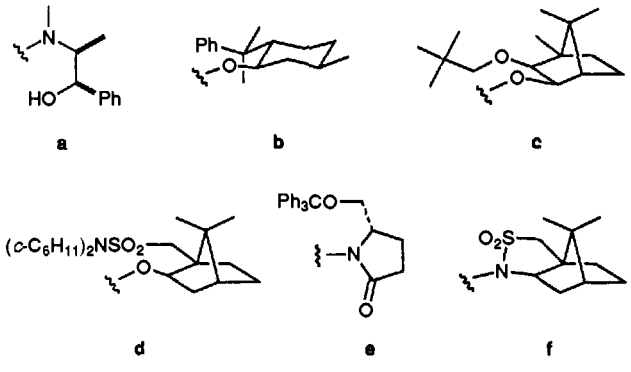
Diastereoselectivity in the Preparation of β-Silyl Esters from αβ-Unsaturated Esters and Amides Attached to Chiral Auxiliaries

Ian Fleming* and Nicholas D. Kindon
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK

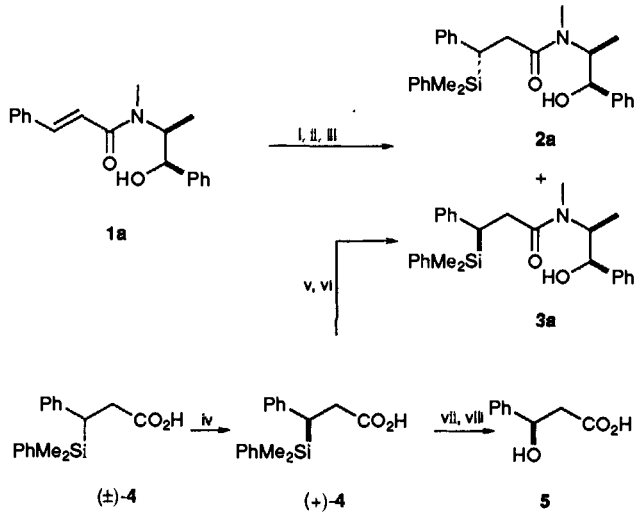
The conjugate addition of the phenyldimethylsilyl-cuprate reagent to cinnamate and crotonate esters and amides **1** of various known chiral auxiliaries, **a–e**, is diastereoselective. The sense of the diastereoselectivity of silyl-cuprate addition to the esters **1b–d**, **8** and **9** is different from established precedent based on carbon-cuprates, but is normal for silyl-cuprate addition to the amide **1a**, the imides **1e** and **21**, and the oxazolidine **6**. The chiral auxiliary **e** gives the best results of those tested, and the silicon-containing group can be removed from the chiral auxiliary using alkoxide ion in aprotic media, making available β-silyl esters **27–29** of high enantiomeric excess, with recovery of the chiral auxiliary **30**.

We have established that the alkylation of β-silyl enolates is highly diastereoselective[1] and that the products can be used in the synthesis of β-hydroxycarbonyl compounds[2] and of allylsilanes.[3,4] To extend this work to the synthesis of homochiral compounds, we needed to induce specific chirality into the conjugate addition of our silyl-cuprate reagent to αβ-unsaturated esters or amides that establishes the stereogenic centre carrying the silyl group. A potentially general and versatile way to do this is to attach a resolved chiral auxiliary at the carbonyl group of the enone system, since this group, when it is part of an ester or amide group, can, in principle, be detached later and recycled. Several ester and amide groups have been recommended for stereocontrol of conjugate additions in general. We chose to test how well some of these, **a–e**, worked with our silyl-cuprate reagent, and reported our results in preliminary form.[5] Our conclusion was that Koga's glutamic acid-derived lactam[6] **e** was the most reliably effective. Shortly before our paper appeared, Oppolzer reported[7] that his camphor-derived sultam **f**, not tested by us, was comparably effective in controlling the diastereoselectivity of the conjugate



addition of several nucleophiles including our silyl-cuprate reagent, and had the advantage that the products were frequently crystalline. We have used his chiral auxiliary since,[4] as well as Koga's,[8] and find that choosing the best for any specific compound can only be done by trial and error. Before, during and since our work, several other chiral auxiliaries for conjugate addition, which we have not tested, have been reported.[9] It is a daunting prospect, but any one of them might be better than the ones we have already studied.

The first substrate **1a** that we tested had Mukaiyama's ephedrine group **a**[10] attached to cinnamic acid, which gave us immediately an unequal mixture of the diastereoisomers **2a** and **3a** but of low d.e. (Table 1, entry 1). Mukaiyama noted that his reactions gave a much higher d.e. when carried out in ether instead of THF, but because the silyl-lithium reagent must be prepared in THF, it was not easy for us to carry out a reaction in ether alone. Instead, we added ether to our mixtures, but this only made matters worse with a lower and inverted d.e. (Table 1, entry 2). We tried simply adding magnesium bromide to the mixture, which was worse still (Table 1, entry 3). However, removing the proton from the hydroxy group first, and then adding magnesium bromide to the mixture before adding the silyl-cuprate, improved matters considerably (Table 1, entry 4). Using other Lewis acids gave some better results (Table 1, entries 10 and 11), and using 2 equiv. of the silyl-cuprate reagent with titanium tetrachloride gave us our best (entry 7). We measured the d.e. of each mixture directly by analysis of its ^{1}H NMR spectrum. We identified the stereochemical sense of the conjugate addition, which had given the same major diastereoisomer **2a** in every case but that of entry 2, by resolving a sample of the β-silylhydrocinnamic acid (±)-**4** (Scheme 1), converting[2]

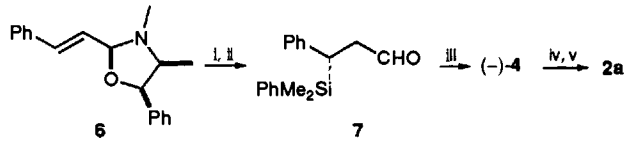


Scheme 1 *Reagents:* i, BuLi; ii, $TiCl_4$; iii, $(PhMe_2Si)_2CuCN\ Li_2$, −78 °C; iv, (+)-$PhCHMeNH_2$ and recrystallise; v, $(COCl)_2$; vi, (−)-ephedrine; vii, HBF_4; viii, AcOOH, Et_3N

some of the acid (+)-**4** into the (+)-β-hydroxy acid **5**, of known absolute configuration, and by joining the rest onto ephedrine to get the diastereoisomer **3a**, which was the minor product from the conjugate additions. Our reactions were, therefore, taking place in the same sense as Mukaiyama's. We had had

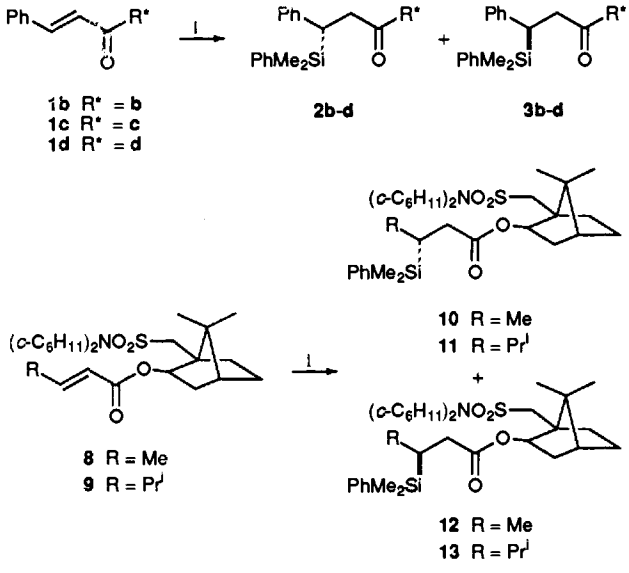
some encouraging success with this group, but we did not pursue it any further, because it proved to be so difficult to remove. We had no success with alkali, which induced decomposition faster than hydrolysis, possibly because we had a benzylsilane, nor were we successful using the method of Borch.[11]

Our second try with ephedrine was to use Normant's and Berland's oxazolidine **6**.[12,13] This overcame the difficulty in removing the chiral auxiliary, but the e.e. of the product **7** (60%, major isomer illustrated), although good, was not remarkably high, nor were we able to raise it. We measured the e.e., and proved that the stereochemical sense of the reaction was the same as Normant's and Berlan's, by oxidising the mixture of aldehydes **7** (major enantiomer illustrated) to the mixture of enantiomeric acids **4** rich in the (−)-enantiomer, and joining them onto ephedrine (Scheme 2).



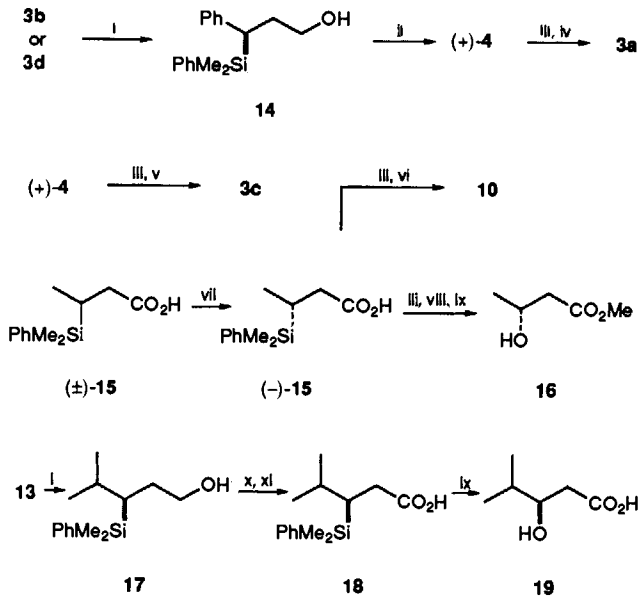
Scheme 2 *Reagents:* i, $(PhMe_2Si)_2CuCN\ Li_2$, −78 °C; ii, NH_4Cl, H_2O; iii, PDC; iv, $(COCl)_2$; v, (−)-ephedrine

Our next three substrates were all esters (Scheme 3), from which we hoped to be able to cleave the chiral auxiliary relatively easily. We used Corey's phenmenthyl group **b**[14] (first



Scheme 3 *Reagents:* i, $(PhMe_2Si)_2CuCN\ Li_2$, −78 °C

used in conjugate additions by Oppolzer),[15] and two of Oppolzer's camphor-derived groups **c**[16] and **d**.[17] Our results are collected in Table 2, with entries 1–5 being for straightforward reactions with our usual 'higher order' cuprate in THF, and the remainder being for variations of our standard conditions. The results (entries 1 and 6–10) with the phenmenthyl auxiliary **b** were not encouraging, nor was the one reaction (entry 2) with the neopentyl ether **c**. One result (entry 3) with the sulfonamide **d** was excellent, but proved not to be general with the substrates **8** and **9** (entries 4 and 5) not derived from cinnamic cid, nor could these substrates be induced to give better results by varying the conditions of the addition (entries 11–13). The use of a copper bromide-derived cuprate (entry 7) reversed the stereochemical sense of the conjugate addition, but other silyl-cuprates (entries 8 and 9) were unremarkable, and a silyl copper reagent with boron trifluoride did not react. We measured the d.e. of each mixture directly from its ^1H NMR spectrum. We proved the stereochemical sense of the reactions by the routes shown in Scheme 4. Alkaline hydrolysis was not,

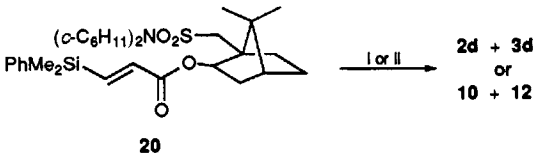


Scheme 4 *Reagents:* i, $LiAlH_4$; ii, PDC, DMF; iii, $(COCl)_2$; iv, (−)-ephedrine; v, **c**-H, AgCN; vi, **d**-H. AgCN; vii, (+)-$PhCHMeNH_2$ and recrystallise; viii, MeOH, Et_3N; ix, $Hg(OAc)_2$, $Pd(OAc)_2$, AcOOH; x, PDC, CH_2Cl_2; xi, CrO_3, H_2SO_4

in fact, easy and we resorted therefore to reduction of the product mixtures rich in **3b** and **3d** from entries 1 and 3 with lithium aluminium hydride to remove the chiral auxiliaries. We oxidised the mixtures rich in the alcohol **14** to the mixture rich in the acid (+)-**4**, and attached it to ephedrine to give mixtures rich in the diastereoisomer **3a** of known relative configuration, as described above. We attached some of the partially resolved acid (+)-**4** to the chiral auxiliary **c** to get a mixture rich in the diastereoisomer **3c**. Similarly, we resolved the acid (±)-**15** derived from crotonic acid, converted[18] some of the (−)-enantiomer (−)-**15** into the (−)-β-hydroxy ester **16** of known absolute configuration, and attached the rest to the chiral auxiliary **d** to get a mixture rich in the diastereoisomer **10**. Finally, we took the product mixture rich in **13** from entry 5, removed the chiral auxiliary, oxidised the alcohol **17** (major enantiomer illustrated) to the acid **18**, and converted it into the (+)-β-hydroxy acid **19** of known absolute configuration.

The most notable feature of the reactions with all three auxiliaries, **b**, **c** and **d**, is that the stereochemical sense of the conjugate addition is opposite to that seen by Oppolzer with alkyl-cuprates. Oppolzer explains his results by suggesting that nucleophilic attack takes place on the less hindered face of the s-*trans* conformation of the αβ-unsaturated esters. We already knew from our earlier work[1] that the silyl-cuprate reagent reacts with the s-*cis* conformation of αβ-unsaturated esters. Since the s-*trans* and s-*cis* conformations expose diastereotopic faces of the double bond, it is reasonable that we should get the opposite result to Oppolzer. We presume that a balance of forces between attack in the s-*trans* conformation, inherently preferred by the system, and attack in the s-*cis* conformation, preferred by the silyl-cuprate reagent, explains the variable degree of selectivity—high for cinnamate and low for crotonate—that detracts from the use of this chiral auxiliary.

We also tested an alternative way of preparing the esters in the **d** series by adding the phenyl and methyl Grignard reagents to the silicon-containing ester **20**, in the presence of copper cyanide (Scheme 5). These reactions worked moderately well



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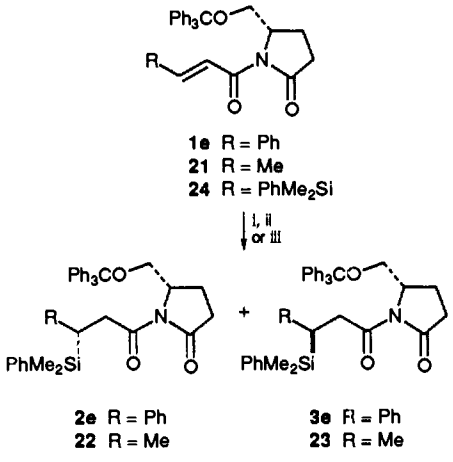
Scheme 5 *Reagents:* i, PhMgBr, CuCN; ii, MeMgI, CuCN or $Cu(OAc)_2$

(Table 2, entries 14–19), taking place as expected in the same stereochemical sense as Oppolzer had found, and hence giving the *same* major diastereoisomers **3d** and **12** as we had obtained in the reactions in Scheme 3. The high but opposite diastereoselectivity in the two ways of forming these compounds is remarkable, given that one gets the same major diastereoisomer regardless of whether the silyl group is added to the cinnamate, or the phenyl group is added to the β-silylenoate.

