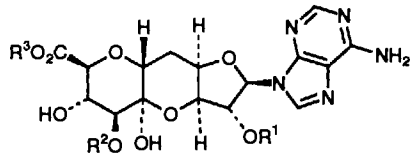
Short Synthetic Route to Congeners of the Undecose Antibiotic Herbicidin

John R. Bearder,[a] Mark L. Dewis[b] and Donald A. Whiting *,[b]
[a] *Shell Research Ltd., Sittingbourne, Kent ME9 8AG, UK*
[b] *Chemistry Department, The University, Nottingham NG7 2RD, UK*

The undecose backbone of the herbicidins has been assembled *via* direct alkylation, hydroxyalkylation, or acylation of the cyclic vinylanion **5** with the xylofuranose triflate **14**, aldehyde **6**, or acid chloride **10**, respectively.

The herbicidins **1a**–**1f** are a group of undecose (C_{11}) antibiotics which have been isolated from strains of *Streptomyces saganonensis*.[1] Herbicidins A and B exhibit potentially valuable herbicidal activity, with selective toxicity towards dicotyledonous plants, and these two compounds also inhibit *Xanthomonas oryzae*, a cause of rice leaf blight.[1a] Inhibitory effects on seed germination and on algal growth were also observed,[1a,c] while the group are markedly non-toxic to animals. The constitutions of these complex undecose nucleosides rest chiefly on a combination of X-ray crystallographic analysis and NMR spectroscopy,[1e] which reveal an unusual furanopyranopyran core ring structure, in which C-1 of a hexose (glucuronic acid derivative) is linked directly to C-5 of a pentose (xylofuranose moiety). Aureonucleomycin[2a] **1g** is closely related to the herbicidins, but very few other undecose-based antibiotics have been characterised. Only hikizimycin[2b] and tunicamycin[2c–e] are known to us, and these have different modes of linkage between the formal hexose-pentose subunits.



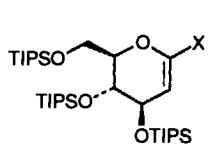
1a Herbicidin A $R^1 = R^3 = Me$, $R^2 = COC(CH_2OH)=CH_2$
1b Herbicidin B $R^1 = R^3 = Me$, $R^2 = H$
1c Herbicidin C $R^1 = R^2 = H$, $R^3 = Me$
1d Herbicidin E $R^1 = R^3 = Me$, $R_2 = COCHMe_2$
1e Herbicidin F $R^1 = R^3 = Me$, $R^2 = (E)$-COC(Me)=CHMe
1f Herbicidin G $R^1 = H$, $R^2 = (E)$-COC(Me)=CHMe, $R^3 = Me$
1g Aureonucleomycin $R^1 = R^2 = R^3 = H$

The potentially valuable biological activity of the herbicidins prompted us to investigate synthetic approaches to this group and related structures, and we focused on the tri-*O*-heterocyclic core ring system. The most expeditious synthesis of this unit would involve union of the appropriate hexose and pentose moieties by formation of the C-1–C-5 bond. However, despite the considerable current interest in *C*-glycosides, we were unable to find literature precedent for such a process. *C*-Glycosides have been formed by a variety of methods.[3] These include (i) using anomeric anions as nucleophiles;[4] (ii) using C-1 vinyl anions as nucleophiles;[5] (iii) by nucleophilic substitution at the anomeric centre;[6] (iv) by intermolecular radical reactions;[7] (v) by palladium cross-coupling processes with stannanes;[5c,8] and (vi) coupling *via* C-1 cationic processes.[9] In the majority of these cases relatively simple new groups have been introduced, and only a few examples involving hexose–hexose C-1–C-6 linkages have been described.[4c,5d,7h,i,10] None of these include substitution at an sp^3 centre in a carbohydrate derivative.

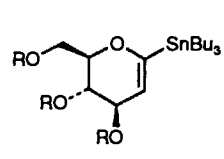
The only published synthetic work in the herbicidin area, to our knowledge, is that of Gallagher and co-workers,[11] who have very recently completed a synthesis of the tri-*O*-heterocyclic system of herbicidin itself, using a 2-ketohexose enolate anion, following earlier model studies. We decided to examine the formation of the undecose skeleton of the herbicidins by using alkylation/acylation of 1-lithiated glucals, in the hope of finding a brief, direct and versatile route, and in this paper we report our progress.

Results and Discussion

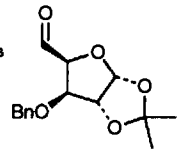
The successful 1-deprotonations of tribenzyl- and tris-(*tert*-butyldimethyl)silyl derivatives of 3,4,6-trihydroxy-D-glucal have been reported by several groups,[5b,d,12] but a number of problems have been noted.[13] We also experienced problems of poor and variable yields from deprotonation of 3,4,6-tris-*O*-(*tert*-butyldimethyl)silyl-D-glucal with *tert*-butyllithium or Schlosser's base, and eventually we adopted the procedure of Friesen *et al.*[13b] Thus, the stannane **3** was prepared (85%) by deprotonation of the tris(triisopropylsilyl) (TIPS) glucal derivative **2** with *tert*-butyllithium (4 mol equiv.), and quenching with tributyltin chloride. The tri-*O*-benzyl stannane **4** was prepared from stannane **3** by the literature method,[5d] but in low and variable yield (10–30%), and was not used in subsequent work.



2 X = H
5 X = Li



3 R = TIPS
4 R = Bn



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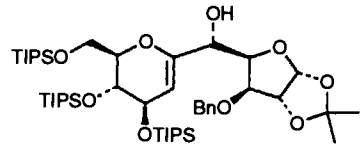

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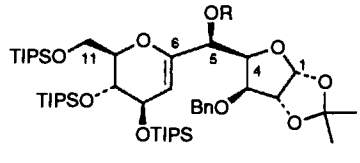


8 R = H
9 R = Ac

Tin–lithium exchange with butyllithium and stannane **3** proceeded smoothly at low temperature. Reactions of the cyclic vinyllithium species **5** with several xylofuranose electrophiles were then investigated, with a view to finding a short route to undecoses of the herbicidin type, suitable for synthesis both of

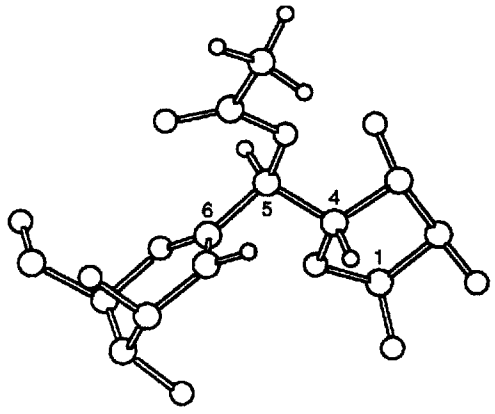
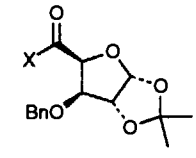


Fig. 1 Computed preferred conformation for acetate **9**

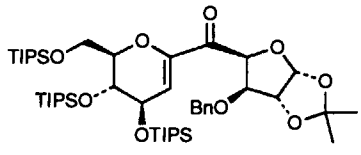
the herbicidins and certain analogues. Reaction with the aldehyde **6** (obtained from diacetone-D-glucose[14]) at −78 °C over a period of 2 h gave the desired *C*-disaccharides **7** and **8**; R = H (2.1:1) in 31% yield from the stannane. The diastereoisomers were separable, and the relative configurations were investigated by ^{1}H NMR spectroscopy. In order to observe 5-H, the acetate **9** was formed from the minor isomer, which displayed $J_{4,5}$ 9.3 Hz. Attempts to acetylate the major alcohol **7** were unsuccessful, as were attempts at the formation of xanthate and phenylthiocarbonate *O*-esters of both alcohols **7** and **8**, indicating marked steric crowding of the 5-hydroxy function. Molecular modelling of both 5-epimers of acetate **9** was carried out using Macromodel (version 3.1) software. Preferred conformations were determined from the results of Monte Carlo conformer searches starting from previously minimised structures of the two epimers. Minimisation employed the MM2 forcefield and included treatment of the chloroform solvent. Sets of conformers close to the minimum were found for each epimer, essentially with minor variations in dispositions of the TIPS group. It was observed that the minimum-energy conformations (Fig. 1) for the 5*S*-acetate had 4-H, 5-H dihedrals in the range 172–176°, consistent with the observed coupling, whereas the 5*R* epimer minimised to conformations with 4-H, 5-H dihedrals in the range 72–76° with a projected *J*-value close to zero. The C-5 configurations shown for alcohols **7** and **8** were thus indicated. Further progress towards the herbicidin core required 5-deoxygenation; however, this was frustrated by the problems of derivatisation of the free hydroxy functions in alcohols **7** and **8**.

