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# INTRAMOLECULAR HYDROSILYLATIONS II: THE ANTI-SELECTIVE REDUCTION OF β-HYDROXYKETONES

S.ANWAR and A.P.DAVIS*

Department of Chemistry, Trinity College, Dublin 2, Ireland

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Abstract - A study was made of the synthesis and intramolecular hydrosilylation of silyloxyketones (2) (Scheme 2). It was found that with a variety of Lewis acid catalysts, anti-selective hydrosilylation took place to give (3) and, after desilylation, (5). With $SnCl_4$, the most effective and practical catalyst, ratios (3):(4) ranged between 40:1 and 120:1 for a number of substrates. An explanation for the stereoselectivity is proposed based on (C1) as a transition state model. The net result is an anti-selective reduction of β-hydroxyketones, summarised in Scheme 4.

## INTRODUCTION

Perhaps the most notable aspect of organosilicon reagents is their lack of potency. Only in certain circumstances and to a very modest extent will a silicon atom induce reactivity in a molecule. This property renders organosilicon reagents easy to control and capable of wide structural variation, features which have been widely exploited by synthetic organic chemists over the past two decades. Nonetheless, until quite recently one mode of variability has been largely ignored by the synthetic community. Almost exclusively, the early applications of organosilicon chemistry employed silicon compounds which were "monofunctional" in the sense that only one bond to silicon played a part in their reactivity. Organosilicon reagents were generally of the form $R_3SiX$, where R represents an alkyl group used merely to occupy a silicon valency. Notable exceptions were certain applications of difunctional silicon compounds $R_2SiXY$ in derivatisation/protection[1], and the methodology employing $RSiF_5^{2-}$ developed by the Kumada group[2].

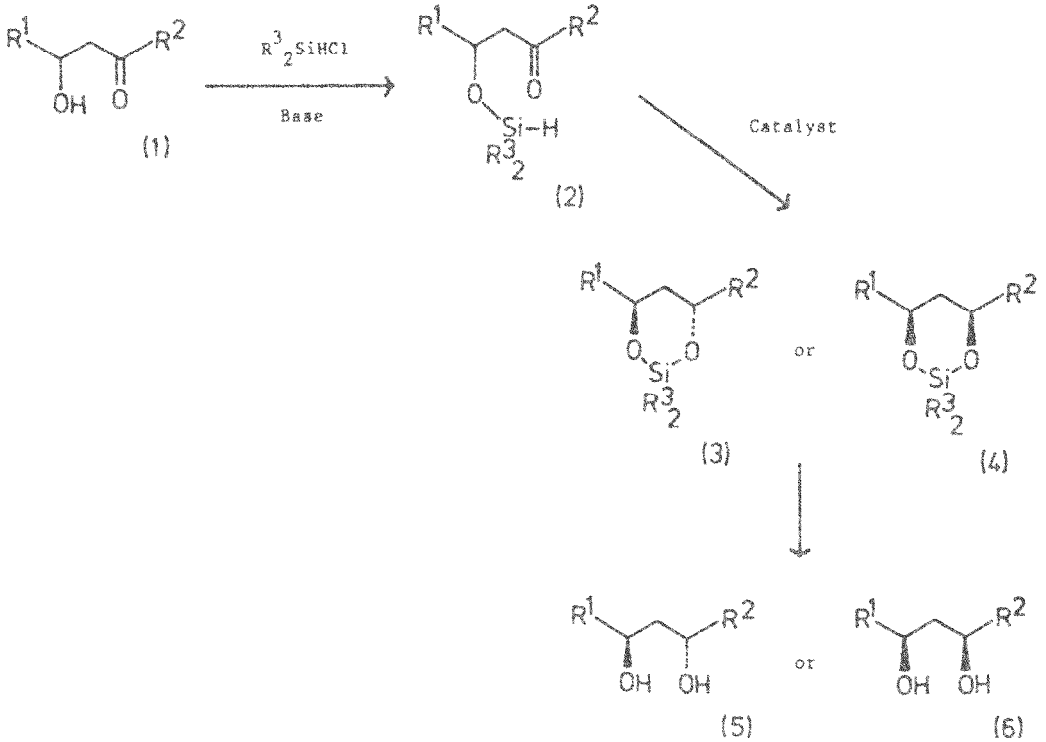
Recently there has been a perceptible increase in interest in polyfunctional organosilicon reagents. One stimulus has been the work of the Kumada[3] and Fleming[4] groups on the oxidative cleavage of organosilicon compounds. As a result, it is now possible to transform $R'SiR_2X$ (X = any moiety labile to $F^-$ or HF) to R'OH, apparently irrespective of the nature of R'. A second factor has been the realisation in a number of laboratories, including our own, that silicon has substantial potential as a bridging element in intramolecular reactions (Scheme 1).


Scheme 1

Intramolecularity is widely appreciated as a means of achieving stereo- and regiocontrol in synthesis. In rigid systems it can sometimes effect complete control, and in flexible acyclic systems it can often impose constraints on possible transition states such that one stereochemical possibility is very strongly favoured. If nothing else, it is quite likely that an intramolecular reaction will have a complementary stereochemical bias to an intermolecular analogue.