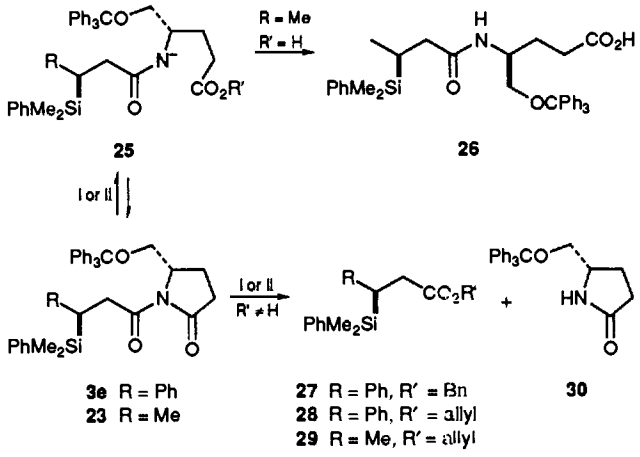
Finally, we turned to Koga's auxiliary **e** (Scheme 6). This had



Scheme 6 *Reagents:* i, $MgBr_2$, $(PhMe_2Si)_2CuLi$, −78 °C; ii, PhMgBr, $CuBr{\cdot}SMe_2$ or $Cu(OAc)_2$; iii, MeMgBr or MeMgI, $CuBr{\cdot}SMe_2$

two advantages: the products would be imides, which ought to be easier to cleave, and Koga's results implied that nucleophilic attack of carbon-cuprates took place in the s-*cis* conformation, just as we expected would occur with the silyl-cuprate. These hopes were borne out in practice (Table 3) as long as we used a magnesium halide as a Lewis acid to chelate the two carbonyl groups. The major products from addition of the silyl-cuprate to the imides **1e** and **21** were the imides **3e** and **23**. Other Lewis acids (entries 5–8) were less effective than magnesium bromide. Adding carbon-cuprates to the silicon-containing substrate **24** gave largely the complementary diasteroisomers **2e** and **22**, both sets of results taking place in the same stereochemical sense as Koga's. We measured the d.e. of each mixture directly from its ^1H NMR spectrum. We proved the relative configuration of these compounds by attaching the partially resolved acid (+)-**4** to the chiral auxiliary to make a mixture rich in **3e**, and by removing (see below) the chiral auxiliary from the product mixture of entry 4 rich in **23**, and attaching the acid so obtained to the chiral auxiliary **d** to make a mixture rich in the ester **12**, to which we had already assigned a relative configuration.

Koga's group is easily removed (Scheme 7). He used acid-catalysed esterification,[6] which had the unfortunate effect of removing the trityl group from the chiral auxiliary. We found that alkaline hydrolysis of the mixture of imides rich in **23** gave largely the open-chain acid **26** from cleavage of the lactam group. However, we also found that, although alkoxide treatment initially opens the ring **3e** or **23** ⟶ **25**, leaving the mixture in an aprotic solvent for a longer time releases the β-silyl esters **27**–**29**, presumably because the ring-opening step is



Scheme 7 *Reagents:* i, BnOLi; ii, allylOLi

reversible. In these conditions the trityl group is retained, and the chiral auxiliary **30** is readily isolated and can be recycled. Since we completed this work, we have found two useful modifications to the cleavage step that we mention here. In general, lithium alkoxides, as used in Scheme 7, are not the best choice. In our subsequent experience, although benzyl and allyl oxides work tolerably well, lithium methoxide does not. This problem is overcome by using the corresponding bromomagnesium alkoxide, when any of the alcohols works well. As a short cut, it is possible to add 1 equiv. of the alcohol directly to the reaction mixture at the end of the conjugate addition step. The alcohol protonates the enolate intermediate, and the bromomagnesium alkoxide so produced cleaves the chiral auxiliary off. It is considerably easier to maintain anhydrous conditions this way, and the overall yields are, therefore, usually higher. This protocol leaves no opportunity to crystallise the intermediate, and hence improve its d.e., but since Koga's auxiliary has rarely given us crystalline products, we have not found this to be much of a sacrifice.

Experimental

Starting Materials.—The silyl-cuprate reagent[19] and anhydrous magnesium bromide and chloride[20] were prepared by the cited methods. The amide **1a** was prepared (80%) by the method of Mukaiyama;[10] R_F(EtOAc–hexane, 1:1) 0.2; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3600 (NH), 3500–3100 (OH), 1640 (C=O), 1600 and 1580 (Ph); $\delta(CDCl_3$, 60 MHz) 7.6 (1 H, *J* 16, PhC*H*=CH), 7.30–7.20 (10 H, m, 2Ph), 6.7 (1 H, d, *J* 16, PhCH=C*H*), 5.0–4.3 (2 H, m, PhC*H*OH and NC*H*Me), 2.85 (3 H, s, NMe) and 1.2 (3 H, d, *J* 7, NCH*Me*). The oxazolidine **6** was prepared by the method of Berlan,[13] needles, m.p. 95–96 °C (from hexane) (lit.,[13] 95–96 °C); R_F(EtOAc–hexane, 1:10) 0.2; $\delta(CDCl_3$, 60 MHz) 7.5–6.9 (10 H, m, 2Ph), 6.6 (1 H, d, *J* 18, PhC*H*=CH), 6.1 (1 H, dd, *J* 8 and 18, PhCH=C*H*), 4.9 (1 H, d, *J* 8, OCHN), 4.15 (1 H, d, *J* 7, PhC*H*O), 3.0–2.5 (1 H, m, MeC*H*N), 2.25 (3 H, s, NMe) and 0.7 (3 H, d, *J* 7, *Me*CHN). The chiral auxiliaries were prepared by the methods of Herzog and Scharf,[21] Oppolzer[17,22] and Koga.[6]

(E)-3-*Dimethyl(phenyl)silylprop*-2-*en*-1-*ol*.—Freshly distilled prop-2-ynyl alcohol (0.5 g, 8.9 mmol) in dry THF (5 cm^3) was added dropwise over 5 min to a stirred solution of the dimethyl(phenyl)silyl-cuprate reagent (8.9 mmol, based on CuCN) in THF (30 cm^3) at 0 °C under nitrogen. After 3 h, basic aqueous ammonium chloride (15 cm^3) was added to the mixture which was then extracted with ether (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$), filtered through Celite and evaporated under reduced pressure. Chromatography

(SiO_2, EtOAc–hexane, 1:7) of the residue gave the *alcohol* (1.43 g, 82%); R_F(EtOAc–hexane, 1:5) 0.25; ν_{max}(film)/cm^{-1} 3700–2900 (OH), 1610 (C=C), 1250 (SiMe) and 1110 (SiPh); δ(CCl_4) 7.5–7.1 (5 H, m, Ph), 6.15 (1 H, dt, *J* 18 and 4.5, SiCH=C*H*), 5.85 (1 H, d, *J* 18, SiC*H*=CH), 3.9 (2 H, d, *J* 4.5, CH_2OH) and 0.2 (6 H, s, $SiMe_2$); *m*/*z* 177 (21%, M^+ – Me), 137 (25, SiPhMeOH), 135 (30, $SiPhMe_2$), 121 (15), 99 (12) and 75 (100) (Found: M^+ – Me, 177.0739. $C_{11}H_{16}OSi$ – Me requires *M* – Me, 177.0736) and its regioisomer 2-*dimethyl*(*phenyl*)*silylprop*-2-*en*-1-*ol* (0.22 g, 13%); R_F(EtOAc–hexane, 1:5) 0.3; ν_{max}(film)/cm^{-1} 3700–2900 (OH), 1250 (SiMe) and 1110 (SiPH); δ($CDCl_3$, 250 MHz) 7.5–7.45 (2 H, m, aromatic Hs *ortho* to Si), 7.37–7.25 (3 H, m, aromatic Hs *meta* and *para* to Si), 5.90 (1 H, dt, *J* 2.5 and 1.9, C$H_A$$H_B$=C), 5.48 (1 H, dt, *J* 2.5 and 1.6, CH$_A$$H_B$=C), 4.23 (2 H, t, *J* 1.75, CH_2OH) and 0.40 (6 H, s, $SiMe_2$); *m*/*z* 177 (15%, M – Me), 135 (30, $PhMe_2Si$) and 75 (100) (Found: M^+ – Me, 177.0731. $C_{11}H_{16}OSi$ requires *M* – Me, 177.0736).

(E)-3-*Dimethyl*(*phenyl*)*silylprop*-2-*enal*.—(*E*)-3-Dimethyl(phenyl)silylprop-2-en-1-ol (1.4 g, 7.3 mmol) in dry dichloromethane (10 cm^3) was added to a stirred solution of pyridinium dichromate (PDC) (3.3 g, 8.8 mmol) in dry dichloromethane (10 cm^3) at room temperature under nitrogen. After 24 h, ether (150 cm^3) was added to the reaction mixture which was then filtered through Celite and evaporated under reduced pressure. Chromatography of the residue (SiO_2, EtOAc–hexane, 1:5) gave the *aldehyde* (1.08 g, 78%); R_F(EtOAc–hexane, 1:5) 0.75; ν_{max}(film)/cm^{-1} 2700 (CH of CHO), 1680 (C=O), 1650 (C=C), 1250 (SiMe) and 1110 (SiPh); δ($CDCl_3$, 80 MHz) 9.53 (1 H, d, *J* 7.35, CHO), 7.6–7.2 (6 H, m, Ph and SiC*H*=CH), 6.55 (1 H, dd, *J* 7.35 and 18.7, SiCH=C*H*) and 0.47 (6 H, s, $SiMe_2$); *m*/*z* 190 (4.5%, M^+), 189 (50, M – H), 175 (40, M – Me), 163 (30), 137 (50, PhMeSiOH), 135 (100, $PhMe_2Si$) and 121 (35) (Found: M^+, 190.0806. $C_{11}H_{14}OSi$ requires *M*, 190.0814).

(E)-3-*Dimethyl*(*phenyl*)*silylpropenoic Acid*.—Chromium trioxide (2.4 g, 24 mmol) in sulfuric acid (98% solution; 3.48 g, 34.2 mmol) and water (10.5 cm^3) was added dropwise to a stirred solution of the aldehyde (3.3 g, 17.4 mmol) in acetone (14 cm^3) at 0 °C. After 4 h at room temperature, water (40 cm^3) was added to the mixture which was then extracted with ether (4 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered through Celite and evaporated under reduced pressure (to 20 cm^3). The solution was extracted with aqueous potassium hydroxide (1 mol dm^{-3}; 3 × 15 cm^3). The combined alkaline extracts were acidified to pH 1 (1 mol dm^{-3} HCl solution) and extracted with ether (3 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, Et_2O) of the residue gave the β-*silyl acid* (2.9 g, 80%); R_F(EtOAc–hexane, 1:1) 0.7; ν_{max}(film)/cm^{-1} 3700–2300 (OH), 1690 (C=O), 1580 (Ph), 1250 (SiMe) and 1110 (SiPh); δ(CCl_4, 90 MHz) 7.5–6.8 (6 H, m, Ph and SiC*H*=CH), 6.0 (1 H, d, *J* 20, SiCH=C*H*) and 0.3 (6 H, s, $SiMe_2$); *m*/*z* 206 (20%, M^+), 205 (35, M – H), 191 (70, M – Me), 137 (30, PhMeSiOH), 135 (55, $PhMe_2Si$), 121 (20), 105 (20) and 75 (100) (Found: M^+, 206.0769. $C_{11}H_{14}O_2Si$ requires *M*, 206.0763).

The Esters **1b–d**, **8**, **9** *and* **20**.—Typically, following Yamaguchi,[23] the alcohol (2.6 mmol), the acid chloride (6.37 mmol) and silver cyanide (3.9 mmol) were refluxed in dry benzene (25 cm^3) under nitrogen for 5 h. Ether (30 cm^3) was added to the mixture which was then filtered through Celite and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:20) of the residue gave the following esters.

(1R,2S,5R)-5-*Methyl*-2-(2′-*phenylpropan*-2′-*yl*)*cyclohexyl cinnamate* **1b** (97%) as needles, m.p. 65–66 °C (from hexane at –20 °C); [α]$_D$ +10.3 (*c* 2.23, $CHCl_3$); R_F(EtOAc–hexane, 1:10) 0.45; ν_{max}(CH_2Cl_2)/cm^{-1} 1700 (C=O), 1640 (C=C), 1600 and 1580 (Ph); δ($CDCl_3$, 250 MHz) 7.5–7.1 (11 H, m, 2Ph and PhC*H*=CH), 5.77 (1 H, d, *J* 16.0, PhCH=C*H*), 4.92 (1 H, dt, *J* 4.3 and 10.75, HCOC=O), 2.12 (1 H, dt, *J* 3.4 and 10.75, $PhMe_2CC$*H*), 2.05–0.9 (7 H, m, aliphatic Hs), 1.34 (3 H, s, C*Me*$_A$Me$_B$), 1.24 (3 H, s, CMe$_A$*Me*$_B$) and 0.9 (3 H, d, *J* 6.5, *Me*CH); *m*/*z* 362 (0.74%, M^+), 214 (10), 131 (30, PhCHCHCO), 119 (100) and 118 (40) (Found: C, 82.8; H, 8.4%; M^+, 362.2258. $C_{25}H_{30}O_2$ requires C, 82.0; H, 8.3%; *M*, 362.2247).

(1R,2S,3R,4S)-2-(2′,2′-*Dimethylpropoxy*)-1,7,7-*trimethylbicyclo*[2.2.1]*heptan*-3-*yl cinnamate* **1c** (93%); [α]$_D$ –8.8 (*c* 1.07, $CHCl_3$); R_F(EtOAc–hexane, 1:8) 0.4; ν_{max}(film)/cm^{-1} 1710 (C=O) and 1640 (C=C); δ($CDCl_3$, 250 MHz) 7.63 (1 H, d, *J* 16.0, PhC*H*), 7.5–7.45 (2 H, m, aromatic Hs *ortho* to Si), 7.37–7.33 (3 H, m, aromatic Hs *meta* and *para* to Si), 6.41 (1 H, d, *J* 16.0, PhCH=C*H*), 4.84 (1 H, d, *J* 6.8, HCOC=O), 3.32 (1 H, d, *J* 6.8, *H*COCH$_A$H$_B$), 3.12 (1 H, d, *J* 7.8, HCOC*H*$_A$H$_B$), 3.01 (1 H, d, *J* 7.8, HCOCH$_A$*H*$_B$), 1.8–0.8 (5 H, m, aliphatic Hs), 1.19 (3 H, s, Me), 0.92 (3 H, s, Me) and 0.81 (3 H, s, Me) and 0.82 (9 H, s, Me_3C); *m*/*z* 370 (0.06%, M^+), 283 (10, M – Me_3CCH_2O) and 153 (100, M – Me_3CCH_2O – PhCH=CHCO + H) (Found: M^+, 370.2510. $C_{24}H_{34}O_3$ requires *M*, 370.2508).

(1S,2R,4R)-1-(N,N-*Dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl cinnamate* **1d** (70%) as needles, m.p. 195–196 °C (from hexane); [α]$_D$ –62.30 (*c* 4.21, $CHCl_3$); R_F(EtOAc–hexane, 1:3) 0.55; ν_{max}(CH_2Cl_2)/cm^{-1} 1710 (C=O), 1640 (C=C), 1580 (Ph), 1310 and 1160 (SO_2N); δ($CDCl_3$, 80 MHz) 7.5–7.1 (6 H, m, Ph and PhC*H*=CH), 5.9 (1 H, d, *J* 16, PhC*H*), 3.4–3.0 (2 H, m, NCH), 3.25 (1 H, d, *J* 13.25, SC*H*$_A$H$_B$), 2.65 (1 H, d, *J* 13.25, SCH$_A$*H*$_B$) and 2.2–0.8 (33 H, m, aliphatic Hs); *m*/*z* 527 (3%, M^+), 380 (5, *M* – $C_9H_7O_2$), 244 [20, $SO_2N(C_6H_{11})_2$] and 180 [100, $N(C_6H_{11})_2$] (Found: C, 70.8; H, 8.5; N, 2.65%; M^+, 527.3089. $C_{31}H_{45}NO_4S$ requires C, 70.6; H, 8.5; N, 2.65%; *M*, 527.3069).

