SYNTHETIC ASPECTS OF ORGANOSILICON CHEMISTRY

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Degree of Doctor of Philosophy

in the

University of Oxford

by

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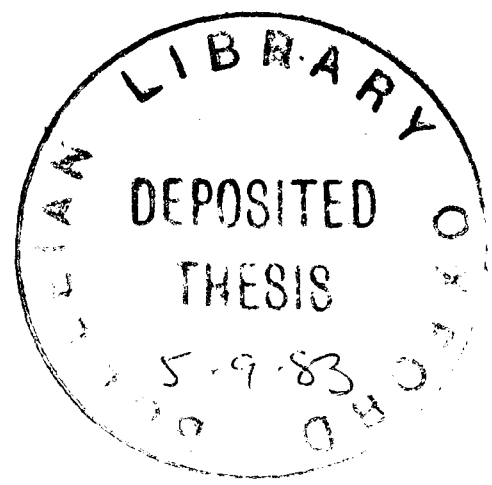

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This thesis is dedicated to

Professor D.J. Weatherall and

all the Doctors and Nurses at the

John Radcliffe and Churchill Hospitals

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ABSTRACTS

GENERAL INTRODUCTION

GENERAL INTRODUCTION

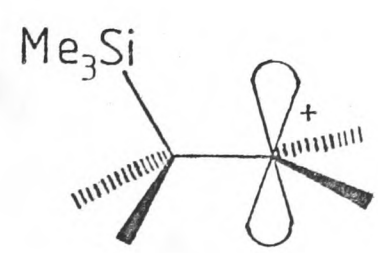
The use of organosilicon compounds as intermediates in organic synthesis is now widely established. The substitution of a proton for a trimethylsilyl group on a substrate enables transformations to be brought about which could not otherwise be achieved, and these transformations often occur with a high degree of stereo- and regiospecificity.

Four main features of silicon's chemistry can be identified from which stem its utility in organic synthesis, these are summarized below.

1. The difference in bond energies (Si-X)-(Si-C) is very much greater than the difference (C-X)-(C-C), where X=F,N or O[1,2]. This provides the driving force for many reactions of organosilicon compounds, the Si-F bond in particular is one of the strongest known single bonds.

2. Nucleophilic substitution at silicon is much easier than the corresponding nucleophilic substitution at carbon. The ease with which a silyl group can be added and removed depends upon this property. Substitution generally takes place in a bimolecular fashion[3,4], it is sensitive to steric hindrance which can be useful.

3. A silicon-carbon bond stablizes a carbonium ion β to itself. This has been explained by bridging[5] or as is now preferred, by (p-σ)π hyperconjugation[6,7](1).



1

4. Silicon stabilizes a negative charge on the α-carbon. The role of (p-d)π back bonding from carbon to silicon[8] as an explanation for this is controversial. An alternative explanation is that the filled orbitals of the carbon-metal bond overlap with the unoccupied antibonding σ^* orbital of adjacent C-Si bond, a process called "negative hyperconjugation"[9].

Most of the reactions of organosilicon compounds can be rationalized in terms of one or more of the above features. The work described in the two parts of this thesis concerns the development of two methods for carbon-carbon double bond formation involving the use of organosilicon intermediates. The Peterson elimination reaction of β-hydroxysilanes (2) is central to both sections, a discussion follows of the reaction and a classification of the methods available for the preparation of β-hydroxysilanes. Several recent reviews[9-15] have been written which give general accounts of organosilicon chemistry, but these do not give such a discussion in detail which also includes more recent examples. Background material specific to the two projects is dealt with separately in the introductory chapters of the two parts.

2

Elimination Reactions of β-Hydroxysilanes

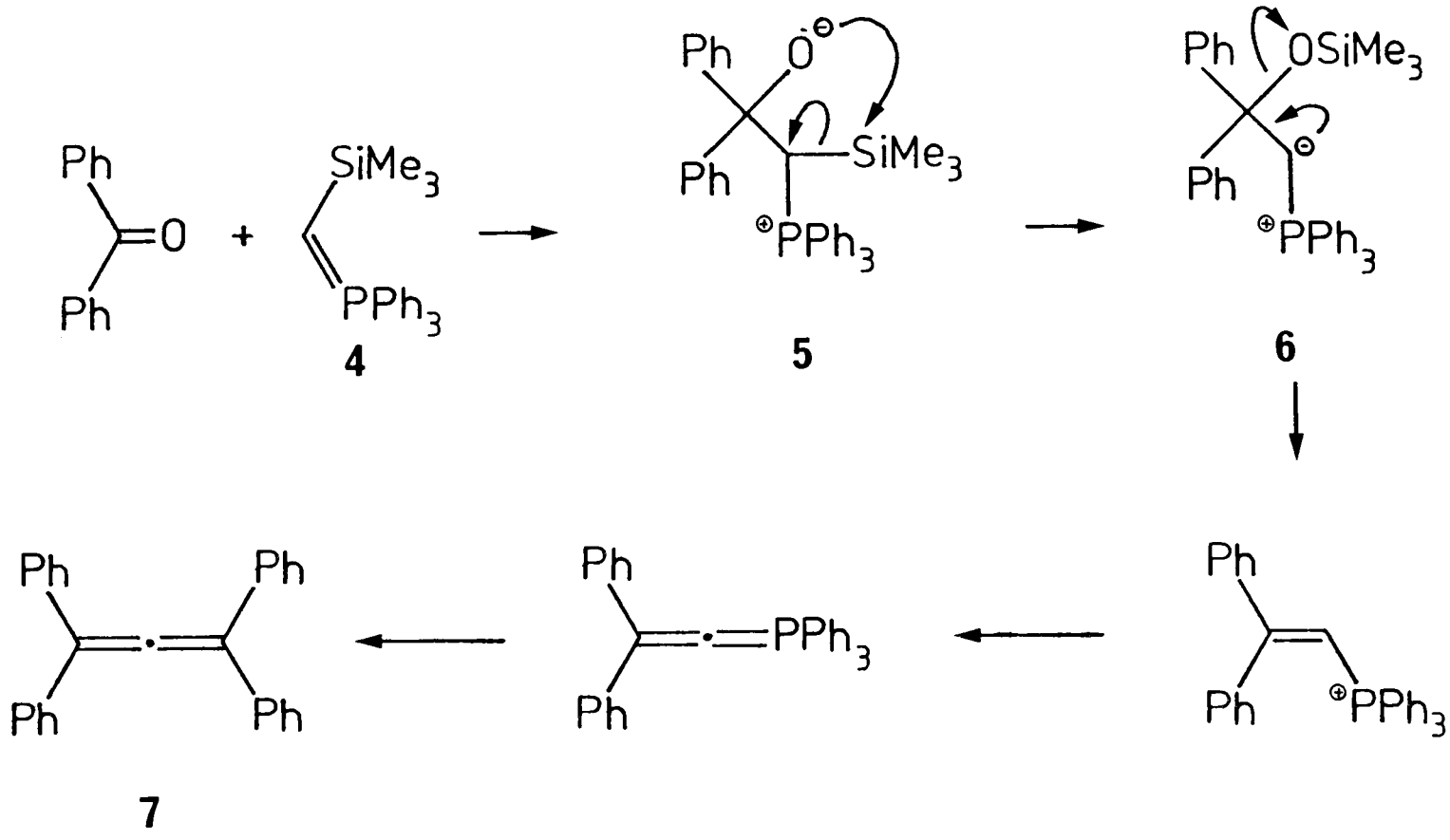
The original observation that β-hydroxysilanes undergo elimination was made in connection with a study of the behaviour of organosilanes with a leaving group in the β-position[16]. 1-Trimethylsilyl-2-propanol (3) was shown to give rise to propene when treated with acid[17] (Scheme 1).

3

Reagents: i, 10% H_2SO_4

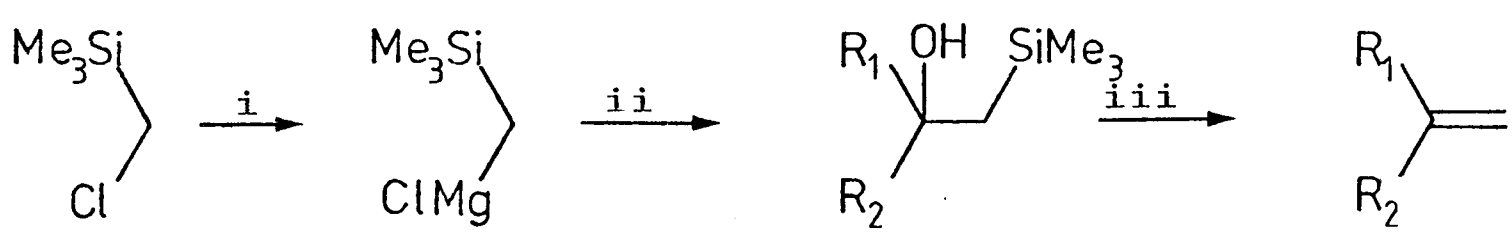
Scheme 1.

Later, a mechanism effectively involving elimination from a β-hydroxysilane under basic conditions (5)→(6) was proposed to account for the formation of tetraphenylallene (7) from the reaction of the silyl substituted ylide (4) with benzophenone[18] (Scheme 2).



Scheme 2.

It is only since the work of Peterson[19], however, that the utility of the elimination reactions of β-hydroxysilanes has been established. He showed that elimination could be brought about under acidic or basic conditions from β-hydroxysilanes of the type (8), thus providing overall a means of carbonyl olefination (Scheme 3).



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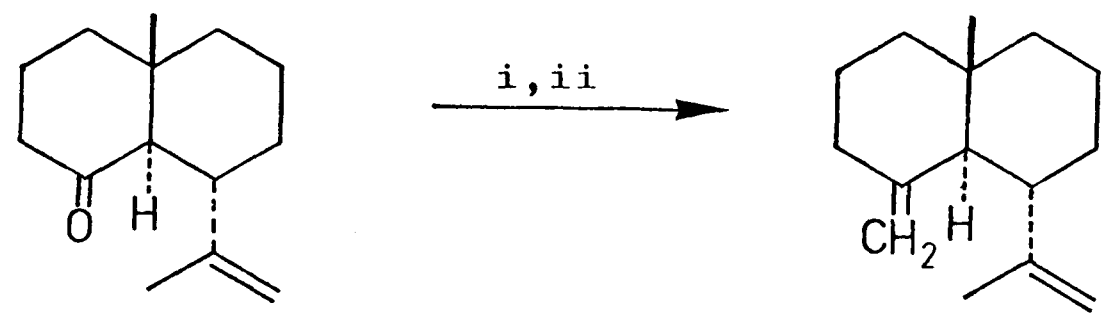
Reagents: i, Mg/THF, ii, R_1COR_2 then H^+,
iii, NaH, KH or H_2SO_4

Scheme 3.

Such a transformation provides a useful alternative to the Wittig reaction. For example it is possible to achieve methyleneation of hindered ketones such as (9) which fail to react with the corresponding Wittig reagent[20] (Scheme 4). Another advantage is that the by-products of the Peterson reaction, hexamethyldisiloxane and trimethylsilanol, are volatile and easier to remove than triphenylphosphine oxide from the product.



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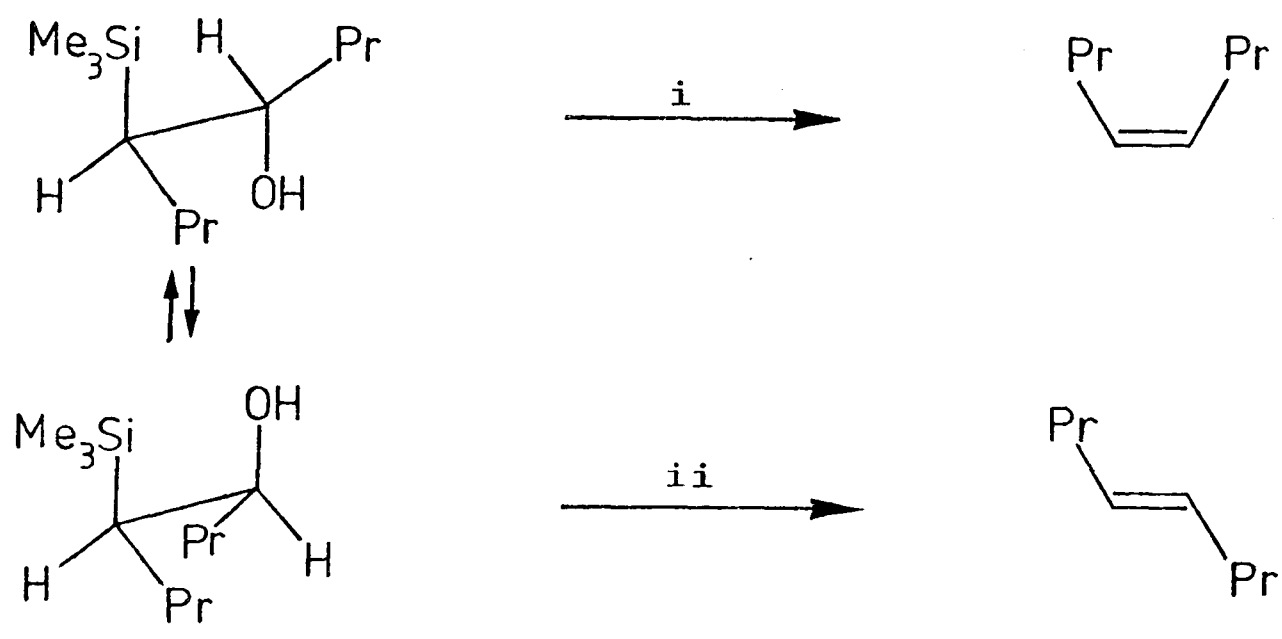
Reagents: i, Me_3SiCH_2MgCl; ii, NaOAc/AcOH

Scheme 4.

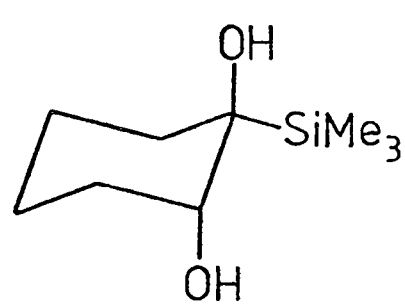
The elimination reactions of β-hydroxysilanes have been shown to be stereospecific[21]. The acid promoted reaction requires an <u>anti</u> arrangement of the departing groups and the base promoted reaction a <u>syn</u> arrangement, thus olefins of opposite stereochemistry can be prepared from a diastereoisomerically pure β-hydroxysilane (Scheme 5).



Reagents: i, H_2SO_4 or $BF_3.Et_2O$; ii, KH

Scheme 5.

In the acid promoted reaction the trimethylsilyl group is analogous to hydrogen as the electrofugal group in E2 type HX eliminations. The mechanism is corroborated by the reluctance of the β-hydroxysilanes (10) and (11) to undergo elimination under acidic conditions. In the preferred conformations of these compounds the trimethylsilyl and β-hydroxyl groups do not have the required anti-periplanar geometry[22].



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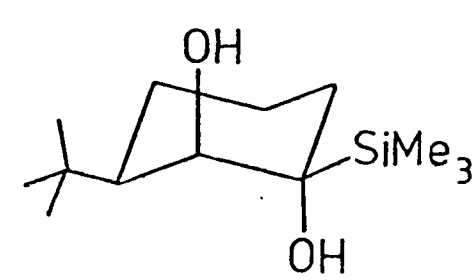

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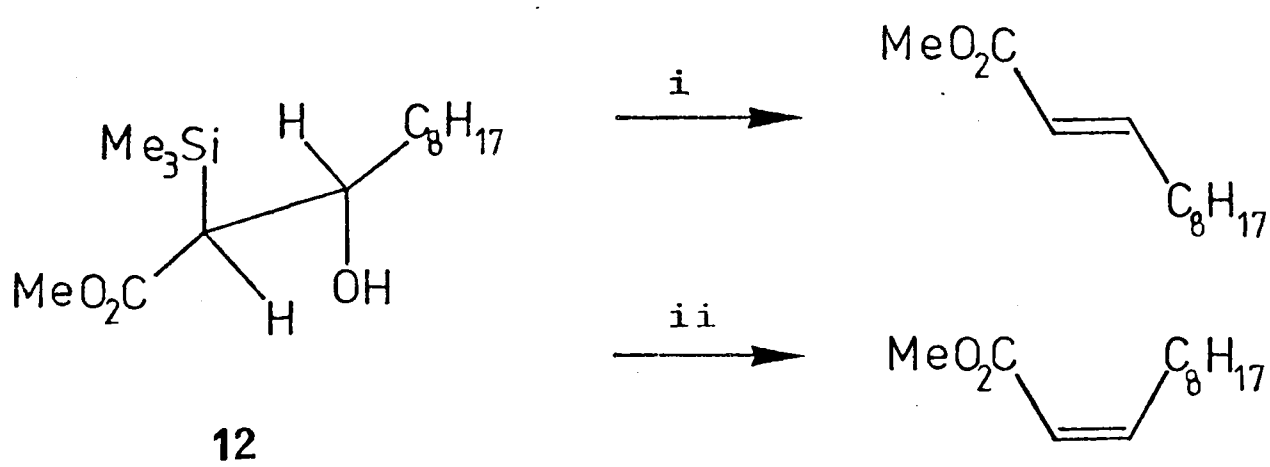
Both Brönsted and Lewis acids can be used to bring about elimination. Unusually, syn-elimination occurs when the β-hydroxysilane (12) is treated with aluminium trichloride whereas normal anti-elimination is brought about by boron trifluoride or titanium tetrachloride[24] (Scheme 6).



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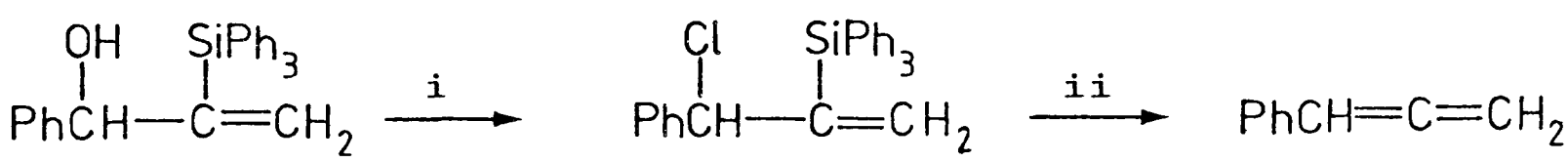
Reagents: i, $TiCl_4$ or $BF_3.Et_2O$, ii, $AlCl_3$

Scheme 6.

The use of acids can be avoided by conversion of the hydroxyl into a better leaving group followed by treatment with fluoride to bring about elimination. This approach has been used to bring about formation of allenes (14) from β-hydroxysilanes such as (13) which do not undergo elimination of trimethylsilanol under other conditions[25,26] (Scheme 7).

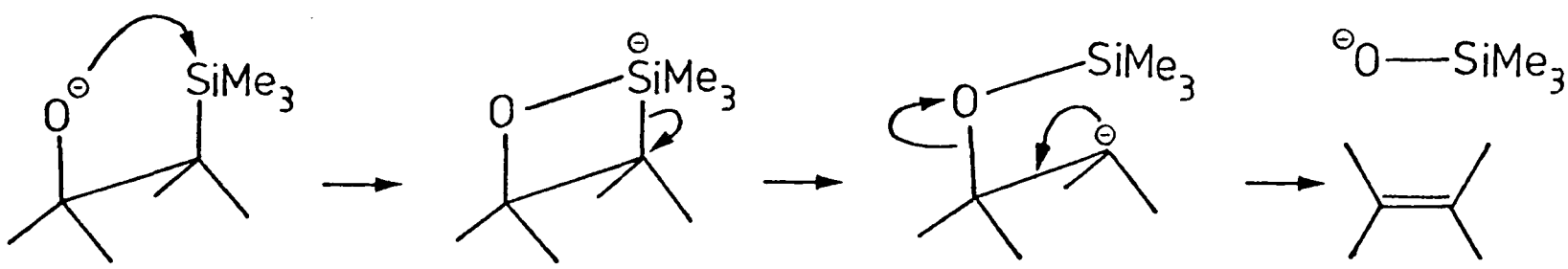


13 **14**

Reagents: i, $SOCl_2/CCl_4$; ii, $Et_4NF/MeCN$

Scheme 7.

The base promoted elimination of β-hydroxysilanes is thought to proceed via a mechanism analogous to that of the Wittig reaction. Molecular orbital calculations[27] indicate that the intermediate is nearer a four membered ring in the Wittig reaction than in the Peterson reaction. In the latter case (Scheme 8) it might be better represented as a carbanion (15), although presumably the exact mechanism depends upon the substituents present.



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Scheme 8.

The bases most commonly used to bring about Peterson elimination are sodium hydride[19,21,28-30], potassium hydride[19,21,28,29] or potassium t-butoxide[19].

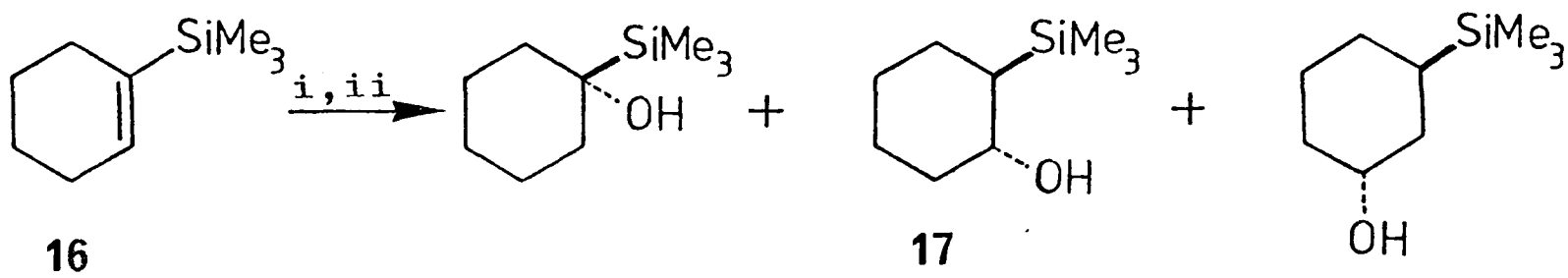
Preparation of β-Hydroxysilanes

Applications of the Peterson elimination in organic synthesis were initially limited by a paucity of routes to β-hydroxysilanes, particularly ones which were stereospecific. A number of routes are, however, now available and the main types are classified below in terms of the silyl containing precursor.

(A) From Vinylsilanes[15,31]

(i) Hydroboration-Oxidation. Hydroboration-oxidation of vinylsilanes such as (16) gives mixtures of hydroxysilanes, the proportion of the β-hydroxysilane (17) depends upon conditions[32,33] (Scheme 9). The variation in the orientation

of hydroboration can be rationalized in terms of interplay between the steric and electronic effects of the trimethylsilyl group.



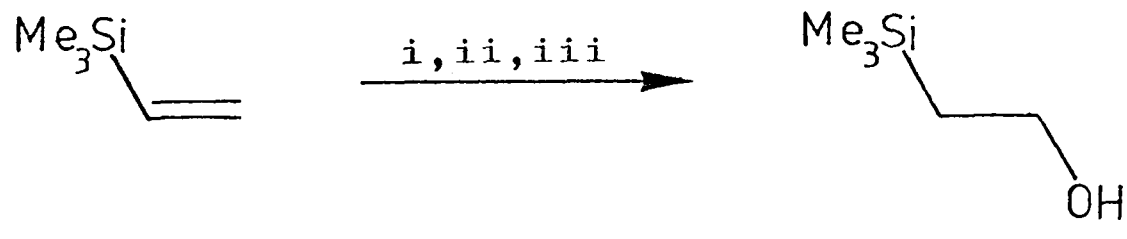
16 **17**

(a)	92	:	8	
(b)			83	: 17

Reagents: i, RBH_2; ii, H_2O_2/OH^-. Conditions: (a), BH_3/-20°/15 min, (b), thexylborane/25°/8h

Scheme 9.

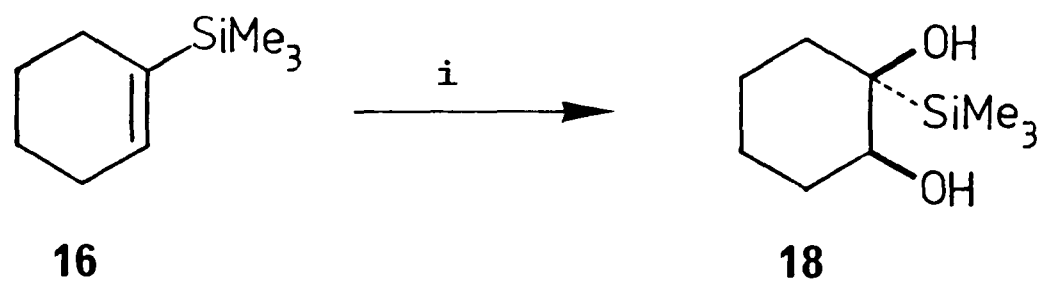
(ii) Oxymercuration. Oxymercuration of vinylsilanes followed by reduction of the adducts obtained gives β-hydroxysilanes[32,34] but yields are generally low (Scheme 10).



Reagents: i, $Hg(OAc)_2/H_2O$; ii, NaCl; iii, Na.Hg

Scheme 10.

(iii) Direct Oxidation. 1-Trimethylsilyl-cis-cyclohexane-1,2-diol (18) has been prepared in 11% yield[35] by potassium permanganate oxidation of the vinylsilane (16) (Scheme 11) (see page 28).

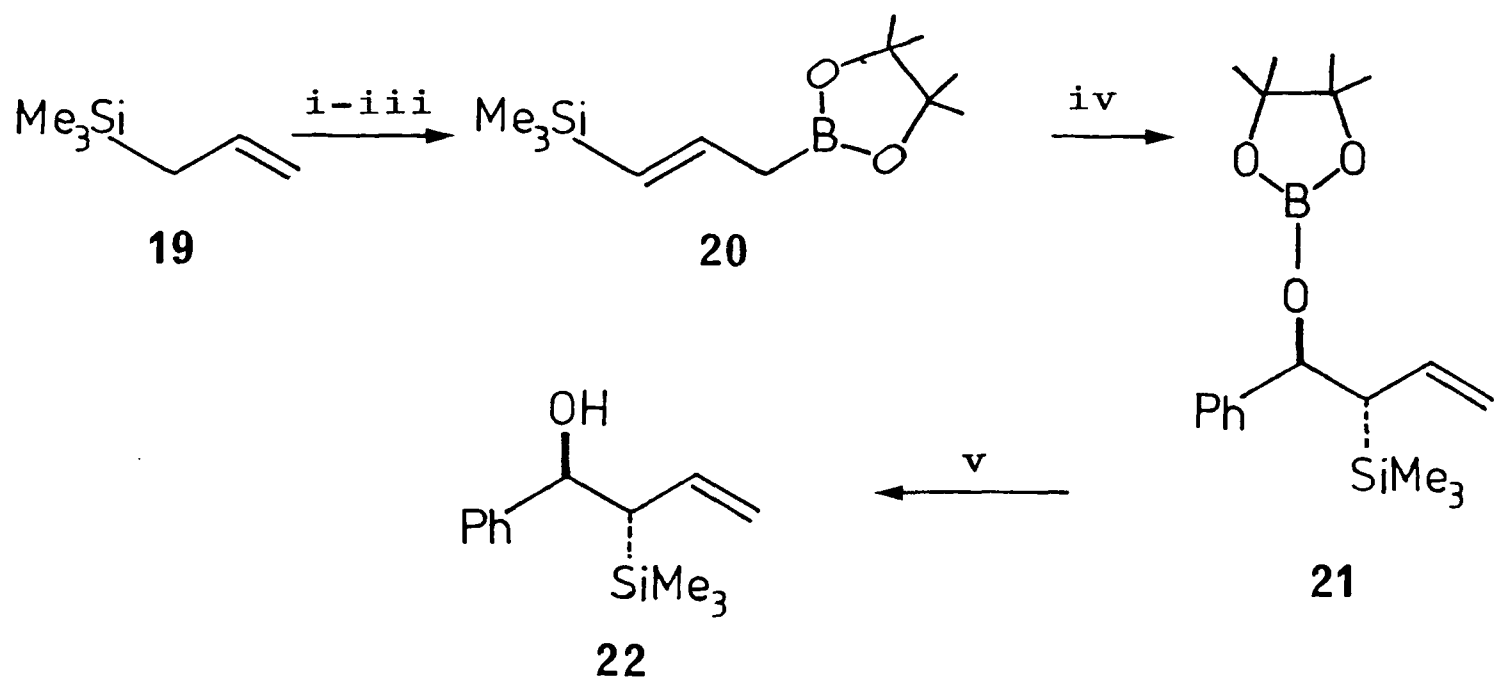


16 **18**

Reagents: i, $KMnO_4$/NaOH/H_2O/t-BuOH

Scheme 11.

(iv) From Substituted Vinylsilanes. Addition of the vinylsilane borate ester (20) to aldehydes[36] takes place in a highly diastereoselective manner, forming β-silyl borates (21) which are easily cleaved to give β-hydroxysilanes (22). The starting material is prepared from allyltrimethylsilane (19) (Scheme 12).

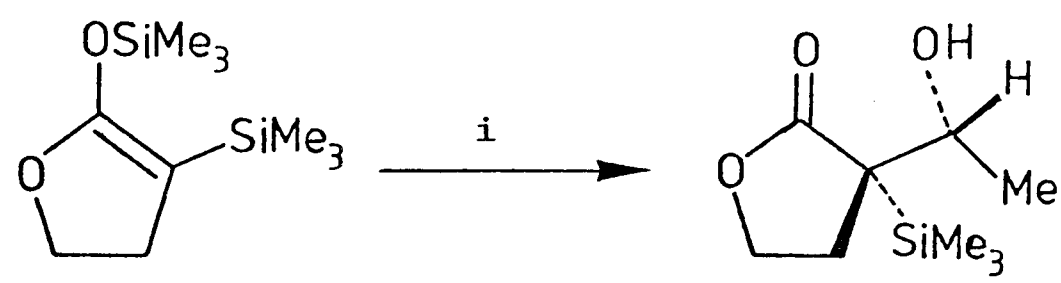


19 **20** **21** **22**

Reagents: i, n-BuLi/THF; ii, $B(OMe)_3$; iii, NH_4^+/pinacol; iv, PhCHO; v, triethanolamine

Scheme 12.

Lewis acid mediated reaction of β-trimethylsilyl silyl enol ethers with aldehydes gives β-hydroxysilanes[24,37]. In the case of the γ-lactone derivative (23), the addition is diastereoselective (Scheme 13).



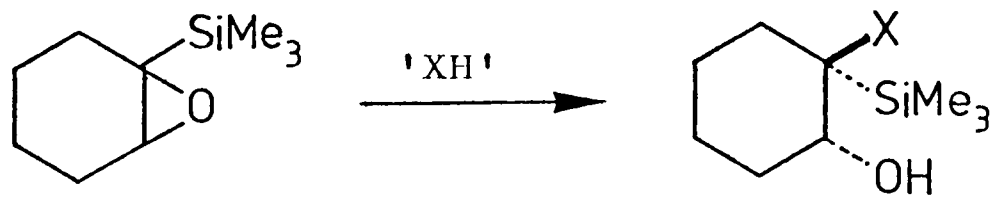
23

Reagents: i, $MeCHO/TiCl_4/CH_2Cl_2$

Scheme 13.

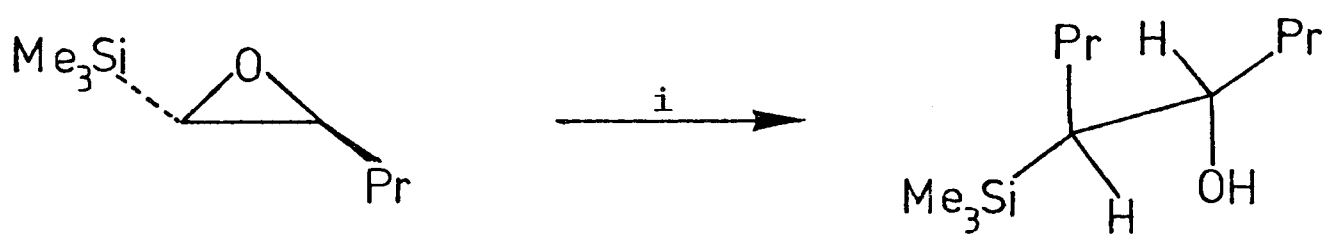
(B) From α,β-Epoxysilanes

The chemistry of α,β-epoxysilanes, which are readily obtainable from vinylsilanes by peracid oxidation, has been extensively explored in recent years[10,38]. Of particular interest are their ring opening reactions since attack of the nucleophile generally occurs at the carbon bearing silicon and a β-hydroxysilane is produced. This regiospecificity has been explained in terms of an S_N2 type mechanism in which the silyl group assists attack of the nucleophile by complexation, thus directing it to the α-carbon. Since these reactions are usually stereopecific, like other epoxide ring openings[39] they provide possibly the most versatile stereoselective route to substituted β-hydroxysilanes. Ring opening by a wide variety of species is known[38,40] including carbon nucleophiles[28] (Scheme 14).



24

X=H,OMe,OH,$OCH_2CH=CH_2$,SCN,NCS,NHAc,Cl,Br,I

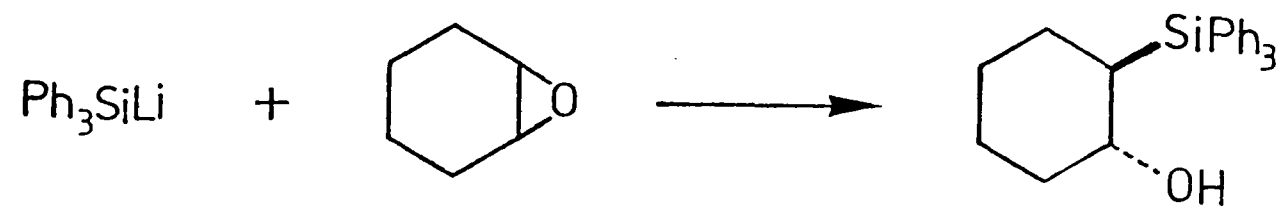


Reagents: i, Pr_2CuLi/Et_2O

Scheme 14.

(C) From Organosilyl Anions

The reaction of silyl anions with epoxides such as (25) provides another route[41,42] to β-hydroxysilanes. Usually, however, the β-hydroxysilane is not isolated as is the case in Scheme 15, which is an application[43] of the reaction to provide a means of inversion of olefin stereochemistry (26)→(27).



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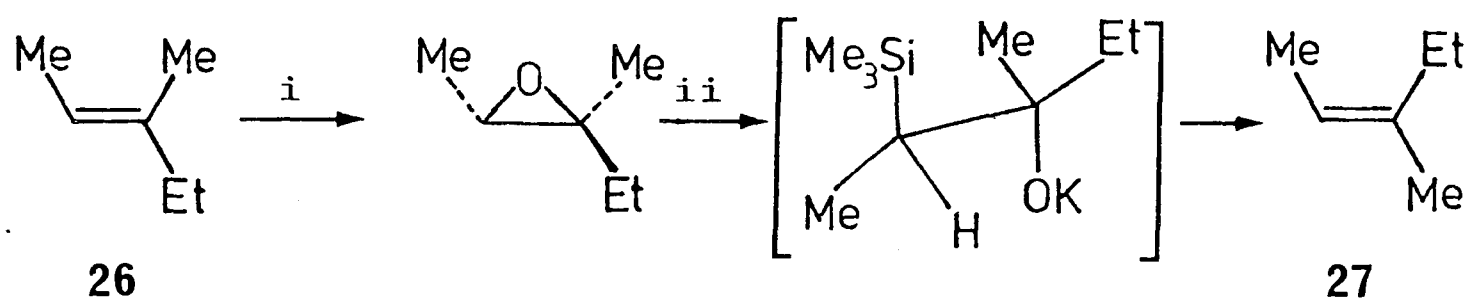


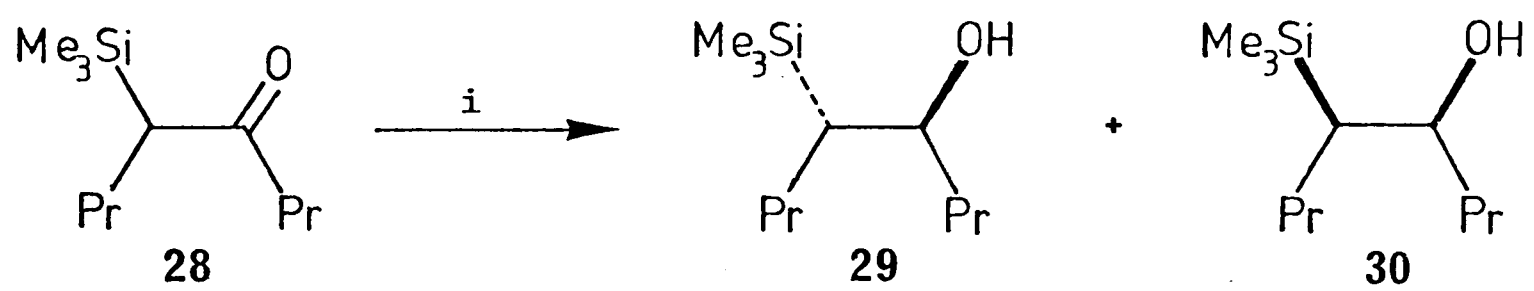
26 **27**

Reagents: i, m-$ClC_6H_4CO_3H/CH_2Cl_2$; ii, $KOMe/Me_3SiSiMe_3$/HMPA

Scheme 15.

(D) From α-Silyl Carbonyl Compounds

β-Hydroxysilanes are produced when α-silyl ketones are reduced by hydrides or treated with Grignard or alkyllithium reagents. Such procedures are especially useful when they occur with a degree of stereoselectivity. This is often the case. The more abundant diastereoisomer in the product is that predicted on the basis of Cram's rule[44], with the silyl group taken as being the largest. Thus reduction[21] of the α-silyl ketone (28) by the bulky hydride reducing agent diisobutylaluminium hydride (DIBAL) gives predominantly the threo β-hydroxysilane (29). Similarly the β-hydroxysilane (32) is produced with 91% stereoselectivity when the α-silyl ketone (31) is treated[45] with n-propyllithium (Scheme 16)



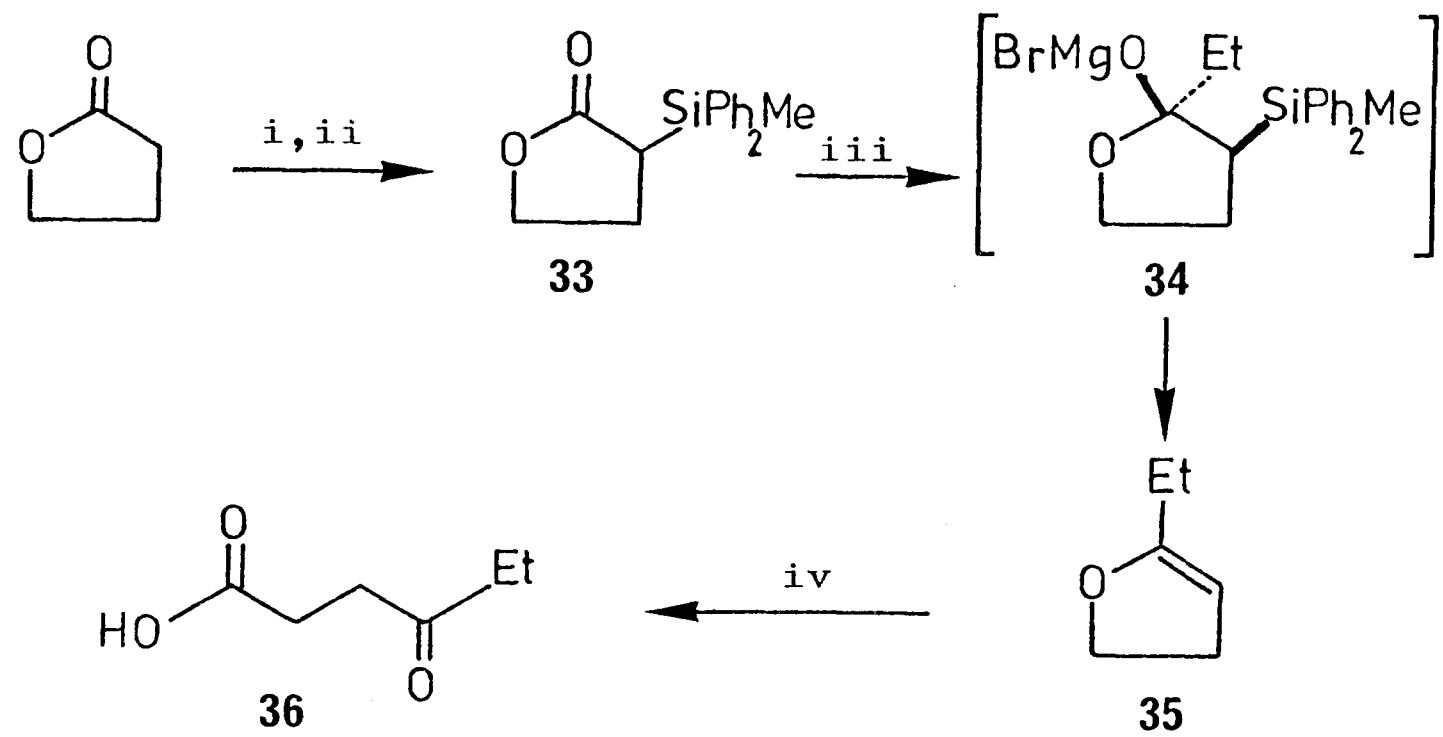
Reagents: i, DIBAL/pentane; ii, n-PrLi/Et_2O

Scheme 16.

The stereoselectivity of the reduction makes it possible to prepare predominantly one diastereoisomer of a β-hydroxysilane from a mixture of diastereoisomers by oxidation using chromium trioxide-pyridine followed by treatment with DIBAL[21]. Other methods of preparing α-silyl ketones are acylation of α-metallated organosilanes[21,46] and in one case α-silylation of ketones[47].

β-Hydroxysilanes can be prepared analogously from silylated derivatives of other carbonyl compounds. For example reaction of the silylated γ-lactone (33) with ethylmagnesium bromide gives (34) which undergoes Peterson

elimination rather than ring opening to give the enol ether (35). This transformation forms part of an overall synthesis[48] of γ-keto acids (36) (Scheme 17).

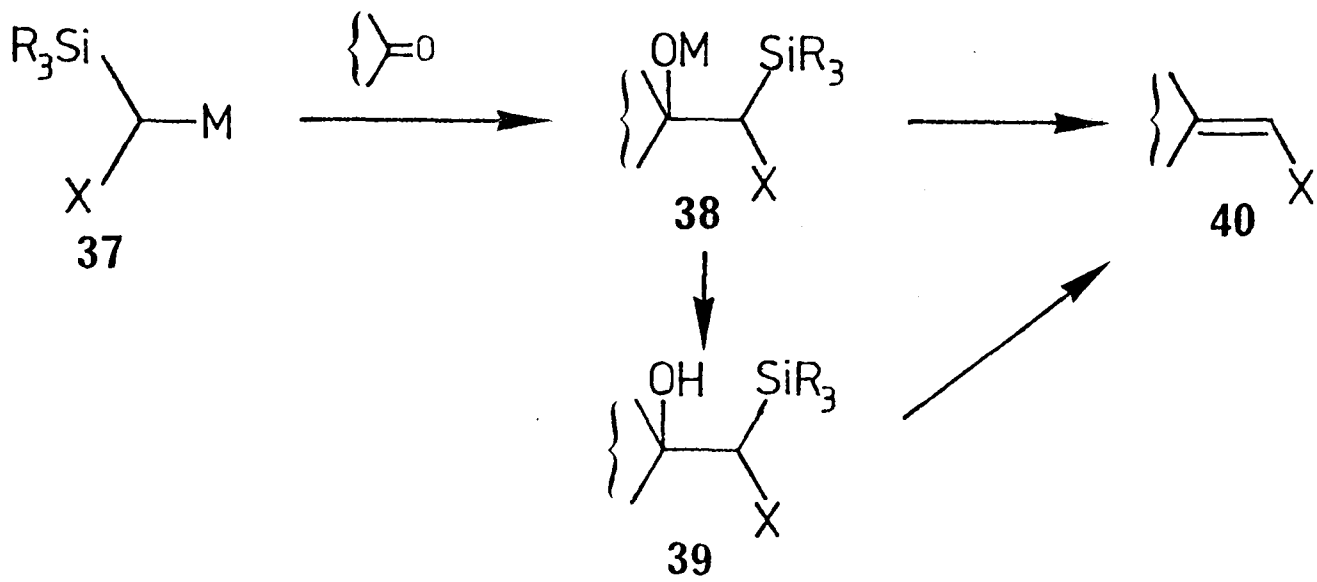


Reagents: i, LDA/THF; ii, $Ph_2MeSiCl$; iii, $EtMgBr/Et_2O$; iv, H_2CrO_4

Scheme 17.

(E) From α-Metallated Organosilanes

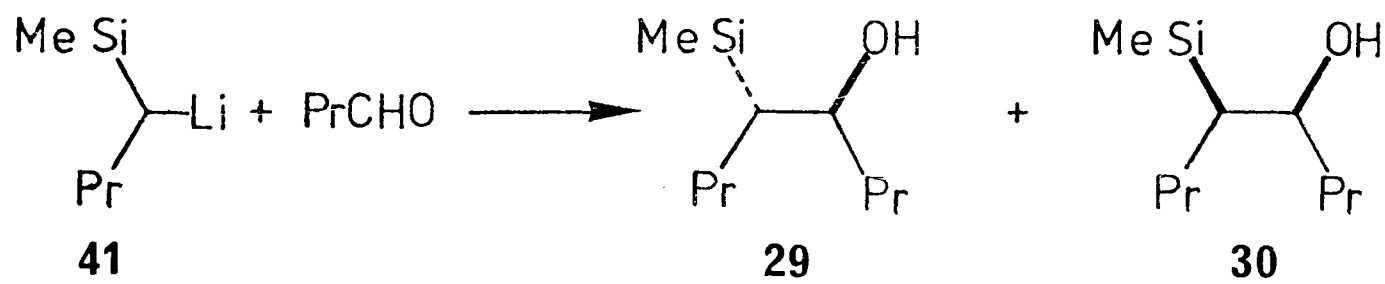
The reaction of an α-metallated organosilane (37) with an aldehyde or ketone is a versatile route to β-hydroxysilanes (Scheme 18).



Scheme 18.

If the metal M is sodium or potassium, the intermediate (38) cannot be isolated and undergoes fast Peterson elimination to give the olefin (40) directly. The β-hydroxysilane (39) can, however, generally be isolated by protonation of (38) if the metal is magnesium, and also if it is lithium except when the carbon bearing silicon also carries an electron withdrawing group, X[9].

The addition step often proceeds with a degree of stereoselectivity. For example the organolithium reagent (41) reacts with butyraldehyde to give[49], after work up, a mixture of β-hydroxysilanes containing a predominance of the threo isomer (29) (Scheme 19).

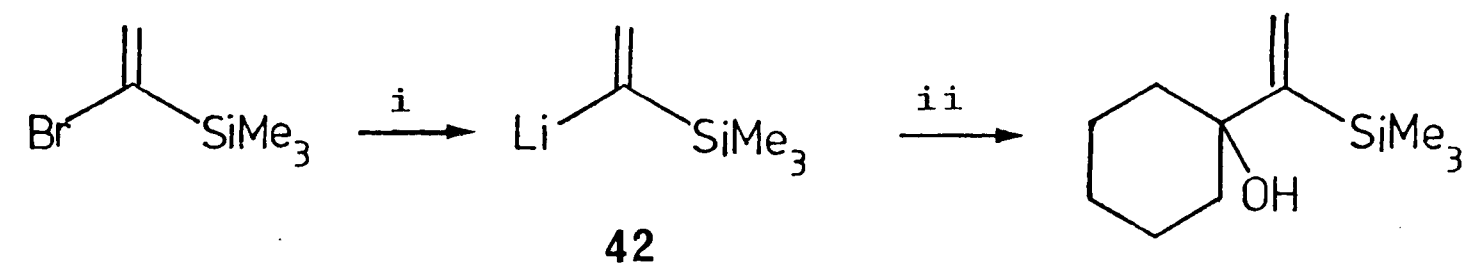


41 **29** **30**

72 : 28

Scheme 19.

Vinyl-[25,50] (42) and allenyl-[51,52] organometallic reagents react analogously. In the case of the allenyllithium reagent (43), which has two bulky silyl groups, addition to aldehydes takes place in a highly diastereoselective manner so that, after elimination, Z-enynes (44) are obtained almost exclusively (Scheme 20).



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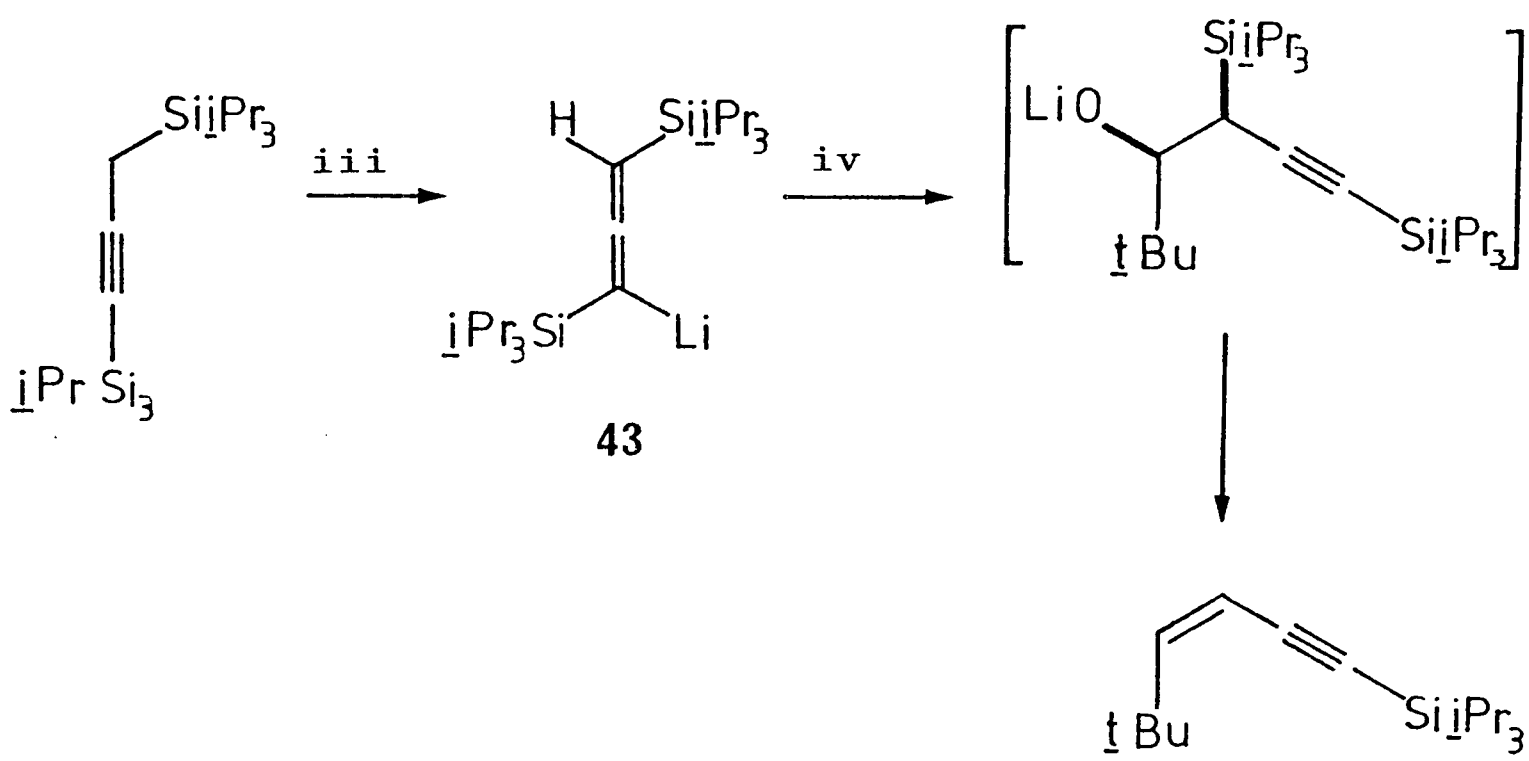


43

44

Z/E > 20:1

Reagents: i, t-BuLi/THF; ii, cyclohexanone;
iii, n-BuLi/THF; iv, pivaldehyde

Scheme 20.

The approach to β-hydroxysilanes using α-substituted-α-metallated organosilanes is the basis of the work described in Part II of this thesis. Part I is concerned with the development of an enol ether synthesis which uses the Peterson elimination as the double bond forming reaction.

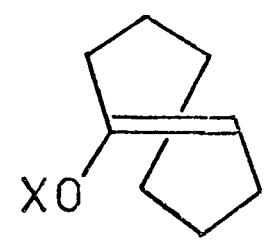
PART I

ENOL ETHER SYNTHESIS FROM 1-TRIMETHYLSILYL-1,2-DIOLS

CHAPTER I

INTRODUCTION

During the course of earlier work,[22,23,38,40] stereospecific routes to 1-trimethylsilylcyclohexane-1,2-diols were developed. The object of the project described here was to develop a route whereby these compounds could be transformed into an enol derivative and then to use the route for the preparation of an analogous trans-cyclooctene derivative (45), with an oxygenated substituent on the double bond. No compound of this type had previously been reported; it would be of particular interest to compare its stability with that of trans-cyclooctene and the known 1-substituted derivatives.

