DOCTOR OF PHILOSOPHY

Asymmetric reactions of organosilicon compounds and properties of novel optically active organosilanes

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ASYMMETRIC REACTIONS OF ORGANOSILICON COMPOUNDS and Properties of Novel Optically Active Organosilanes.

BY

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SUMMARY.

Partial reduction of racemic methoxysilanes by 1:1 complexes of lithium aluminium hydride with optically active cinchona and ephedra alkaloids give optically active silanes and methoxysilanes. Optical yields depend on the groups attached to silicon and the alkaloid used but in some cases approach 50%. The method has been used to prepare novel optically active organosilanes, possessing an asymmetric silicon centre, which are either inaccessible by any of the other available routes or would require a time consuming preparation. Such compounds are of use in the study of the mechanism of substitutions at silicon.

Attempts have been made to rationalize the results of the asymmetric reductions in terms of differences in steric and electronic interactions in diastereoisomeric transition states.

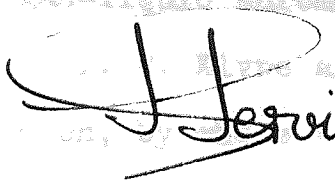
Circular dichroism and optical rotatory dispersion spectra have been obtained for the optically active products in an attempt to elucidate the absolute configurations of the novel asymmetric organosilanes. The results from these studies provide a useful addition to the data so far accumulated for asymmetrically perturbed aromatic chromophores.

Nuclear magnetic resonance studies of diastereoisomeric (-)-menthoxysilanes show that these compounds possess resonances extremely useful in the determination of optical purities for asymmetric organosilanes which possess an aromatic group. The effect of variable temperature on the spectra has revealed evidence for the conformational

preferences in these compounds. Other diastereoisomeric alkoxysilanes have been prepared and their n.m.r. spectra studied in the hope of establishing trends.

Exploratory studies for other asymmetric reactions proceeding at silicon have proved unfruitful.

This work was carried out between 1967 and 1970 at the University of Aston in Birmingham. It has been done independently and has not been submitted for any other degree.



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I

GENERAL INTRODUCTION

1. Optically active asymmetric organosilicon compounds.

It is evident that stereochemical studies of organic reactions have contributed greatly to our knowledge of the mechanisms of substitutions of carbon compounds.[1] However, prior to 1958, it was not even known whether substitution reactions at silicon atoms are stereospecific. At that time, Sommer and co-workers resolved the first optically active organosilicon compound bearing a reactive functional group on silicon.[2] The compound was (+)-1-naphthylphenylmethylsilane, which being a crystalline solid allowed its absolute configuration to be found by application of a X-ray technique.[3]

Once the relative configurations of a number of optically active substituted silanes had been established,[4] Sommer was able to show that a very large number of nucleophilic substitution reactions at silicon proceed with a high stereospecificity.[5,6] The stereochemistry of these reactions has revealed details of mechanism not easily available by other means.

Work carried out on other closely related optically active silicon systems[7], prepared from 1-naphthylphenylmethylsilane, has shown that the stereochemistry of substitution reactions for the latter system is fairly general. However, a completely unrelated optically active silicon system, prepared by Corriu and co-workers[8], exhibits different stereochemistry[9] in a number of reactions from that for the 1-naphthylphenylmethylsilicon system. Since it would appear that the stereochemistry of substitution reactions at silicon depends to some extent on the non-reacting groups attached, a facile means of preparing a wide series of optically active

organosilanes was needed. Asymmetric synthesis presented an alternative possibility.

2. Asymmetric synthesis.

Over the last fifteen years the organic chemist has developed a qualitative and, in some cases, a quantitative understanding of the forces that conspire to produce asymmetric synthesis at carbon. The steric interactions responsible may be delineated by the techniques of conformational analysis, and with a little mechanistic reasoning one can predict when an asymmetric reaction is likely to occur. The absolute configuration of the predominant isomer formed or destroyed in these reactions can sometimes be inferred by empirical models.

The vast amount of work done on asymmetric reactions at carbon has been recently reviewed.[10,11] Compared with this the instances of asymmetric reactions at other atoms are relatively few, and at the onset of the investigation there was only one reported asymmetric synthesis at silicon.[12] This asymmetric reaction involved differences in stability between diastereoisomeric silaoxazolidones.

Interest has recently been concerned with the stereochemistry of organosilicon compounds particularly directed towards the production of siloxane polymers.[13,14] In this field, knowledge of the effects of non-bonded interactions are important, particularly in attempts to produce stereoregular siloxanes. One means of studying this problem is by asymmetric synthesis and this appeared to be quite attractive in view of the high stereospecificities reported by Sommer.[5,6]

Furthermore, asymmetric reactions may prove to be sensitive probes for detecting subtle steric and electronic

disparities in diastereoisomeric transition states leading to substitution.

3. Choice of Asymmetric Reactions.

The asymmetric reactions initially studied involved the reductions of racemic methoxy- and chloro- 1-naphthylphenylmethylsilanes for a number of reasons:

a) the considerable body of evidence available from asymmetric reductions at carbon,[10]

b) the reductions of methoxy- and chloro-silanes proceed with high stereospecificity,

c) the 1-naphthylphenylmethylsilyl system has been thoroughly studied and the rotatory powers and absolute configuration of the compounds concerned have been unambiguously established,

d) all the compounds concerned are crystallisable solids,

e) the 1-naphthylphenylmethylsilane formed as a result of the reduction forms a racemic mixture and therefore its enantiomeric purity may be increased by fractional crystallisation should one enantiomer be in excess,

f) the 1-naphthylphenylmethylsilane is easily separated from the methoxysilane by column chromatography and is configurationally and chemically stable to such treatment.

II

ASYMMETRIC REACTIONS.

The preferential formation, transformation or destruction of one of two (or more) stereoisomers in a given reaction, by reason that that isomer is formed, or reacts at a faster rate than the other(s), is termed 'kinetic asymmetric transformation'.[15]

Within this definition three specific cases may be distinguished.[16] Two diastereoisomers may be formed or react at unequal rates without their asymmetric atoms being directly affected. This has been termed 'kinetic method of resolution' although the term is rather flexible. A second case arises when a reaction is involved which creates a new asymmetric centre either in a compound already possessing asymmetry or under the influence of an asymmetric reagent, catalyst or an external physical influence. Reactions of this type are known as 'asymmetric inductions' or 'asymmetric syntheses'. Finally there is the case where two enantiomers react with, or are destroyed by, an asymmetric reagent at unequal rates leading to a partial resolution. This is called 'asymmetric destruction'.

Work prior to 1964 on asymmetric reductions at a carbon centre has been extensively reviewed by Morrison.[17] In this article he confines himself to an account of 'asymmetric synthesis'. The asymmetric reductions studied in the present work belong to the class of 'asymmetric destruction'.

Theoretical considerations.

All three above cases essentially possess the same kinetic requirements. For two reactions involving chemically

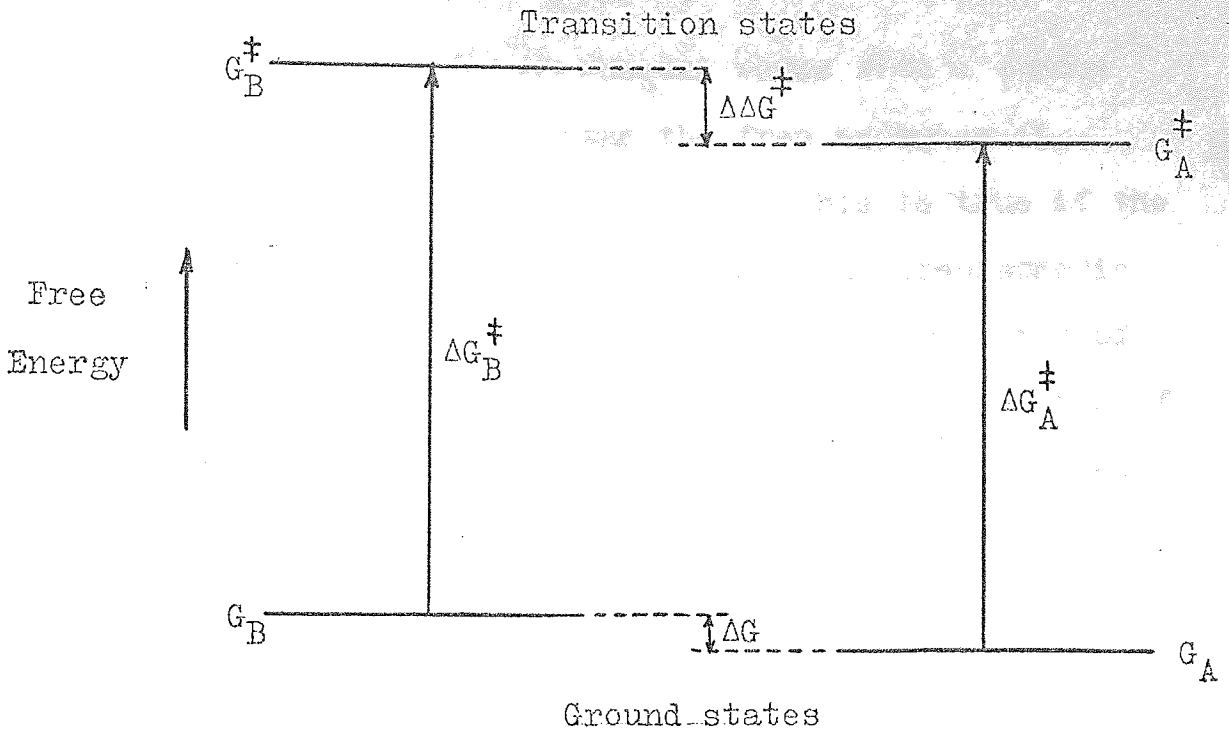


Fig. 1. Kinetic resolution when $\Delta\Delta G^{\ddagger} \neq \Delta G$ for diastereoisomers A and B.

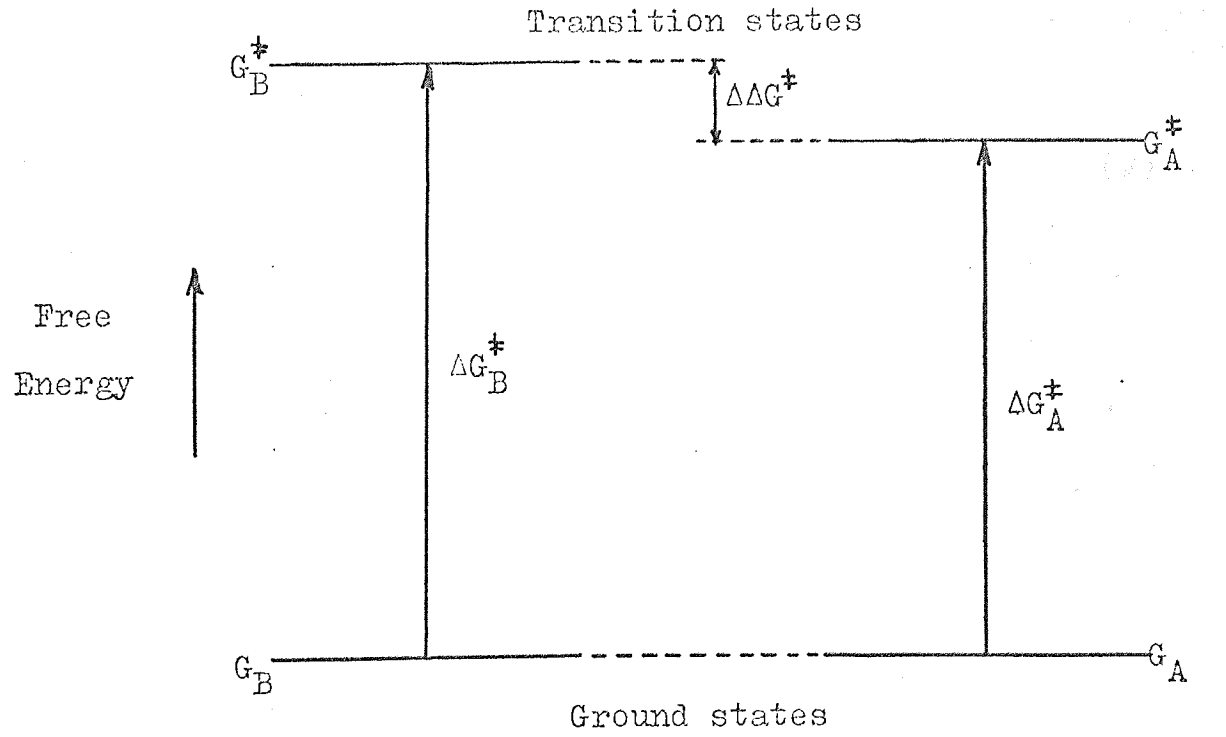


Fig. 2. Asymmetric synthesis or destruction when $\Delta\Delta G^{\ddagger} \neq 0$

similar substrates to occur at unequal rates with a common reagent under identical conditions the free energies of activation must be different. In general this is true if the transition states leading to reaction are diastereoisomeric and so of unequal free energy. However, in the reaction of diastereoisomers (fig. 1) differences in the free energies of the reactants have to be considered since it is differences in the free energies of activation that are important (i.e. change in the free energy from reactant to transition state). These considerations do not arise in the cases of asymmetric synthesis or asymmetric destruction (fig. 2).

The rate constant for a reaction is related to the free energy of activation by the following equation:

$$k = e^{-\Delta G/RT} \qquad (1)$$

which is expressed in $\log_{10}$ form as:

$$\log_{10} k = -\Delta G/2.303\ RT \qquad (2)$$

Suppose now that the two enantiomers A and B react with an asymmetric reducing agent to form two diastereoisomeric transition states with free energy $G_A^{\ddagger}$ and $G_B^{\ddagger}$ (see fig. 2). If the free energies of activation are expressed as $\Delta G_A^{\ddagger}$ and $\Delta G_B^{\ddagger}$ two equations of type (2) may be written:

$$\log_{10} k_A = -\Delta G_A^{\ddagger}/2.303\ RT \qquad (3)$$

$$\log_{10} k_B = -\Delta G_B^{\ddagger}/2.303\ RT \qquad (4)$$

subtracting (4) from (3) gives:

$$\log_{10}(k_A/k_B) = (\Delta G_B^{\ddagger} - \Delta G_A^{\ddagger})/2.303\ RT \qquad (5)$$

$$= \Delta\Delta G^{\ddagger}/2.303\ RT$$

The optical purity of the product is related to the ratio of products A' and B' by the equation:

$$\frac{[\alpha]}{[\alpha']} = \left(\frac{A'}{B'} - 1\right) \Big/ \left(\frac{A'}{B'} + 1\right) \qquad (6)$$

$[\alpha]$ is the observed rotation; $[\alpha]$ is the rotation of the pure enantiomer A'. The relative rates of the reaction of the two enantiomers A and B with the asymmetric reducing agent C can be determined by allowing A and B to react with C and then analysing the mixture. The competing reactions can be represented as follows:

$$A + nC \longrightarrow A' \qquad (7)$$

$$B + nC \longrightarrow B' \qquad (8)$$

where n is the order of the reaction with respect to C. The following treatment is essentially that given by T.S.Lee ref. 18 p. 108. The rate equations (9) and (10) apply to reactions (7) and (8) respectively.

$$-d[A]/dt = k_A[A][C]^n \qquad (9)$$

$$-d[B]/dt = k_B[B][C]^n \qquad (10)$$

Division of (9) by (10) and integrating yields:

$$r = \frac{k_A}{k_B} = \frac{\log_{10}([A]/[A_o])}{\log_{10}([B]/[B_o])} \qquad (11)$$

or

$$[A]/[A_o] = ([B]/[B_o])^r \qquad (12)$$

where $[A_o]$ is the initial concentration of A.

Three experimental techniques for the evaluation of r are available.

1. The ratio of the products formed in the early stages of reaction is approximataly equal to r.

$$[A']/[B'] \approx r$$

2. Calculation of r using equation (11) by analysis of [A] and [B] or [A'] and [B'] at any point in the reaction.

3. Analysis of the products at various stages of the reaction and plotting the $\log_{10}$ of fraction of A remaining against $\log_{10}$ of fraction of B remaining. The graph should be linear with slope r.

The last method has the advantage that it tests for the two reactions being competitive in the sense of following the same order with respect to A and B. In the asymmetric reductions dealt with here, it follows that the reactions are homocompetitive since A and B are enantiomers; method 2 was therefore used.

It is possible to show that r can be determined with the greatest accuracy when:

$$[A_o] = [B_o]$$

and when the extent of reaction is:

$$[A]/[A_o] = r^{r/(1-r)} \text{ and } [B]/[B_o] = r^{1/(1-r)}$$

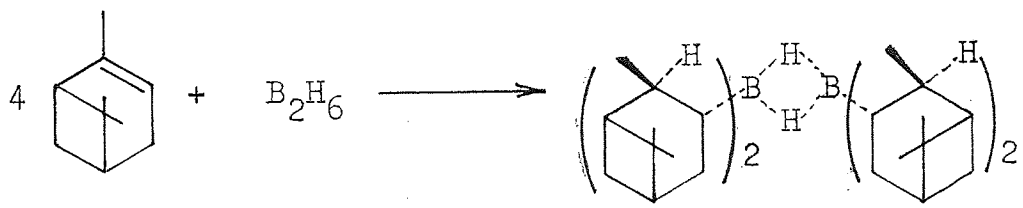
The optimum stage of reaction gives the extent of reaction when asymmetric reduction is at a maximum for a given value of r. Clearly this is an important consideration in an asymmetric destruction of the type under study.

To summarise, from the optical yield at any stage in an asymmetric reduction it is possible to calculate the difference in free energies of the diastereoisomeric transition states and the optimum stage of the reaction.

III

ATTEMPTS AT ASYMMETRIC REDUCTION USING DI-ISOPINOCAMPHEYL-BORANE.

Very high optical yields of secondary alcohols are reported for the hydroboration of cis 1,2-disubstituted olefins with (-)-sym-tetraisopinocampheyldiborane.[19] The hydroboration of (+)-α-pinene (I) proceeds readily to give the asymmetric adduct (II) by stereospecific cis addition of the boron-hydrogen bond to the double bond of the pinene from the less hindered side of the molecule.

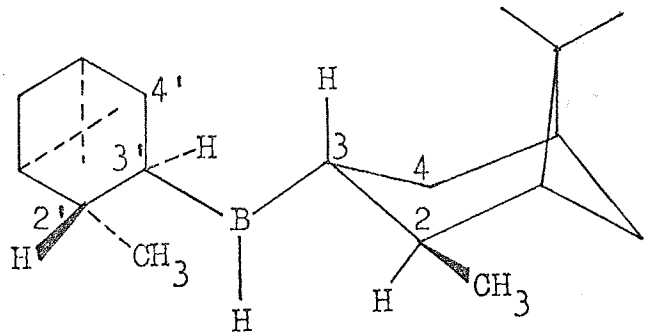


(I) (II)

Reaction of cis-butene with (II), followed by oxidation of the resulting di-isopinocampheyl-2-butylborane with alkaline hydrogen peroxide, gives R-(-)-butan-2-ol of 87% optical purity.[19] The exceptionally high optical yields have been described as due to an unusually good steric fit of the olefin and a particular conformation of the borane (II) in a model in which the boron-hydrogen cis addition occurs via a four centred transition state. (-)-Sym-di-isopinocampheyl-borane is considered in models of the transition states. (Transition states for asymmetric hydroboration involving the dimer have been described in a recent publication by D.R. Brown et al.[20])

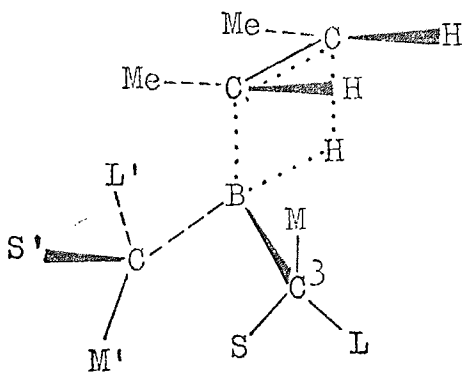
The absolute configuration of (+)-α-pinene is known and, therefore, in a simplified form di-isopinocampheylborane may

may be represented in conformation (III). In this hydrogen atoms at C(3) and C(3')may be replaced by S and S', methylene groups at C(4) and C(4') by M and M', and $-CHCH_3-$ at C(2) and C(2') by L and L'.

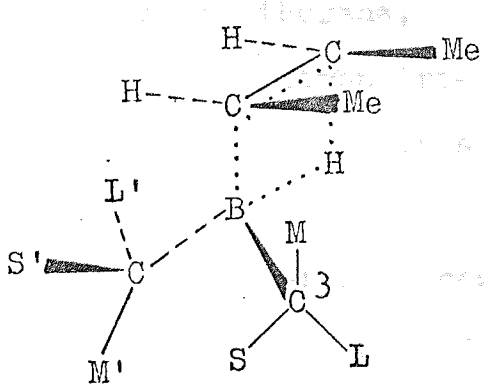


(III)

Hydroboration of a number of cis alkenes with (II) has enabled Brown and co-workers to propose models of the diastereoisomeric transition states that control the product formation typified by the models (IV) and (V) shown below:



(IV)



(V)

The major steric interactions in the transition state models (IV) and (V) are thought to be those between the methyl and hydrogen groups of the olefin and the C(3') hydrogen and the methylene C(4) of the borane, These considerations lead to (IV) being preferred to (V) and so resulting in R-(-)-butan-2-ol predominating in the product after oxidation of the borane intermediate.

Asymmetric hydroboration of trans and hindered olefins,

however, cannot be rationalised in terms of the above transition states.[21] This inconsistency illustrates the dangers in application of a model from one system to another, even if closely related, for the purpose of determining absolute configuration. The discrepancy here was traced to a change of mechanism brought about by dissociation of the tetraisopinocampheyldiborane into (+)-α-pinene and triisopinocampheyldiborane.

(-)-1-Naphthylphenylmethylchlorosilane is very easily reduced by sodium borohydride in diglyme solution to (-)-1-naphthylphenylmethylsilane with inversion of configuration.[4] In view of this, it appeared that if racemic chlorosilane could be partially reduced by the asymmetric diborane (II) an asymmetric reduction might be achieved.

The (-)-sym-tetraisopinocampheyldiborane was prepared by the procedure of Brown[19] by the addition of diborane, generated in situ from sodium borohydride and boron trifluoride etherate, to (+)-α-pinene in diglyme. Attempts at reduction of 1-naphthylphenylmethylchlorosilane were unsuccessful (experiment 5.) and even a twelve-fold excess of borane adduct, left overnight at room temperature gave no indication of any reduction. Further attempts at asymmetric reduction using (-)-sym-tetraisopinocampheyldiborane were abandoned.

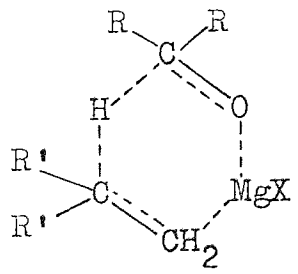
IV

ATTEMPTS AT ASYMMETRIC GRIGNARD REDUCTION.

1. Grignard reduction of carbonyl compounds.

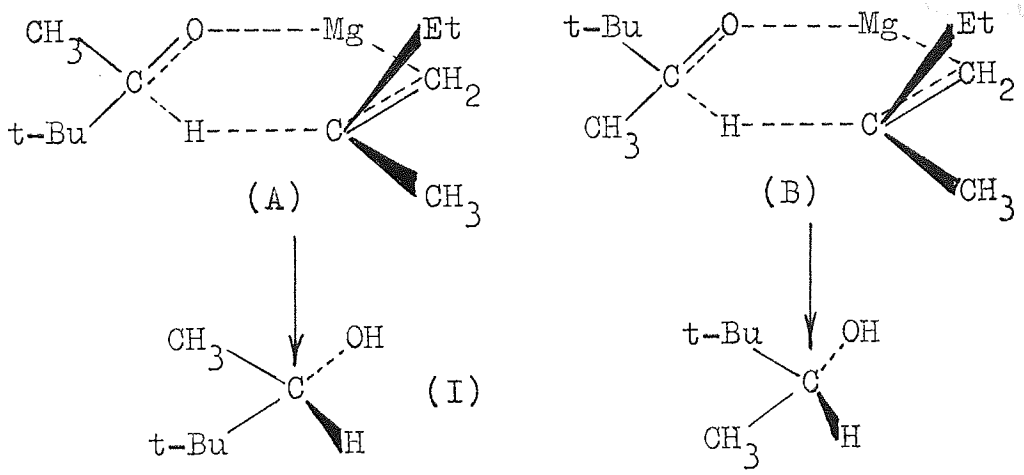
When sterically hindered Grignard reagents react with an organic carbonyl compound the products are predominantly those resulting from a reduction and not a normal addition. Reaction of benzophenone and isobutylmagnesium bromide gives diphenylcarbinol and isobutylene in equivalent amounts.[22] The carbon atom to which the magnesium was originally bonded undergoes a change in hybridisation from sp^3 to sp^2. Consequently, the net result of the reduction involves β elimination of the magnesium and hydrogen from the Grignard reagent. Further support is provided by the observation that no reduction occurs with sterically hindered Grignard reagents not possessing a hydrogen atom bound to a β carbon atom.

Studies on reductions with Grignard reagents deuterated in various positions have shown conclusively that the carbonyl reduction involves the βcarbon atom of the Grignard reagent. The results are consistent with a transition state in which reduction proceeds via an essentially planar six-membered ring structure:[23]



The above reduction has been successfully the subject of considerable study from the point of asymmetric synthesis and was the result of one of the first applications of the concept of steric control.

Using the above model for the transition state it was predicted that the alcohol resulting from the reaction of t-butyl methyl ketone and (+)-2-methylbutylmagnesium chloride would contain an excess of the S-(+)-enantiomer (I).[24]



It was envisaged that there would be less non-bonded interactions in the suggested transition state (A) in which the largest groups (ethyl of the Grignard reagent and the t-butyl of the ketone) were in a trans configuration. Accordingly, (A) would possess less energy than (B) and the reaction would proceed more rapidly through transition state (A) to give predominantly the product (I). When the reaction was conducted at 20° the enantiomer (I) was, indeed, found to be 13% in excess.[25] Many other unsymmetrical ketones were reduced using (+)-2-methylbutylmagnesium chloride and optical yields varied from 25% for phenyl cyclohexyl ketone to 2.1% for isopropyl cyclohexyl ketone. Difficulties arise in deciding whether the above interpretation is consistent with the experimental results and amongst these the arrangement of the groups in order of effective size presents one of the greatest problems. Mosher's results appear to be consistent at first sight if the order of effective size for the three largest groups of the ketones studied is taken to be phenyl >

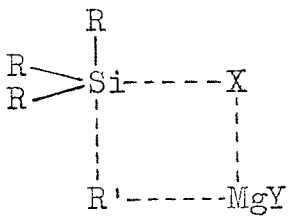
t-butyl > cyclohexyl.

However, recent results of Mosher and co-workers[26] have shown that differences in compression in the transition states are not the only cause of the stereoselectivity in these asymmetric reductions.

Studies using other optically active Grignard reagents have shown that extremely high optical yields of alcohols can be obtained using this type of reduction. Thus reduction of isopropyl phenyl ketone with the Grignard reagent from (+)-1-chloro-2-phenylbutane gives isopropylphenylmethanol in 82% optical yield.

2. Grignard reduction of silanes.

The mechanism of most substitution reactions at silicon can be described as involving nucleophilic attack of the carbanion moiety of the Grignard reagent on the silicon. In the case where the substrate is an alkoxysilane, the alkoxy group is coordinated with the magnesium atom of the Grignard reagent in the transition state. The mechanism, therefore, provides an electrophilic 'pull' from the magnesium together with a nucleophilic 'push' from the carbanion, the combination of which aids the removal of the 'poor leaving group'. The retention of configuration observed for these reactions is in accordance with the flank attack at the silicon described above. The transition state is described as S_Ni-Si and is supposed to be a cyclic four-centred structure:



X is a 'poor leaving group'

Consideration of such a transition state makes the feasibility of normal substitution dependant upon the ability of the α-carbon atom of the Grignard reagent to approach the silicon centre. This ability will obviously be influenced by:

a) bulky substituents on the silicon,

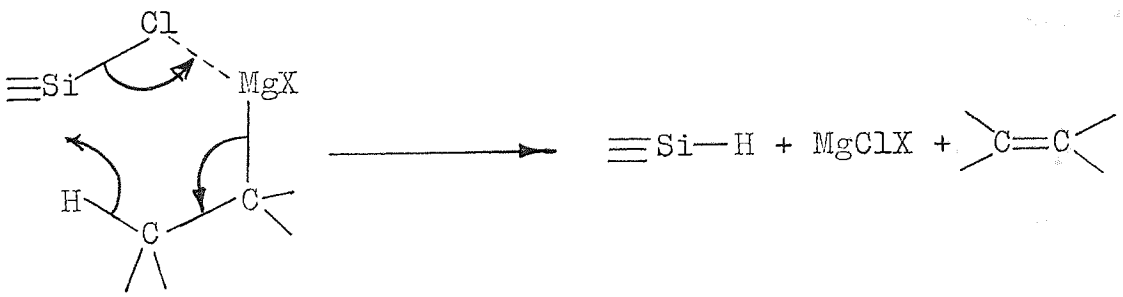
b) steric nature of the Grignard reagent.

Considerable experimentation has been conducted on the study of steric effects on the reactions of organolithiums and Grignard reagents with halo- and alkoxy-silanes. Schumb and Saffer[27] showed that reaction of silicon tetrachloride with p-, m-, and o-tolylmagnesium bromides led to yields of the corresponding tetratolylsilanes that were 35%, 8%, and 0% respectively. Their unsuccessful attempt to prepare tetra-o-tolylsilane is attributable to steric factors. Subsequent work by Gilman and Smart[28] showed that steric effects are of prime importance in the case of the substitution reactions of o-tolyl and mesityl silanes by bulky Grignard reagents and organolithiums. The vast amount of work conducted on studies of this type is too large to be treated satisfactorily here and reference is made to the relevant Chapters in ref. 29. However, it must be mentioned that Cusa and Kipping[30] reported that the principal product of the reaction of phenyltrichlorosilane and cyclohexylmagnesium bromide, under an inert atmosphere at approximately 100°, was dicyclohexylphenylsilane. Reduction had, therefore, occurred in preference to the introduction of the third cyclohexyl group. The mechanism proposed by these workers involved the formation of dicyclohexylphenylsilylmagnesium bromide, which upon hydrolysis gave the silane.

Failure to form stable silyl Grignard reagents led Harvey and co-workers[31] to reinvestigate the reaction.

Detection of dicyclohexylphenylsilane prior to hydrolysis and the presence of cyclohexene as a reaction product (apparently overlooked by the previous workers) compelled Harvey to disregard the earlier mechanism. Studies of the reaction of other sterically hindered Grignard reagents on phenyltrichlorosilane were undertaken since it appeared that the steric size of the cyclohexyl Grignard reagent was instrumental in determining the course of the reaction. Grignard reagents prepared from cyclopentyl-, t-butyl-, and isopropyl halides all form the corresponding silanes, viz. dicyclopentylphenylsilane, di-t-butylphenylsilane, and di-isopropylphenylsilane, together with the corresponding alkenes.

The results from the reaction of triphenylchlorosilane and cyclohexyl Grignard reagent led Brook and Wolfe[32] to propose a six-membered quasi-cyclic intermediate, analogous to that postulated for Grignard reduction of ketones:

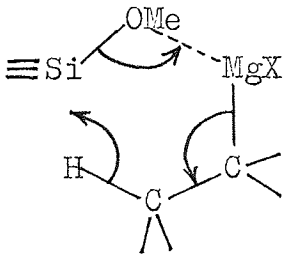


Related reductions were observed in the reaction of tetrabromosilane with s- or t-butylmagnesium bromide.[33] Small amounts of the butyltribromosilanes were obtained, but side reactions mostly occurred to form Si-H bonds with butene evolution or Si-Si bonds with octane formation.

Silicon alkoxides react fairly readily with Grignard reagents with formation of silicon-carbon bonds. However,

generally they are much less reactive than chlorosilanes, their reactivity falling with increasing chain length and branching in the alkoxy group.[34] Sometimes, silicon alkoxides give hydrides when heated with Grignard reagents, however, the presence of large groups does not appear to be essential. Methyltriethoxysilane reacts with n-propylmagnesium chloride at 150° to give some methyldi-n-propylsilane along with methyldi-n-propylethoxysilane.[35]

Reaction of methoxysilanes with t-butylmagnesium chloride at 95° occurs with retention of configuration at the silicon atom and this has led Sommer to propose a transition state analogous to that written for the reduction of silicon chlorides under comparable conditions:



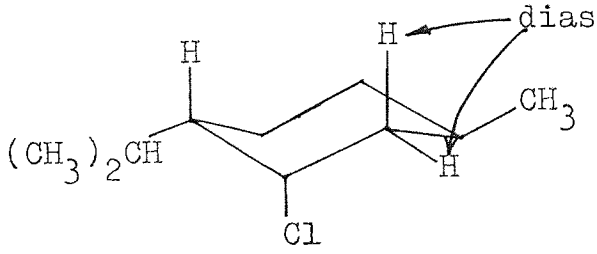
Valade and co-workers,[36] however, suggest that reduction does not involve a six-membered intermediate but that reaction occurs by attack of a hydride of magnesium formed by elimination from the Grignard reagent. Grignard reagents derived from t-butyl and isopropyl chlorides are known to have the greatest reducing effect on chlorosilanes and this suggests that the ability to reduce is conferred by their steric nature. However, these are also compounds which most easily undergo elimination.

In the light of this controversy it was hoped that the successful asymmetric reduction of (±)-1-naphthylphenylmethylmethoxysilane using Grignard reagents possessing a chiral

centre β to the magnesium atom would provide decisive evidence for the mechanism of the reduction.

Preliminary work using 1-naphthylphenylmethylmethoxysilane and Grignard reagents from isobutyl and isoamyl chlorides has shown that very little reduction occurs[37] and that the major product is the normal coupled product. This is perhaps a little surprising in that there is ample evidence to suggest that isobutylmagnesium chloride is capable of reducing triphenylchlorosilane.

It was, therefore, thought possible that asymmetric Grignard reduction might be achieved using the reagent prepared from (+)-neomenthyl chloride. It was expected that the normal coupling reaction would be prevented by the sterically challenging nature of the reagent and hoped that steric interactions would not be prohibitive to reduction. Although the β-hydrogens, most likely for reduction, are not on a chiral centre they are diastereoisomeric by internal comparison and would, therefore, be expected to give rise to asymmetric reduction (c.f. ref 38).



Considerable difficulty was found in the preparation of the Grignard reagent from neomenthyl chloride and successful preparation required the addition of small quantities of ethylmagnesium bromide to initiate the reaction. However, this proved unsuitable, since after baking for 3 days at 100°C with methoxysilane preferential formation of the

ethylsilane had occurred.

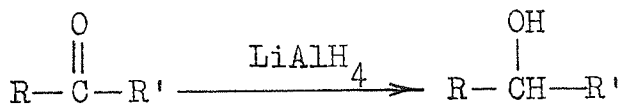
The reaction was repeated using a 2:1 excess of Grignard reagent, prepared by initiation of (+)-neomenthyl chloride with ethylene dibromide (does not form a stable Grignard reagent). Baking at 100° for 4 days failed to give any indication of silane in the infrared spectrum of the separated products. The spectra and thin-layer chromatography showed them to be mainly methoxysilane and hydrocarbon products from the neomenthyl Grignard reagents.

At this time successful asymmetric reduction of (±)-1-naphthylphenylmethylmethoxysilane with a complex of (+)-quinidine and lithium aluminium hydride caused the above work to be discontinued. However, successful asymmetric reduction using a Grignard reduction would remain of considerable interest from the point of the mechanism of these reactions.

V.

ASYMMETRIC REDUCTION BY OPTICALLY ACTIVE ALKOXY LITHIUM ALUMINIUM HYDRIDES.

The reduction of unsymmetrical ketones with metal hydrides yield racemic disubstituted carbinols provided that



the reduction is not affected by either an optically active reagent or other asymmetric influence. The early report by Bothner-By[39] that (+)-camphor could induce the formation of excess of one of the enantiomeric dialkylcarbinols during lithium aluminium hydride reduction of 2-butanone and pinacolone has now been shown to be in error.[40] Although the lithium di-isobornyloxyaluminohydride, presumably formed, does not appear to asymmetrically reduce these ketones, other optically active alkoxy lithium aluminium hydrides have been found to be quite effective. The asymmetric addends used have been amino-alcohols and carbohydrates. Extensive studies by Cervinka and co-workers have been conducted on the asymmetric reduction of methyl alkyl ketones,[41] methyl aryl ketones,[41] phenyl aryl ketones,[42] and cyclohexyl aryl ketones,[43] using complexes of lithium aluminium hydride and amino-alcohol alkaloids.

Cervinka had also reported the asymmetric reduction of 1-methyl-2-alkyl-Δ'-pyrrolinium and -piperidinium perchlorates with complexes between optically active terpene alcohols and lithium aluminium hydride.[44,45] Reduction of alkyl phenyl ketimines by complexes of lithium aluminium hydride and (-)-menthol and (+)-borneol are reported to occur asymmetrically.[46]

The use of carbohydrates for preparing optically active lithium aluminium hydrides was first reported by Landor and co-workers.[47] More recent work on the use of other monosaccharide complexes has established that the highest optical yields of secondary alcohols are achieved by use of 3-O-benzyl-1,2-O-cyclohexylidene-α-D-glucofuranose (I).[48] Further improvements were found by using standardized, ethereal solutions of lithium aluminium hydride and by the addition of ethanol to modify the complex. Addition of ethanol produces optically active alcohols with the opposite absolute configuration to those formed in its absence. Optical purities up to 64% have been obtained using this procedure. Explanations have been offered which account adequately for the configurations of the alcohols formed by the reductions with (I) both in the presence[49] and absence of ethanol.[50]

1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose and 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose have been used by Cervinka[51] for complex formation with lithium aluminium hydride. The optical purities of asymmetric reductions using these complexes, however, have been low (<5%).

Landor and co-workers have reduced certain allylic alcohols with lithium aluminium hydride and (I) to optically active allenols.[52]

$$R'-C\equiv C-CH=CHCH_2OH \xrightarrow{LiAlH_4} R'-CH=C=CCH_2CH_2OH$$

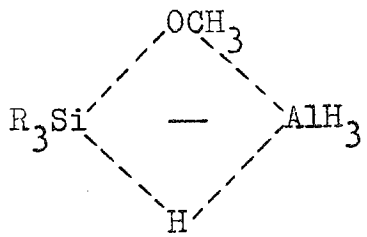
R(-)

$R' = CH_3,\ C_2H_5,\ n\text{-}C_4H_9,\ t\text{-}C_4H_9C\equiv C,\ C_6H_5C\equiv C,\ H(C\equiv C)_2,\ CH_3(C\equiv C)_2$

In the light of this previous work, the partial reduction of racemic methoxysilanes using asymmetric

complexes of lithium aluminium hydride seemed to offer an excellent reaction for the production of optically active silanes.