Organosilicon reagents have clear advantages in the design of intramolecular synthetic methodology. Their general lack of reactivity enables reagent/substrate combinations to be built into molecules, and to exist together until a catalyst is added. The potential of organosilicon chemistry in cyclisation reactions has been realised for some time[5]. Incorporating the silicon as a bridging element in an intramolecular reaction (as in Scheme 1) opens up further possibilities, including the stereoselective synthesis of acyclic molecules. In the last few years silicon-bridged free radical cyclisations[6], carbonyl allylations[7] and C=C hydrosilylations[8] have been reported. Our own interest has been principally in intramolecular carbonyl hydrosilylations, and we now wish to follow up our preliminary communication[9] with a fuller discussion of our work.

Hydrosilanes are capable of adding to carbonyl compounds, but only in the presence of catalysts[10]. Thus, in principle, it should be possible to attach a hydrosilane to a molecule and then use it in an intramolecular carbonyl reduction. We saw an opportunity to exploit this concept in the transformations shown in Scheme 2.




Scheme 2

We were drawn to this possibility for a number of reasons; (i) The chances of stereoselectivity seemed high, especially if a six-membered cyclic transition state were operative (see later). (ii) The 1,3-diol substructure is common in biologically active natural products. (iii) The hydroxyketone starting materials are readily available via the directed aldol condensation. (iv) The achievement of 1,3-asymmetric induction in carbonyl addition reactions could still be seen as a challenge[11]. Indeed, while a good method had been reported for the syn-selective reduction of β-hydroxyketones[12], no anti-selective method was available. In the event, our greatest success was in achieving anti-selectivity, thus remedying this deficiency[13].

## RESULTS AND DISCUSSION

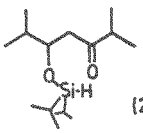
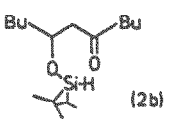
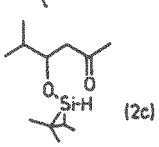
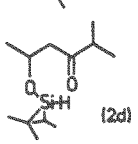
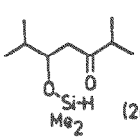
Synthesis of β-silyloxyketones (2) (see Table). Two types of derivatives (2) were used in this work. Some experiments (see below) were undertaken with the dimethylsilyloxy compound (2e), synthesized by silylation of the corresponding hydroxyketone with $Me_2SiHCl$/pyridine. Although this chlorosilane is commercially available at a modest price, its derivatives are moisture-sensitive and relatively hard to handle. We preferred in general to use di-isopropysilyl derivatives, as in (2a-d). These were prepared in yields of 72% or better by treatment of hydroxyketones (1) with $Pr^i_2SiHCl$ and either pyridine or triethylamine/dimethylaminopyridine (Table). The latter seemed to be the method of choice, giving good yields in cases when the method employing pyridine had proved disappointing[9]. The $Pr^i_2SiHCl$ was prepared from $Pr^iMgCl$ and $HSiCl_3$, using a variant of a published method[1b]. An unusual feature of our procedure is the subjection of the reaction mixture to an "aqueous" work-up, using conc. hydrochloric acid. Excess Grignard reagent is thus quenched, allowing the $MgCl_2$ side-product to be removed by filtration before distillation.

Intramolecular Hydrosilylations. The hydrosilylation of carbonyl compounds can be catalysed by Lewis acids[10a], Bronsted acids[10b], nucleophilic catalysts (especially $F^-$)[10c] and transition metal complexes[10d]. We found that catalysts from all these categories were capable of converting silyloxyketones (2) to mixtures of the 2-sila-1,3-dioxanes (3) and (4) or, in one case, directly to diols (5) and (6). The results are summarised in the Table. Unless noted otherwise in the Table, the stereoselectivities were determined by g.l.c. analysis of the crude product mixtures, the two siladioxanes being the only substantial components observable. Standard samples of the individual siladioxanes were prepared by non-stereoselective reduction of the β-hydroxyketones (1) ($NaBH_4$ or $LiAlH_4$) followed by derivatisation with $Me_2SiCl_2$ or $Pr^i_2Si(OTf)_2$[1d] ($T_f$- = $CF_3SO_2$). The isomers were separated by flash chromatography either at the diol or siladioxane stage, and were identified by comparison with literature data (diols) or by n.m.r. (see Experimental).

The most striking feature of the results in the Table is the remarkable level of anti-selectivity observed with Lewis and Bronsted acid catalysts when applied to the di-isopropylsilyloxyketones (2a-d). In the series of experiments with (2a), the selectivity observed with $BF_3.OEt_2$ was particularly impressive. However, as this reaction was not entirely clean, we settled on $SnCl_4$ as our preferred catalyst. The poorest selectivity observed with this catalyst was 40:1, and the reactions were clean and high-yielding. Di-isopropylsiladioxanes are recognised as useful, protected forms of 1,3-diols[1d]. Desilylation with aqueous HF/MeCN gave diols (5) and (6) in excellent yields.

