Preparation of Some Novel Prostanoids Based on a Tetrahydropyran Ring System

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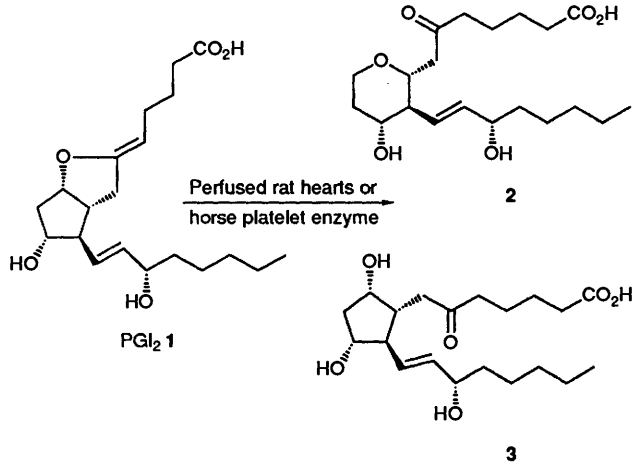
The prostanoids **31**, **33** and **42** have been prepared from tri-*O*-acetyl-D-glucal **5**. The key step in the formation of the prostaglandin analogues **31** and **33** involves the photocatalysed reaction between the thiocarbonate **4** and the allylstannane **21** leading to the stereocontrolled formation of a new carbon–carbon bond through a C-centred radical addition–elimination process.

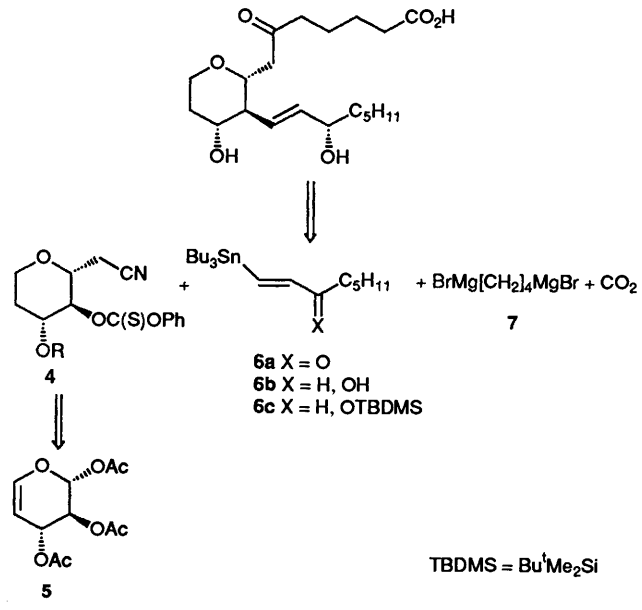
The prostaglandins (PG) are important, naturally occurring compounds exhibiting many diverse pharmacological properties.[1] Since their isolation and structure elucidation many chemists have developed methods for the synthesis of the natural compounds and selected analogues (prostanoids).[2]

Recently, Gryglewski reported that a novel metabolite of prostacyclin (PGI_2) **1**, designated Stable Metabolite X (SMX) **2**, possessed fibrinolytic activity.[3] When PGI_2 was treated with either perfused rat hearts or horse platelet enzyme, SMX was produced as a minor component; the major product was 6-oxo-$PGF_{1\alpha}$ **3**, the expected product from acid-catalysed hydrolysis (Scheme 1). In this paper the synthesis of the compound possessing the structure assigned to SMX (and the two analogues **33** and **42** is described. Note that the mechanism of conversion of PGI_2 into the structure assigned to SMX is not obvious.



Scheme 1

The quintessential structural feature of SMX is a tetrahydropyran ring possessing three contiguous chiral centres. This directed our retrosynthetic approach toward the use of a carbohydrate precursor[4] (Scheme 2). A convenient synthesis of compound **4** was foreseen which would utilize the readily available tri-*O*-acetyl-D-glucal **5**. It was anticipated the C^{13}–C^{20} side-chain (PG numbering) could be introduced with good stereoselectivity *via* a radical addition–elimination reaction[5] utilizing the vinylstannane **6**, and the C^1–C^5 part of the C^1–C^7 side-chain (PG numbering) could be introduced by addition of Grignard reagent **7** followed by a carbon dioxide quench.[6]



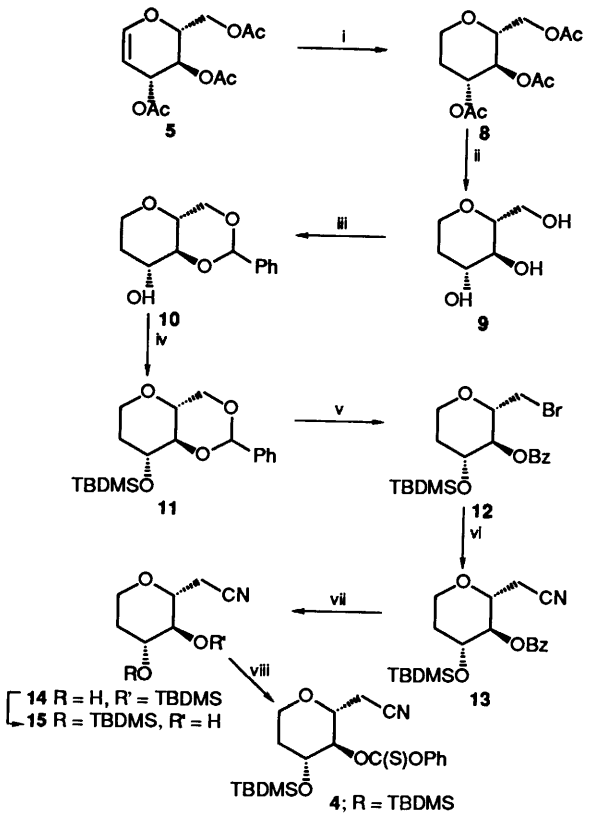
Scheme 2

Results and Discussion

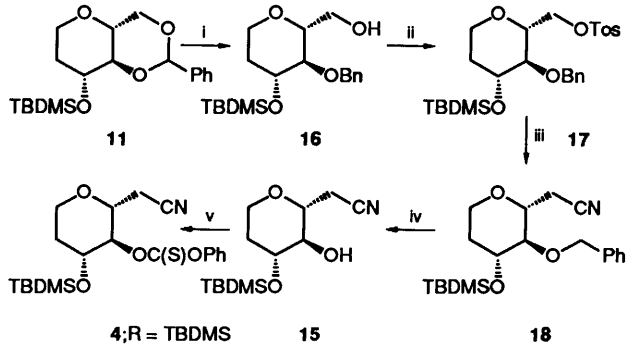
Tri-*O*-acetyl-D-glucal **5** was converted into the known acetal **10**, *via* **8** and **9**, by a modified literature procedure.[7] Protection of the free hydroxy group as the t-butyldimethylsilyl ether **11** (75% from **5**) followed by an Hanessian reaction[8] furnished the bromide **12**. Displacement of the bromine atom by cyanide ion (89%) and methanolysis of the benzoate ester provided the alcohols **14** and **15** in the ratio 1:3, respectively. Formation of the thiocarbonate moiety from alcohol **15** (Scheme 3) gave the key intermediate **4**; R = TBMDS (89%) which was required in order to introduce the C^{13}–C^{20} side-chain (PG numbering) by using the Barton radical deoxygenation methodology.[9]

The route to compound **15**, described above, suffered from two drawbacks. First, on scaling up the Hanessian reaction the yields plummeted to *ca.* 50% (from >90% on a 1 g scale) and, although we could achieve a 93% yield of compound **15** from benzoate **13**, the necessary isomerization reaction (**14** ⟶ **15**) was very tedious, needing four repetitions to maximize the yield. Thus, an alternative route was adopted (Scheme 4).

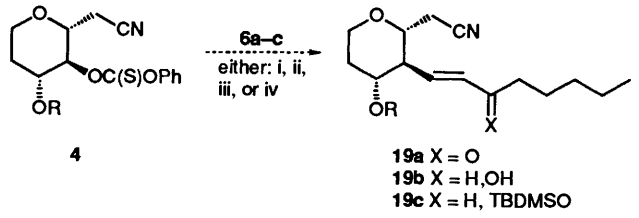
Reduction of compound **11** with diisobutylaluminium hydride[10] (DIBAL) liberated the free primary hydroxy group in compound **16**, which was subsequently converted into the nitrile moiety in product **18** *via* tosylation to give ester **17** and displacement of the tosyl group with cyanide ion (89% yield of **18** from **11**). Removal of the benzyl group could not be effected under the standard conditions of hydrogenation, sodium/liquid ammonia, or ammonium formate.[11,12] However, this group was removed in good yield (82%) when treated with *N*-bromosuccinimide (NBS) under radical benzylic bromination conditions,[13] completing an efficient synthesis of the thiocarbonate **4**



Scheme 3 *Reagents and conditions:* i, 5% Pd–C, H_2, MeOH, room temp., 4 h; ii, MeONa, MeOH, room temp., 2 h; iii, $ZnCl_2$, PhCHO, 80 °C, 3 h; iv, imidazole, Bu^tMe_2SiCl, DMF, room temp., 18 h; v, NBS, AIBN, CCl_4, *hν*, reflux, 10 min; vi, NaI, NaCN, DMSO, 50 °C, 5 h; vii, MeONa, MeOH, room temp., 18 h; viii, PhOC(S)Cl, DMAP, CH_2Cl_2, reflux, 20 h



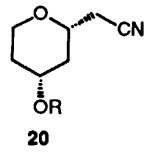
Scheme 4 *Reagents and conditions:* i, DIBAL, CH_2Cl_2, room temp., 3 h; then MeOH; then 2 mol dm^{-3} HCl, −78 °C to room temp.; ii, TosCl, DMAP, pyridine, CH_2Cl_2, room temp., 48 h; iii, NaI, NaCN, DMSO, 50 °C, 5 h; iv, NBS, AIBN, CCl_4, *hν*, reflux, 1 h; v, PhOC(S)Cl, DMAP, CH_2Cl_2, reflux, 20 h



Scheme 5 *Reagents and conditions:* i, C_6H_6, AIBN, reflux; ii, toluene, AIBN, reflux; iii, C_6H_6, *hν*, Pyrex; iv, C_6H_6, *hν*, quartz

(55% from **5**) that could be performed on the desired multi-gram scale.

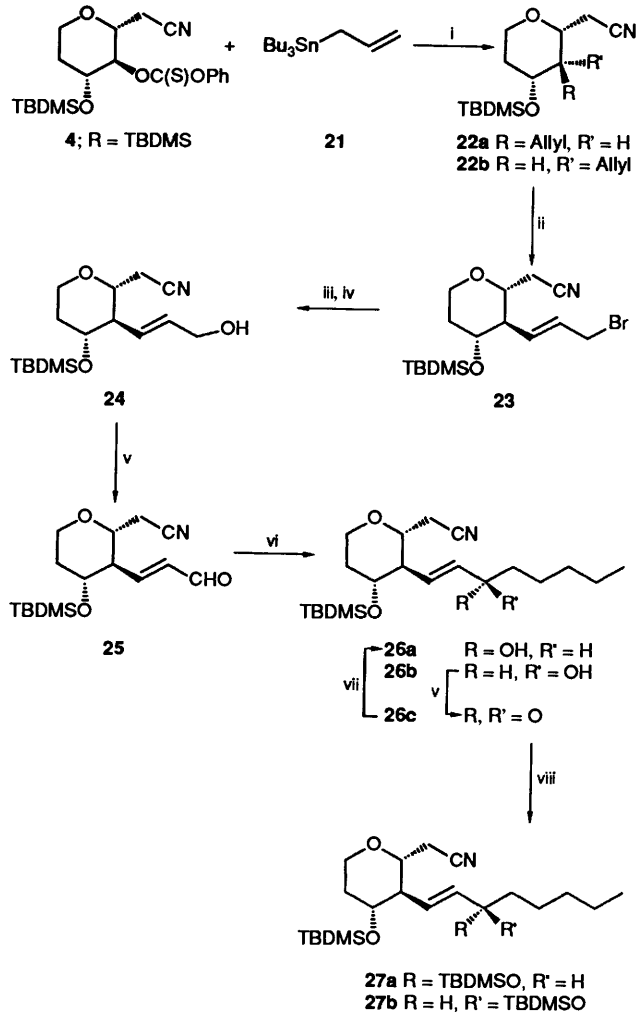
The vinylstannanes **6a**, **6b** and **6c** required to investigate the introduction of the C^{13}–C^{20} side-chain (PG numbering) are known compounds and were prepared following literature methods.[5,14] The radical addition–elimination reaction of compound **4** with all three compounds (**6a–c**) (Scheme 5) was attempted. Under both thermal and photochemical initiation conditions the only product isolated was compound **20** which resulted from deoxygenation; adducts **19a–c** were not obtained.



