Stereocontrol in organic synthesis using silicon-containing compounds. A synthesis of the (±)-Prelog–Djerassi lactone

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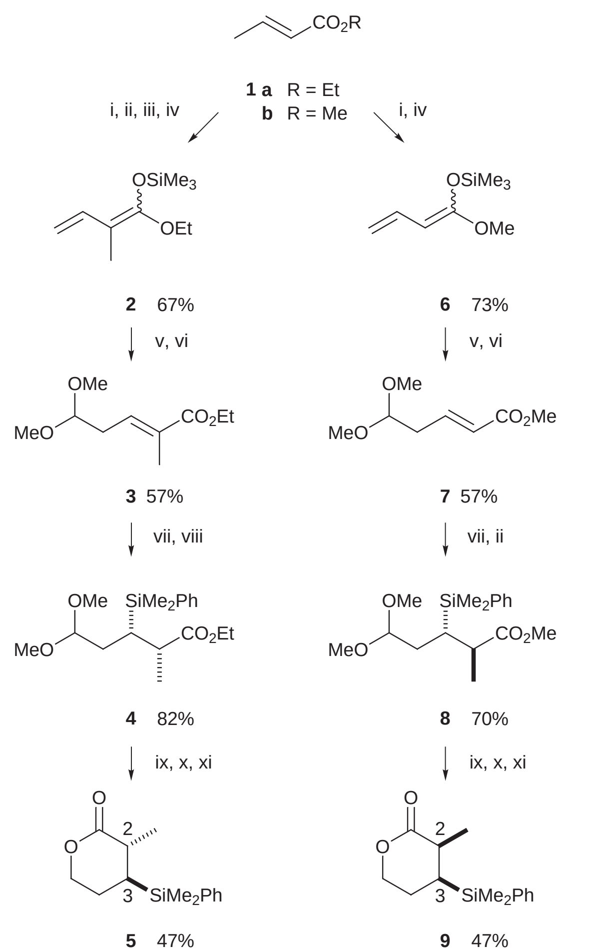
Each of the relative stereochemical relationships present in the Prelog–Djerassi lactone 34 was set up by a stereocontrolled reaction based on the presence of a silyl group. These were the enolate protonation 3→4 of a β-silyl ester, the enolate alkylation 11→12 of a β-silyl ester, silyl-to-hydroxy conversion with retention of configuration 13→14, and stereospecifically *anti* protodesilylation of the allylsilanes 26 and 27 giving largely the alkene 28. These allylsilanes had themselves been prepared in a stereocontrolled, convergent synthesis from the allylic acetates 24 and 25, providing thereby a general solution to the controlled synthesis of a new stereogenic centre relative to a resident centre without regard to their distance apart, except insofar as it influences a necessary separation of diastereoisomers (18 and 19 in this case). Using the opposite double bond geometries, the allylic acetates 29 and 30 gave the complementary pair of allylsilanes 31 and 32, which underwent stereospecifically *anti* protodesilylation to give largely the alkene 33 diastereoisomeric to 28 at C-6. The alkenes 28 and 33 were converted into the Prelog–Djerassi lactonic acid 34 and its C-6 epimer 35, respectively.

Introduction

The Prelog–Djerassi lactone **34** has been a favourite synthetic target on which to test and demonstrate new methods of stereocontrol. The subject has been comprehensively reviewed from the first synthesis in 1963 up to 1990,[1] and new syntheses continue to appear.[2] We now report our own synthesis, already published in preliminary form,[3] in which we used the stereochemistry of electrophilic attack on a double bond adjacent to a silicon-bearing stereogenic centre to control *all* the relative stereochemistry in this molecule. In this synthesis, we used three of the methods listed in the first paper of this series:[4] successively the protonation and alkylation of enolates carrying an adjacent silyl group,[5] silyl-to-hydroxy conversion,[6] and the *anti* S_E2' reaction of allylsilanes.[7] The synthesis is notable for the last of these reactions, which we used to control the relative stereochemistry of two centres having a 1,3 relationship without using rings or cyclic transition structures in any way. Furthermore, each of the stereochemistry-determining reactions that we used could have been redesigned to give the opposite stereochemistry, making our route capable, in principle, of being used for the synthesis of any of the diastereoisomers. To illustrate this point we used the last to set up the opposite relative stereochemistry.

Results and discussion

We began (Scheme 1) by using discoveries that we had made in our work on silyl enol ethers. In particular, we had established, following a lead from Mukaiyama,[8] that silyl dienol ethers react with electrophiles as d^4-synthons predominantly at the γ-position,[9] in contrast to lithium dienolates, which react as d^2-synthons predominantly at the α-position. We also established some of the features that encouraged γ-attack, including the observation that relatively well-stabilised cationic electrophiles were most likely to behave well in this sense.[10] The reaction that we actually used was the combination of the silyl dienol ether **2** and the cation derived from trimethyl orthoformate in the presence of a catalytic amount of zinc bromide. In practice, we obtained the product **3** of γ-attack in 57% yield together with the product of α-attack in 14% yield. This was not as high a degree of γ-selectivity (80 : 20) as we had expected from our experience with highly stabilised electrophiles.[10] Nevertheless,



Scheme 1 *Reagents:* i, LDA, HMPA; ii, MeI; iii, LDA, THF; iv, Me_3SiCl; v, $(MeO)_3CH$, $ZnBr_2$ cat.; vi, separate from α product by distillation; vii, $(PhMe_2Si)_2CuLi$, THF; viii, NH_4Cl, H_2O; ix, TsOH, Me_2CO; x, $NaBH_4$, MeOH; xi, HCl

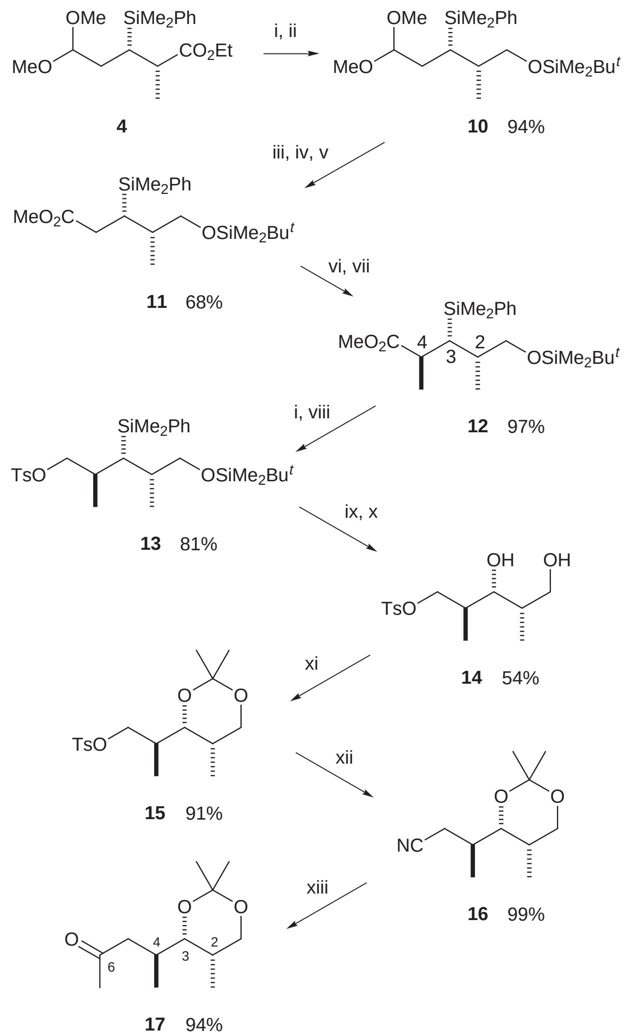
the products were easy to separate by fractional distillation, and the starting materials cheap, so we did not try the methods that we had developed for improving the degree of γ-selectivity, such as using a diisopropylmethyl ester[9] in place of the ethyl ester or a triarylsilyl dienol ether[10] in place of the trimethylsilyl dienol ether. The silyl dienol ether **2** was derived from ethyl crotonate **1a** by methylation of the lithium dienolate at the α-position,[11] followed by the preparation of the silyl dienol ether, so that we actually used successively the capacities of lithium and silyl dienolates to be d^2- and d^4-synthons, respectively. We also carried out a γ-selective reaction with the silyl dienol ether **6** without the C-2 methyl group. The selectivity for γ-attack was slightly less (70:30), but again we easily separated the α,β-unsaturated ester **7** by fractional distillation from the product of α-attack in 57% yield.

Conjugate addition of the silylcuprate reagent to the α,β-unsaturated ester **3** and protonation of the resultant enolate gave selectively (92:8) the product **4** with the silyl and methyl groups *syn*, as we expected from our exploratory work on this type of reaction.[5] We have used this same reaction sequence in another context, and obtained closely similar results, which we have already reported in full.[12] To make absolutely sure of the relative stereochemistry, we also prepared the methyl ester **8** with the opposite relative stereochemistry, by methylation of the enolate derived from the ester **7**, which was selective (83:17) in favour of the isomer with the silyl and methyl groups *anti*. With each of the esters **4** and **8**, we hydrolysed the acetal, reduced the aldehyde group with sodium borohydride, and made the diastereoisomeric δ-lactones **5** and **9**, respectively, by treatment with hydrochloric acid. The double quartets from the protons on C-2 in the ^{1}H NMR spectra were identifiable for both lactones, and showed a diagnostic coupling constant to the proton on C-3 of 11 Hz in the case of the isomer **5** and 7 Hz in the case of the isomer **9**.

It was now necessary to mask the carboxylic ester function, in order to distinguish it from the ester we needed to set up on the other side of the silyl group. We chose to do this safely, but somewhat inelegantly, by reducing it to the alcohol and protecting it as the *tert*-butyldimethylsilyl ether **10** (Scheme 2), at which stage we were able to separate it from the small amount of its diastereoisomer. Hydrolysis of the acetal, oxidation of the aldehyde and esterification gave the methyl ester **11**. We methylated the ester using the lithium enolate and obtained only one diastereoisomer **12**, in happy contrast to our expectation (85:15)[5] based on having an isopropyl group as the carbon substituent on the stereogenic centre. We now had two of the stereochemical relationships safely in hand, and the scene was set for the more critical operation of controlling the stereochemistry at C-6 relative to the existing centres at C-2, C-3 and C-4.

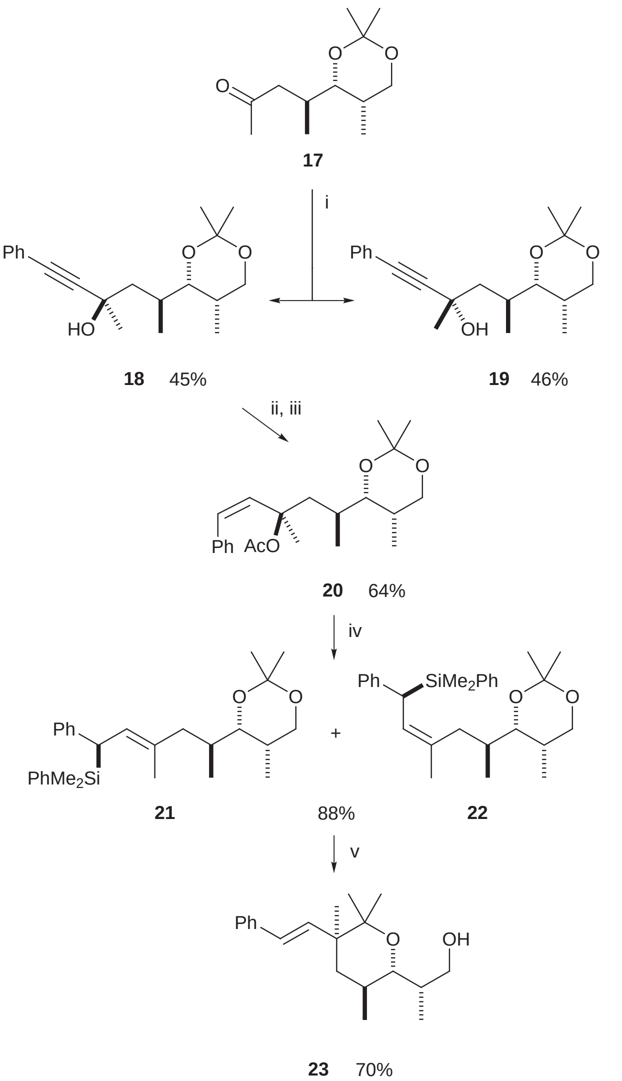
First we had to introduce the necessary carbon atoms and appropriate functionality (Scheme 2). We reduced the ester, and made the toluene-*p*-sulfonate **13** of the alcohol. At this stage we chose to carry out the silyl-to-hydroxy conversion **13**→**14** using our earlier protocol based on protodesilylation of the phenyl group and oxidation with peracid. Although the protodesilylation appeared to work well (97% crude), the second step did not (54% overall). Both steps have since been improved,[6,13] and no doubt better overall yields could be obtained today. The advantage of carrying out the silyl-to-hydroxy conversion at this stage was that it allowed us to tie down both hydroxy groups as the acetal **15**. We then displaced the sulfonate group with cyanide ion to give the crystalline nitrile **16**, and treated this with the methyl Grignard reagent to obtain the ketone **17**.

The ketone carbon, C-6 in **17**, is too remote from the influence of the resident stereogenic centre on C-4, let alone from those on C-3 and C-2, to expect a high level of open-chain stereocontrol in any reactions on the ketone group. We even returned to this subject with an elaborate study of what factors might allow direct 1,3 control in open-chain systems.[14] In the present context, it is a rather artificial problem, since methods for controlling C-6 in the Prelog–Djerassi lactone late in the synthesis are easy in this specific case. However, we wanted to use our methods of open-chain stereocontrol as a demonstration that a carefully placed silyl group could be used *in general to solve the problem of setting up a new stereogenic centre when it is remote from the influence of resident centres*. Our solution is not even limited to 1,3 relationships, although it is most likely to work best there, given that it involves a separation of diastereoisomers that is most likely to be easy when they have their stereocentres not too far apart.



