Stereocontrol in organic synthesis using silicon-containing compounds. A synthesis of methyl (+)-nonactate

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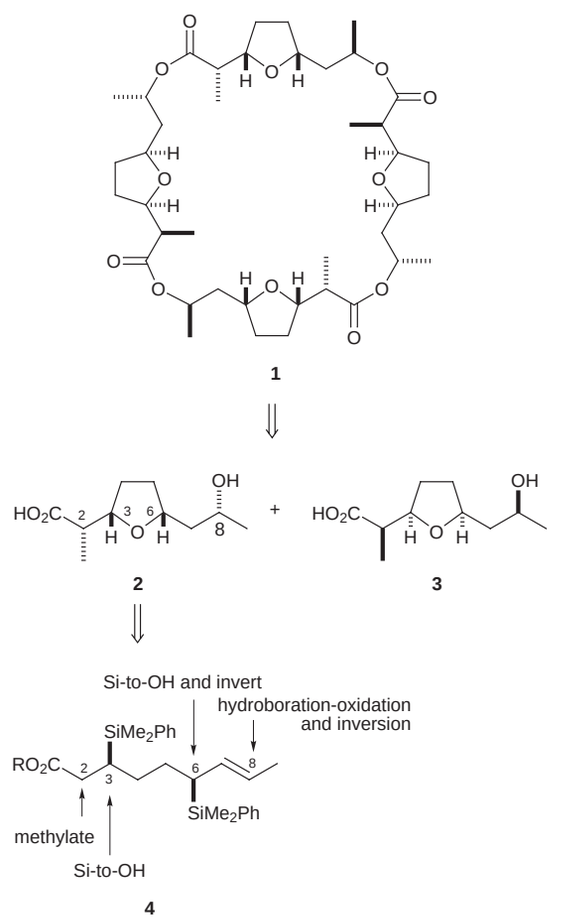
(3*Z*,2*S*)-7,7-Ethylenedioxyhex-3-en-2-yl *N*-phenylcarbamate 7 gave the allylsilane 8, (2*E*,4*S*)-7,7-ethylenedioxy-4-dimethyl(phenyl)silylhept-2-ene, introducing one stereogenic centre carrying a silyl group. Hydroboration–oxidation gave (2*S*,4*S*)-7,7-ethylenedioxy-4-dimethyl(phenyl)silylheptan-2-ol 9, controlling a second stereogenic centre. Conjugate addition of the phenyldimethylsilylcuprate reagent to the α,β-unsaturated imide (2′*E*,6′*S*,8′*R*,5*S*)-1-[8′-benzyloxy-6′-dimethyl(phenyl)silylnon-2′-enoyl]-5-triphenylmethoxymethylpyrrolidin-2-one 11 introduced a third stereogenic centre, and methylation of the ester derived from the product introduced a fourth. Ester hydrolysis and a double silyl-to-hydroxy conversion gave (2*S*,3*S*,6*S*,8*R*)-8-benzyloxy-3,6-dihydroxy-2-methylnonanoic acid 16, from which methyl (+)-nonactate 2 was prepared by differentiating the hydroxy groups with the selective formation of a β-lactone 17 rather than a seven-membered lactone.

Introduction

The (+)- and (−)-nonactic acids **2** and **3**, degradation products of the macrocyclic lactone nonactin **1**, have been synthesised many times, and the syntheses fully reviewed.[1] A high proportion of those syntheses were carried out, using the stereogenic centres at C-6 and C-8, to demonstrate the effectiveness of new methods for setting up 1,3-diols with stereocontrol. Many of them also demonstrate a method for controlling the relative stereochemistry of C-2 and C-3, the stereogenic centres α and β to the carboxylic acid group. In our work on stereocontrol using silicon compounds, we had developed solutions to both of these problems, illustrated in the preceding papers, and we were therefore attracted by nonactic acid as a target for our methods. We were especially attracted because we had not developed a solution to the 1,4-relationship, between C-3 and C-6, embedded in these structures, which therefore presented us with the challenge how to extend our methods to cope with this problem. We have solved the 1,4 problem in two quite different ways, and report the first of them here, having published it before only as a lecture which was given on only one occasion.[2]

The idea is quite simple: to derive each of the oxygen substituents on C-3 and C-6 from phenyldimethylsilyl groups **4** (Scheme 1), having introduced each separately with absolute stereocontrol. Since we have developed two methods for introducing phenyldimethylsilyl groups with absolute stereocontrol, we were able successively to demonstrate both methods, by using one[3] to place a silyl group on C-3 and the other[4] to place a silyl group on C-6, automatically controlling the relative stereochemistry between these two stereocentres. There is another advantage to using two successive enantiocontrolled reactions, as we shall see later. The silyl group on C-3 can then be used to control the 1,2-relationship between C-2 and C-3 by methylation or protonation,[5] and the silyl group on C-6 can be used to control the 1,3-relationship by hydroboration–oxidation.[6] Since it is quite easy to introduce a silyl group in either absolute sense, and since both the 1,2- and 1,3-relationships can be controlled in either sense, it ought to be easy to make any of the isomers of nonactic acid, including, of course, both enantiomers **2** and **3**. It is only necessary to convert the silyl groups on C-3 and C-6 into hydroxy groups in some way that allows them to be differentiated, in order to control which of the hydroxy groups is to be displaced with inversion of configuration when forming the tetrahydrofuran ring. In the plan actually brought to fruition, making (+)-nonactic acid **2** as its methyl ester, we set up C-3 in the absolute sense *S*, we methylated the enolate to control C-2 as *S*, we set up C-6 in the absolute sense *S*, but inverted it later in the formation of the tetrahydrofuran ring, and we used hydroboration of a *trans* double bond to set up C-8 as *S*, and inverted that too to obtain the correct configuration *R*.



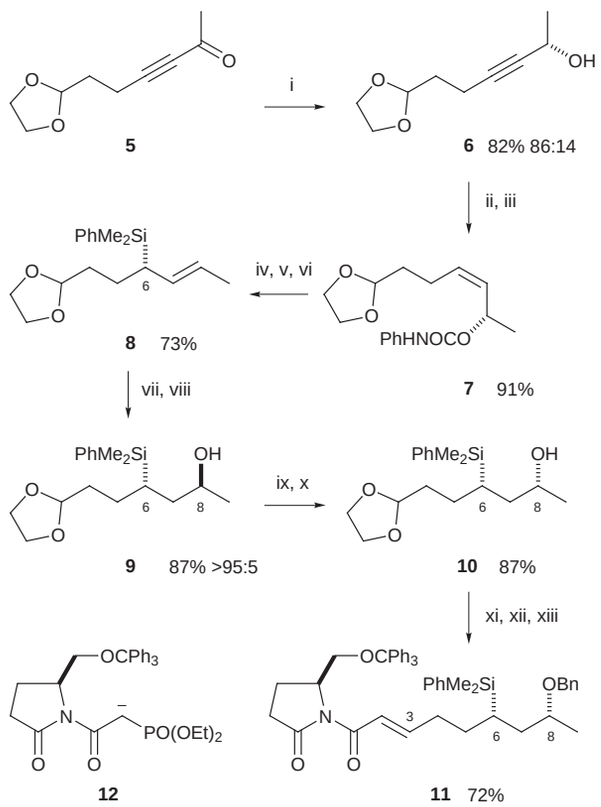
Scheme 1

Results and discussion

The successful route

We prepared the acetylenic ketone **5** in an overall yield of 58%

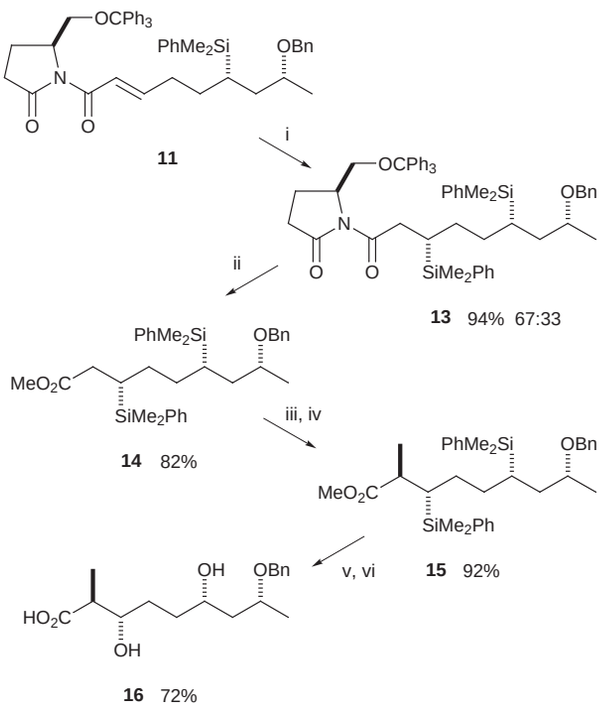
by alkylating the anion of acetylene with 2-(2-bromoethyl)-1,3-dioxolane, and then making the anion at the other end and acetylating that. We introduced the first stereogenic centre using Brown's[7] and Midland's[8] *S*-Alpine-Borane reduction of the acetylenic ketone **5** to give the alcohol **6** (Scheme 2) together



Scheme 2 *Reagents:* i, *S*-Alpine-Borane; ii, PhNCO, Et_3N; iii, H_2, Pd/$CaCO_3$, PbO, MnO_2; iv, BuLi; v, CuI, Ph_3P; vi, $PhMe_2SiLi$; vii, thexylborane; viii, NaOH, H_2O_2; ix, *p*-$O_2NC_6H_4CO_2H$, DEAD, Ph_3P; x, NaOH; xi, $BnOCHNCCl_3$, TfOH; xii, TsOH, Me_2CO; xiii, **12**

with its enantiomer in a ratio of 86:14, measured (^{1}H NMR) by making the diastereoisomeric camphorsulfonate esters. This ratio can be improved by recrystallising the 3,5-dinitrobenzoate of the propargylic (prop-2-ynylic) alcohol **6**, with two recrystallisations raising the enantiomer ratio to 99.4:0.6. However, we only worked this out after we had completed the synthesis, so it remains a formal improvement. We made the *N*-phenylcarbamate and reduced the triple bond to a *cis* double bond **7**, on which we carried out one of our allylsilane syntheses,[4] which we knew to be stereospecifically *syn* and highly regioselective for allylic displacement, to give cleanly the allylsilane **8** with the silyl group on C-6 (nonactic acid numbering). It is an unfortunate consequence of this route that the double bond is always selectively produced as the *trans* double bond, for we would have preferred *cis*, hydroboration–oxidation of which would have given directly the correct configuration at C-8. The hydroboration of *trans* double bonds takes place with lower levels of stereocontrol than of *cis* double bonds, and high levels of control are only observed with hindered hydroborating agents like 9-BBN.[6] In the event, hydroboration of the allylsilane **8** with 9-BBN was too slow, and diborane was, as usual, not highly stereoselective. Fortunately, thexylborane proved to be fast enough and selective enough (>95:5) in favour of the formation of the *anti* alcohol **9**. It was a simple matter to invert the configuration, using a Mitsunobu reaction by way of the *p*-nitrobenzoate,[9] to give the *syn* alcohol **10** with the correct configuration at C-8. We protected the alcohol as its benzyl ether, using the acid-catalysed method,[10] necessarily, because of the ease with which the phenyl group was displaced in base.[11] We removed the acetal protecting group and joined the aldehyde onto Koga's chiral auxiliary[12] using the phosphonate anion **12** in a Horner–Wadsworth–Emmons reaction to give the imide **11**.

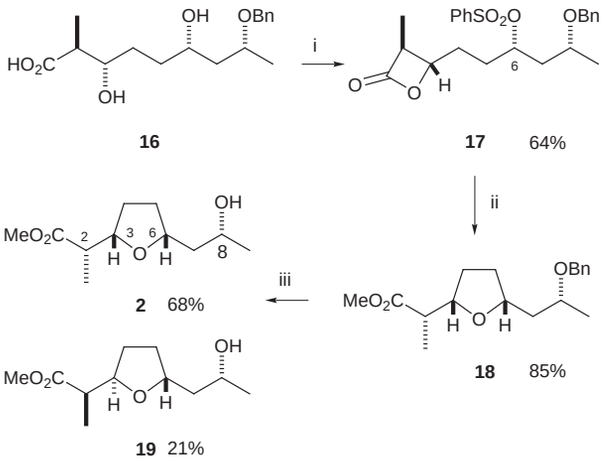
We were now ready to use the second of our methods for introducing a silyl group with absolute stereocontrol using conjugate addition of the silylcuprate reagent. We have been used to high levels of control in this reaction giving the diastereoisomers, typically in a ratio of 95:5. On this occasion we have had to put up with the worst ratio we have yet suffered—the major product was the isomer **13** (Scheme 3), but in a ratio of



Scheme 3 *Reagents:* i, $(PhMe_2Si)_2CuLi$, $MgBr_2$; ii, MeOMgBr; iii, LHMDS; iv, MeI; v, $Hg(OAc)_2$, AcOOH, AcOH; vi, LiOH, MeOH

only 67:33 with its diastereoisomer at C-3. This ratio is perhaps to be taken as no more than an estimate, since we are integrating peaks very close together in the ^{1}H NMR spectrum. This reaction needs more work, and perhaps a different chiral auxiliary, although Koga's has usually proved to be the best. For now we continued with this material, and found, as it turned out, that we had enough to complete the synthesis. We removed the chiral auxiliary, and methylated the ester **14** to give the ester **15** with all the stereogenic centres now in place. We were not able to measure the degree of selectivity with any confidence, because of the number of isomers present at this stage, but it appeared to be high. We converted the silyl groups to hydroxy groups with the usual retention of configuration,[13] and hydrolysed the ester to give the carboxylic acid **16**. This was the first time that we had carried out a silyl-to-hydroxy conversion on a molecule with two phenyldimethylsilyl groups, so we were pleased to find that it still gave a tolerably good yield.

