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The synthesis and potential applications of asymmetric silacycles

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The Synthesis and Potential Applications of Asymmetric Silacycles

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Ph.D. Thesis

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DECLARATION

The work contained in this thesis was carried out in the Department of Chemistry at the University of Durham between October 1991 and September 1994. All the work is my own, unless otherwise indicated. It has not previously been submitted for a degree at this or any other university.

To Mum, Dad and Ian

This is not the end.

It is not even the beginning of the end.

But it is, perhaps, the end of the beginning.

(Winston Churchill, 1942)

Acknowledgements

Abbreviations

Ac	: acetyl
9-BBN	: 9-borabicyclo[3.3.1]nonane
BDPP	: 2,4-bis(diphenylphosphino)pentane
BINAP	: 2,2'-bis(diphenylphosphino)-1,1'-binapthyl
BMPP	: benzylmethylphenylphosphine
Bn	: benzyl
b.p.	: boiling point
BPPFA	: (S)-α-[(R)-1',2-bis(diphenylphosphino)ferrocenyl]ethyldimethylamine
Bu	: butyl
CHIRAPHOS	: 2,3-bis(diphenylphosphino)butane
CI	: chemical ionisation
COD	: 1,5-cyclooctadiene
Cx	: cyclohexyl
d	: doublet
DCI	: desorption chemical ionisation
DCC	: 1,3-dicyclohexylcarbodiimide
de	: diastereomeric excess
DEAD	: diethyl azodicarboxylate
DEPT	: distortionless enhanced polarisation transfer
DIBAL-H	: diisobutylaluminium hydride
DIPAMP	: 1,2-bis-(o-anisylphenylphosphino)ethane
DMAP	: 4-dimethylaminopyridine
DMPU	: 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
dppb	: 1,4-bis(diphenylphosphino)butane
dppe	: 1,2-bis(diphenylphosphino)ethane
DIOP	: 2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
ee	: enantiomeric excess
EI	: electron impact
Et	: ethyl
FAB	: fast atom bombardment
GC	: gas chromatography
GC-MS	: gas chromatography - mass spectroscopy
Hal	: halogen
hfc	: 3-(heptafluoropropylhydroxymethylene)-(+)-camphorato
HOMO	: highest occupied molecular orbital
HPLC	: high performance liquid chromatography

IMDA	: intramolecular Diels-Alder reaction
Ipc	: isopinocampheyl
IR	: infra red
LDA	: lithium diisopropylamide
LUMO	: lowest unoccupied molecular orbital
m	: multiplet
mcpba	: 3-chloroperbenzoic acid
MDPP	: menthyldiphenylphosphine
Me	: methyl
mesyl	: methanesulfonyl
MOP	: 2-(diphenylphosphino)-2'-methoxy-1,1'-binapthyl
m.p.	: melting point
MS	: mass spectroscopy
NMDPP	: (S)-(+)-neomenthyldiphenylphosphine
NMR	: nuclear magnetic resonance
Ph	: phenyl
PPFA	: (S)-α-[(R)-2-diphenylphosphinoferrocenyl]ethyldimethylamine
q	: quartet
s	: singlet
t	: triplet
TBAF	: tetrabutylammonium fluoride
TBDMS	: *tert* -butyldimethylsilyl
Tf	: trifluoromethanesulfonate
THF	: tetrahydrofuran
tlc	: thin layer chromatography
TMEDA	: N,N,N',N'-tetramethylethylenediamine
TMS	: trimethylsilyl
TRIPHOS	: 1,1,1-Tris(diphenylphosphinomethyl)ethane

ABSTRACT

The Synthesis and Potential Applications of Asymmetric Silacycles

Jennifer Louise Matthews
Ph.D. 1994

Although the use of silicon-based reagents has undergone rapid development during the last twenty years, the application of organosilicon chemistry to asymmetric synthesis has been somewhat slower to develop.

The many problems associated with the use of 'Si-centred' chiral organosilicon compounds has led to the application of 'C-centred' chiral organosilicon compounds. This work has been aimed at the synthesis and application of cyclic silicon species.

Routes towards the synthesis of medium-sized rings have been investigated as a potential application of enantiomerically pure silacycles. This work has led to the discovery of an unusual tandem cycloaddition-bond fragmentation reaction of 3-(dienylacyloxy)cycloalk-2-en-1-ones, which affords α-tetralone as the principal product.

Most work has been directed at the synthesis of asymmetric silacycles. Two routes have been explored. Firstly, the double asymmetric hydrosilylation of dienes, catalysts based on many transition metals were used but little evidence of hydrosilylation was observed. The second route is that of the double asymmetric hydroboration of divinylsilanes. Asymmetric stoichiometric hydroboration led to products of moderate to high enantiomeric excess, whilst rhodium-catalysed hydroboration led to high yields of the achiral *syn* isomer. The diastereoselectivity has been found to vary according to the length of the tether between two phosphine ligands, with maximum diastereoselectivity being observed for butanodiphosphines. NMR studies have investigated the possibility that this is related to the stability of a divinylsilane-diphosphine rhodium complex.

Finally, the formation of a variety of silacycles has been attempted. Boron-redistribution of the product of hydroboration with (-)-diisopinocampheylborane has been shown to occur with retention of stereochemistry and subsequent carbonylation led to the formation of asymmetric silacyclohexanones. Oxidation of the hydroboration product led to the formation of a silyldiol species. Reactions of this silyldiol have provided the basis for encouraging preliminary attempts at the formation of other heterosilacycles.

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PART A
INTRODUCTION AND BACKGROUND

PART A : Introduction and Background

Chapter 1
Silicon Reagents in Organic Chemistry

1.1 Introduction

Over the last 20 years, the use of silicon-based reagents has undergone a somewhat explosive development. Their range of uses are found within protection, functional group transformation and carbon-carbon bond formation steps. Furthermore, with the ever increasing interest in asymmetric synthesis, the role of organosilicon chemistry within this area has also become an area attracting considerable attention.

This chapter will give an overview of some of the applications of organosilicon chemistry, with particular emphasis on those areas in which the presence of the silicon atom results in enhanced reactivity or selectivity when compared to the carbon analogue.

1.2 A Comparison of Silicon and Carbon

At the turn of the century, Kipping began to study the chemistry of silicon compounds.[1] It soon became apparent that, although carbon and silicon belong to the same group, there are some tremendous differences between the two elements. This section gives a brief overview of the differences between carbon and silicon, which begin to explain the differences in their chemistry. Some of their properties are outlined below, figure 1.1.

	C	Si
Electronic Configuration	$1s^2 2s^2 2p^2$	$1s^2 2s^2 2p^6 3s^2 3p^2 3d^0$
Atomic Radius	77pm	117pm
Electronegativity	2.5	1.8
C-El Bond Length	1.54Å	1.90Å

Figure 1.1

The atomic radius of silicon is considerably larger than that of carbon and hence, π bonds are much less stable than their carbon counterparts. The lower electronegativity of silicon means that Si-El bonds are more polar than C-El bonds, this has a dramatic effect on the reactivity and can provide a considerable driving force for the reactions of organosilicon compounds.

It is, perhaps, the differences in electronic properties that can often best explain the differences encountered in the chemistry of carbon and silicon compounds. Many of the reactions of organosilicon compounds occur due to the ability of a silicon atom to stabilise carbocations that are β to the silicon atom or carbanions that are α to the silicon atom. The stabilisation of carbocations has become known as the β-effect, the precise cause of which still remains a subject of great debate. Whilst many factors may be involved, the most important is generally accepted to be associated with $(\sigma$-$p)\pi$ overlap between the vacant p-orbital on the β-carbon with the σ-orbital between silicon and the α-carbon, figure 1.2.
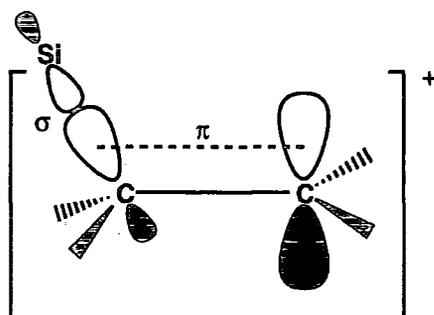
Figure 1.2

For significant π-overlap, the C-Si σ bond must be in the same plane as the vacant p-orbital. This presents no problems in acyclic cases but it is not always possible in cyclic systems.

In a similar manner, α-carbanion stabilisation can be attributed to $(\sigma^*$-$p)\pi$ overlap between the antibonding σ^* level of the C-Si bond and the filled p-orbital of the carbanion, figure 1.3.
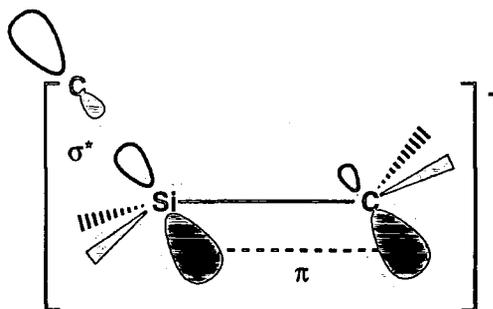
Figure 1.3

It has frequently been suggested that low-lying d-orbitals may have a role in the effects seen in organosilicon chemistry and there is still no conclusive evidence to support only one theory.[2] One area where d-orbitals must be involved is in the formation of penta-coordinate intermediates. This effect is particularly well demonstrated in the often encountered racemisation of chiral silicon compounds, scheme 1.1.
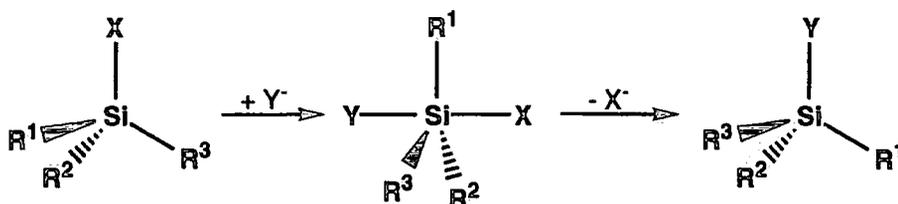
Scheme 1.1

The Berry pseudorotation mechanism[3] allows rapid interchange of substitutents between axial and equatorial sites in the penta-coordinate intermediate, subsequent loss of a group to return to tetrahedral silicon results in the complete scrambling of any chirality associated with the silicon centre. This pseudorotation at the silicon centre is one reason why chiral silicon compounds have found little effective use in asymmetric synthesis, see section 1.10.

In the following sections, some of the major uses of organosilicon reagents in organic synthesis will be discussed.

1.3 Organosilicon Reagents as Protecting Groups

In the early 1970's, silyl ethers were first introduced as a potential protection for hydroxy groups. In the last 20 years, the field has undergone an amazingly rapid development and it is now unusual to see any synthesis of reasonable length accomplished without the use

of an organosilicon protecting group. There is now a vast range of silyl protecting groups and many different ways of achieving the protection and deprotection steps. There has been much written[4] on the use of organosilicon protecting groups for heteroatoms. This thesis is, however, not concerned with the use of organosilicon compounds as protecting groups and, although in a chapter discussing organosilicon reagents, they cannot go completely without mention, they will not be discussed further here.

This chapter will now concentrate on the use of organosilicon compounds in functional group transformations and carbon-carbon bond forming reactions.

1.4 The β-Effect in Synthesis

The ability of silicon to stabilise β-carbocations has been shown to be of use over a wide area of organic synthesis. This section will discuss some of the areas where the β-effect is often put to good use.

1.4.i Electrophilic Substitution of Allyl-, Vinyl- and Arylsilanes

The electrophilic substitution chemistry of all types of organosilanes has been thoroughly reviewed[5] by Chan and Fleming. This section will concentrate on three types of organosilane, namely allyl-, vinyl- and arylsilanes.

Allylsilanes react with a wide range of electrophiles in Lewis acid mediated reactions. A β-carbocation is generated when addition takes place at the γ-carbon and then subsequent attack at the silyl group results in the production of a new alkene,[6] scheme 1.2.
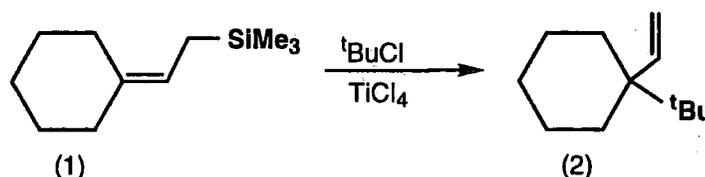
Scheme 1.2

Substitution reactions of this type occur with total regiochemical control - a great asset when compared to reactions of non-silylated allylic reagents.

Lewis acids are often used to aid the reaction and their addition to reactions between allylsilanes and carbonyl compounds has become known as the Sakurai reaction.[7] This reaction generates γ,δ-unsaturated alcohols from starting carbonyl compounds, scheme 1.3.
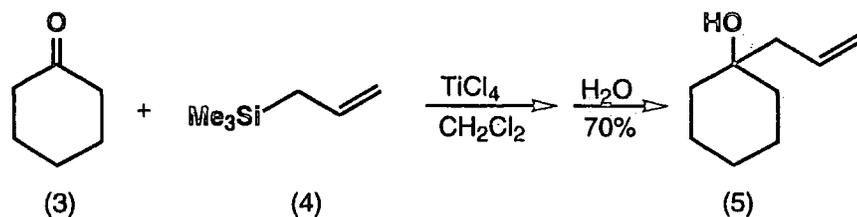
Scheme 1.3

This reaction has also been exploited by Taddei and co-workers in the synthesis of substituted tetrohydropyrans, scheme 1.4. The Sakurai reaction and Taddei's synthesis of tetrahydropyrans have both been the subject of research into possible asymmetric induction in organosilicon chemistry. They will be discussed further in section 1.10.
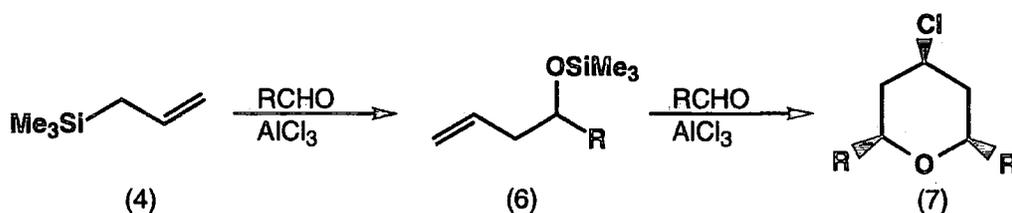
Scheme 1.4

The electrophilic substitution of vinylsilanes has become a well-used method for the synthesis of substituted alkenes. The silyl group is replaced stereospecifically and hence, the synthesis[8] of any one isomer of the alkene is possible, scheme 1.5.
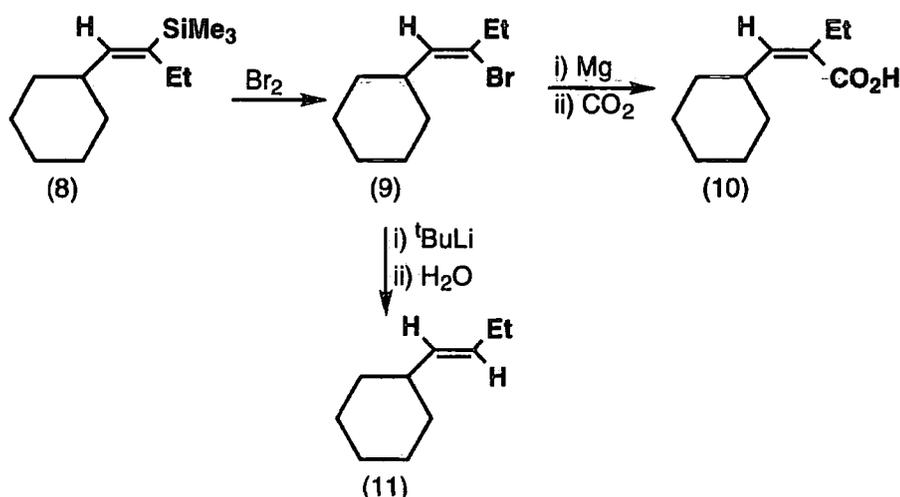
Scheme 1.5

This method can be used to synthesize a wide range of highly functionalised substituted dienes.

Arylsilanes react with electrophiles in a process known as *ipso*-desilylation. This reaction can be used in the synthesis of substituted benzene derivatives. The synthesis[9] of 1,2-cyclopropa-4,5-cyclobutabenzene by Saward and Vollhardt, scheme 1.6, demonstrates the use of the *ipso*-desilylation procedure. The application of this type of reaction to the formation of halosilanes is discussed in more detail in chapter 3.
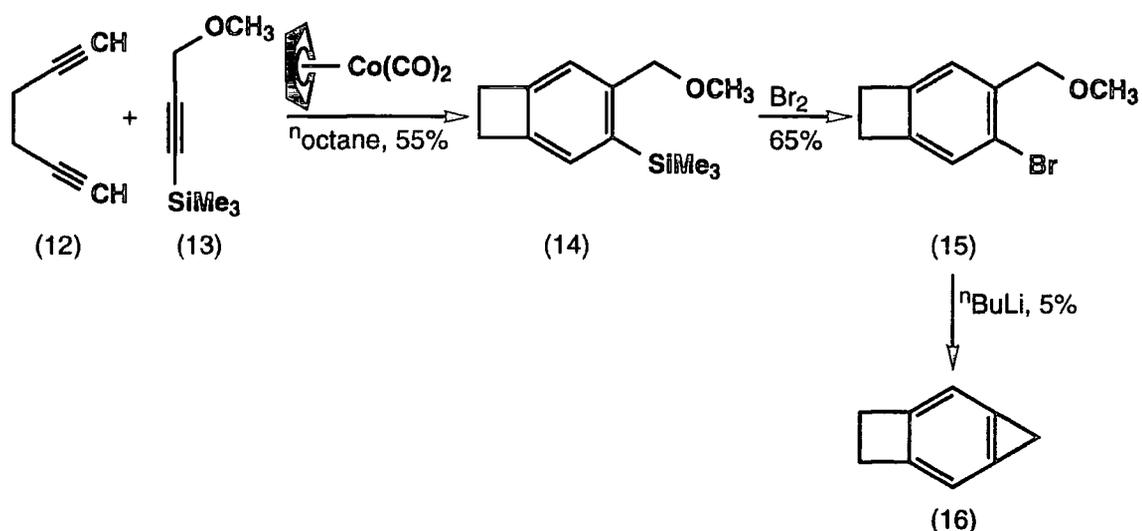
Scheme 1.6

1.4.ii The Rearrangement of Carbocations

The β-effect stabilisation has been shown to be useful in the control of rearrangements of carbocations and also in cyclisations induced by carbocations.[10]

Many carbocation rearrangements are complicated by the formation of many isomeric products. The introduction of a silicon group has been frequently shown to overcome these problems and result in the formation of only one of the possible isomeric products.

This effect is particularly well demonstrated by the Nazarov cyclisation of dienones. When unsymmetrical dienones are used in this reaction, the resulting product is a mixture of the two isomeric cyclopentenones. The introduction of a silyl group β to the carbonyl carbon results in greater stabilisation of one of the possible intermediate carbocations and hence, leads to the formation of only one cyclopentenone product.[11] This is demonstrated in the synthesis[12] of $(\pm)\Delta^{9(12)}$-Capnellane, scheme 1.7, where the silicon directed Nazarov cyclisation is used

twice. In this synthesis, the usual catalyst for Nazarov cyclisations, $FeCl_3$, was found to give only low yields of the required cyclopentenone. This problem was overcome by using $BF_3.Et_2O$ in place of $FeCl_3$.
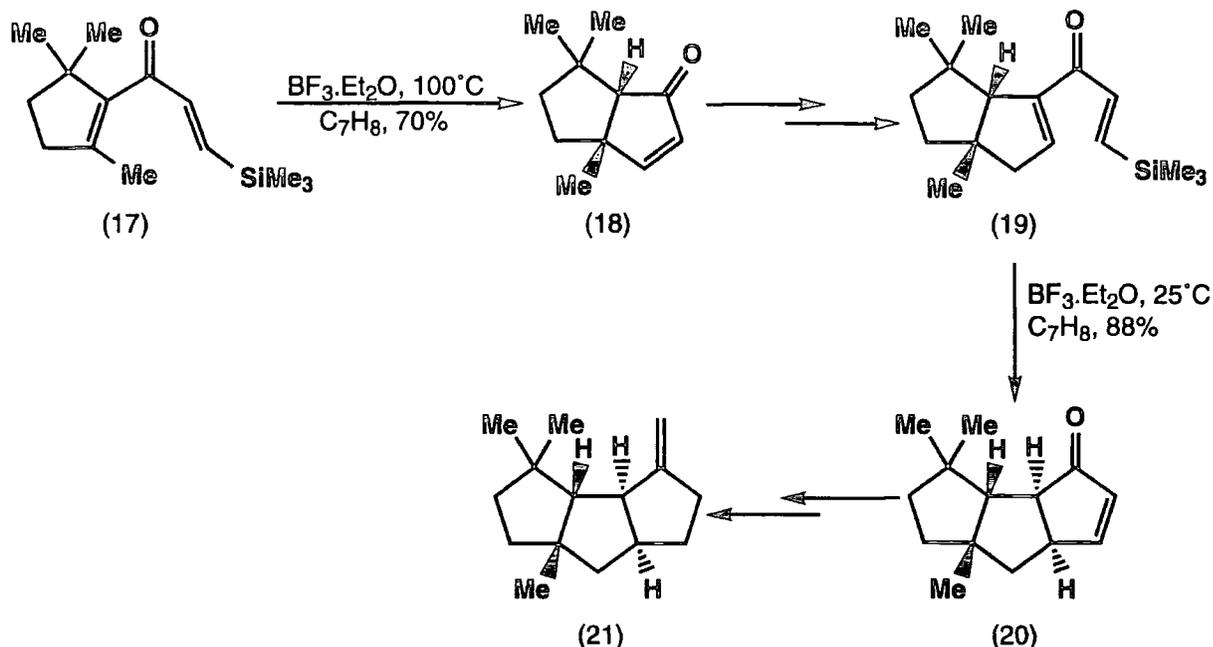
Scheme 1.7

The use of the β-effect is particularly effective in the Nazarov cyclisation and other carbocation rearrangements, since it removes all problems associated with the mixtures of isomeric products.

1.4.iii Alkynylsilanes in Polyolefin Cyclisations

Alkynylsilanes undergo electrophilic substitution reactions in a similar fashion to alkenylsilanes. Addition reactions of alkynylsilanes are also well documented and the ethynylsilane group has been shown to be particularly useful in polyolefin cyclisations,[13] scheme 1.8 (overleaf).

The inclusion of the alkynylsilyl group alters the regioselectivity of the reaction. It is thought that in the methyl substituted case (25), the linear vinylic cation (26) is the most stable and hence, leads to a steroid skeleton containing a 5-membered D ring (27). However, the ability of the silyl group to stabilise a β-carbocation induces the formation of the 6-membered ring intermediate (23) and hence, the final product is a steroid with a six-membered D ring (24).
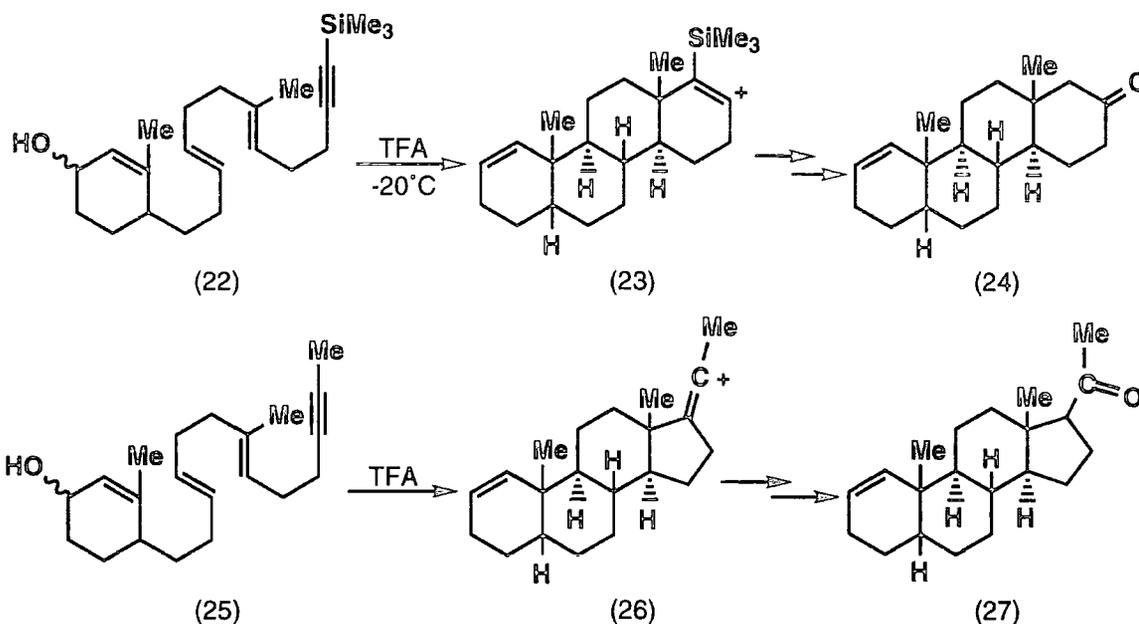
Scheme 1.8

1.4.iv Silyl Enol Ethers in Organic Synthesis

Silyl enol ethers are stable, isolable molecules. Their chemistry extends over a wide range of organic synthesis and has been extensively reviewed.[14] This section will discuss only a few examples of their uses in synthesis.

Silyl enol ethers formed from kinetic enolates are particularly useful since it is possible to use them as a source of isomerically pure enolate ions. Regiochemically pure silyl enol ethers provide a starting point for the alkylation of kinetic enolates, scheme 1.9, and remove the problems associated with isomerisation to the thermodynamically preferred enolate before alkylation can occur.
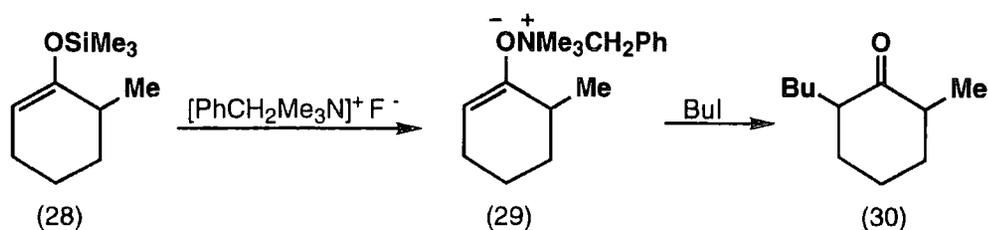
Scheme 1.9

Alkylation of silyl enol ethers, which is usually achieved under Lewis acid catalysis, is also straightforward. It is possible to achieve alkylation with tertiary halides[15] under these

conditions, scheme 1.10. The equivalent alkylation process with enolate ions is usually impossible due to competing elimination reactions.

OSiMe₃
Me

(31) → ᵗBuCl / TiCl₄ → (32)
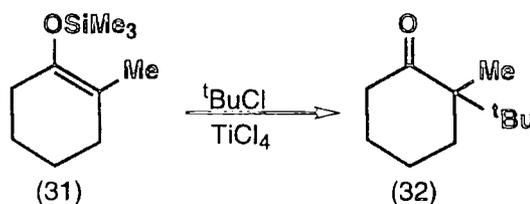
Scheme 1.10

The Lewis acid catalysed aldol condensation of silyl enol ethers, which has become known as the Mukaiyama reaction,[16] has become an extensively studied and useful reaction in synthesis.[17] Titanium tetrachloride[18] has been shown to give consistently good results although Lewis acids based on a vast array of metals have been shown to be active catalysts. The reaction occurs readily with aldehydes at low temperatures (-78°C), scheme 1.11. The reaction with ketones is also possible although higher temperatures are necessary (0°C).

OSiMe₃

(33) → PhCHO, TiCl₄, CH₂Cl₂ / -78°C, 1hr, 92% → H₂O →

(34)
(threo : erythro)
(69 : 23)
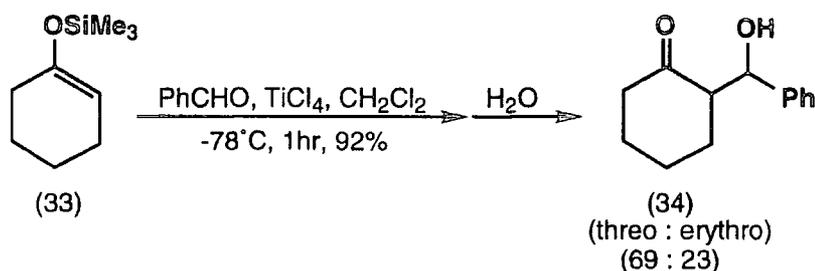
Scheme 1.11

The reactions of acetals and ketals have several advantages over their parent carbonyl compounds. They can act only as electrophiles and it is likely that they coordinate more strongly to the Lewis acid than the simple carbonyl compound. The reaction of the dimethyl acetal of benzaldehyde (35) has been shown to occur with high selectivity (93:7) for the erythro isomer, scheme 1.12. Asymmetric aldol reactions of acetals will be discussed in section 1.10.

OSiMe₃

(33) + Ph—CH(OCH₃)—OCH₃ (35) → TMSOTf / 5 mol% → (36)
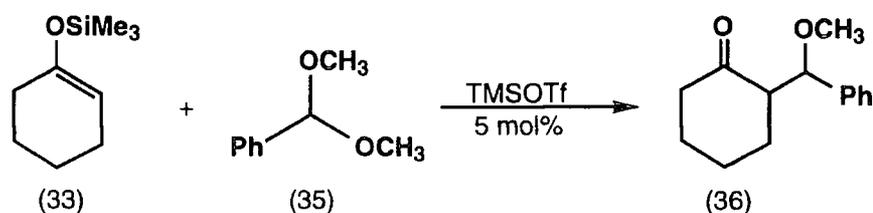
Scheme 1.12

Silyl enol ethers also participate in the Michael reaction with α,β-unsaturated ketones. These Lewis acid catalysed reactions provide a high yielding route to 1,5-dicarbonyl compounds, scheme 1.13.
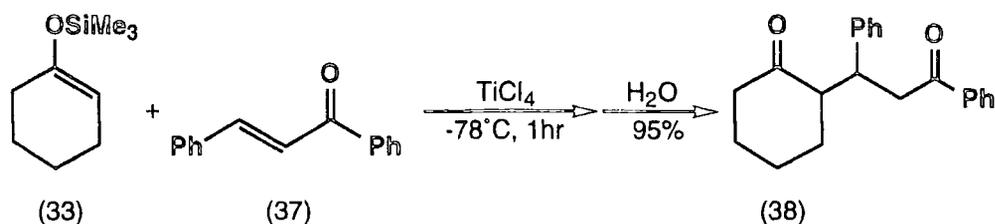
Scheme 1.13

These acid catalysed Michael reactions have also become the subject of research into enantioselective reactions and will be discussed further in section 1.10.

1.5 The Stabilisation of α-Carbanions

The ability of silicon to stabilise β-carbocations has seen wide use in synthesis. The stabilisation of α-carbanions has, however, seen far fewer applications. This section will discuss the application of silicon stabilised α-carbanions in Michael reactions and subsequent annelation reactions. It will also look briefly at the chemistry of α,β-epoxysilanes and the use of two α-lithiosilane anions : α-chloro-α-lithio-α-trimethylsilane and the (trimethylsilyl)allyl anion.

1.5.i The Michael Reaction and Robinson Annelation

The annelation of 2-alkylcyclohexanones (39) with methyl vinyl ketone (40) is an important reaction in the synthesis of polycyclic systems such as steroids, scheme 1.14.
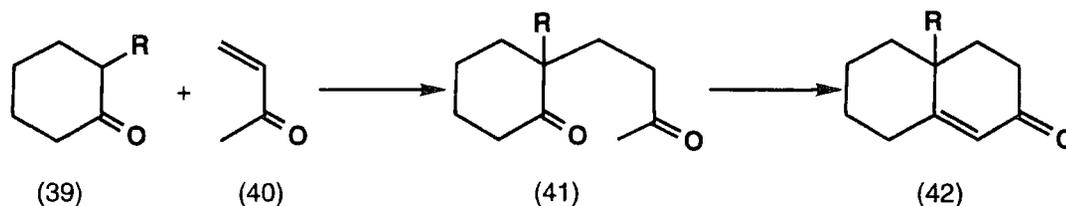
Scheme 1.14

Substitution at the less substituted α-carbon of the ketone can be achieved using enamine chemistry. However, the required substitution at the more substituted carbon is

difficult to achieve and the basic reaction conditions required often result in polymerisation of the vinyl ketone and only low yields of the desired Michael adduct, which can also be accompanied by other structural isomers due to enolate equilibration.

Stork and Ganem demonstrated[19] that use of an α-silylated vinyl ketone (44) overcomes all the difficulties with the use of methyl vinyl ketone (40). The silyl group stabilises the anion of the Michael adduct and also discourages the equilibration of unstable enolates, scheme 1.15.
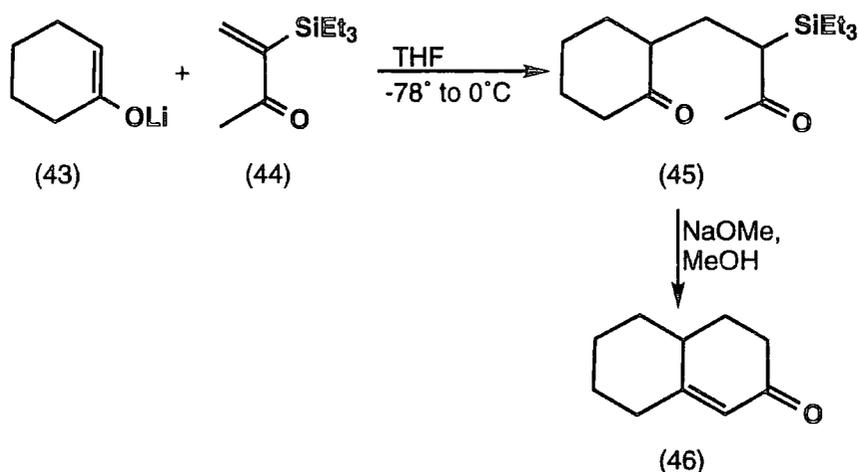
Scheme 1.15

This reaction results in an 80% yield of the desired bicyclic ketone (46), whereas the reaction with methyl vinyl ketone gave less than 5% yield.

Boeckmann have gone on to demonstrate[20] the application of this type of reaction in a wide range of annelation methodology.

1.5.ii Synthesis and Applications of α,β-Epoxysilanes

α,β-Epoxysilanes are useful intermediates in organosilicon chemistry. Their synthesis from aldehydes and ketones and subsequent conversion to aldehydes provides a method for the homologation of both aldehydes and ketones. This demonstrates the use of α-chloro-α-lithio-α-trimethylsilane, scheme 1.16.
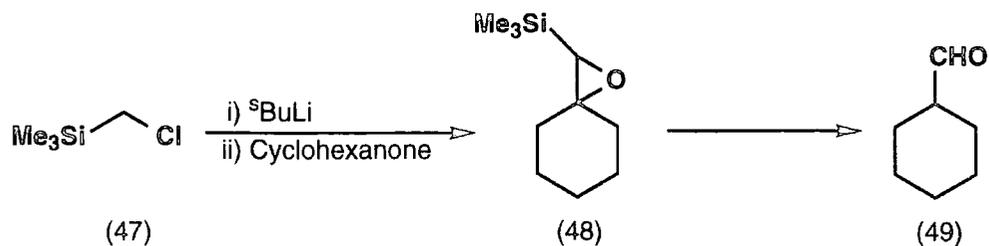
Scheme 1.16

The (trimethylsilyl)allyl anion can also be applied to the synthesis of α,β-epoxysilanes and subsequent BF₃.Et₂O catalysed rearrangement and oxidation provides a useful synthesis of γ-lactones from ketones, scheme 1.17.
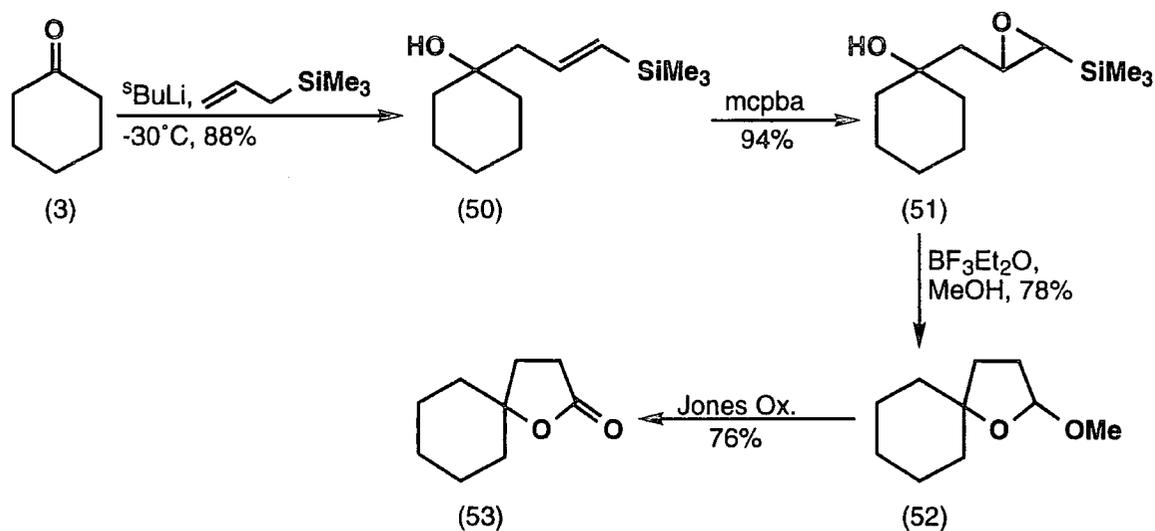
Scheme 1.17

The stabilisation of α-carbanions is also useful in the reaction of organocuprate reagents with α,β-epoxysilanes, scheme 1.18.
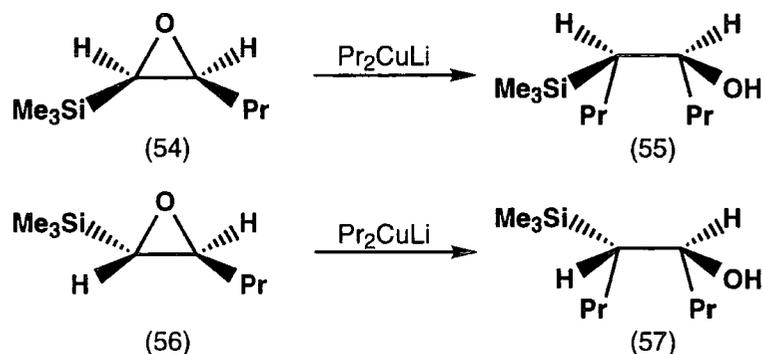
Scheme 1.18

Since the (Z)-epoxide can be formed diastereomerically pure, this method enables the synthesis of diastereomerically pure β-hydroxysilanes which are the substrates required for the Peterson reaction, see section 1.6.

1.6 The Peterson Reaction

The silicon version of the Wittig reaction is known as the Peterson reaction.[21] Although it is used far less than the Wittig reaction in synthesis, it has several advantages. At its simplest, the reaction involves the elimination of trimethylsilanol from a β-hydroxyalkyltrimethylsilane, the silicon containing product of the reaction is hexamethyldisiloxane which is volatile and hence, far simpler to remove than triphenylphosphine oxide. Furthermore, if a single diastereomer of the hydroxysilane is used, both E- and Z- forms of the alkene can be obtained separately, depending on whether basic or acidic conditions are used in the elimination step, scheme 1.19.
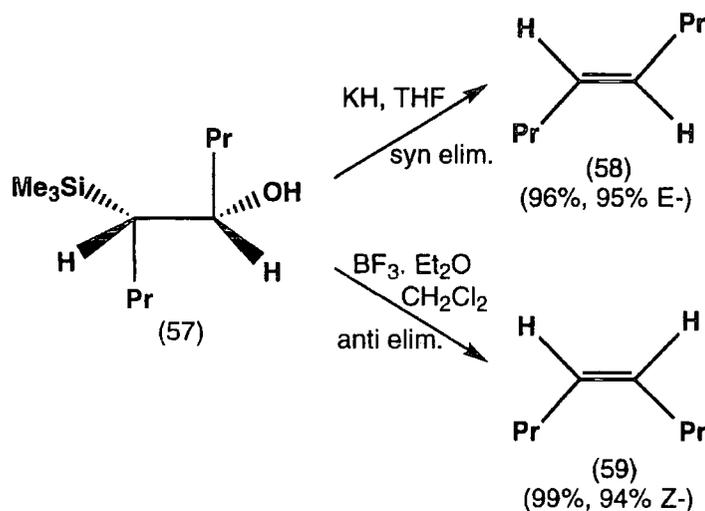
Scheme 1.19

The β-hydroxysilane substrates required for the reaction can be formed from a variety of methods including i) the addition of α-metallated silanes to carbonyl compounds, ii) the addition of dialkylcuprates to α,β-epoxysilanes and iii) the reduction of β-ketosilanes.

The Peterson reaction has been found to be particularly useful in the reactions of sterically hindered ketones, scheme 1.20.
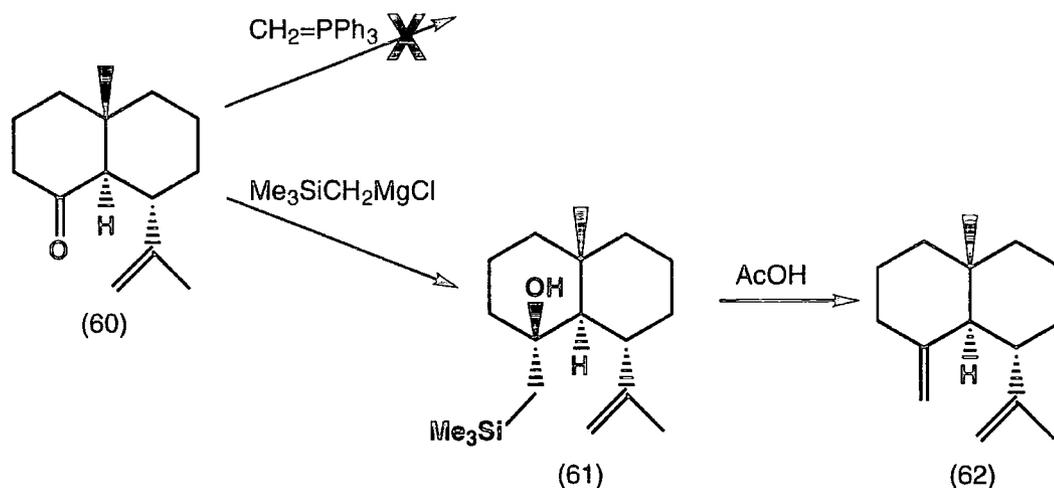
Scheme 1.20

In this synthesis[22] of β-Gorgonene (62), the success of the Peterson reaction, after the failure of the Wittig reaction, is attributed to the length of the carbon-silicon bond, which makes the initial carbanion less sterically demanding.

The Peterson reaction, like so many reactions involving organosilicon reagents, is rapidly becoming a far more exploited alternative procedure in organic synthesis.

1.7 Cycloaddition and Rearrangement Reactions

Organosilicon species have found many applications in cycloaddition and rearrangement reactions. There are many rearrangement reactions which involve the migration of silicon, with perhaps the most well-known being the Brook rearrangement of silylmethanols. All these rearrangement reactions have been thoroughly reviewed.[23] This section will focus on three reactions where modifications involving silicon have been shown to be particularly useful in synthesis : the Diels-Alder reaction, the modified Acyloin condensation and the modified Claisen rearrangement of silyl ketene acetals.

1.7.i The Diels-Alder Reaction

2-Trimethylsiloxybutadienes have become well used as the diene component in Diels-Alder reactions.[24] The polarisation of these molecules ensures that the Diels-Alder reaction occurs regiospecifically,[25] scheme 1.21.
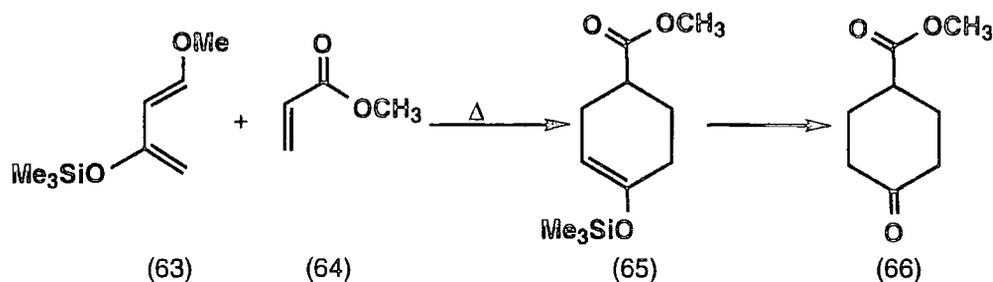
Scheme 1.21

Perhaps the most widely used diene of this type is 1-methoxy-3-trimethylsilyloxybutadiene (64), the Danishefsky diene. This diene has become widely used in natural product syntheses. Danishefsky demonstrated it's use in the synthesis of (±)-disodium prephenate (69),[26] scheme 1.22.
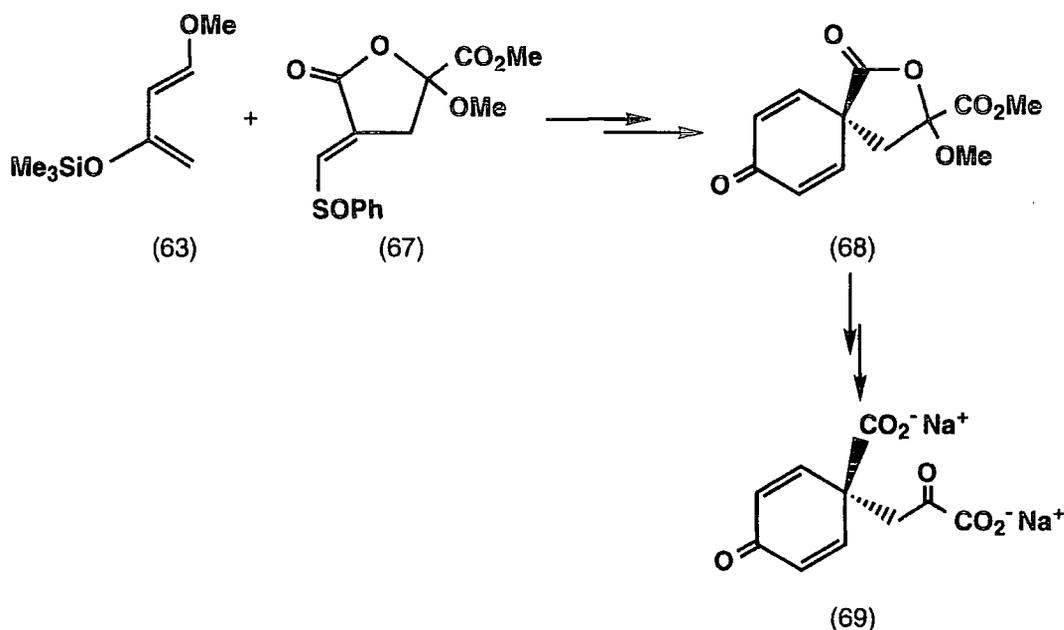
Scheme 1.22

Other silicon substituted dienes, particularly vinyl ketene acetals, have been shown to be useful in Diels-Alder reactions. These have been thoroughly reviewed by Colvin.[27]

1.7.ii The Modified Acyloin Condensation

The reaction of esters with sodium metal to give α-hydroxyketones is known as the acyloin condensation. The generation of the by-product, sodium ethoxide, can catalyse several side-reactions including other condensations of carbonyl derivatives, such as the Dieckmann condensation. These side reactions are particularly severe in the small-membered ring

formations. The addition of at least 4 equivalents of trimethylsilyl chloride to the reaction is known as the Rühlmann modification. It serves two purposes i) the reaction of TMSCl with any ethoxide generated minimises side reactions and ii) it traps the unsaturated dianion intermediate to yield 1,2-bissiloxy alkenes (72), subsequent hydrolysis yields the acyloin product (73). This is demonstrated by the reaction of diethyl adipate (70), scheme 1.23.
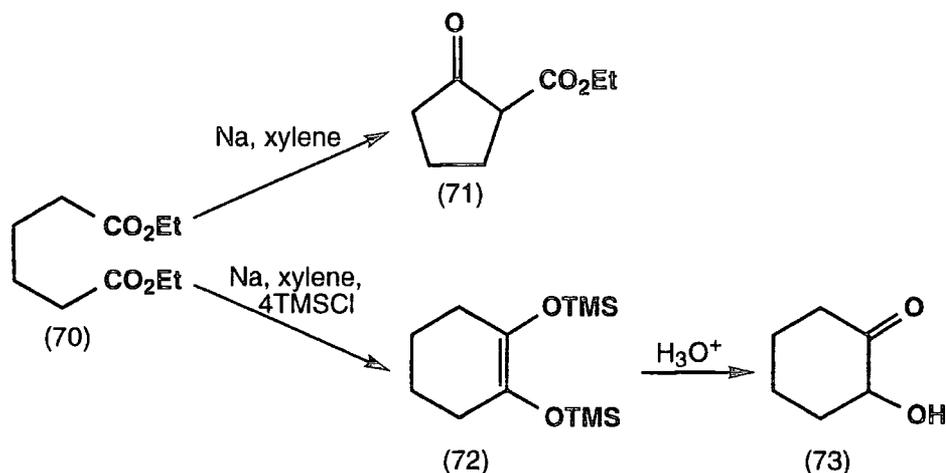
Scheme 1.23

In the reaction of diethyl adipate (70), the Dieckmann condensation proceeds faster than the acyloin condensation, only the addition of TMSCl allows the formation of the acyloin product.

