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ACETONIDES OF HEPTONOLACTONES: POWERFUL CHIRONS

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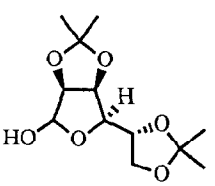
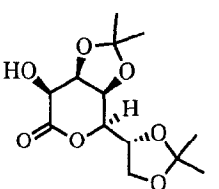
Heptonolactones, in which all the functional groups except one can be protected with a single ketal protecting group, have great potential as starting materials within the chiral pool. The practical synthesis and characterisation of acetonides of *glycero-talo-* and *glycero-galacto-*heptono-lactone are described. X-ray crystal structures of **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone and 2,3:5,6-di-O-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone are reported.

Heptonic acids, readily available from the Kiliani ascension[1,2] of hexoses, contain seven adjacent functional groups and five contiguous chiral centres. Since the carboxylic acid and one of the hydroxyl groups of a heptonolactone are protected within the lactone functionality, additional protection of four hydroxyl groups may in principle be achieved with the use of two equivalents of acetone. Thus, a sole protecting group may give immediate access to a single hydroxyl group in a highly functionalised seven carbon sugar. Such sugars are likely to provide a set of very powerful starting materials for the synthesis of homochiral compounds with a high concentration of functional groups and chiral centres. Among other applications,[3] these compounds provide relatively easy access to highly substituted piperidines such as homomannojirimycin,[4] and to pyrrolizidines[5,6] castanospermines,[7] and alexines;[8,9] additionally, they may readily be transformed into complex 2,5-disubstituted tetrahydrofurans[10] and have considerable potential for the unambiguous synthesis of C-glycopyranosides and of very highly functionalised carbocycles,[11] such as the mannostatins.[12] This paper describes the synthesis of some δ-lactones of heptonic acids - derived from cyanide chain extension of 2,3:5,6-di-*O*-isopropylidene-hexoses - in which the carbon substituent on the lactone ring is adjacent and *cis* to an isopropylidene ketal function; the scope of such readily available materials is shown by examples of the isolation of other hydroxyl groups of the δ-lactones and also in the formation of γ-lactone derivatives which access different hydroxyl groups of the sugar.



(1)



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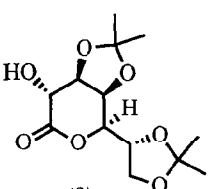
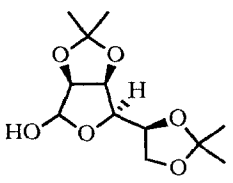


(3)

α-Hydroxy-δ-Lactones

The conversion of diacetone mannose (1) to a mixture of **D**-*glycero*-**D**-*talo*- (2) and **D**-*glycero*-**D**-*galacto*- (3) lactones in a ratio of between 3:1 and 2:1, and a combined yield of 35-40% on a small scale has been previously reported;[13] procedures for this reaction on 100 g and 5 kg scales are given, demonstrating that this reaction works equally well on large scales. A report has appeared[14] for the preparation of a mixture of the acetates of (2) and (3) in approximately 50% yield, but deprotection of the acetates to the free 2-hydroxyl groups is not easy.



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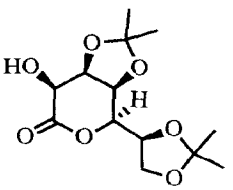

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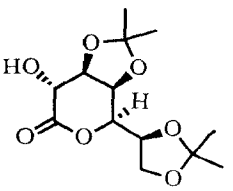

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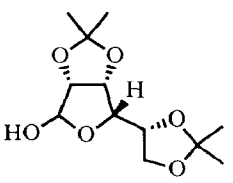

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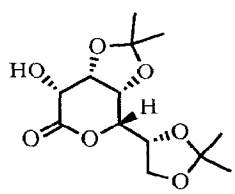

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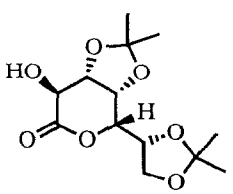

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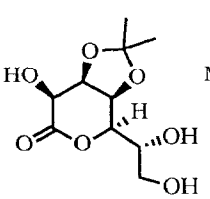
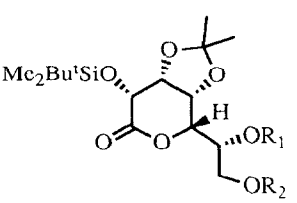


(10)



(11) R_1,R_2 = Me_2C

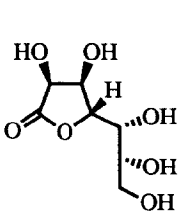
(12) R_1 = R_2 = H

(13) R_1 = H R_2 = Me_2Bu^tSi

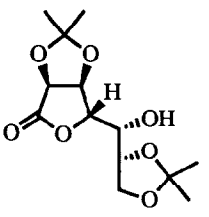
The diisopropylidene derivative of **L**-gulose (4), epimeric with diacetone mannose at C-5, on treatment with aqueous sodium cyanide and subsequent acidification, gives a mixture of the lactones (5) and (6) in yields of 18% and 13% respectively; similar treatment of 2,3:5,6-di-*O*-isopropylidene-**D**-gulonofuranose (7)[15] gave the enantiomers (8) and (9) in respective yields of 16% and 12%. The side chain isopropylidene ketal of the diacetonides (2), (3), (5), (6), (8), (9), can be selectively hydrolysed in excellent yield; for example, treatment of the diacetonide (2) with 80% aqueous acetic acid affords the monoacetonide (10) in 96% yield with the C-2, C-6 and C-7 hydroxyl groups free. The structure of (10) is confirmed by its high yield conversion back into the diacetonide (2) on treatment with acetone and camphor sulphonic acid, indicating that there is no acid catalysed isomerisation of the acetonides under these reaction conditions.

Alternatively, the 2-hydroxyl group in the diacetonides can be protected as the *tert*-butyldimethylsilyl ether, prior to removal of the side chain acetonide. Thus, reaction of **D**-*glycero*-**L**-*talo* lactone (8) with *tert*-butyldimethylsilyl chloride in dimethylformamide gives the fully protected lactone (11) [82% yield] which undergoes selective hydrolysis by aqueous acetic acid to give the diol (12) [82% yield]. Both the triol (10) and the diol (12) undergo preferential reaction with selective electrophilic reagents at the primary hydroxyl on C-7. Further reaction of the diol (12) with *tert*-butyldimethylsilyl chloride gives the bis-silyl ether (13) [70% yield] in which only the C-6 hydroxyl group of the lactone is unprotected.

