VINYLSILANES AND ALLYLSILANES IN ELECTROPHILIC SUBSTITUTION REACTIONS. STEREOCONTROLLED SYNTHESIS OF INSECT SEX PHEROMONES.

by

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Ph.D. Chemistry

Vinylsilanes and Allylsilanes in Electrophilic Substitution Reactions. Stereocontrolled Synthesis of Insect Sex Pheromones

ABSTRACT

Trialkylsilylallyl carbanions, from metalation of trialkylallylsilanes with Schlosser's base (n-BuLi/KO^{t}Bu), react with various alkyl halides to give predominantly γ-addition products. The relative ratio of γ/α products increases significantly by increasing the steric hindrance on the silicon. A stereoselective synthesis of E-vinylsilanes by this method is described.

The electrophilic substitution reaction of E-vinylsilanes with halogens has been investigated. Under iodine monochloride reaction conditions, inversion of configuration at the double bond was observed and Z-vinyliodides are provided stereoselectively. The Lewis acid mediated iododesilylation reaction has been found to proceed with retention of configuration to give mainly E-vinyliodides. Therefore, either the Z- or E-vinyliodides could be prepared stereoselectively from the same precursor.

1,2-Disubstituted alkenes have been prepared stereoselectively from vinyliodides by a coupling reaction with

organozinc compounds in the presence of a palladium catalyst. This methodology has been applied to the stereoselective synthesis of a number of insect sex pheromones.

A new concept of a "tunable" synthesis of a mixture of E- and Z-alkenes has been proposed. The application of this idea to the synthesis of insect sex pheromones has been developed. It consists of the synthesis of a specific blend of E- and Z-alkenes in a one pot reaction.

Ph.D. Chimie

Les Vinylsilanes et les Allylsilanes dans des Reactions de Substitution Electrophile. Synthèse Stéréocontrôlée de Phéromones d'Insectes.

RESUME

Les carbanions trialkylsilylallyles dérivés de la métalation des trialkylallylsilanes à l'aide de la base de Schlosser (n-BuLi/KO^{t}Bu), réagissent avec les halogénures d'alkyle pour conduire à des produits d'addition c_γ de façon prépondérante. Le rapport des produits d'addition c_γ versus c_α augmente considérablement avec l'encombrement stérique autour de l'atome de silicium. Nous dérivons ici une synthèse stéréoselective des vinylsilanes terminales de stéréochimie E basée sur cette approche.

Notre étude a également porté sur les réactions de substitution électrophile des vinylsilanes préparées. Le traitement avec le chlorure d'iodonium (ICl) donne lieu à l'inversion de configuration autour de la double liaison pour conduire à des iodures vinyliques de stéréochimie Z. Nous avons d'autre part trouvé que la réaction de désilylation des vinylsilanes par l'iode en présence d'acides de Lewis s'opère avec rétention de configuration au niveau de la double liaison; et par conséquent, les iodures vinyliques

de stéréochimie E our Z peuvent être préparées séparément, de manière stéréoselective à partir d'un même précurseur.

La réaction de couplage des iodures vinyliques avec des composés organozinciques en présence du catalyseur palladium (O), nous a permis de préparer des oléfines 1,2-disubstituées stéréosélectivement. Cette méthodologie a été appliquée à la synthèse stéréosélective de quelques phéromones d'insectes.

Nous avons par ailleurs proposé un nouveau concept de synthèse de mélange spécifique d'oléfines de stéréochimie E et Z en une seule étape réactionnelle. L'utilité de cette nouvelle approche a été démontrée dans la synthèse de phéromone d'insecte dont la composante biologiquement active est un mélange spécifique des deux isomères oléfiniques E et Z.

Acknowledgements

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Finally, I would like to thank Miss B. Brown for typing this thesis.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Ac	Acetyl
Bu	Butyl
BM	Base
Cp	Cyclopentadienyl
DMF	N'N-Dimethylformamide
Et	Ethyl
GC	Gas chromatography
HPLC	High pressure liquid chromatography
Hz	Hertz
MHz	Megahertz
HMPA or HMPT	Hexamethylphosphotriamide
Hex	Hexyl (n-C_6H_{11}-) or hexane as solvent
HRMS	High resolution mass spectra
INEPT	Insensitive nuclei enhanced by polarization transfer
Me	Methyl
MCPBA	m-Chloroperbenzoic acid
PTSA	Para-toluenesulfonic acid
Pr	Propyl
THF	Tetrahydrofuran
THP	Tetrahydropyran
DHP	Dihydropyran
TMEDA	Tetramethylethylenediamine
TLC	Thin layer chromatography

CHAPTER I

INTRODUCTION

1 - The Development of Organosilicon Chemistry

Naturally occurring silicon compounds, such as silicates, have been of service to men for thousands of years. Since remote antiquity, men have used sand and shaped stones of granite to survive over their surroundings. The later discovery and use of pottery, vitreous enamel, glass and cement in that order all preceded modern silicon chemistry[1]. This oldest and versatile use of silicon results from its availability. Silicon is the second most abundant element in nature after oxygen. It occurs mainly as silicon dioxide[2] (SiO_2).

The pure Si element was first isolated in 1811 by Gay Lussac and Thenard by treatment of tetrafluorosilane with potassium[2].

$$SiF_4 + 4\ K \longrightarrow Si + 4\ KF$$

In 1823 Berzelius prepared elementary silicon from potassium fluorosilicate by an analogous method and then converted the pure silicon into silica (SiO_2) by combustion.

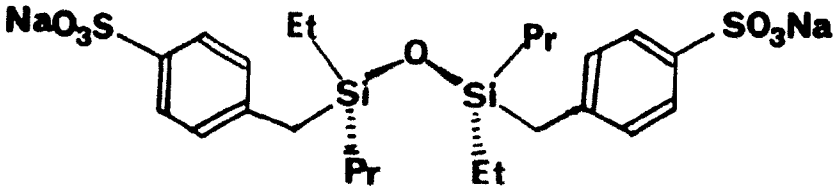
The first organosilicon compound to occur in organic synthesis was tetraethylsilane. This compound was prepared in 1863 by Friedel and Crafts when silicon tetrachloride was

treated with diethylzinc[3]. After Grignard reagent was discovered in France, important advances were made in alkylsilane synthesis. In 1904, Kipping and Dilthey independently used the new organometallic reagent to form a silicon-carbon bond from silicon tetrachloride[4,5]. Advantageously, this method was applied in the next three decades until 1945 when Rochow[6-10] discovered a synthesis of organo-chlorosilanes by passing a vapour of organic chlorides over heated silicon in the presence of a catalyst. Dialkylchlorosilanes are thus readily provided and employed in silicon polymer production.

$$CH_3Cl + Si \xrightarrow{300°C} (CH_3)_2SiCl_2 \longrightarrow \text{Methyl silicones}$$

By this process a new era was opened in organosilicon chemistry, the establishment of a silicone polymer industry. Earlier in 1909, Kipping[11] reported that, when poured into cold water, ethylchlorosilane gave an oil of about the same consistency as glycerol. Jellies, glues, and uncrystallizable solids were obtained as the degree of condensation increased. At that time, Kipping had no notion of the polymeric phenomenon occurring. In all his work, he felt driven to prepare, isolate and characterize a pure crystalline compound containing silicon-carbon bond. Successful results were obtained when he reported the first optically active

organosilicon compound[12] 1 where silicon bears four covalent bonds in tetrahedral structure.



1

Silicon polymer products are used today in different forms. They are oil, emulsion, rubbers, resins, etc., and tremendous developments have been done in recent years[13]. One of the most frequently applied and technologically advantageous processes of forming a silicon-carbon bond is the hydrosilylation reaction[10] as illustrated below.

$$Cl_3SiH + CH_2{=}CH{-}CF_3 \xrightarrow{Pt} Cl_3Si{-}CH_2{-}CH_2{-}CF_3$$

Despite the wide abundance of silicon in nature, especially in the mineral kingdom, its involvement in living organisms is very limited[2]. The most primitive sea algae and sea animals contain large amounts of silicon compounds (diatoms, silicon sponges). They are also contained in plants, in animal tissues and bones of vertebrates. However, the composition of the silicon compounds in which the element appears and their part in the biological activity of plants and animals are not yet properly understood.

Interest in the use of organosilicon compounds in organic synthesis came later. In 1968, the trialkylsilyl group was first introduced as a protecting group for hydroxy functions[15-22]. The silyl ether produced has higher solubility in organic solvents than the parent compound. The thermal stability is also increased. The silyl derivative is more volatile, facilitating its use in gas chromatography experiments. On the other hand, the silyl protecting group is cleaved in extremely selective conditions (Scheme 1.1).

Since the Mukaiyama reaction[23,24] was first reported (Scheme 1.2), silyl enol ethers as protected enolates have found a great deal of use in synthesis. Many reviews[25,26] have been published accounting for the exciting developments which have been made in this area.

$$R\text{-}OH \underset{ii}{\overset{i}{\rightleftharpoons}} RO\text{-}Si(CH_3)_2R'$$

a) i = $(CH_3)_3SiCl$/base, $[(CH_3)_3Si]_2NH$, $(CH_3)_3SiNH\text{-}CO\text{-}CH_3$
$(CH_3)_3Si{=}N(CH_3)_2$ etc....
R' = CH_3-

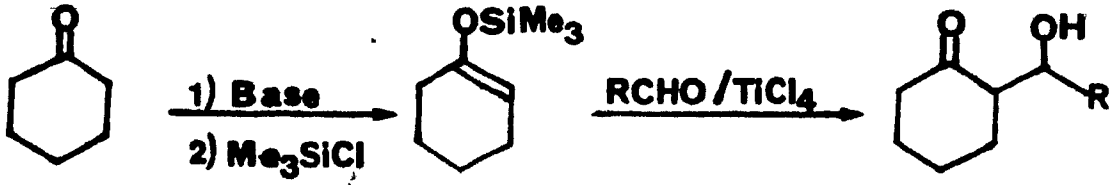
ii = CH_3OH .

b) i = t-Bu$(CH_3)_2SiCl$, DMF/imidazole

ii = n-Bu_4NF

R' = t-Bu-

Scheme 1.1



Scheme 1.2

From another point of view, silanes are used as reducing reagents[27] for carbonyl compounds, unsaturated molecules, halogenated derivatives, etc. Recently, introduction of a carbon-silicon bond as a convertible functional group into a complex molecule has received considerable attention. Organosilicon compounds are then used as versatile intermediates in synthetic routes to natural products[28]. Their prevalent utility is well understood based on the following principles.

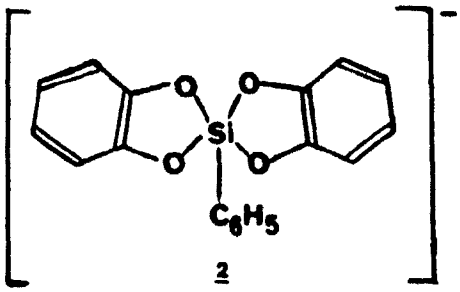
2 - Structural properties of silicon compounds

Silicon mostly forms tetravalent bonds in tetrahedral structure. This fact reveals the similarity of silicon with carbon. Both belong to the Group IV elements. Silicon is in the second row in the periodic table. Its valence shell electronic configuration is $3s^2 3p^2 3d^0$ and differing from carbon in its possession of vacant d-orbitals.

Electronic configuration: C He $2s^2 2p^2$

Si Ne $3s^2 3p^2 3d^0$

Silicon has the ability to utilize the 3 d-orbitals in the formation of penta- or hexacovalent compounds as illustrated by the example K_2SiF_6. In a number of cases, penta-[29] or hexacoordination[30] with oxygen are also known (2 and 3).



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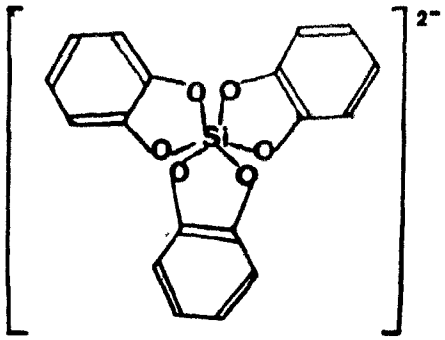

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3 - Silicon-carbon bond polarization

The reactivity of organometallic[31,32] compounds varies with the ionic character of the carbon-metal bond. For example, organopotassium, lithium and magnesium have, respectively, 51, 43 and 35% ionic character according to the Pauling electronegativity scale (Table 1.1). These compounds are known to be highly reactive compared to alkylsilanes in which the C-Si bond has only 12% ionic character. This makes organosilicon compounds more stable than other organometallic reagents. The observed polarizability is reflected on the C-Si bond length. Silicon and carbon atoms have radii of 1.17 Å and 0.77 Å respectively, thus the calculated length of a covalent bond is 1.94 Å which differs slightly from the measured value of 1.88 Å. This small

difference is considered to be due to the disparity between the electronegativities.

Table 1.1

Percentage ionic character of carbon-metal according to Pauling electronegativities

Metal	K	Na	Li	Mg	Zn	Cd	Si	H
Ionic character	51	47	43	35	18	15	12	4

In all respects, the chemical behavior of organosilicon compounds is associated with a greater atomic volume, a lower electronegativity (Table 1.2), and more polarizable bonds of silicon compared to carbon. Owing to the carbon-silicon bond polarization, it is cleaved by oxygen anion, fluoride or chloride ions with nucleophilic attack on the silicon[34]. The bond formed is usually stronger than that which is broken[36,37] (Table 1.3).

Table 1.2

Electronegativities*

Element	Electronegativity
Silicon	1.8
Hydrogen	2.1
Carbon	2.5
Oxygen	3.5
Phosphorus	2.3
Nitrogen	3.0
Sulfur	2.3
Chlorine	3.0

* L. Pauling, "The Nature of Chemical Bonds", Cornell University Press, Ithaca, N.Y. 1948.

4 - Silicon stabilizes an adjacent carbon-metal bond

In spite of the fact that silicon is more electropositive than hydrogen and carbon, silicon stabilizes the carbon-metal bond at the C-1 center, as do phosphorus and sulfur. One of the easiest ways of preparing α-silyl carbanion is the reaction of α-halosilanes with magnesium, sodium or lithium[38-40]. The rate constant[41] of C-Cl bond dissociation in halogen-metal exchange of silyl substituted methylene chloride with sodium is found to be higher than that of the corresponding organohalide compound (Table 1.4).

Table 1.3

Relative bond strengths[35]: Approximate bond dissociation energies (D) and bond lengths (r) for Si-X

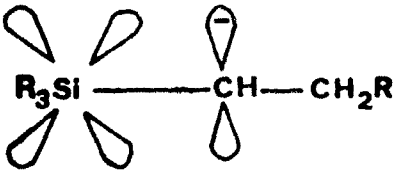
Bond	Compound	D/KJ mol^{-1}	r/nm	Bond	D/KJ mol^{-1}	r/nm
Si-C	Me_4Si	318	0.189	C-C	334	0.153
Si-H	Me_3SiH	339		C-H	420	0.109
	Cl_3SiH	378,382				
	D_3SiH		0.148			
Si-O	Me_3SiOMe	531		C-O	340	0.141
	$(Me_3Si)_2O$	812				
	$(H_3Si)_2O$		0.163			
Si-S	$(H_3Si)_2S$ Ca	293	0.214	C-S	313	0.180
Si-N	$(Me_3Si)_2NH$	320(E)		C-N	335	0.147
	$(H_3Si)_3N$		0.174			
Si-F	Me_3SiF	807		C-F	452	0.139
	H_3SiF		0.16			
Si-Cl	Me_3SiCl	471		C-Cl	335	0.178
	H_3SiCl		0.205			
Si-Br	Me_3SiBr	403		C-Br	268	0.194
	H_3SiBr		0.221			
Si-I	Me_3SiI	322		C-I	213	0.214
	H_3SiI		0.244			

Table 1.4

Rate constants of chloride-sodium exchange

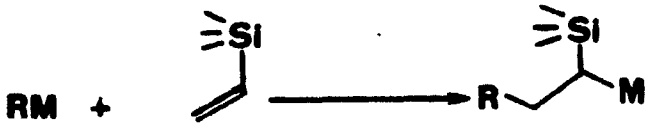
α-halosilanes	$k = 10^{11}$ mL mol^{-1} sec^{-1} 520 K
Me_3SiCH_2Cl	16.2
$(Me_3Si)_2CHCl$	230
Me_3CCH_2Cl	1.06

A convincing argument to justify the α-carbon-metal stabilization is the energy lowering overlap of the empty d-orbital with the occupied p-orbitals as shown below.

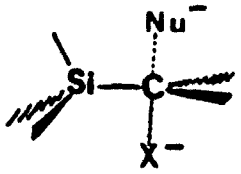


(d-p) π overlapping

The demonstration of this stabilization is provided in organolithium reaction with vinylsilane. The addition occurs regioselectively at the C-2 center to generate the α-silyl carbanion.



α-Silyl carbanion chemistry has recently found many interesting applications in organic synthesis, and various methods to prepare the reagent are provided[42-47]. Another manifestation of this phenomenon is in the high rate of bimolecular nucleophilic substitution reactions at the carbon adjacent to the silyl group (Scheme 1.3).



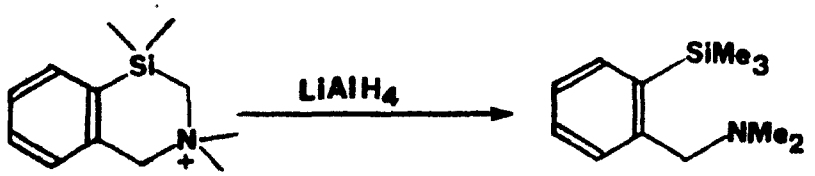
Scheme 1.3

Trimethylsilylmethyl chloride reacts 16 times faster than n-butyl chloride in the halogens exchange process[48].

$$Me_3SiCH_2Cl \xrightarrow{I^-/Me_2CO} Me_3SiCH_2I \quad \text{(eq.1)}$$

$$n\text{-BuCl} \xrightarrow{I^-/Me_2CO} n\text{-BuI} \quad \text{(eq.2)}$$

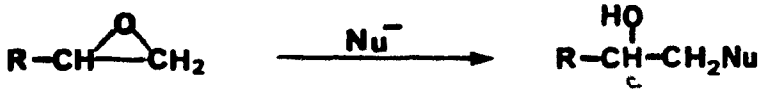
More interestingly the aluminum hydride reduction of compound[49] 4 occurs regioselectively with cleavage of the bond next to the silicon as illustrated in eq. 3.

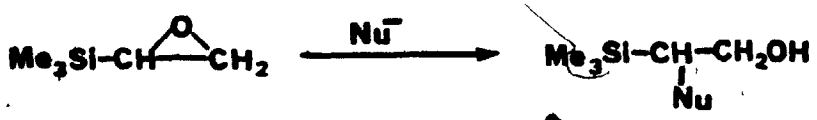


(eq.3)

4 5

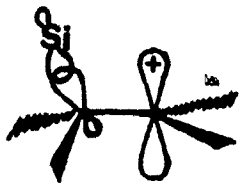
Similarly, α-silylepoxides[50,51] are opened mostly by nucleophilic addition at the α-position contrasting with the regioselectivity usually observed when a silyl group is not involved.





5 - β-Effect

The higher electropositivity of silicon relative to carbon results in increasing the electron density around the carbon in the C-Si bond. Therefore, a β-carbonium ion is more stabilized. In other words, the C-Si bond may better stabilize a positive charge at the β-position than the carbon-carbon, or hydrogen-carbon bond does. Conceptually this is depicted in the covalent C-Si bond overlapping with the empty p-orbital, called hyperconjugation, which may lower the energy of the system (Scheme 1.4).



(σ-p) ⇌ Hyperconjugation

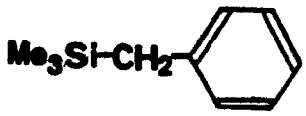
Scheme 1.4

The following observations support this statement: 1-chloro-2-trimethylsilylethane solvolysis is remarkably faster than that of t-butyl chloride[52]. On the other hand, the protodesilylation of silylbenzene is faster relative to proton exchange in benzene[53].

$$Me_3SiCH_2CH_2Cl \xrightarrow{\text{solvolysis}} Me_3SiCH_2CH_2OH$$

$$Me_3CCl \xrightarrow{\text{solvolysis}} Me_3COH$$

Further evidence is provided by the σ^+p values calculated from reaction rates or by the charge transfer spectra with tetracyanoethene[54a-c]. The σ^+p value for the trimethylsilyl methyl group in 6 is between -0.56 and -0.66, which is more negative than that of the methyl group in 7. Thus the trimethylsilylmethyl group has a more significant electron donating effect than the methyl group.



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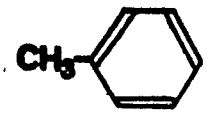

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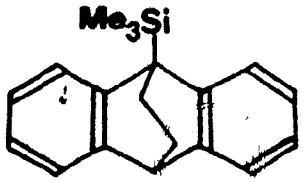
$\sigma + p$	-0.56 to -0.66	-0.31
λ_{max} (TCNE)	486 nm	411nm

From the silane 8 in which the Si-C bond cannot overlap with the π-orbitals of the benzene rings, the CT spectrum is similar to that of the unsubstituted compound 9.

This suggests that the effect is not inductive but depends essentially on (σ-p) π hyperconjugation.



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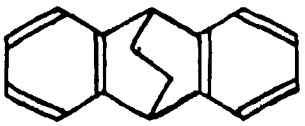


9

λ_{max} (TCNE) 424 nm

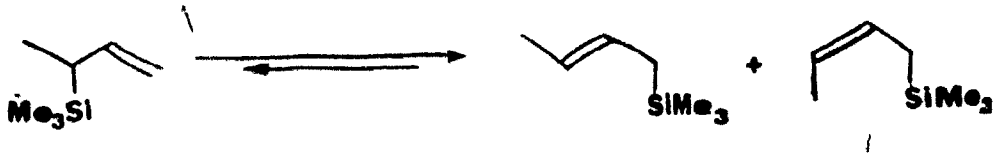
424 nm

CHAPTER II

ALLYLSILANES IN ELECTROPHILIC SUBSTITUTION REACTIONS

1 - General Considerations

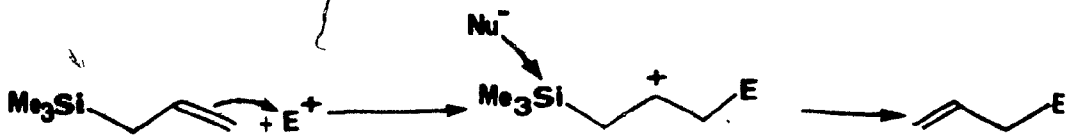
In the recent development of organosilicon chemistry, allylsilanes have been extensively employed as useful intermediates in synthesis for many reasons. As mentioned above, they are relatively stable compared to many other allylic metal compounds, even though they do undergo 1,3-sigmatropic rearrangement only at high temperature[55].



Allylsilanes are reasonably accessible by conventional synthetic methods[56-63]. The Si-C covalent bond overlapping with the π-bond orbitals raises the energy of the HOMO and hence makes the molecule more reactive to electrophiles.

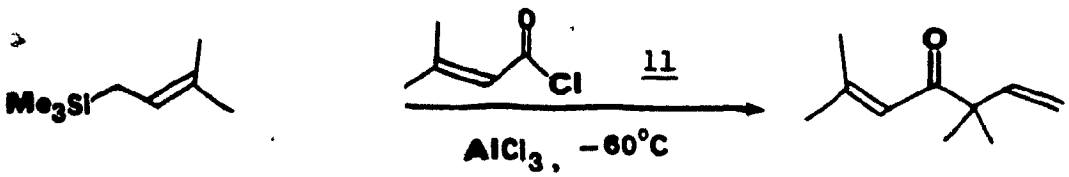
2 - Regioselectivity in Electrophilic Substitution of Allylsilanes

Electrophilic substitution of allylsilanes preferentially takes place at C-3 to induce positive charge formation at the β-position. This carbonium ion is accomodated by the (σ-p) π hyperconjugation. This is followed with nucleophilic attack on silicon resulting in the loss of the silyl group and shifting of the double bond.



Even though halogens[64] (bromine, iodine) or hydrochloric acid addition to allylsilanes occurs without the need of any activation, carbon electrophiles in most cases react in the presence of Lewis acids to form a carbon-carbon bond with a high degree of regioselectivity. Allylsilanes used in the electrophilic substitution reaction gave, normally, selectively, only one isomeric product whereas the corresponding allylic Grignard reagents may lead to a mixture of allylic products. For these reasons, various electrophiles, such as ketone, aldehyde, acyl chloride, enone, chlorosulfonyl isocyanate, tertiary alkyl halide, etc., have been used. The following representative examples clearly demonstrate the efficiency of this type of reaction in organic synthesis.

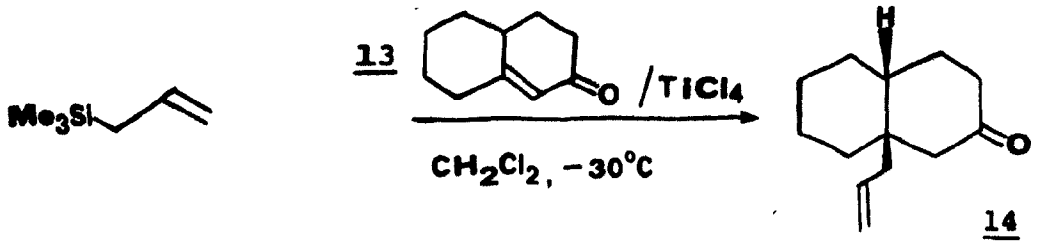
Artemisia ketone 12 is a natural product extracted from Artemisia annua L. or Santolina chamaecyparissus L. oils. It has very interesting organolectic properties and hence is used in the perfume industry. The initial synthesis[65] of this compound required many steps and the final product was obtained in poor yield. However, the allylsilane 3-methyl-1-trimethylsilyl but-2-ene (10) reacts with senicioyl chloride 11 under Friedel Crafts conditions (using $AlCl_3$) to provide Artemisia ketone[66] in 90% yield.



10 12

It is noteworthy that the electrophilic addition is directed exclusively to the more hindered position on the allylsilane moiety.

Introducing a functional group in a fused cyclic compound is in general a serious challenge in organic synthesis. In this respect, Sakurai[67] reported that alkylation of α,β-enone 13 with trimethylallylsilane in the presence of titanium tetrachloride was achieved stereoselectively to give the cis-compound 14.



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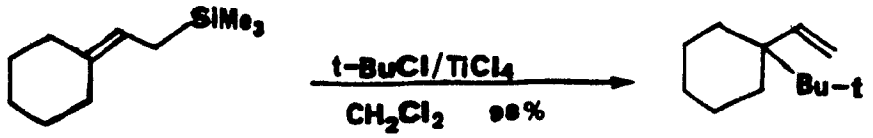
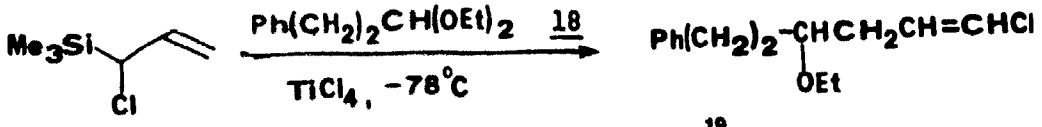
Fleming[68] also reported on the reaction of t-butyl chloride in a similar way. The regioselectivity and high yield of t-butyl alkylation of compound 15 are striking.



15 16

The α-halogen substituted allylsilane 17 could also react with aldehydes, ketones or ketals exclusively at the C-3 center to give predominantly the Z-vinylhalide[69] 19 which is often used in alkene synthesis via a Grignard reagent crosscoupling reaction.



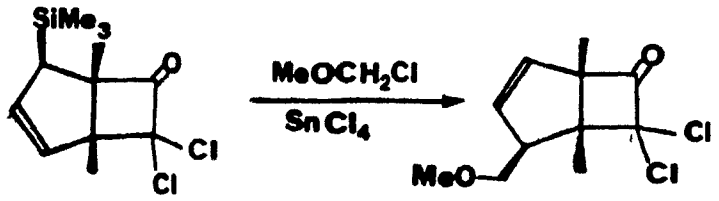
17 19

Z:E = 90 : 10

3 - Stereochemistry in SE' Reactions

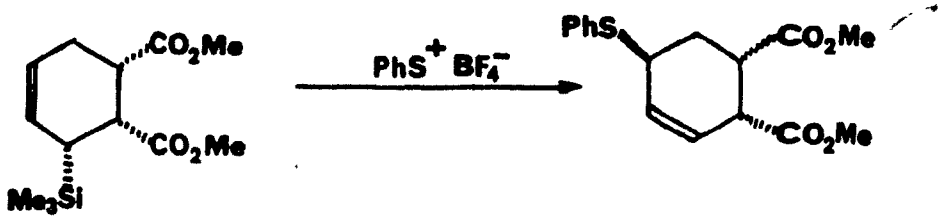
More recently, many investigations have focused on the stereochemistry in the allylsilane electrophilic substitution reaction. Since one or two chiral centers are created, it should be possible to control the enantio- or diastereoselectivity of the reaction. The selectivity depends on the structural constraints, the preferential conformation of the allylsilane or the electrophile. In few particular cases, syn addition has been observed. For example, in the fused

cyclic compound 20 the system is biased because of the concave shape of the [3, 2.0] cis rings. Consequently, the electrophile attacks only the exo-face resulting in retention of configuration[70].



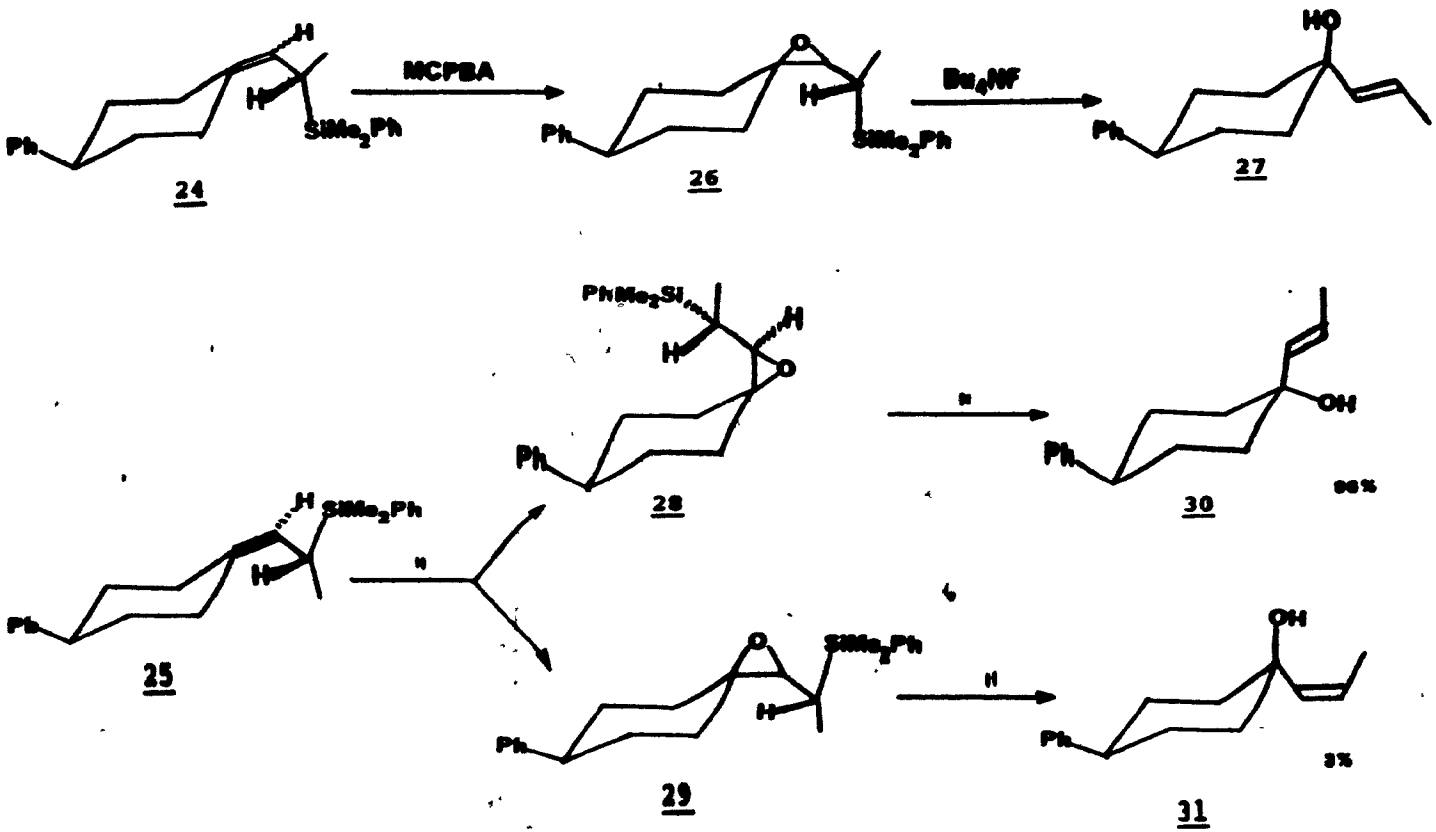
20 21

It is also comprehensible that the electrophile approaches the cyclohexenyl system[71] 22 by the less hindered face to give an anti addition product. The silyl group directing effect, if it exists, may not strongly influence the stereochemistry of the reaction.



