The Diastereoselectivity of Electrophilic Attack on Trigonal Carbon Adjacent to a Stereogenic Centre: Diastereoselective Aldol Reactions of Open-chain Enolates having a Stereogenic Centre carrying a Silyl Group at the β Position

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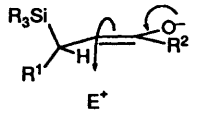
Trigonal electrophiles react with lithium enolates having β-silyl groups **2**, or with the corresponding silyl enol ethers **7**, with high diastereoselectivity in the sense **1**, to give largely the *anti* products **3**. Aldehydes react with the same lithium enolates **2**, and the analogues **10**, with high diastereoselectivity, not only in the sense **1**, but also with high diastereoselectivity for the formation of *anti* aldols **11** from the *E*-enolates and *syn* aldols **12** from the *Z*-enolates. Three adjacent stereogenic centres are set up in one operation, with easy control over the aldol geometry, because of the ease with which the enolate geometry can be controlled.

In the preceding paper in this series,[1] we reported that the alkylation and protonation of enolates having a β-silyl group is highlty diastereoselective in the sense **1**. In that paper the



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electrophiles were alkyl halides and proton sources, and only two stereogenic centres were set up. In this paper, we report in full our observations, already reported in a preliminary communication,[2] that the same high diastereoselectivity in the same sense is also found for reactions with trigonal electrophiles. With aldehydes in particular, a third stereogenic centre is set up with predictably high levels of stereocontrol governed by the forces operating on the aldol transition structure.

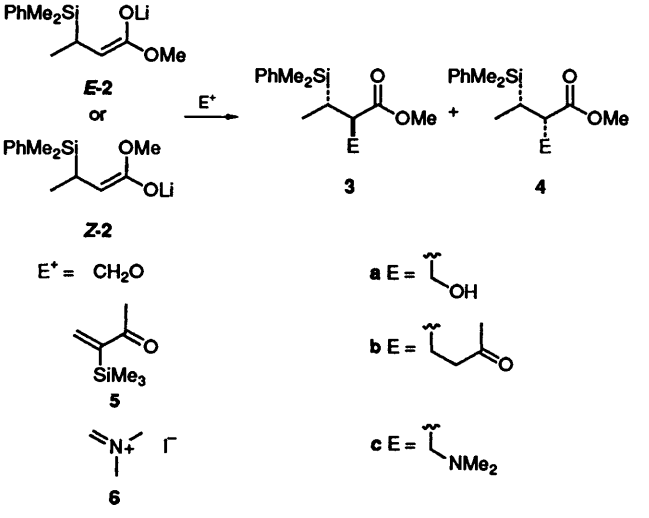
Results and Discussion

We first established that simple trigonal electrophiles, not introducing a third stereogenic centre, reacted with enolates having a β-silyl group with high diastereoselectivity, just as the alkyl halides reported in the preceding paper had. Thus we treated the enolate **2**, available as either the *E* or the *Z* isomer,[1] with formaldehyde, with Stork's α-silylated methyl vinyl ketone **5**[3] and with Eschenmoser's salt **6**.[4] In all six cases the reaction was highly diastereoselective (Table 1) in the formation of the products **3** and **4**, although we did not prove the sense of the diastereoselectivity. The work on the aldol reaction described below makes it clear that the major product in each case has, almost certainly, the relative stereochemistry shown as **3**.

Since silyl enol ethers have many uses in organic synthesis as alternative carbon nucleophiles to lithium enolates,[5] we also carried out a series of reactions using the silyl enol ethers **7**, again available as either the *Z*- or the *E*-isomer. The electrophiles were Eschenmoser's salt **6**, the dithienium fluorborate **8**,[6] phenylthiomethyl chloride and methoxymethyl chloride in the presence of zinc bromide,[7,8] and the dimethyl acetal of acetone in the presence of titanium tetrachloride.[9] Six of these reactions were highly diastereoselective, three of them were diastereoselective but not highly so, and one was not diastereoselective at all (Table 2). The poor or absent selectivity with Eschenmoser's salt is in contrast to the high diastereoselectivity shown by this electrophile when it reacted with the

Table 1 Diastereoselectivity in the reaction of trigonal electrophiles with the enolates **2**

		Products from *E*-**2**		Products from *Z*-**2**	
Products	E^+	Ratio **3**:**4**	Yield (%)	Ratio **3**:**4**	Yield (%)
3a + **4a**	CH_2O	71:29	64	81:19	78
3b + **4b**	**5**	93:7	70	91:9	66
3c + **4c**	**6**	87:13	51	82:18	43



corresponding lithium enolates (Table 1). The poor selectivity with Eschenmoser's salt is easily explained by Danishefsky's finding that when this electrophile reacts with silyl enol ethers, the intermediate regenerates a silyl enol by losing a proton, rather than giving a ketone by losing the silyl group.[10] His examples were silyl enol ethers of ketones and ours are the silyl enol ethers of an ester (often called silyl ketene acetals), but if the same thing happens in our case, as it probably does, the stereochemical relationship originally set up when the electrophile attacked will be destroyed. What we are probably seeing is the stereochemistry created when the silyl enol ethers are hydrolysed in the work-up.

We proved the relative stereochemistry of the products of the reactions with the dithienium ion and with phenylthiomethyl chloride by treating them with Raney nickel.[11] We obtained overall the products of a methylation reaction, which were

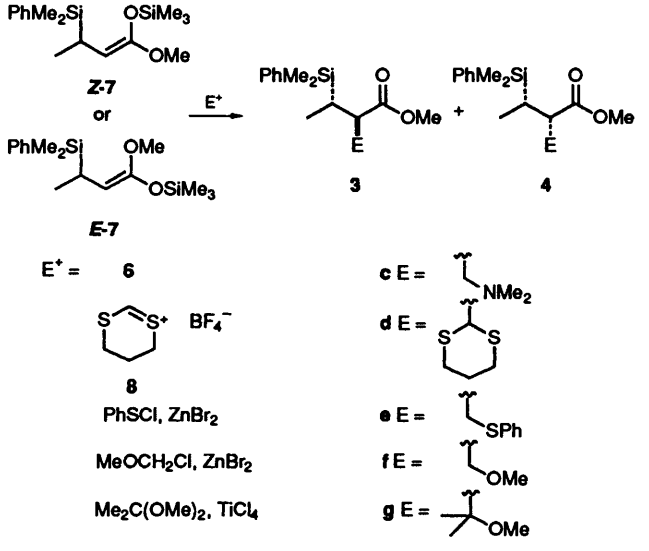
Table 2 Diastereoselectivity in the reaction of trigonal electrophiles with the silyl enol ethers **7**

Products	E^+	Products from *Z*-**7**		Products from *E*-**7**	
		Ratio **3**:**4**	Yield (%)	Ratio **3**:**4**	Yield (%)
3c + **4c**	**6**	66:34	65	50:50	60
3d + **4d**	**8**	97:3	85	88:12	66
3e + **4e**	$PhSCH_2Cl$, $ZnBr_2$	87:13	73	88:12	66
3f + **4f**	$MeOCH_2Cl$, $ZnBr_2$	91:9	79	90:10	83
3g + **4g**	$Me_2C(OMe)_2$, $TiCl_4$	67:33	75	63:37	80

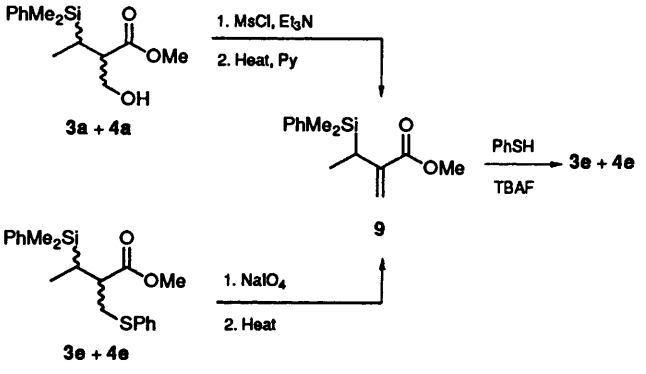
Table 3 Diastereoselectivity in the reaction of aldehydes R^2CHO with the enolates **2** and **10**

R^1	R^2	Products from *E*-enolate		Products from *Z*-enolate	
		Ratio **11**:**12**	Yield (%)	Ratio **11**:**12**	Yield (%)
Me	Me	89:11	73	6:94	81
Me	Ph	94:6	90	9:91	79
Ph	Me	85:15[a]	81[a]	9:91	78
Ph	Ph	91:9	81	10:90	79

[a] Contaminated with *ca.* 4% of the diastereoisomer between C-2 and C-3.