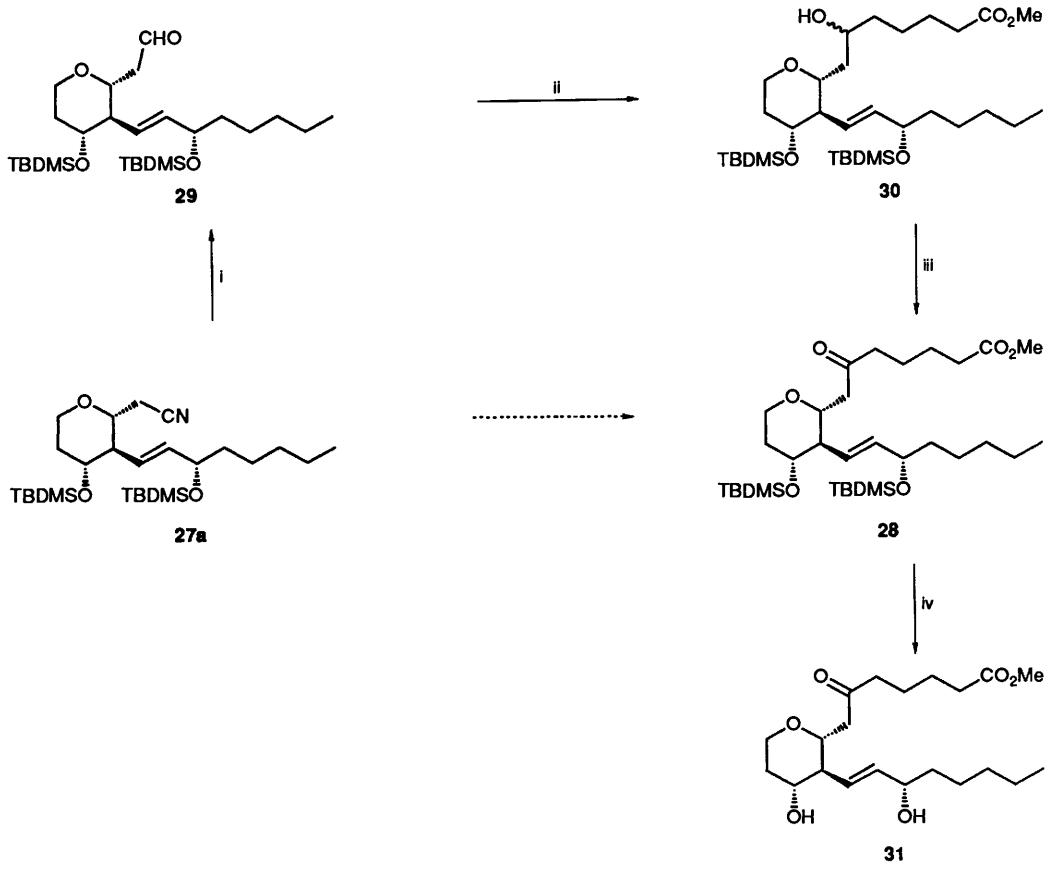
20

Owing to these negative results, attention was directed to work reported by Keck *et al.*[15] on the use of allyltributylstannane **21** as a trap for carbon-centred radicals.

The photochemically initiated reaction of the thiocarbonate **4** with this allylstannane reagent proved to be very efficient, and the allyl compounds **22a** and **22b** were obtained as an inseparable mixture (83%) in the approximate ratio 6:1 (by ^{13}C NMR spectroscopy). Treatment of this mixture with NBS under radical conditions afforded the bromide **23** (71%), which was transformed into the requisite α,β-unsaturated aldehyde **25** *via* a standard series of reactions (75% from **23**) (Scheme 6). Reaction



Scheme 6 *Reagents and conditons:* i, C_6H_6, *hν*, room temp., 26 h; ii, NBS, AIBN, CCl_4, *hν*, reflux, 2.5 h; iii, KOAc, 18-crown-6, Me_2CO, reflux, 2 h; iv, MeONa, MeOH, room temp., 12 h; v, $(COCl)_2$, DMSO, then Et_3N, −60 °C (Swern); vi, $Me[CH_2]_3CH_2MgBr$, $MgBr_2$, Et_2O, 0 °C, 2 h; vii, (*S*)-BINAL-H, THF, −100 °C, 2 h, then −78 °C, 2 h; viii, Bu^tMe_2SiCl, DMF, imidazole, room temp., 18h



Scheme 7 *Reagents and conditions:* i, DIBAL, toluene, −78 to 0 °C to −90 °C, then add MeOH, then $NH_4Cl_{(aq)}$ and warm to room temp.; ii, **7**, $MgBr_2$, 5 °C, THF, 1.5 h; then $CO_{2(s)}$, THF, −78 °C to room temp.; then 20% tartaric acid (aq.); CH_2N_2, Et_2O, room temp., 2 h; iii, Swern; iv, TBAF, THF, room temp., 4 h

of the aldehyde **25** with pentylmagnesium bromide did not give the desired addition compound **26a**, but instead afforded the reduced compound **24** as the sole product. This is a known problem with some Grignard reactions[16] and was readily overcome by saturating the reaction mixture with anhydrous magnesium bromide. With this modification the addition products **26a** and **26b** (66%) were formed in the isolated ratio 1.4:1. The minor component of the mixture was separated, oxidized and then reduced with Noyori's reagent, (*S*)-BINAL-H,[17] to give material identical with the major diastereoisomer **26a**. Protection of the free hydroxy group as the t-butyldimethylsilyl ether **27** completed the construction of the C^{13}–C^{20} side-chain (PG numbering). Further confirmation of the *S*-configuration at the chiral centre destined to become the 15-position (PG numbering) in the target prostanoid came from CD measurements. Compound **27a** gave a more positive CD curve at *ca.* 190 nm than did its diastereoisomer **27b**, as expected for the *S*-epimer of prostanoids.[18]

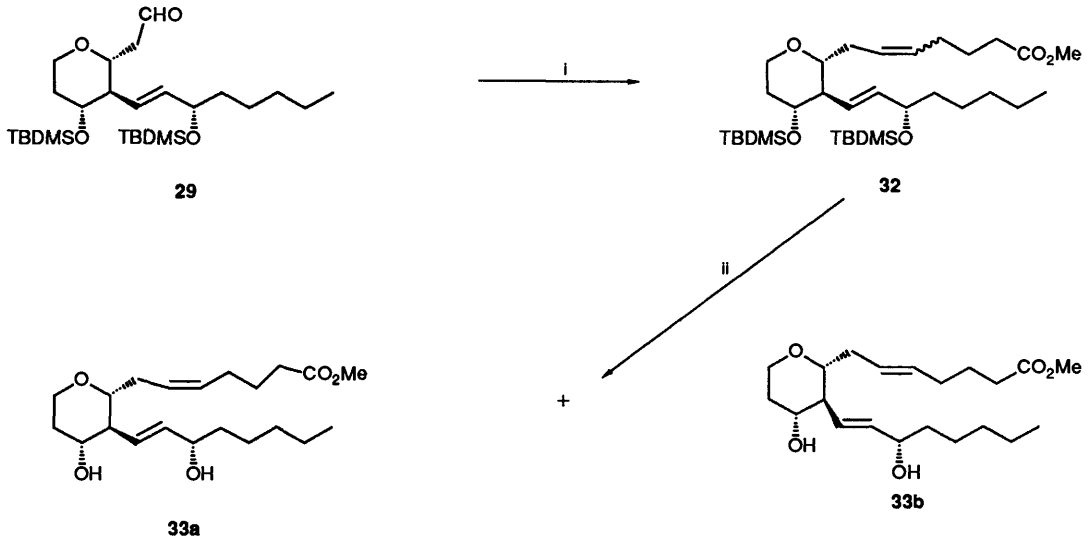
Introduction of the C^1–C^5 part of the top side-chain of SMX (PG numbering) was not as straightforward as we had anticipated. It was envisaged that either addition of the Grignard reagent **7** would afford the target compound, after subsequent minor modification (Scheme 7). However, all attempts to add the reagent **7** to the nitrile **27a** gave complex mixtures. Hence, the way forward was *via* reduction of the nitrile **27a** to the aldehyde **29**. The reduction of nitriles to aldehydes does not always occur readily.[20] After investigation of the use of several reducing agents,[21] DIBAL in toluene solution was found to give the best results. Hence, the nitrile **27a** was converted into the aldehyde **29** in modest yield (42%) with the recovery of some starting material (34%). Addition of reagent **7**, followed by a CO_2 quench* at −78 °C and esterification with diazomethane, afforded the alcohol **30**. Swern[22] oxidation of the crude reaction mixture gave the ketone **28**, which was deprotected using tetrabutylammonium fluoride (TBAF) to afford the methyl ester of SMX, compound **31** (34% from **29**).

The transformation of aldehyde **29** into the prostaglandin analogue **33** was also accomplished (Scheme 8). Hence, compound **29** was treated with the Wittig reagent **34** and the product, after esterification to afford compound **33** and desilylation, afforded an inseparable mixture of unsaturated esters **33a** and **33b** in the ratio 3:1, respectively (52% from **29**).

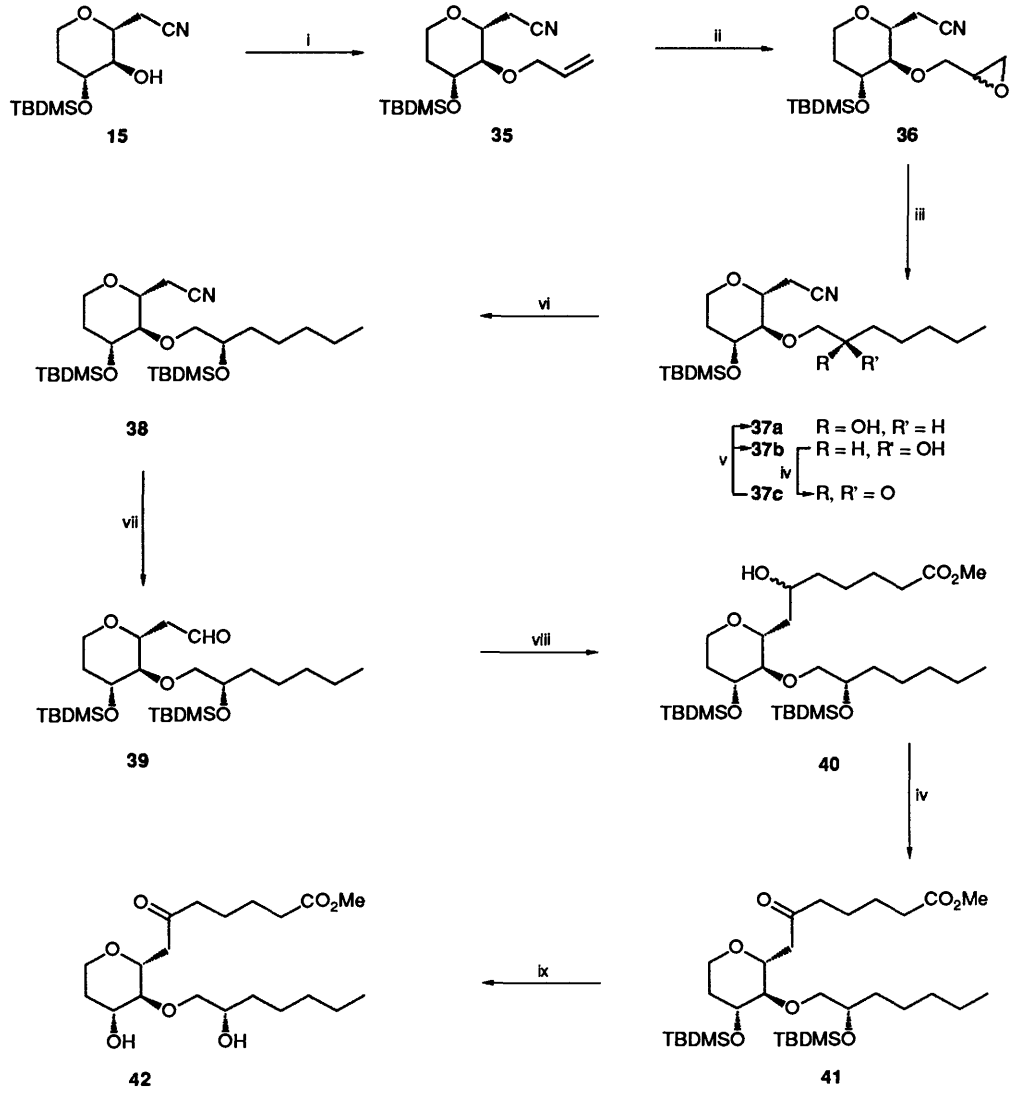
The alcohol intermediate **15** was converted into the 13-oxa-prostaglandin analogue (PG numbering) **42** (Scheme 9) as follows. Reaction of the alcohol **15** with allyl bromide followed by peracid oxidation afforded the epoxide **36** (80% from **15**) as an inseparable mixture of diastereoisomers, in the approximate ratio 2.7:1 (by ^{13}C NMR spectroscopy). On opening of the epoxide ring with dibutylcuprate (75%), the minor component of the mixture (compound **37b**) (20%) was separated and converted into the major 15*S*-component (PG numbering) by a sequence of reactions similar to those described above. Protection of the free hydroxy group as the t-butyldimethylsilyl ether afforded compound **38** (92%) and this compound was converted into analogue **42**, *via* compounds **39**–**41**, in much the same way as adopted for the synthesis of compound **31**.