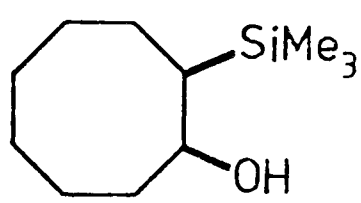


45

Section A: trans-Cyclooctene

trans-Cyclooctene is the smallest isolable trans-cycloalkene. It is strained because of its twisted olefinic linkage and the strain energy associated with this has been estimated as 58.9kJ mol^{-1}.[53] It was first prepared, together with the cis-isomer, by Hofmann elimination[54,55]; a number

of stereospecific preparations are now available[56]. The Peterson elimination has been used to prepare trans-cyclooctene[38,57], treatment of mixtures of the two isomeric β-hydroxysilanes (46) and (47) with sodium hydride in DMSO gave cis- and trans-cyclooctene in the same ratio as the cis- and trans-isomers in the precursor. This indicates that a syn-elimination pathway is still followed even when a strained olefin is produced.



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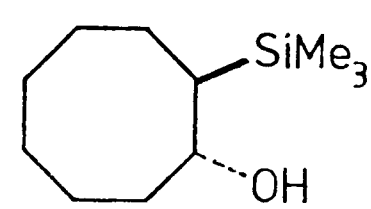


47

Many studies have been made of the chemistry of trans-cyclooctene[58,59], its unusual reactivity has been rationalized in terms of the distortion in the double bond. A great deal of structural work has also been carried out[60]. An X-ray crystal structure[61] of trans-2-cyclooctenyl-3',5'-dinitro-benzoate[62] showed that the molecule has a twist conformation (Figure 1), in agreement with electron diffraction results[63].

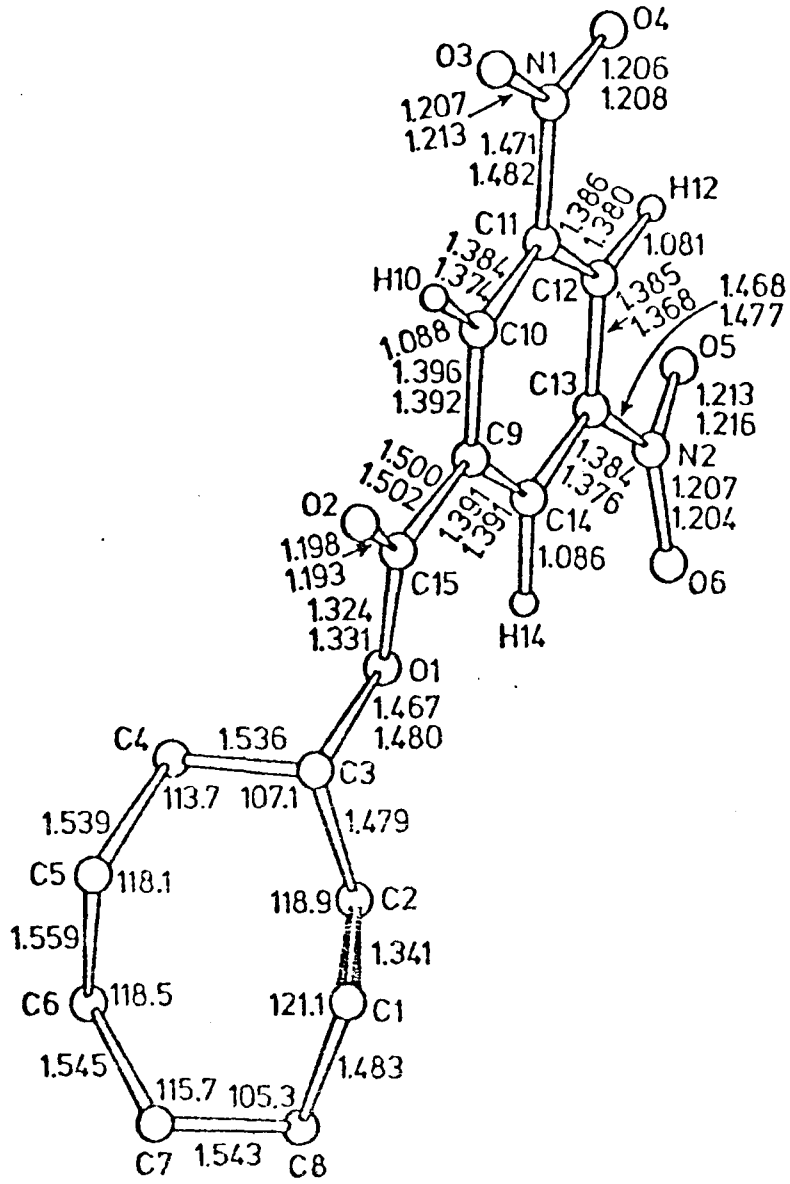


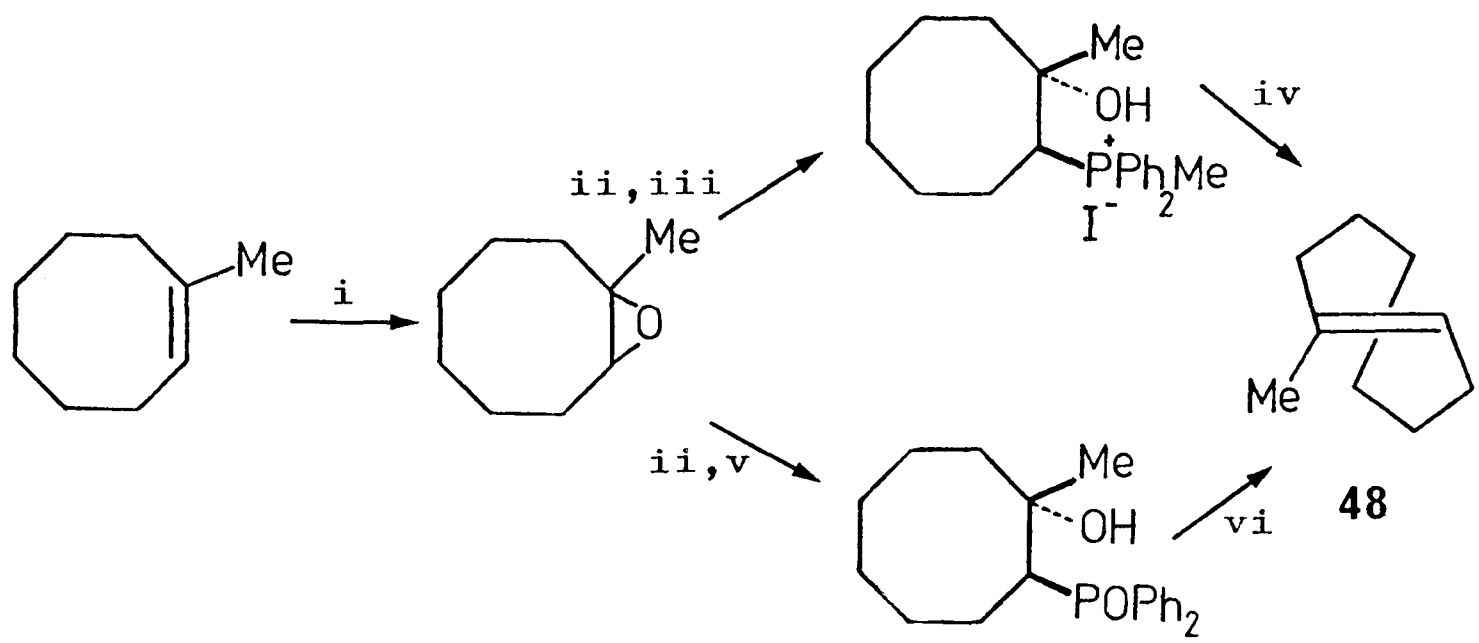
Figure 1. Bond lengths (in Å) and bond angles in trans-2-cyclooctenyl-3',5'-dinitrobenzoate

Because of its helical shape, trans-cyclooctene is chiral. It was first resolved via a diastereoisomeric Pt(II) complex[64].

Section B: trans-Cyclooctenes with Substituents on the Carbon-Carbon Double Bond

1,2-Dideutero-trans-cyclooctene has been prepared[65] from the corresponding cis-cyclooctene by application of the β-hydroxyphosphine oxide olefin inversion procedure[56,66]. The

same procedure[67], and a related one[68] have been used to prepare 1-methyl-trans-cyclooctene (48) (Scheme 21).

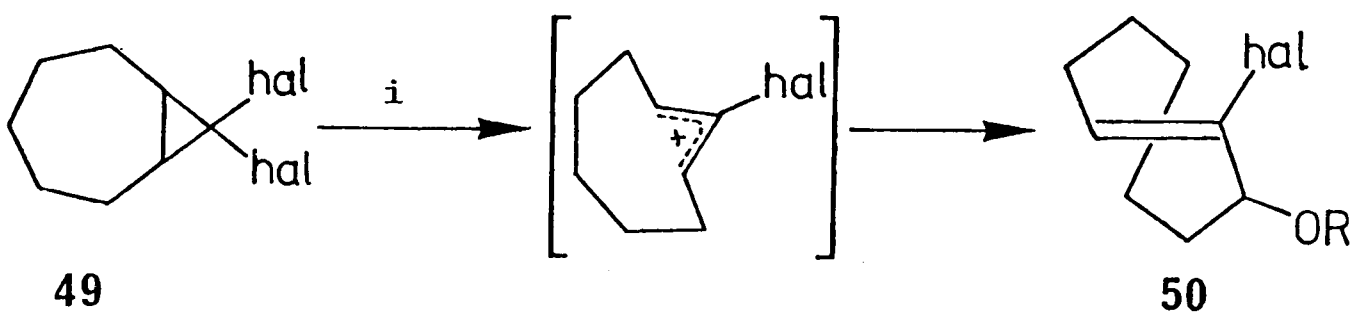


Reagents: i, $CH_3CO_3H/CH_2Cl_2/Na_2CO_3$; ii, $LiPPh_2$/THF; iii, MeI; iv, 1,5-diazabicyclo[5.4.0]undec-5-ene/THF; v, H_2O_2/CH_3CO_2H; vi, NaH/DMF

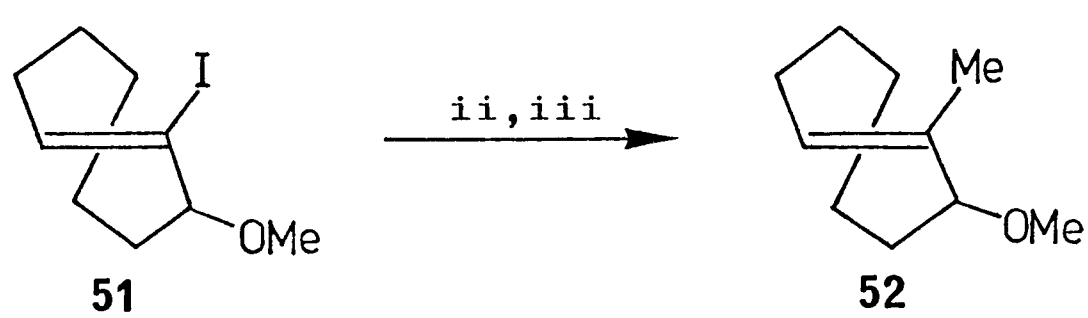
Scheme 21.

The chemistry of 1-methyl-trans-cyclooctene (48) is similar to that of trans-cyclooctene, except in eletrophilic addition reactions where the methyl derivative is more reactive[56,67] because the methyl group stabilizes the incipient tertiary carbonium ion. The molecular structure of (48) has recently been studied by electron diffraction; the results are similar to those calculated by molecular mechanics, they show[69] that the structure of the double bond is similar to that of trans-cyclooctene.

Silver perchlorate promoted solvolysis of dihalocarbene adducts of cycloheptene (49) has been used to prepare a number of 2,3-disubstituted trans-cyclooctenes (50)[70]; these compounds are sufficiently stable to permit further chemical transformation[71,72], for example (51)→(52) (Scheme 22).



49 **50**

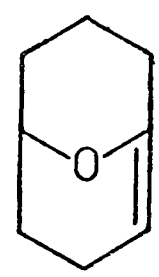


51 **52**

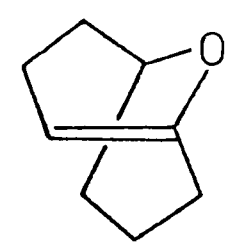
Reagents: i, $AgClO_4$/ROH; ii, MeLi/Et_2O; iii, MeI

Scheme 22.

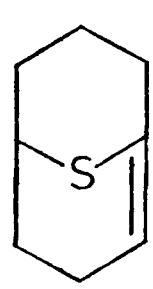
A number of hetero substituted bridgehead alkenes (53)[73], (54)[74], and (55)[75] have been prepared; these are related structurally to <u>trans</u>-cyclooctene derivatives as can be seen in the representation (53a).



53



53a



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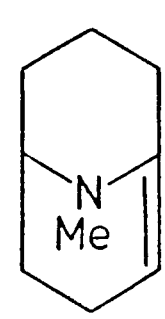

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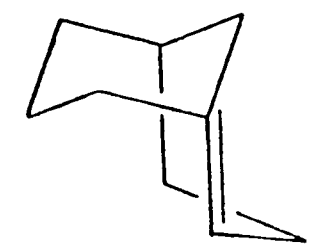
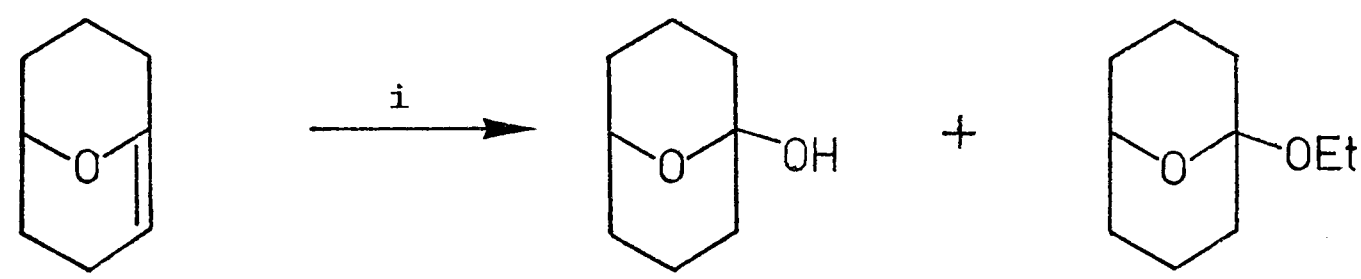
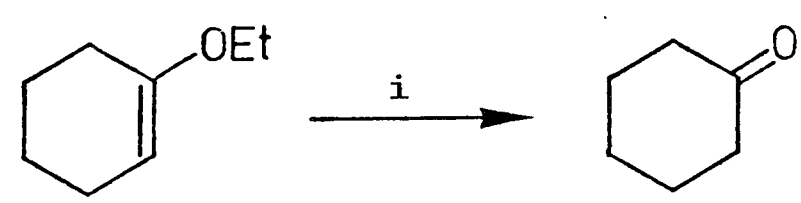


56

Chemically, however, (53) does not have the properties of an enol ether. This is because the fixed geometry of the bicyclic ring system (53a) results in the oxygen lone pairs not being in conjugation with the double bond so resonance stabilization of the carbonium ion which would be derived by protonation of (53) is not possible. Thus (53) is 1400 times less reactive to protonation[76,77] than its parent olefin (56)[78], and its rate of acid catalyzed hydrolysis is 10^5 times slower than that of 1-ethoxycyclohexene (57) (Scheme 23), despite the strain energy of (53) which might be expected to accelerate the reaction. An additional incentive behind preparation of a 1-alkoxy-trans-cyclooctene would be comparison of its chemistry with that of (53).



53



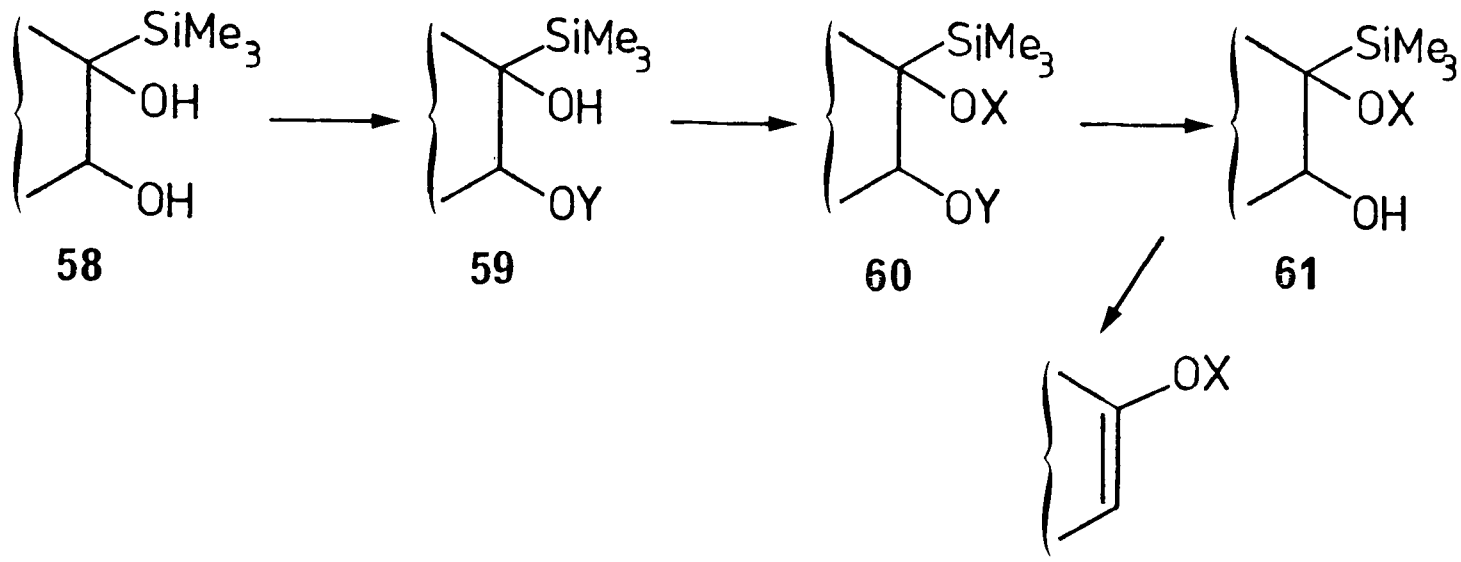
57

Reagents: i, $HClO_4/H_2O/EtOH$

Scheme 23.

Section C: Strategy for the Synthesis of Enol Ethers from 1-Trimethylsilyl-1,2-diols

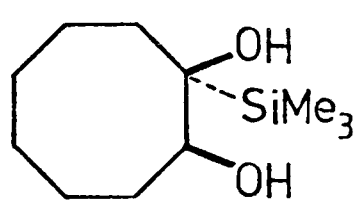
The route which was envisaged to an enol ether (62) starting from a silyl-1,2-diol (58) is shown in scheme 24. If the diol could not be transformed directly to a substituted β-hydroxysilane (61), intermediate protection-deprotection of the secondary hydroxyl group of the diol would be necessary.



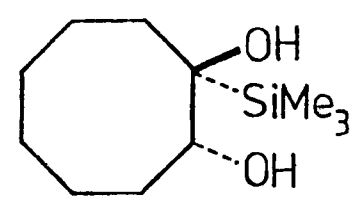
Scheme 24.

Given the availability of cyclic cis- and trans- starting diols, the final step could in principle be achieved stereospecifically by either syn- or anti-elimination of trimethylsilanol from (61). However preparation of a trans-cyclooctene derivative (45) by this route is only likely to be possible via the cis-diol (63) so that the final step involves syn-elimination. Attempts had already been made to prepare trans-cyclooctene by an anti-elimination reaction of the cis-β-hydroxysilane (46) but these were unsuccessful[38,57], and there

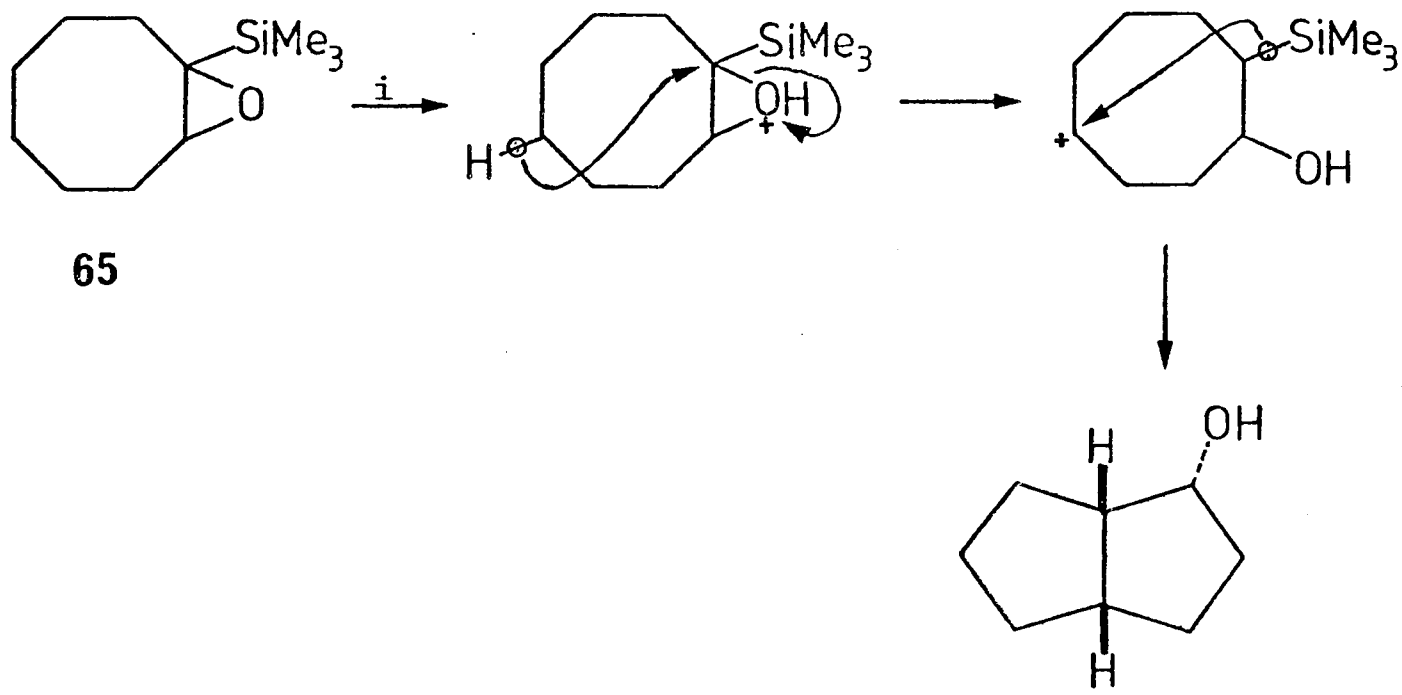
are indeed no examples of any substrate which gives a trans-cyclooctene by anti-elimination of two vicinal substituents. Furthermore the trans-diol (64) is not accessible; at least not stereospecifically by acid catalyzed ring opening of the epoxide (65). Such reactions[38,57,79] give mainly the bicyclic alcohol (66) via a mechanism involving transannular hydride migration (Scheme 25).



63



64



65

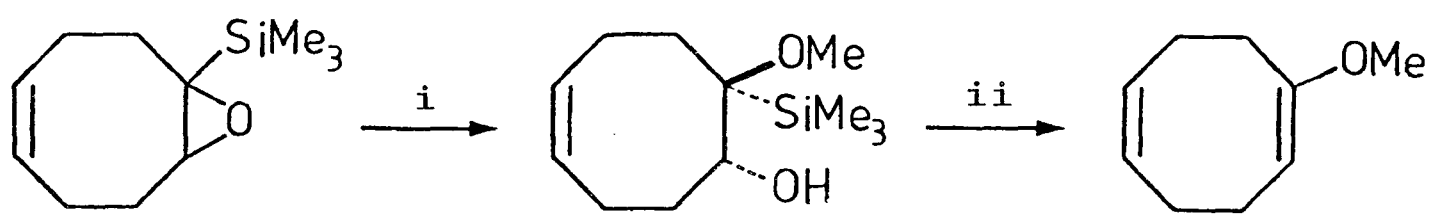
66

Reagents: i, H_2SO_4/MeOH or H_2SO_4/H_2O/dioxane

Scheme 25.

In contrast to the above reactions of (65), when the unsaturated epoxysilane (67) is treated with sulphuric acid in methanol the major product[31] is the methoxy alcohol (68).

The latter is produced via the usual attack by the nucleophile on the carbon bearing silicon[38], although an accompanying minor product is produced via transannular participation of the double bond. The enol ether (69) can be produced from (68) by a Peterson elimination reaction (Scheme 26).

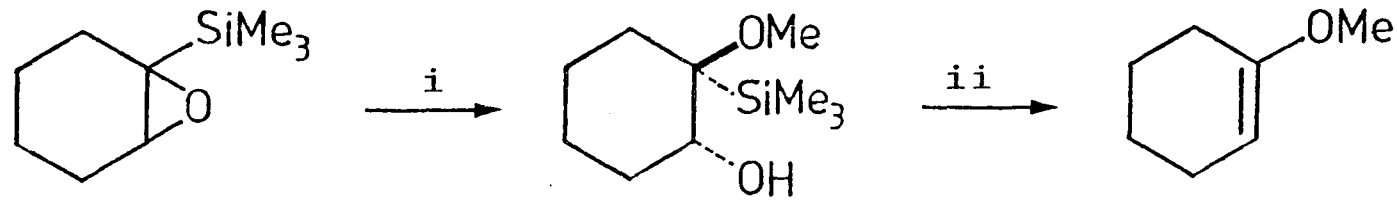


67 **68** **69**

Reagents: i, H_2SO_4/MeOH; ii, NaH/DMSO

Scheme 26.

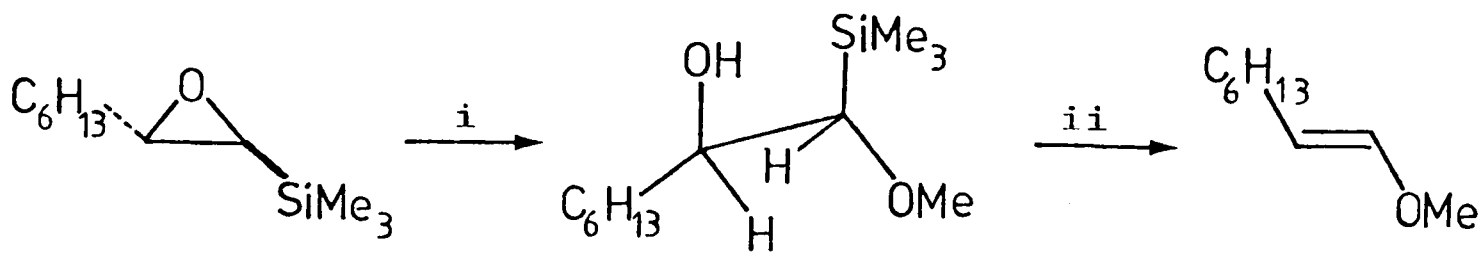
Other examples of the use of the Peterson reaction for the synthesis of enol ethers are known in cyclic[22,38] (Scheme 27) and acyclic[80] (Scheme 28) systems. The stereospecificity of the Peterson reaction is such that 97% of the enol ether produced from (72) is the E-isomer (73).



24 **70**

Reagents: i, H_2SO_4/MeOH; ii, NaH/DMF

Scheme 27.

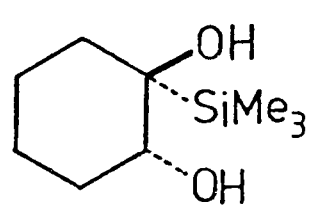


71 **72** **73**

Reagents: i, $BF_3.Et_2O/MeOH$; ii, KH/THF

Scheme 28.

During the course of the work which is to be described, it was often found difficult to prepare certain cyclooctane derivatives because of instability associated with their precursors and the anomalous reactivity of medium ring compounds in general[81]. The transformations to be used were therefore developed initially on the 1-trimethylsilylcyclohexane-1,2-diols (10) and (18) which served as model compounds. A discussion of these reactions follows in chapter 2, approaches to the trans-cyclooctene derivatives are discussed in chapter 3.



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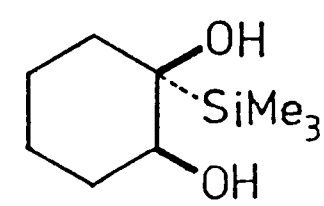


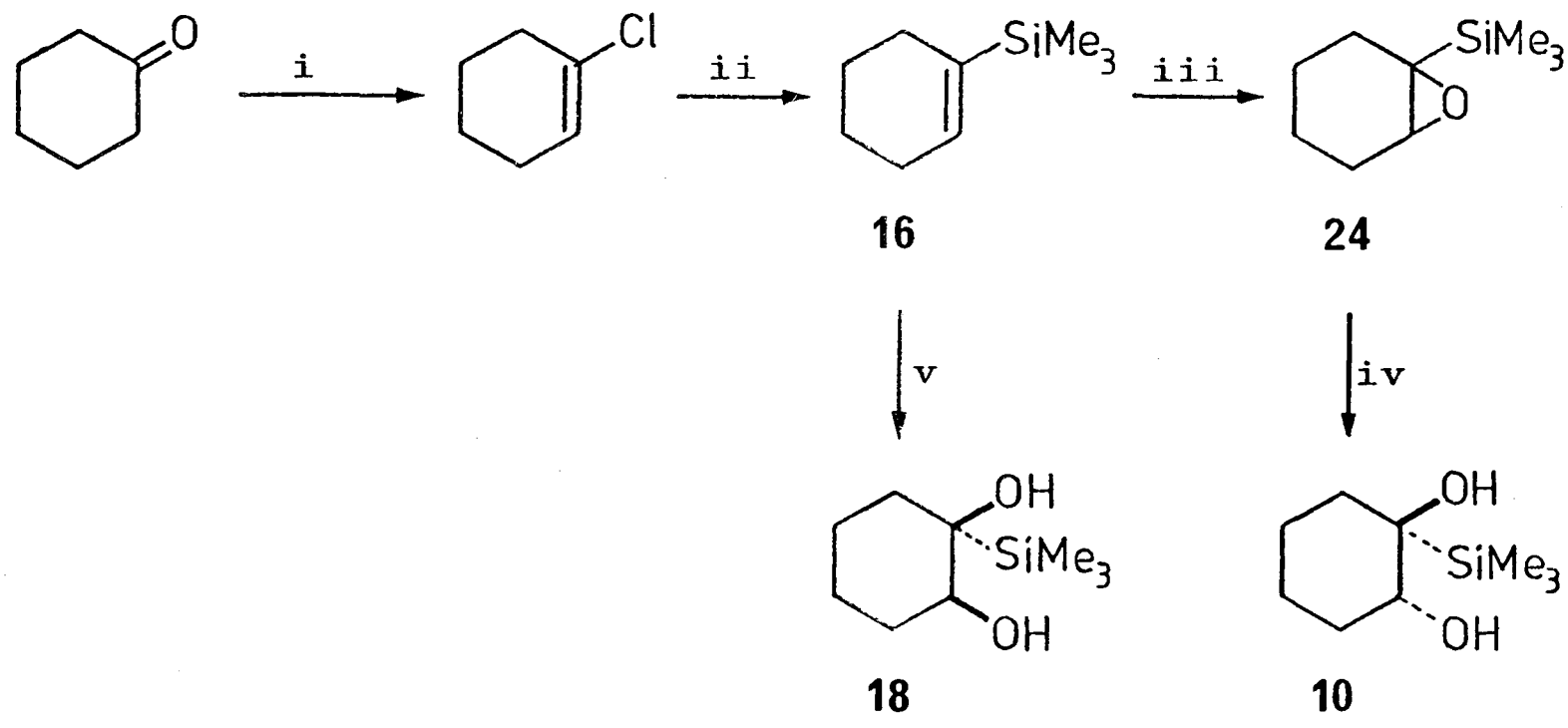
18

CHAPTER 2

THE CHEMISTRY OF CIS- AND TRANS-1-TRIMETHYLSILYCYCLOHEXANE-1,2-DIOLS

Section A: Preparation of cis- and trans-1-Trimethylsilylcyclohexane-1,2-diols

The route to the two diols is summarized in Scheme 29 Chlorination[82] of cyclohexanone followed by silylation[83] gave 1-trimethylsilylcyclohexene (16), this was converted to the trans-diol (10) by epoxidation and ring opening of the epoxide (24) with aqueous acid[22,38]. The cis-diol (18) was prepared[40] in 70% yield from the vinylsilane (16) using a procedure[84] which involves oxidation with osmium tetroxide in the presence of N-methylmorpholine-N-oxide.

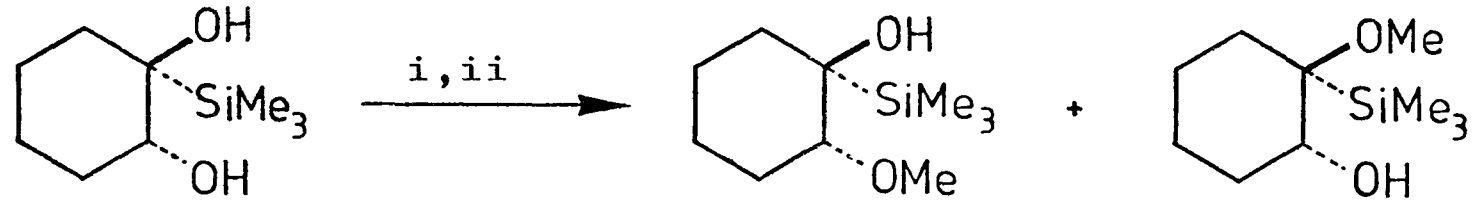


Reagents: i, PCl_5/Et_2O; ii, $Na/Me_3SiCl/Et_2O$;
iii, $CH_3CO_3H/NaOAc/CH_2Cl_2$; iv, H_2SO_4/H_2O/acetone;
v, OsO_4/N-methylmorpholine-N-oxide/H_2O/acetone

Scheme 29.

Section B: Methylation of cis- and trans-1-Trimethylsilyl-cyclohexane-1,2-diols

The first attempts to produce monoprotected derivatives of the silyl diols involved methylation. It is reported[35] that the trans-diol (10) can be transformed into a mixture of the isomeric methoxysilanes (74) and (70) by treatment with methyllithium followed by methyl iodide (Scheme 30).



10 **74** **70**

3 : 1

Reagents: i, MeLi; ii, MeI

Scheme 30.

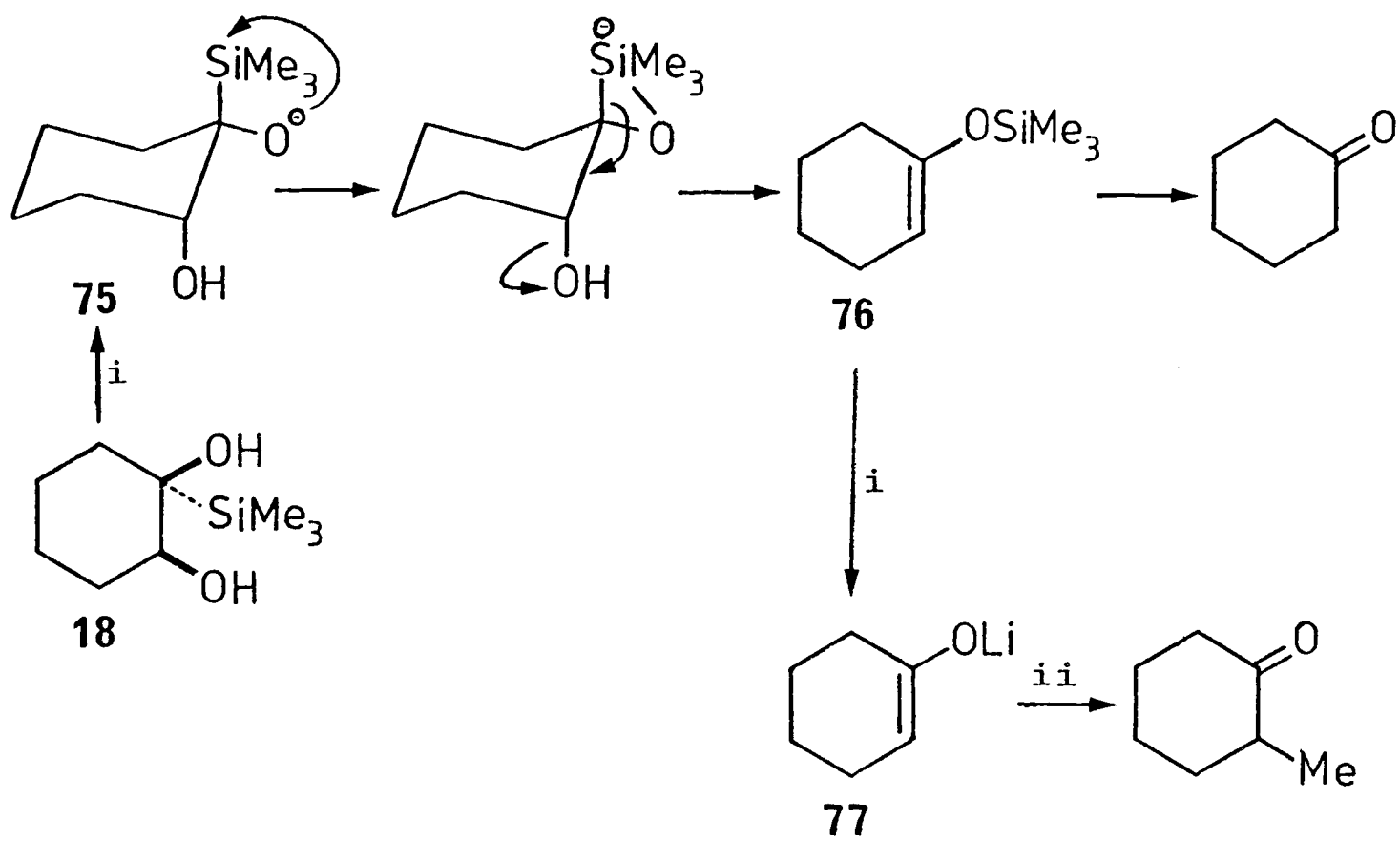
The reaction thus provides a direct route to the 1-substituted diol derivative (70). If this could be repeated and applied to other 1-trimethylsilyl-1,2-diols, it would obviate the need for intermediate protection-deprotection of the secondary hydroxyl group of the diol in the proposed enol ether synthesis (Scheme 24), assuming the mixture could be separated.

It was not, however, found possible to reproduce the above result. When the trans-diol (10) was treated with methyllithium followed by methyl iodide in dry ether, no reaction occurred and even after prolonged reaction time the starting material was recovered. When the reaction was

carried out in dry DMSO, a product was produced which was adjudged by its n.m.r. spectrum to contain about 70% of (74). Attempts were made to purify this compound by preparative t.l.c., but these were unsuccessful owing to loss of trimethylsilyl from the product. There was no indication that any of the desired product (70) had been formed by this procedure. An authentic sample of it was available for identification purposes, this had been produced by acid catalyzed reaction of the epoxide (24) with anhydrous methanol (Scheme 27). The latter procedure is not, however, a general way of preparing such derivatives. The eight membered ring epoxysilane (65) gives mainly the bicyclic alcohol (66) when treated under the same conditions and derivatives of cis-diols cannot, of course, be produced by epoxide ring opening.

On treatment with methyllithium followed by methyl iodide in DMSO, the cis-diol (18) gave rise to a mixture consisting mainly of cyclohexanone and 2-methylcyclohexanone. A possible mechanism for this transformation is shown in Scheme 31. Deprotonation of the tertiary hydroxyl group of the diol, followed by intramolecular attack on silicon and displacement of the β-hydroxyl group gives the silyl enol ether (76). The deprotonated cis-diol can achieve a conformation (75) in which the trimethylsilyl and β-hydroxyl groups are in a trans-antiparallel relationship favourable for elimination, in the case of the trans-diol (10) this is not possible. The enol ether (76) could either be hydrolyzed on work up to give cyclohexanone or cleaved by excess methyllithium[85] to give cyclohexanone lithium enolate (77) which would react with

methyl iodide to give 2-methylcyclohexanone.

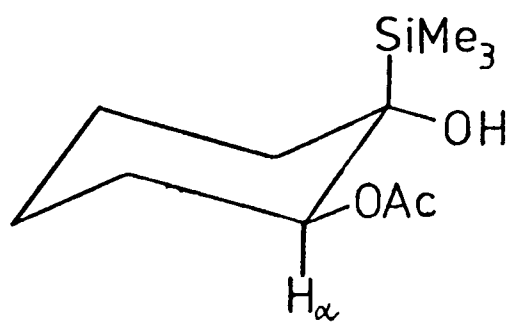


Reagents: i, MeLi/DMSO; ii, MeI

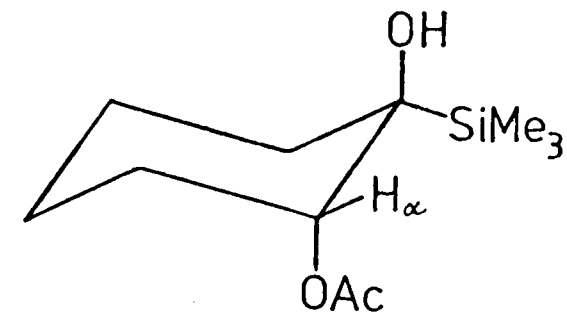
Scheme 31.

Section C: Acetylation of cis- and trans-1-Trimethylsilyl-cyclohexane-1,2-diols

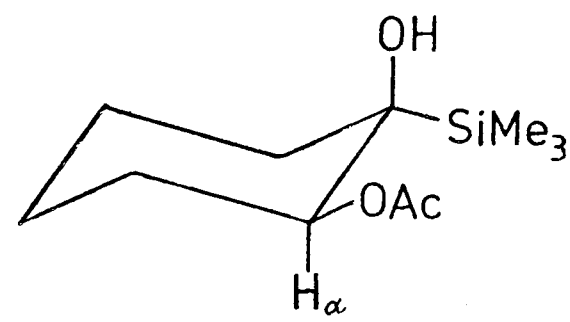
The failure of the methylation procedure to provide a direct route to a 1-substituted diol derivative necessitated the more circuitous route via intermediate protection-deprotection of the β-hydroxyl group (Scheme 24). Since the acetate group can be introduced and removed under fairly mild conditions [86,87], preparation of the trans- and cis-diol monoacetates (78) and (79) was attempted. These were obtained cleanly and in high yield from the diols by straightforward room temperature treatment with acetic anhydride in pyridine.



78a



78b

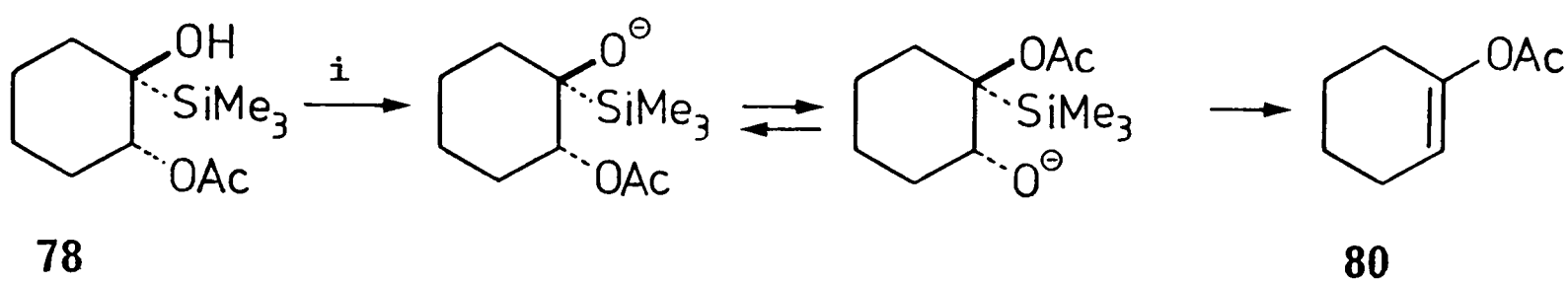


79

Information about the conformations of the two acetates could be obtained from their n.m.r. spectra. The signal due to the proton α to acetate of the cis-hydroxy acetate (79) had a width at half height (W_H) of 17.5Hz, attributable to an axial proton[88,89] in the conformation indicated. In the trans-isomer (78), however, the signal due to the corresponding proton had a W_H of 13Hz. This indicates that there are significant contributions to the conformational equilibrium from both (78a), favoured by intramolecular hydrogen bonding between acetate and hydroxyl, and (78b), favoured by having an equatorial trimethylsilyl group. In the i.r. spectra of both hydroxy acetates, there were two carbonyl bands at about 1740 and 1720cm^{-1}. This is expected on the basis of intramolecular hydrogen bonding in the conformations (78a) and (79), the two bands relate to the free and hydrogen bonded carbonyl groups[90,91].

It was thought that treatment of the hydroxy acetates with base might lead to equilibration of the acetate group

between the two hydroxyls. This would lead to the enol acetate (80) via Peterson elimination in the case of (78) (Scheme 32).



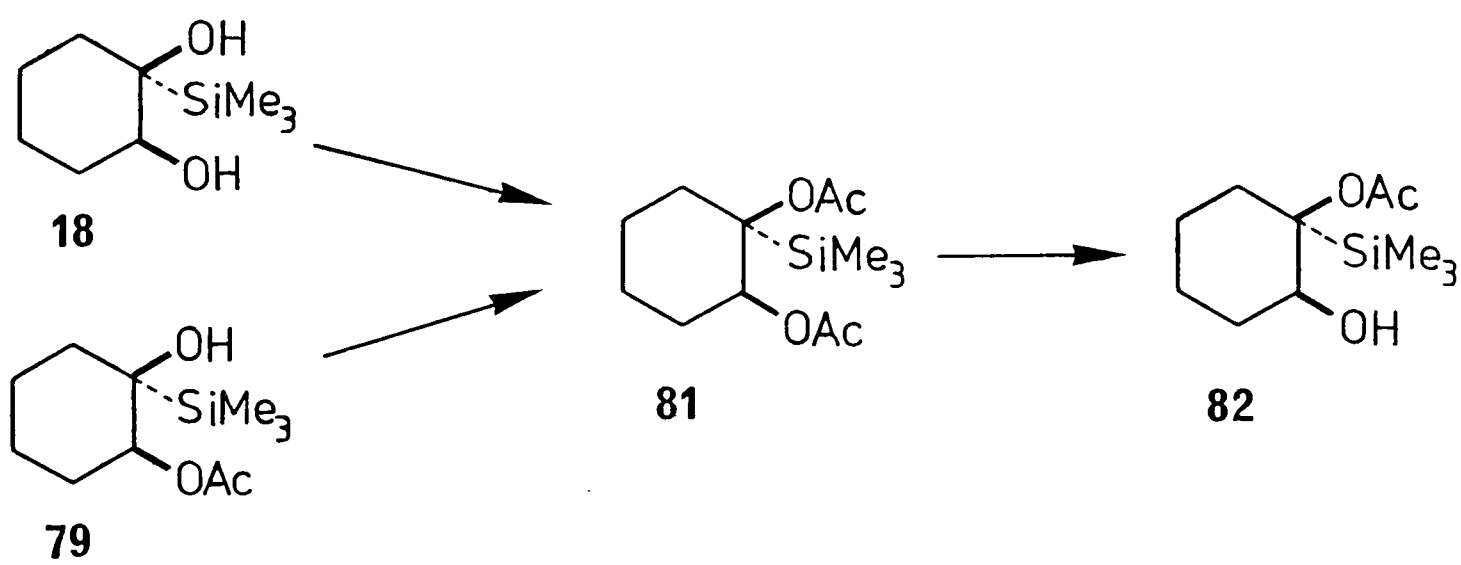
78 **80**

Reagents: i, base

Scheme 32.

When the trans-hydroxy acetate (78) was treated with sodium hydride in DMF, conditions known to bring about Peterson elimination of β-hydroxysilanes[19,22], acetate hydrolysis occurred and the diol (10) was formed. The cis-hydroxy acetate (79) was recovered unchanged after it was treated under the same conditions.

Another possible route to a 1-monoacetate derivative (82) was via the diacetate (81) as shown in Scheme 33, with the less hindered secondary acetate group removed by selective hydrolysis.



Scheme 33.

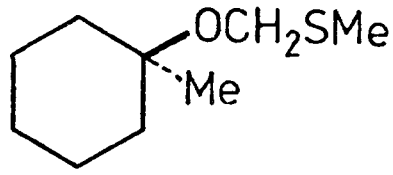
Conditions were required whereby tertiary hydroxyl groups can be acetylated. None of the diacetate was, however formed when the diol (18) was treated with acetyl chloride and N,N-dimethylaniline in ether[92] or when the hydroxy acetate (79) was treated with acetic anhydride and pyridine in dichloromethane containing a catalytic amount of 4-dimethylaminopyridine[93,94].

Section D: Methylthiomethylation of cis- and trans-2-Acetoxy-1-trimethylsilylcyclohexanols

Given that acetylation of the hydroxy acetates (78) and (79) did not seem possible, there was a limited choice of other groups which were suitable for attachment to the hindered tertiary hydroxyl. Tertiary alcohols can be methylated, for example by diazomethane and either boron trifluoride[95] or fluoboric acid[96], but it was unlikely that the rather sensitive silylated substrates would be compatible with such conditions. The methylthiomethyl group seemed worthy of attention since methylthiomethyl ethers[97-99] of even hindered tertiary alcohols[100] can be prepared under mild conditions and such ethers can be converted to methyl ethers by treatment with Raney nickel[99]. Methylthiomethyl ethers are also reported as being stable to basic and mildly acidic conditions as would be used for elimination reactions involving β-hydroxysilanes.

In order to test the procedure for methylthiomethylation, the ether (83) was prepared by treatment of 1-methylcyclohexanol with dimethyl sulphoxide, acetic anhydride, and acetic

acid. Methylthiomethyl acetate was also formed as a by-product, this was removed by treatment with methanolic potassium hydroxide. Following the same procedure as used to prepare (83), the methylthiomethyl ethers (84) and (85) were prepared in 87 and 75% yield respectively from the hydroxy acetates (78) and (79). Purification could be brought about satisfactorily by distillation by virtue of the large difference in boiling point between the ethers and methylthiomethyl acetate. In the n.m.r. spectra of (84) and (85), the signals due to the protons α to acetate had W_H of 13.5 and 14Hz, indicating that both exist as mixtures of the two possible chair conformations.



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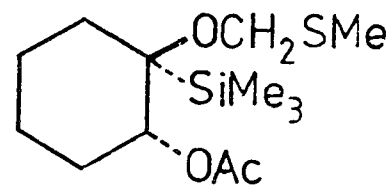

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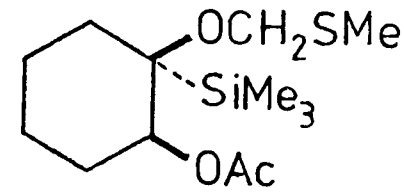
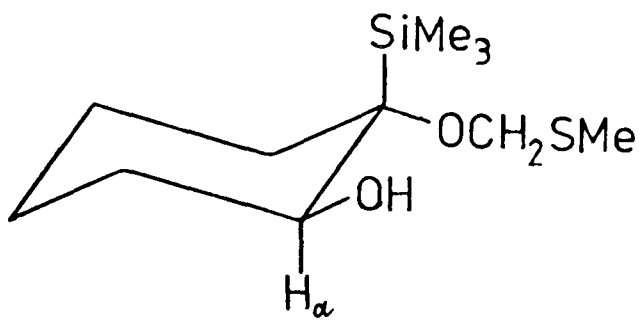


85

The β-hydroxysilanes (86) and (87) were obtained in 80 and 72% yield respectively from (84) and (85) by treatment with methanolic potassium hydroxide. The proton α to hydroxyl in the n.m.r. spectrum of (87) resonated at δ3.5, W_H=17.5Hz, attributable to an axial proton in the conformation shown. The analogous proton in (86) resonated at δ4.05, W_H=16Hz, also attributable to a predominantly axial proton in the conformation shown which could perhaps be favoured by intramolecular hydrogen bonding although it has an axial trimethylsilyl group. The appearance of the signal due to the

methylene protons of the methylthiomethyl group of (86) as an AB quartet, rather than the usual singlet is possibly another indication of intramolecular hydrogen bonding.



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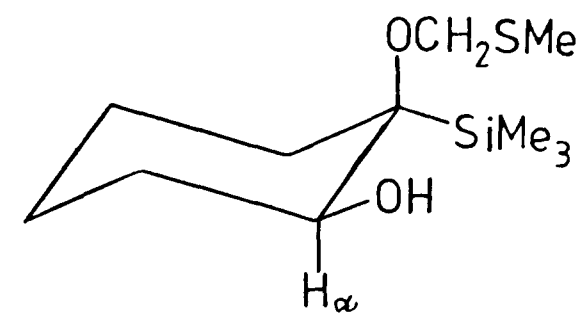
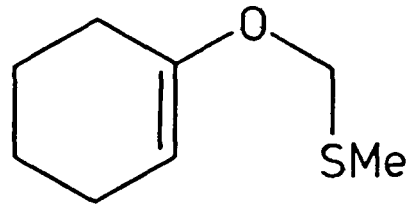


87

Section E: Elimination Reactions Involving cis- and trans-2-Trimethylsilyl-2-methylthiomethoxycyclohexanols

Although the original plan was aimed at the preparation of methyl enol ethers, the availability of the α-methylthiomethoxy-β-hydroxysilanes (86) and (87) made the novel methylthiomethyl ether (88) potentially available by either syn-elimination starting from the cis-β-hydroxysilane (86) or anti-elimination involving the trans-β-hydroxysilane (87).



