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# Stereoselective synthesis of the C13–32 spiroacetal fragment of spirangien A

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ABSTRACT

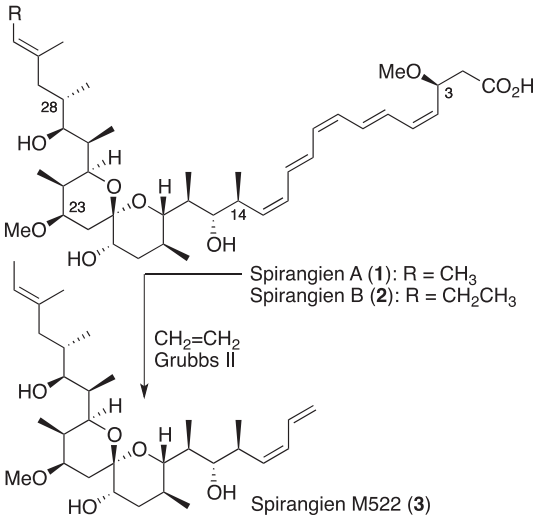
Stereoselective synthesis of an advanced intermediate towards the highly cytotoxic polyketide metabolite spirangien A was achieved. A key step in the synthesis was installation of the C23 stereocentre by a substrate controlled C22–23 aldol reaction. Comparison of this result with previous literature reports suggests that the facial preference of the aldehyde controls the outcome of the C22–23 aldol coupling and depends on the O27/25 protecting groups when reacting with complex ketones, which contain the C17–15 stereochemistry.



## 1. Introduction

Spirangiens A (**1**) and B (**2**) (Scheme 1) are two structurally related polyketide metabolites isolated from the epothilone-producing myxobacterium *Sorangium cellulosum*, strain So ce90.[1,2] Spirangien A (**1**) exhibited potent antifungal activity and was highly cytotoxic against the L929 mouse fibroblast cell line ($IC_{50}$ 0.7 ng $mL^{-1}$).[3] It was later found to be a potent inhibitor of IL-8 expression ($IC_{50}$ 7.2±0.9 nM).[4] Spirangiens A (**1**) and B (**2**) differ in structure only by an additional methylene unit at C32 in spirangien B and both compounds contain a complex pentaene side-chain, a highly functionalised 6,6-spiroacetal core, 14 stereocentres and a terminal carboxyl group. The absolute configuration of the remote C3 stereocentre was determined by chemical degradation of spirangien A and subsequent fragment analysis by GC.[3]

Ethylene cross-metathesis of spirangien A (**1**) afforded a spirangien diene analogue **3** (later named spirangien M522)[4] (Scheme 1), which retained one tenth the cytotoxic activity of spirangien A ($IC_{50}$ 7 ng $mL^{-1}$) and is also a potent inhibitor of IL-8 expression ($IC_{50}$ 90.7±19.8 nM).[3] X-ray crystal structure analysis of spirangien M522 by Höfle et al.[3] allowed for the assignment of the relative configuration of C14–28, while the absolute configuration of spirangiens A and B was later determined by total synthesis of spirangien diene **3** and spirangien A (**1**) by Paterson et al.[5–7] A number of other reports have emerged describing synthetic efforts towards spirangien A, including our own studies on the stereoselectivity of the C22–23 aldol coupling for spirangiens A and B.[5–14] Herein, we describe our synthesis of the C13–32 spiroacetal fragment of spirangien A (**1**).




**Scheme 1.** Spirangiens A (**1**) and B (**2**) and cross-metathesis to produce spirangien M522 (**3**).

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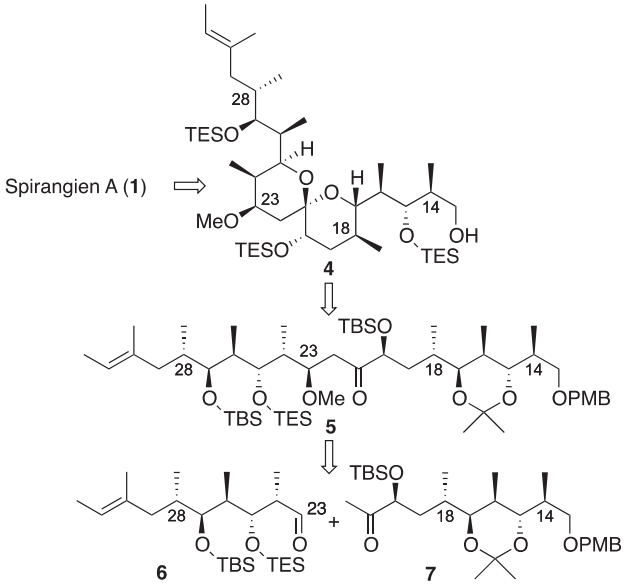
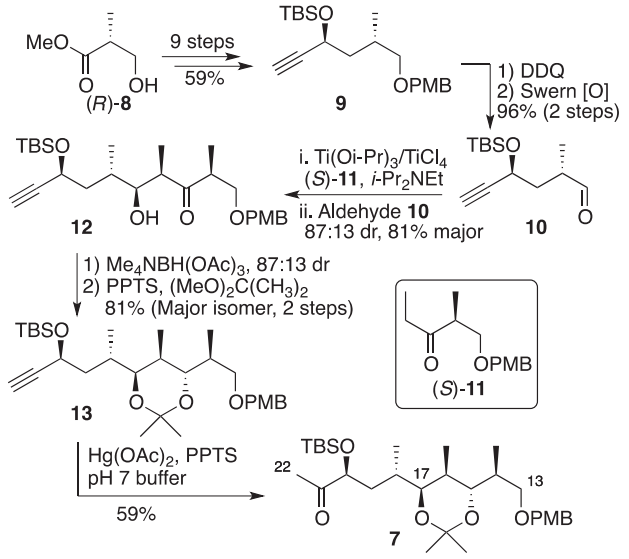
We envisaged a synthesis of spirangien A (**1**) via advanced intermediate **4** that could be used to furnish both spirangien M522 (**3**) and spirangien A (**1**). Spiroacetal **4** was anticipated to arise from the spirocyclization of linear precursor **5**, which in turn can be prepared by the aldol union of aldehyde **6** and ketone **7** (Scheme 2).




**Scheme 2.** Retrosynthesis of spirangien A (**1**) via advanced intermediate **4**.

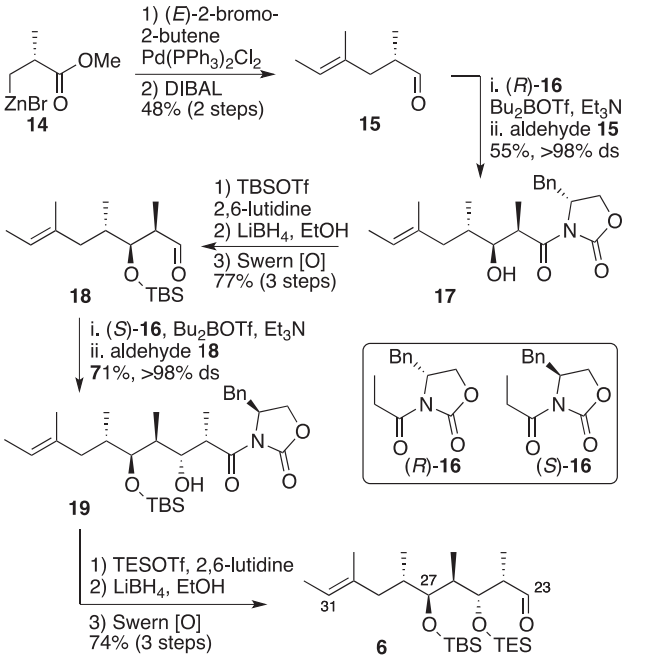
## 2. Results and discussion

Synthesis of methyl ketone **7** began with preparation of known[13] alkyne **9** from commercially available (*R*)-Roche ester [(*R*)-**8**] in 59% yield over nine steps (Scheme 3). Cleavage of the PMB ether with DDQ and subsequent Swern[15] oxidation furnished aldehyde **10** (96%, two steps) in preparation for aldol elaboration. The *Z*-enolate of Roche ester derived chiral ketone (*S*)-**11** was generated using modified Ti aldol conditions ($Ti(Oi\text{-}Pr)Cl_3/i\text{-}Pr_2NEt$)[16] and the ensuing double stereodifferentiating aldol reaction with chiral aldehyde **10** proceeded in 87% ds and purification gave novel aldol adduct **12** as a single isomer in 81% yield. The C14–17 stereotetrad was completed by directed reduction using $Me_4NBH(OAc)_3$ to give the *anti*-1,3-diol (O17/15 *anti*) as an 87:13 mixture of isomers, which was treated with 2,2-dimethoxypropane/PPTS and after purification acetonide **13** was obtained as a single isomer (81%, two steps). Finally, treatment with $Hg(OAc)_2$/PPTS/pH 7 buffer in THF brought about hydration of the terminal alkyne, giving ketone **7** (59%).




**Scheme 3.** Synthesis of ketone **7**.

Synthesis of aldehyde **6** was achieved via the sequence shown in Scheme 4. Palladium-catalysed cross-coupling of zinc homoenolate **14** with (*E*)-2-bromo-2-butene, followed by DIBAL reduction at −78 °C gave ready access to chiral aldehyde **15**.[17] The highly diastereoselective boron mediated aldol addition of Evans' oxazolidinone auxiliary[18–20] (*R*)-**16** to chiral aldehyde **15** gave the *anti–syn* aldol adduct **17** (>98% ds). TBS protection (TBSOTf/2,6-lutidine)[21] of the new hydroxyl was followed by reductive cleavage of the auxiliary ($LiBH_4$/EtOH)[22] and Swern[15] oxidation to furnish aldehyde **18**. Aldol addition of the other enantiomer of Evans' auxiliary[18–20] (*S*)-**16** to aldehyde **18** gave the desired *syn–anti–syn* configuration of the C24–27 stereotetrad of aldol adduct **19** in high selectivity (>98% ds) and afforded the opportunity for differential protection of the *anti*-1,3-diol (O27/25 *anti*). To this end, protection of the C25 hydroxyl was achieved (2,6-lutidine/TESOTf), followed by reductive cleavage of the auxiliary and Swern[15] oxidation to give desired aldehyde **6** (11% yield, 10 steps).

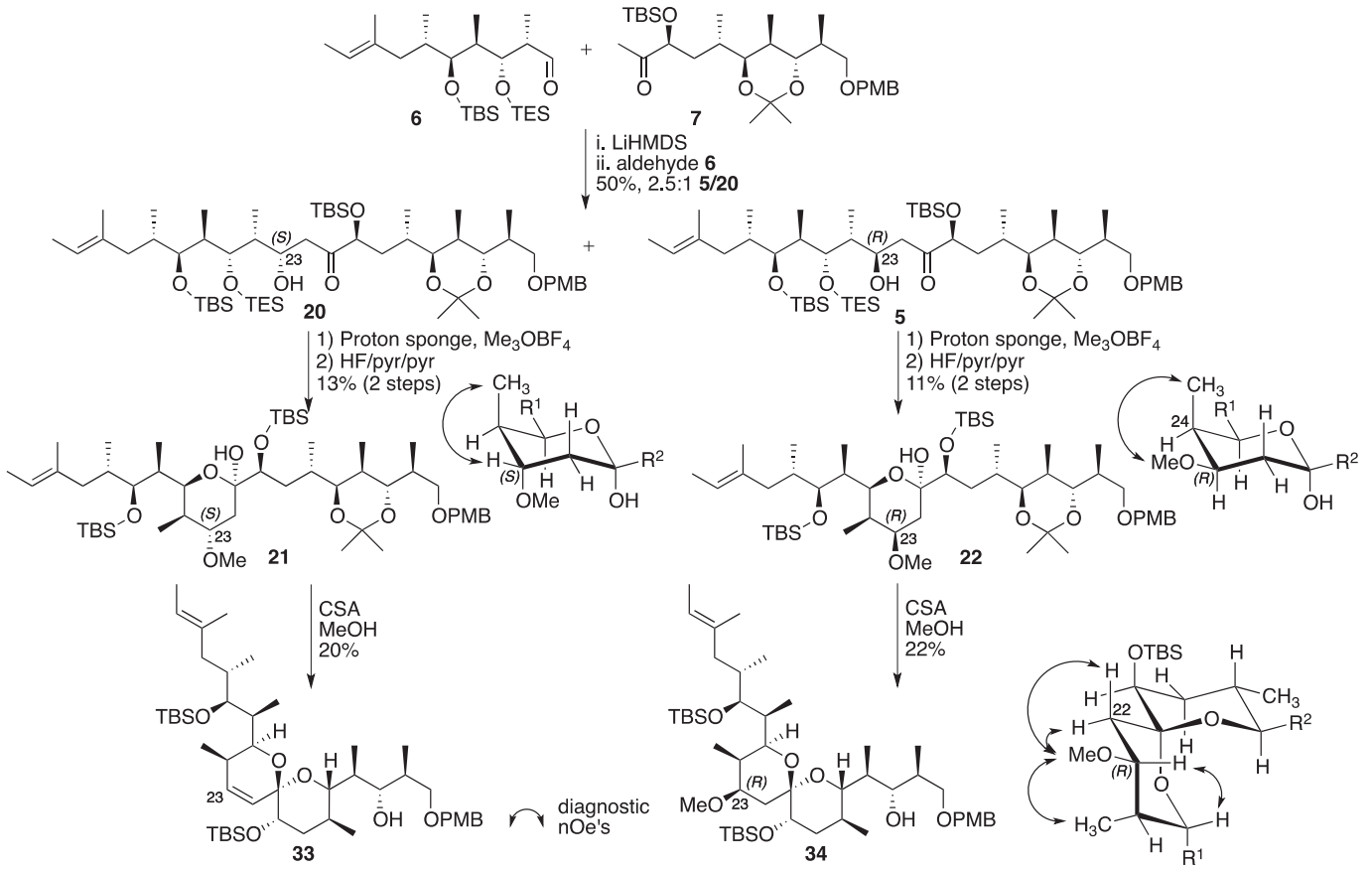



**Scheme 4.** Synthesis of aldehyde **6**.

The aldol coupling of ketone **7** with aldehyde **6** was achieved using LiHMDS (2 equiv) at −78 °C for 3 h to give adducts **5** and **20** in a 2.5:1 ratio. Diastereomeric aldol adducts **5** and **20** were separable by column chromatography and were treated independently for stereochemical determination.