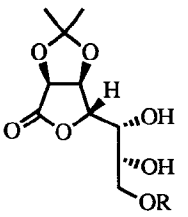
γ-Lactones



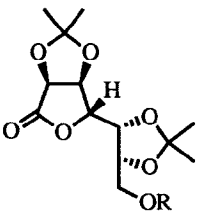
(14)



(15)



(16)
(17) R = Ph_2Bu^tSi



(18) R = Ph_2Bu^tSi
(19) R = H

The acid catalysed removal of the protecting groups from a 4-hydroxy-δ-lactone is generally accompanied by isomerisation to the corresponding 5-hydroxy-γ-lactone; thus all the above δ-lactones may be converted to γ-lactones which provide an alternative set of intermediates with accessibility to alternative hydroxyl functions. The range of opportunities provided by this isomerisation may be illustrated by the chemistry of the **D**-*glycero*-**D**-*talo* diacetonide (2). Treatment of (2) with aqueous trifluoroacetic acid resulted in rapid loss of the side chain acetonide, followed by a relatively slow hydrolysis of the second isopropylidene group to give the unprotected 1,4-lactone (14), m.p. 132-134°C [lit. 130°C,[16] 131-132°C,[17] 152°C[18]], $[\alpha]_D^{20}$ -35.7 (*c*, 1.00 in H_2O) [Lit. -35.7 (*c*, 4 in H_2O),[16] -34.9 (*c*, 0.6 in H_2O),[17] +35.3 (*c*, 0.2 in H_2O)[18]]. Because of this ambiguity in the literature in regard to the physical properties of (14), the crystalline material was subjected to single X-ray crystal structure analysis (Figure 1)[19] which confirmed the original data[16,17] reported for **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14).

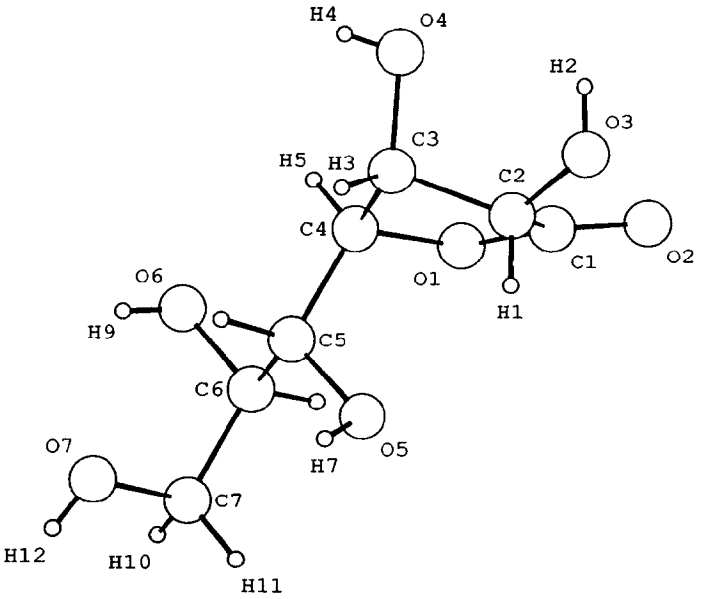


Figure 1. X-Ray molecular structure of **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14), showing crystallographic numbering scheme.

The diacetonide (15), in which only the C-6 hydroxyl group remains unprotected, may be prepared by reacting the crude unprotected lactone (14) in acetone with acetone and 2,2-dimethoxypropane in the presence of camphor sulphonic acid [69% overall yield from (2)]. The side chain acetonide in (15) is very susceptible to acid hydrolysis and considerable care must be exercised in storing (15) for any length of time, since this leads to contamination of (15) with the monoacetonide (16).The side chain acetonide in the γ-lactone (15) was selectively removed with aqueous acetic acid at room temperature to give the monoacetonide (16) [78% yield] in which the primary hydroxyl group could be protected by reaction with *tert*-butylchlorodiphenylsilane to afford the diol (17) in which the C-5 and C-6 hydroxyl groups are free [91% yield]. Reaction of the diol (17) with acetone, dimethoxypropane and camphor sulphonic acid gave the fully protected γ-lactone (18) [92% yield] which on subsequent treatment with tetra-*n*-butylammonium fluoride in tetrahydrofuran gave the diacetonide (19) [73% yield]; the structure of (19), with only the primary hydroxyl group at C-7 unprotected, was firmly established by single X-ray crystal structure analysis (Figure 2).

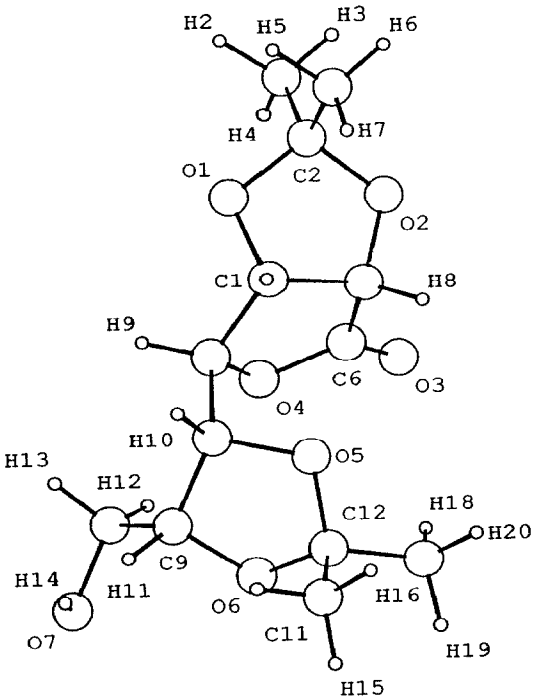


Figure 2. X-Ray molecular structure of 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19), showing crystallographic numbering scheme

In summary, this paper reports the synthesis on moderate to large scales of acetonides of *glycero-talo*- and *glycero-galacto*-lactones as intermediates for the synthesis of highly functionalised targets with up to five adjacent chiral centres; although these syntheses at present only proceed in modest yield, diacetonides of heptonolactones provide a diverse and powerful class of chirons. The accompanying paper describes the characterisation of some α-hydroxy-δ-lactone derivatives in which the isopropylidene protected ketal is trans, rather than cis, to the adjacent carbon substituent of the lactone.[20]

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X-Ray Crystal Structure Analyses.