The reduction of (+)-1-naphthylphenylmethylmethoxysilane with lithium aluminium hydride in diethyl ether is reported to occur by retention of configuration.[4] The mechanism, in non-polar media, is said to involve a four centred transition state which minimizes charge separation. This is clearly in accord with the low ion-solvating nature of such solvents. Sommer has labelled these retention reactions as S_Ni-Si.[5]



The S_Ni-Si mechanism is the most common for reactions involving 'poor leaving groups' i.e. bases whose conjugate acids have $pK_a > 10$.

'Good leaving groups' ($pK_a < 6$) normally react by inversion of configuration. The usual invariance of this stereochemistry for groups such as Cl, Br, and esters has led Sommer to postulate the 'good leaving group rule'.[5] Sommer has designated this mechanistic path as S_N2-Si.

1. Partial reduction of (±)-1-naphthylphenylmethylmethoxysilane with 1:1 complexes of alkaloids and lithium aluminium hydride (Experiment 8).

The exploratory work on the asymmetric reduction of (±)-1-naphthylphenylmethylmethoxysilane (II) with the 1:1 complex of (+)-quinidine and lithium aluminium hydride has been reported.[53] This reaction constituted the first kinetic

asymmetric formation of an optically active organosilane.

The quinidine complex was prepared in situ by the addition of the alkaloid to a suspension of an equivalent molar weight of hydride in diethyl ether. Reaction at reflux for 30 minutes ensured complex formation. At the concentration used the complex is reported to be dimeric in tetrahydrofuran.[54] Although there is no reason to suppose that the degree of association is necessarily the same in diethyl ether and tetrahydrofuran, the concentration used by Cervinka[54] was adopted for the sake of consistency.

Reaction of (+)-quinidine complex and the methoxysilane (II) in the molar ratio 1:3.16 for 4 hours at reflux gave a product which on column chromatographic separation on silica gel using benzene/light petroleum eluant yielded 33% 1-naphthylphenylmethylsilane (III). This silane was found to be dextrorotatory with an optical purity of about 6%. The unreacted methoxysilane, recovered from the column using benzene, was laevorotatory (also with an optical purity of 6%). Nuclear magnetic resonance, infrared, and ultraviolet spectra of these fractions confirmed their chemical integrity.

Fractional crystallisation of the optically active silane from n-pentane at ice-bath temperatures yielded a white crystalline solid whose m.p. and specific rotation showed it to be optically pure (+)-1-naphthylphenylmethylsilane (III).

Attempts to purify the active methoxysilane by a similar procedure failed. Complete reduction with lithium aluminium hydride followed by fractional crystallisation yielded the substantially pure laevorotatory silane.

In this asymmetric reduction the (+)-silane (III) and the (-)-methoxysilane (II) possess opposite absolute configur-

ations, and by the Cahn, Ingold, Prelog nomenclature[55] may be assigned the R configuration. This corresponds to an overall retention of configuration for the asymmetric reduction, in agreement with the findings of Sommer for normal lithium aluminium hydride reductions of alkoxysilanes.

The results of the asymmetric reductions, using other alkaloids as complexing reagents, are given in Table 1.

Table 1.

Asymmetric reductions of (±)-1-naphthylphenylmethylmethoxysilane with 1:1 alkaloid $LiAlH_4$ complexes.

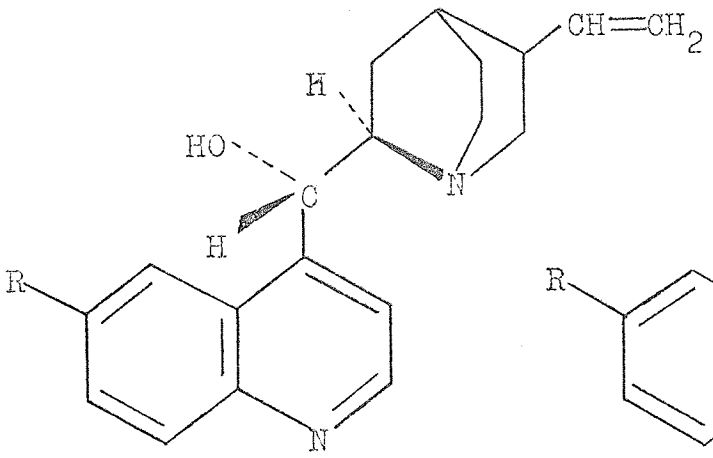
Alkaloid	IVa	IVb	Va	Vb	VI	VII
% redn.	35	28	33	43	23	27
$[\alpha]_{588}$ silane	+1.52°	-0.64°	+1.96°	+1.24°	+0.26°	+4.53°
purity[a]	4.3	1.8	5.5	3.5	0.7	12.8
$[\alpha]_{588}$ methoxy	-0.24°	+0.13°	-0.93°	-0.40°	0.00°	-0.86°
purity[b]	1.4	0.8	5.5	2.4	0.0	5.1
absolute config.	R	S	R	R	R	R

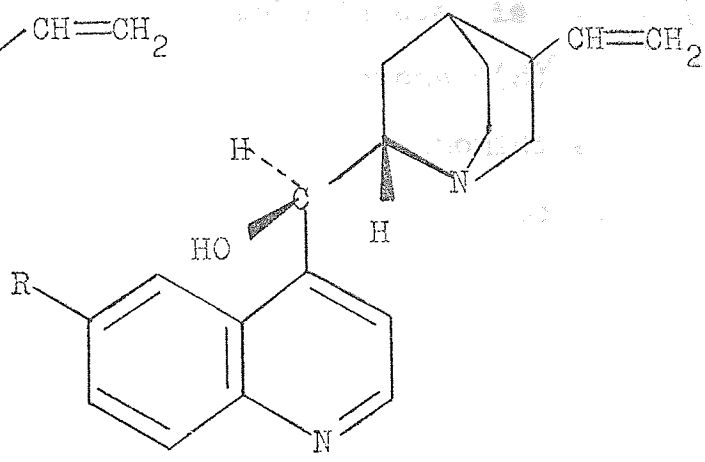
Optical activities have been corrected for the optical purity of the alkaloid used.

a) Optical purity calculated as % of $[\alpha]_D$ +35.5° for the silane[4]

b) " " " " " " $[\alpha]_D$ +17° for the methoxysilane.[4]

IVa	(-)-quinine	Vb	(+)-cinchonine
IVb	(-)-cinchonidine	VI	(-)-ephedrine
Va	(+)-quinidine	VII	(+)-ψ-ephedrine



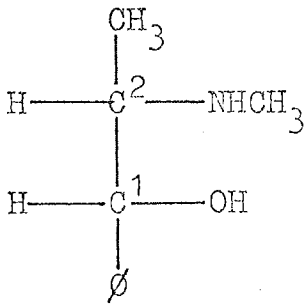


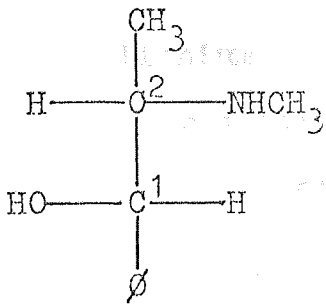
IVa R = CH_3O; (–)-quinine

IVb R = H; (–)-cinchonidine

Va R = CH_3O; (+)-quinidine

Vb R = H; (+)-cinchonine





VI (–)-ephedrine

VII (+)-ψ-ephedrine

Fig. 3

Absolute configurations of optically active cinchona and ephedra alkaloids used to prepare complexes with lithium aluminium hydride.

The absolute configuration of the alkaloids used is shown in Fig. 3. The configurations of carbon atoms C(8) and C(9) in (-)-quinine (IVa R = OCH_3) and (-)-cinchonidine (IVb R = H) are enantiomeric to the same centres of asymmetry in (+)-quinidine (Va R = OCH_3) and (+)-cinchonine (Vb R = H). (-)-Ephedrine (VI) and (+)-ψ-ephedrine (VII) are diastereoisomers differing only in absolute configuration at C(1).

Inspection of Table 1. shows that the extent of reduction depends on the nature of the complex with lithium aluminium hydride. In general, the cinchona alkaloids, (-)-quinine, (+)-quinidine and (+)-cinchonine give yields of silane between 30 and 40% after 4 hours reflux. (-)-Ephedrine and (+)-ψ-ephedrine give noticeably less. This is explained by the presence of the -NH group in the latter compounds which is able to displace a second hydride atom from the lithium aluminium hydride, leaving only two for subsequent reduction of the methoxysilane. Measurements of the hydrogen liberated from lithium aluminium hydride by ephedrine and ψ-ephedrine confirm that both the -OH and -NH protons are displaced.

Clearly the results of asymmetric reductions using the above series of alkaloids cannot be explained in terms of steric factors alone since anomalous behaviour is shown in the case of the reduction with (-)-quinine complex.

Most notable from Table 1. is the vast difference in the efficiency with which ephedrine and ψ-ephedrine promote asymmetric reduction. This may be attributable to the respective nature of the complexes. In the case of ψ-ephedrine steric interactions between the methyl on C(2) and the phenyl group on C(1) cause the amine and hydroxyl groups to be in a gauche conformation (Fig. 4.):

(+)-ψ-ephedrine (-)-ephedrine

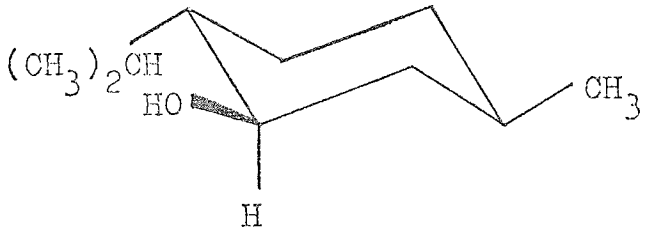
Fig. 4.

However in ephedrine the same interactions cause the amino and hydroxyl groups to be in a trans conformation with respect to one another. These considerations lead to the realization that complexing, in the case of ψ-ephedrine, is likely to be of a cyclic type with both the nitrogen and oxygen atoms bound to the same aluminium atom. The ephedrine complex, however, is more likely to be oligomeric with consequential lack of conformational rigidity. The higher optical yields obtained using alkaloids compared with saturated terpene alcohols (c.f. Table 2.) may be similarly due to the rigidity imposed on the complexes by bonding or coordination of the nitrogen atom of the alkaloids to the aluminium atom. Further discussion of the factors influencing the course of the reductions is left until Chapter VII.

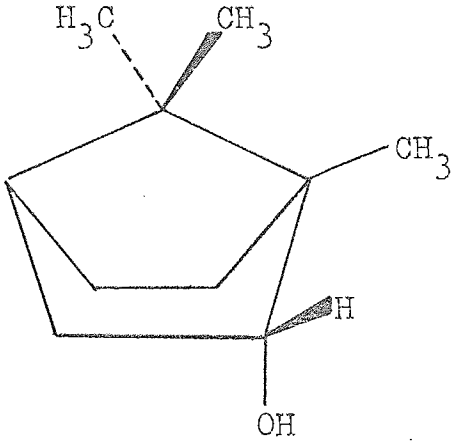
2. Asymmetric reduction of (±)-1-naphthylphenylmethylmethoxysilane with 1:1 complexes of optically active alcohols and lithium aluminium hydride.

The reductions using saturated cyclic terpene alcohols (Experiment 9) were carried out in an effort to simplify the analysis of the results. All the alcohols used possessed only one site for complexing and with the exception of one acyclic alcohol were conformationally locked.

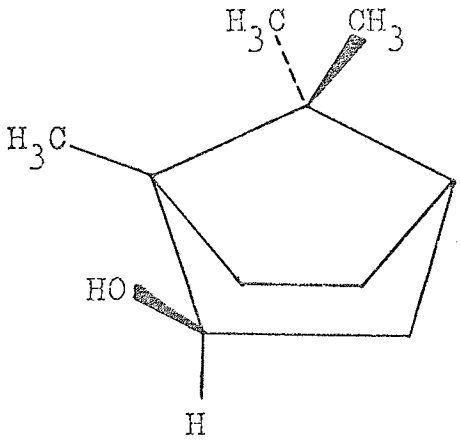
Fig. 5 Absolute configurations of asymmetric alcohols.



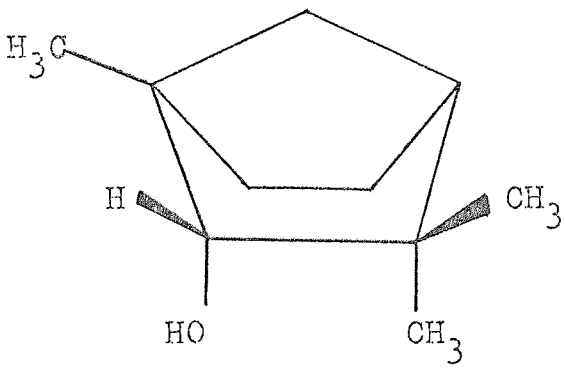
VIII (-)-menthol



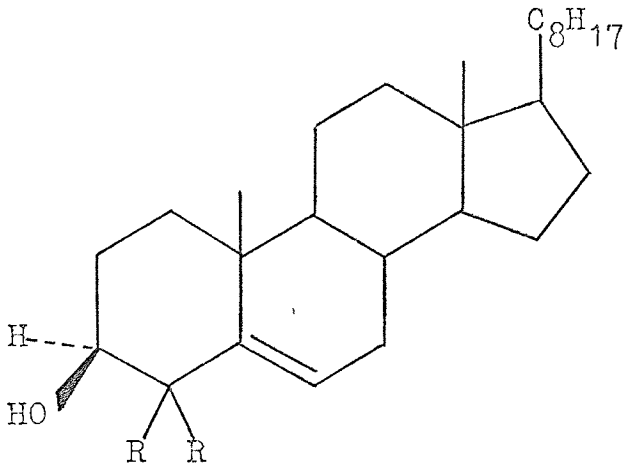
IX (-)-borneol



X (-)-isoborneol

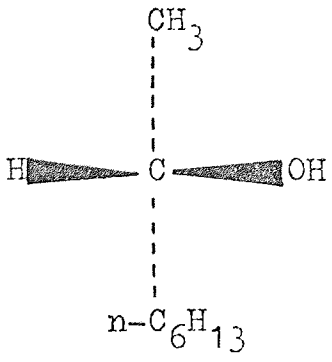


XI (+)-α-fenchol



XIII R = H; cholesterol

XIV R = CH_3; lanosterol



XII (+)-2-octanol

Figure 5. shows the absolute configurations of the alcohols used.

Table 2.

Alcohol	VIII	IX	X	XI	XII	XIII	XIV
% redn.	49	56	47	31	24	31	0
$[\alpha]_{588}$ silane	+0.71°	+0.34°	0.00°	+0.34°	+0.33°	0.00°	-
purity[a]	2.0	1.0	0	1.0	0.9	0	-
$[\alpha]_{588}$ methoxy	-0.20°	0.00°	0.00°	-0.10°	0.00°	0.00°	-
purity[b]	1.2	0	0	0.6	0	0	-
Absolute Config.	R	R	-	R	R	-	-

a. and b. as in the footnotes to Table 1.

VIII (-)-menthol
IX (-)-borneol
X (-)-isoborneol
XI (+)-α-fenchol
XII (+)-2-octanol
XIII cholesterol
XIV lanosterol

It is evident from Table 2. that the reaction is very sensitive to steric factors as evidenced by the considerable difference in reduction rate when lanosterol is used instead of cholesterol. Furthermore, examination of Courtauld's Models makes it clear that the extent of reaction, shown in Table 2., reflects the magnitude of the steric hindrance which the groups about the hydroxyl bearing carbon atom exert on the hydride atoms of the lithium aluminium hydride complex.

A pattern seems to be apparent in the results from the three cyclic terpene alcohols. The result of the reduction

using the acyclic (+)-2-octanol is difficult to rationalize with the others, but the difference may be due to greater disproportionation of the lithium alkoxyaluminium hydride of this alcohol.

3. Partial asymmetric reduction of (±)-1-naphthylphenylmethylchlorosilane (Experiment 11).

In view of the successful asymmetric reductions of (±)-methoxysilane it was wondered what differences might occur when the stereochemistry of the reaction was changed from retention to inversion. Accordingly the partial asymmetric reduction of (±)-1-naphthylphenylmethylchlorosilane (XV) with complexes of alkaloids and lithium aluminium hydride was studied.

The procedure followed was essentially the same as that for the methoxysilane (II) except this time the reduction was terminated by addition of methanol to convert the unreacted chlorosilane to methoxysilane. The results for a reaction time of 4 hours are given in Table 3.

Table 3.

Alkaloid	IVa	IVb	Va	Vb
% redn.	16	25	25	22
$[\alpha]_{588}$ silane	-0.17°	-0.26°	+0.27°	+1.03°
purity[a]	0.5	0.8	0.8	2.9
$[\alpha]_{588}$ methoxy	0.00°	0.00°	+0.12°	-
purity[b]	0.0	0.0	0.7	-
Absolute Config.	S	S	R	R

a. and b. as in the footnotes to Table 1.

It can be seen that the absolute configuration of the silane (III) produced follows the change in absolute configuration of the hydroxyl bearing C(9) of the alkaloid. The optical activity of the methoxysilane formed from the excess chlorosilane was unfortunately zero in two cases. The reduction using (+)-cinchonine (Vb) complex followed by addition of methanol did not yield any methoxysilane in spite of repeated attempts. The (+)-quinidine-lithium aluminium hydride reduction (Va) yielded dextrorotatory methoxysilane after methanol addition. Assuming that the methanol reacted with excess chlorosilane (XV) by inversion of configuration, then this would mean that the asymmetric reduction had taken place by retention of configuration. This is clearly most unusual for reduction of (XV) by lithium aluminium hydride.[56]

In view of the unusual stereochemistry and the failure to form methoxysilane in the case of the reduction with cinchonine complex it is concluded that the reaction does not involve the simple reduction of chlorosilane by lithium aluminium hydride complex. Possibly the chlorosilane reacts with the complex to form diastereoisomeric silyl alkaloid alkoxy compounds. Should these diastereoisomeric siloxy alkaloids be formed in unequal amounts then the remaining unreacted chlorosilane (the chlorosilane is in excess with respect to the alkaloid) would be optically active. Reduction of this would then give optically active silane. On addition of methanol alkoxy exchange occurs by inversion of configuration, in view of the high excess of methanol present,[6d] and optically active methoxysilane would be recovered.

This postulated reaction scheme accounts for the

recovered silane and methoxysilane possessing the same absolute configuration, provided that inversion of configuration is taken to be the predominant stereochemistry for reactions involving chlorosilane. Further evidence of possible siloxy alkaloid participation may be inferred from the reduction with cinchonine complex. In this case methanol does not appear to cause alkoxy exchange of the siloxy alkaloid and it requires aqueous sulphuric acid to cause breakdown during workup with formation of silanol.

Whatever the reaction mechanism, it is likely that the asymmetric reduction of 1-naphthylphenylmethylchlorosilane proceeds by a complex route and is unsuitable for study from the point of view of asymmetric synthesis.

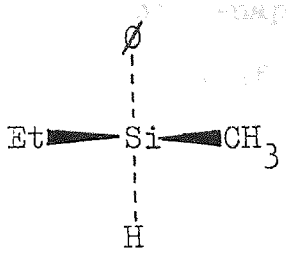
4. Asymmetric reduction of (±)-phenylethylmethylmethoxysilane (XVI) with alkaloid-lithium aluminium hydride complexes. (Experiment 14.)

Optically active (-)-phenylethylmethylbromosilane has been prepared by Sommer and co-workers by stereospecific bromodearylation of the 1-naphthyl group from (-)-1-naphthylphenylethylmethylsilane with bromine.[7a] Reduction with lithium aluminium hydride gave (+)-phenylethylmethylsilane (XVII). The reaction scheme used by Sommer is given below:

$$(+)\text{-1-Np}\emptyset\text{MeSiH} \xrightarrow[\text{ret}]{Cl_2} (-)\text{-1-Np}\emptyset\text{MeSiCl} \xrightarrow[\text{inv}]{\text{EtLi}}$$

$$(+)\text{-}\emptyset\text{MeEtSiH} \xleftarrow[\text{inv}]{LiAlH_4} (-)\text{-}\emptyset\text{EtMeSiBr} \xleftarrow[\text{inv}]{Br_2} (-)\text{-1-Np}\emptyset\text{MeSiEt}$$

The absolute configuration can therefore be written in a Fischer projection for S-(+)-phenylethylmethylsilane as:



The above preparation of this optically active silane is tedious, involves many steps, and results in a low overall yield. The route by asymmetric reduction of (±)-phenylethylmethylmethoxysilane (XVI) involves a single step and results in a fair yield of silane, possessing a good optical purity when (+)-cinchonine is used. Furthermore, optically active methoxysilane is also obtained the preparation of which has not previously been reported.

The asymmetric reduction of (XVI) with alkaloid-lithium aluminium hydride complexes was attempted for two further reasons:

i) the absolute configuration of the silane was known,

ii) considered from a steric point of view, the system presented the greatest challenge to the selectivity of the asymmetric reduction; success made the procedure extremely attractive for the partial resolution and study of novel optically active systems.

The results of the asymmetric reductions are shown in Table 4. (see next page).

It was found that the reduction of (XVI) with complexes of lithium aluminium hydride proceeded at a greatly reduced rate compared with 1-naphthylphenylmethylmethoxysilane. In order to obtain comparable yields of silane it was found necessary to increase the quantity of complex hydride by a factor of two and prolong the reaction time to 24 hours.

It is likely that in the case of 1-naphthylphenylmethylmethoxysilane the reaction rate is affected by electronic factors far more than by steric effects since the latter would act in the opposite sense to the direction observed. The enhanced reactivity of 1-naphthylphenylmethylmethoxysilane may be explained by the cumulative electron withdrawing properties of aryl groups on silicon [57] making attack by nucleophilic hydride ions more readily achieved.

Table 4.

Asymmetric reductions of (±)-phenylethylmethylmethoxysilane

Ratio of methoxysilane : complex 3:2 based on molecular weights; reductions were refluxed for 24 hours prior to work-up.

Alkaloid[a]	IVa	IVb	Va	Vb	VII
% redn.[b]	64	51	54	56	34
$[\alpha]_{588}$ silane	<+0.01°[c]	-0.18°[d]	+0.44°[d]	+0.50°[c]	+0.05°[c]
purity	<0.5[f]	7.1[e]	17.4[e]	41.2[f]	4.1[f]
$[\alpha]^{c}_{588}$ methoxy	-0.03°	+0.59°	-1.35°	-3.89°	0.00°
Absolute Config.	S	R	S	S	S

a) See text and p. 25.

b) Yields based on g.l.c. analysis.

c) $[\alpha]_{588}$ measured in hexane solution.

d) $[\alpha]_{588}$ measured in CCl_4 solution.

e) Optical purity calculated as % of $[\alpha]_D$+2.53° (CCl_4)

f) Optical purity calculated as % of $[\alpha]_D$+1.22° (hexane)

Due to the sensitivity of phenylethylmethylmethoxysilane to treatment with aqueous acid, aqueous ammonium chloride was used for the workup procedure.

The results from the asymmetric reductions further indicate the complex nature of the interactions involved. It appears that the reduction with (-)-quinine (IVa) complex leads to a silane possessing opposite absolute configuration to that from the reduction using (-)-cinchonidine (IVb), although the two alkaloids have the same relative configurations (see fig. 3.). The presence of the 6'-methoxy group on the quinoline moiety is responsible for the changeover but the nature of the involvement is not clear at present.

It it apparent from Table 4, however, that the optical purities of the products obtained from the reductions using (-)-quinine and (-)-cinchonidine were lower than when (+)-quinidine (Va) and (+)-cinchonine (Vb) were used. It may be, therefore, possible that the asymmetric direction of the reductions with (-)-quinine and (-)-cinchonidine is decided on a fine balance of two or more opposing interactions. With the (+)-cinchonine and (+)-quinidine these interactions appear to act in the same direction and lead to the high optical yields found for reductions using these alkaloids. It may be argued that the high optical yield obtained with (+)-cinchonine cannot be explained solely by the differences in steric hindrance of the ethyl and methyl groups on silicon alone. Some other interaction in the diastereoisomeric transition states is clearly involved.

Comparison of the results of the asymmetric reductions of 1-naphthylphenylmethylmethoxysilane and phenylethylmethylmethoxysilane leads to some interesting possibilities.

In general it can be seen that the reductions of the phenylethylmethylmethoxysilane give silanes of opposite absolute configuration to those from the 1-naphthylphenylmethylsilyl system. Furthermore, the extent of asymmetric selectivity for the latter case is markedly lower than for the phenylethylmethylmethoxysilane. The reasons for these observations are not at present understood but may be due in some degree to the ability of the naphthyl group on silicon to coordinate with the aluminium atom[58,59] in the transition state. Results of asymmetric reductions of other organomethoxysilanes (see next Chapter) also indicate that the asymmetric reductions of the naphthyl system may involve a different transition state topology.

5. Asymmetric reduction of (±)-phenylethylmethylmethoxysilane with 1:1 (-)-menthol-lithium aluminium hydride complex. (Experiment 15)

Reduction of the methoxysilane with this complex in the molar ratio of 3:2 at reflux for 4 hours gave a 65% yield of silane. Therefore the rate of reaction is very similar to those observed for 1-naphthyl- and benzyl-phenylmethyl methoxysilanes with 1:1 complexes of terpene alcohols and lithium aluminium hydride.

The silane, separated in the usual way, was very slightly , but significantly, laevorotatory $[\alpha]_{588}$ <-0.03°, $[\alpha]_{303}$ -0.40° in carbon tetrachloride. This corresponds to an optical purity of about 1% at most. The methoxysilane was markedly dextrorotatory $[\alpha]_{588}$+0.11°; $[\alpha]_{313}$+1.51° (hexane). The reduction had therefore proceeded with retention of configuration and the absolute configuration of the predominating silane enantiomer was R.

VI.

PREPARATION OF NOVEL OPTICALLY ACTIVE ORGANOSILICON SYSTEMS.

The high optical yields obtained by asymmetric reduction of (±)-phenylethylmethylmethoxysilane with alkaloid complexes of lithium aluminium hydride made the method attractive as a general preparative technique for novel optically active organosilanes inaccessible by previous routes.

1. Benzylphenylmethylsilane (Experiment 19)

The asymmetric reduction of (±)-benzylphenylmethylmethoxysilane was chosen for study on the basis that it would yield a novel optically active silane whose synthesis from optically active 1-naphthylbenzylphenylmethylsilane by the usual methods might present problems. Due to the way in which benzylsilanes readily undergo electrophilic substitution,[60] it may be anticipated that nuclear bromination of the benzyl group will occur during the normal bromodearylation reaction.

The electrophilic reactivity,[60] bathochromic shifts in the electronic spectra,[57b] and the donor strength of benzylsilanes in charge transfer spectra[59] have been explained by the σ-π conjugation involving the $-CH_2SiR_3$ group. The effect of this electron withdrawal from the silicon on the rate of reaction and stereochemistry may be studied by asymmetric reduction.

Racemic benzylphenylmethylmethoxysilane was prepared in good yield by the reaction of benzylmagnesium chloride on phenylmethyldimethoxysilane in diethyl ether (Experiment 16)

Asymmetric reductions were carried out using very similar conditions to those required for the reductions of phenylethylmethylmethoxysilane. The work-up again involved using aqueous ammonium chloride and not acid. (It is interesting to note that treatment of benzylphenylmethylmethoxysilane with aqueous acid (Experiment 18) gave the silanol only; no significant amount of disiloxane was formed.) The results are shown in Table 5.

Table 5.

Asymmetric reduction of (±)-benzylphenylmethylmethoxysilane with 1:1 alkaloid-lithium aluminium hydride complexes.

Reduction time 24hrs. Molar ratio of methoxysilane:complex = 3:2

Alkaloid	IVa	IVb	Va	Vb	VI	VII
% redn.[a]	47	48[b]	29	42[b]	7	20
$[\alpha]^{c}_{588}$ silane	+1.77°	+3.64°	-1.64°	-7.80°	-0.64°	-5.69°
$[\alpha]^{c}_{588}$ methoxy	-0.28°	-0.86°	+0.16°	+1.86°	+0.00°	+0.46°
Absolute[d] Config.	S	S	R	R	R	R

a) Yields calculated on weights of silane isolated.

b) Calculated on intensity of νSi-H at 2120 cm^{-1} in the mixture.

c) Optical rotations measured in hexane solution.

d) Inferred absolute configuration (see text).

The extent of reduction was calculated on the weight of silane recovered after separation. Analysis of the reduction mixtures, prior to separation, by infrared gave results in

close agreement. (Plot of optical density of the νSi-H peak, calculated using a Si-Ø peak as an internal comparison, against percentage silane in methoxysilane mixtures is linear.) Therefore, loss of silane during separation is minimal. In general it can be seen from Table 5 that the extent of reduction is only slightly lower than that of phenylethylmethylmethoxysilane (cf. Table 4.). This is probably due to greater steric interactions of the benzyl compared with the ethyl group in the course of the reaction. The electron withdrawal of the benzyl group does not appear to be a major factor in the rate of reduction.

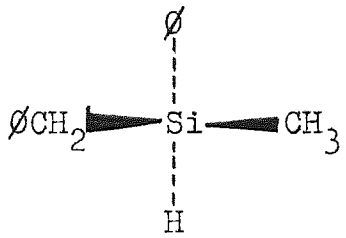
The partial reductions of (±)-benzylphenylmethylmethoxysilane (XVIII) with lithium aluminium hydride in the presence of (+)-quinidine (Va), (+)-cinchonine (Vb) and (+)-ψ-ephedrine (VII) form preferentially (-)-benzylphenylmethylsilane (XIX). Reductions using (-)-quinine (IVa) and (-)-cinchonidine (IVb) gave, on the other hand, excess of the dextrorotatory enantiomer. The results from the reductions using (-)-ephedrine (VI) and (+)-ψ-ephedrine (VII) show, once again, (cf. Table I) that the threo-configuration of the ψ-ephedrine leads to a silane with a much higher optical purity than the product from reduction with ephedrine, possessing the erythro-configuration

As in the case of the reductions of phenylethylmethylmethoxysilane, the silane with the highest optical purity is obtained using (+)-cinchonine (Vb). However, unlike the latter system, reduction with (+)-ψ-ephedrine also gives a silane of high optical activity.

The results show that the configuration of the silane enantiomer formed in excess is related to the absolute

configuration of the hydroxyl-bearing carbon atom C(9) in the cinchona alkaloid.

From optical rotatory dispersion studies (see Chapter IX) and use of the principle of an "isoconfigurational series", defined by Brook,[61] the absolute configuration of (+)-1,2-diphenylpropane[62] may be related with (+)-benzylphenylmethylsilane. Accordingly, the absolute configuration of (+)-benzylphenylmethylsilane is taken to be:



S-(+)-benzylphenylmethylsilane

Use of Brewster's rules for conformational asymmetry leads to the conclusion that S-benzylphenylmethylsilane should be dextrorotatory at the D-line of sodium. However, it should be borne in mind that the above assignment is only provisional. The sign of the optical rotation is governed by the nature of the asymmetrically perturbed electronic transitions of the aromatic groups. It has been shown that the electronic behaviour of a benzyl group on silicon is different from that of the carbon anologue[57b] and so there may reason to suppose that the principle of an "isoconfigurational series" is inapplicable in this case. Nevertheless, Brewster's rules of atomic asymmetry[63] have been applied with success to 1-naphthylphenylmethylsilane and germane[64] where similar objections could be raised.[57a]

In every reduction the recovered, unreacted methoxysilane possessed the opposite sign of rotation to the silane. The optical rotatory dispersion and circular dichroism spectra

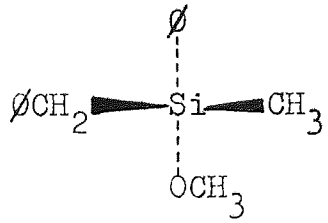
(see Chapter IX) showed that (–)-benzylphenylmethylsilane possessed the opposite relative configuration to (+)-benzylphenylmethylmethoxysilane. Therefore, the reductions of benzylphenylmethylmethoxysilane had proceeded with retention of configuration. This result was confirmed by the reduction of (+)-benzylphenylmethylmethoxysilane to (+)-benzylphenylmethylsilane (Experiment 21) with lithium aluminium hydride in diethyl ether. The stereospecificity was estimated to be about 99% retention, based on:-

a) The extent of the reduction in the preparation of the active methoxysilane,

b) the specific rotation of the silane from the asymmetric reduction,

c) the specific rotation of the silane from the normal reduction of the active methoxysilane.

The absolute configuration of (+)-benzylphenylmethylmethoxysilane was taken to be:



R-(+)-benzylphenylmethylmethoxysilane

In view of the high values in optical rotation found in the asymmetric reductions using alkaloids it was considered of interest to compare the results with reductions using optically active terpene alcohols (Experiment 20). Furthermore, a direct comparison with the asymmetric reductions of 1-naphthylphenylmethylmethoxysilane could be made in cases where a simpler asymmetric reducing agent is employed. The results for three terpene alcohols are shown in Table 6.

Table 6.

Alcohol	VIII	IX	XI
% redn.[a]	60	79	59
$[\alpha]^{b}_{588}$ silane	+0.28°	0.00°	0.00°
$[\alpha]^{b}_{588}$ methoxy	-0.69°	0.00°	0.00°
Absolute Config.	S	-	-

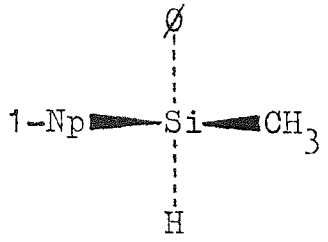
a) Yields calculated on the weight of silane isolated.

b) Optical activities have been corrected for the optical purity of the alcohol used.

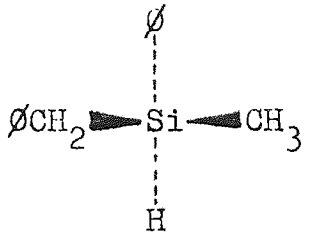
It is interesting to note that the reductions of (±)-benzylphenylmethylmethoxysilane using 1:1 complexes of these alcohols proceed very much faster than the reductions with the alkaloid complexes. In fact the reductions proceed at a similar rate to those of 1-naphthylphenylmethylmethoxysilane with menthol (VIII), borneol (IX), and α-fenchol (XI) complexes of lithium aluminium hydride (c.f. Table 2.). Therefore, alkaloid complexes of lithium aluminium hydride are more selective in reductions of methoxysilanes than simple lithium alkoxyaluminium hydrides. This selectivity appears to be dependent on the nature of the organic groups present on the silicon atom.

Unfortunately, asymmetric reduction was only achieved in the case of (-)-menthol. The slightly more symmetrical (-)-borneol and (+)-α-fenchol were unable to induce asymmetry in the reductions. The absolute configurations of the predominating silane enantiomers from the asymmetric

reductions of 1-naphthyl- and benzylphenylmethylmethoxy-silanes using (-)-menthol are shown below.



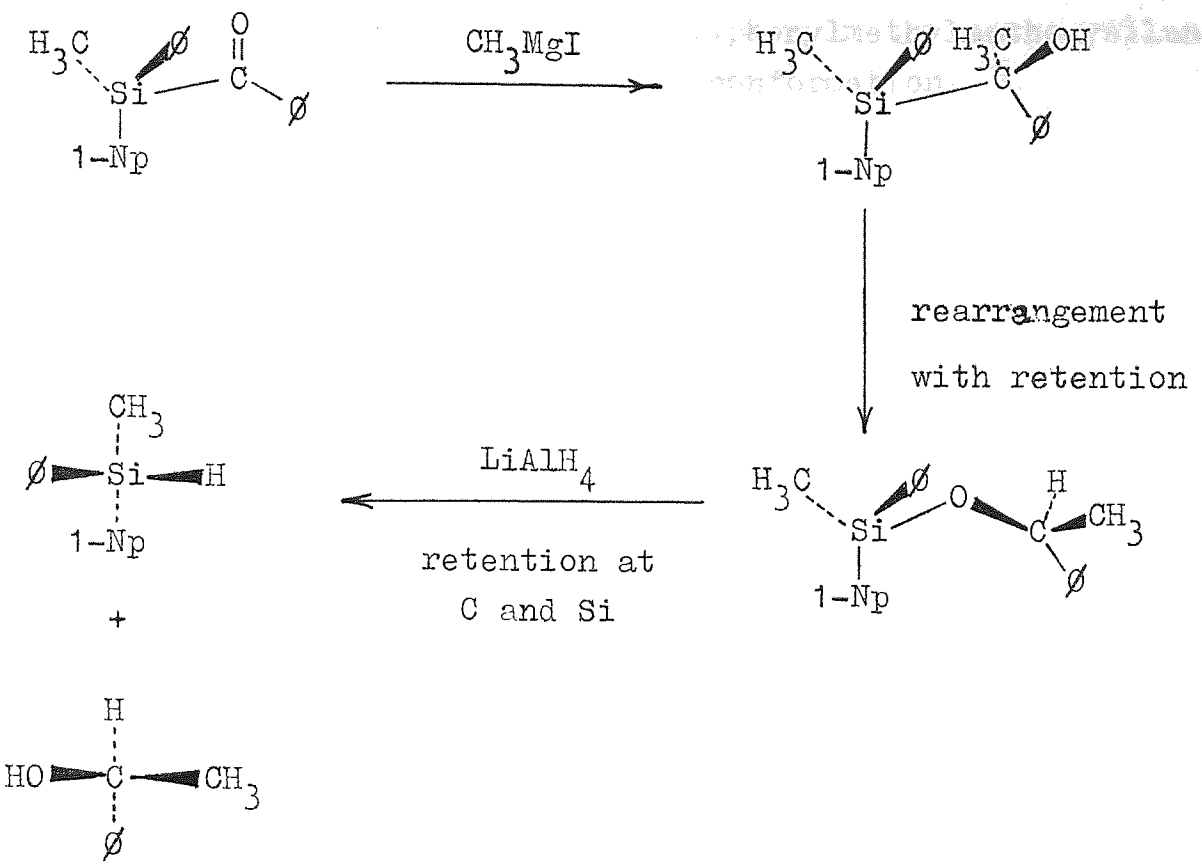
R-(+)-1-naphthylphenyl-methylsilane



S-(+)-benzylphenylmethyl-silane.