In a second variation, anion **5** was added to a suspension of the acid chloride **10** in tetrahydrofuran (THF) at −78 °C. The latter was prepared from the crude acid **11** formed by silver oxide oxidation (rather than the literature method[15] with sodium chlorite/hydrogen peroxide) of the aldehyde **6**. The major product proved to be the enone **12**, but in only 21% yield, and this, and the connected problems of 5-deoxygenation, deterred further work on this product.

We finally decided to examine direct alkylation of anion **5** with iodide **13**[16] and the corresponding benzyl ether triflate **15**. The alcohol precursor to the latter was prepared from the commercially available 1,2-*O*-isopropylidene-α-D-xylofuranose **16**, using a sequence which in our hands proved to be a more convenient and reliable method (60% overall) than the literature route.[17] The mono-(*tert*-butyldimethylsilyl) ether **17** of diol **16** was readily formed and converted into the benzyl ether **18** (selecting reaction conditions which avoided bis-benzylation with concurrent desilylaton). Removal of the silyl group afforded the primary alcohol **19**, which yielded triflate **15** on treatment with triflic anhydride–pyridine at −40 °C. The iodide, sterically hindered and prone to elimination, gave only a multi-component mixture, but we were pleased to find that the triflate afforded the undecose **20** (41%) in reactions in THF, −78 to 0 °C, over a period of 2 h. This represents, to the best of our knowledge, the first example of substitution by a pyranose C-1 anion at an sp^3 carbon in a pentose or hexose. Although the yield is modest the sequence is short, and product **20** is suitably functionalised to facilitate entry into the herbicidin field. Only a limited investigation of further functional manipulations of the undecose **20** was possible. Epoxidation with *m*-chloroperbenzoic acid (MCPBA) or dimethyldioxirane was ineffective, but treatment with trifluoroperacetic acid in buffered dichloromethane at reflux eventually afforded the epoxide **21** (undetermined stereochemistry) in 73% yield. Unfortunately, we were unable to find reaction conditions for the rearrangement of epoxide **21** to the desired ketone **22**, although a minor carbonyl-containing product was formed from treatment with boron trifluoride. Future efforts will be directed towards removal of the sterically demanding TIPS groups from compound **20** before further manipulation.



10 X = Cl
11 X = OH



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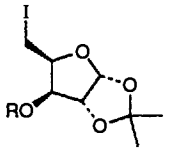
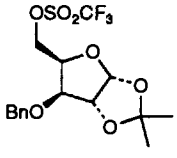


13 R = TBDMS
14 R = H



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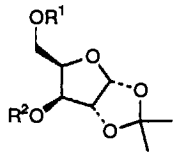
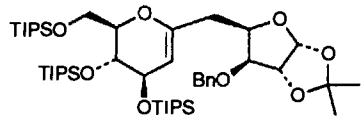


16 $R^1 = R^2 = H$
17 R^1 = TBDMS, R^2 = H
18 R^1 = TBDMS, R^2 = Bn
19 R^1 = H, R^2 = Bn



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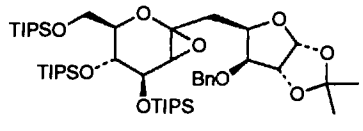

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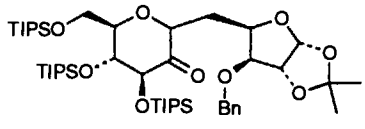

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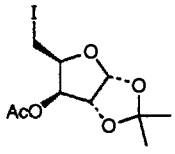
In view of the current interest in radical-coupling methodology[7] for *C*-disaccharide synthesis, we briefly examined its potential in the present work. Thus the iodide **23**[18] was treated with methyl acrylate (5 mol equiv.), tris(trimethyl-

silyl)silane, and azoisobutyronitrile (AIBN) in toluene gave the octanoate **24** (30%). However, iodo alcohol **14** (with the required C-4 stereochemistry) reacted very sluggishly with the enone **25** (equimolar), to give only traces (~5%) of the undecose **26** as a mixture of stereoisomers; the major product was the reduced iodide substrate. Obviously, enone **25** is insufficiently reactive, and cannot efficiently be used in large excess. These studies were not pursued further.



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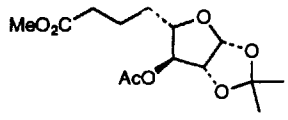

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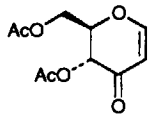

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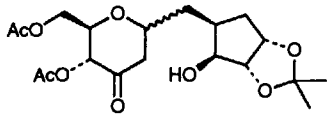

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Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H NMR spectra were recorded on either a JEOL FX 90Q (90 MHz), Bruker WM 250 (250 MHz), JEOL EX 270 (270 MHz), Nicolet QE 300 (300 MHz) or a Bruker AM 400 (400 MHz) instrument. The spectra were recorded as dilute solutions in deuteriochloroform unless otherwise stated. Chemical shifts are recorded relative to an internal tetramethylsilane standard and the multiplicity of a signal is designated by: s, singlet; d, doublet; dd, double doublet; ddd, double double doublet; dt, double triplet; t, triplet; q, quartet; br, broad; m, multiplet. Coupling constants, *J*, are reported in Hertz. ^{13}C NMR were recorded on JEOL FX 90Q (22.5 MHz), JEOL EX 270 (67.8 MHz) or a Bruker AM 400 (100.6 MHz) instruments. Chemical shifts are reported relative to internal tetramethylsilane (0.00 ppm) or chloroform (77.0 ppm) on a broad-band-decoupled mode, and the multiplicities were obtained using a DEPT sequence. Mass spectra were recorded on an AEI MS-902 or a MM-701CF instrument, using electron-impact ionisation at 70 eV unless otherwise stated. Optical rotations were obtained using a JASCO DIP-370 instrument, and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Column chromatography was performed using Flash (60 mesh) silica and the solvents were redistilled before use. All reactions were monitored by TLC using Camlab silica gel 60 F254 precoated plastic plates which were visualised with UV light, acidic anisaldehyde, polyphosphomolybdic acid (PPMA) in ethanol, or sulfuric acid in ethanol. All organic solvents and reagents were purified by standard literature procedures. Organic extracts were dried over magnesium sulfate and the solvent was removed by rotary evaporation. Light petroleum refers to the fraction with distillation range (40–60 °C).

