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6*R*-, and 6*S*, -6*C*-Methylglucose from D-Glucuronolactone: Efficient Synthesis of a Seven Carbon Fucose Analogue: Inhibition of Some Enzymes of Primary Metabolism

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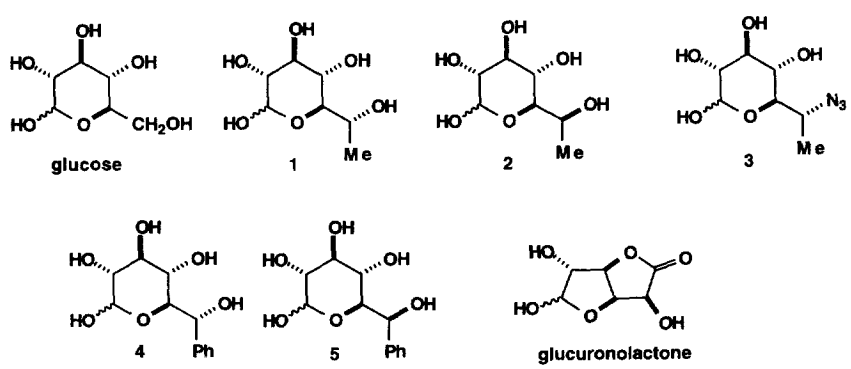
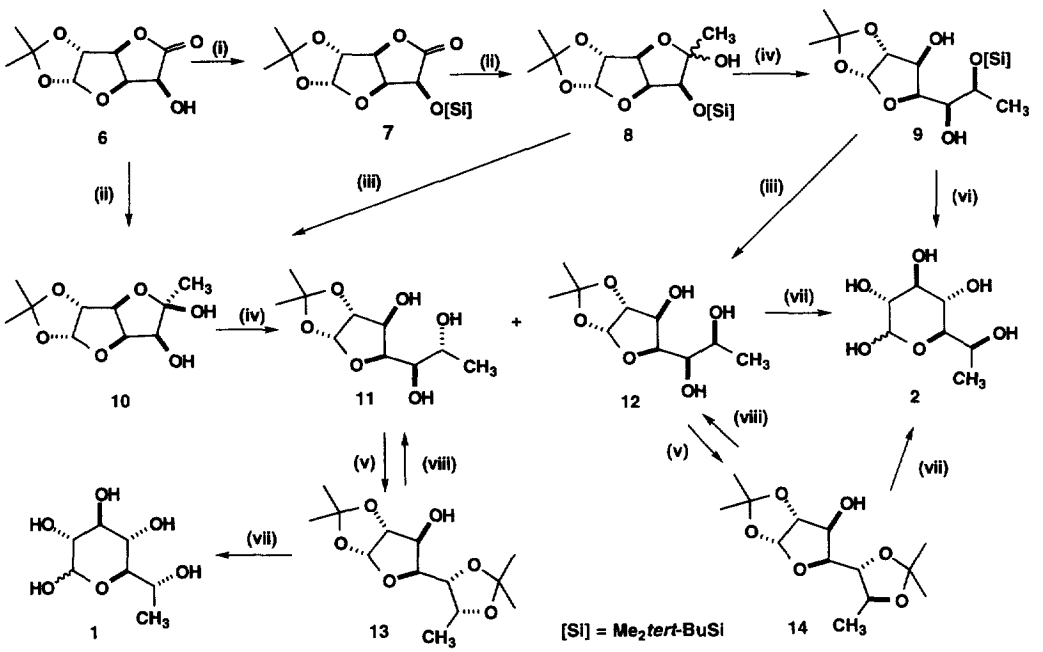
Abstract: Syntheses of the two epimeric 6*C*-methylglucoses from D-glucuronolactone rely on a non-stereoselective reduction of an intermediate lactol. A highly stereoselective reduction of a silylated lactol, which is accompanied by a silyl migration, gives easy access to 6*S*-6*C*-methylglucose - a seven carbon fucose analogue - in five steps from glucuronolactone in an overall yield of 40%. An azido analogue of 6*R*-6C-methylglucose is also reported. Such compounds may provide new materials for the selective inhibition of various enzymes of primary metabolism including glucokinase, glucose-6-phosphatase, and phosphoglucomutase. X-ray crystal structures of *(1S,3R,4S,5S,7R,8R)*-3-methyl-7,8-O-isopropylidene-3,4,7,8-tetrahydroxy-2,6-dioxabicyclo[3,3,0]-octane and 7-deoxy-1,2-5,6-di-*O*-isopropylidene-L-*glycero*-α-D-*gluco*-heptofuranose are reported.

There are very few reported examples of unprotected carbohydrates in which one of the prochiral hydrogens of the hydroxymethyl group of a hexose has been replaced by an alkyl group.[1] One such analogue of glucose is 6*R*-6*C*-methylglucose **1** which has been isolated as a natural product from *Streptomyces*[2] and may inhibit carbon dioxide fixation in dark-grown *Scenedesmus obliquus*.[3] The 6*R*-methyl-D-sugar **1** inhibits both glucose-6-phosphatase (Glc-6-Pase) and, weakly, glucokinase; in contrast, the 6*S*-methyl epimer, a seven carbon L-fucose analogue, **2** inhibits only glucokinase.[4] Larger groups than methyl may be accommodated by glucokinase. Thus, both D-phenyl **4** and L-phenyl **5** analogues inhibit glucokinase, at least partly competitively; the order of inhibition of glucokinase is L-phenyl **5** > D-phenyl **4** ≡ L-methyl **2** >>> D-methyl **1**.[5] Inhibition of Glc-6-Pase by **2** causes intracellular Glc-6-P levels to rise thereby enhancing the catalytic activity of glycogen synthase; this may provide a new strategy for the treatment of late-onset diabetes.[6] These were the first reports of such compounds acting as enzyme inhibitors; such materials may allow the development of specific inhibitors of some of the enzymes involved in primary metabolism, such as those with phosphorylation, dephosphorylation or phosphomutase activity.



This paper reports details of the synthesis of the methyl epimers **1** and **2** and of the azide derivative **3** by routes involving attack of methyl lithium on C-6 of a protected form of glucuronolactone; an efficient sequence with a highly diastereoselective reduction provides easy access in good overall yield to **2**, which is a seven carbon analogue of L-fucose; some of this work has been reported in a preliminary form.[4] The following paper reports the effects of these compounds, and of the corresponding butyl analogues, on phosphoglucomutase. The original synthesis[7] of the epimeric methyl glucoses **1** and **2** involved attack of methyl lithium on an aldehyde derived from oxidation of the C-6 alcohol in a protected form of glucose, but the acetonide of the readily available glucuronolactone **6** provides a much shorter and more convenient route to such compounds.



Scheme 1: (i) Me_2*tert*-BuSiCl, DMF, imidazole (ii) MeLi, THF, -70°C (iii) Bu_4NF, THF (iv) $NaBH_4$, EtOH (v) Me_2CO, CSA (vi) Amberlyst resin (H^+ form), aq. dioxan (vii) aq. CF_3COOH (viii) aq. MeCOOH

The remaining free hydroxyl group in the acetonide of glucuronolactone **6**[8] was converted to its silyl ether **7** in 92% yield as previously described[5] [Scheme 1]. Addition of methyl lithium to the fully protected lactone **7** gave a mixture of the two epimeric lactols **8** in 80% yield on a 15 g scale. Removal of the silyl ether protecting group in **8** by treatment with tetrabutyl ammonium fluoride (TBAF) gave a single crystalline lactol **10** in 58% yield. The configuration of the anomeric position in the lactol **10** was firmly established by X-ray crystallographic analysis (Figure 1). Direct addition of methyl lithium to the unprotected acetonide **6** also afforded the methyl lactol **10** but only in 20% isolated yield; the route *via* initial silyl protection gave a better overall yield of 43%.