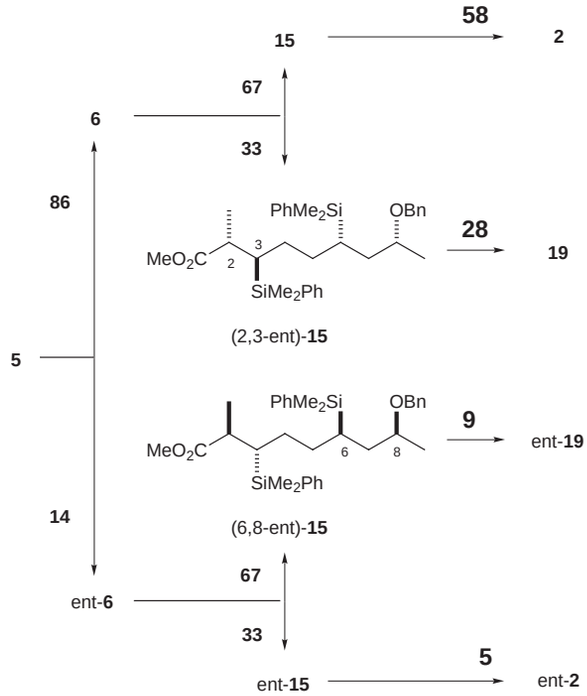
We had done nothing to differentiate the two hydroxy groups up to this point, trusting that one or other of the functional groups at each end of the molecule could be used to protect one of them. And so it proved, with benzenesulfonyl chloride selectively converting the β-hydroxy acid into the β-lactone, leaving the hydroxy at C-6 free to form the benzenesulfonate **17** in the same pot (Scheme 4). When we carried out this reaction, we had not been able to forecast whether the four- or the seven-membered ring would be formed, both ring sizes lying between the five- and six-membered that are classified as fast, and the medium-sized rings that are classified as slow. Selectivity in favour of a four-membered ring has been seen since in a completely different reaction, the samarium(II) induced attack of an



Scheme 4 *Reagents:* i, $PhSO_2Cl$, Py; ii, TsOH, MeOH; iii, H_2, Pd/C and separate diastereoisomers

alkyl halide on an ester group, and may be general.[14] Acidic methanol then opened the lactone **17** and the tetrahydrofuran **18** formed immediately with inversion of configuration at C-6. Deprotection of the benzyl ether and chromatographic separation gave methyl (+)-nonactate **2** (68%) and its C-3 diastereoisomer **19** (21%) in a ratio confirming that our estimate of the diastereoselectivity in the conjugate addition step **11**→**13** had been about right. The two esters were readily identifiable by their ^1H and ^{13}C NMR spectra, which were already known,[15] and they were also in the expected enantiomeric series, as judged by the sense of their optical rotations.

We measured the enantiomeric purity of both products by attaching (4*R*,5*R*)-2-chloro-4,5-dimethyl-1,2,3-dioxaphospholane 2-oxide.[16] The major product **2** proved to consist of the (+)- and (−)-enantiomers in a respectable ratio of 92:8, which agreed reasonably well with the degree of enrichment calculated from the optical rotation. In contrast, the minor product **19** was almost racemic (55:45). With an indifferent ratio of enantiomers 86:14 in the first enantiocontrolled step **5**→**6**, and a feeble 67:33 ratio in the second **11**→**13**, it might at first seem surprising that the major product **2** is present with such a high level of enantiomeric purity. The reason was first enunciated by Horeau,[17] and has been reviewed recently.[18] Attention is only occasionally drawn to the phenomenon,[19,20] and only occasionally credited to Horeau.[20] It has loomed large in our considerations, because we have had occasion to use his principle in the present work, and an alternative version of it in the work described in the following paper. His principle, applied to our case, is summarised in Scheme 5, where the large bold numbers on the right identify the calculated proportions, using the estimates of 86:14 and 67:33 for our ratios, normalised to add up to 100%, of the two major diastereoisomers, each a pair of enantiomers, that ought to be present, assuming no chiral recognition of the resident stereocentres on C-6 and C-8 in the step **11**→**13**. The minor amounts of other diastereoisomers stemming from incomplete control from C-3 to C-2 and from C-6 to C-8 are discounted—they were not detectable, although they must, of course, have been present to some extent. Thus the effect of two successive enantiocontrolled reactions is to create a pair of diastereoisomers in which the major diastereoisomer **2** has an enhanced level of enantiomeric purity (58:5 = 92:8) and the minor **19** a reduced level (28:9 = 76:24). Separation of the diastereoisomers then gives the major product in a more or less acceptable state of enantiomeric purity, at the expense of some loss in yield. It was this arithmetic that had attracted us to using two successive enantiocontrolled reactions as a solution to the 1,4 problem embedded in the structure of nonactic acid. In practice, the measured enantiomeric purity of the major product was exactly that calculated from the scheme in Scheme 5, but the minor product proved to



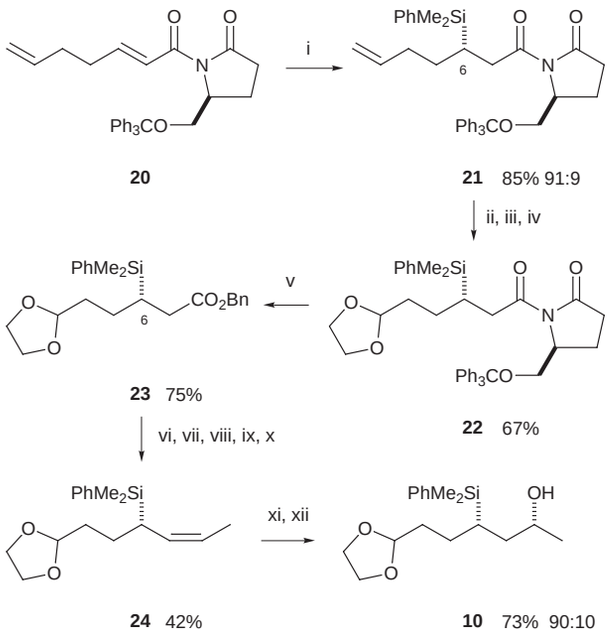
Scheme 5

be rather worse, showing that our estimates of the degrees of selectivity must have been about right but not exactly right. If we had used the recrystallisation of the 3,5-dinitrobenzoate of the propargylic alcohol **6** in the succeeding steps, the methyl nonactate **2** would have been contaminated with only 0.3% of its enantiomer. We did not use it, because we turned instead to a second, better controlled synthesis of nonactic acid derivatives,[21] having established that the approach described in this paper was not without its advantages.

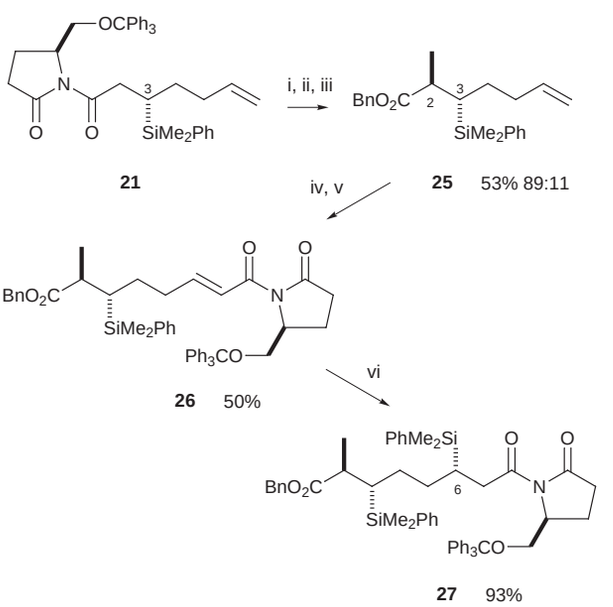
Some other routes

Some of the features of the route described above were far from perfect, and were not in fact our first choices. In particular, we had managed to control the relative and absolute stereochemistry between C-6 and C-8 in an alternative synthesis of the alcohol **10** using a *cis* allylsilane **24**, set up using our long **23**→**24** but versatile method for synthesising unsymmetrical allylsilanes, and using conjugate addition **20**→**21** as the means of establishing the absolute stereochemistry at C-6 (Scheme 6). We made the imide **20** in 39% overall yield by allylation of crotonic acid using the copper(I) enolate.[22] The disadvantages of this route are that it is longer, and that, for all that we were using a *cis* double bond in the hydroboration step, avoiding the inelegant inversion step **9**→**10**, the diastereoselectivity was in the end slightly worse. Again, 9-BBN, which would have given a very high ratio of diastereoisomers, was too slow and so was dicyclohexylborane—we had to use borane, with a small loss of diastereoselectivity. The overall yield of the alcohol **10** from **20** was 15% in 12 steps, which compares unfavourably with an overall yield of 36% from **5** in 10 steps. One advantage of the route in Scheme 6 was that we were easily able to separate the diastereoisomers of the acetal **22**, and that consequently we prepared the allylsilane **24** enantiomerically pure.

We also essayed a route that set up C-2 and C-3 first, using the same intermediate **21** redrawn in Scheme 7. Removal of the chiral auxiliary and methylation of the ester gave largely the *anti* isomer **25**. The aldehyde derived from the terminal double bond of this intermediate could be joined on to the chiral auxiliary to give the imide **26** using the Horner–Wadsworth–Emmons reaction and the phosphonate **12**. A second conjugate addition probably gave the isomer **27** as the major product, but the number of diastereoisomers present at this stage made it



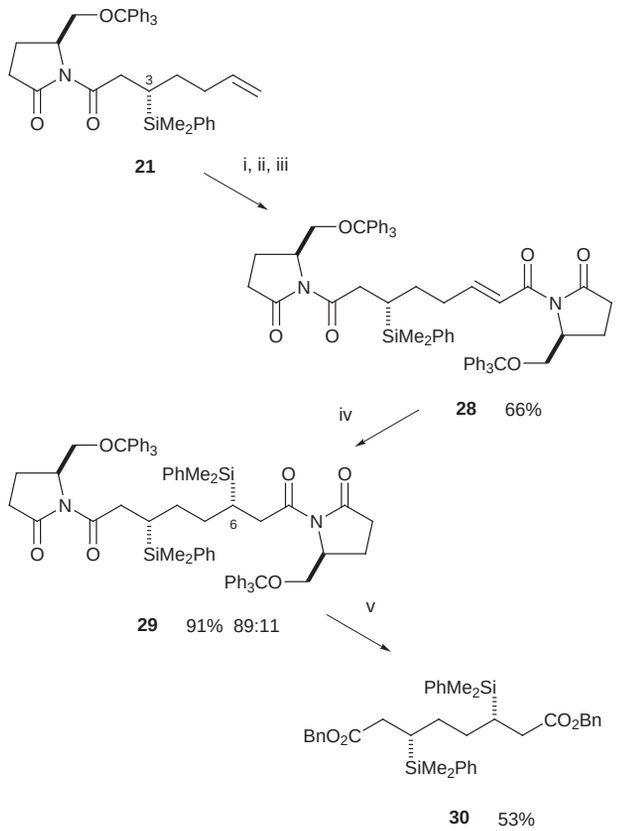
Scheme 6 *Reagents:* i, $(PhMe_2Si)_2CuLi$, $MgBr_2$; ii, OsO_4, $NaIO_4$; iii, $HOCH_2CH_2OH$, PyH^+ TsO^-; iv, separate diastereoisomers; v, LiOBn; vi, LHMDS, THF; vii, MeCHO; viii, H_2, Pd/C; ix, $PhSO_2Cl$; x, collidine, reflux; xi, BH_3, THF; xii, NaOH, H_2O_2



Scheme 7 *Reagents:* i, LiOBn; ii, NHMDS; iii, MeI; iv, O_3; v, **12**; vi, $(PhMe_2Si)_2CuLi$, $MgBr_2$

impossible to determine what the level of selectivity had been, and we were uncomfortable continuing with this mixture.

We also omitted the methylation step, and set up the 3*S*,6*S*-bis-silyl derivative of dibenzyl suberate **30** (Scheme 8). We were able to separate the diastereoisomers of the aldehyde derived from the terminal double bond of the imide **21**, before joining it to the chiral auxiliary **12**, and so the bis-imide **28** was enantiomerically pure. Conjugate addition to this compound gave a mixture (89 : 11) of the bis-imide **29** and its diastereoisomer at C-6. The diester **30** is the 1,4-member of a family of compounds having 1,*n*-related silicon-bearing centres and terminal functionality, which we pointed out in the preceding paper[23] were versatile synthons with which to push stereochemical information out along each chain. For the present purposes, we had hoped that it would be possible separately to alkylate at one end and then to carry out the *cis* allylsilane synthesis at the other, with a bonus that these operations could be carried out in either



Scheme 8 *Reagents:* i, OsO_4, $NaIO_4$; ii, separate diastereoisomers; iii, **12**; iv, $(PhMe_2Si)_2CuLi$, $MgBr_2$; iv, LiOBn

order. The problem was that the first-formed enolate might simply give the Dieckmann product with a seven-membered ring before we could intercept it. Whether or not the Dieckmann reaction was the cause of the problem, we were unable to recognise the products from any base-induced reactions on this diester. We might have tried the device for avoiding the Dieckmann reaction, used in the following paper, of hydrolysing one of the ester groups, but we have not done so yet.

Experimental

Light petroleum refers to the fraction bp 30–40 °C; ether refers to diethyl ether.

5,5-Ethylenedioxypentyne

2-(2-Bromoethyl)-1,3-dioxolane (30 cm^3, 0.255 mol) was stirred with a suspension of lithium acetylide–ethylenediamine complex (47 g, 0.511 mol) and *N*,*N*,*N*,*N*′-tetramethylethylenediamine (77 cm^3, 0.51 mol) in dry THF (500 cm^3) at room temperature under argon for 48 h. The mixture was poured slowly into saturated aqueous ammonium chloride (400 cm^3), extracted with ether (3 × 200 cm^3) and the combined organic extracts were washed with water (300 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was filtered through Celite, and distilled to give the *acetylene* (25 g, 0.198 mol, 78%), bp 62–64 °C at 12 mmHg; R_f (CH_2Cl_2) 0.45; $\nu_{max}(CHCl_3)/cm^{-1}$ 3307 (C≡CH), 2253 (C≡C) and 1140–1096 (C–O–C); δ_H(250 MHz; $CDCl_3$) 4.92 (1 H, t, *J* 4.7, OCHO), 3.99–3.78 (4 H, m, OCH_2CH_2O), 2.25 (2 H, dt, *J* 2.7 and 7.5, $CH_2C{\equiv}C$), 1.91 (1 H, t, *J* 2.7, C≡CH) and 1.82 (2 H, dt, *J* 4.7 and 7.5, CH_2CHO); *m*/*z* 125 (2.48%, $M^+ - H$) and 73 (100, CHO-CH_2CH_2O) (Found: C, 66.70, H, 8.19%; $M^+ - H$, 125.0593. $C_7H_{10}O_2$ requires C, 66.68; H, 7.93%; *M* − H, 125.0603).

