205.5 (C-2); (Found: M^+, 288.1091. $C_{17}H_{20}O_2S$ requires M, M, 288.1079).

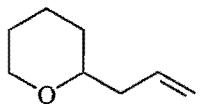
(1*Z*,4a*R,8a*R**)-4-(Phenylsulfonyl)methylene-4a,5,6,7,8,8a-hexahydro-2*H*-naphthalene 113**



A solution of the tetraene **112** (100 mg, 0.35 mmol) in toluene (2 ml) was flushed with nitrogen and heated at 180 °C in a sealed tube for 20 h. The solvent was removed and the residue chromatographed using silica gel with ethyl acetate-toluene as eluent (1:50) to yield the *cycloadduct* **113** (30 mg, 30 %) as a gum; ν_{max}/cm^{-1} 1321 and 1146 (SO); δ_H (400 MHz, C_6D_6) 1.20 – 1.85 (8H, m, 5-, 6-, 7- and 8-H_2), 2.12 (1H, dd, *J* 15.1 and 6.1, 2α-H), 2.27 (1H, ddt, *J* 15.1, 4.8 and 2 x 2.9, 2β-H), 2.70 (1H, br m, *W* 29, 8a-H), 5.43 (1H, dddd, *J* 8.8 , 6.1, 4.8 and 2.9, 3-H), 5.52 (1H, dt, *J* 8.8 and 2.9, 4-H), 5.85 (1H, m, *W* 4.5, CHS) and 6.84 – 7.82 (5H, dd, *J* 7.6

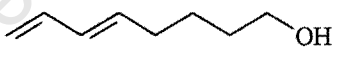
and 1.3, SO_2Ph); δ_C (100 MHz, C_6D_6) 26.3, 26.8, 31.6, 33.4 (t, C-5, C-6, C-7 and C-8), 36.5 (t, C-2), 42.3 (d, C-4a), 45.1 (d, C-8a), 124.0 (d, C-1′), 124.6 (d, C-4), 127.0 (d, SO_2Ph), 128.6 (d, SO_2Ph), 132.1 (d, SO_2Ph), 135.9 (d, C-3), 143.7 (s, SO_2Ph) and 160.7 (s, C-1); (Found: M^+, 288.1192. $C_{17}H_{20}O_2S$ requires M, 288.1183).

2-Allyltetrahydropyran 114



Allyltrimethylsilane (4.50 ml, 40 mmol) was added to a solution of 2-methoxytetrahydropyran (3.5 g, 29 mmol) in dichloromethane (15 ml) at -50 °C, followed by a solution of trimethylsilyl trifluoromethanesulfonate (0.67 ml, 3.5 mmol) in dichloromethane (5 ml). The solution was allowed to slowly warm to room temperature (~ 1 h) at which time aq. $NaHCO_3$ was added. The mixture was extracted (Et_2O), the organic phase was washed (brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was flash chromatographed on silica gel with ether-hexane (1:19) as eluent to yield the allyl derivative **114** (2.26 g, 62 %) as an oil. Spectroscopic data were in agreement with previously reported data. [113]

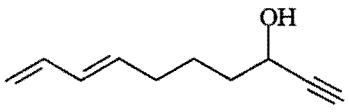
(5*E*)-Octa-5,7-dienol 115



Freshly prepared potassium *tert*-butoxide (1.8 ml, 1.8 mmol, 1M solution in THF) was added to a solution of lithium diisopropylamide [prepared by treatment of diisopropylamine (2.34 ml, 17.9 mmol) in THF (2 ml) with *n*-BuLi (7.2 ml, 17.9 mmol, 2.5M solution in hexanes)] at -78 °C. After 30 min, 2-allyltetrahydropyran **114** (2.26 g, 17.9 mmol) was added and the reaction stirred at -50 °C for 1 h, after which it was allowed to warm to room temperature. After a further 2 h, water was added and the reaction product was extracted (hexane). The organic phase was dried ($MgSO_4$), evaporated under reduced pressure and the residue flash chromatographed on silica gel using ethyl acetate-hexane (2:10) as eluent to yield the (*E*)-dienol **115** (1.46 g, 66 %, 97 % (*E*) by NMR); δ_H (400 MHz) 1.45 – 1.60 (4H, m, 2- and 3-H_2), 2.05 (2H, m, 4-H_2), 3.65 (2H, t, *J* 6.4, 1-H_2), 4.93 (1H, dd, *J* 10.2 and 2.7, 8-H_{cis}), 5.09 (1H, dd, *J* 17.0 and 2.7, 8-H_{trans}), 5.70 (1H, dt, *J*

15.1 and 2 x 6.7, 5-H), 6.05 (1H, br dd, *J* 15.1 and 10.2, 6-H) and 6.32 (1H, dt, *J* 17.0 and 2 x 10.2, 7-H), in accordance with literature values. [117a]

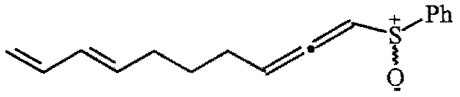
(7*E*)-Deca-7,9-dien-1-yn-3-ol 116



Dienol **115** (150 mg, 1.19 mmol) in dichloromethane (2 ml) was added to a stirred solution of pyridinium chlorochromate (384 mg, 1.78 mmol) in dichloromethane (2 ml) and the resulting mixture was stirred at room temperature for 16 h. The supernatant was poured into a separate flask and the residue was washed repeatedly with ether. The washings were combined and the solvent evaporated to yield dienal (140 mg, 95 %) as a pungent oil, which was used directly in the following step.

Treatment of the crude aldehyde (2.4 g, 19 mmol) with acetylene in the presence of ethylmagnesium bromide (35 mmol), as described previously, gave *dienynol* **116** (1.92 mg, 67 %) as a colourless oil; ν_{max}/cm^{-1} 3684 (OH) and 3305 (C≡C); δ_H 1.50 – 1.80 (4H, m, 4 and 5-H_2), 2.15 (2H, q, *J* 6.7, 6-H_2), 2.47 (1H, d, *J* 2.3, 1-H), 4.38 (1H, td, *J* 2 x 6.3 and 2.3, 3-H), 4.95 (1H, dd, *J* 10.2 and 2.7, 10-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 10-H_{trans}), 5.70 (1H, dt, *J* 15.2 and 2 x 6.7, 7-H), 6.05 (1H, dd, *J* 15.1 and 10.3, 8-H) and 6.32 (1H, dt, *J* 17.0 and 2 x 10.2, 9-H); δ_C 24.6 (C-5), 32.1 (C-6), 37.1 (C-4), 62.1 (C-3), 73.0 (C-1), 84.8 (C-2), 115.0 (C-10), 131.9 (C-8), 134.4 (C-7) and 137.0 (C-9); (Found: M^+, 150. $C_{10}H_{14}O$ requires M, 150).

(7*E*,*S*-*R)- and (7*E*,*S*-*S**)-1-Phenylsulfinyldeca-1,2,7,9-tetraene 117a and 117b**

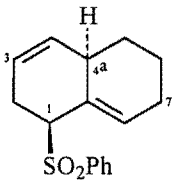


Treatment of alcohol **116** (1.75 g, 11.6 mmol) with triethylamine (1.75 ml, 12.6 mmol) and benzenesulfenyl chloride (1.3 ml, 12.6 mmol) was carried out as before. Work-up and chromatography [silica gel, ethyl acetate-hexane (1:10)] gave a mixture of *phenylsulfinylallenyl* diastereomers **117a** and **117b** (1.95 g, 65 %); ν_{max}/cm^{-1} 1950 (C=C=C) and 1037 (SO); δ_H 1.65 (2H, m, 5-H_2), 2.10 – 2.25 (4H, m, 4- and 6-H_2), 4.96 (1H, dd, *J* 10.2 and 2.7, 10-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 10-H_{trans}), 5.70 (2H, m, 3-H and 7-H), 6.05 (2H, m, 1-H and 8-H), 6.30 (1H, dt, *J* 17.0 and 10.2, 9-H) and 7.50 (5H, m, SOPh); δ_C (C-5), 28.5 (C-4), 31.7 (C-6), 98.9 (C-1), 102.8 (C-3), 115.2 (C-10), 124.2 (SOPh), 129.1 (SOPh), 130.9 (SOPh), 131.2 (C-8), 134.7 (C-7), 137.0 (C-9), 144.8 (SOPh) and 203.7 (C-2); (Found: M^+, 258.1070. $C_{16}H_{18}OS$ requires M, 258.1077).

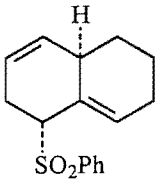
(7*E*)-1-Phenylsulfonyldeca-1,2,7,9-tetraene 118

Oxidation of sulfinyl tetraenes **117a** and **117b** (1.95 g, 7.56 mmol) with *m*-CPBA (1.95 g, 67 %, 7.56 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:5)] gave *phenylsulfonylallene* **118** (1.1 g, 53 %); ν_{max}/cm^{-1} 1956 (C=C=C), 1307 and 1149 (SO); δ_H (400 MHz) 1.49 (2H, quint, *J* 4 x 7.5, 5-H_2), 2.10 – 2.15 (4H, m, 4- and 6-H_2), 4.96 (1H, dd, *J* 10.2 and 2.7, 10-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 10-H_{trans}), 5.60 (1H, dt, *J* 15.2 and 2 x 6.7, 7-H), 5.85 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.05 (1H, dd, *J* 15.2 and 10.2, 8-H), 6.20 (1H, dt, *J* 6.2 and 2 x 3.1, 1-H), 6.28 (1H, dt, *J* 17.0 and 2 x 10.2, 9-H) and 7.56 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 27.0 (C-5), 27.7 (C-4), 31.6 (C-6), 100.9 (C-1), 101.2 (C-3), 115.2 (C-10), 127.6 (SO_2Ph), 129.1 (SO_2Ph), 131.7 (SO_2Ph), 133.3 (C-8), 133.8 (C-7), 137.0 (C-9), 141.4 (SO_2Ph) and 205.7 (C-2); (Found: $M+H^+$, 275. $C_{17}H_{19}O_2S$ requires M, 275).

(1*S,4a*R**)- and (1*R**,4a*R**)-1-Phenylsulfonyl-1,2,4a,5,6,7-hexahydronaphthalene 119 and 120**



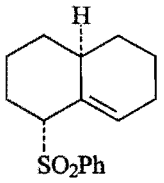
119



120

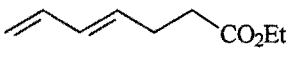
A solution of the tetraene **118** (400 mg, 1.46 mmol) in toluene (30 ml) was flushed with nitrogen and was heated in a sealed tube at 80 °C for 20 h. The solvent was evaporated and the residue chromatographed on silica gel using ethyl acetate-toluene (1:50) as eluent to yield the *cycloadduct* **119** (70 mg, 18 %), mp 110 – 113 °C (from isopropanol); ν_{max}/cm^{-1} 1306 and 1142 (SO); δ_H (400 MHz) 1.18 (1H, qd, *J* 3 x 12.9 and 2.8, 5β-H), 1.50 (1H, qdd, *J* 3 x 12.9, 6.3 and 2.8, 6α-H), 1.75 (1H, m, *W* 29, 6-H), 1.90 (1H, m, *W* 25, 5-H), 2.20 (3H, m, 2-H and 7-H_2), 2.61 (1H, m, *W* 36, 2-H), 2.76 (1H, br m, $W_{½}$ 7.0, 4a-H), 3.82 (1H, ddd, *J* 9.4, 3.5 and 1.3, 1-H), 5.43 (1H, br d, *J* 9.9, 4-H), 5.52 (1H, dddt, *J* 9.9, 7.7 and 2 x 2.4, 3-H), 6.55 (1H, br d, *J* 2.0, 8-H) and 7.55 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 21.4 (t, C-6), 25.5 (t, C-2), 28.8 (t, C-7), 30.2 (t, C-5), 37.6 (d, C-4a), 64.5 (d, C-1), 122.4 (d, C-3), 125.1 (d, C-8), 128.6 (d, SO_2Ph), 128.8 (s, C-8a), 128.9 (d, SO_2Ph), 132.2 (d, C-4), 133.5 (d, SO_2Ph) and 139.1 (s, SO_2Ph); (Found; C, 70.0; H, 6.5; S, 11.6 %: M^+, 274. Requires for $C_{16}H_{18}O_2S$: 274; C, 70.1; H, 6.6; S, 11.7 %). This was followed by the major *cycloadduct* **120** (214 mg, 54 %), mp 123 – 125 °C (from ethanol); ν_{max}/cm^{-1} 1302 and 1146 (SO); δ_H (400 MHz) 0.95 (1H, qd, *J* 3 x 12.4 and 2.4, 5β-H), 1.49 (1H, qdd, *J* 3 x 12.4, 5.6 and 2.8, 6α-H), 1.80 – 1.95 (4H, m, 5-,6- and 7-H_2), 2.55 (1H, dddd, *J* 19.8, 8.4, 6.4 and 2.4, 2β-H), 3.00 (1H, dd, *J* 19.8 and 4.8, 2α-H), 3.06 (1H, m, $W_{½}$ 7.0, 4a-H), 3.72 (1H, d, *J* 8.4, 1-H), 5.25 (1H, m, $W_{½}$ 4.4, 8-H), 5.57 (1H, br d, *J* 10.4, 4-H), 5.65 (1H, dddd, *J* 10.4, 6.4, 4.8 and 2.4, 3-H) and 7.50 – 7.85 (5H, m, SO_2Ph); δ_C (100 MHz) 21.0 (t, C-6), 24.5 (t, C-2), 26.0 (t, C-7), 29.8 (t, C-5), 33.7 (d, C-4a), 67.9 (d, C-1), 121.4 (d, C-3), 128.6 (d, SO_2Ph), 128.9 (s, SO_2Ph), 129.2 (s, C-8a), 130.9 (d, C-4), 132.2 (d, C-8), 133.3 (d, SO_2Ph) and 137.6 (s, SO_2Ph); (Found; C, 70.2; H, 6.7; S, 11.9 %: M^+, 274. Requires for $C_{16}H_{18}O_2S$: 274; C, 70.1; H, 6.6; S, 11.7 %).

(1*R,4a*R**)-1-Phenylsulfonyl-1,2,3,4,4a,5,6,7-octahydronaphthalene 121**



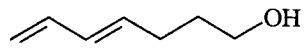
The major cycloadduct **120** (30 mg, 0.11 mmol) in ethyl acetate (3 ml) was hydrogenated in the presence of palladium on carbon (50 mg, 10 mol %) under mild hydrogen pressure (~ 2 atmosphere). After 1 h, the solution was filtered through Celite, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-toluene (1:50) as eluent to give the title compound **121** (27 mg, 89 %); mp 117 – 119°C (from ethanol); ν_{max}/cm^{-1} 1302 and 1146 (SO); δ_H (400 MHz) 0.95 (1H, qd, *J* 3 x 13.0 and 3.5, 4β-H), 1.09 (1H, qd, *J* 3 x 12.9 and 2.9, 5β-H), 1.40 (1H, qdd, *J* 3 x 12.9, 5.4 and 2.7, 6α-H), 1.65 – 1.85 (8H, m, 2-, 3-, 4-, 6- and 8-H and 7-H_2), 2.09 (1H, dt, *J* 13.4 and 2 x 3.4, 3-H), 2.60 (1H, br, $W_{½}$ 9.5, 4a-H), 2.65 (1H, m, *W* 16.5, 2-H), 3.54 (1H, d, *J* 8.4, 1-H), 5.00 (1H, br, $W_{½}$ 5, 8-H) and 7.50 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 21.3 (t, C-5), 21.6 (t, C-7), 25.3 (t, C-3), 26.1 (t, C-6), 31.0 (t, C-2), 33.8 (t, C-4), 34.2 (d, C-4a), 69.3 (d, C-1), 128.5 (SO_2Ph), 128.9 (d, SO_2Ph), 132.0 (s, C-8a), 132.3 (d, C-8), 133.1 (d, SO_2Ph) and 137.8 (d, SO_2Ph); (Found; C, 69.6; H, 7.4; S, 11.7 %; requires for $C_{16}H_{20}O_2S$; C, 69.6; H, 7.3; S, 11.6 %); (Found: *M-SO₂Ph*$^+$, 135. $C_{10}H_{15}$ requires M, 135).

Ethyl (4*E*)-hepta-4,6-dienoate 123



Penta-1,4-dien-3-ol **122** (4 ml, 41 mmol) was dissolved in toluene (20 ml). Triethyl orthoacetate (60 ml, 0.33 mol) and propionic acid (0.7 ml, 9 mmol) were added and the solution was refluxed for 16 h. The solvent was removed and the residue was flash chromatographed on silica gel using ethyl acetate-hexane (1:19) as eluent to afford the dienoate **123** (6.21 g, 98 %, 95 % (*E*)-isomer by NMR) The yield and *E*/*Z* ratio were in close agreement with literature precedent.[117]

(4*E*)-Hepta-4,6-dien-1-ol 124



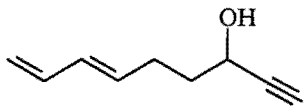
a) The ester **124** (560 mg, 3.6 mmol) was dissolved in THF (5 ml) and the solution was cooled to 0 °C. Diisobutylaluminum hydride (4 ml, 6 mmol, 1.5 M solution in toluene) was added and the reaction mixture was stirred for 1 h before dil. HCl (1M) was added. The product was extracted (EtOAc) and the organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield the alcohol **125** (350 mg, 86 %) as a colourless oil. Spectroscopic data were in agreement with reported data.[117]

b) 1-(*t*-Butyldiphenylsilyloxy)-pent-4-yne (prepared from the reaction of pent-4-yn-1-ol and *t*-butyldiphenylsilyl chloride in the presence of pyridine, 1.54 g, 4.78 mmol) was added to a slurry of zirconocene hydrogen chloride (1.23 g, 4.78 mmol) in dichloromethane (20 ml) in a vessel protected from sunlight. The resulting homogenous solution was stirred at room temperature for 4 h before iodine (1.34 g, 5.3 mmol) in dichloromethane (15 ml) was added. After a further 1 h stirring, water was added and the mixture was extracted (Et_2O). The extract was washed ($Na_2S_2O_3$, water, brine), dried ($MgSO_4$) and the solvent removed under reduced pressure to yield the crude vinyl iodide **125** (2.05 g), as a yellow oil; δ_H 1.05 (9H, s, Bu^t), 1.65 (2H, m, 2-H_2), 2.20 (2H, m, 3-H_2), 3.66 (2H, t, *J* 6.1, 1-H_2), 5.97 (1H, br d, *J* 14.3, 5-H), 6.50 (1H, dt, *J* 14.3 and 2 x 7.1, 4-H) and 7.40 – 7.80 (10H, m, 2 x Ph).

Bis-triphenylphosphinepalladium(II)chloride (170 mg, 0.24 mmol) was dissolved in *N*,*N*-dimethylformamide (20 ml). Vinyltributyltin (1.26 ml, 4.3 mmol) and the iodide were sequentially added and the resulting solution stirred at room temperature for 72 h. Ammonium hydroxide (10 % v/v, 20 ml) was added and the reaction mixture extracted (Et_2O). The extract was washed (water, brine), dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate-hexane (1:19) as eluent to yield the diene **126** (1.16 g, 70 %) as a pale-yellow oil; δ_H 1.05 (9H, s, Bu^t), 1.68 (2H, m, 2-H_2), 2.20 (2H, m, 3-H_2), 3.66 (2H, t, *J* 6.1, 1-H_2), 4.95 (1H, br d, *J* 10.3, 7-H_{cis}), 5.08 (1H, br d, *J* 17.0 , 7-H_{trans}), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 4-H), 6.05 (1H, dd, *J* 15.2 and 10.3, 5-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 6-H) and 7.40 – 7.80 (10H, m, 2 x Ph).

The diene (1.10 g, 3.14 mmol) was dissolved in THF (10 ml). Tetrabutylammonium fluoride (3.2 ml, 1M solution in THF, 3.2 mmol) was added and the resultant solution stirred at room temperature for 2 h. Brine was added and the product extracted (Et_2O). The extract was washed (brine), dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate-hexane (1:3) as eluent to yield the *dienol* **124** (147 mg, 42 %).

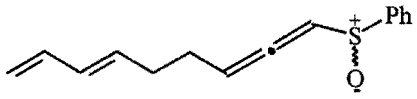
(6*E*)-Nona-6,8-dien-1-yn-3-ol 127



The following is a typical procedure carried out for all Dess-Martin Periodinane (12-I-5 Triacetoxyperiodinane) oxidations. Alcohol **124** (890 mg, 7.95 mmol) was added to a stirred solution of periodinane (4.45 g, 10.5 mmol) in dichloromethane (25 ml) and the resulting solution was stirred for 1 h at room temperature. Saturated $NaHCO_3/Na_2S_2O_3$ (5:1) was added and the solution was stirred for a further 1 h. The mixture was extracted (Et_2O) and the organic phase was washed ($NaHCO_3$, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield the aldehyde **124a** (800 mg, 92 %) as a pungent volatile oil.

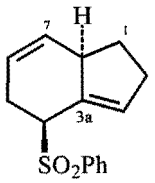
Treatment of the crude aldehyde with ethynylmagnesium bromide (35 mmol), as described previously, gave *dienynol* **127** (900 mg, 91 %) as a colourless oil; ν_{max}/cm^{-1} 3684 (OH) and 3305 (C≡C); δ_H (400 MHz) 1.60 (2H, m, 4-H_2), 2.30 (2H, q, *J* 6.7, 5-H_2), 2.48 (1H, d, *J* 1.8, 1-H), 4.40 (1H, br t, *J* 5.8, 3-H), 4.95 (1H, dd, *J* 10.2 and 2.7, 9-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.70 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.10 (1H, dd, *J* 15.5 and 10.2, 7-H) and 6.32 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H); δ_C (100 MHz) 28.0 (C-5), 36.9 (C-4), 61.7 (C-3), 73.2 (C-1), 84.6 (C-2), 115.4 (C-9), 131.9 (C-7), 133.4 (C-6) and 136.9 (C-8); (Found: M^+, 136.0868. $C_9H_{12}O$ requires M, 136.0888).

(6*E*,*S*-*R)- and (6*E*,*S*-*S**)-1-Phenylsulfinylnona-1,2,6,8-tetraene 128a and 128b**

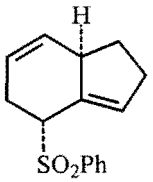


Alcohol **127** (400 mg, 2.93 mmol) was treated with triethylamine (0.6 ml, 4.76 mmol) and benzenesulfenyl chloride (0.44 ml, 4.76 mmol) as before. Work-up and chromatography [silica gel, ethyl acetate-hexane (1:4)] gave *sulfinyl tetraenes* **128a/b** (495 mg, 69 %); ν_{max}/cm^{-1} 1950 (C=C=C) and 1037 (SO); δ_H (400 MHz) 2.25 (4H, m, 4- and 5-H_2), 5.00 (1H, dd, *J* 10.2 and 2.7, 9-H_{cis}), 5.12 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.60-5.75 (2H, m, 3-H and 6-H), 6.05 (2H, m, 1-H and 7-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H) and 7.50 – 7.65 (5H, m, SO*Ph*); δ_C (100 MHz, $CDCl_3$) 27.7 (C-4) 31.5 (C-5), 98.5 (C-1), 103.1 (C-3), 115.7 (C-9), 124.2 (SOPh), 129.1 (SOPh), 130.9 (SOPh), 132.3 (C-7), 132.7(C-6), 136.9 (C-8), 144.8 (SOPh) and 203.6 (C-2); (Found: $M+H^+$, 245. $C_{15}H_{17}OS$ requires M, 245).

