Stereocontrol of stereogenic centres *para* on a benzene ring using the S_E2'' reaction of a pentadienylsilane

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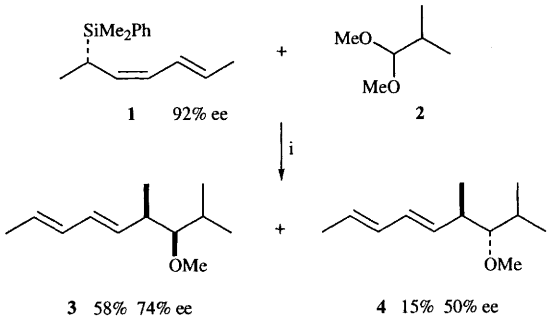
The pentadienylsilane 9 and the dimethyl acetal 2 of isobutyraldehyde react with high (80:20) *anti* stereospecificity to give largely the diene 10a, which was converted into the *para*-disubstituted benzene 11a, having 1,6-related stereogenic centres.

We have shown in the preceding paper,[1] that chiral (*Z*,*E*)-pentadienylsilanes **1** react with electrophiles in S_E2'' reactions, moving stereochemical information five atoms along a carbon chain, with surprisingly high levels (up to 90:10) of stereocontrol in the *anti* sense for both diastereoisomeric products **3** and **4** (Scheme 1).

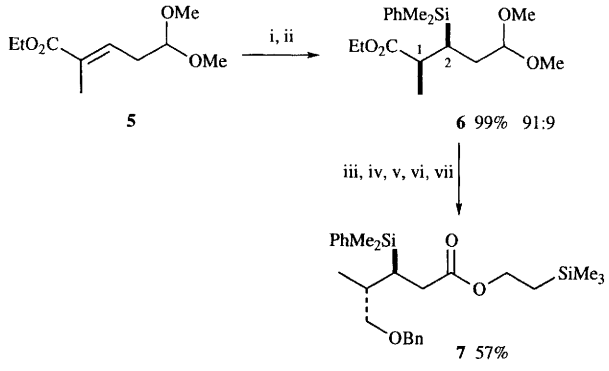


Scheme 1 *Reagents:* i, $BF_3{\cdot}OEt_2$

Most of our work in this area, recorded in the preceding paper, has been concerned with trying to find out whether the stereoselectivity is steric or electronic in origin. Our conclusion is that it is mainly steric when the electrophile is large, but large in this context means such electrophiles as isobutyraldehyde or its acetal **2** in the presence of a Lewis acid. We actually had to work quite hard to find an electrophile, a deuteron or a tethered formaldehyde fragment, that did not show high stereoselectivity. We now report that the high levels of stereospecificity in these S_E2'' reactions can be used to set up stereogenic centres with a 1,6 relationship, and that it is particularly easy to set them up *para* across a benzene ring, an arrangement that is particularly difficult to achieve unless each centre is set up independently with absolute stereocontrol. Separately setting up each centre with absolute control is not suited to the synthesis of racemic material, which is what we are doing here, but obviously specifically synthesising racemic material is not usually important. Roush has recently reported an elegant and indeed better solution to the problem of setting up stereocentres 1,6-related across a butadiene.[2]

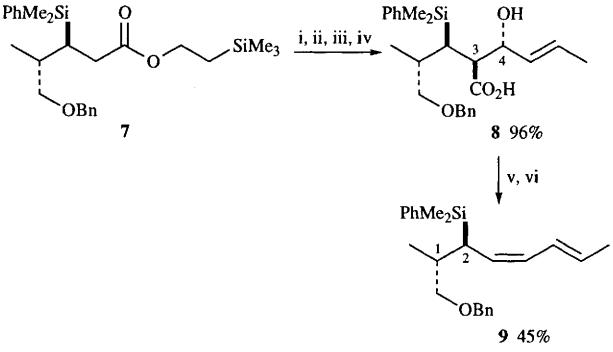
Results and discussion

Following our earlier work,[3] we added successively our phenyldimethylsilyl-cuprate reagent and a proton to the α,β-unsaturated ester **5** to give the ester **6** with selectivity (91:9) in favour of the *syn* relationship between the silyl and the methyl group, as usual in protonations of β-silyl enolates (Scheme 2).[4] We then reduced the ester group and protected the alcohol as its benzyl ether. The benzyl triflate method[5] was superior to the acid-catalysed method using benzyl trichloroacetimidate,[6] because it avoided the easy formation of a cyclic acetal, and base-catalysed methods using benzyl halides give displacement of the phenyl group from the silicon.[7] We oxidised the aldehyde derived from the acetal group into the corresponding carboxylic acid and esterified it to give the ester **7** (Scheme 2).



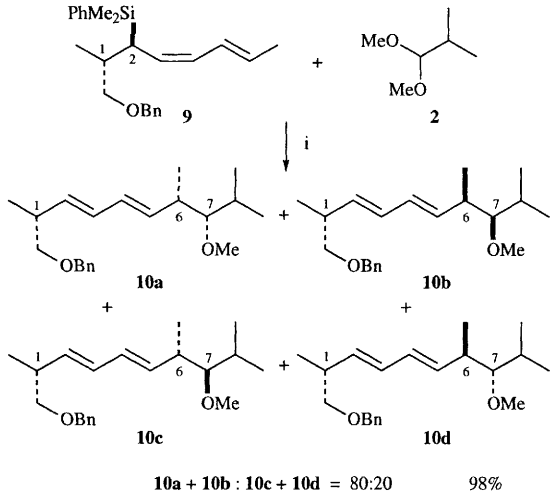
Scheme 2 *Reagents:* i, $(PhMe_2Si)_2CuCNLi_2$, THF, −23 °C, 2 h and −23 °C→0 °C, 30 min; ii, NH_4Cl, H_2O; iii, $LiAlH_4$, THF, 0 °C, 2 h; iv, BnOTf, 2,6-Bu^t_2Py, CH_2Cl_2, −78 °C→−20 °C, 30 min; v, Amberlyst-15, H_2O, Me_2CO, room temp., 24 h; vi, $NaClO_2$, KH_2PO_4, Bu^tOH, H_2O, 2-methylbut-2-ene, room temp., 1 h; vii, $HO(CH_2)_2$-$SiMe_3$, DCC, DMAP, CH_2Cl_2, 0 °C→room temp. 1 h

Having established a relationship between the adjacent centres, numbered C-1 and C-2, on one side of the silyl group, we then used our standard sequence[1,8] for pentadienylsilane synthesis, so that we could move stereochemical information five atoms in the other direction. We carried out an aldol reaction between the ester **7** and *trans*-but-2-enal to give as the major product, a β-hydroxy ester with the usual stereochemistry[8] between C-3 and C-4. Decarboxylative elimination of the corresponding β-hydroxy acid **8** gave largely the (*Z*,*E*)-pentadienylsilane **9** in a *syn* stereospecific reaction, and we removed the small amount of (*E*,*E*)-diene by Diels–Alder reaction with *N*-phenylmaleimide (Scheme 3).



Scheme 3 *Reagents:* i, LDA, THF, −78 °C, 1 h; ii, *trans*-but-2-enal, −78 °C, 3 h; iii, NH_4Cl, H_2O; iv, TBAF, THF, room temp., 3 h; v, $PhSO_2Cl$, Py, 0 °C, 24 h, 100 °C, 1 h; vi, *N*-phenylmaleimide, toluene, 60 °C, 72 h

We then carried out the S_E2'' reaction on the pentadienylsilane **9** with the acetal **2** of isobutyraldehyde to give a mixture of inseparable diastereoisomeric ethers **10** (Scheme 4). By analogy