22 23

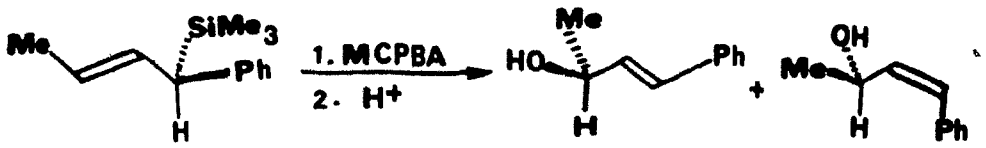
Recently, Fleming reported that the anti-addition is predominant in the epoxidation of chiral allylsilanes[72] 24



Scheme 2.1

and 25, even though there is some small axial preference of the electrophile with regard to the ring system (Scheme 2.1).

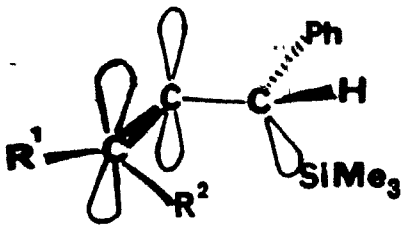
This confirms the result published earlier by Kumada. In an acyclic system, he found that by using the optically active allylsilane 32, the MCPBA enters the double bond anti with respect to the silyl leaving group and optically active allylic alcohol is obtained[73]. Addition of t-butyl chloride, acetyl chloride[74], aldehyde[75], or deuterodesilylation[76], all proceed by the same anti fashion consistently.



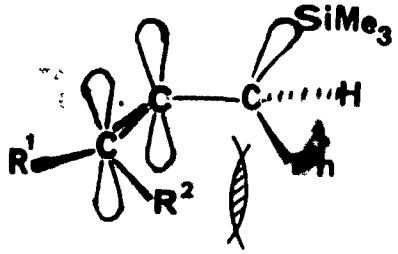
32 R(E) 33 81% 34 19%

An explanation for the stereochemistry is that the steric constraint induced by the phenyl group determines the approach of the electrophile to the double bond. Due to the Si—C bond overlapping with the π lobes of the C-C double bond, the allylsilane exists in two conformations, A and B (Scheme 2.2). Consequently, the electrophile will attack the allylsilane in the favorable conformation A by the side opposite to the trimethylsilyl group (anti).

To conclude, the anti stereochemistry should be considered to be the norm in electrophilic substitution reactions of allylsilanes. Exceptions to this principle occur when the molecule is biased.



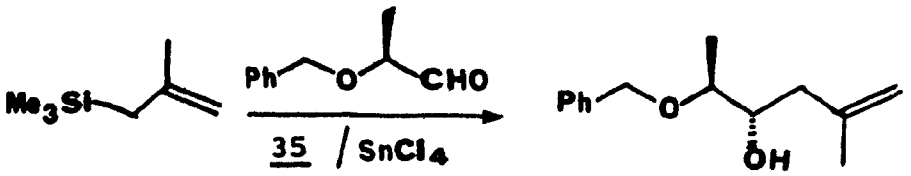
A



B

Scheme 2.2

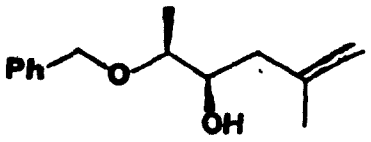
The enantio- or diastereoselectivity in allylsilane reactions with aldehydes and ketones is commonly based on the assumption that the reaction may proceed by a six-membered ring transition state. It is also possible to reach high control of stereochemistry in an acyclic mode when appropriate constraint is set. Recently, Heathcock used chiral aldehydes in the SE' reaction of allylsilanes. Aldehyde 35 and other analogous compounds were involved[77]. The diastereofacial selectivity varies with the substrate and the Lewis acid used. Particularly, the tin chloride mediated reaction of 35 with allylsilane 36 led to compounds 37 and 38 in the ratio of 45:1.



36

37

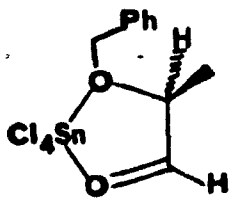
+



38

37 : 38 = 45 : 1.

The high diastereoselectivity observed is interpreted in terms of chelation of $SnCl_4$ by the α-alkoxy and the carbonyl oxygen to form a rigid five-membered ring 39. In this conformation the front side is hindered due to the methyl group, therefore the allylsilane will come from the back side to provide mainly compound 37.



39

39

Of several approaches to obtain optically active erythro or threo β-hydroxy carbonyl compounds, the enantioselective aldol type reaction[78-81] with many variations remains an efficient method to achieve high stereoselectivity, up to 90%, especially when chiral boron or zirconium enolates are used. It is now possible that the electrophilic substitution of allylsilanes or allyl stannanes[82-84] with carbonyl compounds will become a promising alternative for the coming years.

CHAPTER III

α-SILYLALLYL ANION CHEMISTRY

1 - Introduction: Heterosubstituted Allyl Carbanion Preparation - Stability and Reactivity

In general, substituted allylic systems, 40, can be easily metalated using an appropriate base to the corresponding allylic carbanions[85] 41.

40 41

X = $-SiR_3$, $-OR$, $-SR$, $-SO_2R$, $-NR_2$, $-SeR$, $-P(O)R_2$.

The success and the usefulness of this allylic carbanion in organic synthesis depend upon the stability and the regioselectivity of the carbanion[86]. Due to its ambivalent reactivity, it can react as a nucleophile at either the α- or the γ-position, giving a mixture of regioisomers which seriously affect the efficiency of the carbanion in synthesis. The regioselectivity could change significantly according to the heteroatom substituent, the counterion, the solvent and the electrophile used[87].

For instance, the carbanion 43 prepared from 42 in THF by n-butyllithium treatment was allowed to react with a number of electrophiles in the presence of different complexing agents: diazabicyclooctane (DABCO), N,N'-tetramethylethylene diamine (TMEDA), hexamethylphosphotriamide (HMPA) and macrobicyclic diamino polyether [2,2,2]. The results are presented in Table 3.1. When the reaction is run without any complexing agent (entries 5 and 9), the carbanion 43 exists as an ion pair. The lithium ion is closely associated with the α-carbon and only the α-alkylation product was obtained with alkyl halide electrophiles (methyl iodide), whereas carbonyl compounds predominantly gave the γ-product (entry 9). The regioselectivity in the alkylation reaction of 43 depends on the degree of dissociation between the carbanion and the counterion (Li). It also depends on the nature of the electrophile involved and the solvent (Table 3.1).

42 43

Table 3.1

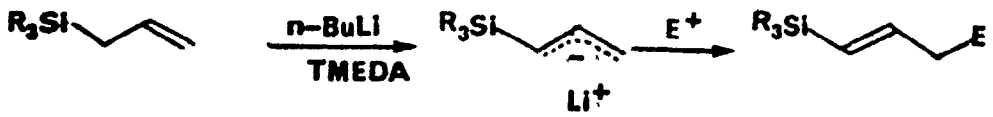
Regioselectivity in the alkylation of 43 with various electrophiles. Solvent effect.

Entry	Temp. °C	Complexing Agent	Reagent	Yield (%)	Proportion of reaction at the α-carbon	Proportion of reaction at the γ-carbon
1	-20	DABCO	MeI	100	99	1
2		DABCO		100	87	12
3		DABCO		100	94	6
4		DABCO		100	--	100
5	-78	none	MeI	100	95	--
6		HMPT	MeI	100	98	Trace
7		[2,2,2]	MeI	80	60	40
8		[2,2,2]		60	50	50
9		none		100	25	75
10		TMEDA	"	100	Trace	90
11		HMPA	"	100	40	60
12		[2,2,2]	"	60	100	0

2 - α-Trialkylsilylallyl Carbanions

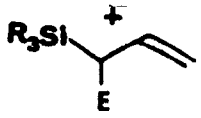
α-Silylallyl carbanions are prepared from allylsilanes by treatment with butyllithium in ether or tetrahydrofuran in the presence of TMEDA or HMPA at relatively low temperature. They are stabilized by allylic resonance and by (p-d)

bonding from Si 3d empty orbital overlapping with the filled p-lobe of the carbon anion. Their reaction with various electrophiles has been studied and a mixture of α and γ addition products could be obtained.



44 45 46

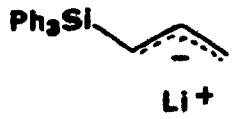
γ-product



47

α-product

The original work concerning the reactivity of α-trialkylsilylallyl carbanions toward electrophiles was first reported by Corriu[88] in 1975. Triphenylsilylallyl lithium 45d and the analogous Grignard reagent 48 were prepared. It was noticed that the lithium compound 45d preferred γ-addition whereas the magnesium compound 48 lead to the α-product in many cases.



45d

48

Table 3.2

Relative reactivity of 45d and 48 toward electrophiles

Electrophiles	45d α-attack (%)	45d γ-attack (%)	48 α-attack (%)	48 γ-attack (%)
H_3O^+	30-40	60-70	90	-
Ph_2CO	-	95	-	65
	40	60	90	10
CH_3I	-	100	No reaction at 20°C	

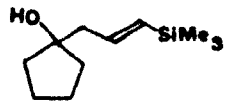
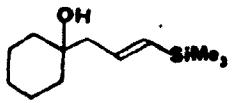
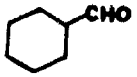
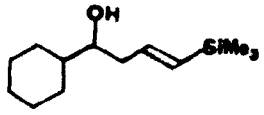
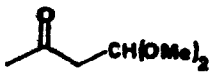
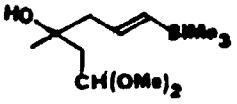
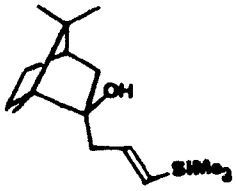
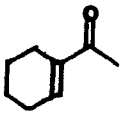
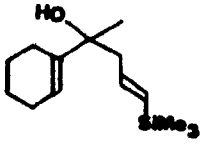
3 - Reaction of α-Silylallyl Anions with Carbonyl Electrophiles

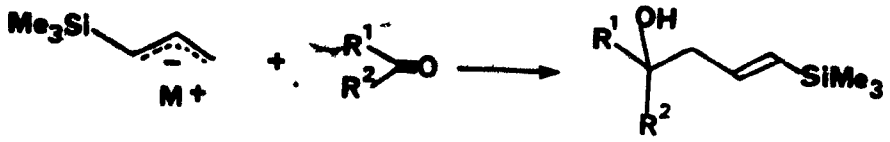
3.1 γ-Selectivity

Another comprehensive work was provided by Magnus[85]. The γ-product was obtained predominantly from the reaction of trimethylsilylallyl anion 45a with aldehydes and ketones. The geometry of the resultant vinylsilane double bond was trans in all cases.

Table 3.3

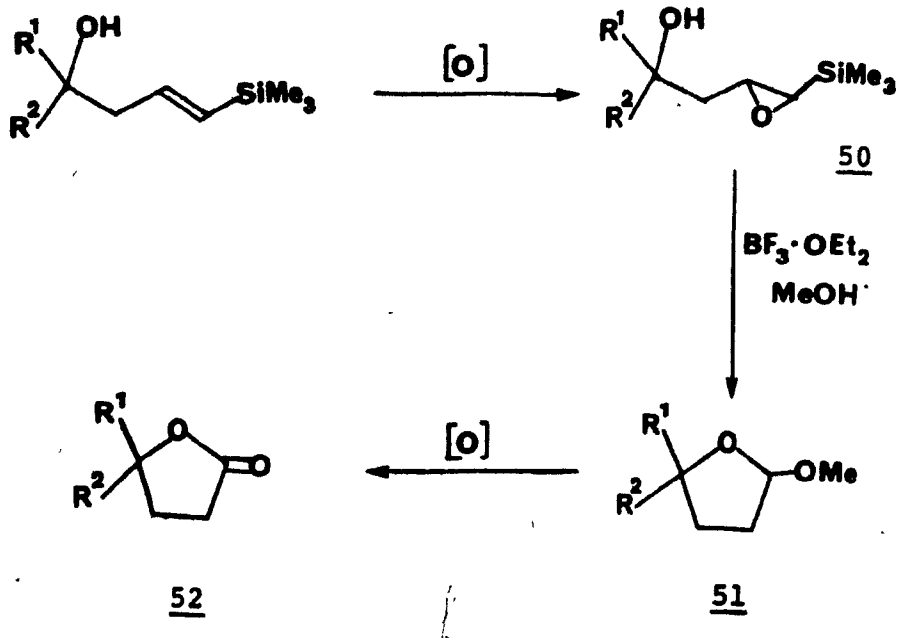
Trimethylsilylallyl anion 45a reaction with various carbonyl electrophiles[85]

Entry	Electrophiles	Equivalent of 45a	Temp. (°C)	Product	Yield (%)
1		2.6	-30		84
2		2.5	-30		88
3		2.0	-78		96
4		3.0 M=ZnCl	-20		66
5		6.5 M=ZnCl	0		89
6		1.5	-75 to-26		80



45a 49

The vinylsilane moiety 49 produced in the electrophilic addition reaction is considered to be a masked carbonyl compound. The carbonyl functional group could be easily regenerated by successive epoxidation and acid treatment to give γ-O-methyl lactol 51 or γ-lactone 52 as shown below.

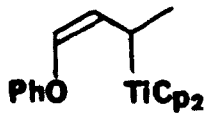
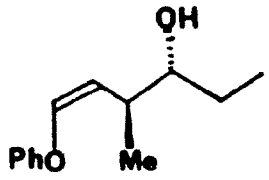
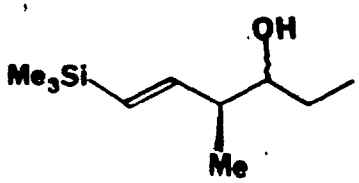
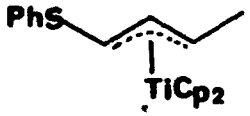
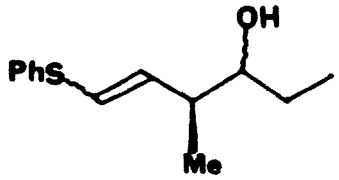


50 52 51

1,3-Disubstituted allyl carbanions were converted into η^3-allyltitanium compounds[89] 53, 54 and 55 under $(C_5H_5)_2TiCl$

Table 3.4

Regio- and stereoselective reaction of 1,3-disubstituted allyl anions with propanal via η^3-allyltitanium compounds

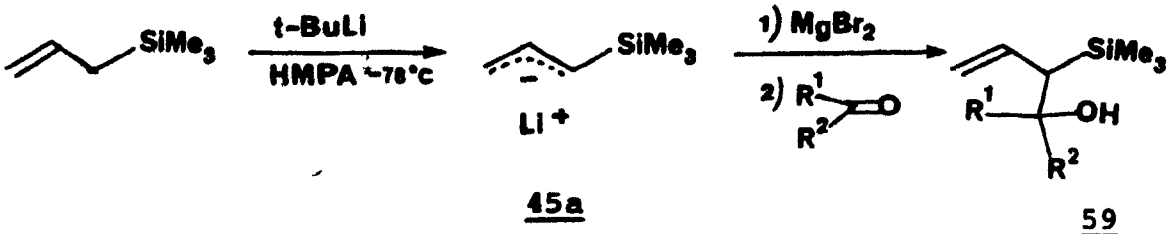
Entry	Allyl anion complex	Products	Stereoselectivity	Yield (%)
1	 53	 56	4R, Cis	88
2	 54	 57	4R:4S=86:14 trans	85
3	 55	 58	4R:4S=66:34 Cis/trans=1:1	93

treatment and reacted with propanol and the γ-addition product was obtained. It is remarkable that only the silyl allyl complex 54 provided the trans double bond geometry exclusively. Cis isomers were obtained with the phenoxy substituted compound 53, whereas 55 gave both stereoisomers in a ratio of 1:1. The reaction is highly diastereoselective giving rise to the threo product 57 (Table 3.4).

3.2 α-Selectivity

The ambivalent α-silylallyl anion reactivity with regard to electrophiles could vary by changing the counterions. Considerable efforts have been made to successfully direct the reaction to the α-position selectively. The first example in this series came from the work of Lau and Chan[90]. In 1978, they reported that trimethylsilylallyl anion 45a, prepared by the usual method, reacted with aldehydes and ketones at the α-carbon mainly when magnesium bromide was added to the reaction mixture.

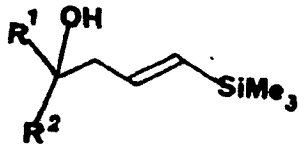
This precedent was followed with other examples. Strong Lewis acid salts or organometallic compounds have been used as additives. The regio- and stereoselectivity increased to give the threo derivative in most cases (Table 3.5). It seems that the metal-carbon covalent bond formation as shown in Scheme 3.1 (step 2) is crucial for such a control. For instance, when trimethylsilylallyl lithium



45a

59

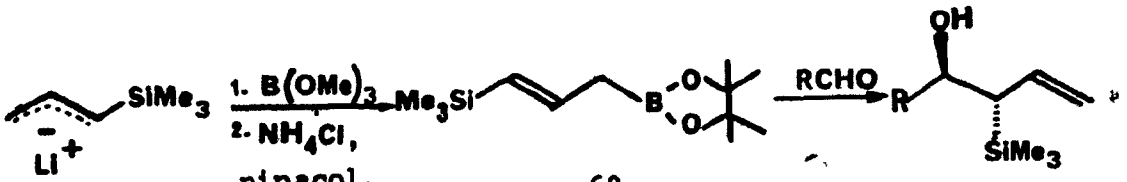
+



49

minor product.

solution was treated with trimethylborate and pinacol, the 3-boronate 60 could be isolated by distillation (b.p. 46-50°C/0.15 torr). The geometry was trans at the double bond. Subsequent reaction of 60 with aldehyde gave the threo (R,S)-3-trimethylsilyl-4-hydroxy-1-alkene[91] 59.



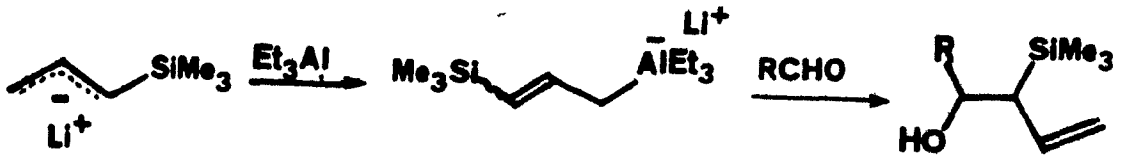
60

59

Step 2

Scheme 3.1

Using the same approach, the aluminum "ate" complex[92] 61, formed in situ, reacts with aldehydes or ketones at the α-position.



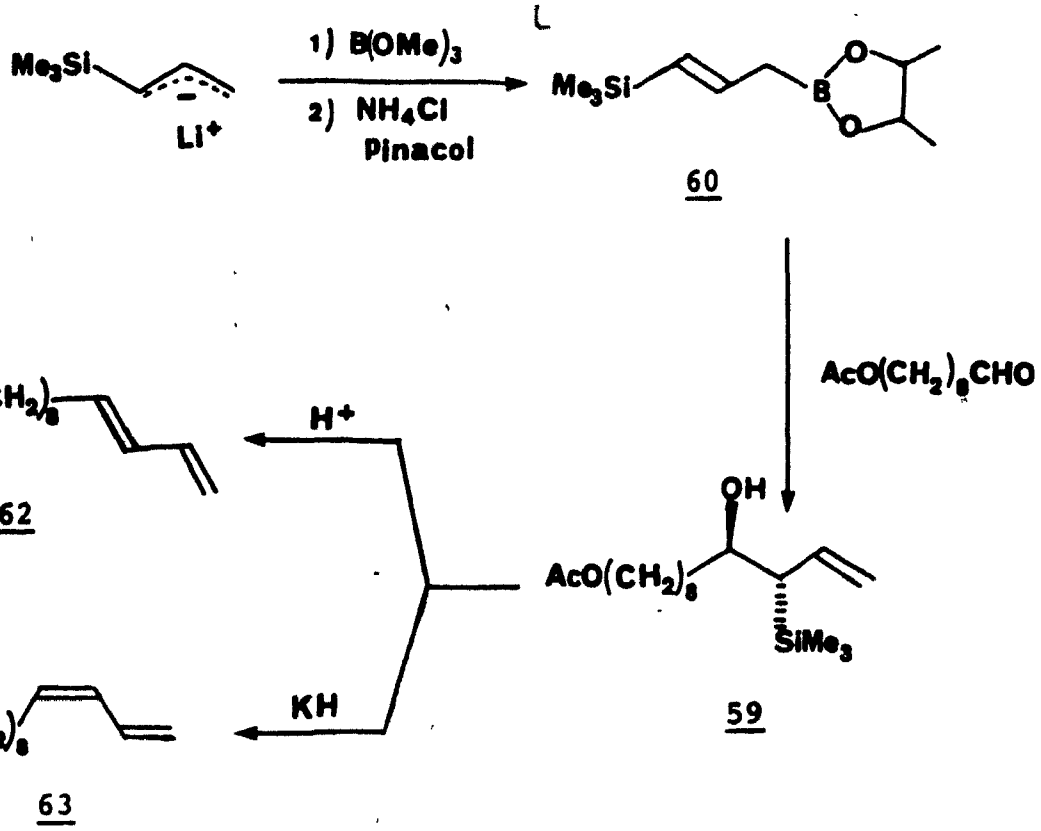
61 59

Table 3.5

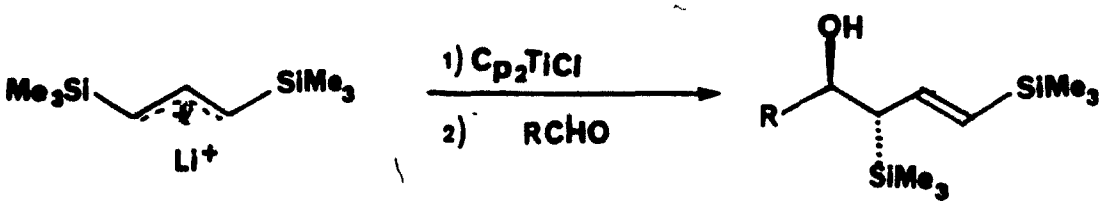
Regio- and stereoselectivity in the reaction of trimethylsilylallyl "ate" complexes with aldehydes

Entry	Aldehydes	Additives	α-Products Threo	α-Products Erythro	γ-Products (Ref.)
1	CH_3CH_2CHO	Et_3Al	94	--	6 (92)
2	$ACO(CH_2)_8CHO$	$B(OCH_3)_3$	79	--	- (91)
3	t-BuCHO	Cp_2TiCl	98	--	- (93)
4	$Br(CH_2)_4CHO$	Cp_2TiCl	92	--	- (93)
5	$CH_3(CH_2)_8CHO$	$Bu_3SnCl-BF_3$	--	100	- (94)
6	Me_2CHCHO	Cp_2BCl	100	--	- (94)
7	$CH_3CH=CHCHO$	$EtAlCl_2$	86	14	- (94)

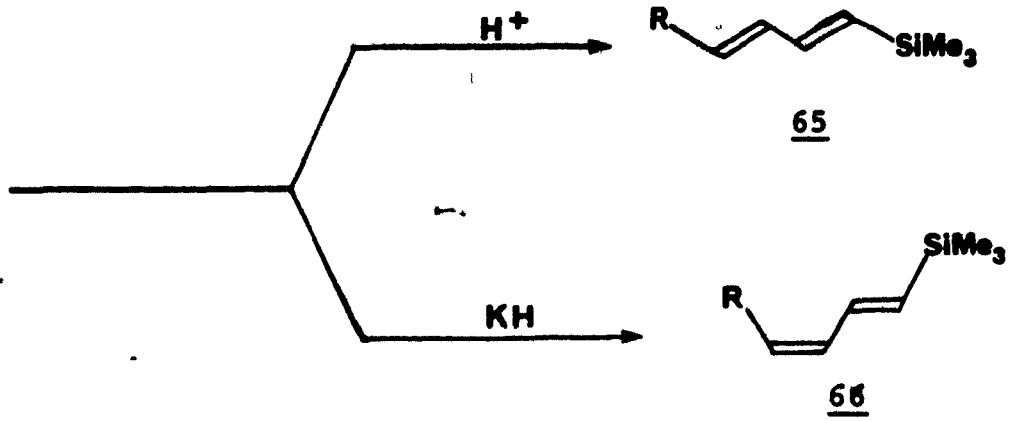
As a convenient alternative to the Wittig reaction, the β-hydroxyvinylsilane 59 obtained from the α-silylallyl carbanion reaction with carbonyl electrophile can undergo a Peterson olefination process to give 1,3-diene in a stereospecific manner. This methodology has been applied to the synthesis of bollworm moth (Dioparopsis castenea) sex pheromone[91] 62.



The same procedure is also used to prepare 1-trimethylsilyl-4-alkyl butadienes in a stereocontrolled manner. 1,3-Bis(trimethylsilyl)propenyl carbanion 64 reacts with the aldehyde to give the threo compound 59 which can eliminate to 65 and 66 stereoselectively[95].



64 59



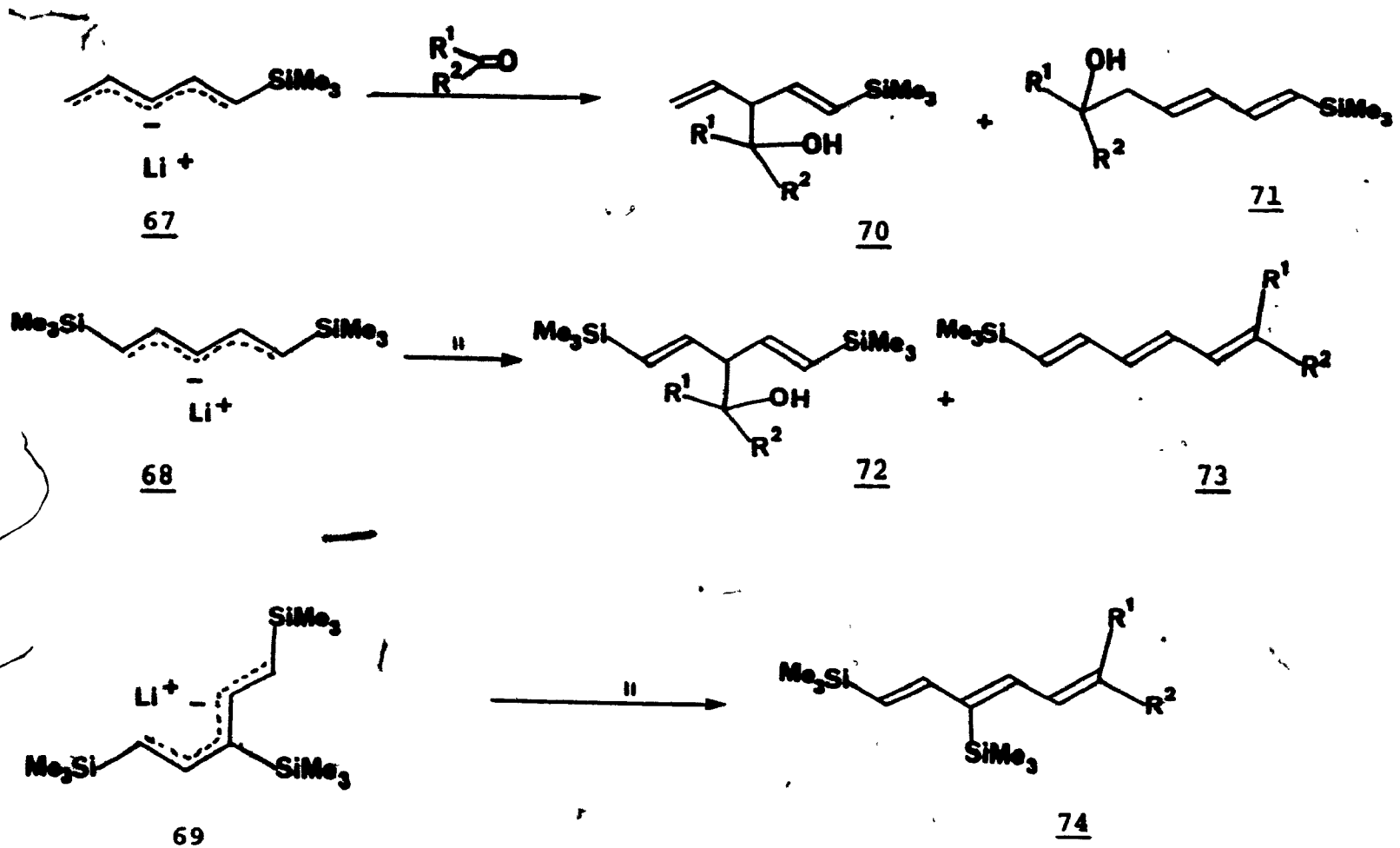
65 66

4 - Pentadienylation of Carbonyl Compounds

More recently, pentadiethylation of carbonyl compounds using [1,5-bis(trimethylsilyl)pentadienyl] lithium 67 and other analogous reagents (68, 69) has been investigated[96]. Although the regioselectivity is not satisfactory in all cases, the reaction is conceptually useful in organic synthesis for elongation of carbon chains. It is also potentially applicable to the synthesis of polyunsaturated molecules such as insect sex pheromones or leucotrienes.

The regioselectivity in the reaction of mono- and disilylated pentadienyl anions 67 and 68 varies, depending

on the bulkiness of the carbonyl group. It is however interesting to see that whatever the electrophile size, compound 69 reacts only at its terminal carbon. A single isomer of triene 74 with E,E configuration is obtained after elimination of the siloxy moiety.

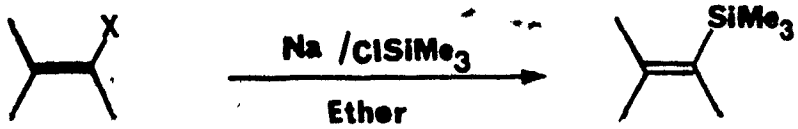

SiMe3
Li+
R1
R2
O
OH
Me3Si
67
70
71
68
72
73
69
74

CHAPTER IV

GENERAL METHODS FOR VINYLSILANE SYNTHESIS

There any many methods to prepare substituted or functionalized vinylsilanes in a stereoselective manner[32]. It is not our goal to undertake a detailed retrospection on alkenylsilane synthesis in this chapter. Appropriate reviews and books are available for that purpose. However, some aspects should be discussed according to the efficiency of the method and the role played by silicon in the stereochemical control. More attention will be paid to the recent developments in this area.

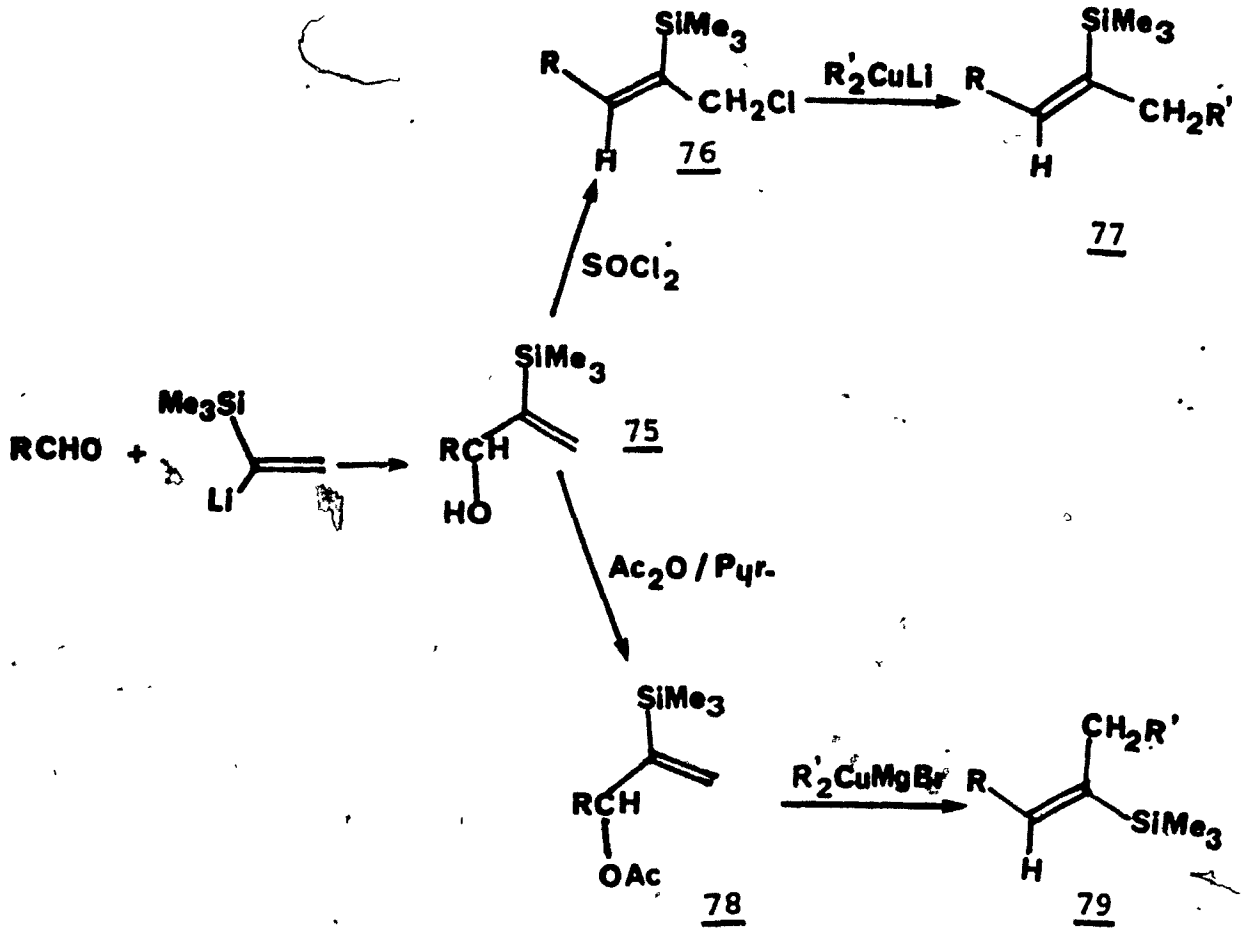
The classical Wurtz type silylation reaction[97,98] usually proceeds in a stereospecific manner with retention of configuration (Scheme 4.1). However, it is useful only when the vinyl halide is provided in a pure isomeric form.



