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PAPER

An approach to aliphatic 1,8-stereocontrol: diastereoselective syntheses of (±)-patulolide C and (±)-epipatulolide C†

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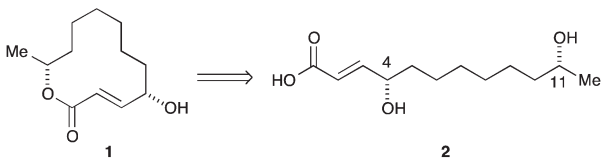
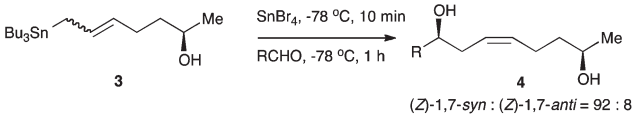
The tin(IV) bromide promoted reaction of 7-hydroxy-7-phenylhept-2-enyl(tributyl)stannane **11** with benzaldehyde gave a mixture of the epimeric 1,8-diphenyloct-3-ene-1,8-diols **12** and so indirect methods were developed for aliphatic 1,8-stereocontrol to complete diastereoselective syntheses of (±)-patulolide C **1** and (±)-epipatulolide C **40**. (5*Z*)-3,7-*syn*-7-(2-Trimethylsilylethoxy)methoxyocta-1,5-dien-3-ol **17** was prepared from the tin(IV) chloride promoted reaction of 4-(2-trimethylsilylethoxy)methoxypent-2-enyl (tributyl)stannane **16** with acrolein (1,5-*syn* : 1,5-*anti* = 96 : 4). An Ireland–Claisen rearrangement of the corresponding benzoyloxyacetate **21** with *in situ* esterification of the resulting acid using trimethylsilyldiazomethane gave methyl (4*E*,7*Z*)-2,9-*anti*-2-benzyloxy-9-(2-trimethylsilylethoxy) methoxydeca-4,7-dienoate **22** together with 10–15% of its 2,9-*syn*-epimer **26**, the 2,9-*syn*- : 2,9-*anti*-ratio depending on the conditions used. An 88 : 12 mixture of esters was taken through to the *tert*-butyldiphenylsilyl ether **38** of (±)-patulolide C **1** together with 6% of its epimer **39**, by reduction, a Wittig homologation and deprotection/macrocyclisation. Following separation of the epimeric silyl ethers, deprotection of the major epimer **38** gave (±)-patulolide C **1**. The success of 2,3-Wittig rearrangements of allyl ethers prepared from (5*Z*)-3,7-*syn*-7-(2-trimethylsilylethoxy)methoxyocta-1,5-dien-3-ol **17** was dependent on the substituents on the allyl ether. Best results were obtained using the pentadienyl ether **56** and the cinnamyl ether **49** that rearranged with >90 : 10 stereoselectivity in favour of (1*E*,5*E*,8*Z*)-3,10-*syn*-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundeca-1,5,8-trien-3-ol **50**. This product was taken through to the separable silyl ethers **38** and **39**, ratio 7 : 93 by regioselective epoxidation and alkene reduction using diimide, followed by deoxygenation, ozonolysis, a Wittig homologation and selective deprotection/macrocyclisation. Deprotection of the major epimer **39** gave (±)-epipatulolide C **40**.

Introduction

Patulolide C **1**[1] is a naturally occurring 12-membered ring containing macrolide with antifungal and antibiotic activity that has been of considerable interest to synthetic chemists.[2] Its seco-acid **2** is characterised by the presence of stereogenic centres at the 4- and 11-positions, *i.e.* two stereogenic centres with a *syn*-1,8-relationship.



Tin(IV) halide promoted reactions of alkoxyalk-2-enylstannanes with aldehydes have been found to proceed with useful levels of 1,5-, 1,6- and 1,7-stereocontrol.[3,4] For example, 1,7-stereocontrol in favour of the (*Z*)-1,7-*syn*-oct-3-ene-1,7-diols **4** was found for tin(IV) bromide promoted reactions of the 6-hydroxyhept-2-enyl(tributyl)stannane **3** with aldehydes.[3] It was of interest to see whether this chemistry could be applied to 1,8-stereocontrol in aliphatic systems. In the event, direct 1,8-stereocontrol was found not to be viable using allylstannanes, but was achieved by coupling 1,5-stereocontrol with a subsequent sigmatropic rearrangement. We here report details of this work together with diastereoselective syntheses of (±)-patulolide C **3** and its epimer using this chemistry.[5,6]



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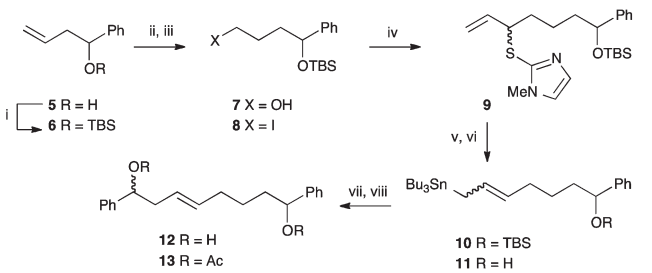
Results and discussion

Studies of direct 1,8-stereocontrol

Following protection of 1-phenylbut-3-en-1-ol **5** as its *tert*-butyldimethylsilyl ether **6**,[7] hydroboration with an oxidative work-up gave the butanol **7**[8] that was converted into the corresponding iodide **8**, see Scheme 1. This was used to alkylate 3-methylimidazol-2-yl prop-2-enylsulfide[9] to give the hept-1-en-3-yl sulfide **9**, as a mixture of epimers. Treatment of this mixture with tributyltin hydride under free radical conditions[3] gave the hept-2-enylstannane **10** as a 67 : 33 mixture of (*E*)- and (*Z*)-isomers and desilylation gave the 7-hydroxyhept-2-enylstannane **11**. Tin(IV) bromide promoted reactions of stannane **11** with benzaldehyde gave the (*E*)-1,8-diphenyloct-3-ene-1,8-diol **12**, the *trans*-geometry of the double-bond being consistent with the vinylic coupling constant of 15.8 Hz. Two isomers were apparent in the reverse phase HPLC of the diol **12** and its bis-acetate **13**, in a ratio of *ca.* 68 : 32. These were identified as the 1,8-*syn*- and 1,8-*anti*-(*E*)-epimers of the diol **12** and bis-acetate **13** but which was which was not investigated. Tin(IV) halide promoted reactions of 7-hydroxyhept-2-enylstannanes with aldehydes would appear not to proceed with useful levels of 1,8-stereocontrol.

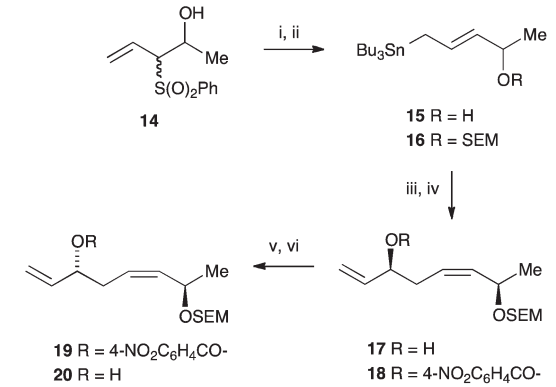
It was decided to see whether useful 1,8-stereocontrol could be achieved combining the 1,5-*syn*-stereocontrol known for 4-alkoxypent-2-enylstannanes[4] with a subsequent sigmatropic rearrangement, specifically with an Ireland–Claisen rearrangement[10] or with a 2,3-Wittig rearrangement.[11] If successful, this chemistry could be used to complete a diastereoselective synthesis of racemic patulolide C **1**.



Scheme 1 Attempted 1,8-stereocontrol using 7-hydroxy-7-phenylhept-2-enylstannane **11**. Reagents and conditions i, TBSCl, imid., DCM, r.t., 15 h (95%); ii, 9-BBN, THF, r.t., 2.5 h, then NaOH, H_2O, EtOH, 30% H_2O_2 (86%); iii, Ph_3P, imid., I_2, THF, r.t., 1.5 h (90%); iv, 3-methylimidazol-2-yl prop-2-enyl sulfide, BuLi, hexanes, THF, −78 °C, 30 min, HMPA, −78 °C, 30 min, add **8**, 1 h (74%); v, Bu_3SnH, AIBN (cat.), benzene, heat under reflux, 1 h [89%, (*E*) : (*Z*) = 67 : 33]; vi, TBAF, THF, r.t., 4 h (69%); vii, $SnBr_4$, DCM, −78 °C, 5 min, benzaldehyde, −78 °C, 20 min (81%, 68 : 32 mixture of epimers); viii, Ac_2O, Et_3N, DMAP (cat.), DCM, r.t., 3 h (82%).

1,8-Stereocontrol by combining (*Z*)-1,5-*syn*-stereoselectivity with an Ireland–Claisen rearrangement

The (*E*)-4-(2-trimethylsilylethoxy)methoxypent-2-enylstannane **16** was prepared by treatment of the allylic sulfone **14**[12] with tributyltin hydride under free radical conditions followed by protection of the resulting hydroxypentenylstannane **15** using (2-trimethylsilylethoxy)methyl chloride, see Scheme 2. The



Scheme 2 Synthesis of the 4-alkoxypent-2-enylstannane **16** and its reaction with acrolein. Reagents and conditions i, Bu_3SnH, AIBN (cat.), benzene, 65 °C, 1.5 h (89%); ii, SEMCl, $^iPr_2NEt$, DCM, 0 °C to r.t., 3 h (83%); iii, $SnCl_4$, DCM, −78 °C, 10 min, then add acrolein, −78 °C, 10 min (77%; 1,5-*syn*-**17** : 1,5-*anti*-**20** = 96 : 4); iv, 4-$NO_2C_6H_4COCl$, Et_3N, DMAP (cat.), DCM, r.t., 2 h (78%); v, DEAD, Ph_3P, 4-$NO_2C_6H_4CO_2H$, benzene, r.t., 2 h (60%); vi, LiOH·H_2O, MeOH–H_2O, r.t., 15 h (89%).

2-trimethylsilylethoxymethoxy (SEM) group was chosen with a view to its selective removal at the end of the synthesis; only the (*E*)-pent-2-enylstannane was isolated in this case.

The tin(IV) chloride promoted reaction of the stannane **16** with acrolein was carried out under the usual conditions at −78 °C and gave the (5*Z*)-3,7-*syn*-7-(2-trimethylsilylethoxy)methoxyocta-1,5-dien-3-ol **17** with excellent 1,5-stereoselectivity, see Scheme 2. The *cis*-geometry was assigned to the internal double-bond of the product **17** on the basis of the vinylic coupling constant of 11 Hz and its 1,5-*syn*-configuration was assigned by analogy with earlier work.[3,13] The major product **17** was converted into its epimer **20** by a Mitsunobu reaction using 4-nitrobenzoic acid followed by saponification of the resulting 4-nitrobenzoate **19**. The ^1H and ^{13}C NMR spectra of the epimeric alcohols **17** and **20** were very similar but one of the diastereotopic OCH_2O hydrogens had slightly different chemical shifts for the two epimers, at δ 4.73 for **17** and at δ 4.69 for **20**, and this enabled the stereoselectivity of the reaction of acrolein with the allylstannane **16** to be estimated as 96 : 4. The alcohol **17** was also converted into its 4-nitrobenzoate **18** with retention of configuration but the nitrobenzoates **18** and **19** could not be distinguished by NMR.

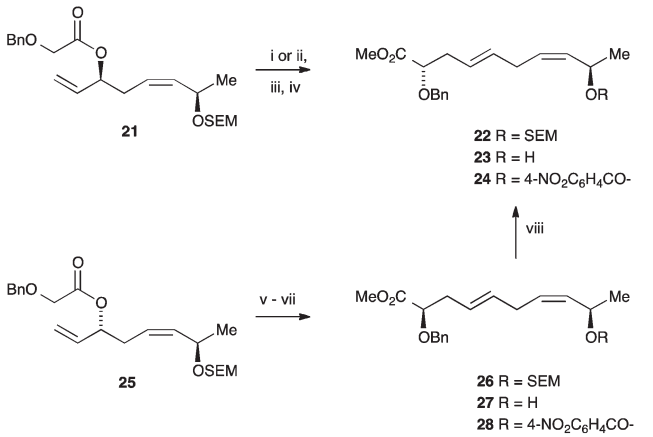
The 3,7-*syn*- and *anti*-octadienols **17** and **20** were esterified using benzyloxyacetyl chloride to give the esters **21** and **25**. Ireland–Claisen rearrangements[10,14,15] involve the formation of ketene silyl acetals from allylic esters, trimethylsilyl chloride either being present during the deprotonation step[16] or added to the preformed enolate. The silyl ketene acetals then undergo the required [3,3]-sigmatropic shift and an aqueous work-up with subsequent esterification provides rearranged products. Both procedures were investigated using the esters **21** and **25**.

The Ireland–Claisen rearrangement of the 3,7-*syn*-ester **21** using lithium hexamethyldisilazide as the base and trimethylsilyl chloride at −78 °C, after esterification of the initially formed acid using trimethylsilyl diazomethane, gave what appeared to be a single ester, subsequently identified as predominantly the

2,9-*anti*-dialkoxydeca-4,7-dienoate **22**. Better yields, 89%, could be obtained if the trimethylsilyl chloride was present during the deprotonation, but the procedure whereby trimethylsilyl chloride was added after the deprotonation was more reliable with yields of *ca.* 78%. Rearrangement of the 3,7-*anti*-ester **25** using the *in situ* trimethylsilyl chloride procedure, after esterification using trimethylsilyl diazomethane, gave the 2,9-*syn*-ester **26**.

The Ireland–Claisen products **22** and **26** were indistinguishable by ^{1}H or ^{13}C NMR. Deprotection of ester **26** using butanethiol and magnesium bromide under buffered conditions[17] gave alcohol **27** that was esterified directly using 4-nitrobenzoyl chloride to give the 2,9-*syn*-ester **28** and with inversion of configuration using Mitsunobu conditions to give the inverted 2,9-*anti*-ester **24**. The *anti*- and *syn*-esters **24** and **28** were found to have slightly different ^{1}H NMR spectra in benzene-d_6. For example, the doublets assigned to 10-H_3 were observed at δ 1.25 and at δ 1.26 for the 2,9-*anti*- and 2,9-*syn*-epimers **24** and **28**, respectively, and could be used to estimate the ratio of the two epimers. The product ratios from the rearrangements of the 3,7-*syn*- and 3,7-*anti*-esters **21** and **25** were then estimated by deprotection and conversion of the resulting alcohols into their 4-nitrobenzoates. The rearrangement of the 3,7-*anti*-ester **25** when trimethylsilyl chloride was present during the deprotonation step took place with 89 : 11 stereoselectivity in favour of the 2,9-*syn*-epimer **26**. The stereoselectivity of the rearrangement of the 3,7-*syn*-ester **21** was found to depend slightly on the conditions used. Lower stereoselectivity was found if the trimethylsilyl chloride was present during the deprotonation step, 2,9-*anti*-**22** : 2,9-*syn*-**26** = 67 : 33, but better stereoselectivity, 2,9-*anti*-**22** : 2,9-*syn*-**26** = 88 : 12, was observed if the trimethylsilyl chloride was added after the base. Better yields were obtained using lithium hexamethyldisilazide, 78–89%, rather than lithium diisopropylamide, 50–55% or potassium hexamethyldisilazide (Scheme 3).

The structures of the rearrangement products **22** and **26** were consistent with their spectroscopic data. The configurations of their double-bonds were confirmed by their vinylic coupling constants. The relative configurations of their stereogenic centres were assigned on the basis of participation of (*Z*)-ketene acetals generated from chelated lithium enolates of the esters **21** and **25** that rearrange through chair-like transition structures,[14,16] *e.g.* the ketene acetal **29** derived from the 3,7-*syn*-ester **21** gives the 2,9-*anti*-epimer **22**. These structures were confirmed by the completion of a synthesis of patulolide C **1**, *vide infra*. Of interest was the fact that the 96 : 4 mixture of epimeric octa-1,5-dien-3-ols **17** and **20** gave an 88 : 12 mixture of the epimeric 2,9-dialkoxydecadienoates **22** and **26** *via* the Ireland–Claisen rearrangement of the 3,7-*syn*-ester **21**, and an 89 : 11 mixture of the 2,9-dialkoxydienoates **26** and **22** *via* rearrangement of the 3,7-*anti*-ester **25**. It would appear that there had been about an 8% loss of stereochemical integrity during these [3,3]-sigmatropic rearrangements (Fig. 1).



Scheme 3 Ireland–Claisen rearrangements of the esters **21** and **25**. Reagents and conditions i, (a) TMSCl, THF, −78 °C, 5 min, add LiHMDS, −78 °C, r.t., 20 min, (b) $TMSCHN_2$, hexanes, MeOH, benzene, r.t., 1 h (89%; **22** : **26** = 67 : 33); ii, (a) LiHMDS, THF, −78 °C, 1.5 min, TMSCl, −78 °C, 20 min, r.t., 20 min, (b) Me_3SiCHN_2, hexanes, MeOH, benzene, r.t., 1 h (78%; **22** : **26** = 88 : 12); iii, 40% HF in H_2O, MeCN, r.t., 5 h (75%); iv, 4-$NO_2C_6H_4$-COCl, Et_3N, DCM, r.t., 2 h (90%; **24** : **28** = 88 : 12); v, (a) TMSCl, THF, −78 °C, 5 min, add LiHMDS, −78 °C, r.t., 20 min, (b) $TMSCHN_2$, hexanes, MeOH, benzene, r.t., 1 h (76%; **26** : **22** = 89 : 11); vi, BuSH, K_2CO_3, $MgBr_2{\cdot}Et_2O$, ether, r.t., 7 h (53%); vii, 4-$NO_2C_6H_4COCl$, Et_3N, DCM, r.t., 2 h (79%; **28** : **24** = 89 : 11); viii, DEAD, Ph_3P, 4-$NO_2C_6H_4CO_2H$, benzene, r.t., 2 h (60%; **24** : **28** = 89 : 11).

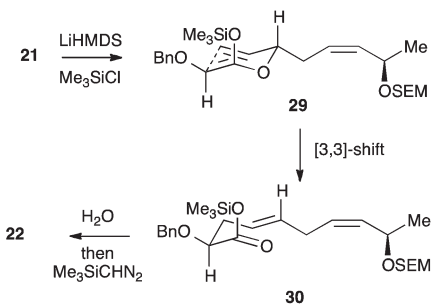
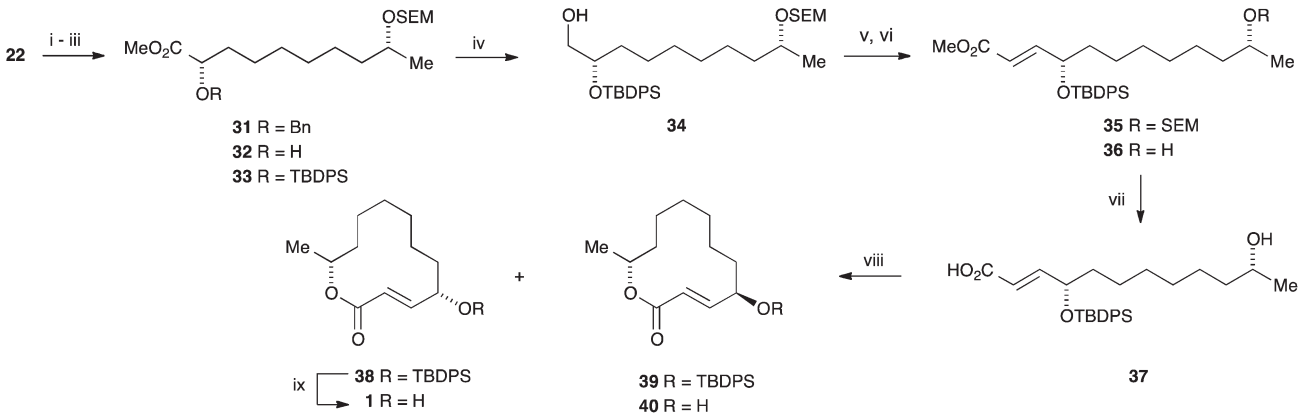


Fig. 1 Participation of the (*Z*)-ketene silyl acetal **29** in the Ireland–Claisen rearrangement of ester **21**.