The structures of **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14) (crystallised from ethanol/ethyl acetate) and 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19) (from ether/hexane) were established by single crystal X-ray analysis. For both compounds, cell dimensions and intensity data were measured with an Enraf-Nonius CAD4-F diffractometer up to $\theta = 75^{o}$ (Cu-Kα radiation). The data were corrected for absorption, Lorentz and polarisation effects. All calculations were carried out on a Microvax 3800 computer using SHELXS-86[21] for direct methods and CRYSTALS[22] for all other calculations. Atomic scattering factors were taken from International Tables.[23] Atomic coordinates for both compounds have been deposited at the Cambridge Crystallographic Data Centre.[19] The coordinates of all non-hydrogen atoms were given by SHELXS-86. The hydrogen atoms were placed geometrically except for the hydroxyl hydrogens which were found by Fourier difference maps. The structures were refined by full-matrix least-squares with isotropic temperature factors for the hydrogen atoms and anisotropic temperature factors for all other atoms using data with merged Friedel pairs. Corrections for secondary extinction were applied,[24] and the models refined almost to convergence. The data were fully refined using Chebyshev weighting schemes[25] to give a final value of R = 0.0263 for **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14) and a final value of R = 0.0381 for 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19).

Crystal Data for **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14).

Molecular formula $C_7H_{12}O_7$ Formula weight 208.17

Crystal data: Crystal system monoclinic primitive

a/Å 5.458(0.001) $\alpha/^{o}$ 90

b/Å 9.935(0.001) $\beta/^{o}$ 91.63(0.02)

c/Å 8.048(0.002) $\gamma/^{o}$ 90

space group $P2_1$ D_C/g cm^{-3} 1.595 linear absorption coeff. /cm^{-1} 12.144

Crystal size /mm 0.05 x 0.2 x 0.4

Data collection: X-radiation λ = 1.5418 Å Cu-Kα θ min., max. /^{o} 0, 72

ω-scan parameters: A, B (^{o}) (A + B tanθ) A = 0.80 B = 0.15

Horizontal aperture parameters: A, B (mm) (A + B tanθ) A = 3.5 B = 0

Scan speed/^{o} min^{-1} 1.3 (min.) to 6.7 (max.) Total data 907

Observed data 838 for [I>nσ(I)] where n = 3

Absorption correction: min 1.00, max 1.17 Merging R 2.62%

Refinement:

Weighting Scheme type Chebyshev 4 coefficients 0.231, 9.054, -1.149, 2.377

Extinction parameter 35.53

Maximum residual electron density/ eÅ^{-3} 0.09 Final R 2.63% R_w 3.42%

Fractional atomic coordinates and equivalent isotropic temperature factors U(equ) with standard devia parentheses for **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14)

Atom	x/a	y/b	z/c	U(equ)
C(1)	0.2248(4)	-0.3797(2)	0.0664(3)	0.0225
C(2)	0.2195(4)	-0.4987(2)	-0.0540(2)	0.0224
C(3)	0.4907(4)	-0.5298(2)	-0.0684(2)	0.0227
C(4)	0.5906(3)	-0.4935(2)	0.1064(2)	0.0220
C(5)	0.6033(4)	-0.6098(2)	0.2301(2)	0.0218
C(6)	0.7182(4)	-0.5689(2)	0.3984(3)	0.0247
C(7)	0.7297(5)	-0.6859(2)	0.5196(3)	0.0315
O(1)	0.4267(3)	-0.3873(1)	0.1652(2)	0.0251
O(2)	0.0799(3)	-0.2893(2)	0.0759(2)	0.0324
O(3)	0.0849(3)	-0.4762(2)	-0 2022(2)	0.0282
O(4)	0.5865(3)	-0.4424(2)	-0.1913(2)	0.0268
O(5)	0.3642(3)	-0.6626(2)	0.2511(2)	0.0310
O(6)	0.9552(3)	-0.5127(2)	0.3727(2)	0.0318
O(7)	0.8670(4)	-0.7915(2)	0.4456(2)	0 0344

Final anisotropic temperature factors with standard deviations in parentheses for **D**-*glycero*-**D**-*talo*-hept lactone (14)

Atom	U(11)	U(22)	U(33)	U(23)	U(13)	U(12)
C(1)	0.0199(9)	0.020(1)	0.0291(9)	-0.0028(8)	0.0032(7)	0.0010(7)
C(2)	0.0213(9)	0.0221(9)	0.0241(8)	-0.0022(8)	-0.0019(7)	0.0008(8)
C(3)	0.025(1)	0.021(1)	0.0225(8)	-0.0012(7)	-0.0016(7)	-0.0029(7)
C(4)	0.0213(9)	0.0199(9)	0.0254(9)	-0.0024(8)	-0.0020(7)	0.0010(8)
C(5)	0.0244(9)	0.0189(8)	0.0227(9)	-0 0012(7)	-0.0021(7)	-0.0005(8)
C(6)	0.032(1)	0.021(1)	0.0227(9)	0.0014(8)	-0.0017(8)	-0.0030(9)
C(7)	0.045(1)	0.030(1)	0.023(1)	-0.0030(9)	0.0004(8)	-0.003(1)
O(1)	0.0290(7)	0.0191(7)	0.0298(7)	0.0030(6)	-0.0046(6)	-0.0018(6)
O(2)	0.0303(8)	0.0246(7)	0.049(1)	-0.0008(7)	0.0029(7)	-0.0066(7)
O(3)	0.0234(7)	0.0361(9)	0.0295(7)	-0.0061(7)	-0.0064(6)	0.0044(6)
O(4)	0.0237(7)	0.0337(9)	0.0274(7)	-0.0077(6)	0.0033(6)	-0.0066(6)
O(5)	0.0309(8)	0.0249(7)	0.0425(9)	-0.0063(7)	-0.0004(6)	0.0064(7)
O(6)	0.0363(9)	0.0269(8)	0.0365(8)	0.0003(7)	-0.0093(6)	0.0051(7)
O(7)	0.062(1)	0.0268(8)	0.0290(8)	-0.0021(6)	-0.0095(8)	-0.0118(8)

Bond lengths (in Å) for the non-hydrogen atoms with standard deviations in parentheses for **D**-*glycero* heptono-1,4-lactone (14)

C(1) - C(2)	1.528(3)	C(1) - O(1)	1.343(3)
C(1) - O(2)	1.201(3)	C(2) - C(3)	1.519(3)
C(2) - O(3)	1.401(2)	C(3) - C(4)	1.537(3)
C(3) - O(4)	1.427(3)	C(4) - C(5)	1.526(3)
C(4) - O(1)	1.470(2)	C(5) - C(6)	1.531(3)
C(5) - O(5)	1.421(2)	C(6) - C(7)	1.518(3)
C(6) - O(6)	1.429(3)	C(7) - O(7)	1.429(3)

Bond angles (in degrees) for the non-hydrogen atoms with standard deviations in parentheses for **D**-*glycero* heptono-1,4-lactone (14)

