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**SILACYCLES: NOVEL REAGENTS IN  
ASYMMETRIC SYNTHESIS**

**Ph D THESIS**

**CRAIG DOUGLAS B.Sc. (Hons)**

**UNIVERSITY OF DURHAM  
1998**

**16 APR 1999**



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## **DECLARATION**

The work contained in this thesis was carried out in the Department of Chemistry at the University of Durham or Zeneca Pharmaceuticals, Process Development Department, Macclesfield between October 1994 and September 1997. All the work is my own, unless otherwise indicated. It has not previously been submitted for a degree at this or any other university

For Amanda, Mum, Dad, and Lisa.

## **Acknowledgments**

Many thanks go to my supervisor, Dr. Patrick Steel.. Thanks too to my industrial supervisor Dr. Joe de Sousa who made my short time at Zeneca so worthwhile and enjoyable and all funding from EPSRC and Zeneca is gratefully acknowledged.

Thanks to everyone in the Steel group, past and present - Lee, Andy Byerley, Andy Ridge, Alison, Phil, Willy, Ed, Russell, Bill and Darren.

A special mention to all the project students - Russell, John and Martin - who have had to endure my mad rantings over the last past couple of years.

Thanks to Emma for the MOP, Lenny for all the GC analysis, Alan Kenwright, Ian McKeag and Julia for all their NMR expertise, Sandra, Jean, Hazel and Brenda for having to clean the lab and office from under my clumsy feet, and finally Ray and Gordon should be thanking me for keeping them in a job! Thanks to Toq and Liz for their help with this thesis.

Finally, a big shout to all my friends and family who helped to keep me sane over the last 8 years.

## Abbreviations

AIBN	: $\alpha,\alpha'$ - azoisobutyronitrile
Ar	: aromatic
Ac	: acetyl
9-BBN	: 9-borabicyclo[3.3.1]nonane
BDPP	: 2,4-bis(diphenylphosphino)pentane
BINAP	: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BMPP	: benzylmethylphenylphosphine
BMS	: borane dimethylsulphide
Bn	: benzyl
b.p.	: boiling point
Bu	: butyl
BuLi	: butyl lithium
Bz	: benzoyl
CI	: chemical ionisation
d	: doublet
de	: diastereomeric ionisation
DEAD	: diethyl azodicarboxylate
DCME	: dichloromethyl methylether
DIBAL	: diisobutylaluminium hydride
DMAP	: 4-dimethylaminopyridine
ee	: enantiomeric excess
EI	: electron impact
Et	: ethyl
GC	: gas chromatography
GCMS	: gas chromatography mass spectroscopy
hfc	: 3-(heptafluoropropylhydroxymethylene)-(+)-camphorato
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	: menthylidiphenylphosphine
Me	: methyl
MOP	: 2-(diphenylphosphino)-2'-methoxy-1,1'-binaphthyl
m.p.	: melting point
MS	: mass spectroscopy
NMR	: nuclear magnetic resonance
Ph	: phenyl
q	: quartet
s	: singlet
t	: triplet
TBAF	: tetrabutylammonium fluoride
TBDMS	: tert-butyldimethylsilyl
Tf	: trifluoromethanesulfonyl
THF	: tetrahydrofuran
tlc	: thin layer chromatography
TMEDA	: N,N,N',N'-tetramethylethylenediamine
TMS	: trimethylsilyl

## ABSTRACT

### **C<sub>2</sub> Symmetric Silacycles : Novel Reagents for Asymmetric Synthesis**

*Craig Douglas*

*Durham University*

1994-1998

Silicon based organic reagents have enjoyed a wealth of applications in the last thirty years. However, the development of organosilanes for asymmetric synthesis has been less prolific.

The drawbacks of using 'Si-centred' chiral organosilanes has led to 'C-centred' organosilicon compounds being the substrate of choice. This research has been directed at the synthesis and application of C<sub>2</sub> symmetric 'C-centred' cyclic organosilicon species and their potential applications in asymmetric synthesis.

A variety of synthetic methods have been considered, the most successful of which has been the double asymmetric hydroboration of substituted divinylsilanes. This has allowed the use of unusual boron redistribution chemistry to give access to both acyclic and cyclic *trans*-substituted organosilicon compounds with high stereoselectivity.

A new method for the synthesis of dichlorosilanes from their diphenyl analogue has been developed and has been shown to occur almost instantaneously and in good yield. Finally, the application of dichlorosilacycles in tethered Diels-Alder reactions has been investigated and has been shown to give enhanced rates of reaction when compared to acyclic silicon tethers.

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## **CHAPTER ONE**

### **INTRODUCTION**

## The Role of Silicon in Organic Synthesis

### A.1. Introduction:

In the last few decades organosilicon reagents have played an ever increasing role in organic synthesis. The near ubiquitous use of silicon protecting groups, has been accompanied by the growing use of organosilicon reagents, particularly in carbon-carbon bond forming reactions and functional group transformations.

The aim of this project, at the outset, was the asymmetric synthesis of enantiomerically pure  $C_2$  symmetric silacycles with the general structure **(1)**, Figure A.1, and a study of their applications as possible chiral resolving agents, biologically active compounds, and chiral auxiliaries.

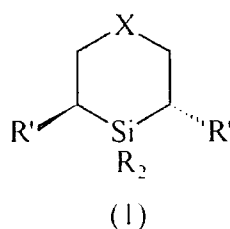


Figure A.1

We chose this structural type for three reasons:

- 1) C-centred chirality is more stable than Si-centred chirality:  $\alpha$ -substitution is desired for maximum asymmetric effect although all positions are of interest.
- 2) The conformational preferences of a cyclic structure will dictate the most favourable transition state, hence limiting the number of possible stereoisomers.
- 3)  $C_2$  symmetry reduces the number of possible competing diastereomeric transition states.<sup>1</sup>

### A.2. A Comparative Study of Silicon and Carbon

The vast potential of organosilicon chemistry has been matched by the depth of research, and a number of excellent reviews and textbooks have been published.<sup>2</sup>

Many of these reviews have drawn analogies between silicon and carbon chemistry, and comparisons have been made between organosilicon and organometallic species. This chapter will focus on the synthetic applications of organosilicon compounds and latterly the synthesis and applications of chiral organosilanes. In essence, it aims to provide an illustrative guide to organosilicon chemistry rather than a comprehensive review.

Silicon's utility in organic synthesis depends on three contributory factors : relative elemental bond strengths, the involvement of valence p-orbitals and empty d-orbitals, and the comparative electronegativity with carbon. These are summarised below, Table 1.<sup>2</sup>

PHYSICAL PROPERTY	CARBON	SILICON
atomic radius	77pm	117pm
electronegativity	2.5	1.8
electronic configuration	$1s^2 2s^2 2p^2$	$1s^2 2s^2 2p^6 3s^2 3p^2 3d^0$
C-El bond length	1.54Å	1.9Å
El-O bond dissociation energy	340kJmol <sup>-1</sup>	531 kJmol <sup>-1</sup>
El-Halogen bond dissociation energy	268 kJmol <sup>-1</sup>	403 kJmol <sup>-1</sup>

Table 1

As can be seen from Table 1, the atomic radius of silicon is significantly larger than that of carbon and as a result it forms longer covalent bonds with other elements. This has some important steric consequences for the reactivity of organosilicon compounds, and researchers have often been surprised by the effect of silyl substitution when compared to analogous *tert*-butyl systems. Silicon is also significantly more electropositive than carbon, resulting in the polarisation of carbon-silicon bonds and a tendency for nucleophilic attack to occur at silicon. However, in comparison to other C-El species, organosilanes are relatively unreactive. In general, tetrasubstituted organosilicon reagents are far more stable than analogous organometallic reagents, can be handled more easily, (these do not normally need

anhydrous or inert atmospheres) and are inert in the presence of most organic functional groups. A variety of reactions have been performed on organosilicon compounds without cleavage of the C-Si bond, yet they have a dormant reactivity that can be revealed at the appropriate moment, in various mechanistic fashions. These are described below and all play key roles in the reactions of organosilanes.

### **A.3. Nucleophilic substitution at silicon**

Nucleophilic substitution at a silicon centre could in principle proceed by either an  $S_N2$  or  $S_N1$  type mechanism. In practice the reaction normally follows an  $S_N2$  type pathway because the alternative unimolecular reaction is so much slower.

The mechanism of nucleophilic substitution reactions at silicon, so called **Si- $S_N2$** , is characterised by the ability of silicon to form hypervalent intermediates. Substitution at silicon can take place with retention or inversion of stereochemistry, and the outcome is dependent on a variety of contributing factors including the choice of leaving group, nucleophile or solvent. Theoretical chemists have postulated different mechanisms for inversion and retention of stereochemistry.<sup>3</sup> The mechanism for inversion, Figure A.2, involves approach of the nucleophile and departure of the leaving group from a trigonal bipyramidal intermediate. This geometry suggests the formation of three equatorial  $3sp^2$  orbitals and two elongated axial  $3p_zd_z^2$  orbitals. The mechanism that permits retention is believed to be similar to that postulated for phosphorus and involves a pseudorotation mechanism. Berry pseudorotation, as it has become known, involves the rapid exchange of ligands on a hypervalent intermediate,<sup>4</sup> and retention at silicon is characterised by the axial entry of the nucleophile, followed by a pseudorotation process and finally axial exit of the leaving group, Figure A.2.<sup>5</sup>

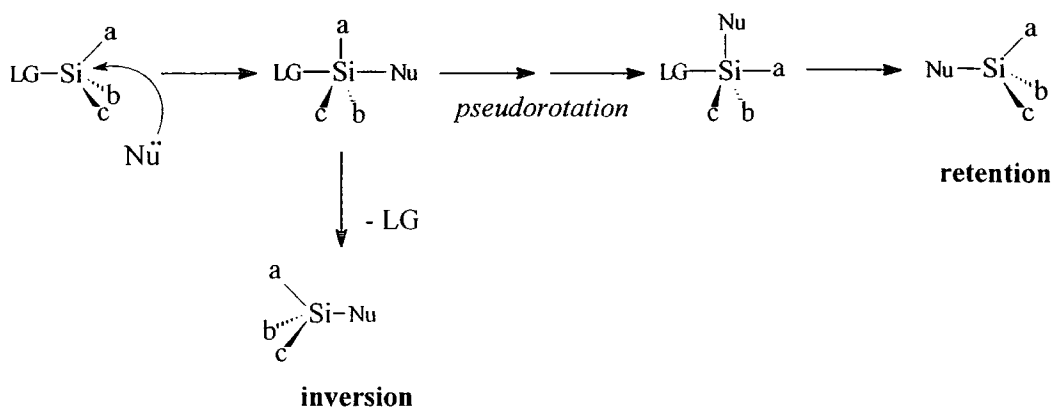


Figure A.2

## **A.4. Activating And Directing Effects of Silicon**

### **A.4.1. Introduction**

The versatility of organosilicon compounds in organic synthesis has been attributed to the relative inertness under a variety of conditions and the selective lability exhibited by silicon.<sup>2</sup> To this should be added its electron donor-acceptor abilities.

Under appropriate conditions proximate silicon groups can stabilise negative or positive charges and can strongly perturb the  $\pi$ -system in a variety of molecules. In any given situation the total electronic effect from silicon can be attributed to a combination of inductive,  $\pi$ -bonding and hyperconjugative effects.

### **A.4.2. $\beta$ -Carbocation Stabilisation**

The ability of silicon to stabilise carbocations  $\beta$  to the silyl moiety (the  $\beta$  effect) has wide ranging consequences for regio- and stereospecificity in the reactions of organosilanes. An electron deficient centre  $\beta$  to silicon is stabilised by  $(\sigma-p)\pi$  conjugation between vacant p orbitals on the  $\beta$  carbon and the  $\sigma$  orbital of the adjacent silicon carbon bond, Figure A.3.<sup>6</sup> In addition, to maximise  $\pi$  overlap, the C-Si  $\sigma$  bond must be coplanar to the vacant p orbital. This last factor provides the rationale behind the stereoselectivity of many organosilicon reactions.

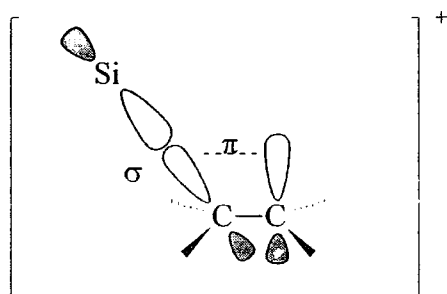
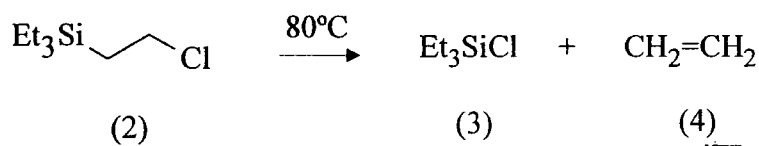


Figure A.3

The  $\beta$  effect has some important consequences for the reactions of organosilicon compounds. Many  $\beta$ -substituted organosilanes exhibit abnormally high reactivity.<sup>7</sup> For example,  $\beta$ -halogenoalkylsilanes such as the chlorosilane (2), Scheme A.1, are far more reactive under a wide variety of conditions than the corresponding  $\alpha$  and  $\gamma$  analogues, undergoing facile thermal  $\beta$  fragmentation leading to the production of alkenes.<sup>7</sup>



Scheme A.1

Similarly, many unsaturated organosilicon compounds show enhanced reactivity in electrophilic substitution reactions with the regiochemistry being controlled by the presence of the silyl moiety in the starting material.<sup>8</sup> The silyl group usually encourages attack at the site which will generate a carbocation  $\beta$  to silicon, with loss of the silyl moiety as the final step of the reaction.

#### A.4.3. Stabilisation of $\alpha$ -Carbanions

Stabilisation of an  $\alpha$ -carbanion can be attributed to  $(\sigma^*-p)\pi$  overlap between the antibonding  $\sigma^*$  orbital of the adjacent carbon-silicon bond and the p orbital of the carbanion, Figure A.4.<sup>5</sup>

$\alpha$ -Carbanion stabilisation also has wide-ranging consequences for the reactions of organosilanes, for example,  $\alpha$ -carbanion stabilisation facilitates nucleophilic addition to vinyl silanes, Section A.5.1.

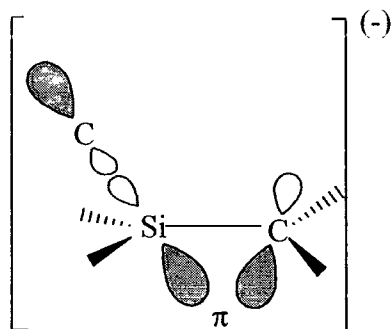


Figure A.4

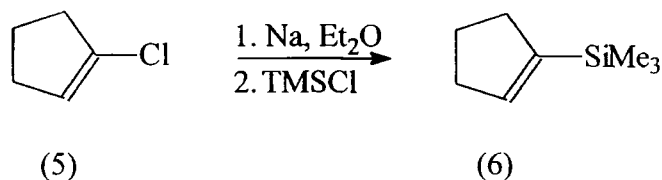
## **A.5. Synthesis and Reactions of Organosilanes**

Until recently the utility of organosilanes in organic synthesis has focused primarily on the reactions of silyl ethers as protecting groups.<sup>9</sup> However, this area has been extensively reviewed and will not be discussed further here. This section will focus on the preparation and reactions of organosilicon compounds and will attempt to draw analogies, where appropriate, between these compounds and analogous organic functional groups or organometallic reagents.

### **A.5.1. Vinylsilanes**

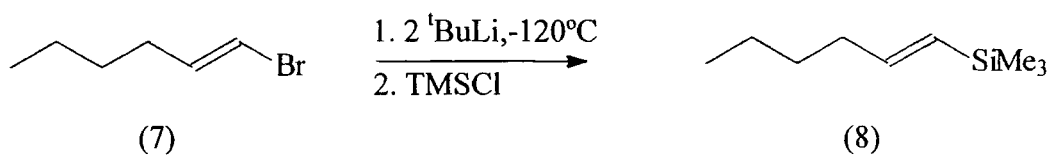
There are a variety of possible synthetic routes to vinylsilanes: most utilise vinyl halides, alkynes or carbonyl compounds and these are summarised below.

The reaction of a nucleophilic carbon species with electrophilic silicon is the most common method of synthesising vinylsilanes. For example, metallation of the vinyl chloride (**5**) and reaction with chlorotrimethylsilane gave vinylsilane (**6**) in good yield, Scheme A.2.<sup>10</sup>



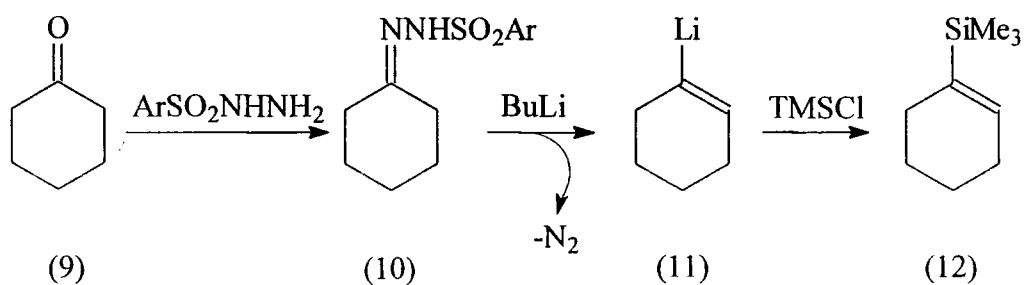
Scheme A.2

Terminal vinyl bromides such as 1-bromohex-1-ene (7), Scheme A.3, have been shown to proceed through this sequence with complete retention of stereochemistry.<sup>11</sup>



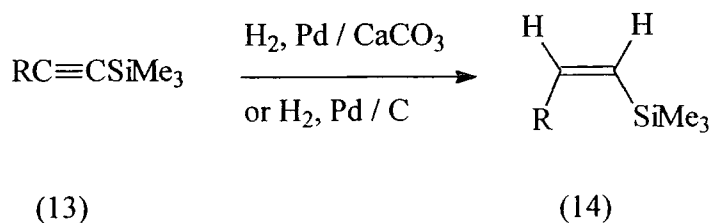
Scheme A.3

Vinyl anions are generated from ketones in the Shapiro reaction and may be trapped by chlorosilanes to give the corresponding vinylsilane.<sup>12</sup> For example, arylsulfonyl hydrazone (10) was deprotonated by butyllithium to form the vinyl carbanion (11) with loss of nitrogen. This was trapped with a variety of electrophiles including chlorotrimethylsilane to produce the vinylsilane (12), Scheme A.4.



Scheme A.4

The silylation and reduction of alkynes affords a variety of preparative routes to vinylsilanes. One such method is the catalytic hydrogenation of alkynylsilanes and this is readily achieved by the use of transition metal catalysts.<sup>13</sup> Addition generally proceeds with *cis*- geometry giving largely the (*Z*)-alkene. For example, the silylalkyne (13) undergoes Pd-catalysed hydrogenation to form the (*Z*)-alkene (14), Scheme A.5.<sup>13</sup>



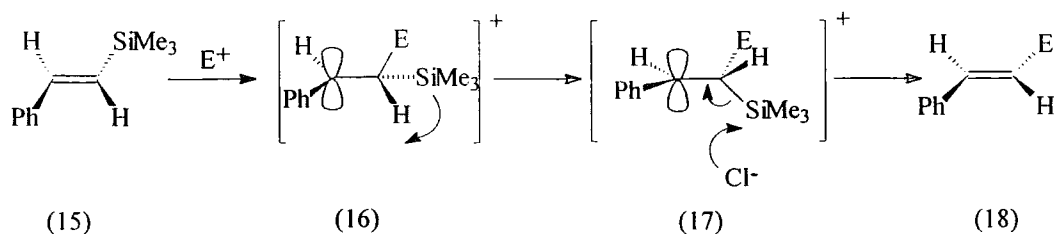
Scheme A.5

Considerable stereoselectivity and flexibility are also attainable from the hydrometallation and subsequent protonolysis of alkynylsilanes. Hydroboration occurs regiospecifically with the boron becoming attached to the silicon bearing carbon atom. Protonolysis then affords the  $\beta$ -substituted vinylsilane with complete *cis*-selectivity.<sup>14</sup>

Alternatively, the hydroalumination of alkynylsilanes allows the synthesis of both *cis*- and *trans*-vinylsilanes. Hydroalumination proceeds with *trans*-geometry in hydrocarbon solvents, whereas in donor solvents clean *cis*-addition is observed.<sup>15</sup>

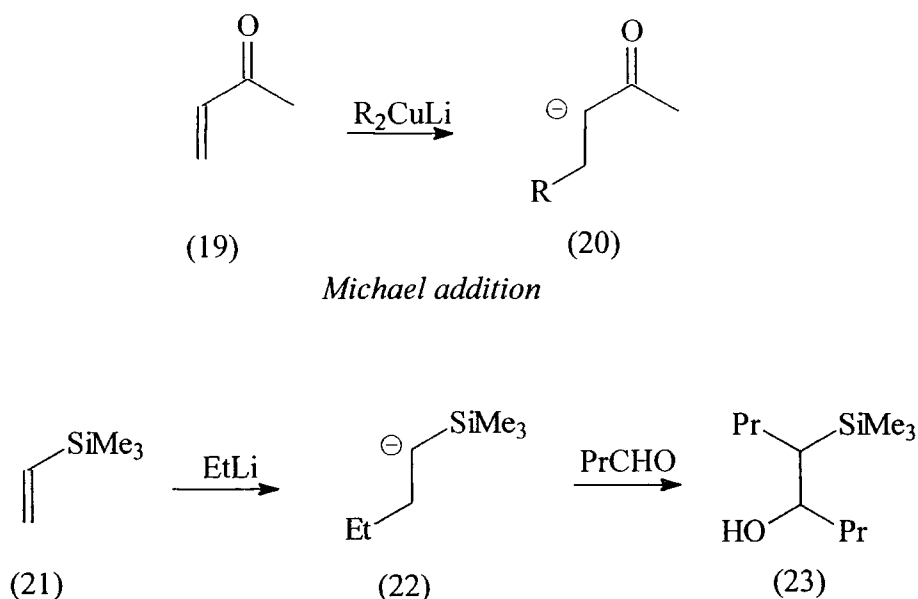
One final method for the preparation of vinylsilanes involves the hydrosilylation of alkynes. This is commonly promoted by transition metal catalysis and give either *cis*- or *trans*-addition products, (see Section A.7 for a more in depth discussion of hydrosilylation).<sup>16</sup>

Vinylsilanes react with electrophiles by the formation of a stabilised electron deficient centre  $\beta$  to the silicon atom. The silyl moiety is displaced in the last step, regenerating the alkene normally with retention of stereochemistry.<sup>17</sup> This can be explained by rotation of the central C-C bond which brings the empty p orbital and the C-Si bond into the same plane, and stabilises the carbonium ion, so that elimination can take place, Scheme A.6. Rotation occurs in the direction which avoids placing the empty p orbital and the C-Si bond at 90°, a high-energy situation in which orbital overlap is zero.



Scheme A.6

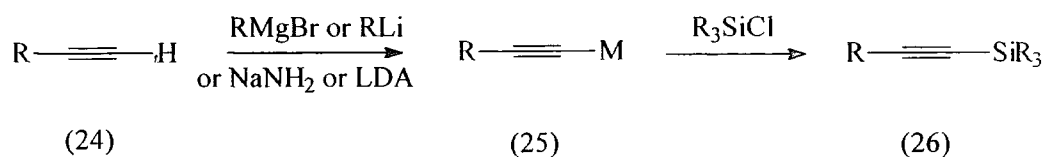
Nucleophilic addition to vinylsilanes is also possible and is facilitated by the formation of a stabilised anion  $\alpha$  to silicon. The reaction can be compared to the Michael reaction in which the anion is stabilised by an adjacent carbonyl group. In the case of vinylsilanes,  $\alpha$ -carbanion stabilisation allows access to  $\beta$ -hydroxysilanes through reaction with aldehydes, Scheme A.7.<sup>18</sup>



Scheme A.7

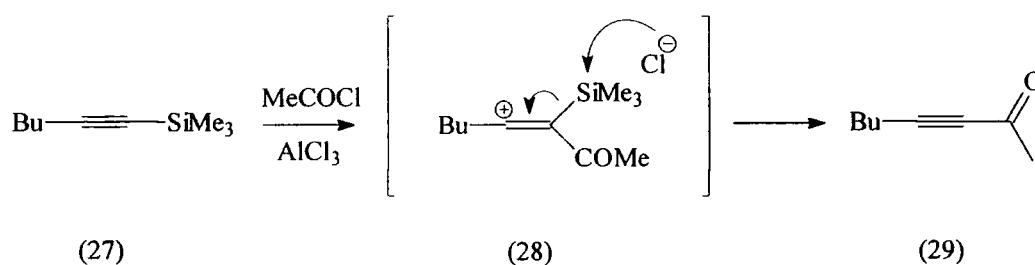
### A.5.2. Alkynylsilanes

Like vinylsilanes, the predominant method for the synthesis of alkynylsilanes is the reaction between a nucleophilic carbon and an electrophilic silicon species. For example, terminal alkynes are readily converted into alkynylsilanes by metallation and reaction with a chlorotrialkylsilane, Scheme A.8.<sup>13</sup>



Scheme A.8

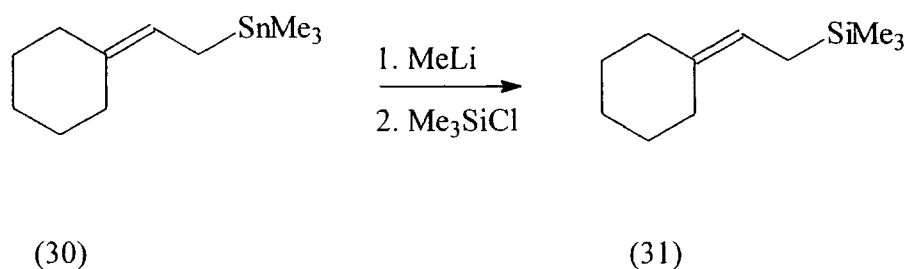
Silylation of the terminal carbon can be utilised to prevent loss of the relatively acidic alkyne hydrogen during subsequent synthetic steps. Alternatively, silylation can regioselectively activate the triple bond towards electrophilic attack. In a similar fashion to vinylsilanes, electrophilic substitution reactions of alkynylsilanes are controlled by the presence of a silyl moiety. Their reactivity is controlled by attack at the site that will generate a carbocation  $\beta$  to silicon. For example, the alkynyl ketone (29) was synthesised by the Lewis acid-catalysed addition of ethanoyl chloride, Scheme A.9.<sup>19</sup>



Scheme A.9

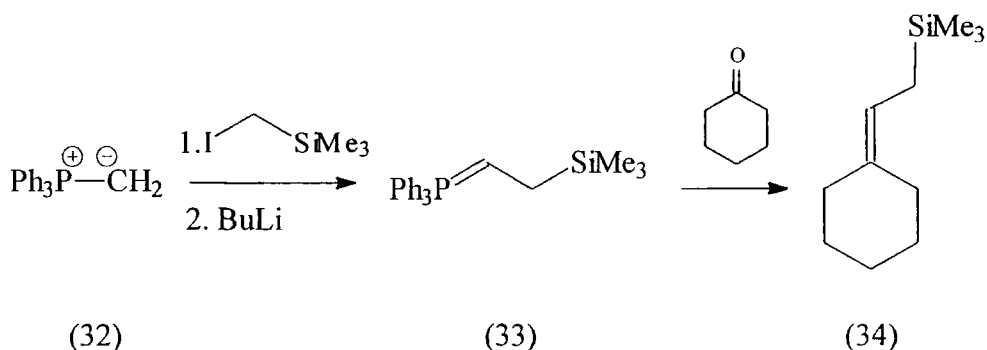
### A.5.3. Allylsilanes

The chemistry of allylsilanes has been extensively reviewed.<sup>20</sup> In a manner analogous to vinylsilanes, allylsilanes are readily prepared by silylation of a metal-allyl species, Scheme A.10<sup>20,21</sup> Occasionally regiochemical problems with this method can arise with silylation occurring at the  $\gamma$ -carbon.



Scheme A.10

There are a number of alternative strategies. For example, the Seyferth-Wittig method utilises carbonyl compounds and phosphosilane derivatives, Scheme A.11.<sup>22</sup>



Scheme A.11

Allylsilanes react with electrophiles at their  $\gamma$ -carbon, as attack at this position generates a carbocation  $\beta$  to silicon, Figure A.5. Regiospecific displacement of the silyl group produces the new alkene. It is this control that renders allylsilanes valuable reagents in organic synthesis.

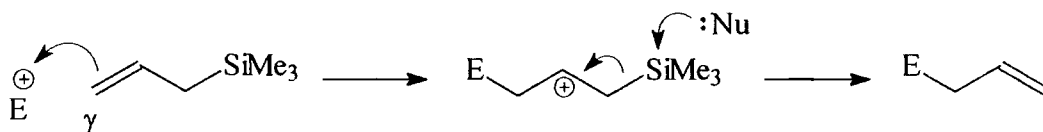
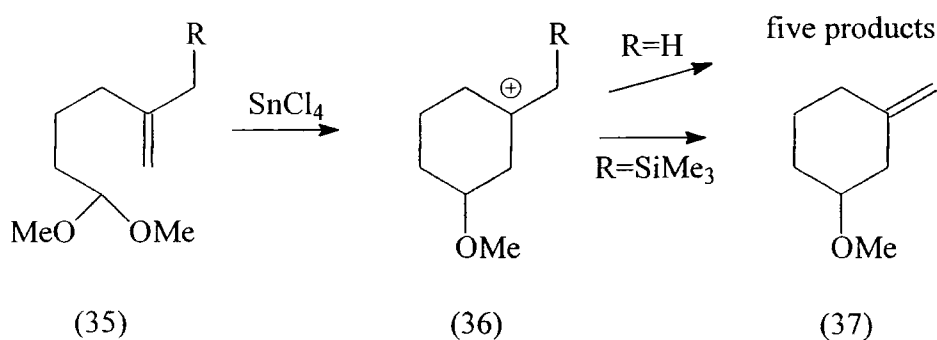


Figure A.5

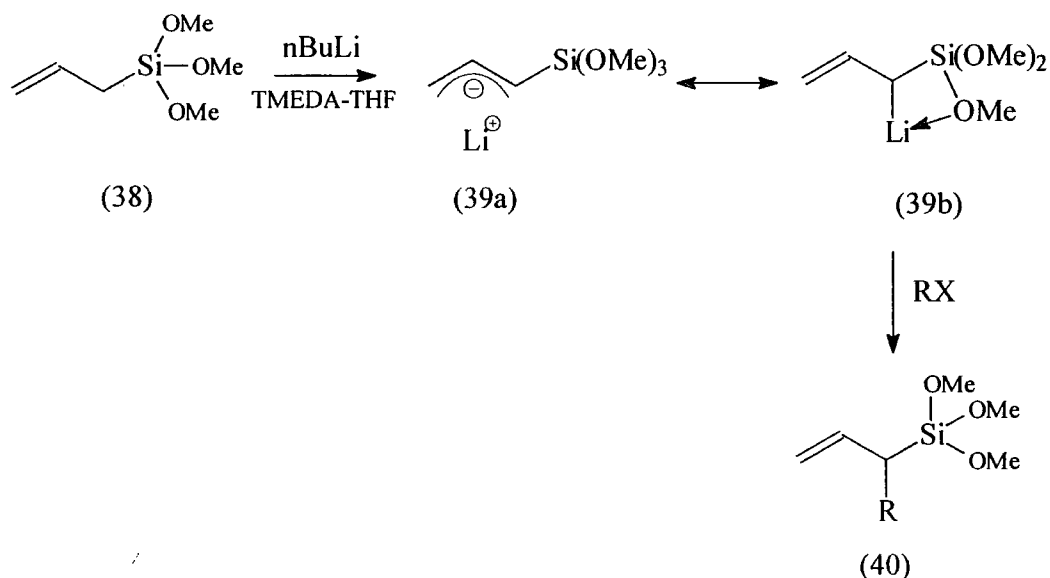
For example, in the cyclisation of allyl acetal (35) the terminal alkene ( $\text{R}=\text{H}$ ) gives a number of different products whereas the allylsilane analogue ( $\text{R}=\text{SiMe}_3$ ) gave exclusively methylenecyclohexane (37), Scheme A.12.<sup>23</sup>



Scheme A.12

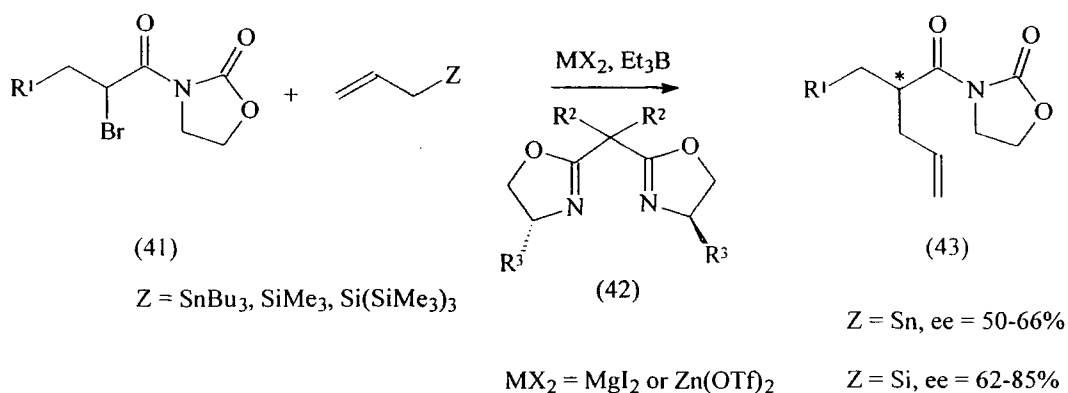
In addition to their reaction as electrophiles, allylsilanes can be deprotonated to give silyl stabilised carbanions which react with electrophiles in either the  $\alpha$  or  $\gamma$  positions. The regioselectivity is dependent upon a variety of factors including the nature of the base, electrophile and silyl substituents. For example, alkylations using Schlosser's base (KOtBu/nBuLi in hexane) have been shown to give enhanced  $\gamma$ -selectivity and similar results are realised by increasing the steric bulk around silicon.<sup>24</sup>

$\alpha$ -Regioselectivity may be enhanced by the use of silylalkoxy groups, with  $\alpha$ -alkylation being attributed to chelation of the lithium cation with the lone pair on the alkoxy group, thus localising the lithium ion at the  $\alpha$ -position (**39b**), Scheme A.13.<sup>25</sup>



Scheme A.13

More recently allylsilanes have been shown to undergo free radical allyl transfer reactions in the presence of a Lewis acid. These offer advantages over corresponding alkylstannanes. For example, Scheme A.14, allyltrimethylsilane ( $Z=\text{SiMe}_3$  /  $\text{Si}(\text{SiMe}_3)_3$ ) reacts in the presence of a chiral Lewis acid with higher selectivity than the allylstannane ( $Z=\text{SnMe}_3$ ).<sup>26</sup>

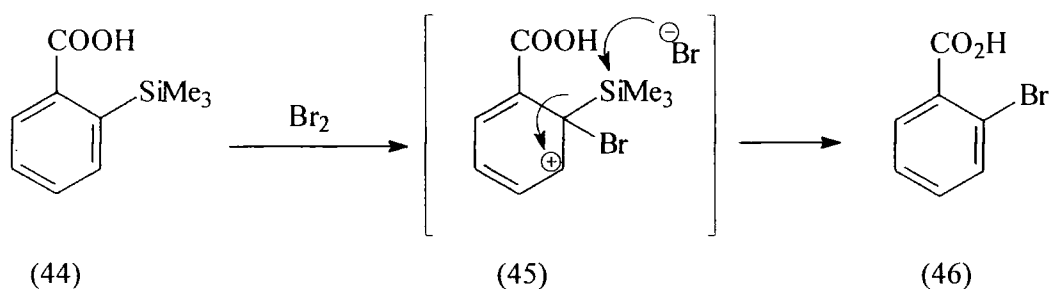


Scheme A.14

### A.5.4. Arylsilanes

The synthesis of arylsilanes has been comprehensively surveyed.<sup>27</sup> Arylsilanes are obtained by silylation of an arylorganometallic with a chlorotrialkylsilane. This process is very general and is only limited by the availability of the requisite arene anion.

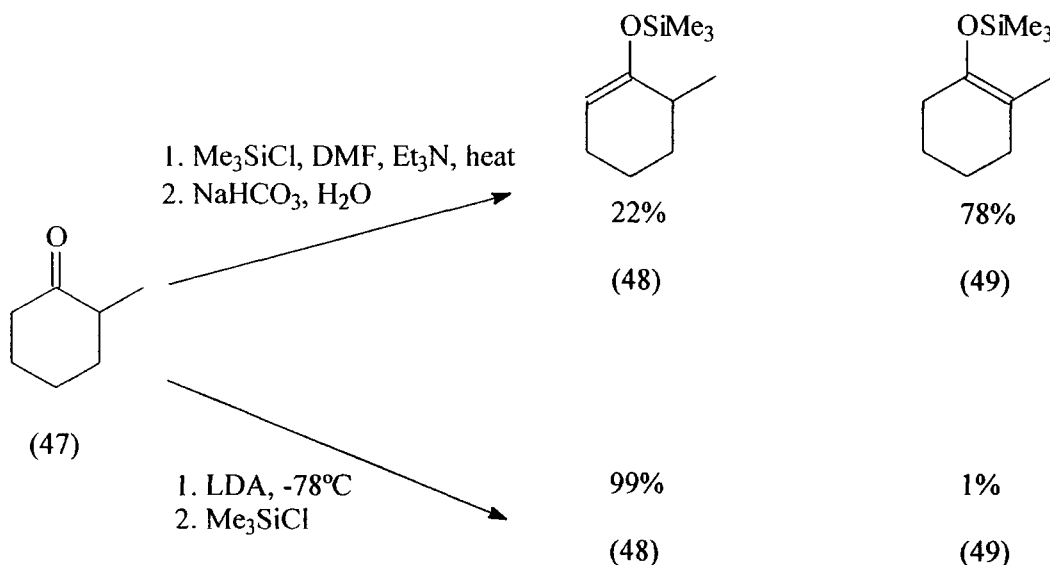
Substitution of arylsilanes occurs with a variety of electrophilic reagents. This is attributed to the formation of a stabilised carbonium ion  $\beta$  to the silyl moiety. This offers significant advantages when compared with classical electrophilic aromatic substitution. For example, bromination of (44) occurs in a highly selective manner, *ortho* to the carboxylic acid group, Scheme A.15.<sup>28</sup>



Scheme A.15

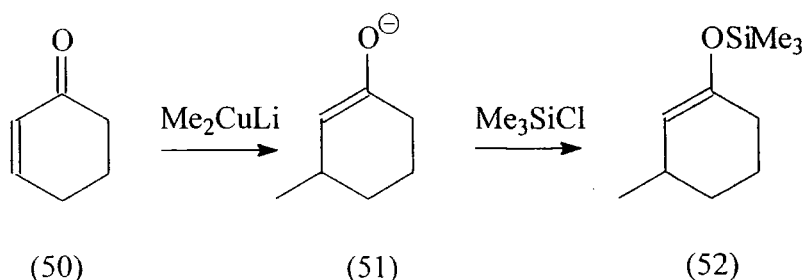
### A.5.5. Silyl Enol Ethers

Silyl enol ether have found widespread application as isolable enol derivatives. They can be prepared, Scheme A.16, by trapping the enolate anion under kinetic or thermodynamic conditions preferentially giving (48) or (49) respectively.<sup>29</sup>



Scheme A.16

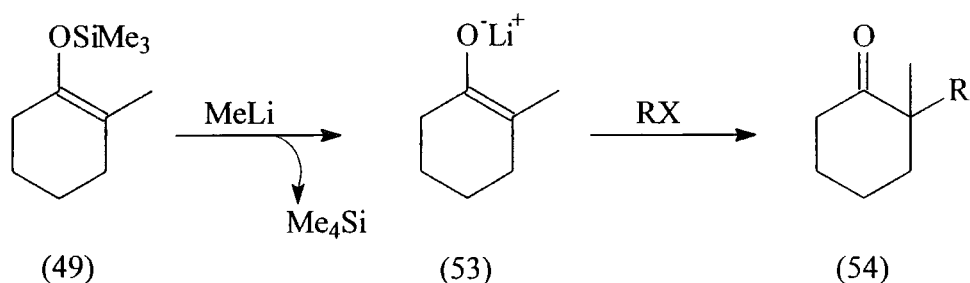
Silyl enol ethers can also be accessed by conjugate addition to an  $\alpha,\beta$ -unsaturated ketone. For example, cuprate addition to cyclohexenone (50) gives the enol intermediate (51) with subsequent silylation affording the regiochemically pure silyl enol ether (52), Scheme A.17.<sup>30</sup>



Scheme A.17

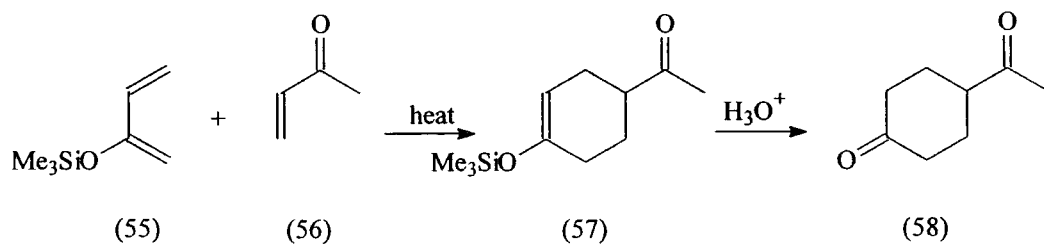
Silyl enol ethers may be used to give regiochemically pure enolate anions. For example, reacting with methyl lithium or benzyltrimethylammonium fluoride,<sup>31</sup>

affords the corresponding lithium (53) or quaternary ammonium enolate under non-equilibrating conditions, Scheme A.18.



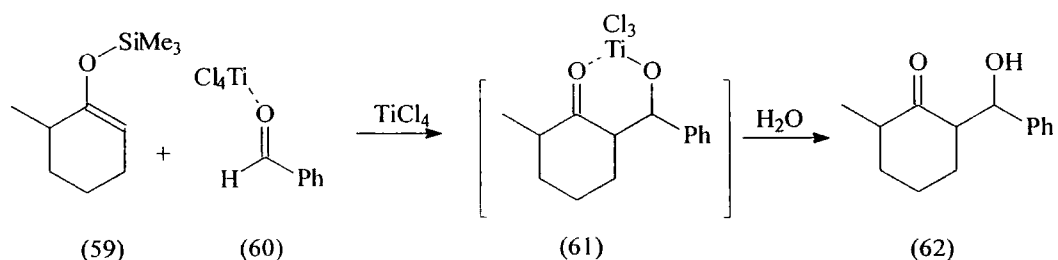
Scheme A.18

Silyl enol ethers provide a source of functionalised olefins and masked carbonyl group. For example, the trimethylsiloxydiene (55) underwent regiospecific Diels-Alder reaction with methyl vinyl ketone (56) to give, following acid hydrolysis, the cyclohexanone derivative (58), Scheme A.19.<sup>32</sup>



Scheme A.19

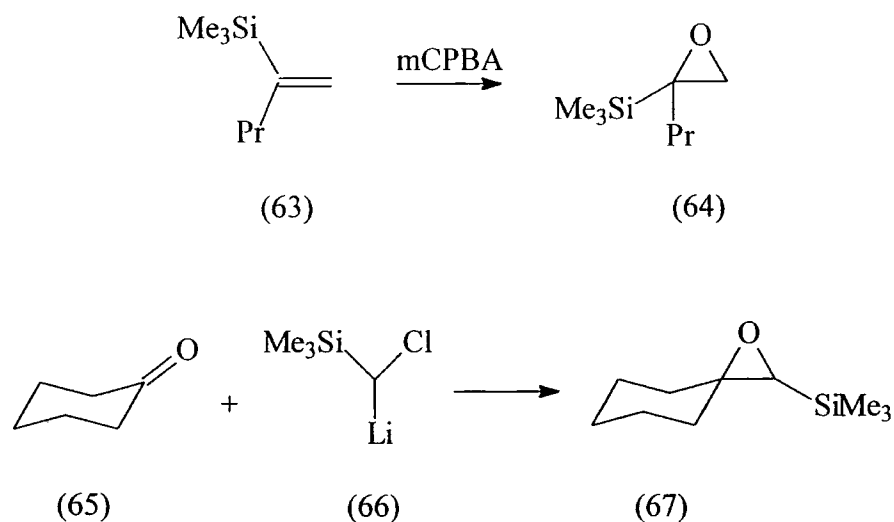
The major use of silyl enol ethers has been in Lewis acid initiated processes, notably the Mukaiyama aldol reaction, Scheme A.20.<sup>33</sup> In this they effectively function as oxygenated allylsilanes.



Scheme A.20

### A.5.6. $\alpha\beta$ -Epoxyasilanes

Epoxyasilanes are commonly synthesised in one of two ways. Either by the epoxidation of vinylsilanes,<sup>34</sup> or through a Darzens type condensation using  $\alpha$ -chloro- $\alpha$ -lithiotrimethylsilanes (**66**), Scheme A.21.<sup>35</sup>



Scheme A.21

In most cases  $\alpha,\beta$ -epoxyasilanes undergo highly regioselective ring opening, Figure A.6. Under nucleophilic conditions attack occurs at the carbon bearing the silyl moiety. It is believed that a transition state with limited carbocationic character exists with the nucleophile being assisted to attack on the  $\alpha$ -carbon by an empty d orbital on silicon.<sup>36</sup> Under acid conditions the regiochemistry is controlled by an intermediate with extensive carbocationic character  $\beta$  to the silicon. Analogous reactions with unsilylated epoxides, give completely different products, as carbocation stabilisation occurs  $\beta$  to the R group.