A pattern can be observed in the reductions using (-)-menthol. If the groups attached to the asymmetric silicon atom are arranged in decreasing order of size then the predominating silane enantiomer formed, in both cases, is that in which the order is anticlockwise when viewed along the H-Si bond. This means that 1-naphthyl>phenyl>methyl and benzyl>phenyl>methyl. The work of Brook and Limburg,[65] outlined overleaf, clearly illustrates that Cram's rule of asymmetric induction[66] is obeyed by the 1-naphthylphenyl-methylsilyl system with 1-naphthyl>phenyl>methyl in order of size.

Examination of Courtauld's and Dreiding Models of benzylphenylmethylmethoxysilane clearly shows the larger steric compression caused by the benzyl group than by the phenyl in certain conformations. Fig. 6. illustrates the argument. The model assumes two preferential conformations. The first, A, is quite acceptable since the trans arrangement of the phenyl groups clearly possesses the least energy

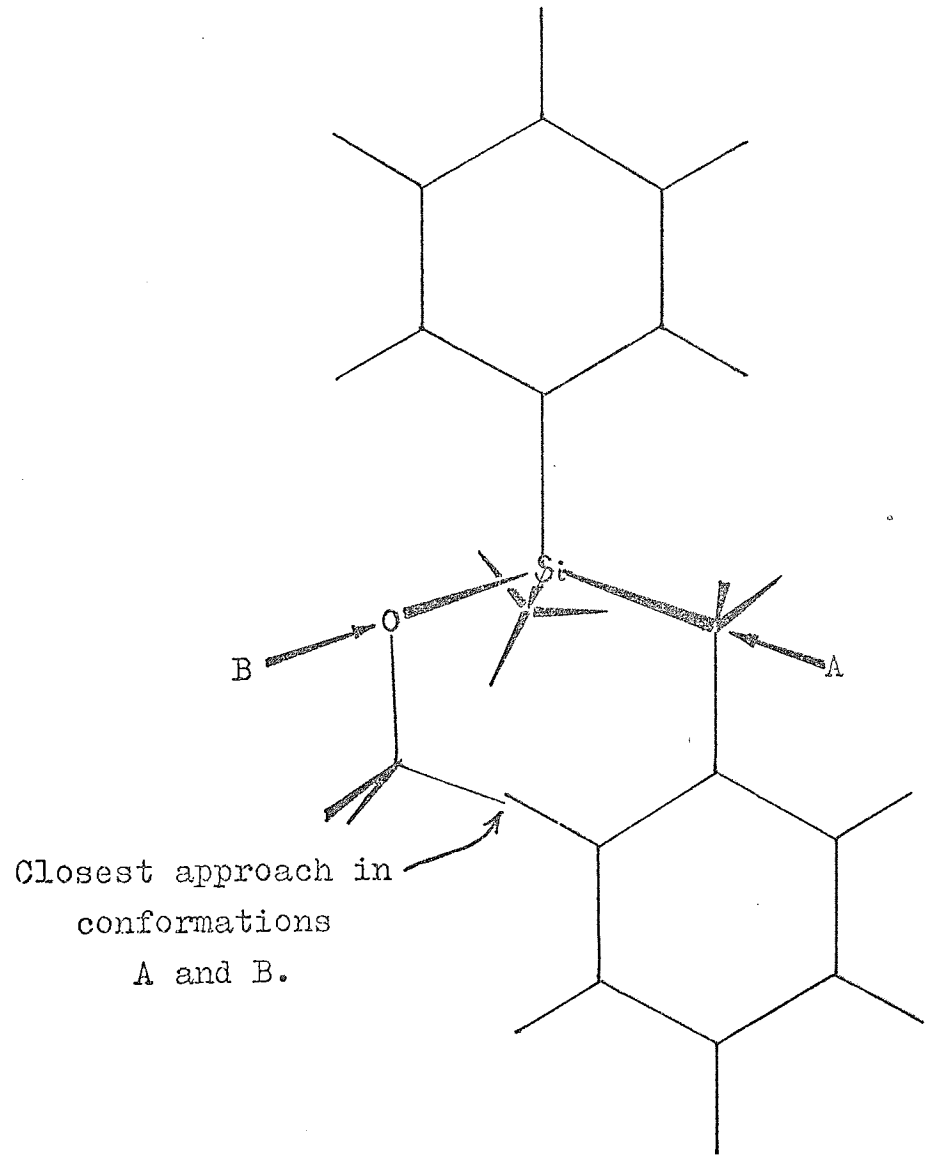


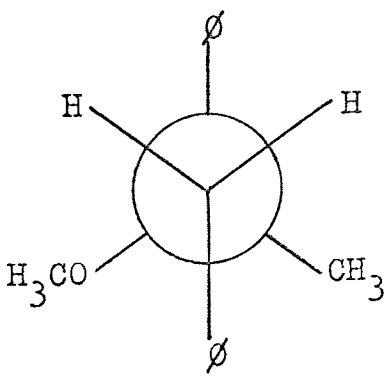
content. The second conformation, B, is also reasonable if the phenyl and not the benzyl is taken to be the largest group. However, the steric compression of the phenyl of the benzyl and the methyl of the methoxy that results from the combination of these two conformations clearly shows one to be incorrect. Since conformation A is unlikely to be at fault, B must be regarded as suspect. If we now assume that the benzyl group is the cause of greatest steric hindrance in conformations of type B we can construct a model which is more free of steric strain.

There is, however, another possible explanation for the results of the menthol catalysed asymmetric reductions of the benzyl- and 1-naphthyl-phenylmethylmethoxysilanes, that is given some credence by the recent work of Bock and Alt.[59] Their investigations on charge transfer complexes of silyl benzenes with tetracyanoethylene show that the benzyl group

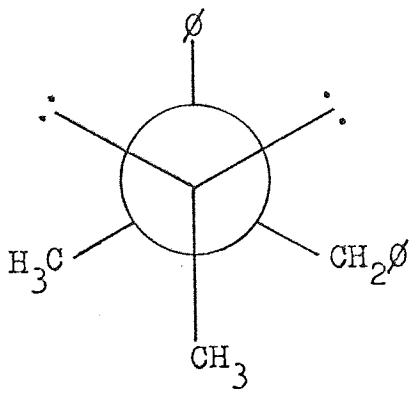
Fig. 6

Steric compression in benzylphenylmethylmethoxysilane as a result of conformation.





A



B

on silicon possesses donor properties almost as strong as those found for naphthalene.[67] These unusual properties are attributed to the very large σ-πconjugation effect involving the $-CH_2SiR_3$ group. In view, therefore, of the similar electronic interactions possible for benzyl and naphthyl on silicon towards electron deficient species, similar interactions with the aluminium atom of the menthoxy complex can be envisaged. The dissimilarity in the reductions using alkaloid complexes may be explained as due to the coordination of a nitrogen atom to the aluminium so reducing its ability to interact with the slightly weaker benzyl donor.

The rationalisation of the results of the asymmetric reductions of compounds of type RØMeSiOMe with (-)-menthol and lithium aluminium hydride when R = 1-naphthyl and benzyl clearly requires considerable further study before any model can be adopted. The hypotheses in the above discussion are advanced only tentatively and with considerable reserve; however, they do suggest definite lines of useful future study.

2. Mesitylphenylmethylsilane (Experiment 24.)

The discovery that the asymmetric reductions of (±)-RØMeSiOMe with alkaloid lithium aluminium hydride complexes appear to give the opposite antipode when R = 1-naphthyl to when R = ethyl or benzyl made it of interest to see what happened when R was another aryl group. It was decided to use the mesityl group since this appeared to offer the best chance of success due to its sterically challenging nature. Furthermore, success would give another optically active organosilane system inaccessible by any of the present

available routes, due to the ease with which the mesityl group is cleaved from silicon with bromine.[57c]

(±)-Mesitylphenylmethylmethoxysilane was prepared in 52% yield from the reaction of phenylmethyldimethoxysilane with excess mesitylmagnesium bromide (experiment 22).

The results from the asymmetric synthesis using the procedure already adopted for the benzyl and ethyl series are tabulated in Table 7. The extent of reduction is significantly lower than when R = benzyl or ethyl, due to the bulkiness of the mesityl group. Because of the sensitivity of the mesityl on silicon to protodearylation in acid media[57d] care has to be exercised in ensuring that reagents and apparatus are acid-free.

It is evident from Table 7 that the sign of rotation of the silane is dependant on the absolute configuration of C(9) in the alkaloid and in this respect the behaviour is similar to when R = benzyl (cf Table 5). The greatest optical purity for the mesitylsilane is when (-)-quinine (IVa) is used and not (+)-cinchonine (Vb), as was the case for the ethyl and benzyl silanes. Surprisingly the (+)-ψ-ephedrine (VII) reduction did not give on optically active product whereas when R = 1-naphthyl reduction using this alkaloid gave the highest optical purity.

As in all cases so far studied, the $[\alpha]_D$ of the methoxysilane was opposite in sign to that of the silane. However, the reduction cannot be assumed to have proceeded by retention of configuration since the optical rotatory dispersion curve of the mesitylphenylmethylsilane changed sign at 310 n.m. On the basis that the sign of the Cotton effect at about 260 n.m. determines the relative configur-

ations of optically active arylic compounds, within a series of closely related compounds,[68] it must be assumed that the (-)-methoxy and (+)-silane possess the same configuration and the reduction has proceeded with inversion. Further work on this interesting system is therefore clearly desirable before a change in stereochemistry can be reported with certainty.

Table 7.

Asymmetric reduction of (±)-mesitylphenylmethylmethoxysilane with 1:1 complexes of alkaloids and $LiAlH_4$.

Molar ratio of methoxysilane : alkoxyhydride 3:2.

Refluxed 24 hours.

Alkaloids	IVa	IVb	Va	Vb	VII
% redn.[a]	27	34	34	31	15[b]
$[\alpha]_{588}$ silane	-4.02°	-1.83°	+1.77°	+1.32°	0.00°
$[\alpha]_{588}$ methoxy	+2.52°	+1.04°	-1.01°	-0.47°	0.00°

a) Yields based on the weights of silane isolated.

b) Reaction mixture refluxed 48 hours.

The absolute configuration of the (-)-mesitylphenylmethylsilane cannot be inferred quite so easily as was the case for the benzylphenylmethylsilane. Unfortunately there is no optically active carbon analogue with which to compare it. The only reported optically active carbon compound containing a mesityl and phenyl group on an asymmetric centre, whose absolute configuration is known, is S-(-)-mesitylphenylcarbinol. Applying Brewster's rule of atomic polarizabilities[63] leads to the conclusion that the mesityl

group has a higher polarizability than the phenyl. On this basis (-)-mesitylphenylmethylsilane may be assigned the S configuration. It is realized, however, that the basis on which this assignment is made may be unjustified since steric interactions of the ortho methyls might prevent the apparently necessary conformational mobility of the aromatic chromophore.[69] Further, the anomalous nature of the optical rotatory dispersion curve of mesitylphenylmethylsilane urges extreme caution in inferring absolute configuration from differences of atomic polarizabilities.

3. Phenylisopropylmethylsilane (Experiment 27.)

With the successful asymmetric reduction of phenylethylmethylmethoxysilane it was considered important to investigate what change (if any) occurred when one of the alkyl groups was made more sterically challenging. The asymmetric reduction of (±)-phenylisopropylmethylmethoxysilane was, therefore, studied.

Table 8 shows the results of the asymmetric reductions of phenylisopropylmethylmethoxysilane. The Table also includes the basic data found for the corresponding reductions of phenylethylmethylmethoxysilane for direct comparison. The highest optical purities in both cases is obtained when (+)-cinchonine (Vb) and (+)-quinidine (Va) are used as asymmetric reagents and the silanes formed in both cases are dextrorotatory for these alkaloids.

Once again, the unreacted methoxysilanes for all the reductions have the opposite sign of rotation to the corresponding silane. The unexpected lack of optical activity of the methoxysilane fraction from the (+)cinchonine (Vb) reduction is, presumably due to the ease with which

racemization takes place. The reason for its occurrence in this case is not clear, however. The reductions using (-)-quinine (IVa) and (-)-cinchonidine (IVb) give lower optical yields and it is in these cases that the direction of asymmetric reduction appears to be unpredictable.

Table 8.

Asymmetric reductions of (±)-phenylisopropylmethylmethoxysilane with 1:1 complexes of alkaloids and $LiAlH_4$.

Molar ratio of methoxysilane:alkoxyhydride 3:2.

Refluxed 24 hours.

Alkaloid	IVa	IVb	Va	Vb
% redn.	57[a] (64)[c]	41[b] (51)	58[b] (54)	27[a] (56)
$[\alpha]^d_{588}$ silane	-0.03° (0.0)	+0.13° (-0.09°)	+0.30° (+0.21°)	+0.73° (+0.50°)
$[\alpha]^d_{588}$ methoxy	+0.66° (-0.03°)	-0.57° (+0.59°)	-4.61° (-1.35°)	0.00° (-3.89°)
Absolute Config.	R	S	S	S

a) Yields determined by infrared analysis of the mixture.

b) Yields determined by g.l.c. analysis of the mixture.

c) The figures in parentheses are the results of the corresponding asymmetric reduction of (±)-phenylethylmethylmethoxysilane (cf. Table 4.) included for comparison.

d) Optical rotations measured in hexane solvent.

Use of Brewster's rules of conformational asymmetry for (+)-phenylisopropylmethylsilane predicts that its absolute configuration like the (+)-ethylsilane (XVII) is S.

Comparison of the optical rotatory dispersion curves of the (+)-isopropylsilane and the (-)-isopropylmethoxysilane

indicates that the asymmetric reductions had occurred with retention of configuration.

The extents of reduction, determined by g.l.c. analysis on the unseparated products are very similar to those found for the ethylmethoxysilane under the same conditions. Replacement of the ethyl group by the larger isopropyl does not cause a marked decrease in overall rate of reaction.

4. Cyclohexylethylmethylsilane (Experiment 31).

Correlation of the results of asymmetric reductions of compounds of the type RØMeSiOMe, where R is either alkyl or aryl, has proved difficult due probably to electronic factors associated with the presence of the aromatic groups. Asymmetric reduction of compounds not possessing this drawback is clearly of prime importance. Furthermore, the preparation of optically active trialkylsilanes for stereochemical studies is of interest, particularly in view of the widespread commercial use of simple alkyl substituted organosilicon compounds. At the time of writing only one optically active trialkylsilane had been prepared and some of its substitution reactions studied.[7b] The route, involving hydrogenation of (-)-1-naphthylphenylmethylfluorosilane at high temperature and pressure, led to a complex trialkylsilane, which being a 1-substituted decalin, exists as four geometric isomers. The asymmetric reduction of cyclohexylethylmethylmethoxysilane constitutes an exciting advance in the study of substitution reactions at silicon.

The (±)-cyclohexylethylmethylmethoxysilane prepared in this study contained small amounts of cyclohexylmethyldimethoxysilane and cyclohexyldiethylmethylsilane as impurities.

All three compounds possessed very similar boiling points and so purification would prove difficult. The impure product was, therefore, used without further treatment since both impurities would yield optically inactive products in the asymmetric reduction.

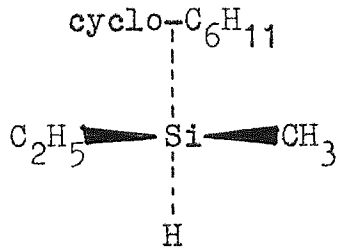
Partial reduction with (+)-cinchonine complex of lithium aluminium hydride in diethyl ether was chosen because of the high optical yields generally found using this reagent. The reduction required forcing conditions to obtain a 24% yield of silane. Separation of the products was achieved in the manner previously described.

Gas-liquid chromatographic analysis of the silane found it to be contaminated only with the diethylsilane and optical rotatory dispersion curves run on this fraction showed it to have a small, but definite laevorotation. Unfortunately, the product contained minute quantities of aromatic impurities which prevented measurements below 286 n.m. Attempts at their removal with activated charcoal were unsuccessful.

The optical rotatory dispersion curve of the methoxysilane was also plain and negative and possessed a greater rotatory power than that recorded for the silane. High absorption caused by aromatic impurities, however, once again made measurements below 312 n.m. impossible. Gas-liquid chromatography of this fraction showed it to be completely free of the silane. Extensive breakdown on the silica gel during the separation resulted in a low recovery of unreacted methoxysilane. Attempts to remove aromatic impurities from this fraction, using activated charcoal, caused extensive racemisation accompanied by formation of silanol and disiloxane. The reason for this was traced to the slightly

alkaline nature of the charcoal used. Under these conditions alkoxy exchange can readily occur.[70]

The absolute configuration of (-)-cyclohexylethylmethylsilane may be inferred by two ways. The carbon analogue has been resolved and assigned the S configuration.[71] It is reasonable to suppose that the rule of 'isoconfigurational series' can in this case be applied in view of the unlikelihood of interactions of the silicon atom with the organic groups. Secondly, calculations based on Brewster's rules of conformational asymmetry predict the S configuration for (-)-cyclohexylethylmethylsilane.



S-(-)-cyclohexylethylmethylsilane

The optical rotatory dispersion spectra of the optically active silane and methoxysilane lead to a significant result. If it can be assumed, in the absence of accessible ultraviolet absorptions associated with the above compounds, that the signs of the optical rotatory dispersion curves are indicative of the relative configurations of the two compounds then the reduction must have proceeded with inversion of configuration. The assumption is generally true and, therefore, we are left with a result that is difficult to rationalise with the retention of configuration universally found for lithium aluminium hydride reductions of methoxysilanes under these conditions.

Repetition of this reaction led to the same unprecedented result.

VII.

DISCUSSION AND GENERAL CONCLUSIONS OF THE ASYMMETRIC REDUCTIONS OF RACEMIC METHOXYSILANES WITH CHIRAL LITHIUM ALUMINOALKOXYHYDRIDES.

Before any satisfactory model can be postulated to account for the selectivity found in an asymmetric reaction the nature of the reagent and (or) the probable topology of the transition state has to be found. Generally the first of these problems is easiest to overcome being usually soluble by the various techniques available to the physical chemist. However, knowledge of the nature of the transition state involved is very much more difficult to obtain. This difficulty arises from the unsuitability of physical techniques for its direct examination. Structures of transition states can be only inferred by indirect experimentation and consequently the evidence is far more circumstantial than that for the nature of the reactant. Therefore the model proposed to account for an asymmetrical reaction is only the best hypothesis consistent with the currently available evidence and may require modification or rejection as the result of further studies.

Nature of lithium aluminium hydride and alkoxyhydrides in solution.

The solubility of lithium aluminium hydride in diethyl ether appears to vary from 10.8 moles/1,000 g. solvent[72] to 0.83 moles $l.^{-1}$ solvent[73] depending on the quality of the material. It is insoluble in non-polar solvents. The essential role in its solubility in ether appears to be connected with the solvation of the alkali metal ion because

the other alkali metal aluminium hydrides are insoluble.[74] Wiberg and co-workers[75] found by ebullioscopy that the molecular weight of lithium aluminium hydride in diethyl ether increases with concentration and corresponds to a dimer at 0.08 M and a trimeric form at 0.8 M. However infrared studies show that there is no change in the Al-H stretching frequency up to a concentration of 3.4 M to indicate hydrogen bond formation.[76,77] In tetrahydrofuran lithium aluminium hydride is essentially monomeric,[78] whereas Cervinka has found that the quinine/lithium aluminium hydride complex is dimeric.[54] This would appear to be unusual considering that generally formation of donor-acceptor bonds decreases the formal positive charge on the aluminium and leads to loss of the ability to form hydrogen bridges.

Lithium aluminium hydride forms comparatively stable complexes with dioxan and tertiary amines and the general order of bond strength in the complex is:

$$Et_2O < T.H.F. < Dioxan \approx NR_3$$

The anion AlH_4^- possesses sp^3 valency[79] and is tetrahedral[73,74] with an Al-H bond distance between 1.61[80] and 1.66 Å[81].

Introduction of an alkoxy group into a hydride molecule has been found to graduate the reductive ability of the reagent,[82] and to influence its stereoselectivity.[83] However, not all alkoxy hydrides of the type $LiAlH_{4-n}(OR)_n$ are stable in solution and disproportionation may take place:

$$2\ Li^+[(RO)_2\bar{A}lH_2] \rightleftharpoons Li^+[(RO)_4\bar{A}l] + LiAlH_4$$

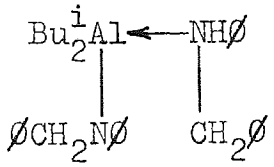
This is particularly so when the alkoxy group is secondary and Haubenstock and Eliel found that lithium aluminium hydride

complexes with these alcohols give low selectivity in the reduction of dihydroisophorone.[84] They attributed this observation to the reduction of the ketone by lithium aluminium hydride and not by the complex due to disproportionation. Tertiary alkoxy hydrides are found to disproportionate only with difficulty. However, the results of Cervinka[44] and the present work illustrate the temporary existence of alkoxy hydrides $LiAlH_{4-n}(OR)_n$ in solution where (-)-menthol, (+)-borneol and (+)-α-fenchol are used for complexing. The sterically challenging nature of these alcohols clearly prevents disproportionation as is the case for tertiary alcohols. Even in the case of less bulky alcohols the existence of alkoxyaluminium hydrides is evidenced by the asymmetric reductions afforded by the use of (-)-1-phenyl-1-ethanol, (-)-3,3-dimethyl-2-butanol[54] and (+)-2-octanol.

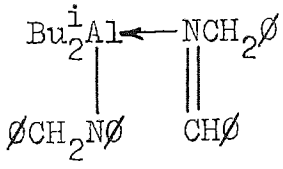
Unfortunately there is little known about the nature of lithium alkoxyaluminium hydrides in solution. In view of the assorted sites for complexing in the case of the alkaloids it is a difficult matter to decide which parts of the complex will offer greatest electronic or steric interactions in a transition state. Clearly more work is required along these lines if the mechanism of these types of reductions are to be understood. However at this point, it might be useful to indicate the major points available for complexing in the alkaloids.

The aluminium atom is obviously bonded to the alkaloid through the oxygen atom at C(9) [see Fig. 3.]. The relatively high optical yields found in reductions using α-amino-alcohols indicate that coordination of the aluminium atom to the nitrogen atom of the amino group takes place. This would

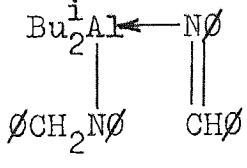
account for the failure to asymmetrically reduce ketones in the presence of (-)-menthol or (+)-borneol[43] and the low optical purities obtained in asymmetric reduction of methoxysilanes using these reagents. Furthermore it has already been stated that tertiary amines coordinate with aluminium very strongly. Infrared studies in solution indicate that instances exist where the coordination number of the aluminium is six.[85] If this is so, there is still one further ligand site available for complexing. This is probably involved in intermolecular complexing since one still has to account for the dimeric nature of the complexes. The colour of the complexes, which are not completely soluble in diethyl ether may give a tentative clue to the nature of this further coordination. Complexes of lithium aluminium hydride with (+)-cinchonine and (-)-cinchonidine are strongly butter yellow coloured. This may indicate the involvement of the quinoline ring nitrogen in complexing in view of the interesting colours observed for the following complexes.[86]



colourless



yellow-orange



deep red

Furthermore the complex between quinoline and aluminium triethyl has a high heat of formation,[87] although it is reported that the corresponding heats of formation for R_2AlH complexes are less than for R_3Al.[88]

(-)-Quinine and (+)-quinidine also give yellow coloured complexes with lithium aluminium hydride but the colour takes very much longer to develop (several hours at reflux). This may, possibly, be due to involvement of the methoxy group at

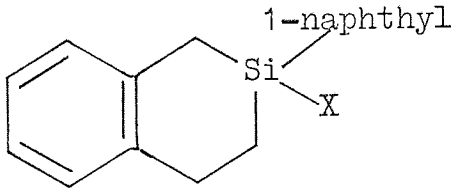
position 6' in coordination. It is interesting, for comparison, to note that the complexes formed between lithium aluminium hydride and ephedrine and ψ-ephedrine are greyish in colour.

The structure of the lithium alkoxyaluminium hydrides of menthol, borneol, and α-fenchol are easier to infer. The absence of functional groups other than the hydroxyl make coordination other than through the oxygen impossible. However, the greatest difficulty may lie in the problem of disproportionation and the presence of a number of species in solution.

The nuclear magnetic resonance spectra of (±)-1-naphthylphenylmethyl-(-)-menthoxysilane features resonances that are typical of the individual diastereoisomers.[89] Mislow and co-workers[90] have discovered similar differences in the spectra of menthyl-n-alkylphenylphosphinates and have shown that the shifted resonances are due to the protons residing on the pro-S-methyl group in the menthoxy moiety (see Chapter X.). Furthermore, they were able to present a conformational analysis which served to accomodate their results. A similar study was conducted on the menthoxysilane diastereoisomers, using variable temperature nuclear magnetic resonance, in the hope of obtaining evidence for the conformational preferences of these compounds (Chapter X.). Since AlH_4^- is isoelectronic with SiH_4, and may be expected, therefore, to possess the same geometry it was hoped that evidence adduced for the menthoxysilanes might be of use in understanding the nature of interactions in menthoxyaluminium hydride anion of the type AlH_3^-OR. The results of this study are discussed in full in Chapter X.

Stereochemistry.

Sommer and co-workers have demonstrated that retention of configuration is the usual stereochemistry involved in reactions of compounds of the type RØMeSiOR' in non-polar solvents, when R is 1-naphthyl, benzhydryl or neopentyl, and R' is methyl cyclohexyl or t-butyl. The present work has shown that the same stereochemistry is involved in lithium aluminium hydride reductions in ether of compounds when R is ethyl, isopropyl or benzyl and R' is methyl. Studies by Corriu using the optically active methoxysilane (Ia) have also established that reactions involving this compound proceed with retention of configuration in non-polar solvents.[8] It would, therefore, appear that reactions involving alkoxy-silanes in solvents of poor ionizing ability proceed, generally, by retention of configuration.



1,2,3,4-tetrahydro-2-X-2-α-naphthyl-2-silanaphthalene

Ia X = OCH_3 Ib X = Cl

Change in stereochemistry is not, however, unknown for reactions involving 'poor leaving groups' such as methoxy. The change is dependant on the polarity of the solvent and the nature of the reagent. Eaborn and co-workers have shown that each act of substitution in the neutral, acid-catalysed and base-catalysed methoxy-methoxy exchange reactions of 1-naphthylphenylmethylmethoxysilane in methanol solvent occurs with inversion of configuration.[70] Subsequent work by Sommer on alkoxy-alkoxy exchange reactions of 1-naphthylphenyl-

methylalkoxysilanes with alkali metal alkoxides has shown that stereochemical crossover is sensitive to the alcoholic content of the solvent and the nature of the cation.[6d] The recent finding of inversion in the hydride exchange of 1-naphthylphenylmethylsilane with lithium aluminium hydride in tetrahydrofuran has also been explained by high solvent polarity.[91]

The effect of the structure of the reagent has been demonstrated by studies of the coupling reactions of 1-naphthylphenylmethylmethoxy- and -fluoro- silanes with organolithium reagents.[6b] Inversion of configuration was found when charge delocalized reagents such as benzyl-lithium were used, whereas simple alkyllithiums gave retention with the same compounds.

Studies, carried out by Corriu, using the complex silyl system (Ib) have shown that the nature of the non-reacting groups affects the stereochemistry of reactions involving 'good leaving groups' such as chlorine. However, no work has been published to suggest that the stereochemistry of reactions involving 'poor leaving groups' is dependant on the non-reacting groups on silicon.

The results of the present work show that the stereochemistry of lithium aluminium hydride reductions of methoxysilanes may depend on the nature of the non-reacting groups. The successful asymmetric reduction of (±)-cyclohexylethylmethylmethoxysilane with (+)-cinchonine-lithium aluminium hydride complex in diethyl ether gives optically active silane and methoxysilane consistent with inversion of configuration. The argument for this conclusion is shown schematically overleaf.

$$(+)\text{-}R_3SiOMe \xrightarrow[\text{inv}]{k_1} (-)\text{-}R_3SiH$$

$$+ \qquad\qquad +$$

$$(-)\text{-}R_3SiOMe \xrightarrow[\text{inv}]{k_2} (+)\text{-}R_3SiH$$

(excess recovered)

$$k_1 > k_2$$

If the sign of rotation of cyclohexylethylmethylsilane and methoxysilane is indicative of relative configuration at silicon the reduction can be assumed to have occurred with inversion. This result differs from that found by Spialter and Buell[7b] for the reduction of 1-decalylcyclohexylmethyl-(-)-menthoxysilane and so the change in stereochemistry is not due solely to the absence of aromatic groups.

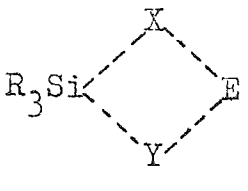
The asymmetric reductions of (±)-mesitylphenylmethyl-methoxysilane may also exhibit stereochemical cross-over. The optical rotatory dispersion curve of (-)-mesitylphenyl-methylsilane shows anomalous behaviour and both this and (+)-mesitylphenylmethylmethoxysilane show strong dextro-rotation at 300 n.m. If the sign of rotation at wavelengths approaching the phenyl absorption at 272 n.m. indicates the relative configuration of the two compounds then the reductions have proceeded with inversion of configuration. Preliminary circular dichroism measurements made on the two compounds support this conclusion since both compounds have positive Cotton effects at 281 n.m. (see Chapter IX)

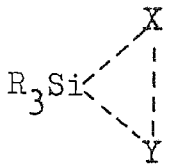
The rationalisation of the results from investigations of the effect of non-bonded organic groups on the stereo-chemistry of reactions at silicon has not been possible so far in view of the relatively few examples studied. An extensive study is required and it is hoped that the present work may aid experiments designed with this end in

view.

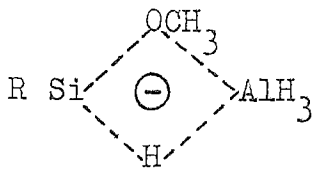
Mechanism.

Sommer has stated for the S_Ni-Si mechanism ".....probably the most common retention mechanism for organosilicon reactions. It is a mechanism which involves quasi-cyclic rate controlling transition states which are generally four-centre but may also be three centre....."



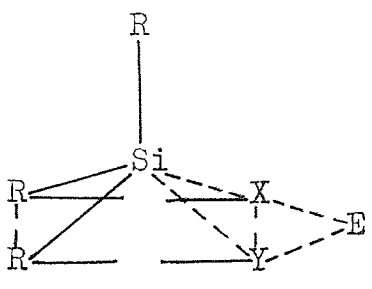


The lithium aluminium hydride reduction of methoxysilanes is supposed to be via the transition state:

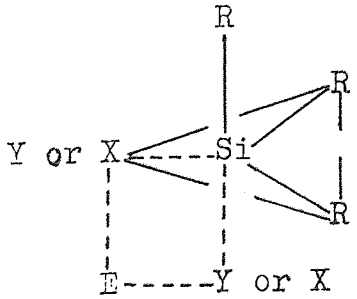


Unlike the S_Ni reaction mechanism for carbon the S_Ni-Si mechanism does not involve ion-pair formation in cases where attack by strong nucleophiles takes place.

Two models are postulated for the S_Ni-Si transition state that involve different 3d orbitals. Consequently the geometries of these structures differ. Fig. 7. shows the possibilities.



A



B

Fig. 7.

In A deformation of the R-Si-R bond angle below the tetrahedral value is supposed to occur in order to reduce non-bonded interactions between the R groups and X and Y. This amounts to about 10° per angle and the strain involved can be expected to be about the same as that incurred in the formation of the S_N2-Si inversion transition state (Fig. 8.). The tetragonal pyramid arrangement of non-reacting groups in A (with silicon out of the basal plane) can be expected to involve Si $3d_{x^2-y^2}$ orbitals.

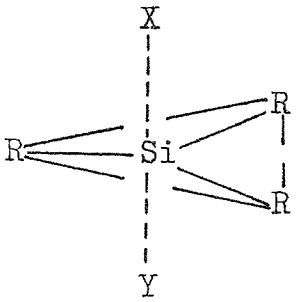


Fig. 8.

The other possibility for S_Ni-Si transition state (Fig. 7B.) also requires a pyramid arrangement of R groups but the arrangement of X and Y is such that the overall geometry is trigonal bipyramidal. This type of transition state indicates involvement of Si $3d_{z^2}$ orbitals. In practice the actual geometries of S_Ni-Si transition states may lie anywhere between 7A and 7B.

The participation of silicon 3d orbitals does not necessarily require the formation of an intermediate and is only of importance when the free energy of activation for the reaction is lowered.[5] Moreover, the bonds involved in the above transition states are not made equivalent by 3d participation. Only the bonds between silicon and the non-reacting groups may be regarded as strong.

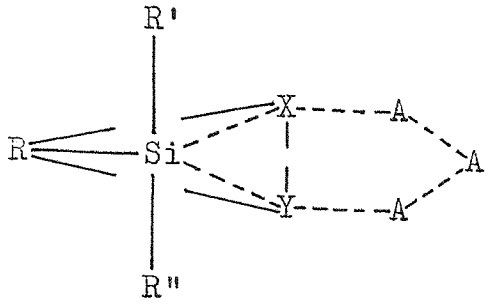
Sommer has done naive calculations [5] of the distance

between terminal carbon atoms of the R groups in the transition state 7A for S_Ni-Si. For an assumed R-Si-R angle of 100° the carbon - carbon distance is 2.98Å. These non-bonded carbon - carbon distances are larger than between two carbons making a tetrahedral angle with a central carbon (2.52Å). Therefore the non-bonded interactions would not be expected to be prohibitive for the formation of transition states with tetragonal pyramid geometry.

The high stereospecificities of reactions at silicon and the stability of optically active organosilanes to thermal racemisation have led Sommer to propose the principle of 'least motion' of non-reacting groups.[5] [Recent work has[155] shown that (-)-1-naphthylphenylmethylchlorosilane undergoes thermal racemisation at 200-300°. The mechanism is not, however, elucidated.] The usual angle deformation in the transition states postulated is of the order of 10°. Expansion of the R-Si-R to 120° is expected for inversion reactions, whereas contraction to 100° is usual in retention reactions.

The assumption of non-linear R-Si-R angles, based on the principle of least motion, is especially pertinent for S_Ni-Si reactions proceeding with pure retention of configuration. Sommer argues that the S_Ni-Si reaction found in the Grignard reduction of 1-naphthylphenylmethylmethoxysilane could be explained by a six-membered transition state which has the entering group Y and leaving group X equatorial in a trigonal bipyramid arrangement about silicon (see next page). Detailed analysis of this type of transition state, however, results in formation of RR'R"SiY with overall inversion of configuration. This is not in accordance with the experimental

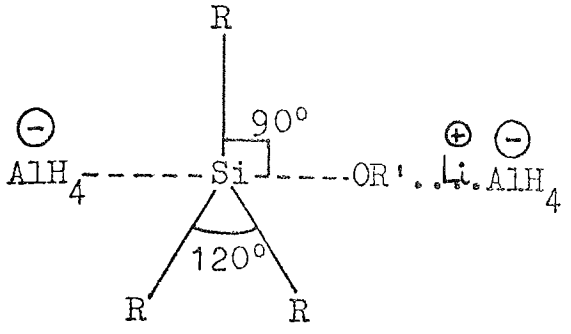
observation of retention and so may be regarded as negative evidence for the principle of least motion.

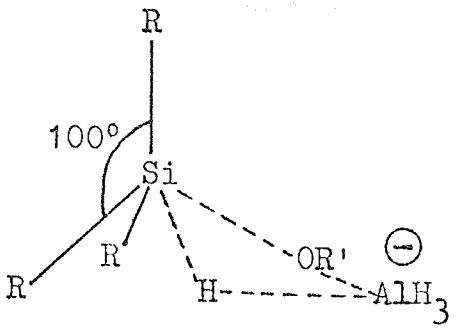


In the light of the above discussion it may be expected that large non-reacting groups on silicon may cause the transition state, in which the R-Si-R angles are opened up to 120° to possess lower energy than that in which the R-Si-R angles are about 100°. This could cause stereochemical crossover from retention to inversion with increasing size of groups R. This may account for the inversion of configuration observed in the reduction of cyclohexylethylmethylmethoxy silane; similarly it may explain the inversion in the reduction of mesitylphenylmethylmethoxysilane, should further studies corroborate the indications of the optical rotatory dispersion curves. However, reduction of 1-decalylcyclohexylmethyl-(-)-menthoxysilane is reported to proceed by retention.[7b] In this case the non-reacting groups are very large but so is the size of the leaving group. The large bulk of the leaving group would be expected to lower the relative energy of the S_Ni-Si transition state, where interactions between the leaving group and the non-reacting R groups are less than in the S_N2-Si transition state.

The stereochemistry observed in some cases may well be a fine balance of steric interactions between the non-reacting

groups and leaving group on one side and the non-reacting groups themselves on the other.





Any model proposed to account for the results of asymmetric reductions at silicon must embody the presently held hypotheses outlined above.

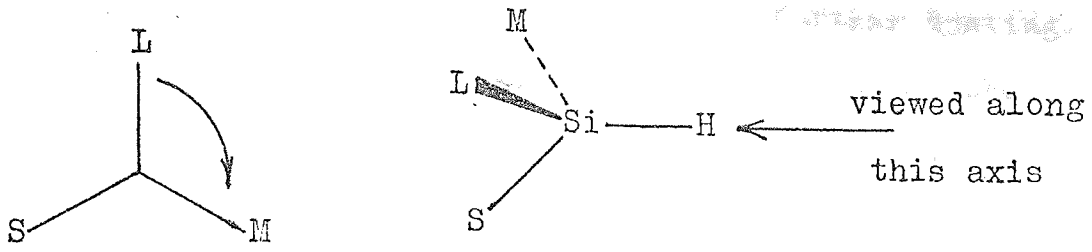
Asymmetric reductions.

The previous Chapters have shown that the asymmetric reductions of RØMeSiOMe compounds with alkaloid complexes of lithium aluminium hydride are generally more highly selective when (+)-cinchonine or (+)-quinidine is used. Furthermore, it is with these alkaloids that the configuration of the silanes, formed in excess, is always consistent with the absolute configuration of the C(9) of the alkaloid.

Table 9 summarises the results from these reductions. Results of asymmetric reductions where R is mesityl and of cyclohexylethylmethylmethoxysilane are not included in view of the uncertainty in the absolute configuration of the predominating silane enantiomer and the possible change in stereochemistry involved.

If the non-reacting groups on the silicon are arranged in decreasing order of size i.e. L > M > S and this arrangement is viewed along the H-Si bond then the silane enantiomer formed in excess using (+)-cinchonine and (+)-

quinidine has an order that is clockwise.



For reasons that are not at present completely understood, but may be due to electronic interactions, the above model fails to predict the absolute configuration of the silane enantiomer formed from the asymmetric reductions of (±)-1-naphthylphenylmethylmethoxysilane.

Table 9.

Results from asymmetric reductions of methoxysilanes with (+)-quinidine (Va) and (+)-cinchonine (Vb) complexes of lithium aluminium hydride.