This modification of the acyloin condensation has been successfully used[28] in the synthesis of four-membered rings, scheme 1.24.
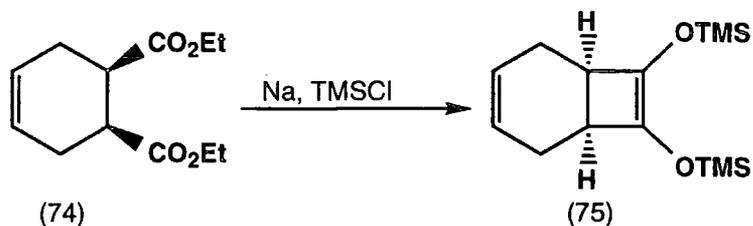
Scheme 1.24

The successful isolation of the bis(siloxy)alkene intermediates also allows these to be used as intermediates in other synthetic sequences.

1.7.iii [3,3]-Sigmatropic Rearrangements

The silyl ketene acetals derived from allyl esters undergo [3,3]-sigmatropic Claisen rearrangements. The stereochemistry of the product is derived from the geometry of the double

bond in the substrate. Since judicious choice of reaction conditions[29] allows the formation of either the (Z)- or (E)- silyl ketene acetal, this method has been used to provide excellent stereocontrol in many natural product syntheses.

One example of this can be seen in the synthesis[30] of (±)-methyl santolinate (78), scheme 1.25.
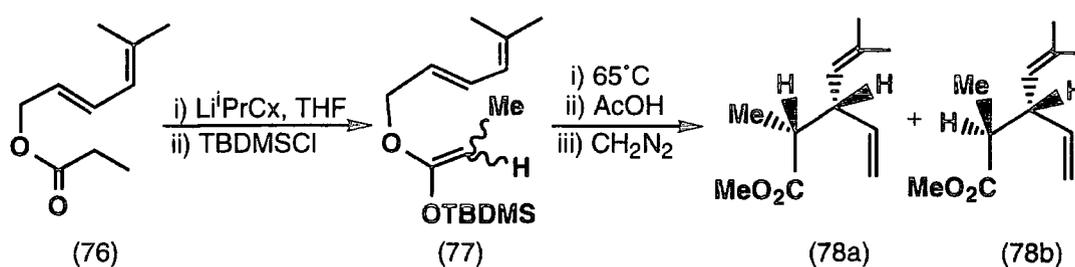
Scheme 1.25

The diastereomeric products (78a:78b) are formed in an 8:1 ratio, which indicates that the (E)-silyl ketene acetal must have been formed predominantly.

1.8 Silanes as Reducing Agents

The addition of Si-H across any multiply bonded system has become an important method of reduction. This addition can occur either catalytically, the process of hydrosilylation, or under ionic conditions, the process of ionic hydrogenation. The process of reductive silylation, which involves the use of a chlorotrimethylsilane-metal system as been extensively studied by Calas, Dunoguès and co-workers. This work has been extensively reviewed[31] and will not be considered further in this section. More recently, tris(trimethylsilyl)silane has been shown to be a useful radical-based reagent. Some of this work will be briefly discussed.

1.8.i   Hydrosilylation

The term hydrosilylation describes the addition of Si-H across a multiple bond. Although there has been work on alkyne hydrosilylation, it is in the hydrosilylation of double bonds where most progress has been made. In this section, the hydrosilylation of carbonyl compounds will be briefly discussed. The hydrosilylation of alkenes will be considered in chapter 3.

Considering the strength of the silicon-oxygen bond, it is not surprising that the hydrosilylation of carbonyl compounds has proved to be simpler to accomplish than the hydrosilylation of alkenes. It is also not surprising that the reaction proceeds completely regiospecifically with silicon forming a new bond to oxygen and carbon to the hydride. Since hydrolysis of the resulting silyl ether is usually facile, hydrosilylation is often a viable alternative to hydrogenation.

Prior to 1972, the hydrosilylation of carbonyl compounds had received little attention although there had been considerable work on the hydrosilylation of alkenes. In 1972, it was, however, found that Wilkinson's complex, $Rh(PPh_3)_3Cl$, was a highly efficient catalyst for the hydrosilylation of carbonyl compounds.[32] The hydrosilylation of ketones has now been shown to be possible under mild conditions with few unwanted side reactions. The range of possible catalysts has developed rapidly with complexes of most transition metals showing a variety of both activity and selectivity and in recent years, as will be seen in section 1.10, considerable attention has focussed on asymmetric hydrosilylation.

Perhaps one of the most useful early discoveries was in the hydrosilylation of α,β-unsaturated ketones, scheme 1.26.
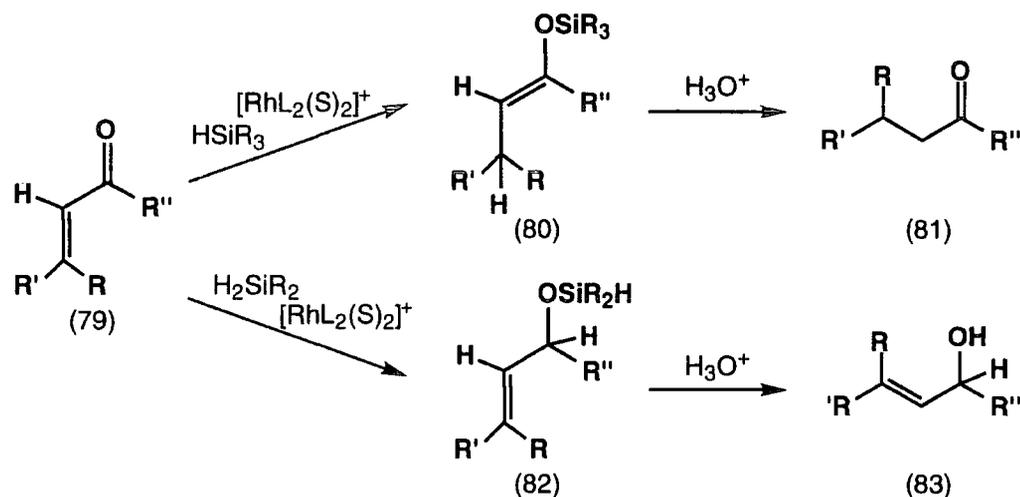
Scheme 1.26

It was found that with monohydrosilanes, the products of 1,4-addition (81) were found exclusively, whereas with di- or tri- hydrosilanes only 1,2-addition (83) to the carbonyl group occurred.[33] This regioselectivity has provided a good method for selective reduction of α,β-unsaturated carbonyl compounds.[34]

1.8.ii   Ionic Hydrogenation

The electronegativity of silicon results in the polarisation of Si-H bonds in a similar fashion to both boron and aluminium hydrides. It is therefore possible to induce hydride transfer from hydridosilane reagents.[35] They are, however, considerably less reactive than their boron and aluminium counterparts and hence, require the addition of Lewis or protic acids to activate the carbon centre before hydride transfer can occur. Triethylsilane has become the reagent of choice due to its rate of reaction and ease of handling. When combined with boron trifluoride etherate, triethylsilane has proved to be a highly selective method for the deoxygenation of lactols,[36] scheme 1.27.
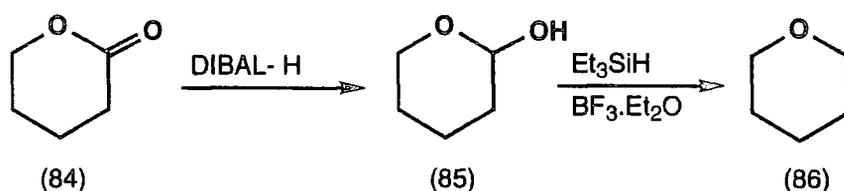
Scheme 1.27

At low temperatures, simple alcohols are unaffected, even those in an allylic position. In unsaturated lactones, the double bond remains unchanged.

Ionic hydrogenation using triethylsilane and a variety of acids has become an extensively used procedure for the reduction of many carbonyl and related compounds.

1.8.iii The use of (Me₃Si)₃SiH in Synthesis

Tributyltin hydride has become a frequently used reagent in radical-based synthesis. However, the disadvantages associated with the use of tin derivatives (toxicity, difficulties encountered in elimination from reaction products) have meant that the search for alternative reagents has begun. Tris(trimethylsilyl)silane has emerged as a compound with great potential.[37]

(Me₃Si)₃SiH has become a valuable radical based reducing agent for ketones and alkenes. Reactions also occur at lower temperatures after initiation by ultra violet irradiation, scheme 1.28.

(87)

(Me₃Si)₃SiH,
hv, 20°C

OSi(SiMe₃)₃   +

OSi(SiMe₃)₃

98
(88a)

:

2
(88b)
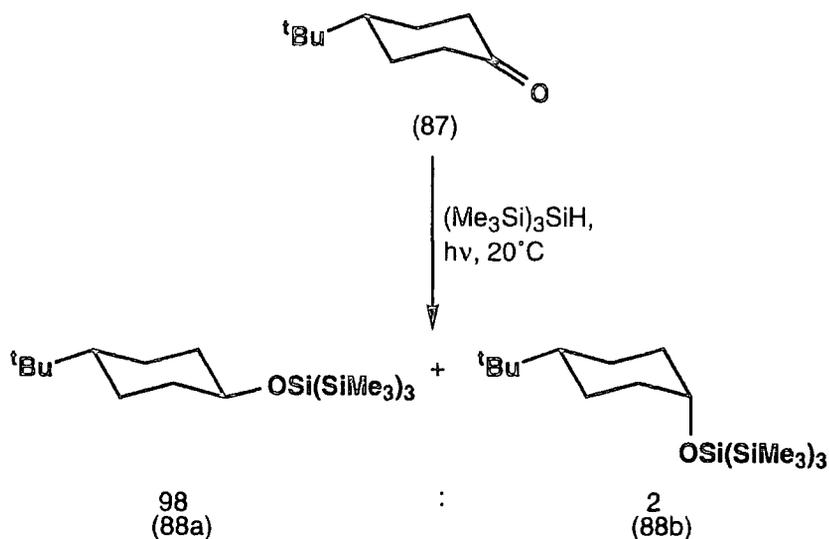
Scheme 1.28

The high selectivity of the reaction of 4-ᵗbutylcyclohexanone (87) demonstrates that axial attack of the intermediate radical is favoured, α-substitution of the ketone can however drastically effect the ratios of products seen.[38]

This reagent has also been of use in cyclisation reactions,[39] scheme 1.29.

Me

Br $\xrightarrow[\text{AIBN, 70°C}]{R_3MH}$ +   +

(89)   (90)   (91)   (92)

	(90)	(91)	(92)
(Me₃Si)₃SiH	93%	2%	4.1%
Bu₃SnH	83%	1.2%	15%
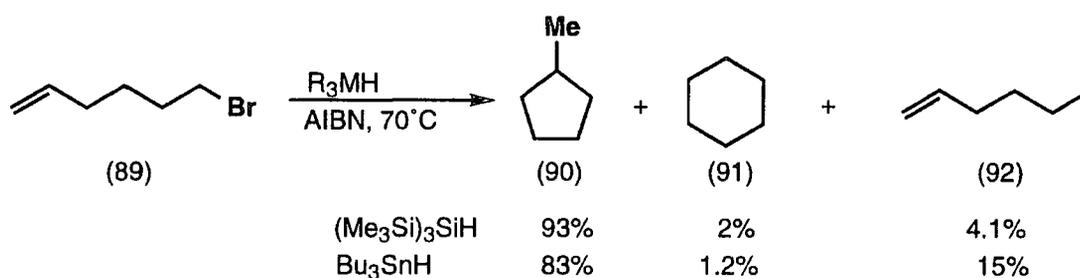
Scheme 1.29

(Me₃Si)₃SiH gives higher yields of cyclised products compared to the analogous reaction with Bu₃SnH.

(Me₃Si)₃SiH has been shown to be a reagent which overcomes the disadvantages of tin reagents and also provides some improvements over a range of uses in synthesis.

1.9 Temporary Silicon Tethers in Intramolecular Reactions

The use of intramolecular reactions as a way of improving stereocontrol has become an area of considerable interest. In recent years, attention has focussed on the use of temporary

"tethers" to link together the reactive species. These tethers must be easily removed and not interfere with the reactive species. Stork and co-workers have demonstrated the application of temporary silicon tethers to carbohydrate synthesis.[40] The variety of procedures available for removing silicon also make the use of silicon-based tethers a versatile method for the introduction of other functional groups if required.[41] Silicon tethers have now been shown to be of use in a variety of intramolecular processes and some examples are detailed below.

1.9.i Intramolecular Diels-Alder Reactions

Intramolecular Diels-Alder reactions (IMDA) are well known to be a method of introducing a high degree of regio- and stereocontrol. It has been shown, however, that tethers such as esters,[42] ethers,[43] amides[44] and carbonates[45] often have a detrimental effect on the regio- and stereocontrol. The use of silaketals as IMDA tethers has been shown to give a high degree of regio- and stereocontrol, scheme 1.30.

| | R=H | 9 | : | 1 |
| | R=Me | >99 | : | <1 |
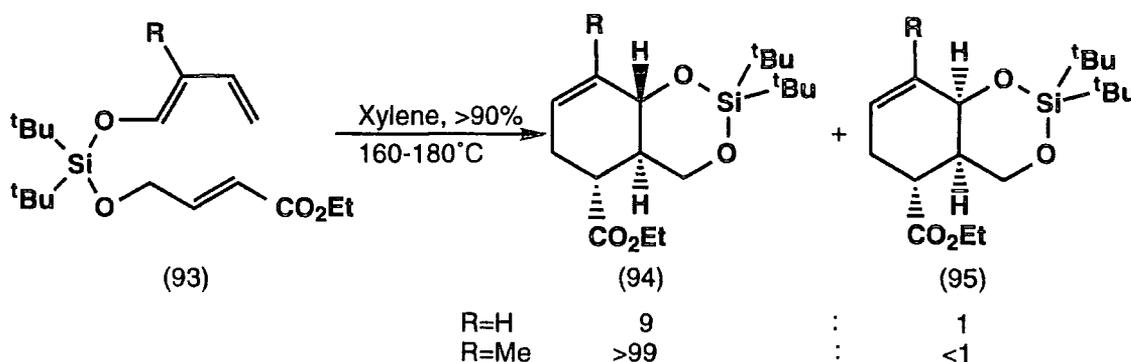
Scheme 1.30

The introduction of the methyl substituent on the diene means that the product of endo cyclisation (94) was found exclusively.[46]

Different silicon tethers have now seen applications in many intramolecular cycloadditions, these include the Diels-Alder reaction of vinylsilanes[47] and also in [2+2] photocycloadditions.[48]

1.9.ii Radical Cyclisations

Radical cyclisations of (bromomethyl)dimethylsilyl allyl ethers have been used[49] in the synthesis of 1,3-diols. Similar reactions of propargyl ethers are currently being studied as a

method of synthesising triquinane skeltons. The synthesis[50] of the diquinane skeleton (99) has been achieved in a one-pot reaction, scheme 1.31.

R^1

R^2

O

Si

Br

Me Me

(96)

Ph$_3$SnH, AIBN

C_6H_6, Δ

R^2

O

Si

Me Me

(97)

EWG

...$\iota\iota$EWG

R^2

O

Si

Me Me

(98)

H_2O_2

...$\iota\iota$EWG

R^2

HO OH

(99)
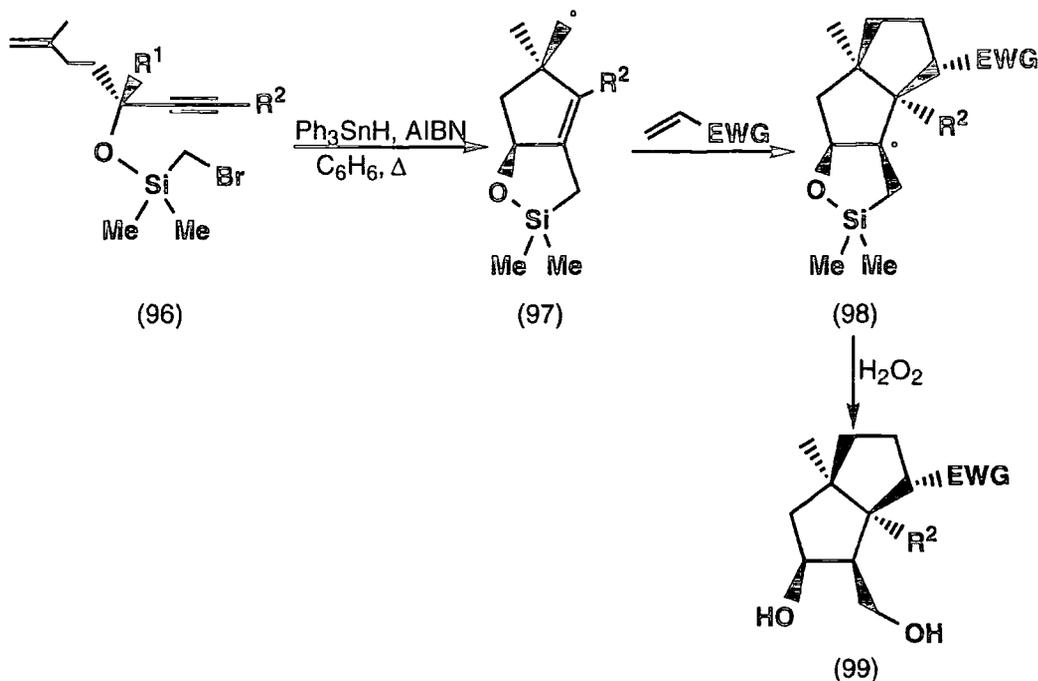
Scheme 1.31

This reaction involves the formation of 4 carbon-carbon bonds with 2 neighbouring quaternary centres and it also controls the stereoselective formation of 4 stereogenic centres. Hydrogen peroxide can be replaced by $^nBu_4NF$ or MeLi to provide other functionalisation in the final product.

Radical cyclisations of (bromomethyl)silyl ethers have, like many other silicon tethered reactions, been shown to take place with high regio-, chemo- and stereoselectivity. This makes them valuable in a wide variety of synthesis.

1.10 Organosilicon Compounds in Asymmetric Synthesis

With the growing interest in organosilicon compounds in recent years, attention has also become focussed on their applications in asymmetric synthesis.

Paquette has suggested[51] that chiral organosilicon compounds can be divided into 2 classes : "Si-centred", where the chirality resides on silicon or "C-centred", where the chirality resides on the carbon of one of the substituents on silicon. This section will look at both types

of reagent. The use of chiral organosilicon compounds in asymmetric synthesis was thoroughly reviewed[52] by Chan and Wang in 1992, this section will focus on some of the major achievements mentioned in that review and the improvements seen after that date.

1.10.i Si-Centred Chiral Organosilicon Compounds in Synthesis

In the early 1960's, Sommer and co-workers pioneered the synthesis[53] of optically active Si-centred chiral organosilicon compounds. There have been frequent attempts to apply these compounds to enantioselective synthesis.

Allylmethyl-α-napthylphenylsilane (100) has been used in the Sakurai reaction,[51] scheme 1.32.

Np
\
Meⁱⁱⁱ·Si   OMe   OMe
/   Ph—| BF₃.Et₂O   ⌇⌇⌇ Ph
Ph   OMe   ——30%——→   H
(100)   (35)   (101)
                                   5%ee
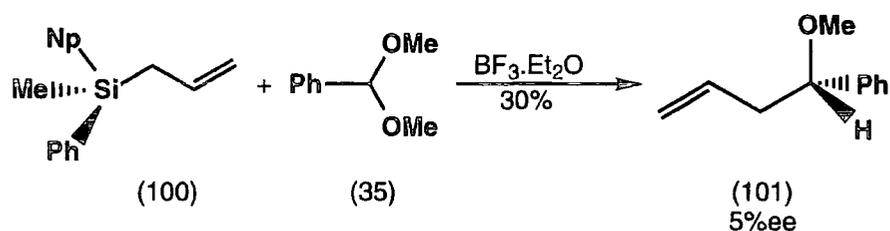
Scheme 1.32

The yield of this reaction was found to be low and the values of enantiomeric excess (ee) disappointing. This ee value is thought to be low because of the elongated transition state. The chiral silicon centre is positioned away from the centres and is therefore unable to have an effect.

The α-silylcarbanion, derived from the reaction of LDA with the α-silylester (102), can be methylated[54] to yield the methyl substituted product (103) in 81% yield and 80% diastereomeric excess (de), scheme 1.33. The asymmetric induction seen in this reaction is high. Although the reasons for this are not entirely clear, it could provide a route for the synthesis of optically active α-substituted acids and esters.

Np   Me
\   Np   \
Meⁱⁱⁱ·Si   CO₂ᵗBu   i) LDA   Meⁱⁱⁱ·Si   CO₂ᵗBu
/   ——————→   /
Ph   ii) MeI   Ph
(102)   (103)
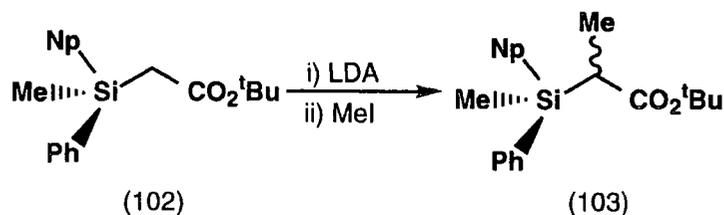
Scheme 1.33

Si-centred chiral organosilanes have seen some use[55] in the hydrosilylation of ketones, scheme 1.34. The disappointing ee values were accompanied by considerable racemisation at the silicon centre. This is likely to arise from pseudorotation of a fluorine containing intermediate and is possible explanation for the low ee value. These low values mean the reaction has not fulfilled it's potential as a route to chiral alcohols.
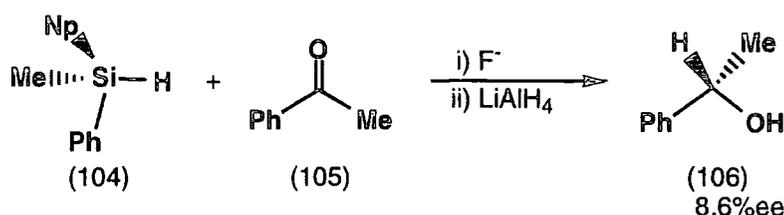
Scheme 1.34

Other reactions studied include the epoxidation of Si-centred chiral vinylsilanes,[56] radical reductions of α-halosilanes[57] and addition reactions of both acylsilanes[58] and α-silylthione.[59] In all cases, only modest enantioselectivity is seen.

Si-centred chiral organosilicon compounds have been generally found to show only modest stereoselectivity. The vast majority of work has examined reactions of methyl-α-napthylphenylsilyl derivatives and it is not unlikely that the stereoselectivity arises from purely steric effects.

1.10.ii C-Centred Chiral Organosilicon Compounds in Synthesis

The problems associated with using Si-centred chiral organosilicon compounds in asymmetric synthesis has meant increasing attention has focused on the use of C-centred chiral silicon compounds. This section will focus on compounds where the chiral carbon centre is a non-reactive substituent on silicon but is the source of asymmetric induction in the product, reactions at the chiral centre will not be covered.

Since the low ee values found in the reaction of allylsilanes with carbonyl compounds are thought to be due to the linear transition state, it is not surprising that similar reactions using C-centred allylsilanes also result in products of low ee. Recent work[60] on this reaction has involved the introduction of a chiral group attached to silicon which is also capable of coordinating to a Lewis acid, scheme 1.35. This aims to favour a synclinal transition state and hence bring the chiral group closer to the reacting centres.
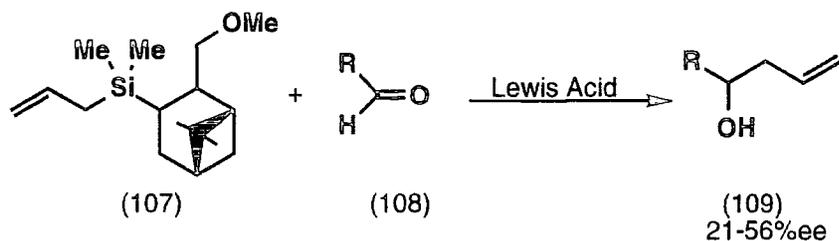
Scheme 1.35

The higher ee values observed imply that this approach does indeed lead to the hoped for results, however, the alkoxy group needs very careful positioning to ensure the necessary coordination and at present, it is certainly not a general method.

This reaction has seen some application in asymmetric natural product synthesis. One example is the synthesis[61] of the chiral tetrahydropyran derivative (113), a compound isolated from a glandular secretion of the Civet cat, scheme 1.36.
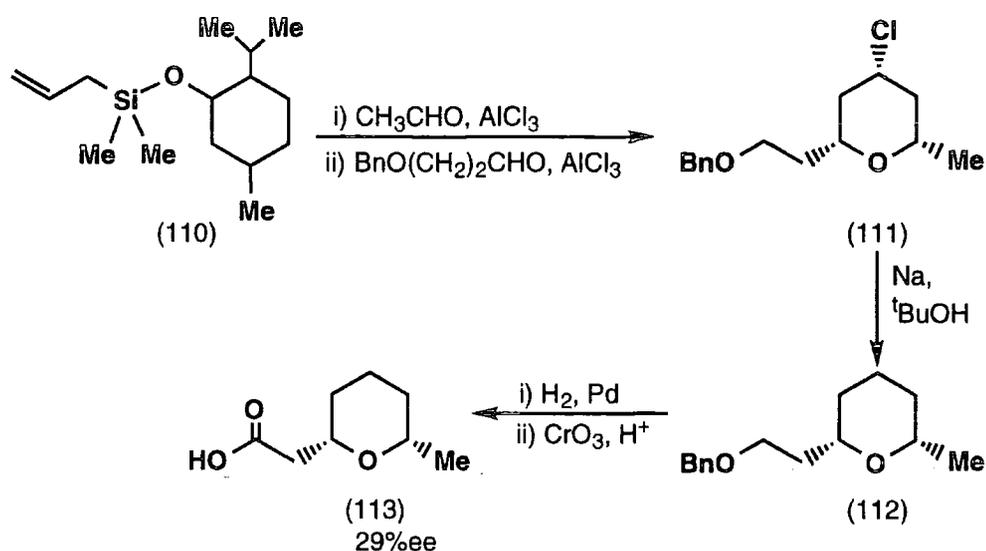
Scheme 1.36

C-centred chiral allylsilanes have also seen use in the synthesis[62] of allylic alcohols (109) of modest to high ee, scheme 1.37.
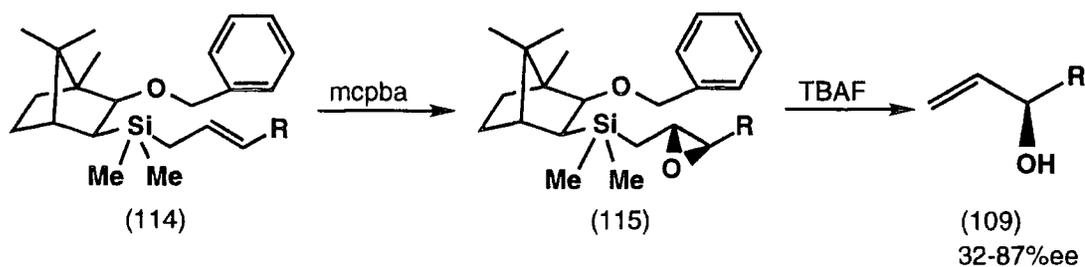
Scheme 1.37

If the chiral auxiliary could be more readily synthesised, the reaction could see considerable application in asymmetric synthesis.

Chiral silyl enol ethers have seen some applications, although products are again usually of low ee. A noteworthy example is the use[63] of the binapthyl silyl enol ether (116) in a Mukaiyama aldol reaction, scheme 1.38.

(116)   (36a)   (36b)
                                         17.2%ee   35%ee
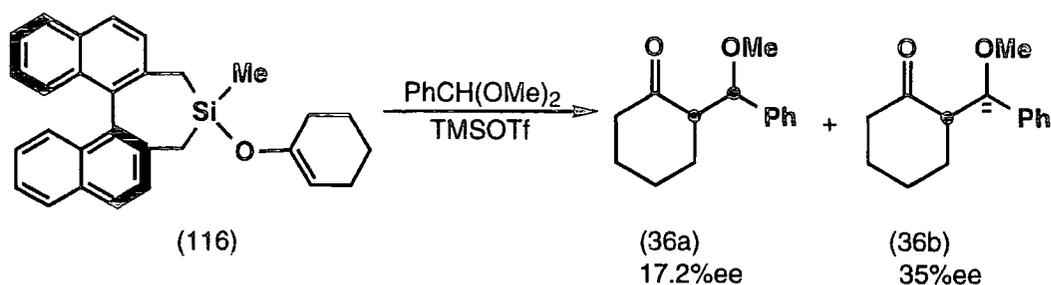
Scheme 1.38

The separable isomeric products are formed in a 4.4:1 ratio. Chiral cyclic silicon species of this type will be discussed further in chapter 3.

The reactions of Si-centred chiral α-silyl carbanions have been shown to be the most stereoselective and the same reactions with C-centred chiral species have also been shown to be highly selective,[64] scheme 1.39. Both the mechanism and structure of the intermediate of this reaction are unclear but there are numerous other examples of the use of α-silyl carbanions, all yielding products of modest to high ee. This type of reaction does, however, appear to have considerable potential in asymmetric synthesis.

(117)   (118)   (119)

(120)
>95%ee
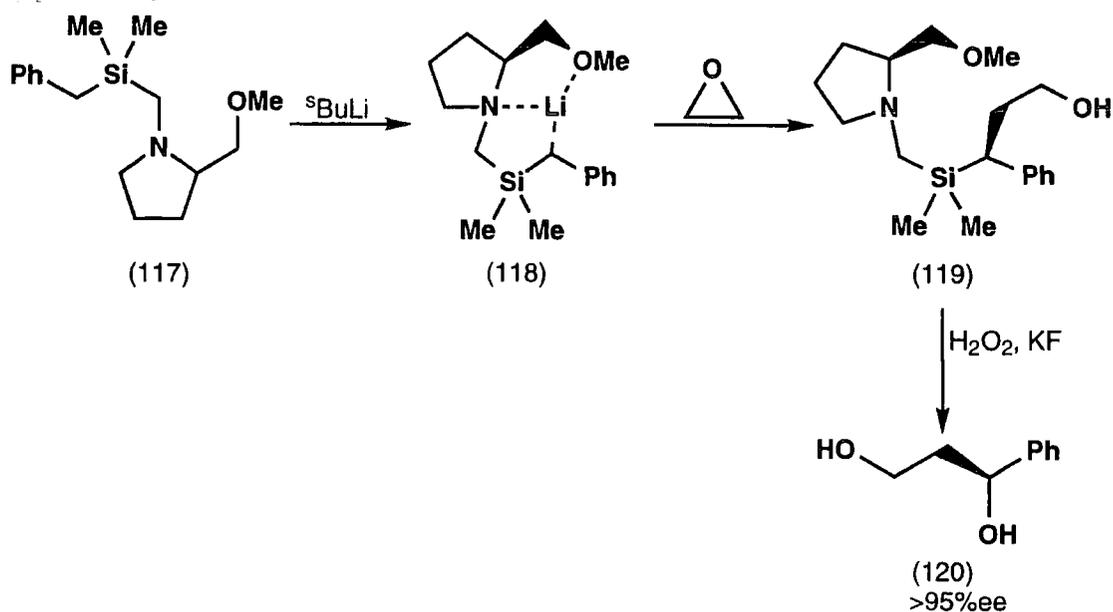
Scheme 1.39

Some of the first uses of C-centred chiral organosilicon compounds were in the hydrosilylation reaction. The silane (122) derived from β-pinene was used in the synthesis[65] of alcohols, the ee values are again still low. Jung has used[63] the binapthyl substituted silane (121) in the hydrosilylation of ketones. It has, however, also been shown to give unsatisfactory ee values, scheme 1.40.
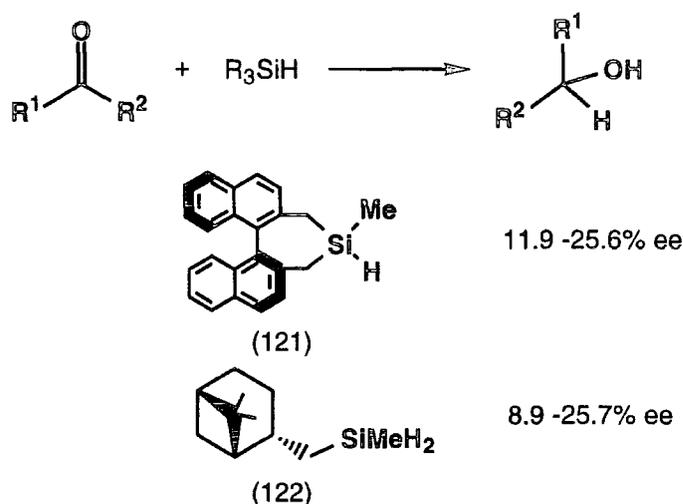
Scheme 1.40

In general, C-centred chiral organosilicon compounds have been shown to give only modest enantioselectivity. They are, however, frequently easier to prepare and handle than Si-centred chiral organosilicon compounds and certainly remove the problems associated with the facile racemisation of the silicon centre.

1.10.iii Chiral Catalysis of Reactions of Organosilicon Compounds

One of the most rapidly growing fields of research in organic synthesis is the application of chiral catalysts in asymmetric synthesis.[66] Organosilicon chemistry has not escaped this and there have been some excellent uses of chiral catalysts within this field.

For many years, catalytic hydrosilylation has been known to give modest ee values when catalysts with chiral ligands are used. Recently, ee values up to 62% have been found in the hydrosilylation of acetophenone (123) using the catalyst derived from $[Rh(COD)Cl]_2$ and (R)-Cystphos, scheme 1.41.
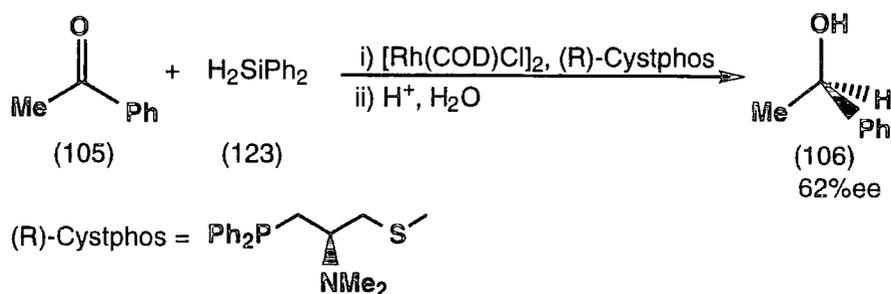
Scheme 1.41

One other example of chiral catalysis is in the Michael reaction of silyl enol ethers,[67] scheme 1.42.
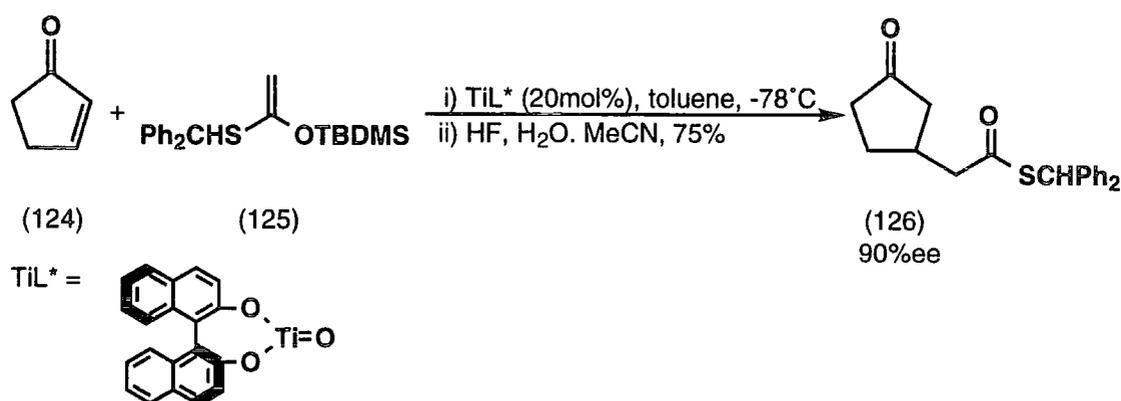
Scheme 1.42

This new application of chiral catalysts suggests that high ee values can be obtained and hence this reaction could become very valuable in synthesis.

1.11 Conclusion

The chemistry of organosilicon compounds is an area of growing interest and application. The great potential of organosilicon chemistry in asymmetric synthesis has now been recognized. Considerable improvements in ee values have been seen in recent years and some of the potential applications of these reactions in asymmetric synthesis are now being realised.

PART B
POTENTIAL APPLICATIONS OF SILACYCLES

PART B : Potential Applications of Silacycles

Chapter 2
The Synthesis of Medium-Sized Carbocyclic Rings

2.1 Introduction

Since compounds containing medium-sized carbocyclic rings found in nature have been shown to be biologically active, increasing interest has focused on their synthesis.[68] This chapter will discuss the available synthetic routes and the difficulties encountered in medium ring synthesis, followed by a description of an alternative strategy and some work related to it.

2.2 Approaches to the Synthesis of Medium-Sized Rings

There are three major routes to ring formation :- i) ring closure of an acyclic precursor ii) pericyclic rearrangement of substituted small ring compounds and iii) fragmentation of a system containing fused small rings, these can be seen schematically below, scheme 2.1.
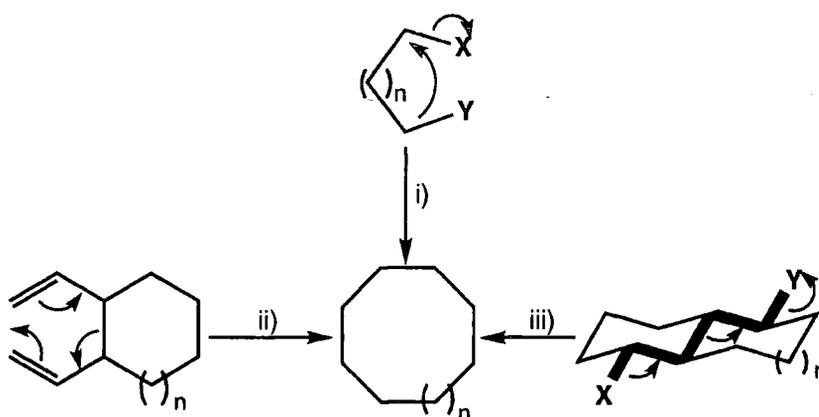
Scheme 2.1

This section will look at each of these methods and, where possible, give some examples of their successful application in the synthesis of medium-sized rings.

2.2.i Ring Closure of an Acyclic Precursor

Ring closure processes can be said to be governed by two main factors, firstly an entropic factor - the frequency at which atoms at the end of a chain come within reacting distance of one another and secondly an enthalpic factor - the interactions observed as the chain takes up the ring shape in the transition state of the reaction. The effects of the entropic factor can be countered in several ways :

i) reactions performed at high dilution will increase the chance of intramolecular reaction and decrease the competing intermolecular processes.

ii) the restriction of the movement of the terminal groups by adsorption onto a surface on which the cyclisation takes place also increases the yield of intramolecular reactions.

iii) making use of effects such as the Thorpe-Ingold effect[69] has also been shown to aid these processes. It is thought that this effect arises through the restriction of the number of conformations available to the molecule hence allowing greater population of the reactive conformation, there has however, been recent evidence[70] against this explanation.

The enthalpic factor is somewhat harder to overcome. The difficulties arise from the bad steric interactions found in the transition state. In cyclooctane derivatives, the transannular interactions between hydrogen atoms at C1 and C5 in all possible conformations of the ring give an indication of the problems in synthesis. The imperfect staggering of bonds (Pitzer Strain) and the deformation of bond angles (Baeyer Strain) in the ring, coupled with the bad steric interactions of substituents, give an indication as to the cause of the high level of strain found in the ring when compared to an acyclic molecule.

It is a combination of all these problems that result in standard ring closure methods being unable to efficiently produce medium-sized carbocycles.[71]

2.2.ii Pericyclic Rearrangements

Pericyclic rearrangements such as the Cope,[72] Claisen[73] and oxy-Cope[74] rearrangements have found many uses in the synthesis of natural products containing medium-sized rings. Grieco's synthesis of (+)-Costunolide (128), which contains a 10-membered carbocyclic ring, is one example of the use of the Cope rearrangement. Dehydrosaussurea

lactone (127) rearranges when heated to produce the required skeleton in 20% yield, scheme 2.2.

(127)   (128)
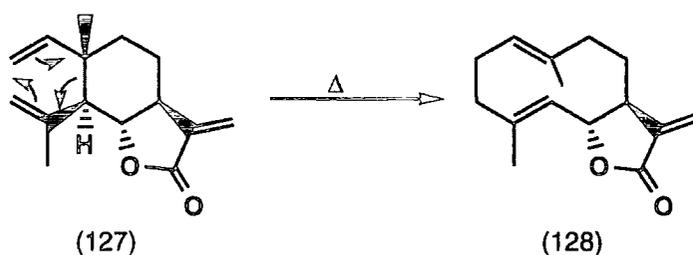
Scheme 2.2

Although pericyclic rearrangements can give high yields of medium-sized carbocycles, the synthesis of the necessary precursors often involves many steps and the need for considerable stereochemical control. These factors lead to the conclusion that pericyclic rearrangement processes are often less attractive than they may first appear for medium-sized ring formation.

2.2.iii Fragmentation of Fused Small Rings

The fragmentation of systems containing two fused small rings is elegantly demonstrated in Eschenmoser's synthesis[75] of (5E,8Z)-6-methyl-5,8-undecadien-11-olide (130), scheme 2.3.

(129)   (130)
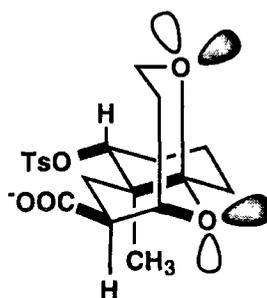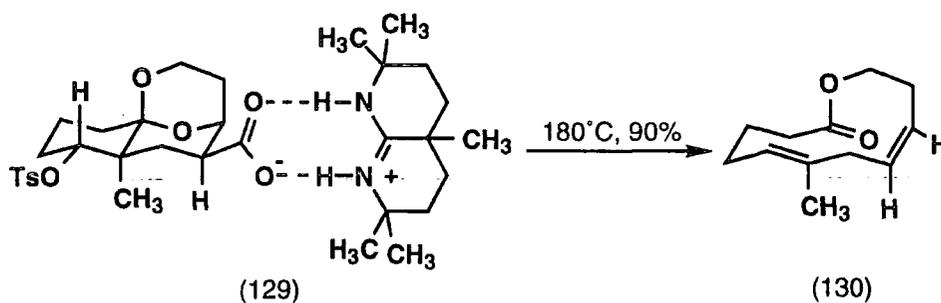
Scheme 2.3

The precursor (129) is ideally set up to allow a double fragmentation - the central C-C bond lies antiperiplanar to the equatorial tosylate group as well as the two 'equatorial' sp³ axes associated

with the electron pairs of the oxygens of the acetal group. Heating the crystalline salt (129) to it's melting point for three minutes under argon gives the required 10 membered carbocycle in 90% yield.

It is again problems associated with precursor formation that complicate the use of the fragmentation route in medium-sized ring synthesis. The complex precursors can be as difficult to form as those necessary for the pericyclic rearrangement routes. Taking all the necessary steps into consideration means that the overall yield for a synthesis can still be very low.

It was hoped that the new approach outlined below would overcome many of the difficulties of both precursor synthesis and medium-sized ring formation.

2.3 An Intramolecular Diels-Alder Route

Intramolecular Diels-Alder reactions are a well known route for the synthesis of polycyclic species. Our initial approach aimed to use a silicon tethered Diels-Alder reaction to produce a polycyclic ring species (132), a subsequent fragmentation reaction would yield the medium-sized ring, scheme 2.4.
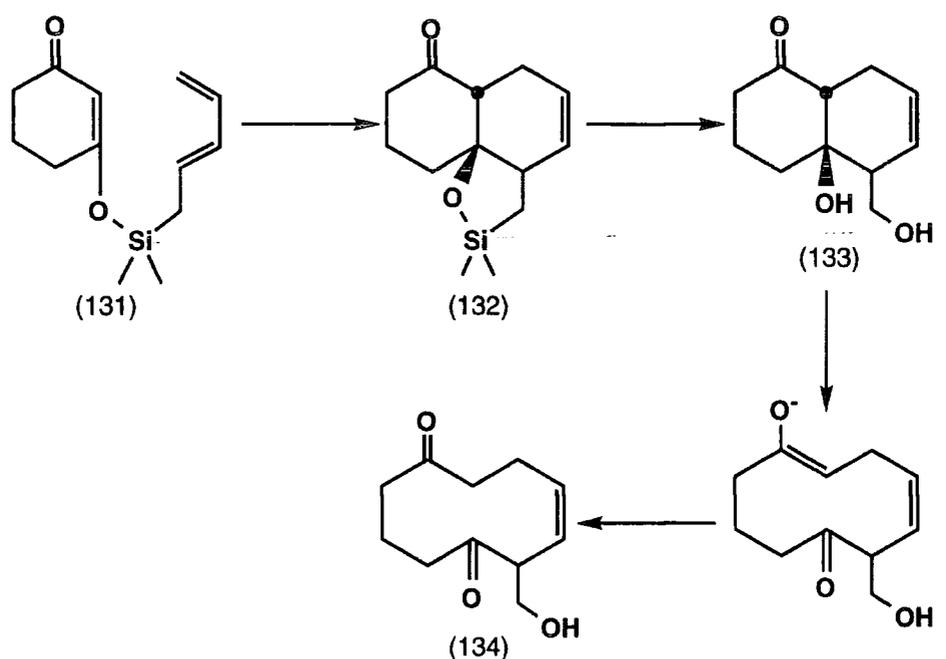
Scheme 2.4

The cleavage of the silacyclic ring resulting from the Diels-Alder reaction, by a Tamao oxidation,[76] produces a bicyclic diol (133) which should be perfectly aligned to allow a Grob-

type fragmentation[77] to be induced across the ring hence producing the required carbocycle, figure 2.1.

