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Synthesis of the novel 1,7,9-trioxadispiro[4.1.5.2]-tetradecane ring system present in the spirolides

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Abstract—A synthesis of bis-spiroacetal **13** which constitutes the bis-spiroacetal moiety of the complex marine biotoxins, spirolides **1** and **2** is described. The synthetic strategy adopted is based on assembly of a suitably protected acyclic hydroxyketone precursor. Key intermediate **25** was synthesised as a mixture of diastereomers from 1,3-propanediol using an iterative Grignard addition/hydroboration strategy and converted to *cis*-enone **28**. Attempted acid catalysed cyclisation of **28** to a spiroacetal was unsuccessful, however, the analagous saturated precursor **30** readily afforded spiroacetal **31**. Oxidative cyclisation of **31** then gave bis-spiroacetal **32**. In an alternative route, bis-spiroacetal **32** was synthesised by selective deprotection of diketone **34**. Selective deprotection of acetylene **25** gave methoxyl acetal **36** which formed unsaturated spiroacetal **37** upon semi-hydrogenation. Finally, oxidative cyclisation of bis-spiroacetal **37** afforded the target bis-spiroacetal **13**.

1. Introduction

Spirolides B **1** and D **2** were isolated in 1995 from the digestive glands of mussels (*Mytilus edulis*) and scallops (*Placopecten magellanicus*) collected off the coast of Nova Scotia.[1] They cause potent and characteristic symptoms in the mouse bioassay (LD_{100} 250 μgkg^{-1} i.p.) and were discovered to be weak activators (1.7 $\mu mol.dm^{-3}$ of type L calcium channels. However, their mode of action has not been established and their toxicological properties are still under investigation. These compounds contain a 6,5,5 bis-spiroacetal moiety as well as a seven-membered spiro-linked cyclic iminium group and are structurally related to the pinnatoxins **3–6**, which are potent calcium channel activators and are responsible for outbreaks of shellfish poisoning in China and Japan.[2,3] To date, there has been no reported synthesis of the spirolides and the relative and absolute stereochemistry of these molecules is yet to be determined. However, Kishi et al. have reported a total synthesis of pinnatoxin A **3** which allowed assignment of the absolute stereochemistry of these molecules (Fig. 1).[4]

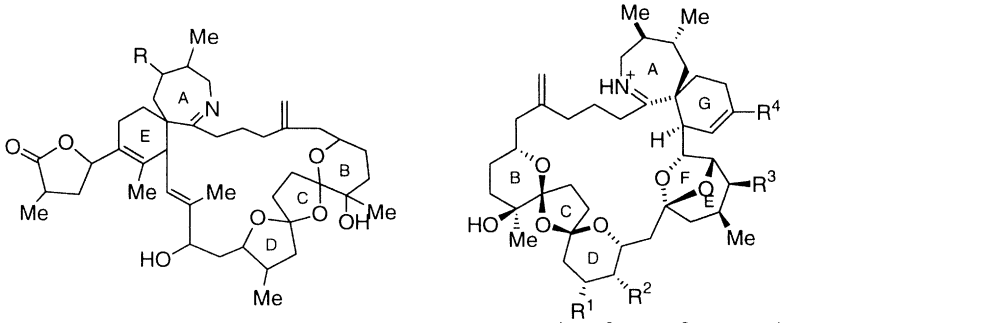

Figure 1.

Keywords: spirocetals; spirolides; oxidative cyclisation.

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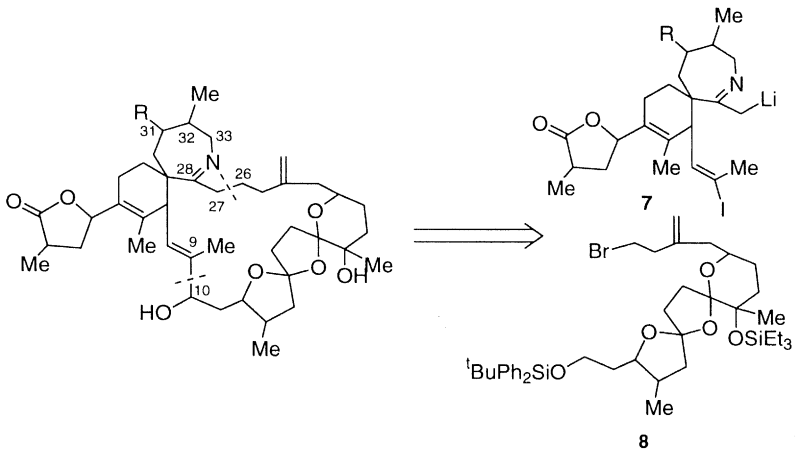


Scheme 1.

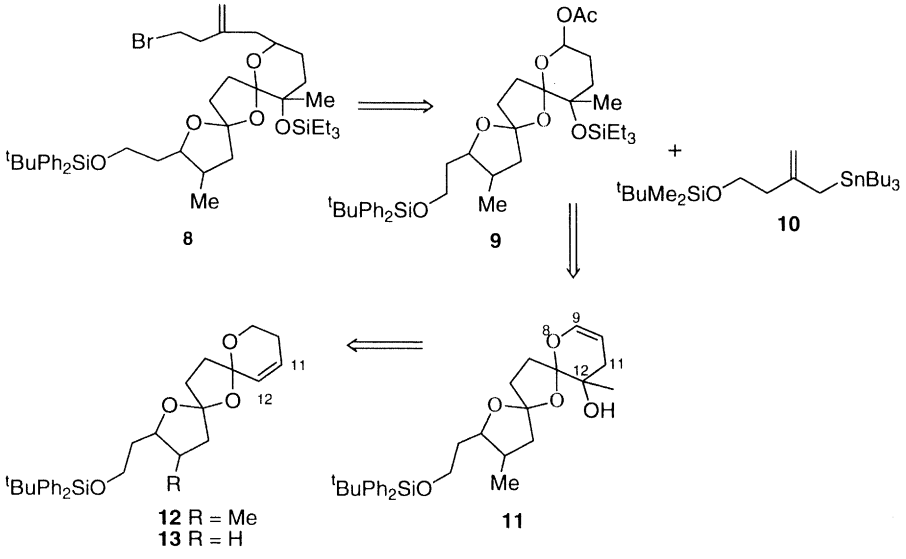
The novel structure and potent biological activity of the spirolides prompted us to embark on their synthesis. The synthetic strategy we adopted hinged on formation of the C27–C26 bond via alkylation of a pre-assembled spiro imine **7** with a functionalised bis-spiroacetal **8** (Scheme 1). The final C9–C10 bond is then constructed using a Ni(II)-Cr(II)-mediated, Kishi–Nozaki coupling between the vinyl iodide moiety at C9 and an aldehyde functionality at C10.[5a–c]

The retrosynthetic plan for the synthesis of **8** is based on studies previously carried out in our research group on related bicyclic spiroacetal systems. It is planned to introduce the allyl side chain using a Lewis acid mediated addition of a functionalised allyl stannane **10** to anomeric acetate **9** (Scheme 2).[6] Acetate **9** is available from hydration of unsaturated bis-spiroacetal **11** which, in turn is synthesised from alkene **12**. Thus, epoxidation of **12** followed by base induced rearrangement of the epoxide, using conditions previously developed for an analogous bicyclic system[7]provides a hydroxyl group at C12 required for introduction of the necessary tertiary alcohol.

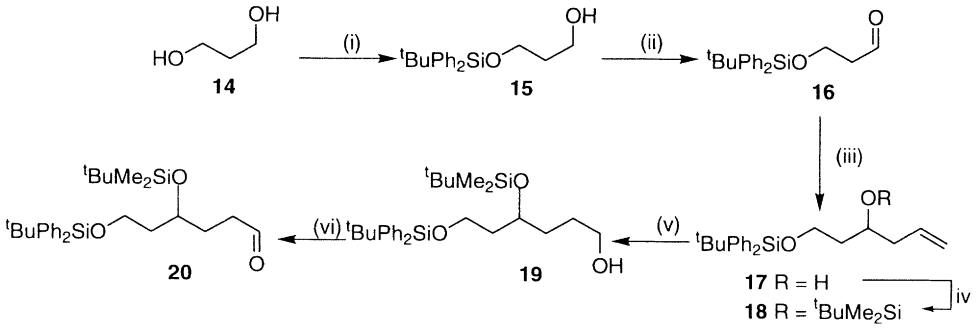
Unsaturated bis-spiroacetal **12**, which possesses all the functionality required for conversion to key intermediate **8** is therefore our initial target. Given that our synthetic strategy would aid the stereochemical assignment of the natural products it was desired that our route to **12** be sufficiently flexible such that fragments of varying relative and absolute stereochemistry be synthesised with relative ease. In order to test the viability of the key bond forming steps on a simple, model system we synthesised bis-spiroacetal **13** as a racemic mixture of diastereomers and the results of this study are reported herein. It is envisaged that these preliminary findings will form the basis for development of a synthetic programme directed towards the synthesis of **12** in a stereocontrolled manner.

2. Results and discussion

Our approach to the synthesis of the bis-spiroacetal core hinges on the cyclisation of a suitably protected, acyclic hydroxy ketone precursor. We chose a synthetic route that is based on the stepwise addition of small carbon fragments



Scheme 2.



Scheme 3. *Reagents and conditions*: (i) TBDPSCl, Et_3N, CH_2Cl_2, 25°C, 12 h, 90%; (ii) DMSO/$(COCl)_2$, CH_2Cl_2, −78°C, 20 min, then Et_3N, −78°C to 25°C, 90%; (iii) Allylmagnesium bromide, Et_2O, 0°C, 0.5 h, 94%; (iv) TBSCl, imidazole, DMAP, CH_2Cl_2, 12 h, 81%; (v) $BH_3.SMe_2$, THF, 0°C to 25°C, 3 h, then $NaOH/H_2O_2$, 82%; (vi) DMSO/$(COCl)_2$, CH_2Cl_2, −78°C, 20 min, then Et_3N, −78°C to 25°C, 95%.

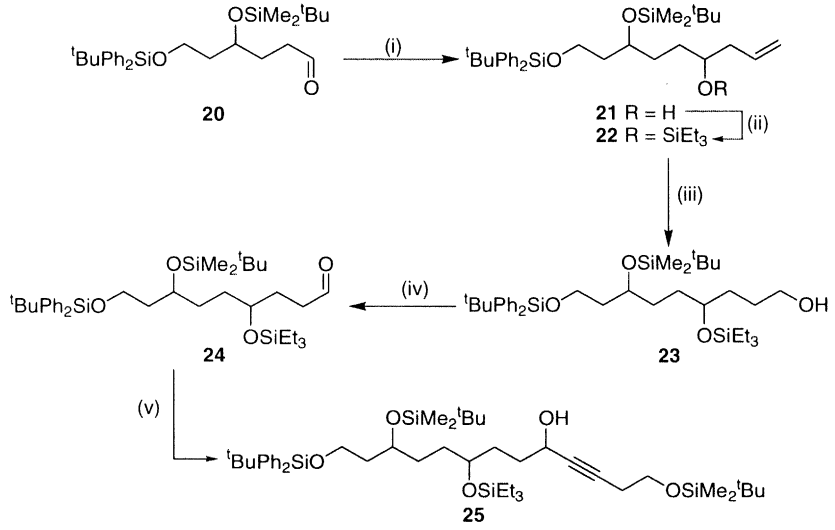
and is relatively simple in design yet incorporates a degree of flexibility such that large quantities of intermediates of varying stereochemistry could be easily obtained. Acetylene **25** is a key precursor to the unsaturated bis-spiroacetal **13** and was the initial focus of our synthetic efforts.

