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Graphical Abstract

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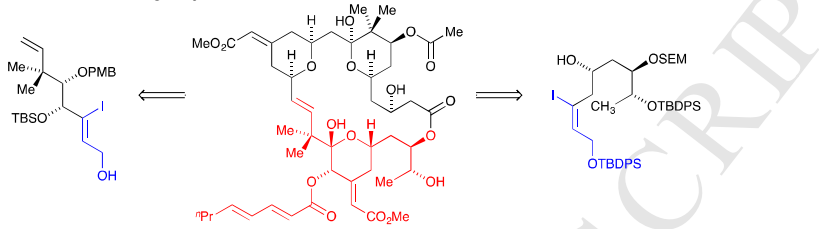

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Synthesis of vinylic iodides for incorporation into the C17-C27 fragment of bryostatins

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ABSTRACT

Vinylic iodides were identified as useful intermediates for the synthesis of the C17-C27 fragment of the bryostatins with control of the geometry of the exocyclic methoxycarbonylmethylene group. Following literature precedent, the Piers (*E*)-stereoselective addition of tributyltin hydride to an alkynoate followed by ester reduction and tin-iodine exchange gave vinylic iodides that could be used to form the C20-C21 bond of the bryostatins. Chelation controlled addition of lithiated 3-silyloxypropynes to 2-alkoxyaldehydes followed by reductive iodination was used to prepare vinylic iodides that could be used in the complementary assembly of the C21-C22 bond of the bryostatins. Initial studies of the synthesis of intermediates for metathesis studies using metal catalysed reactions of a vinylic iodide for C21-C22 bond formation were complicated by cyclisation reactions.

1. Introduction

The bryostatins, e.g. bryostatin 1 (**1**),[1] are an important group of natural products with an impressive array of biological activities including potentially useful anticancer behaviour. However, they are difficult to produce from natural sources and so have been studied extensively by synthetic organic chemists.[2] To date several outstanding total syntheses have been completed[3] and macrocyclic analogues have been prepared that show both the anticancer activity of the bryostatins and the tumour promoting activity of phorbol.[4,5]

It was recognised that approaches to the bryostatins based on a late-stage assembly from C1-C16 and C17-C27 fragments could lead to a convergent synthesis. Indeed the early total syntheses were based on this strategy and used Julia reactions to assemble the core structure by formation of the 16,17-double-bond.[3a-c] The formation of this double-bond by ring-closing metathesis (RCM) has also been considered albeit with mixed success.[6]

Intermediates that are equivalent to the C17-C27 keto-esters **2** and **3** could be useful for Julia and RCM based approaches to bryostatins, see Figure 1. These trisubstituted alkenes should be available from the (*E*)- and (*Z*)-vinylic iodides **4** and **5**. Indeed in their landmark syntheses, Masumune and Yamamura used vinylic iodides related to **4** and **5**.[3a,c] A vinylic iodide **4** was also used in an alternative synthesis of the C17-C27 fragment.[7] We now describe our syntheses of (*E*)- and (*Z*)-vinylic iodides **4** and **5** that may be useful for the synthesis of bryostatins.

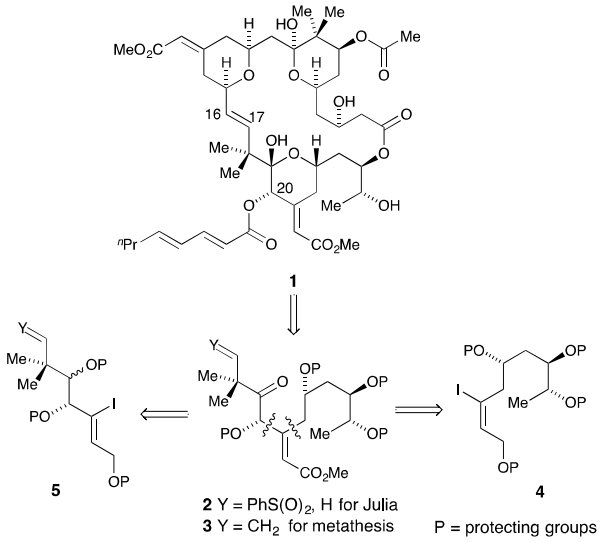

Figure 1 Vinylic iodides for the synthesis of bryostatins

2. Results and discussion

(*E*)-Vinylic iodides **4** were readily available from the alkynyl ester **6** that had been prepared in eight steps from (*R*)-pantolactone during studies of the synthesis of the C17-C27 fragment of the 20-deoxybryostatins.[8] Following the literature

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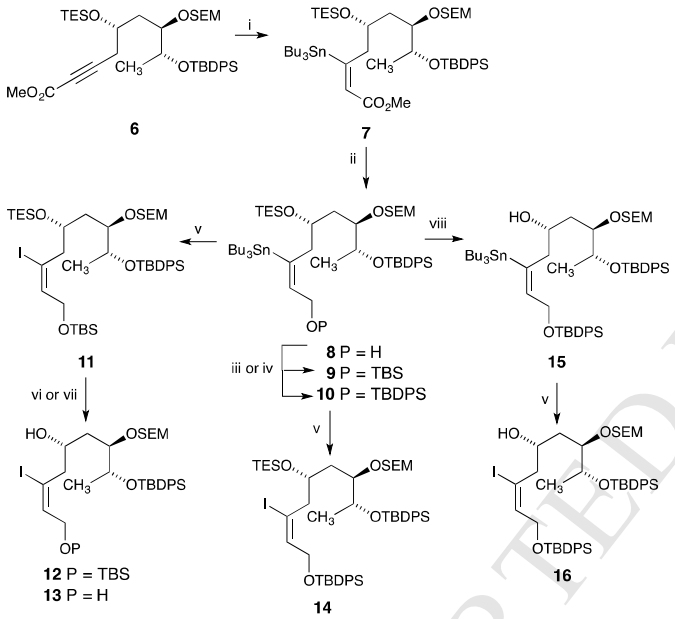
precedent,[7] the addition of tributyltin lithium to the ester **6** according to the procedure of Piers[9] gave the (*E*)-alkenoate **7** with excellent stereoselectivity. Following reduction using di-isobutylaluminium hydride and protection of the ensuing alcohol **8** as its *tert*-butyldimethylsilyl ether **9**, tin-iodine exchange gave the vinylic iodide **11**. However, attempts to remove the triethylsilyl group selectively were accompanied by partial loss of the allylic *tert*-butyldimethylsilyl protecting group and gave mixtures of the alcohol **12** and diol **13** with diol **13** being the dominant product with longer reaction conditions (see Scheme 1). The lability of *tert*-butyldimethylsilyl ethers of allylic alcohols relative to triethylsilyl ethers of secondary alcohols was also characteristic of more advanced bryostatin intermediates.[10]

The *tert*-butyldiphenylsilyl ether **10** of alcohol **8** was prepared and tin-iodine exchange gave the vinyl iodide **14**. The triethylsilyl ether could also be removed selectively from the fully silylated stannane **10** to give the seondary alcohol **15** (see Scheme 1). This on tin-iodine exchange gave the hydroxyvinylic iodide **16**. This was also available in an 85% yield by the selective silylation of the diol **13**.



Scheme 1 Synthesis of vinylic iodides analogous to **4** Reagents and conditions i, *n*BuLi, Bu_6Sn_2, THF, 0 °C, 25 min, add to CuBr.DMS, THF, –50 °C, 25 min, add **6** and MeOH, THF, –78 °C, 4 h (78%); ii, DIBAL-H, THF, –78 °C to rt, 3 h (86%); iii, TBSCl, imid., DCM, rt, 16 h (78% from **6**); iv, TBDPSCl, imid., DCM, rt, 16 h (90% from **6**): v, NIS, DCM, rt, 1.5 h (**11**, 96%; **14**, 96%; **16**, 95%); vi, HF, MeCN, rt, 1.5 h (**12**, 25%; **13**, 50%); vii, HF, MeCN, rt, 4.5 h (**13**, 72%); viii, dil. HF, MeCN, rt, 2 h (71%).

Approaches to the (*Z*)-vinylic iodides **5** were based on the stereoselective reductive iodination[11] of alkyn-1-ols **17**, see Figure 2. The ring opening of the benzyl ether **18** of (*R*)-pantolactone using the Weinreb reagent followed by immediate *O*-silylation gave the amide **19** but only in modest yields due to recovery of the lactone **18**. After reduction, addition of lithiated 3-*tert*-butyldimethylsilyloxypropyne to the resulting aldehyde **20** gave a mixture of the *syn*- and *anti*-alcohols **21** and **22** with stereoselectivity in favour of the *syn*-isomer **21**, ratio *ca*. 70 : 30 (see Scheme 2). The configuration shown was assigned to the major product **21** on the basis of the relative shifts of its (*R*)- and (*S*)-*O*-acetylmandelates.[12]

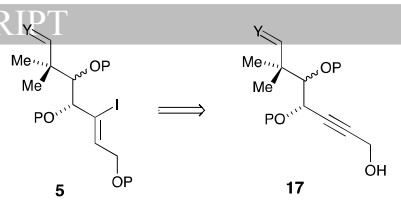
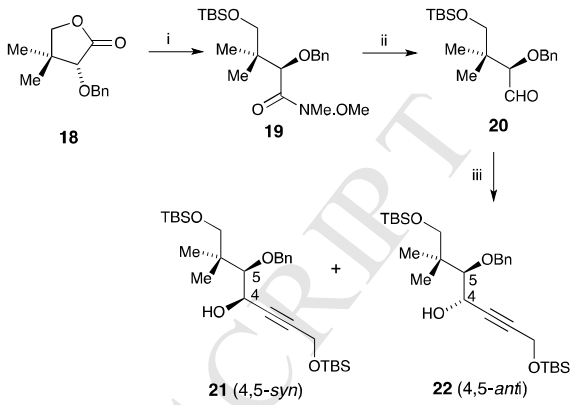


Figure 2 Proposed reductive iodination of alkynols **17**

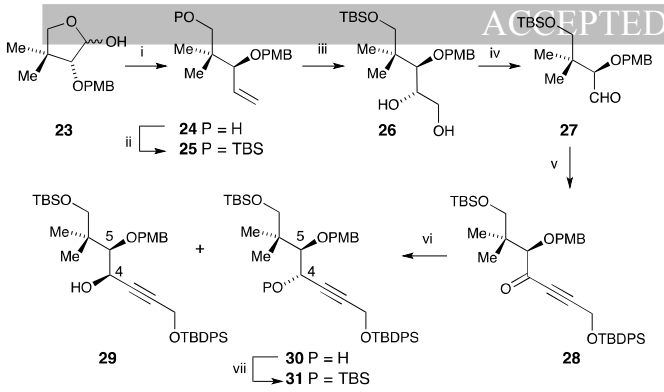


Scheme 2 Synthesis of the alkynol **21** Reagents and conditions i, (a) MeONHMe.HCl, benzene, Me_3Al, 0 °C to rt, 2 h, add **18**, rt, 1 h (b) TBSCl, imid., DCM, DMAP (cat.), TBAI (cat.), rt, 1 h (**19**, 30%; recovered **18**, 48%); ii, DIBAL-H, DCM, –78 °C, 2 h (45%); iii, *n*BuLi, 3-*tert*-butyldimethylsilyloxypropyne, THF, 0 °C, 30 min, cool to –78 °C, add **20**, 1.75 h (**21**, 42%; **22**, 17%).

The configuration at C-4 of the major *syn*-alkyne **21** does not correspond to that in the required alkynols **17**. This was not surprising since it is consistent with both chelation[13] and Felkin-Anh[14] control. However, the selectivity was not as high as expected and so it was decided to use an oxidation – reduction sequence to access intermediates **17** with the required configuration at C-4 from alkynes analogous to **21** and **22** available from (*R*)-pantolactone. The ring opening of (*R*)-*O*-benzylpantolactone **18** using the Weinreb amide had also been capricious and a better synthesis of the aldehyde was required.

Lactol **23**[15] was available by reduction of PMB-protected (*R*)-pantolactone, and was converted into the silyloxypentene **25** *via* a Wittig reaction and *O*-silyation. Hydroxylation appeared to give a single diastereoisomer **26** that was assigned the *anti*-configuration by analogy with the literature,[16] and oxidative cleavage gave aldehyde **27**. As expected, addition of lithiated *tert*-butyldiphenylsilyloxypropyne to this aldehyde gave a mixture of the *syn*- and *anti*-alcohols, *syn*:*anti* = 75 : 25, and this mixture was oxidised to give the ketone **28**, see Scheme 3.

The reduction of this ketone was investigated with chelation control expected to give the required 4,5-*anti*-alcohol **30**, the minor alcohol in the mixture of alcohols obtained from aldehyde **27**. Reduction using di-isobutyaluminium hydride and sodium borohydride in the presence of cerium(III) chloride gave more of the 4,5-*syn*-alcohol **29**, in ratios of 68 : 32 and 86 : 14, respectively. However, zinc borohydride[17] was usefully selective in favour of the chelation controlled product **30**, **29** : **30** = 14 : 86, and the use of the chiral reducing agent (*R*)-methylCBS/BMS[18] led to stereoselectivity, 80 : 20 in favour of the required 4,5-*anti*-epimer **30**. The configurations shown for the alcohols **29** and **30** were assigned by comparison of their ^{1}H NMR spectra with those of analogous alkynols, *vide infra*, and by analogy with the selectivity for formation of the *syn*-adducts **21** and **29** in addition to aldehydes **20** and **27**.

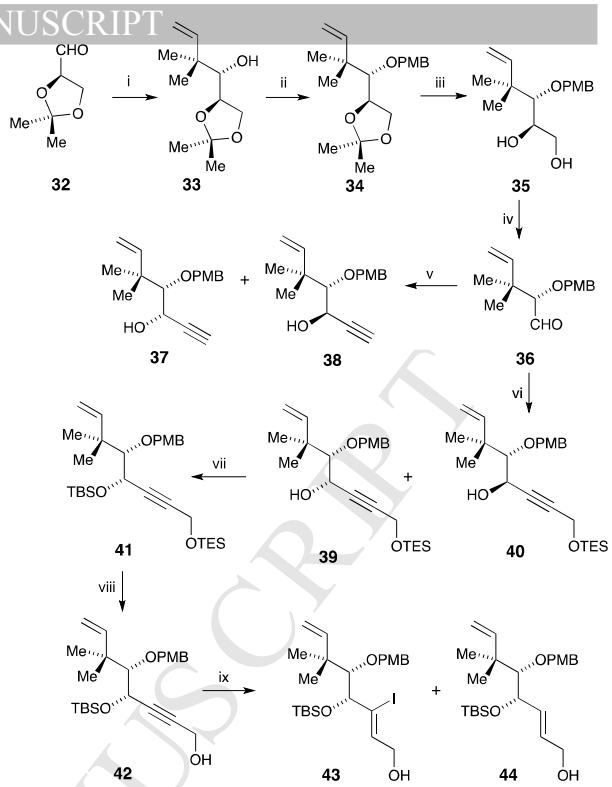


Scheme 3 Synthesis of the 4,5-*anti*-hept-2-yn-4-ol **30** Reagents and conditions i, Ph_3MePBr, KO^{t}Bu, rt, 30 min, THF, rt, 1 h, **23**, 0 ^{o}C to rt, 3.5 h (75%); ii, TBSCl, imid., DMAP (cat.), TBAI (cat.), rt, 1 h (63%); iii, NMO, OsO_4 (cat.), acetone, water, ^{t}BuOH, rt, 18 h (59%); iv, $NaIO_4$, THF, water, rt, 30 min (*ca*. 99%); v, (a) *n*BuLi, *tert*-butyldiphenylsilyloxypropyne, 0 ^{o}C, 30 min, **27**, −78 ^{o}C to 0 ^{o}C, 2 h (84%; **29** : **30** = 75 : 25) (b) Dess-Martin periodinane, DCM, rt, 45 min (*ca*. 99%); vi, (a) $NaBH_4$, $CeCl_3.6H_2O$, MeOH, rt, 1.5 h (85%, **29** : **30** = 86 : 14) (b) $ZnBH_4$, ether, −30 ^{o}C to 0 ^{o}C, 3 h (86%, **29** : **30** = 14 : 86) (c) (*R*)-2-methyl-CBS oxazaborolidine, tol., $BH_3.Me_2S$, −30 ^{o}C to −15 ^{o}C, 2 h (75%, **29** : **30** = 20 : 80); vii, TBSCl, imid., DCM, rt, 18 h (96%).