Completion of a stereoselective synthesis of (±)-patulolide C

To avoid hydrogenolysis of the allylic carbon–oxygen bond, the 2,9-*anti*-dialkoxydecadienoate **22** was reduced using diimide to give the 2,9-*syn*-ester **31**. This was then hydrogenolysed using hydrogen and 10% palladium on charcoal to give the alcohol **32**, see Scheme 4. Following protection of this alcohol as its *tert*-butyldiphenylsilyl ether **33**, reduction of the ester to the primary alcohol **34** was achieved using lithium triethylborohydride. Oxidation to the corresponding aldehyde was then carried out using Swern conditions and the aldehyde was immediately converted into the (*E*)-αβ-unsaturated ester **35** by a Wittig reaction with the (*E*)-configuration of the alkene being confirmed by ^{1}H NMR. Selective removal of the SEM-protecting group using butanethiol and magnesium bromide diethyl etherate under buffered conditions gave the alcohol **36** and saponification gave the seco-acid **37**. Macrolactonisation was carried out using the modified Yamaguchi procedure and gave the epimers **38** and **39**,[2h] ratio 94 : 6, that could be separated by chromatography. Desilylation of the major macrolide **38** using tetrabutylammonium fluoride gave (±)-patulolide C **1**.[1]

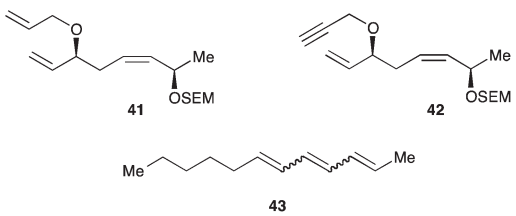


Scheme 4 Completion of a synthesis of (±)-patulolide C **1**. Reagents and conditions i, $TsNHNH_2$, NaOAc, DME, heat under reflux, 5 h (93%); ii, 10% Pd/C, EtOH, r.t., 72 h (87%); iii, TBDPSCI, imid., DCM, r.t., 2 h (98%); iv, $LiBHEt_3$, THF, −10 °C, 30 min (89%); v, (a) DMSO, $(COCl)_2$, DCM, −78 °C, 10 min, add **34**, −78 °C, 5 h, Et_3N, r.t., (b) $Ph_3P{=}CHCO_2Me$, DCM, r.t., 15 h (72%); vi, BuSH, K_2CO_3, $MgBr_2{\cdot}Et_2O$, ether, r.t., 2 h (89%); vii, $LiOH{\cdot}H_2O$, MeOH, H_2O, r.t., 15 h; viii, Et_3N, 2,6-$Cl_2C_6H_3COCl$, THF, r.t., 2 h, toluene, add to DMAP, toluene, heat under reflux, 5 h (**38**, 47%; **39**, 3%); ix, TBAF, THF, r.t., 3 h (76%).

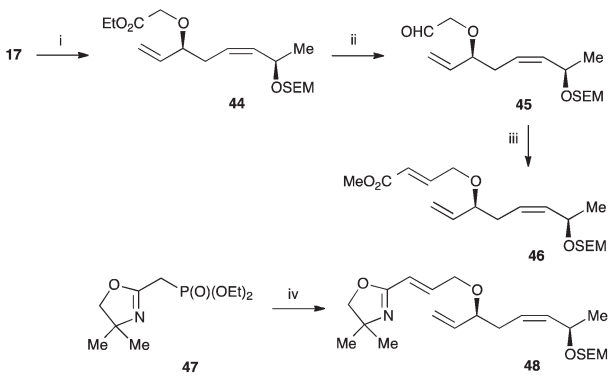
The structures of the intermediates along this series were consistent with their spectroscopic data. Both patulolide C **1**, its epimer **40** and the *tert*-butyldiphenylsilyl ethers **38** and **39** are known compounds with distinctive ^1H NMR spectra.[1,2h] The formation of macrolide **38**, the precursor of patulolide C **1**, as the dominant product from the macrocyclisation, confirmed the *anti*-configuration assigned to the ester **22** on the basis of the proposed mechanism of the [3,3]-sigmatropic rearrangement. It is likely that the 88 : 12 mixture of epimers **22** and **26** translated into a 94 : 6 mixture of macrolides **38** and **39** during this synthesis due to peak shaving during chromatography of the intermediates. The selectivity of formation of **38** also indicated that little epimerisation had taken place during the Swern oxidation of alcohol **34** and the Wittig reaction of the resulting aldehyde.

1,8-Stereocontrol by combining (*Z*)-1,5-*syn*-stereoselectivity with a 2,3-Wittig rearrangement

The prop-2-enyl and prop-2-ynyl ethers **41** and **42** were prepared from the alcohol **17** but gave the linear triene **43**[17] as a mixture of geometrical isomers on treatment with butyllithium.

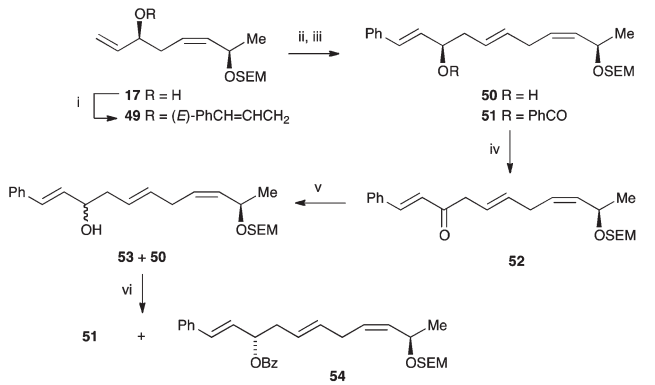


More acidic 2,3-rearrangement precursors were prepared by alkylation of the octadienol **17** using ethyl diazoacetate.[18] Reduction of the resulting alkoxyacetate **44** using diisobutylaluminium hydride gave the aldehyde **45** and a Wittig condensation provided the αβ-unsaturated ester **46**. A condensation of the aldehyde **45** with the phosphonate **47**[19] gave the oxazoline **48**, see Scheme 5. However, attempted 2,3-Wittig rearrangements of the esters **44** and **46**, and the oxazoline **48**, in our hands gave complex mixtures of products.



Scheme 5 Synthesis of precursors of Wittig rearrangements. Reagents and conditions: i, N_2CHCO_2Et, $Rh_2(OAc)_4$, DCM, r.t., 30 min (61%); ii, DIBAL-H, DCM, −60 to −45 °C, 1 h (61%); iii, Ph_3PCHCO_2Me, DMF, r.t., 15 h [(*E*)-isomer 70%; (*Z*)-isomer 4%); iv, **47**, DBU, LiCl, MeCN, r.t., add **45**, r.t., 48 h (60%).

It was decided to study 2,3-Wittig rearrangements of precursors that would be just slightly more acidic than the propenyl and propynyl ethers **41** and **42**. Alkylation of the 3,7-*syn*-octadienol **17** using (*E*)-cinnamyl bromide gave the ether **49**. In this case, treatment with butyllithium initiated a clean 2,3-Wittig rearrangement to give the 3,10-*syn*-undeca-1,5,8-trien-3-ol **50**, see Scheme 6. The ^1H NMR spectrum of this 2,3-Wittig rearrangement product confirmed its gross structure and double-bond geometry. To see whether the *syn*- and *anti*-3,10-epimers could be distinguished, alcohol **50** was oxidised to the ketone **52** that was reduced using sodium borohydride to give a mixture of the epimeric alcohols **50** and **53**. This mixture was esterified to give a mixture of esters **51** and **54**, the former also having been prepared by direct acylation of the *syn*-alcohol **50**. The ^1H and expanded ^{13}C NMR spectra of the mixtures of epimeric alcohols **50** and **53** and esters **51** and **54** showed the presence of a *ca.* 50 : 50 mixture of two isomers. Examination of the Wittig rearrangement product **50** and its benzoate **51** indicated that the rearrangement had given the 3,10-*syn*- and *anti*-products in a ratio of *ca.* 90 : 10.



Scheme 6 2,3-Wittig rearrangement of the (*E*)-cinnamyl ether **49**. Reagents and conditions i, NaH, THF, $^{n}Bu_4NI$ (cat.), (*E*)-PhCH=CHCH$_2$Br, r.t., 15 h (70%); ii, ^{n}BuLi, −78 °C, THF, 3 h (72%); iii, PhCOCl, Et$_3$N, DMAP (cat.), r.t., 2 h (79%); iv, DMSO, (COCl)$_2$, DCM, −78 °C, 10 min, add **50**, −78 °C, 1 h, Et$_3$N, 15 min (38%); v, NaBH$_4$, EtOH, 0 °C to r.t., 15 h (52%); vi, PhCOCl, Et$_3$N, DMAP (cat.), r.t., 2 h (51%; **51** : **54** = 50 : 50).

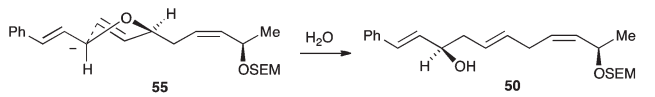
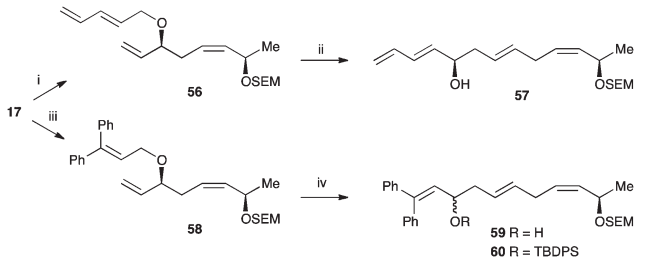


Fig. 2 Formation of the 3,10-*syn*-undecatrienol **50**.

The 3,10-*syn*-configuration of the two stereogenic centres in the major Wittig rearrangement product **50** was assigned on the basis that the rearrangement of the lithiated ether had proceeded *via* an envelope conformation with the cinnamyl group in a pseudo-equatorial position, see Fig. 2.[20] This was confirmed by the completion of a synthesis of (±)-epipatulolide C **40**.

2,3-Wittig rearrangements of other ethers were also briefly investigated. *O*-Alkylation of the 3,7-*syn*-octadienol **17** with (*E*)-1-bromopenta-2,4-diene gave the ether **56**. This underwent a stereoselective 2,3-Wittig rearrangement on treatment with butyllithium to give the trideca-1,3,7,10-tetraen-5-ol **57**. By ^{1}H NMR this appeared to be essentially a single compound, the 5,12-*syn*-configuration being assigned by analogy to the stereoselectivity of rearrangement of the cinnamyl ether **49**. In contrast, rearrangement of the 3,3-diphenylprop-2-enyl ether **58**, also prepared by *O*-alkylation of the *syn*-octadienol **17**, gave a mixture of products. The expected alcohol **59** could not be separated from this mixture, but silylation of the crude reaction mixture gave a modest yield of a 2 : 1 mixture of epimeric silyl ethers **60**, see Scheme 7.



Scheme 7 Further 2,3-Wittig rearrangements. Reagents and conditions i, NaH, THF, (*E*)-CH$_2$=CH·CH=CH·CH$_2$Br, $^{n}Bu_4NI$ (cat.), r.t., 15 h (76%); ii, ^{n}BuLi, hexanes, THF, −78 °C, 3 h (70%); iii, NaH, THF, 30 min, $^{n}Bu_4NI$ (cat.), 1-bromo-3,3-diphenylprop-2-ene, r.t., 15 h (83%); iv, (a) ^{n}BuLi, hexanes, THF, −78 °C, 2.5 h, (b) $^{t}BuPh_2SiCl$, imid., DMF, r.t., 5 h (35%).

Completion of a stereoselective synthesis of (±)-epipatulolide C

To convert the *syn*-3,10-undecatrienol **50** into epipatulolide C **40**, it was necessary to cleave oxidatively the 1,2-double-bond, hydrogenolyse the remaining double-bonds, homologate and effect macrocyclisation. Regioselective epoxidation of the undecatrienol **50** directed by the hydroxyl group using *tert*-butyl hydroperoxide and vanadyl acetoacetate gave epoxide **61** as a mixture of two diastereoisomers together with a small amount of a bis-epoxide. The mixture of hydroxyepoxides **61** was protected as its *tert*-butyl dimethylsilyl ether **62** and the remaining double-bonds reduced using diimide to give the saturated epoxide **64**, see Scheme 8.

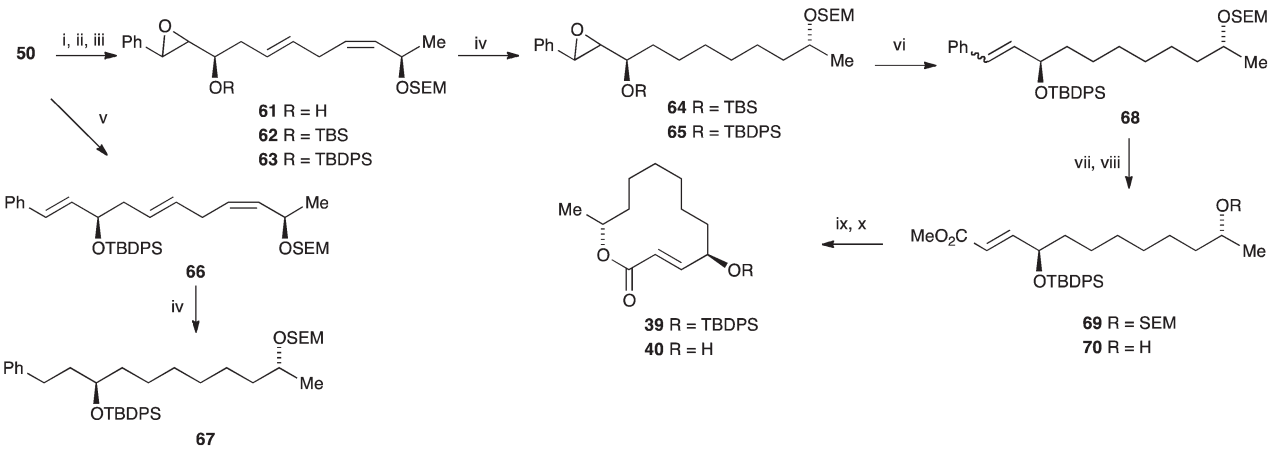
However, epoxide **64** was found to be relatively inert to periodic acid, perhaps because of solubility problems, and although ring-opening was achieved using sodium acetate in glacial acetic acid, this gave a mixture of regio- and stereo-isomeric hydroxyacetates. To see whether the double-bonds in the undecatrienol could be differentiated before epoxidation, the *tert*-butyldiphenylsilyl ether **66** was prepared but reduction of this hindered silyl ether using diimide gave the dialkoxyundecane **67** with no intermediate alkenes being isolated.

Reverting to the hydroxyepoxide **61**, protection using *tert*-butyldiphenylsilyl chloride gave the silyl ether **63** and this was reduced using diimide to give the saturated epoxide **65**. Treatment with samarium iodide[21] then effected a deoxygenation to give the undecene **68** albeit as a 66 : 34 mixture of (*E*)- and (*Z*)-isomers. This mixture was not separated, instead ozonolysis with a reductive work-up gave the corresponding aldehyde that was taken through to the αβ-unsaturated ester **69** using a Wittig condensation. Selective removal of the SEM-group, saponification and macrocylisation then gave the macrolide **39** together with its epimer **38**, ratio **39** : **38** = 93 : 7,[2h] and desilylation of the major silyl ether **39** completed a synthesis of epipatulolide C **40**,[1] see Scheme 8.

In this synthesis the structures of the intermediates were consistent with spectroscopic data and the structures of the macrolides were confirmed by comparison with samples prepared earlier during the synthesis of patulolide C **1** outlined in Scheme 4.

Summary and conclusions

The synthesis of aliphatic compounds with remote stereogenic centres is usually achieved by joining together two enantiomerically enriched starting materials to avoid the formation of diastereoisomers. The work outlined in this paper has illustrated an alternative approach whereby stereocentres that have a 1,8-relationship can be introduced diastereoselectively using a single chiral starting material. The stereogenic centre in a 4-alkoxyalk-2-enylstannane is used to control the configuration of a new stereogenic centre five carbons down an aliphatic chain and the



Scheme 8 Synthesis of (±)-epipatulolide C **40**. Reagents and conditions i, ^{t}BuOOH, $VO(acac)_2$, benzene, r.t., 10 min (76%); ii, $^{t}BuMe_2SiCl$, imid., DMF, r.t., 15 h (77%); iii, $^{t}BuPh_2SiCl$, imid., DCM, r.t., 18 h (93%); iv, $TsNHNH_2$, NaOAc, H_2O, DME, heat under reflux, 4–4.5 h (**64**, 87%; **65**, 85%; **67**, 68%); v, $^{t}BuPh_2SiCl$, imid., DCM, r.t., 2.5 h (82%); vi, SmI_2, THF, r.t., 3 h [56%; (*E*) : (*Z*) = 75 : 25]; vii, (a) O_3, DCM, −78 °C, 1.5 h, Me_2S, r.t., (b) Ph_3PCHCO_2Me, DCM, r.t., 15 h (61%); viii, BuSH, K_2CO_3, $MgBr_2{\cdot}Et_2O$, ether, r.t., 2 h (79%); ix, (a) $LiOH{\cdot}H_2O$, MeOH, H_2O, r.t., 15 h, (b) Et_3N, 2,6-$Cl_2C_6H_3COCl$, THF, r.t., 2 h, toluene, add to DMAP, toluene, heat under reflux, 5 h (**39**, 56%); x, TBAF, THF, r.t., 3 h (61%).

chirality at this centre is then migrated down the chain to effect overall 1,8-stereocontrol. The optical purity of the products depends on the optical purity of the starting materials, but as the original stereogenic centre in the stannane is used to control the relative configuration of the remote stereogenic centre, this chemistry can also be used to effect diastereoselective syntheses of racemic compounds with remote stereogenic centres as illustrated by the stereoselective syntheses of (±)-patulolide C **1** and its epimer **40**. This approach could be extended to include compounds with even more widely dispersed stereocentres and has been applied to effect 1,9-stereocontrol.[22] It has also been used to develop an approach to the total synthesis of epothilones[23,24] and should be useful for the stereoselective synthesis of other aliphatic compounds with remote stereocentres.

Experimental

General experimental procedures

^{1}H and ^{13}C NMR spectra were recorded on Varian Unity 500, Varian Unity Inova 400 and Varian Unity Inova 300 spectrometers. IR spectra were recorded on an ATI Mattson Genesis FTIR, as thin films, produced by evaporation of a chloroform solution, or as liquid films, on sodium chloride plates. Mass spectra were recorded on Fisson VG Trio 2000 and Kratos Concept spectrometers. Chemical ionisation (CI) was performed using ammonia. Typical clusters of isotope peaks were observed for tin containing compounds. Only those corresponding to ^{120}Sn are reported. Chromatography refers to flash column chromatography using silica gel 60 (230–400 mesh).

Tetrahydrofuran (THF) was dried and distilled from sodium metal using benzophenone as an indicator under an atmosphere of nitrogen. Dichloromethane (DCM) was dried and distilled from calcium hydride under an atmosphere of nitrogen. Ether refers to diethyl ether, which was dried and distilled from sodium metal using benzophenone as an indicator under an atmosphere of nitrogen. Light petroleum refers to the fraction of petroleum ether distilled between 40–60 °C. Benzene and hexane were dried over sodium metal. Butyllithium (1.6 M in hexanes) was titrated against a solution of propan-2-ol in xylene with 2,2′-bipyridine as an indicator. Triethylamine and diisopropylamine were dried over potassium hydroxide pellets. Brine refers to saturated aqueous sodium chloride.

General procedure: Ireland–Claisen rearrangement with *in situ* trimethylsilyl chloride

Trimethylsilyl chloride (4.2 equiv.) was added to the ester in THF at −78 °C. After 5 min, the lithium hexamethyldisilazide (4.0 equiv.) was added and the solution stirred for 20 min then warmed to room temperature and stirred for a further 20 min. Saturated aqueous ammonium chloride was added and aqueous phase extracted with ethyl acetate. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure.

General procedure: Ireland–Claisen rearrangement with trimethylsilyl chloride added after the base

Lithium hexamethyldisilazide (1.3 equiv.) was added to the ester in THF at −78 °C. After 90 s, trimethylsilyl chloride (1.6 equiv.) was added and the solution stirred for 20 min then warmed to room temperature and stirred for a further 20 min. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with ethyl acetate. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure.

General procedure: methylation of acids with trimethylsilyldiazomethane

Trimethylsilyldiazomethane (2.0 M in hexanes, 1.2 equiv.) was added to the crude acid in methanol–benzene (1 : 4) and the

solution stirred for 1 h. Concentration under reduced pressure and chromatography gave the methyl ester.

1-*tert*-Butyldimethylsilyloxy-1-phenylbut-3-ene 6.[7] Imidazole (5.52 g, 81.0 mmol) and *tert*-butyldimethylsilyl chloride (5.88 g, 39.0 mmol) were added to the alcohol **5** (4.80 g, 32.0 mmol) in DCM (40 mL) and the solution stirred overnight. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (3%), gave the title compound **6**[7] (7.98 g, 95%) as a colourless oil (Found: M^+ + H, 263.1829. $C_{16}H_{27}SiO$ requires *M*, 263.1831); ν_{max}/cm^{-1} 3077, 3029, 2954, 2931, 2857, 1641, 1467, 1362, 1254, 1089, 1069, 1005, 915, 836, 776 and 699; δ_H (300 MHz, $CDCl_3$) 0.00 and 0.16 (each 3 H, s, $SiCH_3$), 1.01 [9 H, s, $SiC(CH_3)_3$], 2.56 (2 H, m, 2-H_2), 4.81 (1 H, dd, *J* 5.2, 7.1, 1-H), 5.14 (2 H, m, 4-H_2), 5.91 (1 H, m, 3-H) and 7.40 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.0, −4.7, 18.2, 25.8, 45.5, 74.9, 116.8, 125.8, 126.9, 127.9, 135.2 and 145.0; *m*/*z* (CI) 263 (M^+ + 1, 1%), 188 (2), 171 (3) and 131 (100).

4-*tert*-Butyldimethylsilyloxy-4-phenylbutan-1-ol 7.[8] The butene **6** (2.0 g, 7.63 mmol) in THF (15 mL) was added to 9-borabicyclo-[3.3.1]nonane (16.8 mL, 0.5 M in THF, 8.40 mmol). The solution was stirred for 2.5 h, after which time a mixture of aqueous sodium hydroxide (6 mL, 0.5 M) and ethanol (5 mL) was added, followed by aqueous hydrogen peroxide (3 mL, 30%). Saturated aqueous potassium carbonate was added and the layers separated. The aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave the title compound **7**[8] (1.82 g, 86%) as a clear, colourless oil (Found: M^+ + H, 281.1943. $C_{18}H_{29}SiO_2$ requires *M*, 281.1937); ν_{max}/cm^{-1} 3453, 2926, 2857, 1470, 1451, 1413, 1326, 1299, 1250, 1164, 1092, 1034, 837, 776 and 700; δ_H (300 MHz, $CDCl_3$) −0.09 and 0.07 (each 3 H, s, $SiCH_3$), 0.93 [9 H, s, $SiC(CH_3)_3$], 1.50–1.93 (4 H, m, 2-H_2 and 3-H_2), 3.65 (2 H, m, 1-H_2), 4.76 (1 H, dd, *J* 4.0, 6.0, 4-H) and 7.33 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.0, −4.6, 18.3, 25.9, 28.6, 37.2, 63.0, 74.8, 125.9, 126.9, 128.1 and 145.2; *m*/*z* (CI) 281 (M^+ + 1, 4%), 172 (58) and 144 (100).