To elucidate the C23 stereochemistry, the C23 hydroxyl in minor diastereomer **20** was methylated as per the natural product using Meerwein's salt.[23], then subjected to buffered HF–pyridine for 4 h to cleave only the more labile TES protecting group. Cyclisation of the newly liberated hydroxyl onto C21 ensued to afford hemiacetal **21** (Scheme 5).

Analysis of the diagnostic NOE interactions in hemiacetal **21** was indicative of an (*S*)-configuration at C23, the unnatural isomer. Major aldol diastereomer **5** was treated as per the minor isomer to form hemiacetal **22** (Scheme 5). Analysis of the diagnostic NOE correlations in hemiacetal **22** was complicated due to interfering




**Scheme 5.** Aldol coupling of aldehyde **6** and ketone **7**.

NOESY signals for H23 and H25. However, there was a clear NOE interaction between the methoxy protons and the C24 methyl protons, which only occurs in the (23*R*) configuration. Notably, there was also an absence of NOESY correlations between C24-Me and H23. This was further evidence that the major aldol isomer **5** was the desired (23*R*) isomer.

In an attempt to complete the preparation of the desired spiroacetals the hemiacetals **21** and **22** were treated with CSA/MeOH.[5,12a] However, when minor hemiacetal diastereomer **21** was subjected to these conditions, elimination of MeOH across C22–23 was observed in the resulting spiroacetal **33**, removing the crucial C23 stereocentre. Fortunately, when major hemiacetal diastereomer **22** was treated under the same conditions, there was no elimination of MeOH and spiroacetal **34** resulted (Scheme 5). Again the diagnostic NOE interactions in spiroacetal **34** confirmed the (*R*)-stereochemistry at C23, as evident from correlations between C23-OMe and C24-Me, as well as correlations between C23-OMe and both H22a and H22b. An NOE interaction between H23 and H25 was also observed, which is indicative of the (23*R*) isomer.

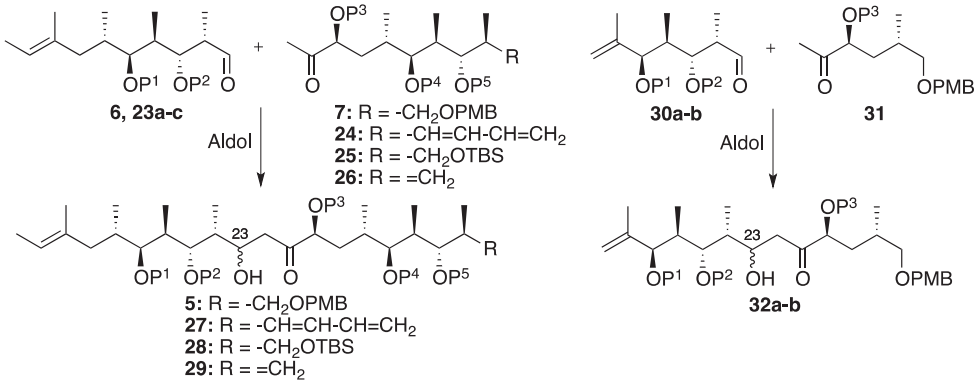
The selectivity observed (2.5:1) for the aldol coupling of O17/15 acetonide protected ketone **7** with O27/25 silyl protected aldehyde **6** is similar to the results of Kalesse and Lorenz[9] and Cossy et al.[12] who each obtained a 3:1 dr in favour of the desired isomers (23*R*)-**27** and (23*R*)-**28**, respectively, in the Li mediated aldol reaction of an analogous aldehyde (O27/25 silyl) with an O17/15 silyl protected ketone (Table 1). This suggests that the nature of the O17/15 protecting groups on the ketone does not control the outcome of the aldol reaction. On the other hand, Paterson et al.[5] obtained the opposite selectivity (3.5:1) in favour of the unnatural isomer (23*S*)-**29** in the Li aldol reaction between cyclic acetonide protected aldehyde **23c** and ketone **26** (Table 1). Ketone **26** is analogous to our ketone **7**, while our aldehyde **6** has unconstrained silyl protecting groups at O27/25 compared to Paterson's cyclic acetonide, thus implying that the aldehyde facial preference depends on the O27/25 protecting groups and controls the outcome of the aldol reaction.

This contrasts with the results for our model system[13] (Table 1). We now conclude that in this model Li aldol coupling (with both O27/25 silyl and acetonide protected aldehydes, **30a** and **b**), the 1,4-*anti* preference[10] of the simplified ketone **31** (lacking C17–15) dominates, giving 3.5:1 and 3:1 dr in favour of the unwanted isomers (23*S*)-**32a** and (23*S*)-**32b**, respectively. Thus the choice of O27/25 protecting groups effects the facial preference of the aldehyde and controls the outcome of the aldol reaction only when reacting with the more complex ketones containing the C17–15 stereocentres, but not the simple ketone **31**.

## 3. Conclusion

In summary, a stereoselective synthesis of advanced C13–32 spiroacetal fragment **34** towards the synthesis of spirangien A (**1**) and spirangien M522 (**3**) was achieved. A key step in the synthesis was a substrate controlled C22–23 aldol reaction to install the C23 stereochemistry. Notably, protecting group manipulation of spiroacetal **34** would constitute a formal synthesis[5,7] of spirangien A (**1**) and work will continue to convert this compound to spirangien A (**1**) and spirangien M522 (**3**). Comparison of the C22–23 aldol coupling with previous literature reports[5,9,12,13] suggests that the facial preference of the aldehyde depends on the O27/25 protecting groups and controls the outcome of the C22–23 aldol

**Table 1**
Comparison of previous C22–23 aldol coupling results for spirangien A (**1**)




| Authors | Aldehyde | Ketone | Conditions | Product | dr (*R*):(*S*) |
|---|---|---|---|---|---|
| This work | **6**: $P^1$=TBS, $P^2$=TES | **7**: $P^3$=TBS; $P^4$=$P^5$=$C(CH_3)_2$ | LiHMDS | **5** | 2.5:1 |
| Lorenz & Kalesse[9] | **23a**: $P^1$=$P^2$=TES | **24**: $P^3$=$P^4$=$P^5$=TES | LiHMDS | **27** | 3:1 |
| Cossy et al.[12] | **23b**: $P^1$=$P^2$=TBS | **25**: $P^3$=$P^4$=$P^5$=TBS | LDA | **28** | 3:1 |
| Paterson et al.[5] | **23c**: $P^1$=$P^2$=$C(CH_3)_2$ | **26**: $P^3$=TES | LDA | **29** | 1:3.5 |
| | | $P^4$=$P^5$=$C(CH_3)_2$ | (*c*-Hex)$_2$BCl/$Et_3$N | **29** | 1:5 |
| | | | (−)-Ipc$_2$BCl/$Et_3$N | **29** | 2.5:1 |
| Gregg & Perkins[13] | **30a**: $P^1$=TBS; $P^2$=TES | **31**: $P^3$=TBS | LiHMDS | **32a** | 1:3.5 |
| | **30b**: $P^1$=$P^2$=$C(CH_3)_2$ | **31**: $P^3$=TBS | LiHMDS | **32b** | 1:3 |

coupling when reacting with ketones, which contain the C17–15 stereochemistry.

## 4. Experimental

### 4.1. General

All reactions were carried out under an atmosphere of nitrogen ($N_2$) or argon (Ar) in oven-dried glassware. Most commercial starting materials and reagents were used as supplied, or dried and distilled using standard procedures.[24] Tetrahydrofuran (THF) was dried using sodium metal and then distilled, as required, from sodium-benzophenone under $N_2$. Dichloromethane ($CH_2Cl_2$) was distilled from calcium hydride under $N_2$ as required. Other solvents used for reactions, extractions and purification were distilled prior to use. Room temperature (rt) varied between 20 and 25 °C. Analytical thin layer chromatography (TLC) was conducted on aluminium-backed 0.2 mm thick silica gel 60 $F_{254}$ plates (Merck) and the plates were visualised under a 254 nm UV lamp and/or by treatment with either anisaldehyde dip (*p*-anisaldehyde, 9.2 mL; $H_2SO_4$, 12.5 mL; $CH_3CO_2H$, 3.75 mL; EtOH, 338 mL) or potassium permanganate dip ($KMnO_4$, 3 g; $K_2CO_3$, 20 g; 5% NaOH, 5 mL; $H_2O$, 300 mL), followed by heating. Column chromatography was conducted using silica gel 60 (mesh size 0.040–0.063 mm) as the stationary phase and the analytical reagent (AR) solvents indicated. When purifying compounds with acid sensitivity, column chromatography was performed on buffered silica as indicated. Buffered silica was prepared by spinning 100 g of silica gel 60 (mesh size 0.040–0.063 mm) with 10 mL of pH 7 phosphate buffer on a rotary evaporator overnight at atmospheric pressure.

Proton ($^1$H) and carbon ($^{13}$C) NMR spectra were recorded on a Bruker Avance II spectrometer at 400 or 600 MHz for proton and 100 or 151 MHz for carbon nuclei, respectively. Chemical shifts were recorded as $\delta$ values in parts per million (ppm). Spectra were acquired in deuterochloroform ($CDCl_3$) at ambient temperature and the peak due to residual $CHCl_3$ ($\delta$ 7.26) was used as the internal reference. For proton-decoupled $^{13}$C NMR spectra recorded in $CDCl_3$, the central peak ($\delta$ 77.16) of the $CDCl_3$ triplet was used as the internal reference and all data are given as chemical shift ($\delta$). $^1$H and $^{13}$C assignments were confirmed by conducting homonuclear ($^1$H–$^1$H) correlation spectroscopy (COSY), nuclear Overhauser effect (NOE) spectroscopy (NOESY) and heteronuclear ($^1$H–$^{13}$C) correlation spectroscopy (HMQC) experiments. Optical rotations were recorded on a PolAAR 21 polarimeter, referenced to the sodium D line (589 nm) at 20 °C, using the spectroscopic grade solvent specified ($CHCl_3$ or $CH_2Cl_2$) and at the concentration (*c*, g/100 mL) indicated. Measurements were carried out in a cell with a 1 dm path length. Infrared (IR) spectra were recorded on either a Perkin–Elmer 1600 series FTIR, BIO-RAD FTS-40-A or Nicolet Avatar 370 DTGS Fourier Transform spectrophotometer, with the absorptions recorded in wavenumbers ($n_{max}$/cm$^{-1}$). Liquid samples were analysed as thin films on NaCl discs, with solids being dissolved in $CH_2Cl_2$ or $CHCl_3$ before being applied to the discs and the solvent evaporated. High resolution mass spectra were recorded on either a Bruker BioApex II 47e FTMS fitted with an Analytica ESI source (in positive or negative ion mode) or an Agilent G1969A LC-TOF utilising an Agilent 1100 Series LC.

### 4.2. Preparative procedures

*4.2.1. (2S,4S)-4-(tert-Butyldimethylsilyloxy)-2-methyl-hex-5-ynyl-1-ol (**35**).* To a stirred solution of PMB ether **9** (481 mg; 1.33 mmol) in $CH_2Cl_2$ (66 mL) at 0 °C was added pH 7 phosphate buffer (13 mL), followed by DDQ (452 mg; 1.99 mmol) and the resultant slurry was stirred at 0 °C for 3 h. The mixture was diluted with $CH_2Cl_2$ (75 mL) and quenched with satd aq $NaHCO_3$ (120 mL). The layers were separated and the organic phase was washed with satd aq $NaHCO_3$ (150 mL), $H_2O$ (150 mL) and brine (150 mL), then dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 5% $Et_2O/CH_2Cl_2$) gave alcohol **35** (313 mg; 97%) as a colourless oil. $R_f$=0.31 (5% $Et_2O/CH_2Cl_2$); $[\alpha]_D^{20}$ −56.4 (*c* 1.46, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 4.45 (1H, ddd, *J*=8.3, 5.1, 2.1 Hz, H20), 3.46 (2H, d, *J*=5.9 Hz, H17), 2.38 (1H, d, *J*=2.1 Hz, H22), 2.28 (1H, br s, O*H*), 1.88 (1H, m, H18), 1.82 (1H, ddd, *J*=13.8, 8.3, 5.6 Hz, H19a), 1.49 (1H, ddd, *J*=13.7, 7.6, 5.1 Hz, H19b), 0.93 (3H, d, *J*=6.8 Hz, C18–C$H_3$), 0.88 (9H, s, SiC(C$H_3$)$_3$), −0.13 (3H, s, Si(C$H_3$)CH$_3$), −0.10 (3H, s, Si(CH$_3$)C$H_3$); $\delta_C$ (100 MHz; $CDCl_3$) 85.9, 72.5, 68.1, 61.2, 42.5, 32.5, 25.8, 18.3, 16.9, −4.4, −5.0; IR (film, cm$^{-1}$) 3311, 2956, 2930,

2858, 2361, 2338; HRESIMS calculated for $C_{21}H_{36}O_3SiH^+$: 243.1775; found: 243.1783.

