

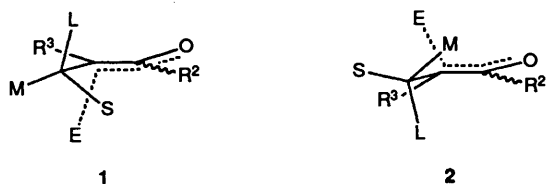
## The Diastereoselectivity of Electrophilic Attack on Trigonal Carbon Adjacent to a Stereogenic Centre: Diastereoselective Alkylation and Protonation of Open-chain Enolates Having a Stereogenic Centre Carrying a Silyl Group at the $\beta$ Position

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The alkylation and protonation of enolates having a  $\beta$ -silyl group, prepared by conjugate addition of a silyl-cuprate reagent to enone systems, are almost always highly diastereoselective in the sense **3** in a wide variety of reactions. The effects of varying the type of enolate (Scheme 1) and its geometry, the size of the medium-sized group  $R^1$  on the stereogenic centre (Scheme 3), the nature of the alkylating agent  $R^3X$  or proton source (Scheme 4), and the size of the substituents  $R^4$  and  $R^5$  on the silyl group (Scheme 6) are reported. The stereoselectivity is also high in the creation of some quaternary centres (Scheme 7). Because the phenyldimethylsilyl group can be converted into a hydroxy group with retention of stereochemistry at the  $\beta$  carbon atom, the reaction allows the stereocontrolled synthesis of  $\beta$ -hydroxycarbonyl compounds. The major limitation, as a synthetic method, is that the diastereoselectivity is low, and even occasionally reversed, when the group  $R^3$  on the nucleophilic centre is much larger than a methyl group. There is some inconclusive evidence that some of the stereocontrol may be electronic in origin, rather than just steric. Whatever the extent of electronic control, a  $\beta$ -silyl group is an effective control element in electrophilic attack on a double bond, because its electronic and steric effects are likely to operate in the same direction. Neither the kinetic acidity of the esters nor the nucleophilicity of the enolates is noticeably affected by the presence of a  $\beta$ -silyl group.

In the first paper in this series,<sup>1</sup> we discussed the steric factors governing the diastereoselectivity of electrophilic attack on a double bond adjacent to a stereogenic centre, and left out of that discussion whatever polar contributions there might be when one of the substituents was a heteroatom. In summary, reactions like the alkylation and protonation of the enolates of an ester or ketone can be expected to take place with transition structures like **1** rather than **2**, because allylic 1,3 interactions favour the arrangement with the medium-sized group 'outside', as in **1**



rather than 'inside', as in **2**. In this paper we discuss first how a contribution from the electronic effect of a polarised bond overlapping with the  $\pi$ -bond complicates the argument for a general rule, and we conclude that when the heteroatom is electropositive relative to carbon, the rule is more orderly than when the heteroatom is electronegative. We then discuss in full our results on the alkylation and protonation of enolates carrying a silyl group in the  $\beta$ -position, many of which have been reported in preliminary form.<sup>2</sup>

Most of the work on the diastereoselectivity of electrophilic attack on a double bond adjacent to a stereogenic centre having polar substituents has been carried out on allylic alcohols and their derivatives, so that the atoms attached to the stereogenic centre are oxygen, carbon and hydrogen. Reactions that have been examined include halogeno-lactonisation and related processes, hydroboration, nitrile oxide and Diels–Alder cycloadditions, the Simmons–Smith reaction, epoxidation, hydrogenation, and osmium tetroxide-based bishydroxylation. In some of these reactions, the oxygen atom probably serves to

deliver the reagent, either by hydrogen bonding, as first suggested by Henbest,<sup>3</sup> or by Lewis base–Lewis acid coordination. This distorts the steric arguments used to create the pictures **3–6** in the first paper in this series, and takes the reaction from being a true open-chain reaction into one that has a cyclic transition structure, with which we are not concerned here. In other cases, when it is not participating by delivering the reagent, there is a reasonable probability that the electronegative element, the oxygen-based group, will be more or less orthogonal to the  $\pi$ -system in the transition structure. The argument is that electrophilic attack will be slower when such a group is able to overlap with the  $\pi$ -system, because of negative hyperconjugation, and having it orthogonal avoids this rate-retarding effect. In calculations, the preferred arrangement for hydroboration appears to be similar to **5** in the first paper in this series,<sup>4</sup> and for nitrile oxide cycloaddition it appears to be similar to **6** in the first paper in this series,<sup>5</sup> in both of which the oxygen substituent occupies the position, M, where it is nearly orthogonal to the  $\pi$ -system, and not antiperiplanar to one of the developing bonds. The ground state is also delicately balanced between having the oxygen substituent orthogonal 'inside' and orthogonal 'outside', with only a very small difference in energy between them.<sup>6</sup> A transition structure similar to **6** in the first paper in this series, with an oxygen or other electronegative substituent occupying the M position, has been proposed, without computational support, for a number of other reactions such as osmium tetroxide-based bishydroxylation,<sup>7,8</sup> epoxidations,<sup>8,9</sup> the alkylation<sup>10</sup> and protonation<sup>11</sup> of nitronates, the alkylation and protonation of enolates,<sup>12</sup> oxymercuration,<sup>13</sup> a  $\beta$ -lactam-forming cycloaddition<sup>14</sup> and iodo-etherification.<sup>15</sup>

There is another possibility with allylic alcohol reactions, in which the electronegative substituent might show a preference, for electronic reasons, for taking up a position antiperiplanar to the incoming bond rather than being nearly orthogonal to it. In one version, used to explain the diastereoselectivity for osmium tetroxide-based bishydroxylation,<sup>16</sup> the lone pairs on the

oxygen overlap, through space, with the  $\pi$ -bond orbitals on the lower surface, making the upper surface the more nucleophilic; the outcome is the same as the explanation more commonly used, in which the conformation attacked is similar to that in **6** in the first paper in this series, with the oxygen substituent occupying the position M. In another version,<sup>17</sup> the electronegative substituent, is seen as electronically stabilising the transition structure when it is antiperiplanar to the incoming bond. This idea is related to the explanations offered for the corresponding reactions involving nucleophilic attack on a carbonyl group, where Anh proposed<sup>18</sup> that the lowest-energy transition structure would have the new bond antiperiplanar to the electronegative substituent. The problem with this idea is that intuitively one would expect nucleophilic and electrophilic reactions to have opposite preferences. For nucleophilic attack on a carbonyl group, Anh's perception was that an antiperiplanar  $\pi$ -acceptor would lower the LUMO energy and hence speed up nucleophilic attack, but Cieplak provocatively pointed out<sup>19</sup> that the incompletely formed bond in the transition structure was, in essence, electron deficient, and should therefore be stabilised, both for nucleophilic and for electrophilic attack, by an antiperiplanar  $\pi$ -donor substituent. Certainly, an  $\alpha$ -silyl substituent, which is a  $\pi$ -donor, leads to high levels of Cram selectivity in nucleophilic attack on a ketone group,<sup>20</sup> and this corresponds to attack *anti* to the silyl group in the usual Felkin model.<sup>21</sup> Whether Cieplak's suggestion proves to be generally true for nucleophilic attack on a carbonyl group, and it is still currently the subject of much debate, it is very probably true for electrophilic attack on a double bond. Electron deficiency in the incomplete bond in electrophilic attack on a C=C double bond ought to be stabilised by an antiperiplanar  $\pi$ -donor substituent—the HOMO energy is raised by such a substituent, so that the conformation in which it overlaps with the  $\pi$ -bond is more reactive, in contrast to the situation when the heteroatom is electronegative.

Relatively little work has been done with electropositive substituents compared to the vast amount of work with electronegative substituents like the oxygen-based groups discussed above, largely because there is a relatively small selection of electropositive heteroatomic candidates, of which silicon and tin are the most likely to have been looked at. Nevertheless, the prediction is clear—electropositive substituents on the stereogenic centre will occupy a position that allows the bond to overlap with the  $\pi$ -system, and electrophiles will attack *anti* to this group, as in the transition structures **1** and **2** with the electropositive element occupying the position L. Since silyl and stannyl groups are almost always relatively large, this argument for an electronic effect leads to the same prediction for the sense of the diastereoselectivity of electrophilic attack as the argument for a steric effect. With the steric and electronic effects working in the same direction, the sense of the diastereoselectivity of electrophilic attack should be relatively easy to predict. The major thesis of all our work in this area has been how well silyl and stannyl groups fulfil the role of being both electronically activating and sterically controlling substituents, with none of the ambiguity about their conformational preference at the time of reaction inherent in having oxygen-based substituents on the stereogenic centre. The major area of doubt in making a prediction is the problem of knowing how the other two substituents, the small and the medium-sized groups, will be arranged in the transition structure. In some cases, there is clearly room in a transition structure like **2** for the medium-sized group to occupy the 'inside' position, as it may be doing for some nitrile oxide cycloadditions and for the protonation of the enol ether **15** discussed in the earlier paper. However, with the enolates of esters and ketones, there is inevitably allylic 1,3 strain between the 'inside' group and the groups *syn* to it on the enolate double bond, and this

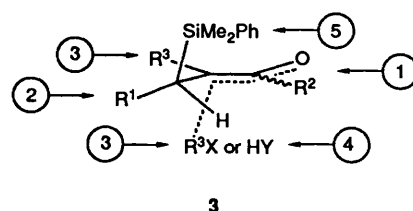
factor makes the transition structure **1** clearly preferred over **2**.

Similar arguments for a high diastereoselectivity in the methylation of enolates carrying silyl, stannyl and oxymethyl groups on an adjacent stereogenic centre have been advanced by McGarvey and Williams,<sup>22</sup> who conclude from the similarity of the results with these three  $\pi$ -donating groups that an electronic component must be present.

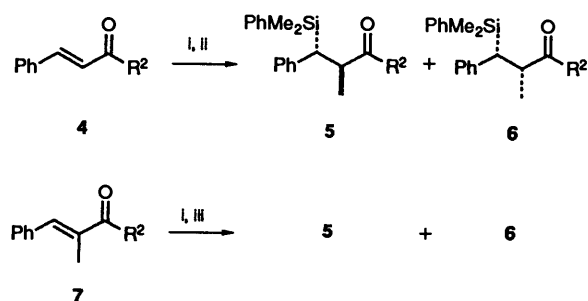
Caution ought perhaps to be exercised at this stage in invoking electronic effects. In the first place, two striking demonstrations that electronic effects seem not to be operating have come from Vedejs. In one, the epoxidation and the osmium tetroxide-based bishydroxylation of allylic systems showed very similar diastereoselectivity, whether the substituent on the stereogenic centre was an electron-withdrawing, sulfonyl, or an electron-donating, silyl, group.<sup>23</sup> In the other, the diastereoselectivity in the epoxidation of an exocyclic double bond was unaffected by whether an  $\alpha$ -methoxy substituent was held orthogonal to or overlapping with the  $\pi$ -bond.<sup>24</sup> In the second place, it is not certain that the C–Si bond is polarised enough to exert a significant electronic effect. What is clear is that the degree of diastereoselectivity that we see in the reactions to be described in this paper is significantly higher than that seen in the reactions described in the two preceding papers, which did not have the benefit of a silyl group on the stereogenic centre. While this might mean that the silyl group is exerting a significant electronic effect, it remains possible that it is a consequence only of its undeniable bulk.

## Results and Discussion

Given that the argument in favour of the transition **1** is made stronger when the large group L is an electropositive element, it is clear that we can expect electrophilic attack on an enolate carrying a  $\beta$ -silyl group to take place by way of the approximate transition structure **3**. To find out just how effective a silyl group



is as a control element, we have investigated all the variables ringed as 1–5, with most of our experiments carried out by adding our phenyldimethylsilyl cuprate reagent to an enone system, and quenching the reaction mixture with an alkyl halide or a proton source. In the following sections, we discuss each of the variables 1–5 in that order.

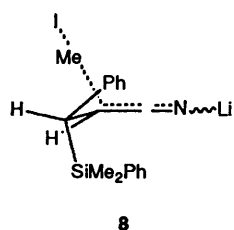


**Scheme 1** Reagents: i,  $(\text{PhMe}_2\text{Si})_2\text{CuCN Li}_2$ ; ii, MeI, iii,  $\text{NH}_4\text{Cl}$ ,  $\text{H}_2\text{O}$

1. Varying the carbonyl group, COR<sup>2</sup>.—We carried out

**Table 1** Varying the carbonyl group (Scheme 1): diastereoselectivity in the methylation of enolates derived from **4** and in the protonation of enolates derived from **7**

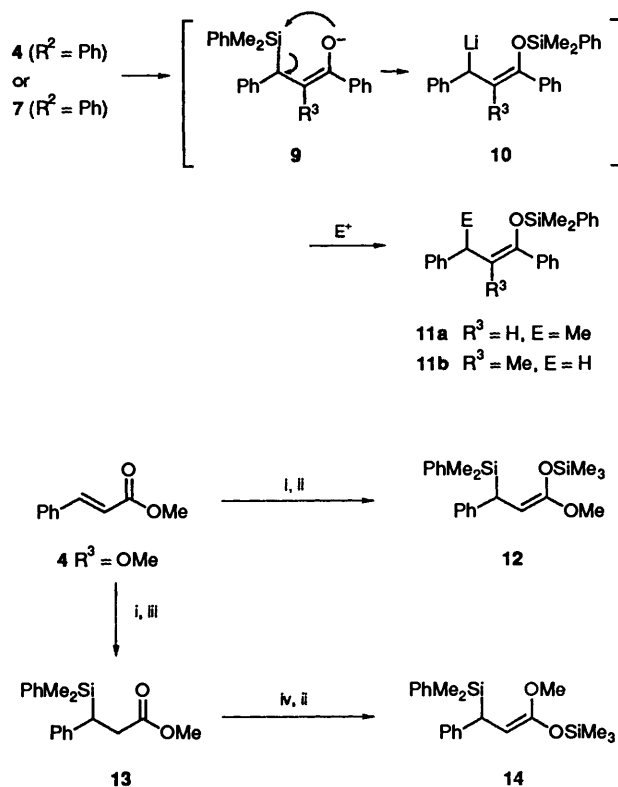
Entry	Identifying letter for compound numbers	R <sup>2</sup>	Methylation from <b>4</b>		Protonation from <b>7</b>	
			Ratio <b>5</b> : <b>6</b>	Yield (%)	Ratio <b>5</b> : <b>6</b>	Yield (%)
1	<b>a</b>	OMe	97:3	88	15:85	84
2	<b>b</b>	Me	98:2	57	30:70	
3	<b>c</b>	H	92:8	74	11:89	93
4	<b>d</b>	Ph	high	70	—	
5	<b>e</b>	NMe <sub>2</sub>	97:3	86	18:82	83
6	<b>f</b>	OLi <sup>d</sup>	64:36	63	—	—
7	<b>g</b>	CN for COR <sup>2</sup>	54:46	65	14:86	77



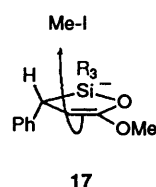
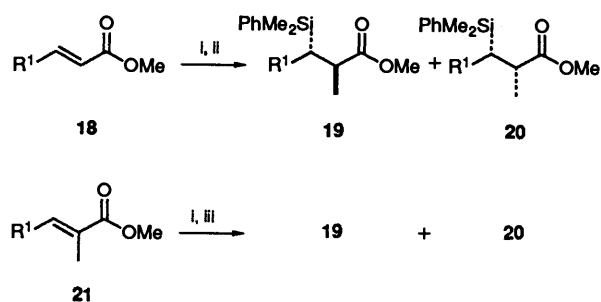
additions to methyl cinnamate **4** ( $R^2 = \text{OMe}$ ), and to the corresponding methyl ketone, aldehyde, phenyl ketone, dimethylamide, and nitrile, in each case using methyl iodide as the electrophile. For the protonation reactions, we carried out the additions to methyl  $\alpha$ -methylcinnamate **7** ( $R^2 = \text{OMe}$ ) and the same derivatives, using aqueous ammonium chloride as the proton source. The diastereoselectivity was uniformly high in most of the alkylation reactions, and moderately high in the protonation reactions (Scheme 1 and Table 1), and the stereochemistry does indeed prove to be that enshrined in the transition structure **3**. The major product in the methylation reactions is the diastereoisomer **5**, and in the protonation reactions it is **6**. The only poor results were in the methylation of the enediolate, entry 6, and the methylation of the nitrile, entry 7. The latter, which is almost completely unselective, is relatively easy to explain—uniquely with the nitrile anion, there is no allylic 1,3 strain in the conformation **8**, corresponding to **2**. This conformation is much more similar in energy to the usual alternative, the nitrile anion equivalent of **3**, and the reaction is correspondingly unselective. The disappointingly low selectivity with the enediolate might be explained similarly, in that the substituent on the enolate double bond *cis* to the stereogenic centre is an oxyllithium group, which might be considered small, but this group is also *cis* to the stereogenic centre in the ester enolate, and that is highly diastereoselective. Furthermore, the enolate in the aldehyde case, entry 3, has only a hydrogen atom *cis* to the stereogenic centre, and the diastereoselectivity of methylation, although not especially high, is still good.

The phenyl ketone case, entry 4, is somewhat more complicated. Only one diastereoisomer was visible in the <sup>1</sup>H NMR spectrum, and so we cannot give a ratio, and the protonation sequence gave none of the expected product **6** ( $R^2 = \text{Ph}$ ). Instead, we isolated only the silyl enol ether **11b**, presumably by way of a 1,4 silyl transfer **9**→**10** in a *Z* enolate. In the methylation series, starting from **4**, there was a by-product from the same pathway, but in this case, quenching with methyl iodide caused the intermediate benzyllithium to give the methylated silyl enol ether **11a**.

In the experiments described in the first paper in this series, we could not control the double bond geometry of the enolate, and were unable seriously to investigate its effect on the diastereoselectivity. In the present work, we have been able easily to control the geometry of the enolate starting from the

**Scheme 2** Reagents: i,  $(\text{PhMe}_2\text{Si})_2\text{CuCN Li}_2$ ; ii,  $\text{Me}_3\text{SiCl}$ ; iii,  $\text{NH}_4\text{Cl}$ ,  $\text{H}_2\text{O}$ ; iv, LDA

esters **4** ( $R^2 = \text{OMe}$ ) (Scheme 2). Conjugate addition of the silyl cuprate to methyl cinnamate and trapping with trimethylsilyl chloride gave what appeared to be a single silyl enol ether **12** with doublets at  $\delta$  3.3 and 3.8. In contrast, when we prepared it by treating the ester **13**, itself prepared by protonating the intermediate enolate from the ester **4** ( $R^2 = \text{OMe}$ ), with lithium diisopropylamide (LDA) and quenching with trimethylsilyl chloride, we obtained a different silyl enol ether **14**, with doublets at  $\delta$  4.15 and 3.5. The latter recipe is well known<sup>25</sup> to give *E*-silyl enol ethers like **14**, and we have assumed that our  $\beta$ -silyl group has not interfered. It follows that the conjugate addition of the silyl-cuprate must be taking place very largely in the *s-cis* conformation of the ester to give the *E*-enolate and hence the *Z*-silyl enol ether **12**. This useful device has played a large part in our being able to control the reactions of these silicon-containing enolates with aldehydes, as described in the next paper in this series. We also investigated the geometry of the enolates in the methyl ketone and aldehyde series, entries 2 and 3. In these cases we could not prepare both isomers, but the conjugate addition reactions appeared to give only one product. In the methyl ketone case, the derived silyl enol ether was the

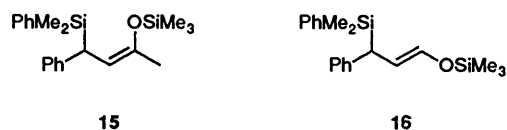


Scheme 3 Reagents: i,  $(\text{PhMe}_2\text{Si})_2\text{CuCN Li}_2$ ; ii, MeI; iii,  $\text{NH}_4\text{Cl}$ ,  $\text{H}_2\text{O}$

Table 2 Varying the medium-sized group (Scheme 3): diastereoselectivity in the methylation of enolates derived from **18** and in the protonation of enolates derived from **21**

Entry	Identifying letter for compound numbers	R <sup>1</sup>	Methylation from <b>18</b>		Protonation from <b>21</b>	
			Ratio <b>19:20</b>	Yield (%)	Ratio <b>19:20</b>	Yield (%)
1	a	Ph	97:3	88	15:85	84
2	b	Me	91:9	78	13:87	82
9	c	Pr <sup>i</sup>	85:15	95	4:96	56
10	d	Bu <sup>i</sup>	66:34	83	4:96	62

*Z*-isomer **15**, as shown by a 13% NOE effect from the *C*-methyl group to the olefinic hydrogen. In the aldehyde case, however, it was probably the *E*-isomer **16**, with a coupling constant of 12 Hz between the two olefinic hydrogens, comparing with literature values of 12 Hz for an *E*-silyl enol ether and 6 Hz for a *Z*-silyl enol ether.<sup>26</sup>



Having both *Z*- and *E*-enolates in the ester series, we could methylate them both and compare the diastereoselectivity. As shown in entry 1 in Table 1, the *E*-enolate from the conjugate addition gave the products **5** and **6** ( $R^2 = \text{OMe}$ ) in a ratio of 97:3, as determined by <sup>1</sup>H NMR integration and by reverse phase HPLC. The *Z*-enolate generated from the ester **13** gave the same products in the same ratio. Clearly there is no reason why they have to be exactly the same, it must be coincidence, but that both enolates are highly diastereoselective shows that the double bond geometry is not necessarily important, as we have argued in the first paper in this series. As long as there is a substituent larger than hydrogen *cis* to the stereogenic centre the conformation is well controlled and high diastereoselectivity follows. This result is important in another respect, since it rules out an alternative explanation for the high diastereoselectivity in these alkylations. The oxyanion group in the enolate might be coordinated to the silyl group to give a cyclic intermediate **17**, alkylation of which on the less hindered surface of the ring would give the same major product **5**. Such an intermediate is only possible with the *E*-enolate and this cannot be the explanation for the diastereoselectivity shown by the *Z*-enolate. Clearly our results are only compatible with genuine open-chain stereocontrol.