Scheme 4.1

The α-silylvinyl anion reaction with aldehydes[45,99] is also a convenient method to prepare disubstituted vinylsi-

lanes. The overall transformation is depicted in Scheme 4.2.

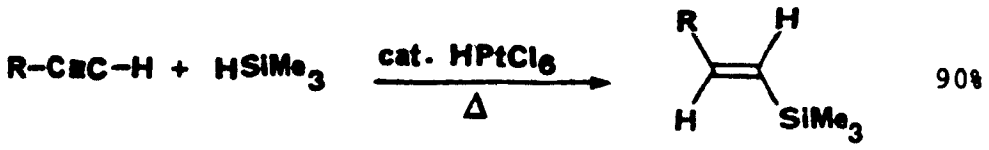


Scheme 4.2

Under thionylchloride treatment, the alcohol 75 is converted into the chlorocompound 76. The allylic rearrangement is assisted by the silicon to give stereoselectively the Z-isomer. No isomerization occurs in the subsequent organocopper lithium coupling reaction. Silicon may also play a critical role in the conversion of 78 into 79.

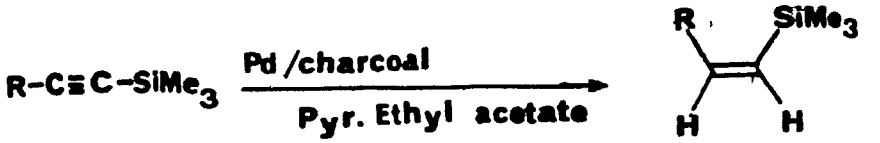
The synthesis of vinylsilanes from acetylenic precursors is the preferred method. This route offers the advantage that either the Z- or E-isomers can be obtained stereoselectively.

Catalytic hydrosilylation[100] of terminal acetylenes undergoes syn-addition to give the trans compound 80 in good yield.



80

The Z-stereoisomer could be obtained by semi-hydrogenation of the silylacetylenic compound 81.



81

82

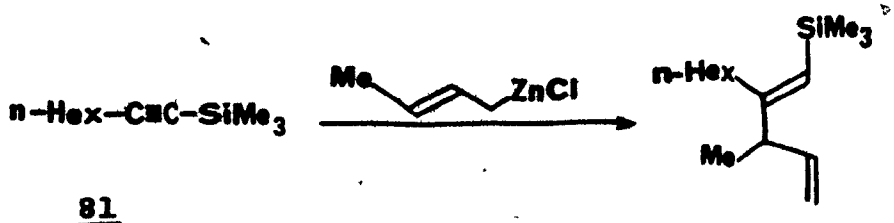
When hydroboration[103], hydroalumination[101,102] or carbometallation of acetylenic precursors is employed, the

addition of the metal hydride or the organometallic compound always proceeds by syn-addition to the triple bond. However, isomerization of the alkenylmetal intermediate could occur depending on the solvent system used. It is stabilized when ether or tertiary amine is added to the reaction mixture. In less polar solvents, it isomerizes to the thermodynamically more stable compound (Scheme 4.3).

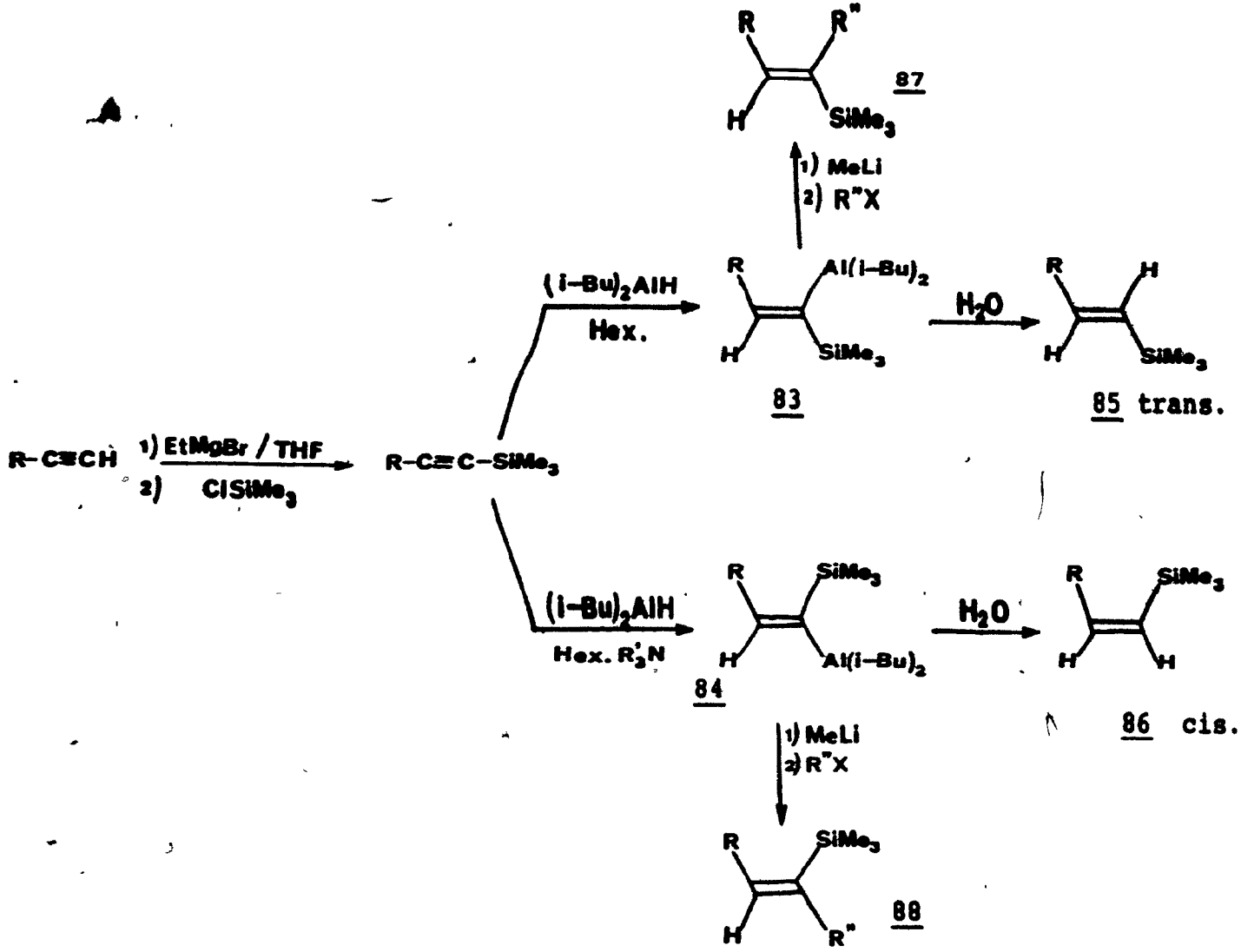
Hydrolysis of 83 and 84 gave the trans and cis vinylsilanes, respectively. Treatment with methyllithium and alkylhalide (R"X) may provide 1,2-disubstituted vinylsilanes 87 and 88.

Similarly, the carbocupration[104,105] of the silylacetylene 89 could be used to prepare α-functionalized vinylsilanes by addition of various electrophiles to the alkenyl copper compound 90.

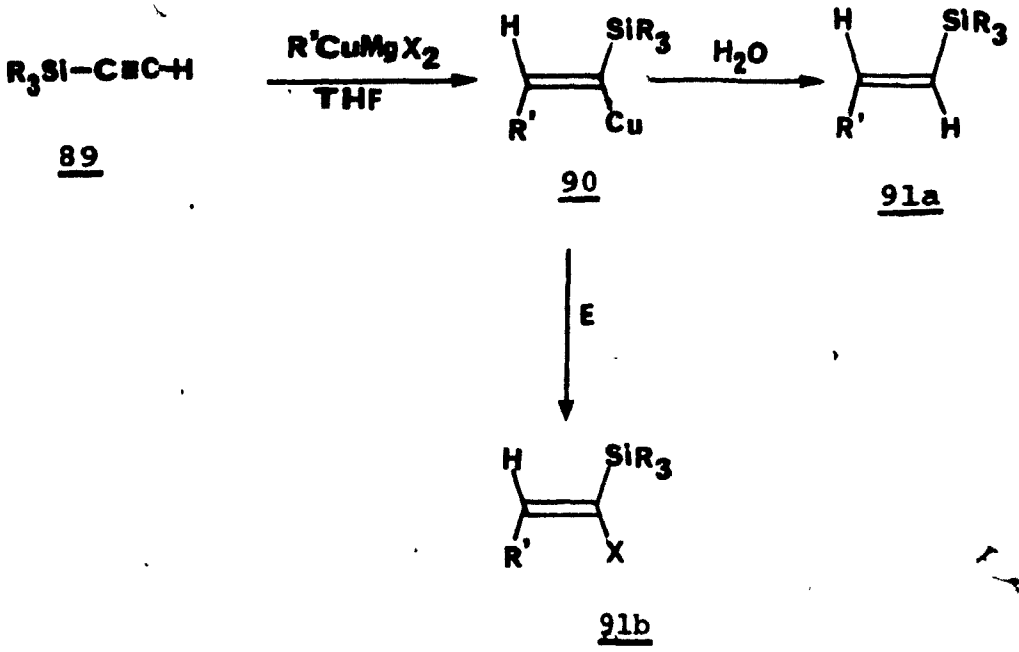
It is interesting to note that the opposite regioselectivity[106] occurs in the (E)-crotylzinc compound reaction with the acetylenic precursor 81 (R = n-C_6H_{13}).



81 92


R-C≡CH
1) EtMgBr / THF
2) ClSiMe3
R-C≡C-SiMe3
(i-Bu)2AlH
Hex.
(i-Bu)2AlH
Hex. R'3N
H2O
H2O
1) MeLi
2) R"X
1) MeLi
2) R"X
83
84
85 trans.
86 cis.
87
88

Scheme 4.3



89 90 91a 91b

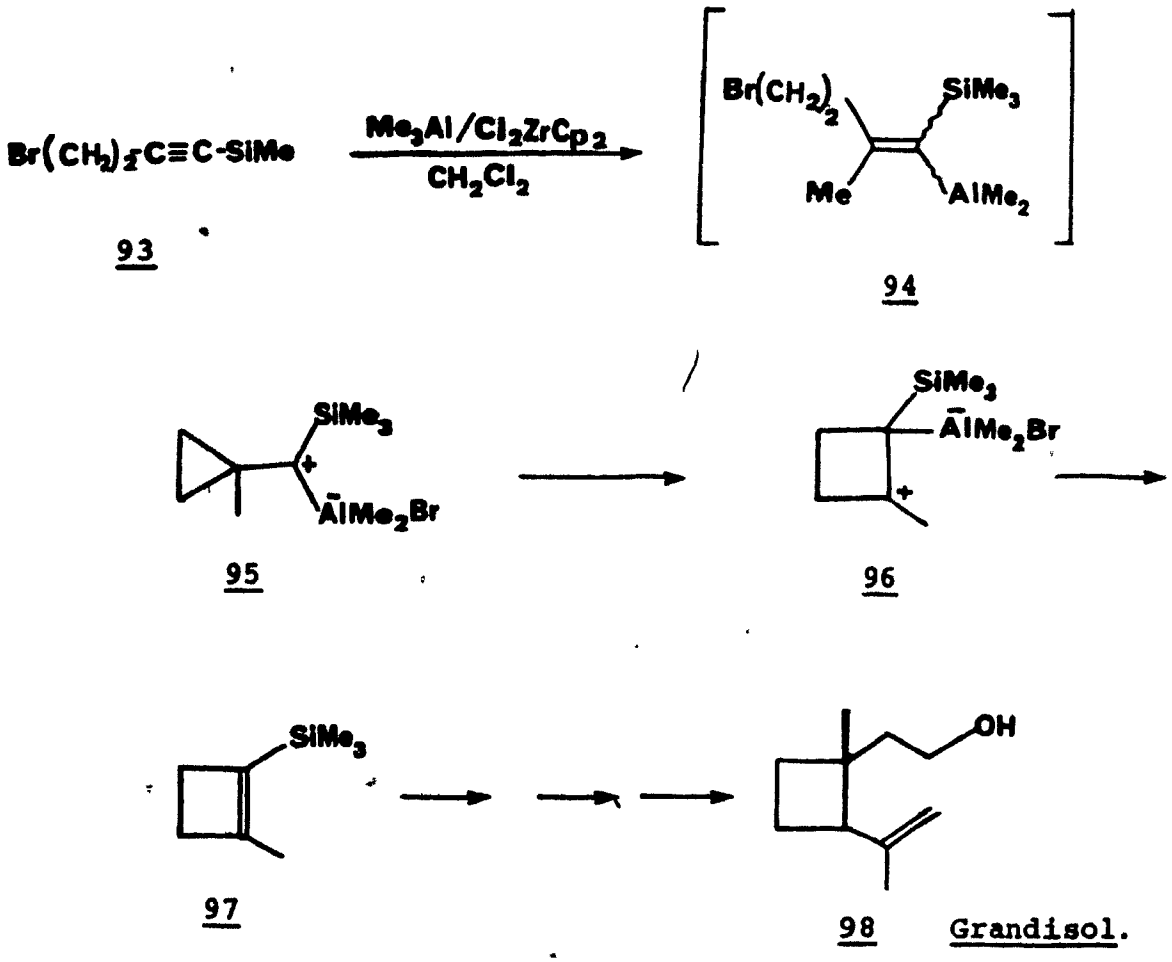
E = I_2, NCS, NBS, MeI

X = I, Cl, Br, Me.

In the recent development of the carbometallation reaction, cyclic vinylsilanes are prepared from acyclic starting compounds, especially when the silylalkyne contains a ω-functional group.

The most striking example is found in the Zr-catalyzed carboalumination reaction[107] of 1-(trimethylsilyl)-4-bromo-1-butyne 93. The cyclobutenylsilane 97 was obtained in 92%

yield. Surprisingly, the protonolysis of 94 does not give the expected 2,2-disubstituted vinylsilane. From the mechanistic aspect, it has been postulated that compound 94 is converted into 95 which rearranges to produce the intermediate 96 (Scheme 4.4).

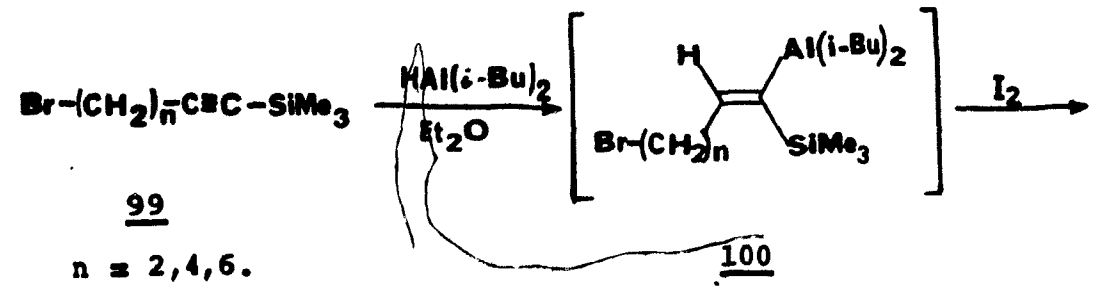


Scheme 4.4

This process may involve interaction between the π-orbital and the C-Br bond in an S_N2 type displacement of the

bromide ion. The preferred elimination of the aluminum moiety to give cyclobutenylsilane 97 is an unexpected precedent in organosilicon chemistry.

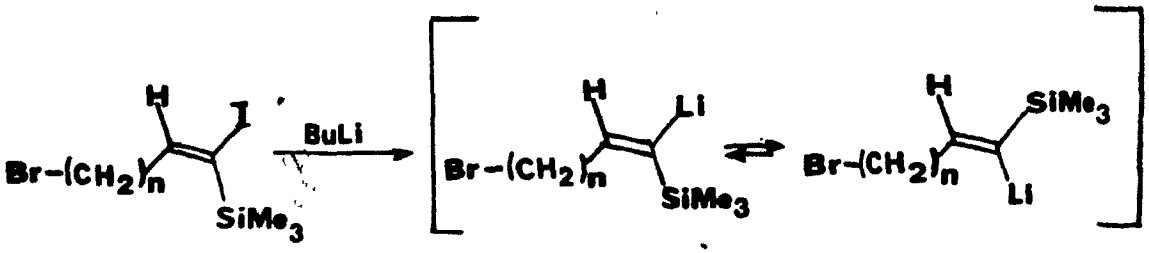
Alternatively, and in a more general approach, the functionalized alkenylmetal 100, prepared by hydroalumination of 99, is quenched with iodine to produce 101 which cyclizes under butyllithium treatment[90] in ether.



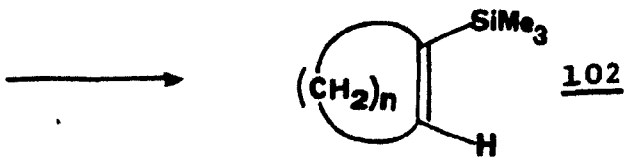
99

n = 2,4,6.

100



101



102

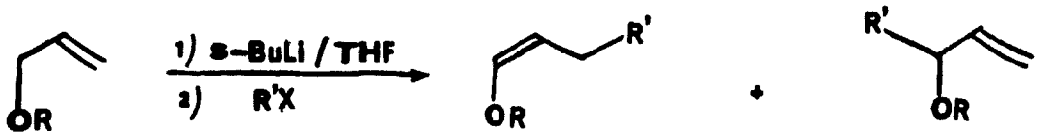
The silicon may play a critical role in promoting this cyclization as well. For instance (E)-1-iodo-6-bromo-1-hexene does not produce cyclohexene upon treatment with 2 equivalents of t-butyllithium.

CHAPTER V

OUTLINE OF THE PRESENT WORK

From the preceding account of α-silylallyl anion reaction with carbonyl electrophiles, successful control of regiochemistry was achieved by changing the nature of the counterion in the allylic anion systems. Therefore, δ-hydroxyvinylsilane and β-hydroxyvinylsilane compounds were prepared with appropriate stereochemistry in some instances. The usefulness of these compounds in organic synthesis has also been demonstrated.

Surprisingly, less attention has been paid to alkyl halide addition to the α-silylallyl carbanions. The analogous alkylation of allyloxy carbanions[108,109] gave rise to a mixture of both regioisomeric products. The geometry is exclusively cis at the double bond in the predominant γ-addition product (Table 5.1, Scheme 5.1).



Scheme 5.1

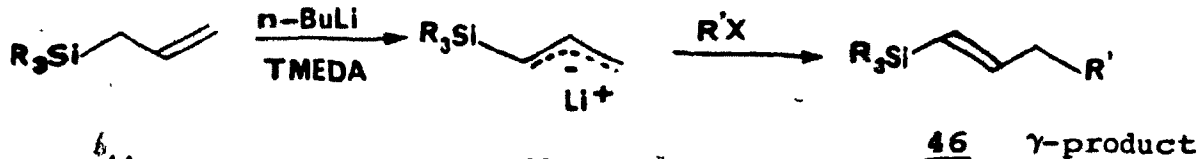
With regard to the α-silylallyl anion alkylation reaction, the original work provided by Corriu[88] in this area lacks sufficient detail. Reaction of triphenylsilylallyl lithium with methyl iodide was reported, in which only the

Table 5.1

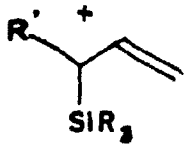
Allyloxy carbanion alkylation with alkylhalide electrophiles

Entry	R	R'X	γ-Product (%)	α-Product (%)	Overall Yield (%) (Isol.'d)
1	$Si(C_2H_5)_3$	CH_3I	97	3	> 95
2	$Si(C_2H_5)_3$	$n\text{-}C_3H_7I$	84	16	> 95
3	$Si(C_2H_5)_3$	Cyclohexyl-I	39	61	80
4	$Si(C_2H_5)_3$	$n\text{-}C_3H_7Br$	75	25	> 95
5	$Si(C_2H_5)_3$	Allyl-Br	68	32	> 95
6	t-Bu	$n\text{-}C_6H_{13}I$	89	11	85
7	C_2H_5	$n\text{-}C_6H_{13}I$	90	11	79
8	C_2H_5	$(CH_3)_2C{=}CHCH_2Br$	63	37	26

γ-addition compound was obtained. It is not clear whether such regioselectivity is general with respect to other alkyl halides.



44 45 46 γ-product



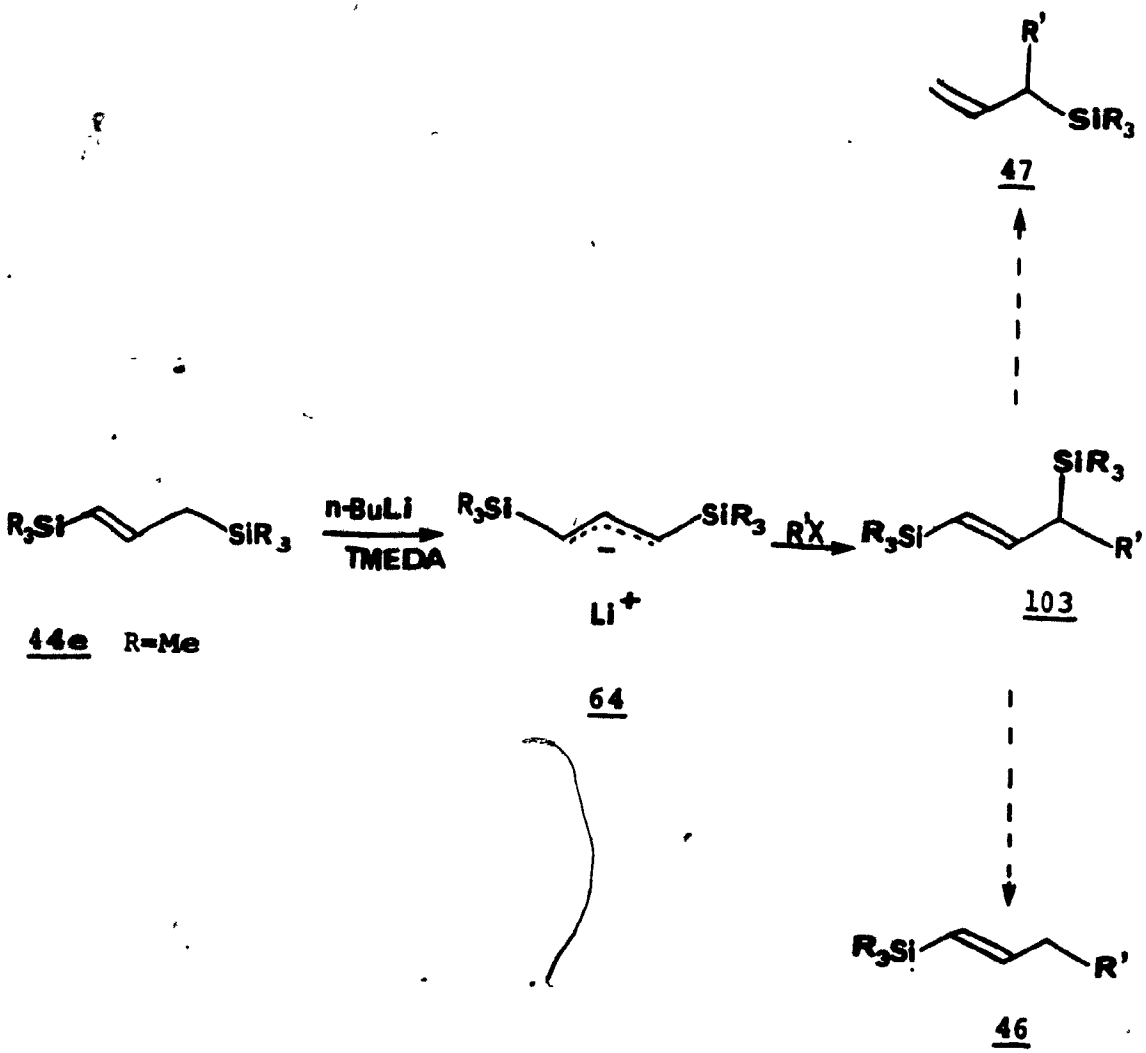
47 α-product.

The expected trans stereochemistry in compound 46 is acknowledged to be inherent to silicon in the heterosubstituted allylic carbanion reaction with electrophiles. This approach could be useful in the synthesis of E-vinylsilanes or α-substituted allylsilanes (type 48) if we assumed that the alkylation could occur selectively at either the C-3 center or the C-1 position of the silylallyl anion species.

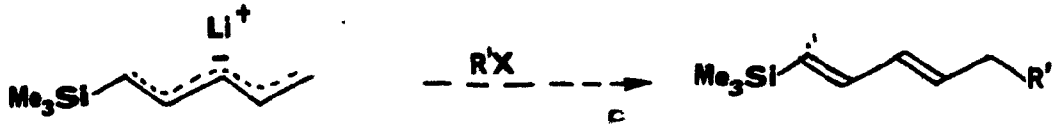
Another approach to overcome the regioselectivity problem is to use the 1,3-bis(trimethylsilyl)propenyl lithium reagent which would give a single isomeric product in the alkylation step due to its symmetrical nature (Scheme 5.2).

Compound 103 is a potentially versatile synthon in organic synthesis with respect to both the vinyl- and the allylsilyl functions. A specific desilylation reaction on the intermediate 103 should lead to compounds 46 or 47.

Another extension to this methodology would be the pentadienylation of alkyl halides according to Scheme 5.3. The question is whether the reaction could be regioselective by analogy to the carbonyl electrophile reactions mentioned in Chapter III, paragraph 4.


R'
SiR3
47
R3Si
SiR3
n-BuLi
TMEDA
R3Si
SiR3
R'X
R3Si
SiR3
R'
103
44e R=Me
Li+
64
R3Si
R'
46

Scheme 5.2



67 104

Scheme 5.3

The present research project is therefore to study the regioselectivity of the alkylation reaction of the silylallyl anion. The prospect of applying such methodology to the synthesis of natural products, especially the insect sex pheromones, will be explored.

CHAPTER VI

INVESTIGATIONS ON THE ALKYLATION OF TRIALKYLSILYLALLYL CARBANIONS WITH ALKYL HALIDES

1 - Starting Compounds

The required allylsilanes and alkyl halides are prepared by appropriate methods as described below.

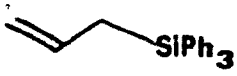
1.1 Allylsilanes

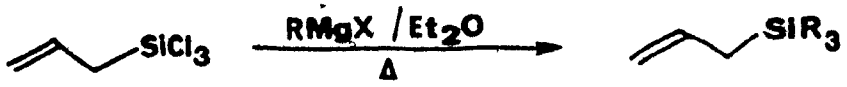
The reaction of allylmagnesium halides with silyl halides (R_3SiX, X = chloride) has been commonly used to produce allylsilanes in acceptable yields[66]. However, its usefulness is somewhat limited by the lack of selectivity when substituted allylic Grignard reagents are employed. In connection with our work, this method has been found to give satisfactory results. Thus triphenyl or diphenylmethylchlorosilanes were reacted with allylmagnesium bromide giving good yields of the corresponding allylsilanes (Table 6.1).

Alternatively, the commercially available allyltrichlorosilane could be alkylated with Grignard reagents to the corresponding allylsilanes (Scheme 6.1). This approach was used for the synthesis of triethyl- and tripropylallylsilane.

Table 6.1

Allylmagnesium bromide reaction with silylchlorides

Silylhalides	Allylsilanes	Yields
Ph_3SiCl		77%
$Ph_2(CH_3)SiCl$		72-80%



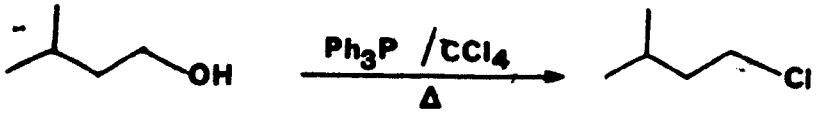
X = Br, Cl

44b R=Et 78%
44c R=n-Pr 88%

Scheme 6.1

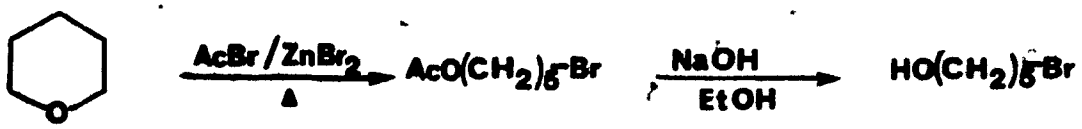
1.2 Alkylhalides

4-Methyl pentyl chloride 106, which was not commercially provided, was prepared from the alcohol 105 using triphenylphosphine in carbon tetrachloride[110].



105 106 68%

The halohydrins were produced in two different ways: 5-bromopentanol (108a) was derived from tetrahydropyran cleavage[111-113] with acetyl bromide and anhydrous zinc bromide followed by hydrolysis of the intermediate bromoacetate 107.



107 108a

Also, semi-halogenation of glycols under HBr treatment was used. A mixture of the diol 10 (n = 6, 9, 10), HBr, water and toluene was refluxed at moderate temperature with continuous extraction in the same manner as described in 6-chlorohexan-1-ol preparation[114]. Compounds 108 (b, c, d) could be readily obtained.

$$HO(CH_2)_nOH \xrightarrow[\text{continuous extraction}]{HBr/Toluene} HO(CH_2)_n\text{-}Br$$

109 n = 6, 9, 10

108b n = 6
108c n = 9
108d n = 10

The bromohydrins were protected as the tetrahydropyranyl ether in the usual manner[115] (Table 6.2).

$$HO(CH_2)_nBr \xrightarrow[Ether]{DHP/PTSA} THPO(CH_2)_nBr$$

108 110

110a n = 5 110c n = 9
110b n = 6 110d n = 10

2 - Regioselectivity in the alkylation of trimethylsilylallyl anion

Following the method reported by Corriu, trimethylsilylallyl lithium was readily generated from the reaction of trimethylallylsilane and n-butyllithium in TMEDA-THF at low temperature. Reactions of the anion with a number of alkylhalides were examined.

Surprisingly, in contrast to the claim of γ-selectivity in the reaction of 45d with methyl iodide, we obtained

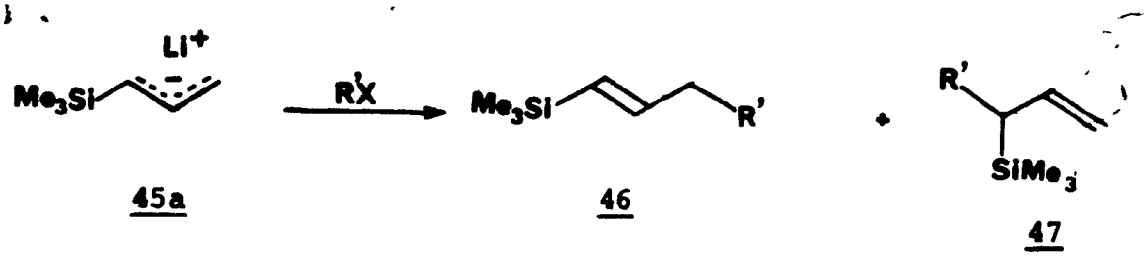
Table 6.2

Results of bromohydrins preparation and their conversion into tetrahydropyranyl ether compounds 110

n	Bromohydrins	Yield (%)	bp/mp °C	$THPO(CH_2)_nBr$	Yield (%)	bp/torr
5	$HO(CH_2)_5Br$ 108a	62*	-	$THPO(CH_2)_5Br$ 110d	98	-
6	$HO(CH_2)_6Br$ 108b	80	b.p. 58-62°C/0.15	$THPO(CH_2)_6Br$ 110b	93	-
9	$HO(CH_2)_9Br$ 108c	88	m.p. 32-33°C	$THPO(CH_2)_9Br$ 110c	96	122°C/0.05
10	$HO(CH_2)_{10}Br$ 108d	72	b.p. 117-120°C/0.03	$THPO(CH_2)_{10}Br$ 110d	91	128-130°C/0.1

* n = 5. Overall yield from tetrahydropyran cleavage and hydrolysis of 107.

a mixture of both γ- and α-regioisomers in a ratio around 2:1 (Table 6.3).