The synthesis of acetylene **25** uses aldehyde **20** as a key intermediate, which in turn is prepared from 1,3-propanediol (Scheme 3). Protection of diol **14** under mild conditions using triethylamine and *tert*-butyldimethylsilyl chloride followed by Swern oxidation gave protected aldehyde **16**.[8] Subsequent addition of allylmagnesium bromide gave secondary alcohol **17** which was then protected as *tert*-butyldimethylsilyl ether **18**. Hydroboration of the terminal alkene **18** afforded primary alcohol **19** which underwent Swern oxidation to aldehyde **20**.

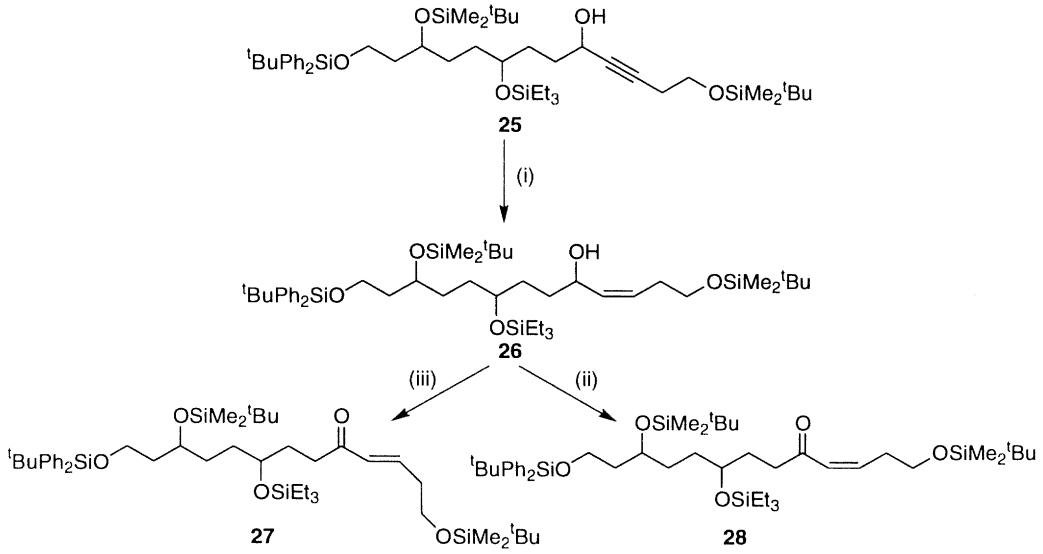
The remaining seven carbons in acetylene **25** were introduced in a similar fashion. Addition of allylmagnesium bromide to aldehyde **20** gave secondary alcohol **21** which was protected as triethylsilyl ether **22** (scheme 4). Hydroboration followed by oxidation using Dess–Martin periodinane[9] buffered with pyridine gave the nine carbon aldehyde **24** in good yield. The final, unsaturated four carbon fragment required was then introduced by addition of the lithium acetylide of 1-*tert*-butyldimethylsilyloxy-3-butyne to aldehyde **24** affording alcohol **25** in 19% overall yield from 1,3-propanediol **14**.

With large quantities of **25** in hand, we next investigated its conversion to an acyclic precursor which could be transformed into bis-spiroacetal **12**. We first attempted to synthesise the desired 6,5,5 bis-spiroacetal ring system by oxidative cyclisation of a suitable bicyclic 6,5 hydroxyalkylspiroacetal precursor. This methodology has been used successfully for the synthesis of the 6,6,5 bis-spiroacetal moiety of *epi*-17-deoxy-(*O*-8)-salinomycin. A double oxidative cyclisation strategy has also been used by Suarez et al., to assemble related bis-spiroacetals.[10,11]

Given that our ultimate goal was the synthesis of unsaturated, bis-spiroacetal **13**, semi-hydrogenation of the triple bond in acetylene **25**, which ultimately provides the double bond at C11 in **13** was carried out. Acetylene **25** was reduced to *cis*-alkene **26** over Lindlar catalyst then oxidation of alcohol **26** was attempted using Dess–Martin periodinane (Scheme 5). Under these conditions however, isomerisation of the double bond occurred and only



Scheme 4. *Reagents and conditions*: (i) Allylmagnesium bromide, Et_2O, 0°C, 0.5 h, 90%; (ii) TESCl, 2,6-lutidine, CH_2Cl_2, 25°C, 12 h, 86%; (iii) $BH_3.SMe_2$, THF, 0°C to 25°C, 3 h, then $NaOH/H_2O_2$, 82%; (iv) Dess–Martin periodinane, pyridine, CH_2Cl_2, 20 min, 73%; (v) 1-*tert*-butyldimethylsilyloxy-3-butyne, ^{n}BuLi, THF, −78°C, 1 h, then **24**, −78° to 25°C, 86%.

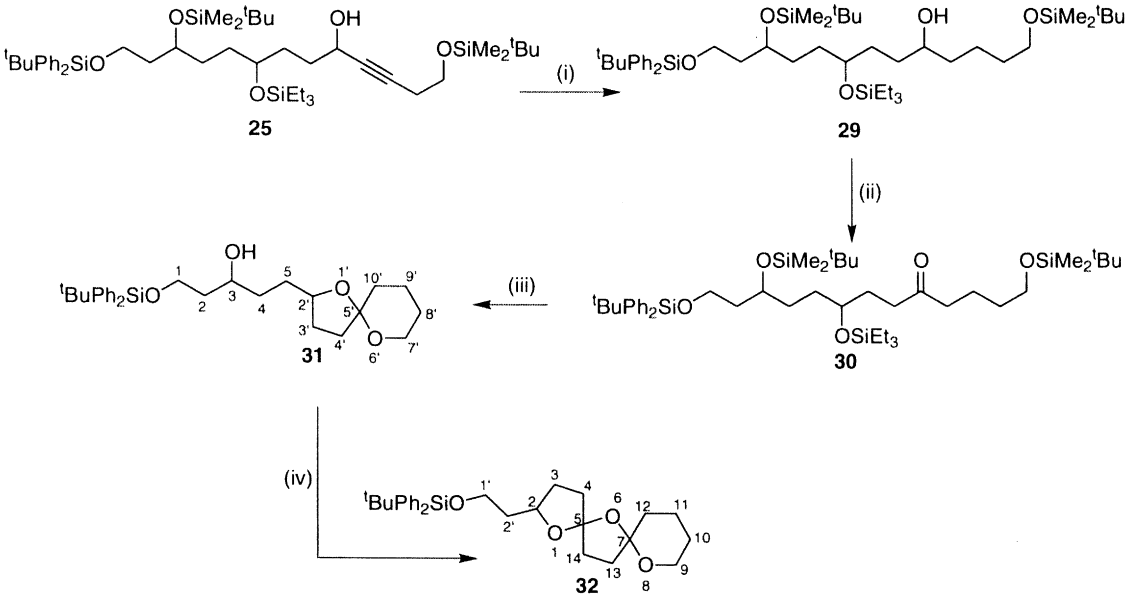


Scheme 5. *Reagents and conditions*: (i) Lindlar catalyst, H_2, THF, 25°C, 4 h, 90%; (ii) TPAP, NMO, 4 Å mol. sieves, CH_2Cl_2, 25°C, 0.5 h, 83%; (iii) Dess–Martin periodinane, pyridine, CH_2Cl_2, 25°C, 1 h, 67%.

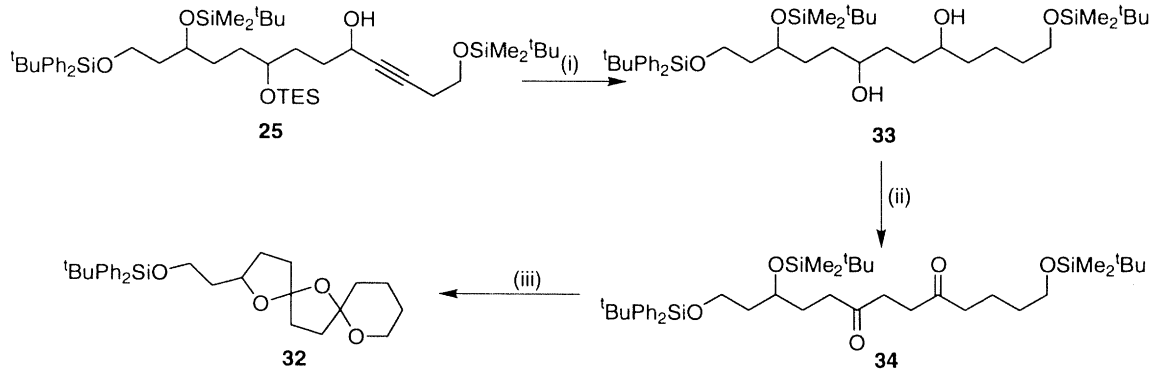
trans-enone **27** was isolated. Oxidation of alcohol **26** using tetrapropylammonium perruthenate and NMO[12a] afforded *cis*-enone **28** in high yield, however, these results raised the possibility that *cis–trans* isomerism would occur upon attempted deprotection of the silyl ether protecting groups under acidic conditions, thereby preventing spirocyclisation from taking place. We therefore decided to initially develop our synthetic protocol on a saturated precursor.

The triple bond in **25** was removed over palladium on carbon in the presence of sodium bicarbonate to give hydroxyalkane **29** (Scheme 6). Oxidation using tetrapropylammonium perruthenate and NMO as co-oxidant then gave ketone **30**. Selective deprotection of the triethyl silyl ether and *tert*-butyldimethylsilyl ethers was successfully achieved by stirring **30** in ethanol in the presence of pyridinium *p*-toluenesulphonate affording the desired hydroxyspiroacetal **31** in good yield.[13] Finally, irradiation of a solution of **31**, iodine and iodobenzene diacetate in cyclohexane led to clean oxidative cyclisation to give saturated bis-spiroacetal **32** as an equimolar mixture of four diastereoisomers.

Bis-spiroacetal **32** could also be obtained in one step from acyclic diketone **34**. This spirocyclisation precursor was easily prepared by reduction of hydroxyacetylene **25** over palladium on carbon without sodium bicarbonate followed by oxidation of the resulting diol. When sodium bicarbonate was not present in the reduction step concomitant deprotection of the C8 triethylsilyl ether occurred (Scheme 7). Oxidation of diol **33** with excess TPAP/NMO gave diketone



Scheme 6. *Reagents and conditions*: (i) Pd/C, EtOAc, 25°C, 3 h, 96%; (ii) TPAP, NMO, 4 Å mol. sieves, CH_2Cl_2, 25°C, 0.5 h, 82%; (iii) PPTS, EtOH, 60°C, 10 h, 67%; (iv) $PhI(OAc)_2$, I_2, cyclohexane, hν, 0.5 h, 56%.