The final column in the Table gives the overall yields of (5) and (1), employing $SnCl_4$ as catalyst. For the sequences employing (2a-d) as intermediates the figures are quite respectable, being in the range of 60 - 70%. It is notable that the differences between these

TABLE; Synthesis of β-silyloxyketones (2), and subsequent transformations into siladioxanes (3) and (4), and diols (5)

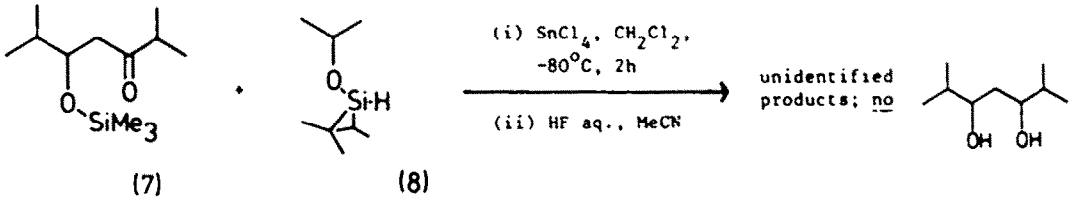
| β-Silyloxyketone | Method of Formation[a] (yield) | Hydrosilylation Catalyst (quantity in mol. eq.) and conditions[b] | Ratio (3):(4)[c] | Overall Yield of anti-diol (5) from ketone (1)[d] |
|---|---|---|---|---|
|  (2a) | A (72%) | $SnCl_4$(0.1),-80°,2h | 120 : 1 | 67% |
| (2a) | | $MgBr_2.OEt_2$(0.1), RT, 24h | 60 : 1 | |
| (2a) | | $TiCl_4$(0.5), -80°, 30 min | 30 : 1 | |
| (2a) | | $BF_3.OEt_2$(0.5), -80°, 2h | 320 : 1[e] | |
| (2a) | | $ZnBr_2$(0.12), -80°, 8h then RT, overnight | 2 : 1 | |
| (2a) | | $ZnCl_2$(0.25), -80°, 30 min then RT, 15 min | 1 : 2.5 | |
| (2a) | | $CF_3CO_2H$(0.2), -80°, 1h then RT, 1h | 35 : 1[f] | |
| (2a) | | $Bu_4N^+F^-$(0.2), -80°, 30 min[g] | 2 : 1 | |
| (2a) | | $(Ph_3P)_3RhCl$(0.08), benzene, reflux, 12h | 5 : 1[f] | |
|  (2b) | A (75%) | $SnCl_4$(0.1), -80°, 2h | 40 : 1 | 60% |
|  (2c) | B (75%) | $SnCl_4$(0.1), -80°, 2h | 50 : 1 | 67% |
|  (2d) | B (79%) | $SnCl_4$(0.1), -80°, 2h | 40 : 1 | 69% |
|  (2e) | C (60%) | $SnCl_4$(0.05), -80°, 1h | | 37%[h] |
| (2e) | | $MgBr_2.OEt_2$(0.1), RT, 24h | 14 : 1[f] | |
| (2e) | | $BF_3.OEt_2$(0.4), -80°, 2h | 23 : 1[f] | |
| (2e) | | $ZnBr_2$(0.1), -80°, 8h, then RT, overnight | 1 : 6 | |
| (2e) | | $ZnCl_2$(0.2), -80°, 30 min then RT, 15 min | 1 : 4 | |
| (2e) | | $Bu_4N^+F^-$(0.1), -80°, 30 min[g] | 2 : 1 | |

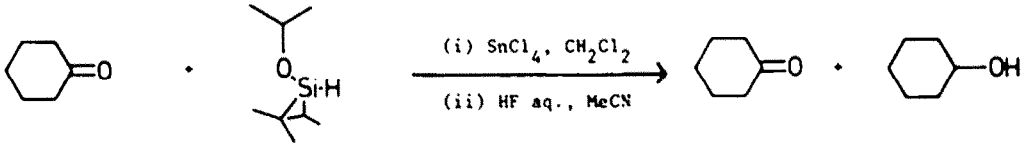
[a]Method A; $Pr^i_2SiHCl$, $Et_3N$, cat. DMAP. Method B; $Pr^i_2SiHCl$, pyridine. Method C; $Me_2SiHCl$, pyridine. [b]Reactions performed in $CH_2Cl_2$ unless otherwise stated. [c]Pure by g.l.c., unless otherwise indicated. [d]After desilylation with HF aq./MeCN, unless otherwise stated. [e]Siladioxanes accompanied by unidentified impurities, ca. 30% by g.l.c. peak areas. [f]Siladioxanes accompanied by unidentified impurities. [g]In the presence of 4A molecular sieves. [h]Siladioxanes (3) and (4) could not be isolated. Syn-diol (6) was isolated in 1.25% yield, implying a 30:1 ratio of (3) to (4) after hydrosilylation.

and the silylation yields are all fairly small, demonstrating the efficiency of the hydrosilylation and desilylation steps.

An intriguing aspect of this work is that $ZnCl_2$ and $ZnBr_2$ behaved very differently from the other Lewis acids. With (2a) the latter gave a modest level of anti-selectivity, while the former was slightly syn-selective. When the dimethylsilyloxyketone (2e) was employed as substrate there was a general decrease in anti-selectivity across the spectrum of Lewis acids, with $ZnCl_2$ and $ZnBr_2$ becoming significantly syn-selective (however not to a synthetically useful extent, in the context of methodology already available[12]).