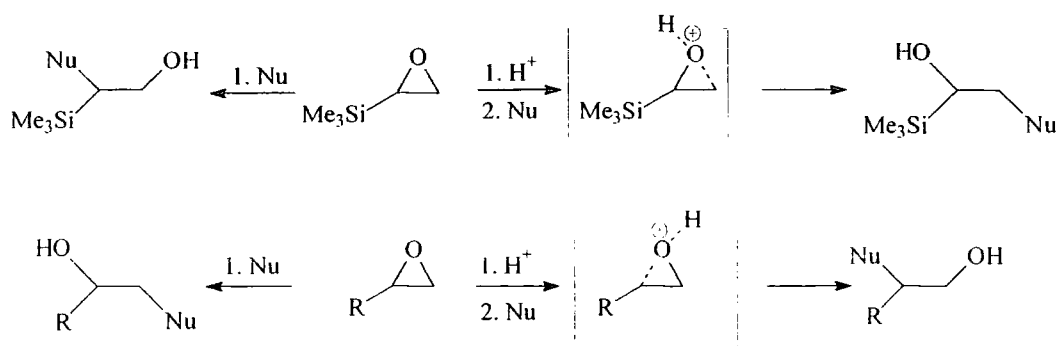


Figure A.6

### A.5.7. The Peterson Reaction and $\beta$ -Hydroxysilanes

The synthesis of alkenes from  $\beta$ -hydroxysilanes is known as the Peterson or silyl-Wittig reaction.<sup>37</sup>  $\beta$ -hydroxysilanes are generally prepared by nucleophilic ring opening of epoxysilanes, Section A.5.6, or by the addition of  $\alpha$ -silyl carbanions to carbonyl compounds.

Depending on the reaction conditions, the Peterson reaction will proceed with *syn*- or *anti*- elimination to afford either the E- or Z-isomer. Under acidic conditions *anti*-elimination occurs, whilst under basic conditions *syn*-elimination occurs, Figure A.7. Consequently by judicious choice of the elimination conditions it is possible to prepare either the Z- or E-alkene from any given  $\beta$ -hydroxysilane.

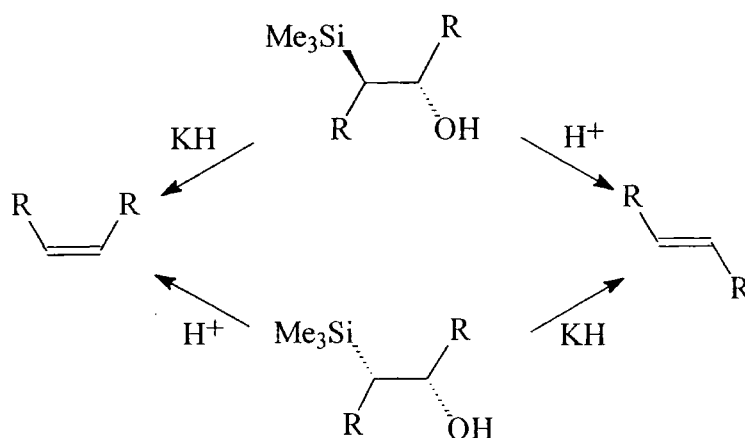
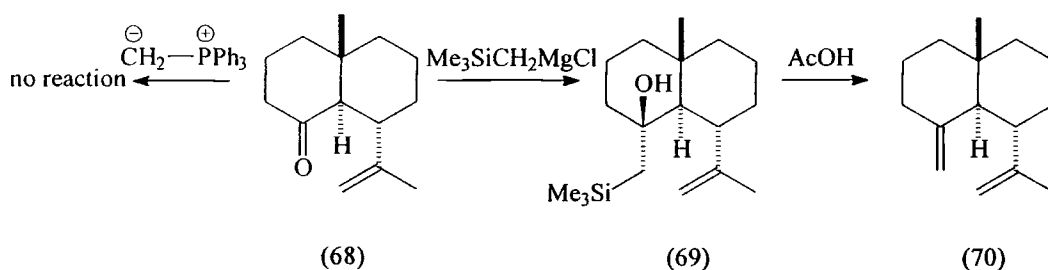


Figure A.7

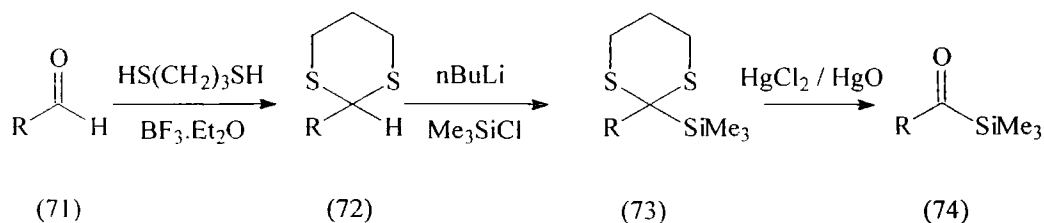
Owing to poor selectivity in the initial addition, the Peterson reaction is far less common than the phosphorus-based Wittig reaction. However, it does offer some distinct advantages. The trialkylsilanol by-products are volatile, making purification simpler, and silyl carbanion reagents are considerably more nucleophilic than the corresponding ylides. Consequently in certain circumstances, the Peterson reaction generates alkenes unobtainable via the Wittig process. For example, a Wittig reaction failed to methylenate the hindered ketone (**68**), Scheme A.22, whereas the silicon based approach gave the required double bond in a synthesis of  $\beta$ -Gorgonene (**70**).<sup>38</sup>



Scheme A.22

### A.5.8. Acylsilanes and the Brook Rearrangement

Acylsilanes are important precursors in the synthesis of silenes,<sup>39</sup> and have been extensively studied by Brook in the synthesis of silyl ethers.<sup>40</sup> Acylsilanes have been synthesised by a variety of methods, including the reductive cleavage of thiol esters, borane reduction of alkynylsilanes and the reverse Brook rearrangement, some of which are outlined below. For example, dithiane (**72**) was readily converted to acylsilane (**74**) by successive deprotonation, silylation and hydrolysis, Scheme A.23.<sup>41</sup>



Scheme A.23

Acylsilanes generally react like ketones. However, they can be transformed into silyl ethers via the Brook rearrangement, Figure A.8.<sup>40</sup> Nucleophilic attack at the carbonyl group is followed by migration of the silyl group onto the oxygen anion. Subsequent reaction with an electrophile generates the silyl ether.

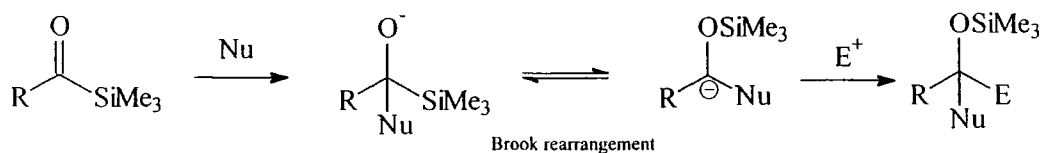
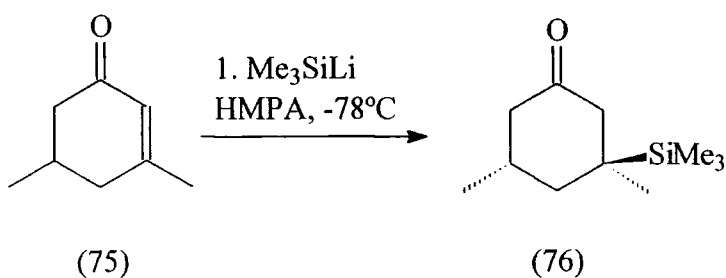


Figure A.8

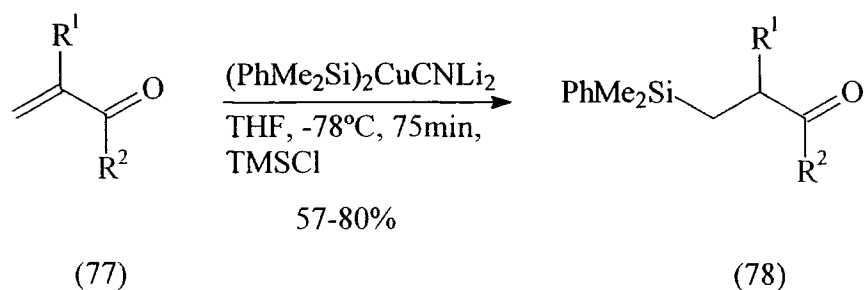
### A.5.9. Silyl Anions

The formation of carbanions allows access to carbon-based nucleophiles for use in a wide variety of reactions. The formation of silyl anions is less well known, although silyllithium reagents have been used in conjugate additions to unsaturated carbonyl compounds, Scheme A.24.<sup>42</sup>



Scheme A.24

Fleming has used silyl cuprates derived from silyllithium precursors in the preparation of phenyldimethylsilane (78), Scheme A.25.<sup>43</sup>

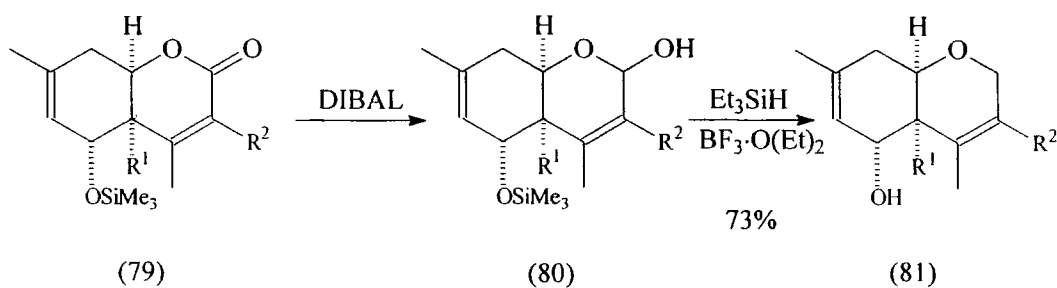


Scheme A.25

### A.6. Silanes as Reducing Agents

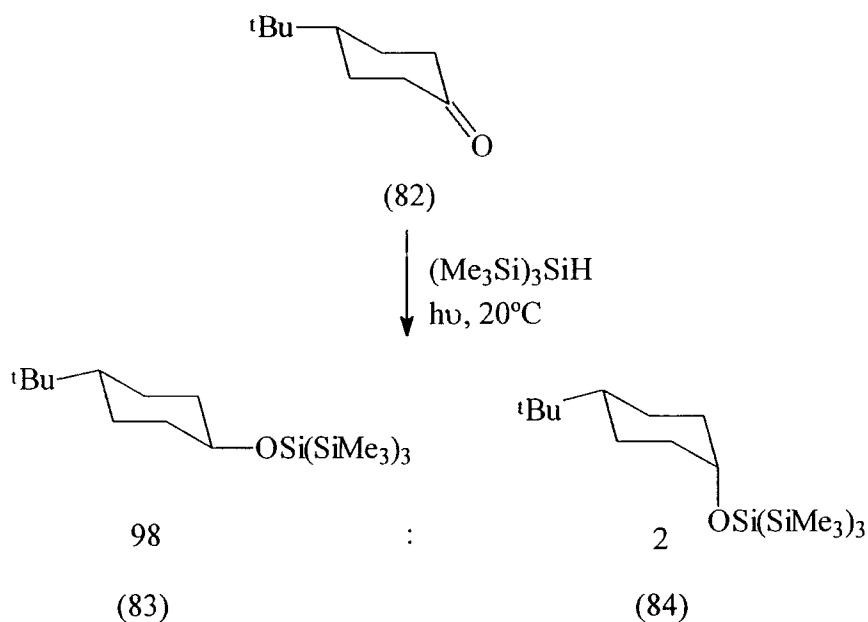
The difficulty in handling metal hydride reducing reagents has meant that silanes have become viable, relatively inert, non-toxic, alternatives. The use of silicon compounds as alternatives to organometallic reagents in the reduction of functional groups will be discussed in this section.

The reduction of ketones and aldehydes with silicon hydrides is well established. However, these reagents have also allowed the reduction of functional groups not normally possible by traditional methods. For example, Colvin has reported the reduction of lactol (**80**) with triethylsilane, Scheme A.26.<sup>44</sup>



Scheme A.26

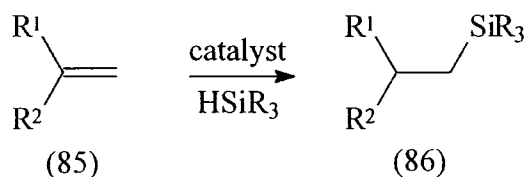
Tris(trimethylsilyl)silane has become valuable as a non-toxic alternative to the radical reducing reagent tributyltin hydride.<sup>45</sup> For example, it has been shown to reduce ketone (**82**) stereoselectively with high de, Scheme A.27.



Scheme A.27

### A.7. Hydrosilylation

This section will cover the hydrosilylation of alkenes, alkynes and carbonyl compounds. The hydrosilylation of carbon-carbon double bonds has been investigated since the 1940's and the reaction is used for the industrial preparation of certain organosilanes, such as adhesives and binders. Hydrosilylation allows easy preparation of various organosilicon compounds, and can be promoted by various methods.<sup>46</sup> These include UV irradiation, heat, electric discharge, peroxides and more commonly transition metal catalysts, Scheme A.28.

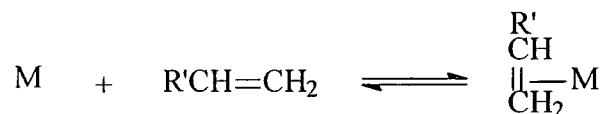


Scheme A.28

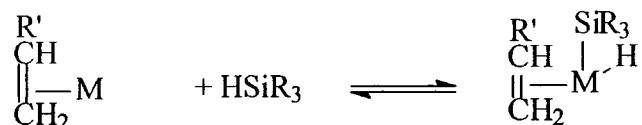
The generally accepted mechanism for transition-metal-catalysed hydrosilylation is shown below, Figure A.9.<sup>47</sup> The formation of an olefin-metal complex is followed by oxidative addition of the silane onto the metal. *Cis*-ligand insertion of the olefin into

the metal hydrogen bond then occurs. Finally reductive elimination affords the hydrosilylated product.

1. Oxidative complex formation



2. Oxidative addition



3. Cis-ligand insertion



4. Reductive elimination

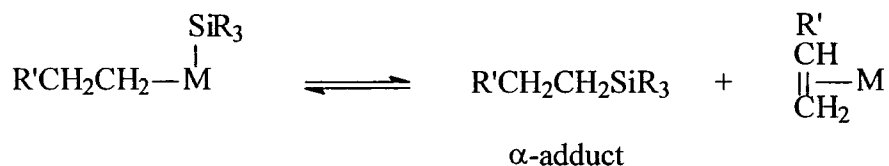
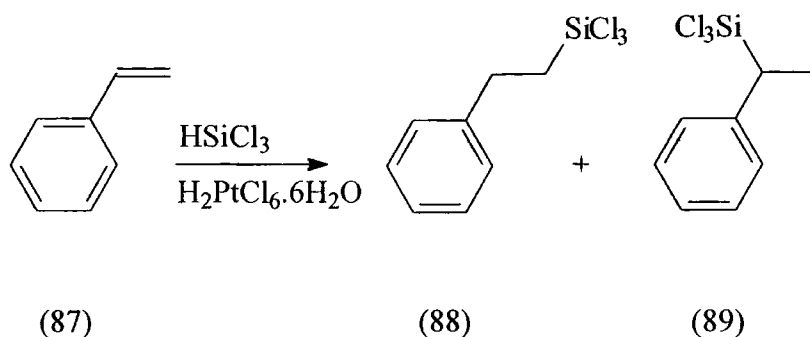


Figure A.9

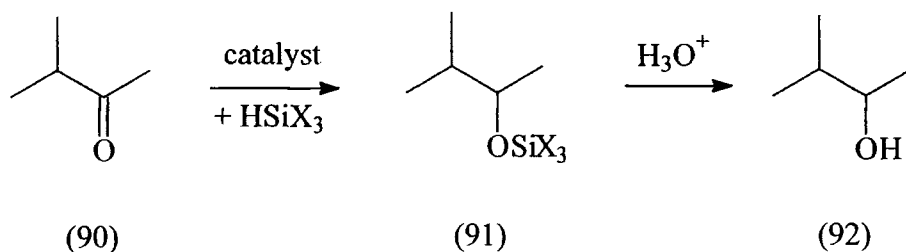
A range of catalysts have been widely used including rhodium, palladium and platinum. Notably, only a very small quantity is required and solvents are not normally needed.

In most cases hydrosilylation of 1-alkenes occurs to give the terminal adduct in high yields. Furthermore, reaction with internal alkenes frequently occurs with isomerisation to give the same terminal product. However, exceptions do exist. For example, hydrosilylation of styrene (**87**) with trichlorosilane gives a mixture of regioisomers, Scheme A.29.<sup>48</sup> Similarly, alkynes typically undergo hydrosilylation with *cis*-addition to give the *trans*-vinylsilane.



Scheme A.29

Ketones and aldehydes undergo transition-metal-catalysed hydrosilylation, providing a convenient non-nucleophilic alternative to metal hydride reagents, with the resultant silicon-oxygen bond being easily hydrolysed to give the desired alcohol, Scheme A.30a.



Scheme A.30a

The increasing interest in methods for generating enantiomerically pure compounds has meant that the asymmetric hydrosilylation of prochiral ketones with chiral catalysts (typically rhodium) has developed as a potential route to optically active alcohols, Figure A.10.<sup>49</sup>

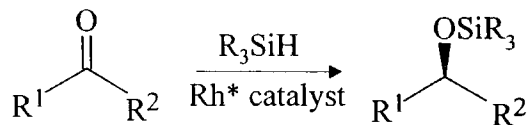
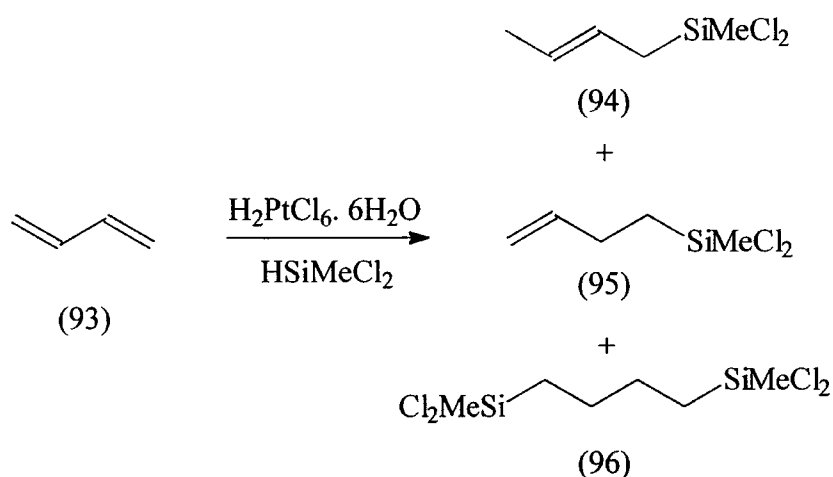


Figure A.10

A vast number of chiral ligands have been developed;<sup>50</sup> however, space precludes a more detailed discussion of this topic. Whilst asymmetric hydrosilylation

of ketones proceeds with high enantioselectivity, olefin hydrosilylation is generally considerably less successful. However, recently, Hayashi has shown that monodentate phosphine ligands have shown considerable potential for this transformation.<sup>51</sup> This is discussed in more detail in the next chapter.

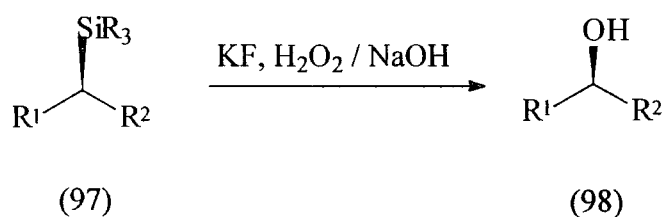
The hydrosilylation of dienes is also feasible but is frequently complicated by double bond isomerisation, Scheme A.30b. This presents a potential method for silacycle synthesis and this will be discussed more fully in the next chapter.



Scheme A.30b

### A.8. Oxidation of Organosilanes: Silicon as a Masked Hydroxy Group

The products of olefin hydrosilylation can be functionalised by a procedure commonly known as the Tamao oxidation.<sup>52</sup> For example, optically active alcohols (**98**) are attainable, without loss of optical activity, through oxidation of silane (**97**), Scheme A.31.



Scheme A.31

Although hydroboration-oxidation is an obvious alternative, the Lewis acidity of boron requires that it is oxidised immediately. In contrast, the neutrality of silicon allows it to survive many synthetic steps. Similarly, the protection-deprotection sequence required for hydroxyl groups during total synthesis may sometimes be troublesome, whereas a silicon group can be converted into a hydroxy group in a single oxidation step. A mechanism for the Tamao oxidation has not been determined; however, Tamao has postulated the mechanism shown below, Figure A.11. This mechanism involves attack of a fluoride ion in a fast and reversible step to afford a pentacoordinate species. The resulting electrophilic silicon is attacked by the nucleophilic oxidant (usually hydrogen peroxide) to produce a hexacoordinate intermediate in the rate determining step.<sup>52</sup> The group *cis* to the peroxide then migrates preferentially. Finally, the new silicon oxygen bond is hydrolysed to produce the expected alcohol.

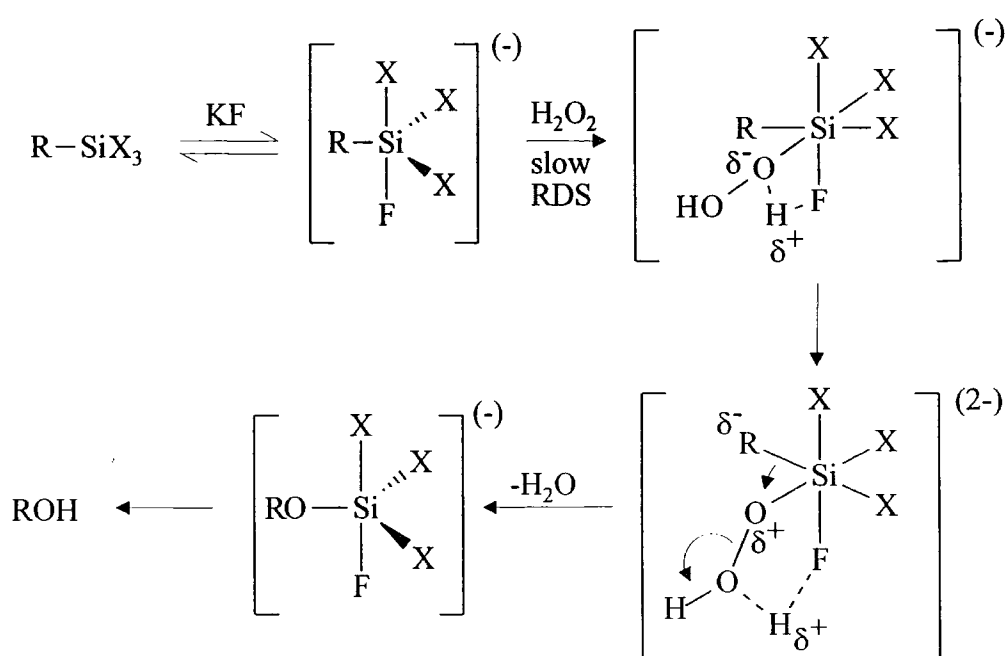


Figure A.11

The oxidation of a silicon - containing compound is only limited by the need for fluoride - labile groups directly attached to silicon (e.g. alkoxy, aromatic, or halogen groups). Since the initial introduction of this method by Tamao, a number of modifications have been reported and these have been discussed in a recent comprehensive review.<sup>53</sup>

## A.8. Silicon Tethered Reactions

In addition to entropic advantages intramolecular reactions are highly regioselective and often display a high degree of stereoselectivity when compared with analogous intermolecular processes. Acyclic reactants may undergo intermolecular reactions by the use of a temporary connection or tether. Removal of a tether gives the acyclic product, Figure A.12.

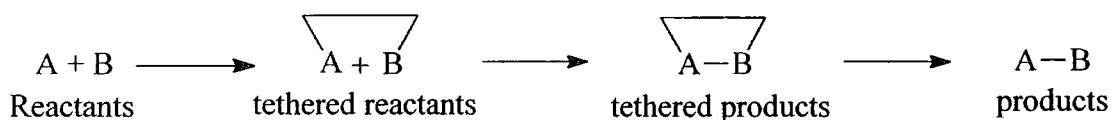


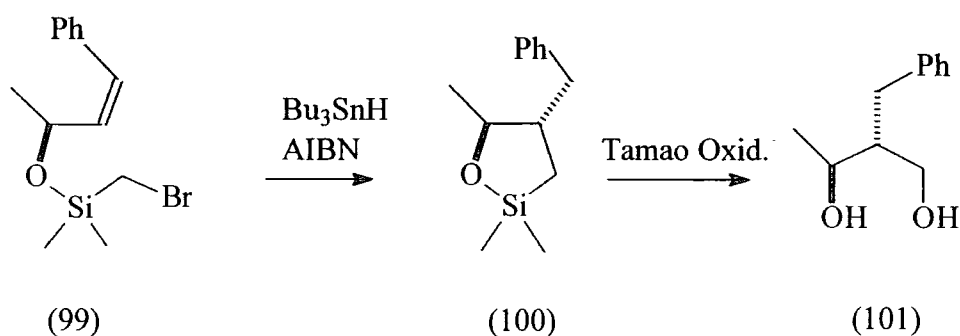
Figure A.12

Silicon tethers are becoming increasingly favoured, being readily available, inert under most reaction conditions, easily and selectively removed and can be transformed into other functionalities.

There have been two major reviews of silicon tethered reaction. Both have described silicon tethers in terms of tether length.<sup>54</sup> However, this approach is slightly confusing as there are many examples where the tether often includes atoms which are involved in the reaction but are not subsequently removed on extrusion of the silicon moiety. It would appear easier, therefore to describe silicon tethered reactions primarily by their reaction type.

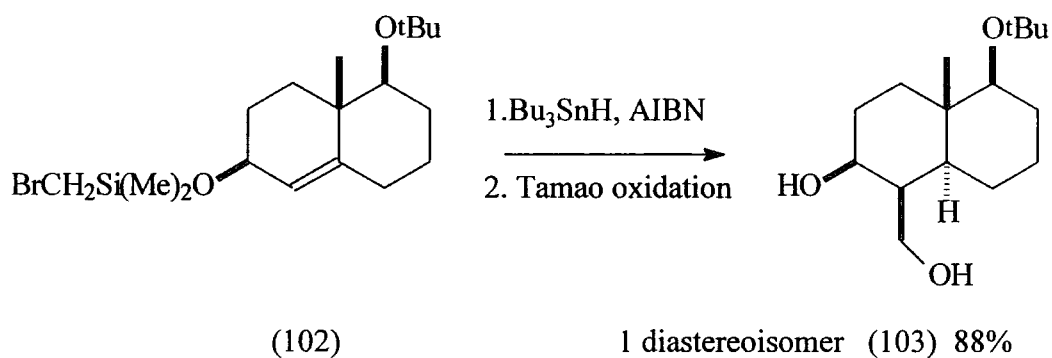
Intramolecular radical cyclisations have been by far the most productive and thoroughly researched area of silicon tethered chemistry. They can display remarkable differences in regiochemistry from their untethered analogues, allowing access to cyclisation products not normally available.

The application of silicon-tethered reactions was first reported by Nishiyama,<sup>55</sup> and Stork.<sup>56</sup> Nishiyama reported that (bromomethyl)dimethylsilyl allyl ethers (**99**) underwent radical cyclisation with high stereoselectivity. Subsequent extrusion of the silicon atom by Tamao type oxidation afforded 1,3-diols (**101**) in good yields and high stereoselectivity, Scheme A.32.<sup>55</sup>



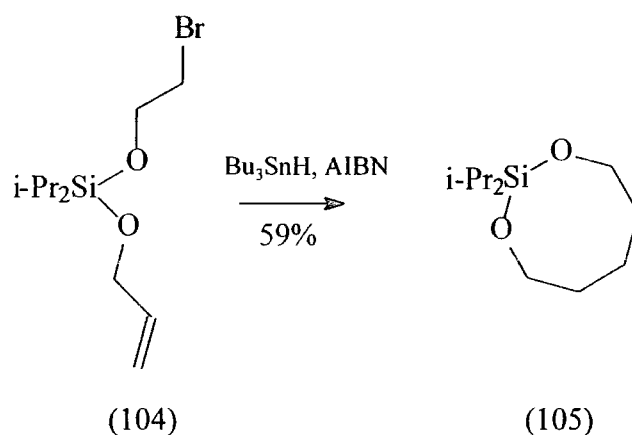
Scheme A.32

Stork has shown that this hydroxymethylation strategy can be used to control the stereochemistry of an adjacent ring junction, Scheme A.33.<sup>56</sup>



Scheme A.33

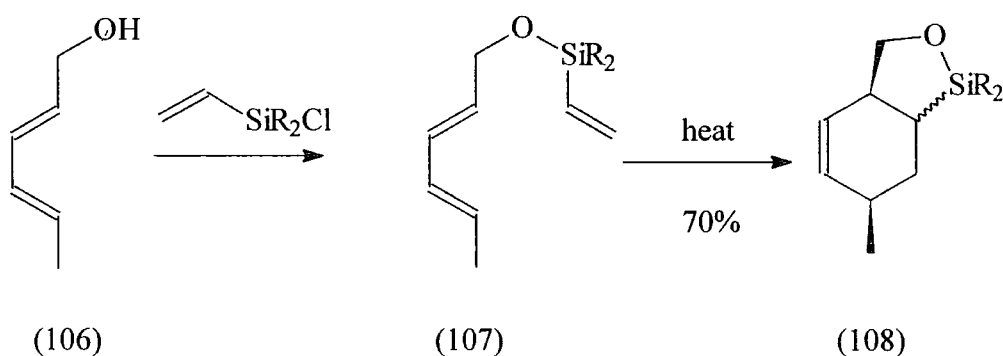
Ketal tethers have also been widely used in radical cyclisation reactions. Hutchinson reported that diisopropylsilyl ketal tethers undergo *endo*-trig cyclisations, to produce 7-, 8- and 9-membered rings. For example, bromide (104) undergoes a clean 8-*endo*-trig cyclisation to give the cyclic ketal (105), Scheme A.34.<sup>57</sup>



Scheme A.34

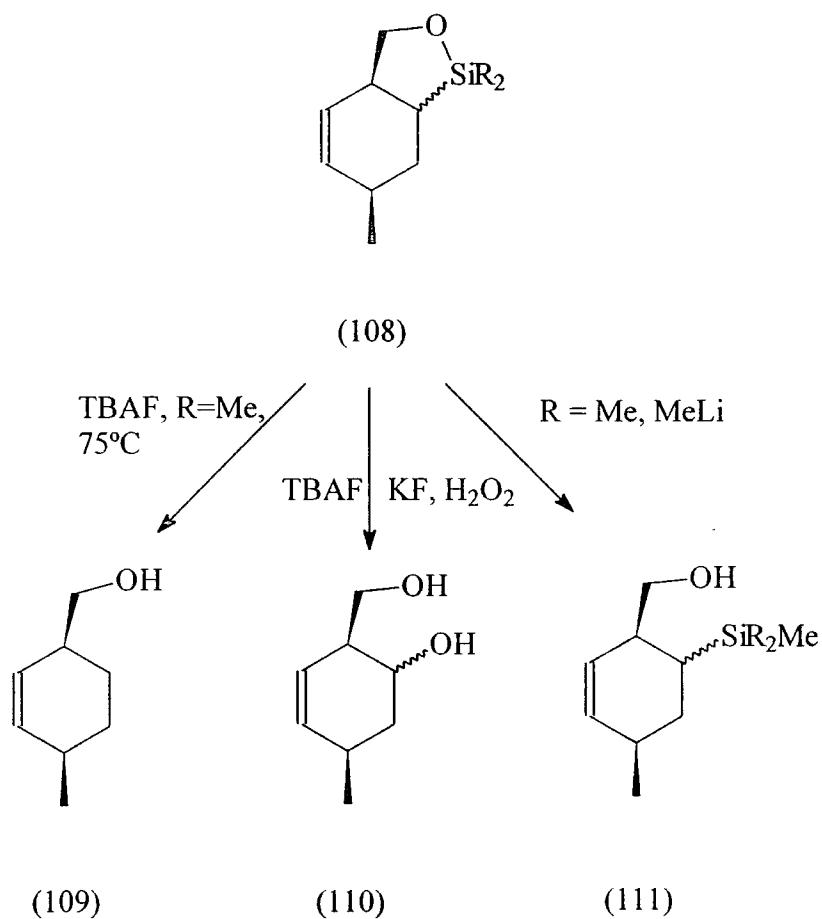
Cycloadditions are ideal for the application of a temporary silicon tether and a variety of cycloadditions, both thermal and photochemical, have been reported. However, Diels-Alder cycloadditions have been the predominant reaction and this section will concentrate on the use of silicon tethers for intramolecular Diels-Alder reactions (IMDA).

For example, Sieburth and Fensterbank have described the thermolysis of the tethered triene (**107**) to give the cyclohexene adduct (**108**) in good yields and moderate selectivities, Scheme A.35.<sup>58</sup> They found that the bulkier the R group on silicon the more the *exo*-transition state is favoured. This was attributed to unfavourable steric interactions between the R groups and the diene in the *endo*-transition state.



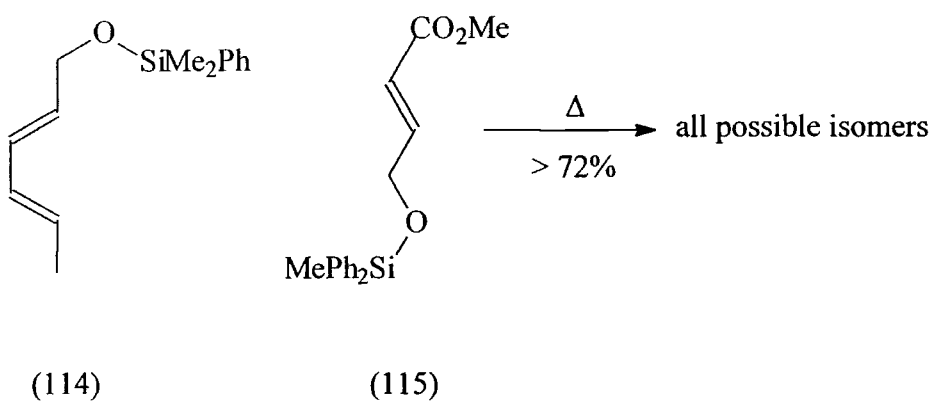
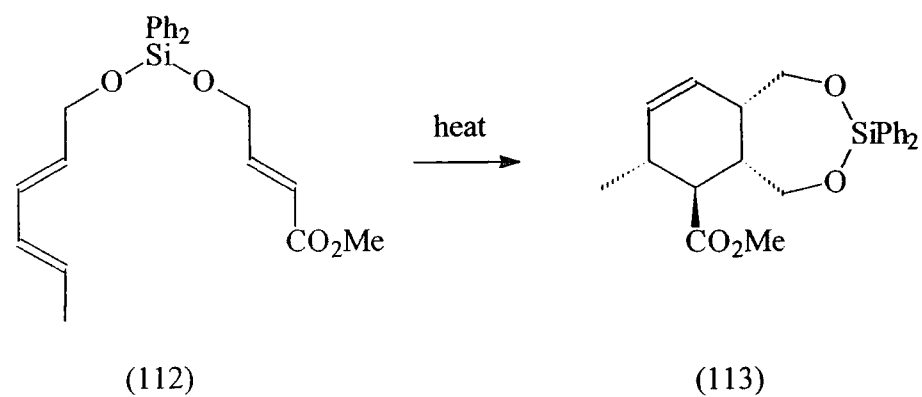
Scheme A.35

In most cases the silyl tether can be functionalised by oxidation or nucleophilic substitution, Scheme A.36.



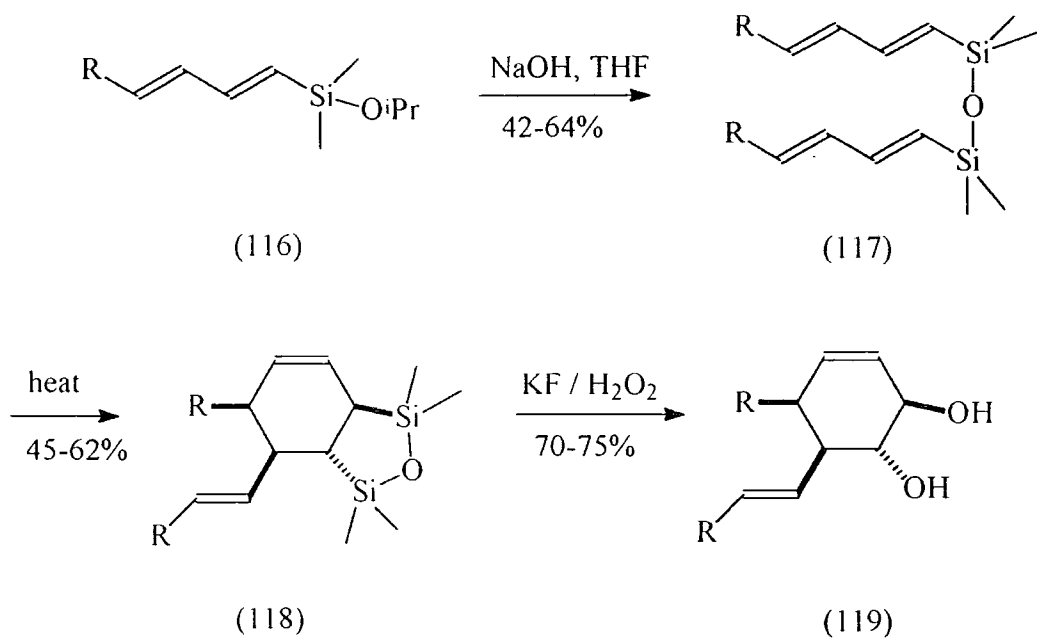
Scheme A.36

Silyl ketal tethers have also been used in IMDA reactions. Craig showed that thermolysis of **(112)** resulted in the formation of a single diastereoisomer **(113)**.<sup>59</sup> By comparison, a related intermolecular reaction resulted in the formation of all possible regio- and stereoisomers, Scheme A.37.



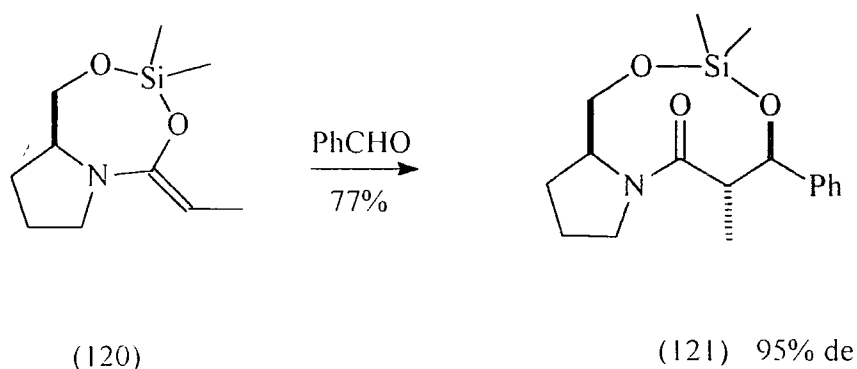
Scheme A.37

A rare example of a siloxane as a tethering unit has been reported by Luh.<sup>60</sup> Treatment of isopropoxyxysilyl dienes (**116**) with aqueous NaOH in THF affords symmetrical siloxane (**117**) in moderate yields, Scheme A.38. Thermolysis gave cycloadduct (**118**) as a single regio- and diastereoisomer. This, on Tamao oxidation, furnished cyclohexenediol (**119**).



Scheme A.38

As discussed in section A.5.5, the Mukaiyama reaction of silyl enol ethers constitutes a very reliable method for the stereoselective construction of carbon-carbon bonds. Silicon tethered aldol reactions have now been developed. Myers has shown that the (*S*)-prolinol-derived silylacetal (**120**) reacts with benzaldehyde at room temperature to give (**121**) in 77% yield in high de, Scheme A.39.<sup>51</sup>



Scheme A.39

A variety of other silicon tethered reactions have been developed, including alkene metathesis, anodic couplings, allylations.<sup>54</sup> The scope of silicon tethered reactions is vast and, if chirality can be incorporated into the temporary silicon tether, the possibilities for asymmetric synthesis are immediately apparent.

## **B. Chiral Silicon**

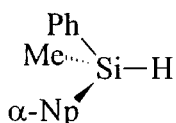
### **B.1. Asymmetric Organosilicon Chemistry**

From this brief introduction to organosilane chemistry it is obvious that organosilicon compounds possess considerable synthetic potential. Whilst high regioselectivity is commonly observed, absolute stereocontrol has been more difficult to attain. This is reflected in the fact that the development of chiral organosilicon compounds has been less well explored. This section will attempt to highlight some of the key syntheses and applications of chiral organosilicon compounds.

The early syntheses and applications of chiral silicon compounds was thoroughly reviewed by Chan and Wang in 1992.<sup>62</sup> This review, and the work described in this thesis, will follow Paquette's suggestion and classify chiral organosilanes into two categories: Si-centred where the chirality resides on the silicon, and C-centred where the chirality resides on a substituent carbon.<sup>63</sup>

#### **B.1.1. Si-Centred Chirality**

Si-centred chiral molecules are fairly limited in structure with most being derived from the methyl- $\alpha$ -naphthylphenylsilyl system (**122**), Figure B.1.