(1S,2R,4R)-1-(N,N-*Dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl crotonate* **8** (93%) as prisms, m.p. 103–104 °C (from hexane) (lit.,[24] 134–135 °C); [α]$_D$ –36.8 (*c* 5.175, $CHCl_3$) [lit.,[24] for the enantiomer of **8**, +39.5 (*c* 1.5, $CHCl_3$)]; R_F(EtOAc–hexane, 1:3) 0.55; ν_{max}(mull)/cm^{-1} 1720 (C=O), 1660 (C=C), 1350 and 1140 (SO_2N); δ($CDCl_3$, 80 MHz) 6.93 (1 H, dq, *J* 15.5 and 6.8, MeC*H*=CH), 5.8 (1 H, dq, *J* 15.5 and 1.7, MeCH=C*H*), 5.05 (1 H, dd, *J* 3.6 and 7.4, HCOC=O), 3.27 (1 H, d, *J* 13.25, SC*H*$_A$H$_B$), 3.4–3.0 (2 H, m, 2NCH), 2.65 (1 H, d, *J* 13.25, SCH$_A$*H*$_B$), 1.95 (3 H, dd, *J* 1.7 and 6.8, *Me*CH), 2.2–0.8 (27 H, m, aliphatic Hs), 0.99 (3 H, s, C*Me*$_A$Me$_B$) and 0.88 (3 H, s, CMe$_A$*Me*$_B$); *m*/*z* 465 (3%, M^+), 380 (10, *M* – $C_4H_5O_2$) and 180 (100, $N(C_6H_{11})_2$) (Found: C, 67.0; H, 9.2%; M^+, 465.2916. $C_{26}H_{43}NO_4S$ requires C, 67.1; H, 9.25%; *M*, 465.2913).

(1S,2R,4R)-1-(N,N-*Dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl* (E)-4′-*methylpent*-2′-*enoate* **9** (60%) as prisms, m.p. 210–211 °C (from hexane); [α]$_D$ –34.4 (*c* 1.35, CH_2Cl_2), R_F(EtOAc–hexane, 1:3) 0.6; ν_{max}(CH_2Cl_2)/cm^{-1} 1720 (C=O), 1650 (C=C), 1350 and 1140 (SO_2N); δ($CDCl_3$, 60 MHz) 6.7 (1 H, dd, *J* 6 and 16, Pr^{i}C*H*=CH), 5.4 (1 H, d, *J* 16, Pr^{i}CH=C*H*), 3.5–2.2 (5 H, m, 2NCH, 2SCH and Me_2C*H*) and 2.1–0.7 (39 H, m, aliphatic Hs); *m*/*z* 493 (3.4%, M^+), 380 (3, *M* – $C_6H_9O_2$), 244 [30, $SO_2N(C_6H_{11})_2$] and 180 [100, $N(C_6H_{11})_2$] (Found: C, 68.0; H, 9.6; N, 2.9%; M^+, 493.3211. $C_{28}H_{47}NO_4S$ requires C, 68.1; H, 9.55; N, 2.8%; *M*, 493.3226).

(1S,2R,4R)-1-(N,N-*Dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl* (E)-3′-*dimethyl*(*phenyl*)*silylpropenoate* **20** (76%) as prisms, m.p. 141–142 °C (from CH_2Cl_2–hexane), [α]$_D$ –40.8 (*c* 1.16, CH_2Cl_2); R_F(EtOAc–hexane, 2:5) 0.67; ν_{max}(mull)/cm^{-1} 1710 (C=O), 1610 (C=C), 1330 and 1150 (SO_2N), 1235 (SiMe) and 1110 (SiPh); δ($CDCl_3$, 250 MHz)

7.55–7.25 (6 H, m, SiPh and SiC*H*=CH), 6.24 (1 H, d, *J* 18.7, SiCH=C*H*), 5.1 (1 H, dd, *J* 3.9 and 7.2, CO_2CH), 3.3–3.0 (2 H, m, 2NCH), 3.27 (1 H, d, *J* 13.25, SCH_AH_B), 2.66 (1 H, d, *J* 13.25, SCH_AH_B), 2.2–0.8 (27 H, m, aliphatic Hs), 1.01 (3 H, s, Me), 0.9 (3 H, s, Me) and 0.39 (6 H, s, $SiMe_2$); *m/z* 585 (6.9%, M^+), 380 (20, $M - PhMe_2SiCHCH_2CO_2$), 298 (80, $M - PhMe_2SiCHCH_2CO_2 - C_6H_{11} + H$), 244 [100, $M - SO_2N(C_6H_{11})_2$], 254 (15), 234 (20), 228 (23) and 205 (20, $PhMe_2SiCHCH_2CO_2$) (Found: C, 67.55; H, 8.75; N, 2.3%; M^+, 585.3315. $C_{33}H_{51}NO_4SSi$ requires C, 67.7; H, 8.7; N, 2.4%; *M*, 585.3308).

The Imides **1e**, **21** *and* **24**.—Typically, butyllithium (1.25 mol dm^{-3} solution in hexane; 0.93 cm, 1.16 mmol) was added to a stirred solution of the lactam **30** (0.41 g, 1.16 mmol) in dry THF (3 cm^3) at −20 °C under nitrogen. After 20 min the solution was cooled to −78 °C and the acid chloride (0.2 g, 1.2 mmol) in dry THF (1 cm^3) added. After 30 min, the solution was allowed to warm to room temperature. Saturated aqueous ammonium chloride (5 cm^3) was added to the mixture which was then extracted with ether (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:6) of the residue gave the following imides.

(5S)-1-*Cinnamoyl*-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **1e** (88%); $[\alpha]_D$ −1.6 (*c* 9.86, $CHCl_3$); R_F(EtOAc–hexane, 1:3) 0.4; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1730 (C=O), 1670 (C=O), 1610 (C=C) and 1580 (Ph); $\delta(CDCl_3$, 80 MHz) 8.05 (1 H, d, *J* 15.6, PhC*H*=CH), 7.76 (1 H, d, *J* 15.6, PhCH=C*H*), 7.7–7.1 (20 H, m, 4Ph), 4.75–4.45 (1 H, m, CHN), 3.65 (1 H, dd, *J* 3.85 and 9.7, $CH_AH_BOCPh_3$), 3.21 (1 H, dd, *J* 2.7 and 9.7, $CH_AH_BOCPh_3$) and 3.1–1.9 (4 H, m, CH_2CH_2CO); *m/z* 487 (0.07%, M^+), 244 (100, $M - CPh_3$) and 243 (80, CPh_3) Found: M^+, 487.2133. $C_{33}H_{29}NO_3$ requires *M*, 487.2147).

(5S)-1-*Crotonoyl*-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **21** (80%) as prisms, m.p. 115–116 °C (from hexane) (lit.,[6] 116–117 °C); R_F(EtOAc–hexane, 1:3) 0.4; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1725 (C=O), 1670 (C=O), 1630 (C=C) and 1600 (Ph); $\delta(CDCl_3$, 80 MHz) 7.6–6.9 (17 H, m, 3Ph and MeC*H*=CH), 4.7–4.4 (1 H, m, CHN), 3.6 (1 H, dd, *J* 5.4 and 10.5, $CH_AH_BOCPh_3$), 3.15 (1 H, dd, *J* 3 and 10.5, $CH_AH_BOCPh_3$), 3.0–1.8 (4 H, m, CH_2CH_2CO) and 1.95 (3 H, d, *J* 6, *Me*CH=CH); *m/z* 425 (0.1%, M^+), 243 (100, CPh_3) (Found: C, 79.0; H, 6.4; N, 3.3%; M^+, 425.1995. $C_{28}H_{27}NO_3$ requires C, 79.05; H, 6.35; N, 3.3%; *M*, 425.1991).

(5S)-1-[3′-*Dimethyl*(*phenyl*)*silylpropenoyl*]-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **24** (100%); $[\alpha]_D$ −51.0 (*c* 2.87, $CHCl_3$); R_F(EtOAc–hexane, 1:3) 0.5; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1730 (C=O), 1670 (C=O), 1590 (C=C) and 1110 (SiPh); $\delta(CDCl_3$, 80 MHz) 7.74 (1 H, d, *J* 18.5, CH=C*H*Si), 7.6–7.0 (21 H, m, 4Ph and C*H*=CHSi), 4.6–4.4 (1 H, m, CHN), 3.55 (1 H, dd, *J* 4 and 9.8, $CH_AH_BOCPh_3$), 3.18 (1 H, d, *J* 2.85 and 9.8, $CH_AH_BOCPh_3$), 3.0–1.8 (4 H, m, CH_2CH_2CO), 0.46 (3 H, s, $SiMe_AMe_B$) and 0.43 (3 H, s, $SiMe_AMe_B$); *m/z* 545 (5%, M^+), 530 (20, M − Me), 302 (35, M − CPh_3) and 243 (100, CPh_3) (Found: M^+, 545.2399. $C_{35}H_{35}NO_3Si$ requires *M*, 545.2386).

(5S)-1-(3′-*Trimethylsilylpropenoyl*)-5-*triphenylmethoxymethylpyrrolidin*-2-*one* (the Me_3Si equivalent of **24**) as prisms, m.p. 104–105 °C (from hexane); $[\alpha]_D$ −64.35 (*c* 2.93, $CHCl_3$); R_F(EtOAc–hexane, 1:4) 0.55; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1730 (C=O), 1670 (C=O) and 1590 (C=C); $\delta(CCl_4$, 90 MHz) 7.7 (1 H, d, *J* 18, CH=C*H*Si), 7.5–7.1 (16 H, m, 3Ph and C*H*=CHSi), 4.5–4.3 (1 H, m, CHN), 3.55 (1 H, dd, *J* 4.5 and 9.0, $CH_AH_BOCPh_3$), 3.20 (1 H, dd, *J* 3.0 and 9.0, $CH_AH_BOCPh_3$), 3.0–1.8 (4 H, m, CH_2CH_2CO) and 0.25 (9 H, s, $SiMe_3$); *m/z* 483 (0.91%, M^+), 468 (10, M − Me), 410 (10, M − Me_3Si), 243 (100, CPh_3), 240 (40), 165 (50) and 127 (45) (Found: C, 74.55; H, 7.1; N, 2.8%; M^+, 483.2259. $C_{30}H_{33}NO_3Si$ requires C, 74.55; H, 6.85; N, 2.9%; *M*, 483.2230).

Conjugate Additions

Tables 1–3 identify the variant procedures that we tried. The following descriptions are the best result for each of the compounds made.

Table 1, *Entry* 7.—Butyllithium (1.3 mol dm^{-3} solution in hexane; 0.77 cm^3, 1 mmol) was added to a stirred solution of the amide **1a** (0.3 g, 1 mmol) in THF (5 cm^3) at −78 °C under nitrogen. After 10 min, titanium tetrachloride (0.19 g, 1 mmol) was added to the solution which was then allowed to warm to −10 °C. The solution was then added dropwise to a stirred solution of the silyl-cuprate reagent (2 mmol, based on CuCN) in THF (15 cm^3) at −78 °C under nitrogen. After 5 h, basic aqueous ammonium chloride (5 cm^3) was added to the mixture which was then allowed to warm to room temperature and extracted with ether (4 × 15 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:2) of the residue gave an inseparable mixture (0.26 g, 60%) of (3S)-3-*dimethyl*(*phenyl*)*silyl*-N-[(1′R,2′S)-1′-*hydroxy*-1′-*phenylpropan*-2′-*yl*]-N-*methyl*-3-*phenylpropanamide* **2a** and (3R)-3-*dimethyl*(*phenyl*)*silyl*-N-[(1′R,2′S)-1′-*hydroxy*-1′-*phenylprop*-2′-*yl*]-N-*methyl*-3-*phenylpropanamide* **3a** in a ratio of 88:12. The ratio was determined by integration of the PhC*H*OH peaks in the NMR spectrum); R_F(EtOAc–hexane, 1:2) 0.2; $\nu_{max}(CHCl_3)/cm^{-1}$ 3500–3100 (OH), 1670 (C=O), 1250 (SiMe) and 1110 (SiPh); $\delta(CDCl_3$, 250 MHz) for **2a**: 7.5–6.9 (15 H, m, 3Ph), 4.57 (1 H, d, *J* 3.2, PhC*H*OH), 4.50–4.35 (1 H, m, NC*H*Me), 3.01 (1 H, dd, *J* 4.9 and 9.9, SiC*H*CH_AH_BCO), 2.75 (1 H, dd, *J* 9.9 and 15.5, SiCHC*H*$_AH_BCO$), 2.51 (1 H, dd, *J* 4.9 and 15.5, SiCHCH_AH_BCO), 2.47 (3 H, s, NMe), 1.01 (3 H, d, *J* 7.15, NCH*Me*), 0.247 (3 H, s, $SiMe_AMe_B$) and 0.243 (3 H, s, $SiMe_AMe_B$); for **3a**: 7.5–6.9 (15 H, m, 3Ph), 4.67 (1 H, d, *J* 3.35, PhC*H*OH), 4.35–4.20 (1 H, m, NC*H*Me), 2.99 (1 H, dd, *J* 4.55 and 10.2, SiC*H*CH_AH_BCO), 2.76 (1 H, dd, *J* 10.2 and 15.7, SiCHC*H*$_AH_BCO$), 2.57 (3 H, s, NMe), 2.52 (1 H, dd, *J* 4.55 and 15.7, SiCHCH_AH_BCO), 1.01 (3 H, d, *J* 7.15, NCH*Me*), 0.27 (3 H, s, $SiMe_AMe_B$) and 0.24 (3 H, s, $SiMe_AMe_B$); *m/z* 431 (10%, M^+), 416 (10, M − Me), 296 (2, M − $PhMe_2Si$) and 135 (100, $PhMe_2Si$) (Found: M^+, 431.2295. $C_{27}H_{33}NO_2Si$ requires *M*, 431.2281).

Conjugate Addition of the Dimethyl(*phenyl*)*silyl-cuprate Reagent to the Oxazolidine* **6**.—The oxazolidine (0.4 g, 1.43 mmol) in dry THF (4 cm^3) was added dropwise (over 15 min) to a stirred solution of the dimethyl(phenyl)silyl-cuprate reagent (2.85 mmol, based on CuCN) in THF (10 cm^3) at −78 °C under nitrogen. After 4.5 h, the mixture was allowed to warm to room temperature overnight. Basic aqueous ammonium chloride (20 cm^3) was added to the mixture which was then extracted with ether (3 × 20 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered through Celite and evaporated under reduced pressure. Flash chromatography (EtOAc–hexane, 1:10) of the residue gave (3*S*)-3-dimethyl(phenyl)silyl-3-phenylpropanal[25] **7** (0.3 g, 79%); R_F(EtOAc–hexane, 1:5) 0.35; ν_{max}(film)/cm^{-1} 3040–3010 (PhH), 2800 and 2700 (CH of CHO), 1720 (C=O), 1250 (SiMe) and 1110 (SiPh); $\delta(CCl_4$, 90 MHz) 9.3–9.1 (1 H, m, CHO), 7.3–6.5 (10 H, m, 2Ph), 2.9–2.4 (3 H, m, PhC*H*CH_2-CHO) and 0.2 (6 H, s, $SiMe_2$), with an enantiomeric excess of 60% determined by oxidation to the acid and attachment to ephedrine.

Table 2, *Entry* 1.—The ester **1b** (0.33 g, 0.9 mmol) in dry THF (1.5 cm^3) was added dropwise to a stirred solution of the dimethyl(phenyl)silyl-cuprate reagent (1.8 mmol, based on CuCN) in THF (9 cm^3) at −78 °C under nitrogen. After 2 h, basic aqueous ammonium chloride (9 cm^3) was added to the

Table 1 Addition of $(PhMe_2Si)_2CuCN\ Li_2$ to the ephedrine-derived cinnamides **1a** (Scheme 1)

Entry	Solvent	Added Lewis acid	Equiv. of Cu	Yield (%)	Recovered **1a**	**2a**:**3a**	D.e. (%)
1	THF	None[a]	1.1	75	—	60:40	20
2	THF, Et_2O (1:5)	None[a]	1.1	75	18	42:58	16
3	THF	$MgBr_2$[a]	1.1	90	—	50:50	0
4	THF	$MgBr_2$	1.1	70	23	70:30	40
5	THF, Et_2O (1:5)	$MgBr_2$	1.1	70	16	65:35	30
6	THF	$TiCl_4$	1.1	48	18	80:20	60
7	THF	$TiCl_4$	2	60	—	88:12	76
8	THF, Et_2O (1:5)	$TiCl_4$	2	63	—	73:27	46
9	THF	$EtAlCl_2$	2	74	22	50:50	0
10	THF	$SnCl_4$	2	79	—	63:37	26
11	THF	$AlCl_3$	2	76	—	66:34	32

[a] The amide **1a** was not treated with BuLi in these cases.