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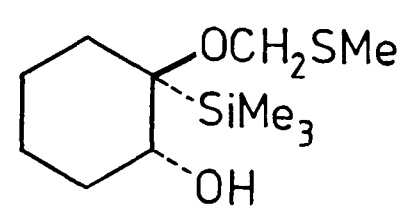

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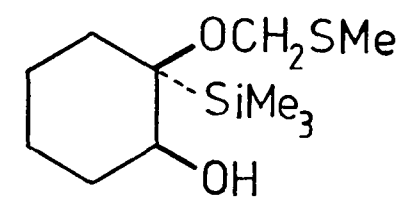
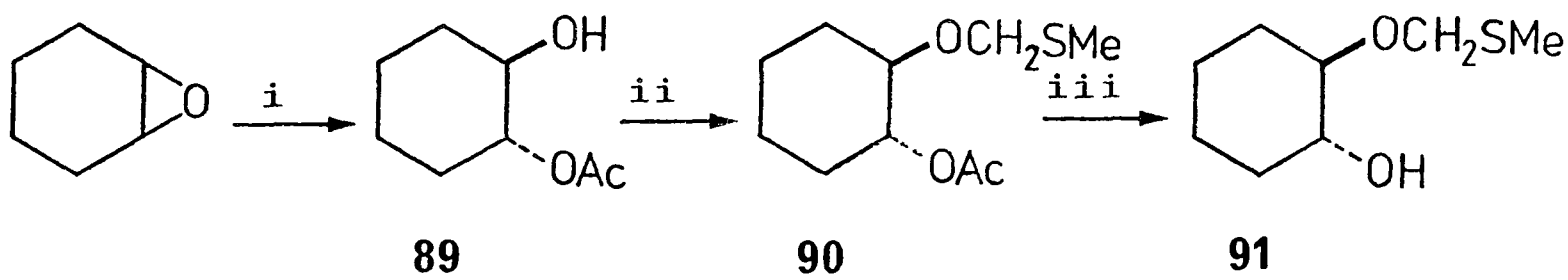


87

(i) Reactions of the cis-β-hydroxysilane (86)

The optimum conditions for bringing about base promoted syn-elimination from a β-hydroxysilane are potassium hydride in THF [19,21,28]. Under these conditions, 1-methylthiomethoxycyclohexene (88) was formed from (86) in 90% yield as an oil which decomposed slowly on standing, the main product from the decomposition was cyclohexanone.

A single product, different from (88), was isolated from the reaction of (86) with potassium t-butoxide in DMSO[19]. The structure (91) was tentatively assigned (^{1}H and ^{13}C n.m.r.), which could arise from (86) by protodesilylation with retention of stereochemistry at the carbon bearing silicon. This structure, and in particular the trans-stereochemistry was proven by the preparation of an authentic sample of (91) from cyclohexene oxide by the route shown in Scheme 34.



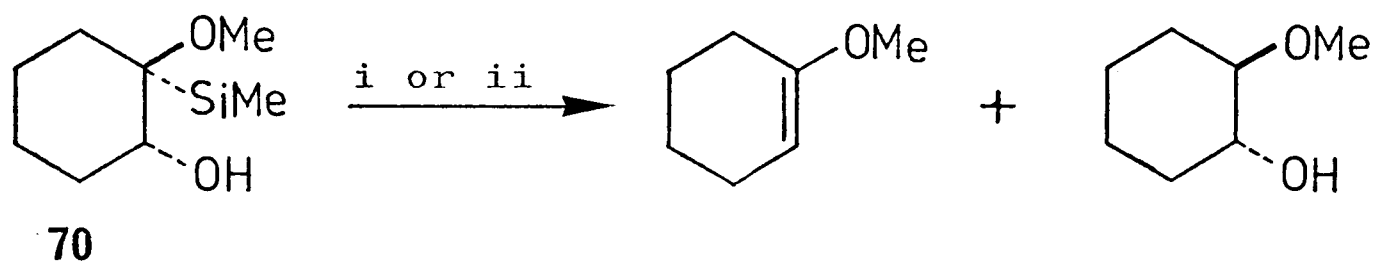
89 90 91

Reagents: i, glacial AcOH; ii, $DMSO/Ac_2O/AcOH$; iii, KOH/MeOH

Scheme 34.

Potassium t-butoxide has previously been shown to bring about desilylation, for example t-butyltrimethylsilyl ether is produced when tetramethylsilane or benzyltrimethylsilane are treated with potassium t-butoxide[101]; and partial desilylation

of the β-hydroxysilane (70) occurs with retention of stereochemistry, when it is treated with potassium t-butoxide in t-butanol under quite vigorous conditions[35] (Scheme 35).



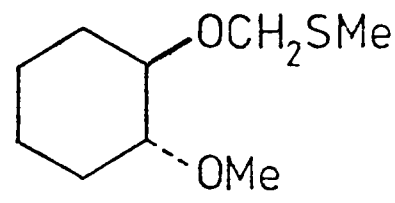
70

i	35	:	65
ii	65	:	35

Reagents and conditions: i, t-BuOK/tBuOH/reflux/24h;
ii, NaH/DMF/25°/1h

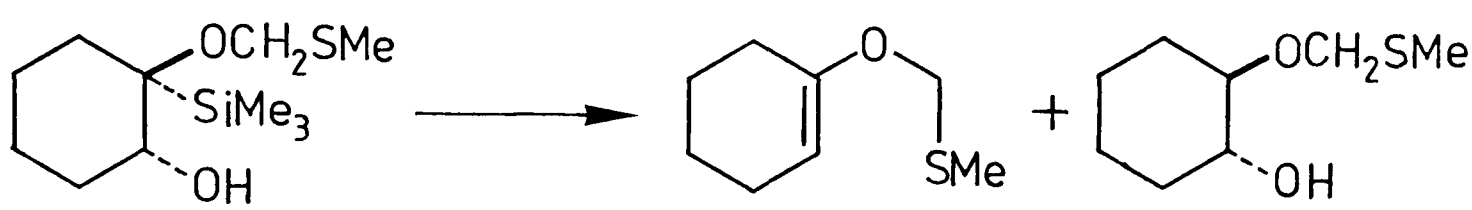
Scheme 35.

In an attempt to find out whether a carbanion intermediate in the desilylation of (86) could be trapped, the reaction with potassium t-butoxide was repeated and quenched with excess methyl iodide. The n.m.r. spectrum of the crude product indicated that it consisted of mainly (91), and its O-methylated derivative (92); the latter was isolated in 69% yield by preparative g.l.c.



92

The reaction of (86) with sodium hydride in DMF gave a mixture of the enol ether (88) and desilylated product (91) in roughly 2:1 ratio (Scheme 36), cf. the corresponding methyl ether (Scheme 35).



86 **88** **91**

66 : 34

Reagents and conditions: NaH/DMF/0 °/1h

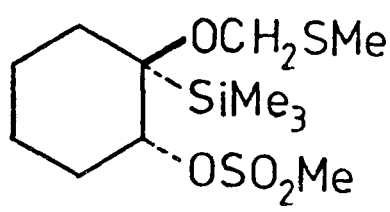
Scheme 36.

(ii) Reactions of the trans-β-hydroxysilane (87)

The preferred procedure for anti-elimination involving (87) was treatment with methanesulphonyl chloride in pyridine[21], which gave (88) in 94% yield. For comparison with this reaction, and with the base promoted eliminations, the cis-β-hydroxysilane (86) was also treated with methanesulphonyl chloride in pyridine. The spectroscopic data of the crude product indicated the presence of starting material, some enol ether (88) (confirmed by co-injection on g.l.c. with an authentic sample), and the methanesulphonate (93). Isolation of the latter compound was attempted by preparative t.l.c., but decomposition was found to occur under these conditions.

Anti-elimination to give (88) from (87) could also be

brought about by treatment with p-toluenesulphonyl chloride in pyridine, but this reaction was much slower than with methanesulphonyl chloride. The use of boron trifluoride etherate[21,28] converted (87) to cyclohexanone; the enol ether (88) may well have been formed but would not be stable to the reaction conditions, as shown in a separate experiment.



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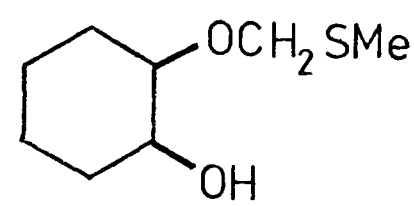


94

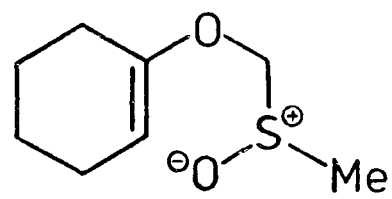
Desilylation of (87) occurred when it was treated with potassium t-butoxide in DMSO. A single product was formed which had spectroscopic data compatible with structure (94), analogous, though not identical to the data of the trans-isomer (91); (94) and (91) gave separate peaks on g.l.c. The above result confirms the high stereospecificity with which desilylation of such β-hydroxysilanes is brought about using potassium t-butoxide.

As expected, reaction of (87) with potassium hydride in THF was much slower than the reaction of (86) under the same conditions. After all the starting material was consumed, the desilylated product (94) was obtained; this was presumably formed via the alkoxide derived from deprotonation of (94), rather than by potassium hydride directly.

A series of transformations has thus been achieved where-

by the same enol ether (88) can be derived from either of the 1-trimethylsilylcyclohexane-1,2-diols (10) or (18) using stereospecific elimination reactions of the β-hydroxysilanes (86) and (87) to form the double bond. The clean reaction of the cis-β-hydroxysilane (86) with potassium hydride in THF in particular indicates the feasibility of bringing about an analogous series of transformations on an eight membered ring substrate to produce a trans-cyclooctene derivative.

The enol ether (88) is apparently the first compound of its type to have been prepared and it and its derivatives may have interesting chemistry; for example on paper at least, electrocyclic rearrangements of its sulphoxide (95), and ylide (96), derivatives would appear possible.



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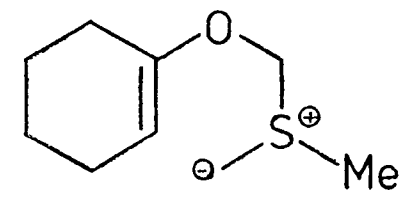
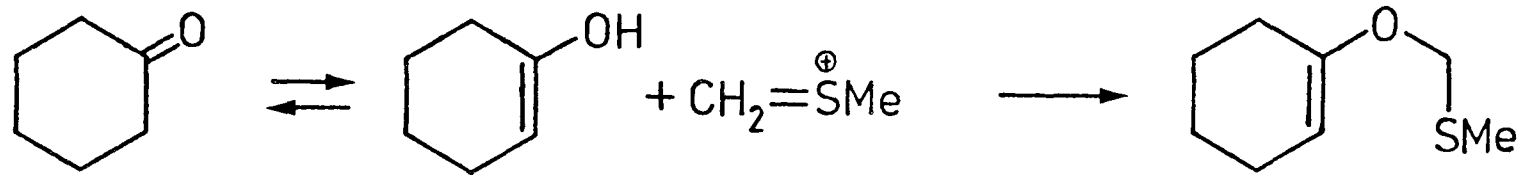


96

Section F: An Alternative Approach to 1-Methylthiomethoxy-cyclohexene

Because of the length of the route to 1-methylthiomethoxy-cyclohexene (88) (8 steps from cyclohexanone), it was of interest to see whether (88) could be produced directly from cyclohexanone by treatment with dimethyl sulphoxide, acetic

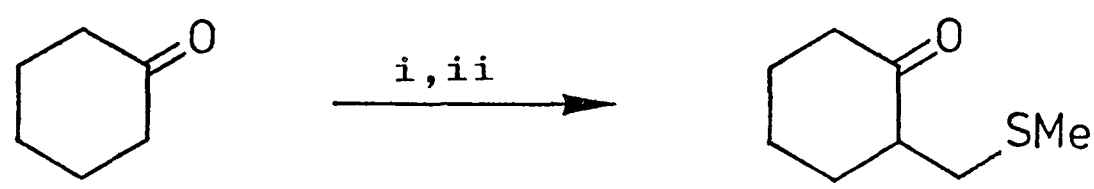
anhydride, and acetic acid. This might take place via a mechanism (Scheme 37) involving O-alkylation of cyclohexanone enol by the same electrophile (97) as that involved in the formation of methylthiomethyl ethers.



97 **88**

Scheme 37.

G.l.c. indicated that the product produced by treatment of cyclohexanone under the above conditions consisted of unreacted cyclohexanone and methylthiomethyl acetate. However when the product was purified using methanolic potassium hydroxide, the C-alkylated derivative of cyclohexanone (98) was apparently produced, together with dialkylated derivatives. This conclusion was corroborated by the production of (98) in 64% yield when cyclohexanone was treated with one equivalent of lithium diisopropylamide, followed by methylthiomethyl acetate (Scheme 38).



98

Reagents: i, lithium diisopropylamide/THF; ii, $MeSCH_2OAc$

Scheme 38.

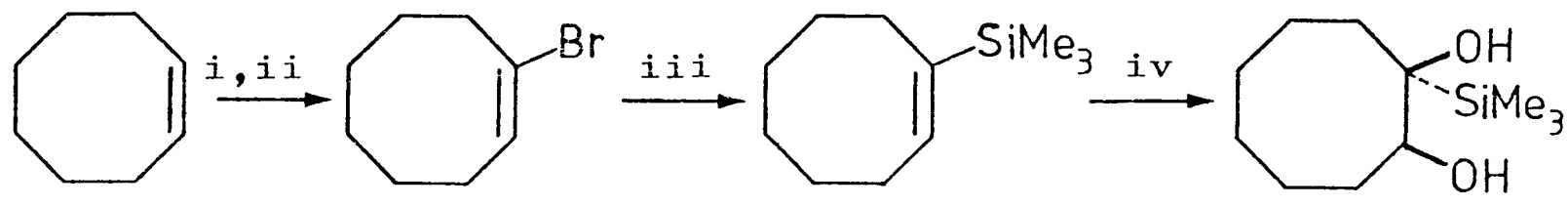
CHAPTER 3

APPROACHES TO 1-ALKOXY-TRANS-CYCLOOCTENES

The work described in this chapter related only to 1-trimethylsilyl-*cis*-cyclooctane-1,2-diol (63) since, for the reasons discussed in chapter 1 the corresponding *trans*-diol (64) was not suitable as a precursor of 1-alkoxy-*trans*-cyclooctenes.

Section A: Preparation and Methylation of 1-Trimethylsilyl-cis-cyclooctane-1,2-diol

The route which was developed to the *cis*-diol (63) (Scheme 41) is analogous to that used for the corresponding *cis*-cyclohexane diol (18), although it starts from the *cis*-cycloalkene rather than the cycloalkanone as the former is much cheaper in the case of the eight membered ring compounds.



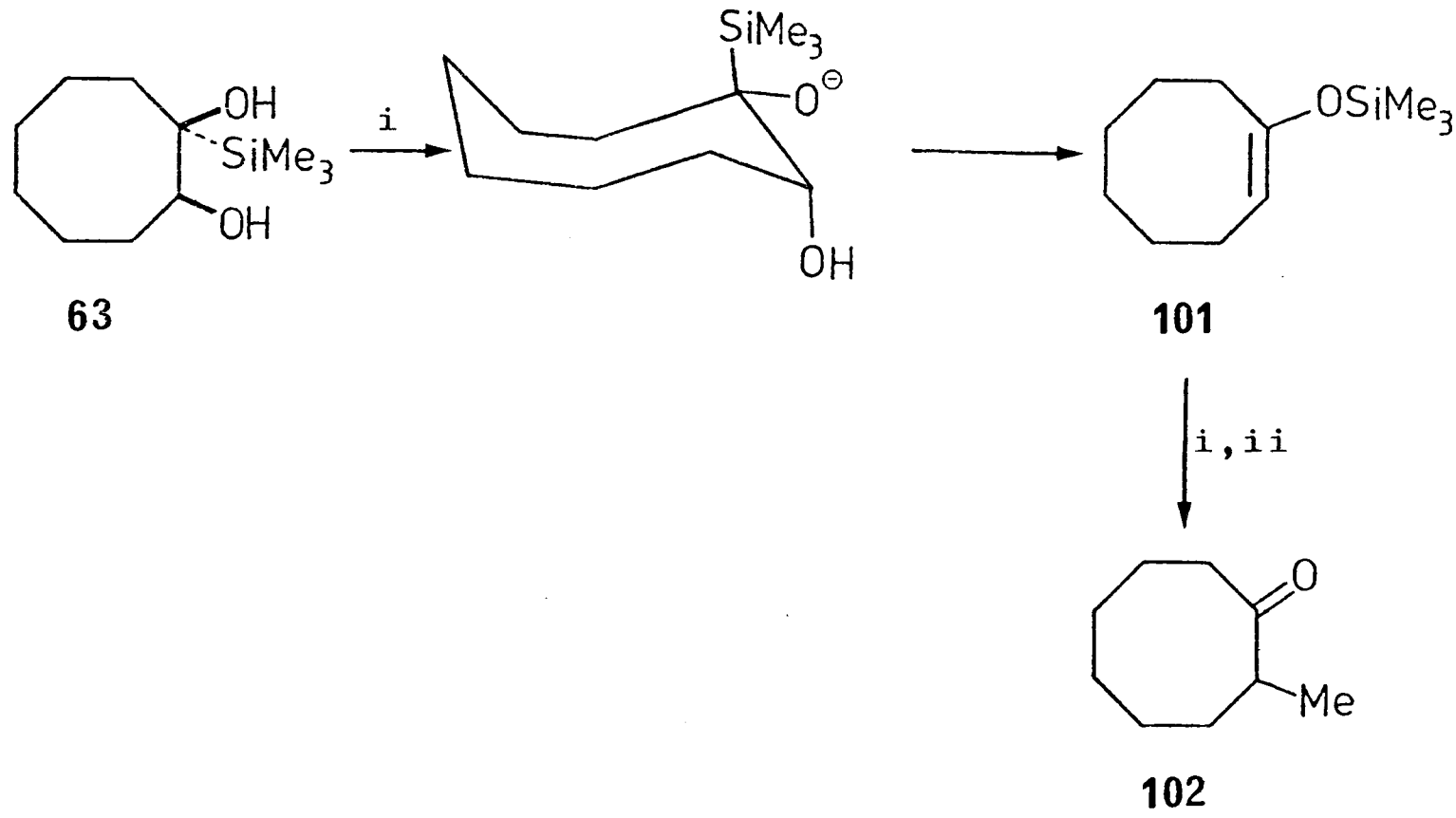
99 **100** **63**

Reagents: i, Br_2/CCl_4; ii, Morpholine/PhMe; iii, $Na/Me_3SiCl/Et_2O$; iv, OsO_4/N-methylmorpholine-N-oxide/H_2O/acetone

Scheme 41.

1-Bromo-cis-cyclooctene (99), prepared by bromination-dehydrobromination of cyclooctene, was converted in 77% yield to the vinylsilane (100) by means of the sodium sand procedure[83]. The organo-lithium procedure[57] which had previously been used for the preparation of (100) gave a poorer yield. The cis-diol (63) was obtained from (100) in 74% yield by oxidation with osmium tetroxide and N-methyl-morphioline-N-oxide.

As was the case for the six membered ring diol (18), no O-methylation occurred when (63) was treated with methyl-lithium followed by methyl iodide in DMSO. The main product of this reaction was 2-methylcyclooctanone (102), presumably formed by an analogous mechanism (Scheme 42) to that by which 2-methylcyclohexanone was formed from (18) (Scheme 31).

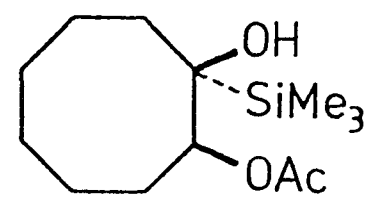


63 101 102

Reagents: i, MeLi/DMSO; ii, MeI

Scheme 42.

Section B: Acetylation of 1-Trimethylsilyl-cis-cyclcoctane-1,2-diol

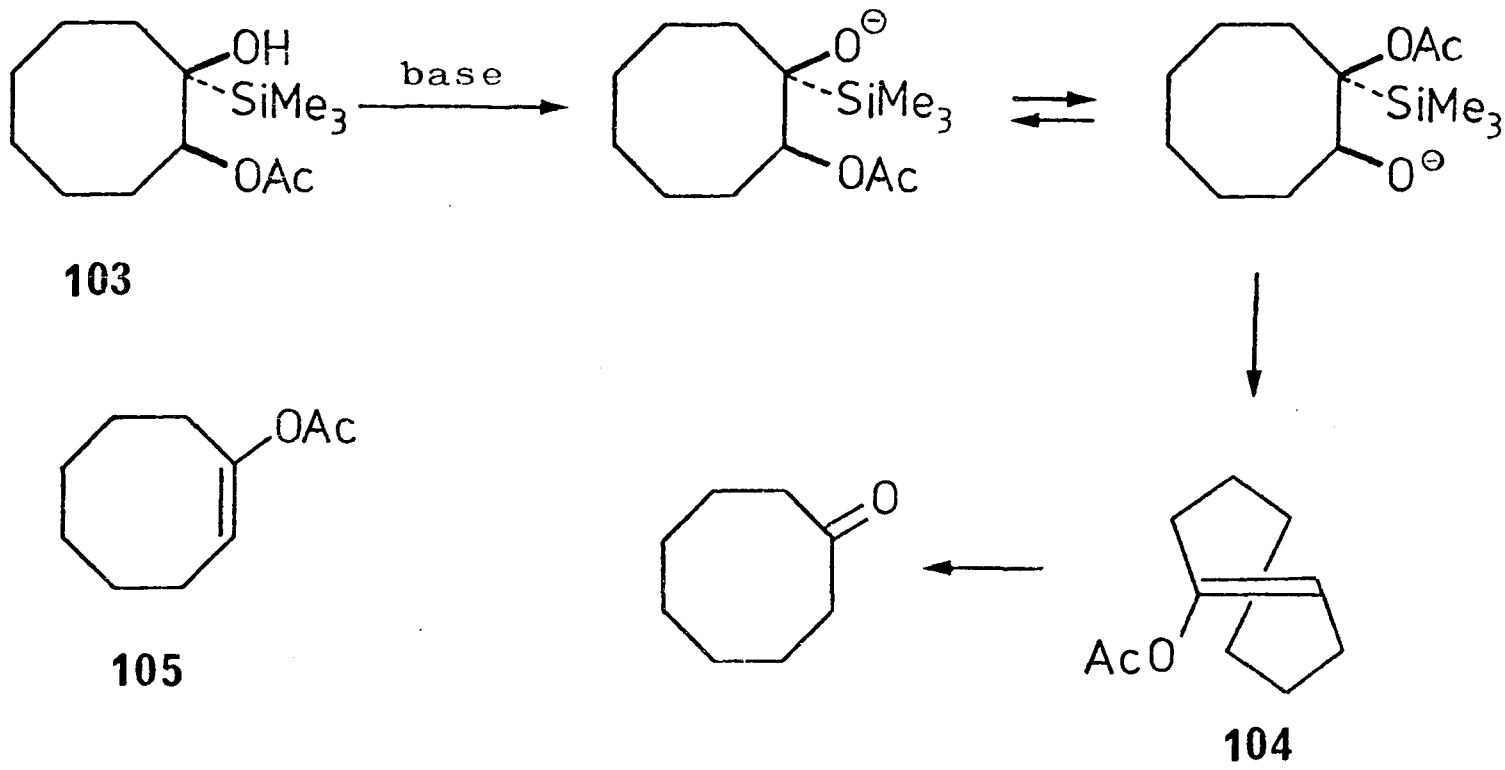


103

On a small scale, the acetate (103) could be prepared from (63) by room temperature treatment with acetic anhydride in pyridine, the same conditions as used for acetylation of the six membered ring diols. This procedure was, however, unsuitable for preparation of (103) on a preparative scale (>1g) because problems associated with the acidic work up led to decomposition of (103) to cyclooctanone. Eventually a reproducible alternative procedure for acetylation was established which involved treatment of the diol (63) at -20^{o} with 2 equivalents of acetic anhydride and pyridine in dichloromethane containing 0.1 equivalent of 4-dimethylamino-pyridine[93,94].

To see whether base induced ester exchange followed by Peterson elimination could be brought about (Scheme 43), (103) was treated with sodium hydride in DMF. The reaction product, cyclooctanone, could have been derived from the hoped for trans-enol acetate (104) but more likely is a mechanism analogous to that in Scheme 42 with acetate rather than hydroxide as the leaving group. The latter mechanism would

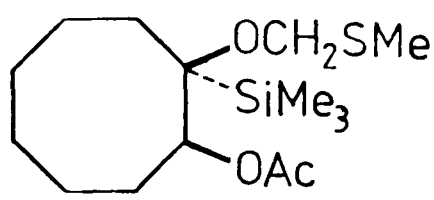
give the silyl enol ether (101) as an initial product; in separate experiments authentic samples of both (101) and the cis-enol acetate (105) were shown to be converted to cyclo-octanone when treated under the same conditions. The reaction of the eight membered ring diol monoacetate (103) with sodium hydride in DMF contrasts with the behaviour of the six membered ring compounds (78) and (79) which did not undergo a corresponding conversion to cyclohexanone.



Scheme 43.

Section C: 1-Methylthiomethoxy-trans-cyclooctene

Methylthiomethylation of the eight membered ring hydroxy acetate (103) was achieved smoothly using dimethylsulphoxide, acetic anhydride, and acetic acid. In contrast to (103), the methylthiomethyl ether (106) was quite stable and could be purified by distillation (72% yield).



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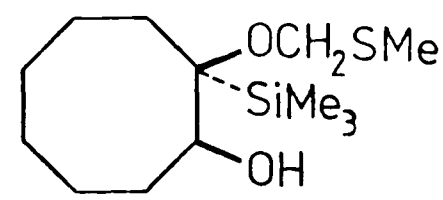
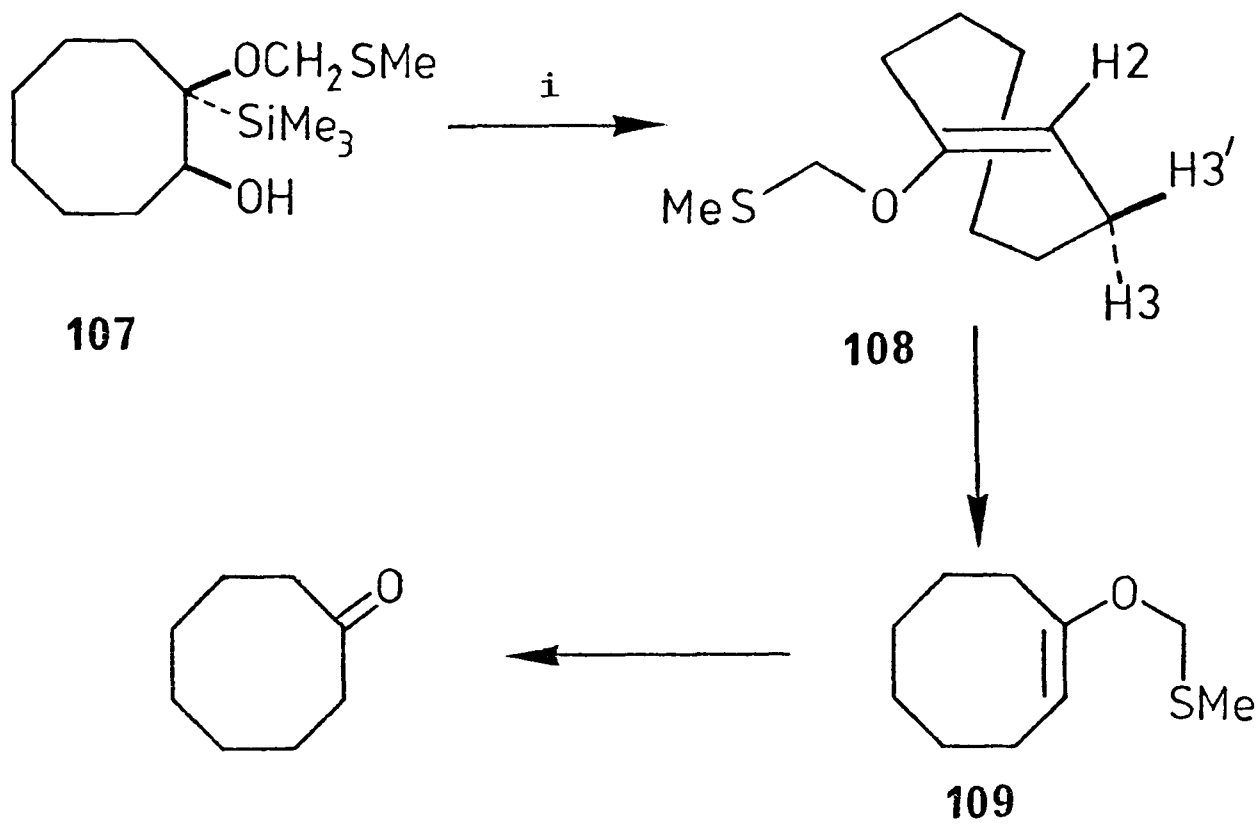


107

The acetate group of (106) was hydrolyzed by treatment with 10% methanolic potassium hydroxide giving the trans-β-hydroxysilane (107) in 73% yield.

Treatment of (107) with potassium hydride in THF, the conditions found best for bringing about Peterson elimination in the six membered ring analogue (86) resulted in all the starting material being consumed. The n.m.r. spectrum of the product showed a doublet of doublets at δ4.93, attributable to an olefinic proton. The coupling constants, J_{H2H3}, 4Hz and J_{H2H3} 12.5Hz, were similar to those of the olefinic proton in trans-cyclooctene (4.5 and 10Hz)[59] and 1-methyl-trans-cyclooctene (48) (5.5 and 10Hz)[67]. Also present were singlets at δ4.88 (methylene α to S and O) and δ2.17 (SMe group). The i.r. spectrum had bands at 3020 (vinylic C-H stretch) and 1660cm^{-1} (C=C stretch) (cf. trans-cyclooctene 1658 and 1-methyl-trans-cyclooctene 1654cm^{-1}). It is therefore concluded that 1-methylthiomethoxy-trans-cyclooctene (108) had been formed (Scheme 44).



Reagents and conditions: i, KH/THF/0°/20min

Scheme 44.

The trans-enol ether (108) was unstable and purification of the compound was not possible. Its behaviour on standing was consistent with the transformations shown in Scheme 44. Initially isomerization to the corresponding cis-enol ether (109) occurred, but that compound was also unstable and decomposed slowly to cyclooctanone. A freshly prepared sample contained about 80% (108) and 20% (109), the latter presumably arising by isomerization. The isomerization could be followed by n.m.r., the spectrum of the product (109) differed from (108) in showing a distinct signal at δ4.53 for the olefinic proton which was a triplet (J 7.5Hz), characteristic of an olefinic proton on a cis double bond in an eight membered ring, rather than a doublet of doublets.

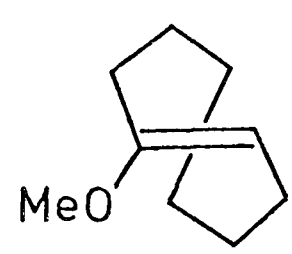
The two compounds could also be distinguished by the singlet at δ4.78 for the methylene α to S and O, the signals for the SMe groups of (108) and (109) were very close in chemical shift, but were just resolved at 300MHz. The half life of (108) was about 40 min in $CDCl_3$ or CCl_4 solution at room temperature, the cis-isomer (109) was much more stable but not sufficiently so to permit purification of an analytical sample. Samples containing (109) did, however, give rise to a symmetrical long retention time peak on g.l.c., and by means of g.l.c.-mass spectroscopy the mass spectrum showing a molecular ion at high resolution were obtained. These were consistent with structure (109).

Attempts were made to obtain an adduct of the trans-enol ether (108) by generating it in the presence of 1,3-diphenyl-isobenzofuran, which is generally a very reactive diene in Diels-Alder reactions[67,74,102]. However no adduct was obtained, possibly because of the mild conditions under which trapping was attempted which were necessary because of the instability of (108).

Section D: 1-Methoxy-trans-cyclooctene

The results of section C showed that the preparation of a 1-alkoxy-trans-cyclooctene was possible and that the Peterson elimination reaction permits the generation of the trans-double bond. It was not clear, however, whether the instability of 1-methylthiomethoxy-trans-cyclooctene (108) was due to its strain, or to it being a methylthiomethyl enol

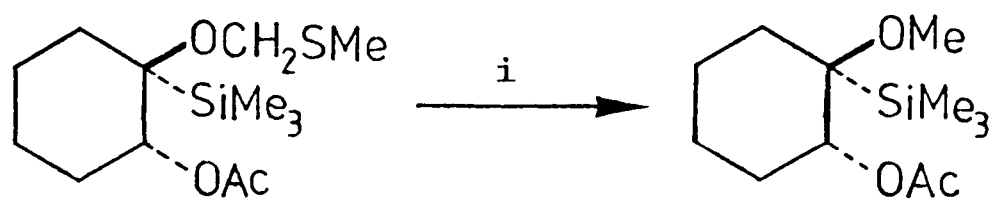
ether. From the behaviour of the unstrained eight and six membered ring compounds (109) and (88), it seemed that such enol ethers have inherent instability. On this basis, it was of interest to prepare the structurally more simple methoxy derivative of trans-cyclooctene (110).



110

It appeared that (110) would be accessible via an analogous series of transformations to those used to prepare (108) since, as mentioned earlier, methyl ethers can be derived from methylthiomethyl ethers by treatment with Raney nickel[99]. Desulphurization by Raney nickel is, of course, a widely used reaction both in organic synthesis and the structure determination of sulphur containing compounds[103], however examples of the reaction as applied to methylthiomethyl ethers are mainly in carbohydrate chemistry[104]. In planning the synthesis of (110), it was considered that it would be best to carry out the desulphurization of the stage of (106) because of the greater stability of this compound.

Desulphurization was initially attempted on the six membered ring compound (84) as a model. Treatment with a tenfold excess of Raney nickel in ethanol at 70-80^{o} for 1h gave the methoxy acetate (111) in 89% yield (Scheme 45).

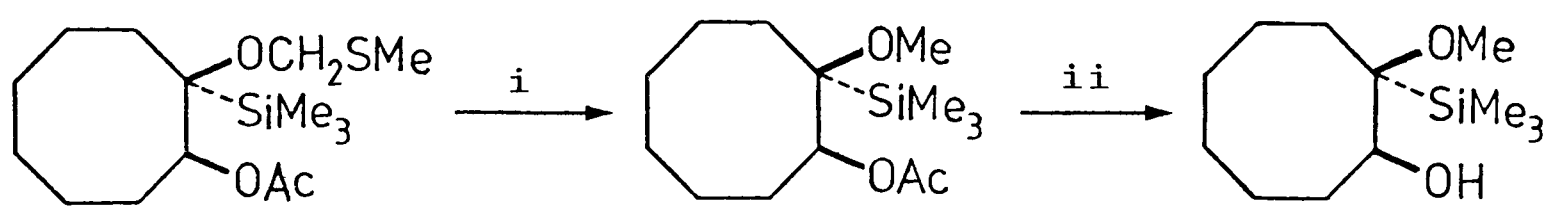


84 **111**

Reagents and conditions: i, Raney Ni/EtOH/70-80°/1h

Scheme 45.

As had been found previously, the eight membered ring compound was much more sensitive than its six membered ring analogue. When (106) was treated under the same conditions as above, some of the desired compound (112) was produced, but the n.m.r. spectrum of the product also indicated that there were several other components present including a compound apparently containing a C-ethyl group, the latter presumably having been derived from solvent. Examples of Raney nickel bringing about such alkylations are known[105]. After attempting the reaction in a number of solvents under various conditions it was found that clean Raney nickel desulphurization of (106) could be achieved in benzene at 25-30° for 1h giving (112) in 94% yield. The acetate group of (112) was removed by hydrolysis to give the β-hydroxysilane (113) in 79% yield (Scheme 46).

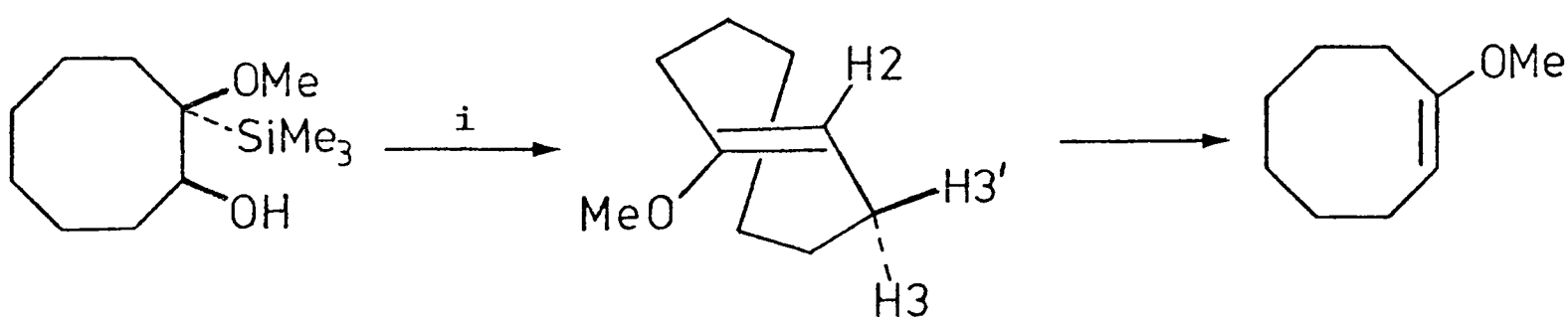


106 **112** **113**

Reagents and conditions: i, Raney Ni/benzene/25-30°/1h;
ii, KOH/MeOH/45°/16h

Scheme 46.

The reaction of (113) with potassium hydride in THF gave an oil, the n.m.r. spectrum of which showed a doubet of doublets at δ4.63, attributable to an olefinic proton. The coupling constants, $J_{H2H3'}$ 4.3Hz and J_{H2H3} 12.3Hz, were similar to those found for 1-methylthiomethoxy-trans-cyclooctene (108) and other trans-cyclooctenes (see page 47). Also present was a sharp singlet at δ3.57 (OMe group). In the i.r. spectrum of the product, there were characteristic bands at 3040 (vinylic C-H stretch) and 1660cm^{-1} (C=C) stretch. We thus conclude that 1-methoxy-trans-cyclooctene (110) had been formed (Scheme 47).



113 **110** **114**

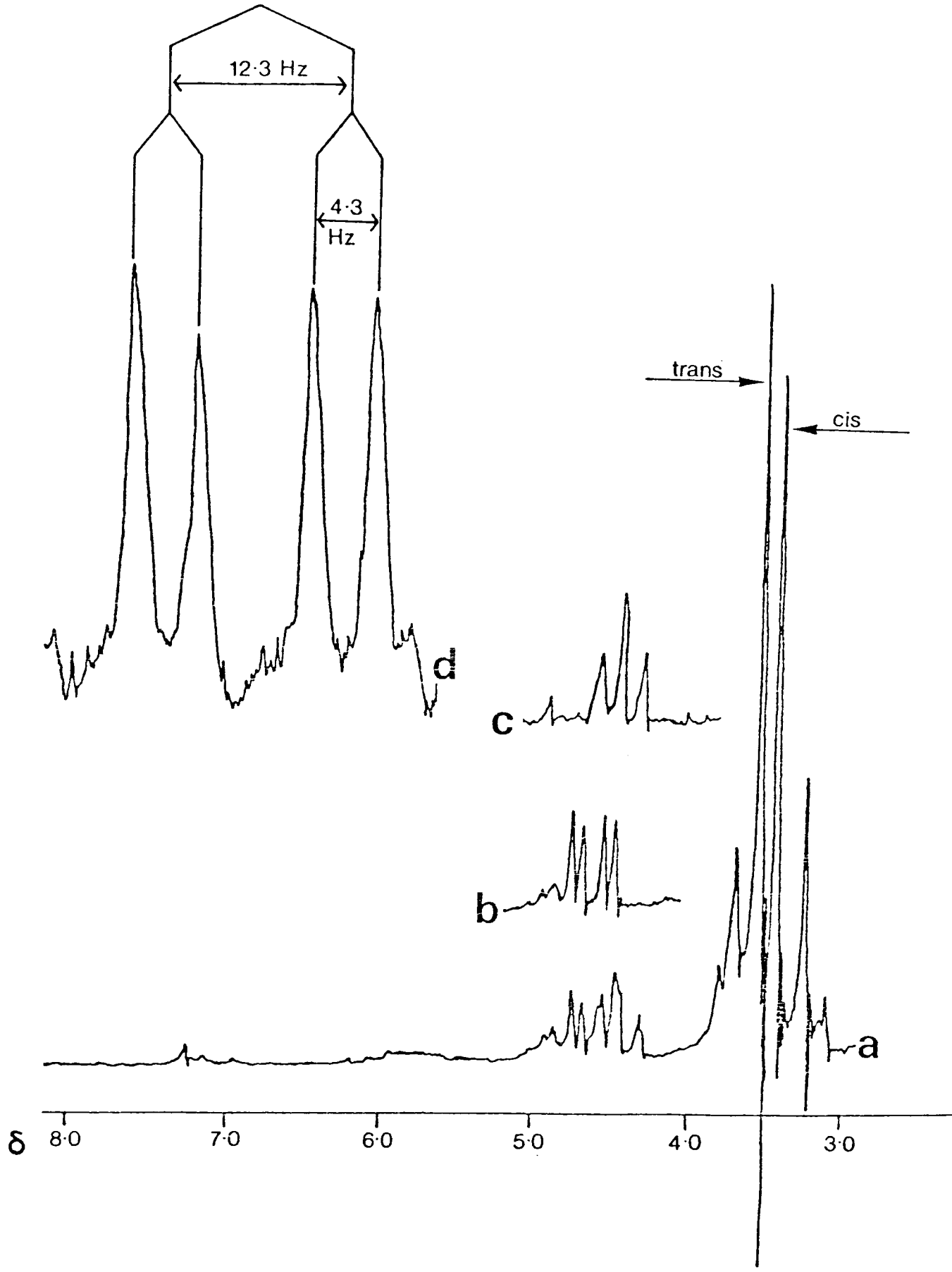
Reagents and conditions: i, KH/THF/0°/30min

Scheme 47.

The behaviour of (110) on standing was reminiscent of (108) in that it isomerized to the cis-enol ether (114). The latter compound, however, unlike the product of isomerization of (108) is stable and well known; an authentic sample of it had been prepared[106] for comparison purposes. A freshly prepared sample contained about 91% trans- (110) and 9% cis-enol ether (114). This proportion is greater than was the case for the methylthiomethoxy compounds (108) and (109) and is presumably a reflection of the fact that (110) is somewhat more stable than (108), the former had a half life in solution of about 70 min at 36°. The isomerization of (110) could conveniently be followed by n.m.r. since the methoxyl and olefinic proton signals were readily distinguished (see figure 2). A rough study of the kinetics of the isomerization could be made by n.m.r., assuming that the peak height, p, of the methoxyl signal of (110) was proportional to the concentration of (110). The approximate straight line plots of ln p vs. time (Figure 3) in both $CDCl_3$ (A) and CCl_4 (B) solution indicate that the isomerization follows first order kinetics although the rate is faster in CCl_4 than $CDCl_3$; the reason for this solvent effect is not clear.

Isolation of a pure sample of (110) was not possible, the isomerization was rapidly accelerated by heating so distillation was excluded and even freshly prepared samples gave only a single long retention time peak on g.l.c. co-incident with that from an authentic sample of the cis-isomer (114).

It is not easy to explain why 1-methoxy-trans-cyclooctene



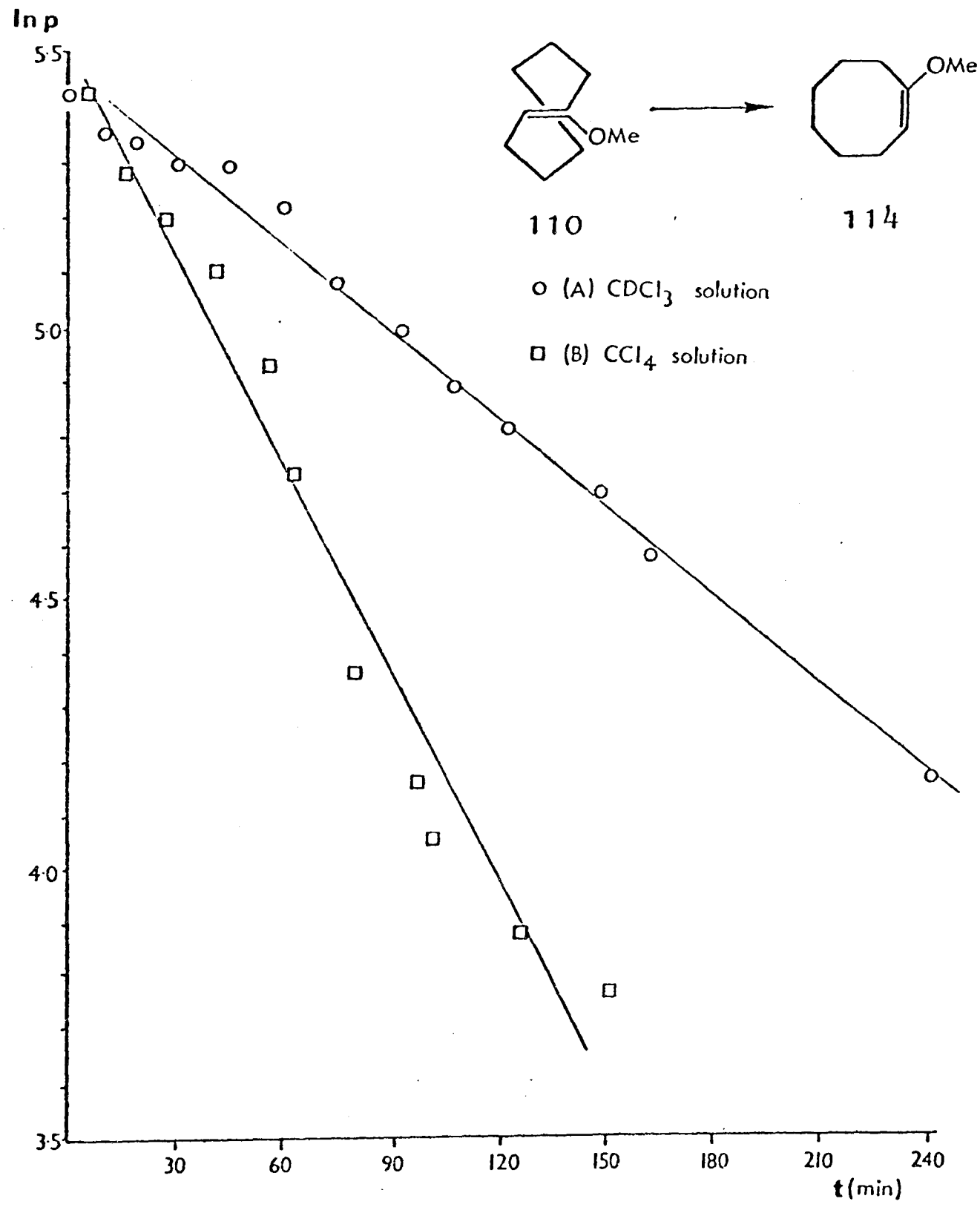
a: A portion of the 60MHz n.m.r. spectrum of a sample containing both trans-(110) and cis-(114) enol ethers, showing the separate methoxyl and overlapping olefinic proton signals.

b: The olefinic proton signal of the trans-isomer (110).

c: The olefinic proton signal of the cis-isomer (114).

d: expansion of b.

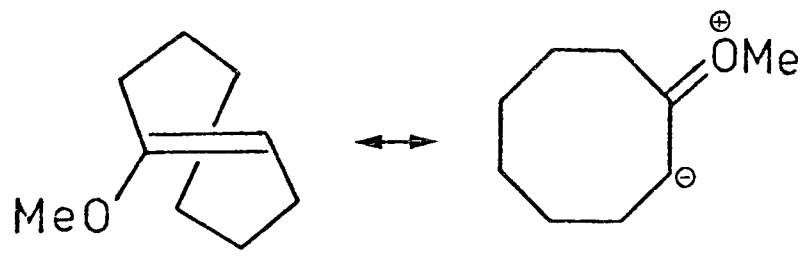
Figure 2.



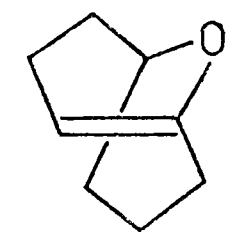
First order plots for the isomerization of 1-methoxy-<u>trans</u>-cyclooctene (110)

Figure 3.

(110) is so unstable. The instability is presumably not due to the steric effect of the methoxy group since 1-methyl-trans-cyclooctene (48) is quite stable. The latter can be purified by preparative g.l.c.[68] and stored for six months without deterioration[67]. The low barrier to isomerization of (110) could perhaps be due to the bond order of the strained double bond being reduced by the electron releasing effect of the methoxyl group (110a)[107,108]. This possibility is corroborated by the much greater stability[73] of the bridgehead bicyclic compound (53) which can be distilled; in (53), the oxygen is not in conjugation with the double bond. On the basis of this argument, a tentative prediction can be made that the corresponding enol thioethers (115) should be more stable than (110) and enamines (116) less stable.



110 **110a**



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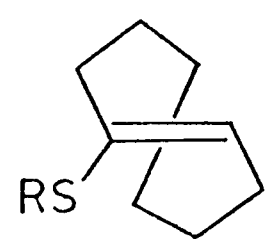

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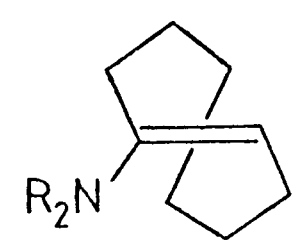


116

The results of the project show that the hitherto unknown 1-alkoxy-trans-cyclooctenes such as (108) and (110) are isolable though unstable compounds. A particularly important aspect of the work is that it provides a further demonstration of the stereospecificity of the Peterson elimination in producing these highly strained unstable compounds.

PART II

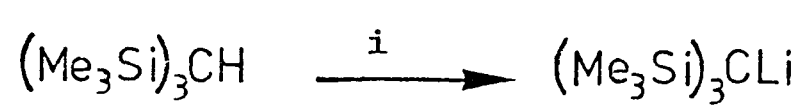
OLFEIN SYNTHESIS USING

α-METALLATED ORGANOSILANES

CHAPTER 4

INTRODUCTION

As discussed in the general introduction, silicon, despite being more electropositive than carbon or hydrogen, has the property of stabilizing an α-carbanion or carbon-metal bond. For example the organolithium reagent (118), which has three stabilizing silyl groups, is readily produced by deprotonation of its parent compound (117) and is a very stable species in solution[109] (Scheme 48).



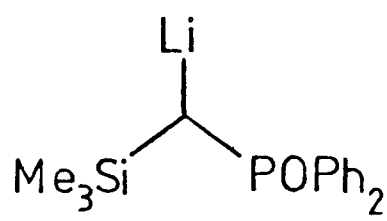
117 **118**

Reagents: i, $MeLi/Et_2O/THF$

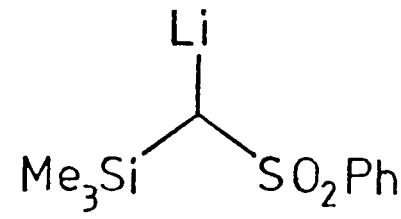
Scheme 48.

Such α-metallated organosilanes have become useful intermediates in organic chemistry by virtue of their availability and reactions with a wide variety of electrophiles. They can be prepared[111] by metal-halogen exchange, metal-metal exchange and addition of an organometallic species to a vinyl-silane as well as by deprotonation as shown in Scheme 48. When the carbon bearing silicon also carries a second anion stabilizing group, X, deprotonation is the easiest way of preparing the derived α-metallated organosilanes. The work described in part II of this thesis is concerned with the reactions of two such organolithium reagents (119) and (120),

these will be discussed in chapters 5 and 6 respectively.

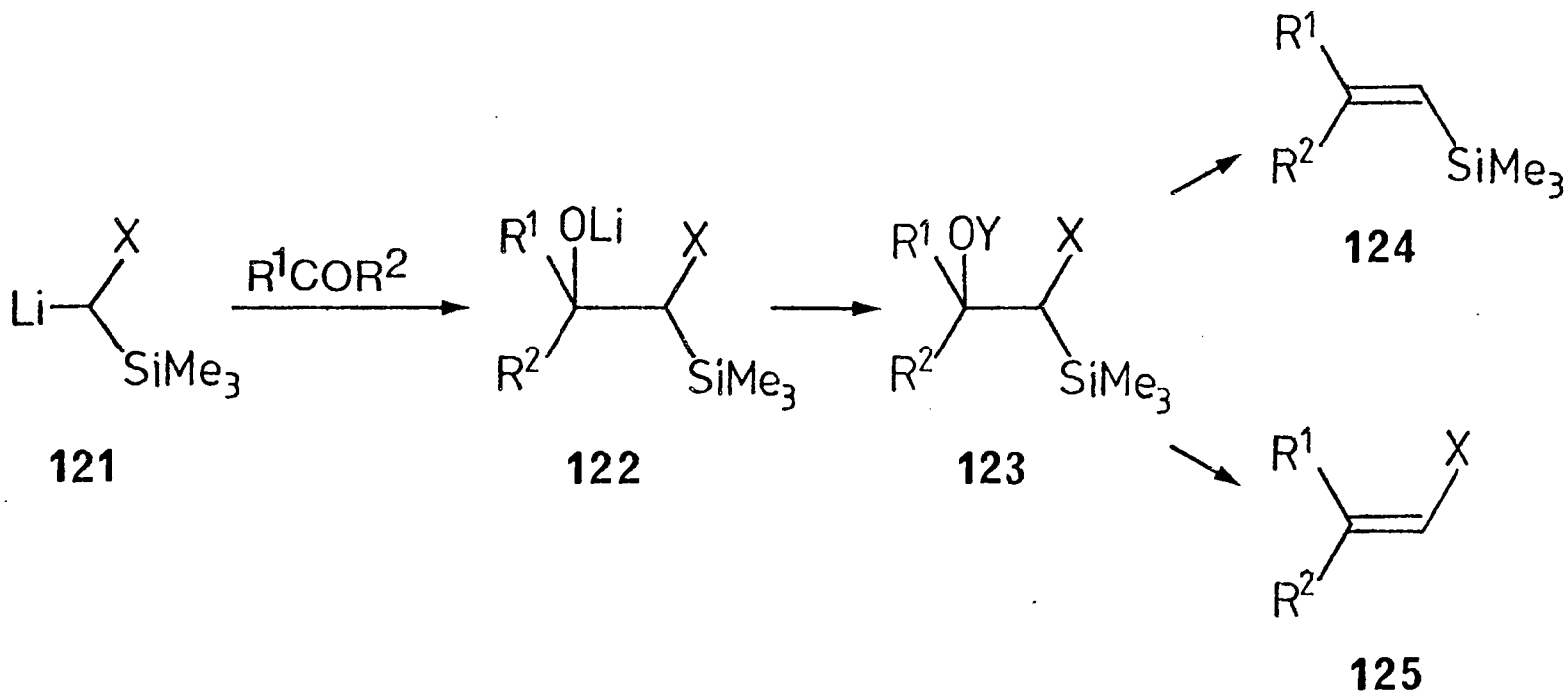


119



120

The object of the work was to isolate (123), the product of addition of (119) or (120) to a carbonyl compound; the former would be derived from the initial adduct (122) by protonation (Y=H) or reaction with some other electrophile. It was hoped that conditions could then be found whereby either the one or the other of the substituted olefins (124) and (125) could then be produced by suitable choice of selective elimination procedures (Scheme 49).