*4.2.2. (2S,4S)-4-(tert-Butyldimethylsilyloxy)-2-methyl-hex-5-ynal (**10**).* To a stirred solution of DMSO (423 μL; 4.92 mmol) in $CH_2Cl_2$ (10 mL) at −78 °C was added $(COCl)_2$ (1.23 mL; 2 M in $CH_2Cl_2$; 2.46 mmol), dropwise and the resulting solution was stirred at −78 °C for 30 min. Alcohol **35** (399 mg; 1.64 mmol) was added dropwise via cannula ($CH_2Cl_2$, 3 mL) and the mixture stirred at −78 °C for 45 min before $Et_3N$ (1.37 mL; 9.84 mmol) was added dropwise. The mixture was stirred at −78 °C for a further 30 min before warming to 0 °C for 30 min and the reaction was quenched by addition of satd aq $NH_4Cl$ (25 mL). The product was extracted with $CH_2Cl_2$ (3×20 mL), the combined organic extracts dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave aldehyde **10** (395 mg; 99%) as a colourless oil. $R_f$=0.56 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ −40.5 (*c* 1.61, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 9.63 (1H, d, *J*=1.6 Hz, H17), 4.46 (1H, ddd, *J*=7.6, 5.2, 2.0 Hz, H20), 2.62 (1H, m, C18), 2.41 (1H, d, *J*=2.0 Hz, H22), 2.21 (1H, ddd, *J*=14.4, 7.6, 6.4 Hz, H19a), 1.64 (1H, ddd, *J*=13.6, 6.4, 5.2 Hz, H19b), 1.13 (3H, d, *J*=7.2 Hz, C18−C*H*$_3$), 0.89 (9H, s, SiC(C*H*$_3$)$_3$), 0.14 (3H, s, Si(C*H*$_3$)CH$_3$), 0.11 (3H, s, Si(CH$_3$)C*H*$_3$); $\delta_C$ (100 MHz; $CDCl_3$) 204.3, 85.0, 73.2, 60.8, 43.3, 39.4, 25.9, 18.3, 13.8, −4.4, −5.0; IR (film, $cm^{-1}$) 3309, 2930, 2885, 2858, 2712, 1727.

*4.2.3. (3S,5S,6S,7R,9S)-3-(tert-Butyldimethylsilyloxy)-6-hydroxy-10-(4-methoxyphenyl)oxy-5,7,9-trimethyl-8-oxo-dec-1-yne (**12**).* Titanium isopropoxide (135 μL; 456 μmol) was added dropwise to a solution of $TiCl_4$ (1.37 mL; 914 μmol) in $CH_2Cl_2$ (3.3 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C and 10 min at rt and diluted with $CH_2Cl_2$ (3.3 mL). The resulting colourless solution was added via cannula to a solution of ketone (*S*)-**11** (385 mg; 1.63 mmol) in $CH_2Cl_2$ (5 mL) at −78 °C. The pale yellow solution was stirred for 2 min and *i*-$Pr_2NEt$ (312 μL; 1.79 mmol) was added dropwise. The resulting red-orange solution was stirred for 30 min at −78 °C before aldehyde **10** (392 mg; 1.63 mmol) was added via cannula. After 3 h at −78 °C the reaction was quenched by addition of satd aq $NH_4Cl$ (30 mL) and vigorously stirred at rt. The mixture was diluted with $Et_2O$ (40 mL) and washed with $H_2O$ (30 mL), satd aq $NaHCO_3$ (30 mL) and brine (30 mL). The aqueous layers were extracted with $Et_2O$ (3×40 mL) and the combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Crude NMR showed a 87:13 mixture of diastereomers, which were able to be separated by column chromatography (buffered silica, 3% $Et_2O$/$CH_2Cl_2$) to give the single isomer, aldol adduct **12** (627 mg; 81%) as a white amorphous solids. $R_f$=0.28 (3% $Et_2O$/$CH_2Cl_2$); $[\alpha]_D^{20}$ −13.8 (*c* 1.38, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 7.18 (2H, d, *J*=8.4 Hz, Ar*H*), 6.86 (2H, d, *J*=8.8 Hz, Ar*H*), 4.55 (1H, ddd, *J*=8.0, 5.6, 2.0 Hz, H20), 4.38 (2H, ABq, *J*=11.6 Hz, OC*H*$_2$PMP), 3.79 (3H, s, OC*H*$_3$), 3.72 (1H, dd, *J*=9.6, 2.0 Hz, H17), 3.59 (1H, dd, *J*=9.2, 7.9 Hz, H13a), 3.41 (1H, dd, *J*=8.8, 4.8 Hz, H13b), 3.17−3.10 (1H, ddq, *J*=9.2, 6.8, 4.1 Hz, H14), 2.96 (1H, br s, O*H*), 2.82 (1H, dq, *J*=7.2, 2.4 Hz, H16), 2.37 (2H, d, *J*=2.0 Hz, H22), 2.18 (1H, ddd, *J*=13.2, 8.0, 4.0 Hz, H19a), 1.86−1.75 (1H, m, H18), 1.40 (1H, ddd, *J*=13.6, 8.0, 5.6 Hz, H19b), 1.05 (3H, d, *J*=7.2 Hz, C14−C*H*$_3$), 1.00 (3H, d, *J*=6.8 Hz, C16−C*H*$_3$), 0.89 (9H, s, SiC(C*H*$_3$)$_3$) 0.84 (3H, d, *J*=6.8 Hz, C18−C*H*$_3$), 0.13 (3H, s, Si(C*H*$_3$)CH$_3$), 0.11 (3H, s, Si(CH$_3$)C*H*$_3$); $\delta_C$ NMR (100 MHz; $CDCl_3$) 218.0, 159.5, 129.8, 129.4, 114.0, 86.3, 74.5, 73.3, 73.1, 72.1, 61.6, 55.3, 48.6, 44.4, 42.8, 31.9, 25.9, 18.3, 16.4, 13.9, 7.8, −4.3, −4.9; IR (film, $cm^{-1}$) 3505, 3307, 2933, 2857, 1711, 1613, 1586, 1513; HRESIMS calculated for $C_{27}H_{44}O_5SiCl^-$: 511.2652; found: 511.2655.

*4.2.4. (3S,5S,6S,7R,8S,9S)-3-(tert-Butyldimethylsilyloxy)-6,8-dihydroxy-10-(4-methoxyphenyl)oxy-5,7,9-trimethyl-dec-1-yne (**36**).* To a stirred solution of β-hydroxyketone **12** (52.5 mg; 110 μmol) in a 1:1 mixture of AcOH/$CH_3CN$ (4.4 mL) was added tetramethylammonium triacetoxyborohydride (467 mg; 2.20 mmol) and the resulting mixture was stirred at rt for 4 days. The mixture was diluted with $Et_2O$ (10 mL) and quenched by careful addition of satd aq $NaHCO_3$ (15 mL). The layers were separated and the aqueous phase was extracted with $Et_2O$ (4×15 mL), the combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 10% $Et_2O$/$CH_2Cl_2$) to give 1,3-diol **36** (45.8 mg; 87%, as a 87:13 *anti*−*syn* mix of isomers) as a yellow oil. $R_f$=0.48 (10% $Et_2O$/$CH_2Cl_2$); $[\alpha]_D^{20}$ −23.0 (*c* 2.14, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 7.23 (2H, d, *J*=8.4 Hz, Ar*H*), 6.87 (2H, d, *J*=8.4 Hz, Ar*H*), 4.56 (1H, ddd, *J*=8.4, 5.2, 2.0 Hz, H20), 4.45 (2H, ABq, *J*=11.2 Hz, OC*H*$_2$PMP), 3.80 (3H, s, OC*H*$_3$), 3.61 (1H, dd, *J*=4.0 Hz, H15), 3.60 (1H, dd, *J*=8.6, 3.3 Hz, H13a), 3.54 (1H, dd, *J*=9.2, 2.8 Hz, H17), 3.47 (1H, dd, *J*=8.6, 6.4 Hz, H13b), 2.38 (1H, d, *J*=2.0 Hz, H22), 2.21 (1H, ddd, *J*=13.6, 8.8, 4.4 Hz, H19a), 2.16−2.10 (1H, m, H14), 1.86−1.78 (1H, m, H18), 1.82−1.78 (1H, m, H16), 1.43 (1H, ddd, *J*=13.6, 7.6, 5.2 Hz, H19b), 1.25 (1H, br s, O*H*), 1.03 (3H, d, *J*=6.8 Hz, C14−C*H*$_3$), 0.90 (9H, s, SiC(C*H*$_3$)$_3$), 0.84 (3H, d, *J*=6.8 Hz, C16−C*H*$_3$), 0.80 (3H, d, *J*=6.8 Hz, C18−C*H*$_3$), 0.15 (3H, s, Si(C*H*$_3$)CH$_3$), 0.12 (3H, s, Si(CH$_3$)C*H*$_3$); $\delta_C$ NMR (100 MHz; $CDCl_3$) 159.5, 129.7, 129.5, 114.0, 86.3, 82.7, 76.1, 75.4, 73.3, 72.2, 61.8, 55.4, 42.9, 35.9, 34.8, 32.9, 25.9, 18.3, 16.6, 14.3, 10.7, −4.3, −4.9; IR (film, $cm^{-1}$) 3423, 3309, 2958, 2931, 2856, 1613, 1513; HRESIMS calculated for $C_{27}H_{46}O_5SiNa^+$: 501.3007; found: 501.3009.

*4.2.5. (3S,5S,6S,7R,8S,9S)-3-(tert-Butyldimethylsilyloxy)-10-(4-methoxyphenyl)oxy-5,7,9-trimethyl-6,8-[(bis-dimethyl-methylene) dioxy]-dec-1-yne (**13**).* To a stirred solution of 1,3-diol **36** (24.3 mg; 50.9 μmol) in $CH_2Cl_2$ (0.85 mL) was added 2,2-dimethoxypropane (0.85 mL) and a few crystals of PPTS and the resulting solution was stirred at rt for 3 h. The reaction mixture was diluted with $CH_2Cl_2$ (5 mL), washed with satd aq $NaHCO_3$ (5 mL) and brine (5 mL), dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave acetonide **13** as a single isomer (24.5 mg; 93%) as a clear, colourless oil. $R_f$=0.55 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ −7.3 (*c* 1.23, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 7.26 (2H, d, *J*=8.8 Hz, Ar*H*), 6.87 (2H, d, *J*=8.4 Hz, Ar*H*), 4.49 (1H, ddd, *J*=8.4, 6.0, 2.0 Hz, H20), 4.42 (2H, ABq, *J*=7.2 Hz, OC*H*$_2$PMP), 3.80 (3H, s, OC*H*$_3$), 3.55 (1H, dd, *J*=9.2, 4.8 Hz, H13a), 3.32 (1H, dd, *J*=8.8, 6.8 Hz, H13b), 3.29 (1H, dd, *J*=10.8, 5.2 Hz, H15), 3.22 (1H, dd, *J*=6.8, 5.6 Hz, H17), 2.37 (1H, d, *J*=2.0 Hz, H22), 2.11 (1H, ddd, *J*=13.2, 8.8, 4.4 Hz, H19a), 1.96−1.85 (1H, m, H14), 1.93−1.86 (1H, m, H16), 1.83−1.74 (1H, m, H18), 1.27 (1H, m, H19b), 1.27 (6H, s, C(C*H*$_3$)$_2$), 1.00 (3H, d, *J*=6.8 Hz, C14−C*H*$_3$), 0.90 (9H, s, SiC(C*H*$_3$)$_3$), 0.84 (3H, d, *J*=6.8 Hz, C16−C*H*$_3$), 0.83 (3H, d, *J*=6.8 Hz, C18−C*H*$_3$), 0.14 (3H, s, Si(C*H*$_3$)CH$_3$), 0.11 (3H, s, Si(CH$_3$)C*H*$_3$); $\delta_C$ NMR (100 MHz; $CDCl_3$) 159.2, 131.0, 129.3, 113.8, 100.4, 76.6, 74.0, 72.9, 72.2, 72.0, 61.6, 55.4, 42.8, 38.0, 35.3, 29.1, 25.9, 25.4, 23.7, 18.3, 15.8, 14.4, 12.5, −4.2, −4.9; IR (film, $cm^{-1}$) 3309, 2959, 2932, 2856, 1613, 1586, 1513; HRESIMS calculated for $C_{30}H_{50}O_5SiH^+$: 519.3500; found: 519.3505.