(133)
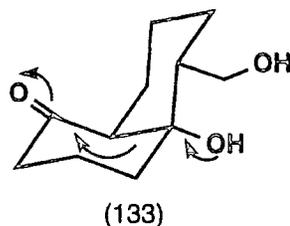
Figure 2.1

Silicon tethers have seen many applications in Diels-Alder reactions, see chapter 1, and have been shown to have little effect on the reactivity on the substrate and hence, the product is recovered in high yield. It was also hoped that the dimethyl substitution of the silicon may aid the ring formation by making use of the Thorpe-Ingold effect.

The Diels-Alder reaction allows the formation of 3 contiguous chiral centres and the intramolecular nature of the reaction increases the control of the stereoselectivity of the reaction. Furthermore, the tricyclic product (132) has a well defined shape, which should allow further functionalisation in a stereocontrolled manner. This means that a considerable degree of the stereochemistry of the products can be introduced in one step and removes the need for the complicated stereocontrol in the synthesis of the precursors, as seen in the pericyclic rearrangement and fragmentation routes. It also seemed likely that the introduction of a chiral 'C-centred' silicon tether would allow the reaction to be made enantioselective.

Furthermore, since less synthetic steps should be necessary in the overall transformation, it was hoped that the yields of medium-sized rings could be considerably improved. The versatility of this synthetic sequence would make it an ideal general method for the synthesis of a wide range of medium-sized rings.

It seemed likely that a relatively simple synthesis of the silicon containing precursor (131) could be developed from a silanol (136) and a cyclohexanone derivative (135), scheme 2.5. In an alternative strategy, the reaction of a silyl chloride with the enol tautomer of 1,3-cyclohexanedione could also be used.
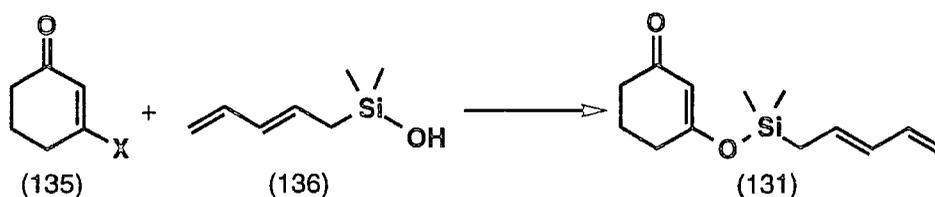
Scheme 2.5

As an initial simplification, it was decided to develop the route without the inclusion of the silicon atom. This carbon tethered case could also be used to determine the potential of the Diels-Alder route. The initial synthetic target therefore became 3-(hexa-3',5'-dienyloxy)-2-cyclohexen-1-one (137), figure 2.2.

(137)
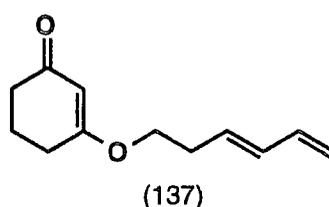
Figure 2.2

The synthesis of this molecule and related derivatives is discussed in the next section.

2.4 The Synthesis and Reactivity of Potential Precursors

2.4.i The Synthesis of 3-(Hexa-3',5'-dienyloxy)-2-cyclohexen-1-one and Derivatives

The first target was to develop a simple synthetic route to hexa-3,5-dienol (141a), which could also be readily adapted to allow the straightforward synthesis of substituted derivatives. This was easily achieved starting with sorbic acid (138), scheme 2.6. Treatment of sorbic acid (138) with diazomethane yielded methyl hexa-2,4-dienoate quantitatively, which was confirmed by the appearance of a singlet at δ3.69 in the ^{1}H NMR spectrum. Shing and Tang have developed[78] a synthesis of hexa-3,5-dienoate esters by the deconjugation of hexa-2,4-dienoate esters. Using a similar procedure, kinetic quenching of the enolate derived from the reaction of the ester with LDA yielded the deconjugated ester in high yields. This procedure could be adapted, by the use of methyl iodide in place of acetic acid, to produce the 2,2-dimethyl substituted ester (140b). In the unsubstituted case, this was confirmed by the appearance of a doublet at δ3.12 in ^{1}H NMR, which is attributable to the CH_2 unit between the

ester and diene functionalities and furthermore, the pattern seen in the olefinic region was dramatically different with the integration suggesting 5 olefinic protons. For the dimethyl substituted case, ^{1}H NMR showed the very distinctive pattern in the olefinic region with integration again showing the presence of 5 olefinic protons. Although the yields are lower in this case, it is likely that optimisation of reaction times and conditions could result in considerable improvement. A straightforward reduction with lithium aluminium hydride yielded the required alcohols, with IR confirming the loss of the carbonyl group and the formation of an OH group.
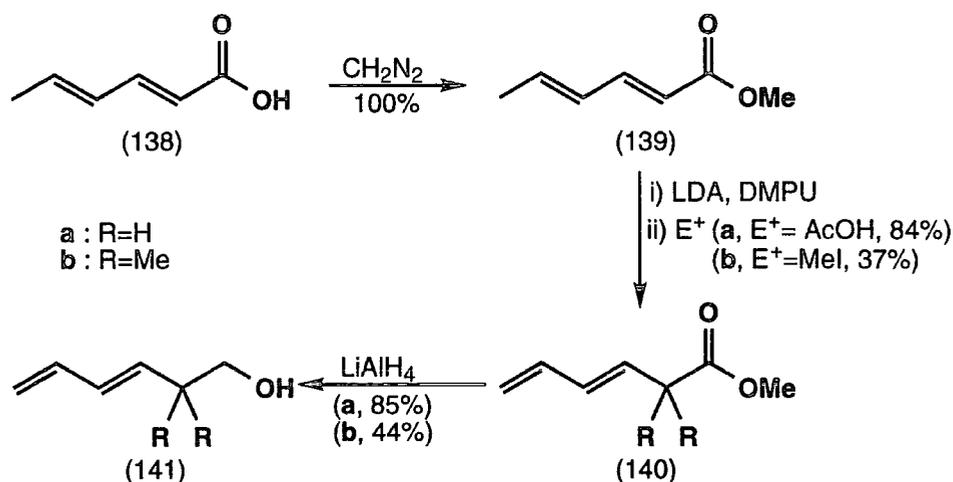
Scheme 2.6

With this synthetic sequence in hand, work began on the coupling reaction necessary to produce the Diels-Alder precursor.

It was thought that 1,3-cyclohexanedione would be the ideal starting point for the synthesis of the required precursors, since it readily reacts as it's acid tautomer. As halogenated derivatives (142) can be prepared in high yields by published methods,[79] it was thought they would provide an ideal basis for a highly versatile route to the required compounds. A simple addition/elimination process would result in the replacement of the halogen by an alkoxide, scheme 2.7.
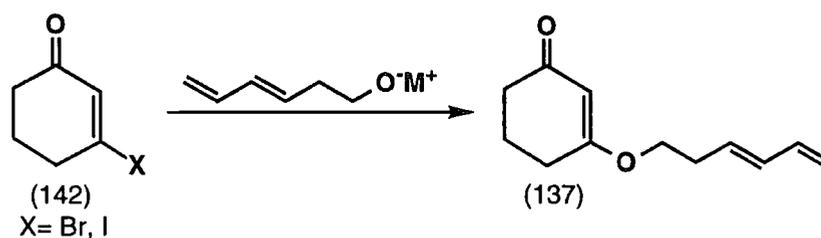
Scheme 2.7

All reactions of this type that were attempted led only to a highly polymeric residue. In an attempt to suppress this polymerisation, it was decided to protect the ketone as a ketal. Shih and Swenton had found[80] that attempted ketalisation of these halogenated substrates with ethylene glycol led mainly to the bis ketal derivative (143), they had found that the formation of the monosubstituted thioketal was much more easily controlled and so the thioketal (144) was prepared by their procedure, scheme 2.8.
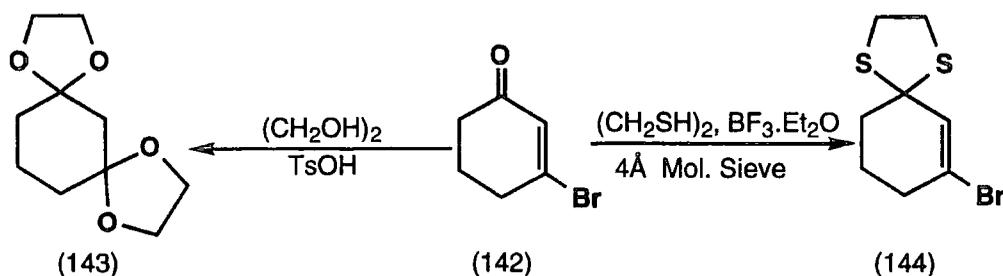
Scheme 2.8

Even the use of these protected derivatives failed to give the required reaction with an alkoxide, with only highly polymeric material being recovered.

The final attempt to use halogenated derivatives lay with the use of thallium salts. Seebach and co-workers have shown[81] that the reaction of a thallium alkoxide with an iodide leads to the formation of solid thallium iodide. This provides an excellent driving force for the displacement reaction, and results in the formation of the required alkoxide substituted product. This reaction, however, again led only to the formation of polymeric residues.

Kowalski and Fields had demonstrated[82] that a mesylate group could be displaced by ethoxide anion, when sodium ethoxide was generated from the addition of sodium to ethanol, and 3-(mesyloxy)-2-cyclohexen-1-one (146) was subsequently added as an ethanolic solution, scheme 2.9.
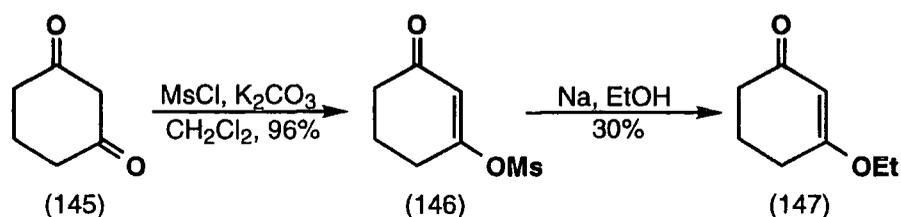
Scheme 2.9

This mesylate (146) was prepared and used in the reactions with alkoxides. Disappointingly, only reactions where the alcohol could be used as the solvent were successful and all reactions in other solvents again failed to yield the required alkoxide substituted product.

Since it was now evident that this route would not provide a versatile synthesis of the required Diels-Alder precursors, a new approach was adopted. Pirrung and Webster had demonstrated[83] that 3-(hexa-3',5'-dienyloxy)-2-cyclohexen-1-one (137a) could be synthesised by the acid catalysed coupling of 1,3-cyclohexanedione (145) with hexa-3,5-dienol (141a), it seemed that this procedure was less versatile than the synthesis originally envisaged, and alternative side reactions may complicate the formation of the silicon derivatives. However, this procedure was followed, scheme 2.10, to allow the potential of these compounds in the Diels-Alder reaction to be investigated.

(145)
a : R=H
b : R=Me

(137)
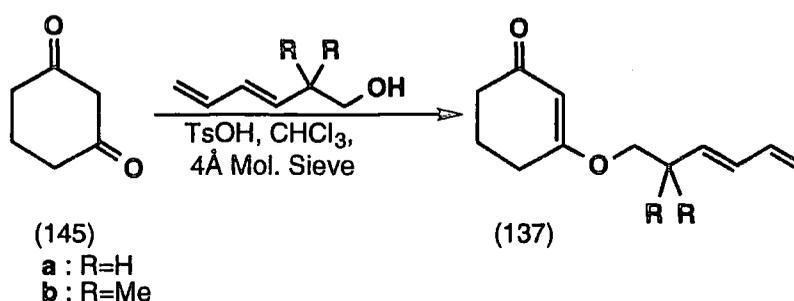
Scheme 2.10

2.4.ii Diels-Alder Reactions of 3-(Hexa-3',5'-dienyloxy)-2-cyclohexen-1-one and Derivatives

Initial attempts at the Diels-Alder cyclisation were made using Lewis acid catalysis. The use of titanium tetrachloride at temperatures below -20°C led only to complete recovery of the starting material. At -20°C the starting material decomposed and led only to the recovery of hexa-3,5-dienol, this decomposition is presumably aided by the Lewis acid. Attempts with other Lewis acids gave the same results.

Attention was then switched to thermal Diels-Alder reactions. Heating a dilute solution (0.04M) under reflux in benzene resulted only in the recovery of the starting material. Heating a solution of the reactant (137a) in benzene in a Carius tube at 250°C yielded only a mixture of starting material and a highly polymeric compound. Reducing the concentration of the solution led to only complete recovery of starting material.

After the failure of 3-(hexa-3',5'-dienyloxy)-2-cyclohexen-1-one (137a) to undergo a Diels-Alder cycloaddition, it was decided to use the analogous dimethyl substituted compound (137b). It was hoped that the Thorpe-Ingold effect may increase the reactivity and hence, aid the cyclisation reaction. This molecule was simply prepared using the modified route described in section 2.4.i. Disappointingly, all attempts at Diels-Alder cycloaddition of this compound also failed.

At this point, it was felt that the failure of the Diels-Alder reaction may be due to the deactivation of the system by the vinylogous ester group. The oxygen directly bound to the dienophile can feed electron density into the dienophile, this would raise the energy of the LUMO and hence, make reaction less likely to occur. If this was the major factor hindering the reactivity, then a simple modification of the starting material should disfavour the donation into the vinylogous ester group, figure 2.3.

(148)
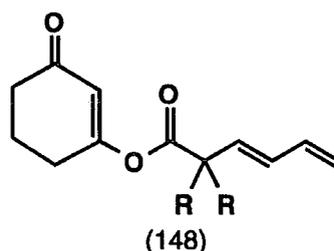
Figure 2.3

By using an ester tether, it was hoped that donation from the oxygen into the directly bound ester would be preferred and this would stop the raising of the LUMO energy of the dienophile.

The next target therefore became the synthesis and application of the 3'-oxocyclohex-1'-enyl hexa-3,5-dienoate (148a), figure 2.3, and it's derivatives.

2.4.iii The Synthesis of 3'-Oxocyclohex-1'-enyl Hexa-3,5-dienoate and Derivatives

A synthetic route similar to that for the vinylogous ester (137) could be followed, scheme 2.11.
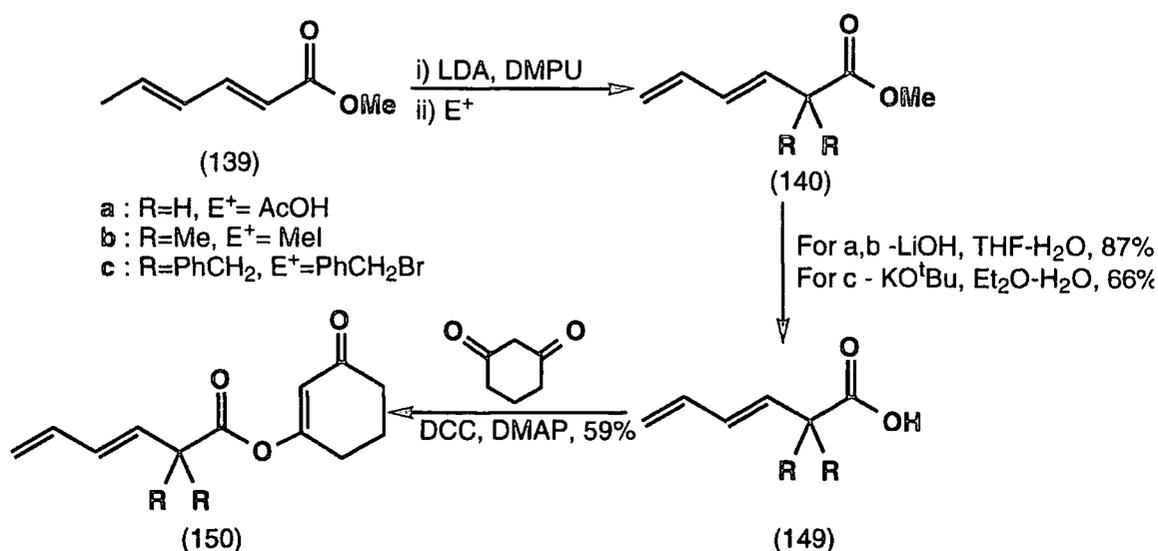
Scheme 2.11

The unsubstituted deconjugated acid (149a) is known to be a very unstable species and the highly complex olefinic region in the ^{1}H NMR spectra showed it could only be obtained as a mixture with the reconjugated species, hexa-2,4-dienoic acid (138). This problem was overcome by the use of 2,2-disubstituted derivatives and hence, further work has largely concentrated on these derivatives. No difficulties were encountered with the synthesis of the dimethyl substituted derivative (149b), however, hydrolysis of the dibenzyl substituted ester (140c) proved impossible with LiOH in THF-water. This problem was overcome by using KO^{t}Bu in Et$_2$O-water, as had been reported[84] by Gassman and Schenk, and resulted in the formation of the required acid (149c) in 66% yield, with ^{1}H NMR clearly showing the loss of the singlet attributable to the methyl ester at $\delta 3.64$. DCC mediated coupling of all three acids with 1,3-cyclohexanedione proved to be easily achieved, with the appearance of a singlet in the olefinic region (e.g. For (150c) $\delta 5.53$) of the ^{1}H NMR spectra confirming the formation of the vinylogous ester. These syntheses, therefore, led to three more potential precursors for the Diels-Alder reaction.

2.4.iv Diels-Alder Reactions of 3'-Oxocyclohex-1'-enyl Hexa-3,5-dienoate and Derivatives

Attempts to carry out the Diels-Alder cycloaddition of these substrates under low temperature Lewis acid catalysed conditions, again yielded only decomposition products.

Thermal Diels-Alder reactions did however, give some success. Heating a dilute solution of the unsubstituted triene (150a) in benzene in a silylated Carius tube at a variety of temperatures up to 300°C, resulted in the reconjugated species, 3'-oxocyclohex-1'-enyl hexa-2,4-dienoate, being the major product recovered. The use of the dimethyl substituted triene (150b) overcame problems of the competing reconjugation and it was hoped, it would further facilitate the cycloaddition reaction by making use of the Thorpe-Ingold effect. However, on heating in benzene in a silylated Carius tube, no reaction was observed at temperatures up to 250°C. When the temperature was raised to 300°C, complete conversion of the starting material was found. Rather surprisingly, the only product isolated was α-tetralone (153), scheme 2.12, which was identified by comparison to an authentic sample.

These observations led to the hypothetical mechanism outlined below, scheme 2.12.
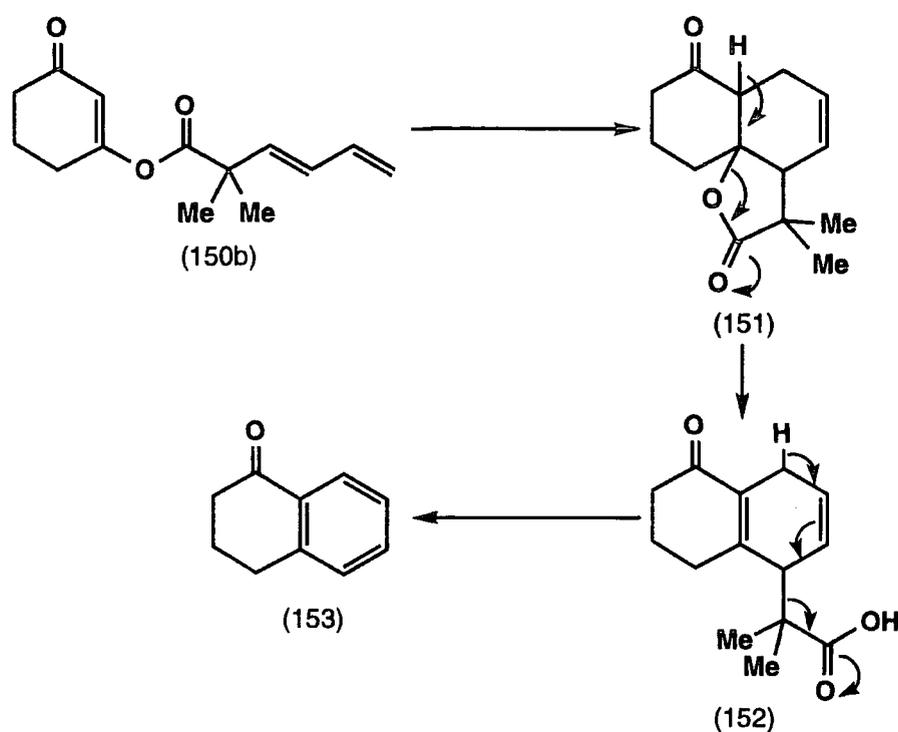
Scheme 2.12

This hypothetical mechanism suggests that the desired intramolecular Diels-Alder reaction does occur to produce the tricyclic lactone (151). However, under these harsh reaction conditions, this species is not stable and undergoes a fragmentation and elimination process. There are two possible routes by which the latter stages can occur. They are either as shown above, scheme 2.12, where initial elimination of the bridgehead lactone is followed by elimination of

isobutyric acid as it's enol form or through initial elimination of dimethylketene and subsequent aromatisation upon dehydration of the resultant tertiary alcohol. Since several attempts to analyse the volatile components from these reactions failed to show any traces of products derived from the ketene and a similar intermolecular reaction also formed trace amounts of α-tetralone, at present the first mechanism seems most likely.

Attempts to isolate the product derived from the lactone bridge also proved unsuccessful. In order to try and identify this product, the Diels-Alder reactions of the dibenzyl substituted triene (150c) was also undertaken. The *gem*-substitution of the compound should further enhance the reactivity in the cycloaddition step and any product resulting from the lactone bridge should be of high enough molecular weight to facilitate isolation. Total reaction occurred when this triene (150c) was heated in a sealed unsilylated tube at 150°C for 6 days, unfortunately the only non-polymeric product resulting from this reaction was α-tetralone (153), which was obtained in 33% yield. Attempts to isolate the acidic product by treating the crude product mixture with diazomethane or *via* a base-acid extraction sequence also proved unsuccessful. It seems likely that the acidic product is further decomposed under the harsh reaction conditions.

By increasing the number of carbons in the diene chain, the second step of the fragmentation process should be prevented since it must now proceed *via* an unstabilised homoenolate anion. It was hoped that a study of the reactivity of the homologous triene, 3'-oxocyclohex-1'-enyl hepta-4,6-dienoate (156a), should therefore allow the isolation of the acidic intermediate and hence, confirm the mechanistic pathway. The synthesis of these homologues, therefore, became the next target.

2.4.v The Synthesis of 3'-Oxocyclohex-1'-enyl Hepta-4,6-dienoate and Derivatives

After the preparation of ethyl hepta-4,6-dienoate via a Claisen rearrangement[85] of penta-1,4-dien-3-ol, the unsubstituted triene was prepared by the same route was as used for the hexa-3,5-dienoate trienes (150), scheme 2.13.

OH

(154)

i) MeC(OEt)$_3$, C$_2$H$_5$CO$_2$H
C$_6$H$_6$, 18h, Δ, 64%
b : ii) LDA, DMPU, MeI, -78°C
and repeat -20°C, 55%

CO$_2$Et
R R
(155)

i) KOH, MeOH, Δ
(a : 100%; b : 72%)
ii)1,3-cyclohexadione,
DCC, DMAP, CH$_2$Cl$_2$, 0°C

O O

OH
(157)

+

O
O

O
R R
(156)

a : R=H   30%   30%
b : R=Me   0%   84%
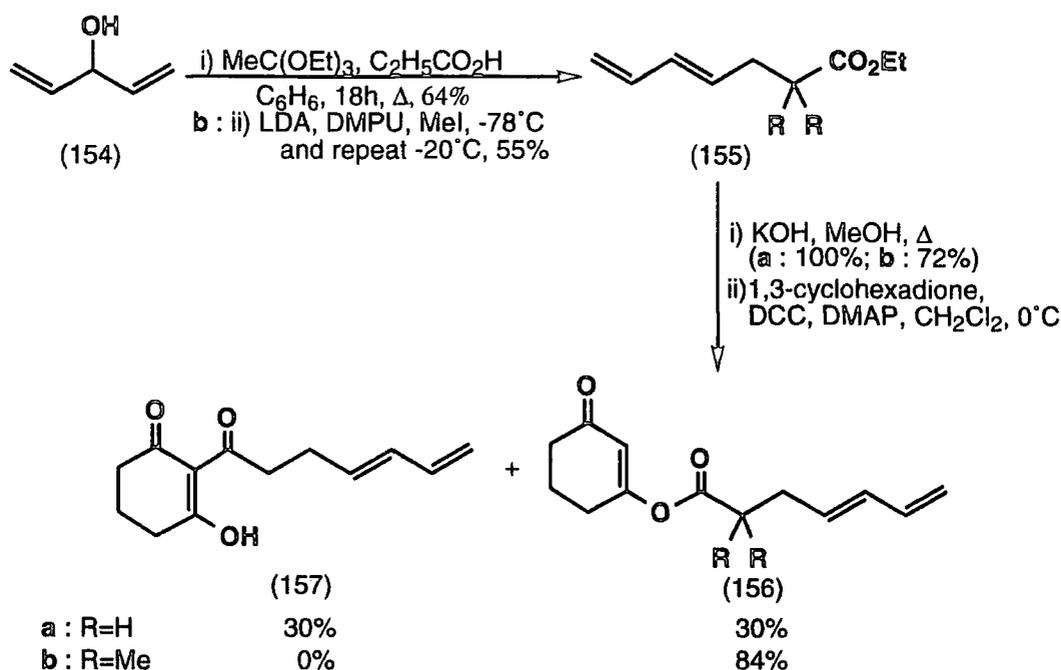
Scheme 2.13

In the unsubstituted case (155a), hydrolysis of the ethyl ester was accomplished by heating to reflux for 2 hours in methanolic KOH solution, with ^{1}H NMR confirming the loss of the quartet (δ4.13) and the triplet (δ1.25) associated with the ethyl group. The ^{13}C NMR spectrum of the resulting acid showed only 6 signals, however one signal (δ132.13) was double the intensity of the other signals and therefore, this signal must be representative of two coincident ^{13}C signals. The coupling reaction with 1,3-cyclohexanedione was complicated by the formation of the corresponding C2-acylated species (157). The two products proved to be separable by column chromatography. Characterisation confirmed the impurity to be the C2-acylated species (157) by the presence of an OH stretch in the IR spectrum and three ^{13}C NMR signals at δ205.01, 197.94 and 195.08 which are attributable to the two ketone and one enol carbons in the molecule. The required vinylogous ester (156a) gives a ^{13}C NMR spectrum containing signals at δ199.31, 169.64 and 169.23 which are attributable to the one ketone and two ester carbons. Although impurities of this type were not observed in the preparation of the earlier trienes, a similar observation has been reported[86] by Tabuchi and co-workers.

The dimethyl substituted triene (156b) was prepared by exhaustive methylation of the ethyl ester followed by hydrolysis and DCC mediated coupling. The carbonyl region of the ^{13}C NMR spectra showed only 3 resonances (δ199.36, 174.07 and 170.28) implying that the

required vinylogous ester (156b), which was obtained in 84% yield, had not undergone a Fries rearrangement. Tabuchi had also noted that compounds with this substitution pattern do not undergo Fries rearrangement.

This synthetic sequence therefore allowed the preparation of the homologous trienes (156) and subsequently, a study of their reactivity in the Diels-Alder reaction.

2.4.vi Diels-Alder Reactions of 3'-Oxocyclohex-1'-enyl Hepta-4,6-dienoate and Derivatives

Under the conditions used in previous attempts at the Diels-Alder reaction, the unsubstituted triene (156a) gave only the product derived from the Fries rearrangement. This process was found to be the only process occurring at a variety of temperatures.

The dimethyl substituted triene (156b) was also subjected to these conditions and, after heating in a Carius tube at 300°C for 48 hours, complete reaction occurred. Analysis of the crude reaction mixture indicated, somewhat surprisingly, the formation of α-tetralone (153). Furthermore, base extraction of the crude reaction mixture failed to produce any of the expected acid formed by elimination of the lactone bridge. Reducing the temperature of the reaction resulted only in recovery of the starting material.

The formation of α-tetralone (153) in this case was unexpected. The elimination of a butyrate enol is not possible for these trienes and therefore, suggests that fragmentation of an unactivated C-C bond or loss of hydride is occurring. The only other alternative is the involvement of radical species, which considering the high reaction temperatures, cannot be totally ignored.

2.5 Conclusion

At the outset of this work, it was envisaged that a new route to medium-sized rings would be developed. Although this has turned out not to be the case, it has uncovered an unusual fragmentation process leading to tetralone products. The mechanism of this fragmentation still remains unclear. There are potentially a variety of reasons, both steric and electronic, that explain the lack of reactivity of these trienes in the Diels-Alder reaction. Boeckmann and Demko have suggested[87] that the low reactivity of vinylogous esters is due to

the difficulties encountered in overcoming the overlap requirements of the ester linkage in the transition state. Parker and Adamchuk have found[88] intramolecular Diels-Alder reactions of furan dienes occur more readily with amide tethers than with ester tethers. Jung and Gervay have also found[89] evidence to suggest that the lower reactivity of ester tethered reactants is due to conformations adopted to minimize dipole effects. They found that tertiary amide linked reactants (which lack strong dipole effects) often participate more readily in intramolecular Diels-Alder reactions. It may be that changing to amide linked reactants would increase the reactivity of our triene systems.

Due to the change of direction during this work, the synthesis of the silicon containing precursors has not been attempted. The rest of this thesis will concentrate on the development of routes for the synthesis of enantiomerically pure silacycles. It is hoped, they will prove to be useful silicon tethers in a variety of intramolecular processes.

PART C
THE SYNTHESIS OF SILACYCLES

PART C : The Synthesis of Silacycles

Chapter 3

Silacycles : Introduction and Background

3.1 Introduction

Work on the use of silicon in asymmetric synthesis has continued and it appears that the use of 'C-centred' chiral silicon reagents has the most promise. Silicon-tethered intramolecular reactions have been found to be very useful. As yet, however, there has only been a single, recent report of reactions where the enantioselectivity is derived from a chiral silicon tether.[90]

This chapter introduces the background behind the work devoted to the synthesis of silacycles. Firstly, it will give a brief outline of some of the long-term aims of the project. It will go on to mention previous work on the biological activity of silacyclic compounds. Finally, there have been reports of many different approaches to silacycle synthesis and these are discussed in section 3.4.

3.2 Potential Uses of Chiral Silacycles

As has been discussed in chapter 1, high diastereoselectivity has been observed in the silicon-tethered intramolecular Diels-Alder reaction.[91] It was envisaged that 'C-centred' chiral silacycles (158), figure 3.1, could be used as tethers to induce some enantioselectivity into these types of reactions.

(158)
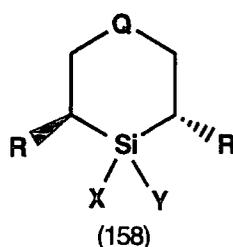
Q= O, NR, R_2C etc.
R= alkyl, aryl etc.
X,Y= alkyl, aryl, OR, Hal, R_2N etc.

Figure 3.1

It was felt that the synthesis of the silacycle would be simplified if the Si-Cl bonds necessary for the formation of the tether links could be introduced at a late stage in the synthetic sequence. Taddei and co-workers have demonstrated, in their synthesis[62,92] of optically active allylsilanes, scheme 3.1, that the addition of HCl to a phenylsilane (159) generates the chlorosilane (160). It was therefore initially hoped to develop a route to a diphenyl substituted silacycle and subsequently use Taddei's procedure to generate the dichlorosilacycle.
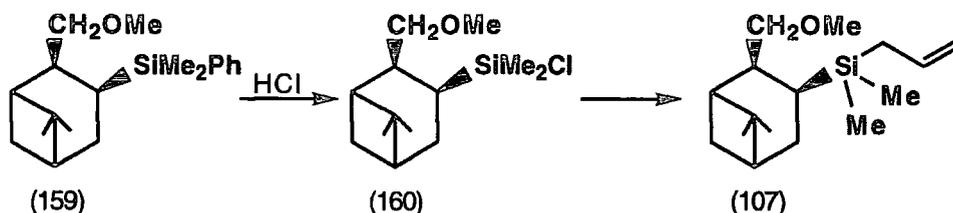
Scheme 3.1

The use of a C_2 symmetric species has several advantages.[93] Consideration of the Diels-Alder reaction, scheme 3.2, shows that C_2 symmetry not only halves the number of possible diastereomeric transition states but also makes the synthesis of the precursor simpler, since the attachment of the diene and dienophile does not create a chiral centre at silicon.
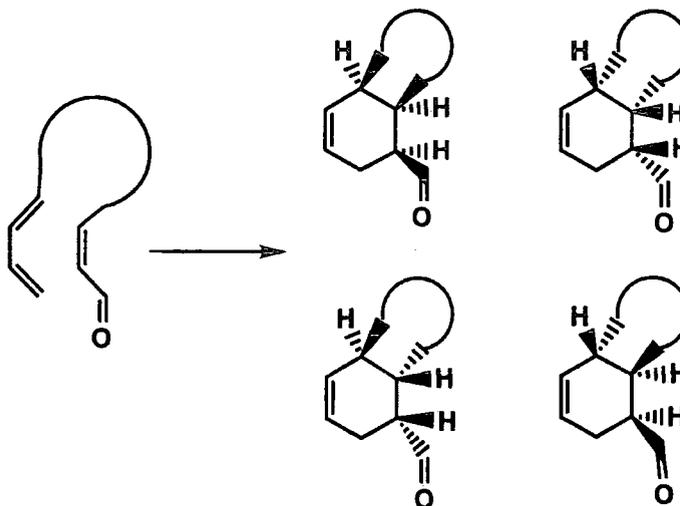
Scheme 3.2

It is hoped that silacycles (158) of this type will have uses in many other processes, one example is in the resolution of chiral diols, scheme 3.3.

Scheme 3.3
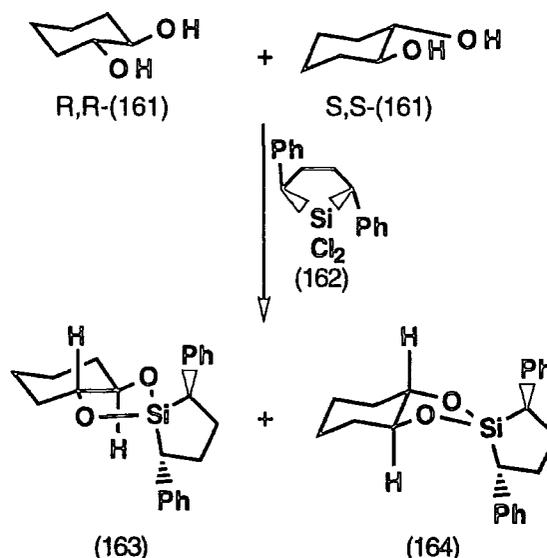
If the silacycle (162) is reacted with trans-1,2-cyclohexanediol (161), the result of double asymmetric induction will mean the reaction with the enantiomer in which the bulky groups [in this case, speculation suggests the silacycle phenyls and the 1,2 axial substituents in the diol] are further apart in space (matched pair, product (164)) should be faster than that where the groups will be closer (mismatched pair, product (163)). Following this scenario, commencing with a racemic mixture and sub-stoichiometric amounts of the silacycle, kinetic resolution should also be possible.

3.3 Silacycles and Their Biological Activity

In addition to their potential as chiral auxiliaries, the possible biological activity of these silacycles is also interesting. Although the only silicon compounds known to be naturally occurring are those which contain Si-O bonds, it has become clear that artificial compounds containing Si-C bonds can often exhibit high and specific biological activity. Cyclic silicon compounds have now seen application in pharmaceuticals, perfumes and biotransformations.[94] This section will outline some of the features of silicon containing compounds with biological activity.

The interest in the biological properties of organosilicon compounds can be grouped into 3 classes :- i) the simple derivatisation of known compounds (e.g. silylation of functional groups), ii) the synthesis and testing of new organosilicon compounds where analogous

carbon compounds have not been studied and iii) the synthesis of silicon compounds analogous to carbon compounds with known activity, a procedure known as sila-substitution.

The differences in the properties between silicon and carbon mean that some silicon compounds are much simpler to prepare than their carbon analogues. Silatranes, figure 3.2, are an interesting class of cyclic silicon compounds[95] with no carbon analogues. Interestingly, they contain a pentacoordinate silicon atom, where a nitrogen atom coordinates across the ring. The carbon substitution at silicon has a dramatic effect. Aryl substitution proves to give highly toxic silatranes (165), which find applications as rodenticides whilst 1-(chloromethyl)silatrane (166) and 1-ethoxysilatrane (167) are non-toxic and have medical applications.
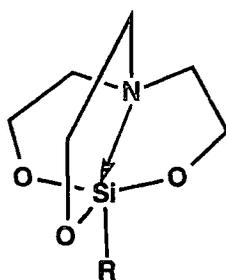
(165) R =C$_6$H$_5$
(166) R = ClCH$_2$
(167) R = EtO

Figure 3.2

It is, perhaps, in the sila-substitution of drugs where the most interesting results with respect to this project lay. In the examples[96] shown overleaf, figure 3.3, the effects of sila-substitution have been studied. The silaazacycle (169) has a variety of derivatives, all of which show improved activity over their carbon counterparts. The synthesis of these silacycles is discussed in section 3.4.

The similarities of these compounds to our synthetic targets are obvious and leads to the possibility of our compounds having properties worthy of investigation.
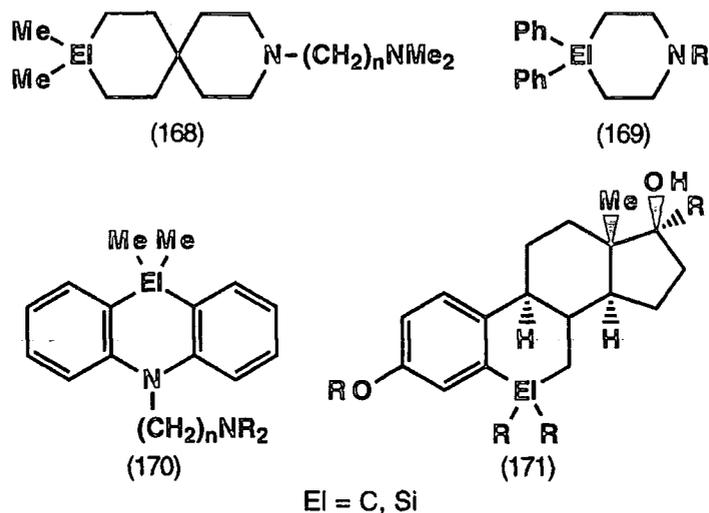
Figure 3.3

3.4 Previous Synthetic Approaches to Silacycles

To the best of our knowledge, there is only one report of the synthesis of an asymmetric silacycle. Jung and co-workers have reported the synthesis of derivatives of the binapthyl substituted silacycle (172), figure 3.4. As has been discussed in chapter 1 (section 1.10), they have gone on to develop the application of this cyclic silicon species to enantioselective reactions.

(172)
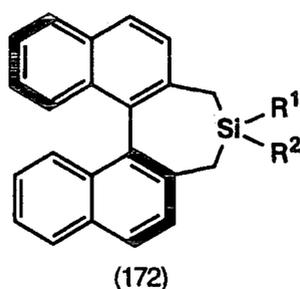
Figure 3.4

This section will consider the synthesis of this silacycle and also discuss the variety of approaches that have been used in the synthesis of achiral silacycles.

3.4.i Approaches with Organometallic Reagents

Grignard and lithiated reagents have been well used in the preparation of silacycles. The route developed by Jung and co-workers for the preparation[63] of the binapthyl silacycle (174) demonstrates the use of lithiated precursors, scheme 3.4.
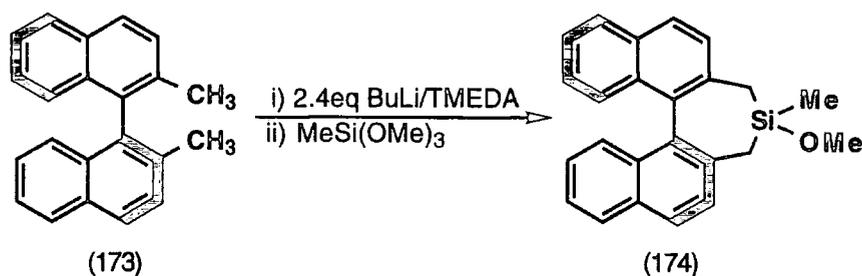
Scheme 3.4

Chong and co-workers have also demonstrated[97] that similar silacycles can be prepared in very high yields from the reactions of the stannepin (176), which is prepared by a Grignard reaction, scheme 3.5.
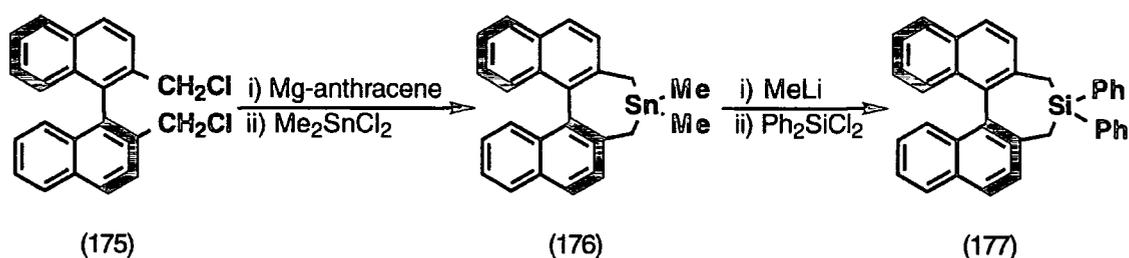
Scheme 3.5

The lithiated derivative of diphenyl ether (178) has also been reacted[98] with phenylsilane to produce the cyclic silicon species (179), scheme 3.6.
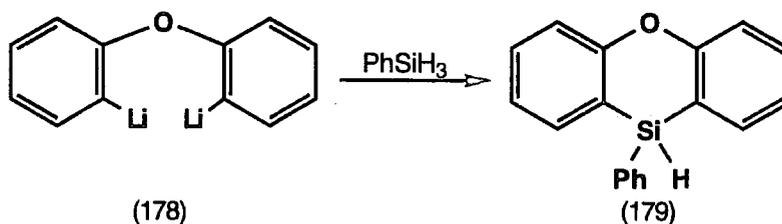
Scheme 3.6

Reagents of this type have been well used in silacycle synthesis, elemental lithium has also seen an interesting application in silacycle synthesis. Weyenberg and co-workers have used[99] lithium in the head to head dimerisation of styrene (180); subsequent reaction with dichlorodimethylsilane yielded 1,1-dimethyl-2,5-diphenyl-1-silacyclopentane (182) as a completely random isomeric mixture at the α-carbons, scheme 3.7.
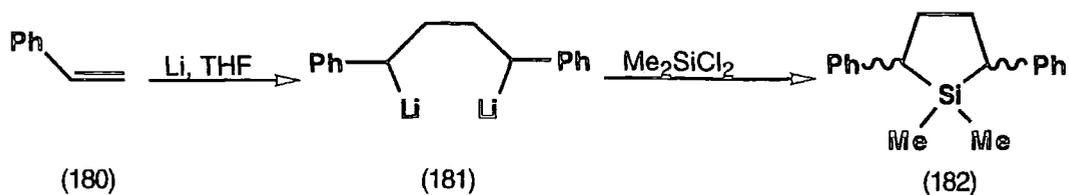
Scheme 3.7

In the synthesis of the α-chiral 'C-centred' silacycles as required in this project, however, these routes cannot be used, since the necessary stereochemistry at the α-carbon cannot be preserved.

3.4.ii Use of Silylene Addition

Dimethylsilylene (183) can be formed by the pyrolysis of 1,2-dimethoxytetramethyldisilane, subsequent reaction[100] of this silylene with cyclopentadiene (184) leads to the bicyclic compound (185), which then rearranges to form isomeric silacyclohexadienes ((186), (187)), scheme 3.8. These compounds can serve as percursors to silacyclohexanes, albeit with no control of stereochemistry.
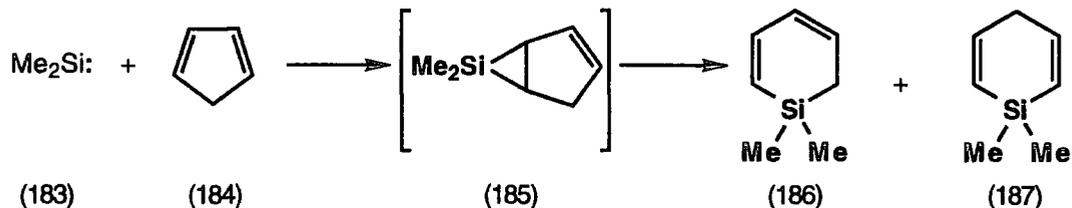
Scheme 3.8

3.4.iii Hydrosilylation of Olefins

Intramolecular hydrosilylation has seen several applications in the synthesis of silacycles. The dimethyl substituted silacycle (189) has been prepared[101] in 73% yield as a 1:1 mixture of cis:trans isomers from the chloroplatinic acid catalysed hydrosilylation of the silane (188), scheme 3.9.
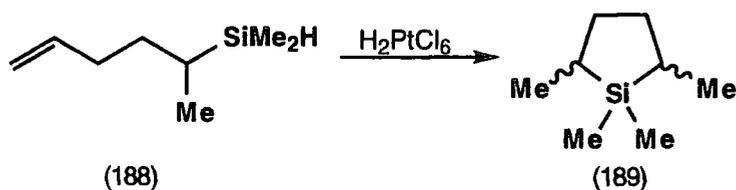
Scheme 3.9

The hydrosilylation of 1,3-butadiene (190) has also resulted[102] in the formation of dichlorosilacyclopentane (192), scheme 3.10.
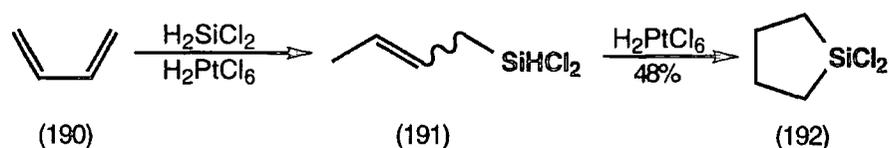
Scheme 3.10

An application of asymmetric hydrosilylation has also resulted[103] in the formation of a silacycle (194) of low but unstated ee, scheme 3.11.
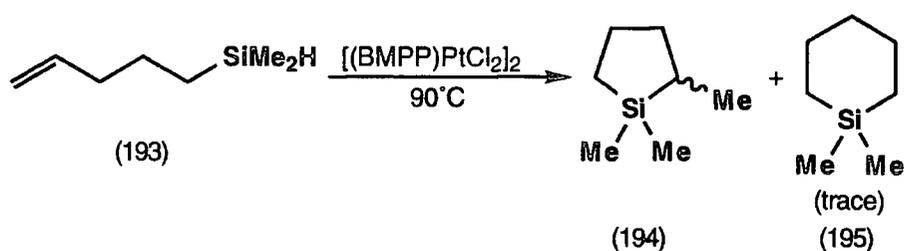
Scheme 3.11

The asymmetric hydrosilylation of olefins is an area of rapidly increasing interest. This methodology forms the basis for one possible route towards the preparation of enantiomerically pure silacycles, it is discussed further in chapter 4.