To assist our mechanistic understanding of the hydrosilylations (see below), we sought experimental support for our view that the reactions are intramolecular. Accordingly, we treated cyclohexanone and the trimethylsilyloxyketone (7) with alkoxysilane (8) and $SnCl_4$ at concentrations matching those used for (2) (Scheme 3). Although the cyclohexanone was reduced slowly at 0°C, no reduction products were observed for either substance at -80°C.




conditions for (i):

| | | | |
|---|---|---|---|
| -80°C, 2h; | 100 | : | 0 |
| 0°C, 3h; | 8 | : | 92 |

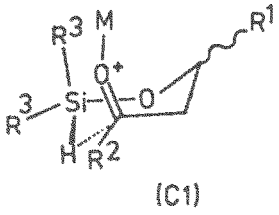
Scheme 3

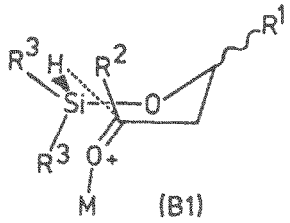
Mechanistic Interpretation. When considering the mechanism of the Lewis acid catalysed, anti-selective hydrosilylations, the following points are pertinent; (i) The facility of these reactions, when compared to those in Scheme 3, strongly suggests that the mechanism is indeed intramolecular; (ii) Mechanisms involving hydride transfer to the Lewis acids are generally unlikely, considering the range of Lewis acids which can be employed; (iii) The fact that $BF_3.OEt_2$ can be used suggests that the substrate oxygens do not chelate to the Lewis acids[14].

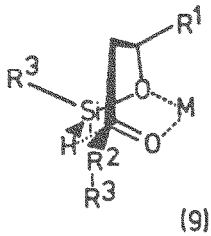
For a direct Si to C=O hydride transfer induced by coordination of a Lewis acid to the carbonyl oxygen, four conformational pairs of (2) can be envisaged as transition state models. Two are chair-like, (C1) and (C2), and two are boat-like, (B1) and (B2). The examination of molecular models reveals that in (B1) and (B2) it is impossible to orient the carbonyl group such that the hydride approaches along the Burgi-Dunitz trajectory[15]. (B2) is also disfavoured by steric interactions between $R^2$ and $R^3$, as is (C2). In contrast, (C1) lacks serious steric

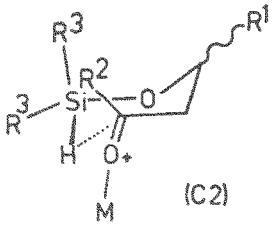
interactions and allows hydride approach along an acceptable trajectory[16]. In either of the chair transition states there will be a strong preference for $R^1$ to be equatorial, and (C1) thus leads to the anti-siladioxane (3).

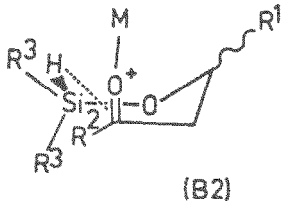
We have no confident explanation for the syn-selectivity observed in some cases with the Zn(II) catalysts, but it is possible that a chelated transition state may be involved. If both substrate oxygens were to bind to the Lewis acid, models suggest that hydride transfer would have to occur from conformation (9) (related to a bicyclo[2.2.2]octane), leading ultimately to the syn-diol.


(C1)


(B1)

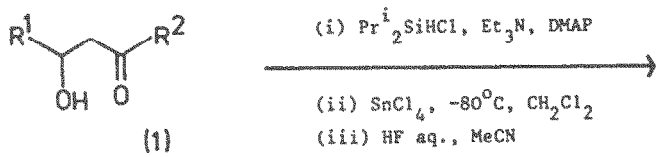

(9)


(C2)


(B2)

## CONCLUSIONS

In the course of investigating the intramolecular hydrosilylation of β-silyloxyketones (2) we have encountered both syn and anti selectivity. Whereas the level of the former is not especially useful, that of the latter is comparable with the best examples of 1,3-asymmetric induction previously observed in carbonyl addition reactions. The work has led to a method for the overall anti-selective reduction of β-hydroxyketones, summarised in Scheme 4. Good selectivity is maintained with a range of substrates, the yields are respectable and the conditions employed are quite mild. The major deficiency in the method is the yield in the initial silylation, and we are optimistic that improvements will be possible in this step[17].




(1)

(5)

Yields 60 - 69%
d.e. 95 - 98.3%

Scheme 4

## EXPERIMENTAL

$^1$H n.m.r. spectra were recorded on a Bruker WP80, with $CDCl_3$ as solvent. TMS was used as internal standard, except where molecules contained MeSi groups. In such cases, $CHCl_3$ was used as reference (taken as δ7.26). IR spectra were recorded as liquid films on a Perkin Elmer 298 instrument. G.l.c. analyses were performed on a Perkin Elmer F11 instrument, using a 2.5 m column packed with OV 225 (5%) on Chromosorb. For all pairs of isomeric siladioxanes (3)/(4), the cis-isomer (4) was eluted first. Microanalyses were carried out in the Department of Chemistry, University College, Dublin. Petroleum ether (b.p. 30-40°C), $CH_2Cl_2$, pyridine and $Et_3N$ were distilled from $CaH_2$. $SnCl_4$ was distilled before use. $MgBr_2.OEt_2$ was prepared from Mg and 1,2-dibromoethane in ether. Hydroxyketones (1) were prepared by directed aldol reactions[12b]. Boiling points quoted for short path distillations refer to oil bath temperatures. Flash chromatography was carried out using Kieselgel 60 (Merck), particle size 0.04-0.063 mm.