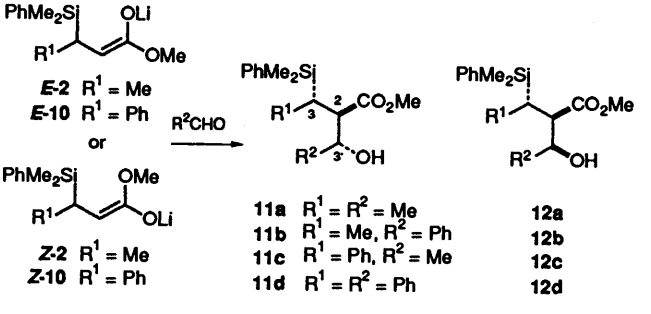


known from the work described in the preceding paper.[1] The relative stereochemistries of the other products were assumed by analogy. Although we had been scrupulous in the work described in the preceding paper to examine the complementary alkylations and protonations in virtually every case, that was not practical here, because the starting materials for the protonation protocol would have been considerably harder to make, and might not have reacted in the same way with the silyl-cuprate reagent. What we were able to do was to prepare the α,β-unsaturated ester **9** in two ways, and try to add to it various nucleophiles. To our surprise, this compound was extraordinarily unreactive towards the kinds of nucleophile that normally can be expected to add to α,β-unsaturated esters. The secondary amines dimethylamine, dibenzylamine and pyrrolidine did not react, nor did their lithium salts, nor did the sodium and potassium salts of methyl acetoacetate. The only reaction of this type that we were able to carry out was the addition of thiophenol,[12] which did give the diastereoisomer **4e** as the major product, although not with high diastereoselectivity (**3e**:**4e**, 33:67). The failure to add methyl acetoacetate and dimethylamine prevented our using this method to prepare selectively the minor diastereoisomers **4b** and **4c**, and



hence to support the stereochemical assignments in these reactions. The failure to add nucleophiles to the α,β-unsaturated ester may be a consequence of the presence of the silyl group, which, as a donor substituent, will make the enone system less electrophilic. Our attempts to follow up this idea, however, showed that a β-silyl group did not greatly affect the kinetic acidity of either esters[1] or ketones.[13]

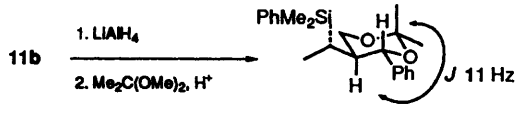
Having established that trigonal electrophiles are not intrinsically different from the electrophiles described in the preceding paper, we investigated the diastereoselectivity of the more complicated reactions when a third stereogenic centre is set up. We took the enolates *E*-and *Z*-**2**, and the enolates *E*- and *Z*-**10**, and treated each with acetaldehyde and benzaldehyde. The products were the β-hydroxy esters **11** and **12**, together, no



doubt, with minor amounts of the diastereoisomers that had the opposite stereochemical relationship between C-2 and C-3. We did not, in every case, separate and identify all four of the diastereoisomers that were produced in each of these reactions. What we were able to do was to separate a major product in each case, for we found that the diastereoselectivity was high not only between C-2 and C-3, as expected from the model reaction with formaldehyde described above, but also between C-2 and C-3′. The *E*-enolates, derived directly from conjugate addition of the silyl-cuprate, gave largely the diastereoisomers **11**, and the *Z*-enolates, derived from the saturated β-silyl esters with LDA, gave largely the diastereoisomers **12** (Table 3). The diastereoisomers with the alternative relative configuration between C-2 and C-3 were not detectable by ^1H NMR

spectroscopy, except in the case of the reaction of *E*-**10** with acetaldehyde, when about 4% of another isomer was detectable, presumably with the relationship corresponding to that in **11c** between C-2 and C-3′ but with the opposite relationship between C-2 and C-3.

We proved the relative stereochemistry in several ways, starting with the less predictable relationship, that between C-2 and C-3′. We reduced the esters **11b** and **12b** with lithium aluminium hydride, and made the acetonides **13** and **14** from



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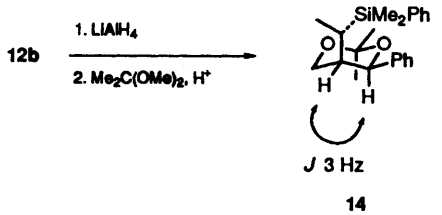

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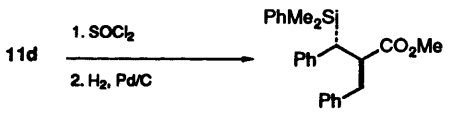

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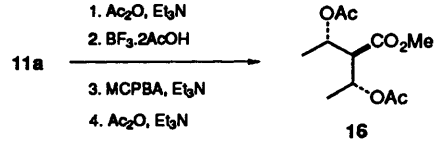
the diols. The coupling constants in the ^{1}H NMR spectra between the protons shown were diagnostic of the relationships. To prove the relative stereochemistry between C-2 and C-3, we converted the hydroxy group of the alcohol **11d** into a chloride, and hydrogenolysed the chloride to give the ester **15**, identical with the product from benzylation of the enolate *E*-**2**, described (as **23e**) in the preceding paper.[1] Finally, we could double check by relating the stereochemistry of C-3 to that of C-3′. Acetylation of the alcohol **11a**, conversion of the phenyldimethylsilyl group into a hydroxy with retention of configuration[14] and acetylation, gave the diacetate **16**, readily identified as a *meso* compound by its ^{1}H NMR spectrum, which showed one acetoxy singlet, one *C*-methyl doublet, one quintet for the protons adjacent to the acetoxy oxygen atoms and a perfect triplet for the proton adjacent to the methoxycarbonyl group. The same sequence carried out on the isomer **12a** gave the unsymmetrical diacetate **17**, easily identified in the ^{1}H



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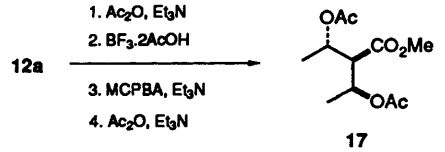

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NMR spectrum by the presence of two equally intense acetoxy singlets, of two *C*-methyl doublets, of two quintets for the protons adjacent to the acetoxy oxygen atoms, and of a double doublet for the proton adjacent to the methoxycarbonyl group.

The relative stereochemistry between C-2 and C-3′, *anti* in **11** and *syn* in **12**, is not that which is commonly found for the reactions of simple enolates with aldehydes, where the usual rule is expressed in the form 'that *Z*-enolates tend to give *syn* aldols.'[15] This rule must be inverted here, because we have adopted the strict Cahn–Ingold–Prelog rule, rather than the convention in which all enolates of the geometry called here *E* are called *Z*, as they would be if the metal were not lithium. This type of reaction is usually carried out with a small group at C-3 and a large group in place of the methoxy group of our methyl esters. In our case, the group at C-3 is large and the methoxy group is small, and this is known to reverse the usual pattern in those few cases that have been studied.[15,16] We have also found that the same kind of aldol reaction with a stannyl group in place of the silyl, although still showing enough diastereoselectivity for the synthesis of allylstannanes,[17] is not as highly diastereoselective for the formation of just one product.

Experimental

Methyl 3-Dimethyl(phenyl)silylbutanoate.—Methyl crotonate (10 mmol) in dry THF (10 cm^3) was added dropwise to the silyl-cuprate reagent[18] (12.5 mmol) under nitrogen at −78 °C and stirred for 3 h. The solution was allowed to warm to room temperature, quenched with aqueous ammonium chloride (25 cm^3) and extracted with ether (3 × 25 cm^3). The organic extracts were washed with aqueous ammonium chloride and with brine, dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography [SiO_2, light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] gave the *ester* (2.2 g, 95%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.42; ν_{max}(CDCl$_3$)/cm^{-1} 1730 (C=O) and 1580 (Ph); δ(CDCl$_3$) 7.55–7.31 (5 H, m, Ph), 3.62 (3 H, s, OMe), 2.39 (1 H, dd, *J* 15 and 4, C*H*$_A$H$_B$CO), 2.07 (1 H, dd, *J* 15 and 11, CH$_A$*H*$_B$CO), 1.43 (1 H, m, MeC*H*), 0.98 (3 H, d, *J* 7, *Me*CH) and 0.29 (6 H, s, $SiMe_2$); *m*/*z* 236 (5%, M$^+$), 221 (20, M − Me) and 135 (100, $PhMe_2Si$) (Found: M$^+$, 236.1228. $C_{13}H_{20}O_2Si$ requires *M*, 236.1233).