45a 46 47

Table 6.3

Relative amounts of γ- and α-products in the alkylation of trimethylsilylallyl lithium in TMEDA-THF

Alkyl halides (R-X)	γ-products (% yield)	α-products (% yield)
$CH_3(CH_2)_3I$	65	33
$CH_3(CH_2)_9I$	65	35
$CH_3(CH_2)_9Br$	57	42

The presence of γ- and α-addition products was verified by GC, GC-MS, ^1H nmr and in some cases by ^{29}Si nmr, as discussed further in the next paragraph. However, the reaction was quantitative and no residue of the starting alkylhalide was detectable from GC or ^1H nmr analysis when 1.1

equivalents of the allyl anion was used. It is also remarkable that the iodo compounds were slightly more regioselective as compared to alkyl bromides.

Furthermore, the ratio of α- to γ-products does not seem to vary significantly with the solvent system used (ether or THF-HMPA), by addition of DABCO, or 12-crown-4 or by addition of various metal salts or organometallic compounds such as magnesium bromide, copper iodide, zinc chloride, cesium fluoride, nickel chloride or tri-i-butyl aluminum.

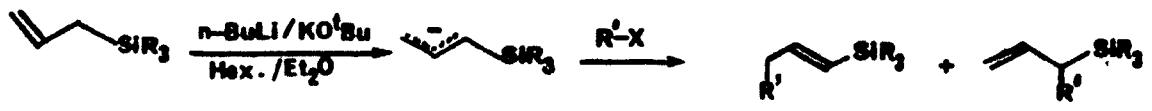
It appears to us that the α-silylallyl lithium alkylation reaction lacks regioselectivity and could not be used as such in a meaningful way for organic synthesis.

3 - The Use of Schlosser's Base

Organolithium reagents are known to react with sodium or potassium alkoxides to give quantitatively mixed metallic compounds with a high degree of reactivity. For instance, addition of n-butyllithium to a suspension of potassium t-butoxide in hexane at 0°C gave a white mixture which turned into a yellowish-orange precipitate at room temperature. The possibility of n-BuK formation by this process was examined by Lochmann et al.[116].

This so-called Schlosser's base undergoes hydrogen-metal exchange with low acidity hydrocarbons to give the

corresponding alkyl anions[117,118]. In connection with our work, when KO^{t}Bu/n-BuLi in hexane was used for the proton abstraction step, the silylallyl anion was readily generated. Alkylation of the carbanion with various alkyl halides unexpectedly gave the γ-addition product predominantly[120] (Table 6.4).



45 46 47

R = Me.

Table 6.4

Relative amounts of γ- and α-products in Schlosser's base condition

Entry	Alkyl halides	γ-products (% yield)	α-products (% yield)		b.p. of pure 46 (/torr)
1	$CH_3(CH_2)_8I$	86	14	46a	120°C/24
2	$CH_3(CH_2)_{11}I$	85	15	46b	180°C/4
3	$CH_3(CH_2)_7Cl$	80	16	46c	146°C/50
4	$CH_3(CH_2)_6Br$	80	18	46d	86°C/24
5	$CH_3(CH_2)_2Br$	83	17	46e	--
6	CH_2=CH-CH_2Br	76	--	46f	--
7	$(CH_3)_2CH(CH_2)_3Cl$	80	20	46g	98°C/760
8*	$THPO(CH_2)_5Br$	90	10	46h	--

* Entry 8 - The reaction time was 36 hours.

It is of interest to try to understand the origin of this improved regioselectivity. Recently Schlosser has provided evidence to suggest that KO^{t}Bu/n-BuLi is not the same as n-BuK[119]. The change in regioselection cannot be due to a change in the counterion in 45a from Li^+ to K^+, nor can we ascribe the change to a greater dissociation of the ion pair since DABCO or 12-crown-4 had no effect on the regioselectivity.

4 - Steric Effect

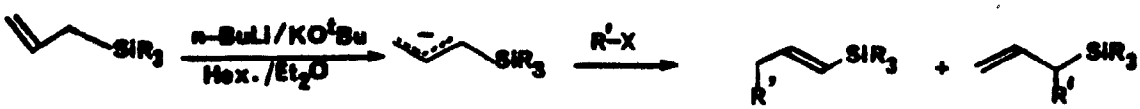
We suspect that a possible role is the association of the t-butoxide anion with the silicon moiety, thus giving greater steric hindrance to α-alkylation. To verify this idea, we prepared a series of silylallyl anions where the substituents on silicon are varied. When the substituent changes from methyl to ethyl to propyl with increasing bulk, the ratio of γ/α-alkylation increases[121] (Table 6.5). With tripropylsilylallyl anions prepared from KO^{t}Bu/n-BuLi in hexane, alkylation with alkyl halides can give a γ/α ratio as high as 40. The phenyl substituent gave a moderate ratio of γ/α-products, presumably due to its inherent electron inductive effect.

In most cases, both γ- and α-regioisomers are clearly identified from GC analysis. The α-product may have a shor-

ter retention time but appears relatively close to the γ-product signal even on an isothermic run. They are not separable by fractional distillation nor by usual chromatography. One could also use INEPT ^{29}Si nmr in decoupling

Table 6.5

Relative amounts of γ- and α-products according to the substitution on silicon in the alkylation of 45 when Schlosser's base was used



45 46 47

R = Me, Et, n-Pr, Ph.

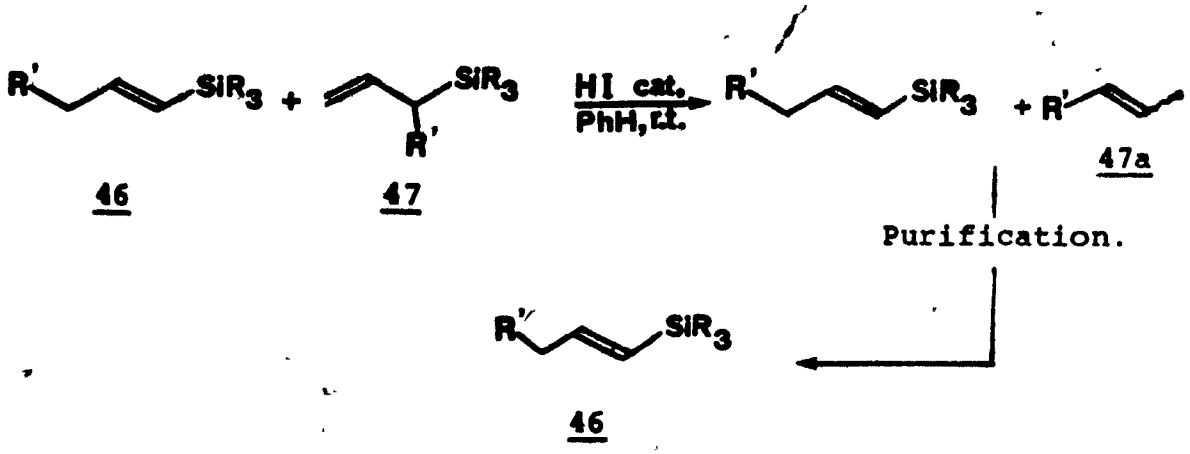
Silylallylanions	Alkyl halides	γ/α ratio	γ-products
$-SiMe_3$	$CH_3(CH_2)_{11}Br$	1/2	46b
	$(CH_3)_2CH(CH_2)_3Cl$	4/1	46g
	$THPO(CH_2)_5Br$	9/1	46h
	$THPO(CH_2)_6Br$	7/1	46i
	$THPO(CH_2)_9Br$	9/1	46j
	$THPO(CH_2)_{10}Br$	17/2	46k
$-SiEt_3$	$CH_3(CH_2)_{11}Br$	18/1	46l
	$CH_3(CH_2)_7I$	16/1	46m
	$(CH_3)_2CH(CH_2)_3Br$	20/1	46n
	$THPO(CH_2)_6Br$	22/1	46p
$-SiPr_3$	$CH_3(CH_2)_2Br$	46/1	46q
	$THPO(CH_2)_6Br$	36/1	46t
$-SiPh_3$	$CH_3(CH_2)_2Br$	16/1	46y

mode to determine the γ- and α-products ratio. For example, with trimethylsilylallyl anion in the alkylation reaction, the spectra of the crude mixture show two ^{29}Si singlets: δ ~ 2 ppm (allylic Si) and δ = -8 ppm (vinylic Si). From ^{1}H nmr spectra, the γ-adduct exhibits the characteristic ABX_2 pattern at δ ~ 6.0 (dt, J_{AB} 18.5 Hz, J_{BX} 6 Hz, 1 H_B) and δ ~ 5.6 (dt, J_{AB} 18.5 Hz, J_{AX} 1.4 Hz, 1 H_A), confirming the trans geometry at the double bond. Protons of the trimethylsilyl group appear as a singlet around 0.2 ppm. With respect to the minor α-product, the terminal olefinic protons are resolved as an unsymmetrical triplet (δ = 4.9 ppm) and the low intensity singlet at δ ~ 0.0 ppm is due to protons of the silyl group.

5 - Selective Protodesilylation

In terms of practical synthesis, the trimethylsilylallyl anion is still preferred since the starting material is commercially available. Furthermore, we found that the minor α-adduct can be readily removed by treating the crude mixture with a catalytic amount of hydroiodic acid (57%) in benzene at room temperature. Under these conditions, the α-product 47 was selectively converted to the olefin 47a but the γ-product 46 remained unchanged. We have been able to isolate the pure γ-product consistently in about 80-90%

yield after distillation or chromatography of the mixture of 46 and 47a.



46 47 47a 46

The selective protodesilylation of allylsilanes 47 could be argued by assuming that they are relatively more reactive than the corresponding vinylsilanes 46. In a general consideration, the Si-C bond overlapping with the π-bond orbitals will raise the energy of the HOMO and hence make the allylsilane more reactive toward electrophiles[32,55]. This overlap can better stabilize the developing positive charge on C-2 in the allylic system, whereas in vinylsilanes the same stabilization would imply a 90° rotation of the Si-C bond.

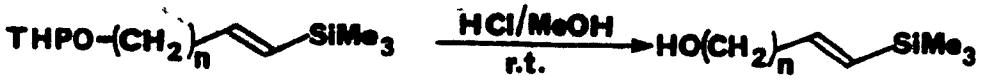
It is also known that at equilibrium, the trimethylallylsilane 44a is about 8 KJ mol^{-1} higher in energy than the corresponding isomeric vinylsilane.

6 - Selective Cleavage of the Tetrahydropyranyl Ether

It is remarkable to see that the tetrahydropyranyl ether group in compounds 46h-k, 46p and 46t survives HI treatment to give the functionalized vinylsilanes in good yields. However, the THP group is cleaved selectively under hydrochloric acid conditions[122] leaving the vinylsilyl group untouched (Scheme 6.2). For example compound 111h (n = 6) was obtained in 92% yield after HCl/methanol treatment of 46h. Its structure was determined by ^{1}H nmr and HRMS. The free alcohol was then acetylated in the usual manner (Ac_2O/Pyr).

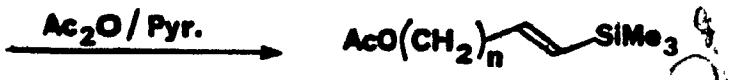
7 - 1,3-Bis(trimethylsilyl)propenyl Lithium Alkylation: A Tentative Approach to Vinylsilanes

As mentioned earlier in this thesis, addition of carbonyl compounds to 1,3-bis(trimethylsilyl)propenyl lithium 64 has been used to prepare 1-trimethylsilylbutadienes[71,95]. In our search of new methods to vinylsilanes, the reagent 64, readily generated from 44e by n-butyllithium treatment in TMEDA-THF at -78°C, was alkylated with dodecenyl bromide to give derivative 103 in quantitative yield (98-100%).



n = 6,10,11.

111		
111h	n=6	92%
111j	n=10	76%
111k	n=11	89%

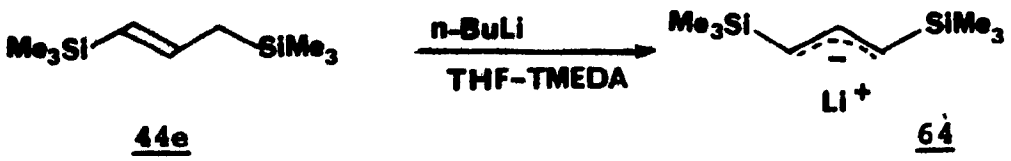


112		
112j	n=10	86%
112k	n=11	93%

Scheme 6.2

This compound was purified by vacuum distillation; b.p. 98-100°C/0.1 torr. From INEPT ^{29}Si nmr analysis (in decoupling mode), it displays two ^{29}Si singlets of equal intensity (δ = 1.9 ppm and δ = -8.1 ppm), characteristic of allylic and vinylic silicon, respectively.

Our attempts to use F^- ion[123] (Bu_4NF/THF or CsF/DMSO/-THF) to selectively cleave one silyl group to obtain either



44e 64

103

vinylsilane or allylsilane unfortunately failed, giving a complex mixture of desilylated products.

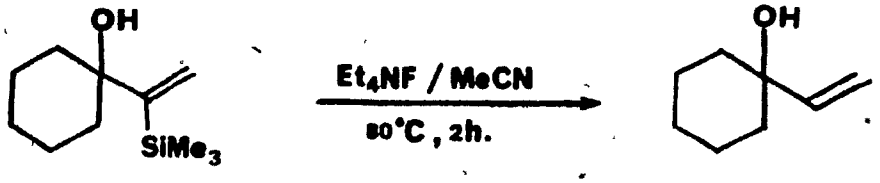
CHAPTER VII

VINYLSILANES IN ORGANIC SYNTHESIS:

ELECTROPHILIC SUBSTITUTION

1 - Introduction

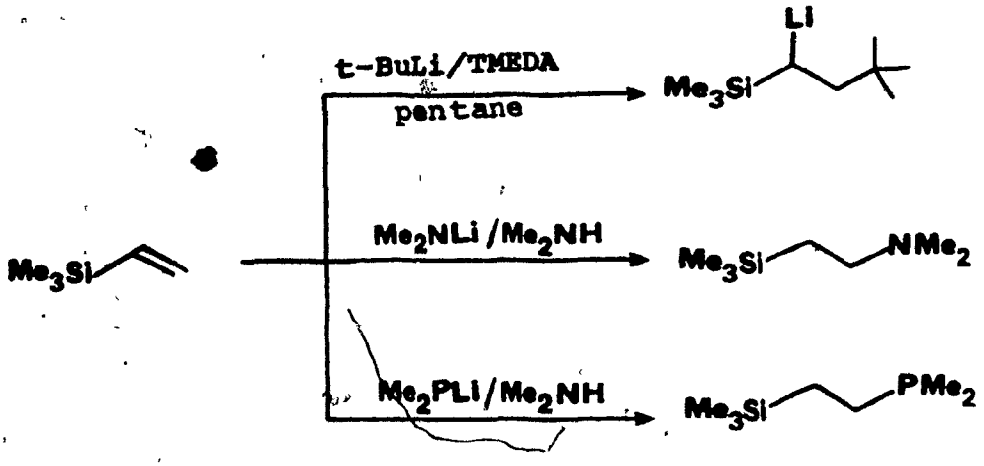
Vinylsilanes are relatively stable compounds. They are quite resistant to nucleophilic cleavage of the silyl group under many reaction conditions. Fluoride ion[124] is so far the most convenient reagent commonly used for desilylation, as illustrated by the conversion of 113 into 114.



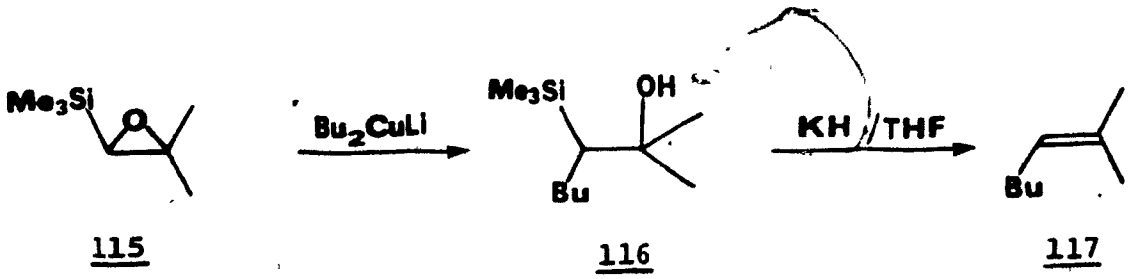
113 114

Their relative stability to mild acid conditions has been exploited advantageously to separate alkylvinylsilanes (γ-products) from allylsilanes as reported in the last chapter.

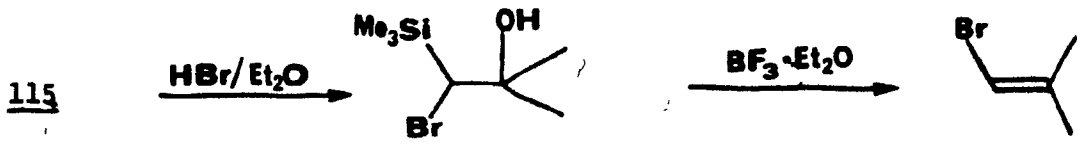
Organometallic carbon[125], nitrogen[126], and phosphorus[127] nucleophiles react with vinylsilanes, not at the silicon, but by addition to the C=C double bond.



The vinylsilanes can be readily epoxidized. The derived α,β-epoxysilanes can serve as vinyl cation equivalents[128], particularly for the stereospecific preparation of heteroatom substituted olefins[129]. For example, the epoxide 115 prepared from isobutenyltrimethylsilane by treatment with m-chloroperbenzoic acid, reacts with di-n-butyl cuprate to give the β-hydroxyalkylsilane 116 in a regio- and stereospecific manner. This silyl alcohol 116 undergoes facile β-elimination to the corresponding olefin 117. On the other hand, compound 115 can react with HBr in ether to give the α-bromo-β-hydroxysilane 118 which is then converted to vinyl bromide 119 by treatment with $BF_3.Et_2O$.



115 116 117

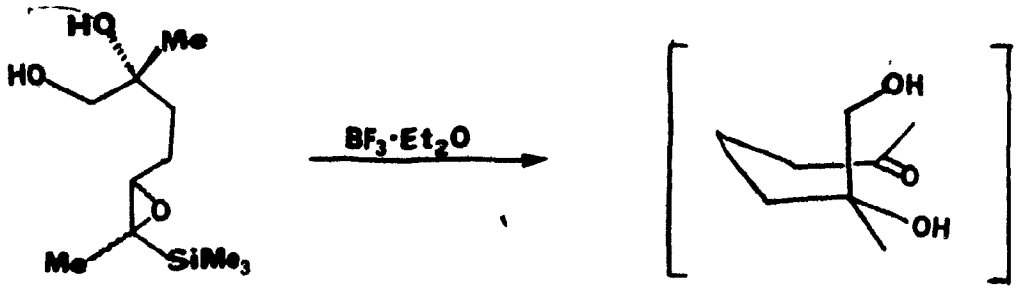


118 119

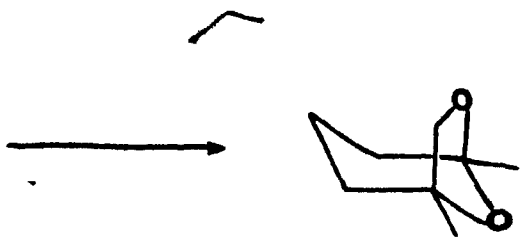
The α,β-epoxysilanes can also be converted into carbonyl compounds allowing vinylsilanes to serve as a latent carbonyl group in organic synthesis[100,130]. Conversion of compound 120 into (R)-(+)-frontalin demonstrates the utility of α,β-epoxysilanes in the synthesis of natural products.

2 - Electrophilic Substitution

Electrophilic substitution of vinylsilanes has attracted much attention during the last few years. They are known to undergo protodesilylation[131,132], acylation[133] and



120

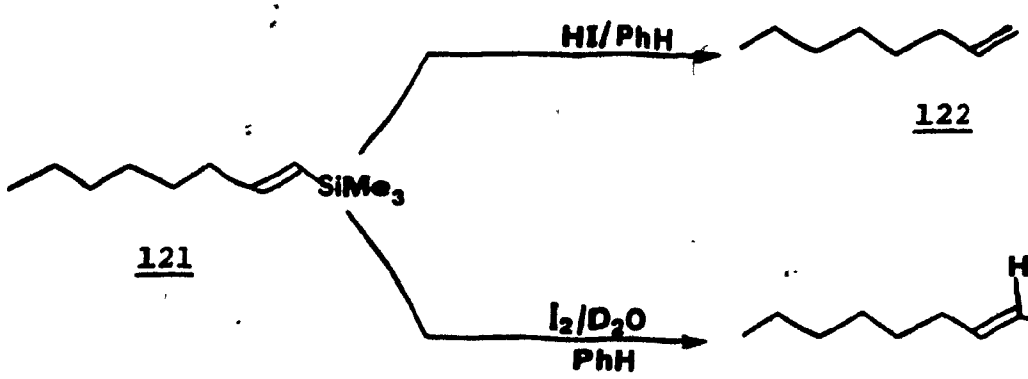


(R)-(+)-Frontalin.

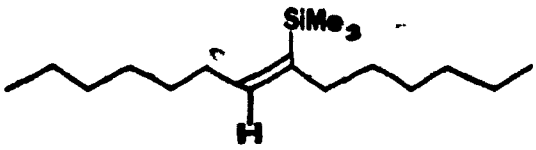
halodesilylation in a stereocontrolled manner. The overall stereochemical result of the electrophilic substitution reaction depends on the electrophile as well as on the reaction conditions.

2.1 Protodesilylation

With a proton as the electrophile, retention of configuration occurs in most cases. HCl, HBr, HI/benzene, or I_2/water, D_2O systems are commonly used. p-Toluenesulfenic acid is recommended when the molecule contains an acid-sen-

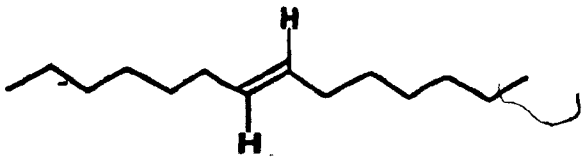


121 122 123 (97%)



124

HI/PhH
91%



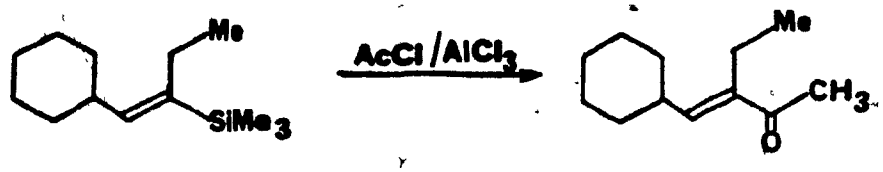
125 (94% E).

sitive functional group, but the reaction appears to be non-stereospecific.

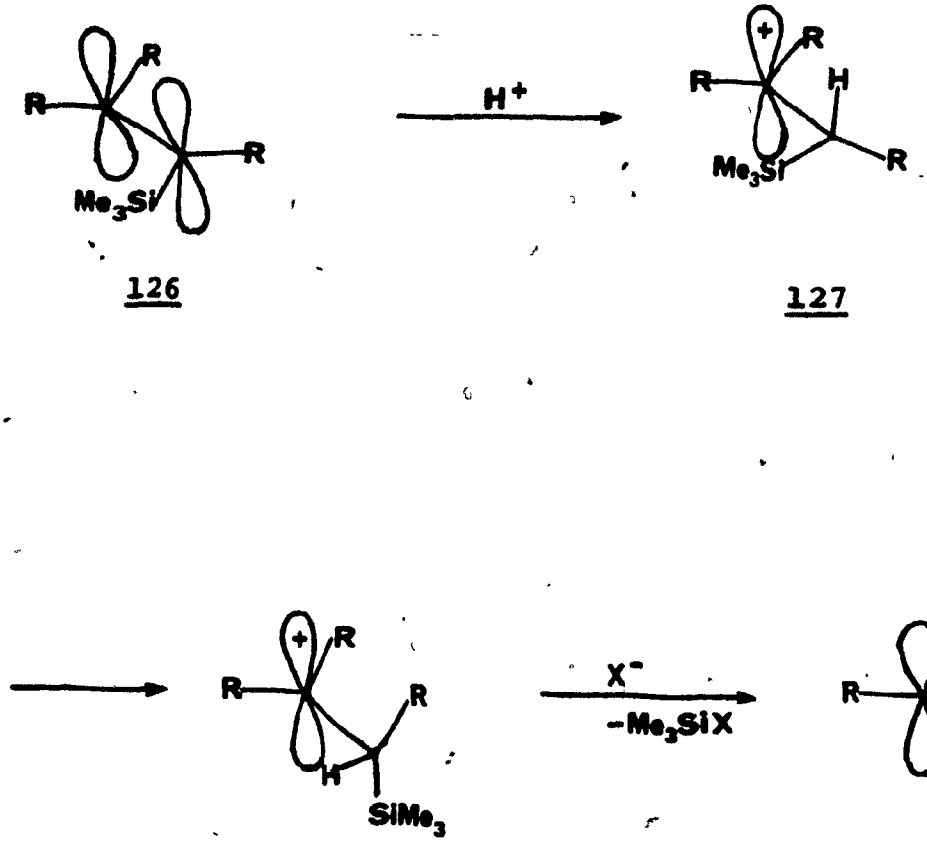
The following mechanistic pathway has been proposed to account for such a retention of configuration. As a proton is added to the double bond to generate the cation 127, the central carbon-carbon bond would rotate by the shortest path to stabilize the β-silyl carbonium ion, followed with nucleophilic attack on silicon to form the double bond (Scheme 7.1).

2.2 Acylation

The same mechanism could be used to argue for the retention of configuration observed in the Friedel-Crafts acylation of vinylsilanes[133] to give α,β-unsaturated carbonyl compounds.



130 E 131

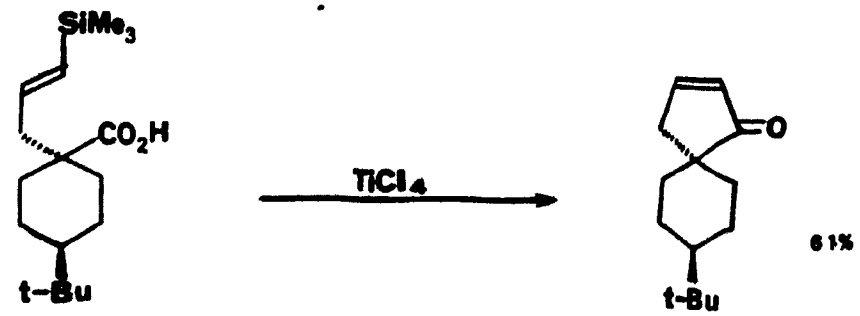


126 127 128 129

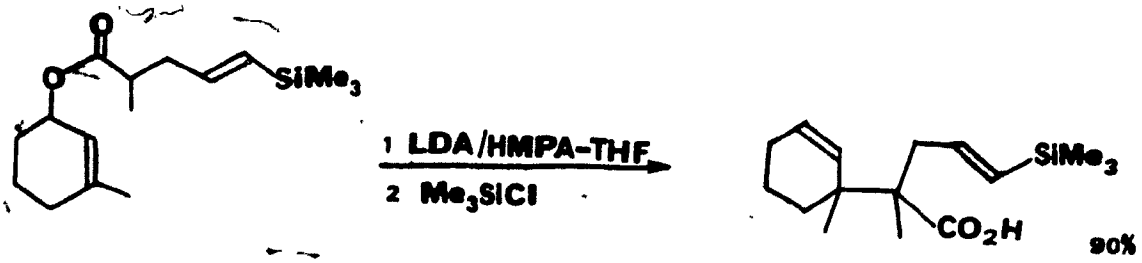
Scheme 7.1

However, the internal acylation of 132 and 135 to form cyclopentenone compounds 133 and 136 occurs with inversion of configuration at the double bond[134].

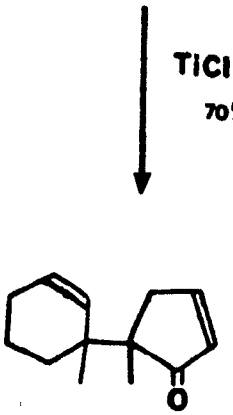
Also, there are some exceptions to the observed regioselectivity, especially when the vinylsilane compound con-



132 133

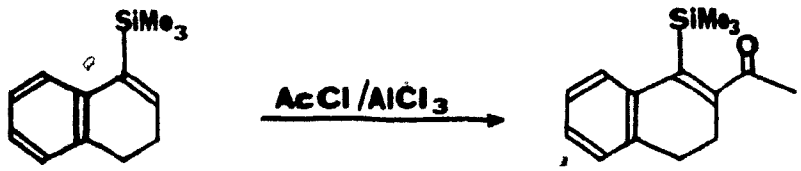


134 135



136

tains an additional group which better stabilizes the carbonium ion. Thus the regiochemistry is determined by the extra-functional group[32].



137 138

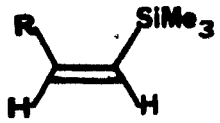
2.3 Halogens as electrophiles

In general, alkenylsilane 126 of defined stereochemistry undergoes anti-addition of bromine or chlorine to form a threo or erythro 1,2-dihalogenated compound which in contact with the nucleophile would eliminate in anti fashion to give the corresponding vinylhalide with overall inversion of configuration at the double bond[135] (Scheme 7.2).

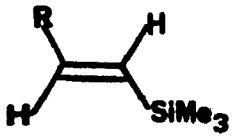
The intermediate 140 is relatively stable and could be isolated, or used in a straightforward manner without purification. Sodium methoxide in methanol, or alumina in pentane or $KF.2H_2O$ in DMSO, are often used for the subsequent halodesilylation process to afford the expected vinylhalides in excellent yield.

The tabulated results (Table 7.1) provided by Miller clearly indicate that the alkylsubstituent (R-) may have an

Table 7.1



142 ;



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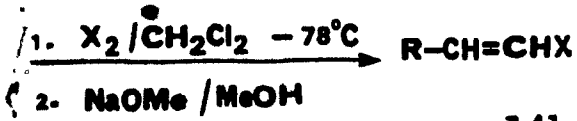
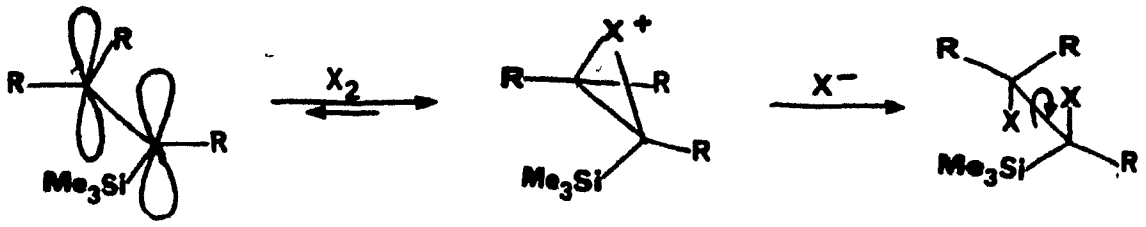


141

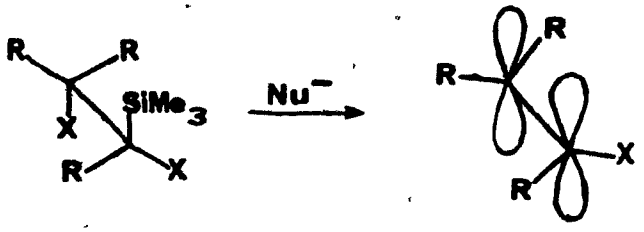
Vinylsilane	R	X	% isolated yield* (% GLC yield)	141 (cis/trans)
142a	n-Bu-	Cl	68 (85)	2:98
		Br	84 (96)	5:95
142b	cyclohexyl-	Cl	97 --	1:99
		Br	98 --	1:99
142c	t-Bu-	Cl	-- (91)[a]	92:8
		Br	70 (96)[a]	99:1
142d	Ph-	Cl	58 --	90:10
		Br	94 --	96:4
143a	n-Bu-	Cl	66 (85)	99:1
		Br	86 (100)	98:2
143b	cyclohexyl-	Cl	88 --	95:5
		Br	93 --	99:1
143c	t-Bu-	Cl	-- (82)	99:1
		Br	31 (58)	87:13
143d	Ph-	Cl	66 --	8:92
		Br	99 --	1:99

* ( )[a] $KF.2H_2O$/DMSO was used as the method of elimination.

important effect on the yield and the stereochemistry outcome of the halodesilylation reaction.