121 **122** **123** **124** **125**

No stereochemical implication is intended in the above representations.

Scheme 49.

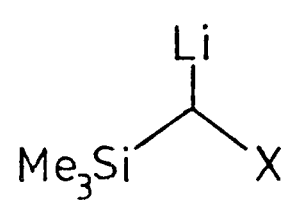
The development of a synthesis of vinylsilanes (124), which are useful synthetic intermediates[31,111] was a particular

incentive. Given that alkylation of (119) or (120) followed by a second deprotonation might also be possible, a wide variety of substituted vinylsilanes could in principle be produced by this route.

The reactions of (119) and (120) were also considered worthy of attention since a number of analogues, including those with the related phosphorus and sulphur containing groups had already been studied[9,15,112,113] (Table 1.)

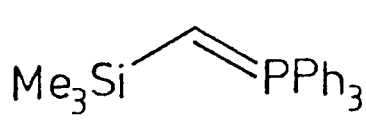
TABLE 1

α-Lithiated Organosilanes of the Type (121) with Phosphorus and Sulphur Containing Groups



121

X	Reference
PPh_2	19
$PSPh_2$	19
$PO(OEt)_2$	114
SMe	19
SPh	114,115
SOPh	116
SOMe	116



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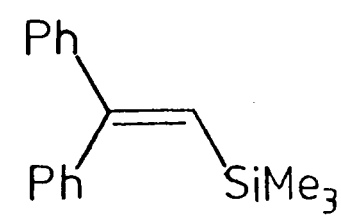
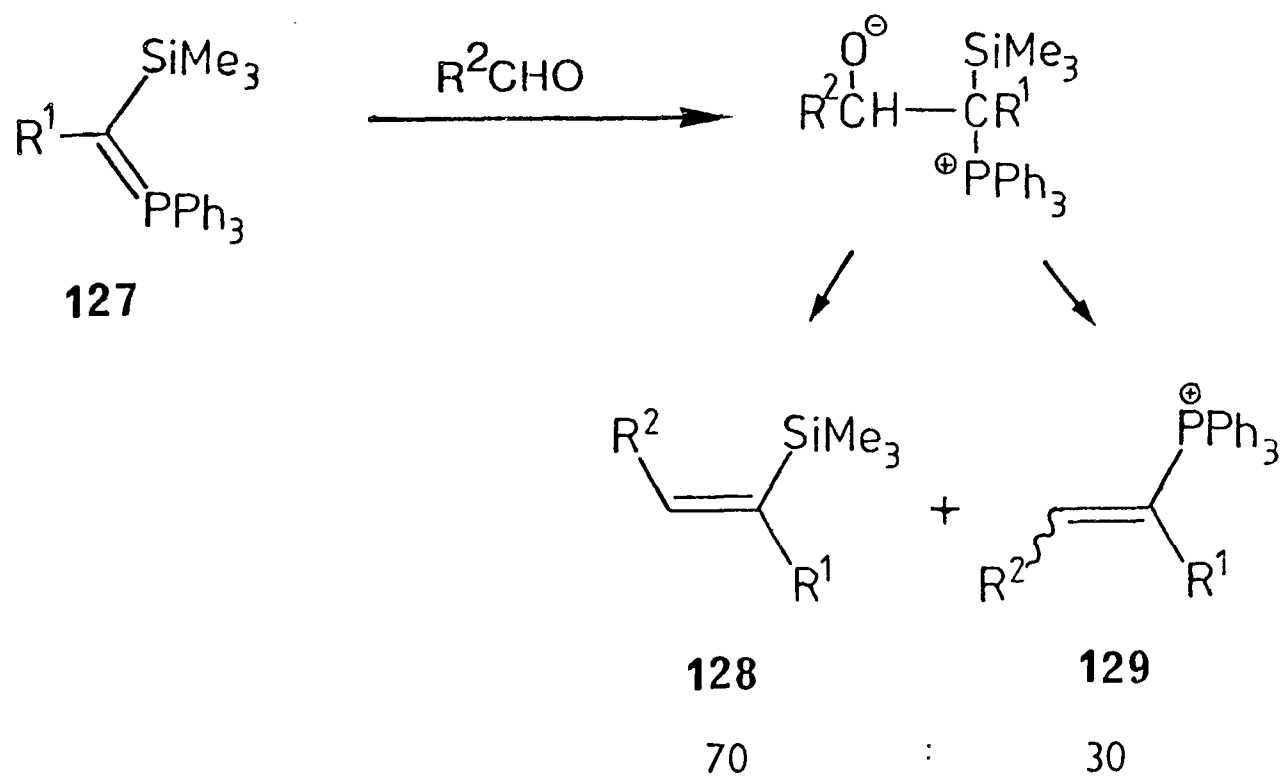


126

In all cases the intermediate (122) is not isolated but rapidly undergoes Peterson elimination to give the appropriate hetero-substituted olefin (125). The ease of elimination can be associated with a change of mechanism to one involving an intermediate with more carbanion-like character (Scheme 8, page 8) when an anion stabilizing group is present.

The reaction of the phosphonium ylide (4) with benzophenone, which was originally reported[18] before the Peterson reaction was established (see page 3), follows an analogous course to that above, but the initially formed vinyl phosphonium ylide then reacts further to produce tetraphenyl allene as the major product. It was mentioned, however, that a small amount of the vinylsilane (126) was produced as a minor component. The reaction of (4) with ketones has since been investigated further and shown to follow the same course as in the benzophenone case[117]. However in the reaction of



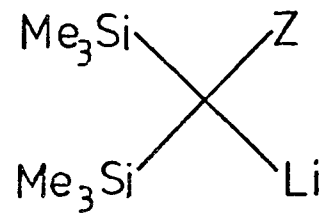
Scheme 50.

(127) with aldehydes a mixture containing mainly vinylsilanes (128) is produced[118,119] the latter with a high degree of stereoselectivity (Scheme 50).

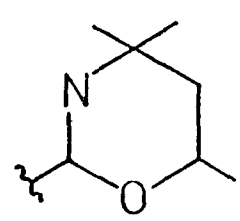
A vinylsilane is, of course, also produced by the reaction of a species of the type (121) with carbonyl compounds if X=$SiMe_3$. The reactions of such reagents (130) (Table 2) have been explored, they generally react with aldehydes or non enolizable ketones only.

TABLE 2

α-Lithiated Organosilanes of the Type (130) with two or more Silyl Groups



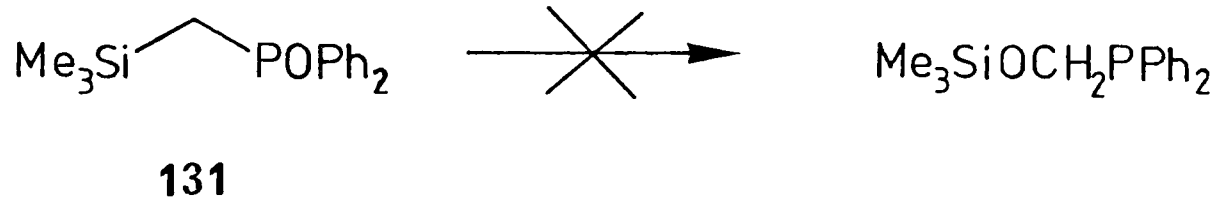
130

Z	Reference
H	120,121,122
$SiMe_3$	120,122
SR	122
Br	123
CO_2tBu	124
	125

CHAPTER 5

THE CHEMISTRY OF DIPHENYL(TRIMETHYLSILYLMETHYL)-PHOSPHINE OXIDE

Little work had previously been carried out concerning the chemistry of diphenyl(trimethylsilylmethyl)phosphine oxide (131). In a study[126] of the rearrangements of organosilicon compounds, it was found that (131) was stable with respect to migration of silicon from carbon to oxygen, in contrast to the corresponding sulphoxide (132) (Scheme 51). However, like (132), (131) was shown to be prone to desilylation, particularly under hydrolytic conditions.



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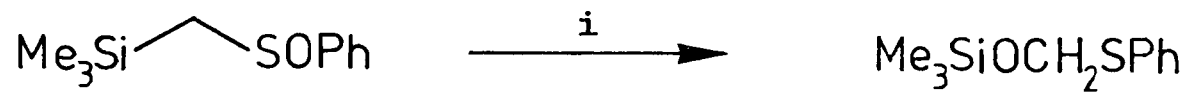


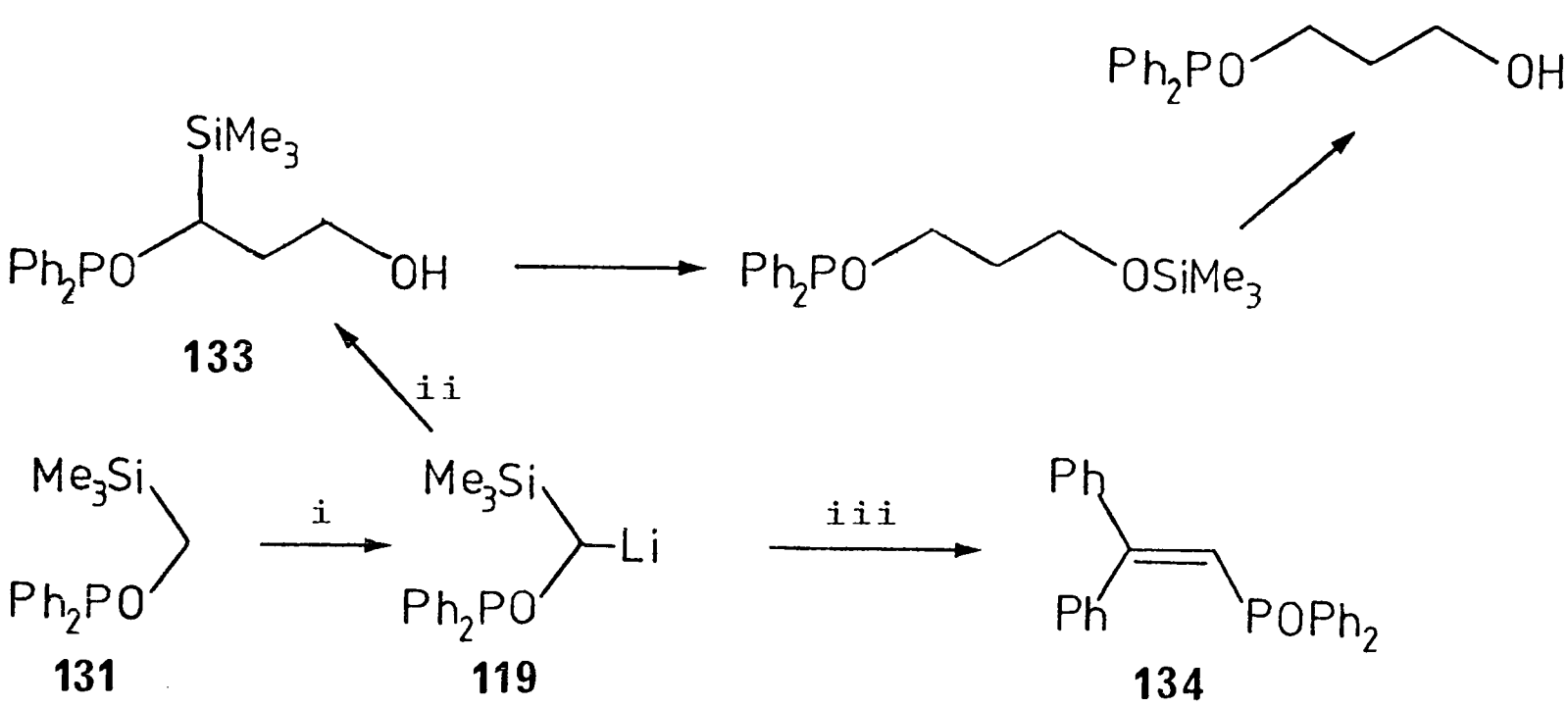
132

Reagents and conditions: i, 60°, 1h

Scheme 51.

More recently, the reaction of the lithiated derivative (119) with ethylene oxide has been investigated[127]. It was found that the initially produced γ-hydroxysilane (133) underwent migration of silicon to oxygen followed by subsequent desilylation. In the same paper, it was stated that (119)

also gave "the usual Peterson product" (134) with benzophenone (Scheme 52), although no reactions with other carbonyl compounds were mentioned.

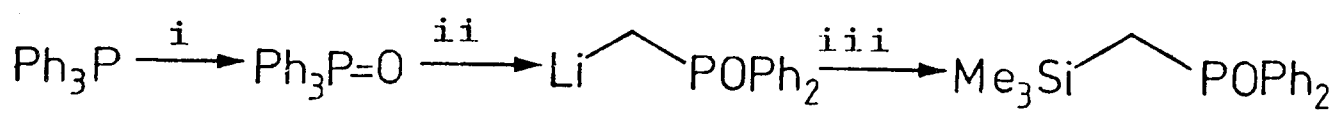


Reagents: i, n-BuLi/Et_2O; ii, ethylene oxide; iii, benzophenone

Scheme 52.

Section A: Preparation of Diphenyl(trimethylsilylmethyl)-phosphine Oxide

The procedure used to prepare diphenyl(trimethylsilylmethyl)phosphine oxide (131) (Scheme 53) was similar to one previously described[128].



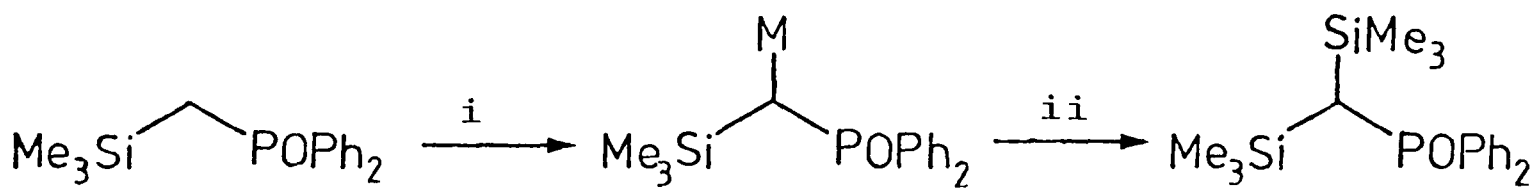
Reagents: i, $K_2S_2O_8/H_2SO_4$/MeOH/EtOH; ii, MeLi/Et_2O; iii, Me_3SiCl

Scheme 53.

Triphenyl phosphine oxide, prepared by straightforward oxidation[56,129] of triphenylphosphine, was treated with methyllithium in ether[130]. The initially formed methyldiphenylphosphine oxide is deprotonated by the phenyllithium also produced in the reaction giving the organolithium reagent (135), this was quenched in situ by trimethylsilyl chloride. The crude reaction product was a mixture of (131) and methyldiphenylphosphine oxide. The silylated product (131) was obtained pure by column chromatography followed by distillation (70% yield). Column chromatography was found to be unsatisfactory when the preparation was carried out on a large scale or when particular grades of silica gel were used, desilylation then took place leading to a low yield of (131). Once purified, however, (131) could be stored indefinitely without deterioration.

Section B: Lithiation and Alkylation of Diphenyl(trimethylsilylmethyl)phosphine Oxide

Having found that (131) was prone to desilylation on chromatography, it was feared that desilylation might compete with deprotonation on treatment with base. Thus, for example, desilylation of (131) occured on treatment with 10% methanolic potassium hydroxide at room temperature. In order to monitor the efficiency of deprotonation, the product from reaction of (131) with one equivalent of base was quenched with trimethylsilyl chloride. It was thought that the latter would react rapidly with deprotonated (131), giving the bis-silyl compound (136) (Scheme 54).



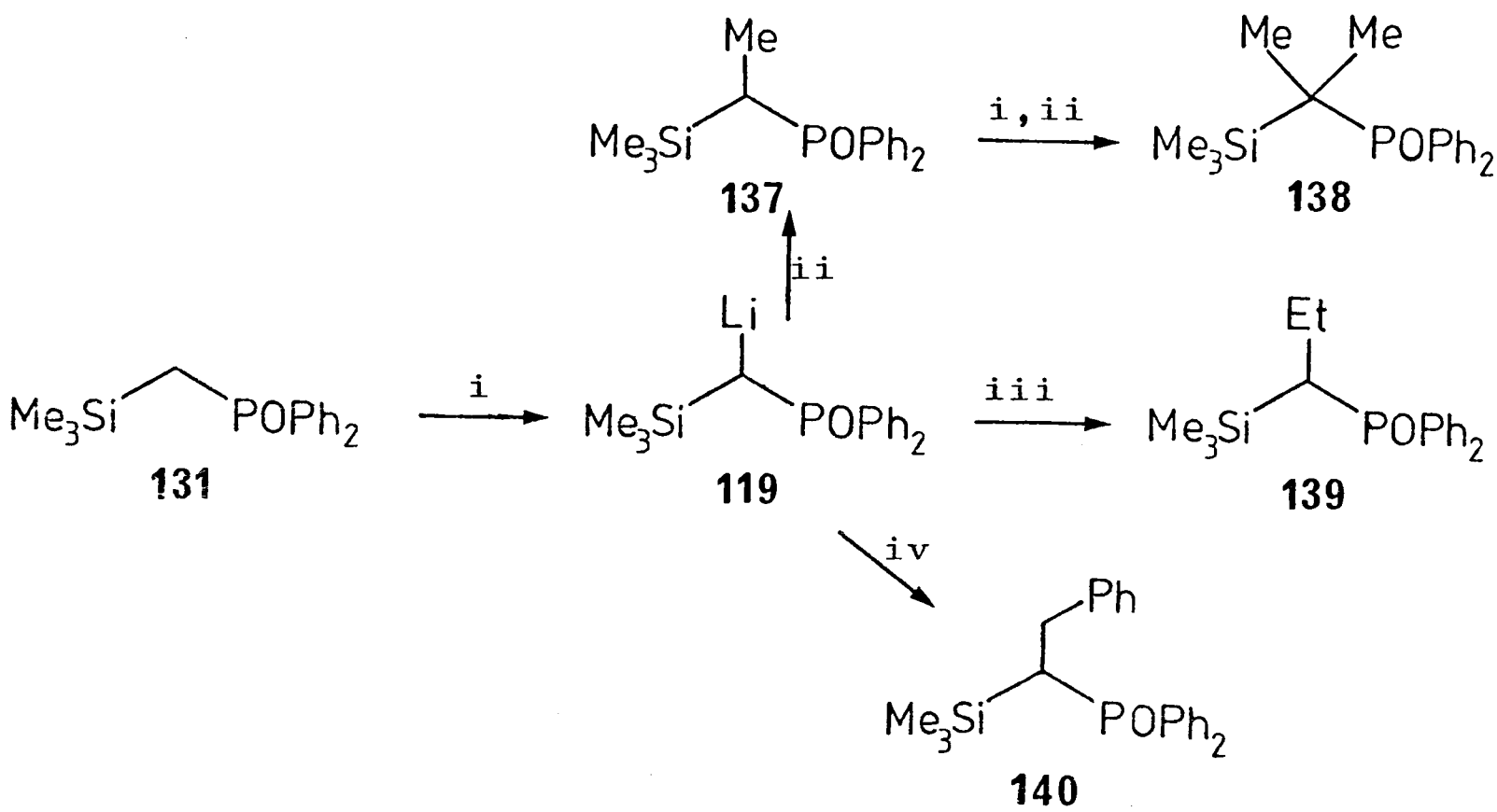
131 **136**

Reagents: i, base; ii, Me_3SiCl

Scheme 54.

The base used initially, methyllithium, apparently brought about good conversion of (131) to (136) although the latter compound was unstable with respect to desilylation and could not be purified. This initial experiment was found difficult to reproduce, however. The low yields of (136) subsequently obtained were associated with desilylation of starting material by the variable amounts of alkoxide base which were also present in the different batches of methyllithium used. A number of bases in various solvents were then tried as alternatives to methyllithium (see experimental) but no conditions were found which brought about formation of (136) in better yield than in the initial experiment. Eventually it was concluded that the capriciousness of the reaction might be due to the inherent instability of the bis-silylated product (136), and thus methyl iodide was used as an alternative electrophile to quench the reaction. The methylated derivative (137) was found to be produced cleanly and in good yield using methyllithium or indeed any of the bases previously tried; n-butyllithium was chosen for subsequent use because of its availability. Analogous ethylation, benzylation, and

dimethylation of (131) could also be brought about in reasonable yields (Scheme 55).



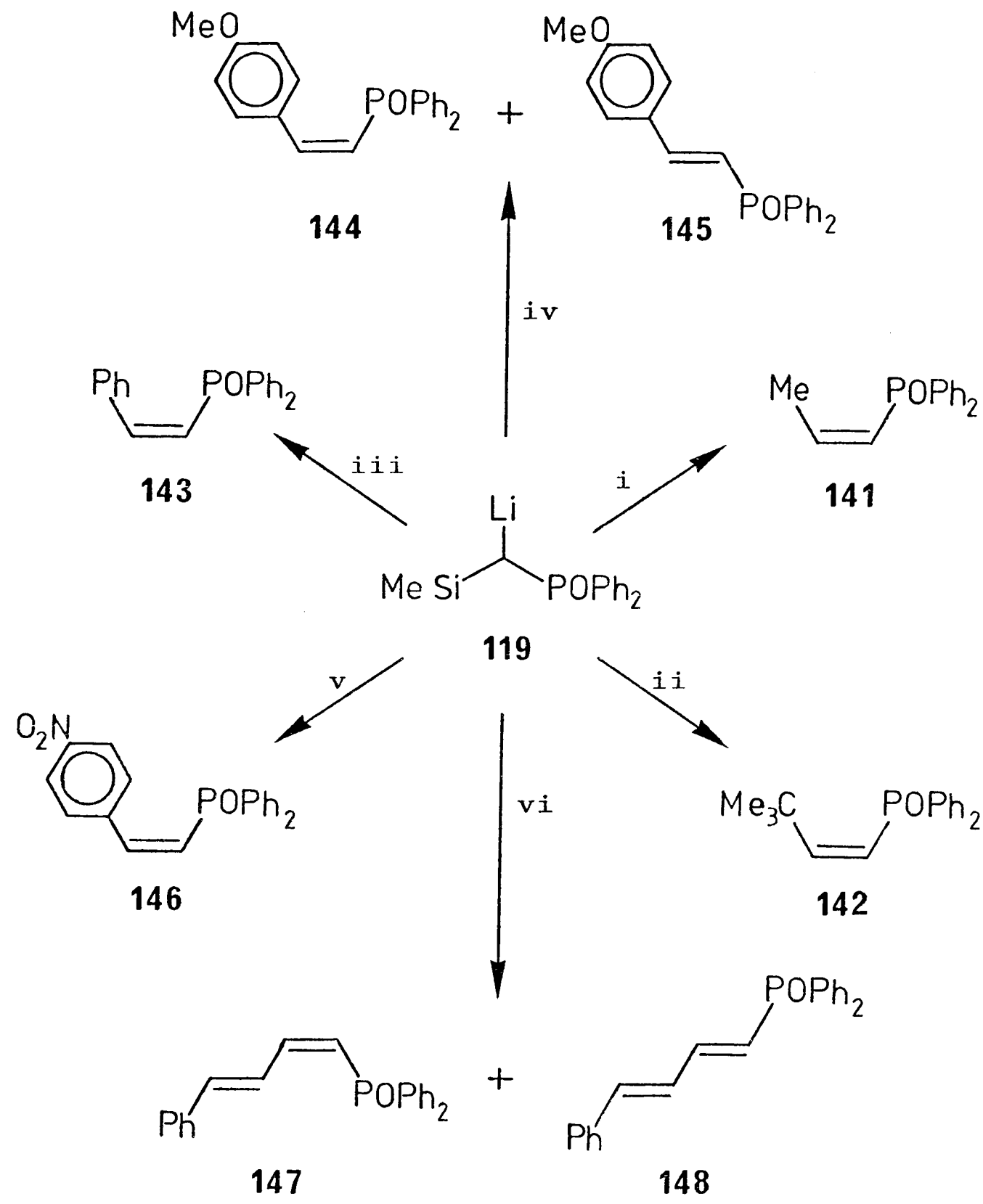
Reagents: i, n-BuLi/Et_2O; ii, MeI; iii, EtI; iv, $PhCH_2Br$

Scheme 55.

Section C: Reaction of Metallated Diphenyl(trimethylsilyl-phosphine Oxide with Aldehydes

The lithiated derivative (119) of (131) was found to react rapidly in ether with a variety of aldehydes, including the sterically hindered pivaldehyde, to give vinyl phosphine oxides (Scheme 56). With simple aldehydes, the vinyl phosphine oxide formed was stereospecifically the Z-isomer, but with p-methoxybenzaldehyde and cinnamaldehyde, the reaction was slower and roughly equal mixtures of the Z- and E-isomers were

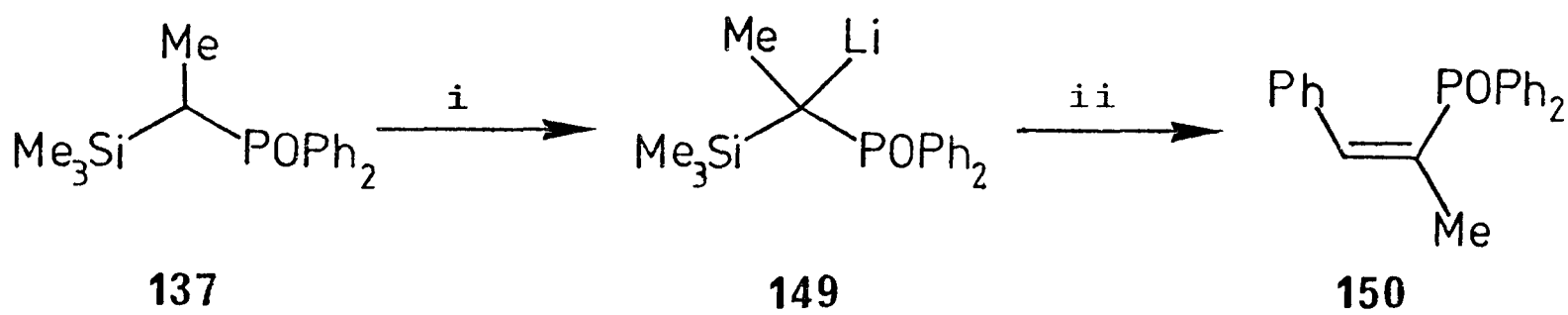
obtained. The product obtained from the reaction of (119) with the latter aldehyde was derived exclusively from 1,2- rather than 1,4-addition.



Reagents: i, acetaldehyde; ii, pivaldehyde; iii, benzaldehyde, iv, p-methoxybenzaldehyde; v, p-nitrobenzaldehyde, vi, E-cinnamaldehyde

Scheme 56.

The reaction of the lithiated derivative (149) of the methylated silyl phospine oxide (137) with benzaldehyde was analogous to the corresponding reaction of (119). A single vinyl phosphine oxide (150) (Scheme 57) was formed which was assigned the stereochemistry shown with the aid of n.m.r. spin decoupling.



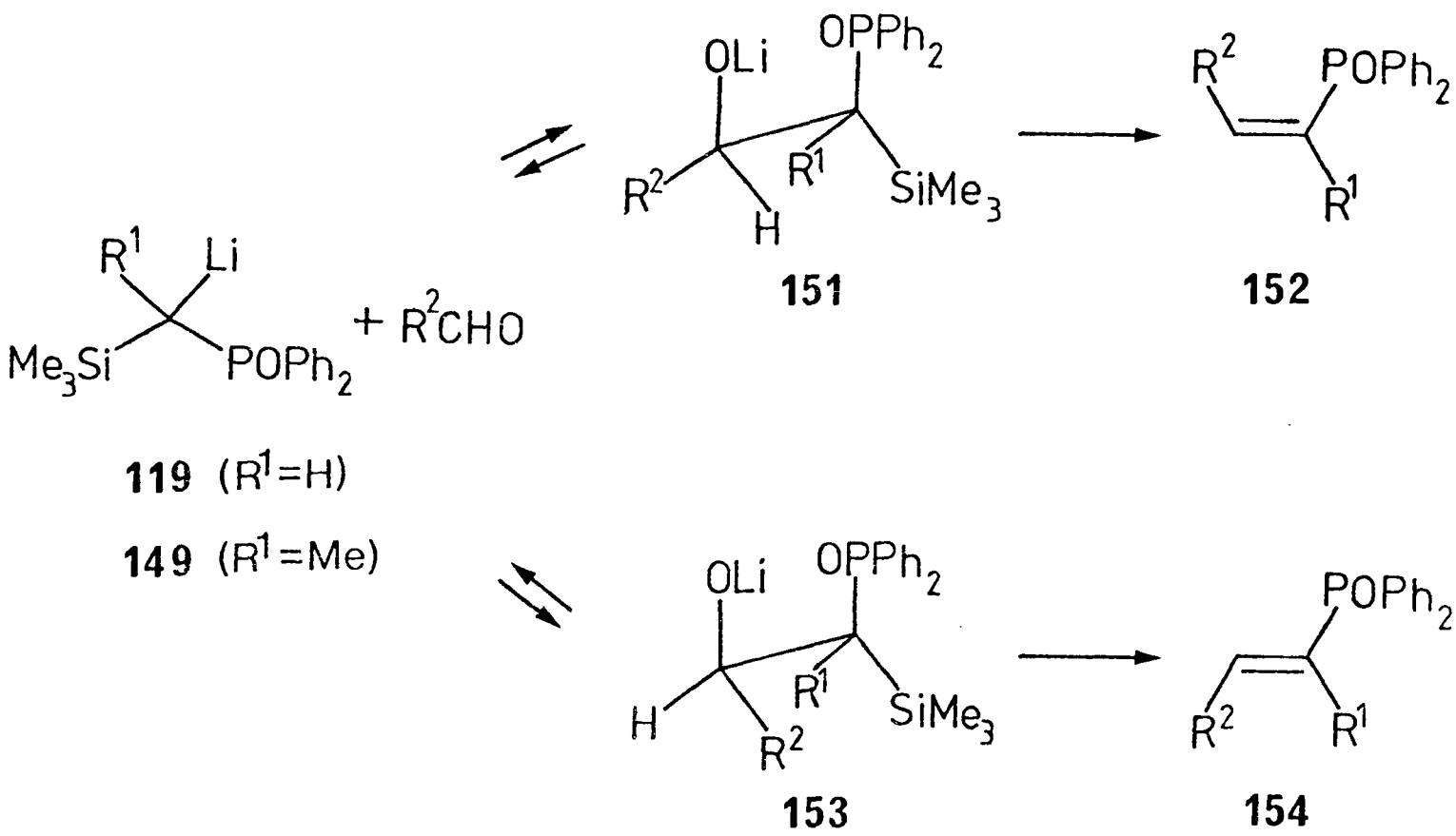
137 **149** **150**

Reagents: i, n-BuLi/Et_2O; ii, PhCHO

Scheme 57.

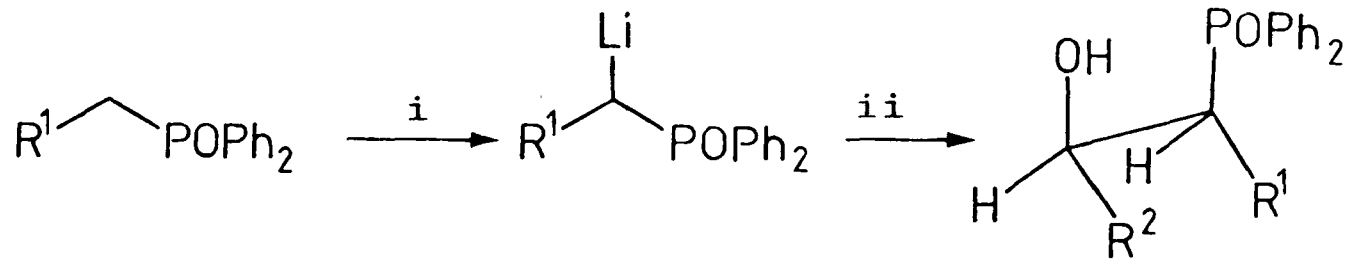
The reason for the stereochemical course of the above reactions of (119) and (149) is not clear. Addition of these reagents to aldehydes can take place to give two possible diastereoisomeric adducts, which are presumably best represented as the conformations (151) and (153), in which the lithium cation is chelated by two oxygen ligands[131]. If the vinyl phosphine oxides are then formed by rotation about the central carbon-carbon bond followed by stereospecific syn-elimination of Me_3SiOLi from these adducts, the preponderance of Z-vinyl phosphine oxides (152) generally produced suggests that the initial addition takes place with high stereoselectively to give the less hindered (threo) adduct (151) (Scheme 58). The factors causing this stereoselectivity are evidently quite sensitive to the aldehyde, however, since the

less reactive p-methoxybenzaldehyde and cinnamaldehyde give rise to roughly equal mixtures of Z- and E-vinyl phosphine oxides which would be derived from the threo (151) and erythro (153) adducts respectively. In the case of the latter aldehydes, the addition is possibly reversible to a greater extent, so interconversion between (151) and (153) could occur.



Scheme 58.

The stereochemistry of the reactions of (119) and (149) is thus in contrast to that of simple monosubstituted lithiated phosphine oxides (155), which undergo addition to aldehydes to give mainly erythro β-hydroxyphosphine oxides[132] (156) (erythro:threo generally >70:30) (Scheme 59).

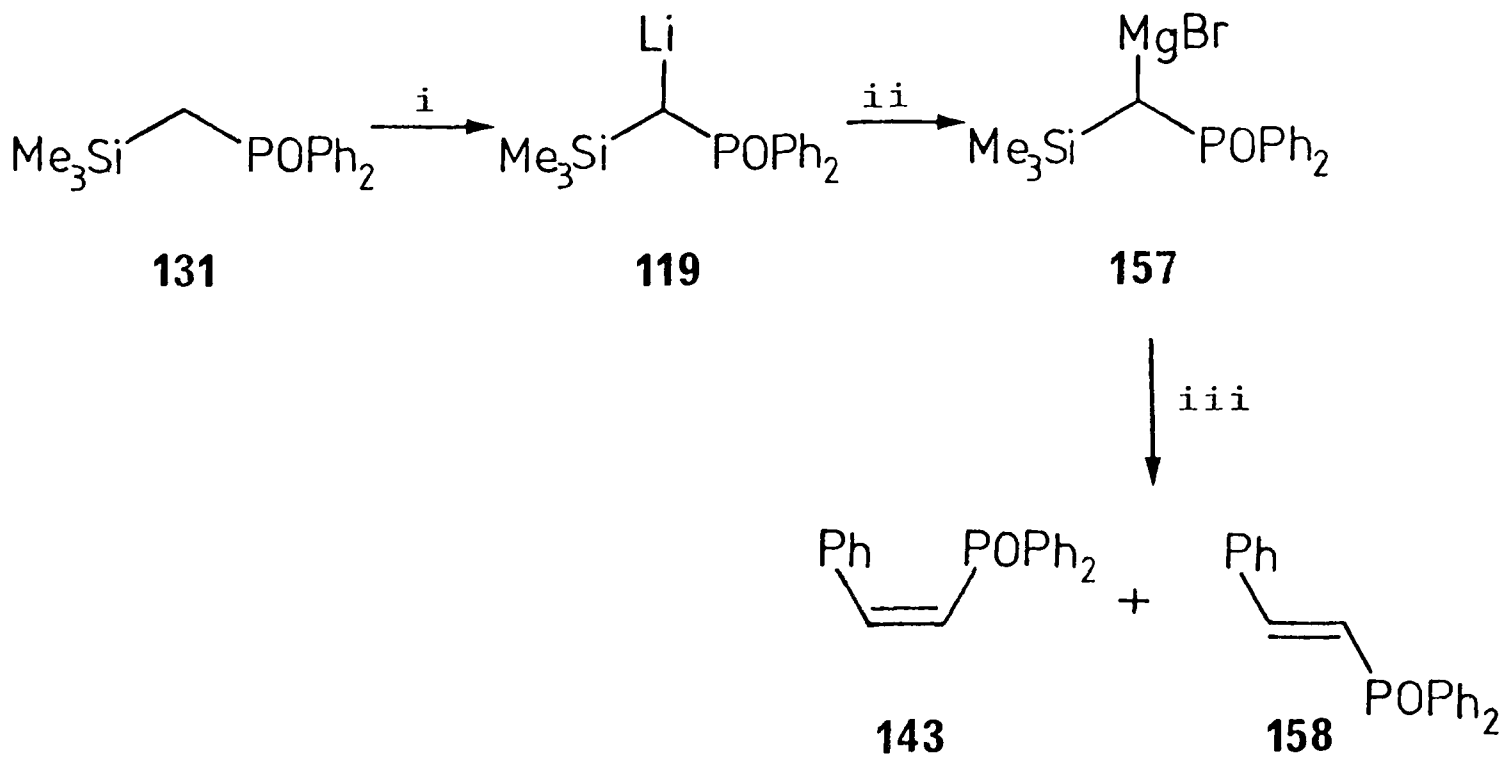


155 **156**

Reagents: i, n-BuLi/THF; ii, R^2CHO

Scheme 59.

The objective had been to isolate the adduct formed by reaction of a lithiated silyl phosphine oxide and a carbonyl compound, but in the reactions of (119) with aldehydes, elimination could not be prevented even by quenching at low temperature (-100^{o}). It was thought, however, that elimination might be prevented by changing the cation. For example with magnesium as the metal, β-silyl alkoxides do not readily undergo Peterson elimination[19,30,133]. The magnesium reagent (157) was produced by the addition of a slight excess of magnesium bromide etherate to an ethereal solution of (119). Reaction of (157) with benzaldehyde gave a roughly equal mixture of the Z and E vinyl phosphine oxides (143) and (158) (Scheme 60), thus elimination was not prevented although the course of the reaction was altered from that of the unmodified lithium reagent (119).



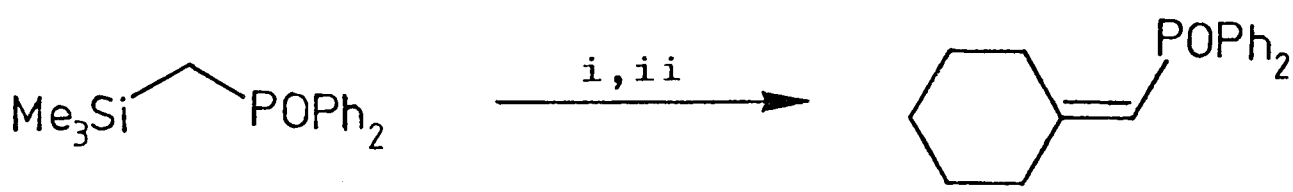
Reagents: i, n-BuLi/Et_2O; ii, $MgBr_2$; iii, PhCHO

Scheme 60.

In an attempt to explore the effect of zinc as cation[134], zinc chloride was added to an ethereal solution of (119); however this reduced the reactivity of the latter to such an extent that no reaction could be achieved with benzaldehyde.

Section D: Reaction of Metallated Diphenyl(trimethylsilylmethyl)phosphine Oxide with Ketones

The reactivity of the lithiated derivative (119) of diphenyl(trimethylsilylmethyl)phosphine oxide (131) towards ketones was very much lower than towards aldehydes. With cyclopentanone, no reaction at all could be achieved and with acetone, the product of ketone self condensation (diacetone alcohol) was produced. With cyclohexanone, after prolonged reaction time, the vinyl phosphine oxide (159) was isolated (60% yield), together with recovered (131) (Scheme 61).

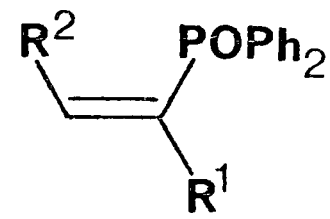


131 159

Reagents and conditions: i, $MeLi/Et_2O$; ii, cyclohexanone/ $18^{o}/18h$

Scheme 61.

Thus the reactions of (119) and (149) with aldehydes make accessible a variety of substituted vinyl phosphine oxides of the type (160). The behaviour of (119) is similar to that of other α-metallated organosilanes in that it reacts readily only with aldehydes[135].

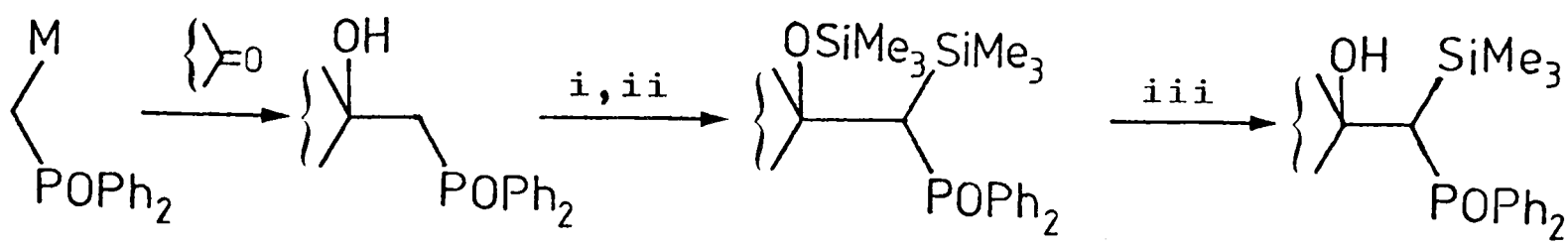


160

Section E: Alternative Approaches to (2-Hydroxy-1-trimethylsilylethyl)phosphine Oxides

In principle, the desired (2-hydroxy-1-trimethylsilyl-ethyl)phosphine oxides (163) could be derived from β-hydroxy-phosphine oxides (161) by bis-silylation, followed by

removal of the more labile O-silyl group (Scheme 62).

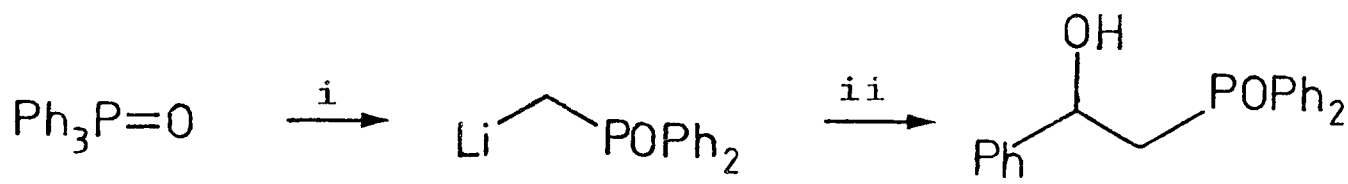


161 **162** **163**

Reagents: i, base (2 eq.); ii, Me_3SiCl; iii, H_3O^+

Scheme 62.

The β-hydroxyphosphine oxide (164) was prepared[136] as shown in Scheme 63. It was not, however, found possible to achieve any silylation of (164); treatment with two equivalents of various bases followed by trimethylsilyl chloride always gave a retro-aldol type reaction and methyl-diphenylphosphine oxide was recovered.



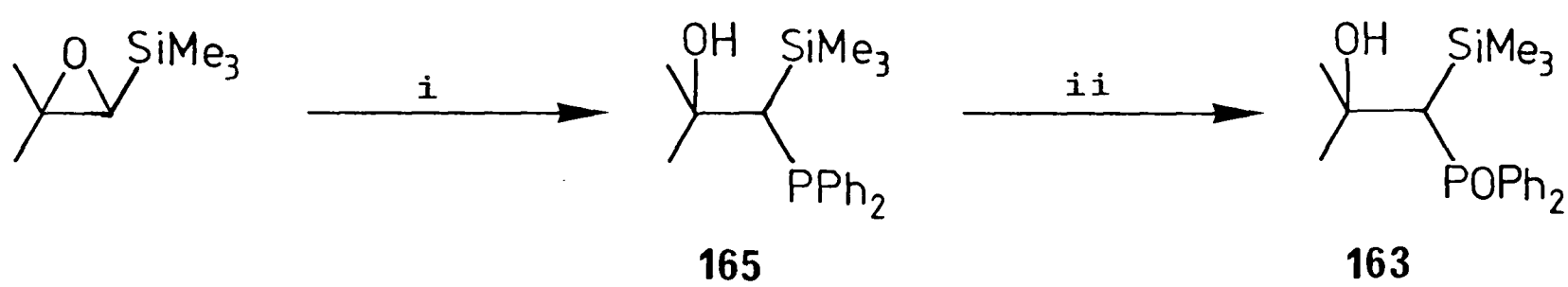
135 **164**

Reagents: i, $MeLi/Et_2O$; ii, PhCHO

Scheme 63.

Another possible route to compounds of the type (163) which was considered involved α,β-epoxysilane ring opening by lithium diphenylphosphide[137]. If attack of the phosphorus nucleophile took place at the carbon bearing silicon in the

manner of other epoxysilane ring opening reactions[38], the silyl phosphine (165) would be produced which could be oxidized to the phosphine oxide (163) (Scheme 64).

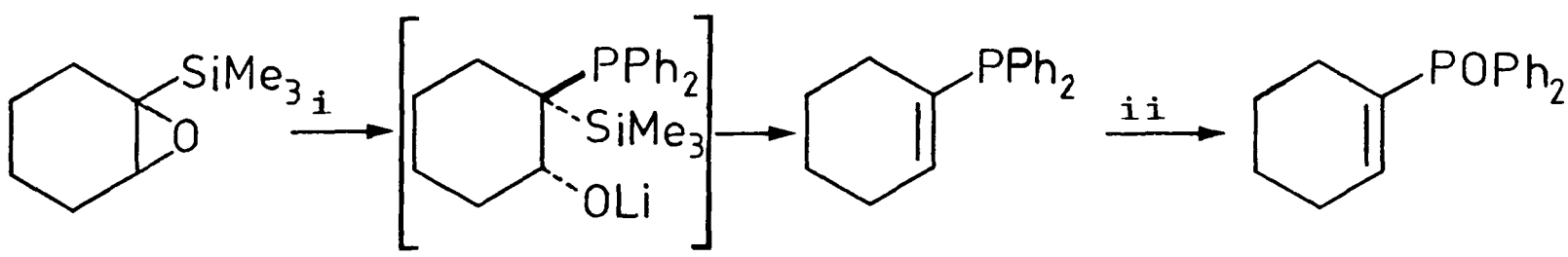


165 **163**

Reagents: i, $LiPPh_2$; ii, oxidation

Scheme 64.

The epoxysilane (24) was chosen for study since it was readily available. Treatment with lithium diphenylphosphide[138] resulted in the formation of the vinyl phosphine (167). Presumably the latter was produced by way of Peterson elimination from the initial adduct (166); the intermediate β-hydroxysilane derived from (166) by protonation was not isolated. The vinyl phosphine (167) was characterized in the form of the phosphine oxide[139] (168) (Scheme 65).



24 **166** **167** **168**

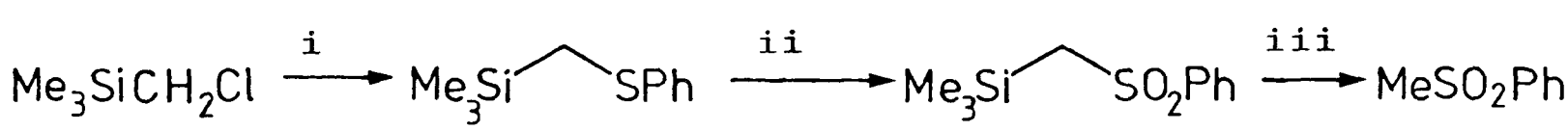
Reagents: i, $LiPPh_2$/THF; ii, H_2O_2/CH_3CO_2H/THF

Scheme 65.

CHAPTER 6

THE CHEMISTRY OF PHENYL TRIMETHYLSILYLMETHYL SULPHONE

The title compound (170) had only been previously reported on two occasions. The first report[140] gave details of its preparation and stability towards acids and bases. It was found to be moderately stable to acid but was rapidly cleaved by aqueous base (Scheme 66). The second report[141], by the same author, was concerned with its possible use as a lubricant or additive.



169 170

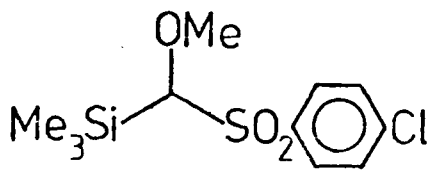
Reagents: i, NaSPh/EtOH; ii, monoperphthalic acid/Et_2O; iii, 5% aq NaOH/5min

Scheme 66.

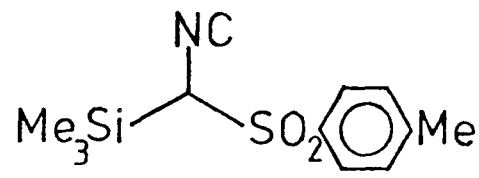
Since (170) could be distilled (b.p. 160° at 6mm Hg), it was evidently much more stable than the corresponding sulphoxide (132) which undergoes migration of silicon to oxygen under mild conditions (see page 63).

Much more recently, the compounds (171)[142] and (172)[143] have been reported. They are related to (170) in that they are both α-silyl sulphones, but differ in having an additional α-substituent. The lithiated derivatives of (171) and (172)

react with aldehydes and ketones to give the corresponding substituted vinyl sulphones (173). The latter were produced via Peterson elimination, but the intermediate β-hydroxy-silanes were not isolated.



171



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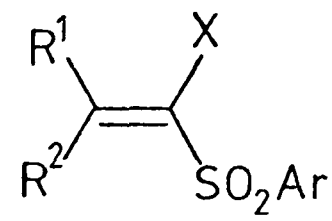
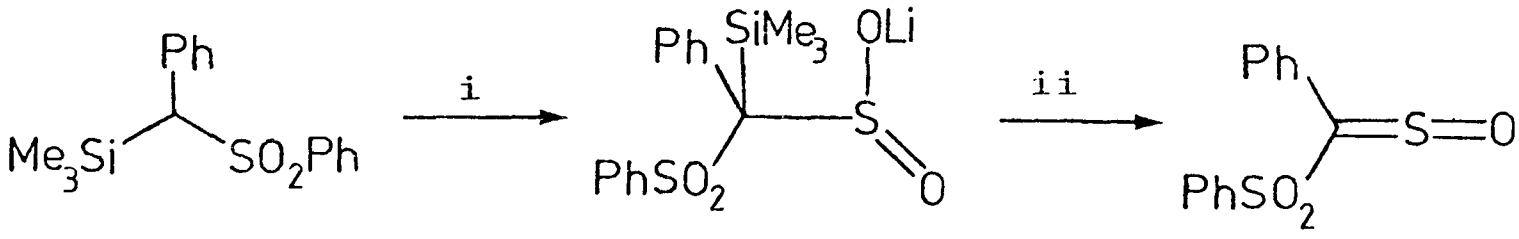


173

Lithiated derivatives of substituted silyl sulphones have also been used in the synthesis of sulphines by means of their reaction with sulphur dioxide[144,145], for example (174)→(176)[146] (Scheme 67). The mechanism of such transformations involves elimination of Me_3SiOLi from the intermediate (175), analogous to the Peterson reaction.



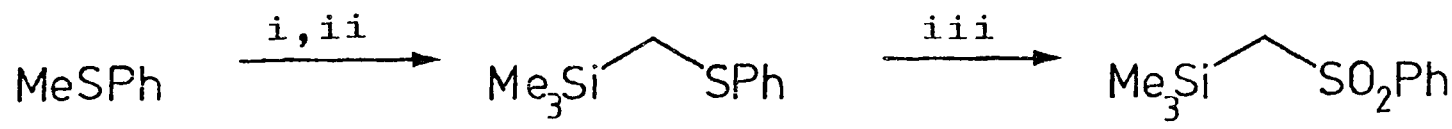
174 175 176

Reagents: i, n-BuLi/THF; ii, SO_2

Scheme 67.

Section A: Preparation of Phenyl Trimethylsilylmethyl Sulphone

The route used to prepare(170) (Scheme 68) was a modification of the original procedure (Scheme 66). Thioanisole was treated with n-butyllithium tetramethylethylenediamine (TMEDA) complex followed by trimethylsilyl chloride to give the sulphide (169)[122]. The latter compound was oxidized to the sulphone (170) using buffered peracetic acid in dichloromethane[147]. It is worth noting that (170) was easier to prepare and purify than the phosphine oxide (131). Both steps in the synthesis were achieved in nearly quantitative yield and (170) was readily distilled at low pressure.



169 **170**

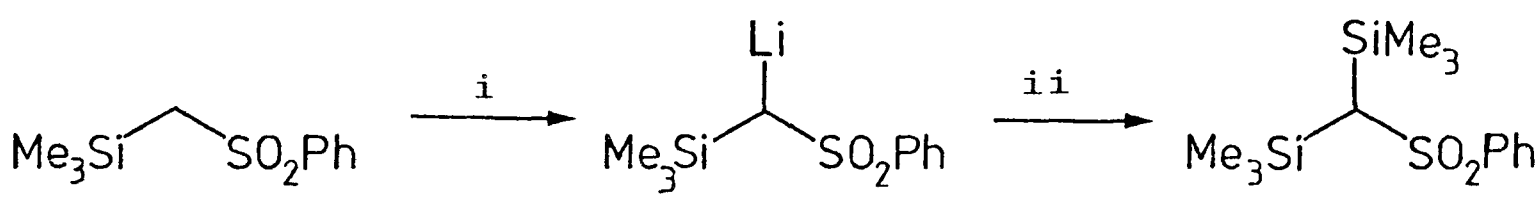
Reagents: i, n-BuLi-TMEDA/THF; ii, Me_3SiCl; iii, CH_3CO_3H/NaOAc/CH_2Cl_2

Scheme 68.