Table 2 Addition of $(PhMe_2Si)_2CuCN\ Li_2$ to the esters **1b–d**, **8** and **9** (Scheme 3) and copper-catalysed addition of PhMgBr and MeMgI to the ester **20** (Scheme 5)

Entry	Substrate	Solvent	Nucleophile[a]	Equiv. of Cu	Yield (%)	**2**:**3**; **10**:**12** or **11**:**13**	D.e. (%)
1	**1b**	THF	$[Si]_2CuCN\ Li_2$	1	80	40:60	20
2	**1c**	THF	$[Si]_2CuCN\ Li_2$	1	74	46:54	8
3	**1d**	THF	$[Si]_2CuCN\ Li_2$	1	77[b]	6:94[c]	88
4	**8**	THF	$[Si]_2CuCN\ Li_2$	1	74	45:55	10
5	**9**	THF	$[Si]_2CuCN\ Li_2$	1	74	22:78	56
6	**1b**	THF, Et_2O (1:3)	$[Si]_2CuCN\ Li_2$	2	82	40:60	20
7	**1b**	THF	$[Si]_2Cu\ Li{\cdot}LiBr$	2	79	60:40	20
8	**1b**	THF	$[Si]_2Cu\ Li{\cdot}LiI$	2	88	50:50	0
9	**1b**	THF	$[Si](Me)CuCN\ Li_2$	2	64	50:50	0
10	**1b**	THF	$[Si]Cu\ BF_3{\cdot}OEt_2$	2	0	—	—
11	**8**	THF	$[Si]_2CuCN\ Li_2$[d]	2	74	45:55	10
12	**8**	THF, Et_2O (1:6)	$[Si]_2CuCN\ Li_2$	2	73	45:55	10
13	**9**	THF[e]	$[Si]_2CuCN\ Li_2$	2	74	21:79	58
14	**20**	Et_2O	$MeCu\ BF_3{\cdot}OEt_2$[f]	10[g]	5	—	—
15	**20**	THF, Et_2O (1:22)[h]	$MeCu\ BF_3{\cdot}OEt_2$[i]	5[g]	5	—	—
16	**20**	THF, Et_2O (1:6)[j]	MeMgI, CuCN[k]	10[g]	30[l]	50:50	0
17	**20**	THF, Et_2O (4:3)[m]	MeMgI, $Cu(OAc)_2$[n]	10[g]	76	24:78	54
18	**20**	THF, Et_2O (1:4)[o]	PhMgBr, CuCN[k]	10[g]	53	24:78	54
19	**20**	THF, Et_2O (1:4)	PhMgBr, CuCN[k]	10[g]	71	13:87	74

[a] [Si] = $PhMe_2Si$. [b] 67% after recrystallisation. [c] 2.5:97.5 (95% d.e.) after recrystallisation. [d] $EtAlCl_2$ added to substrate before adding cuprate. [e] Carried out at −98 °C. [f] Derived from CuI. [g] Ratio of Cu to **20**. [h] Carried out at −20 °C. [i] Derived from CuCN. [j] Carried out at −25 °C. [k] In a ratio of 2:1. [l] Together with **d**-H (43%), (*E*)-4-dimethyl(phenyl)silyl-2-methylbut-3-en-2-ol (21%) and 4-dimethyl(phenyl)silylpentan-2-one (17%). [m] Carried out at −15 °C. [n] In a ratio of 4:1. [o] Carried out at 0 °C.

mixture which was then allowed to warm to room temperature. The solution was extracted with ether (5 × 10 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and chromatography (SiO_2, EtOAc–hexane, 1:15) of the residue gave the inseparable diastereoisomers (1R,2S,5R)-5-*methyl*-2-(1′-*methyl*-1′-*phenylethyl*)*cyclohexyl*-(3″R)-3″-*dimethyl*(*phenyl*)*silyl*-3″-*phenylpropanoate* **3b** and (1R,2S,5R)-5-*methyl*-2-(1′-*methyl*-1′-*phenylethyl*)*cyclohexyl*-(3S″)-3″-*dimethyl*(*phenyl*)*silyl*-3″-*phenylpropanoate* **2b** (0.36 g, 80%) in a ratio of 60:40 determined by integration of the *Me*CPh peaks in the ^1H NMR spectrum; R_F(EtOAc–hexane, 1:10) 0.45; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1725 (C=O), 1250 (SiMe) and 1110 (SiPh); $\delta(CDCl_3$, 250 MHz) for **3b**: 7.4–6.8 (15 H, m, 3Ph), 4.7–4.4 (1 H, m, OCH), 2.38 (1 H, dd, *J* 5.4 and 12, $SiCHCH_AH_B$), 2.30 (1 H, dd, *J* 3.25 and 12, $SiCHCH_AH_B$), 2.2–1.8 (1 H, m, $SiCHCH_AH_B$), 1.7–1.0 (8 H, m, aliphatic Hs), 1.20 (3 H, s, *Me*CPh), 1.12 (3 H, s, *Me*CPh), 0.715 (3 H, d, *J* 6.3, *Me*CH), 0.19 (3 H, s, $SiMe_AMe_B$) and 0.18 (3 H, s, $SiMe_AMe_B$); for **2b**: 7.4–6.8 (15 H, m, 3Ph), 4.7–4.4 (1 H, m, OCH), 2.69 (1 H, dd, *J* 4.7 and 12, $SiCHCH_AH_B$), 2.2–1.8 (2 H, m, $SiCHCH_AH_B$), 1.7–1.0 (8 H, m, aliphatic Hs), 1.24 (3 H, s, *Me*CPh), 1.16 (3 H, s, *Me*CPh), 0.19 (3 H, s, $SiMe_AMe_B$) and 0.18 (3 H, s, $SiMe_AMe_B$); *m/z* 498 (1.0%, M^+), 215 [20, M − $PhMe_2Si(Ph)CHCH_2CO_2$] and 135 (100, $PhMe_2Si$) (Found: M^+ 498.2950. $C_{33}H_{42}O_2Si$ requires *M*, 498.2954).

Table 2, *Entry* 2.—The ester **1c** (0.37 g, 1 mmol) in dry THF (3 cm^3) was added dropwise (over 10 min) to the dimethyl(phenyl)silyl-cuprate reagent (2 mmol, based on CuCN) in THF (9 cm^3) at −78 °C under nitrogen. After 2 h, basic aqueous ammonium chloride (5 cm^3) was added to the reaction mixture which, upon work-up as above, and chromatography (SiO_2, EtOAc–hexane, 1:6) gave the inseparable diastereoisomers (1R,2S,3R,4S)-2-(2′,2′-*dimethylpropoxy*)-1,7,7-*trimethylbicyclo*[2.2.1]*heptan*-3-*yl* (3″R)-3″-*dimethyl*(*phenyl*)*silyl*-3″-*phenylpropanoate* **3c** and (1R,2S,3R,4S)-2-(2′,2′-*dimethylpropoxy*)-1,7,7-*trimethylbicyclo*[2.2.1]*heptan*-3-*yl* (3″S)-3″-*dimethyl*(*phenyl*)*silyl*-3″-*phenylpropanoate* **2c** (0.37 g, 74%) in a ratio of 54:46 determined by integration of the Me peaks in the ^1H NMR spectrum); R_F(EtOAc–hexane, 1:4) 0.60; ν_{max}(film)/cm^{-1} 1740 (C=O), 1250 (SiPh) and 1110 (SiPh); $\delta(CDCl_3$, 250 MHz) for **3c**: 4.48 (1 H, d, *J* 6.8, HCOC=O), 1.07 (3 H, s, Me), 0.85 (3 H, s, Me), 0.78 (9 H, s, Me_3C), 0.73 (3 H, s, Me) and 0.23 (3 H, s, SiMe); for **2c**: 4.43 (1 H, d, *J* 6.8, HCOC=O), 1.02 (3 H, s, Me), 0.845 (3 H, s, Me), 0.80 (9 H, s, Me_3C), 0.71 (3 H, s, Me) and 0.24 (3 H, s, SiMe), with coincident peaks for both diastereo-

Table 3 Addition of $(PhMe_2Si)_2CuLi$ to the imides **1e** and **21**, and of PhMgBr and MeMgI (or MeMgBr) to the imide **24** (Scheme 6)

Entry	Substrate	Solvent	Nucleophile[a]	Added Lewis acid	Yield (%)	2e:3e or 22:23	D.e. (%)
1	**1e**	THF	$[Si]_2CuCN\ Li_2$		78	46:54	8
2	**1e**	THF	$[Si]_2Cu\ Li{\cdot}LiBr$	1.5 $MgBr_2$	80	14:86	72
3	**1e**	THF	$[Si]_2Cu\ Li{\cdot}LiBr$	6 $MgBr_2$	84	11:89	78
4	**21**	THF	$[Si]_2Cu\ Li{\cdot}LiBr$	6 $MgBr_2$	82	11:89	78
5	**21**	THF	$[Si]_2Cu\ Li{\cdot}LiBr$	6 $MgCl_2$	76	14:86	72
6	**21**	THF	$[Si]_2Cu\ Li{\cdot}LiBr$	$EtAlCl_2$	77	50:50	0
7	**1e**	THF	$[Si]_2CuCN\ Li_2$	$TiCl_4$	0[b]	—	—
8	**1e**	THF	$[Si]_2CuCN\ Li_2$	$ZnBr_2$	77	41:59	18
9	**24**	THF, Et_2O, Me_2S 11:2:4[c]	PhMgBr + CuBr·SMe_2 (2:1)		96	96:4	92
10	**24**	THF, Et_2O 5:3[d]	PhMgBr + $Cu(OAc)_2$ (4.5:1)		74	71:29	42
11	**24**	THF, Et_2O, Me_2S 5:1:2[e]	MeMgI + CuBr·SMe_2 (2:1)		82	70:30	40
12	**24**	THF, Et_2O, Me_2S 11:1:4[e]	MeMgBr + CuBr·SMe_2 (2:1)		74	70:30	40
13	**24**	THF, Et_2O, Me_2S 14:1:4.5[e]	MeMgBr + CuBr·SMe_2 (2:1)	1.5 $MgBr_2$	82	76:24	52
14	**24**[f]	THF, Et_2O, Me_2S 7:1:3[g]	MeMgBr + CuBr·SMe_2 (2:1)	1.5 $MgBr_2$	90	82:18[h]	64

[a] [Si] = $PhMe_2Si$. [b] The trityl ether was cleaved. [c] Carried out at −55 °C. [d] Carried out at −30 °C. [e] Carried out at −65 °C and warmed to 0 °C over 3 h. [f] Me_3Si in place of $PhMe_2Si$. [g] Carried out at −78 °C and warmed to 0 °C over 3 h. [h] Relative configuration assigned by analogy.

isomers at 7.4–6.9 (10 H, m, 2Ph), 3.2–2.5 (6 H, m, Me_3CCH_2OCH and $SiCHCH_2CO_2$), 1.6–1.2 (5 H, m, aliphatic Hs) and 0.19 (3 H, s, SiMe); *m/z* 506 (0.06%, M^+), 419 (8, M − Me_3CCH_2O), 223 (10) and 153 (100, M − Me_3CCH_2O − $PhMe_2SiPhCHCH_2CO$ + H) (Found: M^+, 506.3236. $C_{32}H_{46}O_3Si$ requires *M*, 506.3216).

Table 2, *Entry* 3.—The ester **1d** (0.6 g, 1.14 mmol) in dry THF (8 cm^3) was added dropwise (over 20 min) to a stirred solution of the silyl cuprate reagent (2.3 mmol, based on CuCN) in THF (20 cm^3) at −78 °C under nitrogen. After 2 h, basic aqueous ammonium chloride (10 cm^3) was added to the reaction which, upon work-up as above and chromatography (SiO_2, EtOAc–hexane, 1:10) gave the inseparable diastereoisomers (1S,2R,4R)-1-(N,N-*dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl* (3R′)-3′-*dimethyl*(*phenyl*)*silyl*-3′-*phenylpropanoate* **3d** and (1S,2R,4R)-1-(N,N-*dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl* (3S′)-3′-*dimethyl*(*phenyl*)*silyl*-3′-*phenylpropanoate* **2d** (0.58 g, 77%) as needles in a ratio of 94:6 determined by integration of the Me_2C peaks in the ^1H NMR spectrum. Recrystallisation three times from hexane gave a ratio of 97.5:2.5 (0.5 g, 67%), m.p. 129–130 °C; R_F(EtOAc–hexane, 1:5) 0.6; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1725 (C=O), 1250 (SiMe) and 1110 (SiPh); $\delta(CDCl_3$, 250 MHz) for **3d**: 7.4–6.8 (10 H, m, 2Ph), 4.79 (1 H, dd, *J* 3.4 and 7.8, OCH), 3.35–3.10 (2 H, m, 2NCH), 3.15 (1 H, d, *J* 13.35, SCH_AH_B), 2.9–2.6 (3 H, m, $SiCHCH_2CO$), 2.59 (1 H, d, *J* 13.35, SCH_AH_B), 2.0–0.9 (27 H, m, aliphatic Hs), 0.82 (6 H, s, Me_2C) and 0.21 (6 H, s, $SiMe_2$); for **2d**: 7.4–6.8 (10 H, m, 2Ph), 4.76 (1 H, dd, *J* 3.4 and 7.8, OCH), 3.35–3.10 (2 H, m, 2NCH), 3.15 (1 H, d, *J* 13.35, SCH_AH_B), 2.90–2.50 (4 H, m, $SiCHCH_2CO$ and SCH_AH_B), 2.0–0.9 (27 H, m, aliphtic Hs), 0.78 (3 H, s, MeC), 0.70 (3 H, s, MeC), 0.25 (3 H, s, $SiMe_AMe_B$) and 0.19 (3 H, s, $SiMe_AMe_B$); *m/z* 663 (< 1%, M^+), 528 (10, M − Me_2PhSi), 418 [5, M − $SO_2N(C_6H_{11})_2$], 380 (5, M − $Me_2PhSiPhCHCH_2CO_2$) and 135 (100, $PhMe_2Si$) (Found: C, 70.7; H, 8.7; N, 2.1%; M^+, 663.3783. $C_{39}H_{57}NO_4SSi$ requires C, 70.6; H, 8.6; N, 2.1%; *M*, 663.3777). These assignments were aided by the preparation of a 50:50 mixture of the diastereoisomers **2d** and **3d**. Oxalyl chloride (0.09 g, 0.7 mmol) was added to a stirred solution of the β-silyl acid (±)-**4** (0.1 g, 0.35 mmol) in dry dichloromethane (2 cm^3) at room temperature under nitrogen. After 2 h, the solvent and excess of oxalyl chloride were evaporated under reduced pressure to give the crude acid chloride. Dry benzene (3 cm^3), silver cyanide (0.04 g, 0.3 mmol) and the alcohol **d**-H (0.08 g, 0.2 mmol) were added to the mixture which was then refluxed under nitrogen for 16 h. The solution was cooled, diluted with ether (10 cm^3), filtered through Celite and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:10) of the residue gave a 50:50 mixture of the esters (0.0663 g, 50%, based on the alcohol), together with unchanged alcohol **d**-H (0.02 g, 25%), which was inseparable but did not interfere with the assignment of peaks in the NMR spectrum.