3.4.iv Michael Addition to Divinylsilanes

Sila-prodipine (169) is, as seen in section 3.3, a silicon substituted compound of an analogous carbon containing drug, both compounds show similar antiparkinsonian activity.[104] The synthesis of sila-prodipine uses Michael addition to divinylsilanes (197), scheme 3.12.
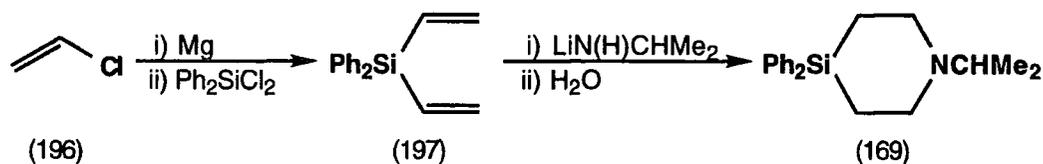
Scheme 3.12

Although there have been no reported attempts to use this reaction in the formation of asymmetric silacycles, it does appear to be an area worthy of further investigation.

3.4.v Hydroboration of Divinylsilanes

In the 1980's, Soderquist and co-workers began investigating the chemistry of divinylsilanes (199) and germanes. Their work resulted in the synthesis[105,106,107] of a variety of silacyclohexanones (202), scheme 3.13.
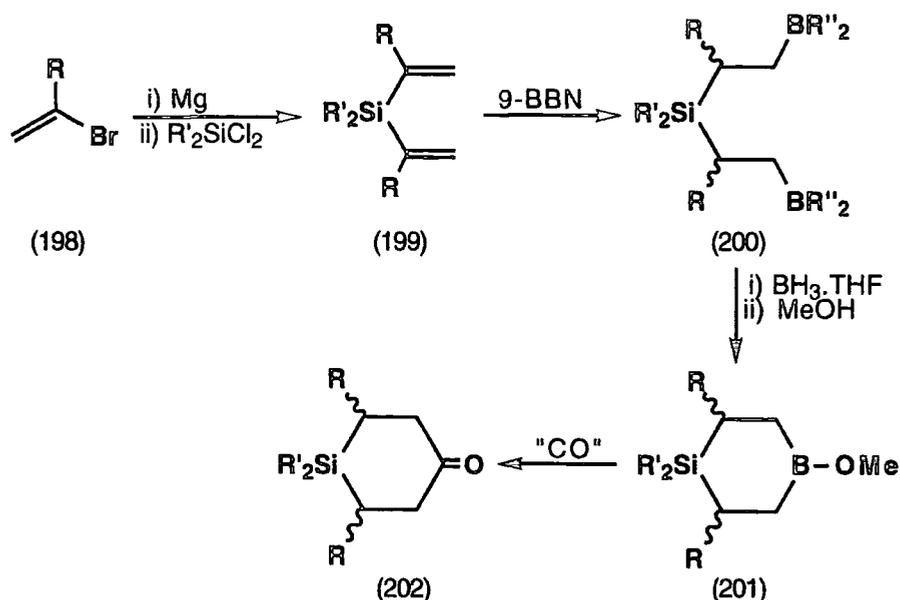
Scheme 3.13

Their work has never investigated the formation of α-chiral silacycles, although they have observed some diastereoselectivity for the *cis* substituted isomer.

This route, which involves the interesting use of a boron redistribution reaction, has become the basis for part of the work described in this thesis and will be considered more fully in chapter 5.

3.5 Potential Approaches to Enantiomerically Pure Silacycles

The possible approaches to silacycles can be divided into 2 classes : i) the last step in the synthesis is the introduction of the silicon containing fragment or ii) the last step is the ring closure of a silicon containing intermediate, scheme 3.14.
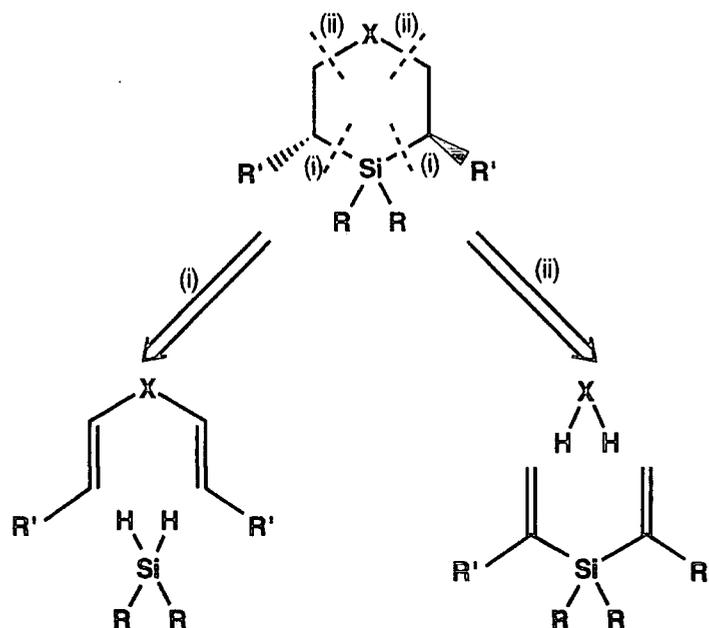
Scheme 3.14

Route (i) can be achieved by the double asymmetric hydrosilylation of a diene. Route (ii) starts with a divinylsilane which can be functionalised to allow subsequent ring closure. Route (ii) is potentially more versatile since it allows the easier introduction of other heteroatoms into the ring.

Work related to the application of the asymmetric hydrosilylation of dienes is discussed in chapter 4. The functionalisation of divinylsilanes is discussed in chapter 5.

<u>PART C : The Synthesis of Silacycles</u>

<u>Chapter 4</u>

Silacycles : Hydrosilylation of Dienes

4.1 Introduction

The addition of silanes across a double bond is known as hydrosilylation, the hydrosilylation of carbonyl compounds has been discussed in chapter 1 and the hydrosilylation of carbon-carbon double bonds is also possible. The first potential route to enantiomerically pure silacycles requires the asymmetric double hydrosilylation of a diene, scheme 4.1.
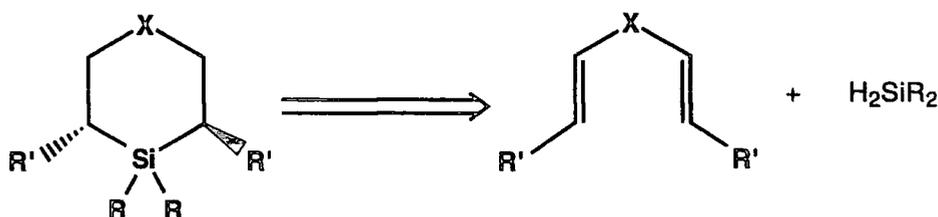
Scheme 4.1

This chapter will discuss the background to olefin hydrosilylation and then describe work related to the synthesis of silacycles by hydrosilylation.

4.2 Hydrosilylation of Alkenes

4.2.i Introduction

Although direct hydrosilylation of olefins can occur at very high temperatures (>300°C), it is more usual and synthetically more efficient to use lower temperatures together with a promoter of some form. Possible promoters include ultraviolet light, γ-irradiation, electric discharge, peroxides and most commonly, a wide range of transition metal based complexes. Since the use of asymmetric metal complexes can make the hydrosilylation reaction enantioselective, this section will focus only on the application of transition metal complexes. The hydrosilylation reaction has been excellently reviewed[108] by Ojima.

4.2.ii Transition Metal Catalysis

Since the metal catalysed addition of silanes to olefins was first reported[109] in the late 1950's, catalysts derived from the late transition metals have been found to be particularly effective. The precise mechanism of the process remains a subject of considerable debate[110] but the most widely accepted version, proposed[111] by Chalk and Harrod, is shown below, scheme 4.2.
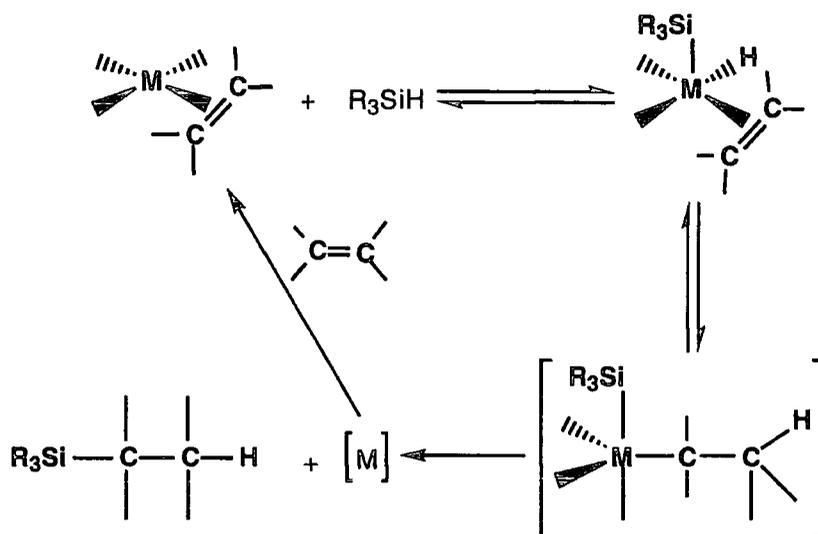
Scheme 4.2

Whether coordination of the olefin occurs before or after the oxidative addition of the hydrosilane is particularly uncertain. It has proved impossible to propose a mechanism that can account for all the observations made about hydrosilylation which include induction periods, radical chain processes, olefin rearrangements and dimerisations and isotopic exchange at both silicon and the olefin.

Despite the complex nature of this process and the many side reactions often associated with it, it has been shown to be very useful in many areas of synthesis, as discussed in the next section.

4.2.iii Hydrosilylation in Synthesis

Early investigations into hydrosilylation found that terminal and internal olefins react particularly well under platinum catalysis. However, the reactions[112] of internal olefins are usually accompanied by isomerisation to give the terminal silane adduct as the major product,

the hydrosilylation of 1-ethylcyclohexene is one example, scheme 4.3. This isomerisation is

thought to occur during the complexation of the olefin to the metal centre.
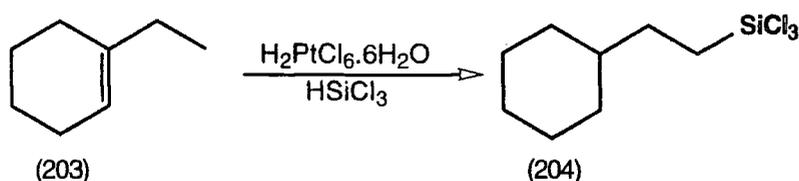
Scheme 4.3

Since the extremely high catalytic efficiency of platinum[103,113] based catalysts was

reported, complexes based on most other late transition metals (particularly palladium[114],

rhodium and nickel[115]) have been found to exhibit some catalytic activity. More recently,

complexes of early transition metals[116] have been investigated. Although the reasons remain

unclear, different metals frequently produce different regiochemical outcomes and this is

particularly well demonstrated in the hydrosilylation of styrene, scheme 4.4.
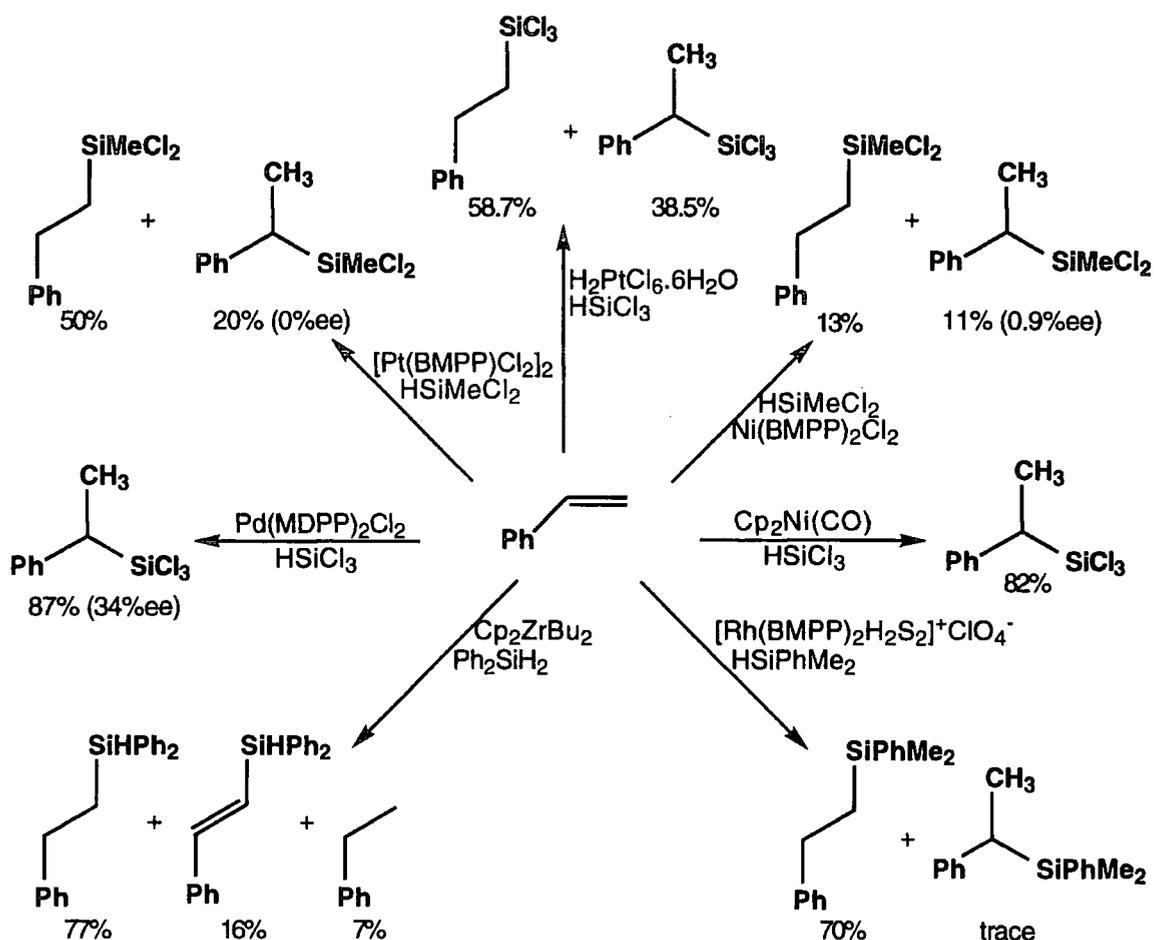
Scheme 4.4

Scheme 4.4 also shows the effect of using asymmetric catalysts. The chiral catalysts are based on the use of chiral phosphine ligands which can be classified into two classes :- (i) those containing a chiral phosphorus atom - (R)-benzylmethylphenylphosphine (BMPP), where 3 different groups are attached to phosphorus, or (ii) those containing a chiral group attached to the phosphorus atom - menthyldiphenylphosphine (MDPP). Initial work demonstrated that in most cases phosphines of class (i) were more effective in asymmetric hydrosilylation, although values of enantiomeric excess were low. However, in the case of catalysts based on palladium, class (i) phosphines were inactive whereas the use of class (ii) phosphines has been found to give moderate ee values.

The increasing interest in the synthesis of enantiomerically pure materials has meant that asymmetric hydrosilylation followed by oxidative cleavage[76] of the Si-C bonds has become recognized as a potential route to optically active alcohols. Investigations into the potential of this reaction has been hampered by the low ee values often encountered in hydrosilylation. It has, however, now been recognized[117] that chelating bis-phosphines are often inactive in simple olefin hydrosilylation reactions and hence, phosphines such as chiraphos and BINAP could not be used. This is an unusual observation and it has been shown not to be the case for intramolecular hydrosilylation reactions of allylic silyl ethers,[118] where rhodium complexes of both BINAP and chiraphos have given products of high ee. Hayashi and co-workers have subsequently developed[119] a monodentate phosphine ligand which allows olefin hydrosilylation to proceed in good yield with high enantioselectivity, scheme 4.5. 2-(Diphenylphosphino)-2'-methoxy-1,1'-binapthyl (MOP) allows the use of the BINAP type ring system to induce the enantioselectivity whilst providing a monodentate phosphine which is highly active in the hydrosilylation reaction.
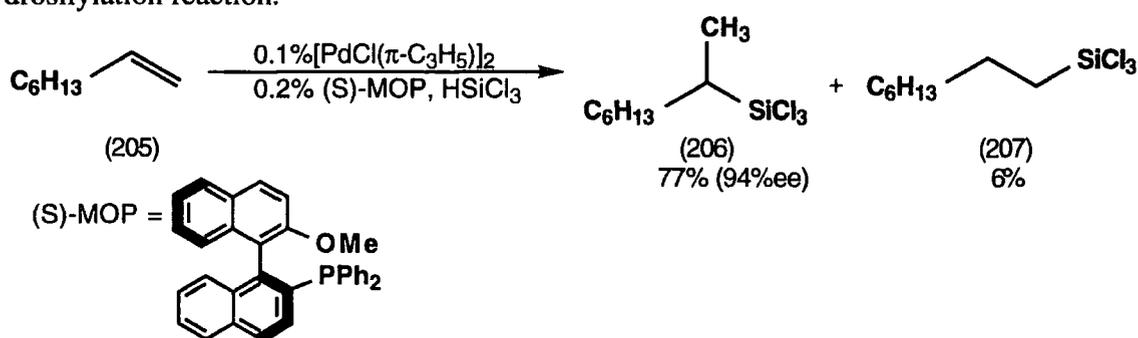
Scheme 4.5

The high ee values now obtainable with these types of phosphine imply that this procedure may become a more synthetically viable route to enantiomerically pure alcohols. Although the sharp changes in ee values often obtained through apparently minor changes in the structure of olefin, silane or catalyst may continue to hamper the application of hydrosilylation in synthesis.

4.3 Hydrosilylation of Dienes

The hydrosilylation of dienes has not been as extensively studied[120] as the hydrosilylation of simple olefins. Unlike olefin hydrosilylation, platinum catalysts show little activity in diene hydrosilylation with reactions occuring only at high temperatures and with low yields. Both palladium and nickel catalysts have been found to catalyse the hydrosilylation of butadiene (190) with triethoxysilane, scheme 4.6. The type of ligands on the metal centre were found to control the distribution of products. With $PdCl_2(PhCN)_2$, the major product (209) was found to be derived from the combination of two molecules of butadiene (190) with one of silane. However, with $[PdCl(\pi\text{-}C_3H_5)]_2$ as catalyst, the yield of the 1:1 product (208) rose to approximately 85% at a reaction temperature of 100°C. The formation of these but-2-enylsilane and octa-2,6-dienylsilane products is typical of the reaction of many butadiene derivatives with a variety of catalysts.[108]
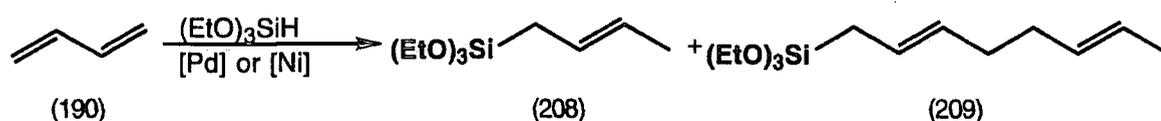
Scheme 4.6

Kumada and co-workers have examined[114] the asymmetric hydrosilylation of cyclopentadiene (184) and 1,4-cyclohexadiene. The hydrosilylation of one double bond was usually accompanied by the isomerisation of the other double bond to form an optically active allylic silyl product (210) of unknown ee, scheme 4.7.
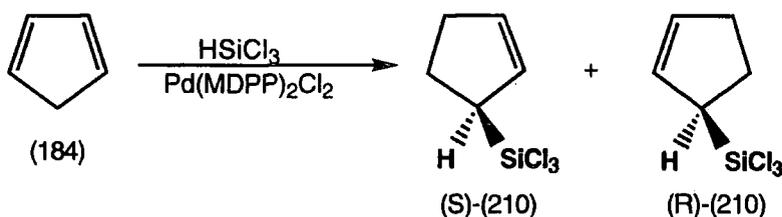
Scheme 4.7

The asymmetric hydrosilylation of 1-aryl-1,3-butadienes (211) has led to some of the highest ee values seen in the hydrosilylation of dienes. The use of the palladium catalyst, PdCl$_2$[(R)-(S)-PPFA] results[121] in both high enantioselectivity and regioselectivity, scheme 4.8.
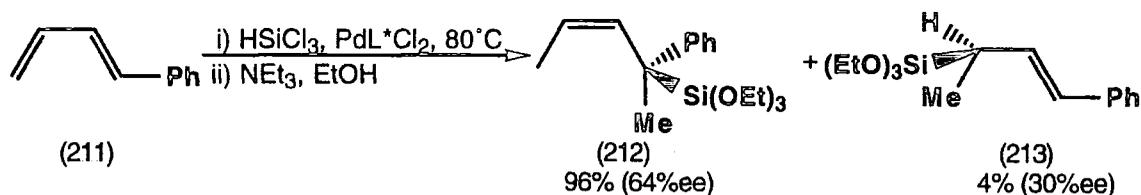
Scheme 4.8

The formation of dichlorosilacyclopentane (192) by the double hydrosilylation of butadiene, discussed in chapter 3 (section 3.4.iii), is the only report of the double hydrosilylation of dienes to form saturated silyl derivatives.

4.4 Silacycles by Asymmetric Hydrosilylation

Given the successful application of intramolecular olefin hydrosilylation to the synthesis of cyclic silicon derivatives discussed in chapter 3, it was hoped that the asymmetric double hydrosilylation of a butadiene derivative (214) would lead to the formation of an enantiomerically pure silacyclopentane (215), scheme 4.9.
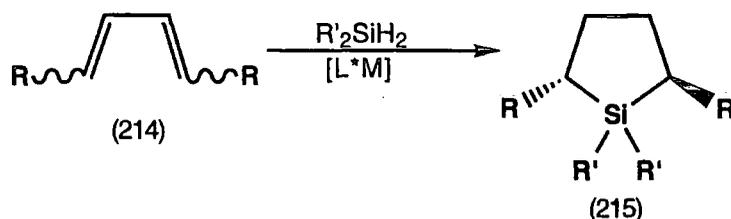
Scheme 4.9

As Kumada and co-workers have demonstrated[103,114,115] that the hydrosilylation of styrene can result in the formation of 1-phenethyl derivatives, it was decided to use 1,4-diphenyl-1,3-butadiene (214, R=Ph), which is available in a pure form as the (E,E) isomer. The use of phenyl groups as substituents also prevents the isomerisation of double bonds to a terminal position and following the first hydrosilylation, it was hoped that the formation of the silacycle would be facilitated by the fact that the second hydrosilylation will be an intramolecular process.

4.5 Attempted Hydrosilylation of 1,4-Diphenylbutadiene

It was decided to test the hydrosilylation of 1,4-diphenylbutadiene with achiral catalysts based on a variety of metals in order to give an indication as to the best catalytic system. Diphenylsilane was selected as the other reagent since it is a readily available, easily handled liquid of low volatility.

Procedures usually followed for the hydrosilylation of olefins involve the addition of the catalyst to a neat mixture of silane and olefin. In this case, diphenylbutadiene is a solid and hence, a solvent must be used. In an attempt to curtail interference from the catalyst, non-coordinating solvents were used. Typically, the diene was dissolved in the minimum amount of benzene or 1,2-dichloroethane and diphenylsilane and the catalyst were added, this mixture was heated in a tap-sealed tube at a variety of temperatures. However, GC analysis of the reaction mixture failed to give any indication of reaction when either chloroplatinic acid, $H_2PtCl_6.6H_2O$, or Wilkinson's catalyst, $(Ph_3P)_3RhCl$, were used. The use of these catalysts in neat reactions with styrene did give some indication, by GC-MS, of the expected products of hydrosilylation together with considerable amounts of ethyl benzene derived from the hydrogenation of styrene.

The use of diethylsilane in place of diphenylsilane also failed to show any reaction. It is, however, known that increasing the electronegativity of the substituents on silicon tends to increase the reactivity of the silane in the hydrosilylation process. The reaction of dichlorosilane, H_2SiCl_2, with diphenylbutadiene in the presence of $(Ph_3P)_3RhCl$ in CD_2Cl_2 was monitored by ^1H NMR. After several days, all the dichlorosilane had been consumed but there had been no loss of the diene, it seemed that the dichlorosilane had taken part in coupling reactions to yield species which still contained Si-H bonds but could not be clearly characterised. The use of $(Ph_3P)_2PdCl_2$ as catalyst in the reaction of diphenylbutadiene with dichlorosilane did result in the loss of some of the diene. Experiments monitored by ^1H NMR, however, imply that the product derived from the diene was an olefin, which was probably 1,4-diphenylbut-2-ene, this product could easily be formed *via* a π-allyl palladium intermediate.

It seems likely that the major problem associated with the use of 1,4-diphenylbutadiene is the fact that it is a solid and therefore requires the use of solvents. The highly conjugated nature of this diene could also affect the complexation to the metal centre. It was, therefore decided to synthesise liquid dienes in order to allow further attempts at hydrosilylation.

4.6 Synthesis of 3,3-Dimethyl-1,5-diphenyl-1,4-pentadiene

It was decided that the use of terminal phenyl substituents should be maintained to prevent isomerisation of the double bonds. Furthermore, in an attempt to suppress internal isomerisation and potential but-2-ene formation, it was decided to use a *gem*-dimethyl substituent group between the double bonds. The target molecule was therefore 3,3-dimethyl-1,5-diphenyl-1,4-pentadiene (216), scheme 4.10.
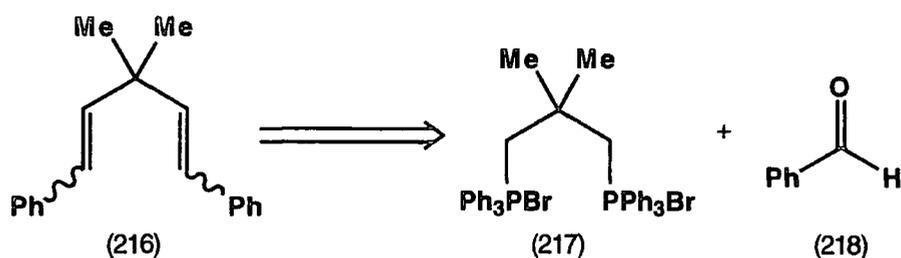
Scheme 4.10

It was envisaged that this molecule could be synthesised from a Wittig reaction of a bis-phosphonium salt (217) and benzaldehyde (218). Tolbert and Ogle have prepared[122] the analogous 1,5-diphenyl-1,4-pentadiene by a similar route.

The procedure used by Horner and co-workers for the preparation[123] of trimethylenebis(triphenylphosphonium) bromide was adapted for the synthesis of the bis-phosphonium salt (217), scheme 4.11.
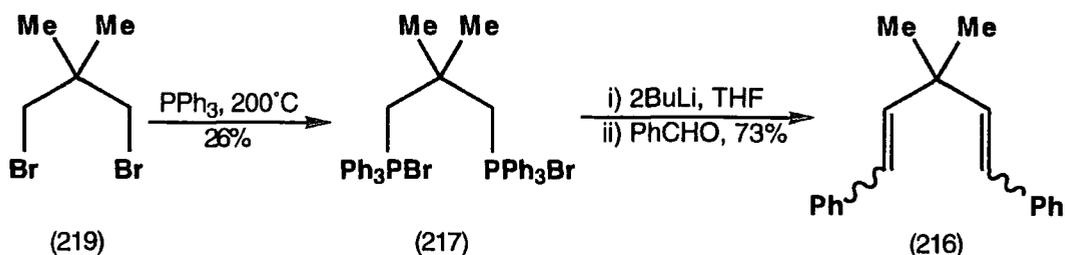
Scheme 4.11

A neat mixture of 1,3-dibromo-2,2-dimethylpropane (219) and triphenylphosphine was heated to 200°C for 18 hours to yield the crude bis-phosphonium salt (217). Recrystallisation from ether/ethanol yielded white crystals, in 26% yield, with one ^{31}P NMR peak at $\delta 19.16$. The presence of only 7 signals in the ^{13}C NMR spectra confirmed the symmetry of the molecule and hence, the formation of the bis-phosphonium salt (217), with the signals of carbons throughout the molecule showing long range couplings to phosphorus. Simple ylid formation and reaction with benzaldehyde yielded a 1:2:1 mixture of (E,E), (E,Z) and (Z,Z) isomers (216) in an overall yield of 73%. Column chromatography allowed the separation of these isomers and ^{1}H NMR gave indicative coupling constant and patterns for the olefinic protons, allowing the identification of each isomer.

4.7 Hydrosilylation of 3,3-Dimethyl-1,5-diphenyl-1,4-pentadiene

It was decided to attempt to monitor the progress of the hydrosilylation of 3,3-dimethyl-1,5-diphenyl-1,4-pentadiene by ^{1}H NMR. Hence, one isomer of the diene was dissolved in CD_2Cl_2 and the catalyst added, this was followed by the appropriate amount of dichlorosilane. The sealed NMR tube was heated at a variety of temperatures and the ^{1}H NMR spectrum was monitored. Yet again, there was no evidence of hydrosilylation of any of the diene isomers. The only new peaks observed appeared to result from hydrogenation reactions and possible silane coupling reactions. This type of complex mixture is frequently observed in hydrosilylation reactions and Kesti and Waymouth have also observed[116] unusual products derived from silicon-silicon coupling reactions.

Despite trying a wide range of combinations of diene isomer, catalyst and silane, no evidence for hydrosilylation could be found.

4.8 Conclusion

The lack of evidence for the hydrosilylation of 1,4-diphenylbutadiene was disappointing although maybe not altogether surprising. The trans geometry of the double bonds is likely to decrease the reactivity,[124] the difficulties in using a solid reagent and the highly conjugated nature of the diene only add to the problems.

The lack of reactivity of 3,3-dimethyl-1,5-diphenyl-1,4-pentadiene (216) was more disappointing, particularly since the (Z,Z) isomer also proved to be unreactive. Neat reactions of the diene may prove to be more successful but to date, these have not been investigated.

The lack of conclusive results from the work on hydrosilylation led to the investigation of the other potential route for the synthesis of silacycles, which is described in chapter 5.

PART C : The Synthesis of Silacycles

Chapter 5

Silacycles : Hydroboration of Divinylsilanes

5.1 Introduction

The second potential route to silacycles, outlined in chapter 3, is the functionalisation of divinylsilanes, scheme 5.1.
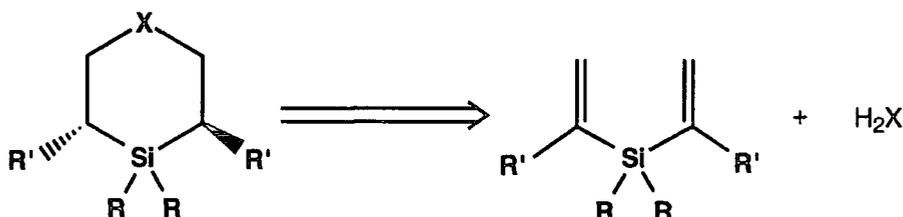
Scheme 5.1

This route is potentially more versatile since it allows the easier introduction of other heteroatoms into the ring. The functionalisation of divinylsilanes has been used in the synthesis of two different silacycles, figure 5.1. The synthesis[104] of the silaazacycle (169) has been discussed in chapter 3 (section 3.4.iv), the silacyclohexanone (202), which was briefly discussed in chapter 3, will be considered in more detail in this chapter.
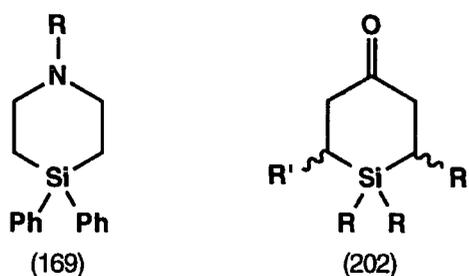
Figure 5.1

5.2 Hydroboration in the Synthesis of Silacycles

Soderquist and Brown have shown[125] that the hydroboration of alkenylsilanes could be used for the preparation of functionalised organosilanes.

Soderquist and his co-workers have gone on to demonstrate[105,106,107] the use of the hydroboration reaction in the functionalisation and subsequent cyclisation of divinylsilanes, scheme 5.2.
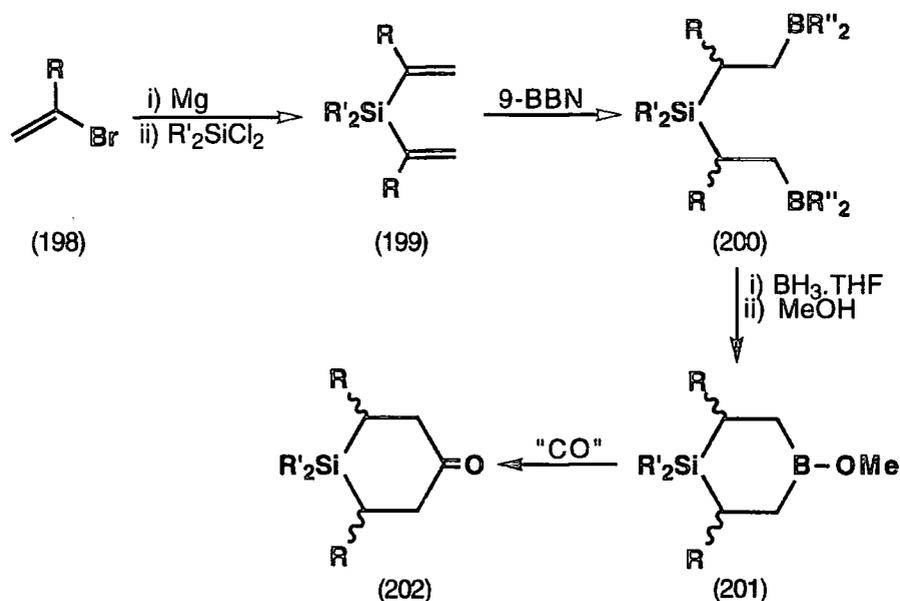
Scheme 5.2

The cyclisation step involves the use of the boron redistribution reaction, which will be discussed in section 5.6.ii.

There have been no attempts to introduce any stereoselectivity into these reactions although Soderquist has noted diastereoselectivity in the hydroboration with 9-BBN, scheme 5.3. It is claimed that when the standard synthetic sequence is employed, total selectivity is seen after cyclisation and only the cis-substituted isomer (221) is found. Since this configuration allows both phenyl groups to be positioned in an equatorial environment, this is not an unlikely outcome.
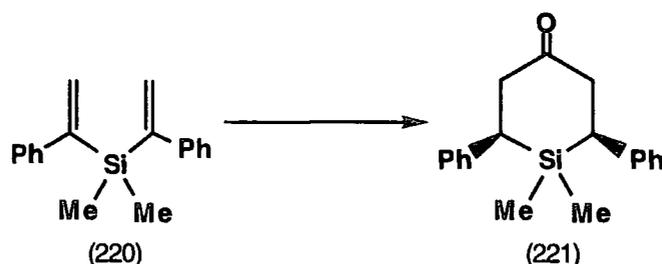
Scheme 5.3

The configuration, figure 5.2, of this compound has been confirmed by crystal structure analysis.[126] When diisopropenyldimethylsilane is used as the starting material, the

diastereomeric excess is reduced to approximately 10% with the *cis* isomer remaining in the majority.

(221)
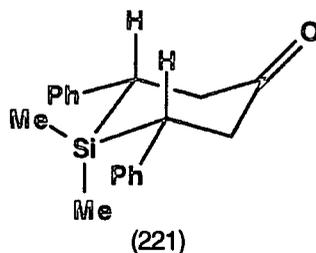
Figure 5.2

It was felt that this methodology could provide a versatile route for the formation of enantiomerically pure silacycles. Asymmetric hydroboration could introduce the required enantioselectivity and it was then hoped that the boron redistribution procedure would lead ultimately to *trans* substituted silacyclohexanones. Furthermore, oxidation of the borane intermediates would lead to a dihydroxy substituted silane and hence, provide a route to further silacycles, scheme 5.4.
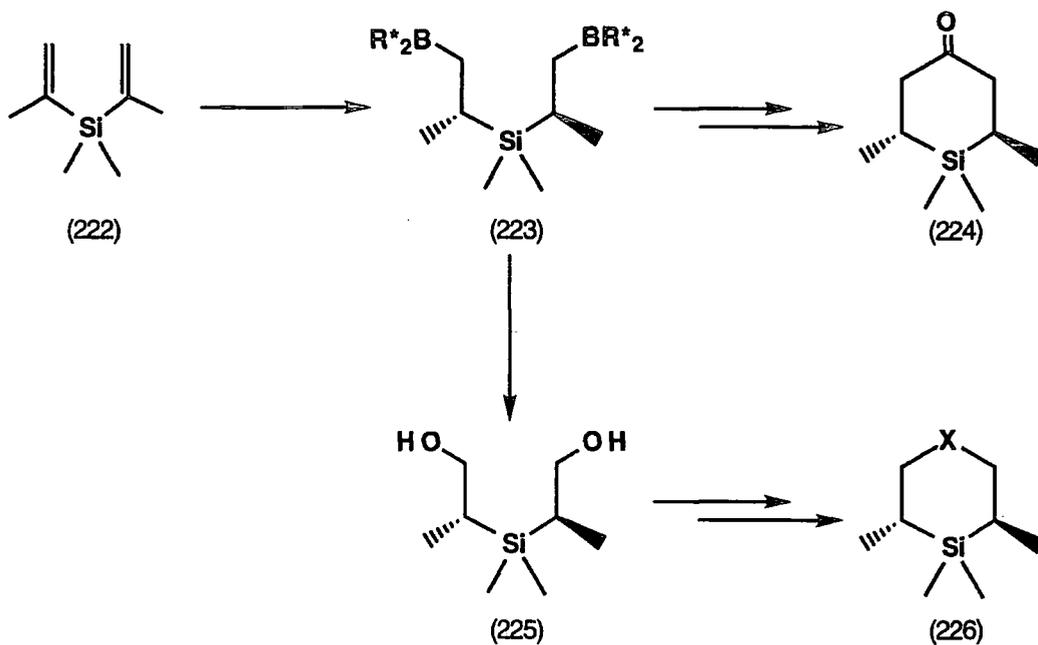
Scheme 5.4

5.3 Synthesis of Divinylsilanes

Soderquist and co-workers have used[105] the reaction of Grignard reagents with dichlorodimethylsilane to produce the required divinylsilanes. This approach was used to produce the variety of divinylsilanes used in this work, scheme 5.5.

(222) R, R'= Me, 81%
(220) R=Me, R'=Ph, 84%
(227) R=Ph, R'=Me, 41%
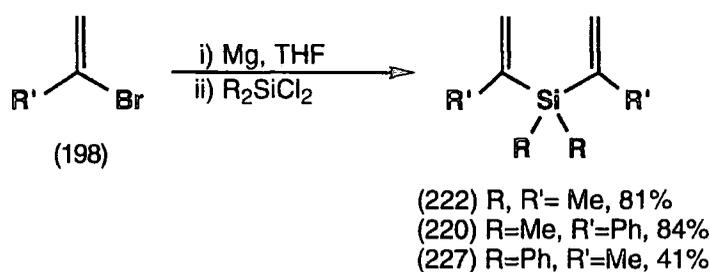
Scheme 5.5

The lower reactivity of dichlorodiphenylsilane, due to steric hindrance, causes some problems not found in the use of dichlorodimethylsilane. The formation of the required product is accompanied by the formation of separable, unidentifiable side products, this results in the lower yield of diisopropenyldiphenylsilane (227). In all cases, mass spectra showed the characteristically small peaks associated with M$^+$ for tetrasubstitutedsilanes and the more intense (M-CH$_3$)$^+$ or (M-Ph)$^+$ peaks resulting from the facile cleavage of an Si-C bond.

α-Bromostyrene is only commercially available at 85% purity and this causes the formation of some unidentifiable impurities during the synthesis of di(α-styryl)dimethylsilane (220), which can be separated only at a later stage in the synthetic sequence. This could be overcome by synthesising α-bromostyrene from styrene and bromine with subsequent elimination of HBr. This process, which was used by Soderquist and co-workers,[105] results in the formation of the pure α-isomer and hence, overcomes problems of impurities. This reaction has now been attempted within the group and does result in high yields of α-bromostyrene in high purity.

Since 2-bromopropene and α-bromostyrene are the only commercially available 2-bromoalkenes, it is an attractive idea to develop an alternative, more versatile route. Bond and co-workers have developed[127] the chemistry of triisopropylsulfonyl hydrazones (229) to allow the preparation of vinylsilanes via a lithiated intermediate (230). Unfortunately, due to time

constraints, this route has not been fully developed but it remains a more attractive synthetic sequence since any methyl ketone can be used as the precursor, scheme 5.6.
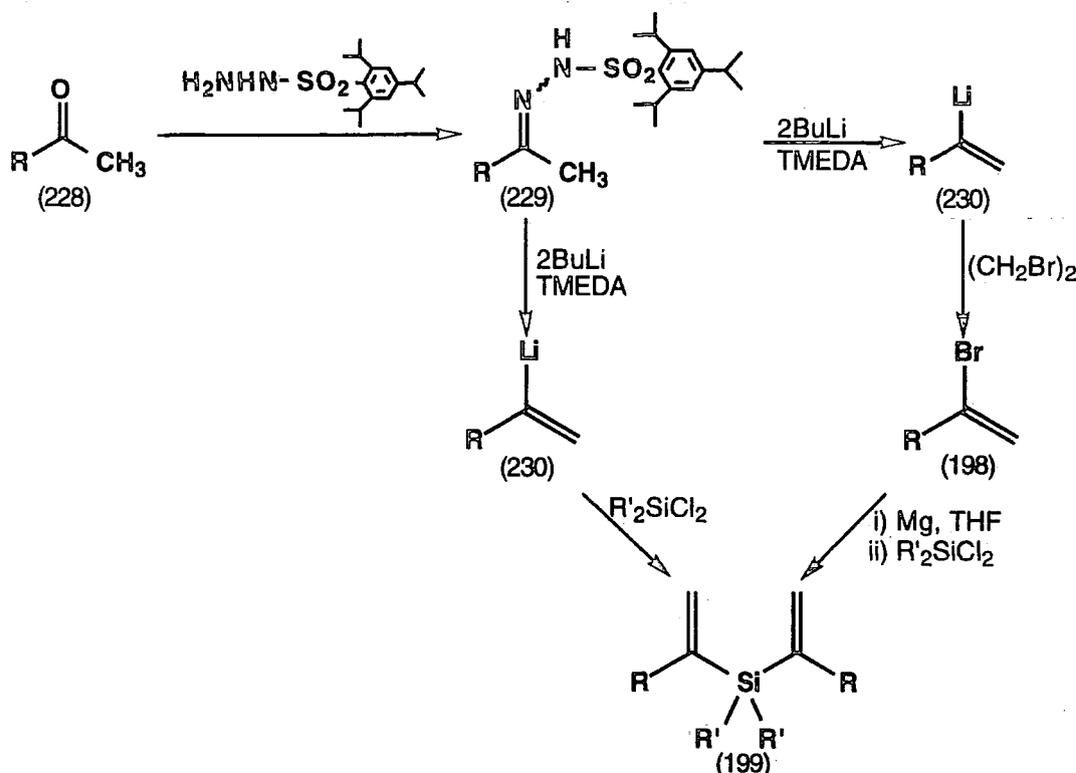
Scheme 5.6

5.4 Asymmetric Stoichiometric Hydroboration

5.4.i Asymmetric Stoichiometric Hydroborating Reagents

The use of chiral hydroborating reagents to induce asymmetry during the reaction is a well-established process.[128]

Several hydroborating reagents derived from terpenes have been synthesised and have been shown to be very useful for the asymmetric hydroboration for some types of alkene. Particularly noteworthy is diisopinocampheylborane, Ipc_2BH (231), figure 5.3, which is readily synthesised[129] from α-pinene. Equilibration of the reagent formed initially with excess α-pinene means that a reagent of >98%ee can be prepared from α-pinene of approximately 90%ee.

(-)-Ipc₂BH
(231)

trans -2,5-dimethylborolane
(232)
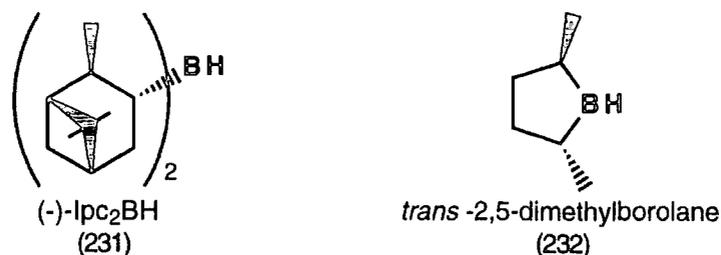
Figure 5.3

Dimethylborolane (232), figure 5.3, has become an increasingly versatile reagent and the resulting products of olefin hydroboration tend to exhibit high values of ee, table 5.1. However, since the preparation of asymmetric hydroborating agents derived from α-pinene remains the simpler procedure, these reagents are still well used.

		Enantiomeric Excess (%) of alcohol obtained from hydroboration and oxidation		
	Class	Ipc₂BH	IpcBH₂	Dimethylborolane
	I	30	1.5	1.4
	II	98.4	24	95.2
	III	13	73	97
	IV	14	53	94.2

Table 5.1

Olefins of class I are the most interesting with respect to this work, since their substitution pattern matches that of the divinylsilanes involved. Unfortunately, this is the one class of olefin where products of high ee have not been obtained. The reagent that gives the best results is diisopinocampheylborane (231) and since the preparation of this reagent is simple, this seems the best reagent to use initially.

5.4.ii Asymmetric Stoichiometric Hydroboration of Divinylsilanes

Since the ee values resulting from the hydroboration of 1,1-disubstituted olefins are low, it was initially felt that the ee value resulting from the hydroboration of the divinylsilanes

should be determined in order to ensure this was a viable way of introducing asymmetry into the synthetic route towards enantiomerically pure silacycles.