The *anti*-alcohol **30** was protected as its *tert*-butyldimethylsilyl ether **31** but attempts to remove the less hindered *tert*-butyldiphenylsilyl group selectively were complicated by loss of both *tert*-butyldimethylsilyl groups to give the corresponding triol.

At this point, it was decided to prepare α-alkoxyaldehydes that were pseudo-enantiomers of aldehydes **20** and **27** so that chelation control of the addition of alkynes would give the required configuration at C-4 directly. As (*S*)-pantolactone is less readily available than its (*R*)-enantiomer it was necessary to vary the synthesis and use a different starting material. It was also decided to target alkynols **17** (Y = CH_2) suitable for use in RCM based approaches to bryostatins.

The zinc mediated Barbier reaction of (*R*)-glyceraldehyde **32** with isoprenyl bromide gave predominantly the *anti*-adduct **33** and this was protected as its PMB-ether **34**. The *anti*-configuration assigned to the major adduct **33** is well precedented[19] and was confirmed using (*R*)- and (*S*)-*O*-acetyl mandelates.[12] Following hydrolysis of the acetonide, periodate cleavage of the diol **35** gave the (*S*)-aldehyde **36**. The addition of ethynylmagnesium bromide to this aldehyde proceeded with only modest stereoselectivity in favour of the *syn*-addduct **37** (see Scheme 4) but the addition of lithiated 3-triethylsilyloxypropyne was much more stereoselective and gave the *syn*-adduct **39** as the dominant product, **39** : **40** = 92 : 8. The configurations of these products were established by comparison of their ^{1}H NMR spectra with those of analogous products prepared earlier with the chemical shifts of the diastereotopic benzylic hydrogens being diagnostic. The *syn*-isomers were also always the less polar. The *syn*-alcohol **39** was then protected as its *tert*-butyldimethylsilyl ether **41** and the triethylsilyl group removed using potassium fluoride in THF-methanol. Under these conditions only traces of the diol formed by competing cleavage of the *tert*-butyldimethylsilyl group were observed.

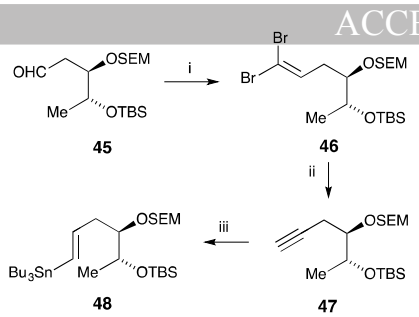


Scheme 4 Synthesis of the vinylic iodide **43** Reagents and conditions i, activated Zn, 1-bromo-3-methylbut-2-ene, **32**, 0 ^{o}C, 4 h (53% plus 6% of its *syn*-epimer); ii, NaH, DMF, 0 ^{o}C to rt, 30 min, PMBCl, 0 ^{o}C to rt, 1 h (98%); iii, aq. AcOH, 48 ^{o}C, 2 h (86%); iv, $NaIO_4$, methanol, water, 0 ^{o}C to rt, 1.25 h (*ca*. 99%); v, ethynylmagnesium bromide, THF, −78 ^{o}C, 2 h, rt, 2 h (**37**, 29%; **38**, 21%); vi, *n*BuLi, 3-triethylsilyloxypropyne, 0 ^{o}C, 1 h, **36**, −78 ^{o}C, 2.5 h (**39**, 74%, **40**, 4%); vii, TBSOTf, 2,6-lut., DCM, 0 ^{o}C, 1 h (92%); viii, KF, methanol, THF, 0 ^{o}C, 2 h (77%); ix, Red-Al, tol., ether, 0 ^{o}C, 1 h, rt, 3 h, iodine flakes, −78 ^{o}C to −10 ^{o}C, 1 h (**43**, 69%; **44**, 14%).

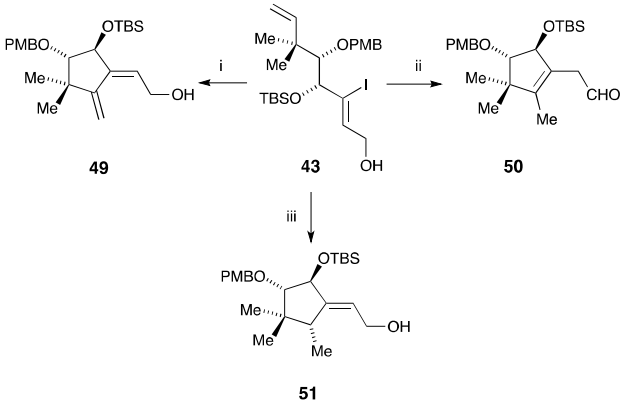
Initial studies of the reductive iodination of the alkynol **42** led to mixtures of the required vinylic iodide **43** and the disubstituted alkene **44**. After optimisation, the use of Red-Al in ether with the addition of iodine at a low temperature gave 65-70% yields of the iodide **43** together with typically 20% of the alkene **44** (see Scheme 4). This synthesis had given the vinylic iodide **43** in eight steps from (*R*)-glyceraldehyde in an overall yield of 14.5%.

The vinylic iodides **12**-**14**, **16** and **43** correspond to the vinylic iodides **4** and **5** and are suitable intermediates for incorporation into syntheses of bryostatins. To check possible reaction conditions, some metal catalysed reactions of the iodide **43** were briefly studied.

To provide substrates for these coupling reactions, aldehyde **45**[8] was converted into the alkyne **47** via the dibromide **46**. Addition of tributyltin hydride under free radical conditions to the alkyne gave the vinyl stannane **48** (see Scheme 5). However, attempts to couple the alkyne **47** or the stannane **48** with the vinylic iodide **43** were unsuccessful as Heck cyclisations dominated instead. The methylenecyclopentane **49** was the dominant product from the attempted Sonogashira reaction with the alkyne **47** and the aldehyde **50** together with traces of the alcohol **49** were formed during the attempted Stille reaction with the stannane **48**. An attempted NHK reaction with benzaldehyde also gave a cyclised product, the methylenecyclopentane **51** (see Scheme 6).



Scheme 5 Synthesis of substrates for test Stille and Sonogashira reactions Reagents and conditions i, CBr_4, Ph_3P, py., DCM, 0 °C, 20 min, **45**, rt, 40 min (74%); ii, *n*BuLi, −78 °C, 15 min, 0 °C, 15 min (87%); iii, Bu_3SnH, AIBN (cat.), tol., 120 °C, 4 h [68%; (*E*) : (*Z*) = 9 : 1].



Scheme 6 Palladium(0) catalysed reactions of the iodide **43** Reagents and conditions i, **47**, $Pd(PPh_3)_4$, CuI, Et_3N, rt, 2 h, CuI, rt, 18 h (80%); ii, **48**, $Pd(PPh_3)_4$, DMF, 80 °C, 17 h (**50**, 30%; **49**, 3%); iii, $CrCl_2$, $NiCl_2$, **43**, PhCHO, DMF, rt, 2 h (62%).

The structures shown were assigned to the products **49** – **51** in Scheme 6 using spectroscopic data. The configuration of the secondary methyl substituent in the methylenecyclopentane **51** was established from nOe studies, see experimental.

3. Summary and conclusions

Several vinylic iodides that could be useful for the synthesis of the C17-C27 fragment of bryostatins have been synthesized. Of some interest is the stereocontrol found for the addition of metalated alkynes to aldehydes, the use of the reductive iodination of alkynols and the application of the Piers conjugated addition of tributyltin hydride to conjugated alkynoates. Although the initial studies of the palladium(0) promoted reactions of the vinylic iodide **43** led to intramolecular Heck products, this reaction would not be a problem with iodides that didn't have the terminal double bond. In addition other procedures could be envisaged to incorporate these iodides into further synthetic studies.

4. Experimental

4.1. General experimental details

Flash column chromatography was performed using Merck silica gel 60. Light petroleum refers to the fraction boiling between 40 and 60 °C and was redistilled before use. Tetrahydrofuran was dried over sodium-benzophenone and distilled under nitrogen prior to use. Dichloromethane was dried over CaH_2 and distilled before use. Ether refers to diethyl ether. Reactions under non-aqueous conditions were carried out under an atmosphere of nitrogen or argon.

Mass spectra used electron impact ionisation (EI^+), chemical ionisation using ammonia (CI^+) or electrospray ionisation in the positive mode (ES^+). Low and high resolution mass spectra were recorded using Micromass Trio 200 and Kratos Concept IS spectrometers, respectively. For organostannanes., molecular ion peaks corresponding to the ^{120}Sn isotope are given. Infra-red spectra were measured using a Genesis FTIR spectrometer on NaBr plates, either neat or as evaporated films. Nuclear magnetic resonance spectra were recorded using Varian Unity 500 (500 MHz), Varian INOVA 400 (400 MHz) and Varian Unity 300 (300 MHz) spectrometers. Spectra are at 300 Mz (^1H) and at 75 Mz (^{13}C) in deuteriated chloroform unless otherwise indicated. Coupling constants (*J*) are given in Hertz (Hz) and chemical shifts are relative to tetramethylsilane. Residual non-deuteriated solvent was used as the internal standard. All products were isolated as pale yellow or colourless oils.

4.2 Experimental procedures

*4.2.1 Methyl (2*E,5R,*7*R,*8*R*)-8*-tert-*butyldiphenylsilyloxy-3-tributylstannyl-5-triethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-enoate (7).* *n*-Butyllithium (1.6 M in hexanes, 5.00 mL, 8.0 mmol) was added to hexa-*n*-butylditin (4.00 mL, 8.0 mmol) in THF (2.6 mL) at 0 °C. After 25 min, this solution was transferred to a suspension of CuBr.DMS (1.64 g, 8.0 mmol) in THF (4.9 mL) at −50 °C and this mixture was stirred for 25 min before cooling to −78 °C. The ester **6** (1.10 g, 1.58 mmol) and anhydrous MeOH (109 µl, 2.7 mmol) in THF (1.6 mL) were added and, after 4 h at −78 °C, MeOH (2 mL) was added. The mixture allowed to warm to rt then diluted with ether and filtered through celite with ether washings. The filtrate was partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:1:98 ether:Et_3N:light petroleum) of the residue gave the *title compound* **7** (1.22 g, 78%), R_f = 0.70 (1:9, ether:light petroleum); $[\alpha]_D^{23}$ −17.6 (*c* 0.5, $CHCl_3$); ν_{max}/cm^{-1} 2955, 2926, 2877, 1721, 1590, 1461, 1427, 1377, 1248, 1167, 1106, 1054, 860, 834; δ_H 0.05 [9H, s, $Si(CH_3)_3$], 0.60 (1H, ddd, *J* 13.8, 11.5, 5.2, C*H*HSi), 0.68 (6H, q, *J* 7.6, 3 × $SiCH_2$), 0.78 (1H, ddd, *J* 13.8, 11.5, 5.2, CH*H*Si), 0.88-1.14 (9H, m, 9-H_3, 3 × $SnCH_2$), 0.93 (9H, t, *J* 7.3, 3 × CH_3), 1.01 (9H, t, *J* 7.6, 3 × $SiCH_2CH_3$), 1.10 [9H, s, $SiC(CH_3)_3$], 1.28-1.42 (6H, m, 3 × CH_2), 1.43-1.62 (7H, m, 3 × CH_2, 6-H), 1.83 (1H, ddd, *J* 13.8, 9.7, 1.4, 6-H′), 3.01 (1H, ddd, *J* 12.1, 5.1, 1.4, 4-H), 3.28 (1H, ddd, *J* 11.6, 9.6, 5.9, C*H*HCH$_2$Si), 3.45 (1H, dd, *J* 12.1, 9.3, 4-H′), 3.51 (1H, ddd, *J* 11.8, 9.4, 5.2, C*H*HCH$_2$Si), 3.75 (3H, s, OCH_3), 3.81 (1H, ddd, *J* 10.9, 4.3, 1.6, 7-H), 4.09 (1H, m, 5-H), 4.18 (1H, dq, *J* 6.1, 4.4, 8-H), 4.54 and 4.60 (each 1H, d, *J* 6.8, OCH*H*O), 6.06 (1H, s, 2-H), 7.36-7.47 (6H, m, ArH), 7.69-7.75 (4H, m, ArH); δ_C −1.3, 5.9, 7.4, 10.5, 13.9, 16.9, 18.1, 19.5, 27.3, 27.7, 29.2, 35.6, 44.3, 51.1, 65.0, 69.4, 69.9, 79.7, 96.4, 127.6, 127.8, 129.6, 129.8, 129.9, 134.3, 135.2, 136.1, 136.2, 164.8, 169.2; *m*/*z* (ES^+) 1013 (M^+ + 23, 100%).

*4.2.2 (2*E,5R,*7*R,*8*R*)-8*-tert-*Butyldiphenylsilyloxy-3-tributylstannyl-5-triethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-en-1-ol (8).* Di-isobutylaluminium hydride (1M in hexanes, 6.15 mL, 6.15 mmol) was added to the ester **7** (2.03 g, 2.05 mmol) in THF (8 mL) at −78 °C and the solution stirred for 1 h at −78 °C and for 3 h at rt. After cooling to 0 °C, ether and saturated aqueous sodium potassium tartrate were added and the mixture was stirred vigorously for 1 h. The aqueous layer was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the alcohol **8** (1.97 g) used directly in the next reaction. Chromatography

(1:1:98 then 10:1:89, ether:Et_3N:light petroleum) of a sample gave the *title compound* **8** (86%), R_f = 0.18 (1:9, ether:light petroleum); $[\alpha]_D^{20}$ –7.3 (*c* 1.2, $CHCl_3$); ν_{max}/cm^{-1} 3449, 2955, 2927, 1725, 1659, 1462, 1425, 1378, 1247, 1105, 1058, 1032, 859, 834; δ_H –0.04 [9H, s, $Si(CH_3)_3$], 0.55-0.71 (1H, m, C*H*HSi), 0.66 (6H, q, *J* 7.6, 3 × $SiCH_2$), 0.80 (1H, ddd, *J* 13.7, 11.7, 5.7, CH*H*Si), 0.87-1.04 (27H, m, 3 × CH_3, 3 × CH_2Sn, 3 × $SiCH_2CH_3$, 9-H_3), 1.10 [9H, s, $SiC(CH_3)_3$], 1.28-1.43 (6H, m, 3 × CH_2), 1.46-1.57 (7H, m, 3 × CH_2, 6-H), 1.80 (1H, ddd, *J* 13.6, 7.6, 1.6, 6-H′), 2.16 (1H, dd, *J* 7.2, 4.6, OH), 2.47 (1H, dd, *J* 13.6, 7.7, 4-H), 2.73 (1H, dd, *J* 13.6, 6.3, 4-H′), 3.30 (1H, ddd, *J* 11.6, 9.8, 5.9, C*H*HCH$_2$Si), 3.51 (1H, ddd, *J* 11.8, 9.5, 5.3, CH*H*CH$_2$Si), 3.70 (1H, ddd, *J* 10.0, 4.1, 2.1, 7-H), 3.89-3.96 (1H, m, 5-H), 4.07-4.23 (2H, m, 1-H, 8-H), 4.36 (1H, ddd, *J* 12.7, 6.9, 4.6, 1-H′), 4.51 and 4.58 (each 1H, d, *J* 6.8, O*H*CHO), 5.95 (1H, t, *J* 6.3, 2-H), 7.36-7.48 (6H, m, ArH), 7.68-7.75 (4H, m, ArH); δ_C –1.3, 5.7, 7.3, 10.0, 14.0, 16.8, 18.1, 19.5, 27.3, 27.8, 29.4, 35.5, 42.7, 46.4, 59.4, 65.2, 69.9, 79.9, 96.0, 127.7, 127.8, 129.8, 129.9, 134.2, 134.9, 136.1, 142.1, 144.4; *m*/*z* (ES^+) 1064 (73%), 984 (100), 962 (40).

