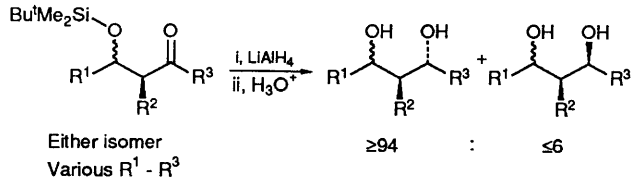
1,3- *versus* 1,2-Asymmetric Induction in the Reduction of β-Hydroxy Ketones by Intramolecular Hydrosilylation

Saeed Anwar, Gavin Bradley and Anthony P. Davis *
Department of Chemistry, Trinity College, Dublin 2, Ireland

The role of 1,2-asymmetric induction has been investigated in the 1,3-*anti*-selective reduction of β-hydroxy ketones *via* intramolecular hydrosilylation. For the α-methyl β-hydroxy ketones **2a**, **3a**, the effect of the α-substituent is negligible except that it appears to reinforce 1,3-asymmetric induction. For the α-ethyl β-hydroxy ketones **2b**, **3b**, 1,3-asymmetric induction is dominant but not overwhelming. The super-acid $TfOH_2^+$ $B(OTf)_4^-$ has been used as a catalyst for the hydrosilylation giving, in one case, an improved result when compared with previous methodology.

There is continuing interest in asymmetric induction from neighbouring centres during addition reactions to C=O and C=C bonds in acyclic molecules.[1] Simple intuition and classical chemical experience both suggest that the closer the asymmetric centre is to the site of reaction, the more powerful the effect should be. Thus, while it has long been established that additions to carbonyl groups may take place with good levels of 1,2-asymmetric induction,[2] it is only recently that useful 1,3-asymmetric induction has been achieved.[3–8]

When 1,3-asymmetric induction is set against 1,2-asymmetric induction (as in, for example, additions to α,β-disubstituted carbonyl compounds) it is natural to assume that the latter will predominate. For carbonyl reductions with conventional hydride reducing agents this is generally the case, as exemplified by the recent work of Bloch *et al.* (Scheme 1).[9] Even in the

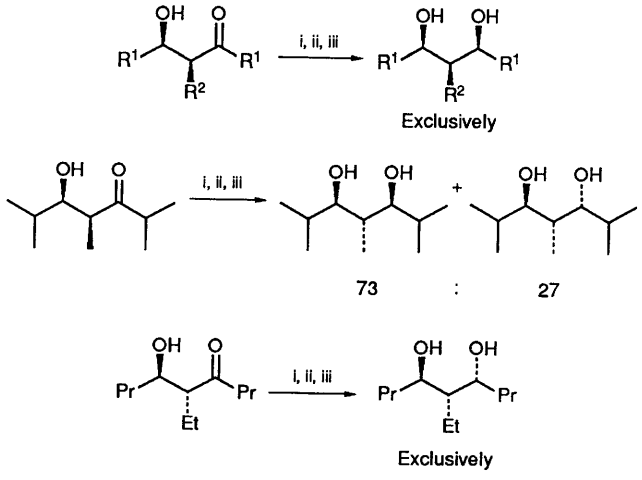


Scheme 1

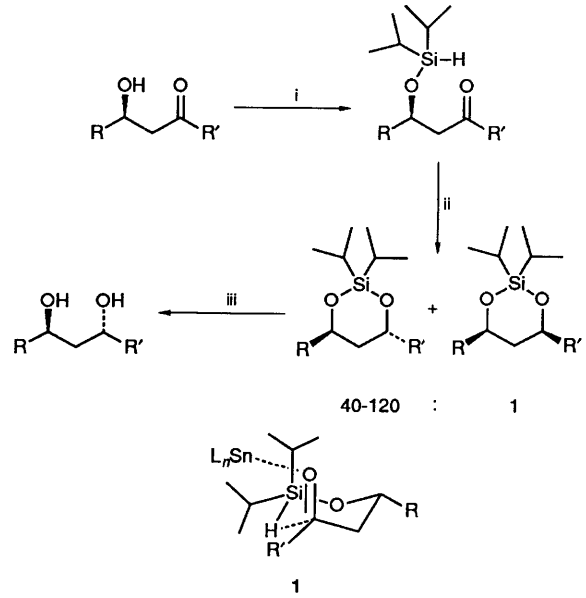
'chelation-controlled' reduction of β-hydroxy ketones due to Narasaka and Pai, generally capable of impressive 1,3-*syn*-selectivity, a substituent in the α position has a significant and sometimes a controlling effect (Scheme 2).[3b]

Recently we reported a method for reducing β-hydroxy ketones which was complementary to that of Narasaka and Pai in that it was highly *anti*-selective.[5] As shown in Scheme 3, it relied on an intramolecular hydrosilylation for which we postulated the chair-like transition state **1** (in the case of the major product). Stereocontrol was presumed to arise from, among other factors, a potential 1,3-diaxial interaction between R and one of the Si–Pr^i groups.

Our hypothesis had one intriguing consequence. In contrast to the β-substituent R, a substituent α to the carbonyl group in **1** seemed unlikely to suffer any severe steric interactions whether axially or equatorially directed. Thus it appeared that, very unusually, the influence of the remote centre should effectively overwhelm that of the neighbouring one. We undertook to investigate this possibility and now report that, with limitations, it is the case. Since we obtained our first results, two other groups have described carbonyl addition reactions which occur through cyclic transition states and show high levels of



Scheme 2 *Reagents and conditions:* i, Bu_3B, THF (tetrahydrofuran); ii, $NaBH_4$, −100 °C; iii, H_2O_2, MeOH, then HCl, MeOH

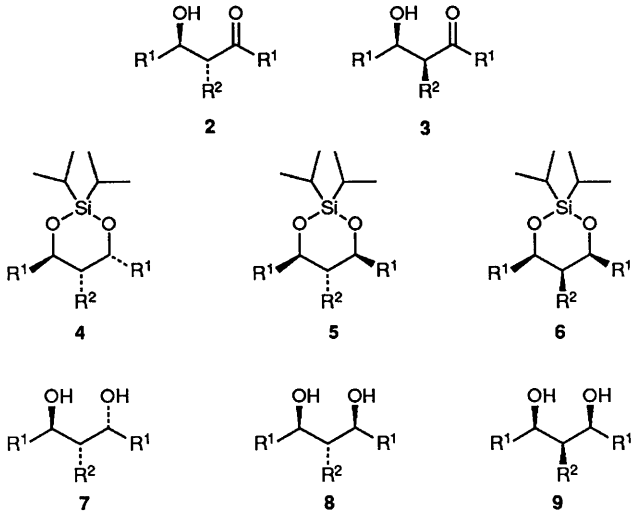


Scheme 3 *Reagents and conditions:* i, Pr^i_2SiHCl, base; ii, $SnCl_4$, CH_2Cl_2, −80 °C; iii, HF aq. MeCN

1,3-asymmetric induction that is unperturbed by α-methyl substituents.[6,7]

Results and Discussion

As substrates for this investigation we chose the three pairs of isomers **2a–c**, **3a–c**.* Each pair was available as a diastereoisomeric mixture from a simple directed aldol condensation. Mixtures **2a**, **3a** and **2b**, **3b** could be separated by flash chromatography (the latter with some difficulty). However, we were unable to separate hydroxy ketones **2c** and **3c** which were therefore used as a mixture (1:2, by ^{13}C NMR spectroscopic analysis).