126 139 140



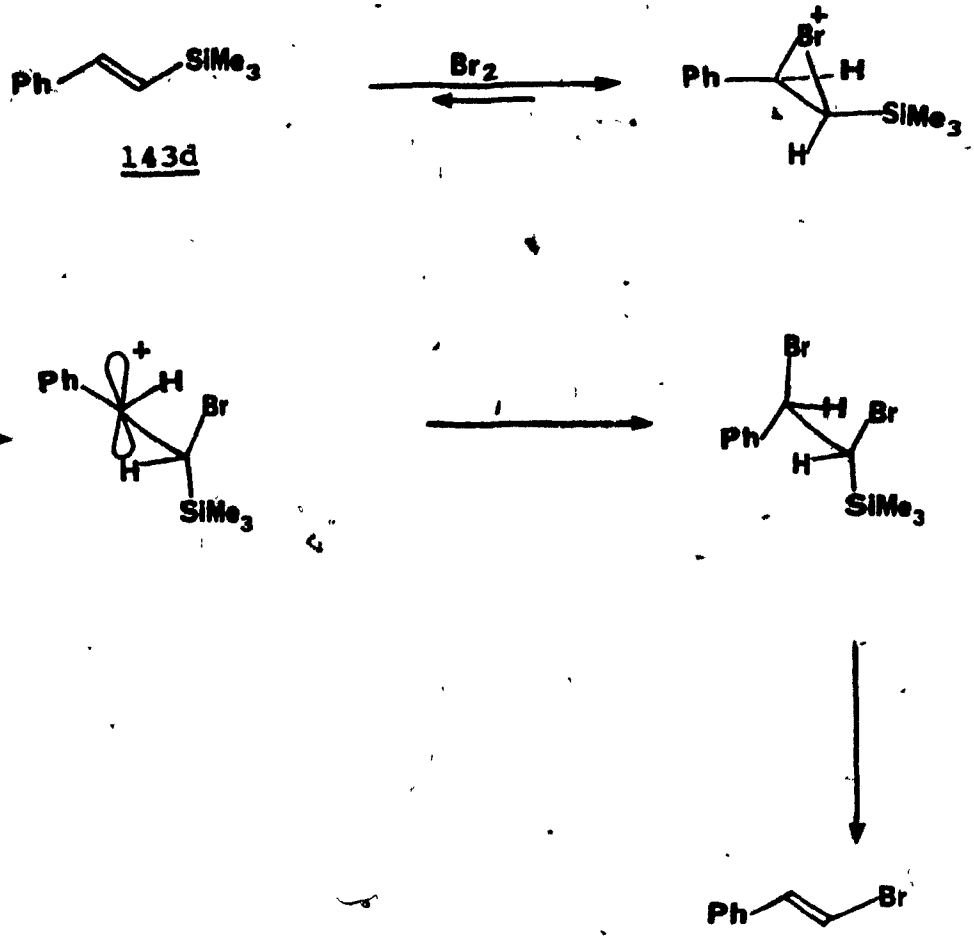
141

X = Br, Cl .

Scheme 7.2

With 2-n-alkylvinylsilanes, such inversion of configuration is observed (Table 7.1). β-Silylstyrenes are special

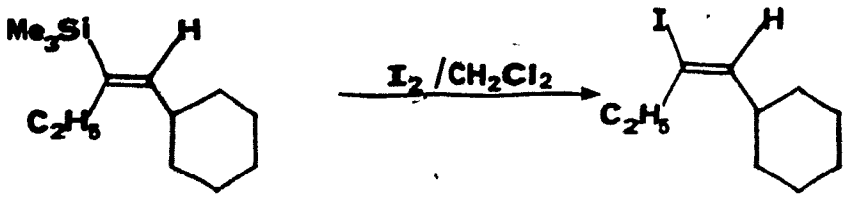
cases. They give retention of stereochemistry even though the reaction takes place by the addition-elimination process. It is established that in this particular situation, syn-addition of bromine or chlorine occurs followed by anti-elimination[136] (Scheme 7.3).



Scheme 7.3

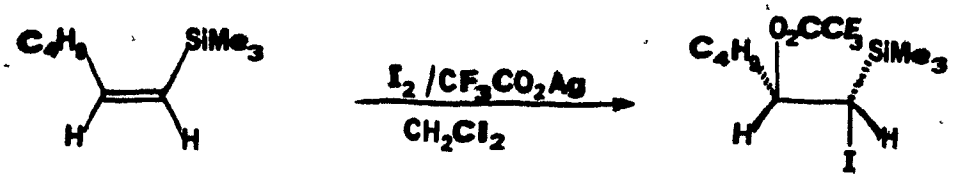
The phenyl group stabilizes the open β-carbonium ion and the bromide ion adds in an anti fashion to the silyl group, presumably for steric reasons, to give the syn-dihalide compounds.

The reaction of vinylsilanes with iodine exhibits some anomalies. Retention of stereochemistry has been observed in a number of instances. The mechanism proposed for the retention of stereochemistry was the same as the protodesilylation reaction (Scheme 7.1). The difference with respect to bromo- or chlorodesilylation is that the iodide counterion has less ability to open the bridged iodonium intermediate due to its size. Hence, the β-carbonium compound formation would result in yielding straightforward vinyliodide with retention of configuration. For example, 1,2-disubstituted alkenylsilane 144 was converted into vinyliodide[137] 145 in 60% yield under iodine treatment in CH_2Cl_2 at room temperature.

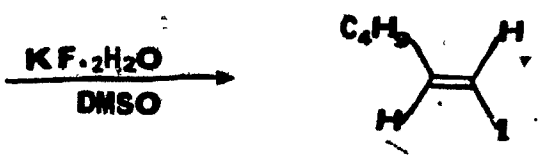


144 145

However, when a similar iododesilylation reaction was performed with iodine in the presence of silver trifluoroacetate[103] in dichloromethane, the vinyliodide 147 was obtained with inversion of configuration.



142a 146

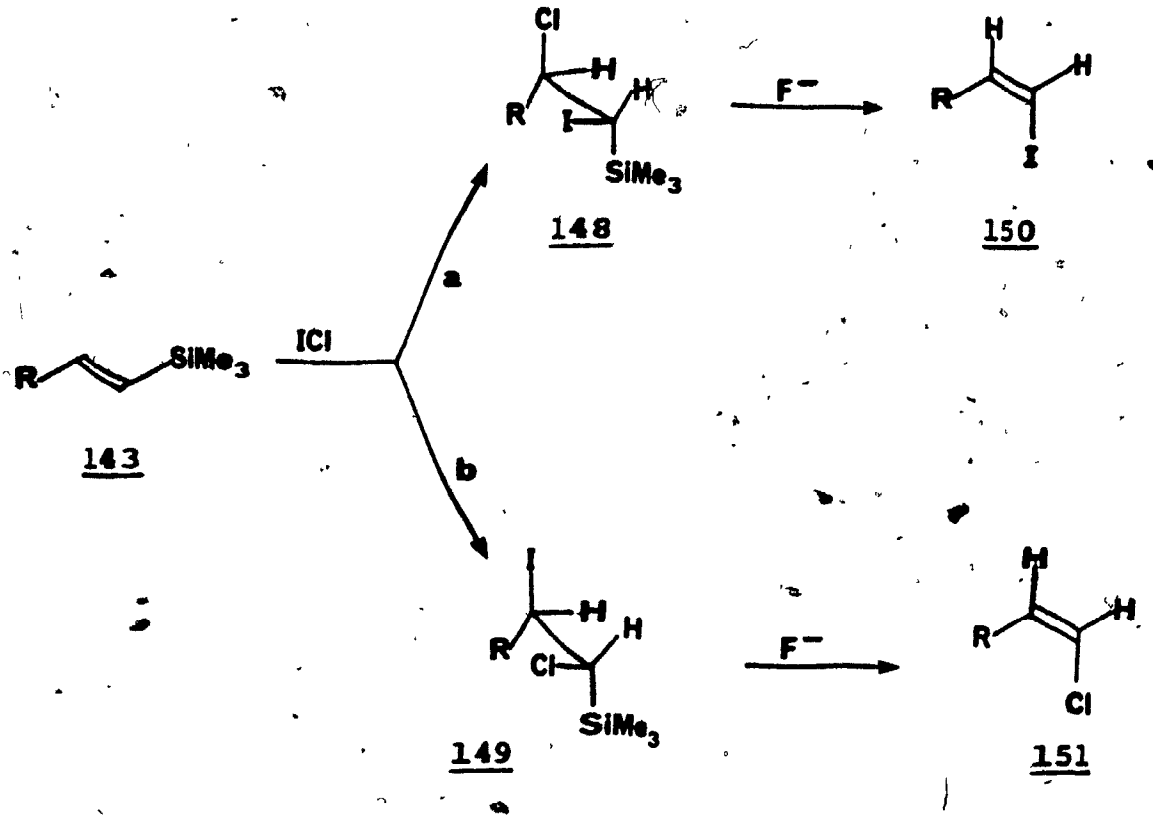


147

Here, the trifluoroacetate counterion acts as the nucleophile with respect to the bridged iodonium ion to give the trans-addition compound 146 which of course would eliminate by the usual anti manner.

Unfortunately, the low yield of the adduct 146 and the use of an expensive silver reagent may affect the usefulness of this approach in organic synthesis. To overcome this

situation, Miller recently employed iodine monochloride[138] as the reagent. The reaction is run in carbon tetrachloride at 0°C to quantitatively afford the dihalide 148. The subsequent fluoride induced elimination gave mainly the vinyliodide, with inversion of configuration at the double bond.



148 150 143 149 151

It is also interesting to see that silicon directs the iodine addition to the α-position selectively in the dihalide 148 formation and the isomeric compound 149 is obtained in very low yield.

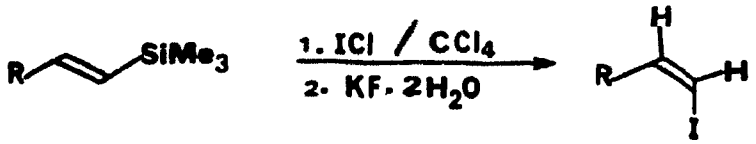
3 - **Results and Discussion**

With this literature precedence, it seems reasonable to expect that E-vinylsilanes can be converted stereoselectively to either Z- or E-vinyliodides depending on the reagents used. We thus examined these reactions. The E-vinylsilanes prepared in Chapter VI have been treated successively with iodine monochloride and $KF.2H_2O$ to provide Z-vinyliodides selectively (Table 7.2). In all cases, the E-isomer is less than 2% base on GC analysis. It is noteworthy that the tetrahydropyranyl ether group once again survives the ICl treatment. It has been possible to isolate the dihalide intermediate for the purpose of ^1H nmr characterization. For example, E-1-trimethylsilyltridecane 46b was allowed to react with 1.1 equivalents of iodine monochloride in carbon tetrachloride at 0°C for 5 to 10 min. The reaction mixture was quenched with 10% $Na_2S_2O_3$. The ^1H nmr of the crude mixture showed it to be the dihalogenated intermediate 148. After subsequent treatment with $KF.2H_2O$ in DMSO, the vinyliodide was obtained, as evidenced by the appearance of the vinyl protons at δ = 6.2 ppm (2 H). Also, the mass spectrum (EI) showed a parent ion at m/e = 336 (11.5%).

It is quite clear from the results in Table 7.2 that in all cases, E-vinylsilane was converted by ICl followed by

Table 7.2

Stereoselective iododesilylation of E-vinylsilanes in ICl/KF conditions



46 150

Entry	E-vinylsilanes (R-)	Isolated % yield of 150	
1	$CH_3(CH_2)_{12}$-	84	150a
2	$CH_3(CH_2)_7$-	86	150b
3	$CH_3(CH_2)_{10}$-	81	150c
4	$(CH_3)_2CH(CH_2)_4$-	85	150d
5	$THPO(CH_2)_6$-	84	150e
6	$THPO(CH_2)_7$-	86	150f

$KF.2H_2O$ to give Z-vinyliodide with a high degree of inversion of stereochemistry.

On the other hand, the electrophilic substitution reaction of vinylsilanes with iodine is expected to give retention of configuration according to literature precedence. It was therefore a surprise that we did not obtain retention of stereochemistry at the double bond when linear (E)-2-alkylvinylsilanes were treated with iodine in dichloromethane at room temperature. Inversion of stereochemistry

was observed and the final product obtained in 30-40% yield was identified as being the Z-vinyliodide. Even though the iodine was resublimed and the starting compound and solvent were perfectly dry, no significant change in stereochemistry was observed.

To account for the different stereochemical outcome than the previous similar work from our laboratory (compound 145), one possibility is that 1,2-disubstituted vinylsilane was used in our previous study. It is possible that the substituents on the vinylsilane moiety may influence the course and the stereochemistry of the iododesilylation reaction.

To argue for the inversion of configuration observed now, we believe that the iodine in fact adds to the double bond in the usual anti manner followed by trans elimination as do Cl_2 and Br_2 (Scheme 7.2). Such an addition is possible for terminal vinylsilanes because the steric hindrance to addition is less.

Attempts to isolate the diiodo intermediate were, however, unsuccessful. If such a mechanism is correct, one way to circumvent the anti-addition would be to decrease the ability of the iodide counterion to open the iodonium ring. In practice, we found that when the iododesilylation reaction was performed with iodine in the presence of various Lewis acids such as aluminum chloride, tin chloride or anti-

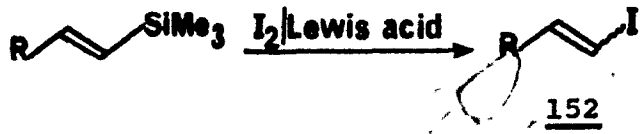
mony pentachloride, the vinyliodide was obtained in good yield and mainly with retention of configuration at the double bond (Table 7.3). The optimum conditions to obtain a high ratio of E/Z isomers are found to require 2 equivalents of Lewis acid and -78°C for the reaction temperature.

The yield and the ratio of E/Z isomers were determined by GC analysis. Also, both stereoisomers are clearly distinguishable by ^1H nmr; the cis vinylic protons appear as a singlet at δ = 6.1 ppm. On the other hand, the vinylic protons in the trans structure have different chemical shifts at δ = 5.93 (dt, J_1 = 14.3 Hz, J_2 = 1.4 Hz, 1 H_A) and δ = 6.43 (dt resolved as quintet, J_1 = 14.3 Hz, J_2 = 7.1 Hz, 1 H_B).

It is also interesting to note that the E/Z ratio could be varied with the amount of Lewis acid added. Conceptually, this may be a convenient method to quantitatively prepare, in a one pot reaction, a specific blend of E- and Z-vinyliodides. For example, the functionalized alkylvinylsilane 112k was treated with iodine in dichloromethane at 0°C in the presence of aluminum chloride or tin chloride. The results are plotted in graph 1 and graph 2, respectively.

Table 7.3

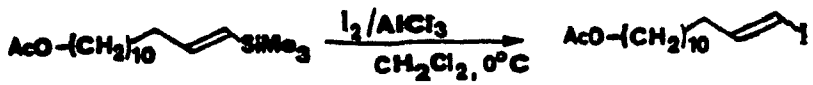
Stereoselectivity in iododesilylation of E-vinylsilanes with iodine in the presence of Lewis acids

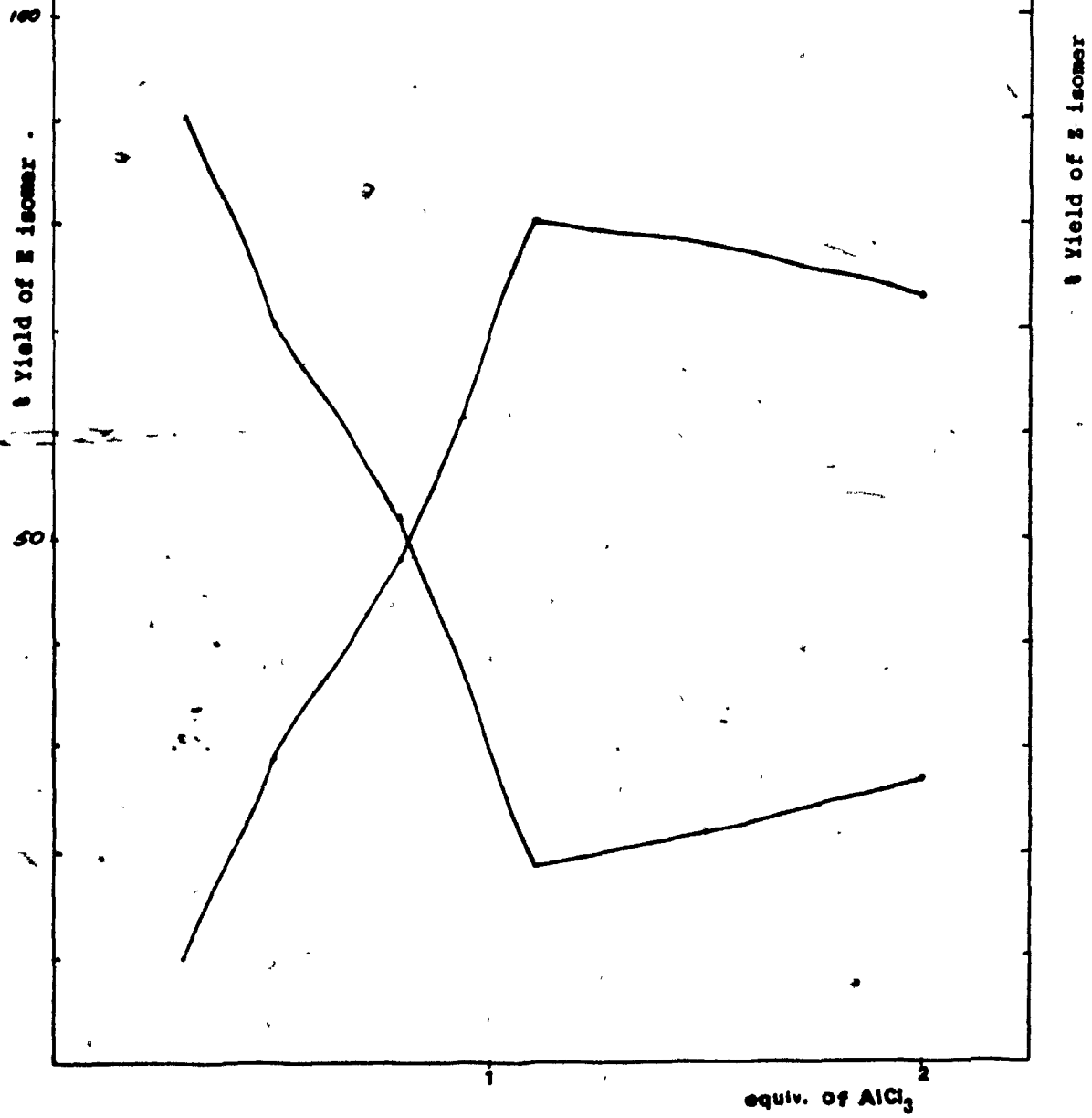


152

Entry	E-vinylsilane (R-)	Lewis acids	Reaction Condition	Yield (%)	E/Z ratio	
1	$CH_3(CH_2)_{12}$-	$SnCl_4$	2 equiv. -78°C	95	18:1	152a
2	$CH_3(CH_2)_{12}$-	$SnCl_4$	1.1 equiv. -78°C	95	14:1	
3	$CH_3(CH_2)_{12}$-	$AlCl_3$	1.1 equiv. 0°C	82	4:1	
4	$AcO(CH_2)_{10}$-	$AlCl_3$	1.1 equiv. r.t.	82	4:1	152b
5	$AcO(CH_2)_{11}$-	$SnCl_4$	2.0 equiv. -78°C	92	13:1	152c
6	$AcO(CH_2)_{11}$-	$SnCl_4$	1.1 equiv. -78°C	90	8:1	

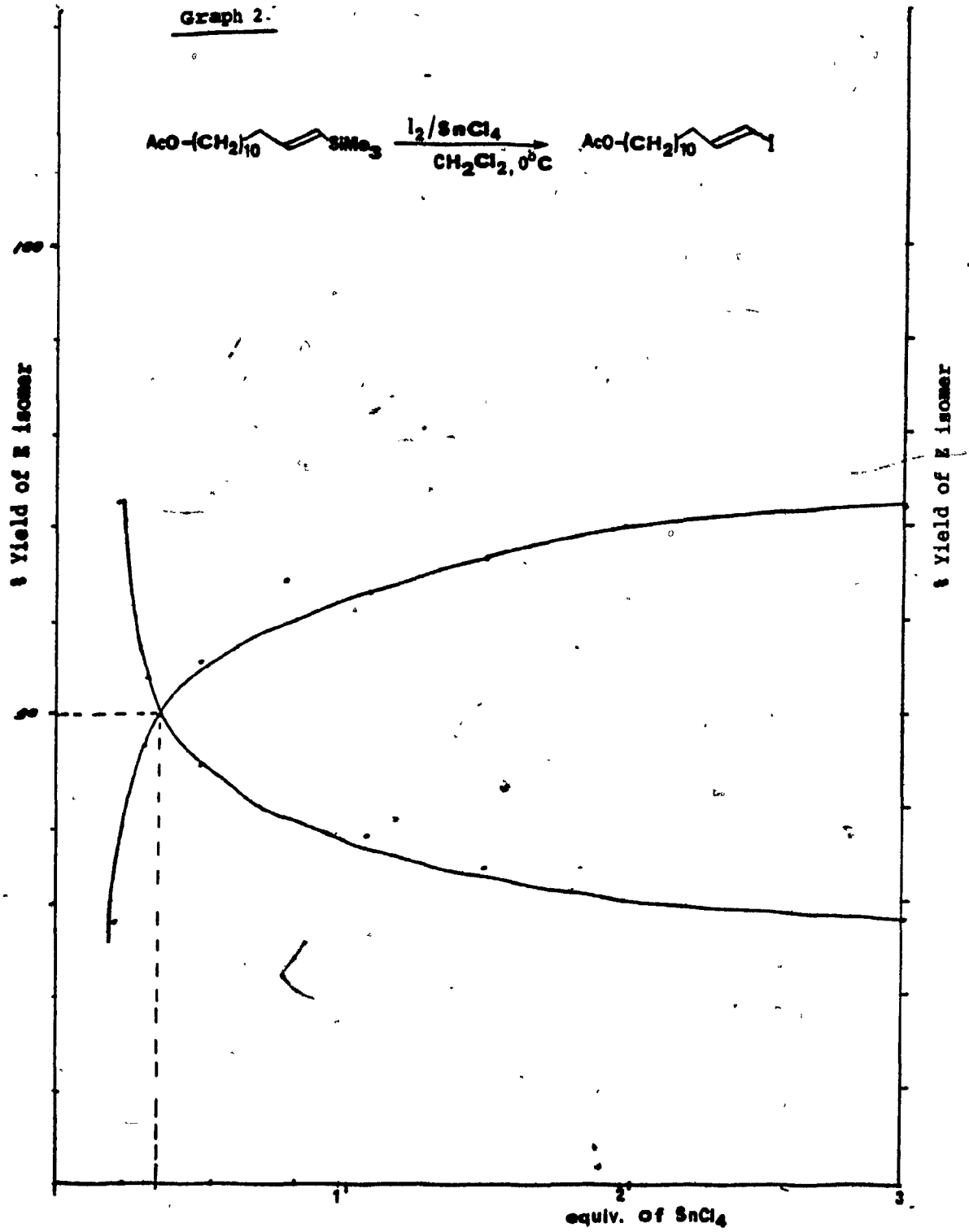
Graph 1.


AcO-(CH2)10
SiMe3
I2/AlCl3
CH2Cl2, 0°C
AcO-(CH2)10
I


% Yield of E isomer
% Yield of Z isomer
50
1
2
equiv. of AlCl3

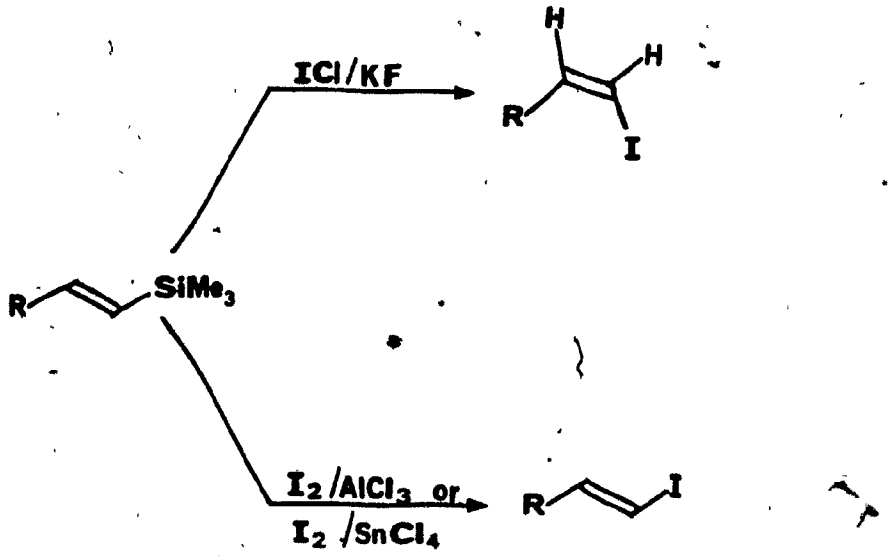
Graph 2.

AcO-(CH2)10
SiMe3
I2/SnCl4
CH2Cl2, 0°C
AcO-(CH2)10
I


% Yield of E isomer
% Yield of E isomer
1
2
3
equiv. of SnCl4

4 - Conclusion

As demonstrated throughout this chapter, electrophilic substitution of vinylsilanes with halogen could be used efficiently to provide vinylhalides in a stereocontrolled manner. Either the Z- or the E-vinyliodides have been prepared from the same precursor.



More interestingly, the iododesilylation reaction in the presence of Lewis acid could be controlled to produce a specific mixture of E- and Z-isomers in a one pot reaction.

Vinyl halides have recently found extensive application in the stereoselective synthesis of biologically important molecules such as insect sex pheromones containing one or two conjugated double bonds. It thus seems interesting to explore the possibility of using the silicon methodology

for the stereocontrolled synthesis of these insect sex pheromones.

CHAPTER VIII

SYNTHESIS OF SOME INSECT SEX PHEROMONES

1 - Introduction

During the past two decades, it has gradually become clear that many behaviours, e.g., metamorphosis, aggregation, and mating of insects are all regulated by chemical substances known as insect hormones and pheromones. Pheromones are chemicals released by an individual and received by another individual of the same species to induce specific behavioral responses or physiological changes. Sex pheromones especially are released by female insects to attract males for the purpose of mating. Most of these biologically active compounds have been isolated and identified even though their biogenetic origin is not well understood so far.

Recent investigations conducted by Bjostad and Roelofs[139] suggest that many moth sex pheromones are produced from fatty acid precursors. For example, the authors provided evidence to show that (Z)-7-dodecenyl acetate, an active component of Tricoplusia m. sex pheromone, is derived from a lipidic source. The hexadecanoate, produced by fatty acid synthetases, may undergo specific desaturation and successive chain shortening, reduction and acetylation (Scheme 8.1).

The possibility that insect pheromones are related to diet has recently been a subject of controversy. The idea

that sex pheromone components would vary with dietary factors and consequently induce an evolutionary mechanism for diversification of certain species of insects has not been universally accepted[140,141].

Hexadecanoate $\xrightarrow{\text{(Z)-11-desaturase}}$ Z-(11)-hexadecenoate

$\xleftarrow{\text{chain shortening}}$ Z-9-tetradecenoate $\xrightarrow{\text{chain shortening}}$

Z-7-dodecenoate $\xrightarrow[\text{2) acetylation}]{\text{1) reduction}}$ Z-7-dodecenyl acetate.

Scheme 8.1

2 - Synthetic Approaches

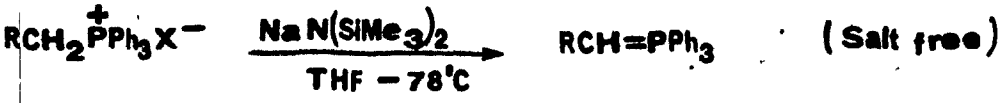
Many insect sex pheromones have general structure 153, where X is an oxygen functional group. For some lepidopterous pheromones, the effective attractant is often a precise mixture of the Z- and E-isomers of the double bond.

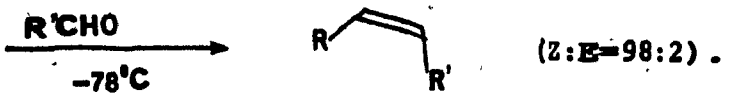
$$CH_3-(CH_2)_n-CH=CH-(CH_2)_m-X$$

153

There are a number of methods for the synthesis of this type of compound[142,143]. The Wittig reaction which has

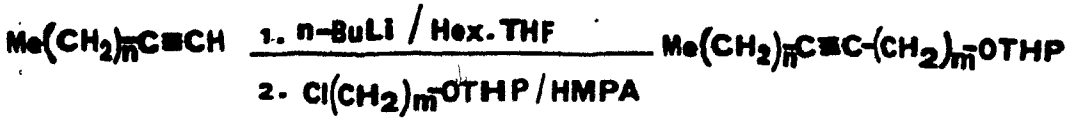
been used extensively in this area, usually gives rise to the Z-olefin selectively[144-149].



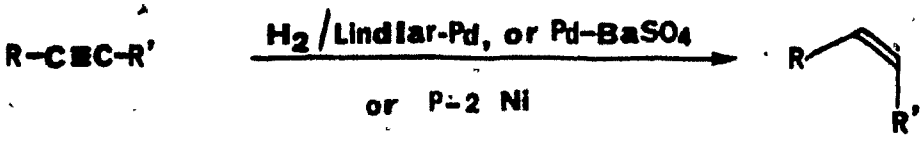


The other method of choice is to proceed by alkylation of the acetylenic compound followed by reduction. This route offers the advantage that either the Z- or E-isomers can be obtained stereoselectively.

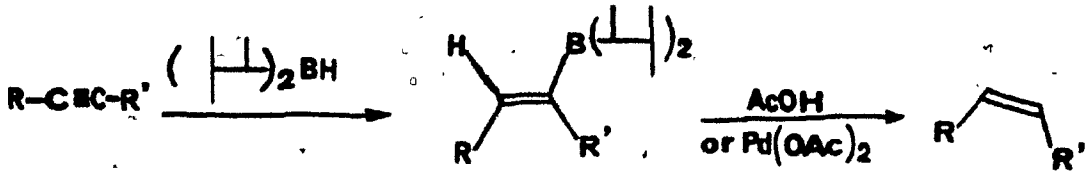
We want to demonstrate that a synthetic methodology based on organosilicon compounds can be developed for the effective synthesis of these compounds.



Ref. 150,151



Ref. 152-156.



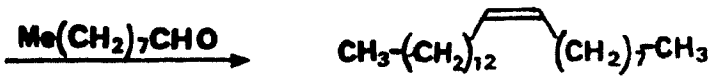
Ref. 157.

Ref. 150, 158.

3 - Synthesis of Z-9-Tricosene (Muscalure)

The first isolation and identification[159] of the house fly (Musca domestica) sex pheromone, Z-9- tricosene, was reported in 1971. This compound is commercially used to increase the effectiveness of fly bait containing insecticides. The initial synthesis of Z-9-tricosene (muscalure) was achieved via a Wittig condensation reaction of triphenylphosphonium tetradecylide 154 with 1-nonanal in dimethylsulfoxide to give both E and Z geometrical isomers in a ratio of 85:15 respectively.

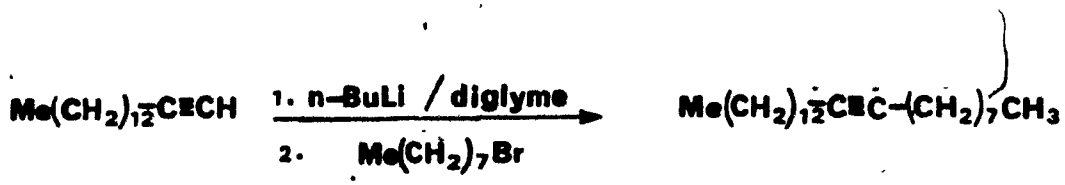
154



155 (Z:E=85:15)

Further modification[146] of this reaction by using potassium in HMPA as the base to generate the ylide increased the Z/E ratio to 94:6. Unfortunately the muscalure was obtained in only 32% yield.

From another approach, semihydrogenation of the acetylenic precursor 156 by using Lindlar-Pd catalyst gave 155 in a stereospecific manner[160].



156 157

155

However, the synthetic routes utilizing copper (II) catalyzed coupling of erucyl 158 or oleyl mesylates[161] 159 with appropriate Grignard reagents were found convenient for production-scale preparation of 155 in the pure Z-isomeric form.

Even though the natural pheromone has Z geometry at the double bond, no masking was observed when the Z- and E-isomers were mixed at ratios up to 1:3 respectively[159].

By using the silicon controlled route described in this thesis, compound 46b can serve as a precursor to 155. When the vinylsilane 46b was reacted with ICl/KF, the Z-

158

159

vinyliodide 150a was obtained in 84% yield. A number of methods are available to couple vinyl halides with organometallic reagents to give alkenes[162-174].

