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PAPER

Total synthesis of C_{19} lipid diols containing a 2,5-disubstituted-3-oxygenated tetrahydrofuran†‡

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The total synthesis of the C_{19} lipid diols **5** and **6**, the enantiomers of the anthelmintic marine natural products **1** and **3**, is described. Key steps in the divergent syntheses include a *syn* selective epoxidation of a homoallylic alcohol, a one-pot alkoxypalladation-carbonylation-lactonisation reaction sequence and a DMEAD promoted Mitsunobu inversion.

Introduction

The commonly occurring brown algae *Notheia anomala* is native to Australian and New Zealand waters.[1,2] This epiphytic species has been the focus of research by Capon and co-workers to uncover biologically active secondary metabolites and examine their chemistry and biochemistry.[3–10] The major metabolite from this species, the C_{19} lipid (6*S*, 7*S*, 9*R*, 10*R*)-6,9-epoxynonadec-18-ene-7,10-diol **1** (Scheme 1), was first isolated in 1980 and displays potent *in vitro* anthelmintic activity.[11] Capon and Barrow hypothesized that this compound was biogenetically derived from the co-isolate *syn* methylene skipped *cis*, *cis*-bis-epoxide **2** through an acid-catalysed endo ring-opening, ring-closing cascade.[5] Supporting this hypothesis, Faber and co-workers have recently demonstrated that the stereochemical outcome of THF formation from methylene skipped bis-epoxides is dependant only on the epoxide-opening reaction being under enzymatic control.[12] The diastereomeric lipid diol **3** was isolated from *N. anomala* in 1998, and also displays anthelmintic activity.[4] It is tempting to hypothesize that this compound arises from either conserved enzymatic action on the as yet unidentified *anti*, methylene skipped *cis*, *cis*-bis-epoxide **4**, or through a disfavoured (perhaps non-enzymatic) exo epoxide-opening, ring-closing cascade on the stereochemically defined bis-epoxide **2** (Scheme 1).[5] In any event, enzymatic involvement in the formation and/or ring-opening of the bis-epoxide precursors means that natural access to the tetrahydrofuran containing C_{19} lipid diols is restricted to one enantiomeric series.

Compounds **1** and **3** provide conspicuous examples of the 2,5-disubstituted-3-oxygenated tetrahydrofuran unit present in many marine natural products. We recently outlined a general synthetic strategy capable of delivering any stereoisomer of this important structural unit.[13] We had initially planned to highlight our approach by completing a total synthesis of **1** and **3**. Upon reflection, however, we revised our targets to the enantiomeric compounds **5** and **6** (Fig.1). Our decision was based on the fact that there is no shortage of compound **1**. Not only have several total syntheses of this molecule been reported,[5,14–21] but the metabolite is available in plentiful quantities from the natural source. Extraction of 25 grams of *N. anomala* delivered more than half a gram of **1**.[10]

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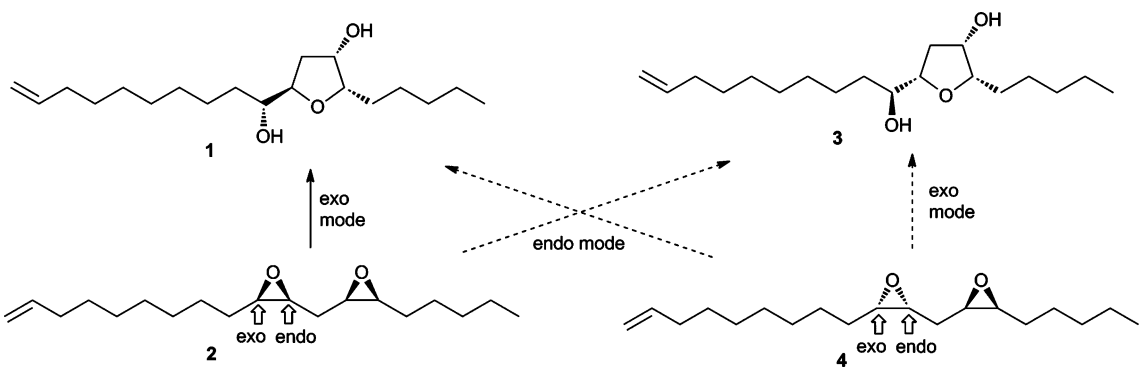


Scheme 1 Proposed biogenetic relationship between C_{19} lipid diols **1** and **3**.

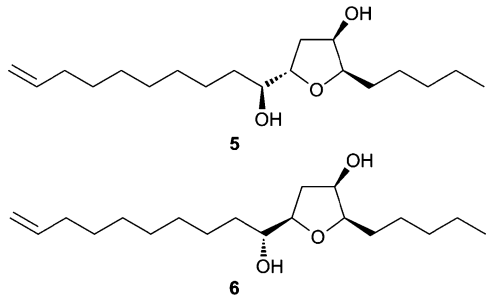
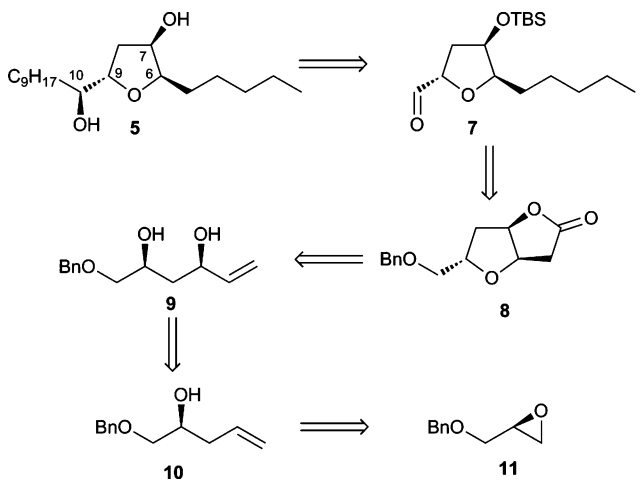


Fig. 1 Target compounds **5** and **6**.

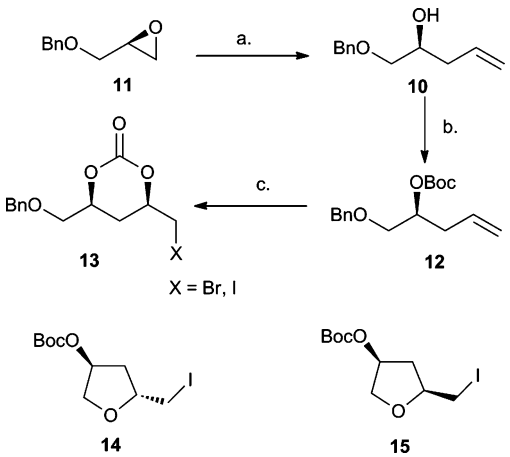
In contrast, the isolation or synthesis of the antipodal compounds **5** and **6** has not been reported. We therefore embarked on a total synthesis of **5** and **6**, the realisation of which is reported below.

Our retrosynthetic analysis is depicted in Scheme 2. Disconnection of the C10–C11 bond revealed the aldehyde **7**. We anticipated that the nine carbon side-chain could be appended using an organometallic reagent that, under appropriate conditions, would facilitate the diastereoselective installation of the C10 stereocentre. The aldehyde **7** was envisaged to arise from the bicyclic lactone **8**, which could be accessed from the enediol **9** using a palladium catalysed carbonylation reaction. The enediol **9** could be generated using one of several methods from the homoallyllic alcohol **10**. The ultimate disconnection revealed benzyl glycidyl ether **11** as the starting material for the sequence. As both isomers of this epoxide are commercially available, the same synthetic sequence could be employed to generate either enantiomeric series.



Scheme 2 Retrosynthetic analysis of target compound **5**.

The synthesis began by opening the (*S*)-configured epoxide **11** with vinylmagnesium bromide under copper catalysis (Scheme 3). We anticipated that the stereochemically defined hydroxyl group which would become C10 in the target molecule could be used to direct the installation of the neighbouring stereocentre. To that end, alcohol **10** was converted into the *tert*-butylcarbonate **12** with the expectation that this group would participate in a Bartlett carbonate-extension reaction.[22,23] It is known that unsubstituted homoallylic alcohols (such as **12**) are the least satisfactory substrates for these cyclisations, and the level of

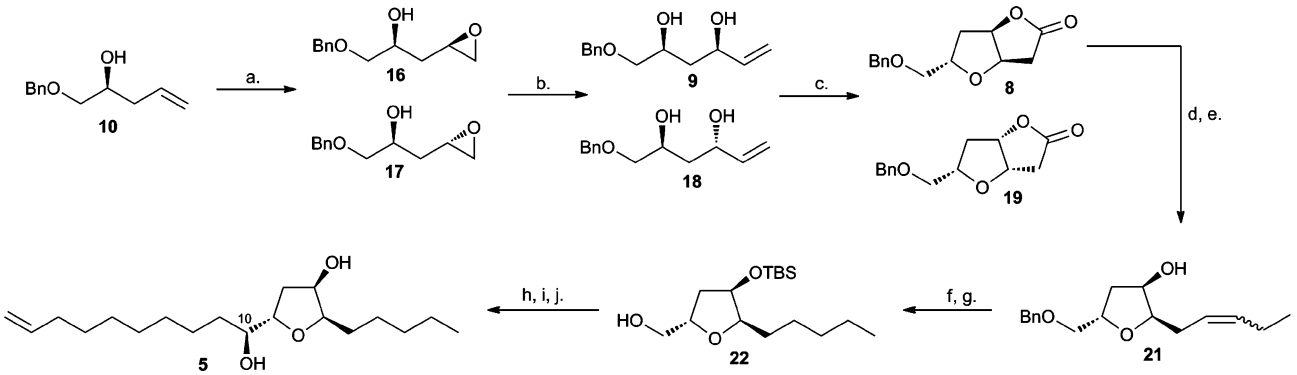


Scheme 3 Carbonate extension strategy. *Reagents and conditions*: (a) $H_2C{=}CHMgBr$, CuCl, 0 °C, 94%; (b) *n*-BuLi, $(Boc)_2O$, −78 °C, 74%; (c) IBr, toluene, −78 °C, 25%.

syn-diastereocontrol can be moderate. Bartlett noted that simply lowering the temperature of the reaction mixture may appear to be a straightforward solution to this problem.[22] Unfortunately, mild iodinating or brominating reagents generally require temperatures approaching ambient in order to participate in the reaction. We thought that we may be able to circumvent this problem by utilising a nucleophilic catalyst to generate a reactive halogenating reagent *in situ* at temperatures favouring formation of the *syn* diastereomer.