Reaction of the lactol **10** with sodium borohydride gave an inseparable mixture of the two triols **12** and **11** in 75% yield and in approximately a 1:1 ratio as judged by NMR; there was very little, if any, stereoselectivity during the reduction. However, acetonation of the mixture of alcohols in acetone in the

presence of camphor sulfonic acid (CSA) allowed the efficient separation of the two diacetonides **14** (19% yield) and **13** (43% yield). The singlets for the $Me_2\underline{C}$ in **14** at δ 109.1 and 111.7 and in **13** at δ 108.3 and 111.7 clearly demonstrated that only five-membered ring acetonides had been formed in this reaction.[9] The structure of the diacetonide **14** was unequivocally determined by X-ray crystallographic analysis to be the homofucose derivative (Figure 2) with the *S* configuration at C-6 of the sugar.

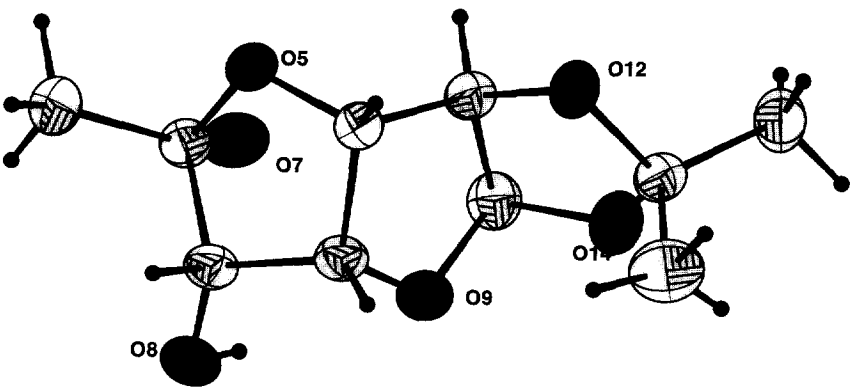


Figure 1 X-Ray structure of(*1S,3R,4S,5S,7R,8R*)-3-Methyl-7,8-O-isopropylidene-3,4,7,8-tetrahydroxy-2,6-dioxabicyclo[3,3,0]-octane **10** showing crystallographic numbering scheme.

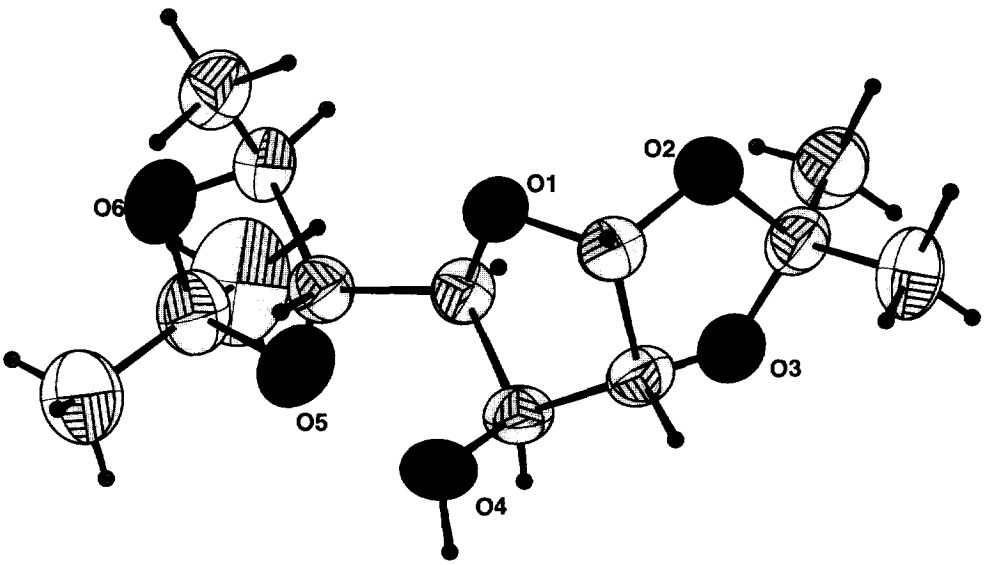
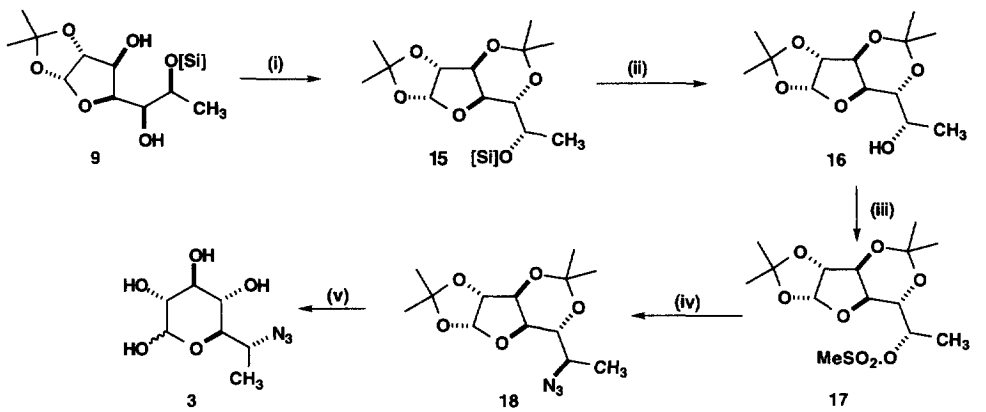
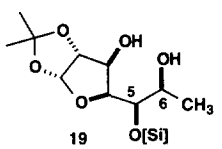


Figure 2 7-Deoxy-1,2-5,6-di-*O*-isopropylidene-**L**-*glycero*-α-**D**-*gluco*-heptofuranose **14** showing crystallographic numbering scheme.

Treatment of the diacetonides **13** and **14** with aqueous acetic acid allowed the isolation of pure samples of the crystalline monoacetonides **11** and **12** in respective yields of 79% and 65%. More vigorous acid hydrolysis of the diacetonides **14** and **13** with aqueous trifluoroacetic acid afforded the unprotected sugars, homofucose **2** and homodeoxyaltrose **1** in yields of 92% and 95% respectively.

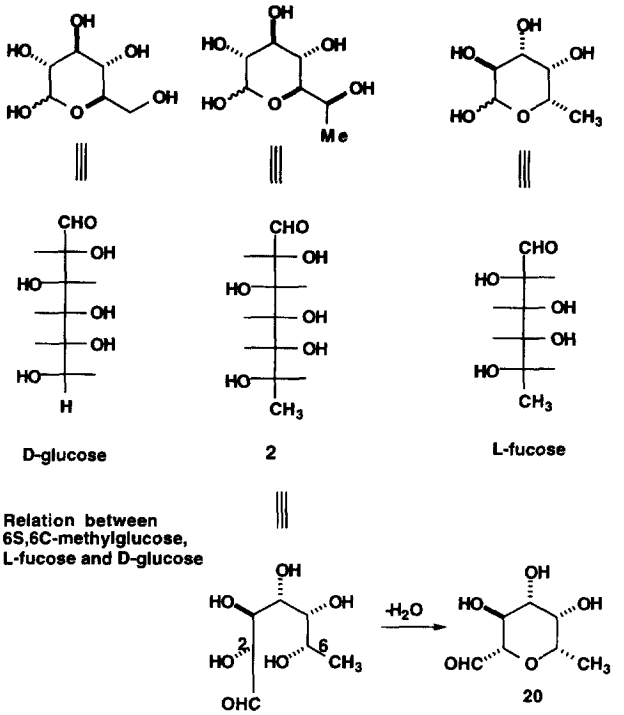


Scheme 2: (i) Me_2CO, $Me_2C(OMe)_2$, CSA (ii) Bu_4NF, THF (iii) $MeSO_2Cl$, DMAP (cat.), pyridine (iv) NaN_3, DMF, 75°C (v) aq. CF_3COOH



In contrast to the non-selective borohydride reduction of the lactol **10**, reduction of the mixture of silyl ethers **8** was highly diastereoselective, allowing the isolation of a single product **9** in 66% yield. Deprotection of **9** by acid hydrolysis gave the homofucose analogue **2** in 92% yield, an overall yield of 43% in four steps from the acetonide **6**.