(4*S,7a*R**)- and (4*R**,7a*R**)-4-Phenylsulfonyl-2,4,5,7a-tetrahydro-1*H*-indene 130 and 131**



130

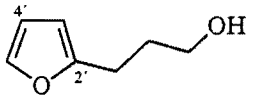


131

To a solution of the sulfinyltetraenes **128a/b** (350 mg, 1.43 mmol) in dichloromethane (50 ml) at 0 °C was added *m*-CPBA (370 mg, 67 %, 1.43 mmol). The solution was stirred for 0.5 h whilst maintaining the temperature at 0 °C. The reaction was quenched with aq. $NaHCO_3$. The reaction products were extracted (CH_2Cl_2) and the organic phase was washed (brine), dried ($MgSO_4$) and evaporated under reduced pressure. This was dissolved in dichloromethane and stirred at 30 °C for 20 min when the solvent was removed. The residue was flash chromatographed on silica gel with ethyl acetate-hexane (1:50) as eluent to yield a mixture of cycloadducts (4:1 by NMR). These were chromatographed with ethyl acetate-toluene (1:49) as eluent to afford the minor *cycloadduct* **130** (63 mg, 18 %); mp 114 – 116 °C (from ethanol); ν_{max}/cm^{-1} 1307 and 1146 (SO); δ_H (400 MHz, C_6D_6) 1.36 (1H, dq, *J* 19.5 and 3 x 9.8, 1β-H), 1.80 (1H, br m, *W* 29.5, 1α-H), 2.15 (3H, m, 2-H_2 and 5-H), 2.60 (1H, m, $W_{½}$ 36.7, 5α-H), 2.80 (1H, m, $W_{½}$ 17.5, 7a-H), 3.78 (1H, m, *W* 21.7, 4-H), 5.18 (1H, ddt, *J* 9.8, 5.0 and 2 x 2.4, 6-H), 5.41 (1H, br d, *J* 9.8, 7-H), 6.42 (1H, t, *J* 2.3, 3-H) and 7.00 – 7.78 (5H, m, SO_2Ph); (400 MHz, $CDCl_3$) 1.40 (1H, dq, *J* 19.5 and 3 x 9.8, 1β-H), 2.20 – 2.45 (5H, m, 1α-H, 2-H_2 and 5-H_2), 3.20 (1H, m, $W_{½}$ 17.5, 7a-H), 4.00 (1H, m, *W* 21.7, 4-H), 5.45 (1H, ddt, *J* 9.8, 5.0 and 2 x 2.4, 6-H), 5.41 (1H, br d, *J* 9.8, 7-H), 6.42 (1H, t, *J* 2.3, 3-H) and 7.00 – 7.78 (5H, m, SO_2Ph); δ_C (100 MHz, C_6D_6) 28.4 (C-5), 30.7 (C-1), 32.5 (C-2), 46.5 (C-7a), 61.8 (C-4), 122.6 (C-6), 126.3 (SO_2Ph), 127.9 (SO_2Ph), 128.1 (C-7), 132.2 (C-3), 133.0 (SO_2Ph) 134.1 (C-3a) and 140.0 (SO_2Ph); (Found; C, 69.1; H, 6.2; S, 12.1 %: Requires for $C_{15}H_{16}O_2S$; C, 69.2; H, 6.2; S, 12.3 %); (Found: M-SO_2Ph^+, 119. C_9H_{11} requires M, 119). This was followed by the major *cycloadduct* **131** (175 mg, 50 %); mp 76 – 78 °C (from ethanol); ν_{max}/cm^{-1} 1334 and 1148 (SO); δ_H (400 MHz) 1.40 (1H, dq, *J* 12.7 and 11.0, 1β-H), 2.20 (3H, m, 1α-H and 2-H_2), 2.53 (1H, ddq, *J* 19.5, 8.4 and 3 x 2.7, 5β-H), 3.00 (1H, ddq, *J* 19.5, 4.4 and 3 x 2.3, 5α-H), 3.38 (1H, m, $W_{½}$ 10.5, 7a-H), 4.04 (1H, d, *J* 8.4, 4β-H), 5.37 (1H, br d, *J* 2.4, 3-H), 5.57 (1H, ddt, *J* 10.0, 4.4 and 2 x 2.7, 6-H), 5.73 (1H, dq, *J* 10.0 and 3 x 2.4, 7-H) and 7.57 – 7.82 (5H, m, SO_2Ph); δ_C (100 MHz) 24.7 (t, C-5), 31.5 (t, C-1), 31.6 (t, C-2), 41.0 (d, C-7a), 62.0 (d, C-4), 121.7 (d, C-6), 128.7 (d, SO_2Ph), 128.8 (d, SO_2Ph), 131.3 (d, C-7), 132.7 (d, C-3), 133.5 (d,

SO_2Ph) 135.0 (s, C-3a) and 137.7 (s, SO_2Ph); (Found; C, 69.3; H, 6.2; S, 12.1 %: Requires for $C_{15}H_{16}O_2S$; C, 69.2; H, 6.2; S, 12.3 %); (Found: $M+H^+$, 261. $C_{15}H_{17}O_2S$ requires M+H, 261).

3-(2-Furyl)propan-1-ol 135

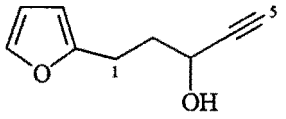


(Methoxycarbonylmethylene)triphenylphosphorane (5 g, 15 mmol) and furfural (1.2 ml, 15 mmol) were stirred in dichloromethane (20 ml) at room temperature for 1 h. Water was added and the products were extracted (CH_2Cl_2). The organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate-hexane (3:7) as eluent to yield the (*E*)-acrylate **134** (2.4 g, 100 %); ν_{max}/cm^{-1} 1706 (CO); δ_H 3.78 (3H, s, OMe), 6.28 (1H, d, *J* 15.7, 2-H), 6.45 (1H, dd, *J* 3.3 and 1.5, 5′-H) 6.60 (1H, br d, *J* 3.3, 4′-H), 7.42 (1H, d, *J* 15.7, 3-H) and 7.45 (1H, br d, *J* 1.5, 3′-H); (Found: M^+, 152. $C_8H_8O_3$ requires M, 152).

Diisobutylaluminum hydride (18 ml, 27 mmol, 1.5 M solution in toluene) was added dropwise to a solution of the ester **134** (1.97 mg, 12.9 mmol) in THF (20 ml) at 0 °C. After 30 min at 0 °C, 1M HCl was cautiously added followed by diethyl ether. The organic phase was washed (water, brine), dried ($MgSO_4$) and the solvent evaporated to yield the crude alcohol (1.42 g, 89 %); ν_{max}/cm^{-1} 3466 (OH); δ_H 4.30 (2H, br s, 1-H_2), 6.20 – 6.38 (3H, m, 2-H, 4′-H and 5′-H), 6.42 (1H, d, *J* 16.3, 3-H) and 7.34 (1H, br d, *J* 1.5, 3′-H); (Found: M^+, 124. $C_7H_8O_2$ requires M, 124).

The crude alcohol (400 mg, 3.22 mmol) dissolved in ethyl acetate (10 ml) was hydrogenated in the presence of palladium on carbon (30 mg, 10 % Pd) in a vessel which had been flushed with hydrogen. After 0.5 h, the slurry was filtered through Celite, whilst washing thoroughly with ethyl acetate. The solvent was removed under reduced pressure to yield the alcohol **135** (365 mg, 90 %) as a colourless oil; ν_{max}/cm^{-1} 3645 (CO); δ_H 1.90 (2H, tt, *J* 2 x 7.4 and 2 x 6.2 2-H_2), 2.70 (2H, t, *J* 7.4, 3-H_2), 3.70 (2H, t, *J* 6.2, 1-H_2), 6.00 (1H, dd, 3.0 and 0.8, 3′-H), 6.28 (1H, dd, *J* 3.0 and 1.6, 4′-H) and 7.30 (1H, dd, *J* 1.6 and 0.8, 5′-H); δ_C 24.4 (C-2), 31.0 (C-3), 62.0 (C-1), 105.0 (C-3′), 110.0 (C-4′), 140.9 (C-5′) and 155.4 (C-2′); (Found: M^+, 126.0677. $C_7H_{10}O_2$ requires M, 126.0681).

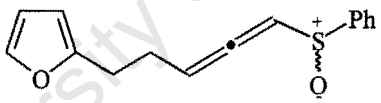
1-(2-Furyl)pent-4-yn-3-ol 136



Treatment of alcohol **135** (810 mg, 6.42 mmol) with Dess-Martin periodinane (3.27 g, 7.7 mmol) was carried out as before. Work-up gave crude aldehyde (743 mg, 93 %) as a pungent oil.

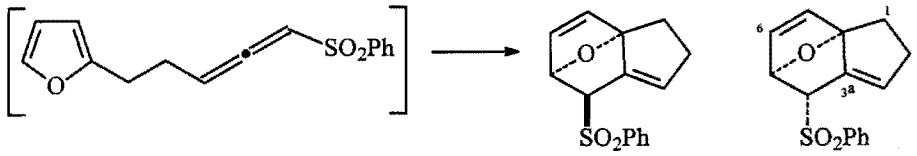
Treatment of the aldehyde (722 mg, 5.82 mmol) with ethynylmagnesium bromide (8.15 mmol), as described previously, gave *dienynol* **136** (772 mg, 88 %) as a colourless oil; ν_{max}/cm^{-1} 3687 (OH) and 3305 (C≡C); δ_H (400 MHz) 2.05 (2H, m, 2-H_2), 2.48 (1H, d, *J* 2.1, 5-H), 2.80 (2H, t, *J* 7.6, 1-H_2), 4.40 (H, br m, 3-H), 6.00 (1H, dd, 3.1 and 0.9, 5′-H), 6.28 (1H, dd, *J* 3.1 and 1.8, 4′-H) and 7.31 (1H, dd, *J* 1.8 and 0.9, 3′-H); δ_C (100 MHz) 23.5 (C-1), 35.8 (C-2), 61.4 (C-3), 73.3 (C-5), 84.3 (C-4), 105.3 (C-3′), 110.0 (C-4′), 141.0 (C-5′) and 154.7 (C-2′); (Found: M^+, 150. $C_9H_{10}O_2$ requires M, 150).

(*S*-*R)- and (*S*-*S**)-5-(2-Furyl)-1-phenylsulfinylpenta-1,2-diene 137a and 137b**



Treatment of alcohol **136** (50 mg, 0.33 mmol) with triethylamine (50 μl, 0.37 mmol) and benzenesulfenyl chloride (38 μl, 0.37 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:7)] gave a mixture of *phenylsulfinylallenyl* diastereomers **137a** + **137b** (42 mg, 49 %) as a colourless oil; ν_{max}/cm^{-1} 1951 (C=C=C) and 1036 (SO); δ_H (400 MHz) 2.45 (2H, m, $W_{½}$ 10.8, 4-H_2), 2.75 (2H, t, *J* 7.5, 5-H_2) 5.75 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.02 (1H, dq, 3.1 and 0.9, 5′-H), 6.05 (1H, dt, *J* 6.2 and 2 x 3.1, 1-H), 6.27 (1H, dd, *J* 3.1 and 1.8, 4′-H), 7.30 (1H, dd, *J* 1.8 and 0.9, 3′-H) and 7.52 – 7.62 (5H, m, SOPh); δ_C (100 MHz) 26.8 (C-4) 27.1 (C-5), 98.1 (C-1), 103.2 (C-3), 105.7 (C-3′), 110.2 (C-4′), 124.3 (SOPh), 129.2 (SOPh), 131.0 (SOPh), 141.2 (C-2′), 144.8 (SOPh), 154.2 (C-5′) and 203.6 (C-2); (Found: M^+, 258. $C_{15}H_{14}O_2S$ requires M, 258).

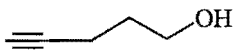
($4R^*,5R^*,7aS^*$) and ($4S^*,5R^*,7aS^*$)-4-Phenylsulfonyl-5,7a-epoxy-2,4,5,7a-tetra-hydro-1*H*-indene 139 and 140



139 **140**

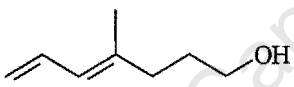
The phenylsulfinylallenyl diastereomers **137a** + **137b** (230 mg, 0.89 mmol) in dichloromethane (30 ml) at -10 °C were treated with *m*-CPBA (230 mg, 67 %, 0.89 mmol) for 30 min. The reaction was quenched with aq. $NaHCO_3$ containing ice. The mixture was extracted (CH_2Cl_2) and the organic phase was washed (brine), dried ($MgSO_4$) and evaporated under reduced pressure. The temperature was maintained at 0 °C during the work up. A ^1H NMR spectrum of the reaction mixture showed the presence of 3 species in the spectrum in the ratio 10:2:1. The major component **140** was isolated (see below) whilst the remaining two compounds were identified as the allenyl sulfone **138**; δ_H (400 MHz) 2.45 (2H, m, 4-H_2) 2.70 (2H, t, *J* 7.5, 5-H_2) 5.87 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.00 (1H, dq, 3.1 and 0.9, 5′-H), 6.20 (1H, dt, *J* 6.2 and 2 x 3.1, 1-H), 6.27 (1H, dd, *J* 3.1 and 1.8, 4′-H), 7.30 (1H, dd, *J* 1.8 and 0.9, 3′-H) and 7.50 – 7.90 (5H, m, SO_2Ph) and cycloadduct **139**; 4.42 (1H, d, *J* 3.6, 4-H), 5.30 (1H, dd, *J* 3.6 and 1.7, 5-H), 5.45 (1H, m, 3-H), 6.54 (1H, d, *J* 5.6, 7-H) and 6.57 (1H, dd, *J* 5.6 and 1.7, 6-H). The residue was flash chromatographed on silica gel with ether-hexane (3:2) as eluent to yield cycloadduct **140** (150 mg, 63 %); mp 87 – 90 °C (from dichloromethane-ether); ν_{max}/cm^{-1} 1307 and 1141 (SO); δ_H (400 MHz) 1.85 (1H, ddd, *J* 13.9, 9.6 and 8.2, 1β-H), 2.28 (1H, ddd, *J* 13.9, 7.4, and 1.6, 1α-H), 2.70 – 2.90 (2H, m, 2-H_2), 3.65 (1H, dt, *J* 3.4 and 2 x 1.9, 4-H), 5.38 (1H, d, *J* 2.1, 5-H), 5.75 (1H, dt, *J* 3.3 and 2 x 1.9, 3-H), 6.41 (1H, dd, *J* 5.7 and 2.1, 6-H), 6.50 (1H, d, *J* 5.7, 7-H) and 7.55 – 7.87 (5H, m, SO_2Ph); δ_C (100 MHz) 26.3 (t, C-1), 37.1 (t, C-2), 66.7 (d, C-4), 83.8 (d, C-5), 101.1 (s, C-7a), 124.4 (d, C-3), 128.7 (d, SO_2Ph), 129.5 (d, SO_2Ph), 133.8 (d, SO_2Ph), 135.0 (d, C-6), 137.8 (s, C-3a) and 137.8 (SO_2Ph) and 140.3 (d, C-7); (Found; C, 66.1; H, 5.1; S, 11.4 %: M^+, 274. Requires for $C_{15}H_{14}O_3S$: 274; C, 65.7; H, 5.1; S, 11.7 %).

Pent-4-yn-1-ol 141



Tetrahydrofurfuryl chloride (2.4 ml, 22.5 mmol) was added to a solution of sodium amide [prepared from sodium (1.66 g, 72 mmol) and anhydrous $FeCl_3$ (116 mg, 0.72 mmol) in refluxing dry ammonia (~15 ml) stirred for 2 h]. The solution was stirred for 1 h, after which excess solid NH_4Cl was cautiously added, followed by Et_2O. After a further 30 min of stirring, the solution was poured into water. The organic phase was washed (1 M HCl, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The resulting oil was purified by Kugelrhor distillation (25 mm Hg, 120 °C) to yield the alcohol **141** (1.62 g, 98 %) as an oil, which was used directly. ^1H NMR showed the presence of pent-4-en-1-ol (~ 5 % by NMR) as contaminant.

(4*E*)-4-Methylhepta-4,6-dien-1-ol 143



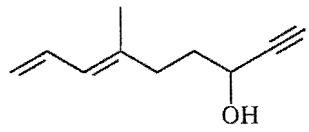
Trimethylaluminum (32 ml, 64 mmol, 2M solution in toluene) was added dropwise to a stirred slurry of Cp_2ZrCl_2 (6.26 g, 21.4 mmol) in dichloromethane (80 ml). The solution was cooled to -15 °C, at which point the alcohol **141** (2 ml, 21.4 mmol) was added in dichloromethane (10 ml). The reaction was then stirred for 16 h at room temperature.

The solution was cooled to -30 °C and iodine (8.2 g, 32 mmol) in THF (20 ml) was added. After 1 h, water was added dropwise (CAUTION!!! - violently exothermic). The mixture was extracted (Et_2O) and the organic phase was washed (1M HCl, $NaHCO_3$, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The product was chromatographed on silica gel using ether-dichloromethane (3:97) as eluent to yield iodide **142** (3.65 g, 75 %) as a yellow oil.

Vinyltributyltin (3.7 ml, 12.7 mmol) in dimethylformamide (DMF) (5 ml) and iodide **142** (2.86 g, 12.7 mmol) in DMF (5 ml) were sequentially added to a stirred solution of bis(triphenylphosphine)palladium chloride (210 mg, 0.63 mmol) in DMF (30 ml) at room temperature. After 18 h stirring, NH_4OH (50 ml, 10 % solution) was added and the solution stirred for a further 30 min. Et_2O was added and the solution repeatedly washed with brine. The

organic phase was dried ($MgSO_4$), the solvent evaporated, and the residue chromatographed on silica gel with ether-dichloromethane (2:48) as eluent to yield the (*E*)-diene **143** (1.46 g, 91 %). Yields and spectroscopic data were in agreement with literature values.[126]

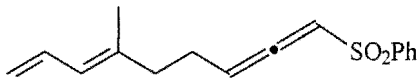
(6*E*)-6-Methylnona-6,8-dien-1-yn-3-ol 144



Oxidation of alcohol **143** (220 mg, 1.74 mmol) with Dess-Martin periodinane (810 mg, 1.91 mmol) was carried out as before to give crude aldehyde (225 mg).

Treatment of the aldehyde with ethynylmagnesium bromide (3.32 mmol), as described previously, followed by chromatography [silica gel, ethyl acetate-hexane (1:5)] gave *dienynol* **144** (181 mg, 74 % over two steps); ν_{max}/cm^{-1} 3687 (OH) and 3305 (C≡C); δ_H (400 MHz) 1.78 (3H, br s, 6-Me), 1.86 (2H, m, 4-H_2), 2.26 (2H, t, *J* 7.8, 5-H_2), 2.48 (1H, d, *J* 2.0, 1-H), 4.37 (1H, m, 3-H), 5.00 (1H, br d, *J* 10.6, 9-H_{cis}), 5.12 (1H, dd, *J* 16.9 and 1.8, 9-H_{trans}), 5.90 (1H, dd, *J* 10.6 and 0.9, 7-H) and 6.58 (1H, dt, *J* 16.9 and 2 x 10.6, 8-H); δ_C (100 MHz) 16.6 (C-Me), 35.0, 35.6 (C-4 and C-5), 61.8 (C-3), 73.2 (C-1), 84.6 (C-2), 115.2 (C-9), 126.1 (C-8), 133.0 (C-6) and 138.0 (C-7); (Found: M^+, 150.1035. $C_{10}H_{14}O$ requires M, 150.1044).

(6*E*)-6-Methyl-1-phenylsulfonylnona-1,2,6,8-tetraene 145

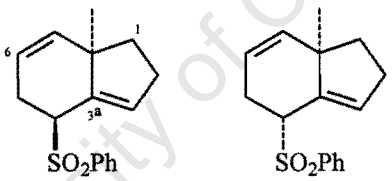


Treatment of alcohol **144** (73 mg, 0.49 mmol) with triethylamine (63 µl, 0.49 mmol) and benzenesulfenyl chloride (56 µl, 0.49 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:4)] gave a mixture of *phenylsulfinylallenyl* diastereomers (72 mg, 57 %); ν_{max}/cm^{-1} 1949 (C=C=C) and 1037 (SO); δ_H (400 MHz) 1.75 (3H, s, 6-Me), 2.15 – 2.30 (4H, m, 4-H_2 and 5-H_2), 5.02 (1H, br d, *J* 9.9, 9-H_{cis}), 5.12 (1H, m, 9-H_{trans}), 5.60 (1H, m, 3-H), 5.85 (1H, m, 7-H), 6.05 (1H, dt, *J* 5.7 and 2 x 2.7, 1-H), 6.30 (1H, m, 8-H) and 7.50 – 7.65 (5H, m, SOPh); δ_C (100 MHz) 16.5 (Me), 26.5 (C-4), 38.5 (C-5), 98.6 (C-1), 103.0 (C-3), 115.4 and

115.6 (C-9), 124.2 and 124.3 (SOPh), 126.6 (C-7), 129.2 (SOPh), 130.9 and 131.0 (SOPh), 133.0 and 132.9 (C-8), 137.3 (C-6), 144.9 (SOPh) and 203.5 (C-2); (Found: M^+, 258.1066. $C_{16}H_{18}OS$ requires M, 258.1078).

Oxidation of the sulfinyl tetraenes **144** (150 mg, 0.58 mmol) with *m*-CPBA (150 mg, 67 %, 0.58 mmol) at 0 °C, followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:5)] gave *sulfonyl tetraene* **145** (79 mg, 50 %); ν_{max}/cm^{-1} 1956 (C=C=C), 1320 and 1148 (SO); δ_H (400 MHz) 1.72 (3H, s, 6-Me), 2.16 (2H, t, *J* 7.6, 5-H_2), 2.28 (2H, m, 4-H_2), 5.02 (1H, br d, *J* 10.5, 9-H_{cis}), 5.08 (1H, dd, *J* 16.9 and 2.0, 9-H_{trans}), 5.85 (2H, m, 7-H), 5.87 (1H, td, *J* 2 x 6.9 and 6.0, 3-H), 6.20 (1H, dt, *J* 6.0 and 2 x 3.0, 1-H), 6.54 (1H, dt, *J* 16.9 and 2 x 10.5, 8-H) and 7.50 – 7.95 (5H, m, SO_2Ph); δ_C (100 MHz) 16.5 (Me), 26.0 (C-4), 38.2 (C-5), 100.5 (C-1), 101.5 (C-3), 115.6 (C-9), 126.6 (C-7), 127.6 (SO_2Ph), 129.1 (SO_2Ph), 132.9 (C-8), 133.4 (SO_2Ph), 137.1 (C-6), 141.4 (SO_2Ph) and 205.6 (C-2); (Found: M^+, 274. $C_{16}H_{18}O_2S$ requires M, 274).

(4*S,7a*R**)- and (4*R**,7a*R**)-7a-Methyl-4-phenylsulfonyl-2,4,5,7a-tetrahydro-1*H*-indene 146 and 147**

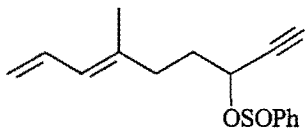


146 **147**

The tetraene **145** (60 mg, 0.21 mmol) was dissolved in toluene (2 ml). The solution was sealed under nitrogen and was heated at 150 °C for 2 h. The solvent was removed and NMR analysis of the residue revealed 3 products in the ratio of 2:7:1. These were chromatographed using silica gel with ethyl acetate-toluene (1:99) as eluent to yield the *endo cycloadduct* **146** (8 mg, 13 %) as an oil; ν_{max}/cm^{-1} 1307 and 1146 (SO); δ_H (400 MHz) 1.60 (3H, s, 7a-Me), 1.69 (1H, td, *J* 2 x 12.3 and 9.6, 1β-H), 1.78 (1H, ddd, *J* 12.3, 7.1 and 1.4, 1α-H), 2.20 (1H, dtd, *J* 16.4, 2 x 5.3 and 1.4, 5-H), 2.38 (1H, m, 2-H), 2.50 – 2.70 (2H, m, 2-H and 5-H), 3.92 (1H, m, *W* 20.7, 4-H), 5.38 (1H, ddd, *J* 9.9, 5.3 and 2.3, 6-H), 5.65 (1H, dd, *J* 9.9 and 2.7, 7-H), 6.10 (1H, br d, *J* 1.8, 3-H) and 7.40 – 7.80 (5H, m, SO_2Ph); δ_C (100 MHz) 24.8 (Me), 28.5 (C-5), 30.3 (C-1), 37.7 (C-2), 49.4 (C-7a), 59.9 (C-4), 119.7 (C-6), 124.3 (SO_2Ph), 128.5 (SO_2Ph), 129.1 (SO_2Ph), 133.6 (C-3), 137.6 (C-7), 138.7 (s, SO_2Ph) and 138.7 (C-3a); (Found: M^+, 274.1012. $C_{16}H_{18}O_2S$ requires M,

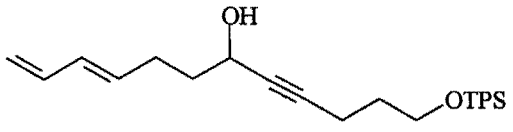
274.1023). This was followed by the *exo cycloadduct* **147** (27 mg, 45 %) as a gum; ν_{max}/cm^{-1} 1306 and 1146 (SO); δ_H (400 MHz) 1.15 (3H, s, 7a-Me), 1.75 (1H, td, *J* 2 x 11.7 and 8.7, 1β-H), 1.83 (1H, dd, *J* 11.7 and 6.7, 1α-H), 2.18 (1H, ddd, *J* 16.5, 8.7 and 3.5, 2β-H), 2.45 (2H, m, 2α-H and 5-H), 2.75 (1H, br d, *J* 18.3, 5-H), 4.14 (1H, m, *W* 16, 4-H), 5.55 (1H, dt, *J* 10.0 and 2 x 3.7, 6-H), 5.60 (1H, m, $W_{½}$ 1.7, 3-H), 5.82 (1H, br d, *J* 10.0, 7-H) and 7.50 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 23.5 (q, Me), 23.8 (t, C-5), 29.6 (t, C-1), 40.9 (t, C-2), 46.0 (s, C-7a), 61.6 (d, C-4), 120.0 (d, C-6), 128.9 (d, SO_2Ph), 129.2 (d, SO_2Ph), 133.3 (d, C-3), 133.5 (d, SO_2Ph), 137.7 (s, C-3a), 138.0 (d, C-7) and 138.3 (s, SO_2Ph); (Found: M^+, 274.1008. $C_{16}H_{18}O_2S$ requires M, 274.1023).

