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Diastereocontrol in open-chain nucleophilic attack on a double bond adjacent to a stereogenic centre carrying a silyl group

Mark S. Betson, Ian Fleming * and Jacqueline V. A. Ouzman
Department of Chemistry, Lensfield Road, Cambridge, UK CB2 1EW.
E-mail: if10000@cam.ac.uk; Fax: +44 (0)1223 336362; Tel: +44 (0)1223 336372

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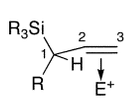
The bis[dimethyl(phenyl)silyl]cuprate reagent introduces a silyl group to the β-position of three α,β-unsaturated esters: methyl *Z*-4-dimethyl(phenyl)silylpent-2-enoate **11**, and methyl *Z*- and *E*-(1′-dimethylphenylsilylbenzyl)but-2-enoates **14** and **15**, diastereoselectively in the unexpected sense, syn to the silyl group in the conformation in which the hydrogen atom is 'inside'. The selectivity is low (58 : 42) in the first case **11**, where the nucleophilic attack is adjacent to the stereogenic centre carrying the silyl group, and moderate (72 : 28) for both *Z*- and *E*-α,β-unsaturated esters **14** and **15**, where the nucleophilic attack is at the other end of the double bond from the stereogenic centre. It is conceivable that nucleophilic attack actually takes place in a conformation in which the donor substituent, the silicon–carbon bond, is out of conjugation with the double bond.

Introduction

Diastereocontrol in electrophilic attack on a C=C bond adjacent to a stereogenic centre carrying a silyl group is well established to take place in the sense **1**. Evidence comes from such disparate reactions as the S_E2' reaction of cationic electrophiles with allylsilanes,[1] the hydroboration of allylsilanes,[2] and the alkylation of enolates derived from β-silyl esters.[3] The frequently high levels of diastereoselectivity are explained by the likelihood that steric and electronic effects reinforce each other in the sense **1**, whether the new bond is forming at C-2 or C-3 or both, but it is not clear whether it is the steric or the electronic effect that is dominant. The corresponding nucleophilic attack **2** is much less well studied, although it is fairly well known for attack on a carbonyl group, which takes place in the sense **3**.[4] Furthermore, although the steric effect ought to be in the same sense as for electrophilic attack, from below in the general sense **2**, there is no agreed way of predicting the electronic effect on the sense of attack, nor any certainty that it would be the same at C-2 as at C-3. We are aware of three pieces of work on this subject. In the first place, Lindeman has shown that nucleophilic attack on the intermediate derived from the acetal **4** takes place predominantly from above (92 : 8), anti to the silyl group, as drawn, and by way of explanation he suggests the obvious conformation **5**, which is in agreement with a straightforward steric effect.[5] His results have more recently been augmented by those of Rychnovsky, who used allylsilanes as the nucleophiles.[6] Using a more rigid system, described in the first paper of this series,[7] we have shown that a dialkylcuprate adds predominantly (96 : 4) to the enone **6** from above, as drawn, again anti to the silyl group, and have suggested that the silyl group, held axially in the cyclohexanone ring, substantially blocks the lower surface. Finally, in some Ireland–Claisen rearrangements described in the immediately preceding paper,[8] we have again seen attack anti to the silyl group, whether the electronic bias was that of nucleophilic attack **7** (98 : 2) or electrophilic attack **8** (86 : 14), where it was notable that the higher of the ratios of diastereoisomers was in the nucleophilic attack series **7**.



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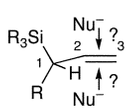

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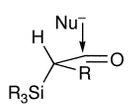

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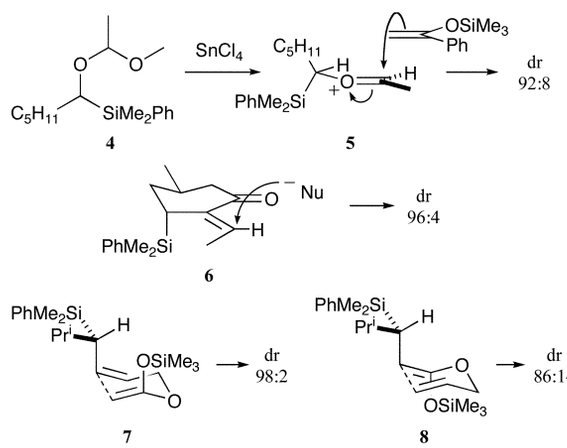

The Lindeman and Rychnovsky work was not on an alkene, and our own work, whether with the rigid cyclic starting material **6** or possessed of a cyclic transition structure **7**, was not simply on open-chain reactions. We therefore sought an example of nucleophilic attack on an alkene in the sense **2**, one for open-chain attack at C-2 and another for open-chain attack at C-3, and report our results for the first time here. In both cases we have used a silylcuprate addition to an α,β-unsaturated ester, since the silylcuprate gave us a reaction taking place under relatively mild conditions, and, at the same time, gave us a handle with which to prove the relative configuration of some of the products. We are well aware that with only one type of reaction, one nucleophile and only two types of substrate, we cannot be confident that our results, unexpected as they proved to be, represent a general pattern.

Results and discussion

Our substrates were the α,β-unsaturated esters **11**, **14** and **15**, which we prepared by the unexceptional routes shown in Scheme 1, where the ester **11** was described in the immediately preceding paper, and the alcohols **12** and **13** were known from earlier work.[9]

The conjugate addition reaction with the first substrate **11** gave both possible diastereoisomers **16** and **17** in a disappointing ratio of 58 : 42 (Scheme 2). We assigned relative configuration to these compounds from the very different coupling constants

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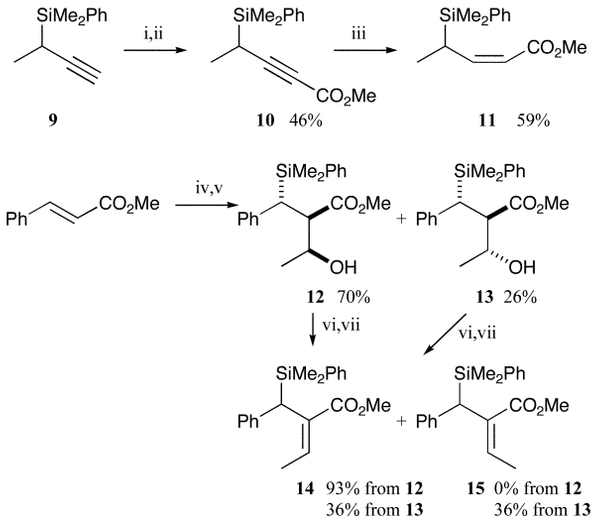
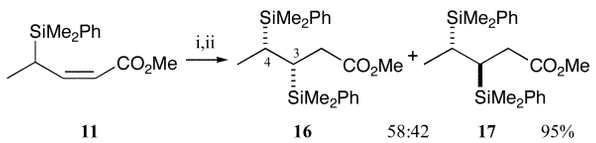


Scheme 1 *Reagents:* i, BuLi; ii, $ClCO_2Me$; iii, H_2, $Pd/BaSO_4$; iv, $PhMe_2SiZnEt_2Li$; v, MeCHO; vi, MsCl, Et_3N; vii, DBU.

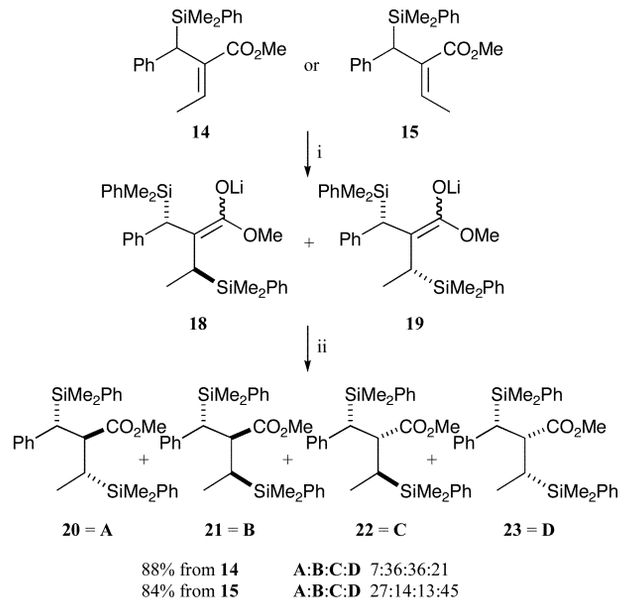


Scheme 2 *Reagents:* i, $(PhMe_2Si)_2CuLi{\cdot}LiCN$; ii, NH_4Cl, H_2O.

between the protons on C-3 and C-4, 1.1 Hz for the major product and 6.7 Hz for the minor. A standard molecular modelling calculation assessing a Boltzmann distribution of the lowest-energy conformations suggested that the coupling constant for the isomer **16** would be 0.6 Hz and for its isomer **17** 6.0 Hz. These are so close to the experimental values, and so different from each other, that we can be reasonably confident of the assignment. We chose a cis double bond in the substrate **11** to minimise any ambiguity about the conformation **37** that will be the most populated. Insofar as it has any significance, the major isomer is not the one anyone would have expected, since it corresponds to attack syn to the silyl group in this conformation. Whatever the explanation, the most important result is that the degree of diastereoselectivity is low, in contrast to cuprate additions in the literature, including silylcuprates, in which the substituents on the stereogenic centre were differentiated either by having an electronegative substituent[10,11] or simply by steric effects.[12]

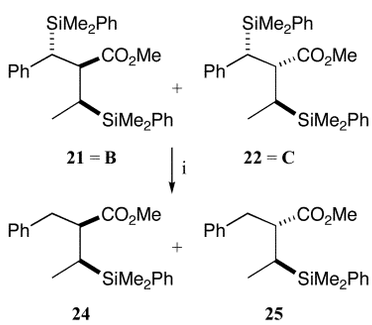
Conjugate addition to the second substrates, **14** and **15**, followed by protonation of the intermediate enolates **18** and **19**, can give four diastereoisomeric products **20**, **21**, **22** and **23** (Scheme 3). All four were detectable, using distinctive signals in ^{1}H-NMR spectra, but they were not all easily separable. Before we were able to assign the relative configurations to them shown in Scheme 3, we labelled the four **A**, **B**, **C** and **D**, in order of elution on chromatography. The isomers **A** and **D** were separable, free of the other isomers, but the isomers **B** and **C** were only obtained as a mixture.