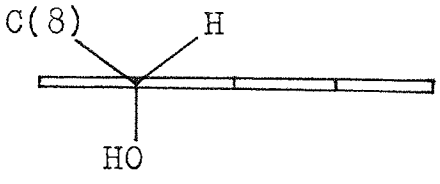
	Absolute configuration of the predominant silane enantiomer.			
	1-NpØMeSiH	$ØCH_2ØMeSiH$	ØEtMeSiH	Øi-PrMeSiH
(Va)	R	R	S	S
(Vb)	R	R	S	S
Order of* Groups	anti-clockwise	clockwise	clockwise	clockwise

*Effective steric order of non-reacting groups when viewed along the Si-H bond axis.

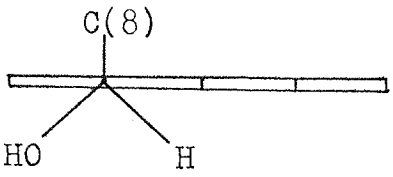
When attempts are made to propose a model for the preferred transition state or activated complex, the result is far more speculative. However, if the severe limitations

and assumptions that are made in proposing such a model are realised, then it serves as a basis for further testing.

First consider the preferred conformation of the quinoline moiety in the cinchona alkaloids. Because of the large bulk of the quinucleidine group at C(8) and the interactions caused by the peri-hydrogen on the quinoline ring, the conformations shown below are likely to be favoured.[92]

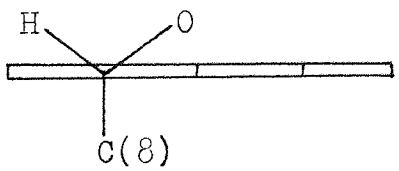


(a)



(b)

However, in the complex, formation of a cyclic five-membered structure by intramolecular nitrogen-aluminium coordination causes great steric interaction of the quinucleidine moiety with the proton at C(3') of the quinoline ring in (a). Examination of Dreiding models of the complex shows that the preferred conformations of the quinoline ring, under these circumstances, are possibly either (b) or (c).



(c)

If a six coordinated aluminium atom in a transition state involving flank attack at silicon with retention of configuration is assumed, it is possible to propose a transition state for (+)-cinchonine and (+)-quinidine reductions of the type shown in Fig. 9.

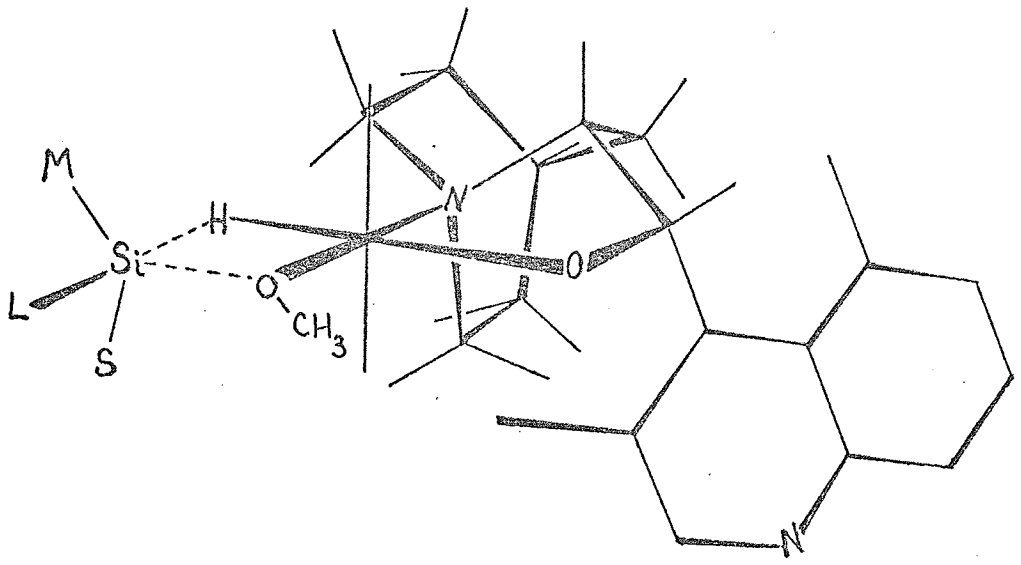


Fig. 9.

Type of transition state proposed to account for the results from the partial asymmetric reductions of (±)-RMeØSiOMe, where R is $ØCH_2$-, Et-, and i-Pr-, with (+)-cinchonine and (+)-quinidine/$LiAlH_4$ complexes.

Asymmetric reductions of methyl aryl ketones with alkaloid-lithium aluminium hydride complexes[41] have been found to give optically active alcohols possessing opposite absolute configuration to those from reductions of methyl alkyl[41] and diaryl ketones.[42] Cervinka has explained this anomaly by the coordination of the aromatic group to the complex in the transition state. He envisages a coordination of the phenyl group with the electron pair of the nitrogen of the alkaloid, which is facilitated by the conjugation of the aromatic nucleus with the carbonyl group. The electron withdrawing effect of the carbonyl group on the phenyl nucleus is further catalysed by the presence of Li^+ ions.

The phenyl group present in MeRØSiOMe does not possess a strong electron withdrawing substituent and, therefore, would be unlikely to coordinate with the nitrogen atom of the alkaloid. If coordination occurs at all, it would be to an electron deficient centre; the aluminium atom is such a centre. Studies on charge transfer complexes of silyl benzenes with acceptors such as iodine and tetracyanoethylene have shown that silyl benzenes possess slightly weaker donor properties than their carbon anologues.[59] Therefore, although coordination of the phenyl group in compounds MeRØSiOMe with the aluminium atom is possible, it is unlikely that the phenomenon outweighs the effect of steric forces.

The naphthyl group, however, has been shown to be a very strong donor and coordination with the aluminium atom in the transition state is more likely. Reversion of the direction of asymmetric reductions could accordingly follow.

The studies on charge transfer complexes have also

shown that the benzyl on silicon is almost as efficient a donor as naphthalene.[59]

The results of asymmetric reductions of ethyl-, isopropyl-, and benzyl- phenylmethylmethoxysilanes with alkaloid-complexes can be explained in terms of overall steric control.

When the (-)-menthoxy complex is used the absence of a nitrogen atom capable of coordinating with the aluminium will increase the ability of the latter to coordinate with the substrate. Under these circumstances it is possible that both the 1-naphthyl and benzyl groups in the relevant silanes will electronically interact with the aluminium. The difference in behaviour for reductions using this complex when R is 1-naphthyl and benzyl, from when R is ethyl, (Table 10), may be due to electronic interactions, of the above type, overcoming the forces associated with the steric compression caused by these groups.

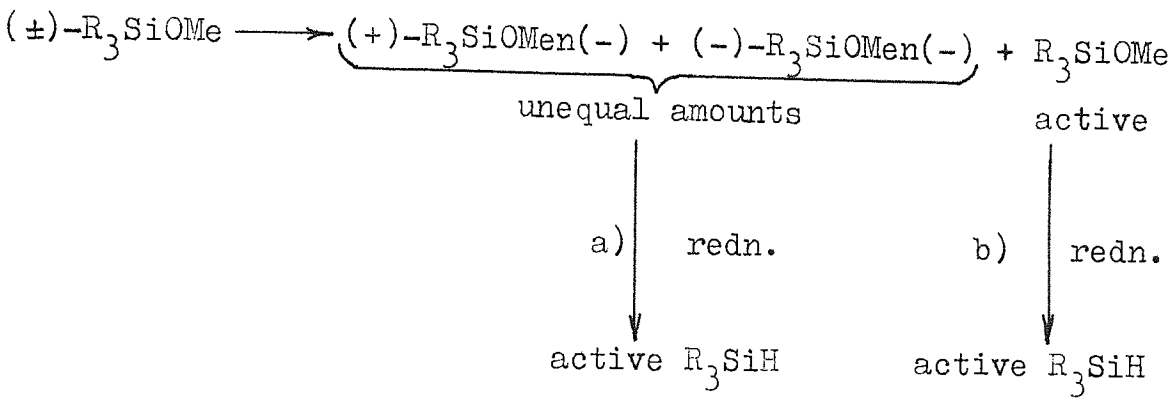
Table 10.

Results from asymmetric reductions of compounds RØMeSiOMe with lithium (-)-menthoxyaluminium hydride.

	Absolute configuration of the predominant silane enantiomer.		
	1-NpØMeSiH	$ØCH_2ØMeSiH$	ØEtMeSiH
	R	S	R
Steric Order of Groups a)	anti-clockwise	anti-clockwise	clockwise

a) Apparent steric order of non-reacting groups when viewed along the H-Si bond axis.

A suggestion has been made[93] that the asymmetric reductions do not involve the direct reduction of racemic methoxysilanes by chiral lithium aluminium hydride species. It was thought possible that alkoxy-alkoxy exchange may first occur, followed by reduction of the unequal amounts of diastereoisomers formed. The scheme is illustrated by the (-)-menthol/lithium aluminium hydride reductions, outlined below:



In the above scheme two possibilities exist:

a) reduction of the unequal amounts of diastereoisomers

b) reduction of the active methoxysilane left by the production of unequal amounts of diastereoisomers.

Both possibilities can be shown to be extremely unlikely. Reduction by path a) is unlikely in view of the slower rate of reduction of menthoxysilanes compared with methoxysilanes. [Complete reduction of 1-naphthylphenylmethyl(-)menthoxysilane requires treatment with a five fold excess of lithium aluminium hydride at 80-90° for 18 hours, whereas the methoxysilane is completely reduced in 16 hours at room temperature.] Reduction by path b) would result in quantities of the menthoxysilanes remaining. Nuclear magnetic resonance spectra and thin-layer chromatography of the separated products, however, showed no evidence of any such

compounds being present (i.e.< 5%). Furthermore, alkoxy exchange was shown not to occur to any measurable extent (i.e.< 2%)in the phenylethylmethylmenthoxysilane system.

$$(\pm)\text{EtMeØSiOMen}(-) \xrightarrow{\text{LiAlH}_2(\text{OMe})_2} (\pm)\text{EtMeØSiOMe}$$

With regard to the asymmetric reductions of RØMeSiOMe it is of interest to compare the magnitudes of the free energy differences for the diastereoisomeric transition states when R = 1-naphthyl and ethyl. The accuracies of the $\Delta\Delta G^{\ddagger}$ values quoted below are difficult to ascertain, due to the low rotatory powers of the products of these asymmetric reactions, but their orders of magnitude may be read with confidence.

Table 11.

$\Delta\Delta G^{\ddagger}$ (cal./mole) for asymmetric reductions of RØMeSiOMe using optically active alkoxy lithium aluminium hydrides.

	R = Et	R = 1-Np
cinchonine	830	57
quinidine	327	73
cinchonidine	127	26
quinine	13	65
menthol	20	36

VIII

OTHER ATTEMPTED ASYMMETRIC REACTIONS AT SILICON.

The successful asymmetric reductions of methoxysilanes prompted exploratory work on other reactions at silicon. The reactions studied do not exhaust the range of possibilities, but were chosen primarily for their ease of study and the accessibility of reagents.

1. Reaction of (+)-peroxycamphoric acid and (±)-1-naphthylphenylmethylsilane. (Experiments 33-34).

The reaction of 1-naphthylphenylmethylsilane with perbenzoic acid has been studied by Sommer.[5] Extensive work has shown that the principal reaction in benzene is:-

$$1\text{-Np}\emptyset\text{MeSiH} + \emptyset\text{COOOH} \xrightarrow[\text{benzene.}]{\text{room temp.}} 1\text{-Np}\emptyset\text{MeSiOH} + \emptyset\text{COOH}$$

The stereochemistry of the reaction has been studied using optically active silane and has been shown to proceed with good retention of configuration.[5] Accordingly, Sommer[5] has proposed an (S_Ni-S_Ei)-Si mechanism.

$$R_3SiH + \emptyset CO_3H \xrightarrow{\text{slow}} \left[R_3Si\overset{H}{\overset{\oplus}{:}}O{-}H\right]\ldots\emptyset CO_2^{\ominus}$$

$$\left[R_3Si\overset{H}{\overset{\oplus}{:}}O{-}H\right] \emptyset CO_2^{\ominus} \xrightarrow{\text{fast}} R_3SiOH + \emptyset COOH$$

Oxidation of unsymmetrical sulphides to sulphoxides with peroxyacids is well known. When optically active peroxyacids are employed asymmetric oxidation occurs and the sulphoxide formed is found to be optically active. Thus, oxidation of n-alkyl phenyl sulphides with (+)-peroxycamphoric acid gave

(+)-n-alkyl phenyl sulphoxides of low optical purity.[94,95] Similarly, reaction with t-butyl phenyl sulphide gave (-)-t-butyl phenyl sulphoxide. Montanari and co-workers[94] have proposed models for the most probable transition state conformations which based on decreasing effective size of the groups attached to sulphur, predict the predominant enantiomer of sulphoxide. However, their model fails to predict the correct configurational assignment for n-alkyl benzyl sulphoxides.[96] Mislow and co-workers[96] pointed out that in using asymmetric synthesis to predict absolute configuration one always has a 50% chance of being correct. They further contend that Montanari's models do not provide a qualitative estimate of the non-bonded interactions which indicate the diastereoisomeric transition state with the lower free energy.[96] (These objections apply equally in proposing a model for the asymmetric reductions of methoxysilanes and due caution has been stressed in the relevant discussion.)

In view of the stereospecificity of the reaction of perbenzoic acid and optically active silane and the proposed mechanism involving a rate determining formation of an activated complex or intermediate, it was hoped that reaction of racemic silane with a dissymmetric peracid would give a partial kinetic resolution via diastereoisomeric transition states of unequal energy. Partial oxidation of racemic 1-naphthylphenylmethylsilane with (+)-peroxycamphoric acid was, therefore, studied. The reaction was done in benzene solvent using excess peroxyacid at room temperature and followed by thin-layer chromatography of samples taken at intervals from the stirred mixture; disappearance of the spot due to the silane indicated complete reaction. Precipitation

of camphoric acid accompanied the reaction. Results from spectroscopic examination of the product after complete reaction are consistent with it being 1-naphthylphenylmethylsilylhydroperoxide. Presumably, this arises from further peroxide attack on the silanol formed initially.[57e] The reaction of racemic silane with a single fold excess of peroxycamphoric acid in benzene at room temperature for six hours was carried out. Chromatographic separation on silica gel yielded 43% unreacted silane. Infrared and nuclear magnetic resonance spectroscopy showed it to be pure 1-naphthylphenylmethylsilane. Optical rotatory dispersion spectra, however, showed it to be optically inactive. Therefore, no asymmetric oxidation had occurred.

2. Attempted hydrolysis of (±)-1-naphthylphenylmethylmethoxysilane with (+)-camphor-10-sulphonic acid in xylene. (Experiment 35).

The hydrolysis of organosilicon alkoxide is usually slow in neutral solution but is strongly catalysed by acids or alkalis.

In acid solution, protonation of the oxygen atom presumably preceeds nucleophilic attack by water on silicon.

$$H_3O^{\oplus} + R_3SiOR' \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_3\overset{\oplus}{S}iOHR' + H_2O$$

$$R_3\overset{\oplus}{S}iOHR' + H_2O \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R_3\overset{\oplus}{S}iOH_2 + R'OH$$

$$R_3\overset{\oplus}{S}iOH_2 + H_2O \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} R_3SiOH + H_3O^{\oplus}$$

Cleavage of the Si-O bond has been experimentally proved by the recovery of pure (+)-2-butanol from the hydrolysis of dimethyldi-(+)-2-butoxysilane.[97] It is probable that k_2 is

the rate determining step and so the rate of reaction may be expected to be dependent on the nature of the protonated alkoxy silane. The nature of this species in acid catalysed hydrolyses is at present unknown. If the acid catalysed cleavage is performed in a solvent of low dielectric constant, for example m-xylene, it is likely that the protonated alkoxysilane will exist as an ion-pair and general acid catalysis would be observed. If then, this ion-pair involves chiral anionic and cationic parts there will exist two types of diastereoisomeric ion-pairs. These diastereoisomeric ion-pairs, differing in energy content, may be expected to react at different rates provided that their transition states do not differ in energy such that their activation energies are equal (see fig. 1). Loss of a proton in the third fast step does not involve the silicon centre and so the configurational integrity of the silicon is maintained.

Therefore, successful asymmetric partial hydrolysis of a methoxysilane in a non-polar solvent catalysed by an optically active acid would be evidence for the existence of ion-pairs in these conditions.

Under the conditions used the amount of free water was kept to a minimum, both in order to maintain a medium of low polarity and to prevent racemisation of the silanol, if formed, which occurs rapidly in acidic polar conditions.

It was anticipated that condensation of silanol to siloxane would occur under the conditions employed.

$$R_3SiOH + R_3SiOMe \rightleftharpoons R_3SiOSiR_3 + MeOH$$

Successful formation of an optically active siloxane or

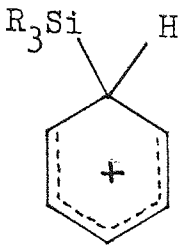
direction of the condensation with the formation of one predominating stereoisomer i.e. meso or dl siloxane by such a method would be of considerable interest in view of the wide spread use of siloxane polymers.

However, the rates of the above reactions appear to be affected to a considerable extent by the steric nature of the substituents on the silicon; triphenylsilanol and triethylsilanol have relative acid catalysed rates for condensation, compared with trimethylsilanol as a standard, that are 10^{-6} and 1.6×10^{-3} respectively.[98] Compounds such as dimethyl-t-butylsilanol and di-t-butylsilane diol are resistant to either acid or base condensation.[99]

Reaction of 1-naphthylphenylmethylmethoxysilane with (+)-camphor-10-sulphonic acid was attempted in m-xylene, a solvent of low polarity, at an elevated temperature. After prolonged treatment, the product was found to consist of a complex mixture of compounds formed by complete cleavage of methoxy and 1-naphthyl groups from silicon. These compounds contained siloxane linkages. In view of the complexity of the products formed the reaction was abandoned from the study of asymmetric reactions.

It is of interest, however, to discuss the results a little further. Apparently the rate of acid catalysed alkoxy cleavage is sufficiently retarded that the competitive proto-dearylation of the 1-naphthyl group occurs. Kinetic studies have been made of the aromatic desilylation by sulphuric[100] and p-toluenesulphonic acids[101-103] in water-acetic acid and by hydrochloric and perchloric acids in aqueous methanol and dioxan.[104,105] The acidity function of the medium appears to govern the rate[105] and the transition state for cleavage is

said to be:



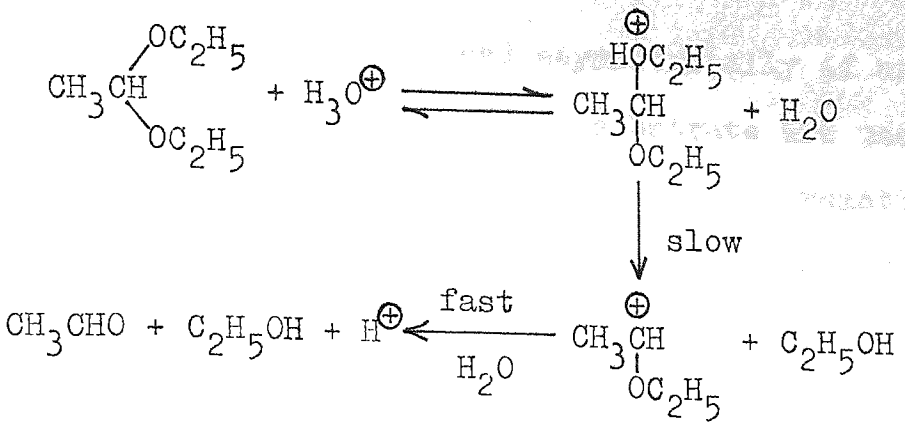
With polynuclear aromatics the rate of cleavage is dependent on the position of the silyl group attachment. In aqueous methanol 1-naphthyltrimethylsilane is cleaved 8.1 times faster than phenyltrimethylsilane with perchloric acid, whereas, the 2-naphthyl group is cleaved only 2.2 times faster.[57f] It is, therefore, not surprising that under the conditions of acid hydrolysis used above, the 1-naphthyl group is cleaved in preference to the phenyl.

3. Attempted base catalysed hydrolysis. (Experiment 36)

Extensive aromatic desilylation during the acid catalysed hydrolysis instigated investigation of the possibility of applying base catalysed hydrolysis of the methoxysilane to asymmetric reaction. The hydrolysis with (±)-1-phenylethylamine in m-xylene was attempted, however, no reaction occurred after 48 hours at 139°.

4. Hydrolysis of (±)-1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane catalysed with (+)-camphor-10-sulphonic acid. (Experiments 38,39)

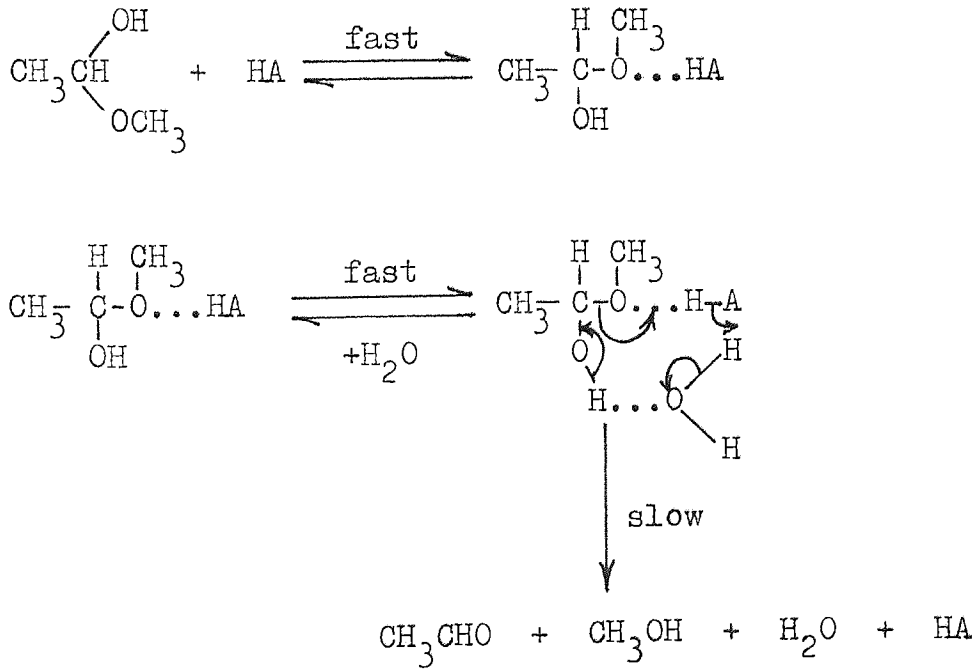
Acetals are generally very readily attacked by acids with subsequent breakdown to form aldehyde and alcohol. The mechanism has been proposed to occur in two steps following an equilibrium protonation process[106] i.e. for diethyl acetal:



The kinetics indicate that the above reaction follows specific acid catalysis i.e.

$$\text{rate} = k[CH_3CH(OC_2H_5)_2][H_3O^{\oplus}]$$

However, considerable study of the acid catalysed hemiacetal fragmentation has shown that in this case the reaction obeys general acid catalysis.[107] This means that the rate involves the concentration of all the acidic species in solution. The mechanism can be written as:



$$CH_3CHO + CH_3OH + H_2O + HA$$

$$\text{rate} = k[CH_3CH(OH)(OCH_3)][HA]$$

It is theoretically possible for a reaction following

general acid catalysis to proceed asymmetrically if an optically active acid and asymmetric substrate are used. Once again there is the proviso that asymmetric reaction will only occur if there is a difference in the free energies of activation for the diastereoisomeric hydrogen bonded complexes.

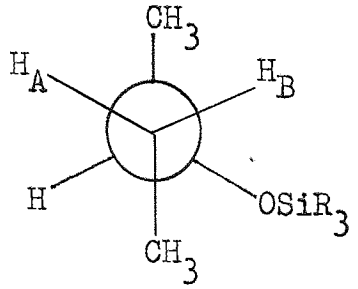
Silyl acetals may be prepared easily by addition of silanol across the double bond of a vinyl ether.[108] The reaction is catalysed by acid and is complete after 18 hours at 65°.

$$R_3SiOH + CH_2{=}CHOC_2H_5 \xrightarrow{H^{\oplus}} R_3Si{-}O{-}\underset{\displaystyle CH_3}{\overset{\displaystyle OC_2H_5}{\overset{|}{\underset{|}{C}}}}{-}H$$

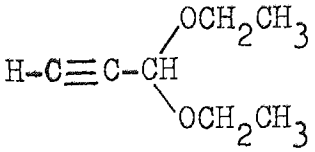
In view of the ease of acid catalysed fragmentation of acetals it was anticipated that the silyl acetal might undergo reaction with camphor-10-sulphonic acid with considerably greater ease than was observed for the methoxysilane. Consequently, the naphthyl cleavage would then only constitute a minor side reaction. Although acetals are reported to fragment by specific acid catalysis, thereby negating the possibility of asymmetric reaction, it was hoped that silyl acetals might not follow the same mechanism in non-polar media. Furthermore, a recent report shows that not all acetals follow specific acid catalysis.[109]

The silyl acetal from 1-naphthylphenylmethylsilanol and vinyl ethyl ether was prepared in quantitative yield by the above method. Since this acetal possesses two centres of asymmetry, one at silicon and the other at carbon, the product exists as a diastereoisomeric dl pair. The nuclear magnetic resonance spectrum of the material exhibited the expected

resonances apart from the indication of non-equivalence for the methylene protons of the ethoxy group. This behaviour has previously been noted for ethoxy acetals[110] and may be explained with reference to the Newman projection below:



The methylene protons view, through the oxygen atom, an asymmetric centre which imposes on the two protons non-equivalent chemical environments. The protons are, therefore, magnetically shielded to different extents irrespective of which rotamer is considered. Accordingly, the protons H_A and H_B are mutually coupled to give an AB quartet, each line of which is further split into a quartet by coupling with the methyl. Therefore a band of sixteen lines would be expected. Normally, however, only eight lines are observed due to overlap[110] and only in the spectrum of the below acetal has the full sixteen lines been observed.



The number of lines observed for the methyleneoxy group of the silyl acetal, prepared in this study, at 100 MH_z however was considerably in excess of sixteen. This is only explicable by superimposition of the spectra of the two diastereoisomers formed, since second order coupling could be ruled out due to the large value of $\Delta\nu/J$. Furthermore, the quartet, due to the methine proton, at 5.00 τ and the doublet of the methyl at 8.75 τ all exhibit shoulders at high field

explicable by the presence of diastereoisomers. The resonances due to the silicon methyl and the methyl of the ethoxy group at 9.20 τ and 9.00 τ respectively were uncomplicated by diastereoisomeric differences.

In consequence of the above diastereoisomeric features of the nuclear magnetic resonance spectrum it was of interest to discover what changes (if any) were apparent in the unreacted acetal after partial reaction with the sulphonic acid.

Once the stability of the acetal on a silica gel coated thin layer plate for long periods of time had been established and a suitable elutive solvent found, the reaction of the silyl acetal with the sulphonic acid was followed by using thin-layer chromatography. The reaction was done in toluene solution. A solution 0.033 M in silyl acetal and 0.004 M in (+)-camphor-10-sulphonic acid reacts so fast at room temperature that all acetal was removed in ten minutes. Decreasing the sulphonic acid concentration by a factor of ten and repeating the reaction at 3° slowed the reaction sufficiently for study; complete reaction was reached after about two hours. Chromatographic separation after thirty minutes under these conditions yielded 24% unreacted silyl acetal. Infrared and nuclear magnetic resonance spectroscopy showed the acetal to be unadulterated with disiloxane or silanol and free of sulphonic acid. Although some change had occurred in the intensity distribution in the methyleneoxy resonances, no measure of change in diastereoisomeric composition could be obtained due to the complexity of the band. Optical rotatory dispersion studies of the acetal, separated from the reaction, in hexane showed it to be without optical activity over the range 588 to 320 n.m. It must, therefore, be assumed that no

asymmetric hydrolysis had occurred and that the reaction either follows specific acid catalysis or the free energy differences were too small to produce observable optical activity.

5. Attempted hydrolysis of 1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane with 1-phenylethylamine in toluene.

With the discovery that the silyl acetal is very rapidly fragmented by acid it was interesting to investigate its stability under basic conditions. The base chosen was 1-phenylethylamine with the view to possible asymmetric reaction.

No observable change occurred even after twenty four hours at reflux.

IX.

OPTICAL ROTATORY DISPERSION AND CIRCULAR DICHROISM OF ASYMMETRIC ORGANOSILICON COMPOUNDS.

Introduction.

The use of optical rotatory dispersion (o.r.d.) and more recently circular dichroism (c.d.) has shown itself to be of paramount importance in the study of stereochemical problems. In suitable cases the relative configurations at asymmetric centres can be determined by comparison with closely related compounds and, where sufficient data is available, the absolute configuration may be inferred. In view of the considerable body of published work on the use of o.r.d. and c.d. for structural studies there is insufficient scope here for a discussion to be of any value. The theoretical aspects and widespread uses of the techniques have been the subject of several texts[111-113] and a number of reviews.[114-116] However, it should be mentioned that the vast majority of the previous work has been the result of structural studies of natural products.

At the onset of the present work no reported o.r.d. or c.d. study of an optically active asymmetric organosilicon compound had penetrated the spectral regions associated with anomolous dispersion. Since then two papers have been published. In 1969 Sommer and McLick reported the results of a comprehensive study of the o.r.d. and c.d. spectra of 1-naphthylphenylmethylsilyl compounds[117] and found Cotton effects useful for the purpose of correlation of configuration. The second, a short communication by Corriu and Massé[118] reported the effect solvent coordination had on the o.r.d. of an asymmetric α-silyl ketone.

O.r.d. and c.d. studies of novel asymmetric organosilicon compounds are, therefore, of obvious interest. Successful asymmetric reductions of several racemic methoxysilanes with chiral lithium aluminium hydride complexes provide a convenient route to such compounds. The features of the o.r.d. and c.d. of these compounds are discussed separately under the individual headings of the silyl system in conjunction with the general ultraviolet spectra of the compounds.

1-Naphthylphenylmethylsilyl system.

Ultraviolet spectra.

The ultraviolet absorption spectra of compounds possessing the 1-naphthylphenylmethylsilyl group display features which are characteristic of a substituted naphthalene. Three band systems are present which are typical of benzenoid hydrocarbons in general. Using Clar's notation these three bands are designated α, para, and β, appear in order of decreasing wavelength, and are successively more intense in that direction. The transitions responsible for these bands are assigned $^1L_b \leftarrow {}^1A$, $^1L_a \leftarrow {}^1A$, and $^1B_b \leftarrow {}^1A$.[119]

The monosilicon compounds[117] possess a small shoulder at 324 n.m. preceding a first maximum at 318 n.m. and a second more intense peak at 313 n.m. ($\log_{10}\epsilon$ 2.5-2.8). These absorptions constitute the α band. The absorption then increases to the para band, consisting of three broad maxima of which the central one at 284 n.m. is most intense ($\log_{10}\epsilon \approx 3.9$). Absorption then subsides below 260 n.m. before rising for the very intense, symmetry allowed, β transition at 225-226 n.m. ($\log_{10}\epsilon$ 4.7-4.8). The α and para

bands are of lower intensity because the transitions are symmetry forbidden. Vibrational interactions introduce a certain measure of allowedness which is responsible for their presence.

Table 12 shows the ultraviolet spectral characteristics of the compounds studied. The data for the 1-naphthylphenylmethylsilyl compounds agree closely with that already published.[117]

Table 12.

Ultraviolet Absorptions of RØMeSiX compounds.

R	X	Absorption characteristics[a,b,c]
1-Np	H	225 (4.8543), 284 (3.9754), 313 (2.7709)
1-Np	OMen(-)	226 (4.7259), 284 (3.9085), 314 (2.6503)
1-Np	OMe	225 (4.8531), 284 (4.0253), 314 (2.5441)
$ØCH_2$	H	205 (4.1875), 267 (2.7657)
$ØCH_2$	OMe	221 (4.1072), 267 (2.7694)
Et	H	217 (3.8344), 260 (2.3711)
Et	OMe	215 (3.8621), 260 (2.3655)
Mes	H	215 (4.3523), 272 (2.8007)
Mes	OMe	212 (4.4387), 272 (2.7910)

a) SpectroSol hexane fraction solvent used in all cases.

b) Wavelength maxima listed for the main absorption bands.

c) Wavelength maxima quoted first are in n.m.; molecular absorptivities ($\log_{10}\varepsilon$) are in parentheses.

Optical rotatory dispersion and circular dichroism.

Prior to 1969 the o.r.d. curves of 1-naphthylphenylmethylsilyl compounds consisted of plain dispersion curves

with a cut-off point of 340 n.m. The incursion of high absorbance at that point prevented penetration of the absorption band and so no Cotton effects were detected. However, the advent of improved instrumentation has enabled the Cotton effects of other compounds possessing strongly absorbing chromophores to be investigated.[115]

In the course of the work on the asymmetric reductions of 1-naphthylphenylmethylmethoxysilane (see previous Chapters), the o.r.d. of the optically pure (+)-silane was determined. The curve down to 318 n.m. was a plain, positive dispersion, however, at that point a small sharp fall in rotation occurred which was followed by steeply rising activity. Cut-off due to unfavourable high absorption occurred at 300 n.m. Because of the limitations of the equipment available, samples were sent to Westfield College, London for c.d. measurements, (by courtesy of Prof. W. Klyne and Dr. P. M. Scopes). The results confirmed and supplemented the data published one month later by Sommer.[117] Since then the c.d. of (-)-1-naphthylphenylmethyl-(-)-menthoxysilane has been determined at Westfield. Figs. 10 and 11 show the c.d. spectra obtained.

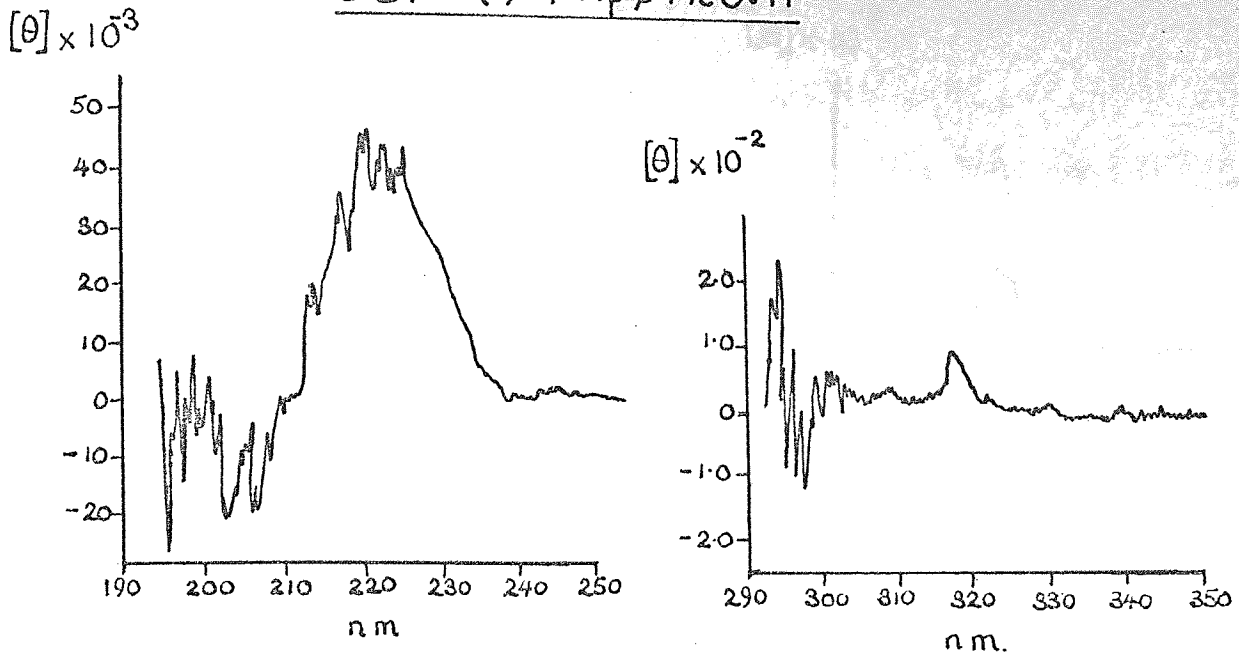
Sommer reports a positive c.d. maximum at 318-319 n.m. for the (+)-silane and a number of compounds possessing this configuration. The menthoxysilane also shows this characteristic. Onset of the para absorption prevented Sommer from studying the c.d. behaviour below 314 n.m. Results obtained at Westfield for the (+)-silane show the presence of multiple Cotton effects at 290-300 n.m. The peak at 297 n.m. is negative and that following at 293 n.m. positive. The region 270-290 n.m. possesses a complexity of negative Cotton effects followed by an equally complex region of positive c.d. peaks

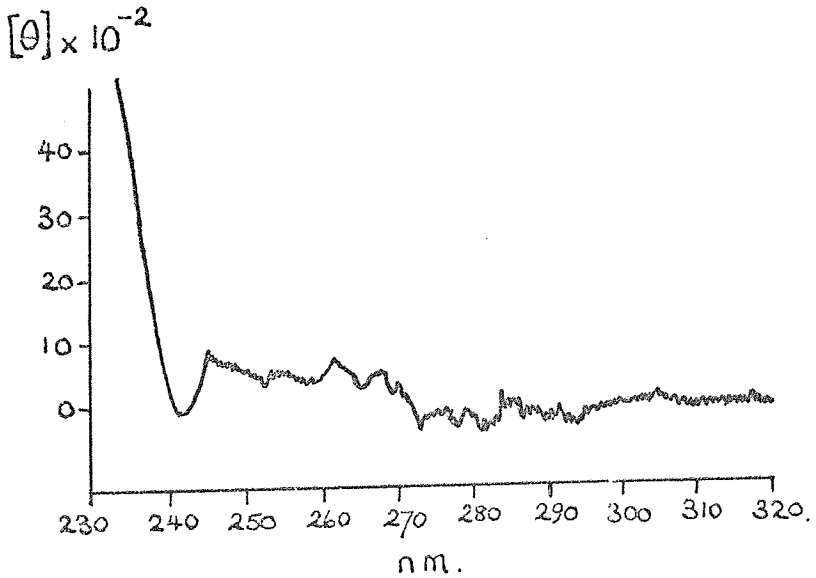
at 240-270 n.m. All the maxima in these regions are of low intensity ([θ] < 1000) and because of this and the high absorption of the para band quantitative determinations of intensities were impossible.