1-*tert*-Butyldimethylsilyloxy-4-iodo-1-phenylbutane 8. Imidazole (0.24 g, 3.57 mmol), triphenylphosphine (0.47 g, 1.79 mmol) and iodine (0.46 g, 1.79 mmol) were added to the alcohol **7** (500 mg, 1.79 mmol) in THF (25 mL) and the solution stirred at room temperature for 1.5 h. Saturated aqueous sodium hydrogen carbonate was added and the mixture stirred for 10 min. Iodine was added portionwise until the organic layer turned purple. The excess iodine was removed with aqueous sodium thiosulfate and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (20%) gave the *title compound* **8** (627 mg, 90%) as a clear, pale yellow oil (Found: M^+ + NH_4, 408.1229. $C_{16}H_{31}NISiO$ requires *M*, 408.1221); ν_{max}/cm^{-1} 3063, 3027, 2952, 2929, 2855, 1467, 1362, 1254, 1092, 1067, 838, 776 and 700; δ_H (300 MHz, $CDCl_3$) 0.00 and 0.18 (each 3 H, s, $SiCH_3$), 1.03 [9 H, s, $SiC(CH_3)_3$], 1.86–2.08 (4 H, m, 2-H_2 and 3-H_2), 3.30 (2 H, m, 4-H_2), 4.83 (1 H, t, *J* 6.3, 1-H) and 7.42 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.1, −4.7, 7.0, 18.1, 25.8, 29.5, 41.4, 73.9, 125.7, 127.0, 128.0 and 145.0; *m*/*z* (CI) 408 (M^+ + 18, 2%), 391 (M^+ + 1, 1), 350 (2), 276 (100), 259 (18) and 148 (22).

1-*tert*-Butyldimethylsilyloxy-5-[(1-methyl-1*H*-2-imidazolyl)-sulfanyl]-1-phenylhept-6-ene 9. Butyllithium (4.7 mL, 1.63 M in hexanes, 7.64 mmol) was added to 2-(prop-2-enylsulfanyl)-1-methyl-1*H*-imidazole (0.98 g, 6.36 mmol) in THF (20 mL) at −78 °C. After 30 min, HMPA (2.2 mL, 12.7 mmol) was added and the solution stirred at −78 °C for 30 min. The iodide **8** (2.48 g, 6.36 mmol) in THF (5 mL) was added and the solution stirred for 1 h. Saturated aqueous ammonium chloride was added and the mixture allowed to warm to room temperature. The aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (30%), gave the *title compound* **9** (1.94 g, 74%) as a clear, colourless oil, a mixture of epimers (^{13}C NMR) (Found: M^+ + H, 417.2391. $C_{23}H_{37}N_2SSiO$ requires *M*, 417.2396); ν_{max}/cm^{-1} 3063, 3028, 2930, 2856, 1455, 1279, 1253, 1093, 1067, 837, 775 and 699; δ_H (300 MHz, $CDCl_3$) 0.00 and 0.17 (each 3 H, s, $SiCH_3$), 1.03 [9 H, s, $SiC(CH_3)_3$], 1.45–1.94 (6 H, m, 2-H_2, 3-H_2 and 4-H_2), 3.81 (3 H, s, NCH_3), 3.93 (1 H, dt, *J* 5.8, 9.2, 5-H), 4.77 (1 H, m, 1-H), 5.03 (2 H, m, 7-H_2), 5.85 (1 H, dt, *J* 16.3, 9.2, 6-H), 7.09 (1 H, br. s, 9-H), 7.25 (1 H, t, *J* 1.1, 8-H) and 7.43 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.0, −4.7, 18.1, 23.2, 23.4, 25.8, 33.6, 34.0, 34.1, 40.4, 40.5, 53.4, 74.7, 74.8, 116.1, 116.0, 122.4, 125.7, 126.7, 127.9, 129.6, 138.4 and 145.5; *m*/*z* (CI) 417 (M^+ + 1, 100%) and 115 (76).

7-*tert*-Butyldimethylsilyloxy-7-phenylhept-2-en-1-yl(tributyl)-stannane 10. Tributyltin hydride (1.43 mL, 5.51 mmol) and AIBN (50 mg) were added to the sulfide **9** (1.91 g, 4.60 mmol) in benzene (20 mL). The mixture was thoroughly degassed then heated under reflux for 1 h. After concentration under reduced pressure, chromatography of the residue, eluting with triethylamine–petrol (1%), gave the *title compound* **10** (2.17 g, 89%) as a clear, colourless oil, a 67 : 33 mixture of (*E*)- and (*Z*)-isomers (^1H NMR) (Found: $M^+ - C_4H_9$, 537.2575. $C_{27}H_{49}Si^{120}SnO$ requires *M*, 537.2373); ν_{max}/cm^{-1} 2955, 2927, 2855, 1460, 1361, 1253, 1092, 836, 775 and 699; δ_H (300 MHz, $CDCl_3$) 0.00 and 0.17 (each 3 H, s, $SiCH_3$), 1.01 (15 H, m, 3 × CH_3CH_2), 1.03 [9 H, s, $SiC(CH_3)_3$], 1.42 (6 H, m, 3 × CH_2), 1.60 (6 H, m, 3 × CH_2Sn), 1.69–1.85 (6 H, m, 1-H_2, 5-H_2 and 6-H_2), 2.09 (2 H, m, 4-H_2), 4.76 (1 H, m, 7-H), 5.12 (0.33 H, m, 3-H), 5.32 (0.67 H, dt, *J* 16.6, 5.8, 3-H), 5.53 (0.33 H, m, 2-H), 5.64 (0.67 H, dt, *J* 16.6, 8.3, 2-H) and 7.42 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) major (*E*)-isomer −4.9, −4.6, 9.1, 9.3 13.8, 14.1, 18.3, 25.9, 27.4, 29.2, 32.7, 40.8, 75.2, 125.6, 125.9, 126.7, 128.0, 129.2 and 146.0; *m*/*z* (EI) 537 ($M^+ - 57$, 1%), 365 (2), 289 (21), 247 (100), 221 (51) and 75 (52).

7-Hydroxy-7-phenylhept-2-en-1-yl(tributyl)stannene 11. Tetrabutylammonium fluoride (4.8 mL, 1.0 M in THF, 4.83 mmol) was added to the stannane **10** (2.17 g, 4.03 mmol) in THF (20 mL) and the solution stirred for 4 h. Saturated aqueous

ammonium chloride was added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10% with 1% TEA), gave the *title compound* **11** (1.33 g, 69%), as a clear, colourless oil, a 67 : 33 mixture of (*E*)- and (*Z*)-isomers (^{1}H NMR) (Found: $M^+ - C_4H_9$, 423.1709. $C_{21}H_{35}{}^{120}SnO$ requires *M*, 423.1709); ν_{max}/cm^{-1} 3368, 2955, 2925, 2852, 1456, 1069, 1021, 961 and 699; δ_H (300 MHz, $CDCl_3$) 0.88 (15 H, m, 3 × CH_3CH_2), 1.30 (6 H, m, 3 × CH_2), 1.46 (6 H, m, 3 × CH_2Sn), 1.68 (2 H, d, *J* 8.0, 1-H_2), 1.70–1.86 (4 H, m, 5-H_2 and 6-H_2), 1.88 (1 H, br. s, OH), 2.00 (2 H, q, *J* 7.2, 4-H_2), 4.67 (1 H, t, *J* 5.4, 7-H), 5.02 (0.33 H, dt, *J* 10.8, 7.2, 3-H), 5.19 (0.67 H, dt, *J* 15.0, 7.2, 3-H), 5.53 (1 H, m, 2-H) and 7.35 (5 H, m, ArH); *m*/*z* (EI) 479 ($M^+ - 1$, 2%), 423 ($M^+ - 57$, 12), 405 (23), 291 (53), 235 (72), 179 (54) and 107 (100).

(*E*)-1,8-Diphenyloct-3-ene-1,8-diol 12. Tin(IV) bromide (2.3 mL, 1.0 M in DCM, 2.34 mmol) was added to the stannane **11** (1.02 g, 2.13 mmol) in DCM (12 mL) at −78 °C. The solution was stirred for 5 min then benzaldehyde (0.65 mL, 6.39 mmol) was added. After 20 min, aqueous ammonium chloride was added and the mixture was allowed to warm to room temperature. The aqueous phase was extracted with DCM and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (50% with 1% TEA), gave the *title compound* **12** (515 mg, 81%) as a clear, colourless oil (Found: $M^+ + NH_4$, 314.2121. $C_{20}H_{28}NO_2$ requires *M*, 314.2120); ν_{max}/cm^{-1} 3374, 3028, 2932, 2859, 1603, 1493, 1452, 1201, 1046, 1027, 972, 760 and 701; δ_H (300 MHz, $CDCl_3$) 1.29–1.59 (2 H, m, 6-H_2), 1.62–1.84 (2 H, m, 7-H_2), 2.06 (2 H, bq, *J* 6.7, 5-H_2), 2.30 (1 H, br. s, OH), 2.39 (1 H, br. s, OH), 2.47 (2 H, m, 2-H_2), 4.67 (2 H, m, 1-H and 8-H), 5.42 (1 H, dt, *J* 15.8, 6.5, 4-H), 5.55 (1 H, dt, *J* 15.8, 6.3, 3-H) and 7.36 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 25.4, 32.3, 38.4, 42.6, 73.5, 74.4, 125.8(2), 127.3, 127.4, 128.3, 128.4, 132.9, 134.3, 144.0 and 144.8; *m*/*z* (CI) 314 (M^+ + 18, 71%), 296 (M^+, 53), 261 (100) and 157 (46). HPLC analysis (Perkin-Elmer LC0480 diode-array system, ODS sphereclone 5u column, 4.6 mm × 25 cm silica) eluting with acetonitrile–water (40 : 60) showed two diastereoisomers in a 33 : 67 ratio.

(*E*)-1,8-Diacetoxy-1,8-diphenyloct-3-ene 13. TEA (0.97 mL, 6.90 mmol), DMAP (10 mg, catalytic) and acetic anhydride (261 μL, 2.77 mmol) were added to the diol **12** (205 mg, 0.69 mmol) in DCM (5 mL) and the solution was stirred for 3 h. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave the *title compound* (214 mg, 82%) as a clear, colourless oil (Found: $M^+ + NH_4$, 398.2330. $C_{24}H_{32}NO_4$ requires *M*, 398.2331); ν_{max}/cm^{-1} 3032, 2939, 2861, 1737, 1371, 1238, 1024, 760 and 700; δ_H (300 MHz, $CDCl_3$) 1.18–1.46 (2 H, m, 6-H_2), 1.70–1.94 (2 H, m, 7-H_2), 2.01 (2 H, br. q, *J* 7.2, 5-H_2), 2.08 and 2.11 (each 3 H, s, CH_3), 2.46–2.73 (2 H, m, 2-H_2), 5.32 (1 H, m, 4-H), 5.43 (1 H, m, 3-H), 5.75 (2 H, m, 1-H and 8-H) and 7.33 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 21.2, 25.1, 25.2, 32.1, 35.6, 39.5, 75.5, 75.9, 125.1, 126.4, 126.5, 127.8, 128.2, 128.3, 132.3, 133.4, 140.1, 140.6, 170.1 and 170.3; *m*/*z* (CI) 398 (M^+ + 18, 100%) and 261 (44). HPLC analysis (Perkin-Elmer LC0480 diode-array system, ODS sphereclone 5u column, 4.6 mm × 25 cm silica) eluting with acetonitrile–water (60 : 40) showed two diastereomers in a 32 : 68 ratio.

(*E*)-4-Hydroxypent-2-eny(tributy)stannane 15. Tributyltin hydride (0.15 mL, 0.55 mmol) and AIBN (5 mg) were added to a thoroughly degassed solution of the sulfone **14** (104 mg, 0.46 mmol) in benzene (5 mL) and the solution heated to 65 °C for 1.5 h. After concentration under reduced pressure, chromatography of the residue, eluting with ether–petrol (20% with 1% triethylamine), gave the *title compound* **15** (153 mg, 89%) as a clear, colourless oil, essentially just the (*E*)-isomer (^{1}H NMR) (Found: $M^+ - C_4H_9$, 319.1093. $C_{13}H_{27}O^{120}Sn$ requires *M*, 319.1083); ν_{max}/cm^{-1} 3344, 2924, 2851, 1652, 1460, 1376, 1291, 1064, 962 and 867; δ_H (300 MHz, $CDCl_3$) 0.89 (15 H, m, 3 × CH_3CH_2), 1.32 (9 H, m, 3 × CH_2 and 5-H_3), 1.53 (6 H, m, 3 × CH_2Sn), 1.75 (2 H, d, *J* 8.7, 1-H_2), 4.26 (1 H, m, 4-H), 5.35 (1 H, dd, *J* 7.3, 15.1, 3-H) and 5.80 (1H, dt, *J* 8.7, 15.1, 2-H); δ_C (75 MHz, $CDCl_3$) 9.3, 13.8, 14.2, 23.6, 27.4, 29.1, 69.6, 129.5 and 131.3; *m*/*z* (CI) 308 (100%) and 244 (21).

(*E*)-4-(2-Trimethylsilylethoxy)methoxypent-2-enyl(tributyl)-stannane 16. Diisopropylethylamine (6.7 mL, 38.4 mmol) and (2-trimethylsilylethoxy)methyl chloride (4.4 mL, 25.0 mmol) were added to the stannane **15** (7.22 g, 19.2 mmol) in DCM (40 mL) at 0 °C. The solution was allowed to warm to room temperature and then stirred for 3 h. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with TEA–petrol (1%), gave the *title compound* **16** (8.08 g, 83%) as a clear, colourless oil (Found: $M^+ - C_4H_9$, 449.1897. $C_{19}H_{41}O_2Si^{120}Sn$ requires *M*, 449.1897); ν_{max}/cm^{-1} (300 MHz, $CDCl_3$) 2956, 2925, 2853, 1651, 1461, 1376, 1248, 1100, 1023 and 836; δ_H 0.05 (9 H, s, 3 × $SiCH_3$), 0.93 (17 H, m, 3 × CH_3CH_2 and CH_2Si), 1.30 (9 H, m, 3 × CH_2 and 5-H_3), 1.51 (6 H, m, 3 × CH_2Sn), 1.75 (2 H, d, *J* 8.8, 1-H_2), 3.69 (2 H, m, OCH_2CH_2), 4.13 (1 H, m, 4-H), 4.61 and 4.73 (each 1 H, d, *J* 6.8, O*H*CHO), 5.54 (1 H, dd, *J* 8.2, 15.1, 3-H) and 5.78 (1 H, dt, *J* 8.8, 15.1, 2-H); δ_C (75 MHz, $CDCl_3$) −1.1, 9.2, 13.7, 14.2, 18.2, 22.0, 27.7, 29.0, 64.8, 65.0, 65.7, 65.9, 91.4, 91.6, 126.4 and 133.3; *m*/*z* (CI) 308 (100%) and 244 (41).

(3*SR*,5*Z*,7*RS*)-3-Hydroxy-7-(2-trimethylsilylethoxy)methoxy-octa-1,5-diene 17. Tin(IV) chloride (16.7 mL, 1.0 M in DCM, 16.7 mmol) was added to the stannane **16** (7.65 g, 15.2 mmol) in DCM (60 mL) at −78 °C. After 10 min, acrolein (5 mL, 75 mmol) was added and the solution stirred for a further 10 min at −78 °C. Water and saturated aqueous ammonium chloride were added and the mixture allowed to warm to room temperature. The aqueous phase was extracted with DCM and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (10% with 1% TEA), gave the *title compound* **17** (2.98 g, 77%) as a clear, colourless oil, a

96 : 4 mixture of epimers (^{1}H NMR) (Found: $M^+ + NH_4$ 290.2148. $C_{14}H_{32}NSiO_3$ requires *M*, 290.2151); ν_{max}/cm^{-1} 3433, 2954, 2893, 1646, 1375, 1249, 1101, 1024, 922, 860, 836 and 756; δ_H (300 MHz, $CDCl_3$) major epimer **17** 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 1.22 (3 H, d, *J* 6.5, 8-H_3), 2.26 and 2.39 (each 1 H, m, 4-H), 2.65 (1 H, d, *J* 5.5, OH), 3.53 and 3.67 (each 1 H, dt, *J* 6.9, 9.8, O*H*CHCH$_2$), 4.41 (1 H, m, 3-H), 4.51 (1 H, dq, *J* 9.2, 6.5, 7-H), 4.60 and 4.73 (each 1 H, d, *J* 7.1, O*H*CHO), 5.09 (1 H, dt, *J* 10.4, 1.5, 1-H), 5.25 (1 H, dt, *J* 17.2, 1.5, 1-H), 5.41 (1 H, dt, *J* 10.0, 11.2, 6-H), 5.58 (1 H, m, 5-H) and 5.87 (1 H, ddd, *J* 5.5, 10.4, 17.2, 2-H); minor epimer **20** 4.69 (1 H, d, *J* 7.1, O*H*CHO); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 35.6, 64.9, 67.0, 71.9, 91.7, 114.2, 128.2, 133.9 and 140.7; *m*/*z* (CI) 290 (M^+ + 18, 100%), 197 (23), 142 (25), 107 (31) and 90 (93).

(3*SR*,5*Z*,7*RS*)-3-(4-Nitrobenzoyl)oxy-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 18. Triethylamine (58 μL, 0.42 mmol), DMAP (5 mg) and 4-nitrobenzoyl chloride (55 mg, 0.30 mmol) were added to the alcohol **17** (54 mg, 0.20 mmol) in DCM (0.5 mL) at room temperature and the resulting solution stirred for 2 h. Saturated aqueous ammonium chloride was added, the aqueous phase extracted with DCM and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (5%), gave the *title compound* **18** (66 mg, 78%) as a clear, colourless oil (Found: $M^+ + NH_4$ 439.2263. $C_{21}H_{35}N_2SiO_6$ requires *M*, 439.2264); ν_{max}/cm^{-1} 3017, 2953, 2889, 1727, 1607, 1530, 1346, 1272, 1102, 1025, 836 and 720; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, t, *J* 8.2, CH_2Si), 1.20 (3 H, d, *J* 6.5, 8-H_3), 2.61 (2 H, m, 4-H_2), 3.50 (1 H, dt, *J* 7.4, 9.5, O*H*CHCH$_2$), 3.70 (1 H, dt, *J* 7.7, 9.6, O*H*CHCH$_2$), 4.52 (1 H, m, 7-H), 4.54 and 4.62 (each 1 H, d, *J* 7.0, O*H*CHO), 5.26 (1 H, d, *J* 10.6, 1-H), 5.35 (1 H, d, *J* 17.1, 1-H), 5.43 (1 H, dd *J* 10.2, 8.1, 6-H), 5.54 (2 H, m, 3-H and 5-H), 5.89 (1 H, ddd, *J* 6.3, 10.6, 17.2, 2-H), 8.20 (2 H, m, ArH) and 8.27 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 21.2, 32.4, 65.0, 66.6, 75.6, 91.7, 117.8, 123.4, 125.9, 130.7, 134.6, 135.1, 135.6, 150.5 and 163.7; *m*/*z* (CI) 439 (M^+ + 18, 30%), 422 (M^+ + 1, 3), 274 (53), 107 (39) and 90 (100).

(3*RS*,5*Z*,7*RS*)-3-(4-Nitrobenzoyl)oxy-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 19. Diethyl azodicarboxylate (135 μL, 0.86 mmol) was added dropwise to the alcohol **17** (156 mg, 0.57 mmol), triphenylphosphine (226 mg, 0.86 mmol) and 4-nitrobenzoic acid (144 mg, 0.86 mmol) in benzene (1.5 mL) at room temperature and the solution stirred for 2 h. Saturated aqueous ammonium chloride was added, the aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (5%), gave the *title compound* **19** (143 mg, 60%) as a clear, colourless oil (Found: $M^+ + NH_4$, 439.2263. $C_{21}H_{35}N_2SiO_6$ requires *M*, 439.2264); ν_{max}/cm^{-1} 2953, 2890, 1727, 1606, 1530, 1346, 1271, 1102, 1024, 836 and 719; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, t, *J* 8.5, CH_2Si), 1.18 (3 H, d, *J* 6.3, 8-H_3), 2.61 (2 H, m, 4-H_2), 3.50 (1 H, dt, *J* 7.3, 9.6, O*H*CHCH$_2$), 3.69 (1 H, dt, *J* 7.7, 9.5, O*H*CHCH$_2$), 4.54 (1 H, m, 7-H), 4.56 and 4.63 (each 1 H, d, *J* 7.0, O*H*CHO), 5.26 (1 H, dt, *J* 10.6, 1.0, 1-H), 5.35 (1 H, dt, *J* 17.2, 1.1, 1-H), 5.43 (1 H, dd, *J* 10.1, 8.2, 6-H), 5.54 (2 H, m, 3-H and 5-H), 5.90 (1 H, ddd, *J* 6.5, 10.6, 17.2, 2-H), 8.19 (2 H, m, ArH) and 8.27 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 32.5, 64.9, 66.5, 75.7, 91.6, 118.0, 123.5, 126.0, 130.6, 134.5, 135.1, 135.6, 150.5 and 163.7; *m*/*z* (CI) 439 (M^+ + 18, 23%), 422 (4), 377 (51), 317 (100), 244 (53) and 90 (65).

