In search of open-chain 1,3-stereocontrol

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1 PERKIN

Methylation of methyl 4-phenylpentanoate 25 gives the diastereoisomers methyl (2*RS*,4*SR*)-2-methyl-4-phenylpentanoate 26 and methyl (2*RS*,4*RS*)- 2-methyl-4-phenylpentanoate 27 in a ratio of 44:56. The aldehydes 3-dimethyl(phenyl)silylbutanal 28, 3-dimethyl(phenyl)silyl-3-phenylpropanal 32 and 3-dimethyl(phenyl)silyl-4-methylpentanal 36, each of which has a stereogenic centre on C-3 carrying a silyl group and successively also a methyl, a phenyl and an isopropyl group, react with a range of methyl, phenyl and isopropyl nucleophiles to give pairs of diastereoisomeric secondary alcohols 40–42, 47–49 and 54–56 having 1,3 related stereocentres. The same alcohols 43–45, 50–52 and 57–59 are also prepared by reduction of the corresponding ketones 29–31, 33–35 and 37–39 with a range of hydride reagents, and three of the ketones, 31, 35 and 39, react with phenyllithium to give mixtures of the tertiary alcohols 46, 53 and 60. The (*E*)- and (*Z*)-α,β-unsaturated methyl esters, 61, 62, 64, 65, 67 and 68, prepared from the same three aldehydes with methoxycarbonylmethyltriphenylphosphorane, react with the phenyldimethylsilyl-cuprate and -zincate reagents to give diastereoisomeric pairs of 1,3-disilylated esters. Likewise, the α,β-unsaturated dimethyl diesters, 63, 66 and 69, prepared from the same three aldehydes with dimethyl malonate, react with phenyldimethylsilyllithium and the corresponding cuprate and zincate reagents to give diastereoisomeric pairs of 1,3-disilylated diesters, and with various methyl and phenyl nucleophiles to give the corresponding pairs of diastereoisomeric diesters with stereogenic centres at C-3 and C-5. The relative stereochemistry of all but two of the products having 1,3-related stereocentres has been proved by silyl-to-hydroxy conversion using mercuric acetate and peracetic acid to give the corresponding alcohols or their derived lactones.

An attempt to identify a purely steric rule by which it might be possible to predict which diastereoisomer would be the major product in each of these reactions was based on arguments about, and molecular mechanics calculations of, the lowest-energy conformations of the starting materials. The only rule that emerges is that ketones are regularly attacked in sense B, defined in the drawings 21 and 23, in a conformation that minimises the interaction between the group M on the stereogenic centre and the group R^1 on the other side of the ketone, but even within this group of reactions, phenyl groups in either or both locations sometimes lead to anomalies.

Krapcho reactions take place more rapidly and in higher yield using four equivalents of lithium chloride in place of the usual sodium chloride, and adding two equivalents of water to the DMSO.

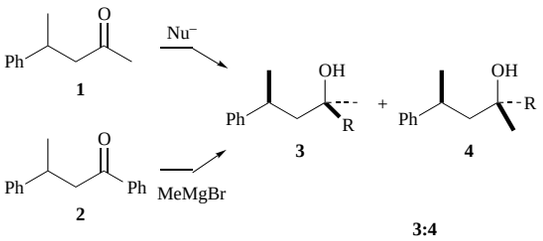
Introduction

Cram's rule[1] for nucleophilic attack on a carbonyl group adjacent to a stereogenic centre is well known, and the explanation, successively advanced by Karabatsos,[2] Felkin,[2] and Anh and Eisenstein,[2] is well accepted. We have pointed out[3] that the corresponding rule for electrophilic attack on a C=C double bond, developed successively by Zimmerman and Chang,[4] Barton *et al.*[4] and Houk *et al.*,[4] is in one sense the opposite of Cram's rule, and we have done a lot of work applying the selectivity of this kind of reaction in synthesis, using a stereogenic centre carrying a silyl group.[5]

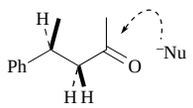
The homologue of these reactions, in which the reaction site and the stereogenic centre are separated by a methylene group, is much less well understood. For good 1,3-control, a cyclic substrate or transition structure is usually needed, as in the methods for controlling the relative stereochemistry of 1,3-diols by reduction of β-hydroxy ketones,[6] by the delivery of chelated carbon nucleophiles to carbonyl groups,[7] and by the intramolecular delivery of electrophiles to a C=C double bond.[8] There are now scores of other reactions having a cyclic component to control the relative stereochemistry of other types of 1,3-related centres,[9] but, in the absence of a ring, it is much more usual to get low levels of diastereocontrol. Thus we found, in our synthesis of the Prelog–Djerassi lactone, that lithium phenylacetylide reacted with a ketone having a stereogenic centre at C-3 to give both possible alcohols in equal amounts.[10] As it happens, that result was not a disappointment, since the whole point of that synthesis had been to demonstrate how our stereochemically complementary allylsilane syntheses,[11] coupled to the predictably *anti* stereospecific protodesilylation of an allylsilane, allowed us to converge on the correct stereochemistry for C-6 from *both* diastereoisomers.

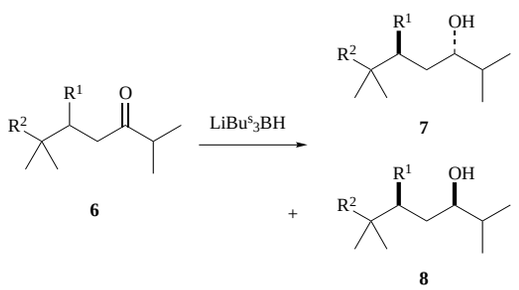
Nevertheless, it would be much easier if one were not obliged to use multi-step sequences to achieve such control. Exploratory work in this area includes that of Tiffenau[12] and Brokaw and Brode,[13] but the first quantitative studies were by Leitereg and Cram[14] and by Jacques[15] in 1968. Cram obtained a good level (83:17) of 1,3-control from the reaction of the phenyl Grignard reagent on the ketone **1** at low temperature, and complementary but lower selectivity (41:59) from the reaction of the methyl Grignard reagent on the ketone **2**. The corresponding lithium reagents were less selective. He explained the stereochemical sense of these reactions by attack of the nucleophile from the less-hindered, rear side in the conformation **5**, giving the alcohol **3** (R = Ph) as the major product from the ketone **1**, and the alcohol **4** (R = Ph) as the major product from the ketone **2**. However, Jacques found only low levels of selectivity (41:59) in the reduction of the ketone **1** by lithium aluminium hydride,[15] and his reaction took place in the opposite sense to Cram's, giving the alcohol **4** (R = H) as the major product. All these results are pretty typical—occasional high levels of stereoselectivity, more often than not low levels, and the sense somewhat unpredictable.

More recently, Evans has looked at this problem, extending Jacques' work on the reduction of ketones using the ketones **6**,



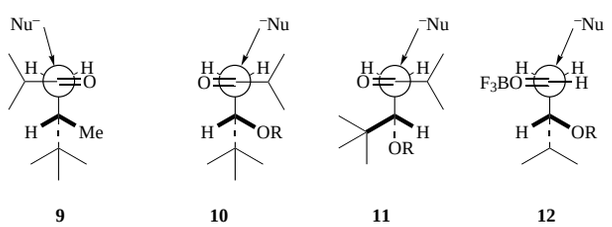
Nu = PhMgBr on **1**	–110 °C	R = Ph	83:17	36%
PhMgBr on **1**	–78 °C	R = Ph	76:24	100%
PhMgBr on **1**	0 °C	R = Ph	67:33	98%
$LiAlH_4$ on **1**	35 °C	R = H	41:59	100%
MeMgBr on **2**		R = Ph	41:59	??%





7:**8**

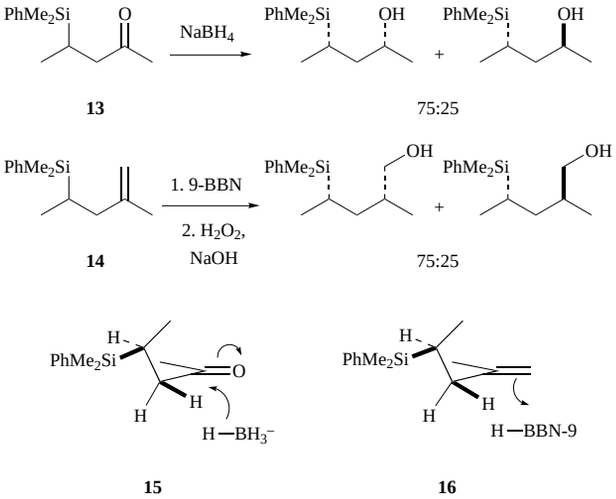
R^1 = Me, R^2 = vinyl	92:8
R^1 = $OSiMe_2Bu^t$, R^2 = Me	3:97



and finds that a hindered reducing agent can sometimes give strikingly high levels of stereoselectivity, with the sense changing dramatically (from 92:8 in favour of the alcohol **7** to 3:97 in favour of the alcohol **8**) when the medium-sized substituent R^1 on the stereogenic centre was changed from a methyl group to a silyloxy substituent.[16] He explains his results with a model **9** for the steric case and a model **10** or possibly **11** for the case with an oxygen substituent, each of which has a stabilising dipolar contribution from the C–O dipole facing away from the carbonyl dipole. Other models that he considers have steric clashes or destabilising electrostatic interactions.

Evans has also studied aldol reactions on aldehydes, using metal enolates or silyl enol ethers as the nucleophiles, and explained his results with a model similar to **10**. The steric-only cases gave low levels of stereoinduction, and not always in the same sense, but the Mukaiyama aldol reactions on aldehydes with β-oxygen functions, using boron trifluoride as the Lewis acid, were often highly selective (≤92:8) in the sense **12** in favour of the *anti* 1,3-diol derivative. This selectivity could be extended to similar reactions with an α-stereogenic centre, which gave very high levels of Cram control (≥97:3) when the β-stereogenic centre was matched so as to give *anti* 1,3 diol derivatives.[17]

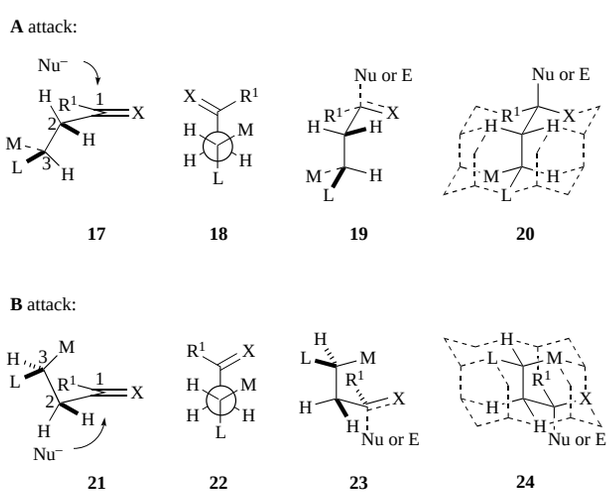
In the course of other work, we also came across examples of moderately high 1,3-selectivity, both in the reduction of the ketone **13** and in the hydroboration of the alkene **14**,[18] the latter



matching some hydroboration results of Evans *et al.*,[19] where he had a large alkyl group and we had a silyl group. We explained our results with the models **15** and **16**, which are similar in concept to Evans's but drawn differently. Stimulated by these observations, we embarked upon a more systematic study of this problem, aiming to find a rule, or to support and flesh out Evans', that predicts the sense of 1,3-control in open-chain systems influenced *only by steric effects*. With such a rule, we might be able to pin down more exactly the features that will lead to high levels of 1,3-stereocontrol, and, if such control is predictable, we can hope to save steps in syntheses. We report our results here, with preliminary reports only in the form of two published lectures.[20]

Since it is not at first sight obvious how a stereogenic centre insulated from the reaction site is able to pass stereochemical information along a chain, it is perhaps important to explain the ideas embedded in the three families of models **5**, **9**–**12**, and **15** and **16**, and to explain the basis of our thinking as we carried out the reactions described here. We may be forgiven for using our version **15** and **16**, which we think gives a somewhat clearer three-dimensional reading of the problem than the other two, although our picture is essentially the same as Evans', which is, in its turn, based on Jacques'. Cram's conformation **5**, with the carbon chain eclipsing the CO–Me bond, is unlikely to be significantly populated, except perhaps with aldehydes, and neither Jacques nor Evans used this idea, and nor have we.

Using the drawings **17**–**24**, we argue that the first consideration is that the large substituent L on the stereogenic centre can be expected to position itself between the two hydrogen atoms of the C-2 methylene group. The nucleophile or electrophile attacking the double bond can then be expected to attack



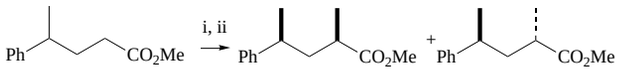
on the opposite side of the double bond from the C-2 to C-3 bond. The two surfaces of the double bond are therefore made different by the direction in which the C-2 to C-3 bond is rotated out of the plane of the double bond, and that in turn is determined by the configuration at the stereogenic centre C-3. Although all our work has been carried out with racemic compounds, we have drawn, throughout this paper, the same absolute configuration at the stereogenic centre C-3, both for our own compounds and for those quoted from Cram's, Jacques' and Evans' work. We can see that if the bond to C-3 is rotated down, as in **17**, the medium-sized group will be positioned in the segment between the group R^1 attached at C-1 and the 'outside' hydrogen atom, as shown more clearly in the Newman projection **18**; if it is rotated up, as in **21**, the medium-sized group will be positioned between the double bond and the 'inside' hydrogen, as seen in the Newman projection **22**. In the former case, the upper surface is more exposed, in the latter it is the lower. The uncertainty lies in which conformation **17** or **21** is the lower in energy. Our feeling was that conformation **21** = **22** would be lower in energy when the group R^1 was large, but the alternative **17** = **18** might be lower in energy when the group R^1 was small. Thus Cram's reactions on the ketones **1** and **2**, Evans' reaction on the ketone **6** (R^1 = Me), and our reactions on the ketone **13** and the alkene **14**, all correspond to attack on the lower surface of the conformation **21**, and all have a group, phenyl, methyl or isopropyl, attached as R^1 to the double bond. Jacques' reaction, which takes place in the opposite sense, has the smallest of these groups as R^1. We label attack on the upper surface as being in the **A** sense, as expected for the conformations variously expressed as **17**–**20**. Similarly, we label attack on the lower surface as being in the **B** sense, as expected for the conformations variously expressed as **21**–**24**. The label **A** or **B** is needed to identify the sense of attack, but is not necessarily associated with any particular explanation. Throughout this paper, all ratios are illustrated and expressed in the order **A**:**B**, and products of attack in the sense **A** are labelled with an **A**, and those from attack in the sense **B** are labelled with a **B**.

One detail should perhaps be clarified. The drawings we are using here are expected to be close to the low energy conformations of the starting material. Following Felkin's argument, we can expect that, at the time of reaction, the C-2 to C-3 bond will be more nearly perpendicular to the plane of the double bond, as in Evans' drawings **9**–**12**. We find that our drawings **17** and **21** are easier to visualise, easier to relate to the results of our modelling work, which is entirely concerned with the ground state, and they do not change the argument significantly, involving as they do only a rotation of 30° or so before reaction. Who knows what the exact angles are at the time of reaction? But if we want to be more refined, we can expect that the transition structures will have the substituents more nearly staggered throughout, as in the drawings **19** and **23**, in which all the atoms more or less occupy the positions of the carbon atoms in a diamond lattice, as illustrated in the versions **20** and **24**. One feature of these pictures, and the rationalisations that go with them, is that we can expect electrophilic attack to take place in the same stereochemical sense as nucleophilic attack, in contrast to Cram's and Houk's rule for 1,2-control. We had already seen in the pair of results **15** and **16**, which are otherwise similar examples of nucleophilic and electrophilic attack, respectively, that this might well prove to be the case.

Results and discussion

1,3-Stereocontrol

Since we had provided the first example[3] of electrophilic attack complementing Cram's work on nucleophilic attack,[1] we looked at one example of electrophilic attack to compare with his results **1** ⟶ **3** + **4**. We chose the enolate methylation **25** ⟶ **26** + **27**, where we found very low selectivity 44:56 in favour of the isomer **27** (Scheme 1). This result does happen to



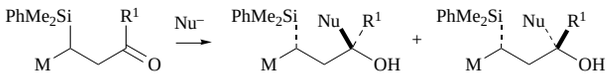
25 **26** 44:56 **27**

Scheme 1 *Reagents:* i, LDA; ii, MeI

give the major product from reaction in the same sense, with the methyl iodide attacking from behind, just as the nucleophile attacks from behind in Cram's picture **5**. In our terminology the sense is **B**. Thus, so far at least, the sense of 1,3-control is the same both for electrophilic and nucleophilic reactions, as we argued above they would be. However, in our later work, described below, it became clear that a double bond with the substitution pattern possessed by the enolate double bond in this reaction is unlikely to demonstrate a reliable level of stereochemical predictability. The fact that it reacts, just, in the same stereochemical sense as the corresponding nucleophilic attack on a carbonyl group can only be regarded as fortuitous.

With the exception of this one result, we have narrowed our study so far to nucleophilic attack, and have uniformly used the phenyldimethylsilyl group as the large group L. This choice is based on our perception that, unlike a hydroxy or protected hydroxy group, it would unambiguously be a larger group than any carbon-based group that we planned to attach to the stereogenic centre. Furthermore, it was unlikely to indulge in coordination to set up a cyclic transition structure, nor would it make a polar contribution, since there is no significant dipole moment associated with a silyl group having four tetrahedrally disposed carbon substituents. Finally, it had the advantage that it could be converted with retention of configuration into a hydroxy group,[21] the ideal group from which to establish the relative stereochemistry in the pairs of products. With an infinite number of other variables to choose among, we then chose to look systematically at the stereochemistry of nucleophilic attack, with a range of hydride and organometallic carbon nucleophiles, on the twelve aldehydes and ketones **28**–**39**, giving mixtures of the alcohols **40A**–**60A** and **40B**–**60B**, with all combinations of R^1 as hydrogen, methyl, phenyl and isopropyl, and the medium-sized group M as methyl, phenyl and isopropyl (Scheme 2). We further studied nucleophilic attack, with a range of organometallic silyl and carbon nucleophiles, on the nine α,β-unsaturated esters **61**–**69**, giving the esters **70A**–**81A** and **70B**–**81B**, with the medium-sized group M as successively methyl, phenyl and isopropyl. The results of our work with aldehydes and ketones are presented in Table 1, and with the α,β-unsaturated esters in Table 2. In all, we have carried out 92 reactions, some of them several times, and have identified the relative stereochemistry of the major product in 24 pairs of diastereoisomers.

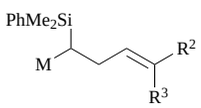
If we start from the idea that the interaction between the medium-sized substituent M and the group R^1 determines which conformation **17** or **21** is populated, we can suggest that the ketones ($R^1 \neq H$) will react in the sense **B**, because the interaction between M and the substituent R^1 will disfavour conformation **17** and make conformation **21** the more populated. In contrast, the aldehydes (R^1 = H) and all the α,β-unsaturated esters **61**–**69** could reasonably react in either sense, but we can try the idea that the conformation **17** might be favoured, since the interaction between the medium-sized group M and the hydrogen atom will be small. Nucleophilic attack on this group of compounds can then be expected to take place in the sense **A**. The data in the Tables, discounting the two pairs of compounds we were unable to assign stereochemistry to, support this idea to some extent—the ratio of correctly to incorrectly predicted results for reactions predicted to take place in sense **A** is 43:19, and the ratio of correctly to incorrectly predicted results for reactions predicted to take place in sense **B** is 20:6. The overall ratio of success to failure is therefore a moderately encouraging but hardly compelling 63:25. Furthermore, an



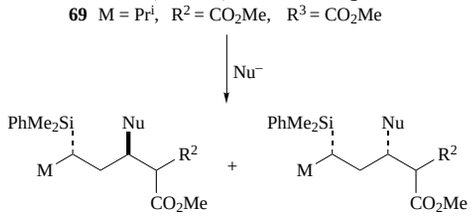
28 M = Me, R^1 = H
29 M = Me, R^1 = Me
30 M = Me, R^1 = Ph
31 M = Me, R^1 = Pr^i
32 M = Ph, R^1 = H
33 M = Ph, R^1 = Me
34 M = Ph, R^1 = Ph
35 M = Ph, R^1 = Pr^i
36 M = Pr^i, R^1 = H
37 M = Pr^i, R^1 = Me
38 M = Pr^i, R^1 = Ph
39 M = Pr^i, R^1 = Pr^i

A **B**

40	M = Me,	R^1 = H	Nu = Me
41	M = Me,	R^1 = H	Nu = Ph
42	M = Me,	R^1 = H	Nu = Pr^i
43	M = Me,	R^1 = Me	Nu = H
44	M = Me,	R^1 = Ph	Nu = H
45	M = Me,	R^1 = Pr^i	Nu = H
46	M = Me,	R^1 = Pr^i	Nu = Ph
47	M = Ph,	R^1 = H	Nu = Me
48	M = Ph,	R^1 = H	Nu = Ph
49	M = Ph,	R^1 = H	Nu = Pr^i
50	M = Ph,	R^1 = Me	Nu = H
51	M = Ph,	R^1 = Ph	Nu = H
52	M = Ph,	R^1 = Pr^i	Nu = H
53	M = Ph,	R^1 = Pr^i	Nu = Ph
54	M = Pr^i,	R^1 = H	Nu = Me
55	M = Pr^i,	R^1 = H	Nu = Ph
56	M = Pr^i,	R^1 = H	Nu = Pr^i
57	M = Pr^i,	R^1 = Me	Nu = H
58	M = Pr^i,	R^1 = Ph	Nu = H
59	M = Pr^i,	R^1 = Pr^i	Nu = H
60	M = Pr^i,	R^1 = Pr^i	Nu = Ph



61	M = Me,	R^2 = CO_2Me,	R^3 = H
62	M = Me,	R^2 = H,	R^3 = CO_2Me
63	M = Me,	R^2 = CO_2Me,	R^3 = CO_2Me
64	M = Ph,	R^2 = CO_2Me,	R^3 = H
65	M = Ph,	R^2 = H,	R^3 = CO_2Me
66	M = Ph,	R^2 = CO_2Me,	R^3 = CO_2Me
67	M = Pr^i,	R^2 = CO_2Me,	R^3 = H
68	M = Pr^i,	R^2 = H,	R^3 = CO_2Me
69	M = Pr^i,	R^2 = CO_2Me,	R^3 = CO_2Me



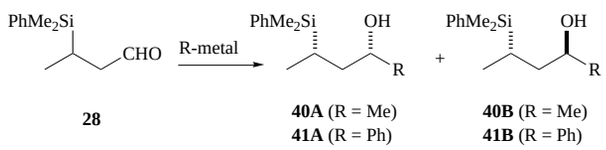
A **B**

70	M = Me,	R^2 = H,	Nu = $SiMe_2Ph$
71	M = Me,	R^2 = CO_2Me,	Nu = $SiMe_2Ph$
72	M = Me,	R^2 = CO_2Me,	Nu = Me
73	M = Me,	R^2 = CO_2Me,	Nu = Ph
74	M = Ph,	R^2 = H,	Nu = $SiMe_2Ph$
75	M = Ph,	R^2 = CO_2Me,	Nu = $SiMe_2Ph$
76	M = Ph,	R^2 = CO_2Me,	Nu = Me
77	M = Ph,	R^2 = CO_2Me,	Nu = Ph
78	M = Pr^i,	R^2 = H,	Nu = $SiMe_2Ph$
79	M = Pr^i,	R^2 = CO_2Me,	Nu = $SiMe_2Ph$
80	M = Pr^i,	R^2 = CO_2Me,	Nu = Me
81	M = Pr^i,	R^2 = CO_2Me,	Nu = Ph

Scheme 2

anomalously large number of the reactions unexpectedly taking place in sense **B** with the aldehydes (*i.e.* R^1 = H) and the diesters **63**, **66** and **69** (*i.e.* $R^2 = R^3 = CO_2Me$) are reactions of methyl- and phenyl-lithium reagents—if these results with lithium reagents are discounted, the ratio of successful to unsuccessful predictions of reaction in the sense **A** changes from 43:19 to a somewhat more respectable 41:9. Clearly a simple rule along these lines is not going to be completely reliable, but there is a trend: *when* $R^1 = H$, *reaction usually takes place in sense* ***A***, *except with lithium reagents, but when* $R^1 \neq H$, *reaction usually takes place in sense* ***B***. In this discussion, we have paid no attention to the degree of selectivity, but there is no trend for the incorrect predictions also to be reactions with low selectivity. Typically, with many of the ratios very low, the degree of selectivity is only rarely high enough to be useful in organic synthesis.

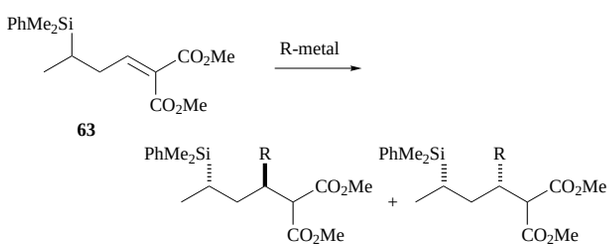
One reason for the lack of correlation can be seen in the large variation in the results depending upon the *reagent* used, as already mentioned in connection with the anomalous results with lithium reagents. Since we have been considering only the conformation of the substrate, all reagents are treated as attacking in the same sense and to more or less the same degree. This is rather plainly not the case in practice, and as seen specifically in the reactions of methyl- and phenyl-lithium with the aldehyde **28**, which take place in the opposite sense to each other, methyllithium in the sense **B** to give more of the alcohol **40B** and phenyllithium in the sense **A** to give more of the alcohol **41A** (Scheme 3). In contrast, the corresponding Grignard



28

40A (R = Me)
41A (R = Ph)
40B (R = Me)
41B (R = Ph)

R-metal	**A**:**B**
MeLi	33:67
PhLi	67:33
MeMgI	60:40
PhMgBr	60:40



63

72A R = Me
73A R = Ph
72B R = Me
73B R = Ph

R-metal	**A**:**B**
MeLi	43:57
PhLi	29:71
$Me_2CuCN\ Li_2$	85:15
$Me_3Zn\ Li$	87:13
$Ph_2CuCN\ Li_2$	50:50
$PhZnMe_2\ Li$	71:29

Scheme 3

reagents both react in the sense **A** to give the same diastereoisomeric relationship in the major products **40A** and **41A**. Also in contrast, both methyl- and phenyl-lithium react with the unsaturated diester **63**, to give as the major products the esters **72B** and **73B**, respectively, corresponding to attack in the sense **B**, whereas the corresponding cuprates and zincates mostly give the opposite result, with the esters **72A** and **73A** as the major products. Clearly, consideration only of the ground state cannot deal with all these variations that depend upon the reagent.

We turned next to molecular modelling, which so far we have used only on the aldehydes and ketones. Alas, modelling the wide range of transition structures was impractical, so we were still obliged to look only at the starting materials, in the hope of finding a better correlation between the sense of the selectivity and which of the diastereotopic surfaces appears to be the more exposed in the model. We first calculated the low-energy conformations within 20 kJ mol^{-1} of the global minimum. Most of these conformations could be assigned as **A**-predictors or **B**-predictors from the dihedral angle of the bond from C-2 to C-3 and the plane of the carbonyl group. With the few conformations where this angle was close to 0 or 180° inspection of a three-dimensional rendering of the structure usually allowed us to make a similar but more tentative assignment. It is perhaps worth noting at this stage that many of the low-energy conformations included in this assessment diverge quite substantially from the paradigms **17**–**24**, indicating that the conformational preferences are not strong. We then calculated the

Table 1 Diastereoisomer ratios for the reactions of the aldehydes and ketones **28**–**39** with nucleophiles

	M	R^1	Nu^-	Solvent	*T*/°C	Yield (%)	A:B	Calc.
28	Me	H	MeLi	THF	−78	72	33:67	62:38
			MeMgBr	THF	−78	36	55:45	62:38
			MeMgI	Et_2O	0	64	60:40	59:41
			PhLi	THF	−78	73	67:33	62:38
			PhMgBr	THF	0	67	60:40	59:41
			Pr^iMgCl	THF	0	60	61:39	59:41
29		Me	$LiAlH_4$	Et_2O	−78	86	30:70	34:66
			$NaBH_4$	MeOH	0	97	25:75	41:59
30		Ph	$LiAlH_4$	Et_2O	−78	86	79:21	74:26
			$NaBH_4$	EtOH	rt	90	71:29	58:42
31		Pr^i	$LiAlH_4$	Et_2O	−78	79	22:78	23:77
			$NaBH_4$	EtOH	rt	78	28:72	37:63[a]
			$Li(Bu^tO)_3AlH$	THF	rt	77	23:77	37:63[a]
			N-Selectride	THF	0	53	21:79	37:63
			PhLi	THF	−78	71	25:75	23:77
			PhMgBr	THF	rt	60	25:75	37:63[a]
32	Ph	H	MeLi	THF	−78	63	48:52	75:25
			MeMgBr	THF	0	60	53:47	69:31
			PhLi	THF	−78	70	22:78	75:25
			PhMgBr	THF	0	70	28:72	69:31
			Pr^iMgCl	THF	0	60	45:55	69:31
33		Me	$LiAlH_4$	Et_2O	−55	81	47:53	75:25
			$NaBH_4$	EtOH	0	85	54:46	64:36
34		Ph	$LiAlH_4$	Et_2O	−55	96	33:67	62:38
			$NaBH_4$	EtOH	0	96	60:40	54:46
35		Pr^i	$LiAlH_4$	Et_2O	−78	66	49:51	60:40
			$NaBH_4$	EtOH	rt	81	47:53	56:44[a]
			$Li(Bu^tO)_3AlH$	THF	rt	70	67:33	56:44[a]
			PhLi	THF	−78	65	55:45[b]	60:40
36	Pr^i	H	MeLi	THF	−78	65	40:60	54:46
			MeMgBr	THF	0	64	53:47	52:48
			PhLi	THF	−78	74	73:27	54:46
			PhMgBr	THF	0	60	72:28	52:48
			Pr^iMgCl	THF	0	68	53:47	52:48
37		Me	$LiAlH_4$	Et_2O	−78	78	33:67	31:69
			$NaBH_4$	EtOH	rt	58	51:49	39:61[a]
38		Ph	$LiAlH_4$	Et_2O	−78	70	12:88	91:9
			$NaBH_4$	EtOH	rt	51	23:77	71:29[a]
39		Pr^i	$LiAlH_4$	Et_2O	−78	76	30:70	24:76
			$NaBH_4$	EtOH	rt	73	23:77	32:68[a]
			$Li(Bu^tO)_3AlH$	THF	rt	71	24:76	32:68[a]
			PhLi	THF	−78	60	23:77	24:76

[a] Calc. for 0 °C. [b] Or the other way round. rt = room temp.