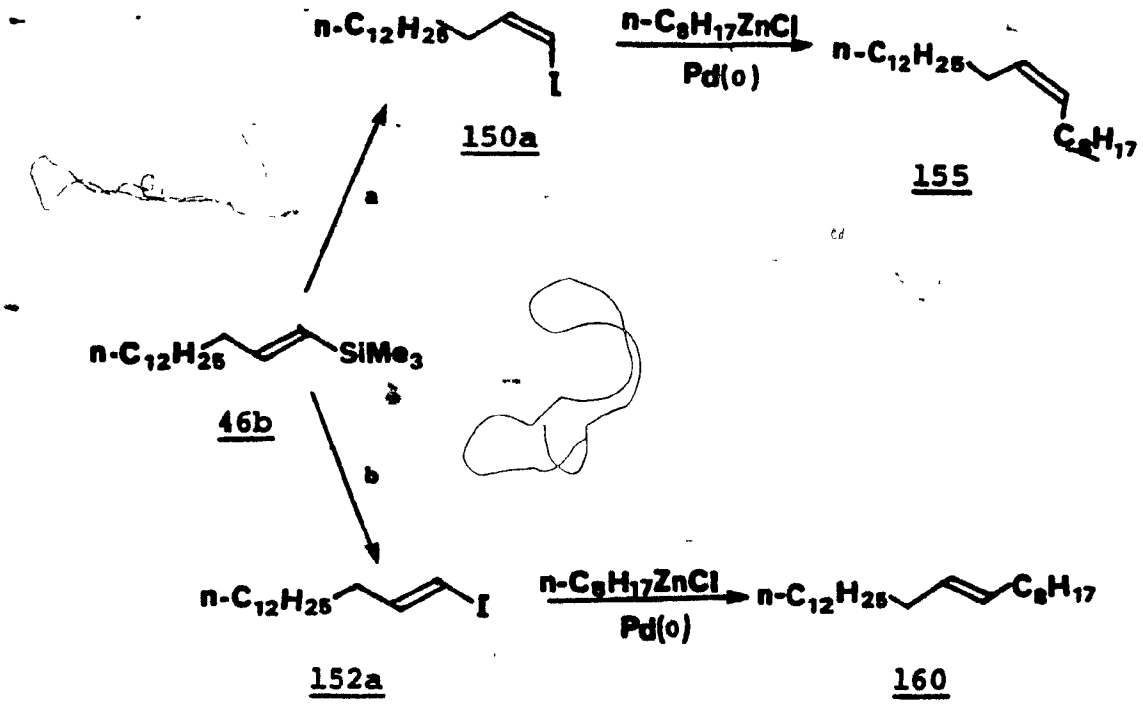
We found that when the octyl copper reagent prepared from octylmagnesium bromide and lithium copper chloride[173] was allowed to react with 150a, the coupled product Z-9-tricosene was obtained quantitatively. Equally effective was the coupling of 150a with octyl zinc chloride[166] in the presence of $(Ph_3P)_4Pd(0)$[175] as catalyst. The palladium (0) catalyst could be generated in situ from Ph_2PdCl_2 treatment with i-Bu_2AlH[165].

The coupling reaction gave a high yield (> 96%) of Z-9-tricosene based on GC analysis. Compound 155 was obtained in 81% yield after fractional distillation. It was

not possible for us to detect the minor E-isomer either by GC, ^{1}H nmr or ^{13}C nmr. However, when an aliquot of 155 was treated with MCPBA in dichloromethane, the corresponding epoxide was obtained. The cis and trans methine protons in the epoxide are clearly distinguishable by ^{1}H nmr, δ = 2.89 ppm (methines cis, 96%) and δ = 2.59 ppm (methines trans, 4%). This transformation allowed us to establish the ratio of Z- and E-isomers in 155 to be 96:4 respectively.

To verify this method of evaluation, the trans isomer of 9-tricosene 160 was prepared selectively from the E-vinyliodide 152a (E/Z = 4:1) (Scheme 8.2). The olefin was converted to the corresponding epoxide. The chemical shifts of cis and trans methine protons are identical in both experiments. It is possible that the slight deviation in the Z/E ratio (96:4) of the coupled product 155 with respect to the vinyliodide Z/E ratio (> 98:2) may be due to the minor self coupling side reaction of 150a.

However, the stereochemical purity of the Z-9-tricosene prepared by the silicon controlled route is higher than that obtained from the usual Wittig reaction. Furthermore, the final product 155 could be obtained in up to 54% overall yield from the starting compound 1-bromododecane.



a. ICl/KF
b. I_2/ $AlCl_3$

Scheme 8.2

4 - Synthesis of Disparlure

The gypsy moth Porthetria dispar (L) is a serious despoiler of forest and shade trees in the northeastern United States and in Europe. The sex pheromone emitted by the female has been identified to be cis-7,8-epoxy-2-methyloctadecane 163 [176]. Experiments with both synthetic enantiomers indicate that the cis-(+)-isomer ((7R,8S)-(+)-disparlure) is the natural sex attractant. The cis-(-)-iso-

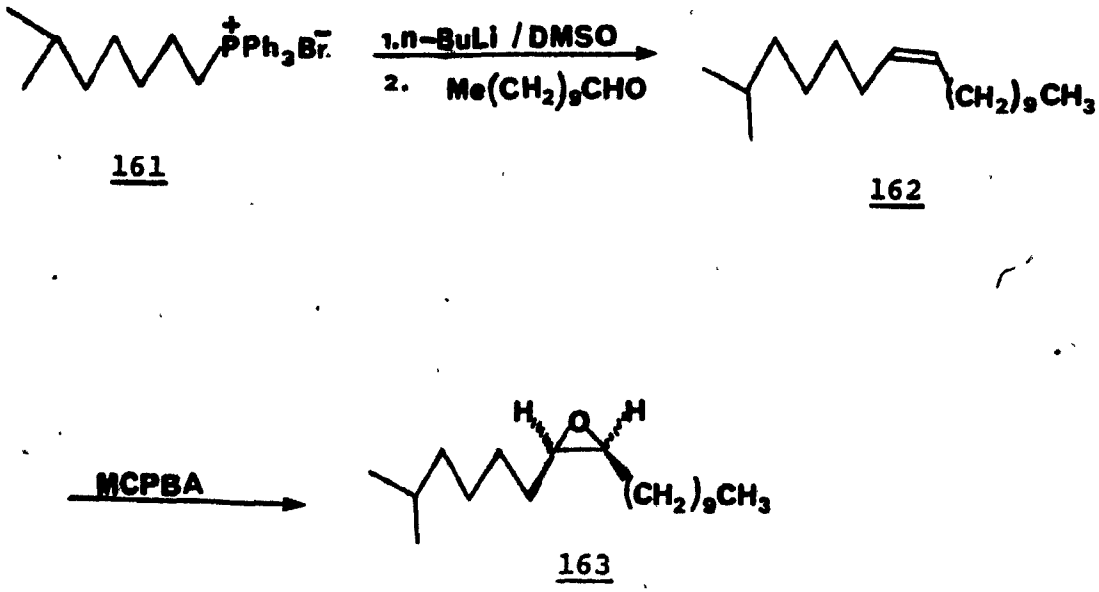
mer shows only very weak or no activity. Furthermore, both trans enantiomers of disparlure are essentially inactive. There is some evidence to suggest that the female gypsy moth may use the olefinic precursor Z-2-methyl-7-octadecene 162 to produce the pheromone by a specific epoxidation[176]. Surprisingly, this intermediate 162 was found to inhibit male attraction to the pheromone. Even though the active component of this sex attractant is the cis-(+)-isomer, mixtures of isomeric compounds containing various amounts of trans epoxide also exhibit appropriate biological activities under field test[177].

A number of synthetic approaches are reported to provide the pheromone as racemate, a mixture of cis and trans isomers, or as a pure cis-(+)-enantiomer.

In the first synthesis of disparlure[176], the authors employed a Wittig reaction to produce the olefinic intermediate 162 as a mixture of both Z and E geometrical isomers in a ratio of 85:15 respectively (Scheme 8.3).

The stereoselectivity of the olefination reaction could be improved to Z/E > 98/2 by employing sodium bis(trimethylsilyl)amide[178] as the base in the ylid formation.

The first synthesis of optically active disparlure from L(+) glutamic acid, reported by Marumo[179] was not stereoselective and required separation, purification by TLC, and repeated recrystallization of diastereomeric reaction



161 162

163

Scheme 8.3

products. Two years later, Mori published a stereoselective synthesis[180] of cis(+) disparlure starting from L-(+)-tartaric acid (164).

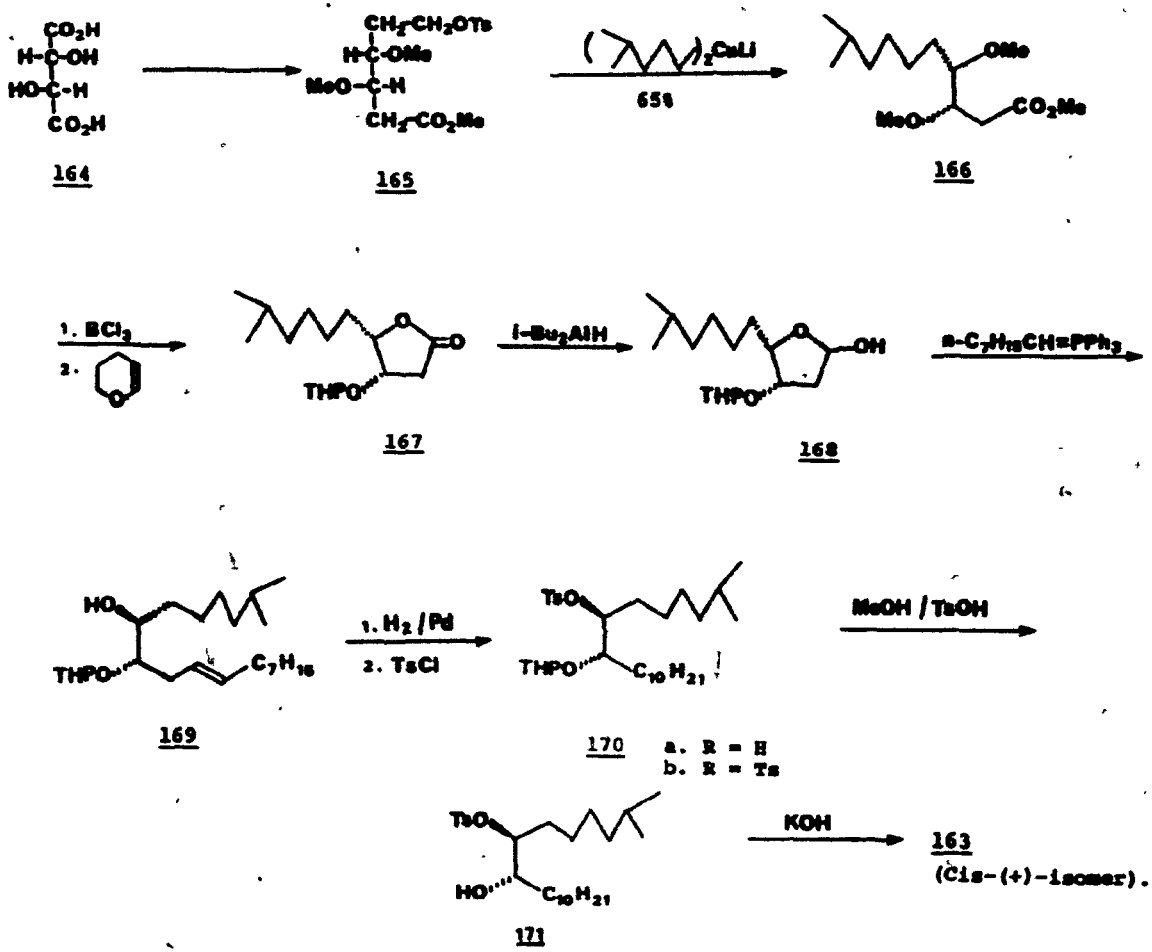
The (2S,3S) threo configuration in 164 is appropriate for the epoxy ring formation. The major problems in this synthesis were discrimination of the two hydroxy groups and carbon chain elongation. Compound 164 was converted into tosylate 165 and treated with i-Am_2CuLi in ether to give the dimethoxy ester 166 in 65% yield. Demethylation of 166 with

an excess of BCl_3 in CH_2Cl_2 gave the hydroxylactone 167 and the discriminated γ-hydroxyl group was protected to the corresponding tetrahydropyranyl ether. Reduction of lactone 167 followed with carbon chain elongation via a Wittig reaction led to compound 170 which was then converted to cis-(+)-7,8-epoxy-2-methyloctadecane 163 by known reactions (Scheme 8.4).

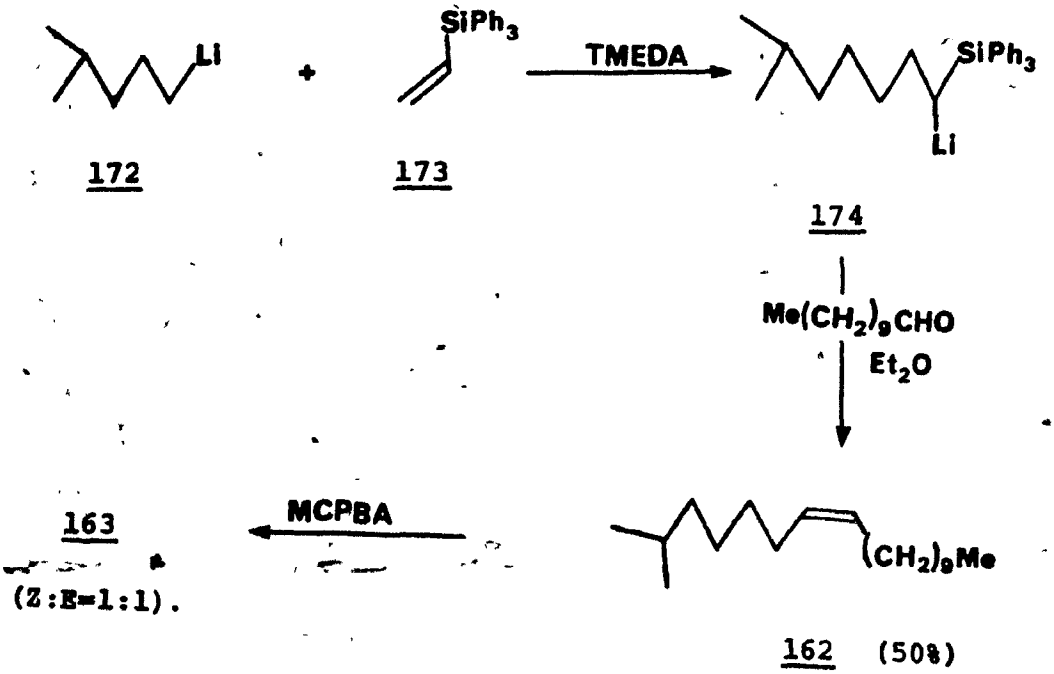
On the other hand, the cis-(-)-isomer of disparlure has been prepared stereoselectively by a similar approach, when n-octyl cuprate was used in the first carbon chain elongation step as described in the original paper[180].

A couple of years ago, our laboratory was involved in the stereoselective synthesis of olefins, using organosilicon compounds as starting materials. Twice already, the gypsy moth sex pheromone has been synthesized[177] via the olefinic intermediate 162. For example, the α-silyl carbanion 174 generated from the reaction of triphenylvinylsilane 173 with 4-methyl-pentyllithium 172 reacts with undecanol to give 162 as a mixture of both geometrical isomers (Z:E = 1:1). Epoxidation of 162 using m-chloroperbenzoic acid gave the corresponding epoxide 163 in quantitative yield. The final compound was found to be a 1:1 mixture of cis and trans isomers (Scheme 8.5).

The second synthesis was stereoselective. Reaction of the α-vinylsilyl carbanion[82], discussed in Chapter IV, was


CO2H
H-C-OH
HO-C-H
CO2H
164
CH2-CH2OTs
H-C-OMe
MeO-C-H
CH2-CO2Me
165
2CuLi
65%
OMe
MeO
CO2Me
166
1. BCl3
2.
THPO
167
i-Bu2AlH
OH
168
n-C7H15CH=PPh3
HO
C7H15
169
1. H2 / Pd
2. TsCl
TsO
C10H21
MeOH / TsOH
170
a. R = H
b. R = Ts
KOH
HO
171
163
(Cis-(+)-isomer).

Scheme 8.4

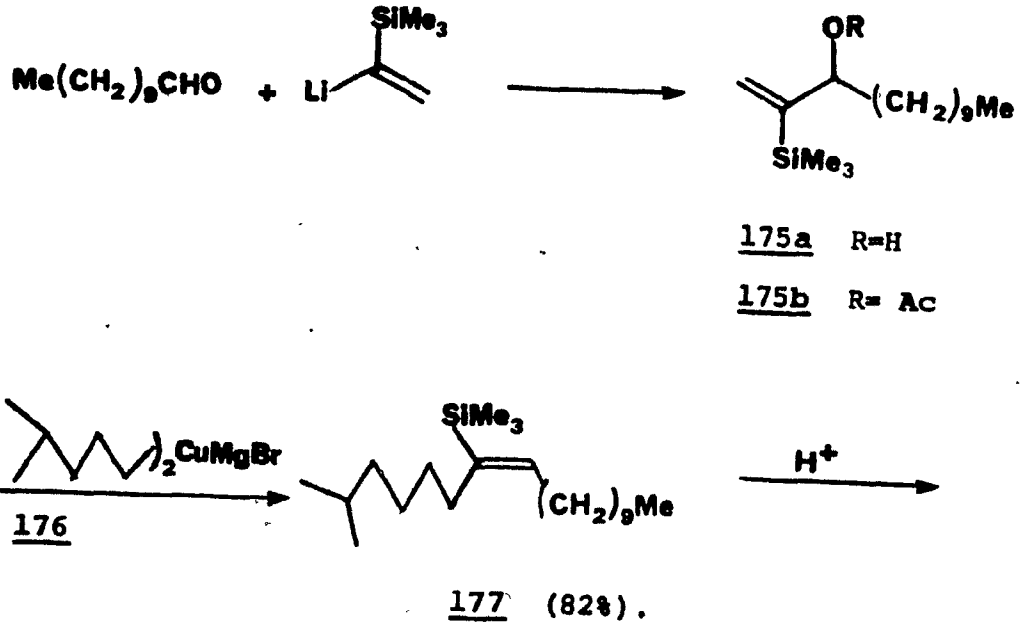


Scheme 8.5

used to provide the E-vinylsilane 177 in good yield and in a stereoselective manner. The reaction of undecanol with α-trimethylsilyl vinyllithium afforded the alcohol 175a (R = H) which was acetylated into 175b.

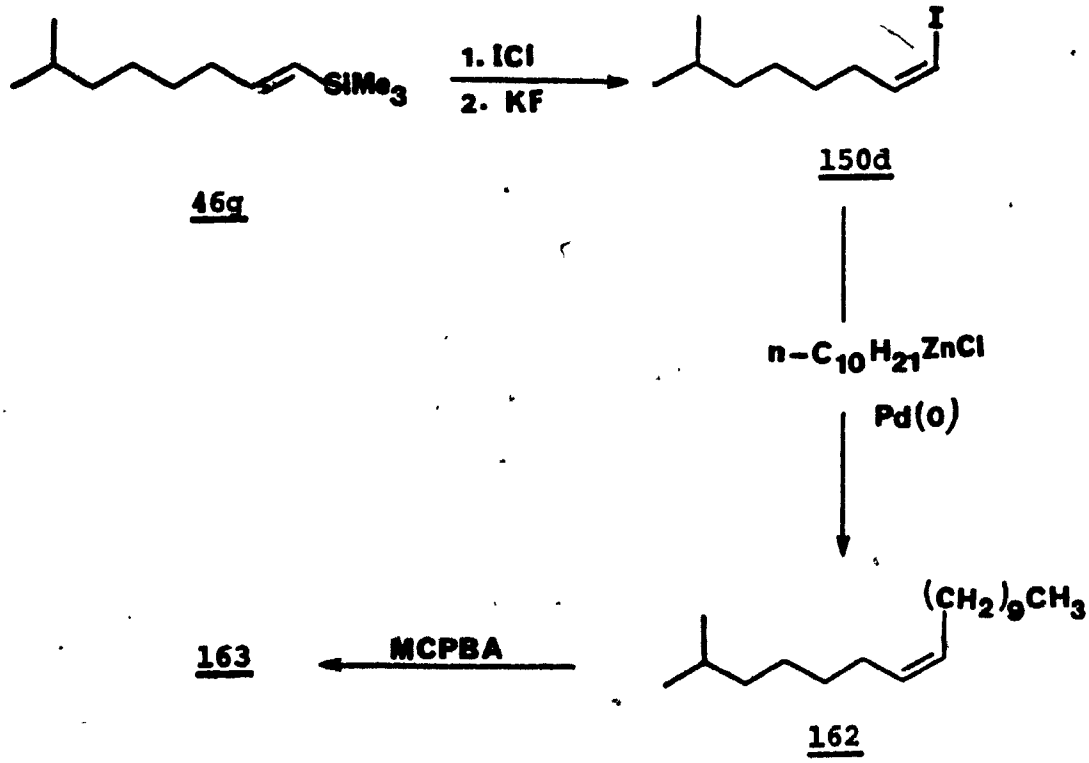
Reaction of 175b with organocopper reagent 176 gave the vinylsilane 177 stereoselectively (E:Z = 87:13). By protodesilylation of 177 with HI (57%) in CH_2Cl_2 the olefin 162 was obtained quantitatively and epoxidized to give the gypsy moth pheromone 163. Both cis and trans isomers were obtained in a ratio of 87:13 respectively.

The recent development in alkylvinylsilane chemistry reported in this thesis has been applied to the synthesis of



Scheme 8.6

disparlure. Interestingly, the stereochemical purity of the final product 163 was improved when compared to both precedent synthesis where silicon compound precursors were used. We obtained the cis and trans epoxides in a ratio of 94:6 respectively. The vinylsilane 46g was reacted with ICl/KF



46g

150d

162

163

to give Z-vinyliodide 150d in 83% yield. Coupling of 150d with n-$C_{10}H_{21}ZnCl$ in the presence of $(Ph_3P)_4Pd$ gave the olefin Z-2-methyl-7-octadecene 162 in 90% yield which was treated with m-chloroperbenzoic acid in dichloromethane to the gypsy moth sex pheromone 163. The methine protons on the epoxide ring appear respectively at δ = 2.8 ppm (cis, 94%) and at δ = 2.6 ppm (trans, 6%).

5 - Synthesis of Z-8-Dodecen-1-yl Acetate (183) and Z-7-Dodecen-1-yl Acetate (186)

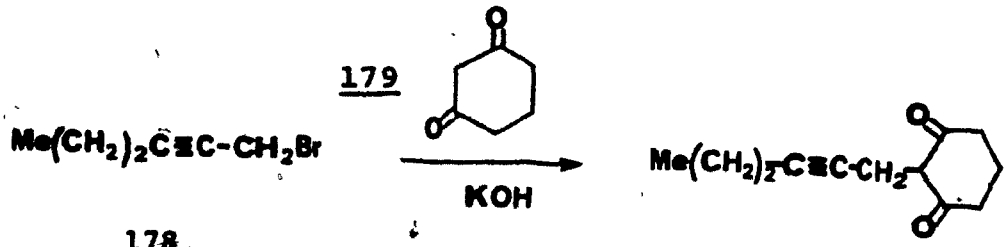
The oriental fruit moth (Grapholita molesta) sex pheromone has been identified to be Z-8-dodecen-1-yl acetate[181] (183). The related geometrical and positional isomers of 183 mixed with the synthetic pheromone exhibit male inhibition by greatly reducing the attractiveness of the acetate 183 in field tests. On the other hand, closely related pest insects G. prunivora, and G. packardi were attracted to the cis and trans-8-dodecenyl acetates, respectively.

In many cases, the acetylenic precursor prepared from various sources was reduced stereoselectively with Pd, Pd-$CaCO_3$, P-2 Ni or $(Sia)_2BH$ to the corresponding alkene up to 98% cis[182-184]. For example, Mori[184] employed a cyclic compound in the carbon chain elongation step, differing from the conventional linear synthesis (paragraph 2 and Scheme 8.7). Cyclohex-

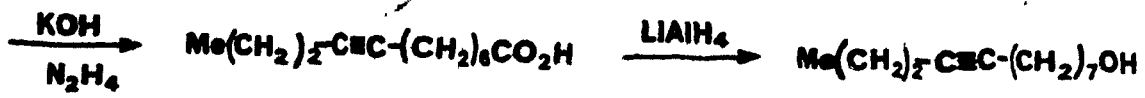
ane-1,3-dione 179 was alkylated with 1-bromo-2-hexyne 178 to give a crystalline compound 180 which was subsequently cleaved with alkali into the acid 181. Reduction of 181 using $LiAlH_4$ followed by semihydrogenation over P-2 Ni gave the alcohol 182 which was then acetylated to afford the insect sex pheromone 183 in 14% overall yield from cyclohexane-1,3-dione.

The "silicon controlled" methodology has been applied to the synthesis of ω-oxy-functionalized alkenes such as 183 and 186 (Scheme 8.8). The vinylsilane 46h (n = 6) was iododesilylated by ICl/KF to give 150e without cleavage of the tetrahydropyranyl protecting group. Coupling of the vinyliodide 150e with C_3H_7ZnCl using $(Ph_3P)_4Pd$ catalyst gave the alkene 184 in 88% yield after purification by chromatography. Compound 184 was converted into 183 by reaction with acetyl chloride in acetic acid. The ratio of Z- and E-isomers in 183 was 96:4 respectively.

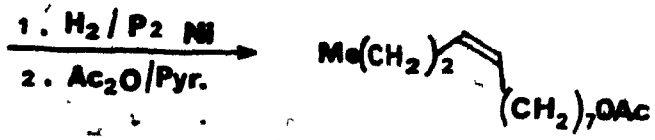
By the same approach described in Scheme 8.8, the cabbage looper (Trichoplusia m.) sex pheromone Z-7-dodecen-1-yl acetate 186 was prepared in 57% overall yield from the vinylsilane 46h. The ratio of Z- and E-isomers was determined by GC to be 92/8 respectively.



178 180

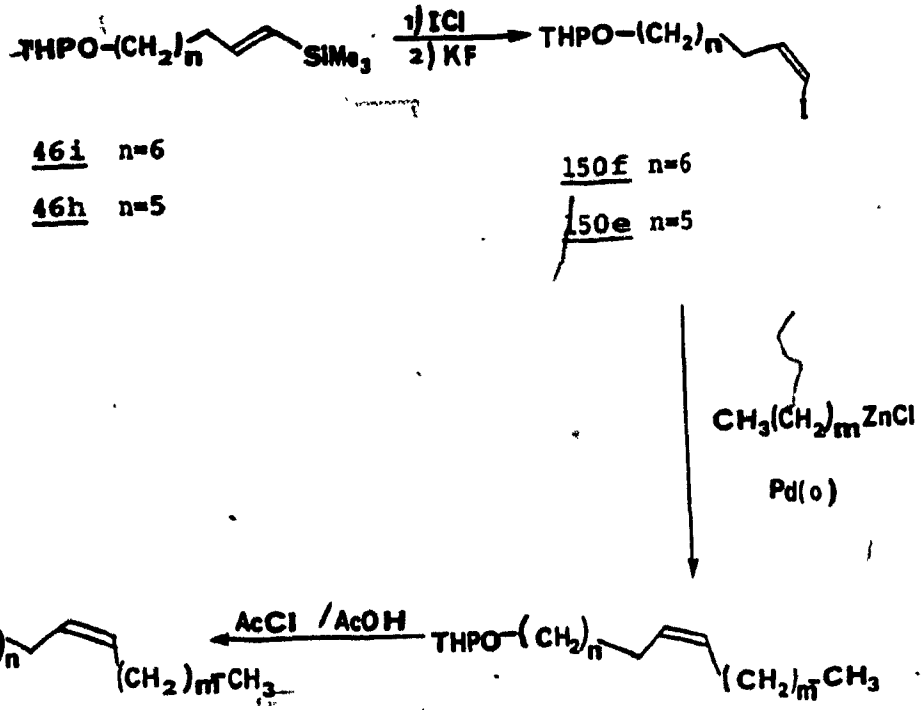


181 182



183

Scheme 8.7



46i n=6
46h n=5

150f n=6
150e n=5

183 n=6, m=2.
186 n=5, m=3.

184 n=6, m=2.
185 n=5, m=3.

Scheme 8.8

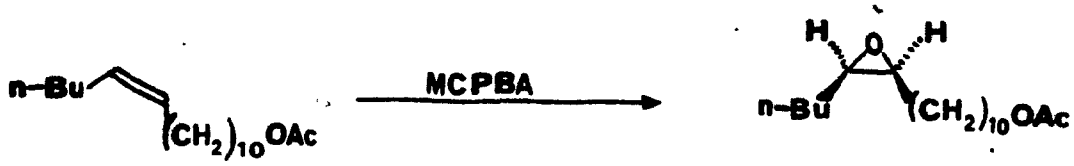
6 - Synthesis of E-11-Hexadecen-1-yl Acetate (189), E-11-Tetradecen-1-yl Acetate (193) and E-11-Tetradecenal (194)

E-11-Hexadecen-1-yl acetate 189 is the sex pheromone emitted by the female sweet potato leaf folder moth (Brachmia macroscopa). It has been prepared from the Z-isomer 187

by inversion of the double bond geometry[185]. Z-11-Hexadecen-1-yl acetate 187 was readily prepared by the conventional Wittig reaction[186]. It was epoxidized by m-chloroperbenzoic acid. Compound 188 was then treated with triphenylphosphine dibromide to give the corresponding dibromo derivative which undergoes trans dehalogenation in a reaction with Zn/DMSO. The E-11-hexadecen-1-yl acetate 189 was obtained in 96% yield (Scheme 8.9).

It is known that the sex pheromone 189 and related compounds 193 or 194 could be provided by the acetylenic routes[187,188], as mentioned earlier in this chapter. However, other approaches could be used to produce the trans olefin in a stereoselective manner. For example, reductive elimination of allylic phosphonate[189] 191 afforded the trans-11-tetradecenal in 73% yield as shown in Scheme 8.10. This compound 192 could be acetylated or oxidized into 193 or 194, respectively.

We have demonstrated in our work that E-alkylvinylsilanes could be converted to either Z- or E-vinyliodides stereoselectively. Consequently, the vinylsilane 112j could serve as a precursor to compounds 189, 193 and 194. When compound 112j was treated with $I_2/AlCl_3$ in dichloromethane at 0°C the E-vinyliodide 152b was obtained in 83% yield, mainly with retention of the geometry at the double bond. The E/Z ratio was 4:1 from GC analysis. Interestingly, we

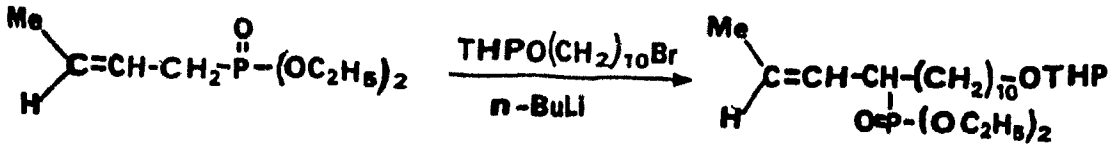


187 188

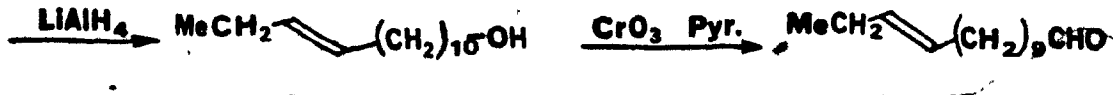
189

Scheme 8.9

found that the E/Z ratio could increase significantly to 13:1 when the reaction is run at -78°C with 2 equivalents of tin chloride instead of aluminum chloride.



190 191



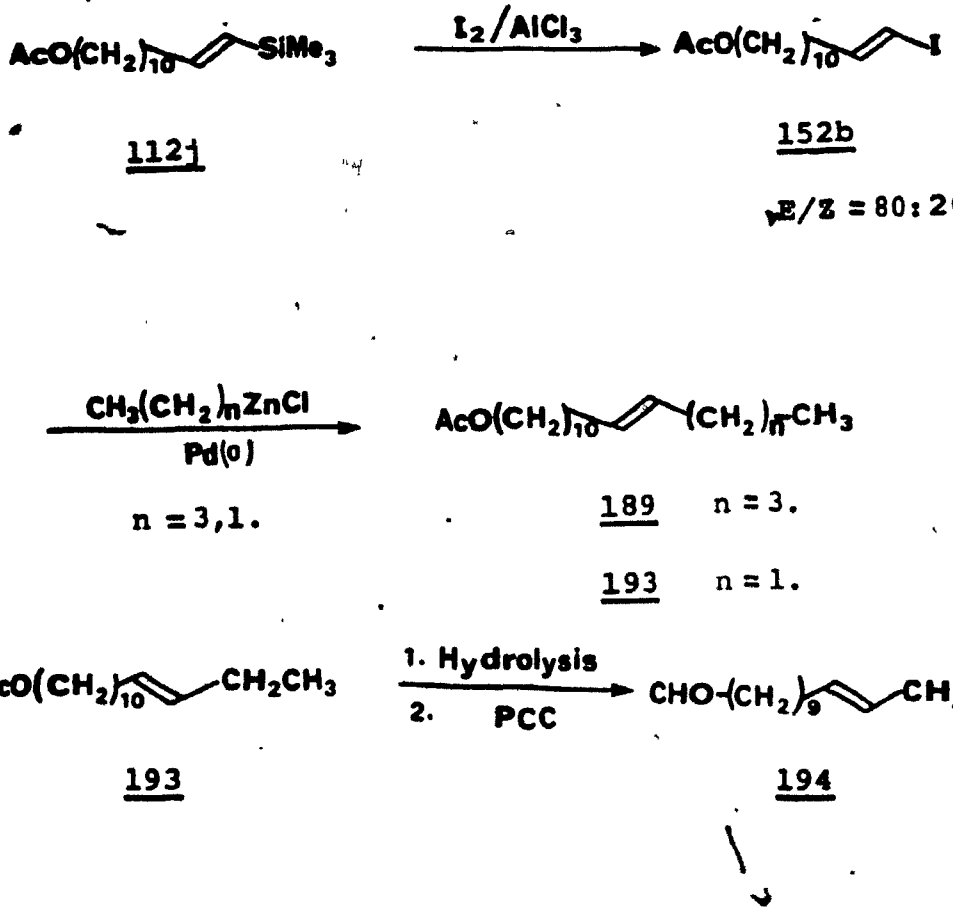
192 194

Scheme 8.10

The sweet potato leaf folder moth sex pheromone was prepared in 82% yield by coupling vinyliodide 152b with n-butylzinc chloride in the presence of a catalytic amount of Pd(0) in the same way as described for compound 186 for instance. A similar coupling reaction of 152b with ethylzinc chloride afforded the oak leaf roller moth pheromone E-11-tetradecen-1-yl acetate 193 in 77% yield after purification by chromatography. In both cases the E/Z ratio = 80/20 was deduced by GC, or via epoxidation and ^{1}H nmr analysis. This ratio could be improved by using tin chloride in the iododesilylation step. On the other hand, the spruce budworm (Choristoneura fumiferana) sex pheromone 194 was prepared from 193 by simple hydrolysis of the acetate protecting group followed by oxidation of the free alcohol to the corresponding aldehyde 194 (Scheme 8.11).