Ishihara's seminal work on phosphine-based nucleophilic promoters for the generation of asymmetric halonium species at low temperature prompted us to investigate the use of nucleophilic catalysts for the iodocyclisation reaction.[24] When the Boc-protected alcohol **12** was treated with *N*- bromosuccinimide and triphenylphosphine in toluene at −78 °C, the desired cyclised product was not observed and the starting material was recovered intact. Switching to a more polar solvent (CH_2Cl_2) offered no improvement. Employing *N*-iodosuccinimide under the same reaction conditions and raising the reaction temperatures to −40 °C were also ineffectual. We reasoned that the lack of reactivity might reflect the low relative nucleophilicity of the phosphine, but the reaction also failed when the highly nucleophilic catalyst, tributylphosphine, was employed. To ensure that the Boc unit was itself nucleophilic enough to react with the initially formed halonium ion, compound **12** was treated with iodine monobromide in toluene at −78 °C.[23] The use of this powerful iodinating reagent delivered the desired iodocarbonate **13** with good levels of *syn*-diastereoselectivity, but in low yield. Competitive cyclisation of the benzyl ether gave tetrahydrofurans **14** and **15** as the major reaction products.[25] This result demonstrated that the Boc unit would participate in ring-forming reaction at low temperatures if the alkene could be halogenated, but the competitive side-reactions rendered this approach untenable. Given the previous success with nucleophilic phosphine catalysts at low temperature to generate highly active halonium species that engage in cyclisations,[24] the current failure may point to the required electronic characteristics of the participating alkene.

Rather than pursue alternative methods to effect the halocyclisation, our attention turned to forming the epoxide **16** directly. We had already reported that treatment of the alcohol **10** with



Scheme 4 Synthesis of **5**. *Reagents and conditions*: (a) $VO(acac)_2$ (2 mol%), t-BuOOH, 81 °C, 63%, **16**:**17** 2 : 1; (b) Me_3SI, *n*-BuLi, 93%; (c) $Pd(OAc)_2$ (10 mol%), NaOAc, $CuCl_2$, HOAc, CO, 47% **8**, 23% **19**; (d) DiBAl-H, −78 °C; (e) $(Ph)_3PPrI$, *n*-BuLi, 0 °C, 59% from **8**; (f) TBSOTf, Et_3N, 0 °C, 96% (g) H_2, Pd/C, 97%; (h) DMSO, SO_3•py, Et_3N; (i) $H_2C{=}CH(CH_2)_6CH_2MgBr$, DCE, 83 °C, 39% from **22**; (j) TBAF, 95%.

m-CPBA gave a 1 : 1 mixture of diastereomeric epoxides **16** and **17** (Scheme 4).[13] That result showed that hydrogen bonding control was unlikely to be effective for selective generation of the *syn*-epoxyalcohol **16**. We therefore examined the vanadium-catalysed *syn*-selective epoxidation.[26] A systematic study of the diastereoselective epoxidation of homoallylic alcohols has been reported by Mihelich,[27] revealing that the direction and magnitude of stereoselection can be predicted by comparing plausible transition state models. That author noted that the observed asymmetric induction was largely the result of minimisation of steric interactions of the various substituents according to the normal principles of conformational analysis. Since compound **10** lacked any vinylic or allylic substitution, we anticipated that the levels of diastereoselection may be low.

As shown in Scheme 4, homoallylic alcohol **10** was subjected to the action of *tert*-butylhydroperoxide in the presence of $VO(acac)_2$. The sluggish epoxidation proceeded only at elevated temperatures, but we were pleased to observe that at 80 °C, the epoxyalcohols **16** and **17** were produced in a 2 : 1 ratio favouring the *syn* diastereomer. At this stage the two compounds were not easily separable and so were carried forward as the mixture.

Reaction with dimethylsulfonium methylide delivered the one carbon homologated allylic alcohols **9** and **18** in quantitative yield. The mixture was then subjected to Semmelhack's alkoxypalladation-carbonylation-lactonisation reaction conditions to give the bicyclic lactones **8** and **19** as a 2 : 1 mixture.[28–30] The two lactones were easily separable by chromatography and the major compound **8** formed crystals suitable for X-ray analysis.[31] As shown in Fig. 2, this demonstrated that the major product had an *anti* relationship between the C5 substituent on the tetrahydrofuran ring and the substituents at the ring junction.

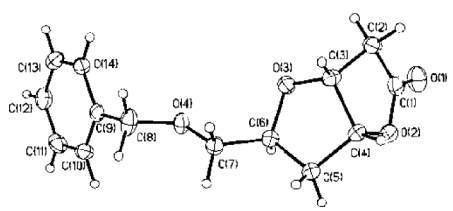
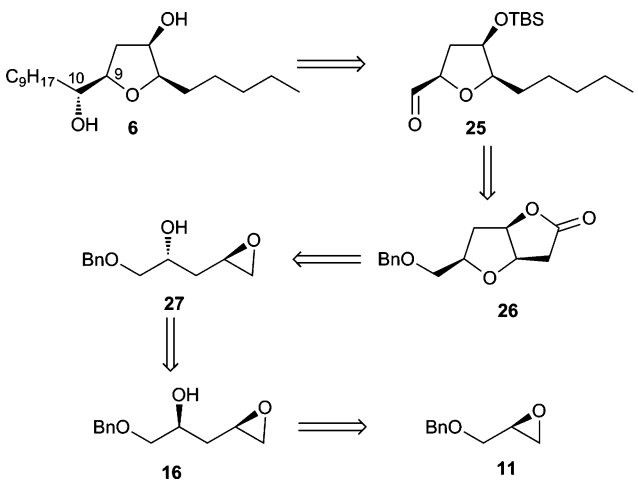


Fig. 2 X-ray crystal structure of compound **8**.

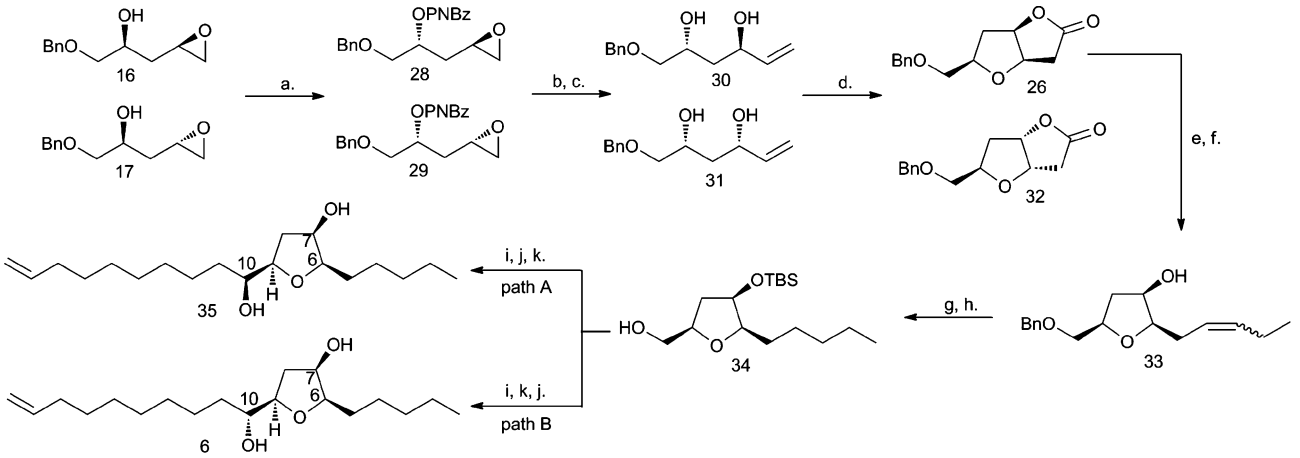
This requires the vanadium epoxidation reaction to have favoured formation of the *syn*-epoxyalcohol **16** as expected.

The lactone **8** was reduced to the lactol **20** and subjected to Wittig olefination to give **21** as an inconsequential mixture of geometric isomers (Scheme 4). After the secondary alcohol was protected as a *tert*-butyldimethylsilyl ether, hydrogenation of the alkene was accompanied by removal of the benzyl ether to give alcohol **22** in good yield. Following the protocol of Britton and co-workers,[18] alcohol **22** was oxidized under Parikh-Doering conditions and the product aldehyde **7** was treated immediately with 8-nonenylmagnesium bromide. This delivered the desired alcohol **23** as the major product in a 4 : 1 mixture with the C10 epimer **24**. This outcome is consistent with chelation-controlled addition of the organometallic reagent, where the carbonyl oxygen and ether-ring oxygen coordinate to magnesium and facilitate addition to the *Si* face of the aldehyde.[32,33] Treatment of **23** with TBAF smoothly effected removal of the TBS group giving the desired product **5**. This synthetic sequence delivered compound **5**, the enantiomer of natural product **1**, in 11 steps from benzyl glycidyl ether **11**.

Our second target, compound **6**, differed from compound **5** in configuration at the C9 and C10 stereocentres. As outlined in Scheme 5, we hoped that the installation of the C10 stereocentre



Scheme 5 Retrosynthetic analysis of target compound **6**.



Scheme 6 Synthesis of **6**. *Reagents and conditions*: (a) *p*-nitrobenzoic acid, PPh_3, DMEAD, 93%, **28**:**29** 2 : 1; (b) MeOH, K_2CO_3, 89%; (c) Me_3SI, *n*-BuLi, 96%; (d) $Pd(OAc)_2$ (10 mol%), NaOAc, $CuCl_2$, HOAc, CO, 44% **26**, 26% **32**; (e) DiBAl-H, −78 °C; (f) $(Ph)_3PPrI$, *n*-BuLi, 0 °C, 82% from **26**; (g) TBSOTf, Et_3N, 0 °C, 99% (h) H_2, Pd/C, 85%; (i) DMSO, SO_3•py, Et_3N; (j) $H_2C{=}CH(CH_2)_6CH_2MgBr$, DCE, 83 °C,; (k) TBAF; Path A, **35**, 74% from **34**; Path B: **6**, 31% from **34**, and **35** 10% from **34**.

could be accomplished under the same reaction conditions used above, with the C9 stereocentre directing the addition. Generation of the appropriate 2,5-disubstituted-3-oxygenated tetrahydrofuran **25** could be accomplished from the bicyclic lactone **26**. The all-*cis* stereochemical arrangement of **26** required the *anti* epoxyaldehyde **27**. We anticipated that **27** could be generated *via* Mitsunobu inversion of **16**.[34] This meant that both of the desired targets **5** and **6** would ultimately be derived from the same starting material **11**.