O(1) - C(1) - C(2)	109.4(2)	O(2) - C(1) - C(2)	128.2(2)
O(2) - C(1) - O(1)	122.4(2)	C(3) - C(2) - C(1)	101.8(2)
O(3) - C(2) - C(1)	114.6(2)	O(3) - C(2) - C(3)	117.1(2)
C(4) - C(3) - C(2)	101.7(2)	O(4) - C(3) - C(2)	107.8(2)
O(4) - C(3) - C(4)	111.4(2)	C(5) - C(4) - C(3)	115.3(2)
O(1) - C(4) - C(3)	105.1(2)	O(1) - C(4) - C(5)	110.5(2)
C(6) - C(5) - C(4)	112.7(2)	O(5) - C(5) - C(4)	109.4(2)
O(5) - C(5) - C(6)	110.3(2)	C(7) - C(6) - C(5)	111.9(2)
O(6) - C(6) - C(5)	109.0(2)	O(6) - C(6) - C(7)	111.8(2)
O(7) - C(7) - C(6)	107.9(2)	C(4) - O(1) - C(1)	110.2(2)

Crystal Data for 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19).

There are two molecules in the asymmetric unit which have an approximate 2 fold axis parallel to c at x = 0.08, y = 0.87). With the exception of 0(7) and 0(27) molecule I maps very closely with molecule II (rms atomic deviation = 0.72Å). In molecule I, 0(7) is approximately trans to C(8) [τ = -176°]; in molecule II, 0(27) is approximately cis to C(208) [τ = -71°].

Molecular formula $C_{13}H_{20}O_7$ Formula weight 288.3

Crystal data: Crystal system orthorhombic primitive

a/Å 11.242(0.002) α/° 90

b/Å 11.421(0.002) β/° 90

c/Å 23.021(0.004) γ/° 90

space group $P2_12_12_1$ D_c/g cm^{-3} 1.296 linear absorption coeff. /cm^{-1} 8.548

Crystal size /mm 0.6 x 0.8 x 0.8

Data collection: X-radiation λ = 1.5418 Å Cu-Kα θ min., max. /° 0, 75

ω-scan parameters: A, B (°) (A + B tanθ) A = 0.90 B = 0.15

Horizontal aperture parameters: A, B (mm) (A + B tanθ) A = 3.5 B = 0

Scan speed/° min^{-1} 1.4 (min.) to 6.7 (max.) Total data 3369

Observed data 2958 for [I>nσ(I)] where n = 3

Absorption correction: min 1.51, max 1.67 Merging R 1.49%

Refinement: Weighting Scheme type Chebyshev 5 coefficients 13.846, -11.906, 9.580, -4.802, -1.645

Extinction parameter 112.80

Maximum residual electron density/ eÅ^{-3} 0.04 Final R 3.81% R_w 4.86%

Fractional atomic coordinates and equivalent isotropic temperature factors with standard deviations in parentheses for 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19)

Atom	x/a	y/b	z/c	U(equ)
O(1)	-0.3679(2)	1.1976(2)	0.25682(9)	0.0649
O(2)	-0.3921(2)	1.1605(2)	0.1609(1)	0.0708
O(3)	-0.3169(2)	0.9105(2)	0.15218(9)	0.0684
O(4)	-0.2521(2)	0.9569(1)	0.24031(7)	0.0537
O(5)	-0.0302(1)	1.0624(2)	0.21740(7)	0.0530
O(6)	0.0270(2)	0.8852(2)	0.25092(7)	0.0540
O(7)	-0.0202(3)	0.7701(2)	0.3605(1)	0.0840
O(21)	0.3790(2)	0.4682(1)	-0.02638(9)	0.0582
O(22)	0.3693(2)	0.4548(2)	0.0724(1)	0.0691
O(23)	0.1916(2)	0.6398(2)	0.09683(8)	0.0647
O(24)	0.2430(1)	0.6884(1)	0.00705(6)	0.0447
O(25)	0.4509(2)	0.8167(1)	0.02220(7)	0.0492
O(26)	0.3181(2)	0.9567(2)	-0.00282(9)	0.0599
O(27)	0.2646(3)	0.8354(2)	-0.14581(9)	0.0890
C(1)	-0.2527(2)	1.1638(2)	0.2367(1)	0.0516
C(2)	-0.4352(2)	1.2318(3)	0.2075(2)	0.0633
C(3)	-0.5640(3)	1.2012(4)	0.2181(2)	0.0980
C(4)	-0.4156(4)	1.3584(3)	0.1934(2)	0.0971
C(5)	-0.2795(2)	1.1164(2)	0.1766(1)	0.0542
C(6)	-0.2858(2)	0.9842(2)	0.1862(1)	0.0509
C(7)	-0.2093(2)	1.0582(2)	0.27187(9)	0.0486
C(8)	-0.0750(2)	1.0553(2)	0.2757(1)	0.0477
C(9)	-0.0145(2)	0.9456(2)	0.3012(1)	0.0528
C(10)	-0.0890(3)	0.8628(3)	0.3363(1)	0.0696

C(11)	0.1793(2)	1.0208(3)	0.2172(1)	0.0640
C(12)	0.0552(2)	0.9706(2)	0.2089(1)	0.0497
C(13)	0.0373(3)	0.9187(3)	0.1493(1)	0.0656
C(201)	0.4196(2)	0.5789(2)	-0.0054(1)	0.0455
C(202)	0.3949(3)	0.3879(2)	0.0205(2)	0.0615
C(203)	0.5210(3)	0.3430(3)	0.0210(2)	0.0732
C(204)	0.3026(3)	0.2929(3)	0.0141(3)	0.0865
C(205)	0.3836(2)	0.5748(2)	0.0584(1)	0.0497
C(206)	0.2634(2)	0.6367(2)	0.05832(9)	0.0462
C(207)	0.3442(2)	0.6749(2)	-0.03188(9)	0.0425
C(208)	0.4125(2)	0.7892(2)	-0.03553(9)	0.0439
C(209)	0.3446(3)	0.8979(2)	-0.0557(1)	0.0541
C(210)	0.2317(3)	0.8772(3)	-0.0903(1)	0.0701
C(211)	0.5192(3)	1.0153(2)	0.0235(2)	0.0681
C(212)	0.4152(2)	0.9344(2)	0.0351(1)	0.0524
C(213)	0.3726(3)	0.9390(4)	0.0971(1)	0.0782

Final anisotropic temperature factors with standard deviations in parentheses for 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19)