The conjugate addition to the *Z*-ester **14** gave the isomers **B** and **C** as the major products. The ratios were much the same whatever proton source was used to quench the reaction medium, and averaged over the seven different runs as 7 : 36 : 36 : 21. The conjugate addition to the *E*-ester **15**, on the other hand, gave the isomers **A** and **D** as the major products with ratios **A** : **B** : **C** : **D** of 27 : 14 : 13 : 45. It therefore seemed to be likely that the conjugate addition to the ester **14** was giving predominantly one enolate **18** or **19**, and that conjugate addition to the ester **15** was giving predominantly the other enolate. The isomers **A** and **D** would then differ from each other only in the stereocentre adjacent to the methoxycarbonyl group, and similarly for the isomers **B** and **C**. If this is the case, then



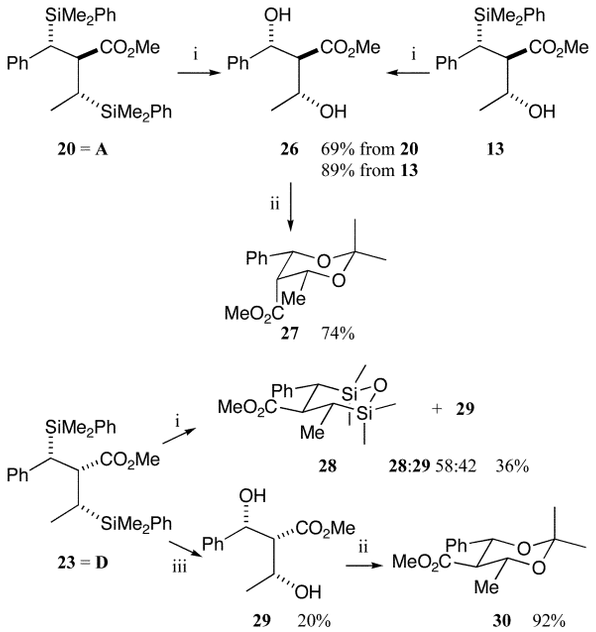
Scheme 3 *Reagents:* i, $(PhMe_2Si)_2CuLi{\cdot}LiCN$; ii, NH_4Cl, H_2O.

the conjugate addition took place in the same stereochemical sense for both isomers—either both were attacked predominantly from the top surface as drawn, or both from the bottom. This analysis was supported by the result of a treatment with tetrabutylammonium fluoride (TBAF), which selectively removed the benzylic silyl group (Scheme 4). A mixture consisting of **B**, **C** and **D** in ratios of 46 : 51 : 3 gave two esters in essentially quantitative yield in a ratio of 55 : 45, which was the same whether the reaction was stopped after 5 minutes or left overnight.



Scheme 4 *Reagent:* i, TBAF

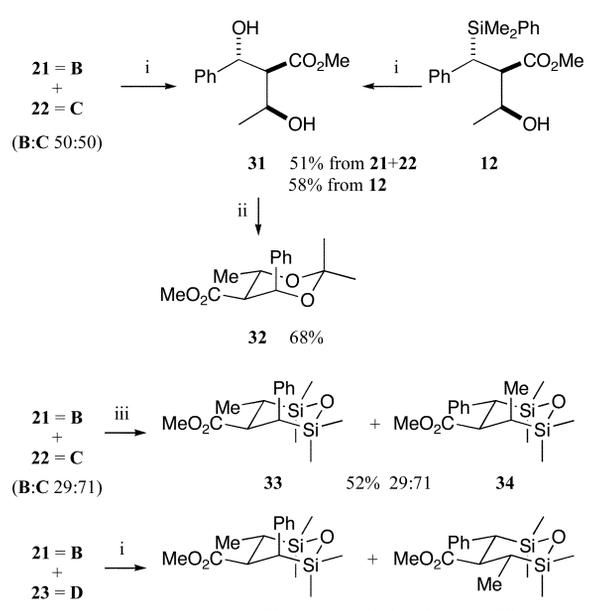
Silyl-to-hydroxy conversion[13] of the isomer **A** using mercuric acetate in peracetic acid gave a diol **26**, which was identical to the diol prepared by silyl-to-hydroxy conversion from the ester **13**. Furthermore, the acetonide **27** derived from this diol had coupling constants and nuclear Overhauser enhancements (see Experimental) consistent with the methyl and phenyl groups being equatorial and the ester group axial as illustrated in Scheme 5. A similar attempt at silyl-to-hydroxy conversion of the isomer **D** using mercuric acetate in peracetic acid did not go to completion, and we isolated a disiloxane **28**, in which both phenyl groups had been removed from the silicon atoms, but the oxidation step had not taken place. The triplet (J 12.5 Hz) for the proton next to the ester group indicated that the ester, phenyl and methyl groups were all trans and all equatorial. On the other hand, silyl-to-hydroxy conversion using potassium bromide in peracetic acid buffered with sodium acetate gave a known diol **29**, which gave a known acetonide **30**.[14] This compound also had coupling constants and nuclear Overhauser enhancements (see Experimental) consistent with the all-equatorial structure. Thus the isomers **A** and **D** differed, as we had deduced earlier, only in the relative configuration at the



Scheme 5 *Reagents:* i, $Hg(OAc)_2$, AcOOH; ii, $Me_2C(MeO)_2$, TsOH, DMF; iii, KBr, AcOOH, NaOAc.

protonation site, and we can assign to them the structures **20** and **23**, respectively.

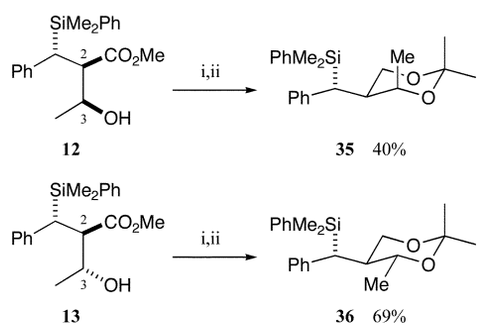
Silyl-to-hydroxy conversion of an approximately 50 : 50 mixture of the isomers **B** and **C** gave in one run only the known diol **31** [14] (Scheme 6), which was identical to a sample obtained by silyl-to-hydroxy conversion of the ester **12**. In addition, we converted the diol from both sources into its acetonide **32**, which is also a known compound [14] and which showed coupling constants and nuclear Overhauser enhancements consistent with a chair conformation having the phenyl group axial, confirming that either **B** or **C** has the structure **21**. On another occasion, starting with a 29 : 71 mixture of **B** and **C**, an incomplete silyl-to-hydroxy conversion gave two cyclic disiloxanes **33** and **34** in the same ratio in 52% yield. The minor product had coupling constants and nuclear Overhauser enhancements consistent with a conformation **33** having the phenyl group axial, and the major product had coupling constants consistent with a conformation **34** having the methyl group axial and the other two groups equatorial. It seemed



Scheme 6 *Reagents:* i, $Hg(OAc)_2$, AcOOH; ii, $Me_2C(MeO)_2$, TsOH, DMF; iii, HBF_4, Et_2O.

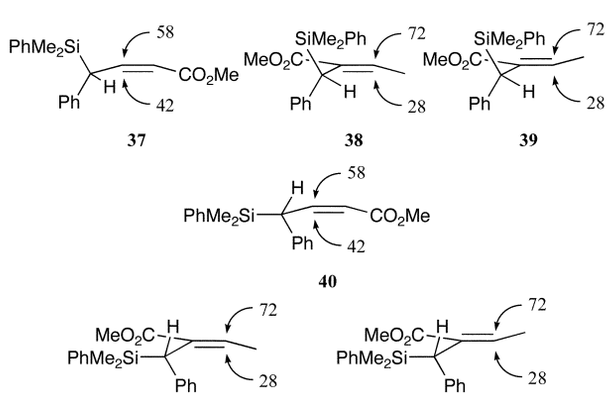
likely that isomer **B** had the structure **21** and that isomer **C** had the structure **22**. This was confirmed when chromatography on yet another occasion gave us a 14 : 86 mixture of the isomers **B** and **D**, unusually free of the isomer **C**. Silyl-to-hydroxy conversion of this mixture failed again to go to completion, but gave the two cyclic disiloxanes **33** and **28** in the same ratio.

The configurations of the esters **12** and **13** played an important part in clinching the assignment of configuration to the diols **26** and **31**, and hence to the esters **20** and **21**. To make sure that we were not being misled by a false assignment to the aldol products **12** and **13**, we confirmed the relative configuration for the two critical stereogenic centres C-2 and C-3 by the sequence of reactions in Scheme 7. The ^{1}H-NMR spectra of the acetonides **35** and **36** showed double quartets for the methine proton adjacent to the methyl group with coupling constants of 3.5 and 7 for the former, indicating that the methyl group was axial, and 9.5 and 7 for the latter, indicating that the methyl group was equatorial.