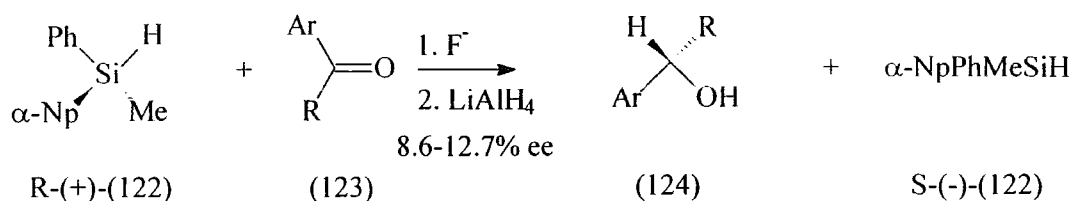


(122)

Figure B.1

Any influence on selectivity is mainly steric in origin and, since C-Si bonds are longer than analogous C-C bonds, this influence tends to be less pronounced. As previously discussed, hydrosilanes are useful reagents in the reduction of ketones and Fry and MacAdam reported that the fluoride-catalysed hydrosilylation of aromatic ketones

with silane **(122)** gave access to optically active alcohols, albeit with low enantioselectivity, Scheme B.1.<sup>64</sup>



Scheme B.1

The inversion at silicon and low ee has been attributed to pseudorotation of the hypervalent intermediates **(125)** and **(126)**, Figure B.2.<sup>4, 64</sup>

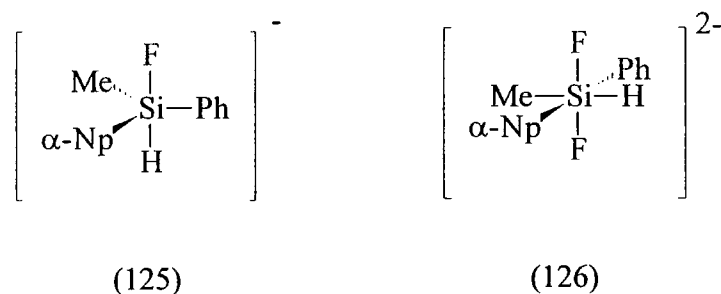
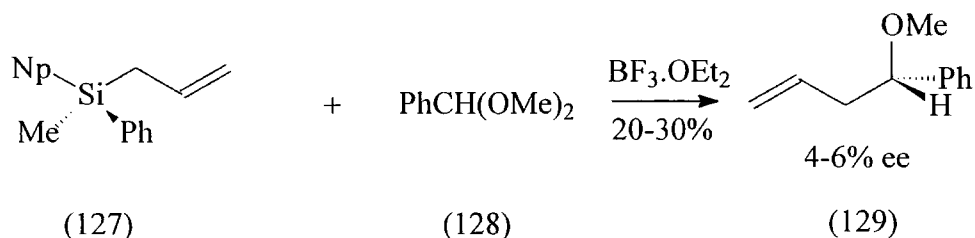


Figure B.2

Similarly, the related chiral allyl silane **(127)** reacts with benzaldehyde dimethyl acetal **(128)**, to give the chiral allyl ether **(129)** in moderate yield but only 4-6% ee, Scheme B.2.<sup>65</sup>



Scheme B.2

Denmark postulated that low ee can be accounted for by an extended open transition state **(130)**, in which the asymmetric silicon is so far removed from the reacting centre that stereocontrol is minimal.<sup>66</sup> However, if a *synclinal* transition state **(131)** can be

encouraged (*e.g.* using ligands on the silicon that allow co-ordination with the reacting centre) asymmetric effect may be enhanced, Figure B.3. However, to date, only C-centred organosilanes with this feature have been developed.<sup>67</sup>

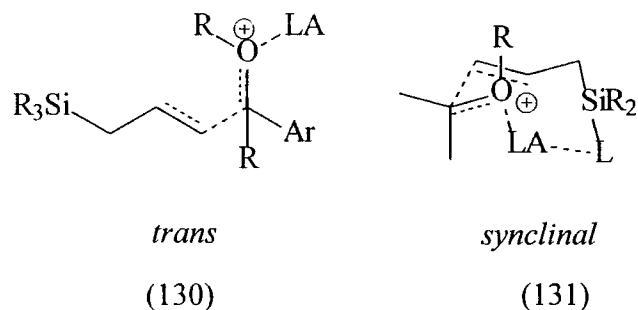


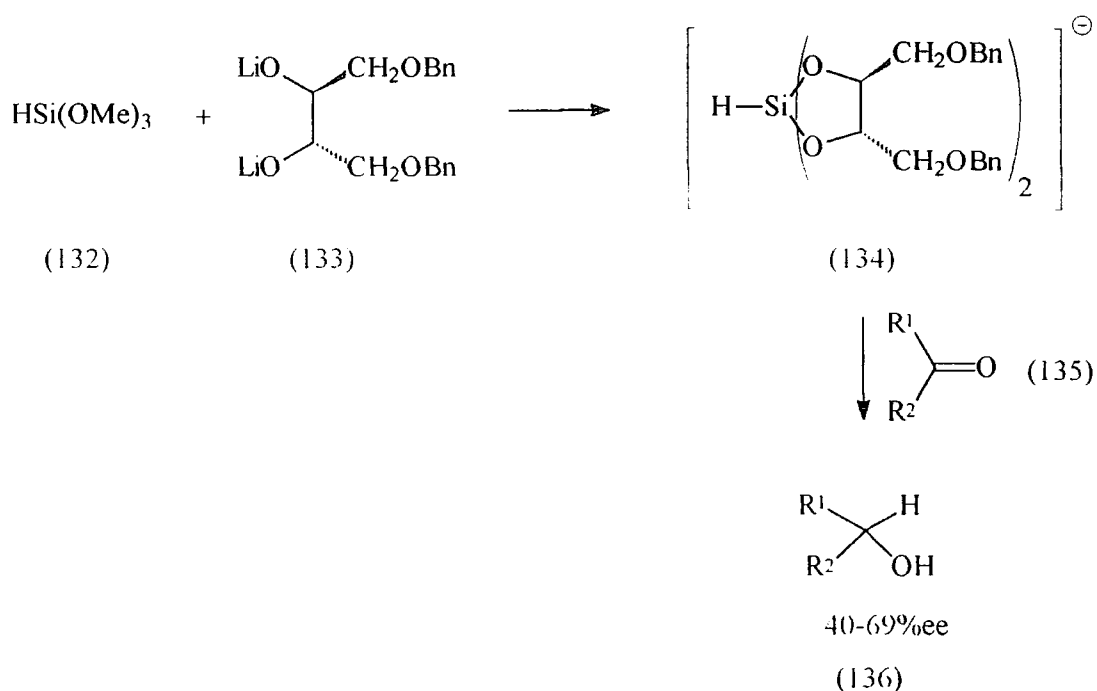
Figure B.3

### **B.1.2. C-Centred Chirality**

The problems associated with using Si-centred chiral silicon compounds has resulted in more work being focused on the use of C-centred chiral organosilanes. In this case, pseudorotation at silicon would not be an issue as long as the integrity of the C-centre remained intact.

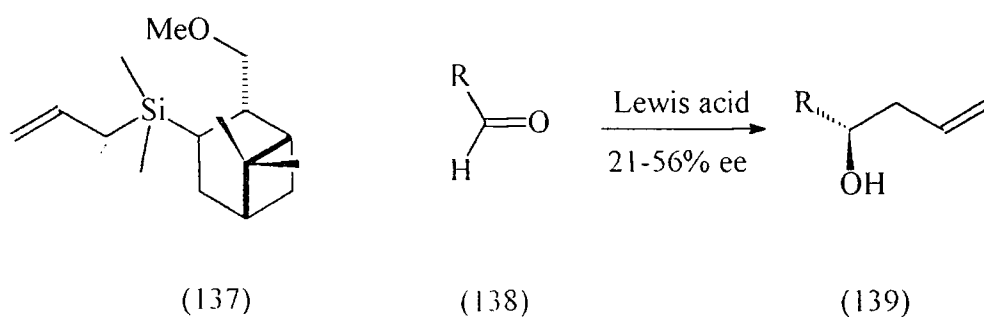
The bulk of the research involving C-centred chiral silicon reagents has concentrated on the asymmetric reduction of ketones and the asymmetric allylation of carbonyl compounds.

Kohra *et al.* have used hypervalent silicon hydrides (**134**) formed by the reaction of trimethoxysilane (**132**) with optically active lithium alkoxides (**133**), derived from diethyl-L(+)-tartrate in the hydrosilylation of ketones (**135**), Scheme B.3.<sup>68</sup>



Scheme B.3

Taddei has incorporated an alkoxy ligand into the  $\beta$ -pinene derived allylsilane (**137**) to give allylic alcohol (**139**) in moderate ee from the alkylation of aldehydes (**138**) Scheme B.4.<sup>67</sup> Presumably the alkoxy functionality encourages the formation of the cyclic *synclinal* transition state, thus bringing the chiral centre closer to the reaction centre.



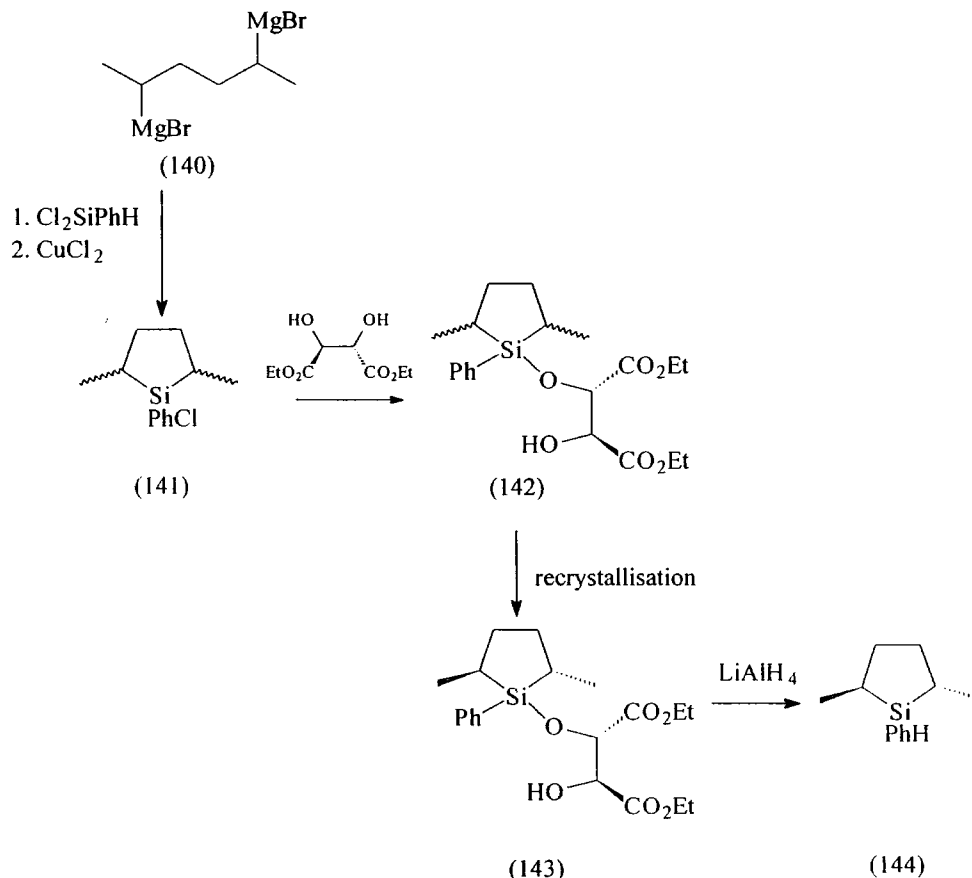
Scheme B.4

The main problem with C-centred chiral silicon compounds is that often they are derived from complex chiral structures that are not readily synthesised. In conclusion, with this proviso, C-centred chiral silicon compounds show greater promise in the efficient induction of asymmetry. Consequently, the main challenge is in the design

and synthesis of readily available C-centred chiral silicon compounds for use in asymmetric synthesis.

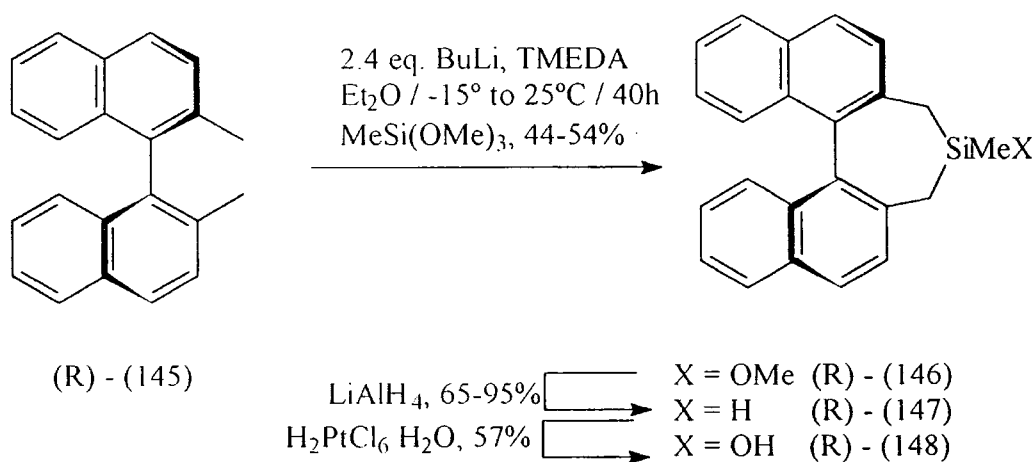
### C. Cyclic Silicon Compounds

Synthetic routes to cyclic silicon compounds have been known for some time and have been recently reviewed.<sup>69</sup> There are a number of cyclic silylketal compounds in the literature, but for the purposes of this review, this section will concentrate on the synthesis of carbocyclic silicon species. The most common method of silacycle synthesis has involved reaction of a nucleophilic carbon with a dichlorosilane. The very first cyclic silicon compound was reported in 1915 by Bygden,<sup>70</sup> who reported the synthesis of dichlorosilacyclopentane and its dimethyl and diethyl derivatives. His method was later improved by West who synthesised twenty one new silacycles using Grignard reagents derived from dibromoalkanes.<sup>71</sup> More recently Roberts has reported the preparation of 2,5-dimethyl-1-phenyl-silacyclopentane (**144**) in good yield by this method.<sup>72</sup> Resolution through exhaustive recrystallisation with diethyl-L-tartrate afforded enantiomerically pure adduct (**143**) and finally treatment with  $\text{LiAlH}_4$ , gave the homochiral silacycle (**144**), Scheme C.1.



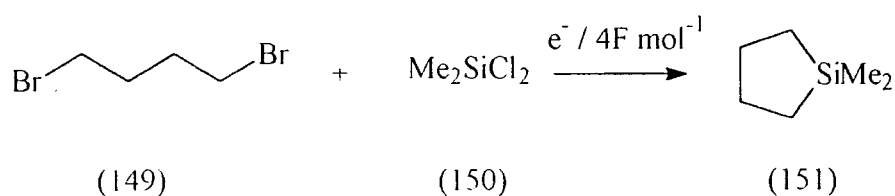
Scheme C.1

There have been other reports of the asymmetric synthesis of enantiomerically pure silacycles. Jung and co-workers have reported the synthesis of the binaphthyl substituted silacycles (**146-148**).<sup>73</sup> Their methodology involved the use of lithiated binaphthyl precursors, Scheme C.2.



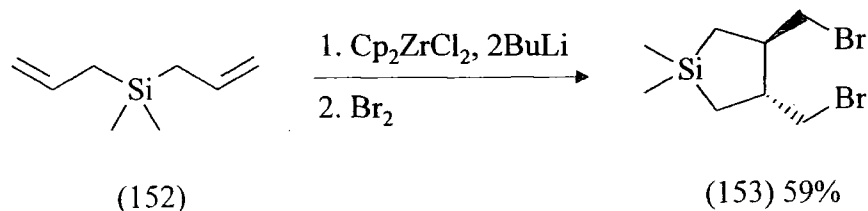
Scheme C.2

Jouikov has reported the use of electrolysis in the reaction of dibromoalkane (**149**) in the presence of dichlorosilanes to afford a variety of silacycle ring sizes in good yields, Scheme C.3.<sup>74</sup>



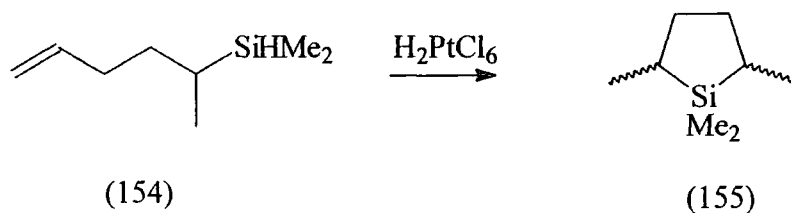
Scheme C.3

The cyclisation of non-conjugated dienes in the presence of a stoichiometric amount of  $\text{Cp}_2\text{ZrCl}_2$  and two equivalents of BuLi was first described by Nugent.<sup>75</sup> This methodology can be used to give access to silacycles if the starting diene contains a  $\text{SiR}_2$  group. For example, dimethyldiallylsilane (**152**) reacts to give the zirconacycle as described above. Subsequent treatment of the reaction mixture with bromine gave the silacyclopentane (**153**), Scheme C.4.<sup>75</sup>



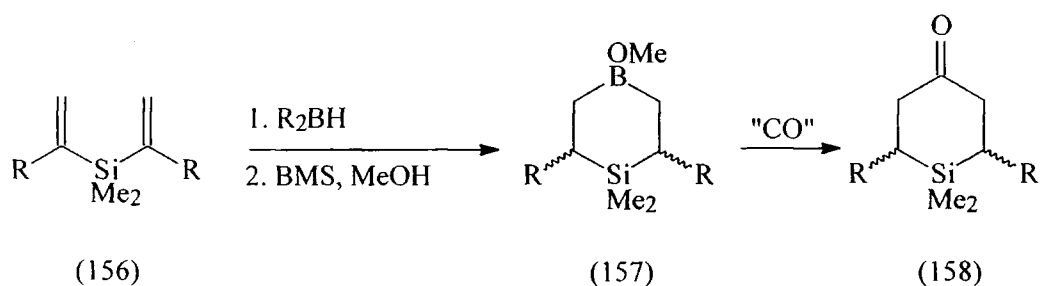
Scheme C.4

The hydrosilylation of alkenes represents one of the most powerful methods for C-Si bond formation. In this vein, silacycle (155) was prepared in good yields as a 1:1 mixture of *cis:trans* isomers from the chloroplatinic acid-catalysed hydrosilylation of the silane (154), Scheme C.5.<sup>76</sup>



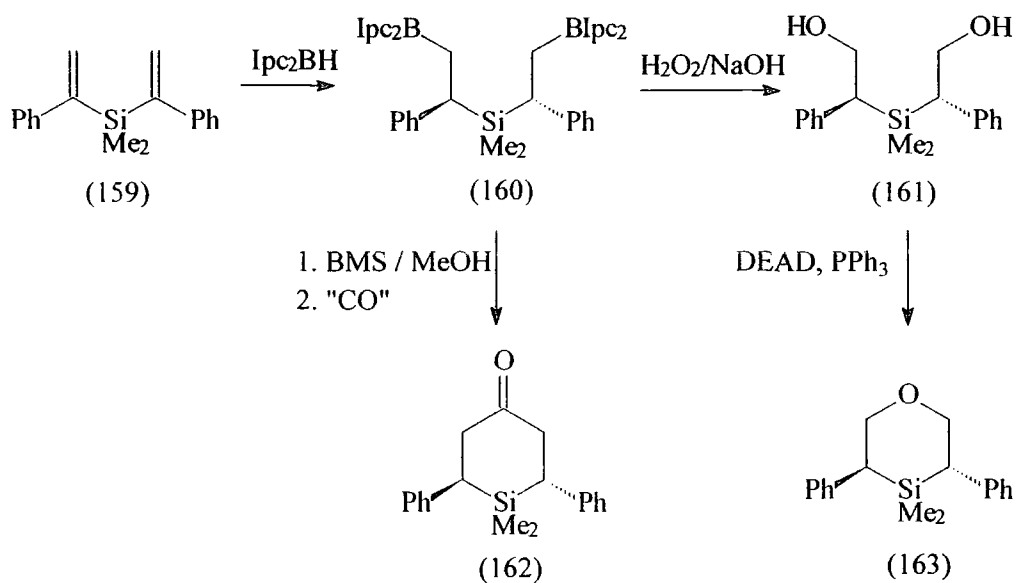
Scheme C.5

Soderquist and co-workers have shown that a variety of silacyclohexanones (158) can be obtained from the double hydroboration of divinyl silanes (156), Scheme C.6.<sup>77</sup>



Scheme C.6

Previous work in the Durham research group has shown that this methodology can be exploited to provide enantiomerically enriched cyclic silanes, Scheme C.7.<sup>78</sup>



Scheme C.7

#### D. Conclusion

From this brief review of some aspects of organic silicon chemistry, it is evident there is a vast depth of well established research in the syntheses and applications of silicon compounds. However, there remains a huge potential for new research, particularly in the area of asymmetric organosilicon chemistry. It is envisaged that a homochiral silacycle may be readily used for a variety of useful applications, particularly in the area of silicon tethered reactions.

**CHAPTER TWO**  
**RESULTS AND DISCUSSION**

## E. Silacycle Synthesis

### E.1. Introduction - Disconnection Approach

The initial challenge of this project was the development of viable synthetic routes to enantiomerically pure  $C_2$  symmetric silacycles. Our target was the disubstituted silacycle (**1**) which can be disconnected in a number of ways, Figure E.1.

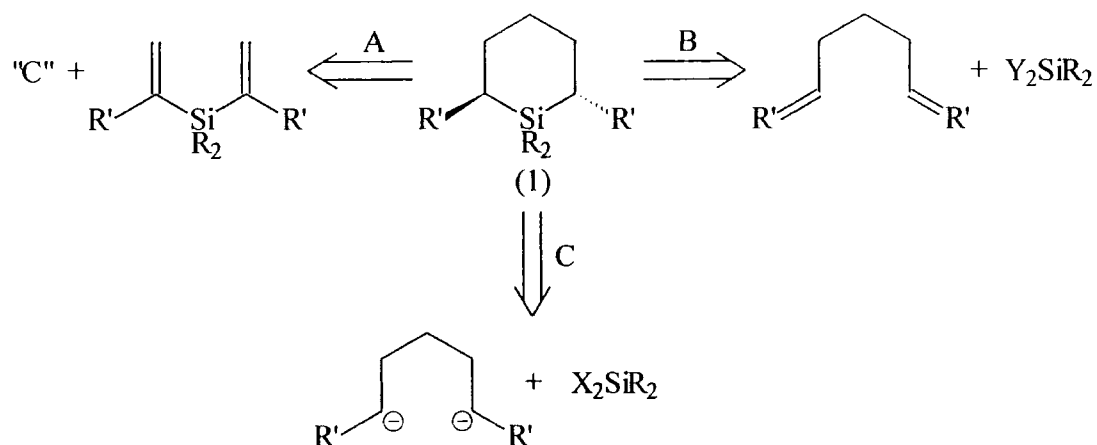


Figure E.1

Disconnection A utilises substituted divinylsilanes as starting materials. As illustrated in the previous section, Soderquist has shown that hydroboration is a possible way to achieve this transformation. Work in this group by Matthews has shown that it is possible to introduce asymmetry into this process.

At the outset of this work it was a priority to develop the conversion of a more stable  $\text{SiR}_2$  unit into the more synthetically useful  $\text{SiCl}_2$  species. Such a strategy would remove the need to handle very reactive dihalosilane moieties. This would allow standard work-up and purification techniques to be used throughout the synthetic route and the dihalosilane could be revealed at the appropriate point. In addition the stereoselectivity of these processes needed to be optimised.

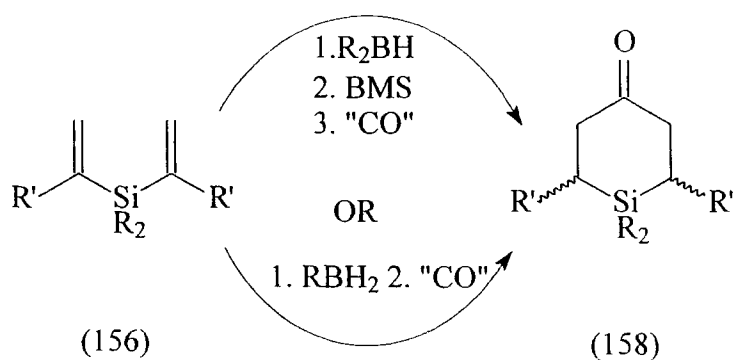
Strategy B involves hydrosilylation of dienes, (section N) or alternatively the hydrometallation, with subsequent silylation. The former approach has been explored with little success. However, recent developments in asymmetric hydrosilylation have afforded new hope and this work is discussed in section N.1. Other hydrometallation

strategies, notably the use of zirconium reagents, have also been considered, section N.2.

Disconnection C involves the formation of a homochiral carbanion species and this is, potentially, a very attractive route, because of the facile reaction between carbanions and electrophilic silicon species. However, this strategy is prohibited by the lack of effective asymmetric deprotonation methodologies and has not been considered further here.

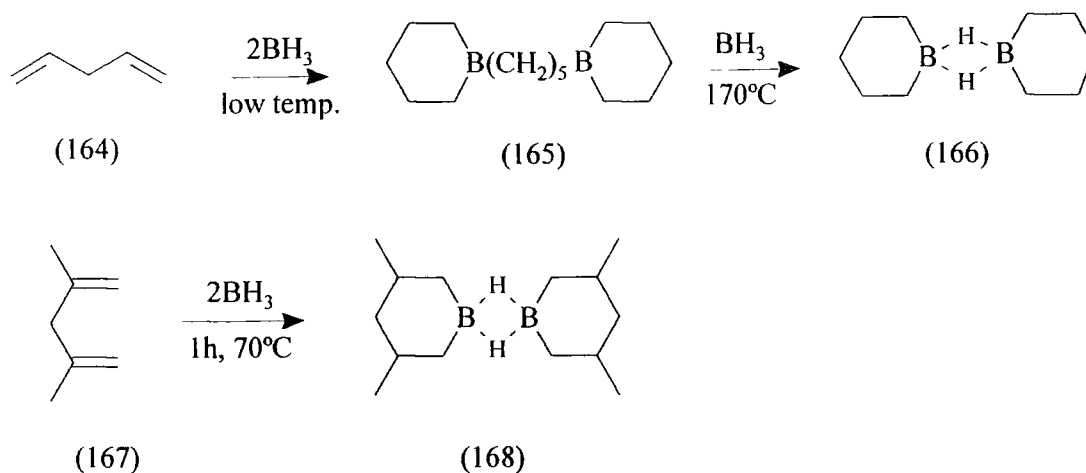
## E.2. Hydroboration as a Tool in the Synthesis of Silacycles

The synthesis of silacycles by the hydroboration of divinylsilanes is a strategy that was initially developed by Soderquist and co-workers and was briefly discussed in the last chapter.<sup>77</sup> Some initial studies have also been carried out in this research group; however these remain largely unpublished.<sup>78</sup> Soderquist reported that divinylsilanes undergo cyclic hydroboration ( $\text{RBH}_2$ ) to give, after carbonylation, silacyclohexanones (**158**), Scheme E.1. When hydroborating reagents incorporating two alkyl substituents ( $\text{R}_2\text{BH}$ ) are used, a cyclisation step is required. Soderquist utilised little known boron redistribution chemistry and our studies into this reaction are discussed in more detail in Section K.3.



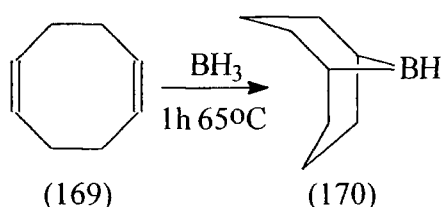
Scheme E.1

The synthesis of cyclic organoboranes by the cyclic hydroboration of dienes has been known for some time, Scheme E.2.<sup>79</sup> Whilst the hydroboration of alkenes is invariably a regiospecific process, the hydroboration of dienes can give complex mixtures, although thermal isomerisation often gives the desired product, Scheme E.2. Notably, in the case of dimethylborinane (**168**), isomerisation is not required as cyclic hydroboration of the disubstituted diene (**167**) is regiospecific.<sup>80</sup>



Scheme E.2

Bicyclic boranes can also be prepared by this strategy. For example, the widely used hydroborating reagent 9-BBN (**170**) is made in this way,<sup>79</sup> Scheme E.3.



Scheme E.3

Organoboranes can be functionalised in a variety of ways including protonolysis, halogenolysis, oxidation and amination to give alkanes, alkyl halides, alcohols and amines respectively.<sup>81</sup> Aldehydes and ketones can be synthesised by the carbonylation of organoboranes with carbon monoxide at elevated temperatures or pressures. The mechanism of most organoborane functionalisations including carbonylation is described below. The empty p orbital on the boron atom of

organoboranes renders the boron electrophilic and highly susceptible to attack by nucleophiles. The tetrahedral species so formed is known as an organoborate. If the nucleophile bears a leaving group, then 1,2-migrations of an alkylborane occur very easily onto the electrophilic centre, Figure E.2.

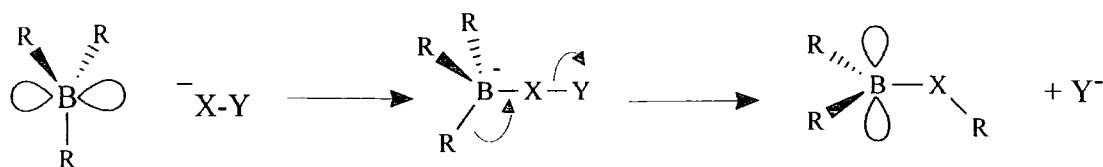
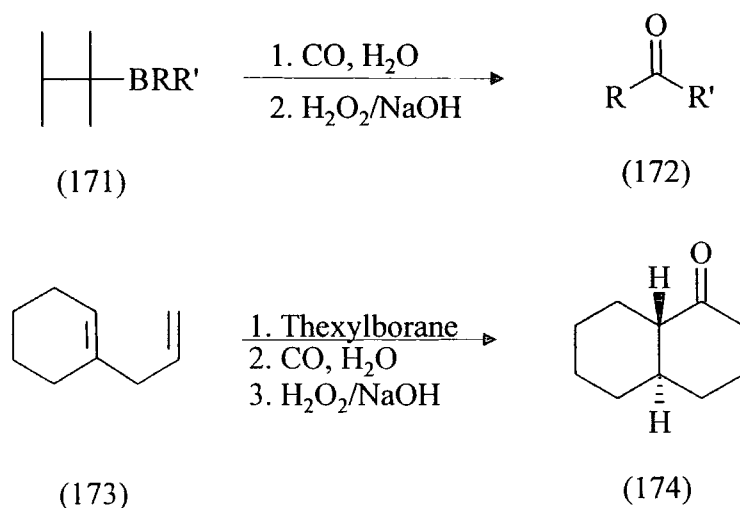


Figure E.2

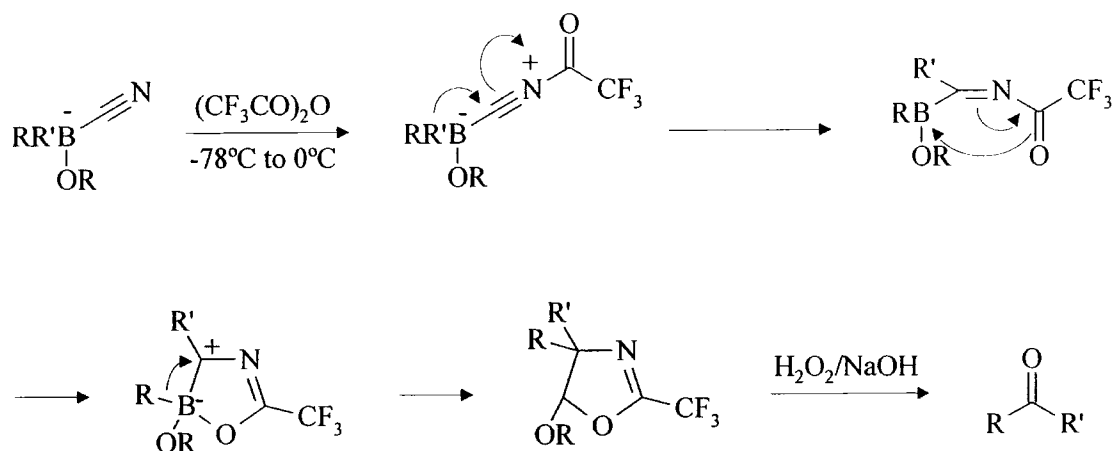
During carbonylation the extent of the migration from boron to carbon can be controlled by the use of additives. For example, the presence of hydride leads to aldehydes, whilst water halts the transfer after two migrations to allow formation of ketones.<sup>79</sup> Alternatively, the migration can be controlled by incorporating a group with low migratory aptitude such as an alkoxy group or the sterically hindered *tert*-hexyl group. *tert*-Hexylborane has been extensively used in the simple conversion of alkenes and dienes into both acyclic ketones (172) and cyclic ketones (174) respectively, Scheme E.4.<sup>79</sup>



Scheme E.4

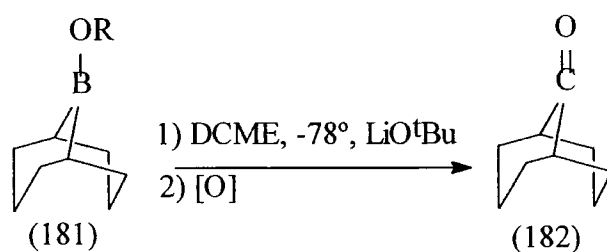
Milder alternatives to carbonylation with carbon monoxide have also been developed. The cyanidation of organoboranes gives cyanoborate intermediates (175), which, on reaction with trifluoroacetic anhydride, give intermediates (176). These are

prone to the migration of alkyl groups from boron to carbon and control of the reaction can yield either a tertiary alcohol or, in this case, a ketone (**180**), Scheme E.5.<sup>82</sup> This process offers advantages over carbon monoxide as elevated pressures are not required and the reaction can proceed at moderate temperatures.



Scheme E.5

Alternatives to both cyanide and carbon monoxide exist. Alkoxydialkylboranes (**181**) undergo rapid reaction with dichloromethyl methyl ether (DCME) at low reaction temperatures, over short time periods, to give the corresponding carbonyl compound, Scheme E.6,<sup>83</sup>. More recently, tris(phenylthio)methane has been used as a solid non-volatile alternative to DCME in some reactions.<sup>84</sup>



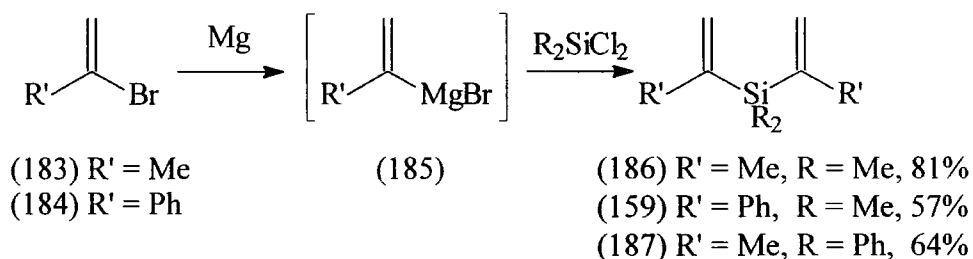
Scheme E.6

Given the relative ease of organoborane functionalisation reactions and the precedent set by Soderquist and Matthews it was envisaged that the asymmetric hydroboration of divinylsilanes might allow efficient access to optically active C<sub>2</sub> symmetric silacycles.

## F. Divinylsilane synthesis

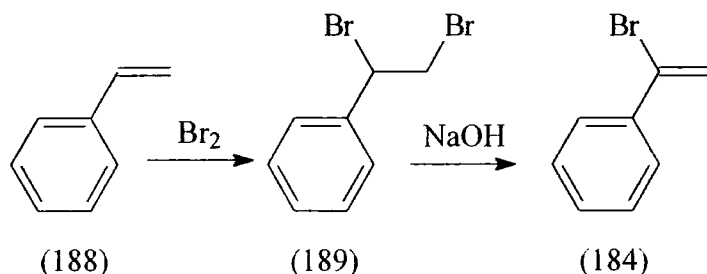
In order to implement the hydroboration strategy a range of substituted divinylsilanes were required for the synthesis of substituted silacycles and for mechanistic studies into the redistribution reaction, (see Section L). Divinylsilanes (**186** and **159**) had been made previously within the group using a Grignard procedure based on a method described by Soderquist, Scheme F.1.<sup>77, 78</sup>

Whilst Matthews had been able to achieve good yields with the dimethylsilanes, other more hindered silanes proved more difficult. This methodology was repeated and  $\alpha$ -disubstituted divinylsilanes (**186** and **159**) were synthesised with the physical data in agreement with that obtained previously.<sup>77, 78</sup>



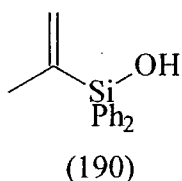
Scheme F.1

However, in our hands the yields of divinylsilane (**159**) were irreproducible and frequently low. This was attributed to the poor quality of commercially available  $\alpha$ -bromostyrene (**184**). Consequently  $\alpha$ -bromostyrene was prepared, using a method described by Soderquist,<sup>77</sup> involving the bromination, dehydrobromination of styrene, Scheme F.2. The formation of  $\alpha$ -bromostyrene (**184**) was confirmed by the appearance of alkene doublets ( $\delta$ 6.13 and  $\delta$ 5.80) in the  $^1\text{H}$  NMR and by comparison with an authentic commercial sample. With this material, divinylsilane (**159**) could be reliably prepared in acceptable yields (55-60%) and on a large scale.



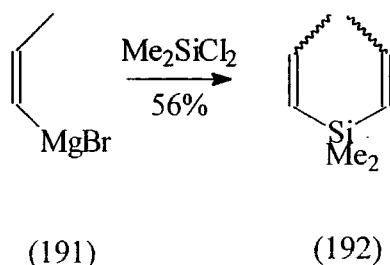
Scheme F.2

As previously discussed, there have been difficulties in achieving reliable yields with the more hindered diphenyl analogue (**187**). Initial attempts afforded divinylsilane (**187**) in low variable yields (20-40%). This was attributed to the steric bulk of the diphenylsilyl unit inhibiting the second addition. Evidence for this was obtained by the isolation of the vinylsilanol (**190**), shown below. Vinylsilanol (**190**) was characterised by GCMS analysis showing a  $M^+$  peak at 240 and an IR band at  $3041\text{ cm}^{-1}$  characteristic of an OH stretch.



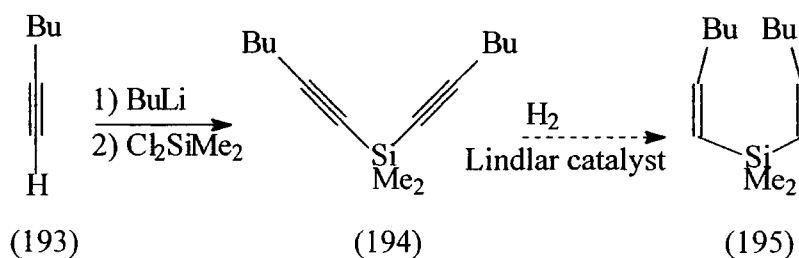
The yield of the divinylsilane (**187**) was found to be significantly enhanced by preparing activated magnesium in the manner of Baker *et al.*<sup>85</sup> Activation of the magnesium occurs by physical agitation under nitrogen which breaks down the oxide layer on the surface thus allowing a quicker, more effective reaction.

$\beta$ -Substituted divinylsilane (**192**) has also been made by this Grignard method. *Cis*-Bromopropene (**191**) was used to give a 83:16:1 mixture of *ZZ:ZE:EE* stereoisomers as determined by GCMS and  $^1\text{H}$  NMR analysis, Scheme F.3. However, the isomers could not be separated by chromatography. These results suggested that divinylsilane (**192**) would not be suitable for the synthesis of homochiral silacycles. However, it would still be of importance for subsequent mechanistic studies into the hydroboration and redistribution of  $\beta$ -substituted divinylsilanes, see section L.



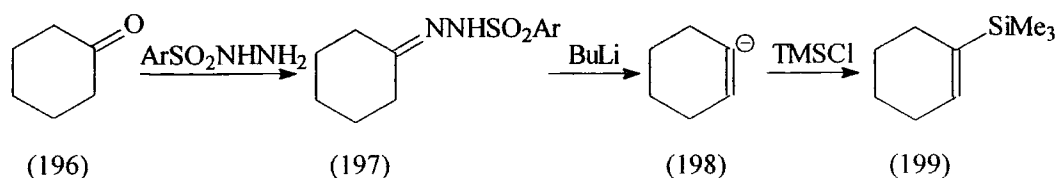
Scheme F.3

The problem of synthesising stereochemically pure  $\beta$ -substituted divinylsilanes forced us to explore alternative methods of vinylsilane synthesis. The stereoselective reduction of alkynylsilanes offers a variety of methods for synthesising vinylsilanes and was discussed in section A.5.1. Consequently, the bis-hexynylsilane (**194**) was prepared by the deprotonation of hexyne (**193**) and trapping with dichlorodimethylsilane, Scheme F.4. It was hoped that reductive hydrogenation with Lindlar catalyst would provide stereochemically pure divinylsilane (**195**). However, the reaction showed little evidence of reduction as ascertained from the  $^{13}\text{C}$  NMR signals ( $\delta$ 84-81) of the triple bond.



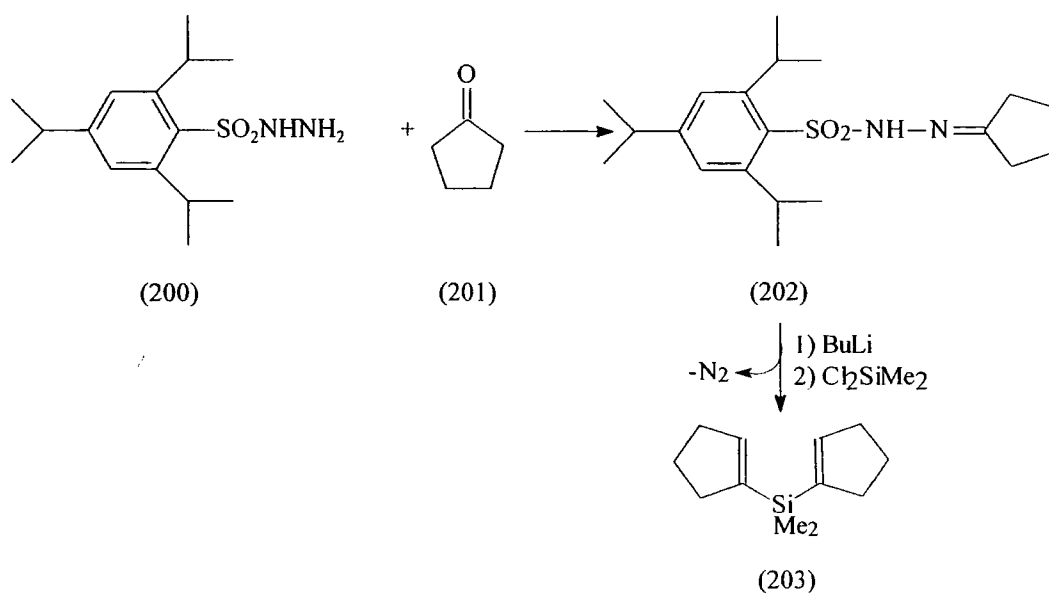
Scheme F.4

At this point attention turned to the synthesis of divinylsilanes with a cycloalkene structure, which would circumvent the problem of alkene stereoisomers. The synthesis of vinylsilanes from cyclic ketones has been reported by Bond and co-workers. For example, the arylsulfonyl hydrazone (**197**) derived from cyclohexanone (**196**) was converted into the anion (**198**) on reaction *in situ* with BuLi, Scheme F.5. This was trapped with a number of electrophiles, for example, chlorotrimethylsilane to produce the vinylsilane (**199**).<sup>86</sup> Interestingly only a GC yield was reported.



Scheme F.5

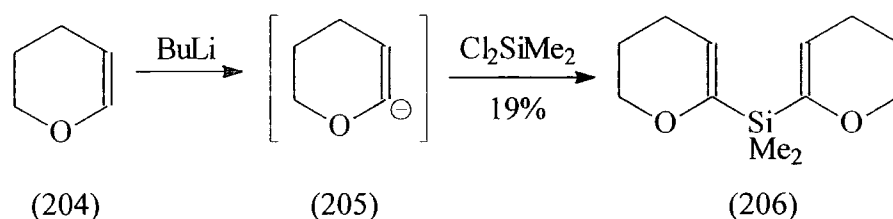
Using Bond's methodology we attempted the synthesis of divinylsilane (**203**) from the cyclic ketone (**201**), Scheme F.6. Whilst the hydrazone (**202**) could be prepared following the literature procedure, metallation and elimination gave divinylsilane (**203**) in low yield and poor quality. Although (**203**) could be identified by GCMS with  $M^+$  peak of 192 it could not be fully characterised or isolated as the synthesis produced a number of unidentifiable side products, that could not be separated by flash column chromatography or distillation. A variety of attempts to modify the reaction conditions were undertaken but were no more successful. Furthermore, similar problems with this procedure have been noted.<sup>87</sup>



Scheme F.6

Vinyl ethers are known to undergo facile metallation and a literature search revealed that the divinylsilane (**206**) has been made previously by Georgyan *et al.*<sup>88</sup> Lithiation of dihydropyran (**204**), with *in situ* trapping using dichlorodimethylsilane

gave divinylsilane (206) in comparable yields to that previously described by Georgyan, Scheme F.7. Attempts to improve this were unsuccessful.



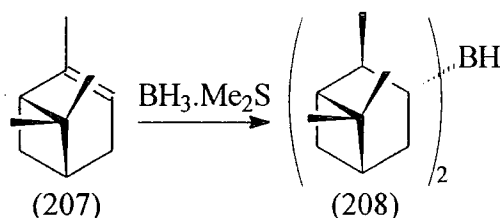
Scheme F.7

In conclusion, a range of  $\alpha$ -substituted divinylsilanes can be synthesised in good yields and on large scale.  $\beta$ -Substituted divinylsilanes can be prepared, albeit, only with moderate stereoselectivity. Cyclic divinylsilanes have been prepared but only in low yields. However, sufficient material could be accumulated to study their applications in asymmetric hydroboration.

## Section G. Asymmetric Hydroboration of Divinylsilanes

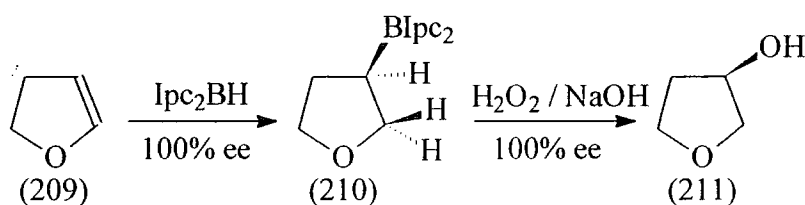
### G.1. Introduction to Asymmetric Hydroboration

Asymmetric hydroboration became firmly established with the advent of the pinene based chiral hydroborating reagent diisopinocampheylborane ( $\text{Ipc}_2\text{BH}$ ) (**208**).<sup>89</sup>  $\text{Ipc}_2\text{BH}$  is readily attainable in excellent enantioselectivity (up to 99% *ee*) from the hydroboration of  $\alpha$ -pinene (**207**) (94% *ee*) with borane dimethyl sulphide complex, Scheme G.1.



Scheme G.1

Brown showed that  $\text{Ipc}_2\text{BH}$  hydroborates *cis*-alkenes with remarkable enantioselectivity. For example alcohol (**211**) is synthesised enantiospecifically by hydroboration of dihydrofuran (**209**), Scheme G.2.<sup>90</sup>



Scheme G.2

However,  $\text{Ipc}_2\text{BH}$  does not exhibit such good selectivity with all olefins and a variety of other chiral hydroborating reagents have since been developed, notably monoisopinocampheylborane (**212**)<sup>91</sup> and Masamune's  $\text{C}_2$  symmetric dimethylborolane (**213**).<sup>92</sup> From Table 2, it can be seen that the asymmetric yield of hydroboration for the four structural classes of olefin varies significantly depending upon olefin substitution and double bond geometry. Often each hydroborating reagent

exhibits a high degree of substrate selectivity. This appears to be a common observation for chiral hydroborating reagents.