Scheme 2 *Reagents:* i, $LiAlH_4$; ii, Bu^tMe_2SiCl; iii, TsOH, Me_2CO; iv, $AgNO_3$, KOH; v, CH_2N_2; vi, LDA, THF; vii, MeI; viii, TsCl, Py; ix, BF_3·2AcOH; x, MCPBA, KF, DMF; xi, TsOH, $Me_2C(OMe)_2$; xii, NaCN, HMPA; xiii, MeMgI

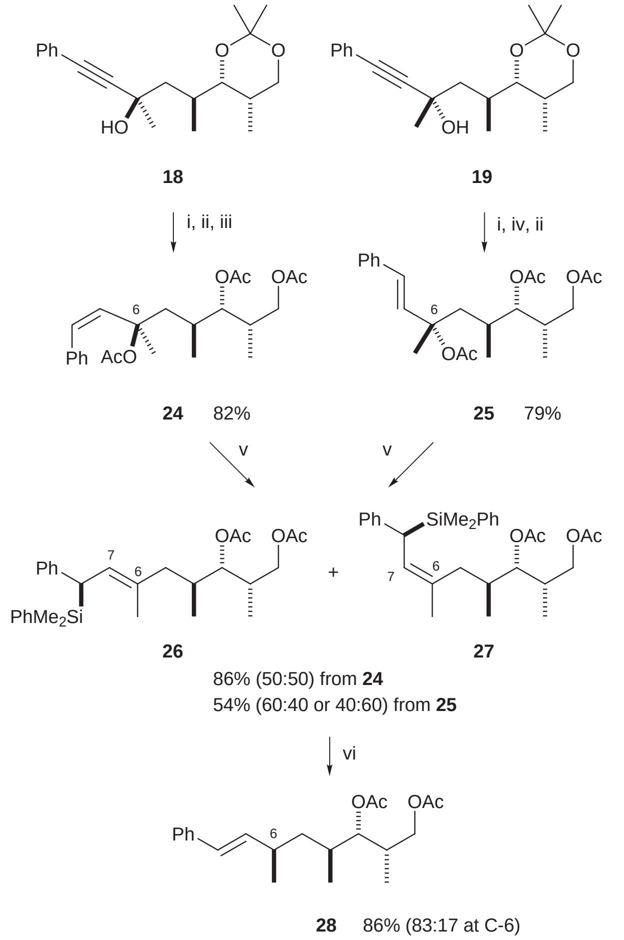
In the event, the lack of 1,3 control was immediately apparent when we found that the ketone **17** reacted with phenylethynyllithium with no selectivity—the two diastereoisomers **18** and **19** were obtained in essentially equal amounts (Scheme 3). This did not matter in the slightest to us; all that was needed was a means to separate them, which fortunately proved to be easy by column chromatography or by preparative HPLC. We did not know which isomer was which, but simply chose arbitrarily the slow running isomer, which later proved to be the isomer **18**. We acetylated the alcohol and reduced the triple bond to the *cis* double bond, to give the allylic acetate **20**. The stereospecifically *anti* S_N2' displacement of the acetate group using the phenyldimethylsilylcuprate reagent gave a pair of allylsilanes **21** and **22** in equal amounts, as expected from our earlier work.[15] The fact that we had a mixture was of no consequence, since both isomers, differing in *two* stereochemical features, were matched to give the same product in a stereospecifically *anti* S_E2' reaction. However, when we tried protodesilylation with our favourite acid, the boron trifluoride–acetic acid complex, a different reaction took place with surprising ease. The product was the pyran **23**, in which a



Scheme 3 *Reagents:* i, PhC≡CLi; ii, Ac_2O, Et_3N; iii, H_2, Lindlar's catalyst; iv, $(PhMe_2Si)_2CuLi$; v, BF_3·2AcOH

bond had been formed between two fully-substituted carbons, as a consequence of the acetal group acting as an intramolecular electrophile. We assigned the stereochemistry at the new centre on the basis that such reactions can be relied upon to be *anti*. There have since been several reactions reported in which allylsilanes react intramolecularly with acetals, and we had seen one ourselves earlier,[16] but we had not expected the acetal to react in competition with the abundant protons. The compounds involved in this dead end, from the acetate of the propargyl alcohols **18** and **19** to the product **23**, since they led nowhere, were not fully characterised, but the ^{1}H NMR spectra were compelling. We now had to backtrack, in order to render the hydroxy group protection inoffensive.

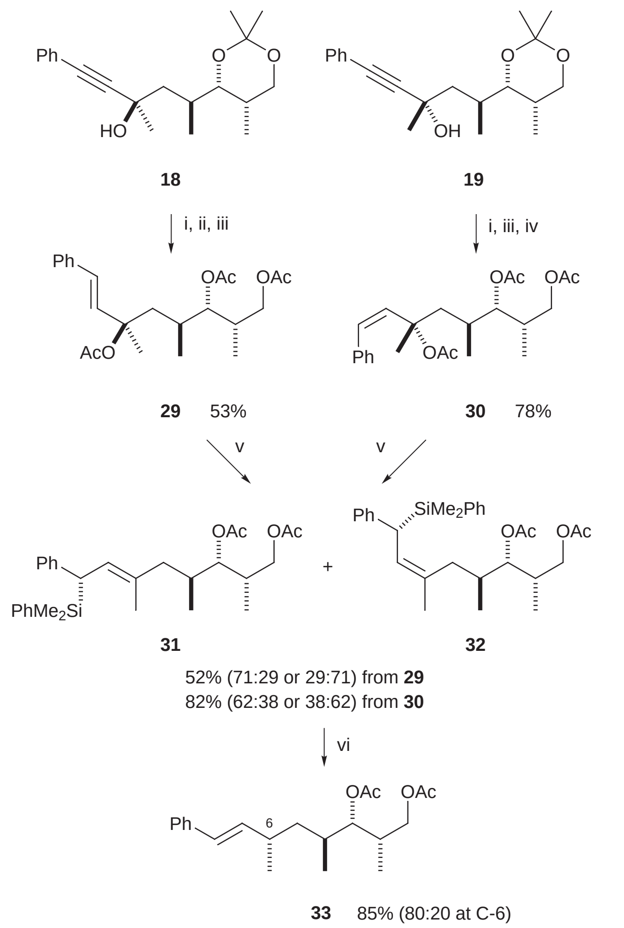
We hydrolysed the acetal group in each of the alcohols **18** and **19**, and reduced the triple bonds in different ways. With the slow-running isomer, derived from **18**, we fully acetylated the three hydroxy groups and again converted the triple to a *cis* double bond to give the triacetate **24**. With the fast-running isomer, we reduced the propargyl alcohol with lithium aluminium hydride to give the *trans* allylic alcohol, and then acetylated all three hydroxy groups to give the triacetate **25** (Scheme 4). These isomers now differ in *two* respects, double bond geometry and the relative stereochemistry at C-6, and therefore the stereospecifically *anti* S_N2' displacement of the allylic acetate groups using the phenyldimethylsilylcuprate reagent gave the same pair of allylsilanes **26** and **27**, which also differ in *two* respects, and remain correlated. In detail, we found that the reaction with the allyl acetate **25** having a *trans* double



Scheme 4 *Reagents:* i, TsOH, PyHOTs, $HO(CH_2)_2OH$; ii, Ac_2O, Et_3N, DMAP; iii, H_2, Lindlar's catalyst; iv, $LiAlH_4$; v, $(PhMe_2Si)_2CuLi$; vi, BF_3·2AcOH

bond reacted more slowly than that with a *cis* double bond **24**, something which we had not noticed before. To make the reaction with the *trans* isomer work at all well, we had to dilute the THF with diethyl ether, and even so the yield was less impressive than we have been used to for reactions with tertiary allylic acetates. Fortunately, the regiochemistry was entirely reliable, with the silyl group attaching itself to the secondary not the tertiary end of the allylic system.[15,17] Once again there was no need to separate the two allylsilanes, protodesilylation of the mixture can be expected to take place in a stereospecifically *anti* S_E2' reaction giving mainly the alkene **28**. The degree of stereospecificity, while high, was somewhat compromised, with the selectivity at C-6 only 83 : 17 in favour of the isomer **28**. We believe that the incomplete stereospecificity is caused by protonation taking place some of the time on C-7, to give a C-6 cation. When this occurs, the stereochemical information embedded in the double bond geometry is lost, and a subsequent hydride shift from C-7 can take place to either surface of the cation at C-6, giving each of the alkenes **28** and **33**. We have shown, without the stereochemical detail, that this pathway is followed in a more simple system.[18] This failure completely to control the stereochemistry at C-6 stimulated us subsequently to find a solution, which we tested only in a model series.[19] We have not, unfortunately, had occasion to return to the specific case in this paper. The solution is to introduce the methyl group in this step instead of the proton. The acetylenic nucleophile would be used to attack an aldehyde instead of a methyl ketone like **17**, and the allylsilanes corresponding to the pair **26** and **27**, but lacking the C-6 methyl group, would then be prepared using the same convergent sequence. Subsequent reaction to achieve overall a stereospecifically *anti* S_E2' replacement of the silyl group by a methyl group would avoid any pathways involving the competitive formation of a tertiary cation, but posed the problem of what the methyl electrophile should be. What we tried, with some success, was methylenation of allylsilanes,[20] and subsequent protodesilylation of the cyclopropylmethylsilanes.[19] Two problems we encountered in this approach were the lack of regioselectivity in the site of proton attack[21] and the susceptibility of the product alkene to further protonation under the acidic conditions necessary to open the cyclopropane ring. More recently, Landais has had some success in solving both problems using mercury(II) ions or electrophilic iodine in the opening of the cyclopropylmethylsilanes.[22] Between our work and that of Landais, it is clear that the C-6 problem could be solved.

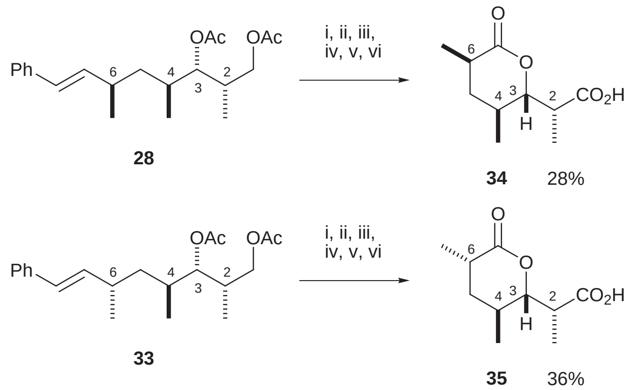
We have repeatedly made the claim that our methods are stereochemically versatile, and can be adapted to the synthesis of any diastereoisomer. In this case we proved our point to some extent by actually carrying out the alternative sequence (Scheme 5), starting with the same propargylic alcohols **18** and



Scheme 5 *Reagents:* i, TsOH, PyHOTs, HO(CH_2)$_2$OH; ii, $LiAlH_4$; iii, Ac_2O, Et_3N, DMAP; iv, H_2, Lindlar's catalyst; v, ($PhMe_2Si$)$_2$CuLi; vi, BF_3·2AcOH

19. All that was required was that we reduce the triple bond to a *trans* double bond where formerly we had made a *cis*, and to a *cis* where formerly we had made a *trans*. In this way we made the correlated pair of allylic acetates **29** and **30**, and hence the correlated pair of allylsilanes **31** and **32**. The lower yield in the sequence **18**→**29** is probably in the reduction step with lithium aluminium hydride, where allene formation[23] can occur, although we did not meet this problem in the sequence **19**→**25**. The ^{1}H NMR spectra, both of the allylic acetates **29** and **30** and of the allylsilanes **31** and **32**, showed distinctive signals that identified them as different from the pairs of their isomers obtained earlier (Scheme 4). Protodesilylation of the mixture of allylsilanes **31** and **32** again gave predominantly the product **33** of a stereospecifically *anti* S_E2' reaction, which was immediately recognisable as having the distinctive ^{1}H NMR signals of the minor product in the earlier series. The stereoselectivity was, disappointingly, a little less (80:20).

The remaining steps were straightforward (Scheme 6). Ozon-



Scheme 6 *Reagents:* i, O_3; ii, Me_2S, PyHOTs; iii, Jones; iv, K_2CO_3, MeOH; v, TsOH; vi, PDC, DMF

olysis of the double bond of the alkene **28**, oxidation of the aldehyde group, hydrolysis of the acetate groups, lactonisation, and oxidation of the free hydroxy group gave the Prelog–Djerassi lactonic acid itself **34**. Each of the intermediates showed the presence of the minor diastereoisomer at C-6 in the same proportion throughout, indicating that there had been no epimerisation at C-6, although this was only true for the ozonolysis step when the reductive work-up included pyridinium toluenesulfonate as a buffer. The lactonic acid itself, however, could be separated from its diastereoisomer by recrystallisation, and now proved to have properties matching (mp, IR, ^{1}H and ^{13}C NMR and MS) those reported in the literature.[24–27] With several of the diastereoisomers known, there can be little doubt about the structural assignment, and we at last knew which isomer **18** or **19** we had been using for which sequence. Repeating the sequence of six reactions on the mixture rich in the C-6 isomer **33** again gave mixtures that remained in the same proportion, but this time in favour throughout of the minor isomer in the earlier series, and giving the known C-6 isomer **35** of the Prelog–Djerassi lactonic acid, having properties matching (IR, ^{1}H and ^{13}C NMR and MS) those reported in the literature. This sequence confirmed that no epimerisation had taken place at C-6, as we had deduced earlier, but without rigorous proof.

Experimental

The details of the preparation of the ester **4**, and of the alcohol derived from it by lithium aluminium hydride reduction, have already been reported.[12] The numbering used in the experimental section is that following IUPAC rules and does not correspond with the numbering used in the text, which is that used for the Prelog–Djerassi lactonic acid. Except where otherwise stated, ether refers to diethyl ether, light petroleum refers to the fraction bp 40–60 °C, and ^{1}H NMR spectra were recorded at 90 MHz, except where otherwise stated. Chemical shifts in ^{1}H NMR spectra reported as using CH_2Cl_2 as an internal standard assume a chemical shift of δ 5.33 relative to Me_4Si.

Methyl (*E*)-5,5-dimethoxypent-2-enoate 7

n-Butyllithium (1.6 mol dm^{-3} in hexane, 68.8 cm^3, 110 mmol) was added dropwise to a stirred solution of diisopropylamine (11.1 g, 110 mmol) and HMPA (19.7 g, 110 mmol) in dry THF (250 cm^3) under nitrogen at −76 °C. After 30 min, methyl crotonate (10.0 g, 100 mmol) in dry THF (25 cm^3) was added over 20 min. The mixture was stirred at −76 °C for another 10 min and then quenched with chlorotrimethylsilane (16.3 g, 150 mmol). The solution was allowed to warm to room temperature and, after stirring for 1.5 h, the solvent was evaporated under reduced pressure in the absence of moisture. Dry pentane (250 cm^3) was added and the precipitated HMPA–lithium chloride complex was removed by filtration. Evaporation of the filtrate under reduced pressure, followed by refiltration and fractional distillation (15 cm Vigreux) gave the silyl ketene acetals **6** (12.56 g, 73%), bp 40–42 °C at 0.5 mmHg. The silyl ketene acetals were stirred with trimethyl orthoformate (10.0 g, 94.2 mmol) and powdered anhydrous zinc bromide (400 mg, 1.8 mmol) in dry dichloromethane (100 cm^3) at room temperature for 4 h. The solvent was evaporated under reduced pressure and the residue was distilled (15 cm Vigreux) to give methyl 2-(dimethoxymethyl)but-3-enoate (3.05 g, 24%), bp 40–45 °C at 0.05 mmHg, and the conjugated *ester* **7** (7.24 g, 57%), bp 52–54 °C at 0.05 mmHg; ν_{max}(neat)/cm^{-1} 2835 (acetal) and 1724 (C=O); $\delta_H(CDCl_3)$ 6.94 (1 H, dt, *J* 17 and 7, C*H*=CCO_2Me), 5.92 (1 H, dt, *J* 17 and 2, C=C*H*CO_2Me), 4.49 [1 H, t, *J* 6, *H*C$(OMe)_2$], 3.75 (3 H, s, CO_2Me), 3.36 (6 H, s, 2 × OMe) and 2.53 (2 H, ddd, *J* 7, 6 and 2, CH_2C=C); *m/z* 174 (1%, M^+), 173 (5, M − H), 143 (55, M − OMe) and 75 [100, $HC(OMe)_2$] (Found: M^+ − OMe, 143.0707. $C_8H_{14}O_4$ requires *M* − OMe, 143.0708).