Scheme 7 *Reagents:* i, $LiAlH_4$, Et_2O; ii, $Me_2C(MeO)_2$, TsOH, DMF.

The remarkable conclusion is that the conjugate addition has taken place predominantly syn to the silyl group in both the *Z*-ester **14** and the *E*-ester **15**, with a syn : anti ratio of 72 : 28 for both isomers. Against all expectation, syn attack is apparently preferred both adjacent to the stereogenic centre **37** (C-2 in **2**), and at the other end of the double bond **38** and **39** (C-3 in **2**) (Scheme 8).



Scheme 8

It is known that alkyl cuprates have two steps influencing the stereochemistry—a reversible coordination step and a copper–carbon bond-forming step.[11] If silylcupration is similar, we cannot be confident that we know at what stage stereochemistry is being determined in these reactions. Also, we cannot be confident in these open-chain systems of the conformation at the time of reaction—with the Curtin–Hammett principle making it necessary to know both relative energies and relative reactivities before predictions can be made. The only comment that is perhaps worth adding is to recall the "inside alkoxy effect",[15] which is seen when some electrophilic reagents are attacking a double bond with an oxygen substituent at an

adjacent stereogenic centre—electrophilic attack can be expected to be faster when the O—C bond is *not* conjugated to the double bond. In our case, nucleophilic attack may be faster when the Si—C bond is *not* conjugated to the double bond, as in the drawings **40**–**42** in the lower part of Scheme 8. To be consistent with the sense of attack that we see, this looks like an "outside-silicon effect", but whether our results here are special cases or not remains to be seen. A referee pointed out that the outside silicon in the structures **41** and **42** might even be co-ordinating to the methoxycarbonyl group, making it a less unlikely and slightly activated conformation. This type of coordination between a weak Lewis base and a weak Lewis acid is detectable in X-ray crystal structures, but there is almost no evidence for it in solution.[16] It must be very weak, and sadly it cannot be invoked to explain the result illustrated in the drawing **37**.

Experimental

General

Infrared spectra were recorded on a Perkin–Elmer 1600 infrared spectrophotometer and wave numbers measured relative to polystyrene (1603 cm^{-1}), using sodium chloride plates or sodium chloride solution cells (0.1 mm path length). ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker NMR spectrometers (AM 400, AC 250). Chemical shifts were measured relative to tetramethylsilane (δ 0.00) or chloroform (δ 7.26) as internal standards. The coupling constant J is expressed in Hertz (Hz) and reported as observed. In ^{13}C attached proton test (APT) spectra, + denotes a signal in the same direction as the solvent signal. Mass spectra were recorded on AE1 MS89, Kratos MS50 or HP5988A spectrometers. Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh ASTM). Thin layer chromatography (TLC) was performed on glass plates coated to a thickness of 1 mm with Kieselgel 60 PF_{254}. Tetrahydrofuran (THF) and ether were freshly distilled from lithium aluminium hydride under argon. Dichloromethane and toluene were freshly distilled from calcium hydride under argon. Light petroleum refers to the fraction boiling between 40 °C and 60 °C. Other solvents and reagents where appropriate were purified before use. Organolithium reagents were titrated using the method of Gilman.[17] Modelling calculations were carried out using the Macromodel programme (version 5.5),[18] applying the Altona equation.[19]

Methyl (2*RS*,3*SR*)-2-[1′*RS*-dimethyl(phenyl)silylbenzyl]-3-hydroxybutanoate 12 and methyl (2*RS*,3*RS*)-2-[1′*RS*-dimethyl(phenyl)silylbenzyl]-3-hydroxybutanoate 13

This reaction is based on the method of Kilburn,[9] but using the zincate[20] rather than the cuprate. Dimethyl(phenyl)silyllithium (1.2 mol dm^{-3} in THF, 14.3 cm^3, 17.2 mmol) was added dropwise to diethylzinc (1.0 mol dm^{-3} in hexane, 17.2 cm^3, 17.2 mmol) in THF (60 cm^3) at 0 °C under nitrogen, and the mixture stirred for 10 min before being cooled to −78 °C. Methyl cinnamate (2.0 g, 12.3 mmol) in THF (5 cm^3) was added dropwise and the solution stirred for 10 min, during which time the solution turned from a dark red to a dark brown colour. Acetaldehyde (1.0 cm^3, 17.2 mmol) was added and the mixture stirred at −78 °C for 10 min before being allowed to warm slowly to room temperature. Water (10 cm^3) was cautiously added, followed by dilute aqueous hydrochloric acid (10 cm^3) and ether (20 cm^3). The layers were separated and the aqueous layer washed with ether (3 × 20 cm^3). The organic layers were combined and washed with water (2 × 20 cm^3), brine (20 cm^3), dried ($MgSO_4$) and solvents removed under reduced pressure. The residue was chromatographed (SiO_2, light petroleum–EtOAc, 8 : 2) to give the major product **12**[9] (2.95 g, 70%); R_f(light petroleum–EtOAc, 9 : 1) 0.02; ν_{max}(film)/cm^{-1} 3434 (OH), 2949 (CH), 1732 (CO), 1249 (SiMe) and 1112 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.38–7.28 (5H, m, SiPh), 7.19 (2 H, t, J 7.6, *m*-PhH), 7.10 (1 H, t, J 7.3, *p*-PhH), 6.91 (2 H, d, J 7.7, *o*-PhH), 3.83 (1 H, dq, J 5.2 and 6.4, C*H*OH), 3.44 (3 H, s, OMe), 3.27 (1 H, dd, J 12.4 and 5.0, C*H*CO_2Me), 2.67 (1 H, d, J 12.4, PhC*H*), 1.2 (3 H, d, J 6.4, *Me*CH), 0.22 (3H, s, SiMe_A-Me_B) and 0.13 (3 H, s, Si$Me_A$$Me_B$); δ_C(125 MHz, $CDCl_3$) 173.5+, 139.8+, 136.7+, 134.4−, 129.1−, 128.7−, 128.3−, 127.5−, 125.3−, 68.0−, 51.8−, 51.4−, 35.9−, 17.7−, −2.9− and −4.5−; *m*/*z* (ESI) 365 (100%, MNa^+)(Found MNa^+, 365.1557, $C_{20}H_{26}O_3Si$ requires M + Na, 365.1549), and the minor isomer **13** (1.1 g, 26%) as a colourless oil: R_f(light petroleum–EtOAc, 9 : 1) 0.05; δ_H(400 MHz; $CDCl_3$) 7.41–7.26 (5H, m, SiPh), 7.20 (2H, t, J 6.6, *m*-PhH), 6.97 (2 H, d, J 7.6, *p*-PhH), 3.55 (1 H, ddq, J 10.1, 2.6 and 6.5, C*H*OH), 3.33 (3 H, s, OMe), 2.99 (1 H, d, J 12.6, PhC*H*), 2.88 (1 H, dd, J 12.6 and 2.6, C*H*CO_2Me), 2.50 (1 H, d, J 10.1 OH), 1.02 (3 H, d, J 6.6 *Me*CH), 0.30 (3 H, s, Si$Me_A$$Me_B$) and 0.04 (3 H, s, Si$Me_A$$Me_B$); δ_C(125 MHz, $CDCl_3$) 174.8+, 140.1+, 136.9+, 134.3−, 129.4−, 128.8−, 128.4−, 127.5−, 125.3−, 65.5−, 51.8−, 51.2−, 32.3−, 21.8−, −2.5− and −5.2−; *m*/*z* (ESI) 365 (MNa^+, 100%)(Found MNa^+, 365.1544).

Methyl (2*RS*,3*SR*)-2-[1′*RS*-dimethyl(phenyl)silylbenzyl]-3-methanesulfonyloxybutanoate

The ester **12** (1.99 g, 5.82 mmol), methanesulfonyl chloride (0.68 cm^3, 8.73 mmol) and triethylamine (1.21 cm^3, 8.73 mmol) were stirred in THF (60 cm^3) at 0 °C for 1.5 h, and then allowed to warm to room temperature and stirred for 1 h. Water (20 cm^3) was added and the mixture was diluted with dichloromethane (50 cm^3). The aqueous phase was extracted with dichloromethane (3 × 30 cm^3), and the combined organic extracts were washed with aqueous citric acid solution (10% w/v, 50 cm^3), dried (Na_2SO_4), filtered and concentrated at reduced pressure to yield the *mesylate* (2.40 g, 98%) as a crystalline solid; ν_{max}(solid)/cm^{-1} 2954 (CH), 1732 (C=O) and 1597 (Ar); δ_H(400 MHz; $CDCl_3$) 7.36–7.27 (5 H, m, Ar), 7.23–7.19 (2 H, m, Ar), 7.12 (1 H, tt, 7.5 and 1.5, *p*-Ar*H*), 6.91 (2 H, m, *o*-Ar*H*), 4.76 (1 H, dq, J 6.5 and 5.0, MeC*H*O), 3.61 (1 H, m, C*H*CO_2Me). 3.40 (3 H, s, CO_2Me), 2.88 (3 H, s, OSO_2Me), 2.63 (1 H, d, J 13.0, PhC*H*), 1.27 (3 H, d, J 6.5, *Me*CHO), 0.25 (3 H, s, Si$Me_A$$Me_B$) and 0.09 (3 H, s, Si$Me_A$$Me_B$); δ_C(100 MHz; $CDCl_3$) 171.70, 134.30, 132.92, 129.27, 129.19, 128.54, 128.41, 127.64, 127.48, 125.69, 78.60, 51.50, 49.01, 38.45, 35.91, 14.96, −3.27 and −5.08; *m*/*z* (ESI) 443 (MNa^+, 70%)(Found MNa^+, 443.1341. $C_{21}H_{28}O_5SSi$ requires M + Na^+, 443.1324).