The synthetic sequence is depicted in Scheme 6. The inseparable 2 : 1 mixture of epoxyalcohols **16** and **17** which was produced by the action of *tert*-butylhydroperoxide and $VO(acac)_2$ (see Scheme 4), was subjected to standard Mitsunobu conditions with *p*-nitrobenzoic acid, triphenylphosphine and diisopropyl azodicarboxylate (DIAD) as the coupling reagent. Disappointingly, the product esters **28** and **29** co-eluted with reaction byproducts. Exhaustive chromatography was required to obtain the purified esters, and consequently the yields were low. We therefore turned to the dimethoxyethyl azodicarboxylate (DMEAD) coupling reagent devised by Sugimura which gives water soluble byproducts, greatly facilitating product isolation.[35,36] Treatment of epoxyalcohols **16** and **17** with *p*-nitrobenzoic acid, triphenylphosphine and DMEAD delivered the esters **28** and **29** as a 1 : 2 mixture in high yield on a gram scale. Ester hydrolysis and epoxide opening with dimethylsulfonium methylide gave the desired enediols **30** and **31**. As in the previous synthesis, the enediols underwent a smooth one-pot alkoxypalladation-carbonylation-lactonisation sequence to give the readily separable bicyclic lactones **26** and **32**. Compound **26**, containing the required stereochemical arrangement was reduced to the lactol, which underwent Wittig olefination to give **33**. The secondary alcohol was protected as a silyl ether and the compound was subjected to the action of hydrogen and palladium-on-charcoal. The debenzylated, fully saturated product **34** was then oxidized under Parikh-Doering conditions and the aldehyde treated with 8-nonenylmagnesium bromide followed by a TBAF mediated deprotection. In contrast to the previous synthetic synthesis, this series of reactions exclusively delivered compound **35**, the C10 epimer of the desired compound.

Capon reported that the C10 epimers of the naturally occurring lipid diols **1** and **3** were the most active compounds in an *in vitro* anthelmintic assay,[4] so efficient access to this compound may be advantageous. We rationalize the stereochemical outcome on the basis of a configurationally driven switch from chelation-control to Felkin-Ahn addition of the organometallic reagent. The all-*cis* stereochemical arrangement around the tetrahydrofuran and the steric bulk of the silyl protecting group, precludes magnesium chelation between the carbonyl and the ether oxygens. Supporting this interpretation is the observation that generally poor levels of stereoselection have been reported using other protecting groups on the C7 hydroxyl group.[16] In contrast, Britton and co-workers reported DFT calculations on a related system that lacked a protecting group on the C7 hydroxyl, and concluded that an intricate network involving the C7 alkoxide, the ether oxygen and the carbonyl unit, predisposed the molecule to undergo a chelation controlled reaction on the desired *Si* face of the aldehyde.[33] We anticipated that removal of the silyl protecting group from compound **34** prior to addition of the organometallic reagent would remove the large steric bulk and favour chelation controlled addition. In the event, compound **34** was oxidized under Parikh-Doering conditions, subjected to TBAF mediated desilylation and then treated with 8-nonenylmagnesium bromide. As shown in Scheme 6, this synthetic sequence delivered compound **6** as a 3 : 1 mixture with the C10 epimer. The synthesis of compound **6**, the enantiomer of natural product **3**, was completed in 13 steps from benzyl glycidyl ether **11**

Conclusions

We have synthesised the two C_{19} lipid diols **5** and **6**, the enantiomers of the marine natural products **1** and **3**. The divergent syntheses began from commercially available benzyl glycidyl ether **11**, and proceeded under substrate control thereafter. The key reaction in both syntheses was the palladium-catalysed transformation of linear enediols into the corresponding fused bicyclic lactones, which engendered the stereochemical framework of the desired

2,5-disubstituted-3-oxygenated tetrahydrofuran. Compounds **5** and **6** were generated in 11 and 13 steps, respectively.

Experimental

All reactions were conducted under an inert atmosphere (nitrogen or argon) in oven-dried glassware. Dichloromethane was freshly distilled from CaH_2 and tetrahydrofuran was freshly distilled from sodium/benzophenone. All other solvents and reagents were used as received from commercial sources. Melting points were determined using a Stanford Research Systems Optimelt automated melting point system and are uncorrected. Infrared spectra were acquired on a Shimadzu FTIR-8400S or Bruker Alpha-E ATR spectrometer as a solution between sodium chloride plates, as a KBR disk or neat. Absorption maxima are expressed in wavenumbers (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX300, or Bruker DPX400 spectrometer (^1H frequencies 300, 400 MHz; ^{13}C frequencies 75 and 100 MHz respectively). ^1H chemical shifts are expressed as parts per million (ppm) with residual chloroform (δ 7.26) or tetramethylsilane as reference and are reported as chemical shift (δ_H); relative integral; multiplicity (s = singlet, br = broad, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, q = quartet, m = multiplet); and coupling constants (J) reported in Hz. ^{13}C NMR chemical shifts are expressed as parts per million (ppm) with residual chloroform (δ 77.2) as internal reference and are reported as chemical shift (δ_C); multiplicity (assigned from DEPT experiments). High resolution mass spectra were recorded on a Bruker ApexII Fourier Transform Ion Cyclotron Resonance mass spectrometer with a 7.0 T magnet, fitted with an off-axis Analytical electrospray source.

(*S*)-1-(Benzyloxy)pent-4-en-2-ol (10)[37]. Vinylmagnesium bromide (1.0 M in THF; 21.8 mL, 21.8 mmol) was added at 0 °C to a suspension of copper (I) chloride (144 mg, 1.45 mmol) in THF (60 mL). After stirring for 15 min, a solution of (*S*)-benzyl glycidyl ether (2.39 g, 14.5 mmol) in THF (60 mL) was added and the mixture was stirred for 40 min at room temperature. The reaction was quenched by the addition of saturated aqueous ammonium chloride (60 mL). The mixture was extracted with ethyl acetate (3 × 60 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 15% ethyl acetate in hexanes gave compound **10** (2.63 g, 94%) as a pale yellow oil. $[\alpha]_D^{25}$ + 3.3 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3580, 3063, 3001, 2908, 2862, 1643; δ_H (300 MHz; $CDCl_3$) 7.39–7.28 (5 H, m), 5.90–5.76 (1 H, m), 5.15–5.09 (2 H, m), 4.56 (2 H, s), 3.89 (1 H, ddd, *J* 13.5, 6.6, 3.3), 3.52 (1 H, ddd, *J* 9.6, 3.3), 3.38 (1 H, dd, *J* 9.6, 7.5), 2.39–2.35 (1 H, m), 2.27 (2 H, dd, *J* 6.9, 6.6); δ_C (75 MHz; $CDCl_3$) 138.1 (CH), 134.4 (C), 128.6 (CH), 127.92 (CH), 127.87 (CH), 117.8 (CH_2), 74.0 (CH_2), 73.5 (CH_2), 69.9 (CH), 38.0 (CH_2).

(*S*)-1-(Benzyloxy)-2-(*tert*-butylcarbonyloxy)pent-4-ene (12). A solution of the alcohol **10** (2.63 g, 13.7 mmol) in anhydrous THF (50 mL) was treated with *n*-butyllithium (2.36 M in hexanes; 8.12 mL, 19.1 mmol) at −78 °C. The resulting solution was transferred *via* cannula to a solution of di-*tert*-butyl dicarbonate (4.61 g, 20.5 mmol) in anhydrous THF (50 mL). After stirring for 12 h at room temperature the reaction mixture was diluted with ether and washed with aqueous NaOH (2 M; 2 × 70 mL). The aqueous layer was extracted with ether (3 × 50 mL) and the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4 and the solvent was removed. Purification by flash chromatography eluting with 1% ethyl acetate in hexanes gave compound **12** as a colourless oil (2.97 g, 74%). $[\alpha]_D^{20}$ + 4.0 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3031, 2980, 2865, 1736, 1250, 1093; δ_H (300 MHz; $CDCl_3$) 7.37–7.27 (5 H, m), 5.77 (1 H, dddd, *J* 17.1, 10.1, 7.1, 7.1), 5.15–5.05 (2 H, m), 4.93–4.85 (1 H, m), 4.58 (1 H, d, *J* 12.1), 4.52 (1 H, d, *J* 12.1), 3.56 (2 H, d, *J* 5.2), 2.47–2.36 (2 H, m), 1.48 (9 H, s); δ_C (75 MHz; $CDCl_3$) 153.3 (C), 138.2 (C), 133.2 (CH), 128.5 (CH), 127.9 (CH), 127.7 (CH), 118.2 (CH_2), 82.1 (C), 75.0 (CH), 73.3 (CH_2), 70.8 (CH_2), 35.7 (CH_2), 27.9 (CH_3).

Iodocarbonate (13)[25,38,39]. A solution of the Boc-protected alcohol **12** (250 mg, 0.86 mmol) in toluene (6.5 mL) was cooled to −78 °C and iodine monobromide (1.0 M in dichloromethane; 3.85 mL, 3.85 mmol) was added. The reaction mixture was stirred in the dark for 2 h then warmed to 0 °C, diluted with ether and quenched by the addition of aqueous sodium thiosulfate (2.0 M; 5 mL) and saturated aqueous sodium hydrogen carbonate (2.5 mL). The layers were separated and the aqueous phase was extracted with ether (2 × 10 mL). The organic extracts were washed with brine (2 × 10 mL), dried over Na_2SO_4 and the solvent was evaporated. Purification by flash chromatography eluting 4% ethyl acetate in hexanes then 100% ether gave, in order of elution, the undesired *anti*-iodocarbonate as a pale yellow oil (19.9 mg, 6.5%). $[\alpha]_D^{20}$ + 2.9 (*c* 5.4, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3022, 2927, 2857, 1746, 1454, 1250; δ_H (300 MHz; $CDCl_3$) 7.40–7.30 (5 H, m), 4.73–4.64 (1 H, m), 4.62–4.58 (2 H, m), 3.70 (1 H, ddd, *J* 18.3, 10.5, 4.8), 3.48 (1 H, dd, *J* 14.1, 7.2), 3.41 (1 H, dd, *J* 10.5, 4.2), 3.25 (1 H, dd, *J* 10.5, 8.1), 2.38 (1 H, dt, *J* 14.4, 4.5), 2.17 (1 H, ddd, *J* 14.1, 8.4, 5.7), 2.04 (1 H, s); δ_C (75 MHz; $CDCl_3$) 148.2 (C), 137.3 (C), 128.8 (CH), 128.3 (CH), 127.9 (CH), 75.4 (CH), 75.1 (CH), 74.0 (CH), 70.8 (CH), 28.5 (CH_2), 4.9 (CH_2); followed by the desired *syn*-iodocarbonate **13** as a pale yellow oil (77.4 mg, 25%). $[\alpha]_D^{20}$ + 16.4 (*c* 0.85, $CHCl_3$) (lit. $[\alpha]_D^{20}$ + 10.9 (*c* 0.73, $CHCl_3$)); ν_{max}/cm^{-1} (neat) 3021, 2921, 2866, 1739, 1496, 1395, 1372; δ_H (300 MHz; $CDCl_3$) 7.39–7.29 (5 H, m), 4.65–4.55 (3 H, m), 4.46 (1 H, m), 3.68 (1 H, dd, *J* 10.5, 4.5), 3.64 (1 H, dd, *J* 10.5, 4.5), 3.41 (1 H, dd, *J* 10.5, 4.5), 3.26 (1 H, dd, *J* 10.5, 7.5), 2.45 (1 H, dt, *J* 14.4, 3.3), 1.91 (1 H, dt, 14.1, 11.7); δ_C (75 MHz; $CDCl_3$) 148.1 (C), 137.5 (C), 128.7 (CH), 128.2 (CH), 128.0 (CH), 77.3 (CH), 77.2 (CH), 74.0 (CH_2), 70.7 (CH_2), 30.3 (CH_2), 5.0 (CH_2).