7,7-Ethylenedioxyhept-3-yn-2-one 5

(Experiment scaled up by U. Ghosh). Following Brandsma,[24] *n*-butyllithium (1.5 mol dm^{-3} in hexane, 166 cm^3, 0.25 mol) was

added dropwise over 35 min to the acetylene (29 g, 0.23 mol) in dry ether (300 cm^3) at −50 °C under argon. The mixture was stirred for 15 min and transferred by cannula over 45 min to freshly distilled acetic anhydride (40 cm^3, 0.41 mol) in dry ether (100 cm^3) at −78 °C under argon. The mixture was stirred for 2 h and saturated aqueous ammonium chloride (150 cm^3) was added dropwise with vigorous stirring, followed by aqueous ammonia (10%) until pH 8. The aqueous layer was extracted with ether (3 × 150 cm^3). The combined organic extracts were washed with saturated aqueous ammonium chloride (120 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (light petroleum–Et_2O; 7:3) gave the *acetylenic ketone* (29 g, 75%); R_f (light petroleum–Et_2O) 0.28; $\nu_{max}(CHCl_3)/cm^{-1}$ 2253–2214 (C≡C), 1672 (C=O) and 1141–1070 (C–O–C); δ_H(250 MHz; $CDCl_3$) 4.95 (1 H, t, *J* 4.4, OCHO), 3.99–3.82 (4 H, m, OCH_2CH_2O), 2.48 (2 H, t, *J* 7.5, $CH_2C{\equiv}C$), 2.30 (3 H, s, MeCO), 1.92 (2 H, dt, *J* 4.4 and 7.5, CH_2CHO); *m*/*z* 168 (12.2%, M^+), 87 (35, $CH_2OCHCH_2CH_2O$) and 73 (100, $CHOCH_2CH_2O$) (Found: C, 64.11; H, 7.30%; M^+, 168.0740. $C_9H_{12}O_3$ requires C, 64.27; H, 7.19%; *M*, 168.0786).

(2*S*)-7,7-Ethylenedioxyhept-3-yn-2-ol 6

(Experiment scaled up by U. Ghosh). *S*-Alpine-Borane[7] (0.5 mol dm^{-3} in THF, 600 cm^3, 0.3 mol) was added to the acetylenic ketone **5** (25 g, 0.15 mol) at room temperature under argon. The mixture was stirred for 3 days at room temperature and then cooled to 0 °C. Acetaldehyde (25.2 cm^3, 0.45 mol) was added and the solution stirred for 15 min. Ether (150 cm^3) was then added followed by ethanolamine (18.1 cm^3, 0.3 mol) and the stirring was continued at 0 °C for 30 min. The was concentrated under reduced pressure and the residue chromatographed (hexane–EtOAc, 6:4) to give the *propargylic alcohol* **6** (20.7 g, 82%); R_f (hexane–EtOAc, 5:5) 0.28; $[\alpha]_D^{20}$ −12.8 (*c* 1, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3590–3300 (OH), 2215 (C≡C) and 1195–1075 (C–O–C); δ_H(250 MHz; $CDCl_3$) 4.94 (1 H, t, *J* 4.7, OCHO), 4.46 (1 H, m, C*H*OH), 3.99–3.78 (4 H, m, OCH_2CH_2O), 2.31 (2 H, td, *J* 7.5 and 1.9, $CH_2C{\equiv}C$), 1.82 (2 H, dt, *J* 4.7 and 7.5, CH_2CHO) and 1.38 (3 H, d, *J* 6.6, MeCH) (Found: C, 63.35; H, 8.37. $C_9H_{14}O_3$ requires C, 63.51; H, 8.29).

(2*S*)-7,7-Ethylenedioxyhept-3-yn-2-yl (1*S*)-camphorsulfonate

(1*S*)-Camphorsulfonyl chloride (33 mg, 0.13 mmol) was stirred with the propargylic alcohol **6** (19 mg, 0.11 mmol) from above, 4-dimethylaminopyridine (5 mg, 0.04 mmol) and triethylamine (0.1 cm^3, 0.13 mmol) in dry dichloromethane (1 cm^3) under argon for 1 h at 0 °C. The mixture was poured onto ice and water and extracted with dichloromethane (2 × 10 cm^3). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Filtration through silica gel (2 g, washing through with light petroleum–Et_2O, 8:2) gave the *camphorsulfonates* (42 mg, 100%) in a ratio of 86:14 (determined by weighing the CH_2SO_2 peaks in the ^1H NMR spectrum); R_f (hexane–EtOAc, 6:4) 0.2; $\nu_{max}(CHCl_3)/cm^{-1}$ 2254 (C≡C), 1415–1367 (O–SO_2) and 1168–1052 (C–O–C and SO_2); δ_H(250 MHz; $CDCl_3$) 5.27 (1 H, tq, *J* 1.9 and 6.6, CHOSO), 4.91 (1 H, t, *J* 4.6, OCHO), 3.96–3.79 (4 H, m, OCH_2CH_2O), 3.74 (1 H, d, *J* 15.0, $CH_AH_BSO_2$ of the *SR* isomer), 3.70 (1 H, d, *J* 15.2, $CH_AH_BSO_2$ of the *SS* isomer), 3.17 (1 H, d, *J* 15.2, $CH_AH_BSO_2$ of the *SS* isomer), 3.05 (1 H, d, *J* 15.0, $CH_AH_BSO_2$ of the *SR* isomer), 2.52–1.34 (11 H, m, $C{\equiv}CCH_2CH_2$ and $CH_2CH_2CHCH_2CO$), 1.58 (3 H, d, *J* 6.6, OCH*Me*), 1.12 (3 H, s, C*Me*Me) and 0.87 (3 H, s, CMe*Me*); *m*/*z* 215 (2%, $C_{10}H_{17}SO_2$), 169 (3.38, $M^+ - C_{10}H_{17}SO_2$) and 73 (100, $CHOCH_2CH_2O$) (Found: $M^+ - C_{10}H_{17}SO_2$, 169.0862. $C_{19}H_{28}SO_6$ requires $M - C_{10}H_{17}SO_2$ 169.0865). Other runs gave us ratios of 85:15 and 88:12.

(2*S*)-7,7-Ethylenedioxyhept-3-yn-2-yl 3,5-dinitrobenzoate

(Experiment by U. Ghosh). 3,5-Dinitrobenzoyl chloride (1.63 g, 7.06 mmol) in dry dichloromethane (6 cm^3) was stirred with the propargylic alcohol (1 g, 5.88 mmol), 4-dimethylaminopyridine (50 mg, 0.41 mmol) and triethylamine (1 cm^3, 7.14 mmol) in dry dichloromethane (10 cm^3) at 0 °C under argon for 2 h. The mixture was diluted with ethyl acetate (30 cm^3) and washed with saturated aqueous sodium hydrogen carbonate (10 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 80:20) gave the 3,5-*dinitrobenzoate* (1.96 g, 91%); R_f (hexane–EtOAc, 7:3) 0.34; $\nu_{max}(CHCl_3)/cm^{-1}$ 3307 (≡CH), 2215 (C≡C) and 1730 (C=O); δ_H(250 MHz; $CDCl_3$) 9.13 (1 H, t, *J* 2.1, *p*-Ar), 9.17 (2 H, d, *J* 2.1, *o*-Ar), 5.74 (1 H, qt, *J* 4.6 and 1.9, CHOC=O), 4.95 (1 H, t, *J* 4.6, OCHO), 4.00–3.80 (4 H, m, OCH_2CH_2O), 2.35 (2 H, td, *J* 7.5 and 1.9, $CH_2C{\equiv}C$), 1.85 (2 H, dt, *J* 4.6 and 7.5, CH_2CHO) and 1.65 (3 H, d, *J* 6.7, *Me*CH); *m*/*z* 364 (0.3%, M^+), 153 (8, $M - C_7H_3N_2O_6$) and 73 (100, $CHOCH_2CH_2O$) (Found: C, 52.56; H, 4.34; N, 7.61%; M^+, 364.0880. $C_{16}H_{16}N_2O_8$ requires C, 52.75; H, 4.43; N, 7.69%; *M*, 364.0907). Recrystallisation from hexane–EtOAc (25 cm^3, 1.5:1) of 1.6 g gave 850 mg, mp 124–125 °C, $[\alpha]_D^{27}$ −9.1 (*c* 1, $CHCl_3$). Hydrolysis and derivatisation with *S*-camphorsulfonyl chloride showed that the ratio *SS* to *SR* was now 97:3. The mother liquor gave 730 mg, mp 108–112 °C, $[\alpha]_D^{27}$ −2.9 with a ratio *SS* to *SR* of 70:30. Recrystallisation from hexane–EtOAc (9 cm^3, 1.3:1) of 387 mg gave 260 mg, mp 125–126 °C, $[\alpha]_D^{27}$ −9.3 (*c* 1, $CHCl_3$). Hydrolysis and derivatisation with *S*-camphorsulfonyl chloride showed that the ratio *SS* to *SR* was now 99.4:0.6. The mother liquor gave 119 mg, mp 124–125 °C, $[\alpha]_D^{27}$ −8.7 with a ratio *SS* to *SR* of 97:3.

(1*S*)-7,7-Ethylenedioxyhept-3-yn-2-yl *N*-phenylcarbamate

(Experiment scaled up by U. Ghosh). The alcohol **6** (10 g, 58.76 mmol), triethylamine (9.82 cm^3, 70.49 mmol) and phenyl isocyanate (6.64 cm^3, 61.15 mmol) were stirred in dry dichloromethane (100 cm^3) at room temperature under argon for 4 h. The mixture was concentrated under reduced pressure and the residue chromatographed (hexane–EtOAc, 8:2) to give the *carbamate* (16 g, 55.3 mmol, 94%); R_f (hexane–EtOAc, 5:5) 0.41; $[\alpha]_D^{20}$ −52 (*c* 1.55 in $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 1733 (C=O) and 1071 (C–O–C); δ_H(250 MHz; $CDCl_3$) 7.38–7.00 (5 H, m, Ph), 6.82 (1 H, br s, NH), 5.46 (1 H, tq, *J* 1.9 and 6.6, MeC*H*OCO), 4.94 (1 H, t, *J* 4.6, OCHO), 3.96–3.79 (4 H, m, OCH_2CH_2O), 2.34 (2 H, dt, *J* 1.9 and 7.5, $CH_2C{\equiv}C$), 1.85 (2 H, dt, *J* 4.6 and 7.5, CH_2CHO) and 1.41 (3 H, d, *J* 6.6, CMe); *m*/*z* 289 (1.23%, M^+), 93 (40, $PhNH_2$) and 73 (100, $CHOCH_2CH_2O$) (Found: C, 66.43; H, 6.79; N, 4.85%; M^+, 289.1316. $C_{16}H_{19}NO_4$ requires C, 66.42; H, 6.62; N, 4.84%; *M*, 289.1314).

(3*Z*,2*S*)-7,7-Ethylenedioxyhept-3-en-2-yl *N*-phenylcarbamate 7

Following Dev,[25] the acetylene (15 g, 51.84 mmol) and catalyst (259 mg) in methanol (25 cm^3) were stirred under hydrogen at 25 °C for 5 h. The mixture was filtered through Celite and the solvent evaporated under reduced pressure. Chromatography (hexane–EtOAc, 6:4) gave the *carbamate* **7** (14.6 g, 97%); R_f (hexane–EtOAc, 7:3) 0.28; $[\alpha]_D^{20}$ +51.9 (*c* 1.9 in $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1726 (C=O), 1602 (C=C) and 1140 (C–O–C); δ_H(250 MHz; $CDCl_3$) 7.40–6.99 (5 H, m, Ph), 6.71 (1 H, br s, NH), 5.66–5.37 (3 H, m, C*H*=C*H*C*H*OCO), 4.87 (1 H, t, *J* 4.6, OCHO), 3.98–3.79 (4 H, m, OCH_2CH_2O), 2.31 (2 H, q, *J* 7.4, CH=CHCH_2), 1.75 (2 H, m, CH_2CHO) and 1.33 (3 H, d, *J* 6.4, CMe); *m*/*z* 291 (0.38%, M^+), 93 (72, $PhNH_2$) and 73 (100, $CHOCH_2CH_2O$) (Found: C, 66.10; H, 7.30; N, 4.96%; M^+, 291.1495. $C_{16}H_{21}NO_4$ requires C, 65.96; H, 7.26; N, 4.80%; *M*, 291.1471).

(2*E*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylhept-2-ene 8

(Experiment scaled up by U. Ghosh). *n*-Butyllithium (31 cm^3, 49.6 mmol) was added to a stirred solution of the carbamate **7** (14 g, 48.05 mmol) in dry THF (300 cm^3) at −78 °C under argon. After 5 min, the mixture was transferred to a stirred slurry of copper iodide (9.33 g, 49 mmol) and triphenylphos-

phine (25.7 g, 98 mmol) in dry ether (50 cm^3) at 0 °C under argon. After 1 h, dimethyl(phenyl)silyllithium (0.7 mol dm^{-3} in THF, 68 cm^3, 47.6 mmol) was added and stirring continued at 0 °C for 4 h. Saturated aqueous ammonium chloride (200 cm^3) was added and the aqueous layer was extracted with ether (2 × 150 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 8:2) gave the trans-*allylsilane* (10.2 g, 73%); R_f (hexane–EtOAc, 7:3) 0.61; $\nu_{max}(CDCl_3)/cm^{-1}$ 3052 (C=CH), 1265 (SiMe) and 1130–1112 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.49–7.46 (2 H, m, Ar *o* to Si), 7.34–7.32 (3 H, m, Ar *m* and *p* to Si), 5.19 (2 H, m, CH=CH), 4.77 (1 H, t, *J* 4.6, OCHO), 3.94–3.76 (4 H, m, OCH_2CH_2O), 1.76 (1 H, m, SiCH), 1.63 (3 H, d, *J* 5.0, *Me*CH), 1.59–1.37 (4 H, m, $SiCHCH_2CH_2$), 0.25 (3 H, s, $SiMe_AMe_B$) and 0.24 (3 H, s, $SiMe_AMe_B$); *m*/*z* 290 (4.13%, M^+) and 135 (100, $SiMe_2Ph$) (Found: C, 69.93; H, 8.78%; M^+, 290.1717. $C_{17}H_{26}O_2Si$ requires C, 70.29; H, 9.02%; *M*, 290.1702).