Treatment of the Enolate E-**2** *with Electrophiles.*—Typically, methyl crotonate (12 mmol) in dry THF (10 cm^3) was added dropwise to the silyl-cuprate reagent (15 mmol) under nitrogen at −78 °C, and stirred for 3 h. The electrophile was added at −78 °C, and the mixture stirred at room temperature for 30 min. Aqueous ammonium chloride (25 cm^3) was added and the mixture extracted with light petroleum (b.p. 60–80 °C) (4 × 25 cm^3). The combined organic extracts were washed with aqueous ammonium chloride and with brine, dried (Na_2SO_4) and evaporated under reduced pressure. The products were purified by flash chromatography [light petroleum (b.p. 60–80 °C)–EtOAc, 2:1].

Treatment of the Enolate Z-**2** *with Electrophiles.*—Typically, methyl 3-dimethyl(phenyl)silylbutanoate (12 mmol) in dry THF (5 cm^3) was added to a stirred solution of LDA, freshly prepared by the addition of butyllithium (1.6 mol dm^{-3} solution in hexane; 9.5 cm^3, 15 mmol), to diisopropylamine (2.1 cm^3, 15 mmol) in THF (50 cm^3) under nitrogen at −78 °C, and the solution stirred for 10 min. The electrophile was added and the mixture worked up as above. The following compounds were prepared by these routes.

Methyl (2RS,3SR)- *and* (2RS,3RS)-3-*dimethyl(phenyl)silyl*-2-*hydroxymethylbutanoate* (**3a** *and* **4a**). As an 89:11 mixture (78%) from the *E*-enolate, and (65%) as a 69:31 mixture from the *Z*-enolate, by blowing formaldehyde, produced by heating dry paraformaldehyde at 150 °C, over the surface of the reaction mixture for 20 min in a stream of dry nitrogen; R_f (light petroleum (b.p. 60–80 °C)–EtOAc, 5:1) 0.15; ν_{max}(CCl$_4$)/cm^{-1} 3400 (OH), 1725 (C=O) and 1580 (Ph); **3a**: δ(CDCl$_3$) 7.55–

7.30 (5 H, m, Ph), 3.90–3.75 (1 H, m, CH_AH_BOH), 3.65–3.50 (1 H, m, CH_AH_BOH), 3.56 (3 H, s, OMe), 2.70–2.60 (1 H, m, CHCO), 2.30 (1 H, br s, OH), 1.52 (1 H, dq, *J* 6 and 8, MeC*H*), 0.96 (3 H, d, *J* 8, *Me*CH), 0.33 (3 H, s, $SiMe_AMe_B$) and 0.31 (3 H, s, $SiMe_AMe_B$); with distinctive signals from **4a**: δ($CDCl_3$) 3.59 (3 H, s, OMe), 0.98 (3 H, d, *J* 8, *Me*CH), 0.32 (3 H, s, $SiMe_AMe_B$) and 0.30 (3 H, s, $SiMe_AMe_B$); *m/z* 266 (8%, M^+), 251 (7, M − Me), 235 (53, M − CH_2OH), 135 (83, $PhMe_2Si$) and 69 (100, C_4H_5O)(Found: M^+, 266.1342. $C_{14}H_{22}O_3Si$ requires *M*, 266.1339). The ratio **3a**:**4a** was measured by integration of the OMe signals in the ^1H NMR spectrum.

Methyl (2RS,1′SR)- *and* (2RS,1′RS)-2-[1-*dimethyl*(*phenyl*)*silylethyl*]-5-*oxohexanoate* **3b** *and* **4b**. As a 91:9 mixture (66%) from the silyl enone[3] **5** and the *E*-enolate, and as a 93:7 mixture (70%) from the *Z*-enolate; R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.19; ν_{max}(film)/cm^{-1} 1725 (ester C=O) and 1715 (ketone C=O); **3b**: δ($CDCl_3$) 7.55–7.30 (5 H, m, Ph), 3.51 (3 H, s, OMe), 2.50–2.20 (3 H, m, CHCO and CH_2CO), 2.05 (3 H, s, MeCO), 1.90–1.60 (2 H, m, CH_2CH_2CO), 1.37 (1 H, dq, *J* 8 and 7, MeC*H*), 0.95 (3 H, d, *J* 7.6, *Me*CH), 0.32 (3 H, s, $SiMe_AMe_B$) and 0.31 (3 H, s, $SiMe_AMe_B$); with distinctive signals from **4b**: δ($CDCl_3$) 3.55 (3 H, s, OMe) and 2.03 (3 H, s, MeCO); *m/z* 306 (5%, M^+), 291 (11, M − Me) and 135 (100, $PhMe_2Si$) (Found: M^+, 306.1663. $C_{17}H_{26}O_3Si$ requires *M*, 306.1652). The ratio **3b**:**4b** was measured by integration of the OMe signals in the ^1H NMR spectrum.

Methyl (2RS,1′SR)- *and* (2RS,1′RS)-3-*dimethyl*(*phenyl*)*silyl*-2-(N,N-*dimethylaminomethyl*)*butanoate* **3c** *and* **4c**. As an 82:18 mixture (43%) from dimethyl(methylene)ammonium iodide[4] and the *E*-enolate, and as an 87:13 mixture (51%) from the *Z*-enolate; R_f [light petroleum (b.p. 40–60 °C)–EtOAc 5:1] 0.07; ν_{max}(film)/cm^{-1} 1735 (C=O) and 1585 (Ph); **3c**: δ($CDCl_3$) 7.54–7.30 (5 H, m, Ph), 3.57 (3 H, s, OMe), 2.70–2.64 (2 H, m, CH_2N), 2.09 (6 H, s, NMe_2), 2.05–2.00 (1 H, m, CHCO), 1.39–1.20 (1 H, m, C*H*Me), 0.97 (3 H, d, *J* 8, CH*Me*), 0.33 (3 H, s, $SiMe_AMe_B$) and 0.31 (3 H, s, $SiMe_AMe_B$); with distinctive signals from **4c**; δ($CDCl_3$) 3.58 (3 H, s, OMe), 2.10 (6 H, s, NMe_2), 0.96 (3 H, d, *J* 8, CH*Me*), 0.32 (3 H, s, $SiMe_AMe_B$) and 0.29 (3 H, s, $SiMe_AMe_B$); *m/z* 293 (3%, M^+) and 58 (100, CH_2NMe_2) (Found: M^+, 293.1818. $C_{16}H_{27}NO_2Si$ requires *M*, 293.1811). The ratio **3c**:**4c** was measured by integration of the Me signals in the ^1H NMR spectrum.

(Z)-3-*Dimethyl*(*phenyl*)*silyl*-1-*methoxy*-1-*trimethylsilyloxybut*-1-*ene* Z-**7**.—Methyl crotonate (10 mmol) in dry THF was added dropwise to the silyl-cuprate reagent (12.5 mmol) under nitrogen at −78 °C and the mixture stirred for 3 h. Trimethylsilyl chloride (30 mmol) was added over 5 min and the mixture kept at room temperature for 1 h. It was then diluted with pentane (20 cm^3) filtered through Celite, and evaporated under reduced pressure, in the absence of moisture. Pentane (20 cm^3) was added to the residue and precipitated lithium chloride was filtered off. Evaporation under reduced pressure of the filtrate, followed (if necessary) by repeating the latter procedure to remove any remaining lithium chloride, gave the *silyl enol ether* (2.3 g, 75%); δ($CDCl_3$) 7.60–7.30 (5 H, m, Ph), 3.49 (3 H, s, OMe), 3.28 (1 H, d, *J* 10, CH=), 1.95 (1 H, dq, *J* 10 and 7, C*H*Me), 0.32 (3 H, s, $SiMe_AMe_B$), 0.29 (3 H, s, $SiMe_AMe_B$) and either 0.36 or 0.21 (9 H, s, $SiMe_3$) (with the uncertainty in the last signal being because there must be some silicon-containing by-product still present).