Chlorodi-isopropylsilane.- The method was adapted from that of Markiewicz[1b]. Dry diethyl ether (250 ml) was added to dry magnesium turnings (19.5 g, 0.8 g. atom) under nitrogen in a three-necked flask equipped with a reflux condenser, a dropping funnel and a mechanical stirrer. A small portion (1 ml) of isopropyl chloride (62.83 g, 0.8 mol) was added. When the reaction had started, the remainder of the isopropyl chloride was added slowly to the refluxing mixture. Reflux was maintained for 20 minutes and trichlorosilane (28 ml, 0.28 mol) mixed with dry ether (20 ml) was added to the flask so that a constant reflux was obtained. The reaction mixture was heated under reflux for a further 4h. Most of the solvent was distilled away and the mixture was cooled to room temperature. Petroleum ether (150 ml) was added to the residue, and the mixture was manipulated and stirred under nitrogen until it formed a white paste. The mixture was cooled in ice and concentrated hydrochloric acid (50 ml) was added cautiously with continuous stirring. The mixture was filtered and the residual precipitate was thoroughly washed with petroleum ether. The combined organic phase was dried ($MgSO_4$). Evaporation of solvent at atmospheric pressure and subsequent distillation under reduced pressure afforded $Pr^i_2SiHCl$ as a colourless liquid (28.5 g, 76.5%), b.p. 81-85°C at 80 mmHg (lit.[18] b.p. 54-55°C at 45 mmHg).

7-Di-isopropylsilyloxyundecan-5-one (2).- $Pr^i_2SiHCl$ (2.408g, 16 mmol), triethylamine (1.62 g, 16 mmol), and 4-(N,N-dimethylamino)pyridine (610 mg, 5 mmol) were dissolved in petroleum ether (20 ml) under a nitrogen atmosphere. 7-Hydroxyundecan-5-one (1; $R^1$,$R^2$ = Bu)[12b] (1.116 g, 6 mmol) in petroleum ether (5 ml) was added, and the reaction mixture was heated under reflux for 3h. Filtration and evaporation of solvent, followed by flash chromatography (hexane-ethyl acetate, 40:1) gave silylated hydroxyketone (2b) (2.9 g, 75%). An analytical sample was prepared by short-path distillation, b.p. 90°C at 0.3 mmHg. (Found: C, 67.75; H, 12.40%. $C_{17}H_{36}O_2Si$ requires C, 67.95; H, 12.05%)[19]; $\nu_{max}$ 2095 (Si-H), 1715 (C=O), 1450, 1370, 1100, 1050, 1000, 880, 840, 810 cm$^{-1}$; $\delta_H$ 4.20 (2H, m, Si-H and O-CH), 2.75-2.25 (4H, m, C4-$H_2$ and C6-$H_2$), 1.75-0.75 (30H, m, Si-isopropyl, Me and remaining $CH_2$).

Similarly prepared from (1; $R^1$,$R^2$ = $Pr^i$)[20] was 2,6-dimethyl-5-di-isopropylsilyloxyheptan-3-one (2a) (72% yield), b.p. 80°C at 0.3 mmHg. Found: C, 65.95; H, 11.85%. $C_{15}H_{32}O_2Si$ requires C, 66.1; H, 11.85%)[19]: $\nu_{max}$ (liquid film) 2100 (Si-H), 1710 (C = O), 1463, 1385, 1370, 1095, 1055, 920, 883 cm$^{-1}$; $\delta_H$ 4.25-4.0 (2H, m, Si-H and O-CH), 2.83-2.2 (3H, m, $CH_2$ and C2-H), 2.0-1.50 (1H, m, C6-H), 1.25-0.65 (26H, m, Si-isopropyl and Me).

5-Methyl-4-di-isopropylsilyloxyhexan-2-one (2c).- $Pr^i_2SiHCl$ (1.17 g, 7.8 mmol) and pyridine (616.9 mg, 7.8 mmol, 631 µl) in petroleum ether (20 ml) were treated with 5-methyl-4-hydroxyhexan-2-one (1, $R^1$ = $Pr^i$, $R^2$ = Me)[20] (780 mg, 6 mmol) under a nitrogen atmosphere. The mixture was heated under reflux for 5h and left stirring overnight at room temperature. Filtration and evaporation gave a clear colourless liquid. Column chromatography (hexane-ether, 40:1) gave silylated hydroxyketone (2c) (1.1 g, 75%). Further purification was possible by short path distillation, b.p. 65°C at 0.3 mmHg[19]. $\nu_{max}$ 2940, 2860, 2080 (Si-H), 1705 (C=O), 1455, 1370, 1100, 1000 cm$^{-1}$; $\delta_H$ 4.25-4.0 (2H, m, Si-H and O-CH), 2.50 (2H, m, $CH_2$), 2.18 (3H, s, Me), 1.95-1.60 (1H, m, C5-H) 1.13-0.78 (20H, m, Me and Si-isopropyl).

Similarly prepared from (1; $R^1$ = Me, $R^2$ = $Pr^i$)[21] was 2-methyl-5-di-isopropylsilyloxyhexan-3-one (2d) (79% yield), b.p. 65°C at 0.3 mmHg[19]. $\nu_{max}$ 2090 (Si-H), 1710 (C=O), 1460, 1375, 1135, 1100, 1055, 1000, 880 cm$^{-1}$; $\delta_H$ 4.52-4.0 (2H, m, Si-H and O-CH), 2.95-2.0 (3H, m, $CH_2$ and C2-H), 1.32-0.83 (23H, m, Si-isopropyl and Me).