*4.2.3 (2*E,*5*R,*7*R,*8*R)*-1*-tert-*Butyldimethylsilyloxy-8*-tert-*butyldiphenylsilyloxy-3-tributylstannyl-5-triethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (**9**).* Alcohol **8** (1.09 g, 1.13 mmol) in DCM (2 mL) was added to *tert*-butyldimethylsilyl chloride (205 mg, 1.36 mmol) and imidazole (184 mg, 2.71 mmol) in DCM (2 mL) at 0 °C and the mixture was stirred at rt for 16 h. Saturated aqueous ammonium chloride was added and the mixture partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:1:98, ether:Et_3N:light petroleum) of the residue gave the *title compound* **9** (949 mg, 78% from **6**), R_f = 0.58 (6% ether in light petroleum); $[\alpha]_D^{20}$ +1.5 (*c* 1.3, $CHCl_3$); ν_{max}/cm^{-1} 2956, 2928, 2859, 1738, 1657, 1464, 1425, 1378, 1255, 1104, 1058, 1036, 834, 776, 739; δ_H –0.05 (6H, s, 2 × $SiCH_3$), 0.11 [9H, s, $Si(CH_3)_3$], 0.58 (1H, ddd, *J* 14.2, 11.8, 5.0, C*H*HSi), 0.65 (6H, q, *J* 8.2, 3 × $SiCH_2$), 0.77 (1H, ddd, *J* 14.0, 12.0, 5.6, CH*H*Si) 0.84-1.04 (6H, m, 3 × CH_2Sn), 0.92 (9H, t, *J* 7.5, 3 × CH_3), 0.95 (3H, d, *J* 6.3, 9-H_3), 0.96 [9H, s, $SiC(CH_3)_3$], 1.01 (9H, t, *J* 8.2, 3 × $SiCH_2CH_3$), 1.10 [9H, s, $SiC(CH_3)_3$], 1.27-1.47 (7H, m, 3 × CH_2, 6-H), 1.44-1.69 (7H, m, 3 × CH_2, 6-H′), 2.47-2.60 (2H, m, 4-H_2), 3.26 (1H, ddd, *J* 9.5, 5.7, 3.6, C*H*HCH$_2$Si), 3.51 (1H, ddd, *J* 9.1, 6.6, 4.2, CH*H*CH$_2$Si), 3.74-3.81 (1H, m, 7-H), 3.87-3.93 (1H, m, 5-H), 4.20 (1H, dq, *J* 6.2, 4.4, 8-H), 4.37 and 4.41 (each 1H, dd, *J* 13.8, 5.5, 1-H), 4.51 and 4.59 (each 1H, d, *J* 6.8, OHC*H*O), 5.77 (1H, t, *J* 5.4, 2-H), 7.36-7.48 (6H, m, ArH), 7.68-7.75 (4H, m, ArH); δ_C –4.7, –1.3, 1.3, 5.8, 7.4, 10.0, 14.0, 16.8, 18.1, 19.5, 26.3, 27.3, 27.8, 29.4, 35.1, 43.8, 61.1, 65.0, 69.3, 69.8, 79.8, 96.4, 127.6, 127.8, 129.7, 129.8, 134.3, 135.1, 136.1, 136.2, 140.3, 143.7; *m*/*z* (ES^+) 1100 (M^+ + 23, 4%), 239 (100).

*4.2.4 (2*E,*5*R,*7*R,*8*R)*-1,8-Bis*-tert-*butyldiphenylsilyloxy-3-tributylstannyl-5-triethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (**10**).* Following the procedure outlined for the preparation of silyl ether **9**, imidazole (335 mg, 4.92 mmol), *tert*-butyldiphenylsilyl chloride (640 μl, 2.46 mmol) and alcohol **8** (1.97 g), after chromatography (1:1:98, ether:Et_3N:light petroleum), gave the *title compound* **10** (2.22 g, 90% from **6**), R_f = 0.79 (1:9, ether:light petroleum); ν_{max}/cm^{-1} 2954, 2926, 2857, 1462, 1426, 1376, 1250, 1106, 1059; δ_H –0.06 [9H, s, $Si(CH_3)_3$], 0.54 (6H, q, *J* 8.2, 3 × $SiCH_2$), 0.54-0.68 (1H, m, C*H*HSi), 0.76 (1H, ddd, *J* 13.6, 11.5, 5.8, CH*H*Si) 0.86-1.12 [45H, m, 3 × $SiCH_2CH_3$, 3 × CH_3, 3 × $SnCH_2$, 2 × $SiC(CH_3)_3$, 9-H_3], 1.21-1.64 (14H, m, 6 × CH_2, 6-H_2), 2.30-2.40 (2H, m, 4-H_2), 3.24 (1H, ddd, *J* 11.3, 9.7, 6.0, C*H*HCH$_2$Si), 3.48 (1H, ddd, *J* 12.1, 9.6, 5.3, CH*H*CH$_2$Si), 3.66-3.73 (1H, m, 7-H), 3.73-3.81 (1H, m, 5-H), 4.13 (1H, dq, *J* 4.7, 6.2, 8-H), 4.38-4.46 (3H, m, 1-H_2, OHC*H*O) 4.52 (1H, d, *J* 6.8, OHC*H*O), 5.84 (1H, t, *J* 5.7, 2-H), 7.25-7.46 (12H, m, ArH), 7.62-7.78 (8H, m, ArH); δ_C –1.2, 4.1, 5.2, 10.1, 14.4, 18.2, 18.4, 19.2, 27.2, 27.3, 27.5, 29.2, 36.5, 41.9, 61.1, 65.5, 67.8, 70.5, 79.4, 96.4, 127.7, 128.0, 129.7, 129.9, 134.0, 134.2, 134.7, 135.8, 135.9, 136.1, 142.7, 143.1; *m*/*z* (ES^+) 1143 (28%), 364 (50), 332 (100).

*4.2.5 (2*E,*5*R,*7*R,*8*R)*-1*-tert-*Butyldimethylsilyloxy-8*-tert-*butyldiphenylsilyloxy-3-iodo-5-triethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (**11**).* The stannane **9** (920 mg, 0.85 mmol) in DCM (9.8 mL) was added to a suspension of *N*-iodosuccinimide (287 mg, 1.27 mmol) in DCM (5.9 mL) at rt and the mixture stirred for 1.5 h. After concentration under reduced pressure, chromatography (2:1:97, ether:Et_3N:light petroleum) of the residue gave the *title compound* **11** (746 mg, 96%), R_f = 0.45 (6% ether in light petroleum); ν_{max}/cm^{-1} 2955, 2930, 2879, 2858, 1466, 1426, 1377, 1256, 1105, 835, 777, 740; δ_H –0.02 (6H, s, 2 × $SiCH_3$), 0.12 [9H, s, $Si(CH_3)_3$], 0.68 (6H, q, *J* 7.9, 3 × $SiCH_2$), 0.77-0.91 (2H, m, $SiCH_2$), 0.94 (3H, d, *J* 5.9, 9-H_3), 0.94 [9H, s, $SiC(CH_3)_3$], 1.01 (9H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.11 [9H, s, $SiC(CH_3)_3$], 1.61 (1H, ddd, *J* 14.1, 10.0, 5.2, 6-H), 1.89 (1H, ddd, *J* 14.1, 7.1, 1.7, 6-H′), 2.67 (2H, d, *J* 6.1, 4-H_2), 3.41 (1H, ddd, *J* 11.5, 9.6, 5.9, C*H*HCH$_2$Si), 3.54 (1H, ddd, *J* 11.7, 9.6, 5.4, CH*H*CH$_2$Si), 3.65 (1H, ddd, *J* 10.0, 4.2, 1.4, 7-H), 4.03-4.18 (2H, m, 5-H, 8-H), 4.22 (2H, t, *J* 6.3, 1-H_2), 4.54 and 4.60 (each 1H, d, *J* 6.8, O*H*CHO) 6.41 (1H, t, *J* 6.3, 2-H), 7.36-7.49 (6H, m, ArH), 7.69-7.76 (4H, m, ArH); δ_C –4.9, –1.2, 5.6, 7.3, 16.9, 18.2, 19.5, 26.2, 27.3, 35.9, 48.6, 61.6, 65.5, 69.8, 70.1, 79.8, 96.0, 100.5, 127.7, 127.9, 128.6, 129.8, 129.9, 134.2, 134.8, 136.1, 136.1, 143.3; *m*/*z* (ES^+) 973 (25%), 935 (M^+ + 23, 100%); HRMS (ES^+): MNa^+, found 935.3789. $C_{43}H_{77}O_5Si_4INa$ requires 935.3785.

*4.2.6 (2*E,*5*R,*7*R,*8*R)*-1*-tert-*Butyldimethylsilyloxy-8*-tert-*butyldiphenylsilyloxy-3-iodo-7-(2-trimethylsilylethoxymethoxy)non-2-en-5-ol (**12**) and (2*E,*5*R,*7*R,*8*R)-8*-tert-*butyldiphenylsilyloxy-3-iodo-7-(2-trimethylsilylethoxymethoxy)non-2-ene-1,5-diol (**13**).* Hydrogen fluoride (1% in MeCN, 1 mL) was added to the triethylsilyl ether **11** (90 mg, 99 μmol) in THF (0.5 mL) in a Teflon container at rt and the mixture stirred for 1.5 h. Saturated aqueous sodium hydrogen carbonate was added and the mixture partitioned between water and EtOAc. The aqueous layer was extracted with EtOAc and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (2:8 then 4:6 ether:light petroleum) of the residue gave the *title compound* **12** (20 mg, 25%), R_f = 0.81 (1:1, ether:light petroleum); ν_{max}/cm^{-1} 3464, 2954, 2929, 2893, 2858, 1467, 1632, 1427, 1376, 1255, 1106, 1058, 1031, 836, 800; δ_H 0.04 (6H, s, 2 × $SiCH_3$), 0.12 [9H, s, $Si(CH_3)_3$], 0.82-1.14 (2H, m, CH_2Si), 0.94 [9H, s, $SiC(CH_3)_3$], 1.04 (3H, d, *J* 6.3, 9-H_3), 1.11 [9H, s, $SiC(CH_3)_3$], 1.54-1.66 (1H, m, 6-H), 1.72 (1H, ddd, *J* 13.6, 10.0, 3.3, 6-H′), 2.49 (1H, dd, *J* 14.2, 4.1, 4-H), 2.78 (1H, dd, *J* 14.4, 8.2, 4-H′), 3.28 (1H, br. s, OH), 3.51 (1H, ddd, *J* 11.1, 9.5, 5.9, C*H*HCH$_2$Si), 3.66-3.76 (2H, m, CH*H*CH$_2$Si, 7-H), 3.97 (1H, dq, *J* 6.5, 5.6, 8-H), 4.02-4.13 (1H, m, 5-H), 4.23 (2H, d, *J* 6.4, 1-H_2), 4.52 and 4.58 (each 1H, d, *J* 6.9, OHC*H*O), 6.50 (1H, t, *J* 6.3, 2-H), 7.38-7.48 (6H, m, ArH), 7.68-7.76 (4H, m, ArH); δ_C –4.9, –1.1, 1.3, 18.0, 18.3, 19.5, 26.2, 27.3, 36.3, 47.4, 61.4, 66.3, 66.8, 71.0, 79.7, 96.3, 101.1, 127.8, 127.9, 129.9, 130.0, 134.6, 136.1, 136.2, 143.4. The second fraction was the *title compound* **13** (34 mg, 50%), R_f = 0.31 (1:1, ether:light petroleum); δ_H 0.06 [9H, s, $Si(CH_3)_3$], 0.85-1.03 (2H, m, CH_2Si), 1.05 (3H, d, *J* 6.3, 9-H_3), 1.10 [9H, s, $SiC(CH_3)_3$], 1.60 (1H, ddd, *J* 14.4, 10.2, 2.9, 6-H), 1.76 (1H, ddd, *J* 13.9, 10.4, 4.2, 6-H′), 2.42 (1H, dd, *J* 14.6, 2.1,

4-H), 3.06 (1H, dd, *J* 14.5, 9.7, 4-H′), 3.50 (1H, ddd, *J* 10.8, 9.6, 6.1, C*H*HCH$_2$Si), 3.57-3.65 (1H, m, 7-H), 3.70-3.82 (2H, m, CH*H*CH$_2$Si, 1-H), 3.92 (1H, dq, *J* 6.2, 5.6, 8-H), 4.04 (1H, tt, *J* 10.2, 2.2, 5-H), 4.19-4.23 (1H, m, 1-H′), 4.46 and 4.58 (each 1H, d, *J* 6.9, OHC*H*O), 6.79 (1H, t, *J* 7.7, 2-H), 7.37-7.53 (6H, m, ArH), 7.68-7.77 (4H, m, ArH); δ_C −1.1, 18.2, 19.5, 27.3, 30.0, 36.7, 47.1, 59.0, 64.7, 66.9, 71.3, 80.2, 96.6, 105.4, 127.9, 128.0, 130.0, 130.2, 133.8, 134.4, 136.1, 136.2, 142.7.

The same procedure using the triethylsilyl ether **11** (365 mg, 0.40 mmol) in THF (1 mL) and hydrogen fluoride (1% in MeCN, 4 mL), after stirring for 4.5 h and chromatography (4:6 ether:light petroleum) gave the diol **13** (197 mg, 72%).

*4.2.7 (2E,5*R*,7*R*,8*R*)-1,8-Bis*-tert-*butyldiphenylsilyloxy-3-iodo-5-triethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (**14**).* Following the procedure outlined for the preparation of iodide **11**, *N*-iodosuccinimide (105 mg, 0.46 mmol) in DCM (4 mL) and the stannane **10** (325 mg, 0.27 mmol) in DCM (9.8 mL), after chromatography (2:1:97, ether:Et$_3$N:light petroleum) gave the *title compound* **14** (271 mg, 96%), R_f = 0.69 (2:8, ether:light petroleum); ν_{max}/cm^{-1} 2956, 2930, 2854, 1613, 1512, 1460, 1423, 1379, 1299, 1243, 1173, 1178, 1110, 1060, 1039, 857, 836, 797; δ_H −0.03 [9H, s, Si(CH$_3$)$_3$], 0.49-0.71 (1H, m, C*H*HSi), 0.59 (6H, q, *J* 8.0, 3 × SiCH$_2$), 0.76-0.99 (1H, m, C*H*HSi), 0.94 (3H, d, *J* 6.3, 9-H$_3$), 0.94 (9H, t, *J* 7.9, 3 × SiCH$_2$C*H*$_3$), 1.07 and 1.08 [each 9H, s, SiC(CH$_3$)$_3$], 1.44-1.60 and 1.73-1.82 (each 1H, m, 6-H), 2.46 (2H, d, *J* 5.9, 4-H$_2$), 3.34-3.60 (3H, m, C*H*$_2$CH$_2$Si, 7-H), 3.95-4.01 (1H, m, 5-H), 4.07-4.12 (1H, m, 8-H), 4.21 and 4.22 (each 1H, dd, *J* 10.5, 6.3, 1-H), 4.49 and 4.56 (each 1H, d, *J* 6.8, OHC*H*O), 6.46 (1H, t, *J* 6.3, 2-H), 7.35-7.47 (12H, m, ArH), 7.66-7.74 (8H, m, ArH); δ_C −1.0, 4.1, 5.2, 18.3, 18.4, 19.5, 19.6, 27.3, 27.6, 36.1, 47.4, 62.3, 66.1, 67.0, 79.8, 96.5, 101.7, 127.8, 127.9, 128.2, 128.7, 129.9, 130.0, 133.5, 133.7, 134.8, 135.9, 136.3, 136.4, 143.2; *m*/*z* (ES$^+$) 1075 (M$^+$ + 39, 5%), 1059 (M$^+$ + 23, 10), 738 (100).

*4.2.8 (2*E*,5*R*,7*R*,8*R*)-1,8-Bis*-tert-*butyldiphenylsilyloxy-3-tributylstannyl-7-(2-trimethylsilylethoxymethoxy)non-2-en-5-ol (**15**).* Hydrogen fluoride (1% in MeCN, 8 mL) was added to the triethylsilyl ether **10** (1.00 g, 0.83 mmol) in THF (4 mL) at rt and the mixture stirred for 2 h. Saturated aqueous sodium hydrogen carbonate was added and the mixture was partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3:1:96, ether:Et$_3$N:light petroleum) of the residue gave the *title compound* **15** (639 mg, 71%), R_f = 0.41 (1:9, ether:light petroleum); $[\alpha]_D^{20}$ −8.1 (*c* 4.0, $CHCl_3$); ν_{max}/cm^{-1} 3463, 3070, 2955, 2927, 2858, 1590, 1465, 1427, 1376, 1251, 1108, 1056, 859, 832, 772, 740; δ_H 0.00 [9H, s, Si(CH$_3$)$_3$], 0.71-1.05 (20H, m, 3 × CH$_3$, 3 × SnCH$_2$, SiCH$_2$, 9-H$_3$), 1.08 [18H, s, 2 × SiC(CH$_3$)$_3$], 1.29-1.58 (14H, m, 6 × CH$_2$, 6-H$_2$), 2.26 (1H, dd, *J* 13.3, 5.6, 4-H), 2.36 (1H, dd, *J* 13.4, 7.7, 4-H′), 3.00 (1H, d, *J* 3.5, OH), 3.39-3.54 (2H, m, C*H*$_2$CH$_2$Si), 3.60-3.73 (2H, m, 5-H, 7-H), 3.96 (1H, dq, *J* 6.1, 5.3, 8-H), 4.32 and 4.41 (each 1H, dd, *J* 13.2, 5.7, 1-H), 4.48 and 4.50 (each 1H, d, *J* 6.4, OHC*H*O), 5.91 (1H, t, *J* 5.6, 2-H), 7.37-7.50 (12H, m, ArH), 7.69-7.77 (8H, m, ArH); δ_C −1.2, 10.2, 14.0, 17.8, 18.2, 19.4, 27.1, 27.3, 27.7, 29.4, 36.5, 41.9, 61.1, 65.5, 67.8, 70.9, 79.4, 96.0, 127.7, 127.9, 129.8, 129.9, 134.0, 134.2, 134.7, 135.9, 136.1, 136.2, 142.5, 142.8; *m*/*z* (ES$^+$) 1145 (75%), 1110 (M$^+$ + 23, 75), 451 (100).