The target compounds **31**, **33** and **42** showed no significant biological activity in either the platelet aggregation or fibrinolytic screens. Recently, Gryglewski has identified another minor

* We discovered that addition of solid CO_2 to the reaction mixture always gave better results than did bubbling dry CO_2 through the reaction mixture.

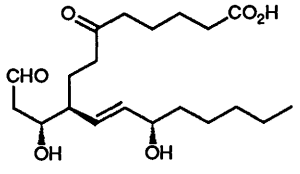


Scheme 8 *Reagents and conditions:* i, $Ph_3P = CH[CH_2]_3CO_2Li$ (**34**), THF, room temp., 2 h; then 20% tartaric acid (aq.); then CH_2N_2, Et_2O, 2 h; ii, TBAF, THF, room temp., 4 h



Scheme 9 *Reagents and conditions:* i, allyl bromide, Ag_2O, DMF, room temp., 48 h; ii, MCPBA, $NaHCO_3$, CH_2Cl_2, room temp., 48 h; iii, $LiCuBu_2$, Et_2O, −78 °C, 10 h; iv, Swern; v, (*S*)-BINAL-H, THF, − 100 °C, 2 h; then −78 °C, 2 h; vi, Bu^tMe_2SiCl, imidazole, DMF, room temp., 18 h; vii, DIBAL, toluene, −78 to 0 to −90 °C; then add MeOH, then NH_4Cl (aq); viii, 7, $MgBr_2$, 0–5 °C, THF, 1.5 h; then CO_2(s), THF, −78 °C to room temp.; then 20% tartaric acid (aq.); then CH_2N_2, Et_2O, room temp., 2 h; ix, TBAF, THF, room temp., 4 h

metabolite resulting from the enzymic degradation of PGI_2 which he has named SMY **43**.[23] The structure of SMY is tentative and it is possible that this compound possesses the fibrinolytic properties originally ascribed to SMX.



43

Experimental

General.—Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. Benzene, diethyl ether, tetrahydrofuran (THF), and toluene were distilled from sodium–benzophenone ketyl immediately prior to use. Other anhydrous solvents were obtained by distillation from the following drying agents and stored over 4 Å molecular sieves under argon: dichloromethane (P_2O_5), dimethylformamide (DMF) (CaH_2), dimethyl sulphoxide (DMSO) (CaH_2), methanol (magnesium methoxide, 3 Å molecular sieves) and triethylamine (KOH). Light petroleum refers to the fraction boiling in the range 40–60 °C. This and ethyl acetate were distilled prior to use. All reactions involving organometallic reagents or other moisture-sensitive reactions were executed under nitrogen or argon. Flash chromatography was carried out using silica gel 60 H (Merck 7385). TLC was performed on Merck 60F-254 (0.25 mm thickness, Art. 5715), glass-backed silica gel plates and R_F-values are quoted for the flash chromatography solvent systems unless noted otherwise. M.p.s were carried out on an 'Electrothermal' device and are uncorrected. IR spectra were recorded on a Perkin-Elmer 881 grating infrared spectrophotometer as solutions in chloroform unless noted otherwise. Optical rotations were performed in chloroform (unless otherwise stated) on a Thorn NPL Automatic Polarimeter Type 243. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM250 spectrophotometer. Unless noted otherwise, spectra are quoted for solutions in $CDCl_3$, with Me_4Si as external standard. *J*-values are given in Hz. Low-resolution mass spectra were run using a VG 12-253 Low Resolution instrument. High-resolution mass spectra were run at the SERC Mass Spectrometry Centre, Swansea, using a VG ZAB-E High Resolution instrument. Elemental analyses were conducted by The Chemical Analysis Department, Glaxo Group Research, Ware.

(−)-(1S,3R,6R,10R)-3-*Phenyl*-2,4,7-*trioxabicyclo*[4.4.0]-*decan*-10-*ol* **10**.—Palladium on activated carbon (5%) (1.00 g) was added to a deoxygenated solution of tri-*O*-acetyl-D-glucal **5** (100.0 g, 376.3 mmol) in dry methanol (250 cm^3) and the mixture was stirred under a slight positive pressure of hydrogen for 4 h at room temperature. The catalyst was removed by filtration and washed with methanol (100 cm^3), and the combined organics were stirred with sodium methoxide (2.00 g, 0.1 mol equiv.) for 2 h at room temperature. This reaction mixture was neutralized using indicator paper with dry, methanolic HCl and concentrated under reduced pressure. The resulting oil was dissolved in freshly distilled benzaldehyde (300 cm^3). $ZnCl_2$ (50.0 g) was added and the mixture was stirred at 80 °C for 3 h. After concentration under reduced pressure, the viscous oil was diluted with CH_2Cl_2 (500 cm^3), washed successively with 2 mol dm^{-3} NaOH (2 × 200 cm^3) and 2 mol dm^{-3} $Na_2S_2O_5$ (200 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. The product crystallized from an ethyl acetate–light petroleum mixture; evaporation of the mother liquor followed by flash chromatography (50% ethyl acetate–light petroleum) yielded a further quantity of compound **10** (68.5 g, 77%), m.p. 105 °C (lit.,[7] 104 °C); R_F 0.53 (Found: C, 66.0; H, 6.8. Calc. for $C_{13}H_{16}O_4$: C, 66.09; H, 6.81%); $[\alpha]_D^{22}$ −43.1° (*c* 0.95, EtOH) {lit., $[\alpha]_D^{22}$ −43.4° (*c* 0.88, EtOH)}; ν_{max}/cm^{-1} 3499 (OH), 3012, 2872, 1383, 1144, 1102, 1072, 1040, 1002 and 699; δ_H 7.60–7.40 (5 H, m, Ph), 5.51 (1 H, s, 3 H), 4.25 (1 H, dd, *J* 10.1, 4.7, 5-H$^\beta$), 3.90 (1 H, ddd, *J* 11.9, 3.8, 1.0, 8-H$^\alpha$), 3.74 (1 H, ddd, *J* 11.0, 8.9, 4.8, 10-H), 3.65 (1 H, at *J* 10.1, 5-H$^\beta$), 3.51–3.16 (4 H, m, 1 and 6 H, 8-H$^\beta$ and OH) and 1.94–1.68 (2 H, m, 9-H); δ_C 137.53 (C); 69.23, 71.22, 84.00, 101.96, 126.39, 128.32 and 129.19 (CH); 33.47, 66.25 and 68.85 (CH_2); *m/z* (EI) 236 $(M)^+$.

(−)-(1S,3R,6R,10R)-10-(*t-Butyldimethylsiloxy*)-3-*phenyl*-2,4,7-*trioxabicyclo*[4.4.0]*decane* **11**.—Imidazole (48.3 g, 2.5 mol equiv.) and Bu^tMe_2SiCl (64.3 g, 1.5 mol equiv.) were added to a solution of compound **10** (67.0 g, 283.9 mmol) in dry DMF (200 cm^3). After being stirred at room temperature for 18 h, the reaction mixture was poured onto saturated aq. NH_4Cl (1 dm^3), and extracted with diethyl ether (3 × 500 cm^3), and the combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification was effected by vacuum distillation (160 °C at 0.2 mmHg), to yield *compound* **11** (96.5 g, 97%) as an oil, R_F 0.32 (10% diethyl ether–petroleum) (Found: C, 65.4; H, 8.9. Calc. for $C_{19}H_{30}O_4Si$: C, 65.10; H, 8.63%); ν_{max}/cm^{-1} 3012, 2957, 2858, 1473, 1464, 1383, 1250, 1130, 1100, 1010 and 701; δ_H 7.55–7.30 (5 H, m, Ph), 5.57 (1 H, s, 3-H), 4.28 (1 H, dd, *J* 10.2, 4.7, 5-H$^\beta$), 4.00–3.82 (2 H, m, 10-H and 8-H$^\alpha$), 3.71 (1 H, t, *J* 10.2, 5-H$^\alpha$), 3.56 (1 H, dt, *J* 11.8, 3.2, 8-H$^\beta$), 3.43 (1 H, t, *J* 8.7, 1-H), 3.36–3.25 (1 H, m, 6-H), 1.98–1.74 (2 H, m, 9-H_2), 0.89 (9 H, s, Bu^tSi), 0.10 (3 H, s, MeSi) and 0.08 (3 H, s, MeSi); δ_C 18.20 and 137.81 (C); 70.37, 71.86, 83.99, 101.57, 126.15, 128.04 and 128.71 (CH); 35.58, 66.41 and 68.96 (CH_2); −4.84, −4.40 and 25.79 (Me); *m/z* (EI) 293 $(M - Bu^t)^+$.

(−)-(2S,3R,4R)-2-*Bromomethyl*-4-(*t-butyldimethylsilyloxy*)-*tetrahydropyran*-3-*yl Benzoate* **12**.—NBS (50.0 g, 1.3 mol equiv.) and azoisobutylnitrile (AIBN) (100 mg) were added to a solution of compound **11** (75.0 g, 213.7 mmol) in CCl_4 (1.5 dm^3). After irradiation with a 200 W tungsten lamp for 20 min, the refluxing reaction mixture was allowed to cool and was then filtered through Celite. The Celite was washed with CCl_4 (100 cm^3) and the combined organics were concentrated under reduced pressure. Purification was effected by flash chromatography (7% diethyl ether–light petroleum) to yield compound **12** (46.9 g, 51%) as a pale yellow oil, R_F 0.20 (Found: C, 53.5; H, 7.1. Calc. for $C_{19}H_{29}BrO_4Si$: C, 53.14; H, 6.81%); $[\alpha]_D^{21}$ −50.5° (*c* 1.00); ν_{max}/cm^{-1} 2956, 2930, 1729 (CO), 1267, 1133, 1094, 838 and 710; δ_H 8.06 (2 H, m, 2 of Ph), 7.65–7.50 (3 H, m, 3 of Ph), 5.01 (1 H, at, *J* 8.9, 3-H), 4.07 (1 H, ddd, *J* 12.0, 4.8, 2.3, 6 H, 3.92 (1 H, ddd, *J* 10.2, 8.9, 5.5, 4-H), 3.68–3.36 (4 H, m, 2-H, 6-H and 1′-H_2), 2.02–1.78 (2 H, m, 5-H_2), 0.76 (9 H, s, Bu^tSi), 0.05 (3 H, s, MeSi) and −0.13 (3 H, s, MeSi); *m/z* (EI) 371 and 373 $(M - Bu^t)$.