Atom	U(22)	U(33)	U(23)	U(13)	U(12)	U(11)
O(1)	0.056(1)	0.078(1)	0.075(1)	-0.019(1)	0.0001(9)	0.0215(9)
O(2)	0.067(1)	0.082(1)	0.085(1)	-0.022(1)	-0.026(1)	0.023(1)
O(3)	0.079(1)	0.069(1)	0.071(1)	-0.026(1)	-0.011(1)	-0.003(1)
O(4)	0.0546(8)	0.0513(8)	0.0575(9)	-0.0039(7)	-0.0030(7)	-0.0091(7)
O(5)	0.0492(8)	0.0579(9)	0.0537(8)	0.0003(7)	0.0046(7)	0.0072(7)
O(6)	0.060(1)	0.0509(8)	0.0551(8)	-0.0094(7)	0.0021(8)	0.0098(8)
O(7)	0.119(2)	0.070(1)	0.077(1)	0.015(1)	-0.005(1)	0.014(1)
O(21)	0.070(1)	0.0348(7)	0.083(1)	-0.0068(8)	-0.008(1)	0.0015(7)
O(22)	0.096(2)	0.047(1)	0.089(1)	0.027(1)	0.010(1)	0.010(1)
O(23)	0.062(1)	0.085(1)	0.059(1)	0.019(1)	0.0150(8)	0.006(1)
O(24)	0.0410(6)	0.0454(7)	0.0507(7)	0.0105(6)	0.0037(6)	0.0011(6)
O(25)	0.0604(8)	0.0384(7)	0.0519(8)	-0.0039(6)	-0.0033(7)	-0.0018(7)
O(26)	0.067(1)	0.0470(8)	0.075(1)	-0.0102(8)	0.0035(9)	0.0131(8)
O(27)	0.154(2)	0.086(2)	0.058(1)	0.013(1)	-0.014(1)	-0.024(2)
C(1)	0.046(1)	0.051(1)	0.063(1)	-0.012(1)	-0.006(1)	0.004(1)
C(2)	0.051(1)	0.060(1)	0.093(2)	-0.016(1)	-0.015(1)	0.008(1)
C(3)	0.053(2)	0.116(3)	0.156(4)	-0.010(3)	-0.007(2)	0.008(2)
C(4)	0.120(3)	0.064(2)	0.139(4)	-0.008(2)	-0.048(3)	-0.000(2)
C(5)	0.050(1)	0.058(1)	0.056(1)	-0.005(1)	-0.005(1)	0.002(1)
C(6)	0.044(1)	0.058(1)	0.053(1)	-0.012(1)	0.0016(9)	-0.002(1)
C(7)	0.047(1)	0.054(1)	0.049(1)	-0.014(1)	0.0008(9)	0.003(1)
C(8)	0.047(1)	0.049(1)	0.050(1)	-0.0117(9)	-0.0011(9)	0.0029(9)
C(9)	0.058(1)	0.055(1)	0.050(1)	-0.010(1)	-0.0073(9)	0.009(1)
C(10)	0.081(2)	0.069(2)	0.063(1)	0.005(1)	0.010(1)	0.014(2)
C(11)	0.047(1)	0.088(2)	0.066(1)	-0.014(1)	-0.003(1)	-0.005(1)
C(12)	0.044(1)	0.059(1)	0.050(1)	-0.0113(9)	-0.0017(9)	0.005(1)
C(13)	0.063(1)	0.087(2)	0.058(1)	-0.023(1)	-0.003(1)	0.001(1)
C(201)	0.049(1)	0.0328(8)	0.059(1)	-0.0038(9)	0.0019(9)	0.0012(8)
C(202)	0.064(1)	0.034(1)	0.111(2)	0.010(1)	-0.008(2)	0.004(1)
C(203)	0.069(2)	0.046(1)	0.129(3)	0.002(2)	-0.012(2)	0.007(1)
C(204)	0.073(2)	0.047(1)	0.209(5)	0.020(2)	-0.023(3)	-0.009(1)
C(205)	0.052(1)	0.044(1)	0.056(1)	0.0098(9)	-0.002(1)	0.004(1)
C(206)	0.046(1)	0.044(1)	0.050(1)	0.0071(9)	0.0017(9)	-0.0002(9)
C(207)	0.0470(9)	0.0385(9)	0.0433(9)	0.0021(8)	0.0052(8)	-0.0006(8)
C(208)	0.052(1)	0.0370(9)	0.045(1)	0.0001(8)	0.0088(9)	-0.0006(8)
C(209)	0.074(1)	0.041(1)	0.055(1)	0.0085(9)	0.006(1)	0.002(1)
C(210)	0.089(2)	0.060(1)	0.073(2)	0.016(1)	-0.012(1)	0.011(2)
C(211)	0.080(2)	0.044(1)	0.096(2)	-0.007(1)	0.013(2)	-0.013(1)
C(212)	0.060(1)	0.042(1)	0.061(1)	-0.011(1)	0.007(1)	-0.000(1)

C(213)	0.085(2)	0.100(2)	0.069(2)	-0.030(2)	0.017(2)	-0.003(2)

Bond lengths (in Å) for the non-hydrogen atoms with standard deviations in parentheses for 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19)

O(1) - C(1)	1.428(3)	O(1) - C(2)	1.420(4)
O(2) - C(2)	1.430(4)	O(2) - C(5)	1.409(3)
O(3) - C(6)	1.202(3)	O(4) - C(6)	1.339(3)
O(4) - C(7)	1.449(3)	O(5) - C(8)	1.436(3)
O(5) - C(12)	1.435(3)	O(6) - C(9)	1.426(3)
O(6) - C(12)	1.410(3)	O(7) - C(10)	1.426(4)
O(21) - C(201)	1.428(2)	O(21) - C(202)	1.427(3)
O(22) - C(202)	1.448(4)	O(22) - C(205)	1.417(3)
O(23) - C(206)	1.200(3)	O(24) - C(206)	1.339(3)
O(24) - C(207)	1.456(2)	O(25) - C(208)	1.432(3)
O(25) - C(212)	1.434(3)	O(26) - C(209)	1.420(3)
O(26) - C(212)	1.421(3)	O(27) - C(210)	1.413(4)
C(1) - C(5)	1.515(3)	C(1) - C(7)	1.532(3)
C(2) - C(3)	1.509(5)	C(2) - C(4)	1.498(5)
C(5) - C(6)	1.527(4)	C(7) - C(8)	1.513(3)
C(8) - C(9)	1.542(3)	C(9) - C(10)	1.498(4)
C(11) - C(12)	1.521(3)	C(12) - C(13)	1.508(3)
C(201)- C(205)	1.524(3)	C(201)- C(207)	1.514(3)
C(202)- C(203)	1.507(4)	C(202)- C(204)	1.509(4)
C(205)- C(206)	1.525(3)	C(207)- C(208)	1.516(3)
C(208)- C(209)	1.529(3)	C(209)- C(210)	1.518(4)
C(211)- C(212)	1.514(4)	C(212)- C(213)	1 506(4)