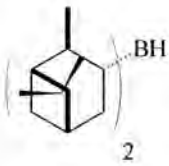


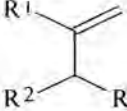


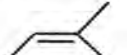
Enantiomeric excess of alcohol obtained from hydroboration and oxidation				
Olefin	Class			
		(208)	(212)	(213)
	I	30	15	14
	II	98.4	24	95.2
	III	13	73	97
	IV	14	53	94.2

Table 2.

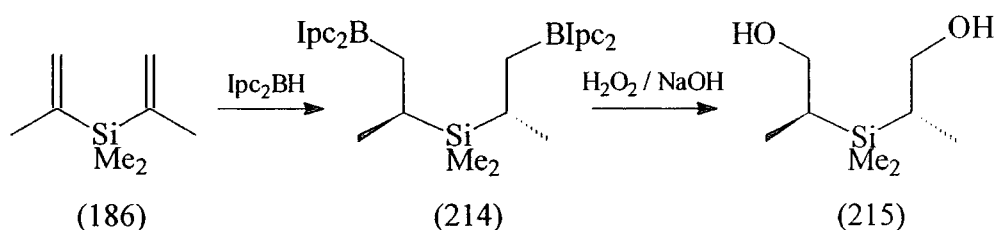
$\alpha$ -Substituted divinylsilanes are analogous to class I olefins and are the easiest of the divinylsilane substrates to prepare. Given that  $\text{Ipc}_2\text{BH}$  has shown to be the most effective reagent for this class of olefin and given the promising preliminary results obtained in this group, we opted to use this reagent as our initial choice. The principal challenge was to enhance the previously reported selectivities.

## G.2. Asymmetric Hydroboration of Substituted Divinylsilanes with $\text{Ipc}_2\text{BH}$

To obtain high yields of the *trans*-substituted diastereoisomers in the double asymmetric hydroboration of dienes it is necessary that the second hydroboration should proceed independently of the newly formed chiral centre. It was, therefore, hoped that enantiomerically pure  $C_2$  symmetric silacycles could be synthesised by double asymmetric hydroboration of substituted divinylsilanes. The synthesis of  $C_2$

symmetric acyclic silicon compounds derived from  $\text{Ipc}_2\text{BH}$  hydroboration of substituted divinylsilanes will be discussed in this section.

The hydroboration of divinylsilane (**186**) with  $\text{Ipc}_2\text{BH}$  has been previously described to give bisorganoborane (**214**), *in situ*.<sup>78</sup> This under standard peroxide oxidation conditions gave diol (**215**), Scheme G.3.



Scheme G.3

This reaction has been repeated for divinylsilanes (**186**) and (**159**). In line with previous results within the group, these diols proved difficult to purify and could not be characterised at this stage.<sup>78</sup> Purification by flash column chromatography often resulted in decomposition, presumably from an acid-catalysed Peterson reaction, Figure G.1. This theory was supported by the attempted purification of the diol derived from divinylsilane (**159**) where flash column chromatography produced styrene as a side product.<sup>78</sup>

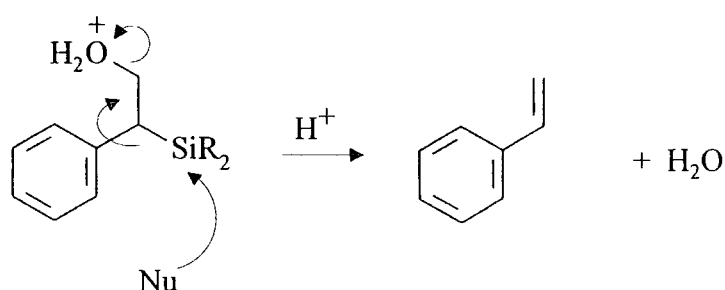
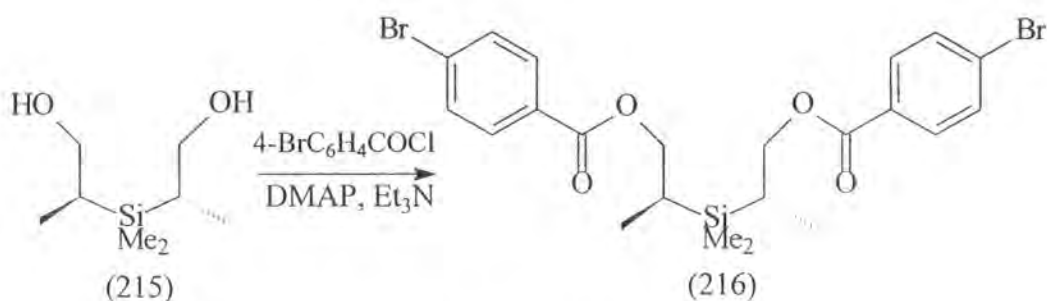


Figure G.1

Matthews had overcome the problem by *in situ* esterification and this procedure has been followed throughout, Scheme G.4.



Scheme G.4

With this procedure the hydroboration study was extended to the other divinylsilanes (**187**) and (**192**). Facile esterification of the crude diols with 4-bromobenzoyl chloride yielded crystalline diesters (**216-219**), Table 3.

Divinylsilane	Diester	% yield	% <i>de</i>	% <i>ee</i>
<p>(186)</p>	<p>(216)</p>	67	31( <i>dl</i> )	73
<p>(159)</p>	<p>(217)</p>	39	60 ( <i>dl</i> )	75
<p>(187)</p>	<p>(218)</p>	49	70 ( <i>dl</i> )	88
<p>(192)</p>	<p>(219)</p>	20	28 (?)	-

Table 3.

The diesters (**216-217**) were characterised by  $^1\text{H}$  and  $^{13}\text{C}$  NMR, and MS analysis and by comparison to data obtained previously.<sup>78</sup>  $^1\text{H}$  NMR analysis on diesters (**216-217**) using lanthanide chiral shift reagent ( $\text{Pr}(\text{hfc})_3$ ) gave the required stereochemical information. This reagent shifts peaks to lower frequency allowing Si-Me signals to be seen without interference from any other peaks in the spectrum. However, this method of chiral analysis is limited to the silicon dimethyl substituted analogues and as these can not provide access to the required dichlorosilanes much effort has been directed to developing more general methods. Chiral HPLC is the most obvious and following some trial and error experiments the *ee* and *de* of the diphenyl silyl ester (**218**) was determined using a Chiracel OD column eluting 2.5% ethanol in iso-hexane. The absolute stereochemistry of diesters (**216-218**) was assigned by analogy with Brown's work on reaction-mediated hydroboration.<sup>93</sup> However, the exact structures of these compounds remains to be confirmed unequivocally by analytical methods.

The structure of the  $\beta$ -substituted diester (**219**) was confirmed by the presence of a triplet signal in the  $^1\text{H}$  NMR assigned to the CH ( $\delta$  5.07) bonded  $\alpha$  to silicon. This would suggest a structure derived from hydroboration  $\alpha$  to silicon, giving the diester (**219**) shown in Table 3. Although hydroboration is normally expected to occur in an *anti*-Markovnikov fashion, there is precedence for  $\alpha$ -hydroboration of vinylsilanes.<sup>94</sup> This is believed to be attributable to the ability of silicon to stabilise  $\alpha$ -carbanions. In this case, it seems likely that the 2-methyl group and the silyl moiety both impart relatively similar steric influence and hence electronic factors take precedence. Owing to the stereochemical mixture of isomers for the divinylsilane (**192**), chiral analysis of the resulting diester proved too complicated for assignment to be confidently undertaken.

These results have established that  $\text{Ipc}_2\text{BH}$  hydroboration does give acyclic silicon compounds with the required  $\text{C}_2$  symmetry in high *de* and *ee*. Furthermore asymmetric efficiency increases as steric bulk around silicon increases. This can be attributed to restriction of bond rotation around the Si-C bond by the bulky nature of the silyl moiety. However, a fundamental problem remained in the moderate yields attained for the synthetically useful diphenyl analogue (**218**). It was speculated that this was because of competing Tamao type processes in the oxidative step.

Consequently a brief survey of organoborane oxidations was undertaken and is discussed in the next section.

## H. Oxidation of Organoboranes

The synthesis of alcohols by the oxidation of organoboranes is a facile process commonly performed with hydrogen peroxide and sodium hydroxide, Figure H.1.<sup>95</sup>

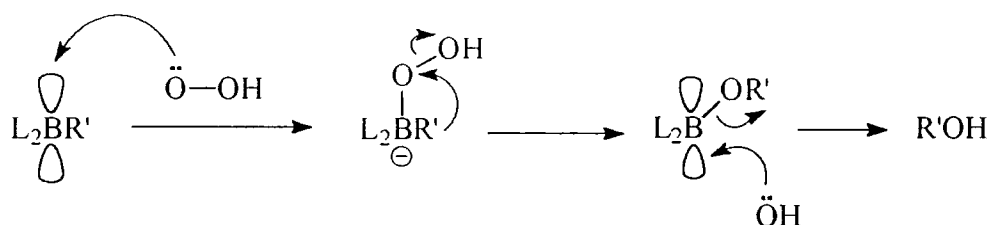
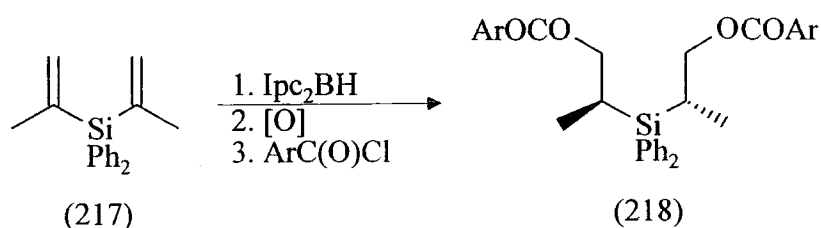


Figure H.1

This can be a relatively harsh procedure and consequently the occurrence of Tamao type oxidations as a competing process in the hydroboration-oxidation of phenylsilanes such as divinylsilane (**187**) would not be unexpected. There are milder alternatives which are particularly useful when used in the presence of oxidatively labile functional groups. For example Kabalka used sodium perborate in the oxidation of organoboranes (derived from the hydroboration of alkenes with  $lpc_2BH$ ) and showed that this gave enhanced yields under milder reaction conditions.<sup>96</sup> Other methods used sodium acetate or a pH 7 buffer instead of sodium hydroxide,<sup>97</sup> and alternative oxidising agents, such as trimethylamine-*N*-oxide, have been reported.<sup>98</sup>

Some of these have been considered with a view to enhancing the yields of diphenylsilyl derivatives. Consequently, the hydroboration, oxidation and esterification of divinylsilane (**187**) was repeated, with the crude reaction mixture being examined for the evidence of phenol which would be a marker for phenylsilyl degradation. The results of these experiments are shown in Table 4.



OXIDATION [O]	YIELD %
H <sub>2</sub> O <sub>2</sub> /NaOH	49
Na <sub>3</sub> BO <sub>4</sub> .H <sub>2</sub> O	48
pH 7 BUFFER H <sub>2</sub> O <sub>2</sub>	20

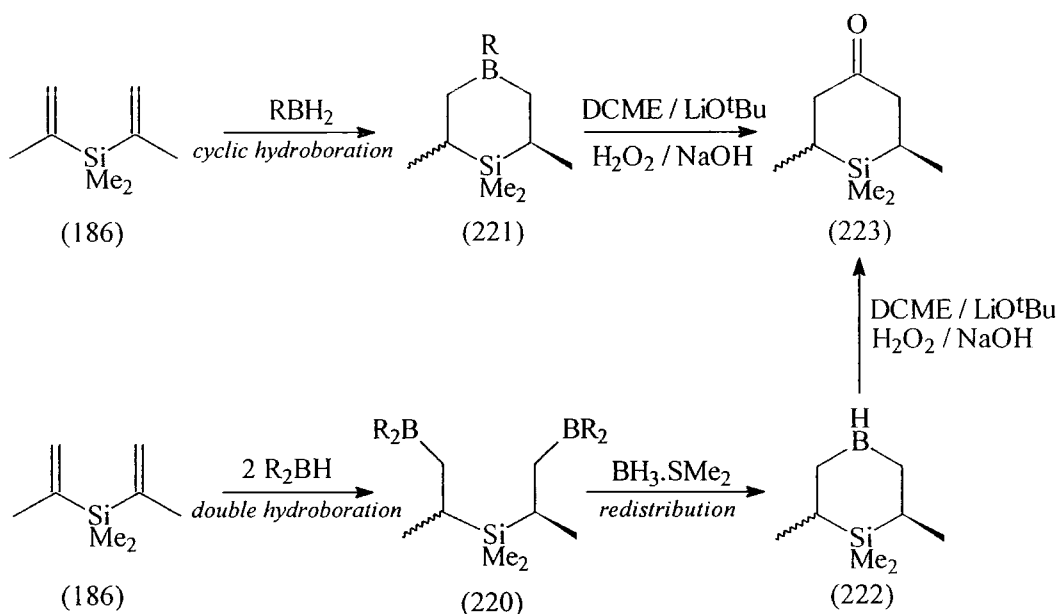
Table 4.

From these results, it can be seen that there was no enhancement in the yield for diester **(218)** with either of the alternatives used. Significantly, no phenol was detected in any of the alternative oxidation procedures and phenol was only detected in the peroxide procedure if excessive reflux times were allowed. Whilst alternative oxidants may prove efficient, this aspect of the study remains to be fully explored.

### **J. Silacycle Synthesis by an Achiral Hydroboration Route**

The asymmetric hydroboration of divinylsilanes has been established as a viable route for the synthesis of C<sub>2</sub> symmetric acyclic silicon compounds, section G. It should be added however, that because both boron redistribution and carbonylation are postulated to occur with retention of stereochemistry, it could be assumed that the *trans*-selectivity observed in the synthesis of acyclic silicon diesters can be adapted to the synthesis of cyclic silicon compounds. Prior to our work, Soderquist had reported that the cyclic hydroboration of divinylsilanes with monoalkylboranes (RBH<sub>2</sub>) and subsequent carbonylation of the resultant borasilacycles gave silacyclohexanones in moderate yields, Scheme J.1.<sup>77</sup> However, when using dialkylboranes (R<sub>2</sub>BH) divinylsilanes undergo a double hydroboration step, Scheme J.1 to give the bisorganoborane **(220)**. Soderquist then used a boron exchange or boron redistribution reaction to give the required borasilacycle **(222)** followed by standard carbonylation

to the required silacyclohexanone. Studies aimed at determining whether redistribution does show retention of stereochemistry are detailed in Section L.



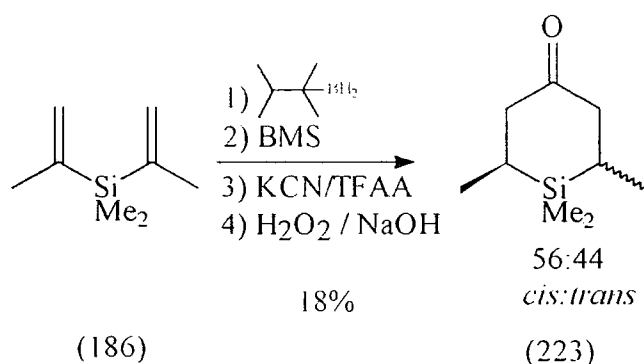
Scheme J.1

The double hydroboration-redistribution route was chosen because it readily allows the application of chiral hydroborating reagents such as  $\text{Ipc}_2\text{BH}$ .<sup>80</sup> However, initial attempts at the synthesis of  $\text{SiPh}_2$  substituted silacycles using this method proved complicated and it seemed prudent to optimise this synthetic strategy using a simple achiral hydroborating reagent. This would provide material for structural characterisation and allow subsequent asymmetric experiments to be monitored by TLC and NMR analysis. Furthermore, it would permit the exploration of the intrinsic diastereoselectivity of both the cyclic hydroboration and hydroboration-redistribution processes. This section will deal with the synthesis of silacycles by the achiral hydroboration of divinylsilanes and the diastereoselectivity thus obtained.

Following the basic protocol of Soderquist a variety of silacyclohexanones have been synthesised. All silacyclohexanones have been identified by their characteristic ketone signals ( $\delta$  211-215) in the  $^{13}\text{C}$  NMR spectra and the results are summarised in Table 5.

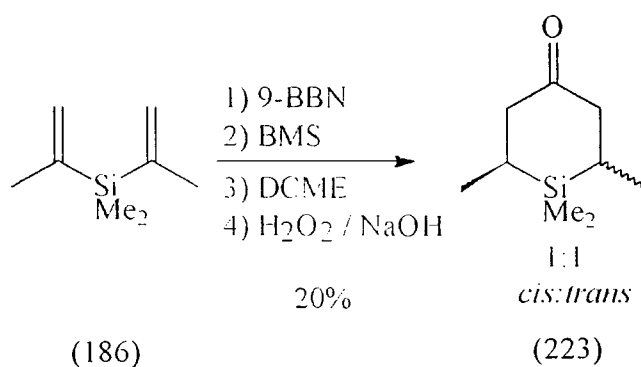
Our initial strategy was to explore the *cyclic hydroboration* route using divinylsilane **(186)** as a model. Consequently the ethylborane hydroboration of

the divinylsilane (**186**) followed by cyanoborate carbonylation gave silacyclohexanone (**223**) in 18% yield as a 56:44 mixture of *cis:trans* diastereoisomers, Scheme J.2. The isomer ratio for silacyclohexanone (**223**) was determined by <sup>1</sup>H NMR analysis and confirmed by GC analysis. Silacyclohexanone (**223**) has spectral and analytical data identical to that reported in the literature.<sup>77</sup> The isolated yield, as a result of a single experiment, is lower than that presented by the original author. However the *cis:trans* isomer ratio is in agreement with that reported previously using these reagents.<sup>77</sup>



Scheme J.2

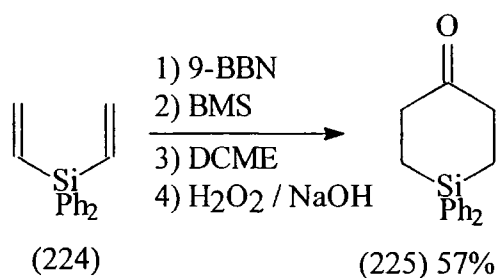
The synthesis of silacyclohexanones by a *double hydroboration* strategy was then investigated. The synthesis of the silacyclohexanone (**223**) has been repeated using 9-BBN and DCME carbonylation, Scheme J.3.<sup>77</sup> Silacyclohexanone (**223**) was obtained in marginally better yield (20%) as a 50:50 mixture of *cis:trans* isomers. This increase in the required *trans*-isomer suggested that the *cis*-selectivity could be overturned and that double asymmetric hydroboration would allow access to C<sub>2</sub> symmetric silacycles.



Scheme J.3

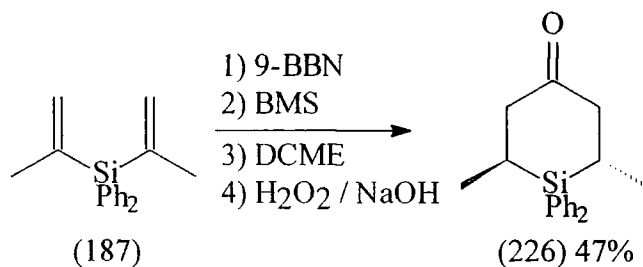
The synthesis of synthetically useful diphenylsilacycles had not been attempted before and it was felt that the increased steric bulk around silicon might affect chemical yields. Consequently, as a model study, the synthesis of the unsubstituted diphenylsilacyclohexanone (**225**) was attempted.

Silacyclohexanone (**225**) was synthesised in good yields using 9-BBN dimer, Scheme J.4. The quality of the 9-BBN was found to be very significant, as yields with the commercially available hexane solution, were significantly lower than those obtained with the crystalline dimer. The yield was also comparable to that obtained in a subsequent report by Mignani and co-workers.<sup>99</sup>



Scheme J.4

The synthesis of the substituted diphenylsilacyclohexanone (**226**) was then attempted. The divinylsilane (**187**) underwent successive 9-BBN hydroboration, redistribution and DCME carbonylation to give silacyclohexanone (**226**) in 47% yield, Scheme J.5. Although not outstanding, this is the highest reported yield for the synthesis of a substituted silacyclohexanone. Silacycle (**226**) was readily identified by the appearance of a signal ( $\delta$  211) in the <sup>13</sup>C NMR attributable to the carbonyl group.



Scheme J.5

The diastereoselectivity was determined by  $^1\text{H}$  NMR analysis and by analogy with data from silacyclohexanone (**223**). Crucially, the *cis:trans* ratio of 44:56 favours the  $\text{C}_2$  symmetric diastereoisomer. Furthermore two recrystallisations from hexane afforded crystals of 50% *de (trans)*. This confirmed that synthetically useful  $\text{C}_2$  symmetric silacycles are obtainable in good yields, and that enantiomerically pure silacycles might be obtained by using an asymmetric hydroboration pathway. Consequently, studies towards the synthesis of  $\text{C}_2$  symmetric silacycles by  $\text{Ipc}_2\text{BH}$  hydroboration of substituted divinylsilanes were undertaken and are discussed in section K. Attempts to resolve silacycle (**226**) by HPLC analysis using the previously successful Chiracel OD column failed to separate the stereoisomers. As a result, it was hoped that manipulation of either the carbonyl group or the silyl moiety might allow separation of the enantiomers at a later stage, Section P.

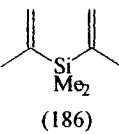
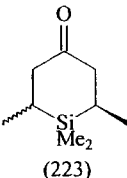
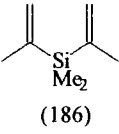
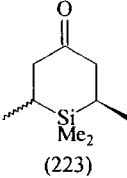
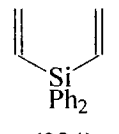
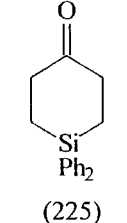
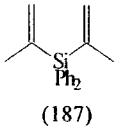
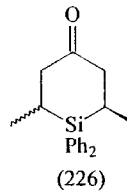
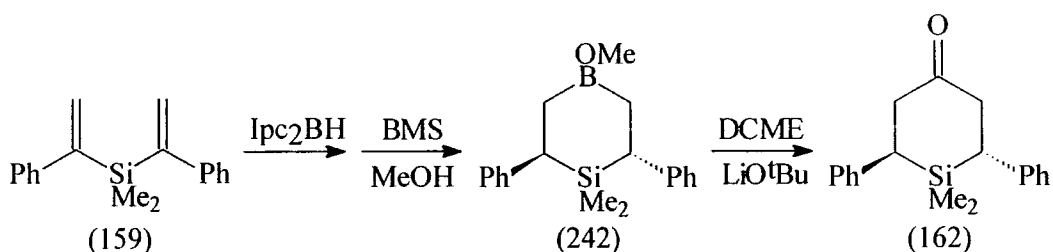
Divinyl silane	Hydroboration	Redistribution	Carbonylation	Silacycle	<i>Cis/trans</i> (yield %)
 (186)	thexylborane	not applicable	KCN/TFAA	 (223)	56:44 (18%)
 (186)	9-BBN	BMS	DCME	 (223)	50:50 (20%)
 (224)	9-BBN	BMS	DCME	 (225)	(57%)
 (187)	9-BBN	BMS	DCME	 (226)	44:56 (47%)

Table 5

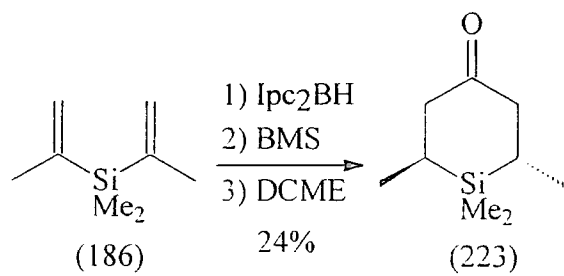
## K. Silacyle Synthesis via Chiral Hydroboration

The double hydroboration of substituted divinylsilanes, with 9-BBN, has shown to give access to *trans*-substituted silacycles and, with  $\text{Ipc}_2\text{BH}$ , was found to be a viable method in the synthesis of  $\text{C}_2$  symmetric acyclic silicon compounds, Section C. It was therefore envisaged that asymmetric hydroboration with  $\text{Ipc}_2\text{BH}$  would give *trans*-substituted silaboranes with high stereoselectivity, undergoing redistribution and carbonylation, as before, to give  $\text{C}_2$  symmetric silacyclohexanones with high *de* and *ee*. In this group, Matthews has reported that  $\text{Ipc}_2\text{BH}$  hydroboration of divinylsilane (**159**) gave after redistribution and carbonylation silacyclohexanone (**162**) in 21% yield, Scheme K.1.<sup>78</sup> Subsequent inspection of the  $^1\text{H}$  NMR suggested that the major isomer was the *trans*-substituted silacycle (**162**).



Scheme K.1

Our initial approach focused on the synthesis of tetramethylsilacyclohexanone (**223**) as a model study. Hydroboration of divinylsilane (**186**) with  $\text{Ipc}_2\text{BH}$  gave after redistribution and carbonylation, silacyclohexanone (**223**) in 24% yield, Scheme K.2.  $^{13}\text{C}$  NMR confirmed the presence of the cyclohexanone product with a signal ( $\delta$  213.4) attributable to the ketone. Furthermore both  $^1\text{H}$  and  $^{13}\text{C}$  NMR analysis showed the presence of two isomers with  $^1\text{H}$  NMR and GC analysis both indicating a 44:56 *cis:trans* isomer ratio, Figure K.1. Unfortunately, chiral HPLC on a Chiracel OD column failed to resolve the enantiomers for *ee* determination. It was hoped that subsequent attempts at *ee* determination by chiral shift analysis would be more successful. However, a lack of time has prevented the successful completion of this aspect of the project.



Scheme K.2

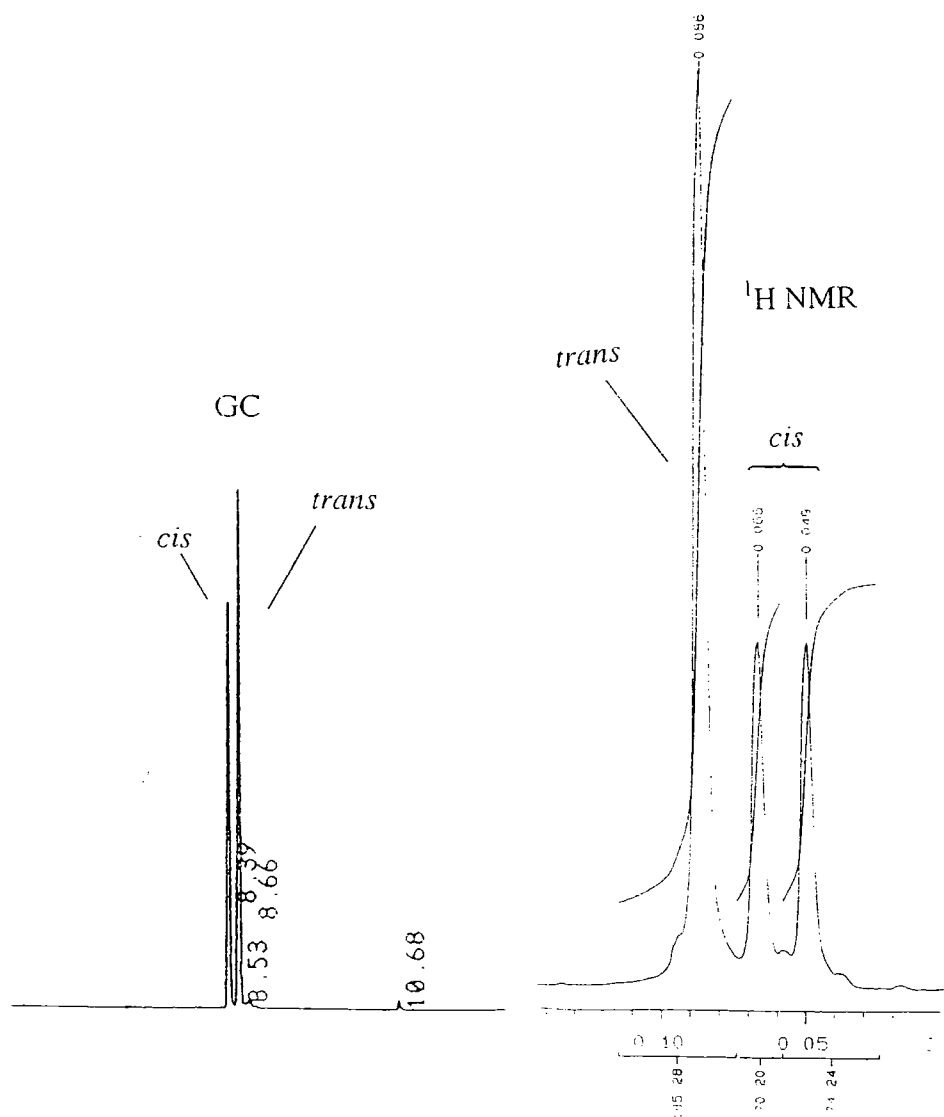
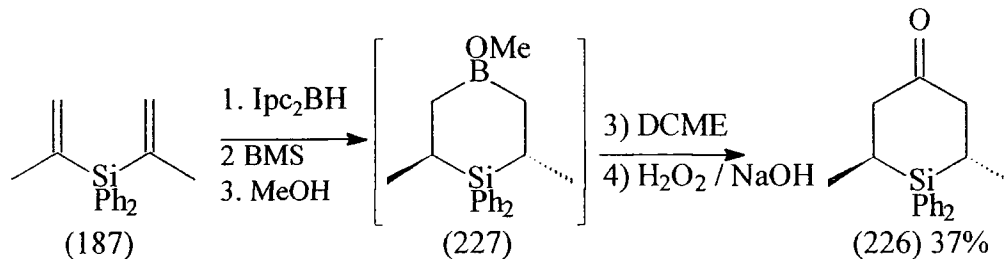


Figure K.1

Our attention then turned to the synthetically more useful diphenyl analogue. Hydroboration of divinylsilane (**187**) with  $\text{Ipc}_2\text{BH}$  after redistribution and carbonylation afforded silacyclohexanone (**226**) in 37% yield, Scheme K.3.



Scheme K.3

$^{13}\text{C}$  NMR analysis again confirmed the presence of the silacyclohexanone product with a signal ( $\delta$  212.71) attributable to the ketone. Integration of the  $\alpha$ -methyl protons signals ( $\delta$  1.12 and  $\delta$  1.05) in the  $^1\text{H}$  NMR indicated a ratio of 15:85 for the *cis*- and *trans*-isomers respectively, corresponding to a 70% *de*. Unfortunately, HPLC and GC analysis failed to give baseline separation and the *ee* remains to be established. Enrichment of the *de* to 85% could be achieved on recrystallisation of (**226**) from hexane. However, this appears to be a stationary state as repeated recrystallisations did not further improve the diastereoselectivity.

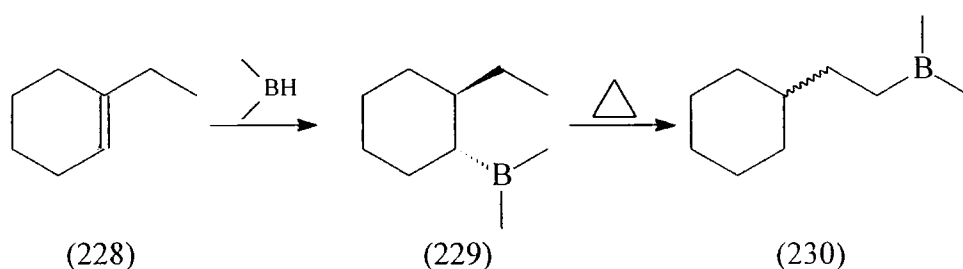
This work has established that asymmetric hydroboration can provide  $\text{C}_2$  symmetric silacycles with excellent diastereocontrol. However yields, are still low and the *ee* remains to be determined. The low yield has been partly attributed to the difficulty in removing diisopinocampheylborane derivatives from the reaction mixture following redistribution. It was hoped that yields could be enhanced by removing the  $\text{Ipc}_2\text{BH}$  derivatives, during the synthetic sequence by distillation. Unfortunately, it transpired that  $\text{Ipc}_2\text{BOMe}$  has a similar boiling range to the corresponding methoxysilaboracycle (**227**). These experiments were complicated by organoborane polymerisation which occurs at the temperatures needed for distillation ( $+100^\circ\text{C}/0.1\text{mbar}$ ). In attempts to circumvent these difficulties other chiral hydroborating reagents were considered and this will be discussed in Section M.

Similarly it was hoped that the enantioselectivity could be determined by manipulation of the carbonyl functionality in the silacyclohexanone and experiments in this direction are discussed in section P.

### L. Borane Redistribution

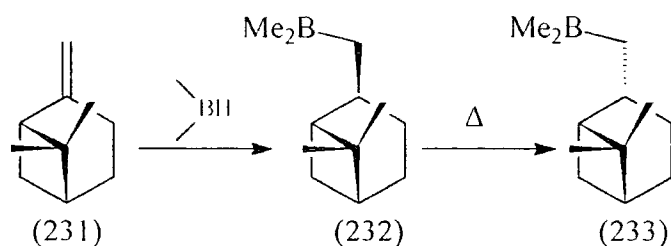
The synthesis of cyclic ketones from the double hydroboration of divinylsilanes required the incorporation of a boron redistribution step. In the synthetic strategy employed it is essential that redistribution does not affect the asymmetric centres introduced in the chiral hydroboration step. Redistribution is one of four processes that can occur on the thermolysis of organoboranes, the others being elimination,<sup>100</sup> redistribution, isomerisation and cycloelimination.<sup>100</sup> Of these, isomerisation and redistribution are the most important in the formation of cyclic organoboranes.

Simple organoboranes undergo isomerisation at temperatures around 160°C. An equilibrium mixture of products is obtained and boron is found at all positions, but predominates at sterically favoured positions, Scheme L.1.<sup>101,102</sup>



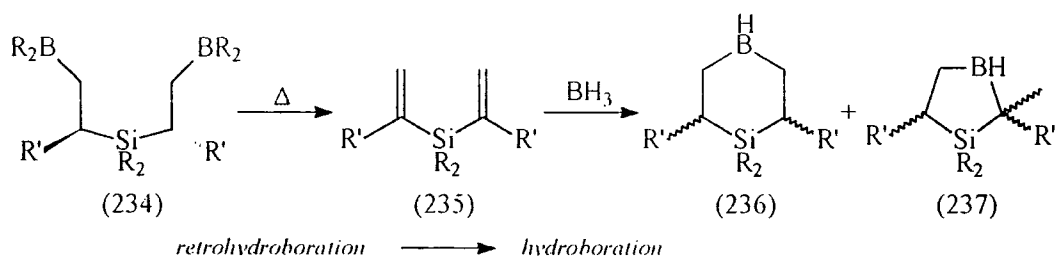
Scheme L.1

Alternatively, stereoisomerisation can occur as a result of migration of boron to give a more stable stereoisomer. For example,  $\beta$ -pinene (**231**) undergoes facile hydroboration with dimethylborane to give the trialkylborane (**232**). Under the action of heat thermal isomerisation gives the thermodynamically more stable stereoisomer (**233**), Scheme L.2.<sup>103</sup>



Scheme L.2

The mechanism of isomerisation has not been determined, but a repeated retrohydroboration - rehydroboration sequence satisfactorily rationalises most of the reported observations. This is a potential pathway for the cyclisation of bisorganoborane (234), Scheme L.3. However, thermal isomerisation would make asymmetric control impossible and isomerisation would also give the regioisomeric borolane (237).



Scheme L.3

Redistribution reactions have been defined as those in which bonds change in relative position but not in total number or type, Figure L.1.<sup>104</sup> The mechanism is believed to proceed via a four-centred transition state, Figure L.2.<sup>105</sup> In contrast to isomerisation, such a mechanism should show retention of stereochemistry at all positions.

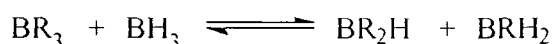


Figure L.1

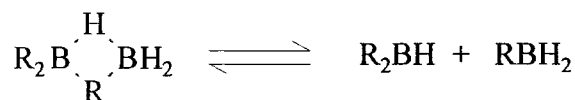
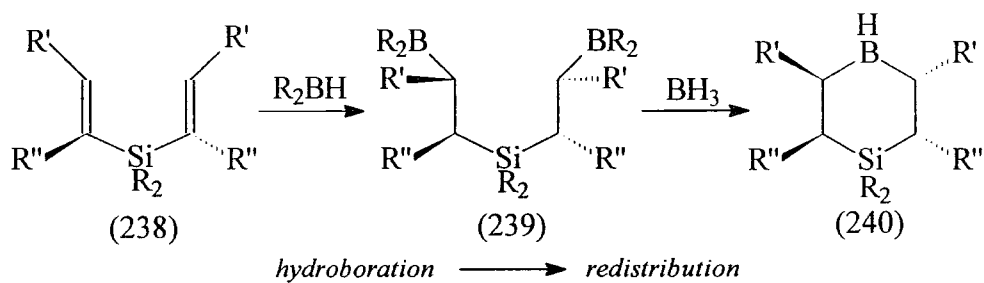


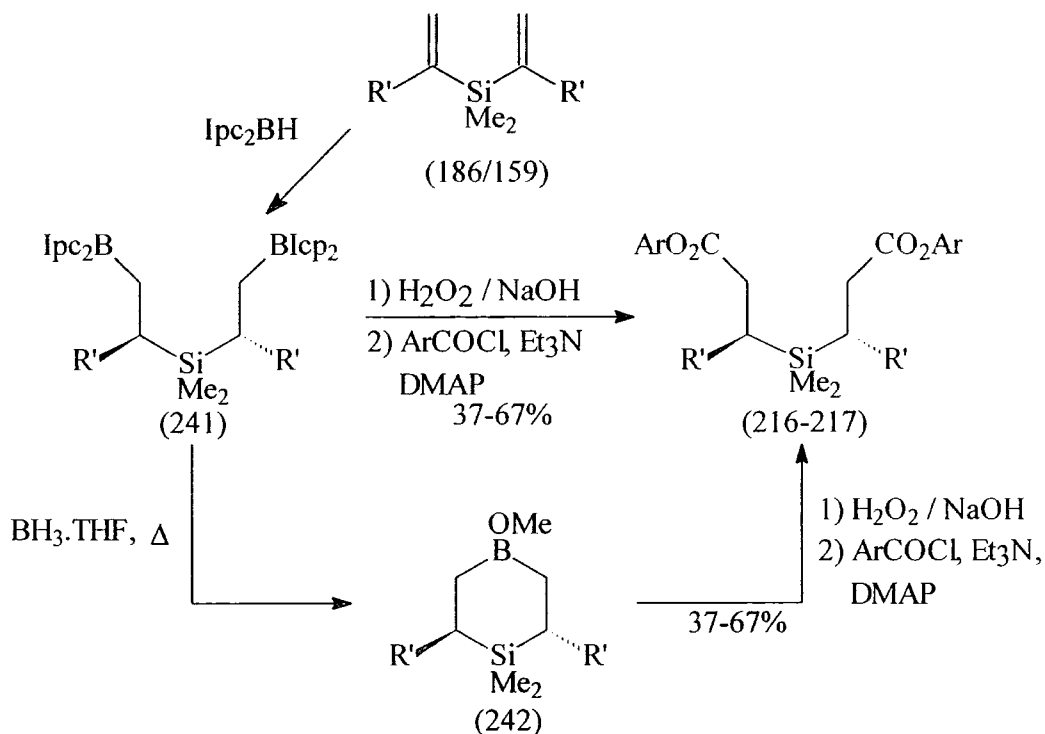
Figure L.2

For hydroboration-redistribution of divinylsilanes, the stereochemical integrity of the borasilacycle should remain intact, Scheme L.4.



Scheme L.4

To fully explore whether the redistribution step does occur and does show retention of stereochemistry, initial experiments aimed to repeat the work previously described within the group.<sup>78</sup> Matthews had described a sequence in which hydroboration-oxidation of divinylsilanes is compared with hydroboration redistribution oxidation from the same reaction mixture, Scheme L.5. The observation was that with  $\alpha$ -substituted divinylsilanes the stereochemical outcome for the corresponding diester was the same whether the redistribution process was followed or not.



Scheme L.5

Consequently it was felt that this area required further exploration and as a result we attempted to ascertain the formation of methoxysilaboracycle (242) either by isolation or by following the reaction by  $^{11}\text{B}$  NMR. The Matthews experiments described above were repeated using divinylsilanes (186) and (159), and were followed by  $^{11}\text{B}$  NMR. This was based on the premise that organoboranes have characteristic  $^{11}\text{B}$  NMR frequencies and it was hoped to be able to detect the presence of silamethoxyboracycle (242) in the reaction mixture.

It was found that, hydroboration of divinylsilanes (186) and (159) afforded bisorganoboranes (241) *in situ*. The reaction mixtures were then divided into two portions. One half was esterified as before, and the other half subjected to the standard redistribution conditions described by Matthews.<sup>78</sup> After standard oxidation and esterification both processes afforded diesters (216-217), Scheme L.5. The diesters (216-217) from both processes were analysed by a combination of chiral shift NMR and chiral HPLC. All spectral ( $\alpha_D$ ) and analytical data and chemical yields were in agreement with compounds that were isolated previously.<sup>78</sup> This suggested that the stereochemical integrity of the  $\alpha$ -chiral centre was retained through redistribution. Whilst this is strong circumstantial evidence that the retrohydroboration pathway does

not take place, no unequivocal evidence for the formation of silacyclomethoxyborane (242) could be obtained as the  $^{11}\text{B}$  NMR spectrum was dominated by the vast excess of IpcBOMe, masking any possible peak for methoxyborane (242). It is not unreasonable to assume, however, that using a redistribution procedure identical to that used for the synthesis of silacycles must give borasilacycle (242). It is anticipated that a further experiment, where the redistribution half is halved again, half of which is oxidised and esterified as above and the other half carbonylated to give the corresponding silacyclohexanones (223/162), would provide ample evidence to support our current findings.

## **M. Other Chiral Hydroborating Reagents**

### **M.1. Introduction**

In using diisopinocampheylborane a number of problems have been encountered and these are summarised below.

Although  $\text{Ipc}_2\text{BH}$  has been shown to give the best optical yields for the hydroboration of class I olefins, Figure M.1 and Table 2, the optical yields obtained for the synthesis of diesters by the hydroboration of divinylsilanes with  $\text{Ipc}_2\text{BH}$  remains moderate at best and it is by no means certain that  $\text{Ipc}_2\text{BH}$  is the best reagent for the asymmetric hydroboration of  $\alpha$ -substituted divinylsilanes. Consequently, it was hoped that optical yields might be improved through the use of other chiral hydroborating reagents.

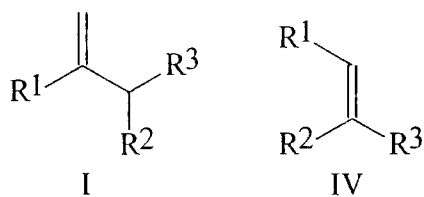


Figure M.1

Secondly, the redistribution studies (section L) have been frustrated by the lack of analytical evidence for the formation of the methoxyborasilacycle (**242**), Figure M.2. The problem appears to lie with the difficulty in removing excess diisopinocampheylborane derivatives from the crude reaction mixture. This "masks" the methoxyborasilacycle signal in the  $^{11}\text{B}$  NMR. Therefore it seemed reasonable that using a more volatile hydroborating reagent would allow purification of this key intermediate by distillation. In this respect studies towards the synthesis of a low molecular weight chiral hydroborating reagent have been investigated (section M.4).

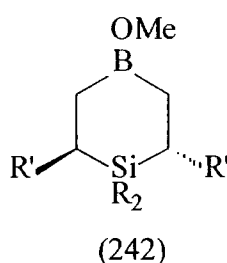


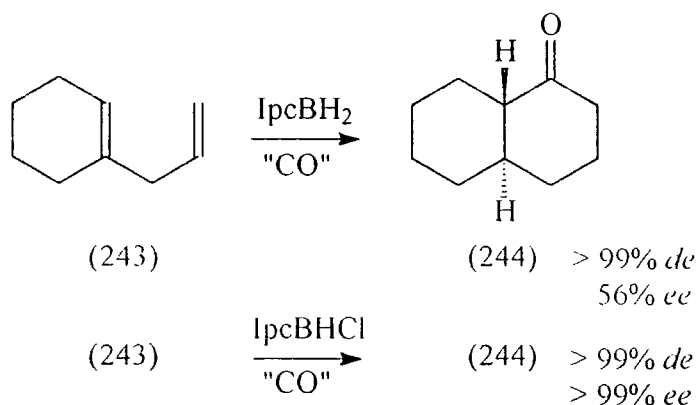
Figure M.2

Finally, the  $\text{Ipc}_2\text{BH}$  hydroboration and oxidation of divinylsilanes is accompanied by the oxidation of the diisopinocampheylborane moiety. This produces an excess of isopinocampheol which complicates the purification of the desired product. This might be avoided by a cyclic hydroboration route as only one equivalent of hydroborating reagent is required and hence purification should prove easier. As a result the synthesis and application of a homochiral monoalkylborane for the cyclic hydroboration has also been investigated and is discussed in sections M.2 and M.3.