With the subsidence of the para band Sommer resumed measurements at 240 n.m. and showed the presence of a strong positive c.d. maximum at 225 n.m. The molecular ellipticity [θ], of the band was +41,000. The results from Westfield showed the presence of a band at 221 n.m. [θ] = +44,900 which exhibited considerable fine structure and a shoulder at 226 n.m. [θ] = +38,300. Sommer reports that further c.d. data below 216 n.m. for the R_3SiX compounds generally, with the exception of the (+)-silane, show adjacent negative Cotton effects. However, unfavourable [θ]/ε ratios prevented quantitative measurements. The results from Westfield are in general agreement, but also reveal negative Cotton effects at 208 n.m. [θ] = -15,800 and 196 n.m. [θ] = -23,800 for the (+)-silane.

Study of the c.d. maxima associated with the β band for (-)-1-naphthylphenylmethylchlorosilane shows a positive peak at 233 n.m. [θ] = +13,500. The position is in close agreement with that reported by Sommer (234 n.m.) but the intensity is lower ([θ] = +29,000). This is followed successively by a negative Cotton effect at 227 n.m. and a positive Cotton effect at 221 n.m. Beyond these, multiple negative c.d. peaks stretch down to 200 n.m. The shift in the c.d. peak from 225 n.m. for the silane to 234 n.m. for other R_3SiX compounds has been explained as possibly due to the overlap of this Cotton effect with other oppositely signed Cotton effects at shorter wavelengths. The result of such

C.D. (+)-1-NpØMeSiH





C.D. (-)-1-NpØMeSiCl.

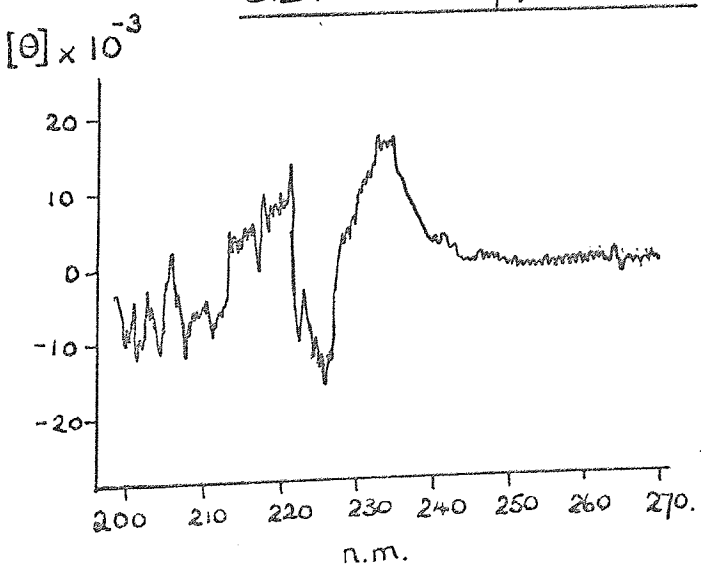
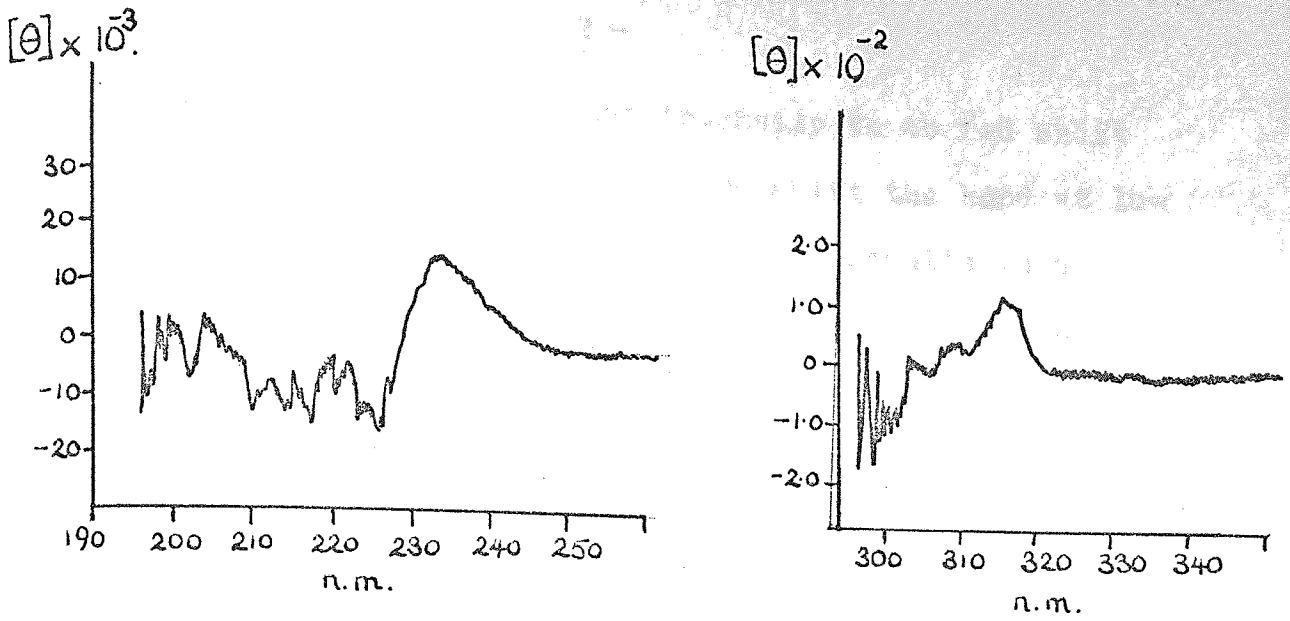


Fig. 10.



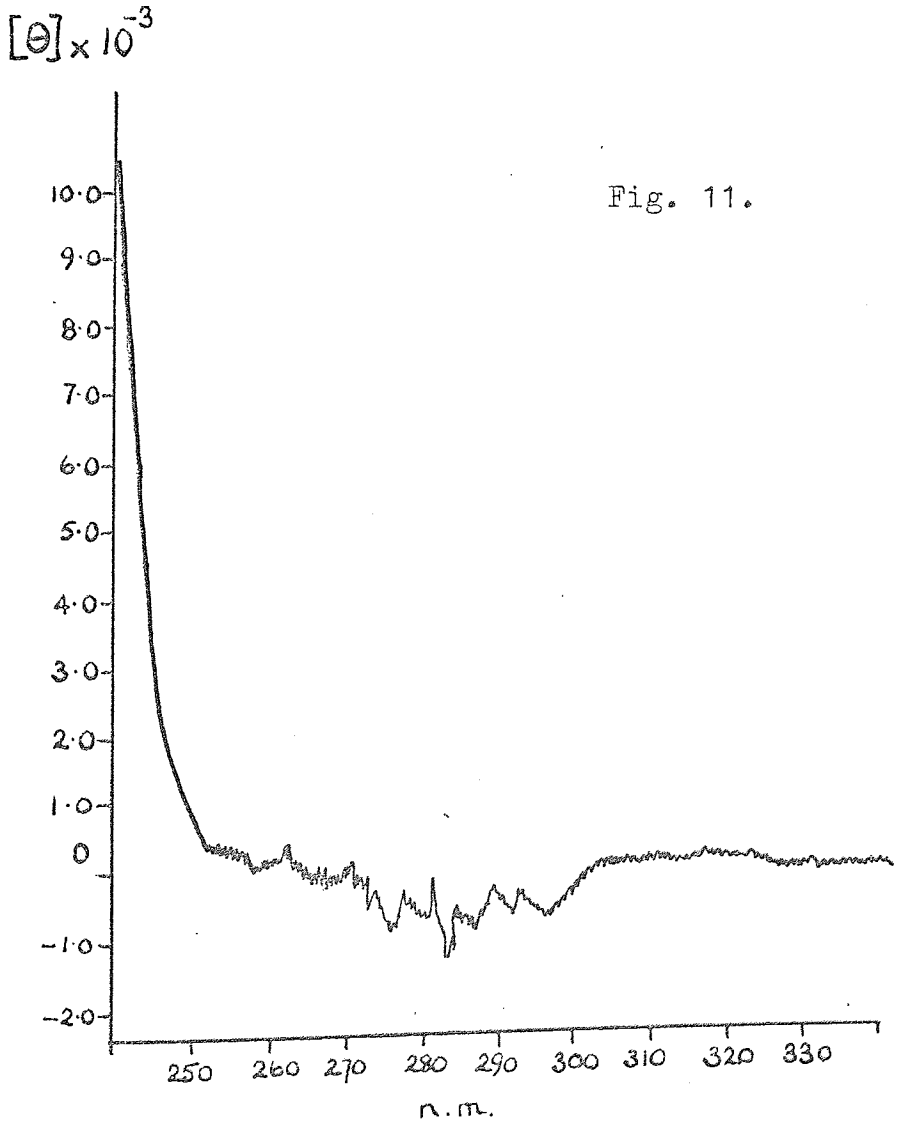


Fig. 11.

C.D. (-)-1-NpØMeSiOMen(-)

coupling of c.d. bands of similar intensity is to red shift the band at higher wavelengths and blue shift the band at low wavelengths.[120] Formation of such couplets results in a mutual cancellation of component c.d. curves and a diminution of rotatory strength. However, this explanation fails to account for the absence of a shift for the silane, since the results from Westfield unambiguously show the presence of negative Cotton effects closely adjacent to the positive one at 221 n.m.

The c.d. of (-)-1-naphthylphenylmethyl-(-)-menthoxysilane (Fig. 11) is basically similar in its major characteristics to the other R_3SiX compounds with the same configuration. A weak positive Cotton effect at 318 n.m. is followed by a complexity of negative Cotton effects $[\theta] = -1,000$ from 250-300 n.m. A positive strong c.d. peak at 233 n.m., characteristic of the absolute configuration, is followed by a complex series of negative c.d. peaks down to 200 n.m. Preliminary work reported by Sommer indicates that simple branching in the X group (e.g., $X = OC(CH_3)_3$) causes increased Cotton activity in the region of the para band. This is responsible for the negative plain dispersion curves of the compounds $X = OCH(CH_3)_2$, $CH_2CH(CH_3)_2$, $CH_2C(CH_3)_3$, O-cyclo-C_6H_{11}, and OMen(-), which possess the (+)-silane configuration. However, branching at the α-carbon centre does not show this effect e.g., (+)-$R_3SiCH(CH_3)_2$. The reason for this behaviour is uncertain but is probably a consequence of conformation. The c.d. results of the menthoxysilane, however, do not show an increased Cotton activity of the para band compared with the silane but a change in sign of some of the peaks in this region is observed. This, together with

the weaker activity of the peak at 233 n.m. is the probable cause of the negative dispersion of (-)-$R_3SiOMen$(-) after allowing for the activity of the (-)-menthoxy group.

Benzylphenylmethylsilyl system.

Ultraviolet Spectra

Despite the change in symmetry of substituted benzenes, compared with the parent hydrocarbon, the spectroscopic behaviour of the substituted compounds is largely uniform and resembles that of benzene itself. The 256 n.m. band ($^1L_b \leftarrow {}^1A$) with its characteristic vibrational structure, and the two shorter wavelength bands (at 203 and 185 n.m. in benzene) are all present. The main effect of substitution is to shift the bands.[119]

The presence of a silicon atom in a side chain β to an aromatic ring produces a marked shift in the α band to 270 n.m. together with a noticeable intensification when the silicon and carbon compounds are compared.[121] This has been explained as a consequence of σ-π hyperconjugation causing electron release from the R_3SiCH_2- to the benzene ring. Large bathochromic shifts of the para band (^1L_a) to 220 n.m. are also found.

Electronic transitions of phenyl groups bonded to silicon occur at very similar positions to those typical of the carbon analogues without great changes in intensity. Aromatic chromophores attached to a common silicon centre are known to possess spectroscopic properties typical of the isolated units. It is not, therefore, unreasonable that the ultraviolet spectra of benzylphenylmethylsilyl compounds show features expected from the addition of the spectral characteristics of phenyl on silicon and benzyl on silicon.

Table 12. gives the data for the main ultraviolet absorptions of the benzylphenylmethylsilane and -methoxysilane. The α band is at 267 n.m. and shows the expected vibrational fine structure. In the case of the silane the absorbance then rises to the first of three maxima at 221 n.m. ($\log_{10}\epsilon$ 4.1568). The central maximum is observed as a shoulder at 210 n.m. and is immediately followed by the most intense of the three at 205 n.m. ($\log_{10}\epsilon$ 4.1875). The ultraviolet spectrum of the methoxysilane differs in that the peak at 221 n.m. is the most intense and the other two suffer a red shift to appear as a shoulder at 215 n.m. ($\log_{10}\epsilon$ 4.1038). The reason for this difference is unknown.

O.r.d. and c.d. characteristics.

The results reported here are for the most optically active samples isolated. Since the pure enantiomers of these compounds have not been prepared, the optical purities of the compounds reported below are unknown.

The (+)-benzylphenylmethylmethoxysilane possessed a plain positive dispersion curve over the range 588-294 n.m.; (-)-benzylphenylmethylsilane gave a plain negative curve. Measurements below 294 n.m. were inaccessible due to the unfavourable $[\emptyset]/\epsilon$ ratio incurred by the ^1L_b transition.

(+)-Benzylphenylmethylmethoxysilane; O.R.D. (c 16.68; hexane), 22°; $[\Phi]_{588}$ +4.11°; $[\Phi]_{500}$ +6.13°; $[\Phi]_{400}$ +12.25°; $[\Phi]_{300}$ +40.3°; $[\Phi]_{294}$ +44.0°.

(-)-Benzylphenylmethylsilane; O.R.D. (c 11.98; hexane) 21°; $[\Phi]_{588}$ -17.1°; $[\Phi]_{500}$ -25.8°; $[\Phi]_{400}$ -46.0°; $[\Phi]_{300}$ -110°; $[\Phi]_{294}$ -116°.

Samples of the above compounds were sent to Westfield College for the determination of their c.d. characteristics.

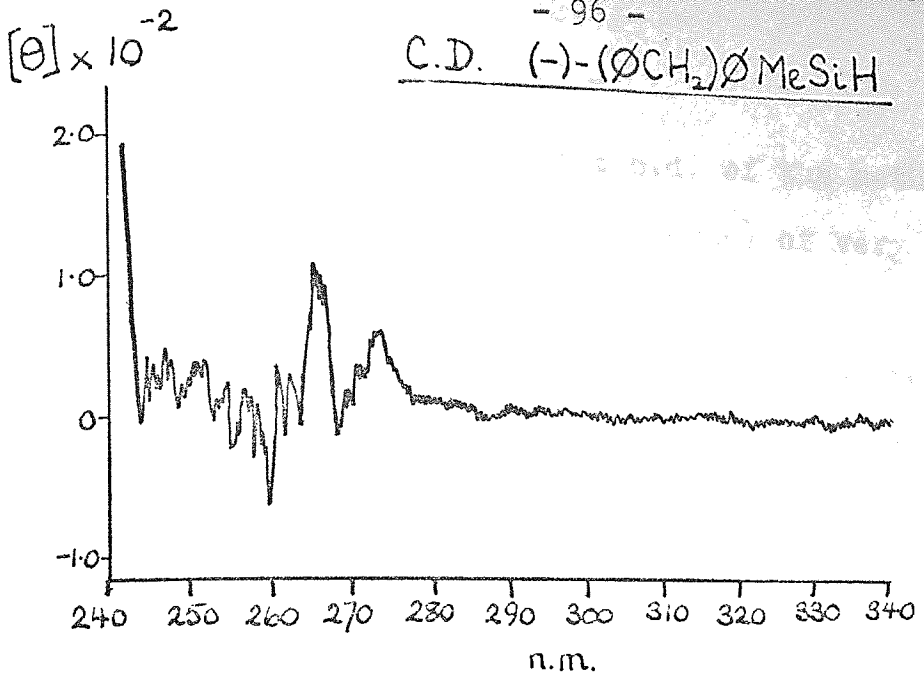
Fig. 12. shows the results which possess some interesting features. As in the 1-naphthylphenylmethylsilyl system the optical activity of these compounds is governed by multiple Cotton effects.

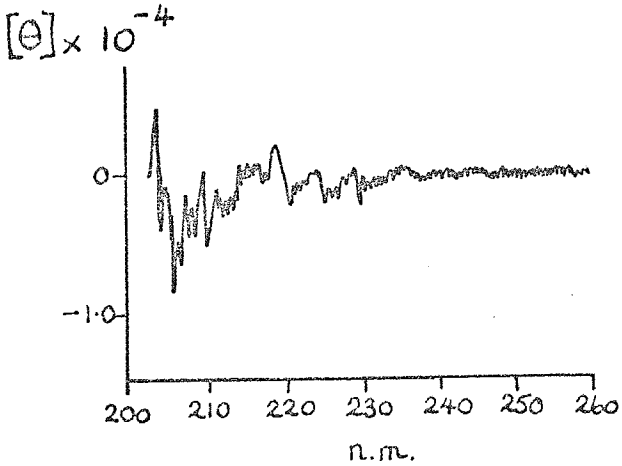
The silane possesses a number of weakly positive , long wavelength, c.d. peaks, which increase in rotatory power with decreasing wavelength. The first, situated at 273 n.m. ([θ] +60) is followed by a minimum at 270 n.m. ([θ] ≈ 0). A second peak beginning at 268 n.m. reaches a maximum at 265 n.m. ([θ] +110) and falls to zero at 264 n.m. An ill-defined region then follows which may contain weakly negative c.d. peaks from 254-260 n.m. and positive ones below this from 254 n.m. to the advent of a stronger positive peak at 242 n.m. Unfortunately the maximum of this peak was not reached and its rotatory power remains unknown. The positive c.d. peaks in the 260-280 n.m. range are associated with the symmetry forbidden α band of the phenyl and benzyl groups on silicon. The origin of the 240 n.m. c.d.peak is uncertain since its position corresponds to the start of the intense para band.

Investigation of the low wavelength region 200-230 n.m. was achieved using greater dilution and a decreased path-length. As expected from the negative o.r.d. curve of the silane, the region is populated with multiple negative Cotton effects which reached a maximum at 206 n.m. ([θ] -6,700).

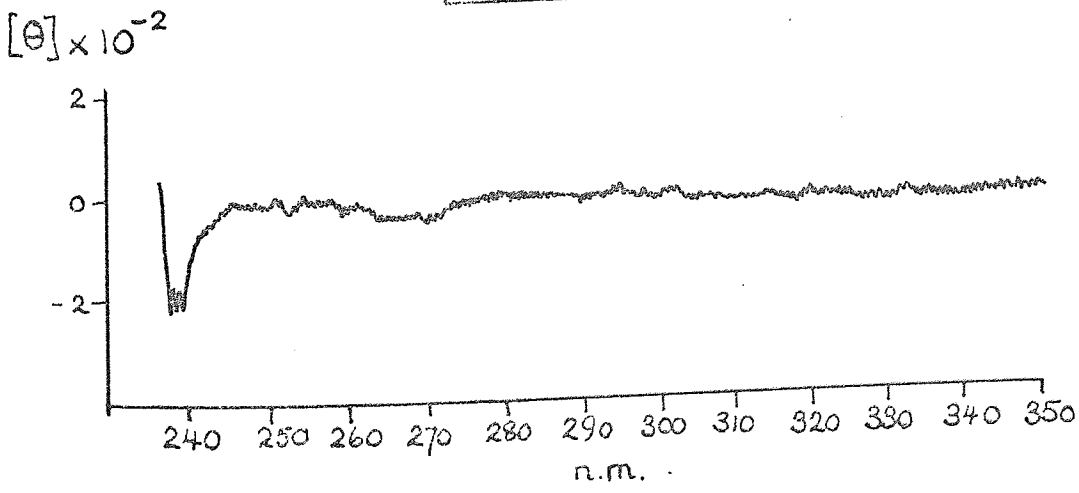
The c.d. spectra of the (+)-methoxysilane exhibited a weak negative Cotton effect at 239 n.m. ([θ] -200). The sign of this peak appears to be indicative of the relative configuration about the silicon in this series of compounds, since it is likely, on the grounds outlined in Chapter V, that the (-)-silane and (+)-methoxysilane have opposite configurations.

C.D. (-)-(ØCH$_2$)ØMeSiH





C.D. (+)-(ØCH$_2$)ØMeSiOMe



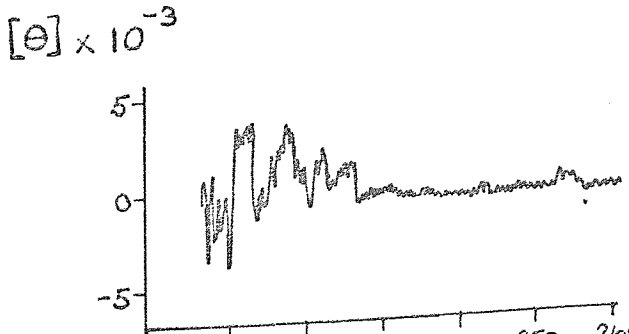


Fig. 12.

The occurrence of this peak in the c.d. of the methoxysilane is preceeded by a Cotton effect (or effects) of very low rotatory power ([θ] -50) at 270 n.m.

The range 210-230 n.m. possesses multiple, positive Cotton effects at 212, 218 and 223 n.m. with decreasing rotatory power in that direction. The most intense at 212 n.m. has [θ] +3,900 and is followed on the low wavelength side by a negative Cotton effect at 209 n.m. ([θ] -4,000). The positive c.d. peaks in this region, therefore, appear to be responsible for the sign of $[\alpha]_{588}$.

Reduction of (+)-benzylphenylmethylmethoxysilane to (+)-benzylphenylmethylsilane with lithium aluminium hydride in diethyl ether (experiment 21) indicates that the methoxysilane used in these studies possessed an optical purity of at least 73% that of the silane used. The positive Cotton effects in the range 210-230 n.m. for the methoxysilane are, therefore, weaker than the negative c.d. peaks of the silane at 210 n.m. This would account for the higher rotatory power of the silane observed at longer wavelengths.

Mesitylphenylmethylsilyl system.

Ultraviolet spectra.

Both the parent silane and the methoxysilane in hexane show the expected ultraviolet benzenoid characteristics. The band, with its vibrational fine structure, rises steeply through a maximum at 284 n.m. ($\log_{10}\epsilon \approx 2.7$) and two shoulders at 279 and 275 n.m. to the band maximum at 272 n.m. ($\log_{10}\epsilon \approx 2.8$). The band then falls through further peaks at 267, 261 and 254 n.m. in diminishing intensity to a minimum at about 250 n.m. The absorbance then increases steeply with the onset of the para band.

The para band consists of an intense peak at 213-214 n.m. ($\log_{10}\varepsilon \approx 4.4$) with a broad shoulder at 230 n.m.

O.r.d. and c.d. characteristics.

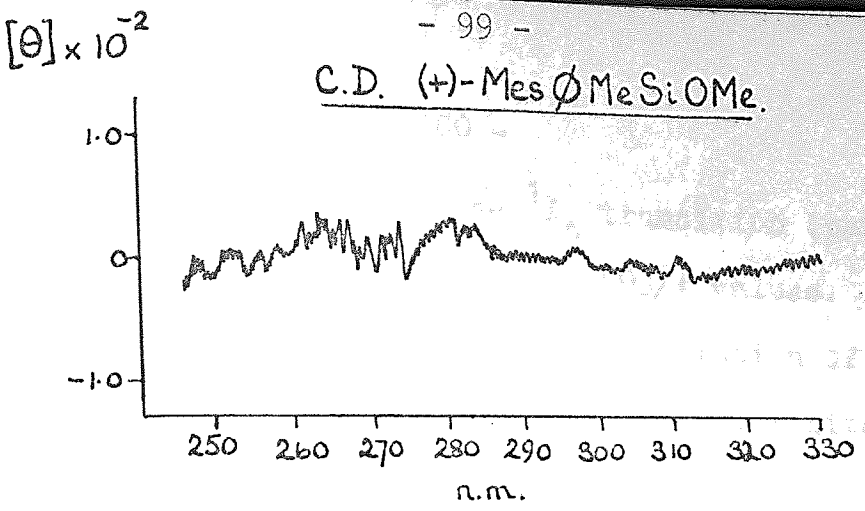
The o.r.d. curves of (+)-mesitylphenylmethylmethoxysilane and (-)-mesitylphenylmethylsilane show interesting and contrasting behaviour. That of the former exhibits a plain, positive dispersion over the range 588-300 n.m. However, the silane, after a slight increase in laevorotation from 588 n.m. to a broad trough at 380-370 n.m., undergoes a change in sign of rotation and becomes increasingly more dextrorotatory until cut-off at 294 n.m. Fig. 13 illustrates the o.r.d. of the compounds.

(+)-Mesitylphenylmethylmethoxysilane; O.R.D. (c 7.28; hexane), 23°; $[\Phi]_{588}$ +6.2°; $[\Phi]_{500}$ +9.05°; $[\Phi]_{400}$ +15.25°; $[\Phi]_{300}$ +27.9°.

(-)-Mesitylphenylmethylsilane; O.R.D. (c 13.57; hexane), 22°; $[\Phi]_{588}$ -9.65°; $[\Phi]_{500}$ -12.95°; $[\Phi]_{400}$ -18.8°; $[\Phi]_{384-370}$ -19.9° (broad trough); $[\Phi]_{310}$ 0.0°; $[\Phi]_{294}$ +24.2°.

The o.r.d. of the silane clearly shows the presence of a positive Cotton effect associated with the ^1L_b aromatic transition (α band) superimposed on a negative background curve. The background rotation is probably the result of a strong negative Cotton effect (or effects) in the short wavelength transitions 210-230 n.m.

C.d. measurements confirm the above inferences, at least with regard to the presence of a positive Cotton effect in the ^1L_b transition of the silane. Fig. 13 shows the presence of a weakly positive c.d. peak at 281 n.m. ([θ] +60). The c.d. of the methoxysilane also shows the presence of a weak, positive Cotton effect at 281 n.m. ([θ] +30). Examination of the


[θ] x 10^-2
C.D. (+)-Mes Ø Me Si OMe.
1·0
0
-1·0
250 260 270 280 290 300 310 320 330
n.m.

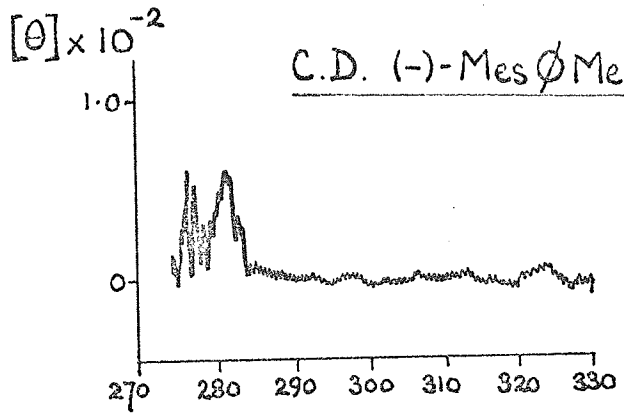
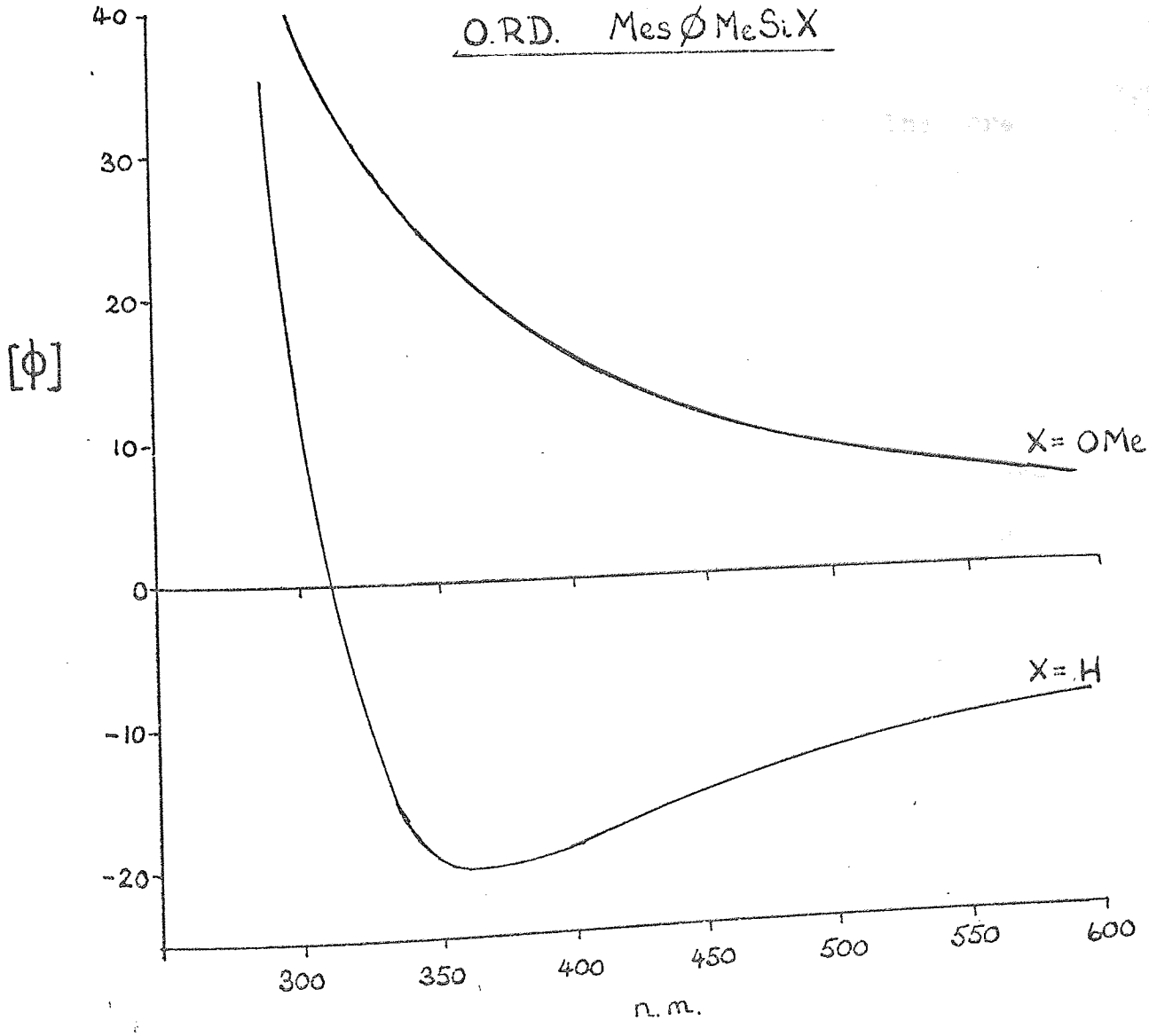

[θ] x 10^-2
C.D. (-)-Mes Ø Me Si H
1·0
0
270 280 290 300 310 320 330

Fig. 13.


O.R.D. Mes Ø Me Si X
[φ]
40
30
20
10
0
-10
-20
X = OMe.
X = H
300 350 400 450 500 550 600
n.m.

region associated with the intense ^1L_a transition (para band) was impossible due to the unfavourable $[\theta]/\epsilon$ values.

An o.r.d. measurement on a very weak solution of the silane in hexane using a 1 m.m. cell showed a definite dextrorotation at 250 n.m. Due to the high absorption in this region the accuracy is not high but the $[\Phi]_{250}$ is estimated to be about +530°. This means that there must be another positive Cotton effect at a wavelength lower than 250 n.m. but higher than the negative 'giant' responsible for the laevorotation at 588 n.m.

Phenylethylmethylsilyl and Phenylisopropylmethylsilyl systems.

Ultraviolet Spectra

As expected, compounds in these series display a typical phenyl chromophore spectrum with a ^1L_b band centred at 260 n.m. ($\log_{10}\epsilon = 2.365$) with vibrational fine structure. The more intense ^1L_a transition occurs at 216 n.m. ($\log_{10}\epsilon \approx 3.8$). The absorption caused by the $^1B \leftarrow {}^1A$ transition (β band) probably occurs at shorter wavelengths (<200 n.m.) and is not observed.

O.r.d. characteristics.

The silanes and methoxysilanes of both these systems gave plain dispersion curves over the range 300-588 n.m. Measurements below 300 n.m. were precluded by the high absorbance for solutions of concentrations sufficient to give measurable rotations. For these reasons no c.d. data was obtained.

(-)-Phenylethylmethylmethoxysilane; O.R.D. (c 19.14; hexane), 23°; $[\Phi]_{588}$ -7.00°; $[\Phi]_{500}$ -9.80°; $[\Phi]_{400}$ -18.5°; $[\Phi]_{300}$ -53.0°.

(+)-Phenylethylmethylsilane; O.R.D. (c 15.97; hexane), 22°; $[\Phi]_{588}$ +0.75°; $[\Phi]_{500}$ +1.18°; $[\Phi]_{400}$ +2.52°; $[\Phi]_{300}$ +8,65°; $[\Phi]_{286}$ +11.0°.

(+)-Phenylethylmethylsilane; O.R.D. (c 19.52; CCl_4) 22°; $[\Phi]_{588}$ +1.43°; $[\Phi]_{500}$ +2.27°; $[\Phi]_{400}$ +4.58°; $[\Phi]_{300}$ +15.4°.

(-)-Phenylisopropylmethylmethoxysilane; O.R.D. (c 17.09; hexane), 23°; $[\Phi]_{588}$ -8.95°; $[\Phi]_{500}$ -14.2°; $[\Phi]_{400}$ -27.6°; $[\Phi]_{312}$ -60.6°.

(+)-Phenylisopropylmethylsilane; O.R.D. (c 14.08; hexane), 21°; $[\Phi]_{588}$ +1.20°; $[\Phi]_{500}$ +2.10°; $[\Phi]_{400}$ +5.45°; $[\Phi]_{300}$ +20.6°.

Cyclohexylethylmethylsilyl system

This fully saturated system possesses no electronic transitions in the accessible ultraviolet region above 200 n.m.[121] Therefore, the Cotton effects responsible for the plain o.r.d. curves are situated at wavelengths below 200 n.m. The optically active compounds isolated from the partial asymmetric reduction with (+)-cinchonine-lithium aluminium hydride complex possessed some aromatic impurity which was found to be difficult to completely remove without causing extensive racemisation. Because of this, and the weak rotatory power of these compounds, measurements below 300 n.m. were impracticable. C.d. measurements at Westfield College showed that this aromatic impurity was not responsible for the optical activity since no Cotton effects associated with aromatic transitions were detected. O.r.d. measurements, also conducted at Westfield College, confirmed the optical activity of the compounds.

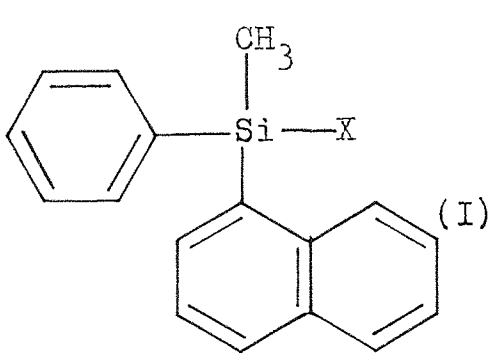
(-)-Cyclohexylethylmethylmethoxysilane; O.R.D. (c 13.30;

hexane), 21°; $[\Phi]_{588}$ -1.10°; $[\Phi]_{500}$ -1.40°; $[\Phi]_{400}$ -2.00°; $[\Phi]_{300}$ -3.38°.

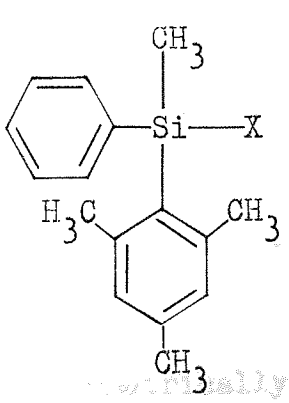
(-)-Cyclohexylethylmethylsilane, O.R.D. (c 18.34; hexane), 20°; $[\Phi]_{588}$ -0.17°; $[\Phi]_{500}$ -0.26°; $[\Phi]_{400}$ -0.47°; $[\Phi]_{325}$ -0.94°.

Discussion of results and conclusions.

The organosilicon compounds (I) and (II) are classed as homoconjugated molecules.[115]

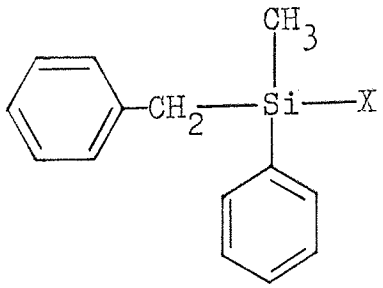


(I)



(II)

Compounds belonging to class (III) may be regarded as di-homoconjugated.



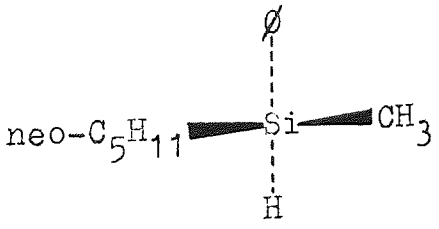
(III)

In all the above cases the compounds are conformationally flexible structures and as such the interpretation of their o.r.d. and c.d. behaviour is made difficult. Homoconjugated optically active compounds are normally characterised by very intense Cotton effects.[116] Moffit[122] has proposed a coupled oscillator model for homoconjugated

compounds and Mason and Vane[123] have successfully applied this model to the consideration of the rigid alkaloid calycanthine. Numerous other examples of rigid homo-conjugated compounds are found in references 115 and 116. However, mention must be made of the studies of diphenyl-propylamines[124] phenylalanine, mandelic acid and phenyl-glycine,[125] substituted phenylacetic and 3-phenylpropionic acids.[126] To this class of flexible, homoconjugated compounds belong the diaryl methanes and some quinones[127] and dihomoconjugated representatives include diaryl ethanes.[128,42]

Sommer in his study of the o.r.d. and c.d. behaviour of compounds of type (I)[117] assumes to a first approximation that the naphthyl and phenyl groups operate as separate, inherently symmetric but dissymmetrically perturbed chromophores. Spectral evidence that phenyl groups bonded to a common silicon or neutral tetrahedral carbon behave as isolated chromophores supports this conclusion.

Although not completely excluding the possibility that the naphthyl and phenyl groups act as coupled oscillators Sommer assumes that the activity of the naphthyl chromophore dominates the o.r.d. and c.d. spectra of compounds of type (I) and that the very weak Cotton effect activity of (+)-neopentylphenylmethylsilane (IV) supports this view.



(IV)

However, the compound (IV) cannot be homoconjugated and so the analogy is not strictly valid. Unfortunately, the importance of interactions through homoconjugation in the spectra of flexible molecules of the type under consideration is not yet known. Study of the c.d. and o.r.d. characteristics of, for example, 1-naphthylcyclohexylmethylsilane may help to resolve this difficulty.