Boltzmann distribution for the low-energy conformations at each of the temperatures at which reactions had been carried out, and hence the proportion of conformations occupied by **A**- and **B**-predictors. These numbers appear as the right hand column in Table 1. All three aldehydes are predicted to react in sense **A**, and of the nine ketones five are predicted to react in sense **A** and four in sense **B**. Making the crude assumption that conformations predicting attack in the **A** sense would react only in the **A** sense, and that conformations predicting attack in the **B** sense would react only in the **B** sense, these numbers could be plotted directly against the corresponding experimental data in a form that ought to place all the points in the upper-right and lower-left quadrants, and more or less in a straight line. The result, shown in Fig. 1, was distinctly disappointing.

The lower-right quadrant was very nearly empty, but the upper left quadrant had a similar number of points to each of the other two, making the 2:1 statistical preference in favour of the predicted sense of attack worse than before. However, by classifying the points, some order is restored—one group, the ketones without a phenyl group, fall in the lower-left quadrant with only one point just outside it, and with most showing healthy, if not dramatic, levels of selectivity. It appears that phenyl groups, perhaps because of the many different conformations that they can fall into, make prediction difficult, but, leaving them out, the other ketones show substantial selectivity in the sense **B**. The uniformity of behaviour of this group

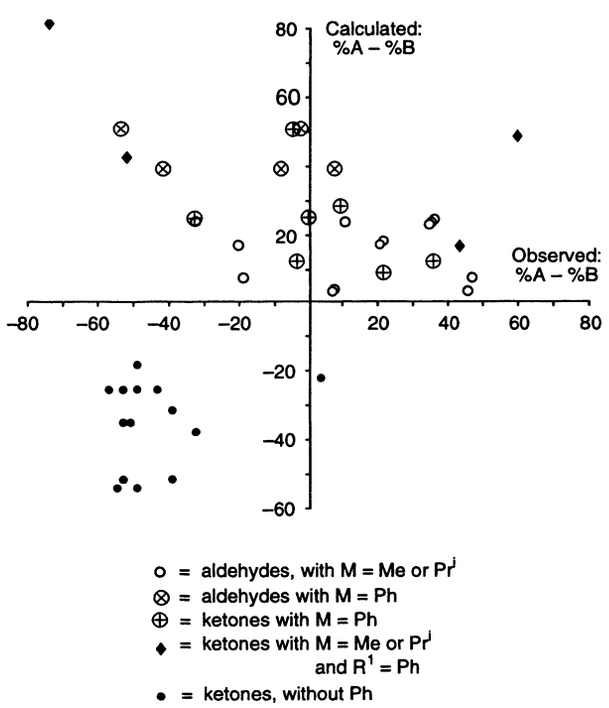


Fig. 1

Table 2 Diastereoisomer ratios for the reactions of the α.β-unsaturated esters **61**–**69** with nucleophiles

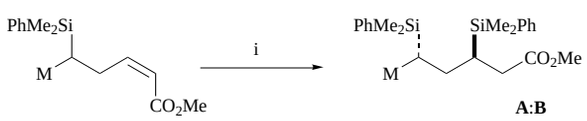
	M	R^2	R^3	Nu^-	*T*/°C	Yield (%)	A:B
61	Me	CO_2Me	H	$(PhMe_2Si)_2Cu$ Li	−78	84	71:29
				$PhMe_2SiZnMe_2$ Li	−78	84	77:23
62		H	CO_2Me	$(PhMe_2Si)_2Cu$ Li	−78	—	variable[a]
				$PhMe_2SiZnMe_2$ Li	−78	76	94:6
63		CO_2Me	CO_2Me	$PhMe_2SiLi$	−78	42	55:45
				$(PhMe_2Si)_2Cu$ Li	−78	75	57:43
				$PhMe_2SiZnMe_2$ Li	−78	81	78:22
				MeLi	−78	25	43:57
				MeMgBr	0	23	67:33
				Me_3ZN Li	−78	70	86:14
				Me_2CuCN Li_2	−78	62	85:15
				PhLi	−78	61	29:71
				$PhZnMe_2$ Li	−78	65	71:29
				Ph_2CuCN Li_2	−78	62	50:50
64	Ph	CO_2Me	H	$(PhMe_2Si)_2Cu$ Li	−78	59	95:5
				$PhMe_2SiZnMe_2$ Li	−78	83	86:14
65		H	CO_2Me	$(PhMe_2Si)_2Cu$ Li	−78	73	48:52
				$PhMe_2SiZnMe_2$ Li	−78	76	95:5
66		CO_2Me	CO_2Me	$(PhMe_2Si)_2Cu$ Li	−78	81	66:34
				$PhMe_2SiZnMe_2$ Li	−78	65	78:22
				$PhMe_2SiLi$	−78	87	82:18
				MeLi	−78	67	48:52
				MeMgBr	0	58	56:44
				Me_3Zn Li	−78	66	60:40
				Me_2CuCN Li_2	−78	63	88:12
				PhLi	−78	89	24:76
				$PhZnMe_2Li$	−78	68	35:65
				PhMgBr	0	77	64:36
				Ph_2CuCN Li_2	−78	96	36:64
67	Pr^i	CO_2Me	H	$(PhMe_2Si)_2Cu$ Li	−78	71	83:17
				$PhMe_2SiZnMe_2$ Li	−78	74	72:28
				$PhMe_2SiAlMe_2$ Li	−78	63	61:39
68		H	CO_2Me	$(PhMe_2Si)_2Cu$ Li	−78	68	53:47
				$PhMe_2SiZnMe_2$ Li	−78	68	78:22
				$PhMe_2SiAlMe_2$ Li	−78	66	72:28
69		CO_2Me	CO_2Me	$(PhMe_2Si)_2Cu$ Li	−78	82	45:55[b]
				$PhMe_2SiZnMe_2$	−78	74	53:47[b]
				$PhMe_2SiAlMe_3$ Li	−78	68	43:57[b]
				$PhMe_2SiLi$	−78	61	45:55[b]
				MeLi	−78	28	46:54
				MeMgBr	0	57	53:47
				Me_3Zn Li	−78	76	51:49
				Me_2CuCN Li_2	−78	88	64:36
				Me_4Al Li	−78	50	52:48
				PhLi	−78	83	37:63
				PhMgBr	0	85	57:43
				$PhZnMe_2$ Li	−78	89	46:54
				Ph_2CuCn Li_2	−78	62	49:51
				$PhAlMe_3Li$	−78	80	37:63

[a] With **A**:**B** always >1. [b] Or other way round.

of ketones confirmed that we had not made a rather doubtful assumption in claiming that the phenyldimethylsilyl group would unambiguously be a larger group than any carbon-based group. It is of course larger than any of the carbon-based groups that we have used, but, because of the long Si–C bond, a silyl group is not always as sterically hindering as its actual size might suggest. That the results with M = Me and M = Pr^i are so similar implies that in our work here, the silyl group is the 'large' group. Thus we have a limited rule for purely steric cases: *when* $R^1 \neq H \neq Ph$, *and when* $M \neq Ph$, *reaction takes place in sense* ***B***. This was where we started—tentatively predicting that M and R^1 would avoid a 1,3-diaxial-like interaction by adopting the conformation **21**, and the modelling supports this idea.

This appears to be about as far as we can go at present. It is consistent with some results of Kobayashi and Ohno[22] on nucleophilic attack on acylsilanes, which inherently have a large group R^1, but aldehydes and α,β-unsaturated esters, both of which have R^1 = H, are still rather unpredictable, with merely a 2:1 bias in favour of reaction in the sense **A**, improved to 4:1 if lithium reagents are taken to be anomalous. Most of Evans' results were with enolates reacting with aldehydes, but with the saving grace of a polar contribution from the dipole-inducing oxygen function on the stereogenic centre. Our results, with large numbers of low ratios, and only steric effects in operation, support his suggestion that a dipole is an important contribution to getting high levels of diastereocontrol.

One of our results deserves highlighting. The conjugate addition of silyl nucleophiles to the (*Z*)-α,β-unsaturated esters **62** and **65** could be made to give, with a careful choice of reagent, a high level of 1,3-control in the sense **A** (Scheme 4). The silyl-



62 M = Me
65 M = Ph
68 M = Pr^i

70A	M = Me	94:6	76%
74A	M = Ph	95:5	76%
78A	M = Pr^i	78:22	68%

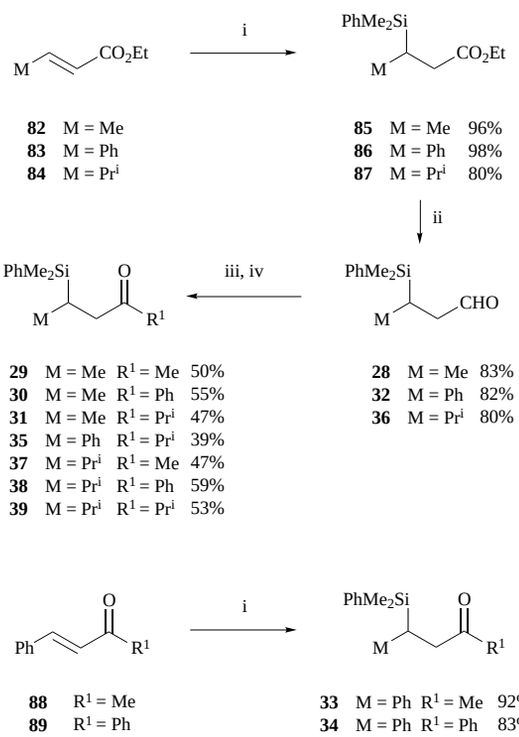
Scheme 4 *Reagents:* i, $PhMe_2SiZnMe_2$ Li, THF, −78 °C

zincate (but not the silylcuprate) gave excellent stereoselectivity in setting up the *anti* related 1,3-disilyl esters **70A** and **74A**. This result gives us an approach to a starting material for a second synthesis of tetrahydrolipstatin,[23] and also gives us a compound

having two silyl groups with correlated stereochemistry. Previously we had found a method for setting up such a compound with 1,2-related silicon-bearing stereocentres;[24] now we have a method for setting up 1,3-related centres. The high level of selectivity, however, fell off with the ester **68** having an isopropyl group on the stereogenic centre, which gave the esters **78A** and **78B** in a ratio of 78:22.

Synthesis of substrates

We prepared the aldehydes **28**, **32** and **36** by DIBAL-H reduction of the corresponding ethyl esters **85**–**87**, themselves prepared by silylzincation[25] of ethyl crotonate **82** and ethyl cinnamate **83** or by silylalumination, which appears to work comparably well, of the ester **84**. The reactions of these aldehydes with lithium and Grignard reagents gave the corresponding secondary alcohols, as recorded in Table 1, and the mixtures of diastereoisomeric secondary alcohols were oxidised to give the corresponding ketones (Scheme 5), ready for the hydride



82 M = Me
83 M = Ph
84 M = Pr^i

85 M = Me 96%
86 M = Ph 98%
87 M = Pr^i 80%

29 M = Me R^1 = Me 50%
30 M = Me R^1 = Ph 55%
31 M = Me R^1 = Pr^i 47%
35 M = Ph R^1 = Pr^i 39%
37 M = Pr^i R^1 = Me 47%
38 M = Pr^i R^1 = Ph 59%
39 M = Pr^i R^1 = Pr^i 53%

28 M = Me 83%
32 M = Ph 82%
36 M = Pr^i 80%

88 R^1 = Me
89 R^1 = Ph

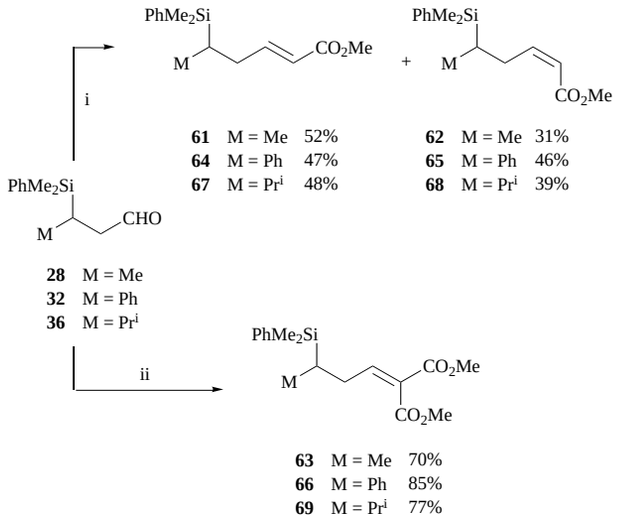
33 M = Ph R^1 = Me 92%
34 M = Ph R^1 = Ph 83%

Scheme 5 *Reagents:* i, $PhMe_2SiZnMe_2$ Li, THF, −78 °C or $PhMe_2SiAlMe_3$ Li, THF, −78 °C; ii, DIBAL-H, toulene, −78 °C; iii, R^{1}Li or R^{1}MgCl, details; iv, PCC, Al_2O_3, light petroleum or CrO_3, Me_2CO

reductions and attack by lithium and Grignard reagents, also recorded in Table 1. We prepared the other two ketones **33** and **34** directly by conjugate addition of the silylzincate to the unsaturated ketones **88** and **89**. We prepared the α,β-unsaturated esters **61**, **62**, **64**, **65**, **67** and **68** by Wittig reaction on the same aldehydes **28**, **32** and **36**, using methanol as a solvent, because it was known to lead to mixtures of the *E* and *Z* isomers (Scheme 6).[26] Since we wanted both, it was easier to separate a mixture than to prepare each individually by stereoselective methods, even though selective methods are available.[27] We prepared the α,β-unsaturated diesters **63**, **66** and **69** by Knoevenagel reaction on the same aldehydes (Scheme 6).[28]

Proof of relative configuration

To assign stereochemistry to the products **26** and **27**, we planned initially to oxidise the phenyl groups in the inseparable mixture of diastereoisomers to the corresponding carboxylic acids,[29] and to esterify them to make the *RR*, *SS* and *RS* isomers of the dicarboxylic esters. The signals of the methylene groups in the ^{1}H NMR spectrum would then have been definitive. However, if one diastereoisomer were to be oxidised



28 M = Me
32 M = Ph
36 M = Pr^i

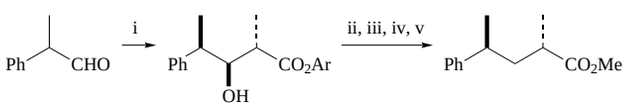
61 M = Me 52%
64 M = Ph 47%
67 M = Pr^i 48%

62 M = Me 31%
65 M = Ph 46%
68 M = Pr^i 39%

63 M = Me 70%
66 M = Ph 85%
69 M = Pr^i 77%

Scheme 6 *Reagents:* i, $Ph_3P{=}CHCO_2Me$, MeOH, 0 °C; ii, $CH_2(CO_2Me)_2$, $(CH_2)_5NH$, AcOH, room temp.

in higher yield than the other, we could easily mis-assign stereochemistry, unless the overall yield were high enough to make the changeover impossible. Unfortunately, we were unable to perform this reaction in the high yield necessary in a case like this, where the diastereoisomers were produced in nearly equal amounts. Instead, we assigned stereochemistry by synthesising an authentic sample of the major isomer **27**, using Heathcock's aldol reaction giving the alcohol **90**, as the major product,[30] and a Barton–McCombie dehydroxylation (Scheme 7).[31]



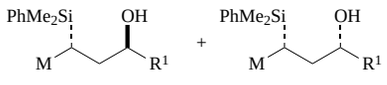
90 57%

27 35%

Scheme 7 *Reagents:* i, $EtCO_2C_6H_3$-2,6-Me_2 + LDA, THF; ii, NaOMe, THF; iii, NaH, CS_2; iv, MeI; v, Bu_3SnH, toluene, reflux

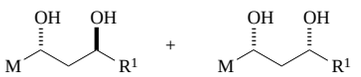
We had already assigned stereochemistry to the pair of alcohols **40**.[18] In order to assign relative stereochemistry to the other pairs of alcohols obtained by the reaction of Grignard and organolithium reagents on the aldehydes **28**, **32** and **36**, we simply converted the silyl groups to hydroxy groups to give the known 1,3-diols **91**–**97** (Scheme 8). The ^{1}H NMR spectra were usually definitive, and we did not need to separate the diastereoisomers either before or after the silyl-to-hydroxy conversion, although we actually did so with the alcohols **44** and **51**. Fortunately, there is some redundancy in the assignments of stereochemistry: the products from the reactions of Grignard or organolithium reagents on the aldehydes are, of course, the same as the products from the reductions of the corresponding ketones. Thus, to take just one example, the alcohol **41A** is the same as the alcohol **44B**. Once we had assigned a configuration to any one pair, we did not need to repeat the degradation, since each pair had at least one pair of signals in either the ^{1}H NMR or the ^{13}C NMR spectrum, or both, that could be integrated to give us the ratio of diastereoisomers. Furthermore, the diols **92** and **94**, derived from the alcohols **45** and **52** are the same as the diols **95** and **96**, derived from the alcohols **57** and **58**, respectively. In this and all our subsequent work, for every pair of compounds and at every stage, we were careful to ensure that the yields were high enough not to have led us to mis-assign stereochemistry because of the selectively higher yielding conversion of a minor diastereoisomer, however unlikely that selectivity might be.

We proved the relative configuration of the tertiary alcohols **46** and **60** by displacing the phenyl group from the silyl



			A:B
44A	M = Me	R^1 = Ph	-
44B	M = Me	R^1 = Ph	-
45	M = Me	R^1 = Pr^i	22:78
51A	M = Ph	R^1 = Ph	-
51B	M = Ph	R^1 = Ph	-
52	M = Ph	R^1 = Pr^i	67:33
57	M = Pr^i	R^1 = Me	33:67
58	M = Pr^i	R^1 = Ph	22:78
59	M = Pr^i	R^1 = Pr^i	23:77

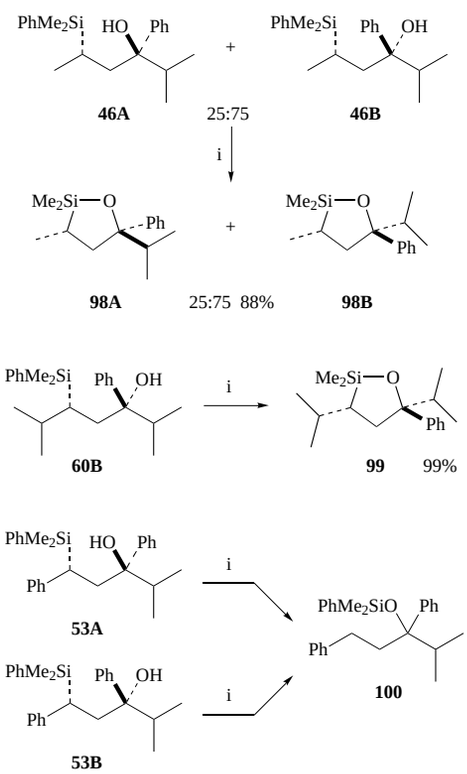
i



			A:B	
91A	M = Me	R^1 = Ph	-	54%
91B	M = Me	R^1 = Ph	-	55%
92	M = Me	R^1 = Pr^i	22:78	55%
93A	M = Ph	R^1 = Ph	-	88%
93B	M = Ph	R^1 = Ph	-	59%
94	M = Ph	R^1 = Pr^i	67:33	74%
95	M = Pr^i	R^1 = Me	33:67	53%
96	M = Pr^i	R^1 = Ph	24:76	57%
97	M = Pr^i	R^1 = Pr^i	23:77	61%

Scheme 8 *Reagents:* i, $Hg(OAc)_2$, AcOOH, AcOH, room temp.

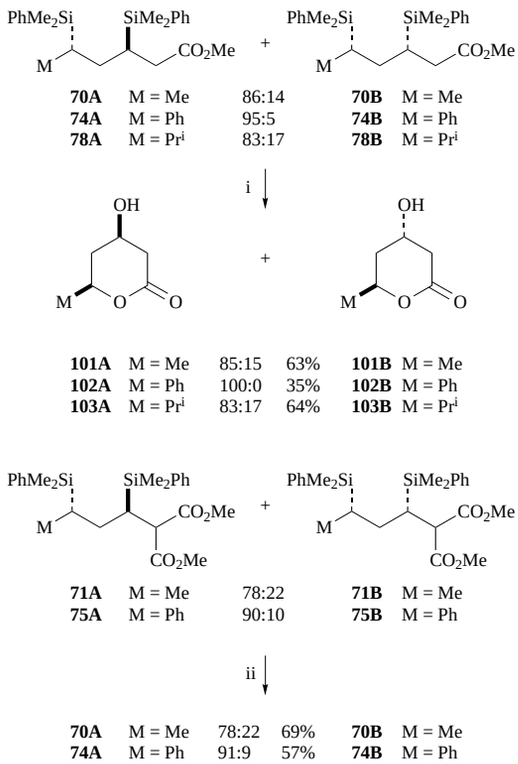
group using the alkoxide derived from the alcohol in a well precedented reaction.[32] The mixture of alcohols **46** gave the mixture of silyl ethers **98**, and the separated alcohol **60B** gave the silyl ether **99** (Scheme 9). The relative stereochemistry of



Scheme 9 *Reagents:* i, NaH, THF, room temp.

these cyclic materials followed from a NOESY experiment. This device did not work for the benzylsilanes **53**, which instead of losing the phenyl group in a 5-*exo*-*tet* reaction, suffered benzylic cleavage in a 5-*endo*-*tet* reaction giving the silyl ether **100** from each of the diastereoisomers. Thus, we were not able easily to determine the sense of attack in the formation of **53A** and **53B**, but with a ratio of only 55:45, this was hardly a critical result.

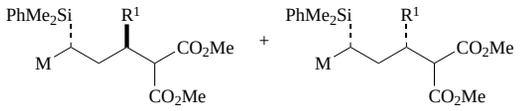
To assign configurations to the products **70**, **74** and **78** from the conjugate additions of the silyl nucleophiles to the α,β-unsaturated esters, we carried out silyl-to-hydroxy conversions, and isolated directly the known lactones **101**–**103** (Scheme 10).



Scheme 10 *Reagents:* i, $Hg(OAc)_2$, AcOOH, AcOH, room temp.; ii, NaCl, H_2O, DMSO, reflux

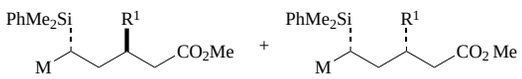
Krapcho reaction[33] on the products **71** and **75** from the conjugate additions of silyl nucleophiles to the α,β-unsaturated diesters gave the mono esters **70** and **74**, to which we had already assigned relative configurations (Scheme 10). Unfortunately, when carried out on the diesters **79**, this reaction did not take place in high enough yield for us to be confident that the major isomer in the starting mixture was still the major isomer in the product mixture. This was made difficult in this case because the ratio of isomers was close to 50:50 (45:55, 53:47, 43:57 and 45:55) with all the silyl nucleophiles. The diesters **79** remain unassigned, both for this reason and because there seemed little point in going to great lengths for such an unselective and inconsistent set of reactions.

Krapcho reaction on the products **72**, **73**, **76**, **77**, **80** and **81** from the conjugate additions of methyl and phenyl nucleophiles to the diesters, followed by silyl-to-hydroxy conversion, gave successively the esters **104**–**109** and the lactones **110**–**115** (Scheme 11). In this case the low yield we experienced in the formation of the mixture of diastereoisomers **108** would have made the assignment ambiguous, so we carried out the conversion on two mixtures with different proportions of diastereoisomers. The products were present in the same proportions in each case, showing that there had not been a selectively more efficient reaction on the minor diastereoisomer. With two of these Krapcho reactions, namely those on the diesters **80** and **81**, we found that using four equivalents of lithium chloride in place of the usual sodium chloride, and adding two equivalents of water, led to significantly shorter reaction times, typically 30 min instead of several hours, for the complete consumption of the starting material, and to cleaner reaction mixtures.



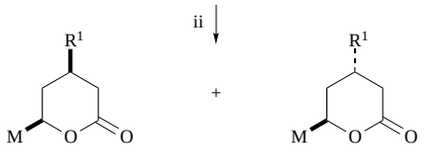
72A	M = Me	R^1 = Me	85:15	**72B**	M = Me	R^1 = Me
73A	M = Me	R^1 = Ph	29:71	**73B**	M = Me	R^1 = Ph
76A	M = Ph	R^1 = Me	81:19	**76B**	M = Ph	R^1 = Me
77A	M = Ph	R^1 = Ph	100:0	**77B**	M = Ph	R^1 = Ph
80A	M = Pr^i	R^1 = Me	64:36	**80B**	M = Pr^i	R^1 = Me
80A	M = Pr^i	R^1 = Me	52:48	**80B**	M = Pr^i	R^1 = Me
81A	M = Pr^i	R^1 = Ph	37:63	**81B**	M = Pr^i	R^1 = Ph

i



104A	M = Me	R^1 = Me	85:15	81%	**104B**	M = Me	R^1 = Me
105A	M = Me	R^1 = Ph	29:71	52%	**105B**	M = Me	R^1 = Ph
106A	M = Ph	R^1 = Me	84:16	71%	**106B**	M = Ph	R^1 = Me
107A	M = Ph	R^1 = Ph	100:0	71%	**107B**	M = Ph	R^1 = Ph
108A	M = Pr^i	R^1 = Me	64:36	68%	**108B**	M = Pr^i	R^1 = Me
108A	M = Pr^i	R^1 = Me	52:48	60%	**108B**	M = Pr^i	R^1 = Me
109A	M = Pr^i	R^1 = Ph	37:63	??%	**109B**	M = Pr^i	R^1 = Ph

ii



110A	M = Me	R^1 = Me	85:15	59%	**110B**	M = Me	R^1 = Me
111A	M = Me	R^1 = Ph	29:71	57%	**111B**	M = Me	R^1 = Ph
112A	M = Ph	R^1 = Me	78:22	67%	**112B**	M = Ph	R^1 = Me
113A	M = Ph	R^1 = Ph	0:100	41%	**113B**	M = Ph	R^1 = Ph
114A	M = Pr^i	R^1 = Me	64:36	65%	**114B**	M = Pr^i	R^1 = Me
115A	M = Pr^i	R^1 = Ph	40:60	83%	**115B**	M = Pr^i	R^1 = Ph

Scheme 11 *Reagents:* i, NaCl or LiCl, H_2O, DMSO, reflux; ii, $Hg(OAc)_2$, AcOOH, AcOH, room temp.

Conclusions

A reliable rule predicting the sense of 1,3-stereocontrol is still not within our grasp. It is possible to make some generalisations that are more often true than not, but a relatively firm prediction is limited only to a small subset of all the reactions that we have investigated: when $R^1 \neq H \neq Ph$, and when $M \neq Ph$, nucleophilic attack takes place on ketone carbonyl groups in the sense **B**, and simple modelling supports this picture. More generally, it is possible to suggest that more often than not, aldehydes and α,β-unsaturated esters with $R^1 = H$ react in the sense **A**, and ketones react in the sense **B**. Notable exceptions to this rule are (i) those reactions in which a lithium reagent is used, for which some but not all the reactions show the opposite sense of stereoselectivity, and (ii) those substrates in which a phenyl group is present either on the stereogenic centre or attached as R^1 to the carbonyl group, which also give inconsistent results not matched to the modelling results.

Experimental

Light petroleum refers to the fraction boiling between 40–60 °C unless otherwise specified. Ether refers to diethyl ether. *J* Values are given in Hz.

Methyl (2*RS*,4*SR*)-2-methyl-4-phenylpentanoate 26 and methyl (2*RS*,4*RS*)-2-methyl-4-phenylpentanoate 27

Butyllithium (1.6 mol dm^{-3} solution in hexanes, 1.43 cm^3, 2.29 mmol) was added dropwise with stirring to diisopropylamine (0.32 cm^3, 2.29 mmol) in THF (20 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 20 min and then cooled to −78 °C. The ester **25** (0.4 g, 2.08 mmol) in THF (20 cm^3) was added dropwise with stirring over 15 min and the mixture kept for a further 1.5 h at this temperature. Methyl iodide (0.39 cm^3, 6.24 mmol) was added to the solution and after 10 min the mixture was allowed to warm to room temperature. Saturated aqueous ammonium chloride (15 cm^3) was added to the mixture followed by dilute hydrochloric acid (30 cm^3). The THF was evaporated under reduced pressure and the residue was extracted with dichloromethane (3 × 50 cm^3). The combined organic extracts were washed with water (100 cm^3), and then brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the *esters* **26** and **27** in a ratio of 44:56. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 15:85) to give a mixture of diastereoisomers of the methylated ester (0.34 g, 80%); ν_{max}(film)/cm^{-1} 1737 (C=O); **26**: δ_H(250 MHz; $CDCl_3$) 7.33–7.09 (5 H, m, Ph), 3.57 (3 H, s, OMe), 2.71 (1 H, m, MeC*H*Ph), 2.41–2.22 (1 H, m, MeO_2CCHMe), 2.05 (1 H, ddd, *J* 13.7, 8.9 and 6.8, CH_AH_B), 1.68–1.54 (1 H, m, CH_AH_B), 1.26 (3 H, d, *J* 6.8, *Me*CHPh) and 1.14 (3 H, d, *J* 6.9, MeO_2CCHMe); **27**: δ_H(250 MHz; $CDCl_3$) 7.33–7.09 (5 H, m, Ph), 3.66 (3 H, s, OMe), 2.71 (1 H, m, MeC*H*Ph), 2.29 (1 H, m, MeO_2CCHMe), 1.98 (1 H, ddd, *J* 13.7, 9.2 and 5.6, CH_AH_B), 1.61 (1 H, ddd, *J* 13.7, 9.5 and 5.2, CH_AH_B), 1.23 (3 H, d, *J* 6.9, *Me*CHPh) and 1.09 (3 H, d, *J* 7.0, MeO_2CCHMe); *m*/*z* (EI) 206 (15%, M^+), 175 (17, M − OMe), 88 (100, M − CH_2CMePh) (Found: M^+, 206.1307. $C_{13}H_{18}O_2$ requires *M*, 206.1307). The ratio of diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum. The above experiment was repeated but the mixture was left for 2 h at −78 °C after addition of methyl iodide and then quenched at this temperature with saturated aqueous ammonium chloride giving the diastereoisomers in the same ratio.