(E)-3-*Dimethyl*(*phenyl*)*silyl*-1-*methoxy*-1-*trimethylsilyloxybut*-1-*ene* E-**7**.—Methyl 3-dimethyl(phenyl)silylbutanoate (10 mmol) in dry THF was added dropwise to a stirred solution of lithium diisopropylamide (LDA), freshly prepared *in situ* by addition of butyllithium (1.6 mol dm^{-3} solution in hexane; 7.8 cm^3, 12.5 mmol) to diisopropylamine (1.75 cm^3, 12.5 mmol) in THF (50 cm^3) under nitrogen at −78 °C over 10 min, and the solution stirred for 10 min. Trimethylsilyl chloride (25 mmol) was added over 5 min to the mixture which was then worked up as described above to give the *silyl enol ether* (2.6 g, 95%); δ($CDCl_3$) 7.60–7.30 (5 H, m, Ph), 3.50 (1 H, d, *J* 11, CH=C), 3.40 (3 H, s, OMe), 1.95 (1 H, dq, *J* 11 and 7, C*H*Me), 0.96 (3 H, d, *J* 7, CH*Me*), 0.25 (6 H, s, $SiMe_2Ph$) and 0.20 (9 H, s, $SiMe_3$).

Methyl (2RS,1′RS)- *and* (2RS,1′RS)-3-*dimethyl*(*phenyl*)*silyl*-2-(N,N-*dimethylaminomethyl*)*butanoate* **3c** *and* **4c** *from the Silyl Enol Ethers*.—Dimethyl(methylene)ammonium iodide[4] (240 mg, 1.3 mmol) and the crude silyl enol ether (1 mmol) in dry dichloromethane (2 cm^3) was stirred at room temperature for 15 min. Dilute hydrochloric acid was added to the mixture which was then stirred for 5 min and then neutralised with dilute aqueous sodium hydroxide. The mixture was extracted with light petroleum (3 × 25 cm^3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and evaporated under reduced pressure. Preparative TLC (EtOAc) gave the dimethylamino esters as a 50:50 mixture (170 mg, 60%) from the *Z*-silyl enol ether, and as a 66:34 mixture (190 mg, 65%) from the *E*-silyl enol ether, otherwise identical (TLC, ^1H NMR) with the sample described above.

Methyl (2RS,3SR)- *and* (2RS,3RS)-3-*Dimethyl*(*phenyl*)*silyl*-2-*dithian*-2-*ylbutanoate* **3d** *and* **4d**.—1,3-Dithienium fluoroborate[6] (550 mg, 2.5 mmol) was added to a stirred solution of the crude silyl enol ether (2 mmol) in dry nitromethane (2 cm^3) at −78 °C. After being stirred for 10 min the mixture was evaporated under reduced pressure. Preparative TLC [light petroleum (b.p. 60–80 °C)–EtOAc 5:1] gave the *esters* as an 88:12 mixture (460 mg, 66%) from the *Z*-silyl enol ether, and as a 97:3 mixture (240 mg, 85%) from the *E*-silyl enol ether (0.8 mmol) R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.37; ν_{max}(film)/cm^{-1} 1730 (C=O) and 1585 (Ph); **3d**: δ($CDCl_3$) 7.62–7.25 (5 H, m, Ph), 3.95 (1 H, d, *J* 9, SCHS), 3.61 (3 H, s, OMe), 2.85–2.55 [5 H, m, $SCH_2CH_2CH_2S$ and CHCO], 2.07–1.75 (3 H, m, $SCH_2CH_2CH_2S$ and C*H*Me), 1.04 (3 H, d, *J* 8, CH*Me*), 0.34 (3 H, s, $SiMe_AMe_B$) and 0.28 (3 H, s, $SiMe_AMe_B$); with distinctive signals from **4d**: δ($CDCl_3$) 3.55 (3 H, s, OMe) and 1.03 (3 H, d, *J* 7, CH*Me*); *m/z* 354 (2%, M^+), 135 (57, $PhMe_2Si$) and 119 (100, $C_4H_7S_2$) (Found: M^+, 354.1140. $C_{17}H_{26}O_2SiS_2$ requires *M*, 354.1144). The ratio **3d**:**4d** was measured by integration of the *O*-Me and *C*-Me signals in the ^1H NMR spectrum.

Methyl (2RS,3SR)- *and* (2RS,3RS)-3-*Dimethyl*(*phenyl*)*silyl*-2-*phenylthiomethylbutanoate* **3e** *and* **4e**.—The crude silyl enol ether (5 mmol), powdered anhydrous zinc bromide (15 mg) and chloromethyl phenyl sulfide[8] (1.0 g, 6.5 mmol) were stirred in dichloromethane (10 cm^3) at room temperature for 5 h. The solvent was evaporated under reduced pressure, and the residue flash chromatographed [light petroleum (b.p. 60–80 °C)–EtOAc] to give the *esters* as an 82:18 mixture (1.15 g, 65%) from the *Z*-silyl enol ether, and as an 88:12 mixture (1.30 g, 73%) from the *E*-silyl enol ether; R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.39; ν_{max}(film)/cm^{-1} 1730 (C=O) and 1600 (Ph); **3e**: δ($CDCl_3$) 7.50–7.20 (10 H, m, SiPh and SPh), 3.57 (3 H, s, OMe), 3.10 (1 H, dd, *J* 11 and 13, CH_AH_BSPh), 2.87–2.71 (2 H, m, CH_AH_BSPh and $CHCH_2SPh$), 1.43 (1 H, dq, *J* 5 and 7, MeC*H*), 1.01 (3 H, d, *J* 7, *Me*CH), 0.25 (3 H, s, $SiMe_AMe_B$) and 0.24 (3 H, s, $SiMe_AMe_B$); with a signal from **4e**: δ($CDCl_3$) 3.58 (3 H, s, OMe); *m/z* 358 (7%, M^+), 343 (10, M − Me), 281 (18, M − Ph), and 135 (100, $PhMe_2Si$)(Found: M^+, 358.1421. $C_{20}H_{26}O_2SiS$ requires *M*, 358.1422). The ratio **3e**:**4e** was measured by integration of the OMe signal in the ^1H NMR spectrum.

Methyl (2RS,3SR)- *and* (2RS,3RS)-3-*Dimethyl(phenyl)silyl*-2-*methoxymethylbutanoate* **3f** *and* **4f**.—The crude silyl enol ether (1.8 mmol), powdered anhydrous zinc bromide (5 mg) and chloromethyl methyl ether (160 mg, 2 mmol) were stirred in dichloromethane (5 cm^3) at room temperature for 30 min. The solvent was evaporated under reduced pressure, and the residue flash chromatographed [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] to give the *esters* as a 90:10 mixture (420 mg, 83%) from the *Z*-silyl enol ether, and as a 91:9 mixture (420 mg, 79%) from the *E*-silyl enol ether (1.9 mmol); R_f (light petroleum–EtOAc 5:1) 0.32; ν_{max}(film)/cm^{-1} 1735 (C=O) and 1585 (Ph); **3f**: δ($CDCl_3$) 7.54–7.33 (5 H, m, Ph), 3.59 (1 H, dd, *J* 9 and 2, CH_AH_BOMe), 3.57 (3 H, s, CO_2Me), 3.37 (1 H, dd, *J* 9 and 5, CH_AH_BOMe), 3.24 (3 H, s, CH_2OMe), 2.74 (1 H, dq, *J* 2 and 5, CHCO), 1.42 (1 H, dq, *J* 5 and 8, C*H*Me), 0.97 (3 H, d, *J* 8, CH*Me*), 0.33 (3 H, s, $SiMe_AMe_B$) and 0.32 (3 H, s, $SiMe_AMe_B$); with distinctive signals from **4f**: δ($CDCl_3$) 3.54 (3 H, s, CO_2Me), 3.21 (3 H, s, CH_2OMe) and 0.98 (3 H, d, *J* 7, CH*Me*); *m*/*z* 280 (6%, M^+), 265 (25, M − Me), 235 (82, M − $MeOCH_2$) and 135 (100, $PhMe_2Si$) (Found: M^+, 280.1488. $C_{15}H_{24}O_3Si$ requires *M*, 280.1495). The ratio **3d**:**4d** was measured by integration of *O*-Me and *C*-Me signals in the ^1H NMR spectrum.