Assuming that the aromatic groups in compounds of the type (I) to (III) act as inherently symmetric chromophores then their optical activity would depend on their respective dissymmetrically perturbing environments. The substituent X could then effect the activity of the chromophores by:

i) electronic interaction with them through the bonding framework,

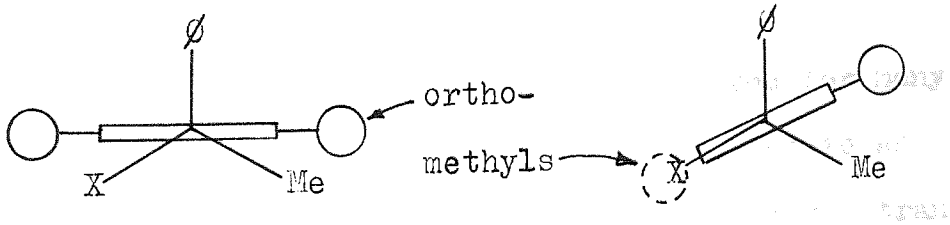
ii) perturbation of the chromophores as an element of their spatial environments,

iii) its simultaneous conformational effects on the molecule as a whole.[117]

Examination of molecular models indicates that the greatest factor determining the conformational distribution in the compounds of type (I) is associated with the steric compression incurred between the peri hydrogen on the naphthyl nucleus and the other groups bonded to the silicon centre. Maximum freedom to intramolecular motions is provided when this hydrogen atom is flanked by the two groups that have the smallest steric requirements. Therefore, the same conformational preferences might be expected in all compounds where X is less sterically challenging than methyl, i.e. X = H, F, OH, OCH_3, Cl. The differences in the c.d. behaviour of the silane (I, X = H) and that

shown by its derivatives may be a consequence of electronic interactions related to the fact that these new substituents contain, in contrast to hydrogen, non-bonding electrons. It is reasonable to expect that the optical activity of aromatic $\pi-\pi^*$ transitions is affected by mixing of $n-\pi^*$ transitions or transitions involving d-orbitals.

The differences observed in the o.r.d. spectra of the mesitylphenylmethylmethoxysilane (II, X = OCH_3) and the silane (II, X = H) may similarly be due to electronic factors associated with the group X. Examination of scaled models shows that the silane may exist in two conformations possessing similar energies. However, due to the increased bulk of the methoxy group over the hydrogen atom only one of these conformations is likely. The conformations are shown below:



Therefore, the striking differences observed may be the result of a change in conformational behaviour. The o.r.d. and c.d. spectra of other derivatives of this system are required in order to see if the above phenomenon is general.

Introduction of a methylene grouping between an asymmetric centre and a chromophore results in an inversion of the associated Cotton effect. This effect, known as the 'proximity rule' and first noted for saturated ketones, now seems rather general. Thus the c.d. band of phenylalanine in the 260 n.m. region has the opposite sign to that of (-)-mandelic acid[125] although both possess the same configuration. Verbit and Heffron also find an inversion of sign

of the Cotton effect at 260 n.m. for substituted phenylacetic and 3-phenylpropionic acids with the same configuration.[126] In this connection the ^1L_b transition associated with the benzyl on silicon would be expected to have a Cotton effect opposite in sign to that of a phenyl in the same perturbed environment. The phenyl and benzyl groups in benzylphenylmethylsilyl derivatives (III) may be considered, to a first approximation, to be enantiomeric in their asymmetric environments. Therefore the two chromophores may be expected to give Cotton effects of the same sign in the ^1L_b region. The c.d. spectra of the silane (III, X = H) and methoxysilane (III, X = OCH_3) both exhibit two optically active transitions at 265 and 240 n.m. which possess the same sign. Whether the 240 n.m. c.d. peak is due to the benzyl on silicon as a separate chromophoric entity, however, is not as yet resolved.

O.r.d. and c.d. studies have been reported for many compounds that bear a single phenyl group bonded to an asymmetric carbon. In these compounds the aromatic transitions are inherently symmetric but are perturbed by their dissymmetric environment. The o.r.d. and c.d. data of optically active (+)-neopentylphenylmethylsilane display very weak, negative, multiple Cotton effects in the α (^1L_b) absorption region. Following these the o.r.d. curve then rises steeply and indicates a positive Cotton effect associated with the ^1L_a absorption band near 213-217 n.m. This behaviour appears to be quite general for asymmetric compounds having the S configuration and a phenyl group attached directly to the centre.[129] Therefore the o.r.d. and c.d. behaviour of the (+)-RMeØSiH compounds where R =

ethyl and isopropyl may be anticipated as exhibiting very similar features. Samples of optically active phenylethylmethylsilane and phenylethylmethylmethoxysilane, prepared by asymmetric reduction failed to show any Cotton effects at 260-270 n.m. Therefore these effects, if present, must be regarded as being extremely weak.

X.

PROTON MAGNETIC RESONANCE OF DIASTEREOISOMERIC ALKOXY-SILANES.

In the course of resolving 1-naphthylphenylmethylsilane via its (-)-menthoxy derivative[4] it was noticed that the nuclear magnetic resonance spectra of the separated diastereoisomers and their mixture featured resonances which are extremely useful in determining the optical purity of the diastereoisomers during resolution.

The instances of magnetic non-equivalence of protons in diastereoisomers are many and Raban and Mislow[131] have recently demonstrated the applicability of nuclear magnetic resonance spectroscopy to the analysis of diastereoisomers as a means of determining optical purity. There are, also, a number of instances reported where this technique has been applied to the analysis of diastereoisomeric organosilicon compounds.[12,130,89] The method is particularly useful in following the purification of the lower melting (+)-1-naphthylphenylmethyl-(-)-menthoxysilane (Ib), where melting point and optical rotation are not very sensitive to purity.

The 60 MHz nuclear magnetic resonance spectrum of the mixed diastereoisomers in carbon tetrachloride features a complex aromatic multiplet at 1.8-2.8 τ, a broad band centred at 6.50 τ, due to the methine proton attached to oxygen, and resonances from 7.4-9.3 τ associated with the aliphatic protons of the menthoxy moiety and the methyl on silicon. In addition, there are four sharp resonances with a intensity of three protons centred at 9.50τ, which are

due to two superimposed doublets, the chemical shifts of which depend on the chirality at the silicon atom.

The spectrum of (-)-1-naphthylphenylmethyl-(-)-menthoxysilane (Ia) showed two major differences from the above (see Fig. 14.). Firstly, in the region 9.0-9.2 τ, the peaks at 9.05 and 9.17 τ, present in the mixture, were absent in the spectrum of the pure (Ia) and in addition there was a considerable intensification of the peak at 9.14 τ. Secondly, the only resonances at high field were a doublet centred at 9.55 τ (J = 7.1 Hz). The spectrum of the lower melting (Ib) recrystallised from ethanol showed resonances at 9.05 and 9.17 τ. The high field resonances consisted of a doublet at 9.51 τ (J = 7.3 Hz) together with a minor doublet due to (Ia) which was only completely removed with great difficulty.

The high field doublets were originally thought[89] to be due to the methyl on C(5) of the menthoxy moiety, based on arguments involving probable steric interactions in the most stable diastereoisomer (see later). However, work by Mislow and co-workers [90] on the nuclear magnetic resonance spectra of related diastereoisomeric phosphinate menthyl esters rigorously proves that similar high field doublets are caused by the pro-S-[132] methyl of the isopropyl group. In view of the analogy and the similar coupling constants for the doublets in the two series (J = 7 Hz for the pro-S-methyl and J = 5 Hz for the methyl at C(5)) it is now thought more likely that the high field resonances observed in this study, are due to the pro-S-methyl group, (H_a, Fig. 15.).

The resonances of the diastereoisomers in the region

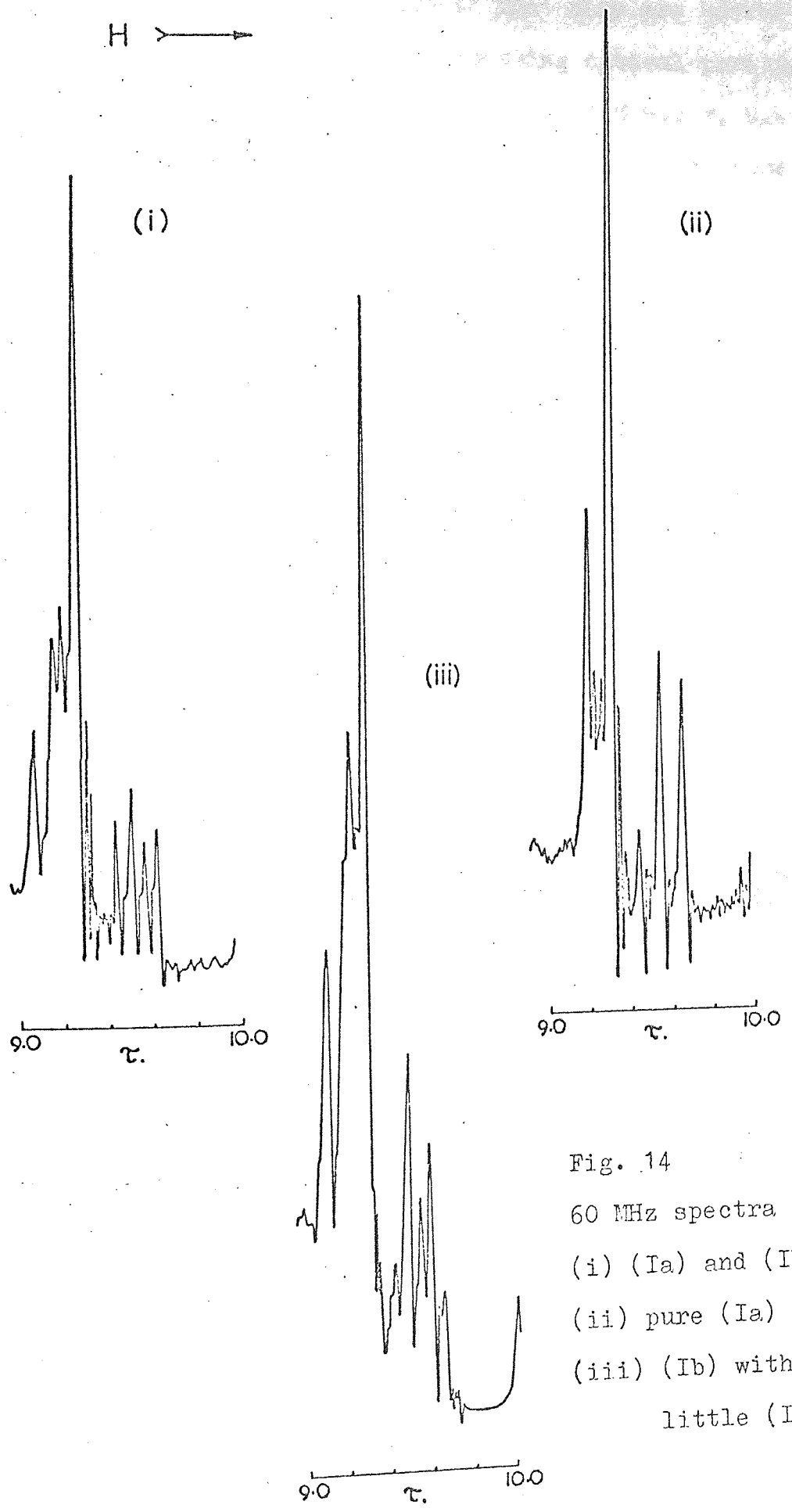
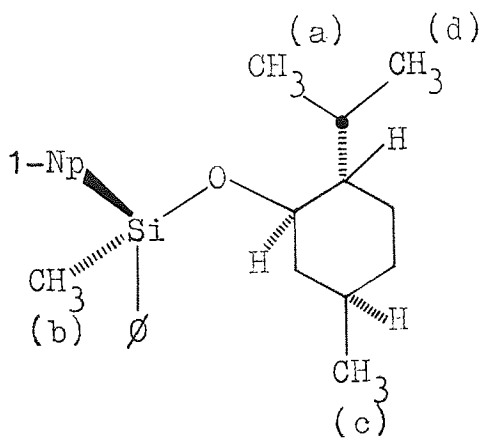


Fig. 14
60 MHz spectra of:
(i) (Ia) and (Ib)
(ii) pure (Ia)
(iii) (Ib) with a little (Ia).

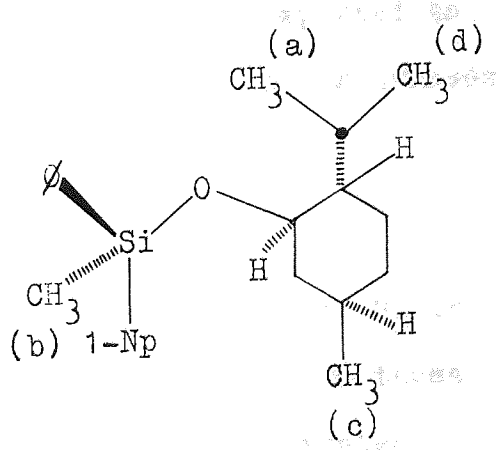
9.5 τ are sufficiently well separated that they are conveniently employed in quantitatively assessing optical purity. Differences in the resonances in the region 9.0-9.2 τ, due to the other methyl groups, provide additional indications of purity, but are too close to the resonances of the methyls on silicon to be of great value on their own.

Examination of the region 9.0-9.3 τ at 100 MHz confirms the above indications but gives no additional information. Under these conditions the high field doublets at 9.4-9.6 τ are separated to the extent that overlap of two peaks occurs and the region has the appearance of an unsymmetrical triplet.

However, the 220 MHz spectra of Ia and Ib allows one to assign the positions of the other methyl doublets (H_c and H_d) of the menthoxy moiety and the methyl on silicon (H_b) [Figs. 17 and 18].



Ia



Ib

Fig. 15

The positions of the C-CH_3 doublets and the SiCH_3 singlets, arising from the protons identified as H_a, H_b, H_c, and H_d in the above formulae, are given in Table 13. The assignments of these protons are based on analogy with

Mislow's results from menthyl n-alkylphenylphosphinates.

Table 13.

Temperature dependence of the n.m.r. spectra[a,b] of (Ia) and (Ib) [Solvent CCl_4].

	21°	0°	-20°	-40°	
Ia	9.55(0)	9.56(8)	9.59(0)	9.60(0)	H_a
Ib	9.48(8)	9.50(1)	9.52(0)	9.53(2)	
Ia	9.25(0)	9.25(0)	9.25(5)	9.25(0)	H_b
Ib	9.23(1)	9.23(4)	9.23(8)	9.23(7)	
Ia	9.18(6)	9.18(4)	9.18(5)	9.17(5)	H_c
Ib	9.23(5)	9.23(6)	9.24(2)	9.23(5)	
Ia	9.18(6)	9.18(4)	9.18(5)	9.17(5)	H_d
Ib	9.10(0)	9.09(8)	9.09(4)	9.08(8)	

a) τ values calculated from T.M.S. internal standard on expanded 220 MHz spectra. The values are reported to three places of decimals but the figures in parentheses are not so reliable.

b) J_{HCH} of H_a and H_d are 7.0 Hz and of H_c 6.0 Hz.

The coupling constants for the doublets H_a and H_d in the two diastereoisomers are 7.0 Hz, identical with those reported for the analogous protons in the phosphinates. The methyl doublet H_c, although not resolved in the spectrum of Ia and only partially in that of Ib, has a coupling constant of only 6.0 Hz (Mislow reports J_{HCH} = 4.5-5.5 Hz). The lower values of the coupling constants for these protons are attributed to broadening of the H_c resonance because of virtual coupling to the ring protons at C(2) and C(6), thus

creating an apparent decrease in coupling constant.[133]

The upfield shift of the H_a doublet in the diastereoisomers Ia and Ib is attributable to the diamagnetic anisotropy of the aromatic groups, rather than to any effect due to the presence of a silicon atom. No upfield shift is observed in the spectrum of a mixture of diastereoisomeric cyclohexylethylmethylmenthoxysilanes.

Table 14.

Proton Magnetic Resonance Spectra of Diastereoisomeric menthoxysilanes.

No.	R_1	R_2	R_3	Chirality at Si.	High field doublet[a] (τ).
Ia	1-Np	Ø	CH_3	S	9.55
Ib	1-Np	Ø	CH_3	R	9.49
2a	$ØCH_2$	Ø	CH_3	-	9.40
2b	$ØCH_2$	Ø	CH_3	-	9.45
3a	Et	Ø	CH_3	-	9.37
3b	Et	Ø	CH_3	-	9.43
4a	Et	cycloC_6H_{11}	CH_3	-	9.27[b]
4b	Et	cycloC_6H_{11}	CH_3	-	9.27[b]

a) J_{HCH} = 7Hz

b) Methyl doublet in pure (-)-menthol is observed at 9.18 τ: R. A. Lewis, O. Korpiun, and K. Mislow, J. Amer. Chem. Soc., 90, 4847, (1968).

The phenomenom appears to be general for menthoxy derivatives of any silane possessing an aromatic group. Table 14 gives the positions of the H_a resonances for

diastereoisomers of benzylphenylmethyl- and phenylethyl-methyl- menthoxysilanes. The method may, therefore, be useful for the determination of the optical purity of any novel optically active organosilane, possessing an aromatic ring, prepared by asymmetric reduction. All that is required is a simple, highly stereospecific synthesis of menthoxysilanes. Preliminary attempts at preparing the menthoxysilanes from optically active benzylphenylmethyl-silane and (-)-menthol using palladium on charcoal as a catalyst indicate that in this particular case extensive racemisation occurs, so making the determination of optical purity inaccessible.

Mislow's results show that in the case of menthyl n-alkylphenylphosphinates the higher field doublet of the H_a protons is due to the diastereoisomer with the S configuration at phosphorus. Therefore, the method is useful for the determination of absolute configuration at phosphorus. Similarly, the diastereoisomer of the menthoxysilanes Ia which gives the H_a doublet at the highest field possesses the S configuration at silicon. The phenomenom may, therefore, also be useful for the determination of the absolute configuration of asymmetric silicon compounds.*

Since the upfield shift of H_a is caused by the diamagnetic anisotropy of the aromatic groups and since the highly shielded protons are situated on the pro-S- methyl

* Mislow has already demonstrated the parallelism that exists between sulphinates and phosphinates. Both form (-)-menthoxy compounds, the S diastereoisomers of which give H_a doublets at highest field (reference 90).

group in the menthoxy moiety of the $\underline{S}_{Si}$ alkoxy compound, it is of interest to know whether the shift is primarily a consequence of conformational preference or of "intrinsic diastereotopism".[134] The results from variable temperature nuclear magnetic resonance studies at 220 MHz (Table 13) show that the positions of H_a in diastereoisomers Ia and Ib are shifted to higher fields by a lowering of temperature. The positions of the other methyl protons H_c and H_d are relatively unaffected. (H_d undergoes a slight shift to lower fields.) This illustrates the importance of the conformer population term ($\Delta\nu_{cp}$[134b]) and shows that the phenomenom is associated with the conformer of lowest energy, the population of which will be expected to increase with lowering of temperature. Change of solvent polarity causes only slight changes to the chemical shifts of H_a; e.g. in carbon disulphide H_a is centred at 9.52τ, in dimethyl sulphoxide at 9.50 τ, and in carbon tetrachloride at 9.55 τ. In view, therefore, of the small changes in chemical shift that are engendered by large changes in solvent polarity it is unlikely that the shifts observed with change in temperature are due to solute-solvent interactions.

Fig. 16 depicts a geometry of the stable conformer of the diastereoisomer Ia in which the pro-S methyl group is situated in a shielded region above the plane of the naphthyl ring system. The naphthyl group possesses a greater shielding effect than the phenyl[135] and so a doublet is found at higher field than in the spectrum of Ib, in which the pro-S methyl is shielded by a phenyl group. In this topology the menthyl group is in an all-equatorial

conformation,[136] the isopropyl group is staggered with respect to the cyclohexane ring and so oriented that there are no $CH_3/OSiR_3$ 1,3-syn-diaxial interactions[137] and the peri-hydrogen of the 1-naphthyl group takes a position between the methyl and the -OMen group.[5]

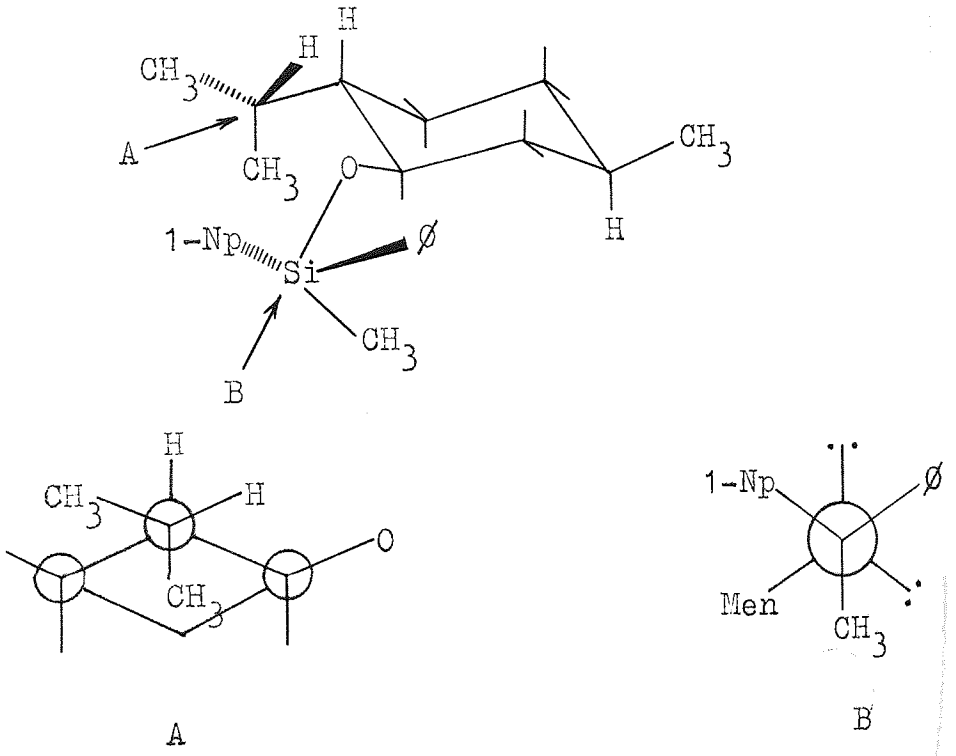


Fig. 16

The $\underline{R}_{Si}$ isomer, placed in a similar conformation, would result in the isopropyl group being shielded by the phenyl group.

Similar results to these have been found by Mislow in a preliminary investigation of menthyl arylphenylphosphinates (unpublished results, see ref. 90) where aryl is 1-naphthyl.

Results of variable temperature on the positions of the high field doublets in the 220 MHz spectrum of the mixture of diastereoisomeric (±)-phenylethylmethyl-(-)-menthoxysilanes (Table 15) shows very similar behaviour to

Fig. 17 220MHz spectrum of (-)-1-naphthylphenylmethyl-(-)-menthoxysilane (Ia).

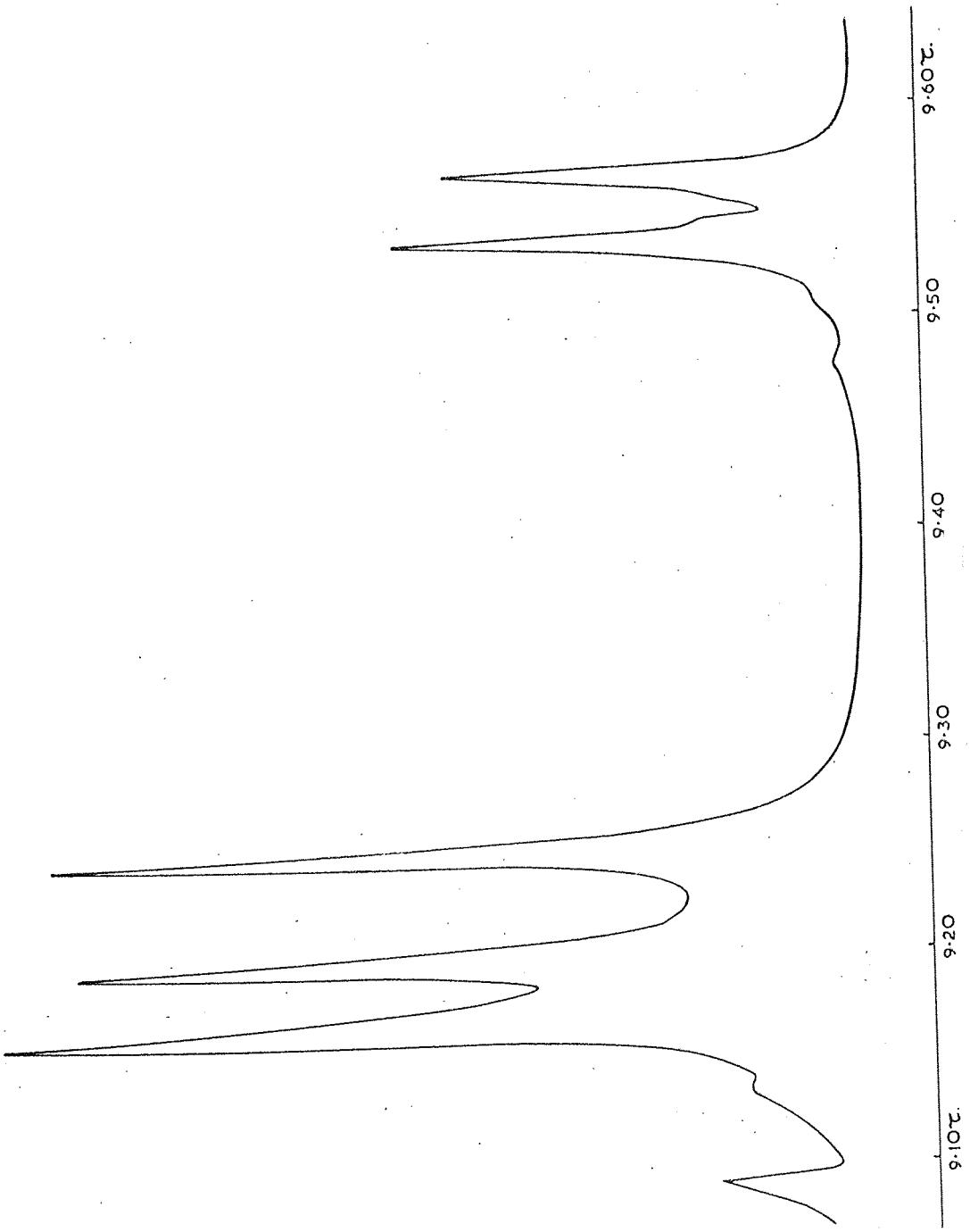


Fig. 18 220MHz spectrum of 1-naphthylphenylmethyl-(-)-menthoxysilanes enriched in diastereoisomer (Ib).

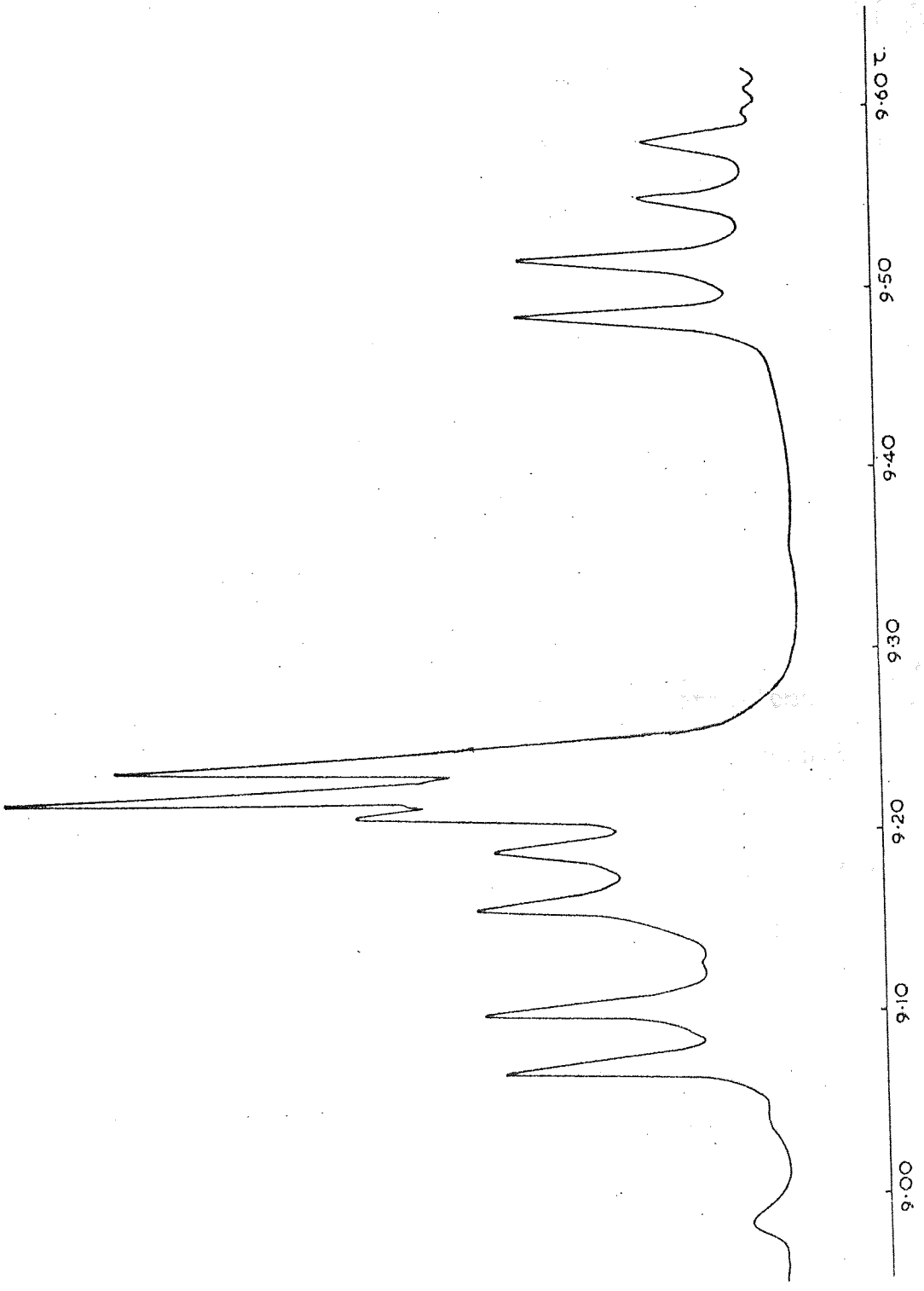


Table 15.

Temperature dependence of the n.m.r. spectra of (±)-phenylethylmethyl-(-)-menthoxysilane diastereoisomers.

Temp.	τ 3a	3b	Δν Hz.
20°	9.35(6)	9.42(2)	14.5
0°	9.39(7)	9.46(4)	14.8
-20°	9.40(3)	9.47(3)	15.5
-40°	9.42(7)	9.50(0)	16.0

Solvent CCl_4.

that observed for the diastereoisomers Ia and Ib. The arguments on which the preceding conformational analysis were based may be extended to the present case. Therefore the diastereoisomers exist in preferential conformations such that the pro-S methyl group is shielded by the phenyl ring in 3b and is less shielded in 3a. The increase in Δν with lowering of temperature is in accord with this view.

Relative Stability of Diastereoisomers Ia and Ib.

Reaction of (±)-1-naphthylphenylmethylsilane with (±)-menthol (experiment 41) using palladium on charcoal as a catalyst[6j,89] gives a mixture of 1-naphthylphenylmethyl-menthoxysilane diastereoisomers. Nuclear magnetic resonance spectroscopy shows that the mixture consists of 55% (-)-1-naphthylphenylmethyl-(-)-menthoxysilane (Ia) and 45% of (+)-1-naphthylphenylmethyl-(-)-menthoxysilane (Ib), together with the same proportions of the mirror image compounds. The reaction of the silane with menthol under

these conditions is reported to proceed with > 95% inversion,[6j] and so the above ratio of products reflects the relative rates in which the two diastereoisomers are formed. The same preferential formation of Ia is observed when Ia and Ib are formed by a method which involves equilibration of configuration at the silicon atom. Therefore the diastereoisomer Ia must be the most thermodynamically favoured.

This at first sight might appear unusual in view of Fig. 16 since in this diastereoisomer the isopropyl group is closer to the 1-naphthyl group than the less sterically demanding phenyl. However, since the conformation of the naphthyl group is such that the peri-hydrogen is well removed from the isopropyl group the naphthyl moiety may offer no greater steric interaction than a phenyl ring. Indeed, it can be visualised that under these considerations the naphthyl group might well provide less steric compression than a phenyl if the latter is regarded as a conformationally freely rotating group.

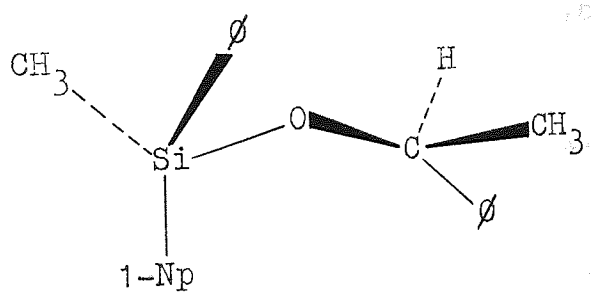
Incidently, since diastereoisomer Ia has the higher melting point it must also possess the most ordered structure in the crystal lattice. This further indicates (but does not prove) that Ia offers the best steric fit for the groups about silicon.

Other Diastereoisomeric Alkoxysilanes.

Reaction of (±)-1-naphthylphenylmethylsilane with (±)-1-phenylethanol using palladium on charcoal in pentane solvent gave a mixture of diastereoisomeric 1-naphthylphenylmethyl-1-phenylethoxysilanes.[130] The nuclear magnetic resonance spectrum of the mixture analysed it as

56% (±)-1-naphthylphenylmethyl-(±)-1-phenylethoxysilane and 44% (∓)-1-naphthylphenylmethyl-(±)-1-phenylethoxysilane.[130]

The above mixture was then equilibrated in toluene at 84° for 24 hours with solid potassium hydroxide in the presence of (±)-1-phenylethanol (Experiment 43) to give a product which analysed as 60% (±)-1-naphthylphenylmethyl-(±)-1-phenylethoxysilane and 40% (∓)-1-naphthylphenylmethyl-(±)-1-phenylethoxysilane. Standard deviation on seven readings of the ratio of the methyl on silicon resonances at 9.34 and 9.39 τ, due to the above compounds, was about 1.0%. (±)-1-Naphthylphenylmethyl-(±)-1-phenylethoxysilane is, therefore, the diastereoisomer of lower energy. The absolute configuration of the (-)-(-) compound determined by Brook and co-workers is given below.[130]



Conformational analysis of this flexible alkoxy compound is difficult. In the most stable diastereoisomers of the 1-naphthylphenylmethyl- menthoxy and 1-phenylethoxy-silanes, it is interesting to note that if the asymmetric silicon centre is viewed from the rear of the Si-O bond and the steric order of groups is clockwise then the steric order of groups about the asymmetric carbon atom is also clockwise when viewed along the O-C bond. This arrangement corresponds to an <u>erythro</u> isomer which on an argument

based on interactions of a purely steric nature may be predicted to be the most stable.[16]

Formation of the diastereoisomeric benzylphenylmethyl-menthoxysilanes from the corresponding racemic silane and racemic menthol by the palladium catalysed reaction gave a mixture of diastereoisomers in the ratio 52:48. The major component gave a high field doublet, due to the pro-S-methyl protons, at 9.40 τ, whereas the other diastereoisomer had resonances centred at 9.45 τ.

The cause of the shielding mainly responsible for the doublet at 9.40 τ is unknown and, therefore, the preferential conformations of the two diastereoisomers cannot be inferred. Examination of molecular models fails to provide a clear-cut decision on this point.

Results from an asymmetric reaction involving partial formation of benzylphenylmethyl-(-)-menthoxysilanes should enable the absolute configurations at silicon to be found for both diastereoisomers. If, by analogy with 1-naphthyl-phenylmethyl- (-)-menthoxy- and -1-phenylethoxy- silanes, the erythro diastereoisomer is most readily formed then the relative steric order of benzyl and phenyl on silicon, in the absence of other factors, may be found for this type of substitution reaction.

In an attempt to extend this study a series of diastereoisomeric alkoxysilanes were prepared from (±)-1-naphthylphenylmethylsilane and various cyclic terpene alcohols using 10% palladium on charcoal as catalyst.(experiment 41).

The 100 MHz nuclear magnetic resonance spectrum of the compound prepared from (-)-isoborneol showed evidence of

the presence of diastereotopic resonances since the number of singlet resonances was more than would be expected from purely enantiotopic groups. However, because the compound contained approximately 35% of the isomeric bornyloxy compound as impurity (isoborneol, prepared from lithium aluminium hydride reduction of camphor, contains some borneol) the relationship of the peaks could not be determined and the ratio of diastereoisomers, therefore, not found.

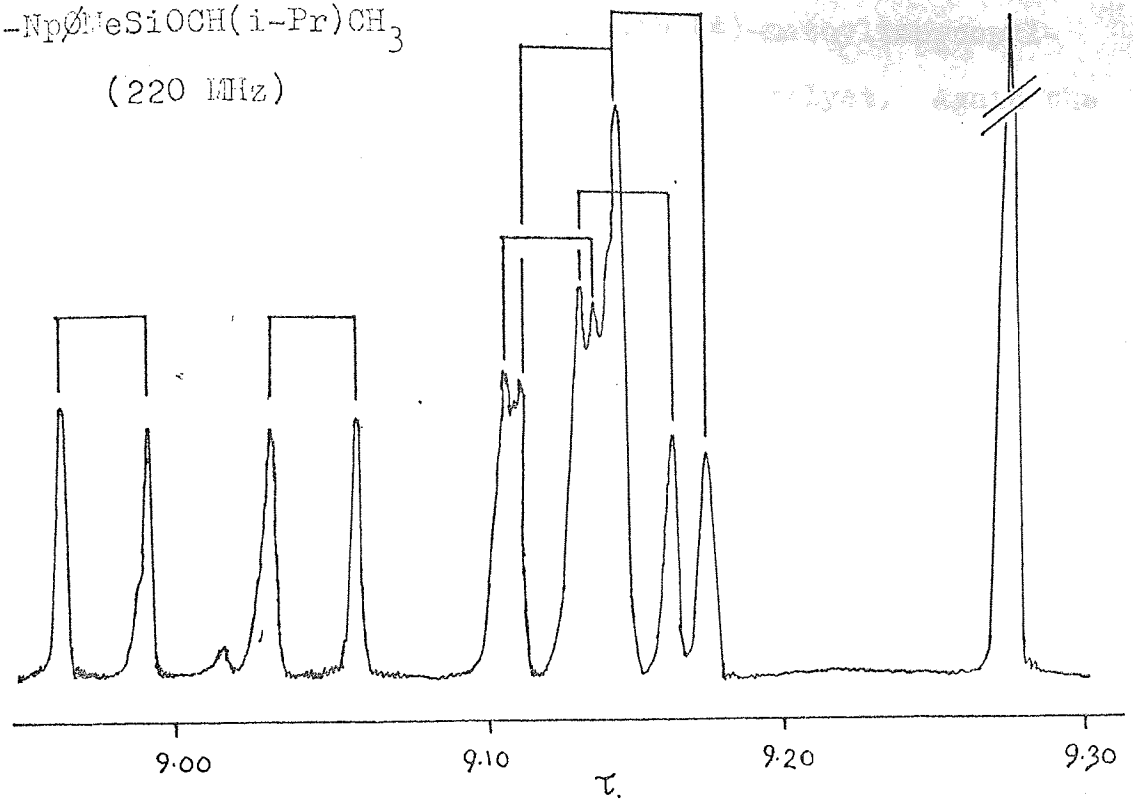
The bornyloxy compound, on the other hand, was formed with greater ease and in much higher purity. The nuclear magnetic resonance spectrum of this compound consisted of three resonances in the range 9.1-9.3 τ at 9.16 τ, 9.20 τ, and 9.27 τ in the ratio 4.3:1.7:6.0 respectively. The only explanation of these observations is that the low field resonance is due to a methyl (a) on carbon in the bornyloxy moiety of both diastereoisomers and in addition contains a peak due to another methyl group (b) in the bornyloxy group of only one diastereoisomer. The peak at 9.20 τ is due to the methyl group (b) of the second diastereoisomer. Resonance at 9.27 τ is explained by the methyl on silicon and the third methyl of the bornyloxy group which shows no diastereoisomeric shift. The ratio of diastereoisomers, therefore, approximates to 57:43.

