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NUCLEOPHILIC DISPLACEMENT AT SILICON
STEREOCHEMISTRY AND MECHANISTIC IMPLICATIONS

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CONTENTS

A - INTRODUCTION AND GENERAL CONSIDERATIONS

During the past years, and mainly from 1960's on, a great number of stereochemical studies of substitution at silicon by nucleophiles have been made. The earlier work, up to 1964, is the subject of an important monograph by Sommer (1) ; more recent studies are also summarized by him (2) and other authors, Prince (3) and Fleming (4) in comprehensive surveys.

The purpose of the present review is :

(i) to include very recent developments in this area with some emphasis on the work performed in our laboratory.

(ii) to discuss in detail the controlling factors of the stereochemistry of substitution and the geometry of attack of the nucleophile ; for this, we shall look at the main factors which may influence the stereochemistry, such as the nature of the leaving group or the nucleophile, the electrophilic assistance by a cation M^+ and the geometry of the organosilane.

Before this, we wish to discuss briefly three following mechanistic questions :

(I) Is the R_3Si^+ cation acting as an intermediate in displacement reactions at silicon ?

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* *The authors are very grateful to Prof. Dietmar Seyferth, who read the text and corrected it with considerable patience and goodwill.*

(II) Are the nucleophilic substitutions at silicon consistent with the occurence of rate-determining formation of a five-coordinate silicon intermediate ?

(III) Is substitution at silicon a nucleophilic or a one-electron transfer process ?

I - ROLE OF R_3Si^+ AS A REACTION INTERMEDIATE

The role of carbonium ions, R_3C^+, as reaction intermediates is well-documented (S_N1 mechanism) (5). In such reactions that are unquestionably first-order, the carbon atom attached to the leaving group undergoes racemization.

Currently, R_3Si^+ siliconium ions are not believed to be intermediates in any reaction in solution (1,2). The device, well-known in carbon chemistry, of placing unsaturated groups next to the developing positive charge, does not change the mechanism in the silicon series (6) : monofunctional triarylsilanes do not solvolyse by way of a R_3Si^+ cation intermediate, and p-methoxy substituents retard substitution relative to unsubstituted phenyl (7). Moreover, nucleophilic substitutions at silicon are found to be very stereoselective, occurring either with retention or inversion of configuration. For instance, vinyl- or ferrocenyl-silanes, the structure of which can favor sp^2 cation formation due to the stabilization from the substituents, do not lead to racemic solvolysis products (Table I) (8, 9, 10).

Finally, it was established that, even in hydroxylic solvents, there is no S_N1-type reaction at silicon. The observed racemization is only a second step, that of reaction products (11). These results and those of racemization of optically active halosilanes by solvents or salts are discussed in a previous review (12).

II - ROLE OF A FIVE-COORDINATE INTERMEDIATE IN DISPLACEMENT REACTIONS AT SILICON

Before we discuss the mechanistic implications of the stereochemical studies of nucleophilic substitutions at silicon, we note that the reactions proceed through an intermediate (13). One can conceive a number of energy diagrams (Scheme 1).

Possibility A, presented in the equation below, can be eliminated :

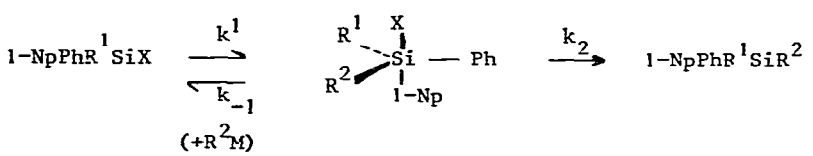


Table I

The stereochemistry of solvolysis of vinyl- and ferrocenyl-silanes

Silane [a]	Reagent	Product	Predominant stereochemistry [d]	ref.
1-NpPhViSiCl $[\alpha]_D = -5.7°$	CH_3CO_2Na/xylene	$R_3Si-OCOCH_3$ $[\alpha]_D = -14°$	87 % IN	(8, 9)
	CH_3OH/pentane	$R_3Si-OCH_3$ $[\alpha]_D = -9.3°$	100 % IN	(8, 9)
	H_2O/Et_2O	R_3Si-OH $[\alpha]_D = -9.2°$	89 % IN	(8, 9)
	KOH/xylene	R_3Si-OK $[\alpha]_D = +24.9°$	98.5% IN	(8, 9)
1-NpPhViSi-H $[\alpha]_D = +17.6°$	KOH/xylene	R_3Si-OK $[\alpha]_D = -21°$	91 % RN	(8, 9)
1-NpPhViSi-OMen $[\alpha]_D = -43.6°$	KOH/xylene [b] (SO_4Me_2)	$R_3Si-OMe$ $[\alpha]_D = +10.6°$	RN [c]	(8)
	KOH/xylene [b] (H_2O)	R_3Si-OH $[\alpha]_D = +9.5°$	RN [c]	(8)
1-NpPhFcSi-Cl $[\alpha]_D = +33.8°$	MeOH/pentane	$R_3Si-OMe$ $[\alpha]_D = -14.8°$	IN [c]	(10)

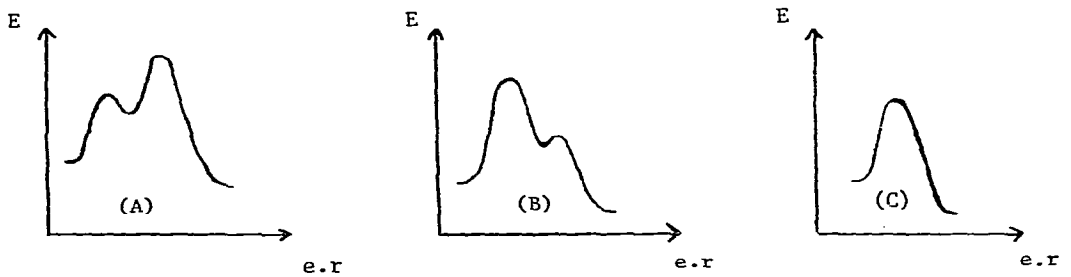
a Vi = vinyl, Fc = ferrocenyl, Men = menthyl, 1-Np = 1-naphthyl.
b R_3SiOK is not isolated as a pure product, but is worked up in situ by reaction with Me_2SO_4 (R_3SiOMe) or H_2O (R_3SiOH) (8).
c The examination of the $[\alpha]_D$ values of these products shows that the corresponding reactions are very stereoselective.
d IN = inversion, RN = retention.

This is because in such a process the intermediate would return to the reactants (k_{-1}) by rupture of a Si-C bond. Thus a mixture of products would be expected since Si-R^1, Si-R^2, Si-Ph or Si-1-Np could be cleaved. The only product observed is that of a normal substitution, and so the mechanism does not involve a rapid preequilibrium.

In order to determine the reaction energy profile, the rates of

Scheme 1

Energy diagrams



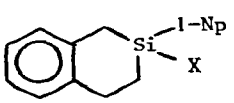
(A : rapid formation of an intermediate complex followed by slow cleavage of the Si-X bond to give the products
B : formation of an intermediate in the rate-determining step, then fast breakdown to the products.
C : synchronous bond-forming and bond-breaking, involving a single transition state).

reactions occurring either with retention or inversion, were studied (13). The results for reactions leading to retention are summarized in Table II, and for reactions giving inversion in Table III.

Two types of behavior are observed, i.e., rate constants being related by a factor of one or a factor > 10^3. The former are in the majo-

Table II

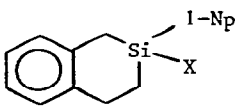
Kinetic data of reactions occurring with retention

Organosilane	α X=	β	RM	solvent	k_α/k_β
	F	OMe	EtMgBr	Et_2O	1.5-2.5
	F	OMe	PhMgBr	Et_2O	2-3
	F	OMe	MeMgBr	THF	1-1.5
	F	OMe	CH_2=$CHCH_2Li$	Et_2O	4-5
	OMe	H	PhLi	Et_2O	1.5-2
	OMe	H	n-BuLi	Et_2O	5-6
1-NpPhEtSi-X	H	D	PhLi	Et_2O	1.3
	H	D	n-BuLi	Et_2O	1
	F	OMe	n-BuLi	Et_2O	50

rity and apply to both retention and inversion while the latter are only found for F and OMe, in reactions giving inversion. Factors approximating to 1 show that the slow step does not involve Si-X bond cleavage. Thus the energy profile (Scheme 1, diagramm C) involving a single transition state can be eliminated. The small kinetic influence of the leaving group agrees with the slow formation of a pentacoordinated intermediate ; the very small deuterium isotope effect confirms this proposal (13).

Table III

Kinetic data of reactions occurring with inversion

Organosilane	α	X= β	RMgX	solvent	k_α/k_β
	F	Cl	CH_3MgBr	Et_2O	1
	F	Cl	allylMgBr	Et_2O	0.9
	F	Cl	crotylMgBr	Et_2O	1
	F	Cl	$PhCH_2MgCl$	Et_2O	1.6
	F	OMe	allylMgBr	Et_2O	$> 10^5$
	F	OMe	$PhCH_2MgBr$	Et_2O	2×10^3-5×10^3
1-NpPhViSi-X	F	Cl	CH_3MgBr	Et_2O	0.32
	F	Cl	allylMgBr	Et_2O	0.5
	F	Cl	$PhCH_2MgBr$	Et_2O	0.7
	F	Cl	crotylMgBr	Et_2O	0.5
	F	Cl	n-propylMgBr	Et_2O	1.7

III - SUBSTITUTION AT SILICON BY NUCLEOPHILES : A NUCLEOPHILIC OR A ONE-ELECTRON TRANSFER PROCESS ?

Coupling reactions of a nucleophilic reagent, Nu^-, with an organosilane, R_3Si-X, usually are represented as a one-stage nucleophilic mechanism (Scheme 2). However, a two-stage reaction pathway could be invoked, the first-step being a single-electron transfer from the electron-rich nucleophile, Nu^-, to the electrophilic silicon atom. The intermediate radicals could recombine in a second step to form the substitution product (Scheme 2).

Scheme 2

- one-stage nucleophilic mechanism :

$$Nu^- + R_3Si - X \longrightarrow R_3Si - Nu + X^-$$

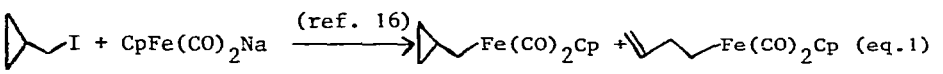
- two-stage electron transfer mechanism :

$$Nu^- + R_3Si - X \xrightarrow[\text{transfer}]{e^-} \overline{Nu^{\bullet} + R_3Si - X^{\bullet}} \longrightarrow R_3SiNu + X^-$$

Such an assumption is suggested by recent studies of coupling reactions between alkyl halides or tosylates and metallated anions R^-M^+ (RLi, RNa or RMgX (14,15,16,17).

Chemical and electrochemical data enable us to discuss these two mechanistic possibilities :

1 - The $CpFe(CO)_2^-$ anion reacts concurrently by S_N2 and free radical processes with alkyl halides (eq. 1). However, it is able to displace easily Cl from Si, leading to the formation of a Fe-Si bond (17) (eq. 2).

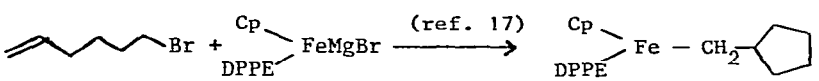


70 % 30 % (eq. 1)

(Cp = cyclopentadienyl)

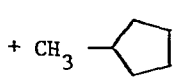
$$CpFe(CO)_2Na + R_3SiCl \xrightarrow{\text{(ref. 17)}} CpFe(CO)_2 - SiR_3 \quad \text{(eq. 2)}.$$

At the opposite extreme, Cp(DPPE)FeMgBr shows very low nucleophilicity and reacts with alkyl halides only by a radical process (17) (eq. 3). Felkin and his collaborators observed that this reagent was completely unreactive towards organosilicon halides, Me_3SiCl or Me_2SiHCl, which are known as very reactive substrates in nucleophilic reaction (eq. 4).

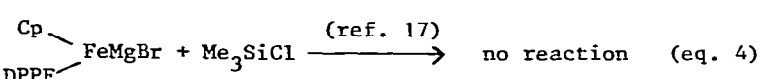


27 % (eq. 3)

(DPPE = bis(diphenylphosphino)-1,2 ethane)



40 %



(eq. 4)

2- The low ability of a M-X bond to react by one-electron transfer pathway is clearly outlined by the electrode potential data derived from the electrochemical reduction of silicon and germanium halides, R_3MX, (Table IV).

It will be noted that the half-wave reduction potentials for all of these silicon and germanium halides are much more negative than the E 1/2 values measured with organic halides, indicating a more difficult addition of an extra electron to a ≡ Si-X or ≡ Ge-X bond.

Table IV

Half-wave reduction potential of some organic halides (18) and organometallic halides R_3MX (M = Si or Ge)(19)

RX or R_3MX	solution	- E (volts)	reference electrode [a]
CH_3Cl	75 % D.O [a]	2.23	S.C.E
CH_3Br	75 % D.O [a]	2.01	S.C.E
CH_3I	75 % D.O [a]	1.63	S.C.E
$PhCH_2Cl$	75 % D.O [a]	1.94	S.C.E
$PhCH_2Br$	D.M.F [a]	1.22	S.C.E
$CH_2=CHCH_2Cl$	D.M.F [a]	1.91	S.C.E
$CH_2=CHCH_2Br$	D.M.F [a]	1.29	S.C.E
$CH_2=CHCH_2I$	D.M.F [a]	1.16	S.C.E
Ph_3Si-F	T.H.F [a]	2.60	S.C.E [b]
Ph_3Si-Cl	T.H.F [a]	2.40	S.C.E [b]
Ph_3Si-Br	T.H.F [a]	2.37	S.C.E [b]
Ph_3Ge-F	T.H.F [a]	2.30	S.C.E [b]
Ph_3Ge-Cl	T.H.F [a]	2.20	S.C.E [b]
Ph_3Ge-Br	T.H.F [a]	2.05	S.C.E [b]

a - T.H.F = tetrahydrofuran, D.O = dioxane, D.M.F = N,N dimethylformamide, S.C.E = saturated calomel electrode.

b - The E 1/2 values are obtained vs Ag/AgI reference electrode and are corrected to S.C.E by adding -0.44 volt.

Thus from these data we can conclude that coupling reactions between organosilanes and nucleophiles occur only by a one-stage nucleophilic mechanism. The halosilanes are not prone to a one-electron transfer.

B - INFLUENCE OF THE LEAVING GROUP ON THE STEREOCHEMISTRY

In this section, we shall examine the effect on the stereochemistry of varying the nature of the leaving group.

I - EXPERIMENTAL FACTS

The Tables V and VI summarize experimental data reported for reactions carried out with reagents which are considered to be predominantly nucleophiles. We have limited our choice to acyclic mono- or bifunctional derivatives. The cyclic organosilanes will be discussed in a later section.

Most of the reported reactions occur with high stereoselectivity either in inversion or in retention, mainly above eighty per cent.

For a constant leaving group, the stereochemical outcome depends upon the nature of the attacking nucleophile : inversion or retention can be observed. We shall examine this later point in a following section.

The stereochemical outcome depends strongly upon the nature of the leaving group :

(i) - The Si-H bond is displaced with retention of configuration, whatever the other substituents attached to silicon (Table V). Inversion occurs only in two cases, i.e., coupling reactions with Ph_2CHLi (20) or with alcohols in presence of Raney nickel (39). In this last case, we are certainly faced with another mechanism, i.e., the activation of the Si-H bond by adsorption on the Ni surface.

(ii) - Chloro- or bromosilanes undergo mainly inversion (Tables V and VI).

(iii) - Both Si-F and Si-SR bonds show parallel behavior, leading either to retention or inversion according to the nature of the nucleophile (Table V). For instance, alkyllithiums react with retention, whereas allyl- or benzyllithiums lead to inversion.

(iiii) - The Si-OR bond is displaced mainly with retention either by organolithiums or Grignard reagents. However, some C_{sp^2} charge delocalized nucleophiles (CH_2=CH-CH_2MgX, $PhCH_2Li$ or $PhCH_2MgX$) react with inversion.

(iiiii) - Bifunctional organosilanes, 1-Np(R)Si(X)Y (R phenyl or

Table V

Stereochemical behavior of monofunctional organosilanes

1-NpPh(R)Si-X + R'M ⟶ 1-NpPh(R)Si-R'

Substrate	Nucleophile(solvent) [a]	Predominant stereochemistry	References
1-NpPh(R)Si-H	R^1Li	RN	(20, 21)
(R = Me, Et, i-Pr, Vi)	(R^1 = Me, Et, n-Pr, n-Bu $p\text{-}CH_3OC_6H_4CH_2$, allyl, $PhCH_2$)		
	R^2Li	IN	(20)
	(R^2 = Ph_2CH)		
	NH_2Li or NH_2Na	RN	(22)
	KOH (xylene)	RN	(8, 23)
	tBuOK (tBuOH)	RN	(24)
1-NpPh(R)SiOMe	R^1Li		
(R = Me, Et, i-Pr, Vi) and PhMe(neo-C_5H_{11})Si-OMe	(R^1 = Me, Et, n-Bu, $p\text{-}CH_3OC_6H_4CH_2$, allyl [b])	RN	(20, 21)
	R^2Li	IN	(20, 21)
	(R^2 = $PhCH_2$, Ph_2CH)		
	R^1MgX	RN	(25, 26)
	(R^1 = Me, Et)		
	R^2MgX	IN	(20, 25)
	(R^2 = $PhCH_2$)		
	$LiAlH_4$	RN	(8, 27, 28)
	KOH (xylene)	RN	(8, 28, 29)

Table V (cont.)

Substrate	Nucleophile(solvent) [a]	Predominant stereochemistry	References
1-NpPh(R)SiF (R = Me, Et, i-Pr, Vi)	R^1Li (R^1 = Me, Et, n-Pr, n-Bu i-Bu, p-MeC_6H_4, PhC ≡ C)	RN	(21, 26)
	R^2Li (R^2 = allyl, benzyl, p-$CH_3OC_6H_4CH_2$)	IN	(21, 26)
	RMgX (R = Me, n-Bu, allyl, benzyl)	IN	(25)
	$LiAlH_4$	IN	(27, 30)
	R_3SiOK/xylene	RN	(26)
1-NpPh(R)Si-X X = SMe, SPh (R = Me)	R^1Li (R^1 = Et, n-Bu, neo-C_5H_{11})	RN	(31, 32)
	R^2Li (allyl, benzyl)	IN	(31, 32)
	RMgX (R = Et, n-Bu, allyl, benzyl)	IN	(32)
	$LiAlH_4$	IN	(31, 32)
	H_2O, CH_3OH	IN	(31)
1-NpPh(R)SiCl (R = Me, Et, i-Pr, Vi) and PhMe(neo-C_5H_{11})SiCl	RLi	IN	(21, 26)
	RMgX	IN	(25)
	$LiAlH_4$	IN	(27, 28)
	$LiNH_2$	IN	(22)
	PhSLi	IN	(32)
	$RCOO^-$	IN	(8, 28, 33)
	c.$C_6H_{11}NH_3^+F^-(CHCl_3)$	IN	(28, 33)
	H_2O, CH_3OH	IN	(8, 28, 33)
	tBuOK (tBuOH)	IN	(8, 33)

Table V (cont.)

Substrate	Nucleophile(solvent) [a]	Predominant stereochemistry	References
	KOH (xylene)	IN	(8, 33)
	R_3SiOK (xylene)	IN	(33)
1-NpPh(R)Si-Br	RLi	IN	(32)
(R = Me, neo-C_5H_{11})	RMgX	IN	(32)
and	$LiAlH_4$	IN	(28, 32, 33
PhMe(R)Si-Br	H_2O, MeOH	IN	(28, 33)
(R = neo-C_5H_{11},	KOH (xylene)	IN	(33)
benzhydryl, Et)	tBuOK (tBuOH)	IN	(33)
	R_3SiOK (xylene)	IN	(33)
	c.$C_6H_{11}NH_3^+X^-$ ($CHCl_3$) ($X^- = F^-$, Cl^-)	IN	(28, 33)

a - When not indicated, the solvent is anhydrous ether.

b - Sommer et al. reported previously retention of configuration as the stereochemical outcome (20). In our hands, the same reaction leads, several times, to predominant retention (85 % RN).

ferrocenyl), are good models to study the relative ability of X and Y leaving groups to be displaced (Table VI) :

- The (H) substituent appears to be the worst leaving group, compared to F and OR, with 1-NpPh(H)SiOR and 1-NpFcSi(H)F derivatives. Only displacement of F and OR groups occurs.

- At the opposite extreme, the chlorine substituent is the best leaving group. With 1-NpPhSi(Cl)OMen and 1-NpFcSi(F)Cl, displacement of Cl only occurs with inversion , whatever the nucleophile.

- Comparison of F and OR substituents is more complex. However, when the reaction takes place with inversion (PhLi, PhC ≡ CLi, $CH_2 = CHCH_2Li$, $CH_2 = CHCH_2MgBr$), only highly stereoselective displacement of the fluorine atom occurs.