Table 2, *Entry* 4.—The ester **8** (0.2 g, 0.43 mmol) in dry THF (3 cm^3) was added dropwise over 10 min to a stirred solution of the dimethyl(phenyl)silyl-cuprate reagent (0.85 mmol, based on CuCN) in THF (8 cm^3) at −78 °C under nitrogen. After 2 h, basic ammonium chloride solution (5 cm^3) was added to the reaction mixture which, upon work-up as above and chromatography (SiO_2, EtOAc–hexane, 1:10), gave the inseparable diastereoisomers (1S,2R,4R)-1-(N,N-*dicyclohexylamino-sulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*hept*-2-*yl* (*3′S*)-*dimethyl*(*phenyl*)*silylbutanoate* **12** and (1S,2R,4R)-1-(N,N-*dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl* (3′R)-3′-*dimethyl*(*phenyl*)*silylbutanoate* **10** (0.19 g, 74%) as prisms (not recrystallised to avoid concentration of one diastereoisomer) in a ratio of 55:45 determined by integration of the methyl doublets at δ 1.0 and 0.95, respectively, in the ^1H NMR spectrum); R_F(EtOAc–hexane, 1:3) 0.6; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1750 (C=O), 1600 (Ph), 1335 and 1150 (SO_2N), 1250 (SiMe) and 1115 (SiPh); $\delta(CDCl_3$, 250 MHz) for **12**: 7.5–7.25 (5 H, m, Ph), 4.91 (1 H, dd, *J* 3.2 and 7.7, HCOC=O), 3.25–3.15 (1 H, m, 2NCH), 3.18 (1 H, d, *J* 13.25, SCH_AH_B), 2.61 (1 H, d, *J* 13.25, SCH_AH_B), 2.32 (1 H, dd, *J* 3.75 and 15.4, $CH_AH_BCO_2$), 1.99 (1 H, dd, *J* 11.05 and 15.4, $CH_AH_BCO_2$), 2.0–1.1 (28 H, m, aliphatic Hs), 1.0 (3 H, d, *J* 7.25, *Me*CH), 0.95 (3 H, s, MeC), 0.86 (3 H, s, MeC) and 0.26 (6 H, s, $SiMe_2$); for **10**: 7.5–7.25 (5 H, m, Ph), 4.91 (1 H, d, *J* 3.2 and 7.7, HCOC=O), 3.25–3.15 (2 H, m, 2NCH), 3.21 (1 H, d, *J* 13.25, SCH_AH_B), 2.63 (1 H, d, *J* 13.25, SCH_AH_B), 2.37 (1 H, dd, *J* 3.15 and 14.6, $CH_AH_BCO_2$), 1.93 (1 H, dd, *J* 12.05 and 14.6, $CH_AH_BCO_2$), 2.05–1.0 (28 N, m, aliphatic Hs), 0.96 (3 H, s, MeC), 0.95 (3 H, d, *J* 7.2, MeCH), 0.86 (3 H, s, MeC) and 0.26 (6 H, s, $SiMe_2$); *m/z* 601 (< 1%, M^+), 180 [10, $N(C_6H_{11})_2$] and 135 (100, $PhMe_2Si$) (Found: C, 67.9; H, 9.25; N, 2.4%; M^+, 601.3626. $C_{34}H_{55}NO_4SSi$ requires C, 67.9; H, 9.15; N, 2.3%; *M*, 601.3621).

Table 2, *Entry* 13.—The ester **9** (0.49 g, 1 mmol) in dry THF (5 cm^3) was added dropwise (over 10 min) to a stirred solution of the dimethyl(phenyl)silyl-cuprate reagent (2 mmol, based on CuCN) in THF (15 cm^3) at −98 °C under nitrogen. After 2 h, basic aqueous ammonium chloride (10 cm^3) was added to the

mixture which, upon work-up as above and chromatography (SiO_2, EtOAc–hexane, 1:12), gave the inseparable diastereoisomers (1S,2R,4R)-1-(N,N-*dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl* (3R')-3'-*dimethyl*(*phenyl*)-*silyl*-4'-*methylpentanoate* **13** and (1S,2R,4R)-1-(N,N-*dicyclohexylaminosulfonylmethyl*)-7,7-*dimethylbicyclo*[2.2.1]*heptan*-2-*yl*(3S')-3'-*dimethyl*(*phenyl*)*silyl*-4'-*methylpentanoate* **11** (0.465 g, 74%) as prisms (not recrystallised to avoid concentrating one diastereoisomer) in a ratio of 79:21 determined by integration of the SiMe peaks in the ^{1}H NMR spectrum; R_F(EtOAc–hexane, 1:5) 0.55; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1725 (C=O), 1320 and 1140 (SO_2N), 1250 (SiMe) and 1110 (SiPh); δ($CDCl_3$, 250 MHz) for **13**: 7.6–7.0 (5 H, m, SiPh), 4.90–4.85 (1 H, m, HCOC=O), 3.2–3.1 (2 H, m, 2NCH), 3.18 (1 H, d, *J* 13.15, SCH_AH_B), 2.62 (1 H, d, *J* 13.15, SCH_AH_B), 2.35 (1 H, dd, *J* 6.7 and 10.0, $CH_AH_BCO_2$), 2.25 (1 H, dd, *J* 6.4 and 10.0, $CH_AH_BCO_2$), 2.0–0.8 (29 H, m, aliphatic Hs), 0.95 (3 H, s, MeC), 0.92 (3 H, d, *J* 6.6, *Me*CH), 0.86 (3 H, s, MeC), 0.81 (3 H, d, *J* 6.8, MeC), 0.31 (3 H, s, $SiMe_AMe_B$) and 0.29 (3 H, s, $SiMe_AMe_B$); for **11**: 7.6–7.0 (5 H, m, SiPh), 4.90–4.85 (1 H, m, HCOC=O), 3.2 (1 H, d, *J* 13.15, SCH_AH_B), 3.2–3.1 (1 H, m, 2NCH), 2.63 (1 H, d, *J* 13.15, SCH_AH_B), 2.5–2.15 (2 H, m, CH_2CO_2), 2.0–0.8 (29 H, m, aliphatic Hs), 0.95 (3 H, s, MeC), 0.87 (3 H, d, *J* 6.6, *Me*CH), 0.86 (3 H, s, MeC), 0.81 (3 H, d, *J* 6.8, MeC*H*), 0.31 (3 H, s, $SiMe_AMe_B$) and 0.30 (3 H, s, $SiMe_AMe_B$); *m*/*z* 629 (< 1%, M^+), 380 (20, M − $PhMe_2SiPr^iCHCH_2CO_2$), 180 [10, $N(C_6H_{11})_2$] and 135 (100, $PhMe_2Si$) (Found: C, 68.6; H, 9.5; N, 2.2%; M^+, 629.3938. $C_{36}H_{59}NO_4SSi$ requires C, 68.7; H, 9.4; N, 2.2%; *M*, 629.3934).

Table 2, *Entry* 19.—The ester **20** (0.13 g, 0.22 mmol) in dry THF (0.5 cm^3) was added dropwise (over 5 min) to a stirred solution of phenylmagnesium bromide (1.5 mol dm^{-3} solution in ether; 1.33 cm^3, 2 mmol) and copper cyanide (0.09 g, 1 mmol) in ether (0.8 cm^3) at −78 °C under nitrogen. After 3 h, saturated aqueous ammonium chloride (2 cm^3) was added to the mixture which, upon work-up as above, gave the inseparable diastereoisomers **3d** and **2d** (0.1 g, 71%), identical (NMR, IR, and mass spectrum) with the compounds above, in a ratio of 87:13.

Table 3, *Entry* 3.—Dimethyl(phenyl)silyllithium (1.1 mol dm^{-3} solution in THF; 3.6 cm^3, 4 mmol) was added to a stirred solution of anhydrous magnesium bromide (0.74 g, 4 mmol) in dry THF (10 cm^3) at 0 °C under nitrogen. After 20 min, this mixture was added by syringe to a stirred solution of freshly recrystallised[26] copper(I) bromide–dimethyl sulfide complex (0.41 g, 2.0 mmol) in dry THF (3 cm^3) at −50 °C under nitrogen. After 30 min the solution was cooled to −78 °C (temperature inside reaction vessel) and a pre-mixed solution of the imide **1e** (0.45 g, 0.92 mmol) and anhydrous magnesium bromide (0.25 g, 1.35 mmol) in THF (2 cm^3) added dropwise to it over 10 min by syringe such that the solution trickled down the sides of the reaction vessel. After 1 h, saturated aqueous ammonium chloride was added to the mixture which was then allowed to warm to room temperature and extracted with ether (4 × 10 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and chromatography (SiO_2, EtOAc–hexane, 1:6) of the residue gave the inseparable diastereoisomers (5S)-1-[(3'R)-3'-*dimethyl*(*phenyl*)*silyl*-3'-*phenylpropanoyl*]-5-*triphenylmethoxymethyl*-*pyrrolidin*-2-*one* **3e** and (5S)-1-[(3'S)-3-*dimethyl*(*phenyl*)*silyl*-3'-*phenylpropanoyl*]-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **2e** (0.48 g, 84%) in a ratio of 89:11 determined by integration of the SiMe peaks and the $CH_AH_BOCPh_3$ peaks in the ^{1}H NMR spectrum; R_F(EtOAc–hexane, 1:3) 0.5; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1730 (C=O), 1685 (C=O), 1600 (Ph) and 1110 (SiPh); δ($CDCl_3$, 250 MHz) for **3e**: 7.8–7.0 (25 H, m, 5Ph), 4.3–4.2 (1 H, m, CHN), 3.80 (1 H, dd, *J* 11.9 and 17.3, $CHCH_AH_BCO$), 3.40 (1 H, dd, *J* 3.9 and 9.8, $CH_AH_BOCPh_3$), 3.10–2.80 (4 H, m, $CHCH_AH_BCO$, $CH_AH_BOCPh_3$ and $CH_2CH_AH_BCO$), 2.5–2.3 (1 H, m, $CH_2CH_AH_BCO$), 2.0–1.8 (2 H, m, $CH_2CH_AH_BCO$), 0.35 (3 H, s, $SiMe_AMe_B$) and 0.24 (3 H, s, $SiMe_AMe_B$); for **2e**: 7.6–6.8 (25 H, m, 5Ph), 4.2–4.1 (1 H, m, CHN), 3.54 (1 H, dd, *J* 10.0 and 17.4, $SiCHCH_AH_BCO$), 3.37 (1 H, dd, *J* 4.0 and 9.8, $CH_AH_BOCPh_3$), 3.33 (1 H, dd, *J* 5.1 and 17.4, $SiCHCH_AH_BCO$), 3.03 (1 H, dd, *J* 5.1 and 10.0, $SiCHCH_AH_BCO$), 2.96 (1 H, dd, *J* 2.4 and 9.8, $CH_AH_BOCPh_3$), 2.83 (1 H, dd, *J* 10.95 and 17.9, $CH_2CH_AH_BCO$), 2.40 (1 H, ddd, *J* 1.3, 9.5 and 17.9, $CH_2CH_AH_BCO$), 2.0–1.6 (2 H, m, $CH_2CH_AH_BCO$), 0.28 (3 H, s, $SiMe_AMe_B$) and 0.26 (3 H, s, $SiMe_AMe_B$); *m*/*z* 623 (12%, M^+), 546 (10, M − Ph) 545 (10, M − Ph − H), 380 (20, M − CPh_3) and 243 (100, CPh_3) (Found: M^+, 623.2859. $C_{41}H_{41}NO_3Si$ requires *M*, 623.2856).

Table 3, *Entry* 4.—Dimethyl(phenyl)silyllithium (1.35 mol dm^{-3} solution in THF; 3.6 cm^3, 49 mmol) was added to a stirred solution of anhydrous magnesium bromide (10.3 g, 56 mmol) in dry THF (200 cm^3) at 0 °C under nitrogen. After 20 min this solution was added to freshly recrystallised copper(I) bromide–dimethyl sulfide complex (5.0 g, 24.5 mmol) in dry THF (100 cm^3) at −50 °C under nitrogen. After 30 min the solution was cooled to −78 °C (temperature inside reaction vessel) and a pre-mixed solution of the imide **21** (5.0 g, 11.7 mmol) and anhydrous magnesium bromide (2.76 g, 15 mmol) in dry THF (35 cm^3) was added dropwise to it over 50 min, such that the solution trickled down the side of the reaction vessel. After 2 h the solution was allowed to warm to room temperature, at which point saturated aqueous ammonium chloride (50 cm^3) was added to it and the whole extracted with ether (4 × 100 cm^3). The combined extracts were dried ($MgSO_4$), filtered through Celite and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:7) of the residue gave the inseparable diastereoisomers (5S)-1-[(3'S)-3-*dimethyl*(*phenyl*)*silylbutanoyl*]-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **23** and (5S)-1-[(3'R)-3-*dimethyl*(*phenyl*)*silylbutanoyl*]-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **22** (5.4 g, 82%) in a ratio of 89:11 determined by integration of the methyl doublet peaks in the ^{1}H NMR spectrum; R_F(EtOAc–hexane, 1:3) 0.5; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1730 (C=O), 1680 (C=O), 1600 (Ph) and 1110 (SiPh); δ($CDCl_3$, 250 MHz) for **23**: 7.7–7.3 (20 H, m, 4Ph), 4.45 (1 H, m, CHN), 3.51 (1 H, dd, *J* 3.8 and 9.75, $CH_AH_BOCPh_3$), 3.17 (1 H, dd, *J* 2.6 and 9.75, $CH_AH_BOCPh_3$), 2.97 (1 H, dd, *J* 3.35 and 16.2, $MeCHCH_AH_BCO$), 2.92 (1 H, dd, *J* 8.9 and 17.8, $CH_2CH_AH_BCO$), 2.77 (1 H, dd, *J* 11.3 and 16.2, $MeCHCH_AH_BCO$), 2.43 (1 H, ddd, *J* 2.0, 9.3 and 17.8, $CH_2CH_AH_BCO$), 2.1–1.9 (2 H, m, $CH_2CH_AH_BCO$), 1.6–1.4 (1 H, m, $MeCHCH_AH_BCO$), 0.935 (3 H, d, *J* 7.35, *Me*$CHCH_AH_BCO$), 0.37 (3 H, s, $SiMe_AMe_B$) and 0.36 (3 H, s, $SiMe_AMe_B$); for **22**: 7.6–7.2 (20 H, m, 4Ph), 4.45–4.35 (1 H, m, CHN), 3.58 (1 H, dd, *J* 3.75 and 9.7, $CH_AH_BOCPh_3$), 3.15 (1 H, dd, *J* 2.65 and 9.7, $CH_AH_BOCPh_3$), 3.14 (1 H, dd, *J* 3.75 and 16.7, $MeCHCH_AH_BCO$), 3.0–2.8 (1 H, m, $CH_2CH_AH_BCO$), 2.72 (1 H, dd, *J* 10.65 and 16.7, $MeCHCH_AH_BCO$), 2.45 (1 H, ddd, *J* 2.1, 9.3 and 17.7, $CH_2CH_AH_BCO$), 2.2–1.8 (2 H, m, $CH_2CH_AH_BCO$), 1.6–1.4 (1 H, m, $MeCHCH_AH_BCO$), 1.02 (3 H, d, *J* 7.3, *Me*$CHCH_AH_BCO$) and 0.36 (6 H, s, $SiMe_2$); *m*/*z* (1.1%, M^+), 546 (10, M − Me), 318 (20, M − Ph_3C) and 243 (100, Ph_3C) (Found: M^+, 561.2678. $C_{36}H_{39}NO_3Si$ requires *M*, 561.2699).

Table 3, *Entry* 9.—Phenylmagnesium bromide (1.5 mol dm^{-3} solution in ether; 0.5 cm^3, 0.72 mmol) was added to a stirred solution of freshly recrystallised copper(I) bromide–dimethyl sulfide complex (0.075 g, 0.36 mmol) in dry THF (2 cm^3) and dry dimethyl sulfide (1 cm^3) at −55 °C under nitrogen. After 30 min a solution of the imide **24** (0.09 g, 0.165 mmol) in THF (0.8

cm^3) was added dropwise to the mixture over 5 min and followed, after 2 h, by basic aqueous ammonium chloride (2 cm^3). The solution was allowed to warm to room temperature and then extracted with ether (4 × 10 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the residue, purified by preparative TLC (SiO_2, EtOAc–hexane, 1 : 3) to give the inseparable diastereoisomers **3e** and **2e** (0.1 g, 96%), identical (NMR, IR) with the compounds above, in a ratio of 4 : 96.