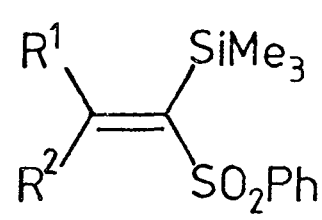
Section B: Lithiation and Alkylation of Phenyl Trimethylsilylmethyl Sulphone

Treatment of (170) with n-butyllithium followed by trimethylsilyl chloride gave the bis-silyl sulphone (177) as a crystalline solid, indicating that lithiation of (170) could be achieved without desilylation (Scheme 69). The bis-

silyl sulphone (177) was purified and characterized, in contrast to the unstable bis-silyl phosphine oxide (136). The former compound is a possible precursor of α,β-unsaturated silyl sulphones of the type (178), such compounds are of interest in that they have the dual reactivity of a vinyl-silane and an α,β-unsaturated sulphone[145,148-150].



170 **120** **177**

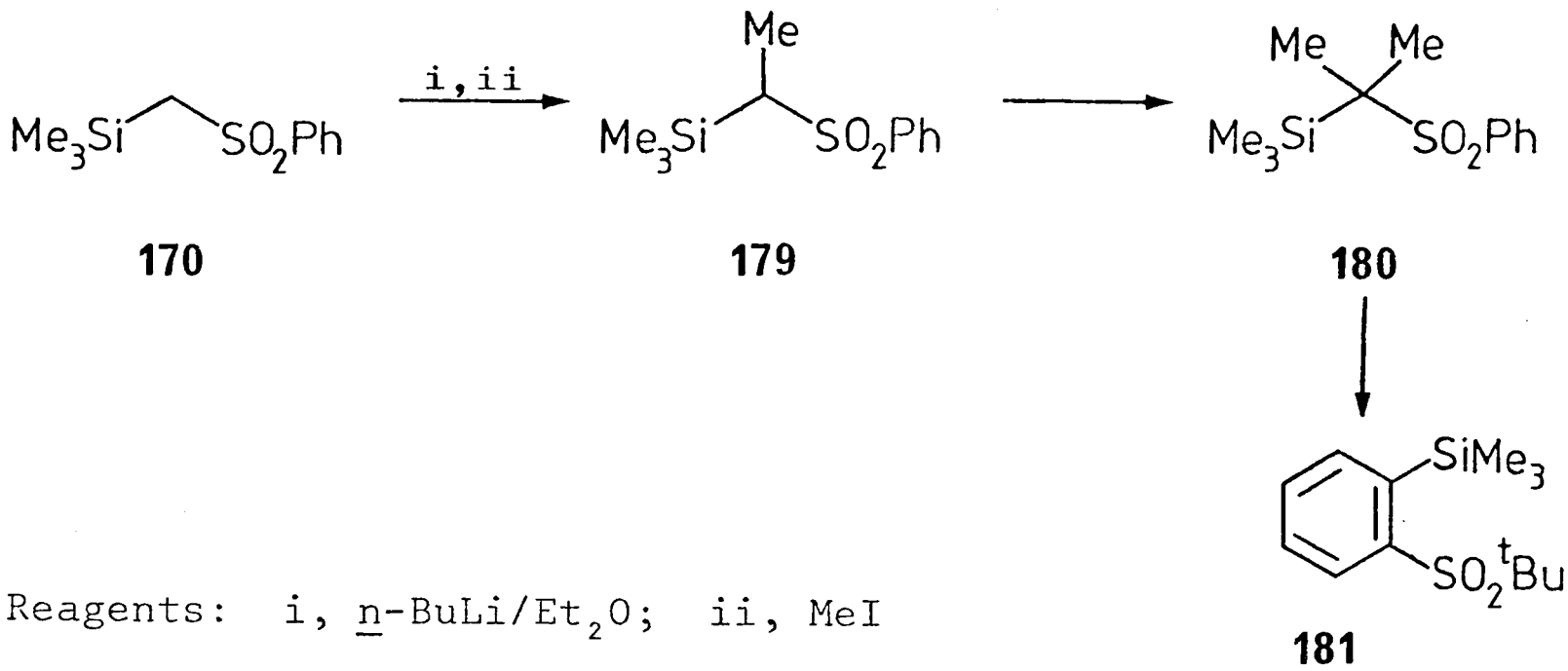


178

Reagents: i, n-BuLi/Et_2O; ii, Me_3SiCl

Scheme 69.

Attempts to methylate (170) are summarized in Scheme 70. Thus treatment with 1.05 equivalents of n-butyllithium followed by methyl iodide produced a mixture consisting mainly of the monomethylated derivative (179), together with some starting material and some of the dimethylated silyl sulphone (180). When this mixture was treated further under the same conditions, the product was a roughly equal mixture of (180) and the t-butyl sulphone (181). Complete conversion to the latter compound was achieved by further methylation, but conditions could not be found for separating the intermediate mixtures.

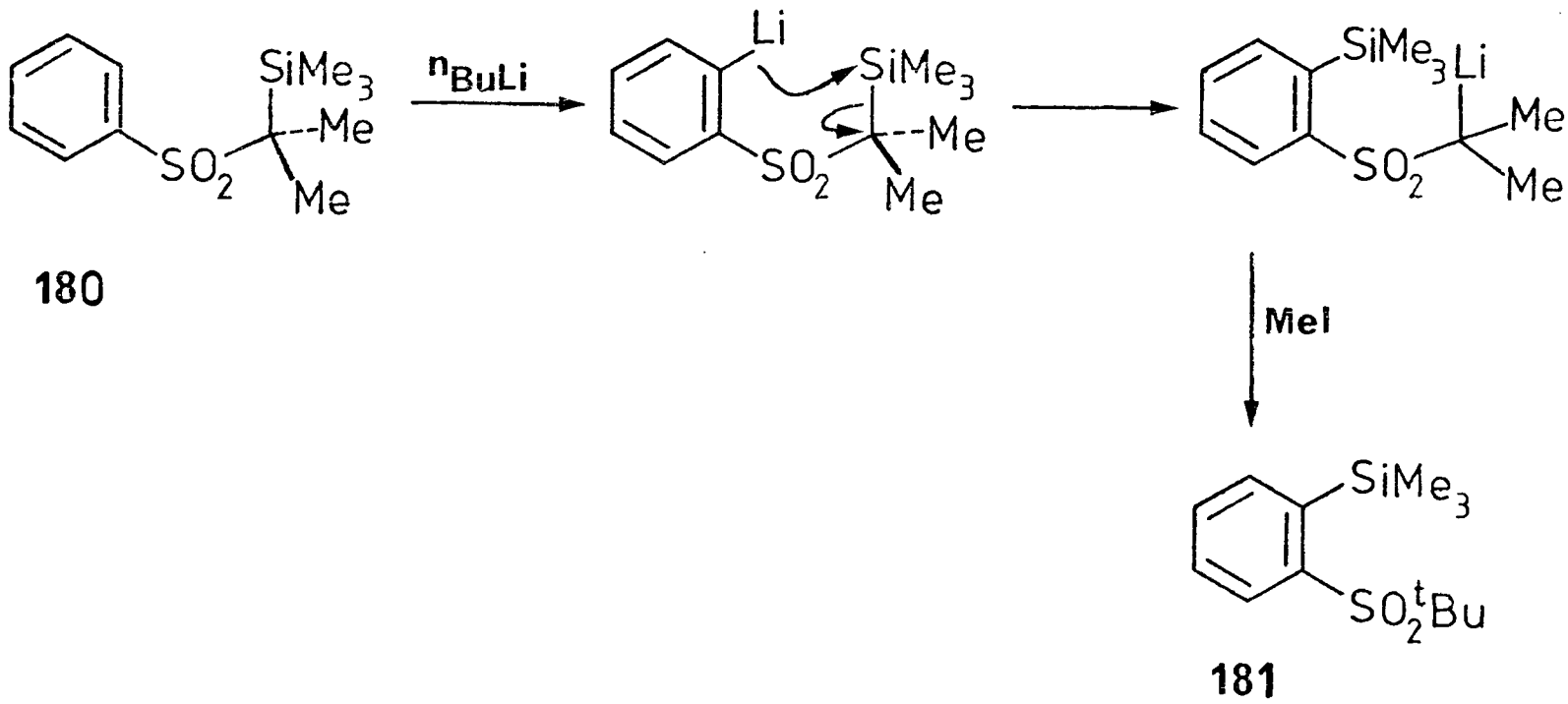


170 **179** **180** **181**

Reagents: i, n-BuLi/Et_2O; ii, MeI

Scheme 70.

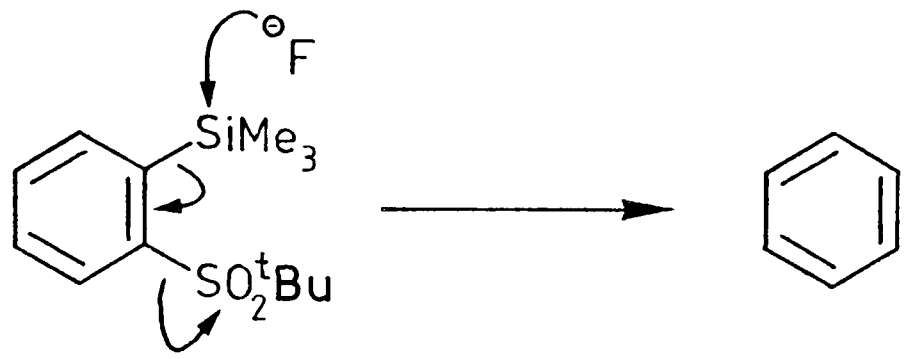
Presumably (181) was formed from (180) by further o-metallation on the aromatic ring followed by intramolecular migration of the trimethylsilyl group (Scheme 71), examples of such lithiations on an aromatic ring facilitated by an adjacent sulphone group are known[151].



180 **181**

Scheme 71.

It is of interest to note that (181) is a possible precursor of benzyne. β-Elimination of the silyl and sulphone groups could perhaps be achieved by fluoride ion[152] (Scheme 72).

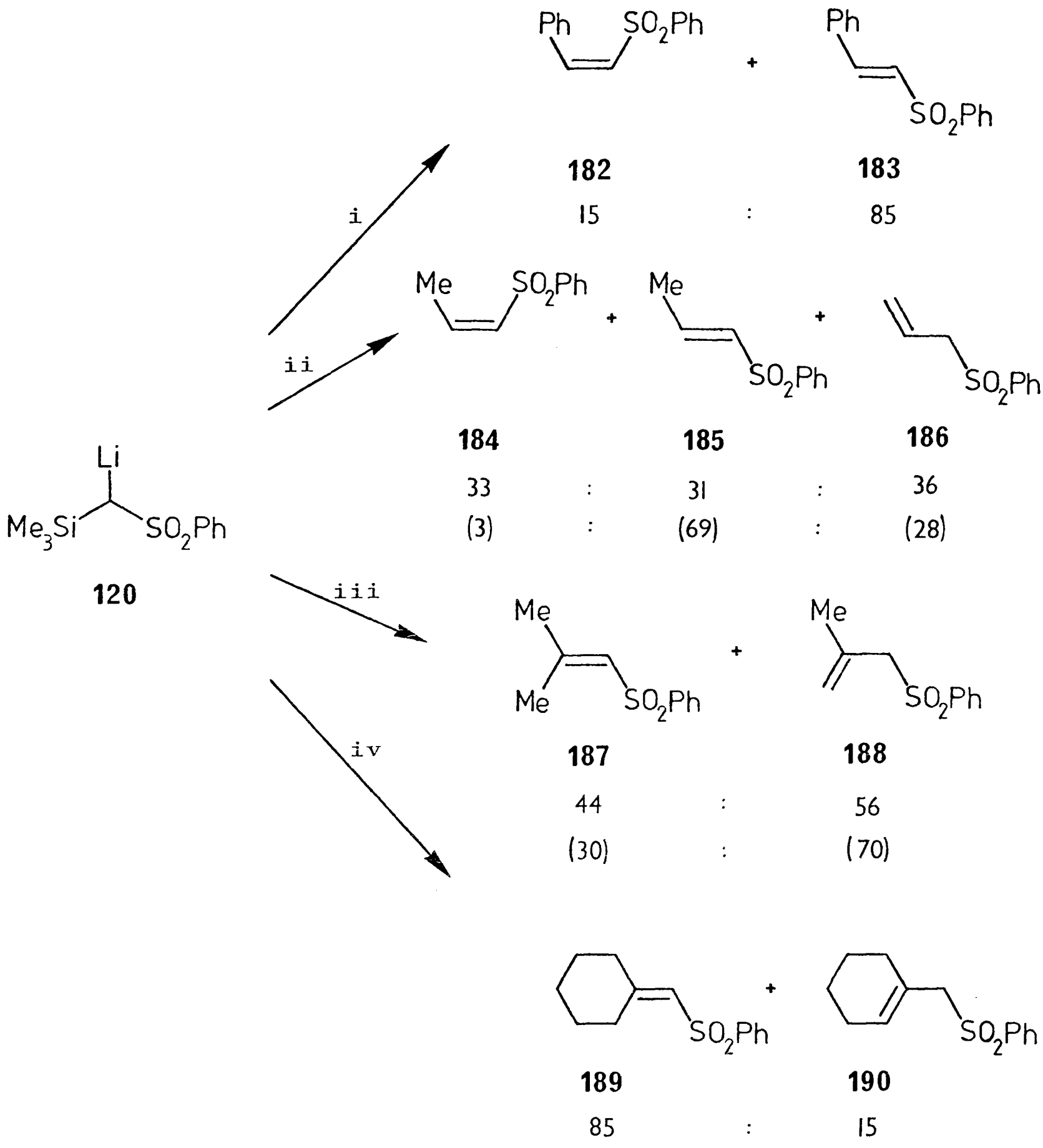


181

Scheme 72.

Section C: Reaction of Metallated Phenyl Trimethylsilylmethyl Sulphone with Aldehydes and Ketones

The products of the reactions of the lithiated derivative (120) of the silyl sulphone (170) with four aldehydes and ketones are shown in Scheme 73. As was the case for the lithiated silyl phosphine oxide (119), reaction occured readily in ether at -78^{o} with aldehydes, although not with corresponding stereoselectivity. With benzaldehyde, a mixture of the Z- and E-vinyl sulphones (182) and (183) was formed. Acetaldehyde gave a roughly equal mixture of the Z- (184) and E- (185) vinyl sulphones and the allyl sulphone (186). Reaction of (120) with the ketones acetone and cyclohexanone could not be achieved in ether but did take place in THF to give mixtures of the vinyl (187) and (189), and allyl (188) and (190) sulphones.

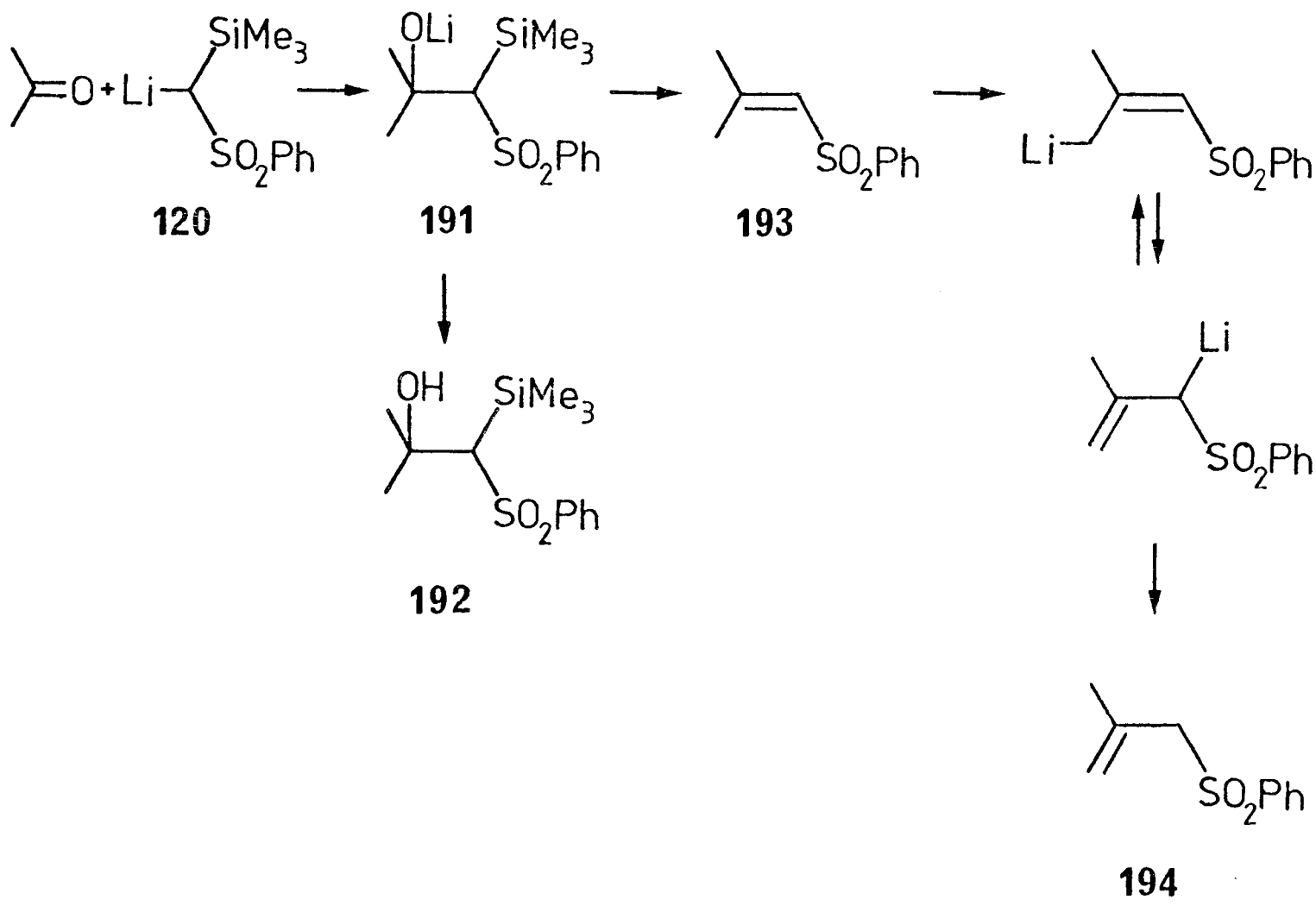


Figures in parentheses refer to the equilibrium positions for the respective unsaturated sulphones, reference 155.

Reagents: i, benzaldehyde/ether; ii, acetaldehyde/ether; iii, acetone/THF; iv, cyclohexanone/THF

Scheme 73.

Presumably the vinyl sulphones (193) were formed by way of Peterson elimination from the intermediate (191), produced by reaction between (120) and the carbonyl compound. The allyl sulphones (194) could then be derived from the respective vinyl compounds (193) by isomerization under the basic conditions of the reaction (Scheme 74). Such isomerizations of vinyl sulphones with a γ-hydrogen are known[153-155]. The mixtures of unsaturated sulphones formed from the reactions of (120) are not equilibrium mixtures, however (cf. the literature[155] equilibrium positions for the sulphones derived from acetaldehyde and acetone also given in Scheme 73).



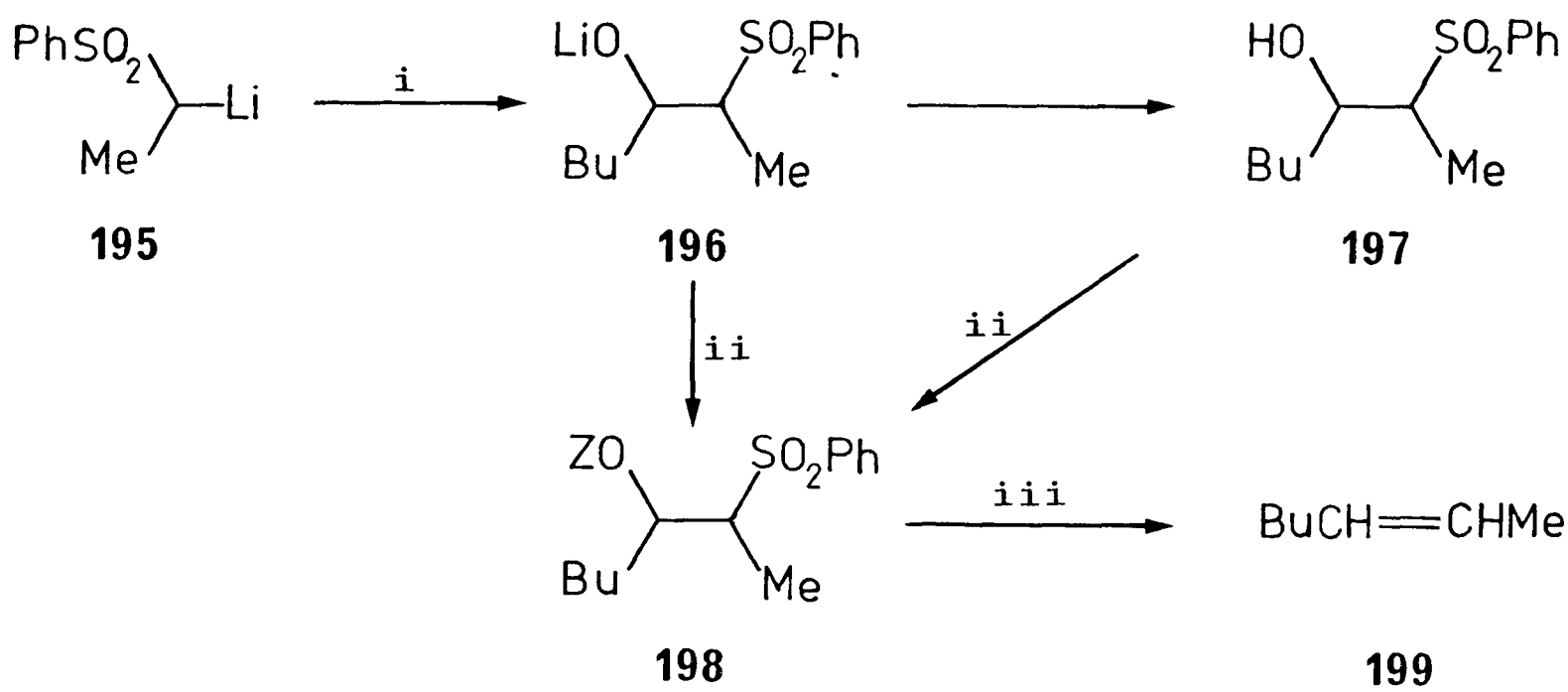
Scheme 74.

Attempts were made to isolate the protonated intermediate (192) before elimination, by protonation of the reactions at

low temperature. Such attempts led either to the formation of unsaturated sulphones as before or to the recovery of starting materials. Although isolation of (192) was not possible it would appear that a wide variety of potentially useful[156,157] unsaturated sulphones are accessible from the reactions of (120).

Section D: 2-Phenyl-2-acetoxy-1-trimethylsilylethyl Phenyl Sulphone

Sulphones with a leaving group in the β-position such as (198), have been shown to lead in good yields to olefins (199) by reductive elimination reactions. Such sulphones can be prepared from α-metallated sulphones and carbonyl compounds either via the β-hydroxysulphone (197) or directly by quenching the intermediate adduct (196) with the appropriate electrophile[158,159] (Scheme 75).



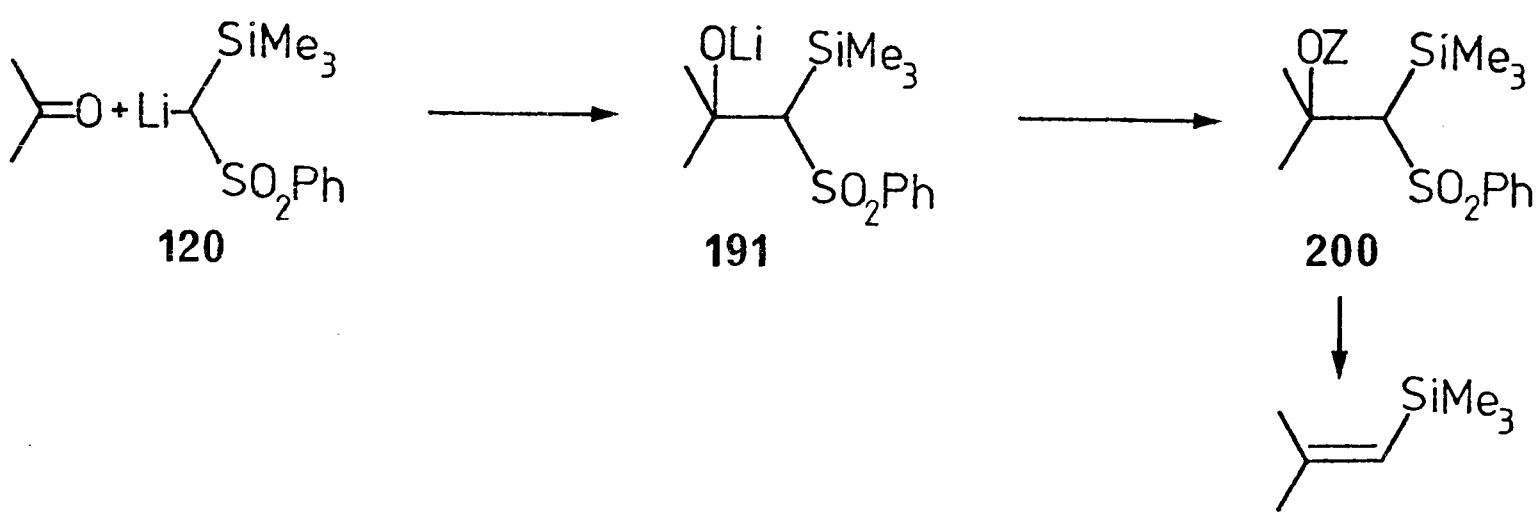
195 196 197 198 199

Z=Ms, Ts or OAc

Reagents: i, BuCHO; ii, MsCl, TsCl or Ac_2O; iii, Na.Hg/Et_2O

Scheme 75.

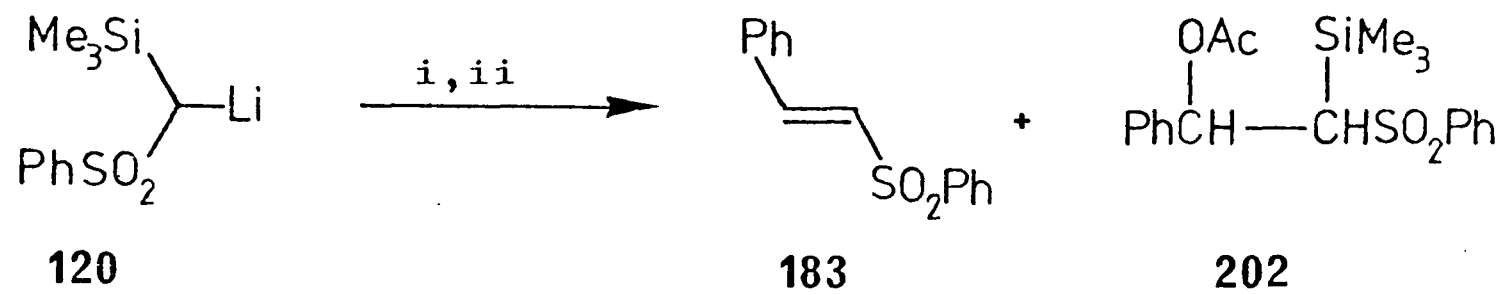
It was thought that by means of a procedure of the latter type, the unstable intermediate (191) formed by reaction of the lithiated silyl sulphone (120) with an aldehyde or ketone might be trapped as a stable adduct (200). The latter could then in principle be transformed by reductive elimination into a vinylsilane (201), which was an original objective of the project (Scheme 76).



Scheme 76.

Reaction of (120) at -78° with benzaldehyde followed immediately by treatment with an excess of acetic anhydride produced a mixture of the E-vinyl sulphone (183), together with a compound which had spectroscopic data consistent with the β-acetoxy-α-silyl sulphone (202) (Scheme 77). Separation of (202) from (183) was possible by virtue of the much greater solubility of the latter in light petroleum. The yield of (202) was not improved when the reaction was quenched by acetic anhydride at different temperatures, or when acetyl chloride was used. The n.m.r. spectrum of (202) showed two well defined doublets at δ6.1 and δ3.65 (both J 7.6Hz), attributable to the protons α to acetoxyl and sulphone respectively. These indicated that (202) was a single diastereoisomer, although

its stereochemistry could not be assigned on the basis of the spectroscopic data.

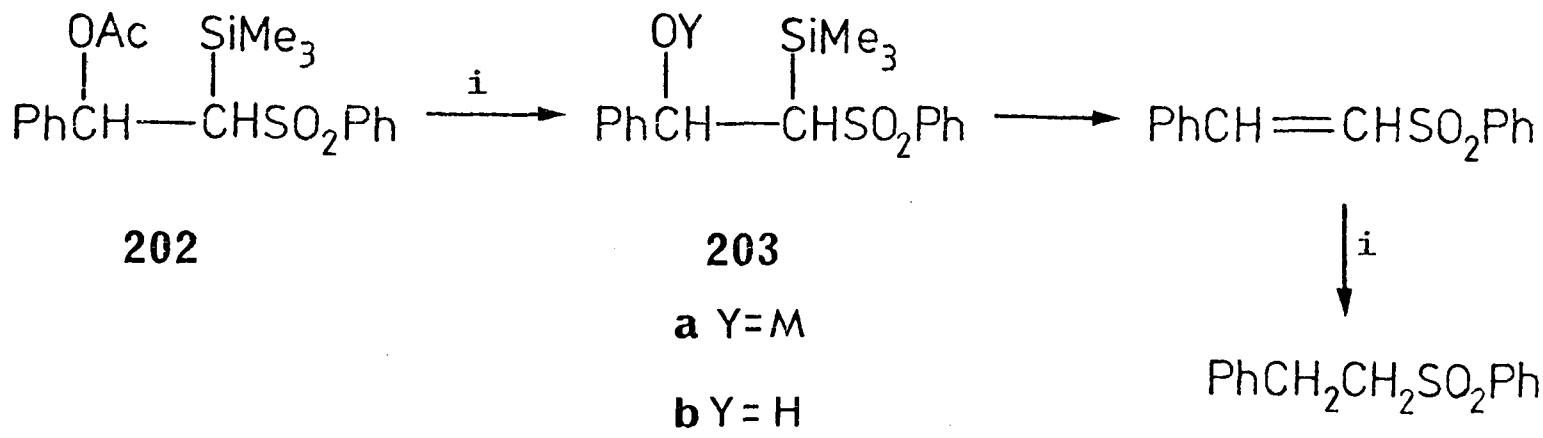


120 **183** **202**

Reagents: i, $PhCHO/Et_2O$; ii, Ac_2O

Scheme 77.

Attempts were made to convert (202) to the β-hydroxy-α-silyl sulphone (203b). Reaction with lithium aluminium hydride gave the saturated sulphone (204) in good yield (Scheme 78). Presumably (204) was formed via reduction of an intermediate vinyl sulphone as shown. Such reductions are known[160].



202 **203** **204**

a Y=M

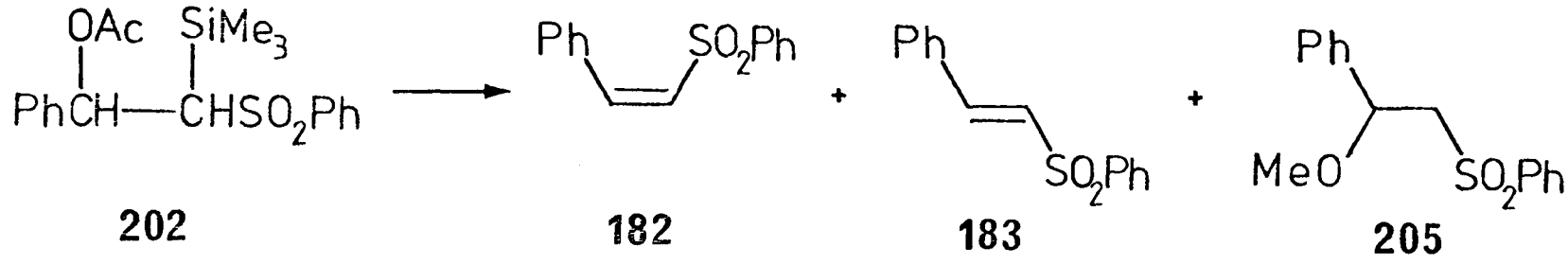
b Y=H

Reagents: i, $LiAlH_4/Et_2O$

Scheme 78.

Treatment of (202) with ammonia in methanol gave a mixture of the Z- and E-vinyl sulphones (182) and (183). With methanolic potassium hydroxide, mixtures of (182), (183)

and the methoxy sulphone (205) were produced (Scheme 79), once again no β-hydroxy-α-silyl sulphone (203) was isolated. The methoxy sulphone (205) was probably formed by nucleophilic addition of methoxide ion to the vinyl sulphones, an authentic sample of (183) was converted completely to (205) when treated under similar conditions. Nucelophilic additions of this type to vinyl sulphones are well known[156,161].



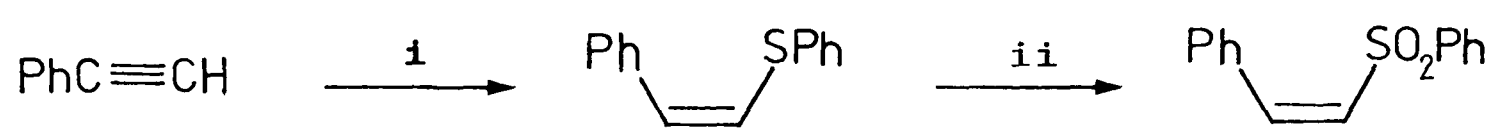
202 **182** **183** **205**

Reagents and Conditions				
NH_3/MeOH/18°/17h	17	:	83	: 0
KOH/MeOH/0°/1h	17	:	33	: 50
KOH/MeOH/18°/17h	0	:	20	: 80

Scheme 79.

Given that (202) was considered to be a single diastereoisomer, it would be expected that the above reactions would produce a single vinyl sulphone if a stereospecific syn-elimination pathway were being followed. The fact that mixtures of the Z- and E-isomers (182) and (183) were produced might be due to the reactions taking place via a non stereospecific elimination, or because partial equilibration of the vinyl sulphone product was occuring, or because (202) was being epimerized under the reaction conditions. Epimerization

could occur via reversible deprotonation at the carbon bearing the silyl and sulphone groups, the intermediate carbanion would thus be stabilized. The possibility of equilibration of the vinyl sulphones was ruled out by treatment of a pure sample of the Z-vinyl sulphone (182) (prepared as shown in Scheme 80) with ammonia in methanol and methanolic potassium hydroxide as before. In both cases, mixtures of (182) and the methoxy sulphone (205) were produced, no E-vinyl sulphone (183) was identified in the product.

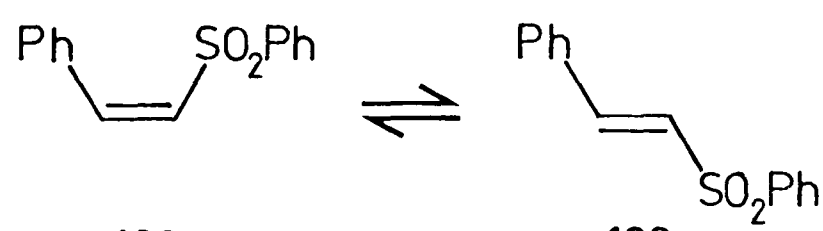


206 **182**

Reagents: i, PhSH/NaOEt/EtOH; ii, $CH_3CO_3H/NaOAc/CH_2Cl_2$

Scheme 80.

To find out the position of equilibrium between (182) and (183), equilibration was brought about by treatment with a catalytic amount of iodine in pentachloroethane at 130° for 6h, i.e. much more vigorous conditions than those above. At equilibrium, nearly all the vinyl sulphone was present as the E-isomer (183) (Scheme 81).



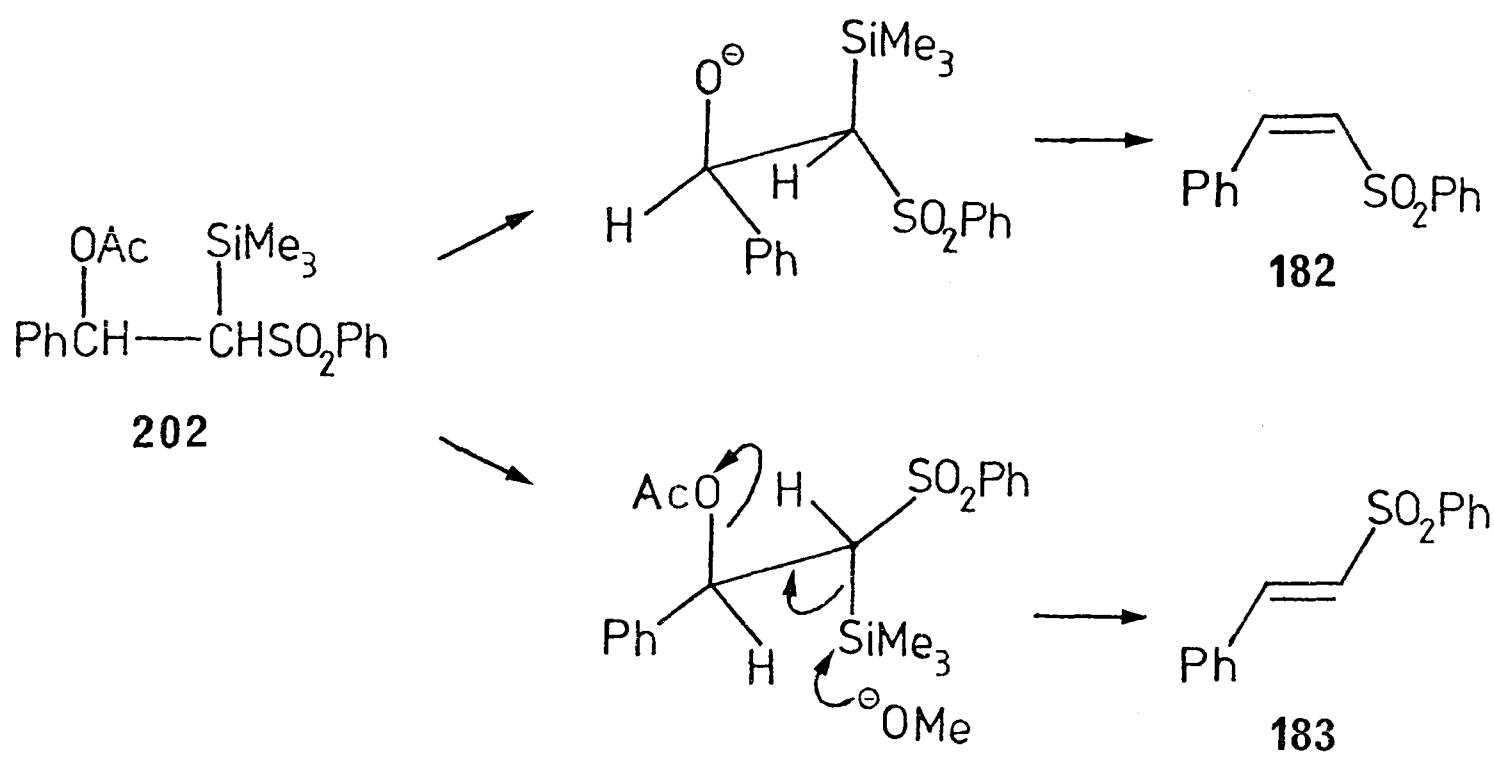
182 **183**

5 : 95

Conditions: $I_2/CHCl_2CCl_3/130^{o}/6h$

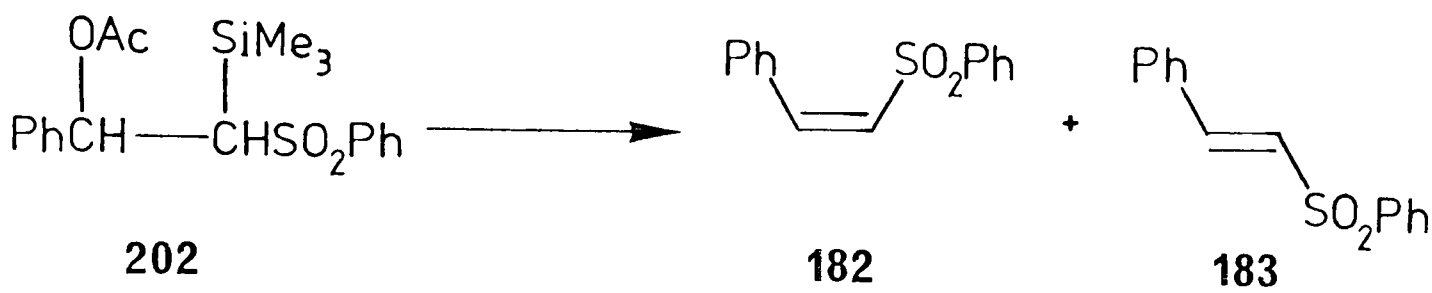
Scheme 81.

Formation of the vinyl sulphones from (202) via non stereospecific elimination could be the result of (202) undergoing both hydrolysis, leading to Peterson (syn) elimination, and direct elimination which might be anti (Scheme 82). An elimination of the latter kind is possibly less likely in methanolic ammonia than methanolic potassium hydroxide.



Scheme 82.

It was thought that anti-elimination similar to that indicated in Scheme 82 might be brought about by fluoride containing reagents[162–165]. However treatment of (202) with potassium fluoride in DMSO and benzyltrimethylammonium fluoride[166] in THF again gave mixtures of the vinyl sulphones (182) and (183) (Scheme 83).

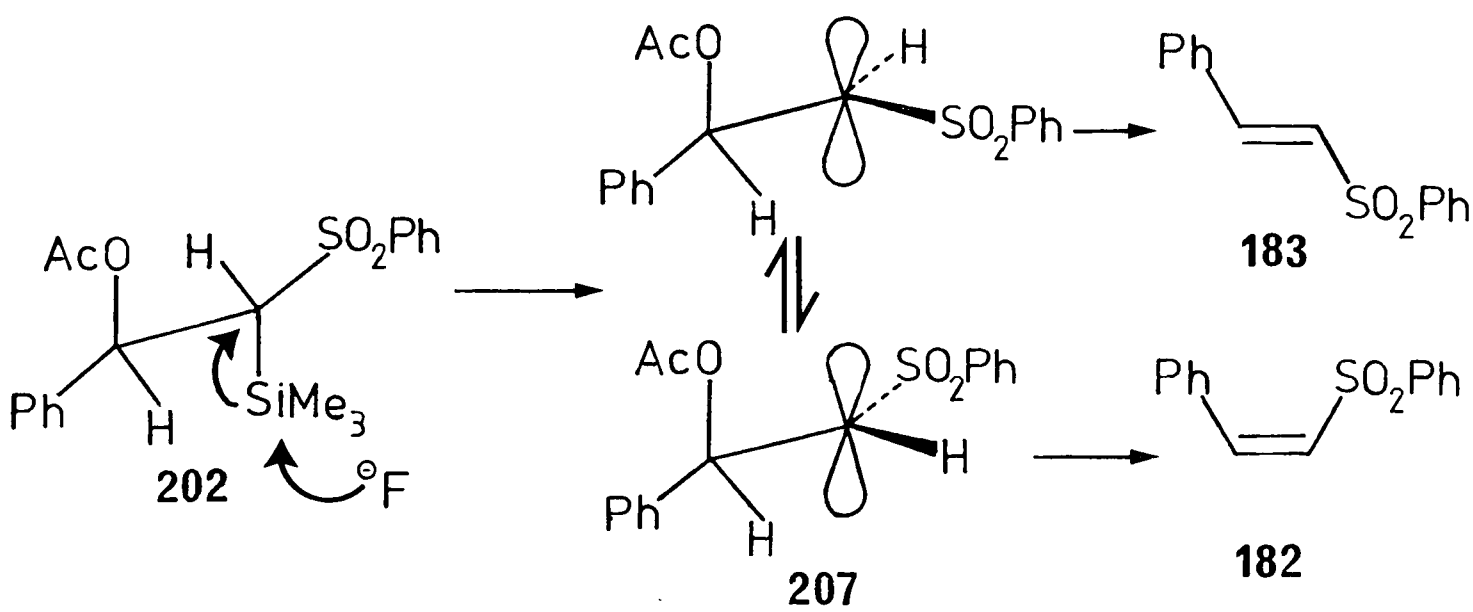


Reagents

(a) KF/DMSO	35	:	65
(b) Me_3BzNF/THF	33	:	67

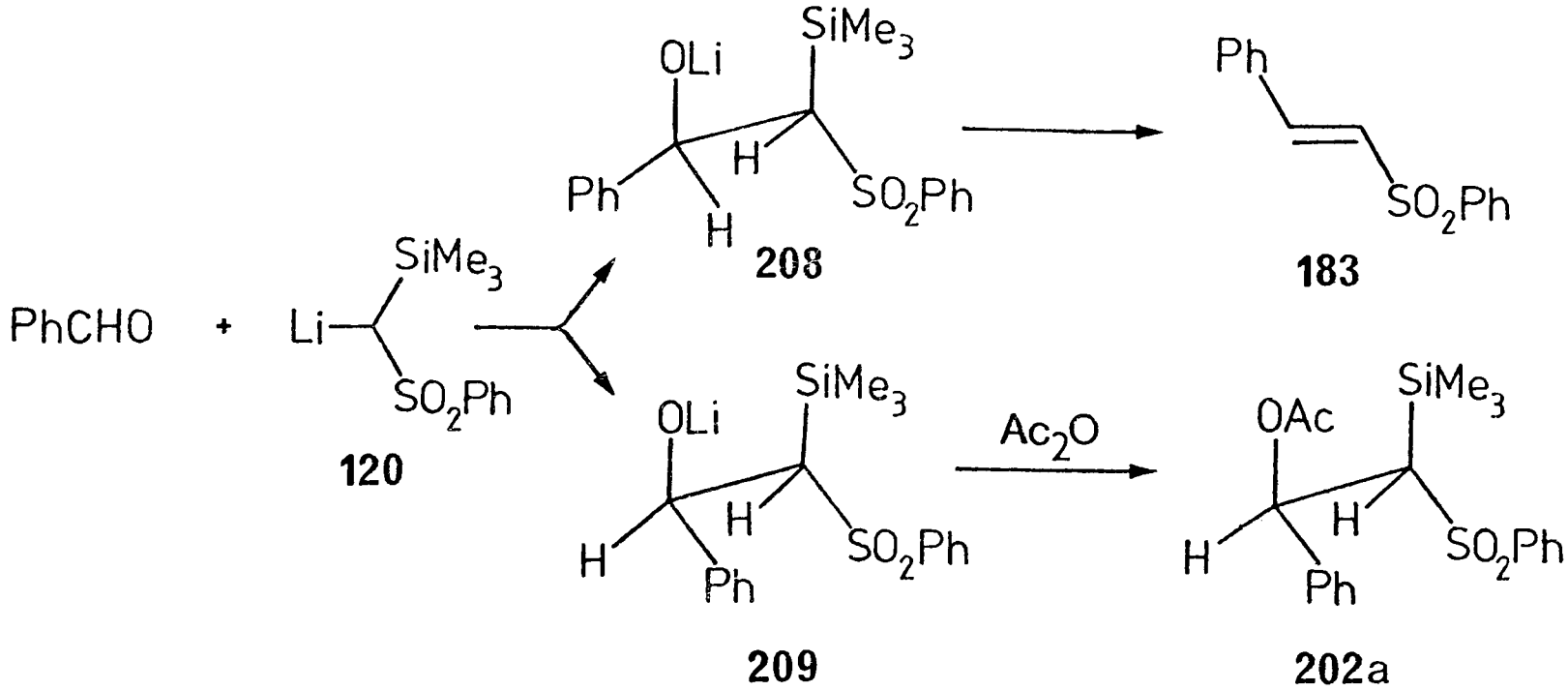
Scheme 83.

Pure samples of the Z-vinyl sulphone (182) were shown not to be equilibrated with the E-isomer (183) when treated under the same conditions; so if (202) is a single stereoisomer, the above elimination reactions are not stereospecific. This is perhaps not too surprising because the presence of the sulphone group would favour a non concerted (ElcB type) type mechanism by stabilizing the carbanion intermediate (207). The latter could lose its stereochemical identity if it had sufficient lifetime for bond rotation to occur before loss of the acetoxy group took place (Scheme 84).



Scheme 84.

It is thus not possible to assign the stereochemistry of (207) on the basis of its chemical reactions. For an unambiguous assignment, a crystal structure would be required. It is noteworthy that only the E-vinyl sulphone (183) was produced as a co-product in the acetic anhydride quenched reaction by which (202) was prepared (Scheme 77) whereas without the acetic anhydride, both Z- and E-vinyl sulphones (182) and (183) were formed. So perhaps only one (209) of the two intermediates formed by reaction of (120) with benzaldehyde reacts further with acetic anhydride and the silyl acetate is thus the (RS,SR) isomer (202a) (Scheme 85).

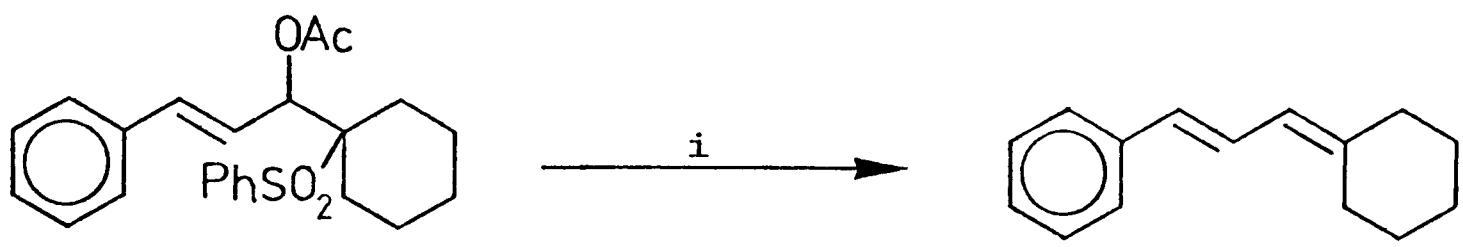


Scheme 85.

Section E: Reaction of 2-Phenyl-2-acetoxy-1-trimethylsilylethyl Phenyl Sulphone with Sodium Amalgam

Reductive eliminations of β-acetoxy sulphones have been carried out in either methanol or ethanol as solvent (Scheme 75)

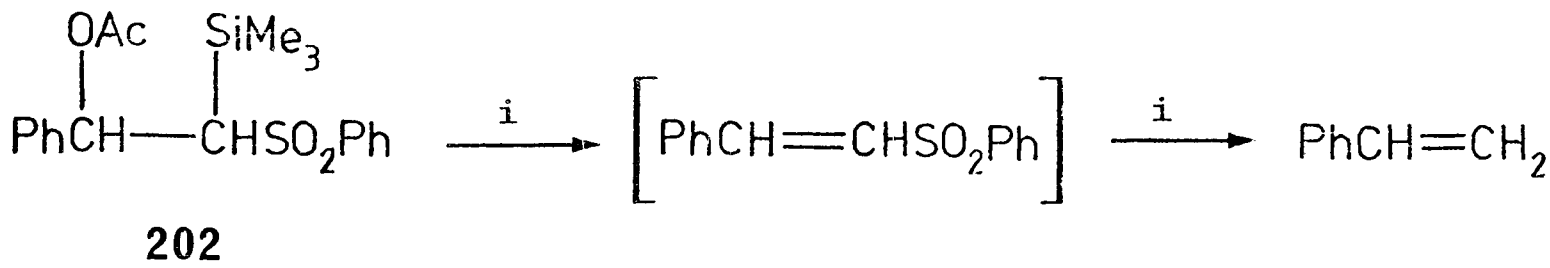
or mixtures of either with ethyl acetate[159] (Scheme 86).



Reagents: i, Na.Hg/MeOH/EtOAc

Scheme 86.

The first attempt to apply such a procedure to (202) was made in methanol at room temperature. The main product of the reaction was styrene, which was presumably formed via initial elimination to vinyl sulphone followed by reduction of the latter by sodium amalgam[158] (Scheme 87).



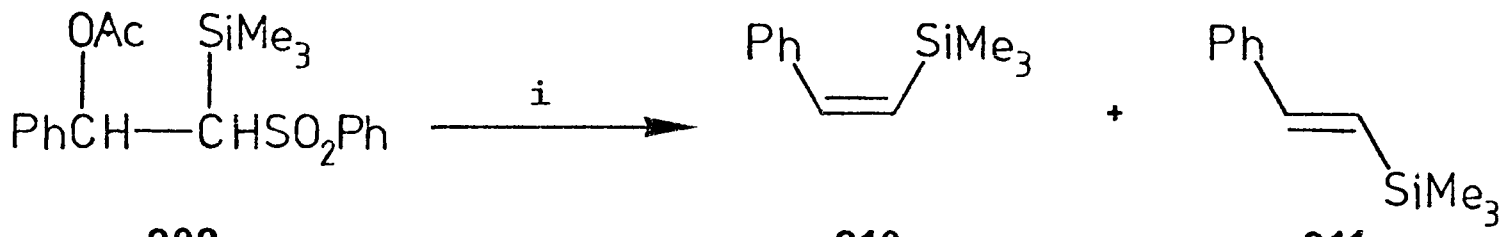
202

Reagents: i, Na.Hg/MeOH/18°/17h

Scheme 87.

