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TETRAHEDRON

An Approach to the Synthesis of the C(17)-C(27) Fragment of Bryostatins

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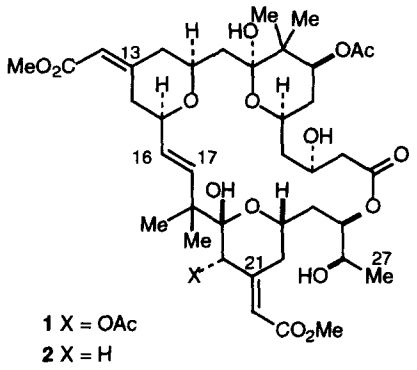
Abstract: The organolithium reagent generated from the vinyl iodide **8** reacts with aldehyde **13** to give a mixture of the *anti*- and *syn*-silyloxy alcohols **14** and **15** together with the regioisomeric *syn*-silyloxy alcohol **16**, ratio **14** : **15** : **16** = 4 : 1 : 1. The major *anti*-alcohol **14** was taken through to the methoxyacetal **27** so confirming this strategy for the stereoselective synthesis of the C(17)-C(23) fragment of bryostatins. The diol **30**, which has configurations at each of its three chiral centres corresponding to the C(23)-C(27) fragment of bryostatins, was prepared in two steps from the aldehyde **28** and converted into the vinylstannane **45**.

The bryostatins are important marine natural products of interest because of their potent anti-neoplastic activity and potential for cancer chemotherapy.[1] Several approaches to the synthesis of fragments of these compounds have been described including a total synthesis of bryostatin 7 **1**.[2,3]



1 X = OAc
2 X = H

One problem which has to be addressed in any synthesis of a bryostatin is the control of the geometry of the exocyclic double-bonds. For example, procedures which have been developed for the stereoselective introduction of the C(13)-double-bond include a stereoselective vinyl radical cyclisation,[4] an intramolecular Wadsworth-Emmons-Horner reaction[5] and an intermolecular Wadsworth-Emmons-Horner reaction on a sterically biased substrate.[6] The C(21)-double-bond of 20-deoxybryostatins, e.g. bryostatin 10 **2**, has been introduced *via* an epoxide ring-opening procedure[7] and by using a palladium(0) catalysed coupling of a vinylic

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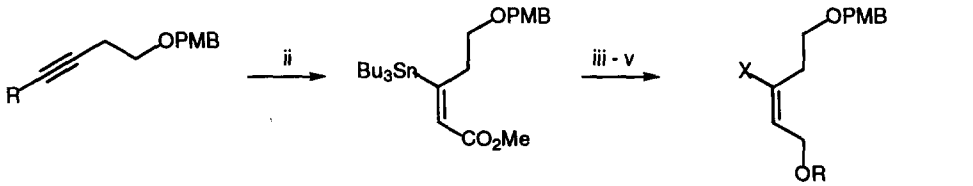
bromide with a tin enolate generated *in situ* by treatment of an enol acetate with tributyltin methoxide.[8] We here report full details of a synthesis of an acetal corresponding to the C(17)-C(23) fragment of bryostatin 7 **1** together with preliminary studies into a stereoselective synthesis of the C(21)-C(27) fragment of the bryostatins. The key step in the synthesis of the acetal is the addition of a vinylic organolithium reagent to a chiral aldehyde derived from (*R*)-pantolactone and follows the strategy pioneered by Masamune.[2]

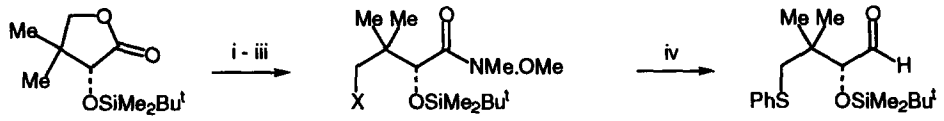
RESULTS AND DISCUSSION

Syntheses of the vinyl iodide **8** and aldehyde **13** required for the key coupling step in the synthesis of the acetal are outlined in Schemes 1 and 2. The iodide was obtained by conjugate addition of a tin cuprate to the alkynoic ester **4** followed by reduction, protection and tin - halogen exchange.[9]



Scheme 1 ***Reagents and Conditions:*** i, butyllithium, -78 °C, 30 min, then $ClCO_2Me$ (93%); ii, $Bu_3SnLi.CuBr.Me_2S$, tetrahydrofuran, -78 °C, 3 h, then methanol (92%); iii, diisobutylaluminium hydride, hexane, -78 °C (98%); iv, *tert*-butyldiphenylsilyl chloride, imidazole, *N,N*-dimethylformamide (95% from **5**); v, iodine, carbon tetrachloride (92%).

The aldehyde **13** was prepared from the *tert*-butyldimethylsilyl ether **9** of (*R*)-pantolactone by ring-opening to the hydroxyamide **10**[10] followed by conversion into the thioether **12**[11] and reduction to the aldehyde.



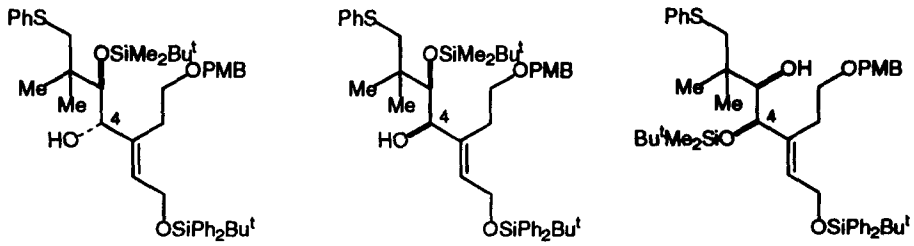
9

10 X = OH
11 X = Br
12 X = PhS

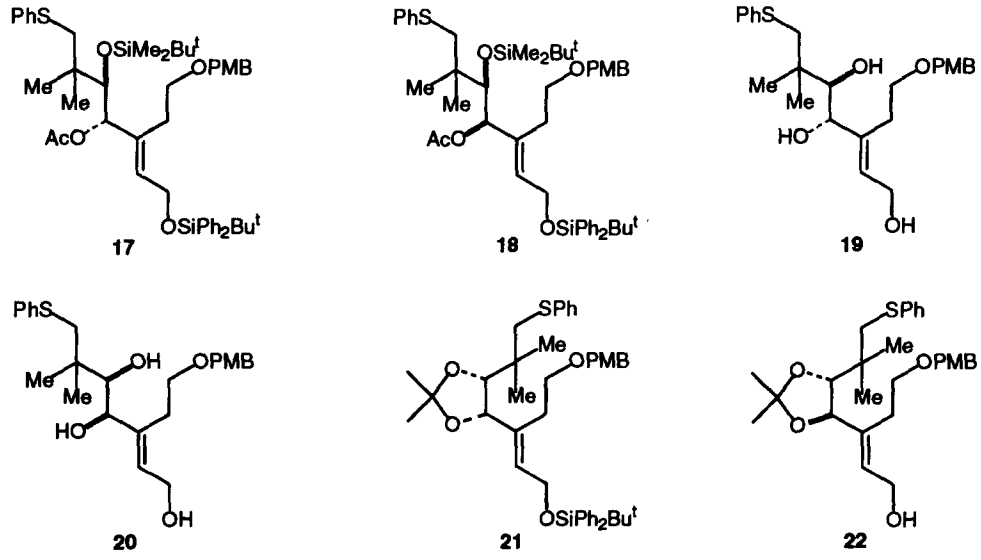
13

Scheme 2 ***Reagents and Conditions:*** i, trimethylaluminium, hexane, *N,O*-dimethylhydroxylamine hydrochloride, benzene (98%); ii, triphenylphosphine, carbon tetrabromide; iii, thiophenol, DBU, benzene, heat under reflux, 48 h (60% from **10**); iv, diisobutylaluminium hydride, hexane, -78 °C (65%).

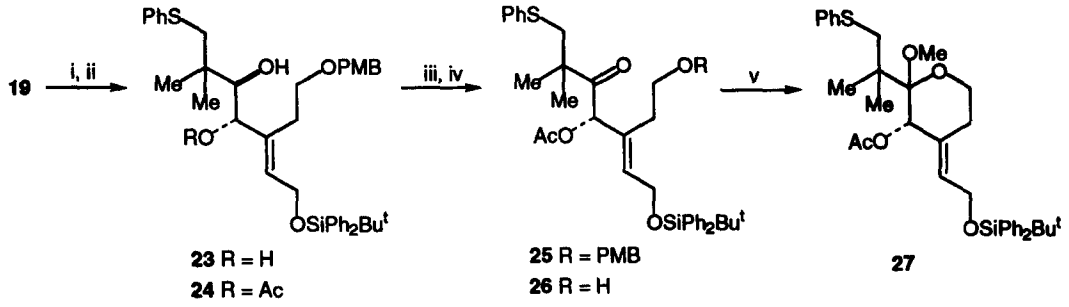
Addition of the aldehyde **13** to a solution of the vinyllithium species generated by treatment of the iodide **8** with butyllithium gave a mixture of three products which were characterised separately and identified as the *anti*-silyloxyalcohol **14**, which has the required configuration at the newly formed hydroxyl-bearing, chiral centre for incorporation into a bryostatin, its *syn*-isomer **15**, and the *syn*-regioisomer **16**, ratio **14** : **15** : **16** = 4 : 1 : 1.



The structures of these products were established by chemical correlation. Acetylation of the alcohols **14** and **15** gave the acetates **17** and **18**, and desilylation of the alcohols **14** - **16** gave the triols **19** and **20** with triol **20** being obtained on deprotection of both **15** and **16**. The configurations of the triols were confirmed using ^{13}C data obtained for the acetonides **21** and **22** which were prepared from the diol **23** and the triol **20**, respectively, since the acetonide methyl carbons were observed at δ 28.83/25.33 for the *cis*-disubstituted acetonide **21** and at δ 27.77/27.68 for the *trans*-disubstituted acetonide **22**.[12] The formation of the *anti*-silyloxy-alcohol **14** as the major product is consistent with Cram-Felkin-Anh control and follows the precedent set by Masamune.[2] Moreover, faster intramolecular migration of the *tert*-butyldimethylsilyl group *via* a *trans*-disubstituted, five-membered ring transition state would be expected for the *syn*-product **15** rather than for the *anti*-product **14**, as observed.



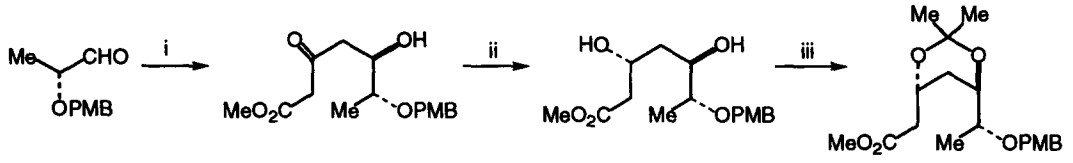
Preliminary attempts to desilylate the acetate **17** were complicated by 1,2-migration of the acetyl group. However, selective silylation of the primary hydroxyl group of the *anti*-triol **19** gave the mono-silyl ether **23** which was regioselectively acetylated to give the acetate **24** then oxidized using pyridinium dichromate (PDC) to the ketone **25**, see Scheme 3. This was deprotected selectively using dichlorodicyanoquinone (DDQ) to give the primary alcohol **26** which was immediately cyclised to give the ketal **27** by treatment with trimethyl orthoformate in methanol containing toluene *p*-sulfonic acid as catalyst.