Methyl 5,5-dimethoxy-3-dimethyl(phenyl)silylpentanoate

Dimethyl(phenyl)silyllithium (30.0 cm^3, 1.0 mol dm^{-3} in THF) was added into a suspension of copper(I) cyanide (1.35 g, 15 mmol) in THF (20 cm^3) under nitrogen at −10 °C. After 10 min, the solution was cooled to −23 °C and the unsaturated ester **7** (2.41 g, 13.9 mmol) in dry THF (10.0 cm^3) was added. The mixture was stirred at −23 °C for 2 h and quenched with saturated aqueous ammonium chloride (5 cm^3). The mixture was extracted with ether (3 × 50 cm^3) and the combined ethereal extracts were washed with saturated aqueous ammonium chloride (4 × 20 cm^3), dried ($MgSO_4$), filtered, evaporated under reduced pressure and distilled to give the *ester* (3.66 g, 85%), bp 116–118 °C at 0.01 mmHg; ν_{max}(neat)/cm^{-1} 2831 (acetal) and 1734 (C=O); $\delta_H(CDCl_3)$ 7.70–7.31 (5 H, m, Ph), 4.36 [1 H, t, *J* 5, *H*C$(OMe)_2$], 3.62 (3 H, s, CO_2Me), 3.25 (3 H, s, OMe), 3.21 (3 H, s, OMe), 2.46–2.30 (2 H, m, C$H_2$$CO_2Me$), 1.91–1.36 (3 H, m, CH_2CHSi) and 0.32 (6 H, s, $SiMe_2$); *m/z* 310 (2%, M^+), 295 (12, M − Me), 278 (7, M − MeOH), 263 (10, M − MeOH − Me), 247 (7, M − MeOH − OMe), 135 (57, $SiMe_2Ph$) and 75 [100, $HC(OMe)_2$] (Found: M^+ − Me, 295.1373. $C_{16}H_{26}O_4Si$ requires *M* − Me, 295.1366).

Methyl (2*R,3*S**)-5,5-dimethoxy-2-methyl-3-dimethyl(phenyl)-silylpentanoate 8**

Methyl 5,5-dimethoxy-3-dimethyl(phenyl)silylpentanoate (11.0 g, 35.5 mmol) in dry THF (100 cm^3) was added dropwise to a stirred solution of LDA [38.0 mmol, prepared from *n*-butyllithium (1.6 mol dm^{-3} in hexane, 23.8 cm^3) and diisopropylamine (4.05 g, 40.0 mmol) at −20 °C] in dry THF (200 cm^3) under nitrogen at −78 °C. After 10 min, methyl iodide (7.0 g, 49.3 mmol) was added and the mixture was stirred at room temperature for 1 h, poured into saturated aqueous ammonium chloride (50 cm^3) and extracted with ether (3 × 50 cm^3). The combined organic extracts were washed with saturated aqueous ammonium chloride (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the ester (11.25 g, 98%) as a mixture of inseparable diastereoisomers in a ratio of 84:16; ν_{max}(neat)/cm^{-1} 2831 (acetal) and 1729 (C=O); $\delta_H(CCl_4)$ 7.76–7.32 (5 H, m, Ph), 4.29 [1 H, t, *J* 5, *H*C$(OMe)_2$], 3.68 (3 H, s, CO_2Me), 3.66 (s, CO_2Me of minor diastereoisomer), 3.22 (3 H, s, OMe), 3.16 (3 H, s, OMe), 2.68 (1 H, dq, *J* 7 and 2.5, CHCO), 1.82–1.50 (3 H, m, $SiCHCH_2$), 1.21 (3 H, d, *J* 7, *Me*CH of the minor diastereoisomer), 1.10 (3 H, d, *J* 7, *Me*CH) and 0.40 (6 H, s, $SiMe_2$); *m/z* 309 (2%, M − Me), 249 [5, M − $HC(OMe)_2$], 135 (57, $SiMe_2Ph$) and 75 [100, $HC(OMe)_2$] (Found: M^+ − Me, 309.1509. $C_{17}H_{28}O_4Si$ requires *M* − Me, 309.1522).

(2*R,3*S**)-5-Hydroxy-2-methyl-3-dimethyl(phenyl)silylpentanoic acid δ-lactone 9**

The ester **8** (228 mg, 0.70 mmol, containing 17% of the diastereoisomer) and anhydrous toluene-*p*-sulfonic acid (10 mg) in dry acetone (10 cm^3) were kept at room temperature for 4 h. The solution was poured into saturated aqueous sodium hydrogen carbonate (20 cm^3) and extracted with ether (2 × 50 cm^3). The combined ethereal extracts were evaporated under reduced pressure to give the *aldehyde*; $\delta_H(CDCl_3)$ 9.68 (1 H, t, *J* 2, HC=O), 7.63–7.05 (5 H, m, Ph), 3.50 (3 H, s, CO_2Me), 2.76–2.44 (3 H, m, CH_2CHO and C*H*Me), 2.22–1.89 (1 H, m, HCSi), 0.98 (3 H, d, *J* 7, CH*Me*), 0.29 (3 H, s, $SiMe_AMe_B$) and 0.28 (3 H, s, $SiMe_AMe_B$). Powdered sodium borohydride (50 mg, 1.32 mmol) was added to the aldehyde in methanol (10 cm^3) at 5 °C and the mixture was stirred at 5 °C for 30 min. The mixture was acidified to pH 3 with hydrochloric acid (6 mol dm^{-3}) and poured into saturated aqueous sodium chloride (10 cm^3) and extracted with chloroform (4 × 25 cm^3). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, 20 g, EtOAc–light petroleum, 1:9) gave the *lactone* (82 mg, 47%); R_f(EtOAc–light petroleum, 1:9) 0.10; ν_{max}(neat)/cm^{-1} 1726 (C=O); $\delta_H(CDCl_3$; 250 MHz) 7.54–7.33 (5 H, m, Ph), 4.43 (1 H, ddd, *J* 11.0, 5.6 and 2.9, CH_AH_BO), 4.26 (1 H, ddd, *J* 11.0, 11.0 and 4.6, CH_AH_BO), 2.87 (1 H, dq, *J* 7.4 and 6.8, CHCO), 2.02–1.60 (3 H, m, $SiCHCH_2$), 1.22 (3 H, d, *J* 7.4, *Me*CH), 0.39 (3 H, s, $SiMe_AMe_B$) and 0.36 (3 H, s, $SiMe_AMe_B$); *m/z* 248 (13%, M^+), 233 (27, M − Me) and 135 (100, $SiMe_2Ph$) (Found: M^+, 248.1224. $C_{14}H_{20}O_2Si$ requires *M*, 248.1232).

(2*R,3*R**)-5-Hydroxy-2-methyl-3-dimethyl(phenyl)silylpentanoic acid δ-lactone 5**

The ethyl ester **4**[12] (150 mg, 0.44 mmol; containing 8% of its diastereoisomer) similarly gave the *lactone* (48 mg, 47%); R_f(EtOAc–light petroleum, 1:9) 0.10; ν_{max}(neat)/cm^{-1} 1726 (C=O); $\delta_H(CCl_4)$ 7.66–7.28 (5 H, m, Ph), 4.16 (2 H, t, *J* 6, CH_2O), 2.47 (1 H, dq, *J* 11 and 7, CHCO), 2.02–1.46 (3 H, m, $SiCHCH_2$), 1.15 (3 H, d, *J* 7, *Me*CH) and 0.45 (6 H, s, $SiMe_2$); *m/z* 248 (10%, M^+), 233 (29, M − Me) and 135 (100, $SiMe_2Ph$) (Found: M^+, 248.1249. $C_{14}H_{20}O_2Si$ requires *M*, 248.1232).

(3*R,4*R**)-5-(*tert*-Butyldimethylsilyloxy)-4-methyl-3-dimethyl-(phenyl)silylpentanal dimethyl acetal 10**

A mixture of the alcohol[12] (19.55 g, 66.0 mmol), *tert*-butyldimethylsilyl chloride (10.50 g, 69.7 mmol) and imidazole (10.00 g, 147 mmol) were stirred in dry DMF (100 cm^3) under nitrogen at 20 °C for 8 h. The solution was poured into water (50 cm^3) and extracted with ether–light petroleum (1:1, 4 × 100 cm^3). The combined organic extracts were washed with water (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, 200 g, EtOAc–light petroleum, 1:25) gave the *silyl ether* (27.06 g, 100%); R_f(EtOAc–light petroleum, 1:25) 0.30; ν_{max}(neat)/cm^{-1} 2830 (acetal) and 1090 (C–O); $\delta_H(CCl_4)$ 7.71–7.23 (5 H, m, Ph), 4.30 [1 H, t, *J* 5, *H*C$(OMe)_2$], 3.50–3.15 (2 H, m, CH_2OSi), 3.20 (3 H, s, OMe), 3.12 (3 H, s, OMe), 1.95 (1 H, br m, C*H*Me), 1.79–1.53 (2 H, m, CH_2CHSi), 1.35 (1 H, br m, CHSi), 0.96 (3 H, d, *J* 7, CH*Me*), 0.94 (9 H, s, Bu^t), 0.40 (6 H, s, SiMe_2Ph) and 0.02 (6 H, s, SiMe_2Bu^t); *m/z* 378 (1%, M − MeOH), 363 (50, M − MeOH − Me), 321 (24, M − MeOH − Bu^t), 263 (22, M − MeOH − $SiBu^tMe_2$), 135 (93, $SiMe_2Ph$) and 75 [100, $HC(OMe)_2$] (Found: M^+ − MeOH, 378.2412. $C_{22}H_{42}O_3Si_2$ requires *M* − MeOH, 378.2410).

(3*R,4*R**)-5-(*tert*-Butyldimethylsilyloxy)-4-methyl-3-dimethyl-(phenyl)silylpentanal**

The acetal **10** (28.41 g, 69.3 mmol) and anhydrous toluene-*p*-sulfonic acid (20 mg) were stirred in anhydrous acetone (500 cm^3) at 20 °C for 6 h. The solution was poured into saturated aqueous sodium hydrogen carbonate (20 cm^3) and the solvent evaporated under reduced pressure. The residue was dissolved in ether (300 cm^3) and washed with saturated aqueous sodium hydrogen carbonate (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a mixture of the acetal and the aldehyde (NMR). This mixture was treated again in the same way until no starting material remained. Chromatography (SiO_2, 200 g, EtOAc–light petroleum, 1:20) gave the *aldehyde* (24.75 g, 98%); R_f(EtOAc–light petroleum, 1:20) 0.36; ν_{max}(neat)/cm^{-1} 2710 (H–CO), 1723 (C=O) and 1092 (C–O); δ_H(CCl_4) 9.60 (1 H, t, *J* 2, HC=O), 7.64–7.27 (5 H, m, Ph), 3.52–3.20 (2 H, m, CH_2O), 2.53–2.34 (2 H, m, C*H*$_2$CHO), 1.73 (1 H, br m, C*H*Me), 1.29 (1 H, br m, CHSi), 0.93 (3 H, d, *J* 7, CH*Me*), 0.91 (9 H, s, Bu^t), 0.37 (3 H, s, Si*Me*$_A$Me$_B$Ph), 0.35 (3 H, s, SiMe$_A$*Me*$_B$Ph) and −0.01 (6 H, s, Si*Me*$_2$$Bu^t$); *m/z* 249 (<1%, M − $SiMe_2Bu^t$), 248 (2, M − $SiMe_2Bu^t$ − H), 233 (8, M − $SiMe_2Bu^t$ − H − Me) and 135 (100, $SiMe_2Ph$) (Found: M^+ − $SiMe_2Bu^t$ − H, 248.1226. $C_{20}H_{36}O_2Si_2$ requires *M* − $SiMe_2Bu^t$ − H, 248.1233).

Methyl (3*R,4*R**)-5-(*tert*-butyldimethylsilyloxy)-4-methyl-3-dimethyl(phenyl)silylpentanoate 11**

Potassium hydroxide (15.35 g, 274 mmol) in ethanol–water (2:1, 370 cm^3) was added dropwise to a stirred solution of silver nitrate (25.50 g, 150 mmol) in water (100 cm^3) at 0 °C. The mixture was stirred in the dark for 10 min and the aldehyde (24.75 g, 68.0 mmol) and potassium hydroxide (1 mol dm^{-3}, 2 drops) in ethanol (300 cm^3) were added over 15 min. The mixture was stirred at 0 °C for 45 min and filtered. The filter cake was washed with ether (3 × 100 cm^3) and the filtrate was neutralised with concentrated hydrochloric acid. The solvents were evaporated off under reduced pressure and the residue was dissolved in ether (500 cm^3). The aqueous layer was separated and washed with ether (3 × 100 cm^3). The combined ethereal layers were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the acid as a pale yellow liquid; δ_H($CDCl_3$) 8.74–8.48 (1 H, br, CO_2H, exchangeable with D_2O), 7.75–7.31 (5 H, m, Ph), 3.66–3.19 (2 H, m, CH_2O), 2.48 (2 H, d, *J* 6, C*H*$_2$$CO_2H$), 1.87–1.14 (2 H, m, CHSi and C*H*Me), 0.97 (3 H, d, *J* 7, CH*Me*), 0.91 (9 H, s, Bu^t), 0.39 (3 H, s, Si*Me*$_A$Me$_B$Ph), 0.37 (3 H, s, SiMe$_A$*Me*$_B$Ph) and 0.00 (6 H, s, Si*Me*$_2$$Bu^t$). The acid was dissolved immediately in ether (100 cm^3) and mixed with an excess of diazomethane. The resulting solution was kept at room temperature for 15 min and the excess diazomethane was destroyed by the addition of glacial acetic acid. The solvent was evaporated off under reduced pressure. Chromatography (SiO_2, 200 g, EtOAc–light petroleum, 1:25) gave the *ester* (18.47 g, 69%); R_f(EtOAc–light petroleum, 1:25) 0.37; ν_{max}(neat)/cm^{-1} 1739 (C=O) and 1091 (C–O); δ_H($CDCl_3$) 7.66–7.26 (5 H, m, Ph), 3.62 (3 H, s, CO_2Me), 3.54–3.22 (2 H, m, CH_2O), 2.37 (2 H, d, *J* 7, C*H*$_2$$CO_2Me$), 1.70 (1 H, br m, CHMe), 1.30 (1 H, br m, CHSi), 0.95 (3 H, d, *J* 7, CH*Me*), 0.91 (9 H, s, Bu^t), 0.37 (6 H, s, Si*Me*$_2$Ph) and −0.02 (6 H, s, Si*Me*$_2$$Bu^t$); *m/z* 394 (1%, M^+), 379 (3, M − Me), 363 (2, M − OMe), 337 (55, M − Bu^t) and 135 (100, $SiMe_2Ph$) (Found: M^+ − Me, 379.2111. $C_{21}H_{38}O_3Si_2$ requires *M* − Me, 379.2125).