Methyl (2RS,3SR)- *and* (2RS,3RS)-3-*Dimethyl(phenyl)silyl*-2-(2-*methoxyallylbutanoate* **3g** *and* **4g**.—The crude *Z*-silyl ketene acetal (2 mmol) in dichloromethane (5 cm^3) was immediately added to a mixture of titanium tetrachloride (0.1 mmol) and 2,2-dimethoxypropane (2.0 mmol) in dichloromethane (4 cm^3) and stirred at −78 °C under nitrogen for 3 h. The mixture was diluted with water and extracted with ether (3 × 25 cm^3) and the combined organic extracts were evaporated under reduced pressure. Preparative TLC (CH_2Cl_2) gave the *esters* as a 63:37 mixture (490 mg, 80%) from the *Z*-silyl enol ether, and as a 67:33 mixture (450 mg, 75%) from the *E*-silyl enol ether; R_f [light petroleum (b.p. 60–80 °C)–EtOAc 5:1] 0.39; ν_{max}(film)/cm^{-1} 1730 (C=O); **3g**: δ($CDCl_3$) 7.56–7.31 (5 H, m, Ph), 3.35 (3 H, s, CO_2Me), 3.12 (3 H, s, Me_2COMe), 2.66 (1 H, d, *J* 11, CHCO), 1.53 (1 H, dq, *J* 11 and 8, C*H*Me), 1.31 (3 H, s, CMe_AMe_B), 1.13 (3 H, s, CMe_AMe_B), 1.07 (3 H, d, *J* 8, C*H*Me), 0.28 (3 H, s, $SiMe_AMe_B$) and 0.27 (3 H, s, $SiMe_AMe_B$); with distinctive signals from **4g**: δ($CDCl_3$) 3.55 (3 H, s, CO_2Me), 2.97 (3 H, s, Me_2COMe), 2.78 (1 H, d, *J* 2, CHCO), 1.37 (1 H, dq, *J* 2 and 8, C*H*Me), 1.18 (3 H, s, CMe_AMe_B), 1.16 (3 H, s, CMe_AMe_B), 1.02 (3 H, d, *J* 8, CH*Me*), 0.30 (3 H, s, $SiMe_AMe_B$) and 0.29 (3 H, s, $SiMe_AMe_B$); *m*/*z* 262 (1%, M − C_2H_6O), 135 (68, $PhMe_2Si$) and 73 (100, Me_2COMe) (Found: $M^+ - C_2H_6O$, 262.1384. $C_{17}H_{28}O_3Si$ requires *M* − C_2H_6O, 262.1389). The ratio **3g**:**4g** was measured by integration of the *O*-Me and *C*-Me signals in the ^1H NMR spectrum.

Raney Nickel Reduction of the Sulfides **3e** *and* **4e**.—A slurry of W-2 Raney nickel[11] (*ca.* 1.5 g) in ethanol was added to the mixture of sulfides (360 mg, 1 mmol) in ethanol (5 cm^3) and the mixture vigorously stirred at room temperature for 2 h. Dichloromethane was added and the nickel cautiously removed by filtration through Celite. Evaporation of the filtrate under reduced pressure followed by preparative TLC [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] gave a mixture of the methyl esters (91% from the 87:13 mixture, 92% from the 82:18 mixture), identical (R_f, ^1H NMR) with an authentic sample described (as **19b**) in the preceding paper.[1] The ratios **3e**:**4e** were measured by integration of the OMe signals in the ^1H NMR spectra, and was identical with the ratio of the starting mixture of sulfides in both cases.

Raney Nickel Reduction of the Dithianyl Esters **3d** *and* **4d**.—The dithians were reduced similarly to give the same pair of diastereoisomeric methyl esters in the same ratios as the starting dithians.

Methyl 2-[1-*Dimethyl(phenyl)silylethyl*]*prop*-2-*enoate* **9**.—*Method A: by dehydration of the alcohols* **3**. The mixture of β-hydroxy esters **3** (1.6 g, 6 mmol), methanesulfonyl chloride (800 mg, 7 mmol) and triethylamine (710 mg, 7 mmol) were mixed in dichloromethane (10 cm^3) at 0 °C, and the mixture then stirred at room temperature for 6 h. Dilute hydrochloric acid was added and the mixture extracted with dichloromethane (4 × 15 cm^3). The combined organic extracts were washed with brine, dried (Na_2SO_4), and the solvent removed under reduced pressure to give the mesylate in quantitative yield. The mesylate was refluxed in pyridine (15 cm^3) for 16 h after which an excess of dilute hydrochloric acid was added and the mixture was extracted with light petroleum (b.p. 60–80 °C) (4 × 25 cm^3). The combined organic extracts were washed with dilute hydrochloric acid and with brine, dried (Na_2SO_4), and evaporated under reduced pressure. Flash chromatography [light petroleum (b.p. 60–80 °C)–EtOAc] gave the acrylate (1.25 g, 72%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.44; ν_{max}(film)/cm^{-1} 1720 (C=O), 1615 (C=C) and 1585 (Ph); δ($CDCl_3$) 7.58–7.27 (5 H, m, Ph), 6.10 (1 H, d, *J* 1, $C{=}CH_AH_B$), 5.21 (1 H, dd, *J* 1 and 1.5, $C{=}CH_AH_B$), 3.60 (3 H, s, OMe), 2.60 (1 H, dq, *J* 1.5 and 7.5, C*H*Me), 1.15 (3 H, d, *J* 7.5, CH*Me*), 0.30 (3 H, s, $SiMe_AMe_B$) and 0.28 (3 H, s, $SiMe_AMe_B$); *m*/*z* 248 (6%, M^+), 233 (42, M − Me) and 135 (100, $PhMe_2Si$) (Found: M^+, 248.1225. $C_{14}H_{20}O_2Si$ requires *M*, 248.1233).

Method B: by oxidative removal of the phenylthio groups from the sulfides **3**. The mixture of sulfides **3e** and **4e** (2.5 g, 7 mmol) and sodium metaperiodate (1.5 g, 7 mmol) were stirred at room temperature in the dark in methanol (70 cm^3) and water (10 cm^3) for 20 h. The mixture was diluted with dichloromethane (100 cm^3) and then poured into water (10 cm^3). The aqueous layer was extracted with dichloromethane (3 × 50 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure. Flash chromatography (EtOAc) gave the sulfoxide (2.1 g, 80%) as a mixture of diastereoisomers; R_f [light petroleum (b.p. 60–80 °C–EtOAc, 1:1] 0.38. The sulfoxide was kept in the dark at 65 °C in carbon tetrachloride (4.5 cm^3) and chloroform (0.5 cm^3) for 4 d. A similar work-up to that above gave the acrylate **9** (900 mg, 65%), identical (R_f, ^1H NMR) with the sample prepared by way of the mesylate.

Addition of Thiophenol to the Acrylate **9**.—Thiophenol (110 mg, 1 mmol), the acrylate **9** (130 mg, 0.5 mmol) and tetrabutylammonium fluoride (25 mg, 0.1 mmol) were stirred at room temp. in THF (1 cm^3) under nitrogen for 20 h. The solvent was removed under reduced pressure and the residue purified by preparative TLC [light petroleum (b.p. 60–80 °C)–EtOAc 5:1] to give the mixture of phenylthiomethyl esters **3e** and **4e** (110 mg, 60%) identical (R_f, ^1H NMR) with the sample described above, in a ratio **3e**:**4e** of 33:67.

Aldol Reactions using the Enolates E-**2** *and* E-**10**.—Typically, methyl crotonate or methyl cinnamate (2 mmol) in dry THF (5 cm^3) was added dropwise to the stirred silyl-cuprate reagent (2.5 mmol) under nitrogen at −78 °C, and stirring continued for 3 h. A solution of acetaldehyde or benzaldehyde (2.5 mmol) in dry THF (5 cm^3) was added, to the mixture, which was then stirred for a further 2 h at −78 °C. Aqueous ammonium chloride (20 cm^3) was added to the mixture, which was then extracted with ether (3 × 30 cm^3). The combined organic extracts were washed with aqueous ammonium chloride and with brine, dried ($MgSO_4$) and evaporated under reduced pressure. Flash chromatography (hexane–EtOAc) gave the products **11**.

Methyl (2RS,3SR)-3-*dimethyl(phenyl)silyl*-2-[(RS)-1-*hydroxyethyl*]*butanoate* **11a** (73%). R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.60; $\nu_{max}(CCl_4)/cm^{-1}$ 3500 (OH), 1720 (C=O) and 1580 (Ph); $\delta(CDCl_3)$ 7.51–7.33 (5 H, m, Ph), 4.01 (1 H, dq, *J* 3 and 6, C*H*OH), 3.39 (3 H, s, OMe), 2.54 (1 H, br s, OH), 2.29 (1 H, dd, *J* 3 and 10, CHCO), 1.59 (1 H, dq, *J* 10 and 7, CHSi), 1.12 (3 H, d, *J* 6, *Me*CHOH), 1.07 (3 H, d, *J* 7, *Me*CHSi), 0.30 (3 H, s, Si*Me*$_A$Me$_B$) and 0.26 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 235 (28%, M − C_2H_5O), 135 (65, $PhMe_2Si$) and 69 (100, C_4H_5O) (Found: $M^+ - C_2H_5O$, 235.1154. $C_{15}H_{24}O_3Si$ requires *M* − C_2H_5O, 235.1155).