(3*RS*,5*Z*,7*RS*)-3-Hydroxy-7-(2-trimethylsilylethoxy)methoxy-octa-1,5-diene 20. Lithium hydroxide monohydrate (320 mg, 7.61 mmol) was added to an emulsion of the ester **19** (641 mg, 1.52 mmol) in methanol–water (10 mL, 3 : 1 v:v) and the mixture stirred vigorously for 15 h. After concentration under reduced pressure, the residue was dissolved in ether and water and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (20%), gave the *title compound* **20** (367 mg, 89%) as a clear, colourless oil, a 96 : 4 mixture of epimers (^{1}H NMR) (Found: M^+ + H, 273.1890. $C_{14}H_{29}SiO_3$ requires *M*, 273.1886); ν_{max}/cm^{-1} 3443, 3013, 2953, 2892, 1422, 1375, 1249, 1101, 1052, 1024, 923, 859, 836 and 756; δ_H (300 MHz, $CDCl_3$) major epimer **20** 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 1.22 (3 H, d, *J* 6.5, 8-H_3), 2.30 (1 H, m, 4-H), 2.41 (1 H, d, *J* 4.1, OH), 2.44 (1 H, m, 4-H), 3.52 (1 H, dt, *J* 7.0, 9.6, O*H*CHCH$_2$), 3.67 (1 H, dt, *J* 7.4, 9.8, O*H*CHCH$_2$), 4.19 (1 H, m, 3-H), 4.53 (1 H, dq, *J* 9.1, 6.5, 7-H), 4.59 and 4.69 (each 1 H, d, *J* 7.0, O*H*CHO), 5.11 (1 H, dt, *J* 10.6, 1.4, 1-H), 5.24 (1 H, dt, *J* 16.9, 1.4, 1-H), 5.42 (1 H, dd, *J* 9.1, 10.9, 6-H), 5.56 (1 H, dt, *J* 10.9, 7.5, 5-H) and 5.87 (1 H, ddd, *J* 5.6, 10.6, 16.9, 2-H); minor epimer **17** 4.73 (1 H, d, *J* 7.0, O*H*CHO) δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 35.0, 64.9, 67.0, 71.8, 91.7, 114.7, 127.2, 134.2 and 140.1; *m*/*z* (CI) 290 (M^+ + 18, 4%), 273 (M^+ + 1, 7), 123 (9), 107 (8) and 90 (100).

(3*SR*,5*Z*,7*RS*)-3-(Benzyloxy)acetoxy-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 21. Benzyloxyacetyl chloride (1.59 mL, 10.1 mmol), TEA (1.96 mL, 14.1 mmol) and DMAP (50 mg) were added to the alcohol **17** (1.83 g, 6.71 mmol) in DCM (15 mL) at room temperature. The solution was heated under reflux for 3 h then allowed to cool to room temperature. Saturated aqueous ammonium chloride was added, the aqueous phase was extracted with DCM and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (7%), gave the *title compound* **21** (2.48 g, 88%) as a clear, colourless oil (Found: $M^+ + NH_4$, 438.2680. $C_{23}H_{40}NSiO_5$ requires *M*, 438.2677); ν_{max}/cm^{-1} 2952, 2891, 1756, 1425, 1249, 1195, 1127, 1027, 836, 742 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.93 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.4, 8-H_3), 2.47 (2 H, m, 4-H_2), 3.49 (1 H, dt, *J* 7.3, 8.0, O*H*CHCH$_2$), 3.78 (1 H, dt, *J* 7.7, 9.5, O*H*CHCH$_2$), 4.08 (2 H, s, O_2CCH_2O), 4.48 (1 H, dq, *J* 8.1, 6.4, 7-H), 4.56 (1 H, d, *J* 7.0, O*H*CHO), 4.61 (3 H, m, C*H*$_2$Ph and O*H*CHO), 5.19 (1 H, dd, *J* 1.1, 10.6, 1-H), 5.25 (1 H, d, *J* 1.0, 17.3, 1-H), 5.41 (3 H, m, 3-H, 5-H and 6-H), 5.78 (1 H, ddd, *J* 6.5, 10.6, 17.2, 2-H) and 7.32 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.4, 18.1, 21.3, 32.4, 65.0, 66.9, 67.2, 73.3, 74.5, 91.9,

117.7, 126.0, 128.0, 128.1, 128.5, 134.5, 135.4, 137.1 and 169.6; *m/z* (CI) 438 (M^+ + 18, 100%), 273 (54) and 107 (46).

Methyl (2*SR*,4*E*,7*Z*,9*RS*)-2-(benzyloxy)-9-(2-trimethylsilylethoxy)-methoxydeca-4,7-dienoate 22. Using the general procedure with the trimethylsilyl chloride *in situ*, the benzyloxyacetate **21** (1.23 g, 2.92 mmol) in THF (30 mL), trimethylsilyl chloride (1.56 mL, 12.28 mmol) and lithium hexamethyldisilazide (11.7 mL, 1.0 M in THF, 11.7 mmol) after reaction with trimethylsilyldiazomethane (1.75 mL, 2.0 M in hexanes, 3.51 mmol) and chromatography, eluting with ethyl acetate–petrol (5%), gave the *title compound* **22** (1.13 g, 89%) as a clear, colourless oil (Found: M^+ + NH_4, 452.2832. $C_{24}H_{42}NSiO_5$ requires *M*, 452.2832); ν_{max}/cm^{-1} 3009, 2952, 2889, 1752, 1451, 1438, 1249, 1202, 1104, 1025, 859, 836, 743 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, m, 3 × $SiCH_3$), 0.91 (2 H, t, *J* 8.5, CH_2Si), 1.20 (3 H, d, *J* 6.4, 10-H_3), 2.45 (2 H, t, *J* 5.6, 3-H_2), 2.78 (2 H, m, 6-H_2), 3.50 (1 H, dt, *J* 7.1, 9.6, O*H*CHCH$_2$), 3.69 (1 H, m, O*H*CHCH$_2$), 3.71 (3 H, s, OCH_3), 3.95 (1 H, t, *J* 6.4, 2-H), 4.41 (1 H, d, *J* 11.8, O*H*CHPh), 4.52 (1 H, dq, *J* 8.9, 6.5, 9-H), 4.55 and 4.62 (each 1 H, d, *J* 7.0, O*H*CHO), 4.68 (1 H, d, *J* 11.8, O*H*CHPh), 5.30 (1 H, m, 8-H), 5.46 (3 H, m, 4-H, 5-H and 7-H) and 7.32 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 21.4, 30.7, 36.1, 51.7, 64.9, 66.6, 72.2, 78.1, 91.7, 125.2, 127.8, 127.9, 128.3, 129.8, 131.6, 131.9, 137.4 and 172.6; *m/z* (CI) 452 (M^+ + 18, 100%), 412 (13), 304 (22), 287 (26) and 90 (63).

The general procedure with addition of trimethylsilyl chloride after the base, the benzyloxyacetate **21** (310 mg, 0.74 mmol) in THF (3.6 mL), lithium hexamethyldisilazide (1.0 mL, 1.0 M in THF, 0.96 mmol) and trimethylsilyl chloride (150 µL, 1.18 mmol) after reaction with trimethylsilyldiazomethane (0.44 mL, 2.0 M in hexanes, 0.89 mmol) and chromatography, eluting with ethyl acetate–petrol (5%), gave the title compound **22** (250 mg, 78%) as a clear, colourless oil.

Methyl (2*SR*,4*E*,7*Z*,9*RS*)-2-benzyloxy-9-hydroxydeca-4,7-dienoate 23. Hydrofluoric acid (0.5 mL, 40% in water, 10 mmol) was added to the ester **22** (78 mg, 0.18 mmol) in acetonitrile (2 mL) and the solution was stirred for 5 h. Ether and saturated aqueous sodium hydrogen carbonate were added until no more effervescence was seen. The aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (30%), gave the *title compound* **23** (41 mg, 75%) as a clear, colourless oil (Found: M^+ + NH_4 322.2017. $C_{18}H_{28}NO_4$ requires *M*, 322.2018); ν_{max}/cm^{-1} 3422, 2966, 2921, 1746, 1438, 1276, 1206, 1112, 972, 741 and 698; δ_H (300 MHz, $CDCl_3$) 1.21 (3 H, d, *J* 6.3, 10-H_3), 1.75 (1 H, br. s, OH), 2.45 (2 H, m, 3-H_2), 2.77 (2 H, m, 6-H_2), 3.71 (3 H, s, OCH_3), 3.95 (1 H, t, *J* 6.3, 2-H), 4.40 (1 H, d, *J* 12.0, O*H*CHPh), 4.59 (1 H, m, 9-H), 4.68 (1 H, d, *J* 12.0, O*H*CHPh), 5.46 (4 H, m, 4-H, 5-H, 7-H and 8-H) and 7.31 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 23.4, 30.5, 36.0, 51.8, 63.6, 72.2, 78.0, 125.0, 127.8, 127.9, 128.0, 128.3, 131.6, 134.8, 137.3 and 172.6; *m/z* (CI) 322 (M^+ + 18, 60%), 287 (100) and 146 (50).

Methyl (2*SR*,4*E*,7*Z*,9*RS*)-2-(benzyloxy)-9-(4-nitrobenzoyl)-oxydeca-4,7-dienoate 24. Diethyl azodicarboxylate (21 µL, 0.13 mmol) was added to the alcohol **27** (31 mg, 0.10 mmol), triphenylphosphine (35 mg, 0.13 mmol) and 4-nitrobenzoic acid (22 mg, 0.13 mmol) in benzene (0.3 mL) at room temperature. The solution was stirred for 2 h and then diluted with ether and water. The aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave the *title compound* (30 mg, 60%) as a clear, pale yellow oil, a mixture of esters **24** and **28**, ratio **24** : **28** = 89 : 11 (^{1}H NMR) (Found: M^+ + NH_4, 471.2124. $C_{25}H_{31}N_2O_7$ requires *M*, 471.2131); ν_{max}/cm^{-1} 3027, 2950, 2872, 1748, 1723, 1605, 1528, 1342, 1273, 1105, 1036 and 720; δ_H (C_6D_6, 400 MHz) 1.25 (2.67 H, d, *J* 6.4, 10-H_3), 1.26 (0.33 H, d, *J* 6.4, 10-H_3), 2.55 (2 H, m, 3-H_2), 2.84 (2 H, t, *J* 6.4, 6-H_2), 3.40 (2.67 H, s, OCH_3), 3.41 (0.33 H, s, OCH_3), 3.96 (1 H, t, *J* 6.0, 2-H), 4.29 (0.11 H, d, *J* 11.6, O*H*CHPh), 4.30 (0.89 H, d, *J* 12.0, O*H*CHPh), 4.70 (1 H, d, *J* 11.6, O*H*CHPh), 5.40–5.52 (3 H, m, 5-H, 7-H and 8-H), 5.60 (1 H, dtq, *J* 15.2, 6.8, 1.6, 4-H), 5.92 (1 H, dq, *J* 8.0, 6.4, 9-H), 7.13 (1 H, m, ArH), 7.21 (2 H, m, ArH), 7.37 (2 H, m, ArH), 7.73 (2 H, m, ArH) and 7.79 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 20.8, 30.9, 36.0, 51.8, 68.7, 72.2, 78.0, 123.4, 125.6, 127.8, 127.9, 128.3, 129.3, 130.6, 130.9, 131.2, 136.0, 137.4, 150.4, 163.8 and 172.5; *m/z* (CI) 471 (M^+ + 18, 100%) and 304 (26).

A solution of the alcohol **23** (41 mg, 0.14 mmol), triethylamine (47 µL, 0.34 mmol), 4-nitrobenzoyl chloride (38 mg, 0.20 mmol) and DMAP (2 mg) in DCM (0.3 mL) was stirred at room temperature for 2 h. DCM and water were added and the aqueous phase was extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave the title compound (57 mg, 90%) as a clear, pale yellow oil, a mixture of esters **24** and **28**, ratio **24** : **28** = 88 : 12 (^{1}H NMR).

(3*RS*,5*Z*,7*RS*)-3-(Benzyloxy)acetoxy-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 25. Triethylamine (81 µL, 0.58 mmol), DMAP (5 mg) and benzyloxyacetyl chloride (74 µg, 0.47 mmol) were added to the alcohol **20** (75 mg, 0.28 mmol) in DCM (0.8 mL) at room temperature and the solution heated under reflux for 3 h then allowed to cool to room temperature. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (7%), gave the *title compound* **25** (101 mg, 86%) as a clear, colourless oil (Found: M^+ + NH_4, 438.2669. $C_{23}H_{40}NSiO_5$ requires *M*, 438.2677); ν_{max}/cm^{-1} 3017, 2952, 2890, 1756, 1374, 1249, 1195, 1027, 859, 836, 743 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.3, 8-H_3), 2.45 (2 H, m, 4-H_2), 3.49 and 3.68 (each 1 H, dt, *J* 7.2, 9.6, O*H*CHCH$_2$), 4.08 (2 H, s, O_2CCH_2O), 4.49 (1 H, dq, *J* 8.4, 6.3, 7-H), 4.56 (1 H, d, *J* 7.0, O*H*CHO), 4.61 (2 H, s, CH_2Ph), 4.62 (1 H, d, *J* 7.0, O*H*CHO), 5.20 (1 H, dt, *J* 10.5, 0.9, 1-H), 5.26 (1 H, dt, *J* 17.1, 1.2, 1-H), 5.41 (3 H, m, 3-H, 5-H and 6-H), 5.78 (1 H, ddd, *J* 6.5, 10.5, 17.1, 2-H) and 7.32 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 32.4, 64.9, 66.6, 67.1, 73.2, 74.5, 91.7, 117.7, 126.1,

127.9, 128.0, 128.4, 134.3, 135.3, 137.0 and 169.5; *m/z* (CI) 438 (M^+ + 18, 88%), 273 (38), 184 (33), 107 (100) and 90 (98).

Methyl (2*RS*,4*E*,7*Z*,9*RS*)-2-(benzyloxy)-9-(2-trimethylsilylethoxy)methoxydeca-4,7-dienoate 26. Using the general procedure with *in situ* trimethylsilyl chloride, the benzyloxyacetate **25** (98 mg, 0.23 mmol) in THF (1.0 mL), trimethylsilyl chloride (124 μL, 0.98 mmol) and lithium hexamethylsilazide (0.93 mL, 1.0 M in THF, 0.93 mmol), after treatment with trimethylsilyldiazomethane (140 μL, 2.0 M in hexanes, 0.28 mmol) and chromatography, eluting with ethyl acetate–petrol (5%), gave the *title compound* **26** (76 mg, 76%) as a clear, colourless oil (Found: M^+ + NH_4 452.2837. $C_{24}H_{42}NSiO_5$ requires *M*, 452.2832); ν_{max}/cm^{-1} 3030, 2951, 2884, 1752, 1438, 1249, 1201, 1103, 1025, 836, 743 and 696; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.21 (3 H, d, *J* 6.4, 10-H_3), 2.45 (2 H, br. t, *J* 6.4, 3-H_2), 2.79 (2 H, m, 6-H_2), 3.50 (1 H, dt, *J* 7.1, 9.5, O*H*CHCH_2), 3.69 (1 H, m, O*H*CHCH_2), 3.71 (3 H, s, OCH_3), 3.94 (1 H, t, *J* 6.4, 2-H), 4.41 (1 H, d, *J* 11.8, O*H*CHPh), 4.53 (1 H, dq, *J* 9.0, 6.4, 9-H), 4.56 and 4.62 (each 1 H, d, *J* 7.0 O*H*CHO), 4.68 (1 H, d, *J* 11.8, O*H*CHPh), 5.29 (1 H, dd, *J* 9.0, 10.9, 8-H), 5.45 (3 H, m, 4-H, 5-H and 7-H) and 7.31 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 21.34, 30.6, 36.1, 51.7, 64.9, 66.6, 72.2, 78.0, 91.7, 125.2, 127.8, 127.9, 128.3, 129.8, 131.6, 131.9, 137.4 and 172.6; *m/z* (CI) 452 (M^+ + 18, 100%), 287 (12) and 90 (13).

Methyl (2*RS*,4*E*,7*Z*,9*RS*)-2-benzyloxy-9-hydroxydeca-4,7-dienoate 27. Butanethiol (0.36 mL, 3.35 mmol) was added to a suspension of potassium carbonate (530 mg, 3.83 mmol), magnesium bromide diethyl etherate (866 mg, 3.35 mmol) and ester **26** (208 mg, 0.48 mmol) in ether (2 mL) at room temperature and the mixture stirred for 7 h. Dilute aqueous hydrogen chloride was added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (30%), gave the *title compound* **27** (77 mg, 53%) as a clear, colourless oil (Found: M^+ + NH_4 322.2019. $C_{18}H_{28}NO_4$ requires *M*, 322.2018); ν_{max}/cm^{-1} 3432, 3009, 2967, 2921, 1747, 1496, 1451, 1438, 1276, 1205, 1114, 1058, 972, 742 and 699; δ_H (300 MHz, $CDCl_3$) 1.28 (3 H, d, *J* 6.3, 10-H_3), 1.84 (1 H, br. s, OH), 2.52 (2 H, t, *J* 5.9, 3-H_2), 2.83 (2 H, m, 6-H_2), 3.77 (3 H, s, OCH_3), 4.02 (1 H, t, *J* 6.3, 2-H), 4.47 (1 H, d, *J* 11.8, O*H*CHPh), 4.66 (1 H, m, 9-H), 4.75 (1 H, d, *J* 11.8, O*H*CHPh), 5.51 (4 H, m, 4-H, 5-H, 7-H and 8-H) and 7.38 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 23.4, 30.5, 36.0, 51.8, 63.6, 72.2, 78.0, 125.0, 127.8, 127.9, 128.0, 128.3, 131.6, 134.8, 137.3 and 172.6; *m/z* (CI) 322 (M^+ + 18, 100%), 304 (M^+, 47), 287 (76) and 164 (42).

Methyl (2*RS*,4*E*,7*Z*,9*RS*)-2-(benzyloxy)-9-(4-nitrobenzoyl)-oxydeca-4,7-dienoate 28. A solution of the alcohol **27** (33 mg, 0.11 mmol), triethylamine (33 μL, 0.24 mmol), 4-nitrobenzoyl chloride (32 mg, 0.17 mmol) and DMAP (2 mg) in DCM (0.5 mL) was stirred for 2 h at room temperature. DCM and water were added and the aqueous phase was extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave the *title compound* **28** (38 mg, 79%) as a clear, pale yellow oil, a mixture of esters **24** and **28**, ratio **24** : **28** = 11 : 89 (^1H NMR) (Found: M^+ + NH_4, 471.2138. $C_{25}H_{31}N_2O_7$ requires *M*, 471.2131); ν_{max}/cm^{-1} 3026, 2950, 2873, 1748, 1723, 1605, 1528, 1343, 1273, 1106, 1037 and 721; δ_H (C_6D_6, 400 MHz) 1.25 (0.33 H, d, *J* 6.4, 10-H_3), 1.26 (2.67 H, d, *J* 6.4, 10-H_3), 2.55 (2 H, m, 3-H_2), 2.84 (2 H, t, *J* 6.8, 6-H_2), 3.39 (0.33 H, s, OCH_3), 3.40 (2.67 H, s, OCH_3), 3.96 (1 H, t, *J* 6.0, 2-H), 4.29 and 4.71 (each 1 H, d, *J* 11.6, O*H*CHPh), 5.46 (3 H, m, 5-H, 7-H and 8-H), 5.60 (1 H, dtq, *J* 15.2, 6.8, 1.6, 4-H), 5.93 (1 H, dq, *J* 8.0, 6.4, 9-H), 7.13 (1 H, m, ArH), 7.21 (2 H, m, ArH), 7.36 (2 H, m, ArH), 7.72 (2 H, m, ArH) and 7.79 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 20.8, 30.9, 36.0, 51.8, 68.7, 72.2, 78.0, 123.4, 125.6, 127.8, 127.9, 128.3, 129.3, 130.6, 130.9, 131.2, 136.0, 137.4, 150.4, 163.8 and 172.5; *m/z* (CI) 471 (M^+ + 18, 100%) and 304 (10).

Methyl (2*SR*,9*RS*)-2-benzyloxy-9-(2-trimethylsilylethoxy)-methoxydecanoate 31. A solution of the diene **22** (915 mg, 2.11 mmol) and toluene 4-sulfonylhydrazine (4.7 g, 25.3 mmol) in DME (35 mL) was heated under reflux and a solution of sodium acetate (5.7 g, 42.2 mmol) in water (7 mL) was added dropwise over 2.5 h. The solution was stirred under reflux for a further 2.5 h, and then allowed to cool to room temperature. Water and ether were added and the aqueous phase extracted with ether. The organic extracts were washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (7%), gave the *title compound* **31** (862 mg, 93%) as a clear, colourless oil (Found: M^+ + NH_4 456.3146. $C_{24}H_{46}NSiO_5$ requires *M*, 456.3145); ν_{max}/cm^{-1} 3031, 2930, 2861, 1752, 1456, 1249, 1200, 1103, 1054, 1030, 859, 836, 739 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.12 (3 H, d, *J* 6.2, 10-H_3), 1.21–1.55 (10 H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2 and 8-H_2), 1.71 (2 H, m, 3-H_2), 3.60 (3 H, m, OCH_2CH_2, 9-H), 3.71 (3 H, s, OCH_3), 3.91 (1 H, t, *J* 6.5, 2-H), 4.37 (1 H, d, *J* 11.7, O*H*CHPh), 4.66 (3 H, m, O*H*CHPh and OCH_2O) and 7.32 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 20.2, 25.1, 25.5, 29.2, 29.4, 32.9, 36.9, 51.7, 64.7, 72.2, 72.8, 78.0, 92.9, 127.7, 127.9, 128.3, 137.5 and 173.3; *m/z* (CI) 456 (M^+ + 18, 100%), 108 (12) and 90 (29).