*4.2.6. (3S,5S,6S,7R,8S,9S)-3-(tert-Butyldimethylsilyloxy)-10-(4-methoxyphenyl)oxy-5,7,9-trimethyl-6,8-[(bis-dimethyl-methylene) dioxy]-decan-2-one (**7**).* To a stirred solution of alkyne **13** (21.5 mg; 41.4 μmol) in THF (0.8 mL) was added sequentially PPTS (15.6 mg; 62.2 μmol), pH 7 buffer (2 μL; 111 μmol) and $Hg(OAc)_2$ (4.0 mg; 12.4 μmol) and the resulting mixture was stirred at 45 °C for 48 h. The reaction was quenched by addition of satd aq $NaHCO_3$ (2 mL) and the mixture was extracted with $Et_2O$ (3×5 mL), the combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 10% EtOAc/hexanes) gave methyl ketone **7** (13.2 mg, 59%) as a colourless oil. $R_f$=0.31 (10% EtOAc/hexanes); $[\alpha]_D^{20}$ −8.1 (*c* 1.24, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 7.25 (2H, d, *J*=8.8 Hz, Ar*H*), 6.87 (2H, d, *J*=8.8 Hz, Ar*H*), 4.41 (2H, ABq, *J*=11.6 Hz, OC*H*$_2$PMP), 4.07 (1H, dd, *J*=9.6, 3.6 Hz, H20), 3.80 (3H, s, OC*H*$_3$), 3.54 (1H, dd, *J*=9.2, 4.8 Hz, H13a),

3.31 (1H, dd, *J*=9.2, 7.2 Hz, H13b), 3.25 (1H, dd, *J*=10.8, 4.0 Hz, H15), 3.22 (1H, dd, *J*=6.8, 5.6 Hz, H17), 2.16 (3H, s, H22), 2.05 (1H, ddd, *J*=13.2, 9.6, 2.8 Hz, H19a), 1.94–1.85 (1H, m, H14), 1.89 (1H, ddd, *J*=13.6, 6.8, 3.6 Hz, H19b), 1.77–1.69 (2H, m, H16 and H18), 1.27 (3H, s, C(C*H*$_3$)CH$_3$), 1.23 (3H, s, C(CH$_3$)C*H*$_3$), 0.99 (3H, d, *J*=6.8 Hz, C14–C*H*$_3$), 0.92 (9H, s, SiC(C*H*$_3$)$_3$), 0.83 (3H, d, *J*=6.8 Hz, C16–C*H*$_3$), 0.80 (3H, d, *J*=6.8 Hz, C18–C*H*$_3$), 0.05 (3H, s, Si(C*H*$_3$)CH$_3$), 0.04 (3H, s, Si(CH$_3$)C*H*$_3$); $\delta_C$ (100 MHz; $CDCl_3$) 212.8, 159.2, 131.0, 129.3, 113.9, 100.5, 77.6, 76.7, 73.5, 72.9, 72.2, 55.4, 38.1, 38.0, 35.3, 28.7, 25.9, 25.3, 25.1, 23.6, 18.3, 15.4, 14.3, 12.5, −4.6, −4.9; IR (film, cm$^{-1}$) 3411, 2957, 2932, 2857, 1715, 1612, 1586, 1513; HRESIMS calculated for $C_{30}H_{52}O_6SiNa^+$: 559.3425; found: 559.3427.

*4.2.7. (2R,4E)-Methyl-2,4-dimethyl-hexanoate (**37**).* To a stirred solution of (*E*)-2-bromo-2-butene (500 μL; 4.93 mmol) in THF (100 mL) at 0 °C was added dropwise over 1 min a solution of (*R*)-3-methoxy-2-methyl-3-oxopropylzinc bromide (**14**) (11.8 mL; 0.5 M in THF; 5.90 mmol). $Pd(PPh_3)_2Cl_2$ (97 mg; 246 μmol) was then added in one portion and the mixture stirred at 0 °C for 10 min, followed by rt for 24 h. The reaction was quenched by addition of satd aq $NH_4Cl$ (100 mL) and the product extracted with $Et_2O$ (3×100 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 50% hexanes/$CH_2Cl_2$) gave methyl ester **37** (526 mg; 68%) as a colourless oil. $R_f$=0.30 (50% hexanes/$CH_2Cl_2$); $[\alpha]_D^{20}$ +3.92 (*c* 1.02, $CH_2Cl_2$); $\delta_H$ (600 MHz; $CDCl_3$) 5.20 (1H, q, *J*=6.6 Hz, H31), 3.62 (3H, s, OC*H*$_3$), 2.59 (1H, ddq, *J*=7.2, 7.2, 6.6 Hz, H28), 2.34 (1H, dd, *J*=13.2, 7.2 Hz, H29a), 2.00 (1H, dd, *J*=13.8, 7.8 Hz, H29b), 1.55 (3H, s, C30–C*H*$_3$), 1.54 (3H, d, *J*=6.6 Hz, H32), 1.06 (3H, d, *J*=6.6 Hz, C28–C*H*$_3$); $\delta_C$ (151 MHz; $CDCl_3$) 177.2, 132.9, 121.1, 44.0, 38.0, 16.6, 15.4, 13.5 (two carbons).

*4.2.8. (2R,4E)-2,4-Dimethyl-hexanal (**15**).* To a stirred solution of ester **37** (449 mg; 2.87 mmol) in $CH_2Cl_2$ (14 mL) at −78 °C was added dropwise a solution of DIBAL (3.01 mL; 1 M in hexanes; 3.01 mmol). The resulting solution was stirred at −78 °C for 1 h, quenched with satd aq $NH_4Cl$ (20 mL) and warmed to rt. A mixture of satd aq potassium sodium tartrate (20 mL) and $Et_2O$ (20 mL) was then added with vigorous stirring for 10 min. Layers were separated and the aqueous layer extracted with $Et_2O$ (3×20 mL). The combined organic extracts were washed with brine (20 mL), dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave aldehyde **15** (256 mg; 71%) as a colourless oil. $R_f$=0.39 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ +6.79 (*c* 2.80, $CH_2Cl_2$); $\delta_H$ (400 MHz; $CDCl_3$) 9.60 (1H, d, *J*=2.0 Hz, H27), 5.25 (1H, m, H31), 2.49 (1H, dddq, *J*=13.6, 8.0, 6.8, 2.0 Hz, H28), 2.40 (1H, m, H29a), 1.97 (1H, m, H29b), 1.59 (3H, m, C30–C*H*$_3$), 1.57 (3H, m, H32), 1.02 (3H, d, *J*=7.2 Hz, C28–C*H*$_3$); $\delta_C$ (100 MHz; $CDCl_3$) 205.4, 132.3, 121.6, 44.6, 41.0, 15.7, 13.5, 13.3.

*4.2.9. [[3-(2R,3S,4S,6E)-4R]-3-(3-Hydroxy-2,4,6-trimethyl-1-oxo-oct-6-enyl)-4-(phenylmethyl)]-2-oxazolidinone (**17**).* To a stirred solution of oxazolidinone (*S*)-**16** (1.57 g; 6.74 mmol) in $CH_2Cl_2$ (10 mL) at 0 °C was added $Bu_2BOTf$ (8.09 mL; 1 M in $CH_2Cl_2$; 8.09 mmol) dropwise giving a red solution. After 30 min $Et_3N$ (1.22 mL; 8.76 mmol) was added and the resulting yellow solution was stirred for a further 30 min before cooling to −78 °C. Aldehyde **15** (850 mg; 6.74 mmol) in $CH_2Cl_2$ (4 mL) was added dropwise via cannula and the reaction mixture stirred at −78 °C for 30 min and then at 0 °C for 4 h, at which time the reaction was quenched by addition of pH 7 buffer (10 mL) and MeOH (10 mL). A solution of 2:1 MeOH/$H_2O_2$ (20 mL) was then added and the mixture stirred at rt for 1 h. The volatiles were removed in vacuo and the resulting slurry was extracted with $CH_2Cl_2$ (3×20 mL), the combined organic extracts washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 5% $Et_2O/CH_2Cl_2$) gave aldol adduct **17** (1.32 g; 55%, >98% ds) as a white solid. $R_f$=0.42 (5% $Et_2O/CH_2Cl_2$); $[\alpha]_D^{20}$ −45.9 (*c* 0.68, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 7.35–7.32 (2H, m, Ar*H*), 7.29–7.26 (1H, m, Ar*H*), 7.22–7.20 (2H, m, Ar*H*), 5.24 (1H, q, *J*=6.6 Hz, H31), 4.69 (1H, m, C*H*CH$_2$Ph), 4.23 (1H, dd, *J*=9.0, 7.2 Hz, CHC*H*$_A$H$_B$O), 4.19 (1H, dd, *J*=9.0, 2.4 Hz, CHCH$_A$*H*$_B$O), 3.97 (1H, dq, *J*=6.6, 2.4 Hz, H26), 3.62 (1H, ddd, *J*=8.4, 2.4, 2.4 Hz, H27), 3.27 (1H, dd, *J*=13.8, 3.6 Hz, C*H*$_A$H$_B$Ph), 2.95 (1H, d, *J*=3.0 Hz, O*H*), 2.79 (1H, dd, *J*=13.2, 9.6 Hz, CH$_A$*H*$_B$Ph), 2.52 (1H, d, *J*=12.6 Hz, H29a), 1.78–1.72 (1H, m, H28), 1.70 (1h, dd, *J*=13.2, 9.6 Hz, H29b), 1.60 (3H, s, C30–C*H*$_3$), 1.58 (3H, d, *J*=6.6 Hz, H32), 1.25 (3H, d, *J*=7.2 Hz, C28–C*H*$_3$), 0.80 (3H, d, *J*=6.6 Hz, C26–C*H*$_3$); $\delta_C$ (151 MHz; $CDCl_3$) 177.7, 153.1, 135.2, 135.0, 129.6, 129.1, 127.6, 120.7, 76.2, 66.3, 55.4, 44.2, 40.0, 37.9, 34.0, 15.7, 15.4, 13.5, 9.7; IR (film, cm$^{-1}$) 3523, 2968, 2919, 1781, 1696; HRESIMS calculated for $C_{21}H_{29}NO_4H^+$: 360.2169; found: 360.2170.

*4.2.10. [[3-(2R,3S,4S,6E)-4R]-3-(3-[tert-Butyldimethylsilyloxy]-2,4,6-trimethyl-1-oxo-oct-6-enyl)-4-(phenylmethyl)]-2-oxazolidinone (**38**).* The procedure used for the preparation of TBS ether **9** was followed with alcohol **17** (1.32 mg; 3.68 mmol), 2,6-lutidine (857 μL; 7.36 mmol), TBSOTf (1.27 mL; 5.52 mmol) and $CH_2Cl_2$ (37 mL). Purification by column chromatography (buffered silica, 50% hexanes/$CH_2Cl_2$) gave TBS ether **38** (1.74 g; 99%) as white solid. $R_f$=0.39 (50% hexanes/$CH_2Cl_2$); $[\alpha]_D^{20}$ +20.7 (*c* 1.02, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 7.36–7.31 (2H, m, Ar*H*), 7.30–7.25 (1H, m, Ar*H*), 7.23–7.20 (2H, m, Ar*H*), 5.14 (1H, q, *J*=6.0 Hz, H31), 4.63 (1H, m, C*H*CH$_2$Ph), 4.19–4.13 (2H, m, CHC*H*$_2$O), 3.97 (1H, dq, *J*=6.4, 6.4 Hz, H26), 3.95 (1H, dd, *J*=6.4, 3.6 Hz, H27), 3.27 (1H, dd, *J*=13.2, 3.2 Hz, C*H*$_A$H$_B$Ph), 2.77 (1H, dd, *J*=13.6, 9.6 Hz, CH$_A$*H*$_B$Ph), 2.19 (1H, d, *J*=13.2 Hz, H29a), 1.76–1.69 (1H, m, H28), 1.60 (1H, dd, *J*=13.2, 10.8 Hz, H29b), 1.55 (3H, d, *J*=6.8 Hz, H32), 1.51 (3H, s, C30–C*H*$_3$), 1.24 (3H, d, *J*=6.8 Hz, C26–C*H*$_3$), 0.93 (9H, s, OSi(C*H*$_3$)$_3$), 0.85 (3H, d, *J*=6.4 Hz, C28–C*H*$_3$), 0.08 (3H, s, OSi(C*H*$_3$)CH$_3$), 0.05 (3H, s, OSi(CH$_3$)C*H*$_3$); $\delta_C$ (100 MHz; $CDCl_3$) 176.3, 153.0, 135.5, 134.3, 129.6, 129.1, 120.3, 76.9, 66.1, 55.8, 42.6, 41.3, 37.8, 36.8, 27.1, 26.3, 15.9, 15.5, 14.2, 14.1, 13.5, −3.6, −3.9; IR (film, cm$^{-1}$) 3531, 3062, 3028, 2928, 2856, 1783, 1681; HRESIMS calculated for $C_{27}H_{43}O_4NSiNa^+$: 496.2854; found: 496.2880.

