Synthesis of Medium Ring Ethers. Part 4.† Stereoselective Claisen-mediated Ring Expansion as a Route to Homochiral Disubstituted Medium Ring Lactones

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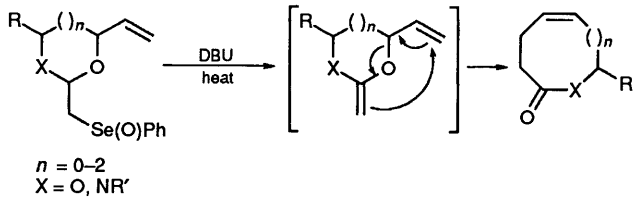
Thermal elimination/Claisen rearrangement of selenoxides derived from the enantiomerically pure phenylselenomethyl-substituted cyclic acetals **4** and **8** proceeds stereospecifically to provide the homochiral 8- and 7-membered lactones **5** and **9** respectively.

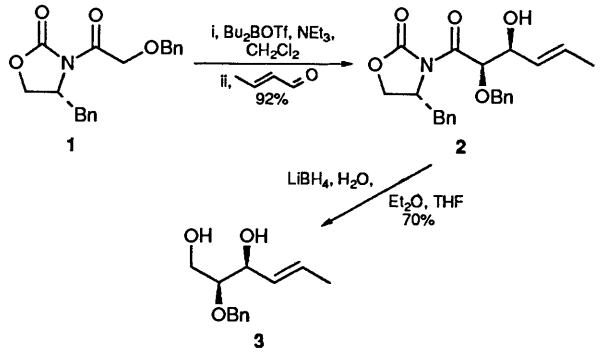
Recent efforts in this laboratory have focussed on the synthesis of medium ring (7–9 membered) heterocycles, including lactones[1] and lactams.[2] A method of increasing generality has been the two-atom ring expansion of a vinyl-substituted cyclic ketene acetal (or aminal) *via* Claisen rearrangement; the desired lactones/lactams are formed in moderate to excellent yields (Scheme 1).



Scheme 1

Results so far have involved only unsubstituted vinyl substituents in the precursor. In those systems, there is no opportunity for the formation of new chiral centres in the Claisen rearrangement itself. In this paper, we report that the methodology can be extended to the synthesis of the optically pure disubstituted lactones **5** and **9** (Scheme 3). Chiral information is transferred from the homochiral precursors, acetals **4** and **8**, during the Claisen rearrangement to the newly formed sp^3 centre in the lactones **5** and **9**.

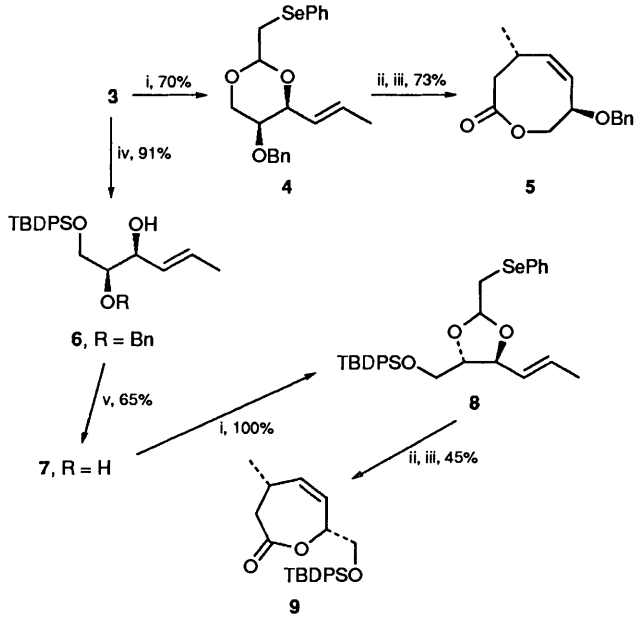
The cyclic acetals **4** and **8** were derived from a common precursor, the (monoprotected) triol **3** (Scheme 2). Evans aldol



Scheme 2

reaction[3] of compound **1** with crotonaldehyde, followed by reductive removal of the chiral auxiliary[4] provided the optically pure triol **3** in 64% overall yield (> 95% e.e.).[5]‡

The conversion of the triol **3** into the cyclic acetal **4** was accomplished by treatment with $PhSeCH_2CH(OEt)_2$ and pyridinium toluene-*p*-sulfonate (PPTS) in refluxing toluene with 70% efficiency (Scheme 3).[1,6] Oxidation of the selenide **4** with sodium periodate provided a quantitative yield of the