Methyl (2*SR*,9*RS*)-2-hydroxy-9-(2-trimethylsilylethoxy)-methoxydecanoate 32. A suspension of palladium on carbon (10%; 175 mg, 0.17 mmol) and the benzyl ether **31** (721 mg, 1.65 mmol) in ethanol (6 mL) was stirred under an atmosphere of hydrogen for 72 h. The mixture was then filtered through celite and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (15%), gave the *title compound* **32** (499 mg, 87%) as a clear, colourless oil (Found: M^+ + NH_4 366.2687. $C_{17}H_{40}NSiO_5$ requires *M*, 366.2676); ν_{max}/cm^{-1} 3442, 2930, 2859, 1742, 1459, 1442, 1377, 1249, 1207, 1098, 1055, 1029, 859 and 836; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.90 (2 H, m, CH_2Si), 1.13 (3 H, d, *J* 6.2, 10-H_3), 1.20–1.82 (12 H, m, 3-H_2, 4-H_2, 5-H_2, 6-H_2, 7-H_2 and 8-H_2), 2.78 (1 H, d, *J* 5.8, OH), 3.62 (3 H, m, OCH_2CH_2, 9-H), 3.77 (3 H, s, OCH_3), 4.16 (1 H, dt, *J* 7.3, 5.4, 2-H) and 4.64 and 4.71 (each 1 H, d, *J* 7.2, O*H*CHO); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 20.2, 24.7, 25.4, 29.2, 29.4, 34.3, 36.9, 52.3, 64.8, 70.4, 72.8, 92.9 and 175.7; *m/z* (CI)

366 (M^+ + 18, 100%), 308 (27), 291 (72), 231 (52), 220 (41), 218 (41) and 90 (42).

Methyl (2*SR*,9*RS*)-2-*tert*-butyldiphenylsilyloxy-9-(2-trimethylsilylethoxy)methoxydecanoate 33. Imidazole (173 mg, 2.55 mmol) and *tert*-butyldiphenylchlorosilane (473 μL, 1.82 mmol) were added to the alcohol **32** (422 mg, 1.21 mmol) in DCM (1.2 mL) and the solution stirred for 2 h at room temperature. DCM and water were added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (3%), gave the *title compound* **33** (695 mg, 98%) as a clear, colourless oil (Found: $M^+ + NH_4$, 604.3852. $C_{33}H_{58}NSi_2O_5$ requires *M*, 604.3853); ν_{max}/cm^{-1} 3049, 2932, 2858, 1757, 1740, 1466, 1429, 1249, 1196, 1110, 1055, 1029, 858, 836 and 704; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × CH_3), 0.89 (2 H, m, CH_2Si), 1.09 [9 H, s, $SiC(CH_3)_3$], 1.14 (3 H, d, *J* 6.2, 10-H_3), 1.17–1.73 (12 H, m, 3-H_2, 4-H_2, 5-H_2, 6-H_2, 7-H_2 and 8-H_2), 3.46 (3 H, s, OCH_3), 3.62 (3 H, m, OCH_2CH_2 and 9-H), 4.21 (1 H, t, *J* 5.5, 2-H), 4.65 and 4.72 (each 1 H, d, *J* 7.1, O*H*CHO), 7.36 (6 H, m, ArH) and 7.64 (4 H, m, ArH); δ_H (75 MHz, $CDCl_3$) −1.5, 18.0, 19.3, 20.2, 24.4, 25.5, 26.8, 29.3, 29.4, 35.1, 36.9, 51.3, 64.8, 72.6, 72.8, 93.0, 127.4, 127.5, 129.6, 129.7, 133.2, 133.4, 135.7, 135.9 and 173.6; *m*/*z* (CI) 604 (M^+ + 18, 100%) and 90 (89).

(2*SR*,9*RS*)-2-*tert*-Butyldiphenylsilyloxy-9-(2-trimethylsilylethoxy)-methoxydecan-1-ol 34. Lithium triethylborohydride (0.96 mL, 1.0 M in THF, 0.96 mmol) was added dropwise to the ester **33** (141 mg, 0.23 mmol) in THF (1 mL) at −10 °C and the solution stirred for 30 min. Water and dilute aqueous hydrogen chloride were added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (15%), gave the *title compound* **34** (114 mg, 89%), as a clear, colourless oil (Found: $M^+ + NH_4$ 576.3903. $C_{32}H_{58}NSi_2O_4$ requires *M*, 576.3904); ν_{max}/cm^{-1} 3439, 3070, 3049, 2931, 2857, 1467, 1428, 1378, 1249, 1110, 1056, 1029, 859, 835 and 703; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.90 (2 H, m, CH_2Si), 1.04 [9 H, s, $SiC(CH_3)_3$], 1.12 (3 H, d, *J* 6.2, 10-H_3), 1.06–1.52 (12 H, m, 3-H_2, 4-H_2, 5-H_2, 6-H_2, 7-H_2 and 8-H_2), 1.81 (1 H, t, *J* 6.3, OH), 3.49 (2 H, m, 1-H_2), 3.61 (3 H, m, OCH_2CH_2 and 9-H), 3.75 (1 H, m, 2-H), 4.63 and 4.70 (each 1 H, d, *J* 7.0, O*H*CHO), 7.37 (6 H, m, ArH) and 7.67 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 19.3, 20.2, 25.0, 25.4, 26.5, 27.0, 29.5, 33.4, 36.9, 64.8, 65.9, 72.8, 74.0, 92.9, 127.5, 127.7, 129.5, 129.7, 133.9, 134.7, 135.6 and 135.8; *m*/*z* (CI) 576 (M^+ + 18, 4%), 363 (10), 333 (12), 196 (18) and 90 (100).

Methyl (2*E*,4*RS*,11*SR*)-4-*tert*-butyldiphenylsilyloxy-11-(2-trimethylsilylethoxy)methoxydodec-2-enoate 35. Dimethylsulfoxide (84 μL, 1.19 mmol) was added to oxalyl chloride (42 μL, 0.47 mmol) in DCM (3 mL) at −78 °C. The solution was stirred for 10 min, then the alcohol **34** (217 mg, 0.39 mmol) in DCM (1 mL) was added *via* a cannula and the resulting solution was stirred for 5 h at −78 °C. Triethylamine (166 μL, 1.19 mmol) was then added and the mixture allowed to warm to room temperature. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure until *ca.* 1 mL of the solution remained. Methoxycarbonylmethylene triphenylphosphorane (261 mg, 0.78 mmol) was added and the solution stirred for 15 h. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (5%), gave the *title compound* **35** (172 mg, 72%) as a clear colourless oil (Found: $M^+ + NH_4$ 630.4002. $C_{35}H_{60}NSi_2O_5$ requires *M*, 630.4010); ν_{max}/cm^{-1} 3070, 2932, 2858, 1727, 1659, 1430, 1272, 1165, 1107, 1054, 859, 835 and 703; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.93 (2 H, m, CH_2Si), 1.08 [9 H, s, $SiC(CH_3)_3$], 1.14 (3 H, d, *J* 6.3, 12-H_3), 1.10–1.54 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 3.63 (3 H, m, OCH_2CH_2 and 11-H), 3.72 (3 H, s, OCH_3), 4.34 (1 H, dq, *J* 1.2, 5.0, 4-H), 4.65 and 4.72 (each 1 H, d, *J* 6.9, O*H*CHO), 5.93 (1 H, dd, *J* 1.5, 15.4, 2-H), 6.87 (1 H, dd, *J* 5.2, 15.4, 3-H), 7.38 (6 H, m, ArH) and 7.63 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 19.3, 20.2, 23.9, 25.5, 27.0, 29.4, 29.5, 36.7, 37.0, 51.4, 66.8, 72.4, 72.9, 93.0, 119.7, 127.5(2), 129.6, 129.7, 133.4, 133.9, 135.7, 150.5 and 167.0; *m*/*z* (CI) 630 (M^+ + 18, 37%), 274 (94), 196 (100) and 90 (89).

Methyl (2*E*,4*RS*,11*SR*)-4-*tert*-butyldiphenylsilyloxy-11-hydroxydodec-2-enoate 36. Butanethiol (0.26 mL, 2.46 mmol) was added to a vigorously stirred suspension of potassium carbonate (388 mg, 2.81 mmol), magnesium bromide diethyl etherate (635 mg, 2.46 mmol) and the SEM-ether **35** (215 mg, 0.35 mmol) in ether (5 mL) at room temperature and the resulting mixture stirred for 2 h. Dilute aqueous hydrogen chloride and water were added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (20%), gave the *title compound* **36** (150 mg, 89%) as a clear, colourless oil (Found: M^+, 482.2841. $C_{29}H_{42}SiO_4$ requires *M*, 482.2852); ν_{max}/cm^{-1} 3431, 2931, 2857, 1725, 1658, 1464, 1431, 1276, 1166, 1108 and 704; δ_H (300 MHz, $CDCl_3$) 1.08 [9 H, s, $SiC(CH_3)_3$], 1.17 (3 H, d, *J* 6.2, 12-H_3), 1.03–1.48 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 3.73 (3 H, s, OCH_3), 3.75 (1 H, m, 11-H), 4.35 (1 H, q, *J* 5.1, 4-H), 5.93 (1 H, dd, *J* 1.4, 15.4, 2-H), 6.88 (1 H, dd, *J* 5.8, 15.4, 3-H), 7.31–7.46 (6 H, m, ArH) and 7.58–7.69 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 19.2, 23.4, 23.8, 25.5, 27.0, 29.3(2), 36.6, 39.2, 51.4, 68.0, 72.3, 119.6, 127.5, 129.7, 129.7, 133.4, 133.9, 135.7, 150.5 and 167.0; *m*/*z* (CI) 500 (M^+ + 18, 18%), 483 (M^+ + 1, 20), 274 (20), 244 (100), 227 (30) and 196 (20).

(4*SR*,11*RS*)- and (4*RS*,11*RS*)-4-*tert*-Butyldiphenylsilyloxy-11-methylundec-2-en-11-olide 38 and 39.[2h] Lithium hydroxide monohydrate (65 mg, 1.54 mmol) was added to the methyl ester **36** (150 mg, 0.31 mmol) in methanol–water (2.5 mL, 3 : 1) and the solution stirred for 15 h. After concentration under reduced pressure, the residue was taken up in water and ethyl acetate. The aqueous phase was extracted with ethyl acetate and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to leave the seco-acid **37** (123 mg, 85%)

that was used without further purification. Triethylamine (24 μL, 171 μmol) and 2,6-dichlorobenzoyl chloride (18 μL, 128 μmol) were added to the seco-acid **37** (40 mg, 85 μmol) in THF (0.5 mL) and the solution stirred for 2 h. The mixture was filtered and diluted with toluene (35 mL). This solution was then added dropwise over 5 h to a solution of DMAP (63 mg, 0.51 mmol) in toluene (5 mL) heated under reflux. The solution was then allowed to cool and water was added. The aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (1%), gave the title compound **39**^{2h} (1.2 mg, 3%) as a clear, colourless oil (Found: $M^+ + NH_4$, 468.2934. $C_{28}H_{42}NSiO_3$ requires *M*, 468.2934); ν_{max}/cm^{-1} 2932, 2857, 1714, 1463, 1428, 1363, 1249, 1110, 822 and 703; δ_H (300 MHz, $CDCl_3$) 0.84–1.74 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 1.09 [9 H, s, $SiC(CH_3)_3$], 1.28 (3 H, d, *J* 6.7, 11-CH_3), 4.50 (1 H, m, 4-H), 5.05 (1 H, dqn, *J* 3.0, 6.9, 11-H), 6.15 (1 H, dd, *J* 1.8, 15.6, 2-H), 7.00 (1 H, dd, *J* 3.6, 15.6, 3-H), 7.39 (6 H, m, ArH) and 7.66 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 19.3, 19.9, 21.1, 23.0, 27.0, 27.7, 27.9, 33.6, 36.3, 72.4, 73.1, 120.2, 127.6, 127.6, 129.7, 133.4, 134.0, 135.7, 135.8, 135.9, 152.2 and 167.5; *m*/*z* (CI) 468 ($M^+ + 18$, 80%), 451 ($M^+ + 1$, 30), 274 (70) and 196 (100). The second fraction was the title compound **38**^{2h} (18.0 mg, 47%) as a clear, colourless oil (Found: $M^+ + NH_4$, 468.2936. $C_{28}H_{42}NSiO_3$ requires *M*, 468.2934); ν_{max}/cm^{-1} 3071, 2934, 2859, 1721, 1649, 1271, 1110 and 703; δ_H (300 MHz, $CDCl_3$) 0.86–1.78 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 1.10 [9 H, s, $SiC(CH_3)_3$], 1.32 (3 H, d, *J* 6.5, 11-CH_3), 4.47 (1 H, q, *J* 5.2, 4-H), 5.09 (1 H, dqn, *J* 3.2, 5.6, 11-H), 6.09 (1 H, d, *J* 15.8, 2-H), 6.79 (1 H, dd, *J* 5.2, 15.8, 3-H), 7.40 (6 H, m, ArH) and 7.65 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 19.2(2), 20.5, 22.0, 26.9, 27.9, 28.5, 32.4, 35.9, 72.0, 72.8, 121.2, 127.5, 127.6, 129.7, 133.4, 133.9, 135.7, 149.8 and 168.5; *m*/*z* (CI) 468 ($M^+ + 18$, 100%), 451 ($M^+ + 1$, 58), 274 (39) and 196 (42).

Patulolide C 1.[1] Tetrabutylammonium fluoride (120 μL, 1.0 M in THF, 0.12 mmol) was added to the silyl ether **38** (36 mg, 80 μmol) in THF (0.3 mL) and the solution stirred for 3 h. Ether and water were added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave patulolide C **1**[1,2] (13 mg, 76%) as a clear, colourless oil (Found: $M^+ + NH_4$ 230.1751. $C_{12}H_{24}NO_3$ requires *M*, 230.1756); ν_{max}/cm^{-1} 3413, 2934, 2859, 1717, 1645, 1461, 1263, 1161 and 992; δ_H (300 MHz, $CDCl_3$) 0.86–1.88 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 1.33 (3 H, d, *J* 6.6, 11-CH_3), 4.54 (1 H, q, *J* 6.0, 4-H), 5.11 (1 H, dqn, *J* 3.3, 6.6, 11-H), 6.13 (1 H, dd, *J* 0.9, 15.7, 2-H) and 6.89 (1 H, dd, *J* 6.6, 15.7, 3-H); δ_C (75 MHz, $CDCl_3$) 19.3, 20.7, 22.1, 27.8, 28.2, 32.8, 35.9, 70.9, 73.1, 121.5, 149.5 and 168.0; *m*/*z* (CI) 230 ($M^+ + 18$, 100%) and 213 ($M^+ + 1$, 32).

(3*RS*,5*Z*,7*SR*)-3-(Prop-2-enyloxy)-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 41. The alcohol **17** (1.51 mg, 5.56 mmol) in DMF (2 mL) was added to a suspension of sodium hydride (289 mg, 60% dispersion in oil, 7.23 mmol) in DMF (5 mL). After the evolution of gas had ceased, the mixture was cooled to 0 °C and tetrabutylammonium iodide (50 mg) and 1-bromoprop-2-ene (0.62 mL, 7.23 mmol) were added. The mixture was stirred overnight at room temperature then saturated aqueous ammonium chloride was added. The aqueous phase was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave the *title compound* **41** (1.34 g, 77%) as a clear, colourless oil (Found: $M^+ + NH_4$ 330.2458, $C_{17}H_{36}NSiO_3$ requires *M*, 330.2464); ν_{max}/cm^{-1} 2953, 2888, 1644, 1421, 1249, 1100, 1027, 924, 836 and 656; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.3, 8-H_3), 2.31 (1 H, dt, *J* 14.6, 7.0, 4-H), 2.42 (1 H, dt, *J* 14.4, 6.3, 4-H), 3.51 (1 H, q, *J* 9.6, 3-H), 3.70 (2 H, m, OCH_2CH_2), 3.82 (1 H, dd, *J* 5.9, 12.8, 1′-H), 4.02 (1 H, dd, *J* 5.1, 12.9, 1′-H), 4.51 (1 H, dq, *J* 8.4, 6.5, 7-H), 4.57 and 4.64 (each 1 H, d, *J* 6.9, O*H*CHO), 5.20 (4 H, m, 1-H_2 and 3′-H_2), 5.35 (1 H, t, J 10.1, 6-H), 5.60 (2 H, m, 2-H, 5-H) and 5.87 (1 H, ddt, *J* 10.4, 16.4, 5.6, 2′-H); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 33.5, 64.8, 67.0, 69.1, 80.0, 91.8, 116.5, 117.3, 127.5, 133.1, 134.9 and 138.2; *m*/*z* (CI) 330 ($M^+ + 18$, 94%), 283 (12), 165 (100) and 97 (88).

(3*RS*,5*Z*,7*SR*)-3-(Prop-2-ynyloxy)-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 42. The alcohol **17** (1.24 mg, 4.56 mmol) in THF (2 mL) was added to a suspension of sodium hydride (237 mg, 60% dispersion in oil, 5.92 mmol) in THF (5 mL). After the evolution of gas had ceased, the mixture was cooled to −78 °C and propargyl bromide (1.02 mL, 80% by wt in toluene, 5.92 mmol) was added. The mixture was stirred overnight at room temperature then saturated aqueous ammonium chloride was added. The aqueous phase was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave the *title compound* **42** (1.20 g, 85%) as a clear, pale yellow oil (Found: $M^+ + NH_4$ 328.2302. $C_{17}H_{34}NSiO_3$ requires *M*, 328.2308); ν_{max}/cm^{-1} 3308, 2953, 2893, 2116, 1642, 1423, 1374, 1249, 1080, 1025, 931, 860, 836, 758 and 693; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, t, *J* 8.2, CH_2Si), 1.21 (3 H, d, *J* 6.3, 8-H_3), 2.33 (1 H, ddt, *J* 1.4, 14.7, 8.1, 4-H), 2.37 (1 H, t, *J* 2.3, 3′-H), 2.41 (1 H, ddt, *J* 1.4, 14.8, 7.7, 4-H), 3.50 and 3.68 (each 1 H, dt, *J* 7.1, 9.6, O*H*CHCH$_2$), 3.91 (1 H, q, *J* 6.6, 3-H), 4.01 and 4.17 (each 1 H, dd, *J* 2.3, 15.7, 1′-H), 4.50 (1 H, dq, *J* 2.6, 6.6, 7-H), 4.57 and 4.64 (each 1 H, d, *J* 6.9, O*H*CHO), 5.24 (1 H, d, *J* 11.5, 1-H), 5.24 (1 H, d, *J* 15.9, 1-H), 5.36 (1 H, ddt, *J* 8.9, 10.7, 1.5, 6-H), 5.54 (1 H, dt, *J* 11.0, 7.3, 5-H) and 5.63 (1 H, ddd, *J* 8.0, 9.9, 17.7, 2-H); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.2, 33.3, 55.2, 64.8, 67.0, 73.9, 79.5, 79.9, 91.8, 118.5, 127.1, 133.4 and 137.0; *m*/*z* (CI) 328 ($M^+ + 18$, 95%), 281 (12), 163 (100) and 107 (71).

Dodeca-2,4,6-triene 43.[17] Butyllithium (0.70 mL, 1.47 M in hexanes, 0.97 mmol) was added to the ether **41** (252 mg, 0.81 mmol) in THF (2 mL) at −78 °C and the mixture stirred for 15 h. Saturated aqueous ammonium chloride was added, the aqueous phase was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under

reduced pressure. Chromatography of the residue, eluting with petrol, gave the title compound **43**[17] (83 mg, 64%), a mixture of two isomers as a clear, colourless oil (Found: M^+ 164.1565. $C_{12}H_{20}$ requires *M*, 164.1565); ν_{max}/cm^{-1} 3013, 2957, 2927, 2857, 1649, 1459, 992 and 926; δ_H (300 MHz, $CDCl_3$) 0.93 (3 H, t, *J* 6.9, 12-H_3), 1.24–1.50 (6 H, m, 9-H_2, 10-H_2 and 11-H_2), 1.81 (3 H, d, *J* 6.8, 1-H_3), 2.13 (2 H, q, *J* 7.0, 8-H_2), 5.71 (2 H, m, 2-H and 7-H) and 6.10 (4 H, m, 3-H, 4-H, 5-H and 6-H); δ_C (75 MHz, $CDCl_3$) 13.3, 14.0, 18.2, 22.5, 28.9, 29.0, 31.4, 32.7, 125.6, 125.7, 128.6, 129.5, 130.3, 130.5, 130.6(2), 131.7, 132.6, 134.4 and 135.2; *m*/*z* (EI) 164 (M^+, 100%), 107 (31), 93 (43), 91 (36), 79 (71) and 41 (28).

