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KETALS OF L-RHAMNOHEPTONOLACTONES: POTENTIAL MIMICS OF L-RHAMNOSE

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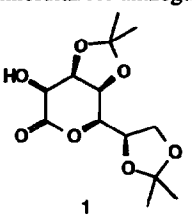
Abstract: Isopropylidene and cyclohexylidene ketals of γ- and δ-heptonolactones derived from Kiliani ascensions of protected L-rhamnose may constitute suitable intermediates for the preparation of mimics of L-rhamnose. The X-ray crystal structure of 7-deoxy-3,4-*O*-isopropylidene-L-*glycero*-L-*galacto*-heptono-1,5-lactone provides an example of a δ-lactone in a boat conformation with a substituent in a flagpole position. The size of ring in the lactones is completely consistent with Hudson's classical lactone rotation rule of 1910.

Mimics of carbohydrates which interact with enzymes and/or receptors may provide access to classes of materials with interesting biological activities specific to the parent sugar. Analogues such as C-glycosides require a seven carbon sugar to mimic a hexose;[1] for example, readily available benzylidene[2] and isopropylidene[3] derivatives of glucoheptonolactones have been used in the synthesis of potential phosphorylase inhibitors.[4,5] The diacetonide **1**,[6,7] derived from the Kiliani ascension of diacetone mannose, has been used for the synthesis of a wide variety of materials[8] such as the specific mannosidase inhibitors homomannojirimycin **2**[9] and homoDIM **3**[10] as well as a new class of glycopeptide, such as the mannofuranose analogue **4**, in which the anomeric position may be incorporated into a peptide chain.[11]



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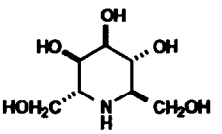

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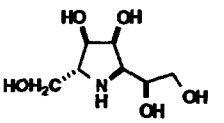

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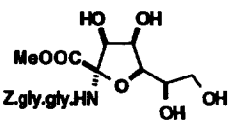

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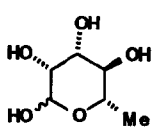
L-Rhamnose **5** is a constituent of cell walls of many plants and mycobacteria; analogues[12] of rhamnose may provide clues to understanding biochemical pathways involved in the biosynthesis of such structures. Thus, azapyranose **6** and azafuranose **7** analogues of rhamnose, as well as the novel peptide **8**, should be readily available from the products of the Kiliani synthesis[13,14] on protected derivatives of L-rhamnose. This paper reports the synthesis and characterisation of isopropylidene and cyclohexylidene derivatives of seven carbon-sugar lactones derived from rhamnose and of other intermediates likely to be useful in the synthesis of a wide range of mimics of L-rhamnose.



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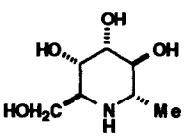

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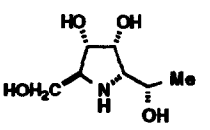

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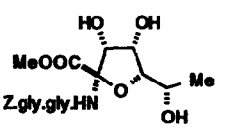

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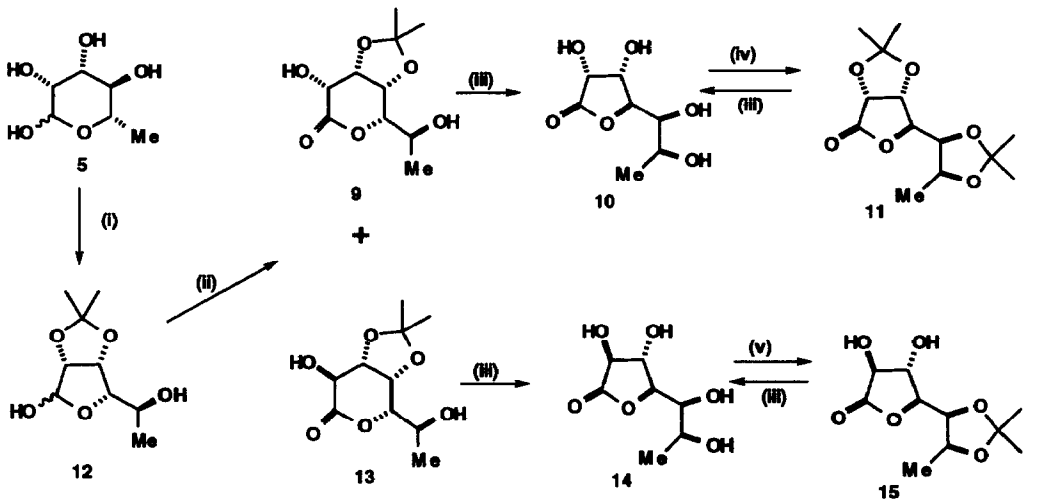


Scheme 1: (i) Me_2CO, $CuSO_4$, conc. H_2SO_4 (ii) NaCN, then H^+ (iii) aq. CF_3COOH (1:1) (iv) Me_2CO, $Me_2C(OMe)_2$, CSA (v) Me_2CO, CSA

Rhamnose **5** was treated with acetone in the presence of anhydrous copper sulphate and concentrated sulphuric acid to give the isopropylidene derivative **12**[15] [Scheme 1] which without purification underwent the Kiliani ascension on treatment with sodium cyanide to give a mixture of the epimeric δ-lactones **9** [29% yield] and **13** [9% yield]. The combined yield of **9** and **13** [38%] and the ratio of the two epimers [3:1] are similar to those in the Kiliani synthesis of diacetone mannose to give **1** and its epimer.[6,7] The structure of the minor component **13** was firmly established by single crystal X- ray analysis [Figure]. Such δ-lactones are usually in a boat conformation; this is the first example of such a sugar lactone with a substituent clearly in a flagpole orientation.

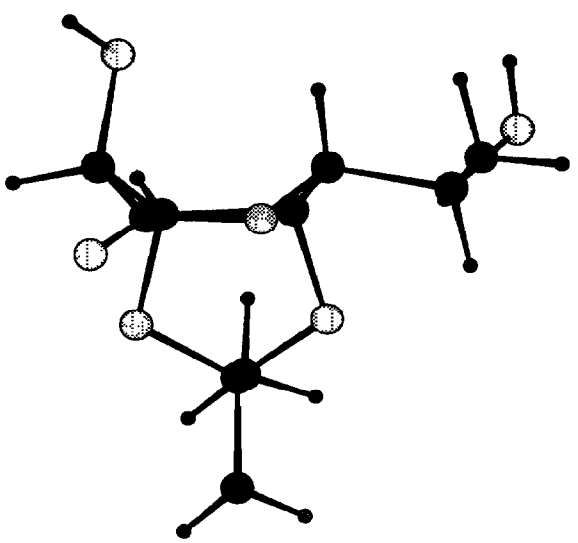
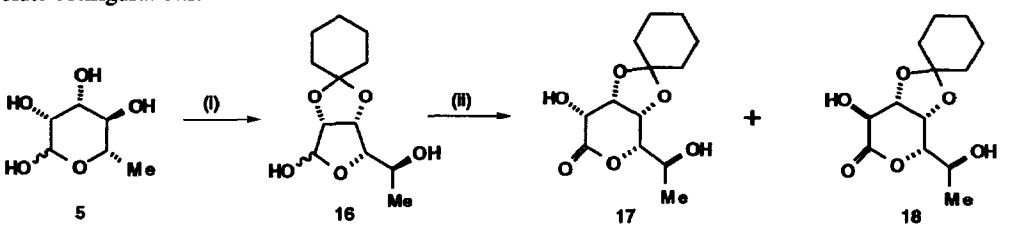