These experimental facts show mainly parallel chemical and stereochemical data for mono- and bifunctional organosilanes. From the studies of the bifunctional organosilanes, the relative ease of displacement is :

$$Cl > F > OR > H$$

Table VI

Influence of the leaving group : the behavior of bifunctional organosilanes

Substrate	Nucleophile (S = Et_2O)	Products	Predominant stereochemistry	Ref.
1-NpPh(Cl)Si-OMen	EtLi (R = Me, n-Bu, p-$CH_3C_6H_4$, CH_2 = $CHCH_2$)	1-NpPh(R)Si-OMen	IN	(34, 35)
	RMgX (R= Me, Et, p-$MeOC_6H_4$, CH_2 = CH-CH_2, $PhCH_2$)	1-NpPh(R)Si-OMen	IN	(34, 35)
1-NpPhSi(F)OMen	RLi (R= p-MeC_6H_4, CH_2 = $CHCH_2$, PhC ≡ C)	1-NpPh(R)Si-OMen	IN	(36)
	CH_2 = $CHCH_2MgBr$	1-NpPh(allyl)Si-OMen	IN	(36)
1-NpPh(H)Si-OMen	RLi (R= Me, Et, n-Bu, p-$CH_3C_6H_4$, CH_2=CH-CH_2)	1-NpPh(H)Si-R	RN	(34, 35)
	R^1MgX (R^1= Me, Et, n-Pr, n-Bu p-$MeOC_6H_4$)	1-NpPh(H)Si-R^1	RN	(34)
	R^2MgX (CH_2 = CH-CH_2, $PhCH_2$)	1-NpPh(H)Si-R^2	IN	(35)
1-NpFc(F)Si-Cl	RLi or RMgX (R= Et, Ph, CH_2 = $CHCH_2$)	1-NpFc(F)Si-R	IN	(37)
1-NpFcSi(F)OEt	RLi (R= Ph, CH_2 = $CHCH_2$, Ph-C ≡ C)	1-NpFc(R)Si-OEt	IN	(36, 38)
	RMgX (R= CH_2=$CHCH_2$)	1-NpFc(CH_2=$CHCH_2$)Si-OEt	IN	(36, 38)
1-NpFc(H)Si-F	RLi (R= Me, Et, Ph, CH_2=$CHCH_2$, Ph-C ≡ C)	1-NpPh(H)Si-R	RN	(37)
	R^1MgX (R= Me, Et, CH_2=$CHCH_2$)	1-NpPh(H)Si-R^1	IN	(37)
	R^2MgX (R= Ph, Ph-C ≡ C)	1-NpPh(H)Si-R^2	RN	(37)

II - DISCUSSION

The above data suggest that a simple relationship between the nature of the leaving group and some of its physical properties may exist. For instance, Sommer et al. classified leaving groups X (R_3Si-X) according to their respective basicity (1, 2) :

- For good leaving groups such as Cl, Br, whose conjugate acids have a pK_a smaller than ca-5, the favored stereochemistry is inversion of configuration.

- For poor leaving groups such as H or OR, whose conjugate acids have a pK_a larger than ca-10, the predominant stereochemistry is retention of configuration.

However, the examination of Tables V and VI shows clearly that this explanation is not sufficiently general. For instance, the ≡Si-SR and ≡Si-F bonds show very close stereochemical behavior, leading either to retention or inversion. Following the Sommer's emperical rule, the SR group (for instance MeSH, $pK_a \sim 10$) would be a poor leaving group and be displaced mainly with retention. At the opposite extreme, the fluoro substituent (HF, $pK_a \sim 3,5-4$) would be a good leaving group and undergo inversion. Moreover, it does not explain why ≡ Si-SR,≡ Si-F and ≡ Si-OR bonds are substituted with inversion or retention according to the nature of the nucleophile.

A more satisfactory explanation cannot be drawn in terms of physical polarisability. The highly polarisable ≡ Si-Cl and ≡ Si-Br bonds are always displaced with inversion. However, the ≡ Si-F bond, which is far less polarisable than ≡ Si-OR or ≡ Si-H bonds, is more easily cleaved by nucleophiles with inversion of configuration. It is also impossible to explain the close behavior of F and SR groups. However, the relative ability of Si-X bonds for inversion and the polarisability order are parallel in a same group of the periodic table :

order of polarisability Br > Cl >> F
and ability for inversion : SR >> OR

So it is quite difficult to state a dependance between the substitution stereochemistry and a physical property of the leaving group (basicity, electronegativity or polarisability). This failure prompted us to draw an empirical relationship between the observed stereochemistry (inversion or retention) and the ability of the leaving group to be displaced (13, 32). Three main experimental facts provide good evidence for such a hypothesis :

(i) - The chemical behavior of bifunctional organosilanes

(Table VI) allows us to state the following relative order of the ability of substituents to be displaced from silicon :

$$Cl > F > OR > H$$

(ii) - Stereochemical data (Tables V and VI) show that this empirical order parallels a general change of the stereochemistry from inversion to retention.

(iii) - This empirical order also is closely parallel to the reactivity order observed in coupling reactions between monofunctional organosilanes, R_3Si-X, and Grignard reagents or organolithiums (13). In general, rate constants vary by a factor between one and fifty for reactions giving either retention or inversion. In the case of the F and OMe leaving groups, for reactions leading to inversion, rate constants are related by a factor 10^3 ($k_F/k_{OMe} > 10^3$) (13).

Thus the above observations are in good agreement with a parallel between the stereochemical paths and the ability of the leaving group to be displaced ; we propose the following order :

- ability of X to be displaced : Br ∿ Cl > SR ∿ F > OMe > H
- stereochemistry : IN ⟶ RN

We can also introduce the OTs and OCOR leaving groups in the above classification near chloro and bromo groups. They show high reactivity and a stereochemical behavior close to that of chlorosilanes, leading only to inversion (40).

Finally, we note the three following points :

(i) - Acyclic fluorosilanes show a general shift of the stereochemistry from inversion to retention of configuration, as indicated below :

$$RN \longrightarrow IN$$

$$R^1R^2Si(H)F > R^1R^2R^3Si-F > R^1R^2\underset{\underset{F}{|}}{Si}-OR$$

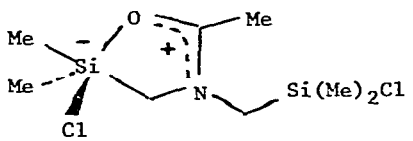
This stereochemical shift is illustrated by the following examples :

RM	$R^1R^2Si(H)F$	$R^1R^2R^3Si-F$	$R^1R^2Si(F)OR$	ref.
allylLi, PhMgBr Ph-C ≡ CMgBr	RN	IN	IN	(21,26,36,37)
ArLi, Ph-C ≡ CLi	RN	RN	IN	(21,26,36,37)

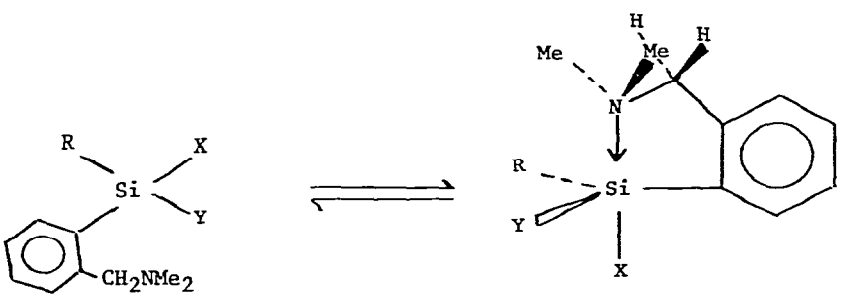
The mutual influence of one of the two leaving groups on the other one changes its lability, and thus the stereochemistry of its displacement by nucleophiles.

(ii) - Inversion of configuration is observed mainly with Si-X bonds which are able to be stretched under the influence of an attacking nucleophile. This fact is well-illustrated by the following data :

- The X-ray crystal structure analysis of the five-membered chloro-(N-chlorodimethylsilylacetamido)methyl-dimethylsilane shows the chlorine atom in an apical position trans to the oxygen (41). Moreover, the Si-Cl bond is considerably longer (2.348 Å instead of 2.01 Å (42) in tetravalent organosilanes).



- To have a good idea about this aptitude, we extend to silicon the interesting study of J.G. Noltes et al.(43) concerning the stabilization of optically active tin centers by intramolecular coordination. The NMR study of *1* at various temperatures (the N-Me groups are diastereotopic) allows us to assess its ability to form a pentacoordinate structure, *2* (44) :



1 *2*

R = 1-Np, X = Me
R = Me, X = H
R = 1-Np, X = H

Y = H, OR, F, SR, Cl

This ability depends greatly upon the nature of the X group and we can state the following order :

- ability of *1* to form *2* = OCOR, Br, Cl > SR, F > OR, H *according to the nature of X.*

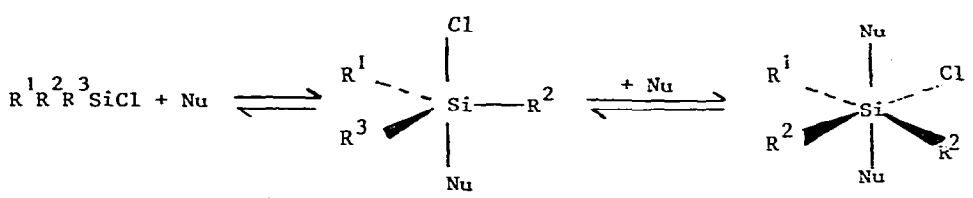
Of particular interest is the close parallel between the above order and the aptitude of X to be displaced with inversion, i.e., OCOR, Br, Cl > SR, F > OR >> H. Thus this study undoubtedly reflects the dominant influence of the aptitude of the Si-X bond to be stretched on the stereochemistry at silicon.

(iii) - The above observation, i.e., inversion of configuration is obtained mainly with Si-X bonds which are able to be stretched under the influence of an attacking nucleophile, is corroborated by data concerning the racemization of halosilanes (12). Their ability to be racemized by nucleophiles (HMPT, etc...) is parallel to the ability of the Si-X bonds to be displaced with inversion :

$$\equiv Si\text{-}Br \; > \equiv Si\text{-}Cl \; > \equiv Si\text{-}F$$

The first step of this process is the reversible coordination of the nucleophile to silicon, leading to a pentacoordinate intermediate in which the nucleophile and the electronegative group X occupy the opposite apical positions (Scheme 3) (12, 45).

Scheme 3



This implies a lengthening of the Si-X bond and thus a far greater ease of racemization of bromo- and chloro-silanes in comparison to the much more electronegative fluoro analogs.

C - INFLUENCE OF THE NATURE OF THE NUCLEOPHILE

The stereochemical outcome is greatly influenced by the nature of the attacking nucleophile (Tables V and VI). For a constant leaving group, both inversion and retention can be observed , depending to the nature of the entering group. For instance, with carbon organometallics, R^-M^+, the na-

ture of the carbanion and of the metal counterion is of importance :

(i) - Aryl, phenylethynyl and alkyl organolithiums, i.e., species with a well-localized negative charge, react mainly with retention. Inversion is observed only with the best Cl or Br leaving groups. On the other hand , allyl, benzyl or benzhydryl lithiums, i.e., reagents with a negative charge which is well delocalized over an sp^2 carbon system, always react with inversion, except with the poorest (H) leaving group (Tables V and VI).

(ii) - Concerning the influence of the metal counterion M^+, the Grignard reagents show a general shift towards inversion compared to organolithiums. For instance, alkyl lithiums lead to retention with the borderline ≡Si-F and ≡Si-SR bonds ; the corresponding Grignard reagents react with predominant inversion (Table V).

It is very clear that these data cannot be explained only in terms of the ability of the leaving group to be cleaved, as we have discussed in the foregoing section. More sophisticated concepts are necessary. The following questions come to mind :

(i) - Can we apply to silicon the concepts used to explain displacement reactions at phosphorus ?

(ii) - Is the stereochemistry governed by electrophilic assistance by the cation of the attacking reagent ?

(iii) - Is the stereochemistry directed by the electronic character of the nucleophile, as suggested by the data given in Tables V and VI ?

I - CAN PSEUDO-ROTATION EXPLAIN STEREOCHEMICAL DATA AT SILICON ?

1) Summary of the mechanistic concepts used to explain data at tetravalent phosphorus compounds (46) :

The interpretation of most of the available data on nucleophilic displacement reactions of tetracoordinate phosphorus compounds is achieved by the consistent application of the following rules (47) :

(i) - The first step of the process is the kinetically determined formation of a pentacoordinate intermediate with a trigonal bipyramidal skeleton (TBP).

(ii) - The intermediate is formed from the tetracoordinate precursor by attack of the nucleophile at one of the tetrahedral faces ; it corresponds to an apical entry. The displacement of the leaving group occurs from an apical position.

(iii) - The first invoked TBP intermediate is the most stable one on the basis of the relative apicophilicity of the groups attached to phosphorus ; the electronegative ligands prefer apical positions.

(iiii) - The intermediate may undergo intramolecular ligand exchange by pseudo-rotation.

2) Can the concepts be carried over the silicon series ?

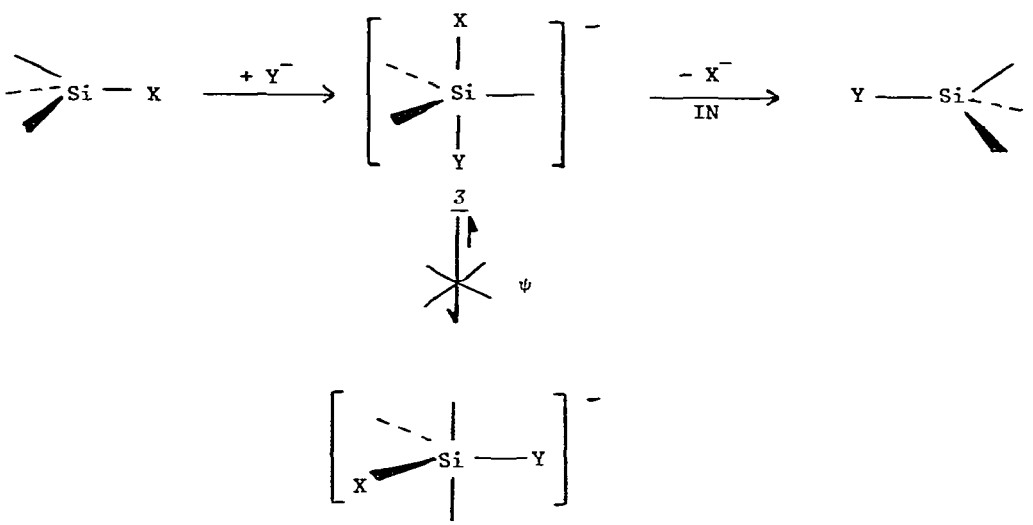
This question can be answered clearly by examining successively the data reported with mono- and bifunctional organosilanes.

a) Case of monofunctional organosilanes R_3Si-X (Table V) :

Only one electronegative group is attached to silicon ; it is also the leaving group. The preference rules cited above must place it always in an apical position of the TBP intermediate.

Inversion of configuration is easily explained. The attack of the nucleophile occurs at an apical position opposite to the leaving group. The most stable trigonal bipyramidal intermediate therefore will be like *3* (Scheme 4).

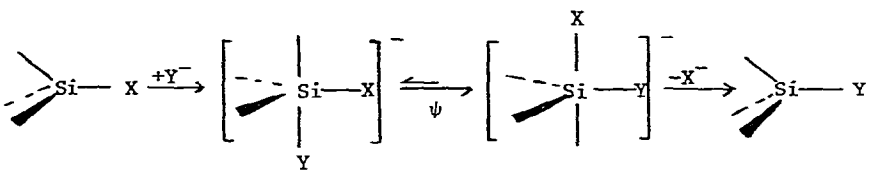
Scheme 4



The leaving group X can leave immediately from the apical position.

At the opposite, it is not possible to explain directly the retention of configuration, since this stereochemistry implies an attack of the nucleophile at 90° with respect to the leaving group. As proposed earlier (4), we must invoke an apical attack of the nucleophile leading to an intermediate like 4 in which the leaving group X is in an equatorial position (Scheme 5).

Scheme 5



4 5

The apical departure of the leaving group X is possible only after one pseudo-rotation which leads to 5.

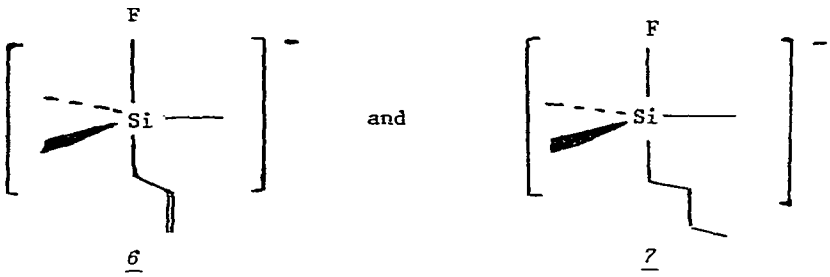
This proposal seems incorrect from two respects :

(i) - The pseudo-rotation does not explain the stereochemistry. It is only invoked to respect the concept which states that the geometry of entry and departure must be the same.

(ii) - The "preference rules" stated with tetravalent phosphorus compounds are not followed when describing nucleophilic substitutions with retention. Apical attack of the nucleophile places the only electronegative group X in an equatorial position (intermediate 4).

In order to illustrate this point, we report the opposite behavior of the allyl and n-butyl anions in the substitution of an optically active fluorosilane R_3Si^*-F (R_3Si = 1-NpPhMeSi). The first leads to inversion (91 % IN) and the latter to retention (98 % RN) (48), when carrying out the reactions with allyl- and n-butyllithium in the presence of a cryptand specific for the lithium cation. The use of a cryptand allows us to discuss the difference in behavior with respect to the anion species alone since it avoids the possibility of electrophilic assistance by Li^+ which could affect the apicophilicity of the fluorine atom.

By NMR spectroscopy, Muetterties et al. (49) have shown that fluorine substituents always occupy the apical positions of pentacoordinated anions such as $RSiF_4^-$ or $R_2SiF_3^-$. Thus, using the rules stated in phosphorus chemistry, the most stable intermediates will be 6 and 7, whatever the entering nucleophile.



6 7

6 and 7 can explain only inversion ; they cannot lead to the substitution of the fluorine atom with retention .

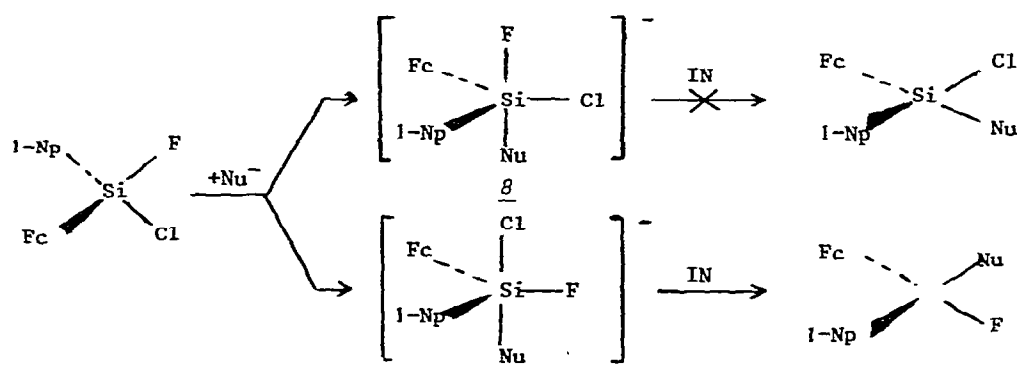
b) Case of bifunctional organosilanes

Bifunctional organosilanes have two electronegative groups attached to silicon. They have the nearest structural resemblance with tetravalent organophosphorus derivatives and thus we are in the best conditions to test the "preference rules" stated above.

To this end, we shall emphasize the following experimental observation (Table VI). The inversion of configuration takes place selectively with the best leaving group. It is always the only one which is displaced, whatever the nature of the other potential leaving group attached at silicon, even if it is more or less electronegative than itself. For instance, with 1-NpFcSi(F)Cl, the chlorine group only is displaced with inversion in all cases.

This fact is in disagreement with an intermediate such as 8 with the most electronegative group, i.e., fluorine atom, in the apical position (Scheme 6) :

Scheme 6



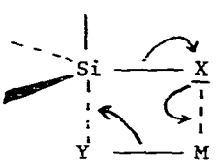
8 would lead to the selective substitution of the fluorine atom with inversion. The observed displacement of the chlorine with inversion can only be explained by the attack of the nucleophile at the opposite side of the most labile ≡Si-X bond, i.e., ≡Si-Cl bond (§ B, influence of the leaving group on the stereochemistry).

Thus, as we have seen also with monofunctional silanes, the "preference rules" stated to explain the stereochemical data reported in phosphorus chemistry, fail in describing the most important experimental facts in organosilicon chemistry. The answer must be found in other concepts and, in particular, in the intimate structure of the nucleophile.