*4.2.9 (2*E*,5*R*,7*R*,8*R*)-1,8-Bis*-tert-*butyldiphenylsilyloxy)-3-iodo-7-(2-trimethylsilylethoxymethoxy)non-2-en-5-ol (**16**).* Following the procedure outlined for the preparation of the iodide **11**, *N*-iodosuccinimide (50 mg, 0.23 mmol) in DCM (1.2 mL) and stannane **15** (165 mg, 0.15 mmol) in DCM (2 mL), after stirring for 1 h and chromatography (1:19, ether:light petroleum) gave the *title compound* **16** (133 mg, 95%), R_f = 0.73 (4:6, ether:light petroleum); ν_{max}/cm^{-1} 3377, 2954, 2928, 2857, 1664, 1613, 1514, 1462, 1427, 1377, 1302, 1249, 1175, 1151, 1109, 1057, 1038, 858, 838, 824, 797, 739; δ_H 0.03 [9H, s, Si(CH$_3$)$_3$] 0.79-1.04 (2H, m, CH$_2$Si), 0.99 (3H, d, *J* 6.1, 9-H$_3$), 1.08 [18H, s, 2 × SiC(CH$_3$)$_3$], 1.44-1.64 (2H, m, 6-H$_2$), 2.28 (1H, dd, *J* 14.5, 4.7, 4-H), 2.53 (1H, dd, *J* 14.4, 8.0, 4-H′), 3.14 (1H, br. s, OH), 3.49 (1H, ddd, *J* 11.1, 9.7, 5.9, C*H*HCH$_2$Si), 3.59-3.73 (2H, m, CH*H*CH$_2$Si, 7-H), 3.93 (1H, quin, *J* 5.9, 8-H), 3.95-4.05 (1H, m, 5-H), 4.23 (2H, d, *J* 6.6, 1-H$_2$), 4.49 and 4.56 (each 1H, d, *J* 6.9, OHC*H*O), 6.54 (1H, t, *J* 6.7, 2-H), 7.38-7.48 (12H, m, ArH), 7.68-7.76 (8H, m, ArH); δ_C −1.1, 18.1, 18.3, 19.4, 19.5, 27.0, 27.3, 36.2, 47.1, 62.1, 66.3, 66.8, 71.1, 79.7, 96.3, 101.5, 127.8, 127.9, 128.0, 128.6, 129.9, 130.0, 133.6, 133.9, 134.6, 135.9, 136.1, 136.2, 142.9.

Imidazole (14 mg, 206 μmol) then *tert*-butyldiphenylsilyl chloride (19 μl, 73 μmol) were added to the diol **13** (50 mg, 73 μmol) in DCM (1 mL) at rt and the mixture stirred for 25 min. Saturated aqueous ammonium chloride was added and the mixture was partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:9, ether:light petroleum) of the residue gave the title compound **16** (55 mg, 85%).

*4.2.10 (2*R*)-2-Benzyloxy-4-*tert*-butyldimethylsilyloxy-*N*-methoxy-*N*,3,3-trimethylbutanamide (**19**).* Trimethylaluminium (2 M in hexanes, 2.09 mL, 4.18 mmol) was added to *N*,*O*-dimethylhydroxylamine.hydrochloride (408 mg, 4.18 mmol) in benzene (6 mL) at 0 °C and the mixture was stirred at rt for 2 h. After cooling to 0 °C, the lactone **18** (460 mg, 2.09 mmol) in benzene (4 mL) was added and the mixture was stirred at rt for 1 h. After cooling to 0 °C, saturated aqueous sodium hydrogen carbonate was added with stirring and, after 10 min at rt, the mixture was diluted with EtOAc and filtered through celite with EtOAc washings. The filtrates were washed with brine then dried ($MgSO_4$) and concentrated under reduced pressure to give (2*R*)-2-benzyloxy-4-hydroxy-*N*-methoxy-*N*,3,3-trimethylbutanamide as an oil mixed with *ca*. 15% pantolactone; δ_H 1.02 and 1.06 (each 3H, s, 3-CH$_3$), 3.16 (1H, m, OH), 3.28 (3H, s, OCH$_3$), 3.42 (1H, dd, *J* 11.4, 8.1, 4-H), 3.61 (3H, s, NCH$_3$), 3.68 (1H, dd, *J* 11.4, 4.3, 4-H′), 4.36 (1H, s, 2-H), 4.38 and 4.69 (each 1H, d, *J* 12.0, Ph*H*CH), 7.28-7.44 (5H, m, ArH).

This amide was azeotroped with benzene, dissolved with DCM (7 mL) and imidazole (449 mg, 6.60 mmol), *tert*-butyldimethylsilyl chloride (299 mg, 1.98 mmol), DMAP (cat.) and TBAI (cat.) were added. After stirring for 1 h, saturated aqueous ammonium chloride was added and the mixture partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:19 then 1:9, ether:light petroleum) of the residue gave recovered lactone **18** (220 mg, 48%) and the *title compound* **19** (160 mg, 30%), R_f = 0.65 (1:1, ether:light petroleum); $[\alpha]_D^{20}$ + 36.0 (*c* 2.8, $CHCl_3$); ν_{max}/cm^{-1} 2955, 2931, 2901, 2857, 1673, 1471, 1391, 1254, 1092, 1000, 854, 837, 776, 738; δ_H 0.00 (6H, s, 2 × SiCH$_3$), 0.85 [9H, s, SiC(CH$_3$)$_3$], 0.87 and 0.94 (each 3H, s, 3-CH$_3$), 3.10 (1H, d, *J* 9.5, 4-H), 3.16 (3H, s, OCH$_3$), 3.45 (3H, s, NCH$_3$), 3.68 (1H, d, *J* 9.5, 4-H′), 4.37 and 4.57 (each 1H, d, *J* 12.0, Ph*H*CH), 4.59 (1H, s, 2-H), 7.18-7.34 (5H, m, ArH); δ_C −5.3, −5.2, 18.5, 19.3, 21.6, 26.1, 32.3, 40.9, 61.1, 69.1, 72.2, 76.1, 127.7, 127.8, 128.5, 128.7, 173.3; *m*/*z* (CI$^+$) 396 (M$^+$ + 1,100%); HRMS (CI$^+$): MH$^+$, found 396.2567. $C_{21}H_{38}NO_4Si$ requires 396.2570.

*4.2.11 (2*R*)-2-Benzyloxy-4-*tert*-butyldimethylsilyloxy-3,3-dimethylbutanal (**20**).* Di-isobutylaluminium hydride (1 M in hexanes, 2.93 mL, 2.93 mmol) was added to the amide **19** (389 mg, 0.98 mmol) in DCM (12 mL) at −78 °C and the mixture stirred at −78 °C for 2 h. Methanol (0.8 mL) was added and the reaction mixture allowed to warm to rt before diluting with ether and pouring into a flask containing saturated Rochelle's salt solution. The mixture was stirred for 1 h and the aqueous layer was extracted with ether. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the aldehyde **20** (343 mg, *ca*. 100%) used in the next reaction. Chromatography (1:19, ether:light petroleum) of a sample gave the *title compound* **20** (45%), R_f = 0.74 (1:9, ether:light petroleum); ν_{max}/cm^{-1} 2955, 2929, 2857, 1730, 1472, 1363, 1252, 1096, 838, 776; δ_H 0.01 and 0.03 (each 3H, s, $SiCH_3$), 0.86 [9H, s, $SiC(CH_3)_3$], 0.94 (6H, s, 2 × 3-CH_3), 3.33 (1H, d, *J* 9.6, 4-H), 3.48 (1H, d, *J* 2.7, 2-H), 3.50 (1H, d, *J* 9.4, 4-H′), 4.44 and 4.64 (each 1H, d, *J* 11.7, PhC*H*CH), 7.24-7.35 (5H, m, ArH), 9.75 (1H, d *J* 3.0, 1-H); δ_C −5.3(2), 18.5, 21.0, 22.0, 26.1, 41.6, 68.3, 73.3, 88.3, 128.1(2), 128.6, 138.0, 204.7; *m*/*z* (CI^+) 354 (M^+ + 18, 14%), 337 (M^+ + 1, 60), 108 (80), 91 (100); HRMS (CI^+): MH^+, found 337.2204. $C_{19}H_{33}O_3Si$ requires 337.2199).

*4.2.12 (4*R,5R*)- and (4*S,5R*)-5-Benzyloxy-1,7-bis-*tert*-butyldimethylsilyloxy-6,6-dimethylhept-2-yn-4-ols (**21**) and (**22**).* *n*-Butyllithium (1.6 M in hexanes, 0.86 mL, 1.38 mmol) was added to 3-*tert*-butyldimethylsilyloxypropyne (250 mg, 1.6 mmol) in THF (8 mL) at 0 °C and the mixture stirred for 30 min at 0 °C then cooled to −78 °C. Aldehyde **20** (323 mg, *ca*. 0.9 mmol) was added in THF (2 mL) and the mixture stirred at −78 °C for 100 min. Saturated aqueous ammonium chloride was added, and the mixture allowed to warm to rt then partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3% ether in light petroleum) of the residue gave *title compound* **21** (205 mg, 42 %), R_f = 0.41 (2:8, ether:light petroleum); $[\alpha]_D^{24}$ −18.5 (*c* 4.8, $CHCl_3$); ν_{max}/cm^{-1} 3506, 2954, 2930, 2886, 2857, 1471, 1390, 1362, 1254, 1125, 1086, 1006, 837, 776, 729; δ_H 0.00, 0.01, 0.06 and 0.07 (each 3H, s, $SiCH_3$), 0.84-0.90 [24H, m, 2 × $SiC(CH_3)_3$, 2 × 6-CH_3], 3.33 and 3.40 (each 1H, d, *J* 9.8, 7-H), 3.42 (1H, d, *J* 7.7, 5-H), 3.59 (1H, s, OH), 4.32 (2H, d, *J* 1.6, 1-H_2), 4.55 (1H, br. d, *J* 7.7, 4-H), 4.67 and 5.02 (each 1H, d, *J* 11.0, PhHC*H*), 7.20-7.38 (5H, m, ArH); δ_C −5.3, −5.2, −4.9(2), 18.5, 18.6, 21.2, 22.8, 26.1, 26.2, 40.7, 52.1, 60.6, 69.5, 75.8, 83.1, 85.2, 86.7, 127.9, 128.1, 128.6, 138.8; *m*/*z* (CI^+) 524 (M^+ + 18, 42%), 507 (M^+ + 1, 100); HRMS (CI^+): MH^+, found 507.3333. $C_{28}H_{51}O_4Si_2$ requires 507.3326). The second fraction was the *title compound* **22** (78 mg, 17%), R_f = 0.34 (2:8, ether:light petroleum); $[\alpha]_D^{24}$ +2.8 (*c* 4.3, $CHCl_3$); ν_{max}/cm^{-1} 3441, 2954, 2930, 2886, 2857, 1471, 1390, 1362, 1255, 1087, 1029, 1006, 838, 777, 732; δ_H 0.00 (6H, s, 2 × $SiCH_3$), 0.02 and 0.03 (each 3H, s, $SiCH_3$), 0.82 and 0.85 [each 9H, s, $SiC(CH_3)_3$], 0.90 and 0.97 (each 3H, s, 6-CH_3), 3.34 and 3.42 (each 1H, d, *J* 10.1, 7-H), 3.55 (1H, d, *J* 6.2, 5-H), 4.39 (2H, d, *J* 1.7, 1-H_2), 4.63-4.69 (2H, m, 4-H, PhHC*H*), 4.96 (1H, d, *J* 11.3, PhHC*H*), 7.29-7.46 (5H, m, ArH); δ_C −5.3(2), −4.9, 18.5, 18.6, 21.6, 22.6, 26.1(2), 40.7, 52.1, 63.7, 70.1, 75.4, 84.6, 85.0, 86.6, 127.7, 128.0, 128.5, 139.1; *m*/*z* (ES^+) 566 (83%), 529 (M^+ + 23, 100); HRMS (CI^+): MH^+, found 507.3324. $C_{28}H_{51}O_4Si_2$ requires 507.3326).

Dicyclohexyl carbodi-imide (130 mg, 0.632 mmol), (*R*)-*O*-acetylmandelic acid (66 mg, 0.316 mmol) and DMAP (cat.) were added to the *syn*-alcohol **21** (80 mg, 0.158 mmol) in THF (2 mL) at 0 °C and the solution stirred for 18 h. After concentration under reduced pressure, chromatography (8% ether in light petroleum) of the residue gave the (*R*)-*O*-acetylmandelate of the alcohol **21** (95 mg, 86%), R_f = 0.38 (2:8, ether:light petroleum); ν_{max}/cm^{-1} 2954, 2932, 2891, 2858, 1754, 1466, 1370, 1254, 1230, 1087, 1052, 934, 840, 778, 738; δ_H 0.00, 0.03, 0.13 and 0.14 (each 3H, s, $SiCH_3$), 0.65 and 0.76 (each 3H, s, 6-CH_3), 0.91 and 0.93 [each 9H, s, $SiC(CH_3)_3$], 2.18 (3H, s, CH_3CO), 3.09 and 3.42 (each 1H, d, *J* 9.5, 7-H), 3.71 (1H, d, *J* 3.5, 5-H), 4.36 (2H, d, *J* 1.6, 1-H_2), 4.54 and 4.86 (each 1H, d, *J* 11.4, PhHC*H*), 5.70 (1H, dt, *J* 3.8, 1.8, 4-H), 6.08 (1H, s, 2′-H), 7.26-7.35 (8H, m, ArH), 7.44-7.50 (2H, m, ArH); δ_C −5.4, −5.3, −5.0, −4.9, 18.5, 20.1, 21.0, 21.9, 26.0, 26.2, 40.4, 52.0, 65.3, 70.2, 74.7, 75.0, 77.5, 81.7, 82.9, 85.9, 127.4, 128.3, 128.4, 128.9, 129.5, 133.8, 139.3, 168.0, 170.2; *m*/*z* (ES^+) 742 (100%), 705 (M^+ + 23, 100%), 383 (57%); HRMS (CI^+): MNa^+, found 705.3618. $C_{38}H_{58}O_7Si_2Na$ requires 705.3613).

Following the same procedure, dicyclohexyl carbodi-imide (130 mg, 0.632 mmol), (*S*)-*O*-acetylmandelic acid (66 mg, 0.316 mmol), DMAP (cat.) and the *syn*-alcohol **21** (50 mg, 99 μmol), after chromatography (8% ether in light petroleum), gave the (*S*)-*O*-acetylmandelate of the alcohol **21** (53 mg, 77%), R_f = 0.38 (2:8, ether:light petroleum); ν_{max}/cm^{-1} 2952, 2930, 2894, 2857, 1753, 1702, 1466, 1369, 1252, 1229, 1088, 838, 776, 733; δ_H 0.00, 0.02, 0.03 and 0.05 (each 3H, s, $SiCH_3$), 0.84 and 0.90 [each 9H, s, $SiC(CH_3)_3$], 0.94 and 0.96 (each 3H, s, 6-CH_3), 2.18 (3H, s, CH_3CO), 3.19 and 3.55 (each 1H, d, *J* 9.5, 7-H), 3.76 (1H, d, *J* 3.4, 5-H), 4.18 (2H, d, *J* 1.6, 1-H_2), 4.64 and 4.97 (each 1H, d, *J* 11.3, PhHC*H*), 5.64-5.72 (1H, m, 4-H), 5.97 (1H, s, 2′-H), 7.27-7.38 (8H, m, ArH), 7.45-7.50 (2H, m, ArH); *m*/*z* (ES^+) 742 (61%), 705 (M^+ + 23, 100); HRMS (CI^+): MNa^+, found 705.3609. $C_{38}H_{58}O_7Si_2Na$ requires 705.3613).