### **M.2. Monoisopinocampheylborane ( $\text{IpcBH}_2$ )**

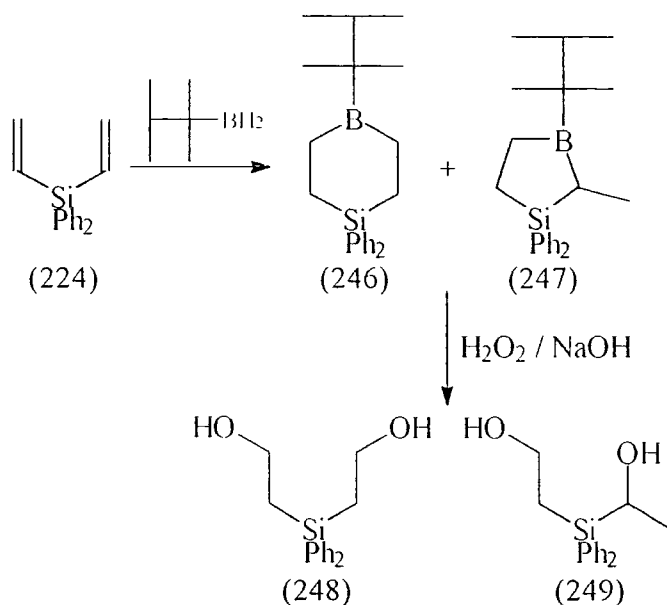
$\text{IpcBH}_2$  has been reported to hydroborate dienes with good stereoselectivity. For example, treatment of allylcyclohexene (**243**) with  $\text{IpcBH}_2$  gave the bicyclic ketone (**244**) diastereospecifically and with moderate enantioselectivity, Scheme M.1.<sup>106</sup> It was felt that  $\text{IpcBH}_2$  could be readily applied to the asymmetric hydroboration of divinylsilanes. Notably the relatively new, more active, chiral hydroborating reagent monoisopinocampheylchloroborane ( $\text{IpcBHCl}$ ) (**245**) has, in

conjunction with  $\text{LiAlH}_4$ , shown much better optical yields for this reaction and the utility of this reagent has also been investigated, section M.3.<sup>106</sup>



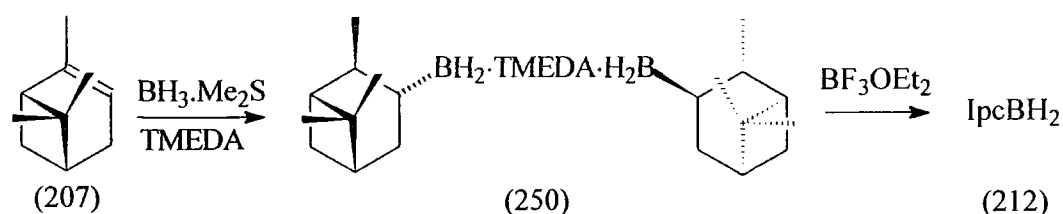
Scheme M.1

In simple cyclic hydroboration there is some precedence for regioisomeric products being formed. For example, Soderquist used tetrylborane for the hydroboration of divinylsilane (**224**), and reported the formation of the regioisomeric diols (**248**) and (**249**), Scheme M.2.<sup>77</sup> It was hoped, that the sterically bulky nature of the isopinocampheyl unit of  $\text{IpcBH}_2$  would prohibit the formation of undesirable regioisomeric products.



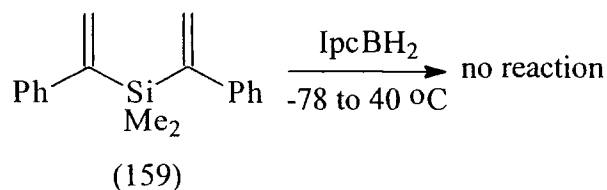
Scheme M.2

Following the procedure developed by Brown, monoisopinocampheylborane (IpcBH<sub>2</sub>) (**212**) was easily prepared through reaction of pinene with borane dimethylsulphide complex generating Ipc<sub>2</sub>BH (**208**) *in situ*.<sup>107</sup> Subsequent displacement of one pinene unit with TMEDA afforded the air-stable crystalline TMEDA complex (**250**) in 95% *ee*, Scheme M.3. IpcBH<sub>2</sub> can then be readily freed from the amine complex by *in situ* reaction with BF<sub>3</sub>OEt<sub>2</sub>. The TMEDA complex was characterised by comparison with literature data.<sup>107</sup>



Scheme M.3

With this reagent in hand the hydroboration of divinylsilane (**159**) by IpcBH<sub>2</sub> was attempted, Scheme M.4. This divinylsilane was chosen because the corresponding diester (**217**) had been prepared previously, Section G.2, thus allowing simple comparison of spectral data. Furthermore the bulky phenyl substituents have been shown to aid regioselectivity.<sup>78</sup> The reaction was followed by <sup>1</sup>H NMR and by TLC and was heated at a variety of temperatures (-78°C to +40°C). However, divinylsilane (**159**) showed no reaction with IpcBH<sub>2</sub> after several days, Scheme M.4.

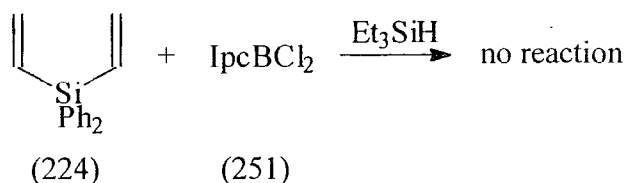


Scheme M.4

In order to circumvent the low reactivity of IpcBH<sub>2</sub> with substituted divinylsilanes, the hydroboration of divinylsilane (**206**) was undertaken, as the presence of the vinyl ether functionality would make this substrate more reactive. Although some hydroboration of divinylsilane (**206**) was evident by <sup>1</sup>H NMR and



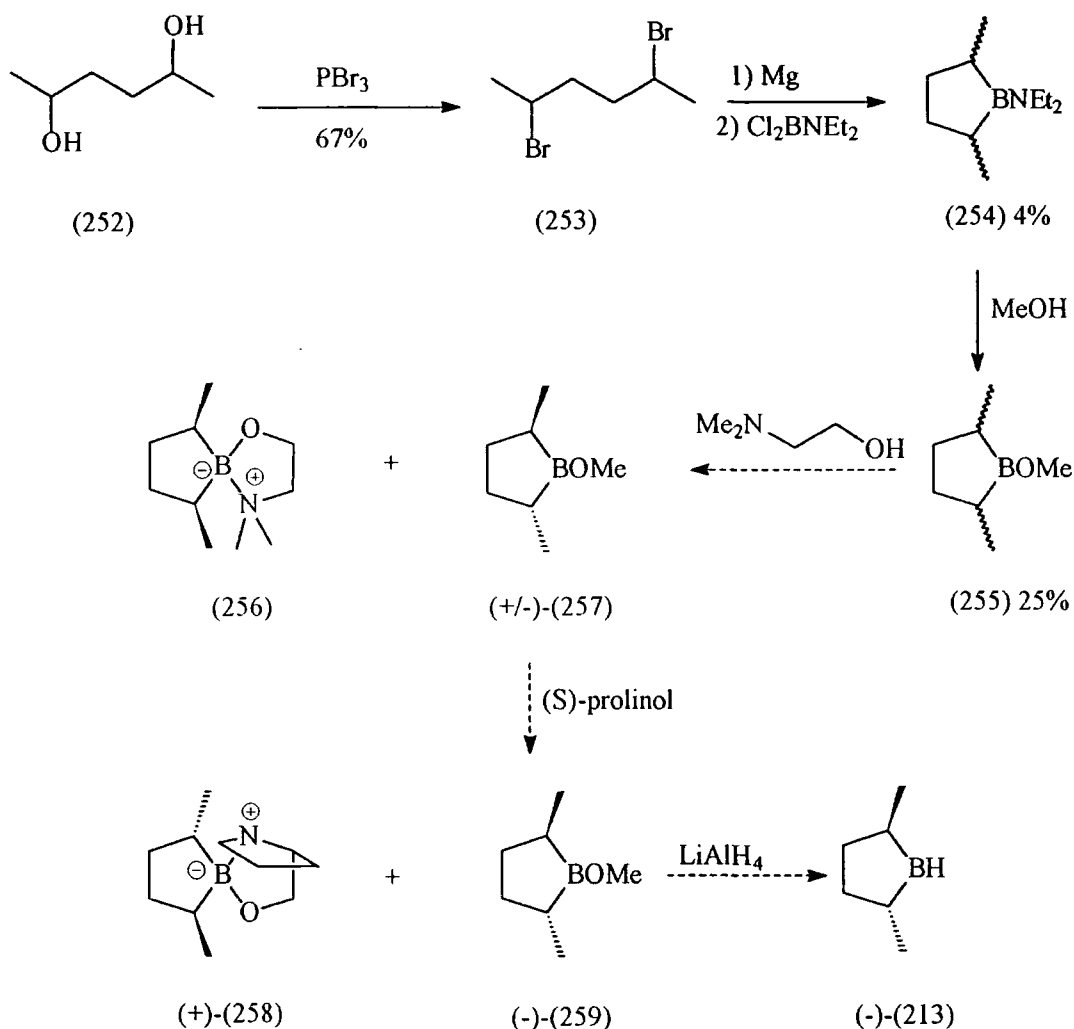
reactivity is surprising and it is difficult to rationalise this observation. With this lack of progress with monoalkylborane reagents it was decided to halt this chemistry at this stage.



Scheme M.7

#### **M.4. Dimethylborolane**

As discussed in the introduction to this section, one problem with the use of Ipc<sub>2</sub>BH is the problem of its removal from the reaction mixture. This was seen in both the redistribution study and in the synthesis of silacycles. The C<sub>2</sub> symmetric dimethylborolane (**213**) developed by Masamune has shown excellent results for the hydroboration of a variety of substituted olefins, Table 2.<sup>92</sup> Furthermore it is of low molecular mass, compared to pinene-based alternatives, and hence should be more volatile, allowing simple purification of key intermediates. Consequently a synthesis of this reagent was undertaken. The reported synthesis involves the preparation of methoxy-borolane (**255**) as a mixture of stereoisomers. Subsequent purification of (**255**) requires initial separation of the diastereoisomers by reaction with N,N'-dimethylethanolamine. This selectively removes the thermodynamically more stable *cis*-isomer as the crystalline amine complex (**256**). Finally the enantiomers are resolved by complexation of the *trans*-methoxyborolane (**257**) with (S)-prolinol to afford enantiomerically pure (S,S)-methoxyborolane (**258**) which can be treated with LiAlH<sub>4</sub> and methyl iodide to give the optically pure borolane (**213**), Scheme M.8.



Scheme M.8

Following this example the initial steps of the synthesis were undertaken. Bromination of hexane-2,5-diol (252) occurred smoothly and on a large scale with  $\text{PBr}_3$ . However, problems occurred on generation of the bis-Grignard intermediate as titration of the THF solution suggested only 20% yield. This is further complicated as it is unclear whether all of this material is a di-Grignard or mono-Grignard species. This latter factor may be behind the low yield of the subsequent step. Although the aminoborolane (254) and the subsequent methoxyborolane (255) could be isolated and characterised by comparison with literature data, the low yields precluded further progression along the synthetic pathway.

Our difficulties have subsequently been substantiated by discussions with other research groups who have worked in this area. It has been revealed that dimethylborolane (213) has seldom been made outside of Masamune's laboratory and

as a result it was decided to abandon the synthesis of dimethylborolane at this stage.<sup>109</sup>

The lack of reactivity and problems associated with preparation have hampered the use of these chiral hydroborating reagents. Although it remains the most successful reagent, the difficulties in using  $\text{Ipc}_2\text{BH}$  prompted us to explore alternative methods for generating  $\text{C}_2$  symmetric silacycles.

### **N. Alternative Strategies for Silacycle Synthesis**

As discussed at the start of this chapter, other disconnections of silacycles have been considered. In particular, disconnection B, Figure N.1. This disconnection requires an asymmetric hydrometallation strategy and two methods have been explored, namely, asymmetric double hydrosilylation and zirconium promoted bicyclisation of dienes. Our investigations towards both of these routes will be discussed in this section.

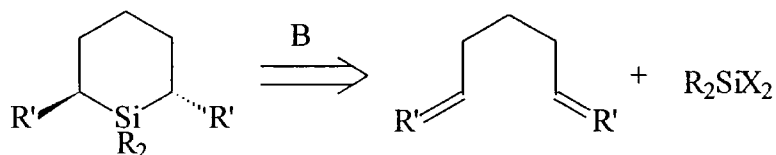
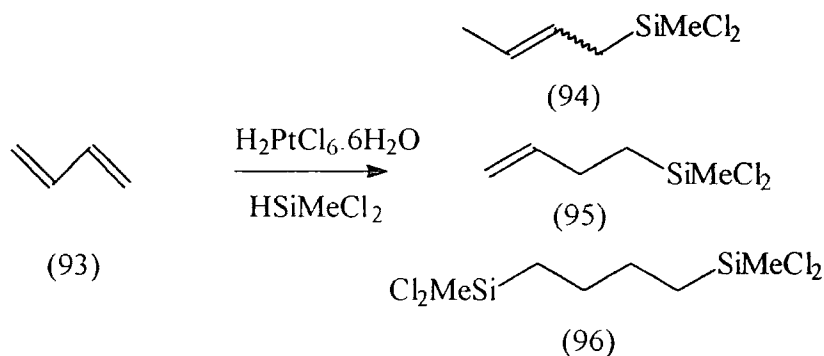


Figure N.1

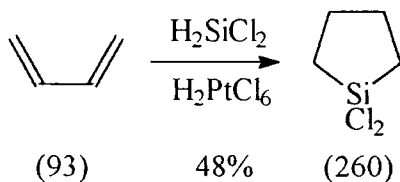
#### **N.1. Hydrosilylation as a Tool in the Synthesis of Silacycles**

Although the hydrosilylation of alkenes has been extensively explored, the hydrosilylation of dienes has not been studied as comprehensively. On hydrosilylation alkenes and dienes often give the terminally substituted adduct and hydrosilylation of conjugated dienes is frequently accompanied by isomerisation of the remaining double bond. For example, the platinum-catalysed hydrosilylation of 1,4-butadiene (**93**) leads to the formation of three regioisomeric adducts, Scheme N.1.<sup>110</sup>



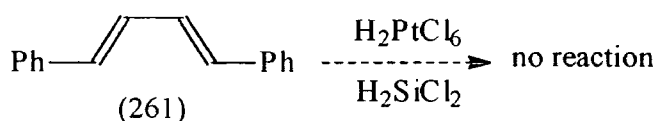
Scheme N.1

There have been few reports of the double hydrosilylation of dienes. However, Benkeser reported the hexachloroplatinic-acid-catalysed synthesis of dichlorosilacyclopentane (**260**), Scheme N.2.<sup>111</sup> It is assumed that the first hydrosilylation is accompanied by isomerisation of the second double bond and that the second hydrosilylation then occurs on a terminal double bond (after another isomerisation).



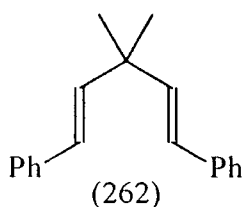
Scheme N.2

To prevent unwanted isomerisation processes, Matthews attempted the hydrosilylation of dienes with blocking groups in the hope that this would prevent isomerisation.<sup>78</sup> In this respect Matthews has prepared diene (**261**) bearing phenyl groups in the terminal position. However, the hydrosilylation of this substrate was unsuccessful, Scheme N.3. Matthews has suggested that there may be two problems with the choice of this diene: (i) isomerisation was still possible due to the conjugation diene system, and (ii) as diene (**261**) is a solid, a solvent was required which may impede the efficiency of the catalyst.



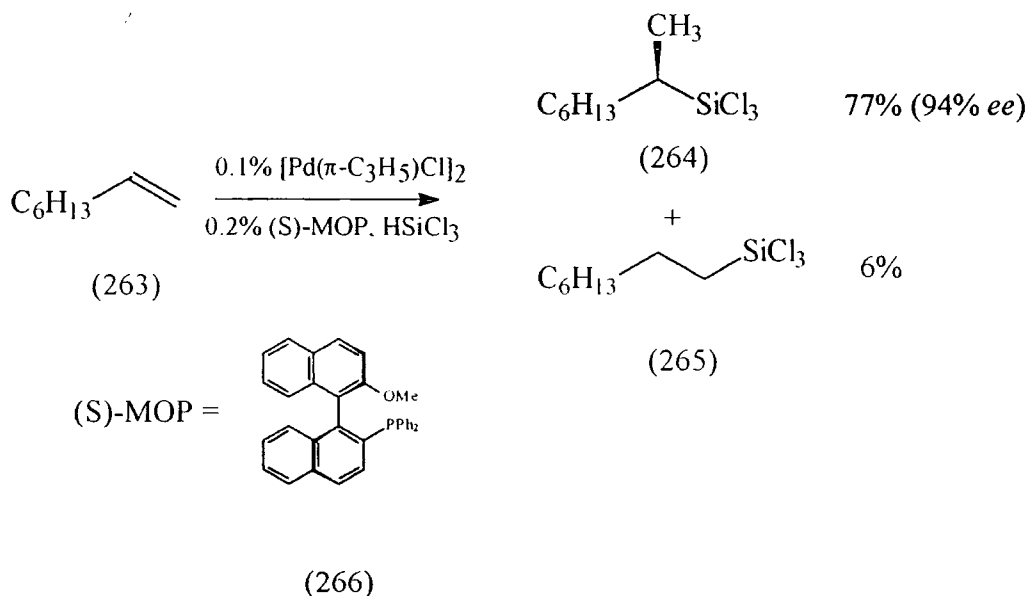
Scheme N.3

As a result Matthews attempted the hydrosilylation of the liquid non-conjugated diene 3,3-dimethyl-1,5-diphenylpentadiene (**262**). However, despite trying a wide range of catalysts and silanes, only hydrogenation and silane coupling products were produced and no evidence for hydrosilylation could be found, Scheme N.4.<sup>78</sup>



Scheme N.4

More recently, Hayashi and co-workers have demonstrated that monodentate phosphine ligand (**266**) directs the hydrosilylation of terminal alkenes regioselectively to the internal position. Furthermore, high enantioselectivity can be realised. For example, oct-1-ene (**263**) underwent palladium catalysed hydrosilylation to give the substituted adduct (**264**) in 94% *ee*, Scheme N.5.<sup>112</sup>

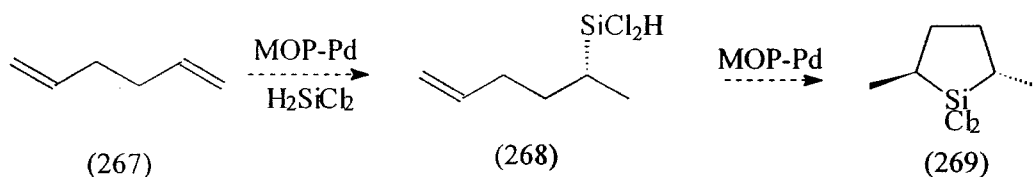


Scheme N.5

This development prompted renewed interest in the double hydrosilylation strategy and consequently (R)-MOP (**266**) has been synthesised within the group.<sup>113</sup>

With this in hand it was hoped that the double hydrosilylation of non-conjugated dienes would allow access to C<sub>2</sub> symmetric silacycles in one step.

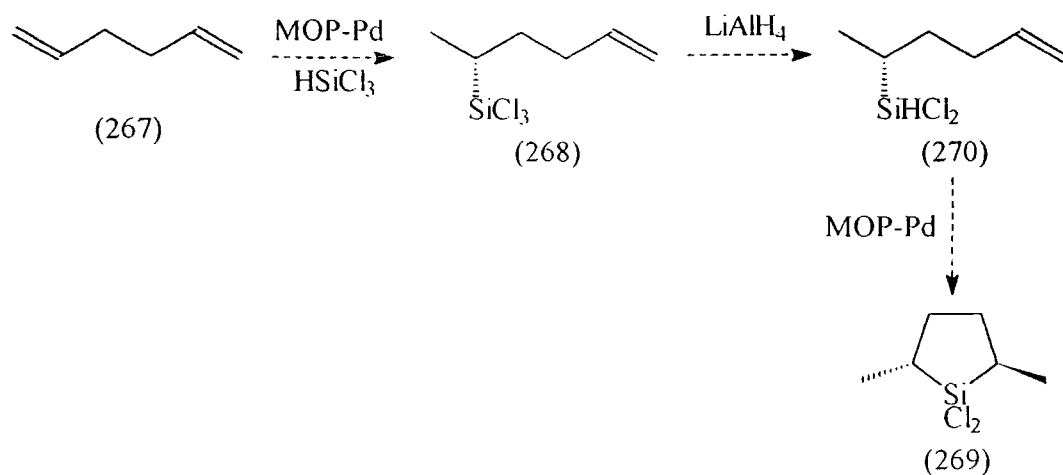
However, at a variety of pressures and temperatures using 1,5-hexadiene (**267**) as a substrate, attempted hydrosilylation with dichlorosilane and MOP catalyst gave no evidence for the formation of (**269**), Scheme N.6. A small amount of crude material was obtained which on analysis by <sup>1</sup>H NMR showed a doublet signal (δ 1.1). This was tentatively assigned to the terminal methyl group of the monosilylated species (**268**). Unfortunately, unequivocal characterisation was not possible as sufficient material could not be isolated.



Scheme N.6

Hydrosilylation involves, as a first step, insertion of the metal into the Si-H bond. The rate of this process is determined by the strength of this bond and this is controlled by the electronegativity of the remaining silyl substituents. It appears that the major problem with this hydrosilylation is that dichlorosilane, in contrast to trichlorosilane, undergoes oxidative addition relatively slowly.

For these reasons it was felt that a two-step procedure using trichlorosilane might be more successful. A possible route would involve hydrosilylation of diene (**267**) with a stoichiometric amount of trichlorosilane. This should give the trichlorosilylalkene (**268**) which could be reduced with LiAlH<sub>4</sub> to give the dichlorosilane (**270**). Subsequent intramolecular hydrosilylation would give the desired silacycle (**269**), Scheme N.7.

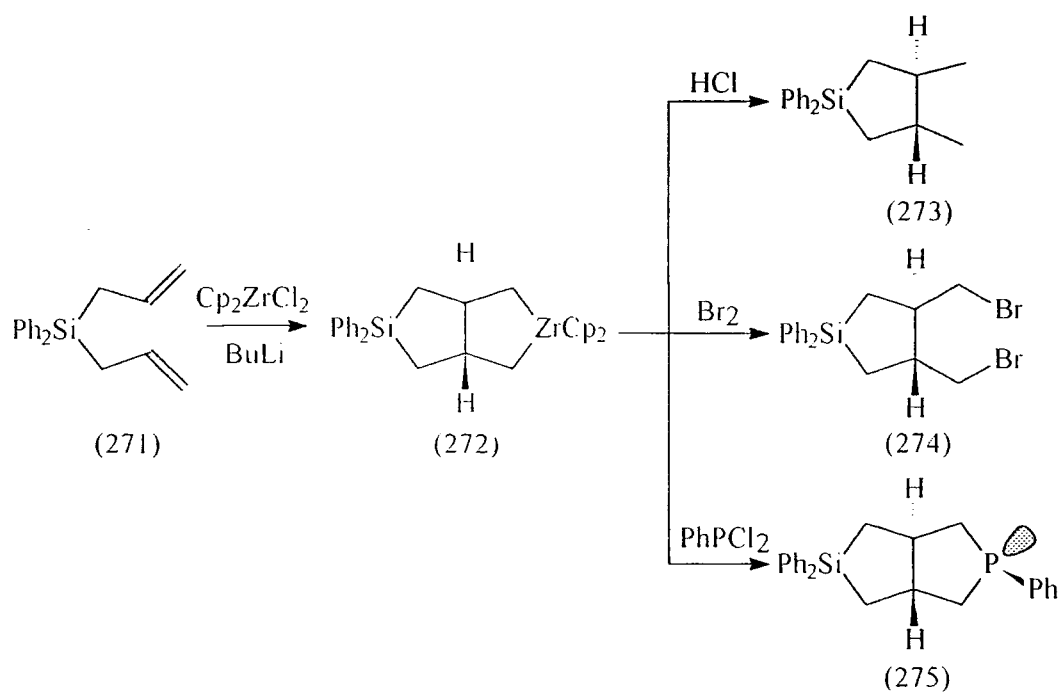


Scheme N.7

At this stage, the constraints of a three year project forced us to focus our efforts on the more advanced hydroboration strategy and as a result this hydrosilylation strategy remains to be attempted.

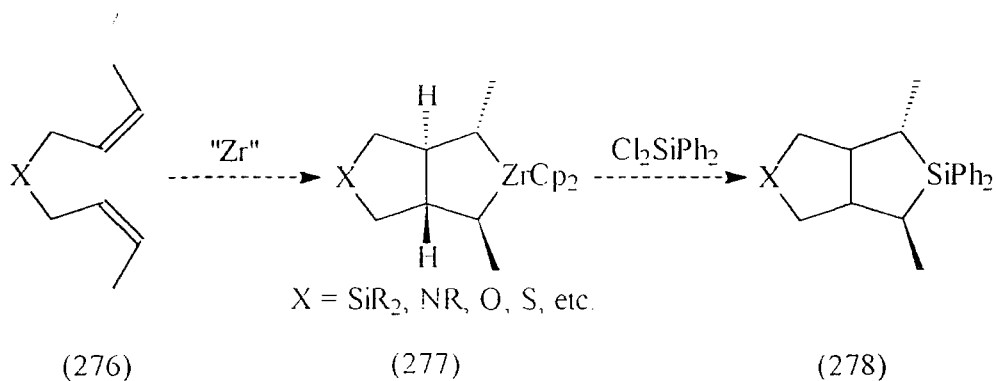
## N.2. Zirconacyclisation as a Tool in the Synthesis of Silacycles

The use of zirconium in organic synthesis has increased rapidly since the development of Schwartz's reagent for the hydrozirconation of unsaturated compounds.<sup>114</sup> More recently Negishi and Nugent have reported the cyclisation of dienes and enynes on treatment with a zirconocene species. This is generated *in situ* by the oxidative elimination reaction of butyllithium and zirconocene dichloride.<sup>115</sup> The resulting cyclic zirconocene intermediate formed on reaction with the diene, has itself been reacted with a variety of electrophiles including CO, I<sub>2</sub>, and Br<sub>2</sub> to give cyclic ketones, diiodo- and dibromo-compounds respectively. Furthermore, silacycles have been synthesised by the zirconacyclisation of silicon-substituted dienes. For example, diallylsilane (271) was treated with zirconocene dichloride and butyllithium to give the zirconasilacycle (272). Subsequent reaction with a variety of electrophiles gave the cyclic products depicted in Scheme N.8.<sup>116</sup>



Scheme N.8

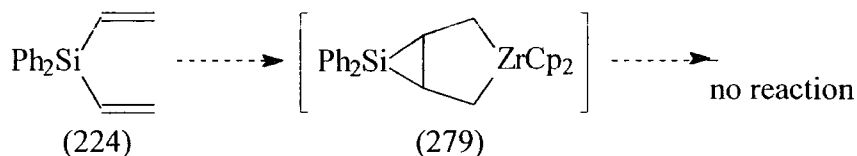
It was anticipated that either zirconacyclisation of a functionalised silyldiene (276) ( $X=\text{SiR}_2$ ) or silyl substitution of the cyclic zirconocene intermediate (277) ( $X=\text{NR/O/R/S/SiR}_2$ ) would allow the synthesis of substituted silacycles (278), Scheme N.9. This zirconocene-promoted cyclisation strategy relies on the use of a suitable chiral zirconium reagent. As yet, enantiomerically pure zirconium compounds are fairly limited in structural type and often require non-trivial resolution steps.<sup>117</sup> However, it seemed reasonable to conduct some model studies in this area.



Scheme N.9

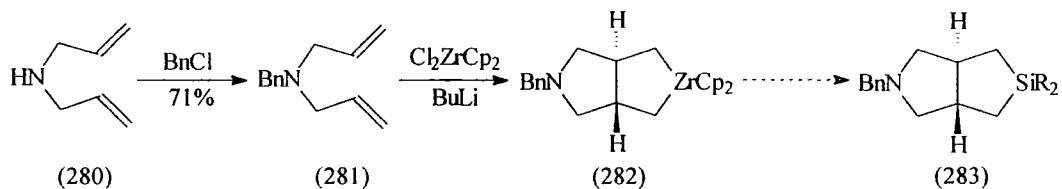
Initial attempts in this area focused on the reaction of divinylsilane (224) and zirconocene dichloride. Divinylsilane (224) failed to react following the conditions

described by Negishi for the zirconocene-promoted bicyclisation of dienes.<sup>115</sup> However, this is not altogether unexpected as the silacyclopropyl intermediate (**279**) would be very strained and, most probably, very difficult to form, Scheme N.10.



Scheme N.10

The alternative strategy involves electrophilic substitution of a zirconocene intermediate with a dichlorosilane species. As a result, benzyldiallylamine (**281**), chosen as a model study, was prepared by benzylation of diallylamine and was characterised by comparison with literature data.<sup>118</sup> However, subsequent reaction with zirconocene dichloride, butyllithium and various dichlorosilanes afforded only complex mixtures of unidentifiable products, Scheme N.11.



Scheme N.11.

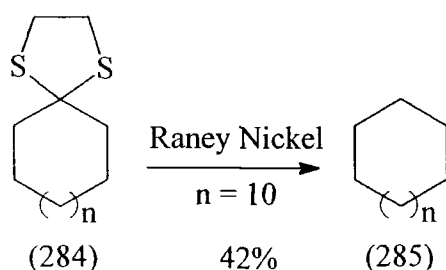
Since there is precedence for trapping zirconacycles such as (**282**) with chlorotrimethylsilane the failure to synthesise silacycles by this strategy was disappointing. Furthermore, informal discussions with the Whitby group at Southampton indicated that transmetalation from zirconium to copper may be necessary to give reaction with silicon.<sup>119</sup> This area remains to be explored.

## P. Silacyclohexanone Reduction and Silacycle Activation Studies

### P.1. Introduction

The asymmetric hydroboration of divinylsilanes has been established as a viable method in the synthesis of  $C_2$  symmetric silacyclohexanones. Our synthetic route relies on the formation of a synthetically useful silyl moiety in the last step. As discussed in section K there remains a need to develop a method to determine the *ee* for silacyclohexanones derived from the asymmetric hydroboration of divinylsilanes. Given that ketals can be readily converted into dithioketals via transketalisation, it was hoped that enantiomerically pure ketals derived from enantiomerically pure diols would aid in the determination of the *ee* and separation of the stereoisomers. This is achieved through the formation of a new set of diastereoisomers which may exhibit different chromatographic profiles.

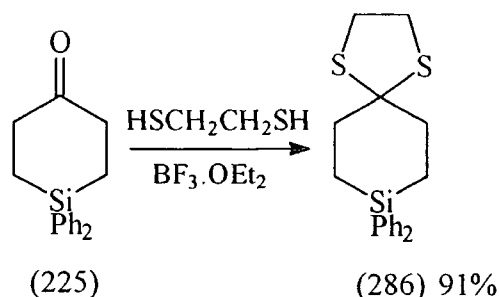
It was felt that, because of possible competing reactions at the  $\alpha$ -keto centre, the activation of the silacycle by phenyl-chloride exchange would be easier to perform on a silacyclohexane rather than the silacyclohexanone. Consequently, removal of the carbonyl functionality is required. A variety of methods exist to convert ketones into alkanes, many involve harsh acidic/basic conditions, which may inadvertently cleave the potentially labile Si-Ph bonds. The neutral Raney nickel reduction was an obvious alternative.<sup>120</sup> For example, the Raney nickel reduction of dithioketals (**284**) gave alkanes (**285**) in acceptable yields, Scheme P.1.



Scheme P.1

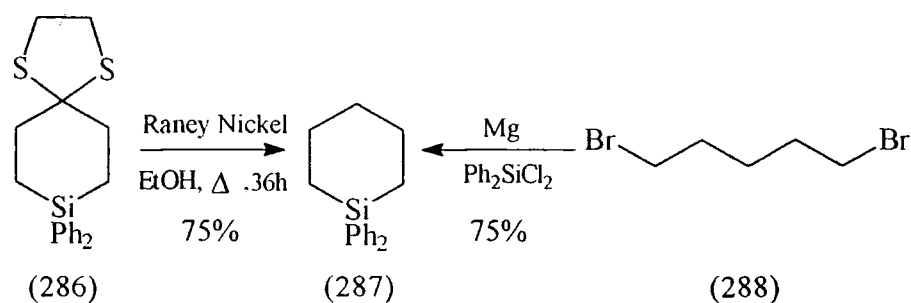
## P.2. A Model Study

It seemed prudent to carry out a model study with the unsubstituted silacyclohexanone (**225**). The corresponding dithiospirodecane (**286**) was synthesised in excellent yields by Lewis-acid-promoted dithioketalisation with ethanedithiol, Scheme P.2. The formation of dithiospirodecane (**286**) was confirmed by the shift in the  $^{13}\text{C}$  NMR for the carbon assigned to the ketone ( $\delta$  214.0) to the spirocentre carbon ( $\delta$  72.0) in the dithioketal (**286**).



Scheme P.2

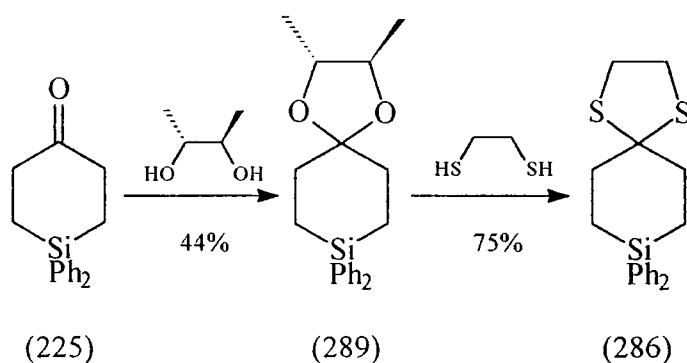
Subsequent Raney nickel reduction on a small scale gave diphenylsilacyclohexane (**287**) in good yield, which was characterised by comparison of a known sample prepared earlier by a Grignard synthesis from 1,5-dibromopentane (**288**), Scheme P.3.



Scheme P.3

With the ketone to methylene conversion secure, attention was then turned to the transketalisation strategy. A model study using ketone (**225**), was undertaken. Reaction of the ketone (**225**) with (*R,R*)-butane-2,3-diol, in the presence of a

catalytic amount of  $\text{BF}_3 \cdot \text{O}(\text{Et})_2$  and 4Å molecular sieves, afforded ketal (**289**) in moderate but acceptable yields, Scheme P.4. The formation of ketal (**289**) was confirmed by the shift of the carbonyl signal ( $\delta$  214.0) in the  $^{13}\text{C}$  NMR to a signal ( $\delta$  109.5) assigned to the spiro carbon. Dioxyspiradecane (**289**) was then converted to the dithioketal (**286**) in good yield, by a Lewis-acid-promoted acetal exchange procedure, Scheme P.4. The formation of dithioketal (**286**) was confirmed by comparison with data previously obtained.

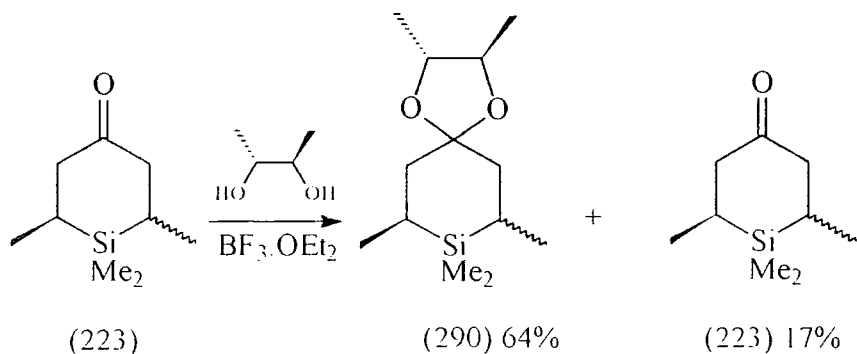


Scheme P.4

### P.3. Ketalisation Studies on $C_2$ Symmetric Silacycles

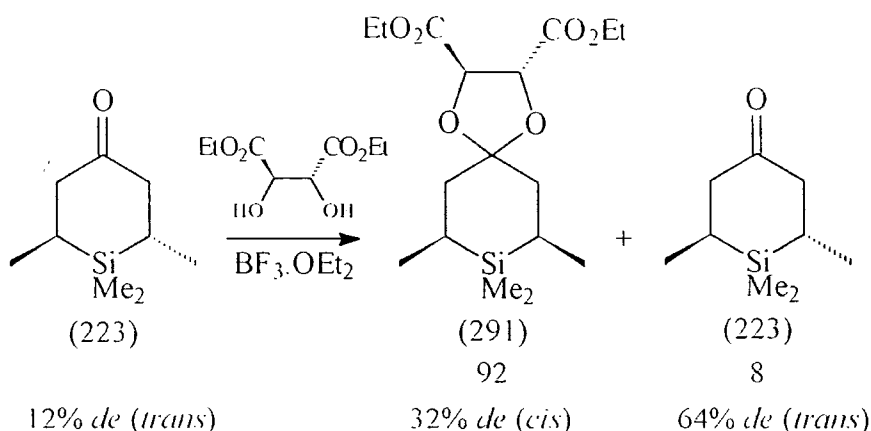
As discussed previously, it was hoped that the ketalisation of  $C_2$  symmetric silacycles may allow enantiomeric purification by separation of the diastereotopic cyclic ketals. In this section the synthesis and analysis of a variety of substituted silaketals will be discussed.

In an identical manner to that utilised for ketal (**289**), silaketal (**290**) was synthesised in good yield by  $\text{BF}_3 \cdot \text{O}(\text{Et})_2$ -promoted acetalisation of the racemic silacyclohexanone (**223**) with (*R,R*)-2,3-butanediol, Scheme P.5. However, the diastereoisomers could not be separated by chromatography and although some unreacted ketone (**223**) (12%) was isolated,  $^1\text{H}$  NMR analysis showed no change in isomer ratio.



Scheme P.5

It was envisaged that another chiral diol may provide enhanced isomeric separation. Consequently treatment of silacyclohexanone (**223**) [12% *de* (*dl*)] with (*2R*, *3R*) diethyl tartrate afforded a mixture of the desired ketal (**291**) and starting material (**223**) in a 92:8 ratio, Scheme P.6. This high conversion required repeated replenishment of the molecular sieves. The formation of cyclic ketal (**291**) was confirmed by the disappearance of the carbonyl signal ( $\delta$  213) and the appearance of the cyclic ether carbon signal ( $\delta$  116.6) in the  $^{13}\text{C}$  NMR. Although chromatographic separation was partially evident by TLC, the isomers of (**291**) could not be separated by flash column chromatography.



Scheme P.6

However,  $^1\text{H}$  NMR analysis of the unreacted silacyclohexanone (**223**) revealed that the *de* of silacyclohexanone (**223**) had risen to 64% (*dl*) suggesting some sort of "kinetic resolution" had occurred. This can be attributed to the *cis*-isomer reacting more quickly with the diol, possibly because of unfavourable 1,3-diaxial interaction

between the axial  $\alpha$ -methyl of the trans-isomer and an oxygen of the ketal ring, Figure P.1.

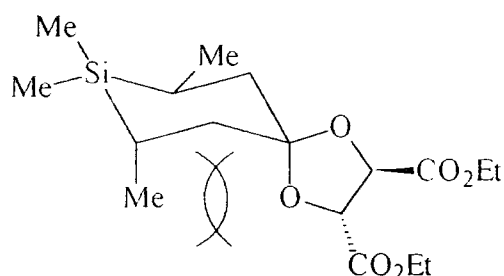
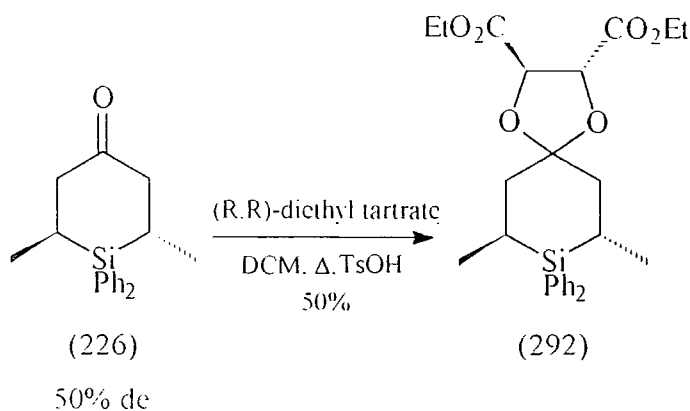


Figure P.1

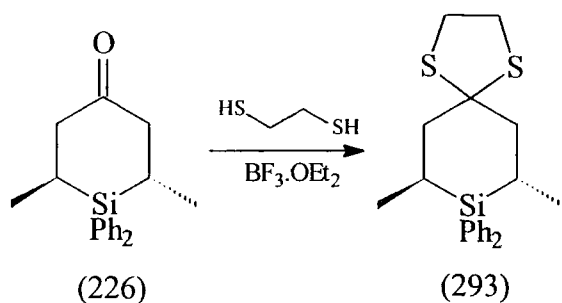
Subsequently, the acetalisation of the diphenyl analogue silacyclohexanone (**226**) was attempted. However, our standard Lewis acid acetalisation procedure gave only low yields of cyclic ketal (**292**). Alternative procedures were investigated: the first of these employed azeotropic removal of water with toluene, using a Dean-Stark apparatus; however, this gave only a complex mixture of unidentifiable products. It seems possible that the high temperatures employed in this process coupled with the acidic medium were enough to cleave the Si-Ph bonds. Reaction at a lower temperature (38°C) was achieved by Soxhlet extraction with DCM over 4Å molecular sieves. Disappointingly even this modification resulted in low conversion to silacycloketal (**292**) with an optimum yield being a moderate 50%, Scheme P.7. The formation of cyclic ketal (**292**) was confirmed by analogy with data obtained from the SiMe<sub>2</sub> analogue (**291**). Unfortunately, at all stages, neither chromatographic separation nor "kinetic resolution" of the diastereoisomers could be observed.



Scheme P.7

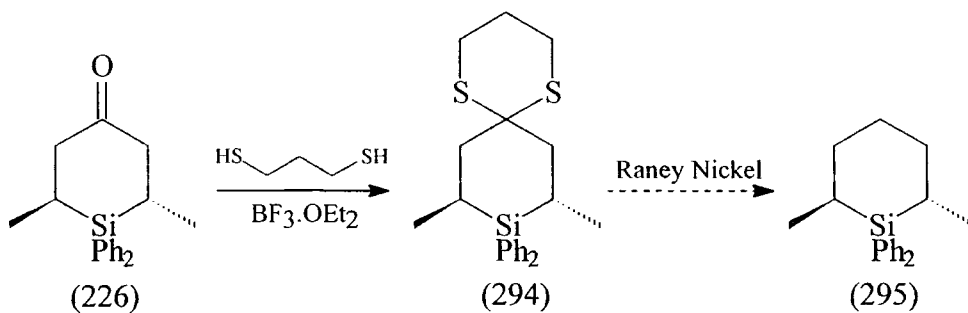
#### P.4. Attempted Functionalisation of Substituted Silacycles

Our attention then turned to the conversion of the  $C_2$  symmetric diphenylsilacyclohexanone (**226**) to silacyclohexane. Lewis-acid-promoted ketalisation, gave dithiaspirodecane (**293**) in almost quantitative yield, as a waxy solid, Scheme P.8. Attempts to recrystallise this material from a variety of solvents proved impossible and flash column chromatography resulted in decomposition of the compound. This has been attributed to degradation of the dithioketal moiety. As a result it seemed prudent to examine the potentially more stable propanedithiol-derived ketal.



Scheme P.8

Consequently siladithiaspirodecane (**294**) was made by the same method as (**293**), Scheme P.9. Concentration of the organic liquors afforded a semi-crystalline solid in good yield and adequate purity. Although TLC indicated no decomposition, no further purification was required. The formation of (**294**) was confirmed by the shift in the <sup>13</sup>C NMR of the signal ( $\delta$  212) assigned to the ketone carbon of the silacyclohexanone (**226**) to the spiro signal ( $\delta$  51.6) in the dithioketal (**294**).

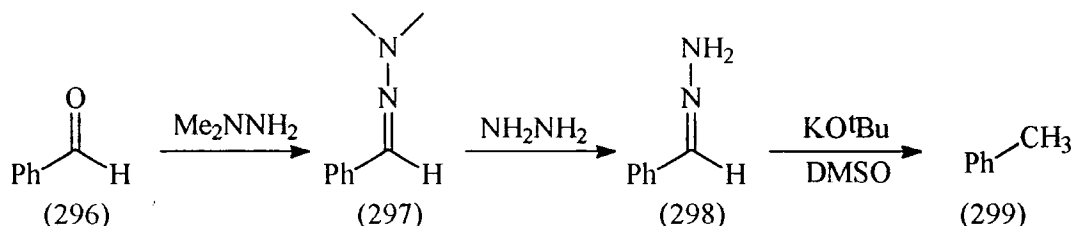


Scheme P.9

However, reduction of dithioketal (**294**) with freshly prepared Raney nickel<sup>121</sup> gave only a complex mixture of unidentifiable side-products. It is unclear why this procedure did not yield the desired silacyclohexane (**295**). However, it was obvious that the need for a large excess (7 equivalents) of Raney nickel hampered the isolation of any product.