Methyl (2RS,3SR)-3-*dimethyl(phenyl)silyl*-2-[(SR)-1-*hydroxybenzyl*]*butanoate* **11b** (90%). R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.13; ν_{max}(film)/cm^{-1} 3500 (OH), 1740, 1720 (C=O) and 1610, 1590 and 1500 (Ph); $\delta(CDCl_3)$ 7.62–7.12 (10 H, m, Ph), 4.97 (1 H, d, *J* 4, C*H*OH), 3.60 (1 H, br s, OH), 3.15 (3 H, s, OMe), 2.67 (1 H, dd, *J* 4 and 9, CHCO), 1.59 (1 H, dq, *J* 9 and 7, CHSi), 1.17 (1 H, d, *J* 7, *Me* CHSi), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.28 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 281 (1%, M − $C_2H_5O_2$) and 135 (100, $PhMe_2Si$) (Found: $M^+ - C_2H_5O_2$, 281.1367. $C_{20}H_{26}O_3Si$ requires *M* − $C_2H_5O_2$, 281.1362).

Methyl (2RS,3RS)-2-[(RS)-1-*dimethyl(phenyl)silyl*]*benzyl*-3-*hydroxybutanoate* **11c** (83%). R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 3:1] 0.68; ν_{max}(film)/cm^{-1} 3480 (OH), 1730 (C=O) and 1600, 1580 and 1500 (Ph); $\delta(CDCl_3)$ 7.45–6.97 (10 H, m, Ph), 3.57 (1 H, m, C*H*OH), 3.33 (3 H, s, OMe), 3.03 (1 H, d, *J* 13, C*H*SiMe$_2$Ph), 2.92 (1 H, dd, *J* 2 and 13, CHCO), 2.60 (1 H, d, *J* 10, OH), 1.03 (3 H, d, *J* 7, *Me*CHOH), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.07 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 327 (2%, M − Me), 297 (47, M − C_2H_5O), 135 (50, $PhMe_2Si$) and 131 (100, C_9H_7O) (Found: M^+ − Me, 327.1417. $C_{20}H_{26}O_3Si$ requires *M* − Me, 327.1417).

Methyl (2RS,3RS)-3-*dimethyl(phenyl)silyl*-2-[(SR)-1-*hydroxybenzyl*]-3-*phenylpropanoate* **11d** (81%). As cubes, m.p. 115.5–116.5 °C (from hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3500 (OH), 1720 (C=O) and 1600 (Ph); $\delta(CDCl_3)$ 7.42–7.09 (15 H, m, Ph), 4.55 (1 H, d, *J* 3, C*H*OH), 3.70 (1 H, br s, OH), 3.26 (1 H, dd, *J* 3 and 13, CHCO), 3.12 (1 H, d, *J* 13, CHSi), 3.04 (3 H, s, OMe), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.07 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 297 (25%, M − C_7H_7O), 135 (52, $PhMe_2Si$) and 131 (100, C_9H_7O) (Found: C, 74.5; H, 7.1. $C_{25}H_{28}O_3Si$ requires C, 74.2; H, 7.0%).

Aldol Reactions using the Enolates Z-**2** *and* Z-**10**.—Typically, methyl 3-dimethyl(phenyl)silylbutanoate or methyl 3-dimethyl(phenyl)silyl-3-phenylpropanoate[19] (2 mmol) in dry THF (5 cm^3) was added dropwise to a stirred solution of LDA, freshly prepared by the addition of butyllithium (1.6 mol dm^{-3} solution in hexane; 1.6 cm^3, 2.5 mmol) to diisopropylamine (0.35 cm^3, 2.5 mmol) in THF (10 cm^3) under nitrogen at −78 °C over 10 min, and the solution stirred for 10 min. Acetaldehyde or benzaldehyde (265 mg, 2.5 mmol) in dry THF (5 cm^3) was added to the mixture which was then stirred for a further 2 h at −78 °C. Work-up as in the aldol reactions described above gave the products **12**.

Methyl (2RS,3SR)-3-*dimethyl(phenyl)silyl*-2-[(SR)-1-*hydroxyethyl*]*butanoate* **12a** (81%). R_f[light petroleum (b.p. 60–80 °C)–EtOAc, 2:1] 0.38; ν_{max}(film)/cm^{-1} 3450 (OH) and 1725 (C=O); $\delta(CDCl_3)$ 7.56–7.30 (5 H, m, Ph), 4.01 (1 H, quintet, *J* 6, C*H*OH), 3.52 (3 H, s, OMe), 2.58 (1 H, dd, *J* 6 and 7, CHCO), 1.64 (1 H, br s, OH), 1.49 (1 H, quintet, *J* 7, CHSi), 1.15 (3 H, d, *J* 6, *Me*CHOH), 1.01 (3 H, d, *J* 7, *Me*CHSi), 0.31 (3 H, s, Si*Me*$_A$Me$_B$) and 0.30 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 265 (1%, M − Me), 235 (22, M − C_2H_5O), 135 (50, $PhMe_2Si$) and 69 (100, C_4H_5O) (Found: M^+ − Me, 265.1265. $C_{15}H_{24}O_3Si$ requires *M* − Me, 265.1260).

Methyl (2RS,3SR)-3-*dimethyl(phenyl)silyl*-2-[(RS)-1-*hydroxybenzyl*]*butanoate* **12b** (79%). R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.18; ν_{max}(film)/cm^{-1} 3500 (OH), 1725 (C=O) and 1495 (Ph); $\delta(CDCl_3)$ 7.64–7.18 (10 H, m, Ph), 4.76 (1 H, d, *J* 10, C*H*OH), 3.33 (3 H, s, OMe), 2.90 (1 H, dd, *J* 4 and 10, CHCO), 1.83 (1 H, br s, OH), 1.65 (1 H, dq, *J* 4 and 8, CHSi), 1.14 (3 H, d, *J* 8, *Me*CHSi), 0.42 (3 H, s, Si*Me*$_A$Me$_B$) and 0.36 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 281 (6%, M − $C_2H_5O_2$) and 135 (100, $SiMe_2Ph$) (Found: $M^+ - C_2H_5O_2$, 281.1370. $C_{20}H_{26}O_3Si$ requires *M* − $C_2H_5O_2$, 281.1362).

Methyl (2RS,3SR)-2-[(RS)-1-*Dimethyl(phenyl)silylbenzyl*]-3-*hydroxybutanoate* **12c** (78%). R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 3:1] 0.62; ν_{max}(film)/cm^{-1} 3480 (OH), 1730 (C=O) and 1600, 1580 and 1500 (Ph); $\delta(CDCl_3)$ 7.38–6.89 (10 H, m, Ph), 3.81 (1 H, dq, *J* 5 and 6, C*H*OH), 3.42 (3 H, s, OMe), 3.28 (1 H, dd, *J* 5 and 12, CHCO), 2.69 (1 H, d, *J* 12, CHSi), 1.90 (1 H, br s, OH), 1.02 (3 H, d, *J* 6, *Me*CHOH), 0.21 (3 H, s, Si*Me*$_A$Me$_B$) and 0.13 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 327 (2%, M − Me), 297 (27, M − C_2H_5O), 135 (40, $PhMe_2Si$) and 131 (100, C_9H_7O) (Found: M^+ − Me, 327.1412. $C_{20}H_{26}O_3Si$ requires *M* − Me, 327.1417).

Methyl 2-(2RS,3RS)-3-*Dimethyl(phenyl)silyl*-2-[(RS)-1-*hydroxybenzyl*]-3-*phenylpropanoate* **12d** (79%). R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.12; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3500 (OH), 1730 (C=O) and 1600 (Ph); $\delta(CDCl_3)$ 7.41–6.97 (15 H, m, Ph), 4.85 (1 H, d, *J* 5, C*H*OH), 3.47 (1 H, dd, *J* 5 and 11, CHCO), 3.22 (3 H, s, OMe), 2.78 (1 H, d, *J* 11, CHSi), 2.44 (1 H, br s, OH), 0.24 (3 H, s, Si*Me*$_A$Me$_B$) and 0.14 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 297 (24%, M − C_7H_7O), 135 (55, $PhMe_2Si$) and 131 (100, C_9H_7O) (Found: $M^+ - C_7H_7O$, 297.1322. $C_{25}H_{28}O_3Si$ requires *M* − C_7H_7O, 297.1310).