The hydroboration of diisopropenyldimethylsilane (222) was followed by oxidation to yield the dihydroxy species (233), scheme 5.7.
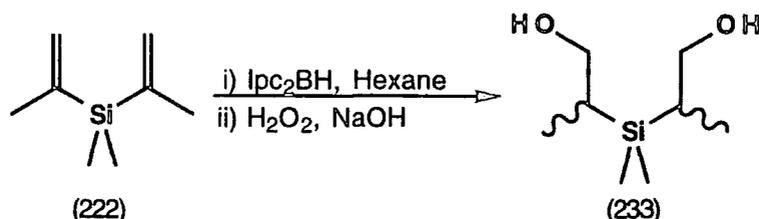
Scheme 5.7

It was hoped that purification to remove the oxidised chiral auxiliary followed by analysis by chiral shift NMR would give the value of enantiomeric excess (ee). Hydroboration and oxidation proceeded smoothly to afford the product mixed with 4 equivalents of isopinocampheol. The ^{1}H NMR spectrum clearly showed the loss of all signals attributable to the olefinic protons. However, subsequent purification by chromatography on silica failed to yield any of the required product and attempted distillation failed to separate the product from the oxidised chiral auxiliary. Silica gel appears to catalyse the decomposition of this β-hydroxysilane derivative, presumably via a Peterson olefination type process. In order to allow purification, it was necessary to esterify the crude mixture, scheme 5.8. Subsequent flash column chromatography allowed facile separation from the esterified chiral auxiliary. The overall yield of the diester (234) based on divinylsilane (222) was 63%. The bromobenzoate derivatives proved to be particularly useful since they allowed clear peak separation in chiral shift NMR studies, see later.
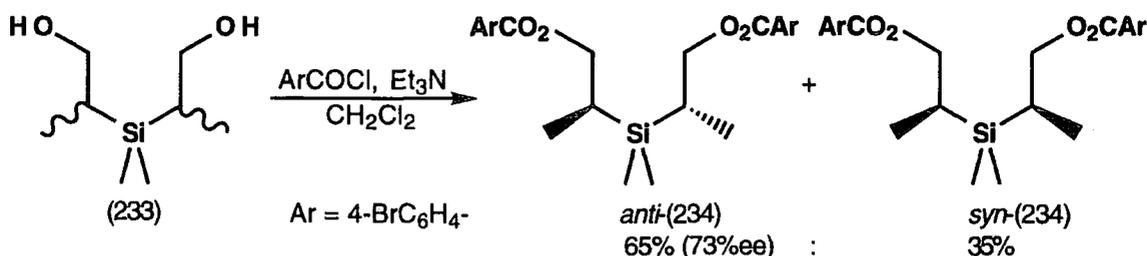
Scheme 5.8

Chiral shift ^{1}H NMR studies using Pr(hfc)$_3$ gave the required information. This reagent shifts peaks to lower frequency and hence, the Si-Me peaks can be seen without interference

from any other peaks in the spectrum. The common observation that far less Pr(hfc)$_3$ was needed than Eu(hfc)$_3$ was also found for these compounds. Eu(hfc)$_3$ is a reagent that shifts peaks to higher frequency and is far more widely used.[130] It seems that the advantages of praseodymium derivatives could be exploited far more than they are at present. The diester (234) was subjected to chiral shift ^{1}H NMR analysis which showed that the diastereomeric excess (de) was 31% in favour of the anti isomer and the enantiomeric excess (ee) of the anti isomer[131] was 73%. Interestingly, in the hydroboration with 9-BBN, a small diastereoselectivity (9%) was also observed. This result does imply that the first hydroboration has some effect on the second.

The success with diisopropenyldimethylsilane led to studies on di(α-styryl)dimethylsilane (220), scheme 5.9. These reactions were performed in the same manner as for diisopropenyldimethylsilane (222). Hydroboration with 9-BBN gave a de value of 16% and the hydroboration with Ipc$_2$BH also proved to be a more selective procedure than that of diisopropenyldimethylsilane, giving a de value of 54% and an ee value of 79%. Furthermore, the diester (235) derived from the hydroboration sequence using Ipc$_2$BH could be recrystallised to give an increase in both diastereomeric and enantiomeric excess (for example, one recrystallisation from hexane resulted in de=92% and ee=91%), implying that enantiomeric purity could be obtained at this point in the synthesis.

i) Ipc$_2$BH, hexane
ii) H$_2$O$_2$, NaOH
iii) ArCOCl, Et$_3$N, CH$_2$Cl$_2$, 53%

(220)   Ar = 4-BrC$_6$H$_4$-

anti-(235)
77% (79%ee) :

syn-(235)
23%
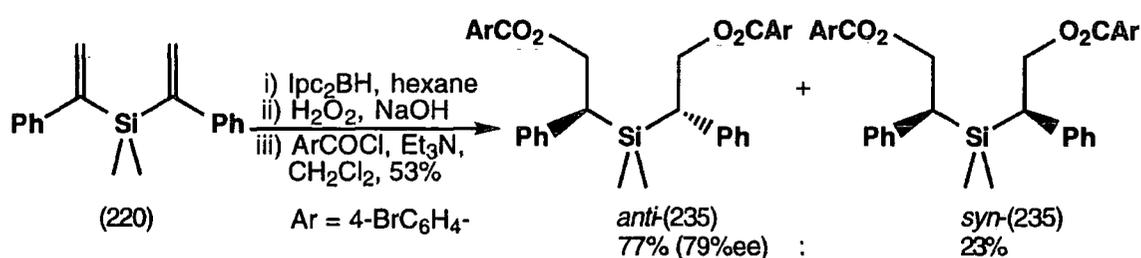
Scheme 5.9

The hydroboration of diisopropenyldiphenylsilane (227) was also attempted with Ipc$_2$BH, scheme 5.10.
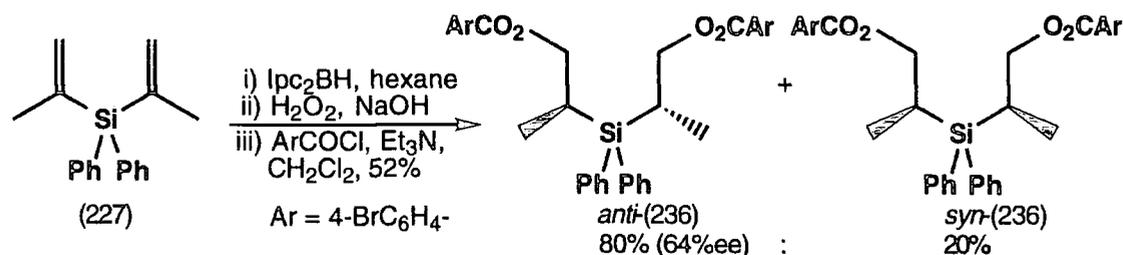
Scheme 5.10

This reaction is complicated by the oxidative cleavage of the Si-Ph bond producing inseparable by-products. This Tamao-like oxidation process was not unexpected since the reagents used for the oxidation, H_2O_2 and NaOH, can also be used in procedures for the oxidative cleavage of Si-C bonds.[76] There are, however, other reagents that can be used, such as H_2O_2 in aqueous buffer solutions at pH7,[132] sodium perborate[133] or sodium percarbonate.[134] The oxidation of Si-C bonds requires harsh highly alkaline conditions and hence, these reactions, which are much milder, should suppress the cleavage of Si-Ph bonds. Lack of time has prevented further study of the asymmetric hydroboration of diisopropenyldiphenylsilane (227) and possible oxidation procedures.

Due to the inseparable side products, determination of the diastereoselectivity and enantioselectivity of this reaction has been difficult. Chiral HPLC suggests a de of 60% and an ee of 64%. Chiral shift ^{1}H NMR cannot be used as before since this compound does not contain Si-CH$_3$ groups and the signal attributable to the SiCH is a highly complex multiplet. In an attempt to devise a simple way to obtain the ee and de for reactions of diisopropenyldiphenylsilane, the use of both ^{13}C and ^{29}Si NMR has been considered. For these reagents, ^{29}Si NMR seemed the obvious choice. Previous experiments had shown that the two diastereomers of 1,5-di(4'-bromobenzoyloxy)-2,3,3,4-tetramethyl-3-silapentane (234) gave separate signals and so these NMR experiments were repeated in the presence of Pr(hfc)$_3$. The spectra did give 3 peaks assignable to the (R,R), (S,S) and (R,S) isomers, although the isomeric ratios were not agreeable with previous results from ^{1}H NMR and HPLC, figure 5.4. It was found that increasing the relaxation delay used in the acquisition of these spectra dramatically altered the values of integration. Increasing the relaxation delay up to 60 minutes still failed to give integrals that gave isomer ratios in agreement with values from HPLC.
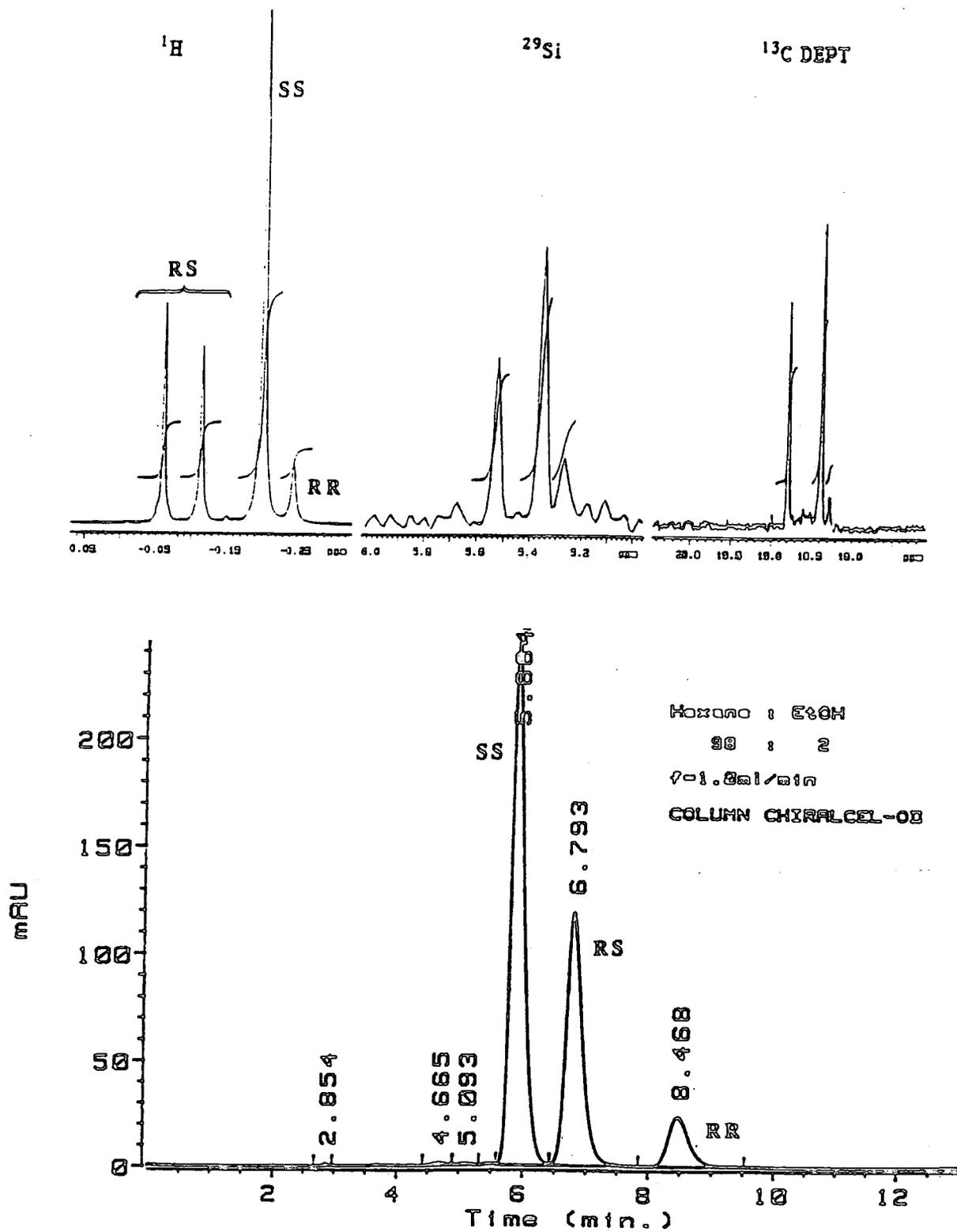
Figure 5.4

Organosilicon compounds are well-known to have very slow rates of relaxation[135] and in this case, the rates of relaxation of the 3 isomers were dramatically different and even very long relaxation delay values were not long enough to allow complete relaxation of all isomers. The long relaxation delay times together with the low natural abundance of ^{29}Si (4.7%) imply that acquisition of these spectra is not practicable. With this problem in mind, the ^{13}C spectra were investigated. The signal associated with the CH adjacent to silicon would split sufficiently to give isomer ratios, however, relaxation rates were still too slow to allow suitable spectra to be collected in a reasonable length of time. Eventually, it was found that a ^{13}C DEPT spectrum would give the correct isomer ratios. This is because the acquisition of DEPT spectra rely on the relaxation rates of the protons attached to the carbon and since the $^1J_{HC}$ value is the same for all isomers (120Hz), the amount of polarisation transfer is identical. The necessary data could be collected using a relaxation delay of 30 seconds, allowing spectra to be obtained in a reasonable length of time. The application of this technique to the other compounds is currently being evaluated, it is hoped that it will provide a reliable second method of determining isomeric ratios of all the Si-Ph substituted compounds that will result from this work.

5.5 Asymmetric Catalytic Hydroboration

5.5.i Introduction

The discovery that asymmetric hydroboration can be catalysed by the use of chiral transition metal complexes is relatively recent.[136] This area has, however, seen very rapid growth and high ee values have been achieved.

Procedures for catalytic hydroboration use catecholborane as the hydroborating reagent. Since the auxiliary derived from oxidation, catechol, is soluble in aqueous base, this procedure is particularly attractive for the hydroboration of divinylsilane, as the direct purification of the dihydroxy substituted silane should be possible. The next section describes work related to the asymmetric hydroboration of olefins and dienes and the catalysts that are normally employed.

5.5.ii Asymmetric Catalysts for Hydroboration

Initial studies on catalytic hydroboration used rhodium complexes and these remain the most highly used.[137] However, complexes based on a variety of transition metals have been successfully used for the promotion of hydroboration.[138]

The enantioselectivity is derived from the use of chiral phosphine ligands. Unlike the hydrosilylation process, chelating diphosphines, figure 5.5, have been found to be the most useful.

(R,R)-DIOP
(237)

(S)-BINAP
(238)

(S,R)-BPPFA
(239)

(S,S)-BDPP
(240)

(S,S)-DIPAMP
(241)

(R,R)-CHIRAPHOS
(242)
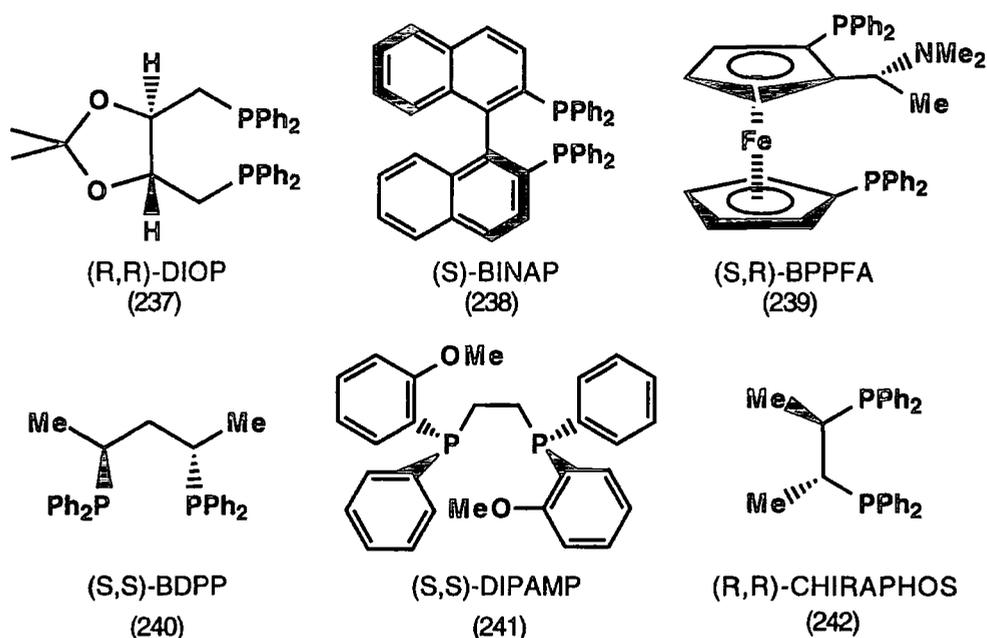
Figure 5.5

Of particular interest is the catalytic hydroboration of 1,1-disubstituted olefins. Stoichiometric asymmetric hydroboration generally fails to give products of high ee whereas the catalytic process can achieve[139] more acceptable results, scheme 5.11.

i) 1 mol% [Rh(COD)Cl]₂, 2 (R,R)-DIOP
THF, Catecholborane
ii) H₂O₂, NaOH

(243)

(244)
(69%ee)
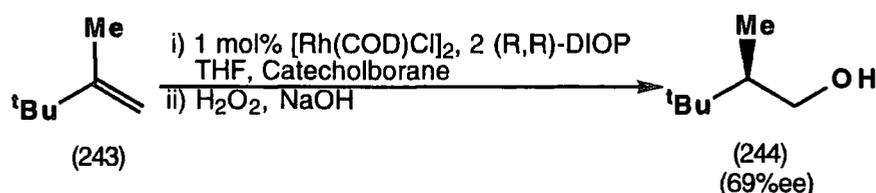
Scheme 5.11

The mechanism of this catalytic hydroboration process has not been conclusively proved. Männig and Nöth have proposed[140] the most generally accepted mechanism, scheme 5.12. The possibility of an "olefin first" mechanism cannot be completely discounted and this remains a subject of considerable debate.[141]
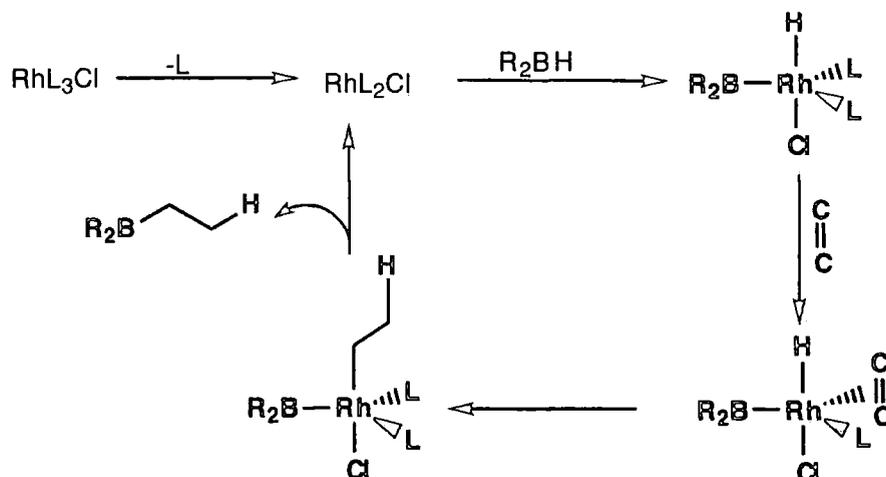
Scheme 5.12

There has been only one report on the double catalytic asymmetric hydroboration of dienes. Matsumoto and Hayashi have studied[142] the hydroboration of 1-phenyl-1,3-butadiene (211), 1,3-decadiene and 1-vinylcycloheptene. Reactions of 1,3-decadiene and 1-vinylcycloheptene gave only terminal allylic and homoallylic alcohols, double hydroboration was only seen in the reactions of 1-phenyl-1,3-butadiene (211) and the products isolated were found to be very dependent upon the phosphine used. Their initial achiral studies showed that with the catalytic system [Rh(COD)$_2$]ClO$_4$/2PPh$_3$, 1-phenyl-1,3-butanediol (245) was obtained in 65% yield with an *anti:syn* ratio of 10:1. However, if one equivalent of dppe was used in place of triphenylphosphine, no diol was formed and instead, a mixture of 4-phenyl-3-butenol (246) and 4-phenyl-2-butenol (247) was formed, scheme 5.13.

[PPh$_3$] = i) [Rh(COD)$_2$]ClO$_4$/2PPh$_3$, R$_2$BH; ii) H$_2$O$_2$, NaOH
[dppe] = i) [Rh(COD)$_2$]ClO$_4$/ dppe, R$_2$BH; ii) H$_2$O$_2$, NaOH
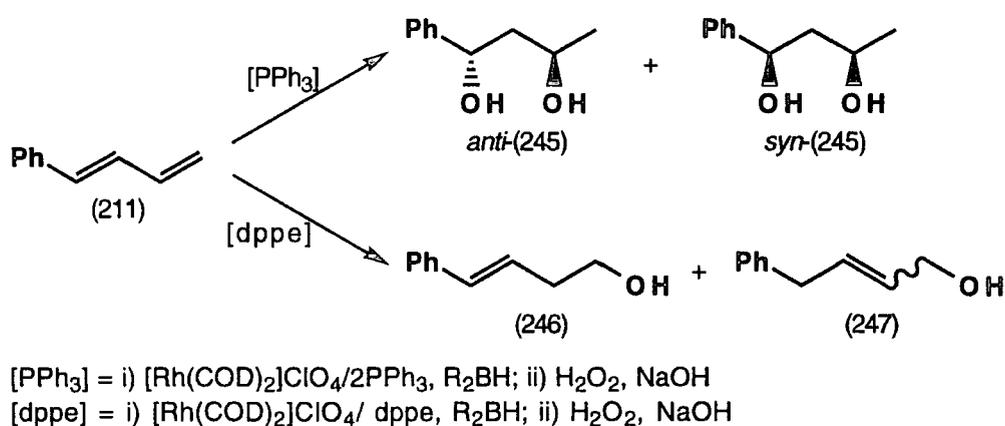
Scheme 5.13

An investigation into the catalytic system derived from [Rh(COD)$_2$]ClO$_4$ with (R)-BINAP at 0°C gave, after oxidation, 1-phenyl-1,3-butanediol in 77% yield with a 3:1 *anti* :*syn* ratio.

Furthermore, the *anti* component had an ee value of 48% and the *syn* component an ee value

of 43%, scheme 5.14.

[BINAP] = i) [Rh(COD)$_2$]ClO$_4$ / (R)-BINAP, Catecholborane
         ii) H$_2$O$_2$, NaOH
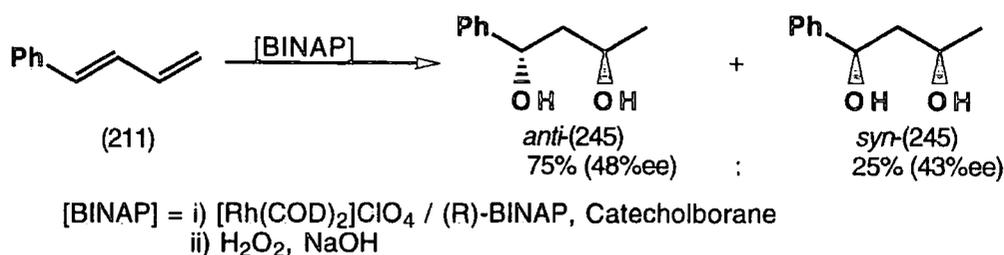
Scheme 5.14

Reduction in the reaction temperature (to -20°C) improved the ee value of the *anti* component

but this was accompanied by a considerable drop in yield. The preference for the *anti* isomer is

suggested to occur due to the catalytic cycle shown below, scheme 5.15.
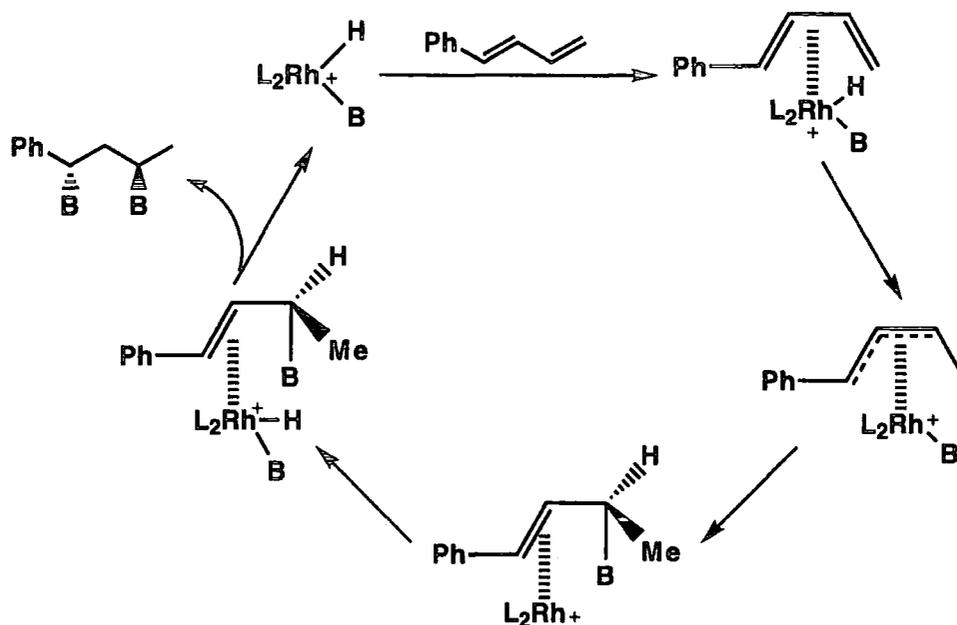
Scheme 5.15

Given the considerable advantages associated with catalytic hydroboration and the high

ee values obtained with 1,1-disubstituted olefins, it was decided to attempt the double

asymmetric catalytic hydroboration of divinylsilanes to give the precursors required for

potential enantiomerically pure silacycles.

5.5.iii Catalytic Hydroboration of Divinylsilanes

It was decided to initially attempt the double asymmetric hydroboration of diisopropenyldimethylsilane using the chiral phosphine (S,S)-DIOP with [Rh(COD)Cl]$_2$ following the procedure used by Burgess and Ohlmeyer.[139] After oxidation, the silyldiol could be isolated in reasonable purity and ^{1}H NMR showed the loss of all signals attributable to olefinic protons. To allow the stereoselectivity of the reaction to be determined, the crude silyldiol was esterified with 4-bromobenzoyl chloride to afford the silyldiester (234) in 67% yield, scheme 5.16.

(222)   Ar = 4-BrC$_6$H$_4$-   anti-(234)   syn-(234)
                                 13% (0%ee) : 87%

i) [Rh(COD)Cl]$_2$/ DIOP, Catecholborane, THF, -25°C, 5 days
ii) H$_2$O$_2$, NaOH
iii) ArCOCl, Et$_3$N, CH$_2$Cl$_2$
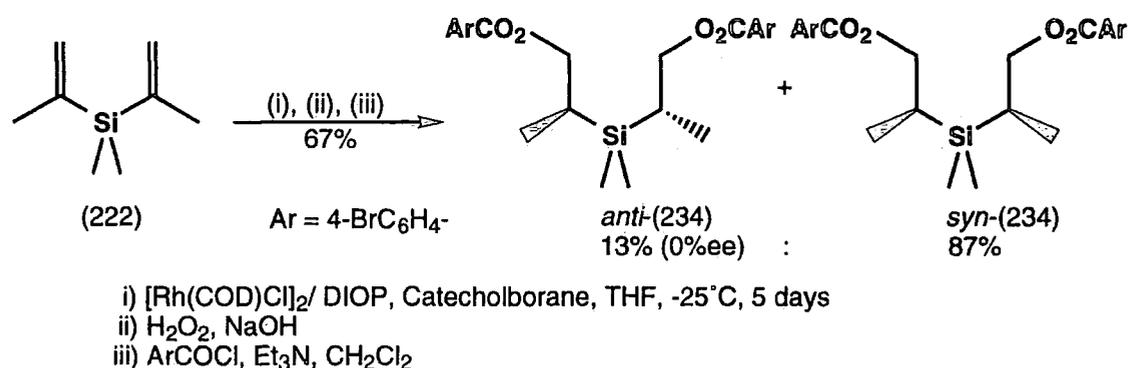
Scheme 5.16

Subsequent chiral shift ^{1}H NMR studies showed that although the reaction was highly diastereoselective, the *syn* isomer was formed predominantly (91.5:8.5). Furthermore, the *anti* component was racemic. This rather unexpected result led to the hypothesis that the diastereoselectivity was controlled by the length of the phosphine tether. To test this hypothesis the reaction using the equivalent achiral phosphine diphenylphosphinobutane (dppb) was attempted, under identical conditions to the DIOP reaction. Chiral shift NMR showed that the diastereoselectivity of this reaction was the same as the DIOP case. Since the length of the carbon chain between the two phosphorus atoms is equivalent in dppb and DIOP, this result suggested that the diastereoselectivity was indeed controlled either by the length of the tether between phosphines or the related chelate bite angle. Consequently, a range of diphosphine ligands were studied under identical reaction conditions, to see how the diastereoselectivty was affected by changes in tether length and bite angle. The results of this study are shown below, table 5.2.

Phosphine	Solvent	Yield	Product Ratio syn : anti
Ph₂P(CH₂)₅PPh₂	THF	35%	48 : 52
(-)-DIOP	THF	67%	87 : 13
(-)-DIOP	Toluene	64%	90.2 : 9.8
Ph₂P(CH₂)₄PPh₂	THF	45%	91.5 : 8.5
Ph₂P(CH₂)₃PPh₂	THF	55%	80 : 20
CH₃C(CH₂PPh₂)₃	THF	37%	82 : 18
Ph₂P(CH₂)₂PPh₂	THF: CH₂Cl₂	14%	65 : 35
Ph₂PCH₂PPh₂	THF	< 5%	62 : 38
PPh₃	THF	42%	54 : 46
(+)-NMDPP	THF	75%	53 : 47

Table 5.2

The highest diastereoselectivity is seen when DIOP or dppb are used and as the length of the tether is reduced the diastereoselectivity decreases. It can be suggested, that the change in diastereoselectivity arises through a rapid hydroboration of a *cis* linked diphosphine-divinylsilane rhodium complex (248). It is possible that with these substrates, the Männig-Nöth mechanism for catalysed hydroboration (see scheme 5.12) is preceeded by complexation of the diene. Hence, the observed product ratios can be related to the relative stability of the monodentate (249) and bidentate (250) divinylsilane complexes, scheme 5.17, which is controlled by the bite angle, θ, created by the diphosphine tether. With diisopropenyldimethylsilane (222), maximum stability of the diphosphine-divinylsilane rhodium complex (248) is achieved with a butano-tether.

In an attempt to increase the percentage of monodentate complex (249) present, the reactivity of a tripodal phosphine, TRIPHOS, was examined to see whether the third phosphine group was able to displace one arm of the silane. However, the ratio obtained was identical to that obtained with diphenylphosphinopropane (both ligands have three carbons between phosphorus atoms) and implies that TRIPHOS has one free phospine arm during the course of the reaction and hence behaves in a similar fashion to the bidentate ligands, this behaviour has been observed[143] in other cases.
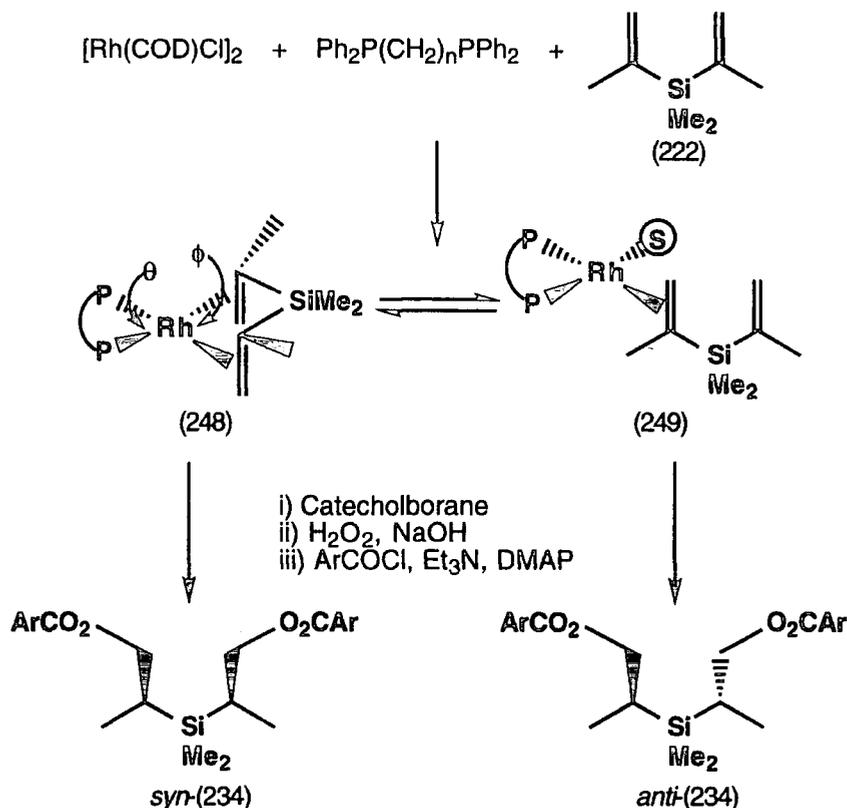
Scheme 5.17

The monodentate phosphines, PPh₃ and NMDPP, and diphenylphosphinopentane do not exhibit high diastereoselectivity. It seems likely that, with these phosphines, a mechanism similar to that described by Männig and Nöth is followed. With diphenylphosphinopentane, it is also possible that *trans* chelation[144] of the metal centre occurs which would inhibit the bidentate complexation of the divinylsilane. In either case, two discrete hydroboration steps would occur which would be consistent with the observed 1:1 ratio of *syn:anti* diastereomers.

In an attempt to confirm the reasons behind the unexpected diastereoselectivity, it was decided to undertake the preparation of some rhodium complexes that would be analogous to the complexes described above, scheme 5.17. It was hoped that a study of the ^{31}P NMR spectra of the resulting complexes would give some information about the ratio of the monodentate and the bidentate complexes present in solution. As [103]Rh is also an NMR-active nuclei, the monodentate complex should exhibit both RhP and PP coupling, whereas the bidentate complex is highly symmetrical and should only exhibit RhP coupling. Data of this kind has been used to identify the nature of intermediate rhodium complexes in asymmetric hydrogenation.[144]

Initially it was hoped that reaction of the bis-divinylsilane complex (251) by one of two possible routes would lead to the formation of the required diphosphine-divinylsilane complex (253), scheme 5.18. The bis-divinylsilane complex (251) was formed by the reaction of μ-dichlorotetraethylene dirhodium(I) with four equivalents of diisopropenyldimethylsilane (222). ^{13}C NMR showed 5 signals, with the two olefinic signals being shifted to lower frequency and showing coupling to rhodium (δ68.11, J_{RhC}=117Hz; δ65.16 J_{RhC}=10Hz) and one of the two signals attributable to Si-CH$_3$ being shifted to δ-5.43. However, it was found, by ^{31}P NMR, that subsequent reactions of this complex appeared to lead only to the bis-diphosphine compound (254).
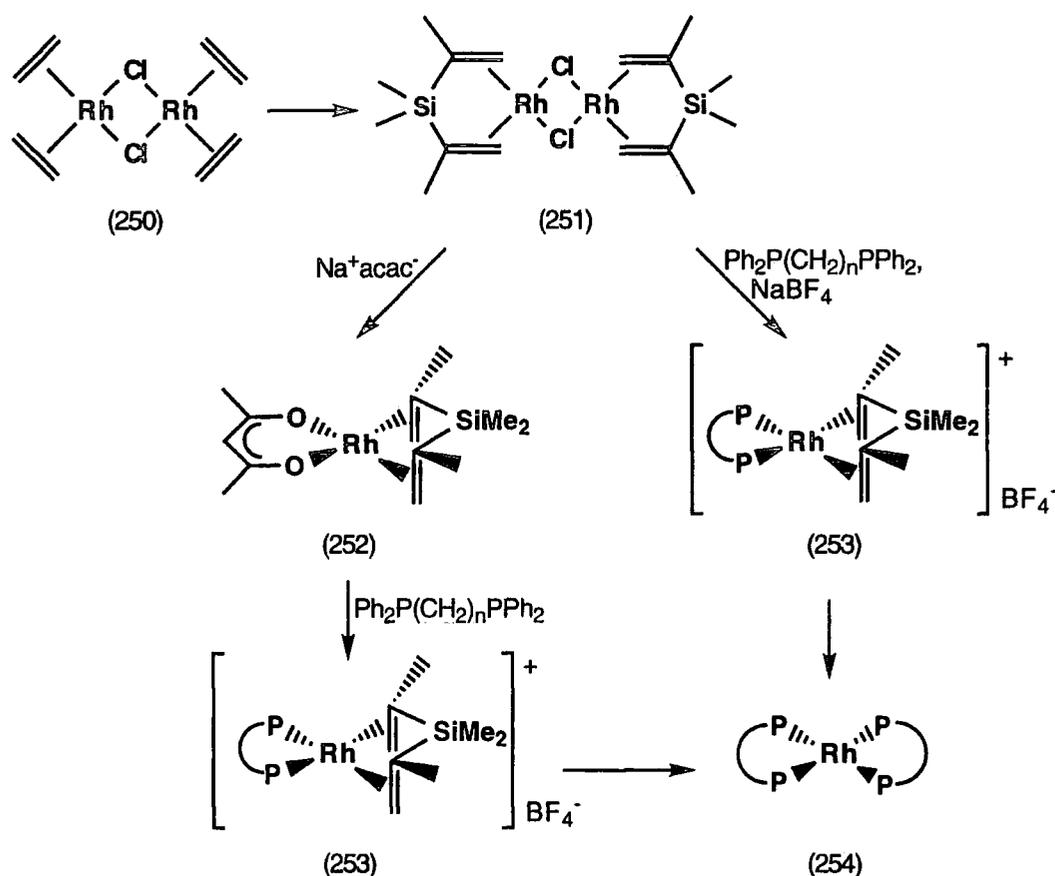
Scheme 5.18

It was eventually found that ^{31}P NMR studies were possible if the complexes were prepared *in situ* by the hydrogenation of a norbornadiene complex and subsequent addition of the divinylsilane, scheme 5.19.
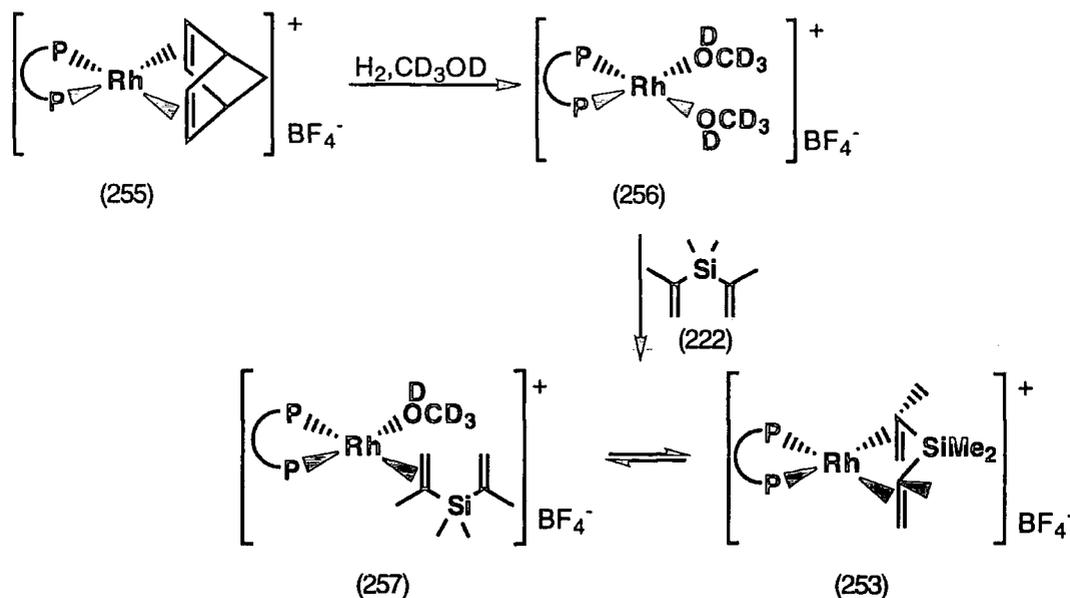
Scheme 5.19

The spectra obtained from these studies proved to be far more complex than originally envisaged. With dppb at -50°C, a doublet that can be assigned to the dimethanol solvate (^{31}P δ=56, J_{RhP}=199Hz) can be clearly seen even in the presence of a large excess of divinylsilane. The many other peaks present imply that there are more than just two species present. The values of phosphorus-phosphorus coupling constants (J_{PP}) are lower than those usually observed for square planar rhodium complexes and may imply that five or six coordinate species are present. Unfortunately, to date, it has proved impossible to gain further indications as to the nature of these complexes by ^{31}P NMR. Attempts to isolate the complexes have proved to be inconclusive and reactions performed in d_8-THF gave no further information. It is possible that the different types of rhodium complex (i.e. 4,5 and 6 coordinate species) will have dramatically different ^{103}Rh NMR spectra. This possibilty has not yet been investigated because of the many difficulties associated with acquisition of ^{103}Rh NMR spectra.

It is also possible that a study of monosubstituted divinylsilanes, scheme 5.20, would give further information since the hydroboration should now become highly enantioselective if the postulated mechanism is operating.
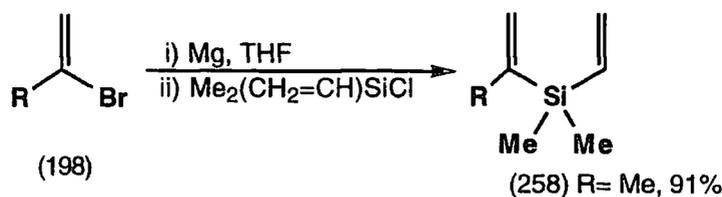
Scheme 5.20

The methyl substituted silane (258) has been studied using DIOP but the reaction was found not to be enantioselective, it is felt this may be due to the methyl group not being bulky enough to induce some enantioselectivity during hydroboration. It is hoped that, using the Shapiro-type chemistry discussed in section 5.3, divinylsilanes with a bulky substituent can be prepared and their catalytic hydroboration can be studied.

The lack of selectivity in the catalytic hydroboration of diisopropenyldimethylsilane is disappointing and means that, at present, this process cannot be used in the synthesis of C_2 symmetrical enantiomerically pure silacycles. However, if the hydroboration of monosubstituted divinylsilanes does prove to be enantioselective, it could provide a route to monosubstituted enantiomerically pure silacycles which may still be useful as chiral auxiliaries.

5.6 Silacycle Formation

5.6.i Introduction

As has been discussed in section 5.2, the hydroboration of divinylsilanes provides precursors for a variety of possible cyclisation procedures. This section will discuss work that has developed Soderquist's methodology for the formation of silacyclohexanones and then go on to discuss attempts to produce other silacycles by the cyclisation of the silyldiol derived from oxidation of the double hydroboration product.

5.6.ii Silacyclohexanone Formation *via* Boron Redistribution

Soderquist and co-workers have used the hydroboration of diisopropenyldimethylsilane (222), boron redistribution and subsequent carbonylation to produce 1,1,2,6-tetramethyl-1-silacyclohexan-4-one (224), see section 5.2. Redistribution reactions are well known and very common in boron chemistry,[145] the mechanism, however, remains uncertain. The postulated mechanism suggests the formation of a bridged transition state (259), scheme 5.21, however, although there has been some evidence to support this it remains inconclusive. The effects on asymmetric substrates have never been considered.

(259)
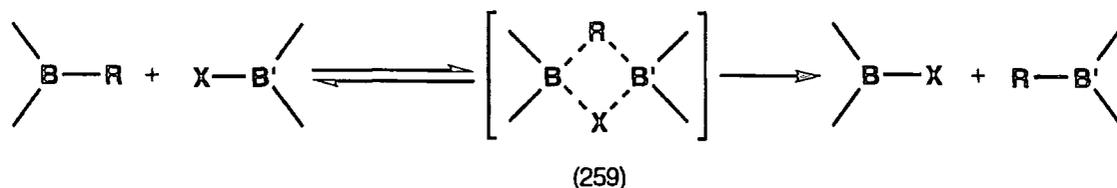
Scheme 5.21

This procedure can only be used for the synthesis of enantiomerically pure silacycles if the stereochemistry is retained during the redistribution step. In Soderquist's work, the boron redistribution process involves heating the product from double hydroboration with 9-BBN with $BH_3.THF$ to reflux. It seemed possible that the high temperatures induce retrohydroboration to reform the initial divinylsilane and this was followed by hydroboration with the less sterically demanding BH_3. If this was the case, all chirality induced in the hydroboration with Ipc_2BH would be lost and a completely racemic mixture would result.

To determine whether the stereochemistry was retained during this procedure, the formation of 1,1,2,6-tetramethyl-1-silacyclohexan-4-one (224) was repeated using the product (260) derived from hydroboration with Ipc_2BH, scheme 5.22.
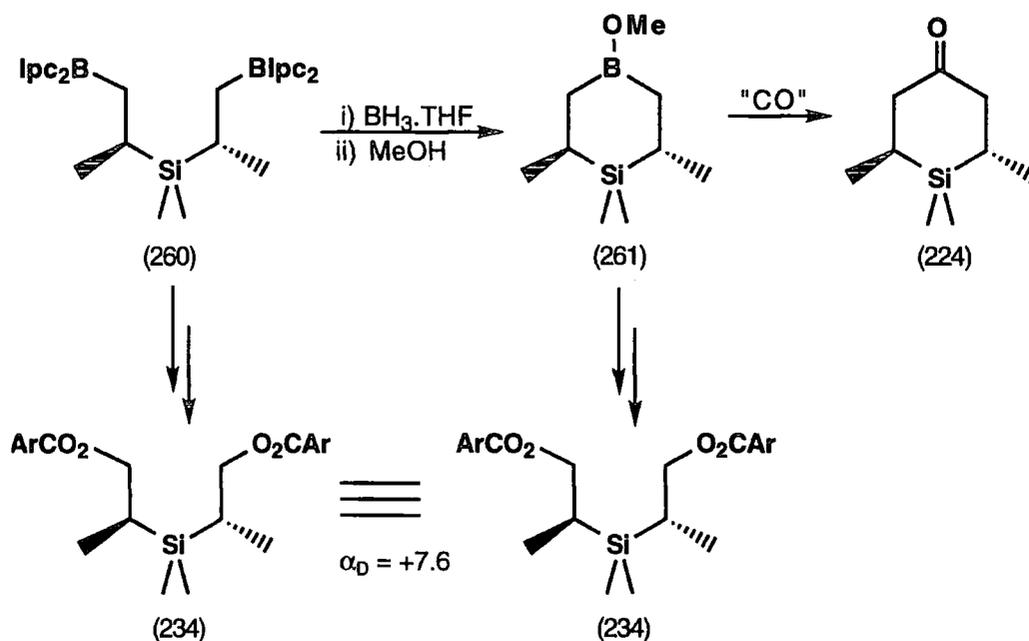
Scheme 5.22

Half of the product of hydroboration with Ipc_2BH was treated with $BH_3.THF$ and the completion of the redistribution reaction was confirmed by comparison of the ^{13}C NMR data for the Si-CH_3 signals with that given by Soderquist. Oxidation and subsequent esterification

yielded that dibromobenzoate ester (234), purification then allowed the measurement of the optical rotation value. This value was then compared to that for the diester derived from oxidation and esterification of the other half of the reaction mixture. The values were found to be identical, this implies that the stereochemistry at these centres is not affected by boron redistribution, which supports the postulated mechanism.