Although the stereoselectivity of the reduction can be explained by the Ahn-Felkin rationale assuming the silyl ether group to be the largest substituent,[10] the migration of the silyl group from the C-5 hydroxyl group during the course of the reduction was unexpected. However, none of **19** was isolated; the site of the silyl ether in **9** was assigned on the basis of NMR spectroscopy; there is essentially no coupling between H-5 and H-6, but H-5 is clearly coupled to a hydroxyl proton whereas there is no coupling from H-6 to any OH. Furthermore, acetonation of the diol **9** gave the diacetonide **15** in high yield [85%]; the singlets for the $Me_2\underline{C}$ at δ 100.7 and 111.8 show that both a five- and a six-membered ring acetonide are present in **15** [Scheme 2]. This intermediate also allows the introduction of other groups into C-6 with inversion, to provide easy access to seven carbon sugars with modification of the C-6 OH group, as exemplified by the azide **3**. Thus, removal of the silyl protecting group in **15** with TBAF gave the alcohol **16** [95% yield] which was esterified with methanesulfonyl chloride in pyridine in the presence of 4-N,N-dimethylaminopyridine (DMAP) to afford the mesylate **17** [82% yield]. Subsequent reaction of the mesylate **17** with sodium azide in dimethyl formamide gave the inverted azide **18** [83% yield], which was completely deprotected with aqueous trifluoroacetic acid to give the azido sugar **3** [97% yield].



6S-Methyl glucose **2**, as well as being a C-6 extended glucose derivative, may also be viewed as a seven carbon analogue of L-fucose [shown as Fischer projection formulae]. There is considerable interest[11,12] in mimics of L-fucose; elimination of water by activation of the hydroxyl group at C-2 of **2** should allow a short synthesis of α-C-glycosides **20** of fucose and such materials might usefully be developed into mimics of L-fucose.

In summary this paper reports an efficient synthesis of the seven carbon fucose analogue, 6*S*-6*C*-methylglucose, **2** in four steps and an overall yield of 43% from the glucuronolactone acetonide **6**. The epimeric 6*R* derivative **1** may also be obtained through a sequence which involves a non-diastereoselective reduction of an unprotected lactol.

Exploration of substitution of the prochiral methylene hydrogens of C-6 of hexoses is likely to provide a novel set of carbohydrate mimics. The fact that the active site of some of the enzymes, such as glucokinase, can accommodate a phenyl group at C-6 - and even be a more potent enzyme inhibitor than the corresponding methyl analogue - means that substantial variations might be made which allow the development of specific and potent inhibitors of enzymes that are responsible for the synthesis, hydrolysis, mutation and isomerisation of sugar phosphates, not only for glucose but also for mannose and galactose. The following paper describes the synthesis of the corresponding butyl analogues[13] indicating that this approach is likely to give general access to a new class of interesting carbohydrate mimics; the effects of these materials on phosphoglucomutase are also reported therein.

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X-Ray Crystal Structure Analysis. The relative configurations of the stereogenic centres in *(1S,3R,4S,5S,7R,8R)*-3-methyl-7,8-*O*-isopropylidene-3,4,7,8-tetrahydroxy-2,6-dioxabicyclo[3,3,0]-octane **10** and 7-deoxy-1,2-5,6-di-*O*-isopropylidene-**L**-*glycero*-α-**D**-*gluco*-heptofuranose **14** were established by X-ray single crystal structure analysis. For both compounds, cell dimensions and intensity data were measured with an Enraf-Nonius Mach3 Diffractometer, and Lorentz, polarisation and psi scan absorption corrections were applied. All calculations were carried out on a 486PC computer. All non-hydrogen atoms were located by SIR92[14] and refined using CRYSTALS.[15] Illustrations were produced using CAMERON.[16] Hydrogen atoms were seen in the difference density map but placed geometrically. Non-hydrogen atoms were refined

anisotropically using atomic scattering factors from International Tables.[17] Structural data for both **10** and **14** have been deposited at the Cambridge Crystallographic Data Centre.[18]

Table 1. Fractional atomic coordinates and equivalent isotropic temperature factors U(iso) with standard deviations in parentheses for *(1S,3R,4S,5S,7R,8R)*-3-methyl-7,8-*O*-isopropylidene-3,4,7,8-tetrahydroxy-2,6-dioxabicyclo[3,3,0]-octane **10**

Atom	x/a	y/b	z/c	U(iso)
C(1)	-0.2064(4)	-0.0587(4)	-0.6610(3)	0.0325
C(2)	-0.4195(4)	-0.1863(4)	-0.6302(3)	0.0342
C(3)	-0.3225(4)	-0.3505(4)	-0.7523(3)	0.0324
C(4)	-0.0397(4)	-0.3671(4)	-0.7775(3)	0.0345
O(5)	-0.0054(4)	-0.1576(3)	-0.7778(3)	0.0376
C(6)	0.0978(5)	-0.4322(5)	-0.9489(4)	0.0491
O(7)	0.0393(4)	-0.5044(3)	-0.6288(3)	0.0444
O(8)	-0.4119(4)	-0.5441(3)	-0.6891(3)	0.0391
O(9)	-0.4563(4)	-0.2837(4)	-0.4495(3)	0.0468
C(10)	-0.2826(5)	-0.2432(4)	-0.3552(3)	0.0407
C(11)	-0.1485(5)	-0.0724(4)	-0.4759(3)	0.0362
O(12)	-0.2580(4)	0.1132(3)	-0.4055(3)	0.0451
C(13)	-0.4348(5)	0.0655(4)	-0.2493(3)	0.0370
O(14)	-0.3976(4)	-0.1589(3)	-0.2058(3)	0.0466
C(15)	-0.6927(6)	0.1549(6)	-0.2893(5)	0.0665
C(16)	-0.3784(6)	0.1534(5)	-0.1014(4)	0.0489

Table 2. Fractional atomic coordinates and equivalent isotropic temperature factors U(iso) with standard deviations in parentheses for 7-deoxy-1,2-5,6-di-*O*-isopropylidene-**L**-*glycero*-α-**D**-*gluco*-heptofuranose **AI**

Atom	x/a	y/b	z/c	U(iso)
O(1)	0.1948(3)	0.5111(1)	0.66803(8)	0.0533
O(2)	0.3120(4)	0.4173(1)	0.75740(9)	0.0606
O(3)	0.0224(3)	0.2984(1)	0.73255(9)	0.0578
O(4)	-0.3074(3)	0.5100(2)	0.65180(1)	0.0625
O(5)	-0.0680(4)	0.4301(2)	0.51866(9)	0.0701
O(6)	0.2078(4)	0.5246(2)	0.46286(9)	0.0746
C(1)	0.1326(4)	0.4795(2)	0.7301(1)	0.0496
C(2)	-0.0793(5)	0.4040(2)	0.7245(1)	0.0514
C(3)	-0.1597(5)	0.4181(2)	0.6570(1)	0.0510
C(4)	0.0690(5)	0.4430(2)	0.6237(1)	0.0487
C(5)	0.0463(5)	0.5028(2)	0.5610(1)	0.0532
C(6)	0.2755(5)	0.5309(2)	0.5282(1)	0.0598
C(7)	0.3689(7)	0.6430(3)	0.5413(2)	0.0781
C(8)	0.2248(5)	0.3089(2)	0.7704(1)	0.0558
C(9)	0.0306(6)	0.4442(3)	0.4569(1)	0.0692
C(10)	0.1651(8)	0.2989(3)	0.8397(1)	0.0763
C(11)	0.4049(6)	0.2270(3)	0.7489(2)	0.0763
C(12)	0.139(1)	0.3380(4)	0.4359(2)	0.1181
C(13)	-0.1511(9)	0.4882(4)	0.4125(2)	0.1021