It was considered that the initial elimination to vinyl sulphone was brought about by sodium methoxide produced under the conditions of the reaction and that this might be prevented by buffering the reaction medium. Sodium dihydrogen phosphate ($NaH_2PO_4.2H_2O$) had been found to be a satisfactory buffer for sodium amalgam reductions of base sensitive compounds[147,167].

When this buffer was used for the reaction of (202) with sodium amalgam in methanol, a different product to that from the unbuffered reaction was produced. Analysis by i.r., n.m.r., and g.l.c. showed that the product was a mixture of the Z- and E- vinylsilanes (210) and (211) (74% combined yield) (Scheme 88), there was no vinyl sulphone or styrene in the product. The fact that a mixture of vinylsilanes was formed by the reductive elimination is not unexpected in this case since such reactions are not stereospecific and generally give a preponderance of the more stable olefin[159].



202 210 211

1 : 2.8

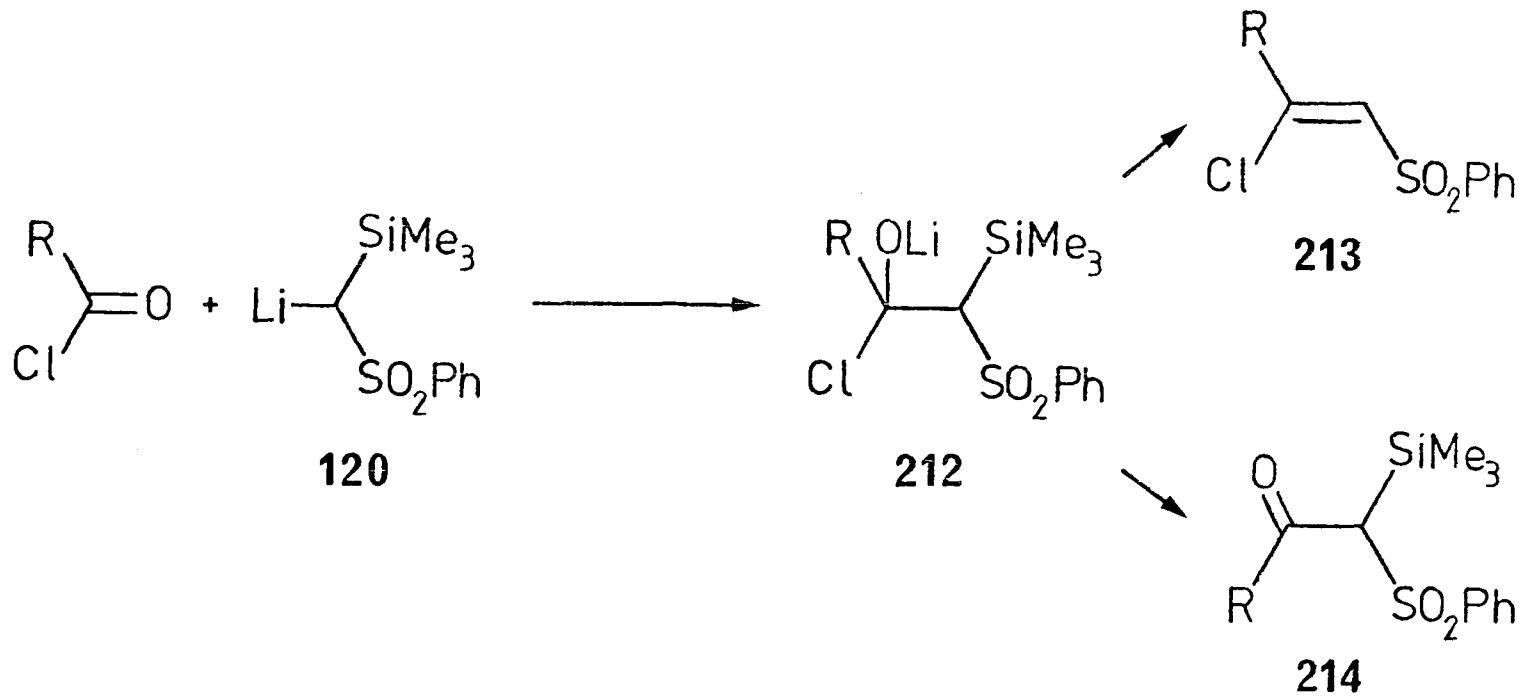
Reagents: i, $Na.Hg/MeOH/NaH_2PO_4$

Scheme 88.

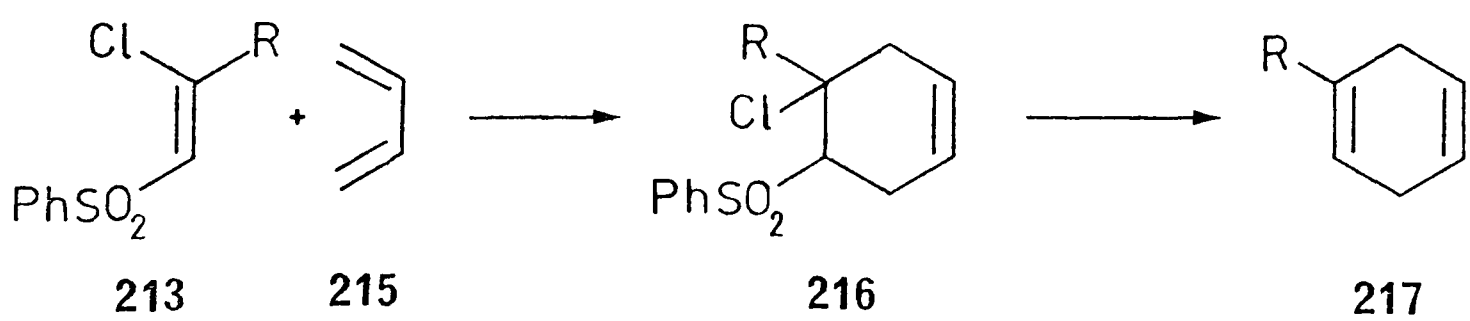
In conclusion, it has been shown that it is possible to prepare from an α-metallated organosilane (120) a compound such as (202) which can be transformed selectively into both vinyl sulphones (for example by treatment with ammonia in methanol) and vinylsilanes (by reductive elimination). An original objective of the project has thus been achieved, but further work is necessary to improve the conversion of (120) to (202) and to prepare adducts of carbonyl compounds other than benzaldehyde.

Section F: Reaction of Metallated Phenyl Trimethylsilylmethyl Sulphone with Acid Chlorides

The reaction of the lithiated derivative (120) of the silyl sulphone (170) with acid chlorides was investigated to see whether products could be derived from Peterson elimination in the intermediate (212) or the usual displacement of chloride (Scheme 89). If the former were the case, such a reaction would provide a route to β-chlorovinyl sulphones of the type (213). Such compounds are of interest as potential "acetylene equivalents" in Diels-Alder reactions[147,168,169], an adduct (216) with a diene (215) could potentially be transformed regiospecifically into a cyclohexa-1,4-diene (217) by a reductive elimination of the type discussed in the previous section (Scheme 90).

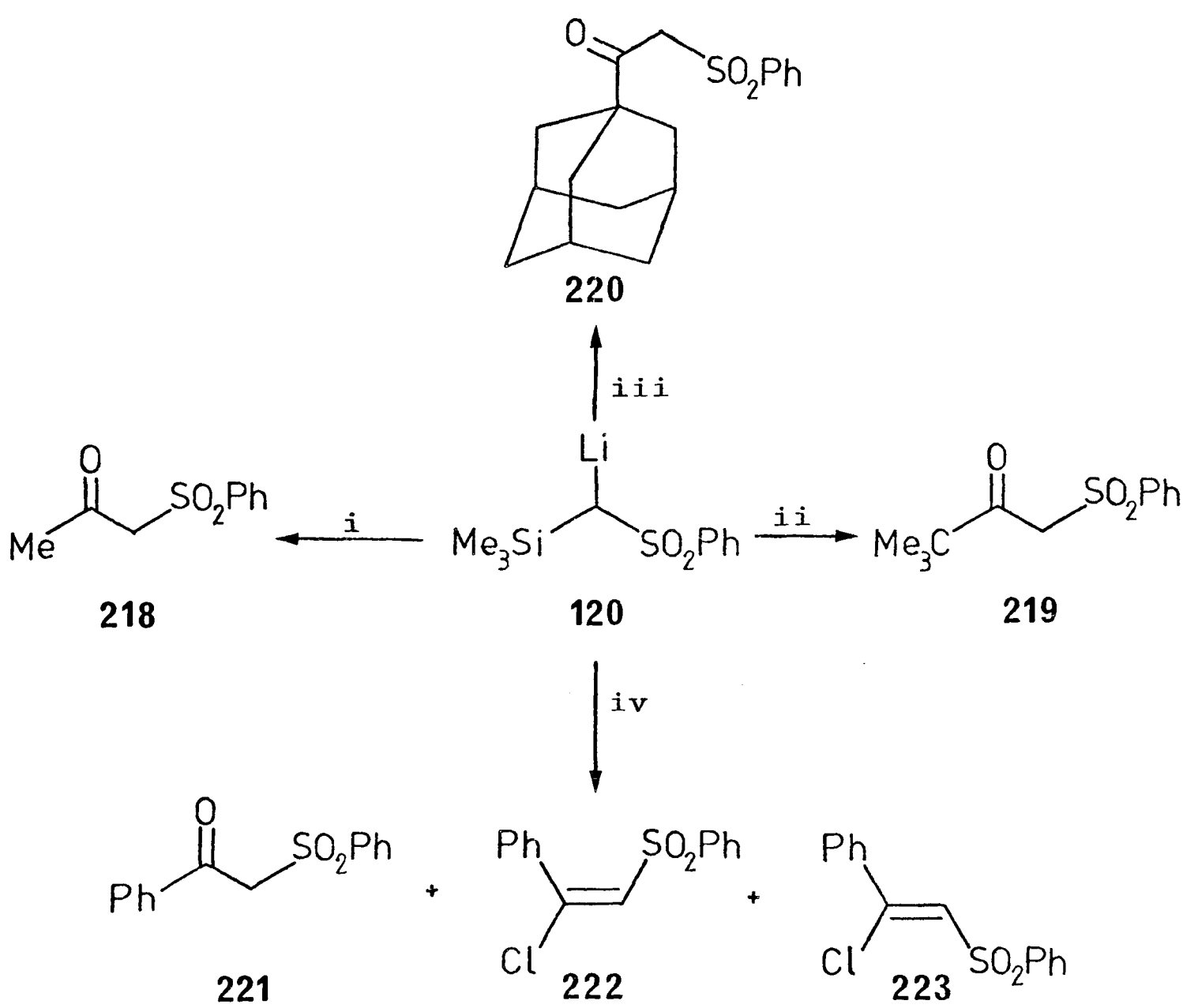


Scheme 89.



Scheme 90.

The products formed from the reactions of (120) witn four acid chlorides are shown in Scheme 91. In each case the main product was a β-ketosulphone, presumably formed by desilylation of an initial product of the type (214). Only the reaction with benzoyl chloride gave an appreciable amount of the β-chlorovinyl sulphones (222) and (223).



Reagents: i, acetyl chloride; ii, pivaloyl chloride; iii, 1-adamantane carboxylic acid chloride; iv, benzoyl chloride

Scheme 91.

β-Ketosulphones are useful synthetic intermediates[156,170] and although the reactions of (120) with acid chlorides would appear to provide a route to a variety of β-ketosulphones, there are more direct methods of preparing them than the one described here.

EXPERIMENTAL

GENERAL

Temperatures are quoted in degrees centigrade.

Infra-red spectra (i.r.) were recorded on Perkin-Elmer 257 or 297 instruments.

Proton nuclear magnetic resonance spectra (n.m.r.) were recorded on Perkin-Elmer R14, R32 or R24 instruments at 100, 90 or 60MHz respectively, or on a Bruker WH300 instrument at 300MHz. Chloroform (δ7.27) or dichloromethane (δ5.25) were used as internal standards for compounds containing a trimethylsilyl group, otherwise tetramethylsilane (δ0.0) was used.

Pulse Fourier transform carbon-13 nuclear magnetic resonance spectra (^{13}C n.m.r.) were recorded on Bruker WH90 or WH300 instruments at 22.63 or 75.57MHz respectively. Solutions in deuterochloroform were used, with the central peak of the solvent signal (77.00ppm) as internal standard.

Mass spectra were recorded on either Varian MATCH7 or VG Micromass 16F or ZAB1F instruments under the supervision of Dr R.T. Aplin. When carried out in conjuction with gas chromatography, a 200m glass capilliary column coated with SP1000 was used, at 140°. Ion intensities are quoted relative to the base peak.

Melting points were determined on a Kofler block and are corrected.

Microanalyses were carried out under the supervision of Dr F.B. Strauss.

Analytical gas-liquid chromatography (g.l.c.) was carried

out using Pye 104 chromatographs. Columns were 5ft long × 4mm bore and were packed with Embacel coated with OV17 (10%), Silicone oil (3%) or PEGA (10%) and were used at the temperature quoted.

Preparative g.l.c. was carried out using a Pye 105 automatic preparative chromatograph with a 15ft long × $^{3}/_{8}$" bore column packed with OV17 (15%).

Thin layer chromatography (t.l.c.) was carried out on plates coated with unbaked Kieselgel $HF_{254+366}$.

Preparative t.l.c. was carried out on 20×20 plates and 100×20cm plates coated with unbaked Kieselgel $HF_{254+366}$, pre-eluted with acetone.

Solvents: Diethyl ether, benzene and xylene were dried over sodium wire. Light petroleum, of boiling range 30-40°, 40-60° or 60-80° as quoted, was redistilled through a 70cm vigreux column before use. Tetrahydrofuran (THF) was dried by heating under reflux with sodium wire and benzophenone until the blue colour of the ketyl radical persisted, and then was distilled under nitrogen. Pyridine was dried by heating under reflux over potassium hydroxide pellets for 2h, followed by distillation. Dimethylformamide (DMF) and dimethyl sulphoxide (DMSO) were dried by heating under reflux over calcium hydride chips for 6h, followed by distillation. Ethanol was dried by reaction with magnesium then distilled.

REAGENTS

Sodium sand.- The required amount of sodium was heated in dry o-xylene in a round bottomed flask until the xylene began to reflux. The air condensor was then removed and the flask tightly corked and shaken vigorously until the molten metal was finely dispersed, and settled to the bottom of the flask as sodium sand. When cool, the xylene was decanted off and the sodium washed with dry ether three times.

Methyllithium in ether[171].- To freshly pressed lithium wire (7.5g, 1.07mol) in dry ether (150ml), was added, with stirring under nitrogen, methyl iodide (51g, 0.36mol) at such a rate as to maintain steady reflux. When cool, the solution was transferred to a dry sealed bottle under a pressure of nitrogen using stainless steel tubing.

The concentration of methyllithium in the solution was determined by titration for "total alkali" and "other alkali" which involves the use of 1,2-dibromoethane[172].

n-Butyllithium and s-Butyllithium were commercially supplied solutions in hexane.

Sodium Hexamethyldisilazide[173].- Sodium pieces (3.57g, 0.155mol) were added, with stirring, slowly to liquid ammonia (ca. 200ml), producing a blue solution. After about $^{1}/_{3}$ of the sodium had been added, ferric nitrate (0.2g) was added and the mixture went grey. Following the addition of the remaining

sodium the mixture was stirred for a further 90 min then left to stand for 16h. Hexamethyldisilazane (25g, 0.155mol) in dry benzene (70ml) was then added and the mixture was heated under reflux until the evolution of ammonia ceased (ca. 12h). The mixture was filtered into a dried bottle and the solution standardized by titration.

Raney Nickel[174].- Nickel-aluminium powder (50g) was added cautiously during 15min to a solution of sodium hydroxide pellets (65g) in water (250ml) maintained at 70°. The mixture was then allowed to cool during 75 min and then transferred to a 1l measuring cylinder. The supernatant liquid was decanted off and the residue washed with water until the washings were pH 7. The supernatant was then again decanted off, ethanol (50ml) was added and the slurry was transferred to a screw-top jar. It was found that the activity of the Raney nickel deteriorated on standing, in general it was used within one week of preparation.

Magnesium Bromide Etherate[176].- To dried magnesium turnings (3g, 0.125mol) in dry ether (125ml) was added slowly, with cooling and stirring under nitrogen, bromine (2ml, 5.8g, 36.7mmol) in dry ether (25ml). When cool, the supernatant solution was transferred to a dry sealed bottle under a pressure of nitrogen using stainless steel capilliary tubing.

p-Toluenesulphonyl chloride was recrystallized before use from light petroleum (b.p. 60-80°).

Trimethylsilylchloride and Benzaldehyde were redistilled before use.

N-Methylmorpholine-N-Oxide was prepared in 80% yield by oxidation of N-methylmorpholine with 50% hydrogen peroxide[84].

5% Sodium Amalgam[176].- Sodium (3.72g, 0.16g atom) was placed in a Buchner flask and covered with mineral oil (40ml). The flask was heated on a hot plate covered with an asbestos sheet, with a stream of nitrogen passing through. After the sodium had melted, mercury (70.4g, 5.2ml) was added quickly from a dropping funnel with swirling. A violent reaction occured and a solid grey mass was deposited at the bottom of the flask. The flask was heated further and above 270° the amalgam softened, it was then broken up with a glass rod and allowed to cool. After cooling, the amalgam was washed with light petroleum and stored under light petroleum (b.p. 60-80°).

PART I

1-Trimethylsilyl-trans-cyclohexane-1,2-diol (10)[22,38].- Concentrated sulphuric acid (5ml) was added to water (10ml) and AR acetone (125ml) at 0°. 7-Oxa-1-trimethylsilylbicyclo-(4,1,0)heptane (24)[22] (5g, 0.029mol) was then added, with stirring, and the mixture was allowed to warm to 18° during 1h then stirred at 18° for a further 25 min. Sodium hydroxide solution (2.5M, 100ml) was added, with cooling, followed by water (50ml). The aqueous layer was extracted with ether (3×50ml), the combined organic layers were washed with brine and dried ($MgSO_4$). Evaporation of solvent followed by recrystallization from ether-light petroleum (b.p. 40-60°) gave the trans-diol (10) as white needles 3.4g, 62%), m.p. 82-83° (lit.[22] m.p. 82-83°), δ($CDCl_3$) 3.65(1H,m,W_H=13Hz,H-2), 1.2-2.1(10H,complex, 8H after D_2O exch.), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(CCl_4) 3390(O-H), 1380,1245,845cm^{-1}(C-Si).

1-Trimethylsilyl-cis-cyclohexane-1,2-diol (18)[40].- 1-Trimethylsilylcyclohexene (16)[83](15g, 0.098mcl), N-methyl-morpholine-N-oxide (18.8g, 0.16mol) and t-butanol (10ml) were added to water (17.5ml) and acetone (170ml). Osmium tetroxide (190mg, 0.7mmol) was then added and the resulting dark brown mixture stirred at 50°. After 36h, g.l.c. (OV17, 150°) showed that all the vinylsilane had been consumed, the acetone was then evaporated under vacuum and water (300ml) was added. The aqueous solution was extracted with ether (4×75ml) and the combined ether extracts were washed with 2M HCl (200ml),

saturated aqueous sodium carbonate and brine then dried ($MgSO_4$). Evaporation of the ether gave a brown solid (12.9g) which was recrystallized from light petroleum (b.p. 60-80°) giving white crystals of the cis-diol (18) (11.8g, 70%), m.p. 85-88° (Found: C,57.7; H,10.8. $C_9H_{20}O_2Si$ requires C,57.4; H,10.7%), δ($CDCl_3$) 3,65(1H,m,W_H=16Hz,H-2), 1.1-1.9(10H,complex, 8H after D_2O exch.), 0.1(9H,s,$SiMe_3$), $\nu_{max.}$(CCl_4) 3580,3720 (br, intramolecularly H bonded OH), 1380,1245,(C-Si),1050, 957cm^{-1}.

1-Trimethylsilyl-cis-cyclooctene (100).- To sodium sand (16g, 0.70mol) in dry ether (200ml) was added, with stirring under nitrogen, trimethylsilyl chloride (32g, 0.29mol), ethyl acetate (1ml) and 1-bromo-cis-cyclooctene (99)[177](1ml). After about 10 min the solution became blue and the ether began to reflux. 1-bromo-cis-cyclooctene (99) (54g, 0.29mol) was then added dropwise during 1h and the mixture was stirred under nitrogen for a further 12h. The solid was filtered off and washed with dry ether (75ml), the washings and filtrate were combined and the ether evaporated giving a yellow oil. This was distilled to give 1-trimethylsilyl-cis-cyclooctene (100) as a colourless liquid (40g, 77%), b.p. 56-64° at 1mm Hg (lit.[178] b.p. 73-74° at 7mm Hg), δ($CDCl_3$) 5.9(1H,t,H-Z), 1.2-2.3(12H,complex), 0.1(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 3030 (=C-H), 1620(C=C), 1250,840cm^{-1} (C-Si).

1-Trimethylsilyl-cis-cyclooctane-1,2-diol (63).- 1-Trimethylsilyl-cis-cyclooctene (100) (17.5g, 0.096mol), N-methylmorpholine-N-oxide (17.5g, 0.15mol) and t-butanol (10ml) were added to water (25ml) and acetone (300ml). Osmium tetroxide (180mg, 0.66mmol) was then added and the resulting dark brown mixture stirred at 50°. After 240h t.l.c. using light petroleum b.p. 40-60°-ether 1:1 as elutant indicated that all the vinyl silane had been consumed. The acetone was evaporated under vacuum and water (280ml) was added. The aqueous solution was extracted with ether (5×60ml) and the combined ether extracts were washed with 2M HCl (180ml), saturated aqueous sodium carbonate and brine then dried ($MgSO_4$). Evaporation of the ether gave a brown solid (14.6g) which was recrystallized from light petroleum (b.p. 60-80°) giving 1-trimethylsilyl-cis-cyclooctane-1,2-diol (63) as a white solid (13.2g, 74%), m.p. 88-90°C (Found: C,61.05; H,11.2. $C_{11}H_{24}O_2Si$ requires C,61.0; H,11.55%), $\delta(CDCl_3)$ 4.05(1H,brd, J 9Hz,H-2), 1.1-2.3(14H,complex,12H after D_2O exch.), 0.2(9H, s,$SiMe_3$), $\nu_{max.}(CHCl_3)$ 3630,3560(br,intramolecularly H bonded OH), 1450,1250,1048,951,844cm^{-1}(C-Si).

Reaction of 1-trimethylsilyl-1,2-diols with Methyllithium and Methyl Iodide. (A) 1-Trimethylsilyl-trans-cycloxhexane-1,2-diol (10).- (a) To a solution of the trans-diol (10) (0.3g, 1.6mmol) in dry ether was added, with stirring under nitrogen methyllithium (1.4M, 1.2ml, 1.7mmol). The mixture was stirred at 15° for 20 min then methyl iodide (0.68g, 4.8mmol) was added.

Stirring was continued and the reaction was monitored on t.l.c. using light petroleum (b.p. 40-60°) - ether (1:1) as elutant. Even after 170h there was no indication of any reaction having occured. Water (5ml) was added and the aqueous layer was extracted with ether (2×4ml). The combined organic layers were washed with brine and dried ($MgSO_4$). Evaporation of solvent gave a white solid (0.26g) which was identified as being mainly starting material by n.m.r. and i.r.

(b) The same procedure was carried out in dry DMSO as solvent. The reaction was worked up as before after 20h using light petroleum (b.p. 40-60°) instead of ether. Evaporation of solvent from the dried extracts followed by short path distillation at 0.1mm Hg and 90-110° gave an oil (0.19g). Analysis by n.m.r. indicated that it was a mixture of ca.30% starting material and 70% t-2-methoxy-t-1-trimethylsilyl-r-1-cyclohexanol* (74), δ($CDCl_3$) 3.3(3H,s,OMe), 3.25(1H,m,H-2), 1.0-2.2(9H, complex), 0.1(9H,s,$SiMe_3$). Attempts were made to isolate the latter compound pure by preparative t.l.c. but these resulted in loss of trimethylsilyl from the product.

There was no indication that either procedure gave rise to any of the compound (70) derived from methylation of the

* For certain derivatives of cyclohexane and cyclooctane with more than two substituents, the nomenclature adopted for designating the relative stereochemistry of substituents is that used by Berti et al.[179], r refers to the substituent chosen as reference, c to substituents cis to the reference and t to substituents trans to the reference.

tertiary hydroxyl group of the diol (10); an authentic sample of it was available[22,23].

(B) 1-Trimethylsilyl-cis-cyclohexane-1,2-diol (18).- The cis-diol (18) gave no reaction under the above conditions in ether. In DMSO after 15h at 15° work up gave an oil; analysis by n.m.r. indicated that it contained a number of components including 2-methylcyclohexanone[180]. There was very little trimethylsilyl containing product present.

(C) 1-Trimethylsilyl-cis-cyclooctane-1,2-diol (63).- The cis-diol (63) (0.2g, 0.93mmol) in dry DMSO (3ml) was treated with methyllithium (1.4M, 0.73ml, 1.0mmol) followed by methyl iodide (0.39g, 2.7mmol) at 15° for 18h under the conditions used for the trans-diol (10). Evaporation of solvent from the dried extracts followed by short path distillation at 25mm Hg and 90-110° gave 2-methylcyclooctanone (102) (72mg, 57%) (lit.[181] b.p. 86° at 12mm Hg), δ($CDCl_3$) 1.05 (3H,d, J 6Hz,Me), 0.9-2.9(13H, complex), $\nu_{max.}$(liquid film) 1700(C=O), 1465,1375,1260,805cm^{-1}. An authentic sample of the product was available[56], it had the same spectroscopic data and gave the same peak of retention time 10.5 min on g.l.c. (OV17, 140°), shown by co-injection.

t-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclohexanol (78).- To a solution of 1-trimethylsilyl-trans-cyclohexane-1,2-diol (10) (4.5g, 23.9mmol) in dry pyridine (25ml) was added acetic

anhydride (5.0ml, 5.37g, 52.7mmol). The mixture was stirred at 40° for 40h then poured into a mixture of ether (100ml) and 2M HCl (100ml). The aqueous layer was extracted with more ether (2×40ml), the combined ether extracts were then washed with saturated aqueous sodium carbonate, brine and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 110-120° gave the trans-hydroxy acetate (78) (5.3g, 96%) as a colourless oil. (Found: C,57.7, H,9.65. $C_{11}H_{22}O_3Si$ requires C,57.35; H,9.6%), δ($CDCl_3$) 4.85 (1H,m,W_H=13Hz,H-2), 2.05(3H,s,CH_3CO), 1.0-2.1(9H, complex, 8H after D_2O exch.), 0.1(9H,s,$SiMe_3$). $\nu_{max.}$(liquid film) 3495 (br,O-H), 1723,1743(C=O), 1240,840cm^{-1} (C-Si).

c-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclohexanol (79).- To a solution of 1-trimethylsilyl-cis-cyclohexane-1,2-diol (18) (3.5g, 18.6mmol) in dry pyridine (20ml) was added acetic anhydride (3.9ml, 4.2g, 40mmol). The mixture was stirred at 15° for 18h then poured into a mixture of ether (80ml) and 2M HCl (80ml). The aqueous layer was extracted with more ether (2×30ml), the combined ether extracts were then washed with saturated aqueous sodium carbonate, brine and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 100-110° gave the cis-hydroxy acetate (79) (4.18g, 97%) as a colourless oil. (Found: C,57.0; H,9.85. $C_{11}H_{22}O_3Si$ requires C,57.35; H,9.6%), δ($CDCl_3$) 4.9(1H,m,H-2, W_H=17.5Hz), 2.1(3H,s,CH_3CO), 1.0-2.1(9H, complex, 8H after D_2O exch.), 0.1(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 3520(br,O-H), 1720,

1740(C=O), 1245,840cm^{-1} (C-Si).

c-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclooctanol (103).- (a) To a solution of 1-trimethylsilyl-cis-cyclooctane-1,2-diol (63) (0.6g, 1.78mmol) in dry pyridine (5ml) was added acetic anhydride (0.53ml, 0.57g, 5.6mmol). The mixture was stirred at 16^{o} for 17h then poured into a mixture of 2M HCl (20ml) and ether (20ml). The aqueous layer was extracted with more ether (2×10ml), the combined ether extracts were then washed with saturated aqueous sodium carbonate, brine, and were dried ($MgSO_4$). Evaporation of solvent followed by removal of volatile impurities under reduced pressure gave the cis-hydroxy acetate (103) (0.61g, 85%). (Found: C,60.1; H,9.9. $C_{13}H_{26}O_3Si$ requires C,60.4; H,10.1%), δ($CDCl_3$) 5.05(1H,brd, J 7.5Hz, H-2), 2.05(3H,s,CH_3CO), 1.0-2.0(13H, complex, 12H after D_2O exch.), 0.1(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 3500(br,O-H), 1737(C=O), 1250,840cm^{-1}(C-Si), m/e 199(54%), 127(100%), 109(33%), 105(55%).

(b)[94] To a solution of 1-trimethylsilyl-cis-cyclooctane-1,2-diol (63) (3.5g, 16.2mmol) in dichloromethane (55ml) was added dry pyridine (2.7ml, 2.6g, 33.4mmol) and acetic anhydride (3.0ml, 3.3g, 32mmol). The mixture was cooled to -20^{o} (carbon tetrachloride-solid CO_2) then 4-dimethylaminopyridine (180mg, 1.5mmol) was added, with stirring, and the temperature was maintained at -20^{o} for a further 75 min. Methanol (1ml) was added then after 5min the mixture was poured into a mixture

of ether (100ml) and water (100ml). The aqueous layer was extracted with more ether (2×50ml), the combined ether extracts were then washed with 2M HCl (75ml), saturated aqueous sodium carbonate, brine and were dried ($MgSO_4$). The ether was evaporated under vacuum using a cold water bath giving the cis-hydroxy acetate (103) (4.05g, 97%).

The cis-hydroxy acetate (103) was unstable and decomposed on standing to give mainly cyclooctanone. Decomposition was also brought about when purification was attempted by distillation or preparative t.l.c. which produced a mixture of products. Attempts were made to characterize the intermediate decomposition products by heating the acetate in a sealed tube or heating a sample in chlorobenzene under reflux but were unsuccessful. Purification was brought about by removal of volatile impurities using an oil pump (0.01mm Hg) and following such treatment the compound was used immediately.

Reaction of 1-Trimethylsilyl-1,2-diol Monoacetates with Sodium Hydride in DMF. (A) t-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclohexanol (78).- Sodium hydride (80% dispersion in oil, 65mg, 2.26mmol) was washed under nitrogen with light petroleum (b.p. 30-40°, 3×3ml). Dry DMF (3ml) was then added and the mixture was cooled to 0°. The trans-hydroxy acetate (78) (0.34g, 1.5mmol) in dry DMF (2ml) was then added, with stirring under nitrogen. The mixture was allowed to warm to 18° during 45 min and was then poured into a mixture of water (50ml) and light petroleum (b.p. 30-40°, 25ml). The aqueous layer was

extracted with more light petroleum (2×15ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave a white solid (0.3g) which was shown by n.m.r. and i.r. to be a mixture of mainly 1-trimethylsilyl-trans-cyclohexane-1,2-diol (10) and some starting material.

(B) c-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclohexanol (79) (0.44g, 1.9mmol) was treated with washed sodium hydride (80% dispersion in oil, 84mg, 2.92mmol) in dry DMF under the conditions used for the trans-hydroxy acetate (78). The crude product was isolated as an oil (0.39g) which was shown to be mainly starting material by n.m.r. and i.r.

(C) c-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclooctanol (103).- The cis-hydroxy acetate (103) (0.53g, 20mmol) was treated with washed sodium hydride (80% dispersion in oil, 90mg, 3.1mmol) in dry DMF under the conditions used for the trans-hydroxy acetate (78). The crude product was isolated as an oil (0.19g) which was shown to be mainly cyclooctanone by comparison (n.m.r., i.r., g.l.c.) with an authentic sample.

In separate experiments, 1-trimethylsiloxy-cis-cyclooctene (101)[182] and 1-acetoxy-cis-cyclooctene (105)[183] were treated with sodium hydride in DMF under the same conditions as above. The major product of both reactions was shown to be cyclooctanone by comparison (n.m.r., i.r., g.l.c.) with an authentic sample.

1-Methylthiomethoxy-1-methylcyclohexane (83).- 1-Methylcyclohexanol[184] (2.0g, 1.75mmol) was added to a mixture of dry DMSO (50ml), glacial acetic acid (10ml) and acetic anhydride (33ml). The mixture was left to stand at 15° for 48h and was then poured into saturated aqueous sodium carbonate (200ml). The aqueous solution was extracted with chloroform (3×100ml), the combined extracts were washed with water (400ml), brine, and dried ($CaCl_2$). Evaporation of solvent gave an oil (2.2g) which was indicated by n.m.r. to be a mixture of the methylthiomethyl ether (83) and methylthiomethyl acetate. The crude product was added to 10% methanolic potassium hydroxide (25ml) and the mixture left to stand for 12h. Ether (50ml) and water (50ml) were then added and the aqueous layer was extracted with more ether (2×30ml). The combined ether layers were washed twice with brine and dried ($MgSO_4$). Evaporation of solvent gave the methylthiomethyl ether (83)[99] (1.65g, 54%), δ($CDCl_3$) 4.4(2H,s,-OCH_2S-), 2.1(3H,s,SCH_3), 1.2-1.9(10H, complex), 1.1 (3H,s,CH_3), $\nu_{max.}$(liquid film) 1450,1225,1050,940cm^{-1}.

c-2-Acetoxy-t-1-Methylthiomethoxy-r-1-trimethylsilyl-cyclohexane (84).- t-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclohexanol (78) (5.3g, 23.0mmol) was added to a mixture of dry DMSO (67ml), glacial acetic acid (18ml) and acetic anhydride (45ml). The mixture was left to stand at 15° for 68h and was then slowly poured into a mixture of chloroform (200ml) and saturated aqueous sodium carbonate (250ml). The aqueous layer was extracted with more chloroform (2×150ml), the combined

organic layers were washed with saturated aqueous sodium carbonate (200ml), water (200ml), brine and dried ($CaCl_2$). Evaporation of solvent followed by short path distillation at 0.005mm Hg and 80-100^{o} give the methylthiomethyl ether (84) as a colourless oil (5.8g, 87%) (Found: C,54.15; H,8.9; S,11.2. $C_{13}H_{26}O_3SSi$ requires C,53.75; H,9.0; S,11.05%), $\delta(CDCl_3)$ 5.2 (1H,m,W_H=13.5Hz,H-2), 4.55(2H,s,-OCH_2S-), 2.2(3H,s,SCH_3), 2.05(3H,s,CH_3CO), 1.2-2.3(8H, complex), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1740(C=O),1370,1240,840cm^{-1}(C-Si).

t-2-Acetoxy-t-1-methylthiomethoxy-r-1-trimethylsilyl-cyclohexane (85).- c-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclohexanol (79) (4.18g, 18.2mmol) was added to a mixture of dry DMSO (52ml), glacial acetic acid (14ml), and acetic ahydride (35ml). The mixture was left to stand at 18^{o} for 55h and was then poured slowly into a mixture of chloroform (200ml) and saturated aqueous sodium carbonate (200ml). The aqueous layer was extracted with more chloroform (2×100ml), the combined organic layers were then washed with saturated aqueous sodium carbonate, (200ml), water, brine, and dried ($CaCl_2$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 110-130^{o} gave the methylthiomethyl ether (85) as a colourless oil (3.95g, 75%) (Found: C,54.05; H,9.05; S,11.2. $C_{13}H_{26}O_3SSi$ requires C,53.75; H,9.0; S,11.05%), $\delta(CDCl_3)$ 4.8(1H,m,W_H=14Hz,H-2), 4.7(2H,s,-OCH_2S-), 2.3(3H,s, SCH_3), 2.1(3H,s,CH_3CO), 1.1-2.2(8H, complex), 0.15(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1730(C=O),1370,1240,840cm^{-1}(C-Si).

c-2-Trimethylsilyl-t-2-methylthiomethoxy-r-1-cyclohexanol (86).- c-2-Acetoxy-t-1-methylthiomethoxy-r-1-trimethylsilylcyclohexane (84) (5.6g, 19.3mmol) was added to 10% methanolic potassium hydroxide (60ml) and the mixture was stirred at 50° for 18h. The mixture was then poured into water (200ml) and ether (200ml). The aqueous layer was extracted with more ether (3×60ml), the combined ether extracts were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (4.2g) which eventually solidified. The solid was recrystallized from light petroleum (b.p. 40-60°) giving the cis-β-hydroxysilane (86) (3.7g, 80%), m.p. 74-75°C (Found: C,53.05; H,9.75; S,12.75. $C_{11}H_{24}O_2SSi$ requires C, 53.2; H,9.75; S,12.9%), δ($CDCl_3$) 4.7(2H,ABq,-OCH_2S-), 4.05(1H, m,W_H=16Hz,H-1), 2.75(1H,brs,D_2O exch.,OH), 2.3(3H,s,SCH_3), 1.2-2.2(8H, complex) 0.28(9H,s,$SiMe_3$), $\nu_{max.}$($CHCl_3$) 3480(br, O-H), 1330,1070,840cm^{-1}(C-Si).

Reactions of c-2-Trimethylsilyl-t-2-methylthiomethoxy-r-1-cyclohexanol (86). (A) With Potassium Hydride in THF.- Potassium hydride (20% dispersion in oil, 0.65g, 3.3mmol) was washed under nitrogen with light petroleum (b.p. 30-40°, 3×5ml) then dry THF (12ml) was added and the mixture was cooled to 0°. The cis-β-hydroxysilane (86) (0.5g, 2.0mmol) in dry THF (2ml) was then added, with stirring under nitrogen, and the mixture became yellow soon after the addition. After 10 min, g.l.c. (silicone oil, 150°) indicated one main component of retention time 4 min and the reaction mixture was slowly

poured into water (20ml) and ether (20ml). The aqueous layer was extracted with more ether (2×20ml), the combined ether extracts were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.36g). Short path distillation at 1.5mm Hg and 100-120° gave 1-methylthiomethoxy-cyclohexene (88) (0.23g, 90%) as a colourless oil (Found: C,60.85; H,8.8; S,19.95. $C_8H_{14}OS$ requires C,60.7; H,8.9; S,20.25%), δ($CDCl_3$) 4.75(2H,s,-OCH_2S-), 4.65(1H,m,H-2), 2.15 (3H,s,SCH_3), 1.3-2.2(8H, complex), $\nu_{max.}$(liquid film) 3080 (=C-H), 1670(C=C), 1380,1150,1009cm^{-1}. After isolation the enol ether (88) showed a single symmetrical peak on g.l.c. (silicone oil, 150°) but decomposed on standing to give a mixture of products on g.l.c., the predominant component being cyclohexanone.

(B) With Potassium t-Butoxide in DMSO.- (a) To a solution of potassium t-butoxide (0.45g, 4.0mmol) in dry DMSO (15ml) at 15°C was added with stirring, the cis-β-hydroxysilane (86) (0.5g, 2.0mmol) in dry DMSO (5ml) and the mixture became red following the addition. After 2h, g.l.c. (silicone oil, 150°) indicated one main component of retention time 8.5 min and the reaction mixture was poured into water (40ml) and light petroleum (b.p. 40-60°, 40ml). The aqueous layer was extracted with more light petroleum (2×20ml), the combined petrol extracts were washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.28g). Short path distillation at 0.9mm Hg and 120-140° gave trans-2-methyl-thiomethoxycyclohexanol (91) (0.25g, 71%) as a colourless oil (Found: C,54.25; H,9.3; S,18.35. $C_8H_{16}O_2S$ requires C,54.5;

H,9.15; S,(8.2%), δ($CDCl_3$) 4.65(2H,ABq,-OCH_2S-), 3.4(2H,m,H-1 and H-2), 2.9(1H,brs,D_2O exch.,OH), 2.2(3H,s,SCH_3), 0.9-2.1 (8H, complex), $\nu_{max.}$(liquid film) 3440(br,O-H), 1500,1070, 845cm^{-1}, ^{13}C n.m.r. δ($CDCl_3$ solvent and ref.) 81.8(d,C-1), 73.6(t,-OCH_2S-), 73.5(d,C-2), 32.4(t), 29.4(t), 24.1(t), 23.8 (t), 14.0(q,SCH_3).

(b) The reaction was carried out in the same way except that methyl iodide (5 mole equivalents) was added immediately following the addition of β-hydroxysilane (86). G.l.c. (silicone oil, 150°C) after 15 min indicated a mixture of two main components of retention time 6 min and 8 min. The latter was the minor component and was shown to be 2-methyl-thiomethoxycyclohexanol (91) by co-injection with an authentic sample (prepared in the previous reaction). After stirring the reaction mixture at 18° for a further 1h the product was isolated as before giving an oil from which the major component was isolated by preparative g.l.c. (OV17, 200°) to give trans-2-methylthiomethoxy-1-methoxycyclohexane (92) 10.26g, 69%) as a colourless oil (Found: C, 56.9; H,9.7; S,16.6. $C_9H_{10}O_2S$ requires C,56.8; H,9.55- S,16.85%), δ($CDCl_3$) 4.8(2H,ABq, -OCH_2S-), 3.5(1H,m,H-2), 3.4(3H,s,OCH_3), 3.1(1H,m,H-1), 2.2(3H, s,SCH_3), 1.2-2.1(8H, complex), $\nu_{max.}$(liquid film) 1450,1350, 1070cm^{-1}.

(c) With Sodium Hydride in DMF.- Sodium hydride (50% dispersion in oil, 78mg, 1.6mmol) was washed, under nitrogen, with light petroleum (b.p. 30-40°, 3×5ml) then dry DMF (4ml)

was added. The mixture was cooled to 0° then the cis-β-hydroxysilane (86) (0.2g, 0.8mmol) in dry DMF (1ml) was added, with stirring under nitrogen. The mixture was allowed to warm to 18° during 1h and was then poured into water (20ml) and light petroleum (b.p. 30-40°, 20ml). The aqueous layer was extracted with more light petroleum (2×10ml), the combined petrol extracts were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.26g) which gave rise to two main peaks on g.l.c. (silicone oil, 150°) of retention time 4 and 8.5 min in the ratio of roughly 2:1. The two products were shown to be 1-methylthiomethoxycyclohexene (88) and trans-2-methylthiomethoxycyclohexanol (91) respectively by co-injection on g.l.c. and comparison of the n.m.r. and i.r. spectroscopic data of the mixture with those of the authentic samples obtained from other reactions of the cis-β-hydroxysilane (86) discussed previously. trans-2-Methylthiomethoxycyclohexanol (91) (38mg) was obtained pure from the mixture by preparative t.l.c. using ether-light petroleum (b.p. 40-60°) (1:1) as elutant.

(d) With Methanesulphonyl Chloride.- To a solution of the cis-β-hydroxysilane (86) (0.4g, 1.6mmol) in dry pyridine (7ml) at 0° was added, with stirring, methanesulphonyl chloride (150µl, 0.22g, 1.9mmol). The mixture was allowed to warm slowly to 18° then stirring was continued at 18° for a further 40h. Water (4 drops) was added followed after 5 min by more water (20ml) and ether (15 min). The aqueous layer was extracted with more ether (2×10ml), the combined ether extracts

were washed with 2M HCl (15ml), saturated aqueous sodium bicarbonate, brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.38g) of which the n.m.r. and i.r, spectroscopic data were recorded. These indicated the product to be a mixture of starting material, 1-methylthiomethoxycyclohexene (88) (i.r. C=C at 1670cm^{-1}) and c-2-methanesulphonyloxy-t-2-methylthiomethoxy-r-1-trimethylsilylcyclohexane (93) $\delta(CDCl_3)$ 4.5(2H,s,$-OCH_2S-$), 4.7(1H,m,H-2), 3.0(3H,s,OSO_2CH_3), 2.15(3H, s,SCH_3), 1.2-2.2(8H, complex), 0.15(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1300cm^{-1}(SO_2). Isolation of the methanesulphonate (93) by preparative t.l.c. was attempted but was unsuccessful because of decomposition taking place. The presence of the enol ether (88) in the reaction product was confirmed by g.l.c. (silicone oil, 150°); co-injection with an authentic sample gave a common peak of retention time 4 min.

trans-2-Acetoxy-1-methylthiomethoxycyclohexane (90).- To a mixture of dry DMSO (42ml), glacial acetic acid (12ml), and acetic anhydride (28ml) was added, with stirring, trans-2-acetoxycyclohexanol (89)[185] (2.3g, 14.6mmol). The mixture was left to stand at 18° for 48h and was then slowly poured into saturated aqueous sodium bicarbonate (250ml). The mixture was extracted with chloroform (3×100ml), the combined extracts were then washed with water, saturated aqueous sodium carbonate, brine, and dried ($MgSO_4$). Evaporation of solvent followed by distillation gave the methylthiomethyl ether (90) (2.8g, 89%), b.p. 85-90° at 0.01mm Hg (Found: C,55.3; H,8.05;

S,14.3. $C_{10}H_{18}O_3S$ requires C,55.0; H,8.3; S,14.7%), δ($CDCl_3$) 4.7(2H,s,-OCH_2S-), 4.7(1H,m,H-2), 3.6(1H,m,H-1), 2.0(3H,s, SCH_3), 2.1(3H,s,$COCH_3$), 1.2-2.2(8H, complex), $\nu_{max.}$(liquid film) 1740(C=O), 1370,1240,1070cm^{-1}.

trans-2-Methylthiomethoxycyclohexanol (91).- trans-2-Acetoxy-1-methylthiomethoxycyclohexane (90) (1.7g, 7.8mmol) was added to 10% methanolic potassium hydroxide (40ml) and the mixture was stirred at 18° for 20h. Water (80ml) was then added and the mixture was extracted with ether (3×50ml), the combined ether layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.9mm Hg and 120-140° gave the alcohol (91) (0.82g, 60%) which had identical n.m.r. and i.r. spectroscopic data to the product of the reaction of the cis-β-hydroxysilane (86) with potassium t-butoxide in DMSO, and gave rise to the same peak of retention time 8.5 min on g.l.c. (silicone oil, 150°), shown by co-injection.

t-2-Trimethylsilyl-c-2-methylthiomethoxy-r-1-cyclohexanol (87).- t-2-Acetoxy-t-1-methylthiomethoxy-r-1-trimethylsilyl-cyclohexane (85) (3.9g, 13.4mmol) was added to 10% methanolic potassium hydroxide (45ml) and the mixture was stirred at 50° for 30h. The mixture was then poured into water (180ml) and ether (100ml). The aqueous layer was extracted with more ether (3×40ml), the combined ether extracts were then washed with

brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (2.8g) which eventually solidified. The solid was recrystallized from light petroleum (b.p. 40-60°) giving the trans-β-hydroxysilane (87) (2.4g, 72%), m.p. 58-61°C (Found: C, 52.8; H,9.55; S,12.8. $C_{11}H_{24}O_2SSi$ requires C,53.2; H,9.75; S,12.9%), δ($CDCl_3$) 4.55(2H,s,-OCH_2S-), 3.5(1H,m,W_H=17.5Hz,H-1), 2.25(3H, s,SCH_3), 1.0-2.1(9H, complex, 8H after D_2O exch.), 0.2(9H,s, $SiMe_3$), $\nu_{max.}$($CHCl_3$) 3470(br,O-H), 1340,1070,840cm^{-1}(C-Si).

Reactions of t-2-Trimethylsilyl-c-2-methylthiomethoxy-r-1-cyclohexanol (87). (A) With Methanesulphonyl Chloride.- To a solution of the trans-β-hydroxysilane (87) (0.29g, 1.17mmol) in dry pyridine (5ml) at 0° was added, with stirring,methanesulphonyl chloride (108µl, 0.16g, 1.38mmol). The mixture was allowed to warm slowly to 18° then stirring was continued at 18° for 18h. Water (4 drops) was added followed after 5 min by more water (15ml) and ether (15ml). The aqueous layer was extracted with more ether (2×10ml), the combined ether extracts were then washed with 2M HCl (15ml), saturated aqueous sodium bicarbonate, brine, and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 1.5mm Hg and 100-130° gave 1-methylthiomethoxycyclohexene (88) (0.18g, 94%), identified by comparison of n.m.r. and i.r. spectra and co-injection on g.l.c. (silicone oil, 150) with the authentic sample produced by reaction of the cis-β-hydroxysilane (86) with potassium hydride in THF.

(B) With p-Toluenesulphonyl Chloride.- The trans-β-hydroxysilane (87) (0.2g, 0.8mmol) in dry pyridine (4ml) was treated with p-toluenesulphonyl chloride (0.17g, 0.89mmol) under the same conditions as those in the above reaction (A). After 72h, n.m.r. indicated that all the starting material had been consumed and work up as above gave 1-methylthiomethoxy-cyclohexene (88) (0.12g, 91%). Attempts to accelerate the reaction by heating were unsuccessful and resulted in a marked reduction in the yield of the enol ether (88).

(C) With Boron Trifluoride Etherate.- To a solution of the trans-β-hydroxysilane (87) (0.2g, 0.8mmol) in dichloromethane (5ml) at 0^{o} was added, with stirring under nitrogen, boron trifluoride etherate (3.2M, 1.1ml, 3.2mmol). The mixture was stirred at 0^{o} for a further 2h then poured into saturated aqueous sodium bicarbonate (20ml). The aqueous layer was extracted with ether (3×15ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.14g) which was shown to be mainly cyclohexanone by n.m.r., i.r. and co-injection on g.l.c. (silicone oil, 150^{o}), there was no indication of any of the enol ether (88) in the product.

(D) With Potassium t-Butoxide in DMSO.- To a solution of potassium t-butoxide (0.41g, 3.6mmol) in dry DMSO (12ml) at 17^{o} was added, with stirring, the trans-β-hydroxysilane (87) (0.45g, 1.8mmol) in dry DMSO (4ml) and the mixture gradually became dark red. After 1.5h, g.l.c. (silicone oil, 150^{o})

indicated one main component of retention time 7.5 min and the reaction mixture was poured into water (30ml) and light petroleum (b.p. 40-60°, 30ml). The aqueous layer was extracted with more light petroleum (2×15ml), the combined petrol layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.3g). Short path distillation at 1.5mm Hg and 100-120° gave cis-2-methylthiomethoxycyclohexanol (94) (0.23g, 79%) as a colourless oil (Found: C,54.25; H,8.9; S, 18.4. $C_8H_{16}O_2S$ requires C,54.5; H,9.15; S,18.2%), δ($CDCl_3$) 4.6(2H,ABq,-OCH_2S-), 3.7(2H,m,H-1 and H-2), 2.3(1H,s,OH,D_2O exch.), 2.1(3H,s,SCH_3), 1.0-2.0(8H, complex), $\nu_{max.}$(liquid film) 3470(br,O-H), 1500,1070,980cm^{-1}, ^{13}C n.m.r. δ($CDCl_3$ solvent and ref.) 76.3(d,C-1), 72.7(t,-OCH_2S-), 68.6(d,C-2), 30.4(t), 26.4(t), 22.2(t), 21.0(t), 13.8(q,SCH_3).

(E) With Potassium Hydride in THF.- Potassium hydride (20% dispersion in oil, 0.14g, 0.71mmol) was washed under nitrogen with light petroleum (b.p. 30-40°, 3×5ml) then dry THF (5ml) was added and the mixture was cooled to 0°. The trans-β-hydroxysilane (87) (0.1g, 0.40mmol) in dry THF (1ml) was then added, with stirring under nitrogen and the mixture became pale yellow after the addition. The mixture was allowed to warm slowly to 18° and the reaction was monitored by g.l.c. (silicone oil, 150°). After 18h, all of the starting material had been consumed and one main component of retention time 7.5 min was present. Water (15ml) was added and the aqueous layer was extracted with ether (3×15ml), the combined organic layers were then washed with brine and dried

($MgSO_4$). Evaporation of solvert gave an oil (0.09g) which was shown to be cis-2-methylthiomethoxycyclohexanol (94) by comparison of n.m.r. and i.r. spectra and co-injection on g.l.c. with the authentic sample produced by procedure (D).

Reaction of Dimethylsulphoxide and Acetic Anhydride with Cyclohexanone.- Cyclohexanone (5g, 51.0mmol) was added to a mixture of dry DMSO (60ml), glacial acetic acid (15ml) and acetic anhydride (40ml). The mixture was left to stand at 18^{o} for 52h and was then poured slowly into a stirred mixture of saturated aqueous sodium carbonate (200ml) and chloroform (200ml). The aqueous layer was extracted with more chloroform (2×80ml), the combined organic layers were then washed with saturated aqueous sodium carbonate (200ml), water, brine, and dried ($CaCl_2$). Evaporation of solvent gave a pale yellow oil (12.2g) which gave rise to two main peaks on g.l.c. (OV17, 155^{o}) of retention time 1.9 min and 2.6 min, shown by co-injection to correspond to methylthiomethyl acetate and cyclohexanone respectively. This conclusion was corroborated by the n.m.r. and i.r. spectroscopic data of the oil.

In order to remove the methylthiomethyl acetate the crude reaction product was treated with 10% methanolic potassium hydroxide (45ml) at 18^{o} for 30h. Water (50ml) was then added and the mixture was extracted with ether (3×20ml). The combined ether extracts were washed with water, brine, and dried ($MgSO_4$). Evaporation of solvent followed by short path

distillation at 1.2mm Hg and 120-130° gave an oil (5.5g) which was considered to be mainly 2-methylthiomethylcyclohexanone (98) on the basis of its n.m.r. and i.r. spectroscopic data compared with those of an authentic sample — see later. Analysis of the product by g.l.c. (OV17, 155°) showed one main component of retention time 10.3 min together with small amounts of longer retention time components. These were considered to be possibly di- and poly-alkylated derivatives of cyclohexanone, as was also indicated by subsidiary SMe peaks in the n.m.r. spectrum (see discussion).