Methyl (2*R,3*S**,4*R**)-5-(*tert*-butyldimethylsilyloxy)-2,4-dimethyl-3-dimethyl(phenyl)silylpentanoate 12**

The ester **11** (18.47 g, 46.9 mmol) in dry THF (100 cm^3) was added dropwise to a stirred solution of LDA (50.0 mmol) in dry THF (300 cm^3) under nitrogen at −78 °C, and the solution was stirred for 10 min. Methyl iodide (8.50 g, 59.9 mmol) was added and the mixture was allowed to warm to room temperature over 2 h. The mixture was poured into saturated aqueous ammonium chloride (50 cm^3), the organic layer was separated and the aqueous layer was washed with ether (3 × 50 cm^3). The combined organic extracts were washed with saturated aqueous ammonium chloride (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the ester (18.55 g, 97%); ν_{max}(neat)/cm^{-1} 1731 (C=O) and 1090 (C–O); δ_H(CCl_4) 7.73–7.29 (5 H, m, Ph), 3.62 (3 H, s, CO_2Me), 3.53–3.12 (2 H, m, CH_2O), 2.75 (1 H, dq, *J* 7 and 4, $CHCO_2$), 1.96 (1 H, br m, CH_2C*H*Me), 1.60 (1 H, br m, CHSi), 1.19 (3 H, d, *J* 7, *Me*CH-CO_2), 1.02 (3 H, d, *J* 7, CH*Me*), 0.93 (9 H, s, Bu^t), 0.47 (3 H, s, Si*Me*$_A$Me$_B$Ph), 0.42 (3 H, s, SiMe$_A$*Me*$_B$Ph) and 0.03 (6 H, s, Si*Me*$_2$$Bu^t$); δ_C($CDCl_3$) 177.3 (C-1), 140.0, 134.0, 128.8, 127.8 (Ar), 68.0 (C-5), 51.4 (CO_2*Me*), 39.4 (C-2), 35.9 (C-4), 32.1 (C-3), 26.0 (SiC*Me*$_3$), 24.9 (Si*C*Me$_3$), 18.0, 15.7 (2 × *Me*CH), −0.7, −0.9 (Si*Me*$_2$Ph) and −5.3 (Si*Me*$_2$$Bu^t$); *m/z* 408 (1%, M^+), 393 (7, M − Me), 351 (71, M − Bu^t), 331 (6, M − Ph), 235 (64, M − $MeCHCH_2OSiMe_2Bu^t$) and 135 (100, $SiMe_2Ph$) (Found: M^+ − Me, 393.2307. $C_{22}H_{40}O_3Si_2$ requires *M* − Me, 393.2281).

(2*R,3*R**,4*R**)-5-(*tert*-Butyldimethylsilyloxy)-2,4-dimethyl-3-dimethyl(phenyl)silylpentan-1-ol**

The ester **12** (18.55 g, 45.5 mmol) in dry THF (100 cm^3) was added dropwise to a stirred suspension of lithium aluminium hydride (1.60 g, 42.2 mmol) in THF (200 cm^3) under nitrogen at 0 °C. After 1.5 h, the mixture was poured into saturated aqueous ammonium chloride (20 cm^3) and extracted with ether (3 × 100 cm^3). The combined organic solvents were dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, 150 g, EtOAc–light petroleum, 1:9) gave the *alcohol* (16.80 g, 97%); R_f(EtOAc–light petroleum, 1:9) 0.10; ν_{max}(neat)/cm^{-1} 3600–3200 (O–H) and 1073 (C–O); δ_H(CCl_4) 7.73–7.25 (5 H, m, Ph), 3.50–2.95 (4 H, m, C*H*$_2$OH and CH_2OSi), 2.59–2.32 (1 H, br, OH, exchangeable with D_2O), 2.22–1.79 (2 H, m, 2 × C*H*Me), 1.65 (1 H, m, HCSi), 0.98 (3 H, d, *J* 7, CH*Me*), 0.92 (9 H, s, $SiBu^t$), 0.86 (3 H, d, *J* 7, CH*Me*), 0.45 (3 H, s, Si*Me*$_A$Me$_B$Ph), 0.38 (3 H, s, SiMe$_A$*Me*$_B$Ph), 0.03 (3 H, s, Si*Me*$_A$Me$_B$$Bu^t$) and 0.01 (3 H, s, SiMe$_A$*Me*$_B$$Bu^t$); *m/z* 380 (<1%, M^+), 365 (<1, M − Me), 323 (1, M − Bu^t), 305 (2, M − Bu^t − H_2O), 248 (4, M − $HOSiMe_2Bu^t$), 245 (4, M − $SiMe_2Ph$), 233 (2, M − $HOSiMe_2Bu^t$ − Me), 135 (100, $SiMe_2Ph$) and 115 (34, $SiMe_2Bu^t$) (Found: M^+ − Bu^t − H_2O, 305.1763. $C_{21}H_{40}O_2Si_2$ requires *M* − Bu^t − H_2O, 305.1757).

(2*R,3*S**,4*R**)-5-(*tert*-Butyldimethylsilyloxy)-2,4-dimethyl-3-dimethyl(phenyl)silylpentyl toluene-*p*-sulfonate 13**

The alcohol (17.02 g, 44.8 mmol) and toluene-*p*-sulfonyl chloride (9.53 g, 50.0 mmol) were kept in pyridine (50 cm^3) under nitrogen at 0 °C for 10 h. The mixture was poured into saturated aqueous ammonium chloride (50 cm^3). The mixture was extracted with ether (4 × 75 cm^3). The combined ethereal layers were washed with water (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, 200 g, EtOAc–light petroleum, 1:25) gave the *tosylate* (20.04 g, 84%); R_f 0.07; ν_{max}(neat)/cm^{-1} 1365, 1177 (S=O) and 1097 (C–O); δ_H(CCl_4) 7.74 (2 H, d, *J* 8, ArH *o* to S), 7.25–7.12 (7 H, m, other ArH), 3.95–3.56 (2 H, m, C*H*$_2$OTs), 3.30–3.10 (2 H, m, C*H*$_2$OSi), 2.48 (3 H, s, *Me*Ar), 2.30–1.20 (3 H, m, CHCH-SiCH), 0.95 (3 H, d, *J* 7, CH*Me*), 0.91 (3 H, d, *J* 7, CH*Me*), 0.85 (9 H, s, Bu^t), 0.38 (3 H, s, Si*Me*$_A$Me$_B$Ph), 0.34 (3 H, s, SiMe$_A$-*Me*$_B$Ph) and −0.04 (6 H, s, Si*Me*$_2$$Bu^t$); *m/z* 477 (1%, M − Bu^t), 171 (46, $TolSO_3$), 135 (100, $SiMe_2Ph$), 115 (23, $SiMe_2Bu^t$) and 91 (27, C_7H_7) (Found: M^+ − Bu^t, 477.1945. $C_{28}H_{46}O_4SSi_2$ requires *M* − Bu^t, 477.1951).

(2*R,3*S**,4*R**)-2,4-Dimethyl-5-(toluene-*p*-sulfonyloxy)pentane-1,3-diol 14**

Boron trifluoride–acetic acid complex (20.0 cm^3) and the phenylsilane **13** (16.29 g, 30.5 mmol) were kept in dry dichloromethane (300 cm^3) under nitrogen at 20 °C for 2 h. The mixture was neutralised by the addition of powdered sodium hydrogen carbonate, poured into water (100 cm^3) and extracted with dichloromethane (2 × 50 cm^3). The combined organic extracts were dried ($NaHCO_3$), filtered and evaporated under reduced pressure to give the fluorosilane (10.75 g, 97%); δ_H(CCl_4) 7.82 (2 H, d, *J* 8, ArH *o* to S), 7.40 (2 H, d, *J* 8, other ArH), 4.14–3.49

(4 H, m, CH_2OTs and CH_2OH), 2.49 (3 H, s, *Me*Ar), 2.40–1.80 (4 H, m, OH and CHCHSiCH), 0.97 (3 H, d, *J* 7, CH*Me*), 0.95 (3 H, d, *J* 7, CH*Me*), 0.17 (6 H, d, *J* 4, $SiMe_2F$). This compound was then kept with anhydrous potassium fluoride (4.43 g, 76.3 mmol) and *m*-chloroperbenzoic acid (16.84 g, 97.6 mmol) in dry DMF (170 cm^3) under nitrogen at room temperature for 7 h and then poured into water (150 cm^3). The solution was extracted with ether (5 × 75 cm^3) and the combined ethereal solvents were washed with saturated aqueous sodium bisulfite (2 × 50 cm^3) and with saturated aqueous sodium hydrogen carbonate (2 × 75 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, 150 g, EtOAc–light petroleum, 4:3) gave the *diol* (4.98 g, 54%); R_f(EtOAc–light petroleum, 4:3) 0.31; ν_{max}(neat)/cm^{-1} 3600–3200 (O–H), 1356, 1176 (S=O) and 1097 (C–O); δ_H($CDCl_3$) 7.90 (2 H, d, *J* 9, ArH *o* to S), 7.42 (2 H, d, *J* 9, other ArH), 4.40–4.02 (2 H, m, CH_2OTs), 3.87–3.54 (3 H, m, CH_2OH and C*H*OH), 2.77 (2 H, br, 2 OH, exchangeable with D_2O), 2.47 (3 H, s, *Me*Ar), 2.10–1.63 (2 H, m, 2 × C*H*Me) and 0.90 (6 H, d, *J* 7, 2 × CH*Me*); *m*/*z* 243 (<1%, M − $MeCHCH_2OH$), 172 (19, $MeC_6H_4SO_3H$), 91 (63, C_7H_7), 71 (76, M − $MeCHCH_2OH$ − TsOH) and 58 (100, C_3H_6O) (Found: M^+ − $MeCHCH_2OH$, 243.0701. $C_{14}H_{22}O_5S$ requires *M* − C_3H_7O, 243.0691).

(2*R,3*S**,4*R**)-3,5-Dihydroxy-3,5-*O*-isopropylidene-2,4-dimethylpent-1-yl toluene-*p*-sulfonate 15**

The diol **14** (4.20 g, 13.91 mmol) and toluene-*p*-sulfonic acid (2 crystals) in 2,2-dimethoxypropane (20 cm^3) were stirred at room temperature for 15 min. The mixture was diluted with ether (100 cm^3) and washed with saturated aqueous sodium hydrogen carbonate (20 cm^3). The organic layer was dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *acetonide* (4.33 g, 91%); R_f(EtOAc–light petroleum, 4:3) 0.81; ν_{max}(neat)/cm^{-1} 1361 and 1178 (S=O); δ_H($CDCl_3$) 7.95 (2 H, d, *J* 8, ArH *o* to S), 7.39 (2 H, d, *J* 8, other ArH), 4.30–3.89 (3 H, m, CH_2OTs and CH_AH_BO), 3.82–3.48 (2 H, m, HCO and CH_AH_BO), 2.40 (3 H, s, *Me*Ar), 2.00–1.32 (2 H, m, 2 × C*H*Me), 1.29 (3 H, s, CMe_AMe_B), 1.27 (3H, s, CMe_AMe_B), 1.00 (3 H, d, *J* 7, CH*Me*) and 0.86 (3 H, d, *J* 7, CH*Me*); *m*/*z* 327 (29%, M − Me), 173 (22, $TolSO_3H_2$), 155 (22, Ts), 95 (35), 91 (42, C_7H_7) and 59 (100, Me_2COH) (Found: M^+ − Me, 327.1275. $C_{17}H_{26}O_5S$ requires *M* − Me, 327.1266).

(3*R,4*R**,5*R**)-4,6-Dihydroxy-4,6-*O*-isopropylidene-3,5-dimethylhexanenitrile 16**

The tosylate **15** (5.19 g, 15.2 mmol) was stirred with sodium cyanide (0.80 g, 16.3 mmol) in dry HMPA (40 cm^3) under nitrogen at 40 °C for 18 h. The mixture was poured into saturated aqueous ammonium chloride (40 cm^3) and extracted with ether (3 × 75 cm^3). The combined organic extracts were washed with water (50 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *nitrile* (2.95 g, 99%) as needles, mp 65–67 °C (from Et_2O); ν_{max}(KBr)/cm^{-1} 2247 (C≡N); δ_H($CDCl_3$) 4.12 (1 H, dd, *J* 12 and 3, CH_AH_BO), 3.68 (1 H, dd, *J* 8 and 2, CHO), 3.62 (1 H, dd, *J* 12 and 2, CH_AH_BO), 2.46 (2 H, d, *J* 6, CH_2CN), 2.10–1.20 (2 H, m, 2 × C*H*Me), 1.42 (3 H, s, CMe_AMe_B), 1.36 (3 H, s, CMe_AMe_B), 1.03 (3 H, d, *J* 7, CH*Me*) and 1.00 (3 H, d, *J* 7, CH*Me*); *m*/*z* 182 (14%, M − Me) and 59 (100, Me_2COH) (Found: C, 67.2; H, 9.50; N, 7.35%; M^+ − Me, 182.1177. $C_{11}H_{19}NO_2$ requires C, 67.0; H, 9.70; N, 7.10%; *M* − Me, 182.1181).

(4*R,5*R**,6*R**)-5,7-Dihydroxy-5,7-*O*-isopropylidene-4,6-dimethylheptan-2-one 17**

The nitrile (2.97 g, 15.1 mmol) was refluxed at 37 °C in dry ether (15 cm^3) with methylmagnesium iodide (1 mol dm^{-3} in Et_2O, 25 cm^3, 25 mmol) under nitrogen for 5 h. The solution was poured into cold saturated aqueous ammonium chloride (20 cm^3) and stirred for another 5 min. The organic solvent was separated and the aqueous layer was washed with ether (2 × 50 cm^3). The combined ethereal solvents were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *ketone* (3.03 g, 94%); ν_{max}(neat)/cm^{-1} 1710 (C=O); δ_H($CDCl_3$) 4.12 (1 H, dd, *J* 12 and 3, CH_AH_BO), 3.64 (1 H, dd, *J* 12 and 2, CH_AH_BO), 3.55 (1 H, dd, *J* 9 and 1.5, CH–O), 2.87–2.29 (2 H, m, CH_2C–O), 2.14 (3 H, s, Ac), 1.95–1.20 (2 H, m, 2 × C*H*Me), 1.40 (3 H, s, CMe_AMe_B), 1.34 (3 H, s, CMe_AMe_B), 1.08 (3 H, d, *J* 7, CH*Me*) and 0.85 (3 H, d, *J* 7, CH*Me*); *m*/*z* 199 (8%, M − Me), 59 (80, Me_2COH) and 43 (100, Ac) (Found: M^+ − Me, 199.1339. $C_{12}H_{22}O_3$ requires *M* − Me, 199.1334).