Reaction of methyllithium with aldehydes

Typically, the aldehyde (2.18 mmol) in THF (5 cm^3) was added dropwise to methyllithium (1.4 mol dm^{-3} solution in Et_2O; 2 cm^3, 2.8 mmol) in THF (12 cm^3) at −78 °C under argon. After 1 h, saturated aqueous ammonium chloride (10 cm^3) was added and the mixture allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure to give the mixture of alcohols. The following compounds were prepared by this method.

(2*RS*,4*SR*)-4-Dimethyl(phenyl)silylpentan-2-ol[18] 40A and (2*RS*,4*RS*)-4-dimethyl(phenyl)silylpentan-2-ol 40B. (72%) Separated by chromatography (SiO_2, Et_2O–CH_2Cl_2, 10:90); **40A**: R_F(Et_2O–CH_2Cl_2, 10:90) 0.42; ν_{max}(film)/cm^{-1} 3356 (OH), 1248 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.51 (2 H, m, *o*-Ph), 7.39–7.31 (3 H, m, *m*- and *p*-Ph), 3.89 (1 H, m, C*H*OH), 1.48 (1 H, m, CH_AH_B), 1.22–1.05 (2 H, m, CH_AH_B and SiCH), 1.16 (3 H, d, *J* 6.1, CHOH*Me*), 0.95 (3 H, d, *J* 6.6, SiCH*Me*) and 0.27 (6 H, s, $SiMe_2$); **40B**: R_F(Et_2O–CH_2Cl_2, 10:90) 0.38; ν_{max}(film)/cm^{-1} 3354 (OH), 1249 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.52 (2 H, m, *o*-Ph), 7.41–7.34 (3 H, m, *m*- and *p*-Ph) 3.86 (1 H, m, C*H*OH), 1.77 (1 H, br s, OH), 1.49–1.40 (2 H, m, CH_2), 1.12 (3 H, d, *J* 6.1, CHOH*Me*), 1.00 (1 H, m, SiCH), 0.98 (3 H, d, *J* 1.8, SiCH*Me*), 0.29 (3 H, s, $SiMe_AMe_B$) and 0.28 (3 H, s, $SiMe_AMe_B$). The ratio of the diastereoisomers was determined by integration of the CHOH*Me* signals in the ^{1}H NMR spectrum. The stereochemistry of the alcohols **40** (= **43**) had already been assigned.[18]

(2*RS*,4*RS*)-4-Dimethyl(phenyl)silyl-4-phenylbutan-2-ol 47A and (2*RS*,4*SR*)-4-dimethyl(phenyl)silyl-4-phenylbutan-2-ol 47B. (63%) Separated by chromatography (SiO_2, Et_2O–CH_2Cl_2, 50:50); **47A**: R_F(Et_2O–light petroleum, 50:50) 0.53; δ_H(200 MHz; $CDCl_3$) 7.44–6.94 (10 H, m, 2 × Ph), 3.62 (1 H, m, C*H*OH), 2.62 (1 H, dd, *J* 12.7 and 3.3, C*H*Si), 1.89 (1 H, ddd,

J 14.2, 12.7 and 2.9, CH_ACH$_B$), 1.68 (1 H, m, CH$_A$CH_B), 1.5 (1 H, br s, OH), 1.09 (3 H, d, *J* 6.2, CH*Me*), 0.28 (3 H, s, SiMe_A-Me$_B$), 0.21 (3 H, s, SiMe$_A$$Me_B$); **47B**; R_F(Et$_2$O–light petroleum, 50:50) 0.43; ν_{max}(film)/cm^{-1} 3362 (OH) and 1598 (Ph); δ_H(200 MHz; CDCl$_3$) 7.44–6.94 (10 H, m, 2 × Ph), 3.62 (1 H, m, C*H*OH), 2.29 (1 H, dd, *J* 12.5 and 2.9, C*H*Si), 2.13 (1 H, dt, *J* 12.5 and 4.9, CH_ACH$_B$), 1.68 (1 H, m, CH$_A$CH_B), 1.5 (1 H, br s, OH), 1.07 (3 H, d, *J* 6.2, CH*Me*), 0.28 (3 H, s, SiMe_AMe$_B$), 0.19 (3 H, s, SiMe$_A$$Me_B$). The ratio of the diastereoisomers was determined by integration of the CHSi signals in the ^{1}H NMR spectrum.

(2*RS*,4*RS*)-4-Dimethyl(phenyl)silyl-5-methylhexan-2-ol 54A and (2*RS*,4*SR*)-4-dimethyl(phenyl)silyl-5-methylhexan-2-ol 54B. (65%) R_F(CH$_2$Cl$_2$) 0.25; ν_{max}(film)/cm^{-1} 3404 (OH), 1250 (SiMe) and 1110 (SiPh); δ_H(250 MHz; CDCl$_3$) **54A**: 7.52 (2 H, m, *o*-Ph), 7.38–7.29 (3 H, m, *m*- and *p*-Ph), 3.65 (1 H, m, C*H*OH), 1.94 (1 H, m, C*H*Me$_A$Me$_B$), 1.63–1.36 (2 H, m, CH$_2$), 1.10–0.97 (1 H, m, C*H*Si), 1.03 (3 H, d, *J* 6.0, CH*Me*), 0.95 (3 H, d, *J* 6.9, CH*Me*), 0.84 (3 H, d, *J* 6.9, CH*Me*), 0.32 (3 H, s, SiMe_CMe$_D$) and 0.31 (3 H, s, SiMe$_C$$Me_D$); **54B**: 7.52 (2 H, m, *o*-Ph), 7.38–7.29 (3 H, m, *m*- and *p*-Ph) 3.65 (1 H, m, C*H*OH), 1.94 (1 H, m, C*H*Me$_A$Me$_B$), 1.63–1.36 (2 H, m, CH$_2$), 1.10–0.97 (1 H, m, C*H*Si), 1.09 (3 H, d, *J* 6.1, CH*Me*), 0.94 (3 H, d, *J* 6.9, CH*Me*), 0.85 (3 H, d, *J* 6.9, CH*Me*), 0.33 (6 H, s, SiMe_2); δ_C(CDCl$_3$) **54A**: 139.9, 133.9, 128.8, 127.8, 67.5, 36.6, 29.1, 28.7, 23.8, 22.7, 21.4, −2.9 and −3.1; **54B**: 140.0, 133.8, 128.8, 127.8, 67.6, 36.1, 29.4, 28.9, 23.4, 22.9, 20.9 and −2.1; *m*/*z* (EI) 235 (13%, M$^+$ − Me), 233 (13, M − OH) and 135 (100, Me$_2$PhSi) (Found: M$^+$ − Me, 235.1516. $C_{15}H_{26}OSi$ requires *M* − Me, 235.1518). The ratio of the diastereoisomers was determined by integration of the CH$_2$ signals in the ^{13}C NMR spectrum (36.6 and 36.1 ppm).

Reaction of methylmagnesium bromide with aldehydes

Typically, the aldehyde (1.9 mmol) in THF (5 cm^3) was added dropwise to a stirred solution of methylmagnesium bromide (3 mol dm^{-3} solution in Et$_2$O, 0.95 cm^3, 2.85 mmol) in THF (12 cm^3) at 0 °C under argon. After 2 h, the mixture was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added, and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with brine, dried (MgSO$_4$) and evaporated under reduced pressure to give the alcohols. The alcohols **40** (36%), **47** (60%) and **54** (64%), identical with the earlier samples, were prepared by this method.

Reaction of methylmagnesium iodide with the aldehyde 28

The aldehyde **28** (0.39 g, 1.89 mmol) in ether (12 cm^3) was added to methylmagnesium iodide (2.83 mmol) freshly prepared in ether (40 cm^3) over 10 min at 0 °C, and the mixture kept for 1 h. An aqueous work-up, as for the reaction with the bromide, and chromatography gave each of the diastereoisomers of the alcohols **40** (0.27 g, 64%).

Reaction of phenyllithium with aldehydes and ketones

Typically, the aldehyde (1.89 mmol) in THF (5 cm^3) was added dropwise to a stirred solution of phenyllithium (1.8 mol dm^{-3} solution in cyclohexane–Et$_2$O, 70:30; 1.4 cm^3, 2.52 mmol) in THF (12 cm^3) at −78 °C under argon. After 1 h (aldehydes) or 3–10 h (ketones), the reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with brine, dried (MgSO$_4$) and evaporated under reduced pressure to give a mixture of alcohols. The following compounds were prepared by this method.

(1*RS*,3*RS*)-3-Dimethyl(phenyl)silyl-1-phenylbutan-1-ol 41A and (1*RS*,3*SR*)-3-dimethyl(phenyl)silyl-1-phenylbutan-1-ol 41B. (73%) Separated by chromatography (SiO$_2$, CH$_2$Cl$_2$); **41A**: R_F(CH$_2$Cl$_2$) 0.30; ν_{max}(film)/cm^{-1} 3380 (OH), 1248 (SiMe) and 1111 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.43–7.19 (10 H, m, Ph), 4.69 (1 H, dd, *J* 8.5 and 6.0, PhC*H*OH), 1.86 (1 H, ddd, *J* 13.5, 8.5 and 3.8, CH_AH$_B$), 1.67 (1 H, ddd, *J* 13.5, 10.3 and 6.0, CH$_A$$H_B$), 1.02 (3 H, d, *J* 7.3, *Me*CHSi), 0.71 (1 H, m, MeC*H*Si), 0.23 (3 H, s, SiMe_AMe$_B$) and 0.21 (3 H, s, SiMe$_A$$Me_B$); δ_C(CDCl$_3$) 144.2, 138.2, 134.0, 129.0, 128.5, 127.8, 127.3, 126.6, 73.9, 40.7, 15.7, 14.6, −4.6 and −5.4; *m*/*z* (EI) 269 (3%, M$^+$ − Me) and 135 (44, Me$_2$PhSi) (Found: M$^+$ − Me, 269.1363. $C_{18}H_{24}OSi$ requires *M* − Me, 269.1362); **41B**: R_F(CH$_2$Cl$_2$) 0.37; ν_{max}(film)/cm^{-1} 3414 (OH), 1248 (SiMe) and 1112 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.53–7.47 (2 H, m, Ph), 7.38–7.21 (8 H, m, Ph), 4.77 (1 H, dd, *J* 10.0 and 2.8, PhC*H*OH), 1.85 (1 H, ddd, *J* 13.5, 10.0 and 2.2, CH_AH$_B$), 1.41 (1 H, ddd, *J* 13.5, 11.6 and 2.8, CH$_A$$H_B$), 1.29 (1 H, m, MeC*H*Si), 1.03 (3 H, d, *J* 6.9, *Me*CHSi), 0.27 (3 H, s, SiMe_AMe$_B$) and 0.26 (3 H, s, SiMe$_A$$Me_B$); δ_C(CDCl$_3$) 145.7, 138.1, 134.0, 128.9, 128.5, 127.8, 127.3, 125.9, 71.6, 41.4, 14.6, 13.6 and −5.0 ; *m*/*z* (EI) 269 (5%, M$^+$ − Me), 177 (56, PhCHOH) and 135 (100, Me$_2$PhSi) (Found: M$^+$ − Me, 269.1346. $C_{18}H_{24}OSi$ requires *M* − Me, 269.1362). The ratio of the diastereoisomers was determined by integration of the PhC*H*OH signals in the ^{1}H NMR spectrum.

(1*RS*,3*SR*)-3-Dimethyl(phenyl)silyl-1,3-diphenylpropan-1-ol 48A and (1*RS*,3*RS*)-3-dimethyl(phenyl)silyl-1,3-diphenylpropan-1-ol 48B. (70%) Separated by chromatography (SiO$_2$, CH$_2$Cl$_2$–light petroleum, 80:20); **48A**: R_F(CH$_2$Cl$_2$–light petroleum, 80:20) 0.33; ν_{max}(film)/cm^{-1} 3600 (OH) and 1600 (Ph); δ_H(400 MHz; CDCl$_3$) 7.4–7.0 (15 H, m, 3 × Ph), 4.47 (1 H, dd, *J* 10 and 2.5, C*H*OH), 2.8 (1 H, dd, *J* 12.7 and 3.3, C*H*Si), 2.12 (1 H, ddd, *J* 14.5, 12.7 and 2.5, CH_ACH$_B$), 2.03 (1 H, ddd, *J* 14.5, 10 and 3.3, CH$_A$CH_B), 1.8 (1 H, br s, OH), 0.3 (3 H, s, SiMe_AMe$_B$) and 0.2 (3 H, s, SiMe$_A$$Me_B$); δ_C(400 MHz; CDCl$_3$) 145.5, 142.1, 137.2, 134.2, 129.1, 128.4, 128.3, 127.7, 127.3, 125.5, 124.9, 71.7, 39.3, 32.7, −4.0 and −5.1 (Found: M$^+$, 346.1747; C, 79.6; H, 7.5%. $C_{23}H_{26}OSi$ requires *M*, 346.1753; C, 79.7; H, 7.6%); **48B**: R_F(CH$_2$Cl$_2$–light petroleum, 80:20) 0.21; ν_{max}(film)/cm^{-1} 3600 (OH) and 1600 (Ph); δ_H(400 MHz; CDCl$_3$) 7.35–6.9 (15 H, m, 3 × Ph), 4.42 (1 H, dd, *J* 9.5 and 4.9, C*H*OH), 2.4 (1 H, ddd, *J* 13.5, 12.6 and 4.9, CH_ACH$_B$), 2.06 (1 H, ddd, *J* 13.5, 9.5 and 3, CH$_A$CH_B), 1.91 (1 H, dd, *J* 12.6 and 3, C*H*Si), 1.73 (1 H, br s, OH), 0.2 (3 H, s, SiMe_AMe$_B$) and 0.08 (3 H, s, SiMe$_A$$Me_B$); δ_C(CDCl$_3$) 143.6, 142.2, 137.03, 134.1, 129.1, 128.4, 128.3, 128.02, 127.8, 127.6, 126.6, 124.8, 74.2, 38.2, 32.8, −4.0 and −5.6 (Found: C, 79.6; H, 7.7. $C_{23}H_{26}OSi$ requires C, 79.7; H, 7.6%).

(1*RS*,3*SR*)-3-Dimethyl(phenyl)silyl-4-methyl-1-phenylpentan-1-ol 55A and (1*RS*,3*RS*)-3-dimethyl(phenyl)silyl-4-methyl-1-phenylpentan-1-ol 55B. (74%) Separated by chromatography (SiO$_2$, CH$_2$Cl$_2$–light petroleum, 80:20); R_F(CH$_2$Cl$_2$–light petroleum, 80:20) 0.33; ν_{max}(film)/cm^{-1} 3422 (OH) and 1492 (Ph); **55A**: δ_H(400 MHz; CDCl$_3$) 7.57–7.14 (10 H, m, 2 × Ph), 4.55 (1 H, t, *J* 6.9, C*H*OH), 2.00 (1 H, dseptet, *J* 3.0 and 6.9, C*H*Me$_2$), 1.80 (2 H, t, *J* 6.6, CH_ACH_B), 1.61 (1 H, br s, OH), 1.11 (1 H, dt, *J* 3.0 and 6.3, C*H*Si), 0.89 (3 H, d, *J* 6.9, CHMe_AMe$_B$), 0.87 (3 H, d, *J* 6.9, CHMe$_A$$Me_B$), 0.38 (3 H, s, Si$Me_AMe_B$) and 0.36 (3 H, s, SiMe$_A$$Me_B$); **55B**: δ_H(400 MHz; CDCl$_3$) 7.57–7.14 (10 H, m, 2 × Ph), 4.50 (1 H, dd, *J* 8.0 and 6.0, C*H*OH), 2.04 (1 H, m, C*H*Me$_2$), 1.92–1.7 (3 H, m, C$H_A$$H_B$ and C*H*Si), 1.61 (1 H, br s, OH), 1.02 (6 H, d, *J* 6.8, CH$Me_A$$Me_B$), 0.33 (3 H, s, Si$Me_AMe_B$) and 0.31 (3 H, s, SiMe$_A$$Me_B$); δ_C(CDCl$_3$) 145.1, 139.9, 134.0, 128.9, 128.4, 127.8, 126.0, 73.9, 36.5, 28.8, 22.5, 21.3, −2.1 and −2.9 (Found: M$^+$ − Me, 297.1668. $C_{20}H_{28}OSi$ requires *M* − Me, 297.1675).

(3*RS*,5*SR*)-5-Dimethyl(phenyl)silyl-2-methyl-3-phenylhexan-3-ol 46A and (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2-methyl-3-phenylhexan-3-ol 46B. (71%) Separated by chromatography (SiO$_2$, Et$_2$O–light petroleum, 10:90); R_F(Et$_2$O–light petroleum,

10:90) 0.30; ν_{max}(film)/cm^{-1} 3591 (OH), 1248 (SiMe) and 1111 (SiPh); **46A**: δ_H(400 MHz; $CDCl_3$) 7.52–7.45 (2 H, m, Ph), 7.39–7.23 (6 H, m, Ph), 7.22–7.12 (2 H, m, Ph), 2.02–1.86 (2 H, m, CH_AH$_B$ and CHMe$_A$Me$_B$), 1.66 (1 H, dd, *J* 14.6 and 10.9, CH$_A$$H_B$), 1.02 (1 H, m, C$H$Si), 1.00 (3 H, d, *J* 7.3, CHMe), 0.94 (3 H, d, *J* 7.6, CHMe), 0.58 (3 H, d, *J* 6.8, CHMe), 0.20 (3 H, s, SiMe_CMe$_D$) and 0.17 (3 H, s, SiMe$_C$$Me_D$); δ_C(400 MHz; $CDCl_3$) 145.5, 138.2, 128.8, 127.9, 127.7, 126.0, 125.8, 81.6, 40.8, 39.0, 17.6, 16.5, 15.6, 15.0, −4.8 and −5.6; **46B**: δ_H(400 MHz; $CDCl_3$) 7.52–7.45 (2 H, m, Ph), 7.39–7.23 (6 H, m, Ph), 7.22–7.12 (2 H, m, Ph), 2.11 (1 H, dd, *J* 14.6 and 3.2, CH_AH$_B$), 1.95 (1 H, m, CHMe$_A$Me$_B$), 1.60 (1 H, dd, *J* 14.6 and 7.8, CH$_A$$H_B$), 0.95 (1 H, m, C$H$Si), 0.81 (3 H, d, *J* 6.7, CHMe), 0.58 (3 H, d, *J* 6.8, CHMe), 0.53 (3 H, d, *J* 7.3, CHMe), 0.25 (3 H, s, SiMe_A-Me$_B$) and 0.23 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 145.6, 138.5, 134.0, 129.0, 127.7, 127.5, 125.9, 78.9, 41.3, 38.0, 17.6, 16.6, 16.2, 13.5, −4.5 and −5.6; *m*/*z* (EI) 283 (7%, M$^+$ − Pr^i), 135 (100, Me$_2$PhSi) (Found: M$^+$ − Pr^i, 283.1524. $C_{21}H_{30}OSi$ requires *M* − Pr^i, 283.1518). The ratio of the diastereoisomers was determined by integration of the CH_2 signals (41.3 and 40.8 ppm) in the ^{13}C NMR spectrum.

(1*RS*,3*RS*)-1-Dimethyl(phenyl)silyl-1,3-diphenyl-4-methylpentan-3-ol 53A and (1*RS*,3*SR*)-1-dimethyl(phenyl)silyl-1,3-diphenyl-4-methylpentan-3-ol 53B. (65%) chromatography (SiO_2, Et_2O–light petroleum, 10:90) gave complete separation of the *alcohols*; **minor isomer**: R_F(Et_2O–light petroleum, 10:90) 0.40; ν_{max}(film)/cm^{-1} 3576 (OH), 1249 (SiMe) and 1113 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.47–6.80 (15 H, m, Ph), 2.47 (1 H, dd, *J* 14.7 and 12.2), 2.17 (1 H, dd, *J* 14.7 and 1.0), 1.93 (1 H, dd, *J* 12.3 and 1.0), 1.80 (1 H, septet, *J* 6.7, CHMe$_A$Me$_B$), 0.90 (3 H, d, *J* 6.7, CHMe_AMe$_B$), 0.53 (3 H, d, *J* 6.8, CHMe$_A$$Me_B$), 0.22 (3 H, s, Si$Me_CMe_D$) and −0.01 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 145.6, 142.8, 137.1, 134.2, 129.2, 128.8, 128.1, 127.7, 126.1, 126.0, 125.3, 82.0, 38.8, 38.5, 31.9, 17.5, 16.7, −4.1 and −6.0; *m*/*z* (EI) 371 (23%, M$^+$ − OH), 345 (45, M − Pr^i) and 135 (100, Me$_2$PhSi) (Found: M$^+$ − OH, 371.2190. $C_{26}H_{32}SiO$ requires *M* − OH, 371.2195); **major isomer**: ν_{max}(film)/cm^{-1} 3581 (OH), 1263 (SiMe) and 1113 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.44–6.67 (15 H, m, Ph), 2.42–2.24 (3 H, m, PhCHSi, CH_AH$_B$ and CH$_A$$H_B$), 1.93 (1 H, septet, *J* 6.8, CHMe$_A$Me$_B$), 0.73 (3 H, d, *J* 6.7, CHMe_AMe$_B$), 0.53 (3 H, d, *J* 6.9, CHMe$_A$$Me_B$), 0.23 (3 H, s, Si$Me_CMe_D$) and 0.07 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 144.5, 144.1, 137.6, 134.2, 129.2, 128.8, 128.0, 127.9, 127.2, 126.1, 126.0, 124.1, 79.8, 40.1, 31.2, 17.6, 16.6, −3.9 and −5.7; *m*/*z* (EI) 371 (35%, M$^+$ − OH), 345 (28, M − Pr^i) and 135 (100, Me$_2$PhSi) (Found: M$^+$ − OH, 371.2167. $C_{26}H_{32}SiO$ requires *M* − OH, 371.2195). The ratio of the diastereoisomers was determined by integration of the CH_2 signals (40.1 to 38.5 ppm) in the ^{13}C NMR spectrum.

(3*RS*,5*RS*)-5-Dimethyl(phenyl)silyl-2,6-dimethyl-3-phenylheptan-3-ol 60A and (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-2,6-dimethyl-3-phenylheptan-3-ol 60B. (60%) Chromatography (SiO_2, Et_2O–light petroleum, 5:95) gave the major *alcohol* **60B**; R_F(Et_2O–light petroleum, 5:95) 0.32; ν_{max}(film)/cm^{-1} 3584 (OH), 1248 (SiMe) and 1108 (SiPh); **60A**: δ_H(400 MHz; $CDCl_3$) (some signals) 7.51–7.09 (10 H, m, Ph), 2.22 (1 H, m, CHMe$_A$Me$_B$), 0.95 (3 H, d, *J* 6.7, CHMe), 0.94 (3 H, d, *J* 7.0, CHMe), 0.71 (3 H, d, *J* 7.1, CHMe), 0.55 (3 H, d, *J* 6.9, CHMe), 0.20 (3 H, s, SiMe_CMe$_D$) and 0.19 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) (some signals) 81.0, 38.6, 37.5, 29.1, 29.0, 23.3, 20.9, 16.4, 1.0 and −0.88; **60B**: δ_H(400 MHz; $CDCl_3$) 7.51–7.09 (10 H, m, Ph), 2.05 (1 H, dd, *J* 14.6 and 6.9, CH_AH$_B$), 1.95 (1 H, septet, *J* 6.8, CPhOHCHMe$_A$Me$_B$), 1.75 (1 H, dd, *J* 14.6 and 4.0, CH$_A$$H_B$), 1.45 (1 H, dseptet, *J* 2.3 and 6.9, CHMe$_C$Me$_D$-CHSi), 0.83–0.77 (1 H, m, CHSi), 0.80 (3 H, d, *J* 4.0, CHMe), 0.67 (3 H, d, *J* 6.9, CHMe), 0.66 (3 H, d, *J* 7.0, CHMe), 0.50 (3 H, d, *J* 6.8, CHMe), 0.38 (3 H, s, SiMe_EMe$_F$) and 0.29 (3 H, s, SiMe$_E$$Me_F$); δ_C($CDCl_3$) 145.4, 140.3, 134.2, 128.9, 128.0, 127.4, 125.9, 79.0, 41.4, 38.3, 36.3, 30.0, 26.5, 21.8, 21.2, 17.7, 16.5, −0.78 and −2.78; *m*/*z* (EI) 311 (8%, M$^+$ − Pr^i), 135 (100, Me$_2$PhSi) (Found: M$^+$ − Pr^i, 311.1814. $C_{23}H_{34}SiO$ requires *M* − Pr^i, 311.1831). The ratio of the diastereoisomers was determined by integration of the CH_2 signals (37.5 to 36.3 ppm) in the ^{13}C NMR spectrum.

Reaction of phenylmagnesium bromide with aldehydes and ketones

Typically, the aldehyde (1.89 mmol) in THF (5 cm^3) was added dropwise with stirring to a solution of phenylmagnesium bromide (3 mol dm^{-3} solution in Et_2O; 0.82 cm^3, 2.46 mmol) in THF (12 cm^3) at 0 °C under argon. After 1 h at 0 °C, the reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of alcohols. The alcohols **41** (67%), **46** (60%), **48** (70%) and **55** (60%), identical with the earlier samples, were prepared by this method.

Reaction of isopropylmagnesium chloride with aldehydes

Typically, the aldehyde (30.6 mmol) in THF (20 cm^3) was added dropwise with stirring to a solution of isopropylmagnesium chloride (2.0 mol dm^{-3} solution in Et_2O; 23.0 cm^3, 46.0 mmol) in THF (60 cm^3) at 0 °C under argon. After 2 h at 0 °C, the mixture was quenched by addition of saturated aqueous ammonium chloride (20 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (50 cm^3) was added and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3) and the combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of the alcohols. The following compounds were prepared by this method.

(3*RS*,5*RS*)-5-Dimethyl(phenyl)silyl-2-methylhexan-3-ol 42A and (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-2-methylhexan-3-ol 42B. (60%) Chromatography (SiO_2, Et_2O–light petroleum, 30:70) gave the *alcohols* as a mixture; R_F(Et_2O–light petroleum, 30:70) 0.32; ν_{max}(film)/cm^{-1} 3398 (OH), 1249 (SiMe) and 1112 (SiPh); **42A**: δ_H(400 MHz; $CDCl_3$) 7.51 (2 H, m, *o*-Ph), 7.38–7.31 (3 H, m, *m*- and *p*-Ph), 3.43 (1 H, m, CHOH), 1.57 (1 H, m), 1.46 (1 H, m), 1.30–1.10 (2 H, m), 0.98 (3 H, d, *J* 6.9, *Me*CH), 0.89 (3 H, d, *J* 6.8, *Me*CH), 0.87 (3 H, d, *J* 6.9, *Me*CH), 0.28 (3 H, s, SiMe_AMe$_B$) and 0.27 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 138.3, 134.0, 128.9, 127.7, 73.5, 35.6, 34.2, 18.9, 17.6, 14.6, 13.4, −5.0 and −5.1; **42B**: δ_H(400 MHz; $CDCl_3$) 7.51 (2 H, m, *o*-Ph), 7.38–7.31 (3 H, m, *m*- and *p*-Ph), 3.43 (1 H, m, CHOH), 1.68–1.60 (1 H, m), 1.30–1.10 (2 H, m), 1.02–0.85 (7 H, m, 2 × *Me*CH and CHSi), 0.75 (3 H, d, *J* 6.8, *Me*CH) and 0.29–0.27 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 138.5, 133.9, 128.9, 127.7, 75.7, 36.9, 31.9, 19.4, 16.5, 15.5, 15.3, −4.6 and −4.7; *m*/*z* (EI) 235 (27%, M$^+$ − Me) and 135 (100, Me$_2$PhSi) (Found: M$^+$ − Me, 235.1517. $C_{15}H_{26}SiO$ requires *M* − Me, 235.1518). The ratio of the diastereoisomers was found by integration of the CH_2 signals (36.9 and 35.6 ppm) in the ^{13}C NMR spectrum.

(3*RS*,5*SR*)-5-Dimethyl(phenyl)silyl-2-methyl-5-phenylpentan-3-ol 49A and (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2-methyl-5-phenylpentan-3-ol 49B. (60%) Chromatography (SiO_2, Et_2O–light petroleum, 30:70) gave the *alcohols* as a mixture; R_F(Et_2O–light petroleum, 30:70) 0.27; ν_{max}(film)/cm^{-1} 3422 (OH), 1249 (SiMe) and 1113 (SiPh); **49A**: δ_H(400 MHz; $CDCl_3$) 7.42–6.88 (10 H, m, Ph), 3.09 (1 H, m, CHOH), 2.61 (1 H, dd, *J* 13.1 and 3.0, PhCHSi), 1.98–1.83 and 1.67–1.46 (3 H, m), 0.81 (3 H, d, *J* 6.7, CHMe_AMe$_B$), 0.80 (3 H, d, *J* 6.6, CHMe$_A$$Me_B$), 0.24 (3 H, s, Si$Me_CMe_D$) and 0.18 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 142.3, 137.4, 134.2, 129.2, 128.3, 128.1, 127.7, 124.6, 74.0, 34.0, 33.3, 32.1, 18.7, 17.7, −4.0 and −5.2; **49B**: δ_H(400 MHz; $CDCl_3$) 7.42–6.88 (10 H, m, Ph), 3.30 (1 H, m, CHOH), 2.27 (1 H, dd, *J* 10.5 and 4.7, PhCHSi), 1.98–1.83 (2 H, m),

1.67–1.46 (1 H, m), 0.78 (3 H, d, *J* 6.8, CH*Me*$_A$Me$_B$), 0.73 (3 H, d, *J* 6.8, CHMe$_A$*Me*$_B$), 0.25 (3 H, s, Si*Me*$_C$Me$_D$) and 0.16 (3 H, s, SiMe$_C$*Me*$_D$); δ_C($CDCl_3$) 142.9, 137.3, 134.1, 129.0, 128.2, 127.9, 127.6, 124.8, 76.6, 34.5, 34.0, 31.5, 19.3, 15.4, −3.9 and −5.6; *m*/*z* (EI) 269 (52%, $M^+ - Pr^i$) and 135 (92, Me_2PhSi) (Found: $M^+ - Pr^i$, 269.1357. $C_{20}H_{28}SiO$ requires $M - Pr^i$, 269.1362). The ratio of the diastereoisomers was found by integration of the C*H*OH signals in the ^{1}H NMR spectrum.