(6*E*)-6-Methylnona-6,8-dien-1-yn-3-yl benzenesulfinate 148



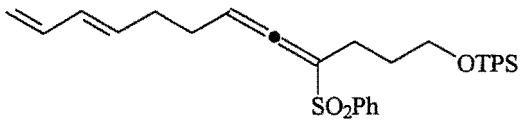
Pyridine (3 μl, 0.35 mmol) and benzenesulfinyl chloride (28 μl, 0.35 mmol) were sequentially added to a solution of the alcohol **144** (53 mg, 0.35 mmol) in THF (3 ml) at -78 °C and the resulting solution stirred for 30 min. HCl (1M) was added, the mixture extracted (Et_2O), and the organic phase washed ($NaHCO_3$, water, brine) and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed on silica gel using ethyl acetate-hexane (1:6) as eluent to yield *sulfinate ester* **148** (75 mg, 78 %); ν_{max}/cm^{-1} 3305 (C≡C) and 1146 (SO); δ_H (400 MHz) 1.76 (3H, s, 6-Me), 2.00 (2H, m, 4-H_2), 2.24 (2H, t, *J* 7.8, 5-H_2), 2.40 (1H, d, *J* 2.1, 1-H), 4.90 (1H, td, *J* 2 x 6.6 and 2.1, 3-H), 5.00 (1H, dd, *J* 10.3 and 2.2, 9-H_{cis}), 5.10 (1H, br d, *J* 16.8, 9-H_{trans}), 5.85 (2H, br d, *J* 10.4 and 1.3, 7-H), 6.54 (1H, dt, *J* 16.8 and 2 x 10.4, 8-H) and 7.56 – 7.78 (5H, m, SOPh); δ_C (100 MHz) 16.6 (Me), 34.6, 34.9 (C-4 and C-5), 65.3 (C-3), 75.5 (C-1), 80.7 (C-2), 115.4 (C-9), 125.4 (SOPh), 126.4 (C-7), 129.0 (SOPh), 132.3 (C-8), 137.0 (SOPh), 137.3 (C-6) and 144.9 (SOPh); (Found: $M+H^+$, 275. $C_{16}H_{19}O_2S$ requires M, 275).

(*9E*)- 1-(*t*-Butyldiphenylsilyloxy)-dodeca-9,11-dien-4-yn-6-ol 150



1-*t*-Butyldiphenylsilyloxy-pent-4-yne (0.9 g, 2.8 mmol) was added to a solution of ethylmagnesium bromide [prepared by treatment of magnesium (62 mg, 2.6 mmol) with bromoethane (0.2 ml, 2.6 mmol) in THF (5 ml), in the presence of iodine (catalytic) and stirring for 1 h]. The aldehyde **124a** (330 mg, 3 mmol) was added and the resulting solution was stirred at room temperature for 30 min. Saturated aq. NH_4Cl was added and the product extracted (Et_2O). The extract was washed (dil. HCl, water, brine), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with ethyl acetate-hexane (1:9) as eluent to afford the starting material (730 mg, 81 %) followed by **150** (149 mg, 14 %) as a colourless oil; ν_{max}/cm^{-1} 3674 (OH) and 2228 (C≡C); δ_H (400 MHz) 1.05 (9H, s, Bu^t), 1.60 (4H, m, 2-H_2 and 7-H_2), 2.24 (2H, q, *J* 6.6, 8-H_2), 2.36 (1H, td, *J* 2 x 7.0 and 2.0, 3-H_2), 3.74 (2H, t, *J* 6.0, 1-H_2), 4.36 (1H, m, 6-H), 4.95 (1H, br d, *J* 10.2, 12-H_{cis}), 5.10 (1H, dd, *J* 17.1 and 1.1, 12-H_{trans}), 5.70 (1H, dt, *J* 15.1 and 2 x 6.6, 9-H), 6.10 (1H, dd, *J* 15.1 and 10.2, 10-H), 6.32 (1H, dt, *J* 17.1 and 10.2, 11-H) and 7.40 – 7.70 (10H, m, Ph); δ_C (100 MHz) 15.1 (C-2), 19.2 (*C*Me_3), 26.8 (C*Me*$_3$), 28.2 (C-8), 31.4 (C-3), 37.3 (C-7), 62.0, 62.3 (C-1 and C-6), 81.1 (C-4), 85.3 (C-5), 115.1 (C-12), 127.6 (Ph), 129.5 (Ph), 131.5 (C-10), 133.7 (C-9), 133.8 (Ph), 135.5 (Ph) and 137.0 (C-11); (Found: *M-Bu*$_t^+$, 375. $C_{24}H_{27}O_2Si$ requires M, 375).

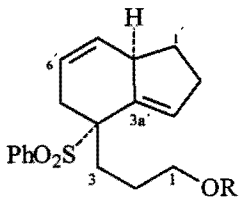
(9*E*)-1-(*t*-Butyldiphenylsilyloxy)-4-phenylsulfonyldodeca-4,5,9,11-tetraene 151



Treatment of alcohol **150** (130 mg, 0.30 mmol) with triethylamine (42 μl, 0.30 mmol) and benzenesulfenyl chloride (35 μl, 0.30 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:10)] gave the presumed mixture of *phenylsulfinylallenyl* diastereomers (110 mg, 68 %); ν_{max}/cm^{-1} 1956 (C=C=C) and 1045 (SO); δ_H (400 MHz) 0.95 (9H, s, Bu^t), 3.58 (2H, m, 1-H_2), 4.95 (1H, m, 12-H_{cis}), 5.10 (1H, m, 12-H_{trans}), 5.66 (2H, m, 6-H and 9-H), 6.07 (1H, m, 10-H), 6.28 (1H, m, 11-H) and 7.40 – 7.70 (15H, m, Ph) as a colourless oil, which were used directly in the next step.

Oxidation of sulfinyl tetraenes (98 mg, 0.18 mmol) with *m*-CPBA (46 mg, 67 %, 0.18 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:10)], gave *phenylsulfonylallene* **151** (71 mg, 70 %); ν_{max}/cm^{-1} 1960 (C=C=C), 1306 and 1149 (SO); δ_H (400 MHz) 1.10 (9H, s, Bu^t), 2.16 (2H, m, 8-H_2), 2.38 (1H, td, *J* 2 x 7.0 and 2.0, 3-H_2), 3.60 (2H, t, *J* 6.2, 1-H_2), 4.95 (1H, br d, *J* 10.2, 12-H_{cis}), 5.10 (1H, dd, *J* 17.1 and 1.1, 12-H_{trans}), 5.65 (1H, dt, *J* 15.1 and 2 x 7.0, 9-H), 5.70 (1H, m, 6-H), 6.02 (1H, dd, *J* 15.1 and 10.2, 10-H), 6.28 (1H, dt, *J* 17.1 and 10.2, 11-H) and 7.30 – 7.70 (15H, m, Ph); δ_C (100 MHz) 19.1 (C-2), 23.3 (CMe_3), 26.8 (CMe_3), 27.7 (C-7), 30.5, 31.3 (C-3 and C-8), 62.5, (C-1), 100.7 (C-6), 113.7 (C-4), 115.6 (C-12), 122.8, 127.6, 128.0, 129.5 (Ph), 130.5 (C-10), 132.1 (Ph), 133.0, 133.2 (Ph), 133.7 (C-9), 135.5 (Ph), 136.7 (C-11), 140.4 (Ph) and 203.8 (C-5); (Found (Electrospray): $M+Na^+$, 579. $C_{34}H_{40}O_3NaSSi$ requires M, 579).

(4′*R,7a′*R**) 1-(*t*-Butyldiphenylsilyloxy)-3-(4′-phenylsulfonyl-2′,4′,5′,7a′-tetrahydro-1′*H*-inden-4′-yl)propane and (4′*R**,7a′*R**)-3-(4′-phenylsulfonyl-2′,4′,5′,7a′-tetrahydro-1′*H*-inden-4′-yl)propan-1-ol 152 and 153**

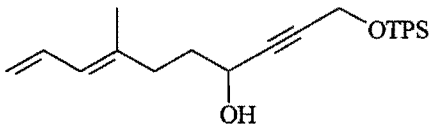


152 R = TBDPS
153 R = H

The tetraene **151** (57 mg, 0.1 mmol) in $CDCl_3$ (2 ml) was heated in a sealed NMR tube at 50 °C for 2 h. The reaction was deemed complete (by NMR) and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-toluene (1:49) as solvent to yield the cycloadduct **152** (43 mg, 75 %); ν_{max}/cm^{-1} 1308 and 1141 (SO); δ_H (400 MHz) 0.95 (9H, s, Bu^t), 1.00 (3H, m, 1′β-H and 3-H_2), 1.40 (2H, m, 2-H_2), 1.98 (1H, ddd, *J* 9.9, 6.5 and 3.0, 1′α-H), 2.25 (3H, m, 2′-H_2 and 5′-H), 3.00 (1H, dt, 18.7 and 2 x 2.5, 5′-H), 3.25 (1H, br, $W_{½}$ 14, 7a′-H), 3.60 (2H, m, 1-H_2), 5.40 (1H, br s, 3′-H), 5.63 (1H, ddd, *J* 9.9, 7.4 and 2.5, 6′-H), 5.70 (1H, br d, *J* 9.9, 7′-H) and 7.35 – 7.80 (15H, m, Ph); δ_C (100 MHz) 19.2 (s, *C*Me_3), 26.6, (t, C-3), 26.8 (q, C-C(*Me*$_3$)$_3$), 28.6 (t, C-5′), 31.2 (t, C-1′), 31.7 (t, C-2′), 31.9 (t, C-2), 43.4 (d, C-7a′), 63.6 (t, C-1), 67.5 (s, C-4′), 122.9 (d, C-6′), 127.6, 128.2, 129.6 (d, Ph), 131.8 (d, C-7′), 132.0 (d, Ph), 133.4 (d, C-3′), 133.7 (s, Ph), 134.8 (d, Ph), 135.2 (s, C-3a′) and 135.5, 137.6 (s, Ph); (Found (Electrospray): *M*+*Na*$^+$, 579. $C_{34}H_{40}O_3NaSSi$ requires M, 579).

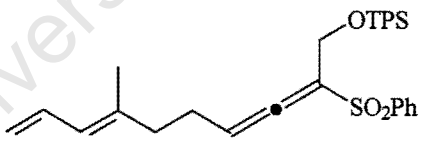
Tetrabutylammonium fluoride (1 ml, 1M, 95 % solution in THF) was added to a solution of the cycloadduct **152** (40 mg, 72 μmol) in THF (2 ml) and the resulting solution was stirred for 30 min at room temperature. Saturated NH_4Cl was added and the mixture was extracted (Et_2O). The extract was washed (water, brine), dried ($MgSO_4$) and evaporated to yield the *alcohol* **153** (10 mg, 44 %); ν_{max}/cm^{-1} 3620 (OH), 1297 and 1141 (SO); δ_H (400 MHz) 1.00 (2H, m, 3-H_2), 1.40 (2H, m, 2-H_2), 1.98 (2H, m, 1′- and 2′-H), 2.25 (3H, m, 1′-,2′- and 5′-H), 3.00 (1H, dq, 18.7 and 2.5, 5′-H), 3.25 (1H, br m, $W_{½}$ 12, 7a′-H), 3.60 (2H, m, 1-H_2), 5.40 (1H, br s, 3-′H), 5.63 (1H, ddd, *J* 9.9, 7.4 and 2.5, 6′-H), 5.70 (1H, br d, *J* 9.9, 7′-H) and 7.35 – 7.80 (5H, m, *Ph*); δ_C (100 MHz) 27.3 (C-3), 29.0 (C-5′), 31.1 (C-1′), 31.7 (C-2′), 32.0 (C-2), 43.5 (C-7a′), 62.9 (C-1), 67.5 (C-4′), 122.8 (C-6′), 128.3, 130.6 (Ph), 131.7 (C-7′), 132.0 (Ph), 133.5 (C-3′), 135.5 (C-3a′) and 137.8 (Ph); (Found: M^+, 314.0980. $C_{18}H_{18}O_3S$ requires M, 314.0972).

(7*E*) 1-(*t*-Butyldiphenylsilyloxy)-7-methyldeca-7,9-dien-2-yn-4-ol 154



The aldehyde **143a** (300 mg, 2.4 mmol) was added to a solution of *t*-butyldiphenylsilyloxy-prop-2-yne (705 mg, 2.4 mmol) and *n*-BuLi (0.95 ml, 2.4 mmol, 2.5M solution in hexanes) in THF (20 ml) at -78 °C. After 1 h, 1M HCl was added and the mixture was then extracted (Et_2O). The organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with ethyl acetate-hexane (1:9) as eluent to yield the *dienynol* **154** (420 mg, 42 %); ν_{max}/cm^{-1} 3603 (OH) and 2252 (C≡C); δ_H (400 MHz) 1.05 (9H, s, Bu^t), 1.72 (2H, m, 5-H_2), 1.74 (3H, s, 7-Me), 2.18 (2H, t, *J* 7.8, 6-H_2), 4.27 (1H, br, *W* 10, 4-H), 4.38 (2H, d, *J* 1.6, 1-H_2), 4.98 (1H, br d, *J* 10.6, 10-H_{cis}), 5.09 (1H, dd, *J* 16.7 and 1.8, 10-H_{trans}), 5.85 (1H, br d, *J* 10.9, 8-H), 6.56 (1H, dt, *J* 16.7 and 2 x 10.6, 9-H) and 7.40 – 7.70 (10H, m, Ph); δ_C (100 MHz) 16.6 (Me), 19.2 (*C*Me_3), 26.7 (C*Me*$_3$), 35.0, 35.6 (C-5 and C-6), 52.7 (C-1), 62.0 (C-4), 83.6 (C-2), 86.0 (C-3), 115.1 (C-10), 126.0 (C-8), 127.7 (Ph), 129.8 (Ph), 133.0 (C-9), 133.3 (Ph), 135.7 (Ph) and 138.3 (C-7); (Found: *M*-Bu_t^+, 361. $C_{23}H_{25}O_2Si$ requires M, 361).

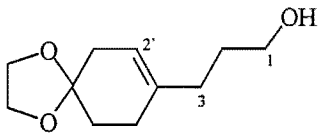
(7*E*)-1-(*t*-Butyldiphenylsilyloxy)-2-phenylsulfonyl-7-methyldeca-2,3,7,9-tetraene 155



Treatment of alcohol **154** (400 mg, 0.98 mmol) with triethylamine (0.14 ml, 0.98 mmol) and benzenesulfenyl chloride (0.11 ml, 0.98 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:5)], gave *sulfinyl tetraenes* (150 mg, 28 %) as a colourless oil; ν_{max}/cm^{-1} 1956 (C=C=C) and 1038 (SO); δ_H (400 MHz) 0.93 (9H, s, Bu^t), 1.71, 1.73 (3H, s, 7-Me), 4.20 (1H, m, 1-H), 4.43 (1H, m,1-H), 4.98 (1H, br m, 10-H_{cis}), 5.09 (1H, br m, 10-H_{trans}), 5.65 (1H, m, 3-H), 5.85 (1H, br m, 8-H), 6.52 (1H, br m, 9-H) and 7.30 – 7.60 (15H, m, Ph); (Found: M^+, 469. $C_{29}H_{29}O_2SiS$ requires M, 469).

Oxidation of sulfinyl tetraenes (130 mg, 0.25 mmol) with *m*-CPBA (65 mg, 67 %, 0.25 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:10)] gave *sulfonyl tetraene* **155** (64 mg, 48 %) as a colourless oil; ν_{max}/cm^{-1} 1959 (C=C=C), 1307 and 1151 (SO); δ_H (400 MHz) 0.93 (9H, s, Bu^t), 1.72 (3H, s, 7-Me), 2.12 (2H, t, *J* 7.8, 6-H_2), 2.25 (2H, m, 5-H_2), 4.48 (2H, m, 1-H_2), 4.98 (1H, br d, *J* 10.6, 10-H_{cis}), 5.10 (1H, dd, *J* 16.7 and 1.8, 10-H_{trans}), 5.80 (2H, m, 4-H and 8-H), 6.53 (1H, dt, *J* 16.7 and 2 x 10.6, 9-H) and 7.30 – 7.90 (15H, m, Ph); δ_C (100 MHz) 16.5 (C-Me), 19.1 (CMe_3), 26.2 (C-5), 26.6 (CMe_3), 38.4 (C-6), 60.3 (C-1), 100.8 (C-4), 113.4 (C-2), 115.5 (C-10), 126.5 (C-8), 127.7, 127.8, 129.8, 132.7 (Ph), 132.9 (C-9), 133.1 (Ph), 133.3 (Ph), 135.4 (Ph), 137.4 (C-7) and 205.3 (C-3); (Found: M^+, 542. $C_{33}H_{38}O_3SiS$ requires M, 542).

3-(4,4-Ethylenedioxycyclohex-1-en-1-yl)propan-1-ol 160

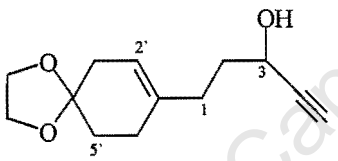


Borane-dimethyl sulfide (10 ml, 165 mmol) was added to a solution of 4-allylanisole (20 g, 135 mmol) in ether (200 ml) at room temperature and the resulting mixture was stirred for 30 min. The solution was cooled to 0 °C and aq. sodium hydroxide (40 ml, 4 M, 160 mmol, CAUTION – violently exothermic) and hydrogen peroxide (25 ml, 30 %) were sequentially added. The mixture was extracted (EtOAc), and the combined extract was washed (water, brine) and dried ($MgSO_4$). The residue was distilled (100 °C, 0.2 mm Hg, lit. 164 – 168 °C, 18 mm Hg) to yield 3-(4-anisyl)propan-1-ol **158** (15.1 g, 67 %) as a colourless oil whose spectroscopic and physical properties were identical those reported in the literature.[153]

Ammonia (30 ml) and ethanol (20 ml) were stirred in a 3-necked round bottomed flask fitted with a dry ice condenser and drying tube. 3-(4-Anisyl)propan-1-ol **158** (830 mg, 5 mmol) in THF (10 mmol) was added, followed by sodium (1 g, 43 mmol, in small portions). The solution was stirred for 0.5 h after which NH_4Cl (s) was added and the ammonia was allowed to evaporate. The remaining solvent was evaporated and the residue redissolved (dichloromethane). This was washed (water), dried ($MgSO_4$) and evaporated under reduced pressure to yield the alcohol **159** (783 mg, 93 %) as a viscous oil, which was used directly.

Ethylene glycol (0.66 ml, 10 mmol) and $BF_3.OEt_2$ (0.2 ml, 1.6 mmol) were added sequentially to a solution of the alcohol **159** (700 mg, 4.06 mmol) in THF (20 ml) at 0 °C, and the resulting solution was stirred for 1 h. This was poured into iced saturated $NaHCO_3$ and the product was extracted (dichloromethane). The combined extract was washed (water, brine) and dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with ethyl acetate-hexane (2:3) as eluent to yield the *ketal* **160** (489 mg, 61 %); ν_{max}/cm^{-1} 3621 (OH); δ_H (400 MHz) 1.70 (2H, m, 2-H_2), 1.74 (2H, t, *J* 6.7, 6′-H_2), 2.07 (2H, t, *J* 7.2, 3-H_2), 2.18 (2H, m, 5′-H_2), 2.24 (2H, br s, 3′-H_2), 3.62 (2H, t, *J* 6.4, 1-H_2), 3.95 (4H, s, O-$(CH_2)_2$O) and 5.35 (1H, br s, 2′-H); δ_C (100 MHz) 27.5 (t, C-5′), 30.6 (t, C-2), 31.1 (t, C-6′), 33.6 (t, C-3), 35.6 (t, C-3′), 62.8 (t, C-1), 64.4 (t, O$(CH_2)_2$O), 108.1 (s, C-4′), 118.5 (d, C-2′) and 137.1 (s, C-1′); (Found: M^+, 198.1250. $C_{11}H_{18}O_3$ requires M, 198.1250).

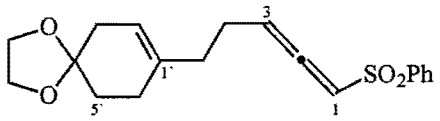
1-(4,4-Ethylenedioxycyclohex-1-en-1-yl)pent-4-yn-3-ol 161



Oxidation of the alcohol **160** (470 mg, 2.37 mmol), using Dess-Martin periodinane (1.31 g, 3 mmol) in dichloromethane (30 ml) at room temperature, was carried out as before to yield the crude aldehyde (412 mg, 89 %) as an oil which was used directly in the next step.

Treatment of the aldehyde with ethynylmagnesium bromide (4.3 mmol), as described previously, gave *ynol* **161** (276 mg, 59 %); ν_{max}/cm^{-1} 3691 (OH) and 3305 (C≡C); δ_H (400 MHz) 2.44 (1H, d, *J* 2.1, 5-H), 3.95 (4H, s, O-$(CH_2)_2$O), 4.45 (1H, td, *J* 2 x 6.4 and 2.1, 3-H) and 5.35 (1H, br, *W* 10.2, 2′-H); δ_C (100 MHz) 27.5 (C-5′), 31.1 (C-6′), 32.4 (C-1), 35.4 (C-2), 35.6 (C-3′), 62.0 (C-3), 64.4 (O$(CH_2)_2$O), 73.0 (C-5), 84.7 (C-4), 108.1 (C-4′), 119.0 (C-2′) and 136.4 (C-1′); (Found: M^+, 222. $C_{13}H_{18}O_3$ requires M, 222).

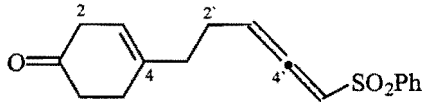
5-(4,4-Ethylenedioxycyclohex-1-en-1-yl)-1-phenylsulfonylpenta-1,2-diene 162



Treatment of the alkynol **161** (900 mg, 4.05 mmol) with triethylamine (0.85 ml, 6.08 mmol) and freshly prepared benzenesulfenyl chloride (0.58 ml, 5 mmol) in dichloromethane (40 ml) at -78 °C, using the same procedure as before gave *sulfinyl trienes* (1.07 g, 80 %); ν_{max}/cm^{-1} 1949 (C=C=C) and 1067 (SO); δ_H (400 MHz) 3.95 (4H, s, $O(CH_2)_2O$), 5.31 (1H, m, 2′-H), 5.66, 5.74 (1H, m, 1-H), 6.05 (1H, m, 3-H) and 7.20 – 7.70 (5H, m, SOPh); (Found: M^+, 330. $C_{19}H_{22}O_3S$ requires M, 330).