II - IS THE RETENTION OF CONFIGURATION GOVERNED BY ELECTROPHILIC ASSISTANCE OF THE CATION OF THE ATTACKING REAGENT ?

Since the retention of configuration implies an attack of the nucleophile at 90° with respect to the leaving group, it is possible, as proposed by Sommer et al.(1,2) tc invoke a quasi-cyclic mechanism (S_Ni-Si, Scheme 7).

Scheme 7



(M = electrophilic part of the attacking reagent)

S_Ni-Si mechanism

In such a process, the electrophilic assistance by the counter ion M^+ determines the apical attack of the nucleophile with the leaving group in an equatorial position*, and thus governs the stereochemistry.

Sommer et al (1, 2) supported their assumption from the stereochemical preference of R_3Si-OR' for retention of configuration, taking into

---

* *This assumption is in complete disagreement with the apicophilicity rule stated in phosphorus chemistry : electrophilic assistance ($P - X \ldots M^+$) increases the electronegativity and the apicophilicity of the X group, and thus its preference to occupy an apical position rather than an equatorial one.*

account the two following points :

(i) - The availability of the unshared electron pairs on oxygen.

(ii) - The necessity of an electrophilic assistance for the displacement of OR' as a negative ion.

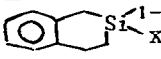
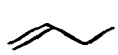
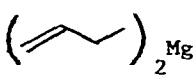
To complete these remarks, experiments were performed in which was varied the basicity of the solvent or in the presence of complexing reagents, such as TMEDA or cryptands. The corresponding stereochemical and kinetic data are discussed in the context of testing the validity of an S_Ni-Si process to explain the retention at silicon.

1) Influence of the solvent on the stereochemistry at silicon

In this section, we shall consider stereochemical data which clearly demonstrate that the stereochemistry (and mechanism) for some lea-

Table VII

Influence of the solvent(S) on the stereochemistry

Nucleophile	S	Vi 1-NpPhSi-F (25)	 (50)
			X = F / X = OMe
CH_3MgBr	- Et_2O		81 % IN
	THF		93 % RN
EtMgBr	- Et_2O	⩾ 65 % IN	
	THF	66 % IN	
	DME	59 % RN	
Et_2Mg	- Et_2O	⩾ 59 % IN	
	THF	⩾ 67 % RN	
	DME	⩾ 67 % RN	
n-BuMgBr	- Et_2O	⩾ 67 % IN	
	THF	⩾ 59 % RN	
	DME	⩾ 71 % RN	
$(n\text{-Bu})_2Mg$	- Et_2O	⩾ 69 % IN	
	THF	⩾ 75 % RN	
	DME	⩾ 74 % RN	
	- Et_2O		93 % IN
	DME		78 % RN
	- Et_2O		72 % IN
	DME		75 % RN

ving groups is extremely sensitive to the nature of the solvent. This is specially so in the case of a borderline leaving group, such as the fluorine atom, which can be displaced either with retention or inversion. We summarized the most striking data in the Table VII.

The above data show clearly the dependance of the stereochemical outcome on the nature of the solvent. The nucleophilic solvents such as DME or THF promote retention of configuration (or decrease the percentage of inversion). Moreover, this general trend is parallel to an increase of the substitution rate (51) (Table VIII).

For all Grignard reagents used, whether there is retention (derivatives *9*, *10*, *11*) or inversion (*11* with benzyl MgCl) or a transition from one to the other (*11* with n-BuMgBr and n-PrMgBr), a net rate increase is observed when increasing the basicity of the solvent (Et_2O < THF < DME).

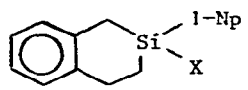
2) Influence of complexing reagents (TMEDA - cryptands) in coupling reactions between organosilanes and organolithiums

In contrast to the covalent Grignard reagents, the organolithiums have ionic character, and thus are of great interest to test the hypothesis of electrophilic assistance by the lithium cation to the cleavage of a ≡Si-X bond (Scheme 7).

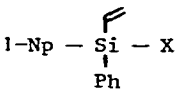
We have reported stereochemical studies carried out with two organolithium reagents, each of which has a well-localized negative charge on an sp^3 carbon atom (n-BuLi and EtLi) (52). The results are given in Table IX.

Table VIII

Stereochemistry and rates of reaction of organosilane derivatives with Grignard reagents in various solvents



(9) , X = F
(10), X = OMe



(11), X = F
(12), X = OMe

Reactant (0.02mol/l)	Organometallic[a] (0.4 mol/l)	Stereochemistry[b]		Absolute rate[c]	$\frac{k_{THF}}{k_{Et_2O}}$	$\frac{k_{DME}}{k_{THF}}$	$\frac{k_{DME}}{k_{Et_2O}}$
(9)	n-PrMgBr	Et_2O	RET	6×10^{-4}	75	24	1800
		THF	RET[b]	4.5×10^{-2}			
		DME	RET[b]	1.1			

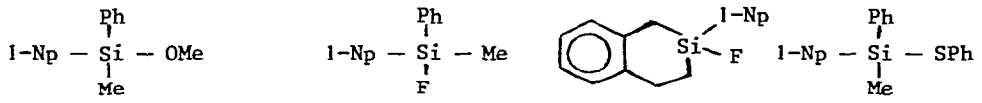
Table VIII (cont.)

Reactant (0.02mol/l)	Organometallic[a] (0.4 mol/l)	Stereochemistry[b]		Absolute rate[c]	$\frac{k_{THF}}{k_{Et_2O}}$	$\frac{k_{DME}}{k_{THF}}$	$\frac{k_{DME}}{k_{Et_2O}}$
(9)	n-BuMgBr	Et_2O	RET	6×10^{-4}			1300
		DME	RET[b]	0.8			
(9)	i-BuMgBr	Et_2O	RET[b]	2.8×10^{-4}	39	14	500
		THF	RET[b]	1.1×10^{-2}			
		DME	RET[b]	0.15			
(10)	n-PrMgBr	Et_2O	RET	4.7×10^{-4}	10	120	1200
		THF	RET[b]	4.9×10^{-3}			
		DME	RET[b]	0.6			
(11)	n-BuMgBr	Et_2O	RET	2.7×10^{-4}	13	108	1400
		THF	RET[b]	3.5×10^{-3}			
		DME	RET[b]	0.38			
(10)	i-BuMgBr	Et_2O	RET[b]	1.7×10^{-5}	3	40	120
		THF	RET[b]	5.3×10^{-5}			
		DME	RET[b]	2×10^{-3}			
(12)	n-PrMgBr	Et_2O	RET	1×10^{-5}	8	20	170
		THF	RET	8.3×10^{-5}			
		DME	RET	1.7×10^{-3}			
(11)	n-PrMgBr	Et_2O	INV	1.7×10^{-4}	36	2.8	100
		THF	RET	6.2×10^{-3}			
		DME	RET	1.7×10^{-2}			
(11)	n-BuMgBr	Et_2O	INV	5×10^{-5}			200-300
		DME	RET	1×10^{-2}			
(11)	BenzMgCl	Et_2O	INV	5.4×10^{-4}	215	≥ 50	$\geq 10^4$
		THF	INV	0.11			
		DME	INV	≥ 5			

[a] Pr, propyl ; Bu, butyl ; Benz, benzyl. [b] Stereochemistry deduced from known stereochemistries.

[c] All results given in min^{-1} using log 10.

Table IX



$[\alpha]_D = -16.5°$ — *13*

$[\alpha]_D = +47°$ — *14*

$[\alpha]_D = -34°$ — *9*

$[\alpha]_D = +27°$ — *15*

Runs	Reagents	*13*	*14*	*9*	*15*
1	EtLi/K_{Li}+/Et_2O[a]	98 % RN[c]	95 % RN	100 % RN	
2	EtLi/TMDA/Et_2O[b]	96 % RN	91 % RN	99 % RN	
3	EtLi/Et_2O	90 % RN	90 % RN	96 % RN	
4	EtLi/benzene	76 % RN	70 % RN		
5	n-BuLi/K_{Li}+/Et_2O	100 % RN	98 % RN		86 % RN
6	n-BuLi/TMDA/Et_2O	90 % RN	82 % RN		
7	n-BuLi/Et_2O	86 % RN	80 % RN		65 % RN
8	n-BuLi/heptane	68 % RN			

[a] K_{Li}+ = kryptofix 211, (tetraoxa-4,7,13,18- diaza-1,10- bicyclo-8,5,5- eicosane), specific for Li^+ cation.

[b] TMDA = tetramethylethylenediamine. [c] Predominant stereochemistry ; the $[\alpha]_D$ of optically pure R_3SiEt and R_3SiBu-n are known (1). A predominant stereochemistry of 90 % inversion indicates a reaction path that is 90 % invertive and 10 % retentive, giving a product which is 80 % optically pure.

Non-polar solvents, such as benzene or n-heptane, in which alkyllithiums are more aggregated, increase the proportion of inversion. At the opposite extreme, complexing agents for the Li^+ cation, such as TMEDA, or better, K_{Li}+ which generates free anions (53), promote retention of configuration.

The kinetic effect of the addition of a lithium cryptand also is very clear (52) (Table X).

It shows that there is a rate increase when a Lewis basic solvent such as ether is used instead of heptane. When the lithium cation is not solvated, and electrophilic assistance is excluded, we get a 10^3-10^4 fold rate acceleration. Thus both Grignard reagents and alkyllithiums show a change of the stereochemistry towards retention and a parallel increase of the substitution rate when the solvent basicity is increased or complexing reagents (TMEDA or K_{Li}+) are added.

Table X

Stereochemistry and rates of reaction of organosilanes with organolithiums (Li^+ cation complexed to various extent)

$$R_3Si - X + n\text{-BuLi (or n-PrLi)} \xrightarrow{S} R_3Si - Bu\text{-}n \text{ (or } R_3SiPr\text{-}n)$$

(R_3Si = 1-NpPhMeSi) (X = F, or OMe)

Runs	Substrate	Solvent	T°C	Complexing reagent	$t_{1/2}$ ratios*
1	R_3Si-OMe	Ether	- 78°C	-	$t_1/t_2 \sim 2$
2	R_3Si-OMe	Ether	- 78°C	TMEDA	
3	R_3Si-OMe	Heptane	0°C	-	$t_3/t_4 \sim 10^2$-10^3
4	R_3Si-OMe	Heptane	0°C	K_{Li}^+	
5	R_3Si-F	Ether	- 78°C	-	$t_5/t_6 \sim 5$
6	R_3Si-F	Ether	- 78°C	TMEDA	
7	R_3Si-F	Heptane	0°C	-	$t_7/t_8 \sim 10^3$-10^4
8	R_3Si-F	Heptane	0°C	K_{Li}^+	

* $t_{1/2}$ ratios = ratio $t_{1/2}$ of reaction carried out without complexing reagent to that of a reaction carried out in the presence of added TMEDA or K_{Li}^+.

These data are in complete opposition to the S_Ni-Si process proposed by Sommer et al. . As the controlling force of such a mechanism is the electrophilic assistance to the cleavage of the ≡Si-X bond (Scheme 7), the use of a more basic solvent or a cryptand would lead to a shift of the stereochemistry to inversion.

We now come to our last assumption, i.e., the electronic character of the nucleophile as the controlling factor of the stereochemistry.

III - IS THE ELECTRONIC CHARACTER OF THE NUCLEOPHILE THE CONTROLLING FACTOR OF THE STEREOCHEMISTRY ?

Small changes in the structure of the nucleophile, the metal or the solvent can lead to dramatic variations in the stereochemistry of substitution. Since no correct interpretation can be made in terms of the stability of the intermediate or on the basis of a mechanism directed by electrophilic assistance to the cleavage of the ≡Si-X bond, we have to discuss the assumption of the nucleophile as the controlling factor of the stereochemistry.

We shall summarize the available experimental data in terms of the following :

(i) - The nucleophilic substitution at silicon by carbon nucleophiles.

(ii) - The coupling reactions with alkoxides and phenoxides.

(iii) - The parallel between the stereochemistry at silicon and the regioselectivity of attack on α-enones.

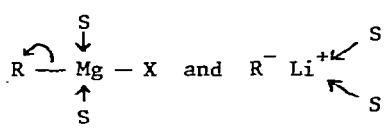
(iiii) - The reduction reactions by alanes, $AlH_nY_{(3-n)}$.

1) Substitution reactions by carbon nucleophiles (RMgX and RLi)

In the case of carbon organometallics, it is possible to modify easily the electronic character of the nucleophile while preserving the same reacting atomic center. Three possibilities are summarized below.

- Nature of the metal. The softer (harder) the cation M^+, the more covalent (ionic) the R-M bond of the organometallic and softer (harder) the anion R^- (54). Thus the organolithiums, RLi, will be harder reagents than the analogous Grignard reagents, RMgX.
- Nature of the solvent. Its basicity or solvating power can modify the electronic character of the anion. A Grignard reagent is softer in ether than in THF or DME (Scheme 8).

Scheme 8



(S = basic solvent, i.e., THF or DME)

Similarly, a basic solvent which favors the dissociation of the R^-Li^+ ion pair increases the negative charge and thus the hardness of R^- when it is an alkyl group.

- Nature of R^-. One can have a large variety of R^- with a more or less delocalized negative charge. For instance, allyl or benzyl anions, with a negative charge well-delocalized on a C sp^2 system, are softer than alkyl anions with a localized charge on a C sp^3 atom (54).

The stereochemical data which are mainly summarized in Tables V and VI, are quite clear :

(i) - Organolithiums react mainly with retention, compared to Grignard reagents (Table V).

(ii) - An increase of the solvating power of the solvent (Et_2O < THF < DME) leads to a shift of the stereochemistry towards retention. The same shift is observed with alkyllithiums when adding TMEDA or a cryptand (Table IX).

(iii) - Hard nucleophiles (alkyl anions) give predominant retention of configuration. At the opposite extreme, softer nucleophiles, such as benzyl or allyl anions, lead mainly to inversion. Quite significant is the case of the Ph_2CH^- anion in which the negative charge is particularly well-delocalized. It leads only to inversion, even with the (H) leaving group (Tables V and VI).

Thus the close relationship between the stereochemistry of substitution at silicon and the electronic character of the attacking nucleophile can be summarized as follows : for a given leaving group at silicon, the tendency of hard reagents is to lead to retention while soft reagents give inversion. These observations have to be generalized to alkoxides, phenoxides, hydrides and alanes.

2) Coupling reactions with alkoxides and phenoxides

a) We have summarized in Table XI the most significant data reported by Sommer et al. concerning nucleophilic substitutions by alkoxides (55) at the ≡Si-OMe, ≡Si-F and ≡Si-SMe bonds.

The most important fact which emerges from these data, is the stereochemical crossover from retention to inversion when increasing the alcohol content of the medium. Whatever the nature of the leaving group (OMe, F, SMe), inversion becomes predominant either with ROLi or RONa. The most striking data are observed with R_3Si-F and $R_3Si-SMe$ for constant ROH/R_3Si-X proportions of 1.1 to 1.4, a change in the ROH/ROM proportion (from 1 to 38) is enough to invert the stereochemistry.

At the opposite extreme, the nature of the metal (Li^+ or Na^+) does not significantly influence the stereochemistry. Under similar conditions (runs 4,7 - 9,12 - 10,13 - 11,14 - 16,18 - 17,19 in Table XI), the predominant stereochemistry is nearly the same in both cases.

These observations suggest an explanation of the above data in terms of electronic factors. The RO^-M^+ species in benzene have a localized negative charge on the oxygen atom, i.e., they act as hard anions and react with retention. On increasing the alcohol ratio, the charge is dispersed by

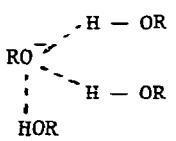
Table XI

$$R_3Si\text{-}X + n\text{-}BuOH/n\text{-}BuOM \xrightarrow{M = Li \text{ or } Na} R_3Si\text{-}OBu\text{-}n$$

Organo-silane	Runs	Metal alkoxide	ROH / ROM mol. mol.	ROH / R_3SiX mol.	ROH vol % in solvent	Predominant stereochemistry
R_3Si-OMe	1	n-BuOLi	10	2.6	2.3	100 % RN
	2	n-BuOLi	10	15	16.7	89 % RN
	3	n-BuOLi	72	47	51.2	65 % IN
	4	n-BuOLi	210	79	100	> 81 % IN
	5	n-BuONa	15	2.6	2.3	95 % RN
	6	n-BuONa	28	15	16.7	76 % IN
	7	n-BuONa	180	49	52.0	82 % IN
	8	n-BuONa	450	83	100	77 % IN
R_3Si-F	9	n-BuOLi	2	1.31	3	92 % RN
	10	n-BuOLi	14.3	1.11	15.8	62 % RN
	11	n-BuOLi	32	1.37	50.0	88 % IN
	12	n-BuONa	1.5	1.16	2.0	94 % RN
	13	n-BuONa	13.7	1.23	15.8	56 % RN
	14	n-BuONa	38	1.19	46.8	80 % IN
R_3Si-SMe	15	n-BuOLi	0.7	1.15	0.8	70 % RN
	16	n-BuOLi	3.0	1.13	3.4	61 % IN
	17	n-BuOLi	39	1.22	50	85 % IN
	18	n-BuONa	2.4	1.30	3.2	58 % IN
	19	n-BuONa	36	1.32	50	72 % IN

- R_3Si = 1-NpPhMeSi
- the reactions were carried out in benzene solvent.

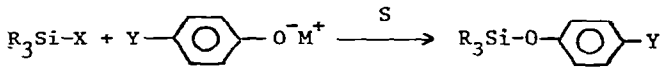
strong hydrogen-bonding interactions :

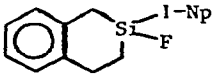


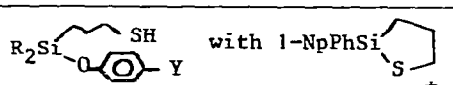
Such dispersal of the negative charge produces a softer species which reacts with predominant inversion.

b) In order to verify this assumption, we studied nucleophilic substitutions with phenoxides. In these the electronic character of the negative charge on the oxygen atom can be changed by varying the substituent Y in the para-position. Our data are summarized in Table XII (56).

Table XII Stereochemistry of reactions of R_3Si-X with phenoxides



Runs	R_3Si-X	Y	M^+	S (solvent)	R_3Si-O $[\alpha]_D$	predominant stereochemistry
1		- MeO	Na^+	benzene	+ 4°	RN
2		- MeO	Na^+	THF	+ 6°	RN
3		- MeO	NR_4^+ [a]	THF	+ 8°	RN
4		- MeO	- [b]	THF	+ 9°	RN
5	(+) 1-Np-Si(Ph)(Me)-SPh	- H	Na^+	benzene	+ 2°	IN
6		- H	Na^+	THF	+ 2°	IN
7		- H	NR_4^+	THF	+ 1.5°	IN
8		- H	- [b]	THF	+ 5°	IN
9		- NO_2	Na^+	benzene	+ 2.5°	IN
10		- NO_2	Na^+	THF	+ 3°	IN
11		- NO_2	NR_4^+	THF	+ 5°	IN
12		- NO_2	- [b]	THF	+ 8°	IN
13	1-Np-Si(Ph)-S (+) [a]	- MeO	Na^+	benzene	+ 8.5°	RN
14		- H	Na^+	benzene	- 2.6°	IN
15	(+)1-Np-Si(Ph)(F)-CH_3	- MeO	Na^+	THF	- 4.5°	RN
16		- MeO	- [b]	THF	- 6°	RN
17		- H	Na^+	THF	+ 3°	RN
18		- H	- [b]	THF	- 2.5°	IN
19		- NO_2	Na^+	THF	+ 0.5°	RN
20		- NO_2	- [b]	THF	- 4°	IN
21		- MeO	Na^+	THF	-24°	RN (≈ 90%)
22		- H	Na^+	THF	- 45°	RN (≈ 90%)

[a] $R_3Si-O-C_6H_4-Y$ =  with 1-NpPhSi(S)

[b] Reactions carried out with a cryptand specific for Na^+.

With a same reaction center (oxygen atom), the stereochemistry depends greatly on the para-substituent Y and on the dissociation of the ion pair :

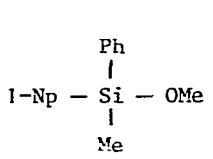
- Influence of the substituent on the phenyl group. An electron-releasing substituent (OMe group) which increases the negative charge on the nucleophilic center and thus its hardness favors retention as stereochemical outcome (runs 1-4, 13, 15, 16, 21). On the other hand, a significant decrease of stereoselectivity in retention or predominant inversion occurs with an electron-withdrawing substituent such as $-NO_2$ (runs 9-12, 19-20). In this case, we are faced with a greater delocalization of the negative charge over the aromatic system and thus with a softer nucleophile.
- Influence of the dissociation of the Aro^-M^+ ion pair. The effect of a variable delocalization of the negative charge is increased when carrying out the reaction in a basic solvent or with a cryptand specific for the Na^+ cation. With p-methoxyphenoxide, the dissociation of the ion pair increases the negative charge on the oxygen atom (runs 2,4 and 16) and the proportion of retention increases. On the other hand, with a softer anion such as p-nitrophenoxide, complexing the Na^+ cation favors the delocalization of the negative charge and thus it favors inversion (runs 10, 12, 20). The same observations can be made when the Na^+ is substituted by the bulky NR_4^+ cation : the dissociation of the ion pair is increased and we recover the above stereochemical shift, i.e., to retention with the -OMe group (run 3) and to inversion with $-NO_2$ (run 11).