Reaction of Cyclohexanone with Methylthiomethyl Acetate.- To a solution of diisopropylamine (6.75ml, 4.9g, 48.4mmol) in dry THF (40ml) was added, with stirring under nitrogen, n-butyllithium (1.5M, 35.5ml, 53.3mmol). The solution was stirred at 18° for 10 min then cooled to 0° and cyclohexanone (5ml, 4.8g, 48.4mmol) was added. After a further 30 min, methylthiomethyl acetate[186] (8.72g, 72.7mmol) was added, with stirring, and the mixture was allowed to warm to 18° during 2h then stirred under nitrogen at 18° for a further 16h. After this time, g.l.c. (OV17, 155°) indicated one main component of retention time 10.3 min. The mixture was poured into water (100ml) and ether (100ml). The aqueous layer was extracted with more ether (2×50ml), the combined organic layers were washed with 2N HCl (100ml), saturated aqueous sodium bicarbonate (2×50ml), brine and dried ($MgSO_4$). Evaporation of solvent gave a pale yellow oil (5.3g) which was distilled to

give 2-methylthiomethylcyclohexanone (98) (4.9g, 64%), b.p. 94-96° at 1.5mm Hg (lit.[187] b.p. 83-84° at 1mm Hg (Found: C, 60.8; H,9.1; S,20.0. $C_8H_{14}OS$ requires C,60.7; H,8.9; S, 20.25%), δ($CDCl_3$) 2.9(1H,m,H-2), 2.0(3H,s,SCH_3), 1.1-2.6(10H, complex), $\nu_{max.}$(liquid film) 171(C=O), 1450,1310,1235,1128cm^{-1}, ^{13}C n.m.r. δ($CDCl_3$ solvent and ref.), 211.2(s,C-1), 50.4(d, C-2), 41.7(t), 33.8(t), 33.1(t), 27.6(t), 24.7(t), 16.1(q, SCH_3). The sample for analysis was purified further after distillation by preparative g.l.c. (OV17, 200°).

t-2-Acetoxy-t-1-methylthiomethoxy-r-1-trimethylsilyl-cyclooctane (106).- c-2-Acetoxy-t-1-trimethylsilyl-r-1-cyclo-octanol (103) (3g, 11.6mmol) was added to a mixture of dry DMSO (34ml), glacial acetic acid (9ml), and acetic anhydride (23ml). The mixture was left to stand at 18° for 40h and was then poured slowly into a mixture of chloroform (100ml) and saturated aqueous sodium carbonate (125ml). The aqueous layer was extracted with more chloroform (2×75ml), the combined organic layers were then washed with saturated aqueous sodium carbonate (100ml), water (100ml), brine and dried ($CaCl_2$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 120-130° gave the methylthiomethyl ether (106) as a colourless oil (2.7g, 72%) (Found: C,56.65; H,9.6; S,9.7. $C_{15}H_{30}O_3SSi$ requires C,56.55; H,9.5- S,10.05%). δ($CDCl_3$) 4.9 (1H,d, J 8Hz,H-2), 4.6(2H,s,-OCH_2S-), 2.2(3H,s,SCH_3), 2.0(3H,s, $COCH_3$), 1.2-2.2(12H, complex), 0.2(9H,s,SiMe), $\nu_{max.}$(liquid film) 1735(C=O), 1379,1245,1043,840cm^{-1}(C-Si).

t-2-Trimethylsilyl-c-2-methylthiomethoxy-r-1-cyclooctanol (107).- t-2-Acetoxy-t-1-methylthiomethoxy-r-1-trimethylsilylcyclooctane (106) (1.27g, 3.99mmol) was added to 10% methanolic potassium hydroxide (20ml) and the mixture was stirred at 50° for 5h. The mixture was then poured into water (80ml) and ether (45ml). The aqueous layer was extracted with more ether (3×30ml), the combined ether extracts were then washed with brine (2×20ml) and dried ($MgSO_4$). Evaporation of solvent gave the trans-β-hydroxysilane (107) (0.80g, 73%) as an oil which eventually solidified to give a sticky solid m.p. 38-43° after recrystallization from light petroleum (b.p. 30-40°) (Found: C,56.3; H,10.45; S,11.35. $C_{13}H_{28}O_2SSi$ requires C,56.45; H,10.2; S,11.6%), δ($CDCl_3$) 4.65(2H,s,-OCH_2S-), 3.95(1H,br d, J 9Hz, sharpened on D_2O exch.,H-2), 2.6(1H,br d, D_2O exch.,OH), 1.2-2.2(12H, complex), 0.3(9H,s,$SiMe_3$), $\nu_{max.}$ ($CHCl_3$) 3580(O-H), 1450,1050,850cm^{-1}(C-Si).

Recrystallization of this low melting point solid was difficult and usually gave poor recovery of material that was spectroscopically not of better quality than the crude product. In general, purification was brought about by removal of volatile impurities under high vacuum (0.01mm Hg) using an oil pump.

Reaction of t-2-Trimethylsilyl-c-2-methylthiomethoxy-r-1-cyclooctanol (107) with Potassium Hydride in THF.- Potassium hydride (20% dispersion in oil, 0.31g, 1.5mmol) was washed under nitrogen with light petroleum (b.p. 30-40°, 3×5ml) then

dry THF (4ml) was added and the mixture was cooled to 0°. The trans-β-hydroxysilane (107) (0.28g, 1.0mmol) in dry THF (1ml) was then added, with stirring under nitrogen. The mixture was stirred at 0° for a further 20 min and was then poured into water (20ml) and light petroleum (b.p. 40-60°, 15ml). The aqueous layer was extracted with more light petroleum (2×15ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent using a cold water bath gave an oil (0.26g) considered to contain mainly 1-methylthiomethoxy-trans-cyclooctene (108), δ($CDCl_3$), 4.93(1H,dd,J4, 12.5Hz,H-2), 4.88(2H,s,-OCH S-), 2.17(3H,s,SCH_3), 0.8-2.6(12H, complex), $\nu_{max.}$(liquid film) 3020(=C-H), 1660(C=C), 1450,1257,1045,843cm^{-1}.

The trans-enol ether (108) was unstable and isolation of the compound pure by distillation or chromatography was not possible. It had a half-life of about 40 min at 15° and isomerized to 1-methylthiomethoxy-cis-cyclooctene (109). (M^+ 186.1078. $C_{10}H_{18}OS$ requires M^+ 186.1078), δ($CDCl_3$) 4.78 (2H,s,-OCH_2S-), 4.53(1H,t,J 7.5Hz,H-2), 2.17(3H,s,SCH_3), 0.8-2.6(12H, complex), $\nu_{max.}$(liquid film) 3062(=C-H), 1665(C=C), 1465,1260,1152,1080cm^{-1}, m/e 186(M^+, 2%), 139(M-SMe^+, 11%), 61 (CH =SMe^+, 100%), 55(14%), 41(16%), 39(10%).

The isomerization of the trans-enol ether (108) to the cis-compound (109) could be followed by n.m.r. and i.r. spectroscopy. Complete conversion took place on g.l.c. (3% silicone oil, 140°) such that even samples containing mainly trans-isomer gave a single peak of retention time 15.9 min corresponding to cis-isomer. The latter compound was also

unstable and decomposed slowly on standing to cyclooctanone which could be detected by g.l.c. Isolation of the cis-isomer pure was thus also not possible, mass spectroscopic data were obtained using g.l.c.-mass spectroscopy (SP1000 Capilliary column, 140°, see discussion and general sections).

Reaction of the trans-β-hydroxysilane (107) with potassium hydride in THF was also carried out in the presence of 1,3-diphenylisobenzofuran, but no Diels-Alder adduct from the trans-enol ether (108) was obtained.

c-2-Acetoxy-t-1-methoxy-r-1-trimethylsilylcyclohexane (111).- To a slurry of Raney nickel (2g) in ethanol (8ml) was added, with vigorous stirring, c-2-acetoxy-t-1-methylthio-methoxy-r-1-trimethylsilylcyclohexane (84) (0.2g, 0.69mmol). The mixture was stirred at 70-80° for 1h then was cooled and filtered through celite. The celite pad was washed with more ethanol (3×10ml), then the combined ethanol solutions were partitioned between water (50ml) and light petroleum (b.p.40-60°, 30ml). The aqueous layer was extracted with more light petroleum (3×10ml), the combined petrol layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 80-100° gave the methoxy acetate (111) (0.15g, 89%) (Found: C,58.85; H,10.0. $C_{12}H_{24}O_3Si$ requires C,59.0; H,9.9%), δ($CDCl_3$) 5.2(1H, m,W_H=12Hz,H-2), 3.3(3H,s,OCH_3), 2.1(3H,s,$COCH_3$), 1.2-2.1(8H, complex), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1740(C=O), 1370, 1230,1080,840cm^{-1}(C-Si).

t-2-Acetoxy-t-1-methoxy-r-1-trimethylsilylcyclooctane (112).- To a slurry of Raney nickel (13g) in benzene (30ml) was added with vigorous stirring, t-2-acetoxy-t-1-methylthiomethoxy-r-1-trimethylsilylcyclooctane (106) (1.3g, 4.09mmol). The mixture was stirred at 25-30° for 1h and then filtered through celite. The celite pad was washed with more benzene (2×20ml) then the combined filtrate and washings were washed with water, brine and were dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 110-120° gave the methoxy acetate (112) (1.05g, 94%). (Found: C,61.8; H,10.4. $C_{14}H_{28}O_3Si$ requires C,61.7; H,10.35%), δ($CDCl_3$) 4.9(1H,d,J 8Hz,H-2), 3.35(3H,s,OCH_3), 2.1(3H,s,$COCH_3$), 1.3-2.3(12H, complex), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1745(C=O), 1367,1245,1080,843cm^{-1}(C-Si).

t-2-Trimethylsilyl-c-2-methoxy-r-1-cyclooctanol (113).- t-2-Acetoxy-t-1-methoxy-r-1-trimethylsilylcyclooctane (112) (0.69g, 2.54mmol) was added to 10% methanolic potassium hydroxide (10ml) and the mixture was stirred at 45° for 16h. The mixture was then poured into water (30ml) and ether (25ml). The aqueous layer was extracted with more ether (3×15ml), the combined ether extracts were then washed with brine (2×15ml) and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.005mm Hg and 115-125° gave the trans-β-hydroxysilane (113) (0.46g, 79%) (Found: C,62.4; H,11.45. $C_{12}H_{26}O_2Si$ requires C,62.55; H,11.35%). δ($CDCl_3$), 3.9(1H,dd, J 9.7, 7.8Hz, collapses to d, J 7.8Hz on D_2O exch.,H-2), 3.35

(3H,s,OCH_3), 2.75(1H,d, J 9.7Hz, D_2O, exch.,OH), 1.2-2.2(12H, complex), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 3660,3460(O-H), 1448,1249,1080,845cm^{-1}(C-Si).

The distilled product eventually solidified to give a sticky solid, m.p. 49-52° after recrystallization from light petroleum (b.p. 40-60°). The recovery of material after recrystallization was poor and on the basis of its n.m.r. and i.r. spectra, its quality was not improved from that of the distilled product. In general, the distilled material was used for subsequent reaction.

Reaction of t-2-Trimethylsilyl-c-2-methoxy-r-1-cyclo-octanol (113) with Potassium Hydride in THF.- Potassium hydride (20% dispersion in oil, 0.26g, 1.3mmol) was washed under nitrogen with light petroleum (b.p. 30-40°, 3×4ml) then dry THF (3.5ml) was added and the mixture was cooled to 0°. The trans-β-hydroxysilane (113) (0.2g, 0.87mmol) in dry THF (1ml) was then added, with stirring under nitrogen. The mixture was stirred at 0° for a further 30 min and was then poured into water (15ml) and light petroleum (b.p. 30-40°, 15ml). The aqueous layer was extracted with more light petroleum (2×12ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent using a cold water bath gave an oil (0.11g) considered to contain mainly 1-methoxy-trans-cyclooctene (110) δ($CDCl_3$) 4.63(1H,dd, J 4.3, 12.3Hz,H-2), 3.57(3H,s,OCH_3), 0.85-2.58(12H, complex), $\nu_{max.}$ (liquid film) 3040(=C-H), 1660(C=C), 1450,1360,1160cm^{-1}.

The trans-enol ether (110) was unstable and isolation of a pure sample by distillation or chromatography was not possible. It isomerized on standing to give 1-methoxy-cis-cyclooctene (114), an authentic sample of which had been prepared (see below). Even freshly prepared samples containing mainly the trans-enol ether (110) gave only a single main peak of retention time 6.4 min on g.l.c. (silicone oil, 107°) which corresponded to the cis-isomer (114) as shown by co-injection. The isomerization of (110) was followed by n.m.r., spectra of separate samples of freshly prepared trans-enol ether (110) in $CDCl_3$(A) and CCl_4(B) solutions were recorded at intervals. The concentration of (110) in the solutions was assumed to be proportional to the peak height, p, of the methoxyl signal. The data for (A) and (B) are given in Table 3 and the plots of $\ln p$ vs. t are given in Figure 3 (see discussion, page 55).

TABLE 3

Data for the Isomerization of 1-Methoxy-trans-cyclooctene (110) in $CDCl_3$(A) and CCl_4(B) solution

(A)			(B)		
time, t (min)	trans peak height, p(mm)	ln p	time, t (min)	trans peak height, p(mm)	ln p
5	225	5.42	0	222	5.40
15	199	5.29	10	210	5.35
25	180	5.19	20	208	5.34
40	166	5.11	30	200	5.30
50	138	4.93	45	199	5.29
65	112	4.72	60	183	5.21
80	78	4.36	75	161	5.08
95	64	4.16	90	144	4.97
110	57	4.04	105	133	4.89
125	48	3.87	120	124	4.82
150	45	3.81	145	110	4.70
			170	98	4.58
			240	65	4.17

During the experiments, both samples were incubated in the probe of the n.m.r. spectrometer at a constant temperature of 36^{o}.

1-Methoxy-cis-cyclooctene (114).- Cyclooctanone (11g, 87.3mmol) was heated with trimethyl orthoformate (15g, 141.3 mmol) and p-toluenesulphonic acid (0.4g) at 120-130° during 16h. The volatile products, methyl formate and methanol, were removed by distillation through a vigreux column then ether (50ml) was added to the cooled residue. The ethereal solution was shaken with saturated aqueous sodium carbonate, then dried ($MgSO_4$). Evaporation of solvent followed by distillation gave 1-methoxy-cis-cyclooctene (114) (7.5g, 63%), b.p. 69-71° at 14mm Hg (lit.[106] b.p. 62-63° at 10mm Hg), $\delta(CDCl_3)$ 4.45(1H, t, J 8Hz,H-2), 3.45(3H,s,OCH_3), 1.3-2.4(12H,complex), $\nu_{max.}$ (liquid film) 3063(=C-H),1667(C=C), 1455,1160,1097cm^{-1}.

PART II

Triphenylphosphine Oxide[56] .- To finely ground potassium persulphate (150g, 0.56mol) was added slowly, with cooling, 97% sulphuric acid (90ml). With swirling, crushed ice (600ml) was then added slowly. The mixture was then added, with stirring, to triphenylphosphine (105g, 0.4mol) dissolved in a mixture of ethanol (500ml) and methanol (500ml). The addition was carried out at such a rate that the temperature never rose above 42°. The mixture was stirred at 18° for a further 24h and was then extracted with benzene (3×500ml). The benzene extracts were then washed with water (500ml), brine then dried ($MgSO_4$). Evaporation of solvent gave a white solid which was recrystallized from benzene-light petroleum (b.p. 60-80°) to give triphenylphosphine oxide (99.7g, 90%), m.p. 154-156° (lit.[188] m.p. 157-158°).

Diphenyl(trimethylsilylmethyl)phosphine Oxide (131).- To a slurry of dried triphenylphosphine oxide (62.6g, 0.23mol) in dry ether (200ml) was added, with stirring under nitrogen, methyllithium (0.7M, 350ml, 0.25mol). The resulting deep red solution was stirred at 18° for a further 1h then trimethylsilyl chloride (45ml, 50g, 0.46mol) in dry ether (100ml) was added during 1h. The mixture was stirred under nitrogen for a further 1.5h after which time the red colour of the solution had been discharged. Water (250ml) and dichloromethane (200ml) were then added, the aqueous layer was extracted with more dichloromethane (2×100ml) and the combined organic layers

were washed with brine and dried ($CaCl_2$). Evaporation of solvent gave an orange solid (55g) which contained diphenyl-(trimethylsilylmethyl)phosphine oxide (131) and methyldiphenyl-phosphine oxide. Chromatography on silica gel (500g) using ethyl acetate as elutant followed by recrystallization from cyclohexane/n-hexane gave diphenyl(trimethylsilylmethyl)-phosphine oxide (131) (46.2g, 69.7%) as white crystals, m.p. 115-117°(lit.[126] m.p.118-119°), δ($CDCl_3$) 7.3-8.1(10H,m,aromatic), 1.8(2H,d, J 15Hz,CH P), 0.1(9H,s,$SiMe_3$), $\nu_{max.}$(nujol mull) 1437(Ph-P), 1247,1177(P=O),1112,842cm^{-1}(C-Si).

The silyl phosphine oxide (131) was prone to desilylation, giving methyldiphenylphosphine oxide. The process seemed to be taking place on chromatography, to an extent which varied according to the grade of silica gel used. Complete desilyl-ation was brought about when the silyl phosphine oxide (131) (0.3g, 1.04mmol) was treated with 10% methanolic potassium hydroxide (5ml) at 18° for 24h. Aqueous work up gave methyl-diphenylphosphine oxide (0.18g, 81%), δ($CDCl_3$) 7.2-8.1(10H,m, aromatic), 2.05(3H,d, J 13Hz,CH_3P).

Reaction of Diphenyl(trimethylsilylmethyl)phosphine Oxide (131) with Base and Trimethylsilyl Chloride.- To a solution of the silyl phosphine oxide (131) (1g, 3.5mmol) in dry ether (20ml) was added with stirring under nitrogen, methyllithium (1.1M, 3.8ml, 3.5mmol). The resulting pale orange solution was stirred at 18° for a further 20 min then trimethylsilyl chloride (0.43ml, 0.5g, 4.6mmol) was added.

A white solid was slowly deposited, the mixture was stirred under nitrogen for a further 16h. Water (20ml) and dichloromethane (20ml) were then added, the aqueous layer was extracted with more dichloromethane (2×20ml) and the combined organic layers were washed with brine and dried ($CaCl_2$). Evaporation of solvent gave a white solid considered to contain mainly diphenyl(bis(trimethylsilyl)methyl)phosphine oxide (136) (1.17g, 93%), $\delta(CDCl_3)$ 7.1-8.1(10H,m,aromatic), 1.35(1H,d, J 12.6Hz,CHP), 0.2(18H,s,$SiMe_3$), $\nu_{max.}(CCl_4)$ 1440 (Ph-P), 1250(C-Si), 1190(P=O), 1110cm^{-1}.

The bis-silyl compound (136) was unstable with respect to loss of one of the silyl groups, all attempts to purify the compound by chromatography or recrystallization failed and the silyl phosphine oxide (131) was obtained. The reaction described was difficult to reproduce and usually gave incomplete conversion to the bis-silyl compound. The same reaction was attempted using the following bases as alternatives to methyllithium in either dry ether or dry THF as solvent: n-butyllithium, s-butyllithium and sodium hexamethyldisilazide; however in no case was more of the bis-silyl compound (136) produced.

Alkylation of Diphenyl(trimethylsilylmethyl)phosphine Oxide (131). (A) Methylation - general procedure.- To a solution of the silyl phosphine oxide (131) (1.4g, 4.9mmol) in dry ether (25ml) was added, with stirring under nitrogen, n-butyllithium (1.7M, 2.9ml, 4.9mmol). The resulting pale

orange solution was stirred at 18° for a further 15 min then methyl iodide (0.6ml, 1.38g, 9.8mmol) in dry ether (5ml) was added. The mixture was stirred under nitrogen for a further 1h then water (15ml) was added. The aqueous layer was extracted with ether (3×10ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave a white solid (1.52g) which was recrystallized from ether-light petroleum (b.p. 40-60°) to give diphenyl-(1-trimethylsilylethyl)phosphine oxide (137) (1.3g, 86%), m.p. 139-142° (Found: C,67.4; H,7.55; P,10.0. $C_{17}H_{23}OPSi$ requires C,67.5; H,7.65; P,9.3%), δ($CDCl_3$) 7.3-8.1(10H,m, aromatic), 1.75(1H,m,H-1), 1.17(3H,dd, J_{HP} 18Hz, J_{HH} 7.5Hz,CH_3), -0.05(9H, s,$SiMe_3$), $\nu_{max.}$ (nujol mull) 1440(Ph-P), 1250(C-Si), 1175(P=O), 840cm^{-1}(C-Si).

(B) Dimethylation.- The methylated silyl phosphine oxide (137) (0.3g, 1.0mmol) in dry ether (8ml) was treated with n-butyllithium (1.7M, 0.6ml, 1.02mmol) followed by methyl iodide (0.13ml, 0.28g, 2.0mmol) in dry ether (2ml) according to the general procedure. The crude product was obtained as a sticky solid (0.31g) which following preparative t.l.c. using ethyl acetate-light petroleum (b.p. 40-60°) (1:1) as elutant gave (1-methyl-1-trimethylsilylethyl)diphenylphosphine oxide (138) as a sticky solid (0.23g, 74%) (Found: C,68.45; H,7.9; P,9.95. $C_{18}H_{25}OPSi$ requires C,68.3; H,7.95; P,9.8%), δ($CDCl_3$) 7.3-8.3(10H,m, aromatic), 1.35(6H,d, J 17.5Hz,CH_3), 0.0(9H,s,$SiMe_3$), $\nu_{max.}$ (nujol mull) 1440(Ph-P), 1260(C-Si), 1180cm^{-1}(P=O).

(C) Ethylation.- The silyl phosphine oxide (131) (0.6g, 2.01mmol) in dry THF (8ml) was treated with n-butyllithium (1.58M, 1.38ml, 2.1mmol) followed by ethyl iodide (0.25ml, 0.49g, 3.1mmol) in dry THF (2ml) according to the general procedure. The crude product was obtained as a gum (0.71g) which following preparative t.l.c. using ethyl acetate as elutant then recrystallization from light petroleum (b.p. 40-60°) gave diphenyl(1-trimethylsilyl-1-propyl)phosphine oxide (139) as white crystals (0.41g, 63%) m.p. 126-130° (Found: C,67.7; H,7.75; P,9.5. $C_{18}H_{25}OPSi$ requires C,68.3; H,7.95; P,9.8%), ($CDCl_3$) 7.3-8.1(10H,M, aromatic) 1.73(2H,m,-CH_2), 1.57(1H, 6 lines,CH-P), 0.92(3H,t, J 6Hz,CH_3), 0.02(9H,s, $SiMe_3$), $\nu_{max.}$(CCl_3), 1440(Ph-P), 1240(C-Si), 1190(P=O), 1110cm^{-1}.

(D) Benzylation.- The silyl phosphine oxide (131) (0.25g, 0.87mmol) in dry ether (5ml) was treated with n-butyllithium (1.7M, 0.51ml, 0.9mmol) followed by benzyl bromide (0.12ml, 0.17g, 1.0mmol) in dry ether (1ml) according to the general procedure. The crude product was obtained as a gum (0.29g) which following preparative t.l.c. using ethyl acetate-light petroleum (b.p. 40-60°) (1:1) as elutant gave (2-phenyl-1-trimethylsilylethyl)diphenylphosphine oxide (140) as a sticky solid (0.17g, 52%) (Found: C,73.2; H,7.05; P,8.4. $C_{23}H_{27}OPSi$ requires C,73.0; H,7.2; P,8.2%), δ($CDCl_3$) 7.0-8.3 (15H, complex, aromatic), 3.2(2H,dd, J_{HP} 14.6Hz, J_{HH} 6.4Hz,-CH_2-), 2.4(1H,dt,J_{HP} 12Hz, J_{HH} 6.4Hz, CH-P), 0.1(9H,s,$SiMe_3$),$\nu_{max.}$(CCl_4), 1440(Ph-P), 1240(C-Si), 1180cm^{-1}(P=O).

Reaction of Diphenyl(trimethylsilylmethyl)phosphine Oxide (131) with Aldehydes. (A) With Acetaldehyde - general procedure.- To a solution of the silyl phosphine oxide (131) (0.5g, 1.74mmol) in dry ether (8ml) was added, with stirring under nitrogen, n-butyllithium (1.6M, 1.1ml, 1.76mmol). The resulting pale orange solution was stirred at 18° for a further 15 min then cooled to -78°. Acetaldehyde (0.13ml, 0.1g, 2.32mmol) was then added and the mixture soon became white. The mixture was allowed to warm to ca. -30° during 1h then methanol (5ml) was added followed by water (15ml). The aqueous layer was extracted with ether (2×10ml) and the combined ether layers were washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil which eventually crystallized. Recrystallization from ethyl acetate-light petroleum (b.p. 40-60°) gave Z-1-diphenylphosphinoylprop-1-ene (141) (0.38g, 90%) m.p.112-4°, (Found: C,73.9, H,6.4; P,12.55. $C_{15}H_{15}OP$ requires C,74.35; H,6.25; P,12.8%), δ($CDCl_3$) 7.2-8.2(10H,m, aromatic), 6.4-7.2(1H,ddd,J_{H2P} 40Hz, J_{H1H2} 13Hz, J_{H2H3} 7Hz H-2), 5.8-6.4(1H,dd, J_{H1P} 25Hz, J_{H1H2} 13Hz, J_{H1H3} 1.5Hz, H-1), 2.07(3H,ddd, J_{H2H3} 7Hz, J_{H3P} 3Hz, J_{H1H3} 1.5Hz, CH_3), the coupling constants were deduced with the aid of double resonance, $\nu_{max.}$(neat) 1620(C=C), 1485,1440(Ph-P), 1175(P=O), 1000cm^{-1}.

(B) With Trimethylacetaldehyde.- The silyl phosphine oxide (131) (0.3g, 1.04mmol) in dry ether (5ml) was treated with n-butyllithium (1.7M, 0.62ml, 1.05mmol) followed by trimethylacetaldehyde (0.112ml, 0.09g, 1.14mmol) according to

the general procedure. The crude product was isolated as an oil which eventually crystallized (0.21g). Purification by preparative t.l.c. using ether-light petroleum (b.p. 40-60°) (1:1) as elutant gave Z-3,3-dimethyl-1-diphenylphosphinoylbut-1-ene (142) (0.21g, 71%), m.p. 97-99° after recrystallization from light petroleum (b.p. 40-60°) (Found: C,75.45; H,7.45; P,10.4. $C_{18}H_{21}OP$ requires C,76.0; H,7.45- P,10.9%). $\delta(CDCl_3)$ 7.0-7.8(10H,m, aromatic) 6.45(1H,dd, J_{H2P} 42Hz, J_{H1H2} 14Hz, H-2), 5.75(1H,dd, J_{H1P} 23Hz, J_{H1H2} 14Hz, H-1), 1.1(9H,s,CH_3), $\nu_{max.}(CCl_4)$ 1605(C=C), 1480,1440(Ph-P), 1190(P=O), 1120, 1030cm^{-1}.

(C) With Benzaldehyde.- (a) The silyl phosphine oxide (131) (1.2g, 4.17mmol) in dry ether (20ml) was treated with n-butyllithium (1.7M, 2.5ml, 4.25mmol) followed by benzaldehyde (0.47ml, 0.48g, 4.5mmol) according to the general procedure. The crude product was isolated as an oil which eventually crystallized (1.65g). Recrystallization from ether-light petroleum (b.p. 40-60°) gave Z-1-phenyl-2-diphenylphosphinoylethene (143) as white crystals (1.01g, 83%), m.p. 105-107° (Found: C,78.7; H,5.75; P,10.05. $C_{20}H_{17}OP$ requires C,78.95; H,5.65; P,10.2%), $\delta(CDCl_3)$ 7.0-8.2(16H, complex, aromatic and H-2), 6.25(1H,dd, J_{HP} 19Hz, J_{HH} 14.3Hz, H-1), $\nu_{max.}(CHCl_3)$ 1595(C=C), 1580,1439(Ph-P), 1170(P=O), 1170(P=O), 1120,690cm^{-1}.

(b) The silyl phosphine oxide (131) (0.5g, 1.74mmol) in dry ether (8ml) was treated with n-butyllithium (1.6M,

1.1ml, 1.8mmol) as before. The solution was cooled to ca. -30^{o} then magnesium bromide etherate (0.25M, 8.4ml, 2.1mmol) was added. The mixture was cooled to -78^{o} and benzaldehyde (0.19ml, 0.2g, 1.8mmol) was added. The mixture was stirred under nitrogen at -78^{o} for a further 20 min then work up as before gave a viscous yellow oil (0.51g). T.l.c. using ethyl acetate as elutant indicated two main components, these were accordingly isolated by preparative t.l.c. using ethyl acetate as elutant. The LR_F component (0.21g) was shown to be Z-1-phenyl-2-diphenylphosphinoylethene (143) by comparison (t.l.c., n.m.r. with the sample prepared previously. The HR_F component (0.16g), a sticky solid was considered to be E-1-phenyl-2-diphenylphosphinoylethene (158), $\delta(CDCl_3)$ 7.1-7.9 (16H, complex, aromatic and H-2), 7.5(1H,dd, J_{HP} 22.5Hz, J_{HH} 18Hz, H-1), by comparison with the spectroscopic data of an authentic sample[189].

(c) The reaction was carried out as in (b) except that zinc chloride (0.24g, 1.75ml) in dry ether (4ml) was added instead of magnesium bromide etherate. Work up gave a product (0.47g) consisting essentially of starting materials.

(D) With p-Methoxybenzaldehyde.- The silyl phosphine oxide (131) (0.3g, 1.04mmol) in dry ether (5ml) was treated with n-butyllithium (1.6M, 0.67ml, 1.07mmol) followed by p-methoxybenzaldehyde (0.127ml, 0.14g, 1.04mmol) according to the general procedure. The crude product was isolated as an

oil which eventually crystallized (0.32g). T.l.c. of the product using ethyl acetate as elutant indicated two main components, these were accordingly isolated by preparative t.l.c. using ethyl acetate as elutant. The LR_F component (0.16g) was considered to be Z-1-(p-methoxyphenyl)-2-diphenylphosphinoylethene (144) m.p. 165-168°, $\delta(CDCl_3)$ 6.6-8.0(15H, complex, aromatic and H-2), 6.1(1H,dd, J_{HP} 20Hz, J_{HH} 14Hz,H-1), 3.6(3H,s,OCH_3), $\nu_{max.}(CCl_4)$ 1610(C=C), 1440 (Ph-P), 1180(P=O), 1120,1040cm^{-1}. The HR_F component was isolated as a gum (0.13g); by comparison with authentic spectroscopic data[189] it was shown to be E-1-(p-methoxyphenyl)-2-diphenylphosphinoylethene (145), $\delta(CDCl_3)$ 6.8-8.0(15H, complex, aromatic and H-2), 6.6(1H,dd, J_{HP} 22.4Hz, J_{HH} 17.5Hz, H-1), 3.75(3H,s,OCH_3), $\nu_{max.}(CCl_4)$ 1605(C=C), 1440(Ph-P), 1307, 1173(P=O), 1120,910cm^{-1}.

(E) With p-Nitrobenzaldehyde.- The silyl phosphine oxide (131) (0.3g, 1.04mmol) in dry ether (5ml) was treated with n-butyllithium (1.6M, 0.67ml, 1.07mmol) followed by p-nitrobenzaldehyde (0.16g, 1.05mmol) in dry THF (2ml) according to the general procedure. Immediately following the addition of benzaldehyde, the solution became deep red. The crude product was isolated as a viscous red oil (0.31g). Its n.m.r. spectrum indicated that ca. 40% of the material was Z-1-(p-nitrophenyl)-2-diphenylphosphinoylethene (146) $\delta(CDCl_3)$ 6.9-8.2(15H, complex, aromatic and H-2, 6.45(1H,dd, J_{HP} 19.2Hz, J_{HH} 14Hz, H-1), however the rest of the product seemed to be polymeric and it was not purified further.

(F) With Cinnamaldehyde.- The silyl phosphine oxide (131) (1.2g, 4.17mmol) in dry ether (20ml) was treated with n-butyllithium (1.6M, 2.7ml, 4.2mmol) followed by E-cinnamaldehyde (0.55ml, 0.58g, 4.3mmol) according to the general procedure. The crude product was isolated as an oil which gave a white solid (1.3g) following trituration with light petroleum (b.p. 40-60°) and cooling. Recrystallization from ether-light petroleum (b.p. 40-60) gave 1-phenyl-4-diphenylphosphinoyl-buta-1,3-diene (1.1g, 80%), m.p. 123-125°, adjudged by n.m.r. and t.l.c. to contain roughly equal amounts of E,Z and E,E isomers (147) and (148). (Found: C,79.65; H, 5.85; P,9.35. $C_{22}H_{19}OP$ requires C,80.0; H,5.8; P,9.4%), $\delta(CDCl_3)$ 7.1-8.05(16H, complex, aromatic and H-4), 5.95-7.1 (3H, complex, =C-H), $\nu_{max.}(CHCl_3)$ 1632(C=C), 1580,1438(Ph-P), 1170(P=O), 1120,997,690cm^{-1}.

Reaction of Diphenyl(1-trimethylsilylethyl)phosphine Oxide (137) with Benzaldehyde.- The methylated silyl phosphine oxide (137) (0.4g, 1.32mmol) in dry ether (5ml) was treated with n-butyllithium (1.6M, 0.85ml, 1.36mmol) followed by benzaldehyde (0.141ml, 0.147g, 1.39mmol) according to the procedure used for reaction of the silyl phosphine oxide (131) with aldehydes. The product was isolated as an oil (0.48g; addition of petroleum (b.p. 40-60°) followed by cooling gave a white solid which was recystallized from ethyl acetate-light petroleum (b.p. 40-60°) giving a white solid considered to be Z-1-phenyl-2-diphenylphosphinoylprop-1-ene (150) (0.31g, 74%)

m.p. 118-120°, δ($CDCl_3$) 6.8-8.2(11H, complex, aromatic and H-2), 1.9(3H,dd, J_{HP} 12.3Hz, J_{HH} 1.7Hz, CH_3), $\nu_{max.}$($CDCl_3$) 1620(C=C), 1592,1440(Ph-P), 1380,1150cm^{-1}(P=O). Attempts to obtain satisfactory analytical data were unsuccessful. T.l.c. of the product indicated a single stereoisomer, its Z-stereochemistry was assigned by comparison of the n.m.r. data with that of the product (141) of the corresponding reaction of the silyl phosphine oxide (131) with benzaldehyde. The stereochemistry could not be confirmed by the spectroscopic data, however.

Reaction of Diphenyl(trimethylsilylmethyl)phosphine Oxide (131) with Acetone.- To a solution of the silyl phosphine oxide (131) (0.3g, 1.04mmol) in dry ether (5ml) was added, with stirring under nitrogen, n-butyllithium (1.7M, 0.65ml, 1.1mmol). The resulting pale orange solution was stirred at 18° for a further 15 min then cooled to -78° and acetone (0.85ml, 0.07g, 1.2mmol) was added. The mixture was allowed to warm to 18° during 1h then water (5ml) followed by more ether (5ml) were added. The aqueous layer was extracted with more ether (2×3ml) and the combined ether layers were washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil which eventually crystallized (0.31g). This was considered on the basis of n.m.r. and t.l.c. to be a mixture of starting silyl phosphine oxide (131) and diacetone alcohol[190], δ($CDCl_3$) 3.4(1H,s,OH), 2.6(2H,s,$-CH_2-$), 2.1(3H,s, CH_3CO), 1.2(6H,s,CH_3).

Reaction of Diphenyl(trimethylsilylmethyl)phosphine Oxide (131) with Cyclohexanone.- To a solution of the silyl phosphine oxide (131) (1g, 3.47mmol) in dry ether (20ml) was added, with stirring order nitrogen, methyllithium (1.1M, 3.3ml, 3.65mmol). The resulting pale orange solution was stirred at 18° for a further 15 min then cyclohexanone (0.38ml, 0.36g, 3.65mmol) was added. The mixture was stirred under nitrogen at 18° for a further 18h then water (15ml) was added. The aqueous layer was extracted with ether (3×10ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave a viscous oil (1.7g) which was considered on the basis of n.m.r., i.r. and t.l.c. to be a mixture of starting materials and ca. 50% (cyclohexylidenemethyl)diphenylphosphine oxide (159)[191] $\delta(CDCl_3)$ 7.3-8.1(10H,m, aromatic), 5.85(1H,brd, J_{HP} 26Hz,=C-H), 1.2-2.5(10H, complex), $\nu_{max.}$(neat) 1625(C=C), 1438(Ph-P), 1180cm^{-1}(P=O).

Reaction of 7-Oxa-1-trimethylsilylbicyclo(4,1,0)heptane (24) with Lithium Diphenylphosphide.- To a solution of triphenylphosphine (1.51g, 5.76mmol) in dry THF (10ml) was added, with stirring under nitrogen, freshly cut lithium (0.15g, 0.02mol) giving a red solution. The mixture was stirred at 18° for a further 2h then t-butyl chloride (0.62ml, 0.53g, 5.7mmol) was added. The mixture refluxed itself for ca. 5min and was then allowed to cool. Stirring was then stopped to allow the solids to separate and the solution was transferred

by syringe to a solution of the silyl epoxide (24) (0.75g, 4.5mmol) in dry THF (3ml) and the mixture was then stirred at 18° under nitrogen for a further 16h. Water (15ml) was then added and the aqueous layer extracted with ether (3×4ml). The combined organic layers were washed with 2N HCl (10ml), saturated aqueous sodium bicarbonate (10ml), brine, and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and 150-170° gave (cyclohex-1-enyl)-diphenylphosphine (147) (1.03g, 83%), δ($CDCl_3$) 7.18(10H,m, aromatic), 6.0(1H,brd, J_{HP} 14.4Hz,=C-H), 1.1-2.3(8H, complex), $\nu_{max.}$(liquid film) 1623(C=C), 1590,1480,1437(Ph-P),840cm^{-1}.

Oxidation of the Vinyl Phosphine (147).- To a solution of the vinyl phosphine (147) (0.37g, 1.39mmol) in dry THF (4ml) was added, with stirring at 0°, glacial acetic acid (0.088ml, 0.092g, 1.53mmol) followed by hydrogen peroxide (27%, 0.21ml, 1.67mmol) in dry THF (2ml). The mixture was allowed to warm slowly to 18° then left to stand during 16h. Water (20ml) followed by dichloromethane (20ml) were then added. The aqueous layer was extracted with more dichloromethane (2×8ml), the combined organic layers were then washed with saturated aqueous sodium bicarbonate (2×20ml), water, brine and dried ($CaCl_3$). Evaporation of solvent gave an oil which eventually crystallized, recrystallization from ether-light petroleum (b.p. 40-60°) gave 1-diphenylphosphinoylcyclohexene[139](148) (0.31g, 79%) m.p. 119-120°(lit.[139] m.p. 122-124°), δ($CDCl_3$) 7.2-8.2(10H, complex, aromatic), 6.38(1H, brd, J_{HP} 20.3Hz, =C-H), 1.2-2.5(8H, complex), $\nu_{max.}$(neat) 1628(C=C), 1592,1435 (Ph-P), 1180(P=O), 1070,940cm^{-1}.

Phenyl Trimethylsilylmethyl Sulphide (169)[122].- A solution of thioanisole (47.5ml, 50g, 0.4mol) and tetramethylethylenediamine (62.5ml, 47.5g, 0.41mol) in dry THF (350ml) was cooled to -40° then n-butyllithium (1.5M, 400ml, 0.6mol) was added, with stirring under nitrogen. The resulting pale yellow solution was maintained at -40° for a further 1h and left to stand for 30 min. The solution was then cooled to -60° and trimethylsilyl chloride (82ml, 70g, 0.64mol) in dry THF was added, with stirring. The mixture was maintained at -60° for a further 30 min then allowed slowly to warm to 18° and left to stand during 12h. Water (500ml) was then added with vigorous stirring, the aqueous layer was extracted with light petroleum (b.p. 40-60°, 2×400ml), the combined organic layers were then washed with 2N HCl (2×300ml), saturated aqueous sodium bicarbonate (2×300ml), brine, and dried ($MgSO_4$). Evaporation of solvent followed by distillation gave the sulphide (169) (78.6g, 99.4%), b.p. 85-88° at 0.8mm Hg (lit.[114] b.p. 159.5° at 52mm Hg), δ($CDCl_3$) 7.0-7.5(5H, complex, aromatic), 2.2(2H,s,-CH_2-), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1580,1480,1250(C-Si),1025,845cm^{-1}(C-Si).

Phenyl Trimethylsilylmethyl Sulphone (170).- To a solution of the sulphide (169) (84g, 0.43mol) in dichloromethane (800ml) at 0° was added dropwise, with stirring, peracetic acid (4.6M, 280ml, 1.3mol) buffered with sodium acetate trihydrate (44g, 0.33mol). Following the addition the mixture was stirred at 0° for a further 90 min, it was then allowed to warm to 18° during 1h and left to stand for 15h. Water (500ml) was then added and the aqueous layer was extracted with dichloromethane

(2×400ml). The combined organic layers were then washed with 2N sodium hydroxide (2×200ml), brine, and dried ($CaCl_2$). Evaporation of solvent followed by distillation gave the silyl sulphone (170) (93.4g, 96%), b.p. 121° at 0.01mm Hg (lit.[140] b.p. 160° at 6mm Hg), δ($CDCl_3$) 7.3-8.1(5H, complex, aromatic), 2.7(2H,s,-CH_2-), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$(liquid film) 1450, 1305(SO_2), 1250(C-Si), 1150(SO_2), 855(C-Si), 795,695cm^{-1}.

Phenyl Bis(trimethylsilyl)methyl Sulphone (177).- To a solution of the silyl sulphone (170) (6g, 26.3mmol) in dry ether (70ml) was added, with stirring under nitrogen, n-butyllithium (1.5M, 19.5ml, 29.25mmol). The mixture was stirred at 18° for 20 min then cooled to -40° and trimethylsilyl chloride (4.4ml, 3.7g, 34.0mmol) was added. The mixture was allowed to warm to 18° during 1h then stirred at 18° for a further 14h. Water (70ml) was then added and the aqueous layer was extracted with ether (2×40ml). The combined organic layers were washed with brine and dried ($MgSO_4$). Evaporation of solvent gave a solid which was recrystallized from ether to give the bis-silyl sulphone (177) (6.46g, 82%), m.p. 114-116° (Found: C,52.15; H,8.25; S,10.65. $C_{13}H_{24}O_2SSi_2$ requires C,51.95; H,8.05, S,10.65%), δ($CDCl_3$) 7.3-8.1(5H, complex, aromatic), 2.75(1H,s,-CH-), 0.3(18H,s,$SiMe_3$), $\nu_{max.}$($CHCl_3$) 1440,1300(SO_2), 1080, 990,855cm^{-1}(C-Si).

Methylation of Phenyl Trimethylsilylmethyl Sulphone (170).- To a solution of the silyl sulphone (170) (6g, 26.3mmol) in dry ether (70ml) was added, with stirring under nitrogen,

n-butyllithium (1.5M, 18.5ml, 27.7mmol). The mixture was stirred at 18° for 20 min then cooled to -40° and methyl iodide (5ml, 11.2g, 78.8mmol) was added. The mixture was allowed to warm to 18° during 1h then stirred at 18 for a further 14h. Water (75ml) was then added and the aqueous layer was extracted with ether (2×20ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (6.46g). Analysis by n.m.r. indicated that it contained ca. 70% phenyl 1-trimethylsilyl-ethyl sulphone (179), δ($CDCl_3$) 7.2-8.1(5H, complex, aromatic), 2.55(1H,q,H-1), 1.0(3H,d,CH_3), 0.2(9H,s,$SiMe_3$) as well as 10% starting material and 20% 1-methyl-1-trimethylsilylethyl phenyl sulphone (180) δ($CDCl_3$) 7.2-8.1(5H, complex, aromatic), 1.1(6H,s,CH_3), 0.2(9H,s,$SiMe_3$). Attempts were made to separate the components of the mixture by t.l.c. using various solvent conditions, column chromatography and short path distillation, however the composition of the mixture remained essentially unchanged.

In order to attempt complete conversion to the dimethylated silyl sulphone (180), a portion of the product (2g) was treated with 1eq. of n-butyllithium followed by methyl iodide as before. The product was isolated as an oil (2.2g). Analysis by n.m.r. indicated that it was a roughly 1:1 mixture of dimethylated silyl sulphone (180) and o-trimethylsilyl-t-butylsulphonyl benzene (181).

Complete conversion to the latter compound was brought about when a portion of the mixture (0.5g) was treated with a further 0.7 eq. of n-butyllithium followed by methyl iodide

under the same conditions as before. The product was isolated as an oil which eventually crystallized (0.47g). Recrystallization from light petroleum (b.p. 40-60°) gave the o-silyl sulphone (181) (0.38g), m.p. 95-98° (Found: C, 57.9; H,8.1; S,11.75. $C_{13}H_{22}O_2SSi$ requires C,57.75; H,8.2; S,11.85%), δ($CDCl_3$) 7.5-8.1(4H,m, aromatic), 1.4(9H,s,t-Bu), 0.5(9H,s,$SiMe_3$), $\nu_{max.}$(CCl_4) 1480,1335,1305(SO_2), 1140,1060, 850cm^{-1}(C-Si).

Reaction of Phenyl Trimethylsilylmethyl Sulphone (170) with Aldehydes and Ketones - general procedure.- To a solution of the silyl sulphone (170) in either dry ether or THF is added, with stirring under nitrogen, n-butyllithium (1.0eq.). The resulting pale yellow solution is stirred at 18 for a further 15 min then cooled to -78° and the carbonyl compound (1.1eq.) is added. The mixture is allowed to warm to ca. -20° during 1h then methanol (5ml) followed by water is added. The aqueous layer is extracted three times with ether, the combined organic layers are then washed twice with brine and dried ($MgSO_4$). The solvent is evaporated to give the crude product.

(A) With Acetaldehyde.- The silyl sulphone (170) (0.3g, 1.32mmol) in dry ether (5ml) was treated with n-butyllithium (1.6M, 0.83ml, 1.33mmol) followed by acetaldehyde (0.81ml, 0.64g, 1.45mmol) according to the general procedure. The crude product was isolated as a sticky solid (0.28g).

Analysis by n.m.r. indicated that it was a mixture containing ca. 36% 2-phenylsulphonylprop-1-ene (186)[192] $\delta(CDCl_3)$ 7.3-8.1(5H, complex, aromatic), 5.35-6.05(1H,m,H-2), 4.85-5.25(2H, m,H-3), 3.7(2H,d,J 6.4Hz,H-1) as well as 33% E-1-phenylsulphonylprop-1-ene (185)[193] 7.3-8.1(5H, complex, aromatic), 6.1-7.3(2H,m,H-1 and H-2), 1.9(3H,s,H-3) and 31% Z-1-phenylsulphonylprop-1-ene (184)[193] 7.3-8.1(5H, complex, aromatic), 6.1-7.3(2H, m, H-1 and H-2), 1.8(3H,s,H-3).

(B) With Benzaldehyde.- (a) The silyl sulphone (170) (0.3g, 1.32mmol) in dry ether 5ml) was treated with n-butyllithium (1.6M, 0.83ml, 1.33mmol) followed by benzaldehyde (0.15ml, 0.15g, 1.44mmol) according to the general procedure. The crude product was isolated as a gum (0.31g) which was recrystallized from methanol to give a white solid (0.29g), m.p. 65-71°. Analysis by n.m.r. indicated that it was a mixture of ca. 85% E-1-phenyl-2-phenylsulphonylethene (183)[193] $\delta(CDCl_3)$ 7.0-8.3(11H, complex, aromatic and H-2), 6.9(1H,d, J 15.5Hz, H-1) and 15% Z-1-phenyl-2-phenylsulphonylethene (182)[194] 7.0-8.2(11H, complex, aromatic and H-2), 6.5(1H,d, J 12Hz,H-1). Even when the reaction was quenched at -78°, the product was essentially of the same composition and contained little or no trimethylsilyl containing material.

(b) The silyl sulphone (170) (5g, 21.9mmol) in dry ether (100ml) was treated with n-butyllithium (1.6M, 14.1ml, 22.6 mmol) followed by benzaldehyde (2.5ml, 2.6g, 24.5mmol) as before. Immediately following the addition of benzaldehyde at -78°, acetic anhydride (4.14ml, 4.48g, 43.9mmol) was added.

The mixture was allowed to warm to -20° during 1h then methanol (10ml) followed by ether (30ml) and water (100ml) were added. The organic layer was separated and dichloromethane (75ml) was added to the aqueous layer to dissolve the residual precipitate. The aqueous layer was extracted with more dichloromethane (2×50ml), the combined organic layers were then washed with saturated aqueous sodium bicarbonate (200ml), brine and ($CaCl_2$). Evaporation of solvent gave a viscous oil (6.74g). Trituration with a small quantity of light petroleum (b.p. 40-60°) and cooling gave a solid which was recrystallized from ether to give white crystals of 2-phenyl-2-acetoxy-1-trimethylsilylethyl phenyl sulphone (202) (2.9g, 35%), m.p. 146-147° (Found: C,60.45; H,6.55; S,8.3. $C_{19}H_{24}O_4SSi$ requires C,6.06; H,6.4; S,8.5%), δ($CDCl_3$) 7.1-7.8 (5H, complex, SO_2Ph), 7.1(5H,brs,Ph), 6.1(1H,d,J 7.6Hz,H-2), 3.65(1H,d,J 7.6Hz,H-1), 1.65(3H,s,CH_3CO), 0.2(9H,s,$SiMe_3$), $\nu_{max.}$($CHCl_3$) 1647(C=O), 1372,1305,1145(SO_2), 1085,850cm^{-1}(C-Si). Following recrystallization, evaporation of the mother liquors gave an oil (3.7g). Short path distillation at 0.01mm Hg and 180-190° gave E-1-phenyl-2-phenylsulphonylethene (183) (3.2g, 60%) which eventually crystallized to give a solid m.p. 67-69° (lit.[193] m.p. 73.5-75°), δ($CDCl_3$) 7.0-8.3(11H, complex, aromatic and H-2), 6.9(J 15.5Hz,H-1), $\nu_{max.}$(liquid film) 1612 (C=C), 1438,1368,1300,1150(SO_2),970,810cm^{-1}.

The n.m.r. spectrum of the silyl acetate (202) indicated that it was a single diastereoisomer, it was tentatively thought to be the (RS,SR) isomer (see discussion).

Attempts were made to improve the conversion to the silyl acetate (202) in the above reaction by quenching with acetic anhydride at different temperatures and by the use of acetyl chloride instead of acetic anhydride, however the proportion of silyl acetate (202) to vinyl sulphone (183) remained essentially unchanged.

(C) With Acetone.- The silyl sulphone (170) (0.3g, 1.32 mmol) in dry THF (5ml) was treated with n-butyllithium (1.6M, 0.83ml, 1.33mmol) followed by acetone (0.11ml, 0.84g, 1.44mmol) according to the general procedure. The crude product was isolated as an oil (0.27g). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 44% 2-methyl-3-phenylsulphonyl-prop-2-ene (187)[195] $\delta(CDCl_3)$ 7.3-8.1(5H, complex, aromatic), 6.15(1H,m,H-3), 1.75(6H,brs,Me groups), and 56% 2-methyl-3-phenylsulphonylprop-1-ene (188)[196] $\delta(CDCl_3)$ 7.3-8.1(5H, complex, aromatic), 5.0(1H,m,H-1), 4.7(1H,m,H-1), 3.7(2H,brs,H-2), 2.95(3H,s,Me).

(D) With Cyclohexanone.- The silyl sulphone (170) (0.3g, 1.32mmol) in dry THF (5ml) was treated with n-butyllithium (1.6M, 0.83ml, 1.33mmol) followed by cyclohexanone (0.147ml, 0.14g, 1.42mmol) according to the general procedure. The crude product was isolated as an oil (0.31g). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 85% cyclo-hexylidenemethyl phenyl sulphone (189)[159] $\delta(CDCl_3)$ 7.3-8.2(5H, complex, aromatic), 6.2(1H,brs,=C-H), 1.2-2.9(10H, complex) and 15% 1-cyclohex-1-enylmethyl phenyl sulphone (190)[159]

$\delta(CDCl_3)$ 7.3-8.2(5H, complex, aromatic), 5.4(1H,brs,H-2), 3.7(2H,s,CH_2SO_2), 1.3-2.9(8H, complex).

Reactions of 2-Phenyl-2-acetoxy-1-trimethylsilylethyl Phenyl Sulphone (202. (A) With Ammonia in Methanol.- To a stirred slurry of the silyl acetate (202) (0.1g, 0.27mmol) in methanol (3ml) was added 0.880 ammonia solution (2ml). The mixture soon became homogeneous and was stirred at 18° for a further 17h. Ether (10ml) and water (10ml) were then added. The aqueous layer was extracted with more ether (2×8ml), the combined organic layers were then washed with 2N HCl, saturated aqueous sodium bicarbonate, twice with brine, and dried ($MgSO_4$). Evaporation of solvent gave an oil (82mg). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 17% Z- (182) and 83% E-1-phenyl-2-phenylsulphonylethene (183), the compounds produced by the reaction of the silyl sulphone (170) with benzaldehyde described earlier.

(B) With Methanolic Potassium Hydroxide.- (a) The silyl acetate (202) (0.1g, 0.27mmol) was added to 10% methanolic potassium hydroxide (3ml) and the mixture was stirred at 18° for 17h. The mixture was then poured into water (10ml) and ether (10ml). The aqueous layer was extracted with more ether (2×8ml), the combined ether extracts were then washed twice with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (75mg). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 80% 2-methoxy-2-phenylethyl phenyl sulphone

(205) and 20% E-1-phenyl-2-phenylsulphonylethene (183).

(b) The same reaction was carried out at 0^{o} and worked up as before after 1h. The crude product was isolated as an oil (80mg). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 50% 2-methoxy-2-phenylethyl phenyl sulphone (205), 17% Z- (182) and 33% E-1-phenyl-2-phenylsulphonylethene (183).