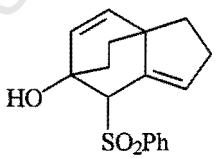
Oxidation of the sulfinyl trienes (1.07 g, 3.24 mmol) with *m*-CPBA (912 mg, 3.24 mmol) in dichloromethane (40 ml) at 0 °C using the same procedure as before yielded the *sulfonyl allene* **162** (461 mg, 41 %); ν_{max}/cm^{-1} 1956 (C=C=C), 1308 and 1148 (SO); δ_H (400 MHz) 1.73 (2H, t, *J* 6.6, 5′-H_2), 2.03 (2H, br t, *J* 7.5, 5-H_2), 3.94 (4H, s, O-$(CH_2)_2O$), 5.26 (1H, br s, *W* 8.2 Hz, 2′-H), 5.85 (1H, td, *J* 2 x 7.0 and 6.0, 3-H), 6.18 (1H, dt, *J* 6.0 and 2 x 3.0, 1-H) and 7.40 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 25.8 (t, C-6′), 27.5 (t, C-4), 31.0 (t, C-5), 35.5, 35.6 (t, C-3′ and C-5′), 64.4 (t, $O(CH_2)_2O$), 100.6 (d, C-1), 101.3 (d, C-3), 107.9 (s, C-4′), 119.4 (d, C-2′), 127.6 (d, SO_2Ph), 129.1 (d, SO_2Ph), 133.4 (d, SO_2Ph), 135.6 (s, C-1′), 141.4 (s, SO_2Ph) and 205.5 (s, C-2); (Found: M^+, 346. $C_{19}H_{22}O_4S$ requires M, 346). This was followed by starting material (422 mg, 40 %).

4-(5′-Phenylsulfonyl-penta-3,4-dienyl)cyclohex-3-en-1-one 163



The ketal **162** (200 mg, 0.58 mmol) and trifluoroacetic acid (1.5 ml) were stirred at room temperature for 0.5 h. The solution was cooled to 0 °C and neutralised with sat. $NaHCO_3$. The mixture was extracted (Et_2O) and the combined extract was washed (water, brine) and dried ($MgSO_4$). The residue was chromatographed on silica gel with ethyl acetate-hexane (2:3) as eluent to yield the *enone* **163** (161 mg, 92 %); ν_{max}/cm^{-1} 1956 (C=C=C), 1713 (CO), 1308 and 1149 (SO); δ_H (400 MHz) 2.20 (2H, t, *J* 2 x 7.4, 1′-H_2), 2.30 (2H, *W* 25, 1-H_2), 2.35 (2H, td, *J* 2 x 6.8 and 1.2, 5-H_2), 2.50 (2H, td, *J* 2 x 6.8 amd 0.8, 6-H_2), 2.82 (2H, m, 2′-H_2), 5.46 (1H, m, 3-H), 5.85 (1H, td, *J* 2 x 6.8 and 5.9, 3′-H), 6.20 (1H, dt, *J* 5.9 and 2 x 2.9, 5′-H) and 7.56 – 7.62 (5H, m, SO_2Ph); δ_C (100 MHz) 25.7 (t, C-5), 27.8 (t, C-2′), 35.5 (t, C-1′), 38.4 (t, C-6), 39.5 (t, C-2), 100.4 (d, C-3′), 101.5 (d, C-5′), 119.3 (d, C-3), 127.6 (d, SO_2Ph), 129.2 (d, SO_2Ph), 133.4 (SO_2Ph), 136.7 (d, SO_2Ph), 141.3 (s, SO_2Ph), 155.4 (s, C-4) and 205.6 (s, C-4′), 210.4 (s, C-1); (Found: M^+, 302. $C_{17}H_{18}O_3S$ requires M, 302).

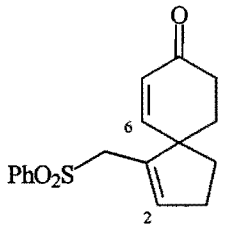
5-Hydroxy-4-phenylsulfonyl-5,7a-ethano-2,4,5,7a-tetrahydro-1*H*-indene 165



n-BuLi (0.28 ml, 0.7 mmol, 2.5M solution in THF) was added to a solution of diisopropylamine (92 µl, 0.7 mmol) in THF (5 ml) at -78 °C and the mixture was stirred for 30 min. Enone **163** (200 mg, 0.66 mmol) was then added followed by trimethylsilyl chloride (0.11 ml, 0.55 mmol) 15 min later. The reaction was stirred at -78 °C for 30 min, was allowed to warm to room temperature, after which it was stirred for a further 2 h. Pentane was added and the solution washed ($NaHCO_3$). The solvent was evaporated under reduced pressure and the residue was flash chromatographed on silica gel using ethyl acetate-hexane (3:7) as eluent to give a mixture of cycloadducts **165** (23 mg, 12 %, 5:1 by NMR); δ_H (400 MHz)(Major cycloadduct) 4.05 (1H, br s, 4-H), 4.45 (1H, br s, OH), 4.90 (1H, q, *J* 3 x 2.2, 3-H), 6.10 (1H, d, *J* 8.6, 7-H), 6.12 (1H, d, *J*

8.6, 6-H), 7.60 – 7.95 (5H, m, SO_2Ph); (Minor cycloadduct) 4.15 (1H, br s, 4-H), 4.95 (1H, br s, OH), 5.60 (1H, d, *J* 8.6, 7-H), 5.65 (1H, q, *J* 3 x 2.0, 3-H), 6.12 (1H, d, *J* 8.6, 6-H), 7.45 – 7.70 (5H, m, SO_2Ph). This was used directly in the next step.

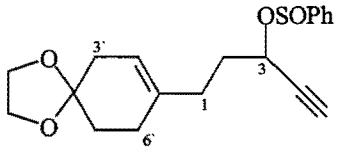
1-Phenylsulfonylmethyl-spiro[4,5]deca-1,6-dien-8-one 166



a) The cycloadducts **165** (10 mg, 0.33 μmol) were dissolved in THF – EtOH (1 ml, 1:1). Aqueous KOH (1 ml, 1 mmol, 1M) was added and the solution was stirred at room temperature for 0.5 h. The mixture was extracted (Et_2O), the combined extract was washed (brine) and dried ($MgSO_4$) to yield the *compound* **166** (7 mg, 70 %) as a colourless oil; ν_{max}/cm^{-1} 1674 (CO), 1309 and 1152 (SO); δ_H (400 MHz) 1.70 – 1.90 (3H, 4-H and 10-H_2), 2.85 (4H, m, 3-H_2 and 9-H_2), 3.68 (1H, dd, *J* 14.4 and 1.2, CH_2S), 3.77 (1H, dd, *J* 14.4 and 1.6, CH_2S), 5.91 (1H, dd, *J* 10.0 and 0.8, 7-H), 6.19 (1H, m, 2-H), 6.50 (1H, dd, *J* 10.0 and 1.6, 6-H) and 7.56 – 7.90 (5H, m, SO_2Ph); δ_C (100 MHz) 30.7, 30.9, 34.2 (t, C-3,C-4 and C-10), 35.1 (t, C-9), 52.5 (s, C-5), 54.6 (t, CSO_2Ph), 128.5 (d, SO_2Ph), 129.2 (d, SO_2Ph), 129.3 (d, C-7), 133.9 (d, SO_2Ph), 134.3 (s, SO_2Ph), 136.5 (d, C-2), 139.3 (s, C-1), 154.9 (d, C-6) and 199.0 (s, C-8); (Found: M^+, 302. $C_{17}H_{18}O_3S$ requires M, 302).

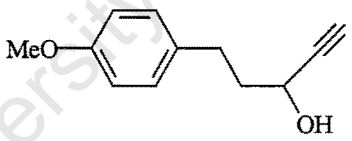
b) In a separate reaction, the allene **162** (460 mg, 1.33 mmol) was dissolved in trifluoroacetic acid (4 ml) and the mixture was stirred for 1 h. This was basified with KOH (1M) and the solution stirred for a further 1 h. Saturated ammonium chloride was added and the product extracted (EtOAc). The extract was washed (NH_4Cl, brine), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with ethyl acetate-hexane (2:3) as eluent to yield compound **165** (340 mg, 85 %).

1-(4,4-Ethylenedioxycyclohex-1-en-1-yl)pent-4-yn-3-yl phenylsulfinate 167



The alcohol **161** (240 mg, 1.08 mmol) was dissolved in dichloromethane (5 ml) and the solution cooled to -78 °C. Triethylamine (0.19 ml, 1.35 mmol) and freshly prepared benzenesulfinyl chloride (0.13 ml, 1.1 mmol) were sequentially added and the reaction was stirred for 1 h. Following this, aq. NH_4Cl was added and the mixture was extracted (CH_2Cl_2). The extract was washed (brine) and dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-hexane (2:3) as eluent to yield diastereomeric *sulfinate ester* **167** (370 mg, 99 %); ν_{max}/cm^{-1} 3306 (C≡C) and 1116 (SO); δ_H (400 MHz) 1.80 – 2.10 (10H, m, 1-,2-,3′-,5′- and 6′-H_2), 2.37 and 2.67 (1H, d, *J* 2.0, 5-H), 3.95 (4H, m, O-$(CH_2)_2$O), 4.90 (1H, m, 3-H), 5.32 (1H, m, 2′-H) and 7.50 – 7.70 (5H, m, Ph); (Found (FAB): $M+H^+$, 347. $C_{19}H_{23}O_4S$ requires M, 347).

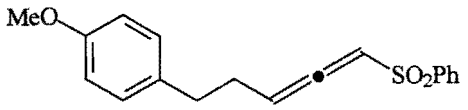
5-(4-Anisyl)pent-4-yn-3-ol 169



Dess Martin oxidation of alcohol **158** (180 mg, 1.1 mmol) with periodinane (480 mg, 1.1 mmol) in dichloromethane (20 ml) followed by work-up gave crude aldehyde (150 mg, 84 %) as an oil which was used directly in the next step.

Treatment of the aldehyde with ethynylmagnesium bromide (3.32 mmol), as described previously, gave *ynol* **169** (100 mg, 49 % over 2 steps); ν_{max}/cm^{-1} 3687 (OH) and 3306 (C≡C); δ_H 2.48 (1H, d, *J* 2.1, 5-H), 2.75 (2H, t, *J* 7.7, 1-H_2), 3.79 (3H, s, O*Me*), 4.35 (1H, td, *J* 2 x 6.6 and 2.1, 3-H), 6.85 (2H, d, *J* 8.7, Ph) and 7.15 (2H, d, *J* 8.7, Ph); δ_C 30.3, 39.3 (C-1 and C-2), 55.2 (O*Me*), 61.5 (C-3), 73.2 (C-5), 84.8 (C-4), 113.9, 129.4, 133.2 and 157.9 (Ph); (Found: M^+, 190. $C_{12}H_{14}O_2$ requires M, 190).

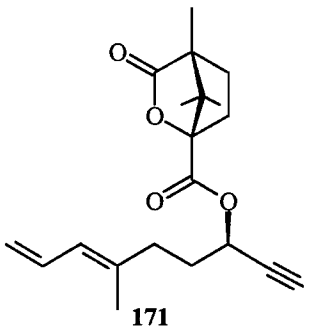
4-(5-Phenylsulfonylpenta-3,4-dienyl)anisole 170



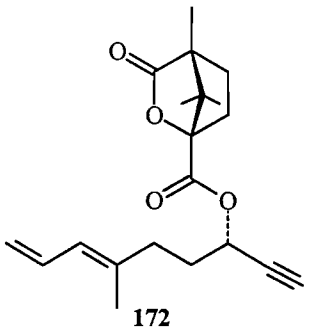
Treatment of the alcohol **169** (100 mg, 0.53 mmol) with triethylamine (83 µl, 0.58 mmol) and benzenesulfenyl chloride (55 µ, 0.63 mmol) at -78 °C, followed by work–up and chromatography [silica gel, ethyl acetate-hexane (2:3)], gave *sulfinyl allenes* (80 mg, 51 %); ν_{max}/cm^{-1} 1950, (C=C=C) and 1036 (SO); δ_H 2.65, 2.70 (2H, t, *J* 7.7, 1-H_2), 3.74, 3.77 (3H, s, OMe), 5.75 (1H, m, 3-H), 6.05 (1H, m, 5-H), 6.85 (2H, d, *J* 8.7, Ph), 7.15 (2H, d, *J* 8.7, Ph) and 7.40 – 7.70 (5H, m, SOPh); δ_C 29.9, 30.1 (C-1), 33.9 (C-2), 55.2 (OMe), 98.4, 98.5 (C-5), 102.9, 103.0 (C-3), 113.8 (Ph), 124.2 (SOPh), 129.1 (SOPh), 129.4 (Ph), 130.9 (SOPh), 132.6, 132.7 (Ph), 144.8 (SOPh), 158.0 (Ph) and 203.7, 203.8 (C-4); (Found: M^+, 298.1018. $C_{18}H_{18}O_2S$ requires M, 298.1023).

Oxidation of the sulfoxides (70 mg, 0.24 mmol) with *m*-CPBA (63 mg, 0.24 mmol) in dichloromethane (5 ml) followed by flash chromatography [silica gel, ethyl acetate-hexane (3:10)] gave *sulfone* **170** (73 mg, 100 %); ν_{max}/cm^{-1} 1955, (C=C=C), 1320 and 1148 (SO); δ_H 2.75 (2H, t, *J* 7.7, 1-H_2), 3.76 (3H, s, O*Me*), 5.80 (1H, td, *J* 2 x 7.0 and 6.2, 3-H), 6.20 (1H, dt, *J* 6.2 and 2 x 3.1, 5-H), 6.80 (2H, d, *J* 8.7, Ph), 7.05 (2H, d, *J* 8.7, Ph) and 7.40 – 7.70 (5H, m, SO_2Ph); δ_C 29.5 (C-1), 33.7 (C-2), 55.2 (OMe), 100.4 (C-5), 101.4 (C-3), 113.9 (Ph), 127.6 (SO_2Ph), 129.1 (SO_2Ph), 129.8 (Ph), 130.2 (SO_2Ph), 133.7 (Ph), 142.0 (SO_2Ph), 158.1 (Ph) and 205.7 (C-4); (Found: M^+, 314.0980. $C_{18}H_{18}O_3S$ requires M, 314.0976).

(3*R*,6*E*)- and (3*S*,6*E*)-6-Methylnona-6,8-dien-1-yn-3-yl (*S*)-camphanoates 171[1] and 172



171



172

The dienynol **144** (400 mg, 2.66 mmol) and (*S*)-camphanic acid (530 mg, 2.66 mmol) were dissolved in dichloromethane (40 ml) at room temperature. DMAP (50 mg, 0.40 mmol) and DCC (604 mg, 2.93 mmol) in dichloromethane (10 ml) were added sequentially and the reaction stirred for 2 h. The solvent was removed under reduced pressure and diluted with ether. The slurry was filtered through a sinter whilst washing with ether. The solvent was evaporated and the residue chromatographed on silica gel using ethyl acetate-toluene (1:33) as eluent to yield the (3*R*,6*E*)-isomer **171** (360 mg, 41 %; *ee* 95 % by NMR) as a colourless oil; $[\alpha]_D$ +13 (1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3306 (C≡C), 1785 (CO) and 1737 (CO); δ_H (400 MHz) 0.98, 1.05, 1.11 (each 3H, s, camphanoate Me), 1.76, (3H, s, 6-Me), 2.22 (2H, t, *J* 7.6, 5-H_2), 2.50 (1H, d, *J* 2.4, 1-H), 5.00 (1H, br d, *J* 10.2, 9-H_{cis}), 5.10 (1H, dd, *J* 16.8 and 1.8, 9-H_{trans}), 5.40 (1H, td, *J* 2 x 6.7 and 2.4, 3-H), 5.86 (1H, br d, *J* 10.5, 7-H) and 6.55 (1H, dt, *J* 16.8 and 2 x 10.5, 8-H); δ_C (100 MHz) 16.6 (6-Me), 32.5 (C-5), 34.8 (C-4), 64.6 (C-3), 74.5 (C-1), 80.1 (C-2), 115.5 (C-9), 126.5 (C-8), 132.9 (C-6) and 136.9 (C-7); (Found: M^+, 330.1820. $C_{20}H_{26}O_4$ requires M, 330.1831). This was followed by the (3*S*,6*E*)-isomer **172** (345 mg, 39 %, *ee* 95 % by NMR); $[\alpha]_D$ -29 (1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3306 (C≡C), 1786 (CO) and 1756 (CO); δ_H (400 MHz) 0.98, 1.09, 1.12 (each 3H, s, camphanoate Me), 1.77, (3H, s, 6-Me), 2.22 (2H, t, *J* 7.6, 5-H_2), 2.51 (1H, d, *J* 2.0, 1-H), 5.05 (1H, br d, *J* 10.2, 9-H_{cis}), 5.10 (1H, dd, *J* 16.9 and 1.8, 9-H_{trans}), 5.43 (1H, td, *J* 2 x 6.6 and 2.0, 3-H), 5.88 (1H, br d, *J* 10.4, 7-H) and 6.55 (1H, dt, *J* 16.9 and 2 x 10.4, 8-H); δ_C (100 MHz) 16.6 (6-Me), 32.6 (C-5), 34.8 (C-4), 64.6 (C-3), 74.7 (C-1), 80.1 (C-2), 115.6 (C-9), 126.5 (C-8), 132.9 (C-6), 136.9 (C-7); (Found: M^+, 330.1823. $C_{20}H_{26}O_4$ requires M, 330.1831).

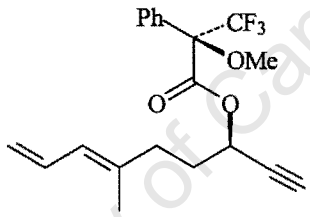
[1] The following spectral data were obtained for *S*-camphanic acid. The ^{13}C reported for **171** and **172** is the result of subtraction of the camphanic signals. δ_C (100 MHz) 9.6 (Me), 2 x 16.6 (2 x 7-Me), 28.9 (C-1), 30.6 (C-2), 54.4 (C-4), 54.9 (C-7), 90.8 (C-1), 171.9 (CO_2H), 177.7 (CO).

(3*R*,6*E*)- and (3*S*,6*E*)-6-Methyl-nona-6,8-dien-1-yn-3-ol 173 and 174

Hydrolysis of ester **171** (300 mg, 0.91 mmol) with KOH (760 mg, 13.6 mmol) in a mixture of THF – H_2O – MeOH (2:2:1, 25 ml) was carried out as before. Work-up and chromatography [silica gel, ethyl acetate-toluene (1:9)] gave *R-ynol* **173** (126 mg, 93 %); $[\alpha]_D$ -18 (1.1 in $CHCl_3$). NMR and infrared analysis were identical to that of **144**.

Hydrolysis of the other diastereomer **172** (250 mg, 0.76 mmol) with KOH (849 mg, 15.1 mmol) in a mixture of THF – H_2O – MeOH (2:2:1, 25 ml) was carried out as before. Work-up and chromatography [silica gel, ethyl acetate-toluene (1:9)] gave *S-ynol* **174** (90 mg, 78 %); $[\alpha]_D$ +17 (1.0 in $CHCl_3$).

(3*R*,2′*R*,6*E*)- and (3*S*,2′*R*,6*E*)-6-Methyl-nona-6,8-dien-1-yn-3-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 175 and 176

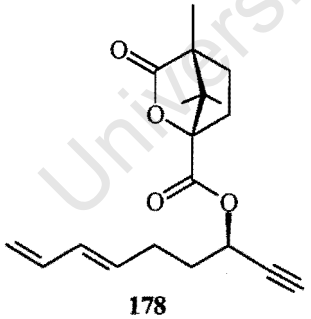


(*R*)-(2-Methoxy-2-trifluoromethyl) phenylacetyl chloride (23 mg, 0.1 mmol) was added to a stirred solution of the (*R*)-alcohol **174** (15 mg, 0.1 mmol), DMAP (cat.) and DCC (22 mg, 0.1 mmol) in dichloromethane (2 ml). The resulting mixture was stirred for 1 h, after which the solvent was removed under reduced pressure. The residue was diluted (Et_2O) and the resulting slurry was filtered through a sinter whilst washing with ether. The solvent was removed and the residue chromatographed on silica gel using ethyl acetate-hexane (1:20) as eluent to yield the *ester* **176** (34 mg, 92 %, *ee* 100 % by NMR) as a colourless oil; $[\alpha]_D$ +59.0 (1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3306 (C≡C) and 1749 (CO); δ_H (400 MHz) 1.71 (3H, s, 6-Me), 1.95 (2H, m, 4-H_2), 2.10 (2H, t, *J* 7.5, 5-H_2), 2.57 (1H, d, *J* 2.1, 1-H), 3.60 (3H, s, OMe), 5.02 (1H, br d, *J* 10.2, 9-H_{cis}), 5.10 (1H, dd, *J* 16.9 and 1.8, 9-H_{trans}), 5.52 (1H, td, *J* 2 x 6.6 and 2.1, 3-H), 5.78 (1H, br d, *J* 10.4, 7-H), 6.54 (1H, dt, *J* 16.9 and 2 x 10.4, 8-H) and 7.40 – 7.80 (5H, m Ph); δ_C (100 MHz) 16.4 (6-Me), 32.5 (C-5), 34.5 (C-4), 55.4 (O-CH_3), 65.2 (C-3), 75.0 (C-1), 79.4 (C-2), 115.5 (C-9), 121.2 (*C*OMe), 124.6 (CF_3), 126.5 (C-7), 127.2 (Ph), 128.4 (Ph), 129.6 (Ph), 131.8 (Ph), 132.9 (C-8), 136.8 (C-6) and 165.6 (CO); (Found: M^+, 336. $C_{20}H_{21}F_3O_3$ requires M, 336).

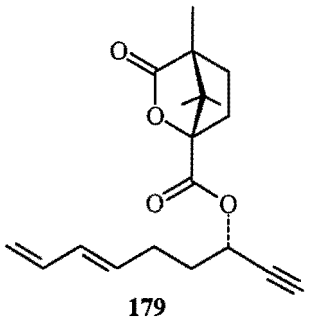
The analogous reaction was carried out on (*S*)-alcohol **174** (80 mg, 0.53 mmol) with DMAP (cat.), triethylamine (73 µl, 0.53 mmol) and (*R*)-(2-methoxy-2-trifluoromethyl) phenylacetyl chloride (0.1 ml, 0.53 mmol). Work-up and chromatography gave *ester* **176** (140 mg, 72 %, *ee* 91 % by NMR) as a colourless oil; $[\alpha]_D$ +7.0 (0.9 in $CHCl_3$); ν_{max}/cm^{-1} 3306 (C≡C) and 1756 (CO); δ_H (400 MHz) 1.76 (3H, s, 6-Me), 2.03 (2H, m, 4-H_2), 2.22 (2H, t, *J* 7.6, 5-H_2), 2.52 (1H, d, *J* 2.1, 1-H), 3.55 (3H, s, OMe), 5.05 (1H, br d, *J* 10.2, 9-H_{cis}), 5.12 (1H, dd, *J* 16.9 and 1.8, 9-H_{trans}), 5.50 (1H, td, *J* 2 x 6.6 and 2.1, 3-H), 5.86 (1H, br d, *J* 10.4, 7-H), 6.57 (1H, dt, *J* 16.9 and 2 x 10.4, 8-H) and 7.40 – 7.80 (5H, m, Ph); δ_C (100 MHz) 16.5 (6-Me), 32.5 (C-5), 34.7 (C-4), 55.4 (O-CH_3), 65.6 (C-3), 75.0 (C-1), 79.4 (C-2), 121.2 (*C*OMe), 124.6 (CF_3),, 115.6 (C-9), 126.6 (C-7), 127.5 (Ph), 128.3 (Ph), 129.6 (Ph), 131.8 (Ph), 132.8 (C-8), 136.8 (C-6) and 165.5 (CO); (Found: M^+, 336. $C_{20}H_{21}O_3F_3$ requires M, 336).

The same reaction was also carried out on the racemic alcohol **144** (50 mg, 0.33 mmol) with DMAP (cat.), triethylamine (45 µl, 0.33 mmol) and (*R*)-(2-methoxy-2-trifluoromethyl) phenylacetyl chloride (60 µl, 0.53 mmol). Work-up and chromatography gave esters **177** (120 mg, 99 %).