*4.2.11. (2S,3S,4S,6E)-3-(tert-Butyldimethylsilyloxy)-2,4,6-trimethyl-octan-1-ol (**39**).* To a stirred solution of oxazolidinone **38** (254 mg; 536 μmol) in $Et_2O$ (5.4 mL) at −10 °C was added EtOH (75 μL; 1.29 mmol) and $LiBH_4$ (643 μL; 1 M in THF; 1.29 mmol) and the resulting mixture was stirred at −10 °C for 4 h. The reaction mixture was warmed to 0 °C and quenched by addition of 1 M NaOH (10 mL). The mixture was poured into brine (10 mL) and extracted with $Et_2O$ (4×15 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 50% $CH_2Cl_2$/hexanes) gave alcohol **39** (126 mg; 78%) as a colourless oil. $R_f$=0.40 (50% $CH_2Cl_2$/hexanes); $[\alpha]_D^{20}$ +7.88 (*c* 1.02, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 5.20–5.16 (1H, m, H31), 3.58 (1H, dd, *J*=5.4, 2.4 Hz, H27), 3.57 (1H, dd, *J*=10.8, 7.8 Hz, H25a), 2.46 (1H, dd, *J*=10.8, 6.6 Hz, H25b), 2.44 (1H, dd, *J*=13.2, 3.6 Hz, H29a), 1.93–1.87 (1H, m, H26), 1.85–1.77 (1H, m, H28), 1.73 (1H, br s, O*H*), 1.66 (1H, dd, *J*=13.2, 10.2 Hz, H29b), 1.57 (3H, d, *J*=9.0 Hz, H32), 1.57 (3H, s, C30–C*H*$_3$), 0.90 (9H, s, OSi(C*H*$_3$)$_3$) 0.88 (3H, d, *J*=7.2 Hz, C26–C*H*$_3$), 0.80 (3H, d, *J*=6.6 Hz, C28–C*H*$_3$), 0.06 (3H, s, OSi(C*H*$_3$)CH$_3$), 0.06 (3H, s, OSi(CH$_3$)C*H*$_3$); $\delta_C$ (151 MHz; $CDCl_3$) 134.6, 120.4, 76.8, 66.8, 43.9, 38.7, 35.3, 26.2, 18.5, 16.2, 15.5, 13.3, 12.0, −3.8, −4.1; IR (film, cm$^{-1}$) 3332, 2957, 2929, 2857; HRESIMS calculated for $C_{17}H_{36}O_2SiH^+$: 301.2557; found: 301.2562.

*4.2.12. (2R,3S,4S,6E)-3-(tert-Butyldimethylsilyloxy)-2,4,6-trimethyl-octanal (**18**).* The procedure used for the preparation of aldehyde **10** was followed with alcohol **39** (111 mg; 369 μmol), DMSO (79 μL; 1.11 mmol), $(COCl)_2$ (277 μL; 2 M in $CH_2Cl_2$; 554 μmol), $Et_3N$ (309 μL; 2.21 mmol) and $CH_2Cl_2$ (4 mL). Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave aldehyde **18**

(110 mg; 100%) as a colourless oil. $R_f$=0.70 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ −24.5 (*c* 1.35, $CHCl_3$); $\delta_H$ (400 MHz; $CDCl_3$) 9.70 (1H, d, *J*=1.2 Hz, H25), 5.17–5.14 (1H, m, H31), 3.97 (1H, dd, *J*=5.2, 3.2 Hz, H27), 2.49 (1H, ddq, *J*=6.8, 3.6, 0.8 Hz, H26), 2.18–2.14 (1H, m, H29a), 1.88–1.76 (1H, m, H28), 1.67 (1H, dd, *J*=13.2, 10.0 Hz, H29b), 1.56 (3H, m, H32), 1.54 (3H, s, C30–C$H_3$), 1.10 (3H, d, *J*=7.2 Hz, C26–C$H_3$), 0.90 (9H, s, OSi(C$H_3$)$_3$) 0.81 (3H, d, *J*=7.2 Hz, C28–C$H_3$), 0.06 (3H, s, OSi(C$H_3$)CH$_3$), −0.02 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (100 MHz; $CDCl_3$) 205.4, 134.0, 120.7, 75.0, 50.1, 43.3, 35.8, 26.0, 18.4, 15.7, 15.4, 13.5, 8.6, −4.0, −4.1; IR (film, $cm^{-1}$) 3435, 2929, 2857, 2708, 1727, 1691.

*4.2.13. [[3-(2S,3R,4S,5S,6S,8E)-4S]-3-(5-[tert-Butyldimethylsilyloxy]-3-hydroxyl-2,4,6,8-tetramethyl-1-oxo-dec-8-enyl)-4-(phenylmethyl)]-2-oxazolidinone (**19**).* The procedure used for the preparation of aldol adduct **17** was followed with oxazolidinone (*S*)-**16** (112 mg; 481 μmol), $Bu_2BOTf$ (577 μL; 1 M in $CH_2Cl_2$; 577 μmol), $Et_3N$ (87 μL; 625 μmol), aldehyde **18** (144 mg; 481 μmol) and $CH_2Cl_2$ (1 mL). Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave aldol adduct **19** (182 mg; 71%) as a white solid. $R_f$=0.56 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ +20.7 (*c* 1.02, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 7.34–7.31 (2H, m, Ar*H*), 7.28–7.26 (1H, m, Ar*H*), 7.22–7.20 (2H, m, Ar*H*), 5.18 (1H, q, *J*=6.6 Hz, H31), 4.71 (1H, m, C*H*CH$_2$Ph), 4.21 (1H, dd, *J*=8.4, 7.8 Hz, CHC$H_A$H$_B$O), 4.17 (1H, dd, *J*=9.0, 3.0 Hz, CHCH$_A$$H_B$O), 3.93 (1H, d, *J*=10.2 Hz, H27), 3.87 (1H, dq, *J*=6.6, 1.8 Hz, H24), 3.80 (1H, dd, *J*=6.0, 1.2 Hz, H25), 3.61 (1H, br s, O*H*), 3.10 (1H, dd, *J*=13.8, 3.6 Hz, C$H_A$H$_B$Ph), 2.77 (1H, dd, *J*=13.8, 9.6 Hz, CH$_A$$H_B$Ph), 2.38 (1H, d, *J*=13.2 Hz, H29a), 1.85–1.78 (2H, m, H26 and H28), 1.57 (1H, m, H29b), 1.57 (3H, d, *J*=6.6 Hz, H32), 1.55 (3H, s, C30–C$H_3$), 1.21 (3H, d, *J*=7.2 Hz, C24–C$H_3$), 0.90 (9H, s, OSi(C$H_3$)$_3$), 0.87 (3H, d, *J*=7.2 Hz, C26–C$H_3$), 0.79 (3H, d, *J*=7.2 Hz, C28–C$H_3$), 0.09 (3H, s, OSi(C$H_3$)CH$_3$), 0.08 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; $CDCl_3$) 177.4, 153.1, 135.4, 134.7, 129.6, 129.1, 127.5, 120.3, 72.3, 66.3, 55.6, 44.2, 40.0, 39.0, 37.9, 34.8, 26.2, 26.0, 18.4, 16.4, 15.5, 13.5, 11.4, 8.7, −3.9, −4.1; IR (film, $cm^{-1}$) 3531, 3062, 3028, 2928, 2856, 1783, 1681; HRESIMS calculated for $C_{30}H_{49}NO_5Si$: 532.3453; found: 532.3454.

*4.2.14. [[3-(2S,3R,4R,5S,6S,8E)-4S]-3-(5-[tert-Butyldimethylsilyloxy]-3-triethylsilyloxyl-2,4,6,8-tetramethyl-1-oxo-dec-8-enyl)-4-(phenylmethyl)]-2-oxazolidinone (**40**).* The procedure used for the preparation of silyl ether **9** was followed with alcohol **19** (492 mg; 925 μmol), 2,6-lutidine (215 μL; 1.85 mmol), TESOTf (314 μL; 1.39 mmol) and $CH_2Cl_2$ (9 mL). Purification by column chromatography (buffered silica, 50% $CH_2Cl_2$/hexanes) gave TES ether **40** (567 mg; 95%) as a clear, colourless liquid. $R_f$=0.49 (50% $CH_2Cl_2$/hexanes); $[\alpha]_D^{20}$ +20.0 (*c* 1.15, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 7.36–7.33 (2H, m, Ar*H*), 7.30–7.26 (1H, m, Ar*H*), 7.23–7.22 (2H, m, Ar*H*), 5.18 (1H, m, H31), 4.60 (1H, m, C*H*CH$_2$Ph), 4.18 (1H, dd, *J*=9.6, 2.4 Hz, CHC$H_A$H$_B$O), 4.13 (1H, dd, *J*=9.0, 7.2 Hz, CHCH$_A$$H_B$O), 4.07 (1H, dd, *J*=6.6, 3.6 Hz, H27), 3.95 (1H, dq, *J*=6.6, 4.2 Hz, H24), 3.57 (1H, dd, *J*=3.6, 3.0 Hz, H25), 3.27 (1H, dd, *J*=13.8, 3.0 Hz, C$H_A$H$_B$Ph), 2.78 (1H, dd, *J*=13.2, 9.6 Hz, CH$_A$$H_B$Ph), 2.15 (1H, d, *J*=10.2 Hz, H29a), 1.86–1.80 (2H, m, H26 and H28), 1.72 (1H, m, H29b), 1.58 (3H, d, *J*=6.0 Hz, H32), 1.58 (3H, s, C30–C$H_3$), 1.21 (3H, d, *J*=7.2 Hz, C24–C$H_3$), 0.99 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.93 (3H, d, *J*=7.2 Hz, C26–C$H_3$), 0.91 (9H, s, OSi(C$H_3$)$_3$), 0.77 (3H, d, *J*=6.6 Hz, C28–C$H_3$), 0.64 (6H, q, *J*=7.8 Hz, OSi(C$H_2$CH$_3$)$_3$), 0.05 (3H, s, OSi(C$H_3$)CH$_3$), 0.05 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; $CDCl_3$) 175.9, 152.9, 135.4, 134.5, 129.6, 129.1, 127.5, 120.0, 76.3, 74.8, 66.0, 55.9, 42.2, 41.8, 40.8, 37.7, 36.9, 34.8, 26.3, 18.7, 16.3, 15.6, 13.5, 11.8, 7.3, 5.7, −3.2, −3.6; IR (film, $cm^{-1}$) 3027, 2956, 2878, 2857, 1784, 1701; HRESIMS calculated for $C_{36}H_{63}NO_5Si_2Na^+$: 668.4137; found: 668.4127.

*4.2.15. (2R,3S,4R,5S,6S,8E)-5-(tert-Butyldimethylsilyloxy)-3-triethylsilyloxyl-2,4,6,8-tetramethyl-dec-8-en-1-ol (**41**).* The procedure used for the preparation of alcohol **39** was followed with oxazolidinone **40** (143 mg; 221 μmol), EtOH (31 μL; 531 μmol), $LiBH_4$ (265 μL; 2 M in THF; 531 μmol) and $Et_2O$ (3 mL). Purification by column chromatography (buffered silica, 50% $CH_2Cl_2$/hexanes) gave alcohol **41** (76.9 mg; 74%) as a colourless oil. $R_f$=0.40 (50% $CH_2Cl_2$/hexanes); $[\alpha]_D^{20}$ −7.44 (*c* 1.21, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 5.19 (1H, q, *J*=6.6 Hz, H31), 3.77 (1H, d, *J*=7.2 Hz, H27), 3.57 (1H, dd, *J*=3.0, 3.0 Hz, H25), 3.52 (1H, dd, *J*=10.0, 7.8 Hz, H23a), 3.46 (1H, dd, *J*=10.0, 6.0 Hz, H23b), 2.11 (1H, d, *J*=10.0 Hz, H29a), 1.84–1.81 (1H, m, H26), 1.84–1.81 (1H, m, H24), 1.75 (1H, d, *J*=10.0 Hz, H29b), 1.76–2.74 (1H, m, H28), 1.57 (3H, d, *J*=6.6 Hz, H32), 1.57 (3H, s, C30–C$H_3$), 1.53 (1H, br s, O*H*), 0.97 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.92 (9H, s, OSi(C$H_3$)$_3$), 0.88 (3H, d *J*=6.6 Hz, C24–C$H_3$) 0.87 (3H, d, *J*=6.6 Hz, C26–C$H_3$), 0.78 (3H, d, *J*=6.0 Hz, C28–C$H_3$), 0.63 (6H, q, *J*=7.8 Hz, OSi(C$H_2$CH$_3$)$_3$), 0.07 (3H, s, OSi(C$H_3$)CH$_3$), 0.06 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; $CDCl_3$) 134.5, 120.1, 77.0, 74.8, 67.2, 42.0, 41.3, 38.0, 37.1, 26.3, 18.7, 15.9, 15.7, 14.3, 13.5, 11.2, 7.2, 5.7, −3.4, −3.4; IR (film, $cm^{-1}$) 3355, 2957, 2878, 2858; HRESIMS calculated for $C_{26}H_{56}O_3Si_2Na^+$: 495.3660; found: 495.3661.