Scheme 3 ***Reagents and Conditions:*** i, *tert*-butyldiphenylsilyl chloride, triethylamine, 4-dimethylaminopyridine (DMAP; cat.) (89%); ii, acetic anhydride, pyridine, DMAP (90%); iii, PDC, 4A sieves, dichloromethane (76%); iv, DDQ, dichloromethane, water; v, trimethyl orthoformate, methanol, toluene *p*-sulfonic acid (cat.) (42% from **25**)

This synthesis of the ketal **27**, which was obtained as a single stereoisomer although the configuration at the anomeric carbon was not confirmed,§ provides a basis for a future preparation of the C(17)-C(23) fragment of the bryostatins. The next stage was to develop a synthesis of a vinylic halide corresponding to the intact C(23)-C(27) fragment. Several approaches to this region of the bryostatins have been reported.[3] Our strategy was based on the chelation controlled addition of methyl acetoacetate to the aldehyde **28** followed by stereoselective reduction and is summarised in Scheme 4.#

Chelation controlled addition of the bis-trimethylsilylenol ether of methyl acetoacetate to (*R*)-2-*p*-methoxybenzyloxypropanal **28** gave the keto-alcohol **29** with excellent stereoselectivity.[14] Selective reduction[15] of the ketone then gave the *anti*-diol **30** which has the required configuration at each of its three chiral centres for incorporation into a synthesis of a bryostatin and which was characterised as its acetonide **31**.



28 **29** **30** **31**

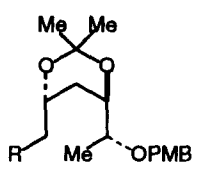
Scheme 4 ***Reagents and Conditions:*** i, $CH_2=C(OSiMe_3)CH=C(OMe)OSiMe_3$, tin(IV) chloride, -100 °C (52%); ii, tetramethylammonium triacetoxyborohydride (82%); iii, 2,2-dimethoxypropane, toluene *p*-sulfonic acid (cat.), acetone (79%).

As part of the preliminary investigation of an assembly of the C(17)-C(27) fragment of the bryostatin, the ester **31** was converted into the aldehyde **33** *via* the alcohol **32**. Aldol addition of 3,3-dimethylpent-4-enone gave the hydroxyketone **34** as a mixture of epimers. However, attempts to convert this hydroxyketone or its methyl ether **35** into the acetal **36** gave rise to mixtures of products in which both of the incipient 23- and 25-hydroxyl

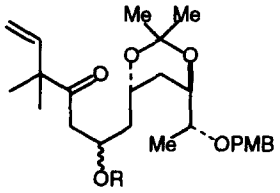
§ This is not important for bryostatin synthesis since the configuration of the hemiacetal will be established by the anomeric effect under conditions of thermodynamic control.

During the course of our work the chelation controlled addition of a keto-ester to an aldehyde followed by *syn*-selective reduction of the hydroxyketone was described.[13]

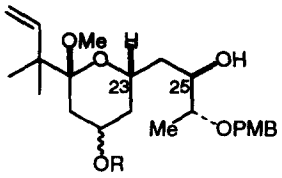
groups (bryostatin numbering) were involved in product formation. It was therefore deemed necessary to use different protecting groups for these hydroxyl groups.



32 R = CH_2OH
33 R = CHO

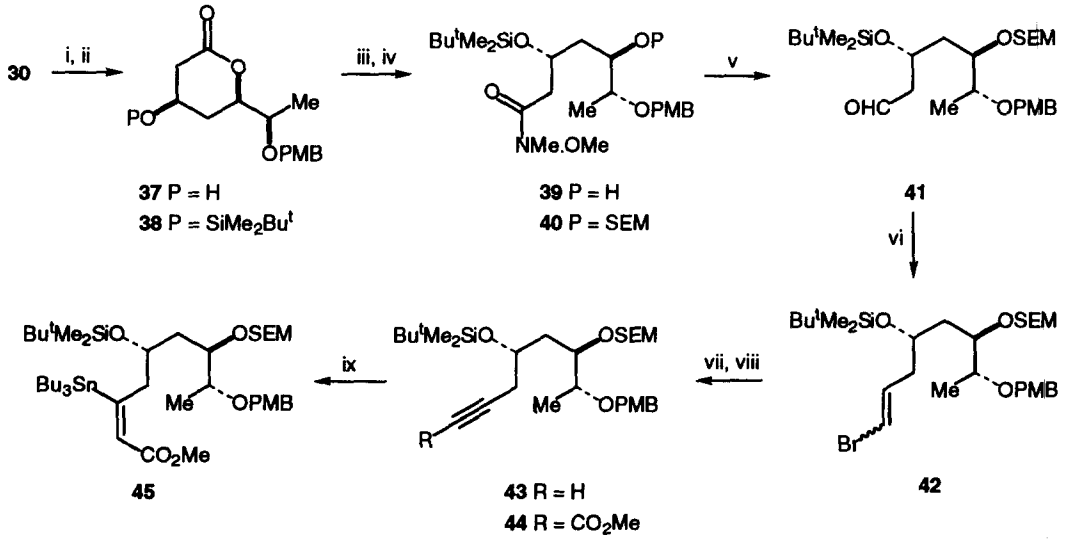


34 R = H
35 R = Me



36 R = H or Me

The diol **30** was cyclised to give the hydroxylactone **37** which was protected as the *tert*-butyldimethylsilyl ether **38**, see scheme 5. Ring-opening gave the Weinreb amide **39** which was further protected as its (2-trimethylsilylethoxy)methyl ether **40**. The three incipient hydroxyl groups in this amide are now protected using different protecting groups and can be manipulated separately. Reduction gave the aldehyde **41** which was converted into the alkyne **43** *via* the vinyl bromide **42** which was prepared as a mixture of geometrical isomers using a Wittig reaction.[16] Finally, after carboxymethylation, stereoselective addition of a tin cuprate[9] gave the (*E*)-vinylstannane **45**.



37 P = H
38 P = $SiMe_2Bu^t$

39 P = H
40 P = SEM

41

42

43 R = H
44 R = CO_2Me

45

Scheme 5 ***Reagents and Conditions:*** i, aqueous NaOH, then H^+, heat in benzene under reflux; ii, *tert*-butyldimethylsilyl chloride, imidazole, *N,N*-dimethylformamide (74% from **30**); iii, trimethylaluminium, *N,O*-dimethylhydroxylamine hydrochloride, benzene (99%); iv, (2-trimethylsilylethoxy)methyl chloride, diisopropylethylamine, dichloromethane (85%); v, diisobutylaluminium hydride, hexane, dichloromethane, -78 °C (94%); vi, bromomethyl(triphenyl)phosponium bromide, lithium hexamethyldisilazide, tetrahydrofuran (65%); vii, butyllithium, tetrahydrofuran, 0 °C (70%); viii, butyllithium, methyl chloroformate, -78 °C to 0 °C (73%); ix, $Bu_3SnLi.CuBr.Me_2S$, -78 °C, then methanol (84%).

CONCLUSIONS

The vinylstannane **45** has the functionality required for incorporation into a synthesis of either a 20-acyloxybryostatin, e.g. **1**, using the vinylic iodide following the route used to prepare the acetal **27**, or a 20-deoxybryostatin, e.g. **2**, by the stereoselective palladium(0) catalysed coupling of the corresponding vinylic bromide with an enol acetate.[8] Work along these lines is in progress.

EXPERIMENTAL

For general experimental details see the first paper in this series.[4] Products were isolated as colourless oils unless otherwise stated.

1-(*p*-Methoxybenzyloxy)but-3-yne **3** (1.75 g, 70 %) was prepared from but-3-yn-1-ol (1 cm^3, 13.2 mmol), sodium hydride (531 mg, 23 mmol) and *p*-methoxybenzyl chloride (1.82 cm^3, 13.4 mmol) with chromatography using light petroleum/ether (92:8) as eluent (Found: M^+, 190.0992. $C_{12}H_{14}O_2$ requires *M*, 190.0994); υ_{max} /cm^{-1} 3292, 1613, 1587, 1514, 1465, 1363, 1303, 1249, 1175, 1099, 1035, 823, 758 and 638; δ_H 2.0 (1 H, t, *J* 3, 4-H), 2.5 (2 H, dt, *J* 3, 7, 2-H_2), 3.58 (2 H, t, *J* 7, 1-H_2), 3.8 (3 H, s, OCH_3), 4.5 (2 H, s, CH_2 Ar) and 6.9 and 7.29 (each 2 H, m, ArH); *m/z* (E.I.) 190 (M^+, 9 %) and 121 (100). Methyl 5-(*p*-methoxybenzyloxy)pent-2-ynoate **4** (1.21 g, 93 %) was prepared from the alkyne **3** (1 g, 5.26 mmol), butyllithium (1.6 M in hexane; 4.04 cm^3, 6.47 mmol) and methyl chloroformate (0.8 cm^3, 10 mmol) with chromatography using light petroleum/ether (70:30) as eluent (Found: $M^+ + NH_4$, 266.1382. $C_{14}H_{20}NO_4$ requires *M*, 266.1392); υ_{max} /cm^{-1} 2241, 1713, 1614, 1586, 1515, 1435, 1363, 1256, 1175, 1079, 1034, 823 and 753; δ_H 2.6 (2 H, t, *J* 7, 4-H_2), 3.6 (2 H, t, *J* 7, 5-H_2), 3.75 and 3.8 (each 3 H, s, OCH_3), 4.48 (2 H, s, CH_2Ar) and 6.9 and 7.25 (each 2 H, m, ArH); δ_C 159.4, 154.0, 129.8, 129.4, 113.9, 86.5, 73.6, 72.8, 66.7, 55.3, 52.6 and 20.2; *m/z* (C.I.) 266 (M^+ + 18, 23 %) and 121 (100).

*Methyl (*E*)-5-(*p*-methoxybenzyloxy)-3-tributylstannylpent-2-enoate* **5**

Butyllithum (1.6 M in hexane; 8.8 cm^3, 14 mmol) was added to a solution of diisopropylamine (2 cm^3, 14.1 mmol) in tetrahydrofuran (24 cm^3) at 0 °C and the mixture stirred at 0 °C for 10 min. Tributyltin hydride (4.2 g, 14.4 mmol) was added and the mixture stirred at 0 °C for 15 min before being cooled to -50 °C and copper(I) bromide-dimethyl sulphide complex (3 g, 14.6 mmol) added in small portions. The mixture was stirred at -50 °C for 20 min, cooled to -78 °C, then a solution of the alkyne **4** (1.17 g, 4.72 mmol) in tetrahydrofuran (20 cm^3) was added dropwise and the reaction mixture stirred at -78 °C for a further 3 h. Methanol (15 cm^3) was added and the mixture stirred for 10 min at -78 °C and then at room temperature for 30 min. The mixture was diluted with water (40 cm^3) and filtered through celite with ethyl acetate washings (5 x 90 cm^3). The filtrate was washed with brine (30 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **5** (2.33, 92 %) (Found: $M^+ - C_4H_9$, 483.1556. $C_{22}H_{35}O_4{}^{120}Sn$ requires *M*, 483.1556); υ_{max} /cm^{-1} 1718, 1614, 1589, 1514, 1464, 1358, 1250, 1169, 1088, 1039, 869 and 821; δ_H 0.89 - 1.6 (27 H, m, Bu_3Sn), 3.24 (2 H, t, *J* 7, 4-H_2), 3.56 (2 H, t, *J* 7, 5-H_2), 3.73 and 3.84 (each 3 H, s, OCH_3), 4.48 (2 H, s, $ArCH_2$), 6.08 (1 H, s, 2-H) and 6.91 and 7.3 (each 2 H, d, ArH); δ_C 171.4, 164.3, 159.4, 131.0, 129.9, 129.4, 114.1, 73.0, 69.8, 55.7, 51.4, 35.9, 29.4, 27.9, 14.2 and 10.6; *m/z* (C.I.) 540 (M^+, 48 %) and 482 (30).