Similarly prepared from (1; $R^1$,$R^2$ = $Pr^i$) and $Me_3SiCl$ was 2,6-dimethyl-5-trimethylsilyloxyheptan-3-one (7) (72% yield), b.p. 70°C at 0.3 mmHg. (Found: C, 63.0; 11.4%. $C_{12}H_{26}O_2Si$ requires C, 62.55; H, 11.35%); $\nu_{max}$ 2960, 1710 (C=O), 1465, 1365, 1250, 1095, 1055, 840, 750 cm$^{-1}$; $\delta_H$ 4.13-3.85 (1H, dt, O-CH), 2.8-2.13 (3H, m, C2-H and C4-$H_2$), 1.58 (1H, m, C6-H), 1.0 (6H, dd, Me), 0.80 (6H, dd, Me), 0.0 (9H, s, Si-Me).

Similarly prepared from isopropanol and $Pr^i_2SiHCl$, but with the omission of chromatography, was 2-di-isopropylsilyloxypropane (8) (77% yield), b.p. 76-78°C at 55 mmHg[19]. $\nu_{max}$ 2930, 2860, 2080, (Si-H), 1455, 1375, 1360, 1170, 1120, 875 cm$^{-1}$; $\delta_H$ 4.17-3.50 (2H, m, Si-H and O-CH), 1.33-0.67 (20H, m, Si-isopropyl and Me).

Similarly prepared from (1 ; $R^1$,$R^2$ = $Pr^i$) and $Me_2SiHCl$, with the omission of chromatography was 2,6-dimethyl-5-dimethylsilyloxyheptan-3-one (2e) (60% yield), b.p. 50°C at 0.1 mmHg. $\nu_{max}$ 2960,

2120 (Si-H), 1710 (C=O), 1465, 1375, 1250, 1055, 890, 830, 765 $cm^{-1}$; $\delta_H$ 4.75-4.50 (1H, m, Si-H), 4.05 (1H, m, O-CH), 3.0-2.13 (3H, m, C2-H and C4-$H_2$), 2.0-1.43 (1H, m, C6-H), 1.25-0.63 (12H, m, Me), 0.18 (3H, d, J 2.6Hz, Si-Me), 0.15 (3H, d, J 2.6Hz, Si-Me).

Anti- and syn-2,6-Dimethyl-3,5-heptanediol (5 and 6 ; $R^1$,$R^2$ = $Pr^i$).- Hydroxyketone (1; $R^1$,$R^2$ = $Pr^i$) (1.0g, 6.32 mmol) dissolved in ethanol 10 ml) was treated with sodium borohydride (212 mg, 5.58 mmol) over a period of 1h at room temperature. The mixture was quenched with sodium hydroxide (1M, 1 ml) and was extracted with ether. After drying ($Na_2SO_4$) and evaporation of solvent, flash chromatography (ether-hexane-ethyl acetate, 1:3:1) afforded (i) anti-diol (5; $R^1$,$R^2$ = $Pr^i$) (369 mg, 36.5%), m.p. 71-72°C after recrystallization (lit[22]. m.p. 72°C); $\delta_H$ 3.80-3.50 (2H, q, C3-H and C5-H), 2.0 (2H, br s, OH), 1.87-1.50 (4H, m, $CH_2$, C2-H), C6-H), 1.08-0.75 (12H, dd, Me) and (ii) syn-diol (6 ; $R^1$,$R^2$ = $Pr^i$) (449 mg, 44.5%) as a colourless liquid. (Found: C, 66.95; H, 13.0%. $C_9H_{20}O_2$ requires C, 67.45; H, 12.6%); $\nu_{max}$ 3360 (OH), 1460, 1362, 1250 $cm^{-1}$; $\delta_H$ 3.77-3.50 (2H, m, C3-H and C5-H), 3.25 (2H, s, OH), 1.87-1.43 (4H, m, $CH_2$, C2-H and C6-H), 0.93 (12H, d, Me).

Anti- and syn-5-Methyl-2,4-hexanediol (5 and 6 ; $R^1$ = $Pr^i$, $R^2$ = Me).- Hydroxyketone (1; $R^1$ = $Pr^i$, $R^2$ = Me) (330 mg, 2.54 mmol) in dry ether (23 ml) was added dropwise to a suspension of lithium aluminium hydride (98 mg, 2.6 mmol) in ether (12 ml). The reaction mixture was heated under reflux for 30 min and was cooled to room temperature. Ice-cold water was added dropwise to the reaction mixture until no more hydrogen was evolved. The aluminium hydroxide precipitate was dissolved by adding 10% sulphuric acid. The organic layer was washed with saturated aqueous sodium hydrogen carbonate and sodium chloride solution then dried ($Na_2SO_4$). Evaporation and flash chromatography (hexane-ethyl acetate, 5:1) gave (i) anti-diol (5; $R^1$ = $Pr^i$, $R^2$ = Me) (100 mg, 30%): $\nu_{max}$ 3380, 1458, 1380, 1255, 1240 $cm^{-1}$; $\delta_H$ 4.18 (1H, m, C2-H), 3.63 (1H, m, C4-H), 2.75 (2H, s, OH), 1.65-1.42 (3H, m, $CH_2$ and C5-H), 1.23 (3H, d, J 6Hz, $CH_3$), 0.96-0.86 (6H, dd, $CH_3$) [lit[22]. n.m.r. $\delta_H$ 4.12, 3.64, 1.23 (d, J 6Hz)] and (ii) syn-diol (6; $R^1$ = $Pr^i$, $R^2$ = Me) (110 mg, 33%): $\nu_{max}$ 3360, 1460, 1380, 1360, 1255 $cm^{-1}$; $\delta_H$ 4.0 (1H, m, C2-H), 3.88 (2H, s, OH), 3.55 (1H, m, C4-H), 1.80-1.28 (3H, m, $CH_2$ and C5-H), 1.12 (3H, d, J 6Hz, $CH_3$), 0.85 (6H, d, $CH_3$) [lit.[22] n.m.r. $\delta_H$ 4.0, 3.58, 1.19 (d, J 6Hz)].