In the protonation reactions, the substituent  $R^3$  in the presumed transition structure **3** is no longer a hydrogen atom, and the preferred conformation at the time of reaction is no longer necessarily close to that shown as **3**. The larger  $R^3$  gets, the less likely is it to be *gauche* to the silyl and medium-sized

groups, and the less predictable is the transition structure, and hence the sense of the diastereoselectivity. As a result, it is not surprising that protonation is not as highly diastereoselective as methylation. It is, however, still in the same sense, corresponding to **3**, and is tolerably selective even with the nitrile (entry 6). There is, however, an alternative explanation, which we advance only tentatively here. We observed, in our results described in the first paper in this series, that there was, in four of the five examples that we measured equilibrium ratios for, a bias in favour of the formation of the thermodynamically more stable product. Thus, methylation gave a higher ratio of diastereoisomers when the major product from methylation was the thermodynamically more stable diastereoisomer, but protonation gave a higher ratio of diastereoisomers when the major product from protonation was the more stable. The same proves to be true in both cases that we have measured in this work—at equilibrium the esters **5a** and **6a** are present in a ratio of 64:36, and the esters **19c** and **20c** are present in a ratio of 41:59, achieved in both cases from both directions by refluxing each diastereoisomer with sodium methoxide in methanol for a week. It would seem that there may be a thermodynamic component affecting the degree of diastereoselectivity. It is most unlikely that there is some degree of equilibration under the conditions of the reactions, but only a little more likely that the factors affecting the relative thermodynamic stability of the products are affecting the transition structures to some extent. This ought not to be a large effect, given that we are looking at an exothermic reaction. Furthermore, there is no necessary correlation between the factors that affect the relative energies of the various populated conformations of the product and the conformations in the transition structures. A plot of the difference between the logarithms of the methylation and protonation ratios and the logarithm of the ratios of the methylation product to the protonation product at equilibrium showed that there was only a very poor quantitative relationship, and we make no more of this point.

Most of the reactions described above were carried out on a 1–3 mmol scale, but there is no problem in scaling up. Selecting the reaction of entry 1, we carried out a reaction on 16.2 g (100 mmol) of methyl cinnamate, hydrolysing the crude ester directly, without purification, to give the crystalline acid **5f** in 59% yield overall.

We proved the relative configuration of most of the products by correlation of the acid derivatives. Thus we have already reported in full<sup>27</sup> the proof of relative configuration for the products of entries 1 and 2 in Table 1. We reduced the products in entries 1 and 3 with lithium aluminium hydride to the same pair of primary alcohols; we treated the carboxylic acid products in entry 6 with diazomethane to give the recognizable esters of entry 1; and we made the major nitrile product in entry 7 from the crystalline carboxylic acid derived by hydrolysis from the major methyl ester of entry 1. We have also reported<sup>28</sup> the conversion of the phenyldimethylsilyl group in the product from the phenyl ketone in entry 4 into a hydroxy group with retention of configuration giving a known alcohol. This leaves only the amide of entry 5, for which we assumed that the major product is in the same sense as all the other derivatives.

2. Varying the Medium-sized Group,  $R^1$ .—Working with the methyl esters **18** and **21**, we tested as medium-sized groups

**Table 3** Relative sizes of relevant groups and the diastereoselectivity of methylation

Group	<i>A</i> -value $r^{*a}$		Diastereoselectivity when set against a dimethyl(phenyl)silyl group, from Table 2	Diastereoselectivity when set against a trimethylstannyl group
Me <sub>3</sub> Si	2.5 <sup>b</sup>	2.1		
Me <sub>3</sub> Sn	1.1 <sup>c</sup>			—
Ph	2.7 <sup>d</sup>	1.6	97:3	96:4 <sup>e</sup> (93:7) <sup>f</sup>
Me	1.7	1.8	91:9	97:3 <sup>g</sup>
Pr <sup>i</sup>	2.1	2.2	85:15	
Bu <sup>t</sup>	~5	3.6	66:34	

<sup>a</sup> Ref. 35. <sup>b</sup> Ref. 33. <sup>c</sup> Ref. 34. <sup>d</sup> Ref. 32. <sup>e</sup> C. J. Urch, Ph.D. Thesis, Cambridge, 1983. <sup>f</sup> Ref. 37 (tributylstannyl in place of trimethylstannyl). <sup>g</sup> Ref. 37.

methyl, isopropyl and *tert*-butyl, as well as phenyl, already described above, and we used methyl iodide as the electrophile (Scheme 3). The results are collected in Table 2. With the phenyl group possibly somewhat out of line, the diastereoselectivity of methylation falls steadily with increasing size of the medium-sized group. We presume that the larger the medium-sized group the more the attack *syn* to it in transition structure 3 is hindered, and that there is certainly a steric component to the diastereoselectivity. Whether the phenyl group is out of line depends upon the size one assigns to it, but we note here that high diastereoselectivity has been found for other trigonal carbon substituents in this position, both by us<sup>29</sup> and by others,<sup>30</sup> who found that vinyl substituents in place of the phenyl also lead to highly diastereoselective methylation. We suggest that this may be because there is an electronic component to the diastereoselectivity, with the phenyl and vinyl groups being less effective donor substituents than the alkyl groups in hyperconjugation with the  $\pi$ -system of the enolate.

It is difficult to find more convincing evidence for an electronic component. Comparing the methylation results in which a methyl group is set against a phenyldimethylsilyl group (91:9, entry 8) with the result in the first paper in this series in which a methyl group is set against an isopropyl group (75:25), there is a clear increase in the diastereoselectivity. When the phenyldimethylsilyl group is set against an isopropyl group there is still high diastereoselectivity (85:15, entry 9). Both results could simply reflect a greater steric hindrance from the silyl group than from the isopropyl group. The problem is to measure the steric hindrance, when it is well known that no one measure of steric hindrance can be safely carried over from one situation to another. Conformational *A*-values<sup>31–34</sup> are much used, and we list these in Table 3, along with Sternhell's parameter  $r^{*}$ ,<sup>35</sup> which measures the steric hindrance exerted by the group towards biphenyl rotation. Both measures of steric hindrance rank the silyl group as less hindering than a *tert*-butyl group, and we suggest that this implies, but does not prove, that there is an electronic component to the diastereoselectivity, since the methylation reaction takes place in the same sense for all the entries in Table 2. Notably, Sternhell's  $r^{*}$ , ranking the carbon groups in the order Bu<sup>t</sup> > Pr<sup>i</sup> > Me > Ph, follows the methylation ratio, but assigns the silyl group a degree of steric hindrance in the middle of the series.

There is, of course, no doubt that the silyl group is larger in overall bulk than the *tert*-butyl group, but the long bond to the silicon atom takes it further away from the site of reaction, making it frequently much less sterically hindering than one might expect merely from its actual size.<sup>36</sup> The same goes, but even more so, for the trimethylstannyl group, which is actually larger still, but which has a smaller *A*-value.<sup>33,34</sup> As far as the evidence goes (unfortunately there is not a complete set of data),

the trimethylstannyl group appears to be very similar to the silyl, perhaps compensating with a larger electronic contribution for a reduced steric requirement. (Some results with the tributylstannyl group<sup>22,37</sup> appear to indicate that the tributylstannyl group is very similar in its effect to the trimethylstannyl.) If all the dihedral angles in the transition structure 3 were known, one might be able to assess the extent of the actual steric hindrance exerted by the silyl group, but in the absence of such knowledge, our claim for detecting some kind of electronic component to the diastereoselectivity must remain tentative.

In the protonations, the selectivity is in the opposite order: Bu<sup>t</sup> = Pr<sup>i</sup> > Me > Ph. It is perhaps curious that a proton, presumably a small electrophile, should be much more selective than the larger electrophiles, but there are so many changes in the steric and electronic requirements for protonation relative to alkylation, and in how early the transition state is, that nothing can be viewed as surprising. As we commented above, with R<sup>3</sup> larger than a hydrogen atom, predictions about the transition structure being close to 3 are less secure.

Some other results belong in this section but are not included in Table 2. Conjugate addition followed by methylation of *ethyl* crotonate (99:1, 82%) gave noticeably better diastereoselectivity than *methyl* crotonate (91:9, entry 8). We have no explanation for this result. Whatever the explanation, we showed, using ethyl crotonate, that the conjugate addition–methylation was not stereospecific in the Zimmerman sense<sup>38</sup>—both the *E*- and *Z*-crotonate gave the same major diastereoisomer 19 (R<sup>1</sup> = Me, OEt in place of OMe) to the same extent [99:1 (82%) and 98:2 (75%), respectively] within experimental error. This stereoselective, but not stereospecific, result is like Mohrig's<sup>39</sup> for the conjugate addition of a deuteriated thiol to ethyl crotonate in ethanol, but is in contrast to Naito's<sup>40</sup> stereospecific conjugate addition of a thiol to several  $\alpha$ -methyl crotonate derivatives in tetrahydrofuran. We also prepared two of the  $\beta$ -silylated enolates by conjugate addition of phenyl and methyl cuprates to the  $\beta$ -silylacrylate 18 (R<sup>1</sup> = PhMe<sub>2</sub>Si), and methylated these enolates to give the same products as before, the esters 19 (R<sup>1</sup> = Ph and Me) and 20 (R<sup>1</sup> = Ph and Me), in ratios (>95:5, 30% and 89:11, 56%) very similar to those in Table 2. The lower yields in these two reactions, and the failure of the ester 21 (R<sup>1</sup> = PhMe<sub>2</sub>Si) to react with either cuprate, point up the difficulty of persuading carbon cuprates to add to  $\alpha,\beta$ -unsaturated esters, whereas the silyl cuprate reacts easily. We also regenerated the enolate in the isopropyl series by treating the ester 18 (R<sup>1</sup> = Pr<sup>i</sup>) successively with the silyl-cuprate reagent, aqueous ammonium chloride, and LDA, and alkylating it with methyl iodide. We obtained in this way the same products 19 and 20 (R<sup>1</sup> = Pr<sup>i</sup>) in a ratio of 80:20 similar to entry 9. The same experiment in the *tert*-butyl series (for comparison with entry 10) gave the usual product from the conjugate addition step, but we were unable to methylate it.

We have assumed that the structures of the products of entry 8 have the appropriate stereochemistry, by analogy with our results on a ketone 4 (C<sub>6</sub>H<sub>13</sub> in place of Ph, R<sup>2</sup> = Me), where we know<sup>27</sup> that the straight-chain alkyl group in the R<sup>1</sup> position does not lead to anomalous stereochemistry. We proved the structures of the products in entries 9 and 10 using the esters 20 (R<sup>1</sup> = Pr<sup>i</sup> and Bu<sup>t</sup>), which were available in a high state of diastereoisomeric purity from the protonation protocol, by converting the phenyldimethylsilyl group into a hydroxy group,<sup>28</sup> to give, in both cases, known<sup>41,42</sup>  $\beta$ -hydroxy esters.

3. *Varying the Alkylating Agent, R<sup>3</sup>X*.—We alkylated the enolate derived from methyl cinnamate 22 with ethyl iodide, butyl iodide, isopropyl iodide, benzyl bromide, allyl bromide and methyl  $\alpha$ -bromoacetate (Scheme 4). In each case, we also

**Table 4** Varying the alkylating agent (Scheme 4): diastereoselectivity in the alkylation of enolates derived from **22** and in the protonation of enolates derived from **25**

Entry	Identifying letter for compound numbers	R <sup>3</sup>	X	Alkylation from <b>22</b>		Protonation from <b>25</b>	
				Ratio <b>23:24</b>	Yield (%)	Ratio <b>23:24</b>	Yield (%)
1	a	Me	I	97:3	88	15:85	84
11	b	Et	I	95:5	83	20:80	77
12	c	Bu	I	94:6	86	27:73	77
13	d	Pr <sup>1</sup>	I	95:5	26	60:40	77
14	e	PhCH <sub>2</sub>	Br	97:3	74	71:29	66
15	f	CH <sub>2</sub> =CHCH <sub>2</sub>	Br	95:5	76	31:69	83
16	g	MeO <sub>2</sub> CCH <sub>2</sub>	Br	98:2	50	10:90	82
17	h	MeCO	Cl	60:40 <sup>a</sup>	87	60:40 <sup>a</sup>	64
18	i	D	OD	55:45 <sup>b</sup>	68	—	—

<sup>a</sup> Or 40:60. <sup>b</sup> 60:40 at -30 °C.

**Table 5** Varying the proton source: diastereoselectivity in the protonation of enolates derived from **7** (R<sup>2</sup> = OMe)

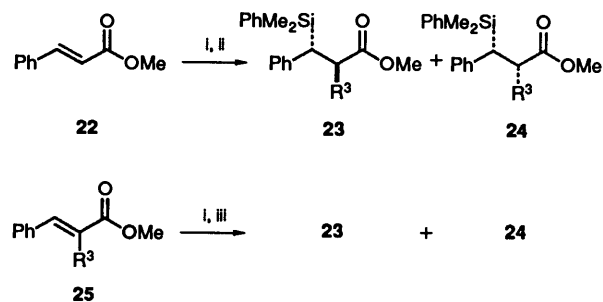
Entry	HY	Protonation from <b>7</b>	
		Ratio <b>5:6</b> <sup>a</sup>	
1	NH <sub>4</sub> Cl, H <sub>2</sub> O	15:85	
19	TFA	15:85	
20	MeOH	17:83	
21	EtOH	14:86	
22	Pr <sup>1</sup> OH	12:88	
23	Bu <sup>1</sup> OH	7:93	
24	Et <sub>3</sub> COH	7:93	
25	CH <sub>2</sub> (CO <sub>2</sub> Me) <sub>2</sub>	13:87	
26	Bu <sup>1</sup> Cl	10:90	

<sup>a</sup> Measured by integration of the C-methyl doublets at δ 1.00 and 1.10, respectively.

prepared the corresponding α,β-unsaturated esters **25** and measured the ratio of diastereoisomers **23** and **24** from conjugate addition and protonation. Our results are collected in Table 4, where it is clear that alkylation continues to be highly diastereoselective with all of the alkylating agents. Although the yield with isopropyl iodide (entry 13) is low, that we were successful at all indicated that the β-silyl enolates might be exceptionally good carbon nucleophiles, a point we return to at the end of this paper. We also carried out one conjugate addition of the silyl cuprate reagent to methyl crotonate in place of methyl cinnamate, followed by benzylation, and obtained a ratio of diastereoisomers of 96:4. The corresponding protonation result, a ratio of 39:61, was also very similar to that for the corresponding cinnamate, showing that the generality of the results in Table 4 is not a fortuitous consequence of having a phenyl group as the medium-sized group on the stereogenic centre. Because of the consistently high level of diastereoselectivity, we did not prove the relative stereochemistry of the products in this series. The following paper describes the extension of these reactions from the alkyl halides described above to trigonal electrophiles like aldehydes, all of which gave high levels of stereocontrol in the same sense, as we proved thoroughly in several cases.

In contrast to the alkylation reactions, protonation proved to be relatively unselective, especially when the group R<sup>3</sup> was much larger than a methyl group. A large group R<sup>3</sup> is unlikely to accept the *gauche* relationship with the silyl and the medium-sized groups in the transition structure **3**, and an alternative conformation is presumably adopted. The wide range of ratios in the protonation results in Table 4 identify the main limitation of this method of stereochemical control. It is not even reliable

in giving the diastereoisomer **24** as the major product—with the isopropyl and benzyl groups in the R<sup>3</sup> position, the major products **23** of alkylation and protonation are the same.

**Scheme 4** Reagents: *i*, (PhMe<sub>2</sub>Si)<sub>2</sub>CuCN Li<sub>2</sub>; *ii*, R<sup>3</sup>X; *iii*, NH<sub>4</sub>Cl, H<sub>2</sub>O

Not surprisingly, acylation of the enolate was unselective (entry 17), and so was the corresponding protonation. We presume that the rather similar ratios represent the thermodynamic ratio for this easily equilibratable system.

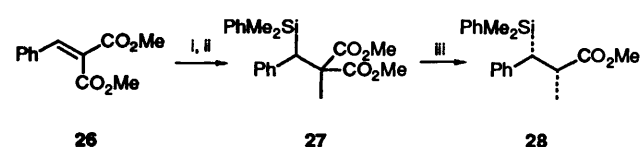
**4. Varying the Proton Source.**—Our efforts to affect the protonation ratio by changing the proton source have met with very limited success, and were not reported in our preliminary communication. Using the ester **6** (R<sup>2</sup> = OMe) and changing from aqueous ammonium chloride to a stronger acid, trifluoroacetic acid, and a weaker acid, methanol, had no very significant effect. The best results were obtained using a series of alcohols of increasing steric hindrance in the delivery of the proton. The effect (Table 5) was very small, but appeared to be a monotonic improvement in the series methanol < ethanol < isopropyl alcohol < *tert*-butyl alcohol, with no improvement beyond that. These ratios are not measurable accurately enough to claim more than that this seems to be a useful trend. There is precedent for methanol and *tert*-butyl alcohol to give different stereoselectivity in the protonation of the nitrile equivalent of an enolate exocyclic to a six-membered ring.<sup>43</sup> The two results with carbon acids (entries 25 and 26) appear to be slightly better than those with the unhindered protic acids.