(E)-1-tert-Butyldiphenylsilyloxy-5-(p-methoxybenzyloxy)-3-tributylstannylpent-2-ene **7**

Diisobutylaluminium hydride (1 M in hexane; 13 cm^3, 13 mmol) was added dropwise to the ester **5** (2.28 g, 4.23 mmol) in tetrahydrofuran (21 cm^3) at -78 °C and the mixture stirred for 1.5 h at -78 °C. Methanol (1.25 cm^3) and saturated aqueous ammonium chloride (4.2 cm^3) were added, and the mixture stirred at 0 °C for 30 min. Ethyl acetate (20 cm^3) was added and the mixture filtered through celite with ethyl acetate washings (5 x 20 cm^3). The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure to yield the alcohol **6** (2.1 g, 98 %).

tert-Butyldiphenylsilyl chloride (1.75 cm^3, 6.7 mmol) was added to a solution of imidazole (620 mg, 7.66 mmol) in *N,N*-dimethylformamide (2 cm^3) at 0 °C. After 5 min, a solution of the alcohol **6** (2.1 g, 4.1 mmol) in *N,N*-dimethylformamide (3 cm^3) was added. The mixture was stirred at room temperature for 16 h, diluted with ether (50 cm^3) and washed with aqueous hydrogen chloride (1 M; 2 x 5 cm^3), brine (5 cm^3), saturated aqueous sodium bicarbonate (5 cm^3) and brine (2 x 5 cm^3). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (90:10) as eluent gave the *title compound* **7** (3 g, 95 %); υ_{max} /cm^{-1} 1614, 1588, 1514, 1464, 1428, 1249, 1112, 1088, 823 and 703; δ_H 1.1 [9 H, s, $SiC(CH_3)_3$], 0.8 - 1.55 (27 H, m, Bu_3Sn), 2.41 (2 H, t, *J* 7.5, 4-H_2), 3.25 (2 H, t, *J* 7.5, 5-H_2), 3.84 (3 H, s, OCH_3), 4.36 (2 H, s, $ArCH_2$), 4.37 (2 H, d, *J* 5.5, 1-H_2), 5.85 (1 H, t, *J* 5.5, 2-H), 6.96 and 7.22 (each 2 H, d, ArH), 7.38 (6 H, m, ArH) and 7.72 (4 H, m, ArH); δ_C 142.8, 141.1, 136.1, 134.2, 130.0, 129.7, 128.1, 114.2, 73.0, 70.0, 61.8, 55.7, 34.2, 29.6, 27.9, 27.3, 19.8, 14.2 and 10.18.

(E)-1-tert-Butyldiphenylsilyloxy-3-iodo-5-(p-methoxybenzyloxy)pent-2-ene **8**

Iodine (2.1 g, 8.3 mmol) was added the stannane **7** (3 g, 4 mmol) in carbon tetrachloride (42 cm^3). The mixture was stirred at room temperature for 10 min, diluted with hexane (170 cm^3) and washed with saturated aqueous sodium thiosulphate (3 x 16 cm^3), saturated aqueous sodium bicarbonate (16 cm^3) and brine (16 cm^3). The organic extract was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography using light petroleum - light petroleum/ether (96:4) as eluent gave the *title compound* **8** (2.16 g, 92 %) (Found: $M^+ + NH_4$, 604.1738. $C_{29}H_{39}NO_3SiI$ requires *M*, 604.1744); υ_{max} /cm^{-1} 1613, 1588, 1514, 1428, 1303, 1249, 1113, 1039, 823 and 703; δ_H (C_6D_6) 1.2 [9 H, s, $SiC(CH_3)_3$], 2.44 (2 H, t, *J* 6, 4-H_2), 3.37 (2 H, t, *J* 6, 5-H_2), 3.38 (3 H, s, OCH_3), 4.23 (2 H, s, $ArCH_2$), 4.25 (2 H, d, *J* 6.5, 1-H), 6.71 (1 H, t, *J* 6.5, 2-H), 6.86 and 7.18 (each 2 H, d, ArH), 7.25 (6 H, m, ArH) and 7.8 (4 H, m, ArH); δ_C (C_6D_6) 143.2, 136.4, 134.1, 131.3, 130,5, 129.7, 114.4, 101.8, 73.2, 68.7, 62.6, 55.2, 40.5, 27.4 and 19.8; *m/z* (C.I.) 604 (M^+ + 18, 7 %).

(R)-N-Methoxy-N-methyl-2-tert-butyldimethylsilyloxy-4-hydroxy-3,3-dimethylbutanamide **10**

Trimethylaluminium (2 M in hexane; 4.2 cm^3, 8.4 mmol) was added dropwise to a suspension of *N,O*-dimethylhydroxylamine hydrochloride (0.25 g, 8.4 mmol) in benzene (8.0 cm^3) at 0 °C. The mixture was stirred at ambient temperature for 2 hours and then cooled to 0 °C. A solution of the protected pantolactone **9** (1.0 g, 4.1 mmol) in benzene (5.0 cm^3) was added dropwise and the mixture stirred at ambient temperature for 1 h. The mixture was then cooled to 0 °C and saturated aqueous sodium bicarbonate (8.0 cm^3) was added. The mixture was stirred for 10 min at ambient temperature, diluted with ethyl acetate (20 cm^3) and filtered through celite with ethyl acetate washings (5 x 20 cm^3). The filtrate was washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **10** (1.21 g, 98 %) (Found: M^+ + H, 306.2104. $C_{14}H_{32}O_4NSi$ requires *M*, 306.2101); υ_{max} /cm^{-1} 3435, 1656, 1473, 1389, 1252, 1114, 1084, 1005, 953, 864, 837 and 777; δ_H (C_6D_6) 0.17 and 0.19 (each 3 H, s, $SiCH_3$), 1.08 [12 H, s, $SiC(CH_3)_3$ and 3-CH_3), 1.13 (3

H, s, 3-CH_3'), 2.86 and 3.2 (each 3 H, s, CH_3), 3.54 (1 H, d, *J* 11, 4-H), 3.7 (1 H, br s, OH), 3.92 (1 H, d, *J* 11, 4-H') and 4.7 (1 H, s, 2-H); δ_C (C_6D_6) 175.2, 73.3, 68.9, 61.0, 40.9, 32.6, 26.5, 24.1, 21.2, 18.7, -4.4 and -5.03; *m/z* (C.I.) 306 (M^+ + 1, 83 %) and 262 (100).

(R)-N-Methoxy-N-methyl-2-tert-butyldimethylsilyloxy-3,3-dimethyl-4-phenylthiobutanamide **12**

Triphenylphosphine (280 mg, 1.04 mmol) and carbon tetrabromide (348 mg, 1.05 mmol) were added to the alcohol **10** (245 mg, 0.8 mmol) in acetonitrile (2 cm^3) at room temperature and the mixture stirred for 2 h before being concentrated under reduced pressure. Repeated chromatography of the residue gave the bromide **11** (Found: M^++ H, 368.1254. $C_{14}H_{31}O_3NSi^{79}Br$ requires *M*, 368.1257); $[\alpha]_D$ -2.32 (c 0.25, $CHCl_3$); υ_{max} /cm^{-1} 1678, 1472, 1387, 1251, 1125, 1097, 1003, 838 and 778; δ_H (C_6D_6) 0.19 [6 H, s, $Si(CH_3)_2$], 1.04 [9 H, s, $SiC(CH_3)_3$], 1.08 and 1.22 (each 3 H, s, 3-CH_3), 2.78 and 3.12 (each 3 H, s, CH_3), 3.2 and 3.72 (each 1 H, d, *J* 9.5, 4-H) and 4.9 (1 H, s, H-2); *m/z* (C.I.) 370, 368 (M^++ 1, 100 %). This bromide **11** (242 mg, 0.66 mmol) in benzene (1 cm^3) was added dropwise to diazabicycloundecane (100 mg, 0.66 mmol) and thiophenol (73 mg, 0.66 mmol) in benzene (2 cm^3) and the mixture stirred under reflux for 48 h. After cooling to room temperature, the mixture was filtered and the filtrate washed with water. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography using light petroleum/ether (85:15) gave the *title compound* **12** (190 mg, 60 % from alcohol **10**), $[\alpha]_D$ -3.69 (*c* 2.25, $CHCl_3$) (Found: M^+ + H, 398.2177. $C_{20}H_{36}NO_3SSi$ requires *M*, 398.2185); υ_{max} /cm^{-1}1678, 1584, 1472, 1387, 1251, 1125, 1002, 838 and 778; δ_H 0.06 and 0.1 (each 3 H, s, $SiCH_3$), 0.95 [9 H, s, $SiC(CH_3)_3$], 1.05 and 1.15 (each 3 H, s, 3-CH_3), 3.1 (1 H, d, *J* 12.5, 4-H), 3.2 (3 H, br s, NCH_3), 3.23 (1 H, d, *J* 12.5, 4-H'), 3.8 (3 H, s, OCH_3), 4.75 (1 H, s, 2-H) and 7.1 - 7.4 (5 H, m, ArH); δ_C 173.4, 138.3, 128.8, 125.4, 71.8, 61.1, 43.2, 40.7, 32.4, 25.9, 23.2, 22.6, 18.2, -4.6 and -5.2; *m/z* (C.I.) 398 (M^+ + 1, 100 %), 370 (44), 368 (57), 340 (20) and 310 (20).

(2R)-2-tert-Butyldimethylsilyloxy-3,3-dimethyl-4-phenylthiobutanal **13**

Di-isobutylaluminium hydride (1 M in hexane, 6.7 cm^3, 6.7 mmol) was added to the amide **12** (895 mg, 2.25 mmol) in dichloromethane (15 cm^3) at -78 °C and the mixture stirred for 2 h before methanol (3.7 cm^3) was added. After 10 min at -78 °C, saturated aqueous ammonium chloride (7.4 cm^3) was added, the mixture stirred at 0 °C for 30 min, then ethyl acetate (35 cm^3) was added. After filtration through celite with ethyl acetate washings (5 x 35 cm^3), the filtrate was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography using light petroleum/ether (92:8) as eluent gave the *title compound* **13** (498 mg, 65 %), $[\alpha]_D$ +19.67 (*c* 8.35, $CHCl_3$) (Found: M^+ + H, 339.1813. $C_{18}H_{31}O_2SSi$ requires *M*, 339.1814); υ_{max} /cm^{-1} 1733, 1584, 1471, 1439, 1389, 1255, 1100, 939, 862, 839 and 779; δ_H (C_6D_6) 0.04 and 0.05 (each 3 H, s, $SiCH_3$), 0.97 [9 H, s, $SiC(CH_3)_3$], 1.02 and 1.04 (each 3 H, s, 3-CH_3), 2.92 and 3.06 (each 1 H, d, *J* 12.5, 4-H), 3.87 (1 H, d, *J* 2.5, 2-H), 6.95 - 7.40 (5 H, m, ArH) and 9.65 (1 H, d, *J* 2.5, 1-H); δ_C (C_6D_6) 203.0, 134.4, 129.9, 129.6, 126.4, 82.8, 43.9, 41.9, 26.4, 24.1, 23.2, 18.9, -4.5 and -4.6; *m/z* (C.I.) 339 (M^+ + 1, 100 %) and 281 (38).