Compound 14. (66.3 mg, 24%); $[\alpha]_D^{20}$ − 5.2 (*c* 1.0, $CHCl_3$) (lit. $[\alpha]_D^{20}$ − 5.2 (*c* 1.1, $CHCl_3$)); ν_{max}/cm^{-1} (neat) 2980, 2934, 2875, 1734, 1369, 1348, 1275; δ_H (300 MHz; $CDCl_3$) 5.20–5.17 (1 H, m), 4.18 (1 H, dd, *J* 10.8, 4.5), 4.11 (1 H, 9.3, 5.7), 3.79 (1 H, d, *J* 10.5), 3.27 (2 H, d, *J* 5.4), 2.29 (1 H, d, *J* 14.1, 5.7), 1.86 (1 H, ddd, *J* 13.8, 9.6, 6.0), 1.47 (9 H, s); δ_C (75 MHz; $CDCl_3$) 153.1 (C), 82.8 (C), 77.9 (CH_2), 77.4 (CH_2), 73.8 (CH), 39.2 (CH), 27.9 (CH_3), 9.4 (CH_2).

Compound 15. (20.6 mg, 7.3%) $[\alpha]_D^{20}$ −27.5 (*c* 4.8, $CHCl_3$); ν_{max}/cm^{-1} (neat) 2922, 2853, 1734, 1461, 1377, 1273; δ_H (300 MHz; $CDCl_3$) 5.16 (1 H, ddd, *J* 9.0, 4.5, 2.1), 4.22–4.13 (1 H, m), 4.10 (1 H, d, *J* 10.2), 3.93 (1 H, dd, *J* 10.8, 4.8), 3.33 (1 H, dd, *J* 9.9, 6.3), 3.27 (1 H, dd, *J* 9.9, 7.5), 2.45 (1 H, dt, *J* 14.4, 7.2), 1.99 (1 H, dddd, *J* 14.4, 5.4, 2.4, 0.9), 1.49 (9 H, s); δ_C (75 MHz; $CDCl_3$)

153.3 (C), 82.8 (C), 79.0 (CH_2), 77.3 (CH_2), 73.7 (CH), 37.9 (CH), 27.9 (CH_3), 8.7 (CH_2).

(2*S*,4*R*)-1-(Benzyloxy)-4,5-epoxy-2-hydroxy-1-pentane (16). To a solution of alkene **10** (2.50 g, 13.0 mmol) in toluene (60 mL) was added $VO(acac)_2$ (69 mg, 0.26 mmol) and the solution was heated to 81 °C. *Tert*-butyl hydroperoxide (5.5 M in decane; 2.6 mL, 14.3 mmol) was added dropwise over 1 h, and the mixture was stirred at 81 °C for 3 h. The reaction was quenched by the addition of aqueous sodium thiosulfate (2 M; 50 mL). The mixture was extracted with ethyl acetate (3 × 50 mL), dried over Na_2SO_4 and the solvent was evaporated. Flash chromatography eluting with 10% ethyl acetate in hexanes followed by 20% ethyl acetate in hexanes gave compound **16** (1.71 g, 63%) as a colourless oil as a 2 : 1 mixture of diastereomers. $[\alpha]_D^{20}$ − 9.8 (*c* 1.0, MeOH); ν_{max}/cm^{-1} ($CHCl_3$) 3580, 3063, 3032, 3016, 2916, 2862; δ_C (75 MHz; $CDCl_3$) 7.45–7.28 (5 H, m), 4.57 (2 H, s), 4.09–4.01 (1 H, m), 3.53 (1 H, ddd, *J* 18.6, 9.3, 3.3), 3.46–3.36 (1 H, m), 3.15–3.07 (1 H, m), 2.79 (1 H, ddd, *J* 12.3, 7.8, 4.5), 2.53 (1 H, ddd, *J* 10.2, 4.8, 2.7), 1.89 (1 H, ddd, *J* 21.6, 12.9, 6.3), 1.51 (1 H, ddd, *J* 21.6, 10.5, 6.6); δ_C (75 MHz; $CDCl_3$) *major isomer* 138.0 (C), 128.5, (CH), 127.9 (CH), 74.1 (CH), 73.59 (CH_2), 73.56 (CH_2), 68.78 (CH), 49.8 (CH), 46.8 (CH_2), 36.1 (CH_2); *minor isomer* 138.0 (C), 128.5, (CH), 128.0 (CH), 74.4 (CH), 73.59 (CH_2), 73.56 (CH_2), 68.54(CH), 49.9 (CH), 47.2 (CH_2), 36.3 (CH_2); HRMS (ESI) for $C_{12}H_{16}O_3Na$ (MNa^+) calcd 231.0992, found 231.0991.

(2*S*,4*R*)-1-(Benzyloxy)-5-hexene-2,4-diol (9)[40,41]. To a stirred mixture of trimethylsulfonium iodide (4.22 g, 20.7 mmol) in anhydrous THF (100 mL) at −10 °C was added *n*-butyllithium (1.26 M in THF; 16.4 mL, 20.7 mmol). The solution was stirred for 30 min then a solution of epoxides **16** and **17** (1.08 g, 5.17 mmol) in dry THF (20 mL) was added and the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched by the addition of saturated aqueous ammonium chloride (60 mL), the aqueous layer was extracted with ethyl acetate (3 × 50 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 40% ethyl acetate in hexanes gave compound **9** (565 mg, 93%) as a pale yellow oil as a 2 : 1 mixture of diastereomers. $[\alpha]_D^{20}$ + 3.2 (*c* 1.0, MeOH); ν_{max}/cm^{-1} (neat) 3587, 3487, 3086, 3040, 3009, 2939, 2916, 2862; δ_H (300 MHz; $CDCl_3$) 7.38–7.26 (5 H, m), 5.96–5.81 (1 H, m), 5.27 (1 H, ddd, *J* 17.1, 7.5, 1.2), 5.11 (1 H, dd, *J* 10.2, 9.0), 4.55 (2 H, s), 4.43–4.35 (1 H, m), 4.18–4.03 (1 H, m), 3.38 (1 H, ddd, *J* 17.1, 9.6, 3.6), 3.40 (1 H, ddd, *J* 16.8, 9.6, 2.4), 3.17 (1 H, br), 2.87 (1 H, br), 1.76 (1 H, ddd, *J* 14.4, 9.0, 3.3), 1.67–1.55 (1 H, m); δ_C (75 MHz; $CDCl_3$) *major isomer* 140.7 (CH), 138.1 (C), 128.7 (CH), 128.1 (CH), 114.8 (CH_2), 74.6 (CH_2), 73.64 (CH_2), 72.9 (CH), 70.9 (CH), 68.1 (CH), 39.8 (CH_2); *minor isomer* 140.9 (CH), 138.1 (C), 128.7 (CH), 128.0 (CH), 114.6 (CH_2), 74.6 (CH_2), 73.64 (CH_2), 73.59 (CH), 70.3 (CH), 68.1 (CH), 39.1 (CH_2); HRMS (ESI) for $C_{13}H_{18}O_3Na$ (MNa^+) calcd 245.1154, found 245.1147.

(3a*R*,5*S*,6a*R*)-5-(Benzyloxymethyl)tetrahydrofuro[3,2-*b*]furan-2(5*H*)-one (8)[42] and (3a*S*,5*S*,6a*S*)-5-(benzyloxymethyl)-tetrahydrofuro[3,2-*b*]furan-2(5*H*)-one (19)[40]. Sodium acetate (337 mg, 4.11 mmol) and copper (II) chloride (552 mg, 4.11 mmol) were dissolved in glacial acetic acid (5.0 mL), and the solution was stirred until the solid dissolved. The mixture of diols **9** and **18** (304 mg, 1.37 mmol) was added as an acetic acid solution (5.0 mL), and the mixture was stirred vigorously while purging with nitrogen, followed by purging the reaction mixture with carbon monoxide. Palladium (II) acetate (30.8 mg, 0.14 mmol) was added and stirring was continued overnight. The solution was poured into water (30 mL), and sodium hydrogen carbonate was added until the solution was neutralised. The solution was extracted with ethyl acetate (3 × 50 mL), dried over Na_2SO_4, and the solvent was evaporated. Purification by column chromatography, eluting with 40% ethyl acetate in hexanes gave compound **19** as a colourless oil (77 mg, 23%): $[\alpha]_D^{20}$ − 53.8 (*c* 1.55, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3040, 2993, 2616, 2862, 1782; δ_H (300 MHz; $CDCl_3$) 7.36–7.27 (5 H, m), 5.03–4.99 (1 H, m), 4.60–4.56 (1 H, m), 4.52 (2 H, d, *J* 12.0), 4.27–4.18 (1 H, m), 3.52–3.50 (2 H, m), 2.79–2.66 (2 H, m), 2.38 (1 H, ddd, *J* 14.7, 7.5, 6.9), 2.03 (1 H, ddd, *J* 14.7, 7.2, 1.5); δ_C (75 MHz; $CDCl_3$) 175.4 (C), 137.9 (C), 128.5 (CH), 127.9 (CH), 127.8 (CH), 84.2 (CH), 79.3 (CH), 79.2 (CH), 73.5 (CH_2), 72.3 (CH_2), 36.6 (CH_2), 35.2 (CH_2); HRMS (ESI) for $C_{14}H_{16}O_4Na$ (MNa^+) calcd 271.0941, found 271.0941; and compound **8** (160 mg, 47%) as a white solid; $[\alpha]_D^{20}$ + 39.0 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3040, 3001, 2932, 2860, 1728 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.37–7.27 (5 H, m), 5.11–5.08 (1 H, m), 4.83 (1 H, ddd, *J* 9.0, 5.4, 2.7), 4.57 (2 H, s), 4.40–4.32 (1 H, m), 3.62 (1 H, dd, *J* 10.5, 3.0), 3.48 (1 H, dd, *J* 10.5, 4.8), 2.71 (2 H, d, *J* 4.8), 2.34 (1 H, dd, *J* 14.1, 6.0), 2.04 (1 H, ddd, *J* 14.1, 9.3, 5.1); δ_C (75 MHz; $CDCl_3$) 175.8 (C), 138.0 (C), 128.6 (CH), 127.9 (CH), 127.8 (CH), 84.8 (CH), 78.6 (CH), 76.7 (CH), 73.6 (CH_2), 71.7 (CH_2), 36.8 (CH_2), 35.0 (CH_2); HRMS (ESI) for $C_{14}H_{16}O_4Na$ (MNa^+) calcd 271.0941, found 271.0941.