*4.2.13 (3S)-3-(4-Methoxybenzyloxy)-2,2-dimethylpent-4-en-1-ol (**24**).*[15] Methyltriphenylphosphonium bromide (8.50 g, 23.8 mmol) was azeotroped in toluene and dried overnight under a high vacuum. Potassium *tert*-butoxide (2.67 g, 23.8 mmol) was added and the solids stirred vigorously together for 30 min under a flow of nitrogen. Tetrahydrofuran (150 mL) was added and the mixture stirred for 1 h at rt before cooling to 0 °C. The lactol **23** (4.00 g, 15.9 mmol) in THF (150 mL) was added and the mixture allowed to warm to rt then stirred for 3.5 h. Water was added and the mixture partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3:17 then 1:3, ether:light petroleum) of the residue gave the title compound **24**[15] (2.97 g, 75%), R_f = 0.21 (3:7, ether:light petroleum); $[\alpha]_D^{20}$ + 40 (*c* 2.2, $CHCl_3$); ν_{max}/cm^{-1} 3425, 2959, 2930, 2871, 2836, 1613, 1513, 1465, 1301, 1275, 1174, 1110, 1036, 821; δ_H 0.91 (6H, s, 2 × 2-CH_3), 2.89 (1H, t, *J* 5.9, OH), 3.58 and 3.55 (each 1H, dd, *J* 11.0, 5.8, 1-H), 3.64 (1H, d, *J* 8.2, 3-H), 3.85 (3H, s, OCH_3), 4.27 and 4.59 (each 1H, d, *J* 11.4, Ar*H*CH), 5.28 (1H, dd, *J* 17.3, 0.7, 5-H), 5.41 (1H, dd, *J* 10.3, 0.7, 5-H′), 5.80-5.90 (1H, m, 4-H), 6.92 and 7.28 (each 2H, d, *J* 8.7, ArH); δ_C 19.7, 22.5, 38.4, 55.2, 69.9, 71.3, 87.7, 113.8, 119.5, 129.4, 130.1, 134.9, 159.1; *m*/*z* (EI^+) 250 (M^+, 4%), 194 (18), 137 (20), 121 (100); HRMS (CI^+): MH^+, found 251.1644. $C_{15}H_{23}O_3$ requires 251.1648.

Alternatively, *n*-butyllithium (1.6 M in hexanes, 1.18 mL, 1.89 mmol) was added to a suspension of methyltriphenylphosphonium bromide (867 mg, 2.43 mmol) in THF (3 mL) at −78 °C and the mixture stirred at 0 °C for 30 min before cooling to −78 °C. The lactol **23** (228 mg, 0.90 mmol) in THF (3 mL) was added and the mixture allowed to warm to rt then stirred for 18 h. Saturated aqueous ammonium chloride was added and the mixture partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts

were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:3, ether:light petroleum) of the residue gave the title compound **24** (135 mg, 60%).

*4.2.14 (3S)-1-*tert*-Butyldimethylsilyloxy-3-(4-methoxybenzyloxy)-2,2-dimethylpent-4-ene (**25**).* Imidazole (2.12 g, 31.2 mmol), *tert*-butyldimethylsilyl chloride (2.36 mL, 15.6 mmol), DMAP (cat.) and TBAI (cat.) were added to the alcohol **24** (2.60 g, 10.4 mmol) in DCM (80 mL) at rt and the mixture stirred for 1 h. Saturated aqueous ammonium chloride was added and the mixture partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:19, ether:light petroleum) of the residue gave the *title compound* **25** (2.40 g, 63%), R_f = 0.79 (3:7, ether:light petroleum); $[\alpha]_D^{20}$ + 8.2 (*c* 4.8, $CHCl_3$); ν_{max}/cm^{-1} 2955, 2930, 2857, 1613, 1513, 1471, 1248, 1172, 1091, 1040, 851, 837, 775; δ_H 0.00 (6H, s, 2 × $SiCH_3$), 0.80 and 0.86 (each 3H, s, 2-CH_3), 0.88 [9H, s, $SiC(CH_3)_3$], 3.26 and 3.45 (each 1H, d, *J* 9.2, 1-H), 3.65 (1H, d, *J* 8.0, 3-H), 3.69 (3H, s, OCH_3), 4.21 and 4.49 (each 1H, d, *J* 11.4, Ar*H*CH), 5.19 (1H, dd, *J* 17.1, 2.1, 5-H), 5.26 (1H, dd, *J* 10.4, 2.1, 5-H′), 5.70-5.84 (1H, m, 4-H), 6.85 and 7.24 (each 2H, d, *J* 8.7, ArH); δ_C −5.6, 18.2, 19.9, 21.0, 25.8, 39.5, 55.2, 69.1, 70.1, 83.9, 113.5, 118.1, 129.0, 131.3, 135.8, 158.8; *m*/*z* (CI^+) 365 (M^+ + 1, 10%), 243 (10), 138 (19), 121 (100); HRMS (CI^+): MH^+, found 365.2512. $C_{21}H_{37}O_3Si$ requires 365.2513.

*4.2.15 (2*RS,*3*R*)-3-(4-Methoxybenzyloxy)-5-*tert*-butyldimethylsilyloxy-4,4-dimethylpentane-1,2-diol (**26**).* *N*-Methylmorpholine *N*-oxide (127 mg, 1.08 mmol) and then a single crystal of osmium tetraoxide were added to the alkene **25** (200 mg, 0.54 mmol) in acetone (5 mL), water (2.5 mL) and *tert*-butanol (5 mL) and the mixture was stirred for 18 h at rt. Saturated aqueous sodium sulfite was added and the mixture partitioned between EtOAc and water. The aqueous layer was extracted with EtOAc and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3:7 then 1:1, ether:light petroleum) of the residue gave the recovered alkene **25** (53 mg, 27%) and the *title compound* **26** (129 mg, 59%) that appeared by ^1H and ^{13}C NMR to be essentially a single diastereoisomer, R_f = 0.14 (1:1, ether:light petroleum); ν_{max}/cm^{-1} 3397, 2955, 2930, 2857, 1613, 1515, 1469, 1250, 1095, 1039, 838, 776; δ_H 0.00 (6H, s, 2 × $SiCH_3$), 0.83 [9H, s, $SiC(CH_3)_3$], 0.86 and 0.91 (each 3H, s, 4-CH_3), 1.52 (1H, s, 2-OH), 2.31 (1H, br. s, 1-OH), 3.20-3.30 (1H, m, 2-H), 3.35 and 3.44 (each 1H, d, *J* 10.3, 5-H), 3.62-3.79 (5H, m, 1-H_2, OCH_3), 4.18-4.28 (1H, m, 3-H), 4.44 and 4.55 (each 1H, d, *J* 10.5, ArHC*H*), 6.79 and 7.18 (each 2H, d, *J* 8.5, ArH); δ_C −5.6, 18.2, 19.7, 23.2, 25.7, 40.5, 55.2, 64.3, 70.4, 71.4, 75.3, 86.0, 113.8, 129.2, 130.6, 159.1; *m*/*z* (CI^+) 399 (M^+ + 1, 13%), 279 (10), 138 (40), 121 (100); HRMS (CI^+): MH^+, found 399.2566. $C_{21}H_{39}O_5Si$ requires 399.2567.

*4.2.16 (2*R*)-4-*tert*-Butyldimethylsilyloxy-2-(4-methoxybenzyloxy)-3,3-dimethylbutanal (**27**).* Sodium periodate (738 mg, 3.45 mmol) was added to the diol **26** (460 mg, 1.15 mmol) in THF (6 mL), water (8 mL) and MeOH (6 mL) at rt and the mixture stirred at rt for 30 min. Saturated aqueous sodium sulfite was added and the mixture partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were washed with aqueous sodium sulfite, dried ($MgSO_4$) and concentrated under reduced pressure to afford the *title compound* **27** (423 mg, *ca*. 99%), R_f = 0.54 (2:8, ether:light petroleum); $[\alpha]_D^{20}$ +25.5 (*c* 1.2, $CHCl_3$); ν_{max}/cm^{-1} 2955, 2930, 2857, 1729, 1613, 1514, 1470, 1250, 1173, 1093, 1037, 838, 776; δ_H 0.06 and 0.07 (each 3H, s, $SiCH_3$), 0.92 [9H, s, $SiC(CH_3)_3$], 0.97 (6H, s, 2 × 3-CH_3), 3.36 (1H, d, *J* 9.5, 4-H), 3.48-3.55 (2H, m, 4-H′, 2-H), 3.85 (3H, s, OCH_3), 4.43 and 4.61 (each 1H, d, *J* 11.4, Ar*H*CH), 6.92 and 7.30 (each 2H, d, *J* 8.7, ArH), 9.73 (1H, d, *J* 3.0, 1-H); δ_C −5.7(2), 18.1, 20.7, 21.6, 25.7, 41.2, 55.1, 67.9, 72.6, 87.5, 113.7, 129.5, 129.7, 159.3, 204.3; *m*/*z* (CI^+) 384 (M^+ + 18, 13%), 367 (M^+ + 1, 9), 247 (35), 231 (62), 217 (30), 121 (100); HRMS (ES^+): MH^+, found 367.2302. $C_{20}H_{35}O_4Si$ requires 367.2299.

*4.2.17 (5*R*)-5-(4-Methoxybenzyloxy)-1-*tert*-butyldiphenylsilyloxy-7-*tert*-butyldimethylsilyloxy-6,6-dimethylhept-2-yn-4-one (**28**).* *n*-Butyllithium (1.6 M in hexanes, 2.15 mL, 3.44 mmol) was added to 3-*tert*-butyldiphenylsilyloxyprop-2-yne (1.09 g, 3.69 mmol) in THF at 0 °C and the mixture stirred at 0 °C for 30 min before cooling to −78 °C. The aldehyde **27** (448 mg, 1.32 mml) in THF was added dropwise and the mixture was allowed to warm to 0 °C and stirred for 2 h. Saturated aqueous ammonium chloride was added and the mixture partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:19 then 1:9, ether:light petroleum) of the residue gave a mixture of the *syn*- and *anti*-alcohols **29** and **30**, ratio 75:25, (using the $PhCH_2$ peaks in the ^1H NMR) (737 mg, 84%). A sample of the less polar, major, *syn*-alcohol **29** was isolated for characterisation; ν_{max}/cm^{-1} 3445, 2951, 2927, 2893, 2852, 1614, 1590, 1513, 1468, 1364, 1249, 1102, 1038, 836, 776, 740; δ_H 0.00 (6H, s, 2 × $SiCH_3$), 0.85 [15H, s, $SiC(CH_3)_3$, 2 × 6-CH_3], 0.98 [9H, s, $SiC(CH_3)_3$], 3.32-3.42 (3H, m, 5-H, 7-H_2), 3.50 (1H, s, OH), 3.73 (3H, s, OCH_3), 4.31 (2H, d, *J* 1.6, 1-H_2), 4.49 (1H, dt, *J* 7.9, 1.6, 4-H), 4.55 and 4.90 (each 1H, d, *J* 10.7, ArHC*H*), 6.78 and 7.22 (each 2H, d, *J* 8.8, ArH), 7.27-7.38 (6H, m, ArH), 7.61-7.67 (4H, m, ArH); δ_C −5.5, 18.2, 19.1, 21.0, 22.4, 25.8, 26.6, 40.3, 52.7, 55.2, 60.2, 69.1, 74.6, 82.3, 84.7, 86.7, 113.6, 127.6, 129.5, 129.7, 130.3, 133.0, 135.5, 159.1; *m*/*z* (CI^+) 661 (M^+ + 1, 52%), 121 (100); HRMS (CI^+): MH^+, found 661.3753. $C_{39}H_5O_5Si_2$ requires 661.3755.

The Dess-Martin periodinane (630 mg, 1.68 mmol) was added to this mixture of diols (737 mg, 1.12 mmol) in DCM (17 mL) at rt and the mixture stirred for 45 min. Aqueous sodium hydroxide (1.3 M) was added and the mixture partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford the *title compound* **28** (730 mg, *ca*. 99%), R_f = 0.74 (2:8, ether:light petroleum); $[\alpha]_D^{20}$ +2.9 (*c* 2.8, $CHCl_3$); ν_{max}/cm^{-1} 3071, 3050, 2954, 2931, 2857, 2213, 1672, 1613, 1588, 1514, 1471, 1428, 1391, 1368, 1302, 1249, 1174, 1104, 1038, 1008, 838, 777, 740; δ_H 0.00 and 0.01 (each 3H, s, $Si(CH_3)$, 0.87 [9H, s, $SiC(CH_3)_3$], 0.92 and 0.94 (each 3H, s, 2 × 6-CH_3), 1.05 [9H, s, $SiC(CH_3)_3$], 3.19 and 3.54 (each 1H, d, *J* 9.3, 7-H), 3.77 (3H, s, OCH_3), 3.82 (1H, s, 5-H), 4.28 (1H, d, *J* 11.0, ArHC*H*), 4.45 (2H, s, 1-H_2), 4.56 (1H, d, *J* 11.0, ArHC*H*), 6.81 and 7.24 (2H, d, *J* 8.6, ArH), 7.34-7.45 (6H, m, ArH), 7.65-7.72 (4H, m, ArH); δ_C −5.6, 18.2, 19.1, 19.8, 21.4, 25.8, 26.5, 40.3, 52.5, 55.1, 68.8, 72.6, 84.6, 87.5, 92.5, 113.6, 127.8, 129.5, 129.9, 132.4, 135.5, 159.1, 190.6; *m*/*z* (CI^+) 660 (10%), 403 (20), 377 (17), 196 (15), 154 (16), 137 (34), 121 (100); HRMS (CI^+): MH^+, found 659.3540. $C_{39}H_{55}O_5Si_2$ requires 659.3589.

*4.2.18 (4*S,*5*R*)-5-(4-Methoxybenzyloxy)-7-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-6,6-dimethyl-hept-2-yn-4-ol (**30**).* (*R*)-2-Methyl-CBS oxazaborolidine (1 M in toluene, 0.40 mL, 0.40 mmol) was added to the ynone **28** (257 mg, 0.40 mmol) in THF (5 mL) at rt. The mixture was stirred for 10 min then cooled to −30 °C and borane dimethyl sulfide (0.114 mL, 1.20 mmol) was added over 5 min. The mixture was stirred

at –30 °C for 1 h then at –15 °C for 1 h. Saturated aqueous ammonium chloride was added then the mixture was partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:19, 1:9 then 1:4, ether:light petroleum) of the residue gave a mixture of diastereoisomers **29** and **30** (192 mg, 75%), **29** : **30** = 20:80. A sample of the more polar *title compound* **30** was isolated for characterisation, $[\alpha]_D^{20}$ +1.9 (*c* 1.7, $CHCl_3$); ν_{max}/cm^{-1} 3441, 3071, 2953, 2929, 2895, 2857, 1657, 1613, 1588, 1513, 1468, 1366, 1249, 1102, 1083, 1038, 1009, 836, 776, 739; δ_H 0.00 (6H, s, 2 × $SiCH_3$), 0.84 [9H, s, $SiC(CH_3)_3$], 0.87 and 0.93 (each 3H, s, 6-CH_3), 0.98 [9H, s, $SiC(CH_3)_3$], 3.30-3.45 (4H, m, 7-H_2, OH, 5-H), 3.72 (3H, s, OCH_3), 4.30 (2H, d, *J* 1.6, 1-H_2), 4.43-4.50 (2H, m, ArHC*H*, 4-H), 4.74 (1H, d, *J* 10.8, ArHC*H*), 6.77 and 7.22 (each 2H, d, *J* 8.5, ArH), 7.25-7.38 (6H, m, ArH), 7.61-7.67 (4H, m, ArH); δ_C –5.2, 18.5, 19.4, 21.7, 22.5, 26.1, 26.9, 40.7, 53.1, 55.5, 63.7, 70.1, 75.0, 84.3, 85.5, 86.2, 114.0, 128.0, 129.7, 130.0, 131.3, 133.4, 135.9, 159.3; *m*/*z* (CI^+) 661 (M^+ + 1, 5%), 643 (8%), 274 (40), 217 (82), 196 (43), 137 (75), 121 (100); HRMS (EI^+): MH^+, found 661.3754. $C_{39}H_{57}O_5Si_2$ requires 661.3755).