(4S,5R,2E)- And (4R,5R,2E)-5-tert-Butyldimethylsilyloxy-1-tert-butyldiphenylsilyloxy-3-[2-(p-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-en-4-ol **14** *and* **15** *and (4R,5R,2E)-4-tert-butyldimethylsilyloxy-1-tert-butyldiphenylsilyloxy-3-[2-(p-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-en-5-ol* **16**

n-Butyllithium (1.6 M in hexane; 0.29 cm^3, 0.46 mmol) was added dropwise to a stirred solution of the iodide **8** (250 mg, 0.426 mmol) in tetrahydrofuran (5 cm^3) at -78 °C. The mixture was stirred at -78 °C for 30 min and a

cooled solution of the aldehyde **13** (120 mg, 0.355 mmol) in tetrahydrofuran (1.5 cm^3) was added *via* a cannula. The mixture was stirred at -78 °C for 45 min, saturated aqueous ammonium chloride (0.5 cm^3) was added, and the reaction mixture was allowed to attain room temperature. The aqueous phase was extracted with ether (3 x 2 cm^3) and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (96:4) as eluent gave the title compounds **14** - **16** (225 mg, 80%) ratio **14** : **15** : **16** = 68 : 16 : 16, respectively. The least polar product was the (4*R*,5*R*,2*E*)-isomer of the *title compound* **16**, $[\alpha]_D$ +3.47 (*c* 2.85, $CHCl_3$) (Found: M^+ - C_4H_9, 741.3475. $C_{43}H_{57}O_5SSi_2$ requires *M*, 741.3465); υ_{max} /cm^{-1} 3506, 1613, 1586, 1514, 1472, 1428, 1362, 1250, 1112, 952, 836, 779 and 703; δ_H 0.00 and 0.04 (each 3 H, s, $SiCH_3$), 0.89 [9 H, s, $SiC(CH_3)_3$], 0.96 and 0.97 (each 3 H, s, Me), 1.05 [9 H, s, $SiC(CH_3)_3$], 2.22 (2 H, m, 1-H_2'), 2.93 (1 H, d, J 12, 7-H), 3.05 (1 H, d, *J* 7, OH), 3.09 (1 H, d, *J* 12, 7-H), 3.31 (1 H, dd, *J* 7, 1.5, 5-H), 3.36 (2 H, t, *J* 6.5, 2'-H_2), 3.75 (3 H, s, OCH_3), 4.2 (3 H, m, 1-H_2, 4-H), 4.26 and 4.29 (each 1 H, d, *J* 11, HC*H*Ar), 5.65 (1 H, t, *J* 6, 2-H), 6.78 (2 H, m, ArH) and 7.09 - 7.72 (17 H, m, ArH); δ_C 138.2, 135.5, 135.0, 133.0, 130.4, 129.6, 129.2, 129.1, 128.7, 128.2, 127.7, 125.5, 113.7, 76.4, 74.0, 72.4, 69.4, 60.4, 55.2, 44.8, 39.6, 28.1, 26.7, 26.0, 23.5, 22.3, 19.2, 18.1, -3.8 and -4.9; *m/z* (FAB) 741 (M^+ - 57, 0.05 %), 667 (43) and 603 (0.7). The next eluted product was the (4*S*,5*R*,2*E*)-isomer of the *title compound* **14**, $[\alpha]_D$ + 44.89 (*c* 0.65, $CHCl_3$) (Found: M^+, 798.4158. $C_{47}H_{66}O_5SSi_2$ requires *M*, 798.4170); υ_{max} /cm^{-1} 3427, 1613, 1586, 1514, 1472, 1428, 1361, 1250, 1089, 835, 778 and 703; δ_H 0.03 and 0.06 (each 3 H, s, $SiCH_3$), 0.88 and 1.01 [each 9 H, s, $SiC(CH_3)_3$], 1.03 (6 H, s, 2 x 6-CH_3), 2.14 (1 H, dt, *J* 15, 4, 1'-H), 2.7 (1 H, ddd, *J* 15, 9.5, 5, 1'-H), 3.05 (2 H, s, 7-H_2), 3.15 (1 H, dt, *J* 9, 4.5, 2'-H), 3.38 (1 H, m, 2'-H'), 3.75 (3 H, s, OCH_3), 3.8 (1 H, br d, OH), 3.81 (1 H, d, *J* 4, 5-H), 4.16 (3 H, m, 1-H_2 and 4-H), 4.30 and 4.34 (each 1 H, d, *J* 8, *H*CHAr), 5.8 (1 H, t, *J* 6, 2-H), 6.8 (2 H, m, ArH), 7.0 - 7.4 (13 H, m, ArH) and 7.64 (4 H, m, ArH); δ_C 138.9, 138.1, 135.5, 133.8, 130.5, 129.6, 129.4, 128.7, 128.2, 127.7, 125.3, 113.7, 80.6, 76.8, 72.9, 69.8, 60.2, 55.2, 44.5, 40.1, 28.8, 26.7, 26.4, 24.5, 23.9, 19.2, 18.6, -3.1 and -4.8; *m/z* (FAB) 799 (M^+ + 1, 0.4 %), 798 (1.6) and 780 (3). The most polar product was the (4*R*,5*R*,2*E*)-isomer of the *title compound* **15**, $[\alpha]_D$ + 31.55 (*c* 0.8, $CHCl_3$) (Found: M^+ - C_4H_9, 741.3457. $C_{43}H_{57}O_5SSi_2$ requires *M*, 741.3465); υ_{max} /cm^{-1} 3518, 1613, 1586, 1514, 1472, 1250, 1112, 1069, 834, 779, 739 and 703; δ_H 0.05 and 0.11 (each 3 H, s, $SiCH_3$), 0.98 and 1.08 [each 9 H, s, 2 x $SiC(CH_3)_3$], 1.12 (6 H, s, 2 x 6-CH_3), 2.15 and 2.44 (each 1 H, m, 1'-H), 3.09 (2 H, br s, 7-H_2), 3.12 (1 H, s, OH), 3.34 (2 H, t, *J* 7, 2'-H_2), 3.78 (4 H, m, 5-H, OCH_3), 4.3 (5 H, m, 1-H_2, 4-H, $ArCH_2$), 5.92 (1 H, t, *J* 6, 2-H), 6.83 (2 H, m, ArH) and 7.15 - 7.77 (17 H, m, ArH); δ_C 138.0, 135.6, 133.9, 133.8, 129.6, 129.1, 128.8, 128.7, 127.6, 126.9, 125.5, 113.7, 77.3, 72.5, 70.4, 69.1, 60.6, 55.2, 43.8, 40.3, 29.0, 26.7, 26.4, 24.7, 24.2, 18.8, 18.1, -3.0 and -3.6; *m/z* (FAB) 781 (M^+ - 17, 0.6%), 741 (M^+ - 57, 0.5) and 543 (1).

*(4S,5R,2E)- and (4R,5R,2E)-4-Acetoxy-5-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-3-[2-(p-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-ene* **17** *and* **18**

Acetic anhydride (0.037 cm^3), triethylamine (0.05 cm^3) and 4-*N*,*N*-dimethylaminopyridine (1 mg) were added to the alcohol **14** (14 mg, 0.018 mmol) in carbon tetrachloride (0.5 cm^3) and the solution stirred for 19 h at room temperature. Saturated aqueous ammonium chloride was added and the mixture extracted with ether. The ethereal extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (95:5) as eluent gave the (4*S*,5*R*,2*E*)-isomer of the *title compound* **17** (14 mg, 95%) (Found: M^+ - C_4H_9, 783.3602. $C_{45}H_{59}O_6SSi_2$ requires *M*, 783.3571); υ_{max} /cm^{-1} 1742, 1613, 1587, 1514,

1473, 1364, 1248, 1112, 835, 777, 739 and 703; δ_H 0.06 and 0.11 (each 3 H, s, $SiCH_3$), 0.9 and 1.0 [each 9 H, s, $SiC(CH_3)_3$], 1.05 and 1.06 (each 3 H, s, 6-CH_3), 1.98 (3 H, s, $COCH_3$), 2.22 and 2.58 (each 1 H, m, 1'-H), 2.99 and 3.04 (each 1 H, d, *J* 12, 7-H), 3.26 (2 H, m, 2'-H_2), 3.76 (3 H, s, OCH_3), 3.87 (1 H, d, *J* 3, 5-H), 4.22 (4 H, m, 1-H_2 and CH_2Ar), 5.4 (1 H, d, *J* 3, 4-H), 5.8 (1 H, t, *J* 5, 2-H), 6.75 (2 H, m, ArH), 7.05 - 7.45 (13 H, m, ArH) and 7.6 (4 H, m, ArH); *m/z* (FAB) 841 (M^+, 1%) and 783 (M^+ - 59, 6).

Similarly the alcohol **15** gave the (4*R*,5*R*,2*E*)-isomer of the *title compound* **18** (Found: $M^+ + NH_4$, 858.4667. $C_{49}H_{72}NO_6SSi_2$ requires *M*, 858.4619); υ_{max} /cm^{-1} 1742, 1614, 1587, 1514, 1473, 1428, 1368, 1249, 1112, 1039, 833, 777, 740 and 703; δ_H 0.00 and 0.03 (each 3 H, s, $SiCH_3$), 0.97 and 1.08 [each 9 H, s, $SiC(CH_3)_3$], 1.12 and 1.14 (each 3 H, s, 6-CH_3), 2.05 (3 H, s, $COCH_3$), 2.20 and 2.39 (each 1 H, m, 1'-H), 3.08 and 3.1 (each 1 H, d, *J* 12, 7-H), 3.37 and 3.45 (each 1 H, m, 2'-H), 3.82 (3 H, s, OCH_3), 4.22 (2 H, d, *J* 5, 1-H_2), 4.35 (2 H, s, CH_2Ar), 4.45 (1 H, d, *J* 3, 5-H), 4.92 (1 H, d, *J* 3, 4-H), 5.82 (1 H, t, *J* 5, 2-H), 6.8 (2 H, m, ArH), 7.15 - 7.45 (13 H, m, ArH) and 7.7 (4 H, m, ArH); *m/z* (C.I.) 858 (M^++ 18, 50%).