(2*S*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylheptan-2-ol 9

(Experiment scaled up by U. Ghosh). Thexylborane,[26] prepared from 2,3-dimethylbut-2-ene (1 mol dm^{-3} in THF, 36.2 cm^3, 36.2 mmol) and borane–THF (1 mol dm^{-3} in THF, 24.8 cm^3, 24.8 mmol), and the allylsilane **8** (6.0 g, 20.6 mmol) were stirred in THF (5 cm^3) at room temperature for 3 days. Sodium hydroxide (3 mol dm^{-3}, 30 cm^3) was then added at 0 °C followed by hydrogen peroxide (30%, 30 cm^3), and the mixture stirred for 1 h at room temperature and then heated at 50 °C for 1 h. Water (100 cm^3) was added, and the mixture extracted with ether (3 × 100 cm^3). The organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 6:4) gave the *alcohol* (5.53 g, 87%); $[\alpha]_D^{20}$ +1.41 (*c* 0.72 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3440 (OH), 1250 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.55–7.47 (2 H, m, *o*-Ar), 7.34–7.26 (3 H, m, *m*- and *p*-Ar), 4.73 (1 H, t, *J* 4.4, OCHO), 3.95–3.74 (5 H, m, OCH_2CH_2O and C*H*OH), 1.82 (1 H, br s, OH), 1.67–1.21 (7 H, m, $CH_2CHSiCH_2CH_2$), 1.05 (3 H, d, *J* 6.1, *Me*CH) and 0.28 (6 H, s, SiMe) (Found: C, 66.02; H, 9.16. $C_{17}H_{28}O_3Si$ requires C, 66.19; H, 9.15%).

(2*R*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylheptan-2-yl *p*-nitrobenzoate

(Experiment scaled up by U. Ghosh). *p*-Nitrobenzoic acid (6.44 g, 38.5 mmol), diethyl azodicarboxylate (6.07 cm^3, 38.5 mmol), the hydroxysilane **9** (4.75 g, 15.4 mmol) and triphenylphosphine (10.1 g, 38.6 mmol) were stirred in dry toluene (30 cm^3) at room temperature under argon for 40 min. The mixture was diluted with ethyl acetate (30 cm^3) and washed with saturated aqueous sodium hydrogen carbonate (30 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the p-*nitrobenzoate* (6.37 g, 90%); $[\alpha]_D^{20}$ −13.8 (*c* 1.3 in $CHCl_3$); R_f (hexane–EtOAc, 7:3) 0.34; $\nu_{max}(CDCl_3)/cm^{-1}$ 3052–2985 (Ar CH), 1720 (C=O), 1528 (CNO_2), 1348 (CNO_2), 1256 (SiMe) and 1139–1015 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 8.25 (2 H, d, *J* 8.8, Ar *o* to NO_2), 8.06 (2 H, d, *J* 8.8, Ar *m* to NO_2), 7.51–7.47 (2 H, m, Ar *o* to Si), 7.38–7.30 (3 H, m, Ar *m* and *p* to Si), 5.21 (1 H, m, CHOC=O), 4.73 (1 H, t, *J* 4.0, OCHO), 3.92–3.74 (4 H, m, OCH_2CH_2O), 1.86 (1 H, m, CHSi), 1.67–1.44 (6 H, m, $CH_2CHSiCH_2CH_2$), 1.27 (3 H, d, *J* 6.1, *Me*CH), 0.32 (3 H, s, $SiMe_AMe_B$) and 0.30 (3 H, s, $SiMe_AMe_B$); *m*/*z* 456 (0.23%, M^+), 135 (100, $SiMe_2Ph$) and 73 (90, $CHOCH_2CH_2O$) (Found: C, 61.43; H, 6.76; N, 2.86%; M^+ − H, 456.1858. $C_{24}H_{31}NO_6Si$ requires C, 62.99; H, 6.82; N, 3.06%; *M* − H, 456.1843).

(2*R*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylheptan-2-ol 10

(Experiment scaled up by U. Ghosh). Sodium hydroxide (1% in MeOH, 200 cm^3) and the *p*-nitrobenzoate (6.30 g, 13.58 mmol) were stirred at room temperature under argon for 1 h. Saturated aqueous ammonium chloride (100 cm^3) was added, and the mixture was extracted with ethyl acetate (3 × 80 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 7:3) gave the *alcohol* **10** (4.12 g, 97%); $[\alpha]_D^{20}$ −12.4 (*c* 1.13 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3440 (OH), 1250 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.55–7.47 (2 H, m, Ph), 7.34–7.26 (3 H, m, Ph), 4.73 (1 H, t, *J* 4.4, OCHO), 3.95–3.74 (5 H, m, OCH_2CH_2O and C*H*OH), 1.72 (1 H, br s, OH), 1.67–1.21 (7 H, m, $CH_2CHSiCH_2CH_2$), 1.10 (3 H, d, *J* 6.1, *Me*CH) and 0.28 (6 H, s, $SiMe_2$) (Found: C, 66.06; H, 9.24. $C_{17}H_{28}O_3Si$ requires C, 66.19; H, 9.15%).

(2*R*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylheptan-2-yl benzyl ether

Trifluoromethanesulfonic acid (0.17 cm^3, 2.75 mmol) was added dropwise at 0 °C to a mixture of benzyl 2,2,2-trichloroacetimidate (3.83 cm^3, 20.6 mmol) in dry cyclohexane (150 cm^3) and the hydroxysilane **10** (4.24 g, 13.76 mmol) in dry dichloromethane (45 cm^3) under argon at room temperature, whereupon a white solid (trichloroacetamide) precipitated. The mixture was stirred for 4.5 h, quenched with saturated sodium hydrogen carbonate (100 cm^3) and extracted with ethyl acetate (3 × 100 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the *benzyl ether* (5.31 g, 93%); R_f (hexane–EtOAc, 8:2) 0.33; $\nu_{max}(CDCl_3)/cm^{-1}$ 3015–2895 (ArH), 1210 (SiMe) and 1132–1045 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.51–7.24 (10 H, m, 2 × Ph), 4.69 (1 H, t, *J* 4.3, OCHO), 4.49 (1 H, d, *J* 11.7, OCH_AH_BPh), 4.31 (1 H, d, *J* 11.7, OCH_AH_BPh), 3.92–3.74 (4 H, m, OCH_2CH_2O), 3.49 (1 H, m, C*H*OBn), 1.77–1.25 (7 H, m, $CH_2CHSiCH_2CH_2$), 1.11 (3 H, d, *J* 6.0, *Me*CH) and 0.27 (6 H, s, $SiMe_2$); *m*/*z* 383 (0.67%, M^+ − Me), 135 (98, $SiMe_2Ph$), 91 (100, CH_2Ph) and 73 (35, $CHOCH_2CH_2O$) (Found: M^+ − Me, 383.2010. $C_{24}H_{34}O_3Si$ requires *M* − Me, 383.2042).

(5*S*)-1-Chloroacetyl-5-triphenylmethoxymethylpyrrolidin-2-one

n-Butyllithium (1.58 mol dm^{-3} in hexane, 2.2 cm^3, 3.4 mmol) was added to a stirred solution of Koga's lactam[12] (1 g, 2.8 mmol) in dry THF (8 cm^3) at −20 °C under argon. After 20 min, the solution was cooled to −78 °C and chloroacetyl chloride (0.27 cm^3, 3.4 mmol) in dry THF (1 cm^3) added dropwise. The solution was kept at room temperature overnight and quenched with aqueous potassium carbonate (1 mol dm^{-3}, 30 cm^3). The mixture was extracted with diethyl ether (3 × 50 cm^3) and the combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 8:2) gave the *imide* (0.85 g, 68%) as prisms, mp 187–189 °C (from EtOH); R_f (hexane–EtOAc, 8:2) 0.20; $\nu_{max}(CHCl_3)/cm^{-1}$ 1755 (C=O), 1720 (C=O) and 1520 (Ph); δ_H(250 MHz; $CDCl_3$) 7.37–7.19 (15 H, m, Ph_3CO), 4.67 (1 H, d, *J* 22, CH_AH_BCl), 4.61 (1 H, d, *J* 22, CH_AH_BCl), 4.43 (1 H, m, CHN), 3.59 (1 H, dd, *J* 3.5 and 10.1, $CH_AH_BOCPh_3$), 3.29 (1 H, dd, *J* 2.6 and 10.1, $CH_AH_BOCPh_3$), 2.98 (1 H, dt, *J* 18.0 and 10.3, $CH_2CH_AH_BCO$), 2.48 (1 H, ddd, *J* 2.1, 9.0 and 18.0, $CH_2CH_AH_BCO$) and 2.19–2.04 (2 H, m, CH_2CH_2CO); *m*/*z* 259 (1.06%, $M^+ - C_7H_9ClNO_2$), 243 (100, CPh_3), 174 (16, M − $OCPh_3$) and 139 (10, M − $OCPh_3$ − Cl) (Found: $M^+ - C_7H_9ClNO_2$, 259.1115. $C_{26}H_{24}ClNO_3$ requires $M - C_7H_9ClNO_2$, 259.1123).

(5*S*)-1-(Diethoxyphosphorylacetyl)-5-triphenylmethoxymethylpyrrolidin-2-one

Triethyl phosphite (2 cm^3, 11 mmol) and the chloroacetylimide (0.25 g, 0.57 mmol) were heated at 120 °C for 5 h. Triethyl phosphite was removed by distillation (50 °C at 1 mmHg) and the residue chromatographed (CH_2Cl_2–MeOH, 96:4) to give the *phosphonate* (0.294 g, 95%) as prisms, mp 80–82 °C (from hexane); R_f (MeOH–CH_2Cl_2, 0.5:9.5) 0.41; $\nu_{max}(CHCl_3)/cm^{-1}$

1735 (C=O), 1685 (C=O), 1250 (P=O) and 1020 (POEt); δ_H(250 MHz; $CDCl_3$) 7.38–7.21 (15 H, m, 3 × Ph), 4.48 (1 H, m, CHN), 4.13 [4 H, dq, *J* 13.8 and 6.9, P(OCH_2Me)$_2$], 3.54–2.80 (4 H, m, CH_2OCPh$_3$ and PCH_2CO), 2.56–1.92 (4 H, m, CH_2CH_2CO) and 1.34 [6 H, dt, *J* 3.9 and 6.9, P(OCH$_2$*Me*)$_2$]; *m*/*z* 292 (19.05%, $M^+ - CPh_3$), 243 (100, CPh_3), 179 [76, COCH_2P(O)(OEt)$_2$] and 151 [17, CH_2P(O)(OEt)$_2$] (Found: $M^+ - CPh_3$, 292.0951. $C_{30}H_{34}NO_6P$ requires $M - CPh_3$, 292.0951).

(2′*E*,6′*S*,8′*R*,5*S*)-1-[8′-Benzyloxy-6′-dimethyl(phenyl)silylnon-2′-enoyl]-5-triphenylmethoxymethylpyrrolidin-2-one 11

The acetal (3.66 g, 9.2 mmol) was refluxed in acetone (100 cm^3) and water (50 cm^3) with toluene-*p*-sulfonic acid (1.35 g, 7.1 mmol) for 1.5 h. The acetone was evaporated off under reduced pressure and ether (150 cm^3) was added. Saturated aqueous sodium hydrogen carbonate (60 cm^3) was added at 0 °C, the organic layer dried ($MgSO_4$) and evaporated under reduced pressure to give the aldehyde (3 g, 98%), which was used without further purification. Meanwhile, sodium bis(trimethylsilyl)-amide (1 mol dm^{-3} in THF, 9.6 cm^3, 9.6 mmol) was added to a stirred solution of the phosphonate (7.9 g, 14.7 mmol) in dry THF (40 cm^3) at room temperature under argon and the mixture stirred for 45 min to prepare the anion **12**. The aldehyde (3 g, 8.1 mmol) in dry THF (5 cm^3) was added dropwise, the mixture was stirred for 3 h, and poured into saturated aqueous ammonium chloride (100 cm^3). The mixture was extracted with ether (3 × 100 cm^3), the combined organic extracts were dried ($MgSO_4$) and the solvents were evaporated under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the *imide* **11** (5.2 g, 77%); R_f (hexane–EtOAc, 8:2) 0.28; $[\alpha]_D^{20}$ −52.9 (*c* 1.75, $CHCl_3$); ν_{max}($CDCl_3$)/cm^{-1} 3053–2985 (ArH), 1733 (C=O), 1673 (C=O), 1629 (C=C), 1264 (SiMe) and 1153–1021 (SiPh and C–O–C); δ_H(250 MHz; $CDCl_3$) 7.51–7.17 (26 H, m, 5 × Ph and COC*H*=CH), 6.93 (1 H, dt, *J* 15.4 and 6.9, COCH=C*H*), 4.50 (1 H, d, *J* 11.6, OCH_AH$_B$Ph), 4.48 (1 H, m, CHN), 4.30 (1 H, d, *J* 11.6, OCH$_A$$H_B$Ph), 3.49 (2 H, m, C*H*OBn and CH_AH$_B$OCPh$_3$), 3.12 (1 H, d, *J* 8.8, CH$_A$$H_B$OCPh$_3$), 2.94 (1 H, dt, *J* 17.9 and 10.3, CH_AH$_B$CON), 2.47 (1 H, dd, *J* 9.1 and 17.9, CH$_A$$H_B$CON), 2.17–1.20 (9 H, m, CH_2CH$_2$CON and CH$_2$CH$_2$-CHSiCH$_2$), 1.13 (3 H, d, *J* 5.9, CH*Me*) and 0.27 (6 H, s, SiMe$_2$); *m*/*z* 492 (1.59%, $M^+ - CPh_3$), 243 (100, CPh_3) and 135 (40, SiMe$_2$Ph); *m*/*z* (LREIMS) 735 (M^+) (Found: $M^+ - CPh_3$, 492.2567. $C_{48}H_{53}NO_4Si$ requires $M - CPh_3$, 492.2570).