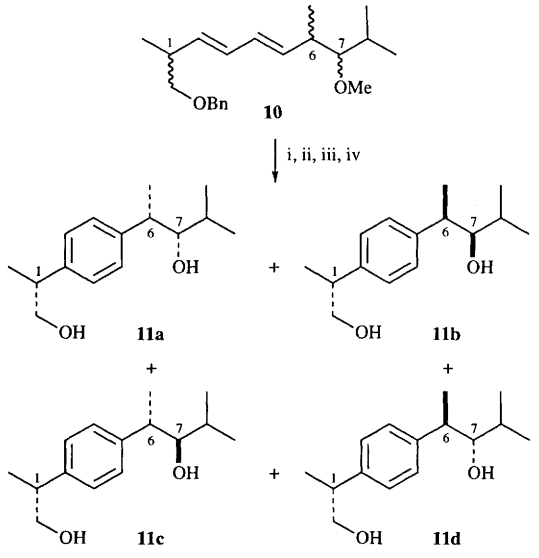


Scheme 4 *Reagents:* i, BF_3·OEt_2, CH_2Cl_2, −78 °C, 5 h, −40 °C, 2 h

with earlier examples of this type of reaction, we can expect to have something like a 4:1 mixture of *syn* (**10a** and **10b**) and *anti* (**10c** and **10d**) diastereoisomers with respect to the relationship between the atoms labelled C-6 and C-7. The ^1H NMR spectrum showed clearly signals from two of the four possible diastereoisomers, in a ratio of 80:20, which we assumed were the isomers differing in their relative stereochemistry at these centres. We can also expect to have a mixture with respect to the relationship between C-1 and C-6, with the products (**10a** and **10c**) of an *anti* reaction significantly more abundant than the products (**10b** and **10d**) of a *syn* reaction. There was no sign of any splitting of the NMR signals (^1H or ^{13}C) from there being mixtures of diastereoisomers **10a** and **10b**, and **10c** and **10d**, which we assumed was because C-1 was too far away from C-6 to show any influence.

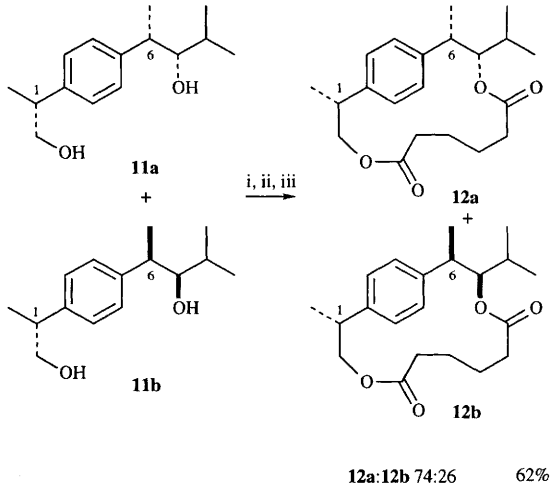
We converted the (*E*,*E*)-diene unit into a benzene ring, using 1-nitro-2-phenylsulfonylethene as an acetylene equivalent.[9] The aromatic product also showed two isomers in the ^1H NMR spectrum with no further splitting of the signals, and still no sign of any possibility of chromatographic separation. We therefore removed both ether groups, using trimethylsilyl chloride and sodium iodide, to give the mixture of diols, which were now separable into the pairs of isomers **11a** + **11b** and **11c** + **11d**, isomeric in their relationships between C-6 and C-7 (Scheme 5). If the stereochemistry has been transferred from C-2 to C-6 with 90% *anti* and 10% *syn* stereoselectivity, which is probably as good as we can hope for, the proportion of the products (**11a**:**11b** and **11c**:**11d**) ought to be 83:17, given that the starting material **6** was actually a 91:9 mixture of diastereoisomers, which we had not separated, although in principle we could have by derivatisation. However, there was no sign, either chromatographically or in the ^1H and ^{13}C NMR spectra, of the diastereoisomeric pairs which must still be present as a result of the presence of a stereogenic centre at C-1. Both pairs of diastereoisomers **11a** + **11b** and **11c** + **11d** gave the sharp signals typical of a single compound, although they could not have been other than mixtures.

To measure the degree of success with which we had controlled the relative stereochemistry between C-1 and C-6, we tied the two hydroxy groups of the mixture of major diastereoisomers **11a** + **11b** into a dilactone, hoping that a restricted range of conformations would increase the probability of differentiating the diastereoisomers spectroscopically. In the event, the mixture of dilactones **12a** and **12b** was formed in good yield using an adipic acid link, which we



Scheme 5 *Reagents:* i, $PhSO_2CH{=}CHNO_2$, toluene, 100 °C, 10 h; ii, Bu_3SnH, AIBN, toluene, reflux, 3 h; iii, DDQ, benzene, room temp., 30 min; iv, TMSCl, NaI, MeCN, room temp., 12 h

attached in two stages, and two diastereoisomers were now clearly present in a ratio of 74:26 (Scheme 6).



Scheme 6 *Reagents:* i, $HO_2C(CH_2)_4CO_2(CH_2)_2SiMe_3$, DCC, DMAP, CH_2Cl_2, 0 °C→room temp., 4 h; ii, TBAF, THF, room temp., 4 h; iii, DCC, DMAP, DMAP·HCl, $CHCl_3$, reflux, 3 h

We assume here that the S_E2'' reaction is *anti* stereospecific, having proved that it was in all our earlier examples. Correcting for the starting material having been a mixture, this indicates that the reaction had taken place with 60% *anti* stereospecificity, and the stereogenic centres between C-1 and C-6 (and C-7, of course) had been substantially controlled, in spite of their distance apart. This was somewhat below what we might have expected from our earlier experience of the S_E2'' reaction,[1] but an 80:20 ratio of attack on the diastereotopic faces of the double bond five atoms from the stereogenic centre is still high, and this remarkable level of 1,6-stereocontrol was achieved entirely with open-chain reactions, with no help from the stereochemical effects in cyclic transition structures.

Experimental

(*Z*-1-Ethoxy-1-trimethylsilyloxy-2-methylbuta-1,3-diene and (*E*)-1-ethoxy-1-trimethylsilyloxy-2-methylbuta-1,3-diene

Butyllithium (1.45 mol dm^{-3} in hexanes; 113 cm^3, 164 mmol) was added dropwise with stirring to diisopropylamine (23.1

cm^3, 16.7 g, 165 mmol) and hexamethylphosphoramide (HMPA) (28.7 cm^3, 29.6 g) in dry tetrahydrofuran (THF) (400 cm^3) under argon at −78 °C. After 30 min, ethyl *trans*-but-2-enoate (17.1 g, 150 mmol) in dry THF (50 cm^3) was added dropwise. The mixture was stirred for a further 10 min and quenched with methyl iodide (10.3 cm^3, 23.4 g, 165 mmol) in dry THF (20 cm^3). The solution was allowed to warm to 0 °C over 50 min and then re-cooled to −78 °C. A solution of LDA [prepared by addition of butyllithium (1.45 mol dm^{-3} in hexanes; 113 cm^3, 164 mmol) to a stirred solution of diisopropylamine (23.1 cm^3, 16.7 g, 165 mmol) in dry THF (200 cm^3) under argon at −20 °C] was added dropwise over 20 min at −78 °C. The mixture was stirred for a further 10 min and quenched with chlorotrimethylsilane (24.5 g, 19.7 cm^3, 225 mmol). The solution was allowed to warm to room temperature, stirred for 1.5 h and the solvent evaporated under reduced pressure. Dry pentane (500 cm^3) was added to the residue, and the resulting mixture filtered to remove the precipitated HMPA–lithium chloride complex and evaporated under reduced pressure. The residue was fractionally distilled under reduced pressure (15 cm Vigreux, 45–46 °C at 1.5 mmHg) to give an inseparable mixture of the *silyl enol ethers* (21.2 g, 70%); ν_{max}(film)/cm^{-1} 1655 (C=C) and 1250 and 845 ($SiMe_3$); δ_H(250 MHz; $CDCl_3$) major isomer: 6.79 (1 H, dd, *J* 10.9 and 17.5,† (C*H*=CH_2), 4.90–4.70 (2 H, m, CH=CH_2), 3.82 (2 H, q, *J* 7.1, CH_2O), 1.62 (3 H, s, MeC=C), 1.23 (3 H, t, *J* 7.1, *Me*CH_2) and 0.22 (9 H, s, $SiMe_3$); minor isomer: 6.63 (1 H, dd, *J* 10.8 and 17.4, C*H*=CH_2), 4.90–4.70 (2 H, m, CH=CH_2), 3.84 (2 H, q, *J* 7.1, CH_2O), 1.67 (3 H, s, MeC=C), 1.23 (3 H, t, *J* 7.1, *Me*CH_2) and 0.22 (9 H, s, $SiMe_3$).