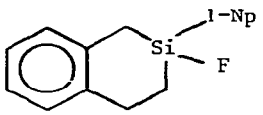
Thus the changes of stereochemistry depend always on electronic factors : the more delocalized nucleophilic anions react mainly with inversion, the ones with more concentrated charge with retention.

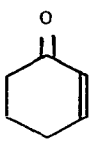
3) Parallel between the stereochemistry at silicon and the regioselectivity of attack at α-enones

In order to check our assumption, we have compared the stereochemistry at silicon and the regioselectivity of nucleophilic additions to α-enones. For instance, it is quite interesting to consider the very close parallel observed in reactions with $LiAlH_4$ (Table XIII p. 44). In presence of the [2.1.1] cryptand (KLi^+) specific for the Li^+ cation, $LiAlH_4$ in Et_2O (naked AlH_4^- anions) adds to α-enones at carbon-4 (57) and gives inversion at silicon (58), whereas $LiAlH_4$ in the absence of the macrocyclic ether adds at carbon-2 and leads to retention at silicon.

Table XIII







$LiAlH_4/Et_2O$	95 % RN	Rac	2 % 1,4
$LiAlH_4$/THF			16 % 1,4
$LiAlH_4/K_{Li}^+$ /Et_2O	75 % RN	65 % IN	70 % 1,4
$LiAlH_4/K_{Li}^+$/THF			85 % 1,4

The regioselectivity of these nucleophilic additions to α-enones has been extensively studied (59). The experimental data (especially of Seyden-Penne et al. (60)) and theoretical studies (61, 62, 63, 64) showed clearly that the proportion of 1,2/1,4-addition is controlled mainly by electronic factors.

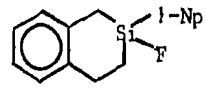
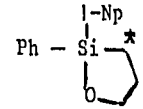
The following table reports some parallel studies of nucleophilic reactions of organometallics such as organolithiums, Grignard reagents and organocuprates (65) at a silicon center and with α-enones.

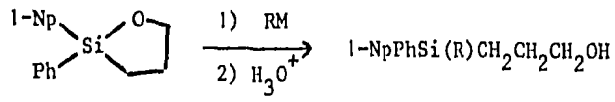
Concerning the influence of the nature of the nucleophile, we observe that for a given leaving group the change from inversion to retention is in the order: R_2CuMgX > RMgX > RLi . Examination of data given in literature for α-enones reactions leads to similar conclusions, viz., (a) organolithium derivatives give 1,2-addition (59), (b) organocuprates lead only to attack at carbon-4 (66) and (c) organomagnesium reagents show intermediate behavior (59).

This parallel is strengthened by the inversion at silicon observed in the substitution of the Si-OMe bond by $(PhCHCN)^-Li^+$. This soft reagent is known to give predominant 1,4-addition with α-enones (67) (Scheme 9).

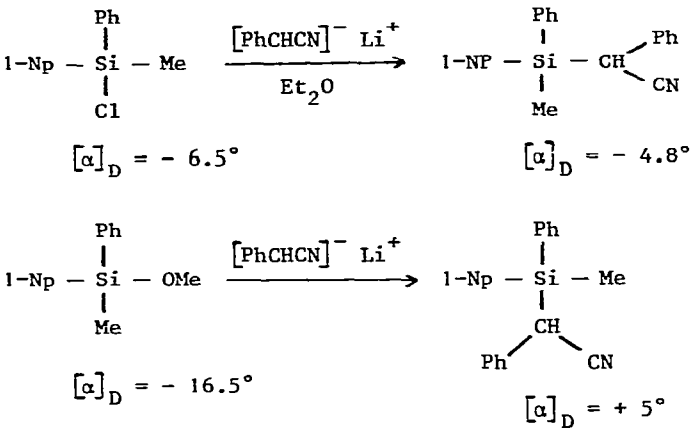
Thus we have shown that organometallics which favor 1,2-addition to α-enones react with retention at silicon, whereas those which favor 1,4-addition react with inversion. This is consistent with our hypothesis which holds that the dominant influence on the stereochemistry at silicon for a given leaving group is the electronic character of the nucleophile. It is well-supported by data concerning reduction reactions of organosilanes and α-enones by various alanes.

Table XIV

Runs	reagents	1-NpPhMeSiSPh			α-enones (regioselectivity of addition)
1	MeLi			$[\alpha]_D$ = - 8° RN	1,2
2	MeMgBr			$[\alpha]_D$ = - 8° RN	1,2 + 1,4
3	$Me_2CuMgBr$			rac	1,4
4	EtLi	92 % IN	96 % RN		1,2
5	EtMgBr	95 % IN	61 % RN		1,2 + 1,4
6	$Et_2CuMgBr$	95 % IN	84 % IN		1,4
7	PhLi		96 % RN		
8	PhMgBr		95 % RN		
9	$Ph_2CuMgBr$		55 % RN		

* 

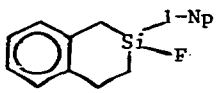
Scheme 9



4) Reduction reactions with alanes $AlH_{3-n}Y_n$

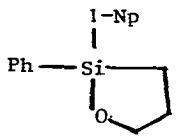
Table XV gives the stereochemical data for reduction of the optically active silanes *13*, *14*, *9*, *16* ($R_3SiX + AlH_{(3-n)}Y_n \longrightarrow R_3Si-H$), and ratios of 1,2 and 1,4-additions to the representatative α-enones, cyclohexenone and benzalacetone (65).

1-NpPhMeSiOMe = *13*



9

1-NpPhMeSi-F = *14*

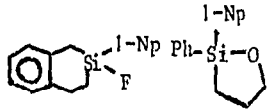


16

Two interesting effects have to be discussed in detail : substituent and solvent effects on the reactivity of alanes. Ashby et al. (68, 69) reported changes in the regioselectivity of α-enone reduction with changes in the nature of the substituents on the aluminium atom. For some alanes, $AlH_{(3-n)}Y_n$these changes on the 1,4-addition ratio are very close to those observed in their stereochemical behavior at silicon. For instance, substitution of hydrogen atoms in AlH_3 by OR or SR groups leads to increased inversion when the resulting reagent attacks at silicon (experiments 6, 8, 9 or 5 and 7 in Table XIVa). In the case of H_2AlI, there is only 1,4-addition with benzalacetone, and a very high selectivity towards inversion of configuration at silicon. These observations are in good agreement with our hy-

Table XIVa

Reduction reactions of the optically active silanes *13*, *14*, *9* and *16* and the representative enones

Reaction number	Reagent (solvent)[a]	1-NpPhMeSiX				cyclo-hexenone [d]	benzal-acetone [d]
		X = OMe	X = F				
1	Dibal(hexane)	100% RN(70)	98% RN(70)	100% RN	$[\alpha]_D$+19°RN(71)	100 % 1,2	100 % 1,2
2	Dibal(Et_2O)	99% RN(70)	90% IN(70)	80% RN	$[\alpha]_D$+16°RN	92 % 1,2	75 % 1,2
3	Dibal(TMEDA hexane)	95% RN(70)	90% IN(70)	70% RN	$[\alpha]_D$+15°RN	60 % 1,2	14 % 1,2
4	Dibal(THF)				$[\alpha]_D$+10°RN	85 % 1,2	10 % 1,2
5	$AlH_3(Et_2O)$	92% RN	96% IN	100% RN	$[\alpha]_D$+16°RN	97 % 1,2	80 % 1,2
6	AlH_3(THF)	90% RN	100% IN	70% IN	$[\alpha]_D$+ 8°RN	87 % 1,2	25 % 1,2
7	$(t\text{-BuO})_2AlH$ (Et_2O)	90% RN	100% IN	75% IN		87 % 1,2	10 % 1,2
8	$(t\text{-BuO})_2AlH$ (THF)	90% RN	100% IN	80% IN	$[\alpha]_D$-14°IN	80 % 1,2	8 % 1,2
9	$(EtS)_2AlH$(THF)	85% RN	100% IN	85% IN	$[\alpha]_D$-16°IN	40 % 1,2	6 % 1,2
10	H_2AlI(THF)	55% RN		80% IN	$[\alpha]_D$-18°IN	no reaction (68)	0 % 1,2

[a] TMEDA = tetramethylethylenediame, THF = tetrahydrofuran, Dibal = $i\text{-Bu}_2AlH$

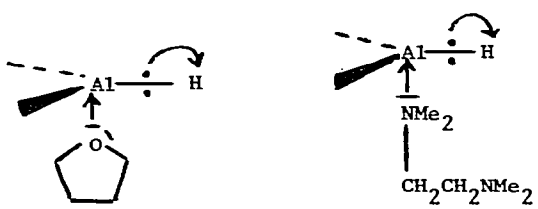
[b] Predominant stereochemistry (*13*, *14*, *9*) : the $[\alpha]_D$ for optically pure R_3Si^*H are known (1,72). A predominant stereochemistry of 90 % inversion indicates reaction path that is 90 % invertive and 10 % retentive, giving a product that is 80 % optically pure. [c] Predominant stereochemistry for *16* : we give the $[\alpha]_D$ of the alcohol, $(1\text{-Np})Ph(H)Si(CH_2)_3OH$. [d] % 1,4-addition = 100 %-(1,2-addition) %.

pothesis that a change in the nature of the Y group leads to a change in the electronic character of the Al-H bond.

The solvent effect is also very clear. For AlH_3, $(t\text{-}BuO)_2AlH$ and $(EtS)_2AlH$, an increase of the basicity of the solvent leads to increased 1,4-addition and increased inversion at silicon (experiments 5 and 6, 7 and 8). $i\text{-}Bu_2AlH$ is especially interesting in this respect (experiments 1, 2, 3 and 4). In hexane it is a very efficient reagent for 1,2-addition to α-enones, and it substitutes all Si-X bonds (X = Cl, SR, F and OR) with retention (70). Moreover, the addition at carbon-4 of α-enones and the percentage of inversion at silicon increase with the basicity of the solvent (hexane < Et_2O < THF) or the use of a complexing agent such as TMEDA.

We have already mentioned that the "naked" AlH_4^- anion leads mainly to 1,4-addition to α-enones (Table XIII) (57). The stereochemistry at silicon is changed to inversion. Thus the more localized on the hydrogen atom is the negative charge, greater is the 1,4-addition ratio and also, the easier the inversion at silicon. This fact is well-illustrated by the behavior of $i\text{-}Bu_2AlH$ or AlH_3 in hexane as solvent. The Al-H bond is slightly polarized and these species behave as hard reagents (1,2-addition to α-enones and retention at silicon, even with chlorosilanes (70). On the other hand, when used in a basic solvent, (Et_2O-THF) or with TMEDA, the coordination of the solvent at the aluminium atom delocalizes the negative charge on hydrogen (Scheme 10). Consequently, under these conditions $i\text{-}Bu_2AlH$ and AlH_3 behave as soft species and the inversion ratio at silicon and the 1,4-addition ratio to α-enones increase.

Scheme 10



In concluding this section on the influence of the nature of the nucleophile, it is important to stress the dominant influence of the nucleophile on the stereochemistry at silicon. This effect cannot be interpreted in terms of the stability of the intermediate on the basis of the apicophilicity rule as stated in phosphorus chemistry. It fails to explain the retention of configuration as the stereochemical outcome. No better explanation can be extracted from the quasi-cyclic mechanism proposed by Sommer et al. (1). On the other hand, we present much data obtained with nucleophiles other than carbon organometallics (RLi, RMgX), i.e., alkoxides, phenoxides

and alanes, $AlH_nY_{(3-n)}$ which all show clearly that the stereochemistry is controlled by the electronic character of the nucleophile. Finally, this dependance is supported by the parallel stated between the stereochemistry of nucleophilic displacements at silicon and the regioselectivity of attack on α-enones, this latter reaction being known as directed by electronic factors.

D - OTHER FACTORS

The foregoing data and discussions clearly indicate that the stereochemistry is mainly controlled by two following factors :

(i) - The ability of the leaving group to be substituted by a nucleophile. For acyclic silicon systems, the stereochemical trends which have been found experimentally show that increased capacity of the leaving group to be cleaved leads to a change of the stereochemistry to inversion.

(ii) - The electronic character of the nucleophile. For a given leaving group, the stereochemistry is extremely sensitive to the nature of the reagent. We provide strong evidence that nucleophiles in which the negative charge can be highly delocalized lead mainly to inversion, whereas charge-localized reagents favor retention.

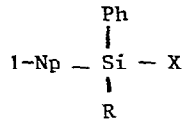
It seems appropriate at this point to discuss other factors which can influence the stereochemistry in borderline cases :

(i) - First, all of the optically active systems discussed above only contained acyclic silicon. We also have to consider the structures in which silicon is present in a ring, particularly a strained ring.

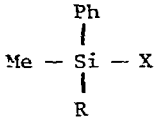
(ii) - We shall discuss the effect of external or internal electrophilic assistance on the stereochemistry.

I - INFLUENCE OF THE STRUCTURE OF THE ORGANOSILANE ON THE STEREOCHEMISTRY

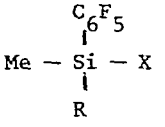
The stereochemical patterns reported for optically active 1-naphthylphenylmethylsilanes can be generally extended to other acyclic R_3Si^* - X systems. The following compounds have been investigated :



R = Me, Et, i-Pr, Vi



R = t-$BuCH_2$ (28)
i-Pr (28)
Et (28)
Ph_3Si (73)
Ph_3Ge (74)



R = 1-Np (75)
Ph (75)

The examination of the stereochemical data reported with the above optically active derivatives, in which the substituents attached to silicon encompass significant variation in their steric and polar effects, leads to the following comments :

(i) - Concerning possible steric effects on the stereochemistry, it seems clear from results (see for instance Table V or ref. 28) that the introduction of R groups of moderate to large steric requirements leaves the stereochemistry unchanged.

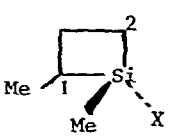
(ii) - Concerning possible polar effects on the stereochemistry, comparison of 1-NpPhMeSi-X and 1-NpC_6F_5MeSi-X systems is interesting. Although the pentafluorophenyl group is a powerful electron-withdrawing group relative to phenyl (76), these two systems do not differ to any significant extent. A similar comparison can be made with the 1-NpPhEtSi-X and 1-NpPhViSi-X derivatives.

On the other hand, structures in which silicon is included in a ring, particularly a strained ring, have stereochemical behavior which is strongly influenced by the geometry of the substrate.

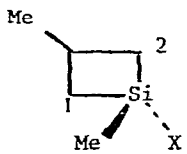
1) Experimental facts

a) Stereochemical behavior of exocyclic leaving groups :

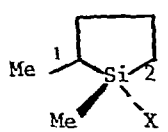
Important changes of stereochemistry, compared to acyclic silanes, were reported with the following cyclic systems :



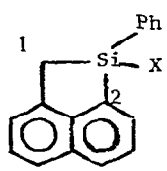
17 (77,78)



18 (77)



19 (79)



20 (80)

Table XV

Influence of an angle strain at silicon on the stereochemistry

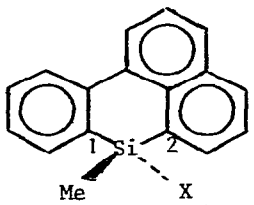
Substrate	Angle (c_1-Si-c_2)	$LiAlH_4$	RLi (R = alkyl)	RLi (R = aryl)	RLi (R = benzyl or allyl)	RMgX (R = alkyl)	RMgX (R = aryl)	RMgX (R = allyl or benzyl)	ref.
17 (Si-Cl)	< 90°(83)	RN					RN		(77,78)
17 (Si-F)	< 90°	RN	RN			RN			(77,78)
17 (Si-OR)	< 90°	RN	RN			RN			(77,78)
18 (Si-F)	< 90°		RN			RN			(77)
18 (Si-OR)	< 90°	RN	RN			RN			(77)
18 (Si-NMe_2)	< 90°					RN			(77)
20 (Si-Cl)	93.4°	RN							(80)
21 (Si-Cl)	≈ 90° [a]	IN							(81)
21 (Si-F)	≈ 90°	RN							(81)
19 (Si-Cl)	92-96°(84)	IN		IN		IN			(79)
19 (Si-F)	92-96°	Rac							(79)
19 (Si-H)	92-96°			RN					(79)

Table XV (cont.)

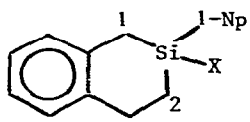
Substrate	Angle (c_1-Si-c_2)	$LiAlH_4$	RLi (R = alkyl)	RLi (R = aryl)	RLi (R= benzyl or allyl)	RMgX (R=alkyl)	RMgX (R=aryl)	RMgX (R= allyl or benzyl)	ref.
22 (Si-Cl)	≃ 105°(85)	IN	RN	RN	IN	IN	RN	IN	(87,88)
22 (Si-F)	≃ 105°	Rac	RN	RN	RN	RN	RN	IN	(87,88)
22 (Si-OMe)	≃ 105°	Rac	RN	RN	RN	RN	RN	RN	(87,88)
22 (Si-H)	≃ 105°	-	RN	RN	RN	-	-	-	(87,88)
R_3Si-Cl [b]	≃ 109°(86)	IN	IN	IN	IN	IN	IN	IN	(89)
R_3Si-F	≃ 109°	IN	RN		IN	IN	IN	IN	(89)
R_3Si-OMe	≃ 109°	RN	RN	RN	RN				(89)
R_3Si-H	≃ 109°	-	RN	RN					(89)

[a] No experimental value is reported in literature ; we give an approximative value calculated with the following bond lengths[85], Si-Ph = 1.87 Å, Si-1-Np = 1.85 Å, $>C-C<$ (Aryl) = 1.38 Å

[b] R_3Si-X = 1-NpPhMeSiX



21 (81)



22 (82)

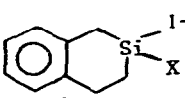
Some of the more interesting experiments are summarized in Table XV.

These stereochemical data lead to the following comments :

(i) - An increased angle strain at silicon leads always to a significant change of the stereochemistry to retention. This general trend is in particular increased with the most angle-strained systems 17 , 18 and 20. Both silacyclobutanes 17 and 18 react with retention, whatever the nature of the nucleophile. Even coupling reactions between 17 (Si-Cl) and $LiAlH_4$ or Grignard reagents (R = p-$MeOC_6H_4$ or p-MeC_6H_4), occur with complete retention of configuration, whereas the same reactions carried out with 1-NpPhMeSi-Cl lead to complete inversion. In compound 20 (C_2-Si-C_1 angle = 93.4°), the Si-Cl bond is cleaved by $LiAlH_4$ with retention of configuration (stereoselectivity = 87.5 %).

(ii) - A small angular strain is enough to raise such a stereochemical change. 1-Naphthyl-2 sila-2-tetrahydro-1,2,3,4 naphthalene, 22

Table XVI

Stereochemical behavior of 

: comparison with 1-NpPhMeSi-X[89] (X = Cl, F, OMe, H)

RM	Predominant stereochemistry (*) Si-Cl	SiF	SiOMe	Si-H
EtLi	63%RN(100%IN)	96%RN (90%RN)	94%RN (90%RN)	100%RN
n-BuLi	82%RN(59%IN)	98%RN (80%RN)	96%RN (86%RN)	100%RN (100%RN)
CH_2=$CHCH_2Li$	86%IN(100%IN)	95%RN (71%IN)	97%RN (85%RN)	85%RN (89%RN)
$PhCH_2Li$	99%IN(100%IN)	70%RN (85%IN)	75%RN (79%IN)	96%RN (90%RN)

* The stereochemical data reported with 1-NpPhMeSiX are given in parenthesis.

(C_1-Si-C_2 = 105°), shows significant deviations compared to 1-naphthylphenylmethylsilane (R_3Si-X) (bond angle = 109°).

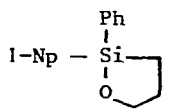
22 (Si-Cl) reacts with alkyl lithiums, leading to complete retention of configuration instead of inversion with R_3SiCl : allyl- or benzyllithium and the alkyl Grignard reagents cleave also the Si-F bond of *22* with retention, instead of inversion with R_3SiF.

(ii) - It is noteworthy that the cyclic strain does not change the main factors which govern the stereochemistry, i.e., the nature of the leaving group and the electronic character of the nucleophile (Table XVI).