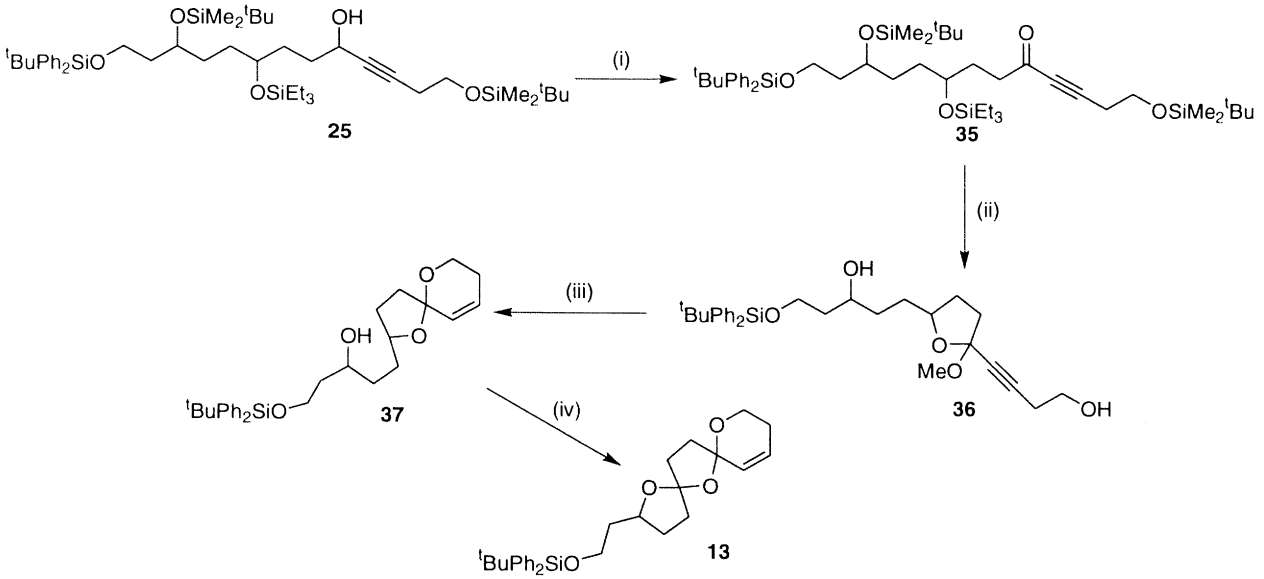
Scheme 7. *Reagents and conditions*: (i) Pd/C, H_2, EtOAc, 25°C, 6 h, 69%; (ii) TPAP, NMO, 4 Å mol. sieves, 25°C, 1 h, 70%; (iii) PPTS, EtOH, 60°C, 7 h, 50%.

34 which cyclised to bis-spiroacetal **32** in moderate yield upon stirring with PPTS in ethanol.

With the synthesis of saturated bis-spiroacetal **32** in hand, our attention next focussed on introducing the key double bond at C11 of unsaturated spiroacetal **12**. Unfortunately, treatment of *cis*-enone **28** with PPTS in ethanol led to formation of a complex reaction mixture. The ^{1}H NMR spectrum of the crude reaction mixture indicated incorporation of an ethoxy group onto the 6,5 spiroacetal structure, presumably via 1,4-addition of ethanol to the *cis*-enone prior to cyclisation. Deprotection using HF.pyridine in THF also resulted in the formation of a complex mixture suggesting that some isomerism of the double bond takes place under these conditions thereby preventing clean cyclisation to a spiroacetal.

We reasoned that semi-hydrogenation of a suitable hydroxy-ynone precursor would afford a masked *cis*-enone which would then undergo spontaneous cyclisation upon addition of a catalytic amount of acid. This would avoid prolonged exposure of a *cis*-enone to acidic conditions circumventing any problems associated with *cis–trans* isomerism. Towards this end, hydroxyalkyne **25** was oxidised to ynone **35** which when treated with a catalytic quantity of camphorsulfonic acid in methanol to give methyl acetal **36** (Scheme 8). Semi-hydrogenation of alkyne **36** over Lindlar catalyst followed by addition of a catalytic amount of PPTS then effected clean conversion to spiroacetal **37**. Finally, oxidative cyclisation under standard conditions gave the desired unsaturated bis-spiroacetal **13**.

Having established our synthetic methodology to construct the novel 6,5,5 bis-spiroacetal ring system of the spirolides, work is now being directed towards incorporating the C3 methyl group in enantiopure form. The work reported herein has elucidated the pathway for the synthesis of this bis-spiroacetal moiety of these complex natural products making use of a key oxidative cyclisation. Moreover, the precise nature of the functional group manipulations required in combination with appropriate protecting group strategies for construction of the key cyclisation precursors has been demonstrated.



Scheme 8. *Reagents and conditions*: (i) TPAP, NMO, 4 Å mol. sieves, CH_2Cl_2, 25°C, 30 min, 79%; (ii) CSA, MeOH, 25°C, 1 h, 55%; (iii) Lindlar catalyst, THF, 25°C, 3 h., then PPTS, THF/CH_2Cl_2, 5 min, 79%; (iv) $PhI(OAc)_2$, I_2, cyclohexane, hν, 25°C, 1 h, 78%.

3. Experimental

3.1. General details

All reactions were conducted in flame-dried or oven-dried glassware under a dry nitrogen atmosphere unless otherwise noted. Tetrahydrofuran and diethyl ether were dried over sodium/benzophenone and distilled prior to use. Cyclohexane, ethyl acetate, dichloromethane and triethylamine were distilled from calcium hydride and used immediately. Flash chromatography was performed by using Merck Kieselgel 60 (230–400 mesh) with the indicated solvents. Thin layer chromatography (tlc) was carried out on precoated silica plates (Merck Kieselgel $60F_{254}$) and compounds were visualised by UV fluorescence or by staining with alkaline potassium permanganate solution or vanillin in methanolic sulfuric acid and heating. Infrared spectra were recorded with a Perkin–Elmer Spectrum One Fourier–Transform IR spectrometer as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers (cm^{-1}) with the following abbreviations: s=strong, m=medium, w=weak and br=broad. ^1H and ^{13}C NMR spectra were obtained using a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz respectively. All chemical shifts are given in parts per million (ppm) downfield from tetramethylsilane as internal standard (^1H) or relative to $CDCl_3$ (^{13}C) and *J* values are given in Hz. ^1H NMR data are tabulated as s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet, br, broad. The ^1H and ^{13}C NMR spectra of compounds **12** and **21** to **37** are complicated by the presence of a mixture of diastereomers. Resonances for individual diastereomers are denoted by asterisks. High resolution mass spectra were recorded using a VG70-SE spectrometer operating at nominal accelerating voltage of 70 eV. Chemical ionisation (CI) mass spectra were obtained with ammonia as the reagent gas. Fast atom bombardment (FAB) mass spectra were obtained with 3-nitrobenzyl alcohol as the matrix.

3.1.1. 1-(*tert*-Butyldiphenylsilyloxy)propan-3-ol 15. Triethylamine (5.2 mL, 38.2 mmol) was added to a solution of 1,3-propanediol (5.8 g, 76.4 mmol) and *tert*-butyldiphenylsilyl chloride (7.0 g, 25.5 mmol) in dichloromethane (50 mL) at room temperature. The mixture was stirred for 12 h then diluted with dichloromethane (200 mL), washed with water (3×80 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash column chromatography using hexane:diethyl ether (7:3) as eluent to afford the *title compound* **15** (7.2 g, 90%) as a colourless oil. All spectral data was consistent with that reported in the literature.[8]

3.1.2. 1-(*tert*-Butyldiphenylsilyloxy)hex-5-en-3-ol 17. A solution of allyl bromide (6.7 mL, 43.2 mmol) in diethyl ether (40 mL) was added to a slurry of magnesium turnings (4.7 g, 195.5 mmol) in diethyl ether (40 mL) dropwise. After initiation of the reaction, the mixture was stirred for 0.5 h at room temperature and then transferred via cannula to a solution of aldehyde **16**[8] in diethyl ether (40 mL) at 0°C. The mixture was stirred at 0°C for 0.5 h then warmed to room temperature. Saturated, aqueous ammonium chloride (80 mL) was added and the mixture extracted with ethyl acetate (3×100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* (6.5 g, 94%) as a colourless oil; ν_{max}(film)/cm^{-1} 3432 (br, s, OH), 3071 (m, C=C–H), 2957, 2931 (s, CH), 1472, 1112; δ_H (400 MHz; $CDCl_3$) 1.06 (9H, s, Bu^t), 1.67–1.77 (2H, m, 2-H), 2.28 (2H, td, $J_{3,4}=J_{4,5}$ 7.1, $J_{4,6}$ 1.0, 4-H), 3.78–3.92 (2H, m, 1-H), 3.94–4.00(1H, m, 3-H), 5.07–5.15 (2H, m, 6-H), 5.61–5.96 (1H, m, 5-H), 7.26–7.45 (6H, m, ArH), 7.66–7.75 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.0 (quat., Bu^t), 26.8 (CH_3, Bu^t), 37.8 (CH_2, C-2), 41.9 (CH_2, C-4), 63.3 (CH_2, C-1), 70.8 (CH, C-3), 117.4 (CH_2, C-6), 127.7 (CH, Ar-C), 129. 8 (CH, Ar-C), 133.0 (CH, C-5), 135.0 (quat., Ar-C), 135.5 (CH, Ar-C); *m/z* (CI, NH_3) 355 (MH^+, 42%), 277 (12) and 199 (35); Found: MH^+, 355.2093. $C_{22}H_{30}O_2Si$ requires *MH*, 355.2093.