Similarly prepared, but without use of chromatography, was a mixture of anti and syn-5,7-undecandiols (5 and 6; $R^1$,$R^2$ = Bu).

trans-2,2,4,6-Tetraisopropyl-1,3-dioxa-2-silacyclohexane (3; $R^1$,$R^2$,$R^3$ = $Pr^i$).- The method was adapted from that of Corey and Hopkins[1d]. The solution of anti-diol (5: $R^1$,$R^2$ = $Pr^i$) (116.6 mg, 0.725 mmol) and 2,6-lutidine (253 µl, 2.175 mmol) in $CDCl_3$ (1.45 ml) at 0°C was treated with $Pr^i_2Si(OTf)_2$ (358.4 µl, 0.87 mmol). The solution was warmed to room temperature. After 5 min. proton n.m.r. showed that the reaction was complete. The $CDCl_3$ was evaporated and the crude siladioxane product was passed through silica gel (ether-hexane-ethyl acetate 1:3:1) to give the trans-siladioxane (156 mg, 78%). An analytical sample was prepared by short path distillation, b.p. 80°C at 0.25 mmHg. (Found: C, 65.7; H, 11,85%. $C_{15}H_{32}O_2Si$ requires C, 66.1; H, 11.85%): $\nu_{max}$ 1463, 1385, 1244, 1135, 1110 $cm^{-1}$; $\delta_H$ 3.86-3.57 (2H, m, O-CH), 1.78 (t, J 5Hz, $CH_2$)[23], 2.0-0.75 (m, isopropyl; 30H together with foregoing t).

Similarly prepared from the corresponding diols were: (i) cis-2,2,4,6-Tetraisopropyl-1,3-dioxa-2-silacyclohexane (4; $R^1$,$R^2$,$R^3$ = $Pr^i$) (77% yield), b.p. 80°C at 0.25 mmHg. (Found: C, 65.9: H, 11.7%. $C_{15}H_{32}O_2Si$ requires C, 66.1: H, 11.85%); $\nu_{max}$ 1460, 1245, 1135 $cm^{-1}$; $\delta_H$ 3.87-3.37 (2H, m, O-CH), 1.87-0.75 (30H, m, $CH_2$ and isopropyl). (ii) trans-2,2,4-Tri-isopropyl-6-methyl-1,3-dioxa-2-silacyclohexane (3; $R^1$,$R^3$ = $Pr^i$, $R^2$ = Me) (79% yield), b.p. 70°C at 0.3 mmHg. (Found: C, 63.6: H, 11.4%. $C_{13}H_{28}O_2Si$ requires C, 63.85; H, 11.55%); $\nu_{max}$ 1460, 1380, 1240, 1130 $cm^{-1}$; $\delta_H$ 4.58-4.15 (1H, m, O-CH), 3.95-3.65 (1H, m, O-CH), 2.10-0.75 (26H, m, Si-isopropyl, C-isopropyl, $CH_3$, and $CH_2$) (iii) cis-2,2,4-Tri-isopropyl-6-methyl-1,3-dioxa-2-silacyclohexane (4; $R^1$,$R^3$ = $Pr^i$, $R^2$ = Me) (86% yield) b.p. 70°C at 0.3 mmHg. (Found: C, 64.05; H, 11.3%. $C_{13}H_{28}O_2Si$ requires C, 63.85; H, 11.55%); $\nu_{max}$ 1466, 1375, 1240 $cm^{-1}$; $\delta_H$ 4.34 (1H, m, O-CH), 3.8 (1H, m, O-CH), 1.98-0.75 (26H, m, Si-isopropyl, C-isopropyl, $CH_3$ and $CH_2$). (iv) trans-2,2-Di-isopropyl-4,6-dibutyl-1;3-dioxa-2-silacyclohexane (3; $R^1$,$R^2$ = Bu, $R^3$ = $Pr^i$) b.p. 80°C at 0.2 mmHg. (Found: C, 68.35; H, 12.2%. $C_{17}H_{36}O_2Si$ requires C, 67.95; H, 12.05%); $\nu_{max}$ 2940, 1455, 1370, 1110, 940 $cm^{-1}$; $\delta_H$ 4,25-3.87 (2H, br m, O-CH), 1.70 (2H, t, J 5Hz, C5-$H_2$)[23], 1.20-0.50 (32H, m, n-butyl and Si-isopropyl). (v) cis-2,2-Di-isopropyl-4,6-dibutyl-1,3-dioxa-2-silacyclohexane (4; $R^1$,$R^2$ = Bu, $R^3$ = $Pr^i$), b.p. 80°C at 0.2 mmHg. (Found: C, 68.05; H, 12.3%. $C_{17}H_{36}O_2Si$ requires C, 67.95; H, 12.05%); $\nu_{max}$ 2940, 1455, 1370, 1240, 1110, 1050, 940 $cm^{-1}$; $\delta_H$ 4.0 (2H, m, O-CH), 1.75-0.75 (34H, m, C5-$H_2$, n-butyl and Si-isopropyl).