3,4,6-*Tris*-O-(*triisopropylsilyl*)-D-*glucal* **2**.—1,5-Anhydro-2-deoxy-D-*arabino*-hex-1-enitol (D-glucal) (2.0 g, 13.69 mmol) was dissolved in dry dimethylformamide (DMF) (60 cm^3). Imidazole (6.71 g, 98.5 mmol) and triisopropylsilyl chloride (9.64 g, 50 mmol) were added and the stirred mixture was headed at 70–95 °C under nitrogen for 2 days. The mixture was cooled, poured into diethyl ether (200 cm^3), washed successively with water (5 × 100 cm^3) and brine, dried and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (15:1)] gave 3,4,6-tris-*O*-(triisopropylsilyl)-D-glucal[13b] **2** as a thick syrup (6.08 g, 76%) (Found: M$^+$ + NH$_4$, 632.492. Calc. for $C_{33}H_{74}NO_4Si_3$: *m/z*, 632.493); ν_{max}(film)/cm^{-1} 2943, 2867, 1646 (C=C), 1464, 1063 and 882; δ_H(400 MHz) 6.35 (1 H, d, *J* 6.4, 1-H), 4.80 (1 H, ddd, *J* 6.4, 5.3 and 1.7, 2-H), 4.23 (1 H, m, 5-H), 4.1–4.04 (2 H, m, 4- and 6-H), 3.96–3.94 (1 H, dt, *J* 5.3 and 1.9, 3-H), 3.83 (1 H, dd, *J* 11.3 and 3.8, 6-H) and 1.05 (63 H, s, TIPS-H); δ_C($CDCl_3$; 67.8 MHz) 142.9 (CH, C-1), 100.3 (CH, C-2), 80.7 (CH, C-5), 70.3 (CH, C-4), 65.1 (CH, C-3), 62.1 (CH$_2$, C-6), 18.1 (Me), 12.5 (CH), 12.35 (CH) and 12.05 (CH); *m/z* (FAB$^+$) 615 (M$^+$, 0.4%), 614 (0.8), 613 (2), 571 (8), 441 (6), 397 (17), 157 (64) and 43 (100).

1-(*Tributylstannyl*)-3,4,6-*tris*-O-(*triisopropylsilyl*)-D-*glucal* **3**.—3,4,6-Tris-*O*-(triisopropylsilyl)-D-glucal **2** (4.3 g, 6.99 mmol) was dissolved in dry THF (18 cm^3; 0.388 mol dm^{-3}) and the solution was stirred under nitrogen, cooled to −78 °C, and treated with Bu^{t}Li (1.7 mol dm^{-3}; 16.45 cm^3, 27.96 mmol) in one addition. The solution was warmed to 0 °C and stirred for 1.5 h, then was cooled to −78 °C, and tributyltin chloride (5.69 g, 17.45 mmol) was added. The solution was again warmed to 0 °C and stirred for 45 min before the reaction was quenched with water (50 cm^3). The solution was poured into diethyl ether (50 cm^3) and the organic phase was separated. The aqueous phase was extracted with diethyl ether and the combined extracts were washed successively with water and brine, dried and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (15:1)] gave 1-(tributylstannyl)-3,4,6,tris-*O*-(triisopropylsilyl)-D-glucal[13b] **3** as an oil (5.34 g, 85%) (Found: M$^+$ + H, 905.560. Calc. for $C_{45}H_{97}O_4Si_3Sn$: *m/z* 905.572); ν_{max}(film)/cm^{-1} 2943, 2867, 1605 (C=C), 1464, 1383, 1089 and 883; δ_H(270 MHz) 4.83 (1 H, dd, *J* 4.9 and 1.6, 2-H), 4.15–4.05 (2 H, m), 4.00–3.88 (2 H, m), 3.85 (1 H, m), 1.6–1.4 (6 H, m), 1.38–1.20 (6 H, m), 1.05 (63 H, s, TIPS-H) and 1.0–0.8 (15 H, m); δ_C($CDCl_3$; 67.8 MHz) 162.4 (C), 111.3 (CH), 80.6 (CH), 70.3 (CH), 65.1 (CH), 62.4 (CH$_2$), 29.0 (CH$_2$), 27.4 (CH$_2$), 18.1 (Me), 13.7 (Me), 12.6 (CH), 12.5 (CH) and 9.5 (CH$_2$); *m/z* (CI$^+$) 905 (M$^+$ + H, 100%), 731 (25), 632 (12), 458 (30) and 441 (15).

3,4,6-*Tri*-O-*benzyl*-1-(*tributylstannyl*)-D-*glucal* **4**.—A solution of 1-(tributylstannyl)-3,4,6-tris-*O*-(triisopropylsilyl)-D-glucal **3** (1.0 g, 1.11 mmol) in dry THF (4 cm^3) was treated with tetrabutylammonium fluoride (TBAF) (3.89 cm^3, 3.89 mmol) and stirred for 2 h. Sodium hydride (60% in mineral oil; 0.16 g, 4 mmol) was added along with THF (5 cm^3). After 10 min, benzyl bromide (0.67 g, 3.89 cm^3) and tetrabutylammonium iodide (TBAI) (1.43 g, 3.89 mmol) were added and the mixture was stirred for 24 h. Water (10 cm^3) was added and the reaction mixture was extracted into diethyl ether. The ether layer was washed with water, dried, and evaporated. The crude product was chromatographed [silica; light petroleum–ethyl acetate (10:1)] to remove the more polar products. Benzyl halides and triisopropylsilyl fluoride were partly removed from the reaction products by distillation (150 °C; 1 mmHg), and then column chromatography [silica; light petroleum–ethyl acetate (20:1)] gave 3,4,6-tri-*O*-benzyl-1-(tributylstannyl)-D-glucal[5d] **4** as a viscous syrup (237 mg, 30%) (Found: M$^+$ − Bu, 649.227. Calc. for $C_{35}H_{45}O_4Sn$: *m/z*, 649.234); ν_{max}(film)/cm^{-1} 3031, 2955, 2870, 1605, 1496, 1454, 1097 and 696; δ_H(270 MHz) 7.61–7.21 (15 H, m, ArH), {4.85 (1 H, d, *J* 11.2) and 4.68 (1 H, d, *J* 11.2), PhCH_2}, 4.85 (1 H, d, *J* 2.4, 2-H), 4.72–4.58 (4 H, m, 2 × PhCH_2), 4.27–4.21 (1 H, m), 3.90–3.74 (4 H, m), 1.59–1.46 (6 H, m), 1.38–1.24 (6 H, m) and 0.99–0.82 (15 H, m); δ_C($CDCl_3$; 67.8 MHz) 164.9 (C), 138.7 and 138.5 (C) (one obscured), 128.3 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.7 (CH), 127.5 (CH), 127.5 (CH), 127.4 (CH), 127.3 (CH), 110.9 (CH), 77.5 (CH), 77.3 (CH), 74.8 (CH), 73.8 (CH$_2$), 73.4 (CH$_2$), 70.3 (CH$_2$),

69.0 (CH_2), 27.2 (CH_2), 13.7 (Me) and 9.7 (CH_2); *m/z* 649 (M^+ − Bu, 3%), 252 (3), 237 (11), 181 (23), 119 (33) and 91 (100).