(3*RS*,5*Z*,7*SR*)-3-(Ethoxycarbonyl)methoxy-7-(2-trimethylsilylethoxy)methoxyocta-1,5-diene 44. Ethyl diazoacetate (0.47 mL, 4.43 mmol) was added dropwise to the alcohol **17** (241 mg, 0.89 mmol) and rhodium diacetate dimer (39 mg, 2 mol% wrt ethyl diazoacetate) in DCM (2.5 mL). After the evolution of gas had ceased (30 min), saturated aqueous ammonium chloride was added and the aqueous phase was extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–light petroleum (15%), gave the *title compound* **44** (193 mg, 61%) as a clear, colourless oil (Found: $M^+ + NH_4$ 376.2509. $C_{18}H_{38}NSiO_5$ requires *M*, 376.2519); ν_{max}/cm^{-1} 2973, 2867, 1736, 1452, 1370, 1313, 1101, 931, 738 and 699; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.21 (3 H, d, *J* 6.5, 8-H_3), 1.26 (3 H, t, *J* 7.1, CH_3CH_2), 2.37 (1 H, ddt, *J* 1.2, 14.7, 8.0, 4-H), 2.48 (1 H, ddt, *J* 1.5, 13.3, 7.0, 4-H), 3.60 (2 H, m, OCH_2CH_2), 3.79 (1 H, q, *J* 6.6, 3-H), 3.97 and 4.08 (each 1 H, d, *J* 16.4, 1′-H), 4.18 (2 H, q, *J* 6.2, CH_3CH_2), 4.51 (1 H, dq, *J* 6.5, 9.1, 7-H), 4.57 and 4.64 (each 1 H, d, *J* 6.9, O*H*CHO), 5.21 (2 H, m, 1-H_2), 5.36 (1 H, dd, *J* 10.7, 11.0, 6-H), 5.58 (1 H, dt, *J* 11.0, 7.4, 5-H) and 5.66 (1 H, ddd, *J* 8.0, 10.4, 17.0, 2-H); δ_C (75 MHz, $CDCl_3$) −1.5, 14.1, 18.0, 21.2, 33.3, 60.6, 64.8, 65.5, 67.0, 81.4, 91.8, 118.6, 127.0, 133.4, 137.1 and 170.5; *m*/*z* (CI) 376 (M^+ + 18, 56%), 359 (M^+ + 1, 7), 329 (8), 228 (22), 107 (100), 90 (53) and 56 (22).

(3*RS*,5*Z*,7*SR*)-3-(Formylmethoxy)-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 45. Diisobutylaluminium hydride (5.74 mL, 1.0 M in hexanes, 5.74 mmol) was added to the ester **44** (1.37 g, 3.82 mmol) in DCM (10 mL) at −78 °C. The solution was stirred between −45 °C and −60 °C for 1 h then cooled to −78 °C and triethanolamine (2 equiv.) in DCM was added. The mixture was allowed to warm to 0 °C, then saturated aqueous ammonium chloride and celite were added and the mixture allowed to warm to room temperature. After filtration through celite, the filtrate was concentrated under reduced pressure. Chromatography of the residue, with ether–light petroleum (20%) as the eluent, gave the starting material **44** (92 mg) and the *title compound* **45** (733 mg, 61%) as a clear colourless oil (Found: $M^+ + NH_4$ 332.2257. $C_{16}H_{34}NSiO_4$ requires *M*, 332.2257); ν_{max}/cm^{-1} 2954, 2894, 1738, 1374, 1249, 1104, 1026, 933, 860, 836, 759 and 694; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.22 (3 H, d, *J* 6.4, 8-H_3), 2.37 (1 H, ddt, *J* 1.4, 14.3, 6.5, 4-H), 2.51 (1 H, ddt, *J* 1.2, 13.7, 6.2, 4-H), 3.50 (1 H, dt, *J* 7.3, 9.6, O*H*CHCH$_2$), 3.69 (1 H, dt, *J* 8.5, 10.7, O*H*CHCH$_2$), 3.75 (1 H, q, *J* 6.6, 3-H), 3.95 and 4.07 (each 1 H, d, *J* 18.0, 1′-H), 4.52 (1 H, dq, *J* 9.1, 6.4, 7-H), 4.57 and 4.64 (each 1 H, d, *J* 7.0, O*H*CHO), 5.21 (1 H, d, *J* 17.2, 1-H), 5.26 (1 H, d, *J* 9.6, 1-H), 5.38 (1 H, dd, *J* 9.1, 11.0, 6-H), 5.55 (1 H, dt, *J* 11.0, 7.3, 5-H), 5.66 (1 H, ddd, *J* 8.0, 9.6, 17.2, 2-H) and 9.69 (1 H, s, CHO); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.2, 33.3, 64.9, 66.8, 73.8, 82.0, 91.7, 118.9, 126.8, 133.7, 136.9 and 201.1; *m*/*z* (CI) 332 (M^+ + 18, 34%), 184 (57), 107 (100) and 90 (42).

(3*RS*,5*Z*,7*SR*)-3-(3-Methoxycarbonylprop-2-enyl)oxy-7-(2-trimethylsilylethoxy)methoxyocta-1,5-diene 46. Methoxycarbonyl triphenyl phosphorane (1.23 g, 3.68 mmol) was added to the aldehyde **45** (577 mg, 1.83 mmol) in DMF (12 mL) at room temperature and the solution stirred overnight. Water and DCM were added and the aqueous phase extracted with DCM. The organic extracts were washed with water then brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (4%), gave the (2′*Z*)-isomer of the *title compound* **(2′*Z*)-46** (30 mg, 4%) as a clear, colourless oil (Found: $M^+ + NH_4$ 388.2526. $C_{19}H_{38}NSiO_5$ requires *M*, 388.2519); ν_{max}/cm^{-1} 2952, 2890, 1723, 1652, 1438, 1194, 1096, 1025, 926, 836, 757 and 694; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.90 (2 H, m, CH_2Si), 1.21 (3 H, d, *J* 6.3, 8-H_3), 2.37 (2 H, m, 4-H_2), 3.50 (1 H, dt, *J* 7.1, 9.6, O*H*CHCH$_2$), 3.69 (3 H, s, OCH_3), 3.70 (2 H, m, O*H*CHCH$_2$ and 3-H), 4.47 (1 H, ddd, *J* 2.5, 5.9, 16.8, 1′-H), 4.50 (1 H, m, 7-H), 4.54 (1 H, ddd, *J* 2.5, 4.9, 16.8, 1′-H), 4.57 and 4.63 (each 1 H, d, *J* 6.9, O*H*CHO), 5.20 (2 H, m, 1-H_2), 5.35 (1 H, ddt, *J* 9.2, 11.0, 1.4, 6-H), 5.53 (1 H, dt, *J* 11.0, 7.8, 5-H), 5.66 (1 H, ddd, *J* 7.6, 9.9, 17.6, 2-H), 5.78 (1 H, dt, *J* 11.7, 2.5, 3′-H) and 6.37 (1 H, dt, *J* 11.7, 4.9, 2′-H); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 33.5, 51.2, 64.9, 66.6, 66.9, 80.8, 91.8, 117.7, 118.6, 127.4, 133.3, 137.8, 149.1 and 166.4; *m*/*z* (CI) 388 (M^+ + 18, 27%), 223 (38), 99 (100) and 56 (38). The second fraction was the (2′*E*)-isomer of the *title compound* **(2′*E*)-46** (457 mg, 70%) as a colourless oil (Found: $M^+ + NH_4$ 388.2509. $C_{19}H_{38}NSiO_5$ requires *M*, 388.2519); ν_{max}/cm^{-1} 2952, 2880, 1727, 1662, 1437, 1301, 1271, 1249, 1170, 1101, 1025, 928, 836, 758 and 693; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.90 (2 H, m, CH_2Si), 1.21 (3 H, d, *J* 6.5, 8-H_3), 2.33 (1 H, ddt, *J* 1.6, 14.7, 6.3, 4-H), 2.43 (1 H, ddt, *J* 1.5, 14.7, 6.0, 4-H), 3.50 (1 H, dt, *J* 7.2, 9.5, O*H*CHCH$_2$), 3.71 (2 H, m, O*H*CHCH$_2$ and 3-H), 3.73 (3 H, s, OCH_3), 3.99 (1 H, ddd, *J* 2.1, 4.4, 16.5, 1′-H), 4.17 (1 H, ddd, *J* 2.1, 3.8, 16.4, 1′-H), 4.51 (1 H, dq, *J* 9.1, 6.3, 7-H), 4.57 and 4.64 (1 H, d, *J* 6.9, O*H*CHO), 5.19 (2 H, m, 1-H_2), 5.36 (1 H, ddt, *J* 9.1, 11.0, 1.4, 6-H), 5.54 (1 H, dt, *J* 11.0, 7.8, 5-H), 5.66 (1 H, ddd, *J* 7.7, 10.7, 16.9, 2-H), 6.07 (1 H, dt, *J* 15.7, 2.2, 3′-H) and 6.93 (1 H, dt, *J* 15.7, 3.9, 2′-H); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.2, 33.4, 51.5, 64.9, 66.7, 66.8, 80.9, 91.7, 117.8, 120.5, 127.2, 133.4, 137.7, 144.9 and 166.8; *m*/*z* (CI) 388 (M^+ + 18, 53%), 240 (61), 155 (100) and 99 (82).

(3*RS*,5*Z*,7*SR*)-3-[3-(4,5-Dihydro-1,3-oxazol-2-l)prop-2-enyl]-oxy-7-(2-trimethylsilylethoxy)methoxyocta-1,5-diene 48. Butyllithium (26.9 mL, 1.6 M in hexanes, 44.9 mmol) was added to diisopropylamine (6.43 mL, 46.0 mmol) in THF (20 mL) at 0 °C. The solution was allowed to warm to room temperature, stirred for 20 min and then cooled to −78 °C. 2,4,4-Trimethyl-2-oxazoline

(1.02 g, 8.98 mmol) in THF (3 mL) was added and the solution stirred for 1 h. Diethyl chlorophosphate (1.6 mL, 10.8 mmol) was added and the solution stirred for a further 1 h. Saturated aqueous ammonium chloride was added and the aqueous phase was extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to leave phosphonate **47** (1.24 g, 55%) as a clear yellow oil used without further purification.

Lithium chloride (66 mg, 1.55 mmol) and 1,8-diazabicyclo [5.4.0]undec-7-ene (0.21 mL, 1.42 mmol) were added to the phosphonate **47** (387 mg, 1.55 mmol) in acetonitrile (6 mL) at room temperature. The aldehyde **45** (409 mg, 1.29 mmol) in acetonitrile (2 mL) was added and the solution stirred for 48 h. Saturated aqueous ammonium chloride and DCM were added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (25%), gave the *title compound* **48** (315 mg, 60%) as a clear, colourless oil (Found: M^+ + H, 410.2632. $C_{22}H_{40}NSiO_4$ requires *M*, 410.2726); ν_{max}/cm^{-1} 2965, 2890, 1678, 1646, 1615, 1459, 1355, 1307, 1248, 1102, 1025, 925, 836, 757 and 694; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.86 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.4, 8-H_3), 1.28 (6 H, s, 2 × CH_3), 2.36 (2 H, m, 4-H_2), 3.50 and 3.68 (each 1 H, dt, *J* 7.3, 9.6, O*H*CHCH_2), 3.72 (1 H, q, *J* 6.6, 3-H), 3.94 (2 H, s, 5′-H_2), 3.96 (1 H, m, 1′-H), 4.15 (1 H, ddd, *J* 1.9, 4.4, 15.0, 1′-H), 4.50 (1 H, dq, *J* 8.7, 6.4, 7-H), 4.57 and 4.64 (1 H, d, *J* 6.9, O*H*CHO), 5.19 (2 H, m, 1-H_2), 5.35 (1 H, ddt, *J* 9.1, 11.0, 1.5, 6-H), 5.55 (1 H, dt, *J* 11.0, 7.6, 5-H), 5.66 (1 H, m, 2-H), 6.17 (1 H, dt, *J* 15.7, 1.8, 3′-H) and 6.55 (1 H, dt, *J* 15.7, 4.7, 2′-H); δ_C (75 MHz, $CDCl_3$) major isomer −1.5, 18.0, 21.2, 22.5, 28.2, 33.4, 41.2, 64.8, 66.9, 67.1, 78.6, 80.5, 91.7, 117.7, 118.3, 127.2, 133.2, 137.8, 139.0 and 161.0; *m*/*z* (CI) 410 (M^+ + 1, 100%), 256 (9), 194 (7), 140 (17) and 90 (23).

(3*RS*,7*SR*,5*Z*,2′*E*)-3-Cinnamyloxy-7-(2-trimethylsilylethoxy)-methoxyocta-1,5-diene 49. The alcohol **17** (259 mg, 0.95 mmol) in THF (1 mL) was added to a suspension of sodium hydride (50 mg, 60% dispersion in oil, 1.24 mmol) in THF (2 mL). After the evolution of gas had ceased, the mixture was cooled to 0 °C and tetrabutylammonium iodide (25 mg, catalytic) and (*E*)-cinnamyl bromide (244 mg, 1.24 mmol) in THF (0.5 mL) were added. The mixture was stirred overnight at room temperature then saturated aqueous ammonium chloride was added. The aqueous phase was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave the *title compound* **49** (257 mg, 70%) as a clear, pale yellow oil (Found: M^+ + NH_4 406.2773. $C_{23}H_{40}NSiO_3$ requires *M*, 406.2777); ν_{max}/cm^{-1} 3021, 2951, 2886, 1448, 1374, 1248, 1100, 1026, 966, 926, 836, 744 and 692; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, t, *J* 8.5, CH_2Si), 1.21 (3 H, d, *J* 6.3, 8-H_3), 2.35 (1 H, ddt, *J* 1.4, 14.4, 6.4, 4-H), 2.46 (1 H, ddt, *J* 1.4, 14.7, 6.4, 4-H), 3.51 and 3.68 (each 1 H, dt, *J* 7.1, 9.6, O*H*CHCH_2), 3.78 (1H, q, *J* 6.7, 3-H), 4.00 and 4.19 (each 1 H, ddd, *J* 1.2, 5.8, 12.8, 1′-H), 4.53 (1 H, dq, *J* 8.7, 6.3, 7-H), 4.58 and 4.65 (each 1 H, d, *J* 6.9, O*H*CHO), 5.20 (1 H, d, *J* 16.2, 1-H), 5.22 (1 H, d, *J* 12.1, 1-H), 5.36 (1 H, ddt, *J* 9.2, 11.0, 1.4, 6-H), 5.56 (1 H, dt, *J* 10.6, 7.4, 5-H), 5.70 (1 H, m, 2-H), 6.25 (1 H, dt, *J* 15.9, 5.8, 2′-H), 6.57 (1 H, d, *J* 15.9, 3′-H), 7.22 (1 H, d, *J* 9.3, ArH), 7.29 (2 H, t, *J* 7.6, ArH) and 7.36 (2 H, d, *J* 7.0, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 21.3, 33.5, 64.9, 67.0, 68.8, 80.1, 91.8, 117.4, 126.3, 126.4, 127.5, 128.4, 131.9, 133.2, 136.8 and 138.2; *m*/*z* (CI) 406 (M^+ + 18, 41%), 241 (21), 134 (86), 117 (100) and 90 (33).

(10*RS*,3*RS*,1*E*,5*E*,8*Z*)-3-Hydroxy-1-phenyl-10-(2-trimethyl-silylethoxy)methoxyundeca-1,5,8-triene 50. Butyllithium (1.76 mL, 1.54 M in hexanes, 2.71 mmol) was cooled to −78 °C and added slowly to the ether **49** (525 mg, 1.35 mmol) in THF at −78 °C. The solution was stirred at −78 °C for 3 h then saturated aqueous ammonium chloride was added at −78 °C and the mixture allowed to warm to room temperature. The aqueous phase was extracted with ether and organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (20%), gave the *title compound* **50** (377 mg, 72%) as a clear, colourless oil, 90 : 10 mixture of epimers (^{13}C NMR) (Found: M^+ + NH_4 406.2775. $C_{23}H_{40}NSiO_3$ requires *M*, 406.2777); ν_{max}/cm^{-1} 3434, 3025, 2953, 2893, 1447, 1374, 1249, 1100, 1023, 967, 836, 749 and 693; δ_H (500 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.93 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.4, 11-H_3), 2.30 (2 H, m, 4-H and OH), 2.36 (1 H, ddt, *J* 1.1, 14.1, 7.1, 4-H), 2.77 (1 H, ddt, *J* 1.3, 14.3, 5.8, 7-H), 2.85 (1 H, m, 7-H), 3.49 and 3.70 (each 1 H, dt, *J* 6.2, 9.8, O*H*CHCH_2), 4.28 (1 H, q, *J* 6.0, 3-H), 4.54 (1 H, d, *J* 7.1, O*H*CHO), 4.57 (1 H, m, 10-H), 4.64 (1 H, d, *J* 6.8, O*H*CHO), 5.29 (1 H, ddt, *J* 9.2, 10.7, 1.5, 9-H), 5.47 (1 H, ddt, *J* 0.6, 15.2, 7.3, 6-H), 5.54 (2 H, m, 5-H and 8-H), 6.20 (1 H, dd, *J* 6.0, 15.8, 2-H), 6.56 (1 H, d, *J* 15.8, 1-H), 7.21 (1 H, m, ArH), 7.29 (2 H, m, ArH) and 7.32 (2 H, m, ArH); δ_C (125 MHz, $CDCl_3$) major epimer **50** −1.4, 18.1, 21.4, 30.8, 40.9, 64.9, 66.4, 71.8, 91.5, 126.0, 126.4, 127.5, 128.5, 129.9, 130.0, 131.8, 132.0, 132.1 and 136.8; minor epimer **53** 71.9, 126.1, 130.0 and 131.7; *m*/*z* (CI) 406 (M^+ + 18, 3%), 371 (3), 313 (4), 253 (100), 223 (48) and 90 (48).

(3*RS*,10*RS*,1*E*,5*E*,8*Z*)-3-Benzoyloxy-1-phenyl-10-(2-trimethyl-silylethoxy)methoxyundeca-1,5,8-triene 51. Benzoyl chloride (7 μL, 0.06 mmol), triethylamine (22 μL, 0.15 mmol) and DMAP (2 mg) were added to the alcohol **50** (20 mg, 0.05 mmol) in DCM (0.3 mL) and the solution stirred for 2 h. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave the *title compound* **51** (20 mg, 79%) as a clear, colourless oil (Found: M^+ + NH_4 510.3046. $C_{30}H_{44}NSiO_4$ requires *M*, 510.3039); ν_{max}/cm^{-1} 3027, 2952, 2894, 1791, 1720, 1601, 1451, 1268, 1109, 1025, 836 and 711; δ_H (500 MHz) 0.00 (9 H, s, 3 × $SiCH_3$), 0.89 (2 H, m, CH_2Si), 1.16 (3 H, d, *J* 6.4, 11-H_3), 2.55 (2 H, m, 4-H_2), 2.77 (2 H, m, 7-H_2), 3.46 (1 H, m, O*H*CHCH_2), 3.66 (1 H, dt, *J* 7.0, 9.7, O*H*CHCH_2), 4.50 (1 H, dq, *J* 9.0, 6.4, 10-H), 4.52 and 4.59 (each 1 H, d, *J* 7.1, O*H*CHO), 5.25 (1 H, dd, *J* 9.2, 10.7, 9-H), 5.48 (3 H, m, 5-H, 6-H and 8-H), 5.65 (1 H, q, *J* 7.1, 3-H), 6.22 (1 H dd, *J* 7.1, 16.0, 2-H), 6.67 (1 H, d, *J* 16.0, 1-H), 7.22 (1 H, m, ArH), 7.29 (2 H, m, ArH), 7.36 (2 H, m, ArH), 7.43 (2 H, m,

ArH), 7.51 (1 H, m, ArH) and 8.05 (2 H, m, ArH); δ_C (125 MHz) −1.4, 18.1, 21.4, 30.8, 38.1, 64.9, 66.5, 74.6, 91.7, 125.2, 126.6, 127.2, 127.9, 128.3, 128.5, 129.6, 129.9, 130.5, 131.9, 132.0 132.6, 132.9, 136.3 and 165.7; *m/z* (CI) 510 (M^+ + 18, 1%), 253 (26), 223 (24), 105 (100) and 90 (41).

(1*E*,5*E*,8*Z*)-1-Phenyl-10-(2-trimethylsilylethoxy)methoxyundeca-1,5,8-trien-3-one 52. Dimethyl sulfoxide (0.35 mL, 4.89 mmol) was added to a solution of oxalyl chloride (0.17 mL, 1.96 mmol) in DCM (9 mL) at −78 °C and the mixture stirred for 10 min. A solution of the alcohol **50** (633 mg, 1.63 mmol) in DCM (1 mL) was added and the solution stirred at −78 °C for 1 h. Triethylamine (0.68 mL, 4.98 mmol) was added and the solution stirred for 15 min before being warmed to room temperature. Saturated aqueous ammonium chloride was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (10%), gave the *title compound* **52** (240 mg, 38%) as a clear, colourless oil (Found: M^+ + H, 387.2340. $C_{23}H_{35}SiO_3$ requires *M*, 387.2355); ν_{max}/cm^{-1} 3015, 2953, 2885, 1691, 1665, 1611, 1449, 1249, 1100, 1025, 836, 753 and 693; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 1.22 (3 H, d, *J* 6.3, 11-H_3), 2.87 (2 H, t, *J* 6.2, 7-H_2), 3.37 (2 H, d, *J* 5.8, 4-H_2), 3.50 and 3.69 (each 1 H, dt, *J* 7.0, 9.6, O*H*CHCH$_2$), 4.56 (1 H, m, 10-H), 4.57 and 4.64 (each 1 H, d, *J* 6.9, O*H*CHO), 5.33 (1 H, t, *J* 9.9, 9-H), 5.48–5.72 (3 H, m, 5-H, 6-H and 8-H), 6.74 (1 H, dd, *J* 0.7, 16.1, 1-H), 7.38 (3 H, m, ArH) and 7.56 (3 H, m, ArH and 2-H); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 21.3, 30.7, 44.8, 64.9, 66.5, 91.7, 123.0, 125.4, 128.2, 128.9, 129.5, 130.4, 132.2, 132.5, 134.4, 142.9 and 198.0; *m/z* (CI) 404 (M^+ + 18, 8%), 387 (M^+ + 1, 4), 256 (29), 239 (100), 131 (31) and 90 (29).