We also tested an alternative methods for creating an enolate for protonation that does not depend upon having the R<sup>3</sup> group already present in the starting material **5**. Conjugate addition of the silyl-cuprate to benzyldenemalonate **26** (Scheme 5), followed by methylation gave the diester **27**. Krapcho decarboxylation<sup>44</sup> of this material should take place by way of an enol, which ought to be protonated stereoselectively. In the event, the ratio **5:6** (R<sup>2</sup> = OMe) was 30:70, in other words the ester **28** was the major diastereoisomer. Since the temperature

**Table 6** Varying the silyl group (Scheme 6): diastereoselectivity in the methylation of enolates derived from **18** and in the protonation of enolates derived from **21**

Entry	Identifying letter for compound numbers	R <sup>1</sup>	R <sup>4</sup>	R <sup>5</sup>	Methylation from <b>18</b>		Protonation from <b>21</b>	
					Ratio <b>29:30</b>	Yield (%)	Ratio <b>29:30</b>	Yield (%)
1	a	Ph	Ph	Me	97:3 <sup>a</sup>	88	15:85	84
27	b	Ph	Me	Me	94:6	67	—	—
28	c	Ph	Ph	Ph	>99:1	75	17:83	48
29	d	Ph	Bu <sup>t</sup>	Ph	99:1	70	34:66	56
9	e	Pr <sup>i</sup>	Ph	Me	85:15 <sup>a</sup>	95	4:96	56
30	f	Pr <sup>i</sup>	Ph	Ph	70:30 <sup>a</sup>	47	8:92	41
31	g	Pr <sup>i</sup>	Bu <sup>t</sup>	Ph	90:10	55	—	—

<sup>a</sup> Carried out by directly quenching the enolate from conjugate addition of the silyl-cuprate to the unsaturated ester with methyl iodide.

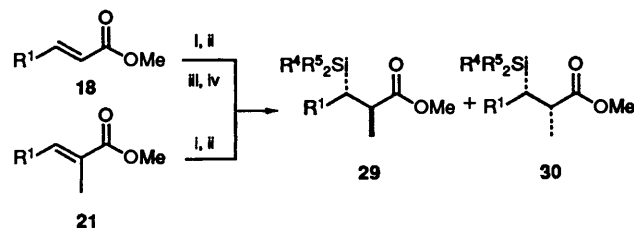


**Scheme 5** Reagents: i, (PhMe<sub>2</sub>Si)<sub>2</sub>CuCN Li<sub>2</sub>; ii, MeI; iii, LiCl, DMSO, reflux

for the Krapcho decarboxylation was that of refluxing DMSO, and the temperature for the protonation of the enolates in Table 5 is  $-78^{\circ}\text{C}$ , the drop in selectivity from 15:85 to 30:70 was remarkably small.

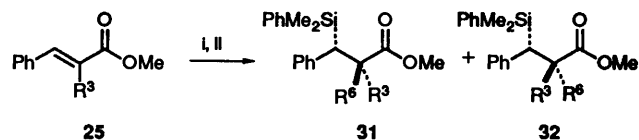
**5. Varying the Silyl Group.**—There was some possibility that we could improve the ratio of diastereoisomeric products by changing the size and electronic nature of the silyl group (Scheme 6). Furthermore, we hoped that this might shed some light on the question of whether there was an electronic component to the diastereoselectivity. In the event, changing the size and nature of the silyl group made only a small difference, and not always a consistent one, just like the change from a silyl to a stannyl group. Our results, which were not in our preliminary communication, are summarised in Table 6. No reliable trends emerged. Both the triphenyl and the *tert*-butyl(diphenyl)silyl groups made the methylation in the cinnamate series (entries 28 and 29) even more selective than it was with the dimethyl(phenyl)silyl group (entry 1), whereas the trimethylsilyl group (entry 27) was marginally worse. This seems to imply a steric rather than an electronic component, but it does not hold up in the second group of results with R<sup>1</sup> as an isopropyl group, where the triphenylsilyl group (entry 30) made methylation less selective, while the *tert*-butyl(diphenyl)silyl group (entry 31) made methylation more selective than the standard reaction (entry 9). The protonation results are even less informative, with the *tert*-butyldiphenylsilyl group (entry 29) inducing rather poor selectivity in the cinnamate series, and the triphenylsilyl group making little difference in both series (entries 28 and 30). We were unable to measure the protonation ratio for entry 31, because the *tert*-butyl(diphenyl)silyl-cuprate reagent could not be induced to add to the  $\alpha,\beta$ -unsaturated ester **21c**. The stereochemistry given for the products in this section is assumed by analogy with the earlier results. Unfortunately, the coupling constants between the methine protons are not reliably diagnostic. In all the work in sections 1–5 described above, the *J* values for the protons on C-2 and C-3 are very similar, and more often than not essentially equal, for every pair of *anti* and *syn* isomers. The only trend is that the *J* values for R<sup>1</sup> = Ph are higher in both diastereoisomers (typically 11–15 Hz) than when R<sup>1</sup> = isopropyl or *tert*-butyl (typically 1–6 Hz).

There is a small but regular trend in the *R<sub>f</sub>* values—the *anti* isomers, of those compounds for which we have been able to prove the stereochemistry, are, when there is any difference, less polar than the *syn* isomers. In agreement with this, the esters to which we have assigned the structures **29b**, **29c** and **29d** are the faster running, but the other two pairs of esters run together on TLC plates.



**Scheme 6** Reagents: i, (R<sup>4</sup>R<sup>5</sup>Si)<sub>2</sub>CuCN Li<sub>2</sub>; ii, NH<sub>4</sub>Cl, H<sub>2</sub>O; iii, LDA; iv, MeI

**6. Creating Quaternary Centres.**—Given the relatively low diastereoselectivity of protonation when the resident group, R<sup>3</sup>, on the enolate is much larger than a methyl group (Table 4), the possibility of stereocontrol in forming quaternary centres by alkylating these enolates was limited. Nevertheless, by restricting ourselves to R<sup>3</sup> groups that were not too large, we found that conjugate addition of the silyl-cuprate reagent to the esters **25** (Scheme 7) followed by alkylation gave the products **31** and



**Scheme 7** Reagents: i, (PhMe<sub>2</sub>Si)<sub>2</sub>CuCN Li<sub>2</sub>; ii, R<sup>6</sup>X

**32** having quaternary centres with good diastereoselectivity in almost every case (Table 7). The only reaction showing poor stereocontrol, entry 37, was that in which R<sup>3</sup> was the largest of those we ventured to try, namely isopropyl. We note again that isopropylation (entry 33) was remarkably successful both in diastereoselectivity and in yield.

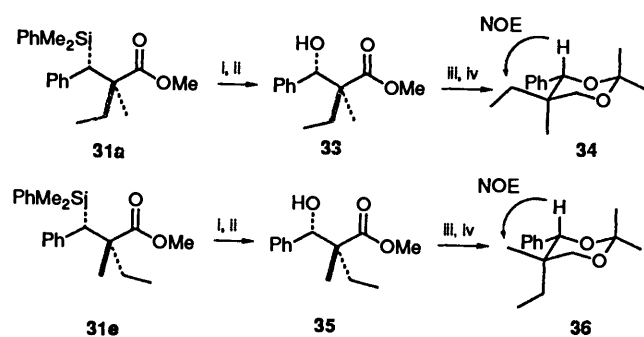
The selectivity in the alkylation reactions (Table 7) appears to be marginally higher in the expected sense than in the corresponding protonation reactions (Table 4). Thus, methylation of the isopropyl-containing enolate, entry 37, although the least selective of all these reactions, at least gives the isomer **31** as the major product, whereas protonation of the same enolate, entry 13, gives the isomer **23** as the major product, even though this is the isomer we normally associate with an alkylation.

We proved the relative stereochemistry of the products **31a**

**Table 7** Forming quaternary centres (Scheme 7): alkylation of enolates derived from **25**

Entry	Identifying letter for compound numbers	R <sup>3</sup>	R <sup>6</sup> X	Ratio 31:32	Yield (%)
32	<b>a</b>	Me	EtI	83:17	94
33	<b>b</b>	Me	Pr <sup>i</sup> I	90:10	63
34	<b>c</b>	Me	CH <sub>2</sub> =CHCH <sub>2</sub> Br	83:17	90
35	<b>d</b>	Me	MeO <sub>2</sub> CCH <sub>2</sub> Br	92:8	45
36	<b>e</b>	Et	MeI	89:11 <sup>a</sup>	95
37	<b>f</b>	Pr <sup>i</sup>	MeI	60:40 <sup>b</sup>	77
38	<b>g</b>	CH <sub>2</sub> CH=CH <sub>2</sub>	MeI	80:20 <sup>c</sup>	90
39	<b>h</b>	CH <sub>2</sub> CO <sub>2</sub> Me	MeI	90:10 <sup>d</sup>	83

<sup>a</sup> The major diastereoisomer in this reaction is the minor diastereoisomer in the reaction in entry 31. <sup>b</sup> The major diastereoisomer in this reaction is the minor diastereoisomer in the reaction in entry 32. <sup>c</sup> The major diastereoisomer in this reaction is the minor diastereoisomer in the reaction in entry 33. <sup>d</sup> The major diastereoisomer in this reaction is the minor diastereoisomer in the reaction in entry 34.



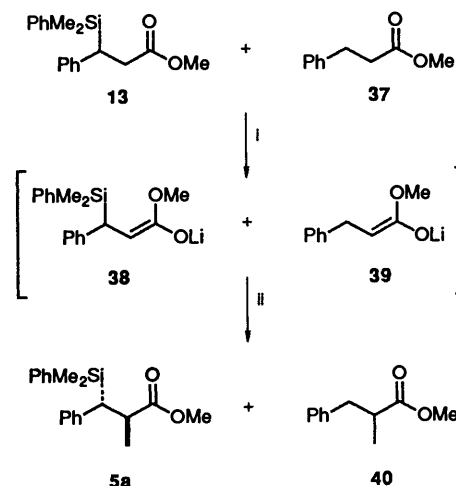
**Scheme 8** Reagents: i, BF<sub>3</sub>·2AcOH; ii, MCPBA; iii, LiAlH<sub>4</sub>; iv, Me<sub>2</sub>C(OMe)<sub>2</sub>, TsOH

and **31e** (Scheme 8) (corresponding to entries 32 and 36 in Table 7) by converting the dimethyl(phenyl)silyl groups into hydroxy groups<sup>28</sup> to give the esters **33** and **35**, respectively, reducing the esters to the corresponding primary alcohols, and forming the acetals **34** and **36**. Irradiation at the resonance frequency of the benzylic hydrogen in the <sup>1</sup>H NMR spectra of these compounds showed unambiguous NOE enhancements in the signals of the ethyl group and the methyl group, respectively. We have assigned relative stereochemistry to all the other products by analogy, which seems reasonable in view of the high levels of diastereoselectivity in these reactions.

**7. Does the β-Silyl Group increase the Nucleophilicity of the Enolate?**—We drew attention earlier to the comparatively easy isopropylation of our enolates. We wondered if the presence of the β-silyl group might have increased the nucleophilicity of the enolate. If the enolates react in a conformation close to **3**, the Si-C bond will overlap with the π-bonding orbitals, raising the HOMO energy. For cationic attack on an allylsilane, this effect is large, allyldimethyl(phenyl)silane reacting 10<sup>5</sup> times faster than propene with a diarylmethyl cation.<sup>45</sup> We can expect that the enolate oxygens present in our enolate ions will dilute this effect considerably, as will the fact that the electrophile, methyl iodide, is both uncharged and attacking the carbon atom adjacent to the silylmethyl group, but we hoped that it might be detectable. We also wondered about the effect of the silyl group on the kinetic acidity of the esters, where we might expect it to be deactivating, although our earlier experience with β-silyl ketones implied that this effect would be quite small.<sup>46</sup>

We used the pair of esters **13** and **37** (Scheme 9). In a control experiment with an excess of LDA followed by treatment with an excess of methyl iodide, a 1:1 mixture of these esters gave an essentially 1:1 mixture of the methylated products **5a** and **40**. Repeating this experiment, but with only enough LDA to deprotonate half the mixture, gave the methylated products **5a**

and **40** in a ratio of 46:54. In agreement with our earlier experience with ketones,<sup>46</sup> there is evidently little if any difference in kinetic acidity between these esters. Repeating the experiment using an excess of LDA, but treating the mixture of enolates **38** and **39** with only 1 equiv. of methyl iodide, gave only a trace of the methylated products **5a** and **40** in a ratio close to 50:50. Repeating this experiment with 3 equiv. of methyl iodide gave the same methylated products in a ratio of 60:40, with enough recovered starting material to indicate that they had been consumed to approximately equal extents. Clearly, there is no striking difference in nucleophilicity between the ester enolates with and without a β silyl group.



**Scheme 9** Reagents: i, LDA; ii, MeI

## Experimental

2-Methyl-1,3-diphenylpropen-1-one **7d**,<sup>47</sup> α,*N,N*-trimethylcinnamide **7e**,<sup>48</sup> α-methylcinnamionitrile **7g**,<sup>49</sup> methyl 4-methylpent-2-enoate **18c**,<sup>50</sup> methyl 4,4-dimethylpent-2-enoate **18d**,<sup>51</sup> methyl 2,4-dimethylpent-2-enoate **21c**,<sup>52</sup> ethyl (*Z*)-crotonate,<sup>53</sup> methyl 2-ethyl-3-phenylpropenoate **25b**,<sup>54</sup> methyl 2-butyl-3-phenylpropenoate **25c**,<sup>54</sup> methyl α-benzylcinnamate **25e**,<sup>55</sup> methyl 2-allylcinnamate **25f**,<sup>56</sup> dimethyl benzylidenesuccinate **25g**,<sup>57</sup> methyl benzylideneacetoacetate **25h**<sup>58</sup> and dimethyl benzylidenemalonate **26**,<sup>59</sup> were prepared by the methods cited. Ether refers to diethyl ether throughout.

**Methyl (E)-2,4,4-Trimethylpent-2-enoate 21d.**—*tert*-Butyl chloride (3.6 g, 28 mmol) in ether (30 cm<sup>3</sup>) was added to magnesium (0.8 g, 32 mmol) during 5 h under reflux. The clear solution was cannulated into a dropping funnel under nitrogen



and added dropwise to a stirred mixture of methyl 2-bromo-methacrylate<sup>60</sup> (5.0 g, 28 mmol) and copper(i) cyanide (1.0 g, 11 mmol) in ether (50 cm<sup>3</sup>) at 0 °C. After 3 h the mixture was diluted with saturated aqueous ammonium chloride (200 cm<sup>3</sup>) and extracted with ether (4 × 50 cm<sup>3</sup>). The organic layer was washed with brine (4 × 50 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and distilled to give the ester (3.6 g, 82%), b.p. 70–71 °C/15 mmHg (lit.,<sup>60</sup> 84–86 °C/12 mmHg);  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1710 (C=O) and 1640 (C=C);  $\delta(\text{CDCl}_3)$  6.68 (1 H, q, *J* 1.5, =CH), 3.63 (3 H, s, OMe), 1.90 (3 H, d, *J* 1.5, =CMe) and 1.18 (9 H, s, Bu<sup>t</sup>).

**Methyl 2-Isopropyl-3-phenylpropenoate 25d.**—Methyl isovalerate (5.8 g) was added to a solution of LDA at –78 °C, prepared by addition of butyllithium (34.7 cm<sup>3</sup>) to diisopropylamine (7.7 cm<sup>3</sup>) in dry THF (100 cm<sup>3</sup>). Stirring was continued for 15 min at –78 °C after which benzaldehyde (5.3 g) was added to the mixture which was then allowed to warm slowly to room temp. Stirring was continued for 1 h after which time the mixture was diluted with water (50 cm<sup>3</sup>) and extracted with ether (3 × 50 cm<sup>3</sup>). The combined organic extracts were washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure. A portion of the crude product (2 g) was dissolved in toluene (50 cm<sup>3</sup>) containing toluene-*p*-sulfonic acid (200 mg) and refluxed with a Dean–Stark apparatus for 18 h. The mixture was cooled to room temperature, washed with aqueous sodium carbonate (25 cm<sup>3</sup>) and brine (25 cm<sup>3</sup>), dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure. TLC [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] gave the ester as a mixture of *E* and *Z* isomers;  $R_f$  [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.35 and 0.40;  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1720 (C=O) and 1640 (C=C);  $\delta(60 \text{ MHz}, \text{CDCl}_3)$  7.10 (5 H, m, Ph), 6.40 (1 H, s, HC=), 3.70 and 3.60 (3 H, s, OMe), 2.75 (1 H, m, *H*CMe<sub>2</sub>), 1.30 (3 H, d, *J* 7, *CH*Me<sub>2</sub>) and 1.25 (3 H, d, *J* 7, *CH*Me<sub>2</sub>).

**Methyl (E)-3-Trimethylsilylpropenoate.**—(*E*)-3-Trimethylsilylpropenoic acid<sup>61</sup> (1.30 g, 9 mmol) in methanol (20 cm<sup>3</sup>) was refluxed with concentrated hydrochloric acid (0.5 cm<sup>3</sup>) for 2 h. The methanol was removed under reduced pressure, concentrated aqueous ammonium chloride added and the solution extracted (Et<sub>2</sub>O). The ether layer was washed with brine, dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. The residue was chromatographed (EtOAc–hexane, 1:10) to give the ester<sup>62</sup> (0.51 g, 36%) as an oil;  $R_f$  (EtOAc–hexane, 1:10) 0.40;  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1730 (C=O), 1605 (C=C) and 840 (SiMe);  $\delta_{\text{H}}(250 \text{ MHz}, \text{CDCl}_3)$  7.22 (1 H, d, *J* 18.9, *CH*CO), 6.20 (1 H, d, *J* 18.9, *CH*CHCO), 3.70 (3 H, s, OMe) and 0.09 (9 H, s, SiMe<sub>3</sub>).

**Methyl (RS)-3-Phenyl-3-trimethylsilylpropenoate.**—Phenylmagnesium bromide (3.0 mol dm<sup>-3</sup> solution in ether; 4.6 cm<sup>3</sup>, 13.8 mmol) was added at –30 °C to a stirred suspension of copper(i) bromide (1.01 g, 7.0 mmol) in THF (12 cm<sup>3</sup>). The solution was stirred at 0 °C for 0.5 h and then brought to –20 °C when methyl (*E*)-3-trimethylsilylpropenoate (0.20 g, 1.25 mmol) in THF (2 cm<sup>3</sup>) was added. The solution was stirred for 0.5 h after which the reaction was quenched (NH<sub>4</sub>Cl) and extracted (Et<sub>2</sub>O). The extract was washed with brine, dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. The residue was chromatographed (EtOAc–hexane, 1:10) to give the ester<sup>63</sup> (0.21 g, 71%) as an oil;  $R_f$  (EtOAc–hexane, 1:10) 0.32;  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1740 (C=O) and 1580 (Ph);  $\delta_{\text{H}}(250 \text{ MHz}, \text{CDCl}_3)$  7.25–7.0 (5 H, m, Ph), 3.45 (3 H, s, OMe), 2.9–2.5 (3 H, m, *CH*Si and *CH*<sub>2</sub>CO) and –0.05 (9 H, s, Me<sub>3</sub>Si).

**Conjugate Addition of the Silyl-cuprate Reagent followed by Alkylation or Protonation.**—Typically, dimethyl(phenyl)silyllithium,<sup>64</sup> *tert*-butyl(diphenyl)silyllithium<sup>65</sup> or triphenylsilyl-

lithium<sup>64</sup> (0.85 mol dm<sup>-3</sup> solution in THF; 4 cm<sup>3</sup>, 3.4 mmol) was added to copper(i) cyanide (153 mg, 1.7 mmol) in THF (3 cm<sup>3</sup>) under nitrogen either at 0 °C and the mixture stirred for 30 min or at –23 °C and the mixture stirred for 3 h. The solution was cooled to –78 °C and the  $\alpha,\beta$ -unsaturated ester, ketone, amide, nitrile or aldehyde (1.8 mmol) added. On several occasions, the mixture was allowed to warm to higher temperatures and stirring continued for 1–3 h to complete the conjugate addition. For the alkylation reactions, the alkyl halide (6 mmol) was added, and the mixture stirred for 1–18 h. The solution was brought to room temperature, and either ether or light petroleum (10 cm<sup>3</sup>), followed by basic aqueous ammonium chloride (5 cm<sup>3</sup>), were added. Alternatively, for the protonation reactions, ether or light petroleum (10 cm<sup>3</sup>) was added at –78 °C, followed by saturated aqueous ammonium chloride (10 cm<sup>3</sup>), and the mixture brought to room temp. In both cases, the aqueous layer was washed with ether or light petroleum (10 cm<sup>3</sup>), and the combined organic layers were washed with basic aqueous ammonium chloride. The organic layer was dried (MgSO<sub>4</sub>) and evaporated under vacuum. Pure samples of the products were obtained by flash chromatography [typically light petroleum (b.p. 60–80 °C)–EtOAc, 15:1]. The many reactions of these two types, carried out by several different hands over several years, varied in what we believe to be only minor ways from the general recipes given above. We have not noticed that the minor variations have had any significant effect on the yields or ratios reported here, except that the conjugate addition reactions were slower, and therefore needed higher temperatures, with the  $\alpha$ -substituted and with the  $\beta$ -hindered unsaturated esters. Perhaps, most surprisingly, the protonation reactions were little different, whether they were quenched at –78 °C or at higher temperatures. The following compounds were prepared by these methods.