7 - A "Tunable" Stereoselective Synthesis of Sex Pheromones

The sex pheromones of a number of insects are often specific blends of E and Z geometrical isomers of alkenes. For instance, the 11-tetradecenyl acetate produced by the female oak leaf roller moth (Archips semiferanus) is a specific blend of 67:33 of E- and Z-isomers[140]. The same two pheromone components are produced by other species but in a different ratio:



112j

152b

E/Z = 80:20.

n = 3,1.

189 n = 3.

193 n = 1.

193

194

Scheme 8.11

Archips agyrospilus 30/70 (E/Z),

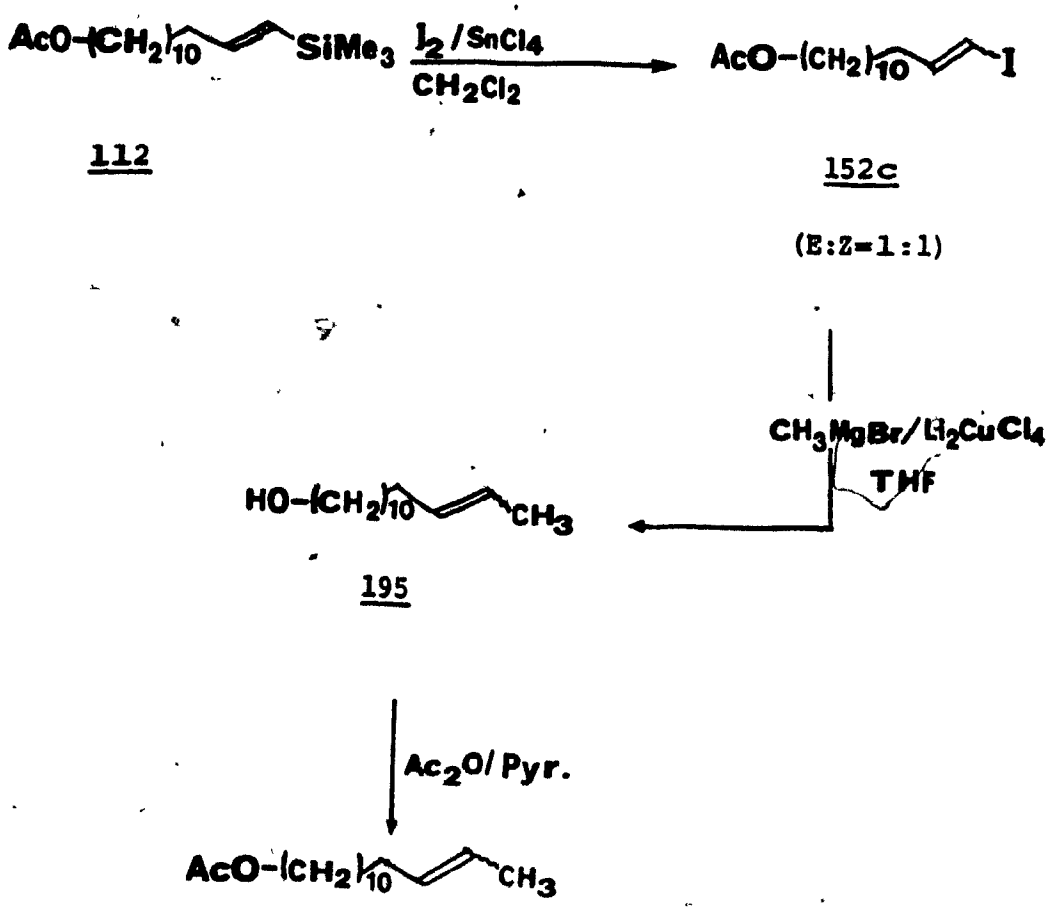
Argyroteania velutinana 7/93,

Archips podana of Europe 50/50.

The most common approach to the synthesis of alkenes with a specific E/Z ratio is done by stereospecific semihydrogenation of alkyne precursors to give the E- and Z-alkenes separately, followed by blending the two geometrically pure isomers in the required ratio. Conceptually such

an approach is inherently inelegant. Since we found that the E-vinylsilane treatment with iodine in the presence of Lewis acids could be used to produce a specific blend of E- and Z-vinyliodides in a one pot reaction (Chapter VII), subsequent coupling with organometallic compounds would provide the desired sex pheromone in the required ratio of E and Z geometrical isomers.

This concept has been applied to the synthesis of Asian corn borer moth (Ostrinia furnicalis) sex pheromone 12-tetradecen-1-yl acetate 196 (E/Z = 50/50) (Scheme 8.12). Compound 112k was reacted with iodine in dichloromethane at 0°C in the presence of 0.4 equivalents of tin chloride to afford vinyliodide 152c (80%) in a ratio of 1:1 for E- and Z-isomers. Subsequent treatment with an excess of methyl magnesium bromide and a catalytic amount of Li_2CuCl_4 gave the coupled product 195. The acetate protecting group was cleaved in this process. Reacetylation with acetic anhydride in pyridine gave the pheromone 196 in 72% overall yield from the vinylsilane 112k. The E/Z ratio = 50/50 was determined by capillary GC analysis.



112

152c

(E:Z=1:1)

195

196 (E:Z=1:1).

Scheme 8.12

EXPERIMENTAL SECTION

Common chemicals were obtained from commercial sources. Iodine and potassium t-butoxide were resublimed before use. n-Butyllithium was titrated according to literature procedure[190,191]. Zinc chloride was dried overnight under vacuum at 75-80°C before use. The organozinc chloride compounds were prepared in the following manner[165,166]. A suspension of alkyl halides, magnesium (1.5 equivalents) and anhydrous zinc chloride (1.5 equivalents) in tetrahydrofuran was refluxed for 3-4 h. A standard solution of dilithium tetrachlorocuprate[173] (~ 0.1 M) was prepared by treating lithium chloride (2 mmol) with copper (II) chloride (1 mmol) in 10 mL of tetrahydrofuran. Tetra-bis(triphenylphosphine)-palladium (0) was prepared according to literature procedure[175]. The palladium (0) catalyst was also prepared in situ by treating dichloro bis(triphenylphosphine)palladium with 2 equivalents of diisobutylaluminum hydride in tetrahydrofuran. The amount of catalyst used in each coupling reaction was 5 mole %.

Organic solvents were dried and distilled prior to use. Hexanes and tetrahydrofuran were distilled from sodium and benzophenone, ether from $LiAlH_4$, dichloromethane (CH_2Cl_2), and carbon tetrachloride (CCl_4) from P_2O_5. Benzene was dried over sodium, tetramethylethylene diamine (TMEDA) over CaH_2, dimethylsulfoxide (DMSO) over NaOH, hexamethylphosphoramide (HMPA) over BaO or CaO, then distilled.

Boiling points and melting points are reported uncorrected. Nuclear magnetic resonance spectra were recorded on Varian XL-200 and T-60A spectrometers using tetramethylsilane (TMS) or chloroform as an internal reference. Chemical shifts were given in the δ scale in parts per million (ppm). Doublet (d), triplet (t), and quartet (q) were recorded at the center of the peaks; other abbreviations used are singlet (s) and broad (b). ^{29}Si and ^{13}C nmr spectra were recorded on Varian XL-200 or Bruker WH spectrometers. Low and high resolution mass spectra were determined on Dupont 21-492B or Hewlett-Packard 5980A instruments. Analytical gas chromatography was performed on a Hewlett-Packard 5730A instrument equipped with a 10 ft. × 0.125 in. column, 6% OV 101 on chromosorb W/HP 80/100 or on a Hewlett-Packard 5890 instrument equipped with a 50 m × 0.2 mm high performance capillary column (crosslinked methyl silicone, film thickness 0.33 μm). Infrared spectra (ir) were obtained on Perkin 297 or Nicolet 7002 MC spectrophotometers. Spectra were calibrated with a 1601 cm^{-1} or 1028 cm^{-1} band of polystyrene film.

Analytical thin layer chromatography (TLC) was performed on Merck Silica Gel 60 F_{254} aluminum-backed plates and visualized by dipping into a solution of ammonium molybdate (2.5 g) and ceric sulfate (1 g) in conc. H_2SO_4/H_2O (10 mL/90 mL) and heated on a hot plate. Purification of reac-

tion products by flash chromatography was performed according to literature procedure using Merck Silica Gel (Kieselgel 60, 40-63 μ or Keiselgel 60 HF_{254}). Preparative high pressure liquid chromatography was performed on Waters Prep 500A liquid chromatograph.

Triethylallylsilane 44b

To a solution of trichloroallylsilane (15.8 g, 90.4 mmol) in 20 mL ether, ethylmagnesium bromide in ether (143 mL, 2.85 M) was added dropwise and the mixture refluxed overnight. It was then quenched with NH_4Cl and washed with a saturated solution of NH_4Cl. The organic layer was dried over Na_2SO_4, evaporated and the residue distilled under vacuum to give 78% of 44b, b.p. 48°C/2 torr, lit.[193c] b.p. 44-46°C/8 torr. ^1H nmr ($CDCl_3$): δ = 5.2 (m, 1 H), 4.4 (m, 2 H), 1.2 (d, J = 8 Hz, 2 H), 0.9-0.4 (m, 15 H). MS (EI): m/e = 150 (M^+, 12%), 127 (21), 115 (76), 99 (27), 97 (11), 88 (27), 87 (100), 71 (42), 59 (57).

Tripropylallylsilane 44c

Tripropylallylsilane 44c was prepared by the same procedure described above in 88% yield after distillation, b.p. 216°/760 torr, lit.[193d] b.p. 216-217°C/748 torr. ^1H nmr ($CDCl_3$): δ = 5.2 (m, 1 H), 4.35 (m, 2 H), 1.7-0.3 (m, 23 H). MS (EI): m/e = 198 (M^+, 2%), 157 (66), 155 (50), 115 (87), 85 (38), 73 (100), 71 (63), 59 (56), 45 (76).

Triphenylallylsilane 44d

A solution of allylbromide (2.06 g, 20 mmol) in 20 mL of ether was added dropwise to a suspension of magnesium (487 mg, 20 mmol) in ether. The mixture was refluxed for one hour and cooled to r.t. before adding 2.95 g (10 mmol) of chlorotriphenylsilane in 20 mL of ether. The mixture was refluxed overnight, filtered and washed with a saturated solution of NH_4Cl. The organic layer was then dried over Na_2SO_4, evaporated, and the crystalline residue purified by chromatography (hexane) to give 2.3 g (77%) of 44d, recrystallized from petroleum ether, m.p. 85-87°C, lit.[193a] m.p. 90°C. ^1H nmr ($CDCl_3$): δ = 7.40 (m, 15 H), 5.9 (m, 1 H), 4.9 (m, 2 H), 2.39 (d, J = 8 Hz, 2 H). MS (EI): m/e = 300 (M^+, 0.4%), 260 (36), 259 (100), 238 (125), 199 (12), 181 (21).

Diphenylmethylallylsilane 44e

Compound 44e was prepared in 72-80% yield from the procedure described above and purified by vacuum distillation, b.p. 117-118°C/0.8 torr, lit.[193b] b.p. 310-311°C/750 torr. ^1H nmr ($CDCl_3$): δ = 7.4 (m, 10 H), 5.9 (m, 1 H), 4.9 (m, 2 H), 2.1 (d, J = 8 Hz, 2 H), 0.53 (s, 3 H).

4-Methyl-1-chloropentane 106

A mixture of 4-methylpentanol (105, 10.218 g, 100 mmol) and 34.1 g of triphenylphosphine in 100 mL of carbon tetrachloride was refluxed for one hour. The white precipi-

tate was then filtered and evaporated. The reaction product was extracted once again with pentane and the organic layer evaporated. The final residue was purified by distillation to give 8.3 g (69%) of 106[177], b.p. 125-126°C/760 torr. ^{1}H nmr ($CDCl_3$): δ = 3.33 (t, J = 6 Hz, 2 H), 1.4 (m, 5 H), 0.8 (d, J = 7 Hz, 6 H).

5-Bromopentan-1-yl-acetate 107

Compound 107 was prepared by literature procedure[112,113]. A mixture of tetrahydropyran (30.1 g, 0.35 mol), acetyl bromide (33.2 g, 0.27 mol) and 8.33 g of zinc bromide was stirred at r.t. for 15 min, then heated in a steam bath for 1 h. The reaction mixture was diluted with benzene (75 mL), and washed with water and sodium bicarbonate (10%). The organic layer was dried over Na_2SO_4, evaporated, and the residue distilled under vacuum to give 46.3 g (82%) of 5- bromopentan-1-yl acetate, b.p. 101°C/0.5 torr, lit.[194] b.p. 90-95°C/0.7 torr. ^{1}H nmr ($CDCl_3$): δ = 4.16 (t, J = 6 Hz, 2 H), 3.4 (t, J = 6 Hz, 2 H), 2.0 (s, 3 H), 1.8 (m, 2 H), 1.5 (m, 4 H). MS (EI): m/e = 150 (30%), 148 (39), 86 (74), 84 (76), 61 (68), 69 (100).

5-Bromopentanol 108a

A mixture of 107 (9.907 g, 47.4 mmol) in ethanol (50 mL) was treated with NaOH (2 N, 100 mL) for 2 h. The ethanol was evaporated, CH_2Cl_2 added to the residue and the

solution washed with diluted HCl, then dried over K_2CO_3. The solvent was evaporated and pure 5-bromopentanol was obtained in quantitative yield (7.815 g, 98%), b.p. 76°C/0.5 torr, lit.[195] b.p. 75-76°C/0.5 torr. ^1H nmr ($CDCl_3$): δ = 3.60 (t, J = 6.4 Hz, 2 H), 3.39 (t, J = 6.7 Hz, 2 H), 1.85 (m, 2 H), 1.70 (s, 1 H), 1.5 (m, 4 H). MS (EI) m/e = 150 (M^+-OH, 5%), 109 (2), 107 (2), 86 (87), 85 (93), 69 (30), 67 (37), 56 (93), 43 (57), 41 (100), 29 (54).

6-Bromo-1-hexanol 108b

Compound 108b was prepared by literature procedure. A mixture of 1,6-hexanediol (20.0 g, 0.169 mol), HBr (70 mL, 48%), and water (50 mL) was heated at 110-120°C and extracted continuously with toluene for 17 h. The organic layer was washed with a saturated solution of K_2CO_3, dried over anhydrous K_2CO_3 and evaporated. The residue was distilled to give 108b[114,115] (24.5 g, 80%), b.p. 100-104°C/9 torr. ^1H nmr ($CDCl_3$): δ = 3.63 (t, J = 6.3 Hz, 2 H), 3.39 (t, J = 6.3 Hz, 2 H), 1.85 (m, 2 H), 1.63 (s, 1 H), 1.5 (m, 6 H). MS (EI): m/e = 164 (3%), 163 (2), 136 (31), 134 (39), 83 (71), 67 (72), 55 (100).

9-Bromononan-1-ol 108c

Compound 108c was prepared by the same procedure described above. The compound was obtained in 88% yield and recrystallized from petroleum ether, m.p. 32-33°C, lit. m.p.

31.5-33°C, lit.[196,197] m.p. 31-33°C. ^{1}H nmr ($CDCl_3$): δ = 3.66 (t, J = 6.3 Hz, 2 H), 3.40 (t, J = 6.5 Hz, 2 H), 1.85 (m, 2 H), 1.59 (s, 1 H), 1.58 (m, 2 H), 1.3 (b, s, 10 H). MS (EI): m/z = 208 (10%), 207 (91), 206 (10), 205 (M^+-1-H_2O, 100), 165 (12), 163 (11), 151 (6), 149 (8), 125 (38). Exact mass of (M^+-H_2O) ion calcd. for $C_9H_{17}Br$: 204.0514, found: 204.0507.

10-Bromodecan-1-ol 108d

Compound 108d was prepared as above in 72% yield, b.p. 114-120°C/0.03 torr, lit.[198] b.p. 153-155°C/0.8 torr. ^{1}H nmr ($CDCl_3$): δ = 6.65 (t, J = 6.3 Hz, 2 H), 3.40 (t, J = 6.5 Hz, 2 H), 1.86 (m, 2 H), 1.6 (s, 1 H, OH), 1.58 (m, 2 H), 1.3 (b, s, 12 H). MS (EI): m/z = 222 (10%), 221 (90), 220 (12), 219 (M^+-1-H_2O, 100), 179 (18), 177 (18), 165 (20), 163 (21), 139 (22).

1-(2-Tetrahydropyranyloxy)-5-bromopentane 110a

A catalytic amount of p-toluenesulfonic acid (0.2 g) was added to a solution of 5-bromopentanol (20.0 g, 0.12 mol) and dihydropyran (15.3 g, 0.18 mol) in ether (100 mL). The mixture was stirred at r.t. for 2 h, washed with a saturated solution of K_2CO_3 and dried over K_2CO_3. The solvent was evaporated and the residue distilled in the presence of a small amount of K_2CO_3 to give 29.9 g (98%) of 110a, b.p.

110°C/2 torr, lit.[195] b.p. 84°C/0.4 torr. ^{1}H nmr ($CDCl_3$): δ = 4.5 (b, s, 1 H), 3.28 (m, 4 H), 3.18 (t, J = 6 Hz, 2 H), 1.8 (m, 2 H), 1.25 (m, 10 H). MS (EI): m/e = 252 (5%), 251 (38), 250 (M^+, 5), 249 (39), 194 (4), 192 (3), 151 (93), 149 (100).

1-(2-Tetrahydropyranyloxy)-6-bromohexane 110b

A mixture of 6-bromo-1-hexanol (23 g, 0.13 mol) and 16.1 g (0.19 mol) of dihydropyran in ether was treated with a catalytic amount of p-toluenesulfonic acid for 2 h to give 31.5 g (93%) of 110b[115] after flash chromatography (hexane:-ethyl acetate 9:1). ^{1}H nmr ($CDCl_3$): δ = 4.5 (b, s, 1 H, 3.7 (m, 2 H), 3.4 (m, 2 H), 3.37 (t, J = 7 Hz, 2 H), 1.83 (m, 2 H), 1.51 (m, 12 H). MS (EI): 265 (100%), 263 (92), 208 (10), 193 (21), 191 (19), 165 (69), 163 (69), 137 (9), 135 (10), 123 (33), 121 (33).

1-(2-Tetrahydropyranyloxy)-9-bromononane 110c

Compound 110c was prepared by the same procedure described above, yield (96%), b.p. 122°C/0.05 torr, lit.[197] b.p. 130-133°C/0.07 torr. ^{1}H nmr ($CDCl_3$): δ = 4.58 (b, s, 1 H), 3.62 (m, 4 H), 3.38 (t, J = 6.8 Hz, 2 H), 1.78 (m, 4 H), 1.62 (m, 4 H), 1.31 (b, s, 12 H). MS (EI): m/e = 241 (11%), 239 (8), 139 (12), 114 (15), 113 (13), 109 (13), 99 (12), 95 (14), 91 (12), 83 (22), 75 (100), 73 (41), 69 (17), 67 (17), 61 (14), 59 (36).

1-(2-Tetrahydropyranyloxy)-10-bromodecane 110d

Compound 110d was prepared by the same procedure as above in 91% yield, b.p. 128-130°C/0.1 torr, lit.[199] b.p. 132°C/0.01 torr. ^{1}H nmr ($CDCl_3$): δ = 4.56 (br, s, 1 H), 3.61 (m, 4 H), 3.38 (t, J = 6.8 Hz, 2 H), 1.77 (m, 4 H), 1.62 (m, 4 H), 1.30 (b, s, 14 H). MS (EI): m/z = 324 (16%), 323 (97), 322 (18), 321 (M+1, 100), 221 (4), 219 (4), 169 (3). Exact mass of (M^+-1) ion calcd. for $C_{15}H_{28}O_2Br$: 319.1273, found: 319.1311.

Alkylation of trimethylsilylallyl lithium with alkyl halides. Typical reaction

A solution of allyltrimethylsilane (571 mg, 5 mmol) and 0.8 mL (5 mmol) of TMEDA in 5 mL of THF was cooled down to -78°C, n-butyllithium (4.2 mL, 1.2 M) was added dropwise and the mixture allowed to warm up to r.t. It was then cooled back to -78°C,alkyl halide 1-bromodecane (1.06 g, 4.8 mmol) in THF was added slowly and the mixture stirred at r.t. overnight. The reaction mixture was quenched with cold water, extracted with ether and the organic layer dried over $MgSO_4$. The residue was purified by distillation to give 1.160 g (96%) of isomeric γ- and α-alkylation products, b.p. 144°C/18 torr. The γ/α ratio = 57/43 was determined by GC-MS (2 m × 6 mm, OV. 101 column; 150 + 8°C/min), RT. 5.78 min and 6.26 min, respectively. MS (EI): m/e 255 (14%), 254

(M^+, 56), 240 (15), 239 (100) for γ-product and m/e = 254 (M^+, 0.5%), 240 (23), 239 (100) for α-product. INEPT ^{29}Si nmr with decoupling experiment: δ = 1.92 ppm (s, allylic Si), and -7,91 ppm (s, vinylic Si).

Synthesis of E-vinylsilanes. Alkylation of trialkylsilylallyl anions with alkyl halides

General Procedure

A suspension of KO^tBu (2.47 g, 22 mmol) in dried hexane (15 mL) was cooled in an ice bath and n-BuLi (13.8 mL, 1.6 M) was added dropwise. The ice bath was removed and the mixture was stirred for 30 min, then cooled down to -78°C. Freshly distilled ether (10 mL) was added, followed with allyltrialkylsilane (22 mmol) in 10 mL ether. The solution was allowed to warm to r.t. for 3.5 h and cooled back to -78°C before addition of the appropriate alkyl halide (10 mmol) in 10 mL ether. The reaction mixture was stirred from -78°C to r.t. for 17 h, then washed with brine, dried over $MgSO_4$ (or K_2CO_3) and evaporated. The residue was dissolved in pentane and filtered through a 2 in. layer of silica gel or purified by flash chromatography. The yield was quantitative. The ratio of γ to α products was determined by GC, ^1H nmr or INEPT ^{29}Si NMR (with decoupling experiment), δ ~ 2 ppm (allylic Si), -8 ppm (vinylic Si).

Selective desilylation

The mixture obtained from the alkylation reaction was diluted with benzene (100 mL), and 0.10 mL of hydroiodic acid (57%) was added. The solution was stirred for 4-6 h and the reaction was followed by GC or ^1H nmr. The reaction mixture was washed with $Na_2S_2O_3$ (10%), dried and evaporated. The residue was purified by fractional distillation or by flash chromatography.

1,3-Bis(trimethylsilyl)propene 44e

To a solution of trimethylallylsilane (10.78 g, 94.4 mmol) in 100 mL ether, 15 mL of TMEDA was added, cooled to -78°C, followed by dropwise addition of n-BuLi (59 mL, 1.6 M). The mixture was allowed to warm up for 2.5 hours, then cooled back to -78°C before addition of 10.272 g (94.6 mmol) of trimethylchlorosilane. The reaction mixture was stirred overnight, washed with ice water. The ether was evaporated and the residue distilled to give 14.66 g (83%) of 44e[95], b.p. 63°C/10 torr. ^1H nmr ($CDCl_3$): δ = 6.05 (dt, J_1 = 18 Hz, J_2 = 6 Hz, 1 H), 5.4 (d, J = 18 Hz, 1 H), 1.67 (d, J = 8 Hz, 2 H), 0.1 (s, 9 H), 0.00 (s, 9 H). MS (EI): m/e = 186 (M^+, 12%), 171 (16), 147 (6), 98 (71), 73 (100). Exact mass of ($M-CH_3$) ion calcd. for $C_8H_{19}Si_2$: 171.1025, found: 171.1063.

1-Trimethylsilyl-1-(E)-dodecene 46a

The ratio of γ/α products was determined by GC to be 6/1 and 80% of 46a was obtained after distillation, b.p. 120°C/24 torr. ^{1}H nmr ($CDCl_3$): δ = 6.05 (dt, J_1 = 18.5 Hz, J_2 = 6.1 Hz, 1 H), 5.67 (dt, J_1 = 18.5 Hz, J_2 = 1.4 Hz, 1 H), 2.1 (m, 2 H), 1.3 (b, s, 16 H), 0.9 (t, J = 6 Hz, 3 H), 0.07 (s, 9 H). MS (EI): m/z = 240 (20%), 239 (47), 205 (3), 114 (31), 99 (29), 85 (19), 81 (20), 73 (100), 59 (49). Exact mass calcd. for $C_{15}H_{32}Si$: 240.2273, found: 240.2291.

1-Trimethylsilyl-1-(E)-pentadecene 46b

The reaction was performed as described above (γ/α = 11/2). Compound 46b was obtained after desilylation and fractional distillation, b.p. 170°C/4 torr. ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.6 (dt, J_1 = 18.5 Hz, J_2 = 1.4 Hz, 1 H), 2.06 (m, 2 H), 1.24 (b, s, 22 H), 0.86 (t, J = 6.5 Hz, 3 H), 0.00 (s, 9 H). IR (neat): 2950, 2920, 2890, 1620, 1410, 1245, 980, 860-830 cm^{-1}. MS (EI): m/e = 282 (5%), 267 (68), 114 (48), 111 (16), 99 (26), 73 (100), 67 (15), 59 (54). Exact mass calcd. for $C_{18}H_{38}Si$: 282.2743, found: 282.2738.

1-Trimethylsilyl-1-(E)-undecene 46c

Compound 46c was prepared from n-chlorooctane. The γ/α ratio was 5/1 and 75% of 46c was obtained after desilylation, b.p. 140°C/50 torr. ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1

= 18.0 Hz, J_2 = 6 Hz, 1 H), 5.8 (d, J = 18 Hz), 2.1 (m, 2 H), 1.4 (b, s, 14 H), 0.9 (t, J = 6 Hz, 3 H), 0.2 (s, 9 H). MS (EI) m/e = 226 (M^+, 13%), 212 (16), 211 (70), 114 (17), 99 (27), 85 (17), 73 (100). Exact mass calcd. for $C_{12}H_{30}Si$: 226.2117, found: 226.2144.

1-Trimethylsilyl-1-(E)-hexene 46e

The γ/α ratio was 5/1 and 80% of pure 46e was obtained after filtration and evaporation. ^1H nmr ($CDCl_3$): δ = 6.1 (dt, J_1 = 18 Hz, J_2 = 6.0 Hz, 1 H), 5.6 (d, J = 18 Hz, 1 H), 2.1 (m, 2 H), 1.4 (m, 4 H), 1.0 (t, J = 6 Hz, 3 H), 0.1 (s, 9 H). MS (EI): m/e = 156 (M^+, 4%), 146 (26), 142 (49), 141 (100), 115 (16), 114 (55), 113 (29), 99 (50), 85 (40), 83 (31), 81 (28), 73 (63), 59 (99). Exact mass calcd. for $C_9H_{20}Si$: 156.1334, found: 156.1320.

1-Trimethylsilyl-7-methyl-1-(E)-octene 46g

The γ/α ratio was 4/1 and compound 46g (70%) was obtained after desilylation and distillation, b.p. 98-103°C/760 torr. ^1H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.54 (dt, J_1 = 18.5 Hz, J_2 = 1.4 Hz, 1 H), 2.05 (m, 2 H), 1.28 (m, 7 H), 0.82 (d, J = 7.2 Hz, 6 H), 0.01 (s, 9 H). MS (EI): m/e = 198 (M^+, 5%), 184 (14), 183 (34), 181 (13), 127 (12), 125 (19), 111 (21), 99 (35), 85 (25), 73 (100). Exact mass calcd. for $C_{12}H_{26}Si$: 198.1804, found: 198.1786.

8-Trimethylsilyl-1-(2-tetrahydropyranyloxy)-7-(E)-octene 46h

The reaction time was 36 h, γ/α = 9/1. A yield of 88% of pure 46h was obtained after desilylation and chromatography. ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18 Hz, J_2 = 6 Hz, 1 H), 5.5 (d, J = 18 Hz, 1 H), 4.6 (b, s, 1 H), 3.6 (m, 4 H), 2.0 (m, 2 H), 1.6-1.25 (m, 14 H), 0.00 (s, 9 H). MS (EI): m/z = 284 (M^+, 3%), 211 (10), 200 (22), 167 (49), 159 (84), 156 (28), 143 (28), 141 (100), 129 (67), 126 (14), 125 (37).

9-Trimethyl-1-(2-tetrahydropyanyloxy)-8-(E)-nonene 46i

The vinylsilane 46i was obtained in 85% yield after desilylation and chromatography (hexane/ethyl acetate 9/1). ^{1}H nmr ($CDCl_3$): δ = 6.1 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.6 (d, J = 18.5 Hz, 1 H), 4.5 (b, s, 1 H), 3.7 (m, 2 H), 3.2 (m, 2 H), 2.1 (m, 2 H), 1.5-1.28 (m, 16 H), 0.01 (s, 9 H). MS (EI): m/z = 298 (M^+, 2%), 297 (7), 213 (11), 197 (28), 173 (28), 159 (100), 156 (74), 141 (77), 129 (51), 123 (35).

12-Trimethylsilyl-1-(2-tetrahydropyranyloxy)-11-(E)-dodecene 46j

The vinylsilane 46j was obtained in 89% yield after desilylation and purification by HPLC (hexane:ethyl acetate 10:1). ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6

Hz, 1 H), 5.56 (d, J = 18.5 Hz, 1 H), 4.55 (b, s, 1 H), 3.76 (m, 2 H), 3.39 (m, 2 H), 2.04 (m, 2 H), 1.54 (m, 6 H), 1.25 (b, s, 16 H), 0.1 (s, 9 H). MS (EI): m/e = 341 (M+1, 2%), 269 (7), 257 (19), 160 (17), 159 (100).

13-Trimethylsilyl-1-(2-tetrahydropyranyloxy)-12-(E)-tridecene 46k

Compound 46k was obtained in 85% yield after desilylation and purification by HPLC (hexane:ethyl acetate 10:1). ^{1}H nmr ($CDCl_3$): δ = 6.1 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.56 (d, J = 18.5 Hz, 1 H), 4.55 (b, s, 1 H), 3.75 (m, 2 H), 3.39 (m, 2 H), 2.05 (m, 2 H), 1.54 (m, 6 H), 1.25 (b, s, 18 H).

1-Trimethylsilyl-1-(E)-pentadecene 46ℓ

The γ/α ratio was 18/1. A yield of 91% of 46ℓ was obtained after desilylation and distillation, b.p. 168°C/0.4 torr. ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6.5 Hz, 1 H), 5.5 (dt, J_1 = 18.5 Hz, J_2 = 1.4 Hz, 1 H), 2.1 (m, 2 H), 1.29 (b, 22 H), 0.9 (t, J = 7.5 Hz, 9 H), 0.86 (t, J = 6.5 Hz, 3 H), 0.5 (q, J = 7.8 Hz, 6 H). MS (EI): m/z = 324 (1.5%), 296 (62), 295 (100). Exact mass calcd. for $C_{12}H_{44}Si$: 324.3212, found: 324.3212.

1-Triethylsilyl-1-(E)-hexene 46m

The γ/α ratio was 16/1. A yield of 92% of 46m was obtained after desilylation and distillation, b.p. 81°C/20 torr. ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.4 (d, J = 18.5 Hz, 1 H), 2.0 (m, 2 H), 1.2-0.9 (m, 16 H), 0.5 (m, 6 H). MS (EI): m/e = 198 (M^+, 15%), 170 (24), 169 (100), 142 (17), 141 (75), 113 (40), 99 (15), 87 (26), 73 (15), 71 (13), 69 (12), 59 (37). Exact mass calcd. for $C_{12}H_{26}Si$: 198.1803, found: 198.1772.

9-Triethylsilyl-1-(2-tetrahydropyranyloxy)-8-(E)-nonene 46p

The alkylation reaction was performed for 36 h (γ/α = 22/1). The residue obtained after desilylation was purified by HPLC (hexane/ethyl acetate 10:0.1) to give a colourless oil of 46p (91%). ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.6 Hz, J_2 = 6.5 Hz, 1 H), 5.5 (d, J = 18.6 Hz, 1 H), 4.5 (b, s, 1 H), 3.7 (m, 2 H), 3.3 (m, 2 H), 2.04 (m, 2 H), 1.5-1.28 (m, 16 H), 0.86 (t, J = 6 Hz, 9 H), 0.5 (q, J = 6 Hz, 6 H). MS (EI): m/e = 340 (M^+, 4%), 339 (3), 311 (19), 255 (11), 225 (81), 227 (85), 187 (32), 169 (19), 159 (41), 131 (100).