(2RS,3RS)-3-*Dimethyl(phenyl)silyl*-2-[(RS)-1-*hydroxybenzyl*]*butan*-1-*ol*.—The hydroxy ester **11b** (140 mg, 0.4 mmol) in ether (3 cm^3) was stirred with a suspension of lithium aluminium hydride (40 mg) in ether at 0 °C for 3 h. Dilute hydrochloric acid was added to the mixture which was then extracted with ether (5 × 10 cm^3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. Flash chromatography (hexane–EtOAc) gave the *diol* (94%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.08; ν_{max}(film)/cm^{-1} 3600 (OH) and 3400 (OH); $\delta(CDCl_3)$ 7.53–7.22 (10 H, m, Ph), 4.78 (1 H, d, *J* 6, PhC*H*OH), 3.76–3.59 (2 H, m, CH_2OH), 2.73 (2 H, br s, OH), 1.85 (1 H, m, C*H*CH$_2$OH), 1.19 (1 H, dq, *J* 5 and 6, CHSi), 1.13 (3 H, d, *J* 6, *Me*CHSi), 0.36 (3 H, s, Si*Me*$_A$Me$_B$) and 0.31 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 219 (7%, M − Ph − H_2O) and 135 (100, $PhMe_2Si$) (Found: $M^+ - C_6H_7O$, 219.1208. $C_{19}H_{26}O_2Si$ requires *M* − C_6H_7O, 219.1205).

(2RS,3RS)-3-*Dimethyl(phenyl)silyl*-2-[(SR)-1-*hydroxybenzyl*]*butan*-1-*ol*.—The hydroxy ester **12b** was similarly reduced to give the *diol* (110 mg, 86%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.09; ν_{max}(film)/cm^{-1} 3600 (OH) and 3400 (OH); $\delta(CDCl_3)$ 7.58–7.21 (10 H, m, Ph), 5.55 (1 H, d, *J* 8, PhC*H*OH), 3.41 (1 H, dd, *J* 5 and 11, C*H*$_A$H$_B$OH), 3.31 (1 H, dd, *J* 6 and 11, CH$_A$*H*$_B$OH), 2.10 (1 H, m, C*H*CH$_2$OH), 1.43 (1 H, dq, *J* 4 and 7, CHSi), 1.12 (3 H, d, *J* 7, *Me*CHSi), 0.39 (3 H, s, Si*Me*$_A$Me$_B$) and 0.35 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* 219 (16%, M − Ph − H_2O) and 135 (100, $PhMe_2Si$) (Found: $M^+ - C_6H_7O$, 219.1211. $C_{19}H_{26}O_2Si$ requires *M* − C_6H_7O, 219.1205).

(3RS,4RS)-4-[(RS)-1-*dimethyl(phenyl)silylethyl*]-1,1-*dimethyl*-3-*phenyl*-2,4-*dioxane* **13**.—The (2*RS*,3*RS*,1′*RS*)-diol (20 mg, 0.064 mmol), 2,2-dimethoxypropane (50 mg) and toluene-*p*-sulfonic acid (5 mg) were stirred at room temperature in dimethylformamide (5 cm^3) for 3 h. The mixture was diluted with ether (30 cm^3), washed with water (4 × 10 cm^3) and brine, dried ($MgSO_4$) and evaporated under reduced pressure. Flash

chromatography (hexane–EtOAc) gave the *acetonide* (15 mg, 67%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.42; ν_{max}(film)/cm^{-1} 3000–2900 (CH); δ($CDCl_3$) 7.54–7.25 (10 H, m, Ph), 4.37 (1 H, d, *J* 11, PhC*H*O), 3.95 (1 H, t, *J* 11, CH_AH_BO), 3.88 (1 H, dd, *J* 5 and 11, CH$_A$$H_B$O), 2.12 (1 H, ddt, *J* 2, 5 and 11, C*H*CH$_2$O), 1.37 (3 H, s, CMe_AMe$_B$), 1.30 (3 H, s, CMe$_A$$Me_B$), 0.92 (3 H, d, *J* 8, *Me*CHSi), 0.79 (1 H, dq, *J* 2 and 8, CHSi), 0.35 (3 H, s, SiMe_AMe$_B$) and 0.19 (3 H, s, SiMe$_A$$Me_B$); *m/z* 281 (3%, M − C_4H_9O) and 135 (100, PhMe$_2$Si) (Found: M$^+$ − C_4H_9O, 281.1367. $C_{22}H_{30}O_2Si$ requires *M* − C_4H_9O, 281.1362).

(3RS,4SR)-1,1-*Dimethyl*-4-[(SR)-1-*dimethyl*(*phenyl*)*silyl*-*ethyl*]-3-*phenyl*-2,4-*dioxane* **14**.—The (2*RS*,3*RS*,1′*SR*)-diol was treated similarly to give the *acetonide* (15 mg, 67%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.48; ν_{max}(film)/cm^{-1} 3000–2900 (CH); δ($CDCl_3$) 7.46–7.17 (10 H, m, Ph), 5.21 (1 H, d, *J* 3, PhC*H*O), 4.09 (1 H, dd, *J* 3 and 12, CH_AH_BO), 3.76 (1 H, dd, *J* 2 and 12, CH$_A$$H_B$O), 1.85 (1 H, m, C*H*CH$_2$O), 1.52 (3 H, s, C$Me_AMe_B$), 1.49 (3 H, s, CMe$_A$$Me_B$), 1.41 (1 H, quintet, *J* 7, CHSi), 0.49 (3 H, d, *J* 7, *Me*CHSi), 0.29 (3 H, s, SiMe_AMe$_B$) and 0.26 (3 H, s, SiMe$_A$$Me_B$); *m/z* 281 (2%, M − C_4H_9O) and 135 (100, PhMe$_2$Si) (Found: M$^+$ − C_4H_9O, 281.1381. $C_{22}H_{30}O_2Si$ requires *M* − C_4H_9O, 281.1362).

Methyl (2RS,3RS)-3-*Chloro*-2-[(RS)-1-*dimethyl*(*phenyl*)*silyl*-*benzyl*]-3-*phenylpropanoate*.—The β-hydroxy ester **11d**, thionyl chloride (45 mg, 0.45 mmol) and triethylamine (62 l, 0.45 mmol) were stirred in dichloromethane (5 cm^3) at room temp. for 1 h. The mixture was then diluted with ether (15 cm^3), washed with dilute hydrochloric acid and brine, dried ($MgSO_4$) and evaporated under reduced pressure. Flash chromatography (hexane–EtOAc) gave the *chloride* (151 mg, 72%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 2:1] 0.49; ν_{max}($CDCl_3$)/cm^{-1} 1725 (C=O) and 1600 (Ph); δ($CDCl_3$) 7.62–6.92 (15 H, m, Ph), 4.86 (1 H, d, *J* 5, CHCl), 3.39 (1 H, dd, *J* 5 and 11, CHCO), 3.28 (3 H, s, OMe), 3.00 (1 H, d, *J* 11, CHSi), 0.24 (3 H, s, SiMe_AMe$_B$) and 0.12 (3 H, s, SiMe$_A$$Me_B$); *m/z* 407 (7%, M − Me), 386 (4, M − HCl) and 297 (100, M − C_7H_6Cl) (Found: M$^+$ − Me, 407.1242. $C_{25}H_{27}ClO_2Si$ requires *M* − Me, 407.1234).