(−)-(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-2-(*cyanomethyl*)-*tetrahydrofuran*-3-*yl Benzoate* **13**.—Sodium iodide (19.9 g, 4 mol equiv.) and sodium cyanide (6.5 g, 4 mol equiv.) were stirred at 80 °C with a solution of compound **12** (14.23 g, 33.17 mmol) in DMSO (150 cm^3) for 5 h. After having cooled, the reaction mixture was poured onto water (500 cm^3) and the mixture was extracted with diethyl ether (3 × 500 cm^3). The combined

* Throughout this section, unprimed NMR locants refer to the pyran moiety, primed locants to the side-chain at the pyran C-2, and doubly primed locants to the side-chain at the pyran C-3.

extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (30% diethyl ether–light petroleum) to yield *compound* **13** (11.78 g, 95%) as a solid, m.p. 92 °C; R_F 0.25 (Found: C, 64.0; H, 7.7; N, 3.6. Calc. for $C_{20}H_{29}NO_4Si$: C, 63.97; H, 7.78; N, 3.73%); $[\alpha]_D^{21}$ −35.1° (*c* 1.00); ν_{max}/cm^{-1} 3010, 2958, 2932, 2259 (CN), 1726. (CO), 1265, 1136, 1093, 839 and 710; δ_H 8.10–8.00 (2 H, m, 2 of Ph), 7.65–7.50 (3 H, m, 3 of Ph), 4.94 (1 H, t, *J* 9.0, 3-H), 4.05 (1 H, ddd, *J* 12.2, 4.9, 1.8, 6-H$^{\alpha}$), 3.92 (1 H, ddd, *J* 10.3, 9.0, 5.5, 4-H), 3.66 (1 H, ddd, *J* 9.0, 6.8, 5.1, 2-H), 3.55 (1 H, dt, *J* 12.2, 2.9, 6-H$^{\beta}$), 2.59 (2 H, dd, *J* 6.8, 5.1, 2′-H_2), 2.04–1.78 (2 H, m, 5-H_2), 0.75 (9 H, s, Bu^{t}Si), 0.07 (3 H, s, MeSi) and −0.11 (3 H, s, MeSi); δ_C 17.67, 116.82, 129.48 and 165.57 (C); 71.07, 74.20, 75.89, 128.44, 129.81 and 133.41 (CH); 21.66, 34.73 and 65.41 (CH_2); −4.95, −4.45 and 25.44 (Me); *m/z* (EI) 318 (M − Bu^t).

(−)-[(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-*hydroxytetrahydropyran*-2-*yl*]*acetonitrile* **15**.—Sodium methoxide (0.45 g, 1 mol equiv.) was stirred with a solution of compound **13** (3.10 g, 8.27 mmol) in dry methanol (25 cm^3) for 10 h at room temperature. The reaction mixture was poured into saturated aq. NH_4Cl (50 cm^3) and the mixture was extracted with diethyl ether (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (20% ethyl acetate–light petroleum) separated compounds **14** and **15** (1:3 ratio, R_F 0.26 and 0.35; 35% ethyl acetate–light petroleum). Compound **14** was treated with catalytic amounts of sodium methoxide in dry methanol. Isolation as described above afforded a further quantity of compound **15**. This silyl-migration reaction was repeated four times to maximize the yield of *title compound* **15** (2.08 g, 93%), m.p. 66 °C (Found: C, 57.75; H, 9.4; N, 5.1. Calc. for $C_{13}H_{25}NO_3Si$: C, 57.52; H, 9.28; N, 5.16%); $[\alpha]_D^{21}$ −3.1° (*c* 1.00); ν_{max}/cm^{-1} 3492 (OH), 2955, 2932, 2859, 2256 (CN), 1257, 1144, 1124, 1096, 914, 836 and 778; δ_H 3.97 (1 H, ddd, *J* 12.0, 4.8, 1.8, 6-H$^{\alpha}$), 3.59 (1 H, ddd, *J* 10.7, 8.1, 5.3, 4-H), 3.47 (1 H, dt, *J* 12.1, 2.8, 6-H$^{\beta}$), 3.40–3.33 (1 H, m, 2-H), 3.26 (1 H, dt, *J* 8.2, 2.4, 3-H), 2.88–2.61 (2 H, ABX_q, *J* 16.8, 6.2, 3.5, 2′-H_2) 2.39 (1 H, d, OH), 1.88–1.65 (2 H, m, 5-H), 0.92 (9 H, s, Bu^{t}Si), 0.16 (3 H, s, MeSi), and 0.12 (3 H, s, MeSi); δ_C 17.90 and 117.41 (C); 73.92, 74.96 and 75.10 (CH); 21.24, 34.40 and 65.62 (CH_2); −4.62, −4.38 and 25.73 (Me); *m/z* (EI) 214 (M − Bu^t).

(+)-[(2R,3R,4R)-(*t-Butyldimethylsiloxy*)*tetrahydropyran*-2-*yl*]*acetonitrile* **18**.—A 1.2 mol dm^{-3} toluene solution of DIBAL (100 cm^3, 5.6 mol equiv.) was added to a solution of compound **11** (7.40 g, 21.10 mmol) in dry CH_2Cl_2 (100 cm^3) at 0 °C. The reaction mixture was stirred for 3 h at room temperature prior to careful quenching at −78 °C with methanol (20 cm^3) followed by addition of 2 mol dm^{-3} HCl (100 cm^3). The reaction mixture was warmed to room temperature and extracted with diethyl ether (4 × 200 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure.

The resultant foam was dissolved in dry CH_2Cl_2 (100 cm^3) and 4-(dimethylamino)pyridine (DMAP) (100 mg), dry pyridine (6.0 cm^3, 3.5 mol equiv.) and tosyl chloride (12.10 g, 3 mol equiv.) were added. After being stirred for 48 h at room temperature the reaction mixture was washed successively with 2 mol dm^{-3} HCl (2 × 50 cm^3) and saturated aq. $NaHCO_3$ (50 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure.

The solid residue was dissolved in DMSO (100 cm^3), and sodium iodide (13.2 g, 4 mol equiv.) and sodium cyanide (4.30 g, 4 mol equiv.) were added. This mixture was stirred for 5 h at 50 °C and, after cooling to room temperature, was poured onto 2 mol dm^{-3} aq. sodium chloride (500 cm^3). This mixture was extracted with diethyl ether (3 × 500 cm^3) and the combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (10% ethyl acetate–light petroleum) to afford *compound* **18** (6.79 g, 89%) as a solid, m.p. 91 °C; R_f 0.29 [Found: C, 66.1; H, 8.4; N, 3.9. Calc. for $C_{20}H_{31}NO_3Si$: C, 66.44; H, 8.64; N, 3.87%. Found: *m/z* (CI, NH_3) ($M^+ + NH_4$), 379.2417. $C_{20}H_{31}NO_3Si$ requires ($M + NH_4$) 379.2413]; $[\alpha]_D^{34}$ +47.4° (*c* 1.00); ν_{max}/cm^{-1} 3003, 2957, 2932, 2888, 2256 (CN), 1461, 1380, 1201, 1128, 1089, 905, 834 and 711; δ_H 7.34 (5 H, br s, Ph), 5.05–4.60 (2 H, AB_q, *J* 11.2, PhCH_2), 3.94 (1 H, ddd, *J* 11.5 4.9, 1.2, 6-H$^{\alpha}$), 3.81 (1 H, ddd, *J* 10.5, 8.5, 5.4, 4-H), 3.42 (1 H, dt, *J* 11.5, 2.0, 6-H$^{\beta}$), 3.38–3.31 (1 H, m, 2-H), 3.21 (1 H, t, *J* 8.5, 3-H), 2.71–2.43 (2 H, ABX_q, *J* 17.0, 5.9, 3.4, 2′-H_2), 1.95–1.68 (2 H, m, 5-H_2), 0.90 (9 H, s, Bu^{t}Si) and 0.18 (6 H, s, 2 × MeSi); δ_C 17.94, 117.39 and 138.06 (C); 74.37, 74.92, 82.09, 127.96, 128.01 and 128.57 (CH); 21.32, 35.17, 65.48 and 75.39 (CH_2); −4.49, −4.21 and 25.89 (Me).

Alternative Preparation of Compound **15**.—NBS (3.54 g, 1.2 mol equiv.) and AIBN (50 mg) were added to a solution of compound **18** (6.00 g, 16.59 mmol) in CCl_4 (250 cm^3). This mixture was irradiated, with a 200 W tungsten lamp, under reflux for 1 h. On cooling, the reaction mixture was filtered through Celite and concentrated under reduced pressure. Purification was effected by flash chromatography (30% ethyl acetate–light petroleum) to afford compound **15** (3.69 g, 82%) as a solid. M.p., R_f-value, $[\alpha]_D$, IR, ^1H and ^{13}C NMR spectral data compared to those previously reported.

(−)-O-(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-2-*cyanomethyl*)*tetrahydropyran*-3-*yl* O-*Phenyl Thiocarbonate* **4**.—DMAP (27.0 g, 4 mol equiv.) and PhOC(S)Cl (23.0 cm^3, 3 mol equiv.) were refluxed with compound **15** (15.0 g, 55.4 mmol) in dry CH_2Cl_2 (400 cm^3) for 16 h. After cooling, the reaction mixture was partitioned with water (500 cm^3). The aqueous layer was further extracted with CH_2Cl_2 (2 × 500 cm^3) and the combined organics were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (50% CH_2Cl_2–light petroleum ⟶ 100% CH_2Cl_2) to yield *compound* **4** (20.1 g, 89%) as a solid, m.p. 142 °C; R_f 0.38 (35% ethyl acetate–light petroleum) (Found: C, 59.1; H, 7.1; N, 3.3. Calc. for $C_{20}H_{29}NO_4SSi$: C, 58.93; H, 7.17; N, 3.44%); $[\alpha]_D^{21}$ −16.6° (*c* 1.00); ν_{max}/cm^{-1} 3023, 2958, 2934, 2861, 2257 (CN), 1491, 1358, 1210 (CS), 1126, 1095, 1058, 1024, 839 and 695; δ_H 7.50–7.10 (5 H, m, Ph), 5.33 (1 H, at, *J* 8.8, 3-H), 4.03 (1 H, ddd, *J* 12.0, 4.8, 2.1, 6-H$^{\alpha}$), 3.98 (1 H, ddd, *J* 10.7, 8.8, 5.4, 4-H), 3.70 (1 H, ddd, *J* 8.8, 7.2, 4.9, 2-H), 3.55 (1 H, dt, *J* 12.0. 2.9, 6-H$^{\beta}$), 2.84–2.62 (2 H, ABX_q, *J* 16.9, 7.2, 4.9, 2′-H_2), 2.05–1.79 (2 H, m, 5-H), 0.89 (9 H, s, Bu^{t}Si), 0.18 (3 H, s, MeSi) and 0.14 (3 H, s, MeSi); δ_C 17.88, 116.68, 153.55 and 195.19 (C); 70.98, 74.05, 84.79, 121.88, 126.74 and 129.59 (CH); 21.89, 34.66 and 65.39 (CH_2); −4.83, −4.51 and 25.67 (Me); *m/z* (EI) 350 (M − Bu^t)$^+$.