**Methyl (2RS,3RS)- and (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropionate 5a and 6a.** Prepared by methylation (–23 °C, 1 h) and protonation (–23 °C) respectively, were reported with full details earlier.<sup>66</sup>

**(3RS,4RS)- and (3RS,4SR)-4-Dimethyl(phenyl)silyl-3-methylbutan-2-one 5b and 6b.** Prepared by methylation (–23 °C, 1 h) and protonation (TFA, –78 °C) respectively, were reported with full details earlier.<sup>27</sup>

**(2RS,3RS)-3-Dimethyl(phenyl)silyl-2-methyl-3-phenylpropanal 5c.** Prepared by methylation (–78 °C, 1.5 h, room temp., 1 h);  $\delta(60 \text{ MHz}, \text{CCl}_4)$  9.50 (1 H, d, *J* 3, CHO), 7.60–6.80 (10 H, m, Ph), 2.90 (1 H, m, MeCH), 2.65 (1 H, d, *J* 10, PhCH), 1.15 (3 H, d, *J* 6, MeC) and 0.45 (6 H, s, SiMe<sub>2</sub>). The aldehyde was too unstable for reliable characterisation as such, and was immediately reduced with lithium aluminium hydride (100 mg, 2.5 mmol) in ether (20 cm<sup>3</sup>) for 15 min at room temp. An aqueous work-up gave a mixture rich in the known<sup>66</sup> (2RS,3RS)-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropan-1-ol (74%). Similarly, (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropanal **6c**, prepared by protonation (–78 °C), was reduced with sodium borohydride to give a mixture rich in (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropanol (93%);  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  3350 (OH), 1255 (SiMe) and 1140 (SiPh);  $\delta_{\text{H}}(250 \text{ MHz}, \text{CDCl}_3)$  6.9–7.6 (10 H, m, Ph), 3.39 (1 H, dd, *J* 3 and 10.5, *CH*<sub>A</sub>*H*<sub>B</sub>O), 3.20 (1 H, dd, *J* 6 and 10.5, *CH*<sub>A</sub>*H*<sub>B</sub>O), 2.2 (2 H, m, CHCH), 1.02 (3 H, d, *J* 6, CMe), 0.31 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.09 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 268 (10%, M – Me), 253 (5, M – CH<sub>2</sub>OH) and 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup> – Me, 268.1297. C<sub>18</sub>H<sub>24</sub>OSi requires M – Me, 268.1283). Integration of the signals at  $\delta$  0.86 and 1.02 gave the ratios reported in Table 1.

**(2RS,3RS)-3-Dimethyl(phenyl)silyl-2-methyl-1,3-diphenylpropan-1-one 5d (70%).** By methylation (–78 °C and warming to room temp);  $R_f$  [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.40;  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1685 (C=O), 1600, 1580 and 1500

(Ph);  $\delta$ (90 MHz,  $\text{CCl}_4$ ) 7.90 (2 H, m, *o*-HPhCO), 7.70–6.90 (13 H, m, remaining Ph), 3.90 (1 H, dq, *J* 10 and 6, CHMe), 2.95 (1 H, d, *J* 10, CHPh), 0.95 (3 H, d, *J* 6, MeC), 0.50 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.20 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 35 (22%,  $\text{M}^+$ ), 343 (25, M – Me) and 135 (100,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$ , 358.1749.  $\text{C}_{24}\text{H}_{26}\text{OSi}$  requires *M*, 358.1753); together with 1-dimethyl(phenyl)silyloxy-1,3-diphenylbut-1-ene **11a** (20%);  $R_f$  [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.54;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1645 (C=C) and 1600 (Ph);  $\delta$ (60 MHz,  $\text{CCl}_4$ ) 7.80–6.90 (15 H, m, Ph), 5.40 (1 H, d, *J* 9, HC=), 3.90 (1 H, m, MeCH), 1.50 (3 H, d, *J* 7, MeC) and 0.60 (6 H, s,  $\text{SiMe}_2$ ). The silyl enol ether was hydrolysed to 1,3-diphenylbutan-1-one, plates, m.p. 69–71 °C [from light petroleum (b.p. 60–80 °C)] (lit.<sup>67</sup> 70.5–71 °C);  $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$  1680 (C=O) 1600, 1580 and 1500 (Ph);  $\delta$ (60 MHz;  $\text{CDCl}_3$ ) 7.80 (2 H, m, *o*-H PhCO), 7.60–6.90 (8 H, m, remaining Ph), 3.65–3.00 (3 H, m,  $\text{CHCH}_2$ ) and 1.30 (3 H, d, *J* 6, CMe).

(2RS,3RS)- and (2RS,3SR)-3-Dimethyl(phenyl)silyl-2,N,N-trimethyl-3-phenylpropionamide **5e** and **6e**. Prepared by methylation (–78 °C, 3 h), were separated by flash chromatography [light petroleum (b.p. 40–60 °C)–EtOAc, 97.5:2.5]; **5e** (86%);  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1640 (C=O);  $\delta_{\text{H}}(250 \text{ MHz}, \text{CCl}_4)$  6.9–7.4 (10 H, m, Ph), 3.07 (1 H, m, CHCO), 2.86 (1 H, d, *J* 11.5, CHSi), 2.76 (3 H, s, NMe), 2.75 (3 H, s, NMe), 0.88 (3 H, s, *J* 6.5, CMe), 0.30 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ), 0.00 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 325 (30%,  $\text{M}^+$ ), 310 (100, M – Me), 234 (30, M –  $\text{C}_7\text{H}_7$ ) and 135 (90,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$ , 325.1874.  $\text{C}_{20}\text{H}_{27}\text{NOSi}$  requires *M*, 325.1862); **6e** (3%);  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1642 (C=O);  $\delta_{\text{H}}(250 \text{ MHz}, \text{CCl}_4)$  6.8–7.4 (10 H, m, Ph), 3.15 (1 H, m, CHO), 2.90 (1 H, m, CHSi), 2.72 (3 H, br s, NMe), 2.61 (3 H, br s, NMe), 1.10 (3 H, d, *J* 6, CMe), 0.35 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ), 0.18 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 325 (10%,  $\text{M}^+$ ), 310 (50%, M – Me), 234 (15, M –  $\text{C}_7\text{H}_7$ ) 135 (100,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$ , 325.1860). The same compounds (83%) were prepared by protonation (–78 °C) in a ratio, measured by isolation, of 18:82.

(2RS,3RS)- and (2RS,3SR)-3-Dimethyl(phenyl)silyl-2-methyl-3-phenylpropionitrile **5g** and **6g** (65%). Prepared by methylation (–78 °C and warming, to room temp.) and further purified by distillation (Kugelrohr, 125–135 °C/0.05 mmHg);  $R_f$  [light petroleum (b.p. 60–80 °C)–EtOAc, 3:1] 0.47;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  2240 (CN), 1600 (Ph), 1250 (SiMe) and 1120 (SiPh);  $\delta$ (250 MHz,  $\text{CDCl}_3$ ) 7.4–7.2 (10 H, m, Ph), 2.90 (1 H, m, CHCN), 2.40 (1 H 5g, d, *J* 11, CHPh), 2.27 (1 H 6g, d, *J* 6, CHPh), 1.17 (3 H, d, *J* 7, MeC), 0.49 (3 H, 6g, s,  $\text{SiMe}_A\text{Me}_B$ ), 0.47 (3 H 5g, s,  $\text{SiMe}_A\text{Me}_B$ ), 0.25 (3 H 5g, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.22 (3 H 6g, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 279 (10%,  $\text{M}^+$ ), 135 (27,  $\text{PhMe}_2\text{Si}$ ) and 118 (100,  $\text{PhC}_3\text{H}_5$ ) (Found:  $\text{M}^+$ , 279.1443.  $\text{C}_{18}\text{H}_{21}\text{NSi}$  requires *M*, 279.1443). The ratio **5g**:**6g** of 54:46 was measured by integration of the SiMe signals in the  $^1\text{H}$  NMR spectrum. The same compounds (78%) were prepared by protonation (–78 °C) in the ratio of 14:86. In this mixture the signal at  $\delta$  2.90 was more clearly resolved (1 H, dq, *J* 6 and 7, CHCN) (Found:  $\text{M}^+$ , 279.1437.  $\text{C}_{18}\text{H}_{21}\text{NSi}$  requires *M*, 279.1443).

Methyl (2RS,3SR)-3-Dimethyl(phenyl)silyl-2-methylbutanoate **19b**. Prepared by methylation (–78 °C and warming to room temp., experiment carried out by J. D. Kilburn) (78%) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80 °C)–EtOAc 5:1] 0.40;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O) and 1590 (Ph);  $\delta$ (250 MHz,  $\text{CDCl}_3$ ) 7.54–7.30 (5 H, m, Ph), 3.57 (3 H, s, OMe), 2.58 (1 H, dq, *J* 2 and 7, CHCO), 1.49 (1 H, dq, *J* 2 and 7, CHSi), 1.04 (3 H, d, *J* 7, MeCHCO), 0.93 (3 H, d, *J* 7, MeCHSi), 0.32 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.30 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 250 (6%,  $\text{M}^+$ ), 235 (19, M – Me) and 135 (100,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$ , 250.1399.  $\text{C}_{14}\text{H}_{22}\text{O}_2\text{Si}$  requires *M*, 250.1389). The (2RS,3RS) isomer **20b** had recognisable signals at  $\delta$ (250 MHz,  $\text{CDCl}_3$ ) 3.58 (3 H, s, OMe) and 1.10 (3 H, d, *J* 7, MeCHCO). The ratio of isomers **19b**:**20b** was measured at 66:34 by integration of the OMe signals.

Methyl (2RS,3SR)-3-dimethyl(phenyl)silyl-2,4-dimethyl-pentanoate **19c** (86%). Prepared by methylation (–78 °C, 3 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] 0.30;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1630 (C=O);  $\delta$ (250 MHz,  $\text{CDCl}_3$ ) 7.55 (2 H, m, *o*-Ph), 7.36–7.32 (3 H, m, *m*- and *p*-Ph), 3.59 (3 H, s, OMe), 2.65 (1 H, dq, *J* 3 and 7, CHCO), 1.95 (1 H, octet, *J* 7, CHMe<sub>2</sub>), 1.48 (1 H, dd, *J* 3 and 6, CHSi), 1.15 (3 H, d, *J* 7, CHMe), 0.93 (3 H, d, *J* 7, CHMe<sub>A</sub>Me<sub>B</sub>), 0.84 (3 H, d, *J* 7, CHMe<sub>A</sub>Me<sub>B</sub>), 0.41 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.38 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 263 (7% M – Me), 235 (50, M –  $\text{C}_3\text{H}_7$ ), 135 (90,  $\text{PhMe}_2\text{Si}$ ) and 69 (100) (Found:  $\text{M}^+$  – Me, 263.1476.  $\text{C}_{16}\text{H}_{26}\text{O}_2\text{Si}$  requires *M* – Me 263.1467). The ratio of isomers **19c**:**20c** was measured as 84:16 by reverse phase HPLC (ODS column, 60% aqueous methanol) and as 86:14 by GC (SE-54 capillary column at 150 °C).

Methyl (2RS,3RS)-3-dimethyl(phenyl)silyl-2,4-dimethyl-pentanoate **20c** (56%). By protonation (–78 °C) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] 0.23;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1728 (C=O);  $\delta$ (250 MHz,  $\text{CDCl}_3$ ) 7.52 (2 H, m, *o*-Ph), 7.35–7.30 (3 H, m, *m*- and *p*-Ph), 3.61 (3 H, s, OMe), 2.79 (1 H, quintet, *J* 7, CHCO), 1.87 (1 H, octet, *J* 7, CHMe<sub>2</sub>), 1.57 (1 H, t, *J* 6, CHSi), 1.16 (3 H, d, *J* 7, CHMe), 0.93 (3 H, d, *J* 7, CHMe<sub>A</sub>Me<sub>B</sub>), 0.89 (3 H, d, *J* 7, CHMe<sub>A</sub>Me<sub>B</sub>), 0.37 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.29 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 263 (5% M – Me), 235 (40, M –  $\text{C}_3\text{H}_7$ ), 201 (15, M – Ph), 135 (90,  $\text{PhMe}_2\text{Si}$ ) and 69 (100) (Found:  $\text{M}^+$ , 263.1471.  $\text{C}_{16}\text{H}_{26}\text{O}_2\text{Si}$  requires *M* – Me, 263.1467). The ratio of isomers **19c**:**20c** was measured as 4:96 by GC (SE-54 capillary column at 150 °C, He carrier).

Methyl (2RS,3SR)-3-dimethyl(phenyl)silyl-2,4,4-trimethyl-pentanoate **19d** (83%). By methylation (–78 °C, 3 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60 °C)–EtOAc, 97.5:2.5] 0.17–0.23. The major diastereoisomer was separated by preparative TLC;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1365 (CMe<sub>3</sub>);  $\delta$ ( $\text{CCl}_4$ ) 7.55 (2 H, m, *o*-Ph), 7.3 (3 H, m, *m,p*-Ph), 3.63 (3 H, s, OMe), 2.79 (1 H, q, *J* 7.5, CHCO), 1.38 (1 H, d, *J* 1.5, CHSi), 1.27 (3 H, d, *J* 7.5, CHMe), 0.92 (9 H, s, Bu<sup>3</sup>) 0.56 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.37 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 277 (10%, M – Me), 237 (100, M – Bu<sup>3</sup>) and 135 (80,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$  – Me, 277.1630.  $\text{C}_{17}\text{H}_{28}\text{O}_2\text{Si}$  requires *M* – Me, 277.1624). The ratio of isomers **19d**:**20d** was measured as 66:34 by reverse phase HPLC (ODS column, 70% aqueous methanol) and as 71:29 by isolation.

Methyl (2RS,3RS)-3-dimethyl(phenyl)silyl-2,4,4-trimethyl-pentanoate **20d** (62%). By protonation (0 °C) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60 °C)–EtOAc, 97.5:2.5] 0.13;  $\nu_{\text{max}}(\text{CCl}_4)/\text{cm}^{-1}$  1720 (C=O);  $\delta$ ( $\text{CCl}_4$ ) 7.7–7.1 (5 H, m, Ph), 3.62 (3 H, s, OMe), 2.80 (1 H, q, *J* 7, CHCO), 1.4 (1 H, br s, CHSi), 1.25 (3 H, d, *J* 7, CHMe), 0.93 (9 H, s, Bu<sup>3</sup>), 0.65 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ) and 0.50 (3 H, s,  $\text{SiMe}_A\text{Me}_B$ ); *m/z* 277 (M – Me), 235 (100, M – Bu<sup>3</sup>) and 135 (100%,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$ , 277.1642.  $\text{C}_{17}\text{H}_{28}\text{O}_2\text{Si}$  requires *M* – Me, 277.1624). The ratio of isomers by **19d**:**20d** was measured as 4:96 by reverse phase HPLC (ODS column, 60% aqueous methanol).

Ethyl (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methylbutanoate (82%). From ethyl (*E*)-crotonate by methylation (–23 °C);  $R_f$  [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] 0.35;  $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$  1730 (C=O) and 1115 (SiPh);  $\delta_{\text{H}}(90 \text{ MHz}, \text{CCl}_4)$  7.65–7.30 (5 H, m, Ph), 4.05 (2 H, q, *J* 8, CH<sub>2</sub>Me), 2.55 (1 H, dq, *J* 6 and 8, CHCO), 1.50 (1 H, dq, *J* 6 and 8, CHSi), 1.25 (3 H, t, *J* 8, CH<sub>2</sub>Me), 1.05 (3 H, d, *J* 8, MeCCO or MeCSi), 0.95 (3 H, d, *J* 8, MeCSi or MeCCO) and 0.35 (6 H, s,  $\text{SiMe}_2$ );  $\delta_{\text{C}}(\text{CDCl}_3)$  176.6, 138.0, 133.8, 128.9, 127.7, 60.0, 40.0, 22.5, 14.2, 13.6, 10.2, –3.9 and –4.0; *m/z* 264 (15%,  $\text{M}^+$ ), 249 (25, M – Me) and 135 (100,  $\text{PhMe}_2\text{Si}$ ) (Found:  $\text{M}^+$ , 264.1559.  $\text{C}_{15}\text{H}_{24}\text{O}_2\text{Si}$  requires *M*, 264.1559). The minor isomer showed additional peaks at  $\delta$  176.4, 138.8, 42.1, 24.0, 17.3, 14.1 and

13.0, from which the ratio of 99:1 was estimated. The same reaction with ethyl (*Z*)-crotonate gave the same products (75%) in a ratio of 98:2.

**Methyl (2RS,3RS)-3-dimethyl(phenyl)silyl-2-ethyl-3-phenylpropanoate 23b** (83%). By ethylation ( $-23^{\circ}\text{C}$ , 1 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.40;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1740 (C=O) 1600, 1580 and 1500 (Ph);  $\delta(90\text{ MHz, CCl}_4)$  7.65–6.85 (10 H, m, Ph), 3.40 (3 H, s, OMe), 2.85 (1 H, m, CHCO), 2.65 (1 H, d, *J* 11, CHPh), 1.45 (2 H, m, CH<sub>2</sub>Me), 0.80 (3 H, t, *J* 7, CH<sub>2</sub>Me), 0.35 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  326 (19%, M<sup>+</sup>), 291 (40, M – Et), 135 (78, PhMe<sub>2</sub>Si) and 131 (100, PhC<sub>4</sub>H<sub>7</sub>) (Found: M<sup>+</sup>, 326.1696. C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M*, 326.1702). The ratio of diastereoisomers **23b**:**24b** of 95:5 was measured by integration of the OMe and SiMe signals.

**Methyl (2RS,3SR)-3-dimethyl(phenyl)silyl-2-ethyl-3-phenylpropanoate 24b** (77%). By protonation ( $-78^{\circ}\text{C}$ ) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.36;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.55–6.90 (10 H, m, Ph), 3.30 (3 H, s, OMe), 2.85 (1 H, m, CHCO), 2.60 (1 H, d, *J* 11, CHPh), 1.55 (2 H, m, CH<sub>2</sub>Me), 0.80 (3 H, t, *J* 7, CH<sub>2</sub>Me), 0.30 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.10 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  326 (2%, M<sup>+</sup>), 297 (30, M – Et), 135 (73, PhMe<sub>2</sub>Si) and 131 (100, PhC<sub>4</sub>H<sub>7</sub>) (Found: M<sup>+</sup>, 326.1716. C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M*, 326.1702). The ratio of diastereoisomers **23b**:**24b** of 20:80 was measured by integration of the OMe and SiMe signals.

**Methyl (2RS,3RS)-2-butyl-3-dimethyl(phenyl)silyl-3-phenylpropanoate 23c** (86%). By butylation (room temp., 18 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.37;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.50–6.80 (10 H, m, Ph), 3.35 (3 H, s, OMe), 2.90 (1 H, dt, *J* 12 and 6, CHCO), 2.65 (1 H, d, *J* 12, CHPh), 1.60–0.60 (9 H, m, Bu), 0.30 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.10 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  354 (2%, M<sup>+</sup>), 297 (15, M – Bu), 135 (57, PhMe<sub>2</sub>Si) and 131 (100, PhC<sub>3</sub>H<sub>2</sub>O) (Found: M<sup>+</sup>, 354.2019. C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>Si requires *M*, 354.2015). The ratio of diastereoisomers **23c**:**24c** of 94:6 was measured by integration of the SiMe signals.