(3*R,5*S**,6*S**,7*S**)-6,8-Dihydroxy-6,8-*O*-isopropylidene-3,5,7-trimethyl-1-phenyloct-1-yn-3-ol 18 and (3*R**,5*R**,6*R**,7*R**)-6,8-dihydroxy-6,8-*O*-isopropylidene-3,5,7-trimethyl-1-phenyloct-1-yn-3-ol 19**

n-Butyllithium (1.6 mol dm^{-3} in hexane, 4.0 cm^3, 6.4 mmol) was added dropwise to a stirred solution of phenylacetylene (0.80 g, 7.83 mmol) in dry ether (20 cm^3) under nitrogen at 0 °C. The mixture was stirred at 0 °C for 20 min and the ketone **17** (1.10 g, 5.14 mmol) in dry ether (10 cm^3) was added over 5 min. The solution was stirred at 0 °C for 30 min and quenched with saturated aqueous ammonium chloride (20 cm^3). The mixture was extracted with ether (3 × 50 cm^3) and the combined organic extracts were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a mixture of the alcohols. They were separated by HPLC to give the faster running alcohol **19** (747 mg, 46%); R_f(EtOAc–light petroleum, 1:7) 0.22; t_R (EtOAc–light petroleum, 1:6, solvent flow rate 6.72 cm^3 min^{-1}) 12.7 min; ν_{max}(neat)/cm^{-1} 3600–3200 (O–H) and 2240 (C≡C); δ_H($CDCl_3$; 250 MHz) 7.50–7.27 (5 H, m, Ph), 4.28–4.12 (1 H, br, OH, exchangeable with D_2O), 4.09 (1 H, dd, *J* 11.6 and 2.6, CH_AH_BO), 3.63 (1 H, dd, *J* 11.6 and 1.3, CH_AH_BO), 3.56 (1 H, dd, *J* 9.9 and 2.2, CHO), 2.16 (1 H, dd, *J* 14.3 and 5.0, CH_AH_BCOH), 1.96–1.78 (1 H, m, C*H*Me), 1.72 (1 H, dd, *J* 14.3 and 4.1, CH_AH_BCOH), 1.67–1.58 (1 H, m, C*H*Me), 1.56 (3 H, s, *Me*COH), 1.47 (3 H, s, CMe_AMe_B), 1.43 (3 H, s, CMe_AMe_B), 1.09 (3 H, d, *J* 6.8, CH*Me*) and 0.97 (3 H, d, *J* 7.1, CH*Me*); δ_C($CDCl_3$) 131.6, 128.1, 127.8, 123.4 (Ar), 99.1 (CMe_2), 94.9 (C-1), 82.1 (C-2), 76.8 (C-6), 67.3 (C-3), 66.9 (C-8), 48.2 (C-4), 30.9, 29.6 (C-5 and C-7), 30.1, 29.5, 19.0, 17.2 and 10.2; *m*/*z* 316 (7%, M^+), 301 (5, M − Me), 145 (28, PhC≡CCMeOH), 129 (22) and 59 (100, Me_2COH) (Found: M^+, 316.2033. $C_{20}H_{28}O_3$ requires *M*, 316.2038), and the slower running alcohol **18** (731 mg, 45%); R_f(EtOAc–light petroleum, 1:7) 0.19; t_R (EtOAc–light petroleum, 1:6, solvent flow rate 6.72 cm^3 min^{-1}) 16.1 min; ν_{max}(neat)/cm^{-1} 3600–3200 (O–H) and 2232 (C≡C); δ_H($CDCl_3$; 250 MHz) 7.50–7.28 (5 H, m, Ph), 5.33–5.25 (1 H, br, OH, exchangeable with D_2O), 4.09 (1 H, dd, *J* 11.6 and 2.5, CH_AH_BO), 3.64 (1 H, dd, *J* 11.6 and 1.5, CH_AH_BO), 3.59 (1 H, dd, *J* 10.6 and 2.1, CH-O), 2.33–1.60 (4 H, m, CH_2CHMe and C*H*Me), 1.56 (3 H, s, *Me*COH), 1.48 (3 H, s, CMe_AMe_B), 1.45 (3 H, s, CMe_AMe_B), 1.12 (3 H, d, *J* 6.7, CH*Me*) and 0.98 (3 H, d, *J* 7.0, CH*Me*); δ_C($CDCl_3$) 131.6, 128.1, 127.8, 123.5 (Ar), 99.2 (CMe_2), 93.6 (C-1), 82.8 (C-2), 77.5 (C-6), 67.3 (C-3), 66.9 (C-8), 50.3 (C-4), 32.4, 30.3 (C-5 and C-7), 31.3, 29.3, 19.0, 18.0 and 10.2; *m*/*z* 316 (16%, M^+), 301 (5, M − Me), 145 (50, PhC≡CCMeOH), 129 (31) and 59 (100, Me_2COH) (Found: M^+, 316.2053. $C_{20}H_{28}O_3$ requires *M*, 316.2038).

(2*R,3*R**,4*R**,6*S**)-2,4,6-Trimethyl-8-phenyloct-7-yne-1,3,6-triol**

The acetonide **18** (924 mg, 2.92 mmol), pyridinium tosylate (20 mg) and toluene-*p*-sulfonic acid (40 mg) in chloroform–ethyl acetate–ethylene glycol (7:13:25, 45 cm^3) were stirred under nitrogen at room temperature for 24 h. The solution was poured into saturated aqueous sodium hydrogen carbonate (20 cm^3) and extracted with chloroform (5 × 30 cm^3). The combined organic extracts were dried ($NaHCO_3$), filtered and evaporated under reduced pressure to give the *triol* (734 mg, 89%) as needles, mp 119–120 °C (from CH_2Cl_2); R_f(EtOAc–light petroleum, 2:1) 0.30; ν_{max}(KBr)/cm^{-1} 3600–3100 (O–H) and 2229 (C≡C); δ_H($CDCl_3$; 250 MHz) 7.47–7.18 (5 H, m, Ph), 5.31–4.31 (3 H, br, 3 × OH, exchangeable with D_2O), 3.87–3.50 (3 H, m, C*H₂*OH and C*H*OH), 2.23 (1 H, br m, C*H*Me), 1.96 (1 H, dd, *J* 14.6 and 6.7, C$H_A$$H_B$COH), 1.83 (1 H, br m, C*H*Me), 1.73 (1 H, dd, *J* 14.6 and 1.4, $CH_A$$H_B$COH), 1.59 (3 H, s, *Me*COH), 0.94 (3 H, d, *J* 6.9, CH*Me*) and 0.93 (3 H, d, *J* 7.0, CH*Me*); δ_C($CDCl_3$) 131.7, 128.2, 128.0, 123.2 (Ar), 93.4 (C-8), 83.5 (C-7), 79.0 (C-3), 67.8 (C-6), 67.7 (C-1), 50.1 (C-5), 36.2, 34.0, 31.7, 19.6 and 8.7; *m/z* 276 (1%, M$^+$), 258 (1, M − H_2O), 199 (16, M − Ph), 145 (100, PhC≡CCMeOH) and 129 (44, PhC≡CCO) (Found: C, 73.8; H, 8.70%; M$^+$, 276.1708. $C_{17}H_{24}O_3$ requires C, 73.9; H, 8.75%; *M*, 276.1725).

(2*R**,3*R**,4*R**,6*R**)-2,4,6-Trimethyl-8-phenyloct-7-yne-1,3,6-triol

This compound was prepared by a similar procedure to that described for its diastereoisomer. The acetonide **19** (936 mg, 2.96 mmol) gave the *triol* (687 mg, 84%) as needles, mp 102.5–103.5 °C (from $CHCl_3$); R_f(EtOAc–light petroleum, 2:1) 0.30; ν_{max}(KBr)/cm^{-1} 3680–3100 (O–H) and 2240 (C≡C); δ_H($CDCl_3$; 250 MHz) 7.50–7.23 (5 H, m, Ph), 5.50–4.00 (3 H, br, 3 × OH, exchangeable with D_2O), 3.85–3.53 (3 H, m, C*H₂*OH and C*H*OH), 2.24–1.72 (4 H, m, C*H₂*C*H*Me and C*H*Me), 1.58 (3 H, s, *Me*COH), 0.96 (3 H, d, *J* 6.8, *Me*CH) and 0.89 (3 H, d, *J* 7.0, *Me*CH); δ_C($CDCl_3$) 131.7, 128.2, 128.1, 123.1 (Ar), 94.5 (C-8), 82.9 (C-7), 78.6 (C-3), 67.9 (C-1), 67.7 (C-6), 48.4 (C-5), 36.3, 33.0, 29.9, 19.0 and 8.8; *m/z* 276 (1%, M$^+$), 258 (1, M − H_2O), 199 (22, M − Ph), 145 (100, PhC≡CCMeOH) and 129 (29, PhC≡CCO) (Found: C, 74.0; H, 8.95%; M$^+$, 276.1724. $C_{17}H_{24}O_3$ requires C, 73.9; H 8.75%; *M*, 276.1725).

(3*R**,5*S**,6*S**,7*S**)-3,6,8-Triacetoxy-3,5,7-trimethyl-1-phenyloct-1-yne

The triol (482 mg, 1.75 mmol) derived from **18**, acetic anhydride (900 mg, 8.78 mmol) and DMAP (60 mg, 0.49 mmol) in dry triethylamine (10 cm^3) were stirred under nitrogen at 0 °C for 6 h. The mixture was diluted with ether (100 cm^3) and washed with water (2 × 20 cm^3). The ether layer was dried ($MgSO_4$), filtered and evaporated. Chromatography (SiO_2, EtOAc–light petroleum, 1:5) gave the *triacetate* (664 mg, 95%); R_f(EtOAc–light petroleum, 1:5) 0.20; ν_{max}(neat)/cm^{-1} 2240 (C≡C) and 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 7.48–7.38 (2 H, m, ArH *o* to C≡C), 7.35–7.25 (3 H, m, other ArH), 4.90 (1 H, dd, *J* 6.7 and 4.9, C*H*OAc), 3.99 (1 H, dd, *J* 11.2 and 6.9, C$H_A$$H_B$OAc), 3.93 (1 H, dd, *J* 11.2 and 6.1, $CH_A$$H_B$OAc), 2.28–2.10 (4 H, m, C*H₂*C*H*Me and C*H*Me), 2.09 (3 H, s, Ac), 2.05 (6 H, s, 2 × Ac), 1.79 (3 H, s, *Me*COAc), 1.15 (3 H, d, *J* 6.8, CH*Me*) and 0.96 (3 H, d, *J* 6.8, CH*Me*); *m/z* 402 (1%, M$^+$), 257 (15, M − PhC≡C − CO_2), 201 (22, M^{2+}), 160 (100), 145 (47, PhC≡CCMeOH) and 105 (70) (Found: M$^+$, 402.2062. $C_{23}H_{30}O_6$ requires *M*, 402.2042).

(3*R**,5*R**,6*R**,7*R**)-3,6,8-Triacetoxy-3,5,7-trimethyl-1-phenyloct-1-yne

Similarly, the triol (169 mg, 0.61 mmol) derived from **19** gave the *triacetate* (235 mg, 96%); R_f(EtOAc–light petroleum, 1:5) 0.20; ν_{max}(neat)/cm^{-1} 2237 (C≡C) and 1740 (C=O); δ_H($CDCl_3$) 7.46–7.40 (2 H, m, ArH *o* to C≡C), 7.32–7.28 (3 H, m, other ArH), 4.90 (1 H, dd, *J* 7.5 and 4.3, C*H*OAc), 3.97 (1 H, dd, *J* 11.1 and 7.1, C$H_A$$H_B$OAc), 3.90 (1 H, dd, *J* 11.1 and 6.2, $CH_A$$H_B$OAc), 2.33–2.14 (2 H, br m, 2 × C*H*Me), 2.05 (3 H, s, Ac), 2.04 (3 H, s, Ac), 2.03 (3 H, s, Ac), 1.87 (2 H, d, *J* 5.2, C*H₂*COAc), 1.78 (3 H, s, *Me*COAc), 1.13 (3 H, d, *J* 6.8, CH*Me*) and 0.97 (3 H, d, *J* 6.8, CH*Me*); *m/z* 402 (2%, M$^+$), 257 (26, M − PhC≡C − CO_2), 201 (30, M^{2+}), 160 (100), 145 (42, PhC≡CCMeOH) and 105 (59) (Found: M$^+$, 402.2041. $C_{23}H_{30}O_6$ requires *M*, 402.2042).

(1*E*,3*R**,5*R**,6*R**,7*R**)-3,6,8-Triacetoxy-3,5,7-trimethyl-1-phenyloct-1-ene 25

This compound was prepared by a similar procedure to that described for the acetylenic triols. The *trans*-triol (244 mg, 0.88 mmol) derived from **19** gave the trans-*triacetate* (210 mg, 59%); R_f(EtOAc–light petroleum, 1:5) 0.20; ν_{max}(neat)/cm^{-1} 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 7.40–7.19 (5 H, m, Ph), 6.51 (1 H, d, *J* 16.3, PhC*H*=CH), 6.36 (1 H, d, *J* 16.3, PhCH=C*H*), 4.84 (1 H, dd, *J* 7.1 and 4.4, C*H*OAc), 3.93 (1 H, dd, *J* 11.0 and 7.0, C$H_A$$H_B$OAc), 3.83 (1 H, dd, *J* 11.0 and 6.3, $CH_A$$H_B$OAc), 2.21–1.77 (4 H, m, C*H₂*C*H*Me and C*H*Me), 2.03 (3 H, s, Ac), 2.02 (3 H, s, Ac), 2.01 (3 H, s, Ac), 1.67 (3 H, s, *Me*COAc), 0.99 (3 H, d, *J* 6.7, CH*Me*) and 0.91 (3 H, d, *J* 7.0, CH*Me*); *m/z* 404 (1%, M$^+$), 284 (9, M − 2 HOAc), 224 (66, M − 3 HOAc), 209 (36, M − 3 HOAc − Me), 171 (48, M − HOAc − AcOCHCHMe-CH_2OAc), 147 (100, PhCH=CHCMeOH), 131 (68, PhCH=CHCO) and 91 (82, C_7H_7) (Found: M$^+$, 404.2185. $C_{23}H_{32}O_6$ requires *M*, 404.2199).