Figure X-Ray structure of 7-deoxy-3,4-O-isopropylidene-L-*glycero*-L-*galacto*-heptono-1,5-lactone **13**

The isopropylidene groups were removed from **9** and **13** by treatment with aqueous trifluoroacetic acid to give the 1,4-lactones **10** and **14** in quantitative yield. Reaction of **10** with dimethoxypropane in acetone in the presence of camphor sulphonic acid gave a diacetonide **11** in 84% yield whereas similar reaction of **14** - with a *trans*-diol unit in the γ-

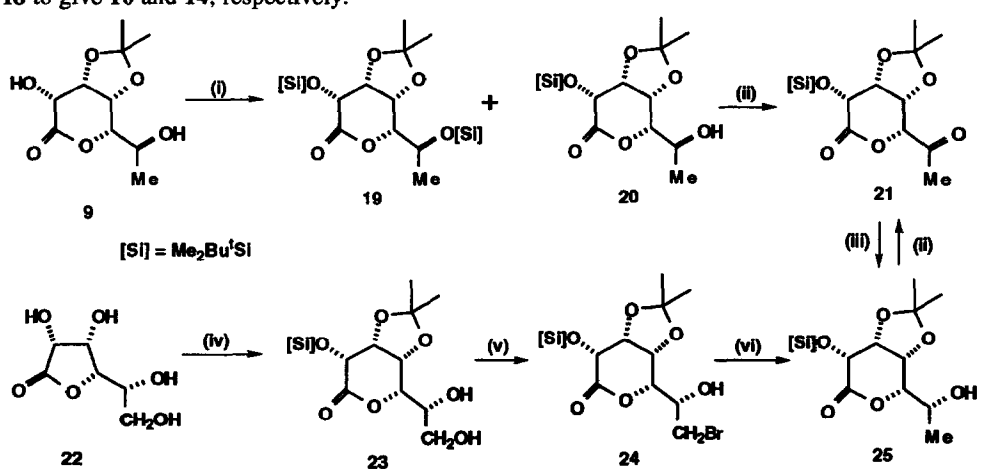
lactone moiety - afforded a monoisopropylidene derivative **15** in 88% yield. Both the di- **11** and mono- **15** acetonides gave the unprotected lactones **10** and **14**, respectively, on treatment with aqueous trifluoroacetic acid in excellent yields. The lactone **10** is the minor - and **14** the major - component in the Kiliani reaction of unprotected rhamnose;[16,17] thus, as in the case of diacetone mannose *versus* unprotected mannose,[6,7] there is a similar inversion in the diastereoselectivity of the protected and unprotected rhamnose Kiliani reactions.

It is noteworthy that all the δ-lactones of the rhamnoheptonic acids have negative specific rotations whereas all the γ-lactones have positive rotation values; this is completely in agreement with Hudson's classical rotation rules for lactones,[18] in which the rotation of the compound depends solely on the absolute configuration of the carbon bearing the ring oxygen. Thus, the sign of rotation in this series of lactones is a good guide as to whether the structure is a γ- or a δ-lactone in *this* case, becuase the C atoms have opposite absolute configurations.



Scheme 2: (i) cyclohexanone, $CuSO_4$, conc. H_2SO_4 (ii) NaCN, then H^+

The use of cyclohexylidene in comparison with isopropylidene protection of a sugar usually increases the ease of solubility of such derivatives and changes the rate of acid hydrolysis of the ketal group. Accordingly, the cyclohexylidene derivatives of the heptonolactones were also prepared [Scheme 2]. Rhamnose was treated with cyclohexanone in the presence of acid to give a crude preparation of the cyclohexylidene derivative **16** which underwent a Kiliani reaction on treatment with sodium cyanide to give a mixture of **17** [37% yield] and **18** [13% yield], in which both the ratio of the two δ-lactones and the stereochemistry of the cyanohydrin ascension are very similar to those of the acetonide reaction above. The structures of the lactones were clearly demonstrated by the acid hydrolysis of the cyclohexylidene ketals in **17** and **18** to give **10** and **14**, respectively.



Scheme 3: (i) Bu^tMe_2SiCl, imidazole, DMF (ii) PCC, molecular sieve, CH_2Cl_2 (iii) $NaBH_4$, aq. EtOH

(iv) ref. 6 (v) Ph_3P, CBr_4, THF (vi) H_2, Pd black, Et_3N, EtOAc

For the synthesis of piperidine analogues of L-rhamnose, such as **6**, from **9** and/or **13**, it is necessary to achieve the introduction of nitrogen at C-6 of the lactones with overall retention of configuration. Reaction of **9** with *tert*-butyldimethylsilyl chloride in dimethylformamide in the presence of imidazole [Scheme 3] gave a highly selective reaction in which a small amount of the disilyl ether **19** was formed [10% yield] with the C-2 *O*-silyl ether **20** as the major product [89% yield, based on recovered starting material]. It is generally the case that hydroxyl groups α- to a lactone carbonyl functionality are more nucleophilic than any other secondary hydroxyl group in a carbohydrate lactone. Oxidation of the remaining free hydroxyl group in **20** by pyridinium chlorochromate in dichloromethane in the presence of molecular sieve afforded the crystalline ketone **21** in 86% yield. Treatment of the ketone **21** with sodium borohydride in aqueous ethanol gave the epimeric alcohol **25** [90% yield] in a highly diastereoselective reaction which is the anticipated result of either chelated or non-chelated control during the reduction. This provides easy access to intermediates which should allow the unambiguous synthesis of materials such as **6**. The inverted alcohol was also prepared from D-gulonolactone **22** by initial transformation to **23** as previously described.[6] Thus, reaction of **23** with triphenylphosphine and carbon tetrabromide in tetrahydrofuran afforded the primary bromide **24** [90% yield] which on hydrogenation in ethyl acetate in the presence of palladium black and triethylamine gave **25** [94% yield] identical to the material prepared from rhamnose. The alcohol **25** could also be oxidised by pyridinium chlorochromate to the ketone **21**. Although the route from rhamnose to **21** and **25** is much more efficient for the preparation of larger quantities of material, the preparation from D-gulonolactone secures the structures of all the compounds in Scheme 3 and in particular confirms that no epimerisation of the carbon α- to the ketone functionality in **21** has occurred.

In summary the intermediates described in this paper may provide easy access to seven-carbon analogues of L-rhamnose which may provide new strategies for the control of plant growth processes and/or the chemotherapy of diseases such as leprosy initiated by mycobacteria.