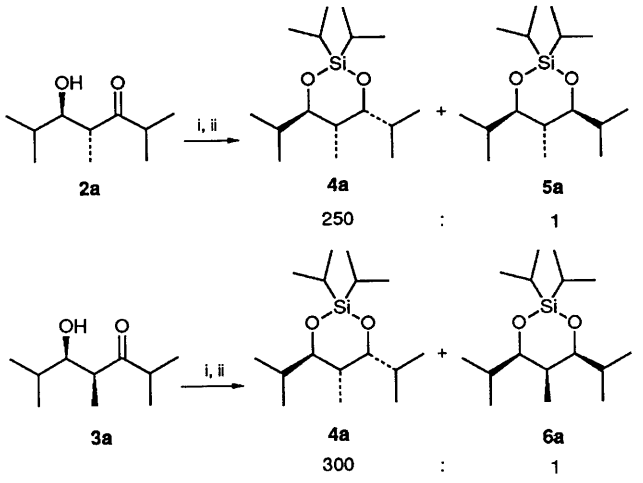


a; $R^1 = Pr^i$, $R^2 = Me$
b; $R^1 = Pr$, $R^2 = Et$
c; $R^1 = Et$, $R^2 = Me$

As we proposed to assess the stereoselectivity of the reduction by GC analysis of the intermediate 2-sila-1,3-dioxanes **4–6** (*cf.* Scheme 3), we required standard samples of the latter. For the 4,6-diisopropyl-5-methyl series **4–6a**, the individual hydroxy ketones **2a** and **3a** were subjected to non-stereoselective reductions with sodium borohydride to give diol mixtures **7a**, **8a** and **7a**, **9a**. Flash chromatography led to a pure sample of each diol, which was then treated with diisopropylsilyl bis-(trifluoromethanesulphonate) [$Pr^i_2Si(OTf)_2$] and 2,6-dimethylpyridine to give the corresponding siladioxane.[10] Control experiments demonstrated that small amounts of either **5a** or **6a** could be detected by conventional packed-column GC in the presence of the *cis,trans*-isomer **4a**.

A similar sequence (omitting the chromatography) was used to convert a mixture of hydroxy ketones **2b** and **3b** into a mixture of the 5-ethyl-4,6-dipropyl siladioxanes **4–6b**. The latter could be resolved by capillary GC (CGC) into three peaks, identifiable on the basis of subsequent results from the hydrosilylation experiments (*vide infra*). The 4,6-diethyl-5-methylsiladioxanes **4–6c** were similarly prepared as a mixture which could again be resolved by CGC.

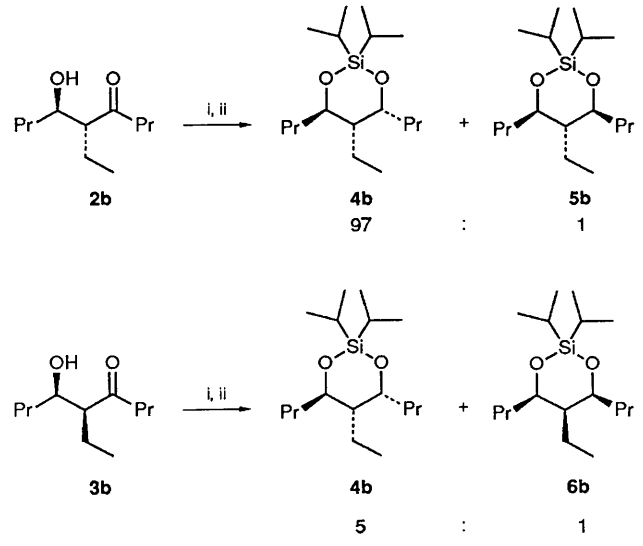
As shown in Scheme 4, application of our intramolecular reduction method to the hydroxy ketones **2a** and **3a** gave the results we had expected, except that in both cases the selectivity was better than we had previously observed with any other substrate. Thus, the *anti*-hydroxy ketone **2a** was diisopropylsilylated (82% yield) and treated with tin tetrachloride to give the siladioxanes **4a** and **5a** in a ratio of 250:1. After desilylation with aqueous hydrofluoric acid in acetonitrile, the *syn,anti*-diol **7a** was isolated in 90% yield (74% overall, based on **2a**). The *syn*-hydroxy ketone **3a** was treated similarly, giving a 75% yield on



Scheme 4 *Reagents and conditions:* i, Pr^i_2SiHCl, Et_3N, hexane, DMAP (4-dimethylaminopyridine) cat.; ii, $SnCl_4$, CH_2Cl_2, −80 °C

silylation, a siladioxane ratio **4a**:**6a**, 300:1, and a 58% yield of diol **7a** (44% overall from **3a**). These results may be compared with the *anti*:*syn* ratio of 120:1 obtained earlier when the same sequence was applied to the analogous substrate lacking the α-methyl substituent **2** ($R^1 = Pr^i$, $R^2 = H$).[5]

We then turned our attention to the hydroxy ketones **2b**, **3b**. It seemed that the two competing chiral centres would be better matched in these substrates than in **2a**, **3a**, and that a fairly rigorous test of the 1,3-*anti* selectivity would be provided. As shown in Scheme 5, our methodology passed the test, but not



Scheme 5 *Reagents and conditions:* i, Pr^i_2SiHCl, Et_3N, hexane, DMAP cat.; ii, $SnCl_4$, CH_2Cl_2, −80 °C

with great facility. The *anti*-hydroxy ketone **2b** was diisopropylsilylated (66% yield) and treated with tin tetrachloride. Quantitative analysis by CGC indicated that the siladioxanes **4b** and **5b** were formed in 39% yield with a ratio of 97:1. However, for the *syn*-isomer **3b**, diisopropylsilylation (70% yield) followed by treatment with tin tetrachloride resulted in the siladioxanes **4b** and **6b** in a ratio of only 5:1 (47% yield). The GC peaks could be identified at this stage, simply on the basis that only *cis,trans*-siladioxane **4b** could be accessed from both hydroxy ketones.

Although the hydrosilylation yields were rather low, this was probably due in part to the small scale of the experiments, which arose in turn from the difficulty of preparing isomerically pure starting materials. Analysis of the crude products by ^{13}C NMR

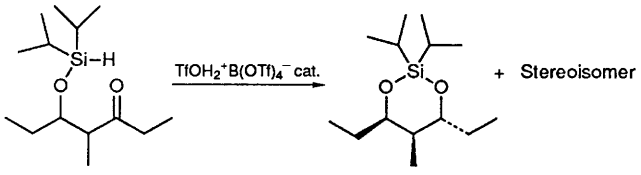
* The hydroxy ketones **2**/**3a**, **b** had been used in the investigation of Narasaka and Pai; *cf.* Scheme 2.

spectroscopy suggested that in each case a major side-reaction was desilylation of the starting material to give the recovered hydroxy ketone **2b** or **3b**, probably promoted by adventitious water. Larger scale reactions on mixtures of **2b** and **3b** gave better yields. For example, in one run, a mixture of composition **2b**:**3b**, 2:3 was silylated in 77% yield, then treated with tin tetrachloride and desilylated with aqueous hydrofluoric acid in acetonitrile to give a mixture of the diols **7–9b** in 68% yield (52% overall from the hydroxy ketones). For all key reactions the product mixtures of siladioxanes and/or diols were analysed by ^{13}C NMR spectroscopy and at no stage was there any indication that the siladioxane ratio as measured by GC was unreliable as a measure of stereoselectivity.