Further information about the redistribution mechanism could be gained by using a precursor which possesses a chiral centre α to boron. The silanes shown below, figure 5.6, could be used to give this information.

(262)   (263)
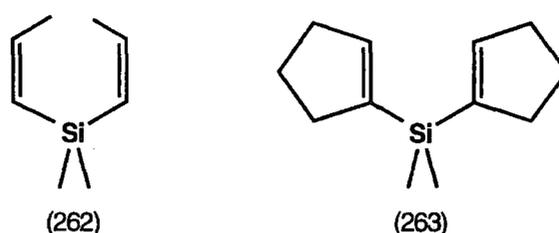
Figure 5.6

The synthesis of the terminal methyl subsitituted silane (262) via Grignard methodology is complicated by facile isomerisation of the double bond which produces a complex mixture of all possible isomers of the silane, it is possible that low temperature lithium-halogen exchange procedures could overcome this problem. It is envisaged that the cyclopentene substituted silane (263) can be synthesised from cyclopentanone using the Shapiro-type chemistry outlined in section 5.3. Lack of time has prevented the synthesis of these silanes and further study of the redistribution process.

The formation of 1,1-dimethyl-2,6-diphenyl-1-silacyclohexan-4-one (266) has also been attempted, scheme 5.33.

(264)   (265)   (266)
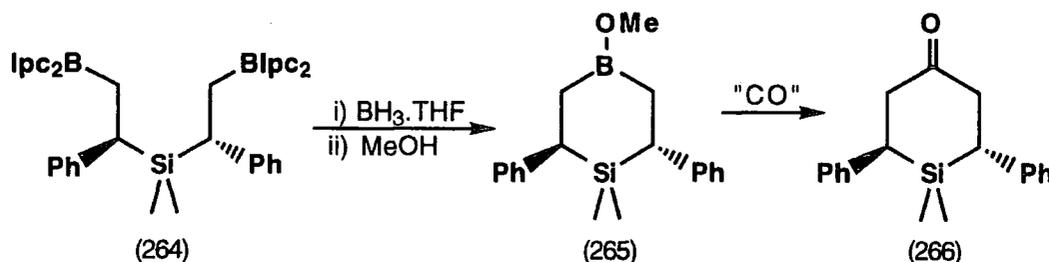
Scheme 5.33

As discussed in section 5.2, Soderquist has suggested that the hydroboration and cyclisation of dimethyldi(α-styryl)silane (220) leads only to the *cis* substituted silacyclohexanone (221). Following hydroboration of dimethyldi(α-styryl)silane with Ipc_2BH, Soderquist's procedure for redistribution was followed. Subsequent carbonylation using LiO^tBu and dichloromethyl methyl ether, in a procedure[146] analogous to that of Brown and co-workers, produced the silacyclohexanone (266) in 21% yield based on dimethyldi(α-styryl)silane. ^{13}C NMR confirmed the presence of the cyclohexanone product with a signal attributable to the ketone at $\delta212.58$. Furthermore, both ^{1}H and ^{13}C NMR suggested the presence of two isomers. Comparison of the ^{13}C spectra of the product to Soderquist's data[105] showed that the minor isomer present was the *cis* substituted silacyclohexanone (221) and the remaining peaks could be accounted for by the presence of the *trans* C_2 symmetric isomer (266). This is particularly well demonstrated by the ^{13}C signals associated with the $Si-CH_3$ carbons, the *cis* isomer (221) has two signals ($\delta= -5.89$, -10.00) and the *trans* isomer has only one ($\delta=-5.88$).

This work has established that the boron redistribution and subsequent cyclisation methodology can be used in the synthesis of *trans* substituted C_2 symmetric silacycles. Furthermore, it may be possible to produce other silacycles by manipulation of the carbonyl group, this possibilty remains to be investigated.

5.6.iii Formation of other Silaheterocycles

It is hoped, that further silacycles could be prepared by reactions of the silyldiol species derived from oxidation of the hydroboration product, see section 5.2. Since separation of the silyldiol and isopinocampheol has proved impossible, it was decided to use the silyldiol (225) derived from either a rhodium catalysed hydroboration procedure or from the hydrolysis of the dibromobenzoate ester (234) with LiOH in THF:water. Carlock and Mack have used[147] a mixture of diethyl azodicarboxylate (DEAD) and PPh_3 to cyclise α,ω-diols in the synthesis of a variety of oxygen containing heterocycles. To allow the reaction to be monitored by ^{1}H NMR, the diol (225) was dissolved in $CDCl_3$ and DEAD and PPh_3 were added simultaneously, scheme 5.34. ^{1}H NMR suggested that reaction had taken place but the signals due to the reaction by-products meant that the product could not be identified by the ^{1}H NMR.
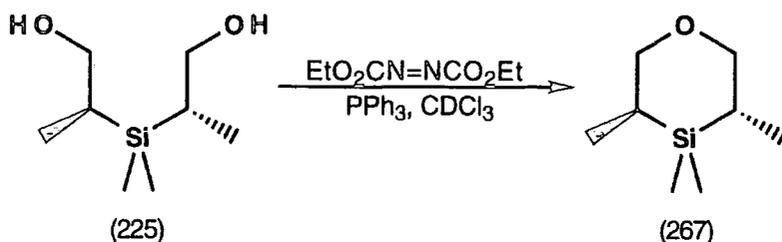
Scheme 5.34

All attempts to isolate the product of the reaction failed, it is felt that this is due to the likely high volatility of the oxasilacycle (267). Therefore, it was decided to use the diphenyl substituted diol for future studies.

Hydrolysis of the dibromobenzoate ester (235) with LiOH in THF:water failed to produce the silyldiol required for cyclisation studies, the only product isolated was styrene which presumably comes from the Peterson olefination reaction of the diol after hydrolysis. Several attempts to avoid this problem by changing the temperature and solvents of the reaction still failed to give the required product. In an attempt to overcome this problem, other ester derivatives were prepared, scheme 5.35.

(i) Ipc$_2$BH, Hexane; (ii) H$_2$O$_2$, NaOH
(268) iii) ClCH$_2$COCl, NEt$_3$, DMAP, CH$_2$Cl$_2$
(269) iii) (CH$_3$CO)$_2$O, pyridine, DMAP, CH$_2$Cl$_2$
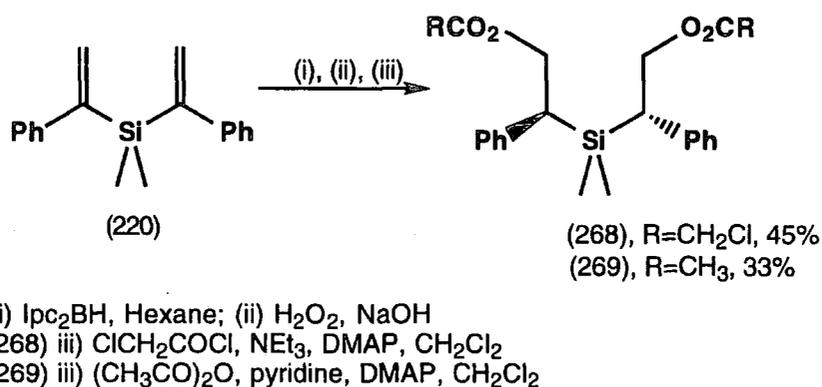
Scheme 5.35

Although these derivatives were easily prepared and purified by chromatography, attempts at hydrolysis still only yielded styrene. Attempted enzyme hydrolysis in pH7 buffer solution resulted in recovery of the starting material. It was eventually found that reduction of the diacetate derivative (269) with 4 equivalents of DIBAL-H, scheme 5.36, gave the silyl diol (270) in near quantitative yields and high purity. ^{1}H NMR indicated the complete loss of the acetate groups.
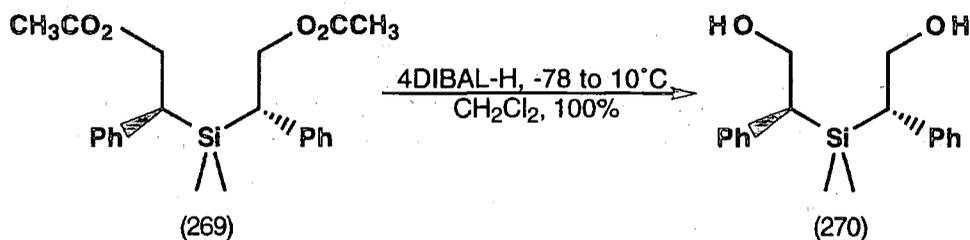
Scheme 5.36

The cyclisation reaction was then attempted, using the procedure described above, with this silyldiol (270) as the substrate. Addition of DEAD and PPh_3 to the diol in $CHCl_3$ led only to the isolation of styrene. It was eventually found that addition of the diol to a preformed DEAD/PPh_3 complex in benzene gave more promising results, scheme 5.37.
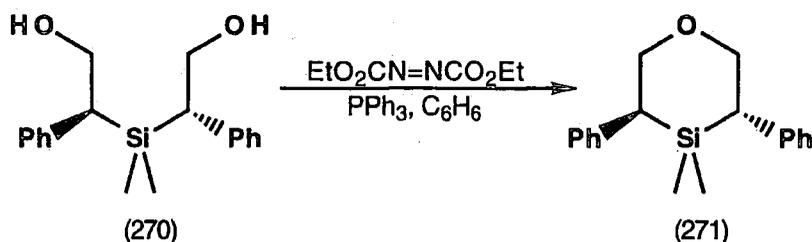
Scheme 5.37

Consideration of the Si-CH_3 signals in ^1H NMR suggests that the *syn* isomer cyclises preferentially, this is not unexpected since it would allow both phenyl substitutents to be placed in equatorial positions on the ring. As yet, it has proved impossible to isolate the oxasilacycle (271) but all indications suggest the presence of both *cis* and *trans* isomers of the cyclic product. It is hoped that altering the reaction conditions and purification procedures will allow the formation and purification of this silacycle. Lack of time has prevented further attempts at this reaction.

Falck and co-workers have shown[148] that the intramolecular condensation of α,ω-diols with bis(phenylsulfonyl)methane leads to bis-sulfone substituted carbocycles (273) in high yields, scheme 5.38.
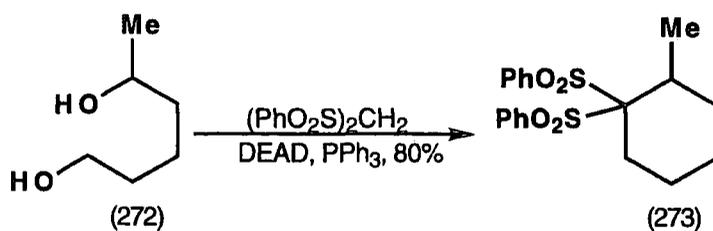
Scheme 5.38

It is possible that this type of procedure could lead to bis-sulfonyl substituted silacycles (274), scheme 5.39.
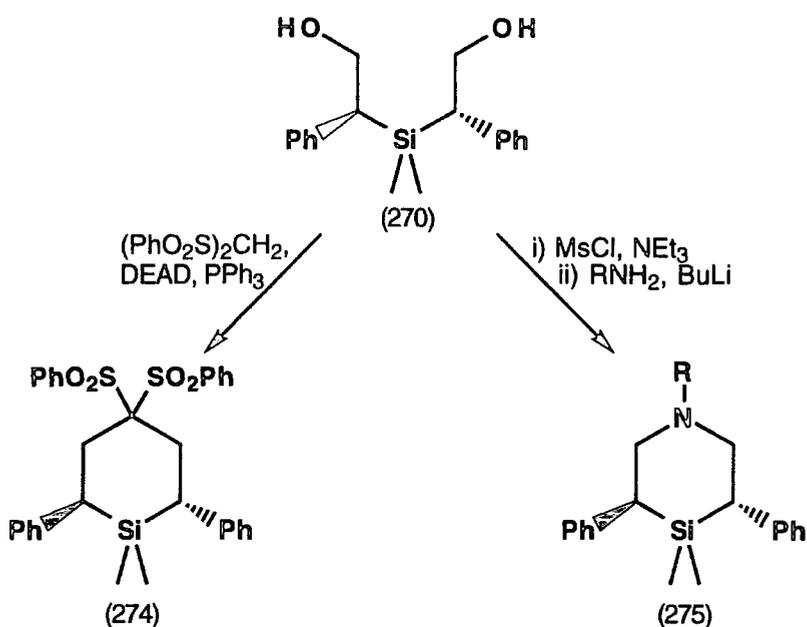
Scheme 5.39

The formation of silaazacycles (275) could also be possible by mesylation and subsequent substitution, the silacycles formed in this way have many similarities to the silaazacycles (169) discussed in section 3.4.iv and it would be interesting to investigate the possible biological activity of these molecules. Attempts at formation of these silacycles has not been investigated due to time constraints.

5.7 Conclusion

The hydroboration of divinylsilanes has produced a route to C_2 symmetric silacyclohexanones. Future work will hopefully develop the use of the boron-redistribution procedure to produce a wide range of asymmetric silacycles.

During the studies on asymmetric hydroboration, the unusual *syn* selectivity, which is dependant upon phosphine tether, has been found in the rhodium catalysed hydroboration reaction. It is hoped that further work on this process will lead to the formation of monosubstituted enantiomerically pure silacycles which may still be useful chiral auxiliaries.

The cyclisation reactions of the silyldiol have not been fully investigated but initial studies look promising. Hopefully, future work will show that the silyldiol is a useful intermediate in the production of a range of enantiomerically pure silacycles and go on to investigate the potential biological activity of these species and the applications of these silacycles in asymmetric synthesis.

PART D
EXPERIMENTAL DETAIL

Part D : Experimental

Chapter 6
Experimental Detail

6.1 Introduction

All reactions were carried out under an atmosphere of dry nitrogen or argon in pre-dried glassware.

Nuclear magnetic resonance (NMR) spectra were obtained on Varian Gemini 200 (^{1}H at 199.975 MHz, ^{13}C at 50.289 MHz), Varian XL-200 (^{1}H at 200.057 MHz), Bruker AC-250 (^{1}H at 250.133 MHz, ^{13}C at 62.257 MHz, ^{31}P at 101.256MHz), Varian VXR-400(S) (^{1}H at 399.952 MHz, ^{13}C at 100.577 MHz), and Bruker AMX-500 (^{1}H at 500.137 MHz, ^{13}C at 125.771 MHz and ^{29}Si at 99.4 MHz) spectrometers with deuterochloroform as solvent (residual $CHCl_3$: $\delta(^1H) = 7.26$, $\delta(^{13}C) = 77.0$) and are recorded in ppm (δ units). ^{29}Si spectra are referenced to an external standard of tetramethylsilane ($\delta=0$) in C_6D_6. ^{31}P spectra are referenced to an external standard of 85% H_3PO_4. Signal splitting patterns are described as singlet (s), doublet (d), triplet (t), quartet (q) or multiplet (m). Infra-red (IR) spectra were recorded on a Perkin Elmer FT-IR 1720X or 1600 spectrometer. Low resolution mass spectra were recorded on a VG Analytical 7070E Organic Mass Spectrometer, and gas chromatography-mass spectra (GC-MS) were recorded using a Hewlett Packard 5890 Series II gas chromatograph, equipped with a 25m SE30 column, connected to a VG Mass Lab Trio 1000. High resolution mass spectra were performed by the EPSRC service at the University of Swansea. Reactions were followed by gas chromatography (GC) using Hewlett Packard 5890A or 5890 Series II gas chromatographs or by thin-layer chromatography (tlc). Flash Column Chromatography was performed according to the method[149] of Still et al using silica gel, (60-240 mesh) or alumina (Merck. Art. 1097, activity II-III, 0.063-0.200mm). Melting points were determined using Gallenkamp melting point apparatus and are uncorrected.

All solvents were distilled prior to use. Petrol refers to the fraction of petroleum spirit boiling in the 30-60°C range unless otherwise stated. Ether refers to diethyl ether. Solvents were dried from the following agents under a nitrogen atmosphere : tetrahydrofuran and ether (sodium benzophenone ketyl); benzene, hexane and dichloromethane (calcium hydride); chloroform (phosphorus pentoxide); methanol (magnesium methoxide); ethanol (magnesium ethoxide). All other reagents were reagent grade and used as supplied unless otherwise stated.

Silylated Carius tubes were prepared by heating a Carius tube containing 3:1 pyridine: N,O-bis(trimethylsilyl)acetamide (BSA) at 65°C for 4 hours under an argon atmosphere. After cooling and washing with dry ether, the silylated tubes were stored in an oven until required.

6.2 Experimental Detail

Methyl hexa-2,4-dienoate (139)[150]
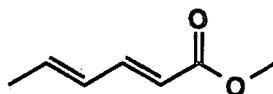
Hexa-2,4-dienoic acid (7g, 63mmol) was dissolved in ether (200ml). An ethereal solution of diazomethane was produced[151] by the addition of N-methyl-N-nitroso-p-toluenesulfonamide (27g, 126mmol) in ether (200ml) to a solution of potassium hydroxide (8g) in ethanol (40ml) and water (12ml) which was heated to 65°C. The solution of diazomethane was added to the acid solution until the yellow colour persisted, acetic acid was then added dropwise until the solution became colourless. Drying (MgSO$_4$) and concentration under reduced pressure yielded methyl hexa-2,4-dienote as a yellow liquid (7.9g, 99%). v$_{max}$ (Thin Film) 2998, 2951, 1720, 1646, 1618, 1436, 1378, 1332, 1266, 1194, 1143, 1000cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.21 (1H, dd, J=15.6, 10.0Hz, C$\underline{H}$=CH-CO$_2$Me), 6.12 (2H, m, H$_3$C-C$\underline{H}$=C$\underline{H}$-CH=), 5.73 (1H, d, J=15.6Hz, CH=C$\underline{H}$-CO$_2$Me), 3.69 (3H, s, OC$\underline{H}_3$), 1.81 (3H, d, J=5.6Hz, $\underline{H}_3$C-CH=CH-CH=); δ(^{13}C) (100MHz; CDCl$_3$) 167.61, 145.07, 139.29, 129.66, 118.44, 51.28, 18.49; MS (EI) m/z 126 (M$^+$, 46%), 111 (77), 95 (69), 67 (100).

Methyl hexa-3,5-dienoate (140a)[152]
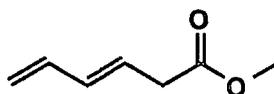
^{n}Butyllithium (13ml, 1.4M solution in hexane, 18mmol) was added dropwise to a solution of diisopropylamine (2.7ml, 20mmol) in dry THF (20ml) at -78°C. This was followed by the dropwise addition of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (3ml, 25mmol). The resulting solution was stirred for 15 minutes at -78°C. A solution of methyl hexa-2,4-dienoate (139) (1.50g, 12mmol) in dry THF (12 ml) was added dropwise at -78°C and the resulting mixture was stirred at -78°C for 4 hours. The reaction was quenched at -78°C with 25ml of 10% (v/v) acetic acid in 1:1 THF:water and then warmed in a warm water bath. THF was removed under reduced pressure and the remaining aqueous layer was extracted with ether (3x20ml). The organic layer was dried (MgSO$_4$) and solvent removed under reduced pressure. Flash column chromatography, eluting 9:1 petrol:ether, yielded methyl hexa-3,5-dienoate (1.25g, 84%) as a colourless liquid. v_{max} (Thin Film) 3022, 2953, 1741, 1654, 1603, 1436, 1407, 1344, 1263, 1173, 1005cm^{-1}; $\delta(^1H)$ (200MHz; CDCl$_3$) 6.30 (1H, ddd, J=16.8, 10.4, 10.4,Hz, H$_2$C=CH-CH=), 6.14 (1H, dd, J=15.2, 10.4Hz, H$_2$C=CH-CH=CH-), 5.78 (1H, m, H$_2$C=CH-CH=CH-), 5.16 (1H, d, J=16.8Hz, (Z)-HCH=CH-CH=), 5.06 (1H, d, J=10.4Hz, (E)-HCH=CH-CH=), 3.69 (3H, s, OCH$_3$), 3.12 (2H, d, J=7.2Hz, =CHCH$_2$CO$_2$Me); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 171.85, 136.28, 134.38, 125.46, 116.98, 51.85, 37.72; MS (EI) m/z 127 (MH$^+$, 37%), 126 (M$^+$, 9), 95 (23), 85 (100), 67 (48), 59 (58).

Hexa-3,5-dienol (141a)[153]
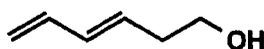
Lithium aluminium hydride (19mg, 0.5mmol) was suspended in dry ether (5ml) and cooled to 0°C. Methyl hexa-3,5-dienoate (140a) (40mg, 0.5mmol) was added dropwise as a solution in dry ether (3ml) and the resulting mixture was stirred at room temperature for 2 hours. After cooling to 0°C, water (0.02ml), 15% NaOH (0.02ml) and water (0.06ml) were added

sequentially. The resulting mixture was filtered and the white precipitate was washed with ether (50ml). The ether extracts were dried (MgSO$_4$) and solvent was removed under reduced pressure. Flash column chromatography, eluting 3:1 petrol:ether, yielded hexa-3,5-dienol (25mg, 85%) as a colourless liquid. v$_{max}$ (Thin Film) 3356(broad), 2932, 2882, 1652, 1603, 1416, 1374cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 6.32 (1H, ddd, J=16.8, 10.0, 10.4Hz, H$_2$C=C**H**-CH=), 6.15 (1H, dd, J=15.0, 10.4Hz, H$_2$C=CH-C**H**=CH-), 5.68 (1H, ddd, J=15.6, 7.6, 7.2Hz, H$_2$C=CH-CH=C**H**-), 5.13 (1H, d, J=16.8Hz, (Z)-**H**CH=CH-CH=), 5.01 (1H, d, J=10.0Hz, (E)-HC**H**=CH-CH=), 3.68 (2H, t, J=6.0Hz, C**H**$_2$OH), 2.35 (2H, m, C**H**$_2$CH$_2$OH), 1.61 (1H, broad s, O**H**); δ(^{13}C) (100MHz; CDCl$_3$) 136.74, 133.71, 130.53, 115.92, 61.85, 35.88; MS (EI) m/z 98 (M$^+$, 94%), 81 (86), 67 (100).

3-(Hexa-3',5'-dienyloxy)-2-cyclohexen-1-one (137a)[83]
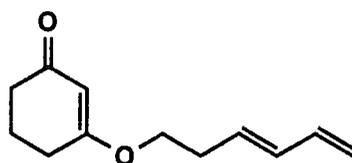
1,3-Cyclohexanedione (308mg, 2.75mmol), hexa-3,5-dienol (141a) (225mg, 2.3mmol) and *p*-toluene sulphonic acid (40mg, 0.23mmol) were dissolved in dry chloroform (10ml) and 4Å Molecular Sieves (0.5g) were added. The resulting mixture was heated to reflux for 18 hours. After cooling, the mixture was diluted with chloroform, filtered and washed with saturated sodium bicarbonate solution. The organic layer was dried (MgSO$_4$) and solvent was removed under reduced pressure. Flash column chromatography, eluting 1:1 petrol:ether, gave 3-(hexa-3',5'-dienyloxy)-2-cyclohexen-1-one (209mg, 47%) as a colourless oil. v$_{max}$ (Thin Film) 3090, 2950, 2900, 1650, 1600, 1370, 1220, 1180cm^{-1}; δ(^{1}H) (250MHz) 6.31 (1H, ddd, J= 16.8, 10.4, 10.4Hz, H$_2$C=C**H**-CH=), 6.14 (1H, m, H$_2$C=CH-C**H**=CH-), 5.64 (1H, m, H$_2$C=CH-CH=C**H**-), 5.35 (1H, s, 2-C**H**), 5.15 (1H, d, J=16.8Hz, (Z)-**H**CH=CH-CH=), 5.04 (1H, d, J=10.4Hz, (E)-HC**H**=CH-CH=), 3.87 (2H, t, J=6.6Hz, -O-C**H**$_2$), 2.52 (2H, m, O-CH$_2$-C**H**$_2$-CH=CH-), 2.38 (4H, m, 4-C**H**$_2$ and 6-C**H**$_2$), 1.98 (2H, m, 5-C**H**$_2$), δ(^{13}C) (50MHz) 200.20, 178.25, 137.09, 134.15, 129.68, 116.89, 103.36, 68.09, 37.25, 32.18, 29.46, 21.20; MS (CI, (NH$_3$)) m/z 193 (MH$^+$, 100%), 141 (37), 81 (25).

Hexa-3,5-dienoic acid (149a)[150]
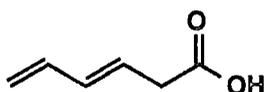
Methyl hexa-3,5-dienoate (140a) (378mg, 3mmol) was dissolved in 3:1 methanol: water (8ml), lithium hydroxide monohydrate (625mg, 15mmol) was added and the resulting mixture was stirred at -5°C for 18 hours. The mixture was diluted with water and the methanol removed under reduced pressure. The resulting aqueous layer was extracted with ether (20ml). The aqueous layer was acidified with 1M HCl to pH3 and then extracted with ethyl acetate (4x 20ml). The combined organic layers were dried (MgSO$_4$) and solvent was removed under reduced pressure to afford a crude colourless liquid (200mg, 59%) consisting mainly of hexa-3,5-dienoic acid with a trace of hexa-2,4-dienoic acid. This mixture was not purified further and was used immediately. v_{max} (Thin Film) 3088(broad), 3022, 1714, 1645, 1506, 1417, 1275, 1221, 1152, 1003cm^{-1}; δ(^{1}H) (200MHz; CDCl$_3$) 11.55 (1H, broad s, COO**H**), 6.28 (2H, m, H$_2$C=C**H**-C**H**=), 5.75 (1H, m, H$_2$C=CH-CH=C**H**-), 5.16 (1H, dd, J=15.7, 1.6Hz, (Z)-**H**CH=CH-CH=), 5.06 (1H, dd, J=10.4, 1.6Hz, (E)-HC**H**=CH-CH=), 3.17 (2H, d, J=7.2Hz, =CH-C**H**$_2$-); δ(^{13}C) (50MHz; CDCl$_3$) 178.67, 136.71, 135.36, 125.18, 117.80, 38.12; MS (EI) *m/z* 112 (M$^+$, 59%), 97 (16), 67 (100).

3'-Oxocyclohex-1'-enyl hexa-3,5-dienoate (150a)
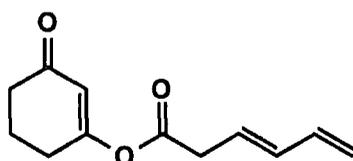
1,3-Dicyclohexylcarbodiimide (0.88mmol, 200mg) and 4-dimethylaminopyridine (10mg, 0.08mmol) were added to a solution of hexa-3,5-dienoic acid (90mg, 0.8mmol) in dry dichloromethane (5ml). 1,3-Cyclohexanedione (100mg, 0.9mmol) was dissolved in dichloromethane (3ml) and added dropwise to the acid mixture at 0°C. The resulting mixture was stirred for 18 hours and solvent was then removed under reduced pressure to afford a crude solid. Dry ether (20ml) was added and the resulting suspension was filtered through celite. The solvent was removed under reduced pressure, the resulting crude product was purified by flash column chromatography, eluting 2:1 petrol:ether. This yielded a 3:2 mixture

of 3'-oxocyclohex-1'-enyl hexa-3,5-dienoate and 3'-oxocyclohex-1'-enyl hexa-2,4-dienoate (77mg, 42%) as a colourless liquid. v_{max} (Thin Film) 2953, 1735, 1673, 1641, 1611, 1521, 1455, 1428, 1368, 1326, 1232, 1208, 1124cm⁻¹; δ(¹H) (400MHz; CDCl₃) 6.50-5.00 (6H, m, all olefinic protons), 3.25 (2H, d, J=6.5Hz, =CH-C**H**₂-COO-), 2.55 (2H, m, 4-C**H**₂), 2.39 (2H, m, 6-C**H**₂), 2.05 (2H, m, 5-C**H**₂); δ(¹³C) (100MHz; CDCl₃) 199.58, 170.07, 163.47, 148.06, 141.88, 129.46, 117.16, 116.98, 36.69, 28.37, 21.26, 18.76; MS (CI, (NH₃)) m/z 207 (MH⁺, 37%), 113 (12), 95 (100); HRMS (CI, (NH₃)) C₁₂H₁₅O₃ m/z Calc. 207.1021; Found 207.1021.

Methyl 2,2-dimethylhexa-3,5-dienoate (140b)[154]
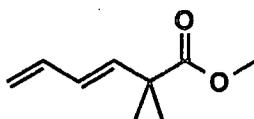
ⁿButyllithium (22ml, 1.6M solution in hexane, 35.2mmol) was added dropwise to a solution of diisopropylamine (5.12ml, 38.4mmol) in dry THF (200ml) at -78°C. This was followed by the dropwise addition of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (6ml, 51.2mmol). The resulting solution was stirred for 15 minutes at -78°C. A solution of methyl hexa-2,4-dienoate (139) (2.02g, 16mmol) in dry THF (10ml) was added dropwise at -78°C and the resulting mixture was stirred at -78°C for 4 hours. Methyl iodide (4ml, 64mmol) was then added dropwise and stirring was continued at -78°C for a further 4 hours. The reaction was quenched at -78°C with saturated aqueous NH₄Cl solution (25ml) and warmed in a warm water bath. THF was removed under reduced pressure and the remaining aqueous layer was extracted with ether (5 x 20ml). The combined organic extracts were washed with water, dried (MgSO₄) and the solvent was removed under reduced pressure. Flash column chromatography, eluting 10:1 petrol:ether, yielded a mixture of the mono- and di- methylated products. This mixture was again subjected to the reaction conditions described above to yield, after column chromatography, methyl 2,2-dimethylhexa-3,5-dienoate (0.9g, 37%). v_{max} (Thin Film) 3088, 2975, 2952, 1733, 1649, 1603cm⁻¹; δ(¹H) (400MHz; CDCl₃) 6.33 (1H, ddd, J=16.8, 10.4, 10.4Hz, H₂C=C**H**-CH=), 6.10 (1H, dd, J=15.6, 10.4Hz, H₂C=CH-C**H**=CH-), 5.87 (1H, d, J=15.6Hz, H₂C=CH-CH=C**H**-), 5.19 (1H, dm, J=16.8Hz, (Z)-**H**CH=CH-

CH=), 5.06 (1H, dm, J=10.4Hz, (E)-$\underline{H}$CH=CH-CH=), 3.67 (3H, s, OC$\underline{H}_3$), 1.32 (6H, s, (C$\underline{H}_3)_2$C); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 176.68, 138.42, 136.80, 128.97, 116.83, 52.11, 44.29, 24.98; MS (EI) m/z 155 (MH$^+$, 15%), 154 (M$^+$, 17), 95 (100).

2,2-Dimethylhexa-3,5-dienol (141b)[155]
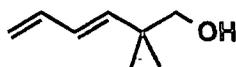
Lithium aluminium hydride (76mg, 2mmol) was suspended in dry ether (10ml) and cooled to 0°C. Methyl 2,2-dimethylhexa-3,5-dienoate (140b) (308mg, 2mmol) was added dropwise as a solution in dry ether (5ml) and the resulting mixture was stirred at room temperature for 2 hours. After cooling to 0°C, water (0.76ml), 15% NaOH (0.76ml) and water (1.50ml) were added sequentially. The resulting mixture was filtered and the white precipitate was washed with ether (50ml). The ethereal extracts were dried (MgSO$_4$) and solvent was removed under reduced pressure. Flash column chromatography, eluting 3:1 petrol:ether, yielded 2,2-dimethylhexa-3,5-dienol (110mg, 44%) as a clear colourless liquid. v_{max} (Thin Film) 3368(broad), 2961, 2870, 1648, 1603, 1473, 1385, 1287cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 6.34 (1H, dddd, J=16.8, 10.4, 10.0, 0.8Hz, H$_2$C=C$\underline{H}$-CH=), 6.10 (1H, dd, J=15.6, 10.4Hz, H$_2$C=CH-C$\underline{H}$=CH-), 5.66 (1H, dd, J=15.6, 0.8Hz, H$_2$C=CH-CH=C$\underline{H}$-), 5.18 (1H, dm, J=16.8Hz, (Z)-$\underline{H}$CH=CH-CH=), 5.04 (1H, dm, J=10.0Hz, (E)-HC$\underline{H}$=CH-CH=), 3.36 (2H, s, C$\underline{H}_2$OH), 1.05 (6H, s, (C$\underline{H}_3)_2$C); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 141.17, 137.14, 129.70, 116.08, 71.59, 38.65, 23.72; MS (EI) m/z 126 (M$^+$, 7%), 95 (100).

3-(2',2'-Dimethylhexa-3',5'-dienyloxy)-2-cyclohexen-1-one (137b)
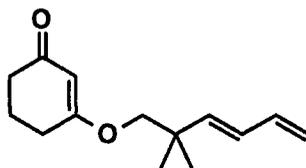
1,3-Cyclohexanedione (117mg, 1.04mmol), 2,2-dimethylhexa-3,5-dienol (141b) (110mg, 0.87mmol) and p-toluene sulphonic acid (16mg, 0.09mmol) were dissolved in dry chloroform (10ml) and 4Å Molecular Sieves (0.3g) were added at room temperature. The resulting mixture was heated to reflux for 18 hours. After cooling, the mixture was diluted with chloroform,

filtered and washed with saturated sodium bicarbonate solution. The organic layer was dried (MgSO$_4$) and solvent was removed under reduced pressure. Flash column chromatography, eluting 1:1 petrol:ether gave initially pure 3-(2',2'-dimethylhexa-3',5'-dienyloxy)-2-cyclohexen-1-one (60mg, 27%). 2,2-dimethylhexa-3,5-dienol (80mg, 0.63mmol, 72%) was also recovered. v$_{max}$ (Thin Film) 2962, 2873, 1654, 1650, 1605, 1401, 1216, 1182cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 6.32 (1H, ddd, J=16.8, 10.0, 10.0Hz, H$_2$C=CH-CH=), 6.06 (1H, dd, J=15.6, 10.0Hz, H$_2$C=CH-CH=CH-), 5.71 (1H, d, J=15.6Hz, H$_2$C=CH-CH=CH-), 5.33 (1H, s, 2-CH), 5.18 (1H, dm, J=16.8Hz, (Z)-HCH=CH-CH=), 5.05 (1H, dm, J=10.0Hz, (E)-HCH=CH-CH=), 3.55 (2H, s, CH$_2$O), 2.43 (2H, t, J=6.0Hz, 4-CH$_2$), 2.35 (2H, t, J=6.4Hz, 6-CH$_2$), 1.98 (2H, m, 5-CH$_2$), 1.12 (6H, s, (CH$_3$)$_2$C); δ(^{13}C) (100MHz; CDCl$_3$) 199.74, 178.00, 140.27, 137.14, 128.86, 116.30, 102.83, 76.46, 36.76, 36.70, 28.88, 24.26, 21.17; MS (EI) m/z 221 (MH$^+$, 100%), 205 (11), 149 (15), 113 (60); HRMS (EI, MH$^+$) C$_{14}$H$_{21}$O$_2$ m/z Calc. 221.1542; Found 221.1542.

2,2-Dimethylhexa-3,5-dienoic acid (149b)[154]
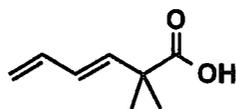
Methyl 2,2-dimethylhexa-3,5-dienoate (140b) (555mg, 3.6mmol) was dissolved in 3:1 methanol: water (16ml) and lithium hydroxide monohydrate (900mg, 21.6mmol) was added. The resulting mixture was stirred at 5°C for 18 hours. The mixture was diluted with water and methanol was then removed under reduced pressure. The resulting aqueous layer was extracted with ether (20ml). The aqueous layer was acidified with 1M HCl to pH3 and then extracted with ethyl acetate (4 x 20ml). The combined organic layers were dried (MgSO$_4$) and solvent was removed under reduced pressure. This yielded 2,2-dimethylhexa-3,5-dienoic acid (479mg, 95%) which was not purified further. This acid polymerises rapidly at room temperature and was therefore used immediately. v$_{max}$ (Thin Film) 2976(broad), 1703, 1652, 1604, 1472, 1409, 1297cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 6.27 (1H, ddd, J=16.8, 10.0, 10.0Hz, H$_2$C=CH-CH=), 6.08 (1H, dd, J=15.6, 10Hz, H$_2$C=CH-CH=CH-), 5.82 (1H, d, J=15.6Hz, H$_2$C=CH-CH=CH-), 5.14 (1H, dm, J=16.8Hz, (Z)-HCH=CH-CH=), 5.02 (1H,

dm, J=10Hz, (E)-HC**H**=CH-CH=), 1.29 (6H, s, (C**H**$_3$)$_2$C); δ(^{13}C) (100MHz; CDCl$_3$)

181.65, 137.70, 136.74, 129.66, 117.31, 44.09, 24.88; MS (EI) m/z 140 (M$^+$, 24%), 95

(94).

3'-Oxocyclohex-1'-enyl 2,2-dimethylhexa-3,5-dienoate (150b)
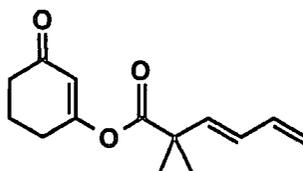
1,3-Dicyclohexylcarbodiimide (430mg, 1.90mmol) and 4-dimethylaminopyridine (25mg,

0.2mmol) were added to a solution of 2,2-dimethylhexa-3,5-dienoic acid (149b) (262mg,

1.87mmol) in dry dichloromethane (10ml). 1,3-Cyclohexanedione (224mg, 2mmol) was

dissolved in dichloromethane (4ml) and added dropwise to the acid mixture at 0°C. The

resulting mixture was stirred at room temperature for 18 hours and solvent was then removed

under reduced pressure. Dry ether (50ml) was added to the resulting solid and the suspension

was filtered through celite. The solvent was removed under reduced pressure. Flash column

chromatography, eluting 2:1 petrol:ether, yielded 3'-oxocyclohex-1'-enyl 2,2-dimethylhexa-

3,5-dienoate (328mg, 75%) as a colourless oil. ν$_{max}$ (Thin Film) 2975, 1757, 1681, 1643,

1470, 1365, 1119cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 6.34 (1H, ddd, J=16.8, 10.0, 10.0Hz,

H$_2$C=C**H**-CH=), 6.16 (1H, dd, J=15.6, 10.0Hz, H$_2$C=CH-C**H**=CH-), 5.86 (1H, d,

J=15.6Hz, H$_2$C=CH-CH=C**H**-), 5.86 (1H, t, J=1.2Hz, 2'-C**H**), 5.24 (1H, dd, J=1.2,

16.8Hz, (Z)-**H**CH=CH-CH=), 5.13 (1H, dd, J=1.2, 10.0Hz, (E)-HC**H**=CH-CH=), 2.51

(2H, dt, J=1.2, 6.0Hz, 6'-C**H**$_2$), 2.40 (2H, t, J=7.2Hz, 4'-C**H**$_2$), 2.06 (2H, m, 5'-C**H**$_2$),

1.40 (6H, s, (C**H**$_3$)$_2$C); δ(^{13}C) (100MHz; CDCl$_3$) 199.46, 172.96, 170.30, 136.69, 136.48,

130.34, 117.88, 117.70, 44.77, 36.82, 28.24, 24.87, 21.34; MS (EI) m/z 235 (MH$^+$,

100%), 113 (34), 95 (63); HRMS (EI, MH$^+$) C$_{14}$H$_{19}$O$_3$ m/z Calc. 235.1334; Found

235.1334.

Diels-Alder Reaction of 3'-oxocyclohex-1'-enyl 2,2-dimethylhexa-3,5-dienoate

3'-oxocyclohex-1'-enyl 2,2-dimethylhexa-3,5-dienoate (150b) (50mg, 0.21mmol) was dissolved in benzene (5ml, 0.04M) and transferred to a dry silylated Carius tube. The solution was degassed (four freeze-thaw cycles) and heated at 300°C for 48h. Upon cooling, the mixture was concentrated and the resultant viscous oil was purified by flash column chromatography to afford α-tetralone (X) (7.5mg, 24%), (which was identified by comparison to an authentic sample) as the only non-polymeric material.

Methyl 2,2-dibenzylhexa-3,5-dienoate (140c)
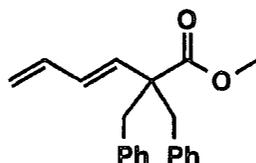
^{n}Butyllithium (15ml, 1.6M solution in hexane, 24mmol) was added dropwise to a solution of diisopropylamine (3.69ml, 26.4mmol) in dry THF (100ml) at -78°C. This was followed by the dropwise addition of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (4.35ml, 36mmol). The resulting solution was stirred for 15 minutes at -78°C. A solution of methyl hexa-2,4-dienoate (139) (1.01g, 8mmol) in dry THF (10ml) was added dropwise at -78°C and the resulting mixture was stirred at -78°C for 4 hours. Benzyl bromide (3.81ml, 32mmol) was then added dropwise and stirring was continued at -78°C for a further 16 hours. The reaction was quenched at -78°C with saturated aqueous NH_4Cl solution (25ml) and warmed in a warm water bath. THF was removed under reduced pressure and the remaining aqueous layer was extracted with ether (5 x 20ml). The combined organic extracts were washed with water, dried ($MgSO_4$) and solvent was removed under reduced pressure. Flash column chromatography, eluting 98:2 petrol:ether, yielded initially excess benzyl bromide and then methyl 2,2-dibenzylhexa-3,5-dienoate (1.49g, 61%) as a colourless oil. v_{max} (Thin Film) 3030, 2949, 1729, 1646, 1602, 1496, 1455, 1435 cm^{-1}; $\delta(^{1}H)$ (400MHz; CDCl$_3$) 7.28-7.12 (10H, m, 2(C$_6$H$_5$-)), 6.37 (1H, ddd, J=16.8, 10.4, 10.4Hz, H$_2$C=CH-CH=), 6.21 (1H, dd, J=15.6, 10.4Hz, H$_2$C=CH-CH=CH-), 5.94 (1H, d, J=15.6Hz, H$_2$C=CH-CH=CH-), 5.20 (1H, dm, J=16.8Hz, (Z)-HCH=CH-CH=), 5.12 (1H, dm, J=10.4Hz, (E)-HCH=CH-CH=), 3.64 (3H,

s, OC$\underline{H}_3$), 3.19 (4H, AB System, J_{AB}=13.6Hz, PhC$\underline{H}_2$); δ(^{13}C) (100MHz; CDCl$_3$) 174.46,

137.00, 136.94, 134.90, 131.83, 130.19, 127.90, 126.48, 116.76, 54.24, 51.70, 44.29;

MS (EI) m/z 306 (M$^+$, 3.7%), 215 (17), 155 (39), 91 (100); HRMS (CI,M(NH$_4$)$^+$)

C$_{21}$H$_{26}$O$_2$Nm/z Calc. 324.1964; Found 324.1964.

2,2-Dibenzylhexa-3,5-dienoic acid(149c)[84]
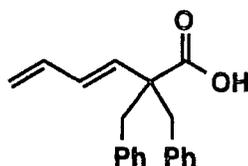
Potassium ^{t}butoxide (0.74g, 7.2mmol) was suspended in dry ether (50ml) and cooled to 0°C.

Distilled water (0.033ml, 1.8mmol) was added and the resulting slurry was stirred for 5

minutes. Methyl 2,2-dibenzylhexa-3,5-dienoate (140c) was dissolved in ether (3ml) and was

added dropwise to the slurry at 0°C. The reaction was allowed to warm to room temperature

and was stirred for a further 18 hours. Iced water was added to form two distinct layers and the

resulting aqueous layer was extracted with ether (1x20ml). The aqueous layer was acidified

with 1M HCl to pH 3 and then extracted with ether (3x50ml). These latter organic extracts

were combined and dried (MgSO$_4$). Removal of solvent under reduced pressure yielded 2,2-

dibenzylhexa-3,5-dienoic acid contaminated with a little ^{t}butanol (237mg, ~99%). This crude

product was used without further purification. v_{max} (Thin Film) 3087(broad), 3030, 2975,

1705, 1603, 1496, 1455, 1261 cm^{-1}; δ(^{1}H) (200MHz; CDCl$_3$) 7.28-7.12 (10H, m, 2(C$_6$$\underline{H}_5$-)),

6.30 (2H, m, H$_2$C=C$\underline{H}$-C$\underline{H}$=), 5.94 (1H, d, J=15.5Hz, H$_2$C=CH-CH=C$\underline{H}$-), 5.20 (2H, dm,

J=16.8Hz, $\underline{H}_2$C=CH-CH=), 3.21 (4H, AB System, J_{AB}=13.6Hz, PhC$\underline{H}_2$); MS (CI, (NH$_3$))

m/z 292 (M$^+$, 4.6%), 247 (95, (M-(CO$_2$H))$^+$), 113 (100).

### 3'-Oxocyclohex-1'-enyl 2,2-dibenzylhexa-3,5-dienoate (150c)

1,3-Dicyclohexylcarbodiimide (791mg, 3.49mmol) and 4-dimethylaminopyridine (47mg, 0.37mmol) were added to a solution of 2,2-dibenzylhexa-3,5-dienoic acid (149c) (1.02g, 3.49mmol) in dry dichloromethane (30ml). 1,3-Cyclohexanedione (418mg, 3.73mmol) was dissolved in dichloromethane (8ml) and added dropwise to the acid mixture at 0°C. The resulting mixture was stirred at room temperature for 18 hours and the solvent was then removed under reduced pressure. Dry ether (50ml) was added to the resulting solid and the suspension was filtered through celite. The solvent was removed under reduced pressure. Flash column chromatography, eluting 3:1 petrol:ether, yielded 3'-oxocyclohex-1'-enyl 2,2-dibenzylhexa-3,5-dienoate (727mg, 54%) as a white, waxy solid. m.p. 61-62°C; v_{max} (CDCl$_3$ Solution) 3065, 2957, 1752, 1673, 1644, 1602, 1496, 1427, 1148cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.20-7.05 (10H, m, 2(C$_6$H$_5$-)), 6.30 (1H, ddd, J=16.8, 10.0, 10.0Hz, H$_2$C=CH-CH=), 6.17 (1H, dd, J=16.0, 10.0Hz, H$_2$C=CH-CH=CH-), 5.87 (1H, d, J=16.0Hz, H$_2$C=CH-CH=CH-), 5.53 (1H, s, 2'-CH), 5.14 (1H, d, J=16.8Hz, (Z)-HCH=CH-CH=), 5.06 (1H, d, J=10.0Hz, (E)-HCH=CH-CH=), 3.14 (4H, AB system, J$_{AB}$=14.0Hz, PhCH$_2$), 2.26 (2H, t, J= 6.4Hz, 6'-CH$_2$), 2.11 (2H, t, J=6.0Hz, 4'-CH$_2$), 1.86 (2H, m, 5'-CH$_2$); δ(^{13}C) (100MHz; CDCl$_3$) 199.27, 170.96, 169.97, 136.53, 136.29, 133.80, 132.45, 130.14, 128.09, 126.86, 117.77, 117.61, 54.41, 44.53, 36.63, 27.84, 21.10; MS (EI) m/z 235 (MH$^+$, 13%), 247 (100), 203 (34); Analysis Found: C, 80.57%; H, 6.77%. C$_{26}$H$_{26}$O$_3$ requires C, 80.80%; H, 6.78%.