Reaction of 1-(*Tributylstannyl*)-3,4,6-*tris*-O-(*triisopropylsilyl*)-D-*glucal* **3** *with* 3-O-*Benzyl*-1,2-O-*isopropylidene*-α-D-*xylo*-*pentodialdo*-1,4-*furanose* **6**.—A stirred solution of 1-(tributylstannyl)-3,4,6-tris-*O*-(triisopropylsilyl)-D-glucal **3** (1.0 g, 1.11 mmol) in dry THF (5 cm^3) was cooled to −78 °C. Butyllithium (2.5 mol dm^{-3}; 0.54 cm^3, 1.33 mmol) was added and the reaction mixture was stirred for 15 min. 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose **6** (0.37 g, 1.33 mmol) was added as a solution in THF (4 cm^3) and the reaction mixture was stirred for 2 h, during which time it went from colourless to orange and then yellow. The reaction mixture was quenched with water (5 cm^3), and treated with dichloromethane (50 cm^3), and the organic phase was washed copiously and successively with water (3 × 50 cm^3) and brine (20 cm^3), dried, and evaporated to give an orange oil. Careful column chromatography [silica; light petroleum–ethyl acetate (15:1 ⟶ 1:1)] gave the separate *secondary alcohols* **7** and **8** as syrups (5*R*, 21% and 5*S*, 10%, respectively) (Found: M^+, 892.855. $C_{48}H_{88}O_9Si_3$ requires M, 892.574); ν_{max}(film)/cm^{-1} (very similar for each epimer) 3498, 3032, 2943, 2866, 1677, 1463, 1383 and 883; δ_H(250 MHz) (**8**) (*S*) epimer 7.33–7.26 (5 H, m, ArH), 6.04 (1 H, d, *J* 3.9, 1-H), 5.10 (1 H, m, 7-H), 4.58–4.41 (5 H, m), 4.36–4.26 (2 H, m), 4.09–3.94 (4 H, m), 3.85 (1 H, dd, *J* 11.4 and 4.1, 11-H), {1.46 (3 H, s) and 1.31 (3 H, s), 2 × Me}, and 1.09–1.04 (63 H, br, TIPS-H); δ_H(250 MHz) (**7**) (*R*)-epimer 7.36–7.26 (5 H, m, ArH), 5.97) 1 H, d, *J* 3.8, 1-H), 4.97 (1 H, dd, *J* 5.1 and 1.3, 7-H), 4.61–4.57 (2 H, m), 4.48–4.43 (2 H, m), 4.38–4.32 (2 H, m), 4.07–4.05 (1 H, m), 4.02–3.95 (4 H, m), 3.90–3.83 (1 H, dd, *J* 11.1 and 4.7, 11-H), {1.46 (3 H, s) and 1.32 (3 H, s), 2 × Me}, 1.08 (21 H, s), 1.03 (21 H, s) and 1.00 (21 H, s); δ_C($CDCl_3$; 67.8 MHz) 152.3 (C), 136.8 (C), 128.4 (CH), 128.2 (CH), 127.8 (CH), 111.5 (C), 105.0 (CH), 96.2 (CH), 84.9 (CH), 82.1 (CH), 81.3 (CH), 78.8 (CH), 72.9 (CH_2), 71.1 (CH), 70.3 (CH), 66.0 (CH), 61.9 (CH_2) 26.8 (CH_3) 26.3 (Me), 18.2 (Me), 18.1 (Me), 18.0 (Me), 12.4 (CH), 12.3 (CH) and 12.0 (CH); *m/z* 892 (M^+, 2%), 849 (2), 413 (13), 385 (16), 157 (71) and 91 (100).

On treatment of a solution in dichloromethane with pyridine, acetic anhydride, and 4-(dimethylamino) pyridine (DMAP) under standard conditions, the 5 *S*-epimer **8** gave the corresponding acetate **9** (87%); δ_H(400 MHz) 7.40–7.25 (5 H, m, ArH), 5.84 (1 H, d, *J* 3.7, 1-H), 5.40 (1 H, d, *J* 9.3, 5-H), 5.07 (1 H, d, *J* 5.2, 7-H), {4.60 (1 H, d, *J* 11.7) and 4.43 (1 H, d, *J* 11.7), PhCH_2}, 4.57 (1 H, d, *J* 3.7, 2-H), 4.54 (1 H, dd, *J* 9.3 and 3.2, 4-H), 4.30–4.10 (3 H, m, 9-, 10- and 11-H), 4.07–4.02 (1 H, m, 8-H), 3.94 (1 H, d, *J* 3.2, 3-H), 3.74 (1 H, dd, *J* 3 and 10, 11-H), 1.85 (3 H, s), {1.41 (3 H, s) and 1.28 (3 H, s), 2 × Me} and 1.05 (63 H, br, TIPS-H); δ_C($CDCl_3$; 100 MHz) 168.7 (C), 147.6 (C, C-6), 137.2 (C), 128.5 (CH), 128.2 (CH), 127.9 (CH), 111.6 (C), 105.2 (CH, C-1), 102.0 (CH, C-7), 82.0 (CH, C-2), 80.9 (CH, C-3), 80.2 (CH, C-10), 77.7 (CH, C-4), 72.0 (CH_2, PhCH_2), 71.2 (CH, C-5), 69.4 (CH, C-9), 66.0 (CH, C-8), 61.4 (CH_2, C-11), 27.0 (Me), 26.6 (Me), 20.9 (Me), 18.2 (Me), 18.1 (Me), 18.0 (Me), 12.5 (CH), 12.4 (CH) and 12.0 (CH).

3-O-*Benzyl*-1,2-O-*isopropylidene*-α-D-*xylofuranuronic Acid* **11**.—A stirred solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose **6** (1.45 g, 5.21 mmol) in ethanol (10 cm^3) containing freshly prepared silver(I) oxide (3.0 g, 12.95 mmol) was treated with aq. sodium hydroxide (1 g in 100 cm^3) slowly over a period of 15 min. The mixture was stirred at room temperature for 2 h. The aqueous mixture was washed with diethyl ether and the aqueous phase was acidified to pH 2 (conc. H_2SO_4) and extracted with dichloromethane. The organic phase was dried and evaporated to give 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronic acid[15] **11** as a powdery solid (1.36 g, 88%); m.p. 128–130 °C [lit.,[15] 141–142 °C (from ethyl acetate)] (Found: M^+ − Me, 279.086. Calc. for $C_{14}H_{15}O_6$: *m/z*, 279.086); ν_{max}(KBr disc)/cm^{-1} 3064–2500 (acid OH, CH stretches), 1741 (C=O), 1605, 1498, 1217 and 1078; δ_H(270 MHz) 9.26 (1 H, br, OH), 7.34–7.20 (5 H, m, ArH), 6.08 (1 H, d, *J* 3.6, 1-H), 4.86 (1 H, d, *J* 3.6, 4-H), 4.65–4.50 (3 H, m, PhCH_2, 2-H), 4.31 (1 H, d, *J* 3.6, 3-H) and {1.46 (3 H, s) and 1.30 (3 H, s), 2 × Me}; δ_C($CDCl_3$; 67.8 MHz) 171.7 (C), 136.5 (C), 128.4 (CH), 128.1 (CH), 127.7 (CH), 112.8 (C), 105.5 (CH, C-1), 82.3 (CH), 81.9 (CH), 79.6 (CH), 72.6 (CH_2, PhCH_2), 26.9 (Me) and 26.3 (Me); *m/z* 279 (M^+ − Me, 4%), 236 (8), 219 (8), 107 (25) and 91 (100).

3-O-*Benzyl*-1,2-O-*isopropylidene*-α-D-*xylofuranuronyl Chloride* **10**.—A solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronic acid **11** (400 mg, 1.36 mmol) in dichloromethane (16 cm^3) was cooled to 0 °C and treated with oxalyl dichloride (0.14 cm^3, 1.43 mmol) and DMF (1 drop). The reaction mixture was stirred for 1 h and then was allowed to warm to room temperature. The mixture was evaporated to leave a pale yellow solid, 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronyl chloride[19] **11**, which was characterised by IR spectroscopy and used immediately: ν_{max}(film)/cm^{-1} 2989, 2938, 1825 (C=O), 1654 and 1078.