Ethyl (*E*)-5,5-dimethoxy-2-methylpent-2-enoate 5 and ethyl 2-dimethoxymethyl-2-methylbut-3-enoate

Powdered anhydrous zinc bromide (0.75 g, 3.4 mmol) was added with stirring to the silyl enol ethers (16.0 g, 85.1 mmol) and trimethyl orthoformate (20 cm^3, 19.5 g, 183 mmol) in dry dichloromethane (200 cm^3) under argon at room temperature. The suspension was stirred overnight and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95) to give the *ester* **5** (8.38 g, 49%); R_f(EtOAc–hexane, 20:80) 0.45; ν_{max}(film)/cm^{-1} 1705 (C=O); δ_H(250 MHz; $CDCl_3$) 6.71 (1 H, tq, *J* 7.2 and 1.4, CH=C), 4.47 (1 H, t, *J* 5.7, C*H*OMe), 4.19 (2 H, q, *J* 7.1, CH_2O), 3.32 (6 H, s, 2 × OMe), 2.48 (2 H, ddd, *J* 1.0, 5.7 and 7.2, C=CCH_2), 1.83 (3 H, q, *J* 1.2, C=CMe) and 1.27 (3 H, t, *J* 7.1, *Me*CH_2) (Found: M^+ − OMe, 171.1028. $C_{10}H_{18}O_4$ requires *M* − OMe, 171.1021); and *ethyl 2-dimethoxymethyl-2-methylbut-3-enoate* (1.9 g, 11%); R_f(EtOAc–hexane, 20:80) 0.53; ν_{max}(film)/cm^{-1} 1740 (C=O) and 1640 (C=C); δ_H(250 MHz; $CDCl_3$) 5.90 (1 H, dd, *J* 10.9 and 17.5, C*H*=CH_2), 5.08 (1 H, dd, *J* 0.7 and 10.8, CH=C$H_A$$H_B$), 5.05 (1 H, dd, *J* 0.7 and 17.5, CH=C$H_A$$H_B$), 4.45 (1 H, s, C*H*OMe), 4.06 (2 H, dq, *J* 2.1 and 7.1, CH_2O), 3.40 (6 H, s, 2 × OMe), 1.19 (3 H, s, MeCC=O) and 1.16 (3 H, t, *J* 7.1, *Me*CH_2).

Ethyl (2*RS*,3*RS*)-5,5-dimethoxy-2-methyl-3-dimethyl(phenyl)-silylpentanoate 6

Dimethyl(phenyl)silyllithium (0.83 mol dm^{-3}; 132 cm^3, 110 mmol) was added dropwise to a stirred suspension of copper(I) cyanide (5.00 g, 55.2 mmol) in dry THF (20 cm^3) under argon at −5 °C. The mixture was stirred for 15 min and then cooled to −23 °C. The ester **5** (8.38 g, 41.5 mmol) in dry THF (50 cm^3) was added dropwise and the resulting mixture was stirred for 2 h at −23 °C and 30 min at 0 °C, quenched with saturated aqueous ammonium chloride (100 cm^3), filtered through Celite and extracted with ether‡ (3 × 50 cm^3). The extract was washed with saturated aqueous ammonium chloride (3 × 50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95–10:90) to give the *ester* (13.95 g, 99%) as a 91:9 mixture (determined by integration of the ^1H NMR signals of the C-2 methyl groups) with its C-2 epimer; R_f(EtOAc–hexane, 20:80) 0.62; ν_{max}(film)/cm^{-1} 1730 (C=O), 1250 ($SiMe_2$), 1110 (SiPh) and 830 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.62–7.46 (2 H, m, *o*-SiPh), 7.40–7.31 (3 H, m, *m*- and *p*-SiPh), 4.26 (1 H, t, *J* 5.7, C*H*OMe), 4.02 (2 H, dq, *J* 3.5 and 7.1, CH_2O), 3.18 (3 H, s, OMe_A), 3.12 (3 H, s, OMe_B), 2.70 (1 H, dq, *J* 3.8 and 7.1, C*H*Me), 1.75–1.65 (2 H, m, CH_2CSi), 1.30–1.05 (1 H, m, CHSi), 1.23 (3 H, t, *J* 7.1, *Me*CH_2), 1.15 (3 H, d, *J* 7.1, MeCC=O), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.29 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 175.8, 139.1, 134, 128.9, 127.7, 104.6, 60.1, 53.5, 52.4, 40.2, 31.2, 25.2, 16.3, 14.2, −2.6 and −3.2; *m*/*z* 338 (10%, M^+), 323 (13, M − Me), 306 (11, M − MeOH), 291 (23, M − Me − MeOH), 275 (11, M − OMe − MeOH), 263 [42, M − $CH(OMe)_2$], 135, (95, $PhMe_2Si$) and 75 [100, $CH(OMe)_2$] (Found: M^+, 338.1904. $C_{18}H_{30}O_4Si$ requires *M*, 338.1913). The minor diastereoisomer had distinctive signals at δ 4.26 [1 H, t, *J* 5.7, C*H*$(OMe)_2$], 4.07 (2 H, q, *J* 7.1, OCH_2), 3.18 (3 H, s, OMe), 3.12 (3 H, s, OMe), 2.63 (1 H, dq, *J* 7.3 and 2.6, C*H*Me), 1.24 (3 H, t, *J* 7.0, OCH_2*Me*), 1.05 (3 H, d, *J* 7.1, CH*Me*) and 0.36 (6 H, s, $SiMe_2$).

(2*RS*,3*RS*)-5,5-Dimethoxy-2-methyl-3-dimethyl(phenyl)silyl-pentan-1-ol

The ester **6** (12.00 g, 35.5 mmol) in dry THF (80 cm^3) was added dropwise with stirring to a suspension of lithium aluminium hydride (1.30 g, 34.2 mmol) in dry THF (80 cm^3) at 0 °C under argon. After stirring for 2 h, the mixture was quenched with saturated aqueous ammonium chloride (10 cm^3) and filtered through Celite, washing with pyridine–ether (250 cm^3, 0.5:99.5). The filtrate was washed with saturated aqueous ammonium chloride (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 10:90) to give the *alcohol* (10.12 g, 96%); R_f(EtOAc–hexane, 20:80) 0.16; ν_{max}(film)/cm^{-1} 3430 (OH), 1250 ($SiMe_2$), 1120 (SiPh) and 830 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.56–7.49 (2 H, m, *o*-SiPh), 7.36–7.31 (3 H, m, *m*- and *p*-SiPh), 4.21 (1 H, t, *J* 5.8, C*H*OMe), 3.41 (1 H, dd, *J* 6.6 and 10.9, C$H_A$$H_B$O), 3.33 (1 H, dd, *J* 5.9 and 10.9, CH$_A$*H*$_B$O), 3.24 (3 H, s, OMe_A), 3.07 (3 H, s, OMe_B), 1.85–1.75 (1 H, m, C*H*Me), 1.68 (1 H, dd, *J* 5.9 and 14.6, C$H_A$$H_B$CSi), 1.59 (1 H, dd, *J* 5.8 and 14.6, CH$_A$*H*$_B$CSi), 1.20–1.05 (1 H, m, CHSi), 0.95 (3 H, d, *J* 7.0, CMe), 0.35 (3 H, s, Si*Me*$_A$Me$_B$) and 0.33 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 249 (1%, M^+ − Me − MeOH), 135 (50, $PhMe_2Si$) and 75 [100, $CH(OMe)_2$] (Found: M^+ − Me − MeOH, 249.1301. $C_{16}H_{28}O_3Si$ requires *M* − Me − MeOH, 249.1310).

(3*RS*,4*RS*)-5-Benzyloxy-4-methyl-3-dimethyl(phenyl)silyl-pentanal dimethyl acetal

Benzyl alcohol (4.18 cm^3, 4.36 g, 40.4 mmol) and 2,6-di-*tert*-butylpyridine (9.2 cm^3, 7.83 g, 41 mmol) in dichloromethane (60 cm^3) were added dropwise with stirring to trifluoromethanesulfonic anhydride (6.8 cm^3, 11.4 g, 40.4 mmol) in dichloromethane (150 cm^3) at −78 °C under argon. The solution was stirred for 5 min and a solution of the alcohol (7.51 g, 25.4 mmol) and 2,6-di-*tert*-butylpyridine (14.8 cm^3, 12.67 g, 66 mmol) in dichloromethane (100 cm^3) was added dropwise. The resulting solution was stirred for 30 min, allowed to warm to −20 °C and stirred for a further 30 min. The solution was quenched with pyridine (8 cm^3), washed with water (3 × 100 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95) to give the *acetal* (8.66 g, 88%); R_f(EtOAc–hexane, 20:80) 0.62; ν_{max}(film)/cm^{-1} 1250 ($SiMe_2$), 1120 (SiPh) and 830 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.56–7.48 (2 H, m, *o*-SiPh), 7.39–

† *J* Values are given in Hz.
‡ 'Ether' refers to diethyl ether.