(C) With Lithium Aluminium Hydride.- A solution of the silyl acetate (202) (0.16g, 0.43mmol) in dry THF (2ml) was added dropwise with stirring to lithium aluminium hydride (0.04g, 1.0mmol) in dry ether (5ml) cooled in ice. The mixture was allowed to warm to 18^{o} during 2h then methanol (1ml) followed by water (5ml) were added cautiously. Sufficient 2M HCl was then added to dissolve the precipitate. The aqueous layer was extracted with ether (2×8ml), the combined organic layers were then washed with saturated aqueous sodium bicarbonate, brine, and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 0.01mm Hg and $160-170^{o}$ gave 2-phenylethyl phenyl sulphone (204) (95mg, 91%) which later crystallized on standing to give a solid m.p. $52-53^{o}$ (lit.[197] m.p. 58^{o}), $\delta(CDCl_3)$ 7.0-8.0(10H, complex, aromatic), 3.25(AA'BB', H-1 and H-2) $\nu_{max.}$(liquid film) 1502,1453,1310,1153(SO_2), 990,745cm^{-1}.

(D) With Potassium Fluoride.- The silyl acetate (202) (0.1g, 0.27mmol) was added to a stirred slurry of potassium fluoride (18mg, 0.31mmol) in DMSO (2ml). The mixture was

stirred at 18° for 100 min then water (5ml) and light petroleum (b.p. 30-40°, 5ml) were added. The aqueous layer was extracted with more light petroleum (2×5ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (60mg). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 35% Z- (182) and 65% E-1-phenyl-2-phenylsulphonyl ethene (183).

(E) With Benzyltrimethylammonium Fluoride.- The silyl acetate (202) 0.1g, 0.27mmol) was added to a stirred solution of anhydrous benzyltrimethylammonium fluoride[166] in THF (2ml). The mixture was stirred at 18° for 100 min then water (5ml) was added. The aqueous layer was extracted with ether (3×3ml), the combined organic layers were then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil (63mg). Analysis by n.m.r. indicated that it was mainly a mixture of ca. 37% Z- (182) and 63% E-1-phenyl-2-phenyl-sulphonylethene (183).

2-Methoxy-2-phenylethyl Phenyl Sulphone (205).- E-1-Phenyl-2-phenylsulphonylethene (183) (0.4g, 1.64mmol) was added to 10% methanolic potassium hydroxide (15ml). The mixture was stirred at 50° for 4h then water (12ml) and ether (10ml) were added. The aqueous layer was extracted with more ether (2×10ml), the combined ether layers were then washed twice with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil which eventually crystallized (0.44g). Re-crystallization from ether-light petroleum (b.p. 40-60°)

gave the methoxy sulphone (205) (0.37g, 82%), m.p. 83-85° (Found: C,64.8; H,5.9; S,11.65. $C_{15}H_{16}O_3S$ requires C,65.2; H,5.85; S,11.6%), δ($CDCl_3$) 7.1-8.1(10H,m, aromatic), 4.7(1H, dd, J 8.7, 3.3Hz, H-2), 3.3(2H,m,H-1), 3.0(3H,s,OMe), $\nu_{max.}$($CHCl_3$) 1450,1305,1150(SO),1105,1083,984cm^{-1}.

Z-1-Phenyl-2-phenylthioethene (206)[194].- To dry ethanol (90ml) was added, in pieces, sodium (2.48g, 1.08mol). The sodium dissolved and after the solution had cooled, thiophenol (10.3ml, 11g, 0.1mol) followed by phenylacetylene (10.8ml, 10g, 0.098mol) were added. The mixture was heated under reflux for 22h then allowed to cool and water (300ml) was added. The resulting precipitate was collected and recrystallized from methanol giving the Z-vinyl sulphide (206) (16.73g, 81%), m.p. 43-45° (lit.[194] m.p. 43-44°), δ($CDCl_3$) 6.9-7.8(10H, complex, aromatic), 6.4(2H,ABq,=C-H), $\nu_{max.}$($CHCl_3$) 1590(C=C),1355,1090, 1022cm^{-1}.

Z-1-Phenyl-2-phenylsulphonylethene (182).- To a solution of the vinyl sulphide (206) (10g, 47.2mmol) in dichloromethane (85ml) at 0° was added, dropwise with stirring, peracetic acid (4.6M, 28ml, 129mmol) buffered with sodium acetate trihydrate (33.8mmol). Following the addition, the mixture was stirred at 0° for a further 2h then allowed to warm to 18° during 1h and left to stand for 17h. Water (100ml) was then added and the aqueous layer was extracted with dichloromethane (2x70ml).

The combined organic layers were washed with saturated aqueous sodium bicarbonate (2×80ml), brine and dried ($CaCl_2$). Evaporation of solvent gave an oil which crystallized on cooling (11.28g). Recrystallization from methanol gave white crystals of Z-vinyl sulphone (182) (10.4g, 91%), m.p. 63-65° (lit.[194] m.p. 64-65°), δ($CDCl_3$) 7.0-8.2(10H,complex, aromatic), 7.0(1H,d, J 12Hz,H-1), 6.45(1H,d, J 12Hz,H-2), $\nu_{max.}$($CHCl_3$) 1610(C=C),1450,1305,1150(SO_2),1087,1030cm^{-1}.

Reactions of Z-1-Phenyl-2-phenylsulphonylethene (182).

(A) With Ammonia in Methanol.- The Z-vinyl sulphone (182) (0.2g, 0.82mmol) was treated with 0.880 ammonia solution (4ml) in methanol (6ml) under the same conditions as used for the silyl acetate (202). The crude product was isolated as an oil 0.19g). Analysis by n.m.r. indicated that it was mainly a mixture of starting material and 2-methoxy-2-phenylethyl sulphone (205) in roughly equal proportions, no E-vinyl sulphone (183) was identified.

(B) With Methanolic Potassium Hydroxide.- The Z-vinyl sulphone (182) (0.2g, 0.82mmol) was treated with 10% methanolic potassium hydroxide (6ml) at 0° under the conditions used for the silyl acetate (202). The crude product was isolated as an oil (0.20g). Analysis by n.m.r. indicated that it was a mixture of ca. 70% starting material and 30% 2-methoxy-2-phenylethyl phenyl sulphone (205), no E-vinyl sulphone (183) was identified.

(C) With Fluoride Reagents.- The Z-vinyl sulphone (182) was treated with potassium fluoride in DMSO and benzyltrimethylammonium fluoride in THF under the same conditions as used for the silyl acetate (202). In both cases, the starting material was recovered unchanged, no E-vinyl sulphone (183) was identified.

(D) Isomerization to the E-Isomer (183).- A solution of the Z-vinyl sulphone (182) (50mg, 0.2mmol, 0.5M) in pentachloroethane containing a crystal of iodine was heated at 130°. After 15 min, analysis by n.m.r. indicated that the isomerization was approximately 50% complete. After 6h the proportion of E-1-phenyl-2-phenylsulphonylethene (183) in the solution was ca. 95%, there was very little Z-isomer remaining.

Reaction of 2-Phenyl-2-acetoxy-1-trimethylsilylethyl Phenyl Sulphone (202) with Sodium Amalgam.- (a) To a vigorously stirred solution of the silyl acetate (202) (0.2g, 0.53mmol) in methanol (5ml) was added 5% sodium amalgam lumps (2.4g, 5.2mmol). The mixture was stirred at 18° for 17h and was then poured into water (15ml) and light petroleum (b.p. 30-40°, 40ml). The organic layer was then washed with brine and dried ($MgSO_4$). Evaporation of solvent gave an oil considered to contain mainly styrene (49mg, 90%) by comparison (n.m.r., i.r., g.l.c.) with an authentic sample.

(b) To a vigorously stirred suspension of $NaH_2PO_4.2H_2O$ (3.2g, 20.6mmol) in methanol (12ml) was added 5% sodium

amalgam lumps (6g, 13mmol) followed immediately by the silyl acetate (202) (0.5g, 1.33mmol). The mixture was stirred at 20° for 2h and was then poured into water (35ml) and light petroleum (b.p. 30-40°, 75ml). The organic layer was then washed with brine and dried ($MgSO_4$). Evaporation of solvent followed by short path distillation at 12mm Hg and 118-123° gave an oil (0.17g) which gave rise to two main peaks on g.l.c. (OV17, 125°) of retention time 7.2 min and 10.2 min, relative area 1:2.8. Analysis by n.m.r. indicated that these corresponded to Z-1-phenyl-2-trimethylsilylethene (210)[198] (lit.[199] b.p. 81° at 5mm Hg), δ($CDCl_3$) 7.1-7.6(6H, complex, aromatic and H-2), 5.8(1H,d,J 14.5Hz,H-1), 0.05(9H,s,$SiMe_3$), and E-1-phenyl-2-trimethylsilylethene (211)[121] (lit.[199] b.p. 85° at 6mm Hg), δ($CDCl_3$) 7.1-7.6(5H, complex, aromatic), 6.95(1H, d,J 18Hz,H-2), 6.4(1H,d,J 18Hz,H-1), 0.2(9H,s,$SiMe_3$). The i.r. spectrum of the mixture also showed the expected vinylsilane absorption, $\nu_{max.}$(liquid film) 3020(=C-H), 1602(C=C), 1493,1247,985,860,840cm^{-1}(C-Si). The combined yield of the two vinyl silanes was 74% after distillation, g.l.c. showed that the ratio of (210) to (211) was unchanged in the crude product to that in the distilled material.

Reaction of Phenyl Trimethylsilylmethyl Sulphone (170) with Acid Chlorides. (A) With Acetyl Chloride - general procedure.- To a solution of the silyl sulphone (170) (0.8g, 3.5mmol) in dry ether (8ml) was added, with stirring under nitrogen, n-butyllithium (1.6M, 2.2ml, 3.5mmol). The mixture was stirred at 18° for 15 min then cooled to -78° and acetyl

chloride (0.26ml, 0.285g, 3.65mmol) was added. The mixture was allowed to warm to 18° during 2h then water (15ml was added. The aqueous layer was extracted with ether (2×8ml), the combined organic layers were then washed with saturated aqueous sodium bicarbonate, brine, and dried ($MgSO_4$). Evaporation of solvent gave an oil (0.81g). Analysis by n.m.r. indicated that it was mainly a mixture in roughly equal proportions of starting silyl sulphone and 1-phenylsulphonyl-propan-2-one (218)[200], δ($CDCl_3$), 7.2-8.1(5H, complex, aromatic), 4.15(2H,s,CH_2), 2.3(3H,s,CH_3CO) $\nu_{max.}$(liquid film) 1720cm^{-1} (C=O).

(B) With Trimethylacetyl Chloride.- The silyl sulphone (170) (1.0g, 4.38mmol) in dry ether (10ml) was treated with n-butyllithium (1.6M, 2.8ml, 4.48mmol) followed by trimethyl-acetyl chloride (0.60ml, 0.59g, 4.8mmol) according to the general procedure. The crude product was isolated as a white solid (1.2g). Recrystallization from ether-light petroleum (b.p. 40-60°) gave 1-phenylsulphonyl-3,3-dimethylbutan-2-one (219) (0.87g, 83%), m.p. 83-85° (Found: C,60.1; H,6.6; S,13.5. $C_{12}H_{16}O_3S$ requires C,60.0; H,6.7- S,13.35%), δ($CDCl_3$) 7.4-8.0 (5H, complex, aromatic), 4.3(2H,s,CH_2) 1.2(9H,s,t-Bu), $\nu_{max.}$($CHCl_3$) 1720(C=O),1320,1150(SO_2),1050,1000cm^{-1}.

(C) With 1-Adamantanecarboxylic Acid Chloride.- The silyl sulphone (170) (1.0g, 4.38mmol) in dry ether (10ml) was treated with n-butyllithium (1.6M, 2.8ml, 4.48mmol) followed by 1-adamantanecarboxylic acid chloride (0.90g, 4.5mmol) in dry

ether (2ml) according to the general procedure. The crude product was isolated as a white solid (1.6g). Recrystallization from ether gave 1-adamantane phenylsulphonylmethyl ketone (220) (1.32g, 95%), m.p. 113-114° (Found: C,67.75; H, 6.9; S,10.15. $C_{18}H_{22}O_3S$ requires C,67.9; H,6.95; S,10.05%), $\delta(CDCl_3)$ 7.4-8.1(5H, complex, aromatic), 4.3(2H,s,CH_2), 1.4-2.3(15H, complex), $\nu_{max.}(CHCl_3)$ 1710(C=O),1450,1320,1150(SO_2), 1085,1008cm^{-1}.

(D) With Benzoyl Chloride.- The silyl sulphone (170) (0.8g, 3.5mmol) in dry ether (8ml) was treated with n-butyllithium (1.6M, 2.2ml, 3.5mmol) followed by benzoyl chloride (0.43ml, 0.52g, 3.7mmol) according to the general procedure. The crude product was isolated as a white solid (0.72g). Analysis by n.m.r. indicated that it was a mixture containing ca. 68.5% phenacyl phenyl sulphone (221)[201] $\delta(CDCl_3)$ 7.25-8.2 (10H, complex, aromatic), 4.7(2H,s,CH_2), $\nu_{max.}$(liquid film) 1685cm^{-1}(C=O), as well as 21% E-1-chloro-1-phenyl-2-phenylsulphonylethene (222)[202] 7.3-8.2(10H, complex, aromatic), 7.05(1H,s,H-1) and 10.5% Z-1-chloro-1-phenyl-2-phenylsulphonylethene (223)[202] 7.3-8.2(10H, complex, aromatic), 7.2(1H,s,H-1). Recrystallization of the product from methanol gave a white solid (0.6g), m.p. 80-89°; its composition was essentially unchanged from that of the crude material.

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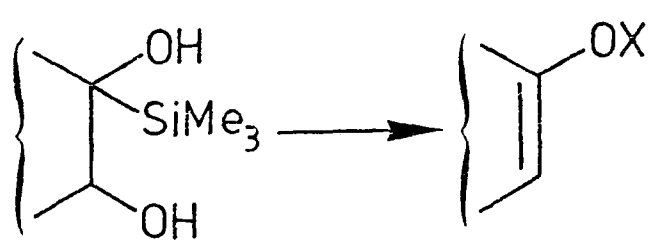
ABSTRACT

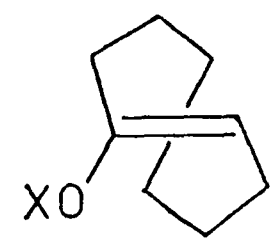
The work described in the two parts of this thesis is concerned with the development of two methods for the synthesis of substituted olefins. Both methods involve elimination reactions of β-hydroxysilanes[1,2] to form the double bond, therefore in the general introduction these reactions are discussed together with the methods available for the preparation of β-hydroxysilanes.

Part I: Enol Ether Synthesis from 1-Trimethylsilyl-1,2-diols

The object of this project was to develop a route whereby cyclic 1-trimethylsilyl-1,2-diols (1) could be transformed stereospecifically to enol ethers (2), such that the route could then be used for the preparation of an analogous *trans*-cyclooctene derivative (3). No compound of the latter type had previously been reported.

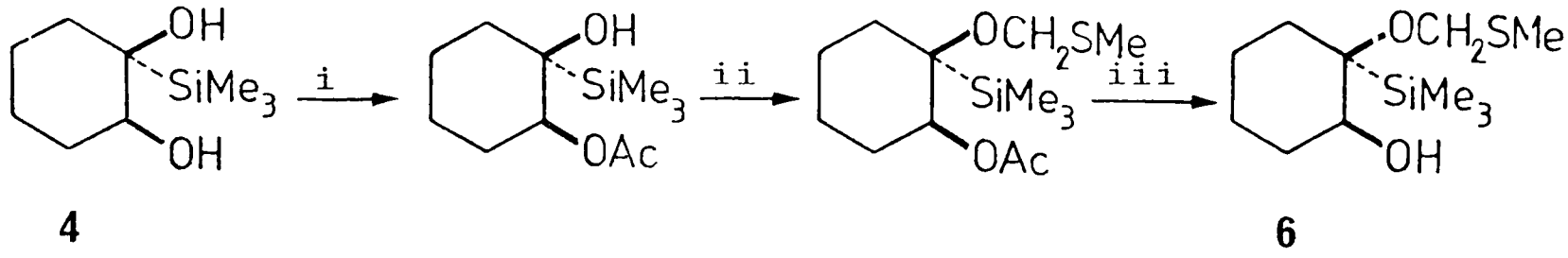


1 2

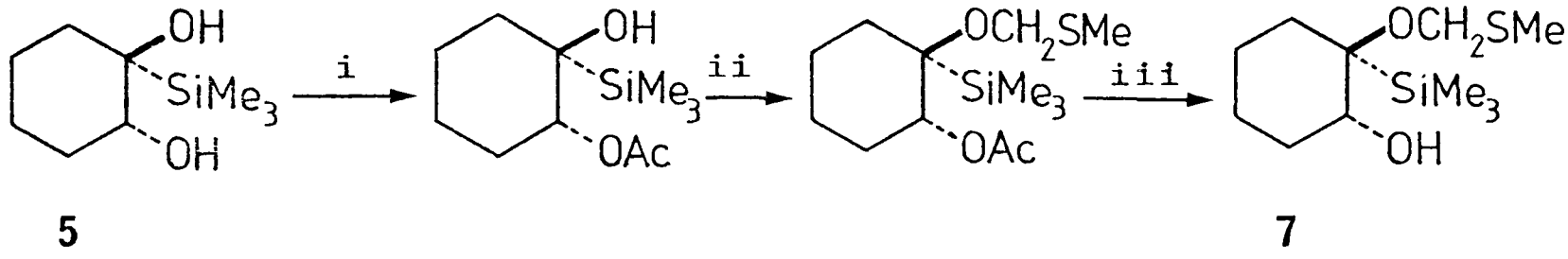


3

The route to enol ethers was developed initially starting from *cis*- and *trans*-1-trimethylsilylcyclohexane-1,2-diols (4) and (5)[3-5], these were transformed to the α-methylthiomethoxy-β-hydroxysilanes (6) and (7) as shown (Scheme 1).



4 **6**

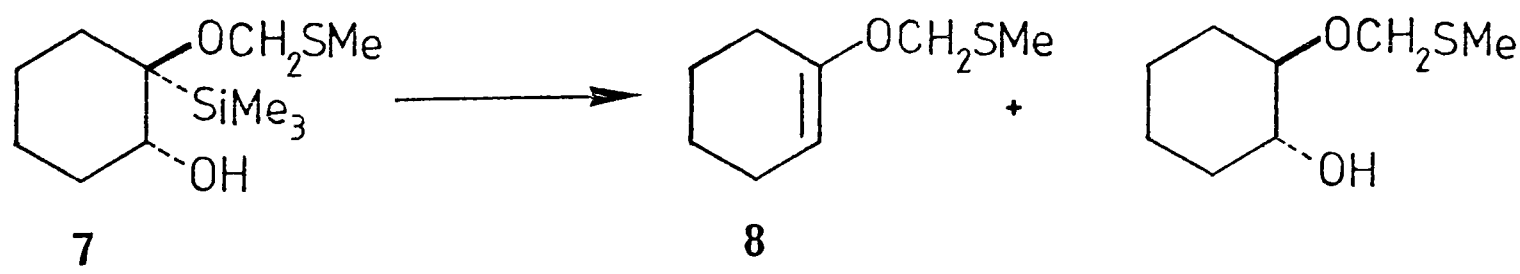


5 **7**

Reagents: i, Ac_2O/pyridine; ii, Ac_2O/DMSO/AcOH; iii, KOH/MeOH

Scheme 1.

syn-Elimination of Me_3SiOH from (7) to give the enol ether (8) was brought about by treatment with potassium hydride in THF; however (7) was desilylated by potassium t-butoxide in DMSO and also to some extent by sodium hydride in DMF (Scheme 2).



7 **8**

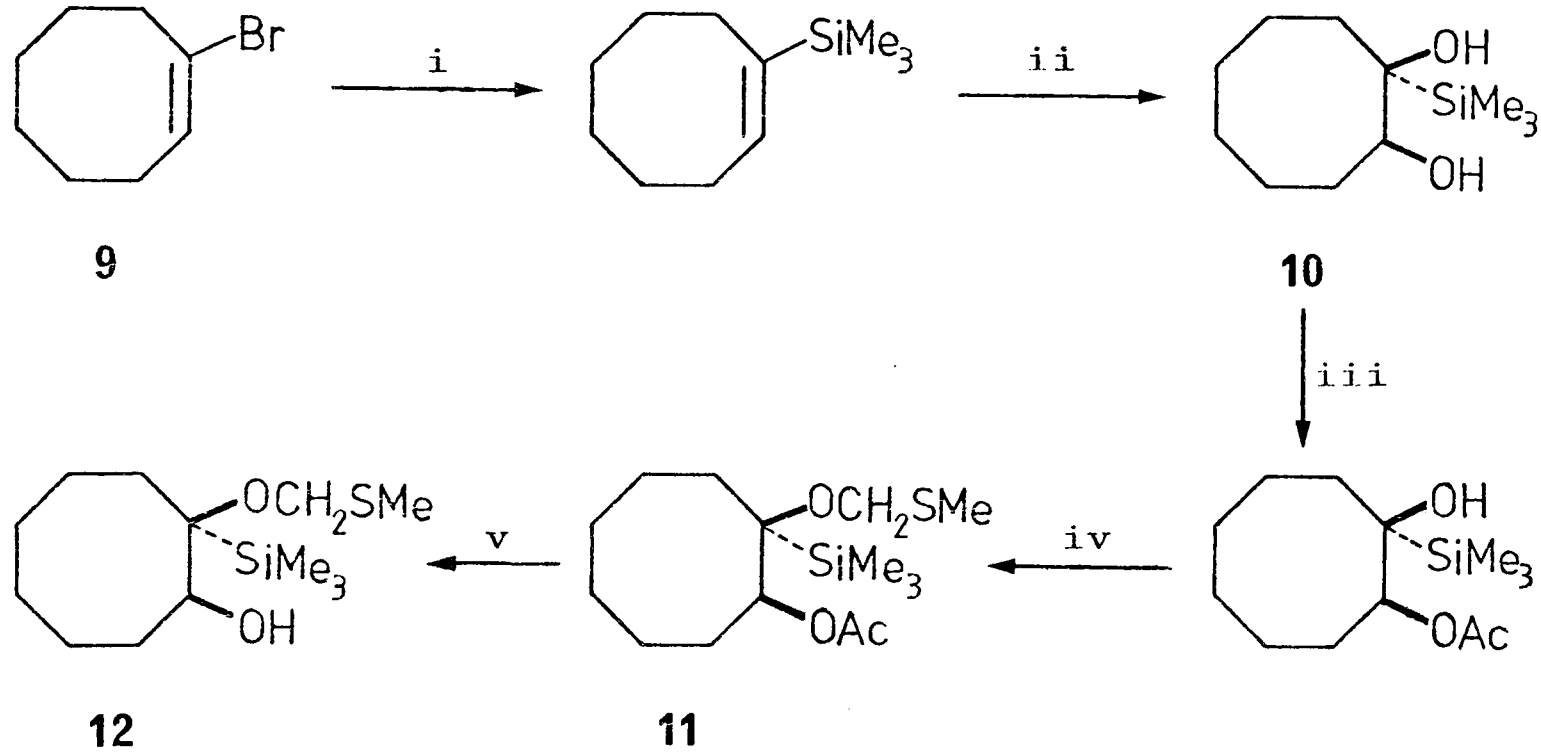
i	100	:	0
ii	0	:	100
iii	66	:	33

Reagents: i, KH/THF; ii, KOtBu/DMSO; iii, NaH/DMF

Scheme 2.

anti-Elimination of Me_3SiOH from (6) to give (8) was brought about by treatment with either methanesulphonyl chloride or p-toluenesulphonyl chloride in pyridine.

1-Trimethylsilyl-cis-cyclooctane-1,2-diol (10), prepared as shown from 1-bromo-cis-cyclooctene (9), was converted to the trans-β-hydroxysilane (12) by means of a series of transformations (Scheme 3) analogous to those used on the six membered ring diols (4) and (5).



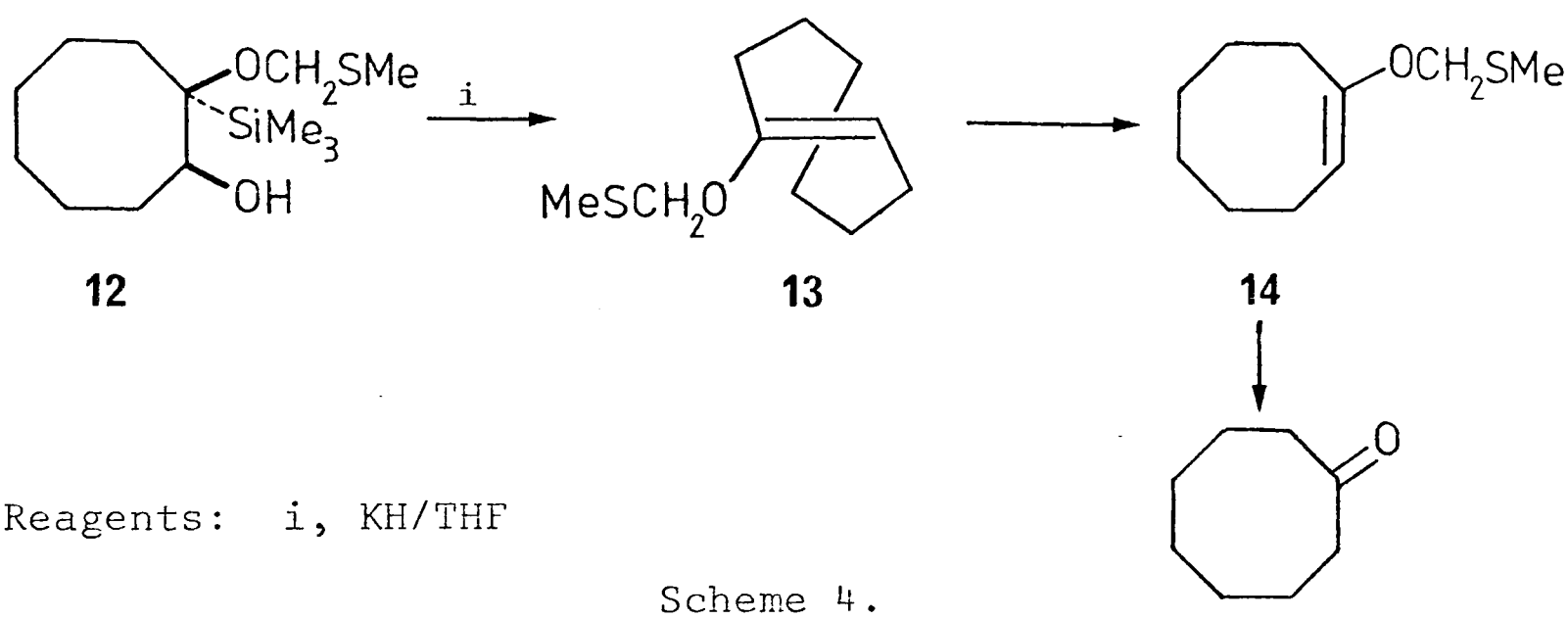
9 **10** **11** **12**

Reagents: i, $Na/Me_3SiCl/Et_2O$; ii, OsO_4/N-methylmorpholine-N-oxide/H_2O/acetone; iii, Ac_2O/pyridine/4-dimethylaminopyridine/CH_2Cl_2; iv, Ac_2O/DMSO/AcOH; v, KOH/MeOH.

Scheme 3.

Treatment of (12) with potassium hydride in THF gave mainly 1-methylthiomethoxy-trans-cyclooctene (13) which was identified by n.m.r. The latter compound had a half life of about 40 min at 18^{o}, it isomerized to the corresponding cis-enol ether (14)

which was also unstable and decomposed on standing to cyclo-octanone (Scheme 4).

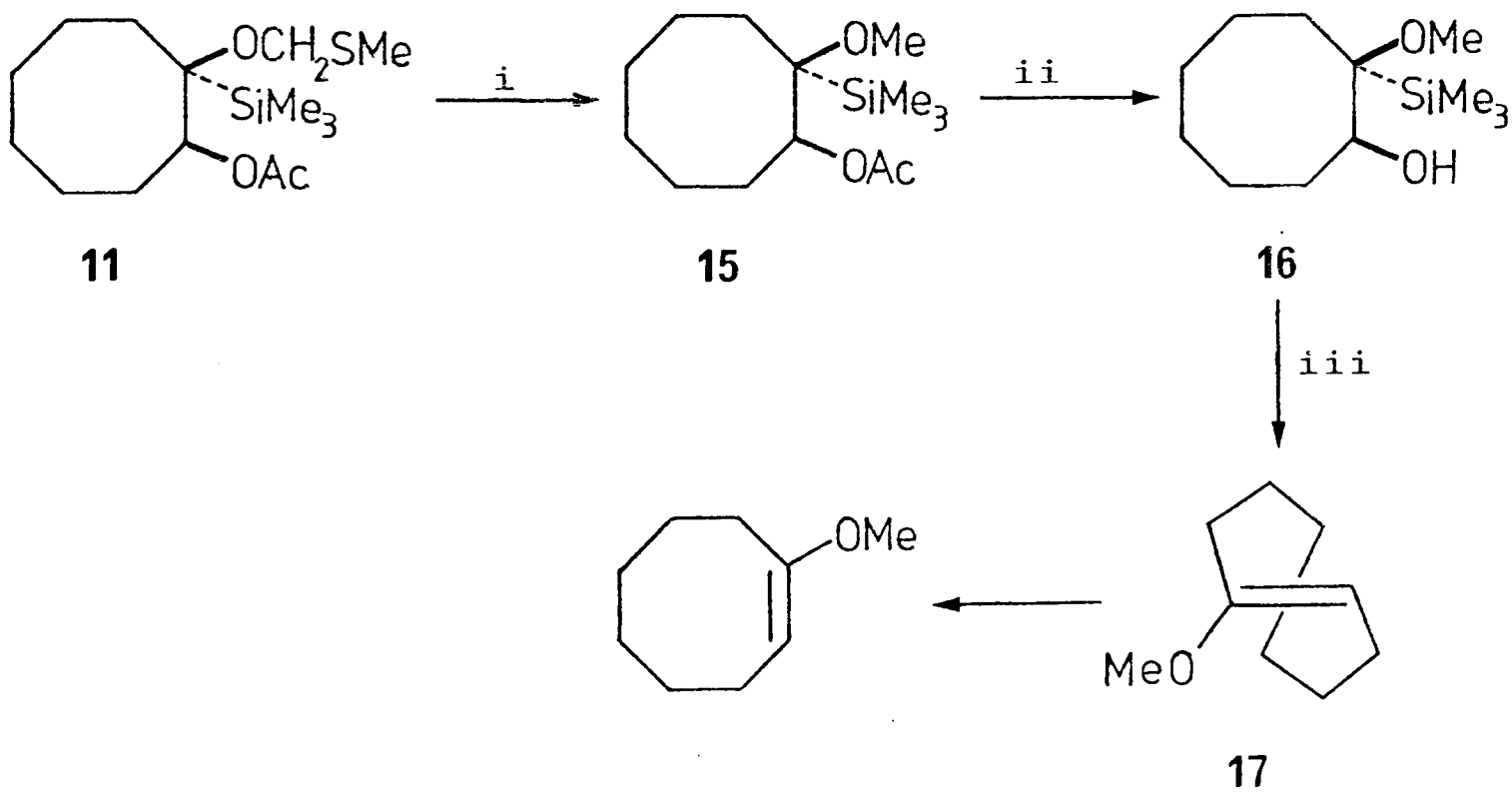


12 13 14

Reagents: i, KH/THF

Scheme 4.

The methylthiomethyl ether (11) was converted via the methyl ether (15) to the α-methoxy-β-hydroxysilane (16) and treatment of the latter with potassium hydride in THF gave 1-methoxy-trans-cycloctene (17) (Scheme 5).



11 15 16 17

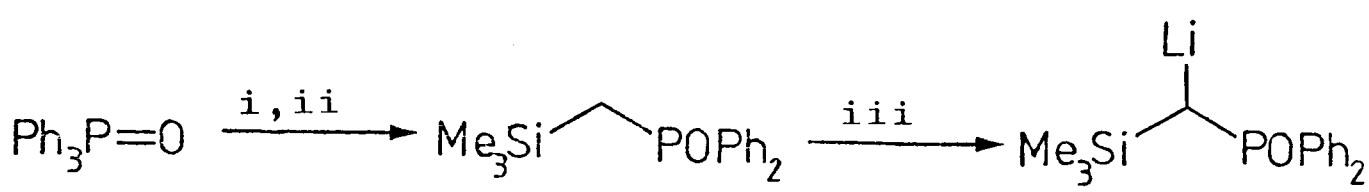
Reagents: i, Raney Ni/benzene; ii, KOH/MeOH; iii, KH/THF

Scheme 5.

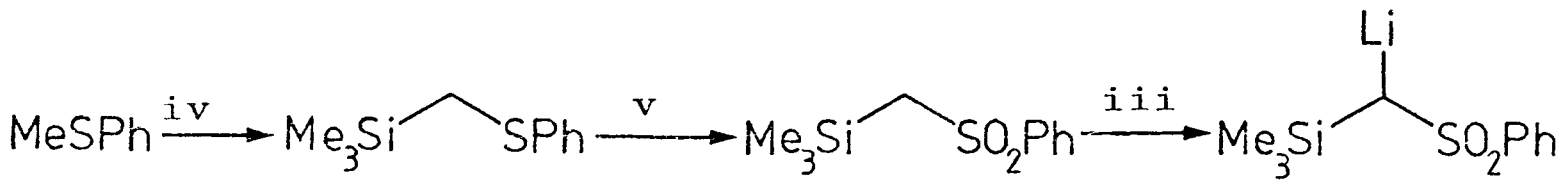
Like (14), (17) was unstable with respect to isomerization, the half life of (17) was about 70 min in $CDCl_3$ solution at 36°.

Part II: Olefin Synthesis Using α-Metallated Organosilanes

This project was concerned with the chemistry of the α-substituted-α-metallated organosilanes[6] (18) and (19), they were prepared as shown in Scheme 6.



18

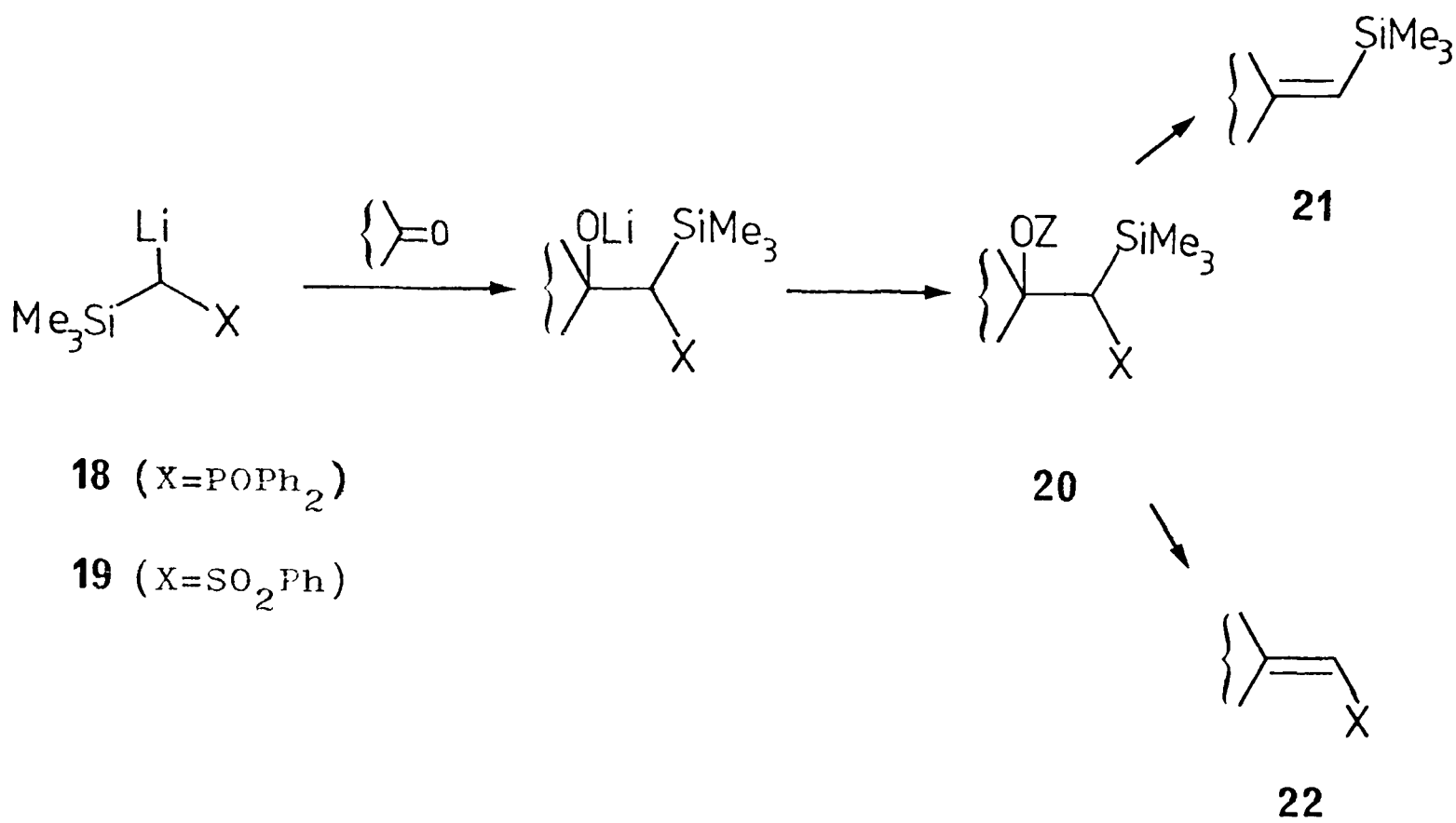


19

Reagents: i, MeLi; ii, Me_3SiCl; iii, n-BuLi; iv, n-BuLi/TMEDA/THF; v, $CH_3CO_3H/NaOAc/CH_2Cl_2$

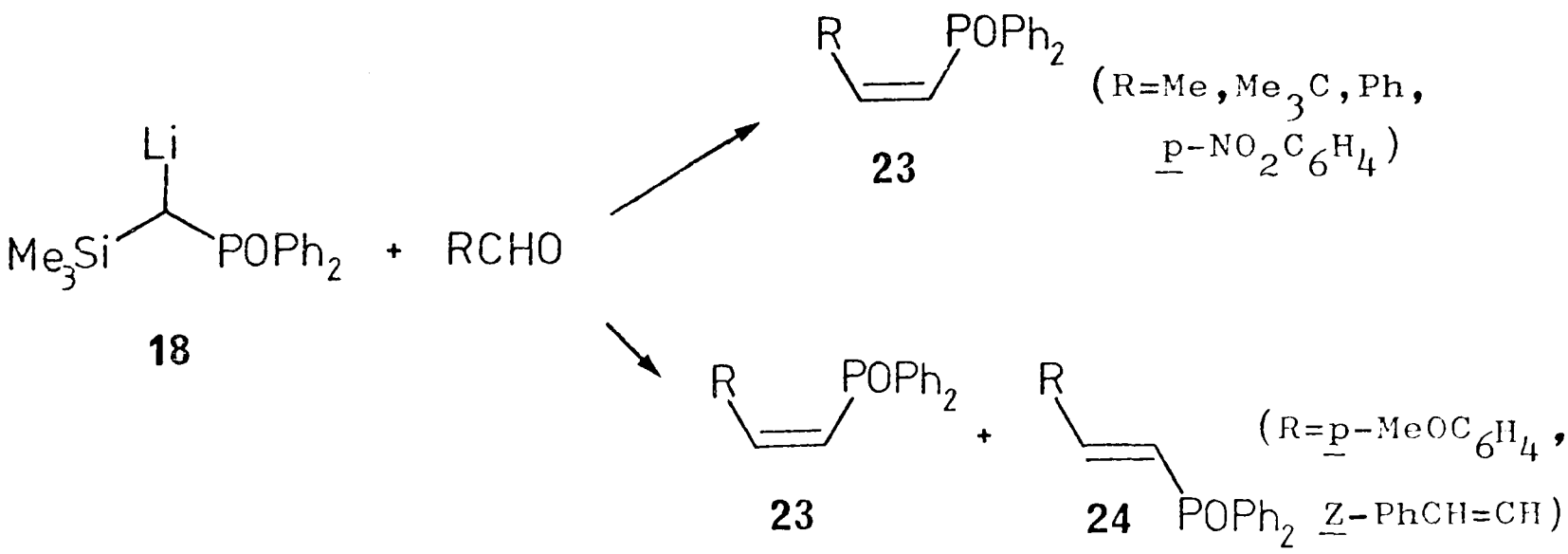
Scheme 6.

The idea was to achieve an adduct (20) of (18) or (19) with a carbonyl compound, such that the adduct could be transformed into either a vinylsilane (21) or the appropriate substituted olefin (22) using suitable selective elimination procedures (Scheme 7).



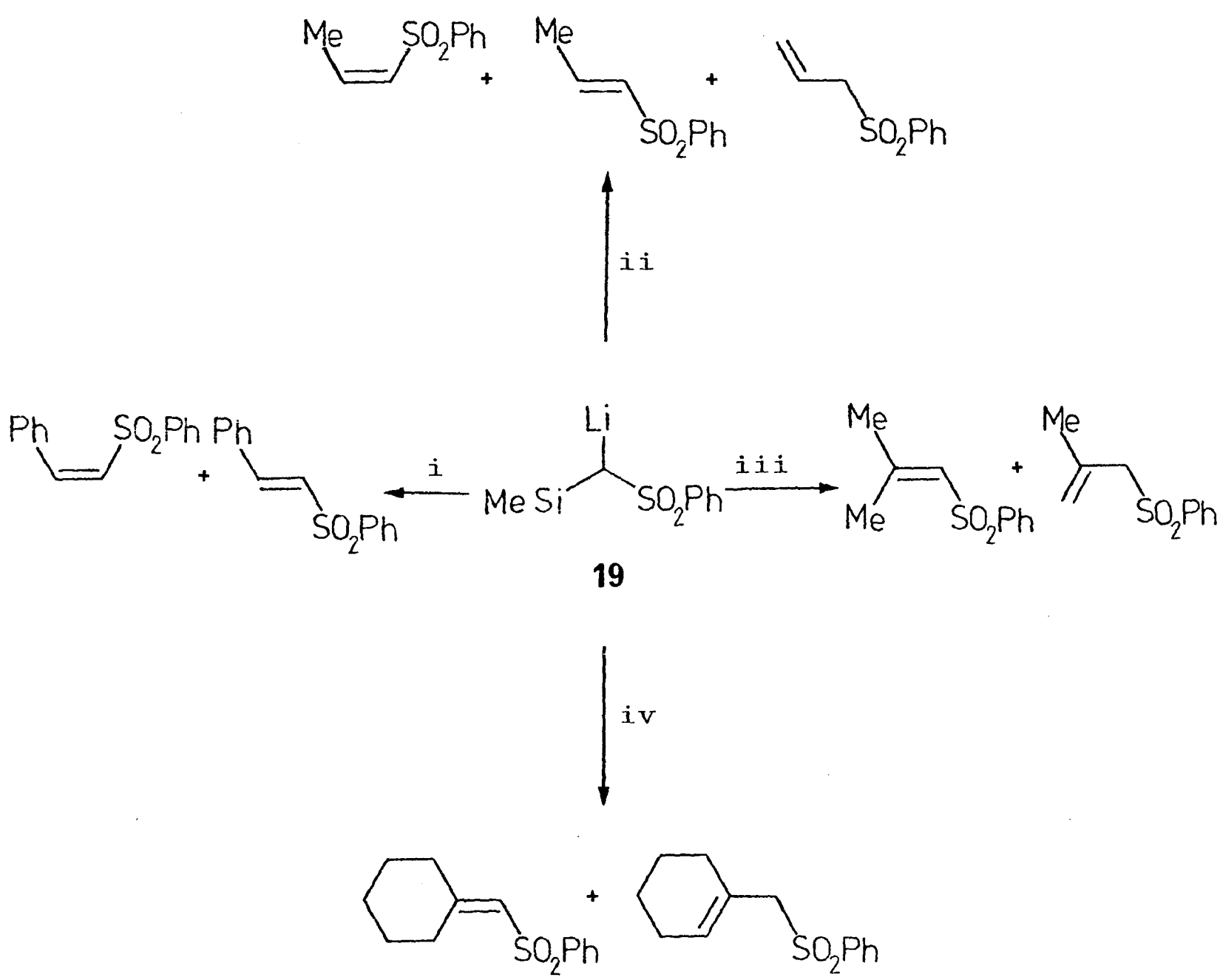
Scheme 7.

Reaction of α-lithiated silyl phosphine oxide (18) occurred rapidly with a number of aldehydes to give generally the Z-vinyl phosphine oxide (23) except in two cases where mixtures of Z- and E-vinyl phosphine oxides (23) and (24) were formed (Scheme 8). Unsuccessful attempts were made to isolate the intermediate β-hydroxy-α-trimethylsilyl phosphine oxides involved in the above reactions.



Scheme 8.

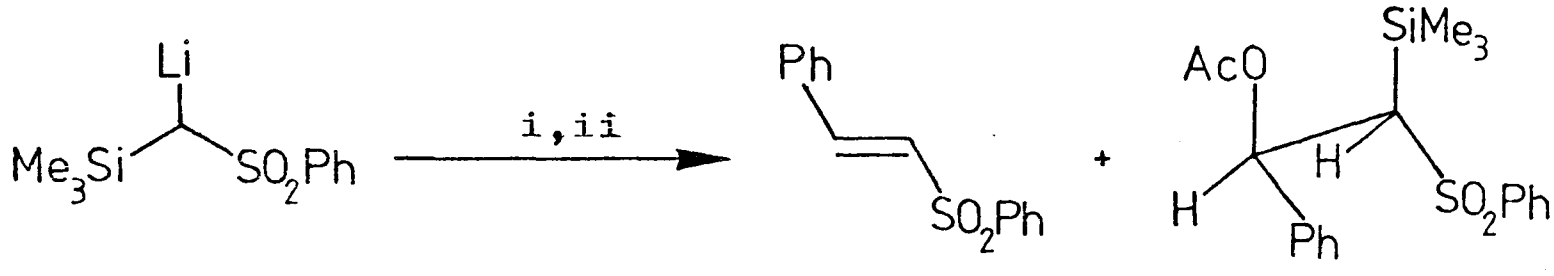
Reaction of the α-lithiated silyl sulphone (19) could be achieved with acetaldehyde and benzaldehyde in ether and with acetone and cyclohexanone in THF. In each case, mixtures of unsaturated sulphones were formed (Scheme 9).



Reagents: i, benzaldehyde/ether; ii, acetaldehyde/ether; iii, acetone/THF; iv, cyclohexanone/THF

Scheme 9.

When the reaction of (19) with benzaldehyde was quenched with acetic anhydride, a mixture of the E-vinyl sulphone (25) and the β-acetoxy-α-silyl sulphone (26) were formed (Scheme 10). The latter was apparently a single stereoisomer, its stereochemistry was tentatively assigned as the (RS,SR) isomer as drawn.

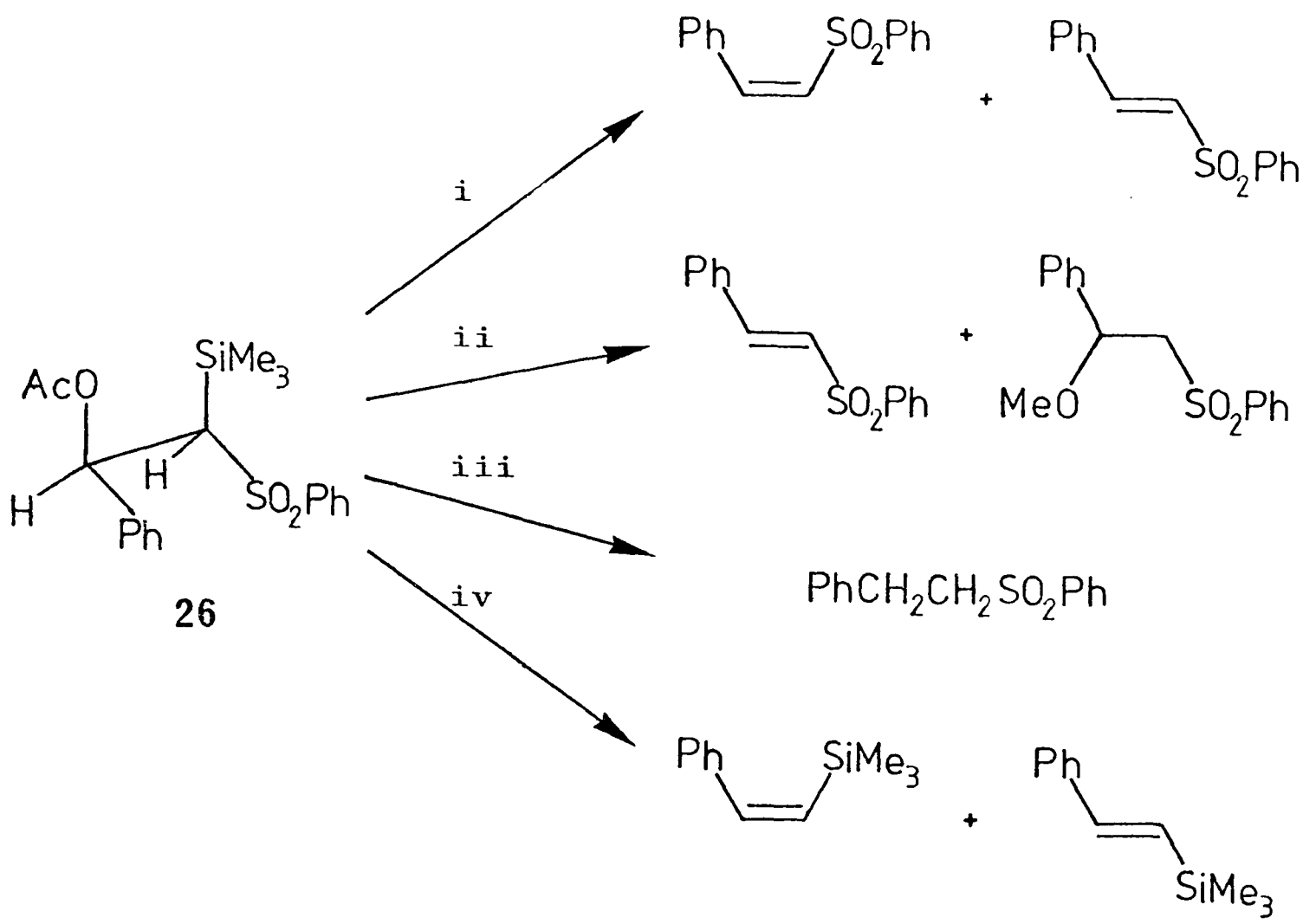


19 **25** **26**

Reagents: i, PhCHO; ii, Ac_2O

Scheme 10.

Treatment of (26) with methanolic ammonia, methanolic potassium hydroxide, or potassium hydride gave either vinyl-sulphones or products derived from the latter by nucleophilic addition. The reaction of (26) with buffered sodium amalgam[8,9] gave a mixture of Z- and E-vinylsilanes (27) and (28) (Scheme 11). Thus (26) can be transformed into either vinyl sulphones or vinylsilanes under appropriate conditions. To a limited extent therefore, the original objective was achieved.



Reagents: i, NH_3/MeOH; ii, KOH/MeOH; iii, $LiAlH_4/Et_2O$; iv, $Na.Hg/NaH_2PO_4$/MeOH

Scheme 11.

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SHORT ABSTRACT

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Synthetic Aspects of Organosilicon Chemistry

Part I: Enol Ether Synthesis from 1-Trimethylsilyl-1,2-diols.

A route was developed whereby cis-(1) and trans-(2) 1-trimethylsilylcyclohexane-1,2-diols could be transformed into the novel enol ether 1-methylthiomethoxycyclohexene (3). The route involved acetylation of the 2-hydroxyl group of the diols followed by methylthiomethylation of the 1-hydroxyl group then hydrolysis of the acetate group to give β-hydroxy-silanes. The final step was then achieved by stereospecific anti-elimination of trimethylsilanol in the case of the route starting from (1) and corresponding syn-elimination in the route starting from (2).

1-Trimethylsilylcyclooctane-1,2-diol was synthesized and transformed, by an analogous route to that used to prepare (3) from (2), to 1-methylthiomethoxy-trans-cyclooctene (4). The latter is the first trans-cyclooctene derivative with an oxygenated substituent on the double bond. A modification of the route used to prepare (4) led to the preparation of 1-methoxy-trans-cyclooctene (5). Both (4) and (5) were unstable with respect to isomerization to the corresponding cis-enol ethers. In the case of (5) a kinetic study indicated the isomerization to be a first order process.

Part II: Olefin Synthesis Using α-Metallated Organosilanes

The lithiated derivative of diphenyl(trimethylsilylmethyl)-phosphine oxide reacted with aldehydes to give (1-diphenylphosphinoyl)alkenes, generally of Z-stereochemistry. For example benzaldehyde gave Z-2-diphenylphosphinoylethene.

The lithiated derivative (6) of phenyl trimethylsilylmethyl sulphone reacted with aldehydes and ketones to give mixtures of α,β- and β,γ-unsaturated sulphones. For example cyclohexanone gave cyclohexylidenemethyl phenyl sulphone and 1-cyclohex-1-enylmethyl phenyl sulphone. Reaction of (6) with benzaldehyde followed by acetic anhydride gave E-2-phenyl-1-phenylsulphonylethene and 2-phenyl-2-acetoxy-1-trimethylsilylethyl phenyl sulphone (7). Treatment of (7) with either methanolic ammonia, methanolic potassium hydroxide, or lithium aluminium hydride gave E- and Z-2-phenyl-1-phenylsulphonylethene and/or products derived from the latter by nucleophilic addition. Treatment of (7) with buffered sodium amalgam gave E- and Z-2-phenyl-1-trimethylsilylethene.