Scheme 3 *Reagents and conditions:* i, $PhSeCH_2CH(OEt)_2$, PPTS(cat.), toluene, reflux; ii, $NaIO_4$, $NaHCO_3$, MeOH–H_2O; iii, DBU, 1-*tert*-butyldimethylsiloxy-1-methoxyethene, xylene, 185 °C, sealed tube; iv, *tert*-butyldiphenylsilyl chloride, imidazole, DMF; v, lithium–di-*tert*-butylbiphenyl, THF

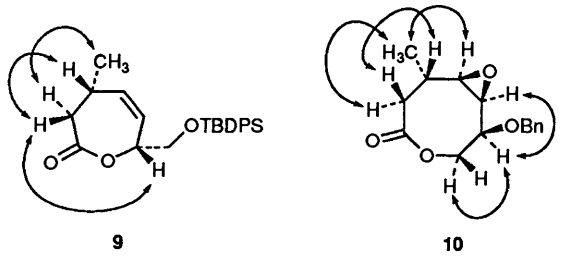
selenoxide, which was generally used without purification. The Claisen rearrangement was carried out in a NaOH-washed sealed tube[7] by heating the selenoxide, diazabicyclo[5.4.0]-undecene (DBU), and a large excess of 1-*tert*-butyldimethylsiloxy-1-methoxyethene[8] in xylene at 185 °C for 14 h. The presence of the silyl ketene acetal was necessary to prevent disproportionation between the liberated benzeneselenenic acid and unchanged selenoxide. The lactone was obtained as a single diastereoisomer in 73% yield {$[\alpha]_D^{20}$ −116.73 (*c* 2.0 in $CHCl_3$) > 95% e.e.}.§

The relative position of the methyl group at the new asymmetric centre to the benzyloxy substituent at the centre

† Part 3, R. W. Carling, J. S. Clark, A. B. Holmes and D. Sartor, *J. Chem. Soc., Perkin Trans. 1*, 1992, 95.

‡ The enantiomeric excess of **3** was determined by protection of the primary alcohol as its triphenylmethyl ether (triphenylmethyl chloride, pyridine), followed by conversion of the secondary alcohol into its (*R*)-(+)-phenyl methoxy(trifluoromethyl)acetate. ^1H and ^{19}F NMR detected only one diastereoisomer, indicating an enantiomeric purity of > 95%.[5]

§ The enantiomeric excesses of the lactones **5** and **9** were determined by ^1H NMR with 30 mol% [Eu(tfc)$_3$]. Only one diastereoisomeric complex was detected, indicating a diastereoisomeric purity of > 95%.



9 10

Fig. 1

of known configuration could not be determined by ^{1}H NMR NOE studies as no effects were observed. Therefore, the double bond was epoxidised to bring the original olefinic protons into close enough proximity with the adjacent protons to ensure an NOE. The epoxidation (MCPBA, 55%) was apparently directed by the benzyloxy group toward the same face to provide the single diastereoisomer **10**. Observed NOEs in the ^{1}H NMR spectrum (Fig. 1) confirmed both the predicted *cis* orientation of the epoxide relative to the benzyloxy substituent, and the *trans* relationship of the methyl and benzyloxy groups.

For the analogous 7-membered lactone synthesis, the primary hydroxy group of the diol **3** (Scheme 3) was protected as its *tert*-butyldiphenylsilyl ether (TBDPSCl, imidazole, dimethylformamide, 91%). The resulting bis-protected triol **6** was debenzylated with lithium di-*tert*-butylbiphenyl[9] to provide the monoprotected triol **7** with 65% efficiency. Acetal formation under the same conditions as described for compound **3** resulted in a quantitative yield of the 5-membered cyclic acetal **8**, which, when subjected to the same oxidation/Claisen conditions as for the 8-membered system, rearranged to a single diastereoisomer of the lactone **9** in 45% yield {$[\alpha]_D^{25}$ −59.77 (*c* 2.0 in $CHCl_3$) >95% e.e.}. ^{1}H NMR NOE studies indicated a *cis* relationship between the methyl and the siloxymethyl substituents (Fig. 1).

The Claisen rearrangement of the above systems is stereospecific, implying a single preferred transition state geometry dictated by the asymmetry of the precursors. Similar transfers of chirality have been observed for carbocyclic systems,[7,10] but these are the first examples in which the products are lactones. This methodology is currently being explored as a route to natural products containing medium ring heterocycles with varying substitution patterns.