(4S,5R,2E)- And (4R,5R,2E)-3-[2-(p-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-ene-1,4,5-triol **19** *and* **20**

Tetrabutylammonium fluoride (1 M in tetrahydrofuran; 1.03 cm^3, 1.03 mmol) was added dropwise to a solution of the silyl ether **14** (284 mg, 0.36 mmol) in tetrahydrofuran (2 cm^3) at 0 °C. The solution was stirred at room temperature for 3 h and then concentrated under reduced pressure. Chromatography of the residue gave the (4*S*,5*R*,2*E*)-isomer of the *title compound* **19** (154 mg, 97 %), $[\alpha]_D$ -5.20 (*c* 0.05, $CHCl_3$) (Found (M^+ + H, 447.2198. $C_{25}H_{35}O_5S$ requires *M*, 447.2205); υ_{max} /cm^{-1} 3387, 1613, 1585, 1514, 1466, 1439, 1250, 1088, 1034, 824 and 739; δ_H 1.07 and 1.1 (each 3 H, s, 6-CH_3), 2.3 (3 H, br s, 3 x OH), 2.51 (2 H, m, 1'-H_2), 3.05 and 3.17 (each 1 H, d, *J* 12, 7-H), 3.5 (1 H, m, 2'-H), 3.58 (2 H, m, 5-H and 2'-H), 3.78 (3 H, s, OCH_3), 4.06 (3 H, m, 1-H_2 and 4-H), 4.42 (2 H, s, CH_2Ar), 5.78 (1 H, t, *J* 7, 2-H), 6.85 (2 H, m, ArH) and 7.2 - 7.36 (7 H, m, ArH); δ_C 141.9, 138.3, 132.0, 130.2, 129.5, 129.4, 129.3, 126.1, 114.4, 78.6, 77.0, 73.6, 69.4, 58.7, 55.8, 45.8, 39.5, 27.8, 24.2 and 23.9; *m/z* (C.I.) 447 (M^+ + 1, 35 %) and 309 (9).

Similarly the silyl ether **15** gave the (4*R*,5*R*,2*E*)-isomer of the *title compound* **20** (Found (M^+ + H, 447.2197. $C_{25}H_{35}O_5S$ requires *M*, 447.2205); υ_{max} /cm^{-1} 3387, 1613, 1584, 1514, 1249, 1087 and 1035; δ_H 1.1 and 1.12 (each 3 H, s, 6-CH_3), 2.42 and 2.61 (each 1 H, m, 1'-H), 3.04 and 3.16 (each 1 H, d, *J* 12, 7-H), 3.1 (1 H, br s, OH), 3.48 (2 H, m, 2'-H and 5-H), 3.61 (2 H, m, 2'-H and OH), 3.84 (3 H, s, OCH_3), 4.12 (2 H, m, 1-H_2), 4.2 (1 H, br s, 4-H), 4.5 (2 H, s, CH_2Ar), 5.84 (1 H, t, *J* 7, 2-H), 6.9 (2 H, m, ArH) and 7.12 - 7.5 (7 H, m, ArH); *m/z* (C.I.) 447 (M^+ + 1, 80 %).

Acetyl chloride (2 drops) was added to a solution of the triol **20** (10 mg, 0.019 mmol) and 2,2-dimethoxypropane (0.016 cm^3) in dichloromethane (1 cm^3) at 0 °C and the mixture stirred for 20 h. Saturated aqueous sodium carbonate was added, the mixture extracted into dichloromethane, and the extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give *(4R,5R,2E)-4,5-di-O-isopropylidene-3-[2-(p-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-en-1-ol* **22** (9 mg, 45%) after chromatography (Found: M^+ + H, 487.2515. $C_{28}H_{39}O_5S$ requires *M*, 487.2518); υ_{max} /cm^{-1} 3416, 1613, 1585, 1514, 1247, 1172 and 1055; δ_H 0.97 and 1.08 (each 3 H, s, 6-CH_3), 1.3 and 1.35 (each 3 H, s, CH_3), 2.43 (2 H, m, 1'-H and OH), 2.56 (1 H, m, 1'-H'), 2.89 and 3.06 (each 1 H, d, *J* 12, 7-H), 3.55 (2 H, m, 2'-H_2), 3.77 (3 H, s, OCH_3), 3.95 (3 H, m, 1-H_2 and 5-H), 4.24 (1 H, d, *J* 7, 4-H), 4.40 and 4.42 (each 1 H, d, *J* 11 HC*H*Ar), 5.9 (1 H, t, *J* 7, 2-H), 6.85 (2 H, m, ArH) and 7.07 - 7.35 (7 H, m, ArH); *m/z* (C.I.) 487 (M^+ + 1, 60%).

*(4S,5R,2E)-1-*tert*-Butyldiphenylsilyloxy-3-[2-(*p*-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-ene-4,5-diol* **23**

Triethylamine (0.096 cm^3, 0.7 mmol) and 4-dimethylaminopyridine (cat.) were added to the triol **19** (154 mg, 0.35 mmol) in dichloromethane (8 cm^3) at 0 °C followed by *tert*-butyldiphenylsilyl chloride (0.183 cm^3, 0.7 mmol) and the mixture stirred at room temperature for 16 h. Water (1 cm^3) was added, the aqueous phase was extracted with ether (3 x 0.5 cm^3) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ethyl acetate (85:15) gave the *title compound* **23** (210 mg, 89 %), $[\alpha]_D$ +41.92 (*c* 0.25, $CHCl_3$) (Found: M^+ + H, 685.3346. $C_{41}H_{53}O_5SSi$ requires *M*, 685.3383); υ_{max} /cm^{-1} 3421, 3071, 1613, 1586, 1514, 1428, 1362, 1250, 1112, 1088, 1036, 824 and 703; δ_H 1.08 [9 H, s, $SiC(CH_3)_3$], 1.12 and 1.15 (each 3 H, s, CH_3), 2.19 (1 H, d, *J* 3.5, OH), 2.22 - 2.46 (2 H, m, 1'-H_2), 3.12 and 3.23 (each 1 H, d, *J* 12, 7-H), 3.27 and 3.47 (each 1 H, m, 2'-H), 3.56 (1 H, dd, *J* 7.5, 3.5, 5-H), 3.63 (1 H, d, *J* 4, OH), 3.81 (3 H, s, OCH_3), 4.06 (1 H, dd, *J* 7.5, 4, 4-H), 4.24 (2 H, d, *J* 6, 1-H_2), 4.4 (2 H, s, $ArCH_2$), 5.79 (1 H, t, *J* 6, 2-H), 6.85 (2 H, m, ArH), 7.1 - 7.5 (13 H, m, ArH) and 7.69 (4 H, m, ArH); δ_C 139.7, 139.0, 135.8, 133.9, 132.7, 130.3, 129.5, 128.9, 128.0, 125.8, 114.2, 78.2, 76.9, 73.3, 70.0, 60.7, 55.9, 45.8, 39.3, 27.9, 27.4, 23.9, 23.7 and 19.7; *m/z* (C.I.) 685 (M^+ + 1, 0.2 %) and 667 (0.07).

Acetyl chloride (2 drops) was added to a solution of the diol **23** (13 mg, 0.019 mmol) and 2,2-dimethoxypropane (0.013 cm^3) in dichloromethane (1 cm^3) at 0 °C and the mixture stirred for 25 h. Saturated aqueous sodium carbonate was added, the mixture extracted into dichloromethane, and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (9:1) as eluent gave (*4S,5R,2E*)-4,5-di-*O*-isopropylidene-3-[2-(*p*-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthio-1-*tert*-butyldiphenylsilyloxyhept-2-ene **21** (Found: M^+ + H, 725.3746. $C_{44}H_{57}O_5SSi$ requires *M*, 725.3696); δ_H 1.01 [9 H, s, $SiC(CH_3)_3$], 1.04 and 1.07 (each 3 H, s, 6-CH_3), 1.3 and 1.48 (each 3 H, s, CH_3), 2.3 (2 H, m, 1'-H_2), 3.0 and 3.05 (each 1 H, d, *J* 12, 7-H), 3.12 and 3.46 (each 1 H, m, 2'-H), 3.75 (3 H, s, OCH_3), 4.2 (5 H, m, 1-H_2, 5-H and CH_2Ar), 4.5 (1 H, d, *J* 6, 4-H), 5.71 (1 H, t, *J* 7, 2-H), 6.71 (2 H, m, ArH), 7.05 - 7.43 (13 H, m, ArH) and 7.63 (4 H, m, ArH); *m/z* (FAB) 725 (M^+ + 1, 4%) and 667 (7).

*(4S,5R,2E)-4-Acetoxy-1-*tert*-butyldiphenylsilyloxy-3-[2-(p-methoxybenzyloxy)ethyl]-6,6-dimethyl-7-phenylthiohept-2-en-5-ol* **24**

Pyridine (0.025 cm^3, 0.307 mmol), 4-dimethylaminopyridine (trace) and acetic anhydride (0.029 cm^3, 0.307 mmol) were added to a solution of the diol **23** (210 mg, 0.307 mmol) in dichloromethane (8 cm^3) at 0 °C and the mixture stirred at room temperature for 10 min, then heated under reflux for 24 h. The mixture was cooled and poured into saturated aqueous ammonium chloride (2 cm^3). The aqueous phase was extracted with dichloromethane (3 x 2 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (85:15) as eluent gave the *title compound* **24** (110 mg, 50 % yield), $[\alpha]_D$ + 7.43 (*c* 0.175, $CHCl_3$) (Found: M^+ + H, 727.3461. $C_{43}H_{55}O_6SSi$ requires *M*, 727.3489); υ_{max} /cm^{-1} 3426, 1741, 1613, 1586, 1514, 1428, 1369, 1235, 1112, 1035, 824, 740, 703 ; δ_H 0.98 (3 H, s, 6-CH_3), 1.02 [12 H, s, $SiC(CH_3)_3$ and 6-CH_3'], 1.95 (3 H, s, CH_3CO), 2.2 (2 H, m, 1'-H_2), 2.91 (1 H, d, *J* 12, 7-H), 3.08 (1H, br s, OH), 3.14 (1 H, d, *J* 12, 7-H), 3.34 (2 H, t, *J* 6.5, 2'-H_2), 3.7 (1 H, d, *J* 8.5, 5-H), 3.74 (3 H, s, OCH_3), 4.21 (2 H, d, *J* 6, 1-H_2), 4.27 (2 H, s, $ArCH_2$), 5.19 (1 H, d, *J* 8.5, 4-H), 5.87 (1 H, t, *J* 6, 2-H), 6.77 (2 H, m, ArH), 7.09 - 7.41 (13 H, m, ArH) and 7.3 (4 H, m, ArH); δ_C 169.8, 138.8, 136.1, 136.0,

134.7, 130.2, 130.0, 129.4, 129.3, 128.2, 125.9, 114.2, 78.5, 74.4, 73.2, 69.1, 61.0, 55.7, 45.7, 39.9, 28.7, 27.3, 24.3, 23.0, 21.9 and 19.8; *m/z* (FAB) 727 (M^+ + 1, 1.5 %), 667 (2.2) and 545 (14).