(2*R*,3*R*,5*S*)-5-((Benzyloxy)methyl)-tetrahydro-2-(pent-2-enyl)-furan-3-ol (21). To a solution of **8** (279 mg, 1.13 mmol) in THF (14 mL) at −78 °C was added diisobutylaluminium hydride (1 M in hexanes; 6.78 mL, 6.78 mmol). The mixture was stirred for 5 h and then quenched by the slow addition of methanol at −10 °C until no more gas was evolved. After warming to room temperature, hydrochloric acid (2 M; 3.39 mL) was added and the mixture was stirred for 30 min. The aqueous layer was extracted with ethyl acetate (3 × 30 mL) and the organic extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 30 mL), brine (2 × 30 mL), then dried over Na_2SO_4. The solvent was evaporated to give the crude lactol as yellow oil which was used without further purification. To a suspension of propyltriphenylphosphonium iodide (1.48 g, 3.39 mmol) in THF (12 mL) at 0 °C was added *n*-butyllithium (2.24 M in hexanes; 1.51 mL, 3.39 mmol). After 15 min, a solution of the lactol (283 mg, 1.13 mmol) in THF (12 mL) was added and the mixture was stirred overnight. The reaction was quenched by the addition of saturated aqueous ammonium chloride (30 mL), the aqueous layer was extracted with ethyl acetate (3 × 30 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 25% ethyl acetate in hexanes gave compound **21** (185 mg, 59%) as a colourless oil and an *ca.* 2 : 1 mixture of geometric isomers. $[\alpha]_D^{20}$ − 20.0 (*c* 0.54, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3625, 2931, 2854, 1080; δ_H (300 MHz; $CDCl_3$) 7.36–7.28 (5 H, m), 5.61–5.36 (2 H, m), 4.60 (2 H, s), 4.49–4.41 (1 H, m), 4.28 (1 H, br), 3.88 (1 H, ddd, *J* 10.8, 8.7, 3.0), 3.56–3.51 (2 H, m), 2.55–2.34 (2 H, m), 2.17–1.93 (4 H, m), 1.76 (1 H, br s), 0.99 (3 H, app t, *J* 7.5); δ_C (75 MHz; $CDCl_3$) *major isomer* 138.4 (C), 134.3 (CH), 128.4 (CH), 127.7 (CH), 127.6 (CH), 124.1 (CH), 82.3 (CH), 76.2 (CH), 73.4 (CH_2), 72.9 (CH),

72.6 (CH_2), 37.7 (CH_2), 27.2 (CH), 20.8 (CH_2), 14.2 (CH_3); *minor isomer* 138.4 (C), 134.9 (CH), 128.4 (CH), 127.7 (CH), 127.6 (CH), 124.7 (CH), 82.3 (CH), 76.3 (CH), 73.4 (CH_2), 73.0 (CH), 72.6 (CH_2), 37.6 (CH_2), 32.4 (CH_2), 25.7 (CH_2), 13.8 (CH_3); HRMS (ESI) for $C_{17}H_{24}O_3Na$ (MNa^+) calcd 299.1618, found 299.1618.

(2*R*,3*R*,5*S*)-3-(*tert*-Butyl)dimethylsilyloxy-5-(benzyloxy-methyl)tetrahydro-2-(pentyl)furan[20]. To a solution of **21** (133 mg, 0.48 mmol) in dichloromethane (10 mL) at 0 °C was added triethylamine (268 μL, 1.92 mmol). After stirring for 5 min, *tert*-butyldimethylsilyl trifluoromethanesulfonate (338 μL, 1.44 mmol) was added and the mixture was stirred for 30 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride (15 mL), the aqueous layer was extracted with ether (3 × 10 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 5% ethyl acetate in hexanes gave silylated alkene (180 mg, 96%) as a pale yellow oil and an *ca.* 2 : 1 mixture of geometric isomers. $[\alpha]_D^{20}$ – 25.7 (*c* 0.92, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 2954, 2931, 1458, 1064; δ_H (300 MHz; $CDCl_3$) 7.35–7.28 (5 H, m), 5.61–5.36 (2 H, m), 4.59 (2 H, s), 4.44–4.35 (1 H, m), 4.29–4.27 (1 H, m), 3.85 (1 H, td, *J* 6.9, 3.3), 3.56–3.52 (2 H, m), 2.49–2.25 (2 H, m), 2.12–1.85 (4 H, m), 0.98 (3 H, app t, *J* 7.5), 0.91 (9 H, s), 0.06 (6 H, s); δ_C (75 MHz; $CDCl_3$) *major isomer* 138.5 (C), 133.6 (CH), 128.4 (CH), 127.7 (CH), 127.6 (CH), 125.2 (CH), 83.4 (CH), 76.3 (CH), 73.4 (CH_2), 73.0 (CH), 72.9 (CH_2), 38.4 (CH_2), 29.7 (CH_2), 25.8 (CH_3), 20.8 (CH_2), 18.1 (C), 14.2 (CH_3), –4.9 (CH_3), –4.4 (CH_3); *minor isomer* 138.5 (C), 134.1 (CH), 128.4 (CH), 127.7 (CH), 127.6 (CH), 125.6 (CH), 83.6 (CH), 76.3 (CH), 73.4 (CH_2), 73.0 (CH), 72.9 (CH_2), 38.4 (CH_2), 32.7 (CH_2), 25.8 (CH_3), 27.5 (CH_2), 18.1 (C), 13.8 (CH_3), –4.9 (CH_3), –4.4 (CH_3); HRMS (ESI) for $C_{23}H_{38}O_3SiNa$ (MNa^+) calcd 413.2482, found 413.2480.

(2*R*,3*R*,5*S*)-3-(*tert*-Butyl)dimethylsilyloxy-5-(hydroxymethyl)-tetrahydro-2-(pentyl)furan (22). To a solution of the silylated alkene (99 mg, 0.25 mmol) in ethyl acetate (15 mL) was added palladium-on-charcoal (10% w/w; 71 mg) and the mixture was stirred overnight under a balloon of hydrogen. After filtration through a plug of celite the solvent was evaporated. Flash column chromatography eluting with 20% ethyl acetate in hexanes gave compound **22** (74 mg, 97%) as a colourless oil. $[\alpha]_D^{20}$ – 11.0 (*c* 0.39, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3043, 2956, 1517, 1251, 1047; δ_H (400 MHz; $CDCl_3$) 4.33–4.21 (2 H, m), 3.79 (1 H, ddd, *J* 6.4, 6.4, 2.8), 3.74–3.70 (1 H, m), 3.50–3.45 (1 H, m) 1.93–1.82 (2 H, m), 1.63–1.55 (3 H, m), 1.32–1.30 (6 H, m), 0.91–0.89 (12 H, m), 0.08 (3 H, s), 0.07 (3 H, s); δ_C (100 MHz; $CDCl_3$) 84.1 (CH), 77.6 (CH), 73.8 (CH), 65.2 (CH_2), 37.7 (CH_2), 32.5 (CH_2), 29.9 (CH_2), 26.4 (CH_2), 26.1 (CH_3), 23.0 (CH_2), 18.4 (C), 14.4 (CH_3), –4.1 (CH_3), –4.7 (CH_3); HRMS for $C_{16}H_{34}O_3NaSi$ (MNa^+) calcd 325.2169, found 325.2169.

(6*R*,7*R*,9*S*,10*R*)-6,9-Epoxy-7-((*tert*-butyldimethylsilyl)oxy)-nonadec-18-ol and (6*R*,7*R*,9*S*,10*S*)-6,9-epoxy-7-((*tert*-butyldimethylsilyl)oxy)nonadec-18-ol. To a solution of alcohol **22** (74 mg, 0.24 mmol) in dimethylsulfoxide (1.1 mL) was successively added triethylamine (526 μL, 2.4 mmol) and SO_3-pyridine complex (195 mg, 1.22 mmol) and the resulting solution was stirred at room temperature for 45 min. The reaction was quenched by the addition of sodium hydrogen sulfate (10% aqueous solution; 7 mL). The aqueous layer was extracted with dichloromethane (3 × 10 mL), and dried over Na_2SO_4. The solvent was evaporated to give the crude aldehyde, which was used without further purification.

To a stirred solution of 8-nonenylmagnesium bromide (0.4 M solution in diethyl ether; 6.0 mL, 2.4 mmol) in 1,2-dichloroethane (2 mL) at 83 °C was added a solution of aldehyde (0.24 mmol) in 1,2-dichloroethane (2.5 mL) and the resulting mixture was stirred at this temperature for 1 h. The reaction mixture was then treated with H_2O (13 mL), and extracted with ether (3 × 13 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and the solvent evaporated to give the crude alcohol and the C10 epimer (dr = 4 : 1). Purification of the crude product by flash chromatography in hexanes (4% ethyl acetate in hexanes) gave (6*R*,7*R*,9*S*,10*R*)-6,9-epoxy-7-((*tert*-butyldimethylsilyl)oxy)-nonadec-18-ol as a colourless oil (39.8 mg, 39%). $[\alpha]_D^{20}$ – 29.2 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3464, 3452, 3077, 2926, 2855, 1733, 1641, 1463, 1361; δ_H (300 MHz; $CDCl_3$) 5.81 (1 H, dddd, *J* 17.1, 10.2, 6.9, 6.6), 4.99 (1 H, dd, *J* 17.4, 1.8), 4.92 (1 H, dd, *J* 10.2, 1.5), 4.23 (1 H, br), 4.01 (1 H, ddd, *J* 9.0, 6.3, 6.3), 3.73 (1 H, ddd, *J* 9.6, 6.6, 6.6), 3.39–3.35 (1 H, m), 2.26 (1 H, d, *J* 4.5), 2.07–2.00 (2 H, m), 1.88–1.80 (2 H, m), 1.56–1.26 (23 H, m), 0.99–0.87 (9 H, m), 0.07 (6 H, d, *J* 4.2); δ_C (75 MHz; $CDCl_3$) 139.4 (CH), 114.3 (CH_2), 83.5 (CH_2), 80.4 (CH), 74.4 (CH), 73.8 (CH), 38.6 (CH), 33.9 (CH_2), 33.8 (CH_2), 32.3 (CH_2), 29.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.2 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 22.8 (CH_3), 18.2 (C), 14.2 (CH_3), –4.3 (CH_3), –4.9 (CH_3); HRMS (ESI) for $C_{25}H_{51}O_3Si$ (MH^+) calcd 427.3608, found 427.3588.