X-Ray Crystal Analysis

The relative configuration of the chiral centres in 7-deoxy-3,4-*O*-isopropylidene-L-*glycero*-L-*galacto*-heptono-1,5-lactone **13** (crystallised from ethyl acetate:hexane) was established by single crystal X-ray analysis. Cell dimensions and intensity data were measured with an Enraf-Nonius CAD4-F diffractometer. A suitable crystal of approximate dimensions 0.17 x 0.20 x 0.28 mm was selected. Molecular formula $C_{10}H_{16}O_6$. Formula weight 232.23; Orthorhombic $P\,2_12_12_1$. No. of molecular units in the cell Z, 8. Calculated Density (gcm^{-3}), 1.39. Reflections for lattice parameters, 25. θ range for lattice parameters, 27.92 - 39.65. Linear absorption coeff.(cm^{-1}), 9.84. Data collection parameters: h range, -1 to 8; k range, -1 to 14; l range, -1 to 35; θ range, 0 to 72° Copper radiation, λ = 1.5418Å. No. of automatic reorientations, 0. Temperature (K), 294. No. of intensity standards, 4. Decay of standards, 4.9%. Total data collected, 3154. Number of data merged including Friedel pairs, 2635. Merging R-factor, 6.32. Number of reflections used, 2398. Criterion for observed, $I > 3\sigma(I)$.Absorption, DIFABS, min, 0.77, max, 1.14. The data were corrected for absorption, Lorentz and polarisation effects. All calculations were carried out on a Microvax 3800 computer. SHELXS-86[19] succeeded in finding all 32 non-hydrogen atoms in the two independent molecules and these were put into CRYSTALS[20] as 20 carbon and 12 oxygen atoms; these were refined to convergence, using full matrix least-squares refinement, of the positional parameters and isotropic temperature factors. Atomic scattering

factors were taken from International Tables.[21] The hydrogen atoms were placed geometrically and refinement completed with all the non-hydrogen atom temperature factors refined anisotropically. Corrections for secondary extinction and anomalous scattering were applied.[22] Refinement: Maximum number of parameters, 418. Ratio of data : parameters, 6.3:1. Flack enantiopole parameter, not refined. $\Delta\rho$, min, -0.17, max, 0.13. The data were refined using Chebyshev three term weighting scheme[23] to give a final value of R = 0.035, R_w = 0.043. Cell parameters 7.070(6), 11.472(2) and 29.093(5) Å. Atomic coordinates for the compound have been deposited at the Cambridge Crystallographic Data Centre.[24]

Fractional atomic coordinates and equivalent isotropic temperature factors U(iso) with standard deviations in parentheses for 7-deoxy-3,4-*O*-isopropylidene-L-*glycero*-L-*galacto*-heptono-1,5-lactone **13**

Atom	x/a	y/b	z/c	U(iso)
O(1)	0.3616(2)	0.1671(1)	0.08250(5)	0.0542
O(2)	0.0481(3)	0.5460(2)	0.04344(6)	0.0640
O(3)	-0.3815(2)	0.6415(1)	0.09991(6)	0.0604
O(4)	-0.6357(3)	0.4326(2)	0.08726(6)	0.0650
O(5)	0.7631(3)	0.0128(2)	0.03499(6)	0.0672
O(6)	0.0957(3)	0.2339(1)	0.11014(7)	0.0692
O(7)	0.3211(3)	0.0156(2)	0.17812(6)	0.0676
O(8)	0.1035(3)	-0.0360(2)	0.06831(7)	0.0677
O(9)	-0.0656(2)	0.4945(2)	0.14202(6)	0.0666
O(10)	0.6044(3)	0.0365(2)	0.14397(6)	0.0699
C(11)	-0.2600(3)	0.5551(2)	0.07804(7)	0.0512
C(12)	-0.3743(4)	0.4217(2)	0.14235(8)	0.0572
C(13)	0.1901(3)	0.1492(2)	0.10143(7)	0.0522
O(14)	-0.3275(3)	0.4694(2)	0.18578(6)	0.0697
C(15)	-0.1267(4)	0.4804(3)	0.18842(8)	0.0692
C(16)	-0.2090(3)	0.4575(2)	0.11110(7)	0.0527
C(17)	0.6608(3)	0.1118(2)	0.05193(8)	0.0602
C(18)	0.4725(3)	0.0656(2)	0.06935(7)	0.0513
O(19)	-0.6427(3)	0.6771(2)	0.1385(1)	0.0871
C(20)	-0.5632(4)	0.4766(2)	0.12914(8)	0.0577
C(21)	0.1339(3)	0.0238(2)	0.11034(8)	0.0562
C(22)	-0.0894(3)	0.6253(2)	0.06142(8)	0.0574
C(23)	0.2977(4)	-0.0369(2)	0.13422(8)	0.0576
C(24)	0.6413(4)	0.2045(3)	0.0155(1)	0.0743
C(25)	-0.5359(4)	0.6063(2)	0.1229(1)	0.0622
C(26)	0.5195(4)	0.0158(3)	0.18773(9)	0.0670
C(27)	0.4878(3)	-0.0165(2)	0.10976(8)	0.0571
C(28)	-0.1412(5)	0.7095(3)	0.0237(1)	0.0710
C(29)	0.5607(8)	0.1174(4)	0.2184(1)	0.0884
C(30)	-0.0789(7)	0.5882(5)	0.2151(2)	0.1016
C(31)	-0.0419(6)	0.3703(5)	0.2083(1)	0.0895
C(32)	0.5796(7)	-0.0994(4)	0.2078(2)	0.0902

Experimental General Methods: Melting points were recorded on a Kofler hot block and are corrected. Proton nuclear magnetic resonance (δ_H) spectra were recorded on Varian Gemini 200 (at 200 MHz), Bruker WH 300 (300 MHz) and Bruker AC 200 (200 MHz) spectrometers or Bruker AM 500 (500 MHz). ^{13}C Nuclear magnetic resonance (δ_C) spectra were recorded on a Varian Gemini 200 (50 MHz) and Bruker AC 200 (50 MHz) spectrometers and multiplicities were assigned using DEPT sequence. All chemical shifts are quoted on the δ-scale. Infra-red spectra were recorded on a Perkin-Elmer 1750 FT spectrophotometer. Mass spectra were recorded on VG Micromass 30F, ZAB 1F, Masslab 20-250 or Trio-1 GCMS (DB-5 column) spectrometers using desorption chemical ionisation (NH_3, DCI), chemical ionisation (CI) or electron impact (EI), 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 (t.l.c.) was carried out on aluminium sheets coated with $60F_{254}$ silica or glass plates coated with silica Blend 41. Plates were developed using a spray of 0.2% w/v cerium (IV) sulphate and 5% ammonium molybdate in 2M sulphuric 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; dichloromethane was refluxed over and distilled from calcium hydride, pyridine was distilled from calcium hydride, and stored over potassium hydroxide; tetrahydrofuran was distilled, under nitrogen, from a solution dried with sodium in the presence of benzophenone. Hexane was distilled at 68°C before use to remove less volatile fractions. **L**-Rhamnose monohydrate **5** and **D**-gulonolactone **22** were purchased from the Sigma Chemical Company; the monosilyl ether **23** was prepared from **D**-gulonolactone as previously described.[6]