<u>Ethyl hepta-4,6-dienoate (155a)</u>[85]

1,4-Pentadien-3-ol (95.3g, 63.5mmol) was dissolved in benzene (60ml). Triethyl orthoacetate (40g, 249mmol) and propionoic acid (0.2ml, 2.7mmol) were added. The resulting mixture was heated to reflux for 18 hours. After cooling to room temperature, the mixture was concentrated under reduced pressure. 0.2M HCl (100ml) was added to the resulting liquid which was then stirred at room temperature for 90 minutes. Saturated aqueous $NaHCO_3$ (50ml) was added and the aqueous layer was extracted with ether (3x50ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (50ml), water (50ml) and saturated brine (50ml) and then dried ($MgSO_4$). The solvent was removed under reduced pressure. Distillation yielded ethyl 4,6-heptadienoate (b.p. 37°C/1mbar (lit.[85] 40-55°C/0.5mmHg)) as a colourless liquid (6.26g, 64%). v_{max} (Thin Film) 3087, 2982, 1735, 1654, 1623, 1604, 1465, 1373, 1249, 1181, 1006cm⁻¹; $\delta(^1H)$ (400MHz; $CDCl_3$) 6.29 (1H, ddd, J=16.8, 10.4, 10.4Hz, $H_2C=C\underline{H}$-CH=), 6.09 (1H, dd, J=15.2, 10.4Hz, $H_2C=CH-C\underline{H}$=CH-), 5.69 (1H, m, $H_2C=CH$-CH=C$\underline{H}$-), 5.11 (1H, d, J=16.8Hz, (Z)-$\underline{H}$CH=CH-CH=), 4.99 (1H, d, J=10.4Hz, (E)-$\underline{H}$CH=CH-CH=), 4.13 (2H, q, J=7.2Hz, $OC\underline{H}_2CH_3$), 2.40 (4H, m, =$CHC\underline{H}_2C\underline{H}_2CO_2Et$), 1.25 (3H, t, J=7.2Hz, $CH_2C\underline{H}_3$); $\delta(^{13}C)$ (100MHz; $CDCl_3$) 172.94, 136.83, 132.65, 131.91, 115.69, 60.35, 33.83, 27.79, 14.23; MS (EI) m/z 154 (M⁺, 74%), 109 (31), 81 (100).

<u>Hepta-4,6-dienoic acid</u>[85]

Ethyl hepta-4,6-dienoate (155a) (1.1g, 7.1mmol) was dissolved in methanol (20ml) and potassium hydroxide (5g, 89mmol) was added. The mixture was refluxed for 2 hours. After cooling to room temperature, water (50ml) was added and the mixture was extracted with ether (1x20ml). The aqueous layer was acidified to pH3 with 1M HCl and then extracted with ethyl acetate (3x50ml). The combined ethyl acetate extracts were dried ($MgSO_4$) and concentrated

under reduced pressure. This yielded hepta-4,6-dienoic acid (0.89g, 100%) as a colourless liquid which was used immediately without further purification. ν_{max} (Thin Film) 3070(broad), 3027, 1700, 1636, 1458, 1420, 1260, 1178cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 11.47 (1H, s (broad), COO$\underline{H}$), 6.33 (1H, ddd, J=17.2, 10.4, 10.0Hz, H$_2$C=C$\underline{H}$-CH=), 6.11 (1H, dd, J=15.2, 10.4Hz, H$_2$C=CH-C$\underline{H}$=CH-), 5.70 (1H, ddd, J=15.2, 6.4, 6.0Hz, H$_2$C=CH-CH=C$\underline{H}$-), 5.13 (1H, dm, J=17.2Hz, (Z)-$\underline{H}$CH=CH-CH=), 5.01 (1H, dm, J=10.0Hz, (E)-$\underline{H}$CH=CH-CH=), 2.46 (4H, m, =CH-C$\underline{H_2}$C$\underline{H_2}$CO$_2$H); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 179.38, 136.72, 132.13, 132.13, 115.95, 33.56, 27.37.

3'-Oxocyclohex-1'-enyl hepta-4,6-dienoate (156a)

1,3-Dicyclohexylcarbodiimide (1.4g, 6.11mmol) and 4-dimethylaminopyridine (75mg, 0.6mmol) were added to a solution of hepta-4,6-dienoic acid (700mg, 5.56mmol) in dry dichloromethane (25ml). 1,3-Cyclohexanedione (694mg, 6.25mmol) was dissolved in dichloromethane (10ml) and added dropwise to the acid mixture at 0°C. The resulting mixture was stirred at room temperature for 18 hours and the solvent was removed under reduced pressure. Dry ether (50ml) was added to the resulting solid and the suspension was filtered through celite. The solvent was removed under reduced pressure. Flash column chromatography, eluting 2:1 petrol:ether, yielded initially pure 2'-hydroxy-6'-oxocyclohex-1'enyl hepta-4,6-dieneone (157a) (369mg, 30%) as a colourless oil. ν_{max} (Thin Film) 3438(broad), 2952, 1666, 1556, 1435, 1190, 1007cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 6.24 (1H, m, H$_2$C=C$\underline{H}$-CH=), 6.05 (1H, m, H$_2$C=CH-C$\underline{H}$=CH-), 5.69 (1H, m, H$_2$C=CH-CH=C$\underline{H}$-), 5.05 (1H, dd, J=17.2, 2.0Hz, (Z)-$\underline{H}$CH=CH-CH=), 4.92 (1H, dd, J=10.0, 2.0Hz, (E)-HC$\underline{H}$=CH-CH=), 3.10 (2H, dt, J=7.6, 4.0Hz, C(=O)CH$_2$C$\underline{H_2}$CH=), 2.62 (2H, m, C(=O)C$\underline{H_2}$CH$_2$CH=), 2.43 (2H, m, 5'-C$\underline{H_2}$), 2.36 (2H, m, 3'-C$\underline{H_2}$), 1.92 (2H, m, 4'-C$\underline{H_2}$); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 205.01, 197.94, 195.08, 136.83, 133.15, 131.58, 115.25, 112.93, 40.12, 38.55, 32.85, 26.96, 18.90; MS (EI) m/z 220 (M$^+$, 42%), 139 (100, (M-

$((CH_2)_2CH=CH-CH=CH_2))^+$); HRMS (CI, MH$^+$) $C_{13}H_{17}O_3$ m/z Calc. 221.1178; Found 221.1178.

This was followed by pure 3'-oxocyclohex-1'-enyl hepta-4,6-dienoate (156a) (366mg, 30%) as a colourless oil. v_{max} (Thin Film) 2933, 1763, 1674, 1644, 1604, 1523, 1427, 1363, 1346, 1120cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 6.23 (1H, m, H$_2$C=C$\underline{H}$-CH=), 6.04 (1H, m, H$_2$C=CH-C$\underline{H}$=CH-), 5.81 (1H, m, 2'-C$\underline{H}$), 5.62 (1H, m, H$_2$C=CH-CH=C$\underline{H}$-), 5.07 (1H, dd, J=17.2, 2.0Hz, (Z)-$\underline{H}$CH=CH-CH=), 4.95 (1H, dd, J=10.0, 2.0Hz, (E)-HC$\underline{H}$=CH-CH=), 2.52-1.97 (10H, m, (C$\underline{H}_2$)$_3$ and (C$\underline{H}_2$)$_2$); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 199.31, 169.64, 169.23, 136.33, 132.34, 131.28, 117.28, 116.07, 36.47, 33.75, 28.10, 27.26, 21.01; MS (CI, (NH$_3$)) m/z 221 (MH$^+$, 32%), 208 (13), 113 (100); HRMS (CI, MH$^+$) $C_{13}H_{17}O_3$ m/z Calc. 221.1178; Found 221.1178.

Ethyl 2,2-dimethylhepta-4,6-dienoate (155b)

^{n}Butyllithium (8.77ml, 2.0M solution in hexane, 17.53mmol) was added dropwise to a solution of diisopropylamine (2.45ml, 17.53mmol) in dry THF (100ml) at -78°C. This was followed by the dropwise addition of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (3.18ml, 26.3mmol). The resulting solution was stirred for 15 minutes at -78°C. A solution of ethyl hepta-4,6-dienoate (155a) (1.08g, 7.01mmol) in dry THF (15ml) was added dropwise at -78°C and the resulting mixture was stirred at -78°C for 6 hours. Methyl iodide (1.87ml, 30mmol) was then added dropwise and stirring was continued at -78°C for a further 18 hours. The reaction was quenched at -78°C with saturated aqueous NH$_4$Cl solution (50ml) and then warmed in a warm water bath. THF was removed under reduced pressure and the remaining aqueous layer was extracted with ether (5 x 20ml). The combined organic extracts were washed with water, dried (MgSO$_4$) and the solvent was then removed under reduced pressure. Flash column chromatography, eluting 48:2 petrol:ether, yielded a mixture of mono- and di-methylated product. This was again subjected to the reaction conditions described above to yield, after column chromatography, pure ethyl 2,2-dimethylhepta-4,6-dienoate (0.70g, 55%)

as a colourless liquid. v_{max} (Thin Film) 2975, 1728, 1653, 1602, 1472, 1384, 1269, 1175, 1143cm⁻¹; δ(¹H) (400MHz; CDCl₃) 6.29 (1H, ddd, J=16.8, 10.0, 10.0Hz, H₂C=C**H**-CH=), 6.05 (1H, dd, J=14.8, 10.0Hz, H₂C=CH-C**H**=CH-), 5.62 (1H, m, H₂C=CH-CH=C**H**-), 5.10 (1H, d, J=16.8Hz, (Z)-**H**CH=CH-CH=), 4.98 (1H, d, J=10.0Hz, (E)-**H**CH=CH-CH=), 4.11 (2H, q, J=7.2Hz, CO₂C**H**₂CH₃), 2.30 (2H, d, J=7.6Hz, H₂C=CH-CH=CH-C**H**₂-), 1.24 (3H, t, J=7.2Hz, CO₂CH₂C**H**₃), 1.17 (6H, s, (C**H**₃)₂C); δ(¹³C) (100MHz; CDCl₃) 177.41, 136.92, 134.01, 130.28, 115.64, 60.33, 43.43, 42.52, 24.88, 14.24; MS (EI) m/z 182 (M⁺, 21%), 109 ((M-CO₂Et)⁺, 50), 67 (100). HRMS (EI) C₁₁H₁₈O₂ m/z Calc. 182.1307; Found 182.1237.

2,2-Dimethylhepta-4,6-dienoic acid

Ethyl 2,2-dimethylhepta-4,6-dienoate (155b) (0.63g, 3.46mmol) was dissolved in methanol (10ml) and potassium hydroxide (2.5g, 45mmol) was added. The mixture was refluxed for 6 hours. After cooling to room temperature, water (50ml) was added and the mixture was extracted with ether (1x20ml). The aqueous layer was acidified to pH3 with 1M HCl and then extracted with ethyl acetate (3x20ml). The combined ethyl acetate extracts were dried (MgSO₄) and concentrated under reduced pressure. This yielded 2,2-dimethylhepta-4,6-dienoic acid (0.38g, 72%) as a white crystalline solid which was used immediately without further purification. v_{max} (CDCl₃ Solution) 3088(broad), 2974, 1701, 1602, 1552, 1472, 1366, 1288cm⁻¹; δ(¹H) (200MHz; CDCl₃) 11.98 (1H, broad s, COO**H**), 6.30 (1H, ddd, J=16.8, 10.2, 10.2Hz, H₂C=C**H**-CH=), 6.05 (1H, dd, J=15.6, 10.2Hz, H₂C=CH-C**H**=CH-), 5.65 (1H, m, H₂C=CH-CH=C**H**-), 5.08 (1H, dd, J=16.4, 2.0Hz, (Z)-**H**CH=CH-CH=), 4.96 (1H, dd, J=10.0, 2.0Hz, (E)-**H**CH=CH-CH=), 2.30 (2H, d, J=7.6Hz, =CH-C**H**₂C(CH₃)₂CO₂H), 1.17 (6H, s, C(C**H**₃)₂); δ(¹³C) (50MHz; CDCl₃) 184.27, 136.71, 134.27, 129.58, 115.69, 42.96, 24.48.

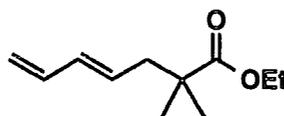3'-Oxocyclohex-1'-enyl 2,2-dimethylhepta-4,6-dienoate (156b)

1,3-Dicyclohexylcarbodiimide (620mg, 2.7mmol) and 4-dimethylaminopyridine (34mg, 0.27mmol) were added to a solution of 2,2-dimethylhepta-4,6-dienoic acid (380mg, 2.47mmol) in dry dichloromethane (25ml). 1,3-Cyclohexanedione (311mg, 2.77mmol) was dissolved in dichloromethane (5ml) and added dropwise to the acid mixture at 0°C. The resulting mixture was stirred at room temperature for 18 hours and the solvent was removed under reduced pressure. Dry ether (50ml) was added to the resulting solid and the suspension was filtered through celite. The solvent was removed under reduced pressure. Flash column chromatography, eluting 3:2 petrol:ether, yielded 3'-oxocyclohex-1'-enyl 2,2-dimethylhepta-4,6-dienoate (515mg, 84%) as a colourless liquid. v_{max} (CDCl$_3$ Solution) 2972, 2933, 1754, 1681, 1643, 1471, 1365, 1120, 1090cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 6.29 (1H, ddd, J=17.2, 10.0, 10.0Hz, H$_2$C=C**H**-CH=), 6.09 (1H, ddd, J=15.2, 10.0, 0.8Hz, H$_2$C=CH-C**H**=CH-), 5.82 (1H, t, J=1.2Hz, 2'-C**H**), 5.62 (1H, m, H$_2$C=CH-CH=C**H**-), 5.12 (1H, dd, J=17.2, 0.4Hz, (Z)-**H**CH=CH-CH=), 5.02 (1H, dd, J=10.0, 0.4Hz, (E)-HC**H**=CH-CH=), 2.49 (2H, t, J= 6.4Hz, 6'-C**H**$_2$), 2.38 (4H, m, =CH-C**H**$_2$C(CH$_3$)$_2$- and 4'-C**H**$_2$), 2.04 (2H, m, 5'-C**H**$_2$), 1.25 (6H, s, C(C**H**$_3$)$_2$); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 199.36, 174.07, 170.28, 136.48, 134.74, 128.87, 117.67, 116.49, 43.27, 43.25, 36.69, 28.26, 24.67, 21.24; MS (EI) m/z 249 (MH$^+$, 9%), 248 (M$^+$, 4), 236 (18), 235 (13), 220 (13), 137 (15), 109 (100); HRMS (EI, MH$^+$) C$_{15}$H$_{21}$O$_3$ m/z Calc. 249.1491; Found 249.1491.

1,3-[Bis(triphenylphosphonium)]-2,2-dimethylpropane dibromide (217)

$$Me \diagdown \diagup Me$$
$$Ph_3PBr \quad PPh_3Br$$

Triphenylphosphine (10.48g, 40mmol) was added to 1,3-dibromo-2,2-dimethylpropane (4.6g, 20mmol) and the mixture was heated to 200°C in a Wood's metal bath for 18 hours. The resulting mixture was recrystallised from ethanol/ether to produce 1,3-[bis(triphenylphosphonium)]-2,2-dimethylpropane dibromide as a white powder (3.96g, 26%). m.p. >260°C; v_{max} 3060, 2941, 1588, 1487, 1439, 1342, 1319, 1241, 1108cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 8.1-7.6 (30H, m, 6(C$_6$H$_5$-)), 4.81 (4H, d, J=12.4Hz, 2(CH$_2$P)), 0.83 (6H, s, C(CH$_3$)$_2$); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 134.45 (s, para-C), 134.22 (t, J=5.0Hz, meta-C), 130.18 (t, J=6.0Hz, ortho-C), 119.29 (dd, J=84.7, 3.4Hz, ipso-C), 38.19 (t, J=3.0Hz, C(CH$_3$)$_2$), 34.55 (dd, J=33.6, 32.8Hz, CH$_2$), 28.21 (s, CH$_3$); $\delta(^{31}P)$ (101MHz; CDCl$_3$) 19.16; Analysis Found : C, 65.32%; H, 5.39 %. C$_{41}$H$_{40}$Br$_2$P$_2$ requires C, 65.25%; H, 5.31%.

3,3-Dimethyl-1,5-diphenyl-1,4-pentadiene (216)

$$Me \diagdown \diagup Me$$
$$Ph \qquad Ph$$

The diphosphonium salt (217) (1.51g, 2mmol) was suspended in THF (20ml) and cooled to -78°C. ^{n}Butyllithium (3ml, 1.6M solution in hexane, 4.8mmol) was added dropwise over one hour. After stirring at -78°C for a further 3 hours, the resulting cloudy, orange solution was warmed to room temperature and stirred for a further hour to give a clear, orange solution. This solution was cooled to -78°C, and a solution of benzaldehyde in THF (5ml) was added dropwise. After stirring for 15 minutes at -78°C, the temperature was allowed to rise slowly to 20°C and the resulting mixture was refluxed for 18 hours. After cooling to room temperature, the reaction was quenched with water (30ml) and extracted with ether (3x30ml). The combined

organic extracts were washed with brine (30ml) and dried (MgSO$_4$). Removal of solvent under reduced pressure and flash column chromatography, eluting neat petrol, yielded 3,3-dimethyl-1,5-diphenyl-1,4-pentadiene (a 1:2:1 mixture of (Z,Z):(E,Z):(E,E) isomers) (360mg, 73%) as a colourless liquid. MS (EI) m/z 248 (M$^+$, 45%), 233 ((M-CH$_3$)$^+$, 63), 205 (45), 157 (43), 91 (100); HRMS (EI) C$_{19}$H$_{20}$ m/z Calc. 248.1566; Found 248.1565. Column chromatography, eluting neat petrol, allowed the separation of the three isomers, eluting in the order (Z,Z), (E,Z) and (E,E).

(Z,Z) v_{max} 3002, 2966, 1599, 1492, 1444, 1167, 1072cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.30-7.18 (10H, m, 2(C$_6$H$_5$-)), 6.26 (2H, d, J=12.5Hz, 2(PhCH)), 5.62 (2H, d, J=12.5Hz, 2(PhCH=CH)), 1.17 (6H, s, C(CH$_3$)$_2$); δ(^{13}C) (100MHz; CDCl$_3$) 141.46, 138.62, 129.07, 127.57, 127.48, 126.30, 38.81, 30.91.

(E,Z) v_{max} 3020, 2965, 1599, 1492, 1447, 1072, 970cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.30-7.10 (10H, m, 2(C$_6$H$_5$-)), 6.53 (1H, d, J=12.5Hz, (Z)-PhCH), 6.28 (1H, d, J=16.2Hz, (E)-PhCH), 6.14 (1H, d, J=16.2Hz, (E)-PhCH=CH), 5.69 (1H, d, J=12.5Hz, (Z)-PhCH=CH), 1.17 (6H, s, C(CH$_3$)$_2$); δ(^{13}C) (100MHz; CDCl$_3$) 140.19, 139.80, 138.31, 137.91, 129.13, 128.61, 128.26, 127.54, 126.68, 126.32, 126.05, 125.48, 39.49, 29.34.

(E,E) v_{max} 3027, 2966, 1599, 1494, 1448, 1217, 1073cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.40-7.20 (10H, m, 2(C$_6$H$_5$-)), 6.39 (2H, d, J=16.2Hz, 2(PhCH)), 6.30 (2H, d, J=16.2Hz, 2(PhCH=CH)), 1.35 (6H, s, C(CH$_3$)$_2$); δ(^{13}C) (100MHz; CDCl$_3$) 138.86, 137.69, 128.50, 127.01, 126.47, 126.14, 39.04, 27.42.

Typical Attempted Hydrosilylation Procedure

(Z,Z)-3,3-Dimethyl-1,5-diphenyl-1,4-pentadiene (0.31mmol) was dissolved in CD$_2$Cl$_2$ (1ml) in an NMR tube equipped with a Young's tap. The catalyst (0.01mmol) was added and the solution was degassed (3 freeze/thaw cycles). Dichlorosilane (1.39mmol) was admitted to the NMR tube. After warming slowly to room temperature, the resulting mixture could be heated to the required temperature and subsequently monitored by NMR.

Diisopropenyldimethylsilane (222)[105]

Magnesium turnings (4.8g, 200mmol) were suspended in dry THF (65ml). 2-bromopropene (17.8ml, 200mmol) was added dropwise, with stirring, so as to maintain a gentle reflux. The resulting mixture was then heated to reflux for 30 minutes. After cooling to room temperature, dichlorodimethylsilane (9.5ml, 78mmol) was added dropwise and the resulting mixture was stirred at room temperature for 18 hours. The mixture was then poured into cold saturated aqueous ammonium chloride solution (50ml). The aqueous layer was extracted with ether (3x20ml). The combined organic layers were dried (MgSO$_4$) and the solvent was removed under reduced pressure. Distillation yielded diisopropenyldimethylsilane (X) (8.78g, 81%) (b.p. 125°C/760mmHg (lit.[105] 126-128°C/760mmHg)) as a colourless liquid. v$_{max}$ (Thin Film) 2948, 1606, 922cm^{-1}; δ(^{1}H) (200MHz; CDCl$_3$) 5.62 (2H, m, 2(HCH=)), 5.29 (2H, m, 2(HCH=)), 1.79 (6H, t, J=1.3Hz, 2(H$_3$C-C=)), 0.16 (6H, s, Si(CH$_3$)$_2$); δ(^{13}C) (50MHz; CDCl$_3$) 145.68, 125.84, 22.34, -4.49; δ(^{29}Si) (99MHz; CDCl$_3$) -9.28; MS (EI) m/z 140 (M$^+$, 5%), 125 ((M-CH$_3$)$^+$, 100), 99 (44), 85 (15), 73 (71).

1,5-Di(4'-bromobenzoyloxy)-2,3,3,4-tetramethyl-3-silapentane (234)

Hydroboration with diisopinocampheylborane

Diisopinocampheylborane (3.62g, 12.7mmol) was suspended in dry hexane (20ml). A solution of diisopropenyldimethylsilane (0.84g, 6mmol) in dry hexane (4ml) was added dropwise. The resulting mixture was stirred at room temperature for 7 days. THF (5ml), 3M

NaOH (4.22ml, 12.7mmol) and 30% H_2O_2 (4.22ml) were added successively and the resulting mixture was heated to reflux for 1 hour. After cooling to room temperature, saturated aqueous potassium carbonate (10ml) was added. The aqueous layer was extracted with ether (3x15ml) and the combined organic extracts were dried (K_2CO_3). The solvent was removed under reduced pressure to afford a mixture of 2,3,3,4-tetramethyl-3-silapenta-1,5-diol and isopinocampheol. This crude mixture was dissolved in dry dichloromethane (20ml) and was added dropwise to a mixture of 4-bromobenzoyl chloride (12.3g, 56mmol), triethylamine (11ml, 75mmol) and 4-dimethylaminopyridine (1.4g, 7.5mmol) in dry dichloromethane (80ml) at 0°C. The resulting mixture was stirred for 5 hours at 20°C. Distilled water (75ml) was added and the aqueous layer was extracted with ether (3x60ml). The combined organic extracts were washed successively with water (75ml) and saturated brine (75ml). The organic layer was dried ($MgSO_4$) and removal of solvent at reduced pressure yielded the crude product. Flash column chromatography,eluting 8% ether in petrol, yielded pure 1,5-di(4'-bromobenzoyloxy)-2,3,3,4-tetramethyl-3-silapentane (2.1g, 63%) as a white, waxy solid. m.p. 61-64°C; α_D=+7.6 (c=5, $CHCl_3$) (de=31%, ee=73%); HPLC (2% ethanol in hexane) (f=1.0ml/min) (UV@230nm) 5.88mins (ent 1, 56.7%), 6.79mins (syn diastereomer, 34.5%), 8.47mins (ent 2, 8.8%).

Hydroboration with 9-BBN

The procedure described for diisopinocampheylborane was used. 9-BBN (0.5M solution in hexane) was substituted for diisopinocampheylborane.

Rhodium catalysed Hydroboration

A Schlenk tube charged with chloro(1,5-cyclooctadiene)rhodium(I) dimer (9.9mg, 0.02mol) and the appropriate phosphine (0.042mmol) was evacuated and flushed three times with nitrogen. THF (2ml) was added and the solution was then cooled to -78°C. Diisopropenyldimethylsilane (280mg, 2mmol) was dissolved in THF (2ml) and added dropwise. The resulting solution was stirred at -78°C for 15 minutes. Catecholborane (4.8ml, 1M Solution in THF, 4.8mmol) was added dropwise and stirring was continued at -78°C for 30 minutes. The reaction mixture was then stirred at -25°C for 5 days. Ethanol (4ml), 3M

NaOH (6.8ml) and 30% H_2O_2(4ml) were added successively at 0°C. After stirring at 0°C for 30 minutes, the reaction mixture was stirred for a further 6 hours at 20°C. 1M NaOH (20ml) was added and the aqueous layer was extracted with ether (3 x 50ml). The combined organic extracts were washed successively with 1M NaOH (50ml), H_2O (50ml) and saturated brine solution (50ml). The organic layer was dried (K_2CO_3) and the solvent was removed under reduced pressure to yield crude 2,3,3,4-tetramethyl-3-silapenta-1,5-diol. The crude product was dissolved in dry dichloromethane (10ml) and was added dropwise to a mixture of 4-bromobenzoyl chloride (1.76g, 8mmol), triethylamine (1.57ml, 10.7mmol) and 4-dimethylaminopyridine (0.2g, 1.07mmol) in dry dichloromethane (40ml) at 0°C. The resulting mixture was stirred for 5 hours at 20°C. Distilled water (50ml) was added and the aqueous layer was extracted with ether (3 x 30ml). The combined organic extracts were washed successively with water (50ml) and saturated brine (50ml). The organic layer was dried ($MgSO_4$) and removal of solvent at reduced pressure yielded the crude product. Flash column chromatography, eluting 8% ether in petrol, yielded pure 1,5-di(4'-bromobenzoyloxy)-2,3,3,4-tetramethyl-3-silapentane as a white solid. m.p. 47-53°C; v_{max} (Thin Film) 2955, 2872, 1718, 1591,1484, 1398, 1273, 1105, 1013cm^{-1}; δ(^{1}H) (500MHz; $CDCl_3$) 7.90-7.55 (8H, m, 2(C_6H_4)), 4.50 (2H, dd, J=11.0, 4.5Hz, 2(CHHOC=O) (anti)), 4.49 (2H, dd, J=11.0, 4.2Hz, 2(CHHOC=O) (syn)), 4.25 (2H, dd, J=11.0, 10.0Hz, 2(CHHOC=O) (anti)), 4.24 (2H, dd, J=11.0, 10.0Hz, 2(CHHOC=O) (syn)), 1.42 (2H, m, 2(SiCHCH$_3$)), 1.15 (6H, d, J=7.2Hz, 2(CHCH$_3$) (syn)), 1.14 (6H, d, J=7.6Hz, 2(CHCH$_3$) (anti)), 0.12 (3H, s, SiCH$_3$ (syn)), 0.11 (6H, s, Si(CH$_3$)$_2$ (anti)), 0.10 (3H, s, SiCH$_3$ (syn)); δ(^{13}C) (125MHz; $CDCl_3$) 166.06, 131.71, 131.01, 129.30, 127.96, 68.54, 19.25, 12.44(anti), 12.36(syn), -6.24(syn), -6.38(anti), -6.39(syn); δ(^{29}Si) (99MHz; $CDCl_3$) 6.25 (anti), 6.18 (syn); MS (CI,(NH$_3$)) (^{79}Br)m/z 558 (M(NH$_4$)$^+$, 1.9%), 299 (36), 274 (56), 257 (98); Analysis Found : C, 48.64%; H, 4.84%. $C_{22}H_{26}Br_2O_4Si$ requires C, 48.72%; H, 4.83%.

μ-Dichlorobis(diisopropenyldimethylsilane) dirhodium(I) (251)

μ-Dichlorotetraethylene dirhodium(I) (1.01g, 2.6mmol) was suspended in ether (10ml). Diisopropenyldimethylsilane (222) (1.46g, 10.4mmol) was added.Stirring at room temperature for 30 minutes led to the formation of a fine orange precipitate. After stirring for a further 90 minutes, the reaction mixture was filtered and the orange solid was washed with cold pentane. After drying *in vacuo* the resulting powder (1.19g, 83%) was used as quickly as possible. $\delta(^1H)$ (400MHz; C_6D_6) 3.58 (2H, broad, =C$\underline{H}$H), 2.70 (2H, broad, =CH$\underline{H}$), 1.60 (6H, broad, 2(C-C$\underline{H}_3$)), 0.50 (3H, broad, Si-C$\underline{H}_3$), -0.44 (3H, broad, Si-C$\underline{H}_3$); $\delta(^{13}C)$ (100MHz; C_6D_6) 68.12 (broad d, J=117Hz, =$\underline{C}H_2$), 65.16 (d, J=10.3Hz, $\underline{C}$=CH$_2$), 24.96 (s, C-$\underline{C}H_3$), 1.38 (s, Si-CH$_3$), -5.43 (s, Si-CH$_3$).

Typical Attempted Rhodium Complex Formation

(Bicyclo[2.2.1]hepta-2,5-diene)[1,4-bis(diphenylphosphino)butane]rhodium(I) tetrafluoroborate (30mg, 0.042mmol) was dissolved in CD_3OD (1ml) in an NMR tube equipped with a Youngs tap. The solution was degassed (three freeze/thaw cycles) and then evacuated and flushed three times with hydrogen. After warming to room temperature, the tube was shaken until the initial orange solution faded to yellow, indicating complete formation of the dimethanol solvate (^{31}P NMR $\delta=56$, $J_{RhP}=199Hz$). Diisopropenyldimethylsilane (24mg, 0.17mmol) was added by vacuum transfer and the resulting mixture was warmed to room temperature under a nitrogen atmosphere. NMR spectra were then obtained at a variety of temperatures.

Diisopropenyldiphenylsilane (227)

Ph   Ph
  \ /
Me   Si   Me

Magnesium turnings (0.92g, 38.5mmol) were suspended in dry THF (12ml). 2-bromopropene

(3.42ml, 38.5mmol) was added dropwise, with stirring, so as to maintain a gentle reflux. The

resulting mixture was then refluxed for 30 minutes. Without cooling, dichlorodiphenylsilane

(3.15ml, 15mmol) was then added dropwise. The resulting mixture was heated to reflux for 18

hours. The mixture was then cooled and poured into cold saturated aqueous ammonium

chloride solution (20ml). The aqueous layer was extracted with ether (3x15ml) and the

combined organic layers were dried (MgSO$_4$). The solvent was removed under reduced

pressure and recrystallisation from hexane yielded white crystals of

diisopropenyldiphenylsilane (1.6g, 41%). m.p. 39-40°C; v_{max} (CHCl$_3$ solution) 3071, 3053,

2947, 1602, 1487, 1452, 1429, 1110, 937cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 7.58-7.35 (10H, m,

Si(C$_6$H$_5$)$_2$), 5.93 (2H, m, 2(HCH=)), 5.43 (2H, m, 2(HCH=)), 1.97 (6H, t, J=1.3Hz,

2(H$_3$C-C=)); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 142.00, 135.92, 133.70, 131.16, 129.33, 127.75,

23.81; $\delta(^{29}Si)$ (99MHz; CDCl$_3$) -14.60; MS (EI) m/z 264 (M$^+$, 67%), 223 ((M-

(H$_3$CC=CH$_2$))$^+$, 100), 197 (70), 183 (65); Analysis Found : C, 81.48%; H, 7.71%. C$_{18}$H$_{20}$Si

requires C, 81.76%; H, 7.62%.

1,5-di(4'-bromobenzoyloxy)-2,4-dimethyl-3,3-diphenyl-3-silapentane (236)

Ph   Ph
  \ /
Me   Si   Me
      | |
      O   O
      | |
  O=   =O
    | |
   Br   Br

Diisopinocampheylborane (1.14g, 2.0mmol) was suspended in dry hexane (16ml). A solution

of diisopropenyldiphenylsilane (227) (0.53g, 2.0mmol) in dry hexane (4ml) was added

dropwise. The resulting mixture was stirred at room temperature for 28 hours. THF (5ml), 3M

NaOH (1.33ml, 4mmol) and 30% H_2O_2 (1.33ml) were added successively and the resulting

mixture was heated to reflux for 1 hour. After cooling to room temperature, saturated aqueous

potassium carbonate (10ml) was added. The aqueous layer was extracted with ether (3x15ml)

and the combined organic extracts were dried (K_2CO_3). The solvent was removed under

reduced pressure to afford a mixture of 2,4-dimethyl-3,3-diphenyl-3-silapenta-1,5-diol and

isopinocampheol. This crude mixture was dissolved in dry dichloromethane (10ml) and added

dropwise to a mixture of 4-bromobenzoyl chloride (3.95g, 18.0mmol), triethylamine (3.52ml,

24.0mmol) and 4-dimethylaminopyridine (0.45g, 2.4mmol) in dry dichloromethane (40ml) at

0°C. The resulting mixture was stirred for 5 hours at 20°C. Distilled water (50ml) was added

and the aqueous layer was extracted with ether (3x30ml). The combined organic extracts were

washed with water (50ml) and saturated brine (50ml). The organic layer was dried ($MgSO_4$)

and removal of solvent at reduced pressure yielded the crude product. Flash column

chromatography, eluting 4% ether in petrol, yielded 1,5-di(4'-bromobenzoyloxy)-2,4-

dimethyl-3,3-diphenyl-3-silapentane as a white solid (0.69g, 52%) with a trace impurity

derived from isopinocampheol. m.p. 47-48°C; v_{max} (Thin Film) 3072, 2958, 2875, 1712,

1592,1485, 1428, 1398, 1272, 1103, 1012cm^{-1}; $\delta(^1H)$ (400MHz; CDCl$_3$) 7.60-7.26 (18H,

m, 2(C$_6$$\underline{H}_5$-) and 2(C$_6$$\underline{H}_4$)), 4.43 (2H, dd, J=10.8, 4.8Hz, 2(CH$\underline{H}$OC=O) (*syn*)), 4.40 (2H,

dd, J=10.8, 5.2Hz, 2(CH$\underline{H}$OC=O) (*anti*)), 3.96 (2H, dd, J=10.8, 10.0Hz, 2(C$\underline{H}$HOC=O)

(*anti*)), 3.95 (2H, dd, J=10.8, 10.4Hz, 2(C$\underline{H}$HOC=O) (*syn*)), 2.11 (2H, m, 2(SiC$\underline{H}$CH$_3$)),

1.04 (6H, d, J=7.2Hz, 2(SiCHC$\underline{H}_3$)); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 165.78, 135.67, 131.50

(*syn*), 131.46 (*anti*), 130.89, 130.67, 129.85, 129.07, 128.12, 127.75, 68.04, 16.88 (*syn*),

16.69 (*anti*), 11.74 (*syn*), 11.65 (*anti*); $\delta(^{29}Si)$ (99MHz; CDCl$_3$) -4.12 (*syn*), -4.15 (*anti*); MS

(DCI,(NH$_3$)) (^{79}Br)*m/z* 682 (M(NH$_4$)$^+$, 12%), 425 (21), 398 (44), 381 (72), 242 (27); HPLC

(2% isopropanol in hexane) (f=0.8ml/min) (UV@230nm) 14.13mins (*syn*, 20%), 15.07mins

(ent 1, 72%), 26.48mins (ent 2, 8%).

Isopropenyldimethylvinylsilane (258)
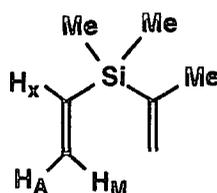
Magnesium turnings (0.6g, 25mmol) were suspended in dry THF (15ml). 2-bromopropene (2.23ml, 25mmol) was added dropwise, with stirring, so as to maintain a gentle reflux. The resulting mixture was then refluxed for 30 minutes. After cooling to room temperature, chlorodimethylvinylsilane (2.73ml, 20mmol) was added dropwise and the resulting mixture was stirred at room temperature for 18 hours. The mixture was poured into cold saturated aqueous ammonium chloride solution (20ml). The aqueous layer was extracted with ether (3x15ml). The combined organic layers were dried (MgSO$_4$) and the solvent was removed under reduced pressure. Distillation at atmospheric pressure yielded isopropenyldimethylvinylsilane together with a little THF (2.3g, ~91%) (b.p. 90-100°C) as a colourless liquid. v_{max} (Thin Film) 3050, 2959, 1594, 1447, 1406, 1250, 1009cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 6.16 (1H, dd, J_{MX}=20.0Hz, J_{AX}=14.8Hz, H_X), 6.00 (1H, dd, J_{AX}=14.8Hz, J_{AM}=4.0Hz, H_A), 5.71 (1H, dd, J_{MX}=20.0Hz, J_{AM}=4.0Hz, H_B), 5.60 (1H, m, CH$_3$-CH=CHH), 5.28 (1H, m, CH$_3$-CH=CHH), 1.82 (3H, dd, J=1.6, 1.2Hz, H_3C-C=CH$_2$), 0.16 (6H, s, Si(CH$_3$)$_2$); δ(^{13}C) (100MHz; CDCl$_3$) 146.33, 137.79, 132.26, 125.63, 22.41, -3.95; MS (GC-MS, EI) m/z 126 (M$^+$, 1.48%), 111 ((M-CH$_3$)$^+$, 100); HRMS (EI) C$_7$H$_{14}$Si m/z Calc. 126.0865; Found 126.0865.

Dimethyldi(α-styryl)silane (220)[105]
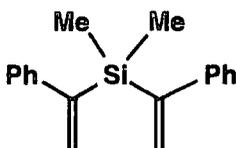
Magnesium turning (4.8g, 200mmol) were suspended in dry THF (64ml). Freshly distilled α-bromostyrene (80% purity from Aldrich) (26ml, 200mmol) was added dropwise, with stirring, so as to maintain a gentle reflux. The resulting mixture was then refluxed for 45 minutes. After removing the heat source, dichlorodimethylsilane (9.5ml, 78mmol) was immediately added.

The resulting mixture was stirred at room temperature for 18 hours. The mixture was then poured into cold saturated aqueous ammonium chloride solution (50ml) and the aqueous layer was extracted with ether (3x50ml). The combined organic layers were dried (MgSO$_4$) and solvent was removed under reduced pressure. Distillation at reduced pressure yielded dimethyldi(α-styryl)silane (b.p. 103-105°C/0.08mmHg (lit.[105] 109-110°C/0.15 torr)) (17.31g, 84% (88% purity)) as a colourless liquid. v_{max} (Thin Film) 3028, 2956, 1597, 1490, 1442, 1400, 1250, 1072, 1022cm^{-1}; $\delta(^1H)$ (500MHz; CDCl$_3$) 7.27 (10H, m, 2(C$_6$H$_5$-)), 6.01 (2H, d, J=3.0Hz, 2(HCH=)), 5.74 (2H, d, J=3.0Hz, 2(HCH=)), 0.33 (6H, s, Si(CH$_3$)$_2$); $\delta(^{13}C)$ (125MHz; CDCl$_3$) 151.05, 144.08, 129.23, 128.09, 126.83, 126.43, -2.07; $\delta(^{29}Si)$ (99MHz; CDCl$_3$) -8.54; MS (EI) m/z 264 (M$^+$, 30%), 135 (100).

1,5-Diacetoxy-3,3-dimethyl-2,4-diphenyl-3-silapentane (269)
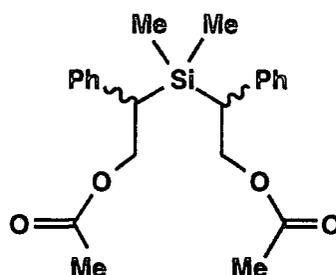
Dimethyldi(α-styryl)silane (220) (3.17g, 12mmol) was dissolved in dry hexane (16ml) and added dropwise to a solution of 9-BBN (56ml, 0.5M solution in hexane, 28mmol). The resulting mixture was heated to reflux for 3 hours. 3M NaOH (9.7ml, 29mmol) and 30% H$_2$O$_2$ (9.7ml) were added successively and the resulting mixture was heated to reflux for 45 minutes. After cooling to room temperature, saturated aqueous potassium carbonate (30ml) was added. The aqueous layer was extracted with ether (3x50ml). The combined organic extracts were washed successively with water (50ml) and brine (50ml) and then dried (K$_2$CO$_3$). The solvent was removed under reduced pressure to afford a mixture of 3,3-dimethyl-2,4-diphenyl-3-silapenta-1,5-diol and 1,5-cyclooctadiol. The crude mixture was dissolved in dry dichloromethane (100ml) and cooled to 0°C. Acetic anhydride (11.3ml, 120mmol), pyridine (14.5ml, 180mmol) and 4-dimethylaminopyridine (3.48g, 18mmol) were added. The resulting mixture was stirred for 18 hours at 20°C. Distilled water (100ml) was added and the aqueous layer was extracted with ether (5x75ml). The combined organic extracts were washed

successively with saturated copper(II) sulphate solution (4x75ml), water (3x75ml) and saturated brine (75ml). The organic layer was dried (MgSO$_4$) and removal of solvent at reduced pressure yielded the crude product. Flash column chromatography, eluting 3:1 petrol:ether, yielded pure 1,5-diacetoxy-3,3-dimethyl-2,4-diphenyl-3-silapentane as a white crystalline solid. m.p. 60-61°C; ν$_{max}$ (CDCl$_3$ Solution) 3028, 2959, 1733, 1601, 1493, 1453, 1386, 1365, 1254, 1027cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.28-7.01 (10H, m, 2(C$_6$H$_5$-)), 4.54 (2H, dd, J=11.2, 10.8Hz, 2(CH$\underline{H}$OC(=O)) (anti)), 4.48 (2H, dd, J=11.2, 10.8Hz, 2(CH$\underline{H}$OC(=O)) (syn)), 4.40 (2H, dd, J=4.4, 4.4Hz, 2(C$\underline{H}$HOC(=O)) (anti)), 4.37 (2H, dd, J=4.4, 4.4Hz, 2(C$\underline{H}$HOC(=O)) (syn)), 2.64 (2H, dd, J=10.8, 4.4Hz, 2(SiC$\underline{H}$Ph) (anti)), 2.56 (2H, dd, J=10.8, 4.4Hz, 2(SiC$\underline{H}$Ph) (syn)), 1.95 (6H, s, 2(O$_2$C(=O)C$\underline{H}_3$) (anti)), 1.94 (6H, s, 2(O$_2$C(=O)C$\underline{H}_3$) (syn)), 0.17 (3H, s, SiC$\underline{H}_3$ (syn)), -0.06 (6H, s, Si(C$\underline{H}_3$)$_2$ (anti)), -0.20 (3H, s, SiC$\underline{H}_3$ (syn)); δ(^{13}C) (100MHz; CDCl$_3$) 171.19, 139.93 (anti), 139.91 (syn), 128.48 (syn), 128.45 (anti), 127.84 (anti), 127.73 (syn), 125.52, 65.40 (anti), 65.34 (syn), 35.17 (anti), 34.80 (syn), 20.96, -4.67 (syn), -5.11 (anti), -5.21(syn); δ(^{29}Si) (99MHz; CDCl$_3$) 3.47; MS (CI,(NH$_3$)) m/z 402 (M(NH$_4$)$^+$, 5%), 246 (36), 134 (100), 117 (76); Analysis Found : C, 68.39%; H, 7.32%. C$_{22}$H$_{28}$O$_4$Si requires C, 68.72%; H, 7.34%.

1,5-Di(2'-chloroacetoxy)-3,3-dimethyl-2,4-diphenyl-3-silapentane (268)
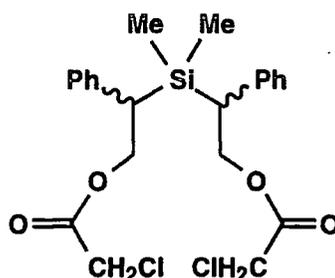
Diisopinocampheylborane (8.19g, 28.6mmol) was suspended in dry hexane (60ml). A solution of dimethyldi(α-styryl)silane (220) (3.58g, 13.6mmol) in dry hexane (16ml) was added dropwise. The resulting mixture was stirred at room temperature for 3 days. 3M NaOH (12ml, 36mmol) and 30% H$_2$O$_2$ (12ml) were added successively and the resulting mixture was heated to reflux for 1 hour. After cooling to room temperature, saturated aqueous potassium carbonate (30ml) was added. The aqueous layer was extracted with ether (3x50ml) and the

combined organic extracts were dried (K_2CO_3). The solvent was removed under reduced pressure to afford a mixture of 3,3-dimethyl-2,4-diphenyl-3-silapenta-1,5-diol and isopinocampheol. This crude mixture was dissolved in dry dichloromethane (150ml) and cooled to 0°C. Chloroacetyl chloride (10.8ml, 136mmol), triethylamine (26.4ml, 180mmol) and 4-dimethylaminopyridine (3.5g, 18mmol) were added. The resulting mixture was stirred for 5 hours at 20°C. Distilled water (100ml) was added and the aqueous layer was extracted with ether (3x100ml). The combined organic extracts were washed with water (100ml) and saturated brine (100ml). The organic layer was dried ($MgSO_4$) and evaporation of solvent under reduced pressure yielded the crude product. Flash column chromatography, eluting 3:1 petrol:ether, yielded pure 1,5-di(2'-chloroacetoxy)-3,3-dimethyl-2,4-diphenyl-3-silapentane as a white crystalline solid. m.p. 97-98°C; v_{max} ($CDCl_3$ Solution) 3029, 2958, 1752, 1601, 1493, 1453, 1413, 1310, 1257, 1180cm^{-1}; $\delta(^1H)$ (400MHz; $CDCl_3$) 7.30-7.00 (10H, m, 2($C_6\underline{H}_5$-)), 4.63 (2H, dd, J=11.0, 11.0Hz, 2(CH$\underline{H}$OC(=O)) (*anti*)), 4.58 (2H, dd, J=11.0, 11.0Hz, 2(CH$\underline{H}$OC(=O)) (*syn*)), 4.49 (2H, dd, J=11.0, 4.4Hz, 2(C$\underline{H}$HOC(=O)) (*syn*)), 4.46 (2H, dd, J=11.0, 4.4Hz, 2(C$\underline{H}$HOC(=O)) (*anti*)), 3.91 (4H, AB system, J_{AB}=15.2Hz, 2(C$\underline{H}_2$Cl) (*anti*)), 3.90 (4H, AB system, J_{AB}=15.2Hz, 2(C$\underline{H}_2$Cl) (*syn*)), 2.68 (2H, dd, J=11.0, 4.4Hz, 2(SiC$\underline{H}$Ph) (*anti*)), 2.61 (2H, dd, J=11.0, 4.4Hz, 2(SiC$\underline{H}$Ph) (*syn*)), 0.20 (3H, s, SiC$\underline{H}_3$ (*syn*)), -0.01 (6H, s, Si(C$\underline{H}_3)_2$ (*anti*)), -0.14 (3H, s, SiC$\underline{H}_3$ (*syn*)); $\delta(^{13}C)$ (100MHz; $CDCl_3$) 167.38, 139.14, 128.63 (*syn*), 128.59 (*anti*), 127.77 (*anti*), 127.66 (*syn*), 125.81, 67.16 (*anti*), 67.09 (*syn*), 40.74, 35.22 (*anti*), 34.85 (*syn*), -4.62 (*syn*), -5.10 (*anti*), -5.10 (*syn*); $\delta(^{29}Si)$ (99MHz; $CDCl_3$) 3.44; MS (CI,(NH_3)) (^{35}Cl)m/z 470 (M(NH_4)$^+$, 7%), 168 (100); Analysis Found : C, 58.30%; H, 5.96%. $C_{22}H_{26}Cl_2O_4Si$ requires C, 58.28%; H, 5.78%.