The second fraction gave (6*R*,7*R*,9*S*,10*S*)-6,9-epoxy-7-((*tert*-butyldimethylsilyl)oxy)-nonadec-18-ol as a colourless oil (17.6 mg, 17%). $[\alpha]_D^{20}$ – 20.0 (*c* 0.5, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3470, 3464, 2927, 2856, 1737, 1641, 1463, 1362; δ_H (300 MHz; $CDCl_3$) 5.86–5.76 (1 H, m), 4.99 (1 H, dd, *J* 17.2, 0.8), 4.93 (1 H, dd, *J* 10.4, 0.8), 4.25 (1 H, br s), 4.13 (1 H, ddd, *J* 9.2, 5.6, 3.2), 3.83–3.86 (1 H, m), 3.80 (1 H, dt, *J* 6.8, 3.2), 2.10–2.04 (2 H, m), 2.00 (2 H, dd, *J* 18.4, 5.6), 1.70 (1 H, dd, *J* 12.4, 5.6), 1.56–1.24 (23 H, m), 0.99–0.87 (9 H, m), 0.08 (3 H, s), 0.07 (3 H, s); δ_C (75 MHz; $CDCl_3$) 139.4 (CH), 114.3 (CH_2), 84.3 (CH_2), 80.3 (CH), 73.6 (CH), 72.0 (CH), 34.7 (CH_2), 33.9 (CH_2), 32.5 (CH_2), 32.3 (CH_2), 29.83 (CH_2), 29.75 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 22.8 (CH_3), 18.2 (C), 14.2 (CH_3), –4.3 (CH_3), –4.9 (CH_3); HRMS (ESI) for $C_{25}H_{50}O_3SiNa$ (MNa^+) calcd 449.3421, found 449.3428.

(6*R*,7*R*,9*S*,10*R*)-6,9-Epoxynonadec-18-en-7,10-diol (5). To a stirred solution of (6*R*,7*R*,9*S*,10*R*)-6,9-epoxy-7-((*tert*-butyldimethylsilyl)oxy)-nonadec-18-ol (22 mg, 0.05 mmol) in THF (10 mL) was added tetrabutylammonium fluoride (1 M in THF; 68 μL, 0.07 mmol). After stirring for 24 h at room temperature, water (10 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 15 mL), and the organic extracts washed with brine (2 × 10 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 30% ethyl acetate in hexanes gave compound **5** (15.5 mg, 95%) as a white solid. $[\alpha]_D^{20}$ – 17.6 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3442, 2920, 2847, 1642, 1464, 1324, 1089; δ_H (300 MHz; $CDCl_3$) 5.81 (1 H, dddd, *J* 17.4, 10.2, 6.6, 6.6), 4.98 (1 H, dd, *J* 17.4, 1.8), 4.93 (1 H, d, *J* 10.2), 4.24 (1 H, br s), 4.02 (1 H, dt, *J* 8.7, 6.6), 3.75 (1 H, ddd, *J* 6.9, 6.9, 2.7), 3.41–3.35 (1 H, m),

2.34 (1 H, br s), 2.01 (3 H, dd, *J* 12.9, 6.6), 1.87 (1 H, ddd, *J* 13.5, 9.0, 4.5), 1.64–1.47 (1 H, m), 1.43–1.25 (20 H, m), 0.89 (3 H, app t, *J* 6.0); δ_C (75 MHz; $CDCl_3$) 139.4, 114.3, 82.7, 80.4, 74.3, 73.7, 38.1, 34.0, 33.4, 32.2, 29.8, 29.6, 29.3, 29.1, 29.0, 26.2, 25.8, 22.8, 14.2; HRMS (ESI) for $C_{19}H_{36}O_3Na$ (MNa^+) calcd 335.2557, found 335.2558.

(2*R*,4*R*)-1-(Benzyloxy)-4,5-epoxy-2-(4-nitrobenzyloxy)-1-pentane 28 and (2*R*,4*S*)-1-(benzyloxy)-4,5-epoxy-2-(4-nitrobenzyloxy)-1-pentane (29). To a solution of the alcohols **16** and **17** (1.0 g, 4.8 mmol), *p*-nitrobenzoic acid (1.12 g, 6.72 mmol) and triphenylphosphine (1.76 g, 6.72 mmol) in toluene (25 mL), was added a solution of DMEAD (1.57 g, 6.72 mmol) in toluene (10 mL) dropwise at room temperature. After 2 h, the mixture was washed with H_2O (40 mL). The aqueous phase was re-extracted with toluene (2 × 20 mL), and the combined organic extracts washed with water (10 mL), brine (20 mL), dried over Na_2SO_4 and the solvent was evaporated. Flash chromatography eluting with 20% ethyl acetate in hexanes gave compound **29** as a pale yellow oil (1.60 g, 93%). $[\alpha]_D^{20}$ + 7.7 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3425, 3055, 2997, 2924, 2866, 1728, 1608, 1542, 1350, 1288; δ_H (300 MHz; $CDCl_3$) 8.29 (2 H, d, *J* 8.7), 8.21 (2 H, dd, *J* 2.4, 9.0), 7.32–7.27 (5 H, m), 5.55–5.48 (1 H, m), 4.61 (1 H, dd, *J* 12.0, 1.2), 4.54 (1 H, d, *J* 12.0), 3.82–3.69 (2 H, m), 3.08–3.00 (1 H, m), 2.78–2.74 (1 H, m), 2.51 (1 H, m), 2.22–2.09 (1 H, m), 1.94–1.84 (1 H, m); δ_C (75 MHz; $CDCl_3$) *major isomer* 164.4 (C), 150.8 (C), 137.9 (C), 135.8 (C), 131.0 (CH), 130.9 (CH), 128.6 (CH), 127.8 (CH), 123.7 (CH), 73.4 (CH_2), 72.7 (CH), 70.8 (CH_2), 49.1 (CH), 46.4 (CH_2), 34.4 (CH_2); *minor isomer* 164.3 (C), 150.8 (C), 137.9 (C), 135.7 (C), 131.0 (CH), 130.9 (CH), 128.6 (CH), 128.0 (CH), 123.7 (CH), 73.4 (CH_2), 72.5 (CH), 70.9 (CH_2), 49.0 (CH), 47.0 (CH_2), 34.6 (CH_2); HRMS (APCI) for $C_{19}H_{19}NO_6Na$ (MNa^+); calcd 380.1110, found 380.1105.

(2*R*,4*R*)- 1-(Benzyloxy)-4,5-epoxy-2-hydroxy-1-pentane and (2*R*,4*S*)-1-(benzyloxy)-4,5-epoxy-2-hydroxy-1-pentane. A mixture of the benzoate esters **28** and **29** (1.40 g, 3.92 mmol) and K_2CO_3 (135 mg, 0.98 mmol) in MeOH (15 mL) was stirred at room temperature for 4 h. The solvent was evaporated and the crude material was purified by flash chromatography (25% ethyl acetate in hexanes) to give *the title compounds* as a colourless oil (728 mg, 89%); $[\alpha]_D^{20}$ + 6.4 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3454, 3006, 2862, 1453, 1090; δ_H (300 MHz; $CDCl_3$) 7.39–7.28 (5 H, m), 4.57 (2 H, s), 4.11–4.04 (1 H, m), 3.54 (1 H, ddd, *J* 9.6, 9.6, 3.6), 3.43 (1 H, ddd, *J* 23.1, 9.6, 7.2), 3.15–3.07 (1 H, m), 2.79 (1 H, ddd, *J* 12.3, 4.5, 4.5), 2.53 (1 H, ddd, *J* 10.2, 5.1, 2.7), 1.86 (1 H, dddd, *J* 14.4, 12.9, 8.7, 4.2), 1.71–1.61 (1 H, m), 1.51 (1 H, ddd, *J* 14.4, 7.2, 4.5); δ_C (75 MHz; $CDCl_3$) *major isomer* 138.0 (C), 128.5, (CH), 128.0 (CH), 74.4 (CH), 73.59 (CH_2), 73.56 (CH_2), 68.54 (CH), 49.9 (CH), 47.2 (CH_2), 36.3 (CH_2); *minor isomer* 138.0 (C), 128.5, (CH), 127.9 (CH), 74.1 (CH), 73.59 (CH_2), 73.56 (CH_2), 68.78 (CH), 49.8 (CH), 46.8 (CH_2), 36.1 (CH_2); HRMS (ESI) for $C_{12}H_{16}O_3Na$ (MNa^+) calcd 230.0992, found 231.0993.

(2*R*,4*R*)-1-(Benzyloxy)-5-hexene-2,4-diol (30) and (2*R*,4*S*)-1-(benzyloxy)-5-hexene-2,4-diol (31). To a stirred mixture of trimethylsulfonium iodide (2.11 g, 10.4 mmol) in anhydrous THF (40 mL) was added *n*-butyllithium (2.07 M in THF; 5.0 mL, 10.4 mmol) at −10 °C under an argon atmosphere. The solution was stirred for 30 min then a solution of the epoxides (540 mg, 2.59 mmol) in dry THF (8 mL) was added and the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched by the addition of saturated aqueous ammonium chloride (30 mL), the aqueous layer was extracted with ethyl acetate (3 × 25 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 40% ethyl acetate in hexanes gave compounds **30** and **31** (556 mg, 96%) as a pale yellow oil as a *ca.* 2 : 1 mixture of diastereomers. $[\alpha]_D^{20}$ + 3.2 (*c* 1.0, MeOH); ν_{max}/cm^{-1} (neat) 3370, 3088, 3030, 2940, 2913, 2862, 1645, 1469, 1072; δ_H (300 MHz; $CDCl_3$) 7.38–7.26 (5 H, m), 5.96–5.81 (1 H, m), 5.27 (1 H, ddd, *J* 17.1, 7.5, 1.2), 5.11 (1 H, dd, *J* 10.2, 9.0), 4.55 (2 H, s), 4.43–4.35 (1 H, m), 4.18–4.03 (1 H, m), 4.38 (1 H, ddd, *J* 17.1, 9.6, 3.6), 3.40 (1 H, ddd, *J* 16.8, 9.6, 2.4), 3.17 (1 H, br), 2.87 (1 H, br), 1.76 (1 H, ddd, *J* 14.4, 9.0, 3.3), 1.67–1.55 (1 H, m); δ_C (75 MHz; $CDCl_3$) *major isomer* 140.9 (CH), 138.1 (C), 128.7 (CH), 128.0 (CH), 114.6 (CH_2), 74.6 (CH_2), 73.64 (CH_2), 73.59 (CH), 70.3 (CH), 68.1 (CH), 39.1 (CH_2); *minor isomer* 140.7 (CH), 138.1 (C), 128.7 (CH), 128.1 (CH), 114.8 (CH_2), 74.6 (CH_2), 73.64 (CH_2), 72.9 (CH), 70.9 (CH), 68.1 (CH), 39.8 (CH_2); HRMS (ESI) for $C_{13}H_{18}O_3Na$ (MNa^+) calcd 245.1154, found 245.1148.