Reaction of 1-(*Tributylstannyl*)-3,4,6-*tris*-O-(*triisopropylsilyl*)-D-*glucal* **3** *with* 3-O-*Benzyl*-1,2-O-*isopropylidene*-α-D-*xylofuranuronyl Chloride* **10**.—A solution of 1-(tributylstannyl)-3,4,6-tris-*O*-(triisopropylsilyl)-D-glucal **3** (1.0 g, 1.11 mmol) in dry THF (5 cm^3) was cooled to −78 °C under nitrogen and BuLi (2.5 mol dm^{-3}; 0.54 cm^3, 1.33 mmol) was added. The reaction mixture was stirred for 30 min. The anion was added to a solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronyl chloride **10** (1.2 mol equiv.) in THF (8 cm^3), which had been cooled to −78 °C. The reaction mixture was stirred for 45 min, quenched with water, poured into dichloromethane (30 cm^3) and the organic phase was washed with water, dried, and evaporated. Careful column chromatography [silica; light petroleum–ethyl acetate (20:1 ⟶ 1:1)] gave the *ketone* **12** as a syrup (208 mg, 21%) (Found: M^+ + H, 892. $C_{44}H_{87}O_9Si_3$ requires *m/z*, 892); ν_{max}(film)/cm^{-1} 2944, 2863, 1729 (C=O), 1642 (C=C), 1464, 1088 and 884; δ_H(270 MHz) 7.30–7.15 (5 H, m, ArH), 6.10 (1 H, dd, *J* 5.2 and 1.4, 7-H), 6.07 (1 H, d, *J* 3.6, 1-H), 5.43, (1 H, d, *J* 3.6, 4-H), 4.68 (1 H, d, *J* 3.6, 3-H), {4.57 (1 H, d, *J* 11) and 4.44 (1 H, d, *J* 11), PhCH_2}, 4.52 (1 H, d, *J* 3.6, 2-H), 4.50–4.40 (1 H, m, 9-H), 4.12–3.98 (3 H, m, 8-, 10- and 11-H), 3.77 (1 H, dd, *J* 11.6 and 3.6, 11-H), {1.49 (3 H, s) and 1.31 (3 H, s), 2 × Me} and 1.06 and 1.05 (63 H, 2 br, TIPS-H); COSY does not show one of $J_{7,9}$ or $J_{10,11}$, therefore 9-H and 10-H assignments may be reversed; δ_C($CDCl_3$; 67.8 MHz) 189.9 (C, C-5), 146.8 (C, C-6), 137.4 (C), 128.2 (CH), 127.5 (CH), 127.2 (CH), 112.1 (C), 105.6 (CH), 105.3 (CH), 83.9 (CH), 83.8 (CH), 82.9 (CH), 82.0 (CH), 72.8 (CH_2, PhCH_2), 70.0 (CH), 65.5 (CH), 61.4 (CH_2, C-11), 27.0 (Me), 26.3 (Me), 18.1 (Me), 18.1 (Me), 18.0 (Me), 12.3 (CH), 12.2 (CH) and 11.9 (CH); *m/z* (FAB$^+$) 892 (M^+ + H, 0.6%), 847 (2), 690 (4), 509 (12), 157 (63), 115 (98) and 91 (100).

5-*Deoxy*-5-*iodo*-1,2-O-*isopropylidene*-α-D-*xylofuranose* **14**.—1,2-*O*-Isopropylidene-α-D-xylofuranose **16** (5.0 g, 26.3 mmol), triphenylphosphine (10.36 g, 39.5 mmol), imidazole (5.38 g, 78.9 mmol) and iodine (10 g, 39.45 mmol) were treated with toluene (500 cm^3) and the mixture was stirred at 70–100 °C for 5 h. The mixture was cooled, saturated aq. sodium hydrogen carbonate (500 cm^3) was added and the mixture was stirred for 5 min. Iodine was added until the toluene layer darkened, then aq. sodium thiosulfate was added to destroy the excess of iodine after 10 min. The organic layer was diluted with toluene and

separated. The organic layer was washed with water, dried, and evaporated. Most of the triphenylphosphine oxide formed was removed by precipitation from an ice-cold ethereal solution, which was evaporated to give a solid. Column chromatography [silica; light petroleum–ethyl acetate (4:1)] gave 5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose[20] **14** as a crystalline solid (5.86 g, 74%) (Found: C, 32.5; H, 4.4; I, 43.5. Calc. for $C_8H_{13}IO_4$: C, 32.02; H, 4.37; I, 42.29%); (Found: M^+, 299.993. Calc. for $C_8H_{13}IO_4$: M, 299.985); ν_{max}(KBr disc)/cm^{-1} 3419 (OH), 2984, 2931, 2855, 1384, 1064 and 1002; δ_H(250 MHz) 5.98 (1 H, d, *J* 3.66, 1-H), 4.57 (1 H, d, *J* 3.66, 2-H), 4.50–4.35 (2 H, m, 3- and 4-H), 3.36–3.18 (2 H, m, 5-H_2), 1.85 (1 H, d, *J* 5.7, OH) and {1.52 (3 H, s) and 1.32 (3 H, s), 2 × Me}; δ_C($CDCl_3$; 100 MHz) 112.0 (C), 105.4 (CH, C-1), 85.0 (CH), 80.8 (CH), 74.7 (CH), 26.8 (Me), 26.2 (Me) and −1.2 (CH_2, C-5); *m*/*z* 300 (M^+, 2%), 285 (31), 241 (23), 151 (27) and 59 (100).

3-O-(tert-*Butyldimethylsilyl*)-5-*deoxy*-5-*iodo*-1,2-O-*isopropylidene*-α-D-*xylofuranose* **13**.—The starting iodide 5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose **14** (3.0 g, 10.0 mmol) was dissolved in dry DMF (20 cm^3) and *tert*-butyldimethylsilyl chloride (1.66 g, 11 mmol) was added along with imidazole (1.57 g, 23 mmol). The mixture was stirred under nitrogen at room temperature for 3 days before being treated with water and extracted into diethyl ether. The ethereal phase was washed with water, dried, and evaporated to give an orange oil. Column chromatography [silica; light petroleum–ethyl acetate (4:1)] gave 3-*O*-(*tert*-butyldimethylsilyl)-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose as a syrup (3.19 g, 77%) (Found: M^+ − Me, 399.045. $C_{13}H_{24}IO_4Si$ requires *m*/*z*, 399.049); ν_{max}(film)/cm^{-1} 2955, 2932, 2858, 1472, 1256 and 1080; δ_H(250 MHz) 5.82 (1 H, d, *J* 3.6, 1-H), 4.36–4.30 (2 H, m, 2- and 4-H), 4.21 (1 H, d, *J* 2.5, 3-H), 3.15–3.11 (2 H, m, 5-H_2), {1.41 (3 H, s) and 1.23 (3 H, s), 2 × Me}, 0.83 (9 H, s, Bu^t) and {0.10 (3 H, s) and 0.09 (3 H, s), $SiMe_2$}; δ_C($CDCl_3$; 100 MHz) 111.9 (C), 105.3 (CH, C-1), 85.1 (CH), 81.9 (CH), 75.1 (CH), 26.9 (Me), 26.3 (Me), 25.7 (Me), 18.0 (C), −0.7 (CH_2, C-5), −4.5 (Me) and −4.7 (Me); *m*/*z* 399 (M^+ − Me, 3%), 357 (3), 299 (14), 257 (54), 129 (90) and 75 (100).

5-O-(tert-*Butyldimethylsilyl*)-1,2-O-*isopropylidene*-α-D-*xylofuranose* **17**.—To a stirred solution of 1,2-*O*-isopropylidene-α-D-xylofuranose **16** (1.0 g, 5.26 mmol) in dry DMF (6 cm^3) under nitrogen were added imidazole (0.54 g, 7.93 mmol) and *tert*-butyldimethylsilyl chloride (0.88 g, 5.84 mmol). The mixture was stirred at room temperature for 6 h and was then poured into diethyl ether. The organic phase was washed with water, dried, and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (6:1)] gave 5-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-xylofuranose **17** as a syrup (1.23 g, 80%) (Found: M^+ − Me, 289.146. $C_{13}H_{25}O_5Si$ requires *m*/*z*, 289.147); ν_{max}(film)/cm^{-1} 3458 (OH), 2932, 1473, 1375, 1256 and 1076; δ_H(270 MHz) 5.96 (1 H, d, *J* 3.6, 1-H), 4.50 (1 H, d, *J* 3.6, 2-H), 4.40 (1 H, br, OH), 4.32 (1 H, br d, *J* 2.3, 3-H), 4.14–4.09 (3 H, m, 4-H and 5-H_2), {1.48 (3 H, s) and 1.32 (3 H, s), 2 × Me}, 0.89 (9 H, s, Bu^t) and 0.11 (6 H, br, $SiMe_2$); δ_C($CDCl_3$; 67.8 MHz) 110.9 (C), 104.4 (CH, C-1), 85.1 (CH), 78.7 (CH), 75.5 (CH), 63.1 (CH_2, C-5), 26.4 (Me), 25.8 (Me), 25.4 (Me) and 17.7 (C); *m*/*z* 289 (M^+ − Me, 5%), 229 (9), 189 (19), 171 (28), 117 (90), 89 (22) and 75 (100).