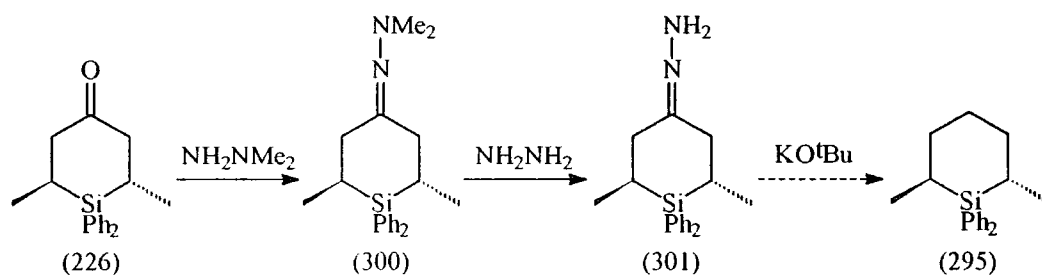
### P.5. Wolff-Kishner Modification

Alternative methods were subsequently considered for the conversion into the silacyclohexane functionality. We focused on the Wolff-Kishner reduction. Given that this process normally requires high temperatures we sought a milder variation. Cram has reported a room temperature version of the Huang-Minlong modification.<sup>122</sup> In this example, benzaldehyde (**296**) was converted into the stable dimethylhydrazone (**297**) on treatment with dimethylhydrazine. Hydrazone (**297**) then reacted with anhydrous hydrazine, to give hydrazone (**298**) which reacted *in situ* with potassium t-butoxide in DMSO at room temperature, to afford toluene (**299**) in good yield, Scheme P.10.



Scheme P.10

Following this precedent a small scale experiment with silacyclohexanone (**226**) was attempted, Scheme P.11. The reaction between the ketone (**226**) and dimethylhydrazine proceeded smoothly, and the synthesis of dimethyl hydrazone (**300**) was confirmed by the appearance of a broad singlet ( $\delta$  2.44) assigned to NMe<sub>2</sub> in the <sup>1</sup>H NMR. The disappearance of the same signal seemed to confirm the formation of hydrazone (**301**) on reaction with hydrazine. Unfortunately the *in situ* KO<sup>t</sup>Bu room temperature reduction gave only a complex mixture of unidentifiable products.



Scheme P.11

Although to date this strategy has not been successful it is possible that further experiments may overcome the problems with this approach. However lack of time prevented any further investigations into this route.

### Q. Activation of Silacycles

This section will focus on model studies towards the activation of diphenylsilacycles and the various methods examined will be discussed. It is known that phenylsilanes undergo electrophilic substitution on the *ipso*-carbon of the aromatic ring to silicon. The mechanism of this chlorination is given in Figure Q.1.<sup>123</sup> Reaction of the phenylsilane creates an electron-deficient centre  $\beta$  to silicon and nucleophilic displacement of silicon re-aromatises the ring and in the case of HCl, gives benzene and the chlorosilane.

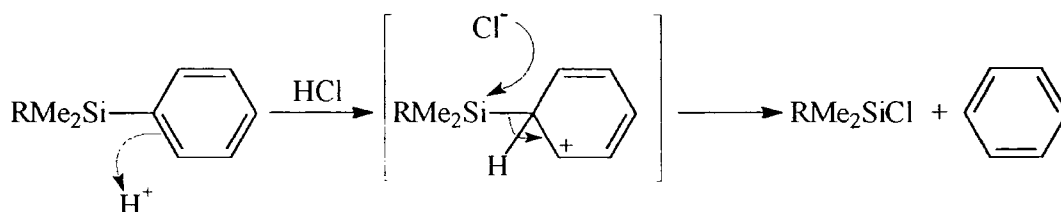
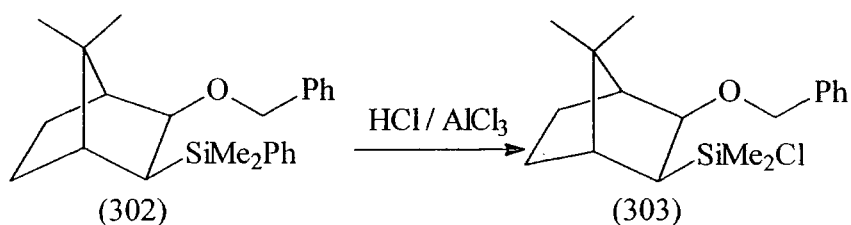


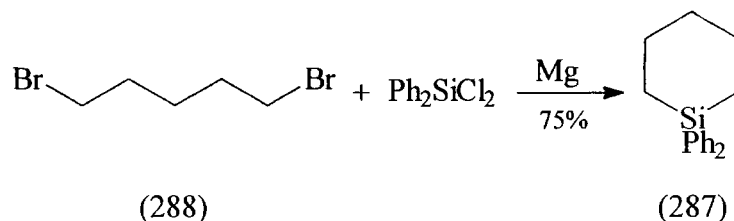
Figure Q.1

Taddei has shown that phenylsilane (**302**) can be readily converted into the chlorosilane (**303**) by reaction with HCl and  $\text{AlCl}_3$ , Scheme Q.1.<sup>124</sup>



Scheme Q.1

It was hoped that a similar procedure would allow the synthesis of dichlorosilacycles from diphenylsilacyclohexanones. We commenced this area of research with a model study using silacycle (287). This was prepared using Grignard methodology. It should be noted that the yield of silacycle (287) was significantly increased by the simultaneous addition of 2,5-dibromopentane (288) and dichlorodiphenylsilane to magnesium in THF, Scheme Q.2. A chemical yield of 75% was attainable compared to the previous best of 40% that could be achieved by preparing the Grignard reagent first, with subsequent addition of the chlorosilane.



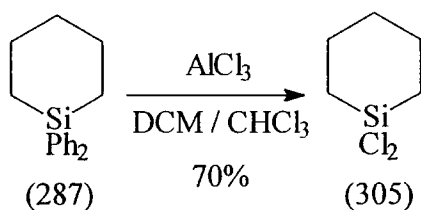
Scheme Q.2

Basing our initial studies on Taddei's work we attempted to chlorinate diphenylsilacycle (287) by bubbling HCl gas through a solution of the diphenylsilane in DCM using a catalytic amount of AlCl<sub>3</sub>. The reaction was followed by GCMS and after several days only the monochloro intermediate (304) could be detected, Figure Q.2. The chlorosilane (304) was not isolated but its presence was confirmed by the mass spectral analysis showing a 3:1 ratio for the parent ion indicating the presence of one chlorine group rather than two.



Figure Q.2

Subsequent attempts to increase the reactivity of the system by varying the halogen nucleophile and initiator electrophile were explored. A variety of analogous bromine systems were tried without success, (these included  $\text{Br}_2/\text{CH}_3\text{COOH}$ , and  $\text{Br}_2/\text{AlBr}_3$ ). Finally we returned to the  $\text{HCl}/\text{AlCl}_3$  system and found that stoichiometric amounts of aluminium chloride gave good yields of the dichlorosilane (305), Scheme Q.3.



Scheme Q.3

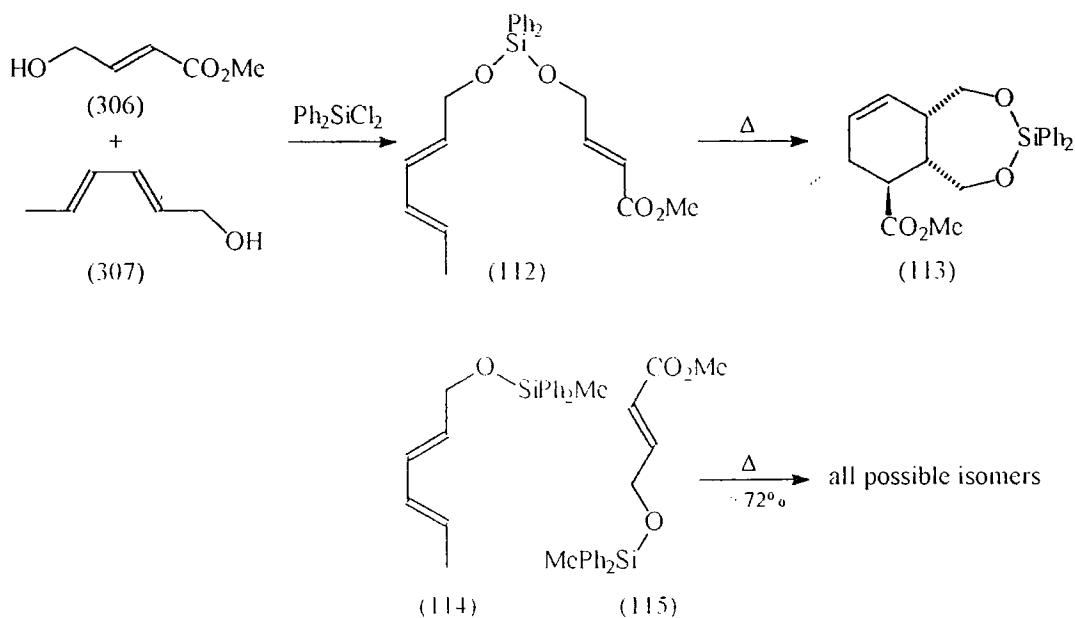
The reaction is extremely rapid, complete conversion occurring in a matter of minutes. Unusually, the use of  $\text{HCl}$  gas was not required and the reaction did not work in hexane. It is likely that there are residual amounts of moisture in the aluminium chloride that encourage the generation of  $\text{HCl}$ , and that this can only occur in polar solvents, where the dielectric constant is sufficient to promote the formation of an ionic electrophilic species. The reaction has not yet been studied in other non-halogenated polar solvents such as diethyl ether or THF so this theory remains to be verified.

## R. Applications of C<sub>2</sub> Symmetric Silacycles

### R.1. Introduction

As discussed in the first chapter, silicon has been used extensively as a temporary tether for intramolecular reactions often resulting in high diastereoselectivity as well as regioselectivity. However, to date, to the best of our knowledge, there have been no examples of asymmetric silicon-bound tethers. It is hoped that an enantiomerically pure silacycle would induce some enantioselectivity to these reactions. In this section a model study involving the use of dichlorosilacyclohexane (**305**) as a tether in a Diels-Alder reaction is discussed.

The use of silicon tethers in intermolecular Diels-Alder reactions is well documented. One such example that has already been discussed, was Craig's use of a diphenylsilyl tether in the reaction between sorbyl alcohol (**307**) and methyl 4-hydroxybutenoate (**306**). This reaction was shown to be highly diastereoselective. In contrast, the untethered version gave a mixture of regio- and diastereomeric products, Scheme R.1.<sup>59</sup>



Scheme R.1

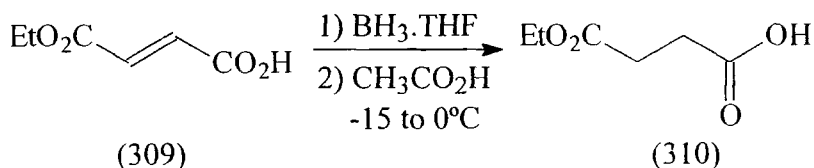
## R.2. Tethered Diels-Alder Model Studies

In order to demonstrate the effect of a cyclic silyl tether, Craig's reaction has been repeated using silacycle (305). Sorbyl alcohol (307) was prepared by LiAlH<sub>4</sub> reduction of ethyl sorbate (308), Scheme R.2. The reaction proceeded smoothly, gave good yields of the desired diene alcohol (307) and was characterised by comparison with the literature data.<sup>125</sup>



Scheme R.2

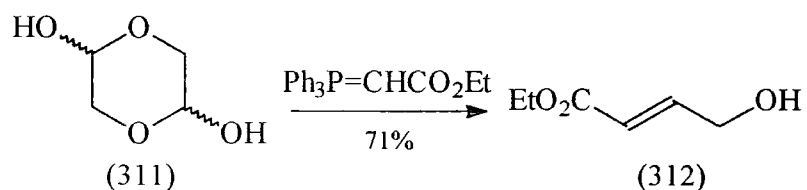
The selective reduction of carboxylic acids in the presence of double bonds and esters has been reported by Kende and Fludzinski using borane-THF at low temperatures.<sup>126</sup> Unfortunately, in our hands, treatment of the carboxylic acid (309) with borane, at a variety of temperatures, resulted in selective reduction of the double bond, Scheme R.3. The formation of the saturated carboxylic acid (310) was confirmed by the disappearance of the alkene signal ( $\delta$  6.9-6.8) in the <sup>1</sup>H NMR and by comparison with literature data.<sup>127</sup>



Scheme R.3

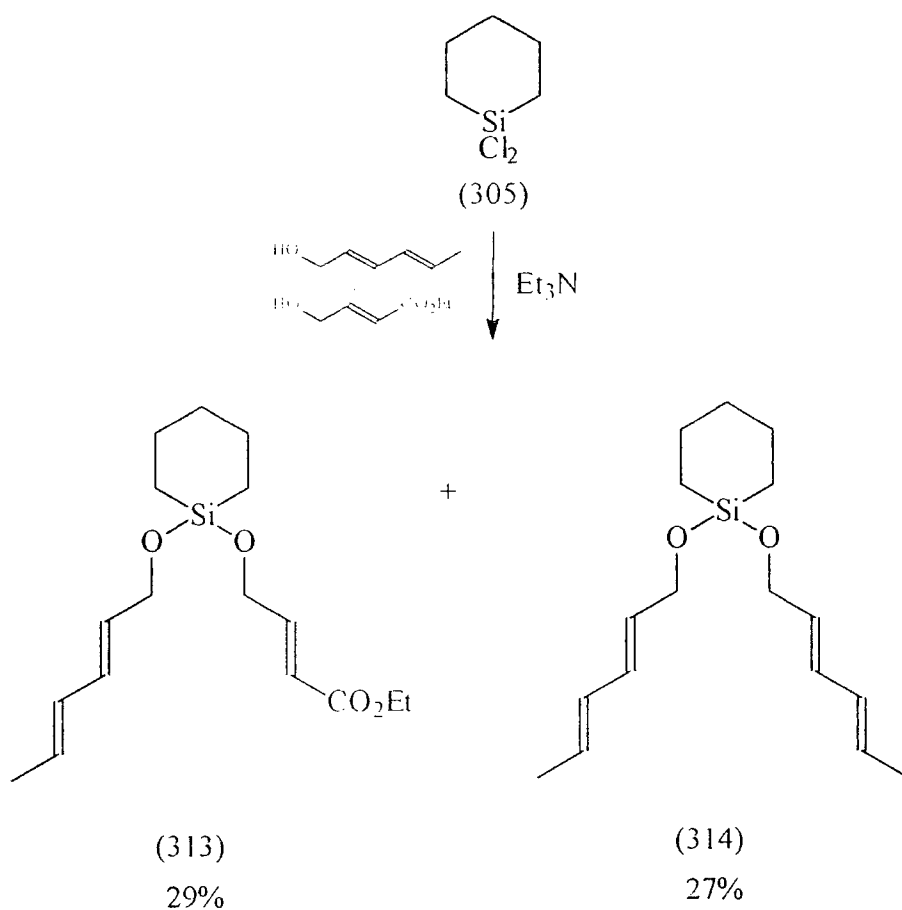
Consequently, the methodology developed by Craig was followed to prepare hydroxyalkene (312).<sup>59</sup> The Wittig reaction between glycolaldehyde (311) and (carboethoxy)triphenylphosphorane proceeded without problems and gave ethyl hydroxybutenoate (312) in good yields, Scheme R.4. Generation of the alkene was confirmed by the appearance of double bond protons ( $\delta$  7.01 and  $\delta$  6.04) in the <sup>1</sup>H NMR which showed a large coupling value confirming the formation of a *trans*

double bond. In all other respects the compound was characterised by comparison with literature data.



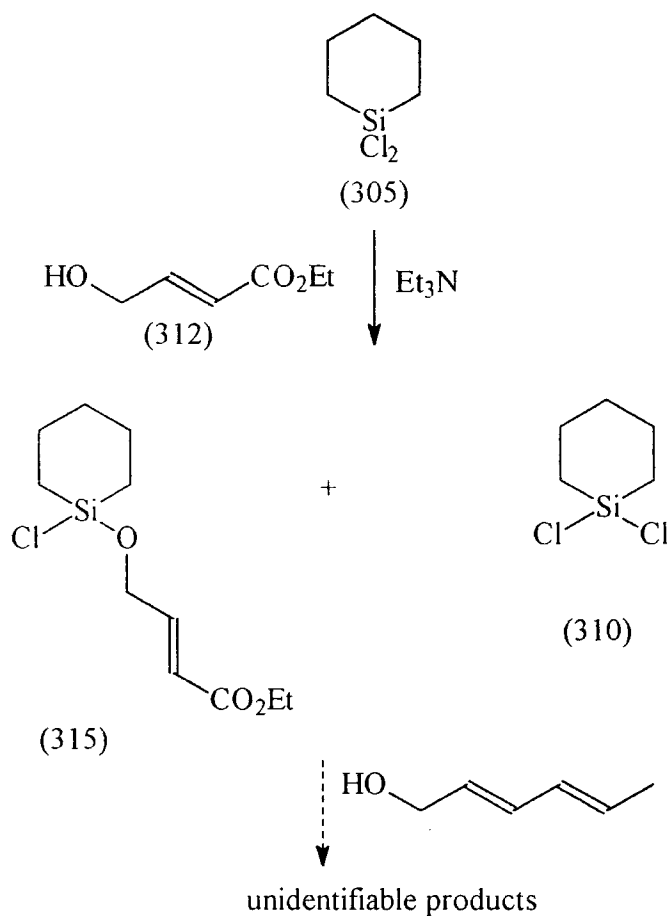
Scheme R.4

To date there have been few reports of the selective tethering of diene and dienophiles by dichlorosilane tethers. In his report Craig had coupled the three reagents in a stoichiometric mixture. Following this procedure, the requisite triene (**313**) was formed unselectively by treatment of the dichlorosilane (**305**) with a stoichiometric mixture of the diene and dienophile, Scheme R.5. This gives a mixture of the desired triene (**313**), and bis-diene (**314**). There was no evidence of the bis-dienophile indicating that the diene is more reactive.



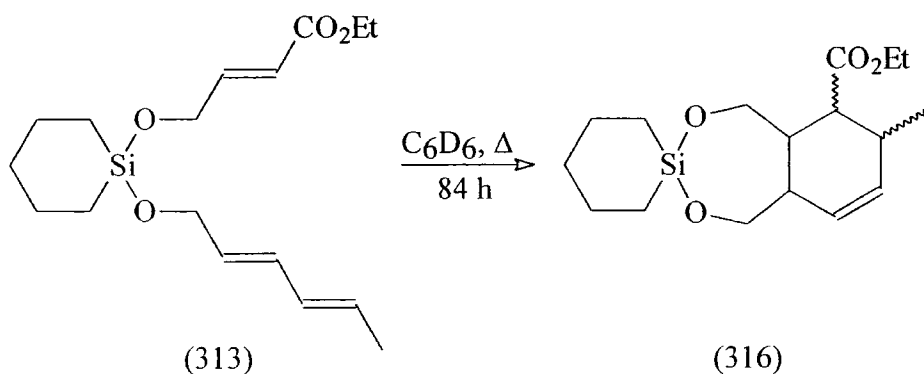
Scheme R.5

Furthermore, in an attempt to increase the yield of (313) a tethering reaction incorporating a sequential addition process was explored. In this, dichlorosilane (305) was treated initially with the dieneophile and after 24 hours the diene was added, Scheme R.6. However, this was not successful, with only a mixture of unidentifiable products being obtained. This may be due to the very slow reaction of the dienophile (312) resulting in hydrolysis of dichlorosilane (305) or intermediate chlorosilylacetal (315).



Scheme R.6

With triene (**313**) in hand we then explored the Diels-Alder reaction. Initially this was carried out on a small scale with NMR monitoring. The triene (**313**) was dissolved in  $\text{C}_6\text{D}_6$  and the sealed NMR tube was then heated under reflux for 80-100 hours, by which time all the starting material had been consumed, Scheme R.7. The tethered cyclohexene (**316**) was isolated in near quantitative yield and the formation of the tricyclic product was confirmed by the disappearance of the double bond signals attributable to the starting triene and the appearance of a double bond signal attributable to the cyclic alkene (**316**).<sup>59</sup> The reaction was significantly quicker than that reported previously and it is predicted that refluxing in toluene may be sufficient to drive this reaction.



Scheme R.7

The significantly lower reaction time is attributed to a reduction in available conformations of the silylketal when compared to Craig's diphenylsilyl ketal tether.<sup>59</sup> Furthermore GCMS analysis indicated an isomer ratio of 93:7 corresponding to a de of 86%. Although <sup>1</sup>H NMR indicated a ratio of 66:33 this is probably because the NMR was indicating a conformational equilibrium rather than the true diastereomeric yield. Further work in this area may yet confirm this, by derivatisation or low temperature NMR experiments. Finally, it is hoped that enantioselectivity can be introduced with use of C<sub>2</sub> symmetric silacycles.

## S. Conclusion

At the start of this study the aim was to synthesise enantiomerically pure silacycles and to study their applications in asymmetric organic synthesis. Significant progress has been made towards realising these goals. The asymmetric hydroboration of divinylsilanes has been firmly established as a viable strategy in the synthesis of  $C_2$  symmetric silacycles. In particular, the diastereoselectivity of the substituted diphenylsilacycle (**226**) is very promising, approaching 90% after one recrystallisation. Unfortunately, we have not yet been able to determine the *ee* for this process. In line with the results obtained for the synthesis of  $C_2$  symmetric diesters (**216-218**) it seems likely that the observed *ee* may well be in excess of the *de* (*i.e.* >90%).

The synthesis of  $\beta$ -substituted divinylsilanes and subsequent asymmetric hydroboration has shown that a competing  $\alpha$ -hydroboration pathway may prohibit the synthesis of silacycles from these substrates.

Our studies of the boron redistribution reaction are consistent with the premise that the redistribution step does occur with retention of stereochemistry.

The oxidation of organoboranes remains an area of some uncertainty and whilst the standard hydrogen peroxide procedure appears to be the best it is anticipated that other oxidants, such as trimethyl-N-oxide may yet provide milder and more effective alternatives.

A preliminary study into the synthesis of silacycles by the asymmetric hydrosilylation of dienes using Hayashi's MOP-Pd-catalysed process has been undertaken. This process requires a regioselective hydrosilylation and whilst some evidence for this has been observed, the conversions are currently too low to be synthetically viable. Unfortunately, time constraints prevented a complete study of this strategy. The zirconocene-promoted cyclisation strategy is similarly underdeveloped and little can be said about the likely outcome of this area of research.

Finally, the conversion of  $C_2$  symmetric silacycles into synthetically useful dichlorosilane species has provided some interesting results. A new procedure for the displacement of phenyl groups on silicon with chlorine has been developed and



allows  $\text{SiPh}_2$  units to be used as  $\text{SiCl}_2$  equivalents. This conversion has been shown to proceed almost instantaneously and in good yield.

The use of dichlorosilacycles as effective tethers for intramolecular Diels-Alder reactions has been demonstrated with silacycles showing enhanced reactivity when compared to acyclic diphenylsilyl counterparts. It is hoped that the introduction of homochiral tethers may yet introduce some enantioselectivity into these reactions.

## **CHAPTER THREE**

### **EXPERIMENTAL**

## **T.1. General Procedures**

All reactions were undertaken in an inert gas atmosphere of dry nitrogen or argon in pre-dried glassware.

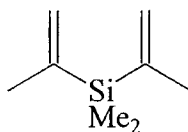
Unless otherwise stated, nuclear magnetic resonance (NMR) spectra were obtained on a Varian Gemini 200 ( $^1\text{H}$  at 199.975MHz,  $^{13}\text{C}$  at 50.289MHz), Varian XL-200 ( $^1\text{H}$  at 200.057MHz), Bruker AC-250 ( $^1\text{H}$  at 250.133MHz,  $^{13}\text{C}$  at 62.257MHz), Varian VXR-400(s) ( $^1\text{H}$  at 399.952MHz,  $^{13}\text{C}$  at 100.577MHz), and Bruker AMX-500 ( $^1\text{H}$  at 500.137MHz,  $^{13}\text{C}$  at 125.771MHz and  $^{29}\text{Si}$  at 99.363MHz) spectrometers with deuteriochloroform containing a trace amount of  $\text{CHCl}_3$  as solvent ( $\delta=7.26$ ) and are recorded in ppm ( $\delta$  units). Infra Red (IR) spectra were recorded on a Perkin Elmer FT-IR 1720X spectrometer. Low resolution mass spectra were recorded on a VG Analytical 7070E organic mass spectrometer, and gas chromatography-mass spectra (GCMS) were recorded using a Hewlett Packard 5890 series II gas chromatograph connected to a VG mass Lab trio 1000. To follow reactions, thin layer chromatography (TLC) or gas chromatography (GC) on Hewlett Packard 5890A or 5890 series II were used. Flash Column Chromatography was performed according to the method of Still *et al.* using silica gel, (60-240 mesh).<sup>128</sup> Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected.

All solvents were distilled prior to use. Petroleum ethers refer to the fraction boiling in the 40-60°C range unless otherwise stated. Solvents were dried from the following reagents under a nitrogen atmosphere: hexane, pentane and benzene (calcium hydride), THF and diethyl ether (sodium benzophenone ketyl), methanol (magnesium methoxide) and ethanol (magnesium ethoxide). All other reagents were used as supplied, unless otherwise stated.

Magnesium turnings used for Grignard reactions were activated, unless otherwise stated, by stirring under nitrogen for 15 hours before use. The magnesium became dark grey in colour and deposited a fine silver mirror on the inside of the flask.

## T.2. Experimental Detail:

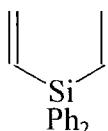
### Di(prop-2-enyl)dimethylsilane (186)<sup>77</sup>



(186)

2-Bromopropene (17.8ml, 200mmol) was added dropwise to a stirred suspension of magnesium (4.8g, 200mmol) in THF (65ml) at a rate sufficient to maintain a gentle reflux. The resulting solution was heated under reflux for a further 30 min. After cooling to room temperature dichlorodimethylsilane (9.5ml, 78mmol) was added dropwise and the resulting solution stirred at room temperature for 18 h. The reaction mixture was then poured onto ice-cold saturated aqueous ammonium chloride (50ml) and the aqueous layer extracted with diethyl ether (3x20ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Distillation yielded the dipropenylsilane (**186**) as a colourless oil (8.78g, 81%); bp. 125°C (lit.<sup>77,78</sup> 126-128°C);  $\nu_{\max}$  (thin film) 1254 (Si-CH<sub>3</sub>) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200MHz) 5.62 (2H, m, HCH=), 5.29 (2H, m, HCH=), 1.79 (6H, t J = 1.3Hz, H<sub>3</sub>CC=), 0.16 (6H, s, Si(CH<sub>3</sub>)<sub>2</sub>);  $\delta_{\text{C}}$  (50MHz) 145.7 (CH<sub>2</sub>=C), 125.8 (CH<sub>3</sub>C=CH<sub>2</sub>), 22.3 (CH<sub>3</sub>C), -4.5 ((SiCH<sub>3</sub>)<sub>2</sub>); MS (EI) *m/z* 140 (M<sup>+</sup>, 5%), 125 (M-CH<sub>3</sub><sup>+</sup>, 100%), 99 (M<sup>+</sup>-CH<sub>2</sub>=CCH<sub>3</sub>, 44%).

### Divinyldiphenylsilane (224)<sup>77</sup>

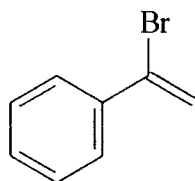


(224)

Dichlorodiphenylsilane (63.1ml, 0.3mol) was added dropwise to vinylmagnesium bromide (600ml, 1.0M in THF, 0.6mol). The reaction was heated under reflux for 1 h

then allowed to cool for a further 1 h. The reaction was poured onto ice-cold saturated ammonium chloride solution (1l) and the product was extracted into ethyl acetate (3x200ml). The combined organic layers were dried ( $\text{MgSO}_4$ ) and concentrated. Purification by distillation afforded divinyl diphenylsilane (**224**) (61g, 89%) as a colourless oil, bp.  $110^\circ\text{C}/0.1\text{mbar}$  (lit.<sup>77</sup>  $130\text{-}131^\circ\text{C}/0.07\text{mbar}$ );  $\nu_{\text{max}}$  (thin film) 1590 ( $\text{CH}_2=\text{C}$ ), 1428, 1401 (SiPh), 1113, 1007, 959  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (100MHz) 7.4-7.8 (10H, m, Ar), 6.6 (2H, dd  $J = 20, 15\text{Hz}$ , HCH=CH), 6.0 (2H, dd  $J = 15, 3.8\text{Hz}$ , HCH=CH), 5.96 (2H, dd  $J = 20, 3.8\text{Hz}$ , CH=CH<sub>2</sub>);  $\delta_{\text{C}}$  (100MHz) 136.5 (Ar), 135.5 (Ar), 134.5 (Ar), 133.7 (Ar), 130.0 (Ar), 129.5 ( $\text{CH}_2=\text{CH}$ ), 127.8 (CHSi);  $\delta_{\text{Si}}$  (99MHz) -20.37; MS (EI)  $m/z$  236 ( $\text{M}^+$ , 17%), 159 ( $\text{M}^+ - \text{Ph}$ , 25%), 105 (SiPh, 100%).

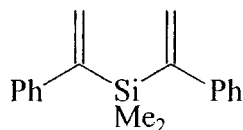
#### $\alpha$ -Bromostyrene (184)<sup>77</sup>



(184)

Bromine (25.8ml, 0.5moles) in DCM (60ml) was added dropwise to a stirred solution of styrene (57ml, 0.5moles) in DCM (450ml) at  $0^\circ\text{C}$ . The solvent was removed under reduced pressure and the resulting crude dibromide dissolved in DMSO (600ml). Aqueous NaOH (260ml, 48% w/v) was added and the mixture stirred at  $20^\circ\text{C}$  for 5 h. Water (450ml) was then added and the organic layer extracted with hexane (3x200ml), dried ( $\text{MgSO}_4$ ) and concentrated. The residue was distilled to afford  $\alpha$ -bromostyrene (**184**), bp.  $100^\circ\text{C}/25\text{mbar}$  (lit.<sup>77</sup> bp  $67\text{-}70^\circ\text{C}/6\text{mbar}$ ) as a pale yellow oil (66.74g, 73%);  $\nu_{\text{max}}$  (thin film) 3032 ( $\text{CH}_2=\text{C}$ ), 1615 ( $\text{C}=\text{C}$ )  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200MHz) 7.50 (5H, m, Ar), 6.13 (1H, d  $J = 2.5\text{Hz}$ , HCH=), 5.80 (1H, d  $J = 2.5\text{Hz}$ , HCH=).

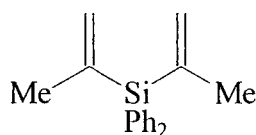
**Di-2-phenylvinyl dimethylsilane (159)**<sup>77</sup>



(159)

$\alpha$ -Bromostyrene (**184**) (7.1ml, 55mmol) was added dropwise to a stirred suspension of magnesium (1.32g) in THF (15ml). The reaction was heated under reflux for 30 min before dichlorodimethylsilane (2.55ml, 21mmol) was added dropwise. The mixture was then stirred for 15 h before being poured onto ice-cold saturated ammonium chloride solution (15ml). The aqueous layer was extracted with ether (3x25ml), and the combined organic layers were dried ( $MgSO_4$ ) and concentrated. Distillation afforded the divinylsilane (**159**) (3.17g, 57%) as a yellow oil, bp. 103-104°C/0.04 mbar (lit.<sup>77,78</sup> 109-110°C/0.19 mbar);  $\nu_{max}$  (thin film) 1250, (Si-CH<sub>3</sub>)  $cm^{-1}$ ;  $\delta_H$  (250MHz) 7.27 (10H, m, Ar), 6.01 (2H, d J = 3.0Hz HCH=), 5.74 (2H, d J = 3.0 Hz, HCH=), 0.33 (6H, s, Si(CH<sub>3</sub>)<sub>2</sub>);  $\delta_C$  (125MHz) 151.05 (Ar), 144.08 (Ar), 129.23 (Ar), 128.09 (Ar), 126.83 (CH<sub>2</sub>=CSi), 126.43 (C=CH<sub>2</sub>), -2.07 (SiMe<sub>2</sub>); MS (EI)  $m/z$  264 (M<sup>+</sup>, 30%), 135 (100, SiMe<sub>2</sub>Ph<sup>+</sup>).

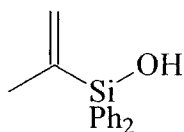
**Di(prop-2-enyl)diphenylsilane (187)**<sup>77</sup>



(187)

2-Bromopropene (6.84ml, 77mmol) was added dropwise to a stirred suspension of magnesium (1.92g, 80mmol) in THF (30ml) at a rate sufficient to generate and maintain a gentle reflux. The reaction was heated under reflux for a further 3 h before dichlorodiphenylsilane (6.3ml, 30mmol) was added dropwise at reflux temperature. After a further 15 h the reaction was allowed to cool before being poured onto ice-cold saturated ammonium chloride solution (50ml). The mixtures was extracted into

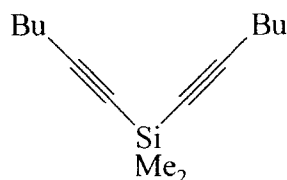
ether (3x25ml) and the combined organic layers washed with brine (30ml), dried ( $\text{MgSO}_4$ ) and concentrated. Flash column chromatography eluting with 2% ethyl acetate in petrol, followed by crystallisation from hexane afforded the divinylsilane (**187**) as a white crystalline solid (5g, 64%), mp. 39-40°C;  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ), 1701 (C=C), 1428 (Si-Ph), 1110, 937  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (400MHz) 7.58-7.35 (10H, m, **Ar**), 5.92 (2H, m, HCH=C), 5.42 (2H, m, HCH=C), 1.95 (6H, t J = 1.3Hz,  $\text{CH}_3$ -C);  $\delta_{\text{C}}$  (100MHz) 143.2 (**Ar**), 134.9 (**Ar**), 134.5 (**Ar**), 130.0 (**Ar**), 129.9 ( $\text{CH}_2$ =C), 128 (C=CH<sub>2</sub>), 22.2 ( $\text{CH}_3$ C);  $\delta_{\text{Si}}$  (99MHz) -14.60; MS (EI)  $m/z$  264 ( $\text{M}^+$ , 64%), 233 (100,  $\text{M}^+$ - $\text{H}_3\text{CC}=\text{CH}_2$ ); Analysis found: C, 81.48%; H, 7.71%.  $\text{C}_{18}\text{H}_{20}\text{Si}$  requires C 81.76%; H 7.62%.



(190)

$\nu_{\text{max}}$  3308 (OH), 1589 (C=C), 1428 (Si-Ph), 1117  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (400MHz) 7.58-7.35 (10H, m, **Ar**), 5.93 (1H, m, HCH=C), 5.43 (1H, m, HCH=C), 1.97 (3H, t J = 1.3Hz,  $\text{CH}_3$ -C);  $\delta_{\text{C}}$  (200MHz) 144, 134.2, 134.1, 130.5, 128, 22; MS (EI)  $m/z$  240 ( $\text{M}^+$ , 18%), 222 ( $\text{M-OH}^+$ , 11.1%), 199 ( $\text{M}^+$ - $\text{CH}_2=\text{CCH}_3$ , 100%).

**Di(hexyn-1-yl)dimethylsilane (194)**<sup>129</sup>



(194)

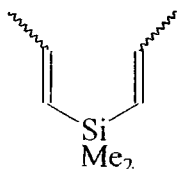
A solution of *n*-BuLi (1.6M in hexanes, 27.5ml, 44mmol) was added dropwise to a stirred solution of 1-hexyne in hexane (15ml) at -78°C. After 30 min

dichlorodimethylsilane (1.38ml, 11mmol) was added dropwise at 0°C and the reaction was stirred for 1 h. A saturated solution of sodium bicarbonate (15ml) was added and the aqueous layer was extracted into diethyl ether (3x25ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Flash column chromatography, eluting with 8% diethyl ether in petrol afforded di(hexyn-1-yl)dimethylsilane (**194**), bp. 74°C/0.25mbar (lit.<sup>129</sup> 68°C/0.2mbar), as a colourless oil (1.54g, 67%).  $\nu_{\max}$  (thin film) 2178 (C≡C), 1261 (Si-CH<sub>3</sub>) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200MHz) 2.23 (4H, m, CH<sub>2</sub>CC), 1.45 (8H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.9 (6H, t J = 6.2Hz, CH<sub>3</sub>CH<sub>2</sub>), 0.08 (6H, s, SiMe<sub>2</sub>);  $\delta_{\text{C}}$  (125MHz) 83.98 (CC), 81.49 (CC), 30.46 (CH<sub>2</sub>CC), 21.86 (CH<sub>2</sub>CH<sub>2</sub>CC), 19.60 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 13.52 (CH<sub>3</sub>CH<sub>2</sub>), 0.76 (SiMe<sub>2</sub>); MS (CI) *m/z* 238 (MNH<sub>4</sub><sup>+</sup>, 100%), 221 (MH<sup>+</sup>, 67%), 156 (MNH<sub>4</sub><sup>+</sup>-HCCBu); HRMS (CI) *m/z* MNH<sub>4</sub><sup>+</sup> for C<sub>18</sub>H<sub>24</sub>NSi calc. 238.1991 obs. 238.1991.

#### **Attempted hydrogenation of di(hex-1-ynyl)dimethylsilane (194)**

A flask containing dihexynyldimethylsilane (**194**) (440mg, 2mmol) in hexane (5ml) and a catalytic amount of Lindlar catalyst (20mg) was flushed with hydrogen (100ml) and the uptake of hydrogen monitored from an graduated container. Once the uptake of hydrogen had levelled off the reaction mixture was filtered and the solvent removed under reduced pressure. The crude NMR data obtained indicated a mixture of starting material and unidentifiable products.

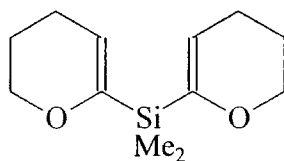
### Di(prop-1-enyl)dimethylsilane (192)



(192)

*Cis*-1-bromopropene (6.85ml, 80mmol) was added dropwise to a stirred suspension of magnesium in THF (20ml). The solution was heated under reflux for 1h. Dichlorodimethylsilane (4.85ml, 40mmol) was then added slowly, with stirring, to the refluxing mixture and the reaction was allowed to stir for a further 15 h before pouring onto ice-cold saturated ammonium chloride solution (15ml). The aqueous layer was extracted with ether (3x25ml) and the combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Distillation yielded di(prop-1-enyl)dimethylsilane (**192**) as a colourless oil (3.12g, 56%) and as a mixture of isomers; (GC 83:16:1 *ZZ:ZE:EE*), b.p. 100°C/70mbar;  $\nu_{\max}$  (thin film) 2961 (CH<sub>3</sub>), 1249 (Si-CH<sub>3</sub>) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 6.43 (0.16H, qd J = 7.1, 14.2Hz, CH<sub>3</sub>CH=CH, *ZE*), 6.42 (1.6H, qd J = 6.8, 13.6Hz, CH<sub>3</sub>CH=CH, *ZZ*), 6.13 (0.16H, qd J = 6.4, 18.4Hz, CH<sub>3</sub>CH=CH, *ZE*), 6.08 (0.08H, qd J = 6.6, 18.0Hz, CH<sub>3</sub>CH=CH, *EE*) 5.58 (1.6H, dq J = 1.2, 13.6Hz, CH<sub>3</sub>CH=CH, *ZZ*), 5.72 (0.16H, dq J = 1.6, 18.4Hz, CH<sub>3</sub>CH=CH, *ZE*), 5.65 (0.08H, dq J = 1.6, 18.6Hz, CH<sub>3</sub>CH=CH, *EE*), 5.50 (0.16H, dq J = 1.6, 14.0Hz, CH<sub>3</sub>CH=CH, *ZE*), 1.83 (0.48H, dd J = 1.6, 6.4Hz, CH<sub>3</sub>CH, *ZE*), 1.82 (0.24H, dd J = 6.0Hz, CH<sub>3</sub>CH, *EE*) 1.78 (4.8H, dd J = 1.6, 6.8Hz, CH<sub>3</sub>CH, *ZZ*), 0.23 (9.6H, s, SiMe<sub>2</sub>, *ZZ*), 0.16 (1.9H, s, SiMe<sub>2</sub>);  $\delta_{\text{C}}$  (100MHz) 143.6 (CH<sub>3</sub>CH=), 129.4 (CH=CHSi), 19.1(CH<sub>3</sub>CH=), -0.1 (SiMe<sub>2</sub>); MS (EI) *m/z* 140 (M<sup>+</sup>, 3%), 125 (M<sup>+</sup>-CH<sub>3</sub>, 84%) 99 (11%), 85 (36%), 59 (SiMe<sub>2</sub>H<sup>+</sup>, 100%); HRMS (EI) M<sup>+</sup> for C<sub>8</sub>H<sub>18</sub>Si calc. 140.1021; obs. 140.1021.

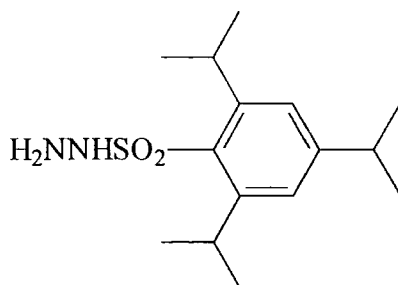
**Bis(dihydropyranyl)dimethylsilane (206)**<sup>88</sup>



**(206)**

A solution of *n*-BuLi (1.6M in hexanes, 68ml, 108mmol) was added slowly to a stirred solution of dihydropyran (9.11ml, 100mmol) in THF (250ml) at -78°C. The resulting yellow solution was stirred at 0°C for 1 h then a further 10 min at rt, before the dropwise addition of dichlorodimethylsilane (6.06ml, 50mmol) at -78°C. The reaction was stirred at -78°C for 20 min then rt for 10 min. Saturated ammonium chloride solution (75ml) was added and the mixture was extracted into diethyl ether (3x25ml). The combined organic layers were washed with water (50ml), dried (MgSO<sub>4</sub>), and concentrated. Purification by fractional distillation afforded bis(dihydropyranyl)dimethylsilane (**206**) as a colourless oil, bp. 74-80°C/0.1mbar (lit.<sup>88</sup> b.p. 120°C/4mbar) (2.8g, 19%);  $\nu_{\max}$  (thin film) 1616 (C=C-O), 1247 (SiMe), 1047 (C-O), 846 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (250MHz) 5.1 (2H, t, *J* = 4.7Hz, CH=CSi), 3.9 (4H, m, CH<sub>2</sub>O), 2.0 (4H, m, CH<sub>2</sub>CH), 1.83 (4H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 0.1 (6H, s, SiMe<sub>2</sub>);  $\delta_{\text{C}}$  (50MHz), 112 (CH=), 110 (C=CH), 66 (CH<sub>2</sub>O), 23 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 21(CH<sub>2</sub>CH=), -5.0(SiMe<sub>2</sub>); MS (EI) *m/z* 224 (M<sup>+</sup>, 23%), 141 (M<sup>+</sup>-dihydropyran); HRMS *m/z* M<sup>+</sup> for C<sub>12</sub>H<sub>20</sub>O<sub>2</sub>Si calc. 224.1233; obs. 224.1233.

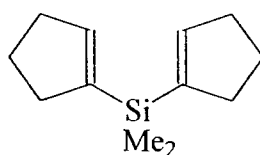
**Triisopropylbenzenesulphonylhydrazide (200)**



**(200)**

Hydrazine hydrate (20.4g, 0.44moles) was added dropwise to a solution of triisopropylbenzenesulphonyl chloride (60.6g, 0.2mol) in THF (250ml), cooled to -10°C. The resulting solution was stirred for 2h at 0°C before H<sub>2</sub>O (4.2ml) was added to dissolve any precipitate. The lower aqueous layer was washed with ether (3x30ml) before being discarded. The upper product layer was then washed with ice-cold brine (3x30ml) before being dried over Na<sub>2</sub>SO<sub>4</sub> for 3h. The solution was then filtered and concentrated below rt. The crude product was then slurried in petrol (30-40°C, 200ml) and then filtered and washed with petrol (30-40°C, 3x40ml). The crude solid was triturated with ice-cold water (3x200ml) to give wet hydrazide (**200**) which was dried over P<sub>2</sub>O<sub>5</sub> to constant mass, (57.8g, 96% yield); m.p. 118-120°C,  $\delta_{\text{H}}$  (200MHz) 7.48 (1H, s, Ar), 7.41 (1H, s, Ar), 4.34 (2H, m, CHMe<sub>2</sub>), 3.66 (3H, bs, NHNH<sub>2</sub>), 3.12 (1H, heptet J= 6.7Hz, CHMe<sub>2</sub>), 1.57 (18H, d J=6.7Hz, CH<sub>3</sub>CH).