(3a*R*,5*R*,6a*R*)-5-(Benzyloxymethyl)tetrahydrofuro[3,2-*b*]furan-2(5*H*)-one (26) and (3a*S*,5*R*,6a*S*)-5-(benzyloxymethyl)-tetrahydrofuro[3,2-*b*]furan-2(5*H*)-one (32). Sodium acetate (295 mg, 3.60 mmol) and copper (II) chloride (484 mg, 3.60 mmol) were dissolved in glacial acetic acid (4.5 mL), and the solution was stirred until the solid dissolved. The diol **3** (267 mg, 1.20 mmol) was added as an acetic acid solution (4.5 mL), and the solution was stirred vigorously while purging with nitrogen, followed by purging the reaction mixture with carbon monoxide gas. Palladium (II) acetate (26.9 mg, 0.12 mmol) was added and stirring was continued overnight under these conditions. The solution was poured into water (30 mL), and sodium hydrogen carbonate was added until the solution was neutralized. The solution was extracted with ethyl acetate (3 × 50 mL), dried over Na_2SO_4, and the solvent was evaporated. Purification by column chromatography, eluting with 40% ethyl acetate in hexanes gave compound **32** as a white solid (77 mg, 26%): $[\alpha]_D^{20}$ − 42.4 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3040, 3001, 2932, 2860, 1728 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.35–7.27 (5 H, m), 5.10 (1 H, dd, *J* 4.5, 4.8), 4.83 (1 H, ddd, *J* 6.6, 4.5, 2.4), 4.57 (2 H, s), 4.40–4.32 (1 H, m), 3.62 (1 H, dd, *J* 10.5, 3.3), 3.48 (1 H, dd, *J* 10.5, 4.8), 2.71 (2 H, d, *J* 4.5), 2.34 (1 H, dd, *J* 14.1, 6.0), 2.05 (1 H, ddd, *J* 14.1, 11.8, 5.1); δ_C (75 MHz; $CDCl_3$) 175.8 (C), 138.0 (C), 128.6 (CH), 127.9 (CH), 127.8 (CH), 84.9 (CH), 78.6 (CH), 78.0 (CH), 73.7 (CH_2), 71.7 (CH_2), 36.8 (CH_2), 35.0 (CH_2); HRMS (ESI) for $C_{14}H_{16}O_4Na$ (MNa^+) calcd 271.0941, found 271.0942; and compound **26** (131 mg, 44%) as a colourless oil; $[\alpha]_D^{20}$ + 58.0 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3533, 2925, 2866, 1772, 1451, 1355, 1067; δ_H (300 MHz; $CDCl_3$) 7.35–7.28 (5 H, m), 5.02 (1 H, ddd, *J* 6.3, 4.2, 1.8), 4.61 (1 H, ddd, *J* 6.3, 4.2, 1.8), 4.59 (1 H, d, *J* 12.0), 4.53 (1 H, d, *J* 12.3), 4.28–4.20 (1 H, m), 3.52–3.50 (2 H, m), 2.81–2.67 (2 H, m), 2.40 (1 H, ddd, *J* 14.4, 7.8, 6.9), 2.04 (1 H, ddd, *J* 14.7, 6.9, 1.5); δ_C (75 MHz; $CDCl_3$) 175.4 (C), 137.9 (C), 128.5 (CH), 128.0 (CH), 127.9 (CH), 84.2 (CH), 79.4 (CH), 79.2 (CH), 73.6 (CH_2), 72.4 (CH_2), 36.7 (CH_2), 35.3 (CH_2); HRMS (ESI) for $C_{14}H_{16}O_4Na$ (MNa^+); calcd 271.0941, found 271.0942.

(2*R*,3*R*,4*R*)-5-((Benzyloxy)methyl)-tetrahydro-2-(pent-2-enyl)-furan-3-ol (33). To a solution of **26** (84.2 mg, 0.34 mmol) in

THF (4 mL) was added diisobutylaluminium hydride (1 M in dichloromethane: 2.03 mL, 2.03 mmol). The mixture was stirred for 5 h and then quenched by the slow addition of methanol at – 10 °C until no more gas was evolved. After warming to room temperature, hydrochloric acid (2 M; 1.02 mL, 2.04 mmol) was added and the mixture was stirred for 30 min. The aqueous layer was extracted with ethyl acetate (3 × 10 mL) and the organic extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 10 mL), brine (2 × 10 mL), then dried over Na_2SO_4 and the solvent was evaporated to give the crude 5-((benzyloxy)methyl)-hexahydrofuro[3,2-*b*]furan-2-ol as a yellow oil. To a suspension of propyltriphenyl-phosphonium iodide (445 mg, 1.02 mmol) in THF (4.5 mL) at 0 °C was added *n*-butyllithium (1.94 M in hexanes; 526 μL, 1.02 mmol). After 15 min, a solution of 5-((benzyloxy)methyl)-hexahydrofuro[3,2-*b*]furan-2-ol (85.1 mg, 0.34 mmol) was added and the mixture was stirred overnight. The reaction was quenched by the addition of saturated aqueous ammonium chloride (10 mL), the organic layer was extracted with ethyl acetate (3 × 10 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash chromatography eluting with 20% ethyl acetate in hexanes gave compound **33** (76.6 mg, 82%) as a yellow oil and an *ca.* 2 : 1 mixture of geometric isomers. $[\alpha]_D^{20}$ + 17.1 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3429, 3029, 2961, 2931, 2871, 1737, 1496; δ_H (300 MHz; $CDCl_3$) 7.37–7.24 (5 H, m), 5.68–5.34 (2 H, m), 4.58 (2 H, s), 4.48–4.39 (1 H, m), 4.27 (1 H, br s), 3.87 (1 H, ddd, *J* 8.1, 6.6, 3.0), 3.55–3.45 (2 H, m), 2.53–2.22 (2 H, m), 2.19–1.91 (4 H, m) 1.70 (1 H, br s), 0.97 (3 H, app t, *J* 7.5); δ_C (75 MHz; $CDCl_3$) *major isomer* 138.5 (C), 134.3 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 124.2 (CH), 82.4 (CH), 76.3 (CH), 73.4 (CH_2), 73.0 (CH), 72.7 (CH_2), 37.8 (CH_2), 27.3 (CH_2), 20.9 (CH_2), 14.3 (CH_3); *minor isomer* 138.5 (C), 135.1 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 124.8 (CH), 82.4 (CH), 76.3 (CH), 73.4 (CH_2), 73.0 (CH), 72.7 (CH_2), 37.7 (CH_2), 32.6 (CH_2), 25.8 (CH_2), 13.9 (CH_3); HRMS (ESI) for $C_{17}H_{24}O_3Na$ (MNa^+) calcd 299.1618, found 299.1620

(2*R*,3*R*,5*R*)-3-(*tert*-Butyl)dimethylsilyloxy-5-((benzyloxy)-methyl)-tetrahydro-2-(pent-2-enyl)furan. To a solution of **33** (158 mg, 0.57 mmol) in dichloromethane (11.5 mL) at 0 °C was added triethylamine (319 μL, 2.29 mmol). After stirring for 5 min, *tert*-butyldimethylsilyl trifluoromethanesulfonate (403 μL, 1.72 mmol) was added and the mixture was stirred for 30 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride (15 mL), the aqueous layer was extracted with ether (3 × 10 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 5% ethyl acetate in hexanes gave *the title compound* (221 mg, 99%) as pale yellow oil and an *ca.* 2 : 1 mixture of geometric isomers. $[\alpha]_D^{20}$ – 15.6 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 2956, 2929, 2856, 1462, 1362, 1253; δ_H (300 MHz; $CDCl_3$) 7.34–7.28 (5 H, m), 5.58–5.29 (2 H, m), 4.61 (1 H, d, *J* 12.0), 4.54 (1 H, d, *J* 12.0), 4.24–4.22 (1 H, m), 4.13 (1 H, m), 3.70–3.65 (1 H, m), 3.63 (1 H, dd, *J* 9.6, 6.6), 3.48 (1 H, ddd, *J* 9.6, 5.4, 2.1), 2.50–2.41 (1 H, m) 2.33 (1 H, app t, *J* 6.6), 2.26 (1 H, app t, *J* 6.3), 2.19 (1 H, ddd, *J* 11.7, 5.4, 3.3), 2.11–1.99 (2 H, m), 1.72 (1 H, ddd, *J* 13.2, 5.1, 2.4), 1.72–1.66 (1 H, m), 0.97 (3 H, app t, *J* 7.5), 0.88 (9 H, s), 0.06 (6 H, s); δ_C (75 MHz; $CDCl_3$) *major isomer* 138.6 (C), 133.5 (CH), 128.4 (CH), 127.9 (CH), 127.6 (CH), 125.4 (CH), 83.9 (CH), 76.6 (CH), 73.8 (CH_2), 73.5 (CH_2), 72.6 (CH_2), 38.7 (CH_2), 27.8 (CH_2), 25.9 (CH_3), 20.9 (CH_2), 18.2 (C), 14.3 (CH_3), –4.3 (CH_3), –5.0 (CH_3); *minor isomer* 138.6 (C), 134.2 (CH), 128.4 (CH), 127.9 (CH), 127.6 (CH), 125.8 (CH), 84.1 (CH), 76.6 (CH), 73.8 (CH_2), 73.5 (CH_2), 72.6 (CH_2), 38.7 (CH_2), 32.9 (CH_2), 27.8 (CH_2), 25.8 (CH_3), 20.9 (CH_2), 18.2 (C), 13.9 (CH_3), –4.3 (CH_3), –5.0 (CH_3); HRMS (ESI) for $C_{23}H_{38}O_3SiNa$ (MNa^+) calcd 413.2482, found 413.2484.