Experimental: Melting points were recorded on a Kofler hot block and are corrected. Proton nuclear magnetic resonance (δ_H) spectra were recorded on a Varian Gemini 200 (200 MHz), Bruker AC 200 (200 MHz) or a Bruker AM 500 (500 MHz) spectrometer. ^{13}C Nuclear magnetic resonance (δ_C) spectra were recorded on a Varian Gemini 200 (50 MHz), a Bruker AC 200 (50 MHz) or a Bruker AM 500 (125 MHz) spectrometer and multiplicities were assigned using DEPT sequence. All chemical shifts are quoted on the δ-scale. The following abbreviations were used to explain multiplicities: s, singlet; d, doublet; t, triplet; q,

quartet; m, multiplet; br, broad; app, apparent. Infra-red spectra were recorded on a Perkin-Elmer 1750 IR FT spectrophotometer. Mass spectra were recorded on a VG Masslab 20-250, BIO-Q by desorption chemical ionisation (DCI NH_3), chemical ionisation (CI NH_3), electrospray or thermospray, or atmospheric pressure chemical ionisation ($APCI^+$ or $APCI^-$) as stated. Optical rotations were measured on a Perkin-Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in g/100 ml. Microanalyses were performed by the microanalysis service of the Dyson Perrins laboratory. Thin layer chromatography (TLC) was carried out on plastic or aluminium sheets coated with $60F_{254}$ silica, and plates were developed using a spray of 0.2% w/v cerium (IV) sulfate and 5% ammonium molybdate in 2M sulfuric acid. Flash chromatography was carried out using Sorbsil C60 40/60 silica. Solvents and commercially available reagents were dried and purified before use according to standard procedures; hexane was distilled at 68°C before use to remove less volatile fractions. D-Glucuronolactone was converted to the isopropylidene derivative **6**[8] and to the silyl ether **7**[5] as previously described.

5-O-tert-Butyldimethylsilyl-7-deoxy-1,2-O-isopropylidene-α-D-gluco-6-heptulofuranose ***8***. Methyl lithium (1.4 M solution in diethyl ether, 43.7 ml, 61.18 mmol, 1.3 eq.) was added to a solution of the fully protected lactone **7**(15.53 g, 47.06 mmol) in dry THF (100 ml) under N_2 at -70° C. After 20 min, TLC (ethyl acetate/hexane 1:1) showed only a trace of starting material (Rf 0.85) and two new spots (Rf 0.75; Rf 0.6). The reaction was then quenched by addition of saturated aqueous ammonium chloride solution (25 ml) and allowed to warm up to room temperature, diluted with ethyl acetate (150 ml) and extracted with brine (100 ml). The aqueous layer was extracted with ethyl acetate (2 x 150 ml). The organic extracts were combined, dried ($MgSO_4$) and the solvent removed under reduced pressure. The resulting oil was purified by flash chromatography (ethyl acetate/hexane 1:3) to afford a mixture of *the epimeric lactols* **8**(13 g, 37.57 mmol, 80 %), as a colourless oil, ν_{max} (film/cm^{-1}) 3457 (br, OH). For *the major epimer*: δ_H (200 MHz, $CDCl_3$): 0.16, 0.18 (6H, 2 x s, $(CH_3)_2Si$), 0.95 (9H, s, $(CH_3)_3CSi$), 1.34, 1.48 (6H, 2 x s, Me_2C), 1.48 (3H, s, Me), 3.85 (1H, d, J 4.5 Hz), 4.51 (1H, d, J 4.4 Hz), 4.68 (1H, d, $J_{1,2}$ 3.7 Hz, H-2), 4.73 (1H, d, J 4.1 Hz), 6.01 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). *m/z* (CI, NH_3): 346 ($M+NH_4^+-H_2O$, 15%), 329 ($M+H^+-H_2O$, 100%). (Found: C, 55.58; H, 9.09; $C_{10}H_{16}O_6$ requires C, 55.46; H, 8.73%).

7-Deoxy-1,2-O-isopropylidene-α-D-gluco-6-heptulofuranose ***10***. Method 1: Tetrabutyl ammonium fluoride (1.1 M in THF, 22.6 mmol, 1.2 eq., 20.5 ml) was added dropwise under N_2 to a solution of the silyl lactols **8** (6.5 g, 18.8 mmol) in dry THF (20 ml) under N_2. After 10 min, TLC (ethyl acetate/hexane 1:1) showed no starting material (Rf 0.85) and a new spot (Rf 0.4). The solvent was removed under reduced pressure and the resulting oil was preadsorbed on silica and purified by flash chromatography (ethyl acetate/hexane 1:1) to afford, after recrystallisation from ethyl acetate, *7-deoxy-1,2-O-isopropylidene-α-D-gluco-6-heptulofuranose* ***10*** as the pure β-furanose anomer, (2.53 g, 58%), m.p. 117-119°C. $[\alpha]_D^{22}$ +25.1 (c, 1.37 in $CHCl_3$). ν_{max} (KBr/cm^{-1}): 3446 (br, OH). δ_H (500 MHz, $CDCl_3$): 1.36, 1.49 (6H, 2 x s, Me_2C), 1.47 (3H, s, Me), 2.93 (1H, s, OH), 3.00 (1H, d, $J_{5,OH}$ 10.3 Hz, OH), 3.75 (1H, dd, $J_{4,5}$ 5.3, $J_{5,OH}$ 10.3 Hz, H-5), 4.58 (1H, d, $J_{3,4}$ 4.8 Hz, H-3), 4.70 (1H, d, $J_{1,2}$ 3.7 Hz, H-2), 4.83 (1H, app. t, J 4.8 Hz, H-4), 6.03 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, $CDCl_3$): 24.9 (q, Me), 27.0, 27.5 (2 x q, $(\underline{C}H_3)_2C$), 76.2, 81.4, 83.2, 86.5 (4 x d, C-2, C-3, C-4, C-5), 102.8 (s, C-6), 107.3 (d, C-1), 113.2 (s, $\underline{C}Me_2$). *m/z* (DCI, NH_3): 250 ($M+NH_4^+$, 15%), 232 ($M+NH_4^+-H_2O$, 24%), 215 ($M+H^+-H_2O$, 100%). (Found: C, 51.45; H, 7.03; $C_{10}H_{16}O_6$ requires C, 51.70; H, 6.95%).

Method 2: Methyl lithium (1.4 M solution in diethyl ether, 19.8 ml, 27.78 mmol, 1.5 eq.) was added to a solution of the acetonide **6**(4.00 g, 18.52 mmol) in dry THF (50 ml) under N_2 at -65°C. After 30 min, TLC (ethyl acetate) showed a trace of starting material (Rf 0.8) and a new spot (Rf 0.7); further methyl lithium was added (1.8 ml, 2,5 mmol). The reaction was quenched after 50 min by addition of a saturated aqueous

ammonium chloride solution (30 ml) and was stirred for a further hour. The solution was diluted with ethyl acetate (150 ml) and washed with brine (50 ml). The aqueous layer was extracted with ethyl acetate (2 x 100 ml). The organic extracts were combined, dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was preadsorbed on silica and purified by flash chromatography (ethyl acetate/hexane 1:2 then 1:1 then EtOAc) to afford the lactol **10**, slightly contaminated with the anomeric lactol. Recrystallisation from ethyl acetate gave pure **10** (868 mg, 20%), identical to the material above.