Bond angles (in degrees) for the non-hydrogen atoms with standard deviations in parentheses for 2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19)

C(2) - O(1) - C(1)	107.3(2)	C(5) - O(2) - C(2)	108.4(2)
C(7) - O(4) - C(6)	112.0(2)	C(12) - O(5) - C(8)	108.7(2)
C(12) - O(6) - C(9)	107.2(2)	C(202)- O(21) - C(201)	105.9(2)
C(205)- O(22) - C(202)	107.4(2)	C(207)- O(24) - C(206)	111.2(2)
C(212)- O(25) - C(208)	108.2(2)	C(212)- O(26) - C(209)	106.3(2)
C(5) - C(1) - O(1)	102.3(2)	C(7) - C(1) - O(1)	109.3(2)
C(7) - C(1) - C(5)	105.3(2)	O(2) - C(2) - O(1)	105.2(2)
C(3) - C(2) - O(1)	108.5(3)	C(3) - C(2) - O(2)	108.3(3)
C(4) - C(2) - O(1)	111.1(3)	C(4) - C(2) - O(2)	109.7(3)
C(4) - C(2) - C(3)	113.5(3)	C(1) - C(5) - O(2)	106.5(2)
C(6) - C(5) - O(2)	110.4(2)	C(6) - C(5) - C(1)	103.4(2)
O(4) - C(6) - O(3)	121.7(2)	C(5) - C(6) - O(3)	127.7(2)
C(5) - C(6) - O(4)	110.6(2)	C(1) - C(7) - O(4)	104.9(2)
C(8) - C(7) - O(4)	110.1(2)	C(8) - C(7) - C(1)	111.5(2)
C(7) - C(8) - O(5)	107.1(2)	C(9) - C(8) - O(5)	104.3(2)
C(9) - C(8) - C(7)	118.7(2)	C(8) - C(9) - O(6)	103.3(2)
C(10) - C(9) - O(6)	108.4(2)	C(10) - C(9) - C(8)	118.1(2)
C(9) - C(10) - O(7)	112.1(2)	O(6) - C(12) - O(5)	105.2(2)
C(11) - C(12) - O(5)	108.7(2)	C(11) - C(12) - O(6)	112.4(2)
C(13) - C(12) - O(5)	108.8(2)	C(13) - C(12) - O(6)	108.8(2)
C(13) - C(12) - C(11)	112.6(2)	C(205)- C(201)- O(21)	102.4(2)
C(207)- C(201)- O(21)	109.0(2)	C(207)- C(201)- C(205)	105.2(2)
O(22) - C(202)- O(21)	105.1(2)	C(203)- C(202)- O(21)	110.0(3)
C(203)- C(202)- O(22)	111.1(3)	C(204)- C(202)- O(21)	107.6(3)
C(204)- C(202)- O(22)	108.8(3)	C(204)- C(202)- C(203)	113.8(2)
C(201)- C(205)- O(22)	106.2(2)	C(206)- C(205)- O(22)	110.3(2)
C(206)- C(205)- C(201)	102.7(2)	O(24) - C(206)- O(23)	121.5(2)
C(205)- C(206)- O(23)	127.5(2)	C(205)- C(206)- O(24)	110.9(2)
C(201)- C(207)- O(24)	105.4(2)	C(208)- C(207)- O(24)	109.8(2)

C(208)- C(207)- C(201)	111.3(2)	C(207)- C(208)- O(25)	106.8(2)
C(209)- C(208)- O(25)	104.7(2)	C(209)- C(208)- C(207)	117.6(2)
C(208)- C(209)- O(26)	103.2(2)	C(210)- C(209)- O(26)	110.4(2)
C(210)- C(209)- C(208)	116.7(2)	C(209)- C(210)- O(27)	108.0(3)
O(26) - C(212)- O(25)	104.8(2)	C(211)- C(212)- O(25)	108.7(2)
C(211)- C(212)- O(26)	112.1(2)	C(213)- C(212)- O(25)	108.5(2)
C(213)- C(212)- O(26)	109.3(2)	C(213)- C(212)- C(211)	113.0(2)

Experimental

General Methods. - Melting points were recorded on a Kofler hot block and are uncorrected. Proton nuclear magnetic resonance (δ_H) spectra were recorded on Varian Gemini 200 (at 200 MHz) or Bruker WH 300 (300 MHz) spectrometers. ^{13}C Nuclear magnetic resonance (δ_C) spectra were recorded on a Varian Gemini 200 (50 MHz) spectrometer and multiplicities were assigned using DEPT sequence. ^{13}C spectra run in D_2O were referenced to methanol (δ_C 49.6 ppm) as an internal standard. All chemical shifts are quoted on the δ-scale. Infra-red spectra were recorded on a Perkin-Elmer 781, or 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) 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, methanol was distilled from magnesium methoxide, pyridine was distilled from, 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 involatile fractions. D-Mannose, and D- and L-gulonolactones were purchased from the Sigma Chemical Company. 2,3:5,6-Di-*O*-isopropylidene-**L**-gulono-1,4-lactone[26] and 2,3:5,6-di-*O*-isopropylidene-**D**-gulono-1,4-lactone[27] were prepared as reported previously.

2,3:5,6-Di-*O*-isopropylidene-**D**-mannofuranose (1) was prepared on a large scale by minor modifications of the literature procedure.[28] Concentrated sulphuric acid (500 ml, 9.4 mol) was added dropwise over 30 min to a stirred suspension of **D**-mannose (2 kg, 11.1 mol) in acetone (technical grade) (10 l, 136.2 mol) . The temperature rose from 12°C to 25°C and the mannose gradually dissolved to give a straw coloured solution. After 3h, the mixture was added to a stirred solution of potassium carbonate (3.1 kg, 22.5 mol) in water (20 l) with the temperature maintained below 30°C. Very little effervescence was observed, and the crude product precipitated out. The reaction vessel was rinsed through with acetone (2 l, 27.2 mol).The acetone was distilled out of the vessel under a slightly reduced pressure, ensuring that the vessel was not heated above 50°C. The resulting aqueous suspension was cooled to 15°C and the white crystalline solid was filtered off and washed with water (10 l). The crystals were left to air dry to give 2,3:5,6-di-*O*-isopropylidene-**D**-mannofuranose (1), (2.575 kg, 9.9 mol, 89% yield), which was used in the next step without further purification.