Table 3, *Entry* 14.—Methylmagnesium bromide (3 mol dm^{-3} solution in ether; 27.7 cm^3, 83 mmol) was added to a stirred solution of freshly recrystallised copper(I) bromide–dimethyl sulfide complex (8.5 g, 41.5 mmol) in dry THF (165 cm^3) and dry dimethyl sulfide (82.5 cm^3) at −40 °C under nitrogen. After 30 min the solution was cooled to −78 °C and a pre-mixed solution of the imide **24** (Me_3Si in place of $PhMe_2Si$) (8.3 g, 17.2 mmol) and anhydrous magnesium bromide (5.2 g, 28 mmol) in dry THF (30 cm^3) added dropwise to it over 30 min. After 1 h the solution was allowed to warm to −10 °C over 3 h. Saturated aqueous ammonium chloride (30 cm^3) was added to the mixture which was then extracted with ether (4 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1 : 7) of the residue gave the inseparable diastereoisomers (5S)-1-[(3'R)-3'-*trimethylsilylbutanoyl*]-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **22** (Me_2Si in place of $PhMe_2Si$) and (5S)-1-[(3'S)-3'-*trimethylsilylbutanoyl*]-5-*triphenylmethoxymethylpyrrolidin*-2-*one* **23** (Me_3Si in place of $PhMe_2Si$) (7.74 g, 90%) in a ratio of 82 : 18 determined by integration of the Me doublets in the ^1H NMR spectrum; R_F(EtOAc–hexane, 1 : 4) 0.6; ν_{max}(CH_2Cl_2)/cm^{-1} 1730 (C=O), 1680 (C=O), 1600 and 1490 (Ph); δ($CDCl_3$, 250 MHz) for **23** (Me_3Si in place of $PhMe_2Si$): 7.4–7.2 (15 H, m, 3Ph), 4.5–4.4 (1 H, m, CHN), 3.57 (1 H, dd, *J* 3.8 and 9.7, $CH_AH_BOCPh_3$), 3.14 (1 H, dd, *J* 2.65 and 9.7, $CH_AH_BOCPh_3$), 3.08 (1 H, dd, *J* 3.55 and 16.35, $SiCHCH_AH_BCO$), 2.93 (1 H, ddd, *J* 1.25, 9.9 and 17.8, $CH_2CH_AH_BCO$), 2.63 (1 H, dd, *J* 10.9 and 16.35, $SiCHCH_AH_BCO$), 2.46 (1 H, ddd, *J* 1.7, 9.4 and 17.8, $CH_2CH_AH_BCO$), 2.3–1.85 (2 H, m, $CH_2CH_AH_BCO$), 1.26–1.17 (1 H, m, $SiCHCH_AH_BCO$), 0.94 (3 H, d, *J* 7.3, *Me*CH) and 0.01 (9 H, s, $SiMe_3$); for **22** (Me_3Si in place of $PhMe_2Si$): 7.4–7.19 (15 H, m, 3Ph), 4.5–4.4 (1 H, m, CHN), 3.50 (1 H, dd, *J* 4.05 and 9.7, $CH_AH_BOCPh_3$), 3.17 (1 H, dd, *J* 2.8 and 9.7, $CH_AH_BOCPh_3$), 3.04–2.96 (1 H, m, $SiCHCH_AH_BCO$), 2.93 (1 H, ddd, *J* 1.25, 9.9 and 17.8, $CH_2CH_AH_BCO$), 2.61 (1 H, dd, *J* 11.3 and 15.8, $SiCHCH_AH_BCO$), 2.46 (1 H, ddd, *J* 1.7, 9.4 and 17.8, $CH_2CH_AH_BCO$), 2.3–1.85 (2 H, m, $CH_2CH_AH_BCO$), 1.26–1.17 (1 H, m, $SiCHCH_AH_BCO$), 0.89 (3 H, d, *J* 7.3, *Me*CH) and 0.02 (9 H, s, $SiMe_3$); *m*/*z* 499 (0.37%, M^+), 484 (20, M − Me), 256 (15, M − Ph_3C), 244 (20, $Me_3SiCHMeCH_2CO$), 243 (100, Ph_3C), 186 (30) and 165 (50) (Found: M^+, 499.2578. $C_{31}H_{37}NO_3Si$ requires *M*, 499.2543).

Proofs of Relative Configuration

(3RS)-3-*Dimethyl*(*phenyl*)*silyl*-3-*phenylpropanoic Acid* (±)-**4**.—Benzyl (3*RS*)-3-dimethyl(phenyl)silyl-3-phenylpropanoate[3] (10 g, 26.7 mmol) was hydrogenated over 10% palladium on charcoal (0.8 g) in methanol (290 cm^3) at room temperature for 5 h. The solution was filtered through Celite and the methanol evaporated under reduced pressure. The mixture in ether (50 cm^3) was extracted with potassium hydroxide (1 mol dm^{-3} solution; 4 × 30 cm^3). The combined aqueous extracts were acidified to pH 1 (using 1 mol dm^{-3} HCl) and extracted with ether (5 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, Et_2O) of the residue gave the *acid* (6.8 g, 89%) as needles, m.p. 113–114 °C (from hexane); R_F(EtOAc–hexane, 1 : 1) 0.6; ν_{max}(CH_2Cl_2)/cm^{-1} 3600–2400 (OH), 1710 (C=O), 1600 (Ph), 1250 (SiMe) and 1110 (SiPh); δ(CCl_4, 90 MHz) 7.4–6.7 (10 H, m, 2Ph), 3.1–2.6 (3 H, m, $PhCHCH_2CO$), 0.35 (3 H, s, $SiMe_AMe_B$) and 0.3 (3 H, s, $SiMe_AMe_B$); *m*/*z* 269 (20%, M − Me), 207 (20, M − Ph), 206 (55, M − Ph − H), 137 (50, PhMeSiOH), 135 (100, $PhMe_2Si$) and 77 (20, Ph) (Found: C, 71.5; H, 7.1%; M^+ − Me 269.0998. $C_{17}H_{20}O_2Si$ requires C, 71.8; H, 7.05%; M^+ − Me, 269.0998).

[(1'R)-1'-*Phenylethyl*]*ammonium* (3R)-3-*Dimethyl*(*phenyl*)*silyl*-3-*phenylpropanoate*.—(1*R*)-Phenylethylamine (2.9 g, 24 mmol) in ether (20 cm^3) was added dropwise to a stirred solution of the β-silyl acid (6.4 g, 22.5 mmol) in ether (15 cm^3). After 1 h, the white precipitate was collected. Recrystallisation until constant optical rotation gave the *ammonium salt* (0.7 g, 7.5%) as needles, m.p. 159–163 °C (19 × from EtOH–H_2O, 1 : 20); $[\alpha]_D$ +34.0 (*c* 1.2, $CHCl_3$); ν_{max}(CH_2Cl_2)/cm^{-1} 3500–2300 (NH_3), 1700 (C=O) and 1110 (SiPh); δ($CDCl_3$, 90 MHz) 7.3–6.5 (15 H, m, 3Ph), 2.75–2.2 (4 H, m, $PhCHCH_2CO_2$ and NH_3CH), 1.2 (3 H, d, *J* 7, Me), 0.22 (3 H, s, $SiMe_AMe_B$) and 0.19 (3 H, s, $SiMe_AMe_B$) (Found: C, 73.8; H, 7.65; N, 3.4. $C_{25}H_{31}NO_2Si$ requires C, 74.0; H, 7.65; N, 3.45%).

(3R)-3-*Dimethyl*(*phenyl*)*silyl*-3-*phenylpropanoic Acid* (+)-**4**.—The ammonium salt (0.7 g, 1.7 mmol) in ether (15 cm^3) was washed with hydrochloric acid (1 mol dm^{-3} solution; 6 × 5 cm^3). The ethereal solution was dried ($MgSO_4$), passed through a short column (SiO_2, Et_2O) and evaporated under reduced pressure to give the β-silyl carboxylic acid (0.45 g, 94%) as prisms, m.p. 86–87 °C (from hexane–CH_2Cl_2); $[\alpha]_D$ +12.0 (*c* 0.5, $CHCl_3$) identical (NMR, IR) with the racemic acid.

(3R)-3-*Hydroxy*-3-*phenylpropanoic Acid* **5**.—Tetrafluoroboric acid–diethyl ether complex (0.1 cm^3, 0.76 mmol) and the acid (0.11 g, 0.38 mmol) were kept in dichloromethane (3 cm^3) at room temperature for 3 h. Water (5 cm^3) was added to the solution which was then extracted with dichloromethane (3 × 15 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude *silyl fluoride* (0.08 g), which was used without further purification; δ(CCl_4, 60 MHz) 7.4–7.15 (5 H, m, Ph), 3.2–2.7 (3 H, m, $PhCHCH_2CO$), 0.35 (3 H, d, *J* 4, $SiMe_AMe_B$) and 0.25 (3 H, d, *J* 4, $SiMe_AMe_B$). Peracetic acid (36% solution in acetic acid; 0.5 cm^3, ≈1.4 mmol) was added to a stirred solution of the silyl fluoride (0.08 g, 0.36 mmol) and triethylamine (0.1 cm^3, 0.4 mmol) in dry ether (3 cm^3) at room temperature. After 16 h, saturated aqueous sodium carbonate (15 cm^3) was added to the mixture which was then washed with ether (2 × 4 cm^3), acidified to pH 1 (using 1 mol dm^{-3} HCl) and extracted with dichloromethane (3 × 15 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the β-hydroxy acid (0.04 g, 67%) as needles, m.p. 114–115 °C (from cyclohexane–Et_2O) (lit.,[27] 115–116 °C); $[\alpha]_D$ +17.9 (*c* 2.39, EtOH) [lit.,[28] +18.6 (EtOH)]; ν_{max}(CH_2Cl_2)/cm^{-1} 3600 (OH), 3200–2400 (OH of CO_2H) and 1710 (C=O); δ($CDCl_3$, 60 MHz) 7.3–7.1 (5 H, m, Ph), 5.05 (1 H, t, *J* 6, PhC*H*) and 2.75 (2 H, d, *J* 6, CH_2CO).

Preparation of the Amide **3a** *from the Carboxylic Acid* (+)-**4**.—Oxalyl chloride (0.05 cm^3, 0.57 mmol) was added to a stirred solution of the acid (0.08 g, 0.28 mmol) in dry dichloromethane (2 cm^3) at room temperature under nitrogen. After 1.5 h, the solvent and excess of dichloromethane were evaporated under reduced pressure to leave the acid chloride which was then diluted with dry ether (2 cm^3). This solution was then added to a stirred solution of (−)-ephedrine (0.067 g, 0.4 mmol) and dry triethylamine (0.04 g, 0.4 mmol) in ether (2 cm^3). After 1 h, the solution was diluted with ether (10 cm^3) and

filtered through Celite, to remove precipitated triethylamine hydrochloride. The ethereal solution was washed with aqueous sodium hydroxide (1 mol dm^{-3} solution; 2 × 5 cm^3), and aqueous hydrochloric acid (1 mol dm^{-3} solution; 2 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1 : 2) of the residue gave the *amide* (0.10 g, 79%); $[\alpha]_D$ −27.0 (*c* 1.0, CH_2Cl_2), identical (NMR, IR and mass spectrum) with the sample described above.

Oxidation of the Aldehyde **7**.—Pyridinium dichromate[29] (1.15 g, 3 mmol) in dry dimethylformamide (DMF) (2 cm^3) was added to a stirred solution of the aldehyde (0.27 g, 1 mmol) in dry DMF (2 cm^3) at room temperature under nitrogen. After 22 h, water (20 cm^3) was added to the mixture which was then extracted with ether (4 × 30 cm^3). The combined extracts were evaporated under reduced pressure to a smaller volume (20 cm^3), washed with water (2 × 10 cm^3), dried ($MgSO_4$) and passed through a short column (SiO_2, Et_2O). The ethereal solution was evaporated under reduced pressure to give (3S)-3-*dimethyl(phenyl)silyl*-3-*phenylpropanoic acid* (−)-**4** (0.2 g, 70%) as prisms. This acid was used without purification to determine the enantiomeric excess as 60% by attaching it to (−)-ephedrine (89%) as described above.

(3R)-3-*Dimethyl(phenyl)silyl*-3-*phenylpropan*-1-*ol* **14**.—The mixture of esters **2b** and **3b** (Table 2, Entry 1) (0.56 g, 1.13 mmol) in dry ether (2 cm^3) was added dropwise (over 5 min) to a stirred solution of lithium aluminium hydride (0.054 g, 1.42 mmol) in dry ether (2 cm^3) at room temperature. After 2 h, saturated aqueous ammonium chloride (3 cm^3) was added dropwise to the mixture which was then extracted with ether (4 × 10 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1 : 5) gave the chiral auxiliary **b**-H (0.237 g, 90%) and the alcohol[30] (0.27 g, 88%); R_F(EtOAc–hexane, 1 : 5) 0.2; ν_{max}(film)/cm^{-1} 3320 (OH), 1600, 1580 and 1500 (Ph), 1255 (SiMe) and 1120 (SiPh); δ(CCl_4, 60 MHz) 7.6–6.95 (10 H, m, 2Ph), 3.65–3.25 (2 H, m, CH_2OH), 2.50 (1 H, t, *J* 8, PhC*H*), 2.15–1.85 (2 H, m, PhCCH_2) 1.90 (1 H, s, OH), 0.35 (3 H, s, Si$Me_A$$Me_B$) and 0.30 (3 H, s, Si$Me_A$$Me_B$); *m*/*z* 270 (0.06%, M^+), 137 (100, PhMeSiOH) and 135 (63, $PhMe_2Si$) (Found: M^+, 270.1450. $C_{17}H_{22}OSi$ requires *M*, 270.1440). The same alcohol (93%) was prepared from the mixture of esters **2d** and **3d** (Table 2, Entry 3) by the same method; $[\alpha]_D$ −2.0 (*c* 1.1, $CHCl_3$) for a mixture that proved to have an 88% e.e.

Preparation of the Amides **2a** *and* **3a** *from the Alcohol* **14**.—The alcohol derived from **2b** and **3b** (0.25 g, 0.93 mmol) in dry dimethylformamide (DMF) (1.5 cm^3) was stirred with pyridinium dichromate (1.35 g, 3.5 mmol) in DMF (1.5 cm^3) over activated 3 Å molecular sieves (0.3 g) at room temperature under nitrogen for 24 h. Work-up as described above for the acid (−)-**4** gave the mixture of acids rich in the acid (+)-**4** (0.15 g, 57%). This acid without any further purification was converted into the amides **2a** and **3a** (0.1 g, 79%, **2a**:**3a** 40:60), as described above for the preparation of the amide **3a**. A similar sequence from the alcohol derived from **2d** and **3d** gave the same amides in the same yield in a ratio of 7:93.

Preparation of a 50 : 50 *Mixture of the Amides* **2a** *and* **3a**.—As a check that there was no chiral recognition between ephedrine and the acid chloride, we treated the racemic β-silyl acid (0.1 g, 0.35 mmol) by the same procedure and obtained the amides (0.12 g, 80%) in a ratio of 50 : 50.

Assignment of Absolute Configuration to the Esters **2c** *and* **3c**.—Oxalyl chloride (0.09 g, 0.7 mmol) was added dropwise to a stirred solution of a sample of partially resolved (3*R*)-3-dimethyl(phenyl)silyl-3-phenylpropanoic acid (50% e.e.; 0.1 g, 0.35 mmol) in dry dichloromethane (2 cm^3) at room temperature under nitrogen. After 3 h, the solvent and excess oxalyl chloride were evaporated under reduced pressure. Dry benzene (2 cm^3), silver cyanide (0.066 g, 0.49 mmol) and the alcohol (**c**-H) (0.084 g, 0.36 mmol) were added to the residue and the mixture refluxed for 16 h. The solution was cooled, diluted with ether (10 cm^3), filtered through Celite and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1 : 5) of the residue gave the esters **2c** and **3c** (0.15 g, 85%) in a ratio of 25 : 75.

Lithium Aluminium Hydride Reduction of the Esters **11** *and* **13**.—The mixture of esters (Table 2, Entry 5) (1.45 g, 2.3 mmol) in dry ether (7 cm^3) was added dropwise to a stirred solution of lithium aluminium hydride (0.13 g, 3.42 mmol) in dry ether (5 cm^3) at room temperature. After 3 h, work-up and chromatography (SiO_2, EtOAc–hexane, 1 : 8) gave the chiral auxiliary **d**-H (0.75 g, 83%) and a mixture of enantiomers rich in (3R)-3-*dimethyl(phenyl)silyl*-4-*methylpentan*-1-*ol* **17** (0.425 g, 78%), $[\alpha]_D$ −3.1 (*c* 1.1, $CHCl_3$); R_F(EtOAc–hexane, 1 : 5) 0.2; ν_{max}(film)/cm^{-1} 3600–3000 (OH), 1250 (SiMe) and 1110 (SiPh); δ($CDCl_3$, 80 MHz) 7.6–7.2 (5 H, m, Ph), 3.49 (2 H, t, *J* 8.25, CH_2OH), 2.2–1.8 (1 H, m, Me_2CH), 1.8–1.4 (1 H, m, SiCH), 1.65 (2 H, q, *J* 8.25, CH_2CH_2OH), 1.2 (1 H, br s, OH), 0.94 (3 H, d, *J* 7.1, *Me*CH), 0.86 (3 H, d, *J* 7.5, *Me*CH), 0.33 (3 H, s, Si$Me_A$$Me_B$) and 0.32 (3 H, s, Si$Me_A$$Me_B$); *m*/*z* 221 (3.6%, M^+ − Me), 152 (6), 137 (100, PhMeSiOH) and 135 (80, $PhMe_2Si$) (Found: M^+ − Me, 221.1349. $C_{14}H_{24}OSi$ − Me requires M − Me, 221.1362).