*7-Deoxy-1,2-5,6-di-O-isopropylidene-L-glycero-α-D-gluco-heptofuranose **14** and 7-Deoxy-1,2-5,6-di-O-isopropylidene-D-glycero-α-D-gluco-heptofuranose **13***. Sodium borohydride (510 mg, 13.48 mmol, 1.5 eq.) was added to a solution of the lactol **10** (2.09 g, 8.99 mmol) in ethanol (50 ml). After 30 min, TLC (ethyl acetate) showed no trace of starting material (Rf 0.7) and a new product (Rf 0.3). The reaction was quenched by addition of an excess of ammonium chloride; the solution was stirred until evolution of gas has ceased, filtered through Celite eluted with ethanol and the solvent was removed under reduced pressure. Purification of the residue by flash chromatography (ethyl acetate) afforded an inseparable 1:1 mixture of the alcohols **12** and **11** (1.57 g, 75 % yield). A suspension of a 1:1 mixture of the alcohols **12** and **11** (1.41 g, 6.02 mmol) and a catalytic amount of DL-camphor-10-sulfonic acid in acetone (70 ml) was stirred at room temperature under N_2. After 12 hours, TLC (ethyl acetate) showed only a trace of starting material (Rf 0.1) and two new spots (Rf 0.8 and Rf 0.75). The reaction was quenched by addition of an excess of $NaHCO_3$. After filtration of the reaction mixture through Celite and elution with acetone, the solvent was removed under reduced pressure to afford a colourless oil. Purification by flash chromatography (ethyl acetate/hexane 1:2) afforded *the homofucodiacetonide **14*** (309 mg, 19%) as a crystalline white solid, the structure of which was established by X-ray crystallographic analysis, m.p. 140-142°C (ethyl acetate/hexane). $[\alpha]_D^{22}$ -9.7 (c, 1.11 in $CHCl_3$). ν_{max} (KBr/ cm^{-1}): 3463 (br, OH). δ_H (500 MHz, $CDCl_3$): 1.38 (3H, d, $J_{6,7}$ 6.0 Hz, Me); 1.33, 1.42, 1.44, 1.51 (12H, 4 x s, 2 x Me_2C); 2.89 (1H, d, $J_{3,OH}$ 3.3 Hz, OH-3); 3.87 (1H, dd, $J_{4,5}$ 6.7 Hz, $J_{5,6}$ 8.2 Hz, H-5); 4.06 (1H, dd, $J_{4,5}$ 6.7 Hz, $J_{3,4}$ 2.7 Hz, H-4); 4.11 (1H, dq, $J_{6,7}$ 6.0 Hz, $J_{5,6}$ 8.2 Hz, H-6); 4.35 (1H, app. t, H-3); 4.54 (1H, d, $J_{1,2}$ 3.7 Hz, H-2); 5.98 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, $CDCl_3$): 18.0 (q, Me); 26.1, 26.8, 27.3 (4 x q, 2 x ($\underline{C}H_3)_2C$); 75.6, 76.3, 79.7, 80.5, 84.9 (5 x d, C-2, C-3, C-4, C-5, C-6); 105.2 (d, C-1); 109.1 (s, $\underline{C}Me_2$); 111.7 (s, $\underline{C}Me_2$). *m/z* (CI, NH_3): 292 ($M+NH_4^+$, 10%), 275 ($M+H^+$, 100%), 234 (M -acetonide+H^+, 24%). (Found: C, 56.69; H, 8.27; $C_{13}H_{22}O_6$ requires C, 56.92; H, 8.08%).
Further elution gave the *homoaltrose derivative **13*** (720 mg, 43 %) as a colourless oil, $[\alpha]_D^{22}$ -27.3 (c, 1.2 in $CHCl_3$). ν_{max} (film/cm^{-1}): 3467 (br, OH). δ_H ($CDCl_3$, 200 MHz): 1.35 (3H, d, $J_{6,7}$ 6.5 Hz, Me); 1.34, 1.37, 1.46, 1.50 (12H, 4 x s, 2 x Me_2C); 2.36 (1H, br, OH-3); 4.18 (2H, m, H-4 and H-5); 4.33 (1H, m , H-3); 4.44 (1H, m, H-6); 4.53 (1H, d, $J_{1,2}$ 3.6 Hz, H-2); 5.97 (1H, d, $J_{1,2}$ 3.6 Hz, H-1). δ_C ($CDCl_3$, 125 MHz): 14.6 (q, Me); 25.4, 26.3, 27.0, 28.1 (4 x q, 2 x ($\underline{C}H_3)_2C$); 73.2, 76.1, 76.3, 78.0, 84.3 (5 x d, C-2, C-3, C-4, C-5, C-6); 105.7 (d, C-1); 108.3 (s, $\underline{C}Me_2$); 111.7 (s, $\underline{C}Me_2$). *m/z* (CI, NH_3): 292 ($M+NH_4^+$, 8%), 275 ($M+H^+$, 100%). (Found: C, 56.65; H, 8.24. $C_{13}H_{22}O_6$ requires C, 56.92; H, 8.08%).

*7-Deoxy-1,2-O-isopropylidene-L-glycero-β-D-gluco-heptofuranose **12***. Tetrabutylammonium fluoride (1.1 M in THF, 1.29 mmol, 1.5 eq., 1.18 ml) was added dropwise under N_2 to the silyl ether **9**(300 mg, 0.862 mmol) in dry THF (2 ml) under N_2. After 1 hour, TLC (ethyl acetate/hexane 1/1) showed no starting material (Rf 0.85) and a single product (Rf 0.2). The solvent was removed under reduced pressure and purification of the residue by flash chromatography (ethyl acetate) gave *the homofucose acetonide **12***(180 mg, 90 %) as a white solid, m.p. 135-137°C (ethyl acetate). $[\alpha]_D^{22}$ -14.8 (c, 0.85 in acetone). ν_{max} (KBr/cm^{-1}): 3390 (OH, br). δ_H (500 MHz, acetone-d_6): 1.21 (3H, d, $J_{6,7}$ 6.5 Hz, Me); 1.26, 1.40 (6H, 2 x s, Me_2C); 3.54 (1H, d, $J_{6,OH}$ 6.2 Hz, OH-6); 3.65 (1H, m, H-5); 3.81 (1H, d, $J_{5,OH}$ 6.9 Hz, OH-5); 3.87 (1H, dq, $J_{5,6}$ 3.0 Hz, $J_{6,7}$ 6.5 Hz, H-6); 4.11 (1H, dd, $J_{3,4}$ 2.8, $J_{4,5}$ 7.8 Hz, H-4); 4.23 (1H, dd, $J_{3,4}$ 2.8 Hz, $J_{3,OH}$ 6.1 Hz, H-3); 4.29

(1H, d, $J_{3,OH}$ 4.3 Hz, OH-3); 4.47 (1H, d, $J_{1,2}$ 3.7 Hz, H-2); 5.85 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, acetone-d_6): 19.8 (q, Me); 26.0, 26.7 (2 x q, $(\underline{C}H_3)_2C$); 67.4, 72.6, 75.3, 80.6, 85.7 (5 x d, C-2, C-3, C-4, C-5, C-6); 105.4 (d, C-1); 111.2 (s, $\underline{C}Me_2$). *m/z* (CI, NH_3): 252 ($M+NH_4^+$, 75%), 234 ($M+NH_4^+-H_2O$, 25%), 194 (100%). (Found C, 51.44 ; H, 7.83; $C_{10}H_{18}O_6$ requires C, 51.26; H, 7.75%).