### Dicyclopentenyl dimethylsilane (203)

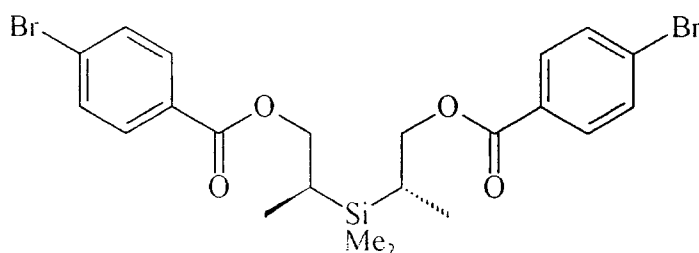


**(203)**

Cyclopentanone (8.42ml, 0.10mol) was added to a stirred suspension of hydrazide (**200**) (29.8g, 0.10 mol) in methanol (100 ml). Concentrated hydrochloric acid (1ml) was then added and the mixture cleared rapidly, after which a fine granular product began to crystallise. The reaction mixture was chilled overnight and filtered. The product was washed with cold methanol (3x25ml) and dried at room temperature at 0.5 mbar to yield cyclopentyl-2,4,6-triisopropylbenzenesulphonylhydrazone (**202**) as white crystals (30g, 81%);  $\delta_{\text{H}}$  (200Mhz) 7.26 (1H, s, Ar), 7.17 (1H, s, Ar), 4.23 (2H, hep J=6.8Hz, CHMe<sub>2</sub>), 2.91 (1H, hep J=6.8Hz, CHMe<sub>2</sub>), 2.34 (2H, t J=6Hz CH<sub>2</sub>C=N), 2.13 (2H, t J=6Hz, CH<sub>2</sub>C=N), 1.9-1.6 (4H, m, CH<sub>2</sub>CH<sub>2</sub>), 1.26 (12H, d J=6.8Hz, (CH<sub>3</sub>)<sub>2</sub>CH), 1.25 (6H, d J=6.8Hz, (CH<sub>3</sub>)<sub>2</sub>CH).

A solution of *n*-BuLi (1.6M, 94ml, 151mmol) in hexane (60ml) was added dropwise to a stirred solution of cyclopentyl-2,4,6-triisopropylbenzenesulphonylhydrazone (19g, 0.06 mol) (202) in hexane (100ml) and TMEDA (100ml) at -78°C. The resulting yellow mixture was allowed to warm to 0°C, during which time a gas (N<sub>2</sub>) evolved and the solution turned orange. Dichlorodimethylsilane (3.6ml, 30mmol) was immediately added dropwise, and the resulting mixture allowed to stir for 1h. Water was then added and the aqueous layer extracted with ether (3x25ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Distillation afforded crude dicyclopentenyldimethylsilane (203) as a yellow oil (2.5g, 43%) (bp. 180°C/9mmHg).  $\nu_{\max}$  (thin film) 3028 (C=CH), 2960, 2842 (CH<sub>2</sub>), 1254 (SiCH<sub>3</sub>)cm<sup>-1</sup>;  $\delta_{11}$  (250 MHz) 6.38 (2H, t J=7.6 Hz, 2(CH=CH<sub>2</sub>)), 2.36 (4H, t J=6.2 Hz 2(CCH<sub>2</sub>-CH<sub>2</sub>)) 1.82 (4H m 2(CH<sub>2</sub>-CH=) 0.04 (6H s SiMe<sub>2</sub>) (MS (EI) m/z 192 (M<sup>+</sup> 34%), 177((M-CH<sub>3</sub>)<sup>+</sup>, 100), 149 (51), 125 ((M-C<sub>5</sub>H<sub>7</sub>)<sup>+</sup>, 24).

**1,5-di- (4-bromobenzoyloxy) 2,3,3,4-tetramethyl-3-silapentane- (216)**<sup>78</sup>



(216)

**Experiment 1**

A solution of diisopropenyldimethylsilane (186) (0.42g, 3mmol) in hexane (5ml) was added dropwise to a stirred suspension of diisopinocampheylborane (1.85g, 6.5mmol) in hexane (15ml) at 0°C. The resulting mixture turned clear after 12h, and was then stirred for a further 6h. The resulting solution was concentrated and THF (15ml) was added to the crude material, 3M NaOH (2ml, 6mmol) and H<sub>2</sub>O<sub>2</sub> (0.68ml, 30% w/v, 6mmol) were then added at 20°C and the reaction mixture heated under reflux for a further 1h. The resulting solution was quenched with saturated potassium carbonate

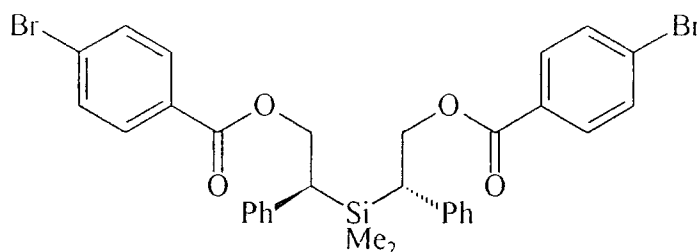
solution (15ml) and the aqueous layer extracted with ether (3x25ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated to give a yellow oil (2.9g). The yellow oil was dissolved in DCM (20ml) and added dropwise to a cooled stirred suspension of bromobenzoyl chloride (6.16g, 28mmol), DMAP (0.7g, 3.85mmol), triethylamine (5.5ml, 37mmol) and dichloromethane (40ml) at 0 °C. The resulting solution was stirred at room temperature for 5h before being quenched with distilled water (35ml) and extracted with diethyl ether (3x60ml). The combined organic layers were washed successively with water (30ml) and saturated brine (30ml), dried (MgSO<sub>4</sub>) and concentrated. Flash column chromatography, with gradient elution, (2% ether in petrol to 25% ether in petrol), afforded the diester (**216**) as a white waxy solid (1.1g, 67%), m.p. 61-64 °C (lit.<sup>78</sup> m.p. 62-64 °C); [ $\alpha$ ]<sub>D</sub> +7.0 (c=5, CHCl<sub>3</sub>) (*de*=26%, *ee*=70%);  $\nu_{\text{max}}$  (CDCl<sub>3</sub>) 2955, 2872, 1718 (C=O), 1273 (Si-Me), 1105 (C-O) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 7.90-7.55 (8H, m, Ar), 4.50 (1.3H, dd J = 11.0Hz, 4.5 Hz, HCHOC=O) (*anti*), 4.49 (0.7H, dd J = 11.0, 4.2 Hz, HCHOC=O) (*syn*), 4.25 (1.3H, dd J = 11.0, 10.0Hz, CHHOC=O) (*anti*), 4.24 (0.7H, dd J = 11.0, 10.0Hz, CHHOC=O) (*syn*), 1.42 (2H, m, SiCHCH<sub>3</sub>) (*syn* and *anti*), 1.15 (2.1H, d J = 7.2, CHCH<sub>3</sub>) (*syn*), 1.14 (3.9H, d, J 7.6, CHCH<sub>3</sub>) (*anti*), 0.12 (1H, s, SiMe<sub>2</sub>) (*syn*), 0.11 (4H, s, SiMe<sub>2</sub>) (*anti*), 0.10 (1H, s, SiMe<sub>2</sub>) (*syn*);  $\delta_{\text{C}}$  (125MHz) 166.1 (C=O), 131.7 (Ar), 131.0 (Ar), 129.3 (Ar), 127.9 (Ar), 68.5 (CH<sub>2</sub>O), 19.2 (CHCH<sub>3</sub>), 12.4 (CH<sub>3</sub>CH) (*anti*), 12.36 (CH<sub>3</sub>CH) (*syn*), -6.24 (SiMe<sub>2</sub>) (*syn*), 6.38 (*anti*) (SiMe<sub>2</sub>); MS (CI) (<sup>79</sup>Br) *m/z* 558 (MNH<sub>4</sub><sup>+</sup>, 1.9%), 299 (MH<sup>+</sup>-BrArCO<sub>2</sub>CH<sub>2</sub>CHCH<sub>3</sub>, 36%); HRMS *m/z* M<sup>+</sup> for C<sub>22</sub>H<sub>26</sub>Br<sub>2</sub>O<sub>4</sub>Si calc. 539.9968; obs. 539.9968.

## Experiment 2

A solution of diisopropenyldimethylsilane (**186**) (0.42g, 3mmol) in hexane (5ml) was added to a stirred suspension of diisopinocampheylborane (1.85g, 6mmol) in hexane (15ml) at 0 °C. The resulting solution turned clear in 12h but was left to stir at room temperature for 3 days. The solvent was removed under reduced pressure and fresh hexane (10ml) was added. A solution of BMS (10M in hexane, 0.3ml, 3mmol) was added dropwise to the stirred reaction mixture at 20 °C and the reaction was heated under reflux for 3 h. Oxidation and esterification as above afforded 1,5-di-(4-

bromobenzoyloxy)-2,3,3,4-tetramethyl-3-silapentane (**216**) (1.0g, 61%) as a white solid, m.p. 61-64<sup>o</sup>C; [ $\alpha$ ]<sub>D</sub> +7.8 (c=5, CHCl<sub>3</sub>) (*de*=33%, *ee*=77%), all other data identical with that obtained from a previously isolated sample.

**1,5-Di (4-bromobenzoyloxy) 2,4-diphenyl-3,3-dimethyl-3-silapentane- (217)**<sup>78</sup>



(217)

**Experiment 1**

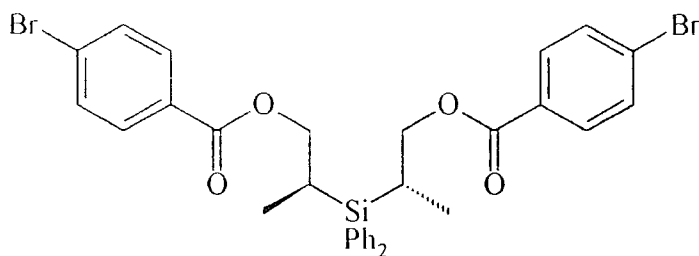
A solution of di( $\alpha$ -styryl)dimethylsilane (**159**) (0.792g, 3mmol) in hexane (3ml) was added dropwise to a stirred suspension of diisopinocampheylborane (1.70g, 6mmol) in hexane (15ml) at 0<sup>o</sup>C. The resulting mixture was left stirring at 20<sup>o</sup>C and went clear within 6 h. After a further 12h the crude mixture was concentrated in an inert atmosphere. The residue was dissolved in THF (10ml) and then methanol (2ml), 3M NaOH (2ml, 6mmol) and H<sub>2</sub>O<sub>2</sub> (0.68ml, 30% w/v, 6mmol) were added successively to the resulting solution. A gentle reflux was maintained for 1 h and the reaction mixture was cooled to rt before addition of saturated potassium carbonate solution (15ml). The aqueous layer was extracted with ether (3x15ml) and the combined organic layers were washed with brine (25ml), dried (MgSO<sub>4</sub>) and concentrated. The yellow oil was dissolved in dichloromethane (20ml) and added dropwise to a cooled stirred suspension of 4-bromobenzoyl chloride (6.16g, 28mmol), DMAP (0.7g, 3.85mmol), triethylamine (5.5ml, 37mmol) and DCM (40ml) at 0<sup>o</sup>C. The resulting solution was stirred at room temperature for 5 h before being quenched with distilled water (35ml), followed by extraction with ether (3x60ml). The combined organic layers were washed successively with water (30ml), and saturated brine (30ml), dried

(MgSO<sub>4</sub>) and concentrated. Flash column chromatography with gradient elution (2%-20% ether in petrol) afforded the diester (**217**) as a white solid (730mg, 38%); (m.p. 114-115 °C); [ $\alpha$ ]<sub>D</sub> -6.1 (c=0.19, CHCl<sub>3</sub>) (*de*=60%, *ee*=75%);  $\nu_{\text{max}}$  (CDCl<sub>3</sub>) 1752 (C=O), 1257 (Si-Me), 1180 (C-O) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 7.70-7.46 (8H, m, O<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>Br), 7.30-7.00 (10H, m, C<sub>6</sub>H<sub>5</sub>CHSi), 4.77-4.65 (4H, m, CH<sub>2</sub>OC=O), 2.82 (1.5H, dd J = 10.8, 4.8Hz, SiCHPh) (*anti*), 2.75 (0.5H, dd J=10.8, 4.8Hz, SiCHPh) (*syn*), 0.26 (0.7H, s, SiMe<sub>2</sub>) (*syn*), 0.05 (4.6H, s, SiMe<sub>2</sub>) (*anti*), -0.08 (0.7H, s, SiMe<sub>2</sub>) (*syn*);  $\delta_{\text{C}}$  (100MHz) 165.9 (C=O), 139.6 (Ar), 131.6 (Ar), 130.9 (Ar), 129.0 (Ar), 128.6 (Ar), 127.96 (Ar), 127.88 (Ar), 127.76 (Ar), 66.12 (CH<sub>2</sub>O) (*anti*), 66.04 (CH<sub>2</sub>O) (*syn*), 35.37 (CHSi) (*anti*), 35.11 (CHSi) (*syn*), -4.59 SiMe<sub>2</sub>) (*syn*), -5.00 (SiMe<sub>2</sub>) (*syn*), -5.06 (SiMe<sub>2</sub>) (*anti*); MS (CI) (<sup>79</sup>Br) *m/z* 682 (MNH<sub>4</sub><sup>+</sup>, 0.5%); Analysis found: C, 57.93%; H, 4.49%. C<sub>32</sub>H<sub>30</sub>Br<sub>2</sub>O<sub>4</sub>Si requires C, 57.84%; H, 4.25%.

## **Experiment 2**

A solution of diphenylethylenedimethylsilane (**159**) (0.792g, 3mmol) in hexane (5ml) was added to a stirred suspension of diisopinocampheylborane (1.7g, 6mmol) in hexane (15ml) at 0°C. The resulting solution turned clear in 12h but was left to stir at room temperature for 3 days. The solvent was removed under reduced pressure and fresh hexane (10ml) was added. A solution of BMS (0.3ml, 3mmol, 10M in hexane) was added dropwise to the stirred reaction mixture at 20°C and the reaction was heated under reflux for 3 h. Oxidation and esterification as above afforded 1,5-di-(4-bromobenzoyloxy)-2,4-diphenyl-3,3-dimethylsilapentane (**217**) as a white solid (1.19g, 60%); m.p. (113-115°C); [ $\alpha$ ]<sub>D</sub> -6.3 (c=0.19, CHCl<sub>3</sub>) (*de*=59%, *ee*=75%), all other data in agreement with that obtained previously.

**1,5-di-(4-bromobenzoyloxy) 2,4-dimethyl-3,3-diphenyl-3-silapentane (218)**



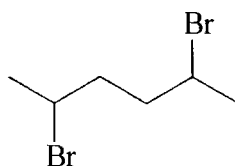
(218)

Diisopropenyldiphenylsilane (**187**) (0.264g, 1mmol) in hexane (5ml) was added to a solution of diisopinocampheylborane (0.6g, 2mmol) in hexane (15ml) at 0°C. The reaction mixture was stirred at rt for 18 h prior to removal of solvent under vacuum. THF (15ml), 3M NaOH (2ml, 6mmol) and H<sub>2</sub>O<sub>2</sub> (0.7ml, 30% w/v, 6mmol) were then added and the solution heated under reflux for 1 h. The reaction was then quenched with saturated potassium carbonate solution (20ml), extracted into ethyl acetate (3x25ml), dried (K<sub>2</sub>CO<sub>3</sub>) and concentrated. The crude diol (0.3g) was dissolved immediately in DCM (5ml) and added to a solution of 4-bromobenzoyl chloride (6.45g, 3mmol) triethylamine (2ml) and DMAP (0.2g, 1.6mmol) in DCM (30ml) at 0°C. The mixture was stirred at rt for 18 h, quenched with water (20ml), extracted into ethyl acetate (3x25ml) washed with brine (20ml) and dried (MgSO<sub>4</sub>). Concentration and flash column chromatography eluting with 5% ethyl acetate in petrol afforded the diester (**218**) as a white crystalline solid (290mg, 49%); (m.p. 46-48°C); [ $\alpha$ ]<sub>D</sub>-8.5 (c=0.2, CHCl<sub>3</sub>) (*de* = 70%, *ee* = 92%);  $\nu_{\max}$  (CHCl<sub>3</sub>) 1712 (C=O), 1485 (SiPh), 1398, 1272, 1012 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 7.4-7.7 (18H, m, Ar), 4.5 (2H, dd, J = 3.0, 5.4Hz, HCHO), 4.05 (2H, t J = 10Hz, HCHO), 2.20 (2H, m, CHCH<sub>3</sub>), 1.17 (1.8H, d J = 5.4Hz, CH<sub>3</sub>CH) (*syn*), 1.16 (4.2H, d J = 5.4Hz, CH<sub>3</sub>CH) (*anti*);  $\delta_{\text{C}}$  (100MHz) 165.8 (C=O), 137 (Ar), 131.5 (Ar), 131.0 (Ar), 130.7 (Ar), 129.9 (Ar), 129.0 (Ar), 128.2 (Ar), 127.8 (Ar), 68.0 (CH<sub>2</sub>O), 16.7 (CHCH<sub>3</sub>) (*syn*), 16.6 (CHCH<sub>3</sub>) (*anti*), 11.65 (CH<sub>3</sub>CH) (*syn*), 11.6 (CH<sub>3</sub>CH) (*anti*);  $\delta_{\text{Si}}$  (99MHz) -4.21; MS (CI) *m/z* 503 (M<sup>+</sup>-Br, 12%); Analysis found: C, 57.93%; H, 4.49%. C<sub>32</sub>H<sub>30</sub>Br<sub>2</sub>O<sub>4</sub>Si requires C, 57.84%; H, 4.25%.



viscous oily material which was dissolved in THF (15ml) and 3M NaOH (2ml, 6mmol) and H<sub>2</sub>O<sub>2</sub> (0.7ml, 30% w/v, 6mmol) were added sequentially. A gentle reflux was maintained for 1 h before quenching the reaction with saturated aqueous potassium carbonate solution (15ml), followed by extracting the aqueous layer with ether (3x25ml). The combined organic layers were washed with saturated brine (20ml), dried (MgSO<sub>4</sub>) and concentrated. The yellow oil thus obtained was dissolved in DCM (20ml) and added dropwise to a cooled stirred suspension of 4-bromobenzoyl chloride (2.1g, 10mmol), DMAP (0.24g, 2mmol), triethylamine (2ml, 15mmol) in DCM (20ml) at 0°C. The resulting solution was stirred at room temperature for 5 h before work-up with distilled water (35ml) and extraction into ether (3x20ml). The combined organic layers were washed successively with water (30ml) and saturated brine (30ml), dried (MgSO<sub>4</sub>) and concentrated. Flash column chromatography by gradient elution (4%-8% diethyl ether in petrol) gave the diester (**219**) as a colourless oil (150mg, 20%) as a mixture of isomers (63:36);  $\nu_{\max}$  (thin film) 1251 (SiCH<sub>3</sub>) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200MHz) 7.65 (8H, dd  $J = 8.0, 108\text{Hz}$ , Ar), 5.07 (1H, t  $J = 7.2\text{Hz}$ , CH<sub>2</sub>CHO), 1.8 (4H, m, CH<sub>3</sub>CH<sub>2</sub>CH), 0.94 (6H, t,  $J = 7.2\text{Hz}$ , CH<sub>3</sub>CH<sub>2</sub>) 0.19 (6H, s, SiMe<sub>2</sub>);  $\delta_{\text{C}}$  (100MHz) 165.9 (C=O), 131.7 (Ar), 130.9 (Ar), 129.2 (Ar), 127.8 (Ar), 69.5 (CHO), 24.4 (CH<sub>2</sub>CH), 11.7 (CH<sub>3</sub>CH<sub>2</sub>), -6.2 (SiMe<sub>2</sub>), -6.4 (SiMe<sub>2</sub>), -6.7 (SiMe<sub>2</sub>); MS (EI) (<sup>79</sup>Br)  $m/z$  301 and 299 (M<sup>+</sup>-ArCO<sub>2</sub>CHCH<sub>2</sub>CH<sub>3</sub>).

### **2,5-Dibromohexane (253)**<sup>130</sup>

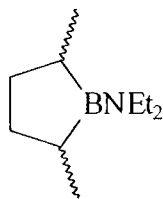


**(253)**

Phosphorus tribromide (1272g, 4.86 moles) was added dropwise to a three-necked flask containing 2,5-hexanediol (261ml, 2.12 moles) at -5°C to 5°C. The dropping funnel was replaced with a reflux condenser and the reaction mixture was allowed to warm to 20°C overnight. The resulting solution was then heated for 1 h on a steam bath, allowed to cool and ice (2kg) poured into the reaction mixture. This was then washed successively with water, 96% sulphuric acid, water, sodium bicarbonate

solution and water. The combined organic layers were dried and filtered. Distillation afforded 2,5-dibromohexane (**253**) as a colourless oil (343.6g, 67%), bp. 95-98°C/19mbar (lit.<sup>130</sup> b.p. 98-100°C/25mbar);  $\delta_{\text{H}}$  (250 MHz) 4.23 (2H, m, CHBr), 1.97 (4H, m, CH<sub>2</sub>CH<sub>2</sub>), 1.73 (6H, d, J = 6.5Hz, CH<sub>3</sub>).

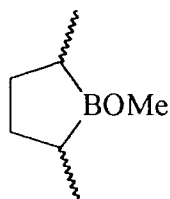
**2,5-Dimethylborolane-1-diethylamine (254)**<sup>92</sup>



(254)

Dibromoethane (11g, 50mmol) was added dropwise to a stirred suspension of magnesium (88g, 3.6 moles) in THF (50ml). This activated the magnesium turnings and the resulting brown solution was removed by cannular filtration and fresh THF (300ml) was added. A solution of 2,5-dibromohexane (**253**) (244g, 1mol) was added at a rate sufficient to maintain an internal temperature between 30-34°C. The resulting mixture was stirred overnight, filtered through glass wool under a positive pressure of nitrogen and titrated against 1.0 M *sec*-butanol and phenanthralene indicator. Several titrations indicated a mean concentration of 0.4 M, corresponding to a 28% yield. Freshly prepared dichloroborane diethylamine<sup>92</sup> (63g, 0.41 moles) in ether (500ml) was added dropwise to the di-Grignard-THF solution at -78°C. The resulting suspension was allowed to warm to room temperature overnight. The solids were allowed to settle and the supernatant liquid removed by cannular filtration. The solids were washed with pentane and the supernatants concentrated by fractional distillation. The resulting residue was vacuum-transferred at 120°C and distillation at reduced pressure gave the diethylaminoborolane (**254**) as a mixture of stereoisomers (10g, 15%), bp. 78-82°C/15mbar (lit.<sup>92</sup> b.p. 79-82°C/20mbar);  $\delta_{\text{H}}$  (400MHz); 3.0-3.2 (4H, m, (CH<sub>2</sub>N)); 1.3-1.2 (6H, m, CH<sub>3</sub>CH<sub>2</sub>N), 1.06 (4H, dt J=1.6, 7.4Hz, CH<sub>2</sub>CH), 0.835 (3H, d J =10Hz, CH<sub>3</sub>CH), 0.95 (2H, d J =8.0Hz, CH<sub>3</sub>CH).

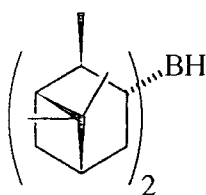
### 2,5-Dimethyl-1-methoxyborolane (255)<sup>92</sup>



(255)

Ethereal HCl (1M, 17.9ml, 61mmol) was added dropwise to a stirred solution of aminoborolane (254) (10g, 60mmol) and methanol (3.18ml, 78mmol) in pentane (100ml). A white precipitate formed during the addition and the reaction was left stirring overnight. The supernatant liquid was removed by cannular filtration and the precipitate washed with pentane. The combined washings were distilled to remove solvent and fractionally distilled to afford the methoxyborolane (255) as a colourless oil (2g, 27%), bp.48-52°C/35mbar, (lit.<sup>92</sup> 47-50°C/35mbar);  $\delta_{\text{H}}$  (200MHz) 3.8 (3H, s, OCH<sub>3</sub>), 1.7-2.1 (4H, m, CHCH<sub>2</sub>CH<sub>2</sub>CH), 1.0-1.2 (2H, m, CHCH<sub>3</sub>), 0.9 (6H, br.s, CH<sub>3</sub>CH);  $\delta_{\text{B}}$  (125MHz) 54.08. The diethylaminoborolane (254) (2g, 20%) was also recovered.

### Diisopinocampheylborane (Ipc<sub>2</sub>BH) (208)



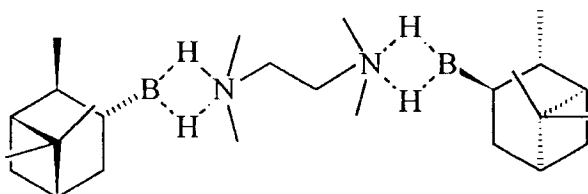
(208)

A solution of BMS (10M in hexane, 5.05ml, 55mmol) in THF (15ml) was cooled to 0°C with ice. ( $\alpha$ )-(-)-Pinene ( $[\alpha]_{\text{D}}$  -42.1°, 84%ee) (15.9ml, 100mmol) was added dropwise and the suspension allowed to stir under nitrogen for 3 hours. A mixture of BMS and THF was then removed at 0°C/30mbar. The reaction flask was then

brought back to atmospheric pressure with nitrogen. More of the  $\alpha$ -pinene (2.38ml, 15mmol) and THF (18ml) were added and the mixture allowed to equilibrate at 0°C for 3 days to give  $\text{Ipc}_2\text{BH}$  (**208**) as a white solid. This was used directly as a suspension in THF.

Oxidation of a sample by refluxing with NaOH and  $\text{H}_2\text{O}_2$  gave isopinocampheol with a m.p. 54.6-56.8°C and  $[\alpha]_{\text{D}} +34.66^\circ$  (c10, benzene) corresponding to 96%ee.

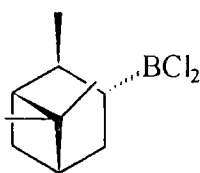
### Monoisopinocampheylborane-TMEDA complex (250)<sup>107</sup>



(250)

$\alpha$ -(+)-Pinene (36.5ml, 230mmol, 87%ee) was added to a solution of BMS (9.5ml, 100mmol) in ether (65ml) at a steady rate to maintain a gentle reflux. The reaction was held at reflux temperature for 0.5 h prior to the addition of TMEDA (7.5ml, 50mmol). The mixture was allowed to reflux for a further 30 min during which time a  $\text{TMEDA}(\text{IpcBH}_2)_2$  complex precipitated as a white solid. The flask was left in the freezer (-20°C) overnight and the supernatant removed by filtration of the cold solution. The white air stable crystals were left to dry under vacuum for 1h at 1mbar to yield the borane (**250**) (12.15g, 69%), m.p. 136°C (lit.<sup>107</sup> m.p. 140°C);  $[\alpha]_{\text{D}} -64.5$  (95%ee);  $\delta_{\text{B}}$ (125MHz,  $\text{C}_6\text{D}_6$ ) 18.15.

### Isopinocampheyl dichloroborane (251)<sup>108</sup>



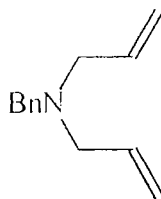
(251)

$\alpha$ -(+)-Pinene (3g, 22mmol) and  $\text{Et}_3\text{SiH}$  (2.6g, 22mmol) were added dropwise into an empty flask. Boron trichloride (1.0M in hexane, 22.05ml, 22mmol) was then added at  $-78^\circ\text{C}$  and purification by distillation afforded isopinocampheyl dichloroborane (**251**) as a colourless oil (4.5ml, 94%), b.p.  $52^\circ\text{C}/0.1\text{mbar}$  (lit.<sup>108</sup> b.p.  $52\text{-}55^\circ\text{C}/0.12\text{mbar}$ ).

### Attempted Hydrosilylation of 1,5-Hexadiene

Dichlorosilane (1.3g, 13mmol) was condensed under vacuum (0.03mbar) and added by vacuum transfer to a neat mixture of 1,5-hexadiene (1.2ml, 10mmol), (S)-MOP (10mol%) and allylpalladium chloride dimer (10mol%). The reaction was stirred at a variety of pressures at  $40^\circ\text{C}$ . After 30 min the heterogenous mixture had turned black and after a further 6 days the volatiles were removed by vacuum transfer at rt. An NMR sample was made up by the vacuum transfer at  $100^\circ\text{C}$  of involatiles into perdeuterated benzene. The  $^1\text{H}$  NMR indicated a strong doublet at 1.1ppm indicative of an internally silylated double bond.

### Benzyldiallylamine (281)<sup>118</sup>



(**281**)

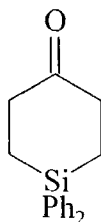
To a solution of diallylamine (1.05g, 18mmol) in water (30ml) and  $\text{NaHCO}_3$  (1.78g) at  $95^\circ\text{C}$  was added dropwise benzyl chloride (1.38g, 10mmol). The mixture was allowed to reflux for 1h. The resulting mixture was cooled, separated and the organic layer dried over  $\text{K}_2\text{CO}_3$ . Distillation afforded benzyldiallylamine (**281**) (1.34g, 67%) as

as a colourless oil, b.p. 50°C/15mbar;  $\delta_{\text{H}}$  (400MHz) 7.4-7.25 (10H, m, Ar), 5.91 (2H, ddt,  $J = 6.4, 16.8, 2.4$  Hz,  $\text{CH}=\text{CH}_2$ ), 5.19 (4H, m,  $\text{CH}=\text{CH}_2$ ) 3.6 (2H, s,  $\text{CH}_2\text{Ph}$ ), 3.1 (4H, d,  $J = 6.4$ Hz,  $\text{BnNCH}_2$ );  $\delta_{\text{C}}$  (100MHz) 139.4, 135.8, 128.9, 128.1, 126.8, 117.4, 57.5, 56.4.

### Zirconocene Cyclisation of Benzyldiallylamine

*n*-BuLi (1.6M, 1.25ml, 2mmol) was added dropwise to a solution of zirconocene dichloride (0.29g, 1mmol) in THF (10ml) held at -78°C. After 1h at -78°C benzyldiallylamine (0.19g, 1mmol) was added and the reaction allowed to reach rt. After a further 1h the reaction was cooled back to -78°C and dichlorodiphenylsilane (0.252g, 1mmol) was added. The reaction left to stir at rt for 72h, by which time TLC eluting with 4:1 iso-hexane/ethyl acetate showed evidence of at least nine different products.

### 4,4-Diphenylsilacyclohexan-1-one (225)<sup>99</sup>

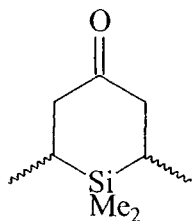


(225)

9-BBN (1.0M in hexane, 20ml, 20mmol) was added dropwise to a stirred solution of divinylidiphenylsilane (**224**) (2.36g, 10mmol) in hexane (15ml), and the mixture was refluxed for 2 h. After cooling to rt, BMS (0.95ml, 10mmol) was added dropwise and the reaction allowed to reflux for a further 1h. After cooling to rt, methanol (35ml) was added and the reaction was allowed to stir at rt for 15h, solvent was then removed under vacuum (0.1mbar/35°C) and THF (30ml) was added. The solution was cooled to 0°C and DCME (0.9ml, 10mmol) was added dropwise. A solution of lithium *t*-butoxide was added [prepared from THF (20ml), 1.6M BuLi (31.2ml, in 50mmol),

and <sup>t</sup>BuOH (4.7ml, 50 mmol), at 0°C for 30 mins then rt for addition]. After 30min at rt, ethanol (12ml) water (3.5ml), NaOH (1.2g, 30mmol) and H<sub>2</sub>O<sub>2</sub> (3.3ml, 30% w/v, 30mmol) were added to the reaction mixture which was heated under reflux for 3h. The mixture was quenched with water (100ml) and extracted into ethyl acetate (3x50ml). The combined organic layers were washed with brine (40ml), dried (MgSO<sub>4</sub>) and concentrated. Purification by flash column chromatography with gradient elution (5-10% ethyl acetate in hexane), afforded 4,4-diphenylsilacyclohexan-1-one (**225**) as a white crystalline solid (1.5g, 56%), m.p. 90-92°C,  $\nu_{\max}$  (CDCl<sub>3</sub>) 1701 (C=O), 1116, 932 (SiPh), 891, 761 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 7.3-7.6 (10H, m, Ar), 1.65 (4H, dt J = 3.5, 5.9Hz, CH<sub>2</sub>CH<sub>2</sub>), 1.54 (4H, dt J = 7.0, 10Hz, CH<sub>2</sub>Si);  $\delta_{\text{C}}$  (100MHz) 214.0 (C=O), 134.2 (Ar), 130.1 (Ar), 129.9 (Ar), 128.2 (Ar), 38.0 (CH<sub>2</sub>CO), 9.0 (CH<sub>2</sub>Si); MS (EI) m/z 266(M<sup>+</sup>, 100%), 237(M<sup>+</sup>-CHO, 18%), 188(M<sup>+</sup>-Ph, 52%), 182(SiPh<sub>2</sub>, 58%), 105(SiPh, 62%).

### 3,4,4,5-Tetramethyl-4-silacyclohexan-1-one (223)<sup>77</sup>



(223)

#### Experiment 1

A solution of diisopropenyldimethylsilane (**186**) (1.26g, 9mmol) in THF (40ml) was added at rt to 9-BBN (1.0M solution in hexanes, 20ml, 20mmol). The reaction was heated under reflux for 2h before cooling to rt. BMS (1ml, 10mmol) was then added and the solution was heated under reflux for a further 1h. After cooling to rt, methanol (3.5ml) was added dropwise and the reaction stirred at rt for a further 18h. The solution was then cooled to 0°C and DCME (0.8ml, 10mmol) followed by LiO<sup>t</sup>Bu [prepared from *n*-BuLi (1.6M, 28ml, 45mmol) and <sup>t</sup>BuOH (3.5ml, 45mmol) in THF

(50ml)] were added sequentially. The resulting solution was stirred at rt for 20 mins before ethanol (10ml), H<sub>2</sub>O (10ml), NaOH (1.2g, 30mmol), and H<sub>2</sub>O<sub>2</sub> (1.1ml, 27.5% w/v, 30mmol) were added sequentially. The reaction mixture was then heated under reflux for a further 18h, cooled to rt, quenched with water (40ml), and extracted into ethyl acetate (3x25ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Flash column chromatography eluting with 5% ether in petrol gave the ketone (**223**) as a colourless oil (30mg, 20%), b.p. 60°C/2.4mbar (lit.<sup>77</sup> b.p. 111-113°C/20mbar);  $\nu_{\text{max}}$  (thin film) 1698 (C=O), 1251 (SiMe) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 2.6-2.4 (4H, m, CH<sub>2</sub>C=O), 1.3-1.2 (2H, m, CHCH<sub>3</sub>), 1.0 (6H, d, J=3.2Hz CH<sub>3</sub>CH), 0.1 (3H, s, SiMe<sub>2</sub>) 0.07 (1.5H, s, SiMe<sub>2</sub>) 0.05 (1.5H, s, SiMe<sub>2</sub>);  $\delta_{\text{C}}$  (100MHz) 213 (C=O), 48 (CHCO), 20 (CH<sub>3</sub>), 18 (CHCH<sub>3</sub>), -4.0 (SiMe<sub>2</sub>).  $\delta_{\text{Si}}$  (99MHz) 3.49; MS (CI) *m/z* 188 (MNH<sub>4</sub><sup>+</sup>, 94%), 171 (MH<sup>+</sup>, 100%) 156 (MH<sup>+</sup>-CH<sub>3</sub>, 12%); HRMS *m/z* MNH<sub>4</sub><sup>+</sup> for C<sub>9</sub>H<sub>22</sub>ONSi calc. 188.14705; obs. 188.1471.

### Experiment 2

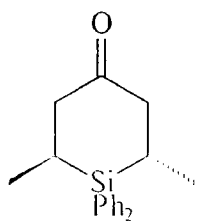
Freshly prepared thexylborane (0.5M in THF, 20ml, 10mmol) was added dropwise to a solution of diisopropenyldimethylsilane (**186**) (1.4g, 10mmol) in THF (10ml). The reaction was heated under reflux for 3 h before cooling to rt. Potassium cyanide was added (0.65g, 10mmol) and the reaction was cooled to -78°C. The reaction was allowed to stir at rt for 18 h before 3M sodium hydroxide (7ml, 21mmol) and hydrogen peroxide (4.5ml, 30%, 45mmol) were added and the solution heated under reflux for 1 h. The reaction was quenched with water, extracted into ether (3x25ml) and the combined organic layers dried (MgSO<sub>4</sub>). Purification by distillation (bp.111-113°C/16mbar) and flash column chromatography eluting with 5% ethyl acetate in petrol afforded the dimethylsilacyclohexan-1-one (**223**) as a colourless oil (300mg, 18%); all data were in agreement to that obtained previously.

### Experiment 3

Diisopropenyldimethylsilane (**186**) (3.1g, 22.5mmol) was added dropwise to a stirred suspension of freshly prepared diisopinocampheylborane (28.5g, 0.1mol,) in pentane (50ml) at 0°C. The suspension was stirred at rt for 3 days by which time the

diisopinocampheylborane had been consumed and the reaction had become clear. The pentane was removed by under vacuum and hexane (50ml) was added. BMS (2.3ml, 23mmol) was then added and the reaction heated under reflux for a further 3h. After cooling to rt, methanol (3ml, 0.1mol) was added dropwise and the reaction stirred for a further 18h at rt. The solvent was removed under vacuum (35°C/0.1mbar), THF (40ml) was added and the reaction was cooled to 0°C. DCME (9ml, 100mmol) was added dropwise followed by a solution of lithium *t*-butoxide [prepared as follows: *n*-BuLi (1.6M, 80ml, 110mmol) was added to *t*-butanol (11ml, 150mmol) and THF (35ml) at 0°C and allowed to stir at 0°C for 30 min before warming to rt for addition to reaction mixture]. After 30 min at rt, ethanol (12ml) water (3.5ml), NaOH (5g, 100mmol) and H<sub>2</sub>O<sub>2</sub> (10ml, 30% w/v, 90mmol) were added to the reaction mixture which was heated under reflux for a further 3h. The reaction was quenched with water (100ml) and extracted into ethyl acetate (3x50ml). The combined organic layers were washed with brine (20ml), dried (MgSO<sub>4</sub>) and concentrated. Purification by flash column chromatography eluting 4% ethyl acetate in petrol gave the ketone (**223**) as a colourless oil (0.89g, 24%), b.p. 60°C/2.4mbar, [ $\alpha$ ]<sub>D</sub> -8.0 (c=0.025, CDCl<sub>3</sub>) (*de*=12%);  $\delta$ <sub>H</sub> (400MHz) 2.6-2.4 (4H, m, CH<sub>2</sub>C=OCH<sub>2</sub>), 1.3-1.2 (2H, m, CHCH<sub>3</sub>), 1.0 (6H, d, J= 3.2Hz CH<sub>3</sub>CH), 0.1 (3.36H, s, SiMe<sub>2</sub>), 0.07 (1.27H, s, SiMe<sub>2</sub>), 0.05 (1.34H, s, SiMe<sub>2</sub>);  $\delta$ <sub>C</sub> (125MHz) 213.4 (C=O) (*syn*), 213 (C=O) (*anti*), 48.0 (CHCO) (*syn*), 47.7 (CHCO) (*anti*), 19.0 (CHCH<sub>3</sub>) (*syn*), 16.9 (CHCH<sub>3</sub>) (*anti*), 16.0 (CH<sub>3</sub>) (*syn*), 15.6 (CH<sub>3</sub>) (*anti*), -6.0 (SiMe<sub>2</sub>) (*syn*), -7.0 (SiMe<sub>2</sub>) (*anti*), -11.0 (SiMe<sub>2</sub>) (*syn*); all other data in agreement with that obtained previously.

### 3,5-Dimethyl-4,4-diphenylsilacyclohexan-1-one (226)



(226)

#### Experiment 1

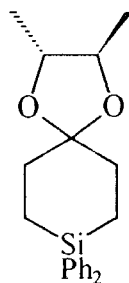
A solution of diisopropenyldiphenylsilane (**187**) (2.0g, 7.8mmol) in hexane (10ml) was added to a suspension of diisopinocampheylborane (7.9g, 27.7mmol) in hexane (20ml) at rt. The reaction was heated under reflux for 2 h, then cooled and BMS (0.8ml, 8mmol) was added at rt. The resulting solution was heated under reflux for 1 h and the reaction was then cooled to rt and methanol (3ml) was added dropwise. The reaction was stirred at rt for 18 h before the solvent was removed under vacuum (35°C/0.1mbar) and THF (20ml) was added. The resulting solution was cooled to 0°C before DCME (0.65ml, 7.5mmol) and a solution of LiO<sup>t</sup>Bu [prepared from THF 20ml, 1.6M BuLi (30ml, 48mmol), <sup>t</sup>BuOH (3.5ml, 45mmol) formed at 0°C before warming to rt. after 30 mins] were added and the reaction stirred at rt for 20 min. Ethanol (15ml), H<sub>2</sub>O (5ml), NaOH (1.5g, 37mmol) and H<sub>2</sub>O<sub>2</sub> (3.8ml, 30% w/v, 37mmol) were then added sequentially and the solution heated under reflux for 18h. The resulting solution was quenched with water (25ml) and extracted into ethyl acetate (3x25ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Purification by flash column chromatography eluting with 4% ethyl acetate in petrol gave ketone (**226**) as a waxy solid (0.775g, 35%); (*de*=70%). Crystallisation from hexane afforded ketone (**226**) as a white crystalline solid; [ $\alpha$ ]<sub>D</sub> -36.0 (*c*=0.1 CHCl<sub>3</sub>) (*de*=85%), m.p. 61-64°C;  $\nu_{\max}$  (CHCl<sub>3</sub>) 1705 (C=O), 1427 (SiPh), 1263, 1112, 701 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 7.36-7.6 (10H, m, Ar), 2.7 (2H, dd *J* = 4.8, 14.0Hz, HCHCHCH<sub>3</sub>), 2.49 (2H, dd, *J* = 11.2, 14.0Hz, HCHCHCH<sub>3</sub>), 1.95 (2H, m, CHCH<sub>3</sub>), 1.12 (0.6H, d *J* = 7.6Hz, CH<sub>3</sub>CH) (*syn*), 1.05 (5.4H, d, *J* = 7.6Hz, CH<sub>3</sub>CH) (*anti*);  $\delta_{\text{C}}$  (100MHz) 212.7 (C=O) (*anti*), 212.5 (C=O) (*syn*), 136.4 (Ar) (*syn*) 135.7 (Ar) (*anti*), 135.1 (Ar) (*anti*), 132.2 (Ar) (*syn*), 129.9 (Ar)

(*anti*), 129.9 (**Ar**) (*syn*), 128.1 (**Ar**) (*anti*), 128.0 (**Ar**) (*syn*), 48.7 (CH<sub>2</sub>CO) (*syn*), 47.8 (CH<sub>2</sub>CO) (*anti*), 18.72 (CHSi) (*syn*), 16.64 (CHSi) (*anti*), 16.4 (CH<sub>3</sub>) (*syn*), 14.7 (CH<sub>3</sub>) (*anti*);  $\delta_{\text{Si}}$  (99MHz; CDCl<sub>3</sub>) -7.55 (*anti*), -9.3 (*syn*); MS (CI) *m/z* 312 (MNH<sub>4</sub><sup>+</sup>, 100%), 295 (M<sup>+</sup>-CH<sub>3</sub>, 3.85%), 253 (M<sup>+</sup>-C(O)C<sub>3</sub>H<sub>6</sub>, 10%), 216 (M-Ph, 24%); HRMS (EI) *m/z* MNH<sub>4</sub><sup>+</sup> for C<sub>19</sub>H<sub>22</sub>OSi calc. 312.1784 ; obs. 312.1784.

## **Experiment 2**

A solution of diisopropenyldiphenylsilane (**187**) (4.1g, 15.2mmol) in hexane (5ml) was added dropwise to a suspension of 9-BBN dimer (4.88g, 20mmol) in hexane (15ml) and the reaction was heated under reflux for 15h. The resulting solution was cooled to rt and BMS (1.5ml, 15mmol) was added. The solution was heated under reflux for a further 3h before cooling to rt again. A white solid precipitated on cooling and the supernatant liquid was removed by filtration. Methanol (3ml) was added to the supernatant and the reaction was stirred at rt for 15h. Solvent was removed under vacuum (35°C/0.1mbar) and THF (45ml) added. DCME (1.3ml, 60mmol) was then added to the reaction at 0°C followed by a solution of LiO<sup>t</sup>Bu [prepared from *n*-BuLi (1.6M, 46ml, 75mmol) was added to *t*-BuOH (7.1ml, 75mmol) in THF (45ml) at 0°C and allowed to stir at 0°C for 30 min before warming to rt for addition to reaction mixture]. After 30min at rt ethanol (9ml), water (3.5ml), NaOH (2g, 40mmol) and H<sub>2</sub>O<sub>2</sub> (5ml, 30% w/v, 45mmol) were added to the reaction mixture which was heated under reflux for a further 3h. The reaction was quenched with water (60ml) and extracted into ethyl acetate (3x30ml). The combined organic layers were washed with brine (10ml), dried (MgSO<sub>4</sub>) and concentrated. Purification by flash column chromatography eluting with 8% ethyl acetate in petrol afforded the ketone (**226**) as a white crystalline solid (2.11g, 47%). All physical data were in agreement with that shown above.