*4.2.16. (2S,3R,4R,5S,6S,8E)-5-(tert-Butyldimethylsilyloxy)-3-triethylsilyloxyl-2,4,6,8-tetramethyl-dec-8-en-1-al (**6**).* The procedure used for the preparation of aldehyde **10** was followed with the above alcohol **41** (23.2 mg; 49.1 mmol), DMSO (10 μL; 147 μmol), $(COCl)_2$ (37 μL; 2 M in $CH_2Cl_2$; 73.7 mmol), $Et_3N$ (41 μL; 295 μmol) and $CH_2Cl_2$ (0.5 mL). Purification by column chromatography (buffered silica, 50% hexanes/$CH_2Cl_2$) gave aldehyde **6** (23.1 mg; 100%) as a colourless oil. $R_f$=0.66 (50% hexanes/$CH_2Cl_2$); $[\alpha]_D^{20}$ +18.2 (*c* 1.16, $CH_2Cl_2$); $\delta_H$ (600 MHz; $CDCl_3$) 9.69 (1H, s, H23), 5.19 (1H, q, *J*=6.6 Hz, H31), 4.17 (1H, dd, *J*=7.2, 1.8 Hz, H27), 3.61 (1H, dd, *J*=3.6, 3.0 Hz, H25), 2.45 (1H, dq, *J*=7.2, 1.8 Hz, H24), 2.10 (1H, d, *J*=10.8 Hz, H29a), 1.82 (1H, ddq, *J*=7.2, 6.6, 2.4 Hz, H26), 1.78–1.72 (1H, m, H28), 1.71 (1H, d, *J*=10.8 Hz, H29b), 1.58 (3H, d, *J*=9.0 Hz, H32), 1.57 (3H, s, C30–C$H_3$), 1.12 (3H, d, *J*=7.2 Hz, C24–C$H_3$), 0.93 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.90 (9H, s, OSi(C$H_3$)$_3$), 0.86 (3H, d, *J*=7.2 Hz, C26–C$H_3$), 0.78 (3H, d, *J*=6.0 Hz, C28–C$H_3$), 0.57 (6H, q, *J*=7.8 Hz, OSi(C$H_2$CH$_3$)$_3$), 0.07 (3H, s, OSi(C$H_3$)CH$_3$), 0.06 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; $CDCl_3$) 205.5, 134.2, 120.2, 76.2, 73.2, 49.7, 42.6, 41.0, 37.6, 26.2, 18.6, 15.6, 15.5, 13.5, 11.9, 7.7, 7.1, 5.6, −3.4, −3.6; IR (film, $cm^{-1}$) 2957, 2878, 2858, 2706, 1728.

*4.2.17. (2S,3S,4R,5S,6S,8S,11R,12R,13S,14R,15S,16S,18E)-1-(8,15-Bis(tert-butyldimethylsilyloxy)-13-triethylsilyloxy-11-hydroxy-4-methoxybenzyl)oxy-2,4,6,12,14,16,18-heptameth3-dimethyl-methylene)dioxy]-icos-18-en-9-one (**5**) and (2S,3S,4R,5S,6S,8S,11S,12R,13S,14R,15S,16S,18E)-1-(8,15-bis(tert-butyldimethylsilyloxy)-13-triethylsilyloxy-11-hydroxy-4-methoxybenzyl)oxy-2,4,6,12,14,16,18-heptamethyl-3,5-[(bis-dimethyl-methylene)dioxy]-icos-18-en-9-one (**20**).* To a stirred solution of ketone **7** (79 mg; 147 μmol) in THF (0.4 mL) at −78 °C was added LiHMDS (294 μL; 1 M in THF; 294 μmol) dropwise and the mixture stirred at −78 °C for 1 h. Aldehyde **6** (70 mg; 148 μmol) was added dropwise via cannula and the reaction mixture was stirred at −78 °C for 5 h. The reaction mixture was diluted with $Et_2O$ (3 mL) and quenched with $NaHCO_3$ (3 mL). The layers were separated and the aqueous layer extracted with $Et_2O$ (3×5 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave aldol diastereomer **5** (51.2 mg; 35%) and aldol isomer **20** (21.8 mg, 15%) (NB on one occasion when the reaction was performed on a larger scale ~130 mg ketone **7** the selectivity was observed to be reduced to ~1.5:1. This was apparently due to lack of temperature control in this latter reaction). Compound **5**: $R_f$=0.57 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ −2.20 (*c* 0.91, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 7.26 (2H, d, *J*=9.0 Hz, Ar*H*), 6.87 (2H, d, *J*=8.4 Hz, Ar*H*), 5.20 (1H, q, *J*=6.0 Hz, H31), 4.42 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 4.13 (1H, d, *J*=7.2 Hz, H27), 4.11 (1H, dd, *J*=9.0, 3.6 Hz, H20), 3.80 (3H, s, OC$H_3$), 3.77 (1H, m, H23), 3.61 (1H, dd, *J*=3.0, 3.0 Hz, H25), 3.54 (1H, dd, *J*=9.0, 4.8 Hz, H13a), 3.32 (1H, s, O*H*), 3.31 (1H, dd, *J*=9.0, 7.2 Hz, H13b), 3.25 (1H, dd, *J*=10.8,

4.2 Hz, H17), 3.22 (1H, dd, *J*=7.2, 6.0 Hz, H15), 2.96 (1H, dd, *J*=18.6, 1.8 Hz, H22a), 2.49 (1H, dd, *J*=18.6, 9.0 Hz, H22b), 2.13 (1H, d, *J*=12.0 Hz, H29a), 2.08 (1H, ddd, *J*=13.2, 9.6, 3.0 Hz, H19a), 1.93–1.88 (1H, m, H14), 1.91–1.86 (1H, m, H16), 1.81–1.76 (1H, m, H28), 1.79–1.75 (1H, m, H26), 1.74–1.68 (1H, m, H18), 1.73 (1H, dd, *J*=12.6, 10.8, H29b), 1.63 (1H, dd, *J*=9.0, 6.6 Hz, H24), 1.58 (3H, d, *J*=7.2 Hz, H32), 1.57 (3H, s, C30–C$H_3$), 1.27 (3H, s, C(C$H_3$)CH$_3$), 1.23 (3H, s, C(CH$_3$)C$H_3$), 1.08 (1H, ddd, *J*=13.2, 9.6, 4.2 Hz, H19b), 0.99 (3H, *J*=6.6 Hz, C14–C$H_3$), 0.97 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.92 (9H, s, OSiC(C$H_3$)$_3$), 0.90 (9H, s, OSiC(C$H_3$)$_3$), 0.84 (3H, d, *J*=7.2 Hz, C28–C$H_3$), 0.83 (3H, d, *J*=6.6 Hz, C16–C$H_3$), 0.81 (3H, d, *J*=6.6 Hz, C18–C$H_3$), 0.78 (3H, d, *J*=6.6 Hz, C26–C$H_3$), 0.77 (3H, d, *J*=6.6 Hz, C24–C$H_3$), 0.65 (3H, q, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.64 (3H, q, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.08 (3H, s, OSi(C$H_3$)CH$_3$), 0.07 (3H, s, OSi(C$H_3$)CH$_3$), 0.06 (3H, s, OSi(CH$_3$)C$H_3$), 0.04 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; CDCl$_3$) 216.7, 159.2, 134.6, 130.9, 129.2, 119.9, 113.8, 100.5, 77.6, 76.7, 76.6, 73.4, 72.9, 72.1, 69.2, 55.38, 55.36, 42.0, 41.6, 41.3, 39.9, 38.07, 38.02, 37.4, 35.3, 28.8, 26.3, 25.9, 25.8, 25.4, 23.6, 18.7, 18.20, 18.17, 15.8, 15.6, 15.4, 13.5, 12.4, 12.41, 12.1, 10.6, 7.3, 5.8, −3.4, −3.5, −4.6, −4.9; IR (film, cm$^{-1}$) 3527, 2957, 1706, 1613, 1586, 1513; HRESIMS calculated for $C_{56}H_{106}O_9Si_3Na^+$: 1029.7037; found: 1029.7045. Compound **20**: $R_f$=0.40 (100% CH$_2$Cl$_2$); $[\alpha]_D^{20}$ −16.0 (*c* 0.38, CHCl$_3$); $\delta_H$ (600 MHz; CDCl$_3$) 7.25 (2H, d, *J*=8.4 Hz, Ar*H*), 6.87 (2H, d, *J*=9.0 Hz, Ar*H*), 5.20 (1H, q, *J*=6.6 Hz, H31), 4.41 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 4.11 (1H, dd, *J*=9.6, 3.6 Hz, H20), 4.06 (1H, ddd, *J*=8.4, 4.2, 4.2 Hz, H23), 3.84 (1H, dd, *J*=5.4, 1.2 Hz, H27), 3.80 (3H, s, OC$H_3$), 3.53 (1H, dd, *J*=9.0, 4.8 Hz, H13a), 3.49 (1H, dd, *J*=4.8, 1.2 Hz, H25), 3.31 (1H, dd, *J*=9.0, 7.2 Hz, H13b), 3.24 (1H, dd, *J*=10.2, 3.6 Hz, H17), 3.22 (1H, dd, *J*=6.0, 5.4 Hz, H15), 3.02 (1H, s, O*H*), 2.73 (1H, dd, *J*=18.0, 4.3 Hz, H22a), 2.66 (1H, dd, *J*=18.0, 8.4 Hz, H22b), 2.09 (1H, d, *J*=9.6 Hz, H29a), 2.06 (1H, ddd, *J*=13.8, 7.8, 3.0 Hz, H19a), 1.93–1.89 (1H, m, H14), 1.91–1.87 (1H, m, H16), 1.90–1.84 (1H, m, H28), 1.80–1.72 (1H, m, H26), 1.79–1.76 (1H, dd, *J*=12.6, 10.8, H29b), 1.76–1.70 (1H, m, H18), 1.72–1.67 (1H, m, H24), 1.59 (3H, s, C30–C$H_3$), 1.58 (3H, d, *J*=7.2 Hz, H32), 1.26 (3H, s, C(C$H_3$)CH$_3$), 1.22 (3H, s, C(CH$_3$)C$H_3$), 1.07 (1H, ddd, *J*=13.2, 10.2, 3.6 Hz, H19b), 0.99 (3H, *J*=7.2 Hz, C14–C$H_3$), 0.97 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.93 (3H, d, *J*=6.6 Hz, C24–C$H_3$), 0.91 (9H, s, OSiC(C$H_3$)$_3$), 0.90 (9H, s, OSiC(C$H_3$)$_3$), 0.90 (3H, d, *J*=7.2 Hz, C28–C$H_3$), 0.83 (3H, d, *J*=6.6 Hz, C16–C$H_3$), 0.82 (3H, d, *J*=6.0 Hz, C18–C$H_3$), 0.78 (3H, d, *J*=6.0 Hz, C26–C$H_3$), 0.64 (6H, q, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.06 (6H, s, OSi(C$H_3$)CH$_3$), 0.05 (3H, s, OSi(CH$_3$)C$H_3$), 0.04 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; CDCl$_3$) 214.4, 159.2, 134.3, 130.9, 129.3, 120.2, 113.86, 100.4, 98.9, 77.3, 76.58, 76.55, 73.3, 72.9, 72.1, 71.4, 55.4, 42.01, 41.98, 41.7, 39.0, 38.0, 37.9, 36.2, 35.3, 33.1, 28.9, 26.3, 25.9, 25.4, 23.6, 18.7, 18.3, 16.1, 15.7, 15.3, 14.3, 13.5, 12.5, 12.3, 9.1, 7.2, 5.76, 5.74, −3.30, −3.35, −4.4, −4.9; IR (film, cm$^{-1}$) 3504, 2951, 1712, 1613, 1586, 1513; HRESIMS calculated for $C_{56}H_{106}O_9Si_3Na^+$: 1029.7037; found: 1029.7040.

*4.2.18. (2S,3S,4R,5S,6S,8S,11S,12R,13S,14R,15S,16S,18E)-1-(8,15-Bis(tert-butyldimethylsilyloxy)-13-triethylsilyloxy-11-methoxy-4-methoxybenzyl)oxy-2,4,6,12,14,16,18-heptamethyl-3,5-[(bis-dimethyl-methylene)dioxy]-icos-18-en-9-one (**42**).* To a stirred solution of aldol diastereomer **20** (53.5 mg; 53.1 μmol) in CH$_2$Cl$_2$ (1.1 mL) at 0 °C was added sequentially 4 Å molecular sieves (100 mg), proton sponge (68.3 mg; 319 μmol) and Me$_3$OBF$_4$ (47.2 mg; 319 μmol). The reaction was warmed to rt for 1 h, before quenching by addition of satd aq NaHCO$_3$ (2 mL). The layers were separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (3×5 mL). The combined organic extracts were dried (Na$_2$SO$_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 100% CH$_2$Cl$_2$) gave methyl ether **42** (41.4 mg; 76%). $R_f$=0.52 (100% CH$_2$Cl$_2$); $[\alpha]_D^{20}$ −11.0 (*c* 1.00, CHCl$_3$); $\delta_H$ (600 MHz; CDCl$_3$) 7.25 (2H, d, *J*=9.0 Hz, Ar*H*), 6.87 (2H, d, *J*=9.0 Hz, Ar*H*), 5.20 (1H, q, *J*=6.0 Hz, H31), 4.42 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 4.16 (1H, dd, *J*=10.2, 3.0 Hz, H20), 3.82 (1H, d, *J*=5.4 Hz, H27), 3.80 (3H, s, ArOC$H_3$), 3.62 (1H, ddd, *J*=7.8, 4.8, 3.0 Hz, H23), 3.54 (1H, dd, *J*=9.6, 5.4 Hz, H13a), 3.47 (1H, d, *J*=5.4 Hz, H25), 3.32 (1H, dd, *J*=9.0, 6.6 Hz, H13b), 3.26 (1H, dd, *J*=9.6, 3.6 Hz, H17), 3.25 (3H, s, C23–OC$H_3$), 3.23 (1H, dd, *J*=6.6, 6.0 Hz, H15), 2.80 (2H, dd, *J*=18.0, 8.4 Hz, H22a), 2.55 (1H, dd, *J*=18.0, 3.0 Hz, H22b), 2.09 (1H, d, *J*=10.2 Hz, H29a), 2.04 (1H, ddd, *J*=12.6, 9.6, 1.8 Hz, H19a), 1.94–1.88 (1H, m, H14), 1.91–1.85 (1H, m, H24), 1.90–1.84 (1H, m, H16), 1.85–1.80 (1H, m, H26), 1.85–1.80 (1H, m, H28), 1.83–1.78 (1H, m, H29b), 1.77–1.72 (1H, m, H18), 1.58 (3H, d, *J*=6.6 Hz, H32), 1.57 (3H, s, C30C$H_3$), 1.26 (3H, s, C(C$H_3$)CH$_3$), 1.22 (3H, s, C(CH$_3$)C$H_3$), 1.12 (1H, ddd, *J*=12.6, 10.2, 4.8 Hz, H19b), 1.00 (3H, d, *J*=6.6 Hz, C14–C$H_3$), 0.98 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.91 (9H, s, OSiC(C$H_3$)$_3$), 0.91 (9H, s, OSiC(C$H_3$)$_3$), 0.89 (3H, d, *J*=6.6 Hz, C26–C$H_3$), 0.87 (3H, d, *J*=7.2 Hz, C24–C$H_3$), 0.83 (3H, d, *J*=6.6 Hz, C18–C$H_3$), 0.81 (3H, d, *J*=6.6 Hz, C28–C$H_3$), 0.79 (3H, d, *J*=6.6 Hz, C16–C$H_3$), 0.65 (6H, q, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.07 (3H, s, OSi(C$H_3$)CH$_3$), 0.06 (3H, s, OSi(C$H_3$)CH$_3$), 0.05 (3H, s, OSi(CH$_3$)C$H_3$), 0.03 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; CDCl$_3$) 212.5, 159.2, 134.4, 131.0, 129.3, 120.0, 113.8, 100.4, 80.0, 77.5, 77.2, 76.6, 73.4, 72.9, 72.5, 72.2, 58.0, 55.4, 42.9, 41.1, 39.5, 38.1, 37.4, 37.2, 35.8, 35.3, 28.9, 26.3, 25.9, 25.2, 23.5, 18.7, 18.4, 16.6, 15.6, 15.0, 14.3, 13.5, 12.5, 12.2, 11.3, 7.4, 5.9, −3.3, −4.4, −4.96, −5.03; IR (film, cm$^{-1}$) 2957, 2857, 1716, 1700, 1615, 1514.