7-Deoxy-1,2-O-isopropylidene-D-glycero-α-D-gluco-heptofuranose ***11.*** The homoaltrose diacetonide **13** (54 mg, 0.182 mmol) was dissolved in 80% aqueous acetic acid (5 ml) at room temperature. After 20 hours, TLC (ethyl acetate) showed no starting material (Rf 0.8) and a new product (Rf 0.2). The solvent was removed under reduced pressure and coevaporated with toluene (2 x 5 ml). Purification of the residue by flash chromatography (ethyl acetate) gave *the homoaltroacetonide* ***11*** (33 mg, 79%) as a white solid, m.p. 145-147°C (ethyl acetate) ν_{max} (KBr/cm^{-1}): 3343 (OH, br). δ_H (500 MHz, acetone-d_6): 1.18 (3H, d, $J_{6,7}$ 6.1 Hz, Me); 1.27, 1.40 (6H, 2 x s, Me_2C); 3.68 (1H, d, $J_{6,OH}$ 4.9 Hz, OH-6); 3.87 (2H, m, H-6, H-5); 4.08 (1H, dd, $J_{3,4}$ 2.8 Hz, $J_{4,5}$ 6.5 Hz, H-4); 4.12 (1H, d, $J_{5,OH}$ 6.5 Hz, OH-5); 4.25 (1H, m, H-3); 4.46 (1H, d, $J_{1,2}$ 3.7 Hz, H-2); 4.53 (1H, d, $J_{3,OH}$ 4.3 Hz, OH-3); 5.86 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, acetone-d_6): 18.4 (q, Me); 26.5, 27.2 (2 x q, $(\underline{C}H_3)_2C$); 69.1, 73.4, 75.8, 81.0, 86.1 (5 x d, C-2, C-3, C-4, C-5, C-6); 105.8 (d, C-1); 111.2 (s, $\underline{C}Me_2$). *m/z* (CI, NH_3): 252 ($M+NH_4^+$, 72%), 234 ($M-H_2O+NH_4^+$, 22%), 194 (M-40, 100%).

7-Deoxy-L-glycero-D-gluco-heptopyranose, Homofucose ***2.***

Method 1: Water (7.5 ml) was added to a solution of the silyl ether **9**(1.02 g, 2.94 mmol) in 1,4-dioxan (7.5 ml). Ion exchange resin (Amberlyst IR-120 (H^+), 2.5 g) was added and the reaction mixture was stirred at 60° C for 8 hours by which time TLC (ethyl acetate/hexane 1:1) showed no starting material (Rf 0.6) and a new baseline product. The resin was removed by filtration and washed with water; the combined filtrates (30 ml) were washed with ethyl acetate (2 x 20 ml) and the aqueous phase was concentrated under reduced pressure and coevaporated with toluene (2 x 15 ml) to afford *homofucose* ***2***(524 mg, 92%), m.p. 168-175°C. $[\alpha]_D^{23}$ + 21.8 (c, 1.05 in H_2O, β anomer), + 95.9 (c, 1.05 in H_2O, α anomer), (lit $[\alpha]_D^{23}$ + 41.0 (c, 1 in H_2O). ν_{max} (KBr/cm^{-1}): 3434 (OH, br). δ_H (500 MHz, D_2O): 1.21 (3H, d, $J_{6,7}$ 6.6 Hz, Meα); 1.25 (3H, d, $J_{6,7}$ 6.6 Hz, Meβ); 3.18 (1H, dd, J 1.8, 9.7 Hz, H-5β); 3.20 (1H, app. t, J 8.6 Hz, H-2β); 3.41-3.54 (5H, m, H-2α, H-3β, H-4α, H-4β, H-5α); 3.66 (1H, app. t, J 9.4 Hz , H-3α); 4.08 (1H, dq, $J_{5,6}$ 1.8 Hz, $J_{6,7}$ 6.6 Hz, H-6β); 4.13 (1H, dq, $J_{5,6}$ 1.8 Hz, $J_{6,7}$ 6.6 Hz, H-6α); 4.57 (1H, d, $J_{1,2}$ 7.9 Hz, H-1β); 5.20 (1H, d, $J_{1,2}$ 3.8 Hz, H-1α). δ_C (125 MHz, D_2O + dioxan): 19.3 (q, Me); 19.5 (q, Me); 65.0, 65.1, 70.4, 70.6, 72.3, 73.8, 74.0, 75.1, 76.8, 78.5 (10 x d, C-2, C-3, C-4, C-5, C-6 α and β); 92.8 (d, C-1α); 96.9 (d, C-1β). *m/z* (DCI, NH_3): 212 ($M+NH_4^+$, 22%), 194 ($M-H_2O+NH_4^+$, 100%). (Found C, 43.57; H, 7.46. $C_7H_{14}O_6$ requires C, 43.30; H, 7.27%).

Method 2: A 3:2 mixture of trifluoroacetic acid/water (5 ml) was added to the diacetonide **14** (212 mg, 0.77 mmol). The solution was stirred overnight at room temperature. After 17 hours, TLC (ethyl acetate) showed no starting material (Rf 0.8) and a new baseline product. The solvent was removed under reduced pressure and coevaporated with toluene (2 x 5 ml) to give *homofucose* **2**(139 mg, 0.72 mmol, 93%), identical to the material above. The diacetonide could also be hydrolysed in a similar yield by acid ion exchange resin.

7-Deoxy-D-glycero-D-gluco-heptopyranose, Homodeoxyaltrose ***1.*** A 3:2 mixture of trifluoroacetic acid/water (7 ml) was added to the altrodiacetonide **13** (323 mg, 1.18 mmol) at room temperature. After 16 hours, TLC (ethyl acetate) showed no starting material (Rf 0.75) and a new baseline product. The solvent was removed under reduced pressure and coevaporated with toluene (2 x 5 ml). The resulting foam was freeze-dried to yield *homodeoxyaltrose* ***1*** (217 mg, 95%), m.p. 29-31°C (melt). $[\alpha]_D^{21}$ + 41.5 (c, 0.8 in H_2O) (lit $[\alpha]_D^{24}$ + 38 (c, 4 in H_2O). ν_{max} (film/cm^{-1}): 3349 (OH, br). δ_H (500 MHz, D_2O): 1.16 (3H, d, $J_{6,7}$ 6.2 Hz, Meα); 1.17 (3H, d,

$J_{6,7}$ 6.4 Hz, Meβ); 3.17 (1H, H-2β); 3.30 (2H, H-4α, H-4β); 3.41 (2H, H-3β, H-5b); 3.47 (1H, H-2α); 3.64 (1H, H-3α); 3.81 (1H, H-5α); 4.09 (2H, H-6α, H-6β); 4.57 (1H, d, $J_{1,2}$ 7.9 Hz, H-1β); 5.17 (1H, d, $J_{1,2}$ 3.8 Hz, H-1α). δ_C (125 MHz, D_2O + dioxane): 14.7 (q, Me); 14.8 (q, Me); 66.1, 70.5, 70.7, 71.2, 72.8, 72.9, 74.0, 75.7, 77.7 (9 x d, C-2, C-3, C-4, C-5, C-6 α and β); 91.9 (d, C-1α); 96.0 (d, C-1β). m/z (DCI, NH_3): 212 ($M+NH_4^+$, 40%), ($M-H_2O+NH_4^+$, 100%). (Found C, 43.24; H, 7.16. $C_7H_{14}O_6$ requires C, 43.30; H, 7.27%).