3.1.3. 1-(*tert*-Butyldiphenylsilyloxy)-3-(*tert*-butyldimethylsilyloxy)hex-5-ene 18. A solution of 4-(dimethylamino)-pyridine (0.35 g, 2.9 mmol), alcohol **17** (6.4 g, 18.1 mmol), *tert*-butyldimethylsilyl chloride (4.1 g, 27.2 mmol) and imidazole (1.8 g, 27.1 mmol) in dichloromethane (40 mL) was stirred at room temperature for 12 h. Saturated, aqueous sodium bicarbonate was added (30 mL) and the mixture extracted with dichloromethane (3×100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography using hexane: diethyl ether (9:1) as eluent, afforded *silyl ether* **18** (6.9 g, 81%) as a colourless oil; ν_{max}(film)/cm^{-1} 3135 (s, C=CH), 2927 (s, CH), 1641, 1589; δ_H (400 MHz; $CDCl_3$) 0.04 (3H, s, SiMe), 0.08 (3H, s, SiMe), 0.90 (9H, s, Bu^t), 1.09 (9H, s, Bu^t), 1.70–1.76 (2H, m, 2-H), 2.21–2.28 (2H, m, 4-H), 3.73–3.77 (2H, m, 1-H), 3.96–4.00 (1H, m, 3-H), 5.02–5.07(2H, m, 6-H), 5.80–5.87 (1H, m, 5-H), 7.38–7.45 (6H, m, ArH), 7.68–7.71 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −4.7 (CH_3, SiMe), −4.4 (CH_3, SiMe), 18.1 (quat., Bu^t), 19.2 (quat., Bu^t), 22.7 (CH_3, Bu^t), 25.8 (CH_3, Bu^t), 39.6 (CH_2, C-2), 42.1 (CH_2, C-4), 60.8 (CH_2, C-1), 68.9 (CH, C-3), 116.8 (CH_2, C-6), 127.8 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.2 (CH, C-5), 135.6 (CH, Ar-C); *m/z* (CI, NH_3) 469 (MH^+, 100%), 429 (10), 411 (9), 337 (32) and 196 (25); Found: MH^+, 469.2954. $C_{28}H_{44}O_2Si_2$ requires *MH*, 469.2958.

3.1.4. 4-(*tert*-Butyldimethylsilyloxy)-6-(*tert*-butyldiphenylsilyloxy)hexan-1-ol 19. A solution of borane-dimethyl sulfide (4.8 mL of a 10 M solution in THF, 48 mmol) was added to a solution of alkene **18** (7.45 g, 15.9 mmol) in THF (100 mL) at 0°C. The reaction mixture was allowed to warm to room temperature then stirred for 3 h. A solution of sodium hydroxide (200 mL of a 3 M solution) followed by H_2O_2 (100 mL of a 35% w/w solution in H_2O) was added at 0°C and the mixture stirred overnight. Solvent was removed under reduced pressure and the residue partitioned between water (100 mL) and ethyl acetate (200 mL). The aqueous layer was further extracted with ethyl acetate (2×150 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography using hexane: diethyl ether (7: 3) as eluent to give the *title compound* **19** (6.3 g, 82%) as a colourless oil; ν_{max}(film)/cm^{-1} 3399 (br s, OH), 3071 (m, Ar-H), 2951 (s, CH), 1589, 1472; δ_H (400 MHz; $CDCl_3$) 0.04 (3H, s, SiMe), 0.06 (3H, s, SiMe), 0.86 (9H, s,

Bu^t), 1.05 (9H, s, Bu^t), 1.52–1.61 (4H, m, 2-H, 3-H), 1.71–1.76 (2H, m, 5-H), 3.55–3.64 (2H, m, 1-H), 3.67–3.78 (2H, m, 6-H), 3.96–3.99 (1H, m, 4-H), 7.38–7.41 (6H, m, ArH), 7.64–7.68 (4H, m, ArH)); δ_C (100 MHz; $CDCl_3$) −4.7 (CH_3, SiMe), −4.5 (CH_3, SiMe), 18.1 (quat., Bu^t), 19.2 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 28.1 (CH_2, C-2), 33.6 (CH_2, C-3), 39.3 (CH_2, C-5), 60.2 (CH_2, C-6), 63.1 (CH_2, C-1), 69.0 (CH, C-4), 127.6 (CH, Ar-C), 129.6 (CH, Ar-C), 133.9 (quat., Ar-C), 135.6 (CH, Ar-C); *m/z* (CI, NH_3) 487 (MH^+, 46%), 297 (30) and 277 (100); Found: MH^+, 487.3059. $C_{28}H_{46}O_3Si_2$ requires *MH*, 487.3064.

3.1.5. 4-(*tert*-Butyldimethylsilyloxy)-6-(*tert*-butyldiphenylsilyloxy)hexanal 20. A solution of DMSO (2.0 mL, 27.4 mmol) in dichloromethane (40 mL) was added to a solution of oxalyl chloride (1.14 mL, 14.3 mmol) in dichloromethane (40 mL), dropwise at −78°C. The mixture was stirred for 20 min at −78°C, then alcohol **19** (5.5 g, 11.4 mmol) in dichloromethane (40 mL) was added dropwise. The mixture was stirred for a further 20 min at this temperature then triethylamine (9.4 mL, 68.4 mmol) was added. The reaction was stirred for 10 min at −78°C then warmed to room temperature. Saturated, aqueous sodium bicarbonate (100 mL) was added and the mixture extracted with dichloromethane (2×200 mL). The combined organic extracts were dried ($MgSO_4$), concentrated under reduced pressure and the residue purified by flash chromatography using hexane: diethyl ether (8:2) as eluent to give the *title compound* **20** (5.2 g, 95%) as a colourless oil; ν_{max}(film)/cm^{-1} 3071 (m, Ar-H), 2954, 2889 (s, CH), 1727 (s, C=O), 1472; δ_H (400 MHz; $CDCl_3$) 0.04 (3H, s, SiMe), 0.06 (3H, s, SiMe), 0.86 (9H, s, Bu^t), 1.05 (9H, s, Bu^t), 1.58–1.88 (4H, m, 3-H, 5-H), 2.44 (2H, dt, $J_{2,3}$7.5, $J_{2,1}$1.5, 2-H), 3.68–3.74 (2H, m, 6-H), 3.94–3.97 (1H, m, 4-H), 7.36–7.45 (6H, m, ArH), 7.64–7.67 (4H, m, ArH), 9.76 (1H, t, $J_{3,2}$1.5, 1-H)); δ_C (100 MHz; $CDCl_3$) −4.6 (CH_3, SiMe), 18.0 (quat., Bu^t), 19.1 (quat., Bu^t), 25.8 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 29.1 (CH_2, C-3), 39.56 (CH_2, C-5), 39.61 (CH_2, C-2), 60.6 (CH_2, C-6), 68.3 (CH, C-4), 127.6 (CH, Ar-C), 129.6 (CH, Ar-C), 133.8 (quat., Ar-C), 135.6 (CH, Ar-C), 202.5 (CO, C-1); *m/z* (CI, NH_3) 485 (MH^+, 36%), 471 (25), 353 (54), 196 (36) and 91 (56); Found: MH^+, 485.2906. $C_{28}H_{44}O_3Si_2$ requires *MH*, 485.2907.

3.1.6. 7-(*tert*-Butyldimethylsilyloxy)-9-(*tert*-butyldiphenylsilyloxy)non-1-en-4-ol 21. A solution of allyl bromide (3.7 mL, 43.2 mmol) in diethyl ether (35 mL) was added to a slurry of magnesium turnings (2.6 g, 108.3 mmol) in diethyl ether (35 mL) dropwise. After initiation of the reaction, the mixture was stirred for 0.5 h at room temperature and then transferred via cannula to a solution of aldehyde **20** (5.2 g, 10.8 mmol) in diethyl ether (40 mL) at 0°C. The mixture was stirred at 0°C for 0.5 h then warmed to room temperature. Saturated, aqueous ammonium chloride (80 mL) was added and the mixture extracted with ethyl acetate (3×100 mL). The combined organic extracts were dried ($MgSO_4$), concentrated under reduced pressure and the residue purified by flash chromatography using hexane: diethyl ether (7:3) as eluent to give the *title compound* **21** (5.0 g, 90%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3413 (br s, OH), 3071 (m, C=CH), 2929, 2856 (s, CH), 1641, 1589, 1462; δ_H (400 MHz; $CDCl_3$) 0.04 (1.5H, s, SiMe), 0.06 (1.5H, s, SiMe), 0.07 (1.5H, s, SiMe*), 0.08 (1.5H, s, SiMe*), 0.89 (9H, s, Bu^t), 1.07 (9H, s, Bu^t), 1.52–1.75 (6H, m, 5-H, 6-H, 8-H), 2.15–2.32 (2H, m, 3-H), 3.60–3.63 (1H, m, 7-H), 3.69–3.79 (2H, m, 9-H), 3.92–4.01 (1H, m, 4-H), 5.11–5.17 (2H, m, 1-H), 5.79–5.89 (1H, m, 2-H), 7.39–7.42 (6H, m, ArH), 7.66–7.69 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −4.6 (CH_3, SiMe), −4.5 (CH_3, SiMe), −4.4 (CH_3, SiMe*), 18.1 (quat., Bu^t), 19.2 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 31.9 (CH_2, C-5), 32.2 (CH_2, C-5*), 32.8 (CH_2, C-6), 33.4 (CH_2, C-6*), 39.4 (CH_2, C-8), 39.6 (CH_2, C-8*), 41.9 (CH_2, C-3), 42.0 (CH_2, C-3*), 60.9 (CH_2, C-9), 69.1 (CH, C-7), 69.3 (CH, C-7*), 70.7 (CH, C-4), 71.0 (CH, C-4*), 117.7 (CH_2, C-1), 117.9 (CH_2, C-1*), 127.6 (CH, Ar-C), 129.6 (CH, Ar-C), 133.9 (quat., Ar-C), 134.9 (CH, C-2), 135.2 (CH, C-2*), 135.6 (CH, Ar-C); *m/z* (CI, NH_3) 527 (MH^+, 35%), 337 (33), 317 (100) and 121 (76); Found: MH^+, 527.3370. $C_{31}H_{50}O_3Si_2$ requires *MH*, 527.3377.

3.1.7. 7-(*tert*-Butyldimethylsilyloxy)-9-(*tert*-butyldiphenylsilyloxy)-4-triethylsilyloxynon-2-ene 22. 2,6-Lutidine (1.99 g, 18.5 mmol) was added to a solution of alcohol **21** (4.9 g, 9.3 mmol) and triethylsilyl chloride (1.8 g, 12.0 mmol) in dichloromethane (20 mL) at room temperature. The mixture was stirred for 12 h then brine (15 mL) was added and the mixture extracted with dichloromethane (3×20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure and the residue purified by flash chromatography using hexane: diethyl ether (9:1) as eluent to give the *title compound* **22** (5.1 g, 86%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3071 (m, Ar-H), 2954, 2857 (s, CH), 1610, 1472; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.03 (3H, s, SiMe), 0.58 (6H, q, J=7.8, $SiEt_3$), 0.85 (9H, s, Bu^t), 0.95 (9H, t, J=7.8, $SiEt_3$), 1.05 (9H, s, Bu^t), 1.35–1.55 (4H, m, 5-H, 6-H), 1.61–1.75 (2H, m, 8-H), 2.22–2.19 (2H, m, 3-H), 3.64–3.75 (3H, m, 7-H, 9-H), 3.84–3.87 (1H, m, 4-H), 5.01–5.06 (2H, m, 1-H), 5.82 (1H, m, 2-H), 7.26–7.42 (6H, m, ArH), 7.64–7.68 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.1 (CH_2, $SiEt_3$), 6.9 (CH_3, $SiEt_3$), 18.1 (quat., Bu^t), 19.2 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 32.4 (CH_2, C-5), 33.0 (CH_2, C-6), 33.1 (CH_2, C-6*), 39.9 (CH_2, C-8), 40.0 (CH_2, C-8*), 42.0 (CH_2, C-3), 61.0 (CH_2, C-9), 69.4 (CH, C-7), 72.2 (CH, C-4), 116.7 (CH_2, C-1), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.3 (CH, C-2), 135.6 (CH, Ar-C); *m/z* (FAB, NBA) Found: MH^+, 641.4233. $C_{37}H_{64}O_3Si_3$ requires *MH*, 641.4242.