(3*RS*,5*SR*)-5-Dimethyl(phenyl)silyl-2,6-dimethylheptan-3-ol 56A and (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2,6-dimethylheptan-3-ol 56B. (68%) Chromatography (SiO_2, Et_2O–light petroleum, 20:80) gave the *alcohols* as a mixture; R_F(Et_2O–light petroleum, 20:80) 0.27; ν_{max}(film)/cm^{-1} 3440 (OH), 1248 (SiMe) and 1109 (SiPh); **56A**: δ_H(400 MHz; $CDCl_3$) 7.52 (2 H, m, *o*-Ph), 7.36–7.29 (3 H, m, *m*- and *p*-Ph), 3.31 (1 H, m, C*H*OH), 2.02–1.89 (1 H, m, C*H*Me$_A$Me$_B$), 1.60–1.47 (2 H, m), 1.32 (1 H, ddd, *J* 14.5, 9.4 and 4.1), 1.11 (1 H, ddd, *J* 8.8, 4.0 and 3.2), 0.93 (3 H, d, *J* 6.9, CH*Me*), 0.87 (3 H, d, *J* 7.0, CH*Me*), 0.83 (3 H, d, *J* 7.3, CH*Me*), 0.81 (3 H, d, *J* 7.1, CH*Me*) and 0.32 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 139.9, 133.9, 128.8, 127.8, 75.8, 33.7, 31.4, 28.9, 28.8, 21.8, 18.9, 16.9, −2.0 and −3.0; **56B**: δ_H(400 MHz; $CDCl_3$) 7.52 (2 H, m, *o*-Ph), 7.36–7.29 (3 H, m, *m*- and *p*-Ph), 3.15 (1 H, m, C*H*OH), 2.02–1.89 (1 H, m, C*H*Me$_A$Me$_B$), 1.60–1.49 (2 H, m), 1.47–1.38 (1 H, m), 1.09–1.04 (1 H, m), 0.95 (3 H, d, *J* 6.9, CH*Me*), 0.86–0.78 (6 H, m, 2 × CH*Me*), 0.73 (3 H, d, *J* 6.8, CH*Me*) and 0.34–0.30 (6 H, m, $SiMe_2$); δ_C($CDCl_3$) 139.9, 133.8, 128.8, 127.8, 75.7, 33.4, 30.5, 28.9, 22.9, 20.7, 19.0, 16.6, −2.0 and −3.0 (Found: C 73.4; H 10.8. $C_{17}H_{30}SiO$ requires C, 73.3; H 10.9%). The ratio of the diastereoisomers was found by integration of the C*H*OH signals in the ^{1}H NMR spectrum.

Reduction of ketones with lithium aluminium hydride

Typically, the ketone (0.682 mmol) in dry ether (15 cm^3) was added with stirring to a suspension of lithium aluminium hydride (0.026 g, 0.682 mmol) in dry ether (40 cm^3) at −78 or −55 °C under argon. After 1 h, the reaction was quenched with methanol (10 cm^3) and the mixture allowed to warm to room temperature. The resulting turbid solution was shaken vigorously with saturated aqueous potassium sodium tartrate (25 cm^3), and the aqueous layer was extracted with ether (3 × 25 cm^3). The combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the alcohols. The pairs of alcohols **43** (=**40**) (86%), **44** (=**41**) (86%), **45** (=**42**) (79%), **50** (=**47**) (81%), **51** (=**48**) (96%), **52** (=**49**) (66%), **57** (=**54**) (78%), **58** (=**55**) (70%) and **59** (=**56**) (76%), identical with the earlier samples, were prepared by this method.

Reduction of ketones with sodium borohydride

Typically, the ketone (0.397 mmol) in ethanol (10 cm^3) was added with stirring to a suspension of sodium borohydride (0.105 g, 2.78 mmol) in ethanol (20 cm^3) at 0 °C or room temperature. After 2 h, the reaction was quenched with dilute hydrochloric acid (15 cm^3). The solvent was evaporated under reduced pressure, the residue taken up into water (50 cm^3) and extracted with ether (3 × 50 cm^3). The combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the alcohols. The pairs of alcohols **43** (=**40**) (97%),[18] **44** (=**41**) (90%), **45** (=**42**) (78%), **50** (=**47**) (85%), **51** (=**48**) (96%), **52** (=**49**) (81%), **57** (=**54**) (58%), **58** (=**55**) (51%) and **59** (=**56**) (73%), identical with the earlier samples, were prepared by this method.

Reduction of ketones with lithium tri-*tert*-butoxyaluminium hydride

Typically, the ketone (0.605 mmol) in THF (10 cm^3) was added with stirring to a solution of lithium tri-*tert*-butoxyaluminium hydride (1.0 mol dm^{-3} solution in THF; 0.85 cm^3, 0.85 mmol) in THF (20 cm^3) at 0 °C under argon. After 1 h, the reaction was allowed to warm to room temperature, and after 24 h, the mixture was quenched with dilute hydrochloric acid (10 cm^3). The resulting turbid solution was shaken vigorously with saturated aqueous potassium sodium tartrate (50 cm^3), and the aqueous layer was extracted with ether (3 × 50 cm^3). The combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of the alcohols. The pairs of alcohols **45** (=**42**) (77%), **52** (=**49**) (70%) and **59** (=**56**) (71%), identical with the earlier samples, were prepared by this method.

Reduction of the ketone 31 with sodium Selectride

The ketone **31** (0.108 g, 0.435 mmol) in THF (10 cm^3) was added with stirring to a solution of N-Selectride (1.0 mol dm^{-3} solution in THF; 0.60 cm^3, 0.60 mmol) in THF (20 cm^3) at 0 °C under argon. The mixture was stirred for 8 h and then quenched with methanol (10 cm^3). The mixture was allowed to warm to room temperature and the solvent was removed under reduced pressure. Light petroleum (40 cm^3) was added to the residue and the mixture was cooled to 0 °C. Aqueous sodium hydroxide (1 mol dm^{-3}; 0.6 cm^3) was added to the stirred mixture, followed by hydrogen peroxide (30% in water; 2 cm^3). After 30 min the mixture was allowed to warm to room temperature and stirred for a further hour. Water (50 cm^3) was added to the mixture and the organic layer was separated off. The aqueous layer was extracted with ether (3 × 50 cm^3) and the combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and the solvent was evaporated under reduced pressure to give a mixture of the alcohols **45A** and **45B** (0.058 g, 53%) after chromatography (SiO_2, Et_2O–light petroleum, 30:70).

Reaction of lithium bis[dimethyl(phenyl)silyl]cuprate with α,β-unsaturated esters and diesters

Typically, dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF; 3.9 cm^3, 3.9 mmol) was added to a stirred suspension of copper(I) cyanide (0.18 g, 2.0 mmol) in THF (15 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 45 min and then cooled to −78 °C. A solution of the α,β-unsaturated ester or diester (1.54 mmol) in THF (5 cm^3) was added dropwise over 5 min. After stirring for 1 h, the reaction was quenched with saturated aqueous basic ammonium chloride (10 cm^3) and allowed to warm to room temperature. The residue was extracted with ether (3 × 25 cm^3). The combined organic fractions were washed with basic ammonium chloride solution until the washings were no longer blue, then washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 10:90) to give the mixtures of β-silyl esters. The following compounds were prepared by this method.

Methyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]hexanoate 70A and methyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]-hexanoate 70B. (71:29, 84% from **61**) (A mixture varying from 71:29 to 86:14 from **62**); R_F(Et_2O–light petroleum, 10:90) 0.34; ν_{max}(film)/cm^{-1} 1737 (C=O) and 1589 (Ph); **70A**: δ_H(400 MHz; $CDCl_3$) 7.47–7.30 (10 H, m, 2Ph), 3.49 (3 H, s, OMe), 2.23 (1 H, dd, *J* 15.4 and 7.1, C*H*$_A$CH$_B$CO$_2$Me), 2.18 (1 H, dd, *J* 15.4 and 6.1, CH$_A$C*H*$_B$CO$_2$Me), 1.54 (1 H, dddd, *J* 11.3, 7.1, 6.1 and 2.8, CH$_2$C*H*SiCH$_2$), 1.37 (1 H, ddd, *J* 14.0, 11.3 and 2.6, CSiC*H*$_A$CH$_B$CSi), 1.24 (1 H, ddd, *J* 14.0, 11.0 and 2.8, CSiCH$_A$-C*H*$_B$CSi), 0.87 (1 H, m, MeC*H*Si), 0.83 (3 H, d, *J* 5.7, *Me*CH-Si), 0.25 (3 H, s, Si*Me*$_A$Me$_B$), 0.24 [3 H, s, SiMe$_{A(or\ D)}$*Me*$_{B(or\ C)}$] and 0.21 (6 H, s, SiMe$_{C+D}$ or SiMe$_A$*Me*$_B$ + SiMe$_C$*Me*$_D$); δ_C($CDCl_3$) 174.7, 138.3, 137.8, 134.0 (2 C), 133.9 (2 C), 129.0, 128.8, 127.7 (2 C), 127.6 (2 C), 51.3, 33.9, 31.3, 18.6, 16.2, 13.0, −4.5, −4.6, −5.1 and −5.2; **70B:** δ_H(400 MHz; $CDCl_3$) 3.56 (3 H, s, OMe), 2.34 (1 H, dd, *J* 15.4 and 9.2, C*H*$_A$CH$_B$CO$_2$Me), 2.11 (1 H, dd, *J* 15.4 and 5.3, CH$_A$C*H*$_B$CO$_2$Me), 1.66 (1 H, m, CH$_2$C*H*SiCH$_2$), 0.22 (3 H, s, Si*Me*$_A$Me$_B$), 0.21 [3 H, s, SiMe$_{A(or\ D)}$*Me*$_{B(or\ C)}$], 0.18 [3 H, s, Si*Me*$_{C(or\ B\ or\ D)}$Me$_{D(or\ A\ or\ C)}$] and 0.17 [3 H, s, SiMe$_{C(or\ A)}$*Me*$_{D(or\ B)}$]; δ_C($CDCl_3$) 174.4, 138.4, 138.1, 129.0, 127.8, 36.3, 32.9, 20.7, 18.5, 14.3, −4.0 and −4.1

(Found: C, 69.4; H, 8.6. $C_{23}H_{34}O_2Si_2$ requires C, 69.3; H, 8.6%). The ratio of the diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum.

Ethyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]hexanoate and ethyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]hexanoate. (86:14, 46%); R_F(Et$_2$O–light petroleum, 10:90) 0.34; ν_{max}(film)/cm^{-1} 1733 (C=O) and 1589 (Ph); major isomer (3*RS*,5*RS*): δ_H(400 MHz; $CDCl_3$) 7.48–7.30 (10 H, m, 2 × Ph), 3.98 (1 H, dq, *J* 14.4 and 7.2, OCH_AH$_B$CH$_3$), 3.95 (1 H, dq, *J* 14.4 and 7.2, OCH$_A$$H_BCH_3$), 2.23 (1 H, dd, *J* 15.6 and 7.0, CH_ACH$_B$CO), 2.16 (1 H, dd, *J* 15.6 and 6.1, CH$_A$CH_BCO), 1.55 (1 H, m, CH$_2$C*H*SiCH$_2$), 1.38 (1 H, ddd, *J* 13.9, 11.5 and 2.6, CSiCH_A-CH$_B$CSi), 1.24 (1 H, ddd, *J* 13.9, 11.1 and 2.8, CSiCH$_A$CH_B-CSi), 1.18 (3 H, t, *J* 7.2, OCH$_2$CH_3), 0.90 (1 H, m, CH$_3$C*H*Si), 0.83 (3 H, d, *J* 6.4, H_3CCHSi), 0.252 (3 H, s, SiMe_AMe$_B$), 0.250 [3 H, s, SiMe$_{A(or\ D)}$$Me_{B(or\ C)}$] and 0.22 (6 H, s, SiMe$_{C+D}$ or SiMe$_A$$Me_B$ + SiMe$_C$$Me_D$); δ_C($CDCl_3$) 174.3, 138.3, 137.9, 134.0 (2 C), 133.9 (2 C), 128.9, 128.8, 127.7 (2 C), 127.6 (2 C), 60.2, 34.2, 31.4, 18.5, 16.2, 14.2, 13.0, −4.5, −4.5, −5.0 and −5.2; minor isomer (3*RS*,5*SR*): δ_H(400 MHz; $CDCl_3$) 4.02 (2 H, q, *J* 7.1, OCH_2CH$_3$), 2.34 (1 H, dd, *J* 15.3 and 4.7, CH_ACH$_B$CO), 2.09 (1 H, dd, *J* 15.3 and 9.4, CH$_A$CH_BCO), 1.19 (3 H, t, *J* 7.1, OCH$_2$$CH_3$), 0.23 (3 H, s, Si$Me_AMe_B$), 0.22 [3 H, s, SiMe$_{A(or\ D)}$ $Me_{B(or\ C)}$], 0.17 [3 H, s, Si$Me_{C(or\ B\ or\ D)}$Me$_{D(or\ A\ or\ C)}$] and 0.16 [3 H, s, SiMe$_{C(or\ A)}$$Me_{D(or\ B)}$]; δ_C($CDCl_3$) 127.7, 36.5, 32.8, 20.6, 18.6 and −4.0 (Found: M$^+$, 412.2255. $C_{24}H_{36}O_2Si_2$ requires *M*, 412.2231). The ratio of the diastereoisomers was determined by integration of the SiMe signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]-2-methoxycarbonylhexanoate 71A and methyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]-2-methoxycarbonylhexanoate 71B. (75%); R_F(Et$_2$O–light petroleum, 20:80) 0.38; ν_{max}(film)/cm^{-1} 1735 (C=O) and 1589 (Ph); **71A**: δ_H(400 MHz; $CDCl_3$) 7.53–7.29 (10 H, m, 2Ph), 3.55 (3 H, s, OMe), 3.55 [1 H, d, *J* 5, C*H*(CO$_2$Me)$_2$], 3.54 (3 H, s, OMe), 1.88 (1 H, m, CH$_2$C*H*SiCH), 1.45 (1 H, ddd, *J* 14.5, 11.6 and 2.7, CSiCH_ACH$_B$CSi), 1.23 (1 H, ddd, *J* 14.5, 11.6 and 3.0, CSiCH$_A$CH_BCSi), 0.86 (1 H, m, MeC*H*Si), 0.74 (3 H, d, *J* 7.1, *Me*CHSi), 0.28 (3 H, s, SiMe_AMe$_B$), 0.27 [3 H, s, SiMe$_{A(or\ D)}$$Me_{B(or\ C)}$], 0.195 [3 H, s, Si$Me_{C(or\ B\ or\ D)}Me_{D(or\ A\ or\ C)}$] and 0.190 [3 H, s, SiMe$_{C(or\ A)}$-$Me_{D(or\ B)}$]; δ_C($CDCl_3$) 170.4, 170.3, 138.8, 138.1, 134.2 (2 C), 133.9 (2 C), 128.8 (2 C), 127.6 (2 C), 127.5 (2 C), 52.2, 52.0, 51.1, 29.6, 23.1, 16.0, 12.8, −2.9, −4.2, −5.21 and −5.24; **71B**: δ_H(400 MHz; $CDCl_3$) 3.61 (3 H, s, OMe), 3.56 (3 H, s, OMe), 3.47 [1 H, d, *J* 5.1, C*H*(CO$_2$Me)$_2$], 1.82 (1 H, m, CH$_2$C*H*SiCH$_2$), 1.09 (1 H, ddd, *J* 13.3, 10 and 3.6, CSiCH$_A$CH_BCSi), 0.78 (3 H, d, *J* 6.4, *Me*CHSi), 0.26 (3 H, s, SiMe_AMe$_B$), 0.22 [3 H, s, SiMe$_{A(or\ D)}$$Me_{B(or\ C)}$], 0.15 [3 H, s, Si$Me_{C(or\ B\ or\ D)}Me_{D(or\ A\ or\ C)}$] and 0.14 [3 H, s, SiMe$_{C(or\ A)}$$Me_{D(or\ B)}$]; δ_C($CDCl_3$) 170.0, 138.2, 134.1, 128.9, 127.7, 53.6, 30.6, 18.1, 13.7, −3.5, −5.1 and −5.3 (Found: M$^+$, 456.2149. $C_{25}H_{36}O_4Si_2$ requires *M*, 456.2152). The ratio of the diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]-5-phenylpentanoate 74A and methyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]-5-phenylpentanoate 74B. (59% from **64**, 73% from **65**); R_F(Et$_2$O–light petroleum, 8:92) 0.28; ν_{max}(film)/cm^{-1} 1736 (C=O) and 1599 (Ph); **74A**: δ_H(400 MHz; $CDCl_3$) 7.40–6.60 (15 H, m, 3 × Ph), 3.4 (3 H, s, OMe), 2.38 (1 H, dd, *J* 12.8 and 3, PhC*H*Si), 2.28 (1 H, dd, *J* 15.0 and 6.4, CH_AH$_B$CO$_2$Me), 2.14 (1 H, dd, *J* 15 and 5.8, CH$_A$$H_BCO_2$Me), 1.95 (1 H, ddd, *J* 14.6, 12.8 and 2.4, CSiCH_AH$_B$CSi), 1.6 (1 H, ddd, *J* 14.6, 11.6 and 3, CSiCH$_A$$H_B$CSi), 1.18 (1 H, m, CH$_2$C*H*SiCH$_2$), 0.21 (3 H, s, Si$Me_AMe_B$), 0.20 (3 H, s, SiMe$_A$$Me_B$), 0.16 (3 H, s, Si$Me_CMe_D$) and 0.13 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 174.2, 141.6, 137.8, 137.3, 134.1, 134.0, 128.9, 128.2, 127.9, 127.8, 127.6, 127.5, 124.5, 51.1, 33.7, 33.3, 28.5, 19.8, −4.1, −4.4, −5.0 and −5.4; **74B**: δ_H(400 MHz; $CDCl_3$) 7.4–6.6 (15 H, m, 3 × Ph), 3.52 (3 H, s, OMe), 2.28 (1 H, dd, *J* 9.9 and 4.7, PhC*H*Si), 2.07 (1 H, dd, *J* 15.2 and 7.5, CH_AH$_B$CO$_2$Me), 2.04 (1 H, dd, *J* 15.2 and 9.8, CH$_A$$H_BCO_2$Me), 1.84–1.81 (2 H, m, CSiC$H_A$$H_B$CSi), 1.35 (1 H, m, CH$_2$C*H*SiCH$_2$), 0.18 (3 H, s, SiMe$_A$$Me_B$), 0.14 (3 H, s, Si$Me_CMe_D$) and 0.03 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 174.0, 142.2, 138.2, 137.4, 134.1, 134.0, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 124.4, 51.2, 36.3, 36.0, 29.9, 21.5, −3.7, −4.3, −4.6 and −5.8 (Found: M$^+$, 460.2244. $C_{28}H_{36}O_2Si_2$ requires *M*, 460.2254). The ratio of the diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]-2-methoxycarbonyl-5-phenylpentanoate 75A and methyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]-2-methoxycarbonyl-5-phenylpentanoate 75B. (81%); R_F(Et$_2$O–light petroleum, 10:90) 0.21; ν_{max}(film)/cm^{-1} 1735 (C=O), 1598 (Ph); **75A**: δ_H(400 MHz; $CDCl_3$) 7.42–6.5 (15 H, m, 3 × Ph), 3.57 [1 H, d, *J* 2.8, C*H*(CO$_2$Me)$_2$], 3.53 (3 H, s, OMe), 3.49 (3 H, s, OMe), 2.33 (1 H, dd, *J* 12.6 and 2.3, PhC*H*Si), 2.00–1.90 (1 H, m, CH_AH$_B$), 1.60–1.55 [2 H, m, CH$_A$$H_B$ and SiC*H*CH(CO$_2$Me)$_2$], 0.26 (3 H, s, SiMe_AMe$_B$), 0.21 (3 H, s, SiMe$_A$$Me_B$), 0.14 (3 H, s, Si$Me_C$-Me$_D$) and 0.11 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 170.4, 170.1, 140.7, 138.7, 137.2, 134.2, 134.1, 129.0, 128.8, 128.0, 127.8, 127.5, 124.6, 52.1, 51.9, 50.5, 33.2, 27.1, 23.6, −2.8, −4.1, −4.7 and −5.5; **75B**: δ_H(400 MHz; $CDCl_3$) 7.42–6.50 (15 H, m, 3 × Ph), 3.57 (3 H, s, OMe), 3.55 (3 H, s, OMe), 3.4 [1 H, d, *J* 4.5, C*H*(CO$_2$Me)$_2$], 2.14 (1 H, ddd, *J* 10.7, 5.9 and 2.2, CH_AH$_B$), 2.11 (1 H, dd, *J* 12.7 and 2.2, PhC*H*Si), 2.00–1.90 (1 H, m, CH$_A$$H_B$), 1.60–1.55 [1 H, m, SiC*H*CH(CO$_2$Me)$_2$], 0.20 (3 H, s, SiMe_AMe$_B$), 0.17 (3 H, s, SiMe$_A$$Me_B$), 0.15 (3 H, s, Si$Me_CMe_D$) and 0.04 (3 H, s, SiMe$_C$$Me_D$) (Found: M$^+$, 518.2308. $C_{30}H_{38}O_4Si_2$ requires *M*, 518.2308). The ratio of the diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]-6-methylheptanoate 78A and methyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]-6-methylheptanoate 78B. (71% from **67**, 68% from **68**); R_F(Et$_2$O–light petroleum, 5:95) 0.28; ν_{max}(film)/cm^{-1} 1736 (C=O), 1249 (SiMe) and 1111 (SiPh); **78A**: δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, m, *o*-Ph), 7.37–7.27 (3 H, m, *m*- and *p*-Ph), 3.48 (3 H, s, OMe), 2.11 (1 H, dd, *J* 15.7 and 6.8, CH_AH$_B$-CO$_2$Me), 2.02 (1 H, dd, *J* 15.6 and 5.9, CH$_A$$H_BCO_2$Me), 1.88 (1 H, dseptet, *J* 2.6 and 6.7, Me$_A$Me$_B$C*H*CHSi), 1.54–1.12 (3 H, m), 0.94–0.83 (1 H, m), 0.80 (3 H, d, *J* 6.5, Me_AMe$_B$CHCHSi), 0.77 (3 H, d, *J* 6.6, Me$_A$$Me_B$CHCHSi), 0.27 (3 H, s, SiMe), 0.25 (3 H, s, SiMe) and 0.23 (6 H, s, 2 × SiMe); δ_C($CDCl_3$) 174.6, 140.0, 137.8, 134.0, 133.9, 129.0, 128.6, 127.7, 127.6, 51.4, 34.1, 30.4, 28.1, 27.8, 22.9, 21.1, 20.1, −1.8, −2.7, −4.5 and −4.6; **78B**: δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, m, *o*-Ph), 7.37–7.27 (3 H, m, *m*- and *p*-Ph), 3.51 (3 H, s, OMe), 2.25 (1 H, dd, *J* 15.6 and 6.3, CH_AH$_B$CO$_2$Me), 2.14 (1 H, dd, *J* 15.7 and 6.9, CH$_A$$H_B$-CO$_2$Me), 1.88 (1 H, m, Me$_AMe_B$C*H*CHSi), 1.54–1.12 and 0.94–0.83 (4 H, m), 0.84 (3 H, d, *J* 6.9, Me_AMe$_B$CHCHSi), 0.68 (3 H, d, *J* 6.8, Me$_A$$Me_B$CHCHSi), 0.23 (3 H, s, SiMe), 0.22 (3 H, s, SiMe), 0.16 (3 H, s, SiMe) and 0.15 (3 H, s, SiMe); δ_C($CDCl_3$) 174.5, 140.0, 137.8, 134.0, 133.9, 129.0, 128.6, 127.7, 127.6, 51.4, 35.1, 31.2, 28.3, 26.9, 21.7, 21.4, 20.9, −1.8, −2.7, −4.4 and −4.6; *m*/*z* (EI) 426 (8%, M$^+$), 411 (35, M − Me) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 426.2426. $C_{25}H_{38}O_2Si$ requires *M*, 426.2410). The ratio of diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*RS*)-3,5-bis[dimethyl(phenyl)silyl]-2-methoxycarbonyl-6-methylheptanoate 79A and methyl (3*RS*,5*SR*)-3,5-bis[dimethyl(phenyl)silyl]-2-methoxycarbonyl-6-methylheptanoate 79B. (82%); R_F(Et$_2$O–light petroleum, 15:85) 0.28; ν_{max}(film)/cm^{-1} 1752 (C=O), 1736 (C=O), 1248 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) major isomer: 7.54–7.27 (10 H, m, Ph), 3.66 (3 H, s, OMe), 3.53 (3 H, s, OMe), 3.50 [1 H, m, C*H*(CO$_2$Me)$_2$], 1.92–1.06 (4 H, m), 0.91 (1 H, m), 0.86–0.57 (6 H, m, Me_AMe$_B$CH and Me$_A$$Me_B$CH), 0.28 (3 H, s, SiMe), 0.25 (3 H, s, SiMe), 0.23 (3 H, s, SiMe) and 0.18 (3 H, s, SiMe); δ_C($CDCl_3$) 52.3 (OMe), 52.1 (OMe) and 24.9 (CH$_2$); minor isomer: δ_H(250 MHz; $CDCl_3$) 7.54–7.27 (10 H, m, Ph), 3.55 (3 H, s,

OMe), 3.50 [1 H, m, C*H*($CO_2Me)_2$], 3.48 (3 H, s, OMe), 1.92–1.06 (4 H, m), 0.91 (1 H, m), 0.86–0.57 (6 H, m, $Me_A$$Me_B$CH and $Me_A$$Me_B$CH), 0.31 (3 H, s, SiMe), 0.27 (3 H, s, SiMe), 0.26 (3 H, s, SiMe) and 0.23 (3 H, s, SiMe); δ_C($CDCl_3$) 52.1 (OMe), 50.8 (OMe) and 26.2 (CH_2); *m*/*z* (EI) 484 (4%, M^+), 469 (20, M − Me), 425 (18, M − CO_2Me) and 135 (100, Me_2PhSi) (Found: M^+, 484.2445. $C_{27}H_{40}O_4Si_2$ requires *M*, 484.2465). The ratio of diastereoisomers was determined by integration of the OMe signals in the ^{1}H NMR spectrum or the CH_2 signals in the ^{13}C NMR spectrum.

Reaction of lithium dimethyl[dimethyl(phenyl)silyl]zincate with α,β-unsaturated esters and diesters

Typically, dimethyl(phenyl)silyllithium (1.05 mol dm^{-3} solution in THF; 2.5 cm^3, 2.6 mmol) was added to a stirred solution of dimethylzinc (2.0 mol dm^{-3} solution in toluene; 1.3 cm^3, 2.6 mmol) in THF (15 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 10 min and then cooled to −78 °C. A solution of the α,β-unsaturated ester or diester (2.1 mmol) in THF (5 cm^3) was added dropwise over 5 min. After stirring for 1 h, the reaction was quenched carefully by dropwise addition of saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (20 cm^3) was added to dissolve the precipitated zinc salts, and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3), the combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum 10:90) to give a mixture of the *disilyl esters*. The pairs of esters **70** (84% from **61**, variable yield from **62**), the corresponding ethyl esters (75:25, 60% from the *E* starting material), **71** (81%), **74** (83% from **64**, 76% from **65**), **75** (65%), **78** (74% from **67**, 68% from **68**) and **79** (74%), identical with the earlier samples, were prepared by this method. Similarly, the following esters and ketones were prepared by this method.

Ethyl 3-dimethyl(phenyl)silylbutanoate[34] 85. (96% on a 32 mmol scale); R_F(Et_2O–light petroleum, 10:90) 0.35; ν_{max}(film)/cm^{-1} 1734 (C=O), 1251 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.49 (2 H, m, *o*-Ph), 7.38–7.31 (3 H, m, *m*- and *p*-Ph), 4.08 (2 H, q, *J* 7.1, OCH_2Me), 2.39 (1 H, dd, *J* 15.2 and 4.1, CH_ACH_B), 2.05 (1 H, dd, *J* 15.2 and 11.2, CH_ACH_B), 1.46 (1 H, m, C*H*SiC$H_A$$H_B$), 1.23 (3 H, t, *J* 7.1, OCH_2*Me*), 0.98 (3 H, d, *J* 7.3, *Me*CHSi) and 0.29 (6 H, s, $SiMe_2$).

Ethyl 3-dimethyl(phenyl)silyl-3-phenylpropanoate[35] 86. (98% on a 31 mmol scale); R_F(Et_2O–light petroleum, 10:90) 0.37; ν_{max}(film)/cm^{-1} 1740 (C=O) and 1599 (Ph); δ_H(200 MHz; $CDCl_3$) 7.48–6.99 (10 H, m, 2 × Ph), 3.50 (3 H, s, OMe), 2.96–2.64 (3 H, m, SiC*H* and CH_2CO), 0.30 (3 H, s, Si$Me_A$$Me_B$) and 0.26 (3 H, s, SiMe$_A$$Me_B$).

4-Dimethyl(phenyl)silyl-4-phenylbutan-2-one[36] 33. (92%); R_F(CH_2Cl_2–light petroleum, 80:20) 0.39; ν_{max}(film)/cm^{-1} 1718 (C=O) and 1599 (Ph); δ_H(200 MHz; $CDCl_3$) 7.45–6.93 (10 H, m, 2 × Ph), 3.00–2.60 (3 H, m, SiC*H* and CH_2CO), 1.96 (3 H, s, MeCO), 0.27 (3 H, s, Si$Me_A$$Me_B$) and 0.23 (3 H, s, SiMe$_A$$Me_B$).