3,4:6,7-Di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (2) and 3,4:6,7-Di-*O*-isopropylidene-**D**-*glycero*-**D**-*galacto*-heptono-1,5-lactone (3). The procedure previously reported[13] on a small scale has been modified for work on intermediate and large scales.

(i) Intermediate Scale: Sodium cyanide (17.0 g, 35 mmol) was added to a vigorously stirred suspension of diacetone mannose (1) (100 g, 39 mmol) in water (800 ml) at room temperature. After 3h, the resulting solid mass was heated at 50°C until a clear solution was obtained (*ca* 1h) and then heated at reflux for 5h. After cooling to room temperature, the dark aqueous solution was extracted with dichloromethane (3 x 200 ml) to remove unreacted diacetone mannose (18.1 g, 18%). The aqueous solution was adjusted to pH 5 by cautious addition of concentrated sulphuric acid with vigorous stirring, and extracted with ethyl acetate (3 x 200 ml). After further acidification to pH 2 and extraction with more ethyl acetate (3 x 200 ml), the combined organic extracts were washed with water (400 ml), dried (magnesium sulphate) and concentrated to a volume of 200 ml. Allowing the mixture to stand for several days resulted in a solution containing two lactones (R_f 0.7 (3) and 0.5 (2), ethyl acetate : hexane, 2 : 1) together with a minor amount of polar material (acid). Addition of dicyclohexylcarbodiimide (1 g) and stirring for several hours converted most of the residual acid to lactones. The mixture was filtered and concentrated (with cooling), whereupon crystals of the major isomer (2) (*ca* 10 g) were deposited on standing. The remaining solution was purified by flash chromatography (hexane : ethyl acetate, 3 : 1) to give 3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**D**-*galacto*-heptono-1,5-lactone (3) (8.0 g, 9% based on unrecovered starting material) m.p. 146-147°C [Lit. 140-141°C][13] and 3,4:6,7-di-O-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (2) (26.3 g total, 29 % based on unrecovered starting material), m.p. 147-149°C [Lit. 157-159°C][13]. In several experiments using reflux times of 2-5h, total yields were in the range 26-40%. The spectroscopic data for the two lactones (2) and (3) were identical with those reported previously.[13]

(ii) Large scale: Sodium cyanide (970 g, 19.8 mol) was added to a stirred suspension of diacetone mannose (5.15 kg, 19.8 mol) in water (50 l) and heated to 50°C for 6 h. The solid gradually dissolved and the solution went brown. The reaction mixture was cooled to 15°C and extracted with dichloromethane (2 x 20 l). The dichloromethane layers were discarded. Sodium chloride (8 kg) was dissolved in the aqueous layer. Ethyl acetate (20 l) was stirred with the aqueous layer, and dilute sulphuric acid (2 M) was added to adjust to pH 3. The ethyl acetate layer was separated and the aqueous layer was extracted with ethyl acetate (4 x 10 l). The combined organic layers were dried over magnesium sulphate and the solvent was removed *in vacuo* to leave a brown oil (2.87 kg) which crystallised on trituration with diethyl ether to give 3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (2) (820 g). The remaining residue was purified by chromatography (43% ethyl acetate : 57% hexane) then recrystallised from ethyl acetate/hexane to give 3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (2) (800 g, making a total of 1620 g, 28% yield) and 3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**D**-*galacto*-heptono-1,5-lactone (3) (515 g, 9% yield). The combined filtrates were evaporated *in vacuo* to leave a brown residue (250 g) which was mainly a mixture of the two lactones in a ratio of approximately 1 : 1.

2,3:5,6-Di-*O*-isopropylidene-**L**-gulonofuranose (4). Di-isobutylaluminium hydride (1.0 M in heptane, 118 ml, 118 mmol, 1.2 equiv) was slowly added to a stirred solution of 2,3:5,6-di-*O*-isopropylidene-**L**-gulono-1,4-lactone (25.44 g, 98.6 mmol) in dry tetrahydrofuran (750 ml) at -70°C over 15 min. The reaction mixture was allowed to warm up to -40°C within 15 min and stirring was continued for 1 h at -40°C. The reaction was then quenched by the addition of saturated ammonium chloride solution (12 ml) and filtered through a

short column of silica (60H) topped with a pad of Celite. The filtrate was evaporated under reduced pressure to give a white solid, which was recrystallised from diethyl ether to afford pure *2,3:5,6-di-O-isopropylidene-L-gulonofuranose* (4), (10.0 g, 38.5 mmol, 39%), as white crystalline solid, m.p. 119 - 120°C (diethyl ether). The mother liquid was then evaporated; after purification by flash chromatography (diethyl ether : hexane, 3 : 7, increasing polarity to diethyl ether : hexane, 7 : 3) afforded a further quantity of the lactol (4) (13.0 g, 50 mmol, 51%; the combined yield was 90%). $[\alpha]_D^{20}$ +0.44 (*c*, 0.68 in $CHCl_3$); υ_{max} (KBr): 3428 (OH) cm^{-1}; δ_H ($CDCl_3$): 1.30 (3H, s, Me), 1.40 (3H, s, Me), 1.46 (6H, s, Me_2C), 2.86 (1H, s, OH), 3.74 (1H, dd, H-6', $J_{5,6'}$ 7.2 Hz, $J_{6,6'}$ 8.1 Hz), 4.15 (1H, dd, H-4, $J_{3,4}$ 3.7 Hz, $J_{4,5}$ 8.5 Hz), 4.23 (1H, dd, H-6, $J_{5,6}$ 6.6 Hz), 4.38 (1H, q, H-5), 4.64 (1H, d, H-2, $J_{2,3}$ 5.9 Hz), 4.76 (1H, H-3), 5.48 (1H, s, H-1); δ_C ($CDCl_3$): 24.5, 25.2, 25.8, 26.5 (4 x q, 4 x MeC), 65.9 (t, C-6), 75.5, 79.8, 82.0, 85.7 (4 x d, C-2, C-3, C-4, C-5), 101.3 (d, C-1), 109.8, 112.9 (2 x s, 2 x CMe_2); *m/z* (NH_3, DCI): 278 ($M+NH_4^+$, 4%), 261 ($M+H^+$, 15%), 203 (M-acetone+H^+, 100%). (Found: C, 55.07; H, 8.05. $C_{12}H_{20}O_6$ requires: C, 55.37, H, 7.75%).