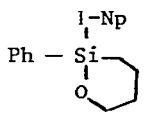
In both cases, the stereochemistry changes from inversion to retention when going from ≡Si-Cl to ≡Si-H. Moreover, charge-delocalized nucleophiles favor inversion,whereas highly charge-localized reagents lead to retention. The cyclic strain is only an additional factor leading to an overall change of the stereochemistry towards retention, at least in borderline cases. A dramatic change is observed only in the case of more highly strained four-membered rings.

b) Stereochemical behavior of endocyclic leaving groups :

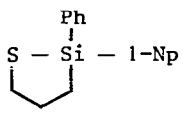
Optically active systems, *16*, *23* and *24*, containing both a silicon atom and leaving group in the ring have been investigated.



16 (65,71)



23 (90)



24 (91)

Stereochemical data are summarized in Tables XVII and XVIII and compared with those observed with 1-NpPhMeSi-OMe and 1-NpPhMeSi-SPh.

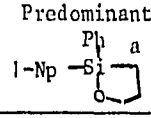
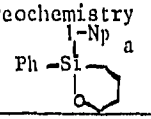
Several points in Tables XVII and XVIII are noteworthy :

(i) - We find again the dominant influence of the leaving group on the stereochemistry, as for acyclic compounds. The SR groups (Table XVIII) favor inversion of configuration, compared to analogous OR groups (Table XVII).

(ii) - Concerning the influence of the nucleophile, cyclic compounds *16* , *23* or *24* show behavior quite similar to that of their acyclic analogs. Charge-localized nucleophiles (alkyllithiums or alkyl Grignard reagents) and $LiAlH_4$ lead to the expected stereochemical outcome in the case of alkoxy leaving groups, i.e., retention of configuration (Table XVII, runs 1-4). Charge-delocalized nucleophiles react with inversion (Table XVII, runs 7, 9, 10). The same observations can be made with -SR leaving groups (Table XVIII).

Table XVII

Stereochemical behavior of endocyclic OR leaving groups

Runs	Nucleophile	Products	1-NpPhMeSi-OMe[1,2]	Predominant stereochemistry 	
1	EtLi	$R_3Si - Et$	95 % RN		
2	CH_3Li	$R_3Si - CH_3$	-	$[\alpha]_D = -8°$ RN	$[\alpha]_D = -2.6°$ RN
3	CH_3MgBr	$R_3Si - CH_3$	-	$[\alpha]_D = -8°$ RN	$[\alpha]_D = -2°$ RN
4	$LiAlH_4$	$R_3Si - H$	90 % RN	$[\alpha]_D = +13°$ RN	$[\alpha]_D = -7°$ RN
5	$LiAlH_4/4CuI/THF$[68]	$R_3Si - H$	55 % RN	$[\alpha]_D = -18°$ IN	$[\alpha]_D = -0.6°$ RN
6	$CH_2=CHCH_2Li$	$R_3SiCH_2-CH=CH_2$	85 % RN [b]	$[\alpha]_D = -5°$ IN	$[\alpha]_D = -2.4°$ RN
7	$CH_2=CHCH_2MgBr$	$R_3SiCH_2-CH=CH_2$	-	$[\alpha]_D = -6.5°$IN	$[\alpha]_D = +3.3°$ IN
8	$p\text{-}CH_3OC_6H_5CH_2Li$	$R_3Si\text{-}CH_2C_6H_5\text{-}(p\text{-}OCH_3)$	90 % RN	$[\alpha]_D = -4°$ IN	$[\alpha]_D = -2°$ RN
9	$C_6H_5CH_2Li$	$R_3Si - CH_2Ph$	79 % IN	$[\alpha]_D = -3°$ IN	$[\alpha]_D = +4°$ IN
10	$C_6H_5CH_2MgBr$	$R_3Si - CH_2Ph$	75 % IN	$[\alpha]_D = -3.7°$IN	$[\alpha]_D = +8°$ IN

[a] *16* + Nu ⟶ $R_1R_2NuSi(CH_2)_3OH$ (= R_3Si-Nu), *23* + Nu ⟶ $R_1R_2NuSi(CH_2)_4OH$ (= R_3Si - Nu)

[b] Cf. note p.14

Table XVIII

Stereochemical behavior of endocyclic -SR leaving groups

Nucleophile	Product	Predominant stereochemistry 1-NpPhMeSi-SMe[31]	1-NpPhMeSi-SPh[32]	24*
Dibal/hexane	R_3Si-H	RN	RN	RN
$LiAlH_4$	R_3Si-H	IN	IN	IN
R'Li (R' = Me, Et, neo-C_5H_{11})	R_3Si-R'	RN	RN	RN
R'MgX (R' = Me, Et)	R_3Si-R'		IN	IN

* 24 + Nu ⟶ $R_1R_2(Nu)Si(CH_2)_3SH$ (R_1 = 1-Np, R_2 = Ph)

(iii) - In borderline cases, some differences are apparent between analogous acyclic and cyclic strained organosilanes. Nucleophiles, such as allyllithium, p-methoxybenzyllithium and the $LiAlH_4$-4CuI reagent lead to inversion in the case of the five-membered ring compound 16 (Table XVII, runs 5, 6, 8).

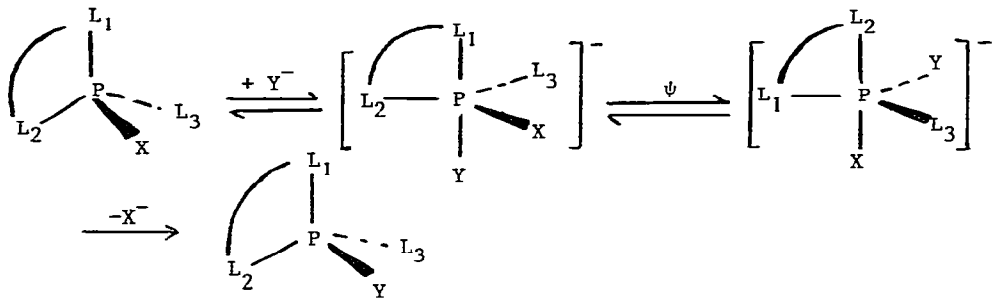
On the other hand, the six-membered ring 23 and the acyclic 1-NpPhMeSi-OMe show the same stereochemical behavior and lead to retention.

(iiii) - A cyclic strained geometry influences the stereochemistry with a general shift to inversion for endocyclic leaving groups. It is opposite to the change towards retention previously mentioned for exocyclic leaving groups when the angle strain at silicon is increased.

2) Discussion

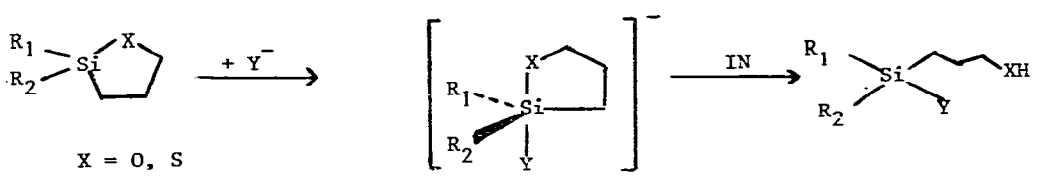
When the phosphorus atom of phospholane oxides and phosphonium ions is incorporated into a four- or five-membered ring, the reduction or displacement reactions proceed, as a rule, with retention of configuration, in contrast to the analogous reactions of acyclic systems where inversion is the normal stereochemistry (92). Ring strain is invoked as the main factor in determining the stability of the intermediate. The analysis takes the following form. Four- or five-membered rings are unable to occupy the diequatorial position of a trigonal bipyramidal intermediate and must occupy the apical-equatorial position. Consequently, the nucleophile Y^- (Scheme 11) displaces the leaving group X with retention.

Scheme 11



With organosilanes, we might also invoke such a factor to explain the stereochemical changes observed with angle strain. It would agree with the general shift towards retention for exocyclic leaving groups. For an endocyclic leaving group, it would agree with a change to inversion. For instance, five-membered rings must occupy the preferred equatorial-apical position of a trigonal bipyramidal intermediate with the most electronegative group (oxygen or sulfur atom) in the apical position (Scheme 12) and thus favor inversion.

Scheme 12



X = O, S

However, in organosilicon chemistry, we have much data obtained from experiments in which the ring size and the nature of the leaving group were varied. They permit a sharper analysis and, in particular, they lead to the following comments :

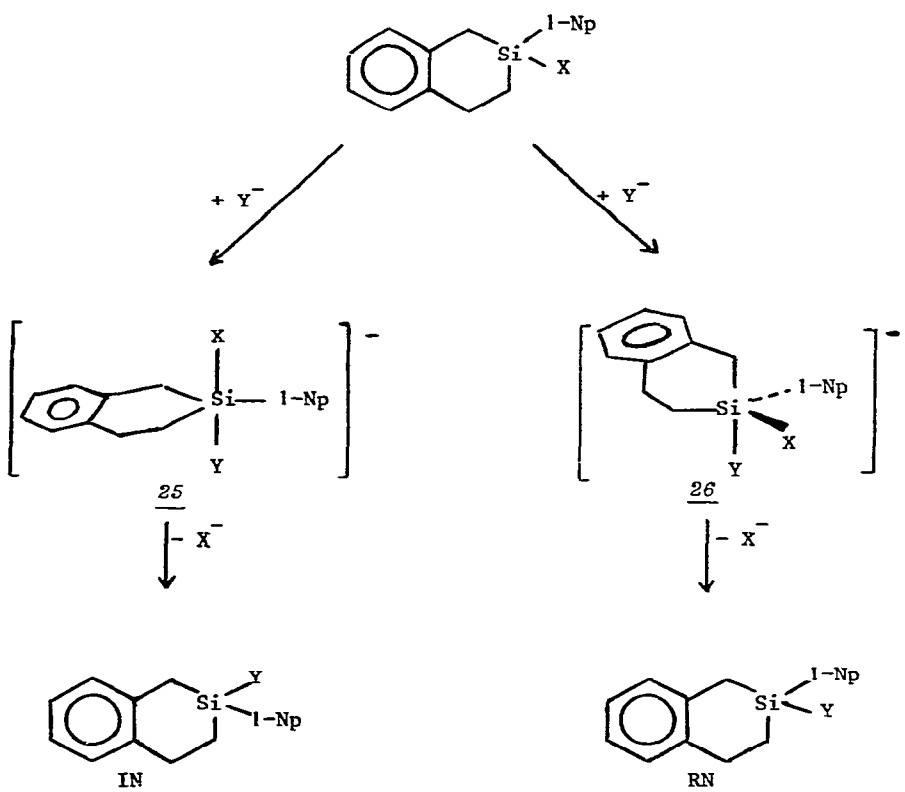
(i) - With the exception of highly strained silacyclobutanes, ring strain does not change the dominant influence of the electronic character of the nucleophile on the stereochemistry. For instance, the oxa-silacyclopentane *16* behaves very similar to the analogous acyclic R_3Si^{*}— OMe. Thus the stability of the intermediate does not govern the stereochemical path. This point will be discussed more in detail in a later section which deals with the geometry of attack of the nucleophile.

(ii) - Experimental data for exocyclic leaving groups show a gradual change of the stereochemistry from inversion to retention when the angle strain at silicon is increased, as indicated in the following scheme :

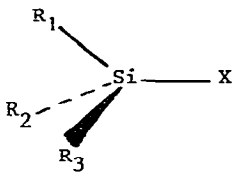
IN ⟶			RN
109°	105°	93-96°	90°
acyclic silanes	six-membered rings	sila-cyclo-pentanes	sila-cyclo-butanes

This fact cannot be easily rationalized from geometric considerations. In particular, the ring strain does not explain why inversion of configuration, compared to retention, is so unfavorable in the case of the six-membered ring [$(C_1\text{-Si-}C_2) = 105°$] . This value suggests that intermediates such as *25* and *26* have energetically equal chances to be formed, and thus both inversion and retention would be expected (Scheme 13).

Scheme 13



For these various reasons, we think that a better explanati is proposed by Nguyễn Trong Anh and C. Minot (93) in terms of change of the hybridization of the Si-R bonds around the tetracoordinated silicon atom :



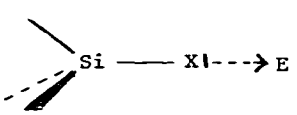
If the R_2SiR_3 angle becomes smaller than the tetrahedral va the R_1SiX angle becomes larger than 109°28'. The four hybrid atomic orbitals of Si are no longer equivalent. The two used for making the SiR_2 and SiR_3 bonds have less s character than a sp^3 hybrid orbital, while th two remaining atomic orbitals acquire more s character. The above author show from molecular orbital calculations that an increase of the s chara ter implies an easier front-side attack at silicon and, therefore, a gre ter ratio of retention (this theoretical approach will be discussed in d tail in the conclusion). It follows that if the Si atom is included in a strained ring while X remains extracyclic, the percentage of retention will increase. A similar reasoning shows that if Si and X are both in th ring, inversion of configuration is favored. These conclusions agree wel with the experimental results. In particular, an attractive explanation of the gradual change of the stereochemistry from inversion to retention when the angle strain at silicon is increased in the case of an extracyclic leaving group,is developed.

II - INFLUENCE OF ELECTROPHILIC ASSISTANCE ON THE STEREOCHEMISTRY OF NUCLEOPHILIC SUBSTITUTIONS AT SILICON

In this section, we shall examine the effect of electrophilic assistance on the stereochemistry of the cleavage of an ≡ Si-X bond. Two different cases must be distinguished :

(i) - The influence of external assistance. The lability an as a consequence, the stereochemistry of displacement of a ≡ Si-X bond c be modified by the complexation of the X group by an electrophile such a H^+, Li^+ or BX_3 (Scheme 14).

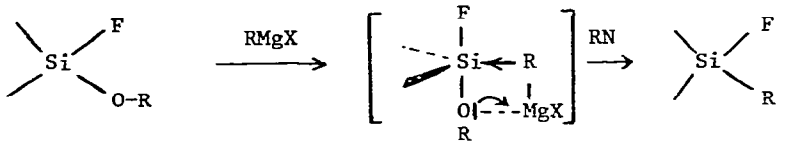
Scheme 14



$E = H^+$, Li^+ or BX_3

(ii) - The influence of internal assistance. The electrophilic part of the attacking nucleophile itself can influence the reactivity of the leaving group. As we shall see later, this effect especially must be taken into account in the case of bifunctional silanes. It does not control the stereochemistry. However, the selectivity of cleavage of two borderline leaving groups with similar labilities can be determined by their respective affinity for the electrophilic portion of the reagent (Scheme 15).

Scheme 15



1) Influence of external assistance

a) Solvolysis of silylamines under acidic or neutral conditions :

In general silicon-nitrogen bonds are far more reactive toward acidic than toward basic reagents. Hexaphenyldisilazane, which undergoes solvolysis readily in presence of acid, reacts slowly even with boiling aqueous-alcoholic alkali (94). To throw some light on the mechanism, several rate and stereochemical studies on the methanolysis and hydrolysis of silylamines have been carried out.

Eaborn et al. have carried out rate studies on the methanolysis of (trialkylsilyl) anilines (95) :

$$MeOH + X\text{-}C_6H_4\text{-}NHSiR_3 \longrightarrow X\text{-}C_6H_4NH_2 + R_3SiOMe$$

(X = H, Me, Cl, OMe, F)

For neutral and acid-catalysed alcoholysis, the results are consistent with specific oxonium ions catalysis, as described in the following reaction sequence (acidic conditions) :

$$ArNHSi(i\text{-}Pr)_3 + MeOH_2^+ \xrightarrow{\text{fast}} \overset{+}{ArNH_2}\text{—}Si(i\text{-}Pr_3) + MeOH$$

$$\overset{+}{ArNH_2}\text{—}Si(i\text{-}Pr)_3 + MeOH \longrightarrow ArNH_2 + (i\text{-}Pr)_3Si\text{—}\overset{+}{\underset{H}{O}}\text{—}Me$$

$$(i\text{-}Pr)_3Si\text{—}\overset{+}{\underset{H}{O}}\text{—}Me + MeOH \longrightarrow (i\text{-}Pr)_3SiOMe + MeOH_2^+$$

The protonation of the silylamine increases the lability of the Si-N bond. $R_3Si-\overset{+}{N}H_2Ph$ is more easily cleaved than $R_3SiNHPh$, as is clearly indicated by the inhibition of these solvolysis reactions when a little alkali is added to neutral solutions.

Moreover, these rate studies are consistent with the stereochemical data (Table XIX) : $-NHR^+$ is a good leaving group and thus the observed inversion of configuration at silicon is the expected stereochemistry.

Table XIX

Hydrolysis and methanolysis of silylamines under neutral or acid-catalysed conditions

Reactant	Nucleophile	Catalyst	Product	Stereochemistry	ref.
R_3SiPyr	H_2O/Et_2O	H^+	R_3SiOH	76 % IN	(22)
$R_3SiNH-i-Bu$	H_2O/Et_2O	H^+	R_3SiOH	95 % IN	(22)
R_3SiNH_2	H_2O/Et_2O	H^+	R_3Si-OH	96 % IN	(22)
$R_3SiNH-CH_3$	H_2O/dioxan	-	R_3Si-OH	IN	(96)
$R_3SiNH-CH_3$	CH_3/OH	-	$R_3Si-OCH_3$	IN	(96)
	n-BuOH	-	$R_3Si-O-n-Bu$	IN	(96)
	$c.C_6H_{11}OH$	-	$R_3Si-O-c.C_6H_{11}$	IN	(96)
$R_3SiN(Et)_2$	CH_3OH/cyclohexan	-	$R_3Si-OCH_3$	IN	(96)
R_3Si-NH_2	CH_3OH/benzene	-	$R_3Si-OCH_3$	IN	(96)

R_3Si = 1-NpPhMeSi

Pyr = 1-pyrrolidinyl

b) Reactions of silicon-oxygen and silicon-nitrogen compounds with boron halides

The boron halides are strong Lewis acids and their reactions with silicon-oxygen bonds to give halosilanes are well-known. In Table

XX are reported the results of stereochemical studies carried out with such reagents (97).

Reactions with BF_3 or its etherate invariably give inversion of configuration at silicon. In contrast, BCl_3 gives high retention of configuration.

The reactions of boron halides with silicon-nitrogen bonds also produce halosilanes, in many cases via demonstrable formation of the aminosilane-boron halide complex at low temperature. Table XXI reports the results of stereochemical studies (97).

Table XX

Stereochemistry of cleavage of silicon-oxygen bonds by boron halides

Substrate	Solvent	Boron halide	Product	Predominant stereochemistry	%
R_3Si^*OMe	pentane	BCl_3	R_3Si^*Cl	RN	92
R_3Si^*OMe	pentane	BF_3	R_3Si^*F	IN	89
R_3Si^*OMe	pentane	BF_3, OEt_2	R_3Si^*F	IN	68
R_3Si^*OMe	Et_2O	BF_3, OEt_2	R_3Si^*F	IN	73
R_3Si^*OH	benzene	BF_3, OEt_2	R_3Si^*F	IN	76
R_3Si^*OK	xylene	BF_3, OEt_2	R_3Si^*F	IN	75
$R_3Si^*OSi^*R_3$	xylene	BF_3, OEt_2	no reaction		
R_3Si^*O-(-)-Men	Et_2O	BF_3, OEt_2	R_3Si^*F	IN	89
R_3Si^*O-t-Bu	Et_2O	BF_3, OEt_2	R_3Si^*F	IN	70
R'_3Si^*OMe	pentane	BCl_3	R_3Si^*Cl	RN	100
R'_3Si^*OMe	pentane	BF_3	R'_3Si^*F	IN	100
R'_3Si^*OMe	pentane	BF_3, OEt_2	R'_3Si^*F	IN	84
R''_3Si^*OMe	pentane	BCl_3	R''_3Si^*Cl	RN	92
R''_3Si^*OMe	pentane	BF_3	R''_3Si^*F	IN	97
R''_3Si^*OMe	pentane	BF_3, OEt_2	R''_3Si^*F	IN	85

* R_3Si = 1-NpPhMeSi , R'_3Si = neopentylphenylmethylSi, R''_3Si = benzhydrylphenylmethylSi.

Table XXI

Stereochemistry of reactions of silylamines with boron halides

Silylamine [a]	Boron halide	Solvent	Product	Predominant stereochemistry	%
R_3Si^*Pyr	BF_3	pentane	R_3Si^*F	RN	54
R_3Si^*Pyr	BF_3, OEt_2	Et_2O	R_3Si^*F	IN	57
R_3Si^*NHBu	BF_3	pentane	R_3Si^*F	IN	62
R_3Si^*NHBu	BF_3, OEt_2	Et_2O	R_3si^*F	IN	74
$R_3Si^*NH_2$	BF_3	pentane	R_3Si^*F	IN	81
R_3Si^*Pyr	BCl_3	pentane	R_3Si^*H [b]	IN	68
R_3Si^*NHBu	BCl_3	pentane	R_3Si^*H [b]	IN	90
R_3Si^*Pyr	BBr_3	pentane	R_3Si^*H [b]	IN	81
R_3Si^*NHBu	BBr_3	pentane	R_3Si^*H [b]	IN	73

[a] R_3Si = 1-NpPhMeSi, pyr = 1-pyrrolidinyl

[b] The initial product was reduced by $LiAlH_4$

With the exception of R_3Si-Pyr which proceeds with slight preference for retention, the reactions in both Tables XX and XXI using BF_3 or its etherate proceed with predominant inversion. The difference between the oxygen and nitrogen compounds lies in their stereochemical behavior with BCl_3. The former react with retention and the latter with inversion of configuration.