3.1.8. 7-(*tert*-Butyldimethylsilyloxy)-9-(*tert*-butyldiphenylsilyloxy)-4-triethylsilyloxynonan-1-ol 23. A solution of borane-dimethyl sulfide (2.4 mL of a 10 M solution in THF, 24.0 mmol) was added to a solution of alkene **22** (5.10 g, 7.9 mmol) in THF (400 mL) at 0°C. The reaction mixture was allowed to warm to room temperature and then stirred for 3 h. A solution of sodium hydroxide (90 mL of a 3 M solution, 270 mmol) followed by H_2O_2 (45 mL of a 35% w/w solution in H_2O, 400 mmol) was added at 0°C and the mixture stirred overnight. Solvent was removed under reduced pressure and the residue partitioned between water (40 mL) and ethyl acetate (100 mL). The aqueous layer was further extracted with ethyl acetate (2×80 mL)

and the combined organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography using hexane: diethyl ether (7:3) as eluent to give the *title compound* **23** (4.3 g, 82%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3400 (br s, OH), 3072 (m, Ar-H), 2928 (s, CH), 1590, 1471; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.03 (3H, s, SiMe), 0.61 (6H, q, J=7.8, $SiEt_3$), 0.85 (9H, s, Bu^t), 1.00 (9H, t, J=7.8, $SiEt_3$), 1.05 (9H, s, Bu^t), 1.17–1.43 (10H, m, 2-H, 3-H, 5-H, 6-H, 8-H), 3.61–3.74 (5H, m, 1-H, 7-H, 9-H), 3.85–3.90(1H, m, 4-H), 7.37–7.40 (6H, m, ArH), 7.64–7.67 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.0 (CH_2, SiEt), 6.9 (CH_3, SiEt), 18.1 (quat., Bu^t), 19.2 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 28.2 (CH_2, C-2), 32.0 (CH_2, C-5), 32.3 (CH_2, C-5*), 33.0 (CH_2, C-6), 33.4 (CH_2, C-3), 33.5 (CH_2, C-3*), 40.0 (CH_2, C-8), 61.0 (CH_2, C-9), 63.2 (CH, C-7), 69.3 (CH, C-1), 69.4 (CH, C-1*), 72.3 (CH, C-4), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.6 (CH, Ar-C); *m/z* (FAB, NBA) Found: MH$^+$, 659.4341. $C_{37}H_{66}O_4Si_3$ requires *MH*, 659.4347.

3.1.9. 7-(*tert*-Butyldimethylsilyloxy)-9-(*tert*-butyldiphenylsilyloxy)-4-triethylsilyloxynonal 24. Dess–Martin periodinane (3.8 g, 9.0 mmol) was added to a solution of alcohol **23** (4.3 g, 6.5 mmol) and pyridine (1.4 g, 18.0 mmol) in dichloromethane (80 mL) at room temperature. The mixture was stirred for 2 h then filtered through a plug of Celite®. The filtrate was concentrated under reduced pressure and the crude product purified by flash chromatography using hexane: diethyl ether (8: 2) as eluent to give the *title compound* **24** (3.13 g, 73%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3071 (m, Ar-H), 2954, 2857 (s, CH), 1727 (s, C=O), 1589, 1472; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.04 (3H, s, SiMe), 0.56 (6H, q, J=7.9, $SiEt_3$), 0.85 (9H, s, Bu^t), 0.95 (9H, t, J=7.9, $SiEt_3$), 1.05 (9H, s, Bu^t), 1.33–1.85 (8H, m, 3-H, 5-H, 6-H, 8-H), 2.46 (2H, dt, $J_{2,3}$ 7.4, $J_{2,1}$ 1.5, 2-H), 3.66–3.72 (3H, m, 7-H, 9-H), 3.83–3.88 (1H, m, 4-H), 7.35–7.42 (6H, m, ArH), 7.64–7.68 (4H, m, ArH), 9.77 (1H, t, J=1.5, 1-H); δ_C (100 MHz; $CDCl_3$) −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.1 (CH_2, $SiEt_3$), 6.9 (CH_3, $SiEt_3$), 18.0 (quat., Bu^t), 19.2 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 29.1 (CH_2, C-2), 32.4 (CH_2, C-5), 32.7 (CH_2, C-6), 33.1 (CH_2, C-3), 39.9 (CH_2, C-8), 60.8 (CH_2, C-9), 60.9 (CH_2, C-9*), 69.3 (CH, C-7), 71.4 (CH, C-4), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.6 (CH, Ar-C), 202.6 (CH, C-1); *m/z* (FAB, NBA) Found: MH$^+$, 657.4174. $C_{37}H_{64}O_4Si_3$ requires *MH*, 657.4191.

3.1.10. 1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytridec-3-yn-5-ol 25. ^{n}Butyllithium (4.4 mL of a 1.6 M solution in hexanes, 7.0 mmol) was added to a solution of 1-(*tert*-butyldimethylsilyloxy)but-3-yne (1.3 g, 7.0 mmol) in THF (20 mL) at −78°C. The mixture was stirred at −78°C for 1 h then aldehyde **24** (3.1 g, 4.7 mmol) in THF (5 mL) was added. The mixture was stirred at −78°C for a further 1 h then warmed to room temperature and saturated, aqueous ammonium chloride (30 mL) was added. The mixture was extracted with ethyl acetate (3×80 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography using hexane: diethyl ether (8:2) as eluent to give the *title compound* **25** (3.4 g, 86%) as a colourless oil and as a 1:1:1:1 mixture of four diastereomers; ν_{max}(film)/cm^{-1} 3435 (br, s, OH), 3050 (m, Ar-H), 2953, 2876 (s, CH), 2243 (w, triple bond) 1471, 1111; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.02 (3H, s, SiMe), 0.04 (6H, s, SiMe), 0.62 (6H, q, *J*7.8, $SiEt_3$), 0.86 (9H, s, Bu^t), 0.90 (9H, s, Bu^t), 0.98 (9H, t, J=7.8, $SiEt_3$), 1.06 (9H, s, Bu^t), 1.35–1.75 (10H, m, 6-H, 7-H, 9-H, 10-H, 12-H), 2.45 (2H, t, $J_{2,3}$ 7.3, 2-H), 2.71 (1H, br s, OH), 3.67–3.74 (5H, m, 1-H, 11-H, 13-H), 3.87 (1H, m, 8-H), 4.32–4.38 (1H, m, 5-H), 7.36–7.43 (6H, m, ArH), 7.65–7.69 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.3 (CH_3, SiMe), −4.6 (CH_3, SiMe), −4.4 (CH_3,SiMe), 5.0 (CH_2, $SiEt_3$), 6.9 (CH_3, $SiEt_3$), 18.0 (quat., Bu^t), 18.3 (quat., Bu^t), 19.1 (quat., Bu^t), 23.1 (CH_2, C-2), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 31.7 (CH_2, C-6), 32.0 (CH_2, C-6*), 32.3 (CH_2, C-7), 32.6 (CH_2, C-7*), 32.7 (CH_2, C-7**), 33.0 (CH_2, C-9), 33.1 (CH_2, C-9*), 33.4 (CH_2, C-10), 33.7 (CH_2, C-10*), 39.9 (CH_2, C-12), 60.9 (CH_2, C-13), 61.9 (CH_2, C-1), 62.3 (CH, C-5), 62.8 (CH, C-5*), 69.3 (CH, C-11), 72.1 (CH_2, C-8), 72.2 (CH_2, C-8*), 81.9 (quat., C-4), 82.4 (quat., C-3), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.5 (CH, Ar-C); *m/z* (FAB, NBA) Found: MH$^+$, 841.5422. $C_{47}H_{84}O_5Si_4$ requires *MH*, 841.5474.

3.1.11. *cis*-1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytridec-3-en-5-ol 26. A mixture of acetylene **25** (250 mg, 0.30 mmol) and Lindlar catalyst (20 mg) in THF (30 mL) was stirred under an atmosphere of hydrogen for 4 h then filtered through Celite®. The filtrate was concentrated under reduced pressure to give the *title compound* **26** (230 mg, 90%) as a colourless oil and as a 1:1:1:1 mixture of four diastereomers; ν_{max}(film)/cm^{-1} 3436 (br, s, OH), 3050, 3071 (m, C=C–H), 2954, 2857 (s, CH), 1590, 1471, 1111; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.04 (3H, s, SiMe), 0.08 (6H, s, SiMe), 0.61 (6H, q, J=7.8, $SiEt_3$), 0.86 (9H, s, Bu^t), 0.91 (9H, s, Bu^t), 0.96 (9H, t, J=7.8, $SiEt_3$), 1.06 (9H, s, Bu^t), 1.27–1.71 (10H, m, 6-H, 7-H, 9-H, 10-H, 12-H), 2.23–2.29 (2H, m, 2-H), 3.58–3.74 (5H, m, 1-H, 11-H, 13-H), 3.38–3.86 (1H, m, 8-H), 4.31–4.36 (1H, m, 5-H), 5.50–5.60 (2H, m, 3-H, 4-H), 7.35–7.42 (6H, m, ArH), 7.65–7.69(4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.5 (CH_3, SiMe), −4.7 (CH_3, SiMe), −4.5 (CH_3, SiMe), 5.0 (CH_2, $SiEt_3$), 6.9 (CH_3, $SiEt_3$), 17.9 (quat., Bu^t), 18.2 (quat., Bu^t), 18.4 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 31.3 (CH_2, C-7), 31.6 (CH_2, C-12), 32.5 (CH_2, C-9), 32.6 (CH_2, C-9*), 32.9 (CH_2, C-10), 33.2 (CH_2, C-10*), 35.9 (CH_2, C-7), 39.9 (CH_2, C-12), 60.8 (CH_2, C-13), 62.3 (CH_2, C-1), 67.1 (CH, C-11), 67.3 (CH, C-11*), 69.3 (CH, C-5), 72.4 (CH, C-8), 127.5 (CH, ArH), 128.3 (CH, C-3), 128.5 (CH, C-3*), 129.4 (CH, Ar-C), 133.9 (quat., Ar-C), 135.2 (CH, C-4), 135.3 (CH, C-4*), 135.4 (CH, Ar-C); *m/z* (FAB, NBA) Found: MH$^+$, 843.5611. $C_{47}H_{87}O_5Si_4$ requires *MH*, 843.5631.