*(4S,5E)-4-Acetoxy-7-*tert*-butyldiphenylsilyloxy-5-[2-(*p*-methoxybenzyloxy)ethyl]-2,2-dimethyl-1-phenylthio-hept-5-en-3-one* **25**

Powered 4A molecular sieves (70 mg) and pyridinium dichromate (158 mg, 0.42 mmol) were added to a solution of the alcohol **24** (150 mg, 0.21 mmol) in dichloromethane (5 cm^3) at 0 °C. After stirring at room temperature for 24 h, the reaction mixture was filtered through celite with dichloromethane washings. The filtrate was concentrated under reduced pressure and chromatography of the residue using light petroleum/ether (70:30) as eluent gave the *title compound* **25** (114 mg, 76 %), $[\alpha]_D$ + 115.69 (*c* 0.85, $CHCl_3$) (Found: M^+ + H, 725.3314. $C_{43}H_{53}O_6SSi$ requires *M*, 725.3332); υ_{max} /cm^{-1} 1742, 1713, 1612, 1585, 1514, 1467, 1439, 1428, 1234, 1112, 824, 740, 703 and 691; δ_H 1.05 [9 H, s, $SiC(CH_3)_3$], 1.32 and 1.36 (each 3 H, s, 2-CH_3), 2.1 (3 H, s, CH_3CO), 2.3 (2 H, m, 1'-H_2), 3.19 and 3.29 (each 1 H, d, *J* 12, 1-H), 3.4 (2 H, m, 2'-H_2), 3.8 (3 H, s OCH_3), 4.32 (2 H, s, $ArCH_2$), 4.33 (2 H, d, *J* 6, 7-H_2), 5.84 (1 H, s, 4-H), 5.92 (1 H, t, *J* 6, 6-H), 6.83 (2 H, m, ArH), 7.13 - 7.58 (13 H, m, ArH) and 7.68 (4 H, m, ArH); δ_C 208.4, 170.5, 137.8, 136.0, 133.3, 130.7, 130.2, 130.0, 129.6, 129.4, 128.8, 128.2, 126.5, 114.2, 79.5, 72.9, 69.1, 61.1, 55.8, 49.1, 44.6, 29.6, 27.2, 25.5, 24.4, 21.0 and 19.5; *m/z* (FAB) 726 (1.5), 725 (M^+ + 1, 1 %), 668 (2) and 667 (2).

*(3S,1'E)-3-Acetoxy-4-(2-*tert*-butyldiphenylsilyloxyethylidene)-2-methoxy-2-(1,1-dimethyl-2-phenylthioethyl)-tetrahydropyran* **27**

A solution of the *p*-methoxybenzyl ether **25** (240 mg, 0.332 mmol) and dichlorodicyanoquinone (92 mg, 0.4 mmol) in dichloromethane (6 cm^3) and water (0.3 cm^3) was stirred at room temperature for 1 h then poured into saturated aqueous sodium bicarbonate and extracted with dichloromethane (3 x 3 cm^3). The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford the hydroxyketone **26** (190 mg) which was used immediately. Toluene *p*-sulphonic acid (trace) and trimethyl orthoformate (0.11 cm^3, 1 mmol) were added to a solution of the hydroxyketone **26** (180 mg) in methanol (10 cm^3) at room temperature. The mixture was stirred for 5 h then saturated aqueous sodium bicarbonate was added. The mixture was concentrated under reduced pressure and the aqueous residue extracted with dichloromethane (4 x 5 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (90:10) as eluent gave the *title compound* **27** (85 mg, 42 % from alcohol **25**, $[\alpha]_D$ +4.35 (*c* 0.25, $CHCl_3$) (Found: M^+, 618.2835. $C_{36}H_{46}O_5SSi$ requires *M*, 618.2835); υ_{max} /cm^{-1} 1742, 1584, 1474, 1428, 1233, 1112, 1082, 824, 739 and 703; δ_H 1.05 [9 H, s, $SiC(CH_3)_3$], 1.16 and 1.43 (each 3 H, s, 1'-CH_3), 2.08 (1 H, m, 5-H), 2.1 (3 H, s, CH_3CO), 2.25 (1 H, m, 5-H'), 3.13 (2 H, s, 2'-H_2), 3.41 (3 H, s, OCH_3), 3.51 (1 H, dt, *J* 11, 2.5, 6-H), 3.74 (1 H, dd, *J* 11 and 5, 6-H'), 4.21 (2 H, m, 2"-H_2), 5.45 (1 H, t, *J* 6, 1"-H), 5.52 (1 H, s, 3-H), 7.08 - 7.42 (11 H, m, ArH) and 7.45 (4 H, m, ArH); δ_C 169.9, 139.1, 136.0, 135.1, 133.3, 130.1, 129.7, 129.3, 128.2, 126.2, 123.2, 102.9, 74.9, 62.5, 60.6, 52.2, 45.2, 44.5, 28.6, 27.3, 24.2, 24.1, 21.8 and 19.9; *m/z* (FAB) 618 (M^+, 0.16 %), 587 (0.8) and 527 (3.7).

Methyl (5R,6R)-5-hydroxy-6-(p-methoxybenzyloxy)-3-oxoheptanoate **29**

A solution of the aldehyde **28** (7.80 g, 40 mmol) in dichloromethane (40 cm^3) was added dropwise to a mechanically stirred, cooled (bath temperature -100 °C) solution of redistilled tin(IV) chloride (10.6 g, 40 mmol)

in dichloromethane (600 cm^3) at such a rate as to maintain the temperature below -95 °C. The mixture was stirred for 10 min at -100 °C then the bis-trimethylsilyl enol ether of methyl acetoacetate (20.3 g, 72 mmol) was added dropwise at such a rate so as to maintain the temperature below -90 °C. The mixture was stirred for a further 30 min at -100 °C, water (100 cm^3) was added and the mixture stirred for 30 min at ambient temperature. The organic layer was extracted with aqueous hydrogen chloride (1 M; 2 x 100 cm^3) and the aqueous washings extracted with dichloromethane (2 x 100 cm^3). The organic extracts washed with saturated aqueous sodium bicabonate (2 x 100 cm^3) and dried ($MgSO_4$) then concentrated under reduced pressure. Chromatography using light petroleum/ether as eluent (4:1 → 1:2) gave the *title compound* **29** (6.5 g, 52 %); υ_{max} /cm^{-1} 3470, 1746, 1715, 1613, 1514, 1249, 1175, 1077 and 1033; δ_H 1.17 (3 H, d, *J* 6.5, 7-H_3), 2.67 (2 H, m, 4-H_2), 3.45 (3 H, m, 2-H_2 and 5-H), 3.71 and 3.79 (each 3 H, s, OCH_3), 3.97 (1 H, quin, *J* 6, 6-H), 4.33 and 4.56 (each 1 H, d, *J* 11.5, HC*H*Ar), 6.87 and 7.21 (each 2 H, m, ArH); δ_C (C_6D_6) 202.2, 167.6, 159.7, 131.0, 129.6, 114.1, 76.7, 70.8, 70.6, 54.9, 51.8, 49.8, 45.9 and 15.0; *m/z* (C.I.) 328 (0.1 %), 296 (1), 241 (1) and 121 (100).

Methyl (3R,5R,6R)-3,5-dihydroxy-6-(p-methoxybenzyloxy)heptanoate **30**

Glacial acetic acid (50 cm^3) was added dropwise to a suspension of tetramethylammonium triacetoxyborohydride (20 g, 76 mmol) in acetonitrile (150 cm^3) and the mixture stirred at ambient temperature for 30 min then cooled to -40 °C. A solution of the ketoester **29** (4.7 g, 15.2 mmol) in acetonitrile (40 cm^3) was added dropwise at such a rate as to maintain the temperature below -30 °C. The mixture was stirred at -40 °C for 24 h then concentrated under reduced pressure. The excess of acetic acid was removed under high vacuum to yield a viscous white suspension which was diluted with water (100 cm^3; effervescence). Sodium bicarbonate (40 g) was added and the mixture diluted with water (300 cm^3) and extracted with dichloromethane (5 x 100 cm^3). The organic extracts were dried Na_2SO_4) and concentrated under reduced pressure. The residue was diluted with ether (3 cm^3), shaken vigorously and allowed to stand for 2.5 h at ambient temperature. The resultant pale yellow solid was repeatedly triturated with a light petroleum/ether mixture (1:1; 5 x 10 cm^3) to yield a white microcrystalline solid which was dried under vacuum (3.64 g). A second crop of diol was obtained by removal of the solvents from the trituration washings and purification of the resultant yellow oil by chromatography using light petroleum/ether (3:1) as eluent. The combined yield of the *title compound* **30** was 3.9 g, 82 %; υ_{max} /cm^{-1} 3427, 1733, 1613, 1587, 1514, 1249, 1174, 1076, 1035, 911, 823 and 731; δ_H (C_6D_6) 1.06 (3 H, d, *J* 6, 7-H_3), 1.57 (2 H, m, 4-H_2), 2.38 (1 H, dd, *J* 5, 16, 2-H), 2.50 (1 H, dd, *J* 8.5, 16.0, 2-H'), 2.72 (1 H, br s, OH), 3.36 (8 H, m, 3-H, 2 x OCH_3 and OH), 3.89 (1 H, m, 5-H), 4.17 and 4.44 (each 1 H d, *J* 11.5, HC*H*Ar), 4.5 (1 H, m, 6-H) and 6.87 and 7.23 (each 2 H, m, ArH); *m/z* (C.I.), 330 (M^+ + 18, 0.1 %), 313 (M^+ + 1, 0.1), 298 (1) and 121 (100).

Methyl (3R,5R,6R)-3,5-di-O-isopropylidene-6-(p-methoxybenzyloxy)heptanoate **31**

Toluene *p*-sulfonic and (0.1 g, 0.53 mmol) was added to a solution of the diol **30** (1.62 g, 5.19 mmol) in acetone (50 cm^3) and 2,2-dimethoxypropane (25 cm^3). The mixture was stirred for 60 min at ambient temperature, triethylamine (5 cm^3) was added and the mixture concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (4:1) as eluent gave the *title compound* **31** (1.47 g, 79 %), $[\alpha]_D$ +35.8 (c 0.011) (Found: M^+ - C_3H_6O, 294.1468. $C_{16}H_{22}O_5$ requires *M*, 294.1467); υ_{max} /cm^{-1} 1741, 1613, 1514, 1381, 1248, 1225, 1175, 1090, 1036 and 824; δ_H 1.11 (3 H, d, *J* 6.5, 7-H_3), 1.33 and 1.35 (each 3 H, s, CH_3), 1.45 and 1.83 (each 1 H, m, 4-H), 2.41 (1 H, dd, *J* 15.5, 5.5, 2-H), 2.53 (1 H, dd, *J* 15.5, 8, 2-H'), 3.49 (1 H,

quin, *J* 6, 6-H), 3.66 and 3.78 (each 3 H, s, OCH_3), 3.82 (1 H, m, 5-H), 4.26 (1 H, m, 3-H), 4.54 (2 H, br s, OCH_2Ar) and 6.85 and 7.26 (each 2 H, m, ArH); *m/z* (E.I.) 337 (0.1 %), 294 (1), 276 (1) and 121 (100).

