An approach to the C(17)–C(24) fragment of bryostatins: applications of stereoselective trisubstituted alkene formation by palladium(0) catalysed coupling of enol acetates and vinylic bromides

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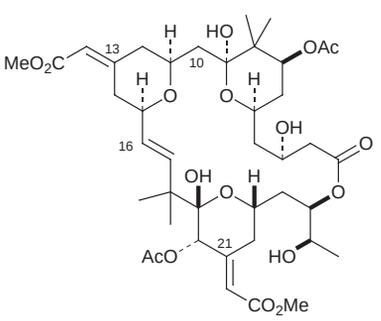
The enol acetate 26 couples stereospecifically with the vinylic bromides 25 and 29 in the presence of tributyltin methoxide and a catalytic amount of dichlorobis(tri-*o*-tolylphosphine)palladium to give the βγ-unsaturated ketones 27 and 30 with retention of double-bond position and geometry. The βγ-unsaturated ketone 42 which has stereochemistry and functionality corresponding to the C(17)–C(24) fragment of the C(20)-deoxybryostatins, is similarly prepared from the enol acetate 26 and the vinylic bromide 41 and can be deprotected to give the hydroxyketone 43.

The bryostatins are natural products isolated from invertebrate filter feeders which display potent antineoplastic activity.[1] Because of this biological activity, they have been the focus of considerable synthetic work to date[2] including a total synthesis of bryostatin 7 **1**.[3] Any stereoselective synthesis of a bryostatin



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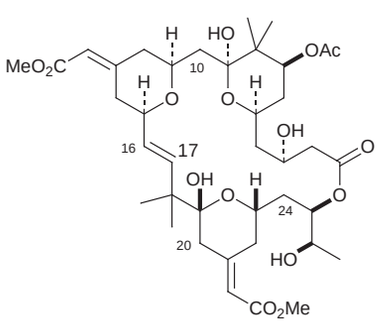

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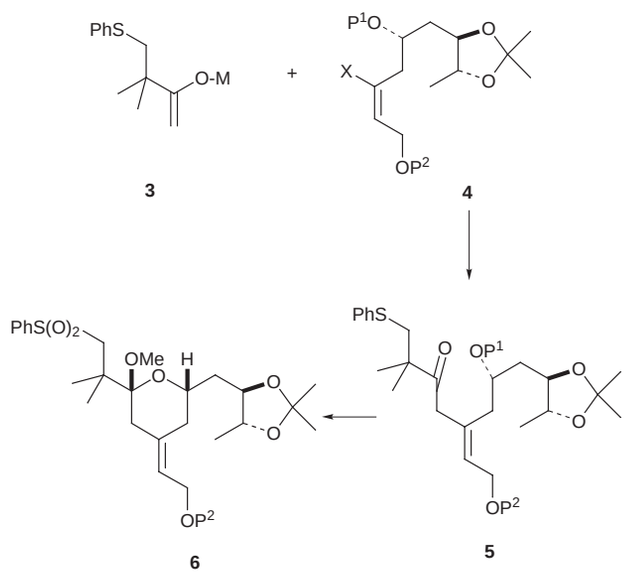
must include procedures for the stereocontrol of the trisubstituted exocyclic double-bonds at C(13) and C(21).[2] In the preceding paper[4] we report a method for the stereoselective synthesis of 2,6-*cis*-disubstituted 4-(methoxycarbonylmethylene)tetrahydropyrans which map onto the C(10)–C(16) fragment of the bryostatins. We now describe a synthesis of the C(17)–C(24) fragment of 20-deoxybryostatins, *e.g.* bryostatin 11 **2**, which makes use of a stereospecific palladium(0) catalysed coupling of a vinylic bromide with a tin enolate which is generated *in situ* from the corresponding enol acetate using tributyltin methoxide. This chemistry is complementary to the reported approach to this fragment of 20-deoxybryostatins which is based upon an epoxide ring-opening sequence.[5]

The synthetic equivalent of coupling an enolate **3** with a suitably functionalised alkene **4** was identified as a possible approach to the trisubstituted alkene **5** which has functionality and stereochemistry corresponding to the C(17)–C(24) fragment of the 20-deoxybryostatins. Ketone protection and oxidation of the sulfide should then provide a sulfone, *e.g.* **6**, for incorporation into a synthesis of a bryostatin using Julia a olefination.[3]

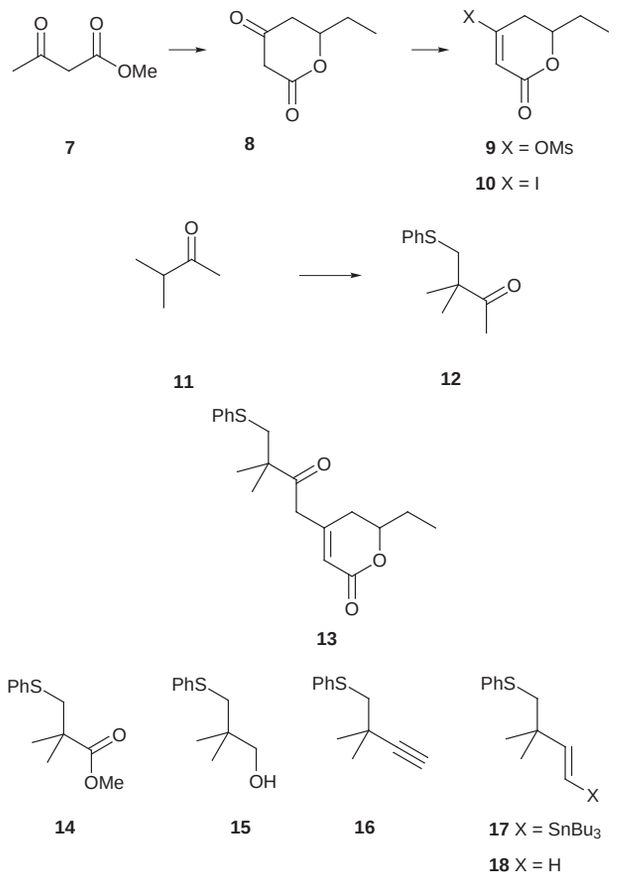


3 **4** **6** **5**

(P^1, P^2 = protecting groups)

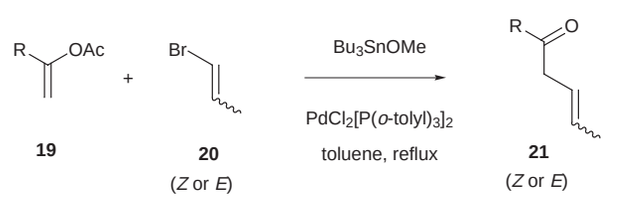
Results and discussion

During preliminary studies, the ketolactone **8** was prepared from methyl acetoacetate **7**[6] and converted into the mesylate **9** and iodide **10**.[7] The ketone **12** was prepared by regioselective alkylation of 3-methylbutan-2-one **11**.[8] However, all attempts to prepare the ketone **13** by condensation of either the mesylate **9** or iodide **10** with an enolate **3** (M = Na, Li) generated from the ketone **12** were unsuccessful with the lactones generally being recovered unchanged. Similar results were obtained with enamines and enol ethers prepared from the ketone **12**. In order to see whether a Stille reaction could be used to prepare a precursor of the ketone **13**, the ester **14** was converted *via* the alcohol **15** into the alkyne **16**.[9] However, although the vinyl stannane **17** could be detected in the crude product from free-radical hydrostannation of the alkyne, attempts to purify the