In the case of the third pair of substrates, the hydroxy ketones **2c**, **3c** we were unable to separate the diastereoisomers and were therefore forced to rely on experiments involving mixtures of the two. Starting with a mixture **2c**:**3c**, 1:2, diisopropylsilylation as above gave the corresponding derivatives in 80% yield (*anti*:*syn*, 2:5). Subsequent treatment with tin tetrachloride gave a mixture of two siladioxanes in the ratio 26:1 and in 74% yield (by quantitative GC). Desilylation gave a mixture of diols (66% yield based on silylated hydroxy ketone) which was shown by ^{13}C NMR spectroscopy to consist mainly of the *syn*:*anti* isomer **7c**. This result is consistent with those described previously, in that it suggests that both hydroxy ketones **2c** and **3c** are reduced with 1,3-*anti* selectivity.*

We had previously observed that trifluoroacetic acid (TFA) could be used as a catalyst for the intramolecular hydrosilylation in Scheme 3, giving a reaction which was exceptionally stereoselective although not entirely clean.[5b] Recent work in this laboratory had shown that the superacid trifluoromethanesulphonylhydroxonium tetrakis(trifluoromethanesulphonyl)boronate [$TfOH_2^+B(OTf)_4^-$] could be used to catalyse the addition of allylsilanes to aldehydes and ketones.[11] It had been suggested that this reagent succeeds where other Brønsted acids fail because the anion $B(OTf)_4^-$ is so stable and non-nucleophilic that it is unable to participate in unwanted side-reactions such as protonolysis of the allylsilane. On this basis, it seemed that $TfOH_2^+B(OTf)_4^-$ might also be useful in the intramolecular hydrosilylations, giving the stereoselectivity of TFA without the side reactions.

As shown in Scheme 6, the superacid was indeed found to



6c

38 : 1

Scheme 6

be effective when applied to the mixture of diisopropylsilyl derivatives of the hydroxy ketones **2c**, **3c**. The ratio of the siladioxanes increased to 38:1, and the yield of diol **7c** obtained after desilylation was 75%. The superacid was also applied successfully in the sequences starting from the hydroxy ketones **2b** and **3b**, although in these cases it appeared to have no particular advantage over tin tetrachloride.

* Given the yields observed, it is theoretically possible that the *syn*-hydroxy ketone **3c** (the major isomer) reacted selectively to give **7c** in good yield, while the *anti* isomer **2c** reacted with low selectivity and in very poor yield. However, in view of the results obtained with the other substrates this seems quite unlikely.

From the foregoing results, we are able to conclude that our original hypothesis was correct, namely that the intramolecular hydrosilylation of β-(diisopropylsilyl)oxy ketones is strongly governed by 1,3-asymmetric induction and that 1,2-asymmetric induction plays, at best, a minor role. This is particularly true for substrates **2a** and **3a** where, remarkably, the α-methyl substituent appears to reinforce the 1,3-asymmetric induction irrespective of its orientation. We have no explanation for this phenomenon, although it may be noted that a similar effect was observed by Evans and Chapman in their work on triacetoxyborohydride reductions.[6a,b] It is slightly disappointing that the control by the β-centre is substantially degraded on moving to substrates **2b**, **3b**, but our results still contrast strongly with those of Narasaka and Pai who observed total control by the α-substituent with these compounds (Scheme 2).

Experimental

^1H and ^{13}C NMR spectra were recorded on a Bruker MSL 300 instrument or, if stated, on a Bruker WP 80 instrument. All spectra were recorded in $CDCl_3$, with TMS (tetramethylsilane) as the internal standard. *J* values are given in Hz. IR spectra were recorded on a Perkin-Elmer 883 spectrophotometer. Conventional (packed-column) gas chromatography was performed with a Perkin-Elmer F11 instrument, using a 2.5 m column packed with OV225 (5%) on Chromosorb. CGC was carried out using a Varian 3300 gas chromatograph with either Carbowax or OV1 columns, 25 m in length. Quantitative gas chromatography was carried out on the latter instrument, using decahydronaphthalene as an internal standard. Tetrahydrofuran (THF) and diethyl ether (Et_2O, referred to as ether) were dried by distillation from sodiobenzophenone. Ethanol was dried by distillation from magnesium ethoxide. Dichloromethane and hexane were dried by distillation from calcium hydride. Triethylamine, diisopropylamine and 2,6-dimethylpyridine were purified by distillation from calcium hydride. Pyridine was dried by heating under reflux over potassium hydroxide pellets for 2 h, followed by distillation. All aldehydes and ketones were purified by distillation. Tin tetrachloride was purified by fractional distillation under an inert atmosphere. Chlorodiisopropylsilane was prepared as described previously.[5b] $Pr^i_2Si(OTf)_2$ was prepared according to the method of Corey and Hopkins[10] and was used immediately after distillation. $TfOH_2^+B(OTf)_4^-$ was prepared after the method of Olah *et al.*[12]

(4RS,5RS)-5-*Hydroxy*-2,4,6-*trimethylheptan*-3-*one* (anti-*Isomer*) **2a** *and* (4RS,5SR)-5-*Hydroxy*-2,4,6-*trimethylheptan*-3-*one* (syn-*Isomer*) **3a**.—Lithium diisopropylamide was prepared by adding diisopropylamine (6.06 g, 60 mmol, 8.4 cm^3) to butyllithium (1.70 mol dm^{-3} in hexane; 32 cm^3, 54.50 mmol) in dry THF (90 cm^3) at −80 °C under an inert atmosphere. The reaction mixture was warmed to −40 °C and, after being stirred for 10 min at this temperature, was recooled to −80 °C. A solution of 2-methylpentan-3-one (5.3 g, 53 mmol) in THF (15 cm^3) was added. Stirring was continued for 10 min after which a solution of 2-methylpropanal (3.82 g, 53 mmol) in THF (15 cm^3) was added in one portion. The mixture was stirred for 20 min at −80 °C and then quenched with saturated aqueous ammonium chloride and extracted with dichloromethane. The extract was dried ($MgSO_4$) and evaporated under reduced pressure. Flash chromatography (ethyl acetate–hexane–ether, 1:5:1) of the residue gave (i) the *anti*-α-methyl-β-hydroxy ketone **2a** (3.5 g, 38%); ν_{max}(liquid film)/cm^{-1} 3490 (OH), 2960, 2930, 1695 (C=O), 1465, 1380, 1010 and 990; δ_H(80 MHz) 3.63–3.30 (1 H, m, 5-H), 3.13–2.50 (3 H, m, 2-H, 4-H and OH), 2.0–1.43 (1 H, m, 6-H) and 1.25–0.80 (15 H, m, CH_3); δ_C(WP80) 219.7 (C=O), 78.6 (COH), 47.2, 41.2 (methine), 30.6, 20.1, 18.1, 15.8 and 14.6 (methyl) (lit.,[6b] δ_C 78.2, 40.8 and

14.3) and (ii) *syn*-α-methyl-β-hydroxy ketone **3a** (1.8 g, 20%); ν_{max}(liquid film)/cm^{-1} 3490 (OH), 2960, 2930, 1695 (C=O), 1460, 1380, 1010 and 985; δ_H(80 MHz) 3.58–3.38 (1 H, m, 5-H), 3.13 (1 H, s, OH), 3.08–2.43 (2 H, m, 2-H and 4-H), 1.95–1.43 (1 H, m, 6-H) and 1.25–0.75 (15 H, m, CH_3); δ_C(WP80) 219.7 (C=O), 76.6 (COH), 40.1 (methine) and 10.1 (methyl) (lit.,[6b] δ_C 76.2, 39.7 and 9.7).