Experimental

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker WM-250 (250 MHz) or on a Bruker AM-400 (400 MHz) instrument. Chemical shifts are measured in ppm relative to tetramethylsilane (TMS) ($\delta = 0$) using $CDCl_3$ or C_6D_6 as internal standard. *J*-Values are given in Hz. IR spectra were recorded on a Perkin-Elmer 1310 spectrophotometer with the sample prepared as a thin liquid film. Calibration was relative to polystyrene. Mass spectra were recorded by the SERC Mass Spectrometry Service, University of Swansea. Optical specific rotations were measured at 20 °C using a Perkin-Elmer 241 polarimeter and are quoted in units of 10^{-1} deg cm^2 g^{-1}. Analytical thin layer chromatography (TLC) was carried out on Merck precoated 0.25 mm thick plates Kieselgel 60 F_{254}. Flash chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Tetrahydrofuran (THF) was distilled from potassium in a recycling still using benzophenone ketyl as indicator. Other solvents were purified by standard techniques.

[3(2R,3S,4E),4R]-4-*Benzyl*-3-(2-*benzyloxy*-3-*hydroxyhex*-4-*enoyl*)*oxazolidin*-2-*one* **2**.—To a cooled (−78 °C) solution of (4*R*)-4-benzyloxazolidin-2-one[4] (4.847 g, 27.35 mmol, 1 equiv.) in THF (100 cm^3) was added BuLi (28.05 mmol, 1.0 equiv.). After 10 min, the mixture was treated with benzyloxyacetyl chloride (5.11 g, 27.67 mmol, 1.0 equiv.) over 10 min. The mixture was stirred for 1.5 h and then allowed to warm to 20 °C; it was poured into brine (0.5 dm^3) and extracted with CH_2Cl_2 (4 × 100 cm^3). The combined extracts were dried ($MgSO_4$), concentrated to a yellow oil, and the residue was filtered through a short flash column (25% EtOAc–hexane). The product was recrystallized from EtOAc–hexane to give compound **1** as white needles (7.15 g, 21.97 mmol, 80%), R_f 0.64 (50% EtOAc–hexane); m.p. 67–69 °C (EtOAc–hexane); $[\alpha]_D^{20}$ −57.45 (*c* 2.0 in $CHCl_3$).

A solution of compound **1** (6.08 g, 18.69 mmol, 1 equiv.) and triethylamine (3.4 cm^3, 24.4 mmol, 1.3 equiv.) in CH_2Cl_2 (100 cm^3) at −74 °C was treated with a CH_2Cl_2 solution of Bu_2BOTf (1 mol dm^{-3}; 22.5 mmol, 1.2 equiv.) at such a rate as to keep the temperature below −65 °C. The solution was stirred for 40 min and then allowed to warm to 0 °C for 1.25 h; it was then cooled to −70 °C and treated with freshly distilled crotonaldehyde (1.86 cm^3, 22.5 mmol, 1.2 equiv.). The mixture was allowed to warm slowly to 0 °C over 1.5 h and was then stirred for a further 1.5 h. The reaction was quenched with a solution of methanol (90 cm^3), pH 7 phosphate buffer (50 cm^3), and H_2O_2 (100 v/v; 20 cm^3). The cooling bath was removed, and the mixture was stirred for 1.5 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 cm^3). The combined extracts were washed with water, combined, dried ($MgSO_4$), and concentrated to a golden oil. Purification of this by flash chromatography (30% EtOAc–hexane) afforded the title compound **2** as a clear oil (6.833 g, 17.28 mmol, 92%), R_f 0.30 (50% EtOAc–hexane); $[\alpha]_D^{20}$ −27.19 (*c* 2.0 in $CHCl_3$); δ_H(250 MHz; $CDCl_3$) 7.41–7.17 (10 H, m, ArH), 5.82–5.67 (1 H, m, CH_2CH), 5.63–5.53 (1 H, dd, *J* 15.4 and 6.8, CH_3CHCH), 5.22 (1 H, d, *J* 4.2, CHOBn), 4.78–4.56 (3 H, m, $NCHCH_2Ph$), 4.32 (1 H, dd, *J* 6.8 and 4.2, CHOH), 4.18 (2 H, d, *J* 4.7, OCH_2Ph), 3.19 [1 H, dd, *J* 13.4 and 3.3, $C(O)OCH_aH_b$], 2.66 [1 H, dd, *J* 13.4 and 9.7, $C(O)OCH_aH_b$] and 1.69 (3 H, d, *J* 6.5, CH_3).