*7-Deoxy-3,4-O-isopropylidene-**L**-glycero-**L**-talo-heptono-1,5-lactone **9** and 7-deoxy-3,4-O-isopropylidene-**L**-glycero-**L**-galacto-heptono-1,5-lactone **13**.* Anhydrous copper sulphate (22.6 g) and concentrated sulphuric acid (0.4 ml) were added to a solution of **L**-rhamnose monohydrate **5** (11.8 g, 64.9 mmol) in acetone (200 ml) and the reaction mixture was stirred at room temperature under nitrogen for 24 h when t.l.c. (ethyl acetate) indicated complete conversion of the starting material (R_f 0.1) to a major product (R_f 0.5). The mixture was filtered through a Celite pad, neutralised by the addition of 33% aqueous ammonia solution (3 ml) and again was filtered through a Celite pad. The solvent was removed *in vacuo* to give the crude acetonide **12**, (13.2 g); the yellow oil **12**, without any further purification, was dissolved in water (120 ml). The solution was treated with sodium cyanide (4.05 g, 82.7 mmol, 1.3 equiv) and the reaction mixture stirred at room temperature for 20 h when t.l.c. (ethyl acetate) indicated complete conversion of the starting material (R_f 0.5) to a baseline spot. The reaction mixture was stirred at 70°C for 3 h after which time all the excess cyanide had been hydrolysed, then cooled to room temperature and washed three times with ethyl acetate (3 x 75 ml). The aqueous layer was acidified to pH 4 by careful addition of 50% aqueous sulphuric acid. The solvent was removed *in vacuo* and the residue dissolved in acetic acid (300 ml) and stirred at 75°C. After 3 h, t.l.c. (ethyl acetate) indicated formation of two products (R_f 0.3) and (R_f 0.6). The solvent was removed and the residue preabsorbed on to silica; flash chromatography (gradient elution from ethyl acetate : hexane, 1 : 4 to 1 : 0) afforded *7-deoxy-3,4-O-isopropylidene-**L**-glycero-**L**-talo-heptono-1,5-lactone **9***, (R_f 0.3), as a white crystalline solid (4.30 g, 29%), m.p. 148-9°C, $[\alpha]_D^{24}$ -89.9 (*c*, 1.05 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3483 (br, OH), 1751 (C=O); δ_H (500 MHz; $CDCl_3$): 1.39 (3H, s, Me), 1.40 (3H, d, *J* 6.2 Hz, H-7), 1.45 (3H, s, Me), 2.10 (1H, d, $J_{OH,6}$ 5.4 Hz, exchanged on D_2O shake, OH-6), 3.31 (1H, d, $J_{OH,2}$ 6.1 Hz, exchanged on D_2O shake, OH-2), 3.89 (1H, dd, $J_{4,5}$ 1.2, $J_{5,6}$ 8.0 Hz, H-5), 4.13-4.19 (1H, m, H-6), 4.35 (1H, dd, $J_{OH,2}$ 6.0, $J_{2,3}$ 2.9 Hz, H-2), 4.80-4.84 (2H, m, H-3, H-4); δ_C ($CDCl_3$): 20.0, 24.3, 25.8 (3 x q, $C\underline{Me}_2$, C-7), 65.5, 68.6, 72.3, 74.8, 79.7 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.8 (s, $\underline{C}Me_2$), 172.0 (s, C-1); *m/z* (DCI; NH_3): 233 ($M+H^+$, 15%), 250 ($M+NH_4^+$, 100%). (Found: C, 51.92; H, 6.91. $C_{10}H_{16}O_6$ requires C, 51.72; H, 6.94%) and *7-deoxy-3,4-O-isopropylidene-**L**-glycero-**L**-galacto-heptono-1,5-lactone **13***, (R_f 0.6), as a white crystalline solid (1.34 g, 9%), m.p. 114-5°C, $[\alpha]_D^{23}$ -114.8 (*c*, 1.5 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3360 (br, OH), 1767 (C=O); δ_H (500 MHz; $CDCl_3$): 1.38 (3H, s, Me), 1.40 (3H, d, *J* 6.3 Hz, H-7), 1.44 (3H, s, Me), 2.16 (1H, s, exchanged on D_2O shake, OH), 3.15 (1H, exchanged on D_2O shake, OH), 4.13 (1H, sex, *J* 6.5 Hz, H-6), 4.42 (1H, dd, $J_{OH,2}$ 4.1, $J_{2,3}$ 2.7 Hz, H-2), 4.58 (1H, dd, $J_{4,5}$ 1.8, $J_{5,6}$ 7.8 Hz, H-5), 4.60 (1H, dd, $J_{2,3}$ 2.7, $J_{3,4}$ 7.5 Hz, H-3), 4.78 (1H, dd, $J_{3,4}$ 7.5, $J_{4,5}$ 1.9 Hz, H-4); δ_C ($CDCl_3$): 19.9, 24.0,

25.9 (3 x q, 2 x Me, C-7), 66.3, 69.2, 71.0, 75.2, 79.3 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.4 (s, $\underline{C}Me_2$), 170.5 (s, C-1); *m/z* (DCI; NH_3): 233 ($M+H^+$, 10%), 250 ($M+NH_4^+$, 100%). (Found: C, 51.97; H, 7.03. $C_{10}H_{16}O_6$ requires C, 51.72; H, 6.94%). The structure of **13** was firmly established by X-ray crystallographic analysis [see above].

7-Deoxy-L-glycero-L-talo-heptono-1,4-lactone ***10****. (a) From 7-deoxy-3,4-O-isopropylidene-L-glycero-L-talo-heptono-1,5-lactone* ***9****.* A solution of the isopropylidene derivative **9** (99 mg, 0.43 mmol) in 50% aqueous trifluoroacetic acid (4 ml) was stirred at room temperature for 16 h. T.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.4) to a single product (R_f 0.3). The solvent was removed *in vacuo* and the residue coevaporated with toluene (3 x 5 ml) to afford *7-deoxy-L-glycero-L-talo-heptono-1,4-lactone* ***10*** as a white solid, (82 mg, quant), m.p. 128-30°C, $[\alpha]_D^{22}$ +51.8 (*c*, 1.0 in CH_3OH) [lit.[16] m.p. 134-38°C, $[\alpha]_D^{20}$ +43.34 (*c*, 10.2 in H_2O)]; ν_{max} (KBr)/cm^{-1}: 3349 (br, OH), 1768 (C=O); δ_H (200 MHz; CD_3OD): 1.23 (3H, d, *J* 6.2 Hz, H-7), 3.38 (1H, dd, $J_{4,5}$ 1.3, $J_{5,6}$ 8.9 Hz, H-5), 3.67 (1H, dq, $J_{5,6}$ 8.9, $J_{6,7}$ 6.2 Hz, H-6), 4.28 (1H, d, *J* 5.9 Hz), 4.61 (1H, d, *J* 5.7 Hz), 4.71 (1H, s); δ_C (CD_3OD): 20.6 (q, C-7), 67.7, 70.3, 72.3, 76.6, 86.5 (5 x d, C-2, C-3, C-4, C-5, C-6), 179.2 (s, C-1); *m/z* (DCI; NH_3): 193 ($M+H^+$, 5%), 210 ($M+NH_4^+$, 100%). (Found: C, 43.47; H, 6.35. $C_7H_{12}O_6$ requires C, 43.75; H, 6.29%).