Sodium borohydride (32 mg, 0.84 mmol) was added to a solution of the ketone **52** (215 mg, 0.56 mmol) in ethanol (1.5 mL) at 0 °C and the solution allowed to warm to room temperature. After 15 h, dilute aqueous hydrogen chloride was added and the mixture concentrated under reduced pressure. The residue was taken up in water and ethyl acetate. The aqueous phase was extracted with ethyl acetate and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (25%), gave the alcohols **50** and **53** (114 mg, 52%) as a clear, colourless oil, a 50 : 50 mixture (^{13}C NMR) (Found: M^+ + NH_4 406.2782. $C_{23}H_{40}NSiO_3$ requires *M*, 406.2777); ν_{max}/cm^{-1} 3438, 3025, 2952, 2893, 1447, 1249, 1100, 1023, 967, 836, 749 and 694; δ_H (500 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.89 (2 H, m, CH_2Si), 1.20 (3 H, m, 11-H_3), 2.19 (1 H, br. s, OH), 2.27 (1 H, dt, *J* 14.5, 7.5, 4-H), 2.36 (1 H, dt, *J* 13.7, 7.1, 4-H), 2.78 (1 H, dt, *J* 13.9, 6.8, 7-H), 2.86 (1 H, dt, *J* 15.4, 7.5, 7-H), 3.51 and 3.70 (each 1 H, dt, *J* 6.6, 9.8, O*H*CHCH$_2$), 4.28 (1 H, br. m, 3-H), 4.54 and 4.55 (each 0.5 H, d, *J* 6.8, O*H*CHO), 4.54 (1 H, m, 10-H), 4.64 (1 H, d, *J* 6.8, O*H*CHO), 5.29 (1 H, m, 9-H), 5.48 (1 H, m, 6-H), 5.55 (2 H, m, 5-H and 8-H), 6.21 (1 H, dd, *J* 6.2, 16.0, 2-H), 6.57 (1 H, d, *J* 16.0, 1-H), 7.21 (1 H, m, ArH), 7.29 (2 H, m, ArH) and 7.35 (2 H, m, ArH); δ_C (125 MHz, $CDCl_3$) −1.4, 18.1, 21.4, 30.7, 40.9, 64.9, 66.4, 71.8, 71.9, 91.5, 126.0, 126.1, 126.4, 127.6, 128.5, 129.9, 130.0, 130.1, 131.7, 131.7, 132.1, 132.2, 132.2 and 136.8; *m/z* (CI) 406 (M^+ + 18, 3%), 388 (M^+, 2), 342 (12), 253 (100), 223 (48) and 90 (70).

Benzoyl chloride (8 μL, 66 μmol), triethylamine (16 μL, 0.12 mmol) and DMAP (2 mg) were added to a mixture of the alcohols **50** and **53** (217 mg, 44 μmol) in DCM (0.3 mL) and the solution stirred for 2 h. Saturated aqueous ammonium chloride was added and the aqueous phase was extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave a mixture of the esters **51** and **54** (11 mg, 51%) as a clear, colourless oil, a 50 : 50 mixture of epimers (^{13}C NMR) (Found: M^+ + NH_4 510.3043. $C_{30}H_{44}NSiO_4$ requires *M*, 510.3039); ν_{max}/cm^{-1} 3029, 2953, 1720, 1449, 1268, 1106, 1025, 965, 836 and 711; δ_H (500 MHz, $CDCl_3$) −0.01 (9 H, s, 3 × $SiCH_3$), 0.86 (2 H, m, CH_2Si), 1.16 (1.5 H, d, *J* 6.4, 11-H_3), 1.16 (1.5 H, d, *J* 6.4, 11-H_3), 2.55 (2 H, m, 4-H_2), 2.78 (2 H, t, *J* 6.0, 7-H_2), 3.47 and 3.66 (each 1 H, m, O*H*CHCH$_2$), 4.49 (1 H, m, 10-H), 4.52 and 4.59 (each 1 H, d, *J* 6.8, O*H*CHO), 5.25 (1 H, m, 9-H), 5.41–5.57 (3 H, m, 5-H, 6-H and 8-H), 5.65 (1 H, q, *J* 6.8, 3-H), 6.23 (1 H dd, *J* 7.1, 16.0, 2-H), 6.67 (1 H, d, *J* 16.0, 1-H), 7.22 (1 H, m, ArH), 7.29 (2 H, m, ArH), 7.36 (2 H, m, ArH), 7.43 (2 H, m, ArH), 7.54 (1 H, m, ArH) and 8.05 (2 H, m, ArH); δ_C (125 MHz, $CDCl_3$) −1.4, 18.1, 21.4, 30.8, 38.1, 64.9, 66.5, 74.7, 91.7, 125.2, 126.6, 127.2, 127.9, 128.3, 128.5, 129.6, 129.9(2), 130.5, 131.8, 131.9, 132.0, 132.6, 132.9, 136.3 and 165.7; *m/z* (CI) 510 (M^+ + 18, 7%), 253 (92), 223 (53), 105 (37) and 90 (100).

(3*RS*,7*SR*,5*Z*)-3-[(2*E*)-Penta-2,4-dienyloxy]-7-(2-trimethylsilylethoxy)methoxyocta-1,5-diene 56. The alcohol **17** (543 mg, 2.00 mmol) in THF (1 mL) was added to a stirred suspension of sodium hydride (104 mg, 60% dispersion in oil, 2.60 mmol) in THF (6 mL). After the evolution of gas had ceased, tetrabutylammonium iodide (100 mg) and (2*E*)-1-bromopenta-2,4-diene (587 mg, 3.99 mmol) in THF (1 mL) were added. The mixture was stirred overnight at room temperature and saturated aqueous ammonium chloride was added. The aqueous phase was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (10%), gave the *title compound* **56** (514 mg, 76%) as a clear, pale yellow oil (Found: M^+ + NH_4 356.2624. $C_{19}H_{38}NSiO_3$ requires *M*, 356.2621); ν_{max}/cm^{-1} 3085, 2953, 2882, 1656, 1605, 1422, 1374, 1249, 1102, 1026, 923, 836 and 693; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.5, 8-H_3), 2.37 (2 H, m, 4-H_2), 3.50 (1 H, dt, *J* 7.1, 9.6, O*H*CHCH$_2$), 3.70 (2 H, m, 3-H and O*H*CHCH$_2$), 3.86 and 4.06 (each 1 H, dd, *J* 6.2, 13.1, 1′-H), 4.51 (1 H, dq, *J* 9.3, 6.5, 7-H), 4.57 and 4.64 (each 1 H, d, *J* 6.8, O*H*CHO), 5.04–5.22 (4 H, m, 1-H_2 and 5′-H_2), 5.35 (1 H, ddt, *J* 9.3, 11.0, 1.5, 6-H), 5.54 (1 H, dt, *J* 11.0, 7.5, 5-H), 5.59–5.79 (2 H, m, 2-H and 2′-H), 6.21 (1 H, m, 3′-H) and 6.32 (1 H, dt, *J* 16.5, 10.2, 4′-H); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 21.3, 33.5, 64.9, 67.0, 68.2, 80.1, 91.8, 117.2, 117.4, 127.5, 130.3, 132.7, 133.2, 136.4 and 138.2; *m/z* (CI) 356 (M^+ + 18, 100%), 339 (M^+ + 1, 8), 309 (9), 191 (87), 123 (38), 90 (36).

(5*RS*,12*RS*,3*E*,7*E*,10*Z*)-5-Hydroxy-10-(2-trimethylsilylethoxy)-methoxytrideca-1,3,7,10-tetraene 57. Butyllithium (3.10 mL,

1.15 M in hexanes, 3.57 mmol) was cooled to −78 °C and added to the ether **56** (514 mg, 1.78 mmol) in THF (3 mL) at −78 °C. The solution was stirred for 3 h before saturated aqueous ammonium chloride was added. After warming to room temperature, the aqueous phase was extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (20%), gave the *title compound* **57** (360 mg, 70%) as a clear, colourless oil (Found: $M^+ + NH_4$ 356.2637. $C_{19}H_{38}NSiO_3$ requires *M*, 356.2621); ν_{max}/cm^{-1} 3437, 2953, 2894, 1654, 1605, 1374, 1249, 1100, 1023, 836 and 693; δ_H (500 MHz, $CDCl_3$) 0.01 (9 H, s, 3 × $SiCH_3$), 0.90 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.4, 13-H_3), 2.15 (1 H, br. s, OH), 2.19 (1 H, dt, *J* 14.5, 7.5, 6-H), 2.27 (1 H, dt, *J* 13.0, 5.3, 6-H), 2.76 (1 H, dt, *J* 15.8, 7.1, 9-H), 2.83 (1 H, dt, *J* 15.6, 7.3, 9-H), 3.48 (1 H, dt, *J* 6.2, 10.3, O*H*CHCH$_2$), 3.69 (1 H, dt, *J* 6.6, 10.0, O*H*CHCH$_2$), 4.15 (1 H, q, *J* 6.0, 5-H), 4.53 (1 H, m, 12-H), 4.54 and 4.62 (each 1 H, d, *J* 7.1, O*H*CHO), 5.05 (1 H, dd, *J* 1.4, 10.0, 1-H), 5.17 (1 H, dd, *J* 1.4, 16.4, 1-H), 5.28 (1 H, dd, *J* 9.2, 10.7, 11-H), 5.42 (1 H, dt, *J* 14.1, 6.8, 8-H), 5.53 (2 H, m, 7-H and 10-H), 5.69 (1 H, dd, *J* 6.0, 15.2, 4-H), 6.21 (1 H, dd, *J* 10.4, 15.2, 3-H) and 6.30 (1 H, dt, *J* 16.4, 10.4, 2-H); δ_C (125 MHz, $CDCl_3$) −1.4, 18.1, 21.4, 30.7, 40.7, 64.9, 66.4, 71.2, 91.5, 117.3, 126.0, 129.9, 130.8, 132.0, 132.1, 135.8 and 136.3; *m*/*z* (CI) 356 (M^+ + 18, 2%), 203 (60), 173 (67), 122 (68) and 90 (100).

(3*SR*,7*RS*,5*Z*)-3-(3,3-Diphenylprop-2-enyloxy)-7-(2-trimethylsilylethoxy)methoxyocta-1,5-diene 58. The alcohol **17** (959 mg, 3.53 mmol) in THF (2 mL) was added slowly to a suspension of sodium hydride (169 mg, 60% dispersion in oil, 4.23 mmol) in THF (6 mL). After 30 min, tetrabutylammonium iodide (50 mg) and 1-bromo-3,3-diphenylprop-2-ene (1.66 g, 6.08 mmol) in THF (2 mL) were added and the mixture stirred overnight. Water was added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (2%), gave the *title compound* **58** (1.36 g, 83%) as a clear, colourless oil (Found: $M^+ + NH_4$ 482.3103. $C_{29}H_{44}NSiO_3$ requires *M*, 482.3090); ν_{max}/cm^{-1} 3022, 2952, 2889, 1669, 1444, 1374, 1248, 1099, 1026, 924, 836, 761 and 699; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.89 (2 H, m, CH_2Si), 1.20 (3 H, d, *J* 6.6, 8-H_3), 2.35 (2 H, m, 4-H_2), 3.50 (1 H, dt, *J* 7.1, 9.6, O*H*CHCH$_2$), 3.65 (1 H, q, *J* 6.6, 3-H), 3.68 (1 H, dt, *J* 7.6, 9.8, O*H*CHCH$_2$), 3.89 and 4.08 (each 1 H, dd, *J* 6.3, 12.2, 1′-H), 4.50 (1 H, dq, *J* 9.1, 6.6, 7-H), 4.57 and 4.66 (each 1 H, d, *J* 6.9, O*H*CHO), 5.07 (2 H, m, 1-H_2), 5.37 (1 H, ddt, *J* 9.1, 11.0, 1.5, 6-H), 5.55 (1 H, dt, *J* 11.0, 7.4, 5-H), 5.62 (1 H, ddd, *J* 7.7, 10.5, 17.2, 2-H), 6.19 (1 H, t, *J* 6.3, 2′-H) and 7.12–7.38 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.0, 21.3, 33.6, 64.9, 66.0, 67.0, 80.2, 91.8, 117.2, 125.7, 127.3, 127.5, 128.0(2), 128.3, 128.5, 129.7, 133.2, 138.2, 139.2, 141.9 and 144.4; *m*/*z* (CI) 482 (M^+ + 18, 42%), 226 (16), 209 (48) and 193 (100).

(5*E*,8*Z*)-3-*tert*-Butyldiphenylsilyloxy-1,1-diphenyl-10-(2-trimethylsilylethoxy)methoxyundeca-1.5,8-triene 60. Butyllithium (14.7 mL, 1.50 M in hexanes, 22.1 mmol) at −78 °C was added to the ether **58** (2.04 g, 4.41 mmol) in THF (10 mL) at −78 °C and the resulting solution stirred for 2.5 h. Saturated aqueous ammonium chloride was added and the mixture allowed to warm to room temperature. The aqueous phase was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dissolved in DMF (3 mL) and imidazole (427 mg, 6.26 mmol) and *tert*-butyldiphenylchlorosilane (0.98 mL, 3.76 mmol) were added. After 5 h, the mixture was diluted with ether and water and the aqueous phase was extracted with ether. The organic extracts were washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (2%), gave the *title compound* **60** (1.09 g, 35%) as a clear, colourless oil, a 2 : 1 mixture of epimers (^{1}H NMR) (Found: $M^+ + NH_4$ 720.4250. $C_{45}H_{62}NSi_2O_3$ requires *M*, 720.4268); ν_{max}/cm^{-1} 3070, 3017, 2953, 2857, 1427, 1249, 1106, 1055, 1027, 859, 835, 763 and 701; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 1.01 [9 H, s, $SiC(CH_3)_3$], 1.20 (3 H, d, *J* 6.0, 11-H_3), 2.52 (2 H, m, 4-H_2), 2.63 (1.33 H, t, *J* 6.6, 7-H_2), 2.74 (0.67 H, m, 7-H_2), 3.51 and 3.69 (each 1 H, m, O*H*CHCH$_2$), 4.32 (1 H, m, 3-H), 4.52 (1 H, m, 10-H), 4.57 and 4.63 (each 1 H, d, *J* 6.9, O*H*CHO), 5.16–5.56 (4 H, m, 5-H, 6-H, 8-H and 9-H), 6.12 (1 H, d, *J* 9.3, 2-H), 6.66 (2 H, m, ArH) and 7.03–7.60 (18 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.5, 18.1, 19.7, 21.4, 25.9, 26.9, 36.4, 64.9, 66.8, 70.7, 91.8, 126.0, 126.8, 127.1, 127.2, 127.3, 127.8, 127.9, 129.2, 129.2, 129.3, 129.5, 130.4, 131.4, 131.6, 133.8, 134.3, 135.8, 135.9, 139.1, 141.0 and 142.0; *m*/*z* (CI) 720 (M^+ + 18, 4%), 329 (29) and 90 (100).

(3*RS*,10*RS*,5*E*,8*Z*)-1,2-Epoxy-3-hydroxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundeca-5,8-diene 61. *tert*-Butylhydroperoxide (2.0 mL, 11.1 mmol) was added to the alcohol **50** (614 mg, 1.58 mmol) and vanadyl acetylacetonate (17 mg, 4 mol%) in benzene (15 mL). After 10 min, the mixture was added to saturated aqueous sodium thiosulfate. The aqueous phase was extracted with ether and the organic extracts were washed with saturated aqueous sodium thiosulfate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (30%), gave the *title compound* **61** (482 mg, 76%) as a clear, colourless oil, a *ca.* 67 : 33 mixture of diastereoisomers (^{1}H NMR) (Found: $M^+ + NH_4$ 422.2725. $C_{23}H_{40}NSiO_4$ requires *M*, 422.2726); ν_{max}/cm^{-1} 3436, 3009, 2953, 2927, 1439, 1374, 1249, 1100, 1024, 839, 836, 751 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.84 (1 H, m, CH_2Si), 0.92 (1 H, m, CH_2Si), 1.21 (2 H, d, *J* 6.5, 11-H_3), 1.22 (1 H, d, *J* 6.5, 11-H_3), 2.34 (3 H, m, OH and 4-H_2), 2.81 (2 H, m, 7-H_2), 3.04 (1 H, m, 2-H), 3.49 and 3.69 (each 1 H, m, O*H*CHCH$_2$), 3.84 (0.5 H, d, *J* 1.9, 1-H), 3.87 (1 H, q, *J* 4.2, 3-H), 3.92 (0.5 H, d, *J* 2.1, 1-H), 4.54 (2 H, m, 10-H and O*H*CHO), 4.63 (1 H, m, O*H*CHO), 5.30 (1 H, m, 9-H), 5.52 (3 H, m, 5-H, 6-H and 8-H) and 7.28 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) major diastereoisomer −1.5, 18.1, 21.3, 30.6, 36.8, 55.2, 64.9, 66.5, 68.7, 91.6, 125.5, 125.6, 128.1, 128.4, 129.7, 131.9, 132.1 and 136.8; minor diastereoisomer 22.5, 37.9, 56.1, 64.3, 68.8, 70.1, 125.4 and 136.7; *m*/*z* (CI) 422 (M^+ + 18, 1%), 329 (2), 274 (2), 239 (22), 137 (22), 107 (46), 91 (55), 90 (100) and 73 (68). The second fraction was (3*RS*,8*Z*,10*RS*)-1,2-epoxy-5,6-epoxy-3-hydroxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxy-undec-8-ene (146 mg, 22%) as

a clear, colourless oil, a mixture of diastereoisomers (Found: $M^+ + NH_4$ 438.2672. $C_{23}H_{40}NSiO_5$ requires *M*, 438.2676); ν_{max}/cm^{-1} 3425, 2953, 2890, 1462, 1373, 1249, 1099, 1054, 1023, 836, 752 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.85–0.95 (2 H, m, CH_2Si), 1.21 (3 H, d, *J* 6.5, 11-H_3), 1.90 (2 H, m, 4-H_2), 2.35 (2 H, m, 7-H_2), 2.63 (1 H, m, OH), 2.80 and 2.98 (each 1 H, m), 3.05 (0.5 H, dd, *J* 2.2, 3.6, 2-H), 3.08 (0.5 H, dd, *J* 2.1, 3.3, 2-H), 3.48 (1 H, m, O*H*CHCH$_2$), 3.68 (1 H, dt, *J* 7.1, 9.9, O*H*CHCH$_2$), 3.92 (0.5 H, d, *J* 2.1, 1-H), 3.94 (0.5 H, d, *J* 2.1, 1-H), 4.04 (1 H, m, 3-H), 4.47 (1 H, dq, *J* 8.7, 6.5, 10-H), 4.56 and 4.63 (each 1 H, d *J* 7.1, O*H*CHO), 5.39 (1 H, dd, *J* 8.7, 10.9, 9-H), 5.53 (1 H, m, 8-H) and 7.28 (5 H, m, ArH); *m*/*z* (CI) 438 (M^+ + 18, 1%), 273 (5), 255 (8), 225 (7), 153 (38), 91 (56), 90 (100) and 73 (52).

(3*RS*,5*E*,8*Z*,10*RS*)-3-*tert*-Butyldimethylsilyloxy-1,2-epoxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundeca-5,8-diene 62. Imidazole (532 mg, 7.81 mmol) and *tert*-butyldimethylsilyl chloride (674 mg, 4.46 mmol) were added to the alcohol **61** (901 mg, 2.23 mmol) in DMF (8 mL) and the solution stirred for 15 h. Ether and water were added and the aqueous phase extracted with ether. The organic extracts were washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave the *title compound* **62** (895 mg, 77%) as a clear, colourless oil, a 67 : 33 mixture of diastereoisomers (^{1}H NMR) (Found: $M^+ + NH_4$ 536.3594. $C_{29}H_{54}NSi_2O_4$ requires *M*, 536.3591); ν_{max}/cm^{-1} 3010, 2954, 2857, 1463, 1371, 1250, 1101, 1026, 836, 778 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.06 (4 H, s, 2 × $SiCH_3$), 0.08 and 0.14 (each 1 H, s, $SiCH_3$), 0.87 [6 H, s, $SiC(CH_3)_3$], 0.87 (2 H, m, $SiCH_2$), 0.91 [3 H, s, $SiC(CH_3)_3$], 1.21 (3 H, d, *J* 6.3, 11-H_3), 2.30 (2 H, m, 4-H_2), 2.78 (2 H, m, 7-H_2), 2.92 (0.7 H, dd, *J* 2.1, 4.3, 2-H), 2.97 (0.3 H, dd, *J* 2.1, 6.3, 2-H), 3.50 (1 H, m, O*H*CHCH$_2$), 3.70 (2.3 H, m, 3-H, 1-H, O*H*CHCH$_2$), 3.79 (0.7 H, d, *J* 2.1, 1-H), 4.52 (1 H, m, 10-H), 4.56 (1 H, d *J* 6.9, O*H*CHO), 4.61 (0.7 H, d, *J* 6.9, O*H*CHO), 4.62 (0.3 H, d, *J* 6.9, O*H*CHO), 5.28 (1 H, dd, *J* 9.0, 10.8, 9-H), 5.46 (3 H, m, 5-H, 6-H and 8-H) and 7.27 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) major diastereoisomer −4.8, −4.5, −1.5, 18.1, 21.4, 25.7, 30.7, 38.4, 55.9, 56.6, 64.7, 64.9, 66.6, 71.0, 91.7, 125.5, 126.2, 127.9, 128.3, 130.0, 131.0, 131.8 and 137.4; minor diastereoisomer 18.1, 25.8, 65.8, 73.8, 128.0, 129.8 and 137.0; *m*/*z* (CI) 536 (M^+ + 18, 2%), 401 (1), 263 (30), 239 (29), 221 (32), 107 (28), 91 (29), 90 (100) and 73 (76).