The identities of the diastereoisomers were not established since a separation could not be affected. Neither were the identities of the methyl groups, responsible for the resonances, found. Deuterium labelling studies should provide the answer to some of these problems.

Fig. 19 shows the 100 MHz spectra of the bornyloxy- and isobornyloxy- silanes together with the 220 MHz spectrum

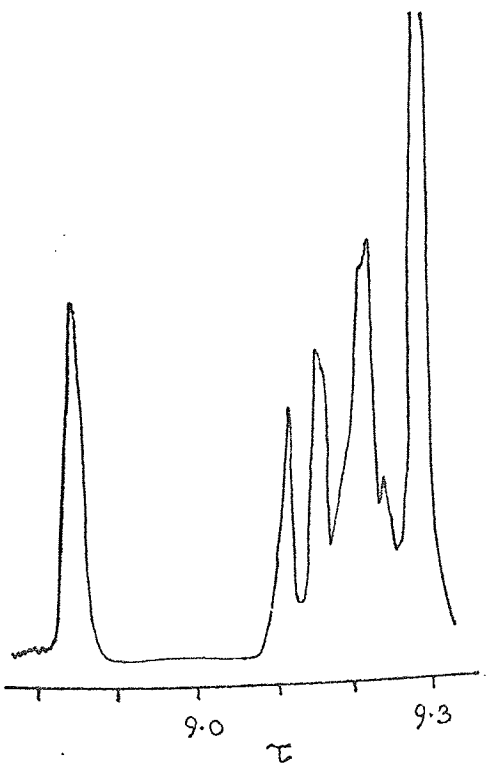
1-NpØMeSiOCH(i-Pr)CH_3

(220 MHz)



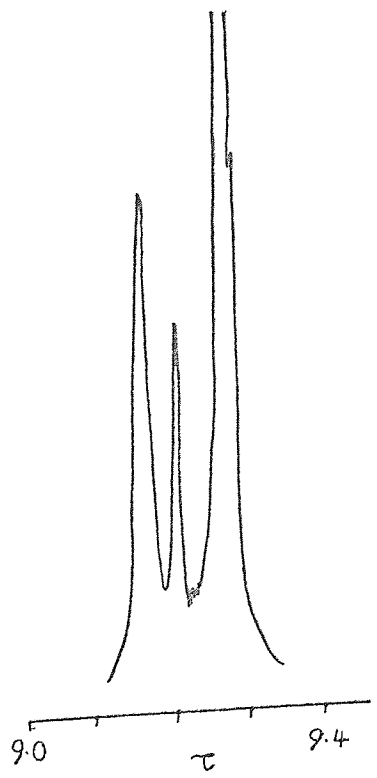
1-NpØMeSiOi-Born

(100 MHz)



1-NpØMeSiOBorn

(100 MHz)



of the diastereoisomeric mixture resulting from the reaction (±)-1-naphthylphenylmethylsilane with (±)-methylisopropylcarbinol using palladium on charcoal as catalyst. Again the

$$1\text{-Np}\emptyset\text{MeSi-O-CH(CH}_3\text{)iPr}$$

1-Naphthylphenylmethyl-2,3-dimethylpropoxysilane.

spectrum of this compound appears to possess two sets of doublet resonances due to an alkoxy methyl group centred at 8.96 and 9.02 τ. At 100 MHz these resonances overlap and give a triplet structure, but at 220 MHz are well separated doublets, J = 6.0 Hz. The identity of this methyl, however, is unknown. Ratio of the peaks indicates an approximate 50:50 composition of diastereoisomers.

Preparation and infrared spectra.

Reaction of 1-naphthylphenylmethylsilane and alcohols in methylene chloride using palladium on charcoal catalyst gives yields of alkoxysilanes that depend on the steric nature of the alcohol used. Thus menthol, borneol, iso-

$$R_3SiH + R'OH \xrightarrow{Pd/C} R_3SiOR' + H_2$$

borneol, methylisopropylcarbinol, and α-fenchol react to give 78%, 47%, 22%, 47%, 0% respectively. Other factors that effect the rate of such reactions are discussed in ref. 6(j).

In all the above reactions quantities of disiloxane and silanol were formed in side reactions. These were removed by chromatography.

All the infrared spectra of the alkoxy compounds formed from 1-naphthylphenylmethylsilane possessed absorptions typical of this system (see Experimental). In the absence

of suitable separation techniques differences due to the diastereoisomers of the bornyloxy-, isobornyloxy-, and 2,3-dimethylpropoxy- compounds were not found.

The infrared spectra of the separated menthoxy compounds, Ia and Ib, clearly showed their diastereoisomeric relationship, particularly in the pattern of absorptions at 1050-1110 cm^{-1}, due to Si-O and C-O stretching. However, because of their complexity they are unsuitable for determining optical purity.

XI.

EXPERIMENTAL.

Boiling points and melting points are uncorrected. Physical constants quoted as Lit. without qualification are from "Organosilicon compounds", volume 2, part 1, by Bazant et al.[138]

60 MHz proton resonance spectra were obtained using either a Perkin-Elmer R.10. Spectrometer operating at 35°C, or a Varian Associates A 60. 100 MHz nuclear magnetic resonance spectra were measured on a Perkin-Elmer R.14 and 220 MHz spectra recorded on a Varian Associates HA 220. Tetramethylsilane was used as an internal reference throughout.

Infrared spectra were recorded on a Perkin-Elmer Infracord 237 and Ultraviolet Absorptions measured on a Perkin-Elmer Infracord 137-U.V.

Optical rotation and optical rotatory dispersion spectra were measured on a Bellingham and Stanley Polarmatic 62 Spectropolarimeter fitted with a 450 watt Xenon filled ultraviolet lamp. Circular dichroism spectra were determined at Westfield College, London, on a Roussel-Jouan Dichrographe by courtesy of Prof. W. Klyne and Dr. P. M. Scopes.

Gas-liquid chromatographic analyses were carried out on a Pye series 104 chromatograph using a katharometer detector and helium as carrier gas. The column and conditions used are described in the appropriate sections.

Infrared assignments were based on the texts of Bellamy[139] and Flett[140] aided by the review of Bajer.[141] The interpretations of the nuclear magnetic resonance

spectra were based on the texts of Mathieson[142] and Emsley, Feeney, and Sutcliffe.[143]

The chemicals used were mainly laboratory reagent grade and obtained from Messrs. Hopkins and Williams. Solvents used for chromatography were A.R. grade and purchased from Fisons Ltd. Silica gel M.F.C. supplied by Messrs. Hopkins and Williams was used without further treatment for column chromatographic separations. Thin-layer plates were spread, in accordance with the manufacturer's recommendations, with a 0.25 mm. thick layer of Silica Gel G, supplied by E. Merck A.G.

1. Preparation of phenylmethyldimethoxysilane.[144]

To redistilled phenylmethyldichlorosilane (80 g. 0.42 mole) b.p.82°/13 mm. (Lit. 82°/13 mm.) in sodium dried diethyl ether (320 ml.) was added dropwise a mixture of methanol (26.8 g. 0.84 mole, freshly distilled from its magnesium salt[145]) and pyridine (66.5 g., dried over solid potassium hydroxide).

The mixture was stirred continuously and kept at 0°C throughout the addition. After 24 hours at room temperature the pyridine hydrochloride was removed and the filtrate fractionated through a 6" x ½" column filled with glass helices to give phenylmethyldimethoxysilane (55 g. 0.30 mole i.e. 72%) b.p. 36-38°/0.3 mm. (Lit. 199°/750 mm.): n.m.r. neat liquid, 9.74 τ, singlet, intensity 3, (methyl on silicon), 6.54 τ, singlet, intensity 6, (methoxy), 2.10-2.70 τ, multiplet, intensity 5, (aromatic): i.r. neat liquid, maxima (cm^{-1}) at 3080m, 3060m, (C-H stretching), 2000-1600w (overtones), 1595m (stretching), 1430s, 1120s, 1030m, 1000m,

740s, 700s, (monosubstituted aromatic ring bendings) - phenyl on silicon; 2970s, 2950s (C-H stretching) 1260s (symmetric deformation), 840s, 800s (rocking mode) - silicon methyl; 2840s, 1190s, 1080s (asymmetric Si-O stretching) - methoxy on silicon.

2. Preparation of (±)-1-naphthylphenylmethylmethoxysilane.

1-Naphthylphenylmethylmethoxysilane was prepared from phenylmethyldimethoxysilane and 1-naphthyl Grignard reagent by the method of Sommer et al.[4] in 77% yield, b.p. 136-138°/0.15 mm. m.p. 57° (Lit. b.p. 143-146°/0.15 mm. m.p. 62.5-63.5°, recrystallized from hexane): n.m.r. (CCl_4), 9.28 τ, singlet, intensity 3, (methyl on silicon), 6.50 τ, singlet, intensity 3, (methoxy), centred at 2.4 τ, broad complex band, intensity 12, (aromatic): i.r. thin film, maxima (cm^{-1}) at 3060m (aromatic C-H stretching), 2000-1600w (overtones), 1590m, 1430s, 1112s, 1023m, 1000w, 740s, 700s (monosubstituted aromatic ring bendings) - phenyl on silicon; 1500m, 1217m, 1145s, 985s - 1-naphthyl on silicon;[9] 2960m, 1255s, 830s, 800s - silicon methyl; 2830m, 1185m, 1080s - methoxy on silicon.

3. Preparation of (±)-1-naphthylphenylmethylsilane.

(±)-1-Naphthylphenylmethylmethoxysilane was reduced with lithium aluminium hydride[4] in diethyl ether to give (±)-1-naphthylphenylmethylsilane in 93% yield, m.p. 40-41° (Lit. m.p. 42°): n.m.r. (CCl_4), 9.32 τ, doublet, J_{CH_3SiH} = 4.0 Hz, integral 3 (methyl on silicon), 4.60 τ, quartet, J = 4.0 Hz, integral 1 (proton on silicon), 1.9-3.0 τ, complex band, integral 12 (aromatic): i.r. thin film, maxima (cm^{-1}) typical of the 1-naphthylphenylmethylsilyl system and at 2120s (Si-H stretching) - silicon hydride.

4. Preparation of (±)-naphthylphenylmethylchlorosilane.

An ethereal solution (200 ml.) containing 1-naphthyl lithium, (0.2 mole) prepared by halogen-metal interconversion by the method of Gilman and Moore,[146] was added dropwise with stirring to redistilled phenylmethyldichlorosilane (36.5 g. 0.181 mole) over a period of 1 hour. The reaction mixture was then allowed to stand overnight at room temperature.

Fractional distillation at reduced pressure gave a fraction (30 g.) b.p. 148-160°/1.0 mm., yield 60% (on dichlorosilane): n.m.r. (CCl_4), 9.00 τ, singlet, intensity 3, (methyl on silicon), centred at 2.67 τ, multiplet, intensity 12, (aromatic): i.r. thin film, absorptions typical of the 1-naphthylphenylmethylsilyl system.

5. Attempted asymmetric reduction of 1-naphthylphenylmethylchlorosilane with di-isopinocampheylborane in diglyme.

Di-isopinocampheylborane was prepared by the method of Brown et al[147] from (+)-α-pinene (50 m.mole) $[\alpha]_{588}$ +54.0° (c 4.0, EtOH) (Lit. $[\alpha]_D$ +51.1°[148]), sodium borohydride (0.71 g.), and redistilled boron trifluoride etherate (3.55 g.).

To this mixture (±)-1-naphthylphenylchlorosilane (7.05 g. 25 m.mole) was added. The temperature was maintained at approximately 0° for 2 hours and then left overnight at room temperature. Work up with 20% aqueous hydrochloric acid gave a viscous oil (6.5 g.): i.r. thin film, maxima (cm^{-1}) at 3450s and 3300s, attributed to silanol (no absorption at 2120 cm^{-1} due to Si-H stretching).

Another attempt at the reduction was made using a twelve-fold excess of di-isopinocampheylborane to chloro-

silane. The mixture was left overnight at room temperature, and worked up in the manner described, to give once more a viscous oil, the i.r. of which was very similar to that outlined above.

6. Preparation of (+)-neomenthyl chloride.

(+)-Neomenthyl chloride was prepared from (-)-menthol by the method of Ingold[149] in 47% yield, b.p. 52°/1.6 mm. $[\alpha]_D$ +11.00°. (Lit. $[\alpha]_D$ +38.5°).

7. Attempted reduction of (±)-1-naphthylphenylmethylmethoxysilane with the Grignard reagent of (+)-neomenthyl chloride.

a) The Grignard reagent of (+)-neomenthyl chloride (4.38 g. 25 m.mole) was prepared using the procedure of Smith and Wright.[150] The reaction required initiation with a small quantity of ethylmagnesium bromide. Volumetric titration of an aliquot from the above reaction indicated that the yield of Grignard reagent was 53%.

To this mixture was added (±)-1-naphthylphenylmethylmethoxysilane (0.5 g. 1.8 m.mole). Ether was then distilled off and under an atmosphere of nitrogen the semi-solid mixture was heated at 98° on a heating bath for 3 days.

Addition of diethyl ether (50 ml.) and destruction of the Grignard with dilute acid gave an oil from the organic layer. Examination of this product by thin-layer chromatography and infrared showed it to consist of hydrocarbons from the Grignard reagent and 1-naphthylphenylethylmethylsilane. No peak at 2120 cm^{-1} due to Si-H was observed.

b) The above reaction was repeated but this time the synthesis of the Grignard reagent was initiated with ethylene dibromide. Product analysis of the mixture of

methoxysilane and Grignard reagent, after heating under an inert atmosphere for 3 days, showed the complete absence of reduced silane. The methoxysilane appeared to be completely unaffected by the above treatment and was recovered in good yield (>80%).

8. Asymmetric reduction of (±)-1-naphthylphenylmethylmethoxysilane with 1:1 complexes formed from optically active alkaloids and lithium aluminium hydride in diethyl ether.

The following alkaloids were used:-

(+)-quinidine, recrystallized from absolute EtOH, dried at 120° to give anhydrous material $[\alpha]_{588}$ +243° (c 0.044, EtOH) [Lit.[148] $[\alpha]_D^{15}$ +243.5° (99% EtOH).

(-)-quinine, dried at 120° overnight $[\alpha]_{588}$ -145° [Lit.[148] $[\alpha]_D^{15}$ -169.3° (in 97% EtOH)].

(+)-cinchonine, dried at 120° overnight $[\alpha]_{588}$ +204° (c 0.41, EtOH) [Lit.[148] $[\alpha]_D$ +229° (EtOH)].

(-)-cinchonidine, dried at 120° overnight $[\alpha]_{588}$ -104.3° (EtOH) [Lit.[148] $[\alpha]_D^{15}$ -107.5° (EtOH)].

(+)-ψ-ephedrine, distilled en vacuo b.p. 132°/18 mm. $[\alpha]_{588}$ +49.4° (EtOH) m.p. 117° [Lit.[148] $[\alpha]_D^{20}$ +51.24° (EtOH) m.p. 117-118°].

(-)-ephedrine, distilled b.p. 129°/4 mm. $[\alpha]_{588}$ -4.96° [Lit.[148] $[\alpha]_D^{20}$ -6.3° (EtOH)].

8a. Reduction with (+)-quinidine-lithium aluminium hydride complex.[53]

The complex hydride was prepared *in situ* by the addition of

(+)-quinidine (3.56 g. 11 m.mole) to lithium aluminium hydride (0.42 g. 11 m.mole) in diethyl ether (100 ml., previously distilled from lithium aluminium hydride). The mixture was refluxed for 30 min. and a solution of (±)-methoxysilane (10 g. 34.8 m.mole) in ether (20 ml.) was added. After refluxing for a further 4 hr. the excess of hydride was decomposed with dilute sulphuric acid, the ether layer washed several times with water, dried over anhydrous sodium sulphate, and the ether removed to give an oil (9.07 g.). This product (8.8 g.) was chromatographed on silica gel, using as eluant a mixture (1:9) of benzene and light petroleum (b.p. 60-80°) to give 1-naphthylphenylmethylsilane (2.93 g.) $[\alpha]_{588}$ +1.96°; $[\alpha]_{400}$ +6.47° (c 13.91, EtOH). Change of eluant to benzene gave unreacted methoxysilane (4.31 g.) $[\alpha]_{588}$ -0.93°; $[\alpha]_{400}$ -3.74° (c 14.34, EtOH). The n.m.r. and i.r. spectra of these products were identical with those of authentic racemic samples. The purity was further established by t.l.c. and by their u.v. extinction coefficients, which agreed very closely with the values for the racemic materials.

8b. Crystallization of the active silane from the partial reduction with (+)-quinidine-lithium aluminium hydride complex.

The crystals of active 1-naphthylphenylmethylsilane were pressed between Whatman's 541 filter paper to remove small quantities of uncrystallized silane.

Three successive crystallizations from SpectroSol hexane fraction, held at -10° in an ice-salt mixture, gave the pure dextro-enantiomer m.p. 63°, $[\alpha]_{588}$ +35.5° (c 0.12, hexane) [Lit.[4] m.p. 64°, $[\alpha]_D$ +35.0°].

Attempts to increase the optical purity of the active methoxysilane by similar fractional crystallization failed and so it was completely reduced with lithium aluminium hydride in diethyl ether. Fractional crystallization of the product gave the laevo-enantiomer of the silane m.p. 59° $[\alpha]_{588}$ -29° (c 0.34, hexane).

8c. Reduction with 1:1 complexes of lithium aluminium hydride and optically active alkaloids.

The method described in 8a. was used on a scale of one fifth. The extents of reduction were calculated on the isolated yields of silane. The purity of the fractions was checked by t.l.c. and i.r. and optical rotations measured at various wavelengths.

The results are given below under the heading of the particular alkaloid used and are also tabulated for comparison in the relevant section of the discussion.

i) (-)-quinine

1-naphthylphenylmethylsilane, 0.63 g. 35.4%
$[\alpha]_{588}$ +1.52°; $[\alpha]_{400}$ +4.83° (c 15.72, hexane);
1-naphthylphenylmethylmethoxysilane, 0.60 g.
$[\alpha]_{588}$ -0.24°; $[\alpha]_{400}$ -0.55° (c 8.21, hexane).

ii) (+)-cinchonine

1-naphthylphenylmethylsilane, 0.76 g. 42.7%
$[\alpha]_{588}$ +1.24°; $[\alpha]_{400}$ +4.05° (c 26.25, hexane);
1-naphthylphenylmethylmethoxysilane, 1.17 g.
$[\alpha]_{588}$ -0.40°; $[\alpha]_{400}$ -1.79° (c 27.91, hexane).

iii) (-)-cinchonidine

1-naphthylphenylmethylsilane, 0.50 g. 28%

$[\alpha]_{588}$ -0.64°; $[\alpha]_{400}$ -2.00° (c 15.47, hexane);

1-naphthylphenylmethylmethoxysilane, 1.12 g.

$[\alpha]_{588}$ +0.13°; $[\alpha]_{400}$ +0.59° (c 19.24, hexane).

iv) (-)-ephedrine

1-naphthylphenylmethylsilane, 0.40 g. 22.5%

$[\alpha]_{588}$ +0.26°; $[\alpha]_{400}$ 0.42° (c 23.01, hexane);

1-naphthylphenylmethylmethoxysilane, 1.28 g.

No observable optical activity (c 36.42, hexane).

v) (+)-ψ-ephedrine

1-naphthylphenylmethylsilane, 0.49 g. 27.5%

$[\alpha]_{588}$ +4.53°; $[\alpha]_{400}$ +14.6° (c 16.67, hexane);

1-naphthylphenylmethylmethoxysilane, 0.95 g.

$[\alpha]_{588}$ -0.86°; $[\alpha]_{400}$ -3.44° (c 13.7, hexane).

9. Asymmetric reduction of 1-naphthylphenylmethylmethoxysilane using 1:1 complexes formed from optically active alcohols and lithium aluminium hydride in diethyl ether.

The following terpene alcohols were used:-

(-)-menthol, supplied by Eastman-Kodak, distilled b.p. 119°/30 mm.

$[\alpha]_{588}$ -32.6° (c 4.07, EtOH) [Lit.[148] b.p. 111°/20 mm. $[\alpha]_D^{18}$ -50.1° (EtOH)];

(-)-borneol, distilled b.p. 212°, m.p. 212-3° (sealed tube)

$[\alpha]_{588}$ -22° (EtOH) [Lit.[148] b.p. 212°, m.p. 208° $[\alpha]_D^{20}$ -37.74°];

(-)-isoborneol, from lithium aluminium hydride reduction of (+)-camphor, $[\alpha]_{588}$ -14.2° (MeOH) [Lit.[148] $[\alpha]_D^{20}$ -32.3°(MeOH)];

(+)-α-fenchol, supplied by Koch-Light, $[\alpha]_{588}$ +10.4° (c 4.67, EtOH) [Lit.[148] $[\alpha]_D$ +10.36° (EtOH)];

cholesterol, supplied by British Drug Houses, $[\alpha]_{588}$ -36.7° (c 1.87, $CHCl_3$) [Lit.[148] $[\alpha]_D$ -31.12° (Et_2O); B.D.H. quote $[\alpha]_D$ -38.5 to -40.5° ($CHCl_3$)];

lanosterol, supplied by Koch-Light, m.p. 130-1°, $[\alpha]_{588}$ +41.2° (c 0.85, $CHCl_3$) [Lit.[148] m.p. 140-1° $[\alpha]_D$ +58° ($CHCl_3$)];

Reductions were also done using:-

(+)-2-octanol, supplied by Koch-Light, $[\alpha]_{588}$ +7.8° (c 13, MeOH) [Lit.[148] $[\alpha]_D^{17}$ +9.9°].

9a. Asymmetric reduction with 1:1 molar complexes of (-)-menthol and lithium aluminium hydride.

To a stirred suspension of lithium aluminium hydride (0.085 g. 2.24 m.mole) in diethyl ether (10 ml. previously distilled from lithium aluminium hydride) was added dropwise 10 ml. of an ethereal solution of (-)-menthol (0.349 g. 2.24 m.mole). The mixture was then refluxed for 30 minutes after complete addition and a solution of (±)-methoxysilane (2 g. 6.96 m.mole) in ether (4 ml.) was added. After refluxing for a further 4 hours the excess hydride was decomposed with dilute sulphuric acid (20% v/v), the temperature being maintained below 10° by an ice-bath. The ether layer was washed several times with dilute sulphuric acid, then with water, and dried over anhydrous sodium sulphate.

Removal of ether gave a product (2.12 g.) which still contained (-)-menthol.

The reaction mixture was chromatographed on silica gel, using a mixture (1:9) of benzene and light petroleum (b.p. 60-80°) to give 1-naphthylphenylmethylsilane (0.879 g.). $[\alpha]_{588}$ +0.46°, $[\alpha]_{400}$ +1.55° and 1-naphthylphenylmethylmethoxysilane (0.69 g.) $[\alpha]_{588}$ -0.13°, $[\alpha]_{400}$ -0.89°.

The n.m.r. and i.r. spectra of these products were identical with those of authentic racemic samples; no trace was found of 1-naphthylphenylmethyl-(-)-menthoxysilane or (-)-menthol.

9b. Asymmetric reduction with 1:1 molar complexes of other optically active alcohols and lithium aluminium hydride.

The procedure detailed in the previous section was followed. The results are given below under the heading of the particular alcohol used.

i) (-)-borneol

1-naphthylphenylmethylsilane, 1.0 g. 56.2%

$[\alpha]_{588}$ +0.20°; $[\alpha]_{400}$ +0.66° (c 13.58, hexane);

1-naphthylphenylmethylmethoxysilane, 0.32 g.

Optical activity too weak to measure.

ii) (-)-isoborneol

1-naphthylphenylmethylsilane, 0.83 g. 46.6%

No observable optical activity;

1-naphthylphenylmethylmethoxysilane, 0.95 g.

Optically inactive.

iii) (+)-α-fenchol

1-naphthylphenylmethylsilane, 0.56 g. 31.5%

$[\alpha]_{588}$ +0.34°; $[\alpha]_{400}$ +1.08° (c 13.97, hexane);

1-naphthylphenylmethylmethoxysilane, 0.84 g.

$[\alpha]_{588}$ -0.10°; $[\alpha]_{400}$ -0.35° (c 15.9, hexane).

iv) cholesterol

1-naphthylphenylmethylsilane, 0.55 g. 31%

No observable optical activity;

1-naphthylphenylmethylmethoxysilane,

No observable optical activity.

v) lanosterol

No reduction occurred and only 1-naphthylphenylmethyl-methoxysilane separated.

vi) Repeat attempt at asymmetric reduction with 1:1 molar complex of lanosterol and lithium aluminium hydride.

The procedure described in section 9a. was followed except that the mixture of methoxysilane and complex hydride was refluxed for 24 hours.

1-naphthylphenylmethylsilane, 0.10 g. 5.6%

No observable optical activity;

1-naphthylphenylmethylmethoxysilane,

No observable optical activity.

vii) (+)-2-octanol

1-naphthylphenylmethylsilane, 0.42 g. 23.6%

$[\alpha]_{588}$ +0.26°; $[\alpha]_{400}$ +0.70° (c 21.19, hexane);

1-naphthylphenylmethylmethoxysilane, 1.05 g.

$[\alpha]_{588}$ 0.0°; $[\alpha]_{400}$ -0.05° (c 15.85, hexane).

10. Attempted asymmetric reduction of (±)-1-naphthylphenylmethylmethoxysilane using a 2:1 molar complex between (-)-menthol and lithium aluminium hydride in diethyl ether.

To a stirred suspension of lithium aluminium hydride

(0.086 g. 2.25 m.mole) in diethyl ether (10 ml.) was added dropwise 10 ml. of an ethereal solution of (-)-menthol (0.701 g. 4.5 m.mole)

The solution was refluxed for 30 min. after complete addition and a solution of (±)-methoxysilane (2 g. 6.96 m.mole) in ether (4 ml.) was added. After refluxing for 4 hours the mixture was worked up using the procedure detailed in section 9a.

Infrared examination of the product revealed that very little reduction had occurred (< 5%).

11. Asymmetric reduction of (±)-1-naphthylphenylmethylchlorosilane with 1:1 (+)-quinidine-lithium aluminium hydride complex in diethyl ether.

a) (+)-Quinidine (0.711 g. 2.20 m.mole) and lithium aluminium hydride (0.084 g. 2.20 m.mole) in diethyl ether (20 ml.) were used to prepare the 1:1 complex in the procedure described in section 8a.

(±)-1-Naphthylphenylmethylchlorosilane (2.0 g. 7.1 m.mole) in diethyl ether (4 ml.) was added and the mixture refluxed for 2 hours. The work up then followed the procedure given in section 8a. Chromatography using a mixture (1:9) of benzene and light petroleum (b.p. 60-80°) on silica gel gave 1-naphthylphenylmethylsilane (0.335 g. 19%).

b) The reduction was repeated but this time refluxed for 4 hours. Anhydrous methanol (5 ml.) was added and the mixture stirred for a further 30 minutes. Work up with dilute sulphuric acid was then followed in the normal manner. Chromatographic separation gave:-

1-naphthylphenylmethylsilane, 0.445 g. 25%

$[\alpha]_{588}$ +0.27°; $[\alpha]_{400}$ +0.70° (c 15.90, hexane);

1-naphthylphenylmethylmethoxysilane, 1.11 g.

$[\alpha]_{588}$ +0.12°; $[\alpha]_{400}$ +0.35° (c 18.35, hexane).

The i.r. spectra of the fractions isolated were identical with authentic racemic samples.

c) Reduction with 1:1 alkaloid-lithium aluminium hydride in diethyl ether.

The procedure detailed in 11b) was followed:

i) (-)-quinine

1-naphthylphenylmethylsilane, 0.284 g. 16%

$[\alpha]_{588}$ -0.17°; $[\alpha]_{400}$ -0.57° (c 17.32, hexane);

1-naphthylphenylmethylmethoxysilane, 0.512 g.

Optically inactive.

ii) (-)-cinchonidine

1-naphthylphenylmethylsilane, 0.444 g. 25%

$[\alpha]_{588}$ -0.25°; $[\alpha]_{400}$ -0.86° (c 16.49, hexane);

1-naphthylphenylmethylmethoxysilane, 0.85 g.

No observable optical activity.

iii) (+)-cinchonine

1-naphthylphenylmethylsilane, 0.395 g. 22%

$[\alpha]_{588}$ +1.03°; $[\alpha]_{400}$ +3.36° (c 18.56, hexane);

No methoxysilane was formed - only silanol.

d) Reduction with 1:1 (-)-menthol-lithium aluminium hydride in diethyl ether.

After refluxing for 4 hours dry methanol (5 ml.) and a few drops of dry pyridine were added. The work up was then followed in the normal way.

Chromatography gave the silane (0.27 g.) but on removal of solvent and heating decomposition occurred and a sublimate formed; the i.r. spectrum and m.p. of which were identical with those of pure naphthalene.

12. Preparation of (±)-phenylethylmethylmethoxysilane.

To an ethereal solution (25 ml.) of phenylmethyldimethoxysilane (8.2 g. 0.1 mole) was added, with stirring, an ether solution of ethylmagnesium bromide (100 ml. 0.1 M). The mixture was left overnight at room temperature and then refluxed for 1 hr. prior to work-up with saturated aqueous ammonium chloride. The ether layer was then washed with water and dried over anhydrous magnesium sulphate.

Solvent was removed by distillation and the residue distilled at atmospheric pressure to give a fraction (14 g. 78%) b.p. 199-202° (Lit.[6j] 110°/23 mm.): n.m.r. 60 MHz neat liquid, 9.70 τ, singlet, intensity 3 (methyl on silicon), 8.6-9.5 τ, complex A_3B_2 type absorptions, intensity 4.38 (ethyl on silicon), 6.63 τ, singlet, intensity 2.16 (methoxy of phenylethylmethylmethoxysilane), 6.53 τ, singlet, intensity 1.08 (methoxy of dimethoxysilane), 2.2-2.9 τ, multiplet, intensity 5 (aromatic): i.r. neat liquid, maxima (c.m.$^{-1}$) at 3070m, 3050m,(C-H stretching, aromatic), 2000-1600w (overtones), 1590w (C=C stretching), 1430m, 1110s, 1000m, 740s, 700s - phenyl on silicon; 2950s, 2940s (C-H stretching), 1250s (symmetric deformation), 830s, 800s (rocking mode) - methyl and ethyl on silicon; 2830s, 1180m, 1080s (asymmetric Si-O stretching) - methoxy on silicon.

G.l.c. at 115°, using a 9' x 1/8" o.d. stainless steel 4 mm. bore column packed with S.E.30 on firebrick and a flow

rate of 50 ml./min. helium carrier gas, gave two peaks with retention times 9 mins and 11.5 mins., corresponding to dimethoxysilane and phenylethylmethylmethoxysilane respectively. Integration found the phenylethylmethylmethoxysilane to be 88% pure.

N.B. N.m.r. 100 MHz, (15% $^{w}/_{v}$ in CCl_4) shows that the ethyl group on silicon in this compound is an A_3B_2 spectrum closely resembling a second order spectrum with $J/\Delta\nu = 0.33$.

13. Preparation of (±)-phenylethylmethylsilane.

(±)-Phenylethylmethylmethoxysilane (2 g. 11.1 m.mole) in diethyl ether (5 ml.) was added to lithium aluminium hydride (0.5 g. 13.2 m.mole) in diethyl ether (20 ml.). The mixture was refluxed for 24 hours and the excess hydride destroyed by addition of saturated aqueous ammonium chloride. The ether layer was separated, washed with water, and dried over anhydrous magnesium sulphate.

Ether was removed by distillation and the pot residue pulled down on a vacuum pump at 40 mm. pressure to remove last traces of solvent and give a colourless oil (1.62 g. 97%). G.l.c. at 115° on a 9' column packed with firebrick, using S.E. 30 silicone gum as liquid phase and helium as carrier gas, gave a major peak with retention time 5 min. and a minor one, due to phenylmethylsilane, at 2.5 min. (from phenylmethyldimethoxysilane in original methoxysilane).

Column chromatography on silica gel using 1:4 benzene-light petroleum (b.p. 60-80°) gave pure phenylethylmethylsilane (1.5 g. 90%) as a colourless oil: n.m.r. 100 MHz (CCl_4), 9.70 τ, doublet, intensity 3, $J_{CH_3-H} = 4.0$ Hz, (methyl on silicon), 8.9-9.4 τ, multiplet, intensity 5

(ethyl on silicon), 5.60 τ, multiplet, intensity 1 (proton on silicon), 2.3-2.7 τ, complex multiplet, intensity 5 (aromatic): i.r. thin film, maxima (cm^{-1}), absorptions typical of the phenylethylmethylsilyl system, 2110s (stretching) - silicon hydride.

14. Asymmetric reduction of (±)-phenylethylmethylmethoxysilane with (+)-cinchonine-lithium aluminium hydride complex.

A 1:1 complex was prepared from lithium aluminium hydride (0.207 g. 5.42 m.mole) and (+)-cinchonine (1.63 g. 5.55 m.mole) in diethyl ether (40 ml.) in the manner described previously. To this was added (±)-phenylethylmethylmethoxysilane (1.495 g. 8.27 m.mole) in ether (20 ml.) and the mixture refluxed for 24 hours.

Excess hydride was then decomposed by the addition of saturated aqueous ammonium chloride (10 ml.) and the alkaloid removed by filtration after precipitation by additions of light petroleum. After drying over anhydrous magnesium sulphate solvents were removed by careful distillation to give a colourless oil (1.54 g.): i.r. thin film, maxima (cm^{-1}) showed strong absorptions at 2830 (methoxy on silicon) and 2120 (Si-H stretching). G.l.c. showed the presence of phenylethylmethylsilane (56%) and phenylethylmethylmethoxysilane (43%), together with a small quantity of phenylmethylsilane (from reduction of phenylmethyldimethoxysilane impurity).

Chromatography on a silica gel column [20 x 2 cm. using 1:4 benzene-light petroleum mixture (b.p. 60-80°)] gave phenylethylmethylsilane (0.57 g. 46%) -

$[\alpha]_{588}$ +0.50°; $[\alpha]_{400}$ +1.68° (c 15.97, hexane) [Lit.[16] $[\alpha]_D$ +1.22° (hexane)]; $[\alpha]_{588}$ +0.95°; $[\alpha]_{400}$ +3.06° (c 19.52; CCl_4) [Lit.[16] $[\alpha]_D$ +2.53° (CCl_4)].

The optical yield of the silane was calculated to be 38-41% based on the two values reported for the optically pure compound.

Change of solvent to benzene eluted phenylethylmethylmethoxysilane (0.216 g. 14.5%) - $[\alpha]_{588}$ -3.89°; $[\alpha]_{400}$ -10.3° (c 19.14, hexane): i.r. and n.m.r. spectra of the fractions were identical with those of the authentic racemic compounds.

i) (-)-cinchonidine

phenylethylmethylsilane, 0.57 g. 46% (by g.l.c. 51%) $[\alpha]_{588}$ -0.18°; $[\alpha]_{400}$ -0.61°; $[\alpha]_{303}$ -1.85° (c 15.89, CCl_4), Optical yield 7.1%;

phenylethylmethylmethoxysilane, 0.31 g. 21% $[\alpha]_{588}$ +0.59°; $[\alpha]_{400}$ +1.71°; $[\alpha]_{303}$ +4.68° (c 16.84, CCl_4).

ii) (+)-quinidine

phenylethylmethylsilane, 0.59 g. 47% (by g.l.c. 54%) $[\alpha]_{588}$ +0.44°; $[\alpha]_{400}$ +1.34°; $[\alpha]_{303}$ +4.30° (c 17.84, CCl_4), Optical yield 17.2%;

phenylethylmethylmethoxysilane, 0.48 g. 32% $[\alpha]_{588}$ -1.35°; $[\alpha]_{400}$ -4.50°; $[\alpha]_{303}$ -13.50° (c 17.02, hexane).

iii) (-)-quinine

phenylethylmethylsilane, 0.65 g. 52% (by g.l.c. 64%) $[\alpha]_{588}$ 0.0°; $[\alpha]_{400}$ 0.0°

phenylethylmethylmethoxysilane, 0.25 g. 17% $[\alpha]_{588}$ -0.08°; $[\alpha]_{303}$ -0.47° (c 17.66, hexane).

iv) (+)-ψ-ephedrine

phenylethylmethylsilane, 0.20 g. 16% (by g.l.c. 34%) $[\alpha]_{588}$ +0.05°; $[\alpha]_{400}$ +0.16°; $[\alpha]_{303}$ +0.47° (c 16.76, hexane), Optical yield 4.1%;

phenylethylmethylmethoxysilane, 0.60 g. 40% $[\alpha]_{588}$ -0.07°; $[\alpha]_{400}$ -0.18°; $[\alpha]_{303}$ -0.50° (c 17.14, hexane).

15. Asymmetric reduction of (±)-phenylethylmethylmethoxysilane with 1:1 (-)-menthol-lithium aluminium hydride complex.

Reaction of methoxysilane (1.5 g. 8.27 m.mole) and 1:1 (-)-menthol-lithium aluminium hydride complex (5.51 m.mole) in refluxing ether (40 ml.) for 4 hours gave a 65% yield of silane.