Cerium trichloride hexahydrate (33 mg, 0.09 mmol) was added to the ketone **28** (30 mg, 0.045 mmol) in MeOH (1 mL) at rt. Sodium borohydride (4 mg, 0.09 mmol) was added and the mixture stirred at rt for 1.5 h. Aqueous hydrogen chloride (2%) was the added until the mixture was neutral. After partitioning between water and ether, the aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give a mixture of the epimeric alcohols **29** and **30**, ratio **29**:**30** = 86:14 (28 mg, 85%).

Zinc chloride (2.5 g) was fused under pressure then a suspension in ether (40 mL) was heated under reflux for 1 h. After allowing to cool to rt, the supernatant was added to a suspension of sodium borohydride (700 mg, 18.4 mmol) in dry ether (20 mL) and the mixture stirred for 2 d. This solution of zinc borohydride (0.3 M, 1 mL) was added to the ketone **28** (35 mg, 0.05 mmol) in dry ether (0.5 mL) at –30 °C and the mixture stirred for 2 h. A further portion of zinc borohydride (1 mL) was added and the reaction stirred at 0 °C. After 1 h, aqueous hydrogen (2%) was added until the mixture was neutral. After partitioning between water and ether, the aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give a mixture of the epimeric alcohols **29** and **30**, ratio **29**:**30** = 14:86 (30 mg, 86%).

*4.2.19 (4*S*,5*R*)-5-(4-Methoxybenzyloxy)-4,7-bis-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-6,6-dimethylhept-2-yne (**31**).* Imidazole (55 mg, 0.81 mmol) and *tert*-butyldimethylsilyl chloride (81 mg, 0.54 mmol) were added to the alcohol **30** (182 mg, 0.27 mmol) in DCM (1 mL) at rt and the solution stirred for 18 h. Saturated aqueous ammonium chloride was added and the mixture was partitioned between water and DCM. The aqueous layer was extracted with DCM, and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:19, ether:light petroleum) of the residue gave the *title compound* **31** (200 mg, 96%), R_f = 0.33 (1:19, ether:light petroleum); $[\alpha]_D^{20}$ +18.4 (*c* 3.7, $CHCl_3$); ν_{max}/cm^{-1} 3071, 2954, 2930, 2894, 2857, 1613, 1588, 1514, 1471, 1428, 1390, 1361, 1301, 1250, 1106, 1087, 1006, 838, 777, 740; δ_H 0.05, 0.06, 0.18 and 0.22 (each 3H, s, $SiCH_3$), 0.94-1.00 [24H, m, 2 × $SiC(CH_3)_3$, 2 × 6-CH_3], 1.08 [9H, s, $SiC(CH_3)_3$], 3.25 and 3.53 (each 1H, d, *J* 9.5, 7-H), 3.56 (1H, d, *J* 2.9, 5-H), 3.82 (3H, s, OCH_3), 4.38 (2H, d, *J* 1.5, 1-H_2), 4.53 (1H, d, *J* 11.0, ArHC*H*), 4.70-4.80 (1H, m, 4-H), 4.99 (1H, d, *J* 11.0, ArHC*H*), 6.84 and 7.34 (each 2H, d, *J* 8.7, ArH), 7.36-7.46 (6H, m, ArH), 7.72-7.77 (4H, m, ArH); δ_C –5.2, –5.1, –4.7, –3.8, 18.4, 18.6, 19.5, 20.9, 22.3, 26.2(2), 26.9, 40.1, 53.2, 55.5, 65.6, 70.3, 74.5, 84.5, 85.5, 86.1, 113.7, 128.0, 128.5, 129.6, 129.2, 130.0, 132.3, 133.5, 135.1, 135.9, 159.1; *m*/*z* (CI^+) 792 (M^+ + 18, 12%), 437 (6), 274 (33), 217 (100), 196 (35), 137 (35), 121 (94); HRMS (CI^+): MNH_4^+, found 792.4885. $C_{45}H_{74}NO_5Si_3$ requires 792.4875.

*4.2.20 (1*S*)-2,2-Dimethyl-1-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]but-3-en-1-ol (**33**).* Zinc was activated by stirring with aqueous hydrogen chloride (5%) for 10 min and washing with water until neutral. This zinc was then washed with ethanol and ether before drying under a high vacuum for 4 h. 1-Bromo-3-methylbut-2-ene (7.3 mL, 47.5 mmol) and the aldehyde **32** (4.98 g, 38.2 mmol) in THF (45 mL) were added to a rapidly stirred suspension of this activated zinc (4.10 g, 76 mmol) in THF (45 mL) at 0 °C and the mixture stirred for 1 h. Water was added and the mixture was filtered through celite with extensive DCM washings. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3:7, ether:light petroleum) of the residue gave the title compound **33** (5.6 g, 76%) together with its *syn*-epimer, ratio 85:15 (^{1}H NMR). Further chromatography (5% ether in light petroleum) gave the *syn*-epimer, (1*R*)-2,2-dimethyl-1-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]but-3-en-1-ol (423 mg, 6%), R_f = 0.50 (4:6, ether:light petroleum); $[\alpha]_D^{20}$ +1.5 (*c* 3.1, $CHCl_3$); ν_{max}/cm^{-1} 3544, 2984, 2935, 2879, 1638, 1465, 1376, 1251, 1217, 1155, 1064, 1006, 915, 857; δ_H 1.07 and 1.08 (each 3H, s, 2-CH_3), 1.38 and 1.43 (each 3H, s, 2′-CH_3), 2.49 (1H, d, *J* 7.0, OH), 3.22 (1H, dd, *J* 7.0, 4.0, 1-H), 3.73 (1H, t, *J* 8.0, 5′-H), 4.00 (1H, dd, *J* 8.0, 6.5, 5′-H′), 4.16 (1H, ddd, *J* 8.0, 6.5, 4.0, 4′-H), 5.60 (1H, dd, *J* 17.1, 1.0, 4-H), 5.75 (1H, dd, *J* 11.1, 1.0, 4-H′), 5.95 (1H, dd, *J* 17.1, 11.1, 3-H); δ_C 21.8, 24.9, 25.9, 26.6, 39.6, 41.2, 68.0, 75.2, 107.7, 113.2, 145.0; *m*/*z* (CI^+) 218 (M^+ + 18, 100%), 201 (M^+ + 1, 85); HRMS (ES^+): MH^+, found 201.1488. $C_{11}H_{21}O_3$ requires 201.1485. After a mixed fraction (1.12 g), the *title compound* **33** (4.03 g, 53%) was eluted (1:1 ether:light petroleum), R_f = 0.44 (4:6, ether:light petroleum); $[\alpha]_D^{20}$ +32.1 (*c* 1.7, $CHCl_3$); ν_{max}/cm^{-1} 3486, 2984, 2932, 2876, 1636, 1465, 1374, 1252, 1217, 1158, 1058, 917, 856; δ_H 1.09 and 1.10 (each 3H, s, 2-CH_3), 1.37 and 1.43 (each 3H, s, 2′-CH_3), 2.03 (1H, d, *J* 2.9, OH), 3.65 (1H, t, *J* 3.1, 1-H), 3.83-3.91 (2H, m, 5′-H_2), 4.18 (1H, ddd, *J* 7.7, 6.4, 3.3, 4′-H), 5.06 (1H, dd, *J* 17.4, 1.3, 4-H), 5.08 (1H, dd, *J* 11.0, 1.3, 4-H′), 5.92 (1H, dd, *J* 17.4, 11.0, 3-H); δ_C 23.5, 24.3, 25.7, 26.7, 40.3, 64.9, 76.7, 107.9, 113.3, 144.7; *m*/*z* (CI^+) 218 (M^+ + 18, 78%), 201 (M^+ + 1, 100); HRMS (ES^+): MH^+, found 201.1484. $C_{11}H_{21}O_3$ requires 201.1485.

(*R*)-(*O*)-Acetylmandelic acid (69 mg, 0.29 mmol), DMAP (cat.) and dicyclohexyl carbodi-imide (91 mg, 0.44 mmol) in THF (1 mL) were added to the alcohol **33** (42 mg, 0.21 mmol) in THF (1.5 mL) at 0 °C and the mixture stirred at rt for 18 h. After concentration under reduced pressure, chromatography of the residue gave the (*R*)-*O*-acetylmandelate of the alcohol **33** (54 mg, 69%), R_f = 0.16 (3:17, ether:light petroleum), $[\alpha]_D^{20}$ –30.5 (*c* 1.2, $CHCl_3$); δ_H 0.72 and 0.87 (each 3H, s, 2-CH_3), 1.35 and 1.41 (each 3H, s, 2′-CH_3), 2.25 (3H, s, CH_3CO), 3.81 (1H, t, *J* 8.2, 5′-H), 3.96 (1H, t, *J* 8.3, 5′-H′), 4.18-4.28 (1H, m, 4′-H), 4.81 (1H, d, *J* 17.4, 4-H), 4.89 (1H, d, *J* 10.8, 4-H′), 5.09 (1H, d, *J* 4.1, 1-H), 5.61 (1H, dd, *J* 17.5, 10.8, 3-H), 6.01 (1H, s, 2″-H), 7.40-7.56 (5H, m, ArH); δ_C 21.0, 23.5, 23.7, 25.6, 26.5, 40.3, 65.6, 74.6, 75.0, 79.8, 108.8, 113.6, 128.0, 128.9, 129.5, 134.2, 143.1, 168.4, 170.3; *m*/*z* (CI^+) 394 (M^+ + 18, 100%), 377 (M^+ + 1, 33); HRMS (ES^+): MH^+, found 377.1963. $C_{21}H_{29}O_6$ requires 377.1959.

Following the same procedure, (*S*)-(*O*)-acetylmandelic acid gave the (*S*)-*O*-acetylmandelate of the alcohol **33** (51 mg, 65%), R_f = 0.16 (3:17, ether:light petroleum); $[\alpha]_D^{20}$ +59 (*c* 1.0, $CHCl_3$); δ_H 0.92, 1.07, 1.13 and 1.22 (each 3H, s, CH_3), 2.24 (3H, s, CH_3CO), 3.34 (1H, t, *J* 7.9, 5′-H), 3.54 (1H, dd, *J* 7.9, 6.3, 5′-H′), 4.11 (1H, ddd, *J* 7.8, 6.3, 4.3, 4′-H), 5.05-5.13 (3H, m, 4-H_2, 1-H), 5.90 (1H, dd, *J* 17.8, 10.8, 3-H), 5.97 (1H, s, 2″-H), 7.40-7.56 (5H, m, ArH); δ_C 20.7, 23.9, 25.0, 25.9, 26.3, 34.7, 66.2, 74.3, 75.6, 86.7, 109.5, 114.3, 127.6, 129.2, 129.8, 134.9, 144.2, 168.9, 171.1; *m*/*z* (CI^+) 394 (M^+ + 18, 100%), 377 (M^+ + 1, 31), 319 (28); HRMS (ES^+): MH^+, found 377.1963. $C_{21}H_{29}O_6$ requires 377.1959.

*4.2.21 (4*R*)-4-[(1*S*)-1-(4-Methoxybenzyloxy)-2,2-dimethylbut-3-enyl]-2,2-dimethyl-1,3-dioxolane (**34**).* The alcohol **33** (627 mg, 3.13 mmol) in DMF (3 mL) was added to a suspension of sodium hydride (60% in mineral oil, 258 mg, 6.46 mmol) in DMF (7 mL) at 0 °C and the mixture allowed to warm to rt and stirred for 30 min. After cooling to 0 °C, 4-methoxybenzyl chloride (875 µl, 6.46 mmol) was added and, after 10 min, the mixture was allowed to warm to rt and was stirred for 1 h. Saturated aqueous ammonium chloride was added and the mixture was partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (1:9, ether:light petroleum) of the residue gave the *title compound* **34** (978 mg, 98%), R_f = 0.44 (2:8, ether:light petroleum); $[\alpha]_D^{20}$ +21 (*c* 4.1, $CHCl_3$); ν_{max}/cm^{-1} 2983, 2935, 2906, 1613, 1514, 1463, 1374, 1248, 1215, 1172, 1062, 1041, 915, 859, 823; δ_H 1.01 and 1.07 (each 3H, s, 2′-CH_3), 1.36 and 1.45 (each 3H, s, 2-CH_3), 3.56 (1H, d, *J* 1.5, 1′-H), 3.82 (3H, s, OCH_3), 3.89 (1H, t, *J* 7.2, 5-H), 4.00 (1H, t, *J* 7.8, 5-H′), 4.27 (1H, td, *J* 7.8, 1.5, 4-H), 4.55 and 4.85 (each 1H, d, *J* 10.8, ArHC*H*), 4.96-5.04 (2H, m, 4′-H_2), 5.92 (1H, dd, *J* 17.7, 10.5, 3′-H), 6.89 and 7.31 (each 2H, d, *J* 8.7, ArH); δ_C 23.6, 24.9, 25.3, 26.7, 41.2, 55.5, 64.9, 75.6, 77.4, 85.4, 107.6, 112.4, 113.9, 129.5, 131.4, 145.3, 159.2; *m*/*z* (CI^+) 338 (M^+ + 18, 33%), 155 (24), 138 (83), 121 (100); HRMS (ES^+): MNH_4^+, found 338.2325. $C_{19}H_{32}NO_4$ requires 338.2326).

*4.2.22 (2*R*,3*S*)-3-(4-Methoxybenzyloxy)-4,4-dimethylhex-5-ene-1,2-diol (**35**).* The dioxolane **34** (3.20 g, 10 mmol) was dissolved in aqueous acetic acid (70%, 28 mL) and the solution was warmed to 48 °C and stirred for 2 h. After concentration under reduced pressure, the residue was taken up in EtOAc and solid $NaHCO_3$ and $MgSO_4$ were added. The slurry was stirred vigorously, then filtered and concentrated under reduced pressure. Chromatography (7:3 then 8:2, ether:light petroleum) of the residue gave the *title compound* **35** (2.48 g, 86%), R_f = 0.35-0.15 (1:1, ether:light petroleum); $[\alpha]_D^{20}$ +23.5 (*c* 5.1, $CHCl_3$); ν_{max}/cm^{-1} 3405, 2961, 2936, 2878, 1613, 1514, 1464, 1302, 1248, 1175, 1071, 1037, 916, 821; δ_H 1.12 and 1.13 (each 3H, s, 4-CH_3), 2.31 and 2.45 (each 1H, br. s, OH), 3.39 (1H, d, *J* 4.0, 3-H), 3.75-3.79 (3H, m, 1-H_2, 2-H), 3.81 (3H, s, OCH_3), 4.62 and 4.64 (each 1H, d, *J* 10.6, ArHC*H*), 5.02-5.12 (2H, m, 6-H_2), 6.04 (1H, dd, *J* 18.0, 9.5, 5-H), 6.89 and 7.28 (each 2H, d, *J* 8.0, ArH); δ_C 22.9, 25.5, 41.9, 55.5, 64.2, 72.7, 76.1, 88.7, 112.7, 114.1, 129.7, 130.7, 145.8, 159.6; *m*/*z* (CI^+) 298 (M^+ + 18, 32%), 218 (27), 155 (32), 138 (100), 121 (93); HRMS (EI^+): M^+, found 280.1673. $C_{16}H_{24}O_4$ requires 280.1674.

*4.2.23 (2*S*)-2-(4-Methoxybenzyloxy)-3,3-dimethylpent-4-enal (**36**).* Sodium periodate (916 mg, 4.28 mmol) was added to the diol **35** (600 mg, 2.14 mmol) in MeOH (14 mL) and water (7 mL) at 0 °C and the mixture was allowed to warm to rt and stirred for 1 h 10 min. The mixture was partitioned between water and DCM and the aqueous layer was extracted with DCM. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **36** (530 mg, *ca*. 99%), R_f = 0.62 (4:6, ether:light petroleum); $[\alpha]_D^{20}$ −57.6 (*c* 2.2, $CHCl_3$); ν_{max}/cm^{-1} 2963, 2930, 2867, 1729, 1612, 1513, 1464, 1370, 1302, 1248, 1175, 1083, 1035, 921, 822; δ_H 1.09 and 1.10 (each 3H, s, 3-CH_3), 3.36 (1H, d, *J* 3.3, 2-H), 3.82 (3H, s, OCH_3), 4.39 and 4.60 (1H, d, *J* 11.5, ArHC*H*), 5.03 (1H, d, *J* 17.5, 5-H), 5.06 (1H, d, *J* 10.8, 5-H′), 5.96 (1H, dd, *J* 17.6, 11.0, 4-H), 6.88 and 7.26 (each 2H, d, *J* 8.5, ArH), 9.60 (1H, d, *J* 2.9, 1-H); δ_C 23.4, 23.5, 40.9, 55.4, 72.8, 89.1, 113.4, 113.9, 129.6, 129.8, 143.3, 159.6, 204.4; *m*/*z* (CI) 266 (M^+ + 18, 21%), 138 (25), 121 (100); HRMS (EI^+): M^+, found 248.1411. $C_{15}H_{20}O_3$ requires 248.1407.