(5RS,6RS)-5-*Ethyl*-6-*hydroxynonan*-4-*one* (anti-*Isomer*) **2b** *and* (5RS,6SR)-5-*Ethyl*-6-*hydroxynonan*-4-*one* (syn-*Isomer*) **3b**.—The preparation was carried out as for the previous experiment, employing diisopropylamine (3.74 g, 37 mmol), butyllithium (1.76 mol dm^{-3} in hexanes; 18.75 cm^3, 33 mmol) heptan-4-one (3.42 g, 30 mmol) and butanal (2.16 g, 30 mmol). Flash chromatography (hexane–ethyl acetate, 7:3) yielded a mixture of the hydroxy ketones **2b** and **3b** as a colourless liquid (3.69 g, 66%). The chromatography was repeated several times in order to isolate samples of the individual diastereoisomers. In each case the fractions were analysed by CGC (Carbowax column; *anti*-isomer **2b** eluted first) and only those fractions containing almost exclusively **2b** or **3b** were retained, the remainder being rechromatographed. This resulted in (i) the *anti*-hydroxy ketone **2b** (168 mg); ν_{max}(liquid film)/cm^{-1} 3453 (OH), 1704 (C=O), 1460, 1404, 1380, 1269, 1123 and 946; δ_H($CDCl_3$) 3.6–3.7 (1 H, m, 6-H), 2.75 (1 H, d, *J* 6.1, OH), 2.44 (1 H, dt, *J* 7.71, 5.91, 5-H), 2.39 (2 H, t, *J* 7.2, 3-H), 1.1–1.7 (8 H, m, CH_2) and 0.7–0.9 (9 H, m, CH_3); δ_C($CDCl_3$) 216.4 (C=O), 71.8 (C-6), 58.0 (C-5), 46.6 (C-3), 37.5 (C-7), 22.1, 18.8, 16.4, 13.8, 13.5 and 11.7 (lit.,[3b] 72.2, 22.3), and (ii) the *syn*-hydroxy ketone **3b** (390 mg); ν_{max}(neat)/cm^{-1} 3465 (OH), 1702 (C=O), 1461, 1405, 1379, 1175, 1144 and 1009; δ_H($CDCl_3$) 3.65–3.75 (1 H, m, 6-H), 2.73 (1 H, br s, OH), 2.3–2.5 (3 H, m, 3-H and 5-H), 1.1–1.8 (8 H, m, CH_2) and 0.7–1.0 (9 H, m, CH_3); δ_C($CDCl_3$) 215.3 (C=O), 71.1 (C-6), 58.2 (C-5), 46.3 (C-3), 36.6 (C-7), 19.7, 19.0, 16.4, 13.7, 13.4 and 12.1 (lit.,[3b] 71.6 and 21.0).

5-*Hydroxy*-4-*methylheptan*-3-*one* (*Mixture of* anti-*Isomer* **2c** *and* syn-*Isomer* **3c**.—The preparation was carried out as for the previous experiment, employing diisopropylamine (3.74 g, 37 mmol), butyllithium (1.76 mol dm^{-3} in hexanes; 18.75 cm^3, 33 mmol), pentan-3-one (2.58 g, 30 mmol) and propanal (1.74 g, 30 mmol). Flash chromatography (hexane–ethyl acetate, 6:4) yielded the hydroxy ketones **2c** and **3c** as a colourless liquid (2.97 g, 68.7%); ν_{max}(liquid film)/cm^{-1} 3447 (OH), 1706 (C=O), 1460, 1411, 1376, 1243, 1101, 1029, 970 and 804; δ_H($CDCl_3$) 3.4–3.7 (1 H, 2m, 5-H), 2.8–2.9 (1 H, 2d, *J* 3.4 and 6.3, OH), 2.3–2.6 (3 H, m, 2-H, 4-H), 1.2–1.5 (2 H, m, 6-H) and 0.7–1.1 (9 H, m, CH_3); δ_C($CDCl_3$) 216.8, 216.1, 75.0, 72.8, 50.8, 49.7, 36.1, 35.2, 27.5, 27.1, 14.1, 10.5, 10.2, 9.8, 7.6 and 7.5 (lit.,[13] **2c** 74.9 (C-5), 13.9 (C4-CH_3); **3c** 73.4 (C-5), 10.9 (C4-CH_3). Integration of the ^{13}C NMR spectrum and comparison with the literature data indicated that the diastereoisomers were present in the approximate ratio of **2c**:**3c**, 1:2.

Reduction of (4RS,5RS)-5-*Hydroxy*-2,4,6-*trimethylheptan*-3-*one* **2a** *with Sodium Borohydride*.—The hydroxy ketone **2a** (86 mg, 0.5 mmol) in ethanol (2 cm^3) was treated with sodium borohydride (76 mg, 2 mmol) at room temperature over a period of 2 h. The reaction mixture was left overnight and then quenched with aqueous sodium hydroxide (1 mol dm^{-3}; 1.5 cm^3) and extracted with ether. The ethereal layer was dried ($MgSO_4$) and evaporated to afford a clear viscous solution. Flash chromatography (ether–hexane–ethyl acetate 1:5:1) of this gave (i) *syn,anti*-diol **7a** (24 mg, 28%), ν_{max}(Nujol mull)/cm^{-1} 3250 (OH), 1455, 1375, 1155, 1080, 1060 and 970 [lit.,[3b] ν_{max}/cm^{-1} 3250 (OH)]; δ_H(80 MHz, $CDCl_3$) 3.40 (1 H, d, *J* 9, 5-H), 3.23 (1 H, dd, *J* 8, 4, 3-H), 2.53 (2 H, br s, OH), 2.13–1.40 (3 H, m, 2-H, 4-H and 6-H) and 1.13–0.70 (15 H, m, CH_3) and (ii) *anti,anti*-diol **8a** (35 mg, 40%), ν_{max}(Nujol mull)/cm^{-1} 3330 (OH), 1455, 1375, 1100 and 985 [lit.,[3b] ν_{max}/cm^{-1} 3330 (OH)]; δ_H(80 MHz, $CDCl_3$) 3.88 (2 H, br s, OH), 3.45 (2 H, dd, *J* 8.4, 2.2, 3-H and 5-H), 2.13–1.38 (3 H, m, 2-H, 4-H and 6-H), 1.13–0.83 (12 H, m, Me) and 0.75 (3 H, d, *J* 6.4, 4-Me).