3.1.12. *trans*-1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytridec-3-en-5-one 27. Dess–Martin periodinane (60 mg, 0.12 mmol) was added to a solution of alcohol **26** (50 mg, 0.06 mmol) and

pyridine (19 mg, 0.24 mmol) in dichloromethane (1 mL) at room temperature. The mixture was stirred for 1 h then filtered through a plug of Celite®. The filtrate was concentrated under reduced pressure and the residue purified by flash chromatography using hexane: diethyl ether (9: 1) as eluent to give the *title compound* **27** (33 mg, 67%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3071, 3050 (m, C=CH), 3954, 2930 (s, CH), 1698, (m, C=O), 1471, 1111; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.02 (3H, s, SiMe), 0.06 (6H, s, SiMe), 0.60 (6H, q, J=7.8, $SiEt_3$), 0.85 (9H, s, Bu^t), 0.90 (9H, s, Bu^t), 0.94 (9H, t, J=7.8, $SiEt_3$), 1.04 (9H, s, Bu^t), 1.26–1.68 (8H, m, 7-H, 9-H, 10-H, 12-H), 2.40–2.43 (2H, m, 6-H), 2.41–2.60 (2H, m, 2-H), 3.66–3.75 (5H, m, 1-H, 11-H, 13-H), 3.83–3.86 (1H, m, 8-H), 6.11 (1H, dt, $J_{4,3}$ 16.0, $J_{4,2}$ 1.4, 4-H), 6.80 (1H, dt, $J_{3,4}$ 16.0, $J_{3,2}$ 7.0, 3-H), 7.35–7.41 (6H, m, ArH), 7.64–7.67 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.3 (CH_3, SiMe), −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.1 (CH_2, SiEt), 7.0 (CH_3, SiEt), 18.0 (quat., Bu^t), 19.2 (quat., Bu^t), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 30.9 (CH_2, C-2), 32.5 (CH_2, C-9), 32.8 (CH_2, C-7), 33.1 (CH_2, C-10), 35.6 (CH_2, C-6), 35.9 (CH_2, C-6*), 39.9 (CH_2, C-12), 60.9 (CH_2, C-13), 61.6 (CH_2, C-1), 69.3 (CH, C-11), 71.6 (CH, C-8), 127.7 (CH, Ar-C), 129.5 (CH, Ar-C), 131.9 (CH, C-4), 134.0 (quat., Ar-C), 135.5 (CH, Ar-C), 143.6 (CH, C-3), 201.2 (quat., C-5); *m/z* (FAB, NBA) Found: MH$^+$, 841.5506. $C_{47}H_{84}O_5Si_4$ requires *MH*, 841.5474.

3.1.13. *cis*-1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytridec-3-en-5-one 28. Tetra-*n*-propylammonium perruthenate (1 mg, 2.8×10^{-3} mmol) was added to a mixture of alcohol **26** (23 mg, 0.027 mmol), *N*-methylmorpholine-*N*-oxide (5 mg, 0.045 mmol) and 4 Å mol. sieves (5 mg) in dichloromethane (2 mL) at room temperature. The mixture was stirred for 0.5 h, then filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure to give the *title compound* **28** (19 mg, 83%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3071 (m, C=CH), 2877, 2954 (s, CH), 1695 (m, C=O), 1472, 1111; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.02 (3H, s, SiMe), 0.06 (6H, s, SiMe), 0.60 (6H, q, J=7.8, $SiEt_3$), 0.86 (9H, s, Bu^t), 0.90 (9H, s, Bu^t), 0.91 (9H, t, J=7.8, $SiEt_3$), 1.06 (9H, s, Bu^t), 1.34–1.80 (8H, m, 7-H, 9-H, 10H, 12-H), 2.52 (2H, t, $J_{6,5}$ 7.6, 6-H), 2.82–2.87 (2H, m, 2-H), 3.67–3.76 (5H, m, 1-H, 11-H, 13-H), 3.84–3.88 (1H, m, 8-H), 6.19 (2H, br s, 3-H, 4-H), 7.35–7-43 (6H, m, ArH), 7.65–7.68 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.4 (CH_3, SiMe), −4.7 (CH_3, SiMe), −4.5 (CH_3, SiMe), 5.0 (CH_2, $SiEt_3$), 6.9 (CH_3, $SiEt_3$), 18.0 (quat., Bu^t), 19.1 (quat., Bu^t), 25.8 (CH_3, Bu^t), 26.8 (CH_3, Bu^t), 30.6 (CH_2, C-2), 30.7 (CH_2, C-2*), 32.3 (CH_2, C-9), 32.5 (CH_2, C-9*), 32.7 (CH_2, C-7), 33.0 (CH_2, C-10), 33.1 (CH_2, C-10*), 35.9 (CH_2, C-6), 39.8 (CH_2, C-12), 60.9 (CH_2, C-13), 62.2 (CH_2, C-1), 69.3 (CH_2, C-11), 72.4 (CH, C-8), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 131.9 (CH, C-4), 133.9 (quat., Ar-C), 135.5 (CH, Ar-C), 144.9 (CH, C-3), 200.3 (quat., C-5) 201.3 (quat., C-5*); *m/z* (FAB, NBA) Found: MH$^+$, 841.5431. $C_{47}H_{84}O_5Si_4$ requires *MH*, 841.5474.

3.1.14. 1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytetradecan-5-ol 29. A mixture of acetylene **25** (0.5 g, 0.06 mmol), palladium on carbon (12 mg) and sodium bicarbonate (0.15 g, 1.8 mmol) in ethyl acetate (50 mL) was stirred under an atmosphere of hydrogen at room temperature for 3 h. The mixture was then filtered through Celite® and the filtrate concentrated under reduced pressure to give the *title compound* **29** (0.48 g, 96%) as a colourless oil and a 1:1:1:1 mixture of four diastereomers; ν_{max}(film)/cm^{-1} 3440 (br, s, OH), 3071, (m, Ar-H), 2930 (s, CH), 1471, 1428; δ_H (400 MHz; $CDCl_3$) 0.03 (3H, s, SiMe), 0.04 (3H,s, SiMe), 0.07 (6H, s, SiMe), 0.60 (6H, q, J=7.8, $SiEt_3$), 0.85 (9H, s, Bu^t), 0.89 (9H, s, Bu^t), 0.95 (9H, t, J=7.8, $SiEt_3$), 1.05 (9H, s, Bu^t), 1.30–1.73 (16H, m, 2-H, 3-H, 4-H, 6-H, 7-H, 9-H, 10-H, 14-H), 3.60–3.73 (6H, m, 1-H, 8-H, 11-H, 13-H), 3.85–3.86 (1H, m, 5-H), 7.36–7.42 (6H, m, ArH), 7.64–7.68 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.3 (CH_3, SiMe), −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.1 (CH_2, $SiEt_3$), 7.0 (CH_3, $SiEt_3$), 18.1 (quat., Bu^t), 18.4 (quat., Bu^t), 19.2 (quat., Bu^t), 22.0 (CH_2, C-3), 25.9 (CH_3, Bu^t), 26.0 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 32.3 (CH_2, C-6), 32.6 (CH_2, C-10), 32.9 (CH_2, C-9), 33.4 (CH_2, C-7), 37.2 (CH_2, C-2), 37.3 (CH_2, C-4), 39.9 (CH_2, C-12), 61.0 (CH_2, C-1), 63.2 (CH_2, C-13), 69.4 (CH, C-11), 71.8 (CH, C-8), 72.1 (CH, C-8*), 72.6 (CH, C-5), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.6 (CH, Ar-C); *m/z* (FAB, NBA) Found: MH$^+$, 845.5750. $C_{47}H_{88}O_5Si_4$ requires *MH*, 845.5787.

3.1.15. 1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytridecan-5-one 30. Tetra-*n*-propylammonium perruthenate (3.3 mg, 9.4×10^{-3} mmol) was added to a mixture of alcohol **29** (80 mg, 0.095 mmol), *N*-methylmorpholine-*N*-oxide (17 mg, 0.14 mmol) and 4 Å mol. sieves (20 mg) in dichloromethane (5 mL) at room temperature. The mixture was stirred for 0.5 h then filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure to give the *title compound* **30** (66 mg, 82 %) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3071 (m, Ar-H), 2953 (s, CH), 1715 (s, C=O), 1471, 1110; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.02 (3H, s, SiMe), 0.05(6H, s, SiMe), 0.60 (6H, q, J=7.8, SiEt), 0.86 (9H, s, Bu^t), 0.90 (9H, s, Bu^t), 0.95 (9H, t, J=7.8, SiEt), 1.05 (9H, s, Bu^t), 1.32–1.68 (12H, 2-H, 3-H, 7-H, 9-H, 10-H, 12-H), 2.37–2.49 (4H, m, 4-H, 6-H), 3.52–3.71 (5H, m, 1-H, 11-H, 13-H), 3.73–3.82 (1H, m, 8-H), 7.34–7.42 (6H, m, ArH), 7.64–7.68 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.4 (CH_3, SiMe), −4.5 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.1 (CH_2, $SiEt_3$), 7.0 (CH_3, $SiEt_3$), 20.3 (CH_2, C-3), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 30.5 (CH_2, C-9), 32.2 (CH_2, C-7), 32.4 (CH_2, C-10), 32.9 (CH_2, C-2), 38.3 (CH_2, C-6), 39.9 (CH_2, C-4), 42.6 (CH_2, C-12), 60.9 (CH_2, C-1), 62.8 (CH_2, C-13), 69.3 (CH, C-11), 71.6 (CH, C-8), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.5 (CH, Ar-C), 211.0 (quat., C-5); *m/z* (FAB, NBA) Found: MH$^+$, 843.5644. $C_{47}H_{86}O_5Si_4$ requires *MH*, 843.5631.

3.1.16. 1-(*tert*-Butyldiphenylsilyloxy)-5-(1,6-dioxaspiro-[4.5]dec-2-yl)pentan-3-ol 31. Pyridinium *p*-toluenesulphonate (5 mg, 0.02 mmol) was added to a solution of ketone **25** (50 mg, 0.06 mmol) in ethanol (0.5 mL). The solution was heated to 60°C and stirred for 10 h. Saturated, aqueous sodium bicarbonate (1mL) was added and the mixture extracted with diethyl ether (3×3 mL). The combined organic extracts were dried (K_2CO_3) and concentrated

under reduced pressure and the residue purified by flash chromatography using hexane: diethyl ether (1:1) as eluent to gave the *title compound* **30** (20 mg, 67%) as a colourless oil and as a 1:1:1:1 mixture of four diastereomers; ν_{max}(film)/cm^{-1} 3437 (br, s, OH), 3070 (m, Ar-H), 2941 (s, CH), 1589, 1427; δ_H (400 MHz; $CDCl_3$) 1.06 (9H, s, Bu^t), 1.46–2.10 (16H, m, 2-H, 3′-H, 4′-H, 8′-H, 9′-H, 10′-H), 3.38–3.71 (1H, m, 3-H), 3.79–3.94 (4H, m, 1-H, 7′-H), 4.04–4.11 (1H, m, 2′-H), 7.37–7.45 (6H, m, ArH), 7.67–7.69 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.0 (quat., Bu^t), 20.3 (CH_2, C-9′), 22.6 (CH_2, C-3′), 25.6 (CH_2, C-8′), 26.8 (CH_3, Bu^t), 29.7 (CH_2, C-5), 30.1 (CH_2, C-5*), 31.5 (CH_2, C-4), 32.1 (CH_2, C-4*), 34.0 (CH_2, C-4′), 34.2 (CH_2, C-4′*), 37.5 (CH_2, C-10′), 38.5 (CH_2, C-2), 38.7 (CH_2, C-2*), 61.5 (CH_2, C-7′), 63.0 (CH_2, C-1), 70.9 (CH, C-3), 71.1 (CH, C-3*), 78.0 (CH, C-2′), 80.9 (CH, C-2′*), 105.4 (quat., C-5′), 105.5, (quat., C-5′*), 106.7 (quat., C-5′**), 106.8 (quat., C-5′***), 127.7 (CH, Ar-C), 129.7 (CH, Ar-C), 133.2 (quat., Ar-C), 135.5 (CH, Ar-C); *m/z* 482 (EI) (M^+, 1%), 425 (34) and 407 (15); Found: M^+, 482.2844. $C_{29}H_{42}O_4Si$ requires *M*, 482.2852.