(3R)-3-*Dimethyl(phenyl)silyl*-4-*methylpentanal*.—The alcohol (0.28 g, 1.19 mmol) in dry dichloromethane (1 cm^3) was added to a stirred solution of pyridinium dichromate (PDC) (0.59 g, 1.57 mmol) in dry dichloromethane (2.5 cm^3) at room temperature under nitrogen. After 24 h, the mixture was diluted with ether (10 cm^3), filtered through Celite and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1 : 8) of the residue gave the aldehyde (0.16 g, 57%); R_F(EtOAc–hexane, 1 : 5) 0.75; ν_{max}(film)/cm^{-1} 2700 (CHO), 1720 (C=O), 1250 (SiMe) and 1110 (SiPh); δ(CCl_4, 90 MHz) 9.6 (1 H, m, CHO), 7.6–7.2 (5 H, m, Ph), 2.5–2.2 (2 H, m, CH_2CHO), 2.1–1.8 (1 H, m, Me_2CH), 1.7–1.4 (1 H, m, SiCH), 0.90 (3 H, d, *J* 6, Me), 0.85 (3 H, d, *J* 6, Me) and 0.3 (6 H, s, $SiMe_2$).

(3R)-3-*Dimethyl(phenyl)silyl*-4-*methylpentanoic Acid* **18**.—Chromium trioxide (0.08 g, 0.8 mmol) and sulfuric acid (98%; 0.12 g, 1.2 mmol) in water (0.3 cm^3) were stirred with the aldehyde (0.16 g, 0.68 mmol) in acetone (0.3 cm^3) at 0 °C for 12 h. After this, water (4 cm^3) was added to the mixture which was then extracted with ether (3 × 5 cm^3). The combined extracts were dried ($MgSO_4$), filtered through Celite and extracted with aqueous sodium hydroxide (1 mol dm^{-3} solution; 3 × 4 cm^3). The combined alkaline extracts were acidified to pH1 (HCl, 1 mol dm^{-3}) and extracted with ether (4 × 8 cm^3). The combined organic extracts were dried ($MgSO_4$), evaporated under reduced pressure and passed through a short column (SiO_2, Et_2O) giving the β-*silyl acid* (0.09 g, 53%); $[\alpha]_D$ −7.35 (*c* 2.23, $CHCl_3$); R_F(EtOAc–hexane, 1 : 1) 0.7; ν_{max}(film)/cm^{-1} 3600–2400 (OH), 1700 (C=O), 1250 (SiMe) and 1110 (SiPh); δ(CCl_4, 90 MHz) 7.5–6.9 (5 H, m, SiPh), 2.15 (2 H, d, *J* 6, CH_2CO_2H), 2.0–1.6 (1 H, m, Me_2CH), 1.5–1.2 (1 H, m, SiCH), 0.85 (3 H, d, *J* 6, Me), 0.75 (3 H, d, *J* 6, Me) and 0.25 (6 H, s, $SiMe_2$); *m*/*z* 235 (3.5%, M − Me), 137 (40, PhMeSiOH), 135 (80, $PhMe_2Si$), 130

(40) and 129 (100) (Found: M^+ − Me, 235.1154. $C_{14}H_{22}O_2Si$ − Me requires M − Me, 235.1154).

(3R)-3-*Hydroxy*-4-*methylpentanoic Acid* **19**.—The β-silyl acid **18** (0.05 g, 0.21 mmol) in peracetic acid (36% solution in acetic acid; 0.5 cm^3) was added to a stirred solution of mercury(II) acetate (0.013 g, 0.04 mmol, 0.2 equiv.) and palladium(II) acetate (0.0045 g, 0.02 mmol, 0.1 equiv.) in peracetic acid (36% solution in acetic acid; 2 cm^3) at room temperature. After 2 h, the peracetic acid and acetic acid were evaporated off under reduced pressure and the residue was redissolved in ether (5 cm^3). The ethereal solution was washed with brine (2 × 2 cm^3) and extracted with aqueous potassium hydroxide (1 mol dm^{-1} solution; 3 × 4 cm^3). The combined alkaline extracts were acidified to pH 1 (HCl, 1 mol dm^{-3}) and extracted with ether (4 × 10 cm^3). The combined ethereal extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Preparative TLC (SiO_2, Et_2O) gave the β-hydroxy acid (0.015 g, 56%); $[\alpha]_D$ +26.05 (*c* 1.26, $CHCl_3$) [lit.,[31] −42.1 for (3*S*)-enantiomer], this optical rotation corresponds to a 62% e.e. in favour of the (3*R*)-enantiomer; R_F(Et_2O) 0.5; ν_{max}(film)/cm^{-1} 3600–2400 (OH) and 1715 (C=O); δ($CDCl_3$, 250 MHz) 4.4–3.8 (2 H, br s, 2OH, signal disappears after D_2O shake), 3.8 (1 H, m, C*H*OH), 2.55 (1 H, dd, *J* 3.2 and 16.4, $CH_AH_BCO_2H$), 2.45 (1 H, dd, *J* 9.16 and 16.4, $CH_AH_BCO_2H$), 1.7 (1 H, m, Me_2CH), 0.95 (3 H, d, *J* 6.3, Me) and 0.92 (3 H, d, *J* 6.5, Me).

(3RS)-3-*Dimethyl(phenyl)silylbutanoic Acid* (±)-**15**.—Benzyl (3RS)-3-dimethyl(phenyl)silylbutanoate[3] (6.55 g, 21 mmol) in methanol (200 cm^3) was hydrogenated over 10% palladium on charcoal (0.5 g) for 5 h. The solution was filtered through Celite and evaporated under reduced pressure and the residue was dissolved in ether (50 cm^3). This solution was extracted with aqueous potassium hydroxide (1 mol dm^{-3} solution; 4 × 30 cm^3). The combined alkaline extracts were acidified to pH1 (HCl, 1 mol dm^{-3}) and extracted with ether (5 × 50 cm^3). The combined extracts were dried ($MgSO_4$), passed through a short column (SiO_2, Et_2O) and evaporated under reduced pressure to give the *acid* (4.2 g, 90%); R_F(EtOAc–hexane, 1:1) 0.7; ν_{max}(film)/cm^{-1} 3600–2400 (OH), 1710 (C=O), 1250 (SiMe) and 1110 (SiPh); δ($CDCl_3$, 90 MHz) 7.5–7.35 (5 H, m, Ph), 2.43 (1 H, dd, *J* 3.9 and 15.5, $CHCH_AH_BCO$), 2.07 (1 H, dd, *J* 11.3 and 15.5, $CHCH_AH_BCO$), 1.47–1.41 (1 H, m, $CHCH_AH_BCO$), 1.01 (3 H, d, *J* 7.3, *Me*CH) and 0.3 (6 H, s, $SiMe_2$); *m*/*z* 207 (10%, M − Me) and 135 (100, $PhMe_2Si$) (Found: M^+ − Me, 207.0845. $C_{12}H_{18}O_2Si$ requires M − Me, 207.0841).

[(1'R)-1'-*Phenylethyl*]*ammonium* (3R)-3-*Dimethyl(phenyl)silylbutanoate*.—The acid (5 g, 22.5 mmol) was resolved using (1*R*)-1-phenylethylamine (2.9 g, 24 mmol) in dry hexane (15 cm^3), with recrystallisation from cyclohexane to give the *ammonium salt* (1.18 g, 15%) as needles, m.p. 116–117 °C (12 times from cyclohexane); $[\alpha]_D$ +3.05 (*c* 3.05, $CHCl_3$); ν_{max}(CH_2Cl_2)/cm^{-1} 3500–2300 (NH_3), 1700 (C=O) and 1110 (SiPh); δ($CDCl_3$, 80 MHz) 7.6–7.0 (13 H, m, 2Ph and NH_3), 4.05 (1 H, q, *J* 6.7, MeC*H*N), 2.18 (1 H, dd, *J* 3.4 and 14.5, $SiCHCH_AH_BCO$), 1.75 (1 H, dd, *J* 10.8 and 14.5, $SiCHCH_AH_BCO$), 1.44 (3 H, d, *J* 6.7, *Me*CHN), 1.5–1.1 (1 H, m, $SiCHCH_AH_BCO$), 0.84 (3 H, d, *J* 6.7, *Me*$CHCH_AH_BCO$) and 0.22 (6 H, s, $SiMe_2$) (Found: C, 69.75; H, 8.35; N, 3.9. $C_{20}H_{29}NO_2Si$ requires C, 70.0; H, 8.45; N, 4.1%).

(3R)-3-*Dimethyl(phenyl)silylbutanoic Acid* (−)-**15**.—A solution of the above salt (1.10 g, 3.2 mmol) in ether (15 cm^3) was washed with dilute hydrochloric acid (1 mol dm^{-3} solution; 6 × 5 cm^3), dried ($MgSO_4$), passed through a short column (SiO_2, Et_2O) and evaporated under reduced pressure to give the β-*silyl acid* (0.67 g, 95%); $[\alpha]_D$ −6.1 (*c* 2.07, $CHCl_3$), identical (NMR, IR) with the racemic acid.

Methyl (3R)-3-*Dimethyl(phenyl)silylbutanoate*.—Oxalyl chloride (0.13 g, 1 mmol) was added to a stirred solution of the β-silyl acid (0.12 g, 0.54 mmol) in dry dichloromethane (1.5 cm^3) at room temperature under nitrogen. After 1.5 h the dichloromethane and excess of oxalyl chloride were evaporated off under reduced pressure. Dry ether (1 cm^3) was added to the residue followed by a mixture of dry methanol (0.5 cm^3) and dry triethylamine (0.07 g, 0.7 mmol) added slowly. After 1.5 h the solution was diluted with ether (10 cm^3), filtered through Celite (to remove the precipitated triethylamine hydrochloride) and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:10) gave the *ester* (0.12 g, 94%); $[\alpha]_D$ −2.4 (*c* 3.74, $CHCl_3$); R_F(EtOAc–hexane, 1:10) 0.4; ν_{max}(film)/cm^{-1} 1730 (C=O), 1250 (SiMe) and 1110 (SiPh); δ($CDCl_3$, 80 MHz) 7.6–7.2 (5 H, m, Ph), 3.61 (3 H, s, OMe), 2.41 (1 H, dd, *J* 4.6 and 15.0, $CH_AH_BCO_2$), 2.04 (1 H, dd, *J* 10.1 and 15.0, $CH_AH_BCO_2$), 1.6–1.2 (1 H, m, MeC*H*Si), 0.97 (3 H, d, *J* 6.9, *Me*CHSi) and 0.28 (6 H, s, $SiMe_2$); *m*/*z* 236 (12%, M^+), 221 (25, M − Me), 151 (20) and 135 (100, $PhMe_2Si$) (Found: M^+, 236.1229. $C_{13}H_{20}O_2Si$ requires M, 236.1233), spectroscopically identical with a racemic sample.[2]

Methyl (3R)-3-*Hydroxybutanoate* **16**.—Peracetic acid (15% solution of peracetic acid in acetic acid; 5 cm^3, 12 mmol) was added to a mixture of the β-silyl ester (0.12 g, 0.5 mmol), palladium(II) acetate (0.004 g, 0.018 mmol) and mercury(II) acetate (0.016 g, 0.05 mmol) at room temperature. After 2 h the solution was cooled to 0 °C and to it were added, over 5 min, sodium acetate (0.25 g, 3 mmol) and then sodium thiosulfate (approximately 12 mmol, enough to reduce the peracetic acid). After 5 min the mixture was diluted with ether (30 cm^3), dried ($MgSO_4$), filtered and the ether removed by evaporation under reduced pressure (bath temp. < 30 °C). The acetic acid was then distilled off under reduced pressure (14 mmHg, bath temp. < 40 °C) and the residue diluted with ether (10 cm^3). This solution was filtered and evaporated under reduced pressure and the residue subjected to preparative TLC (SiO_2, EtOAc–hexane, 1:1) to give the β-hydroxy ester (0.025 g, 43%); $[\alpha]_D$ −43.2 (*c* 1.2, $CHCl_3$) [lit.,[31] −45.8 (*c* 1.7, $CHCl_3$)]; R_F(EtOAc–hexane, 1:3) 0.2; ν_{max}(film)/cm^{-1} 3500–3100 (OH) and 1740 (C=O); δ($CDCl_3$, 80 MHz) 4.4–4.0 (1 H, m, C*H*OH), 3.70 (3 H, s, OMe), 2.55 (1 H, d, *J* 11.2, CH_AH_BCO), 2.34 (1 H, dd, *J* 1.85 and 11.2, CH_AH_BCO), 2.6–2.3 (1 H, br s, OH, disappears after D_2O shake) and 1.22 (3 H, d, *J* 6.3, *Me*CHOH).

Preparation of the Ester **10** *from the Acid* (−)-**15**.—Oxalyl chloride (0.25 g, 1.97 mmol) was added to a stirred solution of the β-silyl acid (0.16 g, 0.72 mmol) in dry dichloromethane (15 cm^3) at room temperature under nitrogen. After 1.5 h, the dichloromethane and excess of the oxalyl chloride were evaporated under reduced pressure to give the acid chloride. Dry benzene (2 cm^3), silver cyanide (0.07 g, 0.5 mmol) and the alcohol (0.12 g, 0.3 mmol) were added to the acid chloride and the mixture refluxed under nitrogen for 16 h. After cooling the solution was diluted with ether (10 cm^3), filtered through Celite and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–hexane, 1:10) of the residue gave the ester (0.17 g, 93%) as prisms, m.p. 136–137 °C (from hexane); $[\alpha]_D$ −28.6 (*c* 1.25, $CHCl_3$), identical (NMR, IR) with the earlier sample (Table 2, Entry 4).

Assignment of the Absolute Configuration of the Imides **2e** *and* **3e**.—Oxalyl chloride (0.12 g, 1 mmol) was added to a stirred solution of a sample of partially resolved (3*R*)-3-dimethyl(phenyl)silyl-3-phenylpropanoic acid (0.1 g, 0.35 mmol, 80%

e.e.) in dry dichloromethane (2 cm^3) at room temperature under nitrogen. After 2 h the dichloromethane and excess of oxalyl chloride were evaporated off under reduced pressure to leave the crude acid chloride. Butyllithium (1.2 mol dm^{-3} solution in hexane; 0.29 cm^3, 0.35 mmol) was added to the lactam **30** (0.12 g, 0.35 mmol) in dry THF (2 cm^3) at −20 °C under nitrogen. After 20 min, the solution was cooled to −78 °C and the acid chloride (0.35 mmol) in dry THF (1 cm^3) was added to it. After 30 min the solution was allowed to warm to room remperature and saturated aqueous ammonium chloride (2 cm^3) was added to it. Work-up and purification as in the first preparation of these compounds above, gave the imides (0.2 g, 91%) in a ratio **2e**:**3e** of 10:90.

Assignment of the Absolute Configuration of the Imides **22** *and* **23**.—The ester **29** (see below) (0.18 g, 0.68 mmol) in ether (1 cm^3) was added dropwise to a solution of lithium dimethylcuprate (3 mmol) in ether (3 cm^3) at −20 °C under nitrogen and the mixture kept for 1 h. The mixture was then warmed to room temperature and aqueous hydrochloric acid (2 mol dm^{-3}; 3 cm^3) was added to it and the whole extracted with ether (3 × 5 cm^3). Work-up gave the (3*S*)-acid (+)-**15** (0.106 g, 70%), identical (^{1}H NMR) with the earlier samples of (±)- and (−)-**15**. The acid (0.1 g, 0.45 mmol) was kept with oxalyl chloride (0.254 g, 2 mmol) in dichloromethane (2 cm^3) for 3 h at room temperature. Benzene (2 cm^3), silver cyanide (0.134 g, 1 mmol) and the alcohol **d**-H (0.18 g, 0.45 mmol) were added to the mixture which was then refluxed under nitrogen for 16 h. Work-up and chromatography gave the ester **12** (0.246 g, 92%) with the ^{1}H NMR signals from the isomer **12** clearly present, and those from the isomer **10** not detectable.