[(2R,3R,4R)- *and* (2R,3S,4R)-4-(*t-Butyldimethylsiloxy*)-3-(*prop*-2-*enyl*)*tetrahydropyran*]*acetonitrile* **22a** *and* **22b**.—A degassed solution of compound **4** (2.00 g, 4.91 mmol) and allyltributylstannane (3.00 cm^3, 2 mol equiv.) in dry benzene (20 cm^3) was irradiated, with a 400 W halogen lamp, in a quartz photolysis tube for 26 h. After concentration of the reaction mixture under reduced pressure, the pale yellow oil was partitioned between hexane (50 cm^3) and acetonitrile (50 cm^3). The hexane layer was washed with a further portion of acetonitrile (20 cm^3) and the combined acetonitrile layers were washed successively with 2 mol dm^{-3} NaOH (25 cm^3), water (25 cm^3) and saturated brine (25 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by careful flash chromatography (80% CH_2Cl_2–hexane to 100% CH_2Cl_2) to yield an inseparable mixture of *epimers* **22a** and **22b** in the approximate ratio 6:1 (1.20 g, 83%), R_f 0.49 (CH_2Cl_2) (Found: C, 65.15; H, 9.9; N, 5.0. Calc. for $C_{16}H_{29}NO_2Si$: C, 65.03; H, 9.89;

N, 4.74%); ν_{max}/cm^{-1} 3080, 2931, 2858, 2252 (CN), 1640 (C=C), 1256, 1097, 916, 857, 775 and 666; δ_H 5.72 (1 H, m, 2″-H), 5.01 (2 H, m, 3″-H_2), 3.85 (1 H, m, 6-H^{α}), 3.56 (1 H, m, 4-H), 3.33 (2 H, m, 2-H and 6-H^{β}), 2.60 (2 H, m, 2′-H_2), 2.24 (2 H, m, 1″-H_2), 1.80 (1 H, m, 5-H_{α}), 1.55 (2 H, m, 3-H and 5-H_{β}), 0.89 (9 H, s, Bu^{t}Si) and 0.01 (6 H, br s, 2 × MeSi); δ_C 17.88 and 120.89 (C); 43.56, 46.99, 69.57, 69.97, 74.18, 74.50, 134.92 and 138.16 (CH); 20.69, 22.46, 31.21, 31.63, 35.29, 64.83, 115.89, 117.24 and 117.31 (CH_2); −4.86, −4.83, −4.61, −3.87 and 25.76 (Me); *m/z* (EI) 238 (M − Bu^t)$^+$.

(+)-{(2R,3R,4R)-3-[(E)-3″-*Bromoprop*-1″-*enyl*]-4-(*t-butyldimethylsiloxy*)*tetrahydropyran*-2-*yl*}*acetonitrile* **23**.—NBS (1.00 g, 1.1 mol equiv.) and AIBN (cat.) were added to a solution of the mixture of compounds **22a** and **22b** (1.50 g, 5.08$_5$ mmol) in CCl_4 (30 cm^3). This mixture was irradiated with a 200 W tungsten lamp for 2.5 h. On cooling, the reaction mixture was filtered through Celite, which was washed with CCl_4 (10 cm^3), and the combined organics were concentrated under reduced pressure. Purification was effected by flash chromatography (15% ethyl acetate–light petroleum) to yield *compound* **23** (1.40 g, 85% from **22a** in starting mixture), m.p. 80.5–82 °C; R_f 0.31 (20% ethyl acetate–light petroleum) [Found: *m/z* (CI, NH_3) ($M^+ + NH_4$), 391.1416. $C_{16}H_{28}BrNO_2Si$ requires ($M + NH_4$), 391.1416]; $[\alpha]_D^{24}$ +1.62° (*c* 0.62); ν_{max}/cm^{-1} 2955, 2861, 2255 (CN), 1695 (C=C), 1466, 1363, 1200, 1099, 1000, 968, 912 and 831; δ_H 5.89 (1 H, dt, *J* 15.1, 7.5, 2″-H), 5.40 (1 H, tdd, *J* 15.1, 9.6, 0.9, 1″-H), 4.03 (1 H, ddd, *J* 12.0, 4.6, 1.8, 6-H^{α}), 3.92 (2 H, m, 3″-H), 3.54 (1 H, ddd, *J* 10.3, 9.6, 4.9, 4-H), 3.46 (1 H, dt, *J* 12.0, 2.3, 6-H^{β}), 3.37 (1 H, ddd, *J* 9.6, 6.5, 3.5, 2-H), 2.69–2.42 (2 H, ABX_q, *J* 16.8, 6.5, 3.5, 2′-H_2), 2.13 (1 H, aq, *J* 9.6, 3-H), 1.90–1.60 (2 H, m, 5-H), 0.92 (9 H, s, Bu^{t}Si), 0.10 (3 H, s, MeSi) and 0.06 (3 H, s, MeSi); δ_C 17.97 and 117.12 (C); 53.36, 71.46, 74.56, 131.63 and 132.66 (CH); 23.08, 31.54, 35.10 and 65.85 (CH_2); −4.55, −4.18 and 25.72 (Me).

(+)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[(E)-3″-*hydroxyprop*-1″-*enyl*]*tetrahydropyran*-2-*yl*}*acetonitrile* **24**.—Potassium acetate (0.73 g, 4 mol equiv.) and 18-crown-6 (50 mg) were added to a solution of compound **23** (650 mg, 1.74 mmol) in acetone (20 cm^3) and this mixture was refluxed for 2 h. The reaction mixture was allowed to cool and was then poured into saturated aq. $NaHCO_3$ (20 cm^3) and extracted with diethyl ether (4 × 30 cm^3). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure to yield a pale yellow oil. This was dissolved in dry MeOH (15 cm^3) containing sodium methoxide (20 mg). After being stirred at room temperature for 12 h, the reaction mixture was diluted with saturated aq. NH_4Cl (20 cm^3) and extracted with diethyl ether (4 × 30 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (30% ethyl acetate–light petroleum) to yield *compound* **24** (448 mg, 83%) as a viscous oil, R_f 0.35 [Found: *m/z* (CI, NH_3) ($M^+ + NH_4$), 329.2224. $C_{16}H_{29}NO_3Si$ requires ($M + NH_4$), 329.2256]; $[\alpha]_D^{22}$ + 9.4° (*c* 0.98); ν_{max}/cm^{-1} 3480 (OH), 2958, 2933, 2860, 2256 (CN), 1464 (C=C), 1251, 1100, 1002, and 837; δ_H 5.83 (1 H, td, *J* 15.4, 5.2, 2″-H), 5.34 (1 H, tdd, *J* 15.4, 9.7, 1.6 Hz, 1″-H), 4.13 (2 H, m, 3″-H_2), 4.01 (1 H, ddd, *J* 11.9, 4.7, 1.9, 6-H^{α}), 3.61–3.33 (3 H, m, 2- and 4-H and 6-H^{β}), 2.70–2.43 (2 H, ABX_q, *J* 16.8, 6.3, 4.0, 2′-H_2), 2.10 (1 H, aq., *J* 9.7, 3-H), 1.88–1.59 (2 H, m, 5-H_2), 1.57(1 H, br s, OH), 0.86 (9 H, s, Bu^{t}Si), 0.04 (3 H, s, MeSi) and 0.00 (3 H, s, MeSi); δ_C 17.98 and 117.46 (C); 53.73, 71.50, 74.70, 128.28 and 134.83 (CH); 23.17, 35.17, 62.97 and 65.85 (CH_2); −4.60, −4.22 and 25.67 (Me).

(+)-{2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-2-[(E)-2″-*formylvinyl*]*tetrahydropyran*-2-*yl*}*acetonitrile* **25**.—Dry DMSO (0.50 cm^3, 2.2 mol equiv.) was added to a solution of oxalyl dichloride (0.31 cm^3, 1.1 mol equiv.) in dry CH_2Cl_2 (10 cm^3) at −60 °C followed, after 2 min, by a solution of the addition of compound **24** (1.00 g, 3.21 mmol) in dry CH_2Cl_2 (10 cm^3). After the solution had been stirred for 15 min at −60 °C, dry Et_3N (2.20 cm^3) was added and the reaction mixture was allowed to warm to room temperature before being poured onto saturated aq. NH_4Cl (20 cm^3); the aqueous layer was then extracted with CH_2Cl_2 (3 × 30 cm^3). The combined organics were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (30% ethyl acetate–light petroleum) to afford *compound* **25** (0.96 g, 96%) as a solid, m.p. 66 °C; R_f 0.44 (40% ethyl acetate–light petroleum) (Found: C, 62.25; H, 9.0; N, 4.35. Calc. for $C_{16}H_{27}NO_3Si$: C, 62.10; H, 8.79; N, 4.53%); $[\alpha]_D^{22}$ +24.6° (*c* 0.80); ν_{max}/cm^{-1} 2959, 2934, 2861, 2255 (CN), 1693 (CO), 1253, 1109 and 838; δ_H 9.48 (1 H, d, *J* 7.4, 3″-H), 6.48 (1 H, dd, *J* 15.7, 9.6, 1″-H), 6.22 (1 H, dd, *J* 15.7, 7.4, 2″-H), 4.02 (1 H, ddd, *J* 12.0, 4.8, 1.9, 6-H^{α}), 3.66 (1 H, ddd, *J* 10.4, 9.6, 4.9, 4-H), 3.54–3.41 (2 H, m, 2-H and 6-H^{β}), 2.62–2.31 (3 H, m, 3-H and 2′-H_2), 1.90–1.58 (2 H, m, 5-H), 0.98 (9 H, s, Bu^{t}Si), −0.03 (3 H, s, MeSi) and −0.09 (3 H, s, MeSi).

{(2R,3R,4R)- *and* (2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[3″(S)-*and* (R)-(E)-*hydroxyoct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}-*acetonitrile* **26a** *and* **26b**.—A vigorously stirred solution of compound **25** (206 mg, 0.67 mmol) in dry diethyl ether (2 cm^3) was saturated with anhydrous magnesium bromide (400 mg) and cooled to 0 °C. To this solution was added an ethereal solution of freshly prepared pentylmagnesium bromide (2 cm^3, 4 mol equiv.) and the reaction mixture was stirred at 0–5 °C for 2 h and then quenched with saturated aq. NH_4Cl (10 cm^3) and this mixture was extracted with diethyl ether (3 × 20 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (10% Et_2O–CH_2Cl_2) separated the two epimers **26a** (112 mg, 44%), R_f 0.32 and **26b** (66 mg, 26%), R_f 0.22 as viscous oils.

Compound **26a**: [Found: *m/z* (CI, NH_3) ($M^+ + NH_4 - H_2O$), 381.2937. $C_{21}H_{39}NO_3Si$ requires ($M + NH_4 - H_2O$), 381.2936]; $[\alpha]_D^{21}$ +26.2° (*c* 1.00); ν_{max}/cm^{-1} 3460 (OH), 2959, 2933, 2860, 2255 (CN), 1464, 1362, 1250, 1106, 1001, 973, 910 and 837; δ_H 5.73 (1 H, dd, *J* 15.4, 6.0, 2″-H), 5.30 (1 H, ddd, *J* 15.4, 9.6, 1.2, 1″-H), 4.12–3.98 (2 H, m, 6-H^{α} and 3″-H), 3.56 (1 H, ddd, *J* 11.0, 9.6, 5.5, 4-H), 3.46 (1 H, dt, *J* 12.0, 2.4, 6-H^{β}), 3.35 (1 H, ddd, *J* 9.6, 6.3, 3.8, 2-H), 2.68–2.40 (2-H, ABX_q, *J* 16.8, 6.3, 3.8, 2′-H_2), 2.10 (1 H, aq., *J* 9.6, 3-H), 1.89–1.22 (11 H, m, 5-, 4″-, 5″-, 6″-, 7″-H_2 and OH), 0.88 (12 H, m, Bu^{t}Si and 8″-H_3), 0.05 (3 H, s, MeSi) and 0.03 (3 H, s, MeSi); δ_C 18.00 and 117.33 (C); 53.62, 71.65, 72.41, 74.71, 127.62 and 138.84 (CH); 22.55, 23.12, 25.34, 31.68, 35.22, 37.37 and 65.81 (CH_2); −4.46, −4.10, 13.95 and 25.76 (Me).