(2S,3S)-2-*Benzyloxyhex*-4-*ene*-1,3-*diol* **3**.—To a solution of compound **2** (7.905 g, 19.99 mmol, 1 equiv.) and water (0.360 cm^3, 19.98 mmol, 1.0 equiv.) in diethyl ether (400 cm^3) at 0 °C was added a suspension of $LiBH_4$ (0.429 g, 19.70 mmol, 1.0 equiv.) in THF (14 cm^3). After 20 min, dilute aqueous NaOH (300 cm^3) was added to the mixture which was then stirred at 20 °C for 1 h. The layers were separated, and the aqueous layer extracted with diethyl ether (2 × 300 cm^3); the combined extracts were dried ($MgSO_4$) and concentrated. Purification of the residue by flash chromatography (10% → 30% EtOAc–hexane) afforded the diol **3** as a clear oil (3.64 g, 14.00 mmol, 70%); R_f 0.18 (50% EtOAc–hexane); $[\alpha]_D^{20}$ +16.83 (*c* 2.0 in $CHCl_3$) (Found: C, 70.2; H, 8.2. $C_{13}H_{18}O_3$ requires C, 70.2; H, 8.2%); ν_{max}(film)/cm^{-1} 3610–3110 (OH), 1090 (ether) and 960 (*trans* olefin); δ_H(250 MHz; $CDCl_3$) 7.40–7.28 (5 H, m, Ar*H*), 5.88–5.69 (1 H, dq, *J* 15.3 and 6.4, CH_3CH=C), 5.49 (1 H, ddq, *J* 15.3, 7.0 and 1.5, CH_3CH=C*H*), 4.71 (1 H, d, *J* 11.5, OCH_aH_bPh), 4.65 (1 H, d, *J* 11.5, OCH_aH_bPh), 4.19 (1 H, t, *J* 7.0, CHOH), 3.80 (1 H, dd, *J* 11.8 and 3.6, CH_aH_bOH), 3.36 (1 H, dd, *J* 11.8 and 3.6, CH_aH_bOH), 3.46–3.38 (1 H, m, CHOBn), 2.45 (1 H, br s, OH), 1.92 (1 H, br s, OH) and 1.72 (3 H, dd, *J* 6.4 and 1.5, CH_3); δ_C(250 MHz; $CDCl_3$) 137.9 (4° ArC), 129.7 (olefin C), 128.6 (olefin C), 128.1 (ArC), 128.0 (ArC), 82.3 (CHOH), 73.1 ($PhCH_2$), 73.0 (CHOBn), 61.5 (CH_2OH) and 17.9 (CH_3); *m/z* (CI, NH_3) 240 [$(M + NH_4)^+$, 5%], 219 (5), 205 (12), 187 (17), 169 (9), 157 (11), 143 (8), 131 (6), 108 (25), 91 (100) and 69 (5) [Found: $(M + NH_4)^+$ 240.1600. $C_{13}H_{22}NO_3$ requires *M*, 240.1600].

(4S,5S)-5-*Benzyloxy*-2-*phenylselenoylmethyl*-4-(*prop*-1-*enyl*)-1,3-*dioxane* **4**.—A solution of the diol **3** (0.940 g, 4.23 mmol, 1 equiv.), phenylselenoacetaldehyde diethyl acetal (1.411 g, 5.16 mmol, 1.2 equiv.), and PPTS (0.03 g, 0.12 mmol, 0.03 equiv.) in dry toluene (50 cm^3), was heated at reflux for 1 h. The mixture was cooled, poured into water (300 cm^3), and extracted with diethyl ether (3 × 200 cm^3). The combined extracts were dried ($MgSO_4$) and concentrated. The residue was subjected to flash chromatography (5% EtOAc–hexane) to provide the cyclic acetal **4** as a light straw-coloured oil (1.195 g, 2.96 mmol, 70%); R_f 0.47 (30% EtOAc–hexane); $[\alpha]_D^{20}$ +23.0 (*c* 2.0 in $CHCl_3$) (Found: C, 62.2; H, 6.1. $C_{21}H_{24}O_3Se$ requires C, 62.5; H, 6.0%); ν_{max}(film)/cm^{-1} 1580 (phenyl) and 1110 (ether); δ_H(250 MHz, $CDCl_3$) 7.55–7.47 (2 H, m, Se-*m*-ArH), 7.36–7.18 (8 H, m, ArH), 5.80–5.62 (2 H, m, C*H*=CH), 4.79 [1 H, t, *J* 5.3, $CH(OR)_2$], 4.74 (1 H, d, *J* 12.6, OCH_aH_bPh), 4.54 (1 H, d, *J* 12.6, CH_aH_bPh), 4.24 (1 H, dd, *J* 12.5 and 1.4, CH_aH_bOR), 4.13 (1 H, m, C=CHC*H*OR), 3.72 (1 H, dd, *J* 12.5 and 1.4, CH_aH_bOR), 3.17–3.14 (3 H, m, CH_2Se and CHOBn) and 1.71 (3 H, d, *J* 4.5, CH_3); δ_C(250 MHz; $CDCl_3$) 138.0 (4° ArC), 132.4 (ArC), 130.6 (4° ArC), 129.3 (ArC), 129.0 (ArC), 128.3 (ArC), 128.1 (ArC), 127.8 (olefin C), 127.7 (ArC), 126.8 (olefin C), 101.3 (acetal C), 80.2 (allylic C), 71.9 (CHOBn), 71.5 ($PhCH_2$), 68.3 (CH_2CHOBn), 30.9 ($SeCH_2$) and 17.9 (CH_3); *m*/*z* (CI, NH_3) 422 [$(M + NH_4)^+$, 35%], 405 (9), 291 (12), 222 (100), 205 (82), 187 (52), 169 (13), 143 (7), 108 (75), 91 (54) and 78 (4) (Found: 422.1234. $C_{21}H_{28}NO_3Se$ requires *M*, 422.1236).