Reduction of (4RS,5SR)-5-*Hydroxy*-2,4,6-*trimethylheptan*-3-*one* **3a** *with Sodium Borohydride*.—The hydroxy ketone **3a** (120 mg, 0.698 mmol) in ethanol (1 cm^3) was treated with sodium borohydride (49 mg, 1.30 mmol) over a period of 3 h at room temperature. The mixture was quenched with aqueous sodium hydroxide (1 mol dm^{-3}; 1 cm^3) and extracted with ether. The extract was dried ($MgSO_4$) and evaporated and flash chromatography (ether–hexane–ethyl acetate, 1:5:1) of the residue afforded (i) a mixture of *syn,anti*-diol **7a** and *syn,syn*-diol **9a** (72 mg, 59%) and (ii) pure *syn,syn*-diol **9a** (40 mg, 33%); ν_{max}(Nujol mull)/cm^{-1} 3320 (OH), 1455, 1375, 1155, 1065 and 970; δ_H(80 MHz, $CDCl_3$) 3.45–3.20 (2 H, dd, *J* 9, 2, 3-H and 5-H), 3.0 (2 H, br s, OH), 2.0–1.40 (3 H, m, 2-H, 4-H and 6-H) and 1.13–0.75 (15 H, m, Me) [lit.,[3b] 3.22 (2 H, d, *J* 9)].

Reduction of 5-*Ethyl*-6-*hydroxynonan*-4-*one* (*Mixture of* **2b** *and* **3b**) *with Sodium Borohydride*.—A mixture of the hydroxy ketones **2b** and **3b** (1.8 g, 9.7 mmol) in dry ethanol (20 cm^3) was treated with sodium borohydride (369 mg, 9.7 mmol) for a period of 4 h at room temp. The reaction was quenched with sodium hydroxide (2 mol dm^{-3}; 1 cm^3) and extracted with ether (×8). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure. Flash chromatography (hexane–ethyl acetate, 6:4) of the residue yielded a mixture of the diols **7b**, **8b** and **9b** as a slightly discoloured oil (1.38 g, 76%), ν_{max}(liquid film)/cm^{-1} 3358 (OH), 2961, 2936, 2875, 2732, 1459, 1378, 1323, 1153, 1121 and 1065; δ_H($CDCl_3$) 3.6–4.1 (2 H, m, 4-H, 6-H), 3.2–3.6 (2 H, 2 br s, OH), 1.1–1.7 (11 H, m, CH_2, 5-H) and 0.7–1.0 (9 H, m, CH_3); δ_C($CDCl_3$) 77.3, 74.5, 72.7, 71.7, 48.9, 48.4, 47.6, 38.2, 38.0, 37.7, 36.3, 21.9, 19.5, 19.3, 18.8, 17.8, 15.7, 14.4, 14.1, 12.6 and 11.0. By comparison with literature data [3b] and consideration of other experiments (*vide infra*) the following ^{13}C NMR spectroscopic assignments were made: *syn,anti*-diol **7b**; 72.7 and 71.7 (C-3, C-7), 47.6 (C-5) and 38.0 and 36.3 (C-4, C-6): *anti,anti*-diol **8b**; 74.5 (C-3, C-7), 48.9 (C-5) and 38.2 (C-4, C-6): *syn,syn*-diol **9b**; 77.3 (C-3, C-7), 48.4 (C-5) and 37.7 (C-4, C-6).

Reduction of 5-*Hydroxy*-4-*methylheptan*-3-*one* (*Mixture of* **2c** *and* **3c**) *with Sodium Borohydride*.—A mixture of the hydroxy ketones **2c** and **3c** (1.6 g, 11.1 mmol) in dry ethanol (20 cm^3) was treated with sodium borohydride (422 mg, 11.1 mmol) as described above. Flash chromatography (hexane–ethyl acetate, 1:1) of the product yielded a mixture of the diols **7c**, **8c** and **9c** as a slightly discoloured oil (1.18 g, 73%);[14] ν_{max}(neat)/cm^{-1} 3383 (OH), 2966, 1460, 1380, 1340, 1256, 1156 and 968; δ_H($CDCl_3$) 3.4–3.9 (2 H, m, 3-H, 5-H), 3.2–3.9 (2 H, OH), 1.3–1.8 (5 H, m, 2-H, 4-H and 6-H) and 0.8–1.1 (9 H, m, CH_3); δ_C($CDCl_3$) 78.7, 77.6, 77.2, 73.9, 42.4, 40.1, 39.0, 28.6, 27.9, 27.4, 26.6, 13.0, 11.1, 10.3, 10.2, 9.9, 9.0 and 3.8.

2,2-r-4-t-6-*Tetraisopropyl*-5-*methyl*-1,3-*dioxa*-2-*silacyclohexane* **4a**.—The *syn,anti*-diol **7a** (20 mg, 0.115 mmol) and 2,6-dimethylpyridine (40 mm^3, 0.344 mmol) in dichloromethane (300 mm^3) were treated with $Pr^i_2Si(OTf)_2$ (57 mg, 0.138 mmol) at 0 °C under a nitrogen atmosphere. The reaction mixture was brought to room temperature and stirred for 1 h. After removal of the solvent, the crude product was filtered through silica gel (hexane–ethyl acetate, 40:1) to give *siladioxane* **4a** (17 mg, 52%); ν_{max}(liquid film)/cm^{-1} 2250, 2860, 1460, 1380, 1360, 1240, 1130, 1100, 1060, 990, 945, 880 and 845; δ_H(80 MHz, $CDCl_3$) 3.63–3.23

(2 H, m, 4-H and 6-H), 2.13–1.50 (3 H, m, C4-C*H*, 5-H and C6-C*H*) and 1.13–0.70 (29 H, m, Si-isopropyl, Me).

2,2-r-4-c-6-*Tetraisopropyl*-t-5-*methyl*-1,3-*dioxa*-2-*silacyclohexane* **5a**.—The *anti,anti*-diol **8a** (40 mg, 0.229 mmol) and 2,6-dimethylpyridine (80 mm^3, 0.688 mmol, 3 equiv.) in dichloromethane (0.5 cm^3) at 0 °C were treated with $Pr^i_2Si(OTf)_2$ (114 mg, 0.275 mmol) as described above to give the *siladioxane* **5a** (37 mg, 56%); ν_{max}(liquid film)/cm^{-1} 2950, 2860, 1460, 1380, 1365, 1355, 1180, 1160, 1130, 1040, 880 and 845; δ_H(80 MHz, $CDCl_3$) 3.65–3.40 (2 H, dd, 4-H and 6-H), 2.1–1.25 [3 H, m, C(4)-C*H*, 5-H and C(6)-C*H*] and 1.15–0.60 (29 H, m, Si-isopropyl and Me).

2,2-r-4-c-6-*Tetraisopropyl*-c-5-*methyl*-1,3-*dioxa*-2-*silacyclohexane* **6a**.—The *syn,syn*-diol **9a** (25 mg, 0.144 mmol) and 2,6-dimethylpyridine (50 mm^3, 0.431 mmol) in dichloromethane (250 mm^3) were treated with $Pr^i_2Si(OTf)_2$ as describe above, to give the *siladioxane* **6a** (28 mg, 68%); ν_{max}(liquid film)/cm^{-1} 2940, 2860, 1640, 1380, 1360, 1350, 1290, 1240, 1180, 1160, 1095, 1075, 990, 950, 910, 880, 840, 810 and 695; δ_H(80 MHz, $CDCl_3$) 3.45 (2 H, dd, 4-H and 6-H), 2.08–1.38 [3 H, m, C(4)-C*H*, 5-H and C(6)-C*H*] and 1.18–0.63 (29 H, m, Si-isopropyl and Me).