Compound **26b**: [Found: *m/z* (CI, NH_3) ($M^+ + NH_4 - H_2O$), 381.2937. $C_{21}H_{39}NO_3Si$ requires ($M + NH_4 - H_2O$), 381.2936]; $[\alpha]_D^{21}$ +4.0° (*c* 0.40); ν_{max}/cm^{-1} identical with that of compound **26a**; δ_H 5.74 (1 H, dd, *J* 15.4, 5.6, 2″-H), 5.32 (1 H, ddd, *J* 15.4, 9.6, 1.2, 1″-H), 4.10 (1 H, aq., *J* 9.6, 3″-H), 4.08 (1 H, ddd, *J* 11.9, 4.7, 1.9, 6-H^{α}), 3.55 (1 H, ddd, *J* 10.4, 9.7, 4.9, 4-H), 3.46 (1 H, dt, *J* 11.9, 2.4, 6-H^{β}), 3.36 (1 H, ddd, *J* 9.7, 6.1, 4.2, 2-H), 2.69–2.44 (2 H, ABX_q *J* 16.8, 6.1, 4.2, 2′-H), 2.08 (1 H, aq., *J* 9.7, 3-H), 1.89–1.2 (11 H, m, 5-, 4″-, 5″-, 6″- and 7″-H_2 and OH), 0.89 (12 H, m, Bu^{t}Si and 8″-H_3), 0.04 (3 H, s, MeSi) and 0.00 (3 H, s, MeSi); δ_C 17.97 and 117.58 (C); 53.79, 71.63, 72.02, 74.76, 127.45 and 138.81 (CH); 22.53, 23.15, 24.98, 31.75, 35.23, 37.40 and 65.82 (CH_2); −4.54, −4.17, 13.96 and 25.72 (Me).

(+)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[(E)-3″-*oxooct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}*acetonitrile* **26c**.—Compound **26b** (100 mg, 0.26 mmol) was oxidized following the Swern procedure described in the preparation of compound **25**.

Purification was effected by bulb-to-bulb distillation (144 °C at 0.15 mmHg) to yield *compound* **26c** (94 mg, 95%) as an oil, R_f 0.21 (CH_2Cl_2) [Found: *m/z* (CI, NH_3) ($M^+ + H$), 380.2621. $C_{21}H_{37}NO_3Si$ requires (M + H), 380.2617]; $[\alpha]_D^{25}$ +7.1° (*c* 0.34); ν_{max}-cm^{-1} 2957, 2931, 2858, 2255 (CN), 1696 (CO), 1631 (C=C), 1128, 1103 and 840; δ_H 6.45 (1 H, dd, *J* 15.6, 9.2, 1″-H), 6.33 (1 H, d, *J* 15.6, 2″-H), 4.06 (1 H, ddd, *J* 11.9, 4.7, 1.8, 6-H_α), 3.64 (1 H, ddd, *J* 10.5, 9.2, 4.9, 4-H), 3.50 (1 H, dt, *J* 11.9, 2.4, 6-H^β), 3.46 (1 H, ddd, *J* 9.2, 6.0, 3.6, 2-H), 2.65–2.37 (4 H, ABX_q, *J* 16.9, 6.0, 3.6, 2′-H_2 and t, *J* 7.4, 4″-H_2), 2.29 (1 H, aq., *J* 9.2, 3-H), 1.92–1.55 (4 H, m, 5- and 5″-H_2), 1.40–1.2 (4 H, m, 6″- and 7″-H_2), 0.89 (3 H, t, *J* 5.0, 8″-H_2), 0.84 (9 H, s, Bu^{t}Si), 0.04 (3 H, s, MeSi) and −0.04 (3 H, s, MeSi); δ_C 18.00, 116.71 and 199.09 (C); 53.56, 71.08, 73.78, 133.92 and 141.63 (CH); 22.45, 23.39, 23.55, 31.43, 34.82, 41.52 and 65.92 (CH_2); −4.66, −4.17, 13.91 and 25.63 (Me).

Alternative Preparation of Isomer **26a**.—A 1 mol dm^{-3} THF solution of $LiAlH_4$ (396 mm^3, 3 mol equiv.) was added to a 1 mol dm^{-3} THF solution of ethanol (396 mm^3, 3 mol equiv.) at 0 °C. A solution of (*S*)-(−)-1,1′-bi-2-naphthol (113 mg, 3 mol equiv.) in dry THF (0.50 cm^3) was added and the resulting mixture was stirred at room temperature for 1 h. A solution of compound **26c** (50 mg, 0.13 mmol) in dry THF (0.50 cm^3) was added to the mixture at −100 °C, and the mixture was stirred for 2 h at this temperature and then for 2 h at −78 °C. MeOH (50 mm^3) was added, and the mixture was warmed to room temperature, poured into saturated aq. NH_4Cl (5 cm^3), and extracted with diethyl ether (3 × 10 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (CH_2Cl_2 to 10% Et_2O–CH_2Cl_2), and the two epimers **26a** (46 mg, 91%) and **26b** (1 mg, 2%) were isolated as oils. R_f-Values (mixed spot), $[\alpha]_D$ for **26a**, IR and ^1H NMR spectra for both compounds were in full agreement with those previously reported.

(+)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[3″(S)-(E)-(*t-butyldimethylsiloxy*)*oct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}*acetonitrile* **27a**.—The hydroxy group in compound **26a** (224 mg, 0.59 mmol) was protected as the Bu^tMe_2Si ether following the procedure previously described in the preparation of compound **11**. Purification was effected by flash chromatography (CH_2Cl_2) to yield *compound* **27a** (251 mg, 96%) as a solid, R_f 0.52; m.p. 66–67 °C (Found: C, 65.3; H, 10.8; N, 2.8. $C_{27}H_{53}NO_3Si_2$ requires C, 65.40; H, 10.77; N, 2.82%); $[\alpha]_D^{21}$ +23.9° (*c* 1.00); ν_{max}/cm^{-1} 2959, 2933, 2900, 2860, 2255 (CN), 1464, 1251, 1142, 1124, 1099, 910, 836 and 739; δ_H 5.73 (1 H, dd, *J* 15.6, 3.9, 2″-H), 5.31 (1 H, ddd, *J* 15.6, 9.5, 2.8, 1″-H), 4.16–4.07 (1 H, m, 3″-H), 4.02 (1 H, ddd, *J* 11.9, 4.4, 1.8, 6-H^α), 3.57 (1 H, ddd, *J* 10.4, 9.5, 4.7, 4-H), 3.47 (1 H, dt, *J* 11.9, 2.3, 6-H^β), 3.32 (1 H, ddd, *J* 9.5, 6.5, 3.6, 2-H), 2.71–2.41 (2 H, ABX_q, *J* 16.5, 6.5, 3.6, 2′-H_2), 2.10 (1 H, aq., *J* 9.5, 3-H), 1.90–1.60 (2 H, m, 5-H_2), 1.52–1.20 (8 H, m, 4″-, 5″-, 6″- and 7″-H_2), 0.90 (21 H, m, 2 × Bu^{t}Si and 8″-H_3), 0.05 (6 H, br s, 2 × MeSi), 0.03 (3 H, s, MeSi) and 0.01 (3 H, s, MeSi); δ_C 17.95, 18.14 and 117.33 (C); 53.14, 71.70, 72.63, 74.91, 126.31 and 139.50 (CH); 22.55, 23.00, 24.42, 31.89, 35.26, 38.12 and 65.63 (CH_2); −4.45, −4.41, −4.35, −3.96, 13.97, 25.80 and 25.85 (Me); *m/z* (EI) 438 ($M - Bu^t$); Δε (MeCN; 191 nm) +7.25.

(+)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[3″(R)-(E)-(*t-butyldimethylsiloxy*)*oct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}*acetonitrile* **27b**.—The hydroxy group in compound **26b** (42 mg, 0.10 mmol) was protected as the Bu^tMe_2Si ether following the procedure previously described for the preparation of compound **11**. Purification was effected by flash chromatography (CH_2Cl_2) to yield *compound* **27b** (45 mg, 93%) as a viscous oil., R_f 0.55 (Found: C, 65.6; H, 10.7; N, 3.0. $C_{27}H_{53}NO_3Si_2$ requires C, 65.40; H, 10.77; N, 2.82%); $[\alpha]_D^{21}$ +16.2° (*c* 0.90); ν_{max} identical with that of compound **27a**; δ_H 5.66 (1 H, dd, *J* 15.9, 5.7, 2″-H), 5.18 (1 H, ddd, *J* 15.9, 10.0, 1.3, 1″-H), 4.15–4.07 (1 H, m, 3″-H), 4.01 (1 H, ddd, *J* 12.0, 4.8, 1.9, 6-H^α), 3.53 (1 H, ddd, *J* 10.0, 9.0, 5.0, 4-H), 3.45 (1 H, dt, *J* 12.0, 2.2, 6-H^β), 3.35 (1 H, ddd, *J* 10.0, 6.7, 3.5, 2-H), 2.72–2.41 (2 H, ABX_q, *J* 16.8, 6.7, 3.5, 2′-H_2), 2.06 (1 H, aq., *J* 10.0, 3-H), 1.90–1.40 (10 H, m, 5-, 4″-, 5″-, 6″- and 7″-H_2), 0.87 (21 H, m, 2 × Bu^{t}Si and 8‴-H_2), 0.05 (3 H, s, MeSi), 0.04 (3 H, s, MeSi), 0.03 (3 H, s, MeSi) and 0.01 (3 H, s, MeSi); δ_C 18.01, 18.14 and 117.39 (C); 53.05, 71.80, 71.91, 74.93, 125.81 and 138.80 (CH); 22.54, 22.93, 25.18, 31.87, 35.26, 38.27 and 65.65 (CH_2); −4.70, −4.39, −4.36, −4.24, 13.97, 25.84 and 25.86 (Me); *m/z* (EI) 438 ($M - Bu^t$)$^+$; Δε (MeCN; 191 nm) −2.00.

(−)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[3″(S)-(E)-(*t-butyldimethylsiloxy*)*oct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}*acetaldehyde* **29**.—A 1 mol dm^{-3} solution of Dibal (400 mm^3, 2.0 mol equiv.) in toluene was added to a mixture of compound **27a** (94 mg, 0.19 mmol) and dry toluene (2 cm^3)) at −78 °C. The reaction mixture was warmed to 0 °C and, after being stirred for 10 min, was then cooled to −90 °C. Methanol (1 cm^3) was added, followed by saturated aq. NH_4Cl (1 cm^3), and the reaction mixture was allowed to warm to room temperature before being poured into saturated aq. NH_4Cl (10 cm^3) and extracted with diethyl ether (3 × 20 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (CH_2Cl_2) separated the starting material (32 mg, 34% recovery) and *compound* **29** (40 mg, 42%) as a viscous oil, R_f 0.30 [Found: *m/z* (CI, NH_3) ($M^+ + NH_4$) 516.3904. $C_{27}H_{54}O_4Si_2$ requires ($M + NH_4$), 516.3898]; $[\alpha]_D^{24}$ −0.8° (*c* 0.80); ν_{max}/cm^{-1} 2959, 2900, 2859, 2738 (CH ald), 1726 (CO), 1464, 1362, 1249, 1095, 972, 915 and 834; δ_H 9.73 (1 H, dd, *J* 3.1, 1.5, 1′-H), 5.61 (1 H, dd, *J* 15.4, 3.8, 2″-H), 5.30 (1 H, ddd, *J* 15.4, 9.1, 1.6, 1″-H), 4.09 (1 H, adq., *J* 5.9, 1.3, 3″-H), 3.95 (1 H, ddd, *J* 11.7, 4.6, 1.8, 6-H^α), 3.55 (1 H, ddd, *J* 10.6, 9.3, 4.8, 4-H), 3.44 (1 H, dt, *J* 11.7, 2.2, 6-H^β), 3.31 (1 H, m, 2-H) 2.72–2.43 (2 H, d of ABX_q, *J* 16.4, 8.7, 3.3, 3.1, 1.5, 2′-H_2), 2.00 (1 H, aq., *J* 9.5, 3-H), 1.90–1.16 (10 H, m, 5-, 4″-, 5″-, 6″- and 7″-H_2), 0.88 (21 H, m, 2 × Bu^{t}Si and 8″-H_2), 0.06 (3 H, s, MeSi), 0.04 (3 H, s, MeSi), 0.03 (3 H, s, MeSi) and 0.00 (3 H, s, MeSi); δ_C 18.04 and 18.14 (C); 53.76, 71.92, 72.29, 75.14, 126.55, 138.23 and 201.24 (CH); 22.55, 25.17, 31.88, 35.65, 38.28, 47.64 and 65.71 (CH_2); −4.71, −4.39, −4.33, −4.21, 13.97 and 25.87 (Me).