These reactions are known to proceed as rapidly as the Lewis acid is added. This fact, taken together with the low-temperature isolation of coordination complexes of boron halides with silicon-nitrogen and silicon-oxygen compounds (98), strongly suggests that the first step in the BX_3 reactions involves the conversion of the $-NR_2$ and $-OR$ groups to better leaving groups by coordination with BX_3.

$$\equiv Si-Y- + BX_3 \longrightarrow \equiv Si-\underset{\downarrow}{Y}-BX_3$$

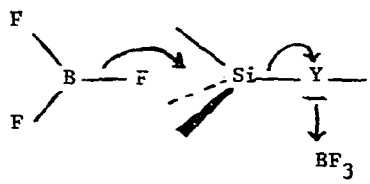
(Y = N, O)(X = Cl, F)

The inversion of configuration is well-explained by attack of a second molecule of BF_3, via fluorine, at the rear of the silicon : it displaces the oxygen or nitrogen, whose leaving group ability has been enhanced by coordination (Scheme 16).

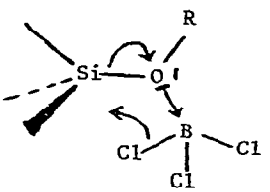
BCl_3 is known to have a greater Lewis acid strength than BF_3 (99). It would be expected to favor inversion of configuration by enhanced coordination of the oxygen or nitrogen atom. This assumption is confirmed with the silicon-nitrogen reactants : in all cases, BCl_3 leads to a far greater stereoselectivity in inversion.

The only exception is observed in the reaction of the Si-OCH_3 bond with BCl_3 which gives a very high ratio of RN instead of the good inversion observed with BF_3 or BF_3, Et_2O. This latter stereochemistry is well-explained by the complexation of the oxygen atom which increases the lability of the Si-O bond. For BCl_3, we believe that we are faced with an unique case and that the retention has to be explained by an another mechanism ; BCl_3 could lead to the formation of a very unstable complex with the oxygen atom of the OR group which decomposes intramolecularly, leading to retention as stereochemical outcome (Scheme 16).

Scheme 16



displacement of the Si-OR bond by BF_3 , Et_2O



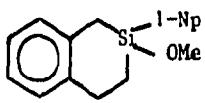
displacement of Si-OR bond by BCl_3

c) Electrophilic assistance by Li^+ and Mg^{2+} cations

In several cases, it has been reported that the stereochemistry depends on the nature of dissolved salts. We shall discuss here data reported for coupling reactions with organometallic reagents. From a general point of view, they show clearly a stereochemical shift towards inversion when external electrophilic assistance is operative. The most significant experimental observations are :

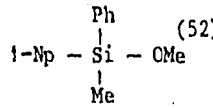
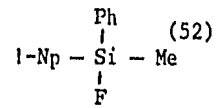
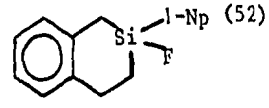
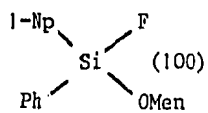
(i) - Coupling reactions between EtMgBr and 1-NpPhViSiF in Et_2O or THF lead to inversion (Table VII). Retention only occured in DME

Table XXII

Organosilane	Nucleophile (solvent)	Added salt	Product	Predominant stereochemistry		Ref.
	$CH_3-CH=CHCH_2MgBr$ (Et_2O)	-	$R_3Si-CH_2CH=CHCH_3$	92 %	RN	(50)
	$CH_3-CH=CHCH_2MgBr$ (Et_2O)	$MgBr_2$	$R_3Si-CH_2CH=CHCH_3$	57 %	IN	(50)
1-NpPh(-)MenOSiOMe	$CH_2=CH-CH_2MgBr$ (Et_2O)	-	$R_2(OMe)SiCH_2-CH=CH_2^*$	69 %	IN	(50)
	$CH_2=CH-CH_2MgBr$ (Et_2O)	$MgBr_2$	$R_2(OMe)SiCH_2-CH=CH_2^*$	88 %	IN	(50)

* R_2Si= : 1-NpPhSi=

Table XXIII

Reagents	 (52)	 (52)	 (52)	 (100)
$EtLi/Et_2O$	90 % RN (R_3SiEt)	90 % RN (R_3SiEt)	96 % RN (R_3SiEt)	$R_2(Et)SiF$ (40 %) $R_2(Et)SiOMen$ (60%) 60 % RN
$EtLi/LiClO_4/Et_2O$	85 % RN (R_3SiEt)	57 % (R_3SiEt)	75 % RN (R_3SiEt)	$R_2(Et)SiF$ (29 %) $R_2(Et)SiOMen$ (71%) 54 % RN

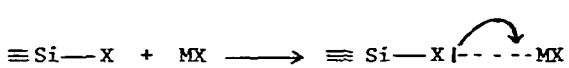
(25). When the same reactions are carried out with Et_2Mg (free of $MgBr_2$), a shift towards retention is observed (Table VII).

(ii) - A net shift of the stereochemistry towards inversion also is observed on the dissolution of $MgBr_2$ (Table XXII) in the reaction mixture in the case of displacement of OR from silicon (50, 35).

(iii) - The stereochemistry of displacement of a fluorine atom is influenced by added Li^+ cation (as $LiClO_4$). A decrease of the stereoselectivity in retention or a change from retention to inversion is observed (Table XXIII) (52). Moreover, with 1-NpPhSi(OMen)F, it is parallel with an enhanced selectivity in the cleavage of the Si-F bond (100). In contrast, alkoxysilanes are insensitive to added $LiClO_4$.

These various data show clearly the effect of an external electrophilic assistance on the stereochemistry of substitution. In all cases, Lewis-acid-type salts can facilitate inversion. We have shown previously that a shift of the stereochemistry from retention to inversion is always parallel to an increase of the ability of the leaving group to be substituted. These observations are then explained in terms of conversion of a given leaving group to a better leaving group by coordination with Li^+ or $MgBr_2$ (Scheme 17).

Scheme 17



MX = $LiClO_4$ or $MgBr_2$

The above assumption is well-illustrated in the case of the (EtLi + $LiClO_4$) system. Ashby et al. have shown that $LiClO_4$ does not complex with an organolithium (69). Thus a change in the stereochemical outcome when $LiClO_4$ is added can only be explained by a modification of the leaving group by electrophilic assistance. The very small effect observed with a Si-OMe bond implies a reluctance to complex the Li^+ cation (Table XXIII). In contrast, the slight shift to inversion observed with the fluorine group results from its greater affinity towards the Li^+ cation.

2) Influence of internal electrophilic assistance

In this case, it is the electrophilic part of the attacking nucleophile itself which influences the chemical behavior of the leaving group. Results are summarized in Table XXIV.

Table XXIV

Chemical behavior of bifunctional organosilanes with organometallics : influence of an electrophilic assistance

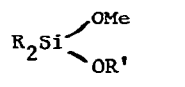
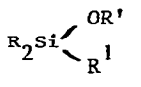
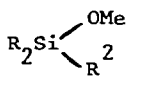
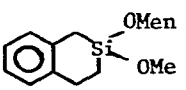
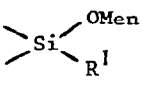
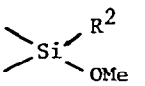
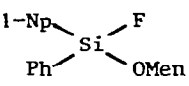
Organosilane	Nucleophile	Products(yield)	stereochemistry	ref.
 (R = 1-Np, Ph R' = bornyl cyclohexyl)	R^1MgX = alkyl aryl		-	(102)
	R^2MgX = allyl, benzyl		-	(102)
	R^1MgX = alkyl, aryl		-	(102)
	R^2MgX = allyl, benzyl		-	(102)
	MeLi	1-NpPh(Me)Si-OMen (100%)	RN	(103)
	EtLi	1-NpPh(Et)Si-OMen (60%) + 1-NpPh(F)Si-Et (40%)	RN (not isolated)	(103)
	n-PrLi	1-NpPh(n-Pr)SiOMen (56%) 1-NpPh(F)Sin-Pr (44%)	RN (not isolated)	(103)
	n-BuLi	1-NpPh(n-Bu)SiOMen (75%) 1-NpPh(F)Sin-Bu (25%)	RN (not isolated)	(103)

Table XXIV cont.

Organosilane	Nucleophile	Products(yield)	stereo-chemistry	ref.
	$neo\text{-}C_5H_{11}Li$	1-NpPh(neo-C_5H_{11})SiOMen 1-NpPh(F)Si(neo-C_5H_{11})(90%)	(not isolated) RN	(103)
	RMgX (R = Me, Et, n-Pr, p.$CH_3C_6H_4$)	1-NpPh(F)SiR	RN	(103)
1-NpFc(F)Si-OEt	MeLi	1-NpFcMeSi-OEt	RN	(103)
	EtLi	1-NpFc(Et)Si-OEt (52%) + 1-NpFc(F)Si-Et (19%)	IN RN	(103)
	n-PrLi	1-NpFc(n-Pr)Si-OEt (48%) + 1-NpFc(F)Si-n-Pr (17%)	IN RN	(103)
	RMgBr (R = Me, Et, n-Pr, Ph)	1-NpFc(F)Si-R	RN	(103)
1-NpPh(MeO)SiOMen	MeLi	1-NpPh(Me)Si-OMen (73%) + 1-NpPh(MeO)Si-Me (27%)	RN RN	(104,105)
	EtLi	1-NpPh(Et)Si-OMen (85%) + 1-NpPh(MeO)Si-Et (15%)	RN RN	(104,105)
	n-PrLi	1-NpPh(n-Pr)Si-OMen (>80%) 1-NpPh(MeO)Sin-Pr (<20%)	RN RN	(104,105) (104,105)

Table XXIV (cont.)

Organosilane	Nucleophile	Products(yield)	Stereo-chemistry	ref.
1-NpPh(MeO)SiOMen	n-BuLi	1-NpPh(n-Bu)Si-OMen (87%) + 1-NpPh(MeO)Si-n-Bu (13%)	RN RN	(104,105)
	R^1MgX R^1 = Me, Et, n-Pr, i-Pr	1-NpPh(R^1)Si-OMen	RN	(104)
	R^2MgX (CH_2 = CH-CH_2, $PhCH_2$)	1-NpPh(MeO)Si-R^2	IN	(35)

Bifunctional organosilanes, where the two potential leaving groups have close abilities to be substituted, i.e., for instance, $R_2Si(OMe)OR'$ (R' = Men, cyclohexyl, bornyl) and 1-Np(R)Si(F)OR' (R = Ph or Fc, R' = Men or Et), show particular behavior. Attack by organolithiums and by Grignard reagents are to be distinguished :

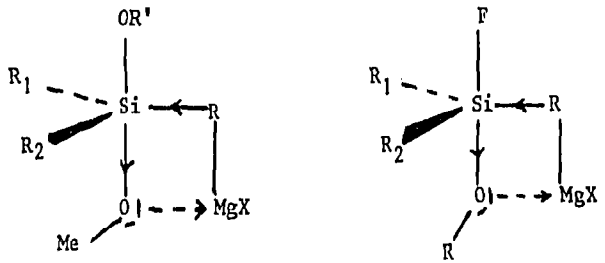
(i) - Soft organolithiums and Grignard reagents which lead to inversion, cleave only the best leaving group (F vs OR group, Table VI).

(ii) - Hard organolithiums show a lack of selectivity. They substitute concurrently the two leaving groups with predominant cleavage of the better one due either to electronegativity (F vs OR group) or for steric reasons (OMen vs OMe).

(iii) - In contrast, saturated Grignard reagents, which react with predominant retention, lead to the selective cleavage of the alkoxy group (F vs OR). Moreover, with dialkoxysilanes, the less bulky group only is cleaved (OMe vs OMen).

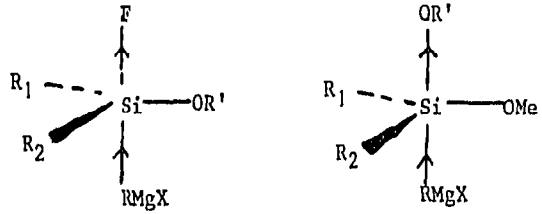
All these comments show clearly that in borderline cases, i.e., for leaving groups having close abilities to be substituted, the assistance by the electrophilic part of the nucleophile can direct the substitution selectivity. The Li^+ cation has no great affinity either for OR or F groups. This explains the lack of selectivity with hard organolithiums which give retention, and the best leaving group is predominantly cleaved (Scheme 18) (the retention is explained by an equatorial attack, that will be discussed in detail in the next section).

Scheme 18



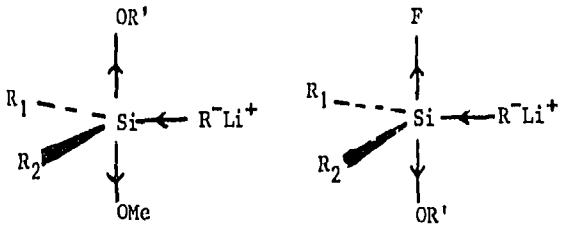
RN

(for RMgX, R = alkyl or aryl)



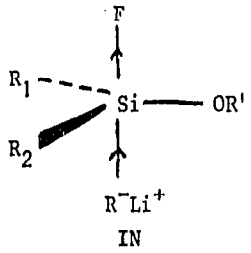
IN

(for RMgX, R = allyl, benzyl)



RN

(for RLi, R = alkyl)



IN

(for RLi, R = Ph, CH_2=CH-CH_2, Ph-C≡C)

(R' = Et, Men, cyclohexyl, bornyl)

In contrast, the magnesium atom is known to have a great affinity toward oxygen. With Grignard reagents which react with retention, it explains that the OR group complexed by the magnesium becomes a better leaving group than fluorine ; it is cleaved selectively (Scheme 18). With dialkoxysilanes, $R_2Si(OMe)OR'$, the complexation by magnesium occurs only with the oxygen atom of the less bulky alkoxy group. This serves to explain its greater readiness to be substituted, compared to the OR' group (Scheme 18).

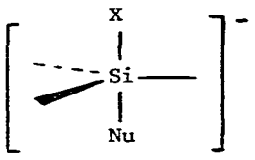
Finally, these data show clearly that in any case, this factor controls the stereochemistry. Softer anions (allyl, benzyl) react with inversion and the better leaving group is cleaved. For hard reagents (alkyl anions),it is the electronic character of the anion whichat first determines the geometry of attack ; then electrophilic assistance may influence the selectivity in changing the respective ability to be cleaved of the two potential leaving groups. With Li^+, which has a low affinity for electrophilic assistance towards Si-F and Si-OR bonds, a lack of selectivity is observed. In contrast, the Mg atom has a better affinity towards the oxygen atom and the alkoxy leaving group only is displaced with retention.

E - GEOMETRY OF ATTACK OF THE NUCLEOPHILE AT SILICON. HOW IS IT POSSIBLE TO EXPLAIN INVERSION AND RETENTION OF CONFIGURATION ?

In the above sections,we discussed in detail the main factors which control the stereochemistry of nucleophilic displacements at silicon. Either retention or inversion of configuration can occur, and the change in stereochemistry clearly is a function of the nature of the leaving group (§ B) and of the electronic character of the nucleophile (§ C). In borderline cases, other factors, such as the geometry of the starting organosilanes (§ D-I) or electrophilic assistance by the cationic part of the attacking reagent (§ D-II) can have a substantial influence.

Our purpose is now to propose a reasonable explanation of these results, and, in particular, to discuss the geometry of attack of the nucleophile at silicon which leads in a first determinant step to the formation of a pentacoordinate intermediate (§ A-II).

Concerning the reactions occurring with inversion, the mechanistic interpretation is quite easy. This stereochemistry requires a backside attack of the nucleophile opposite the leaving group. With regard to the skeleton of the intermediate, it corresponds to apical entry and departure (intermediate *27*).



27

(Nu^- = nucleophile)

Concerning substitution at silicon occurring with retention, it requires a nucleophilic attack at 90° with respect to the leaving group. Two different mechanisms can be advanced :

(i) - Apical attack of the nucleophile, leading to an intermediate such as *28* with the electronegative leaving group in an equatorial position.

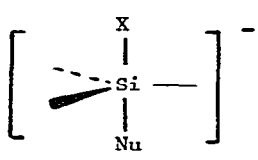
(ii) - Equatorial attack of the nucleophile, the leaving group being apical in a trigonal bipyramid like the intermediate *29*

28 *29*

(Nu^- = nucleophile, X = leaving group).

Two preliminary remarks can be made at this point :

(i) - The apical entry of the nucleophile implies that the leaving group is equatorial. In the case of monofunctional organosilanes, R_3SiX, for instance, fluorosilanes (R_3Si-F), X is also the most electronegative group around the silicon atom. Muetterties et al. (49) have shown by NMR spectroscopy that the electronegative fluorine atoms always occupy the apical positions of pentacoordinated anions such as $R_3SiF_4^-$ or $R_2SiF_3^-$. Thus we can assume that the most stable intermediate resulting from apical attack of the nucleophile is *27* and not *28* :



27

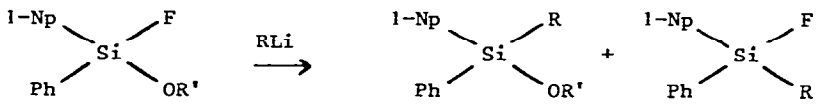
This intermediate, *27* , only explains the inversion at silicon.

(ii) - Opposed to the second hypothesis, we are faced with an unusual process.

We wish now to present the evidence supporting the second hypothesis and show how it explains easily the retention of configuration at silicon. For this purpose, we turn now to a discussion of the following data :

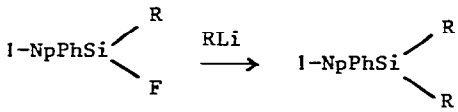
I - COUPLING REACTIONS BETWEEN ALKYLLITHIUMS AND BIFUNCTIONAL ORGANOSILANES

Hard nucleophiles, such as alkyllithiums (RLi = MeLi, EtLi, n-PrLi or n-BuLi), lead to a competitive cleavage of the two electronegative groups attached at silicon in fluoroalkoxysilanes, $R_2Si(F)OR'$ (103).



The most striking data, obtained in the reactions of RLi in the presence of a cryptand specific for the Li^+ cation (in order to avoid the possible interactions between Li^+ and the leaving group) are reported in Table XXV. In the case of 1-NpPh(F)SiOMen, the concurrent substitution takes place with retention on the both leaving groups, with stereoselectivities up to 96 %

The fluorosilanes were not isolated because of the fast substitution of the fluorine atom by RLi taking place in situ :



However, in the case of neo-$C_5H_{11}Li$, the formation of 1-NpPhSiR_2 is impossible for steric reasons and the stereochemistry of displacement of the OMen group is retention (85 % RN). Moreover, the alkyl organolithiums cleave always the Si-F bonds with retention (Cf § C-I). Thus the concurrent cleavage of both (F) and (OMen) groups occurs with retention.

The first step of the mechanism is the apical attack of the

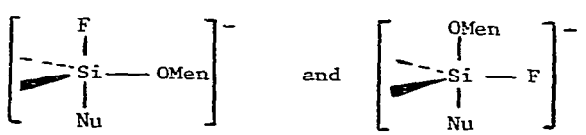
Table XXV

Stereochemical behavior of 1-NpPhSi(F)OMen with alkyl organolithiums (reactions carried out in presence of a cryptand specific for the Li^+ cation, except in the case of the neo-$C_5H_{11}Li$)

Nucleophile	Products*	Yield	Predominant stereochemistry
MeLi	≻Si(Me)OMen	99 %	96 % RN
	≻Si(F)Me	1 %	
EtLi	≻Si(Et)OMen	90 %	90 % RN
	≻Si(F)Et	10 %	
n-PrLi	≻Si(n-Pr)OMen	77 %	84 % RN
	≻Si(F)n-Pr	21 %	
n-BuLi	≻Si(n-Bu)OMen	82 %	81 % RN
	≻Si(F)n-Bu	18 %	
neo-Pent Li	≻Si(neo-Pent)OMen	-	-
	≻Si(F)neo-Pent	90 %	85 % RN

* Cf.ref. 103, ≻Si = 1-NpPhSi.

nucleophile and two possible intermediates *29* and *30* can be proposed :

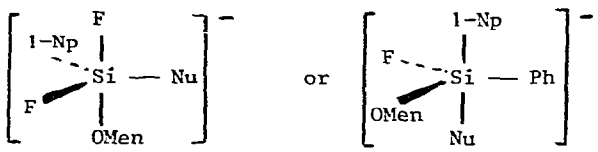


29 *30*

The intermediate *29* with the most electronegative group (fluorine atom) in apical position, is energetically favored compared to *30* . It can explain the displacement of the fluorine atom with inversion and of the menthoxy group with retention, that is strictly oppo-

site to the experimental data. The intermediate *30* can only rationalize the retention for displacement of the fluorine atom ; also, it implies inversion for the alkoxy group instead of the observed retention. The concurrent formation of these intermediates, *29* and *30* , would lead to the competitive cleavage of the fluorine and alkoxy groups with low stereoselectivity.