5-*Ethyl*-2,2-*diisopropyl*-4,6-*dipropyl*-1,3-*dioxa*-2-*silacyclohexane* (*Mixture of Diastereoisomers* **4b**, **5b** *and* **6b**).—To a mixture of the diols **7b**, **8b** and **9c** (1.10 g, 5.85 mmol) in dry dichloromethane (30 cm^3) at 0 °C under argon was added dry 2,6-dimethylpyridine (2.04 cm^3, 17.55 mmol). The mixture was stirred for 20 min after which $Pr^i_2Si(OTf)_2$ (2.90 g, 7.02 mmol) was added. The reaction mixture was allowed to warm to room temp. and was then stirred for 2 h. After this it was evaporated under reduced pressure and flash chromatography (hexane–ethyl acetate, 50:1) of the residue yielded a mixture of the *siladioxanes* **4b**, **5b** and **6b** (1.11 g, 63%). An analytical sample was prepared by short path distillation; bath temperature 110–113 °C at 0.3 mmHg (Found: C, 67.9; H, 12.15. $C_{17}H_{36}SiO_2$ requires C, 67.93; H, 12.07%); ν_{max}(neat)/cm^{-1} 2964, 2871, 2727, 1463, 1380, 1247, 1159 and 1117; δ_H($CDCl_3$) 3.8–4.1 (2 H, m, 4-H, 6-H), 1.25–1.70 (11 H, m, CH_2, 5-H) and 0.8–1.2 (23 H, m, CH_3, Si-isopropyl); δ_C($CDCl_3$) 78.5, 75.6, 74.3, 73.4, 48.9, 48.7, 48.4, 38.7, 37.7, 37.6, 35.1, 21.0, 19.9, 19.5, 19.3, 18.8, 18.0, 17.7, 17.3, 17.2, 17.1, 17.0, 16.9, 16.4, 14.5, 14.1, 14.0, 13.6, 13.5, 12.9, 12.6, 12.4, 12.3 and 10.2. On the basis of later experiments (*vide infra*) the following ^{13}C NMR spectroscopic assignments were made: *cis,trans*-siladioxane **4b**; 74.3 and 72.4 (C-4, C-6), 48.4 (C-5) and 38.7 and 35.1 [C(4)-*C*H_2, C(6)-*C*H_2]; *trans,trans*-siladioxane **5b**; 75.6 (C-4, C-6), 48.9 (C-5) and 37.7 [C(4)-*C*H_2, C(6)-*C*H_2]; *cis,cis*-siladioxane **6b**; 77.5 (C-4, C-6), 48.7 (C-5) and 37.6 [C(4)-*C*H_2, C(6)-*C*H_2]. The three components could be resolved by capillary GC (OV1), being eluted in the order **5b**, **6b**, **4b**.

4,6-*Diethyl*-2,2-*diisopropyl*-5-*methyl*-1,3-*dioxa*-2-*silacyclohexane* (*Mixture of Diastereoisomers* **4c**, **5c** *and* **6c**).—To a mixture of the diols **7c**, **8c** and **9c** (1.00 g, 6.8 mmol) in dry dichloromethane (30 cm^3) at 0 °C under argon was added dry 2,6-dimethylpyridine (2.37 cm^3, 20.4 mmol). The mixture was stirred for 20 min after which $Pr^i_2Si(OTf)_2$ (3.8 g, 8.16 mmol) was added. The reaction mixture was allowed to warm to room temp. after which it was stirred for 2 h. The solvent was evaporated under reduced pressure and flash chromatography (hexane–ethyl acetate, 30:1) yielded the mixture of *siladioxanes* **4c**, **5c** and **6c** (1.22 g, 69%). An analytical sample was prepared by short path distillation; bath temperature 85–88 °C at 0.3 mmHg (Found: C, 64.75; H, 11.6. $C_{14}H_{30}SiO_2$ requires C, 65.05; H, 11.70%); ν_{max}/cm^{-1} 2963, 2873, 2726, 1462, 1383, 1247, 1165 and 1117; δ_H($CDCl_3$) 3.5–4.0 (2 H, 4-H, 6-H), 1.3–1.9 (5 H, m, CH_2, 5-H) and 0.7–1.2 (23 H, m, CH_3, Si-isopropyl); δ_C($CDCl_3$) 79.5, 79.2, 77.3, 76.7, 42.2, 41.0, 39.0, 29.0, 28.4, 28.3, 25.2, 17.7, 17.2, 17.1, 16.8, 13.8, 13.7, 13.4, 12.8, 12.3, 10.9, 10.4, 9.5, 8.7 and 4.0. The three components could be resolved by CGC (OV1). Later experiments established that the *cis,trans*-siladioxane **6c** was the last to be eluted.

Diisopropylsilylation of the anti-*Hydroxy Ketone* **2a**.—Chlorodiisopropylsilane (361 mg, 2.4 mmol, 413 mm^3), triethylamine (243 mg, 2.4 mmol, 335 mm^3), and 4-(*N*,*N*-dimethylamino)-pyridine (DMAP) (86 mg, 0.704 mmol) were dissolved in hexane (20 cm^3) under a nitrogen atmosphere. The hydroxy ketone **2a** (344.5 mg, 2 mmol) dissolved in hexane (5 cm^3) was added *via* a syringe. The reaction mixture was heated under reflux for 5 h and left overnight at room temperature. After filtration and removal of solvent, flash chromatography (hexane–ethyl acetate, 40:1) gave (4RS,5RS)-5-(*diisopropylsilyl*)*oxy*-2,4,6-*trimethylheptan*-3-*one** as a clear colourless liquid (470 mg, 82%); ν_{max}(liquid film)/cm^{-1} 2950, 2855, 2090 (Si–H), 1705 (C=O), 1455, 1375, 1045, 995, 875, 845 and 800; δ_H(80 MHz, $CDCl_3$) 4.13 (1 H, br s, Si-H), 3.78 (1 H, dd, *J* 8, 2.4, 5-H), 3.13–2.45 (2 H, m, 2-H and 4-H), 2.0–1.45 (1 H, m, 6-H) and 1.38–0.78 (29 H, m, Si-isopropyl and Me).

Diisopropylsilylation of the syn-*Hydroxy Ketone* **3a**.—A similar procedure involving chlorodiisopropylsilane (301 mg, 2 mmol), triethylamine (202.4 mg, 2 mmol, 279 mm^3), DMAP (86 mg, 0.704 mmol) and the hydroxy ketone **3a** (172.3 mg, 1 mmol) yielded (4RS,5SR)-5-(*diisopropylsilyl*)*oxy*-2,4,6-*trimethylheptan*-3-*one* (214 mg, 75%); ν_{max}(liquid film)/cm^{-1} 2960, 2850, 2090 (Si–H), 1705 (C=O), 1455, 1375, 1360, 1050, 1000 and 850; δ_H(80 MHz, $CDCl_3$) 4.28 (1 H, s, Si-H), 3.95–3.78 (1 H, dd, 5-H), 3.08–2.55 (2 H, m, 4-H and 2-H) and 2.0–0.80 (30 H, m, 6-H, Me and Si-isopropyl).