Methyl (2*RS*,3*RS*)-2-[1′*RS*-dimethyl(phenyl)silylbenzyl]-3-methanesulfonyloxybutanoate

The ester **13** (350 mg, 1.02 mmol) was similarly converted into the *mesylate* (429 mg, 100%) as a colourless oil; ν_{max}(film)/cm^{-1} 2954 (CH), 1746 (C=O) and 1599 (Ar); δ_H(400 MHz; $CDCl_3$) 7.37–7.28 (5 H, m, Ar), 7.25–7.19 (2 H, m, Ar), 7.12 (1 H, tt, 7.5 and 1.5, *p*-Ar*H*), 6.91 (2 H, m, *o*-Ar*H*), 4.71 (1 H, dq, J 6.5 and 3.0, MeC*H*), 3.39 (3 H, s, CO_2*Me*), 3.09 (1 H, dd, J 12.0 and 4.0, C*H*CO_2Me). 2.90 (1 H, d, J 12.0, PhC*H*), 2.73 (3 H, s, OSO_2*Me*), 1.28 (3 H, d, J 6.5, *Me*CH), 0.23 (3 H, s, Si$Me_A$$Me_B$) and 0.12 (3 H, s, Si$Me_A$$Me_B$); δ_C(100 MHz; $CDCl_3$) 171.33, 139.15, 136.32, 134.32, 129.11, 128.76, 128.31, 127.41, 125.62, 77.41, 51.81, 51.37, 38.63, 34.96, 20.06, −2.74 and −4.59; *m*/*z* (ESI) 443 (MNa^+, 100%)(Found MNa^+, 443.1325. $C_{21}H_{28}SiSO_5$ requires M + Na, 443.1324).

Methyl (*Z*)-(1′*RS*-dimethylphenylsilylbenzyl)but-2-enoate 14

The mesylate (1.00 g, 2.381 mmol) derived from the alcohol **12** and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.0 cm^3, 6.7 mmol) were refluxed in hexane (15 cm^3) for 3 h and then stirred at room temperature for 14 h. Water (10 cm^3) was added and the organic

phase was separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Flash column chromatography (SiO_2, hexane) gave the *ester* **14** (733 mg, 95%) as an oil; R_f(hexane) 0.27; ν_{max}(film)/cm^{-1} 2950 (CH), 1710 (ester C=O) and 1492 (Ar); δ_H(400 MHz; $CDCl_3$) 7.43 (2 H, m, *m*-Ar*H*), 7.33–7.29 (3 H, m, *o*- and *p*-Ar*H*), 7.17 (2 H, m, *m*-Ar*H*), 7. 08 (1 H, tt, *J* 7.5 and 2.0, *p*-Ar*H*), 7.04 (2 H, m, *o*-Ar*H*), 6.87 (1 H, q, *J* 7.0, MeC*H*), 3.70 (1 H, s, PhC*H*), 3.66 (3 H, s, OMe), 1.73 (3 H, d, *J* 7.0, *Me*CH), 0.35 (3 H, s, Si*Me*$_A$Me$_B$) and 0.31 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 169.11+, 141.67+, 139.73+, 138.16−, 134.76+ 133.85−, 128.66−, 128.31−, 128.07−, 127.50−, 124.66−, 51.50−, 36.35−, 14.47−, −2.53− and −2.74−; *m*/*z* (ESI) 347 (MNa$^+$, 30%) and 247 (M$^+$ − Ph, 100%)(Found M$^+$, 347.1430. $C_{20}H_{24}O_2Si$ requires *M* + Na$^+$, 347.1443).

Methyl (*E*)-(1′*RS*-dimethylphenylsilylbenzyl)but-2-enoate 15

A similar reaction on the mesylate (351 mg, 0.836 mmol) derived from the alcohol **13** gave a 1 : 1 mixture of *esters* **14** and **15** (197 mg, 73%) from which the *E*-ester could be separated with difficulty; R_f(hexane) 0.27; δ_H(400 MHz; $CDCl_3$) 7.37 (2 H, m, *m*-Ar*H*), 7.31–7.28 (3 H, m, *o*- and *p*-Ar*H*), 7.16 (2H, m, *m*-Ar*H*), 7.11 (1H, tt, *J* 7.5 and 1.5, *p*-Ar*H*), 7.03 (2 H, m, *o*-Ar*H*), 5.97 (1 H, dq, *J* 7.0 and 1.0, MeC*H*), 3.66 (1 H, s, PhC*H*), 3.57 (3 H, s, OMe), 1.88 (3 H, dd, *J* 7.0 and 1.0, *Me*CH), 0.32 (3 H, s, Si*Me*$_A$Me$_B$) and 0.26 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(125 MHz, $CDCl_3$) 169.1+, 141.0+, 137.7+, 135.6−, 133.9−, 133.7+, 129.0−, 128.8−, 128.3−, 127.5−, 125.2−, 51.2−, 41.3−, 15.9−, −2.9− and −3.4−.

Methyl (*3RS,4RS*)-3,4-bisdimethyl(phenyl)silylpentanoate 16 and methyl (*3RS,4SR*)-3,4-bisdimethyl(phenyl)silylpentanoate 17

A suspension of copper(I) cyanide (0.046 g, 0.5 mmol) in dry THF (1 cm^3) was treated with dimethyl(phenyl)silyllithium (1.1 mol dm^{-3} solution in THF, 0.90 cm^3, 1.0 mml) at 0 °C under nitrogen. The mixture was stirred for 30 min and then cooled to −78 °C. (*Z*)-Methyl 4-dimethyl(phenyl)silylpent-2-enoate (**11 = 12a** in the preceding paper) (0.095 g, 0.38 mmol) in THF (0.5 cm^3) was added and the mixture stirred at −78 °C for 5 min and then allowed to warm to −20 °C, stirred at that temperature for 1 h and then cooled to −78 °C. Basic saturated aqueous ammonium chloride solution (2 cm^3) was added and the mixture allowed to warm to room temperature. Ether (1 cm^3) was added and the layers separated. The aqueous layer was washed with ether (3 × 2 cm^3), the combined organic layers were washed with water (2 × 2 cm^3), brine (3 cm^3), dried ($MgSO_4$) and solvents removed under reduced pressure. The residue was chromatographed (SiO_2, light petroleum–EtOAc, 95 : 5) to give the mixture of *esters* (0.14 g, 95%, 58 : 42, **16** : **17**) as a colourless oil; R_f(light petroleum–EtOAc, 95 : 5) 0.35; ν_{max} (film)/cm^{-1} 2952 (CH), 1736 (C=O), 1249 (SiMe) and 1111 (SiPh); δ_H(400 MHz; $CDCl_3$) (major isomer **16**) 7.50–7.39 (2 H, m, SiPh), 7.37 (3 H, m, SiPh), 3.43 (3 H, s, CO_2Me), 2.27 (1 H, dd, *J* 15.8 and 10.1, C*H*$_A$H$_B$CO$_2$Me), 2.17 (1 H, dd, *J* 15.8 and 4.2, CH$_A$*H*$_B$CO$_2$Me), 1.77 (1 H, ddd, *J* 10.1, 4.2 and 1.1, SiC*H*-CH$_2$CO$_2$Me), 1.17 (1 H, dq, *J* 1.0 and 7.5, SiC*H*Me), 0.82 (3 H, d, *J* 7.6, SiCH*Me*), 0.25 [9 H, s, (Si*Me*$_A$Me$_B$)$_2$ and SiMe$_A$*Me*$_B$] and 0.17 (3 H, s, Me$_A$*Me*$_B$), and (minor isomer **17**, where different from the major isomer) 3.47 (3 H, s, CO_2Me), 2.34 (2 H, d, *J* 6.7, CH_2CO_2Me), 1.68 (1 H, q, *J* 6.7, SiC*H*CH$_2$CO$_2$Me) and 1.0 (3 H, d, *J* 7.6, SiCH*Me*); and for the mixture δ_C(125 MHz, $CDCl_3$) 174.4+, 174.1+, 139.5+, 139.3+, 133.9−, 128.8−, 127.6−, 51.3−, 36.3+, 32.1+, 24.6−, 22.0−, 21.0−, 19.1−, 15.7−, 11.5−, −1.9−, −2.7−, −3.5−, −3.6−, −4.1− and −4.5−; *m*/*z* (EI) 384.2 (3%, M), 135.1 (100%, PhMe$_2$Si) and 249.1 (18%, M − PhMe$_2$Si)(Found M$^+$, 384.1944. $C_{22}H_{32}O_2Si$ requires *M*, 384.1941).