1,5-Di(4'-bromobenzyloxy)-3,3-dimethyl-2,4-diphenyl-3-silapentane (235)
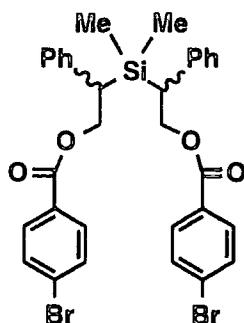
Diisopinocampheylborane (3.02g, 10.58mmol) was suspended in dry hexane (20ml) and cooled to 0°C. A solution of dimethyldi(α-styryl)silane (220) (1.32g, 5mmol) in dry hexane (4ml) was added dropwise. The resulting mixture was stirred at room temperature for 18 hours. The resulting cloudy solution was warmed to 40°C to dissolve all remaining solids. After cooling to room temperature (the solution remained clear), 3M NaOH (3.33ml, 10mmol) and 30% H_2O_2 (3.33ml) were added successively and the resulting mixture was heated to reflux for 1 hour. After cooling to room temperature, saturated aqueous potassium carbonate (10ml) was added. The aqueous layer was extracted with ether (3x15ml) and the combined organic extracts were dried (K_2CO_3). The solvent was removed under reduced pressure to afford a mixture of 3,3-dimethyl-2,4-diphenyl-3-silapenta-1,5-diol and isopinocampheol. This crude mixture was dissolved in dry dichloromethane (20ml) and was added dropwise to a mixture of 4-bromobenzoyl chloride (10.2g, 47mmol), triethylamine (9.1ml, 62mmol) and 4-dimethylaminopyridine (1.2g, 6.2mmol) in dry dichloromethane (80ml) at 0°C. The resulting mixture was stirred for 5 hours at 20°C. Distilled water (75ml) was added and the aqueous layer was extracted with ether (3 x 60ml). The combined organic extracts were washed with water (75ml) and saturated brine (75ml). The organic layer was dried ($MgSO_4$) and removal of solvent at reduced pressure yielded the crude product. Flash column chromatography with gradient elution (2% ether in petrol to 25% ether in petrol), yielded pure 1,5-di(4'-bromobenzoyloxy)-3,3-dimethyl-2,4-diphenyl-3-silapentane as a white, crystalline solid. (Repeated recrystallisation from hot hexane improved both de and ee values given below.) m.p. 114-115°C; α_D=-7.21 (c=5.5, CHCl$_3$) (de=54%, ee=79%); HPLC (2% ethanol in heptane) (f=0.5ml/min) (UV@230nm) 14.77mins (ent 1, 69%), 15.83 (ent 2, 8%), 18.66

(*syn*, 23%); ν_{max} (CDCl$_3$ Solution) 3029, 2958, 1752, 1601, 1493, 1453, 1413, 1310, 1257, 1180cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.70-7.46 (8H, m, 2(O$_2$CC$_6$H$_4$Br)), 7.30-7.00 (10H, m, 2(C$_6$H$_5$CHSi)), 4.77-4.65 (4H, m, 2(CH$_2$OC(=O))), 2.82 (2H, dd, J=10.8, 4.8Hz, 2(SiCHPh) (*anti*)), 2.75 (2H, dd, J=10.8, 4.8Hz, 2(SiCHPh) (*syn*)), 0.27 (3H, s, SiCH$_3$ (*syn*)), 0.06 (6H, s, Si(CH$_3$)$_2$ (*anti*)), -0.07 (3H, s, SiCH$_3$ (*syn*)); δ(^{13}C) (100MHz; CDCl$_3$) 165.91, 139.63, 131.60, 130.93, 129.04 (*syn*), 129.00 (*anti*), 128.60 (*syn*), 128.56 (*anti*), 127.94 (*syn*), 127.87 (*anti*), 127.75, 125.66, 66.11 (*anti*), 66.02 (*syn*), 35.36 (*anti*), 35.10 (*syn*), -4.59 (*syn*), -4.98 (*syn*), -5.06(*anti*); δ(^{29}Si) (99MHz; CDCl$_3$) 3.31 (*anti*), 3.21 (*syn*); MS (DCI,(NH$_3$)) (^{79}Br)m/z 682 (M(NH$_4$)$^+$, 0.5%), 407 (28), 363 (15), 259 (100); Analysis Found : C, 57.93%; H, 4.49%. C$_{32}$H$_{30}$Br$_2$O$_4$Si requires C, 57.84%; H, 4.25%.

1,1-Dimethyl-2,6-diphenyl-1-silacyclohexan-4-one (266)[105]
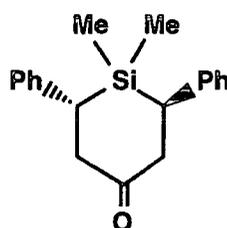
Diisopinocampheylborane (0.6g, 2.1mmol) was suspended in dry hexane (3ml) and cooled to 0°C. A solution of dimethyldi(α-styryl)silane (220) (0.26g, 1.0mmol) in dry hexane (2ml) was added dropwise and the resulting mixture was stirred at room temperature for 18 hours. The resulting cloudy solution was warmed to 40°C to dissolve all remaining solids. Borane-dimethyl sulfide complex (0.1ml, 1.0mmol) was added dropwise and the resulting mixture was refluxed for 3 hours. After cooling to room temperature, methanol (0.12ml) was added and solvent was removed *in vacuo*. The crude mixture was dissolved in THF (10ml) and cooled to 0°C. 1,1-Dichlorodimethyl ether (0.32ml, 3.5mmol) was added dropwise. ^{t}Butanol (1.30g, 17.5mmol) was dissolved in THF (10ml) and cooled to 0°C. ^{n}Butyllithium (9ml, 2M solution in hexane, 18mmol) was added dropwise and the resulting solution was stirred for 10 minutes at 0°C. The resulting solution of lithium ^{t}butoxide was added dropwise to the reaction mixture at 0°C. It was stirred at 0°C for 10 minutes and then at room temperature for 30 minutes. Ethanol (3ml), water (0.8ml), sodium hydroxide pellets (0.42g, 10.5mmol) and 30% H$_2$O$_2$

(1.37ml) were added and the resulting mixture was heated to reflux for 90 minutes. After cooling to room temperature, brine (20ml) was added and the resulting aqueous layer was extracted with ether (3x20ml). The combined organic extracts were dried (K_2CO_3) and solvent was removed under reduced pressure. Distillation (75°C/0.02mmHg) removed most of the isopinocampheol. Column chromatography on alumina, eluting neat petrol to remove styrene and then 8:1:0.1 petrol:ether:isopropanol, yielded pure 1,1-dimethyl-2,6-diphenyl-1-silacyclohexan-4-one (62mg, 21%) as a white crystalline solid. m.p. 109-111°C; v_{max} (CDCl$_3$ Solution) 3010, 2959, 1700, 1598, 1495, 1450, 1252, 1114, 1080cm^{-1}; $\delta(^1H)$ (500MHz; CDCl$_3$) 7.20-7.00 (10H, m, 2(C$_6$H$_5$-)), 3.17 (2H, dd, J=12.8, 11.2Hz, 2(CHHC(=O)) (syn)), 3.05 (2H, dd, J=15.6, 12.8Hz, 2(CHHC(=O)) (anti)), 2.88 (2H, dd, J=15.6, 4.4Hz, 2(CHHC(=O)) (anti)), 2.79 (2H, dd, J=11.2, 4.1Hz, 2(CHHC(=O)) (syn)), 2.68 (2H, dd, J=12.8, 4.4Hz, 2(SiCHPh) (anti)), 2.64 (2H, dd, J=12.8, 4.1Hz, 2(SiCHPh) (syn)), 0.02 (3H, s, SiCH$_3$ (syn)), -0.10 (6H, s, Si(CH$_3$)$_2$ (anti)), -0.11 (3H, s, SiCH$_3$ (syn)); $\delta(^{13}C)$ (100MHz; CDCl$_3$) 212.58, 141.85, 128.61 (anti), 128.55 (syn), 126.44, 125.23 (syn), 125.06 (anti), 45.21 (syn), 43.71 (anti), 34.14 (syn), 29.98 (anti), -5.89 (syn), -5.88 (anti), -10.00 (syn); $\delta(^{29}Si)$ (99MHz; CDCl$_3$) -3.95; MS (EI) m/z 294 (M$^+$, 27%), 190 (100), 175 (49), 75 (70).

3,3-Dimethyl-2,4-diphenyl-3,-silapentane-1,5-diol (270)
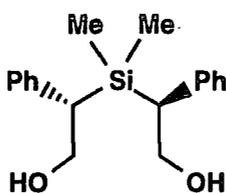
1,5-Diacetoxy-3,3-dimethyl-2,4-diphenyl-3-silapentane (192mg, 0.5mmol) was dissolved in dichloromethane (5ml) and cooled to -78°C. Diisobutylaluminium hydride (2.8ml, 1M solution in hexane, 2.8mmol) was added dropwise. Stirring was continued as the reaction mixture was allowed to slowly reach 10°C. Afer cooling to -78°C, methanol (0.46ml, 22.4mmol) was added and the reaction was warmed to 20°C. Water (0.41ml, 22.4mmol) was added and the reaction stirred until a gel formed. Celite was added to the gel and the resulting solid was filtered through a celite plug which was washed with ethyl acetate. Removal of solvent under

reduced pressure yielded 3,3-dimethyl-2,4-diphenyl-3,-silapentane-1,5-diol as a white crystalline solid (150mg, 100%). This was used without further purification. m.p. 75-78°C (dec.); ν_{max} (CDCl$_3$ Solution) 3594 (sharp), 3429 (broad), 3026, 2959, 2881, 1600, 1490, 1452, 1389, 1253, 1041cm^{-1}; δ(^{1}H) (400MHz; CDCl$_3$) 7.30-7.04 (10H, m, 2(C$_6$H$_5$-)), 4.00 (2H, m, 2(CHHOH)), 3.88 (2H, m, 2(CHHOH)), 2.52 (2H, dd, J=10.0, 5.2Hz, 2(PhCH) (*anti*)), 2.43 (2H, dd, J=10.8, 4.8Hz, 2(PhCH) (*syn*)), 2.08 (2H, broad s , 2(OH) (*anti*)), 1.84 (2H, broad s , 2(OH) (*syn*)), 0.11 (3H, s, SiCH$_3$ (*syn*)), -0.10 (6H, s, Si(CH$_3$)$_2$ (*anti*)), -0.24 (3H, s, SiCH$_3$ (*syn*)); δ(^{13}C) (100MHz; CDCl$_3$) 140.32 (*anti*), 140.17 (*syn*), 128.63 (*syn*), 128.55 (*anti*), 128.13 (*anti*), 128.04 (*syn*), 125.48 (*syn*), 125.42 (*anti*), 63.32 (*anti*), 63.21 (*syn*), 39.49 (*anti*), 39.30 (*syn*), -4.68 (*syn*), -5.20 (*anti*), -5.41 (*syn*); MS (CI, (NH$_3$)) m/z 318 (M(NH$_4$)$^+$, 5%), 219 (40), 196 (21), 179 (93), 144 (100).

Attempted Formation of 1-Oxa-4,4-dimethyl-3,5-diphenyl-4-silacyclohexane (271)
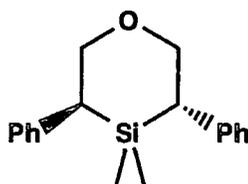
Triphenylphosphine (1.69g, 6.43mmol) was dissolved in benzene (60ml) under an atmosphere of argon. Diethyl azodicarboxylate (1.01ml, 6.43mmol) was added dropwise and the resulting reaction mixture was stirred for 5 minutes at room temperature. 3,3-Dimethyl-2,4-diphenyl-3,-silapentane-1,5-diol (270) (0.64g, 2.14mmol) was dissolved in benzene (30ml) and added dropwise to the reaction. The resulting solution was stirred for one hour. Removal of solvent at reduced pressure and the addition of hexane led to precipitation of a white solid which was removed by filtration through a celite plug. Subsequent removal of hexane under reduced pressure led to the crude product. δ(^{1}H) (400MHz; CDCl$_3$) 7.50-7.25 (10H, m, 2(C$_6$H$_5$-)), 4.70-4.20 (4H, m, 2(CH$_2$O)), 1.30-1.00 (2H, m, 2(PhCH)), 0.37, 0.07, -0.20 (6H, 3s, Si(CH$_3$)$_2$).

APPENDIX

Appendix

UNIVERSITY OF DURHAM

Board of Studies in Chemistry

COLLOQUIA, LECTURES AND SEMINARS FROM INVITED SPEAKERS

1991 - 1994

1991

October 17   Dr. J. A. Salthouse, University of Manchester
               * *Son et Lumiere - a demonstration lecture.*

October 31   Dr. R. Keely, Metropolitan Police Forensic Science
               * *Modern Forensic Science.*

November 6   Prof. B. F. G. Johnson†, University of Edinburgh
               Cluster-Surface Analogies.

November 7   Dr. A. R. Butler, St. Andrews University
               * *Traditional Chinese Herbal Drugs.*

November 13   Prof. D. Gani†, St. Andrews University
               * *The Chemistry of PLP Dependant Enzymes.*

November 20   Dr. R. More O'Ferrall†, Dublin
               * *Some Acid-Catalysed Rearrangements in Organic Chemistry.*

November 28   Prof. I. M. Ward, Leeds University
               The Science & Technology of Orientated Polymers.

December 4   Prof. R. Grigg†, Leeds University
               * *Palladium Catalysed Cyclisation and Ion Capture Processes.*

December 5   Prof. A. L. Smith, ex Unilever
               Soap Detergents and Black Puddings.

December 11   Dr. W. A. Cooper†, Shell Research
               Colloid Science, Theory, and Practice.

1992

January 16   Dr. N. J. Long, University of Exeter
               Metallocenophanes-Chemical sugar-tongs.

January 22   Dr. K. D. M. Harris†, University of St. Andrews
               Understanding the Properties of Solid Inclusion Compounds.

January 29   Dr. A. Holmes†, University of Cambridge
               * *Cycloaddition Reactions in the Service of the Synthesis of Piperidine and ndolizidine Natural Products.*

January 30   Dr. M. Anderson, Sittingbourne Research Centre, Shell Research
                * *Recent Advances in the Safe and Selective Chemical Control of Insect Pests.*

February 12   Dr. D. E. Fenton†, University of Sheffield
                Polynuclear Complexes of Molucular Clefts as Models for Copper Biosites.

February 13   Dr. J. Saunders, Glaxo Group Research Limited
                * *Molecular Modelling in Drug Discovery.*

February 19   Prof. E. J. Thomas†, University of Manchester
                * *Application of Organo-Stannanes to Organic Synthesis.*

February 20   Prof. E. Vogel, University of Cologne
                * *The Musgrave Lecture: Porrphyrins, Molecules of Interdisciplinary Interest.*

February 25   Prof. J. F. Nixon, University of Sussex
                * *Phosphoalkylenes, New Building Blocks in Inorganic and
                Organometallic Chemistry.*

February 26   Prof. M. L. Hitchman†, University of Strathclyde
                Chemical Vapour Deposition.

March 5   Dr. N. C. Billingham, University of Sussex
                Degradable Plastics - Myth or Magic ?

March 11   Dr. S. E. Thomas†, Imperial College London
                * *Recent Advances in Organoiron Chemistry.*

March 12   Dr. R. A. Hann, ICI Image Data
                * *Electronic Photography - An Image of the Future*

March 18   Dr H. Maskill†, University of Newcastle
                * *Concerted or stepwise fragmentation in a deamination-type reaction.*

April 7   Prof. D. M. Knight, Philosophy Department, University of Durham
                Interpreting experiments: the begining of electrochemistry.

May 13   Dr. J-C. Gehret, Ciba Geigy, Basel
                * *Some aspects of Industrial Agrochemical Research.*

October 15   Dr M. Glazer & Dr. S. Tarling, Oxford University & Birbeck College, London
                * *It Pays to be British! - The Chemist's Role as an Expert Witness in
                Patent Litigation.*

October 20   Dr. H. E. Bryndza, Du Pont Central Research
                * *Synthesis, Reactions and Thermochemistry of Metal (Alkyl) Cyanide
                Complexes and Their Impact on Olefin Hydrocyanation Catalysis.*

October 22   Prof. A. Davies, University College London
                * *The Ingold-Albert Lecture The Behaviour of Hydrogen as a Pseudometal.*

October 28   Dr. J. K . Cockcroft, University of Durham
                Recent Developments in Powder Diffraction.

October 29   Dr. J. Emsley, Imperial College, London
                * *The Shocking History of Phosphorus.*

November 4   Dr. T. P. Kee, University of Leeds
              * *Synthesis and Co-ordination Chemistry of Silylated Phosphites.*

November 5   Dr. C. J. Ludman, University of Durham
              * *Explosions, A Demonstration Lecture.*

November 11   Prof. D. Robins†, Glasgow University
              * *Pyrrolizidine Alkaloids : Biological Activity, Biosynthesis and Benefits.*

November 12   Prof. M. R. Truter, University College, London
              * *Luck and Logic in Host - Guest Chemistry.*

November 18   Dr. R. Nix†, Queen Mary College, London
              Characterisation of Heterogeneous Catalysts.

November 25   Prof. Y. Vallee. University of Caen
              * *Reactive Thiocarbonyl Compounds.*

November 25   Prof. L. D. Quin†, University of Massachusetts, Amherst
              * *Fragmentation of Phosphorous Heterocycles as a Route to Phosphoryl Species with Uncommon Bonding.*

November 26   Dr. D. Humber, Glaxo, Greenford
              * *AIDS - The Development of a Novel Series of Inhibitors of HIV.*

December 2   Prof. A. F. Hegarty, University College, Dublin
              Highly Reactive Enols Stabilised by Steric Protection.

December 2   Dr. R. A. Aitken†, University of St. Andrews
              * *The Versatile Cycloaddition Chemistry of Bu3P.CS2.*

December 3   Prof. P. Edwards, Birmingham University
              * *The SCI Lecture - What is a Metal?*

December 9   Dr. A. N. Burgess†, ICI Runcorn
              The Structure of Perfluorinated Ionomer Membranes.

1993

January 20   Dr. D. C. Clary†, University of Cambridge
              Energy Flow in Chemical Reactions.

January 21   Prof. L. Hall, Cambridge
              * *NMR - Window to the Human Body.*

January 27   Dr. W. Kerr, University of Strathclyde
              * *Development of the Pauson-Khand Annulation Reaction : Organocobalt Mediated Synthesis of Natural and Unnatural Products.*

January 28   Prof. J. Mann, University of Reading
              * *Murder, Magic and Medicine.*

February 3   Prof. S. M. Roberts, University of Exeter
              * *Enzymes in Organic Synthesis.*

February 10   Dr. D. Gillies†, University of Surrey
              NMR and Molecular Motion in Solution.

February 11   Prof. S. Knox, Bristol University
               * *The Tilden Lecture: Organic Chemistry at Polynuclear Metal Centres.*

February 17   Dr. R. W. Kemmitt†, University of Leicester
               Oxatrimethylenemethane Metal Complexes.

February 18   Dr. I. Fraser, ICI Wilton
               Reactive Processing of Composite Materials.

February 22   Prof. D. M. Grant, University of Utah
               Single Crystals, Molecular Structure, and Chemical-Shift Anisotropy.

February 24   Prof. C. J. M. Stirling†, University of Sheffield
               Chemistry on the Flat-Reactivity of Ordered Systems.

March 10   Dr. P. K. Baker, University College of North Wales, Bangor
               * *Chemistry of Highly Versatile 7-Coordinate Complexes*

March 11   Dr. R. A. Y. Jones, University of East Anglia
               * *The Chemistry of Wine Making.*

March 17   Dr. R. J. K. Taylor†, University of East Anglia
               * *Adventures in Natural Product Synthesis.*

March 24   Prof. I. O. Sutherland†, University of Liverpool
               * *Chromogenic Reagents for Cations.*

May 13   Prof. J. A. Pople, Carnegie-Mellon University, Pittsburgh, USA
               The Boys-Rahman Lecture: Applications of Molecular Orbital Theory

May 21   Prof. L. Weber, University of Bielefeld
               Metallo-phospha Alkenes as Synthons in Organometallic Chemistry

June 1   Prof. J. P. Konopelski, University of California, Santa Cruz
               * *Synthetic Adventures with Enantiomerically Pure Acetals*

June 2   Prof. F. Ciardelli, University of Pisa
               Chiral Discrimination in the Stereospecific Polymerisation of Alpha Olefins

June 7   Prof. R. S. Stein, University of Massachusetts
               Scattering Studies of Crystalline and Liquid Crystalline Polymers

June 16   Prof. A. K. Covington, University of Newcastle
               * *Use of Ion Selective Electrodes as Detectors in Ion Chromatography.*

June 17   Prof. O. F. Nielsen, H. C. Arsted Institute, University of Copenhagen
               Low-Frequency IR - and Raman Studies of Hydrogen Bonded Liquids.

September 13   Prof. Dr. A. D. Schlüter, Freie Universität Berlin, Germany
               Synthesis and Characterisation of Molecular Rods and Ribbons.

September 13   Prof. K. J. Wynne, Office of Naval Research, Washington, U.S.A.
               Polymer Surface Design for Minimal Adhesion

September 14   Prof. J. M. DeSimone, University of North Carolina, Chapel Hill, U.S.A.
               *Homogeneous and Heterogeneous Polymerisations in Enviromentally
               Responsible Carbon Dioxide.*

September 28   Prof. H. Ila., North Eastern University, India
* *Synthetic Strategies for Cyclopentanoids via OxoKetene Dithiacetals.*

October 4   Prof. F. J. Feher†, University of California at Irvine
Bridging the Gap between Surfaces and Solution with Sessilquioxanes.

October 14   Dr. P. Hubberstey, University of Nottingham
* *Alkali Metals: Alchemist's Nightmare, Biochemist's Puzzle and Technologist's Dream.*

October 20   Dr. P. Quayle†, University of Manchester
* *Aspects of Aqueous Romp Chemistry.*

October 23   Prof. R. Adams†, University of S. Carolina
The Chemistry of Metal Carbonyl Cluster Complexes Containing Platinum and Iron, Ruthenium or Osmium and the Development of a Cluster Based Alkyne Hydrogenating Catalyst.

October 27   Dr. R. A. L. Jones†, Cavendish Laboratory
'Perambulating Polymers'.

November 10   Prof. M. N. R. Ashfold†, University of Bristol
High-Resolution Photofragment Translational Spectroscopy: A New Way to Watch Photodissociation.

November 17   Dr. A. Parker†, Laser Support Facility
Applications of Time Resolved Resonance Raman Spectroscopy to Chemical and Biochemical Problems.

November 24   Dr. P. G. Bruce†, University of St. Andrews
Synthesis and Applications of Inorganic Materials.

November 25   Dr. R.P. Wayne, University of Oxford
* *The Origin and Evolution of the Atmosphere*

December 1   Prof. M. A. McKervey†, Queens University, Belfast
* *Functionlised Calixarenes.*

December 8   Prof. O. Meth-Cohen, Sunderland University
* *Friedel's Folly Revisited.*

December 16   Prof. R. F. Hudson, University of Kent
Close Encounters of the Second Kind.

1994

January 26   Prof. J. Evans†, University of Southhampton
* *Shining Light on Catalysts.*

February 2   Dr. A. Masters†, University of Manchester
Modelling Water Without Using Pair Potentials.

February 9   Prof. D. Young†, University of Sussex
* *Chemical and Biological Studies on the Coenzyme Tetrahydrofolic Acid.*

February 16   Prof. K. H. Theopold, University of Delaware, U.S.A
* *Paramagnetic Chromium Alkyls: Synthesis and Reactivity.*

February 23   Prof. P. M. Maitlis†, University of Sheffield
               * *Why Rodium in Homogenous Catalysis.*

March 2   Dr. C. Hunter†, University of Sheffield
               Non Covalent Interactions between Aromatic Molecules.

March 9   Prof. F. Wilkinson, Loughborough University of Technology
               Nanosecond and Picosecond Laser Flash Photolysis.

March 10   Prof. S.V. Ley, University of Cambridge
               New Methods for Organic Synthesis.

March 25   Dr. J. Dilworth, University of Essex
               * *Technetium and Rhenium Compounds with Applications as Imaging Agents.*

April 28   Prof. R. J. Gillespie, McMaster University, Canada
               The Molecular Structure of some Metal Fluorides and OxoFluorides: Apparent Exceptions to the VSEPR Model.

May 12   Prof. D. A. Humphreys, McMaster University, Canada
               * *Bringing Knowledge to Life*

(* Indicates lectures attended by the author)
(† Invited specially for the graduate training programme)

RESEARCH CONFERENCES ATTENDED

December 1991	Modern Aspects of Stereochemistry at SheffieldUniversity
December 1992	Modern Aspects of Stereochemistry at SheffieldUniversity
December 1993	Modern Aspects of Stereochemistry at SheffieldUniversity

SEMINARS, COLLOQUIA AND POSTER PRESENTATIONS

December 1993	¥	ICI Poster Competition, University of Durham
January 1994	¤	Zeneca Medicinal Chemistry Workshop
April 1994	¤	SCI Postgraduate Symposium, Heriot Watt University
June 1994	¤	University of Durham Graduate Colloquia

(¤ indicates oral presentation by author)
(¥ indicates poster presentation by author)

PAPERS PUBLISHED

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REFERENCES

1. F.S. Kipping, *Proc. R. Soc. London, Ser. A*, 1937, 159, 139.

2. J.S. Panek, in *Comprehensive Organic Synthesis*, ed. B.M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 1, p. 579.

3. R.S. Berry, *J. Chem. Phys.*, 1960, 32, 933; R.S. Berry, *Rev. Mod. Phys.*, 1960, 32, 447.

4. M. Lalonde and T.H. Chan, *Synthesis*, 1985, 817.

5. T.H. Chan and I. Fleming, *Synthesis*, 1979, 761.

6. I. Fleming and I. Paterson, *Synthesis*, 1979, 445.

7. A. Hosomi and H. Sakurai, *Tetrahedron Lett.*, 1976, 1295.

8. T.H. Chan, P.W.K. Lau and W. Mychjlowskij, *Tetrahedron Lett.*, 1977, 3317.

9. C.J. Saward and K.P.C. Vollhardt, *Tetrahedron Lett.*, 1975, 4539.

10. I. Fleming, *Chem. Soc. Rev.*, 1981, 10, 83.

11. S.E. Denmark and T.K. Jones, *J. Am. Chem. Soc.*, 1982, 104, 2642.

12. G.T. Crisp, W.J. Scott and J.K. Stille, *J. Am. Chem. Soc.*, 1984, 106, 7500.

13. W.S. Johnson, T.M. Yarnell, R.F. Myers and D.R. Morton, *Tetrahedron Lett.*, 1978, 2549.

14. P. Brownbridge, *Synthesis*, 1983, 1 and 85.

15. T.H. Chan, I. Paterson and J. Pinsonnault, *Tetrahedron Lett.*, 1977, 4183.

16. T. Mukaiyama, K. Banno and K. Narasaka, *J. Am. Chem. Soc.*, 1974, 96, 7503.

17. T. Mukaiyama, in *Organic Reactions*, ed. W.G. Dauben, John Wiley and Sons, Inc., New York, 1982, 28, 203.

18. T. Mukaiyama, *Angew. Chem. Int. Ed. Engl.*, 1977, 16, 817.

19. G. Stork and B. Ganem, *J. Am. Chem. Soc.*, 1973, 95, 6152; G. Stork and J. Singh, *J. Am. Chem. Soc.*, 1974, 96, 6181.

20. R.K. Boeckmann, *Tetrahedron*, 1983, 39, 925.

21. D.J. Peterson, *J. Org. Chem.*, 1968, 33, 781.

22. R.K. Boeckmann and S.M. Silver, *J. Org. Chem.*, 1975, 40, 1755.

23.   A.G. Brook and A.R. Bassindale, in *Rearrangements in Ground and Excited States*, ed. P.de Mayo, Academic Press, New York, 1980, Vol. 2, pp. 149-227.

24.   S. Danishefsky, *Acc. Chem. Res.*, 1981, 14, 400.

25.   M.E. Jung, C.A. McCombs, Y. Takeda and Y.-G. Pan, *J. Am. Chem. Soc.*, 1981, 103, 6677.

26.   S. Danishefsky and M. Hirama, *J. Am. Chem. Soc.*, 1977, 99, 7740.

27.   E. Colvin, 'Silicon in Organic Synthesis', Butterworth, London, 1981, Chapter 17, p 243.

28.   J.J. Bloomfield and J.M. Nolke, *Organic Reactions*, 1976, 23, 259.

29.   R.E. Ireland and C.S. Wilcox, *Tetrahedron Lett.*, 1977, 2839; R.E. Ireland, S. Thaisrivongs and C.S. Wilcox, *J. Am. Chem. Soc.*, 1980, 102, 1155.

30.   J. Boyd, W. Epstein and G. Frater, *J. Chem. Soc. Chem. Commun.*, 1976, 380.

31.   R. Calas and J. Dunoguès, *J. Organomet. Chem. Rev.*, 1976, 2, 277; R. Calas, *J. Organomet. Chem.*, 1980, 200, 11.

32.   I. Ojima, M. Nihonyanagi and Y. Nagai, *Chem. Commun.*, 1972, 938; I. Ojima, M. Nihonyanagi, T. Kogure, M. Kumagai, S. Horuichi, K. Nakatsugawa, *J. Organometal. Chem.*, 1975, 94, 449.

33.   I. Ojima, T. Kogure and Y. Nagai, *Tetrahedron Lett.*, 1972, 5035.

34.   I. Ojima, K. Yamamoto and M. Kumada, in *Aspects of Homogeneous Catalysis*, ed. R. Ugo, Reidel, Dordrecht, Nederland, 1977, vol. 3, chapter 3.

35.   D.N. Kursanov, Z.N. Parnes and N.M. Loim, *Synthesis*, 1974, 633.

36.   G.A. Kraus, K.A. Frazier, B.D. Roth, M.J. Taschner and K. Neuenschwander, *J. Org. Chem.*, 1981, 46, 2417.

37.   C. Chatgilialoglu, *Acc. Chem. Res.*, 1992, 25, 188; M. Ballestri, C. Chatgilialoglu, K.B. Clark, D. Griller, B. Geise and B. Kopping, *J. Org. Chem.*, 1991, 56, 678.

38.   K.J. Kulicke and B. Giese, *Synlett*, 1990, 91.

39.   B. Giese and B. Kopping, *Tetrahedron Lett.*, 1989, 30, 681.

40. G. Stork and G. Kim, *J. Am. Chem. Soc.*, 1992, **114**, 1087; G. Stork, H.S. Suh and G. Kim, *J. Am. Chem. Soc.*, 1991, **113**, 7054.

41. E.W. Colvin, in *The Chemistry of the Metal-Carbon Bond*, ed. F.R. Hartley , John Wiley & Sons, New York, 1987, Vol. 4, Chapter 6, p. 539.

42. J.D. White and B.J. Sheldon, *J. Org. Chem.*, 1981, **46**, 2273.

43. R.L. Funk, C.J. Mossman and W.E. Zeller, *Tetrahedron Lett.*, 1984, 1655.

44. G. Frater, *Tetrahedron Lett.*, 1976, 4517.

45. G.A. Kraus, D. Gougie, R.A. Jacobson and S. Ying Zhong, *J. Org. Chem.*, 1989, **54**, 2425.

46. J.W. Gillard, R. Fortin, E.L. Grimm, M. Maillard, M. Tjepkema, M.A. Bernstein and R. Glaser, *Tetrahedron Lett.*, 1991, **32**, 1145.

47. S.McN. Sieburth and L. Fensterbank, *J. Org. Chem.*, 1992, **57**, 5279.

48. M.T. Crimmins and L.E. Guise, *Tetrahedron Lett.*, 1994, **35**, 1657.

49. N. Nishiyama, T. Kitajama, M. Matsumoto and K. Itoh, *J. Org. Chem.*, 1985, **49**, 2298; G. Stork and M. Kahn, *J. Am. Chem. Soc.*, 1985, **107**, 500.

50. M. Journet and M. Malacria, *J. Org. Chem.*, 1992, **57**, 3085.

51. S.J. Hathaway and L.A. Paquette, *J. Org. Chem.*, 1983, **48**, 3351.

52. T.H. Chan and D. Wang, *Chem. Rev.*, 1992, **92**, 995.

53. L.H. Sommer, 'Stereochemistry, Mechanism and Silicon', McGraw Hill, New York, 1965.

54. G. Larson, S. Sandoval, F. Cartledge and F.R. Froonczek, *Organometallics*, 1983, **2**, 810.

55. J.L. Fry and M.A.McAdam, *Tetrahedron Lett.*, 1984, **25**, 5859.

56. R.G. Daniels and L.A. Paquette, *Organometallics*, 1982, **1**, 1449.

57. G.L. Larson and E. Torres, *J. Organometal. Chem.*, 1985, **293**, 19.

58. A.G. Brook and J.D. Pascoe, *J. Am. Chem. Soc.*, 1971, **93**, 6224.

59. B.F. Bonini, G. Mazzanti, P. Zani and G.J. Maccagani, *J. Chem. Soc., Chem. Commun.*, 1988, 365.

60.　L. Coppi, A. Mordini and M. Taddei, *Tetrahedron Lett.*, 1987, **28**, 965 and 969.

61.　L. Coppi, A. Ricci and M. Taddei, *J. Org. Chem.*, 1988, **53**, 911.

62.　C. Nativi, A. Ricci and M. Taddei, in *Frontiers in Organosilicon Chemistry*, ed. A.R. Bassindale and P.P. Gaspar, Royal Society of Chemistry, Cambridge, 1991, p. 332.

63.　M.E. Jung and K.T. Hogan, *Tetrahedron Lett.*, 1988, **29**, 6199.

64.　T.H. Chan and K.T. Nwe, *J. Org. Chem.*, 1992, **57**, 6107.

65.　D. Wang and T.H. Chan, *Tetrahedron Lett.*, 1983, **24**, 1573.

66.　R.O. Duthaler and A. Hafner, *Chem. Rev.*, 1993, **93**, 807; K. Soai and S. Niwa, *Chem. Rev.*, 1993, **93**, 833; H.B. Kagan and O. Riant, *Chem. Rev.*, 1993, **93**, 1007; K. Mikami and M. Shimizu, *Chem. Rev.*, 1993, **93**, 1021.

67.　S. Kobayashi, S. Suda, M. Yamada and T. Mukaiyama, *Chem. Lett.*, 1994, 97.

68.　M. Norte, A.G. Gonzalez. P. Arroyo, M. Zarraga, C.Perez, M.L. Rodriguez, C. Ruiz-Perez and L. Dorta, *Tetrahedron*, 1990, **46**, 6125; G. Konig, A.D. Wright and O. Sticher, *Tetrahedron*, 1991, **47**, 1399; D. Faulkner, *J. Nat. Prod. Rep.*, 1984, **1**, 251; D. Faulkner, *J. Nat. Prod. Rep.*, 1984, **1**, 551; M.O. Ishitsuka, T. Kusumi and H. Kakisawa, *J. Org. Chem.*, 1988, **53**, 5010; H. Ngaoka, K. Kobayashi and Y. Yamada, *Tetrahedron Lett.*, 1988, **29**, 5945.

69.　M.E. Jung and J. Gervay, *Tetrahedron Lett.*, 1988, 2429.

70.　A.L. Parrill and D.P. Dolata, *Tetrahedron Lett.*, 1994, **35**, 7319.

71.　J. Sicher, in *Progress in Stereochemistry*, ed. P.B.D. de la Mare and W. Klyne, Butterworth, 1962, **3**, 222.

72.　P.A. Grieco and M. Nishizawa, *J. Org. Chem.*, 1977, **42**, 1717.

73.　S. Raucher, K.N. Chui, K.J. Hwang and J.E. Burks, *J. Org. Chem.*, 1986, **51**, 5503.

74.　W.C. Still, *J. Am. Chem. Soc.*, 1979, **101**, 2493.

75.　D. Sternbach, M. Shibuya, F. Jaisli, M. Bonetti and A. Eschenmoser, *Angew. Chem. Int. Ed. Engl.*, 1979, **18**, 634.

76.　K. Tamao, N. Ishida, T. Tanaka and M. Kumada, *Organometallics*, 1983, **2**, 1694.

77. C.A. Grob, *Angew. Chem. Int. Ed. Eng.*, 1969, **8**, 535.

78. T.K.M. Shing and Y. Tang, *Tetrahedron*, 1990, **46**, 2187.

79. E. Piers, J.R. Grierson, Cheuk Kun Lau and I. Nagakura, *Can. J. Chem.*, 1982, **60**, 210.

80. Chuan Shih and J.S. Swenton, *J. Org. Chem.*, 1982, **47**, 2825.

81. H.-O. Kalwowski, G. Crauss and D. Seebach, *Chem. Ber.*, 1981, **114**, 477.

82. C.J. Kowalski and K.W. Fields, *J. Org. Chem.*, 1981, **46**, 197.

83. M.C. Pirrung and N.J.G. Webster, *J. Org. Chem.*, 1987, **52**, 3603.

84. P.G. Gassman and W.N. Schenk, *J. Org. Chem.*, 1977, **42**, 918.

85. T. Hudlicky, J. Koszyk, T.M. Kutchan and J.P. Seth, *J. Org. Chem.*, 1980, **45**, 5020.

86. H. Tabuchi, T. Hamamoto and A. Ichihara, *Synlett*, 1993, 651.

87. R.K. Boeckmann, Jr. and D.M. Demko, *J. Org. Chem.*, 1982, **47**, 1792.

88. K.A. Parker and M.R. Adamchuk, *Tetrahedron Lett.*, 1978, 1689.

89. M.E. Jung and J. Gervay, *J. Am. Chem. Soc.*, 1989, **111**, 5469.

90. K.J. Shea and D.R. Gauthier, *Tetrahedron Lett.*, 1994, **35**, 7311.

91. J.W. Gillard, R. Fortin, E.L. Grimm, M. Maillard, M. Tjepkema, M.A. Bernstein and R. Glaser, *Tetrahedron Lett.*, 1991, **32**, 1145.

92. L. Coppi, A. Ricci and M. Taddei, *Tetrahedron Lett.*, 1987, **28**, 965.

93. J.K. Whitesell, *Chem. Rev.*, 1989, **89**, 1581.

94. R. Tacke and H. Linoh, in *The Chemistry of Organic Silicon Compounds*, ed. S. Patai and Z. Rappoport, Wiley, New York, 1989, vol. 2, chapter 18, pp 1143-1206.

95. M.G. Voronkov, in *Biochemistry of Silicon and Related Problems*, ed. G. Bendz and I. Lindqvist, Plenum Press, New York/London, 1978, pp 395-434.

96. L.M. Rice, B.S. Sheth and J.W. Wheeler, *J. Heterocycl. Chem.*, 1973, **10**, 731; M. Gerlach, P. Jutzi, J.-P. Stasch and H. Przuntek, *Z. Naturforsch.*, 1982, **37b**, 657; D. Wiese, R. Tacke and U. Wannagat, *Liebigs Ann. Chem.*, 1981, 1285; C.G. Pitt, A.E. Friedman, D. Rector and M.C. Wani, *Tetrahedron*, 1975, **31**, 2369.

97.   J.M. Chong, G.K. MacDonald, S.B. Park and S.H. Wilkinson, *J. Org. Chem.*, 1993, 58, 1266.

98.   H. Gilman and W.J. Trepka, *J. Org. Chem.*, 1962, 27, 1418.

99.   D.R. Weyenberg, L.H. Toporcer and A.E. Bey, *J. Org. Chem.*, 1965, 30, 4096.

100.   R.-J. Hwang, R.T. Conlin, P.P. Gaspar, *J. Organometal. Chem.*, 1975, 94, C38.

101.   R.J. Fessenden and W.D. Kray, *J. Org. Chem.*, 1973, 38, 87.

102.   R.A. Benkeser, E.C. Mozden, W.C. Muench, R.T. Roche and M.P. Siklosi, *J. Org. Chem.*, 1979, 44, 1370.

103.   K. Yamamoto, T. Hayashi, M. Zembayashi and M. Kumada, *J. Organometal. Chem.*, 1976, 118, 161

104.   M. Gerlach, P. Jutzi, J.-P. Stasch and H. Przuntek, *Z. Naturforsch.*, 1982, 37b, 657.

105.   J.A. Soderquist and A. Hassner, *J. Org. Chem.*, 1983, 48, 1801.

106.   J.A. Soderquist, F.-Y. Shiau and R.A. Lemesh, J. Org. Chem., 1984, 49, 2565.

107.   J.A. Soderquist and A. Negron, *J. Org. Chem.*, 1989, 54, 2462.

108.   I. Ojima, in *The Chemistry of Organic Silicon Compounds*, ed. S. Patai and Z. Rappoport, John Wiley, Chichester, 1989, vol 2, p. 1479.

109.   J.L. Speier, J.A. Webster and G.H. Barnes, *J. Am. Chem. Soc.*, 1957, 79, 974.

110.   S.H. Bergens, P. Noheda, J. Whelan and B.Bosnich, *J. Am. Chem. Soc.*,1992, 114, 2128.

111.   A.J. Chalk and J.F. Harrod, *J. Am. Chem. Soc.*, 1965, 87, 16.

112.   H.M. Bank, J.C. Saan and J.L. Speier, *J. Org. Chem.*, 1964, 29, 792.

113.   M. Capka, P. Svoboda and J. Hetflejs, *Collect. Czech. Chem. Commun.*, 1973, 38, 3830.

114.   K. Yamamoto, Y. Kiso, R. Ito, K. Tamao and M. Kumada, *J. Organomet. Chem.*, 1981, 210, 9.

115.   P. Svoboda, P. Sedlmayer and J. Hetflejs, *Collect. Czech. Chem. Commun.*, 1973, 38, 1783; K. Yamamoto, T. Hayashi, Y. Uramoto, R. Ito and M. Kumada, *J. Organomet. Chem.*, 1976, 118, 331.

116. M.R. Kesti and R.M. Waymouth, *Organometallics*, 1992, 11, 1095.

117. T. Hayashi and Y. Uozumi, *Pure Appl. Chem.*, 1992, 64, 1911.

118. S.H. Bergens, P. Noheda, J. Whelan and B. Bosnich, *J. Am. Chem. Soc.*, 1992, 114, 2121.

119. T. Hayashi, *J. Synth. Org. Chem., Japan*, 1994, 52, 900.

120. J.L. Speier, in *Advances in Organometallic Chemistry*, ed. F.G.A. Stone and R. West, Academic Press, 1979, Vol. 2, p.407.

121. T. Hayashi and K. Kabeta, *Tetrahedron Lett.*, 1985, 25, 3023.

122. L.M. Tolbert and M.E. Ogle, *J. Am. Chem. Soc.*, 1990, 112, 9519.

123. L. Horner, H. Hoffman, W. Klink, H. Ertel and V.G. Toscano, *Chem. Ber.*, 1962, 95, 581.

124. A.J. Chalk, *J. Organomet. Chem.*, 1970, 21, 207.

125. J.A. Soderquist and H.C. Brown, *J. Org. Chem.*, 1980, 45, 3571.

126. C.L. Barnes and J.A. Soderquist, *Acta Crystallogr., Sect. C*, 1992, C48, 2222.

127. A.R. Chamberlin, J.E. Stemke and F.T. Bond, *J. Org. Chem.*, 1978, 43, 147.

128. K. Smith and A. Pelter, in *Comprehensive Organic Synthesis*, ed. B.M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 8, p. 703.

129. H.C. Brown, M.C. Desai and P.K. Jadhav, *J. Org. Chem.*, 1982, 47, 5065.

130. D. Parker, *Chem. Rev.*, 1991, 91, 1441.

131. The major isomer is assigned the (S,S) configuration by analogy with literature precedent for the hydroboration of 1,1-disubstituted alkenes with this reagent . H.C. Brown, P.K. Jadhav and A.K. Mandal, *Tetrahedron*, 1981, 37, 3547.

132. I. Paterson, J.M. Goodman, M.A. Lister, R.C. Schumann, C.K. McClure and R.D. Norcross, *Tetrahedron*, 1990, 46, 4663.

133. G.W. Kabalka, T.M. Shoup and N.M. Goudgaon, *Tetrahedron Lett.*, 1989, 30, 1483.

134. G.W. Kabalka, P.P. Wadgaonkar and T.M. Shoup, *Tetrahedron Lett.*, 1989, 30, 5103.

135. C. Brevard and P. Granger, 'Handbook of High Resolution Multinuclear N.M.R.', John Wiley and Sons, Chichester, 1981.

136. K. Burgess and M.J. Ohlmeyer, *Chem. Rev.*, 1991, **91**, 1179.

137. D.A. Evans, G.C. Fu and A.H. Hoveyda, *J. Am. Chem. Soc.*, 1992, **114**, 6671.

138. K. Burgess and M. Jaspers, *Tetrahedron Lett.*, 1993, **34**, 6813; K. Burgess and W.A. van der Donk, *Organometallics*, 1994, **13**, 3616.

139. K. Burgess and M.J. Ohlmeyer, *J. Org. Chem.*, 1988, **53**, 5178.

140. D. Männig and H. Nöth, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 878.

141. D.A. Evans, G.C. Fu and B.A. Anderson, *J. Am. Chem. Soc.*, 1992, **114**, 6679.

142. Y. Matsumoto and T. Hayashi, *Tetrahedron Lett.*, 1991, **32**, 3387.

143. E.G. Thaler, K. Folting and K.G. Caulton, *J. Am. Chem. Soc.*, 1990, **112**, 2664.

144. J.M. Brown, P.A. Chaloner, A.G. Kent, B.A. Murrer, P.N. Nicholson, D. Parker and P.J. Sidebottom, *J. Organomet. Chem.*, 1981, **216**, 263.

145. J.D. Odom, in *Comprehensive Organometallic Chemistry*, ed. G. Wilkinson, F.G.A. Stone and E.W. Abel, Pergamon, Oxford, 1982, vol. 1, p. 253.

146. H.C. Brown and B.A. Carlson, *J. Am. Chem. Soc.*, 1973, **95**, 6876.

147. J.T. Carlock and M.P. Mack, *Tetrahedron Lett.*, 1978, 5153.

148. J. Yu, H.-S. Cho and J.R. Falck, *J. Org. Chem.*, 1993, **58**, 5892.

149. W.C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.

150. Y.Ueda, C.E. Damas and B.Belleau, *Can. J. Chem.*, 1983, **61**, 1996.

151. A. Vogel, 'Vogel's Textbook of Practical Organic Chemistry', Longman, London, 1989, 5th Edition.

152. R.V. Stevens, R.E. Cherpeck, B.L. Harrison, J. Lai and R. Lapalme, *J. Am. Chem. Soc.*, 1976, **98**, 6317.

153. B. Nader, T.R. Bailey, R.W. Franck and S.M. Weinreb, *J. Am. Chem. Soc.*, 1981, **103**, 7573.

154. D.B. Wigley and R.H. Weatherhead, *J. Chem. Soc., Perkin Trans. 2*, 1976, 704.

155. B.B. Snider, G.B. Phillips and R. Cordova, *J. Org. Chem.*, 1983, **48**, 3003.