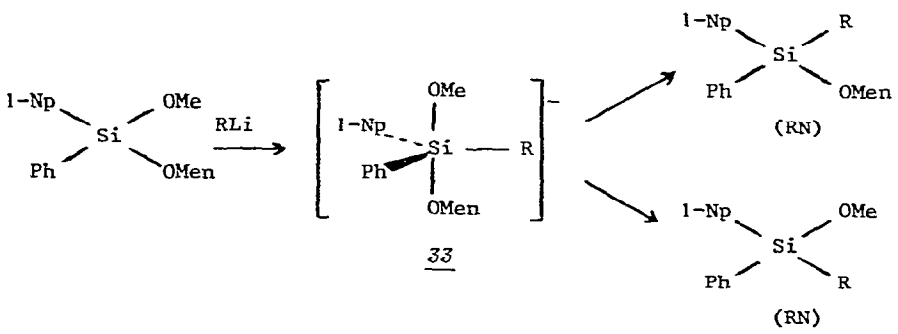
The substitution of F and OMen groups with high stereoselectivity in retention implies a nucleophilic attack at 90° with respect to the two leaving groups. Thus we can only explain the stereochemical data either by an equatorial attack of the nucleophile leading to *31* or by an apical attack leading to *32*.



31 *32*

31 is energetically more favorable than *32* , because the two electronegative groups (F and OMen) are in apical position. Equatorial attack of the nucleophile provides the most reasonable description of the observed results.

Similar experimental data are obtained with 1-NpPhSi(OMen)OMe and alkyllithiums (Table XXIV) (105), i.e., both cleavage of the two alkoxy groups with retention (stereoselectivity up to 97 %). The simple process is also an equatorial attack of the nucleophile, leading to the intermediate *33*.



33

II - NUCLEOPHILIC SUBSTITUTIONS IN THE CASE OF OXA- AND THIASILACYCLOPENTANES

That equatorial attack can explain the retention at silicon, is also well-supported by stereochemical data obtained with optically active oxa- and thiasilacyclopentanes (Tables XXVII and XXVIII).

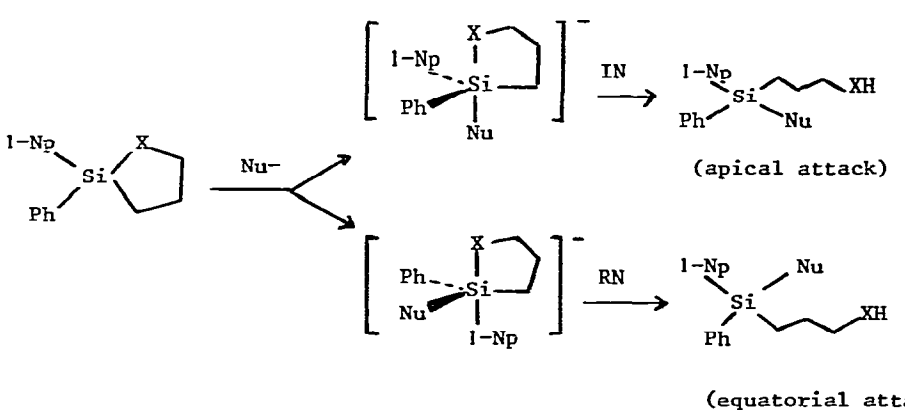
In spite of angle strain at silicon, these two five-membered ring systems show very close stereochemical behavior compared to their acyclic analogs $R_3Si-OMe$ and R_3Si-SR' (R_3Si = 1-NpPhMeSi). The stereochemistry is controlled by electronic factors (§ D-III) and both inversion and retention are possible stereochemical outcomes according to the nature of the nucleophile.

A comparison of the oxa- and thiasilacyclopentanes shows also that contrary to the apicophilicity rule, the most electronegative leaving group, i.e., the oxygen atom, leads preferentially to retention. The less electronegative leaving group,i.e., the sulfur atom, reacts mainly with inversion.

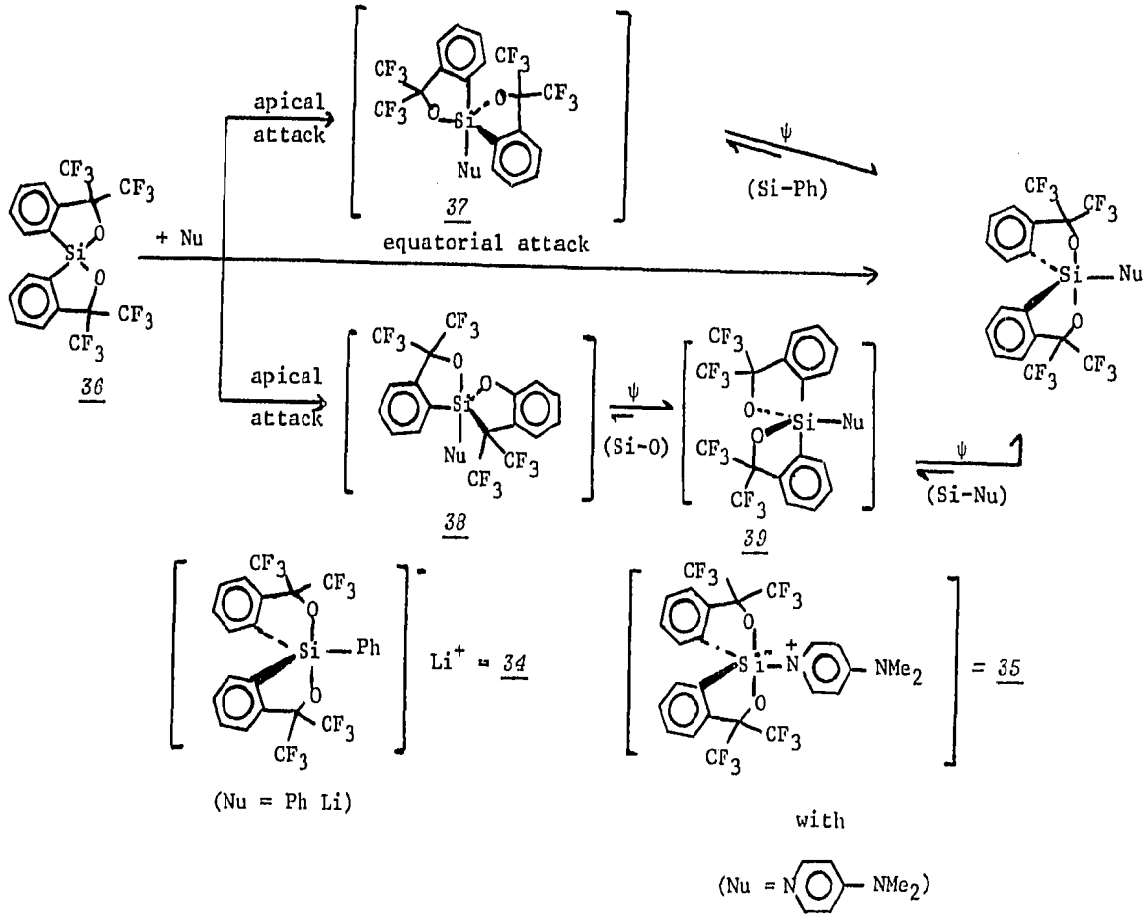
We find again the two main factors which govern the stereochemistry at silicon, i.e., the nature of the leaving group and the electronic character of the nucleophile. The ring strain has only a marginal effect in borderline cases (§ D-I).

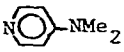
If we assume reasonably that the electronegative group is apical and the five-membered ring equatorial-apical, the apical attack of the nucleophile explains inversion. In contrast, the equatorial entry of the nucleophile is the only possible mechanistic explanation for retention, taking into account the necessary 90° angle between the nucleophile and the leaving group (Scheme 19).

Scheme 19



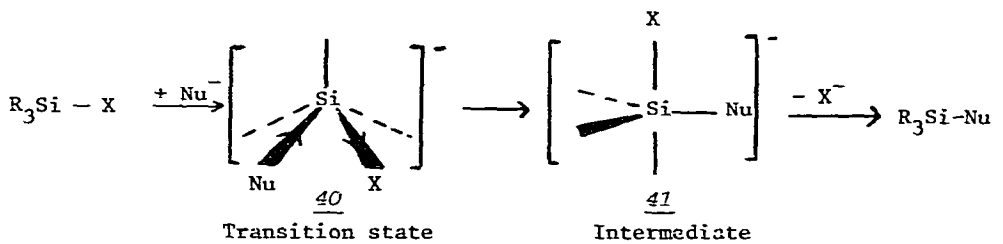
Scheme 20


apical attack
+ Nu
equatorial attack
apical attack
(Si-Ph)
(Si-O)
(Si-Nu)
Li+ = 34
= 35
(Nu = Ph Li)
with
(Nu = NMe2)

In conclusion, we note that the equatorial attack is strongly supported by Martin's elegant structural investigations on pentacoordinated silicon species (106). The siliconates *34* and *35* are obtained by a nucleophilic attack (Ph^- or )at a tetravalent silicon atom (compound *36* in Scheme 20). Their structures, established by NMR spestroscopy, confirm clearly that the electronegative groups (oxygen atoms) are apical, the two five-rings apical-equatorial, and the entering group in an equatorial position. This result can be only described as resulting from equatorial attack of the nucleophile. The other possibility way, i.e., apical attack of the nucleophile followed by a permutational isomerization, would lead to the energetically highly disfavored intermediates *37*, *38* or *39* (Scheme 20).

Consequently, equatorial attack seems the most reasonable and simplest way to describe an approach of the nucleophile at 90° with respect to the leaving group, leading to the most stable pentacoordinated intermediate. However, it is also possible to postulate a square pyramidal structure such as *40* as a transition state which would change into intermediate *41* (Scheme 21).

Scheme 21



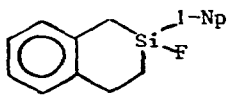
Such a structure was previously proposed in phosphorus chemistry by Hudson et al., to explain the alkaline hydrolysis of cyclic phosphonamidates (107).

The evidence which we have presented on equatorial nucleophilic attack at silicon do not rule out the objection of the principle of microscopic reversibility (P.M.R.) (46c). By its application, an apical entry as a consequence of an apical departure (or vice versa) implies a symmetric energy profile. This is the case with similar leaving and entering groups. But when these groups are different in nature (electronegativity, nucleophilicity ...), this application of the P.M.R. is not correct since the energy profile does not admit a mirror symetry. In such cases, as Mislow et al. pointed out for nucleophilic displacements at phosphorus (108), equatorial attack followed by apical departure (or vice versa) cannot be dismissed on the only consideration of violating the P.M.R.

F - CONCLUSION

Nucleophilic displacements at silicon are usually highly stereoselective processes, taking place either with retention or inversion. However, in a few cases, the substitution reaction proceeds with racemization or with low stereoselectivity. We believe that this fundamental question could be answered in terms of inversion or retention of configuration as competing pathways. If our assumption is right, it implies that the proportion of inversion or retention can vary with the experimental conditions for a given nucleophile. The most striking data are reported in the case of the $LiAlH_4$ reduction of an optically active silicon fluoride (82b, 58) (Table XXVI). Either the addition of LiBr or the complexation of the Li^+ cation by a specific cryptand (naked AlH_4^- anions) leads respectively to retention and inversion of configuration.

Table XXVI

Substrate	Reagent (solvent)	Predominant stereochemistry
	$LiAlH_4$/LiBr (Et_2O)	95 % RN
	$LiAlH_4$ (Et_2O)	racem.
	$LiAlH_4/KLi^+$ (Et_2O)	65 % IN

Similar conclusions can be drawn from reactions with alkyllithiums (Table IX) or with phenoxides (Table XII). Thus, all these data clearly suggest that inversion and retention of configuration are two competing pathways. Racemization results from fortuitously cancelling rates.

We will now summarize the factors which govern the stereochemistry at silicon : among them, we pointed out the dominant influence of the leaving group and of the electronic character of the nucleophile :

(i) - Nature of the leaving group. Chloro- and bromosilanes are mainly displaced with inversion. In contrast, the Si-H bond is cleaved with retention. The Si-SR, Si-F and Si-OR bonds show intermediate behavior, leading either to retention or inversion according to the nature of the nucleophile. A good empirical relationship between the stereochemistry and

the ability of the leaving group to be substituted can be stated :

- Predominant stereochemistry : IN ——————————→ RN
- Ability of the leaving group to be substituted : Br ∿ Cl > SR, F > OR >> H

Moreover, we outlined the aptitude of the leaving group to be stretched under the influence of an attacking nucleophile as an important factor which contributes to direct the stereochemistry at silicon.

(ii) - Electronic character of the nucleophile. For the same leaving group, the stereochemistry is governed by the nature of the nucleophile. The thorough investigation of various nucleophiles (carbon, oxygen and hydride nucleophiles) shows clearly that the stereochemistry is not controlled by electrophilic assistance of the counter cation to the cleavage of the Si-X bond (S_Ni-Si mechanism). The dominant factor is the electronic character of the nucleophile. We suggest the following empirical rule, according to which "the harder (softer) the nucleophile, the more retention (inversion) of configuration". Nucleophilic reagents with well-localized negative charge (alkyl or p-methoxyphenoxide anions, for instance) lead mainly to retention. In contrast, softer anions with a more delocalized negative charge (allyl, benzyl, p-nitrophenoxide anions) usually react with inversion. This interpretation is in agreement with the effect of solvating solvents and complexing agents on the stereochemistry. Finally, this dependance is supported by the parallel between the stereochemistry of nucleophilic displacements at silicon and the regioselectivity of attack of α-enones, this latter reaction being known as directed by electronic factors.

(iii) - Secondary factors. In borderline cases, we also have to take into account side factors, such as the geometry of the organosilane or the electrophilic assistance by the counter cation of the attacking reagent. The experimental trends are as follows :

- Cyclic silicon compounds show more retention of configuration than their open-chain analogs, if the leaving group is extracyclic. In contrast, when Si and the leaving group X are both in a strained ring, the stereochemistry is somewhat displaced towards inversion. An increased angle strain at silicon in small rings leads to an increase of the s character of the exocyclic bonds. It favors retention. In contrast, the p character of the endocyclic bonds increases ; this explains the opposite stereochemical shift to inversion (§ D-I).

- External electrophilic assistance facilitates inversion by increasing the ability of the leaving group to be substituted.

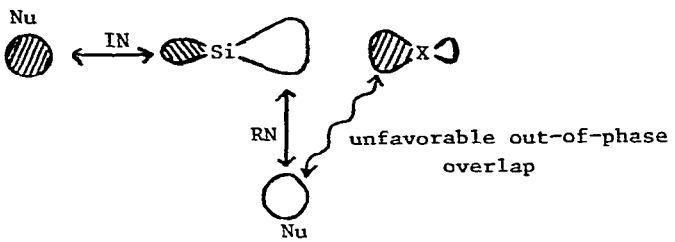
- In the case of bifunctional organosilanes with two different leaving groups with similar abilities to be substituted, assistance by the counter ion of the nucleophile can direct the substitution selectivity.

In any case, these side factors do not control the stereochemistry. They only act as additional factors which can modify the stereochemical pathway in borderline reactions.

Before we discuss all of these experimental observations in mechanistic terms, we wish to introduce Nguyên Trong Anh and C. Minot's theoretical calculations (109) and their important implications. These authors reproduced the experimental trends using a perturbation argument which is an extension of Salem's orbital treatment of the Walden inversion (110). The frontier-orbital approximation is assumed for both inversion and retention ; the major interaction during the reaction occurs between the nucleophile's HOMO and the substrate's LUMO, (σ^*_{Si-X}). The calculated structure of the latter is shown below, with the big lobes of the hydrid AO's pointing towards each other :

Scheme 22

Structure of the substrate's LUMO (σ^*_{Si-X})



Front-side attack, corresponding to an attack on the big lobe of silicon, leads to retention. When the unfavorable, out-of-phase overlap between the nucleophile and the leaving group orbitals predominates nucleophilic attack occurs at the rear of the molecule opposite to X ; this leads to inversion. Therefore, retention and inversion can be considered the result of a fine balance between the in-phase and out-of-phase orbital overlap between the nucleophile and the substrate's LUMO (σ^*_{Si-X}).

Another approach in terms of energy levels has been put forward by Nguyên Trong Anh and C. Minot to explain inversion. They propose the involvement of a substrate's superjacent MO (111) in which the big lobe of the Si hybrid orbital points to the rear (Scheme 23).

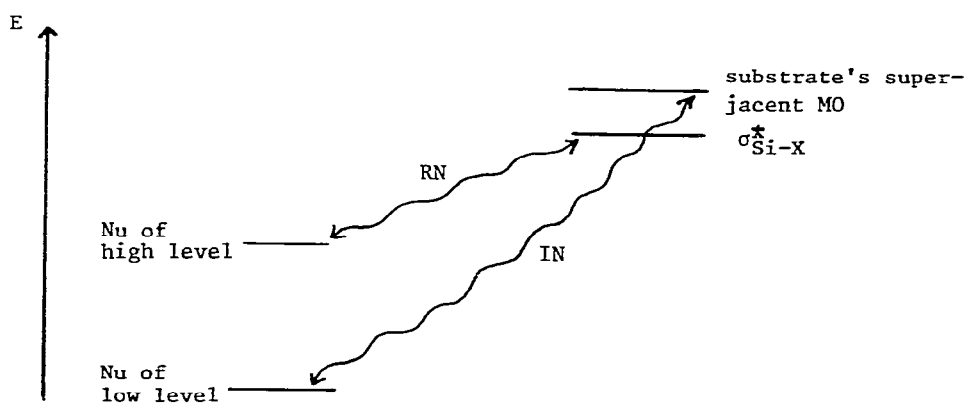
Scheme 23

(favorable
in-phase overlap)

Structure of the substrate's superjacent MO

When the nucleophile has a high energy level (hard reagent), frontier-orbital interaction (nucleophile's HOMO and substrate's LUMO, Scheme 24)is predominant. When the nucleophile has a low energy level (soft reagent with a delocalized charge), the relative importance of the nucleophile's HOMO-substrate's superjacent MO interaction increases. Because of the structure of the latter, inversion is favored (Scheme 24).

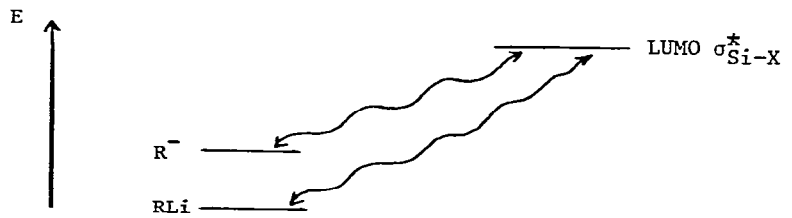
Scheme 24



This theoretical approach leads to the following implications (109) :

(i) - Nucleophilic displacements at silicon may be reproduced as frontier-orbital controlled processes. Therefore, a change in the nucleophile's HOMO level must imply a modification of the stereochemistry. The most striking data which illustrates this assumption is the large rate increase in the case of nucleophilic displacements with alkyllithiums plus a cryptand specific of Li^+ (Table X). This parallels an increase of the percentage of retention (Table IX). Trapping Li^+ corresponds to a higher energy level for the nucleophile (Scheme 25).

Scheme 25



We have then an increase of the frontier-orbital interactions between the nucleophile's HOMO and the substrate's LUMO ; therefore retention is kinetically favored.

(ii) - <u>It explains the stereochemical behavior of silicon compared to carbon in nucleophilic displacement reactions</u>. *By replacing C by Si, it is possible to obtain stereoselective reactions with either retention or inversion of configuration, whereas there is still no proven example of an S_N2 reaction with retention at carbon. This replacement (C by Si) for a given leaving group X, corresponds to a Si-X bond which is longer than the C-X bond. This bond lengthening will diminish the unfavorable interaction between X and the nucleophile for the front-side RN attack (Scheme 23). The valence orbitals also change from 2s and 2p for carbon to 3s and 3p for Si ; i.e., they become more diffuse and overlap better with the nucleophile at longer distances. Therefore, the probability of attack with retention is enhanced.*

(iii) - <u>Influence of the leaving group</u> (X = Cl and F). *When one replaces X = Cl by X = F, besides the favorable electronegativity change, the valence orbitals of X become more contracted, and this decreases the overlap between X and the nucleophile. At the same time, the Si-X bond shortens, increasing the X-Nu overlap in an attack with retention. Numerical calculations indicate that in this example (Cl → F), the Si-X bond shortening does not compensate for the two former effects. Therefore, the retention is favored and generally, replacing X by an element of smaller atomic number in the same column of the periodic table (X = Cl to X = F) generally will increase the percentage of retention.*

(iiii) - <u>Particular behavior of X = H</u>. *The importance of the size of the valence orbitals comes to the fore when X = H. Although the Si-H bond is quite short and the electronegativity of hydrogen quite low, retention is commonly observed. The main requirement for retention is a feeble repulsion between the leaving group and the nucleophile. The hydrogen 1s orbital is small and overlaps little with the nucleophile's orbitals. Furthermore, hydrogen is the only leaving group with no lone pair and no core electrons ; the H-Nu repulsion is therefore drastically reduced and retention favored.*

(iiiii) - Influence of the nucleophile. *A hard reagent is usually a small one, with contracted valence orbitals. Its long range out-of-phase, unfavorable overlap with the leaving group will be negligible and front-side attack leading to retention is therefore possible. On the other hand, a soft nucleophile usually has diffuse valence orbitals. It has therefore a sizable out-of-phase overlap with the leaving group and the stereochemistry is shifted towards inversion (rear-side attack).* This shows the dominant influence of the size of the valence orbitals on the reactive atom. This will be discussed more in detail later.