**Methyl (2RS,3SR)-2-butyl-3-dimethyl(phenyl)silyl-3-phenylpropanoate 24c** (77%). By protonation (0  $^{\circ}\text{C}$ ) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.29;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.55–6.90 (10 H, m, Ph), 3.35 (3 H, s, OMe), 3.00 (1 H, m, CHCO), 2.70 (1 H, d, *J* 11, CHPh), 1.60–0.70 (9 H, m, Bu), 0.35 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  354 (1%, M<sup>+</sup>), 297 (41, M – Bu), 135 (62, PhMe<sub>2</sub>Si) and 131 (100, PhC<sub>3</sub>H<sub>2</sub>O) (Found: M<sup>+</sup>, 354.2009. C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>Si requires *M*, 354.2015). The ratio of diastereoisomers **23c**:**24c** of 27:73 was measured by integration of the SiMe signals.

**Methyl (2RS,3RS)-3-dimethyl(phenyl)silyl-2-isopropyl-3-phenylpropanoate 23d** (26%). By isopropylation (room temp., 18 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.41;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.45–6.80 (10 H, m, Ph), 3.40 (3 H, s, OMe), 3.00 (1 H, dd, *J* 4 and 15, CHCO), 2.75 (1 H, d, *J* 15, CHPh), 1.75 (1 H, d, septet, *J* 4 and 6, CHMe<sub>2</sub>), 0.80 (3 H, d, *J* 6, CMe<sub>A</sub>Me<sub>B</sub>), 0.75 (3 H, d, *J* 6, CMe<sub>A</sub>Me<sub>B</sub>), 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.15 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  325 (0.2%, M – Me), 297 (18, M – Pr), 135 (46, PhMe<sub>2</sub>Si) and 131 (100, PhC<sub>3</sub>H<sub>2</sub>O) (Found: M<sup>+</sup> – Me, 325.1639. C<sub>21</sub>H<sub>28</sub>O<sub>2</sub>Si requires *M* – Me, 325.1624). The ratio of diastereoisomers **23d**:**24d** of 95:5 was measured by integration of the OMe signals.

**Methyl (2RS,3SR)-3-dimethyl(phenyl)silyl-2-isopropyl-3-phenylpropanoate 24**. Separated by preparative TLC from the mixture (77%) in a protonation experiment (0  $^{\circ}\text{C}$ );  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.32;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.60–6.95 (10

H, m, Ph), 3.35 (3 H, s, OMe), 2.95 (1 H, dd, *J* 3.5 and 11.5, CHCO), 2.80 (1 H, d, *J* 11.5, CHPh), 2.00 (1 H, d, septet, *J* 3.5 and 7, CHMe<sub>2</sub>), 0.90 (3 H, d, *J* 7, CMe<sub>A</sub>Me<sub>B</sub>), 0.80 (3 H, d, *J* 7, CMe<sub>A</sub>Me<sub>B</sub>), 0.30 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.15 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  340 (2.2%, M<sup>+</sup>), 297 (100, M – Pr), 135 (40, PhMe<sub>2</sub>Si) and 131 (72, PhC<sub>3</sub>H<sub>2</sub>O) (Found: M<sup>+</sup>, 340.1889. C<sub>21</sub>H<sub>28</sub>O<sub>2</sub>Si requires *M*, 340.1859). The ratio of diastereoisomers **23d**:**24d** of 60:40 was measured by integration of the OMe signals.

**Methyl (2RS,3RS)-2-benzyl-3-dimethyl(phenyl)silyl-3-phenylpropanoate 23e** (74%). By benzylation ( $-78^{\circ}\text{C}$ , 3 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60  $^{\circ}\text{C}$ )–EtOAc, 95:5] 0.23;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1731 (C=O);  $\delta(\text{CCl}_4)$  6.9–7.3 (15 H, m, Ph), 3.12 (3 H, s, OMe), 3.10 (1 H, m, CHCO), 2.71 (1 H, d, *J* 12, CH<sub>2</sub>Ph), 2.55 (1 H, dd, *J* 1.5 and 11, CHSi), 0.28 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.08 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  373 (15%, M – Me), 357 (12, M – OMe), 311 (25, M – Ph), 297 (25, M – CH<sub>2</sub>Ph) and 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup> – Me, 373.1645. C<sub>25</sub>H<sub>28</sub>O<sub>2</sub>Si requires *M* – Me, 373.1625). The ratio of diastereoisomers **23e**:**24e** of 97:3 was measured by reverse phase HPLC (ODS column, 70% aqueous methanol).

**Methyl (2RS,3SR)-2-Benzyl-3-dimethyl(phenyl)silyl-3-phenylpropanoate 24e**. Identified in the mixture (66%) obtained in the protonation experiment ( $-78^{\circ}\text{C}$ );  $R_f$  [light petroleum (b.p. 40–60  $^{\circ}\text{C}$ )–EtOAc, 95:5] 0.38;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O);  $\delta(\text{CCl}_4)$  7.6–6.7 (15 H, m, Ph), 3.12 (3 H, s, OMe), 3.10 (1 H, m, CHCO), 2.71 (2 H, d, *J* 8, CH<sub>2</sub>Ph), 2.5 (1 H, m, CHSi), 0.38 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>, minor diastereoisomer), 0.21 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>, minor diastereoisomer), 0.28 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.21 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  373 (8%, M – Me), 357 (100, M – OMe), 311 (35, M – Ph), 297 (23, M – CH<sub>2</sub>Ph), 135 (58, PhMe<sub>2</sub>Si) and 131 (100) (Found: M<sup>+</sup> – Me, 373.1651. C<sub>25</sub>H<sub>28</sub>O<sub>2</sub>Si requires *M* – Me, 373.1625). The ratio of diastereoisomers **23e**:**24e** of 71:29 was measured by reverse phase HPLC (ODS column, 65% aqueous methanol).

**Methyl (2RS,3RS)-2-allyl-3-dimethyl(phenyl)silyl-3-phenylpropanoate 23f** (76%). By allylation ( $-78^{\circ}\text{C}$ , 3 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60  $^{\circ}\text{C}$ )–EtOAc, 95:5] 0.26;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O), 1255 (SiMe) and 1122 (SiPh);  $\delta(\text{CCl}_4)$  7.3–6.9 (10 H, m, Ph), 5.58 (1 H, m, CH<sub>2</sub>=CHCH<sub>2</sub>), 4.86 (2 H, m, CH<sub>2</sub>=CH), 3.30 (3 H, s, OMe), 2.95 (1 H, dt, *J* 12 and 3.5, CHCO), 2.62 (1 H, d, *J* 12, CHSi), 2.1 (2 H, m, CH<sub>2</sub>=CHCH<sub>2</sub>), 0.26 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.09 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  323 (8%, M<sup>+</sup> – Me), 307 (25, M – OMe), 297 (20%, M – C<sub>3</sub>H<sub>5</sub>), 135 (60, PhMe<sub>2</sub>Si) and 131 (100) (Found: M<sup>+</sup> – Me, 323.1480. C<sub>20</sub>H<sub>23</sub>O<sub>2</sub>Si requires *M* – Me, 323.1467). The ratio of diastereoisomers **23f**:**24f** of 95:5 was measured by reverse phase HPLC (ODS column, 70% aqueous methanol).

**Methyl [(2RS,3SR)-2-allyl-3-dimethyl(phenyl)silyl]-3-phenylpropanoate 24f**. Identified in the mixture (83%) obtained in the protonation experiment ( $-78^{\circ}\text{C}$ );  $R_f$  [light petroleum (b.p. 40–60  $^{\circ}\text{C}$ )–EtOAc, 95:5] 0.22;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1738 (C=O) and 1640 (C=C);  $\delta(\text{CCl}_4)$  7.4–6.8 (10 H, m, Ph), 5.6 (1 H, m, CH<sub>2</sub>=CHCH<sub>2</sub>), 4.9 (2 H, m, CH<sub>2</sub>=CH), 3.30 (3 H, s, OMe), 2.9 (1 H, m, CHCO), 2.7 (1 H, m, CHSi), 2.2 (2 H, t, *J* 6, CH<sub>2</sub>=CHCH<sub>2</sub>), 0.42 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.25 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  323 (12%, M – Me), 297 (25, M – OMe), 135 (65, PhMe<sub>2</sub>Si) and 131 (100%) (Found: M<sup>+</sup> – Me, 323.1448. C<sub>21</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M* – Me, 323.1467). The ratio of diastereoisomers **23f**:**24f** of 31:69 was measured by reverse phase HPLC (ODS column, 70% aqueous methanol).

**Methyl (2RS,3RS)-3-dimethyl(phenyl)silyl-2-methoxycarbonylmethyl-3-phenylpropanoate 23g** (50%). By methoxycarbonylmethylation ( $-78^{\circ}\text{C}$ , 3 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 40–60  $^{\circ}\text{C}$ )–EtOAc, 90:10] 0.18;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1738 (C=O);  $\delta(\text{CCl}_4)$  7.4–6.8 (10 H, m, Ph), 3.55 (3 H, s, OMe), 3.31 (3 H, s, OMe), 2.62 (2 H, d,

*J* 9, CH<sub>2</sub>CO), 2.4 (2 H, m, CHCO and CHSi), 0.40 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.14 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 370 (1%, M<sup>+</sup>), 339 (10, M – OMe), 297 (15, M – CH<sub>2</sub>CO<sub>2</sub>Me), 135 (80, PhMe<sub>2</sub>Si) and 131 (100) (Found: M<sup>+</sup>, 370.1597. C<sub>21</sub>H<sub>26</sub>O<sub>4</sub>Si requires *M*, 370.1600). The ratio of diastereoisomers **23g**:**24g** of 98:2 was measured by reverse phase HPLC (ODS column, 60% aqueous methanol).

**Methyl (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methoxy-carbonylmethyl-3-phenylpropanoate 24g**. Identified in the mixture (82%) obtained in the protonation experiment (–78 °C); *R<sub>f</sub>* [light petroleum (b.p. 40–60 °C)–EtOAc, 90:10] 0.13; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1736 (C=O), 1230 (SiMe) and 1170 (SiPh); *δ*(CCl<sub>4</sub>) 7.6–6.9 (10 H, m, Ph), 3.58 (3 H, s, OMe), 3.40 (3 H, s, OMe), 3.34 (1 H, m, CHCO), 3.0–2.5 (3 H, m, CH<sub>2</sub> and CHSi), including *δ* 2.56, dd, *J* 10 and 16.5, CH<sub>A</sub>CH<sub>B</sub>CO), 0.35 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.05 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 370 (4%, M<sup>+</sup>), 297 (60%, M – CH<sub>2</sub>CO<sub>2</sub>Me) and 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup>, 370.1587. C<sub>21</sub>H<sub>26</sub>O<sub>4</sub>Si requires *M*, 370.1600). The ratio of diastereoisomers **23g**:**24g** of 10:90 was measured by reverse phase HPLC (ODS column, 80% aqueous methanol).

**Methyl 2-acetyl-3-dimethyl(phenyl)silyl-3-phenylpropanoate 23h and 24h (87%)**. By acetylation (–78 °C, 3 h) as a 60:40 mixture of diastereoisomers; *R<sub>f</sub>* [light petroleum (b.p. 40–60 °C)–EtOAc, 90:10] 0.20; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1736 (CO<sub>2</sub>Me) and 1716 (COMe); *δ*(CCl<sub>4</sub>) 7.4–6.8 (10 H, m, Ph), 3.95 (1 H, d, *J* 12, CHCO), 3.41 (3 H, s, OMe), 3.24 (1 H, d, *J* 12, CHPh), 1.93 (3 H, s, COMe), 0.46 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>, minor diastereoisomer), 0.34 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>, major diastereoisomer), 0.22 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>, minor diastereoisomer) and 0.28 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>, major diastereoisomer); *m/z* 323 (20%, M – Me), 297 (30, M – COMe), 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup>, 325.1259. C<sub>20</sub>-H<sub>24</sub>O<sub>3</sub>Si requires *M* – Me, 323.1260). The same products (64%) in essentially the same ratio were obtained by protonation (–78 °C) following conjugate addition to methyl benzylideneacetate.

**Methyl (2RS,3SR)-2-benzyl-3-dimethyl(phenyl)silylbutanoate (92%)**. By benzylation with benzyl bromide (–78 °C, 3 h) following conjugate addition to methyl crotonate, as a mixture with its diastereoisomer; *R<sub>f</sub>* (5%) in [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] 0.21; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1728 (C=O); *δ*(CCl<sub>4</sub>) 7.0–7.6 (10 H, m, Ph), 3.49 (3 H, s, OMe), 2.92 (2 H, m, CH<sub>2</sub>Ph), 2.85 (1 H, m, CHCO), 1.4 (1 H, m, CHSi), 1.15 (3 H, d, *J* 6, CHMe), 0.49 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.46 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 311 (2%, M – Me), 235 (30, M – C<sub>7</sub>H<sub>7</sub>), 135 (60, PhMe<sub>2</sub>Si) and 69 (100) (Found: M<sup>+</sup>, 311.1478. C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M* – Me, 311.1467). The ratio of diastereoisomers **23**:**24** of 96:4 was measured by reverse phase HPLC (ODS column, 70% aqueous methanol).

**Methyl (2RS,3RS)-2-benzyl-3-dimethyl(phenyl)silylbutanoate (88%)**. By protonation (–78 °C) following conjugate addition to methyl 2-benzylbut-2-enoate,<sup>68</sup> as a mixture with its diastereoisomer; *R<sub>f</sub>* [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] 0.23; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1728 (C=O); *δ*(CCl<sub>4</sub>) 7.0–7.7 (10 H, m, Ph), 3.55 and 3.50 (3 H, s, OMe), 2.92 (2 H, m, CH<sub>2</sub>Ph), 2.79 (1 H, m, CHCO), 1.4 (1 H, m, CHSi), 1.2 (3 H, d, *J* 3, CHMe), 0.43 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.39 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 311 (2%, M – Me), 249 (10, M – Ph), 235 (30, M – C<sub>7</sub>H<sub>7</sub>), 135 (60, PhMe<sub>2</sub>Si) and 69 (100) (Found: M<sup>+</sup> – Me, 311.1469. C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M* – Me, 311.1467). The ratio of the diastereoisomers **23**:**24** of 39:61 was measured by reverse phase HPLC (ODS column, 70% aqueous methanol).

**Methyl (RS)-3-phenyl-3-triphenylsilylpropanoate (75%)**. By protonation as prisms, m.p. 146–147 °C (from hexane); *R<sub>f</sub>* (EtOAc–hexane, 1:10) 0.22; *v<sub>max</sub>*(Nujol)/cm<sup>–1</sup> 1740 (C=O), 1600 (Ph) and 1110 (SiPh); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 8.0–6.8 (20 H, m, 4 × Ph), 3.58 (1 H, dd, *J* 3.6 and 11.8, SiCH), 3.48 (3 H, s, OMe), 3.02 (1 H, dd, *J* 3.6 and 16.0, CH<sub>A</sub>CH<sub>B</sub>CO) and 2.90 (1 H, dd, *J* 11.9 and 15.9, CH<sub>A</sub>CH<sub>B</sub>CO); *m/z* 422 (6.4%, M<sup>+</sup>), 391 (0.5,

M – OMe) and 259 (100, Ph<sub>3</sub>Si) (Found: M<sup>+</sup>, 422.1661. C<sub>28</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M*, 422.1202) (Found: C, 79.5; H, 6.1. C<sub>28</sub>H<sub>26</sub>O<sub>2</sub>Si requires C, 79.6; H, 6.2%).

**Methyl (RS)-3-tert-butyl(diphenyl)silyl-3-phenylpropanoate (63%)**. By protonation as prisms, m.p. 100–101.5 °C (from hexane); *R<sub>f</sub>*(EtOAc–hexane, 1:10) 0.29; *v<sub>max</sub>*(Nujol)/cm<sup>–1</sup> 1730 (C=O) and 1110 (SiPh); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 7.7–6.9 (15 H, m, 3 × Ph), 3.49 (1 H, dd, *J* 2.6 and 12.6, SiCH), 3.44 (3 H, s, OMe), 2.83 (1 H, dd, *J* 2.6 and 15.9, CH<sub>A</sub>CH<sub>B</sub>CO), 2.49 (1 H, dd, *J* 12.7 and 15.9, CH<sub>A</sub>CH<sub>B</sub>CO) and 0.82 (9 H, s, Bu<sup>t</sup>); *m/z* 402 (3%, M<sup>+</sup>), 387 (2, M – Me), 345 (60, M – Bu) and 239 (43, Bu<sup>t</sup>Ph<sub>2</sub>Si) (Found: M<sup>+</sup>, 402.2045. C<sub>26</sub>H<sub>30</sub>O<sub>2</sub>Si requires *M*, 402.2015) (Found: C, 77.8; H, 7.5. C<sub>26</sub>H<sub>30</sub>O<sub>2</sub>Si requires C, 77.6; H, 7.5%).

**Methyl (RS)-4-methyl-3-triphenylsilylpentanoate (77%)**. By protonation; *R<sub>f</sub>* (EtOAc–hexane, 1:10) 0.32; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1740 (C=O), 1600 (Ph) and 1110 (SiPh); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 7.8–7.3 (15 H, m, 3 × Ph), 3.58 (3 H, s, OMe), 2.7–2.4 (3 H, m, CH<sub>A</sub>CH<sub>B</sub>CO, CH<sub>A</sub>CH<sub>B</sub>CO and CHSi), 2.24 (1 H, dsp, *J* 6.8 and 2.9, CHMe<sub>2</sub>), 0.97 (3 H, d, *J* 6.8, CMe<sub>A</sub>Me<sub>B</sub>) and 0.72 (3 H, d, *J* 6.8, CMe<sub>A</sub>Me<sub>B</sub>); *m/z* 388 (6.4%, M<sup>+</sup>), 345 (45, M – Pr<sup>i</sup>) 311 (85, M – Ph) and 259 (100, Ph<sub>3</sub>Si) (Found: M<sup>+</sup>, 388.1820. C<sub>25</sub>H<sub>28</sub>O<sub>2</sub>Si requires *M*, 388.1859).

**Methyl (RS)-3-tert-butyl(diphenyl)silyl-4-methylpentanoate (71%)**. By protonation; *R<sub>f</sub>* (EtOAc–hexane, 1:10) 0.38; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1740 (C=O) and 1110 (SiPh); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 7.7–7.2 (10 H, m, 2 × Ph), 3.63 (3 H, s, OMe), 2.7–2.1 (4 H, m, CH<sub>A</sub>CH<sub>B</sub>CO, CH<sub>A</sub>CH<sub>B</sub>CO, CHSi and CHMe<sub>2</sub>), 1.10 (9 H, s, Bu<sup>t</sup>), 0.90 (3 H, d, *J* 6.9, CMe<sub>A</sub>Me<sub>B</sub>) and 0.54 (3 H, d, *J* 6.9, CMe<sub>A</sub>Me<sub>B</sub>); *m/z* 367 (0.02%, M<sup>+</sup> – H), 353 (0.4, M – Me), 337 (2, M – OMe), 325 (4, M – Pr<sup>i</sup>) and 311 (100, M – Bu<sup>t</sup>) (Found: M<sup>+</sup> – H, 367.2128. C<sub>23</sub>H<sub>32</sub>O<sub>2</sub>Si requires *M* – H, 367.2093).