Diisopropylsilylation of the anti-*Hydroxy Ketone* **2b**.—To a solution of the hydroxy ketone **2b** (40 mg, 0.22 mmol) in dry hexane (1 cm^3) under argon was added DMAP (11 mg, 0.09 mmol) and dry triethylamine (26.1 mg, 0.26 mmol). The mixture was stirred for 10 min after which chlorodiisopropylsilane (42.3 mg, 0.28 mmol) was added. The mixture was stirred for 1.5 h, filtered through Celite and the filtrate evaporated under reduced pressure. Flash chromatography (hexane–ethyl acetate, 40:1) of the residue yielded anti-5-*ethyl*-6-(*diisopropylsilyl*)*oxynonan*-4-*one* as a colourless liquid (43 mg, 66%); δ_H($CDCl_3$) 4.11 (1 H, t, *J* 1.2, Si-H), 3.86 (1 H, dt, *J* 6.5 and 4.9, 6-H), 2.54 (1 H, ddd, *J* 4.3, 6.7, 10.6, 5-H), 2.3–2.5 (2 H, m, 3-H), 1.2–1.7 (8 H, m, CH_2) and 0.7–1.0 (23 H, m, CH_3, Si-isopropyl); δ_C($CDCl_3$) 213.4 (CO), 74.9 (C-6) 58.8 (C-5), 46.8 (C-3), 35.8 (C-7), 20.7, 17.5, 17.4, 17.3, 16.4, 14.1, 13.7, 12.5, 12.4 and 12.1.

Diisopropylsilylation of the syn-*Hydroxy Ketone* **3b**.—A similar procedure involving the hydroxy ketone **3b** (80 mg, 0.43 mmol), DMAP (22 mg, 0.17 mmol), dry triethylamine (52.5 mg, 0.52 mmol) and chlorodiisopropylsilane (84.5 mg, 0.56 mmol) yielded syn-5-*ethyl*-6-(*diisopropylsilyl*)*oxynonan*-4-*one* (91 mg, 70%); δ_H($CDCl_3$) 4.20 (1 H, s, Si-H), 3.75–3.80 (1 H, m, 6-H), 2.58 (1 H, ddd, *J* 9.7, 5.6, 4.2, 5-H), 2.2–2.5 (2 H, m, 3-H), 1.1–1.7 (8 H, m, CH_2) and 0.7–1.0 (23 H, m, CH_3, Si-isopropyl); δ_C($CDCl_3$) 213.0 (CO), 75.1 (C-6), 59.4 (C-5), 46.8 (C-3), 36.5 (C-7), 21.2, 18.8, 17.5, 17.4, 16.6, 14.0, 13.7, 12.7, 12.4 and 12.2.

* In our earlier work, we had found that the microanalysis of (diisopropylsilyl)oxy ketones gave irreproducible results.[5b] Thus, microanalyses were not attempted on the corresponding derivatives described herein.

Diisopropylsilylation of 5-*Hydroxy*-4-*methylheptan*-3-*one* (*Mixture of* anti-*Isomer* **2c** *and* syn-*Isomer* **3c**).—A similar procedure involving a mixture of the hydroxy ketones **2c** and **3c** (2.00 g, 13.9 mmol) DMAP (680 mg, 5.6 mmol), triethylamine (1.69 g, 16.7 mmol) and chlorodiisopropylsilane (2.73 g, 18.1 mmol) yielded 5-(*diisopropylsilyl*)*oxy*-4-*methylheptan*-3-*one* as a colourless liquid (2.87 g, 80%); ν_{max}(neat)/cm^{-1} 2097, (Si–H), 1712 (C=O), 1462, 1411, 1102, 1053, 1004 and 880; δ_H($CDCl_3$) 4.22, 4.18 (1 H, 2s, Si-H), 3.9–4.0 (1 H, m, 5-H), 2.4–2.8 (3 H, m, 2-H, 4-H), 1.4–1.6 (2 H, m, 6-H) and 0.8–1.2 (23 H, m, CH_3, Si-isopropyl); δ_C($CDCl_3$) 214.1 (CO), 213.6 (CO), 76.7 (C-5), 76.5 (C-5), 50.5 (C-4), 49.9 (C-4), 36.5 (C-2), 35.4 (C-2), 27.2 (C-6), 25.6 (C-6), 17.4, 17.3, 12.5, 12.4, 11.5, 9.8, 7.9, 7.5 and 7.3. Integration of the ^{13}C NMR spectrum indicated that the diastereoisomers were present in the approximate ratio of *anti*:*syn*, 2:5.

Treatment of (4RS,5RS)-5-(*Diisopropylsilyl*)*oxy*-2,4,6-*trimethylheptan*-3-*one* (*as Prepared from the* anti-*Hydroxy Ketone* **2a**) *with Tin Tetrachloride*.—The silylated hydroxy ketone (200 mg, 0.699 mmol) in dichloromethane (7 cm^3) was treated with tin tetrachloride (8 mm^3) at −80 °C, under a nitrogen atmosphere over a period of 4 h. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (0.5 cm^3), allowed to warm gradually to room temp. and extracted with ether. The organic phase was dried (Na_2SO_4) and evaporated to give a colourless liquid (196 mg, 98%). Analysis by GC (packed-column) showed that the siladioxanes **4a** and **5a** were present in the ratio 99.6:0.4. Acetonitrile (3 cm^3) was added to the crude product and the solution was treated with aqueous hydrofluoric acid (40%; 5 drops) for 30 min. After completion of the desilylation, the reaction mixture was partitioned between chloroform and water, and the organic phase was dried ($MgSO_4$) and evaporated. Flash chromatography (ether–hexane–ethyl acetate, 1:5:1) of the residue gave the *syn*,*anti*-diol **7a** (109 mg, 92%), identical (NMR, TLC, IR) with the authentic sample prepared as described earlier.

Treatment of (4RS,5SR)-5-(*Diisopropylsilyloxy*)-2,4,6-*trimethylheptan*-3-*one* (*as Prepared from the* syn-*Hydroxy Ketone* **3a**) *with Tin Tetrachloride*.—The silylated hydroxy ketone (120 mg, 0.419 mmol) in dichloromethane (8 cm^3) was treated with anhydrous tin tetrachloride (6 mm^3) at −80 °C under a nitrogen atmosphere over a period of 3 h. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (1 cm^3), warmed to room temp. and extracted with ether. The organic phase was dried (Na_2SO_4). Evaporation of solvent, followed by flash chromatography (hexane–ethyl acetate, 40:1) gave a clear colourless liquid (74 mg, 62%). Analysis by GC (packed-column) showed that the siladioxanes **4a** and **6a** were present in the ratio 99.7:0.3. The siladioxane mixture was dissolved in acetonitrile (2 cm^3) and aqueous hydrofluoric acid (40%; 3 drops) was added to it; the reaction mixture was then stirred at room temp. for 2 h. After completion of desilylation, the reaction mixture was partitioned between chloroform and water. The organic phase was dried ($MgSO_4$). Evaporation of solvent gave *syn*,*anti*-diol **7a** (42 mg, 93%) identical (NMR, IR, TLC) with the authentic sample prepared as described earlier.