The size of the reagent is not the only controlling factor. A change in the nucleophile's hardness implies a modification of its valence orbitals, and also of its HOMO level. When the level is high (i.e., hard nucleophile with contracted negative charge), frontier-orbital interaction is predominant (Scheme 24). When the level is low (i.e., soft nucleophile with voluminous valence orbitals), the relative importance of the nucleophile's HOMO- substrate's superjacent MO interaction is increased (Scheme 24) ; inversion is favored.

Therefore, these two approaches lead to the same conclusions concerning the dominant influence of the nucleophile on the stereochemistry. Because of the difficulty of evaluating the relative stability of various anions, we shall give preference to the first approach. Moreover, it allows to reproduce simply, as we shall discuss later, most of our experimental data.

Additional data were reported by C. Minot (109 b) for the calculation of the HOMO of a pentacoordinate D_{3h} intermediate (SiX_5^-). The geometry of SiH_5^- with nearly equal bond lengths in the equatorial and apical positions suggests the two kinds of stereochemistry. Moreover, it allows us to discuss the mutual influence of ligands attached at the silicon atom. Briefly we can summarize the main conclusions as follows (109 b).

(i) - A substituent of low level (soft reagent) shows a high ability to stabilize a negative charge in the apical position. It weakens the bond in the other apical position, whereas it strengthens the bond equatorial. The consequence is an approach of a soft nucleophile at 180° with respect to the leaving group, and therefore, the decomposition of the intermediate with inversion.

(ii) - Equatorial groups of high level (hard or small reagents) stabilize a negative charge in a perpendicular apical position. They weaken a perpendicular apical bond ; in contrast, they strengthen the trans equatorial bond. The stereochemical consequence is an approach of the nucleophile at 90° with respect to the leaving group. Therefore, it implies the retention as stereochemical outcome.

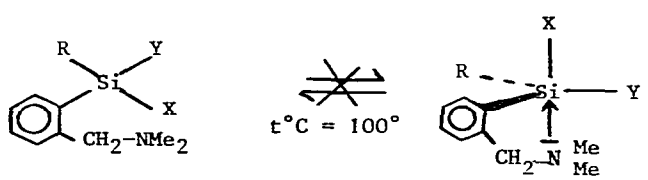
The above experimental data and theoretical approaches allow us to define the factors which, either in the structure of the substrate or in the geometry of a pentacoordinate intermediate, control the stereochemistry. We wish now to propose the following concerning the mechanism of nucleophilic displacement reactions at silicon. To this end, we shall conduct our discussion with respect to the nature of the leaving group :

(i) - Case of bad leaving groups such as X = OR, H. Three main factors determine their stereochemical behavior :

- From an extension of Nguyên Trong Anh and C. Minot's conclusions (109), it is reasonable to suppose for the Si-OMe bond that the substrate's LUMO σ^{*}_{Si-X} shows a big lobe pointing towards the leaving group X. It has a strong s character and therefore favors front-side attack. With H as the leaving group, the unfavorable H-Nu repulsion is drastically reduced and does not disturb in any way a front-side attack. This argument is far more satisfactory than our previous proposal, i.e., that the retention is explained by a charge-controlled process (105). For instance, it was in disagreement with the stereochemical behavior of the Si-H bond. Although it is the far less polarized bond at silicon, it is only cleaved with retention, whatever the nucleophile.

- They show a low aptitude to be stretched under the influence of an attacking nucleophile. In our opinion, this is the most important fact which characterizes these groups. The best illustration is given by the NMR study of the stabilization of a silicon center by intramolecular coordination (44) (§ B-Influence of the leaving group). For instance, with OR group, even at -100°C, the N-Me protons do not coalesce and therefore no (or very weak) intramolecular coordination occurs (Scheme 26).

Scheme 26



R = 1-Np, Y = H, OMe
R = 1-Np, Y = Me
X = OMe

- With respect to the structure of the intermediate, they stabilize a negative charge in a position perpendicular to them as clearly indicated by C. Minot's calculations and the experimental data reported by J. Martin et al. (§ E - Geometry of attack of the nucleophile). It implies

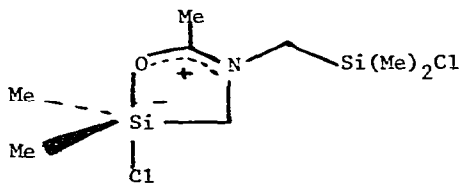
an equatorial entry of the nucleophile, perpendicular to the leaving group.

As a consequence, they lead mainly to retention. Inversion is only observed for nucleophiles whose the negative charge is localized in a big lobe. The unfavorable out-of-phase overlap with the leaving group is certainly dominant and an attack at the rear of the molecule becomes possible. However, the reaction occurs slowly, as in the case of CH_2=$CHCH_2MgBr$ attack on a methoxysilane (13), or of the displacement of the Si-H bond by Ph_2CHLi (20). In contrast, with nucleophiles having either a concentrated negative charge or a small lobe, the reaction is very fast. The best example is given by an alkyllithium or a neutral reagent such as dibal in hexane. In this case, the valence orbitals around the hydrogen atom are small and, therefore, the out-of-phase overlap with the leaving group is feeble and does not mind the overlap with the big lobe at silicon (Scheme 22).

(ii) - Case of good leaving groups (X = OCOR, Cl, Br). The stereochemistry is controlled by the following factors :

- The substrate's LUMO σ^*_{Si-X} is not directed towards the inside of the Si-X bonds. It has much p character. Moreover, the valence orbitals of the leaving group are more diffuse and the unfavorable out-of-phase overlap with the nucleophile is not negligible. Therefore, rear-side attack is favored.

- Furthermore, these leaving groups show a high aptitude to be stretched under the influence of an attacking nucleophile ; they can stabilize a negative charge (or a lone pair) in an opposite position. For instance, for these groups (X = OCOR, Cl, Br), the temperature of coalescence of the NMe_2 group (Scheme 26) is always the highest, even when the silicon atom is surrounded by three carbon atoms. The X-ray crystal structure of the five-coordinate chloro-(N-chlorodimethylsilylacetamido)methyldimethylsilane (§ B, p. 21) is also very significant. The only isolated complex which thus corresponds to the most favorable geometry around silicon shows the soft chlorine substituent opposite the other soft group of the molecule :



Therefore, an apical entry of the nucleophile opposite the leaving group is here the favored pathway. We also note that the aptitude to be stretched under the influence of a nucleophile is the most important factor which characterizes such good leaving groups. This experimental conclusion is fully in agreement with the theoretical calculation of the HOMO

of a pentacoordinate D_{3h} intermediate and its implications with chlorine atom as reported by C. Minot (109b).

As a consequence, all the nucleophiles react with inversion. For such leaving groups, retention can be only observed with reagents having very small valence orbitals. One example is known : dibal in hexane cleaves Si-Cl and Si-Br bonds with retention (70, 32).

(iii) - Borderline leaving groups (X = SR or F). These leaving groups show an intermediate aptitude to be stretched and they can also stabilize a negative charge in a perpendicular position. Concerning the LUMO σ^{*}_{Si-X}, its structure shows a lobe on silicon which points both towards X and also in the opposite direction. As a consequence, the stereochemistry will be essentially controlled by the nature of the nucleophile. Small nucleophiles with contracted valence orbitals will give retention, while a nucleophile with a diffuse negative charge will lead to the opposite stereochemistry.

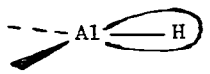
A common factor appears in all of these comments. For a given leaving group, the stereochemistry is controlled by the electronic character of the nucleophile. At this point, it is interesting to ask the following question : how is it possible to describe this factor ? We can have a good idea about it by taking into account the size of the probable valence orbitals around the nucleophilic center. We shall suppose that a hard reagent will have contracted valence orbitals, while a softer nucleophile will have a diffuse negative charge in a bigger lobe. This must be confirmed by theoretical calculations of the orbitals of the corresponding anions.

To support our assumption, we point out the following examples :

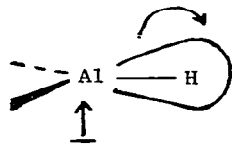
(i) - The alanes $AlH_{(3-n)}Y_n$ (Y = OR, SR or I) are quite interesting reagents. The hydrogen atom has no unshared electron pairs and, therefore, the electrons of the nucleophile are those of the Al-H bond. In hexane, valence orbitals around the hydrogen points towardsthe aluminium atom. In solvents such as THF, TMEDA, i.e., those able to coordinate at Al, the structure of the nucleophile's HOMO is modified by diffusing the valence orbitals around H (Scheme 27).

In the first case (non-coordinating solvent), we are faced with contracted valence orbitals for the nucleophile. The unfavorable out-

Scheme 27



Structure of σ_{Al-H}



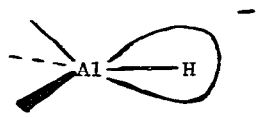
Structure of σ_{Al-H}

of-phase overlap with the leaving group is feeble and whatever its nature, retention is observed*.

In the second case, since the valence orbitals around hydrogen are more diffuse, the out-of-phase repulsion with the leaving group is dominant. A rear-side attack at silicon is favored and inversion is observed with fluoro-,chloro- and bromosilanes, i.e., with the best leaving groups.

The above discussion shows more clearly than in the case of alanes, that the more displaced towards the hydrogen is the negative charge, more voluminous the valence orbitals are around it. It seems interesting to introduce at this point the case of the naked AlH_4^- anion. In the latter, the negative charge is completely localized in the hydrogen atoms. Therefore, we can reasonably suppose diffuse valence orbitals around it (Scheme 28) and this explains the general shift of stereochemistry to inversion which is observed when naked AlH_4^- anions are used as reducting agents (Table XIII).

Scheme 28



Supposed AlH_4^-'s valence orbitals

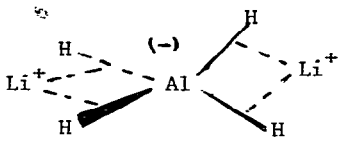
---

* *dibal in hexane cleaves very quickly the Si-OMe bond ;in contrast, the others are displaced slowly ($k_{OR}/k_{Br} \sim 10^4$). The following rate order has been reported (70) :*

$$Si-Br < Si-Cl < Si-SCH_3, \; Si-F < Si-OR$$

The reaction is much faster when the σ^*_{Si-X} orbital is centered at the inside of the Si-X bond (for instance, X = OR compared to X = Cl or Br).

In contrast, when using $LiAlH_4$ or $LiAlH_4$/LiBr, we observe an increase of the RN ratio. Li^+ and AlH_4^- are tightly associated in aggregates, but their structure is unknown. Our results and those of others (112) suggest aggregates in which the Li^+ cations prevent the delocalization of the negative charge ; a possibility could be :



Such assumptions are supported by the crystal structures of $LiAl(Et_4)$ (113) and $KAl(Me_4)$ (114). The structure of the latter compound consists of isolated K^+ and $Al(Me)_4^-$ ions : the bonding between the central atoms and ligands shows a highly polar character which causes a considerable weakening of the Al-C bond. We can find here a good model for the naked AlH_4^-'s structure : the negative charge is highly delocalized around the H atoms. On the other hand, the structure of $LiAl(Et)_4$ consists of linear chains of alternating lithium and aluminium : there is some evidence of weak covalent interaction involving lithium. Such an interaction would explain the behavior of $LiAlH_4$/LiBr aggregates in preventing the delocalization of the negative charge to hydrogen atoms.

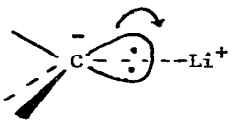
(ii) - A similar approach serves for alkoxides. RO^-M^+ in benzene can be considered as a small nucleophile with contracted valence orbitals ; Si-SR and Si-F bonds are cleaved with retention. On addition of alcohol to the medium, the solvatation of the RO^- anion by hydrogen bonding implies an increase of the bulk of the nucleophile. The out-of-phase interaction with the leaving group increases and, therefore, inversion is promoted (Table XI).

(iii) - We wish to finish these comments with a consideration of carbon nucleophiles which have often been used as reagents in mechanistic studies at silicon. Their influence on the stereochemistry also can be discussed in terms of the size of the valence orbitals around carbon. Alkyllithiums have a negative charge on carbon which is in part transfered to the Li^+ cation. When the Li^+ cation is trapped (naked anion), the negative charge is concentrated on the carbon reactive center (Scheme 29).

In the latter case, as the valence orbitals are smaller, the out-of-phase overlap with the leaving group is diminished and, therefore, retention is favored. This is in agreement with the experimental data.

This cryptand effect which results in increases of retention ratio and of the rate, also can be explained by an higher level of the naked

Scheme 29



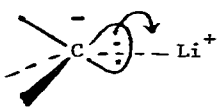
Structure of the HOMO
of alkyllithiums

Structure of the HOMO
of naked alkyl anions

anion's HOMO (Scheme 25). As a consequence, the frontier-orbital interaction is increased. Therefore, retention is kinetically favored.

Alkyl Grignard reagents are also quite interesting. Compared to organolithiums, we have at first to note the covalent character of the carbon-magnesium bond. As a consequence, the electrons of the nucleophile are those of the C-Mg bond which are localized in a MO pointing towards each other. It is more voluminous than the small valence orbitals around the nucleophilic carbon of an alkyl organolithium (Scheme 30).

Scheme 30



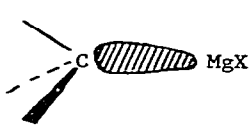
Alkyl organolithium

Alkyl Grignard reagent

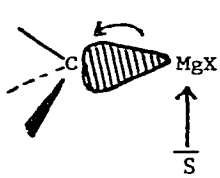
We can so explain the greater aptitude of Grignard reagents to give inversion compared to organolithiums (Tables V and VI).

Similar arguments allow us to discuss the change of stereochemistry observed with Grignard reagents when increasing the solvent basicity. The addition of a basic solvent (THF, DME) implies a modification of the carbon-magnesium MO. The latter becomes more contracted on the carbon atom (Scheme 31). As a consequence, we are faced with a nucleophile of smaller size and the stereochemistry is shifted to retention (Table VII).

Scheme 31



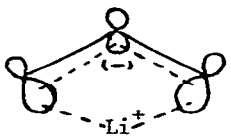
RMgX's HOMO
(R = alkyl)



RMgX's HOMO
(S = basic solvent)

With softer nucleophiles such as allyl- or benzyllithium, it is also possible to explain their stereochemical shift to inversion when the Li^+ cation is complexed (87, 115). For instance, we can propose the following argument. In the case of the allyllithium (Scheme 32), the valence orbitals are centered towards Li^+, while for the naked allyl anion they are more disposable or, in other words, more diffuse. Therefore, in the latter case, the unfavorable out-of-phase overlap with the leaving group is increased : the rear-side attack of the nucleophile is promoted and, therefore, inversion.

Scheme 32



Supposed structure for allyllithium's HOMO

Supposed structure for naked allyl anion's HOMO

The noteworthy behavior of Ph_2CHLi, which leads to inversion even with a Si-H bond, suggests also a high delocalization of the negative charge over the phenyl groups which is parallel to an important increase of the valence orbitals around the nucleophilic center.

Our above mechanistic arguments allow to access to a better understanding of nucleophilic displacements at silicon. They lead also to an attractive approach of the influence of a nucleophilic assistance on the stereochemistry. For instance, hydrolysis (or alcoholysis) of chlorosilanes is activated by HMPT, DMSO or DMF:it takes place with retention instead of inversion (116). The most reasonable mechanism which can be proposed implies coordination of the nucleophile (HMPT, DMSO or DMF) at silicon as the determining step :

$$R_1R_2R_3SiCl + Nu \rightleftharpoons \left[R_1 \; R_2 \; Si(Cl)(Nu) \; R_3 \right] \xrightarrow{ROH} R_1R_2R_3SiOR$$

(Si^{IV}) (Si^{V})

We propose that the nucleophilic coordination certainly introduces a lengthening of the Si-X bond. This lengthening has two effects : it reduces the unfavorable out-of-phase overlap between Nu and X, and it increases the volume of the lobe on silicon (σ^*_{Si-X}) at the inside of the Si-X

bond. As a consequence, front-side attack of the second molecule of nucleophile (H_2O, MeOH) is favored and the stereochemistry is displaced to complete retention.

For the case of silicon compounds, it is thus possible to discuss the experimental trends without introduction of silicon d orbitals. Whether this factor plays a role is still an open question. For instance, the aptitude of a group attached at silicon to be streched under the approach of an attacking nucleophile can be reasonably explained by the intervention of a d_z2 orbital. It is the same problem when a bad leaving group, such as an alkoxy group, stabilizes a negative charge in a perpendicular position (equatorial-apical stabilization). It can be interpreted by the intervention of another kind of perpendicular d orbital ($d_{x^2-y^2}$, d_{yx}, d_{xz} or d_{yz}).

Two other questions remain unanswered after our discussion based on an HOMO-LUMO interaction as the major interaction during the reaction :

(i) - In our first works (105), we outlined a charge-controlled process to explain retention as the dominant stereochemical outcome observed with hard nucleophiles. This explanation is in complete disagreement with the behavior of the Si-H bond which is a bond of low polarity and which leads only to retention. This stereochemical behavior is well explained by theoretical studies carried out by Nguyễn Trong Anh and C. Minot and reported above. In contrast, with the other leaving groups, the charge is certainly an important factor. When the Li^+ cation is complexed by a cryptand (alkyllithiums), the substitution rate increases. This acceleration is the highest with fluorosilanes in which the reaction center(silicon atom) is the most electropositive (Table XXVII) (52).

This shows clearly that a charge effect cannot be completely ruled out, even if the dominant factor is a frontier-orbital interaction.

(ii) - The mutual influence of two potential leaving groups attached to silicon in the case of bifunctional compounds is the last open question. It remains an intriguing problem because of the difficulty to describe the structure of the LUMO corresponding to each bond.

Finally, we note that our mechanistic proposals can be easily generalized to other nucleophilic substitution reactions :

(i) - The stereochemical data reported in the case of germanium compounds by Eaborn (117), Brook (118) or Corriu (117) are quite parallel to those discussed here. The nature of the leaving group and the electronic character of the nucleophile, rationalized in terms of hard and soft reagents, are also the dominant factorswhich govern the stereochemistry. Some recent data, communicated to us by P. Mazerolles and J. Dubac, are summarized in Table XXVIII (120).

Table XXVII

Charge effect in nucleophilic substitutions at silicon

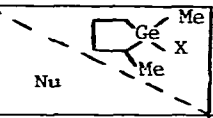
t_1/t_2 (nucleophile)	R_3Si-H	$R_3Si-OMe$	R_3Si-F
t_1/t_2 (n-BuLi)	~ 1	$\sim 10^3$	$\sim 10^4$
t_1/t_2 (n-PrLi)	~ 1	$\sim 10^2$	$\sim 10^3$

R_3Si = 1-NpPhMeSi

$t_1 = t_{1/2}$, reaction being carried out with RLi in ether

$t_2 = t_{1/2}$, reaction being carried out in the presence of a cryptand specific of the Li^+ cation.

Table XXVIII

	Ge-OMe	Ge-OEt	$Ge-NEt_2$	Ge-St-Bu	$Ge-PEt_2$
$LiAlH_4$/Ether	RN 100 %	RN 94 %	RN 88 %	IN 100 %	RN 100 %
$LiAlH_4$/THF	IN 67 %	IN 75 %	RN 100 %	IN 100 %	RN 80 %
n-BuLi/Ether-hexane	RN 100 %	RN 100 %	-	RN 97 %	RN 100 %
AllylLi/Ether	RN 85 %	RN 78 %	RN 90 %	IN 100 %	RN 95 %
EtMgBr/Ether	RN 98 %	RN 100 %	RN 92 %	-	-
AllylMgBr/Ether	IN 80 %	IN 85 %	IN 90 %	IN 92 %	-

(ii) - Many data concerning nucleophilic displacements at phosphorus can also be rationalized using similar arguments, i.e., the aptitude of the leaving group to be cleaved and the electronic character of the nucleophile (121). Studies are now in progress which completely justify this proposal.

ACKNOWLEDGEMENTS(Professor R. CORRIU)

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