**Methyl (2RS,3SR)-2,4-dimethyl-3-triphenylsilylpentanoate 29f (47%)**. By methylation (–78 °C, 2.5 h) as a 70:30 mixture with its diastereoisomer; *R<sub>f</sub>* (EtOAc–hexane, 1:10) 0.31; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1740 (C=O), 1600 (Ph) and 1110 (SiPh); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 7.7–7.3 (15 H, m, 3 × Ph), 3.56 (3 H, s, OMe), 2.86 (1 H, dq, *J* 7.2 and 2.5, CHCO), 2.20 (2 H, m, CHMe<sub>2</sub> and CHSi), 1.06 (3 H, d, *J* 7.2, MeCHCO), 0.90 (3 H, d, *J* 6.8, CMe<sub>A</sub>Me<sub>B</sub>) and 0.82 (3 H, d, *J* 6.6, CMe<sub>A</sub>Me<sub>B</sub>); *m/z* 387 (1.4%, M<sup>+</sup> – Me), 357 (8, M – Pr<sup>i</sup>) and 325 (6, M – Ph) (Found: M<sup>+</sup> – Me, 387.1771. C<sub>26</sub>H<sub>30</sub>O<sub>2</sub>Si requires *M* – Me, 387.1780). The ratio of diastereoisomers **29f**:**30f** was measured by integration of the OMe signals.

**Methyl (2RS,3SR)-2-methyl-3-phenyl-3-triphenylsilylpropanoate 30c (56%)**. By protonation (–78 °C) as an 83:17 mixture with its diastereoisomer, as prisms, m.p. 153–155 °C (from hexane); *R<sub>f</sub>* (EtOAc–hexane, 1:10) 0.22; *v<sub>max</sub>*(Nujol)/cm<sup>–1</sup> 1715 (C=O) and 1590 (Ph); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 7.4–6.8 (20 H, m, 4 × Ph), 3.35–3.20 (2 H, m, CHSi and CHCO), 3.27 (3 H, s, OMe) and 1.16 (3 H, d, *J* 6.4, CHMe); *m/z* 436 (67%, M<sup>+</sup>), 421 (30, M – Me), 405 (4, M – OMe), 359 (13, M – Ph) and 259 (100, Ph<sub>3</sub>Si) (Found: M<sup>+</sup>, 436.1842. C<sub>29</sub>H<sub>28</sub>O<sub>2</sub>Si requires *M*, 436.1859) (Found: C, 80.0; H, 6.4. C<sub>29</sub>H<sub>28</sub>O<sub>2</sub>Si requires C, 79.8; H, 6.5%). The ratio of isomers **30c**:**29c** was measured by integration of the OMe signals.

**Methyl (2RS,3SR)-3-tert-butyl(diphenyl)silyl-3-phenyl-2-methylpropanoate 30d (56%)**. By protonation (–78 °C) as a 66:34 mixture with its diastereoisomer; *R<sub>f</sub>* (EtOAc–hexane, 1:10) 0.28; *v<sub>max</sub>*(film)/cm<sup>–1</sup> 1730 (C=O) and 1100 (SiPh); *δ<sub>H</sub>*(250 MHz; CDCl<sub>3</sub>) 7.9–6.8 (15 H, m, 3 × Ph), 3.20 (1 H, d, *J* 6.9, CHSi), 3.18 (3 H, s, OMe), 2.96 (1 H, qn, *J* 7.1, CHCO), 1.06 (3 H, d, *J* 6.9, CHMe) and 0.73 (9 H, s, Bu<sup>t</sup>); *m/z* 416 (1%, M<sup>+</sup>) and 239 (5, Bu<sup>t</sup>Ph<sub>2</sub>Si) (Found: M<sup>+</sup>, 416.2190. C<sub>27</sub>H<sub>32</sub>O<sub>2</sub>Si requires *M*, 416.2172). The ratio of isomers **30d**:**29d** was measured by integration of the OMe signals.

**Methyl (2RS,3RS)-2,4-dimethyl-3-triphenylsilylpentanoate 30f**

(41%). By protonation ( $-78^{\circ}\text{C}$ ) as a 92:8 mixture with its diastereoisomer;  $R_f$  (EtOAc-hexane, 1:10) 0.31;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O), 1600 (Ph) and 1110 (SiPh);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.7–7.3 (15 H, m, 3  $\times$  Ph), 3.47 (3 H, s, OMe), 2.95 (1 H, qn,  $J$  7.1, CHCO), 2.46 (1 H, dd,  $J$  7.0 and 4.8, CHSi), 2.20 (1 H, m, CHMe<sub>2</sub>) 1.13 (3 H, d,  $J$  7.2, MeCHCO), 0.91 (3 H, d,  $J$  6.8, CMe<sub>A</sub>Me<sub>B</sub>) and 0.83 (3 H, d,  $J$  6.8, CMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  359 (34.6%,  $\text{M}^+ - \text{Pr}^+$ ) and 259 (100, Ph<sub>3</sub>Si) (Found:  $\text{M}^+ - \text{Pr}^+$ , 359.1468.  $\text{C}_{26}\text{H}_{30}\text{O}_2\text{Si}$  requires  $M - \text{Pr}^+$ , 359.1467). The ratio of isomers **30f**:**29f** was measured by integration of the OMe signals.

*Methyl* (2RS,3SR)-3-dimethyl(phenyl)silyl-2-ethyl-2-methyl-3-phenylpropanoate **31a** (94%). By ethylation (room temp., 18 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.41;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.50–6.90 (10 H, m, Ph), 3.40 (3 H, s, OMe), 2.85 (1 H, s, CHPh), 1.60 (1 H, m, MeCH<sub>A</sub>H<sub>B</sub>), 1.30 (3 H, s, MeCC=O), 1.15 (1 H, m, MeH<sub>A</sub>H<sub>B</sub>), 0.65 (3 H, t,  $J$  7, MeCH<sub>2</sub>), 0.35 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.15 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  340 (4%,  $\text{M}^+$ ), 311 (28,  $\text{M} - \text{Et}$ ), 145 (62, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+$ , 340.1850.  $\text{C}_{21}\text{H}_{28}\text{O}_2\text{Si}$  requires  $M$ , 340.1858). The ratio of diastereoisomers **31a**:**31e** of 83:17 was measured by integration of the OMe signals.

*Methyl* (2RS,3RS)-3-dimethyl(phenyl)silyl-2-ethyl-2-methyl-3-phenylpropanoate **31e** (95%). By methylation (room temp., 18 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.41;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1600 and 1500 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.50–6.90 (10 H, m, Ph), 3.35 (3 H, s, OMe), 2.70 (1 H, s, CHPh), 1.55 (2 H, m, CH<sub>2</sub>Me), 1.25 (3 H, s, MeCC=O), 0.70 (3 H, t,  $J$  7, MeCH<sub>2</sub>), 0.45 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.15 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  340 (0.4%,  $\text{M}^+$ ), 311 (11,  $\text{M} - \text{Et}$ ), 145 (82, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+$ , 340.1862.  $\text{C}_{21}\text{H}_{28}\text{O}_2\text{Si}$  requires  $M$ , 340.1858). The ratio of diastereoisomers **31e**:**31a** of 89:11 was measured by integration of the OMe signals.

*Methyl* (2RS,3SR)-3-dimethyl(phenyl)silyl-2-isopropyl-2-methyl-3-phenylpropanoate **31b** (63%). By isopropylation (room temp., 18 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.45;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.45–6.80 (10 H, m, Ph), 3.60 (3 H, s, OMe), 2.90 (1 H, s, CHPh), 1.95 (1 H, septet,  $J$  7, HCMe<sub>2</sub>), 1.15 (3 H, s, MeCC=O), 0.80 (3 H, d,  $J$  7, CMe<sub>A</sub>Me<sub>B</sub>), 0.75 (3 H, d,  $J$  7, CNe<sub>A</sub>Me<sub>B</sub>), 0.40 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  339 (4%,  $\text{M} - \text{Me}$ ) and 311 (100,  $\text{M} - \text{Pr}$ ) (Found:  $\text{M}^+ - \text{Me}$ , 339.1769.  $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Si}$  requires  $M - \text{Me}$ , 339.1780). The ratio of diastereoisomers **31b**:**31f** of 90:10 was measured by integration of the OMe and MeCCO signals.

*Methyl* (2RS,3RS)-3-dimethyl(phenyl)silyl-2-isopropyl-2-methyl-3-phenylpropanoate **31f** (77%). By methylation (room temp., 2 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.45;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.50–6.80 (10 H, m, Ph), 3.55 (3 H, s, OMe), 2.70 (1 H, s, CHPh), 2.00 (1 H, septet,  $J$  7, HCMe<sub>2</sub>), 1.25 (3 H, s, MeCC=O) 0.80 (3 H, d,  $J$  7, CMe<sub>A</sub>Me<sub>B</sub>), 0.75 (3 H, d,  $J$  7, CMe<sub>A</sub>Me<sub>B</sub>), 0.40 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  354 (9%,  $\text{M}^+$ ), 311 (97,  $\text{M} - \text{C}_3\text{H}_7$ ), 145 (75, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+$ , 354.2002.  $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Si}$  requires  $M$ , 354.2015). The ratio of diastereoisomers **31f**:**31b** of 60:40 was measured by integration of the OMe and MeCCO signals.

*Methyl* (2RS,3SR)-2-allyl-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropanoate **31c** (90%). By allylation (room temp., 20 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.34;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O), 1640 (C=C) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.70–6.95 (10 H, m, Ph), 5.55 (1 H, m, CH=CH<sub>2</sub>), 4.85 (2 H, m, C=CH<sub>2</sub>) 3.40 (3 H, s, OMe), 2.90 (1 H, s, CHPh), 2.45 (1 H, dd,  $J$  6 and 13, CH<sub>A</sub>H<sub>B</sub>CH=), 1.80 (1 H, dd,  $J$  7 and 13, CH<sub>A</sub>H<sub>B</sub>CH=), 1.30 (3 H,

s, MeC), 0.40 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  337 (2%,  $\text{M} - \text{Me}$ ), 311 (34,  $\text{M} - \text{C}_3\text{H}_5$ ), 145 (98, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+ - \text{Me}$ , 337.1613.  $\text{C}_{22}\text{H}_{28}\text{O}_2\text{Si}$  requires  $M - \text{Me}$ , 337.1624). The ratio of diastereoisomers **31c**:**31g** of 83:17 was measured by integration of the OMe and MeCCO signals.

*Methyl* (2RS,3RS)-2-allyl-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropanoate **31g** (90%). By methylation (room temp., 1 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 10:1] 0.32;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O), 1640 (C=C) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.60–6.90 (10 H, m, Ph), 5.50 (1 H, m, CH=CH<sub>2</sub>), 4.90 (2 H, m, C=CH<sub>2</sub>) 3.35 (3 H, s, OMe), 2.70 (1 H, s, CHPh), 2.50 (1 H, dd,  $J$  6 and 13, CH<sub>A</sub>H<sub>B</sub>CH=), 2.10 (1 H, dd,  $J$  7 and 13, CH<sub>A</sub>H<sub>B</sub>CH=), 1.25 (3 H, s, MeC), 0.45 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  337 (3%,  $\text{M} - \text{Me}$ ), 311 (82,  $\text{M} - \text{C}_3\text{H}_5$ ), 145 (78, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+ - \text{Me}$ , 337.1623.  $\text{C}_{22}\text{H}_{28}\text{O}_2\text{Si}$  requires  $M - \text{Me}$ , 337.1624). The ratio of diastereoisomers **31g**:**31c** of 80:20 was measured by integration of the OMe and MeCCO signals.

*Methyl* (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methoxycarbonylmethyl-2-methyl-3-phenylpropanoate **31d** (45%). By methoxycarbonylmethylation (room temp., 1.5 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 3:1] 0.50;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1740 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.55–6.95 (10 H, m, Ph), 3.50 (3 H, s, OMe), 3.40 (3 H, s, OMe), 2.80 (1 H, d,  $J$  16, CH<sub>A</sub>H<sub>B</sub>C=O), 2.75 (1 H, s, CHPh), 2.10 (1 H, d,  $J$  16, CH<sub>A</sub>H<sub>B</sub>C=O), 1.35 (3 H, s, MeC), 0.40 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.15 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  384 (4%,  $\text{M}^+$ ), 311 (27,  $\text{M} - \text{CH}_2\text{CO}_2\text{Me}$ ), 145 (65, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+$ , 384.1775.  $\text{C}_{22}\text{H}_{28}\text{O}_4\text{Si}$  requires  $M$ , 384.1757). The ratio of diastereoisomers **31d**:**31h** of 92:8 was measured by integration of the OMe, MeCCO and SiMe signals.

*Methyl* (2RS,3RS)-3-dimethyl(phenyl)silyl-2-methoxycarbonylmethyl-2-methyl-3-phenylpropanoate **31h** (83%). By methylation (room temp., 1 h) as a mixture with its diastereoisomer;  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 3:1] 0.50;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1740 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.70–6.95 (10 H, m, Ph), 3.55 (3 H, s, OMe), 3.40 (3 H, s, OMe), 2.90 (1 H, d,  $J$  16, CH<sub>A</sub>H<sub>B</sub>C=O), 2.70 (1 H, s, CHPh), 2.35 (1 H, d,  $J$  16, CH<sub>A</sub>H<sub>B</sub>C=O), 1.40 (3 H, s, MeC), 0.50 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.20 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  384 (4%,  $\text{M}^+$ ), 311 (65,  $\text{M} - \text{CH}_2\text{CO}_2\text{Me}$ ), 145 (90, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (100, PhMe<sub>2</sub>Si) (Found:  $\text{M}^+$ , 384.1741.  $\text{C}_{22}\text{H}_{28}\text{O}_4\text{Si}$  requires  $M$ , 384.1757). The ratio of diastereoisomers **31h**:**31d** of 90:10 was measured by integration of the OMe, MeCCO and SiMe signals.

(2RS,3RS)- and (2RS,3SR)-3-Dimethyl(phenyl)silyl-2-methyl-3-phenylpropanoic Acid **5f** and **6f**.—3-Dimethyl(phenyl)silyl-3-phenylpropanoic acid<sup>69</sup> (0.284 g) in THF (5 cm<sup>3</sup>) was added dropwise with stirring to a solution of lithium diisopropylamide [prepared from butyllithium (1.6 mol dm<sup>-3</sup> solution in hexane; 7 cm<sup>3</sup>) and diisopropylamine (3 cm<sup>3</sup>) in THF (5 cm<sup>3</sup>)] at 0  $^{\circ}\text{C}$  and the mixture stirred for 30 min. The mixture was then stirred at room temp. for 30 min, cooled to 0  $^{\circ}\text{C}$ , and methyl iodide (0.28 g) in THF (5 cm<sup>3</sup>) added. After 30 min, the mixture was poured into water, and worked up in the usual way with ether to give the mixture of acids **5f** and **6f** (0.19 g, 63%), of which the former is known;<sup>27</sup>  $R_f$  [light petroleum (b.p. 60–80  $^{\circ}\text{C}$ )–EtOAc, 1:1] 0.24;  $\nu_{\text{max}}(\text{CCl}_4)/\text{cm}^{-1}$  3200–2500 (OH) and 1695 (C=O);  $\delta(250\text{ MHz, CDCl}_3)$  7.51–6.88 (10 H, m, Ph), 3.08–2.55 (2 H, m, CHSi and CHCO), 1.19 (3 H, **5f**, d,  $J$  6.9, Me), 1.03 (3 H, **6f**, d,  $J$  6.8, Me), 0.28 (3 H, **5f**, s, SiMe<sub>A</sub>Me<sub>B</sub>), 0.26 (3 H **5f**, s, SiMe<sub>A</sub>Me<sub>B</sub>), 0.25 (3 H **6f**, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.19 (3 H **6f**, s, SiMe<sub>A</sub>Me<sub>B</sub>). Treatment with diazomethane gave a mixture of the corresponding esters identical (<sup>1</sup>H NMR) with authentic samples.<sup>66</sup>

*Silylcupration of  $\alpha$ -Methylchalcone.*— $\alpha$ -Methylchalcone **7d**

(300 mg, 1.35 mmol) in dry THF (3 cm<sup>3</sup>) was added dropwise to the silyl-cuprate reagent (2.43 mmol) at  $-78^{\circ}\text{C}$  and stirring continued for 2 h. The mixture was allowed to warm slowly to room temp. and was quenched with basic aqueous ammonium chloride and extracted with light petroleum. The organic extracts were washed with basic aqueous ammonium chloride and brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure. Preparative TLC [light petroleum (b.p. 60–80 °C)–EtOAc, 10:1] gave 1-dimethyl(phenyl)silyloxy-2-methyl-1,3-diphenylprop-1-ene **11b** (280 mg, 58%);  $\delta$ (60 MHz, CCl<sub>4</sub>) 7.55–6.95 (15 H, m, Ph), 3.60 (2 H, s, PhCH<sub>2</sub>), 1.65 (3 H, s, MeC) and 0.35 (6 H, s, SiMe<sub>2</sub>). The silyl enol ether underwent hydrolysis to give 2-methyl-1,3-diphenylpropan-1-one b.p. 105–120 °C/0.05 mmHg (Kugelrohr) (lit.,<sup>70</sup> 113–115 °C/0.05 mmHg);  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup> 1680 (C=O);  $\delta$ (60 MHz, CDCl<sub>3</sub>) 7.90 (2 H, m, *o*-HCOPh), 7.80–7.10 (8 H, m, remaining Ph), 3.5 (1 H, m, HCCO), 2.60 (2 H, m, CH<sub>2</sub>Ph) and 1.25 (C H, d, J 6, CMe).

**Silyl Enol Ether 12.**—Methyl cinnamate (400 mg, 2.47 mmol) in dry THF (3 cm<sup>3</sup>) was added dropwise to the silylcuprate reagent (4.45 mmol) at  $-78^{\circ}\text{C}$  and stirring continued for 70 min. Chlorotrimethylsilane (1.5 cm<sup>3</sup>) was added, the cold bath removed and the solution allowed to warm to room temperature, where stirring was continued for 1 h. Pentane was added and the solution filtered through Celite. The solvent was removed under reduced pressure and the residue redissolved in pentane. The solution was filtered through Celite and then evaporated under reduced pressure to give the silyl enol ether which was characterised by signals at  $\delta$ (60 MHz, CCl<sub>4</sub>) 3.80 (1 H, d, J 10, HC=), 3.60 (3 H, s, OMe) and 3.30 (1 H, d, J 10, PhCH), together with signals in the phenyl region and the SiMe region masked by silicon-containing by-products.

**Silyl Enol Ether 14.**—The ester **13**<sup>66</sup> (250 mg, 0.84 mmol) was added dropwise to a solution of LDA at  $-78^{\circ}\text{C}$  [prepared by addition of butyllithium (0.72 cm<sup>3</sup>) to diisopropylamine (0.17 cm<sup>3</sup>) in dry THF (5 cm<sup>3</sup>)]. Stirring was continued for 10 min at  $-78^{\circ}\text{C}$  after which chlorotrimethylsilane (0.25 cm<sup>3</sup>) was added and the cold bath removed. Stirring was continued at room temp. for 50 min after which pentane was added and the mixture worked up as described above. The silyl enol ether was characterised by signals at  $\delta$ (60 MHz, CCl<sub>4</sub>) 4.15 (1 H, d, J 10, HC=), 3.55 (3 H, s, OMe) and 3.50 (1 H, d, J 10, PhCH), together with signals in the phenyl region and the SiMe region masked by silicon-containing by-products.

**Silyl Enol Ether 15.**—Benzylideneacetone (500 mg, 3.42 mmol) in dry THF (5 cm<sup>3</sup>) was added dropwise to the silylcuprate reagent (3.77 mmol) at  $-78^{\circ}\text{C}$  and stirring continued for 2.5 h. Chlorotrimethylsilane (2.2 cm<sup>3</sup>) was added and the cold bath removed. Stirring was continued at room temp. for 18 h and the mixture then worked up as described above. The silyl enol ether was characterised by signals at  $\delta$ (90 MHz, CCl<sub>4</sub>) 4.80 (1 H, d, J 11, HC=), 3.50 (1 H, d, J 11, PhCH) and 1.85 (3 H, s, CMe), together with signals in the phenyl region and the SiMe region masked by silicon-containing by-products. Irradiation at  $\delta$  1.85 gave an NOE enhancement of 13% at  $\delta$  4.80 and 0% at  $\delta$  3.50.