Conjugate additions of the silylcuprate reagent to the α,β-unsaturated esters 14 and 15

Dimethyl(phenyl)silyllithium (0.9 mol dm^{-3}, 8.7 cm^3, 8.2 mmol) was added dropwise to a suspension of copper(I) cyanide (370 mg, 4.1 mmol) in dry THF (20 cm^3) at 0 °C under nitrogen. The mixture was stirred for 15 min, and then cooled to −78 °C. The *Z*-ester **14** (1.0 g, 3.2 mmol) in dry THF (5 cm^3) was added. The mixture was stirred for a further 1 h at −78 °C, allowed to warm to −20 °C and kept at that temperature for 1.5 h, and finally allowed to warm to 0 °C and stirred at that temperature for 1 h before being cooled back to −78 °C. The reaction was then quenched by the addition of saturated aqueous basic ammonium chloride solution (20 cm^3) and allowed to warm to room temperature. Ether (20 cm^3) was added and the layers separated. The aqueous layer was extracted with ether (2 × 20 cm^3) and the combined organic layers washed with water (2 × 20 cm^3), brine (20 cm^3), dried ($MgSO_4$) and the solvents removed under reduced pressure. The residue was chromatographed (SiO_2, light petroleum–EtOAc, 99 : 1) to give the *esters* (typical total yield 1.28 g, 88%; average ratios of 7 : 36 : 36 : 21 **20 : 21 : 22 : 23**) as colourless oils. (Quenching with basic ammonium chloride solution, methanol, or 2,6-di-*tert*-butylphenol gave the esters in similar ratios.) A similar experiment on the *E*-ester **15** (78 mg, 0.24 mmol) gave the same esters (91 mg, 84%; in ratios of 27 : 14 : 13 : 45, **20 : 21 : 22 : 22**). The esters **20** and **23** were obtained free enough of the other isomers. The esters **21** and **22** were obtained as a mixture, but the ratios from different runs were different enough to identify characteristic signals for each. The following compounds were prepared by this method: *methyl (2*SR*,3*RS*)-2-[1′(*RS*)-dimethyl(phenyl)silylbenzyl]-3-dimethylphenylsilylbutanoate* **20**: R_f(light petroleum–EtOAc, 95 : 5) 0.40; ν_{max}(KBr)/cm^{-1} 2953 (CH), 1733 (C=O), 1598 (aromatic C=C), 1427 (CH) and 1249 (SiMe); δ_H(400 MHz; $CDCl_3$) 7.42–7.21 (10 H, m, ArH), 7.19 (2 H, t, *J* 7.4, *m*-ArH), 7.17 (1 H, t, *J* 7.7, *p*-ArH), 6.78 (2 H, d, *J* 7.5, *o*-ArH), 3.23 (3 H, s, OMe), 2.97 (1H, dd, *J* 12.5 and 3.0, C*H*CO$_2$Me), 2.77 (1 H, d, *J* 12.5, PhC*H*), 1.13 (1H, dq, *J* 7.5 and 3.0, MeC*H*), 0.88 (3H, d, *J* 7.5, *Me*CH), 0.33 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.15 (3H, s, SiMe) and 0.02 (3H, s, SiMe); δ_C(100 MHz, $CDCl_3$) 175.4+, 140.7+, 139.7+, 137.1+, 134.1−, 133.8−, 132.8−, 128.6−, 128.2−, 127.8−, 127.6−, 127.2−, 124.6−, 50.6−, 50.4−, 37.6−, 22.1−, 16.3−, −1.8−, −2.8−, −4.8− and −5.0−; *m*/*z* (ESI) 483 (MNa$^+$, 23%)(Found M$^+$, 483.2176. $C_{28}H_{36}O_2Si_2$ requires *M* + Na$^+$, 483.2152); for the mixture of esters **21** and **22**: R_f(light petroleum–EtOAc, 95 : 5) 0.38; ν_{max}-(film)/cm^{-1} 3069 (CH), 2951 (CH), 1732 (CO), 1598 (PhH), 1494 (PhH), 1249 (SiMe) and 1112 (SiPh); δ_C(125 MHz, $CDCl_3$) 175.1+, 174.4+, 142.3+, 140.2+, 138.9+, 138.4+, 138.1+, 134.3−, 134.1−, 133.9−, 133.8−, 137.1+, 129.2−, 128.8−, 128.7−, 128.3−, 127.9−, 127.8−, 127.6−, 127.5−, 127.4−, 127.3−, 124.9, 124.8−, 52.3−, 50.7−,47.1−, 44.1−, 38.3−, 36.0−, 22.3−, 20.0−, 16.2−, 8.3−, −1.5−, −2.3−, −2.7−, −4.5−, −4.55−, −4.6, −4.7− and −4.8−; *m*/*z* (ESI) 483.2 (100%, M$^+$)(Found MNa$^+$ 483.2144. $C_{28}H_{36}O_2Si_2$ requires *M*Na$^+$ 483.2152); *methyl (2*SR*,3*SR*)-2-[1′(*RS*)-dimethyl(phenyl)silylbenzyl]-3-dimethylphenylsilylbutanoate* **21**: δ_H(400 MHz; $CDCl_3$) 7.46 (2 H, m, *m*-Ar*H*), 7.38 (2 H, m, *o*-Ar*H*), 7.32–7.23 (6 H, m, Ar*H*), 7.14 (2 H, m, *m*-Ar*H*), 7.07 (1 H, m, *p*-Ar*H*), 6.73 (2 H, m, *o*-Ar*H*), 3.18 (1 H, s, OMe), 3.10 (1 H, dd, *J* 12.5 and 3.0, C*H*CO$_2$Me), 2.90 (1 H, d, *J* 12.5, PhC*H*), 1.11 (1 H, qd, *J* 7.5 and 2.5, MeC*H*), 0.82 (3 H, d, *J* 7.5, *Me*CH), 0.19 (3 H, s, SiMe), 0.16 (3 H, s, SiMe), 0.13 (3 H, s, SiMe) and 0.05 (3 H, s, SiMe); *methyl (2*RS*,3*SR*)-2-[(1′(*RS*)-dimethyl(phenyl)silylbenzyl]-3-dimethylphenylsilylbutanoate* **22**: δ_H(400 MHz; $CDCl_3$) 7.46 (2 H, m, *m*-Ar*H*), 7.38 (2 H, m, *o*-Ar*H*), 7.32–7.23 (6 H, m, Ar *H*), 7.15 (2 H, m, *m*-Ar*H*), 7.06 (1 H, m, *p*-Ar*H*), 6.88 (2 H, m, *o*-Ar*H*), 3.19 (1 H, s, CHCO$_2$*Me*), 2.99 (1 H, dd, *J* 11.0 and 4.0, C*H*CO$_2$Me), 2.70 (1 H, d, *J* 11.0, PhC*H*), 1.35 (1 H, qd, *J* 7.5 and 4.0,

MeC*H*), 0.95 (3 H, d, *J* 7.5, *Me*CH), 0.28 (3 H, s, SiMe), 0.25 (3 H, s, SiMe), 0.17 (3 H, s, SiMe) and 0.05 (3 H, s, SiMe); *methyl (2*RS*,3*RS*)-2-[(1′(*RS*)-dimethyl(phenyl)silylbenzyl]-3-dimethylphenylsilylbutanoate* **23**: R_f(light petroleum–EtOAc, 95 : 5) 0.36; ν_{max}(film)/cm^{-1} 2952 (CH), 1725 (ester C=O), 1599 and 1574 (Ar); δ_H(400 MHz; $CDCl_3$) 7.48 (2 H, m, *m*-Ar*H*), 7.39 (2 H, m, *o*-Ar*H*), 7.36–7.28 (6 H, m, Ar*H*), 7.16 (2 H, m, *m*-Ar*H*), 7.04 (1 H, tt, *J* 7.5 and 1.0, *p*-Ar*H*), 6.99 (2 H, m, *o*-Ar*H*), 3.25 (1 H, dd, *J* 12.5 and 2.5, C*H*CO_2Me), 3.15 (3 H, s, OMe), 2.99 (1 H, d, *J* 12.5, PhC*H*), 1.25 (1 H, qd, *J* 7.5 and 2.5, MeC*H*), 0.72 (3 H, d, *J* 7.5, *Me*CH), 0.19 (3 H, s, SiMe), 0.17 (3 H, s, SiMe), 0.12 (3 H, s, SiMe) and 0.01 (3 H, s, SiMe); δ_C(100 MHz; $CDCl_3$) 173.94+, 142.45+, 138.41+, 133.93−, 129.05−, 128.27−, 127.97−, 127.60−, 124.92−, 50.48−, 47.08−, 36.69−, 21.48−, 8.89−, −1.57−, −4.16−, −5.12− and −5.52−; *m*/*z* (ESI) 483 (MNa^+, 100%)(Found MNa^+, 483.2168. $C_{28}H_{36}O_2Si_2$ requires *M* + Na^+, 483.2152).