*4.2.24 (3*S*,4*S*)- and (3*R*,4*S*)-4-(4-Methoxybenzyloxy)-5,5-dimethylhept-6-en-1-yn-3-ols (**37**) and (**38**).* The aldehyde **36** (60 mg, 0.24 mmol) in ether (1 mL) was added to ethynylmagnesium bromide (0.5 M in THF, 960 µl, 0.48 mmol) at −78 °C and the solution stirred at −78 °C for 2 h. The mixture was allowed to warm to 0 °C over 1 h and was stirred for a further 30 min, then warmed to rt, and stirred for 2 h. Saturated aqueous ammonium chloride was added and the mixture partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave recovered aldehyde **36** (30 mg, 50%) followed by the *title compound* **37** (19 mg, 29%), R_f = 0.30 (2:8, ether:light petroleum); $[\alpha]_D^{20}$ +8.5 (*c* 1.1, $CHCl_3$); ν_{max}/cm^{-1} 3486, 3291, 2961, 2930, 1612, 1514, 1465, 1377, 1303, 1248, 1174, 1079, 1037, 919, 826; δ_H 1.06 (6H, s, 2 × 5-CH_3), 2.47 (1H, s, 1-H), 2.96 (1H, br. d, *J* 8.5, OH), 3.43 (1H, s, 4-H), 3.81 (3H, s, OCH_3), 4.43 (1H, br. d, *J* 8.5, 3-H), 4.68 and 4.92 (each 1H, d, *J* 9.5, ArHC*H*), 5.04 (1H, d, *J* 16.0, 7-H), 5.05 (1H, d, *J* 11.5, 7-H′), 5.85 (1H, dd, *J* 17.5, 11.0, 6-H), 6.89 and 7.32 (each 2H, d, *J* 8.5, ArH); δ_C 22.3, 25.1, 42.2, 55.6, 60.2, 72.8, 75.9, 86.2, 87.2, 113.4, 114.1, 130.1, 130.2, 145.0, 159.7; *m*/*z* (CI^+) 292 (M^+ + 18, 8%), 138 (17), 121 (100); HRMS (ES^+): MNH_4^+, found 292.1900. $C_{17}H_{26}NO_3$ requires 292.1907. The second product was the *title compound* **38** (14 mg, 21%), R_f = 0.22 (2:8, ether:light petroleum); $[\alpha]_D^{20}$ −7.3 (*c* 0.6, $CHCl_3$); ν_{max}/cm^{-1} 3434, 3302, 2955, 2930, 1723, 1612, 1513, 1462, 1383, 1299, 1247, 1173, 1103, 1035, 918, 827; δ_H 1.14 (6H, s, 2 × 5-CH_3), 1.98 (1H, br. d, *J* 6.2, OH), 2.56 (1H, d, *J* 2.0, 1-H), 3.34 (1H, d, *J* 3.8, 4-H), 3.83 (3H, s, OCH_3), 4.49-4.55 (1H, m, 3-H), 4.69 and 4.81 (each 1H, d, *J* 11.2, ArHC*H*), 5.05 (1H, d, *J* 10.7, 7-H), 5.08 (1H, d, *J* 17.5, 7-H′), 6.00 (1H, dd, *J* 17.5, 10.7, 6-H), 6.91 and 7.35 (each 2H, d, *J* 8.6, ArH); δ_C 22.3, 25.5, 41.7, 55.5, 64.6, 75.3, 77.5, 83.6, 88.3, 112.8, 114.1, 129.8, 131.0, 145.7, 159.5; *m*/*z* (CI^+) 292 (M^+ + 18, 2%), 138 (7), 121 (100); HRMS (ES^+): MNH_4^+, found 292.1904. $C_{17}H_{26}NO_3$ requires 292.1907.

*4.2.25 (4*S*,5*S*)- and (4*R*,5*S*)-5-(4-Methoxybenzyloxy)-6,6-dimethyl-1-triethylsilyloxyoct-7-en-2-yn-4-ols (**39**) and (**40**).* *n*-Butyllithium (1.6 M in hexanes, 4.6 mL, 7.34 mmol) was added to 3-triethylsilyloxypropyne (1.31 g, 7.71 mmol) in THF (8 mL) at 0 °C and the solution stirred for 1 h. After cooling to −78 °C, the aldehyde **36** (910 mg, 3.67 mmol) in THF (4.2 mL) was added over 10 min and the solution stirred for 2.5 h at −78 °C. Saturated aqueous ammonium chloride was added and the mixture was allowed to warm to rt then partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the title compounds as a mixture of diastereoisomers, **39**:**40** = 92:8 (^{1}H NMR). Chromatography (1:9, ether:light petroleum with 1% Et_3N) of the mixture gave recovered aldehyde **36** (88 mg, 10%) followed by the *title compound* **39** (1.13 g, 74%), R_f = 0.45 (3:7, ether:light

petroleum); $[\alpha]_D^{20}$ +16.3 (*c* 0.6, $CHCl_3$); ν_{max}/cm^{-1} 3507, 2956, 2913, 2878, 1613, 1514, 1463, 1372, 1245, 1123, 1082, 1040, 1009, 807, 726; δ_H 0.66 (6H, q, *J* 8.0, 3 × $SiCH_2$), 0.99 (9H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.07 (6H, s, 2 × 6-CH_3), 2.92 (1H, d, *J* 8.5, OH), 3.43 (1H, d, *J* 1.5, 5-H), 3.83 (3H, s, OCH_3), 4.37 (2H, d, *J* 1.4, 1-H_2), 4.49 (1H, dq, *J* 8.3, 1.5, 4-H), 4.68 and 4.92 (1H, d, *J* 10.6, ArHC*H*), 5.00-5.10 (2H, m, 8-H_2), 5.87 (1H, dd, *J* 17.9, 10.5, 7-H), 6.90 and 7.3 (each 2H, d, *J* 8.5, ArH); δ_C 4.7, 7.0, 22.3, 25.0, 42.1, 51.7, 55.5, 60.4, 75.7, 83.1, 86.8, 87.2, 113.2, 114.0, 130.1, 130.3, 145.1, 159.7; *m/z* (CI^+) 436 (M^+ + 18, 81%), 138 (30), 121 (100); HRMS (CI^+): MNH_4^+, found 436.2889. $C_{24}H_{42}NO_4Si$ requires 436.2883. The second product was the *title compound* **40** (66 mg, 4%)**,** R_f = 0.36 (3:7, ether:light petroleum); $[\alpha]_D^{20}$ –3.2 (*c* 2.7, $CHCl_3$); ν_{max}/cm^{-1} 3446, 3409, 2955, 2915, 2878, 1613, 1513, 1463, 1369, 1302, 1246, 1082, 1037, 1008, 812, 740; δ_H 0.61 (6H, q, *J* 7.9, 3 × $SiCH_2$), 0.93 (9H, t, *J* 7.9, 3 × CH_3), 1.09 and 1.10 (each 3H, s, 6-CH_3), 1.91 (1H, d, *J* 5.8, OH), 3.28 (1H, d, *J* 3.8, 5-H), 3.78 (3H, s, OCH_3), 4.31 (2H, s, 1-H_2), 4.47-4.55 (1H, m, 4-H), 4.61 and 4.75 (each 1H, d, *J* 11.0, ArHC*H*), 4.99 (1H, d, *J* 10.8, 8-H), 5.02 (1H, d, *J* 17.5, 8-H′), 5.96 (1H, dd, *J* 17.5, 10.8, 7-H), 6.85 and 7.29 (each 2H, d, *J* 8.5, ArH); δ_C 4.7, 7.0, 22.6, 25.4, 41.7, 51.8, 55.5, 64.8, 75.3, 84.3, 85.5, 88.5, 112.5, 114.0, 129.7, 131.2, 145.9, 159.4; *m/z* (CI^+) 436 (M^+ + 18, 29%), 138 (42), 121 (100); HRMS (CI^+): MNH_4^+, found 436.2892. $C_{24}H_{42}NO_4Si$ requires 436.2883.

*4.2.26 (4*S*,5*S*)-4-*tert*-Butyldimethylsilyloxy-5-(4-methoxybenzyloxy)-6,6-dimethyl-1-triethylsilyloxyoct-7-en-2-yne (**41**).* 2,6-Lutidine (907 µl, 7.8 mmol) and *tert*-butyldimethylsilyl triflate (894 µl, 3.9 mmol) were added to the alcohol **39** (1.08 g, 2.6 mmol) in DCM (26 mL) at 0 °C and the solution stirred for 1 h. Water was added and the aqueous layer was extracted with DCM. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1% ether, 1% Et_3N in light petroleum) of the residue gave the *title compound* **41** (1.27 g, 92%), R_f = 0.64 (1:9, ether:light petroleum); ν_{max}/cm^{-1} 2955, 2933, 2880, 1613, 1513, 1464, 1249, 1125, 1083, 1008, 838, 778, 741; δ_H 0.09 and 0.16 (each 3H, s, $SiCH_3$), 0.66 (6H, q, *J* 8.0, 3 × $SiCH_2$), 0.93 [9H, s, $SiC(CH_3)_3$], 1.00 (9H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 1.09 and 1.13 (each 3H, s, 6-CH_3), 3.26 (1H, d, *J* 4.7, 5-H), 3.83 (3H, s, OCH_3), 4.34 (2H, s, 1-H_2), 4.56-4.48 (2H, m, 4-H, Ar*H*CH), 4.93 (1H, d, *J* 11.2, ArHC*H*), 4.99 (1H, d, *J* 10.6, 8-H), 5.00 (1H, d, *J* 17.5, 8-H′), 6.04 (1H, dd, *J* 17.5, 10.7, 7-H), 6.89 and 7.32 (each 2H, d, *J* 8.4, ArH); δ_C –4.5, –4.1, 4.7, 7.0, 18.5, 23.9, 25.3, 26.1, 41.9, 51.7, 55.5, 63.7, 74.7, 84.8, 86.6, 88.2, 111.5, 113.7, 129.3, 131.7, 146.2, 159.0; *m/z* (CI^+) 550 (M^+ + 18, 35%), 532 (M^+, 12), 121 (100); HRMS (CI^+): M^+, found 532.3398. $C_{30}H_{52}O_4Si_2$ requires 532.3399.

*4.2.27 (4*S*,5*S*)-4-*tert*-Butyldimethylsilyloxy-5-(4-methoxybenzyloxy)-6,6-dimethyloct-7-en-2-yn-1-ol (**42**).* Potassium fluoride (2.15 g, 37.0 mmol) was added to the triethylsilyl ether **41** (1.27 g, 2.38 mmol) in THF (8.5 mL) and MeOH (34 mL) at 0 °C and the mixture stirred for 2 h. Saturated aqueous sodium hydrogen carbonate was added and the mixture partitioned between water and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3:7, ether:light petroleum) of the residue gave recovered silyl ether **41** (113 mg, 9%) followed by the *title compound* **42** (767 mg, 77%), R_f = 0.50 (1:1, ether:light petroleum); $[\alpha]_D^{20}$ +4.0 (*c* 1.6, $CHCl_3$); ν_{max}/cm^{-1} 3411, 2955, 2932, 2859, 1613, 1514, 1467, 1353, 1249, 1093, 1036, 839, 778; δ_H 0.11 and 0.18 (each 3H, s, $SiCH_3$), 0.85 [9H, s, $SiC(CH_3)_3$], 1.14 and 1.16 (each 3H, s, 6-CH_3), 1.64 (1H, br. s, OH), 3.28 (1H, d, *J* 5.3, 5-H), 3.85 (3H, s, OCH_3), 4.37-4.41 (2H, m, 1-H_2), 4.52 (1H, d, *J* 5.2, 4-H), 4.58 and 4.91 (each 1H, d, *J* 11.3, ArHC*H*), 5.01 (1H, d, *J* 10.8, 8-H), 5.03 (1H, d, *J* 17.5, 8-H′), 6.09 (1H, dd, *J* 17.5, 10.7, 7-H), 6.92 and 7.36 (each 2H, d, *J* 8.6, ArH); δ_C –4.4, –4.1, 18.5, 24.0, 25.4, 26.2, 42.0, 51.6, 55.5, 63.9, 74.9, 84.6, 87.8, 88.2, 111.6, 113.8, 129.3, 131.5, 146.4, 159.1; *m/z* (CI^+) 436 (M^+ + 18, 3%), 154 (32), 138 (45), 121 (100); HRMS (CI^+): MNH_4^+, found 436.2892. $C_{24}H_{42}NO_4Si$ requires 436.2883. The second product was (4*S*,5*S*)-5-(4-methoxybenzyloxy)-6,6-dimethyloct-7-en-2-yne-1,4-diol (24 mg, 3%), R_f = 0.10 (1:1, ether:light petroleum); $[\alpha]_D^{20}$ +24.5 (*c* 1.3, $CHCl_3$); ν_{max}/cm^{-1} 3401, 2960, 2928, 2876, 1613, 1586, 1514, 1302, 1249, 1174, 1119, 1034, 916, 822; δ_H 1.11 and 1.12 (each 3H, s, 6-CH_3), 1.81 (1H, br. s, 1-OH), 3.03 (1H, d, *J* 8.3, 4-OH), 3.46 (1H, d, *J* 1.9, 5-H), 3.86 (3H, s, OCH_3), 4.34 (2H, br. s, 1-H_2), 4.52 (1H, dt, *J* 8.2, 1.8, 4-H), 4.73 and 4.92 (each 1H, d, *J* 10.5, ArHC*H*), 5.09 (1H, d, *J* 17.5, 8-H), 5.10 (1H, d, *J* 10.5, 8-H′), 5.91 (1H, dd, *J* 17.5, 10.5, 7-H), 6.94 and 7.37 (each 2H, d, *J* 8.7, ArH); δ_C 22.4, 25.0, 42.1, 51.4, 55.5, 60.4, 75.9, 82.9, 87.3, 87.8, 113.3, 114.1, 128.9, 130.1, 144.9, 159.7; *m/z* (CI^+) 322 (M^+ + 18, 20%), 138 (22), 121 (100); HRMS (CI^+): MNH_4^+, found 322.2019. $C_{18}H_{28}NO_4$ requires 322.2018.