3-Dimethyl(phenyl)silyl-1,3-diphenylpropan-1-one[36] 34. (83%) Mp 67–69 °C; R_F(Et_2O–light petroleum, 15:85) 0.3; ν_{max}(film)/cm^{-1} 1687 (C=O) and 1597 (Ph); δ_H(200 MHz; $CDCl_3$) 7.83–6.98 (15 H, m, 3 × Ph), 3.51 (1 H, dd, *J* 17.0 and 10.0, SiC*H*), 3.28–3.1 (2 H, m, CH_2CO), 0.32 (3 H, s, Si$Me_A$$Me_B$) and 0.26 (3 H, s, SiMe$_A$$Me_B$).

Reaction of lithium trimethyl[dimethyl(phenyl)silyl]aluminate with α,β-unsaturated esters and the diester 69

Typically, dimethyl(phenyl)silyllithium (1.2 mol dm^{-3} solution in THF; 1.15 cm^3, 1.38 mmol) was added with stirring to a solution of trimethylaluminium (2.0 mol dm^{-3} solution in hexanes; 0.35 cm^3, 0.70 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 15 min and then cooled to −78 °C. The α,β-unsaturated ester or diester (0.63 mmol) in THF (20 cm^3) was added dropwise over 5 min, and the mixture kept for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (50 cm^3) was added and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3), washed with brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and chromatographed (SiO_2, Et_2O–light petroleum, 5:95) to give a mixture of the esters. The pairs of esters **78** (63% from **67**, 66% from **68**) and **79** (68%), identical with the earlier samples, were prepared by this method. Similarly, the following *ester* was prepared by this method.

Ethyl 3-dimethyl(phenyl)silyl-4-methylpentanoate 87. (80% on 28 mmol scale); R_F(Et_2O–light petroleum, 5:95) 0.25; ν_{max}(film)/cm^{-1} 1735 (C=O), 1250 (SiPh) and 1111 (SiMe); δ_H(250 MHz; $CDCl_3$) 7.52 (2 H, m, *o*-Ph), 7.38–7.30 (3 H, m, *m*- and *p*-Ph), 4.01 (2 H, q, *J* 7.1, OCH_2Me), 2.37 (1 H, dd, *J* 15.9 and 7.7, CH_ACH_B), 2.28 (1 H, dd, *J* 15.9 and 6.2, CH_ACH_B), 1.91 (1 H, m, C*H*Me$_A$Me$_B$), 1.51 (1 H, ddd, *J* 7.6, 6.2 and 3.9, C*H*SiC$H_A$$H_B$), 1.20 (3 H, t, *J* 7.1, *Me*CH_2O), 0.91 (3 H, d, *J* 6.8, CHMe_AMe$_B$), 0.83 (3 H, d, *J* 6.9, CHMe$_A$$Me_B$), 0.33 (3 H, s, Si$Me_CMe_D$) and 0.32 (3 H, s, SiMe$_C$$Me_D$); δ_C($CDCl_3$) 174.7, 138.8, 133.9, 128.9, 127.7, 60.3, 31.9, 29.2, 28.8, 22.8, 20.9, 14.2, −2.6 and −3.0; *m*/*z* (EI) 278 (M^+, 4%), 263 (M − Me, 69) and 135 (Me_2PhSi, 100) (Found: M^+, 278.1706. $C_{16}H_{26}O_2Si$ requires *M*, 278.1702).

Reaction of dimethyl(phenyl)silyllithium with α,β-unsaturated diesters

Typically, dimethyl(phenyl)silyllithium (0.94 mol dm^3 solution in THF; 0.67 cm^3, 0.633 mmol) in THF (30 cm^3) was added dropwise over 5 min with stirring to a solution of diester (0.575 mmol) in THF (20 cm^3) under argon at −78 °C, and the mixture kept for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (15 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (50 cm^3) was added and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3), washed with brine (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure, and chromatographed (SiO_2, Et_2O–light petroleum, 15:85) to give the mixtures of β-silyl diesters. The pairs of esters **71** (42%), **75** (87%) and **79** (61%), identical with the earlier samples, were prepared by this method.

Reaction of methyllithium with α,β-unsaturated diesters

Typically, the diester (1.56 mmol) in THF (15 cm^3) was added dropwise with stirring to a solution of methyllithium (1.4 mol dm^{-3} solution in ether; 1.45 cm^3, 2.03 mmol) in THF (60 cm^3) at −78 °C under argon, and the mixture kept for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give the mixtures of diesters. The following compounds were prepared by this method.

Methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-3-methylhexanoate 72A and methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-3-methylhexanoate 72B. (25%); R_F(Et_2O–light petroleum, 25:75) 0.33; ν_{max}(CH_2Cl_2)/cm^{-1} 1737 (C=O), 1249 (SiMe) and 1112 (SiPh); **72A**: δ_H(400 MHz; $CDCl_3$) 7.48 (2 H, m, *o*-Ph), 7.40–7.28 (3 H, m, *m*- and *p*-Ph), 3.69 (3 H, s, OMe), 3.62 (3 H, s, OMe), 3.38 [1 H, d, *J* 5.8, C*H*(CO_2Me)$_2$], 2.34 (1 H, m), 1.51 (1 H, m), 1.08 (1 H, m), 0.98 [3 H, d, *J* 6.8, *Me*CHCH(CO_2Me)$_2$], 0.92 (3 H, d, *J* 1.8, *Me*CHSi), 0.91 (1 H, m), 0.26 (3 H, s, Si$Me_A$$Me_B$) and 0.25 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 169.8, 169.0, 138.2, 134.0,

128.9, 127.7, 54.8, 52.3, 51.9, 36.9, 31.9, 17.9, 16.7, 14.5 and −5.0; **72B**: δ_H(400 MHz; $CDCl_3$) 7.48 (2 H, m, *o*-Ph), 7.40–7.28 (3 H, m, *m*- and *p*-Ph), 3.69 (3 H, s, OMe), 3.67 (3 H, s, OMe), 3.16 [1 H, d, *J* 8.6, C*H*(CO_2Me)$_2$], 2.34 (1 H, m), 1.30–1.16 (2 H, m), 0.92 (3 H, d, *J* 1.8, *Me*CHSi), 0.88 [3 H, d, *J* 5.6, *Me*CH-CH(CO_2Me)$_2$], 0.81 (1 H, m), 0.26 (3 H, s, Si$Me_A$$Me_B$) and 0.24 (3 H, s, SiM$e_A$$Me_B$); δ_C($CDCl_3$) 169.8, 169.2, 138.2, 133.9, 128.9, 127.7, 58.4, 52.3, 52.0, 35.9, 31.1, 17.9, 16.0, 13.0 and −5.3; *m*/*z* (EI) 336 (9%, M^+), 321 (27, M − Me) and 135 (100, Me_2PhSi) (Found: M^+, 336.1756. $C_{18}H_{28}O_4Si$ requires *M*, 336.1757). The ratio of diastereoisomers was determined by integration of the C*H*(CO_2Me)$_2$ signals in the ^{1}H NMR spectrum. In addition to the esters **72** produced from 1,4-addition of methyllithium to **63**, 1,2-addition also occurred to give the tertiary alcohol 1,1-*dimethyl*-5-*dimethyl*(*phenyl*)*silyl*-2-*methoxycarbonylhex*-2-*en*-1-*ol* (18%); R_F(Et_2O–light petroleum, 25:75) 0.12; ν_{max}(film)/cm^{-1} 3448 (OH), 1719 (C=O), 1648 (C=C), 1249 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.49 (2 H, m, *o*-Ph), 7.39–7.31 (3 H, m, *m*- and *p*-Ph), 5.93 (1 H, dd, *J* 7.7 and 7.3, C*H*CCO_2Me), 3.67 (3 H, s, OMe), 2.32 (1 H, ddd, *J* 14.9, 7.3 and 4.4, C$H_A$$H_B$), 2.04 (1 H, ddd, *J* 14.9, 8.8 and 7.7, C$H_A$$H_B$), 1.34 (6 H, s, C$Me_2$OH), 0.98 (1 H, m, MeC*H*Si), 0.95 (3 H, d, *J* 5.1, *Me*CHSi), 0.27 (3 H, s, Si$Me_A$$Me_B$) and 0.26 (3 H, s, SiM$e_A$$Me_B$); δ_C($CDCl_3$) 169.8, 139.6, 138.2, 135.0, 134.0, 129.0, 127.9, 71.7, 51.3, 31.5, 29.3, 29.2, 20.2, 14.3, −4.6 and −5.3; *m*/*z* (EI) 305 (29%, M^+ − Me), 302 (56, M − H_2O), 135 (100, Me_2PhSi) (Found: M^+ − H_2O, 302.1688. $C_{18}H_{28}O_3Si$ requires *M* − H_2O, 302.1702).

Methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-3-methyl-5-phenylpentanoate 76A and methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-3-methyl-5-phenylpentanoate 76B. (67%); R_F(Et_2O–light petroleum, 10:90) 0.20; ν_{max}(film)/cm^{-1} 1735 (C=O), 1598 (Ph); from which **76A** could be separated after a second chromatography stage as cubes, mp 72–74 °C (from light petroleum); δ_H(400 MHz; $CDCl_3$) 7.40–6.90 (10 H, m, 2 × Ph), 3.59 (3 H, s, OMe), 3.58 (3 H, s, OMe), 3.36 [1 H, d, *J* 5.9, C*H*(CO_2Me)$_2$], 2.30 (1 H, dd, *J* 11.6 and 3.6, C*H*Si), 2.15 (1 H, m, C*H*Me), 1.84 (1 H, ddd, *J* 14.5, 11.6 and 5.4, C$H_A$$H_B$), 1.74 (1 H, ddd, *J* 14.5, 8.3 and 3.6, C$H_A$$H_B$), 0.87 (3 H, d, *J* 6.8, *Me*CH), 0.23 (3 H, s, Si$Me_A$$Me_B$) and 0.15 (3 H, s, SiM$e_A$$Me_B$); δ_C($CDCl_3$) 169.4, 169.0, 142.3, 137.2, 134.1, 129.0, 128.2, 127.8, 127.6, 124.7, 54.3, 52.1, 51.9, 34.2, 34.1, 32.8, 17.7, −4.1 and −5.5; **76B**: 7.4–6.9 (10 H, m, 2 × Ph), 3.70 (3 H, s, OMe), 3.6 (3 H, s, OMe), 3.16 [1 H, d, *J* 8.0, C*H*(CO_2Me)$_2$], 2.37 (1 H, dd, *J* 13.2 and 3.2, C*H*Si), 2.09 (1 H, m, C*H*Me), 1.99 (1 H, dt, *J* 2.9 and 13.5, C$H_A$$H_B$), 1.42 (1 H, ddd, *J* 13.9, 11.0 and 3.2, C$H_A$$H_B$), 0.82 (3 H, d, *J* 6.7, CH*Me*) and 0.21 (6 H, s, Si$Me_A$$Me_B$) (Found: M^+, 398.1912. $C_{23}H_{30}O_4Si$ requires *M*, 398.1913). The ratio of the diastereoisomers was determined by integration of the C*H*(CO_2Me)$_2$ signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*RS*)-3,6-dimethyl-5-dimethyl(phenyl)silyl-2-methoxycarbonylheptanoate 80A and methyl (3*RS*,5*SR*)-3,6-dimethyl-5-dimethyl(phenyl)silyl-2-methoxycarbonylheptanoate 80B. (28%); R_F(Et_2O–light petroleum, 15:85) 0.23; ν_{max}(CH_2Cl_2)/cm^{-1} 1750 (C=O), 1736 (C=O), 1249 (SiMe) and 1110 (SiPh); **80A**: δ_H(250 MHz; $CDCl_3$) 7.51 (2 H, m, *o*-Ph), 7.37–7.29 (3 H, m, *m*- and *p*-Ph), 3.71 (3 H, s, OMe), 3.65 (3 H, s, OMe), 3.22 [1 H, d, *J* 6.9, C*H*(CO_2Me)$_2$], 2.19 (1 H, m), 1.93 (1 H, m), 1.46 (1 H, m, C$H_A$$H_B$), 1.28 (1 H, m, C$H_A$$H_B$), 1.11 (1 H, m, C*H*Si), 0.94–0.73 (9 H, m, 3 × CH*Me*), 0.34 (3 H, s, Si$Me_A$$Me_B$) and 0.32 (3 H, s, SiM$e_A$$Me_B$); δ_C($CDCl_3$) 169.5, 169.0, 139.3, 133.9, 128.7, 127.7, 57.0, 52.3, 52.2, 32.7, 30.9, 30.0, 28.6, 22.5, 20.6, 16.8, −2.5 and −2.6; **80B**: δ_H(250 MHz; $CDCl_3$) 7.51 (2 H, m, *o*-Ph), 7.37–7.29 (3 H, m, *m*- and *p*-Ph), 3.69 (3 H, s, OMe), 3.68 (3 H, s, OMe), 3.15 [1 H, d, *J* 8.0, C*H*(CO_2Me)$_2$], 2.19 (1 H, m), 1.93 (1 H, m), 1.46 (1 H, m, C$H_A$$H_B$), 1.28 (1 H, m, C$H_A$$H_B$), 0.96 (1 H, m, C*H*Si), 0.94–0.73 (9 H, m, 3 ×CH*Me*), 0.31 (3 H, s, Si$Me_A$$Me_B$) and 0.29 (3 H, s, SiM$e_A$$Me_B$); δ_C($CDCl_3$) 169.3, 169.1, 139.2, 133.9, 128.7, 127.7, 57.7, 52.2, 52.1, 32.6, 32.0, 30.0, 28.4, 22.2, 21.9, 16.5, −1.9 and −3.0; *m*/*z* (EI) 364 (12%, M^+), 349 (52, M − Me) and 135 (100, Me_2PhSi) (Found: M^+, 364.2069. $C_{20}H_{32}O_4Si$ requires *M*, 364.2070). The ratio of diastereoisomers was determined by integration of the C*H*(CO_2Me)$_2$ signals in the ^{1}H NMR spectrum.

Reaction of methylmagnesium bromide with α,β-unsaturated diesters

Typically, the diester (1.56 mmol) in THF (10 cm^3) was added dropwise with stirring to a solution of methylmagnesium bromide (3 mol dm^{-3} in Et_2O; 0.7 cm^3, 2.03 mmol) in THF (60 cm^3) at 0 °C under argon and the mixture kept for 2 h. The reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give mixed diesters. The pairs of esters **72** (23%), **76** (58%) and **80** (57%), identical with the earlier samples, were prepared by this method. A by-product in the reaction with the ester **63** was the deconjugated starting material *methyl* 5-*dimethyl*(*phenyl*)*silyl*-2-*methoxycarbonylhex*-3-*enoate* (47%); R_F(Et_2O–light petroleum, 15:85) 0.20; ν_{max}(CH_2Cl_2)/cm^{-1} 1738 (C=O), 1652 (C=C), 1250 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.47 (2 H, m, *o*-Ph), 7.39–7.30 (3 H, m, *m*- and *p*-Ph), 5.70 (1 H, dd, *J* 15.5 and 7.6, CHSiC*H*), 5.44 [1 H, ddd, *J* 15.5, 8.9 and 1.3, C*H*CH(CO_2Me)$_2$], 4.00 [1 H, d, *J* 8.9, C*H*(CO_2Me)$_2$], 3.74 (3 H, s, OMe), 3.73 (3 H, s, OMe), 1.88 (1 H, ddq, *J* 7.6, 1.3 and 7.1, MeC*H*Si), 1.06 (3 H, d, *J* 7.1, *Me*CHSi), 0.26 (3 H, s, SiMe_A-Me_B) and 0.25 (3 H, s, SiM$e_A$$Me_B$); δ_C($CDCl_3$) 169.0, 139.8, 137.3, 134.0, 129.1, 127.8, 117.5, 55.6, 52.6, 26.3, 13.3, −5.1 and −5.3; *m*/*z* (EI) 320 (28%, M^+), 261 (92, M − CO_2Me), 135 (97, Me_2PhSi) (Found: M^+, 320.1446. $C_{17}H_{24}SiO_4$ requires *M*, 320.1444). This compound could also be made deliberately (85%) by treating the diester **63** (4.7 mmol) with DABCO (4.7 mmol) in dichloromethane (50 cm^3) at room temperature for 24 h.

Reaction of lithium trimethylzincate with α,β-unsaturated diesters

Typically, methyllithium (1.4 mol dm^{-3} solution in Et_2O; 1.0 cm^3, 1.40 mmol) was added with stirring to a solution of dimethylzinc (2.0 mol dm^{-3} solution in toluene; 0.35 cm^3, 0.70 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 15 min and then cooled to −78 °C. A solution of the diester (0.625 mmol) in THF (20 cm^3) was added dropwise over 5 min, and the mixture kept for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (30 cm^3) was added and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3), washed with brine (50 cm^3), dried ($MgSO_4$), the solvent evaporated under reduced pressure and the residue chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give the mixtures of diesters. The pairs of esters **72** (70%), **76** (66%) and **80** (76%), identical with the earlier samples, were prepared by this method.

Reaction of dilithium cyanodimethylcuprate with α,β-unsaturated diesters

Typically, methyllithium (1.4 mol dm^{-3} solution in Et_2O; 1.2 cm^3, 1.68 mmol) was added to a stirred suspension of pre-dried copper(I) cyanide (0.073 g, 0.813 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 45 min and then cooled to −78 °C. The diester (0.625 mmol) in THF (20 cm^3) was added dropwise over 5 min and the mixture

kept for 1 h. The reaction was quenched with saturated basic aqueous ammonium chloride (50 cm^3) and allowed to warm to room temperature. The mixture was extracted with ether (3 × 50 cm^3), the combined organic fractions were washed with basic aqueous ammonium chloride until the washings were no longer blue (3 × 50 cm^3), washed with brine (50 cm^3), dried ($MgSO_4$), and the solvent evaporated off under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give the mixture of diesters. The pairs of esters **72** (62%), **76** (63%) and **80** (88%), identical with the earlier samples, were prepared by this method.

Reaction of lithium tetramethylaluminate with the α,β-unsaturated diester 69

Methyllithium (1.4 mol dm^{-3} solution in Et_2O; 1.1 cm^3, 1.54 mmol) was added with stirring to trimethylaluminium (2.0 mol dm^{-3} solution in hexanes; 0.38 cm^3, 0.76 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 20 min and then cooled to −78 °C. A solution of diester **69** (0.2 g, 0.575 mmol) in THF (20 cm^3) was added dropwise over 5 min. After 1 h, the reaction was quenched with saturated aqueous ammonium chloride (15 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (50 cm^3) was added and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3), the extracts were washed with brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and the residue chromatographed (SiO_2, Et_2O–light petroleum, 15:85) to give the mixture of esters **80** (0.105 g, 50%), identical with the earlier samples.

Reaction of phenyllithium with α,β-unsaturated diesters

Typically, the diester (0.50 mmol) in THF (5 cm^3) was added dropwise with stirring to a solution of phenyllithium (1.8 mol dm^{-3} solution in cyclohexane–Et_2O; 0.36 cm^3, 0.65 mmol) in THF (12 cm^3) at −78 °C under argon, and the mixture kept for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (5 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 25 cm^3) and the combined organic fractions were washed with dilute aqueous sodium hydroxide (50 cm^3), brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and the residue chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give a mixture of the diesters. The following compounds were prepared by this method.

Methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-3-phenylhexanoate 73A and methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-3-phenylhexanoate 73B. (61%); R_F(Et_2O–light petroleum, 25:75) 0.27; ν_{max}(CH_2Cl_2)/cm^{-1} 1740 (C=O), 1250 (SiMe) and 1113 (SiPh); **73A**: δ_H(400 MHz; $CDCl_3$) 7.50 (1 H, m, Ph), 7.40–7.16 (7 H, m, Ph), 7.10–7.01 (2 H, m, Ph), 3.70 (3 H, s, OMe), 3.53 [1 H, d, *J* 10.2, C*H*(CO_2Me)$_2$], 3.38 (3 H, s, OMe), 3.37 (1 H, m, C*H*Ph), 1.73 (1 H, m, CH_AH_B), 1.60–1.47 (1 H, m, CH$_A$$H_B$), 0.76 (1 H, m, MeC*H*Si), 0.75 (3 H, s, *Me*CHSi), 0.31 (3 H, s, SiMe_AMe$_B$) and 0.28 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 168.3, 168.1, 141.3, 138.5, 134.1, 128.9, 128.5, 128.4, 128.3, 126.9, 59.1, 52.5, 52.1, 45.6, 37.3, 17.7, 16.5, −4.5 and −4.9; **73B**: δ_H(400 MHz; $CDCl_3$) 7.50 (1 H, m, Ph), 7.40–7.16 (7 H, m, Ph), 7.10–7.01 (2 H, m, Ph), 3.73 (3 H, s, OMe), 3.60–3.47 [2 H, m, C*H*(CO_2Me)$_2$ and C*H*Ph], 3.38 (3 H, s, OMe), 1.76 (1 H, m, CH_AH_B), 1.35 (1 H, m, CH$_A$$H_B$), 0.97 (3 H, d, *J* 7.3, *Me*CHSi), 0.55 (1 H, m, MeC*H*Si), 0.18 (3 H, s, SiMe_AMe$_B$) and 0.14 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 168.8, 168.3, 140.0, 137.9, 134.1, 128.9, 128.5, 128.3, 128.2, 126.9, 59.1, 52.5, 52.2, 43.4, 35.0, 15.4, 12.8, −4.7 and −5.8; *m*/*z* (EI) 398 (4%, M^+), 383 (36, M − Me) and 135 (100, Me_2PhSi) (Found: M^+, 398.1898. $C_{23}H_{30}O_4Si$ requires *M*, 398.1913). The ratio of diastereoisomers was determined by integration of the SiMe$_A$$Me_B$ signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-3,5-diphenyl-2-methoxycarbonylpentanoate 77A and methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-3,5-diphenyl-2-methoxycarbonylpentanoate 77B. (89%) The major isomer **77B** could be separated by crystallisation as prisms, mp 98–100 °C (from light petroleum); R_F(Et_2O–light petroleum, 10:90) 0.17; ν_{max}(film)/cm^{-1} 1737 (C=O), 1598 (Ph) and 1494 (Ph); **77A**: δ_H(400 MHz; $CDCl_3$) 7.36–6.70 (15 H, m, 3 × Ph), 3.66 (3 H, s, OMe), 3.57 [1 H, d, *J* 10.8, C*H*(CO_2Me)$_2$], 3.36 (3 H, s, OMe), 3.36 [1 H, m, C*H*Ph-CH(CO_2Me)$_2$], 2.27 (1 H, m, CH_AH_B), 2.18–2.10 (2 H, m, CH$_A$$H_B$ and C*H*Si), 0.26 (3 H, s, SiMe_AMe$_B$) and 0.10 (3 H, s, SiMe$_A$$Me_B$); **77B**: δ_H(400 MHz; $CDCl_3$) 7.36–6.70 (15 H, m, 3 × Ph), 3.72 (3 H, s, OMe), 3.55 [1 H, d, *J* 10.8, C*H*(CO_2Me)$_2$], 3.3 (3 H, s, OMe), 3.2 [1 H, dt, *J* 10.8 and 2.6, C*H*PhCH-(CO_2Me)$_2$], 2.15 (1 H, m, CH_AH_B), 1.89–1.82 (2 H, m, CH$_A$$H_B$ + C*H*Si), 0.18 (3 H, s, SiMe_AMe$_B$) and 0.01 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 168.6, 168.1, 141.1, 139.8, 137.2, 134.0, 129.0, 128.5, 128.2, 128.1, 127.8, 127.6, 126.9, 124.8, 58.6, 52.4, 52.0, 43.7, 33.0, 32.7, −3.8 and −5.95 (Found: M^+, 460.2070. $C_{28}H_{32}O_4Si$ requires *M*, 460.2070). The ratio of the diastereoisomers was determined by integration of the Si*Me* signals in the ^{1}H NMR spectrum.

Methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-6-methyl-3-phenylheptanoate 81A and methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-2-methoxycarbonyl-6-methyl-3-phenylheptanoate 81B. (83%); R_F(Et_2O–light petroleum, 20:80) 0.39; ν_{max}(film)/cm^{-1} 1758 (C=O), 1739 (C=O), 1494 (Ph) and 1454 (Ph); **81A**: δ_H(400 MHz; $CDCl_3$) 7.52–6.73 (10 H, m, 2 × Ph), 3.77 (3 H, s, OMe), 3.51 [1 H, d, *J* 10.9, C*H*(CO_2Me)$_2$], 3.33 (3 H, s, OMe), 3.24 (1 H, dt, *J* 10.9 and 4.4, C*H*Ph), 1.8–1.56 [3 H, m, CH_AH_B and C*H*(Me)$_2$], 0.71 (1 H, d, *J* 6.9, Me_AMe$_B$-CH), 0.64 (3 H, d, *J* 6.8, Me$_A$$Me_B$CH), 0.56 (1 H, dt, *J* 2.7 and 9.9, C*H*Si), 0.45 (3 H, s, SiMe_AMe$_B$) and 0.29 (3 H, s, SiMe$_A$$Me_B$); **81B**: δ_H(400 MHz; $CDCl_3$) 7.52–6.73 (10 H, m, 2 × Ph), 3.74 (3 H, s, OMe), 3.56–3.49 [2 H, m, C*H*(CO_2Me)$_2$ and C*H*Ph], 3.35 (3 H, s, OMe), 2.06 [1 H, dseptet, *J* 2.4 and 7.0, C*H*(CH_3)$_2$], 1.80–1.56 (2 H, m, CH_AH_B), 0.98 (3 H, d, *J* 6.9, Me_AMe$_B$CH), 0.84 (3 H, d, *J* 7.1, Me$_A$$Me_B$CH), 0.62 (1 H, m, C*H*Si), 0.19 (3 H, s, SiMe_AMe$_B$) and 0.18 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 168.6, 139.7, 139.4, 133.8, 128.6, 128.5, 128.2, 127.9, 127.7, 127.5, 126.7, 59.0, 52.6, 44.5, 31.6, 29.3, 27.9, 23.0, 21.7, −1.4 and −3.2 (Found: M^+, 426.2234. $C_{25}H_{34}O_4Si$ requires *M*, 426.2226). The ratio of the diastereoisomers was determined by integration of the Si*Me* signals in the ^{1}H NMR spectrum.

Reaction of phenylmagnesium bromide with α,β-unsaturated diesters

Typically, a stirred solution of the diester (0.606 mmol) in dry THF (50 cm^3) was added to phenylmagnesium bromide (3 mol dm^{-3} solution in Et_2O; 0.3 cm^3, 0.9 mmol) at 0 °C under argon and the mixture kept for 1.5 h at 0 °C. The reaction was quenched with saturated aqueous ammonium chloride (15 cm^3) and allowed to warm to room temperature. The mixture was extracted with ether (3 × 15 cm^3). The organic layers were combined, washed with brine, dried ($MgSO_4$), evaporated under reduced pressure and chromatographed (SiO_2, Et_2O–light petroleum, 20:80) to give a mixture of the diesters. The pairs of esters **77** (77%) and **81** (85%), identical with the earlier samples, were prepared by this method.

Reaction of lithium dimethyl(phenyl)zincate with α,β-unsaturated diesters

Typically, phenyllithium (1.8 mol dm^{-3} solution in cyclohexane–Et_2O; 0.76 cm^3, 1.37 mmol) was added to a stirring solution of dimethylzinc (2.0 mol dm^{-3} solution in toluene; 0.35 cm^3, 0.70 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 15 min and then cooled to −78 °C. A solution of diester (0.625 mmol) in THF (20 cm^3) was added dropwise over 5 min, and the mixture kept

for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (30 cm^3) was added and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3), washed with dilute sodium hydroxide (50 cm^3), brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give a mixture of diesters. The pairs of esters **73** (65%), **77** (68%) and **81** (89%), identical with the earlier samples, were prepared by this method.

Reaction of dilithium cyanodiphenylcuprate with α,β-unsaturated diesters

Typically, phenyllithium (1.8 mol dm^{-3} solution in cyclohexane–Et_2O; 0.9 cm^3, 1.63 mmol) was added to a stirred suspension of pre-dried copper(I) cyanide (0.073 g, 0.813 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 45 min and then cooled to −78 °C. A solution of the diester (0.625 mmol) in THF (20 cm^3) was added dropwise over 5 min, and the mixture kept for 1 h. The reaction was quenched with saturated basic aqueous ammonium chloride (10 cm^3) and the mixture allowed to warm to room temperature. The mixture was extracted with ether (3 × 50 cm^3). The combined organic fractions were washed with basic aqueous ammonium chloride until the washings were no longer blue (3 × 50 cm^3), washed with dilute sodium hydroxide (50 cm^3) and brine (50 cm^3), dried ($MgSO_4$), evaporated under reduced pressure and the residue chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give a mixture of diesters. The pairs of esters **73** (62%), **77** (96%) and **81** (62%), identical with the earlier samples, were prepared by this method.

Reaction of lithium trimethyl(phenyl)aluminate with the α,β-unsaturated diester 69

Phenyllithium (0.63 cm^3; 1.8 mol dm^3 solution in cyclohexane–ether) was added with stirring to a solution of trimethylaluminium (2.0 mol dm^3 solution in toluene; 0.28 cm^3, 0.57 mmol) in THF (30 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 15 min and then cooled to −78 °C. A solution of the diester **69** (0.099 g, 0.284 mmol) in THF (20 cm^3) was added dropwise over 5 min, and the mixture kept for 1 h. The reaction was quenched with saturated aqueous ammonium chloride (25 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (15 cm^3) was added to dissolve the aluminium salts, and the residue was extracted with ether (3 × 25 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), evaporated under reduced pressure and chromatographed (SiO_2, Et_2O–light petroleum, 20:80) to give a mixture of the two esters **81** (0.097 g, 80%).

Preparation of the aldehydes 28, 32 and 36

Typically, diisobutylaluminium hydride (1.0 mol dm^{-3} solution in hexanes; 43.7 cm^3, 43.7 mmol) in toluene (15 cm^3) was added dropwise over 30 min to a stirred solution of the ester **85**, **86** or **87** (33.6 mmol) in toluene (80 cm^3) at −78 °C under argon. The mixture was stirred for a further 1 h, quenched with methanol (20 cm^3) and allowed to warm to room temperature. The resulting turbid solution was shaken vigorously with saturated aqueous potassium sodium tartrate (100 cm^3). The aqueous layer was further extracted with light petroleum (3 × 50 cm^3) and the combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, CH_2Cl_2) to give the aldehyde. The following aldehydes were prepared by this method.