**Silyl Enol Ether 16.**—Cinnamaldehyde (400 mg, 3.03 mmol) in dry THF (5 cm<sup>3</sup>) was added dropwise to the silylcuprate reagent (3.4 mmol) at  $-78^{\circ}\text{C}$  and stirring continued for 1.5 h. Chlorotrimethylsilane (1.5 cm<sup>3</sup>) was added, the cold bath removed and the solution allowed to warm to room temperature, where stirring was continued for 30 min. Work-up as described above gave the silyl enol ether which was characterised by signals at  $\delta$ (90 MHz, CCl<sub>4</sub>) 6.10 (1 H, d, J 12, HCO), 5.30 (1 H, dd, J 11 and 12, HC=CO) and 2.95 (1 H, d, J 11,

PhCH), together with signals in the phenyl region and the SiMe region masked by silicon-containing by-products.

**Large-scale Preparation of the Acid 5f.**—The silyllithium solution<sup>64</sup> (1.2 mol dm<sup>-3</sup> solution in THF; 200 cm<sup>3</sup>, 220 mmol) was added to copper(i) cyanide (9.845 g, 110 mmol) at 0 °C under argon and the mixture stirred for 30 min. The solution was cooled with a solid CO<sub>2</sub>–acetone bath and methyl cinnamate (16.2 g, 100 mmol) added slowly. The mixture was stirred for 6 h and then at room temperature overnight. Work-up using basic aqueous ammonium chloride and light petroleum (b.p. 60–80 °C) gave the crude ester, which was dissolved in a two-phase mixture of methanol (400 cm<sup>3</sup>), water (100 cm<sup>3</sup>) and lithium hydroxide (7.2 g). This mixture was refluxed for 24 h and then concentrated under reduced pressure to 100 cm<sup>3</sup>. Water (200 cm<sup>3</sup>) and ether (100 cm<sup>3</sup>) were added and the organic phase washed with aqueous lithium hydroxide (6 mol dm<sup>-3</sup>; 2 × 100 cm<sup>3</sup>). The combined aqueous phases were acidified to pH 2 with concentrated sulfuric acid and extracted with ether (5 × 100 cm<sup>3</sup>). The combined organic extracts were washed with brine (100 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and evaporated under reduced pressure and the residue crystallised to give the known acid (17.5 g, 59%), m.p. 98–99 °C (from pentane–Me<sub>2</sub>CO) (lit.,<sup>27</sup> 99–101 °C);  $\delta$ (90 MHz, CCl<sub>4</sub>) 7.45–6.83 (10 H, m, Ph), 2.97 (1 H, dq, J 11 and 7, CHMe), 2.60 (1 H, d, J 11, CHSi), 1.06 (3 H, d, J 7, CHMe), 0.31 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.29 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>).

(2RS,3SR)-3-Dimethyl(phenyl)silyl-2-methyl-3-phenylpropionitrile.—Oxalyl chloride (0.82 cm<sup>3</sup>, 9.4 mmol) in dichloromethane (3 cm<sup>3</sup>) was added dropwise to a mixture of the acid (2 g, 6.7 mmol) and potassium carbonate (0.5 g) in dichloromethane (7 cm<sup>3</sup>) and the mixture was stirred under nitrogen overnight. The mixture was concentrated under reduced pressure, diluted with light petroleum (b.p. 60–80 °C) (50 cm<sup>3</sup>), filtered, and evaporated to give (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropionyl chloride (2.2 g, 100%);  $\nu_{\text{max}}$ (film)/cm<sup>-1</sup> 1785 (C=O), 1595 and 1490 (Ph) and 1260 (SiMe);  $\delta$ (90 MHz, CDCl<sub>3</sub>) 7.5–6.9 (10 H, m, PhC), 3.36 (1 H, dq, J 10 and 7, CHMe), 2.76 (1 H, d, J 10, CHSi), 1.19 (3 H, d, J 7, CHMe), 0.38 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.29 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 281 (3%, M – Cl), 135 (96, PhMe<sub>2</sub>Si) and 118 (100) (Found: M<sup>+</sup> – Cl, 281.1366. C<sub>18</sub>H<sub>21</sub>ClOSi requires M – Cl, 281.1361). The acid chloride (2.12 g) in ether (5 cm<sup>3</sup>) and THF (10 cm<sup>3</sup>) was added to aqueous ammonia (35%; 20 cm<sup>3</sup>) at 0 °C with vigorous stirring. The mixture was extracted with dichloromethane (3 × 60 cm<sup>3</sup>) and the combined extracts were washed with brine, dried (MgSO<sub>4</sub>) and evaporated under reduced pressure to give (2RS,3SR)-3-dimethyl(phenyl)silyl-2-methyl-3-phenylpropionamide (1.97 g, 100%) as needles, m.p. 122–123 °C (from CHCl<sub>3</sub>–hexane);  $\nu_{\text{max}}$ (CHCl<sub>3</sub>)/cm<sup>-1</sup> 3515 and 3395 (NH<sub>2</sub>), 1675 (C=O), 1595 (Ph), 1585 (amide II), 1490 (Ph), 1255 (SiMe) and 1120 (SiPh);  $\delta$ (90 MHz, CDCl<sub>3</sub>) 7.5–6.85 (10 H, m, Ph), 5.9 (1 H, br s, NH<sub>A</sub>H<sub>B</sub>), 5.55 (1 H, br s, NH<sub>A</sub>H<sub>B</sub>), 2.69 (2 H, m, CHMe and CHSi), 1.00 (3 H, d, J 6, CHMe), 0.32 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.19 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $\delta$ (90 MHz, [<sup>2</sup>H<sub>6</sub>]DMSO) showed better resolved signals 2.35 (1 H, dq, J 10 and 6, CHMe) and 2.15 (1 H, d, J 10, CHSi); *m/z* 297 (18%, M<sup>+</sup>), 282 (65, M – Me), 204 (53) and 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup>, 297.1547. C<sub>18</sub>H<sub>23</sub>NOSi requires M, 297.1549) (Found: C, 73.3; H, 8.05; N, 4.5. C<sub>18</sub>H<sub>23</sub>NOSi requires C, 72.7; H, 7.8; N, 4.7%). The amide (1.97 g, 6.63 mmol), pyridine (1.1 cm<sup>3</sup>, 13.6 mmol) and trifluoroacetic anhydride (1.1 cm<sup>3</sup>, 7.79 mmol) in dry THF (20 cm<sup>3</sup>) were stirred under nitrogen at 0 °C for 24 h and then poured into water (100 cm<sup>3</sup>). The water was extracted with dichloromethane (2 × 50 cm<sup>3</sup>) and the combined organic extracts were washed with brine, dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The residue was chromato-



graphed to give the nitrile **5g** (1.63 g, 88%);  $\nu_{\max}(\text{CCl}_4)/\text{cm}^{-1}$  2245 (CN), 1595 and 1490 (Ph), 1260 (SiMe) and 1120 (SiPh);  $\delta(90 \text{ MHz}, \text{CCl}_4)$  7.6–6.85 (10 H, m, Ph), 2.89 (1 H, dq, *J* 10 and 7, CHMe), 2.40 (1 H, d, *J* 10, CHSi), 1.17 (3 H, d, *J* 7, CHMe), 0.56 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.27 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 279 (9%, M<sup>+</sup>), 135 (33, PhMe<sub>2</sub>Si) and 118 (100, M – PhMe<sub>2</sub>Si – CN) (Found: M<sup>+</sup>, 279.1427. C<sub>18</sub>H<sub>21</sub>NSi requires *M*, 279.1443).

*Methyl (2RS,3RS)-3-Dimethyl(phenyl)-2-methyl-3-phenylpropanoate 5a* by Conjugate Addition of Phenyl-cuprate to Methyl  $\beta$ -Silylacrylate.—Copper(I) cyanide (270 mg, 3 mmol) was suspended in ether (10 cm<sup>3</sup>) at –78 °C and phenyllithium (4 cm<sup>3</sup> of a 1.5 mol dm<sup>–3</sup> solution in Et<sub>2</sub>O) was added. The mixture was stirred at 0 °C until the copper(I) cyanide dissolved and methyl 2-dimethyl(phenyl)silylacrylate<sup>71</sup> (220 mg, 1.36 mmol) was added. After 3 h, methyl iodide (0.2 cm<sup>3</sup>, 3.2 mmol) was added and stirring continued for 3 h. The black mixture was diluted with saturated aqueous ammonium chloride and extracted with ether (3 × 20 cm<sup>3</sup>). The organic layer was washed with saturated aqueous ammonium chloride (20 cm<sup>3</sup>) and brine (2 × 25 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. Flash column chromatography [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] of the residue gave largely the (2*RS*,3*RS*)-ester (128 mg, 30%) identical (<sup>1</sup>H NMR) with authentic material.<sup>66</sup>

*Methyl (2RS,3SR)-3-Dimethyl(phenyl)silyl-2-methylbutanoate 19b* by Conjugate Addition of Methylcuprate to Methyl  $\beta$ -Silylacrylate.—Similarly, methyl 2-dimethyl(phenyl)silylacrylate and lithium dimethylcuprate gave the ester **19b** and its diastereoisomer **20b** (56%), identical (<sup>1</sup>H NMR) with the authentic mixture described above, in a ratio measured by integration of the OMe signals of 89:11.

*Methyl 3-Dimethyl(phenyl)silyl-2-methylacrylate*.—Methyl 2-bromomethacrylate<sup>60</sup> (895 mg, 5 mmol) in THF (10 cm<sup>3</sup>) was added slowly to the silyl-cuprate reagent (6 mmol) in THF (20 cm<sup>3</sup>) at –78 °C and the mixture stirred for 3 h. Work-up with saturated aqueous ammonium chloride (50 cm<sup>3</sup>) and ether (50 cm<sup>3</sup>), followed by flash chromatography [light petroleum (b.p. 60–80 °C)–EtOAc, 95:5] and distillation (Kugelrohr, 90–92 °C/0.5 mmHg) gave the ester (705 mg, 60%);  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1710 (C=O) and 1605 (C=C);  $\delta(\text{CCl}_4)$  7.5–6.9 (5 H, m, Ph), 6.75 (1 H, br s, CH=), 3.61 (3 H, s, OMe), 1.90 (3 H, =CMe) and 0.49 (6 H, s, SiMe<sub>2</sub>); *m/z* 233 (3%, M<sup>+</sup>) and 218 (100, M – Me) (Found: M<sup>+</sup>, 233.0995. C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>Si requires *M*, 233.0998). This ester failed to react with either lithium diphenylcuprate or lithium dimethylcuprate even at 0 °C after 3 h in ether.

*Methyl 3-Dimethyl(phenyl)silyl-4-methylpentanoate*.—Methyl 4-methylpent-2-enoate was treated with the silyl-cuprate and the intermediate protonated as described above to give the ester (93%); *R<sub>f</sub>* [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] 0.27;  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1730 (C=O);  $\delta(\text{CCl}_4)$  7.4–7.0 (5 H, m, Ph), 3.50 (3 H, s, OMe), 2.33 (2 H, d, *J* 7, CH<sub>2</sub>), 1.90 (1 H, m, CHSi), 1.50 (1 H, m, CHMe<sub>2</sub>), 1.05 (3 H, d, *J* 5, CHMe<sub>A</sub>Me<sub>B</sub>), 0.96 (3 H, d, *J* 5, CHMe<sub>A</sub>Me<sub>B</sub>) and 0.47 (6 H, s, SiMe<sub>2</sub>); *m/z* 249 (15%, M – Me), 221 (70, M – C<sub>3</sub>H<sub>7</sub>) and 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup>, 249.1305. C<sub>15</sub>H<sub>24</sub>O<sub>2</sub>Si requires *M* – Me, 249.1311).

*Methyl (2RS,3SR)-3-Dimethyl(phenyl)silyl-2,4-dimethylpentanoate 19c* by Methylation of the Enolate Derived from Methyl 3-Dimethyl(phenyl)silyl-4-methylpentanoate.—The ester (264 mg, 1 mmol) in THF (5 cm<sup>3</sup>) was added dropwise to a solution of LDA (2 mmol) in THF (5 cm<sup>3</sup>) at –78 °C. After 3 h, methyl iodide (0.5 cm<sup>3</sup>, 8 mmol) was added and stirring

continued for 3 h. The mixture was brought to room temp., when aqueous work-up and flash chromatography [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] gave the ester **19c** and its diastereoisomer **20c** (258 mg, 93%) identical (<sup>1</sup>H NMR) with the authentic mixture described above, in a ratio measured by the integration of the SiMe signals of 80:20.

*Methyl 3-Dimethyl(phenyl)silyl-4,4-dimethylpentanoate*.—Methyl 4,4-dimethylpent-2-enoate was treated with the silyl-cuprate, and the intermediate protonated, as described above, to give the ester (83%); *R<sub>f</sub>* [light petroleum (b.p. 40–60 °C)–EtOAc, 95:5] 0.24;  $\nu_{\max}(\text{film})/\text{cm}^{-1}$  1733 (C=O);  $\delta(\text{CCl}_4)$  7.5–7.1 (5 H, m, Ph), 3.59 (3 H, s, OMe), 2.08 (2 H, d, *J* 6, CH<sub>2</sub>), 1.79 (1 H, t, *J* 6, CHSi), 1.1 (9 H, s, Bu<sup>t</sup>) 0.55 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.47 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>); *m/z* 263 (2%, M – Me), 221 (40, M – Bu<sup>t</sup>) and 135 (100, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup> – Me, 263.1489. C<sub>16</sub>H<sub>26</sub>O<sub>2</sub>Si requires *M* – Me, 263.1467). This ester failed to react with LDA followed by methyl iodide.

*Methyl (2RS,3SR)-3-Hydroxy-2,4-dimethylpentanoate*.—Methyl 3-dimethyl(phenyl)silyl-2,4-dimethylpentanoate **20c** (278 mg, 0.67 mmol) and boron trifluoride–acetic acid complex (0.2 cm<sup>3</sup>, 1.6 mmol) were stirred in dichloromethane (3 cm<sup>3</sup>) for 2 h. The dark brown solution was diluted with saturated aqueous sodium hydrogen carbonate (20 cm<sup>3</sup>) and extracted with ether (2 × 20 cm<sup>3</sup>). The ether layer was dried (MgSO<sub>4</sub>) and evaporated under reduced pressure to give the fluorodimethylsilyl compound (134 mg, 93%), which was dissolved in anhydrous DMF (1 cm<sup>3</sup>) and added to a suspension of potassium fluoride (206 mg, 3.55 mmol) in DMF (4 cm<sup>3</sup>) at 0 °C. A solution of *m*-chloroperbenzoic acid (630 mg, 3.57 mmol) in anhydrous DMF (3 cm<sup>3</sup>) was added dropwise, and the mixture stirred for 12 h at room temp. The solution was diluted with ether (50 cm<sup>3</sup>) and washed successively with water (100 cm<sup>3</sup>), aqueous sodium bisulfite (3 × 25 cm<sup>3</sup>, 10%) and aqueous sodium hydrogencarbonate (5%; 3 × 25 cm<sup>3</sup>), dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. Preparative TLC [light petroleum (b.p. 40–60 °C)–EtOAc, 80:20] gave the  $\beta$ -hydroxy ester (64 mg, 60%);  $\delta_{\text{C}}(\text{CDCl}_3)$  176.9, 76.9, 51.7, 41.9, 30.7, 19.1, 18.5 and 10.25 [lit.,<sup>41</sup> 76.7, 42.0 and 10.3 for the (2*RS*,3*SR*)-isomer and 78.0, 42.6 and 14.4 for (2*RS*,3*RS*)-isomer].

*Methyl (2RS,3RS)-3-Hydroxy-2,4,4-trimethylpentanoate*.—The ester **20d** (314 mg, 1 mmol) similarly gave the fluorodimethylsilyl compound (239 mg, 100%);  $\delta_{\text{H}}(\text{CCl}_4)$  3.60 (3 H, s, OMe), 2.74 (1 H, m, CHCO), 1.70 (1 H, m, CHSi), 1.35 (3 H, d, *J* 7, MeCCO), 1.14 (9 H, s, Bu<sup>t</sup>), 0.36 (3 H, d, *J* 8, SiMe<sub>A</sub>SiMe<sub>B</sub>), 0.35 (3 H, d, *J* 8, SiMe<sub>A</sub>SiMe<sub>B</sub>) which was similarly oxidised to give the  $\beta$ -hydroxy ester (183 mg, 100%);  $\delta_{\text{H}}(\text{CCl}_4)$  3.71 (3 H, s, OMe), 3.65 (1 H, s, CHOH), 2.6 (1 H, m, CHCO), 1.45 (3 H, d, *J* 7, MeCCO), 1.16 (9 H, s, Bu<sup>t</sup>),  $\delta_{\text{C}}(\text{CDCl}_3)$  175.5, 78.3, 51.7, 41.15, 35.6, 26.5 and 12.8 [lit.,<sup>42</sup> 78.3, 41.2 and 12.8 for the (2*RS*,3*RS*)-isomer and 82.5, 38.6 and 17.9 for (2*RS*,3*SR*)-isomer. The entries in the third and sixth columns of Table 1 entry 25 of ref. 42 should be reversed.<sup>72</sup>

*Varying the Proton Source: Protonation of the Enolate Derived from the Ester 7a*.—Methyl  $\alpha$ -methylcinnamate (100 mg, 0.57 mmol) in THF (3 cm<sup>3</sup>) was added to the silyl-cuprate reagent at –23 °C and the mixture quenched with the acids listed in Table 5. The ratios of the isomers were measured by reverse phase HPLC (ODS column, 70% aqueous methanol) and by integration of the CMe signals in the <sup>1</sup>H NMR spectrum at 250 MHz. The values varied from run to run, and measurement to measurement by  $\pm 2$ –3%. Yields were in the region of 87%.

*Dimethyl 2-[ $\alpha$ -Dimethyl(phenyl)silylbenzyl]-2-methylmalonate 27*.—The ester **26** (800 mg, 3.64 mmol) in dry THF (5

$\text{cm}^3$ ) was added dropwise to the silyl-cuprate reagent (6.4 mmol) at  $-78^\circ\text{C}$  and stirring continued for 1 h. Methyl iodide ( $1.85\text{ cm}^3$ ) was added and the reaction mixture allowed to warm to room temp. After 18 h, standard work-up of the reaction mixture followed by flash chromatography [light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )–EtOAc, 5:1] of the residue gave the ester (1.22 g, 90%);  $R_f$  [light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )–EtOAc, 3:1] 0.44;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O) and 1600 (Ph);  $\delta(80\text{ MHz, CDCl}_3)$  7.55–6.75 (10 H, m, Ph), 3.75 (3 H, s, OMe), 3.55 (3 H, s, OMe), 3.20 (1 H, s, CHPh), 1.40 (3 H, s, MeC), 0.40 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.25 (3 H, s, SiMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  370 (4%, M<sup>+</sup>), 311 (48, M – CO<sub>2</sub>Me), 145 (100, PhC<sub>4</sub>H<sub>4</sub>O) and 135 (58, PhMe<sub>2</sub>Si) (Found: M<sup>+</sup>, 370.1575. C<sub>21</sub>H<sub>26</sub>O<sub>4</sub>Si requires M, 370.1600).

**Demethoxycarbonylation of 27.**—The malonate was refluxed in DMSO (12 cm<sup>3</sup>) containing lithium chloride (100 mg) and water (0.05 cm<sup>3</sup>) for 25 min. Water (30 cm<sup>3</sup>) was added at room temp. and the mixture extracted with ether (3 × 20 cm<sup>3</sup>). The combined organic extracts were washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure. Preparative TLC [light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )–EtOAc, 10:1] of the residue gave (68%) of a 30:70 mixture (<sup>1</sup>H NMR) of **5a** and **6a** = **28**.