(b) From 3,4-O-cyclohexylidene-7-deoxy-L-glycero-L-talo-heptono-1,5-lactone ***17****.* A solution of the cyclohexylidene ketal **17** (118 mg, 0.43 mmol) in 50% aqueous trifluoroacetic acid (4 ml) was stirred at 50°C. After 3 h, t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.5) to a single product (R_f 0.3). The solvent was removed *in vacuo* and the residue dissolved in methanol, preabsorbed on to silica and purified by flash chromatography (gradient elution from ethyl acetate to ethyl acetate : methanol, 9 : 1) to afford the 1,4-lactone **10** as a white solid (38 mg, 46%) identical to that described above.

(c) From 7-deoxy-2,3:5,6-di-O-isopropylidene-L-glycero-L-talo-heptono-1,4-lactone ***11****.* The diacetonide **11** (57 mg, 0.21 mmol) was dissolved in 50% aqueous trifluoroacetic acid (4 ml) and the solution stirred at 50°C. After 3 h, t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.7) to a single product (R_f 0.3). The solvent was removed *in vacuo* to give the 1,4-lactone **10** as a white solid (40 mg, 99%) identical to the material described above.

7-Deoxy-L-glycero-L-galacto-heptono-1,4-lactone ***14****. (a) From 7-deoxy-3,4-O-isopropylidene-L-glycero-L-galacto-heptono-1,5-lactone* ***13****.* The isopropylidene derivative **13** (96 mg, 0.41 mmol) in 50% aqueous trifluoroacetic acid (4 ml) was stirred at room temperature for 16 h when t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.7) to a single product (R_f 0.3). The solvent was removed *in vacuo* and the residue coevaporated with toluene (3 x 5 ml) to give *7-deoxy-L-glycero-L-galacto-heptono-1,4-lactone* ***14*** as a white solid, (74 mg, quant), m.p. 172-174°C, $[\alpha]_D^{22}$ +82.8 (*c*, 0.75 in CH_3OH) [lit.[17] m.p. 171-171.5°C, $[\alpha]_D^{20}$ +87.3 (*c*, 0.8 in H_2O)]; ν_{max} (KBr)/cm^{-1}: 3387, 3271 (br, OH), 1759 (C=O); δ_H (500 MHz; CD_3OD): 1.29 (3H, d, *J* 6.2 Hz, H-7), 3.38 (1H, dd, $J_{4,5}$ 1.8, $J_{5,6}$ 8.6 Hz, H-5), 3.76 (1H, dq, $J_{5,6}$ 8.6, $J_{6,7}$ 6.2 Hz, H-6), 4.28 (1H, t, *J* 8.5 Hz, H-3), 4.35 (1H, d, $J_{2,3}$ 8.9 Hz, H-2), 4.41 (1H, dd, $J_{3,4}$ 8.2, $J_{4,5}$ 1.8 Hz, H-4); δ_C (CD_3OD): 20.8 (q, C-7), 68.0, 74.0, 74.6, 75.8, 80.7 (5 x d, C-2,

C-3, C-4, C-5, C-6), 176.4 (s, C-1); *m/z* (DCI; NH_3): 210 ($M+NH_4^+$, 100%). (Found: C, 43.70; H, 6.02. $C_7H_{12}O_6$ requires C, 43.75; H, 6.29%).

(b) From 3,4-O-cyclohexylidene-7-deoxy-L-glycero-L-galacto-heptono-1,5-lactone ***18.*** The ketal **18** (117 mg, 0.43 mmol) in 50% aqueous trifluoroacetic acid (4 ml) was stirred at 50°C for 3 h when t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.7) to a single product (R_f 0.3). The solvent was removed *in vacuo* and the residue dissolved in methanol, preabsorbed on to silica and purified by flash chromatography (gradient elution from ethyl acetate to ethyl acetate : methanol, 9 : 1) to give the 1,4-lactone **14** as a white solid (55 mg, 67%) identical to that described above.

(c) From 7-deoxy-5,6-O-isopropylidene-L-glycero-L-galacto-heptono-1,4-lactone ***15.*** The monoketal **15** (65 mg, 0.28 mmol) was dissolved in 50% aqueous trifluoroacetic acid (2 ml) and the solution stirred at room temperature. After 16 h t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.6) to a single product (R_f 0.3). The solvent was removed *in vacuo* and the residue coevaporated with toluene (3 x 5 ml) to yield 1,4-lactone **14**, a white solid (54 mg, quant), identical to that described above.

7-Deoxy-2,3:5,6-di-O-isopropylidene-L-glycero-L-talo-heptono-1,4-lactone ***11.*** A solution of the 1,4-lactone **10** (120 mg, 0.63 mmol) in acetone (5 ml) was adjusted to pH 2 by the addition of **dl**-10-camphorsulphonic acid. The reaction mixture was stirred at 45°C under nitrogen for 30 min when t.l.c. indicated the formation of three products. 2,2-Dimethoxypropane (0.38 ml, 3.13 mmol, 5 equiv) was then added and the mixture stirred for a further 30 min at 45°C under nitrogen, when t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.3) to a single product (R_f 0.7). The reaction mixture was concentrated, then diluted with ethyl acetate (50 ml) and filtered through a silica plug. The solvent was removed *in vacuo* to afford *7-deoxy-2,3:5,6-di-O-isopropylidene-L-glycero-L-talo-heptono-1,4-lactone* ***11*** as a white solid (143 mg, 84%), m.p. 119-20°C, $[\alpha]_D^{25}$ +19.8 (*c*, 1.05 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 1784 (C=O); δ_H (500 MHz; $CDCl_3$): 1.33, 1.38, 1.40 (3 x 3H, 3 x s, 3 x Me), 1.46 (3H, d, *J* 6.5 Hz, H-7), 1.48 (3H, s, Me), 4.17 (1H, d, *J* 7.2 Hz), 4.49 (1H, qn, *J* 6.7 Hz), 4.55 (1H, s), 4.69 (1H, d, *J* 5.5 Hz), 4.78 (1H, d, *J* 5.5 Hz); δ_C ($CDCl_3$): 14.9, 24.5, 25.4, 25.9, 26.7 (5 x q, 4 x Me, C-7), 72.4, 75.2, 77.2, 79.0, 80.3 (5 x d, C-2, C-3, C-4, C-5, C-6), 108.8, 112.9 (2 x s, 2 x $\underline{C}Me_2$), 174.3 (s, C-1); *m/z* (DCI; NH_3): 273 ($M+H^+$, 30%), 290 ($M+NH_4^+$, 100%); (Found: C, 57.55; H, 7.52. $C_{13}H_{20}O_6$ requires C, 57.34; H, 7.40%).