(3*RS*,10*RS*,5*E*,8*Z*)-3-*tert*-Butyldiphenylsilyloxy-1,2-epoxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundeca-5,8-diene 63. Imidazole (681 mg, 10.0 mmol) and *tert*-butyldiphenylchlorosilane (1.8 mL, 6.8 mmol) were added to the alcohol **61** (1.62 g, 4.0 mmol) in DCM (7 mL) at room temperature. The solution was stirred for 18 h and water was added. The aqueous phase was extracted with DCM and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (3%), gave the *title compound* **63** (2.38 g, 93%) as a clear, colourless oil, a 67 : 33 mixture of two diastereoisomers (^{1}H NMR) (Found: $M^+ + NH_4$ 660.3903. $C_{39}H_{58}NSi_2O_4$ required *M*, 660.3904); ν_{max}/cm^{-1} 3013, 2953, 2859, 1467, 1428, 1368, 1249, 1106, 1026, 834, 743 and 701; δ_H (300 MHz, $CDCl_3$) 0.00 (3 H, s, 3 × $SiCH_3$), 0.01 (6 H, s, 3 × $SiCH_3$), 0.91 (2 H, m, CH_2Si), 1.04 [6 H, s, $SiC(CH_3)_3$], 1.10 [3 H, s, $SiC(CH_3)_3$], 1.19 (1 H, d, *J* 6.5, 11-H_3), 1.21 (2 H, d, *J* 6.3, 11-H_3), 2.13–2.38 (2 H, m, 4-H_2), 2.69 (0.67 H, m, 7-H_2), 2.78 (1.33 H, m, 7-H_2), 3.01 (0.67 H, dd, *J* 2.1, 5.8, 2-H), 3.08 (0.33 H, dd, *J* 2.1, 6.2, 2-H), 3.45 (0.67 H, d, *J* 2.1, 1-H), 3.51 (1 H, dt, *J* 8.2, 10.7, O*H*CHCH$_2$), 3.66 (2.33 H, m, O*H*CHCH$_2$, 3-H and 1-H), 4.42–4.59 (1 H, m, 10-H), 4.58 and 4.64 (each 1 H, d, *J* 7.0, O*H*CHO), 5.20–5.56 (4 H, m, 5-H, 6-H, 8-H and 9-H) and 7.03–7.76 (15 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.4, 18.1, 19.3, 19.4, 21.4, 26.9, 27.0, 30.6, 30.8, 38.2, 38.2, 56.5, 57.3, 64.2, 64.9, 65.6, 66.5, 66.6, 72.6, 74.2, 91.7, 125.5, 125.7(2), 127.5(2), 127.6, 127.9, 128.0, 128.2, 128.3, 129.6, 129.8(2), 130.1, 131.3, 131.7, 131.8, 133.3, 133.7, 134.1, 135.8, 135.9(2), 137.0 and 137.1; *m*/*z* (CI) 660 (M^+ + 18, 51%), 495 (24), 417 (64), 405 (51), 196 (51) and 90 (100).

(3*RS*,10*RS*)-3-*tert*-Butyldimethylsilyloxy-1,2-epoxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundecane 64. Sodium acetate (2.83 g, 34.6 mmol) in water (20 mL) was added dropwise over 2 h to the diene **62** (895 mg, 1.73 mmol) and toluene 4-sulfonylhydrazine (3.86 g, 20.7 mmol) in DME (65 mL) heated under reflux. The solution was heated under reflux for a further 2 h and then allowed to cool to room temperature. The aqueous phase was extracted with ether and the organic extracts washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether–petrol (5%), gave the *title compound* **64** (785 mg, 87%) as a clear, colourless oil, a 67 : 33 mixture of diastereoisomers (^{1}H NMR) (Found: $M^+ + NH_4$ 540.3915. $C_{29}H_{58}NSi_2O_4$ requires *M*, 540.3904); ν_{max}/cm^{-1} 2930, 2857, 1464, 1376, 1250, 1102, 1055, 1032, 836, 777, 753 and 697; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.06 and 0.07 (each 2 H, s, $SiCH_3$), 0.08 and 0.15 (each 1 H, s, $SiCH_3$), 0.87 [6 H, s, $SiC(CH_3)_3$], 0.87 (2 H, m, CH_2Si), 0.91 [3 H, s, $SiC(CH_3)_3$], 1.13 (3 H, d, *J* 6.2, 11-H_3), 1.20–1.58 (12 H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2, 8-H_2 and 9-H_2), 2.89 (0.7 H, dd, *J* 2.1, 4.4, 2-H), 2.96 (0.3 H, dd, *J* 2.2, 6.5, 2-H), 3.45 (1 H, m, O*H*CHCH$_2$), 3.65 (2.3 H, m, O*H*CHCH$_2$, 1-H and 3-H), 3.79 (0.7 H, d, *J* 1.8, 1-H), 4.58 (1 H, m, 10-H), 4.64 and 4.71 (each 1 H, d, *J* 7.1, O*H*CHO) and 7.28 (5 H, m, ArH); *m*/*z* (CI) 540 (M^+ + 18, 2%), 317 (4), 285 (13), 215 (14), 177 (13), 90 (100) and 73 (39).

(3*RS*,10*RS*)-3-*tert*-Butyldiphenylsilyloxy-1,2-epoxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundecane 65. Sodium acetate (4.56 g, 33.0 mmol) in water (15 mL) was added dropwise over 2 h to the diene **63** (1.06 g, 1.65 mmol) and 4-sulfonylhydrazine (3.69 g, 19.8 mmol) in DME (40 mL) heated under reflux. The solution was heated under reflux for a further 2.5 h then allowed to cool to room temperature. The aqueous phase was extracted with ether and the organic extracts were washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (3%), gave the *title compound* **65** (904 mg, 85%) as a clear, colourless oil, a 67 : 33 mixture of two diastereoisomers (^{1}H NMR) (Found: $M^+ + NH_4$ 664.4219. $C_{39}H_{62}NSi_2O_4$ requires *M*, 664.4217); ν_{max}/cm^{-1} 3048, 2932, 2858, 1465, 1428, 1248, 1107, 1055, 1031, 836, 742 and 702; δ_H (300 MHz, $CDCl_3$)

0.00 (3 H, s, 3 × $SiCH_3$), 0.01 (6 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 1.02 [6 H, s, $SiC(CH_3)_3$], 1.11 [3 H, s, $SiC(CH_3)_3$], 1.05–1.62 (12 H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2, 8-H_2 and 9-H_2), 1.14 (3 H, d, *J* 6.3, 11-H_3), 2.97 (0.67 H, dd, *J* 1.9, 5.9, 2-H), 3.05 (0.33 H, dd, *J* 2.1, 6.3, 2-H), 3.42 (0.67 H, d, *J* 1.9, 1-H), 3.62 (4.33 H, m, O*C*H_2CH_2, 10-H, 3-H and 1-H), 4.64 (0.33 H, d *J* 6.5, OHC*H*O), 4.66 (0.67 H, d, *J* 6.5, OHC*H*O), 4.69 (0.33 H, d, *J* 6.5, O*H*CHO), 4.71 (0.67 H, d, *J* 6.5, O*H*CHO) and 7.05–7.75 (15 H, m, ArH); *m*/*z* (CI) 664 (M^+ + 18, 78%), 409 (42), 256 (26) and 90 (100).

(3*RS*,10*RS*,1*E*,5*E*,8*Z*)-3-*tert*-Butyldiphenylsilyloxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundeca-1,5,8-triene 66. Imidazole (99 mg, 1.45 mmol) and *tert*-butyldiphenylchlorosilane (189 μL, 0.73 mmol) were added to the alcohol **50** (141 mg, 0.36 mmol) in DCM (200 μL) at room temperature. The mixture was stirred for 2.5 h then diluted with DCM and water. The aqueous phase was extracted with DCM and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (5%), gave the *title compound* **66** (189 mg, 82%) as a clear, colourless oil (Found: M^+ + NH_4 644.3935. $C_{39}H_{58}NSi_2O_3$ requires *M*, 644.3955); ν_{max}/cm^{-1} 3025, 2955, 2892, 1654, 1591, 1471, 1428, 1248, 1108, 1054, 1026, 966, 859, 835, 741 and 702; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.91 (2 H, t, *J* 8.4, CH_2Si), 1.08 [9 H, s, $SiC(CH_3)_3$], 1.19 (3 H, d, *J* 6.6, 11-H_3), 2.25 (2 H, m, 4-H_2), 2.74 (2 H, m, 7-H_2), 3.50 (1 H, dt, *J* 7.3, 9.6, O*H*CHCH_2), 3.69 (1 H, dt, *J* 7.6, 9.5, O*H*CHCH_2), 4.31 (1 H, q, *J* 6.2, 3-H), 4.51 (1 H, dq, *J* 8.4, 6.6, 10-H), 4.54 and 4.61 (each 1 H, d, *J* 6.9, O*H*CHO), 5.22–5.50 (4 H, m, 5-H, 6-H, 8-H and 9-H), 6.10 (1 H, dd, *J* 6.3, 15.9, 2-H), 6.22 (1 H, d, *J* 15.9, 1-H), 7.17–7.44 (11 H, m, ArH) and 7.67 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.4, 18.1, 19.3, 21.4, 27.0, 30.8, 41.4, 64.9, 66.6, 74.3, 91.7, 126.4, 126.5, 127.2, 127.3, 127.4, 128.3, 129.4, 129.5, 129.8, 130.2, 130.7, 131.6, 132.1, 134.1, 134.3, 135.9, 136.0 and 137.1; *m*/*z* (CI) 644 (M^+ + 18, 2%), 371 (5), 274 (10), 253 (13), 196 (20), 90 (100) and 58 (63).

(3*RS*,10*RS*)-3-*tert*-Butyldiphenylsilyloxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundecane 67. Sodium acetate (791 mg, 5.81 mmol) in water (2 mL) was added dropwise over 2 h to the triene **66** (182 mg, 0.29 mmol) and toluene 4-sulfonylhydrazine (650 mg, 3.49 mmol) in DME (8 mL) heated under reflux. The solution was heated under reflux for a further 2.5 h and then allowed to cool to room temperature. The aqueous phase was extracted with ether and the organic extracts washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (5%), gave the *title compound* **67** (125 mg, 68%) as a clear, colourless oil (Found: M^+ + NH_4 650.4416. $C_{39}H_{64}NSi_2O_3$ requires *M*, 650.4425); ν_{max}/cm^{-1} 3069, 3026, 2931, 2857, 1428, 1459, 1375, 1249, 1107, 1056, 858, 835 and 702; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 1.06 [9 H, s, $SiC(CH_3)_3$], 1.13 (3 H, d, *J* 6.2, 11-H_3), 1.04–1.52 (12 H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2, 8-H_2 and 9-H_2), 1.72 (2 H, m, 2-H_2), 2.55 (2 H, m, 1-H_2), 3.63 (3 H, m, 10-H, O*C*H_2CH_2), 3.78 (1 H, quin., *J* 5.5, 3-H), 4.65 and 4.71 (each 1 H, d, *J* 7.0, O*H*CHO), and 6.99–7.74 (15 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −1.4, 18.1, 19.4, 20.2, 24.8, 25.5, 27.1, 29.6, 31.3, 36.3, 37.0, 38.1, 64.8, 72.8, 93.0, 125.5, 127.4(2), 128.2(2), 129.4, 134.6(2), 135.9 and 142.6; *m*/*z* (CI) 650 (M^+ + 18, 27%), 447 (100) and 90 (86).

(3*RS*,10*RS*)-3-*tert*-Butyldiphenylsilyloxy-1-phenyl-10-(2-trimethylsilylethoxy)methoxyundec-1-ene 68. The epoxide **65** (904 mg, 1.40 mmol) in THF (2 mL) was added to samarium diiodide in THF (28 mL, 0.1 M in THF, 2.8 mmol) and the mixture stirred at room temperature for 3 h. Dilute aqueous hydrogen chloride was added and the aqueous phase extracted with ether. The organic extracts were washed with saturated aqueous sodium hydrogen carbonate, water, saturated aqueous sodium thiosulfate, water, then brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (3%), gave the *title compound* **68** (493 mg, 56%) as a clear, colourless oil, a 75 : 25 mixture of (*E*)- and (*Z*)-isomers (^1H NMR) (Found: M^+ + NH_4 648.4260. $C_{39}H_{62}NSi_2O_3$ requires *M*, 648.4268); ν_{max}/cm^{-1} 3028, 2931, 2858, 1466, 1428, 1249, 1108, 1055, 836, 742 and 701; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.92 (2 H, m, CH_2Si), 0.98–1.62 (12 H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2, 8-H_2 and 9-H_2), 1.01 [2.25 H, s, $SiC(CH_3)_3$], 1.07 [6.75 H, s, $SiC(CH_3)_3$], 1.12 (2.25 H, d, *J* 6.1, 11-H_3), 1.13 (0.75 H, d, *J* 6.0, 11-H_3), 3.63 (3 H, m, O*C*H_2CH_2 and 10-H), 4.27 (1 H, q, *J* 5.9, 3-H), 4.64 (0.75 H, d, *J* 7.1, O*H*CHO), 4.65 (0.25 H, d, *J* 7.0, O*H*CHO), 4.71 (0.75 H, d, *J* 7.0, O*H*CHO), 4.72 (0.25 H, d, *J* 7.1, O*H*CHO), 5.71 (0.25 H, dd, *J* 9.2, 11.7, 2-H), 6.05–6.29 (1.75 H, m, 2-H and 1-H) and 6.80–7.72 (15 H, m, ArH); *m*/*z* (CI) 648 (M^+ + 18, 12%), 392 (16), 375 (13), 274 (68), 257 (86) and 90 (100).

Methyl (4*RS*,11*RS*,2*E*)-4-*tert*-butyldiphenylsilyloxy-11-(2-trimethylsilylethoxy)methoxydodec-2-enoate 69. Oxygen was bubbled through a solution of alkene **68** (697 mg, 1.11 mmol) in DCM (40 mL) at −78 °C for 10 min followed by ozonolysed oxygen for 1.5 h. After this time, the solution had turned pale blue. Oxygen was bubbled through the solution for a further 10 min and then dimethyl sulfide (0.81 mL, 11.1 mmol) was added. The mixture was allowed to warm to room temperature and concentrated under reduced pressure to leave the corresponding undecanal (183 mg, 69%) as a clear, colourless oil. This was dissolved in DCM (5 mL) and methoxycarbonylmethylene triphenyl phosphorane (1.11 g, 3.3 mmol) was added. After 15 h, water was added and the aqueous phase extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with ethyl acetate–petrol (1%) gave the *title compound* **69** (411 mg, 61%) as a clear colourless oil (Found: M^+ + NH_4 630.3998. $C_{35}H_{60}NSi_2O_5$ requires *M*, 630.4010); ν_{max}/cm^{-1} 3048, 2932, 2859, 1727, 1660, 1431, 1273, 1166, 1107, 1054, 859, 835 and 704; δ_H (300 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.90 (2 H, m, CH_2Si), 1.04 [9 H, s, $SiC(CH_3)_3$], 1.12 (3 H, d, *J* 6.3, 12-H_3), 1.10–1.55 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 3.62 (3 H, m, O*C*H_2CH_2 and 11-H), 3.70 (3 H, s, OCH_3), 4.32 (1 H, dq, *J* 1.2, 5.0, 4-H), 4.68 and 4.70 (each 1 H, d, *J* 6.9, O*H*CHO), 5.92 (1 H, dd, *J* 1.5, 15.4, 2-H), 6.85 (1 H, dd, *J* 5.2, 15.4, 3-H), 7.36 (6 H, m, ArH) and 7.62 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$)

−1.5, 18.0, 19.3, 20.2, 23.9, 25.5, 27.0, 29.4(2), 36.6, 36.9, 51.4, 64.7, 72.3, 72.8, 92.9, 119.6, 127.5(2), 129.6, 129.7, 133.4, 133.9, 135.7, 150.5 and 167.0; *m*/*z* (CI) 630 (M^+ + 18, 2%), 274 (35), 196 (32) and 90 (100).

Methyl (2*E*,4*RS*,11*RS*)-4-*tert*-butyldiphenylsilyloxy-11-hydroxydodec-2-enoate 70. Butanethiol (0.50 mL, 4.7 mmol) was added to a vigorously stirred suspension of potassium carbonate (740 mg, 5.4 mmol), magnesium bromide diethyl etherate (1.21 g, 4.7 mmol) and the SEM-ether **69** (411 mg, 0.67 mmol) in ether (6 mL) at room temperature and the resulting mixture stirred for 1.5 h. Dilute aqueous sodium bicarbonate and water were added and the aqueous phase extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (20%), gave the *title compound* **70** (254 mg, 79%) as a clear, colourless oil (Found: $M^+ + NH_4$, 500.3192. $C_{29}H_{46}SiNO_4$ requires *M*, 500.3196); ν_{max}/cm^{-1} 3347, 2931, 2857, 1725, 1659, 1463, 1430, 1276, 1166, 1108 and 703; δ_H (300 MHz, $CDCl_3$) 1.08 [9 H, s, SiC$(CH_3)_3$], 1.17 (3 H, d, *J* 6.2, 12-H_3), 1.00–1.50 (12 H, m, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 3.72 (3 H, s, OCH_3), 3.74 (1 H, m, 11-H), 4.35 (1 H, q, *J* 5.1, 4-H), 5.94 (1 H, dd, *J* 1.4, 15.4, 2-H), 6.87 (1 H, dd, *J* 5.8, 15.4, 3-H), 7.31–7.46 (6 H, m, ArH) and 7.58–7.69 (4 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 19.3, 23.4, 23.8, 25.5, 27.0, 29.3(2), 36.6, 39.2, 51.4, 68.0, 72.3, 119.6, 127.5, 129.6, 129.7, 133.4, 133.9, 135.7, 150.5 and 167.0; *m*/*z* (CI) 500 (M^+ + 18, 18%), 483 (M^+ + 1, 20), 274 (80), 244 (85), 227 (100) and 196 (80).

Lithium hydroxide monohydrate (111 mg, 2.63 mmol) was added to the methyl ester **70** (254 mg, 0.53 mmol) in methanol–water (4 mL, 3 : 1) and the solution stirred for 15 h. After concentration under reduced pressure, the residue was taken up in water and ethyl acetate. The aqueous phase was extracted with ethyl acetate and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to leave the seco-acid (204 mg, 82%) that was used without further purification.

Triethylamine (18 μL, 13 μmol) and 2,6-dichlorobenzoyl chloride (17 μL, 12 μmol) were added to the seco-acid (55 mg, 12 μmol) in THF (1 mL) and the solution stirred for 6 h. The mixture was filtered and diluted with toluene (50 mL). This solution was then added dropwise over 3.5 h to a solution of DMAP (85 mg, 0.69 mmol) in toluene (10 mL) heated under reflux. The solution was then allowed to cool and water and ether were added. The aqueous phase was extracted with ether and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (1%), gave the macrolide **39**[2h] (28 mg, 52%) as a clear, colourless oil (Found: M^+, 451.2658. $C_{28}H_{38}SiO_3$ requires *M*, 451.2668). The second fraction was the macrolide **38**[2h] (2 mg, 4%) as a clear, colourless oil.

Epipatulolide C 40.[1] Tetrabutylammonium fluoride (124 μL, 1.0 M in THF, 124 μmol) was added to the silyl ether **39** (28 mg, 62 μmol) in THF (0.4 mL) and the solution stirred for 5 h at ambient temperature. Ethyl acetate was added and the solution washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate–petrol (10%), gave the title compound **40**[1,2h] (8 mg, 61%) as a clear, colourless oil (Found: M^+ + H, 213.1494. $C_{12}H_{21}O_3$ requires *M*, 213.1491); ν_{max}/cm^{-1} 3433, 2934, 2860, 1711, 1644, 1459, 1356, 1249, 1100 and 1000; δ_H (300 MHz, $CDCl_3$) 1.15–1.70 (10 H, m, 6-H_2, 7-H_2, 8-H_2, 9-H_2 and 10-H_2), 1.29 (3 H, d, *J* 6.5, 11-CH_3), 1.81 (1 H, d, *J* 4.0, OH), 1.88 (2 H, m, 5-H_2), 4.50 (1 H, m, 4-H), 5.05 (1 H, dquin, *J* 3.0, 6.5, 11-H), 6.05 (1 H, dd, *J* 2.0, 16.0, 2-H) and 7.02 (1 H, dd, *J* 4.5, 16.0, 3-H); δ_C (75 MHz, $CDCl_3$) 19.7, 21.4, 22.8, 27.7, 28.0, 33.4, 36.4, 71.5, 73.2, 120.3, 151.2 and 167.3; *m*/*z* (CI) 230 (M^+ + 18, 48%), 213 (100) and 195 (12).

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