(4R,7R)-7-*Benzyloxy*-4-*methyl*-7,8-*dihydro*-4-*oxacin*-2(3H)-*one* **5**.—A mixture of the acetal **4** (1.235 g, 3.064 mmol, 1 equiv.), $NaIO_4$ (2.002 g, 9.360 mmol, 3.1 equiv.), and $NaHCO_3$ (0.508 g, 6.047 mmol, 2.0 equiv.) in methanol (200 cm^3) and water (30 cm^3) was stirred vigorously at 20 °C for 1 h. The reaction mixture was poured into water (600 cm^3) and extracted with CH_2Cl_2 (4 × 300 cm^3). The combined extracts were dried ($MgSO_4$) and concentrated to give a quantitative yield of the selenoxide (1.291 g); δ_H(250 MHz; $CDCl_3$) 7.77–7.73 [2 H, m, Se(O)*m*-ArH], 7.75–7.47 [3 H, m, Se(O)*o*- and *p*-ArH], 7.35–7.28 (5 H, m, ArH), 5.83–5.64 (2 H, m, C*H*=CH), 4.98 (1 H, m, C*H*CH_2Se), 4.73 (1 H, dd, *J* 12.4 and 6.6, CH_aH_bPh), 4.54 (1 H, dd, *J* 12.4 and 2.3, CH_aH_bPh), 4.31–4.08 (2 H, m, C*H*CH=CH and CH_aH_bOR), 3.81–3.65 (1 H, dd, *J* 12.5 and 1.4, CH_aH_bOR), 3.25–3.17 (3 H, m, $OSeCH_2$ and CHOBn) and 1.75–1.67 (3 H, m, CH_3).

A solution of the selenoxide (0.108 g, 0.256 mmol, 1 equiv.), DBU (0.12 cm^3, 0.802 mmol, 3.1 equiv.), and 1-*tert*-butyldimethylsiloxy-1-methoxyethene (0.95 g, 5.04 mmol, 20 equiv.) in dry xylene (10 cm^3) was heated in a NaOH-washed sealed tube at 180 °C for 14 h. The xylene was removed under high vacuum, and the residue was subjected to flash chromatography (hexane → 2% EtOAc–hexane) to give the lactone **5** as a clear oil (0.0464 g, 0.189 mmol, 73%); R_f 0.47 (30% EtOAc–hexane); $[\alpha]_D^{20}$ −116.73 (*c* 2.05 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1755 (C=O) and 1220 (ester C–O); δ_H(250 MHz; $CDCl_3$) 7.38–7.28 (5 H, m, ArH), 5.71 (1 H, dd, *J* 11.7 and 8.8, CH_3CHCH=CHR), 5.59 (1 H, dd, *J* 11.7 and 6.2, CH=C*H*CHOBn), 4.66 (1 H, d, *J* 12.0, $OCH_{ax}H_{eq}$-CHOBn), 4.66 (1 H, d, *J* 11.6, OCH_aH_bPh), 4.39 (1 H, d, *J* 11.6, OCH_aH_bPh), 4.13 (1 H, dd, *J* 12.0 and 2.0, $OCH_{ax}H_{eq}$CHOBn), 3.89 (1 H, dt, *J* 6.2 and 2.0, CHOBn), 3.83–3.64 (1 H, m, CH_3CH), 2.90 [1 H, dd, *J* 13.4 and 6.1, $C(O)CH_{ax}H_{eq}$], 2.13 [1 H, dd, *J* 13.4 and 11.5, $C(O)H_{ax}H_{eq}$] and 1.10 (3 H, d, *J* 6.7, CH_3); δ_C(250 MHz; $CDCl_3$) 176.3 (CO), 143.0 (olefin C), 137.7 (4° ArC), 128.5 (*m*-ArC), 128.1 (*o*-ArC), 127.8 (*p*-ArC), 126.1 (olefin C), 75.0 (CHOBn), 70.5 [$CH_2OC(O)$], 69.5 ($PhCH_2$), 45.7 [$CH_2C(O)$], 32.4 ($CHCH_3$) and 20.1 (CH_3); *m*/*z* (CI, NH_3) 264 [$(M + NH_4)^+$, 26%], 247 (25), 229 (9), 211 (4), 187 (2), 174 (8), 155 (6), 139 (23), 125 (7), 108 (33), 91 (100) and 65 (5) (Found: 264.1600. $C_{15}H_{22}NO_3$ requires *M*, 264.1601).