(2*R*,3*R*,5*R*)-3-(*tert*-Butyl)dimethylsilyloxy-5-(hydroxymethyl)-tetrahydro-2-(pentyl)furan (34). To a solution of 3-(*tert*-butyl)-dimethylsilyloxy-5-((benzyloxy)-methyl)-tetrahydro-2-(pent-2-enyl)furans (186 mg, 0.48 mmol) in ethyl acetate (27.5 mL) was added palladium-on-charcoal (10% w/w; 133 mg) and the mixture was stirred overnight under a balloon of hydrogen. After filtration through a plug of celite the solvent was evaporated. Flash column chromatography eluting with 20% ethyl acetate in hexanes gave compound **34** (123 mg, 85%) as a colourless oil. $[\alpha]_D^{20}$ – 35.6 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 3443, 2953, 2929, 2857, 1463, 1362, 1252; δ_H (300 MHz; $CDCl_3$) 4.17–4.11 (2 H, m), 3.73 (1 H, ddd, *J* 11.4, 5.1, 2.7), 3.63 (1 H, ddd, *J* 8.7, 7.2, 3.0), 3.54 (1 H, ddd, *J* 10.2, 5.4, 4.5), 2.53 (1 H, dd, *J* 5.4, 5.4), 2.24 (1 H, ddd, *J* 13.8, 9.6, 5.4), 1.80 (1 H, dd, *J* 13.5, 4.2), 1.71–1.49 (2 H, m), 1.42–1.25 (6 H, m), 0.90–0.87 (12 H, m), 0.08 (3 H, s), 0.07 (3 H, s); δ_C (75 MHz; $CDCl_3$) 84.2 (CH), 77.8 (CH), 73.0 (CH), 65.1 (CH_2), 37.6 (CH_2), 32.2 (CH_2), 29.4 (CH_2), 26.3 (CH_2), 25.9 (CH_3), 22.8 (CH_2), 18.2 (C), 14.2 (CH_3), –4.1 (CH_3), –4.7 (CH_3); HRMS (ESI) for $C_{16}H_{34}O_3NaSi$ (MNa^+) calcd 325.2169, found 325.2172.

(6*R*,7*R*,9*R*,10*S*)-6,9-Epoxy-7-(*tert*-butyldimethylsilyloxy)-nonadec-18-ol. To a solution of alcohol **34** (73 mg, 0.24 mmol) in dimethylsulfoxide (1.2 mL) was added triethylamine (400 μL, 2.8 mmol) and SO_3-pyridine complex (235 mg, 1.45 mmol) and the mixture was stirred at room temperature for 45 min. The reaction was quenched by the addition of sodium hydrogen sulfate (10% aqueous solution; 7 mL). The aqueous layer was extracted with dichloromethane (3 × 15 mL), and dried over Na_2SO_4. The solvent was evaporated to give the crude aldehyde which was used without further purification. To a stirred solution of 8-nonenylmagnesium bromide (0.4 M solution in diethyl ether; 6.3 mL, 2.4 mmol) in 1,2-dichloroethane (2.2 mL) at 83 °C was added a solution of aldehyde (0.24 mmol) in 1,2-dichloroethane (2.65 mL) and the mixture was stirred at this temperature for 1 h. The reaction mixture was then treated with H_2O (13 mL), and extracted with ether (3 × 13 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and the solvent evaporated to give the crude product. Flash chromatography eluting with 4% ethyl acetate in hexanes gave *the title compound* as a colourless oil (76 mg, 75%). $[\alpha]_D^{20}$ – 18.0 (*c* 1.0, $CHCl_3$) ν_{max}/cm^{-1} (neat) 3511, 3077, 2927, 2856, 1731, 1641, 1463, 1439, 1289, 1052; δ_H (300 MHz; $CDCl_3$) 5.80 (1 H, dddd, *J* 17.1, 10.2, 6.6, 6.6), 4.98 (1 H, dd, *J* 17.1, 1.8), 4.94–4.90 (1 H, m), 4.18–4.15 (1 H, m), 3.94 (1 H, ddd, *J* 8.7, 4.8, 2.4), 3.84–3.80 (1 H, m), 3.55 (1 H, ddd, *J* 7.2, 6.0, 3.3), 2.80–2.64 (1 H, m), 2.10–1.99 (2 H, m), 1.89 (2 H, ddd, *J* 13.5, 5.1, 1.2), 1.64–1.25 (23 H, m), 0.98–0.87 (9 H, m), 0.09 (3 H, s), 0.07 (3 H, s); δ_C (75 MHz; $CDCl_3$) 139.4 (CH), 114.2 (CH_2), 83.5 (CH_2), 80.7 (CH), 72.8 (CH), 71.7 (CH), 34.6 (CH), 33.9 (CH_2), 33.8 (CH_2), 32.3 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.3 (CH_2), 26.0 (CH_2), 22.8 (CH_3), 18.3 (C), 14.2 (CH_3), –4.4 (CH_3), –4.9 (CH_3); HRMS (ESI) for $C_{25}H_{50}O_3NaSi$ (MNa^+) calcd 427.3602, found 427.3611.

(6*R*,7*R*,9*R*,10*S*)-6,9-Epoxynonadec-18-en-7,10-diol (35). To a stirred solution of alcohol (42 mg, 0.10 mmol) in THF (20 mL) was added tetrabutylammonium fluoride (1 M in THF; 129 μL, 0.13 mmol). After stirring for 24 h at room temperature water (20 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 30 mL) and the organic extracts washed with brine (2 × 20 mL), dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography eluting with 30% ethyl acetate in hexanes gave compound **35** (30.5 mg, 99%) as a white solid. $[\alpha]_D^{20}$ – 22.8 (*c* 1.00, $CHCl_3$); ν_{max}/cm^{-1} (MeOH) 3332, 3056, 2943, 2831, 1650, 1447, 1276, 1024; δ_H (300 MHz; $CDCl_3$) 5.80 (1 H, dddd, *J* 16.8, 10.2, 6.6, 6.6), 4.99 (1 H, dd, *J* 17.4, 1.8), 4.93 (1 H, d, *J* 11.1), 4.02–3.97 (2 H, m), 3.83–3.81 (1 H, m), 3.59 (1 H, ddd, *J* 6.9, 6.9, 2.4), 3.26 (1 H, br s), 2.49 (1 H, br s), 2.18 (1 H, ddd, *J* 14.1, 9.9, 5.4), 2.03 (2 H, dd, *J* 13.5, 6.6), 1.92 (1 H, dd, *J* 14.1, 3.3), 1.69–1.62 (1 H, m), 1.36–1.25 (19 H, m), 0.89 (3 H, app t, *J* 6.5); δ_C (75 MHz; $CDCl_3$) 139.3 (CH), 114.3 (CH_2), 84.0 (CH), 80.1 (CH), 72.2 (CH), 71.4 (CH), 34.5 (CH_2), 33.9 (CH_2), 33.5 (CH_2), 32.2 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 29.02 (CH_2), 28.97 (CH_2), 26.2 (CH_2), 26.0 (CH_2), 22.8 (CH_2), 14.2 (CH_3); HRMS (ESI) for $C_{19}H_{36}O_3Na$ (MNa^+) calcd 335.2557, found 335. 2557.

(6*R*,7*R*,9*R*,10*R*)-6,9-Epoxynonadec-18-en-7,10-diol (6). To a solution of alcohol **34** (22.4 mg, 0.07 mmol) in dimethylsulfoxide (460 μL) was successively added triethylamine (124 μL, 0.88 mmol) and SO_3-pyridine complex (72.1 mg, 0.44 mmol) and the resulting solution was stirred at room temperature for 45 min. The reaction was quenched by the addition of sodium hydrogen sulfate (10% aqueous solution; 3 mL). The aqueous layer was extracted with dichloromethane (3 × 5 mL) and dried over Na_2SO_4. The solvent was evaporated to give the crude aldehyde which was used without further purification. To a stirred solution of the aldehyde (22.2 mg, 0.07 mmol) in THF (15 mL) was added tetrabutylammonium fluoride (1 M in THF; 96 μL, 0.10 mmol). After stirring for 30 min at room temperature water (5 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the organic extracts washed with brine (5 mL), dried over Na_2SO_4, and the solvent was evaporated. Crude aldehyde (13.8 mg, 0.07 mmol) was dissolved in 1,2-dichloroethane (800 μL) and added to a stirred solution of 8-nonenylmagnesium bromide (0.4 M solution in diethyl ether; 1.9 mL, 0.74 mmol) in 1,2-dichloroethane (700 μL) at 83 °C. The resulting mixture was stirred at that temperature for 1 h. The reaction mixture was then treated with H_2O (5 mL), and extracted with ether (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 and the solvent evaporated to give the crude product and its C10 epimer (dr = 3 : 1). Flash chromatography, eluting with 20% ethyl acetate in hexanes, gave compound **6** as a white solid (7.2 mg, 31%). $[\alpha]_D^{20}$ –23.1 (*c* 0.4, $CHCl_3$); ν_{max}/cm^{-1} (MeOH) 3346, 3079, 2925, 2855, 1729, 1640, 1465, 1283, 1128; δ_H (400 MHz; $CDCl_3$) 5.81 (1 H, ddd, *J* 16.8, 10.2, 6.9, 6.9), 4.99 (1 H, d, *J* 17.4), 4.93 (1 H, d, *J* 10.2), 4.05 (1 H, m), 3.95 (1 H, d, *J* 9.3), 3.63 (1 H, ddd, *J* 6.9, 6.6, 2.7), 3.48 (1 H, m), 2.38 (2 H, ddd, *J* 14.1, 9.9, 5.4), 2.26 (2 H, dd, *J* 14.1, 7.5), 1.84 (1 H, dd, *J* 13.8, 3.3), 1.67–1.26 (21 H, m), 0.89 (3 H, m); δ_C (100 MHz; $CDCl_3$) 139.4 (CH), 114.3 (CH_2), 84.5 (CH), 79.2 (CH), 74.1 (CH), 71.7 (CH), 38.9 (CH_2), 34.6 (CH_2), 33.9 (CH_2), 32.2 (CH_2), 29.62 (CH_2), 29.55 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 22.8 (CH_2), 14.2 (CH_3); HRMS (ESI) for $C_{19}H_{36}O_3Na$ (MNa^+) calcd 335.2557, found 335. 2557. The 10*S* diastereomer **35** was also obtained as a white solid (2.4 mg, 10%).

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