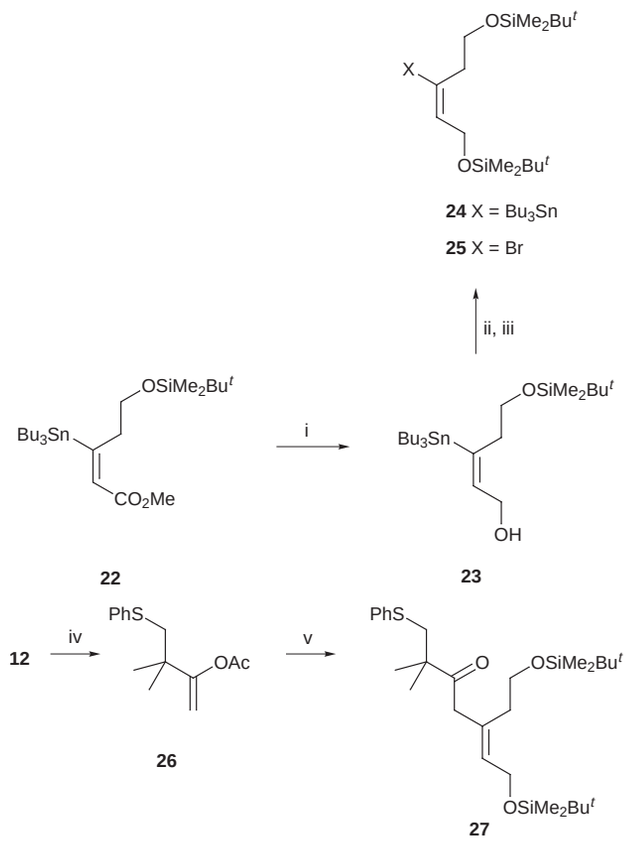
stannane were accompanied by destannylation to the alkene **18**, and the use of impure stannane in a Stille reaction with the iodide **10** was unsuccessful.

As these early investigations were not promising, an alternative approach was conceived based on the palladium(0) catalysed coupling of tin enolates generated *in situ* from enol acetates and vinyl bromides as reported by Migita and co-workers.[10,11] This reaction is known to preserve the geometry of the double-bond derived from the vinyl bromide[10] and leads to the formation of βγ-unsaturated ketones, *e.g.* **21** from the enol acetate **19** and vinyl bromide **20**.

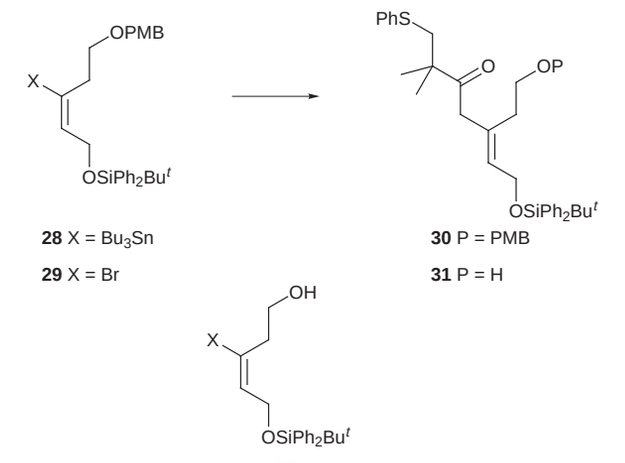


To establish the viability of this approach, the 3-tributylstannylpent-2-enoate **22**[4] was reduced to the alcohol **23** which was converted into the vinylic bromide **25** by *O*-silylation and tin–bromine exchange.[12] The ketone **12** was converted into its enol acetate **26** by acid-catalysed exchange with isopropenyl acetate[13] (Scheme 1). The enol acetate **26** and the vinylic bromide **25** were then coupled by treatment with tributyltin methoxide and a catalytic amount of dichlorobis(tri-*o*-tolylphosphine)palladium[11] in toluene heated to 100 °C. This reaction gave a single product which isolated in a 78% yield and identified as the βγ-unsaturated ketone **27**. This had been formed with complete retention of the position and geometry of the double-bond as expected on the basis of precedent[10] and confirmed using spectroscopic methods, in particular ^{1}H NMR (see Experimental section).

The differentially protected dihydroxypentenyl bromide **29** was prepared from the vinyl stannane **28**[14] by treatment with *N*-bromosuccinimide. In this case, attempted tin–bromine

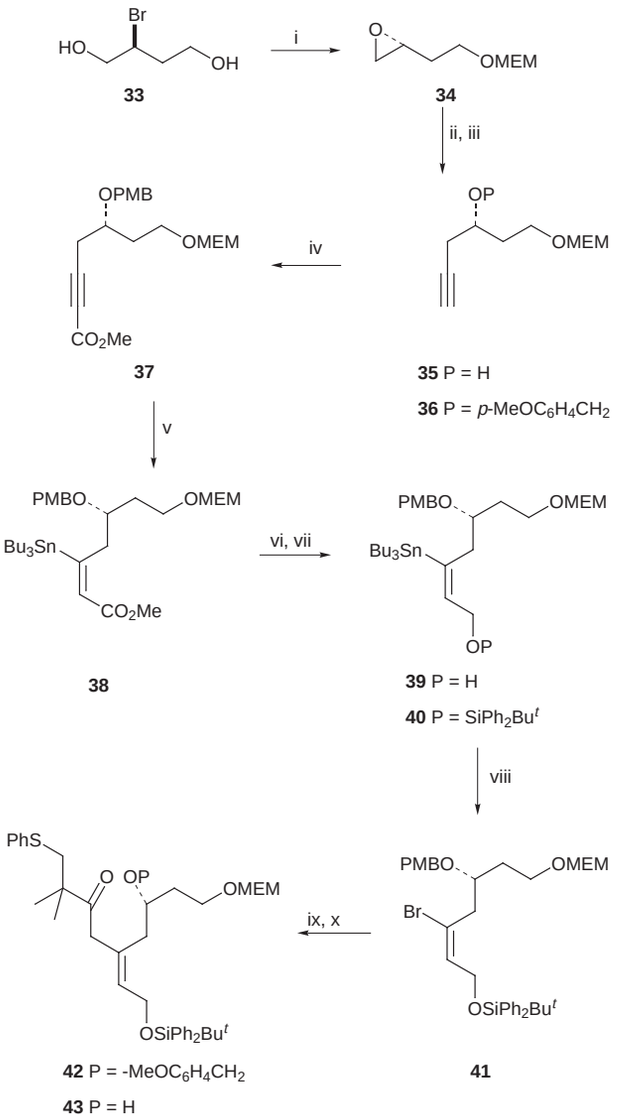


Scheme 1 *Reagents and conditions*: i, diisobutylaluminium hydride, hexane, THF (92%); ii, *tert*-butyldimethylsilyl chloride, imidazole, *N*,*N*-dimethylformamide (87%); iii, bromine, carbon tetrachloride, −20 °C (93%); iv, isopropenyl acetate, toluene-*p*-sulfonic acid (cat.), reflux, 48 h (40–50%); v, **25**, $PdCl_2[P(o\text{-tolyl})_3]_2$, tributyltin methoxide, toluene, 100 °C (78%)



exchange gave mixtures of products including those formed by bromination of the aromatic ring of the *p*-methoxybenzyl group. The use of *N*-bromosuccinimide avoided these side reactions and was more convenient for large-scale reactions. The bromide **29** underwent efficient coupling with the enol acetate **26** to give the unsaturated ketone **30**. The hydroxypentenyl bromide **32** available by selective deprotection of the *p*-methoxybenzyl ether **29** did not participate cleanly in the coupling reaction, although the hydroxyketone **31** could be prepared by selective deprotection of the coupled *p*-methoxybenzyl ether **30**.