7-Deoxy-5,6-O-isopropylidene-L-glycero-L-galacto-heptono-1,4-lactone ***15.*** The pH of a solution of unprotected 1,4-lactone **14** (59 mg, 0.31 mmol) in acetone (5 ml) was adjusted to pH 2 by the addition of **dl**-10-camphorsulphonic acid and the reaction mixture was stirred at 45°C under nitrogen for 45 min when t.l.c. (ethyl acetate : methanol, 9 : 1) indicated complete conversion of the starting material (R_f 0.3) to a single product (R_f 0.6). The reaction mixture was diluted with ethyl acetate (50 ml) and filtered through a silica plug. The solvent was removed *in vacuo* to afford *7-deoxy-5,6-O-isopropylidene-L-glycero-L-galacto-heptono-1,4-lactone* ***15*** as a white solid (63 mg, 88%), m.p. 118-21°C, $[\alpha]_D^{23}$ +97.8 (*c*, 1.05 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3305 (br, OH), 1792 (C=O); δ_H (500 MHz; $CDCl_3$): 1.39 (3H, s, Me), 1.43 (3H, d, *J* 6.5 Hz, H-7), 1.45 (3H, s, Me), 2.99 (1H, br s, exchanged on D_2O shake, OH), 3.35 (1H, br s, exchanged on D_2O shake, OH), 4.15 (1H, dd, *J* 0.6 Hz, *J* 7.1 Hz), 4.26 (1H, d, *J* 6.8 Hz), 4.39 (1H, d, *J* 7.7 Hz), 4.48 (1H, t, *J* 7.4 Hz), 4.51 (1H, qn, *J* 6.5 Hz, H-6); δ_C ($CDCl_3$): 14.6, 25.2, 26.4 (3 x q, 2 x Me, C-7), 72.5, 74.1,

74.7, 78.7 (4 x d, C-2, C-3, C-4, C-5, C-6), 109.2 (s, $\underline{C}Me_2$), 175.1 (s, C-1); *m/z* (DCI; NH_3): 233 ($M+H^+$,90%), 250 ($M+NH_4^+$,100%). (Found: C, 51.41; H, 6.87. $C_{10}H_{16}O_6$ requires C, 51.72; H, 6.94%).

3,4-O-Cyclohexylidene-7-deoxy-L-glycero-L-talo-heptono-1,5-lactone ***17*** *and 3,4-O-Cyclohexylidene-7-deoxy-L-glycero-L-galacto-heptono-1,5-lactone* ***18***. A solution of **L**-rhamnose monohydrate **5** (16.0 g, 87.8 mmol) in cyclohexanone (240 ml) was treated with anhydrous copper sulphate (29.8 g) and concentrated sulphuric acid (0.64 ml) and the resulting reaction mixture stirred at room temperature under nitrogen for 24 h. T.l.c. (ethyl acetate) indicated complete conversion of the starting material (R_f 0.1) to a major product (R_f 0.5). The mixture was filtered through a Celite pad, neutralised with 33% aqueous ammonia solution (2.4 ml), and again filtered through Celite. The solvent was removed *in vacuo* and the residue purified by flash chromatography (gradient elution from ethyl acetate : hexane, 1 : 4 to 2 : 3) to give crude the cyclohexylidene derivative **16** (21.2 g) which was dissolved in a mixture of water (120 ml) and dioxan (10 ml). The resulting solution was reacted with sodium cyanide (5.2 g, 106.1 mol, 1.2 equiv) and then stirred at room temperature for 20 h, after which time t.l.c. (ethyl acetate) indicated complete conversion of the starting material (R_f 0.5) to a baseline spot. The reaction mixture was stirred at 70°C for 3 h after which time all the excess cyanide had been hydrolysed, cooled to room temperature and extracted three times with ethyl acetate (3 x 75 ml). The aqueous layer was acidified to pH 4 with careful addition of 50% aqueous sulphuric acid. The solvent was removed *in vacuo* and the residue dissolved in acetic acid (300 ml) and stirred at 70°C for 3 h. T.l.c. (ethyl acetate) indicated the formation of two products (R_f 0.3) and (R_f 0.7) which were purified by flash chromatography (gradient elution from ethyl acetate : hexane, 1 : 4 to 1 : 0) to give *3,4-O-cyclohexylidene-7-deoxy-L-glycero-L-talo-heptono-1,5-lactone* ***17***, (R_f 0.3), as a foam (8.81 g, 37%), $[\alpha]_D^{22}$ -74.5 (*c*, 1.2 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3436 (br, OH), 1757 (C=O); δ_H (500 MHz; $CDCl_3$): 1.40 (3H, d, *J* 6.3 Hz, H-7), 1.52-1.66 (10H, m, cyclohexylidene), 2.10 (1H, br s, exchanged on D_2O shake, OH), 3.26 (1H, d, *J* 5.2 Hz, exchanged on D_2O shake, OH), 3.88 (1H, d, *J* 7.8 Hz), 4.15-4.21 (1H, m, H-6), 4.33 (1H, bs), 4.79-4.83 (2H, m); δ_C ($CDCl_3$): 20.0 (q, C-7), 23.5, 23.8, 24.9, 33.9, 35.5 (5 x t, cyclohexylidene) 65.7, 68.8, 72.0, 74.4, 79.7 (5 x d, C-2, C-3, C-4, C-5, C-6), 111.6 (s, cyclohexylidene), 172.0 (s, C-1); *m/z* (CI; NH_3): 273 ($M+H^+$, 20%), 290 ($M+NH_4^+$, 100%). (Found: C, 57.46; H, 7.23. $C_{13}H_{20}O_6$ requires C, 57.34; H, 7.40%) and *3,4-O-cyclohexylidene-7-deoxy-L-glycero-L-galacto-heptono-1,5-lactone* ***18***, (R_f 0.7), as a white solid (2.06 g, 13%), m.p. 114-7°C, $[\alpha]_D^{22}$ -98.2 (*c*, 1.05 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3372 (br, OH), 1749 (C=O); δ_H (500 MHz; $CDCl_3$): 1.40 (3H, d, *J* 6.3 Hz, H-7), 1.53-1.64 (10H, m, cyclohexylidene), 2.29 (1H, bs, exchanged on D_2O shake, OH), 3.36 (1H, br s, exchanged on D_2O shake, OH), 4.13-4.17 (1H, m, H-6), 4.43 (1H, t, *J* 3.2 Hz, H-2), 4.58 (1H, dd, *J* 2.0, *J* 7.7 Hz), 4.59 (1H, dd, *J* 2.7, *J* 7.5 Hz, H-3), 4.78 (1H, dd, *J* 7.5, *J* 2.0 Hz); δ_C ($CDCl_3$): 19.8 (q, C-7), 23.5, 23.8, 24.9, 33.5, 35.6 (5 x t, cyclohexylidene) 66.4, 69.3, 70.7, 75.0, 79.3 (5 x d, C-2, C-3, C-4, C-5, C-6), 111.1 (s, cyclohexylidene), 170.6 (s, C-1); *m/z* (DCI; NH_3): 273 ($M+H^+$, 25%), 290 ($M+NH_4^+$, 100%). (Found: C, 57.06; H, 7.59. $C_{13}H_{20}O_6$ requires C, 57.34; H, 7.40%).