7.28 (8 H, m, *m*- and *p*-SiPh and CPh), 4.39 (2 H, s, PhCH_2), 4.32 (1 H, t, *J* 5.8, C*H*OMe), 3.25–3.10 (2 H, m, CH_2CMe), 3.22 (3 H, s, OMe_A), 3.13 (3 H, s, OMe_B), 2.14 (1 H, d sextet, *J* 2.8 and 6.9, C*H*Me), 1.77–1.61 (2 H, m, CH_2CSi), 1.34–1.27 (1 H, m, CHSi), 1.00 (3 H, d, *J* 6.9, CMe), 0.33 (3 H, s, Si$Me_A$$Me_B$) and 0.32 (3 H, s, Si$Me_A$$Me_B$); *m*/*z* 309 (1%, M^+ − Ph), 135 (100, $SiMe_2$Ph), 107 (15, $PhCH_2O$) and 91 (65, $PhCH_2$) (Found: C, 71.5; H, 8.9. $C_{23}H_{34}O_3Si$ requires C, 71.5; H, 8.9%).

(3*RS*,4*RS*)-5-Benzyloxy-4-methyl-3-dimethyl(phenyl)silylpentanal

Amberlyst-15 (1.8 g) was added to the acetal (10.67 g, 27.6 mmol) in water (1.8 cm^3) and acetone (150 cm^3) at room temperature under argon. The mixture was stirred overnight, filtered and evaporated under reduced pressure to give the *aldehyde* (9.38 g, 100%); R_f(EtOAc–hexane, 20:80) 0.62; ν_{max}(film)/cm^{-1} 2715 (aldehyde CH), 1720 (C=O), 1250 ($SiMe_2$), 1110 (SiPh) and 830 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 9.57 (1 H, dd, *J* 1.5 and 2.6, CHO), 7.50–7.44 (2 H, m, *o*-SiPh), 7.37–7.26 (8 H, m, *m*- and *p*-SiPh and CPh), 4.35 (2 H, s, PhCH_2), 3.21 (1 H, dd, *J* 6.3 and 9.3, C$H_A$$H_B$CMe), 3.16 (1 H, dd, *J* 6.4 and 9.3, $CH_A$$H_B$CMe), 2.43 (1 H, ddd, *J* 2.6, 8.3 and 16.5, C$H_A$$H_B$C=O), 2.38 (1 H, ddd, *J* 1.5, 5.0 and 16.5, $CH_A$$H_B$C=O), 2.05–1.95 (1 H, m, C*H*Me), 1.74 (1 H, dt, *J* 8.2 and 4.9, CHSi), 0.95 (3 H, d, *J* 6.9, CMe), 0.32 (3 H, s, Si$Me_A$$Me_B$) and 0.31 (3 H, s, Si$Me_A$$Me_B$); *m*/*z* 325 (19%, M^+ − Me), 263 (65, M − Ph), 249 (45, M − $PhCH_2$), 135 (100, $SiMe_2$Ph) and 91 (90, $PhCH_2$) (Found: M^+ − Me, 325.1625. $C_{21}H_{28}O_2Si$ requires *M* − Me, 325.1624).

(3*RS*,4*RS*)-5-Benzyloxy-4-methyl-3-dimethyl(phenyl)silylpentanoic acid

Sodium chlorite (4.0 g, 80%, 35.6 mmol) and potassium dihydrogen phosphate (4.0 g, 29.4 mmol) in water (100 cm^3) were added dropwise with stirring to the aldehyde (9.28 g, 27.3 mmol) in *tert*-butyl alcohol (200 cm^3) and 2-methylbut-2-ene (50 cm^3) at room temperature under argon. The mixture was stirred vigorously for 1 h, diluted with EtOAc (1500 cm^3), washed with brine (3 × 150 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 20:80–50:50) to give the *acid* (7.15 g, 74%); ν_{max}(film)/cm^{-1} 3400–2500 (acid OH), 1705 (C=O), 1250 ($SiMe_2$), 1110 (SiPh) and 835 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.54–7.45 (2 H, m, *o*-SiPh), 7.38–7.26 (8 H, m, *m*-and *p*-SiPh and CPh), 4.37 (2 H, s, PhCH_2), 3.26 (1 H, dd, *J* 5.9 and 9.2, C$H_A$$H_B$CMe), 3.17 (1 H, dd, *J* 7.1 and 9.2, $CH_A$$H_B$CMe), 2.44 (1 H, dd, *J* 7.9 and 16.3, C$H_A$$H_B$C=O), 2.38 (1 H, dd, *J* 5.9 and 16.3, $CH_A$$H_B$C=O), 2.15–2.00 (1 H, m, C*H*Me), 1.66 (1 H, ddd, *J* 4.3, 6.1 and 7.7, CHSi), 0.98 (3 H, d, *J* 6.9, CMe), 0.34 (3 H, s, Si$Me_A$$Me_B$) and 0.33 (3 H, s, Si$Me_A$$Me_B$); *m*/*z* 356 (4%, M^+), 341 (45, M − Me), 279 (50, M − Ph), 135 (95, $SiMe_2$Ph) and 91 (100, $PhCH_2$) (Found: M^+, 356.1810. $C_{21}H_{28}O_3Si$ requires *M*, 356.1808) (Found: C, 70.5; H, 7.9. $C_{21}H_{28}O_3Si$ requires C, 70.7; H, 7.9%).

2-Trimethylsilylethyl (3*RS*,4*RS*)-5-benzyloxy-4-methyl-3-dimethyl(phenyl)silylpentanoate 7

Dicyclohexylcarbodiimide (3.50 g, 16.96 mmol) in dry dichloromethane (7 cm^3) was added dropwise to a stirred solution of the acid (5.49 g, 15.42 mmol), 2-trimethylsilylethanol (2.43 cm^3, 2.01 g, 16.96 mmol) and 4-dimethylaminopyridine (100 mg, 0.8 mmol) in dry dichloromethane (30 cm^3) at 0 °C under argon. The mixture was stirred at room temperature for 1.5 h, filtered through Celite, diluted with dichloromethane (400 cm^3), washed with dilute hydrochloric acid (1 mol dm^{-3}; 2 × 100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95) to give the *ester* (5.88 g, 84%); R_f(EtOAc–hexane, 20:80) 0.70; ν_{max}(film)/cm^{-1} 1730 (C=O), 1250 ($SiMe_2$), 1110 (SiPh) and 835 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.50–7.46 (2 H, m, *o*-SiPh), 7.35–7.26 (8 H, m, *m*- and *p*-SiPh and CPh), 4.35 (2 H, s, PhCH_2), 4.06–3.99 (2 H, m, $SiCH_2CH_2$), 3.24 (1 H, dd, *J* 5.8 and 9.2, C$H_A$$H_B$CMe), 3.13 (1 H, dd, *J* 7.4 and 9.2, $CH_A$$H_B$CMe), 2.40–2.25 (2 H, m, CH_2C=O), 2.15–2.00 (1 H, m, C*H*Me), 1.66 (1 H, ddd, *J* 4.0, 6.3 and 7.8, CHSi), 0.96 (3 H, d, *J* 6.9, CMe), 0.95–0.85 (2 H, m, $SiCH_2$), 0.30 (3 H, s, Si$Me_A$$Me_B$), 0.29 (3 H, s, Si$Me_A$$Me_B$) and 0.01 (9 H, s, $SiMe_3$); *m*/*z* 413 (40%, M^+ − C_2H_4 − Me), 351 (25, M − C_2H_4 − Ph), 135 (95, $SiMe_2$Ph), 91 (100, $PhCH_2$) and 73 (80, $SiMe_3$) (Found: C, 68.5; H, 8.7. $C_{26}H_{40}O_3Si$ requires C, 68.4; H, 8.8%).