**Methylation of Regenerated Enolates.**—Typically, butyllithium (1.6 mol dm<sup>-3</sup> solution in hexane; 2.5 cm<sup>3</sup>, 4.0 mmol) was added at  $-78^\circ\text{C}$  to diisopropylamine (0.51 cm<sup>3</sup>, 3.6 mmol) in THF (12 cm<sup>3</sup>) and stirred at  $0^\circ\text{C}$  for 0.5 h. The solution was cooled to  $-78^\circ\text{C}$ , the ester (2.4 mmol) in THF (12 cm<sup>3</sup>) injected, and the solution stirred for 2 h. Methyl iodide (0.75 cm<sup>3</sup>, 12 mmol) was injected and the solution stirred for 2–3 h. The mixture was quenched at  $-78^\circ\text{C}$  with aqueous ammonium chloride solution, and worked up in the usual way. The following esters were prepared by this method.

**Methyl (2RS,3RS)-2-methyl-3-phenyl-3-trimethylsilylpropanoate 29b** (67%). As a 94:6 mixture with its diastereoisomer;  $R_f$  (EtOAc–hexane, 1:20) 0.30;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1735 (C=O) and 1600 (Ph);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.3–6.9 (5 H, m, Ph), 3.69 (3 H, s, OMe), 2.97 (1 H, dq,  $J$  6.8 and 11.5, CHCO), 2.34 (1 H, d,  $J$  11.5, CHSi), 1.02 (3 H, d,  $J$  6.8, CHMe) and  $-0.10$  (9 H, s, Me<sub>3</sub>Si);  $m/z$  250 (0.5%, M<sup>+</sup>), 235 (30, M – Me) and 177 (13, M – Me<sub>3</sub>Si) (Found: M<sup>+</sup>, 250.1389. C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>Si requires M, 250.1392). The ratio of isomers **29b**:**30b** was measured by integration of the OMe signals.

**Methyl (2RS,3RS)-2-methyl-3-phenyl-3-triphenylsilylpropanoate 29c** (75%). As a single diastereoisomer (>99:1) as prisms, m.p.  $124\text{--}126^\circ\text{C}$  (from hexane);  $R_f$  (EtOAc–hexane, 1:10) 0.28;  $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$  1720 (C=O) and 1580 (Ph);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.4–6.8 (20 H, m, 4 × Ph), 3.34–3.17 (2 H, m, CHSi and CHCO), 2.97 (3 H, s, OMe) and 0.93 (3 H, d,  $J$  6.1, CHMe);  $m/z$  436 (7%, M<sup>+</sup>), 421 (80, M – Me), 359 (20, M – Ph) and 259 (100, Ph<sub>3</sub>Si) (Found: M<sup>+</sup>, 436.1877. C<sub>29</sub>H<sub>28</sub>O<sub>2</sub>Si requires M, 436.1859) (Found: C, 79.5; H, 6.3. C<sub>29</sub>H<sub>28</sub>O<sub>2</sub>Si requires C, 79.8; H, 6.5%).

**Methyl (2RS,3RS)-3-tert-butyl(diphenyl)silyl-2-methyl-3-phenylpropanoate 29d** (70%). As a 99:1 mixture with its diastereoisomer;  $R_f$  (EtOAc–hexane, 1:10) 0.30;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1100 (SiPh);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.9–7.0 (15 H, m, 3 × Ph), 3.42 (1 H, d,  $J$  7.2, CHSi), 3.26 (3 H, s, OMe), 3.08 (1 H, qn,  $J$  7.0, CHCO), 0.75 (9 H, s, Bu<sup>t</sup>) and 0.74 (3 H, d,  $J$  7.0, CHMe);  $m/z$  416 (4.5%, M<sup>+</sup>), 401 (20, M – Me) and 239 (20, Bu<sup>t</sup>Ph<sub>2</sub>Si) (Found: M<sup>+</sup>, 416.2169. C<sub>27</sub>H<sub>32</sub>O<sub>2</sub>Si requires M, 416.2172). The ratio of isomers **29d**:**30d** was measured by integration of the OMe signals.

**Methyl (2RS,3SR)-3-tert-butyl(diphenyl)silyl-2,4-dimethylpentanoate 29g** (55%). As a 90:10 mixture with its diastereoisomer;  $R_f$  (EtOAc–hexane, 1:10) 0.38;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1100 (SiPh);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.8–7.2 (10 H,

m, 2 × Ph), 3.68 (3 H, s, OMe), 3.06 (1 H, dq,  $J$  7.3 and 2.0, CHCO), 2.52 (1 H, dd,  $J$  5.7 and 2.1, CHSi), 2.23 (1 H, sp,  $J$  6.7, CHMe<sub>2</sub>), 1.03 (3 H, d,  $J$  7.3, MeCHCO), 0.88 (3 H, d,  $J$  6.9, CMe<sub>A</sub>Me<sub>B</sub>) and 0.83 (3 H, d,  $J$  7.0, CMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  367 (0.8%, M<sup>+</sup> – Me), 351 (2.5 M – OMe), 339 (12, M – Pr<sup>i</sup>), 325 (100, M – Bu<sup>t</sup>) and 239 (8, Bu<sup>t</sup>Ph<sub>2</sub>Si) (Found: M<sup>+</sup> – Me, 367.2092. C<sub>24</sub>H<sub>34</sub>O<sub>2</sub>Si requires M – Me, 367.2100). The ratio of isomers **29g**:**30g** was measured by integration of the OMe signals.

**Methyl (2RS)-2-methyl-3-phenylpropanoate 40<sup>73</sup>** (48%);  $R_f$  (EtOAc–hexane, 1:10) 0.31;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1740 (C=O) and 1600 (Ph);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.4–7.1 (5 H, m, Ph), 3.64 (3 H, s, OMe), 3.04 (1 H, dd,  $J$  5.9 and 12.4, PhCH<sub>A</sub>H<sub>B</sub>), 2.9–2.6 (2 H, m, PhCH<sub>A</sub>H<sub>B</sub> and CHCO) and 1.21 (1 H, d,  $J$  9.1, CHMe).

**Methyl (2RS,3SR)-3-Phenyl-3-triphenylsilylpropanoate 30b.**—This ester was prepared for characterisation from its diastereoisomer **29b**. Sodium methoxide (4.0 mol dm<sup>-3</sup> solution in methanol; 0.75 cm<sup>3</sup>, 3.0 mmol) was added to **29b** (0.10 g, 0.4 mmol) in methanol (12 cm<sup>3</sup>) and the solution was heated at reflux under argon overnight. The solvent was removed, ether (10 cm<sup>3</sup>) was added and the solution was shaken with concentrated aqueous ammonium chloride. The ether extract was washed (brine), dried (Na<sub>2</sub>SO<sub>4</sub>) and chromatographed (EtOAc–hexane, 1:20) to give the ester (0.034 g, 34%) as an oil;  $R_f$  (EtOAc–hexane, 1:20) 0.18;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1740 (C=O) and 1600 (Ph);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.3–6.9 (5 H, m, Ph), 3.37 (3 H, s, OMe), 3.05 (1 H, dq,  $J$  7.0 and 11.3, CHCO), 2.32 (1 H, d,  $J$  11.4, CHSi), 1.30 (3 H, d,  $J$  7.0, CHMe) and  $-0.03$  (9 H, s, Me<sub>3</sub>Si);  $m/z$  250 (0.8%, M<sup>+</sup>), 235 (30, M – Me) and 177 (13, M – Me<sub>3</sub>Si) (Found: M<sup>+</sup>, 250.1382. C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>Si requires M, 250.1392).

**Methyl (2RS,3RS)-3-tert-Butyl(diphenyl)silyl-2,4-dimethylpentanoate 30g.**—This ester was prepared for characterisation from its diastereoisomer **29g**. Butyllithium (1.7 mol dm<sup>-3</sup> solution in hexane; 0.34 cm<sup>3</sup>, 0.58 mmol) was added at  $-78^\circ\text{C}$  to diisopropylamine (0.074 cm<sup>3</sup>, 0.52 mmol) in THF (10 cm<sup>3</sup>) and the mixture stirred at  $0^\circ\text{C}$  for 0.5 h. It was then cooled to  $-78^\circ\text{C}$  and the ester **29g** (0.040 g, 0.10 mmol) in THF (1.5 cm<sup>3</sup>) was injected into it; the solution was then stirred for 2 h. After this it was quenched at  $-78^\circ\text{C}$  with aqueous ammonium chloride and worked up in the usual way to give a 40:60 mixture of **30g** and **29g** (0.026 g, 65%);  $R_f$  (EtOAc–hexane, 1:10) 0.38;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  1730 (C=O) and 1110 (SiPh);  $\delta_{\text{H}}(250\text{ MHz; CDCl}_3)$  7.8–7.2 (10 H, m, 2 × Ph), 3.64 (3 H, s, OMe), 2.80 (1 H, dq,  $J$  7.3 and 3.9, CHCO), 2.38 (1 H, dd,  $J$  3.8 and 2.3, CHSi), 2.22 (1 H, sp,  $J$  6.7, CHMe<sub>2</sub>), 1.03 (3 H, d,  $J$  7.3, MeCHCO), 0.86 (3 H, d,  $J$  6.9, CMe<sub>A</sub>Me<sub>B</sub>) and 0.57 (3 H, d,  $J$  7.0, CMe<sub>A</sub>Me<sub>B</sub>);  $m/z$  382 (2%, M<sup>+</sup> – Me), 351 (2, M – OMe), 339 (19, M – Pr<sup>i</sup>) and 239 (8, Bu<sup>t</sup>Ph<sub>2</sub>Si) (Found: M<sup>+</sup>, 382.2341. C<sub>24</sub>H<sub>34</sub>O<sub>2</sub>Si requires M, 382.2328).

**Methyl (2RS,3RS)-2-Ethyl-3-hydroxy-2-methyl-3-phenylpropionate 33.**—The silane **31a** (0.91 g, 2.67 mmol) and boron trifluoride–acetic acid complex (0.37 cm<sup>3</sup>, 3.2 mmol) in dichloromethane (8 cm<sup>3</sup>) were stirred for 3 h at room temperature under nitrogen. The usual work-up gave the fluorosilane (0.67 g, 89%);  $\delta(60\text{ MHz, CCl}_4)$  7.28 (5 H, s, Ph), 3.81 (3 H, s, MeO), 2.70 (1 H, d,  $J$  8, CHSiF), 1.75 (2 H, m, CH<sub>2</sub>Me), 1.43 (3 H, s, MeCCO), 0.95 (3 H, t,  $J$  7, CH<sub>2</sub>Me), 0.30 (3 H, d,  $J$  8, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.18 (3 H, d,  $J$  8, SiMe<sub>A</sub>Me<sub>B</sub>). The fluorosilane (0.64 g), *m*-chloroperbenzoic acid (1.44 g) and potassium fluoride (0.4 g) were stirred in DMF (30 cm<sup>3</sup>).<sup>74</sup> After work-up with water and ether, flash chromatography [light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )–EtOAc, 1:1] gave the alcohol (0.45 g, 79%);  $R_f$  [light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )–EtOAc, 5:1] 0.24;  $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$  3400 (OH), 1710 (C=O) and 1480 (Ar);  $\delta(80\text{ MHz, CDCl}_3)$  7.29 (5 H, s, Ph), 4.88 (1 H, s, CHOH), 3.73 (3 H, s, MeO), 2.91 (1 H, br s,



OH, disappears on D<sub>2</sub>O shake), 1.82 (1 H, dq, *J* 14.7 and 7.4, CH<sub>A</sub>H<sub>B</sub>Me), 1.29 (1 H, m, CH<sub>A</sub>H<sub>B</sub>Me), 1.06 (3 H, s, MeCCO) and 0.85 (3 H, t, *J* 7.4, CH<sub>2</sub>CH<sub>3</sub>); *m/z* 222 (9%, M<sup>+</sup>), 191 (9, M - MeO), 116 (100, M - C<sub>7</sub>H<sub>6</sub>O), 101 (70, M - C<sub>8</sub>H<sub>9</sub>O) and 77 (22, Ph) (Found: M<sup>+</sup>, 222.1239. C<sub>13</sub>H<sub>18</sub>O<sub>3</sub> requires *M*, 222.1256).

**Methyl (2RS,3SR)-2-Ethyl-3-hydroxy-2-methyl-3-phenylpropionate 35.**—The silane **31e** (0.39 g, 1.14 mmol) was treated similarly to give the fluorosilane (0.31 g, 96%); δ(60 MHz, CCl<sub>4</sub>) 7.20 (5 H, br s, Ph), 3.61 (3 H, s, MeO), 2.64 (1 H, d, *J* 6, CHSiF), 1.90 (2 H, m, CH<sub>2</sub>Me), 1.52 (3 H, s, MeCCO), 1.00 (3 H, t, *J* 7.4, CH<sub>2</sub>Me), 0.45 (3 H, d, *J* 6, SiMe<sub>A</sub>Me<sub>B</sub>) and 0.32 (3 H, d, *J* 6, SiMe<sub>A</sub>Me<sub>B</sub>). The fluorosilane (0.27 g) was then similarly oxidised to give the alcohol (0.16 g, 74%); R<sub>f</sub> [light petroleum (b.p. 60–80 °C)–EtOAc, 5:1] 0.23; ν<sub>max</sub>(film)/cm<sup>-1</sup> 3450 (OH) and 1720 (C=O); δ(80 MHz, CDCl<sub>3</sub>) 7.29 (5 H, s, Ph), 4.89 (1 H, s, CHOH), 3.66 (3 H, s, MeO), 2.85 (1 H, br s, OH, disappears on D<sub>2</sub>O shake), 1.90 (1 H, dq, *J* 13.3 and 7.4, CH<sub>A</sub>H<sub>B</sub>Me), 1.13 (1 H, dq, *J* 13.3 and 7.4, CH<sub>A</sub>H<sub>B</sub>Me), 1.08 (3 H, s, MeCCO) and 0.87 (3 H, t, *J* 7.4, –CH<sub>2</sub>Me); *m/z* 222 (11%, M<sup>+</sup>), 191 (12, M - MeO), 116 (100, M - C<sub>7</sub>H<sub>6</sub>O), 101 (60, M - C<sub>8</sub>H<sub>9</sub>O) and 77 (19, Ph) (Found: M<sup>+</sup>, 222.1272. C<sub>13</sub>H<sub>18</sub>O<sub>3</sub> requires *M*, 222.1256).

**(2RS,3RS)-5-Ethyl-2,2,5-trimethyl-5-phenyl-1,3-dioxane 34.**—The β-hydroxy ester **33** (0.45 g) in ether (7.5 cm<sup>3</sup>) was added dropwise over 0.5 h to a stirred suspension of lithium aluminium hydride (0.105 g) in ether (2.5 cm<sup>3</sup>) at room temperature under nitrogen. After the mixture had been stirred for 1.5 h excess ethyl acetate was added, followed by water. The product was extracted with ether and ethyl acetate. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure, to give the diol (0.35 g, 89%); δ(60 MHz, CDCl<sub>3</sub>) 7.25 (5 H, s, Ph), 4.95–4.20 (2 H, m, OH), 4.59 (1 H, br s, CHOH), 3.58 (2 H, m, CH<sub>2</sub>OH), 1.50 (2 H, m, CH<sub>2</sub>Me), 1.02 (3 H, m, CH<sub>2</sub>Me) and 0.80 (3 H, s, MeCCO). The diol (0.35 g) and toluene-*p*-sulfonic acid (catalytic amount) were stirred in 2,2-dimethoxypropane (25 cm<sup>3</sup>) for 40 min at room temperature under nitrogen. An equal volume of water was then added and the mixture washed with aqueous sodium hydrogen carbonate and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated under reduced pressure. The residue was chromatographed [preparative TLC, light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] to give the dioxane (0.39 g, 82% overall); R<sub>f</sub> [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.64; ν<sub>max</sub>(film)/cm<sup>-1</sup> 2960 (CH), 1600 and 1490 (Ph) and 1100 (C–O), δ(250 MHz, CDCl<sub>3</sub>) 7.40–7.21 (5 H, m, Ph), 4.71 (1 H, s, CHPh), 3.86 (1 H, d, *J* 11.2, CH<sub>A</sub>H<sub>B</sub>O), 3.52 (1 H, d, *J* 11.2, CH<sub>A</sub>H<sub>B</sub>O), 1.53 (3 H, s, CMe<sub>A</sub>Me<sub>B</sub>), 1.52 (3 H, s, CMe<sub>A</sub>Me<sub>B</sub>), 1.40–1.10 (2 H, m, CH<sub>2</sub>Me), 0.91 (3 H, s, CMe) and 0.77 (3 H, t, *J* 7.6, CH<sub>2</sub>Me); *m/z* 234 (8%, M<sup>+</sup>), 165 (23, C<sub>4</sub>H<sub>7</sub>O), 107 (75, C<sub>7</sub>H<sub>7</sub>O), 70 (100, C<sub>5</sub>H<sub>10</sub>), 59 (20, C<sub>3</sub>H<sub>7</sub>O) and 55 (22, C<sub>4</sub>H<sub>7</sub>) (Found: M<sup>+</sup>, 234.1615. C<sub>15</sub>H<sub>22</sub>O<sub>2</sub> requires *M*, 234.1620).

**(2RS,3SR)-5-Ethyl-2,2,5-trimethyl-4-phenyl-1,3-dioxane 36.** The β-hydroxy ester **35** (0.15 g) was treated similarly to give the diol (0.06 g, 46%); δ(60 MHz, CCl<sub>4</sub>) 7.27 (5 H, s, Ph), 4.50 (1 H, br s, CHOH), 3.44 (2 H, m, CH<sub>2</sub>OH) and 2.00–0.75 (10 H, m, remaining Hs). The diol (0.05 g) was similarly converted into the dioxane (0.04 g, 30% overall); R<sub>f</sub> [light petroleum (b.p. 60–80 °C)–EtOAc, 1:1] 0.63, δ(250 MHz, CDCl<sub>3</sub>) 7.38–7.22 (5 H, m, Ph), 4.74 (1 H, s, CHPh), 3.69 (1 H, d, *J* 11.8, CH<sub>A</sub>H<sub>B</sub>O), 3.62 (1 H, d, *J* 11.8, CH<sub>A</sub>H<sub>B</sub>O), 1.53 (3 H, s, CMe<sub>A</sub>Me<sub>B</sub>), 1.52 (3 H, s, CMe<sub>A</sub>Me<sub>B</sub>), 0.88–0.69 (5 H, m, Et) and 0.67 (3 H, s, CMe).

**Kinetic Acidity and Nucleophilicity of β-Silyl Esters.**—LDA (0.24 mmol) and the esters **13**<sup>66</sup> (0.066 g, 0.22 mmol) and **37** (0.036 g, 0.22 mmol) were kept at –78 °C in THF (7 cm<sup>3</sup>) for 2 h. Methyl iodide (0.14 cm<sup>3</sup>, 2.2 mmol) was added and the

solution stirred for 2 h. Aqueous ammonium chloride was added at –78 °C, and the mixture worked up in the usual way. The ratio 46:54 of isomers **5a**:**40** was measured by integration of the OMe signals. A similar experiment using LDA (0.61 mmol), the two esters (0.11 mmol each) and methyl iodide (0.11 mmol) gave only a trace of the methylated products in a ratio of 1:1, and the recovered starting materials in a ratio of 2:1. However, a blank experiment, with omission of the methyl iodide, also gave the recovered starting materials in a ratio of 2:1. This indicated that methyl 3-phenylpropanoate was partly consumed under these conditions, probably by Claisen condensation, since submitting the mixture of esters merely to the work-up procedure caused virtually no change in the ratio. Finally, using LDA (0.90 mmol), the two esters (0.16 mmol each) and methyl iodide (0.48 mmol) gave the methylated products in a ratio of 60:40, with a little of the recovered starting materials in a ratio of 2:1.

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Paper 2/03392E

Received 29th June 1992

Accepted 8th September 1992