2-O-tert-Butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-L-glycero-L-talo-heptono-1,5-lactone ***20*** *and 7-Deoxy-2,6-di-O-tert-butyldimethylsilyl-3,4-O-isopropylidene-L-glycero-L-talo-heptono-1,5-lactone* ***19***. A stirred solution of the 1,5-lactone **9** (1.56 g, 6.72 mmol) and imidazole (1.14 g, 16.81 mmol, 2.5 equiv) in dimethylformamide (15 ml) under nitrogen at -20°C was treated with *tert*-butyldimethylsilyl chloride (1.32 g,

8.74 mmol, 1.3 equiv). After 3.5 h, t.l.c. (ethyl acetate : hexane, 1 : 1) indicated partial conversion of the starting material (R_f 0.05) to two products (R_f 0.4) and (R_f 0.9). The solvent was removed *in vacuo* and the residue dissolved in ethyl acetate, preabsorbed on to silica and purified by flash chromatography (gradient elution from ethyl acetate : hexane, 1 : 4 to 1 : 0) to give some starting material (0.52 g, 33%) and *2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-L-glycero-L-talo-heptono-1,5-lactone* ***20***, (R_f 0.4), as a white crystalline solid (1.38 g, 59%, 89% based on recovered starting material), m.p. 104-6°C, $[\alpha]_D^{25}$ -45.1 (*c*, 1.05 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3501 (br, OH), 1775 (C=O); δ_H (200 MHz; $CDCl_3$): 0.15, 0.24 (2 x 3H, 2 x s, $SiMe_2$), 0.95 (9H, s, CMe_3), 1.39 (3H, d, H-7), 1.38, 1.47 (2 x 3H, 2 x s, CMe_2), 2.11 (1H, d, $J_{OH,6}$ 5.1 Hz, exchanged on D_2O shake, OH-6), 3.81 (1H, dd, $J_{4,5}$ 1.8, $J_{5,6}$ 8.0 Hz, H-5), 4.09-4.19 (1H, m, H-6), 4.39 (1H, d, $J_{2,3}$ 2.6 Hz, H-2), 4.68 (1H, dd, *J* 1.8, *J* 7.8 Hz, H-3 or H-4), 4.76 (1H, dd, *J* 1.8, *J* 7.8 Hz, H-3 or H-4); δ_C ($CDCl_3$): -5.4, -4.4 (2 x q, $SiMe_2$), 18.6 (s, $\underline{C}Me_3$), 20.2, 24.6, 26.0 (3 x q, 2 x Me, C-7), 25.8 (q, $C\underline{Me}_3$), 65.7, 70.2, 72.6, 76.3, 79.6 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.8 (s, $\underline{C}Me_2$), 169.3 (s, C-1); *m/z* (CI; NH_3): 347 ($M+H^+$, 100%), 364 ($M+NH_4^+$, 5%). (Found: C, 55.74; H, 8.85. $C_{16}H_{30}O_6Si$ requires C, 55.46; H, 8.73%) and *7-deoxy-2,6-di-O-tert-butyldimethylsilyl-3,4-O-isopropylidene-L-glycero-L-talo-heptono-1,5-lactone* ***19***, (R_f 0.9) as a white crystalline solid (0.21 g, 7%, 10% based on recovered starting material), m.p. 95-7°C, $[\alpha]_D^{25}$ -32.5 (*c*, 1.1 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 1769 (C=O); δ_H (500 MHz; $CDCl_3$): 0.10, 0.11, 0.14, 0.23 (4 x 3H, 4 x s, 2 x $SiMe_2$), 0.90, 0.95 (2 x 9H, 2 x s, 2 x CMe_3), 1.29 (3H, d, *J* 6.1 Hz, H-7), 1.33, 1.44 (2 x 3H, 2 x s, CMe_2), 3.73 (1H, dd, $J_{4,5}$ 0.9, $J_{5,6}$ 8.8 Hz, H-5), 4.09 (1H, dq, $J_{5,6}$ 8.8, $J_{6,7}$ 6.1 Hz, H-6), 4.35 (1H, d, $J_{2,3}$ 2.8 Hz, H-2), 4.64 (1H, dd, $J_{2,3}$ 2.9, $J_{3,4}$ 7.9 Hz, H-3), 4.67 (1H, dd, $J_{3,4}$ 7.9, $J_{4,5}$ 1.4 Hz, H-4); δ_C ($CDCl_3$): -5.4, -5.2, -4.5, -4.4 (4 x q, 2 x $SiMe_2$), 17.9, 18.6 (2 x s, 2 x $\underline{C}Me_3$), 21.0, 24.2, 26.0 (3 x q, 2 x Me, C-7), 25.7, 25.8 (2 x q, 2 x $C\underline{Me}_3$), 65.7, 70.3, 72.0, 76.0, 79.9 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.0 (s, $\underline{C}Me_2$), 169.4 (s, C-1); *m/z* (CI; NH_3): 461 ($M+H^+$, 100%). (Found: C, 57.03; H, 9.81. $C_{22}H_{44}O_6Si_2$ requires C, 57.35; H, 9.63%).

2-O-tert-Butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-L-talo-6-heptulosono-1,5-lactone ***21***.

(a) From 2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-L-glycero-L-talo-heptono-1,5-lactone ***20***. Pyridinium chlorochromate (2.56 g, 11.9 mmol, 3 equiv) was added to a stirred solution of the L-*glycero*-1,5-lactone **20** (1.38 g, 3.97 mmol) and dried powdered molecular sieve (3 g) in dry dichloromethane (25 ml). The reaction mixture was stirred at room temperature for 3 h when t.l.c. (ethyl acetate:hexane, 1 : 1) indicated complete conversion of the starting material (R_f 0.4) to a single product (R_f 0.6). Ether (300 ml) was added and the mixture filtered through a silica plug topped with Celite. The solvent was removed *in vacuo* and the residue purified by flash chromatography (ethyl acetate : hexane, 1 : 4), to afford *2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-L-talo-6-heptulosono-1,5-lactone* ***21*** (1.18 g, 86%) as a white crystalline solid, m.p. 63-5°C; $[\alpha]_D^{20}$ +23.9 (*c*, 1.0 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 1766 (lactone C=O), 1732 (keto C=O); δ_H (200MHz; $CDCl_3$): 0.14, 0.24 (2 x 3H, 2 x s, $SiMe_2$), 0.95 (9H, s, CMe_3), 1.33, 1.48 (2 x 3H, 2 x s, CMe_2), 2.36 (3H, s, H-7), 4.32 (1H, d, *J* 3.0 Hz, H-2 or H-5), 4.46 (1H, d, *J* 2.1 Hz, H-2 or H-5), 4.69 (1H, dd, *J* 3.0, 7.7 Hz, H-3 or H-4), 4.81 (1H, dd, *J* 2.1, 7.7 Hz, H-3 or H-4); δ_C ($CDCl_3$): -5.6, -4.6 (2 x q, $SiMe_2$), 18.5 (s, $\underline{C}Me_3$), 24.1 (q, C-7), 24.6, 28.1 (2 x q, CMe_2), 25.7 (q, CMe_3), 70.8, 74.9, 76.0, 80.1 (4 x d, C-2, C-3, C-4, C-5), 111.3 (s, $\underline{C}Me_2$), 168.4 (s, C-1), 204.6 (s, C-6); *m/z* (NH_3, CI): 287 ($M+H^+$-acetone, 100%), 345 ($M+H^+$, 13%), 362 ($M+NH_4^+$, 2%). (Found C, 56.11; H, 8.31. $C_{16}H_{28}O_6Si$ requires C, 55.79; H, 8.19%).