Methyl (2*RS*,3*RS*)-2-benzyl-3-dimethylphenylsilylbutanoate 24 and methyl (2*RS*,3*SR*)-2-benzyl-3-dimethylphenylsilylbutanoate 25

Tetrabutylammonium fluoride (1.0 mol dm^{-3} in THF, 0.06 cm^3, 0.06 mmol) was added to a mixture of isomers **B**, **C** and **D** (**B** : **C** : **D**, 46 : 51 : 3, 24 mg, 0.05 mmol) in THF (1 cm^3). and the mixture stirred for 5 min at room temperature. Water (1 cm^3) was added and the layers separated. The aqueous layer was washed with ether (2 × 1 cm^3) and the combined organic layers washed with water (1 cm^3), brine (1 cm^3), dried ($MgSO_4$) and solvents removed under reduced pressure. The residue was chromatographed (SiO_2, light petroleum–EtOAc, 95 : 5) to give the *esters* (16 mg, 100%, 55 : 45) as an oil; R_f(light petroleum–EtOAc, 95 : 5) 0.28; ν_{max}(film)/cm^{-1} 3068 (CH), 2952 (CH), 1732 (CO), 1603 (PhH), 1495 (PhH), 1250 (SiMe) and 1112 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.58–7.52 (2 H, m, Ar), 7.50–7.45 (2 H, m, Ar), 7.39–7.32 (6 H, m, Ph), 7.25–7.10 (6 H, m, Ar), 7.02–6.96 (4 H, m, Ar), 3.45 (3 H, s, OMe), 2.95–2.70 (2 H m, PhCH_AH_BC*H*), 2.64 (1 H, dd, *J* 13.0 and 3.1, PhC$H_A$$H_B$) common to both isomers, and with signals for the major isomer **25**, assuming equal yields from the two substrates, at 1.26 (1 H, quintet, *J* 7.7, CHSi), 1.03 (3 H, d, *J* 7.5, CH*Me*), 0.33 (3 H, s, Si$Me_A$$Me_B$) and 0.30 (3 H, s, Si$Me_A$$Me_B$), and for the minor isomer, probably **24**, at 3.39 (3 H, s, OMe), 1.45 (1 H, dq, *J* 7.6 and 5.0, CHSi), 1.08 (3 H, d, *J* 7.6, CH*Me*), 0.38 (3 H, s, SiMe_A-Me_B) and 0.35 (3 H, s, Si$Me_A$$Me_B$); δ_C(125 MHz, $CDCl_3$) 175.4+, 175.3+, 140.2+, 139.7+, 138.3+, 137.8+, 134.0−, 133.8−, 129.1−, 129.0−, 128.8−, 128.7−, 128.3−, 128.2−, 127.8−, 127.7−, 126.1−, 126.0−, 50.9−, 49.2−, 37.8+, 35.4+, 23.2−, 22.5−, 11.8−, 11.5−, −3.7−, −3.8−, −3.9− and −4.1−; *m*/*z* (EI) 326.2 (8%, M^+), 311.1 (22%, *M* − Me), 249.1 (33%, *M* − Ph) and 235.1 (88%, *M* − $PhCH_2$), 135.1 (100%, $PhMe_2Si$)(Found M^+, 326.1698. $C_{20}H_{26}O_2Si$ requires *M*, 326.1702).

Silyl-to-hydroxy conversions

Method A. Typically, the substrate (0.5 mmol) and mercury(II) acetate (560 mg, 1.75 mmol) were stirred with a solution of peracetic acid in acetic acid (15%, with 1% H_2SO_4, 6 cm^3) at room temperature for 16–24 h. Sodium thiosulfate solution (30 cm^3) and ether (30 cm^3) were added, and the mixture separated. The organic layer was washed with sodium thiosulfate solution (10%, 30 cm^3), water (2 × 30 cm^3) and brine (30 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed (SiO_2, hexane to Et_2O) to give the products.

Method B. Typically, the substrate (0.20 mmol), potassium bromide (29 mg, 0.24 mmol) and anhydrous sodium acetate (507 mg, 0.61 mmol) were stirred in glacial acetic acid (1 cm^3) at 0 °C. Peracetic acid (15% solution in acetic acid with 1% H_2SO_4, 1 cm^3, 1.2 mmol) was then added dropwise, and the mixture was stirred at room temperature for 14 h. Ether (30 cm^3) and sodium thiosulfate solution (30 cm^3) were added. The resulting suspension was stirred vigorously for 30 min, filtered through Celite and concentrated under reduced pressure. The residue was dissolved in ether (30 cm^3), washed with sodium bicarbonate solution (30 cm^3), brine (30 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was chromatographed (SiO_2, ether–hexane, 1 : 1 to ether) to give the products.

Method C. A 29 : 71 mixture of the silanes **21** and **22** (25 mg, 0.05 mmol) and hydrofluoroboric acid (54% w/v Et_2O, 0.02 cm^3, 0.15 mmol) in dichloromethane (1 cm^3) were stirred at 0 °C at room temperature for 10 h. The mixture was diluted with dichloromethane (10 cm^3) and saturated aqueous sodium hydrogencarbonate solution (20 cm^3), and extracted with dichloromethane (3 × 10 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. In an attempt to oxidise the products, they were stirred with *m*-chloroperbenzoic acid (28 mg, 0.17 mmol) and triethylamine (0.08 cm^3, 0.06 mmol) at room temperature for 2 h, and worked up in the usual way, but this treatment evidently had no effect. Chromatography (SiO_2; hexane–Et_2O, 90 : 10) gave the mixture of disiloxanes **33** and **34** described below. The following compounds were prepared by these methods.

Methyl (2*SR*,3*RS*)-2-(1′*RS*-hydroxybenzyl)-3-hydroxybutanoate 26. By method A from **20** (6 mg) as an oil (2 mg, 69%) and from **12** (200 mg, 0.58 mmol) as a solid (117 mg, 89%); R_f(Et_2O) 0.35; ν_{max}(solid)/cm^{-1} 3467, 3371 (OH), 1707 (C=O), 1609 (MeO) and 1493 (Ar); δ_H(400 MHz; $CDCl_3$) 7.41–7.29 (4 H, m, Ar), 7.27 (1 H, tt, *J* 6.5 and 2.0, *p*-Ar*H*), 5.08 (1 H, d, *J* 7.5, PhC*H*), 3.73 (1 H, qd, *J* 6.5 and 3.5, MeC*H*OH), 3.69 (1 H, s, OMe), 2.71 (1 H, dd, *J* 7.5 and 3.5, CHCO) and 1.18 (3 H, d, *J* 6.5, *Me*CHOH); δ_C(100 MHz; $CDCl_3$) 173.77+, 141.19+, 128.11−, 127.65−, 125.73−, 73.83−, 66.87−, 58.43−, 51.39− and 21.80−; *m*/*z* (EI) 224 (M^+, 40%) and 77 (Ph, 90%)(Found M^+, 224.1050. $C_{12}H_{16}O_4$ requires *M*, 224.1049).

Methyl (4*RS*,5*SR*,6*RS*)-1,1,3,3,6-pentamethyl-4-phenyl-[1,2,3]oxadisilinane-5-carboxylate 28. By method A from **23** (190 mg) as a solid (33 mg, 36%), which was a mixture (**28** : **29**, 58 : 42). Further chromatography gave the disiloxane **28** (12 mg, 9%) as an oil; ν_{max}(film)/cm^{-1} 2954 (CH), 1724 (ester C=O), 1600 (Ar), 1431 (CH) and 1250 ($SiMe_3$); δ_H(400 MHz; $CDCl_3$) 7.20–7.01 (5 H, m, Ar), 3.35 (3 H, s, OMe), 3.07 (1 H, t, *J* 12.5, CHCO), 2.50 (1 H, d, *J* 12.5, PhC*H*), 1.17 (1 H, dq, *J* 12.5 and 7.5, MeC*H*), 0.87 (3 H, d, *J* 7.5, *Me*CH), 0.20 (3 H, s, SiMe), 0.19 (3 H, s, SiMe), 0.15 (3 H, s, SiMe) and 0.08 (3 H, s, SiMe); δ_C(125 MHz; $CDCl_3$) 175.57+, 140.27+, 128.07−, 127.96−, 125.02−, 50.88−, 49.34−, 41.95−, 25.24−, 13.10−, −0.86−, −0.94−, −2.35− and −3.08−; *m*/*z* (ESI) 345 (*M* + Na^+, 100%), 307 (*M* − Me, 43%) and 263 (*M* − CO_2Me, 63%)(Found MNa^+, 345.1316. $C_{16}H_{26}O_3Si_2$ requires *M* + Na, 345.1318), and the diol **29** (10 mg, 11%).

Methyl (2*RS*,3*RS*,)-3-hydroxy-2-(1′*RS*-hydroxybenzyl)-butanoate 29[14]. By method B from **23** (93 mg, 0.20 mmol) as a solid (9 mg, 20%); ν_{max}(solid)/cm^{-1}3237 (OH) and 1728 (C=O); δ_H(400 MHz; $CDCl_3$) 7.35–7.28 (5 H, m, Ar), 5.10 (1 H, d, *J* 9.0, PhC*H*), 4.34 (1 H, dq, *J* 8.0 and 6.0, MeC*H*OH), 3.38 (3 H, s, OMe), 2.81 (1 H, dd, *J* 9.0 and 8.5, C*H*CO) and 1.25 (3 H, d, *J* 6.0, *Me*CHOH); δ_C(125 MHz; $CDCl_3$) 171.559+, 141.26+, 131.57−, 128.40−, 126.55−, 76.88−, 70.05−, 60.64−, 51.50− and 21.81−; *m*/*z* (ESI) 247 (MH^+, 100%)(Found MNa^+, 247.0945. $C_{12}H_{16}O_4$ requires *M* + Na, 247.0946).