(3*R*,6*E*)- and (3*S*,6*E*)-Nona-6,8-dien-1-yn-3-yl (*S*)-camphanoate 178 and 179



178



179

DMAP (50 mg, 0.40 mmol) and DCC (1.03 g, 5 mmol) in dichloromethane (20 ml) were added to a stirred solution of dienynol **127** (540 mg, 3.97 mmol) and (*S*)-camphanic acid (786 mg, 4.0 mmol) in dichloromethane (50 ml) at room temperature, and the mixture was stirred for 2 h. The solvent was removed under reduced pressure and the residue was diluted with ether. The resultant slurry was filtered through a sinter whilst washing with ether. The solvent was evaporated and the residue chromatographed on silica gel using ethyl acetate-toluene (1:33) as eluent to yield the 3*R*,6*E* (*ee* 100 % by NMR) diastereomer **178** (320 mg, 26 %) as a colourless oil; $[\alpha]_D$ +16 (1.1 in

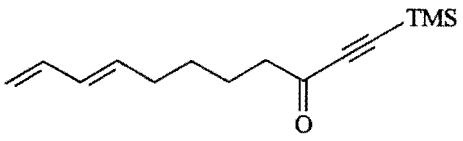
$CHCl_3$); ν_{max}/cm^{-1} 3306 (C≡C), 1785 (CO) and 1737 (CO); δ_H (400 MHz) 0.98, 1.05, 1.11 (each 3H, s, camphanoate Me), 2.51 (1H, d, *J* 2.2, 1-H), 5.00 (1H, br d, *J* 10.3, 9-H_{cis}), 5.12 (1H, br d, *J* 16.9, 9-H_{trans}), 5.45 (1H, td, *J* 2 x 6.6 and 2.2, 3-H), 5.68 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.08 (1H, dd, *J* 15.2 and 10.3, 7-H) and 6.30 (1H, dt, *J* 16.9 and 2 x 10.3, 8-H); δ_C (100 MHz) 27.8 (C-5), 33.8 (C-4), 64.4 (C-3), 74.5 (C-1), 80.1 (C-2), 115.7 (C-9), 132.3 (C- 6 and 7) and 136.7 (C-8); (Found: M^+, 316.1666. $C_{19}H_{24}O_4$ requires M, 316.1674). This was followed by the 3*S*,6*E* (*ee* 91 % by NMR) diastereomer **179** (160 mg, 12 %); $[\alpha]_D$ -40 (1.0 in $CHCl_3$) as an oil; ν_{max}/cm^{-1} 3306 (C≡C), 1786 (CO) and 1756 (CO); δ_H (400 MHz) 0.97, 1.08, 1.12 (each 3H, s, camphanoate Me), 2.51 (1H, d, *J* 2.2, 1-H), 5.00 (1H, br d, *J* 10.3, 9-H_{cis}), 5.12 (1H, br d, *J* 16.9, 9-H_{trans}), 5.44 (1H, td, *J* 2 x 6.6 and 2.2, 3-H), 5.66 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.08 (1H, dd, *J* 15.2 and 10.3, 7-H) and 6.30 (1H, dt, *J* 16.9 and 2 x 10.3, 8-H); δ_C (100 MHz) 27.8 (C-5), 33.8 (C-4), 64.3 (C-3), 74.7 (C-1), 80.0 (C-2), 115.8 (C-9), 132.2 (C-7), 132.3 (C-6) and 136.7 (C-8); (Found: M^+, 316.1662. $C_{19}H_{24}O_4$ requires M, 316.1674).

(3*R*,6*E*)- and (3*S*,6*E*)-Nona-6,8-dien-1-yn-3-ol 180 and 181

Hydrolysis of ester **178** (310 mg, 0.98 mmol) with KOH (382 mg, 6.8 mmol) in a mixture of THF – H_2O – MeOH (2:2:1, 10 ml) was carried out as before. Work-up and chromatography [silica gel, ethyl acetate-toluene (1:9)] gave (*R*)-*ynol* **180** (85 mg, 64 %); $[\alpha]_D$ -22 (1.0 in $CHCl_3$). NMR and infrared spectra were identical to those of **127**.

Similarly, hydrolysis of ester **179** (150 mg, 0.47 mmol) with KOH (310 mg, 5.5 mmol) in a mixture of THF – H_2O – MeOH (2:2:1, 6 ml) was carried out as before. Work-up and chromatography [silica gel, ethyl acetate-toluene (1:9)] gave (*S*)-*ynol* **181** (39 mg, 61 %); $[\alpha]_D$ +20 (1.0 in $CHCl_3$).

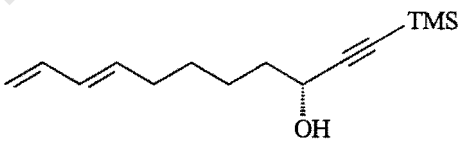
1-Trimethylsilylundeca-8,10-dien-1-yn-3-one 182



n-BuLi (3.4 ml, 8.5 mmol, 2.5M solution in hexanes) was added to a solution of trimethylsilylacetylene (1.2 ml, 8.6 mmol) in THF (20 ml) at room temperature, and the resulting solution stirred for 10 min after which crude aldehyde **109** (1.2 g, 8.6 mmol, (*E*/*Z*) 3/1 by NMR) was added. After 1 h, ethereal HCl (9 ml, 9 mmol, 1M solution in Et_2O) was added and the resulting solution was poured into a separation funnel containing iced water. The mixture was extracted (Et_2O) and the combined extract was washed (brine) and dried. The solvent was evaporated under reduced pressure to yield the crude alcohol.

Oxidation of the alcohol with Dess-Martin periodinane (3.6 g, 8.5 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:100) as eluent] gave *ynone* **182** (1.07 g, 54 %) as a colourless oil; δ_{max}/cm^{-1} 2150 (C≡C) and 1669 (CO); δ_H (400 MHz,(*E*)- isomer shown) 0.24 (9H, s, $Si(Me)_3$), 2.56 (2H, t, *J* 7.4, 4-H_2), 4.95 (1H, dd, *J* 10.3 and 1.9, 11-H_{cis}), 5.20 (1H, m, 11-H), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 8-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H), and 6.05 (1H, m, 9-H); (Found: M^+, 234. $C_{14}H_{22}OSi$ requires M, 234).

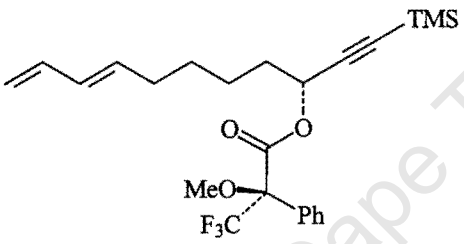
(3*R*)-1-Trimethylsilylundeca-8,10-dien-1-yn-3-ol 183



The following is a typical procedure for all Alpine-Borane reductions carried out in this investigation. 9-BBN dimer (520 mg, 2.14 mmol) and (+)-α-pinene (0.68 ml, 4.28 mmol, 98 %, 91 % *ee*/GLC) were stirred at 65 °C for 5 h. The ynone **182** (500 mg, 2.14 mmol) was then added in THF (2 ml) and the yellow solution stirred at room temperature for 24 h, after which the excess reagent was quenched with acetaldehyde (excess). The volume was reduced using a water aspirator whilst heating the flask at 60 °C for 2 h. The residual oil was dissolved in anhydrous diethyl ether (20 ml) to which ethanolamine (0.26 ml, 4.4 mmol) was added and the solution was

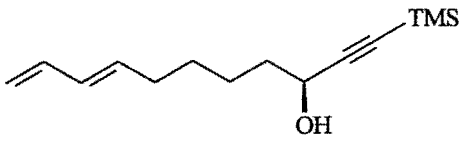
stirred for a further 1 h. The resultant slurry was filtered through a sinter whilst washing with ether. The solvent was evaporated and the residue chromatographed on silica gel using ethyl acetate-hexane (1:9) as eluent to yield the (*R*)-*ynol* **183** (351 mg, 69 %); $[\alpha]_D$ -3.4 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 3601 (OH) and 2169 (C≡C); δ_H ((*E*)- isomer shown) 0.17 (9H, s, $SiMe_3$), 2.10 (2H, t, *J* 6.2, 7-H_2), 4.35 (1H, t, *J* 6.1, 3-H), 4.95 (1H, dd, *J* 10.3 and 1.9, 11-H_{cis}), 5.20 (1H, br d, 17.0, 11-H_{trans}), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 8-H), 6.05 (1H, m, 9-H) and 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 10-H); δ_C -0.12 ($SiMe_3$), 24.7 (C-5), 28.8 (C-6), 32.4 (C-7), 37.6 (C-4), 62.8 (C-3), 89.5 (C-1), 106.8 (C-2), 114.7 (C-11), 131.1 (C-9), 135.0 (C-8) and 137.2 (C-10); (Found: M^+, 236. $C_{14}H_{24}OSi$ requires M, 236).

(2′*R*,3*R*)-1-Trimethylsilylundeca-8,10-dien-1-yn-3-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 184



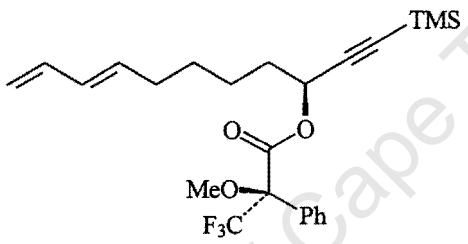
The following procedure is a typical procedure for future Mosher esterification reactions carried out in this investigation. The alcohol **183** (30 mg, 0.13 mmol) and (*R*)-methoxy-trifluoromethylphenylacetic acid (30 mg, 0.09 mmol) were stirred in dichloromethane (5 ml). DMAP (5 mg, cat.) and DCC (0.2 ml, 0.2 mmol, 1M solution in THF) were sequentially added and the reaction was stirred at room temperature for 1 h. The resultant slurry was filtered through a sinter whilst washing with ether. The solvent was evaporated and the residue chromatographed on silica gel with ethyl acetate-hexane (1:49) as eluent to yield the ester **184** (96 % *ee* by F^{19} NMR, 50 mg, 87 %); $[\alpha]_D$ +46.4 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2115 (C≡C) and 1751 (CO); δ_H (400 MHz, (*E*)-isomer shown) 0.18 (9H, s, $SiMe_3$), 2.10 (2H, t, *J* 6.2, 7-H_2), 3.60 (3H, s, OMe), 4.95 (1H, dd, *J* 10.3 and 1.9, 11-H_{cis}), 5.20 (1H, br d, *J* 17.0, 11-H_{trans}), 5.57 (1H, t, *J* 6.6, 3-H), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 8-H), 6.05 (1H, m, 9-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 10-H) and 7.40 – 7.60 (5H, m, Ph); δ_C (100 MHz) -0.34 ($SiMe_3$), 24.7 (C-5), 28.8 (C-6), 32.2 (C-7), 34.9 (C-4), 55.8 (OMe), 66.2 (C-3), 91.8 (C-1), 101.3 (C-2), 114.8 (C-11), 121.8 (*C*OMe), 124.6 (CF_3), 128.3 (Ph), 129.6 (Ph), 131.3 (C-9), 134.6 (C-8), 137.2 (C-10) and 165.7 (CO); δ_F (188 MHz) 80.7 (CF_3); (Found: $M+H^+$, 453. $C_{24}H_{32}F_3O_3Si$ requires M, 453).

(3*S*)-1-Trimethylsilyl-undeca-8,10-dien-1-yn-3-ol 185



Reduction of the ynone **181** (500 mg, 2.14 mmol) with (*S*)-Alpine Borane [prepared from 9-BBN dimer (520 mg, 2.14 mmol) and (-)-α-Pinene (0.68 ml, 4.28 mmol)], followed by work-up using ethanolamine (0.26 ml, 4.4 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:10)], gave (*S*)-*ynol* **185** (320 mg, 63 %); $[\alpha]_D$ +3.8 (*c* 1.0 in $CHCl_3$).

(2′*R*,3*S*)-1-Trimethylsilylundeca-8,10-dien-1-yn-3-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 186



Mosher ester formation was carried out on the *S*-enantiomer in an identical reaction to give *diastereomer* **186** (96 % *ee* by F^{19} NMR, 54 mg, 93 %); $[\alpha]_D$ –4.9 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2116 (C≡C), 1750 (CO); δ_H (400 MHz, (*E*)-isomer shown) 0.16 (9H, s, $SiMe_3$), 2.10 (2H, t, *J* 6.2, 7-H_2), 3.57 (3H, s, OMe), 4.95 (1H, dd, *J* 10.3 and 1.9, 11-H_{cis}), 5.18 (1H, dd, *J* 17.0 and 1.9, 11-H_{trans}), 5.55 (1H, t, *J* 6.6, 3-H), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 8-H), 6.05 (1H, m, 9-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 10-H) and 7.40 – 7.60 (5h, m, Ph); δ_C (100 MHz) -0.34 ($SiMe_3$), 24.5 (C-5), 28.8 (C-6), 32.2 (C-7), 34.2 (C-4), 55.4 (OMe), 66.6 (C-3), 91.7 (C-1), 100.9 (C-2), 114.9 (C-11), 121.8 (*C*OMe), 124.6 (CF_3), 128.3 (Ph), 129.6 (Ph), 131.4 (C-9), 134.6 (C-8), 137.1 (C-10) and 165.6 (CO); δ_F (188 MHz) 80.3 (CF_3); (Found: $M+H^+$, 453. $C_{24}H_{32}F_3O_3Si$ requires M, 453).

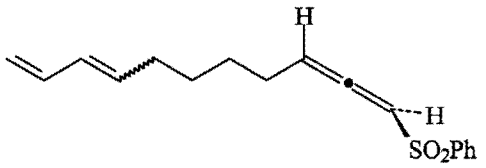
(3*R*)- and (3*S*)-Undeca-8,10-dien-1-yn-3-ol 187 and 188

The (*R*)-alcohol **183** (300 mg, 1.27 mmol) was dissolved in MeOH (5 ml). Saturated potassium carbonate (20 ml) was added and the mixture was stirred for 0.5 h. The MeOH was removed

under reduced pressure and the solution partitioned with Et_2O. The organic phase was washed (NH_4Cl, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to give the (*R*)-*ynol* **187** (181 mg, 87 %) as a colourless oil; $[\alpha]_D$ +0.9 (*c* 1.0 in $CHCl_3$). NMR and infrared spectra were identical to that of **110**.

The (*S*)-alcohol **184** (255 mg, 1.08 mmol) was treated as above to yield desilylated (*S*)-*ynol* **188** (151 mg, 85 %); $[\alpha]_D$ -0.8 (*c* 1.0 in $CHCl_3$).

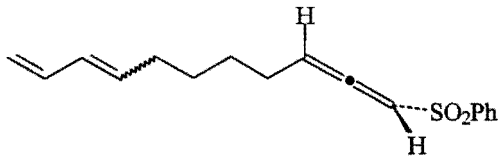
(*M*)-1-Phenylsulfony-undeca-1,2,8,10-tetraene 189



Treatment of (*R*)-ynol **187** (181 mg, 1.1 mmol) with triethylamine (0.23 ml, 1.65 mmol) and benzenesulfenyl chloride (0.14 ml, 1.21 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:7)] gave a mixture of (*M*) *phenylsulfinyallenes* (189 mg, 63 %); $[\alpha]_D$ -43.3 (*c* 1.0 in $CHCl_3$). These were used directly.

Oxidation of sulfoxides (65 mg, 0.24 mmol) with *m*-CPBA (66 mg, 62 %, 0.24 mmol) in dichloromethane (3 ml) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:4)] gave (*M*)-*phenylsulfonylallene* **189** (37 mg, 54 %); $[\alpha]_D$ -135.2 (*c* 0.8 in $CHCl_3$). All data were identical to that of **112**.

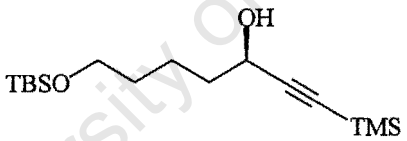
(*P*)-1-Phenylsulfonylundeca-1,2,8,10-tetraene 190



Treatment of (*S*)-ynol **188** (150 mg, 0.92 mmol) with triethylamine (0.19 ml, 1.38 mmol) and benzenesulfenyl chloride (0.13 ml, 1.10 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:7)], gave a mixture of *(P)-phenylsulfinylallenes* (153 mg, 62 %); $[\alpha]_D$ +44.4 (*c* 1.0 in $CHCl_3$).

Oxidation of sulfoxides (150 mg, 0.56 mmol) with *m*-CPBA (156 mg, 62 %, 0.56 mmol) in dichloromethane (3 ml), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:4)], gave *(P)-phenylsulfonylallene* **190** (75 mg, 43 %); $[\alpha]_D$ +136.5 (*c* 1.0 in $CHCl_3$).

(5*R*)- and (5*S*)-7-trimethylsilylhept-6-yn-1,5-diol 1-(*t*-butyldimethylsilyl)ether 193 and 194



n-Butyllithium (8.7 ml, 21.6 mmol, 2.5M solution in hexanes) was added to a solution of trimethysilylacetylene (3.05 ml, 21.6 mmol) in THF (20 ml) at -78 °C. This was allowed to warm to 0 °C and was then *trans*ferred via cannula to a solution of δ-valerolactone (2 ml, 21.6 mmol) in THF (20 ml) at -78 °C. The resulting solution was maintained at -78 °C for 1 h and then quenched with ethereal HCl (1M, 22 ml, 22 mmol). This was stirred rapidly for 10 min, then poured into a separation flask containing brine, and the mixture was extracted (Et_2O). The extract was washed (brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield crude 7-hydroxy-1-(trimethylsilyl)-hept-1-yn-3-one **191** as a colourless oil which was used without purification.

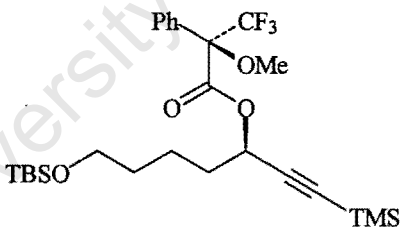
A solution of the crude ketone, *tert*-butyldimethylsilylchloride (3.6 g, 24 mmol), imidazole (2.2 g, 32.4 mmol) and dichloromethane (30 ml) was stirred at room temperature for 1.5 h. Water was

added and the mixture was extracted (hexane). The extract was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to afford crude 7-(*tert*-butyldimethysilyloxy)-1-(trimethylsilyl)-hept-1-yn-3-one **192** as a light yellow liquid. Spectral analysis were identical to literature values.[145]

Reduction of ynone **192** with (*R*)-Alpine-Borane [prepared from 9-BBN dimer (5.27 g, 21.6 mmol) and (+)-α-Pinene (6.85 ml, 43.2 mmol)] followed by work-up with ethanolamine (2.60 ml, 43.2 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:5)] gave (*R*)-*alcohol* **193** (5.87 g, 87 %); $[\alpha]_D$ -0.5 (*c* 1.0 in $CHCl_3$). Spectroscopic data were in agreement with literature values. [145]

Reduction of ynone **192** (4 g, 12.8 mmol) with (*S*)-Alpine-Borane [9-BBN dimer (3.12 g, 12.8 mmol) and (-)-α-Pinene (4.03 ml, 25.6 mmol)], followed by work-up with ethanolamine (1.53 ml, 25.6 mmol) and chromatography [silica gel, ether-hexane (1:5)], gave (*S*)-*ynol* **194** (3.5 g, 87 %); $[\alpha]_D$ +0.6 (*c* 1.0 in $CHCl_3$). [145]

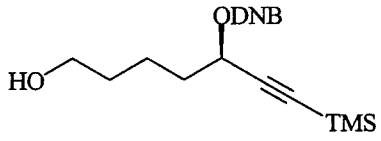
(2′*R*,3*R*)-7-(*t*-Butyldimethylsilyloxy)-1-trimethylsilylhept-1-yn-3,7-diol-3-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 195



Mosher ester formation was carried out on (*R*)-alcohol **193** (200 mg, 0.64 mmol) as before, using (*R*)-methoxy-trifluoromethylphenylacetic acid (150 mg, 0.64 mmol), DMAP (50 mg, 0.41 mmol) and DCC (0.7 ml, 0.7 mmol, 1M solution in CH_2Cl_2). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)] gave diastereomer **195** (95 % *ee* by F^{19} NMR, 265 mg, 79 %); $[\alpha]_D$ +39.4 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2179 (C≡C) and 1751 (CO); δ_H (400 MHz) 0.04 (6H, s, $SiMe_2$), 0.18 (9H, s, $SiMe_3$), 1.50 - 1.80 (6H, m, 4-,5- and 6-H_2), 3.57 (2H, t, *J* 6.2, 7-H_2), 3.62 (3H, d, *J* 0.8, OMe), 5.57 (1H, t, *J* 6.6, 5-H) and 7.40 – 7.60 (5H, m, *Ph*); δ_C (100 MHz) -5.4 (q, $SiMe_2$), -0.2 (q, $SiMe_3$), 18.3 (s, CMe_3), 21.3 (t, C-5), 25.9 (q, C(*Me*$_3$)), 32.1 (t, C-6), 34.2 (t, C-4), 55.4 (q, OMe), 62.8 (t, C-7), 66.3 (d, C-3), 91.8, 101.3 (s, C-1 and C-2), 121.9 (s, *C*OMe), 124.7 (s, CF_3),

127.4 (d, Ph), 128.3 (d, Ph), 129.6 (d, Ph), 132.5 (s, Ph) and 165.6 (CO); δ_F (188 MHz) 80.8 (s, CF_3); (Found (FAB): $M+H^+$, 531. $C_{26}H_{42}F_3O_4Si_2$ requires M, 531).

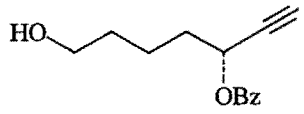
(5*R*)-7-Trimethylsilylhept-6-yne-1,5-diol-5-yl (3,5)-dinitrobenzoate 197



The (*R*)-alcohol **193** (1.98 g, 6.3 mmol), 3,5-dinitrobenzoic acid (1.47 g, 6.9 mmol) and DMAP (125 mg, 1.01 mmol) were stirred in dichloromethane (30 ml). DCC (1.56 g, 7.6 mmol, in dichloromethane (5 ml)) was added to the suspension and the reaction mixture was stirred at room temperature for 30 min. The resultant slurry was filtered through a sinter whilst washing with dichloromethane. The solvent was removed and the yellow crystalline product adsorbed onto silica gel. This was chromatographed on silica gel using ethyl acetate-hexane (3:7) as eluent to yield the *dinitrobenzoylester* **196** as a yellow crystals (2.54 g, 80 %); mp 62 – 64 °C (from EtOH); $[\alpha]_D$ +11.1 (*c* 0.9 in $CHCl_3$); δ_{max}/cm^{-1} 2178 (C≡C), 1735 (CO), 1548 and 1345 (NO); δ_H (400 MHz) 0.05 (6H, s, $SiMe_2$), 0.20 (9H, s, $SiMe_3$), 0.89 (9H, s, Bu^t), 1.60 (4H, m, 2- and 3 -H_2), 2.00 (2H, m, 4-H_2), 3.65 (2H, t, *J* 5.8, 1-H_2), 5.71 (1H, t, *J* 6.6, 5-H), 9.18 (2H, d, *J* 2.0, Ph) and 9.22 (1H, t, *J* 2.0, Ph); δ_C (100 MHz) -5.3 (q, $SiMe_2$), -0.3 ($SiMe_3$), 18.3 (s, CMe_3), 21.6 (t, C-3), 25.9 (q, CMe_3), 32.1 (t, C-4), 34.7 (t, C-2), 62.7 (t, C-1), 67.3 (d, C-5), 92.3, 101.6 (s, C-6,7), 124.4, 129.6, 133.8, 148.7 (d, Ph) and 161.5 (s, CO); (Found: $M+Rb^+$, 593. $C_{23}H_{36}N_2O_7Si_2Rb$ requires M, 593).

The ester (824 mg, 1.62 mmol) was dissolved in methanol (5 ml). Pyridinium *p*-toluenesulfonate (200 mg, 0.8 mmol) was added and the solution stirred for 16 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel using ethyl acetate-hexane (2:5) as eluent to yield the *hydroxydinitrobenzoyl ester* **197** (576 mg, 90 %); mp 112 – 114 °C (from EtOH); $[\alpha]_D$ +15.0 (*c* 0.9 in $CHCl_3$); δ_{max}/cm^{-1} 3619 (OH), 2178 (C≡C), 1734 (CO), 1549 and 1345 (NO); δ_H (400 MHz) 0.18 (9H, s, $SiMe_3$), 1.65 (4H, m, 2- and 3-H_2), 2.05 (2H, m, 4-H_2), 3.69 (2H, t, *J* 6.2, 1-H_2), 5.72 (1H, t, *J* 6.6, 5-H), 9.16 (2H, d, *J* 2.0, Ph_2) and 9.22 (1H, t, *J* 2.0, Ph); δ_C (100 MHz) -0.3 ($SiMe_3$), 21.5, 31.9, 34.6 (C-2, C-3 and C-4), 62.5 (C-1), 67.1 (C-5), 92.5, 100.9 (C-6,7), 122.5, 129.6, 133.8, 148.7 (Ph) and 161.5 (CO); (Found: C, 51.7; H, 5.8; N, 6.7 %; (FAB) $M+Rb^+$, 479; Requires for $C_{17}H_{22}N_2O_7Si$: 479; C, 51.8; H, 5.6; N, 7.1 %).