6-O-tert-Butyldimethylsilyl-7-deoxy-1,2-O-isopropylidene-L-glycero-α-D-gluco-heptofuranose ***9***. Sodium borohydride (2.052 g, 54.26 mmol, 1.5 eq.) was added to a solution of the lactols **8** (12.51 g, 36.17 mmol) in ethanol (100 ml) at room temperature, and the reaction mixture stirred at room temperature. After 2 hours, TLC (ethyl acetate/hexane 1:1) showed complete conversion of the starting material (Rf 0.75) into a new product (Rf 0.55). The reaction was quenched with solid ammonium chloride and the solution was stirred until effervescence has ceased, filtered through Celite and eluted with ethyl acetate. The solvent was removed and the residue purified by flash chromatography (ethyl acetate/hexane 1:2) to afford *the diol* ***9*** (8.33 g, 66 %) as a white solid, m.p. 97-99°C (hexane). $[\alpha]_D^{22}$ +2.9 (c, 0.95 in $CHCl_3$). ν_{max} (KBr/cm^{-1}): 3515 (br, OH). δ_H (500 MHz, $CDCl_3$): 0.12 (6H, s, Me_2Si), 0.91 (9H, s, $(CH_3)_3CSi$), 1.25 (3H, d, $J_{6,7}$ 6.6 Hz, Me), 1.31, 1.47 (6H, 2 x s, Me_2C), 2.70 (1H, d, $J_{5,OH}$ 8.5 Hz, OH-5), 2.96 (1H, d, $J_{3,OH}$ 3.1 Hz, OH-3), 3.59 (1H, app. dt, $J_{5,6}$ 2.4, $J_{4,5}$ 8.3 Hz, H-5), 4.03 (1H, dd, $J_{4,5}$ 8.3 Hz, $J_{3,4}$ 2.8 Hz, H-4), 4.07 (1H, dq, $J_{5,6}$ 2.4 Hz, $J_{6,7}$ 6.6 Hz, H-6), 4.32 (1H, m, H-3), 4.53 (1H, d, $J_{1,2}$ 3.7 Hz, H-2), 5.93 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, $CDCl_3$): -4.8, -4.3 (2 x q, $(CH_3)_2Si$), 18.0 (s, $(CH_3)_3\underline{C}Si$), 20.5 (q, Me), 25.8 (q, $(\underline{C}H_3)_3CSi$), 26.1, 26.7 (2 x q, $(\underline{C}H_3)_2C$), 67.9, 73.2, 75.5, 80.0, 85.0 (5 x d, C-2, C-3, C-4, C-5, C-6), 105.1 (d, C-1), 111.3 (s, $\underline{C}Me_2$). *m/z* (CI, NH_3): 366 ($M+NH_4^+$, 3%), 349 ($M+H^+$, 100%), 291 ($M-(CH_3)_3C$, 27%). (Found: C, 55.00; H, 9.59; $C_{16}H_{32}O_6Si$ requires C, 55.14; H, 9.26%).

6-O-tert-Butyldimethylsilyl-7-deoxy-1,2:3,5-di-O-isopropylidene-L-glycero-α-D-gluco-heptofuranose ***15***. The silyl protected diol **9** (600 mg, 1.71 mmol) was dissolved in acetone (27 ml) and 2,2-dimethoxypropane (3 ml) with a catalytic amount of camphor sulfonic acid and the solution stirred at room temperature under N_2. After 12 hours, TLC (ethyl acetate/hexane 1:2) showed some starting material (Rf 0.2) and a new product (Rf 0.8). Ethyl acetate was added (60 ml) and the reaction was quenched with $NaHCO_3$. The solution was filtered through Celite eluted with ethyl acetate, the solvent removed and the residue purified by flash chromatography (ethyl acetate/hexane 1:4 then ethyl acetate) to afford *the six-ring acetonide* ***15*** (570 mg, 85 %) as a colourless oil, $[\alpha]_D^{24}$ +23.1 (c, 1.54 in $CHCl_3$). ν_{max} (KBr/cm^{-1}): 2936 (CH). δ_H (500 MHz, $CDCl_3$): 0.05, 0.06 (6H, 2 x s, Me_2Si); 0.88 (9H, s, $(CH_3)_3CSi$); 1.19 (3H, d, $J_{6,7}$ 6.4 Hz, Me); 1.32, 1.33, 1.34, 1.48 (12H, 4 x s, 2 x Me_2C); 3.32 (1H, app. t, J 6.8 Hz, H-5); 3.82 (1H, app. qt, $J_{6,7}$ 6.4 Hz, H-6); 4.13 (1H, d, $J_{3,4}$ 3.6 Hz, H-3); 4.25 (1H, dd, $J_{4,5}$ 3.6 Hz, $J_{3,4}$ 7.0 Hz, H-4); 4.54 (1H, d, $J_{1,2}$ 3.7 Hz, H-2); 5.98 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, $CDCl_3$): -4.6, -4.5 (2 x q, $(CH_3)_2Si$); 18.2 (s, $(CH_3)_3\underline{C}Si$); 19.1 (q, Me); 25.8 (q, $(\underline{C}H_3)_3CSi$); 23.6, 24.3, 26.6, 27.1 (4 x q, 2 x $(\underline{C}H_3)_2C$); 69.3, 75.1, 76.3, 80.1, 83.7 (5 x d, C-2, C-3, C-4, C-5, C-6); 100.7 (s, $\underline{C}Me_2$ dioxane ring), 106.3 (d, C-1); 111.8 (s, $\underline{C}Me_2$ dioxolane ring). *m/z* ($APCI^+$): 389.48 ($M+H^+$, 18%), 273.52 ($M+H^+$-TBDMS, 69%). (Found: C, 58.73; H, 9.64; $C_{19}H_{36}O_6Si$ requires C, 58.37; H, 9.34%).

7-Deoxy-1,2:3,5-di-O-isopropylidene-L-glycero-α-D-gluco-heptofuranose ***16***. A 1M solution of tetrabutyl ammonium fluoride (0.60 ml, 0.60 mmol) was added to a stirred solution of the silyl diacetonide **15** (200 mg, 0.52 mmol) in THF (10 ml) under N_2 at room temperature. After 16 hour, TLC (ethyl acetate/hexane 1:4) showed only traces of starting material (Rf 0.88) and one major compound (Rf 0.25). The solvent was

removed *in vacuo* and the residue purified by flash chromatography (ethyl acetate/hexane 1:4) to yield *the diacetonide* ***16*** (135 mg, 95%) as a colourless oil, $[\alpha]_D^{22}$ +41.1 (c, 1.40 in CH_3OH). ν_{max} (film/cm^{-1}): 3502 (OH). δ_H (500 MHz, $CDCl_3$): 1.26 (3H, d, $J_{6,7}$ 6.4 Hz, Me); 1.33, 1.36, 1.37, 1.50 (12H, 4 x s, 4 x CH_3); 2.26 (1H, d, $J_{OH,6}$ 4.2 Hz, exch. in D_2O, OH); 3.33 (1H, t, J 6.7 Hz, H-5), 3.77-3.82 (1H, m, H-6); 4.17 (1H, d, $J_{3,4}$ 3.7 Hz, H-3); 4.32 (1H, dd, $J_{3,4}$ 3.7, $J_{4,5}$ 7.0 Hz, H-4); 4.57 (1H, d, $J_{1,2}$ 3.8 Hz, H-2); 6.00 (1H, d, $J_{1,2}$ 3.8 Hz, H-1). δ_C (125 MHz, $CDCl_3$): 17.9 (C-7); 23.8, 24.0, 26.5, 27.1 (4 x CH_3); 68.5 (C-6); 75.1, 76.1, 79.9, 83.7 (C-2, C-3, C-4, C-5); 101.0 (<u>C</u>Me_2 dioxane ring); 112.0 (<u>C</u>Me_2 dioxolane ring). *m/z* (APCI$^+$): 275 (M+H$^+$, 11%). (Found C, 56.50; H, 8.33; $C_{19}H_{38}O_6Si$ requires C, 56.92; H, 8.08%).