1-Tripropylsilyl-1-(E)-hexene 46q

The γ/α ratio was 46/1. A yield of 95% of pure vinylsilane 46q was obtained after desilylation and distillation, b.p. 90-92°C/1 torr. ^{1}H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5

Hz, J_2 = 6 Hz, 1 H), 5.58 (d, J = 18.5 Hz, 1 H), 2.07 (m, 2 H), 1.28 (m, 9 H), 0.9 (m, 22 H), 0.53 (m, 6 H). MS (EI): m/e = 240 (23%), 197 (85), 155 (100), 113 (56), 99 (35), 97 (221), 85 (59), 57 (34). Exact mass calcd. for $C_{15}H_{32}Si$: 240.2273, found: 240.2286.

9-Tripropylsilyl-1-(2-tetrahydropyranyloxy)-8-(E)-nonene 46t

The alkylation reaction was performed as described above for 36 h (γ/α = 36/1). Compound 46t (93%) was obtained after desilylation and chromatography (HPLC). ^1H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.5 (dt, J_1 = 18.5 Hz, J_2 = 1.4 Hz, 1 H), 4.5 (b, s, 1 H), 3.7 (m, 2 H), 3.37 (m, 2 H), 2.04 (m, 2 H), 1.52-1.3 (m, 16 H), 0.92 (t, J = 7.1 Hz, 9 H), 0.51 (m, 6 H). MS (EI): m/z = 382 (M^+, 4%), 339 (6), 255 (56), 213 (31), 211 (79), 173 (100), 169 (17), 159 (25), 157 (29), 131 (88).

1-Triphenylsilyl-1-(E)-hexene 46y

The reaction time was 36 h (γ/α = 16/1) and 77% of 46y was obtained after desilylation and chromatography (hexane). The final product was recrystallized from petroleum ether, m.p. 60-61°C. ^1H nmr ($CDCl_3$): δ = 7.47 (m, 18 H), 6.1 (s, 2 H), 2.2 (b, s, 2 H), 1.3 (m, 4 H), 0.87 (t, J = 6.6 Hz, 3 H). MS (EI): m/e = 324 (25%), 285 (56), 259 (61), 207 (38),

183 (100), 105 (56), 53 (22). Exact mass calcd. for $C_{24}H_{26}Si$: 342.1804, found: 342.1786.

1,3-Bis(trimethylsilyl)-1-(E)-pentadecene 103

A solution of 1,3-bis(trimethylsilyl)propene (5.6 g, 30 mmol), and 4.6 mL TMEDA in 60 mL THF was cooled to -78°C, n-BuLi (18.8 mL, 1.6 M) was added dropwise and the mixture allowed to warm up for 3.5 h, then cooled back to -78°C, after which 4.985 g (20 mmol) of bromododecane in 10 mL of THF was slowly added. The mixture was stirred overnight, washed with brine, dried over Na_2SO_4 and evaporated. The residue was distilled to give 9.1 g (86%) of 103, b.p. 95-100°C/0.1 torr. ^1H nmr (60 MHz): δ = 6.0 (dd, J_1 = 18 Hz, J_2 = 6 Hz, 1 H), 5.4 (d, J = 18 Hz, 1 H), 1.9 (m, 1 H), 1.3 (b, 22 H), 1.0 (t, J = 6 Hz, 3 H), 0.1 (s, 9 H), 0.00 (s, 9 H). ^{29}Si nmr (decoupling mode): δ = 1.56 ppm (s, allylic silyl), -8.5 (s, vinylic silyl). MS (EI): m/e = 354 (1%), 151 (21), 149 (27), 137 (59), 135 (100), 85 (42), 75 (30), 73 (82), 71 (51), 69 (34), 54 (56), 43 (74).

Selective cleavage of tetrahydropyranyl ether in the presence of the vinylsilane functional group. Preparation of 8-trimethylsilyl-7-octen-1-ol 111h

Hydrochloric acid (5 drops, 3 N) was added to a solution of 46h (1.61 g, 5.66 mmol) in methanol (20 mL), the mixture was stirred at r.t. for 5 h, then concentrated.

Dichloromethane was added to the residue and the solution washed with Na_2CO_3 (10%), dried over K_2CO_3 and evaporated. The final residue was purified by chromatography (hexane: ethyl acetate = 7:3) to give 1.042 g (92%) of 111h. ^1H nmr ($CDCl_3$): δ = 6.0 (dt, J_1 = 18.5 Hz, J_2 = 6.1 Hz, 1 H), 5.5 (dt, J_1 = 18.5 Hz, J_2 = 1.4 Hz, 1 H), 3.6 (m, 2 H), 2.06 (m, 2 H), 1.56 (s, 1 H, OH), 1.55 (m, 2 H), 1.34 (m, 16 H), 0.01 (s, 9 H). MS (EI): m/z = 200 (M^+, 0.5%), 111 (14), 97 (13), 85 (15), 82 (24), 74 (100), 73 (64). Exact mass calcd. for $C_{11}H_{24}SiO$: 200.1595, found: 200.1599.

12-Trimethylsilyl-11-(E)-dodecen-1-yl acetate 112j

To a solution of 1.88 g (5.5 mmol) of 46j in 25 mL methanol, 3 drops of HCl (3 N) were added and the mixture stirred at r.t. for 2 h. A trace of K_2CO_3 was added and the solvent evaporated. Ether was added to the residue and the solution washed twice with K_2CO_3 (10%), dried over K_2CO_3 and evaporated. The crude mixture was treated with acetic anhydride in pyridine overnight, then codistilled with toluene. Ether was added and the solution washed with brine. The organic layer was dried, evaporated and the final residue purified by chromatography (hexane:ethyl acetate = 10:0.1) to give 1.42 g (86% overall yield) of 62b, b.p. 112-114°C/-0.05 torr. ^1H nmr ($CDCl_3$): δ = 6.1 (dt, J_1 = 18.5 Hz, J_2 = 6 Hz, 1 H), 5.6 (d, J = 18.5 Hz, 1 H), 4.0 (t, J = 6 Hz, 2

H), 2.0 (s, 3 H), 1.35 (b, 16 H), 0.2 (s, 9 H). IR (neat): 2940, 2880, 1750, 1620, 1470, 1370, 1250, 1040, 990, 870, 840 cm^{-1}. MS (EI): m/z = 298 (4%), 283 (18), 135 (52), 118 (30), 117 (100), 93 (23), 85 (32), 82 (61), 75 (79), 68 (61), 59 (63), 55 (65), 43 (79). Exact mass calcd. for $C_{17}H_{34}O_2Si$: 298.3338, found: 298.3333.

13-Trimethylsilyl-12-(E)-tridecen-1-yl acetate 112k

Using the procedure described above, 90% of 112k was obtained from compound 46k. ^1H nmr (60 MHz): δ = 6.1 (dt, J_1 = 18 Hz, J_2 = 6.1 Hz, 1 H), 5.6 (d, J = 18.5 Hz, 1 H), 3.9 (t, J = 6 Hz, 2 H), 2.0 (s, 3 H), 1.35 (b, s, 18 H), 0.2 (s, 9 H). MS (EI): m/e = 312 (M^+, 10%), 297 (22), 133 (34), 117 (100), 99 (27), 83 (26), 73 (63), 67 (33). Exact mass calcd. for $C_{18}H_{36}O_2Si$: 312.2484, found: 312.2549.

Bromodesilylation. Preparation of 1-(Z)-bromododecene 141a

To a solution of 46a (480 mg, 2 mmol) in 10 mL dichloromethane at 0°C, bromine (~ 2 mmol) in CH_2Cl_2 was added dropwise. The addition was stopped at the first drop of bromine giving a persistent yellowish colour. The reaction mixture was washed with $Na_2S_2O_3$ (10%), dried over N_2SO_4 and evaporated. The residue was diluted with 4 mL CH_2Cl_2 and treated with NaOMe/MeOH according to literature procedure to give 71% of 141a after chromatography (hexane). ^1H nmr

($CDCl_3$): δ = 6.1 (b, s, 2 H), 2.2 (m, 2 H), 1.3 (b, 16 H), 0.9 (t, J = 6 Hz, 3 H). MS (EI): m/e = 249 (1%), 248 (7), 247 (1), 246 (M^+, 8), 169 (22), 148 (23), 141 (20), 121 (24), 119 (33), 111 (48), 97 (78), 83 (56), 71 (68), 69 (79), 55 (100), 43 (97). Exact mass calcd. for $C_{12}H_{23}Br$: 246.0984, found: 246.0941.

Iododesilylation of E-vinylsilanes with iodine monochloride

General procedure

A solution of vinylsilanes in CCl_4 (~ 5 mmol/10 mL) was cooled to 0°C and iodine monochloride (1.1 equiv.) in CCl_4 was added dropwise. Fifteen minutes after the addition, the reaction mixture was washed with $Na_2S_2O_3$ (10%). The organic solution was dried ($MgSO_4$ or K_2CO_3) and evaporated. A mixture of DMSO (10 mL) and 1.5 equiv. of $KF.2H_2O$ was added to the residue and the mixture stirred at r.t. for 4 h, then extracted three times with ether/water. The ethereal solution was dried, evaporated and the final product purified by flash chromatography.

(Z)-1-Iodo-1-pentadecene 150a

By the procedure described above, 3.38 g (12 mmol) of 46b was treated with ICl and $KF.2H_2O$ to give 3.36 g (84%) of vinyl iodide 150a after chromatography (hexane). ^1H nmr ($CDCl_3$): δ = 6.1 (b, s, 2 H), 1.54 (m, 2 H), 1.23 (b, s, 22

H), 0.86 (t, J = 6.5 Hz, 3 H). IR (neat): 3070, 2960, 2930, 2850, 1610, 1450, 1360, 1260, 820, 745, 705, 666, 610 cm^{-1}. MS (EI): m/z = 336 (12%), 128 (11), 154 (23), 97 (77), 83 (86), 71 (83), 55 (100). Exact mass calcd. for $C_{15}H_{29}I$: 336.1316, found: 336.1306.

(Z)-1-Iodo-decene 150b

Using the same procedure as above, 78% of 150b was obtained after chromatography. ^1H nmr ($CDCl_3$): δ = 6.0 (b, s, 2 H), 2.1 (m, 2 H), 1.2 (b, s, 12 H), 0.9 (t, J = 6 Hz, 3 H). MS (EI): m/z = 266 (M^+, 63%), 197 (9), 183 (4), 167 (29), 154 (27), 97 (48), 83 (100), 70 (41), 69 (82), 67 (34), 57 (91), 55 (75), 41 (97), 39 (37), 28 (48).

(Z)-1-Iodo-tridecene 150c

By the same procedure as above, 81% of 150c was obtained. ^1H nmr ($CDCl_3$): δ = 6.13 (b, s, 2 H), 2.1 (m, 2 H), 1.23 (b, s, 18 H), 0.85 (t, J = 6 Hz, 3 H). MS (EI): m/z = 308 (M^+, 39%), 239 (8), 167 (40), 154 (34), 128 (41), 111 (42), 97 (75), 85 (49), 83 (87), 69 (91), 67 (31), 57 (100), 55 (87).

(Z)-1-Iodo-7-methyl-1-octene 150d

By the same procedure, 1.51 g (6.28 mmol) of vinylsilane 46g was treated with ICl and $KF.2H_2O$, and 1.35 g (85%) of 150d was obtained. ^1H nmr ($CDCl_3$): δ = 6.15 (s, 2 H),

2.1 (m, 2 H), 1.3 (m, 7 H), 0.84 (d, J = 6.5 Hz, 6 H). IR (neat): 3075, 2795, 1604, 1446, 1371, 1356, 1280, 1170, 1070, 1007, 935, 680 cm^{-1}. MS (EI): m/z = 252 (3%), 167 (36), 83 (72), 81 (26), 68 (84), 55 (100). Exact mass calcd. for $C_9H_{17}I$: 252.0377, found: 252.0332.

(Z)-8-Iodo-1-(2-tetrahydropyranyloxy)oct-7-ene 150e

By the general procedure described above, 46h (4.55 g, 15.3 mmol) was converted into 4.33 g (84%) of vinyl iodide 150e. ^1H nmr ($CDCl_3$): δ = 6.14 (s, 2 H), 4.52 (b, s, 1 H), 3.74 (m, 2 H), 3.37 (m, 2 H), 2.08 (m, 2 H), 1.52-1.34 (m, 14 H). ^{13}C nmr: 141.30, 98.79, 82.12, 67.50, 62.21, 34.54, 30.76, 29.76, 29.56, 28.87, 27.85, 26.02, 25.48, 19.65. MS (EI): m/z = 338 (M^+, 2%), 337 (5), 211 (40), 180 (80), 167 (100).

(Z)-9-Iodo-1-(2-tetrahydropyranyloxy)non-8-ene 150f

By the same procedure, 3.57 g (12 mmol) of 46i was allowed to react with ICl and $KF.2H_2O$, and 3.65 g (86%) of 150f was obtained. ^1H nmr ($CDCl_3$): δ = 6.14 (s, 2 H), 4.53 (b, s, 1 H), 3.40 (m, 2 H), 3.74 (m, 2 H), 2.10 (m, 2 H), 1.53-1.20 (m, 16 H). MS (EI): m/z = 352 (0.7%), 180 (46), 167 (270), 124 (3), 123 (22), 85 (100), 84 (21), 56 (60), 55 (95).

Lewis acid mediated iododesilylation

1-(E)-Iodopentadecene 152a

A solution of iodine (508 mg, 2 mmol) and 521 mg (2 mmol) of tin chloride in 10 mL CH_2Cl_2 was cooled to -78°C. Compound 46b dissolved in 10 mL CH_2Cl_2 was added dropwise and the reaction mixture stirred for 2 h, washed with $Na_2S_2O_3$ (10%), dried over Na_2SO_4, and evaporated to give 95% of 152a from GC analysis. The residue was then purified by chromatography (pentane) to give 698 mg (90%) of 152a, E/Z = 18/1. ^1H nmr ($CDCl_3$): δ = 6.49 (dt resolved as quintet, J_1 = 14.3 Hz, J_2 = 7 Hz, 1 H), 5.94 (dt, J_1 = 14.32 Hz, J_2 = 1.4 Hz, 1 H) for the trans isomer, 6.13 (s, 2 H for the cis isomer), 2.0 (m, 2 H), 1.24 (b, s, 22 H), 0.83 (t, J = 6 Hz, 3 H).

12-(E)-Iodododecen-1-yl acetate 152b

A suspension of aluminum chloride (248 mg, 1.86 mmol) and iodine (472 mg, 1.86 mmol) in 10 mL CH_2Cl_2 was cooled to 0°C, then 504 mg (1.7 mmol) of 112j in 5 mL of CH_2Cl_2 was added dropwise. The reaction mixture was stirred at 0°C for 1 h and quenched with $Na_2S_2O_3$ (10%). The organic layer was washed twice with NH_4Cl (10%), dried over Na_2SO_4, concentrated and the residue purified by chromatography to give 468 mg (78%) of 152b, E/Z = 80/20. ^1H nmr ($CDCl_3$): δ = 6.48 (dt resolved as quintet, J_1 = 14.32 Hz, J_2 = 7.1 Hz, 1 H), 5.93

(dt, J_1 = 14.32 Hz, J_2 = 1.4 Hz, 1 H) for the trans isomer, 6.12 (s, 2 H, cis isomer), 4.0 (t, J = 6 Hz, 2 H), 2.02 (s, 3 H), 1.58 (m, 2 H), 1.24 (b, s, 16 H). IR (neat): 3040, 2940, 2860, 1745, 1610, 1465, 1440, 1390, 1370, 1240, 1040, 950, 745, 660, 610. MS (EI): m/e = 353 (M+1, 100%), 293 (37), 251 (3), 237 (10), 223 (8), 167 (11), 166 (12), 165 (79), 109 (15).

(Z)-9-Tricosene 155

To a solution of (Z)-1-iodo-1-pentadecene 150a, 1.41 g, 4.2 mmol) in THF (10 mL), $(Ph_3P)_4Pd$ (242 mg) was added followed with n-octylzinc chloride (10 mL, ~ 1 M in THF). The mixture was kept at room temperature overnight, then diluted with ether and washed with a saturated solution of NH_4Cl. The organic layer was dried over $MgSO_4$ and evaporated. Compound 155 was obtained quantitatively (> 96% from GC analysis). Fractional distillation of the residue gave 1.1 g (81%) of pure compound 155 (Z/E = 96/4), b.p. 136-140°C/0.1 torr. ^1H nmr ($CDCl_3$): δ = 5.31 (t, J = 4.6 Hz, 2 H), 2.0 (m, 4 H), 1.22 (b, 34 H), 0.85 (t, J = 6.5 Hz, 6 H). ^{13}C NMR ($CDCl_3$): δ = 129.92, 31.93, 29.74, 29.56, 29.36, 28.44, 27.26, 22.72, 14.04. MS (EI): m/e = 322 (M^+, 3%), 111 (12), 97 (31), 84 (16), 83 (43), 69 (53), 57 (81), 56 (44), 55 (79), 43 (100). Exact mass calcd. for $C_{23}H_{46}$: 322.3599, found: 322.3566. Determination of Z/E: An aliquot

of 155 was epoxidized in CH_2Cl_2 solution using 1.2 equiv. of MCPBA. The reaction mixture was washed with sodium bicarbonate solution, dried over $MgSO_4$ and evaporated. The product was purified by flash chromatography. ^1H nmr: δ = 2.89 (methines cis, 96%), 2.59 (methines trans, 4%).

(Z)-2-Methyl-7-octadecene 162

To a solution of (Z)-vinyliodide 150d (1.33 g, 5.2 mmol) in THF (10 mL), $(Ph_3P)_4Pd$ (300 mg) was added followed with n-decylzinc chloride (11 mL, ~ 1 M in THF) and the mixture was stirred at room temperature overnight. Ether (30 mL) was added before extraction with a saturated solution of NH_4Cl. The ethereal solution was dried over $MgSO_4$, evaporated and the residue purified by distillation to give 1.32 g (95%) of 162[177,200], b.p. 102°C/0.1 torr, lit.[177] b.p. 101-103°C/0.09 torr. ^1H nmr ($CDCl_3$): δ = 5.34 (t, J = 4.5 Hz, 2 H), 2.0 (m, 4 H), 1.25 (s, 23 H), 0.85 (m, 9 H). ^{13}C nmr: δ = 19.92, 38.96, 31.95, 30.06, 29.68, 29.36, 28.08, 27.26, 27.09, 22.67, 14.09. MS (EI): m/z = 267 (20%), 266 (25), 111 (35), 97 (44), 96 (18), 95 (20), 85 (50), 84 (25), 83 (63), 82 (28), 69 (66), 67 (37), 57 (100), 55 (59). Exact mass calcd. for $C_{19}H_{38}$: 266.2973, found: 266.2935.

Cis-7,8-epoxy-2-methyl-octadecene 163 (disparlure)

A solution of 162 (266 mg, 1 mmol) in CH_2Cl_2 (10 mL) was cooled in an ice bath. MCPBA (1.2 equiv.) in 10 mL CH_2Cl_2 was added. The mixture was stirred for 4-6 h, then washed with sodium bicarbonate solution. The organic layer was dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (pentane) to give 163[177,200] (253 mg, 89%, cis/trans = 94/6). ^1H nmr ($CDCl_3$): δ = 2.85 (b, s, 2 H, methines cis 94%), 2.6 (m, 2 H, methines trans 6%), 1.4- 1.2 (m, 27 H), 0.8 (m, 9 H). IR (neat): 2938, 1379, 1360, 1260, 1165, 1073, 1012, 916, 794 cm^{-1}. MS (EI): m/e = 264 (1%), 260 (3), 128 (4), 105 (24), 92 (25), 78 (43), 70 (22), 69 (23), 56 (35), 55 (41), 44 (100).

(Z)-8-Dodecen-1-yl acetate 183

A mixture of 184 (426 mg, 1.6 mmol), acetic acid (10 mL) and acetyl chloride (0.5 mL) was kept at 60°C for 6 h. The reaction mixture was then diluted with CH_2Cl_2, washed with H_2O and a solution of Na_2CO_3 (10%). The organic layer was dried over $MgSO_4$, evaporated, and the residue purified by flash chromatography (hexane/ethyl acetate = 10/0.5). Z-8-Dodecen-1-yl acetate 183[184] (240 mg, 77%) was obtained. ^1H nmr ($CDCl_3$): δ = 5.3 (t, J = 5 Hz, 2 H), 4.0 (t, J = 6.7 Hz, 2 H), 2.01 (s, 3 H), 1.97 (m, 4 H), 1.5-1.3 (m, 12 H), 0.85 (t, J = 7 Hz, 3 H). MS (EI): m/e = 205 (1%), 166 (24),

110 (30), 108 (24), 96 (85), 95 (68), 82 (90), 68 (87), 55 (100). Exact mass of M^+-AcOH ion calcd. for $C_{12}H_{22}$: 166.1721, found: 166.1750.

(Z)-1-(2-Tetrahydropyranyloxy)dodec-8-ene 184

A solution of 150f (841 mg, 2.4 mmol) in 10 mL THF was treated with n-propylzinc chloride (9 mL, ~ 1 M in THF) in the presence of $(Ph_3P)_4Pd$ (0.05 equiv.) as described above for compound 162. Compound 184 (565 mg, 88%) was obtained after flash chromatography (hexane/ethyl acetate = 9/1). ^1H nmr ($CDCl_3$): δ = 5.3 (t, J = 5 Hz, 2 H), 4.56 (b, s, 1 H), 3.7 (m, 2 H), 3.4 (m, 2 H), 1.98 (m, 4 H), 1.56-1.3 (m, 18 H), 0.88 (t, J = 6.5 Hz, 3 H). MS (EI): m/z = 268 (M^+, 1.8%), 267 (2), 101 (36), 97 (20), 95 (33), 85 (100), 69 (87), 67 (57).

(Z)-1-(2-Tetrahydropyranyloxy)dodec-7-ene 185

(Z)-8-Iodo-(2-tetrahydropyranylox)oct-7-ene 150e (651 mg, 1.9 mmol) was allowed to react with n-butylzinc chloride (4 mL, ~ 1 M in THF) in the presence of $(Ph_3P)_4Pd$ in the same way as described above for compound 162. The final residue was purified by chromatography (hexane/ethyl acetate = 9/1) and 426 mg (82%) of 185 was obtained. ^1H nmr ($CDCl_3$): δ = 5.33 (t, J = 5 Hz, 2 H), 4.53 (b, s, 1 H), 3.7-3.4 (m, 4 H), 1.96 (m, 4 H), 1.5-1.3 (m, 18 H), 0.83 (t,

J = 6 Hz, 3 H). MS (EI): m/z = 205 (11%), 154 (17), 152 (18), 128 (18), 91 (28), 84 (53), 83 (63), 78 (66), 55 (96), 41 (47), 28 (100).

(Z)-7-Dodecen-1-yl acetate 186

The reaction was performed as described above for compound 183. (Z)-1-(2-Tetrahydropyranyloxy)dodec-7-ene 185 (367 mg, 1.4 mmol) was treated with AcOH/AcCl at 60°C for 6 h and 2.49 mg (82%) of 186[201,202] was obtained after chromatography (hexane/ethyl acetate = 99/1). ^{1}H nmr ($CDCl_3$): δ = 5.3 (t, J = 5.6 Hz, 2 H), 4.0 (t, J = 6.7 Hz, 2 H), 1.97 (s, 3 H), 1.96 (m, 4 H), 1.5-1.3 (m, 12 H), 0.8 (t, J = 7 Hz, 3 H). MS (EI): m/z = 225 (1%), 166 (37), 154 (3), 138 (8), 123 (23), 110 (47), 109 (51), 95 (75), 82 (67), 67 (100). Exact mass of M^+-AcOH ion calcd. for $C_{12}H_{22}$: 166.1721, found: 166.1765. The ratio of Z/E in 186 was determined by epoxidation with MCPBA using the procedure developed for 155. ^{1}H nmr: δ = 2.89 (methines cis, 92%), 2.60 (methines trans, 8%).

11-(E)-Hexadecen-1-yl acetate 189

A solution of 152b (713 mg, 2.0 mmol) in 10 mL of THF was treated with n-butylzinc chloride (6 mL, ~ 1 M in THF) in the presence of $(Ph_3P)_4Pd$ as described above for compound 162. The reaction mixture was washed with a saturated solu-

tion of NH_4Cl, dried over Na_2SO_4 and evaporated. The residue was purified by chromatography (pentane/toluene = 7/3) to give 465 mg (82%) of 189[185, 186], E/Z = 80/20. ^1H nmr ($CDCl_3$): δ = 5.36 (m, 2 H), 4.02 (t, J = 6.7 Hz, 2 H), 2.02 (s, 3 H), 1.95 (m, 2 H), 1.56 (m, 2 H), 1.26 (b, s, 20 H), 0.87 (t, J = 7 Hz, 3 H). IR (neat): 2945, 2870, 1750, 1470, 1445, 1395, 1370, 1245, 1095, 970, 745, 610. MS (EI): m/z = 283 (M+1, 100%), 227 (17), 167 (26), 153 (10), 139 (13), 125 (14), 111 (16).

11-(E)-Tetradecen-1-yl acetate 193

As described above, compound 152b (1.06 g, 3 mmol) was treated with ethylzinc chloride (4 mL, ~ 1 M in THF), to give 589 mg (77%) of 193 after chromatography (pentane/toluene, 7/3), E/Z = 80/20. ^1H nmr ($CDCl_3$): δ = 5.2 (m, 2 H), 3.83 (t, J = 6 Hz, 2 H), 2.0 (s, 3 H), 1.9 (m, 4 H), 1.23 (b, s, 16 H), 0.83 (t, J = 7 Hz, 3 H). MS (EI): m/e = 194 (M^+-AcOH, 49%), 165 (6), 152 (11), 138 (11), 123 (27), 110 (42), 96 (56), 81 (93), 68 (95), 55 (100), 43 (99). Exact mass of (M-AcOH) ion calcd. for $C_{14}H_{26}$: 194.2034, found: 194.2014.

11-(E)-Tetradecen-1-ol 109

The acetate 107 (549 mg, 2.1 mmol) was hydrolyzed with NaOH (5 drops, 3 N) in 10 mL methanol for 2 h. The methanol was evaporated, ether was added to the residue and the solu-

tion washed successively with dilute HCl and Na_2CO_3 (10%), dried over K_2CO_3 and evaporated. The final residue was purified by chromatography (hexane/ethyl acetate = 10/1) to give 390 mg (99%) of 109[189]. MS (EI): m/e = 213 (M+1, 100%), 211 (7), 194 (13), 185 (29), 139 (6), 125 (12), 111 (16). Exact mass of (M^+-H_2O) ion calcd. for $C_{14}H_{26}$: 194.2035, found: 194.2062.

11-(E)-Tetradecenal 194

A solution of 11-(E)-tetradecenol (160 mg, 0.75 mmol) in 5 mL CH_2Cl_2 was treated with pyridinium chlorochromate according to literature procedure[203,204] to give 134 mg (85%) of 194[189] after chromatography (hexane:toluene = 7:3), E/Z = 4/1. ^1H nmr ($CDCl_3$): δ = 9.75 (t, J = 1.7 Hz, 1 H), 5.40 (m, 2 H), 2.40 (t, J = 7.3 Hz, 2 H), 1.95 (m, 4 H), 1.60 (m, 2 H), 1.26 (b, s, 12 H), 0.95 (t, J = 7.3 Hz, 3 H). IR (neat): 1730, 967 cm^{-1}. MS (EI): m/e = 210 (M^+, 4%), 205 (5), 192 (22), 121 (35), 111 (40), 95 (53), 83 (56), 81 (67), 69 (80), 67 (58), 55 (84), 43 (66), 41 (100). Exact mass calcd. for $C_{14}H_{26}O$: 210.1983, found: 210.1958.

A "tunable" synthesis of a specific blend of E- and Z-vinyl iodides: Variation in E/Z ratio of 13-iodo-12-dodecen-1-yl acetate versus the amount of aluminum chloride used

Compound 112k (1.028 g, 3.3 mmol) was dissolved in 33 mL of freshly distilled CH_2Cl_2 to give a 1 M solution. A

standard solution of iodine in dichloromethane (· 1 M) was prepared. To a 10 mL round bottom flask containing 1 mL of the iodine solution, variable amounts of Lewis acid ($AlCl_3$) were added. The mixture was stirred for 10 min and cooled to 0°C in an ice bath. The solution of 112k (1 mL) was added and the reaction mixture was kept at 0°C for 2 h, then quenched with $Na_2S_2O_3$ (10%). The organic layer was washed with NH_4Cl (10%), dried over Na_2SO_4 and evaporated. The residue was diluted with 1 mL hexane. Yields and E/Z ratio of 152e were determined by capillary GC, 200 + 8°C/min; RT 6.18 min (Z-isomer), 6.32 min (E-isomer).

Results

Equivalents of $AlCl_3$	Yield (%)	E/Z ratio (%)
2.0	92	73/27
1.5	95	78/22
1.1	96	80/20
0.8	45	48/52
0.5	44	29/71
0.3	42	10/90
0.0	40	10/90

Variation in E/Z ratio of 13-iodo-12-dodecen-1-yl acetate according to equivalents of tin chloride used

Tin chloride (1.563 g, 6 mmol) was dissolved in 60 mL CH_2Cl_2 and used as a standard solution (· 1 M). The reac-

tion was performed in the same conditions as described above.

Results

Equivalents of $SnCl_4$	Yield (%)	E/Z ratio (%)
3.0	92	73/27
2.0	94	70/30
1.5	88	66/34
1.1	87	63/37
0.8	80	64/36
0.5	75	56/44
0.3	63	46/54
0.2	55	27/73
0.0	40	10/90

Preparation of a specific blend of 1/1 ratio of 13-iodo-(E and Z)-12-tridecen-1-yl acetate 152c

Compound 112k (187 mg, 0.6 mmol) was treated with iodine (168 mg) in the presence of 0.4 equivalents of tin chloride as described above. Compound 152e (175 mg, 80%) was obtained after purification by chromatography (hexane:-toluene = 10:1), E/Z = 1/1. ^1H nmr ($CDCl_3$): δ = 6.45 (dt, J_1 = 14 Hz, J_2 = 7 Hz, 1 H), 5.9 (d, J = 14 Hz, 1 H, for trans vinylic protons), 6.10 (s, 2 H, for cis vinylic protons), 4.1 (t, J = 6 Hz, 2 H), 2.05 (s, 3 H), 1.60 (b, s, 18 H). MS (EI): m/e = 306 (M-AcOH, 0.2%), 239 (2), 179 (33),

167 (30), 137 (18), 128 (19), 123 (34), 110 (37), 109 (54), 95 (65), 82 (56), 67 (64), 55 (81), 43 (100).

Synthesis of a specific blend of 1/1 ratio of E- and Z-12-tetradecen-1-yl acetate: Asian corn borer moth pheromone 196

A solution of vinyliodide 152e (205 mg, 0.56 mmol) in 3 mL THF was treated with methylmagnesium bromide (3 mL, 3.1 M in ether), in the presence of Li_2CuCl_4 catalyst (0.3 mL, 1 M in THF). The reaction mixture was stirred at r.t. overnight, diluted with ether and washed with NH_4Cl (10%). The organic layer was dried over Na_2SO_4, evaporated, and the residue purified by flash chromatography (hexane:ethyl acetate = 10:1) to give quantitative yield of coupled product 195 (E/Z = 1/1). The alcohol was reacetylated in Ac_2O/pyridine to give 128 mg (72%) of 196[205] overall yield from 112k, capillary GC 200°C, RT = 4.79 (E-isomer), 4.98 (Z-isomer). ^1H nmr ($CDCl_3$): δ = 5.4 (m, 2 H), 4.0 (t, J = 6 Hz, 2 H), 2.0 (s, 3 H), 1.90 (m, 2 H), 1.60 (m, 3 H), 1.30 (b, s, 18 H). MS (EI): m/e = 194 (M-AcOH, 26%), 138 (26), 137 (17), 124 (26), 117 (18), 110 (39), 109 (46), 96 (54), 82 (85), 68 (57), 67 (57), 43 (100). Exact mass of (M-AcOH) ion calcd. for $C_{14}H_{26}$: ~~194.2034~~, found: 194,1994.

CLAIMS TO ORIGINAL WORK

- **Trialkylsilylallyl** carbanions, readily generated from **trialkylallylsilanes** using Schlosser's base (n-BuLi/-KO^tBu), were found to react with a number of alkyl halides to predominantly give γ-addition products. The regioselectivity was improved significantly and this makes the reaction particularly useful in the stereoselective synthesis of terminal E-vinylsilanes.

- The electrophilic substitution of E-vinylsilanes with halogen (iodine), has been controlled stereoselectively to provide either the Z- or E-vinyliodides from the same precursor.

- A novel approach to transform E-vinylsilanes into E-vinyliodide with retention of configuration at the double bond has been developed. Iodine and strong Lewis acids such as aluminum chloride ($AlCl_3$) or stannic chloride ($SnCl_4$) have been used.

- A new method to provide a specific blend of E- and Z-vinyliodides in a one pot reaction has been developed.

- A novel route to the stereocontrolled synthesis of insect sex pheromones using organosilicon compounds has been developed.

- A new concept of a "tunable" synthesis of insect sex pheromones has been developed. This methodology has been used to prepare an active sex pheromone as a specific blend of E- and Z-isomers of alkenes.

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