(5*R*)- and (5*S*)-Hept-6-yn-1,5-diol-5-yl benzoate 200 and 201



The (*R*)-alcohol **193** (1.70 g, 5.45 mmol) was dissolved in MeOH (5 ml). Saturated potassium carbonate was added and the mixture was stirred for 2 h, after which aq. NH_4Cl was added. The mixture was extracted (Et_2O) and the combined extract was washed (water, brine) and dried ($MgSO_4$). The solvent was evaporated to give (5*R*)-1-*t-butyldimethlsilyloxy-hept-6-yne*-1,5-*diol* **198** (1.22 g, 93 %); $[\alpha]_D$ +0.5 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 3617 (OH) and 3306 (C≡C); δ_H (400 MHz) 0.05 (6H, s, $SiMe_2$) 0.91 (9H, s, Bu^t), 1.50 – 1.80 (4H, m, 2-H_2 and 3-H_2), 2.44 (1H, d, *J* 2.0, 7-H), 3.63 (2H, t, *J* 6.2, 1-H_2), 4.38 (1H, td, *J* 2 x 6.6 and 2.0, 5-H) and 7.40 – 7.90 (10H, m, Ph); δ_C (100 MHz) -5.3 ($SiMe_2$), 14.3 (CMe_3), 21.4 (C-2), 25.9 (CMe_3), 32.3 (C-3), 37.1 (C-4), 62.3 (C-5), 62.9 (C-1), 72.8 (C-7) and 84.9 (C-6); (Found (FAB): $M+H^+$, 243. $C_{13}H_{27}O_2Si$ requires M, 243).

The ynol **198** (1.20 g, 5.0 mmol) was dissolved in pyridine (5 ml). Benzoyl chloride (1.5 ml, 12.8 mmol) was added and the solution was stirred at room temperature for 1 h. The pyridine was azeotropically removed with repeated evaporation of toluene. The residue was diluted with water and the product was extracted (Et_2O). The organic phased was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude ester **199** (2 g) which was used directly.

The ester was dissolved in MeOH (10 ml) and PPTS (720 mg, 2.89 mmol) was added. This was stirred for 16 h following which the solvent was removed under reduced pressure. The residue was chromatographed directly on silica gel with ethyl acetate-hexane (3:7) as eluent to yield the (*R*)-*hydroxyester* **200** (918 mg, 73 %); $[\alpha]_D$ +9.3 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 3625 (OH), 3305 (C≡C) and 1718 (CO); δ_H 1.60 (4H, m, 2- and 3-H_2), 1.95 (2H, m, 4-H_2), 2.50 (1H, d, *J* 2.1 , 7-H), 3.0 (1H, br s, OH), 3.67 (2H, t, *J* 5.9, 1-H_2), 5.60 (1H, td, *J* 2 x 6.5 and 2.1, 5-H) and 7.50 – 8.10 (5H, m, Ph); δ_C 21.4, 32.1, 34.5 (C-2, C-3 and C-4), 62.5 (C-1), 64.3 (C-5), 73.9 (C-7), 81.1 (C-6), 128.4, 129.7, 130.0, 133.3 (Ph) and 165.6 (CO); (Found: M^+, 232. $C_{14}H_{16}O_3$ requires M, 232).

The analogous series of reactions were carried out on the opposite enantiomer (2.2 g, 7 mmol) and gave the (*S*)-*hydroxyester* **201** (1.19 g, 74 % over the 3 steps); $[\alpha]_D$ -12 (*c* 1.0 in $CHCl_3$).

(3*R*,7*E*)-Deca-7,9-dien-1-yn-3-ol 203

Oxidation of the ynol **200** (918 mg, 3.96 mmol) using Dess-Martin periodinane (2.18 g, 5.14 mmol) in dichloromethane (20 ml) followed by work-up gave the corresponding aldehyde (900 mg, 97 %) which was used directly.

A Wittig reaction was carried on the aldehyde using allyltriphenylphosphonium bromide (1.53 g, 4 mol) and *n*-BuLi (1.6 ml, 4 mol, 2.5M solution in hexanes). Work-up followed by flash chromatography [silica gel, ethyl acetate-hexane (1:19)] afforded a mixture (6:4 *E/Z* by NMR) of dienes **202** (350 mg, 40 %); $[\alpha]_D$ +8.0 (*c* 1.1 in $CHCl_3$); δ_{max}/cm^{-1} 3306 (C≡C) and 1720 (CO); δ_H (400 MHz, (*E*)-isomer only) 1.63 – 1.98 (4H, m, 4-H_2 and 5-H_2), 2.48 (1H, d, *J* 2.4, 1-H), 2.18 (2H, br q, *J* 6.8, 6-H_2), 4.95 (1H, dd, *J* 10.3 and 1.9, 10-H_{cis}), 5.18 (1H, dd, *J* 17.0 and 1.9, 10-H_{trans}), 5.41 (1H, m, *W* 15, 3-H), 6.05 (1H, m, 8-H), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 6-H), 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 9-H) and 7.40 – 8.10 (5H, m, Ph); (Found: M^+, 254. $C_{17}H_{18}O_2$ requires M, 254).

Hydrolysis of the ester (270 mg, 1.06 mmol) was carried out as before using NaOH (400 mg, 10 mmol) dissolved in THF – MeOH - H_2O (1:1:1, 5 ml). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)] gave (*R*)-*dienynol* **203** (160 mg, 100 %); $[\alpha]_D$ +0.4 (*c* 1.0 in $CHCl_3$). NMR and infrared data were identical to **116**.

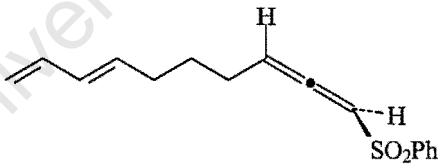
(3*S*,7*E*)-Deca-7,9-dien-1-yn-3-ol 205

Dess-Martin oxidation of the (*S*)-ynol **201** (1.18 g, 5.1 mmol) using periodinane (2.60 g, 6.12 mmol) in dichloromethane (20 ml) followed by work-up gave the corresponding aldehyde (1.10 g, 93 %) which was used directly.

n-BuLi (2 ml, 5 mmol, 2.5M solution in hexanes) was added dropwise over 10 min to a stirred suspension of allyldiphenylphosphine oxide (1.21 g, 5 mmol) in THF (15 ml) and HMPA (1.74 ml, 10 mmol) at -78 °C. This was stirred for 10 min after which the aldehyde was added. The reaction was stirred at -78 °C for 30 min, 0 °C for 2 h and room temperature for 2 h. This was poured into HCl (2M) containing ice and the mixture was extracted (pentane). The organic phase was washed (water, brine), dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude diene **204** (1.52 g) which was used directly.

Hydrolysis of the ester was carried out as before using NaOH (840 mg, 21 mmol) dissolved in THF – MeOH – H_2O (1:1:1, 30 ml). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)] gave (*S*)-*dienynol* **205** (450 mg, 63 % over 2 steps, ~ 86 % (*E*) by NMR); $[\alpha]_D$ -0.4 (*c* 1.0 in $CHCl_3$).

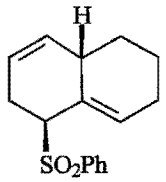
(*M*,7*E*)-1-Phenylsulfonyl-deca-1,2,7,9-tetraene 207



Treatment of (*R*)-ynol **203** (160 mg, 1.06 mmol) with triethylamine (0.24 ml, 1.7 mmol) and benzenesulfenyl chloride (0.14 ml, 1.2 mmol) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:7)] gave a mixture of (*M*)-*phenylsulfinylallene* diastereomers **206** (128 mg, 47 %); $[\alpha]_D$ -18.6 (*c* 1.0 in $CHCl_3$) which was used directly.

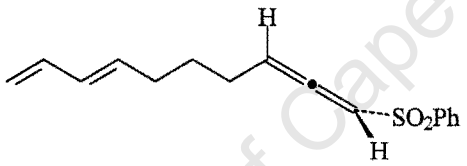
Oxidation of sulfoxide **206** (130 mg, 0.50 mmol) with *m*-CPBA (158 mg, 62 %, 0.56 mmol) in dichloromethane (5 ml) followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:7)] gave (*M*)-*phenylsulfonylallene* **207** (55 mg, 40 %); $[\alpha]_D$ -31.4 (*c* 0.9 in $CHCl_3$). NMR and infrared were identical to that of **118**.

(1*S*,4a*S*)-1-Phenylsulfonyl-1,2,4a,5,6,7-hexahydronaphthalene 208



The tetraene **207** (32 mg, 0.12 mmol, 48 % (*E*) by NMR) in C_7D_8 (2 ml) was heated at 110 °C in a sealed NMR tube. After 16 h, the solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with ethyl acetate-toluene (1:49) as eluent to yield the *exo cycloadduct* **208** (5 mg, 15 %); $[\alpha]_D$ +4.8 (*c* 0.4 in $CHCl_3$). All spectroscopic data were identical to **120**. The unreacted (*Z*)-diene (4 mg, 13 %) was also isolated.

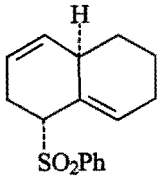
(*P*,7*E*)-1-Phenylsulfinyl-deca-1,2,7,9-tetraene 210



Treatment of the (*S*)-ynol **205** (292 mg, 1.95 mmol) with triethylamine (0.54 ml, 3.89 mmol) and benzenesulfenyl chloride (0.29 ml, 2.54 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:7)], gave a mixture of *(P)-phenylsulfinylallene* diastereomers **209** (220 mg, 44 %); $[\alpha]_D$ +23.4 (*c* 1.1 in $CHCl_3$) which were used directly.

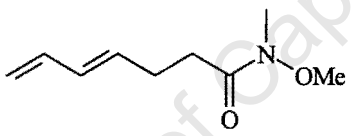
Oxidation of sulfoxides **209** (220 mg, 0.85 mmol) with *m*-CPBA (245 mg, 62 %, 0.89 mmol) in dichloromethane (10 ml), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:10)], gave *(P)-phenylsulfonylallene* **210** (136 mg, 58 %); $[\alpha]_D$ +56.0 (*c* 1.0 in $CHCl_3$).

(1*R*,4a*R*)-1-Phenylsulfonyl-1,2,4a,5,6,7-hexahydronaphthalene 211



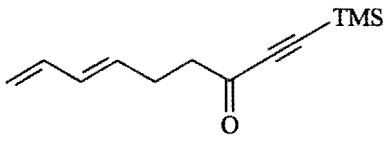
The tetraene **210** (135 mg, 0.49 mmol, ~86 % (*E*) by NMR) in toluene (2 ml) was heated at 110 °C for 16 h, following which the solvent was evaporated and the residue was chromatographed on silica gel with ethyl acetate-toluene (1:49) as eluent to yield the *exo cycloadduct* **211** (70 mg, 52 %); mp 123 – 124 °C (from EtOH); $[\alpha]_D$ -17.2 (*c* 0.8 in $CHCl_3$). All spectroscopic data were identical to those of **120**. This was followed by the *endo* cycloadduct **212** (55 mg, 41 %) which was inseparable from the major cycloadduct **211** (~ 20 % by NMR).

_N_-Methoxy-_N_-Methyl (4*E*)-Hepta-4,6-dienamide 213



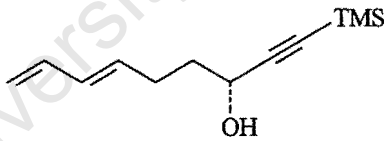
Dimethylaluminumchloride (39 ml, 39 mmol, 1M solution in hexanes) was slowly added to a suspension of *N*-methyl,*N*-methoxy-ammonium chloride (3.78 g, 39 mmol) in dichloromethane (100 ml) at 0 °C. This was stirred for 0.5 h, after which dienylester **123** (2 g, 12.9 mmol) in dichloromethane (5 ml) was slowly added, and the resulting solution was stirred for 1 h. MeOH (15 ml) was cautiously added followed by sodium potassium tartrate (~ 40g) and EtOAc (100 ml). The resultant slurry was stirred vigorously for 1 h and was subsequently filtered through Celite whilst washing with EtOAc. The solvent was evaporated and the residue was chromatographed on silica gel with ethyl acetate-hexane (3:4) as eluent to yield the *amide* **213** (1.68 g, 78 %); δ_{max}/cm^{-1} 1648 (CON); δ_H 2.45 – 2.55 (4H, m, 2- and 3-H_2), 3.17 (3H, s, NMe), 3.67 (3H,s, OMe), 4.95 (1H, dd, *J* 10.3 and 1.9, 7-H_{cis}), 5.08 (1H, dd, *J* 17.0 and 1.9, 7-H_{trans}), 5.65 (1H, dt, *J* 15.2 and 2 x 6.6, 4-H), 6.05 (1H, dd, *J* 15.2 and 10.3, 5-H) and 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 6-H); δ_C 27.4 (C-3), 31.4 (C-2), 34.9 (Me), 61.2 (OMe), 115.4 (C-7), 131.7 (C-5), 133.4 (C-4), 136.9 (C-6) and 176.8 (CO); (Found: M^+, 169. $C_9H_{15}O_2N$ requires M, 169).

(6*E*)-1-Trimethylsilylnona-6,8-dien-1-yn-3-one 214



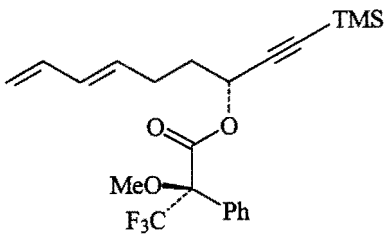
n-BuLi (4 ml, 10 mmol, 2.5M solution in hexanes) was added to a solution of trimethylsilylacetylene (1.4 ml, 10 mmol) in THF (10 ml) at 0 °C. After 15 min, the amide **213** (1.63 g, 9.63 mmol) in THF (10 ml) was added. This was stirred for 1 h after which ethereal HCl (10 ml, 10 mmol, 1M) was added and the solution stirred vigorously for 30 min. This solution was poured into brine and the mixture was extracted (Et_2O). The combined extract was dried, evaporated and the residue flash chromatographed on silica gel with ether-pentane (1:99) as eluent to yield the y*none* **214** (1.26 g, 61 %); δ_{max}/cm^{-1} 2151 (C≡C) and 1671 (CO); δ_H 0.24 (9H, s, $SiMe_3$), 2.45 (2H, br q, *J* 7.0, 5-H_2), 2.65 (2H, t, *J* 7.0, 4-H_2), 4.95 (1H, dd, *J* 10.3 and 1.9, 9-H_{cis}), 5.08 (1H, dd, *J* 17.0 and 1.9, 9-H_{trans}), 5.65 (1H, dt, *J* 15.2 and 2 x 7.0, 6-H), 6.05 (1H, dd, *J* 15.2 and 10.3, 7-H) and 6.30 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H); (Found: M^+, 206. $C_{12}H_{18}OSi$ requires M, 206).

(3*R*,6*E*)-1-Trimethylsilylnona-6,8-dien-1-yn-3-ol 215



Reduction of the ynone **214** (600 mg, 2.91 mmol) with (*R*)-Alpine Borane [prepared from 9-BBN dimer (710 mg, 2.91 mmol) and (+)-α-Pinene (0.92 ml, 5.83 mmol)], followed by work up using ethanolamine (0.36 ml, 6.0 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:12)], gave (*R*)-*ynol* **215** (540 mg, 89 %); $[\alpha]_D$ -31.6 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 3595 (OH) and 2170 (C≡C); δ_H 0.17 (9H, s, $SiMe_3$), 1.80 (2H, m, 4-H_2), 2.30 (2H, q, *J* 6.7, 5-H_2), 4.40 (1H, br t, *J* 5.8, 3-H), 4.95 (1H, dd, *J* 10.2 and 2.7, 9-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.70 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.10 (1H, dd, *J* 15.5 and 10.2, 7-H) and 6.32 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H); δ_C -0.14 ($Si(Me)_3$), 28.2 (C-5), 37.0 (C-4), 62.3 (C-3), 89.8 (C-1), 106.4 (C-2), 115.3 (C-9), 131.8 (C-7), 133.7 (C-6) and 137.0 (C-8); (Found: $M\text{-}H^+$, 207. $C_{12}H_{19}OSi$ requires M, 207).

(2′*R*,3*R*,6*E*)-1-Trimethylsilylnona-6,8-dien-1-yn-3-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 216



Mosher ester formation was carried out as before on (*R*)-alcohol **215** (21 mg, 0.1 mmol) using (*R*)-methoxy-trifluoromethylphenylacetic acid (24 mg, 0.1 mmol), DMAP (2 mg, cat) and DCC (0.2 ml, 0.2 mmol, 1M solution in CH_2Cl_2). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:49)] gave the ester **216** (94 % *ee* by F^{19} NMR, 43 mg, 99 %); $[\alpha]_D$ +22.9 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2116 (C≡C) and 1752 (CO); δ_H (400 MHz) 0.17 (9H, s, $SiMe_3$), 1.80 – 2.00 (4H, m, 4-H_2 and 5-H_2), 3.55 (3H, s, OMe), 4.95 (1H, dd, *J* 10.2 and 2.7, 9-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.57 (1H, br t, *J* 5.8, 3-H), 5.65 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.10 (1H, dd, *J* 15.5 and 10.2, 7-H), 6.32 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H) and 7.40 – 7.60 (5H, m, Ph); δ_C (100 MHz) -0.37 ($SiMe_3$), 28.9 (C-5), 37.0 (C-4), 55.7 (OMe), 65.6 (C-3), 92.2 (C-1), 101.0 (C-2), 115.7 (C-9), 121.8 (*C*OMe), 124.7 (CF_3), 127.5 (Ph), 128.4 (Ph), 129.6 (Ph), 132.3 (C-7), 132.4 (C-6), 136.8 (C-8), 137.2 (Ph) and 165.6 (CO); δ_F (188 MHz) 80.7 (CF_3); (Found: $M+H^+$, 425. $C_{22}H_{27}F_3O_3Si$ requires M, 425).

(3*S*,6*E*)-1-Trimethylsilylnona-6,8-dien-1-yn-3-ol 217

Reduction of the ynone **214** (500 mg, 2.43 mmol) with (*S*)-Alpine Borane [prepared from 9-BBN dimer (710 mg, 2.91 mmol) and (-)-α-Pinene (0.92 ml, 5.83 mmol)] followed by work up using ethanolamine (0.36 ml, 6.0 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:12)] gave (*S*)-*ynol* **217** (434 mg, 86 %); $[\alpha]_D$ +32.8 (*c* 1.0 in $CHCl_3$).

(2′*R*,3*S*,6*E*)-1-Trimethylsilylnona-6,8-dien-1-yn-3-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 218

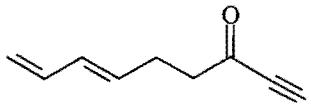
Mosher ester formation was carried out on the (*S*)-enantiomer **217** (28 mg, 0.13 mmol) using (*R*)-methoxy-trifluoromethylphenylacetic acid (31 mg, 0.13 mmol), DMAP (2 mg, cat) and DCC (0.3 ml, 0.3 mmol, 1M solution in CH_2Cl_2). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:50)] gave *ester* **218** (93 % *ee* by F^{19} NMR, 52 mg, 91 %); $[\alpha]_D$ +5.5 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2116 (C≡C) and 1752 (CO); δ_H (400 MHz) 0.15 (9H, s, $SiMe_3$), 1.80 – 2.10 (4H, m, 4-H_2 and 5-H_2), 3.55 (3H, s, OMe), 4.95 (1H, dd, *J* 10.2 and 2.7, 9-H_{cis}), 5.10 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.51 (1H, br t, *J* 5.8, 3-H), 5.65 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.10 (1H, dd, *J* 15.5 and 10.2, 7-H), 6.32 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H) and 7.40 – 7.60 (5H, m, Ph); δ_C (100 MHz) -0.37 ($SiMe_3$), 27.9 (C-5), 34.9 (C-4), 55.7 (OMe), 66.0 (C-3), 92.1(C-1), 100.7 (C-2), 115.7 (C-9), 121.8 (*C*OMe), 124.8 (CF_3), 127.5 (Ph), 128.3 (Ph), 129.6 (Ph), 132.0 (C-7), 132.4 (C-6), 134.5 (Ph), 137.1 (C-8) and 165.5 (CO); δ_F (188 MHz) 80.3 (CF_3); (Found: H^++H^+, 425. $C_{22}H_{27}F_3O_3Si$ requires M, 425).

(3*R*,6*E*)- and (3S,6*E*)-Nona-6,8-dien-1-yn-3-ol 219 and 220

Saturated potassium carbonate (20 ml) was added to a solution of the (*R*)-alcohol **215** (500 mg, 2.40 mmol) in MeOH (5 ml) and the mixture was stirred for 0.5 h, after which sat.NH_4Cl was added. The mixture was extracted (Et_2O) and the organic phase washed (water, brine) and dried ($MgSO_4$). The solvent was removed to yield (*R*)-*ynol* **219** (299 mg, 91 %); $[\alpha]_D$ -20.4 (*c* 1.0 in $CHCl_3$). NMR and infrared analysis were identical to **127**.

The (*S*)-alcohol **216** (400 mg, 1.92 mmol) was treated as above to yield (*S*)-*ynol* **220** (240 mg, 92 %); $[\alpha]_D$ +22.4 (*c* 1.0 in $CHCl_3$).

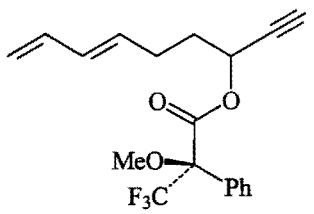
(6*E*)-Nona-6,8-dien-1-yn-3-one 221



a) Periodinane (1.0 g, 2.3 mmol) was dissolved in dichloromethane (10 ml). Alcohol **127** (300 mg, 2.2 mmol) was added and the reaction was stirred for 2 h at room temperature. The solution was diluted with ether and was quenched with saturated $NaHCO_3$ containing $Na_2S_2O_3$. The organic phase was washed ($NaHCO_3$, water, brine), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate-hexane (1:9) as eluent to yield *ynone* **221** (210 mg, 71 %); ν_{max}/cm^{-1} 3297 (C≡C) and 1682 (CO); δ_H (400 MHz) 2.45 (2H, m, 5-H_2), 2.70 (2H, t, *J* 7.4, 4-H_2), 3.22 (1H, s, 1-H), 5.00 (1H, dd, *J* 10.3 and 2.7, 9-H_{cis}), 5.12 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.65 (1H, dt, *J* 15.2 and 2 x 6.7, 6-H), 6.08 (1H, dd, *J* 15.2 and 10.3, 7-H) and 6.29 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H); δ_C (100 MHz) 26.4 (C-5), 44.7 (C-4), 78.6 (C-1), 81.2 (C-2), 115.9 (C-9), 131.8 (C-8), 132.2 (C-6), 136.6 (C-7) and 186.2 (C-3); (Found: M^+, 134.0732. $C_9H_{10}O$ requires M, 134.0723).

b) Treatment of the amide **213** (2.95 mmol) with ethynylmagnesium bromide (3.55 mmol), as described previously, followed by chromatography [silica gel, ethyl acetate-hexane (1:5)] gave starting amide (300 mg, 60 %) followed by *ynone* **221** (115 mg, 29 %).

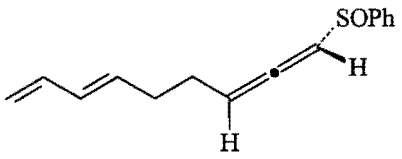
(2′*R*,3*R*,6*E*)-Nona-6,8-dien-1-yn-3-yl 2′-methoxy-2′-trifluromethyl-2′-phenylethanoate 222



Reduction of the ynone **221** (115 mg, 0.86 mmol) with (*R*)-Alpine Borane [prepared from 9-BBN dimer (575 mg, 2.36 mmol) and (+)-α-Pinene (0.75 ml, 4.72 mmol)] followed by work-up using ethanolamine (0.29 ml, 4.9 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:12)] gave *ynol* **219** (104 mg, 88 %); $[\alpha]_D$ -4.3 (*c* 1.0 in $CHCl_3$).