Methyl (2R,3S,4R)-7′-{4-*Hydroxy*-3-[(E)-3″-*hydroxyoct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}-6′-*oxoheptanoate* **31**.—A slurry of dry magnesium powder (140 mg, 40 mol equiv.) in dry THF (5 cm^3) was refluxed for 30 min with 1,4-dibromobutane (345 mm^3, 20 mol equiv.) and a crystal of I_2 before being cooled to 0–5 °C. Anhydrous $MgBr_2$ (1.00 g) was added to the vigorously stirred mixture, followed by the dropwise addition of a solution of compound **29** (60 mg, 0.12 mmol) in dry THF (5 cm^3). After being stirred for 1.5 h at 0–5 °C, the reaction mixture was cooled to −78 °C and excess of CO_2(s) was added. This mixture was allowed to reach room temperature and poured into 20% aq. tartaric acid (10 cm^3). After extraction with diethyl ether (4 × 25 cm^3), the combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. The resultant pale yellow oil was dissolved in diethyl ether (5 cm^3) and excess of diazomethane (CH_2N_2 in Et_2O) was added. After storage for 2 h at room temperature the excess of CH_2N_2 was quenched with acetic acid and the mixture was poured into saturated aq. $NaHCO_3$ (10 cm^3). This mixture was extracted with diethyl ether (3 × 25 cm^3) and the combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure.

Oxidation of this crude mixture following the Swern procedure described in the preparation of compound **25** produced compound **28**. This oil was filtered through silica gel (10%

Et_2O–CH_2Cl_2) to remove baseline material and, after concentration under reduced pressure, was dissolved in dry THF (1 cm^3).

A 1 mol dm^{-3} THF solution of TBAF (1 cm^3) was added and this mixture was stirred for 18 h at room temperature. The reaction mixture was concentrated under reduced pressure and the residual oil was purified by flash chromatography (85% ethyl acetate–light petroleum) to yield *compound* **31** (16 mg, 34%) as a low melting solid, m.p. <40 °C; R_f 0.19 [Found: *m/z* (CI, NH_3) ($M^+ + NH_4$), 402.2856. $C_{21}H_{36}O_6$ requires ($M + NH_4$), 402.2849]; $[\alpha]_D^{24}$ +30.6° (*c* 0.16); ν_{max}/cm^{-1} 3414 (OH), 2931, 2859, 1720br (CO and CO_2Me), 1436, 1371, 1198, 1116, 1045 and 974; δ_H 5.66 (1 H, dd, *J* 15.4, 6.9, 2″-H), 5.30 (1 H, br dd, *J* 15.4, 9.8, 1″-H), 4.05 (1 H, br aq., *J* 7.0, 3″-H), 3.95 (1 H, ddd, *J* 11.8, 6.1, 1.4, 6-H^{α}), 3.67–3.36 (6 H, m, 2- and 4-H, 6-H^{β} and MeO), 2.61–2.26 (8 H, m, 2′-, 5′- and 7′-H_2 and 2 × OH), 1.98–1.79 (2 H, m, 3-H and 5-H^{α}), 1.68–1.23 (13 H, m, 5-H^{β}, 3′-, 4′-, 4″-, 5″-, 6″- and 7″-H_2) and 0.88 (3 H, m, 8″-H_3); δ_C 173.85 and 208.73 (C); 54.76, 70.60, 72.54, 75.49, 128.30 and 139.20 (CH); 22.57, 22.80, 24.34, 25.14, 31.65, 33.52, 33.77, 37.24, 43.48, 46.98 and 65.87 (CH_2); 13.93 and 51.45 (Me).

Methyl {(2R,3S,4R,5′Z)-7′-{4-*Hydroxy*-3-[(E)-3″-*hydroxy*-*oct*-1″-*enyl*]*tetrahydropyran*-2-*yl*}*hept*-5′-*enoate* **33a**.—Butyllithium (340 mm^3, 8 mol equiv.) was added to a vigorously stirred solution of carboxybutyl(triphenyl)phosphonium bromide (128 mg, 4 mol equiv.) in dry THF (2.5 cm^3). After 30 min, a solution of compound **29** (34 mg, 0.07 mmol) in dry THF (1 cm^3) was added and this mixture was stirred at room temperature for 1 h. The reaction mixture was poured into saturated aq. NH_4Cl (10 cm^3), and this mixture was extracted with ethyl acetate (4 × 25 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. The resultant oil was dissolved in diethyl ether (2 cm^3) and treated with excess of CH_2N_2 in Et_2O. After 2 h, the excess of CH_2N_2 was quenched with acetic acid and the reaction mixture was poured onto saturated aq. $NaHCO_3$ (10 cm^3). This mixture was extracted with diethyl ether (3 × 25 cm^3) and the combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. After filtration through silica gel (15% ethyl acetate–light petroleum) to remove baseline material and concentration under reduced pressure, the oily residue was dissolved in dry THF (1 cm^3) and a mol dm^{-3} THF solution of TBAF (1 cm^3) was added. The reaction solution was stirred for 18 h at room temperature and then concentrated under reduced pressure. Purification was effected by flash chromatography (60% EtOAc–CH_2Cl_2) to afford an inseparable mixture of the Z- and E-*isomers* (**33a** and **33b**) (~3:1 by ^{13}C NMR spectroscopy (13 mg, 52%) as an oil, R_f 0.22 [Found: *m/z* (CI, NH_3) ($M^+ + NH_4$), 386.2930. $C_{21}H_{36}O_5$ requires ($M + NH_4$), 386.2901]; ν_{max}/cm^{-1} 3428 (OH), 3000, 2957, 2932, 2860, 1728 (CO_2Me), 1437, 1200, 1118, 1061, and 972; δ_H 5.76–5.38 (4 H, m, 5′-, 6′-, 1″- and 2″-H), 4.16–3.98 (2 H, m, 6-H^{α} and 3″-H), 3.67 (3 H, s, MeO), 3.53–3.36 (2 H, m, 6-H^{β} and 4-H), 3.18–3.08 (1 H, m, 1-H), 2.54–1.26 (21 H, m, 3-H, 5-, 2′-, 3′-, 4′-, 7′-, 4″-, 5″-, 6″-, 7″-H_2 and 2 × OH) and 0.90–0.80 (3 H, m, 8″-H_3); δ_C 174.18 (C); 54.05, 54.34, 70.73, 72.46, 72.82, 78.66, 79.01, 126.75, 127.10, 128.15, 128.62, 130.21, 131.46, 138.70 and 138.86 (CH); 22.57, 24.61, 24.71, 25.17, 26.75, 31.49, 31.72, 31.91, 33.39, 33.54, 36.73, 37.36 and 65.87 (CH_2); 13.96 and 51.46 (Me).

(+)-[(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-(*prop*-2″-*enyloxy*)*tetrahydropyran*-2-*yl*]*acetonitrile* **35**.—Silver(I) oxide (34.0 g, 3 mol equiv.) was slurried with a solution of compound **15** (13.0 g, 47.9 mmol) in dry DMF (200 cm^3). Freshly distilled allyl bromide (17 cm^3, 3 mol equiv.) was added and the reaction mixture was stirred at room temperature for 48 h. After a quench with water (500 cm^3), the reaction mixture was filtered through Celite and extracted with diethyl ether (3 × 500 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (15% ethyl acetate–light petroleum) to afford *compound* **35** (13.4 g, 90%) as a solid, R_f 0.42 (20% ethyl acetate–light petroleum), m.p. 57–58 °C (Found: C, 61.9; H, 9.3; N, 4.3. Calc. for $C_{16}H_{29}NO_3Si$: C, 61.69; H, 9.38; N, 4.50%); $[\alpha]_D^{21}$ +31.5 (*c* 1.00); ν_{max}/cm^{-1} 3086, 2930, 2862, 2254 (CN), 1464, 1381, 1259, 1100, 1005, 911, 844 and 740; δ_H 5.97–5.80 (1 H, m, 2″-H), 5.29–5.13 (2 H, m, 3″-H), 4.45–4.04 (2 H, t of ABX_q, *J* 12.5, 6.2, 5.5, 1.4, 1.3, 1″-H_2), 3.91 (1 H, ddd, *J* 11.9, 4.7, 1.9, 6-H^{α}), 3.70 (1 H, ddd, *J* 10.7, 8.3, 5.4, 4-H), 3.39 (1 H, ddd, *J* 12.1, 12.1, 2.6, 6-H^{β}), 3.34–3.25 (1 H, m, 2-H), 3.04 (1 H, dd, *J* 8.3, 8.0, 3-H), 2.80–2.58 (2 H, ABX_q, *J* 16.8, 5.9, 3.9, 2′-H_2), 1.88–1.62 (2 H, m, 5-H), 0.89 (9 H, br s, Bu^{t}Si) and 0.08 (6 H, 2 s, 2 × MeSi); δ_C 17.87 and 117.30 (C); 74.09, 74.95, 81.91 and 134.40 (CH); 21.38, 35.07, 65.50, 74.24 and 117.37 (CH_2); −4.66, −4.44 and 25.77 (Me); *m/z* (EI) 254 ($M - Bu^t$)$^+$

[(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-(*oxiranylmethoxy*)-*tetrahydropyran*-2-*yl*]*acetonitrile* **36**.—Sodium hydrogen carbonate (8.20 g, 3 mol equiv.) was slurried with a solution of compound **35** (9.00 g, 28.89 mmol) in CH_2Cl_2 (300 cm^3) at 0 °C. *m*-Chloroperbenzoic acid (MCPBA) (12.80 g, 2 mol equiv.) was added and, after being stirred for 10 min at 0 °C, the reaction mixture was allowed to warm to room temperature. It was then stirred for 48 h before being diluted with CH_2Cl_2 (300 cm^3), washed successively with saturated aq. Na_2SO_3 (3 × 200 cm^3), saturated aq. $NaHCO_3$ (200 cm^3), water (200 cm^3), and brine (200 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Purification was effected by flash chromatography (30% ethyl acetate–light petroleum) to afford *compound* **36** (8.45 g, 89%) as an inseparable mixture of *epimers* (~2.7:1, ^{13}C NMR spectroscopy), R_f 0.39 (40% ethyl acetate–light petroleum); m.p. 58–61 °C (Found: C, 58.5; H, 8.9; N, 4.1. Calc. for $C_{16}H_{29}NO_4Si$: C, 58.68; H, 8.93; N, 4.28%); ν_{max}/cm^{-1} 2957, 2862, 2255 (CN), 1464, 1381, 1256, 1105, 1003, 902, 841 and 721; δ_H 4.23 (0.2 H, add, *J* 11.0, 2.2, 2″-H), 3.96–3.81 (2.4 H, m, 6-H^{α} and 1″-H), 3.70 (1 H, br ddd, *J* 10.8, 8.3, 5.3, 4-H), 3.45–3.25 (2.4 H, m, 6-H^{β}, 2- and 1″-H), 3.14–2.99 (2 H, m, 3- and 1″-H), 2.84–2.50 (4 H, m, 2′- and 3″-H_2), 1.89–1.60 (2 H, m, 5-H_2), 0.90 (9 H, br s, Bu^{t}Si) and 0.01 (6 H, br s, 2 × MeSi); δ_C 17.85, 117.33 and 117.42 (C); 50.34, 50.83, 73.98, 74.03, 74.78, 74.99, 83.00 and 83.26 (CH); 21.25, 35.02, 44.25, 44.28, 65.45, 73.26 and 75.20 (CH_2); −4.71, −4.63, −4.34 and 25.76 (Me); *m/z* (EI) 270 [M − Bu^t]$^+$.

(+)-(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[(S)- *and* (*R*)-(2″-*hydroxyheptyloxy*)*tetrahydropyran*-2-*yl*]*acetonitrile* **37a** *and* **37b**.—A 1.6 mol dm^{-3} hexane solution of butyllithium (194 cm^3, 12 mol equiv.) was added dropwise to a slurry of copper(I) iodide (29.5 g, 6 mol equiv.) in dry diethyl ether at −30 °C. This mixture was then stirred for 30 min before being cooled to −78 °C, when a solution of compound **36** (8.45 g, 25.84 mmol) in dry diethyl ether (100 cm^3) was added and the mixture was stirred for 10 h. After a cautious quench with saturated aq. NH_4Cl (250 cm^3) at −78 °C, the reaction mixture was allowed to warm to room temperature and the aqueous layer was extracted with diethyl ether (4 × 100 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (10% Et_2O–CH_2Cl_2) separated the two epimers, **37a** (5.43 g, 55%), R_f 0.32 and **37b** (2.04 g, 20%), R_f 0.25, as viscous oils.