*4.2.19. (2S,3S,4R,5S,6S,8S,11S,12R,13S,14R,15S,16S,18E)-1-(8,15-Bis(tert-butyldimethylsilyloxy)-13-triethylsilyloxy-11-methoxy-4-methoxybenzyl)oxy-2,4,6,12,14,16,18-heptamethyl-3,5-[(bis-dimethyl-methylene)dioxy]-icos-18-en-9-one (**43**).* The procedure used for the preparation of methyl ether **42** was followed with aldol diastereomer **5** (68.4 mg; 67.9 μmol) 4 Å molecular sieves (130 mg), proton sponge (87.3 mg; 407 μmol), Me$_3$OBF$_4$ (60.2 mg; 407 μmol) and CH$_2$Cl$_2$ (1.4 mL). Purification by column chromatography (buffered silica, 100% CH$_2$Cl$_2$) gave methyl ether **43** (53.9 mg; 78%). $R_f$=0.43 (100% CH$_2$Cl$_2$); $\delta_H$ (600 MHz; CDCl$_3$) 7.25 (2H, d, *J*=8.4 Hz, Ar*H*), 6.87 (2H, d, *J*=8.4 Hz, Ar*H*), 5.20 (1H, q, *J*=6.6 Hz, H31), 4.42 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 4.17 (1H, dd, *J*=9.6, 3.0 Hz, H20), 3.83 (1H, d, *J*=5.4 Hz, H27), 3.80 (3H, s, ArOC$H_3$), 3.64 (1H, ddd, *J*=10.2, 7.8, 3.0 Hz, H23), 3.54 (1H, dd, *J*=9.0, 4.8 Hz, H13a), 3.53 (1H, m, H25), 3.31 (1H, dd, *J*=9.0, 6.6 Hz, H13b), 3.25 (1H, dd, *J*=9.0, 3.6 Hz, H17), 3.22 (3H, s, C23–OC$H_3$), 3.22 (1H, m, H15), 2.80 (1H, dd, *J*=17.4, 8.4 Hz, H22a), 2.55 (1H, dd, *J*=17.4, 3.0 Hz, H22b), 2.10 (1H, ddd, *J*=13.2, 10.2, 2.4 Hz, H19a), 2.08 (1H, d, *J*=8.4 Hz, H29a), 1.93–1.89 (1H, m, H14), 1.92–1.86 (1H, m, H24), 1.86–1.81 (3H, m, H16), 1.84–1.79 (1H, m, H26), 1.82–1.77 (1H, m, H28), 1.79 (1H, d, *J*=7.8 Hz, H29b), 1.77–1.71 (1H, m, H18), 1.59 (3H, d, *J*=5.4 Hz, H32), 1.58 (3H, s, C30–C$H_3$), 1.26 (3H, s, C(C$H_3$)CH$_3$), 1.22 (3H, s, C(CH$_3$)C$H_3$), 1.10 (1H, ddd, *J*=13.8, 10.2, 3.6 Hz, H19b), 0.99 (3H, d, *J*=6.6 Hz, C14–C$H_3$), 0.97 (9H, t, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.92 (9H, s, OSiC(C$H_3$)$_3$), 0.91 (9H, s, OSiC(C$H_3$)$_3$), 0.89 (3H, d, *J*=7.2 Hz, C26–C$H_3$), 0.83 (3H, d, *J*=6.6 Hz, C24–C$H_3$), 0.83 (3H, d, *J*=6.6 Hz, C18–C$H_3$), 0.80 (3H, d, *J*=6.0 Hz, C28–C$H_3$), 0.79 (3H, d, *J*=7.2 Hz, C16–C$H_3$), 0.63 (6H, q, *J*=7.8 Hz, OSi(CH$_2$C$H_3$)$_3$), 0.07 (6H, s, OSi(C$H_3$)CH$_3$), 0.06 (3H, s, OSi(CH$_3$)C$H_3$), 0.04 (3H, s, OSi(CH$_3$)C$H_3$); $\delta_C$ (151 MHz; CDCl$_3$) 212.4, 159.2, 134.4, 131.0, 129.3, 120.1, 113.8, 100.4, 79.8, 77.7, 76.6, 76.2. 73.7, 73.4, 72.9, 72.2, 57.2, 55.4, 42.5, 41.7, 40.2, 38.1, 37.7, 37.5, 36.8, 35.3, 28.9, 26.3, 26.0, 25.2, 23.6, 18.7, 18.3, 16.0, 15.7, 15.1, 14.3, 13.5, 12.5, 11.9, 10.3, 7.3, 5.8, −3.4, −3.6, −4.4, −5.0; IR (film, cm$^{-1}$) 2925, 1717, 1613, 1586, 1513; HRESIMS calculated for $C_{57}H_{108}O_9Si_3Na^+$: 1043.7193; found: 1043.7197.

*4.2.20. (2R,4S,5R,6S)-2-[(1S,3S,4S,5R,6S,7S)-1-(tert-Butyldimethylsilyloxy)-8-(4-methoxyphenyl)oxy-3,5,7-trimethyl-4,6-[(bis-dimethyl-methylene)dioxy]-octanyl]-5-[(1S,2S,3S,5E)-2-(tert-butyldimethylsilyloxy)-1,3,5-trimethyl-hept-5-enyl]-2-hydroxy-4-methoxyl-5-methyl-tetrahydro-2H-pyran (**21**).* To a Teflon cylinder containing TES ether **42** (41.4 mg; 40.5 μmol) was added buffered pyridinium

hydrofluoride (1 mL) from a stock solution containing dry THF (10 mL), pyridine (5 mL), pyridinium hydrofluoride (2.1 g) and $H_2O$ (32 μL). The resulting solution was stirred at rt for 5 days, then diluted with $Et_2O$ (15 mL), washed with satd aq $CuSO_4$ (10 mL), satd aq $NaHCO_3$ (10 mL) and brine (10 mL), dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 15% EtOAc/hexanes) gave hemiacetal **21** (6.1 mg; 17%) as a clear, colourless oil. The low yield of this reaction was in part attributed to the limited solubility of the product in the extraction solvent. $R_f$=0.54 (100% $CH_2Cl_2$); $[\alpha]_D^{20}$ +6.57 (*c* 0.31, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 7.25 (2H, d, *J*=9.0 Hz, Ar*H*), 6.87 (2H, d, *J*=9.0 Hz, Ar*H*), 5.17 (1H, q, *J*=6.6 Hz, H31), 4.92 (1H, s, C21−O*H*), 4.42 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 3.92 (1H, d, *J*=5.4 Hz, H23), 3.90 (1H, d, *J*=9.0 Hz, H25), 3.80 (3H, s, ArOC$H_3$), 3.54 (1H, dd, *J*=9.0, 4.8 Hz, H13a), 3.51 (1H, d, *J*=3.0 Hz, H27), 3.47 (1H, d, *J*=9.0 Hz, H20), 3.35 (3H, s, C23−OC$H_3$), 3.32 (1H, dd, *J*=9.0, 7.2 Hz, H13b), 3.22 (1H, dd, *J*=9.6, 3.0 Hz, H17), 3.21 (1H, dd, *J*=6.6, 5.4 Hz, H15), 2.31 (1H, d, *J*=12.6 Hz, H29a), 1.95−1.90 (1H, m, H24), 1.94−1.89 (1H, m, H14), 1.93−1.87 (1H, m, H19a), 1.89−1.85 (1H, m, H22a), 1.88−1.84 (1H, m, H16), 1.71−1.66 (4H, m, H18, H22b, H26 and H28), 1.60−1.55 (1H, m, H29b), 1.57 (3H, d, *J*=7.2 Hz, H32), 1.55 (3H, s, C30−C$H_3$), 1.27−1.23 (1H, m, H19b), 1.24 (3H, s, OC(C$H_3$)$CH_3$), 1.24 (3H, s, OC($CH_3$)C$H_3$), 0.99 (3H, d, *J*=6.6 Hz, C14−C$H_3$), 0.90 (9H, s, OSiC(C$H_3$)$_2$), 0.89 (9H, s, OSiC(C$H_3$)$_2$), 0.87 (3H, d, *J*=7.2 Hz, C24−C$H_3$), 0.84 (3H, d, *J*=6.6 Hz, C16−C$H_3$), 0.79 (3H, d, *J*=7.2 Hz, C28−C$H_3$), 0.77 (3H, d, *J*=6.6 Hz, C18−C$H_3$), 0.75 (3H, d, *J*=6.6 Hz, C26−C$H_3$), 0.12 (3H, s, OSi(C$H_3$)$CH_3$), 0.08 (3H, s, OSi(C$H_3$)$CH_3$) 0.08 (6H, s OSi($CH_3$)C$H_3$); $\delta_C$ (151 MHz, $CDCl_3$) 159.2, 134.9, 131.0, 129.3, 120.0, 113.8, 100.3, 98.7, 81.6, 77.6, 75.8, 72.9, 72.3, 61.8, 56.5, 55.4, 43.9, 38.2, 37.5, 36.9, 35.4, 29.9, 29.4, 26.5, 26.4, 25.8, 25.3, 23.6, 18.8, 18.6, 15.7, 15.5, 15.0, 14.3, 14.2, 13.5, 12.9, 10.1, 9.9, −3.0, −3.82, −3.88, −4.3; IR (film, $cm^{-1}$) 3488, 2930, 2856, 1731, 1613, 1586, 1513.