2-Trimethylsilylethyl (2*RS*,3*SR*,4*E*)-2-[(1*SR*,2*SR*)-1-dimethyl(phenyl)silyl-2-methyl-3-benzyloxypropan-1-yl]-3-hydroxyhex-4-enoate

Butyllithium (1.42 mol dm^{-3} in hexanes; 10.44 cm^3, 14.83 mmol) was added dropwise with stirring to diisopropylamine (2.24 cm^3, 1.62 g, 16 mmol) in dry THF (30 cm^3) under argon at −20 °C, the mixture stirred for 0.5 h and then cooled to −78 °C. The ester **7** (5.88 g, 12.89 mmol) in dry THF (20 cm^3) was added dropwise at −78 °C and the mixture stirred for 1 h at this temperature. Freshly distilled *trans*-but-2-enal (2.24 g, 2.65 cm^3, 32 mmol) was added dropwise at the same temperature. The solution was stirred for 3 h, quenched with saturated aqueous ammonium chloride (40 cm^3), allowed to warm and extracted with ether (3 × 100 cm^3). The extract was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95–10:90) to give the *hydroxy ester* (6.51 g, 96%); R_f(EtOAc–hexane, 20:80) 0.59; ν_{max}(film)/cm^{-1} 3450 (OH), 1730 (C=O), 1250 ($SiMe_2$), 1110 (SiPh) and 835 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.59–7.45 (2 H, m, *o*-SiPh), 7.36–7.26 (8 H, m, *m*- and *p*-SiPh and CPh), 5.52 (1 H, dq, *J* 15.3 and 5.8, CH=C*H*Me), 5.42 (1 H, ddq, *J* 7.1, 15.3 and 1.1, C*H*=CHMe), 4.34 (2 H, s, PhCH_2), 4.10–3.90 (1 H, m, CHO), 3.96–3.86 (2 H, m, $SiCH_2CH_2$), 3.25 (1 H, dd, *J* 4.6 and 9.0, C$H_A$$H_B$CMe), 3.13 (1 H, t, *J* 8.7, $CH_A$$H_B$CMe), 2.69 (1 H, dd, *J* 3.3 and 8.4, CHC=O), 2.25–2.10 (1 H, m, CH_2C*H*Me), 1.72 (1 H, t, *J* 3.3, CHSi), 1.62 (3 H, d, *J* 5.5, C=CMe), 0.99 (3 H, d, *J* 6.8, CH_2C*Me*), 0.91–0.77 (2 H, m, $SiCH_2$), 0.39 (3 H, s, Si$Me_A$$Me_B$), 0.37 (3 H, s, Si$Me_A$$Me_B$) and 0.02 (9 H, s, $SiMe_3$) (Found: C, 68.4; H, 8.9. $C_{30}H_{46}O_4Si_2$ requires C, 68.4; H, 8.8%).

(2*RS*,3*SR*,4*E*)-2-[(1*SR*,2*SR*)-1-Dimethyl(phenyl)silyl-2-methyl-3-benzyloxypropan-1-yl]-3-hydroxyhex-4-enoic acid 8

Tetrabutylammonium fluoride (1.1 mol dm^{-3} in THF; 40 cm^3, 44 mmol) was added dropwise with stirring to the hydroxy ester (6.51 g, 12.38 mmol) in dry THF (100 cm^3) under argon at room temperature. The solution was stirred for 3 h, quenched with ether (250 cm^3) and water (250 cm^3), stirred for 5 min and extracted with ether (2 × 100 cm^3). The extract was washed with dilute hydrochloric acid (1 mol dm^{-3}; 100 cm^3) and brine (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the *hydroxy acid* (5.22 g, 99%) as a pale yellow oil, R_f(EtOAc–hexane, 20:80) 0.06; ν_{max}(film)/cm^{-1} 3500–2500 (acid OH), 1715 (C=O), 1250 ($SiMe_2$), 1110 (SiPh) and 820 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.60–7.44 (2 H, m, *o*-SiPh), 7.37–7.26 (8 H, m, *m*- and *p*-SiPh and CPh), 5.64 (1 H, dq, *J* 15.3 and 6.3, CH=C*H*Me), 5.48 (1 H, ddq, *J* 6.9, 15.3 and 1.3, C*H*=CHMe), 4.38 (2 H, s, PhCH_2), 4.17 (1 H, t, *J* 7.1, CHO), 3.33 (1 H, dd, *J* 6.2 and 9.3, C$H_A$$H_B$CMe), 3.28 (1 H, dd, *J* 5.5 and 9.2, $CH_A$$H_B$CMe), 2.81 (1 H, dd, *J* 2.8 and 7.3, CHC=O), 2.20–2.05 (1 H, m, CH_2C*H*Me), 1.71 (1 H, dd, *J* 2.8 and 3.7, CHSi), 1.66 (3 H, d, *J* 6.3, C=CMe), 0.95 (3 H, d, *J* 6.9, CH_2C*Me*), 0.40 (3 H, s, Si$Me_A$$Me_B$) and 0.38 (3 H, s, Si$Me_A$$Me_B$); *m*/*z* 393 (70%, M^+ − H_2O − Me), 349 (15, M − Ph), 331 (80, M − H_2O − Ph), 135 (95, $SiMe_2$Ph) and 91 (100, $PhCH_2$) (Found: M^+ − Ph, 349.1838. $C_{25}H_{34}O_4Si$ requires *M* − Ph, 349.1835).

(2*RS*,3*SR*,4*Z*,6*E*)-(1-Benzyloxy-2-methylocta-4,6-dien-3-yl)-dimethyl(phenyl)silane 9 and (2*RS*,3*SR*,4*E*,6*E*)-(1-benzyloxy-2-methylocta-4,6-dien-3-yl)dimethyl(phenyl)silane

Benzenesulfonyl chloride (3.5 cm^3, 5.0 g, 28.1 mmol) was added dropwise with stirring to the hydroxy acid **8** (4.00 g, 9.39 mmol) in pyridine (40 cm^3) at 0 °C under argon. The solution was left overnight in the refrigerator, quenched with ice water (50 cm^3) and extracted with ether (3 × 50 cm^3). The extract was washed with saturated aqueous sodium hydrogen carbonate solution (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of the β-lactone of **8** and the *dienes* in pyridine. This mixture was heated at 100 °C for 1 h under argon, diluted with ether (200 cm^3), washed with dilute hydrochloric acid (3 mol dm^{-3}; 3 × 50 cm^3), saturated aqueous sodium hydrogen carbonate (50 cm^3) and brine (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95) to give an inseparable mixture of the *dienes* (1.97 g, 58%) as a colourless oil. Spectroscopic data for diene **9** are recorded below.

(2*RS*,3*SR*,4*Z*,6*E*)-(1-Benzyloxy-2-methylocta-4,6-dien-3-yl)-dimethyl(phenyl)silane 9

N-Phenylmaleimide (8.0 mmol, 1.45 g) was heated with the dienes (1.97 g, 5.41 mmol) in toluene (50 cm^3) at 60 °C for 72 h. The solvent was removed under reduced pressure and the residue chromatographed (SiO_2, EtOAc–hexane, 5:95) to give the pure *diene* (1.42 g, 72%); R_f(EtOAc–hexane, 5:95) 0.52; ν_{max}(film)/cm^{-1} 1250 ($SiMe_2$), 1120 (SiPh), 990 (CH=CH) and 840 ($SiMe_2$); δ_H(250 MHz; $CDCl_3$) 7.53–7.44 (2 H, m, *o*-SiPh), 7.37–7.26 (8 H, m, *m*- and *p*-SiPh and CPh), 6.19 (1 H, ddq, *J* 12.4, 14.9 and 1.4, MeCH=C*H*CH=CH), 5.96 (1 H, t, *J* 10.9, MeCH=CHC*H*=CH), 5.62 (1 H, dq, *J* 14.8 and 6.8, MeC*H*=CHCH=CH), 5.14 (1 H, t, *J* 11.4, MeCH=CHCH=C*H*), 4.36 (2 H, s, PhCH_2), 3.38 (1 H, dd, *J* 4.2 and 9.0, C$H_A$$H_B$CMe), 3.12 (1 H, dd, *J* 7.9 and 8.9, CH$_A$$H_B$CMe), 2.26 (1 H, dd, *J* 7.0 and 12.1, CHSi), 2.00–1.85 (1 H, m, CH_2C*H*Me), 1.73 (3 H, dd, *J* 1.3 and 6.8, C=CMe), 0.94 (3 H, d, *J* 6.8, CH_2C*Me*), 0.28 (3 H, s, Si*Me*$_A$Me$_B$) and 0.27 (3 H, s, SiMe$_A$*Me*$_B$); *m*/*z* 287 (5%, M^+ − Ph), 135 (100, $SiMe_2$Ph) and 91 (60, $PhCH_2$) (Found: C, 78.9; H, 8.9. $C_{24}H_{32}OSi$ requires C, 79.1; H, 8.9%).