3-O-*Benzyl*-5-O-(tert-*butyldimethylsilyl*)-1,2-O-*isopropylidene*-α-D-*xylofuranose* **18**.—A solution of 5-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-xylofuranose **17** (3.34 g, 10.97 mmol) in DMF (50 cm^3) was treated at room temperature with sodium hydride (60% in mineral oil; 0.48 g, 12.0 mmol) and stirred for 5 min. Benzyl bromide (2.25 g, 13.16 mmol) was added in one addition and the mixture was stirred under nitrogen for 1 h. Water (15 cm^3) was added and the mixture was poured into water (100 cm^3), then extracted twice with diethyl ether, and the combined extracts were washed with water, dried, and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (12:1)] gave 3-*O*-benzyl-5-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-xylofuranose **18** as a thick syrup (4.14 g, 96%) (Found: M^+ − Bu^t, 337.154. $C_{17}H_{25}O_5Si$ requires *m*/*z*, 337.147); ν_{max}(film)/cm^{-1} 3033, 2932, 1497, 1374, 1256, 1166, 1078, 839, 735 and 698; δ_H(270 MHz) 7.4–7.25 (5 H, m, ArH), 5.90 (1 H, d, *J* 3.6, 1-H), {4.66 (1 H, d, *J* 11.9) and 4.58 (1 H, d, *J* 11.9), PhCH_2}, 4.58 (1 H, d, *J* 3.6, 2-H), 4.27–4.20 (1 H, m, 4-H), 3.98 (1 H, d, *J* 3.0, 3-H), 3.94–3.80 (2 H, m, 5-H_2), {1.50 (3 H, s) and 1.31 (3 H, s), 2 × Me}, 0.89 (9 H, s, Bu^t) and 0.07 (6 H, br, $SiMe_2$); δ_C($CDCl_3$; 67.8 MHz) 137.7 (C), 128.4 (CH), 127.7 (CH), 127.6 (CH), 111.6 (C), 105.0 (CH, C-1), 82.6 (CH), 81.3 (CH), 80.9 (CH), 72.2 (CH_2, PhCH_2), 59.9 (CH_2, C-5), 26.8 (Me), 26.3 (Me), 25.8 (Me), 18.2 (C) and −5.5 (Me).

3-O-*Benzyl*-1,2-O-*isopropylidene*-α-D-*xylofuranose* **19**.—The aldehyde 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose **6** (1.10 g, 3.95 mmol) was dissolved in 10% aq. methanol (55 cm^3) and treated at room temperature with sodium boranuide (0.15 g, 3.95 mmol). After 2 h the reaction mixture was treated successively with saturated aq. ammonium chloride and water. The mixture was extracted into diethyl ether, and the extract was washed with water, dried, and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (2:1)] gave 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose[17] **19** as a syrup (0.86 g, 77%) (Found: M^+ − Me, 265.106. Calc. for $C_{14}H_{17}O_5$: *m*/*z*, 265.108); $[\alpha]_D^{21}$ −68.7 (*c* 1.02, $CHCl_3$); ν_{max}(film)/cm^{-1} 3469 (OH), 3032, 2937, 1498, 1376, 1216, 1165, 1077, 737 and 700; δ_H(270 MHz) 7.36–7.26 (5 H, m, ArH), 5.97 (1 H, d, *J* 4.0, 1-H), {4.70 (1 H, d, *J* 11.9) and 4.49 (1 H, d, *J* 11.9), PhCH_2}, 4.63 (1 H, d, *J* 4.0, 2-H), 4.31–4.25 (1 H, ddd, *J* 5.3, 5.0 and 3.6, 4-H), 4.00 (1 H, d, *J* 3.6, 3-H), 3.96–3.90 (1 H, dd, *J* 11.9 and 5.3, 5-H), 3.87–3.80 (1 H, dd, *J* 1.9 and 5.0, 5-H), 2.52 (1 H, br, OH) and {1.48 (3 H, s) and 1.32 (3 H, s), 2 × Me};[3] δ_C($CDCl_3$; 67.8 MHz) 137.0 (C), 128.6 (CH), 128.1 (CH), 127.6 (CH), 111.6 (C), 104.9 (CH, C-1), 82.5 (CH), 82.3 (CH), 80.1 (CH), 71.8 (CH_2, PhCH_2), 60.8 (CH_2, C-5), 26.7 (Me) and 26.2 (Me); *m*/*z* 265 (M^+ − Me, 3%), 163 (4), 151 (9), 113 (7) and 91 (100).

3-O-*Benzyl*-1,2-O-*isopropylidene*-5-O-(*trifluoromethylsulfonyl*)-α-D-*xylofuranose* **15**.—3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose **19** (1.0 g, 3.56 mmol) was dissolved in dry dichloromethane (12 cm^3) and the stirred solution was treated with dry pyridine (0.58 cm^3, 7.13 mmol) under nitrogen. The mixture was cooled to −44 °C and triflic anhydride (0.72 cm^3, 4.27 mmol) was added. The reaction mixture was stirred at ~40 °C for 1 h. Methanol (1 cm^3) was added and the mixture was evaporated to give a waxy yellow solid. Column chromatography [silica; light petroleum–ethyl acetate (10:1 ⟶ 2:1)] gave 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-(trifluoromethylsulfonyl)-α-D-xylofuranose[17a] **15** as an unstable syrup (1.26 g, 86%); ν_{max}(film)/cm^{-1} 2991, 1417, 1247, 1213, 1148, 1078 and 955; δ_H(250 MHz) 7.38–7.25 (5 H, m, ArH), 5.96 (1 H, d, *J* 3.7, 1-H), 4.71–4.40 (6 H, m, PhCH_2, 2- and 4-H, and 5-H_2), 4.03 (1 H, d, *J* 3.5, 3-H) and {1.49 (3 H, s) and 1.33 (3 H, s), 2 × Me}; δ_C($CDCl_3$; 67.8 MHz) 136.6 (C), 128.6 (CH), 128.2 (CH), 127.8 (CH), 118.5 (C, q, *J* 320, CF_3), 112.3 (C), 105.4 (CH, C-1), 81.7 (CH), 81.2 (CH), 77.2 (CH), 73.7 (CH_2, C-5), 71.9 (CH_2, PhCH_2), 26.7 (Me) and 26.1 (Me).

Reaction of 1-(*Tributylstannyl*)-3,4,6-*tris*-O-(*triisopropylsilyl*)-D-*glucal* **3** *with* 3-O-*Benzyl*-1,2-O-*isopropylidene*-5-O-*trifluoromethylsulfonyl*-α-D-*xylofuranose* **15**.—1-(Tributyl-