(3′*S*,6′*S*,8′*R*,5*S*)-1-{8′-Benzyloxy-3′,6′-bis[dimethyl(phenyl)-silyl]nonanoyl}-5-triphenylmethoxymethylpyrrolidin-2-one 13

Dimethyl(phenyl)silyllithium (0.7 mol dm^{-3} in THF, 41.5 cm^3, 29 mmol) was stirred with a suspension of dry copper(I) iodide (2.74 g, 14.4 mmol) in dry THF (50 cm^3) at 0 °C under argon for 45 min, and then transferred by cannula to a premixed solution of the imide **11** (3.5 g, 4.75 mmol) and anhydrous magnesium bromide[27] (1.75 g, 9.51 mmol) in dry THF (35 cm^3) at −78 °C under argon. The mixture was stirred for 4 h at −78 °C, quenched with basic aqueous ammonium chloride (120 cm^3) and extracted with ether (3 × 100 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (light petroleum–Et_2O, 8:2) gave the *pyrrolidinone* **13** (3.9 g, 4.47 mmol, 94%); R_f (hexane–EtOAc, 8:2) 0.32; $[\alpha]_D^{20}$ −30.7 (*c* 1.91 in $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 1733 (C=O), 1685 (C=O), 1212 (SiMe) and 1047 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.47–7.16 (30 H, m, 6 × Ph), 4.43 (1 H, d, *J* 11.7, OCH_AH$_B$Ph), 4.26 (1 H, m, CHN), 4.23 (1 H, d, *J* 11.7, OCH$_A$$H_B$Ph), 3.39 (1 H, dd, *J* 4.1 and 9.6, CH_AH$_B$OCPh$_3$), 3.35 (1 H, m, C*H*OBn), 3.12 (1 H, dd, *J* 2.6 and 9.6, CH$_A$$H_B$OCPh$_3$), 3.02 (1 H, dd, *J* 9.0 and 17.6, SiCHCH_AH$_B$CON), 2.79 (1 H, dt, *J* 18.2 and 10.3, CH$_2$CH_AH$_B$CO), 2.68 (1 H, dd, *J* 4.7 and 17.6, SiCHCH$_A$$H_B$CON), 2.40 (1 H, dd, *J* 8.9 and 18.2, CH$_2$CH$_A$$H_B$-CO), 1.89–1.14 (10 H, m, CH_2CH$_2$CON and SiCHCH$_2$CH$_2$-CHSiCH$_2$), 1.05 (3 H, d, *J* 5.9, CH*Me*), 0.21 (3 H, s, SiMe_A-Me$_B$), 0.20 (3 H, s, SiMe$_A$$Me_B$ or SiMe_CMe$_D$), 0.17 (3 H, s, SiMe$_A$$Me_B$ or SiMe$_C$$Me_D$) and 0.16 (3 H, s, SiMe$_A$$Me_B$ or SiMe$_C$$Me_D$); *m*/*z* 614 (3.43%, $M^+ - CPh_3 - Me + H$), 494 (10, $M - CPh_3 - SiMe_2Ph + H$), 243 (88, CPh_3), 135 (100, SiMe$_2$Ph) and 91 (47, CH$_2$Ph); *m*/*z* (LREIMS) 871 (M^+) (Found: $M^+ - CPh_3 - Me + H$, 614.3101. $C_{56}H_{65}NO_4Si_2$ requires $M - CPh_3 - Me + H$, 614.3122).

Methyl (3*S*,6*S*,8*R*)-8-benzyloxy-3,6-bis[dimethyl(phenyl)silyl]-nonanoate 14

Methylmagnesium bromide (3.0 mol dm^{-3} in THF, 15 cm^3, 15 mmol) was added to a stirred solution of freshly distilled methanol (1 cm^3, 25 mmol) in dry THF (10 cm^3) at 0 °C under argon. After 10 min, the imide **13** (4.4 g, 5.04 mmol) in dry THF (5 cm^3) was added and the solution stirred for 20 h at room temperature. Saturated aqueous ammonium chloride (60 cm^3) was added and the mixture extracted with dichloromethane (3 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 8:2) gave the *methyl ester* (2.27 g, 82%) contaminated with its diastereoisomer at C-3 in a ratio of 67:33; R_f (hexane–EtOAc, 8:2) 0.55; $[\alpha]_D^{20}$ −7.36 (*c* 0.62 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1730 (C=O), 1249 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.44–7.21 (15 H, m, 3 × Ph), 4.45 (1 H, d, *J* 11.8, CH_AH$_B$Ph), 4.25 (1 H, d, *J* 11.8, CH$_A$$H_B$-Ph), 3.52 (3 H, s, CO_2*Me*), 3.32 (1 H, m, C*H*OBn), 2.26–2.04 (2 H, m, CH$_2$CO$_2$), 1.69–1.11 (6 H, m, 3 × CH$_2$), 1.06 (3 H, d, *J* 6, *Me*CH) and 0.7 (12 H, s, 2 × SiMe$_2$Ph) with a doublet at 1.07 (*J* 6, *Me*CH) from the minor isomer; *m*/*z* 546 (15%, M^+), 531 (66), 455 (47), 135 (100, PhMe$_2$Si), 91 (93, PhCH$_2$) (Found: M^+, 546.3029. $C_{33}H_{46}O_3Si_2$ requires *M*, 546.2985).

Methyl (2*R*,3*S*,6*S*,8*R*)-8-benzyloxy-3,6-bis[dimethyl(phenyl)-silyl]-2-methylnonanoate 15

n-Butyllithium (1.5 mol dm^{-3} in hexane, 2.35 cm^3, 3.51 mmol) was added dropwise to a solution of 1,1,1,3,3,3-hexamethyldisilazane (0.925 cm^3, 4.38 mmol) in dry THF (20 cm^3) at −5 °C under argon and stirred for 30 min. The ester **14** (1.6 g, 2.92 mmol) in THF (5 cm^3) was added slowly at this temperature under argon. After 40 min, the solution was cooled to −78 °C and methyl iodide (1.82 cm^3, 29.2 mmol) in DMPU (5 cm^3) was added. The mixture was stirred for 8 h at −78 °C, and the temperature then allowed to rise slowly to 0 °C, and quenched by pouring into saturated aqueous ammonium chloride (20 cm^3). After extraction by diethyl ether (3 × 50 cm^3), the combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc; 9:1) gave the *methyl ester* (1.51 g, 92%); R_f (hexane–EtOAc, 8:2) 0.58; $[\alpha]_D^{20}$ +3.32 (*c* 1.05 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1732 (C=O), 1248 (SiMe), 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.46–7.24 (15 H, m, 3 × Ph), 4.45 (1 H, d, *J* 11.76, OCH_AH$_B$Ph), 4.30 (1 H, d, *J* 11.76, OCH$_A$$H_B$Ph), 3.52 (3 H, s, OMe major isomer), 3.50 (s, OMe minor isomer), 3.31 (1 H, m, C*H*OBn), 2.54 (1 H, br q, *J* 7.12, MeC*H*), 1.63 (1 H, ddd, *J* 14.1, 9.3 and 3.7, SiC*H*CHMeCO), 1.40–1.11 [8 H, m, SiCH(CH$_2$)$_2$CHSiCH$_2$], 1.07 (d, *J* 6.5, *Me*CHOBn or CH*Me*CO minor isomer), 1.05 (3 H, d, *J* 6.5, *Me*CHOBn or CH*Me*CO major isomer), 0.95 (3 H, d, *J* 7.12, CH*Me*CO or *Me*CHOBn), 0.24 (s, SiMe minor isomer), 0.22 (3 H, s, SiMe), 0.21 (3 H, s, SiMe) and 0.18 (6 H, s, 2 × SiMe); *m*/*z* 560 (20%, M^+), 483 (51), 469 (84, $M - PhCH_2$), 235 (60), 135 (100, PhMe$_2$Si) and 91 (93, PhCH$_2$) (Found: M^+, 560.3160. $C_{34}H_{48}O_3Si_2$ requires *M*, 560.3142).

Methyl (2*S*,3*S*,6*S*,8*R*)-8-benzyloxy-3,6-dihydroxy-2-methyl-nonanoate

Mercuric acetate (1.13 g, 3.53 mmol) was stirred with the bissilane (0.91 g, 1.62 mmol) in peracetic acid (32% in AcOH, 26 cm^3) at room temperature under argon for 60 min. The mixture was diluted with ether (80 cm^3), washed with water (40 cm^3) then very carefully with saturated aqueous sodium hydrogen

carbonate (40 cm^3) and sodium thiosulfate (60 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 6:4) gave the *diol* (0.39 g, 74%); R_f (hexane–EtOAc, 5:5) 0.20; $[\alpha]_D^{20}$ −24.5 (*c* 0.645 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3680–3450 (OH) and 1720 (C=O); δ_H(250 MHz; $CDCl_3$) 7.36–7.26 (5 H, m, Ph), 4.66 (1 H, d, *J* 11.3, OC$H_A$$H_B$Ph), 4.39 (1 H, d, *J* 11.3, OCH$_A$$H_B$Ph), 3.82 (2 H, m, 2 × C*H*O), 3.68 (3 H, s, and 1 H, m, OMe and C*H*O), 2.52 (1 H, quintet, *J* 7.5, MeC*H*CO), 1.79–1.42 [6 H, m, CHOH-(CH_2)$_2$CHOHCH_2], 1.25 (3 H, d, *J* 4.92, *Me*CHOBn) and 1.16 (3 H, d, *J* 7.04, *Me*CHCO); *m*/*z* 325 (26%, M^+ + H), 200 (36), 157 (36), 91 (100, $PhCH_2$) (Found: M^+ + H, 325.2009. $C_{18}H_{28}O_5$ requires *M* + H, 325.2015).

(2*S*,3*S*,6*S*,8*R*)-8-Benzyloxy-3,6-dihydroxy-2-methylnonanoic acid 16

Following Corey,[28] lithium hydroxide (0.53 g, 12.6 mmol) and the methyl ester (0.41 g, 1.26 mmol) were stirred in water (12 cm^3) and methanol (25 cm^3) for 15 h at room temperature. The solvents were evaporated under reduced pressure, saturated aqueous sodium hydrogen carbonate (5 cm^3) was added and the mixture washed with ether (10 cm^3). The aqueous layer was acidified with hydrochloric acid (6 mol dm^{-3}) and extracted with ethyl acetate (3 × 20 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the *acid* **16** (0.38 g, 97%); R_f (EtOAc) 0.1; ν_{max}(film)/cm^{-1} 3198–2983 (OH) and 1744 (C=O); δ_H(250 MHz; $CDCl_3$) 7.38–7.26 (5 H, m, Ph), 4.68 (1 H, d, *J* 11.2, OC$H_A$$H_B$Ph), 4.39 (1 H, d, *J* 11.2, OCH$_A$$H_B$Ph), 3.88–3.80 (2 H, m, 2 × C*H*O), 3.6 (1 H, m, C*H*O), 2.50 (1 H, quintet, *J* 7.1, MeC*H*CO), 1.81–1.51 [6 H, m, CHOH(CH_2)$_2$CHOHCH_2], 1.25 (3 H, d, *J* 5.8, *Me*CHOBn) and 1.21 (3 H, d, *J* 7.1, *Me*CHCO); *m*/*z* 292 (53%, $M^+ - H_2O$), 251 (46), 223 (100), 215 (54), 197 (70) and 104.9 (55) (Found: $M^+ - H_2O$, 292.1673; M^+ − OBn + H, 204.1367. $C_{17}H_{26}O_5$ requires *M* − H_2O, 292.1675; *M* − OBn + H, 204.1362).

(3*S*,4*S*,3′*S*,5′*R*)-4-(5′-Benzyloxy-3′-phenylsulfonyloxyhexyl)-3-methyloxetan-2-one 17

Following Adam,[29] benzenesulfonyl chloride (0.148 cm^3, 1.16 mmol) and the acid **16** (120 mg, 0.39 mmol) were stirred in anhydrous pyridine (0.625 cm^3) at 0 °C overnight, then stirred for 3 h at room temperature. The mixture was poured onto crushed ice (about 4 cm^3) and extracted with ether (3 × 8 cm^3). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate (5 cm^3) and water (5 cm^3), dried ($MgSO_4$) and the ether evaporated off at reduced pressure. Chromatography (light petroleum–Et_2O; 3:7) gave the β-*lactone* **17** (107 mg, 64%); ν_{max}(film)/cm^{-1} 1825 (C=O), 1360 and 1186 (OSO_2); δ_H(250 MHz; $CDCl_3$) 7.87 (2 H, dd, *J* 8.0 and 2.3, Ar *o* to SO_2), 7.64 (1 H, td, *J* 8.0 and 2.3, Ar *p* to SO_2), 7.51 (2 H, t, *J* 8.0, Ar *m* to SO_2), 7.37–7.17 (5 H, m, OCH_2Ph), 4.76 (1 H, m, C*H*OSO_2), 4.52 (1 H, d, *J* 11.7, C$H_A$$H_B$Ph), 4.27 (1 H, d, *J* 11.7, CH$_A$$H_B$Ph), 3.92 (1 H, m, C*H*OCO), 3.48 (1 H, m, C*H*OBn), 3.06 (1 H, qd, *J* 7.5 and 4.0, MeC*H*CO), 1.93–1.50 [6 H, m, CH_2CHOH(CH_2)$_2$], 1.29 (3 H, d, *J* 7.5, *Me*CHCO) and 1.09 (3 H, d, *J* 6.1, *Me*CHOBn); *m*/*z* 432 (15%, M^+), 298 (69), 274 (71), 246 (58), 173 (60), 91 (100, $PhCH_2$) (Found: M^+, 432.1602. $C_{23}H_{28}O_6S$ requires *M*, 432.1606).

(+)-Methyl (2*S*,3*S*,6*R*,8*R*)-8-*O*-benzylnonactate 18

Toluene-*p*-sulfonic acid (6 mg, 0.027 mmol) and the lactone **17** (60 mg, 0.138 mmol) were stirred in anhydrous methanol (3 cm^3) under argon for 3 days at room temperature. The methanol was evaporated off under reduced pressure and saturated aqueous sodium hydrogen carbonate (5 cm^3) added. The mixture was extracted with ether (3 × 10 cm^3). The extract was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum–Et_2O, 7:3) gave an inseparable mixture of the benzyl ethers of methyl nonactate **18** and its C-2,3-diastereoisomer (36 mg, 85%); R_f (light petroleum–Et_2O, 7:3) 0.34; ν_{max}(film)/cm^{-1} 1738 (C=O); δ_H(250 MHz; $CDCl_3$) 7.38–7.25 (5 H, m, Ph), 4.56 (1 H, d, *J* 11.5, C$H_A$$H_B$Ph), 4.44 (1 H, d, *J* 11.5, CH$_A$$H_B$Ph), 4.16–3.96 (2 H, m, 2 × C*H*O), 3.74–3.54 (1 H, m, C*H*OBn), 3.57 (3 H, s, O*Me*), 2.62–2.45 (1 H, m, MeC*H*CO), 2.07–1.94 (2 H, m, CH_2), 1.75–1.42 (4 H, m, 2 × CH_2), 1.19 (3 H, d, *J* 6.1, CH*Me*, **18**), 1.18 (3 H, d, *J* 6.1, CH*Me* of diastereoisomer), 1.10 (3 H, d, *J* 7.0, CH*Me*, **18**) and 1.09 (3 H, d, *J* 6.1, CH*Me* of diastereoisomer); *m*/*z* 306 (4%, M^+), 219 (28), 200 (55), 157 (23) and 91 (100) (Found: M^+, 306.1850. $C_{18}H_{26}O_4$ requires *M*, 306.1831).