7-Deoxy-1,2:3,5-di-O-isopropylidene-6-O-methylsulfonyl-L-glycero-α-D-gluco-heptofuranose ***17***. Mesyl chloride (134 µl, 1.67 mmol) was added dropwise to a solution of the alcohol **16** (183 mg, 0.67 mmol) and dimethylaminopyridine (catalytic amount) in dry pyridine (1 ml). The reaction mixture was stirred at room temperature under N_2 for 15 hour. After this time, TLC (toluene/acetone 39:1) showed no starting material (Rf 0.10) and a new compound (Rf 0.20). The solvent was removed *in vacuo* and the residue dissolved in chloroform, washed with water, dried and concentrated under reduced pressure. The residue was purified by flash chromatography (ethyl acetate/hexane 1:4) to give *the mesylate* ***17*** (193 mg, 82%) as a white solid, m.p. 119-120°C (hexane). $[\alpha]_D^{22}$ +19.0 (c, 0.96 in CH_3OH). ν_{max} (film/cm^{-1}): 2989, 2940 (CH). δ_H (500 MHz, $CDCl_3$): 1.33, 1.35, 1.36, 1.48 (12H, 4 x s, 4 x CH_3); 1.48 (3H, d, $J_{7,6}$ 6.5 Hz, Me); 3.01 (3H, s, CH_3-S); 3.56 (1H, app. t, J 7.5 Hz, H-5); 4.21 (1H, d, $J_{3,4}$ 3.8 Hz, H-3), 4.25 (1H, dd, $J_{4,3}$ 3.7, $J_{4,5}$ 7.3 Hz, H-4); 4.57 (1H, d, $J_{1,2}$ 3.7 Hz, H-2), 4.73 (1H, app. q, J 6.8 Hz, H-6); 5.99 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, $CDCl_3$): 17.1 (C-7); 23.6, 23.9, 26.5, 27.1 (4 x CH_3); 38.4 (CH_3-S); 74.2, 75.2, 79.6, 79.8, 83.5 (C-2, C-3, C-4, C-5, C-6); 101.2 (<u>C</u>Me_2 dioxane ring); 106.5 (C-1); 112.3 (<u>C</u>Me_2 dioxolane ring). *m/z* (APCI$^+$): 375 (M+Na$^+$, 70%), 353 (M+H$^+$, 26%), 186 (100%). (Found C, 48.03; H, 6.84; $C_{14}H_{24}O_8S$ requires C, 47.72; H, 6.86%).

6-Azido-6,7-dideoxy-1,2:3,5-di-O-isopropylidene-D-glycero-α-D-gluco-heptofuranose ***18***. A mixture of the mesylate **18** (88 mg, 0.25 mmol) and sodium azide (24 mg, 0.37 mg) in DMF (10 ml) was stirred at 75°C under N_2 for 70 hour. After this time, TLC (toluene/acetone 39:1) showed no starting material (Rf 0.20) and a new major spot (Rf 0.58). The solvent was removed *in vacuo* and the residue purified by column chromatography (toluene/acetone 39:1) to afford *the azide* ***18*** (62 mg, 83%) as a colourless oil, $[\alpha]_D^{21}$ +45.0 (c, 0.53 in CH_3OH). ν_{max} (film/cm^{-1}): 2126 (N_3). δ_H (500 MHz, $CDCl_3$): 1.27 (3H, d, $J_{7,6}$ 6.9 Hz, H-7); 1.33, 1.36, 1.37, 1.50 (12H, 4 x s, 4 x CH_3); 3.58 (1H, dd, $J_{5,6}$ 4.0, $J_{5,4}$ 6.7 Hz, H-5); 3.66-3.71 (1H, m, H-6); 4.20 (1H, d, $J_{3,4}$ 3.4 Hz, H-3), 4.44 (1H, dd, $J_{3,4}$ 3.6, $J_{4,5}$ 6.8 Hz, H-4); 4.56 (1H, d, $J_{1,2}$ 3.7 Hz, H-2), 6.00 (1H, d, $J_{1,2}$ 3.7 Hz, H-1). δ_C (125 MHz, $CDCl_3$): 14.7 (C-7); 23.7, 24.0, 26.4, 27.1 (4 x CH_3); 58.4 (C-6); 74.9, 75.3, 79.1, 83.5 (C-2, C-3, C-4, C-5); 101.0 (<u>C</u>Me_2 dioxane ring); 106.4 (C-1); 112.1 (<u>C</u>Me_2 dioxolane ring). *m/z* (APCI$^+$): 272 (M-N_2+H$^+$, 100%). (Found C, 52.05; H, 7.22; N, 14.14; $C_{13}H_{21}N_3O_5$ requires C, 52.16; H, 7.07; N, 14.04%).

6-Azido-6,7-dideoxy-D-glycero-D-gluco-heptopyranose ***3***. A solution of the protected azide **18** (28 mg, 0.1 mmol) in a 3:2 mixture of trifluoroacetic acid/water (5 ml) was stirred for 17 h at room temperature. After this time, TLC (ethyl acetate) showed no starting material (Rf 0.84) and a new product (Rf 0.18). The solvent was removed under reduced pressure and coevaporated with toluene. The residue was purified by flash chromatography (ethyl acetate) to give *the unprotected anomeric azides* ***3*** as a colourless oil, (20 mg, 97% yield), $[\alpha]_D^{23}$ +8.9 (c, 1.11 in MeOH). ν_{max} (film/cm^{-1}): 3368 (OH); 2923 (CH); 2112 (N_3), δ_H (500 MHz, D_2O): 1.17 (3H, d, $J_{7,6}$ 6.9 Hz, CH_3 α); 1.20 (3H, d, $J_{7,6}$ 6.9 Hz, CH_3 β); 3.11 (1H, dd, $J_{2,1}$ 8.0, $J_{2,3}$ 9.2 Hz, H-2β); 3.27 (1H, app. t, J 9.6 Hz, H-4α); 3.28 (1H, app. t, J 9.4 Hz, H-4β); 3.35 (1H, t, J 9.2 Hz, H-

3β); 3.42 (1H, dd, $J_{2,1}$ 3.8, $J_{2,3}$ 9.8 Hz, H-2α); 3.47 (1H, dd, $J_{5,6}$ 2.3, $J_{5,4}$ 9.8 Hz, H-5β); 3.57 (1H, t, J 9.4 Hz, H-3α); 3.75 (1H, dq, $J_{6,5}$ 2.3, $J_{7,6}$ 6.9 Hz, H-6β); 3.80 (1H, dq, $J_{6,5}$ 2.3, $J_{7,6}$ 6.9 Hz, H-6α); 3.85 (1H, dd, $J_{5,6}$ 2.3, $J_{5,4}$ 10.2 Hz, H-5α); 4.54 (1H, d, $J_{1,2}$ 8.0 Hz, H-1β); 5.11 (1H, d, $J_{1,2}$ 3.8 Hz, H-1α). δ_C (125 MHz, D_2O+dioxane) 12.29 (Me β); 12.44 (Me α); 56.88 (C-6β); 56.99 (C-6); 71.19, 72.08, 72.75, 73.59 (C-2α, C-3α, C-4α, C-5α); 70.98, 74.81, 76.48, 77.42 (C-2β, C-3β, C-4β, C-5β); 92.83 (C-1α); 96.80 (C-1β). *m/z* (APCI$^-$): 218 (M-H$^-$, 100%). (Found C, 38.60; H, 6.12; N, 18.89; $C_7H_{13}N_3O_5$ requires C, 38.36; H, 5.98; N, 19.17%).

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