The hydroxyketone **31** corresponds to the C(17)–C(22) fragment of the 20-deoxybryostatins and with suitable ketone protection could be incorporated into a bryostatin synthesis. Alternatively, the coupling reaction could be applied to assemble



Scheme 2 *Reagents and conditions*: i, sodium hydride, (methoxyethoxy)-methyl chloride, THF (79%); ii, lithium acetylide–ethylenediamine, dimethyl sulfoxide, THF (70%); iii, sodium hydride, *p*-methoxybenzyl chloride, tetrabutylammonium iodide, *N*,*N*-dimethylformamide, THF, 20 °C, 16 h (71%); iv, butyllithium, methyl chloroformate, 1 h, −75 °C (93%); v, Bu_3SnLi·CuBr, Me_2S, THF, −78 °C, 3 h, then methanol (96%); vi, diisobutylaluminium hydride, hexane; vii, *tert*-butyldiphenylsilyl chloride, imidazole, *N*,*N*-dimethylformamide (80% from **38**); viii, *N*-bromosuccinimide, dichloromethane, 20 °C (93%); ix, **26**, $PdCl_2[P(o\text{-tolyl})_3]_2$, tributyltin methoxide, toluene, 100 °C (81%); x, dichlorodicyanoquinone, dichloromethane, H_2O (83%)

a more advanced intermediate. To this end, (*S*)-2-bromobutane-1,4-diol **33**, which is readily available from L-aspartic acid,[15] was converted into the protected epoxide **34** in one step by treatment with base and (methoxyethoxy)methyl chloride. Ring-opening of the epoxide using lithium acetylide–ethylenediamine complex[16] gave the alkynol **35** which was taken through to the ester **37** by protection and *C*-acylation. Stereoselective addition of the tributyltin moiety following the procedure of Piers[17] gave the (*E*)-vinyl stannane **38** which was converted into the vinylic bromide **41** by reduction, *O*-silylation and tin–bromine exchange using *N*-bromosuccinimide. The coupling of this bromide with the enol acetate **26** under the usual conditions was very efficient and gave the (*E*)-unsaturated ketone **42** in an excellent yield (81%). Finally selective oxidative removal of the *p*-methoxybenzyl group gave the hydroxyketone **43** which corresponds to the C(17)–C(25) fragment of the 20-deoxybryostatins.

Preliminary attempts[18] to convert the hydroxyketone **43** into a cyclic acetal corresponding to **6** and so effect simultaneous protection of the ketone carbonyl and 25-hydroxy group of the bryostatin precursor were unsuccessful. It may be that the carbonyl group is too hindered by the adjacent *gem*-dimethyl substituents for acetalisation to occur under mild conditions. Nevertheless this work has established a viable stereoselective synthesis of the C(17)–C(25) fragment of the 20-deoxybryostatins and has shown that the palladium(0) catalysed coupling of enol acetates and vinylic bromides[10] is a useful reaction for complex syntheses. Future work will study the use of bromides analogous to **4** in the coupling reaction and the completion of a synthesis of a bryostatin.

Experimental

Proton nuclear magnetic resonance spectra were recorded on Bruker AC-300 and Varian Gemini 200 spectrometers. Carbon nuclear magnetic resonance spectra were recorded on a Varian Gemini 200 spectrometer at 50 MHz. Coupling constants are quoted in hertz (Hz). Infrared spectra were recorded on Perkin-Elmer 1710FT and ATI Mattson Genesis FTIR spectrometers as evaporated films. Low resolution chemical ionisation (CI) and electron impact (EI) mass spectra were recorded on a Fisons TRIO 2000 quadrupole mass spectrometer. All high resolution mass spectra were recorded on a Kratos Concept-1S mass spectrometer coupled to a Mach 3 data system. Optical rotations were recorded at ambient temperature on an Optical Activity AA-100 polarimeter at 589 nm using chloroform as the solvent and are given in units of 10^{-1} deg cm^2 g^{-1}.

Flash column chromatography purifications were performed using Merck 60H silica gel (40–63 μ, 230–300 mesh) as the stationary phase. Light petroleum refers to the fraction which distils between 40 and 60 °C and was redistilled prior to use; ether refers to diethyl ether. Tetrahydrofuran (THF) was dried over sodium–benzophenone and distilled under an atmosphere of dry nitrogen. Dichloromethane was dried over calcium hydride and distilled under an atmosphere of dry nitrogen. All other solvents and commercially available reagents were purified following standard procedures.[19] Butyllithium was supplied as a solution in hexanes, and was titrated in THF with a solution of propan-2-ol in xylene in the presence of 2,2′-bipyridyl.

6-Ethyl-4-methylsulfonyloxy-5,6-dihydro-2*H*-pyran-2-one 9

A solution of methyl acetoacetate **7** (4.64 g, 40 mmol) in tetrahydrofuran (10 cm^3) was added dropwise to a suspension of sodium hydride (60% dispersion; 1.76 g, 44 mmol; washed with light petroleum) in tetrahydrofuran (40 cm^3) at 0 °C. After 10 min, butyllithium (1.5 M in hexane; 28 cm^3, 42 mmol) was added and the mixture stirred for 10 min before being cooled to −78 °C. Propanal (1.6 cm^3, 22 mmol) was added and the mixture stirred at −78 °C for 30 min, then poured into water (150 cm^3). Aqueous hydrogen chloride (1.2 M) was added to adjust the pH to 6 and the mixture was extracted with dichloromethane. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the lactone **8** (3.36 g); δ_H(keto-tautomer) 1.06 (3 H, t, *J* 7, CH_3), 1.79 (2 H, m, CH_2CH_3), 2.46 (1 H, dd, *J* 17, 11, 5-H), 2.65 (1 H, dd, *J* 17, 3, 5-H′), 3.43 and 3.57 (each 1 H, d, *J* 19, 3-H) and 4.6 (1 H, m, 6-H); which was used directly.

Potassium carbonate (9.70 g, 70.2 mmol) and methanesulfonyl chloride (1.84 cm^3, 23.6 mmol) were added to a solution of the lactone **8** (3.36 g) in dichloromethane (150 cm^3) and the mixture stirred at room temperature for 2 h before being poured into water (150 cm^3). The organic layer was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (1 : 4) gave the *title compound* **9** (2.06 g, 42% from propanal) (Found: M$^+$, 220.0408. $C_8H_{12}O_5S$ requires *M*, 220.0405); ν_{max}/cm^{-1} 3023, 1716, 1649, 1464, 1372, 1246, 1190, 1119, 1037, 973, 896, 795 and 721; δ_H 1.05 (3 H, t, *J* 7.5, CH_2CH_3), 1.8 (2 H, m, CH_2CH_3), 2.54 (1 H, dd, *J* 18, 5, 5-H), 2.69 (1 H, ddd, *J* 18, 11,

2, 5-H′), 3.26 (3 H, s, CH_3SO_3), 4.44 (1 H, m, 6-H) and 5.98 (1 H, d, *J* 2, 3-CH); δ_C 8.8, 27.0, 31.6, 38.5, 77.2, 104.9, 162.1 and 164.4; *m*/*z* (CI) 238 (M^+ + 18, 80%) and 221 (M^+ + 1, 100).

Tetrabutylammonium iodide (8.72 g, 23 mmol) and boron trifluoride diethyl etherate (1.2 cm^3, 9.35 mmol) were added to a solution of the methanesulfonate **9** (2.06 g, 9.35 mmol) in dichloromethane (50 cm^3) at room temperature and the mixture stirred at room temperature for 1 h then poured into water. The aqueous layer was extracted with dichloromethane and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (2:1) gave the iodide **10** (1.92 g, 81%); δ_H 0.95 (3 H, t, *J* 7.5, CH_2CH_3), 1.68 (2 H, m, CH_2CH_3), 2.76 (2 H, m, 5-H_2), 4.35 (1 H, m, 6-H) and 6.68 (1 H, d, *J* 3, 3-H); δ_C 8.7, 26.6, 42.1, 78.6, 117.3, 130.0 and 160.9.