(1*E*,3*R**,5*S**,6*S**,7*S**)-3,6,8-Triacetoxy-3,5,7-trimethyl-1-phenyloct-1-ene 29

Similarly, the *trans*-triol (107 mg, 0.38 mmol) derived from **18** gave the trans-*triacetate* (92 mg, 59%); R_f(EtOAc–light petroleum, 1:5) 0.20; ν_{max}(neat)/cm^{-1} 1742 (C=O); δ_H($CDCl_3$; 250 MHz) 7.40–7.21 (5 H, m, Ph), 6.51 (1 H, d, *J* 16.3, PhC*H*=CH), 6.32 (1 H, d, *J* 16.3, PhCH=C*H*), 4.85 (1 H, dd, *J* 7.3 and 4.3, C*H*OAc), 3.93 (1 H, dd, *J* 11.0 and 7.0, C$H_A$$H_B$OAc), 3.86 (1 H, dd, *J* 11.0 and 6.0, $CH_A$$H_B$OAc), 2.18–1.78 (4 H, m, C*H₂*C*H*Me and C*H*Me), 2.08 (3 H, s, Ac), 2.04 (3 H, s, Ac), 2.04 (3 H, s, Ac), 1.66 (3 H, s, *Me*COAc), 0.98 (3 H, d, *J* 6.7, CH*Me*) and 0.92 (3 H, d, *J* 6.8, CH*Me*); *m/z* 404 (1%, M$^+$), 284 (9, M − 2 HOAc), 224 (48, M − 3 HOAc), 209 (31, M − 3 HOAc − Me), 171 (62, M − HOAc − AcOCHCHMeCH_2OAc), 147 (100, PhCH=CHCMeOH), 131 (47, PhCH=CHCO) and 91 (83, C_7H_7) (Found: M$^+$, 404.2179. $C_{23}H_{32}O_6$ requires *M*, 404.2199).

(3*R**,5*S**,6*S**,7*S**)-6,8-Dihydroxy-6,8-*O*-isopropylidene-3,5,7-trimethyl-1-phenyloct-1-yn-3-yl acetate

Similarly, the acetonide **18** gave the acetate; δ_H($CDCl_3$) 7.57–7.17 (5 H, m, Ph), 3.95 (1 H, dd, *J* 11 and 2, C$H_A$$H_B$O), 3.65–3.30 (2 H, m, $CH_A$$H_B$O and CHO), 2.40–1.46 (4 H, m, C*H₂*C*H*Me and C*H*Me), 2.0 (3 H, s, Ac), 1.74 (3 H, s, *Me*COAc), 1.37 (3 H, s, C$Me_A$$Me_B$), 1.33 (3 H, s, C$Me_A$$Me_B$), 1.05 (3 H, d, *J* 7, CH*Me*) and 0.97 (3 H, d, *J* 7, CH*Me*).

(1*Z*,3*R**,5*S**,6*S**,7*S**)-3,6,8-Triacetoxy-3,5,7-trimethyl-1-phenyloct-1-ene 24

The triacetate (661 mg, 1.64 mmol) derived from **18** and quinoline (0.10 cm^3) in absolute ethanol (10 cm^3) were hydrogenated over Lindlar's catalyst (Aldrich, 150 mg) until 1 equivalent of hydrogen had been absorbed. The solvent was evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–light petroleum, 1:5) gave the cis-*triacetate* (642 mg, 97%); R_f(EtOAc–light petroleum, 1:5) 0.20; ν_{max}(neat)/cm^{-1} 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 7.27–7.15 (5 H, m, Ph), 6.43 (1 H, d, *J* 12.8, PhC*H*=CH), 5.67 (1 H, d, *J* 12.8, PhCH=C*H*), 4.78 (1 H, dd, *J* 7.7 and 4.1, C*H*OAc), 3.88 (1 H, dd, *J* 11.0 and 7.3, C$H_A$$H_B$OAc), 3.77 (1 H, dd, *J* 11 and 6.1, $CH_A$$H_B$OAc), 2.20–1.67 (4 H, m, C*H₂*C*H*Me and C*H*Me), 2.00 (3 H, s, Ac), 1.99 (3 H, s, Ac), 1.53 (3 H, s, Ac), 1.48 (3 H, s, AcOC*Me*), 0.99 (3 H, d, *J* 6.7, CH*Me*) and 0.88 (3 H, d, *J* 6.8, CH*Me*); *m/z* 404 (1%, M$^+$), 344 (1, M − HOAc), 284 (5, M − 2 HOAc), 224 (35, M − 3 HOAc), 209 (15, M − 3 HOAc − Me), 171 (33, M − HOAc − AcOCHCHMeCH_2OAc), 147 (100, PhCH=CHCMeOH), 131 (30, PhCH=CHCO) and 91 (32, C_7H_7) (Found: M$^+$, 404.2185. $C_{23}H_{32}O_6$ requires *M*, 404.2199).

(1*Z*,3*R**,5*R**,6*R**,7*R**)-3,6,8-Triacetoxy-3,5,7-trimethyl-1-phenyloct-1-ene 30

Similarly, the triacetate (234 mg, 0.58 mmol) derived from **19** gave the cis-*triacetate* (228 mg, 97%); R_f(EtOAc–light petroleum, 1:5) 0.20; ν_{max}(neat)/cm^{-1} 1738 (C=O); δ_H(CDCl$_3$; 250 MHz) 7.32–7.18 (5 H, m, Ph), 6.51 (1 H, d, *J* 12.8, PhCH=CH), 5.68 (1 H, d, *J* 12.8, PhCH=C*H*), 4.83 (1 H, dd, *J* 7.0 and 4.6, C*H*OAc), 3.94 (1 H, dd, *J* 11.0 and 7.0, CH_AH$_B$OAc), 3.85 (1 H, dd, *J* 11.0 and 6.1, CH$_A$$H_B$OAc), 2.05–1.64 (4 H, m, CH_2C*H*Me and C*H*Me), 2.05 (3 H, s, Ac), 2.04 (3 H, s, Ac), 1.57 (3 H, *Me*CO$_2$CMe), 1.53 (3 H, s, MeCO$_2$C*Me*), 0.98 (3 H, d, *J* 6.7, CH*Me*) and 0.93 (3 H, d, *J* 7.0, CH*Me*); *m*/*z* 404 (1%, M$^+$), 284 (6, M − 2 HOAc), 224 (37, M − 3 HOAc), 209 (20, M − 3 HOAc − Me), 171 (40, M − HOAc − AcOCHCHMeCH$_2$-OAc), 147 (100, PhCH=CHCMeOH), 131 (34, PhCH=CHCO) and 91 (C_7H_7) (Found: M$^+$, 404.2185. $C_{23}H_{32}O_6$ requires *M*, 404.2199).

(1*Z*,3*R**,5*S**,6*S**,7*S**)-6,8-Dihydroxy-6,8-*O*-isopropylidene-3,5,7-trimethyl-1-phenyloct-1-en-3-yl acetate 20

Similarly, the acetate derived from the acetonide **18** gave the *cis*-alkene; δ_H(CDCl$_3$) 7.30–7.20 (5 H, m, Ph), 6.39 (1 H, d, *J* 13, PhC*H*=CH), 5.72 (1 H, d, *J* 13, PhCH=C*H*), 3.97 (1 H, dd, *J* 11 and 2, CH_AH$_B$O), 3.63–3.23 (2 H, m, CH$_A$$H_B$O and CHO), 2.19–1.56 (4 H, m, CH_2C*H*Me and C*H*Me), 1.53 (3 H, s, Ac), 1.48 (3 H, s, *Me*COAc), 1.33 (3 H, s, CMe_AMe$_B$), 1.28 (3 H, s, CMe$_A$$Me_B$), 1.02 (3 H, d, *J* 7, CH*Me*) and 0.86 (3 H, d, *J* 7, CH*Me*).

(2*R**,3*R**,4*R**,6*R**,7*E*)-2,4,6-Trimethyl-8-phenyloct-7-ene-1,3,6-triol

The acetylenic triol (213 mg, 0.77 mol) derived from **19** and lithium aluminium hydride (150 mg, 3.95 mmol) were refluxed in dry ether (10 cm^3) under nitrogen at 37 °C for 5 h. Saturated aqueous ammonium chloride (5 cm^3) was added and the mixture was extracted with ether (3 × 30 cm^3). The combined organic layers were dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the trans-*triol* (210 mg, 98%) as an amorphous solid, mp 117–118 °C (from CH$_2$Cl$_2$); ν_{max}(KBr)/cm^{-1} 3600–3150 (O–H); δ_H(CDCl$_3$; 250 MHz) 7.56–7.21 (5 H, m, Ph), 6.66 (1 H, d, *J* 17, PhC*H*=CH), 6.36 (1 H, d, *J* 17, PhCH=C*H*), 4.92–4.53 (3 H, br, 3 OH, exchangeable with D$_2$O), 3.93–3.40 (3 H, m, C*H*OH and CH_2OH), 2.32–1.52 (3 H, m, CH_2COH and C*H*Me), 1.37 (3 H, s, *Me*COH), 1.33 (1 H, m, C*H*Me), 0.96 (3 H, d, *J* 7, CH*Me*) and 0.88 (3 H, d, *J* 6, CH*Me*); *m*/*z* 260 (35%, M − H$_2$O), 245 (44, M − H$_2$O − Me), 147 [100, PhCH=CHC(Me)OH], 131 (84, PhCH=CHCO) and 91 (48, C_7H_7) (Found: M$^+$ − H$_2$O, 260.1777. $C_{17}H_{26}O_3$ requires *M* − H$_2$O, 260.1777). This product was contaminated with the *cis*-isomer (7%, NMR), which did not separate from it on recrystallisation.

(2*R**,3*R**,4*R**,6*S**,7*E*)-2,4,6-Trimethyl-8-phenyloct-7-ene-1,3,6-triol

Similarly, the acetylenic triol (102 mg, 0.37 mmol) derived from **18** gave the trans-*triol* (102 mg, 100%) as an amorphous solid, mp 126.5–127.5 °C (from CH$_2$Cl$_2$); ν_{max}(KBr)/cm^{-1} 3600–3150 (O–H); δ_H(CDCl$_3$) 7.67–7.14 (5 H, m, Ph), 6.69 (1 H, d, *J* 17, PhC*H*=CH), 6.27 (1 H, d, *J* 17, PhCH=C*H*), 5.43–4.03 (3 H, br, 3 OH, exchangeable with D$_2$O), 3.92–3.48 (3 H, m, C*H*OH and CH_2OH), 2.22–1.55 (3 H, m, CH_2COH and C*H*Me), 1.37 (1 H, m, C*H*Me), 1.36 (3 H, s, *Me*COH), 0.85 (3 H, d, *J* 7, CH*Me*) and 0.81 (3 H, d, *J* 7, CH*Me*); *m*/*z* 260 (21%, M − H$_2$O), 245 (14, M − H$_2$O − Me), 147 [100, PhCH=CHC(Me)OH], 131 (62, PhCH=CHCO) and 91 (68, C_7H_7) (Found: M$^+$ − H$_2$O, 260.1771. $C_{17}H_{26}O_3$ requires *M* − H$_2$O, 260.1777). This product was contaminated with the *cis*-isomer (10%), which did not separate from it on recrystallisation.

(1*R**,2*E*,5*S**,6*S**,7*S**)-6,8-Diacetoxy-3,5,7-trimethyl-1-dimethyl(phenyl)silyl-1-phenyloct-2-ene 26 and (1*R**,2*Z*,5*R**,6*R**,7*R**)-6,8-diacetoxy-3,5,7-trimethyl-1-dimethyl(phenyl)-silyl-1-phenyloct-2-ene 27

Method A. Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} in THF, 2.5 cm^3, 2.5 mmol) was added dropwise to copper(I) cyanide (113 mg, 1.25 mmol) under nitrogen at 0 °C and kept for 10 min. The *cis*-triacetate **24** (542 mg, 1.34 mmol) in dry THF (2.0 cm^3) was added dropwise under nitrogen at −23 °C, and kept for 2 h. Saturated aqueous ammonium chloride (25 cm^3) was added and the mixture extracted with ether (3 × 50 cm^3). The combined organic extracts were washed with saturated aqueous ammonium chloride (3 × 50 cm^3), dried (MgSO$_4$), filtered and evaporated under reduced pressure. Chromatography (SiO$_2$, 25 g, EtOAc–light petroleum, 1:5) gave the allylsilanes contaminated with dimethyl(phenyl)silanol, which was removed by evaporation (60 °C at 0.05 mmHg), to leave the *allylsilanes* (554 mg, 86%) as a 1:1 mixture; R_f(EtOAc–light petroleum, 1:10) 0.25; ν_{max}(neat)/cm^{-1} 1738 (C=O) and 1245 (SiMe$_2$Ph); δ_H(CDCl$_3$; 250 MHz) 7.36–6.89 (10 H, m, Ph and SiPh), 5.64 (1 H, d, *J* 11.7, HC=C, one isomer), 5.55 (1 H, d, *J* 11.3, HC=C, one isomer), 4.86–4.76 (1 H, m, *H*COAc), 3.94–3.72 (2 H, m, CH_2OAc), 3.33 (1 H, d, *J* 11.2, SiCH, one isomer), 3.25 (1 H, d, *J* 11.5, SiCH, one isomer), 2.14–1.63 (4 H, m, CH_2C*H*Me and C*H*Me), 2.02, 2.00, 1.95, 1.92 (total 6 H, 4 × s, Ac), 1.72 (3 H, s, MeC=C, one isomer), 1.44 (3 H, s, MeC=C, one isomer), 0.90, 0.83, 0.75, 0.66 (total 6 H, 4 × d, *J* 6.8, 6.8, 6.4 and 6.7, respectively, CH*Me*), 0.26, 0.24, 0.21 and 0.20 (total 6 H, 4 × s, SiMe$_2$); δ_C(CDCl$_3$) 170.7, 170.5, 170.4, 143.2, 142.9, 137.4, 134.3, 133.6, 132.1, 129.0, 128.0, 127.8, 127.5, 125.9, 125.3, 124.5, 124.4, 77.2, 66.6, 43.6, 38.0, 37.4, 34.6, 34.2, 34.0, 33.6, 32.9, 24.6, 20.7, 16.2, 15.8, 10.9, 10.8, −4.0, −4.3, −4.6 and −4.7; *m*/*z* 480 (1 %, M$^+$), 286 (5, M − SiMe$_2$Ph − OAc), 226 (6, M − SiMe$_2$-PhOAc − HOAc), 184 (14), 171 (12), 145 (28, PhCH=CHCMe$_2$), 144 (90, PhCH=CHMeC=CH$_2$), 135 (40, SiMe$_2$Ph), 129 (41) and 43 (100, Ac) (Found: M$^+$ − SiMe$_2$PhOAc, 286.1929. $C_{29}H_{40}O_4Si$ requires *M* − SiMe$_2$PhOAc, 286.1932).

Method B. Dimethyl(phenyl)silyllithium (1.5 cm^3 of a 1.0 mol dm^{-3} in THF, 1.5 mmol) was added dropwise to a stirred suspension of copper(I) cyanide (68 mg, 0.75 mmol) in dry ether (7 cm^3) under nitrogen at 0 °C and kept for 10 min. The *trans*-triacetate **25** (210 mg, 0.52 mmol) was added and the procedure described for the epimeric *cis*-triacetate then gave, after chromatography (SiO$_2$, EtOAc–light petroleum, 1:5), the allylsilanes **26** and **27** (108 mg, 43%, 54% based on reacted starting material) in a ratio of 2:3 (or 3:2), identical (IR and ^{1}H NMR) to the earlier sample, and the starting material **25** (42 mg, 20%).