(2*RS*,7*SR*,8*SR*,3*E*,5*E*)-1-Benzyloxy-2,7,9-trimethyl-8-methoxydeca-3,5-diene 10a, (2*RS*,7*RS*,8*RS*,3*E*,5*E*)-1-benzyloxy-2,7,9-trimethyl-8-methoxydeca-3,5-diene 10b, (2*RS*,7*SR*,8*RS*,3*E*,5*E*)-1-benzyloxy-2,7,9-trimethyl-8-methoxydeca-3,5-diene 10c and (2*RS*,7*RS*,8*SR*,3*E*,5*E*)-1-benzyloxy-2,7,9-trimethyl-8-methoxydeca-3,5-diene 10d

Boron trifluoride–diethyl ether (0.96 cm^3, 1.11 g, 7.8 mmol) was added dropwise with stirring to the diene **9** (1.42 g, 3.89 mmol) and the acetal **2** (920 mg, 7.8 mmol) in dry dichloromethane (25 cm^3) at −78 °C under argon. The mixture was stirred at −78 °C for 5 h and at −40 °C for 2 h, quenched with water (15 cm^3), diluted with ether (200 cm^3), washed with water (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95) to give an inseparable mixture of the *dienes* (1.21 g, 98%); R_f(EtOAc–hexane, 10:90) 0.35; ν_{max}(film)/cm^{-1} 1095 (C–O) and 990 (CH=CH); δ_H(250 MHz; $CDCl_3$) 7.40–7.26 (5 H, m, Ph), 6.12–5.95 (2 H, m, CH=C*H*CH=CH), 5.67–5.45 (2 H, m, C*H*=CHCH=C*H*), 4.51 (2 H, s, PhCH_2), 3.43 (3 H, s, OMe), 3.37 (1 H, dd, *J* 6.5 and 9.1, C$H_A$$H_B$CMe), 3.28 (1 H, dd, *J* 7.0 and 9.1, CH$_A$$H_B$CMe), 2.66 (1 H, dd, *J* 5.0 and 6.6, CHO), 2.52 (1 H, sept, *J* 6.8, CH_2C*H*Me), 2.36 (1 H, sext, *J* 6.8, CHC*H*Me), 1.75 (1 H, oct, *J* 6.7, C*H*Me_2), 1.04 (3 H, d, *J* 6.8, C=CCH*Me*$_A$), 1.03 (3 H, d, *J* 6.7, C=CCH*Me*$_B$), 0.92 (3 H, d, *J* 6.9, C*Me*$_A$Me$_B$) and 0.88 (3 H, d, *J* 6.9, CMe$_A$*Me*$_B$); *m*/*z* (FAB) 317 (25%, M^+ + H), 315 (50, M − H) and 229 (100, M − MeOCHCHC-Me_2) (Found: M^+ + H, 317.2455. $C_{21}H_{32}O_2$ requires *M* + H, 317.2480). The ratio of **10a** + **10b**:**10c** + **10d** was determined to be 80:20 by integration of ^{1}H NMR peaks, with distinguishable peaks in the ^{1}H NMR spectrum from **10c** + **10d** at δ 2.61 (dd).

***cis*-1-[(2*RS*)-1-Benzyloxypropan-2-yl]-4-[(2*SR*,3*SR*)-3-methoxy-4-methylpentan-2-yl]cyclohexa-2,5-diene, *cis*-1-[(2*RS*)-1-benzyloxypropan-2-yl]-4-[(2*RS*,3*SR*)-3-methoxy-4-methylpentan-2-yl]cyclohexa-2,5-diene, *cis*-1-[(2*RS*)-1-benzyloxypropan-2-yl]-4-[(2*SR*,3*RS*)-3-methoxy-4-methylpentan-2-yl]cyclohexa-2,5-diene and *cis*-1-[(2*RS*)-1-benzyloxypropan-2-yl]-4-[(2*RS*,-3*SR*)-3-methoxy-4-methylpentan-2-yl]cyclohexa-2,5-diene**

The dienes **10** (1.15 g, 3.64 mmol) and 1-nitro-2-phenylsulfonylethene (1.00 g, 4.73 mmol) in toluene (15 cm^3) were heated under argon at 100 °C for 10 h and at 80 °C overnight and the solvent evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 10:90–20:80) to give the Diels–Alder products (1.54 g, 2.91 mmol) which were then heated under reflux under argon as a mixture with AIBN (95 mg, 0.58 mmol) and tributyltin hydride (1.57 cm^3, 1.70 g, 5.82 mmol) in toluene (10 cm^3) for 3 h. The solvent was evaporated under reduced pressure and the crude product chromatographed (SiO_2, hexane then EtOAc–hexane, 5:95) to give an inseparable mixture of the *dienes* (837 mg, 67%); R_f(EtOAc–hexane, 20:80) 0.62; ν_{max}(film)/cm^{-1} 1095 (C–O); δ_H(250 MHz; $CDCl_3$) 7.38–7.26 (5 H, m, Ph), 5.80–5.46 (4 H, m, 2 × CH=CH), 4.50 (2 H, s, PhCH_2), 3.44 (1 H, dd, *J* 6.9 and 9.2, C$H_A$$H_B$CMe), 3.42 (3 H, s, OMe), 3.30 (1 H, dd, *J* 7.2 and 9.2, CH$_A$$H_B$CMe), 3.00–2.75 (3 H, m, CHO and C*H*C=CC*H*), 1.95 (1 H, dsextet, *J* 3.9 and 6.9, CH_2C*H*Me), 1.94–1.80 (1 H, m, CHC*H*Me), 1.75–1.60 (1 H, m, C*H*Me_2), 0.93 (3 H, d, *J* 6.8, CMe$_A$), 0.89 (3 H, d, *J* 6.8, CMe$_B$), 0.88 (3 H, d, *J* 6.9, CMe$_C$) and 0.86 (3 H, d, *J* 6.9, CMe$_D$); *m*/*z* 91 (100, $PhCH_2^+$) and 87 (85, $MeOCHCHMe_2$) (Found: C, 80.5; H, 10.0. $C_{23}H_{34}O_2$ requires C, 80.7; H, 10.0%). The ratio of 2*SR*,3*SR* + 2*RS*,3*RS*:2*SR*,3*RS* + 2*SR*,3*RS* diastereoisomers was determined to be 80:20 by integration of ^{1}H NMR peaks. Distinguishable peaks in ^{1}H NMR spectrum from 2*SR*,3*RS* + 2*SR*,3*RS* diastereoisomers at δ 3.47 (s), 1.01 (d) and 0.64 (d).