*4.2.21. (2R,4R,5R,6S)-2-[(1S,3S,4S,5R,6S,7S)-1-(tert-Butyldimethylsilyloxy)-8-(4-methoxyphenyl)oxy-3,5,7-trimethyl-4,6-[(bis-dimethylmethylene)dioxy]-octanyl]-5-[(1S,2S,3S,5E)-2-(tert-butyldimethylsilyloxy)-1,3,5-trimethyl-hept-5-enyl]-2-hydroxy-4-methoxyl-5-methyl-tetrahydro-2H-pyran (**22**).* The procedure used for the preparation of minor hemiacetal **21** was followed with TES ether **43** (53.9 mg; 52.8 μmol), HF/pyr/pyr (1 mL) and $H_2O$ (40 μL). Purification by column chromatography (buffered silica, 15% EtOAc/hexanes) gave hemiacetal **21** (6.5 mg; 14%) as a clear, colourless oil. The low yield of this reaction was in part attributed to the limited solubility of the product in the extraction solvent. $R_f$=0.43 (15% EtOAc/hexanes); $[\alpha]_D^{20}$ +22.2 (*c* 0.36, $CHCl_3$); $\delta_H$ (600 MHz; $CDCl_3$) 7.25 (2H, d, *J*=9.0 Hz, Ar*H*), 6.87 (2H, d, *J*=8.4 Hz, Ar*H*), 5.14 (1H, q, *J*=6.6 Hz, H31), 4.41 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 3.82 (1H, d, *J*=5.4 Hz, H25), 3.80 (3H, s, ArOC$H_3$), 3.69 (1H, ddd, *J*=11.4, 4.8, 4.2 Hz, H23), 3.58 (1H, dd, *J*=10.2, 1.2 Hz, H27), 3.53 (1H, dd, *J*=9.0, 4.8 Hz, H13a), 3.51 (1H, dd, *J*=9.0, 1.8 Hz, H20), 3.35 (3H, s, C23−OC$H_3$), 3.31 (1H, dd, *J*=9.0, 6.6 Hz, H13b), 3.21 (1H, d, *J*=10.8 Hz, H17), 3.18 (1H, dd, *J*=12.6, 1.8 Hz, H15), 2.18 (1H, d, *J*=13.2 Hz, H29a), 2.08 (1H, m, H22a), 2.03 (1H, ddd, *J*=14.4, 9.0, 3.0 Hz, H19a), 1.94−1.88 (1H, m, H14), 1.89−1.84 (1H, m, H16), 1.73−1.68 (5H, m, H18, H22b, H24, H26 and H28), 1.55−1.50 (1H, m, H29b), 1.55 (3H, d, *J*=6.6 Hz, H32), 1.54 (3H, s, C30−C$H_3$), 1.20 (3H, s, OC(C$H_3$)$CH_3$), 1.18 (3H, s, OC($CH_3$)C$H_3$), 1.09 (1H, ddd, *J*=14.4, 10.2, 1.8 Hz, H19b), 0.99 (3H, d, *J*=6.6 Hz, C14−C$H_3$), 0.92 (9H, s, OSiC(C$H_3$)$_2$), 0.90 (9H, s, OSiC(C$H_3$)$_2$), 0.83 (3H, d, *J*=6.6 Hz, C16−C$H_3$), 0.79 (3H, d, *J*=6.6 Hz, C24−C$H_3$), 0.76 (3H, d, *J*=7.2 Hz, C28−C$H_3$), 0.74 (6H, d, *J*=6.6 Hz, C18−C$H_3$), 0.74 (3H, d, *J*=6.6 Hz, C26−C$H_3$), 0.09 (6H, s, OSi(C$H_3$)$CH_3$), 0.06 (3H, s, OSi($CH_3$)C$H_3$) 0.02 (3H, s OSi($CH_3$)C$H_3$); $\delta_C$ (151 MHz; $CDCl_3$) 159.2, 134.7, 131.0, 129.3, 120.0, 113.8, 100.4, 97.8, 77.4, 76.6, 76.5, 75.1, 73.8, 73.1, 72.9, 72.2, 55.44, 55.41, 44.1, 38.2, 38.1, 36.6, 36.0, 35.3, 31.9, 31.5, 29.5, 26.23, 26.19, 25.9, 25.1, 23.6, 23.3, 18.5, 18.4, 15.7, 15.6, 15.5, 14.7, 14.3, 13.5, 12.8, 10.7, 3.8, −3.68, −3.72, −3.9, −4.3; IR (film, $cm^{-1}$) 3377, 2930, 2857, 1717, 1613, 1513; HRESIMS calculated for $C_{51}H_{94}O_9Si_2Na^+$: 929.6329; found: 929.6323.

*4.2.22. (2S,3R,7R,9S,11S)-2-[(1S,2S,3S,5E)-2-(tert-Butyldimethylsilyloxy)-1,3,5-trimethyl-hept-5-enyl]-8-[(1S,2S,3S)-4-(2-hydroxy-(4-methoxyphenyl)oxy-1,3-dimethyl)-11-(tert-butyldimethylsilyloxy)-3,9-dimethyl-1,7-dioxaspiro[6,6]undec-4-ene (**33**).* To a stirred solution of hemiacetal **21** (6.1 mg; 6.72 μmol) in MeOH (0.5 mL) was added a few crystals of CSA and the resulting solution stirred at rt for 16 h before quenching by addition of satd aq $NaHCO_3$ (5 mL). The mixture was extracted with $CH_2Cl_2$ (3×5 mL) and the combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave elimination product **33** (1.1 mg; 20%). $R_f$=0.61 (100% $CH_2Cl_2$); $\delta_H$ (600 MHz; $CDCl_3$) 7.23 (2H, d, *J*=8.4 Hz, Ar*H*), 6.84 (2H, d, *J*=9.0 Hz, Ar*H*), 5.96 (1H, dd, *J*=10.2, 6.6 Hz, H23), 5.76 (1H, dd, *J*=10.2, 0.6 Hz, H22), 5.20 (1H, q, *J*=6.6 Hz, H31), 3.84 (1H, dd, *J*=10.2, 1.2 Hz, H25), 3.79 (1H, dd, *J*=6.6, 1.8 Hz, H17), 3.79 (3H, s, OC$H_3$), 3.56 (1H, dd, *J*=8.4, 4.8 Hz, H13a), 3.56−3.53 (1H, m, H27), 3.54 (1H, dd, *J*=9.0, 3.0 Hz, H15), 3.47 (1H, dd, *J*=6.6, 6.0 Hz, H13b), 3.38 (1H, dd, *J*=3.6, 1.8 Hz, H20), 3.29 (1H, br s, O*H*), 2.19 (1H, d, *J*=16.2 Hz, H29a), 2.17−2.10 (1H, m, H18), 2.06−2.00 (2H, m, H24 and H28), 1.90−1.86 (3H, m, H14, H16 and H26), 1.76 (1H, ddd, *J*=14.4, 13.2, 1.8 Hz, H19a), 1.71 (1H, dd, *J*=13.2, 10.2 Hz, H29b), 1.58 (3H, s, H32), 1.58 (3H, s, C30−C$H_3$), 1.50 (1H, ddd, *J*=13.2, 3.6, 3.0 Hz, H19b), 1.25 (6H, s, OC(C$H_3$)$_2$), 1.05 (3H, d, *J*=6.6 Hz, C14−C$H_3$), 0.96 (3H, d, *J*=7.2 Hz, C16−C$H_3$), 0.90 (9H, s, OSiC(C$H_3$)$_3$), 0.89 (9H, s, OSiC(C$H_3$)$_3$), 0.86 (3H, d, *J*=7.2 Hz, C24−C$H_3$), 0.84 (3H, d, *J*=6.6 Hz, C28−C$H_3$), 0.78 (6H, d, *J*=6.6 Hz, C18−C$H_3$ and C26−C$H_3$), 0.02 (3H, s, OSi(C$H_3$)$CH_3$), 0.00 (3H, s, OSi(C$H_3$)$CH_3$), 0.00 (3H, s, OSi($CH_3$)C$H_3$), −0.01 (3H, s, OSi($CH_3$)C$H_3$).

*4.2.23. (2S,3R,7R,9S,11S)-2-[(1S,2S,3S,5E)-2-(tert-Butyldimethylsilyloxy)-1,3,5-trimethyl-hept-5-enyl]-8-[(1S,2S,3S)-2-hydroxy-4-(4-methoxyphenyl)oxy-1,3-dimethyl]-11-(tert-butyldimethylsilyloxy)-4-methoxy-3,9-dimethyl-1,7-dioxaspiro[6,6]undecane (**34**).* The procedure used for the preparation of spiroacetal **23** was followed with hemiacetal **22** (6.4 mg; 7.05 μmol), CSA (a few crystals) and MeOH (0.5 mL). Purification by column chromatography (buffered silica, 100% $CH_2Cl_2$) gave spiroacetal **34** (1.3 mg; 22%) as a clear, colourless oil. $R_f$=0.37 (100% $CH_2Cl_2$); $\delta_H$ (600 MHz; $CDCl_3$) 7.23 (2H, d, *J*=9.0 Hz, Ar*H*), 6.85 (2H, d, *J*=8.4 Hz, Ar*H*), 5.19 (1H, q, *J*=6.6 Hz, H31), 4.42 (2H, ABq, *J*=11.4 Hz, OC$H_2$PMP), 3.79 (3H, s, ArOC$H_3$), 3.78 (2H, d, *J*=7.8 Hz, H25), 3.73 (1H, dd, *J*=10.8, 1.2 Hz, H17), 3.64 (1H, dd, *J*=9.0, 4.8 Hz, H13a), 3.50 (1H, m, H23), 3.50 (1H, m, H27), 3.48 (1H, m, H13b), 3.45 (1H, m, H15), 3.37 (1H, br s, H20), 3.31 (3H, s, C23−OC$H_3$), 3.02 (1H, d, *J*=7.8 Hz, O*H*), 2.15 (1H, d, *J*=12.6 Hz, H29a), 2.14−2.09 (1H, m, H26), 2.09−2.04 (1H, m, H18), 2.00 (1H, dd, *J*=13.2, 4.8 Hz, H22a), 1.95−1.90 (1H, m, H28), 1.93−1.88 (1H, m, H14), 1.92−1.87 (1H, m, H24), 1.80 (1H, dq, *J*=7.2, 6.6 Hz, H16), 1.74 (1H, dd, *J*=12.6, 1.8 Hz, H19a), 1.71 (1H, dd, *J*=13.2, 6.0 Hz, H29b), 1.57 (3H, d, *J*=6.6 Hz, H32), 1.55 (3H, s, C30−C$H_3$), 1.49 (1H, ddd, *J*=13.2, 3.6, 3.0 Hz, H19b), 1.17 (1H, dd, *J*=12.6, 12.6 Hz, H22b), 1.09 (3H, d, *J*=7.2 Hz, C14−C$H_3$), 0.91 (3H, d, *J*=6.6 Hz, C16−C$H_3$), 0.89 (9H, s, OSiC(C$H_3$)$_3$), 0.89 (9H, s, OSiC(C$H_3$)$_3$), 0.84 (3H, d, *J*=7.2 Hz, C28−C$H_3$), 0.77 (6H, d, *J*=6.6 Hz, C18−C$H_3$ and C24−C$H_3$), 0.74 (3H, d, *J*=6.6 Hz, C26−C$H_3$), 0.04 (3H, s, OSi(C$H_3$)$CH_3$), 0.04 (3H, s, OSi(C$H_3$)$CH_3$), −0.01 (3H, s, OSi($CH_3$)C$H_3$), −0.03 (3H, s, OSi($CH_3$)C$H_3$); $\delta_C$ (600 MHz; $CDCl_3$) 130.7, 129.3, 119.5, 113.8, 112.8, 98.5, 76.8, 76.7, 73.3, 72.2, 70.8, 55.4, 55.2, 53.6, 40.2, 38.1, 37.9, 36.8, 36.0, 35.7, 33.3, 32.4, 29.9, 26.3, 25.9, 24.3, 18.7, 18.6, 18.1, 17.8, 16.2, 15.6, 13.6, 12.5, 11.0, 4.2, −3.2, −4.3, −4.2, −4.8; HRESIMS calculated for $C_{48}H_{88}O_8Si_2Na^+$: 871.5910; found: 871.5910. $\delta_H$ (600 MHz, $C_6D_6$) $\delta$ 7.16 (2H, d, *J*=9.0 Hz, Ar*H*), 6.81 (2H, d, *J*=9.0 Hz, Ar*H*), 5.44 (1H, q, *J*=6.6 Hz, H31), 4.27 (1H, d, *J*=12.0 Hz, OC$H_AH_B$PMP), 4.26 (1H, s,

O*H*), 4.24 (1H, d, *J*=5.4 Hz, H25), 4.17 (1H, dd, *J*=10.8, 1.8 Hz, H17), 4.16 (1H, d, *J*=11.4 Hz, $OCH_AH_B$PMP), 3.97 (1H, dd, *J*=10.2, 1.8 Hz, H27), 3.86 (1H, ddd, *J*=11.4, 4.8, 4.2 Hz, H23), 3.77 (1H, ddd,=9.0, 9.0, 3.6 Hz, H15), 3.66 (1H, dd, *J*=3.0, 2.4 Hz, H20), 3.62 (1H, dd, *J*=9.0, 3.6 Hz, H13a), 3.32 (3H, s, ArO$CH_3$), 3.27 (1H, dd, *J*=9.0, 3.0 Hz, H13b), 3.12 (3H, s, C23–O$CH_3$), 2.53 (1H, d, 13.8 Hz, H29a), 2.46 (1H, dd, *J*=13.2, 4.2 Hz, H22a), 2.37–2.31 (1H, m, H28), 2.31–2.26 (1H, m, H18), 2.30–2.25 (1H, m, H26), 2.24–2.18 (1H, m, H24), 2.11 (1H, dd, *J*=13.8, 10.2 Hz, H29b), 2.08 (1H, ddd, *J*=13.2, 13.2, 1.2 Hz, H19a), 1.89–1.86 (1H, m, H16), 1.86–1.83 (1H, m, H14), 1.70 (3H, s, C30–$CH_3$), 1.66 (1H, ddd, *J*=13.2, 3.6, 2.4 Hz, H19b), 1.59–1.55 (1H, m, H22b), 1.57 (3H, d, *J*=6.6 Hz, H32), 1.30 (3H, d, *J*=7.2 Hz, C14–$CH_3$), 1.26 (3H, d, *J*=7.2 Hz, C28–$CH_3$), 1.13 (9H, s, OSiC($CH_3$)$_3$), 1.04 (3H, d, *J*=7.2 Hz, C24–$CH_3$), 1.03 (3H, d, *J*=7.2 Hz, C18–$CH_3$), 1.00 (9H, s, OSiC($CH_3$)$_3$), 0.99 (3H, d, *J*=7.2 Hz, C16–$CH_3$), 0.89 (3H, d, *J*=7.8 Hz, C26–$CH_3$), 0.33 (3H, s, OSi($CH_3$)$CH_3$), 0.21 (3H, s, OSi($CH_3$)$CH_3$), 0.01 (6H, s, OSi($CH_3$)$CH_3$).

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## Supplementary data

Copies of NMR spectra for all new compounds are available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.06.012.

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