*(3*R,5R,6R*)-3,5-Di*-O-*isopropylidene-6-(*p-*methoxybenzyloxy)heptanol* **32**

The ester **31**(1.39 g, 3.9 mmol) in tetrahydrofuran (10 cm^3) was added to a suspension of lithium aluminium hydride (0.19 g, 5 mmol) in tetrahydrofuran (10 cm^3) at 0 °C. The mixture was stirred for 2 h at 0 °C and then water (0.2 cm^3), aqueous sodium hydroxide (15 % w/v; 0.2 cm^3) and water (0.6 cm^3) were added. The white suspension was stirred at ambient temperature for 30 min and filtered through celite with tetrahydrofuran washings (5 x 10 cm^3). The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure to yield the *title compound* **32** (1.15 g, 91 %) a sample of which was chromatographed using ether/light petroleum (2:1) as eluent (Found: M^+- C_3H_6O, 266.1523 requires *M*, 266.1518); υ_{max} /cm^{-1} 3398, 1613, 1513, 1380, 1247, 1226 and 1036; δ_H 1.12 (3 H, d, *J* 6.5, 7-H_3), 1.36 and 1.38 (each 3 H, s, CH_3), 1.50 (1 H, ddd, *J* 6.5, 10, 13, 4-H), 1.76 (3 H, m, 2-H_2, 4-H), 2.50 (1 H, br s, OH), 3.49 (1 H, quin, *J* 6, 6-H), 3.74 (2 H, br t, *J* 6, 1-H_2), 3.79 (3 H, s, OCH_3), 3.85 (1 H, dt, *J* 10, 6, 5-H), 4.02 (1 H, m, 3-H), 4.53 and 4.55 (each 1 H, d, *J* 12, HCHAr), 6.85 and 7.26 (each 2 H, m, ArH); *m/z* (C.I.) 342 (M^+ + 18, 1 %), 325 (4), 205 (11) and 121 (100).

*(3*R,5R,6R*)-3,5-Di*-O-*isopropylidene-6-(*p-*methoxybenzyloxy)heptanal* **33**

A solution of dimethylsulfoxide (0.11 cm^3, 1.49 mmol) in dichloromethane (1.5 cm^3) was added to a solution of oxalyl chloride (0.065 cm^3, 0.75 mmol) in dichloromethane (2.0 cm^3) at -70 °C. The mixture was stirred for 30 min at -70 °C and a solution of the alcohol **32** (0.18 g, 0.55 mmol) in dichloromethane (2 cm^3) was added. The mixture was stirred for 10 min at -78 °C and then triethylamine (0.6 cm^3) was added. The mixture was stirred for 5 min at -78 °C and 10 mins at ambient temperature, then diluted with saturated aqueous ammonium chloride (15 cm^3) and extracted with dichloromethane (3 x 10 cm^3). The organic washings were dried and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **33** (0.15 g, 84 %) (Found: M^+ 322.1773. $C_{18}H_{26}O_5$ requires *M*, 322.1780); υ_{max} /cm^{-1} 1727, 1613, 1514, 1380, 1248, 1173, 1103 and 1035; δ_H 1.12 (3 H, d, *J* 6.5, 7-H_3), 1.35 and 1.37 (each 3 H, s, CH_3), 1.48 (1 H, ddd, *J* 6.5, 10, 13, 4-H), 1.88 (1 H, ddd, *J* 6, 10, 13, 4-H'), 2.48 (1 H, ddd, *J* 2, 8, 16.5, 2-H), 2.61 (1 H, ddd, *J* 2.5, 8.5, 16.5, 2-H'), 3.50 (1 H, quin, *J* 6.5, 6-H), 3.79 (3 H, s, OCH_3), 3.85 (1 H, dt, *J* 10, 6, 5-H), 4.32 (1 H, m, 3-H), 4.51 and 4.59 (each 1 H, d, *J* 11, HC*H*Ar), 6.85 and 7.25 (each 2 H, m, ArH) and 9.73 (1 H, t, *J* 2, 1-H); *m/z* (E.I.) 323 (M^+ + 1, 0.5%), 322 (M^+, 2.5). 220 (35) and 121 (100).

*(4*R,6R*)-4-*tert-*Butyldimethylsilyloxy-6-[(*R*)-1-(*p-*methoxybenzyloxy)ethyl]-2-oxo-1-oxacyclohexanone* **37**

Aqueous sodium hydroxide (0.5 M; 12.0 cm^3, 6.0 mmol) was added to a solution of the dihydroxyester **30** (1.56 g, 5.0 mmol) in tetrahydrofuran (20 cm^3) at 0 °C. The mixture was stirred at ambient temperature for 5 min, cooled to 0 °C and acidified to pH 3.5 by the dropwise addition of aqueous hydrogen chloride (1.0 M). The mixture was diluted with brine (50 cm^3) and extracted with dichloromethane (5 x 40 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dissolved in benzene (15 cm^3) and the solution heated under reflux using a Dean-Stark trap for 15 h. Concentration under reduced pressure gave the hydroxylactone **37** (1.40 g) which was used immediately. *tert*-Butyldimethylsilyl chloride (1.12 g, 7.4 mmol) was added to a solution of imidazole (0.89 g, 13.1 mmol) in *N,N*-dimethylformamide (2.0 cm^3) at 0 °C. The mixture was stirred for 10 min at 0 °C and a solution of the lactone **37** (1.22 g, 4.4 mmol) in dry *N,N*-

dimethylformamide (1.0 cm^3) was added and the mixture stirred at room temperature for 20 h. The suspension was diluted with ethyl acetate (50 cm^3) and extracted with aqueous hydrogen chloride (1 M; 2 x 10 cm^3) and brine (3 x 10 cm^3). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **38** (74 %); υ_{max} /cm^{-1} 1741, 1613, 1515, 1250, 1173, 1083, 891, 837 and 779; δ_H (C_6D_6) 0.0 [6 H, s, $Si(CH_3)_2$], 0.96 [9 H, s, $SiC(CH_3)_3$], 1.10 (3 H, d, *J* 6.5, 2'-H_3), 1.61 (1 H, ddd, *J* 9.5, 12, 13.5, 5-H_{ax}), 1.86 (1 H, dddd, *J* 1.5, 3.5, 5, 13.5, 5-H_{eq}), 2.31 (1 H, dd, *J* 8, 17, 3-H_{ax}), 2.58 (1 H, ddd, *J* 1.5, 6, 17, 3-H_{eq}), 3.38 (3 H, s, OCH_3), 3.53 (1 H, dq, *J* 5, 6.5, 1'-H), 3.71 (1 H, m, 4-H), 3.84 (1 H, ddd, *J* 3.5, 5, 12, 6-H), 4.34 and 4.50 (each 1 H, d, *J* 11.5, HC*H*Ar) and 6.87 and 7.26 (each 2 H, m, ArH); δ_C (C_6D_6), 168.6, 159.8, 131.0, 129.5, 114.1, 78.1, 74.9, 71.3, 65.0, 54.8, 40.7, 33.7, 25.8, 18.0, 14.7, -4.7 and -4.8; *m/z* (C.I.) 412 (M^+ + 18, 39 %), 393 (18), 241 (81) and 121 (100).

N-*Methyl*-N-*methoxy (3*R,*5*R,*6*R)-*3*-tert-*butyldimethylsilyloxy-6-(*p-*methoxybenzyloxy)-5-(2-trimethylsilylethoxy)methoxyheptanamide* **40**

Trimethylaluminium (2 M in hexane; 2.0 cm^3, 40 mmol) was added to a suspension of *N,O*-dimethylhydroxylamine hydrochloride (0.38 g, 3.86 mmol) in benzene (3.5 cm^3) at 0 °C. The mixture was stirred at ambient temperature for 2 h, and the lactone **38** (0.73 g, 1.84 mmol) in benzene (3.0 cm^3) was added dropwise. The mixture was stirred for 60 min at ambient temperature and then cooled to 0 °C. Aqueous hydrogen chloride (0.5 M, 4.0 cm^3) was added (effervescence) and the mixture stirred for 10 min at 0 °C then diluted with ethyl acetate (10 cm^3) and filtered through celite with ethyl acetate washings (5 x 20 cm^3). The organic extracts were washed with brine (10 cm^3) and saturated aqueous sodium bicarbonate (10 cm^3) and dried ($MgSO_4$). Concentration under reduced pressure gave the hydroxyamide **39** (0.83 g, 1.82 mmol, 99 %). (2-Trimethylsilylethoxy)methyl chloride (0.7 cm^3, 4.0 mmol) was added to the hydroxyamide (0.83 g, 1.82 mmol) in di-isopropylethylamine (1.3 cm^3, 7.5 mmol) and dichloromethane (2 cm^3) at 0 °C. The mixture was stirred at ambient temperature for 15 h then aqueous hydrogen chloride (1 M; 3 cm^3) was added. The mixture was diluted with ethyl acetate (100 cm^3) and extracted with brine (5 cm^3), aqueous hydrogen chloride (1 M; 2 x 5 cm^3), brine (5 cm^3), saturated aqueous sodium bicarbonate (5 cm^3) and brine (5 cm^3). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (1.5:1) as eluent gave the *title compound* **40** (0.92 g, 85 %); υ_{max} /cm^{-1} 1665, 1613, 1514, 1249, 1033 and 836; δ_H 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 and 0.11 (each 3 H, s, $SiCH_3$), 0.98 - 0.81 [11 H, m, CH_2Si and $SiC(CH_3)_3$], 1.13 (3 H, d, *J* 6.5, 7-H_3), 1.64 (1 H, ddd, *J* 5, 8.5, 14, 4-H), 1.84 (1 H, ddd, *J* 3, 7.5, 14, 4-H'), 2.49 (1 H, dd, *J* 6, 15, 2-H), 2.75 (1 H, dd, *J* 7, 15, 2-H'), 3.16 (3 H, s, NCH_3), 3.5 - 3.8 (8 H, m, 3-H, 5-H, and 2 x OCH_3), 4.38 (1 H, m, 6-H), 4.49 (2 H, s, OCH_2O), 4.73 (2 H, s, OCH_2Ar) and 6.85 and 7.25 (each 2 H, m, ArH); δ_C (C_6D_6) 172.2, 159.6, 131.6, 129.2, 114.0, 95.7, 77.6, 75.7, 70.8, 66.1, 65.6, 60.7, 54.7, 41.3, 38.6, 31.7, 26.3, 18.4, 18.3, 14.4, -1.3, -4.0 and -4.3; *m/z* (C.I.) 586 (M^+ + 1, 1.5 %), 348 (14) and 121 (100).