Compound **37a**: (Found: C, 62.2; H, 10.4; N, 3.7. Calc. for $C_{20}H_{39}NO_4Si$: C, 62.29; H, 10.19; N, 3.63%); $[\alpha]_D^{20}$ +18.1° (*c* 0.60); ν_{max}/cm^{-1} 3507 (OH), 2957, 2933, 2868, 2255 (CN), 1257, 1134, 1092, 1004, 908, 838 and 777; δ_H 3.92 (1 H, ddd, *J* 11.9, 4.8, 1.8, 6-H^{α}), 3.78–3.60 (4 H, m, 4-H, 1″-H_2 and 2″-H), 3.40 (1 H, dt,

J 11.9, 2.4, 6-H$^{\beta}$), 3.35–3.27 (1 H, m, 2-H), 3.14 (1 H, at, *J* 8.7, 3-H), 2.84–2.65 (2 H, ABX_q, *J* 16.8, 5.7, 4.1, 2′-H_2), 2.59 (1 H, d, *J* 2.5, OH), 1.93–1.64 (2 H, m, 5-$H)_2$), 1.60–1.15 (8 H, m, 3″-, 4″-, 5″- and 6″-H_2), 0.90 (12 H, br s, 7″-H_3 and Bu^{t}Si) and 0.15 (6 H, 2 s, 2 × MeSi); δ_C 17.92 and 117.30 (C); 71.07, 74.06, 75.15 and 83.28 (CH); 21.42, 22.51, 25.08, 31.83, 32.97, 35.08, 65.42 and 77.97 (CH_2); −4.45, −4.25, 13.93 and 25.84 (Me); *m/z* (EI) 328 (M − Bu^t).

Compound **37b**: (Found: C, 62.0; H, 10.5; N, 3.9%); $[\alpha]_D^{21}$ +13.8° (*c* 1.00); ν_{max}/cm^{-1} identical with that of **37a**; δ_H 3.97–3.86 (2 H, m, 6-H$^{\alpha}$ and 1″-H$^{\alpha}$), 3.80–3.63 (2 H, m, 4- and 2″-H), 3.46–3.28 (3 H, m, 6-H$^{\beta}$, 1″-H$^{\beta}$ and 2-H), 3.03 (1 H, t, *J* 8.7, 3-H), 2.86–2.65 (2 H, ABX_q, *J* 16.5, 5.8, 4.1, 2′-H_2), 2.20 (1 H, br s, OH), 1.89–1.61 (2 H, m, 5-H_2), 1.60–1.11 (8 H, m, 3″-, 4″-, 5″- and 6″-H_2), 0.90 (12 H, br s, 7-H_3 and Bu^{t}Si) and 0.10 (6 H, 2 s, 2 × MeSi); δ_C 17.87 and 117.45 (C); 70.88, 73.90, 75.10 and 83.13 (CH); 21.41, 22.48, 25.10, 31.77, 33.19, 35.05, 65.43 and 78.20 (CH_2); −4.56, 4.28, 13.90 and 25.76 (Me); *m/z* (EI) 328 (M − Bu^t)$^+$.

(+)-[(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-(2-*oxoheptyloxy*)*tetrahydropyran*-2-*yl*]*acetonitrile* **37c**.—Compound **37b** (468 mg, 1.22 mmol) was oxidized following the Swern procedure described in the preparation of compound **25**. Purification was effected by flash chromatography (CH_2Cl_2) to yield *compound* **37c** (373 mg, 83%) as an oil; R_f 0.09 (Found: C. 62.3; H, 9.8; N, 4.0. $C_{20}H_{37}NO_4Si$ requires C, 62.62; H, 9.72; N, 3.65%); $[\alpha]_D^{21}$ +42.6° (*c* 1.00); ν_{max}/cm^{-1} 2957, 2930, 2858, 2252 (CN), 1731 (CO), 1468, 1382, 1257, 1138, 1090, 842 and 778; δ_H 4.53 (2 H, AB_q, *J* 17.9, 1″-H_2), 3.92 (1 H, ddd, *J* 11.9, 4.8, 1.7, 6-H$^{\alpha}$), 3.76 (1 H, ddd, *J* 10.9, 8.3, 5.3, 4-H), 3.47–3.36 (2 H, m, 2-H and 6-H$^{\beta}$), 3.07 (1 H, dd, *J* 8.9, 9.0, 3-H), 3.05–2.85 (2 H, ABX_q, *J* 17.0, 6.1, 3.7, 2′-H_2), 2.30 (2 H, t, *J* 7.3, 3″-H_2), 1.90–1.52 (4 H, m, 5- and 4″-H_2), 1.40–1.19 (4 H, m, 5″- and 6″-H_2), 0.90 (12 H, br s, 7″-H_3 and Bu^{t}Si) and 0.03 (6 H, br s, 2 × MeSi); δ_C 17.76, 117.73 and 207.21 (C); 74.57, 74.71 and 82.75 (CH); 21.57, 22.30, 23.13, 31.32, 34.97, 38.54, 65.41 and 77.54 (CH_2); −4.73, −4.28, 13.78 and 25.70 (Me); *m/z* (EI) 326 (M − Bu^t)$^+$.

Alternative Preparation of Compounds **37a** *and* **37b**.—Compound **37c** (100 mg, 0.26 mmol) was reduced following the Noyori procedure described in the preparation of compound **26a**. Purification was effected by flash chromatography (CH_2Cl_2 to 10% Et_2O–CH_2Cl_2) to afford compound **37a** (92 mg, 91%) and compound **37b** (2 mg, 2%) as viscous oils. R_f-Values (mixed spot), $[\alpha]_D$ for **37a**, and ^{1}H NMR spectra for both compounds agreed with those previously obtained.

(+)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[(S)-2″-(*t-butyldimethylsiloxy*)*heptyloxy*]*tetrahydropyran*-2-*yl*}*acetonitrile* **38**.—The hydroxy group in compound **37a** (2.86 g, 7.42 mmol) was protected as the Bu^tMe_2Si ether following the procedure previously described in the preparation of compound **11**. Purification was effected by flash chromatography (90% CH_2Cl_2–light petroleum) to yield *compound* **38** (3.41 g, 92%) as a solid; m.p. 58 °C; R_f 0.35 (CH_2Cl_2) (Found: C, 62.6; H, 10.7; N, 2.8. Calc. for $C_{26}H_{53}NO_4Si_2$ C, 62.47; H, 10.69; N, 2.80%); $[\alpha]_D^{21}$ +9.1° (*c* 1.00); ν_{max}/cm^{-1} 2957, 2254 (CN), 1474, 1381, 1246, 1091, 1003, 961, 909, 841 and 695; δ_H 3.98–3.84 (2 H, m, 6-H$^{\alpha}$ and 1″-H), 3.75–3.62 (2 H, m, 4- and 2″-H), 3.44–3.25 (3 H, m, 2-H, 6-H$^{\beta}$ and 1″-H), 2.98 (1 H, dd, *J* 8.6, 8.4, 3-H), 2.95–2.65 (2 H, ABX_q, *J* 16.8, 6.6, 3.5, 2′-H_2), 1.89–1.58 (2 H, m, 5-H_2), 1.58–1.20 (8 H, m, 3″-, 4″-, 5″- and 6″-H_2), 0.93–0.85 (21 H, 2 br s, 7″-H_3 and 2 × Bu^{t}Si) and 0.12–0.02 (12 H, 3 br s, 4 × MeSi); δ_C 17.86, 18.14 and 117.51 (C); 71.96, 74.10, 75.14 and 83.45 (CH); 21.43, 22.57, 24.86, 32.00, 23.26, 35.08, 65.29 and 77.40 (CH_2); −4.67, −4.48, −4.22, −4.14, 13.96, 25.84 and 25.91; *m/z* (EI) 443 (M − Bu^t)$^+$.

(−)-{(2R,3R,4R)-4-(*t-Butyldimethylsiloxy*)-3-[(S)-2″-(*t-butyldimethylsiloxy*)*heptyloxy*]*tetrahydropyran*-2-*yl*}*acetaldehyde* **39**.—Compound **38** (200 mg, 0.40 mmol) was reduced following the procedure used in the preparation of compound **29**. Flash chromatography (CH_2Cl_2) separated the starting material (42 mg, 21% recovery) and compound **39** (86 mg, 43%) as a viscous oil R_f 0.26 [Found: *m/z* (CI, NH_3) (M^+ + NH_4), 520.3853. $C_{26}H_{54}O_5Si_2$ requires (M + NH_4), 520.3846]; $[\alpha]_D^{21}$ −7.6° (*c* 0.85); ν_{max}/cm^{-1} 2957, 2931, 2859, 2725 (CHO), 1731 (C=O), 1257, 1128, 1093, 836 and 775; δ_H 9.76 (1 H, dd, *J* 2.7, 1.8, 1′-H), 3.95–3.59 (5 H, m, 2-, 4-, 1″-H, 2″-H and 6-H$^{\alpha}$), 3.44–3.30 (2 H, m, 6-H$^{\beta}$ and 1″-H), 2.96–2.85 (2 H, m, 3- and 2′-H), 2.55 (1 H, A part of d of ABX_q, *J* 16.2, 8.4, 2.7, 2′-H), 1.89–1.20 (10 H, m, 5-, 3″-, 4″-, 5″- and 6″-H_2), 0.89 (21 H, 2 br s, 7″-H_3 and 2 × Bu^{t}Si) and 0.13–0.02 (12 H, 3 br s, 4 × MeSi); δ_C 17.91 and 18.15 (C); 71.82, 74.37, 74.99, 84.20 and 200.78 (CH); 22.58, 24.78, 32.01, 34.38, 35.42, 46.66, 65.28 and 77.34 (CH_2); −4.66, −4.40, −4.19, −4.15, 13.96, 25.88 and 25.91 (Me).

(+)-*Methyl*{(2R,3S,4R)-7-[4-*Hydroxy*-3-[(S)-2″-*hydroxyheptyloxy*]*tetrahydropyran*-2-*yl*}-6′-*oxoheptanoate* **42**.—Compound **39** (31 mg, 0.062 mmol) was transformed into compound **42** by means of a procedure identical with that described earlier in the preparation of compound **31**. Purification was effected by flash chromatography (85% ethyl acetate–light petroleum) to yield *compound* **42** (10 mg, 42%) as a viscous oil; R_f 0.30 [Found: *m/z* (CI, NH_3) (M^+ + NH_4), 406.2799. $C_{20}H_{36}O_7$ requires (M + NH_4), 406.2797]; $[\alpha]_D^{21}$ +0.86° (*c* 0.51); ν_{max}/cm^{-1} 3418 (OH), 2935, 2864, 1738, (CO_2Me), 1720 (C=O), 1459, 1374, 1121, 1086 and 870; δ_H 3.90–3.63 (7 H, m, 4 H, 6-H$^{\alpha}$, 1″-H, 2″-H and MeO), 3.55 (1 H, ddd, *J* 9.2, 8.5, 3.6, 2-H), 3.49–3.32 (2 H, m, 6-H$^{\beta}$ and 1″-H), 2.94 (1 H, at, *J* 9.2, 3-H), 2.76–2.53 (2 H, ABX_q, *J* 15.0, 8.5, 3.6, 7′-H_2), 2.49 (2 H, br t, *J* 6.0, 5′-H_2), 2.32 (2 H, br t, *J* 6.5, 2′-H_2), 1.98–1.88 (1 H, m, 5-H$^{\alpha}$), 1.76–1.56 (5 H, m, 5-H$^{\beta}$, 3′- and 4′-H_2), 1.46–1.22 (10 H, m, 3″-, 4″-, 5″-, 6″-H_2 and 2 × OH) and 0.90 (3 H, br t, *J* 5.0, 7″-H_3); δ_C 173.85 and 208.30 (C); 72.20, 73.19, 76.08 and 86.34 (CH); 22.50, 22.84, 24.37, 25.01, 31.78, 33.05, 33.80, 33.83, 43.24, 45.56, 65.66 and 78.28 (CH_2); 13.94 and 51.45 (Me).

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