stannyl)-3,4,6-tris-*O*-(triisopropylsilyl)-D-glucal **3** (2.07 g, 2.30 mmol) was dissolved in dry THF (10 cm^3; 0.23 mol dm^{-3}), and cooled to −78 °C under argon. BuLi (1.4 mol dm^{-3}; 1.67 cm^3, 2.35 mmol) was added and the formation of the cyclic vinyl ether anion was monitored by TLC, ~ 10 min. On completion of formation of the anion, 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-(trifluoromethylsulfonyl)-α-D-xylofuranose **15** (950 mg, 2.30 mmol) was added as a solution in anhydrous THF (6 cm^3) and the reaction mixture was allowed to warm to 0 °C over a period of 2 h. The mixture was quickly warmed to room temperature and water (20 cm^3) was added. The mixture was extracted with diethyl ether (30 cm^3) and the extract was washed with water (2 × 20 cm), dried, and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (20:1 ⟶ 2:1)] gave the undecose **20** as a thick syrup (828 mg, 41%); other major products were 3,4,6-tris-*O*-(triisopropylsilyl)-D-glucal **2** and unchanged trifluoromethanesulfonate **15**. For compound **20** (Found: M^+, 877. $C_{48}H_{88}O_8Si_3$ requires M, 887); ν_{max}(film)/cm^{-1} 2944, 2867, 1652 (C=C), 1464, 1383, 1190, 1093 and 883; δ_H(270 MHz) 7.35–7.28 (5 H, m, ArH), 6.02 (1 H, dd, *J* 5.3 and 1.5, 7-H), 5.88 (1 H, d, *J* 4, 1-H), {4.62 (1 H, d, *J* 11.5) and 4.54 (1 H, d, *J* 11.5), PhCH_2}, 4.58–4.39 (5 H, m, 2-, 4- and 10-H and 5-H_2), 4.24–4.18 (2 H, m, 8- and 9-H), 4.02–3.96 (3 H, m, 3-H and 11-H_2), {1.47 (3 H, s) and 1.30 (3 H, s), 2 × Me} and 1.05 (63 H, br, TIPS-H); δ_C($CDCl_3$; 67.8 MHz) 147.0 (C, C-6), 137.1 (C), 128.5 (CH), 127.9 (CH), 127.7 (CH), 112.0 (C), 107.2 (CH, C-7), 105.2 (CH, C-1), 83.6 (CH, C-10), 82.1 (CH, C-2), 81.3 (CH, C-3), 77.7 (CH, C-4), 72.2. CH_2, PhCH_2), 68.8 (CH, C-9), 68.6 (CH_2, C-5), 65.6 (CH, C-8), 60.7 (CH_2, C-11), 26.8 (Me), 26.3 (Me), 18.0 (Me), 17.9 (Me), 17.7 (Me), 12.3 (CH), 12.2 (CH) and 11.9 (CH); carbon assignments for C-2 and C-10 may be interchanged; CI^+ *m/z* 893 (M^+ + CH_4, 58%), 877 (M^+, 15), 849 (20), 719 (41), 175 (78) and 91 (100).

Formation of Epoxide **21**.—A solution of the undecose **20** (250 mg, 0.28 mmol) in dichloromethane (5 cm^3) containing sodium hydrogen carbonate (0.5 g) was heated at reflux. A solution of trifluoroperacetic acid (2 mmol) was added during 30 min *via* a dropping funnel, and a vigorous reaction appeared to take place on commencement of the addition. The reaction mixture was heated for a further 30 min before being allowed to cool. The mixture was filtered, the salts were washed with dichloromethane, and the combined organic phases were dried and evaporated. Column chromatography [silica; light petroleum–ethyl acetate (15:1)] gave the epoxide **21** as an oil, which upon concentration from an ethereal solution gave fine needle crystals (183 mg, 73%), m.p. 101–103 °C; ν_{max}(film)/cm^{-1} 2945, 2867, 1464, 1115, 736 and 685; δ_H(250 MHz) 7.40–7.28 (5 H, m, ArH), 5.91 (1 H, d, *J* 3.7, 1-H), 4.66–4.56 (5 H, m, PhCH_2, 5-H_2 and 2-H), 4.52–4.45 (1 H, m, 4-H), 4.36 (1 H, br, 9-H), 4.15–4.10 (2 H, m, 8- and 10-H), 4.02–3.96 (3 H, m, 3-H and 11-H_2), 3.74 (1 H, br, 7-H), {1.47 (3 H, s) and 1.30 (3 H, s), 2 × Me} and 1.10–1.03 (63 H, br, TIPS-H); δ_C($CDCl_3$; 67.8 MHz) 137.0 (C), 128.5 (CH), 128.0 (CH), 127.8 (CH), 112.0 (C), 105.3 (CH, C-1), 88.2 (C, C-6), 82.1 (2 × CH, C-2 and -10), 81.2 (CH, C-3), 77.8 (CH, C-4), 72.2 (CH_2, PhCH_2), 70.6 (CH_2, C-5), 70.0 (CH, C-8), 67.9 (CH, C-9), 61.8 (CH_2, C-11), 57.2 (CH, C-7), 26.9 (Me), 26.3 (Me), 18.0 (Me), 17.9 (Me), 17.8 (Me), 12.4 (CH), 12.2 (CH) and 11.8 (CH).

3-O-*Acetyl*-5-*deoxy*-5-*iodo*-1,2-O-*isopropylidene*-β-L-*arabino*-*furanose* **23**.—5-Deoxy-5-iodo-1,2-*O*-isopropylidene-β-L-arabinofuranose[21] (3.6 g, 12.0 mmol) was dissolved in dry pyridine (30 cm^3), acetic anhydride (2.0 cm^3, 21.2 mmol) was added to the stirred solution, and the mixture was stirred at room temperature for 3 h before being evaporated to ~ 5 cm^3 and most of the pyridine was removed by azeotroping with toluene (40 cm^3). The residue was dissolved in dichloromethane (20 cm^3), and the solution was washed successively with 2 mol dm^{-3} HCl, 2 mol dm^{-3} aq. sodium hydrogen carbonate and water. The organic phase was dried and evaporated. The yellow solid was crystallised from dichloromethane–light petroleum to give 3-*O*-acetyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-β-L-arabinofuranose[18] **23** as needle crystals (3.84 g, 93%); δ_H(300 MHz) 5.92 (1 H, d, *J* 3.8, 1-H), 5.20 (1 H, s, 3-H), 4.55 (1 H, d, *J* 3.8, 2-H), 4.30 (1 H, t, *J* 7.4, 4-H), 3.40 (2 H, m, 5-H_2), 2.10 (3 H, s, OAc) and {1.53 (3 H, s) and 1.23 (3 H, s), 2 × Me}; δ_C($CDCl_3$; 22.5 MHz) 169.2 (C), 112.8 (C), 106.1 (CH, C-1), 85.7 (CH), 84.4 (CH), 78.3 (CH), 26.7 (Me), 25.6 (Me), 20.6 (Me) and 4.6 (CH_2).

Methyl 3-O-*Acetyl*-5,6,7-*trideoxy*-1,2-O-*isopropylidene*-β-L-*arabinooctofuranuronate* **24**.—To a solution of 3-*O*-acetyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-β-L-arabinofuranose **23** (0.1 g, 0.29 mmol) in dry toluene (2 cm^3) were added methyl acrylate (0.13 g, 1.5 mmol), tris(trimethylsilyl)silane (0.1 cm^3, 0.35 mmol) and AIBN (cat.). The mixture was heated at 90 °C for 5 h, then was evaporated, and column chromatography [silica; light petroleum–ethyl acetate (3:1)] gave the title ester **24** as a syrup (27 mg, 30%) (Found: M^+ − Me, 287.110. $C_{13}H_{19}O_7$ requires *m/z*, 287.113); ν_{max}(film)/cm^{-1} 2953, 1740 (C=O) and 1238; δ_H(400 MHz) 5.90 (1 H, d, *J* 3.9, 1-H), 4.96 (1 H, d, *J* 1.7, 3-H), 4.56 (1 H, d, *J* 3.9, 2-H), 4.03 (1 H, m, 4-H), 3.66 (3 H, s, OMe), 2.36 (2 H, t, *J* 6.8, 7-H_2), 2.08 (3 H, s, OAc), 1.86–1.65 (4 H, m, 5- and 6-H_2) and {1.53 (3 H, s) and 1.31 (3 H, s), 2 × Me}; δ_C($CDCl_3$; 100 MHz) 173.7 (C), 169.9 (C), 112.5 (C), 105.7 (CH, C-1), 85.6 (CH, C-4), 84.6 (CH, C-2), 79.9 (CH, C-3), 51.5 (Me), 33.6 (CH_2, C-7), 33.0 (CH_2), 26.6 (Me), 25.9 (Me), 21.4 (CH_2) and 20.8 (Me); *m/z* 287 (M^+ − Me, 7%), 213 (7), 185 (36) and 43 (100).