(+)-Methyl (2*S*,3*S*,6*R*,8*R*)-nonactate 2 and (+)-methyl (2*R*,3*R*,6*R*,8*R*)-nonactate 19

The mixture of benzyl ethers (48 mg, 0.156 mmol) and palladium on carbon (10% Pd, 12 mg) in absolute ethanol (2 cm^3) were stirred vigorously under hydrogen for 24 h. The mixture was filtered through Celite and evaporated to give the methyl (+)-nonactate **2** and its isomer **19**. Chromatography (SiO_2, CH_2Cl_2–Et_2O, 1:1) gave the ester **2** (23 mg, 68%); R_f (CH_2Cl_2–Et_2O; 1:1) 0.38; $[\alpha]_D^{20}$ +19.1 (*c* 0.45, $CHCl_3$) [lit.,[30] +22.1 (*c* 0.7, $CHCl_3$)]; ν_{max}(film)/cm^{-1} 3700–3100 (OH) and 1730 (C=O); δ_H(250 MHz; $CDCl_3$) 4.20–3.92 (3 H, m, C*H*OH + 2 × C*H*OC), 3.68 (3 H, s, OMe), 2.52 (1 H, quintet, *J* 7, MeC*H*CO), 2.06–1.90 (2 H, m, CH_2), 1.79–1.56 (4 H, m, 2 × CH_2), 1.19 (3 H, d, *J* 6.3, CH*Me*), 1.12 (3 H, d, *J* 7, CH*Me*); *m*/*z* 217 (80%, M^+ + H), 199 (30), 157 (90), 129 (100), 125 (59) (Found: M^+ + H, 217.1436. $C_{11}H_{20}O_4$ requires *M* + H, 217.1440), and its isomer **19** (7 mg, 21%); R_f (CH_2Cl_2–Et_2O; 1:1) 0.42; $[\alpha]_D^{20}$ +3.5 (*c* 0.4, $CHCl_3$); δ_H(250 MHz; $CDCl_3$) 4.28–3.97 (3 H, m, C*H*OH + 2 × C*H*OC), 3.68 (3 H, s, OMe), 2.53 (1 H, quintet, *J* 7, MeC*H*CO), 2.09–1.98 (2 H, m, CH_2), 1.69–1.54 (4 H, m, 2 × CH_2), 1.19 (3 H, d, *J* 6.3, CH*Me*), 1.11 (3H, d, *J* 6.9, CH*Me*) with both spectra in agreement with literature data.[15] The ratio of enantiomers (92:8 and 55:45, respectively) was measured by phosphorus NMR using (4*R*,5*R*)-2-chloro-4,5-dimethyl-1,3,2-dioxaphospholane 2-oxide (Fluka), following Shapiro.[16]

(2*E*)-Hepta-2,6-dienoic acid

Following Katzenellenbogen,[22] *n*-butyllithium (1.5 mol dm^{-3} in hexane, 170 cm^3, 0.255 mol) was added to a solution of distilled diisopropylamine (35.8 cm^3, 0.255 mol) in dry THF (200 cm^3) at −78 °C under argon. The solution was stirred for 20 min at 0 °C and then cooled to −78 °C. Crotonic acid (10 g, 0.116 mol) in dry THF (50 cm^3) was added dropwise, the solution was warmed to 0 °C and stirred for 30 min. The solution was cooled to −78 °C and, maintaining an argon atmosphere, copper iodide (48 g, 0.255 mol) added. The slurry was then stirred vigorously at −78 °C for 1 h. Allyl bromide (21.6 cm^3, 0.232 mol) in dry THF (20 cm^3) was added and stirring continued overnight allowing the mixture to warm to room temperature. Sodium hydroxide (2 mol dm^{-3}, 350 cm^3) was added and the THF evaporated off under reduced pressure. The suspension was then filtered through a pad of Celite and the filtrate extracted with ether (2 × 300 cm^3). The aqueous layer was adjusted to pH 2 with hydrochloric acid (6 mol dm^{-3}) and extracted with ether (3 × 300 cm^3). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 4:6) gave the acid (7.46 g, 51%); R_f (hexane–EtOAc, 4:6) 0.55; ν_{max}($CHCl_3$)/cm^{-1} 3600–2400 (OH), 1715 (C=O) and 1660 (C=C); δ_H(250 MHz; $CDCl_3$) 11.2 (1 H, br s, COH), 7.07 (1 H, dt, *J* 15.6 and 6.4, C*H*CHCO), 5.87–5.71 (2 H, m, CHC*H*CO and CH_2C*H*CH_2), 5.09–4.98 (2 H, m, CH_2=CH) and 2.38–2.16 (4 H, m, CH_2CH_2).

(2′*E*,5*S*)-1-(Hepta-2′,6′-dienoyl)-5-triphenylmethoxymethylpyrrolidin-2-one 20

Oxalyl chloride (0.76 cm^3, 8.7 mmol) and the acid (1 g, 7.9 mmol) were stirred in dichloromethane (5 cm^3) at room tem-

perature for 2 h. The solvent and excess reagent were evaporated off under reduced pressure and the acid chloride dissolved in dry THF (5 cm^3). *n*-Butyllithium (1.63 mol dm^{-3} in hexane, 5.8 cm^3, 9.5 mmol) was added to a stirred solution of Koga's lactam [12] (2.7 g, 7.9 mmol) in dry THF (20 cm^3) at −20 °C under argon. After 0.5 h, the solution was cooled to −78 °C and the acid chloride solution added. The solution was allowed to warm from −78 °C to −20 °C over 4 h and quenched with basic aqueous ammonium chloride (50 cm^3). The mixture was extracted with ether (3 × 100 cm^3), the organic layers dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (light petroleum–Et_2O, 8:2) gave the *pyrrolidinone* **20** (2.68 g, 76%); R_f (light petroleum–Et_2O, 7:3) 0.32; $\nu_{max}(CHCl_3)$/cm^{-1} 1730 (C=O), 1675 (C=O), 1635 (C=C) and 1530 (Ph); δ_H(250 MHz; $CDCl_3$) 7.46–7.18 (16 H, m, Ph_3CO and C=CHCO), 7.07 (1 H, dt, *J* 15.4 and 6.8, C*H*=CHCO), 5.83 (1 H, ddt, *J* 10.1, 16.7 and 5.8, CH_2=C*H*), 5.06 (2 H, m, CH_2=CHCH_2), 4.53 (1 H, m, CHN), 3.55 (1 H, dd, *J* 4.3 and 9.8, C$H_A$$H_B$OCPh$_3$), 3.13 (1 H, dd, *J* 2.7 and 9.8, $CH_A$$H_B$OCPh$_3$), 2.93 (1 H, dt, *J* 10.3 and 17.9, C$H_A$$H_B$CO), 2.55–2.22 (5 H, m, C$H_2$$CH_A$$H_B$CO and C$H_2$CH=$CH_2$) and 2.05 (2 H, m, CH=CHCH_2); *m*/*z* 243 (100%, CPh_3), 222 (43, $M^+ - CPh_3$) and 109 (88, $COCHCH_2CH_2CHCH_2$) (Found: $M^+ - CPh_3$, 222.1161. $C_{31}H_{31}NO_3$ requires $M - CPh_3$, 222.1174).

(5*S*,3′*S*)-1-[3′-Dimethyl(phenyl)silylhept-6′-enoyl]-5-triphenylmethoxymethylpyrrolidin-2-one 21

Dimethyl(phenyl)silyl cuprate (13 mmol, based on CuI) was added by cannula to the imide **20** (3 g, 6.5 mmol) and anhydrous magnesium bromide (3.56 g, 19.5 mmol) in dry THF (40 cm^3) at −78 °C under argon, and the mixture stirred for 3 h. Basic aqueous ammonium chloride (50 cm^3) was added and the mixture extracted with ether (3 × 70 cm^3). The combined organic extracts were washed with basic aqueous ammonium chloride, dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography (light petroleum–Et_2O, 8:2) gave an inseparable mixture of the diastereoisomeric *imides* (3.42 g, 85%) in a ratio of 91:9 (determined by integration of the C*H*CH_2OCPh$_3$ peaks in the ^{1}H NMR spectrum); R_f (light petroleum–Et_2O, 8:2) 0.31; $\nu_{max}(CHCl_3)$/cm^{-1} 1740 (C=O), 1695 (C=O), 1540 (Ph) and 1115 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.53–7.20 (20 H, m, 4 × Ph), 5.69 (1 H, ddt, *J* 10.3, 17.1 and 6.7, C*H*=CH_2), 4.88 (2 H, m, CH=CH_2), 4.36 (1 H, m, CHN), 3.43 (1 H, dd, *J* 4.3 and 9.6, C$H_A$$H_B$OCPh$_3$), 3.15 (1 H, dd, *J* 2.6 and 9.6, $CH_A$$H_B$OCPh$_3$), 3.06 (1 H, dd, *J* 9.1 and 18.2, SiCHC$H_A$$H_B$CO), 2.88–2.83 (2 H, m, SiCHC$H_A$$H_B$CO and CH_2C$H_A$$H_B$CO), 2.41 (1 H, ddd, *J* 1.8, 9.6 and 17.8, $CH_2CH_A$$H_B$CO), 2.03–1.85 (4 H, m, CH_2CH_2CHN and SiCHCH_2CH_2), 1.61–1.53 (2 H, m, SiCHC$H_2$$CH_2$), 1.36 (1 H, m, SiCH), 0.32 (3 H, s, Si*Me*$_A$Me$_B$) and 0.31 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 601 (9.27%, M^+), 586 (7, M − Me), 358 (50, M − CPh_3), 243 (100, CPh_3) and 135 (47, $SiMe_2Ph$) (Found: M^+, 601.3007. $C_{39}H_{43}NO_3Si$ requires *M*, 601.3012).

(5*S*,3′*S*)-1-[3′-Dimethyl(phenyl)silyl-6′-oxohexanoyl]-5-triphenylmethoxymethylpyrrolidin-2-one and (5*S*,3′*R*)-1-[3′-dimethyl(phenyl)silyl-6′-oxohexanoyl]-5-triphenylmethoxymethylpyrrolidin-2-one

Following Corey,[31] osmium tetroxide (0.04 mol dm^{-3} in toluene, 0.5 cm^3, 0.019 mmol) and the imide (1.13 g, 1.8 mmol) were stirred in THF (21 cm^3) and water (7 cm^3) at 0 °C for 10 min. The mixture was allowed to warm to room temperature and sodium periodate (1.16 g, 5.4 mmol) was added over 30 min, and stirring was continued for 2 h. The mixture was poured into saturated aqueous ammonium chloride (50 cm^3), and extracted with ether (2 × 100 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 7:3) gave a mixture of the two diastereoisomers (0.96 g, 83%). A second chromatography (light petroleum–Et_2O, 6:4) gave the (3′S)-*aldehyde*; R_f (light petroleum–Et_2O, 6:4) 0.18; $\nu_{max}(CHCl_3)$/cm^{-1} 1720 (C=O), 1715 (C=O), 1680 (C=O), 1225 (SiMe) and 1105 (SiPh); δ_H(400 MHz; $CDCl_3$) 9.60 (1 H, br s, CHO), 7.55–7.19 (20 H, m, 4 × Ph), 4.34 (1 H, m, CHN), 3.47 (1 H, dd, *J* 4.0 and 9.6, C$H_A$$H_B$OCPh$_3$), 3.16 (1 H, dd, *J* 2.5 and 9.6, $CH_A$$H_B$OCPh$_3$), 3.02 (1 H, dd, *J* 8.6 and 17.2, SiCHC$H_A$$H_B$CO), 2.91–2.84 (2 H, m, SiCHC$H_A$$H_B$CO and CH_2C$H_A$$H_B$CON), 2.45 (1 H, ddd, *J* 9.6 and 17.8, $CH_2CH_A$$H_B$CON), 2.35 (2 H, m, SiCHCH_2-CH_2), 2.02–1.80 (3 H, m, SiCH and C$H_2$$CH_2$CON), 1.58–1.54 (2 H, m, SiCHC$H_2$$CH_2$), 0.37 (3 H, s, Si*Me*$_AMe_B$) and 0.35 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 603 (0.14%, M^+), 243 (100, CPh_3) and 135 (39, $SiMe_2Ph$) (Found: M^+, 603.2818. $C_{38}H_{41}NO_4Si$ requires *M*, 603.2804), and the (3′R)-*aldehyde*; R_f (light petroleum–Et_2O, 6:4) 0.28; $\nu_{max}(CHCl_3)$/cm^{-1} 1720 (C=O), 1715 (C=O), 1680 (C=O), 1225 (SiMe) and 1105 (SiPh); δ_H(400 MHz; $CDCl_3$) 9.55 (1 H, br s, CHO), 7.50–7.20 (20 H, m, 4 × Ph), 4.29 (1 H, m, CHN), 3.45 (1 H, dd, *J* 4.0 and 9.6, C$H_A$$H_B$OCPh$_3$), 3.19–3.13 (2 H, m, $CH_A$$H_B$OCPh$_3$ and SiCHC$H_A$$H_B$CO), 2.86 (1 H, dt, *J* 17.9 and 10.7, CH_2C$H_A$$H_B$-CON), 2.67 (1 H, dd, *J* 7.9 and 17.7, SiCHC$H_A$$H_B$CO), 2.41 (1 H, dd, *J* 9.6 and 17.9, $CH_2CH_A$$H_B$CON), 2.29 (2 H, m, SiCHCH_2CH_2), 2.02–1.87 (2 H, m, C$H_2$$CH_2$CON), 1.80 (1 H, m, SiCH), 1.59–1.47 (2 H, m, SiCHC$H_2$$CH_2$), 0.33 (3 H, s, Si*Me*$_AMe_B$) and 0.30 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 588 (0.13%, M^+ − Me), 243 (93, CPh_3) and 135 (100, $SiMe_2Ph$) (Found: M^+ − Me, 588.2567. $C_{38}H_{41}NO_4Si$ requires *M* − Me, 588.2570).