3-Dimethyl(phenyl)silylbutanal 28. (83%); R_F(CH_2Cl_2) 0.65; ν_{max}(film)/cm^{-1} 1724 (C=O), 1250 (SiMe) and 1111 (SiPh); δ_H(250 MHz; $CDCl_3$) 9.67 (1 H, dd, *J* 3.2 and 1.1, CHO), 7.49 (2 H, m, *o*-Ph), 7.41–7.31 (3 H, m, *m*- and *p*-Ph), 2.43 (1 H, ddd, *J* 16.3, 3.5 and 1.1, CH_ACH_BCHO), 2.15 (1 H, ddd, *J* 16.3, 10.9 and 3.2, CH_ACH_BCHO), 1.50 (1 H, m, HCSi), 0.98 (3 H, d, *J* 7.3, *Me*CHSi) and 0.30 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 203.2, 137.1, 133.9, 129.3, 127.9, 46.0, 14.6, 13.9, −4.9 and −5.3 (Found: M^+, 206.1117. $C_{12}H_{18}OSi$ requires *M*, 206.1127).

3-Dimethyl(phenyl)silyl-3-phenylpropanal[34] **32.** (82%); R_F(Et_2O–light petroleum, 20:80) 0.42; δ_H(200 MHz; $CDCl_3$) 9.6 (1 H, s, C*H*O), 7.45–6.97 (10 H, m, 2 × Ph), 2.94–2.62 (3 H, m SiC*H* and CH_2CO), 0.30 (3 H, s, Si*Me*$_A$Me$_B$) and 0.28 (3 H, s, SiMe$_A$*Me*$_B$).

3-Dimethyl(phenyl)silyl-4-methylpentanal 36. (80%); R_F(Et_2O–light petroleum, 10:90) 0.35; ν_{max}(film)/cm^{-1} 1723 (C=O), 1250 (SiMe) and 1111 (SiPh); δ_H(250 MHz; $CDCl_3$) 9.62 (1 H, dd, *J* 2.5 and 1.8, CHO), 7.50 (2 H, m, *o*-Ph), 7.39–7.30 (3 H, m, *m*- and *p*-Ph), 2.46 (1 H, ddd, *J* 17.2, 7.7 and 2.5, CH_ACH_BCHO), 2.34 (1 H, ddd, *J* 17.2, 5.4 and 1.8, CH_ACH_B-CHO), 1.92 (1 H, m, C*H*Me$_A$Me$_B$), 1.54 (1 H, ddd, *J* 7.7, 5.4 and 3.9, C*H*SiCH_AH$_B$), 0.90 (3 H, d, *J* 6.8, CH*Me*$_A$Me$_B$), 0.83 (3 H, d, *J* 6.9, CHMe$_A$*Me*$_B$), 0.35 (3 H, s, Si*Me*$_C$Me$_D$) and 0.33 (3 H, s, SiMe$_C$*Me*$_D$); δ_C($CDCl_3$) 203.6, 138.4, 133.9, 129.1, 127.9, 41.5, 28.7, 27.0, 23.3, 20.9, −2.5 and −3.2; *m*/*z* (EI) 234 (M^+, 3%), 219 (M − Me, 77) and 135 (Me_2PhSi, 100) (Found: M^+, 234.1440. $C_{14}H_{22}OSi$ requires *M*, 234.1440).

Preparation of the ketones 29 and 30 by PCC oxidation

Typically, PCC on alumina[37] (5.0 g, 5 mmol) was stirred with the diastereoisomeric mixture of alcohols (2.43 mmol) in light petroleum (15 cm^3) at room temperature for 8 h, after which complete consumption of the starting alcohols had occurred (TLC). The mixture was filtered through Celite and the residue was washed with light petroleum. The solvent was evaporated under reduced pressure and the residue was chromatographed (SiO_2, CH_2Cl_2) to give the ketone. The following known ketones were prepared by this method.

4-Dimethyl(phenyl)silylpentan-2-one[34] **29.** (60%); R_F(CH_2Cl_2) 0.48; ν_{max}(film)/cm^{-1} 1717 (C=O), 1247 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.48 (2 H, m, *o*-Ph), 7.39–7.32 (3 H, m, *m*- and *p*-Ph), 2.41 (1 H, dd, *J* 16.3 and 3.5, CH_AH$_B$), 2.17 (1 H, dd, *J* 16.3 and 10.9, CH$_A$$H_B$), 1.49 (1 H, ddq, *J* 10.9, 3.5 and 7.3, MeC*H*Si), 0.92 (3 H, d, *J* 7.3, *Me*CHSi) and 0.27 (6 H, s, $SiMe_2$).

3-Dimethyl(phenyl)silyl-1-phenylbutan-1-one[38] **30.** As needles, mp 84 °C (from light petroleum) (60%); R_F(CH_2Cl_2) 0.60; ν_{max}(CH_2Cl_2)/cm^{-1} 1682 (C=O), 1265 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.82 (2 H, m, Ph), 7.58–7.47 (3 H, m, Ph), 7.45–7.34 (5 H, m, Ph), 3.00 (1 H, dd, *J* 15.8 and 3.3, CH_AH$_B$), 2.65 (1 H, dd, *J* 15.8 and 10.9, CH$_A$$H_B$), 1.61 (1 H, ddq, *J* 10.9, 3.3 and 7.3, MeC*H*Si), 0.98 (3 H, d, *J* 7.3, *Me*CHSi), 0.54 (3 H, s, Si*Me*$_A$Me$_B$) and 0.53 (3 H, s, SiMe$_A$*Me*$_B$).

Preparation of the ketones 31, 35 and 37–39 by chromium(VI) oxidation

Typically, chromium(VI) oxide (26.7 g) was added to concentrated sulfuric acid (23 cm^3), and the mixture was diluted carefully to 100 cm^3 with water at 0 °C. The reagent was then added dropwise with stirring to a mixture of the diastereoisomeric alcohols (9.9 mmol) in acetone (30 cm^3) at 0 °C. When a permanent orange–brown colour was obtained the addition was stopped. Water (100 cm^3) was added, and the solution was extracted with ether (3 × 100 cm^3). The combined organic layers were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 10:90) to give the ketone. The following new ketones were prepared by this method.

2-Methyl-5-dimethyl(phenyl)silylhexan-3-one 31. (77%); R_F(Et_2O–light petroleum, 10:90) 0.40; ν_{max}(film)/cm^{-1} 1711 (C=O), 1249 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.49 (2 H, m, *o*-Ph), 7.39–7.30 (3 H, m, *m*- and *p*-Ph), 2.53 (1 H, septet, *J* 6.9, C*H*Me$_A$Me$_B$CO), 2.41 (1 H, dd, *J* 16.7 and 3.7, CH_AH$_B$), 2.23 (1 H, dd, *J* 16.7 and 10.4, CH$_A$$H_B$), 1.53 (1 H, m, C*H*MeCH$_A$H$_B$), 1.02 (3 H, d, *J* 6.9, CH*Me*$_A$Me$_B$), 1.01 (3 H, d,

J 6.9, CHMe$_A$*Me*$_B$), 0.89 (3 H, d, *J* 7.3, CH*Me*CH$_A$H$_B$) and 0.27 (6 H, s, SiMe$_2$); δ_C(CDCl$_3$) 214.9, 137.7, 133.9, 129.1, 127.8, 42.7, 40.7, 18.3, 18.0, 14.7, −4.7 and −5.2; *m*/*z* (EI) 248 (24%, M$^+$), 233 (31, M − Me), 205 (23, M − Pr^i) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 248.1601. $C_{15}H_{24}OSi$ requires *M*, 248.1601).

1-Dimethyl(phenyl)silyl-4-methyl-1-phenylpentan–3-one 35. As needles, mp 45 °C (from propan-2-ol) (65%); R_F(Et$_2$O–light petroleum, 10:90) 0.30; ν_{max}(film)/cm^{-1} 1713 (C=O), 1249 (SiMe) and 1113 (SiPh); δ_H(250 MHz; C$_6$D$_6$) 7.42–6.93 (10 H, m, 2 × Ph), 3.18 (1 H, dd, *J* 9.5 and 4.9), 2.80 (1 H, dd, *J* 17.3 and 9.5), 2.56 (1 H, dd, *J* 17.2 and 4.9), 2.09 (1 H, septet, *J* 6.9, C*H*Me$_A$Me$_B$), 0.80 (3 H, d, *J* 6.9, CH*Me*$_A$Me$_B$), 0.74 (3 H, d, *J* CHMe$_A$*Me*$_B$) and 0.18 (6 H, s, SiMe$_2$); δ_C(CDCl$_3$) 213.5, 142.6, 136.9, 134.2, 129.3, 128.1, 127.7, 124.8, 41.1, 40.6, 30.7, 18.1, 18.0, −3.9 and −5.1 (Found: C, 77.5; H, 8.55. $C_{20}H_{26}OSi$ requires C, 77.4; H, 8.45%). The ^{1}H NMR spectrum in CDCl$_3$ was not first order.

4-Dimethyl(phenyl)silyl-5-methylhexan-2-one 37. (73%); R_F(Et$_2$O–light petroleum, 15:85) 0.33; ν_{max}(film)/cm^{-1} 1717 (C=O), 1249 (SiMe) and 1110 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.49 (2 H, m, *o*-Ph), 7.37–7.29 (3 H, m, *m*- and *p*-Ph), 2.45 (1 H, dd, *J* 17.6 and 7.0, CH$_A$*H*$_B$CHO) 2.34 (1 H, dd, *J* 17.6 and 5.6, CH$_A$*H*$_B$CHO), 1.99 (3 H, s, CO*Me*), 1.86 (1 H, m, Me$_A$Me$_B$-C*H*), 1.59 (1 H, m, C*H*Si), 0.87 (3 H, d, *J* 6.8, *Me*$_A$Me$_B$CH), 0.81 (3 H, d, *J* 6.9, Me$_A$*Me*$_B$CH), 0.32 (3 H, s, Si*Me*$_C$Me$_D$) and 0.29 (3 H, s, SiMe$_C$*Me*$_D$); δ_C(CDCl$_3$) 209.3, 138.9, 134.0, 128.9, 127.8, 41.4, 29.7, 28.8, 27.5, 23.0, 21.3, −2.3 and −3.0; *m*/*z* (EI) 248 (17%, M$^+$), 233 (65, M − Me) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 248.1595. $C_{15}H_{24}OSi$ requires *M*, 248.1596).

3-Dimethyl(phenyl)silyl-4-methyl-1-phenylpentan-1-one 38. (80%); R_F(Et$_2$O–light petroleum, 20:80) 0.58; ν_{max}(film)/cm^{-1} 1686 (C=O) and 1597 (Ph); δ_H(250 MHz; CDCl$_3$) 7.85–7.25 (10 H, m, 2 × Ph), 3.04 (1 H, dd, *J* 17.1 and 7.3, C*H*$_A$H$_B$), 2.95 (1 H, dd, *J* 17.1 and 5.5, CH$_A$*H*$_B$), 1.98 (1 H, dseptet, *J* 4.1 and 6.8, C*H*Me$_2$), 1.84 (1 H, ddd, *J* 7.3, 5.5 and 4.1, C*H*Si), 0.96 (3 H, d, *J* 6.8, CH*Me*$_A$Me$_B$), 0.92 (3 H, d, *J* 6.9, CHMe$_A$*Me*$_B$), 0.41 (3 H, s, Si*Me*$_A$Me$_B$) and 0.39 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(CDCl$_3$) 201.1, 139.1, 137.2, 134.0, 132.7, 128.7, 128.5, 128.4, 128.1, 36.2, 28.9, 28.2, 23.0, 21.5, −2.1 and −2.5 (Found: M$^+$, 310.1753. $C_{20}H_{26}OSi$ requires *M*, 310.1753).

5-Dimethyl(phenyl)silyl-2,6-dimethylheptan-3-one 39. (78%); R_F(Et$_2$O–light petroleum, 5:95) 0.35; ν_{max}(film)/cm^{-1} 1713 (C=O), 1249 (SiMe) and 1110 (SiPh); δ_H(400 MHz; CDCl$_3$) 7.49 (2 H, m, *o*-Ph), 7.36–7.28 (3 H, m, *m*- and *p*-Ph), 2.54–2.34 (3 H, m), 1.85 (1 H, m, C*H*Me$_A$Me$_B$CHSi), 1.61 (1 H, m), 0.99 (3 H, d, *J* 6.9, CH*Me*), 0.96 (3 H, d, *J* 6.9, CH*Me*), 0.86 (3 H, d, *J* 6.8, CH*Me*), 0.81 (3 H, d, *J* 6.9, CH*Me*), 0.32 (3 H, s, Si*Me*$_C$Me$_D$) and 0.29 (3 H, s, SiMe$_C$*Me*$_D$); δ_C(CDCl$_3$) 214.7, 139.1, 134.0, 128.8, 127.7, 40.6, 38.2, 28.8, 26.8, 26.5, 22.9, 21.4, 18.6, 18.4, −2.4 and −2.9; *m*/*z* (EI) 276 (12%, M$^+$), 233 (27, M − Pr^i) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 276.1906. $C_{17}H_{28}OSi$ requires *M*, 276.1909).

Preparation of the α,β-unsaturated esters 61, 62, 64, 65, 67 and 68

Typically, the aldehyde (17.9 mmol) in methanol (20 cm^3) was stirred with a suspension of methoxycarbonylmethyl(triphenyl)phosphorane (10.30 g, 30.8 mmol) in methanol (80 cm^3) under argon at 0 °C for 3 h when TLC showed no starting material remained. The methanol was removed under reduced pressure, and the residue was dissolved in light petroleum (30 cm^3), filtered and evaporated under reduced pressure. The residue was chromatographed (SiO$_2$, Et$_2$O–light petroleum, 5:95) to give the trans- and the cis-*α,β-unsaturated esters*. The following compounds were prepared by this method.

Methyl (*E*)-5-dimethyl(phenyl)silylhex-2-enoate 61. (52%); R_F(Et$_2$O–light petroleum, 10:90) 0.25; ν_{max}(film)/cm^{-1} 1725 (C=O), 1654 (C=C) and 1589 (Ph); δ_H(250 MHz; CDCl$_3$) 7.55–7.35 (5 H, m, Ph), 6.90 (1 H, ddd, *J* 15.5, 8.3, 6.4, HC=C*H*CO$_2$Me), 5.75 (1 H, dt, *J* 15.5 and 1, *H*C=CHCO$_2$Me), 3.71 (3 H, s, OMe), 2.35 (1 H, dddd, *J* 14.3, 6.4, 3.5 and 1.0, C*H*$_A$CH$_B$CH=CHCO$_2$Me), 1.93 (1 H, ddt, *J* 14.3, 1.0 and 8.3, CH$_A$C*H*$_B$CH=CHCO$_2$Me), 1.03 (1 H, m, HCSi), 0.94 (3 H, d, *J* 6.3, MeCSi) and 0.28 (6 H, s, SiMe$_2$); δ_C(CDCl$_3$) 167.0, 149.9, 137.7, 133.9 (2 C), 129.1, 127.8 (2 C), 121.4, 51.3, 34.7, 19.0, 14.0, −4.8 and −5.1 (Found: C, 68.6; H, 8.45. $C_{15}H_{22}O_2Si$ requires C, 68.7; H, 8.45%).

Methyl (*Z*)-5-dimethyl(phenyl)silylhex-2-enoate 62. (31%); R_F(Et$_2$O–light petroleum, 5:95) 0.35; ν_{max}(film)/cm^{-1} 1723 (C=O) and 1641 (C=C); δ_H(250 MHz; CDCl$_3$) 7.50 (2 H, m, Ph), 7.39–7.32 (3 H, m, Ph), 6.19 (1 H, dt, *J* 11.5 and 7.5, *H*C=CHCO$_2$Me), 5.76 (1 H, dt, *J* 11.5 and 1.7, HC=C*H*CO$_2$Me), 3.67 (3 H, s, OMe), 2.65 (2 H, dt, *J* 7.0 and 1.7, C*H*$_2$CH=CH-CO$_2$Me), 0.99 (1 H, m, HCSi), 0.94 (3 H, d, *J* 4.2, MeCSi) and 0.30 (6 H, s, SiMe$_2$); δ_C(CDCl$_3$) 167.0, 149.9, 137.7, 133.9 (2 C), 129.1, 127.8 (2 C), 121.4, 51.3, 34.7, 19.0, 14.0, −4.8 and −5.1 (Found: M$^+$, 262.1394. $C_{15}H_{22}O_2Si$ requires *M*, 262.1389).

Methyl (*E*)-5-dimethyl(phenyl)silyl-5-phenylpent-2-enoate 64. (48%); R_F(Et$_2$O–light petroleum, 8:92) 0.19; ν_{max}(film)/cm^{-1} 1723 (C=O), 1654 (C=C) and 1599 (Ph); δ_H(400 MHz; CDCl$_3$) 7.39–6.90 (10 H, m, 2 × Ph), 6.76 (1 H, dt, *J* 15.6 and 6.9, *H*C=CHCO$_2$Me), 5.66 (1 H, dt, *J* 15.6 and 1.4, HC=C*H*CO$_2$Me), 3.60 (3 H, s, OMe), 2.65–2.51 (2 H, m, CH$_A$H$_B$), 2.39 (1 H, dd, *J* 11.8 and 3.9, C*H*Si), 0.25 (3 H, s, Si*Me*$_A$Me$_B$) and 0.22 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(CDCl$_3$) 166.8, 149.1, 141.3, 136.8, 134.1, 130.4, 129.3, 128.2, 127.8, 127.7, 124.9, 121.3, 51.2, 35.7, 32.2, −3.9 and −5.5 (Found: M$^+$, 324.1548; C, 74.0; H, 7.4. $C_{20}H_{24}O_2Si$ requires *M*, 324.1545; C, 74.0; H, 7.45%).

Methyl (*Z*)-5-dimethyl(phenyl)silyl-5-phenylpent-2-enoate 65. (45%); R_F(Et$_2$O–light petroleum, 8:92) 0.33; ν_{max}(film)/cm^{-1} 1722 (C=O), 1642 (C=C) and 1599 (Ph); δ_H(400 MHz; CDCl$_3$) 7.41–6.9 (10 H, m, 2 × Ph), 6.03 (1 H, dt, *J* 11.4 and 7.1, *H*C=CHCO$_2$Me), 5.61 (1 H, dt, *J* 11.4 and 1.6, HC=C*H*CO$_2$Me), 3.67 (3 H, s, OMe), 3.22–3.06 (2 H, m, CH$_A$H$_B$), 2.38 (1 H, dd, *J* 12.1 and 4.4, C*H*Si), 0.29 (3 H, s, Si*Me*$_A$Me$_B$) and 0.26 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(400 MHz; CDCl$_3$) 166.9, 151.1, 141.8, 137.03, 134.2, 129.2, 128.1, 128.0, 127.6, 124.8, 119.3, 51.0, 36.7, 28.5, −4.2 and −5.3 (Found: M$^+$, 324.1546; C, 73.9; H, 7.5. $C_{20}H_{24}O_2Si$ requires *M*, 324.1545; C, 74.0; H, 7.45%).

Methyl (*E*)-5-dimethyl(phenyl)silyl-6-methylhept-2-enoate 67. (48%); R_F(Et$_2$O–light petroleum, 10:90) 0.30; ν_{max}(film)/cm^{-1} 1725 (C=O), 1268 (SiMe) and 1110 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.49 (2 H, m, *o*-Ph), 7.38–7.29 (3 H, m, *m*- and *p*-Ph), 6.86 (1 H, dt, *J* 15.6 and 7.6, C*H*CHCO$_2$Me), 5.71 (1 H, dt, *J* 15.5 and 1.4, CHC*H*CO$_2$Me), 3.69 (3 H, s, OMe), 2.28 (2 H, td, *J* 7.1 and 1.5, CHSiC*H*$_2$), 1.92 (1 H, dseptet, *J* 3.6 and 6.8, Me$_A$Me$_B$C*H*CHSi), 1.04 (1 H, td, *J* 6.8 and 3.6, C*H*SiCH$_2$), 0.92 (3 H, d, *J* 6.8, *Me*$_A$Me$_B$CHCHSi), 0.86 (3 H, d, *J* 6.8, Me$_A$*Me*$_B$CHCHSi), 0.32 (3 H, s, Si*Me*$_C$Me$_D$) and 0.31 (3 H, s, SiMe$_C$*Me*$_D$); δ_C(CDCl$_3$) 167.0, 151.4, 139.1, 133.9, 128.9, 127.8, 120.8, 51.4, 33.0, 30.0, 28.6, 22.7, 21.3, −2.1 and −2.7; *m*/*z* (EI) 290 (29%, M$^+$), 275 (30, M − Me) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 290.1702. $C_{17}H_{26}O_2Si$ requires *M*, 290.1702).

Methyl (*Z*)-5-dimethyl(phenyl)silyl-6-methylhept-2-enoate 68. (39%); R_F(Et$_2$O–light petroleum, 10:90) 0.38; ν_{max}(film)/cm^{-1} 1723 (C=O), 1250 (SiMe) and 1110 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.50 (2 H, m, *o*-Ph), 7.36–7.18 (3 H, m, *m*- and *p*-Ph), 6.11 (1 H, ddd, *J* 11.6, 7.8 and 7.0, C*H*CHCO$_2$Me), 5.67 (1 H, dt, *J* 11.5 and 1.8, CHC*H*CO$_2$Me), 3.68 (3 H, s, OMe), 2.91 (1 H, ddt, *J* 16.2, 1.8 and 8.0, CHSiC*H*$_A$H$_B$), 2.78 (1 H, m, CHSiCH$_A$*H*$_B$), 1.91 (1 H, dseptet, *J* 3.4 and 6.9, Me$_A$Me$_B$C*H*-CHSi), 1.01 (1 H, ddd, *J* 8.0, 5.9 and 3.4, C*H*SiCH$_A$H$_B$), 0.93 (3 H, d, *J* 6.8, *Me*$_A$Me$_B$CHCHSi), 0.85 (3 H, d, *J* 6.9, Me$_A$-*Me*$_B$CHCHSi), 0.33 (3 H, s, Si*Me*$_C$Me$_D$) and 0.32 (3 H, s, SiMe$_C$*Me*$_D$); δ_C(CDCl$_3$) 167.0, 153.1, 139.5, 133.9, 128.8, 127.7, 118.7, 51.0, 34.0, 28.8, 26.4, 22.9, 21.3, −2.3 and −2.7; *m*/*z* (EI) 290 (9%, M$^+$), 275 (12, M − Me) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 290.1705. $C_{17}H_{26}O_2Si$ requires *M*, 290.1702).

Horner–Wadsworth–Emmons reactions

Using the reaction procedure of Marmor,[39] sodium hydride (60% dispersion in mineral oil; 1.28 g, 32 mmol) was washed with light petroleum (2 × 10 cm^3) and residual solvent was removed under reduced pressure. Ether (60 cm^3) was added and the stirred suspension cooled to 0 °C. Diethyl ethoxycarbonylmethylphosphonate[40] (6.36 g, 28 mmol) in ether (10 cm^3) was added dropwise over 10 min and the mixture was refluxed for 20 min. After cooling the mixture to 0 °C, a solution of the aldehyde (28 mmol) in ether (10 cm^3) was added dropwise over 10 min. The mixture was stirred at 0 °C for 10 min and refluxed for 30 min. The mixture was cooled to room temperature, the clear ether layer was decanted off, and water (50 cm^3) was added to the residue, which dissolved on warming. The aqueous layer was extracted with ether (3 × 25 cm^3) and the combined ether fractions were washed with aqueous sodium hydrogen carbonate (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 10:90) to give the ester. The following esters were prepared by this method.

Ethyl (*E*)-5-dimethyl(phenyl)silylhex-2-enoate. (81%); R_F(Et_2O–light petroleum, 10:90) 0.28; ν_{max}(film)/cm^{-1} 1718 (C=O), 1651 (C=C) and 1589 (Ph); δ_H(250 MHz; $CDCl_3$) 7.55–7.35 (5 H, m, Ph), 6.90 (1 H, ddd, *J* 15.5, 8.3 and 6.4, CH=C*H*-CO_2Et), 5.75 (1 H, dt, *J* 15.5 and 1.2, C*H*=CHCO_2Et), 4.16 (2 H, q, *J* 7.1, OCH_2CH_3), 2.35 (1 H, dddd, *J* 14.3, 6.4, 3.5 and 1.2, CH_ACH_BCH=CH), 1.93 (1 H, dddd, *J* 14.3, 10.3, 8.3 and 1.2, CH$_A$CH_BCH=CH), 1.27 (3 H, t, *J* 7.1, OCH_2CH_3), 1.02 (1 H, m, HCSi), 0.94 (3 H, d, *J* 6.3, MeCSi) and 0.29 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 166.6, 149.5, 137.7, 133.9 (2 C), 129.1, 127.8 (2 C), 121.8, 60.1, 34.7, 19.0, 14.3, 14.0, −5.1 and −5.3 (Found: C, 69.6; H, 8.65. $C_{16}H_{24}O_2Si$ requires C, 69.5; H, 8.75%).

Methyl (*E*)-4-phenylpent-2-enoate.[41] (74%); R_F(Et_2O–light petroleum) 0.40; ν_{max}(film)/cm^{-1} 1724 (C=O) and 1653 (C=C); δ_H(250 MHz; $CDCl_3$) 7.36–7.15 (5 H, m, Ph), 7.12 (1 H, dd, *J* 15.8 and 6.7, C*H*CHCO_2Me), 5.81 (1 H, dd, *J* 15.8 and 1.6, CHC*H*CO_2Me), 3.72 (3 H, s, OMe), 3.62 (1 H, m, MeC*H*Ph) and 1.42 (3 H, d, *J* 7.0, *Me*CHPh); δ_C($CDCl_3$) 167.2, 152.9, 143.3, 128.7, 127.3, 126.8, 119.7, 51.5, 42.6 and 20.2; *m*/*z* (EI) 190 (24%, M^+), 159 (16, M − OMe) and 131 (65, M − CO_2Me) (Found: M^+, 190.0991. $C_{12}H_{14}O_2$ requires *M*, 190.0994); (*Z*)-isomer: R_F(Et_2O–light petroleum) 0.50; ν_{max}(film)/cm^{-1} 1722 (C=O) and 1650 (C=C); δ_H(250 MHz; $CDCl_3$) 7.32–7.17 (5 H, m, Ph), 6.28 (1 H, dd, *J* 11.3 and 10.4, C*H*CHCO_2Me), 5.74 (1 H, dd, *J* 11.4 and 0.9, CHC*H*CO_2Me), 4.91 (1 H, m, MeC*H*Ph), 3.74 (3 H, s, OMe) and 1.40 (3 H, d, *J* 7.0, *Me*CHPh); δ_C($CDCl_3$) 166.7, 154.1, 144.5, 128.0, 127.1, 126.5, 117.4, 51.2, 37.7 and 20.9; *m*/*z* (EI) 190 (3%, M^+) (Found: M^+, 190.0995. $C_{12}H_{14}O_2$ requires *M*, 190.0994).

Preparation of the α,β-unsaturated diesters 63, 66 and 69

Typically, glacial acetic acid (0.16 cm^3, 2.8 mmol) and piperidine (0.28 cm^3, 2.8 mmol) were added with stirring to a solution of the aldehyde (27.9 mmol) and dimethyl malonate (4.06 g, 30.7 mmol) in dichloromethane (130 cm^3) at 0 °C and the mixture stirred for 45 min at room temperature. Additional glacial acetic acid (0.16 cm^3, 2.8 mmol) and piperidine (0.28 cm^3, 2.8 mmol) were added and the mixture was stirred for a further 30 min. Molecular sieves (4 Å) were added and the mixture kept for a further 4 h. The sieves were removed by filtration and the solvent was evaporated under reduced pressure. The residue was taken up into ether (100 cm^3), washed with saturated aqueous sodium hydrogen carbonate (50 cm^3) and brine (50 cm^3) and dried ($MgSO_4$). The ether was evaporated under reduced pressure and the residue was chromatographed (SiO_2, Et_2O–light petroleum, 15:85) to give the diesters. Use of more than 0.2 equiv. of acetic acid and piperidine reduced the yield of the diesters and promoted the formation of their deconjugated isomers. The following compounds were prepared by this method.

Methyl 5-dimethyl(phenyl)silyl-2-methoxycarbonylhex-2-enoate 63. (61%); R_F(Et_2O–light petroleum, 15:85) 0.20; ν_{max}(film)/cm^{-1} 1732 (C=O), 1642 (C=C), 1264 (SiMe) and 1113 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.47 (2 H, m, *o*-Ph), 7.39–7.30 (3 H, m, *m*- and *p*-Ph), 7.02 [1 H, dd, *J* 8.5 and 7.3, C*H*C-(CO_2Me)$_2$], 3.75 (3 H, s, OMe), 3.72 (3 H, s, OMe), 2.38 (1 H, ddd, *J* 14.7, 7.3 and 3.8, CH_AH$_B$), 2.08 (1 H, ddd, *J* 14.7, 10.0 and 8.6, CH$_A$$H_B$), 1.06 (1 H, m, C*H*SiCH$_A$H$_B$), 0.96 (3 H, d, *J* 6.5, *Me*CHSi) and 0.28 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 165.9, 164.3, 151.1, 137.4, 133.9, 129.1, 128.0, 127.8, 52.3, 52.1, 32.0, 19.7, 14.1, −4.9 and −5.4 (Found: C, 63.8; H, 7.6. $C_{17}H_{24}O_4Si$ requires C, 63.7; H, 7.55%).