The last two were formed from a mixture of the corresponding diols (see above) and separated by flash chromatography (hexane).

trans-2,2-Dimethyl-4,6-di-isopropyl-1,3-dioxa-2-silacyclohexane (3; $R^1$,$R^2$ = $Pr^i$,$R^3$ = Me).- The method was adapted from that of Krieble and Burkhard[24]. $Me_2SiCl_2$ (208 mg, 1.61 mmol, 195 µl) and pyridine (254 mg, 3.22 mmol, 260 µl) were dissolved in petroleum ether (3 ml) under $N_2$. Anti-diol (5; $R^1$,$R^2$ = $Pr^i$) (225 mg, 1.41 mmol), dissolved in petroleum ether (2 ml), was added to the flask via a syringe with stirring. The reaction mixture was heated under reflux for 2h. The mixture was filtered and the precipitate washed with petroleum ether. Removal of solvent, followed by short path distillation, gave the trans-siladioxane (201 mg, 66%), b.p. 60°C at 0.2 mmHg. (Found: C, 60.9; H, 11.20%. $C_{11}H_{24}O_2Si$ requires C, 61.05; H, 11.20%); $\nu_{max}$ 1455, 1380, 1115 $cm^{-1}$; $\delta_H$ 3.75-3.40 (2H, m, O-CH) 1.66 (t, J 5Hz m $CH_2$)[23], 1.87-1.25 (m, isopropyl CH, 4H together with foregoing t), 1.0-0.63 (12H, m, isopropyl Me), 0.1 (6H, s, Si-Me).

Similarly prepared was cis-2,2-Dimethyl-4,6-di-isopropyl-1,3-dioxa-2-silacyclohexane (4; $R^1,R^2$ = $Pr^i$, $R^3$ = Me) (47% yield), b.p. 60°C at 0.2 mmHg. (Found: C, 60.8, 11.25%. $C_{11}H_{24}O_2Si$ requires C, 61.05; H, 11.20%); $\nu_{max}$ 2930, 1455, 1378, 1115 $cm^{-1}$; $\delta_H$ 3.87-3.37 (2H, m, O-CH), 1.87-1.05 (4H, m, $CH_2$ and isopropyl CH), 1.0-0.63 (12H, m, isopropyl Me), 0.25 (3H, s, Si-Me), 0.1 (3H, s, Si-Me).

Treatment of Silyloxyketones (2) with hydrosilylation catalysts.

The following description is typical of the treatment of the di-isopropylsilyloxyketones (2a-d) with $SnCl_4$. The first part (omitting the desilylation with aq. HF/MeCN) serves as a basis for the other experiments in the Table.

Treatment of (2) with $SnCl_4$.- Silyloxyketone (2a) (200 mg, 0.74 mmol) was dissolved in $CH_2Cl_2$ (5 ml) under $N_2$, and cooled to -80°C. $SnCl_4$ (10 µl, 22 mg, 0.08 mmol) was added via syringe. The mixture was stirred for 2h, quenched with aqueous sodium hydrogen carbonate (0.5 ml), allowed to warm gradually to room temperature, and extracted with ether. The organic phase was dried ($Na_2SO_4$) and evaporated. A portion of the crude product (7% of total) was set aside and analysed by g.l.c., showing the siladioxanes (3 and 4: $R^1,R^2,R^3$ = $Pr^i$) to be present in the ratio 120:1, being the only significant volatile components.

The remainder of the crude product was treated with aqueous HF (40%, 5 drops) in acetonitrile (4 ml) at room temperature for 30 min. The mixture was partitioned between chloroform and water, and the organic phases dried ($Na_2SO_4$) and evaporated. Flash chromatography (ether-hexane-ethyl acetate, 1:3:1) gave (i) anti-diol (5; $R^1,R^2$ = $Pr^i$) (102 mg, 93%) and (ii) syn-diol (6; $R^1,R^2$ = $Pr^i$) (ca. 1.5 mg).

From a similar experiment employing (2b) as starting material was isolated (5; $R^1,R^2$ = Bu) (80% yield), m.p. 76-78°C (lit.[12b] m.p. 76-78°C).

Reduction of cyclohexanone with 2-di-isopropylsilyloxypropane(8) and $SnCl_4$.- Cyclohexanone (26µl, 0.25 mmol) and silane (8) (57 mg, 0.325 mmol) were dissolved in $CH_2Cl_2$ under $N_2$, cooled to -80°C and treated with $SnCl_4$ (4µl). The mixture was stirred for 2h, then quenched, worked up and desilylated as described for the previous experiment. Analysis by g.l.c. showed only cyclohexanone.

The other experiments referred to in Scheme 3 were performed similarly.

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