(4S,5S)-5-*Benzyloxy*-6-tert-*butyldiphenylsiloxyhex*-2-*en*-3-*ol* **6**.—A solution of the diol **3** (1.993 g, 8.966 mmol, 1 equiv.) and imidazole (0.911 g, 13.38 mmol, 1.5 equiv.) in DMF (40 cm^3) at 0 °C was treated with *tert*-butyldiphenylsilyl chloride (3.5 cm^3, 13 mmol, 1.5 equiv.). After 2 h, the mixture was poured into water (400 cm^3) and extracted with diethyl ether (3 × 200 cm^3). The combined extracts were washed with water and then with brine, dried ($MgSO_4$), and concentrated. The product was purified by flash chromatography (2.5 → 10% EtOAc–hexane) to give the title compound **6** as a clear oil (3.771 g, 8.185 mmol, 91%); R_f 0.55 (30% EtOAc–hexane); $[\alpha]_D^{20}$ +25.29 (*c* 1.72 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3535–3075 (OH), 1125 (SiOR); δ_H(250 MHz; $CDCl_3$) 7.69–7.64 (4 H, m, Si*m*-ArH), 7.45–7.27 (11 H, m, ArH), 5.80–5.69 (1 H, dq, *J* 15.3 and 6.5, CH_3CH), 5.45 (1 H, dd, *J* 15.3 and 7.0, CH_3CH=C*H*), 4.72 (1 H, d, *J* 11.5, CH_aH_bPh), 4.48 (1 H, d, *J* 11.5, CH_aH_bPh), 4.21 (1 H, m, C*H*OH), 3.84 (1 H, dd, *J* 11.0 and 4.7, CH_aH_bOSi), 3.73 (1 H, dd, *J* 11.0 and 4.7, CH_aH_bOSi), 3.40 (1 H, dd, *J* 10.7 and 4.7, CHOBn), 2.75 (1 H, br s, OH), 1.67 (3 H, d, *J* 6.5, CH_3) and 1.05 (9 H, s, Bu^t); δ_C(250 MHz; $CDCl_3$) 138.2 (4° ArC), 135.7 (ArC), 135.6 (ArC), 133.2 (4° ArC), 133.1 (4° ArC), 130.1 (olefin C), 129.8 (ArC), 128.9 (olefin C), 128.4 (ArC), 127.9 (ArC), 127.8 (ArC), 127.7 (ArC), 82.6 (CHOH), 72.9 ($PhCH_2$), 72.3 (CHOBn), 63.2 (CH_2OSi), 26.8 [$C(CH_3)$], 19.2 [$C(CH_3)$] and 17.9 (CH_3); *m*/*z* (CI, NH_3) 478 [$(M + NH_4)^+$, 1%], 457 (4), 443 (5), 365 (10), 327 (8), 295 (12), 275 (100), 221 (9), 196 (8), 157 (8), 105 (28) and 91 (34).