Methyl 5-dimethyl(phenyl)silyl-2-methoxycarbonyl-5-phenylpent-2-enoate 66. (85%) as an oil; R_F(Et_2O–light petroleum, 15:85) 0.2; ν_{max}(film)/cm^{-1} 1728 (C=O), 1641 (C=C) and 1599 (Ph); δ_H(400 MHz; $CDCl_3$) 7.40–6.80 (10 H, m, 2 × Ph), 6.83 [1 H, dd, *J* 8.4 and 6.9, *H*C=C(CO_2Me)$_2$], 3.68 (3 H, s, OMe), 3.65 (3 H, s, OMe), 2.74 (1 H, ddd, *J* 15.4, 12.0 and 6.9, CH_AH$_B$), 2.65 (1 H, ddd, *J* 15.4, 8.4 and 4.1, CH$_A$$H_B$), 2.38 (1 H, dd, *J* 12.0 and 4.1, CHSi), 0.24 (3 H, s, SiMe_AMe$_B$) and 0.19 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 165.8, 164.2, 150.6, 140.9, 136.6, 134.1, 129.3, 128.3, 127.8, 127.6, 125.2, 52.2, 52.06, 36.05, 29.7, −4.1 and −5.7 (Found: M^+, 382.1609. $C_{22}H_{26}O_4Si$ requires *M*, 382.1600).

Methyl 5-dimethyl(phenyl)silyl-2-methoxycarbonyl-6-methylhept-2-enoate 69. (77%); R_F(Et_2O–light petroleum, 30:70) 0.45; ν_{max}(film)/cm^{-1} 1724 (C=O), 1263 (SiMe) and 1111 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.49 (2 H, m, *o*-Ph), 7.38–7.29 (3 H, m, *m*- and *p*-Ph), 6.94 [1 H, t, *J* 7.7, C*H*C(CO_2Me)$_2$], 3.77 (3 H, s, OMe), 3.62 (3 H, s, OMe), 2.50–2.38 (2 H, m, CHSiCH_AH$_B$), 1.93 (1 H, m, Me$_A$Me$_B$C*H*CHSi), 1.09 (1 H, ddd, *J* 7.8, 6.2 and 3.2, Me$_A$Me$_B$CHC*H*Si), 0.92 (3 H, d, *J* 6.8, *Me*$_A$Me$_B$CHCHSi), 0.86 (3 H, d, *J* 6.9, Me$_A$$Me_B$CHCHSi) and 0.33 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 166.0, 164.3, 152.8, 138.8, 133.9, 128.9, 127.8, 127.1, 52.8, 52.2, 33.8, 28.7, 27.3, 22.7, 21.1, −2.3 and −3.0; *m*/*z* (EI) 348 (19%, M^+), 333 (49, M − Me), 317 (54, M − OMe) and 135 (100, Me_2PhSi) (Found: M^+, 348.1744. $C_{19}H_{28}O_4Si$ requires *M*, 348.1757).

Methyl 4-phenylpentanoate 25

Methyl (*E*)-4-phenylpent-2-enoate (1.0 g, 5.26 mmol) in methanol (5 cm^3) was stirred with a suspension of palladium on carbon (0.2 g) in methanol (10 cm^3) at room temperature under hydrogen for 48 h, when TLC indicated that complete consumption of the starting *trans*-ester had occurred. The hydrogen atmosphere was removed and the system was flushed twice with argon. The catalyst was removed by filtration through Celite. The methanol was removed by evaporation under reduced pressure and the residue was passed through a short column of silica using ether as eluent to give the ester[42] (0.85 g, 85%); ν_{max}(film)/cm^{-1} 1733 (C=O); δ_H(250 MHz; $CDCl_3$) 7.33–7.12 (5 H, m, Ph), 3.61 (3 H, s, OMe), 2.70 (1 H, sextet, *J* 6.9, MeC*H*Ph), 2.24–2.14 (2 H, m, C$H_2$$CO_2$Me), 1.98–1.84 (2 H, m, MeCHPhCH_2) and 1.27 (3 H, d, *J* 7.0, *Me*CHPh).

(2*SR*,3*SR*,4*RS*)-2′,6′-Dimethylphenyl 3-hydroxy-2-methyl-4-phenylpentanoate 90

Butyllithium (1.6 mol dm^{-3} solution in hexanes; 11.6 cm^3, 18.5 mmol) was added dropwise with stirring to a solution of diisopropylamine (2.43 cm^3, 18.5 mmol) in THF (60 cm^3) at 0 °C under argon. After 20 min, the mixture was cooled to −78 °C and 2,6-dimethylphenyl propanoate in THF (20 cm^3) was added slowly. The mixture was stirred for 1.5 h at this temperature and then 2-phenylpropanal (2.24 cm^3, 16.9 mmol) was added. After stirring for a further 5 min the mixture was quenched with saturated aqueous ammonium chloride (15 cm^3) and allowed to warm to room temperature. Dilute hydrochloric acid (50 cm^3) was added to the mixture and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3), washed with brine (100 cm^3),

dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 25:75) to give the ester[30] (3.0 g, 57%) as cubes, mp 89–90 °C (from light petroleum); R_F(Et_2O–light petroleum) 0.30; ν_{max}(CH_2Cl_2)/cm^{-1} 3478 (OH) and 1746 (C=O); δ_H(250 MHz; $CDCl_3$) 7.39–7.21 (5 H, m, Ph), 7.05 (3 H, s, Ph), 3.82 (1 H, m, C*H*OH), 3.05 (1 H, quintet, *J* 6.9, MeC*H*), 2.84 (1 H, quintet, *J* 7.2, MeC*H*), 2.58 (1 H, d, *J* 7.6, CHO*H*), 2.17 (6 H, s, 2 × *Me*Ph), 1.48 (3 H, d, *J* 7.3, *Me*CH) and 1.40 (3 H, d, *J* 7.0, *Me*CH). Heathcock reported that a 4:1 ratio of diastereoisomers of the ester was obtained in this reaction. Although the ^{1}H NMR spectrum of the crude product suggested that a very small amount of the second diastereoisomer, presumably the *anti*,*anti*-Cram product, might have been obtained this was inconclusive. Following chromatography, two minor products were obtained: 2,6-dimethylphenol (0.38 g) and an unidentified product (0.58 g) of R_F(Et_2O–light petroleum, 25:75) 0.15, which had no OH frequency present in the IR spectrum and may have been the elimination product from the minor diastereoisomer.

Methyl (2*SR*,3*SR*,4*RS*)-3-hydroxy-2-methyl-4-phenylpentanoate

Sodium (0.048 g, 2.1 mmol, pre-washed with light petroleum) was added to methanol (20 cm^3) at 0 °C. After the sodium had been completely converted to sodium methoxide, THF (20 cm^3) was added and the solution allowed to warm to room temperature. The ester **90** (0.592 g, 1.90 mmol) was added and the mixture was stirred for 24 h when TLC indicated complete consumption of the starting material. Ether (150 cm^3) was added and the mixture was washed with water (100 cm^3). The water layer was extracted with ether (3 × 50 cm^3). The combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (100 cm^3) and brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 50:50) to give the methyl ester[43] (0.34 g, 80%); R_F(Et_2O–light petroleum, 50:50) 0.28; ν_{max}(film)/cm^{-1} 3504 (OH) and 1736 (C=O); δ_H(250 MHz; $CDCl_3$) 7.35–7.13 (5 H, m, Ph), 3.69 (3 H, s, OMe), 3.63 (1 H, m, C*H*OH), 2.86 (1 H, quintet, *J* 7.0, C*H*Me), 2.74 (1 H, d, *J* 8.1, CHO*H*), 2.47 (1 H, dq, *J* 5.0 and 7.3, C*H*Me), 1.35 (3 H, d, *J* 7.0, CH*Me*) and 1.22 (3 H, d, *J* 7.3, CH*Me*); δ_C($CDCl_3$) 176.9, 144.3, 128.5, 127.7, 126.6, 78.5, 51.7, 43.9, 41.8, 16.3 and 15.4.

Methyl (2*SR*,3*SR*,4*RS*)-3-[(methylthio)thiocarbonyloxy]-2-methyl-4-phenylpentanoate

Following the method of Barton and McCombie,[31] the methyl ester from above in THF (5 cm^3), sodium hydride (0.036 g, 0.90 mmol) and imidazole (0.01 g) in THF (10 cm^3) were stirred for 2 h under argon and then carbon disulfide (0.08 cm^3, 1.35 mmol) was added, and the mixture stirred for 30 min. Methyl iodide (0.085 cm^3, 1.35 mmol) was added and the mixture was stirred for an additional 1 h. Water (50 cm^3) was added and the mixture was extracted with ether (3 × 50 cm^3). The combined organic fractions were washed with dilute hydrochloric acid (100 cm^3), saturated aqueous sodium hydrogen carbonate (100 cm^3) and brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 20:80) to give the dithiocarbonate (0.11 g, 78%); R_F(Et_2O–light petroleum, 20:80) 0.33; ν_{max}(film)/cm^{-1} 1741 (C=O); δ_H(250 MHz; $CDCl_3$) 7.35–7.19 (5 H, m, Ph), 6.27 (1 H, dd, *J* 9.4 and 4.0, C*H*OCS$_2$Me), 3.56 (3 H, s, OMe), 3.36 (1 H, dq, *J* 9.4 and 7.0, C*H*Me), 2.77 (1 H, dq, *J* 4.0 and 7.2, C*H*Me), 2.58 (3 H, s, CS$_2$Me), 1.29 (3 H, d, *J* 7.0, CH*Me*) and 1.15 (3 H, d, *J* 7.2, CH*Me*); δ_C($CDCl_3$) 216.3, 172.7, 142.2, 128.4, 128.3, 127.8, 87.3, 51.7, 42.2, 41.7, 18.7, 18.4 and 13.5; *m*/*z* (EI) 281 (3%, M$^+$ − OMe) and 253 (43, M − CO_2Me) (Found: M$^+$ − OMe, 281.0659. $C_{15}H_{20}O_3S_2$ requires *M* − OMe, 281.0670).

Methyl (2*RS*,4*RS*)-2-methyl-4-phenylpentanoate 27

Following the procedure of Barton and McCombie,[31] the dithiocarbonate from above (0.09 g, 0.288 mmol) in toluene (15 cm^3) was added dropwise over 15 min to a refluxing solution of tributyltin hydride (0.085 cm^3) in toluene (15 cm^3) under argon and the mixture was refluxed for 16 h. The solvent was evaporated under reduced pressure and the residue was chromatographed (SiO_2, Et_2O–light petroleum, 10:90) to give the *ester* **27** (0.033 g, 56%), identical (^{1}H NMR) with the signals assigned to this isomer in the mixture from the methylation experiment; δ_C($CDCl_3$) 177.4, 146.7, 128.4, 127.1, 126.2, 51.5, 42.5, 38.0, 37.6, 22.6 and 18.0.

Silyl-to-hydroxy conversions

Typically, mercuric acetate (0.23 g, 0.72 mmol) was added to a stirring solution of the silane (0.48 mmol) in peracetic acid (35–40% solution in dilute acetic acid; 3 cm^3) and the mixture was stirred for 3 h at room temperature. Toluene (10 cm^3) was added and the mixture of solvents was evaporated under reduced pressure. The residue was taken up in ether, filtered and evaporated under reduced pressure. The residue was chromatographed to give the alcohol. The following compounds were prepared by this method, except that a larger excess of mercuric acetate (typically 1.23 mmol) relative to the amount of the ester (typically 0.493 mol) was used for the doubly silylated esters **70**, **74** and **78**.

(1*RS*,3*SR*)-1-Phenylbutane-1,3-diol 91A. As needles, mp 77 °C (from Et_2O–light petroleum) (lit.,[18] 78 °C) (54%); R_F(Et_2O) 0.37; ν_{max}(CH_2Cl_2)/cm^{-1} 3422 (OH); δ_H(250 MHz; $CDCl_3$) 7.38–7.22 (5 H, m, Ph), 4.89 (1 H, dd, *J* 9.8 and 3.4, PhC*H*OH), 4.11 (1 H, ddq, *J* 9.3, 2.9 and 6.2, C*H*OHMe), 3.67 (2 H, br s, 2 × OH), 1.90–1.67 (2 H, m, CH_2) and 1.19 (3 H, d, *J* 6.2, CHOH*Me*).

(1*RS*,3*RS*)-1-Phenylbutane-1,3-diol 91B. As prisms, mp 62–63 °C (from Et_2O–light petroleum) (lit.,[18] 62–63 °C) (55%); R_F(Et_2O) 0.32; ν_{max}(CH_2Cl_2)/cm^{-1} 3386 (OH); δ_H(250 MHz; $CDCl_3$) 7.33–7.21 (5 H, m, Ph), 5.01 (1 H, dd, *J* 7.3 and 4.2, PhC*H*OH), 4.04 (1 H, m, C*H*OHMe), 3.54 (1 H, br s, OH), 2.94 (1 H, br s, OH), 1.94–1.73 (2 H, m, CH_2) and 1.21 (3 H, d, *J* 6.3, CHOH*Me*).

(2*RS*,4*SR*)-5-Methylhexane-2,4-diol[44] 92A (=95A) and (2*RS*,4*RS*)-5-methylhexane-2,4-diol[44] 92B (=95B). (53%, 33:67 from a 33:67 mixture of **57A** and **57B**; 55%, 22:78 from a 22:78 mixture of **42B** and **42A**); R_F(Et_2O) 0.33 and 0.23; ν_{max}($CDCl_3$)/cm^{-1} 3372 (OH); **92A**: δ_H(250 MHz; $CDCl_3$) 4.12 (1 H, m, MeC*H*OH), 3.67–3.54 (1 H, m, CHC*H*OH), 1.71–1.34 (3 H, m, CH_AH$_B$, CH$_A$$H_B$ and Me$_A$Me$_B$C*H*), 1.22 (3 H, d, *J* 6.4, *Me*CH) and 0.95–0.81 (6 H, m, 2 × *Me*CH); **92B**: δ_H(250 MHz; $CDCl_3$) 4.00 (1 H, m, MeC*H*OH), 3.67–3.54 (1 H, m, CHC*H*OH), 1.71–1.34 (3 H, m, CH_AH$_B$, CH$_A$$H_B$ and Me$_A$Me$_B$C*H*), 1.18 (3 H, d, *J* 6.2, *Me*CH) and 0.95–0.81 (6 H, m, 2 × *Me*CH). The ratio of the diastereoisomers was determined by integration of the MeC*H*OH signals in the ^{1}H NMR spectrum.

(1*RS*,3*RS*)-1,3-Diphenylpropane-1,3-diol[45] 93A. As prisms mp 135–139 °C (from CH_2Cl_2–light petroleum) (88%); R_F(EtO_2–light petroleum, 50:50) 0.24; ν_{max}(film)/cm^{-1} 3391 (OH) and 1492 (Ph); δ_H(250 MHz; $CDCl_3$): 7.42–7.22 (10 H, m, 2 × Ph), 4.97 (2 H, t, *J* 5.8, 2 × C*H*OH), 2.89 (2 H, br s, 2 × OH) and 2.17 (2 H, dd *J* 6.2 and 5.4, C$H_A$$H_B$).

(1*RS*,3*SR*)-1,3-Diphenylpropane-1,3-diol[45] 93B. As prisms mp 107–112 °C (59%); R_F(EtO_2–light petroleum, 50:50) 0.24; ν_{max}(film)/cm^{-1} 3351 (OH) and 1602 (Ph); δ_H(250 MHz; $CDCl_3$) 7.67–6.82 (10 H, m, 2 × Ph), 5.03 (2 H, dd, *J* 10.1 and 2.8, 2 × C*H*OH), 3.31 (2 H, br s, 2 × OH), 2.15 (1 H, dt, *J* 14.7 and 10.1, CH_AH$_B$), 1.96 (1 H, dt, *J* 14.7 and 2.8, CH$_A$$H_B$).

(1*RS*,3*RS*)-4-Methyl-1-phenylpentane-1,3-diol[46] 94A and (1*RS*,3*SR*)-4-methyl-1-phenylpentane-1,3-diol[46] 94B. (74%, 67:33 from a 67:33 mixture of **52A** and **52B**; 57%, 24:76 from a 22:78 mixture of **55B** and **55A**); ν_{max}(film)/cm^{-1} 3364 (OH);

94A: R_f(EtO_2–light petroleum, 50:50) 0.20; δ_H(250 MHz; $CDCl_3$) 7.39–7.20 (5 H, m, Ph), 5.03 (1 H, t, *J* 5.6, PhC*H*OH), 3.59 (1 H, q, *J* 5.9, CHC*H*OH), 1.88–1.60 (3 H, m, CH_AH_B and C*H*Me_AMe_B), 0.89 (3 H, d, *J* 6.7, CH*Me*$_A$Me$_B$) and 0.86 (3 H, d, *J* 6.7, CHMe$_A$*Me*$_B$); δ_C($CDCl_3$) 144.6, 128.4, 127.2, 125.5, 73.8, 71.8, 41.6, 33.7, 18.5 and 17.7; **94B**: R_F(EtO_2–light petroleum, 50:50) 0.28; δ_H(250 MHz; $CDCl_3$) 7.39–7.20 (5 H, m, Ph), 4.90 (1 H, dd, *J* 9.0 and 3.9, PhC*H*OH), 3.72 (1 H, m, CHC*H*OH), 1.88–1.60 (3 H, m, CH_AH_B and C*H*Me_AMe_B), 0.90 (3 H, d, *J* 6.9, CH*Me*$_A$Me$_B$) and 0.89 (3 H, d, *J* 6.6, CHMe$_A$*Me*$_B$); δ_C($CDCl_3$) 144.6, 128.5, 127.6, 125.7, 77.6, 75.6, 42.0, 34.2, 18.2 and 17.4. The ratio of diastereoisomers was determined by integration of the PhC*H*OH signals in the ^{1}H NMR spectrum.

(3*RS*,5*RS*)-2,6-Dimethylheptane-3,5-diol[47] **97A and (3*RS*,5*SR*)-2,6-dimethylheptane-3,5-diol 97B.** (61%, 23:77 from a 23:77 mixture of **59A** and **59B**); R_F(Et_2O–light petroleum, 80:20) 0.37 and 0.28; ν_{max}(film)/cm^{-1} 3388 (OH); **97A**: δ_H(400 MHz; $CDCl_3$) 3.67–3.58 (2 H, m, 2 × C*H*OH), 1.73–1.60 (2 H, m), 1.44–1.33 (2 H, m) and 0.97–0.91 (12 H, m, 4 × CH*Me*); δ_C($CDCl_3$) 74.2, 36.5, 33.7, 18.7 and 18.1; **97B**: δ_H(400 MHz; $CDCl_3$) 3.67–3.58 (2 H, m, 2 × C*H*OH), 1.73–1.60 (2 H, m), 1.58–1.52 (2 H, m) and 0.97–0.91 (12 H, m, 4 × CH*Me*); δ_C($CDCl_3$) 78.2, 35.8, 34.1, 18.4 and 17.8. The ratio of diastereoisomers was determined by integration of the CH_2 signals (36.5 and 35.8 ppm) in the ^{13}C NMR spectrum.

(4*RS*,6*SR*)-4-Hydroxy-6-methyltetrahydro-2*H*-pyran-2-one[48] **101A and (4*RS*,6*RS*)-4-hydroxy-6-methyltetrahydro-2*H*-pyran-2-one**[49] **101B.** (63%, 85:15 from an 86:14 mixture of **70A** and **70B**); R_F(EtOAc) 0.31; **101A**: ν_{max}(film)/cm^{-1} 3414 (OH) and 1726 (C=O); δ_H(400 MHz; $CDCl_3$) 4.33 (1 H, ddq, *J* 11.7, 3.0 and 6.3, C_6-H_{ax}), 4.23 (1 H, m, C_4-H_{ax}), 2.86 (1 H, ddd, *J* 17.1, 5.9 and 1.4, C_3-H_{eq}), 2.73 (1 H, br s, OH), 2.43 (1 H, dd, *J* 17.1 and 7.7, C_3-H_{ax}), 2.25 (1 H, dddd, *J* 13.8, 5.5, 3.0 and 1.4, C_5-H_{ax}), 1.56 (1 H, ddd, *J* 13.8, 11.7 and 9.2, C_5-H_{ax}) and 1.39 (3 H, d, *J* 6.3, Me); δ_C($CDCl_3$) 171.1, 73.8, 63.8, 39.5, 39.9 and 21.4; **101B**: δ_H(400 MHz; $CDCl_3$) 4.83 (1 H, ddq, *J* 12.8, 3.0 and 6.4, C_6-H_{ax}), 2.68 (1 H, dd, *J* 17.7 and 4.8, C_3-H_{eq}), 2.59 (1 H, ddd, *J* 17.7, 3.6 and 1.7, C_3-H_{ax}), 1.97 (1 H, dddd, *J* 14.4, 3.8, 3.3 and 1.8, C_5-H_{eq}), 1.69 (1 H, ddd, *J* 14.4, 11.3 and 3.2, C_5-H_{ax}) and 1.37 (3 H, d, *J* 7.0, Me); δ_C($CDCl_3$) 170.9, 72.5, 62.7, 38.4 and 37.5.

(4*RS*,6*RS*)-4-Hydroxy-6-phenyltetrahydro-2*H*-pyran-2-one 102A and (4*RS*,6*SR*)-4-hydroxy-6-phenyltetrahydro-2*H*-pyran-2-one 102B. (35%, 95:5 from a 95:5 mixture of **74A** and **74B**); R_F(Et_2O–EtOAc, 65:35) 0.30; ν_{max}(film)/cm^{-1} 3607 (OH), 1737 (C=O) and 1602 (Ph); **102A**: δ_H(400 MHz; $CDCl_3$) 7.40–7.25 (5 H, m, Ph), 5.21 (1 H, dd, *J* 12.1 and 3.1, C_6-H_{ax}), 4.40 (1 H, m, C_4-H_{ax}), 3.45 (1 H, ddd, *J* 17.1, 6 and 1.3, C_3-H_{eq}), 2.6 (1 H, dd, *J* 17.1 and 8, C_3-H_{ax}), 2.51 (1 H, dddd, *J* 13.9, 6.8, 3.1 and 1.3, C_5-H_{eq}), 1.92 (1 H, ddd, *J* 13.9, 12.1 and 9.4, C_5-H_{ax}); δ_C($CDCl_3$) 170.2, 138.6, 128.8, 128.7, 125.9, 78.5, 64.1, 40.4, 39.6; **102B**: δ_H(400 MHz; $CDCl_3$) 5.74 (1 H, dd, *J* 11.2 and 3.1, C_6-H_{ax}), 4.40 (1 H, m, C_4-H_{eq}), 2.85 (1 H, dd, *J* 17.9 and 5, C_3-H_{ax}), 2.70 (1 H, ddd, *J* 17.9, 3.7 and 1.5, C_3-H_{eq}), 2.20 (1 H, dtd, *J* 14.4, 3.7 and 1.5, C_5-H_{eq}), 2.05 (1 H, ddd, *J* 14.4 11.2 and 3.1, C_5-H_{ax}); δ_C($CDCl_3$) 170.2, 139.2, 128.7, 128.4, 125.9, 78.5, 62.8, 38.7 and 38.4 (Found: M^+, 192.0778. $C_{11}H_{12}O_3$ requires *M*, 192.0786).

(4*RS*,6*RS*)-4-Hydroxy-6-isopropyltetrahydro-2*H*-pyran-2-one[6] **103A and (4*RS*,6*SR*)-4-hydroxy-6-isopropyltetrahydro-2*H*-pyran-2-one**[6] **103B.** (64%, 83:17 from an 83:17 mixture of **78A** and **78B**; 50%, 53:47 from a 53:47 mixture of **78A** and **78B**); R_F(Et_2O–MeOH, 96:4) 0.30; ν_{max}($CDCl_3$)/cm^{-1} 3422 (OH) and 1717 (C=O); **103A**: δ_H(250 MHz; $CDCl_3$) 4.24 (1 H, m, C*H*OH), 3.99 (1 H, ddd, *J* 12.0, 5.6 and 3.0, C_6-H_{ax}), 2.91 (1 H, ddd, *J* 17.2, 5.9 and 1.5, C_3-H_{eq}), 2.44 (1 H, dd, *J* 17.1 and 8.2, C_3-H_{ax}), 2.21 (1 H, dddd, *J* 13.5, 5.3, 2.9 and 1.5, C_5-H_{eq}), 1.92 (1 H, m, Me_AMe_BCH), 1.59 (1 H, ddd, *J* 13.5, 12.0 and 11.5, C_5-H_{ax}), 1.00 (3 H, d, *J* 5.9, *Me*$_A$Me$_B$CH) and 0.97 (3 H, d, *J* 6.0, Me$_A$*Me*$_B$CH); **103B**: δ_H(250 MHz; $CDCl_3$) 4.49 (1 H, ddd, *J* 11.6, 5.7 and 3.1, C_6-H_{ax}), 4.41 (1 H, m, C*H*OH), 2.71 (1 H, dd, *J* 17.6 and 4.8, C_3-H_{ax}), 2.61 (1 H, ddd, *J* 17.7, 3.7 and 1.6, C_3-H_{eq}), 1.98–1.83 (2 H, m, Me_AMe_BCH and C_5-H_{eq}), 1.74 (1 H, ddd, *J* 14.7, 11.7 and 3.4, C_5-H_{ax}), 1.00 (3 H, d, *J* 6.0, *Me*$_A$Me$_B$CH) and 0.97 (3 H, d, *J* 5.9, Me$_A$*Me*$_B$CH). The ratio of diastereoisomers was determined by integration of the C*H*OH signals in the ^{1}H NMR spectrum.

(4*RS*,6*SR*)-4,6-Dimethyltetrahydro-2*H*-pyran-2-one[50] **110A and (4*RS*,6*RS*)-4,6-dimethyltetrahydro-2*H*-pyran-2-one**[50] **110B.** (59%, 85:15 from an 85:15 mixture of **104A** and **104B**); R_F(Et_2O–CH_2Cl_2, 5:95) 0.37; ν_{max}(CH_2Cl_2)/cm^{-1} 1732 (C=O); **110A**: δ_H(250 MHz; $CDCl_3$) 4.40 (1 H, ddq, *J* 17.9, 6.3 and 2.9, C_6-H_{ax}), 2.64 (1 H, m), 2.19–1.82 (3 H, m), 1.35 (3 H, d, *J* 6.3, C_6-Me), 1.22 (1 H, m) and 1.02 (3 H, d, *J* 6.2, C_4-Me); **110B**: δ_H(250 MHz; $CDCl_3$) (recognisable signals) 4.54 (1 H, ddq, *J* 8.6, 4.3 and 6.3, C_6-H_{ax}), 1.35 (3 H, d, *J* 6.3, C_6-Me) and 1.07 (3 H, d, *J* 6.6, C_4-Me).

(4*RS*,6*SR*)-6-Methyl-4-phenyltetrahydro-2*H*-pyran-2-one 111A and (4*RS*,6*RS*)- 6-methyl-4-phenyltetrahydro-2*H*-pyran-2-one 111B. (57%, 29:71 from a 29:71 mixture of **105A** and **105B**); R_F(CH_2Cl_2) 0.22; ν_{max}(CH_2Cl_2)/cm^{-1} 1731 (C=O); **111A**: δ_H(400 MHz; $CDCl_3$) 7.39–7.15 (5 H, m, Ph), 4.56 (1 H, m, C_6-H_{eq}), 3.19 (1 H, m, C_4-H_{ax}), 2.90 (1 H, ddd, *J* 17.8, 6.0 and 1.9, C_3-H_{eq}), 2.52 (1 H, dd, *J* 17.9 and 11.5, C_3-H_{ax}), 2.16 (1 H, m, C_5-H), 1.73 (1 H, m, C_5-H) and 1.44 (3 H, d, *J* 6.3, C_6-Me); δ_C($CDCl_3$) 170.9, 142.9, 129.0, 127.2, 126.4, 73.9, 38.1, 37.7, 37.3 and 21.9; **111B**: δ_H(400 MHz; $CDCl_3$) 7.39–7.15 (5 H, m, Ph), 4.56 (1 H, m, C_6-H_{eq}), 3.37 (1 H, m, C_4-H_{ax}), 2.80 (1 H, dd, *J* 17.1 and 6.2, C_3-H_{eq}), 2.72 (1 H, dd, *J* 17.1 and 8.5, C_3-H_{ax}), 2.12–1.97 (2 H, m, C_5-H_{ax} and C_5-H_{eq}) and 1.40 (3 H, d, *J* 6.3, C_6-Me); δ_C($CDCl_3$) 171.7, 143.1, 129.0, 127.1, 126.7, 73.9, 36.8, 35.9, 34.7 and 21.3; *m*/*z* (EI) 190 (29, M^+) (Found: M^+, 190.0992. $C_{12}H_{14}O_2$ requires *M*, 190.0994). Irradiation of the proton signal at 4.56 ppm resulted in the enhancement of the signal at 3.19 ppm (but not the signal at 3.37 ppm).

(4*RS*,6*RS*)-4-Methyl-6-phenyltetrahydro-2*H*-pyran-2-one[51] **112A and (4*RS*,6*SR*)-4-methyl-6-phenyltetrahydro-2*H*-pyran-2-one**[51] **112B.** (67%, 78:22 from an 84:16 mixture of **106A** and **106B**); the major isomer **112A** could be separated as needles, mp 89–92 °C (from light petroleum); R_F(Et_2O–light petroleum, 30:70) 0.12; ν_{max}(film)/cm^{-1} 1729 (C=O) and 1493 (Ph); δ_H(400 MHz; $CDCl_3$) **112A**: 7.39–7.29 (5 H, m, Ph), 5.30 (1 H, dd, *J* 12.0 and 3.0, C_6-H_{ax}), 2.80 (1 H, ddd, *J* 16.8, 5 and 2, C_3-H_{eq}), 2.27–2.13 (3 H, m, C_3-H_{ax}, C_4-H_{ax} and C_5-H_{eq}), 1.52 (1 H, dt, *J* 13.9 and 11.5, C_5-H_{ax}) and 1.08 (3 H, d, *J* 6.2, *Me*CH); **112B**: 7.39–7.29 (5 H, m, Ph), 5.52 (1 H, dd, *J* 7.6 and 4.7, C_6-H_{ax}), 2.70 (1 H, ddd, *J* 16.9, 5.8 and 1.0, C_3-H_{eq}), 2.27–2.13 (3 H, m, C_3-H_{ax}, C_4-H_{eq} and C_5-H_{eq}), 1.88 (1 H, m, C_5-H_{ax}) and 1.11 (3 H, d, *J* 6.6, *Me*CH).