*4.2.28 (2*Z*)-(4*R*,5*S*)-4-*tert*-Butyldimethylsilyloxy-3-iodo-5-(4-methoxybenzyloxy)-6,6-dimethylocta-2,7-dien-1-ol (**43**) and (2*E*)-(4*S*,5*S*)-4-*tert*-butyldimethylsilyloxy-5-(4-methoxybenzyloxy)-6,6-dimethylocta-2,7-dien-1-ol (**44**).* The alkynol **42** (546 mg, 1.31 mmol) in ether (5.4 mL) was added to Red-Al™ (65% in toluene, 783 µl, 2.61 mmol) in ether (10.9 mL) at 0 °C and the mixture stirred for 1 h at 0 °C. The mixture was allowed to warm to rt and was stirred for 3 h before cooling to –78 °C. Crushed iodine flakes (663 mg, 2.61 mmol) were added in one portion and the reaction mixture was allowed to warm slowly to –10 °C over 1 h. An aqueous solution of Rochelle's salt was added and the mixture was allowed to warm to rt then ether was added. The mixture was stirred vigorously for 30 min then extracted with ether. The organic extracts were washed with saturated aqueous sodium thiosulfate and the washings extracted with ether. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:9, 2:8, then 3:7, ether:light petroleum with 1% Et_3N) of the residue gave the *title compound* **43** (489 mg, 69%), R_f = 0.37 (4:6, ether:light petroleum); $[\alpha]_D^{20}$ +8.0 (*c* 0.8, $CHCl_3$); ν_{max}/cm^{-1} 3411, 2952, 2859, 1613, 1513, 1464, 1249, 1109, 1075, 1042, 838; δ_H 0.06 (6H, s, 2 × $SiCH_3$), 0.95 [9H, s, $SiC(CH_3)_3$], 1.10 and 1.13 (each 3H, s, 6-CH_3), 1.49 (1H, br. t, OH), 3.35 (1H, d, *J* 5.8, 5-H), 3.85 (3H, s, OCH_3), 4.00 (1H, d, *J* 5.7, 4-H), 4.20-4.24 (2H, m, 1-H_2), 4.56 and 4.83 (1H, d, *J* 11.3, ArHC*H*), 4.96 (1H, dd, *J* 17.6, 1.2, 8-H), 4.99 (1H, dd, *J* 10.8, 1.2, 8-H′), 6.05 (1H, dd, *J* 17.3, 11.1, 7-H), 6.24 (1H, t, *J* 5.6, 2-H), 6.91 and 7.33 (each 2H, d, *J* 8.7, ArH); δ_C –4.0, –3.6, 18.4, 23.6, 25.9, 26.3, 42.2, 55.5, 67.1, 75.5, 79.8, 86.1, 111.6, 113.7, 115.5, 128.8, 131.8, 136.4, 146.1, 159.0; *m/z* (CI^+) 564 (M^+ + 18, 3%), 154 (48), 138 (100), 121 (75); HRMS (CI^+): MNH_4^+, found 564.2012. $C_{24}H_{43}NO_4SiI$ requires 564.2006. The second product was the *title compound* **44** (79 mg, 14%), R_f = 0.24 (4:6, ether:light petroleum); $[\alpha]_D^{20}$ –10.2 (*c* 1.1, $CHCl_3$); ν_{max}/cm^{-1} 3410, 2954, 2930, 2859, 1688, 1612, 1212, 1513, 1465, 1361, 1301, 1251, 1173, 1080, 1039, 835, 777; δ_H 0.04 and 0.07 (each 3H, s, $SiCH_3$), 0.94 [9H, s, $SiC(CH_3)_3$] 1.11 and 1.13 (each 3H, s, 6-CH_3), 3.13 (1H, d, *J* 4.8, 5-H), 3.85 (3H, s, OCH_3), 4.15 (2H, d, *J* 4.8, 1-H_2), 4.36 (1H, t, *J* 5.2, 4-H), 4.54 and 4.73 (1H, d, *J* 11.1, ArHC*H*), 4.94 (1H, d, *J* 10.5, 8-H), 4.95 (1H, d, *J* 17.8, 8-H′), 5.76 (1H, dt, *J* 15.6, 5.1, 2-H), 5.86 (1H, dd, *J* 15.8, 5.7, 3-H), 6.06 (1H, dd, *J* 18.0, 10.4, 7-H), 6.92 and 7.33 (each 2H, d, *J* 8.6, ArH; δ_C –4.3, –4.0, 18.4, 25.0, 25.2, 26.2, 42.2, 55.5, 63.6, 74.4, 74.6, 89.3, 110.7, 113.9, 128.6, 129.2, 131.5, 134.0, 147.3, 159.2; *m/z* (CI^+) 438 (M^+ + 18, 7%), 154 (33), 138 (100), 121

(83); HRMS (CI^+): MNH_4^+, found 438.3026. $C_{24}H_{44}NO_4Si$ requires 438.3040.

*4.2.29 (4*R,*5*R*)*-5-tert-*Butyldimethylsilyloxy-4-(2-trimethylsilylethoxymethoxy)-hex-1-yne (**47**).* Pyridine (674 μl, 8.2 mmol) and then carbon tetrabromide (5.44 g, 16.4 mmol) were added to a suspension of triphenylphosphine (8.59 g, 32.8 mmol) in DCM (60 mL) at 0 °C and the mixture was stirred vigorously for 20 min. The aldehyde **45** (2.33 g, 6.44 mmol) in DCM (8 mL) was added and the mixture allowed to warm to rt then stirred for 40 min. Saturated aqueous sodium hydrogen carbonate (8 mL) was added and the mixture was partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (2% ether in light petroleum) of the residue gave recovered aldehyde **45** (300 mg, 13%) and the dibromoalkene **46** (2.47 g, 74%), R_f = 0.76 (1:9, ether:light petroleum); ν_{max}/cm^{-1} 2953, 2930, 2890, 2859, 1467, 1374, 1252, 1104, 1034, 834, 776; δ_H 0.05 [9H, s, $Si(CH_3)_3$], 0.08 and 0.09 (each 3H, s, $SiCH_3$), 0.91 [9H, s, $SiC(CH_3)_3$], 0.82-1.02 (2H, m, CH_2Si), 1.13 (3H, d, *J* 6.3, 6-H_3), 2.24 (1H, ddd, *J* 15.5, 8.5, 7.2, 3-H), 2.44 (1H, ddd, *J* 15.5, 6.9, 3.9, 3-H′), 3.51-3.72 (3H, m, OCH_2CH_2Si, 4-H), 3.91 (1H, qd, *J* 6.4, 4.6, 5-H), 4.68 and 4.74 (each 1H, d, 7.1, OHC*H*O), 6.56 (1H, t, *J* 7.0, 2-H); δ_C −4.5, −4.4, −1.1, 18.1, 18.3, 18.4, 26.1, 33.7, 65.7, 69.6, 80.2, 89.5, 95.3, 136.6. *m*/*z* (ES^+) 539 (100%).

n-Butyllithium (1.6 M in hexanes, 6.3 mL, 10.1 mmol) was added to the dibromoalkene **46** (2.40 g, 4.6 mmol) in THF (35 mL) at −78 °C and the solution stirred for 15 min, then allowed to 0 °C and stirred for a further 15 min. Saturated aqueous ammonium chloride was added and the mixture allowed to warm to rt then partitioned between brine and ether. The aqueous layer was extracted with ether and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (2% ether in light petroleum) of the residue gave the *title compound* **47** (1.43 g, 87%), R_f = 0.32 (4% ether in light petroleum); $[\alpha]_D^{20}$ −14.1 (*c* 2.3, $CHCl_3$); ν_{max}/cm^{-1} 3314, 2954, 2930, 2890, 2859, 1467, 1379, 1252, 1106, 1056, 1035, 835, 776; δ_H 0.04 [9H, s, $Si(CH_3)_3$], 0.09 (6H, s, 2 × $SiCH_3$) 0.91 [9H, s, $SiC(CH_3)_3$], 0.83-0.99 (2H, m, CH_2Si), 1.14 (3H, d, *J* 6.3, 6-H_3), 1.96 (1H, t, *J* 2.6, 1-H), 2.36 (1H, ddd, *J* 16.9, 7.3, 2.6, 3-H), 2.58 (1H, ddd, *J* 16.9, 4.6, 2.7, 3-H′), 3.58-3.76 (3H, m, OCH_2CH_2Si, 4-H), 4.03 (1H, dq, *J* 6.3, 4.7, 5-H), 4.77 and 4.84 (each 1H, d, *J* 7.1, O*H*CHO); δ_C −4.6, −4.3, −1.2, 18.3, 18.4, 18.5, 20.0, 26.1, 65.5, 69.1, 69.5, 80.0, 82.3, 95.4; *m*/*z* (ES^+) 381 (M^+ + 23, 100%); HRMS (ES^+): MNa^+, found 381.2255. $C_{18}H_{38}O_3Si_2Na$ requires 381.2252.

*4.2.30 (1*E,*4*R,*5*R*)-5-*tert-*Butyldimethylsilyloxy-1-tributylstannyl-4-(2-trimethylsilylethoxymethoxy)hex-1-ene (**48**).* The alkyne **47** (239 mg, 0.67 mmol) in toluene (5 mL) was added to tributyltin hydride (215 μl, 0.80 mmol) and AIBN (17 mg, 0.10 mmol) in toluene (6 mL) and the solution heated under reflux for 4 h. After cooling to rt and concentration under reduced pressure, chromatography (1% ether and 1% Et_3N in light petroleum) of the residue gave the *title compound* **48** (298 mg, 68%), together with its (*Z*)-isomer, 9:1 (^1H NMR), R_f = 0.16 (1:9, ether:light petroleum); ν_{max}/cm^{-1} 2955, 2927, 2857, 1463, 1378, 1251, 1106, 1053, 858, 835, 775; δ_H 0.06 [9H, s, $Si(CH_3)_3$], 0.10 (6H, s, 2 × $SiCH_3$), 0.87-1.00 [17H, m, 3 × CH_3, 3 × $SnCH_2$, $SiCH_2$), 0.93 [9H, s, $SiC(CH_3)_3$], 1.15 (3H, d, *J* 6.3, 6-H_3), 1.28-1.42 and 1.47-1.59 (each 6H, m, 3 × CH_2), 2.20-2.34 and 2.53-2.60 (each 1H, m, 3-H), 3.52 (1H, m, 4-H), 3.57-3.76 (2H, m, OCH_2CH_2Si), 3.96 (1H, dq, *J* 6.3, 4.8, 5-H), 4.75 (2H, s, OCH_2O), 6.01-6.06 (2H, m, 1-H, 2-H); δ_C −4.5, −4.3, −1.2, 9.7, 10.4, 14.0, 18.4, 18.5, 26.2, 27.6, 29.4, 38.5, 65.3, 69.8, 82.1, 95.6, 130.5, 146.4; *m*/*z* (ES^+) 672 (M^+ + 23, 100%).

*4.2.31 (1*S,*2*S*)-2-*tert-*Butyldimethylsilyloxy-5,5-dimethyl-3-[(*Z*)-2-hydroxyethylidene]-1-(4-methoxybenzyloxy)-4-methylidenecyclopentane (**49**).* The vinylic iodide **43** (100 mg, 0.18 mmol) in Et_3N (0.5 mL) was added to a suspension of $P(Ph_3)_4$ (13 mg, 11 μmol) and CuI (1.1 mg, 6 μmol) in Et_3N (0.5 mL) at rt. After stirring for 10 min, the alkyne **47** (72 mg, 0.20 mmol) in Et_3N (0.5 mL) was added. After stirring for 2 h, CuI (3.3 mg, 18 μmol) was added and the mixture stirred for 18 h at rt. Saturated aqueous ammonium chloride was added and the mixture partitioned between water and DCM. The aqueous layer was extracted with DCM and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (10:1:89 ether:Et_3N:light petroleum then 30:1:69 ether:Et_3N:petrol) of the residue gave the *title compound* **49** (60 mg, 80%), R_f = 0.22 (3:7, ether:light petroleum); ν_{max}/cm^{-1} 3447, 2955, 2927, 2857, 1614, 1514, 1466, 1357, 1249, 1070, 1038, 836, 777; δ_H 0.17 (6H, s, 2 × $SiCH_3$), 1.00 [9H, s, $SiC(CH_3)_3$], 1.11 and 1.13 (each 3H, s, 5-CH_3), 3.36 (1H, d, *J* 8.0, 1-H), 3.85 (3H, s, OCH_3), 4.33-4.58 (3H, m, 2′-H_2, 2-H), 4.62 and 4.72 (each 1H, d, *J* 11.3, Ar*H*CH), 5.00 and 5.16 (each 1H, s, 4-CH), 5.82 (1H, ddd, *J* 7.0, 4.9, 2.2, 1′-H), 6.91 and 7.32 (each 2H, d, *J* 8.7, ArH); δ_C −5.3, −5.1, 18.3, 21.2, 21.4, 26.0, 55.9, 60.0, 73.7, 81.0, 103.1, 114.5, 127.4, 128.1, 129.8, 142.1, 160.4; *m*/*z* (CI^+) 437 (M^+ + 28, 15%), 306 (42), 271 (80), 121 (70).

*4.2.32 (3*S,*4*S*)-3-*tert-*Butyldimethylsilyloxy-2-formylmethyl-4-(4-methoxybenzyloxy)-1,5,5-trimethylcyclopentene (**50**).* $Pd(PPh_3)_4$ (26 mg, 23 μmol) and the stannane **48** (298 mg, 0.46 mmol) were added to the vinylic iodide **43** (150 mg, 0.27 mmol) in DMF (2 mL) and the flask was covered in foil before being heated at 80 °C for 17 h. The mixture was allowed to cool to rt then diluted with water and ether. The aqueous layer was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (1:9, ether:light petroleum) of the residue gave recovered iodide **43** (8 mg, 5%) and the *title compound* **50** (35 mg, 30%), R_f = 0.57 (3:7, ether:light petroleum), $[\alpha]_D^{20}$ +38.3 (*c* 2.3, $CHCl_3$); ν_{max}/cm^{-1} 2956, 2930, 2857, 1725, 1613, 1514, 1464, 1386, 1360, 1301, 1249, 1174, 1145, 1064, 868, 837, 777; δ_H 0.08 and 0.12 (each 3H, s, $SiCH_3$), 0.91 [9H, s, $SiC(CH_3)_3$], 1.05 and 1.16 (each 3H, s, 5-CH_3), 1.57 (3H, s, 1-CH_3), 3.02 and 3.16 (each 1H, dd, *J* 16.5, 2.0, 2-CH), 3.60 (1H, d, *J* 5.4, 4-H), 3.83 (3H, s, OCH_3), 4.56 (1H, d, *J* 10.7, ArHC*H*), 4.56-4.60 (1H, m, 3-H), 4.67 (1H, d, *J* 10.7, Ar*H*CH), 6.90 and 7.32 (each 2H, d, *J* 8.6, ArH), 9.55 (1H, t, *J* 2.2, CHO); δ_C −4.4, −4.0, 10.3, 18.2, 21.3, 26.1, 26.9, 41.3, 47.2, 55.4, 73.5, 82.0, 95.1, 113.8, 125.5, 129.5, 130.9, 145.5, 159.3, 199.9; *m*/*z* (CI^+) 436 (M^+ + 18, 4%), 304 (96), 287 (94), 243 (35), 121 (100); HRMS (ES^+): MNH_4^+, found 436.2879. $C_{24}H_{42}NO_4Si$ requires 436.2878. A small amount of the alcohol **49** (4 mg, 3%) was also isolated.

*4.2.33 (1*S,*2*S,*4*R*)-2-*tert-*Butyldimethylsilyloxy-5,5-dimethyl-3-[(*Z*)-2-hydroxyethylidene]-1-(4-methoxybenzyloxy)-4-methylcyclopentane (**51**).* Anhydrous chromium(II) chloride (78 mg, 0.6 mmol) and anhydrous nickel(II) chloride (7.3 mg, 0.06 mmol) were added to vinylic iodide **43** (100 mg, 0.18 mmol) and benzaldehyde (23 μl, 0.23 mmol) in DMF (2 mL) at rt and the mixture was stirred at rt for 2 h. Saturated aqueous ammonium chloride was added and the mixture was partitioned between water and EtOAc. The aqueous layer was extracted with EtOAc and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (2:8 then 3:7, ether:light petroleum) gave the *title compound* **51** (47 mg,

62%), R_f = 0.23 (4:6, ether:light petroleum); ν_{max}/cm^{-1} 3413, 2954, 2932, 2859, 1613, 1513, 1466, 1362, 1249, 1149, 1090, 1035, 838, 777; δ_H 0.13 (6H, s, 2 × $SiCH_3$), 0.89 (3H, s, 5-CH_3), 0.96 [9H, s, $SiC(CH_3)_3$], 0.97 (3H, s, 5-CH_3′), 1.02 (3H, d, *J* 7.3, 4-CH_3), 1.42 (1H, br. s, OH), 2.40 (1H, q, *J* 7.4, 4-H), 3.24 (1H, d, *J* 8.1, 1-H), 3.82 (3H, s, OCH_3), 4.23 (2H, d, *J* 6.7, 2′-H_2), 4.44 (1H, dt, *J* 8.0, 2.2, 2-H), 4.56 and 4.68 (each 1H, d, *J* 11.2, ArHC*H*), 5.61 (1H, tt, *J* 6.8, 2.4, 1′-H), 6.88 and 7.29 (each 2H, d, *J* 8.7, ArH) (irradiation of 4-H gave a significant nOe enhancement of 1-H); δ_C –4.3, –4.1, 15.7, 18.3, 18.4, 26.2, 28.6, 40.0, 42.6, 55.5, 59.9, 73.8, 78.1, 91.8, 113.8, 122.9, 129.4, 131.4, 148.4, 159.2; *m*/*z* (CI^+) 438 (M^+ + 18, 29%), 306 (33), 271 (67), 121 (100); HRMS (ES^+): MNH_4^+, found 438.3035. $C_{24}H_{44}NO_4Si$ requires 438.3034.

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