(2S,3S)-1-tert-*Butyldiphenylsiloxyhex*-4-*ene*-2,3-*diol* **7**.—A solution of 4,4-di-*tert*-butylbiphenyl (1.47 g, 5.52 mmol, 11.2 equiv.) in dry THF (25 cm^3), was degassed (freeze/thaw × 2) and cooled to 0 °C. Lithium (0.054 g, 7.78 mmol, 15.7 equiv.) was washed in hexane, cut several times, and added to the di-*tert*-butylbiphenyl solution which, upon sonication for 2 h at 0 °C, turned a deep green. The reagent was added dropwise to a solution of the alcohol **6** (0.2275 g, 0.494 mmol, 1 equiv.) in THF (3 cm^3) at −78 °C. After all of the reagent had been added, the reaction mixture was dark red, and TLC showed one main product, with a small amount of starting material. The reaction was quenched with saturated aqueous NH_4Cl (10 cm^3), poured into water (100 cm^3), and extracted with diethyl ether (3 × 100 cm^3). The combined extracts were washed with water, dried ($MgSO_4$), and concentrated. Purification of the residue by flash chromatography (hexane → 20% EtOAc–hexane) afforded the diol **7** as a straw-coloured oil (0.1178 g, 0.319 mmol, 65%). Also recovered were 4,4-di-*tert*-butylbiphenyl (0.50 g, 34%) and the benzyl ether **6** (0.0173 g, 8%); R_f 0.26 (30% EtOAc–hexane); $[\alpha]_D^{20}$ + 0.25 (*c* 2.01 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3520–3220 (OH), 1115 (SiOR); δ_H(250 MHz; $CDCl_3$) 7.70–7.62 (4 H, m, *m*-ArH), 7.47–7.35 (6 H, m, *o*- and *p*-ArH), 5.78–5.64 (1 H, dq, *J* 15.3 and 6.4, CH_3CH), 5.41 (1 H, ddq, *J* 15.3, 7.2 and 1.4, CH_3CH=C*H*), 4.11 (1 H, m, CH=CHC*H*OH), 3.76 (1 H, dd, *J* 10.5 and 4.1, CH_aH_bOSi), 3.67 (1 H, dd, *J* 10.5 and 4.9, CH_aH_bOSi), 3.53 (1 H, m, $SiOCH_2CHOH$), 2.62 (2 H, br s, 2 OH), 1.64 (3 H, dd, *J* 6.4 and 1.4, CH_3) and 1.07 (9 H, s, Bu^t); δ_C(250 MHz; $CDCl_3$) 135.6 (*m*-ArC), 132.8 (4° ArC), 132.7 (4° ArC), 129.9 (*p*-ArC), 129.7 (olefin C), 129.5 (olefin C), 127.8 (*o*-ArC), 74.3 (CHOH), 73.2 (CHOH), 64.9 (CH_2), 26.8 [$C(CH_3)$], 19.2 [$C(CH_3)$] and 17.8 (vinyl CH_3); *m*/*z* (CI, NH_3) 388 [$(M + NH_4)^+$, 3%], 370 (4), 353 (10), 295 (15), 275 (100), 265 (4), 215 (8), 196 (6), 157 (10), 136 (4), 117 (5) and 97 (5) [Found: $(M + NH_4)^+$ 388.2308. $C_{22}H_{34}NO_3Si$ requires *M*, 388.2309].

(4S,5S)-4-tert-*Butyldiphenylsiloxymethyl*-2-*phenylselenomethyl*-5-*prop*-1-*enyl*-1,3-*dioxolane* **8**.—A solution of the diol **7** 0.109 g, 0.295 mmol, 1 equiv.), phenylselenoacetaldehyde diethyl acetal (0.1224 g, 0.448 mmol, 1.5 equiv.), and PPTS (0.005 g, 0.020 mmol, 0.07 equiv.) in dry toluene (5 cm^3) was heated at

reflux for 1.5 h. The mixture was cooled, poured into water (20 cm^3), and extracted with diethyl ether (3 × 50 cm^3). The combined extracts were combined, dried ($MgSO_4$) and concentrated. The product was purified by flash chromatography (5% EtOAc–hexane) to give the acetal **8** as a yellow oil (0.164 g, 0.297 mmol, 100%); R_f 0.65 (30% EtOAc–hexane); $[\alpha]_D^{20}$ −71.0 (*c* 3.07 in $CHCl_3$): ν_{max}(film)/cm^{-1} 1135 (SiOR) and 1112 (ether); δ_H(250 MHz; 2 diastereoisomers; $CDCl_3$) 7.69–7.64 (4 H, m, Si-*m*-ArH), 7.56–7.49 (2 H, m, Se-*m*-ArH), 7.40–7.30 (6 H, m, Si-*o*- and *p*-ArH), 7.23–7.15 (3 H, m, Se-*o*- and *p*-ArH), 5.81–5.66 (1 H, m, CH_3CH), 5.53–5.40 (1 H, m, $CH_3CH{=}CH$), 5.34 (*1 H, dd, J* 9.6 and 4.6, CH=CHCHO), 4.47–4.37 (1 H, m, $SeCH_2CH$), 3.86–3.64 (3 H, m, $SiOCH_2CHO$), 3.16–3.05 (2 H, m, $SeCH_2$), 1.69 (3 H, dd, *J* 6.4 and 1.3, CH_3), 1.05 and 1.03 (9 H, 2s, Bu^t); δ_C(250 MHz; 2 diastereoisomers; $CDCl_3$) 135.6 (Si-*m*-ArC), 132.2 (4° SiArC), 132.5 (Se-*m*-ArC), 131.6 (olefin C), 131.0 (Se *p*-ArC), 130.4 (4° SeArC), 129.7 (olefin C), 129.0 (Si *p*-ArC), 127.7 (Si *o*-ArC), 126.8 (Se-*o*-ArC), 103.0 and 102.8 ($SeCH_2CH$), 82.4 and 81.6 (CHOR), 80.3 and 79.4 (CHOR), 62.9 ($SiOCH_2$), 31.9 and 31.7 ($SeCH_2$), 26.7 [$C(CH_3)$], 19.2 [$C(CH_3)$] and 17.8 (vinyl CH_3); *m/z* (CI, NH_3) 570 [$(M + NH_4)^+$, 5%], 370 (8), 353 (10), 295 (12), 275 (100), 229 (5), 196 (4) and 157 (4) [Found: $(M + NH_4)^+$ 570.194. $C_{30}H_{40}NO_8SeSi$ requires *M*, 570.194].