(4*RS*,6*RS*)-4,6-Diphenyltetrahydro-2*H*-pyran-2-one 113A and (4*RS*,6*SR*)-4,6-diphenyltetrahydro-2*H*-pyran-2-one 113B. (35%, 78:22 from an 84:16 mixture of **107A** and **107B**; 41%, **113B** pure from a pure sample of **107B**); R_F(Et_2O–light petroleum, 30:70) 0.20; ν_{max}(film)/cm^{-1} 1730 (C=O), 1599 (Ph); **113A**: δ_H(400 MHz; $CDCl_3$) 7.4–7.2 (10 H, m, 2 × Ph), 5.47 (1 H, dd, *J* 11.9 and 3.0, C_6-H_{ax}), 3.38 (1 H, m, C_4-H_{ax}), 3.05 (1 H, ddd, *J* 17.9, 5.9 and 2.0, C_3-H_{eq}), 2.68 (1 H, dd, *J* 17.9 and 11.5, C_3-H_{ax}), 2.43–2.32 (1 H, m, C_5-H_{eq}) and 2.06 (1 H, dt, *J* 14.0 and 12.1, C_5-H_{ax}); **113B**: needles, mp 63–65 °C (from light petroleum); δ_H(400 MHz; $CDCl_3$) 7.40–7.20 (10 H, m, 2 × Ph), 5.55 (1 H, dd, *J* 7.0 and 5.1, C_6-H_{ax}), 3.3 (1 H, m, C_4-H_{eq}), 2.93 (1 H, dd, *J* 17.3 and 6.2, C_3-H_{eq}), 2.84 (1 H, dd, *J* 17.3 and 9.0, C_3-H_{ax}) and 2.43–2.32 (2 H, m, C_5-H_{eq} and C_5-H_{ax}); **113B**: δ_C($CDCl_3$) 171.2, 142.6, 139.8, 129.1, 128.7, 128.2, 127.3, 126.6, 125.5, 78.7, 37.3, 36.4 and 34.2 (Found: M^+, 252.1147. $C_{17}H_{16}O_2$ requires *M*, 252.1150).

(4*RS*,6*RS*)-6-Isopropyl-4-methyltetrahydro-2*H*-pyran-2-one[52,53] **114A and (4*RS*,6*SR*)-6-isopropyl-4-methyltetrahydro-2*H*-pyran-2-one**[52] **114B.** (65%, 64:36 from a 64:36 mixture of **108A** and **108B**); R_F(Et_2O–CH_2Cl_2, 4:96) 0.37; ν_{max}($CDCl_3$)/

cm^{-1} 1734 (C=O); **114A**: δ_H(500 MHz; $CDCl_3$) 4.07 (1 H, m, C_6-H_{ax}), 2.66 (1 H, m, C_3-H), 2.07–1.95 (2 H, m, C_3-H and C_4-H_{ax}), 1.92–1.78 (2 H, m, C_5-H and C*H*Me$_A$Me$_B$), 1.21 (1 H, m, C_5-H), 1.04 (3 H, d, *J* 6.1, CH*Me*), 0.99 (3 H, d, *J* 6.8, CH*Me*) and 0.96 (3 H, d, *J* 6.7, CH*Me*); δ_C($CDCl_3$) 171.8, 85.3, 38.2, 33.5, 32.8, 26.7, 21.8, 17.8 and 17.6; **114B**: δ_H(500 MHz; $CDCl_3$) 4.07 (1 H, m, C_6-H_{ax}), 2.54 (1 H, m, C_3-H), 2.22–2.15 (2 H, m, C_3-H and C_4-H_{ax}), 1.92–1.78 (2 H, m, C_5-H and C*H*Me$_A$Me$_B$), 1.52 (1 H, m, C_5-H), 1.09 (3 H, d, *J* 6.4, CH*Me*), 1.01 (3 H, d, *J* 6.8, CH*Me*) and 0.95 (3 H, d, *J* 6.1, CH*Me*); δ_C($CDCl_3$) 173.0, 81.7, 37.3, 32.5, 32.0, 23.9, 21.4, 18.1 and 18.0. The ratio of diastereoisomers was determined by integration of the C_3-H signals in the ^{1}H NMR spectrum (2.66 and 2.54 ppm). The assignment was made on the basis of COSY couplings between the following signals: (1) 4.07 to 1.92–1.78 ppm, 1.52 and 1.21 ppm; (2) 2.66 to 2.07–1.95 and 1.04 ppm; (3) 2.54 to 2.22–2.15 and 1.09 ppm; (4) 2.22–2.15 to 2.54, 1.52 and 1.09 ppm; (5) 2.07–1.95 to 2.66, 1.92–1.78, 1.21 and 1.04 ppm; (6) 1.92–1.78 to 4.07, 2.07–1.95, 1.52, 1.21, 1.01, 0.99, 0.96 and 0.95 ppm; (7) 1.52 to 2.22–2.15 and 1.92–1.78 ppm. The assignment of the stereochemistry of this lactone made in the literature[52,53] was confirmed by the presence of an NOE enhancement between the signal at 2.07–1.95 ppm (C_4-H_{ax}) and the signal at 4.07 ppm (C_6-H_{ax}) in **114A**; no such NOE enhancement was present in **114B**.

(4*RS*,6*RS*)-6-Isopropyl-4-phenyltetrahydro-2*H*-pyran-2-one 115A and (4*RS*,6*SR*)-6-isopropyl-4-phenyltetrahydro–2*H*-pyran-2-one 115B. (83%, 40:60 from a 38:62 mixture of **109A** and **109B**); R_F(Et_2O–light petroleum, 30:70) 0.19; ν_{max}(film)/cm^{-1} 1733 (C=O) and 1603 (Ph); **115A**: δ_H(250 MHz; $CDCl_3$) 7.40–7.16 (5 H, m, Ph), 4.22 (1 H, ddd, *J* 11.8, 5.5 and 2.9, C_6-H_{ax}), 3.16 (1 H, tdd, *J* 11.9, 5.9 and 3.7, C_4-H_{ax}), 2.90 (1 H, ddd, *J* 17.8, 5.9 and 2.0, C_3-H_{eq}), 2.53 (1 H, dd, *J* 17.8 and 11.6, C_3-H_{ax}), 2.18–1.94 (3 H, m, C_5-H_{eq}, C_5-H_{ax} and C*H*Me$_2$), 1.02 (3 H, d, *J* 7.0, CH*Me*$_A$Me$_B$) and 1.98 (3 H, d, *J* 7.1, CHMe$_A$*Me*$_B$); δ_C($CDCl_3$) 171.2, 143.1, 129.0, 127.2, 126.5, 85.2, 37.7, 37.6, 32.9, 32.5, 17.9 and 17.7; **115B**: δ_H(250 MHz; $CDCl_3$) 7.4–7.16 (5 H, m, Ph), 4.10 (1 H, ddd, *J* 10.4, 6.5 and 4.3, C_6-H_{ax}), 3.33 (1 H, m, C_4-H_{eq}), 2.77 (2 H, d, *J* 7.3, C_3-H_{eq} and C_3-H_{ax}), 2.11 (1 H, m, C_5-H_{eq}), 1.91 (1 H, m, C*H*Me$_2$), 1.72 (1 H, dt, *J* 13.7 and 12.0, C_5-H_{ax}), 1.01 (3 H, d, *J* 6.7, CH*Me*$_A$Me$_B$) and 0.94 (3 H, d, *J* 6.8, CHMe$_A$*Me*$_B$); δ_C($CDCl_3$) 172.3, 143.4, 129.0, 127.1, 126.6, 82.0, 35.9, 34.8, 33.1, 32.5, 18.1 and 18.0 (Found: M^+, 218.1312. $C_{14}H_{18}O_2$ requires *M*, 218.1307).

Preparation of the silyl ethers 98, 99 and 100

Typically, a mixture of the diastereoisomers of the alcohols **46**, or the single diastereoisomer **60B**, or each of the separate diastereoisomers **53A** and **53B** (0.28 mmol) in THF (5 cm^3) was stirred with a suspension of sodium hydride (60% dispersion in oil pre-washed with light petroleum, 0.067 g, 1.65 mmol) in THF (10 cm^3) under argon at room temperature for 24 h. The mixture was quenched with water (10 cm^3) and extracted with ether (3 × 25 cm^3). The combined organic fractions were washed with brine (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the silyl ethers. The following compounds were prepared by this method.

(3*RS*,5*RS*)-5-Isopropyl-5-phenyl-2,2,3-trimethyl-1-oxa-2-silacyclopentane 98A and (3*RS*,5*SR*)-5-isopropyl-5-phenyl-2,2,3-trimethyl-1-oxa-2-silacyclopentane 98B. (88%, 25:75 from a 25:75 mixture of **46A** and **46B**); ν_{max}(film)/cm^{-1} 1250 (SiMe); **98A**: δ_H(500 MHz; $CDCl_3$) (recognisable signals) 7.39–7.37 (2 H, m, Ph), 7.30–7.26 (2 H, m, Ph), 7.21–7.18 (1 H, m, Ph), 2.59 (1 H, dd, *J* 13.5 and 8.4, CHMeC*H*$_A$H$_B$), 1.85 (1 H, dd, *J* 13.5 and 8.2, CHMeCH$_A$*H*$_B$); δ_C($CDCl_3$) (recognisable signals) 86.9, 44.7, 39.0, 18.2, 15.6, −0.4 and −2.6; **98B**: δ_H(500 MHz; $CDCl_3$) 7.39–7.37 (2 H, m, Ph), 7.30–7.26 (2 H, m, Ph), 7.21–7.18 (1 H, m, Ph), 2.46 (1 H, dd, *J* 13.0 and 7.1, CHMeC*H*$_A$H$_B$), 1.92 (1 H, m, C*H*Me$_A$Me$_B$), 1.76 (1 H, t, *J* 13.1, CHMeCH$_A$*H*$_B$), 1.00 (3 H, d, *J* 7.2, CH*Me*CH$_A$H$_B$), 0.90–0.81 (1 H, m, C*H*MeCH$_A$H$_B$), 0.84 (3 H, d, *J* 6.6, CH*Me*$_A$Me$_B$), 0.77 (3 H, d, *J* 6.9, CHMe$_A$*Me*$_B$), 0.14 (3 H, s, Si*Me*$_C$Me$_D$) and 0.08 (3 H, s, SiMe$_C$*Me*$_D$); δ_C($CDCl_3$) 146.2, 127.6, 126.3, 126.1, 87.2, 42.7, 39.2, 17.9, 17.6, 13.3, 1.05, −0.63 and −2.94; *m*/*z* (EI) 248 (7%, M^+), 205 (73, M − Pr^i) and 135 (100, Me$_2$PhSi) (Found: M^+, 248.1584. $C_{15}H_{24}SiO$ requires *M*, 248.1596). The ratio of the diastereoisomers was determined by integration of the CHMeC*H*$_A$H$_B$ signals in the ^{1}H NMR spectrum. COSY couplings were found for the major diastereoisomer **98B** between the following signals: (1) 2.46 to 1.76, 1.00, (0.90–0.81 + 0.84), 0.77 ppm (weak); (2) 1.92 to (0.90–0.81 + 0.84), 0.77 ppm; (3) 1.76 to 2.46, (0.90–0.81 + 0.84) ppm; and (4) (0.90–0.81 + 0.84) to 2.46, 1.92, 1.76 (weak), 0.14, 0.08 ppm. NOESY enhancements were found for the major diastereoisomer **98B** between the following signals: (1) 1.00 (CH*Me*CH$_A$H$_B$) to 1.76 ppm (CHMeCH$_A$*H*$_B$); (2) 1.76 (CHMeCH$_A$H$_B$) to 1.92 ppm (C*H*-Me$_A$Me$_B$); (3) 2.46 (CHMeC*H*$_A$H$_B$) to 7.39–7.18 ppm (Ph); and (4) no enhancement between 1.76 (CHMeCH$_A$*H*$_B$) and 7.39–7.18 ppm (Ph).

(3*RS*,5*SR*)-2,2-Dimethyl-3,5-diisopropyl-5-phenyl-1-oxa-2-silacyclopentane 99. (99%); ν_{max}(film)/cm^{-1} 1250 (SiMe); δ_H(500 MHz; $CDCl_3$) 7.40–7.35 (2 H, m, Ph), 7.32–7.25 (2 H, m, Ph), 7.20 (1 H, m, Ph), 2.49 (1 H, dd, *J* 12.9 and 7.0, C*H*$_A$H$_B$), 1.92 (1 H, septet, *J* 6.8, C*H*Me$_A$Me$_B$CPh), 1.76 (1 H, t, *J* 13.4, CH$_A$*H*$_B$), 1.60 (1 H, m, C*H*Me$_C$Me$_D$CHSi), 0.92 (3 H, d, *J* 6.5, CH*Me*$_A$Me$_B$CPh), 0.84 (6 H, d, *J* 6.7, CHMe$_A$*Me*$_B$CPh and CH*Me*$_C$Me$_D$CHSi), 0.77 (3 H, d, *J* 6.9, CHMe$_C$*Me*$_D$CHSi), 0.55 (1 H, ddd, *J* 13.6, 10.8 and 7.0, CHMe$_C$Me$_D$C*H*Si), 0.19 (3 H, s, Si*Me*$_E$Me$_F$) and 0.18 (3 H, s, SiMe$_E$*Me*$_F$); δ_C($CDCl_3$) 146.3, 127.4, 126.3, 126.0, 87.1, 39.3, 39.1, 33.7, 29.2, 24.2, 23.4, 17.8, 17.6, 0.84 and −2.4; *m*/*z* (EI) 276 (12%, M^+), 261 (73, M − Me) and 233 (100, M − Pr^i) (Found: M^+, 276. 1908. $C_{17}H_{28}SiO$ requires *M*, 276.1909). COSY couplings were found between the following signals: (1) 2.49 to 2.45, 0.92, 0.84 ppm; (2) 1.92 to 0.84, 0.77 ppm; (3) 1.76 to 2.49, 0.55 ppm; and (4) 1.60 to 0.92, 0.84, 0.55 ppm. NOESY enhancements were found between the following signals: (1) 0.57 to 2.45, 0.92, 0.84 ppm; (2) 2.45 to 7.40–7.18, 1.78 ppm; and (3) 1.78 to 2.45, 0.84, 0.77 ppm.

1,3-Diphenyl-3-dimethyl(phenyl)silyloxy-4-methylpentane 100. ν_{max}(film)/cm^{-1} 1253 (SiMe) and 1117 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.73–7.67 (2 H, m, Ph), 7.44–7.09 (7 H, m, Ph), 6.96–6.91 (2 H, m, Ph), 2.54 (1 H, m), 2.34–2.10 (3 H, m), 2.06 (1 H, septet, *J* 6.8, C*H*Me$_A$Me$_B$), 0.79 (3 H, d, *J* 6.7, CH*Me*$_A$Me$_B$), 0.76 (3 H, d, *J* 6.9, CHMe$_A$*Me*$_B$), 0.53 (3 H, s, Si*Me*$_C$Me$_D$) and 0.52 (3 H, s, SiMe$_C$*Me*$_D$); δ_C($CDCl_3$) 144.2, 142.7, 140.1, 133.5, 129.3, 128.8, 128.3, 128.2, 127.8, 127.5, 126.6, 126.2, 125.6, 84.7, 41.3, 39.5, 30.5, 29.7, 18.1, 17.7, 1.8 and 1.6; *m*/*z* (EI) 345 (100, M^+ − Pr^i) and 135 (100, Me$_2$PhSi) (Found: M^+ − Pr^i, 345.1676. $C_{26}H_{32}OSi$ requires *M* − Pr^i, 345.1675).

Krapcho demethoxycarbonylations

Typically, following Krapcho,[33] sodium chloride (0.04 g, 0.684 mmol) and water (0.012 g, 0.684 mmol) and a mixture of diesters (0.342 mmol) were refluxed in DMSO (40 cm^3) for 24 h when TLC showed complete consumption of the starting diesters. Water (100 cm^3) was added and the mixture extracted with dichloromethane (3 × 50 cm^3). The combined organic fractions were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of monoesters. The following compounds, except **108**, were prepared by this method. Later, we found that reaction could be achieved in higher yield by using lithium chloride (4 equiv.), water (2 equiv.) and fresh DMSO (typically 15 cm^3 for 1 mmol of ester). These conditions not only provided better yields but also achieved complete reaction typically in 30 min. The compounds **108** and **109** was prepared by this method.

Methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-3-methylhexanoate 104A and methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-3-methylhexanoate 104B. (81%, 85:15 from an 85:15 mixture of **72A** and **72B**); R_F(Et_2O–light petroleum, 10:90) 0.33;

ν_{max}(film)/cm^{-1} 1740 (C=O), 1249 (SiMe) and 1112 (SiPh); **104A**: δ_H(400 MHz; $CDCl_3$) 7.48 (2 H, m, *o*-Ph), 7.39–7.30 (3 H, m, *m*- and *p*-Ph), 3.63 (3 H, s, OMe), 2.35 (1 H, dd, *J* 14.2 and 4.2, CH_AH$_B$CO$_2$Me), 2.05 (1 H, m, MeC*H*CH$_A$H$_B$CO$_2$Me), 1.89 (1 H, dd, *J* 14.2 and 9.0, CH$_A$$H_BCO_2$Me), 1.28 (1 H, ddd, *J* 11.7, 4.4 and 2.0, CHSiCH_AH$_B$), 1.17 (1 H, m, CHSiCH$_A$$H_B$), 0.92 (3 H, d, *J* 2.4, *Me*CHSi), 0.90 (3 H, d, *J* 13.0, *Me*CH-CH$_A$H$_B$CO$_2$Me), 0.87 (1 H, m, MeC*H*Si), 0.24 (3 H, s, SiMe_A-Me$_B$) and 0.23 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 173.9, 138.4, 133.9, 128.8, 127.7, 51.3, 40.1, 39.0, 28.3, 21.1, 16.4, 14.2, −5.0 and −5.1; *m*/*z* (EI) 278 (11%, M$^+$), 263 (75, M − Me), 247 (67, M − OMe) and 135 (100, Me$_2$PhSi); **104B**: δ_H(400 MHz; $CDCl_3$) (recognisable signals) 2.40 (1 H, dd, *J* 14.8 and 4.4, CH_AH$_B$-CO$_2$Me) and 1.91 (1 H, dd, *J* 14.6 and 9.5, CH$_A$$H_BCO_2$Me) (Found: M$^+$, 278.1701. $C_{16}H_{26}O_2Si$ requires *M*, 278.1702). The ratio of diastereoisomers was obtained by integration of the CH_AH$_B$CO$_2$Me signals in the ^{1}H NMR spectrum; it could also be measured from the CH_2 resonances in the ^{13}C NMR spectrum (40.1 and 39.0 ppm in **104A** and 40.2 and 38.4 ppm in **104B**).

Methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-3-phenylhexanoate 105A and methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-3-phenylhexanoate 105B. (52%, 29:71 from a 29:71 mixture of **73A** and **73B**); R_F(Et$_2$O–light petroleum, 20:80) 0.42; ν_{max}(film)/cm^{-1} 1738 (C=O), 1248 (SiMe) and 1112 (SiPh); **105A**: δ_H(400 MHz; $CDCl_3$) (recognisable signals) 7.56–7.02 (10 H, m, Ph), 3.53 (3 H, s, OMe), 3.16 (1 H, m, C*H*Ph), 2.62 (1 H, dd, *J* 15.1 and 5.9, CH_AH$_B$CO$_2$Me), 2.42 (1 H, dd, *J* 15.1 and 9.1, CH$_A$$H_BCO_2$Me), 0.28 (3 H, s, Si$Me_AMe_B$) and 0.26 (3 H, s, SiMe$_A$$Me_B$); **105B**: δ_H(400 MHz; $CDCl_3$) 7.56–7.02 (10 H, m, 2 × Ph), 3.55 (3 H, s, OMe), 3.28 (1 H, m, C*H*Ph), 2.51 (2 H, d, *J* 7.5, CH_2CO$_2$Me), 1.75 (1 H, ddd, *J* 13.7, 11.6 and 2.2, CHSiCH_AH$_B$), 1.37 (1 H, ddd, *J* 13.6, 11.9 and 3.6, CHSiCH$_A$$H_B$), 0.96 (3 H, d, *J* 7.3, *Me*CHSi), 0.60 (1 H, m, MeC*H*Si), 0.20 (3 H, s, SiMe_AMe$_B$) and 0.16 (3 H, s, SiMe$_A$-Me_B); δ_C($CDCl_3$) 172.8, 143.2, 138.1, 133.9, 128.9, 128.8, 128.5, 128.4, 127.8, 51.4, 42.6, 39.8, 37.2, 15.2, 13.2, −4.8 and −5.7; *m*/*z* (EI) 325 (37%, M$^+$ − Me), 309 (65, M − OMe) and 135 (100, Me$_2$PhSi) (Found: M$^+$ − Me, 325.1624. $C_{21}H_{28}SiO_2$ requires *M* − Me, 325.1624).

Methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-3-methyl-5-phenylpentanoate 106A and methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-3-methyl-5-phenylpentanoate 106B. (71%, 84:16 from an 81:19 mixture of **76A** and **76B**); R_F(Et$_2$O–light petroleum, 10:90) 0.41; ν_{max}(film)/cm^{-1} 1737 (C=O) and 1599 (Ph); **106A**: δ_H(400 MHz; $CDCl_3$) 7.40–6.91 (10 H, m, 2 × Ph), 3.55 (3 H, s, OMe), 2.33 (1 H, dd, *J* 11.7 and 3.2, C*H*Si), 2.27 (1 H, dd, *J* 14.5 and 4.6, CH_AH$_B$CO$_2$Me), 1.97 (1 H, dd, *J* 14.5 and 8.1, CH$_A$$H_B$-CO$_2$Me), 1.86–1.78 (2 H, m, C*H*Me and CH_AH$_B$CHSi), 1.58 (1 H, ddd, *J* 15.0, 10.1 and 3.2, CH$_A$$H_B$CHSi), 0.84 (3 H, d, *J* 6.5, *Me*CH), 0.24 (3 H, s, SiMe_AMe$_B$) and 0.16 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 173.5, 142.5, 137.3, 134.1, 129.0, 128.0, 127.9, 127.6, 124.5, 51.2, 39.6, 36.1, 33.9, 29.04, 20.8, −4.0 and −5.5; **106B**: δ_H(400 MHz; $CDCl_3$) 7.40–6.91 (10 H, m, 2 × Ph), 3.59 (3 H, s, OMe), 2.38 (1 H, dd, *J* 12.9 and 3.1, C*H*Si), 2.16 (1 H, dd, *J* 14.8 and 7.0, CH_AH$_B$CO$_2$Me), 2.08 (1 H, dd, *J* 14.8 and 7.4, CH$_A$$H_BCO_2$Me), 1.95 (1 H, m, C$H_AH_B$CHSi), 1.80 (1 H, m, C*H*Me), 1.36 (1 H, ddd, *J* 13.7, 10.3 and 3.1, CH$_A$$H_B$CHSi), 0.80 (3 H, d, *J* 6.6, *Me*CH), 0.24 (3 H, s, SiMe_AMe$_B$) and 0.15 (3 H, s, SiMe$_A$$Me_B$) (Found: M$^+$, 340.1853. $C_{21}H_{28}O_2Si$ requires *M*, 340.1858).

Methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-3,5-diphenylpentanoate 107A and methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-3,5-diphenylpentanoate 107B. (71%, 14:86 from a 12:88 mixture of **77A** and **77B**); R_F(Et$_2$O–light petroleum, 10:90) 0.41; ν_{max}(film)/cm^{-1} 1738 (C=O) and 1599 (Ph); **107A**: δ_H(400 MHz; $CDCl_3$) 7.30–6.80 (15 H, m, 3 × Ph), 3.47 (3 H, s, OMe), 3.03 (1 H, m, C*H*PhCH$_2$CO$_2$Me), 2.63 (1 H, dd, *J* 15.3 and 5.8, CH_A-H$_B$CO$_2$Me), 2.46 (1 H, dd, *J* 15.3 and 9.1, CH$_A$$H_BCO_2$Me), 2.36 (1 H, dd, *J* 11.1 and 4.3, C*H*Si), 2.24–2.12 (1 H, m, CH_AH$_B$-CHSi), 2.04 (1 H, ddd, *J* 13.8, 9.2 and 4.3, CH$_A$$H_B$CHSi), 0.26(3 H, s, Si$Me_AMe_B$), 0.16 (3 H, s, SiMe$_A$$Me_B$); **107B**: δ_H(400 MHz; $CDCl_3$) 7.30–6.80 (15 H, m, 3 × Ph), 3.50 (3 H, s, OMe), 2.90 (1 H, m, C*H*PhCH$_2$CO$_2$Me), 2.46 (2 H, d, *J* 7.6, C$H_A$$H_B$-CO$_2$Me), 2.14 (1 H, dt, *J* 3.2 and 13.4, CH_AH$_B$CHSi), 1.91 (1 H, dd, *J* 12.8 and 2.4, C*H*Si), 1.83 (1 H, ddd, *J* 13.8, 11.6 and 2.4, CH$_A$$H_B$CHSi), 0.17 (3 H, s, Si$Me_AMe_B$), 0.01 (3 H, s, SiMe$_A$-$Me_B$); δ_C($CDCl_3$) 172.5, 142.9, 141.7, 137.2, 134.0, 128.9, 128.3, 128.2, 128.1, 127.8, 127.5, 126.4, 124.6, 51.3, 42.0, 40.3, 35.1, 33.3, −3.8 and −5.9 (Found: M$^+$, 402.2006. $C_{26}H_{30}O_2Si$ requires *M*, 402.2015).

Methyl (3*RS*,5*SR*)-3,6-dimethyl-5-dimethyl(phenyl)silylheptanoate 108A and methyl (3*RS*,5*RS*)-3,6-dimethyl-5-dimethyl(phenyl)silylheptanoate 108B. (68%, 64:36 from a 64:36 mixture of **80A** and **80B**; 60%, 52:48 from a 52:48 mixture of **80A** and **80B**); R_F(Et$_2$O–light petroleum, 10:90) 0.33; ν_{max}(film)/cm^{-1} 1739 (C=O), 1249 (SiMe) and 1110 (SiPh); **108A**: δ_H(400 MHz; $CDCl_3$) 7.49 (2 H, m, *o*-Ph), 7.35–7.26 (3 H, m, *m*- and *p*-Ph), 3.64 (3 H, s, OMe), 2.27–1.83 and 1.47–1.06 (7 H, m), 0.92–0.72 (9 H, m, 3 × C*H*Me) and 0.32 (6 H, s, SiMe$_2$); δ_C($CDCl_3$) 173.8, 140.0, 133.9, 128.7, 127.7, 51.4, 41.5, 33.7, 30.1, 29.8, 28.8, 22.5, 21.1, 20.1, −2.7 and −2.8; **108B**: δ_H(400 MHz; $CDCl_3$) 7.49 (2 H, m, *o*-Ph), 7.35–7.26 (3 H, m, *m*- and *p*-Ph), 3.63 (3 H, s, OMe), 2.27–1.83 and 1.47–1.06 (7 H, m), 0.92–0.72 (9 H, m, 3 × C*H*Me) and 0.30 (3 H, s, SiMe$_2$); δ_C($CDCl_3$) 173.7, 139.9, 133.8, 128.7, 127.7, 51.4, 42.0, 34.1, 30.0, 29.7, 28.7, 22.3, 21.9, 19.4, −2.0 and −2.2; *m*/*z* (EI) 306 (18%, M$^+$), 291 (52, M − Me), 275 (44, M − OMe) and 135 (100, Me$_2$PhSi) (Found: M$^+$, 306.2015. $C_{18}H_{30}SiO_2$ requires *M*, 306.2015). The ratio of diastereoisomers was determined by integration of the CH_2 signals in the ^{13}C NMR spectrum (42.0 to 41.5 and 34.1 to 33.7 ppm).

Methyl (3*RS*,5*SR*)-5-dimethyl(phenyl)silyl-6-methyl-3-phenylheptanoate 109A and methyl (3*RS*,5*RS*)-5-dimethyl(phenyl)silyl-6–methyl-3-phenylheptanoate 109B. (70%, 37:63 from a 37:63 mixture of **81A** and **81B**); R_F(Et$_2$O–light petroleum, 10:90) 0.37; ν_{max}(film)/cm^{-1} 1735 (C=O) and 1602 (Ph); **109A**: δ_H(250 MHz; $CDCl_3$) 7.5–6.85 (10 H, m, 2 × Ph), 3.56 (3 H, s, OMe), 2.94 (1 H, m, PhC*H*CH$_2$CO$_2$Me), 2.52 (1 H, dd, *J* 15.1 and 7.2, CH_AH$_B$CO$_2$Me), 2.36 (1 H, dd, *J* 15.1 and 7.8, CH$_A$$H_BCO_2$Me), 1.84 (1 H, dseptet, *J* 2.6 and 6.9, C*H*Me$_2$), 1.72–1.53 (3 H, m, CH_2CHSi and C*H*Si), 0.77 (3 H, d, *J* 6.9, CHMe_AMe$_B$), 0.74 (3 H, d, *J* 6.8 CHMe$_A$$Me_B$), 0.38 (3 H, s, Si$Me_AMe_B$) and 0.31 (3 H, s, SiMe$_A$$Me_B$); **109B**: δ_H(250 MHz; $CDCl_3$) 7.50–6.85 (10 H, m, 2 × Ph), 3.54 (3 H, s, OMe), 3.16 (1 H, m, PhC*H*CH$_2$CO$_2$Me), 2.50 (1 H, dd, *J* 7.3 and 4.9, CH_AH$_B$CO$_2$Me), 2.47 (1 H, dd, *J* 14.6 and 7.3, CH$_A$$H_BCO_2$Me), 2.02 (1 H, dseptet, *J* 2.6 and 7.1, C*H*Me$_2$), 1.72–1.53 (2 H, m, CH_2CHSi), 0.96 (3 H, d, *J* 6.9, CHMe_AMe$_B$), 0.82 (3 H, d, *J* 7.0, CHMe$_A$$Me_B$), 0.68 (1 H, dt, *J* 2.6 and 9.9, C*H*Si), 0.22 (3 H, s, SiMe_AMe$_B$) and 0.21 (3 H, s, SiMe$_A$$Me_B$); δ_C($CDCl_3$) 172.8, 143.3, 139.6, 133.9, 128.3, 128.2, 127.7, 127.6, 126.3, 51.4, 42.0, 41.0, 33.6, 29.6, 28.3, 22.5, 22.1, −1.6 and −3.1 (Found: M$^+$ − Me, 353.1938. $C_{23}H_{32}O_2Si$ requires *M* − Me, 353.1937).

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