Methyl (2*SR*,3*SR*)-3-hydroxy-2-(1′*RS*-hydroxybenzyl)-butanoate 31[14]. By method A from a 1 : 1 mixture of **21** and **22**

(40 mg, 0.09 mmol) as an oil (10 mg, 51%), from **13** (100 mg, 0.29 mmol) as an oil (38 mg, 58%) and by method B from **14** (100 mg, 0.29 mmol) as an oil (27 mg, 42%); R_f(Et_2O–hexane, 1 : 1) 0.1; ν_{max}(film)/cm^{-1} 3398 (OH), 2972 (CH), 1717 (C=O), 1495 (Ar), 1438 (CH) and 1050 (CO); δ_H(400 MHz; $CDCl_3$) 7.44–7.25 (5 H, m, Ar), 5.17 (1 H, dd, *J* 7.5 and 4.5, PhC*H*), 4.20 (1 H, br sextet, *J* 6.5, MeC*H*OH), 3.73 (1 H, d, *J* 7.5, PhCHO*H*), 3.56 (3 H, s, OMe), 2.84 (1 H, dd, *J* 6.5 and 4.5, CHCO), 2.72 (1 H, d, *J* 5.5, MeCHO*H*) and 1.27 (3 H, d, *J* 6.5, *Me*CHOH); δ_C(100 MHz; $CDCl_3$) 173.77+, 141.19+, 128.11−, 127.65−, 125.73−, 73.83−, 66.87−, 58.43−, 51.39− and 21.80−; *m*/*z* (ESI) 247 (*M* + Na^+, 84%)(Found MNa^+, 247.0948. $C_{12}H_{16}O_4$ requires *M* + Na, 247.0946).

Methyl (4*SR*,5*SR*,6*RS*)-1,1,3,3,6-pentamethyl-4-phenyl-[1,2,3]oxadisilinane-5-carboxylate 33. By method A from a 14 : 86 mixture of **21** and **23** (127 mg, 0.276 mmol) as a solid (68 mg, 72%) consisting of a 14 : 86 mixture of disiloxane **33**; δ_H(400 MHz; $CDCl_3$) 7.20–7.01 (5 H, m, Ar), 3.35 (3 H, s, OMe), 3.07 (1 H, t, *J* 12.5, CHCO), 2.50 (1 H, d, *J* 12.5, PhC*H*), 1.17 (1 H, dq, *J* 12.5 and 7.5, MeC*H*), 0.87 (3 H, d, *J* 7.5, *Me*CH), 0.20 (3 H, s, SiMe), 0.19 (3 H, s, SiMe), 0.15 (3H, s, SiMe) and 0.08 (3 H, s, SiMe); δ_C(125 MHz; $CDCl_3$) 174.29+, 139.78+, 130.06−, 128.04−, 125.08−, 50.95−, 49.98−, 38.63−, 18.19−, 13.63−, 0.42−, −0.50−, −0.61− and −2.23−; *m*/*z* (ESI) 345 (MNa^+, 100%), 307 (M – Me, 43%) and 263 (*M* − CO_2Me, 63%)(Found MNa^+, 345.1316. $C_{16}H_{26}O_3Si_2$ requires *M* + Na, 345.1318), and disiloxane **28** with signals (^{1}H-NMR) identifiable from the sample described above.

Methyl (4*SR*,5*RS*,6*SR*)-1,1,3,3,6-pentamethyl-4-phenyl-[1,2,3]oxadisilinane-5-carboxylate 34. By Method A, from a 35 : 65 mixture of B and C, separated clean from a 35 : 65 mixture of disiloxanes **33** and **34**, as an oil (7 mg, 36%); δ_H(400 MHz; $CDCl_3$) 7.21–7.01 (5 H, m, Ar), 3.53 (1 H, dd, *J* 13.5 and 2.5, CHCO), 3.45 (3 H, s, OMe), 2.79 (1 H, d, *J* 13.5, PhC*H*), 1.18 (1 H, qd, *J* 7.5 and 2.5, MeC*H*), 1.12 (3 H, d, *J* 7.5, *Me*CH), 0.27 (3 H, s, SiMe), 0.19 (3 H, s, SiMe), 0.17 (3 H, s, SiMe) and −0.20 (3 H, s, SiMe); δ_C(125 MHz; $CDCl_3$) 174.61, 149.03, 141.86, 135.96, 129.74, 129.48, 128.28, 127.09, 124.72, 122.05, 51.27, 45.17, 33.73, 22.14, 9.59, −0.37, −0.57, −1.34 and −1.60; *m*/*z* (ESI) 345 (*M* + Na^+, 100%), 307 (*M* − Me, 43%) and 263 (M – CO_2Me, 63%)(Found MNa^+, 345.1316. $C_{16}H_{26}O_3Si_2$ requires *M* + Na, 345.1318).

(2*SR*,3*SR*)-2-[1′*RS*-Dimethyl(phenyl)silylbenzyl]butane-1,3-diol

The ester **12** (80 mg, 0.23 mmol) in anhydrous diethyl ether (2 cm^3) was stirred under nitrogen with lithium aluminium hydride (10 mg, 0.26 mmol) at 0 °C for 3 h. Water (2 cm^3) and hydrochloric acid (1 mol dm^{-3}, 5 cm^3) were added, and the mixture was partioned between ether (30 cm^3) and water (20 cm^3). The organic phase was washed with brine (20 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, Et_2O–hexane, 1 : 1) gave the *diol* as an oil (37 mg, 50%); ν_{max}(film)/cm^{-1} 3374 (OH), 2960 (CH) and 1600 (Ar); δ_H(400 MHz; $CDCl_3$) 7.46 (2 H, m, *m*-Ar*H*), 7.34–7.32 (3 H, m, *p*- and *o*-Ar*H*), 7.23 (2 H, m, *m*-Ar C*H*), 7.10 (1 H, tt, 7.5 and 2.0, *p*-ArC*H*), 7.02 (1 H, m, *o*-ArC*H*), 3.80 (1 H, dd, *J* 11.0 and 3.5, CH_AH_BOH), 3.75 (1 H, qd, *J* 6.5 and 3.0, MeC*H*OH), 3.57 (1 H, dd, *J* 11.0 and 9.5, CH_AH_BOH), 2.60 (1 H, dtd, *J* 12.5, 9.0 and 3.5, C*H*CH_2OH), 2.07 (1 H, d, *J* 12.0, PhC*H*), 1.06 (3 H, d, *J* 6.5, *Me*CHOH), 0.35 (3 H, s, Si*Me*$_A$Me$_B$) and −0.14 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(125 MHz; $CDCl_3$) 141.93+, 138.59+, 133.63−, 129.13−, 128.50−, 128.25−, 127.95−, 125.10−, 70.25−, 64.08+, 46.49−, 35.85−, 16.42−, −1.25− and −5.09−; *m*/*z* (ESI) 337 (MNa^+, 100%)(Found MNa^+, 377.1613).

(2*SR*,3*RS*)-2-[1′*RS*-Dimethyl(phenyl)silylbenzyl]butane-1,3-diol

Similarly, the ester **13** (70 mg, 0.21 mmol) gave the *diol* as an oil (47 mg, 73%); ν_{max}(film)/cm^{-1} 3358 (OH), 2967 (CH) and 1598 (Ar); δ_H(400 MHz; $CDCl_3$) 7.53 (2 H, m, *m*-Ar*H*), 7.36–7.35 (3 H, m, *o*- and *p*-Ar*H*), 7.23 (2 H, t, *J* 6.0, *m*-Ar*H*), 7.11 (1 H, tt, *J* 6.0 and 1.0, *p*-ArC*H*), 7.04 (2 H, br d, *J* 5.5, *o*-ArC*H*), 4.07 (1 H, br dt, *J* 12.0 and 2.5, CH_AH_BOH), 3.76 (1 H, ddd, *J* 12.0, 6.0 and 2.5, CH_AH_BOH), 3.70 (1 H, m, MeC*H*OH), 3.02 (1 H, d, *J* 12.0, PhC*H*), 2.30 (1 H, br d, *J* 6.0, MeCHO*H*), 1.92 (1 H, br t, *J* 3.5, CH_2OH), 1.83 (1 H, dq, *J* 12.0 and 2.5, C*H*CH_2OH), 1.14 (3 H, d, *J* 6.5, *Me*CHOH), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.09 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 144.14, 140.26 (Ar*C*), 135.39, 130.78, 130.33, 130.03, 129.59, 126.63 (Ar*C*H), 70.53 (Me*C*HOH), 63.35 (*C*H_2OH), 47.89 (*C*HCH_2OH), 36.57 (Ph*C*H), 23.51 (*Me*CHOH), 0.00 (Si*Me*$_A$Me$_B$) and −2.91 (SiMe$_A$*Me*$_B$); *m*/*z* (ESI) 337 (MNa^+, 100%)(Found MNa^+, 337.1604. $C_{19}H_{26}O_2Si$ requires *M* + Na, 337.1600).

Synthesis of acetonides

Typically, the diol (0.12 mmol), 2,2-dimethoxypropane (0.6 cm^3) and toluene-*p*-sulfonic acid (3 mg) in dimethylformamide (2 cm^3) were stirred at room temperature for 14 h. Ether (30 cm^3) and water (30 cm^3) were added and the layers separated. The organic phase was washed with water (2 × 30 cm^3) and brine (30 cm^3), dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, Et_2O–hexane, 1 : 3) gave the acetonides. The following compounds were prepared by this method.