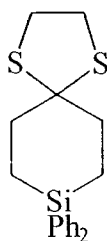
**8,8-Diphenyl-8-sila-1,4-dioxaspiro[4.5]decane (289)**



**(289)**

BF<sub>3</sub>.OEt<sub>2</sub> (0.04ml, 0.44mmol) was added to a stirred solution of (2*R*,3*R*)-Butanediol (34.2mg, 0.38mmol) and silacyclohexanone (**225**) (100mg, 0.38mmol) in DCM (10ml) at -78°C. The reaction was stirred for 1h at -78°C and then allowed to reach rt. The reaction was monitored by TLC for completion (6h). The reaction was quenched with saturated potassium carbonate solution (15ml), extracted into DCM (3x10ml), dried (MgSO<sub>4</sub>) and concentrated. Flash column chromatography eluting with hexane gave the acetal (**289**) as a waxy solid (55mg, 44%); m.p. 100-102°C;  $\nu_{\max}$  1410 (SiPh), 1104 (C-O) cm<sup>-1</sup>;  $\delta_{\text{H}}$  (269MHz) 7.6-7.3 (10H, m, Ar), 3.65 (2H, m, CH<sub>3</sub>CHO), 1.93 (4H, t J = 5.3Hz, CH<sub>2</sub>C), 1.32 (4H, t J = 5.3Hz, CH<sub>2</sub>Si), 1.24 (6H, d J = 5.7Hz, CH<sub>3</sub>CHO);  $\delta_{\text{C}}$  (62MHz) 135.5 (Ar), 134.5 (Ar), 128.1 (Ar), 128.0 (Ar), 109.5 (OCO), 78.1 (CHO), 34.0 (CH<sub>2</sub>C), 17.0 (CH<sub>3</sub>), 8.0 (CH<sub>2</sub>Si); MS (EI) *m/z* 261 (M<sup>+</sup>Ph, 100%); Analysis found: C, 74.50%; H, 7.55%. C<sub>21</sub>H<sub>26</sub>O<sub>2</sub>Si requires C, 74.51% H, 7.74%; O, 9.45%.

### **8,8-Diphenyl-8-sila-1,4-dithiaspiro[4.5]decane (286)**



**(286)**

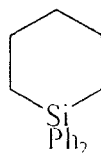
#### **Experiment 1**

BF<sub>3</sub>.OEt<sub>2</sub> (0.04ml, 0.44mmol) was added to a stirred solution of ethanedithiol (0.17ml, 2mmol) and the ketone (**225**) (500mg, 1.9ml) in DCM (10ml) over 4Å molecular sieves at rt. The reaction was stirred at rt for 48h before being quenched with saturated sodium bicarbonate (10ml) and extracted into ether (3x10ml). The combined organic layers were washed (brine), dried (MgSO<sub>4</sub>) and concentrated to afford the dithioketal (**286**) as a waxy semi-crystalline solid (500mg, 91%); mp. 105-107°C,  $\nu_{\max}$  1430, 1156, 1106, 974, 881 (SiPh<sub>2</sub>), 841 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400MHz) 7.65-7.44 (10H, m, SiPh<sub>2</sub>), 3.36 (4H, s, SCH<sub>2</sub>CH<sub>2</sub>S), 2.44 (4H, t J = 6.25Hz, CH<sub>2</sub>CCH<sub>2</sub>), 1.54 (4H, t J = 6.3Hz, CH<sub>2</sub>SiCH<sub>2</sub>),  $\delta_{\text{C}}$  (100MHz) 135.0 (Ar), 134.0 (Ar), 131.1 (Ar), 129.0 (Ar), 72.1 (SCS), 40.0 (SCH<sub>2</sub>CH<sub>2</sub>S), 38.0 (CH<sub>2</sub>SCH<sub>2</sub>), 11.0 (CH<sub>2</sub>SiCH<sub>2</sub>);  $\delta_{\text{Si}}$  (99MHz) -15.2; MS (CI) *m/z* 360 (MNH<sub>4</sub><sup>+</sup>, 0.93%), 343 (MH<sup>+</sup>, 3.7%), 342 (M<sup>+</sup>, 0.8%), 282 (M<sup>+</sup>-C<sub>2</sub>H<sub>4</sub>S, 27%), 190 (MH<sub>2</sub><sup>+</sup>-Ph<sub>2</sub>, 100%); HRMS *m/z* M<sup>+</sup> for C<sub>19</sub>H<sub>22</sub>S<sub>2</sub>Si calc. 342.0966; obs. 342.0965.

#### **Experiment 2**

BF<sub>3</sub>.OEt<sub>2</sub> (0.04ml, 0.44mmol) was added dropwise to a solution of ethanedithiol (0.06ml, 0.66mmol) and the silacycloacetal (**289**) (150mg, 0.44mmol) in DCM at rt. The reaction was stirred at rt for 18h before being quenched with saturated potassium bicarbonate solution (10ml) and extracted into ethyl acetate (3x10ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated to afford the dithioketal (**286**) as a white semi-crystalline solid (110mg, 75%); all data were identical to that obtained previously.

### 1,1-Diphenyl-1-silacyclohexane (292)<sup>131</sup>



(287)

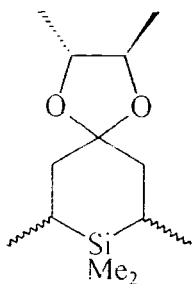
#### Experiment 1

A mixture of 2,5-dibromopentane (6.9g, 30mmol) and dichlorodiphenylsilane (7.56g, 30mmol) was added dropwise to a stirred suspension of activated magnesium (1.44g, 60mmol) in THF (30ml) in order to maintain a gentle reflux. The resulting mixture was heated under reflux for a further 1 h, before leaving to stir at 20°C for 15 h. The resulting material was poured onto ice-cold saturated aqueous ammonium chloride solution (20ml) and the aqueous layer extracted with ether (3x25ml). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. Distillation yielded diphenylsilacyclohexane (**287**) (5.67g, 75%) as a colourless oil, bp. 120°C/0.1mbar (lit.<sup>131</sup> b.p. 122°C/0.15mbar);  $\nu_{\max}$  3066 (Ar), 1112, 987, 907 (Si-Ph), 774 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200MHz) 7.45 (10H, m, Ar), 1.78 (4H, m, CH<sub>2</sub>CH<sub>2</sub>Si), 1.53 (2H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.20 (4H, t, J = 7.2Hz, SiCH<sub>2</sub>); MS (EI)  $m/z$  252 (M<sup>+</sup>, 22%), 174 (M<sup>+</sup>-Ph, 100%).

#### Experiment 2

The dithioketal (**286**) (200mg, 0.8mmol) was added to a suspension of freshly prepared Raney nickel (2g, excess) in EtOH (50ml). The suspension was refluxed for 36h before cooling back to rt and filtering through celite. Concentration afforded diphenylsilacyclohexane (**287**) (120mg, 60%) as a colourless oil;  $\nu_{\max}$  3066 (Ar), 1112, 987, 907 (Si-Ph), 774 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200MHz) 7.45 (10H, m, Ar), 1.78 (4H, m, CH<sub>2</sub>CH<sub>2</sub>Si), 1.53 (2H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.20 (4H, t, J = 7.2Hz, SiCH<sub>2</sub>).

**7,9-Dimethyl-8,8-dimethyl-8-sila-2,3-dimethyl-1,4-dioxaspira[4.5]decane (290)**

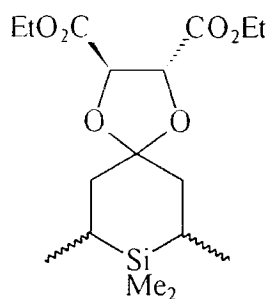


(290)

BF<sub>3</sub>·OEt<sub>2</sub> (0.04ml, 0.44mmol) was added dropwise to a stirred solution of (2*R*, 3*R*)-butanediol (90mg, 1mmol) and the ketone (**223**) (0.17g, 1mmol) in DCM (15ml) over 4Å molecular sieves at rt. The reaction was stirred at rt for 26 h with fresh molecular sieves being added after 18 h. The reaction was quenched with sodium bicarbonate (20ml), and extracted into ethyl acetate (3x25ml). The combined organic layers were washed (brine), dried (MgSO<sub>4</sub>) and concentrated. Purification by flash column chromatography eluting with 1% ethyl acetate in petrol afforded unreacted starting ketone (**223**) (29mg, 17%) and the acetal (**290**) as a colourless oil (150mg, 64%); (50:50 *cis:trans*);  $\nu_{\max}$  (thin film) 1455, 1248 (SiMe), 1105 (C-O), 833 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200MHz) 3.59 (2H, m, OCHCHO), 1.84-1.44 (4H, m, CH<sub>2</sub>CCH<sub>2</sub>), 1.21 (6H, m, CH<sub>3</sub>CHCHCH<sub>3</sub>), 0.95 (8H, m, CH<sub>3</sub>CHSiCHCH<sub>3</sub>), -0.02 (1.5H, s, SiMe<sub>2</sub>) (*syn*), -0.04 (1.5H, s, SiMe<sub>2</sub>) (*anti*), -0.05 (1.5H, s, SiMe<sub>2</sub>) (*anti*), -0.15 (1.5H, s, SiMe<sub>2</sub>) (*syn*);  $\delta_{\text{C}}$  (100MHz) 110.8 (OCO), 110.5 (OCO), 109.7 (OCO), 78.2 (OCHCHO), 77.75 (OCHCHO), 77.7 (OCHCHO), 77.6 (OCHCHO), 44.4 (CH<sub>2</sub>OCH<sub>2</sub>), 43.5 (CH<sub>2</sub>OCH<sub>2</sub>), 42.8 (CH<sub>2</sub>OCH<sub>2</sub>), 42.6 (CH<sub>2</sub>OCH<sub>2</sub>), 17.05 (CHCH<sub>3</sub>), 17.03 (CHCH<sub>3</sub>), 16.9 (CHCH<sub>3</sub>), 16.8 (CHCH<sub>3</sub>), 15.98 (CH<sub>3</sub>CHO), 15.9 (CH<sub>3</sub>CHO), 15.75 (CH<sub>3</sub>CHO), 15.4 (CH<sub>3</sub>CHO), 15.38 (CH<sub>3</sub>CHSi), 15.08 (CH<sub>3</sub>CHSi), 14.4 (CH<sub>3</sub>CHSi), 14.2 (CH<sub>3</sub>CHSi), -6.1 (SiMe<sub>2</sub>), -7.0 (SiMe<sub>2</sub>), -7.1 (SiMe<sub>2</sub>), -11.99 (SiMe<sub>2</sub>);  $\delta_{\text{Si}}$  (99MHz) 3.8, 2.8, 2.5; MS (CI)  $m/z$  243 (MH<sup>+</sup>, 55%), 242 (M, 1.3%), 185 (M<sup>+</sup>-SiMe<sub>2</sub>, 20%); HRMS  $m/z$  M<sup>+</sup> for C<sub>13</sub>H<sub>26</sub>O<sub>2</sub>Si 242.1702 obs. 242.1702 calc.

**7,9-Dimethyl-8,8-dimethyl-8-sila-2,3-diethoxycarbonyl-1,4-dioxaspiro[4.5]decane**

**(291)**

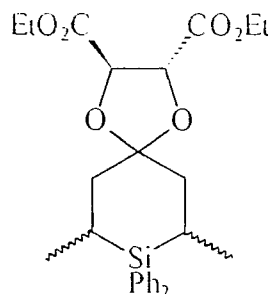


**(291)**

BF<sub>3</sub>·OEt<sub>2</sub> (0.04ml, 0.44mmol) was added dropwise to a solution of (2R,3R)-diethyl tartrate (0.31g, 1.5mmol) and the ketone (**223**) (164mg, 1mmol, 12% *de (anti)*) in DCM (10ml) at rt. The reaction was stirred over 4Å molecular sieves for 48h, with renewal of molecular sieves every 15h. The reaction was then quenched with saturated sodium bicarbonate (15ml) and extracted into ethyl acetate (3x15ml). The combined organic layers were washed with brine (15ml), dried (MgSO<sub>4</sub>) and concentrated. Flash column chromatography eluting with 4% ethyl acetate in petrol afforded the unreacted ketone (**223**) (10mg, 8%, 64% *de (anti)*); δ<sub>H</sub> (400MHz) 0.1 (4.9H, s, SiMe<sub>2</sub>), 0.08 (0.45H, s, SiMe<sub>2</sub>), 0.07 (0.6H, s, SiMe<sub>2</sub>) and the acetal (**291**) as a colourless oil (323mg, 92%, 40%*de, syn*), ν<sub>max</sub> 1739 (C=O), 1248 (SiMe), 1213, 1120 (C-O), 836 cm<sup>-1</sup>; δ<sub>H</sub> (400MHz) 4.78 (2H, d J = 8.8Hz, CHO), 4.25 (4H, m, CH<sub>3</sub>CH<sub>2</sub>O), 1.96-1.5 (4H, m, CH<sub>2</sub>CCH<sub>2</sub>), 1.3 (6H, m, CH<sub>3</sub>CH<sub>2</sub>O), 1.1 (2H, m, CHSiCH), 0.9 (6H, d, J = 7.6Hz, CH<sub>3</sub>CHSiCHCH<sub>3</sub>) -0.01 (2.1H, s, SiMe<sub>2</sub>), -0.04 (1.8H, s, SiMe<sub>2</sub>), -0.14 (2.1H, s, SiMe<sub>2</sub>); δ<sub>C</sub> (100MHz) 170 (C=O), 169.9 (C=O), 169.9 (C=O), 117.0 (OCO), 116.1 (OCO), 77.4 (OCHCHO), 76.8 (OCHCHO), 76.6 (OCHCHO), 61.9 (CH<sub>2</sub>CCH<sub>2</sub>), 61.8 (CH<sub>2</sub>CCH<sub>2</sub>), 43.0 (CH<sub>2</sub>OCO), 42.6 (CH<sub>2</sub>OC=O), 41.7 (CH<sub>2</sub>OC=O), 15.6 (CHCH<sub>3</sub>), 15.4 (CHCH<sub>3</sub>), 15.3 (CH<sub>3</sub>CH<sub>2</sub>), 14.1 (CH<sub>3</sub>CH<sub>2</sub>), 14.08 (CH<sub>3</sub>CH), 14.0 (CH<sub>3</sub>CH), -6.3 (SiMe<sub>2</sub>), -7.15 (SiMe<sub>2</sub>), -7.2 (SiMe<sub>2</sub>), -11.95 (SiMe<sub>2</sub>); δ<sub>Si</sub> (99MHz) 2.7, 2.6, 2.5; MS (EI) *m/z* 359 (M<sup>+</sup>, 13.4%), 358 (M<sup>+</sup>, 9.5%), 315 (6.7%), 285 (M<sup>+</sup>-CO<sub>2</sub>Et, 9.1%), 287 (MH<sub>2</sub><sup>+</sup>-CO<sub>2</sub>Et, 100%); HRMS *m/z* M<sup>+</sup> for C<sub>17</sub>H<sub>30</sub>O<sub>6</sub>Si 358.1812 obs. 358.1812 calc.

**7,9-Dimethyl-8,8-diphenyl-8-sila-2,3-diethoxycarbonyl-1,4-dioxaspiro[4.5]decane**

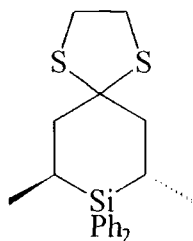
**(292)**



**(292)**

A mixture of the silacyclohexanone (**226**) (294mg, 1mmol, 50%de), (2*R*, 3*R*) diethyl tartrate (0.31g, 1.5mmol) and TsOH (0.19g., 0.1mmol) in DCM (15ml) was heated under reflux with soxhlet extraction over 4Å molecular sieves for 48 h. The resulting solution was quenched with saturated sodium bicarbonate (20ml), extracted into ethyl acetate (3x25ml), washed with brine (15ml) and concentrated. Purification by flash column chromatography eluting with 8% ethyl acetate in petrol afforded the acetal (**292**) as a waxy solid (180mg, 50%); m.p. 94-97°C;  $\delta_{\text{H}}$  (400MHz) 7.53-7.33 (10H, m, SiPh<sub>2</sub>), 4.8 (2H, s, OCHCHO), 4.29 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 2.2-1.85 (4H, m, CH<sub>2</sub>CCH<sub>2</sub>), 1.84-1.78 (2H, m, CH<sub>3</sub>CHSiCHCH<sub>3</sub>), 1.3 (6H, m, CH<sub>3</sub>CH<sub>2</sub>O), 1.02 (6H, d, J = 7.6Hz, CH<sub>3</sub>CHSiCHCH<sub>3</sub>);  $\delta_{\text{C}}$  (100MHz) 169.8 (C=O), 169.4 (C=O), 136.4 (Ar), 135.7 (Ar), 133.4 (Ar), 133.3 (Ar), 129.4 (Ar), 129.3 (Ar), 127.7 (Ar), 127.6(Ar), 116.7 (OCO), 116.6 (OCO), 77.2 (OCHCHO) 76.9 (OCHCHO) 61.8 (CH<sub>2</sub>CCCH<sub>2</sub>), 61.7 (CH<sub>2</sub>CCCH<sub>2</sub>), 41.95 (CH<sub>2</sub>C=O), 41.85 (CH<sub>2</sub>C=O), 16.8 (CHCH<sub>3</sub>), 16.65 (CHCH<sub>3</sub>), 14.03 (CH<sub>3</sub>CH<sub>2</sub>), 14.0 (CH<sub>3</sub>CH<sub>2</sub>), 12.3 (CH<sub>3</sub>CH), 12.2 (CH<sub>3</sub>CH); MS (CI) *m/z* 500 (MNH<sub>4</sub><sup>+</sup>, 22%), 483 (MH<sup>+</sup>, 3.1%), 423 (MNH<sub>4</sub><sup>+</sup>-Ph, 6%), 312 (MH<sub>2</sub><sup>+</sup>-CO<sub>2</sub>EtCHCHCO<sub>2</sub>Et, 100%); HRMS *m/z* M<sup>+</sup> (CI) for C<sub>27</sub>H<sub>38</sub>O<sub>6</sub>NSi obs. 500.247; calc. 500.247.

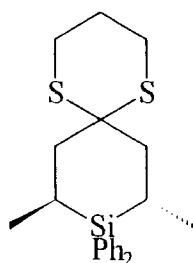
**Attempted Preparation of 7,9-Dimethyl-8,8-diphenyl-8-sila-1,4-dithiaspiro [4.5]decane (293)**



(293)

BF<sub>3</sub>.OEt<sub>2</sub> (0.02ml, 0.22mmol) was added to a stirred solution of the ketone (226) (121mg, 0.4mmol), and ethanedithiol (0.04ml, 0.4mmol) in DCM (7ml) over 4Å molecular sieves at rt. After stirring for 1h at rt the reaction was quenched with saturated sodium bicarbonate (10ml) extracted into ethyl acetate (3x10ml) and concentrated to afford the dithioketal (293) as a semi-crystalline solid (148mg, 100%) which decomposed on attempted purification by flash column chromatography.

**8,10-Dimethyl-9,9-diphenyl-9-sila-1,5-dithiaspiro[5.5]undecane (294)**

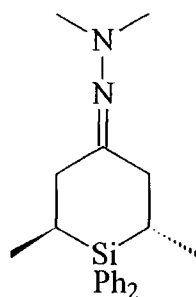


(294)

BF<sub>3</sub>OEt<sub>2</sub> (0.1ml) was added to a solution of the ketone (226) (0.5g, 1.9mmol) and propanedithiol (0.22ml, 2mmol) in DCM (10ml) at rt. The resulting solution was stirred at rt for 1 h before K<sub>2</sub>CO<sub>3</sub> (10ml) was added and the mixture extracted into ethyl acetate (3 x 25ml). Concentration afforded the dithioketal (294) as a semi-crystalline solid (700mg, 75%); m.p. 80-84°C; (de=84%); ν<sub>max</sub> 1430 (SiPh<sub>2</sub>), 1116,

907, 702  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200MHz), 7.54-7.35 (10H, m,  $\text{SiPh}_2$ ), 2.89 (4H, m,  $\text{CH}_2\text{SCSCH}_2$ ), 2.35 (2H, dd  $J = 4.5$  Hz,  $\text{HCHCHCH}$ ), 2.02 (4H, m,  $\text{HCHCHCH}$ ,  $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$ ), 1.83 (2H, m,  $\text{CH}_3\text{CHSiCHCH}_3$ ), 1.0 (0.46H, d,  $J = 7.99$  Hz,  $\text{CH}_3\text{CHSiCHCH}_3$ ) 0.98 (5.54H, d,  $J = 7.44$  Hz,  $\text{CH}_3\text{CHSiCHCH}_3$ );  $\delta_{\text{C}}$  (100MHz) 135.9 (Ar), 132.9 (Ar), 129.5 (Ar), 127.7 (Ar), 51.6 (SCS), 43.5 ( $\text{CH}_2\text{SCSCH}_2$ ), 26.6 ( $\text{CH}_2\text{CCH}_2$ ), 25.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 17.0 ( $\text{CHCH}_3$ ), 11.8 ( $\text{CH}_3\text{CH}$ ); MS (CI)  $m/z$  402 ( $\text{MNH}_4^+$  38%), 300 ( $\text{M}^+ - \text{HSCH}_2\text{CH}_2\text{CH}_2\text{SH}$ , 22%), 258 ( $\text{M}^+ - \text{HSCH}_2\text{CH}_2(\text{CH}_2\text{CH}_2\text{CH}_3)\text{CH}_2\text{SH}$ , 100%).

### **8,10-Dimethyl-9,9-diphenyl-9-sila cyclohexane -1,2,-dimethylhydrazone (300)**



**(300)**

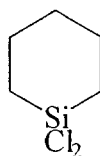
To a solution of the ketone (**226**) (147mg, 0.5mmol) in EtOH (10ml) was added dimethyl hydrazine (90mg, 1.5mmol). The mixture was heated under reflux for 24h. Concentration afforded the hydrazone (**300**) as a waxy solid (200mg);  $\delta_{\text{H}}$  (200Mhz) 7.4-7.15 (10H, m,  $\text{SiPh}_2$ ), 2.44 (6H, s,  $\text{NMe}_2$ ), 1.6-1.3 (4H, m,  $\text{CH}_2\text{CCH}_2$ ), 1.0 (2H, m,  $\text{CHSiCH}$ ), 0.96 (6H, d  $J=7.6\text{Hz}$ ,  $\text{CH}_3\text{CHSi}$ ).

### **Attempted conversion of (300) to silacyclohexane (295)**

Hydrazine hydrate (45mg, 1.5mmol) was added to a solution of (**300**) (200mg) in EtOH (30ml) at rt. The resulting mixture was heated under reflux and stirred at this temperature until the signal ( $\delta$  2.44) attributable to the dimethylamine had disappeared in the  $^1\text{H}$  NMR. The reaction mixture was concentrated and DMSO (2ml) added. The resulting solution was added to a suspension of  $^t\text{BuOK}$  (2g) in DMSO (5ml) dropwise. The

resulting mixture was stirred at room temperature for 15h. Concentration afforded a number of unidentifiable products.

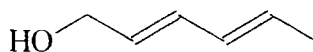
**1,1-Dichloro-1-silacyclohexane (305)**<sup>132</sup>



**(305)**

The silacyclohexane (**287**) (1g, 4mmol) was added dropwise to a stirred suspension of  $\text{AlCl}_3$  (0.5g, 4mmol) in DCM (15ml). The resulting dark red solution was allowed to stir at rt for 2h (30 min is sufficient). The solvent was removed by distillation and 1,1-dichloro-1-silacyclohexane (**305**) was distilled as a colourless oil (0.44g, 70%); b.p.  $62^\circ\text{C}$ , 30mbar (lit.<sup>132</sup> b.p.  $167\text{-}168^\circ\text{C}$ )  $\delta_{\text{H}}$  (400MHz) 1.84 (4H, m,  $\text{CH}_2\text{CH}_2\text{Si}$ ) 1.5 (2H, m,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.20 (4H, t  $J=7.5\text{Hz}$ ,  $\text{CH}_2\text{SiCl}_2$ );  $\delta_{\text{C}}$  (100MHz) 28.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 23.97 ( $\text{CH}_2\text{CH}_2\text{Si}$ ), 20.2 ( $\text{CH}_2\text{Si}$ );  $\delta_{\text{Si}}$  (99MHz) 10.98; GCMS RT 8.344 min (SE30 column); MS  $m/z$  (EI); 168/170 ( $\text{M}^+$ , 33/24%), 133/135 ( $\text{M}^+\text{-Cl}$ , 100/68%), 97( $\text{M-SiCl}_2$ , 15%); HRMS  $m/z$  (EI)  $\text{M}^+$  for  $\text{C}_5\text{H}_{10}\text{SiCl}_2$  obs. 167.9929; calc. 167.9929.

**2,4-Hexadiene-1-ol (307)**<sup>125</sup>

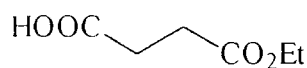


**(307)**

A solution of ethyl sorbate (**308**) (10g, 72mmol) in ether (150ml) was added to a suspension of  $\text{LiAlH}_4$  (1.6g, 42mmol) in ether (150ml) at  $0^\circ\text{C}$ . The reaction was stirred for 18h before being quenched with water (1.6ml, 90mmol),  $\text{NaOH}$  (1.6ml, 15% w/v) and more water (4.8ml). A white solid precipitated. The reaction mixture was filtered and the residue was washed with ethyl acetate (3x30ml). Recrystallisation from hexane afforded the diene alcohol (**307**) as a white crystalline solid (4g, 57%);

(mp. 26-29°C);  $\nu_{\max}$  3372 (OH), 3168, 1435, 1391, 1361  $\text{cm}^{-1}$ ; all data were in agreement with the literature.<sup>125</sup>

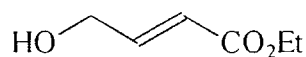
### Succinic Acid Monoethyl Ester (310)<sup>127</sup>



(310)

$\text{BH}_3$ .THF (1.0M, 75ml, 0.075mmol) was added to a solution of monoethyl fumarate (**309**) (10g, 76mmol) in THF (30ml) at -15 to -5°C. The resulting mixture was warmed slowly over 2h before being quenched with water/acetic acid (1:1, approx. 2ml) until no more gas evolved. The reaction was concentrated under vacuum before being poured onto ice-cold saturated  $\text{NaHCO}_3$  (30ml). The aqueous layer was washed with ethyl acetate (20ml) before being acidified to pH 5 by the addition of dilute hydrochloric acid (3.6ml of 3.0M). After removal of water under reduced pressure, the title compound (**310**) was obtained as a yellow oil, b.p. 127-136°C 15mbar, (lit.<sup>127</sup> 134-138°C, 15mbar),  $^1\text{H}$  NMR analysis indicated the disappearance of the double bond signal attributable to the starting material. With all other physical data in agreement with that found in the literature.<sup>127</sup>

### Ethyl 4-Hydroxybut-2-enoate (312)<sup>133</sup>

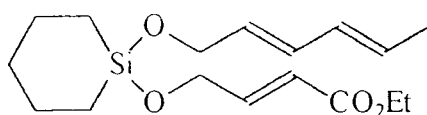


(312)

A solution of (carboethoxymethylene)triphenylphosphorane (10g, 28.7mmol) in benzene (200ml) was added to a refluxing solution of glycolaldehyde dimer (**311**) (1.8g, 15mmol) in benzene (190ml). The resulting solution was heated under reflux for a further 4h, before being concentrated and purified by flash column

chromatography eluting with 8% ethyl acetate in hexane which gave the allylic alcohol (**312**) as a colourless oil (2.67g, 71%). (b.p. 85-90°C/1.25mbar (lit<sup>133</sup> b.p. 88-90°C/1.2mbar)  $\delta_{\text{H}}$  (200MHz) 7.01 (1H, dt  $J = 16, 1.9$  Hz, CH=), 6.04 (1H, dt  $J = 16, 2.1$  Hz, CH=), 4.29 (2H, s, CH<sub>2</sub>), 4.15 (2H, q  $J = 10.6$  Hz, CH<sub>3</sub>CH<sub>2</sub>O), 3.0 (1H, br.s, OH), 1.24 (3H, t  $J = 8.4$  Hz, CH<sub>3</sub>CH<sub>2</sub>).

**Ethyl (E,E,E)-6,6-Pentamethylene-5,7,6-dioxasila-2,14,16-hexadecatrienoate (313)**

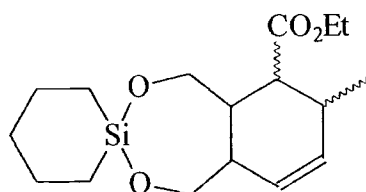


(313)

A mixture of the diene (**307**) (392mg, 4mmol) and the dienophile (**312**) (520mg, 4mmol) in DCM (10ml) was added dropwise to the dichlorosilacycle (**305**) (672mg, 4mmol) in DCM (15ml) and Et<sub>3</sub>N (1.2ml). The resulting mixture was stirred for 1h before petrol (10ml) was added to precipitate Et<sub>3</sub>N.HCl. The reaction mixture was filtered and concentrated. Flash column chromatography by gradient elution (2-10% ethyl acetate in petrol) afforded the **tethered bisdiene (314)** (30mg);  $\nu_{\text{max}}$  1448, 1384, 1110, 1051, 990  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (300MHz) 6.1 (4H, m, CH<sub>2</sub>CH=CH), 5.68 (4H, m, CH=CHCH<sub>3</sub>), 4.25 (4H, d  $J=5.7$ Hz, SiOCH<sub>2</sub>);  $\delta_{\text{C}}$  (300MHz) 131.2 (CH<sub>2</sub>CH=), 130.8 (CHCH=), 129.5(CH=CH), 128.9 (=CHCH<sub>3</sub>), 63.1 (SiOCH<sub>2</sub>), 29.6 (CH<sub>3</sub>CH=), 24.7 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 18.1 (CH<sub>2</sub>CH<sub>2</sub>Si), 12.2 (CH<sub>2</sub>SiCH<sub>2</sub>); MS (EI)  $m/z$  292 (M<sup>+</sup>, 5.3%), 277 (M<sup>+</sup> - CH<sub>3</sub>, 6.9%), 211 (M<sup>+</sup> - CH<sub>2</sub>CH=CH.CH=CH=CH<sub>3</sub>, 43%) 115 (hydroxysilacyclopentamethylene<sup>+</sup>, 100%); and the **tethered triene (313)** as a colourless oil (86mg, 27%),  $\nu_{\text{max}}$  1721 (C=O), 1663 (CH=CH), 1446, 1296 (SiCH<sub>2</sub>), 990  $\text{cm}^{-1}$ ,  $\delta_{\text{H}}$  (400MHz) 6.92 (1H, dt  $J = 15.5, 2.0$ Hz, CH=CHCH<sub>2</sub>), 6.4 (1H, dt  $J = 15.5, 0.6$ Hz, CH=CHCH<sub>2</sub>), 6.26 (1H, m, CH=CH), 6.01 (1H, m, CH=CH), 5.57 (2H, m, CH=CHCH<sub>3</sub>), 4.25 (2H, d  $J = 3.0$ Hz, CO<sub>2</sub>EtCHCHCH<sub>2</sub>O), 4.10 (2H, d  $J = 5.5$ Hz, CH<sub>3</sub>CHCHCHCH<sub>2</sub>O), 4.03 (2H, q  $J = 7.5$  Hz, CH<sub>3</sub>CH<sub>2</sub>O), 1.67 (4H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si), 1.56 (3H, d  $J = 7.0$ Hz, CH<sub>3</sub>CH=), 1.28 (2H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si),

1.22 (3H, t J=7.5 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 0.68 (4H, t J=6.5 Hz, CH<sub>2</sub>SiCH<sub>2</sub>); δ<sub>C</sub> (100 MHz) 166.5 (C=O), 146.6 (CH=CHCO), 131.5 (CH=CHCO), 130.7 (CH=CH), 129.8 (CH=CH), 128.6 (CH=CH), 120 (CH=CH), 63.2 (CH<sub>3</sub>CH<sub>2</sub>O), 61.3 (CH<sub>2</sub>OSi), 60.3 (CH<sub>2</sub>OSi), 29.6 (CH<sub>3</sub>CH=), 24.7 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 18.1 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 14.2 (CH<sub>3</sub>CH<sub>2</sub>CO), 11.9 (CH<sub>2</sub>SiCH<sub>2</sub>); MS (EI) m/z 324 (M<sup>+</sup>, 50%), 226 (M<sup>+</sup>-HOCH<sub>2</sub>CH=CHCH=CHCH<sub>3</sub>, 34%), 115 (hydroxysilacyclopentamethylene<sup>+</sup>, 100%); HRMS m/z (EI) M<sup>+</sup> for C<sub>17</sub>H<sub>28</sub>O<sub>4</sub>Si obs. 324.175343, calc. 324.175688.

**11-Ethoxycarbonyl-10-methyl-4,4-pentamethylene-3,5,4-dioxasilabicyclo[5.4.4]-8-undecane (316)**



**(316)**

The triene **(313)** (20mg, 0.06 mmol) in C<sub>6</sub>D<sub>6</sub> (1ml) was heated at reflux (140°C). in an evacuated NMR tube. After 84h the <sup>1</sup>H NMR indicated complete conversion of the triene **(313)** to the tricyclic Diels-Alder product **(316)**. GCMS (rt 17.9 min. 93%, 18.5 min 7%); ν<sub>max</sub> 1727 (C=O), 1264 (SiCH<sub>2</sub>), 1096, 1021, 802 cm<sup>-1</sup>; δ<sub>H</sub> (300MHz) 5.32 (0.33H, m, CH=CH), 5.29 (0.66H, m, CH=CH), 5.22 (0.66H, m, CH=CH), 5.20 (0.33H, m, CH=CH), 4.0 (2H, q J = 7.2 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 3.87 (1.33H, m, CH<sub>2</sub>OSiOCH<sub>2</sub>), 3.84 (0.66H, m, CH<sub>2</sub>OSiOCH<sub>2</sub>) 3.6 (2H, m, CH<sub>2</sub>OSiOCH<sub>2</sub>), 2.53 (1H, m, CHCH<sub>3</sub>), 2.33 (1H, m, CHCH<sub>2</sub>O), 2.11 (1H, m, CHCH<sub>2</sub>O), 1.69 (4H, m, CH<sub>2</sub>CH<sub>2</sub>SiCH<sub>2</sub>CH<sub>2</sub>), 1.28 (2H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si), 0.96 (6H, m), 0.6-0.4 (4H, m); δ<sub>C</sub> (300MHz) 174.8 (C=O), 133.9 (C=C), 125.5 (C=C), 63.4 (OCH<sub>2</sub>CH<sub>3</sub>), 63.3 (CH<sub>2</sub>OSi) 60.0 (CH<sub>2</sub>OSi), 46.0 (CHCH<sub>3</sub>), 42.4 (CHCH<sub>2</sub>O), 41.5 (CHCH<sub>2</sub>O), 36.0 (CHCO<sub>2</sub>Et), 29.8 (CH<sub>2</sub>CH<sub>2</sub>SiCH<sub>2</sub>CH<sub>2</sub>), 25.0 (CH<sub>2</sub>) 20.2 (CH<sub>3</sub>CH<sub>2</sub>O), 12.4 (CH<sub>3</sub>CH), 12.1 (CH<sub>2</sub>SiCH<sub>2</sub>); MS (EI) m/z 324 (MH<sup>+</sup>, 17%), 294

( $M^+ - CH_3CH_2$ , 100%), 150 ( $M^+ - CO_2Et$ , 16%) 115

(hydroxysilacyclopentamethylene<sup>+</sup>, 43%); HRMS  $m/z$  (EI)  $M^+$  for  $C_{17}H_{27}O_4Si$  obs.

324.302, calc. 324.301734.

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## **APPENDICES**

**UNIVERSITY OF DURHAM**

**Board of Studies in Chemistry**

**COLLOQUIA, LECTURES AND SEMINARS FROM INVITED SPEAKERS**

**1994 - 1995 (August 1 - July 31)**

**1996 - 1997 (August 1 - July 31)**

**1995 - 1996 (August 1 - July 31)**

**1994**

- October 5                    Prof. N. L. Owen, Brigham Young University, Utah, USA  
Determining Molecular Structure - the INADEQUATE NMR way
- #October 19                Prof. N. Bartlett, University of California  
Some Aspects of Ag(II) and Ag(III) Chemistry
- November 2                Dr P. G. Edwards, University of Wales, Cardiff  
The Manipulation of Electronic and Structural Diversity in Metal Complexes -  
New Ligands
- #November 3               Prof. B. F. G. Johnson, Edinburgh University  
Arene-metal Clusters
- #November 9               Dr G. Hogarth, University College, London  
New Vistas in Metal-imido Chemistry
- #November 10              Dr M. Block, Zeneca Pharmaceuticals, Macclesfield  
Large-scale Manufacture of ZD 1542, a Thromboxane Antagonist Synthase  
Inhibitor
- #November 16              Prof. M. Page, University of Huddersfield  
Four-membered Rings and  $\beta$ -Lactamase
- #November 23              Dr J. M. J. Williams, University of Loughborough  
New Approaches to Asymmetric Catalysis
- December 7                Prof. D. Briggs, ICI and University of Durham  
Surface Mass Spectrometry

1995

- #January 11 Prof. P. Parsons, University of Reading  
Applications of Tandem Reactions in Organic Synthesis
- January 18 Dr G. Rumbles, Imperial College, London  
Real or Imaginary Third Order Non-linear Optical Materials
- #January 25 Dr D. A. Roberts, Zeneca Pharmaceuticals  
The Design and Synthesis of Inhibitors of the Renin-angiotensin System
- February 1 Dr T. Cosgrove, Bristol University  
Polymers do it at Interfaces
- February 8 Dr D. O'Hare, Oxford University  
Synthesis and Solid-state Properties of Poly-, Oligo- and Multidecker  
Metallocenes
- #February 22 Prof. E. Schaumann, University of Clausthal  
Silicon- and Sulphur-mediated Ring-opening Reactions of Epoxide
- March 1 Dr M. Rosseinsky, Oxford University  
Fullerene Intercalation Chemistry
- March 22 Dr M. Taylor, University of Auckland, New Zealand  
Structural Methods in Main-group Chemistry
- April 26 Dr M. Schroder, University of Edinburgh  
Redox-active Macrocyclic Complexes : Rings, Stacks and Liquid Crystals
- #May 4 Prof. A. J. Kresge, University of Toronto  
*The Ingold Lecture* Reactive Intermediates : Carboxylic-acid Enols and Other  
Unstable Species
- October 11 Prof. P. Lugar, Frei Univ Berlin, FRG  
Low Temperature Crystallography
- October 13 Prof. R. Schmutzler, Univ Braunschweig, FRG.  
Calixarene-Phosphorus Chemistry: A New Dimension in Phosphorus  
Chemistry
- #October 18 Prof. A. Alexakis, Univ. Pierre et Marie Curie, Paris,  
Synthetic and Analytical Uses of Chiral Diamines

- #October 25            Dr.D.Martin Davies, University of Northumbria  
Chemical reactions in organised systems.
- #November 1           Prof. W. Motherwell, UCL London  
New Reactions for Organic Synthesis
- November 3            Dr B. Langlois, University Claude Bernard-Lyon  
Radical Anionic and Psuedo Cationic Trifluoromethylation
- #November 8           Dr. D. Craig, Imperial College, London  
New Stategies for the Assembly of Heterocyclic Systems
- November 15           Dr Andrea Sella, UCL, London  
Chemistry of Lanthanides with Polypyrazoylborate Ligands
- November 17           Prof. David Bergbreiter, Texas A&M, USA  
Design of Smart Catalysts, Substrates and Surfaces from Simple Polymers
- November 22           Prof. I Soutar, Lancaster University  
A Water of Glass? Luminescence Studies of Water-Soluble Polymers.
- #November 29           Prof. Dennis Tuck, University of Windsor, Ontario, Canada  
New Indium Coordination Chemistry
- #December 8           Professor M.T. Reetz, Max Planck Institut, Mulheim  
Perkin Regional Meeting
- 1996**
- January 10            Dr Bill Henderson, Waikato University, NZ  
Electrospray Mass Spectrometry - a new sporting technique
- #January 17           Prof. J. W. Emsley , Southampton University  
Liquid Crystals: More than Meets the Eye
- #January 24           Dr Alan Armstrong, Nottingham Univesity  
Alkene Oxidation and Natural Product Synthesis
- January 31            Dr J. Penfold, Rutherford Appleton Laboratory,  
Soft Soap and Surfaces

- #February 7 Dr R.B. Moody, Exeter University  
Nitrosations, Nitrations and Oxidations with Nitrous Acid
- February 12 Dr Paul Pringle, University of Bristol  
Catalytic Self-Replication of Phosphines on Platinum(O)
- February 14 Dr J. Rohr, Univ Gottingen, FRG  
Goals and Aspects of Biosynthetic Studies on Low Molecular Weight Natural Products
- February 21 Dr C R Pulham , Univ. Edinburgh  
Heavy Metal Hydrides - an exploration of the chemistry of stannanes and plumbanes
- February 28 Prof. E. W. Randall, Queen Mary & Westfield College  
New Perspectives in NMR Imaging
- #March 6 Dr Richard Whitby, Univ of Southampton  
New approaches to chiral catalysts: Induction of planar and metal centred asymmetry
- March 7 Dr D.S. Wright, University of Cambridge  
Synthetic Applications of Me<sub>2</sub>N-p-Block Metal Reagents
- March 12 RSC Endowed Lecture - Prof. V. Balzani, Univ of Bologna  
Supramolecular Photochemistry
- March 13 Prof. Dave Garner, Manchester University  
Mushrooming in Chemistry
- April 30 Dr L.D.Pettit, Chairman, IUPAC Commission of Equilibrium Data  
pH-metric studies using very small quantities of uncertain purity
- October 9 Professor G. Bowmaker, University Auckland, NZ  
Coordination and Materials Chemistry of the Group 11 and Group 12 Metals :  
Some Recent Vibrational and Solid State NMR Studies
- #October 14 Professor A. R. Katritzky, University of Gainesville, University of Florida,  
USA  
Recent Advances in Benzotriazole Mediated Synthetic Methodology
- #October 16 Professor Ojima, Guggenheim Fellow, State University of New York at Stony  
Brook

## Silylformylation and Silylcarbocyclisations in Organic Synthesis

- #October 22 Professor Lutz Gade, Univ. Wurzburg, Germany  
Organic transformations with Early-Late Heterobimetallics: Synergism and Selectivity
- October 22 Professor B. J. Tighe, Department of Molecular Sciences and Chemistry, University of Aston  
Making Polymers for Biomedical Application - can we meet Nature's Challenge?  
Joint lecture with the Institute of Materials
- #October 23 Professor H. Ringsdorf (Perkin Centenary Lecture), Johannes Gutenberg-Universitat, Mainz, Germany  
Function Based on Organisation
- #October 29 Professor D. M. Knight, Department of Philosophy, University of Durham.  
The Purpose of Experiment - A Look at Davy and Faraday
- October 30 Dr Phillip Mountford, Nottingham University  
Recent Developments in Group IV Imido Chemistry
- November 6 Dr Melinda Duer, Chemistry Department, Cambridge  
Solid-state NMR Studies of Organic Solid to Liquid-crystalline Phase Transitions
- November 12 Professor R. J. Young, Manchester Materials Centre, UMIST  
New Materials - Fact or Fantasy?  
Joint Lecture with Zeneca & RSC
- November 13 Dr G. Resnati, Milan  
Perfluorinated Oxaziridines: Mild Yet Powerful Oxidising Agents
- #November 18 Professor G. A. Olah, University of Southern California, USA  
Crossing Conventional Lines in my Chemistry of the Elements
- #November 19 Professor R. E. Grigg, University of Leeds  
Assembly of Complex Molecules by Palladium-Catalysed Queuing Processes
- November 20 Professor J. Earnshaw, Department of Physics, Belfast  
Surface Light Scattering: Ripples and Relaxation
- November 27 Dr Richard Templer, Imperial College, London

## Molecular Tubes and Sponges

- December 3 Professor D. Phillips, Imperial College, London  
"A Little Light Relief" -
- December 4 Professor K. Muller-Dethlefs, York University  
Chemical Applications of Very High Resolution ZEKE Photoelectron Spectroscopy
- #December 11 Dr Chris Richards, Cardiff University  
Stereochemical Games with Metallocenes
- 1997**
- #January 15 Dr V. K. Aggarwal, University of Sheffield  
Sulfur Mediated Asymmetric Synthesis
- January 16 Dr Sally Brooker, University of Otago, NZ  
Macrocycles: Exciting yet Controlled Thiolate Coordination Chemistry
- January 21 Mr D. Rudge, Zeneca Pharmaceuticals  
High Speed Automation of Chemical Reactions
- January 22 Dr Neil Cooley, BP Chemicals, Sunbury  
Synthesis and Properties of Alternating Polyketones
- January 29 Dr Julian Clarke, UMIST  
What can we learn about polymers and biopolymers from computer-generated nanosecond movie-clips?
- February 4 Dr A. J. Banister, University of Durham  
From Runways to Non-metallic Metals - A New Chemistry Based on Sulphur
- February 5 Dr A. Haynes, University of Sheffield  
Mechanism in Homogeneous Catalytic Carbonylation
- #February 12 Dr Geert-Jan Boons, University of Birmingham  
New Developments in Carbohydrate Chemistry
- #February 18 Professor Sir James Black, Foundation/King's College London  
My Dialogues with Medicinal Chemists

- February 19 Professor Brian Hayden, University of Southampton  
The Dynamics of Dissociation at Surfaces and Fuel Cell Catalysts
- February 25 Professor A. G. Sykes, University of Newcastle  
The Synthesis, Structures and Properties of Blue Copper Proteins
- February 26 Dr Tony Ryan, UMIST  
Making Hairpins from Rings and Chains
- March 4 Professor C. W. Rees, Imperial College  
Some Very Heterocyclic Chemistry
- March 5 Dr J. Staunton FRS, Cambridge University  
Tinkering with biosynthesis: towards a new generation of antibiotics
- March 11 Dr A. D. Taylor, ISIS Facility, Rutherford Appleton Laboratory  
Expanding the Frontiers of Neutron Scattering
- March 19 Dr Katharine Reid, University of Nottingham  
Probing Dynamical Processes with Photoelectrons

# seminars attended by this author