(5*S*,3′*S*)-1-[3′-Dimethyl(phenyl)silyl-6′,6′-ethylenedioxyhexanoyl]-5-triphenylmethoxymethylpyrrolidin-2-one 22 and (5*S*,3′*R*)-1-[3′-dimethyl(phenyl)silyl-6′,6′-ethylenedioxyhexanoyl]-5-triphenylmethoxymethylpyrrolidin-2-one

Following Sterzycki,[32] ethylene glycol (0.39 cm^3, 7.1 mmol), pyridinium toluene-*p*-sulfonate (0.11 g, 0.4 mmol) and the aldehyde (0.86 g, 1.4 mmol) were refluxed in benzene (14 cm^3) for 1 h with a Dean–Stark apparatus. Excess solvent was removed under reduced pressure, ether (40 cm^3) was added and the mixture was washed with saturated aqueous sodium hydrogen carbonate (40 cm^3) and brine (40 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 7:3) gave the *imide* **22** (0.75 g, 81%); R_f (hexane–EtOAc, 7:3) 0.23; $\nu_{max}(CDCl_3)$/cm^{-1} 1732 (C=O), 1689 (C=O), 1250 (SiMe) and 1139–1085 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.54–7.15 (20 H, m, 4 × Ph), 4.71 (1 H, t, *J* 4.0, OCHO), 4.32 (1 H, m, CHN), 3.90–3.72 (4 H, m, OCH_2CH_2O), 3.41 (1 H, dd, *J* 4.2 and 9.6, C$H_A$$H_B$OCPh$_3$), 3.11 (1 H, dd, *J* 2.8 and 9.6, $CH_A$$H_B$OCPh$_3$), 3.06 (1 H, dd, *J* 9.2 and 17.9, SiCHC$H_A$$H_B$CON), 2.87–2.73 (2 H, m, CH_2C$H_A$$H_B$CO and SiCHC$H_A$$H_B$CON), 2.40 (1 H, dd, *J* 9.3 and 17.7, $CH_2CH_A$$H_B$CO), 2.07–1.82 (2 H, m, C$H_2$$CH_2$CON), 1.61–1.55 (4 H, m, SiCHCH_2CH_2), 1.37 (1 H, m, SiC*H*CH_2), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.30 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 570 (1.46%, M^+ − Ph), 243 (68, CPh_3), 135 (100, $SiMe_2Ph$) and 73 (70, $CHOCH_2CH_2O$) (Found: M^+ − Ph, 570.2680. $C_{40}H_{45}NO_5Si$ requires *M* − Ph, 570.2675). When the mixture of aldehydes was used for the reaction, chromatography (hexane–EtOAc, 7:3) separated the diastereoisomers into the (3′*S*)-imide **22** (74%) and the (3′*R*) imide (7%).

Benzyl (3*S*)-3-dimethyl(phenyl)silyl-6,6-ethylenedioxyhexanoate 23

n-Butyllithium (1.5 mol dm^{-3} in hexane, 2.71 cm^3, 4.0 mmol) was added to the benzyl alcohol (0.56 g, 5.2 mmol) in dry THF (4 cm^3) at 0 °C under argon. After 10 min, the imide **22** (0.753 g, 1.2 mmol) in dry THF (4 cm^3) was added and the solution stirred for 24 h at room temperature. Saturated aqueous ammonium chloride (10 cm^3) was added and the mixture extracted with ether (3 × 20 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the

benzyl ester **23** (0.347 g, 0.87 mmol, 75%); R_f (hexane–EtOAc, 8:2) 0.29; $\nu_{max}(CDCl_3)/cm^{-1}$ 1732 (C=O), 1252 (SiMe) and 1144–1031 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.52–7.25 (10 H, m, 2 × Ph), 5.01 (2 H, s, $COCH_2Ph$), 4.74 (1 H, t, *J* 4.4, OCHO), 3.92–3.76 (4 H, m, OCH_2CH_2O), 2.42 (1 H, dd, *J* 5.2 and 15.8, $SiCHCH_AH_BCO$), 2.28 (1 H, dd, *J* 7.9 and 15.8, $SiCHCH_AH_BCO$), 1.70–1.38 (5 H, m, $SiCHCH_2CH_2$) and 0.31 (6 H, s, $SiMe_2$); *m*/*z* 398 (0.13%, M^+), 135 (92, $SiMe_2Ph$), 91 (100, CH_2Ph) and 73 (77, $CHOCH_2CH_2O$) (Found: M^+, 398.1897. $C_{23}H_{30}O_4Si$ requires *M*, 398.1914).

Benzyl (2*R*,3*S*,1′*S*)-2-(1′-hydroxyethyl)-3-dimethyl(phenyl)silyl-6,6-ethylenedioxyhexanoate

Lithium diisopropylamide (0.7 mmol) in dry THF (1.5 cm^3) was added to the benzyl ester **23** (0.2 g, 0.5 mmol) in dry THF (2 cm^3) at −78 °C. After 0.5 h at −78 °C, acetaldehyde (0.08 cm^3, 1.5 mmol) was added, and the mixture stirred for 3 h. Saturated aqueous ammonium chloride (10 cm^3) was added and the mixture extracted with ether (3 × 20 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 7:3) gave the β-*hydroxy esters* (0.143 g, 65%) as a mixture of two major diastereoisomers in a ratio of 88:12 (determined by integration of either the *Me*CH peaks or $SiMe_2$ peaks in the ^1H NMR spectrum); R_f (hexane–EtOAc, 7:3) 0.18; $\nu_{max}(CDCl_3)/cm^{-1}$ 3052–2985 (OH), 1723 (C=O), 1258 (SiMe) and 1153–1032 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.55–7.25 (10 H, m, 2 × Ph), 4.96 (2 H, s, $COCH_2Ph$), 4.68 (1 H, t, *J* 4.0, OCHO), 3.88–3.75 (5 H, m, OCH_2CH_2O and MeC*H*OH), 2.65 (1 H, dd, *J* 3.3 and 8.8, SiCHC*H*CO), 1.65–1.35 (5 H, m, $SiCHCH_2CH_2$), 1.14 (d, *J* 6.1, *Me*CH of the minor isomer), 1.09 (3 H, d, *J* 6.1, *Me*CH of the major isomer), 0.36 (s, $SiMe_AMe_B$ of the minor isomer) and 0.32 (s, $SiMe_AMe_B$ of the minor isomer), 0.34 (3 H, s, $SiMe_AMe_B$ of the major isomer) and 0.30 (3 H, s, $SiMe_AMe_B$ of the major isomer); *m*/*z* 398 (0.59%, $M^+ - MeCHO$), 135 (46, $SiMe_2Ph$), 91 (100, CH_2Ph) and 73 (42, $CHOCH_2CH_2O$) (Found: $M^+ - MeCHO$, 398.1933. $C_{25}H_{34}O_5Si$ requires *M*, 398.1913).

(2*R*,3*S*,1′*S*)-2-(1′-Hydroxyethyl)-3-dimethyl(phenyl)silyl-6,6-ethylenedioxyhexanoic acid

The benzyl ester (4.52 g) was stirred with palladium (45 mg, 10% on charcoal) in methanol (70 cm^3) under hydrogen at room temperature for 5 h. The catalyst was removed by filtration through Celite and the solvent evaporated under reduced pressure. The residue in ether (100 cm^3) was extracted with aqueous sodium hydroxide (5%, 3 × 70 cm^3). The combined alkaline extracts were acidified with concentrated hydrochloric acid at 0 °C and extracted with ethyl acetate (3 × 70 cm^3), the combined organic layers dried ($MgSO_4$) and evaporated under reduced pressure to give the β-*hydroxy acid* (4.61 g, 98%); R_f (EtOAc) 0.32; $\nu_{max}(CDCl_3)/cm^{-1}$ 3070–2890 (OH), 1702 (C=O), 1251 (SiMe) and 1133–1023 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.57–7.46 (2 H, m, Ar *o* to Si), 7.34–7.29 (3 H, m, Ar *m* and *p* to Si), 4.71 (1 H, t, *J* 4.0, OCHO), 3.93–3.68 (5 H, m, OCH_2CH_2O and MeC*H*OH), 2.61 (1 H, dd, *J* 2.8 and 8.7, SiCHC*H*CO), 1.71–1.44 (5 H, m, $SiCHCH_2CH_2$), 1.18 (3 H, d, *J* 6.1, *Me*CH), 0.37 (3 H, s, $SiMe_AMe_B$) and 0.33 (3 H, s, $SiMe_AMe_B$); *m*/*z* 337 (0.29%, $M^+ - Me$), 135 (100, $SiMe_2Ph$) and 73 (28, $CHOCH_2CH_2O$) (Found: $M^+ - Me$, 337.1466. $C_{18}H_{28}O_5Si$ requires $M - Me$, 337.1471).

(3*R*,4*S*,1′*S*)-4-Methyl-3-[6′,6′-ethylenedioxy-1′-dimethyl-(phenyl)silylbutyl]oxetan-2-one

Benzenesulfonyl chloride (0.13 cm^3, 1 mmol) and the β-hydroxy acid (0.185 g, 0.5 mmol) were stirred in anhydrous pyridine (5 cm^3) at 0 °C under argon for 1 h and kept in the refrigerator overnight. The mixture was poured onto crushed ice (25 g) and extracted with ether (3 × 25 cm^3). The combined organic extracts were washed with hydrochloric acid (1 mol dm^{-3}, 3 × 30 cm^3), saturated aqueous sodium hydrogen carbonate (30 cm^3) and brine (30 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 8:2) gave the *lactone* (0.182 g, 96%); R_f (hexane–EtOAc, 8:2) 0.18; $\nu_{max}(CDCl_3)/cm^{-1}$ 1814 (C=O), 1252 (SiMe) and 1131–1112 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.60–7.53 (2 H, m, Ar *o* to Si), 7.37–7.24 (3 H, m, Ar *m* and *p* to Si), 4.69 (1 H, quintet, *J* 6.3, MeC*H*), 4.58 (1 H, t, *J* 4.3, OCHO), 3.90–3.70 (4 H, m, OCH_2CH_2O), 3.61 (1 H, dd, *J* 6.3 and 11.2, SiCHC*H*CO), 1.61–1.20 (5 H, m, $SiCHCH_2CH_2$), 1.44 (3 H, d, *J* 6.3, *Me*CH), 0.46 (3 H, s, $SiMe_AMe_B$) and 0.44 (3 H, s, $SiMe_AMe_B$); *m*/*z* 334 (0.20%, M^+), 135 (100, $SiMe_2Ph$) and 73 (28, $CHOCH_2CH_2O$) (Found: M^+, 334.1571. $C_{18}H_{26}O_4Si$ requires *M*, 334.1600).

(2*Z*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylhept-2-ene 24

The β-lactone (0.169 g, 0.5 mmol) was refluxed in 2,4,6-collidine (4.5 cm^3) for 3 h under argon. The solution was diluted with ether (20 cm^3), washed with hydrochloric acid (1 mol dm^{-3}, 3 × 15 cm^3), saturated aqueous sodium hydrogen carbonate (15 cm^3) and brine (15 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the cis-*allylsilane* (0.1 g, 69%); R_f (hexane–EtOAc, 7:3) 0.61; $\nu_{max}(CDCl_3)/cm^{-1}$ 3052 (C=CH), 1265 (SiMe) and 1130–1112 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.52–7.45 (2 H, m, Ar *o* to Si), 7.37–7.32 (3 H, m, Ar *m* and *p* to Si), 5.43 (1 H, dq, *J* 10.8 and 6.7, MeC*H*=CH), 5.11 (1 H, dq, *J* 10.8 and 1.5, MeCH=C*H*), 4.58 (1 H, t, *J* 4.4, OCHO), 3.95–3.75 (4 H, m, OCH_2CH_2O), 2.01 (1 H, dt, *J* 11.6 and 2.7, SiCH), 1.83–1.17 (4 H, m, $SiCHCH_2CH_2$), 1.44 (3 H, dd, *J* 6.7 and 1.5, *Me*CH), 0.27 (3 H, s, $SiMe_AMe_B$) and 0.26 (3 H, s, $SiMe_AMe_B$); *m*/*z* 290 (4.13%, M^+) and 135 (100, $SiMe_2Ph$) (Found: M^+, 290.1717. $C_{17}H_{26}O_2Si$ requires *M*, 290.1702).

(2*R*,4*S*)-7,7-Ethylenedioxy-4-dimethyl(phenyl)silylheptan-2-ol

Borane–THF complex (1.0 mol dm^{-3} in THF, 1.21 cm^3, 1.2 mmol) was stirred with the allylsilane **24** (0.117 g, 0.4 mmol) at 0 °C under argon for 1.5 h. Sodium hydroxide (3 mol dm^{-3}, 0.47 cm^3, 1.4 mmol) and hydrogen peroxide (30%, 0.47 cm^3, 1.4 mmol) were added and the mixture stirred for 1 h at room temperature and then heated at 50 °C for 1 h. Water (5 cm^3) was added and the mixture extracted with ether (3 × 10 cm^3). The organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 6:4) gave the *alcohol* (0.09 g, 73%) as a mixture of diastereoisomers in a ratio of 90:10 (determined by integration of the *Me*CH peaks in the ^1H NMR spectrum; R_f (hexane–EtOAc, 5:5) 0.18; $\nu_{max}(CDCl_3)/cm^{-1}$ 3699–3667 (OH), 1264 (SiMe) and 1208–1111 (C–O–C and SiPh); δ_H(250 MHz; $CDCl_3$) 7.55–7.47 (2 H, m, Ar *o* to Si), 7.34–7.26 (3 H, m, Ar *m* and *p* to Si), 4.73 (1 H, t, *J* 4.4, OCHO), 3.95–3.74 (5 H, m, OCH_2CH_2O and C*H*OH), 1.82 (1 H, br s, OH), 1.67–1.21 (7 H, m, $CH_2CHSiCH_2CH_2$), 1.11 (3 H, d, *J* 6.1, *Me*CH of the major isomer), 1.05 (3 H, d, *J* 6.1, *Me*CH of the minor isomer) and 0.28 (6 H, s, $SiMe_2$); *m*/*z* 291 (0.55%, $M^+ - OH$) and 135 (100, $SiMe_2Ph$) (Found: $M^+ - OH$, 291.1768. $C_{17}H_{28}O_3Si$ requires $M - OH$, 291.1781).