1-[(2*RS*)-1-Benzyloxypropan-2-yl]-4-[(2*SR*,3*SR*)-3-methoxy-4-methylpentan-2-yl]benzene, 1-[(2*RS*)-1-benzyloxypropan-2-yl]-4-[(2*RS*,3*RS*)-3-methoxy-4-methylpentan-2-yl]benzene, 1-[(2*RS*)-1-benzyloxypropan-2-yl]-4-[(2*SR*,3*RS*)-3-methoxy-4-methylpentan-2-yl]benzene and 1-[(2*RS*)-1-benzyloxypropan-2-yl]-4-[(2*RS*,3*SR*)-3-methoxy-4-methylpentan-2-yl]benzene

Dichlorodicyanobenzoquinone (DDQ) (531 mg, 2.34 mmol) in benzene (10 cm^3) was added dropwise with stirring to the dienes (800 mg, 2.34 mmol) in benzene (10 cm^3) at room temperature under argon. The mixture was stirred for 30 min, filtered washing with dichloromethane (400 cm^3), washed with saturated aqueous sodium hydrogen carbonate (2 × 100 cm^3) and water (100 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 5:95) to give an inseparable mixture of the *ethers* (789 mg, 99%); R_f(EtOAc–hexane, 5:95) 0.27; ν_{max}(film)/cm^{-1} 1510 (Ar) and 1095 (C–O); δ_H(250 MHz; $CDCl_3$) 7.35–7.19 (5 H, m, Ph), 7.13 (4 H, s, R_2ArH), 4.49 (2 H, s, PhCH_2), 3.57 (1 H, dd, *J* 6.3 and 9.2, C$H_A$$H_B$CMe), 3.47 (1 H, dd, *J* 7.6 and 9.2, CH$_A$$H_B$CMe), 3.31 (3 H, s, OMe), 3.04 (1 H, sext, *J* 6.9, CH_2C*H*Me), 2.94 (1 H, dd, *J* 4.6 and 7.1, CHO), 2.85 (1 H, quintet, *J* 6.9, CHC*H*Me), 1.67–1.48 (1 H, m, C*H*Me_2), 1.29 (3 H, d, *J* 6.9, ArCMe$_A$), 1.28 (3 H, d, *J* 6.7, ArCMe$_B$), 0.91 (3 H, d, *J* 6.9, C*Me*$_A$Me$_B$) and 0.85 (3 H, d, *J* 6.7, CMe$_A$*Me*$_B$); *m*/*z* 340 (10%, M^+), 297 (65, M − $CHMe_2$), 91 (35, $PhCH_2$) and 87 (100, $MeOCHCHMe_2$) (Found: M^+, 340.2395. $C_{23}H_{32}O_2$ requires *M*, 340.2402) (Found: C, 81.1; H, 9.5. $C_{23}H_{32}O_2$ requires C, 81.1; H, 9.5%). The ratio of 2*SR*,3*SR* + 2*RS*,3*RS*:2*SR*,3*RS* + 2*SR*,3*RS* diastereoisomers was determined to be 80:20 by integration of ^{1}H NMR peaks. Distinguishable peaks in ^{1}H NMR spectrum from 2*SR*,3*RS* + 2*SR*,3*RS* diastereoisomers at δ 3.11 (s), 1.69 (m) and 0.90 (d).

1-[(2*RS*)-1-Hydroxypropan-2-yl]-4-[(2*SR*,3*SR*)-3-hydroxy-4-methylpentan-2-yl]benzene 11a, 1-[(2*RS*)-1-hydroxypropan-2-yl]-4-[(2*SR*,3*SR*)-3-hydroxy-4-methylpentan-2-yl]benzene 11b, 1-[(2*RS*)-1-hydroxypropan-2-yl]-4-[(2*SR*,3*RS*)-3-hydroxy-4-methylpentan-2-yl]benzene 11c and 1-[(2*RS*)-1-hydroxypropan-2-yl]-4-[(2*RS*,3*SR*)-3-hydroxy-4-methylpentan-2-yl]benzene 11d

Chlorotrimethylsilane (0.11 cm^3, 92 mg, 0.85 mmol) was added dropwise with stirring to the ethers (97 mg, 0.285 mmol) and sodium iodide (127 mg, 0.85 mmol) in acetonitrile (3 cm^3) at room temperature under argon. The mixture was stirred overnight, quenched with water (5 cm^3), diluted with ether (70 cm^3), washed with aqueous sodium thiosulfate (25%, 10 cm^3) and brine (10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (SiO_2, diisopropyl ether) to give the *diols* **11a** + **11b** (32 mg, 48%); R_f(isopropyl ether) 0.17; ν_{max}(film)/cm^{-1} 3380 (OH) and 1510 (Ar); δ_H(400 MHz; $CDCl_3$) 7.16 (4 H, s, ArH), 3.67 (2 H, d, *J* 6.8, CH_2O), 3.36 (1 H, t, *J* 5.9, CHO), 2.92 (1 H, sextet, *J* 7.0, CH_2CHMe), 2.88 (1 H, quintet, *J* 6.9, $CHCHMe$), 1.59 (1 H, octet, *J* 6.5, $CHMe_2$), 1.27 (3 H, d, *J* 7.3, $ArCMe_A$), 1.25 (3 H, d, *J* 7.3, $ArCMe_B$), 0.93 (3 H, d, *J* 6.8, CMe_AMe_B) and 0.90 (3 H, d, *J* 6.7, CMe_AMe_B); δ_C(100 MHz; $CDCl_3$) 143.5, 141.5, 127.9, 127.6, 81.2, 68.7, 42.2, 42.0, 30.3, 19.9, 17.6, 17.0 and 15.3; *m*/*z* 236 (5%, M^+), 164 (90, M − C=OCHMe$_2$) and 146 (65, M − H_2O − C=OCHMe$_2$) (Found: M^+, 236.1778. $C_{15}H_{24}O_2$ requires *M*, 236.1776); and the *diols* **11c** + **11d** (9 mg, 13%); R_f(isopropyl ether) 0.15; ν_{max}(film)/cm^{-1} 3390 (OH) and 1510 (Ar); δ_H(400 MHz; $CDCl_3$) 7.21 (2 H, d, *J* 8.3, ArH_A), 7.18 (2 H, d, *J* 8.5, ArH_B), 3.68 (2 H, d, *J* 6.8, CH_2O), 3.39 (1 H, dd, *J* 4.4 and 7.6, CHO), 2.92 (1 H, sextet, *J* 6.9, CH_2CHMe), 2.84 (1 H, quintet, *J* 7.2, $CHCHMe$), 1.77 (1 H, dseptet, *J* 4.4 and 6.8, $CHMe_2$), 1.25 (3 H, d, *J* 7.0, $ArCMe_A$), 1.23 (3 H, d, *J* 7.1, $ArCMe_B$), 1.01 (3 H, d, *J* 6.8, CMe_AMe_B) and 0.92 (3 H, d, *J* 6.8, CMe_AMe_B); δ_C(100 MHz; $CDCl_3$) 142.4, 141.8, 128.4, 127.6, 80.5, 68.7, 43.0, 42.0, 30.0, 20.4, 18.6, 17.6 and 15.4; *m*/*z* 236 (50%, M^+), 164 (30, M − C=OCHMe$_2$) and 146 (100, M − H_2O − C=OCHMe$_2$) (Found: M^+, 236.1774. $C_{15}H_{24}O_2$ requires *M*, 236.1776).

2-Trimethylsilylethyl hydrogen adipate

A mixture of adipic acid (730 mg, 5.0 mmol), toluene-*p*-sulfonic acid (10 mg, 0.05 mmol) and 2-trimethylsilylethanol (840 mg, 7.1 mmol) in toluene (5 cm^3) was refluxed for 2 h with continuous azeotropic removal of water in a Dean–Stark trap. The solvent was removed under reduced pressure and the residue was chromatographed (SiO_2, EtOAc–hexane, 50:50) to give the *ester* (400 mg, 33%); R_f(EtOAc–hexane, 50:50) 0.39; ν_{max}(film)/cm^{-1} 3600–2500 (acid OH), 1730 and 1715 (C=O) and 1250 and 840 ($SiMe_3$); δ_H(250 MHz; $CDCl_3$) 4.18–4.11 (2 H, m, CH_2O), 2.41–2.26 (4 H, m, 2 × CH_2C=O), 1.66 (4 H, quintet, *J* 3.5, $CH_2CH_2CH_2CH_2$), 1.00–0.93 (2 H, m, CH_2Si) and 0.03 (9 H, s, $SiMe_3$) (Found: C, 53.6; H, 9.0. $C_{11}H_{22}O_4Si$ requires C, 53.6; H, 9.0%).