3,3-Dimethyl-4-phenylthiobutan-2-one 12

Titanium chloride (1 M in dichloromethane; 21 cm^3, 21 mmol) was added dropwise to a solution of 2-methyl-3-trimethylsilyloxybut-2-ene[20] (3.02 g, 19.1 mmol) and chloro(phenylthio)methane (3.61 g, 26.8 mmol) in dichloromethane (25 cm^3) at −25 °C. The red suspension was stirred for 1 h at −25 °C and poured into water (100 cm^3). The mixture was basified using solid sodium carbonate and extracted with dichloromethane. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (95:5) gave the *title compound* **12** (3.58 g, 90%) (Found: C, 69.05; H, 7.95; S, 15.4; M^+, 208.0948. $C_{12}H_{16}OS$ requires C, 69.2; H, 7.75; S, 15.4%; *M*, 208.0922); ν_{max}/cm^{-1} 1706, 1584, 1469, 1439, 1385, 1355, 1109 and 1025; δ_H 1.25 (6 H, s, 2 × 3-CH_3), 2.16 (3 H, s, 1-H_3), 3.16 (2 H, s, 4-H_2) and 7.1–7.4 (5 H, m, ArH); δ_C 24.1, 25.2, 43.8, 48.7, 126.0, 128.7, 129.5, 137.0 and 211.6; *m*/*z* (EI) 208 (M^+, 29%), 165 (22) and 123 (91).

Methyl 2,2-dimethyl-3-phenylthiopropanoate 14

A solution of 1-methoxy-2-methyl-1-trimethylsilyloxypropene[21] (4.27 g, 24.5 mmol), chloro(phenylthio)methane (3.76 g, 29.4 mmol) and anhydrous zinc bromide (55 mg, 0.25 mmol) in dichloromethane (40 cm^3) was stirred at room temperature for 24 h then concentrated under reduced pressure.[8] Chromatography of the residue using light petroleum–ether (95:5) gave the *title compound* **14** (3.69 g, 67%) (Found: M^+, 224.0872. $C_{12}H_{16}O_2S$ requires *M*, 224.0871); ν_{max}/cm^{-1} 1736, 1583, 1472, 1438, 1386, 1302, 1197, 1140 and 742; δ_H 1.29 (6 H, s, 2 × 2-CH_3), 3.18 (2 H, s, 3-H_2), 3.56 (3 H, s, OCH_3) and 7.1–7.4 (5 H, m, ArH); δ_C 21.6, 43.7, 44.6, 51.6, 126.1, 128.7, 129.9, 171.6 and 159.2; *m*/*z* (EI) 225 (M^+ + 1, 4%), 224 (M^+, 30) and 123 (100).

2,2-Dimethyl-3-phenylthiopropanol 15

A solution of the methyl ester **14** (1.50 g, 6.7 mmol) in tetrahydrofuran was added dropwise to a suspension of lithium aluminium hydride (0.30 g, 8.6 mmol) in tetrahydrofuran (10 cm^3), and the resulting mixture was stirred at 0 °C for 2 h. Water (0.4 cm^3), aqueous sodium hydroxide (15%, 0.4 cm^3) and water (1.2 cm^3) were added cautiously and the resulting white mixture was stirred at room temperature for 30 min then filtered through Celite with copious washings with ether. The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (7:3) gave the *title compound* **15** (1.06 g, 81%) (Found: M^+, 196.0923. $C_{11}H_{16}OS$ requires *M*, 196.0922); ν_{max}/cm^{-1} 3379, 1584, 1479, 1439, 1090, 1042, 737, 690 and 666; δ_H 1.03 (6 H, s, 2 × 2-CH_3), 1.51 (1 H, s, OH), 3.00 (2 H, s, 3-H_2), 3.47 (2 H, s, 1-H_2) and 7.1–7.5 (5 H, m, ArH); δ_C 24.0, 36.9, 43.4, 70.2, 125.7, 128.8, 129.0 and 137.6; *m*/*z* (EI) 197 (M^+ + 1, 12%) and 196 (M^+, 100).

3,3-Dimethyl-4-phenylthiobutyne 16

A solution of dimethyl sulfoxide (2.4 cm^3, 33.4 mmol) in dichloromethane (1 cm^3) was added dropwise to a solution of oxalyl chloride (1.51 cm^3, 16.7 mmol) in tetrahydrofuran (33 cm^3) at −78 °C. After 30 min, a solution of the alcohol **15** (1.44 g, 7.3 mmol) in dichloromethane (9 cm^3) was added dropwise followed, after 10 min, by triethylamine (11 cm^3). The mixture was stirred at −78 °C for 10 min then at room temperature for 20 min. Water (20 cm^3) was added and the organic layer washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (95:5) gave 2,2-dimethyl-3-phenylthiopropanal (1.21 g, 85%); ν_{max}/cm^{-1} 1726; δ_H 1.19 (6 H, s, 2 × 2-CH_3), 3.13 (2 H, s, 3-H_2), 7.1–7.4 (5 H, m, ArH) and 9.49 (1 H, s, CHO); δ_C 21.3, 41.8, 47.1, 126.3, 128.9, 129.7, 136.6 and 203.9.

Triphenylphosphine 3.94 g (15.02 mmol) was added portionwise to a solution of carbon tetrabromide (2.49 g, 7.48 mmol) in dichloromethane (30 cm^3) and the mixture was stirred at 0 °C for 1 h. A solution of the aldehyde **15** (0.65 g, 3.32 mmol) in dichloromethane (6 cm^3) was added dropwise and the stirring continued for 30 min before adding the reaction mixture to hexane (100 cm^3) and filtering through Celite. The filtrate was concentrated under reduced pressure and the residue dissolved with hexane (60 cm^3) and filtered again. Concentration of this second filtrate under reduced pressure gave 1,1-dibromo-3,3-dimethyl-4-phenylthiobutene (1.30 g) which was used directly. Butyllithium in hexane (1.6 M; 4.9 cm^3, 7.79 mmol) was added dropwise to a solution of 1,1-dibromo-3,3-dimethyl-4-phenylthiobutene (1.30 g) in tetrahydrofuran (25 cm^3), and the resulting yellow solution stirred at −78 °C for 1 h. The reaction mixture was then warmed to room temperature and stirred for 1 h. Water was added and the mixture extracted with hexane. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (99:1) gave the alkyne **16** (0.50 g, 66% from the alcohol **15**); δ_H 1.36 (6 H, s, 2 × 3-CH_3), 2.18 (1 H, s, 1-H), 3.12 (2 H, s, 4-H_2) and 7.1–7.5 (5 H, m, ArH).

(*E*)-5-*tert*-Butyldimethylsilyloxy-3-tributylstannylpent-2-en-1-ol 23

Diisobutylaluminium hydride (1 M in hexanes; 31 cm^3, 31 mmol) was added dropwise to a solution of the ester **22**[4] (5.40 g, 10.1 mmol) in tetrahydrofuran (50 cm^3) at −78 °C. The mixture was stirred for 90 min at −78 °C then methanol (3.0 cm^3) was added. The mixture was stirred for 5 min at −78 °C, saturated aqueous ammonium chloride solution (10 cm^3) was added and the mixture stirred at 0 °C for 30 min. The resultant suspension was diluted with ethyl acetate (50 cm^3) and filtered through Celite with copious ethyl acetate washes (5 × 50 cm^3). The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **23** (4.68 g, 9.3 mmol, 92%) (Found: $M^+ - C_4H_9$, 449.1890. $C_{19}H_{41}O_2SiSn$ requires *M*, 449.1898); δ_H 0.12 [6 H, s, $Si(CH_3)_2$], 0.93 (9 H, t, *J* 7.5, 3 × CH_3), 0.94 [9 H, s, $SiC(CH_3)_3$], 1.3–1.7 (18 H, m, 9 × CH_2), 2.51 (1 H, br s, OH), 2.62 (2 H, t, *J* 6, 4-H_2), 3.65 (2 H, t, *J* 6, 5-H_2), 4.17 (2 H, t, *J* 6, 1-H_2) and 6.01 (1 H, t, *J* 6, 2-H); $\delta_C(C_6D_6)$ −5.2, 10.0, 13.9, 26.2, 27.8, 29.5, 37.1, 58.7, 62.8, 143.2, 143.52; *m*/*z* (EI) 449 (M^+ − 57, 60%).