(1*R**,2*E*,5*R**,6*R**,7*R**)-6,8-Diacetoxy-3,5,7-trimethyl-1-dimethyl(phenyl)silyl-1-phenyloct-2-ene 31 and (1*R**,2*Z*,5*S**,6*S**,7*S**)-6,8-diacetoxy-3,5,7-trimethyl-1-dimethyl(phenyl)-silyl-1-phenyloct-2-ene 32

Method A. The *cis*-triacetate **30** (503 mg, 1.25 mmol) in dry THF (2.0 cm^3) was treated by method A above to give the *allylsilanes* (490 mg, 82%) as a 5:3 or 3:5 mixture; R_f(EtOAc–light petroleum, 1:5) 0.44; ν_{max}(neat)/cm^{-1} 1738 (C=O) and 1244 (SiMe$_2$Ph); δ_H(CDCl$_3$; 250 MHz) 7.33–6.90 (10 H, m, Ph and SiPh), 5.66 (1 H, d, *J* 11.4, HC=C, one isomer), 5.56 (1 H, d, *J* 11.2, HC=C, one isomer), 4.84–4.78 (1 H, m, *H*COAc), 3.95–3.76 (2 H, m, CH_2OAc), 3.32 (1 H, d, *J* 11.1, SiCH, one isomer), 3.28 (1 H, d, *J* 11.4, SiCH, one isomer), 2.20–1.52 (4 H, m, CH_2C*H*Me and C*H*Me), 2.04, 2.04, 2.03, 2.01 (6 H, 4 × s, Ac), 1.67 (3 H, s, MeC=C, one isomer), 1.41 (3 H, s, MeC=C, one isomer), 0.91, 0.88, 0.70, 0.55 (6 H, 4 × d, *J* 7.0, 6.8, 6.4 and 6.4, respectively, CH*Me*), 0.24, 0.22, 0.21 and 0.20 (6 H, 4 × s, SiMe$_2$); δ_C(CDCl$_3$) 170.7, 170.4, 142.9, 134.3, 131.9, 128.9, 128.3, 128.0, 127.4, 126.1, 125.5, 124.4, 77.4, 77.3, 66.5, 42.7, 42.6, 37.8, 34.1, 34.9, 33.1, 32.9, 23.4, 20.7, 15.5, 15.2, 10.7, −4.4 and −4.8; *m*/*z* 286 (<1%, M − SiMe$_2$Ph − OAc), 226 (4, M − SiMe$_2$PhOAc − HOAc), 145 (14, PhCH=CHCMe$_2$), 144 (100, PhCH=CHMeC=CH$_2$), 135 (27, SiMe$_2$Ph) and 129 (36) (Found: M$^+$ − SiMe$_2$PhOAc, 286.1928. $C_{29}H_{40}O_4Si$ requires *M* − SiMe$_2$PhOAc, 286.1932).

Method B. The *trans*-triacetate **29** (92 mg, 0.23 mmol) was treated by method B above to give the allylsilanes **31** and **32** (46 mg, 42%, 52% based on reacted starting material) in a ratio of 5:2 (or 2:5) identical (IR, ^{1}H NMR) with the earlier sample, and the starting material **29** (18 mg, 20%).

(1*E*,3*R,5*S**,6*S**,7*S**)-6,8-Dihydroxy-6,8-*O*-isopropylidene-3,5,7-trimethyl-1-dimethyl(phenyl)silyl-1-phenyloct-2-ene 21 and (1*Z*,3*R**,5*S**,6*S**,7*S**)-6,8-dihydroxy-6,8-*O*-isopropylidene-3,5,7-trimethyl-1-dimethyl(phenyl)silyl-1-phenyloct-2-ene 22**
Similarly, the *cis*-allylic acetate **20** gave the mixture of allylsilanes; δ_H($CDCl_3$) 7.48–6.86 (10 H, m, Ph and SiPh), 5.58 (1 H, m, CH=C), 4.00 (1 H, m, CH_AH$_B$O), 3.65–3.20 (2 H, m, CH$_A$$H_B$O and CHO), 2.54 (1 H, m, CHSi), 1.78 and 1.50 (total of 3 H, s, MeC=), 2.08–1.40 (4 H, m, CH_2C*H*Me and C*H*Me), 1.38, 1.33 and 1.28 (total of 6 H, s, CMe_2), 1.05, 1.00, 0.62 and 0.60 (total of 6 H, d, *J* 6, 2 × CH*Me*) and 0.25, 0.22 and 0.20 (total of 6 H, s, $SiMe_2$).

(1*E*,3*R,5*S**,6*S**,7*S**)-6,8-Diacetoxy-3,5,7-trimethyl-1-phenyloct-1-ene 28**
A mixture of the allylsilanes **26** and **27** (557 mg, 1.61 mmol) and boron trifluoride–acetic acid complex (0.37 cm^3) in dry dichloromethane (10 cm^3) were stirred under nitrogen at 5 °C for 25 min. The mixture was poured into saturated aqueous sodium hydrogen carbonate (20 cm^3) and extracted with dichloromethane (2 × 50 cm^3). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate (25 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, EtOAc–light petroleum, 1:7) gave the *alkene* (345 mg, 86%) as an 83:17 mixture with its epimer at C-6 **33**; R_f(EtOAc–light petroleum, 1:7) 0.28; ν_{max}(neat)/cm^{-1} 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 7.38–7.19 (5 H, m, Ph), 6.36 (1 H, d, *J* 15.9, PhC*H*=CH), 5.96 (1 H, dd, *J* 15.8 and 8.8, PhCH=C*H*), 4.84 (1 H, dd, *J* 7.7 and 3.7, *H*COAc), 3.97–3.76 (2 H, m, CH_2OAc), 2.40 (1 H, br m, C=CCH), 2.25–1.68 (2 H, m, C*H*Me and C*H*Me), 2.08 (3 H, s, Ac), 2.03 (3 H, s, Ac), 1.45–1.16 (2 H, m, CCH_2C), 1.08 (3 H, d, *J* 6.7, MeCC=C), 0.90 (3 H, d, *J* 6.5, CH*Me*) and 0.88 (3 H, d, *J* 6.7, CH*Me*); *m*/*z* 346 (12%, M$^+$), 286 (5, M − HOAc), 226 (7, M − 2 HOAc), 171 (15, PhCH=CHCMe=CHCHMe), 145 (33, PhCH=CHCMe$_2$), 144 (91, PhCH=CHCMe=CH$_2$), 131 (65, PhCH=CHCHMe), 91 (47, C_7H_7), 77 (5, Ph) and 43 (100, Ac) (Found: M$^+$, 346.2137. $C_{21}H_{30}O_4$ requires *M*, 346.2144).

(1*E*,3*R,5*R**,6*R**,7*R**)-6,8-Diacetoxy-3,5,7-trimethyl-1-phenyloct-1-ene 33**
Similarly, the allylsilanes **32** and **31** (628 mg, 1.31 mmol) gave the *alkene* (386 mg, 85%) as an 80:20 mixture with its epimer at C-6 **28**; R_f(EtOAc–light petroleum, 1:7) 0.28; ν_{max}(neat)/cm^{-1} 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 7.36–7.15 (5 H, m, Ph), 6.35 (1 H, d, *J* 15.9, PhC*H*=CH), 6.12 (1 H, dd, *J* 15.9 and 7.4, PhCH=C*H*), 4.89 (1 H, dd, *J* 7.7 and 3.9, C*H*OAc), 3.99–3.81 (2 H, m, CH_2OAc), 2.40 (1 H, m, C=CCH), 2.30–1.75 (2 H, m, C*H*Me and C*H*Me), 2.07 (3 H, s, Ac), 2.05 (3 H, s, Ac), 1.43–1.16 (2 H, m, CCH_2C), 1.04 (3 H, d, *J* 6.7, MeCC=C), 0.93 (3 H, d, *J* 6.9, CH*Me*) and 0.92 (3 H, d, *J* 6.7, CH*Me*); *m*/*z* 346 (<1%, M$^+$), 286 (2, M − HOAc), 226 (6, M − 2 HOAc), 171 (14, PhCH=CHCMe=CHCHMe), 145 (16, PhCH=CHCMe$_2$), 144 (100, PhCH=CHCMe=CH$_2$), 131 (37, PhCH=CHCHMe) and 91 (20, C_7H_7) (Found: M$^+$, 346.2164. $C_{21}H_{30}O_4$ requires *M*, 346.2144).

(2*R,3*R**,5*R**)-2-[(1*R**)-1-(Hydroxymethyl)ethyl]-3,4,5,6-tetrahydro-3,5,6,6-tetramethyl-5-[(*E*)-2-phenylethenyl]pyran 23**
Similarly, the allylsilanes **21** and **22** gave the alkene; δ_H($CDCl_3$) 7.50–7.18 (5 H, m, Ph), 6.39 (1 H, d, *J* 16, PhC*H*=CH), 6.17 (1 H, d, *J* 16, PhCH=C*H*), 3.90–3.33 (3 H, m, CH_2O and CHO), 2.30–1.40 (5 H, m, CH_2C*H*Me and C*H*Me and OH), 1.30 (3 H, s, *Me*$_A$Me$_B$C), 1.26 (3 H, s, Me$_A$*Me*$_B$C), 1.17 (3 H, s, MeCC=C), 1.03 (3 H, d, *J* 7, CH*Me*) and 0.86 (3 H, d, *J* 7, CH*Me*).

(2*R,4*S**,5*S**,6*S**)-5,7-Diacetoxy-2,4,6-trimethylheptanal**
Ozone and air were passed into the alkene **28** (338 mg, 0.98 mmol) in dry dichloromethane (10 cm^3) and methanol (0.1 cm^3) at −78 °C until the solution turned blue. The reaction was stirred at −78 °C for 15 min and the excess ozone was flushed away with dry nitrogen. Dimethyl sulfide (2 cm^3) and pyridinium tosylate (20 mg) were added and the mixture was allowed to warm to room temperature over 1 h and kept for 5 h. The solvent was evaporated off under reduced pressure and the residue was chromatographed (SiO_2, 20 g, EtOAc–light petroleum, 1:10) to give the *aldehyde* (144 mg, 58%); R_f(EtOAc–light petroleum, 1:10) 0.07; ν_{max}(neat)/cm^{-1} 2716 (H–CO) and 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 9.58 (1 H, d, *J* 1.5, CH=O), 4.85 (1 H, dd, *J* 6.8 and 4.3, *H*COAc), 3.99–3.80 (2 H, m, CH_2OAc), 2.56 (1 H, m, HCC=O), 2.25–1.67 (2 H, m, 2 × C*H*Me), 2.08 (3 H, s, Ac), 2.06 (3 H, s, Ac), 1.65–1.38 (2 H, m, CCH_2C), 1.21 (3 H, d, *J* 6.9, *Me*CCHO), 0.93 (3 H, d, *J* 6.6, CH*Me*) and 0.92 (3 H, d, *J* 6.8, HC*Me*); *m*/*z* 229 (1%, M − Ac), 173 (30, M − MeCHCH$_2$CHMeCHO), 131 (47), 127 (36), 113 (46), 75 (100) and 71 (44, CH$_2$CHMeCHO) (Found: M$^+$ − Ac, 229.1444. $C_{14}H_{24}O_5$ requires *M* − Ac, 229.1440).

(2*R,4*R**,5*R**,6*R**)-5,7-Diacetoxy-2,4,6-trimethylheptanal**
Similarly, the alkene **33** (385 mg, 1.11 mmol) gave the *aldehyde* (194 mg, 64%); R_f(EtOAc–light petroleum, 1:10) 0.07; ν_{max}(neat)/cm^{-1} 2715 (H–CO) and 1738 (C=O); δ_H($CDCl_3$; 250 MHz) 9.65 (1 H, d, *J* 1.5, CH=O), 4.87 (1 H, dd, *J* 7.4 and 4.3, *H*COAc), 3.99–3.82 (2 H, m, CH_2OAc), 2.51 (1 H, m, HCC=O), 2.25–1.70 (2 H, m, 2 × C*H*Me), 2.08 (3 H, s, Ac), 2.06 (3 H, s, Ac), 1.65–1.38 (2 H, m, CCH_2C), 1.16 (3 H, d, *J* 6.9, *Me*C-CHO), 0.93 (3 H, d, *J* 6.9, CH*Me*) and 0.91 (3 H, d, *J* 6.7, CH*Me*); *m*/*z* 229 (1%, M − Ac), 173 (45, M − MeCHCH$_2$-CHMeCHO), 131 (97), 127 (95), 113 (99), 75 (35) and 71 (100, CH$_2$CHMeCHO) (Found: M$^+$ − Ac, 229.1420. $C_{14}H_{24}O_5$ requires *M* − Ac, 229.1440).

(2*R,4*S**,5*S**,6*S**)-5,7-Diacetoxy-2,4,6-trimethylheptanoic acid**
Jones reagent (0.9 mol dm^{-3}, 2.0 cm^3, 1.8 mmol) was added dropwise to a stirred solution of the aldehyde (143 mg, 0.53 mmol) derived from **28** in acetone (2 cm^3) at 0 °C and stirred at 5 °C for 15 min. The mixture was poured into saturated aqueous sodium bisulfite (3 cm^3) and extracted with ether (3 × 25 cm^3). The combined organic layers were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *acid* (120 mg, 79%); R_f(EtOAc–light petroleum, 1:3) 0.12; ν_{max}(neat)/cm^{-1} 3600–3000 (O–H), 1738 (ester C=O) and 1710 (acid C=O); δ_H($CDCl_3$; 250 MHz) 10.8–10.6 (1 H, br, CO_2H, exchangeable with D_2O), 4.85 (1 H, dd, *J* 6.9 and 4.3, *H*COAc), 3.99–3.82 (2 H, m, CH_2OAc), 2.55 (1 H, m, *H*CCO$_2$H), 2.17 (1 H, m, C*H*Me), 2.08 (3 H, s, Ac), 2.06 (3 H, s, Ac), 1.79 (1 H, m, C*H*Me), 1.66–1.40 (2 H, m, CCH_2C), 1.21 (3 H, d, *J* 6.8, *Me*CHCO$_2$H), 0.93 (3 H, d, *J* 6.7, HC*Me*) and 0.92 (3 H, d, *J* 6.9, HC*Me*); *m*/*z* 229 (1%, M − OAc), 173 (39, M − MeCH-CH$_2$ − CHMeCO$_2$H), 131 (75), 127 (100), 113 (88) and 71 (84) (Found: M$^+$ − OAc, 229.1447. $C_{14}H_{24}O_6$ requires *M* − OAc, 229.1440).