Treatment of anti-5-*Ethyl*-6-(*diisopropylsilyl*)*oxynonan*-4-*one* (*as Prepared from the* anti-*Hydroxy Ketone* **2b**) *with Tin Tetrachloride*.—The silylated hydroxy ketone (10 mg, 0.033 mmol) in dry dichloromethane (1 cm^3) at −80 °C under argon was treated with tin tetrachloride (1 mm^3). After being stirred at this temperature for 2 h the reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate, allowed to warm to room temp. and extracted with dichloromethane (× 5). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to yield a crude product (8.9 mg). Quantitative analysis by GC (OV1) indicated that the siladioxanes **4b** and **5b** were present in the ratio of 97:1, in 39% overall yield. Analysis by ^{13}C NMR suggested that the *cis*,*trans*-siladioxane **4b** and the *syn*,*anti*-diol **7b**, totalled approximately 50% of the crude product, and that the *anti*-β-hydroxy ketone **2b** made up most of the remaining material.

Treatment of syn-5-*Ethyl*-6-(*diisopropylsilyl*)*oxynonan*-4-*one* (*as Prepared from* syn-*Hydroxy Ketone* **3b**) *with Tin Tetrachloride*.—The silylated hydroxy ketone (20 mg, 0.066 mmol) was treated with tin tetrachloride (1 mm^3) as described above, to yield a crude product (18.5 mg). Quantitative analysis by GC (OV1) indicated that the siladioxanes **4b** and **6b** were present in the ratio of 5:1, in 47% overall yield. ^{13}C NMR analysis was consistent with this result, and indicated that the major side product of the reaction was the *syn*-β-hydroxy ketone **3b**.

Treatment of 5-(*Diisopropylsilyl*)*oxy*-4-*methylheptan*-3-*one* (*as Prepared from the Mixture of* **2c** *and* **3c**) *with Tin Tetrachloride*.—The mixture of silylated hydroxy ketones (650 mg, 2.52 mmol) (*anti*:*syn*, 2:5) in dry dichloromethane (15 cm^3) at −80 °C under argon was treated with tin tetrachloride (25 mm^3, 0.21 mmol). After stirring at this temperature for 2 h the reaction was quenched with saturated aqueous sodium hydrogen carbonate, allowed to warm to room temp. and extracted five times with dichloromethane. The combined extracts were dried (Na_2SO_4) and the solvent evaporated under reduced pressure to yield a crude product (630 mg). Quantitative analysis by GC (OV1) indicated that *cis*,*trans*-siladioxane **4c** (identified by ^{13}C NMR; see following experiment) and one of the other possible siladioxane products were present in the ratio 26:1, in 73.7% overall yield. Exactly 25% of the crude product was dissolved in acetonitrile (10 cm^3) and treated with hydrofluoric acid (40%, 5 drops). The mixture was stirred for 2 h, distilled water (10 cm^3) was added and the mixture was extracted eight times with dichloromethane. The combined extracts were dried (Na_2SO_4) and the solvent evaporated under reduced pressure. Flash chromatography (hexane–ethyl acetate, 1:1) yielded the diol **7c** as a colourless oil (60.6 mg, 66%), identified by its ^{13}C NMR spectrum; δ_C($CDCl_3$) 77.4 and 74.1 (C-3 and C-5), 40.3 (C-4), 28.2 and 26.8 (C-2 and C-6), 11.3, 10.4 and 10.1.

Treatment of 5-(*Diisopropylsilyl*)*oxy*-4-*methylheptan*-3-*one* (*as Prepared from the Mixture of* **2c** *and* **3c**) *with* $TfOH_2^+$ $B(OTf)_4^-$.—The mixture of silylated hydroxy ketones (160 mg, 0.62 mmol) (*anti*:*syn*, 2:5) in dry dichloromethane (3 cm^3) at −80 °C under argon was treated with $TfOH_2^+B(OTf)_4^-$ (1 drop). The mixture was allowed to warm with stirring to −40 °C over a period of 2 h. Distilled water (2 cm^3) was added, the mixture warmed to room temp. and extracted eight times with dichloromethane. The combined extracts were dried (Na_2SO_4) and the solvent evaporated under reduced pressure to yield a crude product (152 mg). Analysis by ^{13}C NMR spectroscopy indicated that the major product was the *cis*,*trans*-siladioxane **4c**; δ_C($CDCl_3$) 76.9 and 74.4 (C-4 and C-6), 40.6 (C-5), 28.6 and 24.8 (CH_2), 16.9, 16.7, 16.6, 13.4, 13.3, 13.2, 10.6 and 9.2. A trace of a second diastereoisomer (**5c** or **6c**) was also detected. Analysis by capillary GC (OV1) indicated that **4c** and the second siladioxane were present in the ratio 38:1. Exactly 50% of the crude product was dissolved in acetonitrile (2 cm^3) and treated with hydrofluoric acid (40%, 4 drops) over a period of 2 h. Distilled water (2 cm^3) was added and the mixture was extracted with chloroform (× 8). The combined extracts were dried (Na_2SO_4) and the solvent evaporated under reduced pressure. Flash chromatography (hexane–ethyl acetate, 1:1) yielded the diol **7c** (34 mg, 75%).

Acknowledgements

We thank EOLAS, the Irish Science and Technology Agency, for financial support.

References

1 *e.g.* T. Oishi and T. Nakata, *Synthesis*, 1990, 635.
2 E. L. Eliel, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, London, 1983, vol. 2, p. 125.
3 (*a*) K. Narasaka and F.-C. Pai, *Chem. Lett.*, 1980, 1415; (*b*) K. Narasaka and F.-C. Pai, *Tetrahedron*, 1984, **40**, 2233; (*c*) K. Narasaka, S. Yamazaki and Y. Ukaji, *Chem. Lett.*, 1984, 2065.
4 (*a*) M. T. Reetz and A. Jung, *J. Am. Chem. Soc.*, 1983, **105**, 4833; (*b*) M. T. Reetz, A. Jung and C. Bolm, *Tetrahedron*, 1988, **44**, 3889.
5 (*a*) S. Anwar and A. P. Davis, *J. Chem. Soc., Chem. Commun.*, 1986, 831; (*b*) S. Anwar and A. P. Davis, *Tetrahedron*, 1988, **44**, 3761.
6 (*a*) D. A. Evans and K. T. Chapman, *Tetrahedron Lett.*, 1986, **27**, 5939; (*b*) D. A. Evans and K. T. Chapman, *J. Am. Chem. Soc.*, 1988, **110**, 3560; (*c*) D. A. Evans and A. H. Hoveyda, *J. Am. Chem. Soc.*, 1990, **112**, 6447.
7 G. A. Molander and J. B. Etter, *J. Am. Chem. Soc.*, 1987, **109**, 6556.
8 For an early example of 1,4-asymmetric induction, see; T. Fukuyama, B. Vranesic, D. P. Negri and Y. Kishi, *Tetrahedron Lett.*, 1978, 2741.
9 R. Bloch, L. Gilbert and C. Girard, *Tetrahedron Lett.*, 1988, **29**, 1021.
10 E. J. Corey and P. B. Hopkins, *Tetrahedron Lett.*, 1982, **23**, 4871.
11 A. P. Davis and M. Jaspars, *J. Chem. Soc., Chem. Commun.*, 1990, 1176.
12 G. A. Olah, K. Laali and O. Farooq, *J. Org. Chem.*, 1984, **49**, 4591.
13 K. Mori and T. Ebata, *Tetrahedron*, 1986, **42**, 4421.
14 A. Franke and M. Kohn, *Monatsh. Chem.*, 1906, **27**, 1097.

Paper 1/00082I
Received 7*th January* 1991
Accepted 24*th January* 1991