Methyl (4*RS*,5*SR*,6*RS*)-2,2,4-trimethyl-6-phenyl[1,3]dioxane-5-carboxylate 27. From the diol **26** (30 mg, 0.13 mmol) as a solid (26 mg, 74%); ν_{max}(solid)/cm^{-1} 2991 (CH), 1747 (C=O), 1609 (MeO), 1575, 1493 (Ar) and 1432 (CH); δ_H(400 MHz; $CDCl_3$) 7.52–7.24 (5 H, m, ArC*H*), 5.15 (1 H, d, *J* 3.5, PhC*H*), 4.35 (1 H, qd, *J* 6.5 and 3.0, MeC*H*), 3.41 (3 H, s, OMe), 2.68 (1 H, t, *J* 3.5, C*H*CO), 1.62 (3 H, s, (C*Me*$_A$Me$_B$), 1.57 (3H, s, (CMe$_A$*Me*$_B$) and 1.26 (3 H, d, *J* 6.5, *Me*CH); δ_C(100 MHz; $CDCl_3$) 168.39 (*C*=O), 134.95 (Ar*C*), 128.72, 128.46, 127.20, 126.59, 124.48 (Ar*C*H), 98.28 (Ph*C*H), 70.40 (Me*C*H), 64.63 (OMe), 50.02 (*C*HCO), 28.75 (*Me*CH), 18.59 (C*Me*$_A$Me$_B$) and 18.05 (CMe$_A$*Me*$_B$); *m*/*z* (ESI) 287 (MNa^+, 81%)(Found MNa^+, 287.1271).

Methyl (4*RS*,5*RS*,6*RS*)-2,2,4-trimethyl-6-phenyl[1,3]dioxane-5-carboxylate 30[14]. From the diol **29** (6 mg, 0.03 mmol) as an oil (10 mg, 92% yield adjusted for presence of the plasticiser); ν_{max}(film)/cm^{-1} 2924 (CH) and 1739 (C=O); δ_H(400 MHz; $CDCl_3$)[1] 7.32–7.25 (5 H, m, ArC*H*), 5.01 (1 H, d, *J* 10.5, PhC*H*), 4.26 (1 H, qd, *J* 10.0 and 6.0, MeC*H*), 3.48 (3 H, s, OMe), 2.42 (1 H, t, *J* 10.5, C*H*CO), 1.50 (3 H, s, (C*Me*$_A$Me$_B$), 1.42 (3 H, s, (CMe$_A$*Me*$_B$) and 1.19 (3 H, d, *J* 6.0, *Me*CH); δ_C(125 MHz; $CDCl_3$) 171.78 (*C*=O), 139.57 (Ar*C*), 131.63, 128.50, 128.34, 126.63 (Ar*C*H), 99.25 (*C*Me_2), 73.78 (Ph*C*H), 67.21 (Me*C*H), 56.50 (OMe), 51.56 (*C*HCO), 29.91 (*Me*CH), 20.33 (C*Me*$_A$Me$_B$) and 19.63 (CMe$_A$*Me*$_B$); *m*/*z* (ESI) 287 (MNa^+, 50%)(Found MNa^+, 287.1255).

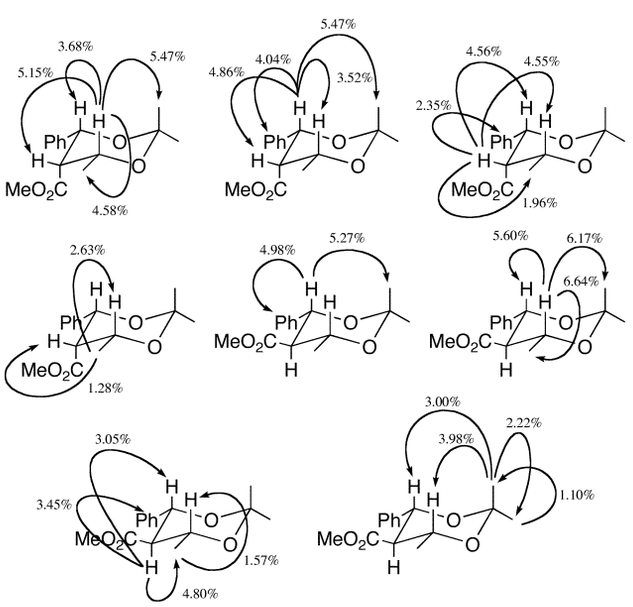
Methyl (4*SR*,5*SR*,6*RS*)-2,2,4-trimethyl-6-phenyl[1,3]dioxane-5-carboxylate 32[14]. From the diol **31** (27 mg, 0.12 mmol, derived from the monosilylmonoalcohol **12**) as an oil (18 mg, 68%), and from the diol **31** (18 mg, 0.080 mmol, derived from the mixture of disilyl esters **21** and **22**) as an oil (21 mg, 99%); ν_{max}(film)/cm^{-1} 2986 (CH), 1732 (C=O), 1490 (Ar), 1379 (Me) and 1134 (CO); δ_H(400 MHz; $CDCl_3$) 7.30–7.29 (4 H, m, Ar), 7.22 (1 H, m, *p*-C*H*), 5.13 (1 H, d, *J* 7.0, PhC*H*), 4.37 (1 H, dq, *J* 9.0 and 7.0, MeC*H*), 3.13 (1 H, s, OMe), 2.89 (1 H, dd, *J* 9.0 and 7.0, C*H*CO), 1.55 (3 H, s, (C*Me*$_A$Me$_B$), 1.41 (3 H, s, (CMe$_A$*Me*$_B$) and 1.26 (3 H, d, *J* 6.0, *Me*CH); δ_C(100 MHz;

$CDCl_3$) 171.70 (*C*=O), 138.44 (Ar*C*), 127.94, 127.43, 125.94 (Ar*C*H) 101.51 (Me_2C), 69.82 (Ph*C*H), 65.56 (Me*C*H), 57.60 (OMe), 51.10 (*C*HCO), 24.51 (CMe_AMe_B), 24.15, (CMe_A*Me*$_B$) and 20.80 (*Me*CH); *m*/*z* (ESI) 287 (*M* + Na^+, 47%)(Found MNa^+, 287.1263. $C_{15}H_{20}O_4$ requires *M* + Na, 287.1259).

(4*SR*,5*SR*)-5-[1′*RS*-Dimethyl(phenyl)silylbenzyl]-2,2,4-trimethyl[1,3]dioxane 35. From the diol (9 mg, 0.03 mmol) derived from the alcohol **12** as an oil (8 mg, 79%); ν_{max}(film)/cm^{-1} 2989 (CH) and 1596 (Ar); δ_H(400 MHz; $CDCl_3$) 7.40 (2 H, m, *m*-Ar*H*), 7.33–7.29 (3 H, m, *o*- and *p*-Ar*H*), 7.16 (2 H, m, *m*-Ar*H*), 7.07 (1 H, tt, *J* 7.5 and 1.5, *p*-Ar*H*), 7.02 (2 H, m, *o*-Ar*H*), 4.01(1 H, dq, *J* 7.0 and 3.5, MeC*H*), 3.88 (1 H, dd, *J* 12.0 and 4.0, CH_AH_BO), 3.80 (1 H, dd, *J* 12.0 and 6.0, CH_AH_BO), 3.66 (1 H, d, *J* 11.5, PhC*H*), 2.41 (1 H, ddt, *J* 11.5, 6.0 and 4.0, MeCHC*H*), 1.38 (3 H, s, (CMe_AMe_B), 1.35 (3 H, s, (CMe_AMe_B), 0.83 (3 H, d, *J* 7.0, *Me*CH), 0.29 (3 H, s, $SiMe_A$-Me_B) and 0.11 (3 H, s, $SiMe_AMe_B$); δ_C(125 MHz; $CDCl_3$) 143.02+, 138.40+, 133.92−, 128.85−, 128.00−, 127.59−, 124.61−, 98.14+, 70.27−, 63.29+, 39.92−, 34.27−, 27.80−, 24.04−, 19.09−, −1.89− and −3.9−; *m*/*z* (ESI) 377 (MNa^+, 28%)(Found MNa^+, 377.1905. $C_{22}H_{30}O_2SiNa$ requires *M* + Na, 377.1913).

(4*RS*,5*SR*)-5-[1′*RS*-Dimethyl(phenyl)silylbenzyl]-2,2,4-trimethyl[1,3]dioxane 36. From the diol (47 mg, 0.15 mmol) derived from the alcohol **13** as an oil (50 mg, 94%); ν_{max}(film)/cm^{-1} 2965 (CH) and 1597 (aromatic C=C); δ_H(400 MHz; $CDCl_3$) 7.45 (2 H, m, *m*-Ar*H*), 7.34–7.32 (3 H, m, *o*- and *p*-Ar*H*), 7.19 (2 H, m, *m*-Ar*H*), 7.10 (1 H, tt, *J* 5.5 and 2.0, *p*-Ar*H*), 7.02 (2 H, m, *o*-Ar*H*), 3.93 (1 H, dd, *J* 11.5 and 5.0, CH_AH_BO), 3.60 (1 H, dq, *J* 9.5 and 6.0, MeC*H*), 3.58 (1 H, dd, *J* 11.5 and 10.5, CH_AH_BO), 2.22 (1 H, d, *J* 7.5, PhC*H*), 2.12 (1 H, dddd, *J* 10.5, 9.5, 7.5 and 5.0, MeCHC*H*), 1.29 (3 H, s, (CMe_AMe_B), 1.20 (3 H, s, (CMe_AMe_B), 0.80 (3 H, d, *J* 6.0, *Me*CH), 0.37 (3 H, s, $SiMe_AMe_B$) and 0.04 (3 H, s, $SiMe_AMe_B$); δ_C(100 MHz; $CDCl_3$) 144.56+, 139.81+, 134.89−, 130.19−, 129.85−, 129.32−, 128.99−, 126.19−, 98.76+, 72.72−, 65.90+, 47.04−, 38.27−, 30.45−, 22.38−, 20.61−, 0.00− and −2.58−; *m*/*z* (ESI) 377 (MNa^+, 76%).

Nuclear Overhauser enhancements for acetonides 27 and 30



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