2-Trimethylsilylethyl (2*RS*)-2-{4-[(2*SR*,3*SR*)-3-hydroxy-4-methylpentan-2-yl]phenyl}propyl adipate and 2-trimethylsilyl (2*RS*)-2-{4-[(2*RS*,3*RS*)-3-hydroxy-4-methylpentan-2-yl]-phenyl}propyl adipate

Dicyclohexylcarbodiimide (33 mg, 0.16 mmol) in dry dichloromethane (1 cm^3) was added dropwise to a stirred solution of the above acid (34 mg, 0.14 mmol), the diols **11a** + **11b** (33 mg, 0.14 mmol), 4-dimethylaminopyridine (20 mg, 0.16 mmol) and 4-dimethylaminopyridine hydrochloride (22 mg, 0.14 mmol) in dry dichloromethane (1 cm^3) at 0 °C under argon. The mixture was allowed to warm to room temperature, stirred for 4 h, filtered and the solvent evaporated under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 20:80) to give the *diesters* (53 mg, 82%); R_f(EtOAc–hexane, 20:80) 0.30; ν_{max}(film)/cm^{-1} 3520 (OH), 1730 (C=O), 1510 (Ar) and 1250 and 835 ($SiMe_3$); δ_H(250 MHz; $CDCl_3$) 7.17 (4 H, s, ArH), 4.18 (1 H, dd, *J* 6.8 and 10.7, $CHCH_AH_BO$), 4.17–4.10 (2 H, m, CH_2CH_2O), 4.08 (1 H, dd, *J* 7.5 and 10.8, $CHCH_AH_BO$), 3.36 (1 H, q, *J* 5.5, CHO), 3.05 (1 H, sextet, *J* 7.0, CH_2CHMe), 2.88 (1 H, quintet, *J* 6.7, $CHCHMe$), 2.30–2.20 (4 H, m, 2 × CH_2C=O), 1.66–1.55 (5 H, m, $CH_2CH_2CH_2CH_2$ and $CHMe_2$), 1.38 (1 H, d, *J* 4.7, OH), 1.25 (6 H, d, *J* 7.0, 2 × ArCMe), 1.00–0.95 (2 H, m, CH_2Si), 0.93 (3 H, d, *J* 6.6, CMe_AMe_B), 0.90 (3 H, d, *J* 6.5, CMe_AMe_B) and 0.03 (9 H, s, $SiMe_3$) (Found: C, 67.3; H, 9.6. $C_{26}H_{44}O_5Si$ requires C, 67.2; H, 9.5%).

(2*RS*)-2-{4-[(2*SR*,3*SR*)-3-Hydroxy-4-methylpentan-2-yl]-phenyl}propyl hydrogen adipate and (2*RS*)-2-{4-[(2*RS*,3*RS*)-3-hydroxy-4-methylpentan-2-yl]phenyl}propyl hydrogen adipate

Tetrabutylammonium fluoride (1.0 mol dm^{-3} in THF; 0.3 cm^3, 0.3 mmol) was added dropwise to a stirred solution of the diesters (47 mg, 0.10 mmol) in dry THF (1 cm^3) under argon at room temperature. The resulting solution was stirred for 4 h, quenched with ether (5 cm^3) and water (5 cm^3), stirred for 5 min and extracted with ether (2 × 5 cm^3). The extract was washed with dilute hydrochloric acid (1 mol dm^{-3} 5 cm^3) and brine (5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the *hydroxy acids* (37 mg, 100%); ν_{max}(film)/cm^{-1} 3460 (OH), 3400–2500 (acid OH), 1730 and 1715 (C=O) and 1510 (Ar); δ_H(250 MHz; $CDCl_3$) 7.16 (4 H, s, ArH), 4.18 (1 H, dd, *J* 7.2 and 10.8, CH_AH_BO), 4.12 (1 H, dd, *J* 6.9 and 10.8, CH_AH_BO), 3.38 (1 H, t, *J* 5.9, CHO), 3.06 (1 H, sextet, *J* 7.0, CH_2CHMe), 2.92 (1 H, quintet, *J* 6.7, $CHCHMe$), 2.34–2.24 (4 H, m, 2 × CH_2C=O), 1.68–1.56 (5 H, m, $CH_2CH_2CH_2CH_2$ and $CHMe_2$), 1.27 (3 H, d, *J* 7.0, $ArCMe_A$), 1.26 (3 H, d, *J* 7.0, $ArCMe_B$), 0.94 (3 H, d, *J* 6.8, CMe_AMe_B) and 0.92 (3 H, d, *J* 6.5, CMe_AMe_B); *m*/*z* 365 (75, M^+ + H) and 292 (40, M − COCHMe$_2$) (Found: M^+ + H, 365.2326. $C_{21}H_{32}O_5$ requires *M* + H, 365.2328).

(1*RS*,2*RS*,12*SR*)-2-Isopropyl-1,12-dimethyl-3,10-dioxa[12]-paracyclophane-4,9-dione 12a and (1*RS*,2*RS*,12*RS*)-2-isopropyl-1,12-dimethyl-3,10-dioxa[12]paracyclophane-4,9-dione 12b

The hydroxy acids (18 mg, 0.050 mmol) in freshly distilled ethanol-free chloroform (0.5 cm^3) were added dropwise over 3 h to a stirred solution of dicyclohexylcarbodiimide (23 mg, 0.11 mmol), 4-dimethylaminopyridine (21 mg, 0.17 mmol) and 4-dimethylaminopyridine hydrochloride (18 mg, 0.11 mmol) in freshly distilled ethanol-free chloroform (4 cm^3) at reflux under argon. The mixture was allowed to cool to room temperature, stirred overnight, the solvent removed under reduced pressure, diluted with ether (15 cm^3), filtered and the solvent removed under reduced pressure. The residue was chromatographed (SiO_2, EtOAc–hexane, 10:90) to give an inseparable mixture of the *diones* **12a** and **12b** (13 mg, 76%) in a ratio of 74:26 (as determined by integration of GLC and ^1H NMR signals) as a white solid, mp 128–131 °C; R_f(EtOAc–hexane, 10:90) 0.34; r.t. (GLC; 60 °C–15 °C/min–200 °C/min) 19.9 (2*RS* diast.) and 20.1 (2*SR* diast.); ν_{max}(CH_2Cl_2)/cm^{-1} 1725 (C=O); δ_H(400 MHz; $CDCl_3$) 7.25–6.98 [4 H, m, ArH (2*RS* and 2*SR* diast.)], 4.99 [1 H, dd, *J* 2.9 and 10.3, CHO (2*RS* diast.)], 4.91 [1 H, dd, *J* 3.0 and 10.3, CHO (2*RS* diast.)], 4.56 [1 H, t, *J* 11.1, $CHCH_AH_BO$ (2′*RS* diast.)], 4.40 [1 H, dd, *J* 5.0 and 10.7, $CHCH_AH_BO$ (2*SR* diast.)], 4.01 [1 H, dd, *J* 4.9 and 11.1, $CHCH_AH_BO$ (2*RS* diast.)], 3.81 [1 H, t, *J* 11.1, $CHCH_AH_BO$ (2*SR* diast.)], 3.20–3.12 [2 H, m, CH_2CHMe and $CHCHMe$ (2*RS* and 2*SR* diast.)], 2.16–2.04 [3 H, m, 2 × CH_AH_BC=O and $CHMe_2$ (2*RS* and 2*SR* diast.)], 1.96–1.88 [2 H, m, 2 × CH_AH_BC=O (2*RS* and 2*SR* diast.)], 1.31 [3 H, d, *J* 7.1, $ArCMeCH$ (2*SR* diast.)], 1.31 [3 H, d, *J* 7.1, $ArCMeCH$ (2*RS* diast.)], 1.25–1.05 [4 H, m, $CH_2CH_2CH_2CH_2$ (2*RS* and 2*SR* diast.)], 1.20 [3 H, d, *J* 7.1, $ArCMeCH_2$ (2*SR* diast.)], 1.31 [3 H, d, *J* 7.1, $ArCMeCH_2$ (2*RS* diast.)], 1.04 [3 H, d, *J* 6.7, CMe_AMe_B(2*RS* and 2*SR* diast.)], 0.86 [3 H, d, *J* 6.5, CMe_AMe_B(2*SR* diast.)] and 0.86 [3

H, d, J 6.6, CMe_AMe_B(2*RS* diast.)]; δ_C(100 MHz; $CDCl_3$) 2*RS* diast. 173.5, 172.9, 141.3, 141.1, 129.4, 128.9, 126.6, 124.4, 81.8, 67.1, 38.7, 38.3, 35.3, 34.0, 30.1, 26.0, 24.7, 20.0, 19.5, 18.8 and 10.5. Distinguishable signals from 2*SR* diast. at 173.1, 141.9, 130.1, 129.3, 126.4, 124.6, 82.0, 69.0, 38.6, 38.2, 35.2, 33.4, 25.6, 24.3, 20.0, 17.6 and 10.9; *m/z* (FAB) 369 (5%, M^+ + Na) and 347 (55, M + H) (Found: M^+ + H, 347.2209. $C_{21}H_{30}O_4$ requires *M* + H, 347.2222).

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