Benzyl (3*S*)-3-dimethyl(phenyl)silylhept-6-enoate

Using the same method as for the preparation of the ester **23**, the imide **21** (0.122 g, 0.19 mmol) gave the *benzyl ester* (0.052 g, 75%); R_f (hexane–EtOAc, 8:2) 0.53; $\nu_{max}(CDCl_3)/cm^{-1}$ 1700 (C=O), 1640 (C=C) and 1500 (Ph); δ_H(250 MHz; $CDCl_3$) 7.38–7.28 (10 H, m, 2 × Ph), 5.69 (1 H, ddt, *J* 9.6, 17.7 and 6.6, CH_2=C*H*), 5.02 (2 H, s, $COCH_2Ph$), 4.94–4.85 (2 H, m, CH_2=CH), 2.41 (1 H, dd, *J* 5.2 and 15.6, $SiCHCH_AH_BCO$), 2.27 (1 H, dd, *J* 8.0 and 15.6, $SiCHCH_AH_BCO$), 2.05–1.89 (2 H, m, CH_2=CHCH_2), 1.63–1.30 (3 H, m, CH_2CH_2CHSi) and 0.29 (6 H, s, $SiMe_2$); *m*/*z* 337 (1.65%, $M - Me$), 135 (57, $SiMe_2Ph$)

and 91 (100, CH_2Ph) (Found: $M^+ - Me$, 337.1633. $C_{22}H_{28}O_2Si - Me$ requires $M - Me$, 337.1624).

Benzyl (2*R*,3*S*)-2-methyl-3-dimethyl(phenyl)silylhept-6-enoate 25

Sodium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF, 0.19 cm^3, 0.19 mmol) was added slowly to the ester (0.068 g, 0.19 mmol) in dry THF (1 cm^3) at 0 °C under argon. After 0.5 h, the solution was cooled to −78 °C and methyl iodide (0.072 cm^3, 1.15 mmol) added. After 18 h at −78 °C, the mixture was poured into saturated aqueous ammonium chloride (5 cm^3) and the mixture extracted with ether (3 × 5 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the *esters* (0.05 g, 71%) in a ratio of 89:11 (determined by integration of the CH*Me* peaks in the ^1H NMR spectrum); R_f (hexane–EtOAc, 8:2) 0.55; $\nu_{max}(CHCl_3)/cm^{-1}$ 1715 (C=O), 1480 (Ph), 1240 (SiMe) and 1120 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.54–7.32 (10 H, m, 2 × Ph), 5.63 (1 H, ddt, *J* 9.7, 17.7 and 6.5, C*H*=CH_2), 5.04 (2 H, s, $COCH_2Ph$), 4.92–4.83 (2 H, m, CH=CH_2), 2.67 (1 H, m, C*H*Me), 1.91–1.46 (5 H, m, $SiCHCH_2CH_2$), 1.08 (3 H, d, *J* 7.1, CH*Me*), 0.35 (3 H, s, $SiMe_AMe_B$) and 0.31 (3 H, s, $SiMe_AMe_B$); *m*/*z* 351 (1.52%, M − Me), 135 (100, $SiMe_2Ph$) and 91 (77, CH_2Ph) (Found: $M^+ - Me$, 351.1809. $C_{23}H_{30}O_2Si - Me$ requires $M - Me$, 351.1780).

Benzyl (2*R*,3*S*)-2-methyl-3-dimethyl(phenyl)silyl-6-oxohexanoate

Following Bertele and Schudel,[33] ozone was bubbled through a solution of the benzyl ester **25** (0.433 g, 1.2 mmol) in ethyl acetate (10 cm^3) at −78 °C for 30 min. Dimethyl sulfide (3 cm^3) was added and the solution allowed to warm to room temperature. The solvent and dimethyl sulfide were removed under reduced pressure. Chromatography (hexane–EtOAc, 9:1) gave the *aldehyde* (0.304 g, 70%); R_f (hexane–EtOAc, 9:1) 0.26; $\nu_{max}(CHCl_3)/cm^{-1}$ 1723 (C=O), 1497 (Ph), 1252 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.52–7.33 (10 H, m, 2 × Ph), 4.99 (2 H, s, $COCH_2Ph$), 2.59 (1 H, m, C*H*Me), 1.59–1.48 (5 H, m, $SiCHCH_2CH_2$), 1.04 (3 H, d, *J* 7.1, CH*Me*) and 0.34 (6 H, s, $SiMe_2$), which was used directly without further purification.

(2′*E*,6′*S*,7′*R*,5*S*)-1-[7′-Benzyloxycarbonyl-6′-dimethyl(phenyl)silyloct-2′-enoyl]-5-triphenylmethoxymethylpyrrolidin-2-one 26

Using the same method as for the preparation of the imide **11**, the aldehyde (0.1 g, 0.27 mmol) was combined with the phosphonate anion **12** (0.32 mmol) to give the *pyrrolidinone* **26** (0.145 g, 71%); R_f (CH_2Cl_2) 0.26; $\nu_{max}(CHCl_3)/cm^{-1}$ 1727 (C=O), 1674 (C=O), 1631 (C=C), 1490 (Ph), 1263 (SiMe) and 1110 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.55–7.16 (26 H, m, 5 × Ph and COC*H*=CH), 6.92 (1 H, dt, *J* 15.3 and 6.8, COCH=C*H*), 5.05 (2 H, s, OCH_2Ph), 4.51 (1 H, m, CHN), 3.55 (1 H, dd, *J* 4.0 and 9.7, $CH_AH_BOCPh_3$), 3.16 (1 H, dd, *J* 2.6 and 9.7, $CH_AH_BOCPh_3$), 2.96 (1 H, dt, *J* 17.9 and 10.3, CH_AH_BCON), 2.70 (1 H, dq, *J* 2.6 and 7.1, COC*H*CHSi), 2.49 (1 H, dd, *J* 9.1 and 17.9, CH_AH_BCON), 2.15–1.52 (7 H, m, CH_2CH_2CON and CH_2CH_2CHSi), 1.10 (3 H, d, *J* 7.1, CH*Me*) and 0.36 (6 H, s, $SiMe_2$); *m*/*z* 614 (0.03%, $M^+ - SiMe_2Ph$), 243 (42, CPh_3), 135 (70, $SiMe_2Ph$) and 91 (100, CH_2Ph) (Found: $M^+ - SiMe_2Ph$, 614.2899. $C_{48}H_{51}NO_5Si$ requires $M - SiMe_2Ph$, 614.2906).

(3′*R*,6′*S*,7′*R*,5*S*)-1-{7′-Benzyloxycarbonyl-3′,6′-bis[dimethyl(phenyl)silyl]octanoyl}-5-triphenylmethoxymethylpyrrolidin-2-one 27

Using the same method as for the preparation of the imide **13**, the imide **26** (0.46 g, 0.61 mmol) and anhydrous magnesium bromide (0.23 g, 1.2 mmol) were treated with lithium bis[dimethyl(phenyl)silyl]cuprate (0.88 mol dm^{-3} in THF, 5.6 cm^3, 4.8 mmol) to give a mixture of diastereoisomers containing the *pyrrolidinone* **27** (0.51 g, 93%); R_f (hexane–EtOAc, 8:2) 0.28; $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (C=O), 1689 (C=O), 1251 (SiMe) and 1111 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.46–7.19 (30 H, m, 6 × Ph), 4.96 (1 H, d, *J* 16.9, OCH_AH_BPh), 4.93 (1 H, d, *J* 16.9, OCH_AH_BPh), 4.32 (1 H, m, CHN), 3.42 (1 H, dd, *J* 4.1 and 9.6, $CH_AH_BOCPh_3$), 3.14 (1 H, dd, *J* 2.6 and 9.6, $CH_AH_BOCPh_3$), 3.05 (1 H, dd, *J* 9.0 and 17.6, $SiCHCH_AH_BCON$), 2.82 (1 H, dt, *J* 18.2 and 10.3, $CH_2CH_AH_BCO$), 2.64 (1 H, dd, *J* 4.7 and 17.6, $SiCHCH_AH_BCON$), 2.56 (1 H, m, SiCHC*H*Me), 2.44 (1 H, dd, *J* 8.9 and 18.2, $CH_2CH_AH_BCO$), 2.05–1.07 (8 H, m, CH_2CH_2CON and $SiCHCH_2CH_2CHSi$), 1.06–0.97 (3 H, 4 × d, *J* 7.0, diastereoisomeric SiCHCH*Me*), 0.26–0.13 (12 H, m, diastereoisomeric $SiMe_2$); *m*/*z* 552 (0.16%, $M^+ - CPh_3 - CHPh$), 243 (100, CPh_3), 135 (63, $SiMe_2Ph$) and 91 (52, CH_2Ph) (Found: $M^+ - CPh_3 - CHPh$, 552.2598. $C_{56}H_{63}NO_5Si_2 - C_{26}H_{21}$ requires $M - CPh_3 - CHPh$, 552.2601).

(2′*E*,5″*S*,6′*S*,5*S*)-1-{7′-[5″-Triphenylmethoxymethyl-2″-oxopyrrolidin-1-ylcarbonyl]-6′-dimethyl(phenyl)silylhept-2′-enoyl}-5-triphenylmethoxymethylpyrrolidin-2-one 28

Using the same method as for the preparation of the imide **23**, the aldehyde (0.23 g, 0.36 mmol) was combined with the phosphonate anion **12** (0.47 mmol) to give the *bis-imide* **28** (0.31 g, 87%); R_f (hexane–EtOAc, 7:3) 0.26; $\nu_{max}(CHCl_3)/cm^{-1}$ 1731 (C=O), 1680 (C=O), 1632 (C=C) and 1448 (Ph); δ_H(250 MHz; $CDCl_3$) 7.54–7.18 (35 H, m, 7 × Ph), 6.97 (2 H, m, CH=CH), 4.51 (1 H, m, CHN), 4.36 (1 H, m, CH′N), 3.54 (1 H, dd, *J* 4.0 and 9.7, $CH_AH_BOCPh_3$), 3.45 (1 H, dd, *J* 4.2 and 9.7, $CH'_AH'_BOCPh_3$), 3.12 (3 H, m, $CH_AH_BOCPh_3$, $CH'_AH'_BOCPh_3$ and $SiCHCH_AH_BCON$), 2.97–2.81 (3 H, m, $CH_2CH_AH_BCO$, $CH'_2CH'_AH'_BCO$ and $SiCHCH_AH_BCON$), 2.49–2.44 (2 H, m, $CH_2CH_AH_BCO$ and $CH'_2CH'_AH'_BCO$), 2.28–0.84 (9 H, m, CH_2CH_2CON, $CH'_2CH'_2CON$ and CH_2CH_2CHSi) and 0.34 (6 H, s, $SiMe_2$); *m*/*z* (FDMS) 984 (M^+).

(5′*S*,3′*S*,6′*S*,5*S*)-1-{7′-[5″-Triphenylmethoxymethyl-2″-oxopyrrolidin-1-ylcarbonyl]-3′,6′-bis[dimethyl(phenyl)silyl]heptanoyl}-5-triphenylmethoxymethylpyrrolidin-1-one 29

Using the same method as for the preparation of the imide **13**, the imide **28** (0.30 g, 0.30 mmol) and anhydrous magnesium bromide (0.13 g, 0.7 mmol) were treated with lithium bis[dimethyl(phenyl)silyl]cuprate (1.22 mmol) to give a mixture (89:11) of diastereoisomers containing the *diimide* **29** (0.31 g, 91%); R_f (hexane–EtOAc, 8:2) 0.28; $\nu_{max}(CHCl_3)/cm^{-1}$ 1731 (C=O), 1691 (C=O), 1489 (Ph), 1249 (SiMe) and 1111 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.63–7.22 (40 H, m, 8 × Ph), 4.29 (2 H, m, 2 × CHN), 3.43 (2 H, dd, *J* 4.2 and 9.6, 2 × $CH_AH_BOCPh_3$), 3.16 (2 H, dd, *J* 2.3 and 9.6, 2 × $CH_AH_BOCPh_3$), 3.07 (2 H, dd, *J* 8.6 and 17.6, 2 × $SiCHCH_AH_BCON$), 2.83 (1 H, dt, *J* 18.0 and 10.4, 2 × $CH_2CH_AH_BCO$), 2.70 (2 H, dd, *J* 4.8 and 17.6, 2 × $SiCHCH_AH_BCON$), 2.43 (2 H, m, 2 × $CH_2CH_AH_BCO$), 1.98–1.20 (8 H, m, CH_2CH_2CON and $SiCHCH_2CH_2CHSi$) and 0.44–0.22 (12 H, several s, diastereoisomeric $SiMe_2$); *m*/*z* (FDMS) 1121 ($M^+ + H$).

Dibenzyl (3*S*,6*S*)-3,6-bis[dimethyl(phenyl)silyl]suberate 30

Using the same method as for the preparation of the ester **23**, the imide **29** (0.75 g, 0.67 mmol) and benzyl alcohol (0.50 g, 4.7 mmol) gave the *dibenzyl ester* (0.22 g, 53%); R_f (hexane–EtOAc, 8:2) 0.43; $\nu_{max}(CDCl_3)/cm^{-1}$ 1728 (C=O), 1251 (SiMe) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.40–7.25 (20 H, m, 4 × Ph), 4.95 (4 H, m, 2 × $COCH_2Ph$), 2.27 (2 H, dd, *J* 5.1 and 15.8, 2 × $SiCHCH_AH_BCO$), 2.12 (2 H, dd, *J* 7.9 and 15.8, 2 × $SiCHCH_AH_BCO$), 1.35–1.17 (4 H, m, $SiCHCH_2CH_2$), 0.84 (2 H, m, 2 × SiCH) and 0.16 (12 H, s, 2 × $SiMe_2$); *m*/*z* 607 (2.1%, $M^+ - Me$), 135 (55, $SiMe_2Ph$) and 91 (100, CH_2Ph) (Found: $M^+ - Me$, 607.2680. $C_{38}H_{46}O_4Si_2$ requires $M - Me$, 607.2712).

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