Separation of the products gave phenylethylmethylsilane with a slight, but significant, laevo-rotation: $[\alpha]_{588}$ -0.03°; $[\alpha]_{303}$ -0.40° (c 16.5; CCl_4). This corresponds to an optical purity of about 1%. The unreacted methoxysilane had $[\alpha]_{588}$ +0.11°; $[\alpha]_{313}$ +1.51° (c 15.9, hexane).

16. Preparation of (±)-benzylphenylmethylmethoxysilane.

Benzylmagnesium chloride was prepared by slowly adding a solution of benzyl chloride (12.7 g. 0.1 mole) in anhydrous diethyl ether (50 ml.) to magnesium turnings (2.6 g.) in diethyl ether (50 ml.) with a trace of iodine present. The light green solution of Grignard reagent was transferred under nitrogen to a dropping funnel and added dropwise to a stirred solution of phenylmethyldimethoxysilane (18.2 g. 0.1 mole) in diethyl ether. The mixture was

stirred overnight at room temperature and worked up with ice-cold saturated aqueous ammonium chloride. The ether layer was washed with water and dried over anhydrous magnesium sulphate.

Removal of solvent and distillation of the product gave a clear, colourless oil (21.2 g. 88%) b.p. 90-91°/0.05 mm.: n.m.r. 100MHz (50% $^{v}/_{v}$ CCl_4), 9.74 τ, singlet, intensity 3 (methyl on silicon), centred at 7.65 τ, AB quartet, $J_{AB}/\Delta\nu_{AB}$ = 1.48, intensity 2, (magnetically and chemically non-equivalent benzylic protons[151]), 6.65 τ,singlet, intensity 3 (methoxy), 2.4-3.1 τ, complex multiplet, intensity 10 (aromatic): i.r. thin film, maxima (cm^{-1}) at 3070s, 3030s (C-H stretching), 2000-1700w (overtones), 1600 with shoulders at 1593 and 1585 (C═C stretching), 1430s, 1120s, 1030m, 1000m, 740s, 700 - phenyl on silicon, 2900m, 1450s (CH_2 deformation), 1210s, 1160s, 905m - benzyl on silicon, 2960s, 2940s (C-H stretching) - methoxy on silicon. (Found: C, 74.4; H, 7.6; Si, 11.8. $C_{15}H_{18}SiO$ requires C, 74.3; H, 7.5; Si, 11.6%).

17. Preparation of (±)-benzylphenylmethylsilane.

Reduction of (±)-benzylphenylmethylmethoxysilane (2 g. 8.25 m.mole) with lithium aluminium hydride (0.5 g.) in refluxing diethyl ether (25 ml.) for 18 hours gave, after acid work up, (±)-benzylphenylmethylsilane as a colourless oil (1.4 g. 80%): n.m.r. 100MHz (CCl_4), 9.73 τ, doublet, intensity 3, J_{CH_3H} = 3.7 Hz (methyl on silicon), 7.65 τ, multiplet, intensity 2, consisting of two AB quartets split by the proton on silicon (magnetically non-equivalent protons of benzylic methylene[151]), centred at 5.50 τ, sextet,

intensity 1, (proton on silicon split by methyl and benzyl methylene protons on silicon), 2.4-3.1 τ, multiplet, intensity 10 (aromatic): i.r. thin film, maxima (cm^{-1}), absorptions typical of the benzylphenylmethylsilyl system (see experiment 16), at 2120s (Si-H stretching), no indication of any methoxy on silicon.

T.l.c. on silica gel developed with 1:9 benzene/light petroleum (b.p. 60-80°) - one spot, R_F 0.79.

18. Acid Hydrolysis of (±)-benzylphenylmethylmethoxysilane.

A solution of (±)-methoxysilane (0.51 g. 2.11 m.mole) in diethyl ether (10 ml.) was shaken with 20% $^{v}/_{v}$ aqueous sulphuric acid for five minutes and then three times with water. After the ether layer had been dried over anhydrous magnesium sulphate the solvent was removed to give an oil (0.41 g.): i.r. thin film, maxima (cm^{-1}), absorptions typical of the benzylphenylmethylsilyl system (c.f. previous experiments), at 3400s (O-H stretching), 860m - silanol; 2840, 1190, 1090 (decreased intensity) - methoxy on silicon.

Continued shaking with 20% $^{v}/_{v}$ aqueous sulphuric acid overnight gave an oil identified as (±)-benzylphenylmethylsilanol: n.m.r. 100MHz (CCl_4), 9.78 τ, singlet, intensity 3, (methyl on silicon), 7.72 τ, singlet, intensity 2, (proton of benzylic methylene), 7.22 τ, broad singlet, intensity 1 (hydroxylic proton), 2.4-3.1 τ, complex multiplet, intensity 10 (aromatic): i.r. thin film, no indication of methoxy on silicon. The spectra showed no evidence of any disiloxane formation.

19. i) Asymmetric reduction of (±)-benzylphenylmethylmethoxysilane with (+)-cinchonine-lithium aluminium hydride complex.

(±)-Benzylphenylmethylmethoxysilane (2.0 g. 8.25 m.mole) was partially reduced by refluxing for 24 hours with a 1:1 molar complex of (+)-cinchonine (1.63 g. 5.54 m.mole) and lithium aluminium hydride (0.207 g. 5.42 m.mole) in diethyl ether (60 ml.). Excess hydride was destroyed with saturated aqueous ammonium chloride (10 ml.) and the alkaloid removed by filtration. The ether layer was washed, dried over anhydrous magnesium sulphate, and the ether removed by distillation. The product (1.96 g.) was chromatographed on a silica gel column using 1:9 benzene/light petroleum (b.p. 60-80°) and gave benzylphenylmethylsilane (0.711 g. 41%), $[\alpha]_{588}$ -7.79°; $[\alpha]_{400}$ -21.4° (c 14.13, hexane) whose n.m.r. was identical with that of racemic benzylphenylmethylsilane. Change of solvent to benzene gave benzylphenylmethylmethoxysilane (0.76 g. 38%), $[\alpha]_{588}$ +1.86°; $[\alpha]_{400}$ +5.23° (c 16.68, hexane).

ii) (-)-cinchonidine
benzylphenylmethylsilane, 0.843 g. 48%
$[\alpha]_{588}$ +3.04°; $[\alpha]_{400}$ +8.16° (c 16.06, hexane);
benzylphenylmethylmethoxysilane, 0.873 g.
$[\alpha]_{588}$ -0.86°; $[\alpha]_{400}$ -2.42° (c 15.35, hexane).

iii) (+)-quinidine
benzylphenylmethylsilane, 0.52 g. 28.5%
$[\alpha]_{588}$ -1.64°; $[\alpha]_{400}$ -4.51° (c 13.29, hexane).
benzylphenylmethylmethoxysilane, 1.09 g. 54.5%
$[\alpha]_{588}$ +0.16°; $[\alpha]_{400}$ +0.59° (c 15.17, hexane).

iv) (-)-quinine

benzylphenylmethylsilane, 0.66 g. 37% (n.m.r. 47%)

$[\alpha]_{588}$ +1.77°; $[\alpha]_{400}$ +4.78° (c 17.37, hexane);

benzylphenylmethylmethoxysilane, 0.73 g. 36.5%

$[\alpha]_{588}$ -0.28°; $[\alpha]_{400}$ -1.08° (c 14.95, hexane).

v) (+)-ψ-ephedrine

benzylphenylmethylsilane, 0.35 g. 20%

$[\alpha]_{588}$ -5.69°; $[\alpha]_{400}$ -15.0° (c 8.79, hexane);

benzylphenylmethylmethoxysilane, 1.43 g. 71.5%

$[\alpha]_{588}$ +0.46°; $[\alpha]_{400}$ +1.29° (c 21.51, hexane).

vi) (-)-ephedrine

benzylphenylmethylsilane, 0.12 g. 6.8% (i.r. 7%)

$[\alpha]_{588}$ -0.64°; $[\alpha]_{400}$ -1.48° (c 8.24, hexane);

benzylphenylmethylmethoxysilane, 1.56 g. 78%

No observable optical activity.

20. Asymmetric reduction of (±)-benzylphenylmethylmethoxysilane with 1:1 molar complexes of lithium aluminium hydride and optically active terpene alcohols.

The procedure was the same as described in the previous section except that the reactions were only carried out at reflux for 4 hours.

i) (-)-menthol

benzylphenylmethylsilane, 1.04 g. 60%

$[\alpha]_{588}$ +0.18°; $[\alpha]_{400}$ +0.47° (c 17.4, hexane);

benzylphenylmethylmethoxysilane, 0.33 g. 17%

$[\alpha]_{588}$ -0.45°; $[\alpha]_{400}$ -1.09° (c 12.3, hexane).

ii) (-)-borneol

benzylphenylmethylsilane, 1.38 g. 79%

optically inactive;

benzylphenylmethylmethoxysilane, 0.20 g. 10%

optically inactive.

iii) (+)-α-fenchol

benzylphenylmethylsilane, 1.03 g. 59%

optically inactive;

benzylphenylmethylmethoxysilane, 0.28 g. 14%

optically inactive.

21. Reduction of (+)-benzylphenylmethylmethoxysilane with lithium aluminium hydride in diethyl ether.

(+)-Benzylphenylmethylmethoxysilane, $[\alpha]_{588}$ +1.86° (0.633 g. 2.62 m.mole) was stirred with lithium aluminium hydride (0.5 g.) in diethyl ether (12 ml.) at reflux for 5 hours. After the usual treatment with aqueous ammonium chloride and drying over magnesium sulphate the solvent was removed to give an oil (0.53 g. 95%).

Chromatography through a silica gel column using 1:4 benzene/light petroleum as eluant gave the benzylphenylmethylsilane, (0.52 g.) $[\alpha]_{588}$ +6.45°; $[\alpha]_{400}$ +16.9° (c 14.29, hexane).

22. Preparation of (±)-mesitylphenylmethylmethoxysilane.

Mesitylmagnesium bromide was prepared by addition of mesityl bromide (30 g. 0.15 mole) and ethylene dibromide (2.81 g. 0.015 mole) in diethyl ether (70 ml.) dropwise to magnesium turnings (4.5 g. 0.188 mole). After the addition was completed the greenish-yellow solution was refluxed for

24 hours and toluene (100 ml.), dried over sodium, was added. The mixture was then refluxed for a further hour and ether (45 ml.) was removed by distillation under a nitrogen atmosphere.

To the Grignard reagent was added phenylmethyldimethoxysilane (18.2 g. 0.10 mole) in toluene (10 ml.) and the mixture refluxed for 66 hours at 70°.

The mixture was treated with ice-cold aqueous ammonium chloride and after washing three times with water, dried over anhydrous magnesium sulphate. Solvents were removed by distillation and the residue distilled under reduced pressure to give a fraction (14.1 g. 52%) b.p. 134°/0.6 mm., as a colourless oil: n.m.r. 60MHz (CCl_4), 9.35 τ, singlet, intensity 3, (methyl on silicon), 7.80 τ, singlet, intensity 3, (p-methyl of mesityl group), 7.70 τ, singlet, intensity 6 (o-methyl of mesityl group), 6.63 τ, singlet, intensity 3, (methoxy on silicon), 3.26 τ, broad singlet, intensity 2, (aromatic mesityl on silicon), centred at 2.70 τ, multiplet, intensity 5, (aromatic): i.r. thin film, maxima (cm^{-1}) at 3065-3000m (aromatic C-H stretchings), 2000-1650w (overtones typical of a monosubstituted benzene with intensification of absorption at 1700 due to 1,2,3,5 trisubstituted benzene), 1610s, 1550m (aromatic C=C stretchings), 1430s, 1115s, 1000m, 850m (C-H deformation of one free hydrogen on an aromatic ring) - phenyl and mesityl on silicon; 2960s, 2940s (aliphatic C-H stretching), 1450m (C-C stretching), 2830, 1185m, 1085s - methoxy on silicon. (Found: C, 75.4; H, 8.2; Si, 10.5. $C_{17}H_{22}SiO$ requires C, 75.5; H, 8.2; Si, 10.4%).

T.l.c. using 1:4 benzene/light petroleum (b.p. 60-80°)

R 0.21

23. Preparation of (±)-mesitylphenylmethylsilane.

(±)-Mesitylphenylmethylmethoxysilane (2.0 g. 7.4 m.mole) was reduced with lithium aluminium hydride (0.5 g.) in diethyl ether (20 ml.). The mixture was refluxed overnight and treated with saturated aqueous ammonium chloride, washed with water, dried, and the solvent removed. The product (1.69 g. 95%) was a clear, colourless oil: n.m.r. 60MHz (CCl_4), 9.39 τ, doublet, J_{CH_3SiH} = 4.0 Hz, intensity 3, (methyl on silicon split by proton on silicon), 7.80 τ, singlet, intensity 3, (p-methyl on mesityl group), 7.69 τ, singlet, intensity 6, (methyl groups o- to silicon), centred at 4.75 τ, quartet, J_{CH_3SiH} = 4.0 Hz intensity 1, (proton on silicon split by methyl), 3.27 τ, broad singlet, intensity 2, (aryl protons on mesityl group), 2.45-2.90 τ, complex multiplet, intensity 5, (aromatic of phenyl): i.r. thin film, maxima (cm^{-1}) absorptions typical of mesitylphenylmethylsilyl system (see previous experiment); at 2140s (stretching) and 880s (bending) - silicon hydride.

T.l.c. eluted with 1:4 benzene/light petroleum (b.p. 60-80°) R_F 0.75.

24. Asymmetric reduction of (±)-mesitylphenylmethylmethoxysilane with 1:1 alkaloid-lithium aluminium hydride complexes.

The method used was the same as that already described for the reductions of (±)-benzylphenylmethylmethoxysilane. The results are given under the heading of the alkaloid used.

i) (+)-quinidine

mesitylphenylmethylsilane, 0.609 g. 34%

$[\alpha]_{588}$ +1.77°; $[\alpha]_{400}$ +3.25°; $[\alpha]_{370}$ +3.34° (maximum); $[\alpha]_{323}$ +2.27° (c 16.66, hexane);

mesitylphenylmethylmethoxysilane, 1.0 g.
$[\alpha]_{588}$ -1.01°; $[\alpha]_{400}$ -2.89°; $[\alpha]_{303}$ -7.35° (c 14.79, hexane).

ii) (-)-quinine
mesitylphenylmethylsilane, 0.48 g. 27%
$[\alpha]_{588}$ -4.02°; $[\alpha]_{400}$ -7.77°; $[\alpha]_{370}$ -8.31° (minimum); $[\alpha]_{328}$ -6.18° (c 13.57, hexane); $[\alpha]_{310}$ 0.0° (c 2.67, hexane)*
mesitylphenylmethylmethoxysilane, 0.80 g.
$[\alpha]_{588}$ +2.52°; $[\alpha]_{400}$ +5.65°; $[\alpha]_{303}$ +13.8° (c 7.28, hexane).

iii) (+)-cinchonine
mesitylphenylmethylsilane, 0.554 g. 31%
$[\alpha]_{588}$ +1.37°; $[\alpha]_{400}$ +2.48°; $[\alpha]_{370}$ +2.60° (maximum); $[\alpha]_{345}$ +2.38° (c 17.05, hexane);
mesitylphenylmethylmethoxysilane, 1.013 g.
$[\alpha]_{588}$ -0.47°; $[\alpha]_{400}$ -1.36°; $[\alpha]_{303}$ -3.45° (c 17.72, hexane).

iv) (-)-cinchonidine
mesitylphenylmethylsilane, 0.61 g. 34%
$[\alpha]_{588}$ -1.82°; $[\alpha]_{400}$ -3.52°; $[\alpha]_{370}$ -3.68° (minimum); $[\alpha]_{333}$ -2.95° (c 17.52, hexane);
mesitylphenylmethylmethoxysilane, 1.0 g.
$[\alpha]_{588}$ +1.04°; $[\alpha]_{400}$ +2.73°; $[\alpha]_{303}$ +6.73° (c 17.09, hexane).

* For complete o.r.d. data see relevant section in Chapter IX.

v) (+)-ψ-ephedrine (Refluxed 48 hours).

mesitylphenylmethylsilane, 0.262 g. 15%

$[\alpha]_{588}$ 0.0°; $[\alpha]_{400}$ 0.0° (c 13.81, hexane);

mesitylphenylmethylmethoxysilane, 0.99 g.

$[\alpha]_{588}$ 0.0°; $[\alpha]_{400}$ 0.0°; $[\alpha]_{333}$ 0.0° (c 15.2, hexane).

25. Preparation of (±)-phenylisopropylmethylmethoxysilane.

Isopropylmagnesium bromide, prepared from isopropyl bromide (12.3 g. 0.1 mole) and magnesium (2.7 g.) in diethyl ether (10 ml.), was added dropwise, with stirring, to phenylmethyldimethoxysilane (18.2 g. 0.1 mole) in diethyl ether (20 ml.). The mixture was refluxed under nitrogen for 7 days and the product isolated in the manner described for phenylethylmethylmethoxysilane (see experiment 12). Distillation under reduced pressure gave a colourless oil (16 g.) b.p. 76°/6 mm: n.m.r. 60MHz (CCl_4), 9.70 τ, singlet, intensity 3, (methyl on silicon), 8.7-9.2 τ, multiplet, intensity 6.3, (isopropyl on silicon), 6.62 τ, singlet, intensity 2.7, (methoxy on silicon), 6.55 τ, singlet, intensity 0.6, (methoxy on silicon - due to some unreacted phenylmethyldimethoxysilane), 2.2-2.9 τ, complex multiplet, intensity 5, (aromatic). Chromatographic purification of the product (5 g.) on silica gel, using benzene as eluant, gave a fraction (4 g.) which was shown by n.m.r. and g.l.c. to be pure phenylisopropylmethylmethoxysilane. I.r. thin film, maxima (cm^{-1}) absorptions typical of methyl and phenyl groups on silicon; at 2840s, 1190s, 1080s - methoxy on silicon; 1380m, 1370m (gem-dimethyl deformation), 1170m -isopropyl on silicon.

26. Preparation of (±)-phenylisopropylmethylsilane.

(±)-Phenylisopropylmethylmethoxysilane (2 g. 10.3 m.mole) was reduced with lithium aluminium hydride in diethyl ether (see experiment 13) to give a colourless oil (1.6 g. 95%). Chromatography on silica gel using 1:4 benzene/light petroleum spirit gave a fraction (1.5 g.): n.m.r. 60MHz (CCl_4), centred at 9.76 τ, doublet, J_{CH_3SiH} = 4.0 Hz, intensity 3, (methyl on silicon), 8.7-9.4 τ, complex multiplet, intensity 7, (isopropyl on silicon), 5.83 τ, multiplet, intensity 1, (proton on silicon), 2.4-2.9 τ, complex multiplet, intensity 5 (aromatic): i.r. thin film, maxima (cm^{-1}) absorptions due to the phenylisopropylmethylsilyl system; at 2105s (Si-H stretching).

27. Asymmetric reduction of (±)-phenylisopropylmethylmethoxysilane by 1:1 alkaloid-lithium aluminium hydride complexes in diethyl ether.

The procedure used to partially reduce the methoxysilane (1.62 g. 8.35 m.mole) was similar to that described for the reduction of (±)-phenylethylmethylmethoxysilane (experiment 14). The results are given under the heading of the alkaloid used.

i) (+)-cinchonine

phenylisopropylmethylsilane, 0.35 g. 25.5% (i.r. 27%) $[\alpha]_{588}$ +0.73°; $[\alpha]_{400}$ +3.32°; $[\alpha]_{303}$ +12.3° (c 11.05, hexane);

phenylisopropylmethylmethoxysilane, 0.51 g. no optical activity detected (n.m.r. indicates 20% disiloxane).

ii) (-)-cinchonidine (1.43 g. (±)-methoxysilane used).

phenylisopropylmethylsilane, 0.34 g. 28.0% (g.l.c. 41.0%) $[\alpha]_{588}$ +0.13°; $[\alpha]_{400}$ +0.59°; $[\alpha]_{333}$ +1.53° (c 14.15, hexane);

phenylisopropylmethylmethoxysilane, 0.89 g. $[\alpha]_{588}$ -0.57°; $[\alpha]_{400}$ -1.84°; $[\alpha]_{303}$ -5.25° (c 18.13, hexane).

iii) (-)-quinine

phenylisopropylmethylsilane, 0.48 g. 35% (i.r. 57%) $[\alpha]_{588}$ -0.03°; $[\alpha]_{303}$ -0.44° (c 16.49, hexane);

phenylisopropylmethylmethoxysilane, 0.28 g. $[\alpha]_{588}$ +0.66°; $[\alpha]_{303}$ +5.26° (c 17.74, hexane).

iv) (+)-quinidine

phenylisopropylmethylsilane, 0.55 g. 40.2% (g.l.c. 58%) $[\alpha]_{588}$ +0.30°; $[\alpha]_{313}$ +4.55° (c 14.08, hexane);

phenylisopropylmethylmethoxysilane, 0.34 g. $[\alpha]_{588}$ -4.61°; $[\alpha]_{313}$ -31.3° (c 17.09, hexane).

28. Preparation of cyclohexylmethyldichlorosilane.

Cyclohexylmethyldichlorosilane, b.p. 74-76°/12 mm. Lit. b.p. 201-202°/760 mm., was prepared in 88% yield by the method of Speier et al.[152]

29. Preparation of (±)-cyclohexylethylmethylchlorosilane.

Ethylmagnesium bromide (82.5 m.mole) in diethyl ether (50 ml.) was added to cyclohexylmethyldichlorosilane (15 g. 76.0 m.mole) at room temperature. After stirring for one hour at room temperature the mixture was refluxed for 2 days under an atmosphere of nitrogen. The magnesium salts were removed by filtration through a glass sinter and the ether

removed by distillation to give a product (10.7 g.) b.p. 80°/9 mm. G.l.c. showed it to consist of cyclohexylethylmethylchlorosilane (73%), cyclohexylmethyldichlorosilane (20%), and cyclohexyldiethylmethylsilane (7%).

30. Preparation of (±)-cyclohexylethylmethylmethoxysilane.

(±)-Cyclohexylethylmethylchlorosilane (5 g. 26.3 m.mole) was methanolysed with anhydrous methanol (3 ml.) and triethylamine (5 ml.) in light petroleum (15ml.).

Removal of the amine hydrochloride by filtration and distillation of the solvent gave a product (4.23 g.). G.l.c. analysis showed the product to be cyclohexylethylmethylmethoxysilane (70%), cyclohexylmethyldimethoxysilane (17%), and cyclohexyldiethylmethylsilane (13%).

31. Asymmetric reduction of (±)-cyclohexylethylmethylmethoxysilane with 1:1 complex of (+)-cinchonine and lithium aluminium hydride in diethyl ether.

(+)-Cinchonine (1.37 g. 4.66 m.mole) and lithium aluminium hydride (0.177 g. 4.66 m.mole) were reacted in anhydrous diethyl ether (40 ml.) for 30 minutes at reflux. (±)-Cyclohexylethylmethylmethoxysilane (0.93 g. above product, 3.8 m.mole) was added in diethyl ether (20 ml.) and the mixture refluxed for 7 days. Removal of solvent, after treatment with saturated aqueous ammonium chloride and drying, gave a product (1.04 g.) whose i.r. showed a strong absorption at 2095 cm^{-1} (Si-H stretching).

Chromatographic separation on silica gel using 1:9 benzene/light petroleum gave a fraction (0.19 g.). G.l.c. examination analysed the mixture as cyclohexylethylmethylsilane (70%) and cyclohexyldiethylmethylsilane (30%).

Change of solvent to benzene gave a second fraction (0.18 g.),

Fraction 1. was treated with activated charcoal in hexane to remove traces of aromatic material and the optical rotatory dispersion spectrum measured. The curve was a plain negative one with a cut-off in transmission at 286 n.m. (presumably still due to aromatic impurities):

$[\alpha]_{588}$ -0.11°; $[\alpha]_{400}$ -0.30°; $[\alpha]_{303}$ -0.76°; $[\alpha]_{286}$ -0.96° (c 14.73, hexane).

Owing to the weak optical rotations of the sample errors of the order of ±0.3° at 286 n.m. were observed. I.r. thin film, exhibited a strong Si-H stretching absorption at 2100 cm^{-1} with no indication of silanol or disiloxane at 3300 and 1080 $cm.^{-1}$ Absorptions characteristic of methoxy on silicon were also absent.

Fraction 2. i.r. thin film, was identical with cyclohexylethylmethylmethoxysilane and had the following o.r.d. data:

$[\alpha]_{588}$ -0.58°; $[\alpha]_{400}$ -1.07°; $[\alpha]_{312}$ -1.82° (c 13.30, hexane).

Aromatic impurities were once again the cause of the cut-off in transmission at 312 n.m. Treatment of the sample with activated charcoal in hexane at room temperature, although succeeding in partial removal of the aromatics, caused extensive racemisation.[70] I.r. examination of the sample after this treatment showed it to consist of a substantial amount of silanol and disiloxane. Examination of the activated charcoal found it to be alkaline in reaction to litmus paper.

G.l.c. on fraction 2, prior to the treatment with charcoal, showed it to consist of cyclohexylethylmethylmethoxysilane (80%) and cyclohexyldiethylmethylsilane (14%).

32. Preparation of (+)-peroxy-camphoric acid.

(+)-Peroxy-camphoric acid was obtained in 90% yield using the method of Milas and McAlevy[153] from camphoric anhydride, m.p. 221-222° $[\alpha]_{588}$ -2.8° (c 4.86, C_6H_6). [Lit.[148] m.p. 223.5° $[\alpha]_D$ -7.7° (C_6H_6)]

33. Reaction of (+)-peroxy-camphoric acid and (±)-1-naphthylphenylmethylsilane.

(±)-1-Naphthylphenylmethylsilane (0.26 g. 1.05 m.mole) and (+)-peroxy-camphoric acid (0.51 g. 2.36 m.mole) were dissolved in benzene (26 ml.) and stirred at room temperature. The progress of the reaction was followed by t.l.c. on silica gel using 1:9 benzene/light petroleum (b.p. 60-80°) as eluant. Disappearance of the spot at R_F 0.74 marked the complete removal of 1-naphthylphenylmethylsilane.

As the reaction proceeded a white crystalline solid was deposited which was shown to be (+)-camphoric acid. The reaction proceeds slowly requiring 48 hours for completion.

Filtration gave (+)-camphoric acid (0.37 g. 78%), m.p. 184-185° $[\alpha]_{588}$ +47.3° (c 1.88, EtOH). [Lit.[148] $[\alpha]_D$ +47.7° m.p. 187°]. Removal of benzene from the filtrate under reduced pressure gave an oil (0.42 g.): n.m.r. 60MHz (CCl_4), 9.34 τ, singlet, intensity 3, (methyl on silicon), 8.7-9.3 τ, complex band, intensity 3.4, (camphoric acid impurity), 3.58 τ, broad singlet, intensity 1.26, (hydroperoxidic proton on silicon), 2.0-2.9 τ, complex multiplet,

intensity 12, (aromatic): i.r. thin film, maxima (cm^{-1}), absorptions typical of the 1-naphthylphenylmethylsilyl system, at 3300s (O-H stretching); at 2850s, 1700s, 1450m - due to camphoric acid residues.

The above spectral data indicate that the product formed in the reaction is 1-naphthylphenylmethylsilyl hydroperoxide since the methyl resonance at 9.34τ is lower than that of 1-naphthylphenylmethylsilanol (9.50τ).

34. Partial reaction of (+)-peroxy-camphoric acid and (±)-1-naphthylphenylmethylsilane.

(±)-1-Naphthylphenylmethylsilane (1.0 g. 4.03 m.mole) and (+)-peroxy-camphoric acid (2.0 g. 9.25 m.mole) in benzene (100 ml.) were reacted at room temperature for 6 hours. The mixture was then filtered to remove the camphoric acid (0.87 g. 47%) and the solution passed through a silica gel column using benzene as eluant to yield 1-naphthylphenylmethylsilane (0.43 g. 43%).

The o.r.d. of the unreacted silane showed no observable optical activity. N.m.r. and i.r. spectra showed the chromatographed material to be free of impurities.

35. Attempted hydrolysis of (±)-1-naphthylphenylmethylmethoxysilane with (+)-camphor-10-sulphonic acid in m-xylene.

1-Naphthylphenylmethylmethoxysilane (0.50 g. 1.8 m.mole) and (+)-camphor-10-sulphonic acid (0.05 g. 0.18 m.mole) in m-xylene (50 ml.) were heated at reflux (139°). The reaction was followed by t.l.c. using benzene as eluant. Complete removal of the methoxysilane, marked by the disappearance of the spot at R_F 0.80, occurred after 40 hours.

The solvent was removed under reduced pressure, sulphonic acid by filtration, and the oil remaining was examined by i.r. Absorptions at 1430 and 1260 cm^{-1} indicated the presence of phenyl and methyl groups on silicon; a strong band at 1100-1020 cm^{-1} indicated the formation of siloxanes and a broad absorption at 3400 cm^{-1} the presence of hydroxyl groups. In addition bands due to sulphonic acid were present.

Chromatography through a silica gel column using benzene as eluant gave an oil (0.406 g.) whose i.r. spectrum was free of absorptions due to hydroxyl groups and sulphonic acid. Absorptions characteristic of naphthyl on silicon at 1505 and 1220 cm^{-1} were very much reduced in intensity. A strong band at 1070 cm^{-1} indicated the presence of siloxanes. N.m.r. showed the aromatic:aliphatic ratio to be 5:3 and, therefore, almost complete cleavage of the naphthyl group had occurred. T.l.c. of this oil using 17% benzene in light petroleum (b.p. 60-80°) showed it to be a complex mixture of products.

36. Attempted base catalysed hydrolysis of (±)-1-naphthylphenylmethylmethoxysilane with (±)-phenylethylamine in m-xylene.

(±)-1-Naphthylphenylmethylmethoxysilane (0.50 g. 1.8 m.mole) and (±)-phenylethylamine (0.027 ml.) in m-xylene (50 ml.) were refluxed with stirring. T.l.c. indicated that no reaction had occurred after 48 hours.

37. Preparation of (±)-1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane.[154]

Prepared by the method of Shostalovskii et al[108] from

(±)-1-naphthylphenylmethylsilanol (2 g. 7.58 m.mole, prepared by hydrolysis of (±)-chlorosilane[4]) and vinyl ethyl ether (1.5 ml. 15.8 m.mole). Heating with concentrated hydrochloric acid (0.004 ml.) in a sealed tube at 65° for 18 hours yielded, after removal of excess ether, a colourless oil (2.48 g. 98%): n.m.r. 100 MHz (CCl_4) 9.20 τ, singlet, intensity 3, (methyl on silicon), centred at 9.00 τ, triplet J = 7Hz, intensity 3, (methyl of ethoxy), centred at 8.75 τ, doublet J = 5Hz, intensity 3, (methyl on carbon), 6.2-6.9 τ, complex multiplet, intensity 2, (methylene of ethoxy, complicated by non-equivalence of protons), centred at 5.00 τ, quartet J = 5Hz, intensity 1, (methine bonded to two oxygens), 1.9-2.8 τ, complex multiplet, intensity 12, (aromatic): i.r. thin film, maxima (cm^{-1}) - bands characteristic of the 1-naphthylphenylmethylsilyl system and absence of the OH stretching band at 3300; at 1380m ($C-CH_3$ deformation), 1140s, 1080s, 1055s, 970s - probably due to Si-O and C-O stretchings.

38. Acid catalysed hydrolysis of (±)-1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane with (+)-camphor-10-sulphonic acid in toluene.

To a solution (23 ml.) of the silyl acetal in toluene (0.0331 M) at a temperature of 3° was added a solution (2.5 ml.) of (+)-camphor -10-sulphonic acid in toluene (0.004 M). The mixture was kept at a temperature of 3° and stirred continuously. Samples were taken every 5 min. and spotted onto a t.l.c. plate spread with silica gel. The plate was then developed with benzene and the spots located by spraying with 1% potassium permanganate in 10% aqueous sulphuric acid.

The extent of reaction was estimated by observing the disappearance of the spot R_F 0.60, due to silyl acetal, and the appearance of a new spot R_F 0.20. This new spot has the same R_F value as that due to 1-naphthylphenylmethylsilanol. After 2 hours the reaction was judged to be virtually complete. The silyl acetal was found to be stable to silica gel and no change occurred after 20 hours on the t.l.c. plate at room temperature.

The solvent was removed under reduced pressure to give an oil:n.m.r. 100 MHz (CCl_4), 9.34 τ, singlet, intensity 3 (methyl on silicon), 1.9-3.0 τ, complex multiplet, intensity 12 (aromatic). No other resonances in the n.m.r. were observed. The position of the methyl resonance at 9.34 τ was identical with that due to 1,3-di-1-naphthyl-1,3-diphenyl-1,3-dimethyldisiloxane (methyl on silicon due to silanol 9.50 τ): i.r. absorptions typical of the 1-naphthylphenylmethylsilyl system used, with a weak band at 3300 cm^{-1} due to silanol; a very strong band at 1050 cm^{-1} indicated the presence of disiloxane.

39. Partial acid hydrolysis of (±)-1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane with (+)-camphor-10-sulphonic acid in toluene.

The reaction described in the previous experiment was repeated on twice the scale. After 30 minutes the mixture was poured onto a silica gel column and eluted using benzene as eluant. Removal of solvent gave an oil (0.128 g.) whose i.r. and n.m.r were identical with (±)-1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane. No indication of disiloxane was found. The o.r.d. of the oil was run in hexane but no optical activity was observed.

The absence of disiloxane in the product eluted from the column with benzene and the absence of a spot R_F 0.90 on the t.l.c. in experiment 38 indicates that the initial product on the hydrolysis of the silyl acetal is silanol. Subsequent acid catalysed condensation accelerated by removal of solvent in experiment 38 leads to disiloxane formation.

40. Attempted base catalysed hydrolysis of (±)-1-ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane with (±)-1-phenylethylamine in toluene.

(±)-1-Ethoxy-1-(1-naphthylphenylmethylsilyloxy)ethane (0.28 g. 0.834 m.mole) in toluene (28 ml.) and (±)-1-phenylethylamine (0.25 ml.) were refluxed for 24 hours. T.l.c. indicated that no reaction had occurred

41. Preparation of diastereoisomeric 1-naphthylphenylmethylalkoxysilanes.[89]

To (±)-1-naphthylphenylmethylsilane (1.5 g. 6.05 m.mole) and synthetic (±)-menthol (1.88 g. 12.0 m.mole) in methylene chloride (12 ml. dried over Molecular Sieve 5A) was added 10% palladium on charcoal (0.1 g.). The mixture was allowed to stand at room temperature until evolution of hydrogen ceased, (time from 30 mins. to 3 hrs. according to activity of catalyst). After removal of the catalyst and solvent the product was separated from silanol and excess menthol by a silica gel column using a 1:4 mixture of benzene and light petroleum (b.p. 60-80°).

The oil (1.85 g. 78%) had i.r. and n.m.r. spectra identical to those of the product prepared by the alkoxy exchange reaction between (±)-1-naphthylphenylmethylmethoxy-

silane and (-)-menthol with potassium hydroxide as catalyst.

The reaction of (±)-1-naphthylphenylmethylsilane with (-)-menthol in the presence of palladium on charcoal in methylene chloride followed by fractional crystallization of the diastereoisomers was found to be an improved step in the route to the preparation of optically active 1-naphthyl-phenylmethylsilane.

Diastereoisomeric alkoxysilanes were prepared in yields dependant on the alcohol used, from (±)-1-phenylethanol (68%), (±)-methylisopropylcarbinol (47%), (-)-borneol (47%),* (-)-isoborneol (22%)* using the above method. Very little alkoxysilane was formed from the palladium catalysed reaction of (±)-1-naphthylphenylmethylsilane and (+)-α-fenchol.

The i.r. and n.m.r. characteristics of these compounds are discussed in the appropriate chapter of the discussion. The high purity of the products was established by their spectra and by t.l.c. using 7% $^{v}/_{v}$ benzene in light petroleum (b.p. 60-80°).

*The preparations of the alkoxysilanes from (-)-borneol and (-)-isoborneol were performed using an excess of (±)-silane in order to detect preferential diastereoisomer formation. The yields are calculated on the quantity of alcohol used.

42. Preparation of (±)-phenylethylmethyl-(-)-menthoxysilane.

(±)-Phenylethylmethylmethoxysilane (10 g. 0.06 moles) and (-)-menthol (8.5 g. 0.06 mole) in dry toluene (20 ml) were refluxed for 2 hours with dry, powdered potassium hydroxide (0.01 g.). The azeotropic mixture of methanol and toluene (b.p. 60°) was slowly distilled off. The mixture remaining was then washed with water and the organic layer

dried over sodium sulphate. The toluene was then removed by distillation and the remaining oil distilled under reduced pressure to give a fraction (9.0 g. 51%) b.p. 106°/0.2 mm: n.m.r. 60 MHz (CCl_4), 9.64 τ, singlet, intensity 3, (methyl on silicon), 9.34 and 9.42 τ, two superimposed doublets J = 7 Hz, total intensity 3, (methyls, diastereotopic by external comparison, associated with the pro-S-methyl of the isopropyl group on the menthoxy moiety), 7.6-9.2τ, complex band, intensity 20,(menthoxy and ethyl on silicon), centred at 6.6τ, complex multiplet, intensity 1, (methine attached to oxygen), 2.3-2.8 τ, intensity 5, (aromatic): i.r. thin film, maxima (cm^{-1}), absorptions typical of the phenylethylmethylsilyl system, 1385m, 1370m (gem-dimethyl), 1080s, 1070s, 1055s (Si-O stretch) - menthoxy on silicon. (Found: C, 74.8; H, 10.4; Si, 9.4. $C_{19}H_{32}SiO$ requires C, 74.9; H, 10.6; Si, 9.2%).

Integrals of the doublets at 9.42 and 9.34τ in the 60 MHz spectrum of the product show it to be a 50:50 mixture of the diastereoisomers.

43. Equilibration of (±)-1-naphthylphenylmethyl-1-phenylethoxysilane with potassium hydroxide in toluene.

(±)-1-Naphthylphenylmethyl-1-phenylethoxysilane (0.846 g.) [diastereoisomeric ratio 56:44] and (±)-1-phenylethanol (1.0 ml.) were heated at 84° for 5 hours with powdered potassium hydroxide (0.006 g.) in sodium dried toluene (50 ml.). Constant stirring was maintained throughout. Removal of potassium hydroxide by passing the product through silica gel and eluting with 1:1 benzene/light petroleum gave (±)-1-naphthylphenylmethyl-1-phenylethoxy-

silane (0.800 g. 95%). N.m.r. analysis at 60 MHz showed the diastereoisomeric ratio to be 60:40.

Further treatment under the above conditions for 20 hours did not alter the ratio of diastereoisomers. The major component in the compound prior to, and after base catalysed equilibration, possessed a resonance for methyl on silicon at 9.34 τ. The other diastereoisomer gave a resonance at 9.39 τ.

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