*(3*R,*5*R,*6*R)-*3*-tert-*Butyldimethylsilyloxy-6-(*p-*methoxybenzyloxy)-5-(2-trimethylsilylethoxy)methoxyheptanal* **41**

Diisobutylaluminium hydride (1 M in hexane; 1.9 cm^3, 1.9 mmol) was added dropwise over 5 min to the amide **40** (0.55 g, 0.93 mmol) in dichloromethane (7 cm^3) at -78 °C. The mixture was stirred for 60 min at -78 °C, methanol (1 cm^3) was added dropwise and the mixture stirred at -78 °C for 5 min. Saturated aqueous ammonium chloride (2 cm^3) was added and the mixture stirred at ambient temperature for 30 min. The resultant suspension

was diluted with ethyl acetate (10 cm^3) and filtered through celite with copious washings of ethyl acetate (5 x 10 cm^3). The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (4:1) gave the *title compound* **41** (0.46 g, 94 %); υ_{max} /cm^{-1} 1727, 1613, 1587, 1514, 1250, 1034, 837 and 777; δ_H (C_6D_6) 0.08 [9 H, s, $Si(CH_3)_3$], 0.19 and 0.23 (each 3 H, s, $SiCH_3$), 1.10 [11 H, m, $SiCH_2$, $SiC(CH_3)_3$], 1.29 (3 H, d, *J* 6.5, 7-H_3), 1.79 (1 H, ddd, *J* 5, 9, 14, 4-H), 2.13 (1 H, ddd, *J* 3, 7.5, 14, 4-H'), 2.45 (2 H, m, 2-H_2), 3.39 (3 H, s, OCH_3), 3.7 (2 H, m, OCH_2), 3.87 (1 H, m, 6-H), 3.98 (1 H, m, 3-H), 4.48 and 4.52 (each 1 H, d, *J* 12, HCHAr), 4.54 (1 H, m, 5-H), 4.79 (2 H, s, OCH_2O), 6.91 and 7.34 (each 2 H, m, ArH) and 9.68 (1 H, t, *J* 2, 1-H); δ_C (C_6D_6) 200.1, 159.7, 131.3, 129.3, 114.1, 95.7, 77.4, 75.5, 70.8, 66.5, 65.6, 54.7, 52.2, 38.3, 26.0, 18.3, 18.2, 14.2, -1.4, -4.2 and -4.2.

*(4R,6R,7R)-1-Bromo-4-*tert*-butyldimethylsilyloxy-7-(*p*-methoxybenzyloxy-6-(2-trimethylsilylethoxy)methoxy-oct-1-ene* **42**

Sodium bis(trimethylsilyl)amide (1 M in tetrahydrofuran; 1.9 cm^3, 1.9 mmol) was added dropwise to a suspension of (bromomethyl)triphenylphosphonium bromide (0.76 g, 1.75 mmol) in tetrahydrofuran (10 cm^3) and the mixture stirred for 4 min at ambient temperature and then cooled to -78 °C. A solution of the adehyde **41** (0.61 g, 1.16 mmol) in tetrahydrofuran (5 cm^3) was added dropwise, the cooling bath was removed and the mixture stirred for 40 min allowing the temperature to rise to room temperature. The solution was then diluted with light petroleum (100 cm^3) and filtered through silica gel with copious washings of light petroleum/ether (9:1; 5 x 20 cm^3). After concentration under reduced pressure, chromatography of the residue using light petroleum/ether (15:1) as eluent gave the *title compound* **42** (0.45 g, 65 %); υ_{max} /cm^{-1} 1613, 1587, 1514, 1249, 1103, 1034, 860 and 836; δ_H (C_6D_6) 0.08 [9 H, s, $Si(CH_3)_3$], 0.17 (0.6 H, s, $SiCH_3$), 0.21 (2.4 H, s, $SiCH_3$), 0.22 (0.6 H, s, $SiCH_3$), 0.26 (2.4 H, s, $SiCH_3$), 1.05 [11 H, m, $SiC(CH_3)_3$ and CH_2Si], 1.33 (0.6 H, d, *J* 7, 8-H_3), 1.30 (2.4 H, d *J* 6.5, 8-H_3), 1.80 (0.8 H, ddd, *J* 3.5, 9, 14, 5-H), 2.1 (1.2 H, m, 5-H, 5-H'), 2.55 (2 H, m, 3-H_2), 3.38 (2.4 H, s, OCH_3), and 3.39 (0.6 H, s, OCH_3), 3.6 - 4.3 (5 H, m, 4-H, 6-H, 7-H and OCH_2), 4.52 (2 H, m, OCH_2Ar), 4.84 (2 H, m, OCH_2O), 5.89 (0.2 H, d, *J* 13.5, 1-H_E), 5.99 (0.8 H, d, *J* 7, 1-H_Z), 6.08 (0.8 H, q, *J* 7, 2-H_E), 6.30 (0.2 H, dt, *J* 13.5, 7.5, 2-H_Z) and 6.9 and 7.37 (each 2 H, m, ArH); δ_C (C_6D_6) 159.7, 134.8, 131.5, 131.4, 131.3, 129.3, 129.1, 114.0, 109.6, 106.5, 96.0, 95.7, 77.8, 77.5, 75.7, 70.8, 69.4, 68.9, 65.5, 54.7, 41.7, 38.9, 37.7, 37.6, 26.1, 18.3, 14.4, -1.7, -3.9, -4.2, -4.0 and -4.2; *m/z* (FAB) 603, 602 (M^+, 4, 3 %) and 473, 472 (each 19).

*(4R,6R,7R)-4-*tert*-Butyldimethylsilyloxy-7-(*p*-methoxybenzyloxy)-6-(2-trimethylsilylethoxy)methoxyoct-1-yne* **43**

Butyllithium (1.6 M in hexane, 0.5 cm^3, 0.8 mmol) was added dropwise to the vinyl bromide **42** (0.18 g, 0.30 mmol) in tetrahydrofuran (1.0 cm^3) at 0 °C. The mixture was stirred at 0 °C for 15 mins, water (0.5 cm^3) was added, and the mixture was diluted with brine (2 cm^3) and extracted with ethyl acetate (3 x 5 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (15:1 → 12:1) as eluent gave the *title compound* **43** (0.11 g, 70 %); υ_{max} /cm^{-1} 1612, 1514, 1249, 1100, 1034 and 836; δ_H 0.01 [9 H, s, $Si(CH_3)_3$], 0.11 and 0.10 (each 3 H, s, $SiCH_3$), 0.88 [11 H, m, $SiC(CH_3)_3$, $SiCH_2$), 1.14 (3 H, d, *J* 6.5, 8-H_3), 1.78 (2 H, m, 5-H_2), 1.98 (1 H, t, *J* 2.5, 1-H), 2.37 (2 H, m, 3-H_2), 3.6 (4 H, m, OCH_2, 4-H and 6-H), 3.80 (3 H, s, OCH_3), 4.0 (1 H, m, 7-H), 4.48 (2 H, s, OCH_2Ar),

4.73 (2 H, s, OCH_2O) and 6.85 and 7.26 (each 2 H, m, ArH); δ_C (C_6D_6) 159.6, 131.6, 129.2, 114.0, 96.0, 81.5, 77.7, 75.8, 70.8, 69.0, 65.5, 54.7, 37.6, 30.2, 28.7, 26.1, 18.3, 14.5, -1.4, -4.0 and -4.3.

*Methyl (5R,7R,8R)-5-*tert*-butyldimethylsilyloxy-8-(*p*-methoxybenzyloxy)-7-(2-trimethylsilylethoxy)methoxy-hept-1-ynoate* **44**

tert-Butyllithium (1.6 M in hexane, 0.04 cm^3, 64 mmol) was added dropwise to a solution of the alkyne **43** (0.03 g, 52 mmol) in tetrahydrofuran (0.2 cm^3) at -78 °C and the mixture stirred for 30 min. Methyl chloroformate (0.008 cm^3, 0.1 mmol) was then added and the mixture stirred for 20 hours allowing the temperature to rise to room temperature. The mixture was diluted with ether (10 cm^3) and exracted with brine (2 x 1 cm^3). The ether extract was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum/ether (6:1) as eluent gave the *title compound* **44** (0.02 g, 73 %); υ_{max} /cm^{-1} 2241, 1719, 1614, 1515, 1251, 1100, 1075, 1034 and 837; δ_H (C_6D_6) 0.10 [9 H, s, $Si(CH_3)_3$], 0.28 [6 H, s, $Si(CH_3)_2$], 1.05 [11 H, m, $SiC(CH_3)_3$ and $SiCH_2$), 1.29 (3 H, d, *J* 6.5, 9-H_3), 1.90 (1 H, ddd, *J* 4, 9, 14, 6-H), 2.12 (1 H, ddd, *J* 2.5, 8, 14, 6-H'), 2.4 (2 H, m, 4-H_2), 3.32 and 3.40 (each 3 H, s, OCH_3), 3.72 (2 H, m, OCH_2), 3.84 (1 H, dq, *J* 5, 6.5, 8-H), 4.0 and 4.24 (each 1 H, m), 4.5 and 4.51 (each 1 H, d, *J* 12, HC*H*Ar), 4.79 and 4.80 (each 1 H, d, *J* 7, OHC*H*O) and 6.9 and 7.36 (each 2 H, m, ArH); δ_C 159.1, 154.1, 130.9, 129.2, 113.7, 95.6, 86.8, 75.5, 74.5, 70.7, 67.9, 65.5, 55.3, 52.5, 37.7, 28.5, 25.8, 18.1, 18.0, 14.5, -1.5, -4.2 and -4.5.

*Methyl (5R,7R,8R,2E)-5-*tert*-butyldimethylsilyloxy-8-(*p*-methoxybenzyloxy)-3-tributylstannyl-7-(2-trimethyl-silylethoxy)methoxyhept-2-enoate* **45**

Butyllithium (1.6 M in hexane; 0.18 cm^3, 0.29 mmol) was added to a solution of diisopropylamine (0.04 cm^3, 0.29 mmol) in tetrahydrofuran (0.5 cm^3) at 0 °C and the mixture stirred for 10 min. Tributyltin hydride (0.08 cm^3, 0.3 mmol) was added dropwise and the mixture stirred at 0 °C for 15 min. The mixture was cooled to -50 °C and copper (I) bromide dimethyl-sulphide (0.06 g, 0.30 mmol) was added in several small portions. The dark green solution was then stirred at -50 °C for 20 min and cooled to -78 °C. A solution of the alkyne **44** (0.056 g, 97 mmol) in tetrahydrofuran (0.4 cm^3) was added and the mixture stirred at -78 °C for 3 h. Methanol (0.3 cm^3) was added dropwise and the mixture stirred at -78 °C for a further 10 min and then at ambient temperature for 30 min. Water (2 cm^3) was added and the mixture filtered through celite with copious ethyl acetate washings (5 x 5 cm^3). The filtrate was washed with brine (5 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **45** (0.064 g, 84 %); δ_H (C_6D_6) 0.08 [9 H, s, $Si(CH_3)_3$], 0.44 and 0.45 (each 3 H, s, $SiCH_3$), 0.99 - 1.75 (38 H, m), 1.93 (1 H, ddd, *J* 2, 10, 14, 6-H), 2.24 (1 H, dd, *J* 10, 13, 6-H'), 3.39 and 3.45 (each 3 H, s, OCH_3), 3.6 (2 H, m, OCH_2), 3.83 (2 H, m, 4-H_2), 4.09 (1 H, dq *J* 4.5, 6, 8-H), 4.35 (1 H, dd *J* 4.5, 9, 7-H), 4.55 (1 H, m, 5-H), 4.61 and 4.64 (each 1 H, d, *J* 12, HC*H*Ar), 5.02 and 4.91 (each 1 H, d, *J* 7, OHC*H*O), 6.45 (1 H, d, *J* 0.7, 2-H) and 6.91 and 7.41 (each 2 H, m, ArH); δ_C (C_6D_6) 169.2, 164.0, 159.6, 131.7, 130.6, 129.2, 114.0, 96.5, 77.5, 75.5, 70.7, 70.1, 65.5, 54.7, 50.5, 44.6, 37.4, 29.4, 27.8, 26.4, 18.5, 18.3, 14.5, 13.8, 10.6, -1.4, -2.8 and -4.0.

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