(b) From 2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone ***25***. Pyridinium chlorochromate (254 mg, 4 equiv) was added to a stirred mixture of the D-*glycero*-1,5-lactone **25** (102 mg, 0.29 mmol) and powdered molecular sieve (*ca.* 180 mg) in dry dichloromethane (6 ml) at 0°C. After 15 min, the mixture was allowed to warm to room temperature and stirring was continued for a further 2 h when t.l.c. (ethyl acetate : hexane, 1 : 1) indicated complete conversion of the starting material (R_f 0.4) to a single product (R_f 0.6). The reaction mixture was diluted with ether (6 ml), treated with magnesium sulphate and filtered through a silica plug topped with Celite. The solvent was removed *in vacuo* and the residue purified by flash chromatography (ethyl acetate : hexane, 1 : 4) to afford the ketone **21** (93 mg, 92%) as a white crystalline solid, identical to the material above.

2-O-tert-Butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone ***25***.
(a) From 2-O-tert-Butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-L-talo-6-heptulosono-1,5-lactone ***21***. A solution of the ketone **21** (889 mg, 2.58 mmol) in ethanol (24 ml) was cooled to -20°C and sodium borohydride (96 mg, 2.58 mmol) in 50% aqueous ethanol (6 ml) was added; the reaction mixture was stirred at -20°C for 30 min when t.l.c. (ethyl acetate:hexane, 1 : 1) indicated complete conversion of the starting material (R_f 0.6) to a single product (R_f 0.4). The reaction was quenched by the addition of excess ammonium chloride (300 mg). The reaction mixture was filtered through a silica plug topped with Celite. The solvent was removed *in vacuo* and the residue purified by flash chromatography (ethyl acetate : hexane, 3 : 7), to give *2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone* ***25*** (808 mg, 90%) as a white crystalline solid, m.p. 99-102°C; $[\alpha]_D^{20}$ -37.8 (*c*, 0.5 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3305 (br, OH), 1766 (C=O); δ_H (300 MHz; $CDCl_3$): 0.14, 0.23 (2 x 3H, 2 x s, $SiMe_2$), 0.94 (9H, s, CMe_3), 1.30 (3H, d, *J* 6.4 Hz, H-7), 1.34, 1.46 (2 x 3H, 2 x s, CMe_2), 3.86 (1H, dd, $J_{5,6}$ 7.5, $J_{4,5}$ 1.8 Hz, H-5), 4.01 (1H, m, H-6), 4.37 (1H, d, $J_{2,3}$ 3.0 Hz, H-2), 4.52 (1H, dd, $J_{3,4}$ 7.7, $J_{4,5}$ 1.8 Hz, H-4), 4.66 (1H, dd, $J_{2,3}$ 3.0, $J_{3,4}$ 7.7 Hz, H-3); δ_C ($CDCl_3$): -5.6, -4.6 (2 x q, $SiMe_2$), 17.4 (q, C-7), 18.4 (s, $\underline{C}Me_3$), 24.3, 25.8 (2 x q, CMe_2), 25.7 (q, CMe_3), 66.4, 70.2, 73.2, 77.6, 81.3 (5 x d, C-2, C-3, C-4, C-5, C-6), 111.0 (s, $\underline{C}Me_2$), 169.4 (s, C-1); *m/z* (DCI; NH_3): 289 ($M+H^+$-acetone, 64%), 347 ($M+H^+$, 100%), 364 ($M+NH_4^+$, 27%). (Found C, 55.72; H, 8.95. $C_{16}H_{30}O_6Si$ requires C, 55.46; H, 8.73%).
(b) From 7-Bromo-2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone ***24***. A solution of the bromide **24** (133 mg, 0.31 mmol) and triethylamine (150 µl, 4 equiv) in ethyl acetate (5 ml) was stirred under an atmosphere of hydrogen in the presence of palladium black (*ca.* 15 mg) for 25 h when t.l.c. (ethyl acetate : hexane, 2 : 1) indicated complete conversion of the starting material (R_f 0.8) to a single product (R_f 0.6). The mixture was filtered through Celite and the solvent removed *in vacuo*. The residue was purified by flash chromatography (ethyl acetate : hexane, 3 : 7) to give the silyl alcohol **25** (102 mg, 94%) as a white crystalline solid, identical to that described above.

7-Bromo-2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone ***24***. A solution of triphenylphosphine (263 mg, 1.5 equiv) in dry tetrahydrofuran (3 ml) was added to a stirred solution of the diol **23**[6] (245 mg, 0.67 mmol) and carbon tetrabromide (289 mg, 1.3 equiv) in dry tetrahydrofuran (3 ml) at 0°C. The reaction mixture was allowed to warm to room temperature and stirring was continued for 40 h when t.l.c. (ethyl acetate : hexane, 2 : 1) indicated complete conversion of the starting material (R_f 0.2) to a single product (R_f 0.8). The reaction mixture was diluted with ether (6 ml), filtered

through a Celite pad, and the solvent was removed *in vacuo*. The residue was purified by flash chromatography (ethyl acetate : hexane, 3 : 7) to afford *7-bromo-2-O-tert-butyldimethylsilyl-7-deoxy-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone* **24** (260 mg, 90%) as a solid, m.p. 82-3°C; $[\alpha]_D^{20}$ -26.8 (*c*, 1.2 in $CHCl_3$); ν_{max} (KBr)/cm^{-1}: 3306 (br, OH), 1766 (C=O); δ_H (300 MHz, $CDCl_3$): 0.15, 0.25 (2 x 3H, 2 x s, $SiMe_2$), 0.95 (9H, s, CMe_3), 1.36, 1.47 (2 x 3H, 2 x s, CMe_2), 3.04 (1H, br s, exchanged on D_2O shake, OH), 3.65 (1H, dd, $J_{7,7'}$ 11.2, $J_{6,7}$ 4.0 Hz, H-7), 3.71 (1H, dd, $J_{6,7'}$ 4.0, $J_{7,7'}$ 11.2 Hz, H-7'), 4.20 (1H, dt, $J_{5,6}$ 6.3, $J_{6,7}$ 4.0 Hz, H-6), 4.28 (1H, dd, $J_{4,5}$ 1.8, $J_{5,6}$ 6.3 Hz, H-5), 4.40 (1H, d, $J_{2,3}$ 2.9 Hz, H-2), 4.62 (1H, dd, $J_{3,4}$ 7.7, $J_{4,5}$ 1.8 Hz, H-4), 4.70 (1H, dd, $J_{2,3}$ 2.9, $J_{3,4}$ 7.7 Hz, H-3); δ_C ($CDCl_3$): -5.2, -4.6 (2 x q, $SiMe_2$), 18.4 (s, $\underline{C}Me_3$), 24.3, 25.8 (2 x q, CMe_2), 25.7 (q, CMe_3), 33.5 (t, C-7), 69.5, 70.1, 73.0, 76.7, 77.6 (5 x d, C-2, C-3, C-4, C-5, C-6), 111.4 (s, $\underline{C}Me_2$), 169.1 (s, C-1); *m/z* (DCI; NH_3): 330 and 328 ($M+H^+$-Br-H_2O, 100%), 444 and 442 ($M+NH_4^+$, 8%). (Found C, 45.56; H, 6.65. $C_{16}H_{29}BrO_6Si$ requires C, 45.18; H, 6.87%).

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