(*E*)-3-Bromo-1,5-bis(*tert*-butyldimethylsilyloxy)pent-2-ene 25

A solution of the pentenol **23** (5.26 g, 10.4 mmol) in *N*,*N*-dimethylformamide (13 cm^3) was added dropwise to a solution of imidazole (2.13 g, 31.0 mmol) in *N*,*N*-dimethylformamide (4 cm^3) followed, after 5 min at 0 °C, by *tert*-butyldimethylsilyl chloride (2.65 g, 17.5 mmol). The mixture was stirred at room temperature for 20 h, diluted with ethyl acetate (150 cm^3) and washed with aqueous hydrogen chloride (1.2 M) and brine. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (98:2) gave the bis-silyl ether **24** (5.60 g, 87%);

δ_H 0.07 and 0.08 [each 6 H, s, $Si(CH_3)_2$], 0.90 and 0.92 [each 9 H, s, $SiC(CH_3)_3$], 0.7–1.7 [27 H, m, $Sn(C_4H_9)_3$], 2.47 (2 H, t, *J* 6, 4-H_2), 3.52 (2 H, t, *J* 6, 5-H_2), 4.30 (2 H, d, *J* 5, 1-H_2) and 5.73 (1 H, t, *J* 5, 2-H).

A solution of bromine (1.44 g, 9.04 mmol) in carbon tetrachloride (10 cm^3) was added slowly to a solution of the stannane **24** (5.60 g, 9.04 mmol) in carbon tetrachloride (10 cm^3) at −20 °C. The mixture was allowed to warm to room temperature and then concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether–triethylamine (94.5 : 5.0 : 0.5) gave the *title compound* **25** (3.44 g, 93%) (Found: M^+ + H, 409.1597; $C_{17}H_{38}BrO_2Si_2$ requires *M*, 409.1594); ν_{max}/cm^{-1} 1471, 1256, 1099, 1058, 1006, 936, 836, 812 and 777; δ_H 0.06 and 0.07 [each 6 H, s, $Si(CH_3)_2$], 0.89 and 0.90 [each 9 H, s, $SiC(CH_3)_3$], 2.67 (2 H, t, *J* 6, 4-H_2), 3.76 (2 H, t, *J* 6, 5-H_2), 4.16 (2 H, d, *J* 7, 1-H_2) and 6.10 (1 H, t, *J* 7, 2-H); δ_C −5.4, −5.2, 18.3, 18.3, 25.7, 60.5, 60.7, 123.7 and 134.1; *m*/*z* (CI) 428, 426 (M^+ + 18, 41, 33%), 411, 409 (M^+ + 1, 17, 12) and 279, 277 (100, 90).

2-Acetoxy-3,3-dimethyl-4-phenylthiobutene 26

A mixture of ketone **12** (1 equiv.), isopropenyl acetate (2 equiv.) and a catalytic amount of toluene-*p*-sulfonic acid was heated under reflux for 48 h, at which time additional isoprenyl acetate (2 equiv.) was added and the heating continued for another 48 h. The resulting mixture was cooled to room temperature, diluted with ether and washed with saturated aqueous sodium hydrogen carbonate. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (98 : 2) gave the *title compound* **26** (40–50%) (Found: M^+, 250.1031. $C_{14}H_{18}O_2S$ requires *M*, 250.1028); ν_{max}/cm^{-1} 1764, 1653, 1584, 1480, 1439, 1369, 1205, 1167, 1131, 1022, 957, 879, 739 and 692; δ_H 1.21 (6 H, s, 2 × 3-CH_3), 2.13 (3 H, s, CH_3CO), 3.05 (2 H, s, 4-H_2), 4.85 and 4.98 (each 1 H, d, *J* 2.5, 1-H) and 7.1–7.4 (5 H, m, ArH); δ_C 21.1, 25.1, 40.5, 44.6, 111.5, 125.8, 126.7, 129.4, 137.6, 158.9 and 168.8; *m*/*z* (EI) 250 (M^+, 34%), 209 (16) and 208 (79).

(*E*)-7-*tert*-Butyldimethylsilyloxy-5-(2-*tert*-butyldimethylsilyloxyethyl)-2,2-dimethyl-1-phenylthiohept-5-en-3-one 27

Tributyltin methoxide (2.4 cm^3, 8.22 mmol) and dichlorobis(tri-*o*-tolylphosphine)palladium (129 mg, 3% mol. equiv.) was added to a solution of the enol acetate **26** (2.06 g, 8.22 mmol) and the bromide **25** (2.24 g, 5.48 mmol) in toluene (25 cm^3) and the resulting suspension stirred at 100 °C until the formation of a black precipitate was observed (19 h). The solvent was then removed under reduced pressure and chromatography of the residue using hexane–ether (9 : 1) gave the *title compound* **27** (2.28 g, 78%) (Found: M^+ + H, 537.3258; $C_{29}H_{53}O_3SSi_2$ requires *M*, 537.3254); ν_{max}/cm^{-1} 1710, 1585, 1471, 1256, 1100, 1067, 837 and 777; δ_H 0.08 and 0.10 [each 6 H, s, $Si(CH_3)_3$], 0.91 and 0.93 [each 9 H, s, $SiC(CH_3)_3$], 1.30 (6 H, s, 2 × 2-CH_3), 2.33 (2 H, t, *J* 6.5, 1′-H_2), 3.19 (2 H, s, 1-H_2), 3.32 (2 H, s, 4-H_2), 3.65 (2 H, t, *J* 6.5, 2′-H_2), 4.28 (2 H, d, *J* 6, 6-H_2), 5.43 (1 H, t, *J* 6, 6-H) and 7.1–7.5 (5 H, m, ArH); δ_C −5.3, −5.1, 18.3, 24.4, 25.9, 34.3, 44.1, 46.1, 49.0, 59.9, 61.0, 126.1, 128.9, 129.5, 131.4, 131.9, 137.2 and 211.6; *m*/*z* (CI) 538 (M^+ + 1, 18%), 537 (M^+, 46), 479 (22), 406 (26) and 405 (100).

(*E*)-3-Bromo-1-*tert*-butyldiphenylsilyloxy-5-(4-methoxybenzyloxy)pent-2-ene 29

N-Bromosuccinimide (0.47 g, 2.67 mmol) in dichloromethane (15 cm^3) was added dropwise to a solution of the vinylstannane **28**[14] (2.00 g, 2.67 mmol) in dichloromethane (15 cm^3) at room temperature. The mixture was stirred for 20 min and then concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (9 : 1) gave the *title compound* **29** (1.45 g, 100%) (Found: M^+ + NH_4, 556.1872. $C_{29}H_{39}BrNO_3Si$ requires *M*, 556.1883); ν_{max}/cm^{-1} 3070, 3048, 3011, 1649, 1613, 1587, 1512, 1463, 1428, 1248, 1111, 1059, 1039, 823, 740 and 703; δ_H 1.08 [9 H, s, $SiC(CH_3)_3$], 2.56 (2 H, t, *J* 6.5, 4-H_2), 3.51 (2 H, t, *J* 6.5, 5-H_2), 3.80 (3 H, s, OCH_3), 4.18 (2 H, d, *J* 6.5, 1-H_2), 4.37 (2 H, s, $OCH_2C_6H_4$), 6.19 (1 H, t, *J* 6.5, 2-H), 6.83 and 7.18 (each 2 H, d, *J* 8.5, ArH) and 7.3–7.8 (10 H, m, ArH); δ_C 19.0, 26.7, 36.8, 55.1, 61.1, 67.3, 72.5, 113.6, 123.6, 127.7, 129.0, 129.7, 130.1, 133.2, 133.4, 135.5 and 159.0; *m*/*z* (CI) 558, 556 (M^+ + 18, 97%).