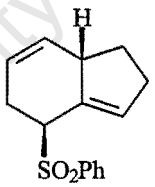
The alcohol **219** (30 mg, 0.22 mmol) was treated as before with Mosher's acid (52 mg, 0.22 mmol), DMAP (cat.) and DCC (0.35 ml, 0.35 mmol, 1M solution in dichloromethane). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)] gave the *ester* **222** (*ee* 33 % by F^{19} NMR, 30 mg, 39 %); $[\alpha]_D$ +61.4 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2116 (C≡C) and 1748 (CO); δ_F (188 MHz) 80.6 (*R*-CF_3), 80.7 (*S*-CF_3); (Found: M^+, 352. $C_{19}H_{19}F_3O_3$ requires M, 352).

(*M*,6*E*)-1-Phenylsulfinylnona-1,2,6,8-tetraene 223



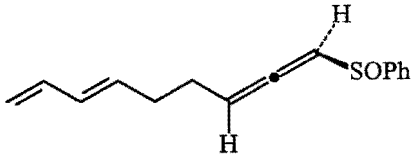
Treatment of (*R*)-ynol **219** (201 mg, 1.48 mmol) with triethylamine (0.31 ml, 2.20 mmol) and benzenesulfenyl chloride (0.18 ml, 1.55 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:10)], gave a mixture of *(M)-phenylsulfinylallenes* **223** (240 mg, 67 %); $[\alpha]_D$ -45.0 (*c* 1.0 in $CHCl_3$), which was used directly.

(4*S*,7a*S*)-4-Phenylsulfonyl-2,4,5,7a-tetrahydro-1*H*-indene 225



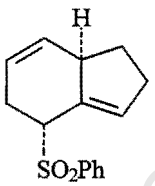
Oxidation of the sulfoxides **223** (217 mg, 0.89 mmol) with *m*-CPBA (245 mg, 62 %, 0.89 mmol) in dichloromethane (3 ml), followed by work-up (as carried out for **129**) and chromatography [silica gel, ethyl acetate-toluene (1:49)], gave diastereopure *cycloadduct* **225** (52 mg, 23 %); mp 82 – 84 °C (from ethanol); $[\alpha]_D$ +47.4 (*c* 0.6 in $CHCl_3$). All spectroscopic data were identical to **130**. This was followed by a mixture of cycloadduct **225** and minor cycloadduct **226** (34 mg, 15 %, 1:1 by NMR).

(*P*,6*E*)-1-Phenylsulfinylnona-1,2,6,8-tetraene 227



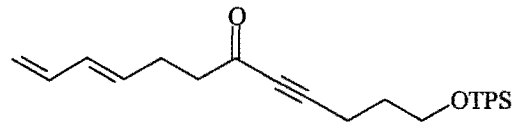
Treatment of (*S*)-ynol **220** (230 mg, 1.71 mmol) with triethylamine (0.36 ml, 2.57 mmol) and benzenesulfenyl chloride (0.23 ml, 2.00 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (3:10)], gave a mixture of (*P*)-*phenylsulfinylallenes* **227** (288 mg, 69 %); $[\alpha]_D$ +45.5 (*c* 0.8 in $CHCl_3$).

(4*R*,7a*R*)-4-Phenylsulfonyl-2,4,5,7a-tetrahydro-1*H*-indene 229



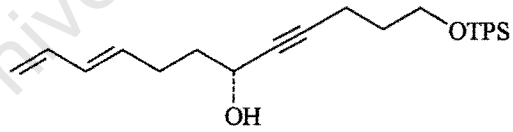
Oxidation of the sulfoxides **227** (214 mg, 0.88 mmol) with *m*-CPBA (245 mg, 62 %, 0.89 mmol) in dichloromethane (3 ml), followed by work-up (as for **129**) and chromatography [silica gel, ethyl acetate-toluene (1:49)], gave diastereopure *cycloadduct* **229** (58 mg, 25 %); mp 84 – 86 °C (from ethanol); $[\alpha]_D$ -47.3 (*c* 1.0 in $CHCl_3$). All spectroscopic data were identical to **131**. This was followed by a mixture of cycloadduct **229** and minor cycloadduct **230** (53 mg, 23 %, 1:1 by NMR).

(9*E*)-1-(*t*-Butyldiphenylsilyloxy)dodeca-9,11-dien-4-yn-6-one 231



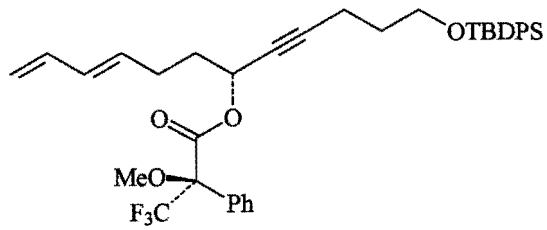
n-BuLi (1.52 ml, 3.8 mmol, 2.5M solution in hexanes) was added to a stirred solution of 1-(*t*-butyldiphenylsilyloxy)pent-4-yne (1.2 g, 3.8 mmol) in THF (10) at room temperature, and the resulting solution was stirred for 30 min. Weinreb amide **213** (600 mg, 3.55 mmol) was added and the solution was stirred for a further 30 min after which HCl (1M) was added. The mixture was extracted (Et_2O) and the combined extract washed (water, brine) and dried ($MgSO_4$). The solvent was evaporated and the residue was chromatographed on silica gel with ethyl acetate-hexane (1:19) as eluent to afford the *ynone* **231** (1.09 g, 72 %) ;ν_{max}/cm^{-1} 2213 (C≡C) and 1668 (CO); δ_H 1.05 (9H, s, CMe_3), 1.60 (2H, quin, *J* 4 x 6.0, 2-H_2), 2.40 – 2.60 (6H, m, 3-, 7- and 8-H_2), 3.74 (2H, t, *J* 6.0, 1-H_2), 4.95 (1H, br d, *J* 10.2, 12-H_{cis}), 5.10 (1H, dd, *J* 17.1 and 1.1, 12-H_{trans}), 5.70 (1H, dt, *J* 15.1 and 2 x 7.0, 9-H), 6.10 (1H, dd, *J* 15.1 and 10.2, 10-H), 6.32 (1H, dt, *J* 17.1 and 2 x 10.2, 11-H) and 7.40 – 7.70 (10H, m, Ph); δ_C 15.6 (C-2), 19.2 (CMe_3), 26.8 (CMe_3), 30.6 (C-3 and C-8), 44.8 (C-7), 62.0 (C-1), 80.8 (C-4), 94.3 (C-5), 115.7 (C-12), 127.6 (Ph), 129.6 (Ph), 132.0 (C-10), 133.6 (C-9), 133.8 (Ph), 135.5 (Ph), 136.8 (C-11) and 187.1 (CO); (Found: *M-Bu*$_t^+$, 373. $C_{24}H_{25}O_2Si$ requires M, 373).

(6*R*,9*E*)-1-(*t*-Butyldiphenylsilyloxy)-dodeca-9,11-dien-4-yn-6-ol 232



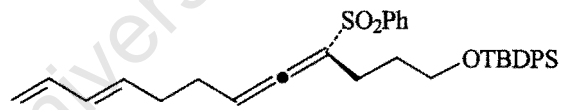
Reduction of the ynone **231** (1.09 g, 2.55 mmol) with (*R*)-Alpine Borane [prepared from 9-BBN dimer (980 mg, 4.0 mmol) and (+)-α-Pinene (1.27 ml, 8.0 mmol)], followed by work-up using ethanolamine (0.49 ml, 8.3 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:3)], gave (*R*)-dienynol **232** (927 mg, 85 %); $[\alpha]_D$ -10.5 (*c* 1.0 in $CHCl_3$). Spectroscopic data were identical to that of **150**.

(2′*R*,6*R*,9*E*)-1-(*t*-Butyldiphenylsiloxy)dodeca-9,11-dien-4-yn-6-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 233



Mosher ester formation was carried out on (*R*)-alcohol **232** (32 mg, 70 μmol) using (*R*)-methoxy-trifluoromethylphenylacetic acid (16 mg, 70 μmol), DMAP (2 mg, cat) and DCC (0.15 ml, 0.15 mmol, 1M solution in CH_2Cl_2). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:19)] gave diastereomer **233** (85 % *de* by F^{19} NMR, 45 mg, 99 %); $[\alpha]_D$ +23.3 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 2116 (C≡C) and 1750 (CO); δ_H 1.04 (9H, s, $C(Me)_3$), 2.44 (2H, td, *J* 2 x 7.0 and 1.9, 3-H_2), 3.57 (3H, s, OMe), 3.70 (2H, t, *J* 6.0, 1-H_2), 4.95 (1H, br d, *J* 10.2, 12-H_{cis}), 5.10 (1H, br d, *J* 17.0, 12-H_{trans}), 5.50 – 5.60 (2H, m, 6-H and 9-H), 6.00 (1H, dd, *J* 15.5 and 10.2, 10-H), 6.28 (1H, dt, *J* 17.0 and 2 x 10.3, 11-H) and 7.40 – 7.60 (15H, m, Ph); δ_F (188 MHz) 80.7 (CF_3); (Found (Electrospray): $M+Na^+$, 671. $C_{38}H_{43}F_3NaO_4Si$ requires M, 671).

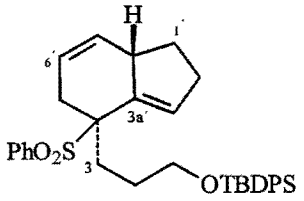
(*M*,9*E*)-1-(*t*-Butyldiphenylsilyloxy)-4-phenylsulfonyldodeca-4,5,9,11-tetraene 234



Treatment of (*R*)-alcohol **233** (900 mg, 2.08 mmol) with triethylamine (0.46 ml, 3.30 mmol) and benzenesulfenyl chloride (0.35 ml, 3.30 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)], gave a mixture of (*M*)-*phenylsulfinylallenes* (705 mg, 63 %); $[\alpha]_D$ -19.4 (*c* 1.1 in $CHCl_3$), which was used directly.

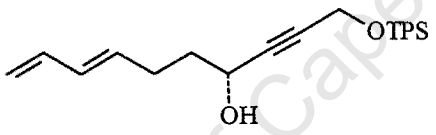
Oxidation of sulfinyltetraene (696 mg, 1.29 mmol) with *m*-CPBA (372 mg, 60 %, 1.29 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:9)], gave (*M*)-*phenylsulfonylallene* **234** (275 mg, 38 %); $[\alpha]_D$ -32.5 (*c* 1.1 in $CHCl_3$). This was followed by starting material (250 mg, 36 %). NMR and infrared spectra were identical to those of **151**.

(4′*S*,7a′*S*)- (1-*t*-Butyldiphenylsilyloxy)-3-(4′-phenylsulfonyl-2′,4′,5′,7a′-tetrahydro-1′*H*-inden-4′-yl)propane 235



The tetraene **234** (160 mg, 0.29 mmol) in CH_2Cl_2 (2 ml) was heated at 40 °C for 3 h whilst the reaction was monitored by NMR. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel with ethyl acetate-hexane (1:9) as solvent to yield the cycloadduct **235** (31 mg, 19 %). Spectroscopic characterisation of cycloadduct was identical to that observed for **152**.

(4*R*,7*E*) 1-(*t*-Butyldiphenylsilyloxy)-deca-7,9-dien-2-yn-4-ol 237

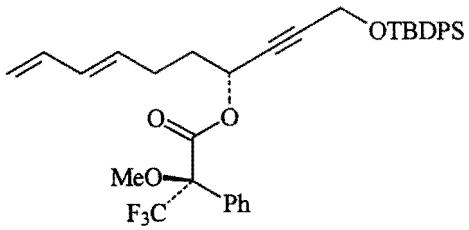


1-*t*-Butyldiphenylsiloxy-prop-2-yne (695 mg, 2.34 mmol) was dissolved in THF (5 ml). *n*-BuLi (0.95 ml, 2.34 mmol, 2.5 M solution in hexanes) was added followed by the amide **213** (295 mg, 1.75 mmol) after 0.5 h, This was stirred for 0.5 h after which dil. HCl (1M) was added. The mixture was extracted (Et_2O) and the combined extract washed (water, brine) and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed on silica gel with ethyl acetate-hexane (1:20) as eluent to afford the *ynone* **236** (546 mg, 1.36 mmol, 78 %);ν_{max}/cm^{-1} 2217 (C≡C), 1669 (CO); δ_H 1.08 (9H, s, C(CH_3)$_3$), 2.40 - 2.60 (4H, m, 5-H_2 and 6-H_2), 4.47 (2H, s, 1-H_2), 4.95 (1H, br d, *J* 10.2, 10-H_{cis}), 5.10 (1H, dd, *J* 17.1 and 1.1, 10-H_{trans}), 5.70 (1H, dt, *J* 15.1 and 7.0, 7-H), 6.10 (1H, dd, *J* 15.1 and 10.2, 8-H), 6.32 (1H, dt, *J* 17.1 and 10.2, 9-H), 7.40 (6Hs, m, Ph), 7.70 (4H, m, Ph); (Found: *M-Bu*$_t^+$, 345. $C_{22}H_{21}O_2Si$ requires M, 345).

Reduction of the ynone **234** (500 mg, 1.24 mmol) with (*R*)-Alpine Borane [prepared from 9-BBN dimer (303 mg, 1.25 mmol) and (+)-α-Pinene (0.39 ml, 2.5 mmol)], followed by work up using ethanolamine (0.17 ml, 2.8 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:4)], gave *ynol* **237** (249 mg, 0.62 mmol, 50 %); $[\alpha]_D$ -12.7 (*c* 1.0 in $CHCl_3$); δ_{max}/cm^{-1} 3600 (OH),

2359 (C≡C); δ_H 1.05 (9H, s, C(CH_3)$_3$), 1.70 – 2.20 (4H, m, 5 and 6 -H_2), 4.35 (1H, m, 4-H), 4.39 (2H, d, *J* 1.7, 1-H_2), 4.97 (1H, br d, *J* 10.3, 11-H_{cis}), 5.10 (1H, br d, *J* 17.0 , 11-H_{trans}), 5.70 (1H, dt, *J* 15.2, 6.6, 8-H), 6.08 (1H, dd, *J* 15.2, 10.3, 9-H), 6.32 (1H, dt, *J* 17.0, 10.3, 10-H); δ_C (100 MHz, $CDCl_3$) 19.2 (C(CH_3)$_3$) 26.8 (C(CH$_3$)$_3$), 28.1 (C-6), 36.8 (C-5), 52.7 (C-1), 61.8 (C-4), 83.6, 86.1 (C-2,3), 115.2 (C-10), 127.7 (Ph), 129.8 (Ph), 131.7 (C-8), 133.7 (C-7), 135.7 (Ph), 137.1 (C-9); (Found: M^+, 404. $C_{26}H_{32}O_2Si$ requires M, 404).

(2′*R*,4*R*,7*E*) 1-(*t*-Butyldiphenylsiloxy)-deca-7,9-dien-2-yn-4-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 238



Mosher ester formation was carried out on (*R*)-alcohol **237** (22 mg, 54 μmol) using (*R*)-methoxy-trifluoromethylphenylacetic acid (18 mg, 75 μmol), DMAP (2 mg, cat) and DCC (0.1 ml, 0.1 mmol, 1 M solution in CH_2Cl_2). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:20)] gave diastereomer **238** (34 mg, 54 μmol, 100 %, 90 % *ee* by F^{19} NMR); $[\alpha]_D$ 29.8 (*c* 1.0 in $CHCl_3$);δ_{max}/cm^{-1} 2243 (C≡C), 1750 (CO); δ_H (300 MHz) 1.05 (9H, s, C(Me)$_3$), 2.44 (2H, td, *J* 7.0 and 1.8, 5-H_2), 3.52 (3H, s, OMe), 4.19 (2H, d, *J* 1.5, 1-H), 5.00 (1H, br d, *J* 10.2, 10-H_{cis}), 5.10 (1H, br d, *J* 17.0, 10-H_{trans}), 5.50 - 5.60 (2H, m, 4-H and 7-H), 6.00 (1H, dd, *J* 15.5 and 10.2, 8-H), 6.28 (1H, dt, *J* 17.0 and 10.3, 9-H), 7.40 - 7.60 (15H, m, Ph);δ_F (188MHz, $CDCl_3$) 80.7 (CF_3); (Found: *M-Bu*$_t^+$, 563. $C_{32}H_{30}F_3O_4Si$ requires M, 563).

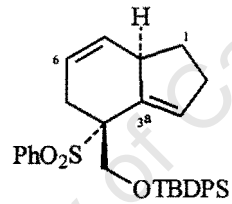
(4*S*,7*E*) 1-(*t*-Butyldiphenylsiloxy)-deca-7,9-dien-2-yn-4-ol 239

Reduction of the Reduction of the ynone **236** (225 mg, 0.55 mmol) with (*S*)-Alpine Borane [prepared from 9-BBN dimer (154 mg, 0.64 mmol) and (+)-α-Pinene (0.19 ml, 1.25 mmol)], followed by work up using ethanolamine (0.09 ml, 1.3 mmol) and chromatography [silica gel, ethyl acetate-hexane (1:4)], gave *ynol* **239** (144 mg, 0.35 mmol, 64 %); $[\alpha]_D$ +12.7 (*c* 1.0 in $CHCl_3$).

(2′*R*,4*S*,7*E*) 1-(*t*-Butyldiphenylsiloxy)-deca-7,9-dien-2-yn-4-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylethanoate 240

Mosher ester formation was carried out on (*S*)-alcohol **239** (30 mg, 74 μmol) using (*R*)-methoxy-trifluoromethylphenylacetic acid (17 mg, 74 μmol), DMAP (2 mg, cat) and DCC (21 mg, 0.1 mmol). Work-up and chromatography [silica gel, ethyl acetate-hexane (1:20)] gave diastereomer **240** (40 mg, 64 μmol, 87 %, 94 % *ee* by F^{19} NMR); $[\alpha]_D$ –1.3 (*c* 0.9 in $CHCl_3$);δ_{max}/cm^{-1} 2243 (C≡C), 1750 (CO); δ_H (300 MHz, C_6D_6) 1.12 (9H, s, $C(Me)_3$), 2.05 (2H, q, *J* 3 x 7.3, 6-H_2), 3.41 (3H, d, *J* 1.2, OMe), 4.19 (2H, d, *J* 1.5, 1-H), 5.00 (1H, br d, *J* 10.2, 10-H_{cis}), 5.10 (1H, br d, *J* 17.0, 10-H_{trans}), 5.50 - 5.60 (2H, m, 4-H and 7-H), 6.00 (1H, dd, *J* 15.5 and 10.2, 8-H), 6.28 (1H, dt, *J* 17.0 and 10.3, 9-H), 7.40 - 7.60 (15H, m, Ph); δ_F (188MHz, $CDCl_3$) 80.4 (CF_3); (Found: *M*-*Bu*$_t$, 563.1889. $C_{32}H_{30}F_3O_4Si$ requires M, 563.1866).

(4*R*,7a*R*)-4- *t*-Butyldiphenylsilyloxymethanol-4-phenylsulfonyl-2,4,5,7a-tetrahydro-1*H*-indene 242

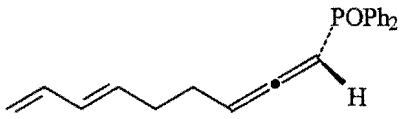


Treatment of (*S*)-alcohol **239** (60 mg, 0.15 mmol) with triethylamine (70 μl, 0.5 mmol) and benzenesulfenyl chloride (30 μl, 0.26 mmol), followed by work-up and chromatography [silica gel, ethyl acetate-hexane (1:20)], gave a mixture of (*P*)-*phenylsulfinylallenyl* diasteromers (34 mg, 44 %); δ_H 0.98 (9H, s, $C(CH_3)_3$), 2.20 (2H, m, 6-H_2), 2.50 (2H, m, 5-H_2), 5.00 (1H, br d, *J* 10.3, 10-H_{cis}), 5.12 (1H, br d, *J* 17.0, 10-H_{trans}), 5.50 – 5.75 (3H, m, 2-H, 4-H and 7-H), 6.05 (1H, dd, *J* 15.4 and 10.3, and 8-H), 6.30 (1H, dt, *J* 17.0 and 10.3, 9-H), 7.30 – 7.90 (15H, m, Ph); (Found: *M*-*Bu*$_t^+$, 455.1501. $C_{28}H_{27}O_2SiS$ requires M, 455.1501) which was partially characterised as it was used directly.

Oxidation of sulfinyltetraene **241** (33 mg, 64 μmol) with *m*-CPBA (16 mg, 65 μmol), followed by work-up gave a product, which contained significant amounts of cycladduct. This residue was dissolved in ethyl acetate and was heated at 50 °C for 30 min. Chromatography of the residue[silica gel, ethyl acetate-hexane (1:19)], gave *exo*-cycloadduct **242** (29 mg, 85 %); $[\alpha]_D$ -

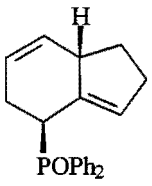
38.2 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} 1303, 1145 (SO); δ_H (300 MHz) 1.20 (10H, 1β-H and $C(CH_3)_3$), 2.20 (3H, m, 1α-H and 2-H_2), 2.53 (1H, m, *W* 26, 5-H), 2.86 (1H, ddt, *J* 17.9, 4.4 and 2 x 2.3, 5-H), 3.10 (1H, m, 7a-H), 3.79 (1H, d, *J* 10.8, CHOSi), 4.12 (1H, d, *J* 10.8, CHOSi), 5.57 (1H, ddt, *J* 9.9, 4.4, and 2 x 3.2, 6-H), 5.69 (1H, br d, *J* 9.9, 7-H) and 7.48 – 7.85 (15H, m, Ph); δ_C (70 MHz) 19.3 (s, *C*(Me)$_3$), 26.9 (q, C(*Me*)$_3$), 29.7, (t, C-5), 31.0 (t, C-1), 31.9 (t, C-2), 43.6 (d, C-7a), 65.6 (t, C-OSi), 68.8 (s, C-4), 122.7 (d, C-6), 127.7 (d, Ph), 128.2 (d, Ph), 129.7 (d, Ph), 130.3 (d, Ph), 131.4 (d, C-3), 132.0 (d, C-7), 132.9 (d, Ph), 133.2 (d, Ph), 135.7 (d, Ph), 136.6 (s, C-3a) and 136.9 (s, Ph); (Found: M^+, 528.2147. $C_{32}H_{36}O_3SiS$ requires M, 528.2155).

(*M*,6*E*)-1-Diphenylphosphonylnona-1,2,6,8-tetraene 245



DMAP (268 mg, 2.2 mmol) and diphenylphosphinyl chloride (0.38 ml, 2.2 mmol) were added to a stirred solution of the *R*-alcohol **219** (200 mg, 1.47 mmol) dissolved in ether (5 ml), and the resultant slurry was stirred for 16 h at room temperature. Water was added, and the mixture was extracted (Et_2O). The organic phase was washed (water, brine), dried and evaporated. The residue was chromatographed on silica gel with ethyl acetate-hexane (8:2) as eluent and gave *phosphonyl allenes* **245** (190 mg, 40 %); $[\alpha]_D$ -72.7 (*c* 1.0 in $CHCl_3$) as an oil; ν_{max}/cm^{-1} 1952 (C=C=C) and 1121 (PO); δ_H 2.00 (4H, m, 4-H_2 and 5-H_2), 5.00 (1H, dd, *J* 10.2 and 2.7, 9-H_{cis}), 5.12 (1H, dd, *J* 17.0 and 2.7, 9-H_{trans}), 5.60 – 5.75 (2H, m, 3-H and 6-H), 6.05 (2H, m, 1-H and 7-H), 6.27 (1H, dt, *J* 17.0 and 2 x 10.3, 8-H) and 7.50 – 7.65 (10H, m, Ph); δ_C 26.9, 27.0 (C-4) 31.7, 31.8 (C-5), 84.6, 86.7 (C-1), 91.9, 92.2 (C-3), 115.5 (C-9), 128.2, 128.5, 128.7 131.3, 131.5 (Ph), 132.3 (C-7), 132.1 (C-6), 133.1 (Ph), 136.9 (C-8), 144.8 (Ph) and 211.5 (C-2); (Found: M^+, 320. $C_{21}H_{21}OP$ requires M, 320).