Methyl (2RS,3RS)-2-*Benzyl*-3-*dimethyl*(*phenyl*)*silyl*-3-*phenylpropanoate* **15**.—The chloride (50 mg, 0.10 mmol) was stirred in methanol (10 cm^3) with 10% palladium on charcoal under a hydrogen atmosphere at 45 p.s.i. for 5 h. The mixture was filtered through Celite and evaporated under reduced pressure. Flash chromatography (hexane–EtOAc) gave the ester (42 mg, 92%) identical (R_f, ^{1}H NMR) with an authentic sample.[1]

Methyl (2RS,3SR)-2-[(RS)-1-*Acetoxyethyl*]-3-*dimethyl*-(*phenyl*)*silylbutanoate*.—The hydroxy ester **11a** (440 mg, 1.57 mmol), acetic anhydride (0.19 cm^3, 2 mmol), triethylamine (0.28 cm^3, 2 mmol) and dimethylaminopyridine (5 mg) were stirred in dichloromethane (10 cm^3) at room temp. for 2 h. The mixture was washed with dilute hydrochloric acid and brine, dried ($MgSO_4$) and evaporated under reduced pressure. Flash chromatography (hexane–EtOAc) gave the *acetoxy ester* (425 mg, 84%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.66; ν_{max}(film)/cm^{-1} 1730 (C=O); δ($CDCl_3$) 7.52–7.32 (5 H, m, Ph), 5.12 (1 H, quintet, *J* 6, C*H*OAc), 3.49 (3 H, s, OMe), 2.47 (1 H, dd, *J* 6 and 8, CHCO), 2.00 (3 H, s, OAc), 1.45 (1 H, quintet, *J* 8, CHSi), 1.19 (3 H, d, *J* 6, *Me*CHOAc), 0.97 (3 H, d, *J* 8, *Me*CHSi), 0.31 (3 H, s, SiMe_AMe$_B$) and 0.28 (3 H, s, SiMe$_A$$Me_B$); *m/z* 307 (2%, M − Me), 235 (38, M − $C_4H_7O_2$) and 135 (100, PhMe$_2$Si) (Found: M$^+$ − Me, 307.1356. $C_{17}H_{26}O_4Si$ requires *M* − Me, 307.1365).

Methyl (2RS,3SR)-2-[(SR)-1-*Acetoxyethyl*]-3-*dimethyl*-(*phenyl*)*silylbutanoate*.—The hydroxy ester **12a** (440 mg, 1.57 mmol) was treated similarly to give the *acetoxy ester* (390 mg, 77%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.71; ν_{max}($CDCl_3$)/cm^{-1} 1725 (C=O); δ($CDCl_3$) 7.49–7.30 (5 H, m, Ph), 5.17 (1 H, quintet, *J* 6, C*H*OAc), 3.43 (3 H, s, OMe), 2.74 (1 H, dd, *J* 6 and 10, CHCO), 1.99 (3 H, s, OAc), 1.40 (1 H, dq, *J* 10 and 8, CHSi), 1.25 (3 H, d, *J* 6, *Me*CHOAc), 0.98 (3 H, d, *J* 8, *Me*CHSi), 0.28 (3 H, s, SiMe_AMe$_B$) and 0.26 (3 H, s, SiMe$_A$$Me_B$); *m/z* 307 (2%, M − Me), 235 (40, M − $C_4H_7O_2$), 135 (77, PhMe$_2$Si) and 69 (100, C_4H_5O) (Found: M$^+$ − Me, 307.1369. $C_{17}H_{26}O_4Si$ requires *M* − Me, 307.1365).

Methyl (2RS,3RS)-3-*Acetoxy*-2-[(SR)-1-*hydroxyethyl*]-*butanoate*.—The (2*RS*,3*SR*,1′*RS*)-acetate (300 mg, 0.93 mmol) and boron trifluoride–acetic acid complex (0.15 cm^3, 1.1 mmol) were stirred in dichloromethane (10 cm^3) under nitrogen at room temperature for 2 h. Saturated aqueous sodium hydrogencarbonate (5 cm^3) was added to the mixture and stirring continued for 10 min. The mixture was then extracted with ether (3 × 20 cm^3) and the organic extracts were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure to give the fluoro(dimethyl)silyl butanoate (240 mg). This was stirred with triethylamine (0.14 cm^3, 1 mmol) and *m*-chloroperbenzoic acid (560 mg, 3.3 mmol) in ether (10 cm^3) under nitrogen at room temperature for 1.5 h. The mixture was then diluted with ether (20 cm^3), washed successively with saturated aqueous sodium bisulfite, aqueous, sodium hydrogen carbonate and brine, dried ($MgSO_4$) and evaporated under reduced pressure. Preparative TLC (hexane–EtOAc, 1:1) of the residue gave the *hydroxy ester* (62%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.24; ν_{max}($CDCl_3$)/cm^{-1} 3500 (OH) and 1725 (C=O); δ($CDCl_3$) 5.29 (1 H, dq, *J* 8 and 6, C*H*OAc), 4.01 (1 H, dq, *J* 5 and 6, C*H*OH), 3.73 (3 H, s, OMe), 2.54 (1 H, dd, *J* 5 and 8, CHCO), 2.00 (3 H, s, OAc), 1.33 (3 H, d, *J* 6, *Me*CHOAc) and 1.24 (3 H, d, *J* 6, *Me*CHOH); *m/z* 204 (1%, M$^+$), 187 (9, M − OH), 173 (14, M − OMe), 101 (85, $C_5H_9O_2$) and 100 ($C_5H_8O_2$) (Found: M$^+$, 204.1016. $C_9H_{16}O_5$ requires *M*, 204.9998).

Methyl (2RS,3SR)-3-*Acetoxy*-2-[(SR)-1-*hydroxyethyl*]-*butanoate*.—The (2*RS*,3*SR*,1′*SR*)-acetate was treated similarly to give the *hydroxy ester* (54%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.27; ν_{max}(CH_2Cl_2)/cm^{-1} 3500 (OH) and 1725 (C=O); δ($CDCl_3$) 5.25 (1 H, dq, *J* 9 and 6, C*H*OAc), 3.98 (1 H, dq, *J* 4 and 6, C*H*OH), 3.74 (3 H, s, OMe), 2.61 (1 H, dd, *J* 4 and 9, CHCO), 2.06 (3 H, s, OAc), 1.25 (3 H, d, *J* 5, *Me*CHOAc) and 1.23 (3 H, d, *J* 6, *Me*CHOH); *m/z* 173 (3%, M − OMe), 101 (66, $C_5H_9O_2$), 100 (88, $C_5H_8O_2$) and 69 (100, C_4H_5O) (Found: M$^+$ − MeO, 173.0802. $C_9H_{16}O_5$ requires *M* − OMe, 173.0813).

Methyl (2RS,3RS)-3-*Acetoxy*-2-[(SR)-1-*acetoxyethyl*]-*butanoate* **16**.—The (2*RS*,3*RS*,1′*SR*)-alcohol (22 mg, 0.11 mmol), acetic anhydride (11 cm^3, 0.12 mmol), triethylamine (17 cm^3, 0.12 mmol) and dimethylaminopyridine (1 mg) were stirred in dichloromethane (2 cm^3) for 1 h. The mixture was diluted with ether (8 cm^3), washed with dilute hydrochloric acid and brine, dried ($MgSO_4$) and evaporated under reduced pressure to give the *diacetate* (20 mg, 73%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.45; ν_{max}($CDCl_3$)/cm^{-1} 1730 (C=O); δ($CDCl_3$) 5.19 (2 H, quintet, *J* 6, C*H*OAc), 3.70 (3 H, s, OMe), 2.69 (1 H, t, *J* 6, CHCO), 2.00 (6 H, s, OAc) and 1.27 (6 H, d, *J* 6, *Me*CHOAc); *m/z* 215 (4%, M − OMe), 101 (95, $C_5H_9O_2$) and 100 (100, $C_5H_8O_2$) (Found: M$^+$ − OMe, 215.0919. $C_{11}H_{18}O_6$ requires *M* − OMe, 215.0920).

Methyl (3RS)-3-*Acetoxy*-2-[(RS)-1-*acetoxyethyl*]*butanoate* **17**.—The (2*RS*,3*SR*,1′*SR*)-acetate was treated similarly to give *diacetate* (25 mg, 93%); R_f [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.50; ν_{max}(film)/cm^{-1} 1730 (C=O); δ($CDCl_3$) 5.19 (2 H, m, C*H*OAc), 3.72 (3 H, s, OMe), 2.77 (1 H, dd, *J* 6 and 9, CHCO), 2.01 (3 H, s, OAc), 1.99 (3 H, s, OAc), 1.25 (3 H, d, *J* 6, *Me*CHOAc) and 1.22 (3 H, d, *J* 6, *Me*CHOAc); *m*/*z* 215 (6%, M − OMe), 204 (4, M − C_2H_2O), 101 (32, $C_5H_9O_2$) and 100 (37, $C_5H_8O_2$) (Found: M^+ − OMe, 215.0915. $C_{11}H_{18}O_6$ requires *M* − OMe, 215.0920).

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