3.1.17. 2-{(2-*tert*-Butyldiphenylsilyloxy)ethyl}-1,6,8-trioxadispiro[4.1.5.2]tetradecane 32. Iodine (92 mg, 0.18 mmol) was added to a solution of hydroxyspiroacetal **32** (90 mg, 0.18 mmol) and iodobenzene diacetate (0.13 g, 0.41 mmol) in cyclohexane (5 mL). The mixture was irradiated using a 40 W tungsten lamp for 0.5 h at room temperature. Saturated, aqueous sodium bicarbonate (4 mL) was added and the reaction mixture extracted with diethyl ether (3×10 mL). The combined organic extracts were dried (K_2CO_3) and concentrated under reduced pressure and the residue purified by flash chromatography using hexane: diethyl ether (9:1) as eluent to give the *title compound* **32** (50 mg, 56%) as a colourless oil and as a 1:1:1:1 mixture of four diastereomers; ν_{max}(film)/cm^{-1} 3048 (m, Ar-H), 2941, 2857 (s, CH), 1472, 1427, 1111; δ_H (400 MHz; $CDCl_3$) 1.05 (9H, s, Bu^t), 1.55–2.11 (16H, m, 1′-H, 3-H, 4-H, 10-H, 11-H, 12-H, 13-H, 14-H), 3.54–3.62 (1H, m, 2′-H), 3.70–3.93 (3H, m, 2′-H, 9-H), 4.17–4.36 (1H, m, 2-H), 7.26–7.47 (6H, m, ArH), 7.67–7.71 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.0 (quat., Bu^t), 20.2 (CH_2, C-11), 26.8 (CH_3, Bu^t), 29.9 (CH_2, C-3), 30.1 (CH_2, C-3*), 30.5 (CH_2, C-3**), 30.9 (CH_2, C-3***), 33.7 (CH_2, C-10), 34.1 (CH_2, C-10*), 34.2 (CH_2, C-10**), 34.5 (CH_2, C-10***), 34.7 (CH_2, C-13), 35.1 (CH_2, C-13*), 35.3 (CH_2, C-13**), 36.8 (CH_2, C-14), 36.9 (CH_2, C-14*), 37.0 (CH_2, C-14***), 37.3 (CH_2, C-4), 37.6 (CH_2, C-4*), 37.8 (CH_2, C-4**), 38.1 (CH_2, C-4***), 38.5 (CH_2, C-12), 38.7 (CH_2, C-12*), 40.2 (CH_2, C-2′), 40.4 (CH_2, C-2′*), 61.2 (CH_2, C-1′), 61.4 (CH_2, C-1′*), 62.0 (CH_2, C-9), 62.1 (CH_2, C-9*), 75.7 (CH, C-2), 76.0 (CH, C-2*), 77.0 (CH_2, C-2**), 77.3 (CH_2, C-2***), 105.6 (quat., C-7), 105.7 (quat., C-7*), 105.8 (quat., C-7**), 105.9 (quat., C-7***), 115.1 (quat., C-5), 115.3 (quat., C-5*), 115.4 (quat., C-5**), 115.5 (quat., C-5***), 127.6 (CH, Ar-C), 129.5 (CH, Ar-C), 134.1 (quat., Ar-C), 136.7 (CH, Ar-C); *m/z*(EI) 480 (M^+, 0.6%), 423 (100), 405 (25) and 462 (2.5); Found: M^+, 480.2695. $C_{29}H_{40}O_4Si$ requires *M*, 480.2696.

3.1.18. 1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)tridecane-5,8-diol 33. A mixture of acetylene **25** (0.10 g, 0.12 mmol) and palladium on carbon (4 mg) in ethyl acetate (10 mL) was stirred under an atmosphere of hydrogen for 6 h. The mixture was then filtered through Celite® and the filtrate concentrated under reduced pressure. The residue was purified by flash chromatography using hexane: diethyl ether (2: 8) as eluent to give the *title compound* **33** (61 mg, 69%) as a colourless oil and as a 1:1:1:1 mixture of four diastereomers; ν_{max}(film)/cm^{-1} 3367 (br, s, OH), 3051, 3071 (m, Ar-H), 2953, 2857 (s, CH), 1589, 1471; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.04 (6H, s, SiMe), 0.05 (3H, s, SiMe), 0.85 (5H, s, Bu^t), 0.86 (4H, s, Bu^{t*}), 0.89 (9H, s, Bu^t), 1.05 (9H, s, Bu^t), 1.47–1.73 (16H, m, 2-H, 3-H, 4-H, 6-H, 7-H, 9-H, 10-H, 12-H), 3.58–3.74 (6H, m, 1-H, 5-H, 11-H, 13-H), 3.90–3.94 (0.5 H, m, 8-H), 3.94–4.01 (0.5H, m, 8-H*), 7.35–7.42 (6H, m, ArH), 7.64–7.67(4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5.3 (CH3, SiMe), −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 18.1 (quat., Bu^t), 19.2 (quat., Bu^t), 22.0 (CH_2, C-3), 25.9 (CH_3, Bu^t), 26.0 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 31.6 (CH_2, C-9), 32.7 (CH_2, C-10), 33.4 (CH_2, C-2), 37.2 (CH_2, C-6), 37.4 (CH_2, C-7), 39.0 (CH_2, C-4), 39.5 (CH_2, C-12), 60.8, (CH_2, C-1), 60.9 (CH_2, C-13), 69.3 (CH, C-11), 71.8 (CH, C-5), 72.2 (CH, C-8), 127.6 (CH, Ar-C), 129.6 (CH, Ar-C), 133.9 (quat., Ar-C), 135.6 (CH, Ar-C); *m/z* (FAB, NBA) Found: MH^+, 731.4930. $C_{41}H_{75}O_5Si_3$ requires *MH*, 731.4922.

3.1.19. 1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)tridecane-5,8-dione 34. Tetra-*n*-propylammonium perruthenate (6 mg, 1.6×10^{-3} mmol) was added to a mixture of diol **29** (60 mg, 0.082 mmol), *N*-methylmorpholine-*N*-oxide (30 mg, 0.24 mmol) and 4 Å mol. sieves (200 mg) in dichloromethane (3 mL) at room temperature. The mixture was stirred for 1 h then filtered through a plug of flash silica gel. The filtrate was concentrated under reduced pressure to give the *title compound* **34** (42 mg, 70%) as a colourless oil; ν_{max}(film)/cm^{-1} 3071 (m, Ar-H), 2930 (s, CH), 1714 (s, C═O), 1471, 1428; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.03 (3H, s, SiMe), 0.04 (6H, s, SiMe), 0.85 (9H, s, Bu^t), 0.89 (9H, s, Bu^t), 1.04 (9H, s, Bu^t), 1.49–1.74 (8H, m, 2-H, 3-H, 10-H, 12-H), 2.43–2.50 (4H, m, 4-H, 9-H), 2.66 (4H, m, 6-H, 7-H), 3.57–3.62 (1H, m, 11-H), 3.69–3.72 (2H, m, 1-H), 3.89–3.96 (2H, m, 13-H), 7.37–7.42 (6H, m, ArH), 7.64–7.66 (4H, m, ArH) δ_C (100 MHz; $CDCl_3$) −5.3 (CH_3, SiMe), −4.7 (CH_3, SiMe), −4.5 (CH_3, SiMe), 18.0 (quat., Bu^t), 19.1 (quat., Bu^t), 20.2 (CH_2, C-3), 22.3 (quat., Bu^t), 25.8 (CH_3, Bu^t), 25.9 (CH_3, Bu^t), 26.8 (CH_3, Bu^t), 29.2 (CH_2, C-10), 30.7 (CH_2, C-2), 32.2 (CH_2, C-9), 36.0 (CH_2, C-6), 36.9 (CH_2, C-7), 38.2 (CH_2, C-4), 42.5 (CH_2-C-12), 59.5 (CH_2, C-1, C-13), 68.3 (CH, C-11), 127.6, CH, Ar-C), 129.6 (CH, Ar-C), 133.9 (quat., Ar-C), 135.5 (CH, Ar-C), 209.3 (2×CO, C-5, C-8); *m/z* (FAB, NBA) Found: MH^+, 727.4617. $C_{41}H_{70}O_5Si_3$ requires *MH*, 727.4609.

3.1.20. 2-(1-*tert*-Butyldiphenylsilyloxethyl-2-)-1,6,8-trioxadispiro[4.1.5.2]tetradecane 32. Pyridinium *p*-toluenesulphonate (5 mg, 0.020 mmol) was added to a solution of diketone **34** (30 mg, 0.041 mmol) in ethanol (0.5 mL). The mixture was stirred at 60°C for 7 h. and then cooled to room temperature and diluted with diethyl ether (1 mL). Saturated, aqueous sodium bicarbonate (2 mL) was added and the mixture extracted with diethyl ether (3×4 mL). The combined organic extracts were dried (K_2CO_3),

concentrated under reduced pressure and the residue purified by flash chromatography to give the *title compound* **32** (10 mg, 50%) as a colourless oil and as a 1:1:1:1 mixture of four diastereomers.

All spectral data was consistent with that obtained above.