(4*S*,7a*S*)-4-Diphenylphospinonyl-2,4,5,7a-tetrahydro-1*H*-indene 246



The tetraene **245** (140 mg, 0.43 mmol) in toluene (2 ml) was heated in a sealed tube at 90 °C for 2 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel with ethyl acetate-hexane (5:1) as eluent to yield the *exo cycloadduct* **246** (90 mg, 64 %); mp 148 – 150 °C (from ethanol); $[\alpha]_D$ –6.1 (*c* 1.0); ν_{max}/cm^{-1} 1118 (PO); δ_H (400 MHz) 1.20 (1H, m, *W* 44.5, 1α-H), 2.20 (3H, m, 1β- and 2-H_2), 2.40 – 2.62 (2H, m, 5-H_2), 3.35 (1H, br, *W* *ca* 25,7a-H), 3.61 (1H, t, *J* 8.4, 4-H), 5.20 (1H, br s, $W_{½}$ 2.2, 3-H), 5.58 (1H, ddd, *J* 9.9, 7.2 and 2.8, 6-H), 5.73 (1H, dq, *J* 9.9 and 3 x 2.2, 7-H) and 7.40 – 7.90 (10H, m, $POPh_2$); δ_C (100 MHz) 25.8 (C-5), 31.2 (C-1), 31.5 (C-2), 36.7, 37.5 (d, *J* 129.6, C-4), 42.7 (C-7a), 122.9 (C-6), 127.1 (C-3), 128.0, 128.1, 128.5, 128.6, 131.1, 131.2, 131.3, 131.4, 131.6 ($POPh_2$) and 132.2 (C-7); δ_p (162 MHz) 31.7 ($POPh_2$); (Found: M^+, 320.1320. $C_{21}H_{21}OP$ requires M, 320.1330).

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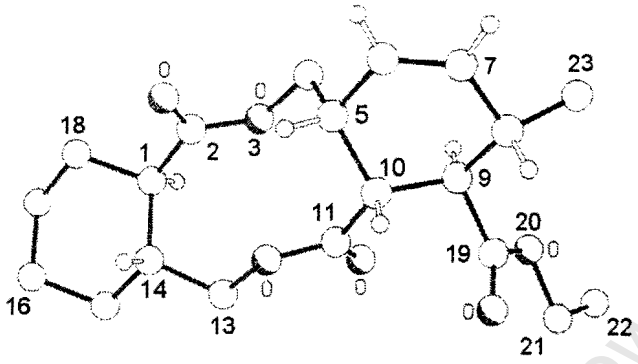
APPENDIX 1: CRYSTAL STRUCTURES

Selected X-ray data for:

(1*R,5*S**,8*R**,9*R**,10*R**,14*R**)-8-METHYL-3,12-DIOXA-2,11-DIOXO-[12.4.0.0^{5,10}]-TRICYCLO-OCTADEC-6-EN-9-CARBOXYLATE** (collected by the Imperial College Crystallography department)



General

Empirical formula	$C_{20}H_{28}O_6$	Formula weight	364.42
Temperature	293(2) K	Wavelength	0.71073 Å
Crystal system	Orthorhombic	Space group	Pbca
Unit cell Dimensions	a = 14.572(1) Å $\alpha = 90°$	Volume	1398.9 Å^3
	b = 10.825 (1) Å $\beta = 90°$	Z	8
	c = 24.135(1) Å $\chi = 90°$		
Density (calc)	1.272 Mg/m^3	Absorp. coeff.	0.093 mm^{-1}
F(000)	1568	Reflections collected	3089
Crystal size	0.73 x 0.40 x 0.23 mm	Indepen. reflections	3089
Index ranges	0<h<17, 0<k<10, -28<l<0	ϕ range for collection	2.49 – 25 °

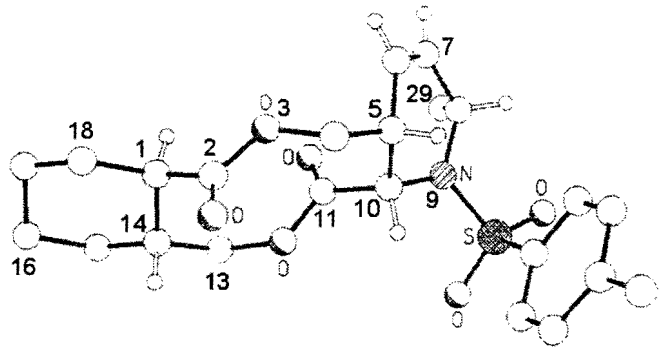
Refinenment method	Full-matrix least-squares on F^2 (Direct)
Goodness-to-fit on F^2	1.026
Final R indices	$R_1 = 0.0496$, $wR_2 = 0.1114$
R indices (all data)	$R_1 = 0.0819$, $wR_2 = 0.1283$
Extinction coeffiecient	0.0006(3)
Largest diff. peak and hole	0.299 and -.0.169 eÅ^{-3}

Tables 1 and 2: Selected bond lengths (Å) and bond angles

Bond	Length Å	Bond	Length Å	Bond	Length Å
C(1) – C(2)	1.516	C(8) – (C23)	1.532	C(15) – C(16)	1.510
C(2) – C(2)	1.205	C(9) – C(10)	1.541	C(16) – (C17)	1.509
C(2) – O(3)	1.340	C(10) – C(19)	1.512	C(17) – C(18)	1.527
O(3) – C(4)	1.459	C(10) – C(11)	1.516	C(18) – C(1)	1.517
C(4) – C(5)	1.530	C(11) – O(11)	1.198	C(19) – O(19)	1.201
C(5) – C(6)	1.507	C(11) – O(12)	1.347	C(19) – O(20)	1.344
C(5) – C(10)	1.548	O(12) – C(13)	1.451	O(20) – C(21)	1.457
C(6) – C(7)	1.316	C(13) – C(14)	1.505	C(21) – C(22)	1.480
C(7) – C(8)	1.507	C(14) – C(15)	1.536		
C(8) – C(9)	1.543	C(14) – C(1)	1.548		

Bond	Angle °	Bond	Angle °	Bond	Angle °
C(19) – C(9) – C(10)	108.9	O(2) – C(2) – O(3)	123.8	O(11) – C(11) – O(12)	124.1
C(8) – C(9) – C(10)	111.2	O(2) – C(2) – C(1)	123.6	O(11) – C(11) – C(10)	125.0
C(7) – C(8) – C(9)	111.6	C(1) – C(2) – O(3)	112.6	C(5) – C(10) – C(11)	112.6
C(6) – C(7) – C(8)	125.6	C(2) – C(1) – C(14)	111.1	C(5) – C(10) – C(9)	112.3
C(5) – C(6) – C(7)	124.0	C(18) – C(1) – C(14)	110.7	C(10) – C(11) – O(12)	110.9
C(23) – C(8) – C(9)	110.9	C(17) – C(18) – C(1)	112.3	C(19) – C(9) – C(8)	109.2
C(7) – C(8) – C(23)	110.7	C(16) – C(17) – (18)	110.2	O(19) – C(19) – C(9)	124.1
C(4) – C(5) – C(6)	108.3	C(15) – C(16) – C(17)	110.7	O(19) – C(19) – O(20)	123.2
C(4) – C(5) – C(10)	115.2	C(14) – C(15) – C(16)	112.4	C(9) – C(19) – O(2O)	112.7
C(6) – C(5) – C(10)	109.8	C(13) – C(14) – C(15)	108.6	C(19) – O(20) – C(21)	114.1
O(3) – C(4) – C(5)	112.8	O(12) – C(13) – C(14)	110.4	O(20) – C(21) – C(22)	108.2
C(2) – O(3) – C(4)	116.6	C(11) – O(12) – C(13)	116.5		

(1*R,5*R**,8*S**,10*S**,14*R**)-8-METHYL-9-*P*-TOLUENESULFONYL-9-AZA-3,12-DIOXA-2,11-DIOXO-[12.4.0.0^{5,10}]-TRICYCLO-OCTADEC-6-ENE** (collected by the Imperial College Crystallography department)



General

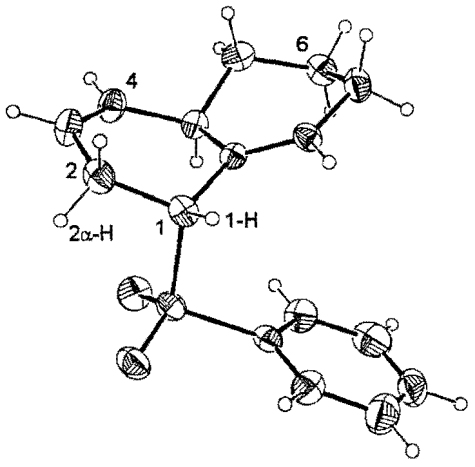
Empirical formula	$C_{23}H_{29}NO_6$		Formula weight	447.53
Temperature	293(2) K		Wavelength	1.54178 Å
Crystal system	Monoclinic		Space group	$P2_1/c$
Unit cell Dimensions	a = 6.9313(1) Å	α = 90°	Volume	1398.9 Å^3
	b = 14.125 (3) Å	β = 94.309°	Z	4
	c = 23.181(2) Å	χ = 90°		
Density (calc)	1.314 Mg/m^3		Absorp. coeff. 1.600 mm^{-1}	
F(000)	952		Reflections collected	3673
Crystal size	0.60 x 0.10 x 0.03 mm		Indepen. reflections	3359
Index ranges	-7<h<0, -15<k<0, -25<l<26		ϕ range for collection	2.67 – 60 °
Refinenment method	Full-matrix least-squares on F^2 (Direct)			
Goodness-to-fit on F^2	1.048			
Final R indices	R_1 = 0.0533, wR_2 = 0.1191			
R indices (all data)	R_1 = 0.0858, wR_2 = 0.1427			
Extinction coeffiecient	0.0010(2)			
Largest diff. peak and hole	0.192 and -.0.222 eÅ^{-3}			

Tables 3 and 4: Selected bond lengths (Å) and bond angles

Bond	Length Å	Bond	Length Å	Bond	Length Å
C(1)-C(2)	1.511	C(15)-C(16)	1.519	O(12)-C(13)	1.452
C(2)-O(2)	1.198	C(17)-C(18)	1.524	C(14)-C(15)	1.533
O(3)-C(4)	1.454	C(1)-C(14)	1.528	C(16)-C(17)	1.504
C(5)-C(6)	1.506	C(2)-O(3)	1.338	C(1)-C(18)	1.535
C(7)-C(8)	1.491	C(4)-C(5)	1.498	S(19)-O (20)	1.430
C(8)-N(9)	1.475	C(6)-C(7)	1.306	S(19)-C (22)	1.761
N(9)-C(10)	1.473	C(8)-C(29)	1.536	S(19)-O (21)	1.433
C(10)-C(11)	1.531	N(9)-S(19)	1.629	C(22)-C(23)	1.378
C(11)-O(12)	1.339	C(10)-C(5)	1.534		
C(13)-C(14)	1.525	C(11)-O(11)	1.192		

Bond	Angle °	Bond	Angle °	Bond	Angle °
S(19) – N(9) – C(10)	115.4	O(2) – C(2) – O(3)	123.6	O(11) – C(11) – O(12)	124.4
S(19) – N(9) – C(8)	120.5	O(2) – C(2) – C(1)	124.0	O(11) – C(11) – C(10)	124.8
C(7) – C(8) – N(9)	111.0	C(1) – C(2) – O(3)	112.3	C(5) – C(10) – C(11)	114.4
C(6) – C(7) – C(8)	124.3	C(2) – C(1) – C(14)	109.4	C(5) – C(10) – N(9)	109.8
C(5) – C(6) – C(7)	122.8	C(18) – C(1) – C(14)	111.3	C(10) – C(11) – O(12)	110.8
C(28) – C(8) – N(9)	111.6	C(17) – C(18) – C(1)	111.8	N(9) – C(10) – C(11)	109.3
C(7) – C(8) – C(28)	111.9	C(16) – C(17) – (18)	111.0	C(10) – N(9) – C(8)	122.4
C(4) – C(5) – C(6)	115.5	C(15) – C(16) – C(17)	110.4	N(9) – S(19) – C(20)	104.7
C(4) – C(5) – C(10)	114.1	C(14) – C(15) – C(16)	113.4	C(1) – C(13) – C(14)	113.0
C(6) – C(5) – C(10)	108.9	C(13) – C(14) – C(15)	106.5	C(1) – C(13) – C(15)	111.9
O(3) – C(4) – C(5)	109.1	O(12) – C(13) – C(14)	112.7		
C(2) – O(3) – C(4)	116.4	C(11) – O(12) – C(13)	117.2		

(1*R,4a*R**)-1-PHENYLSULFONYL-1,2,4A,5,6,7-HEXAHYDRO-NAPHTHALENE** (collected by the University of Cape Town Crystallography department)



General

Empirical formula	$C_{16}H_{18}O_2S$	Formula weight	274.36
Temperature	293(2) K	Wavelength	0.71070 Å
Crystal system	Monoclinic	Space group	C c
Unit cell Dimensions	a = 14.700(1) Å α = 90°	Volume	1398.9 $Å^3$
	b = 8.782 (1) Å β = 103.77°	Z	4
	c = 11.157(1) Å χ = 90°		
Density (calc)	1.303 Mg/m^3	Absorp. coeff. 0.227 mm^{-1}	
F(000)	584	Reflections collected	10417
Crystal size	0.20 x 0.15 x 0.25 mm	Indepen. reflections	1377
Index ranges	0<h<18, 0<k<10, -12<l<12	ϕ range for collection	3.11 – 26 °

Completeness to ϕ	95.9 %
Refinenment method	Full-matrix least-squares on F^2
Goodness-to-fit on F^2	1.158
Final R indices	R_1 = 0.0672, wR_2 = 0.0991
R indices (all data)	R_1 = 0.1163, wR_2 = 0.1113
Extinction coefficient	0.0071
Largest diff. peak and hole	0.2 and – 0.203e$Å^{-3}$

Tables 5 and 6: Selected bond lengths (Å) and bond angles

Bond	Length Å	Bond	Length Å	Bond	Length Å
S(1) – O(1)	1.432	C(4a) – H(5)	1.525	C(8) – H(8)	0.960
S(1) – O(2)	1.449	C(4a) – H(4a)	0.959	C(2) – C(1)	1.517
S(1) – C(Ph)	1.777	C(3) – C(4)	1.306	C(2) – H(2a)	0.959
S(1) – C(1)	1.807	C(3) – C(2)	1.498	C(2) – H(2b)	0.959
C(8a) – C(8)	1.317	C(3) – H(3)	0.960	C(1) – H(1)	0.959
C(8a) – C(1)	1.495	C(7) – C(8)	1.482	C(4) – H(2)	0.960
C(8a) – C(4)	1.515	C(7) – C(6)	1.521		
C(4a) – C(4)	1.493	C(6) – C(5)	1.521		

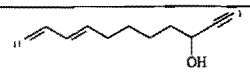
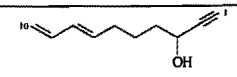
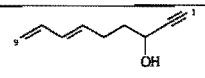
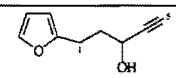
Bond	Angle °	Bond	Angle °	Bond	Angle °
O(2) – S(1) – C(1)	110.0	C(6) – C(7) – H(7a)	107.7	C(1) – C(2) – H(2b)	109.5
O(1) – S(1) – C(1)	107.3	C(8) – C(7) – H(7b)	108.9	H(2a) – C(2) – H(2b)	109.5
C(9) – S(1) – C(1)	104.8	C(6) – C(7) – H(7b)	108.3	C(8a) – C(1) – C(2)	112.9
C(8) – C(8a) – C(1)	121.2	H(7a) – C(7) – H(7b)	109.5	C(8a) – C(1) – S(1)	112.7
C(8) – C(8a) – C(4a)	122.3	C(5) – C(6) – C(7)	109.9	C(2) – C(1) – S(1)	108.3
C(1) – C(8a) – C(4a)	116.6	C(5) – C(6) – H(6a)	108.4	C(8a) – C(1) – H(1)	106.2
C(4) – C(4a) – C(8a)	111.4	C(7) – C(6) – H(6a)	108.3	C(2) – C(1) – H(1)	107.6
C(4) – C(4a) – C(5)	111.5	C(5) – C(6) – H(6b)	110.8	S(1) – C(1) – H(1)	109.0
C(8a) – C(4a) – C(5)	110.3	C(7) – C(6) – H(6b)	109.9	C(3) – C(4) – C(4a)	124.5
C(4) – C(4a) – H(4a)	106.8	H(6a) – C(6) – H(6b)	109.5	C(3) – C(4) – H(4)	120.9
C(8a) – C(4a) – H(4a)	109.6	C(8a) – C(8) – C(7)	125.4	C(4a) – C(4) – H(4)	114.6
C(5) – C(4a) – H(4a)	107.1	C(8a) – C(8) – H(8)	114.7	C(6) – C(5) – C(4a)	111.8
C(4) – C(3) – C(2)	124.0	C(7) – C(8) – H(8)	120.0	C(6) – C(5) – H(5b)	109.3
C(4) – C(3) – H(3)	119.1	C(3) – C(2) – C(1)	113.7	C(4a) – C(5) – H(5b)	107.3
C(2) – C(3) – H(3)	116.9	C(3) – C(2) – H(2a)	107.5	C(6) – C(5) – H(5a)	110.8
C(8) – C(7) – C(6)	112.5	C(1) – C(2) – H(2a)	109.3	C(4a) – C(5) – H(5a)	108.1
C(8) – C(7) – H(7a)	110.0	C(3) – C(2) – H(2b)	107.2	H(5b) – C(5) – H(5a)	109.4

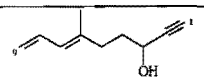
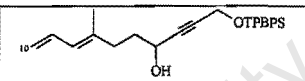
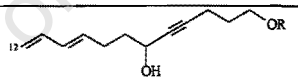
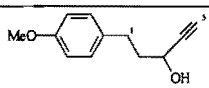
Table 7: Selected torsion angles

Bonds	Torsion angle °	Bonds	Torsion angle °
H(1) – C(1) – C(2) – H(2b)	**-88.9**	C(3) – C(2) – C(1) – C(8a)	34.3
C(8) – C(8a) – C(4a) – C(4)	-141.7	C(3) – C(2) – C(1) – S(1)	-91.2
C(1) – C(8a) – C(4a) – C(4)	37.3	O(2) – S(1) – C(1) – C(8a)	-60.7
C(8) – C(8a) – C(4a) – C(5)	-17.3	O(1) – S(1) – C(1) – C(8a)	169.6
C(1) – C(8a) – C(4a) – C(5)	161.7	C(9) – S(1) – C(1) – C(8a)	54.7
C(8) – C(7) – C(6) – C(5)	41.6	O(2) – S(1) – C(1) – C(2)	64.9
C(1) – C(8a) – C(8) – C(7)	-179.6	O(1) – S(1) – C(1) – C(2)	-64.9
C(4a) – C(8a) – C(8) – C(7)	-0.6	C(9) – S(1) – C(1) – C(2)	-179.8
C(6) – C(7) – C(8) – C(8a)	-12.0	C(2) – C(3) – C(4) – C(4a)	0.0
C(4) – C(3) – C(2) – C(1)	-11.1	C(8a) – C(4a) – C(4) – C(3)	-12.5
C(8) – C(8a) – C(1) – C(2)	129.8	C(5) – C(4a) – C(4) – C(3)	-136.2
C(4a) – C(8a) – C(1) – C(2)	-49.2	C(7) – C(6) – C(5) – C(4a)	-61.4
C(8) – C(8a) – C(1) – S(1)	-107.1	C(4) – C(4a) – C(5) – C(6)	172.3
C(4a) – C(8a) – C(1) – S(1)	73.9	C(8a) – C(4a) – C(5) – C(6)	47.9

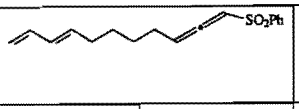
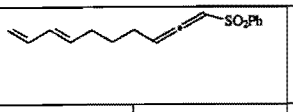
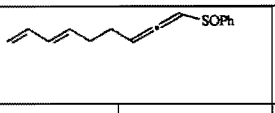
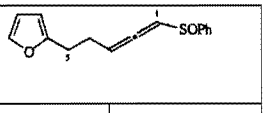
APPENDIX 2: ^{13}C NMR of allenyl precursors and cycloadducts

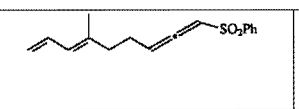
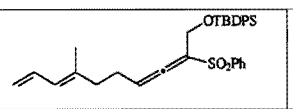
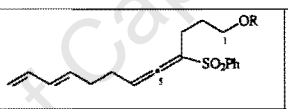
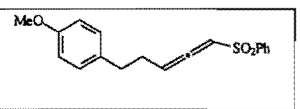
NMR Table 1: ^{13}C NMR of Dienols (protecting groups excluded)

							
24.5	C-5	24.6			C-5		
28.7	C-6					28.0	C-5
32.2	C-7	32.1	23.5	C-1	C-6		
37.4	C-4	37.1	35.8	C-2	C-4	36.9	C-4
62.1	C-3	62.1	61.4	C-3	C-3	61.7	C-3
72.8	C-1	73.0	73.3	C-5	C-1	73.2	C-1
84.9	C-2	84.8	84.3	C-4	C-2	84.6	C-2
114.7	C-11	115.0	105.3	C-3`	C-10	115.4	C-9
131.1	C-9	131.9	110.0	C-4`	C-8	131.9	C-7
134.9	C-8	134.4	141.0	C-5`	C-7	133.4	C-6
137.2	C-10	137.0	154.7	C-2`	C-9	136.9	C-8

							
16.6	Me	16.6	Me	15.1	C-2		
				28.2	C-8		
35.0	C-5	35.0	C-6	31.4	C-3	30.3	C-1
35.6	C-4	35.6	C-5	37.3	C-7	39.3	C-2
61.8	C-3	52.7,62.0	C-1, C-3	62.0,62.3	C-1, C-6	55.2,61.5	OMe,C-3
73.2	C-1	83.6	C-2	81.1	C-4	73.2	C-5
84.6	C-2	86.0	C-3	85.3	C-5	84.8	C-4
115.2	C-9	115.1	C-10	115.1	C-12	113.9	Ph
126.1	C-7	126.0	C-8	131.5	C-10	129.4	Ph
133.0	C-8	133.0	C-9	133.7	C-9	133.2	Ph
138.0	C-6	138.3	C-7	137.0	C-11	157.9	Ph

NMR Table 2: ^{13}C NMR of Sulfones/sulfoxides (Phenyl signals excluded)

							
27.5	C-6						
27.8	C-5	27.0	C-5				
28.3	C-4	27.7	C-4	27.7	C-4	26.8	C-4
32.0	C-7	31.6	C-6	31.5	C-5	27.1	C-5
101.0	C-1	100.9	C-1	98.5	C-1	98.1	C-1
101.2	C-3	101.2	C-3	103.1	C-3	103.2	C-3
114.9	C-11	115.2	C-10	115.7	C-9	105.3	C-3`
131.2	C-9	133.3	C-8	132.3	C-7	110.2	C-4`
134.6	C-8	133.8	C-7	132.7	C-6	141.2	C-5`
137.1	C-10	137.0	C-9	136.9	C-8	154.2	C-2`
205.5	C-2	205.7	C-2	203.6	C-2	203.6	C-2

							
16.5	Me	16.5	Me	19.1	C-2		
				27.7	C-7	29.5	C-1
26.0	C-4	26.2	C-5	30.5	C-3	33.7	C-2
38.2	C-5	38.4 60.3	C-6 C-1	31.3 62.5	C-8 C-1	55.2	OMe
100.5	C-1	100.8	C-4	100.7	C-6	100.4	C-5
101.5	C-3	113.4	C-2	113.7	C-4	101.4	C-3
115.6	C-9	115.5	C-10	115.6	C-12	113.9	Ph
126.6	C-7	126.5	C-8	130.5	C-10	129.8	Ph
132.9	C-8	132.9	C-9	133.7	C-9	133.7	Ph
137.1	C-6	137.4	C-7	136.7	C-11	158.1	Ph
205.6	C-2	205.3	C-2	203.8	C-2	205.7	C-4