7-*tert*-Butyldiphenylsilyloxy-5-[2-(4-methoxybenzyloxy)ethyl]-2,2-dimethyl-1-phenylthiohept-5-en-3-one 30

Tributyltin methoxide (1.33 cm^3, 4.65 mmol) and dichlorobis(tri-*o*-tolylphosphine)palladium (73 mg, 3% mol equiv.) were added to a solution of the enol acetate **26** (1.16 g, 4.65 mmol) and the bromide **29** (1.66 g, 3.10 mmol) in toluene (30 cm^3). The mixture was stirred at 100 °C until the formation of a black precipitate was observed (20 h). The mixture was concentrated under reduced pressure and chromatography of the residue using light petroleum–ether (9 : 1) gave the *title compound* **30** (1.53 g, 74%) (Found: M^+ + NH_4, 684.3545. $C_{41}H_{54}NO_4SSi$ requires *M*, 684.3543); ν_{max}/cm^{-1} 3070, 3050, 1707, 1612, 1585, 1513, 1469, 1248, 1101, 1058, 1039, 823, 741 and 703; δ_H 1.08 [9 H, s, $SiC(CH_3)_3$], 1.27 (6 H, s, 2 × 2-CH_3), 2.17 (2 H, t, *J* 7, 1′-H_2), 3.18 (2 H, s, 1-H_2), 3.3 (2 H, s, 4-H_2), 3.38 (2 H, t, *J* 7, 2′-H_2), 3.82 (3 H, s, OCH_3), 4.31 (2 H, d, *J* 6, 7-H_2), 4.35 (2 H, s, $OCH_2C_6H_4$), 5.52 (1 H, t, *J* 6, 6-H), 6.86 and 7.20 (each 2 H, d, *J* 8.5, ArH) and 7.3–7.8 (10 H, m, ArH); δ_C 18.9, 24.2, 26.7, 30.9, 43.8, 45.7, 48.8, 54.9, 60.6, 68.3, 72.2, 113.5, 126.1, 127.5, 128.7, 128.8, 129.4, 130.3, 130.8, 132.1, 133.6, 135.4, 137.1, 158.9 and 211.2; *m*/*z* (CI) 684 (M^+ + 18, 100%).

(*E*)-3-Bromo-5-*tert*-butyldiphenylsilyloxypent-3-en-1-ol 32

Dichlorodicyanoquinone (0.65 g, 2.87 mmol) and an aqueous buffer (pH 7; 2.5 cm^3) were added to a vigorously stirred solution of the *p*-methoxybenzyl ether **29** (1.41 g, 2.61 mmol) in dichloromethane (48 cm^3) at room temperature. After 3 h, the mixture was diluted with dichloromethane and washed with an aqueous buffer at pH 7. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (95 : 5) gave the *title compound* **32** (0.91 g, 83%) (Found: M^+ + H, 419.1048. $C_{21}H_{28}BrO_2Si$ requires *M*, 419.1042); ν_{max}/cm^{-1} 3385, 3070, 1471, 1428, 1112, 1084, 1047, 823, 740 and 702; δ_H 1.05 [9 H, s, $SiC(CH_3)_3$], 1.68 (1 H, t, *J* 6, OH), 2.57 (2 H, t, *J* 6, 2-H_2), 3.72 (2 H, q, *J* 6, 1-H_2), 4.16 (2 H, d, *J* 7, 5-H_2), 6.24 (1 H, t, *J* 7, 4-H) and 7.3–7.7 (10 H, m, ArH); δ_C 19.0, 26.7, 39.3, 59.6, 60.7, 124.9, 127.7, 129.8, 133.0, 133.6 and 135.5; *m*/*z* (CI) 438, 436 (M^+ + 18, 100%).

(*R*)-4-[(2-Methoxyethoxy)methoxy]-1,2-epoxybutane 34

(*S*)-2-Bromobutane-1,4-diol[15] (8.9 g, 52.7 mmol) was added dropwise to a suspension of sodium hydride (60% dispersion; 6.44 g, 161.0 mmol; washed with hexane) in tetrahydrofuran (100 cm^3) at −10 °C. After 25 min at −10 °C, methoxyethoxymethyl chloride (6.5 cm^3, 57.1 mmol) and tetrabutylammonium iodide (2.01 g, 5.3 mmol) were added and the mixture stirred at −10 °C for 5 min and then at room temperature for 1 h. Saturated aqueous ammonium chloride (50 cm^3) was added and the aqueous layer extracted with ether. The organic extracts were washed with water and brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (1 : 1) gave the *title compound* **34** (7.30 g, 79%), $[\alpha]_D$ +8.8 (*c* 2, $CHCl_3$) (Found: M^+ + NH_4, 194.1391. $C_8H_{20}NO_4$ requires *M*, 194.1392); ν_{max}/cm^{-1} 1116, 1098, 1058 and 1044; δ_H 1.8 (2 H, m, 3-H_2), 2.52 (1 H, dd, *J* 5, 3, 1-H), 2.78 (1 H, t, *J* 9, 5, 1-H′), 3.03 (1 H, m, 2-H), 3.38 (3 H, s, OCH_3), 3.5-3.8 (6 H, m, OCH_2CH_2O and 4-H_2) and 4.73 (2 H, s, OCH_2O); δ_C 33.5, 46.5, 49.6, 58.6, 64.2, 66.4, 71.4 and 95.1; *m*/*z* (CI) 194 (M^+ + 18, 100%).

(*S*)-1-[(2-Methoxyethoxy)methoxy]hex-5-yn-3-ol 35

Lithium acetylide–ethylenediamine complex (90%; 106 g, 103.8

mmol) was added portionwise to a solution of epoxide **34** (7.3 g, 41.5 mmol) in a mixture of dimethyl sulfoxide (30 cm^3) and tetrahydrofuran (20 cm^3) at 0 °C. The mixture was stirred at 0 °C for 6 h and then water (80 cm^3) was added cautiously. The aqueous phase was extracted with ether and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (1:4) gave the *title compound* **35** (5.86, 70%), $[\alpha]_D$ +19.7 (*c* 2.0, $CHCl_3$) (Found: M^+ + H, 203.1285. $C_{10}H_{19}O_4$ requires *M*, 203.1283); ν_{max}/cm^{-1} 3451, 3286, 1111 and 1046; δ_H 1.85 (2 H, m, 2-H_2), 2.03 (1 H, t, *J* 2.5, 6-H), 2.4 (2 H, m, 4-H_2), 3.03 (1 H, d, *J* 4, OH), 3.39 (3 H, s, OCH_3), 3.5–3.9 (6 H, m, OCH_2CH_2O and 1-H_2), 3.96 (1 H, m, 3-H) and 4.71 (2 H, s, OCH_2O); δ_C 26.9, 35.2, 58.6, 64.8, 66.5, 67.7, 70.8, 71.1, 80.7 and 94.9; *m*/*z* (CI) 220 (M^+ + 18, 22%) and 203 (M^+ + 1, 32).

(*S*)-4-(4-Methoxybenzyloxy)-6-[(2-methoxyethoxy)methoxy]-hex-1-yne 36

A solution of the alkynol **35** (3.75 g, 18.5 mmol) in tetrahydrofuran (10 cm^3) was added dropwise to a suspension of sodium hydride (60% dispersion; 0.82 g, 20.4 mmol; washed with hexane) in a mixture of tetrahydrofuran (28 cm^3) and *N*,*N*-dimethylformamide (8 cm^3) at 0 °C. The cooling bath was removed and, after 5 min, *p*-methoxybenzyl chloride (2.75 cm^3, 20.4 mmol) and tetrabutylammonium iodide (0.74 g, 2.0 mmol) were added. The mixture was stirred at room temperature for 16 h then water (40 cm^3) and ether (100 cm^3) were added cautiously. The aqueous layer was extracted with ether and the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of residue using light petroleum–ether (2:1) gave the *title compound* **36** (4.23 g, 71%) (Found: M^+ + NH_4, 340.2127. $C_{18}H_{30}NO_5$ requires *M*, 340.2124); ν_{max}/cm^{-1} 3288, 1613, 1514, 1248, 1173, 1111, 1098 and 1040; δ_H 1.7–2.2 (5 H, m, 1-H, 3-H_2 and 5-H_2), 3.4 (3 H, s, OCH_3), 3.5–3.9 (7 H, m, 4-H, 3 × CH_2), 3.8 (3 H, s, OCH_3), 4.68 (2 H, s, CH_2Ar), and 6.9 and 7.23 (each 2 H, d, *J* 8, ArH); δ_C 23.6, 34.0, 54.9, 58.6, 63.9, 66.4, 70.0, 70.8, 71.4, 73.5, 80.6, 95.2, 116.4, 129.0, 130.1 and 158.9; *m*/*z* (CI) 340 (M^+ + 18, 55%).