3.1.21. 1,11-Bis-(*tert*-butyldimethylsilyloxy)-13-(*tert*-butyldiphenylsilyloxy)-8-triethylsilyloxytridec-3-yn-5-one 35. Tetra-*n*-propylammonium perruthenate (13 mg, 0.036 mmol) was added to a mixture of alcohol **25** (200 mg, 0.24 mmol), *N*-methylmorpholine-*N*-oxide (36 mg, 0.31 mmol) and 4 Å mol. sieves (50 mg) in dichloromethane (6 mL) at room temperature. The reaction mixture was stirred for 0.5 h then filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure to give the *title compound* **35** (160 mg, 80%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max}(film)/cm^{-1} 3050, 3071 (m, Ar-H), 2954, 2930 (s, CH), 2215 (w, triple bond), 1676 (s, C=O), 1472; δ_H (400 MHz; $CDCl_3$) 0.01 (3H, s, SiMe), 0.03 (3H, s, SiMe), 0.08 (6H, s, SiMe), 0.60 (6H, q, J=7.8, $SiEt_3$), 0.85 (9H, s, Bu^t), 0.90 (9H, s, Bu^t), 0.96 (9H, t, J=7.8, $SiEt_3$) 1.04 (9H, s, Bu^t), 1.38–1.80 (8H, m, 7-H, 9-H, 10-H, 12-H), 2.56–2.61 (4H, m, 2-H, 6-H), 3.65–3.87 (6H, m, 1-H, 8-H, 11-H, 13-H), 7.35–7.42 (6H, m, ArH), 7.64–7.67(4H, m, ArH); δ_C (100 MHz; $CDCl_3$) −5,3 (CH_3, SiMe), −4.6 (CH_3, SiMe), −4.4 (CH_3, SiMe), 5.1 (CH_2, $SiEt_3$), 7.0 (CH_3, $SiEt_3$), 18.0 (quat., Bu^t), 18.3 (CH_3, Bu^t), 19.2 (CH_3, Bu^t), 23.4 (CH_2, C-2), 25.9 (CH_3, Bu^t), 26.9 (CH_3, Bu^t), 30.7 (CH_2, C-9), 30.8 (CH_2, C-9*), 32.4 (CH_2, C-7), 32.7 (CH_2, C-7*), 32.8 (CH_2, C-10), 33.1 (CH_2, C-10*), 39.9 (CH_2, C-6), 41.2 (CH_2, C-12), 60.8 (CH_2, C-1), 60.9 (CH_2, C-13), 69.2 (CH, C-11), 71.3 (CH, C-8), 81.6 (quat., C-4), 90.8 (quat., C-3), 127.6 (CH, ArC), 129.5 (CH, Ar-C), 134.0 (quat., Ar-C), 135.5 (CH, Ar-C), 187.9 (quat., C-5); *m/z* (FAB, NBA) Found: MH$^+$, 839.5323. $C_{47}H_{83}O_5Si_4$ requires *MH*, 839.5318.

3.1.22. 4-{5-[5-(*tert*-Butyldiphenylsilyloxy)-3-hydroxypentyl]-2-methoxytetrahydrofuran-2-yl}but-3-yn-1-ol 36. Camphorsulphonic acid (2.5 mg, 0.010 mmol) was added to ketone 35 (50 mg, 0.060 mmol) in methanol (0.5 mL) at room temperature. The mixture was stirred for 1 h then neutralised by the addition of triethylamine (2 drops). The mixture was concentrated under reduced pressure and purified by flash column chromatography using diethyl ether as eluent to give the *title compound* **36** (17 mg, 55%) as a colourless oil and as a 1:1:1:1 mixture of diastereoisomers; ν_{max}(film)/cm^{-1} 2931 (s, CH), 2115 (w, triple bond), 1112; δ_H (400 MHz; $CDCl_3$)1.05 (9H, s, Bu^t), 1.59–1.78 (10H, m, 3′-H, 4′-H, 1″-H, 2″H, 4″-H), 2.49–2.54 (2H, m, 2-H), 3.35 (0.5 H, s, OMe), 3.35 (0.5 H, s, OMe*), 3.35 (0.5 H, s, OMe**), 3.36 (0.5 H, s, OMe***), 3.49 (1H, s, OMe****), 3.69-3.91 (5H, m, 1-H, 3″-H, 5″-H), 4.04–4.26 (1H, m, 5′-H), 7.37–7.46 (6H, m, ArH), 7.64–7.68 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.0 (quat., Bu^t), 22.9 (CH_2, C-2), 23.4 (CH_2, C-2*), 25.3 (CH_2, C-4′) 26.9 (CH_3, Bu^t), 29.7 (CH_2, C-1″), 31.0 (CH_2, C-2″), 31.5 (CH_2, C-2″*), 31.7 (CH_2, C-2″**), 31.9 (CH_2, C-2″***), 33.4 (CH_2, C-3′), 33.6 (CH_2, C-3′*), 34.4 (CH_2, C-3′**), 34.6 (CH_2, C-3′***), 38.1 (CH_2, C-4″), 38.2 (CH_2, C-4″*), 384 (CH_2, C-4″**), 39.3 (CH_2, C-4″***), 42.1 (CH_3, OMe), 42.6 (CH_3, OMe), 60.2 (CH_2, C-5″), 60.8 (CH_2, C-5″*), 61.5 (CH_2, C-5″**), 63.4 (CH_2, C-1), 64.0 (CH_2, C-1*) 70.7 (CH, C-3″), 71.1 (CH, C-3″*), 72.3 (CH, C-3″**), 72.8 (CH, C-3″***), 79.8 (CH, C-5′), 81.5 (quat., C-4), 81.6 (quat., C-3), 91.1 (quat., C-2′), 127.6 (CH, Ar-C), 129.8 (CH, Ar-C), 134.2 (quat., Ar-C), 135.6 (CH, Ar-C); *m/z* (FAB, NBA) 479 (M-OMe) (7%), 421 (7) and 401 (8).

3.1.23. 1-(*tert*-Butyldiphenylsilyloxy)-5-(1,6-dioxaspiro-[4.5]dec-9-en-2-yl)-pentan-3-ol 37. A mixture of acetylene **36** (20 mg, 0.039 mol) and Lindlar catalyst (2 mg) in THF (1 mL) was stirred under an atmosphere of hydrogen at room temperature for 3 h. The mixture was then diluted with dichloromethane (2 mL) and pyridinium *p*-toluenesulphonate (3 mg) was added. The mixture was stirred for 5 min. Two drops of triethylamine were added and the mixture filtered through Celite® and concentrated under reduced pressure. The residue was purified by flash chromatography using diethyl ether: hexane (2: 3) as eluent to give the *title compound* **37** (15 mg, 79%) as a colourless oil and a 1:1:1:1 mixture of four diastereoisomers; ν_{max}(film)/cm^{-1} 3435 (br, s, OH), 3054 (m, Ar-H), 2950, 2858 (s, CH), 1111; δ_H (400 MHz; $CDCl_3$) 1.06 (9H, s, Bu^t), 1.54–2.31 (12H, m, 2-H, 4-H, 5-H, 3′-H, 4′-H, 8′-H), 3.38 (1H, br s, OH), 3.63–3.98 (5H, m, 1-H, 3-H, 7′-H), 4.05–4.21 (1H, m, 2′-H), 5.58–5.65 (1H, m, 10′-H), 5.93–6.04 (1H, m, 9′-H), 7.36–7.44 (6H, m, ArH), 7.67–7.69 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.0 (quat., Bu^t), 24.5 (CH_2, C-4), 30.2 (CH_2, C-3′), 30.3 (CH_2, C-3′*), 30.6 (CH_2, C-5), 31.8 (CH_2, C-8′), 33.7 (CH_2, C-4), 34.0 (CH_2, C-4*), 34.2 (CH_2, C-4**), 37.3 (CH_2, C-4′), 38.6 (CH_2, C-2), 58.7 (CH_2, C-1), 59.2 (CH_2, C-1*), 63.2 (CH_2, C-7′), 63.4 (CH_2, C-7′*), 71,3 (CH, C-3), 71.5 (CH, C-3*), 80.1 (CH, C-2′), 81.0 (CH, C-2′*), 102.4 (quat., C-5′), 127.7 (CH, Ar-C), 128.5 (CH, C-9), 128.9 (CH, C-10′), 129.6 (CH, ArC), 133.1 (quat., ArC), 135.5 (CH, ArC); *m/z* (CI, NH_3) 481 (MH$^+$, 21%) and 463 (100); Found: MH$^+$, 481.2779. $C_{29}H_{40}O_4Si$ requires *MH*, 481.2774.

3.1.24. 2-{2-(*tert*-Butyldiphenylsilyloxy)ethyl}-1,6,8-trioxadispiro[4.1.5.2]tetradec-11-ene 13. A mixture of hydroxyspiroacetal **37** (45 mg, 0.094 mmol), iodine (49 mg, 0.19 mmol) and iodobenzene diacetate (63 mg, 0.20 mmol) in cyclohexane (5 mL) was irradiated with a 40 W tungsten lamp at room temperature for 1 h. Saturated, aqueous sodium thiosulphate (4 mL) was added and the mixture extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with saturated, aqueous sodium bicarbonate (5 mL), dried (K_2CO_3) and concentrated under reduced pressure. The residue was purified by flash chromatography using hexane: diethyl ether (8:2) as eluent to give the *title compound* **12** (35 mg, 78 %) as a colourless oil and a 1:1:1:1 mixture of diastereoisomers; ν_{max}(film)/cm^{-1} 3070 (m, Ar-H), 2958, 2857 (s, CH), 1111; δ_H (400 MHz; $CDCl_3$) 1.05 (9H, s, Bu^t), 1.52–2.29 (12H, m, 1′-H, 3-H, 4-H, 10-H, 13-H, 14-H), 3.71–3.97 (4H, m, 2-H, 9′-H), 4.11–4.33 (1H, m, 1-H), 5.55–5.68 (1H, m, 11-H), 5.91–6.01 (1H, m, 12-H), 7.36–7.45 (6H, m, ArH), 7.67–7.69 (4H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.1 (quat., Bu^t), 24.3 (CH_2, C-3), 29.7 (CH_2, C-13), 29.9 (CH_2, C-13*), 30.6 (CH_2, C-13*), 34.4 (CH_2, C-14), 34.5 (CH_2, C-14*), 34.6 (CH_2, C-14**), 35.0 (CH_2, C-14***), 36.3 (CH_2, C-10), 36.6 (CH_2, C-10*), 36.7 (CH_2, C-10**), 36.8 (CH_2, C-10***), 37.3 (CH_2, C-4), 37.6 (CH_2, C-4*),

38.4 (CH_2, C-1′), 38.6 (CH_2, C-1′*), 39.6 (CH_2, C-1′**), 40.3 (CH_2, C-1′***), 58.9 (CH_2, C-2′), 59.1 (CH_2, C-2′*), 59.2 (CH_2, C-2′**), 59.3 (CH_2, C-2′***), 61.1 (CH_2, C-9), 61.8 (CH_2, C-9*), 76.0 (CH, C-2), 76.1 (CH, C-2*), 77.1 (CH, C-2**), 77.3 (CH, C-2***), 102.8 (quat., C-5), 115.2 (quat., C-5*), 127.5 (CH, Ar-C), 127.9 (CH, C-11), 128.3 (CH, C-11*), 128.9 (CH, C-11**), 129.4 (CH, Ar-C), 129.6 (CH, C-12), 129.9 (CH, C-12*), 133.9 (quat., Ar-C), 135.5 (CH, Ar-C); *m/z* (EI) 479 (M^+, 2%) and 461 (100); Found: MH^+, 479.2608. $C_{29}H_{39}O_4Si$ requires *MH*, 479.2618.

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