(4*R*,7*R*)-7-(tert-*Butyldiphenylsiloxymethyl*)-4-*methyl*-4H,7H-*oxepin*-2(3H)-*one* **9**.—A mixture of the acetal **8** (0.129 g, 0.234 mmol, 1 equiv.), $NaIO_4$ (0.1613 g, 0.754 mmol, 3.2 equiv.) and $NaHCO_3$ (0.043 g, 0.512 mmol, 2.2 equiv.) in methanol (15 cm^3) and water (2.5 cm^3) was stirred vigorously at 20 °C for 2 h. The mixture was poured into water (50 cm^3) and extracted with EtOAc (3 × 50 cm^3). The extracts were washed with water, combined, dried ($MgSO_4$) and concentrated to give the selenoxide as a clear oil (0.128 g, 0.225 mmol, 96%). The selenoxide was generally used without purification.

A solution of the above selenoxide (0.1256 g, 0.221 mmol, 1 equiv.), DBU (0.10 cm^3, 0.669 mmol, 3.0 equiv.), and 1-*tert*-butyldimethylsiloxy-1-methoxyethene (0.937 g, 4.975 mmol, 22.5 equiv. in xylene (10 cm^3) was heated in a dried, NaOH-washed sealed tube at 185 °C for 14 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (25% EtOAc–hexane) to afford the lactone **9** as a straw-coloured oil (0.0392 g, 0.099 mmol, 45%); R_f 0.40 (50% EtOAc–hexane); $[\alpha]_D^{20}$ −59.77 (*c* 1.98 in $CHCl_3$) (Found: C, 72.6; H, 7.6. $C_{24}H_{30}O_3Si$ requires C, 73.0; H, 7.7%); ν_{max}(film)/cm^{-1} 1742 (C=O) and 1261 (ester C–O); δ_H(250 MHz; $CDCl_3$) 7.68–7.64 (2 H, m, *m*-ArH), 7.40–7.35 (3 H, m, *o*- and *p*-ArH), 5.79–5.64 (2 H, m, 2 × olefin H), 5.06–5.00 (1 H, m, CHOCOR), 3.85 (1 H, dd, *J* 10.4 and 6.5, $SiOCH_aH_b$), 3.68 (1 H, dd, *J* 10.4 and 6.5, $SiOCH_aH_b$), 3.28 (1 H, dd, *J* 13.0 and 4.5, $OCOH_aH_b$), 2.68–2.65 (1 H, m, $CHCH_3$), 2.46 (1 H, ddd, *J* 13.0, 3.9 and 1.3, $OCOH_aH_b$) and 1.06 (9 H, s, Bu^t); δ_C(250 MHz; $CDCl_3$) 172.4 (CO), 137.4 (olefin C), 135.6 (*m*-ArC), 133.0 (4° ArC), 129.9 (*p*-ArC), 127.8 (*o*-ArC), 124.8 (olefin C), 74.4 [CHOC(O)], 65.3 [$CH_2C(O)$], 38.0 (CH_2OSi), 30.6 ($CHCH_3$), 26.8 [$C(CH_3)_3$], 20.5 (CH_3) and 19.2 [$C(CH_3)_3$]; *m/z* (CI, NH_3) 412 [$(M + NH_4)^+$, 100%], 395 (60), 377 (7), 354 (2), 334 (16), 317 (50), 299 (4), 276 (10), 259 (22), 239 (4), 216 (9), 199 (9), 181 (8), 157 (33), 138 (3), 121 (8) and 91 (2) [Found: $(M + NH_4)^+$ 412.2308. $C_{24}H_{34}NO_3Si$ requires *M*, 412.2309].

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