(2*R,4*R**,5*R**,6*R**)-5,7-Diacetoxy-2,4,6-trimethylheptanoic acid**
Similarly, the aldehyde (140 mg, 0.51 mmol) derived from **33** gave the *acid* (125 mg, 85%); R_f(EtOAc–light petroleum, 1:3) 0.12; ν_{max}(neat)/cm^{-1} 3600–3000 (O–H), 1738 (ester C=O) and 1708 (acid C=O); δ_H($CDCl_3$; 250 MHz) 11.0–10.3 (1 H, br, CO_2H, exchangeable with D_2O), 4.87 (1 H, dd, *J* 7.4 and 4.3, *H*COAc), 3.98–3.80 (2 H, m, CH_2OAc), 2.51 (1 H, m, HCCO$_2$H), 2.24–2.11 (1 H, m, C*H*Me), 2.08 (3 H, s, Ac), 2.06 (3 H, s, Ac), 1.81 (1 H, m, C*H*Me), 1.66–1.40 (2 H, m, CCH_2C), 1.15 (3 H, d, *J* 7.1, *Me*CHCO$_2$H), 0.93 (3 H, d, *J* 7.1, CH*Me*) and 0.91 (3 H, d, *J* 6.8, CH*Me*); *m*/*z* 229 (1%, M − OAc), 173

[53, M − MeCHCH$_2$CH(Me)CO$_2$H], 131 (73), 127 (100), 113 (77) and 71 (65) (Found: M$^+$ − OAc, 229.1423. C$_{14}$H$_{24}$O$_6$ requires *M* − OAc, 229.1440).

(3*R,5*S**,6*S**)-6-[(1*S**)-1-(Hydroxymethyl)ethyl]-3,4,5,6-tetrahydro-3,5-dimethylpyran-2-one**

Powdered potassium carbonate (200 mg) was stirred with the above diacetate (103 mg, 0.36 mmol) in dry methanol (5 cm^3) at room temperature for 1 h. The mixture was filtered and the filter cake was washed with ether (2 × 30 cm^3). The combined organic extracts were evaporated under reduced pressure. The residue and toluene-*p*-sulfonic acid (10 mg) in dichloromethane (5 cm^3) were stirred for 1 h, the mixture was diluted with dichloromethane (50 cm^3) and washed with saturated aqueous sodium hydrogen carbonate (20 cm^3). The organic layer was dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the lactone[25] (50 mg, 75%); ν_{max}(neat)/cm^{-1} 3600–3200 (O–H) and 1726 (C=O); δ_H(CDCl$_3$; 250 MHz) 4.26 (1 H, m, CHO), 3.78–3.53 (2 H, m, C*H*$_2$OH), 2.82–2.63 (1 H, br, OH, exchangeable with D$_2$O), 2.51 (1 H, m, *H*CCO$_2$), 2.07–1.86 (3 H, m, CC*H*$_A$H$_B$C*H* and C*H*CH$_2$OH), 1.40 (1 H, q, *J* 13, CCH$_A$*H*$_B$C), 1.27 (3 H, d, *J* 7.1, *Me*CCO$_2$), 0.98 (3 H, d, *J* 6.3, CH*Me*) and 0.88 (3 H, d, *J* 6.5, CH*Me*); *m*/*z* 169 (3%, M − Me), 127 (82) and 56 (100, C$_3$H$_4$O) (Found: M$^+$ − Me, 169.1233. C$_{10}$H$_{18}$O$_3$ requires *M* − Me, 169.1229).

(3*R,5*R**,6*R**)-6-[(1*R**)-1-(Hydroxymethyl)ethyl]-3,4,5,6-tetrahydro-3,5-dimethylpyran-2-one**

Similarly, the diacetate (140 mg, 0.49 mmol) derived from **33** gave the *lactone* (76 mg, 84%); ν_{max}(neat)/cm^{-1} 3600–3200 (O–H) and 1726 (C=O); δ_H(CDCl$_3$; 250 MHz) 4.24 (1 H, dd, *J* 10.7 and 1.9, *H*CO), 3.77–3.59 (2 H, m, C*H*$_2$OH), 2.69 (1 H, m, *H*CCO$_2$), 2.06–1.89 (2 H, m, 2 × C*H*Me), 1.71 (2 H, m, CCH$_2$C), 1.66–1.56 (1 H, br, OH, exchangeable with D$_2$O), 1.23 (3 H, d, *J* 6.8, *Me*CCO$_2$), 0.99 (3 H, d, *J* 6.6, CH*Me*) and 0.92 (3 H, d, *J* 6.6, CH*Me*); *m*/*z* 186 (<1%, M$^+$), 127 (78) and 56 (100, C$_3$H$_4$O) (Found: M$^+$, 186.1258. C$_{10}$H$_{18}$O$_3$ requires *M*, 186.1256).

(3*R,5*S**,6*S**)-6-[(1*R**)-1-Carboxyethyl]-3,4,5,6-tetrahydro-3,5-dimethylpyran-2-one 34**

The alcohol (40 mg, 0.22 mmol) and pyridinium dichromate (430 mg, 1.14 mmol) in dry DMF (2.0 cm^3) were stirred at room temperature for 10 h. The mixture was poured into saturated aqueous sodium bisulfite (10 cm^3) and acidified to pH 1 with concentrated hydrochloric acid. Sodium chloride was added to make a saturated solution, which was extracted with ether (5 × 15 cm^3). The combined organic layers were dried (MgSO$_4$), filtered and evaporated under reduced pressure. Chromatography (SiO$_2$, AcOH–Et$_2$O–hexane, 1:66:33) gave the Prelog–Djerassi (±)-lactonic acid (35 mg, 82%) as needles, mp 112–112.5 °C (from Et$_2$O–pentane) (lit., 119–120 °C;[24] 110–113 °C;[25] 114–115 °C;[26] and 116–117 °C[27]); R_f(AcOH–Et$_2$O–hexane, 1:66:33) 0.14; ν_{max}(KBr)/cm^{-1} 3700–2400 (O–H), 1742 (ester C=O), 1710 (acid C=O), 1458, 1385, 1260, 1212, 1192 and 1098; δ_H(CDCl$_3$; 250 MHz) 7.6–7.4 (1 H, br, CO$_2$H, exchangeable with D$_2$O), 4.60 (1 H, dd, *J* 10.4 and 2.2, HCO), 2.77 (1 H, dq, *J* 7.2 and 2.4, C*H*CO$_2$H), 2.57 (1 H, m, CHCO$_2$C), 2.04–1.86 (2 H, m, C*H*$_A$H$_B$C*H*CO), 1.47 (1 H, t, *J* 12.6, CCH$_A$*H*$_B$C), 1.29 (3 H, d, *J* 7.0, *Me*CCO$_2$C), 1.20 (3 H, d, *J* 7.3, *Me*CCO$_2$H) and 1.02 (3 H, d, *J* 6.2, CH$_2$CH*Me*CO); δ_C(CDCl$_3$) 176.6, 174.0, 86.2, 41.2, 37.5, 36.3, 31.1, 17.2, 17.0 and 8.6; *m*/*z* 200 (1%, M$^+$), 182 (1, M − H$_2$O), 158 (7), 130 (53), 127 (97), 99 (75), 98 (45), 83 (48), 69 (62) and 56 (100), matching published data.[24–27,28,29]

(3*R,5*R**,6*R**)-6-[(1*S**)-1-Carboxyethyl]-3,4,5,6-tetrahydro-3,5-dimethylpyran-2-one 35**

Similarly, the alcohol (72 mg, 0.39 mmol) derived from **33** gave the (±)-lactonic acid (62 mg, 80%) as prisms, mp 124–126 °C (from Et$_2$O–pentane) (lit., 92–93 °C[28] and 100–102 °C[30]); R_f(AcOH–Et$_2$O–hexane, 1:66:33) 0.14; ν_{max}(KBr)/cm^{-1} 3700–2400 (O–H), 1740 (ester C=O) and 1709 (acid C=O); δ_H(CDCl$_3$; 250 MHz) 8.5–8.2 (1 H, br, CO$_2$H, exchangeable with D$_2$O), 4.55 (1 H, dd, *J* 10.1 and 2.8, HCO), 2.81–2.65 (2 H, m, C*H*CO$_2$C and C*H*CO$_2$H), 1.99 (1 H, m, CH$_2$C*H*CO), 1.80–1.68 (2 H, m, CCH$_2$C), 1.24 (3 H, d, *J* 6.9, *Me*CCO$_2$C), 1.23 (3 H, d, *J* 7.2, *Me*CCO$_2$H) and 1.04 (3 H, d, *J* 6.6, CH$_2$CH*Me*CO); δ_C(CDCl$_3$) 178.0, 175.8, 82.8, 41.0, 35.1, 32.6, 28.9, 17.5, 16.6 and 9.1; *m*/*z* 200 (4%, M$^+$), 182 (5, M − H$_2$O), 158 (11), 130 (52), 127 (84), 112 (17), 99 (50), 98 (40), 83 (33), 69 (39) and 56 (100), matching published data.[27,28]

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References

1 S. F. Martin and D. E. Guinn, *Synthesis*, 1991, 245.
2 N. Ouvrard, J. Rodriguez and M. Santelli, *Tetrahedron Lett.*, 1993, **34**, 1149; C. Santelli-Rouvier, S. Lefrère and M. Santelli, *Tetrahedron Lett.*, 1994, **35**, 6101; M. Miyashita, M. Hoshimo, A. Yoshikoshi, K. Kawamine, K. Yoshihara and H. Irie, *Chem. Lett.*, 1992, 1101.
3 H.-F. Chow and I. Fleming, *Tetrahedron Lett.*, 1985, **26**, 397.
4 I. Fleming and N. K. Terrett, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 2645.
5 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.
6 I. Fleming, R. Henning, D. C. Parker, H. E. Plaut and P. E. J. Sanderson, *J. Chem. Soc.*, *Perkin Trans. 1*, 1995, 317.
7 I. Fleming and N. K. Terrett, *J. Organomet. Chem.*, 1984, **264**, 99.
8 T. Mukaiyama and A. Ishida, *Chem. Lett.*, 1975, 319, 1201 and 1977, 467.
9 I. Fleming, J. Goldhill and I. Paterson, *Tetrahedron Lett.*, 1979, 3205 and 3209.
10 I. Fleming and T. V. Lee, *Tetrahedron Lett.*, 1981, **22**, 705.
11 J. L. Herrmann, G. R. Kieczykowski and R. H. Schlessinger, *Tetrahedron Lett.*, 1973, 2433.
12 I. Fleming and C. P. Leslie, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 1197.
13 I. Fleming, *Chemtracts: Org. Chem.*, 1996, **9**, 1; G. R. Jones and Y. Landais, *Tetrahedron*, 1996, **37**, 7599; K. Tamao, *Adv. Silicon Chem.*, JAI Press, Greenwich, CT, 1996, **3**, 1.
14 A. Barbero, D. C. Blakemore, I. Fleming and R. N. Wesley, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 1329.
15 I. Fleming and N. K. Terrett, *J. Organomet. Chem.*, 1984, **264**, 99.
16 I. Fleming and A. Pearce, *J. Chem. Soc.*, *Perkin Trans. 1*, 1981, 251; H.-F. Chow and I. Fleming, *J. Chem. Soc.*, *Perkin Trans. 1*, 1984, 1815.
17 I. Fleming and D. Marchi, *Synthesis*, 1981, 560.
18 I. Fleming, D. Marchi and S. K. Patel, *J. Chem. Soc.*, *Perkin Trans. 1*, 1981, 2518.
19 I. Fleming, P. E. J. Sanderson and N. K. Terrett, *Synthesis*, 1992, 69.
20 I. Fleming, N. J. Lawrence, A. K. Sarkar and A. P. Thomas, *J. Chem. Soc.*, *Perkin Trans. 1*, 1992, 3303.
21 For another example, see P. Mohr, *Tetrahedron Lett.*, 1995, **36**, 7221.
22 Y. Landais and L. Parra-Rapado, *Tetrahedron Lett.*, 1996, **37**, 1209; see also R. Angelaud and Y. Landais, *Tetrahedron Lett.*, 1997, **38**, 8841; R. Angelaud, Y. Landais and L. Parra-Rapado, *Tetrahedron Lett.*, 1997, **38**, 8845.
23 A. Claesson and L.-I. Olsson, *J. Am. Chem. Soc.*, 1979, **101**, 7302 and references therein; A. Burger, J.-P. Roussel, C. Hetru, J. A. Hoffmann and B. Luu, *Tetrahedron*, 1989, **45**, 155; J. K. Crandall, D. J. Keyton and J. Kohne, *J. Org. Chem.*, 1968, **33**, 3655; L. G. Damm, M. P. Hartshorn and J. Vaughan, *Aust. J. Chem.*, 1976, **29**, 1017; M. P. Hartshorn, R. S. Thompson and J. Vaughan, *ibid.*, 1977, **30**, 865; J. W. Blunt, M. P. Hartshorn, M. H. G. Munroe, L. T. Soong, R. S. Thompson and J. Vaughan, *J. Chem. Soc.*, *Chem. Commun.*, 1980, 820; C. J. Elsevier, J. Meijer, H. Westmijze, P. Vermeer and L. A. Van Dijk, *J. Chem. Soc.*, *Chem. Commun.*, 1982, 84 and references therein; I. Fleming, Y. Landais and P. R. Raithby, *J. Chem. Soc.*, *Perkin Trans. 1*, 1991, 715.
24 S. Masamune, C. U. Kim, K. E. Wilson, G. O. Spessard, P.-E. Georghiou and G. S. Bates, *J. Am. Chem. Soc.*, 1975, **97**, 3512.
25 J. D. White and Y. Fukuyama, *J. Am. Chem. Soc.*, 1979, **101**, 226.
26 G. Stork and V. Nair, *J. Am. Chem. Soc.*, 1979, **101**, 1315.

27 P. A. Bartlett and J. L. Adams, *J. Am. Chem. Soc.*, 1981, **102**, 337.
28 R. E. Ireland and J. P. Daub, *J. Org. Chem.*, 1981, **46**, 479.
29 P. A. Grieco, Y. Ohfune, Y. Yokoyama and W. Owens, *J. Am. Chem. Soc.*, 1979, **101**, 4749; M. Isobe, Y. Ichikawa and T. Goto, *Tetrahedron Lett.*, 1981, **22**, 4287; S. Masamune, *Aldrichimica Acta*, 1978, **11**, 23; S. Masamune, M. Hirama, S. Mori, S. A. Ali and D. S. Garvey, *J. Am. Chem. Soc.*, 1981, **103**, 1568; K. Maruyama, Y. Ishihara and Y. Yamamoto, *Tetrahedron Lett.*, 1981, **22**, 4235; R. H. Schlessinger and M. A. Poss, *J. Am. Chem. Soc.*, 1982, **104**, 357; S. Danishefsky, N. Kato, D. Askin and J. F. Kerwin, Jr., *J. Am. Chem. Soc.*, 1982, **104**, 360; W. C. Still and K. R. Shaw, *Tetrahedron Lett.*, 1981, **22**, 3725; R. W. Hoffmann, H.-J. Zeiss, W. Ladner and S. Tabche, *Chem. Ber.*, 1982, **115**, 2357; D. A. Evans and J. Bartroli, *Tetrahedron Lett.*, 1982, **23**, 807.
30 D. J. Morgans, Jr., *Tetrahedron Lett.*, 1981, **22**, 3721.

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