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References

1 (*a*) M. Arai, T. Haneishi, N. Kitahara, R. Enokita, K. Kawakuo and Y. Kondo, *J. Antibiot.*, 1976, **29**, 863; (*b*) T. Haneishi, A. Terahara, H. Kayamori, J. Yabe and M. Arai, *J. Antibiot.*, 1976, **29**, 870; Y. Takiguchi, H. Yoshikawa, A. Terahara, A. Torikata and M. Terao, (*c*) *J. Antibiot.*, 1979, **32**, 857; (*d*) *J. Antibiot.*, 1979, **32**, 862; (*e*) A. Terahara, T. Haneishi, M. Arai, T. Hata, H. Kuwano and C. Tamura, *J. Antibiot.*, 1982, **35**, 1711.

2 (*a*) X. Dai, G. Li, D. Wu, D. Lu, H. Wang, Z. Li, L. Zhou, X. Chen and W. Chen, *Faming Zhuanli Shenquing Gongkai Shuomingshu*, CN 87100250 (*Chem. Abstr.*, 1989, **111**, 230661f); (*b*) S. J. Danishefsky and M. P. DeNinno, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 15, and refs. cited therein; R. T. Schwartz and R. Datema, *Trends Biochem. Sci.*, 1980, **5**, 65; (*d*) A. D. Ebein, *Trends Biochem. Sci.*, 1980, **5**, 219; (*e*) M. J. Morin and R. J. Bernacki, *Cancer Res.*, 1983, **43**, 1669.

3 See M. L. Dewis, Ph.D. Thesis, University of Nottingham, 1992, for a recent review.

4 *inter alia* (*a*) J.-M. Lancelin, L. Morin-Allory and P. Sinay, *J. Chem. Soc., Chem. Commun.*, 1984, 355; (*b*) P. LeSimple, J.-M. Beau and P. Sinay, *J. Chem. Soc., Chem. Commun.*, 1985, 894; (*c*) J.-M. Beau and P. Sinay, *Tetrahedron Lett.*, 1985, **26**, 6185, 6189, 6193; (*d*) D. K. Hutchinson and P. L. Fuchs, *J. Am. Chem. Soc.*, 1987, **109**, 4930.

5 *inter alia* (*a*) R. R. Schmidt and H. Dietrich, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1328; (*b*) K. C. Nicolau, C.-K. Hwang and M. E. Duggan, *J. Chem. Soc., Chem. Commun.*, 1986, 925; (*c*) J.-M. Beau and E. Dubois, *Tetrahedron Lett.*, 1990, **31**, 5165; (*d*) S. Hanessian, M. Martin and R. Desai, *J. Chem. Soc., Chem. Commun.*, 1986, 926.

6 *inter alia* J. M. Lancelin, P. H. A. Zollo and P. Sinay, *Tetrahedron Lett.*, 1983, **24**, 4833; R. Bihovsky, C. Selick and I. Giusti, *J. Org. Chem.*, 1988, **53**, 4026; S. Czernecki and G. Ville, *J. Org. Chem.*, 1989, **54**, 610; G. A. Kraus and N. T. Molina, *J. Org. Chem.*, 1988, **53**, 752; A. O. Stewart and R. M. Williams, *J. Am. Chem. Soc.*, 1985, **107**, 4289; S. J. F. Macdonald, W. B. Huizinga and T. C. McKenzie,

J. Org. Chem., 1988, **53**, 3373; V. Bellosta and S. Czernicka, *J. Chem. Soc., Chem. Commun.*, 1989, 199.

7 *inter alia* (*a*) B. Giese and J. Dupuis, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 622; (*b*) B. Giese, J. Dupuis, M. Nix, M. Leising and H. J. Lindner, *Carbohydr. Res.*, 1987, **171**, 329; (*c*) Y. Araki, T. Endo, M. Tanji, J. Nagasawa and Y. Iishido, *Tetrahedron Lett.*, 1987, **28**, 5853; (*d*) B. Giese, T. Linker and R. Muhn, *Tetrahedron*, 1989, **45**, 935; (*e*) B. Giese, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 553; (*f*) J. Dupuis, B. Giese, D. Ruegge, H. Fischer, H.-G. Korth and R. Sustmann, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 896; (*g*) B. Giese, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 969; (*h*) B. Giese and T. Witzel, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 450; (*i*) B. Giese, M. Hoch, C. Lamberth and R. R. Schmidt, *Tetrahedron Lett.*, 1988, **29**, 1375.

8 *inter alia* R. W. Friesen and C. F. Sturino, *J. Org. Chem.*, 1990, **55**, 2572, 5808; R. W. Friesen and A. K. Daljeet, *Tetrahedron Lett.*, 1990, **31**, 6133; J.-M. Beau and E. Dubois, *J. Chem. Soc., Chem. Commun.*, 1990, 1191; R. W. Friesen and R. W. Loo, *J. Org. Chem.*, 1991, **56**, 4821; G. D. Daves, Jr., *Acc. Chem. Res.*, 1990, **23**, 201.

9 *inter alia* R. R. Schmidt and M. Hoffmann, *Tetrahedron Lett.*, 1982, **23**, 409; R. R. Schmidt and G. Effenberger, *Liebigs Ann. Chem.*, 1987, 825; P. Allevi, M. Anastasia, P. Ciuffreda, A. Fiecchi and A. Scala, *J. Chem. Soc., Chem. Commun.*, 1987, 101, 1245; A. Giannis and K. Sandoff, *Tetrahedron Lett.*, 1985, **26**, 1479; J. Herscovici, K. Muleka, L. Boumaiza and K. Antonakis, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1995.

10 J.-L. Reymond, A. A. Pinkerton and P. Vogel, *J. Org. Chem.*, 1991, **56**, 2128; Y. Chen and P. Vogel, *Tetrahedron Lett.*, 1992, **33**, 4917.

11 N. J. Newcombe, M. F. Mahon, K. C. Molloy, K. C. Alker and T. Gallagher, *J. Am. Chem. Soc.*, 1993, **115**, 6430; P. Cox, M. F. Mahon, K. C. Molloy, S. Lister and T. Gallagher, *Tetrahedron Lett.*, 1988, **29**, 1993; P. Cox, M. F. Mahon, K. C. Molloy, S. Lister and T. Gallagher, *Tetrahedron Lett.*, 1989, **30**, 2437; P. Cox, S. Lister and T. Gallagher, *J. Chem. Soc., Perkin Trans. 1*, 1990, 3151; P. Cox, A. M. Griffin, N. J. Newcombe, S. Lister, M. V. J. Ramsay, D. Alker and T. Gallagher, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1443.

12 P. Lesimple, J.-M. Beau, G. Jaurand and P. Sinay, *Tetrahedron Lett.*, 1986, **27**, 6201.

13 (*a*) D. Crich and T. J. Richie, *Tetrahedron*, 1988, **44**, 2319; (*b*) R. W. Friesen, C. F. Sturino, A. K. Daljeet and A. Kolaczewska, *J. Org. Chem.*, 1991, **56**, 1944.

14 M. L. Wolfrom and S. Hanessian, *J. Org. Chem.*, 1962, **27**, 1800.

15 D. D. Dhavale, E. Tagliavini, C. Trombini and A. Umani-Ronchi, *J. Org. Chem.*, 1989, **54**, 4100.

16 V. K. Srivasta and L. M. Lerner, *J. Med. Chem.*, 1979, **22**, 24.

17 (*a*) G. W. J. Fleet and D. R. Witty, *Tetrahedron: Asymmetry*, 1990, **1**, 119; (*b*) T. Nagakawa, H. Toknaka, K. Shinoti, J. Yoshimura and T. Sato, *Bull. Chem. Soc. Jpn.*, 1967, **40**, 2150.

18 L. Hough, R. Khan and B. A. Otter, *Adv. Chem. Ser.*, 1968, No. 74, 120.

19 J. M. J. Tronchet and R. E. Moskalyk, *Helv. Chim. Acta*, 1972, **55**, 2816.

20 P. J. Garegg and B. Samuelsson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2866.

21 P. A. Levene and J. Compton, *J. Biol. Chem.*, 1936, **116**, 189.

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