Unsuccessful Removal of the Chiral Auxiliary

(4S)-4-[(3′S)-3′-*Dimethyl(phenyl)silylbutanamido*]-5-*triphenylmethoxypentanoic Acid* **26**.—Potassium hydroxide (0.073 g, 1.3 mmol) in water (0.7 cm^3) was added to a stirred solution of the imide **23** (78% d.e.; 0.056 g, 0.1 mmol) in methanol (2 cm^3) at 80 °C. After 10 min the methanol was evaporated under reduced pressure and the remaining aqueous solution was acidified to pH 1 (HCl, 1 mol dm^{-3}) and extracted with ether (4 × 2 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Preparative TLC (SiO_2, EtOAc–hexane, 1:1) gave the *acid* (0.035 g, 60%); R_F(EtOAc–hexane, 1:1) 0.4; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3600–2400 (OH), 1710 (C=O), 1670 (C=O), 1210 (SiMe) and 1110 (SiMe); $\delta(CCl_4$, 90 MHz) 7.6–6.9 (20 H, m, 4Ph), 5.4–5.25 (1 H, m, HCN), 4.1–3.8 (2 H, m, CH_2OCPh_3), 3.2–3.0 (2 H, m, CH_2CON), 2.3–1.2 (5 H, m, aliphatic Hs), 0.8 (3 H, d, *J* 7.3, *Me*CH) and 0.25 (6 H, s, $SiMe_2$); *m*/*z* 579 (0.05%, M^+), 243 (100, CPh_3) and 135 (80, $PhMe_2Si$) (Found: M^+, 579.2810. $C_{36}H_{41}NO_4Si$ requires *M*, 579.2805).

Benzyl (4S)-4-[(3′S)-3′-*Dimethyl(phenyl)silylbutanamido*]-5-*triphenylmethoxy-pentanoate*.—Butyllithium (1.5 mol dm^{-3} solution in hexane; 0.15 cm^3, 0.225 mmol) was added dropwise to a stirred solution of benzyl alcohol (dried by distillation)[32] (0.054 g, 0.5 mmol) in dry THF (0.5 cm^3) at 0 °C under nitrogen. After 10 min the imide **23** (78% d.e.; 0.078 g, 0.14 mmol) in dry THF (0.35 cm^3) was added to the mixture which was then stirred for only 5 min. Saturated aqueous ammonium chloride (2 cm^3) was added to the mixture which was then extracted with ether (4 × 3 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under vacuum. Preparative TLC (SiO_2, EtOAc–hexane, 1:3) gave the *ester* (0.047 g, 50%); R_F(EtOAc–hexane, 1:3) 0.4; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3420 (NH), 1730 (C=O), 1670 (C=O), 1600 and 1500 (Ph), 1210 (SiMe) and 1110 (SiPh); $\delta(CCl_4$, 90 MHz) 7.6–6.9 (25 H, m, 5Ph), 5.4–5.25 (1 H, m, CHN), 5.1 (2 H, m, OCH_2Ph), 4.1–3.8 (2 H, m, CH_2OCPh_3), 3.2–3.0 (2 H, m, CH_2CON), 2.3–1.2 (5 H, m, aliphatic Hs), 0.85 (3 H, d, *J* 7.5, *Me*CH) and 0.25 (6 H, s, $SiMe_2$); *m*/*z* 669 (< 1%, M^+), 243 (100, CPh_3) and 135 (70, $PhMe_2Si$) (Found: M^+, 669.3288. $C_{43}H_{47}NO_4Si$ requires *M*, 669.3274).

Successful Removal of the Chiral Auxiliary

Benzyl (3RS)-3-*Dimethyl(phenyl)silyl*-3-*phenylpropanoate* **27**.—Butyllithium (1.4 mol dm^{-3} solution in hexane; 0.5 cm^3, 0.7 mmol) was added dropwise to a stirred solution of benzyl alcohol (dried by distillation)[32] (0.097 g, 0.9 mmol) in dry THF (0.8 cm^3) at 0 °C under nitrogen. After 10 min, a 50:50 mixture of the imides **2e** and **3e** (0.12 g, 0.2 mmol) in dry THF (0.7 cm^3) was added to the solution which was then stirred for 24 h at room temperature. Saturated aqueous ammonium chloride (2 cm^3) was added to the mixture which was then extracted with ether (4 × 4 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by preparative TLC (SiO_2, EtOAc–hexane, 1:6) gave the lactam **30** (0.058 g, 82%) and the ester[3] (0.067 g, 90%).

Allyl (3RS)-3-*Dimethyl(phenyl)silyl*-3-*phenylpropanoate* **28**.—Similar conditions, but using allyl alcohol (dried by distillation from K_2CO_3)[32] (0.058 g, 1 mmol) and preparative TLC (SiO_2, EtOAc–hexane, 1:3), gave the lactam **30** (0.064 g, 72%) and the *ester* (0.068 g, 84%); R_F(EtOAc–hexane, 1:10) 0.35; ν_{max}(film)/cm^{-1} 1740 (C=O), 1250 (SiMe) and 1115 (SiPh); $\delta(CDCl_3$, 80 MHz) 7.5–6.9 (10 H, m, 2Ph), 5.7 (1 H, ddt, *J* 9.5, 17.6 and 5.5, CH=CH_2), 5.25–5.15 (1 H, m, CH=CH_AH_B), 5.05–4.95 (1 H, m, CH=CH_AH_B), 4.37 (2 H, dt, *J* 5.5 and 1.25, OCH_2CH=), 2.95–2.6 (3 H, m, $PhCHCH_2CO$), 0.26 (3 H, s, $SiMe_AMe_B$) and 0.23 (3 H, s, $SiMe_AMe_B$); *m*/*z* 324 (0.24%, M^+) and 135 (100, $PhMe_2Si$) (Found: M^+, 324.1548. $C_{20}H_{24}O_2Si$ requires *M*, 324.1546).

Allyl (3S)-3-*Dimethyl(phenyl)silylbutanoate* **29**.—Similar conditions, but using allyl alcohol (dried by distillation from K_2CO_3)[32] (0.34 g, 6 mmol) and the imide **23** (0.6 g, 1.07 mmol, 78% d.e.) and column chromatography (SiO_2, eluting first with EtOAc–hexane, 1:15) until the ester was collected and then with ethyl acetate to collect the lactam **30** (0.31 g, 80%), gave the *ester* (0.27 g, 96%); $[\alpha]_D$ +1.3 (*c* 3.6, MeOH); R_F(EtOAc–hexane, 1:10) 0.35; ν_{max}(film)/cm^{-1} 1745 (C=O), 1255 (SiMe) and 1115 (SiPh); $\delta(CDCl_3$, 80 MHz) 7.5–7.35 (5 H, m, Ph), 5.95–5.80 (1 H, m, CH=CH_2), 5.33–5.19 (2 H, m, CH=CH_2), 4.50 (2 H, dt, *J* 5.8 and 1.3, OCH_2), 2.40 (1 H, dd, *J* 4.0 and 15.3, CH_AH_BCO), 2.10 (1 H, dd, *J* 11.2 and 15.3, CH_AH_BCO), 1.5–1.4 (1 H, m, $MeCH$), 0.98 (3 H, d, *J* 7.3, *Me*CH) and 0.28 (6 H, s, $SiMe_2$); *m*/*z* 262 (1.62%, M^+), 247 (45, M − Me) and 135 (100, $PhMe_2Si$) (Found: M^+, 262.1409. $C_{15}H_{22}O_2Si$ requires *M*, 262.1389), identical (^{1}H NMR) with a racemic sample.[33]

Allyl (3R)-3-*Trimethylsilylbutanoate* **29** (Me_3Si *in place of* $PhMe_2Si$).—Similar conditions, but using allyl alcohol (dried by distillation from K_2CO_3)[32] (5 cm^3, 74 mmol) and the imide **23** (Me_3Si in place of $PhMe_2Si$) (6.0 g, 12 mmol, 64% d.e.) and column chromatography (SiO_2, eluting first with EtOAc–hexane, 1:5) until the ester was collected and then with ethyl acetate to collect the lactam **30** (3.0 g, 70% after recrystallisation) gave the *ester* (2.0 g, 83%); $[\alpha]_D$ −2.0 (*c* 0.25, $CHCl_3$); R_F(EtOAc–hexane, 1:5) 0.8; ν_{max}(film)/cm^{-1} 3090 (C=CH_2), 1735 (C=O), 1250 (SiMe) and 985 (CH_2=CH); $\delta(CDCl_3$, 250 MHz) 5.90 (1 H, ddt, *J* 10.3, 17.2 and 5.7, CH_2CH=CH_AH_B), 5.31 (1 H, dq, *J* 17.2 and 1.5, CH_2CH=C-H_AH_B), 5.23 (1 H, dq, *J* 10.3 and 1.3, CH_2CH=CH_AH_B), 4.57 (2 H, dt, *J* 5.7 and 1.3, CH_2CH=CH_AH_B), 2.41 (1 H, dd, *J* 4.15 and 15.1, $CHCH_AH_BCO$), 2.08 (1 H, dd, *J* 11.1 and 15.1, $CHCH_AH_BCO$), 1.3–1.1 (1 H, m, $CHCH_AH_BCO$), 0.95 (3 H, d, *J* 7.15, *Me*CH) and −0.025 (9 H, s, $SiMe_3$); *m*/*z* 200 (7%, M^+)

and 73 (100, Me_3Si) (Found: M^+, 200.1243. $C_{10}H_{20}O_2Si$ requires M, 200.1233).

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References

1 R. A. N. C. Crump, I. Fleming, J. H. M. Hill, D. Parker, N. L. Reddy and D. Waterson, *J. Chem. Soc., Perkin Trans 1*, 1992, 3277; I. Fleming and J. D. Kilburn, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3295.
2 I. Fleming, R. Henning and H. Plaut, *J. Chem. Soc., Chem. Commun.*, 1984, 29; I. Fleming and J. D. Kilburn, *J. Chem. Soc., Chem. Commun.*, 1986, 1198; H.-F. Chow and I. Fleming, *Tetrahedron Lett.*, 1985, **26**, 397.
3 I. Fleming, S. Gil, A. K. Sarkar and T. Schmidlin, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3351.
4 M. J. C. Buckle, I. Fleming and S. Gil, *Tetrahedron Lett.*, 1992, **33**, 4479.
5 I. Fleming and N. D. Kindon, *J. Chem. Soc., Chem. Commun.*, 1987, 1177.
6 K. Tomioka, T. Suenaga and K. Koga, *Tetrahedron Lett.*, 1986, **27**, 369.
7 W. Oppolzer, R. J. Mills, W. Pachinger and T. Stevenson, *Helv. Chim. Acta*, 1986, **69**, 1542; see also C. Palomo, J. M. Aizpurua, M. Iiurburu and R. Urchegui, *J. Org. Chem.*, 1994, **59**, 240.
8 I. Fleming, N. D. Kindon and A. K. Sarkar, *Tetrahedron Lett.*, 1987, **28**, 5921; I. Fleming and N. J. Lawrence, *Tetrahedron Lett.*, 1990, **31**, 3645.
9 T. Mukaiyama, T. Takeda and K. Fujimoto, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 3368; J. Fujiwara, Y. Fukutani, M. Haasegawa, K. Maruoka and H. Yamamoto, *J. Am. Chem. Soc.*, 1984, **106**, 5004; S. G. Davies and J. C. Walker, *J. Chem. Soc., Chem. Commun.*, 1985, 209; L. S. Liebeskind and M. E. Welker, *Tetrahedron Lett.*, 1985, **26**, 3079; G. Helmchen and G. Wegner, *Tetrahedron Lett.*, 1985, **26**, 6051; P. Somfai, D. Tanner and T. Olsson, *Tetrahedron*, 1985, **41**, 5973; P. Mangeney, A. Alexakis and J. F. Normant, *Tetrahedron Lett.*, 1986, **27**, 3143; J. d'Angelo and J. Maddalino, *J. Am. Chem. Soc.*, 1986, **108**, 8112; W. Amberg and D. Seebach, *Chem. Ber.*, 1990, **123**, 2413 and 2439; A. I. Meyers, J. D. Brown and D. Laucher, *Tetrahedron Lett.*, 1987, **28**, 5279; E. J. Corey, F. J. Hamon and N. W. Boaz, *Tetrahedron*, 1989, **45**, 545; M. Bergdahl, M. Nilsson, T. Olsson and K. Stern, *Tetrahedron*, 1991, **47**, 9691; M. Uemura, H. Oda, T. Minami and Y. Hayashi, *Tetrahedron Lett.*, 1991, **32**, 4565; C.-L. Fang, H. Suenume and K. Sakai, *J. Org. Chem.*, 1992, **57**, 4300; G. Li, M. A. Jarosinski and V. J. Hruby, *Tetrahedron Lett.*, 1993, **34**, 2561; K. Rück and H. Kunz, *Synthesis*, 1993, 1018; K. Tanaka, J. Matsui, K. Somemiya and H. Suzuki, *Synlett*, 1994, 351.
10 T. Mukaiyama and I. Iwasawa, *Chem. Lett.*, 1981, 913.
11 R. F. Borch, *Tetrahedron Lett.*, 1968, 61.
12 P. Mangeney, A. Alexakis and J. F. Normant, *Tetrahedron Lett.*, 1983, **24**, 373.
13 J. Berlan, Y. Besace, D. Prat and G. Pourcelot, *J. Organomet. Chem.*, 1984, **264**, 399; J. Berlan and Y. Besace, *Tetrahedron*, 1986, **42**, 4767.
14 E. J. Corey and H. E. Ensley, *J. Am. Chem. Soc.*, 1975, **97**, 6908.
15 W. Oppolzer and H. J. Löher, *Helv. Chim. Acta*, 1981, **64**, 2808.
16 W. Oppolzer, R. Moretti, T. Godel, A. Meunier and H. Löher, *Tetrahedron Lett.*, 1983, **24**, 4971.
17 W. Oppolzer, C. Chapuis and G. Bernardinelli, *Tetrahedron Lett.*, 1984, **25**, 5885.
18 I. Fleming and P. E. J. Sanderson, *Tetrahedron Lett.*, 1987, **28**, 4229.
19 I. Fleming, T. W. Newton and F. Roessler, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2527.
20 C. L. Stevens and S. J. Dykstra, *J. Am. Chem. Soc.*, 1954, **76**, 4402.
21 H. Herzog and H.-D. Scharf, *Synthesis*, 1986, 420; O. Ort, *Org. Synth. (N.Y.)*, 1987, **65**, 203.
22 W. Oppolzer, C. Chapuis, G. M. Dao, D. Reichlin and T. Godel, *Tetrahedron Lett.*, 1982, **23**, 4781.
23 S. Takimoto, J. Inanaga, T. Katsuki and M. Yamaguchi, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 2335.
24 W. Oppolzer, R. Moretti and G. Bernardinelli, *Tetrahedron Lett.*, 1986, **27**, 4713.
25 D. J. Ager, I. Fleming and S. K. Patel, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2520.
26 H. O. House, C.-Y. Chu, J. M. Wilkins and M. J. Umen, *J. Org. Chem.*, 1975, **40**, 1460.
27 A. McKenzie and H. B. P. Humphries, *J. Chem. Soc.*, 1910, 121.
28 C. Schöpf and W. Wüst, *Justus Liebigs Ann. Chem.*, 1959, **626**, 150.
29 E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, 1979, 399.
30 I. Fleming and D. Waterson, *J. Chem. Soc., Perkin Trans 1*, 1984, 1809.
31 D. A. Evans, J. Bartroli and T. L. Shih, *J. Am. Chem. Soc.*, 1981, **103**, 2127.
32 D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon, Oxford, 2nd edn., 1966.
33 I. Fleming, A. K. Sarkar, M. J. Doyle and P. R. Raithby, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2023.

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