Methyl (*S*)-5-(4-methoxybenzyloxy)-7-[(2-methoxyethoxy)-methoxy]hept-2-ynoate 37

Butyllithium (1.6 M in hexane; 8.2 cm^3, 13.3 mmol) was added dropwise to a solution of the alkyne **36** (3.51 g, 10.9 mmol) in tetrahydrofuran (45 cm^3) at −78 °C. The mixture was stirred at −78 °C for 30 cm^3 and methyl chloroformate (1.6 cm^3, 20.6 mmol) was added dropwise. After 1 h at −78 °C, saturated aqueous ammonium chloride (8 cm^3) was added and the reaction allowed to warm slowly to room temperature. The aqueous phase was extracted with ether and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (2:3) gave the *title compound* **37** (3.87 g, 93%), $[\alpha]_D$ +25.9 (*c* 2, $CHCl_3$) (Found: M^+ + NH_4, 398.2180. $C_{20}H_{32}NO_7$ requires *M*, 398.2179); ν_{max}/cm^{-1} 2238, 1712, 1612, 1586, 1513, 1435, 1259, 1173, 1110, 1097, 1075 and 1048; δ_H 1.91 (2 H, m, 6-H_2), 2.60 (2 H, d, *J* 5.5, 4-H_2), 3.38 (3 H, s, OCH_3), 3.5–3.7 (6 H, m, OCH_2CH_2O and 7-H_2), 3.76 (3 H, s, CO_2CH_3), 3.79 (3 H, s, OCH_3), 3.79 (1 H, m, 5-H), 4.43 and 4.56 (each 1 H, d, *J* 9, O*H*CHC_6H_4), 4.64 and 4.69 (each 1 H, d, *J* 9, O*H*CHO) and 6.87 and 7.27 (each 2 H, d, *J* 8.5, ArH); δ_C 24.2, 34.3, 52.3, 55.0, 63.8, 66.6, 71.5, 73.1, 74.1, 86.1, 95.3, 113.5, 129.3, 129.9, 153.7 and 159.1; *m*/*z* (CI) 398 (M^+ + 18, 100).

Methyl (5*R*,2*E*)-5-(4-methoxybenzyloxy)-7-[(2-methoxyethoxy)methoxy]-3-tributylstannylhept-2-enoate 38

Butyllithium in hexane (1.6 M; 12.0 cm^3, 19.5 mmol) was added to a solution of diisopropylamine (2.6 cm^3, 19.6 mmol) in tetrahydrofuran (35 cm^3) at 0 °C. After 15 min, tributyltin hydride (5.5 cm^3, 20.0 mmol) was added dropwise and the stirring continued at 0 °C for 15 min. The reaction was then cooled to −50 °C and copper(I) bromide–dimethyl sulfide complex (4.18 g, 20.3 mmol) was added portionwise. The resulting green suspension was stirred at −50 °C for 20 min and then cooled at −78 °C. A solution of the alkyne **37** (2.5 g, 6.6 mmol) in tetrahydrofuran (30 cm^3) was added dropwise. The stirring was continued at −78 °C for 3 h, and methanol (20 cm^3) was added very slowly keeping the temperature at −78 °C for 10 further min. The mixture was then allowed to warm slowly to room temperature and was diluted with water (50 cm^3). The resulting mixture was filtered through Celite, which was washed thoroughly with ethyl acetate, and the filtrate washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (7:3) gave the *title compound* **38** (8.44 g, 96%), $[\alpha]_D$ −1.3 (*c* 1.2, $CHCl_3$) (Found: $M^+ - C_4H_9$, 615.2346. $C_{28}H_{47}O_7Sn$ requires *M*, 615.2344); ν_{max}/cm^{-1} 1716, 1513, 1248, 1195, 1170, 1113 and 1040; δ_H 0.8–1.9 [29 H, m, $Sn(C_4H_9)_3$ and 6-H_2], 3.25 (2 H, m, 4-H_2), 3.41 and 3.72 (each 3 H, s, OCH_3), 3.5–3.8 (7 H, m, OCH_2CH_2O, 5-H and 7-H_2), 3.83 (3 H, s, CO_2CH_3), 4.46 and 4.54 (each 1 H, d, *J* 11, O*H*CHC_6H_4), 4.69 and 4.71 (each 1 H, d, *J* 10, O*H*CHO), 6.09 (1 H, s, 2-H), and 6.88 and 7.27 (each 2 H, d, *J* 8.5, ArH); δ_C 10.0, 13.4, 27.2, 28.7, 34.0, 39.3, 50.5, 54.9, 58.7, 64.2, 66.4, 70.4, 71.6, 76.0, 95.2, 113.8, 129.0, 129.3, 130.6, 158.6, 164.1 and 170.4; *m*/*z* (CI) 690, 688 (M^+ + 18, 6, 8%) and 615, 613 (M^+ − 57, 46, 33%).

(5*R*,2*E*)-1-*tert*-Butyldiphenylsilyloxy-5-(4-methoxybenzyloxy)-7-[(2-methoxyethoxy)methoxy]-3-tributylstannylhept-2-ene 40

Diisobutylaluminium hydride in hexane (1 M; 38.0 cm^3, 38.0 mmol) was added dropwise to a solution of the methyl ester **38** (8.22 g, 12.2 mmol) in tetrahydrofuran (60 cm^3) at −78 °C. The mixture was stirred at −78 °C for 1.5 h and then methanol (3.7 cm^3) was added cautiously. The stirring was continued at −78 °C for 5 min and saturated aqueous ammonium chloride (12 cm^3) was added. The mixture was allowed to reach room temperature and was stirred for 30 min. The mixture was then filtered through Celite and the filtrate dried ($MgSO_4$) and concentrated under reduced pressure to afford the alcohol **39** (7.91 g) which was used directly without further purification.

tert-Butyldiphenylsilyl chloride (5.1 cm^3, 19.8 mmol) was added to a solution of imidazole (1.54 g, 22.6 mmol) in *N*,*N*-dimethylformamide (6 cm^3) at 0 °C. After 5 min at 0 °C, a solution of the alcohol **39** (7.7 g, 12.0 mmol) in *N*,*N*-dimethylformamide (10 cm^3) was added dropwise. The mixture was stirred at room temperature for 18 h, diluted with ether (150 cm^3) and washed with water and brine. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (8:2) gave the *title compound* **40** (8.50 g, 80%), $[\alpha]_D$ +12.5 (*c* 2.2, $CHCl_3$) (Found: $M^+ - C_4H_9$, 825.3541. $C_{43}H_{65}O_6SiSn$ requires *M*, 825.3572); ν_{max}/cm^{-1} 1513, 1248, 1111, 1075 and 1044; δ_H 0.7–1.7 [29 H, m, $Sn(C_4H_9)_3$ and 6-H_2], 1.09 [9 H, s, $SiC(CH_3)_3$], 2.24 (1 H, dd, *J* 8.5, 5, 4-H), 2.48 (1 H, dd, *J* 8.5, 3.5, 4-H′), 3.41 (3 H, s, OCH_3), 3.4–3.7 (7 H, m, OCH_2CH_2O, 7-H_2 and 5-H), 3.82 (3 H, s, OCH_3), 4.32 and 4.45 (each 1 H, d, *J* 11, O*H*CHC_6H_4), 4.36 and 4.40 (each 1 H, d, *J* 5.5, 1-H), 4.64 and 4.66 (each 1 H, d, *J* 10, O*H*CHO), 5.89 (1 H, t, *J* 5.5, 2-H), 6.85 and 7.20 (each 2 H, d, *J* 8.5, ArH) and 7.3–7.8 (10 H, m, ArH); δ_C 9.7, 13.6, 19.1, 26.7, 27.4, 29.0, 34.1, 38.6, 55.1, 58.9, 61.1, 64.4, 66.5, 71.0, 71.7, 75.9, 95.3, 113.6, 127.5, 129.1, 129.4, 130.7, 133.8, 135.5, 140.7, 142.7 and 158.9; *m*/*z* (CI) 898, 900 (M^+ + 18) and 825, 823 (M^+ − 57).

(5*R*,2*E*)-3-Bromo-1-*tert*-butyldiphenylsilyloxy-5-(4-methoxybenzyloxy)-7-[(2-methoxyethoxy)methoxy]hept-2-ene 41

N-Bromosuccinimide (0.60 g, 3.40 mmol) in dichloromethane (15 cm^3) was added dropwise to a solution of the vinylstannane **40** (3.00 g, 3.40 mmol) in dichloromethane (15 cm^3) at room temperature. The mixture was stirred for 20 min and then concentrated under reduced pressure. Chromatography of the

residue using light petroleum–ether–triethylamine (6:4:0.5) gave the *title compound* **41** (2.11 g, 93%), $[a]_D$ +29.7 (*c* 2, $CHCl_3$) (Found: $M^+ + NH_4$, 688.2658. $C_{35}H_{51}BrNO_6Si$ requires *M*, 688.2669); ν_{max}/cm^{-1} 1513, 1248, 1112, 1048 and 703; δ_H 1.08 [9 H, s, $SiC(CH_3)_3$], 1.7 (2 H, m, 6-H_2), 2.36 (1 H, dd, *J* 14.5, 5.5, 4-H), 2.64 (1 H, dd, *J* 14.5, 7, 4-H′), 3.42 (3 H, s, OCH_3), 3.5–3.9 (7 H, m, OCH_2CH_2O, 7-H_2 and 5-H), 3.82 (3 H, s, OCH_3), 4.18 and 4.24 (each 1 H, dd, *J* 12.5, 6.5, 1-H), 4.40 and 4.49 (each 1 H, d, *J* 11, O*H*CHC_6H_4), 4.67 and 4.69 (each 1 H, d, *J* 11, O*H*CHO), 6.22 (1 H, t, *J* 6.5, 2-H), 6.85 and 7.22 (each 2 H, d, *J* 8.5, ArH) and 7.4–7.9 (10 H, m, ArH); δ_C 19.0, 26.7, 34.4, 42.0, 55.1, 58.9, 61.1, 64.2, 66.6, 71.7, 71.8, 74.0, 95.4, 113.6, 127.7, 129.4, 129.7, 130.4, 133.2, 134.0, 135.8 and 159.0; *m*/*z* (CI) 690, 688 (M^+ + 18, 68, 65%).

(*E*)-7-*tert*-Butyldiphenylsilyloxy-5-[(2*S*)-2-(4-methoxybenzyloxy)-4-(2-methoxyethoxy)methoxybutyl)]-2,2-dimethyl-1-phenylthiohept-5-en-3-one 42

Tributyltin methoxide (1.35 cm^3, 4.70 mmol) and dichlorobis(tri-*o*-tolylphosphine)palladium (74 mg, 3% mol equiv.) were added to a solution of the enol acetate **26** (1.18 g, 4.70 mmol) and the vinylic bromide **41** (2.11 g, 3.12 mmol) in toluene (35 cm^3). The resulting suspension was stirred at 100 °C until the formation of a black precipitate was observed (14 h). The solvent was removed under reduced pressure and chromatography of the residue using light petroleum–ether (3:2) gave the *title compound* **42** (2.04 g, 81%), $[a]_D$ +11.1 (*c* 2.1, $CHCl_3$) (Found: $M^+ + NH_4$, 816.4339. $C_{47}H_{66}NO_7SSi$ requires *M*, 816.4329); ν_{max}/cm^{-1} 1708, 1612, 1513, 1469, 1440, 1428, 1248, 1111 and 1051; δ_H 1.08 [9 H, s, $SiC(CH_3)_3$], 1.27 (6 H, s, 2 × 2-CH_3), 1.65 (2 H, m, 3′-H_2), 2.18 and 2.31 (each 1 H, dd, *J* 14, 6, 1′-H), 3.18 (2 H, s, 1-H_2), 3.27 and 3.35 (each 1 H, d, *J* 17, 4-H_2), 3.41 (3 H, s, OCH_3), 3.5–3.7 (7 H, m, OCH_2CH_2O, 2′-H and 4′-H_2), 3.82 (3 H, s, OCH_3), 4.30 (2 H, d, *J* 6, 7-H_2), 4.33 and 4.42 (1 H, d, *J* 11, O*H*CHC_6H_4), 4.61 and 4.63 (each 1 H, d, *J* 10, O*H*CHO), 5.56 (1 H, t, *J* 6, 6-H), 6.84 and 7.21 (each 2 H, d, *J* 8.5, ArH) and 7.2–7.8 (15 H, m, ArH); δ_C 19.0, 24.2, 26.6, 34.9, 35.2, 43.8, 45.8, 48.9, 55.0, 58.8, 60.6, 64.3, 66.5, 70.8, 71.5, 74.6, 77.2, 95.3, 113.5, 125.9, 127.5, 128.7, 129.2, 129.3, 129.4, 130.5, 131.3, 131.9, 133.5, 135.4, 137.1, 158.9 and 211.2; *m*/*z* (CI) 816 (M^+ + 18, 100%).

(*E*)-7-*tert*-Butyldiphenylsilyloxy-5-[(2*S*)-2-hydroxy-4-(2-methoxyethoxy)methoxybutyl]-2,2-dimethyl-1-phenylthiohept-5-en-2-one 43

Dichlorodicyanoquinone (160 mg, 0.69 mmol) and an aqueous buffer (pH 7; 0.5 cm^3) were added to a vigorously stirred suspension of the *p*-methoxybenzyl ether **42** (500 mg, 0.63 mmol) in dichloromethane (10 cm^3) at room temperature. After 1 h, the mixture was diluted with dichloromethane and washed with an aqueous buffer (pH 7). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (2:3) gave the *title compound* **43** (358 mg, 83%) (Found: $M^+ + NH_4$, 696.3779. $C_{39}H_{58}NO_6SSi$ requires *M*, 696.3754); ν_{max}/cm^{-1} 3500, 3070, 3050, 1706, 1584, 1471, 1428, 1110, 1050, 740 and 704; δ_H 1.03 [9 H, s, $SiC(CH_3)_3$], 1.25 (6 H, s, 2 × 2-CH_3), 1.59 (3 H, m, 3′-CH_2 and OH), 1.96 and 2.15 (each 1 H, m, 1′-H), 3.17 (2 H, s, 1-H_2), 3.36 (3 H, s, OCH_3), 3.0–3.8 (9 H, m, 4-H_2, OCH_2CH_2O, 2′-H and 4′-H_2), 4.24 (2 H, d, *J* 6, 7-H_2), 4.63 (2 H, s, OCH_2O), 5.53 (1 H, t, *J* 6, 6-H) and 7.1–7.8 (15 H, m, ArH); δ_C 19.0, 22.5, 24.3, 26.7, 36.6, 39.4, 44.0, 45.9, 58.8, 60.3, 65.1, 66.5, 67.0, 71.6, 95.2, 126.1, 127.5, 128.8, 129.5, 132.1, 132.2, 133.4, 133.5, 135.4, 136.9 and 212.6; *m*/*z* (CI) 696 (M^+ + 18, 24%).

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