3,4:6,7-Di-*O*-isopropylidene-**L**-*glycero*-**D**-*talo*-heptono-1,5-lactone (5) and 3,4:6,7-Di-*O*-isopropylidene-**L**-*glycero*-**D**-*galacto*-heptono-1,5-lactone (6). A mixture of the lactol (4) (8.10 g, 31 2 mmol) and sodium cyanide (2.14 g, 43.7 mmol, 1.4 equiv.) in water (60 ml) were stirred at 100°C with for 3 h (at which point a test for the presence of cyanide was negative). The reaction mixture was then cooled to 0°C and extracted with dichloromethane (4 x 50 ml). The dichloromethane extracts were dried (magnesium sulphate) and the solvent removed to give the unreacted starting material (0.83 g, 10%). The aqueous layer was acidified to pH 3 by dropwise addition of concentrated sulphuric acid and extracted with ethyl acetate (2 x 150 ml). The aqueous layer was further adjusted to pH 1 and then further extracted with ethyl acetate (2 x 150 ml). The combined ethyl acetate extracts were dried (magnesium sulphate) and the solvent removed to afford an oily residue. The residue solidified after standing overnight at room temperature. Purification by flash chromatography (ethyl acetate : hexane, 1 : 4, increasing polarity to ethyl acetate : hexane, 1 : 1) gave the less polar *3,4:6,7-di-O-isopropylidene-L-glycero-D-galacto-heptono-1,5-lactone* (6) (1.08 g, 12% [13% based on recovered starting material]; R_f 0.7 - ethyl acetate : hexane, 2 : 1), m.p. 156-157°C ($CHCl_3$/hexane); $[\alpha]_D^{20}$ +97.8 (*c*, 0.56 in $CHCl_3$); υ_{max} (KBr): 3495 (OH), 1763 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.33 (3H, s, Me), 1.41 (3H, s, Me), 1.43 (3H, s, Me), 1.46 (3H, s, Me), 3.41 (1H, d, OH, J 3.6 Hz), 3.83 (1H, t, H-7', $J_{6,7'}$ 7.9 Hz, $J_{7,7'}$ 8.4 Hz), 4.19 (1H, dd, H-7, $J_{6,7}$ 6.4 Hz), 4.41 (1H, dd, H-5, $J_{4,5}$ 3.0 Hz, $J_{5,6}$ 7.5 Hz), 4.47 (1H, t, H-2, $J_{2,3}$ 2.2 Hz), 4.49 (1H, q, H-6), 4.58 (1H, dd, H-4, $J_{3,4}$ 7.96 Hz), 4.85 (1H, dd, H-3); δ_C ($CDCl_3$): 23.9, 25 3, 25.7, 26.4 (4 x q, 4 x MeC), 65.2 (t, C-7), 68.8, 71.4, 75.0, 75.5, 78.1 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.3, 110.8 (2 x s, 2 x CMe_2), 169.9 (s, C-1); *m/z* (NH_3, DCI): 306 ($M+NH_4^+$, 44%), 289 ($M+H^+$, 76%), 231 (M-acetone+H^+, 100%). (Found: C, 54.40; H, 7.27. $C_{13}H_{20}O_7$ requires: C, 54.16; H, 6.99%),, and the more polar *3,4:6,7-di-O-isopropylidene-L-glycero-D-talo-heptono-1,5-lactone* (5) (1.62 g, 18% [20% based on recovered starting material]; R_f 0.3 in ethyl acetate : hexane, 2 : 1), m.p. 188-189°C ($CHCl_3$/hexane); $[\alpha]_D^{20}$ +74.3 (*c*, 0.44 in $CHCl_3$); υ_{max} (KBr): 3436, 3392 (OH), and 1752 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.35 (3H, s, Me), 1.41 (3H, s, Me), 1.46 (6H, s, Me_2C), 3.32 (1H, d, OH, J 5.3 Hz), 3.83 (1H, dd, H-7', $J_{6,7'}$ 7.2 Hz, $J_{7,7'}$ 8.5 Hz), 4.17 (1H, dd, H-5, $J_{4,5}$ 1.6 Hz, $J_{5,6}$ 7.9 Hz), 4.20 (1H, dd, H-7, $J_{6,7}$ 6.4 Hz,), 4.36 (1H, dd, H-2, $J_{2,3}$ 3.5 Hz), 4.45 (1H, dd, H-4, $J_{3,4}$ 7.7 Hz), 4.48 (1H, q, H-6), 4.81 (1H, dd, H-3); δ_C ($CDCl_3$): 24.2, 25.2, 25.7, 26.5 (4 x q, 4 x MeC), 65.2 (t, C-7), 68.4, 72.8, 74.6, 74.9, 78.3 (5 x d, C-2, C-3, C-4, C-5, C-6), 111.5, 111.5 (2 x s, 2 x CMe_2), 171.3 (s, C-1); *m/z* (NH_3, DCI): 306 ($M+NH_4^+$,

65%), 289 (M+H$^+$, 67%), 231 (M-acetone+H$^+$, 100%). (Found: C, 54.38; H, 7.06. $C_{13}H_{20}O_7$ requires: C, 54.16; H, 6.99%).

2,3:5,6-Di-*O*-isopropylidene-**D**-gulonofuranose (7) was prepared by minor modification of the literature procedure.[15] Di-isobutylaluminium hydride (1.0 M in heptane, 93 ml, 1.5 equiv) was added slowly to a stirred solution of 2,3:5,6-di-*O*-isopropylidene-**D**-gulono-1,4-lactone (15.9 g, 61.7 mmol) in dry tetrahydrofuran (500 ml) at -40°C. The reaction mixture was allowed to warm to -20°C and stirring was continued for 1 h at which time t.l.c. (ether : hexane, 7 : 3) showed no starting material (R_f 0.2) and a single product (R_f 0.4). The reaction was quenched by the addition of saturated ammonium chloride solution (10 ml) and filtered through a short column of silica topped with Celite. The filtrate was evaporated under reduced pressure to give a solid which was recrystallized from ether to yield 2,3:5,6-di-*O*-isopropylidene-**D**-gulonofuranose (7), (15.56 g, 36 mmol, 97%), m.p.106-107°C [Lit. 113°C][15]; $[\alpha]_D^{20}$ -2.2 (*c*, 1.0 in $CHCl_3$); υ_{max} (KBr): 3420 (br, OH) cm^{-1}; δ_H ($CDCl_3$): 1.30 (3H, s, Me), 1.41 (3H, s, Me), 1.47 (6H, s, Me_2C), 3.74 (1H, t, H-6', $J_{5,6'}$ 7.7 Hz, $J_{6,6'}$ 7.9 Hz), 4.16 (1H, dd, H-4, $J_{3,4}$ 3.7 Hz, $J_{4,5}$ 6.4 Hz), 4.24 (1H, dd, H-6, $J_{5,6}$ 6.9 Hz), 4.39 (1H, q, H-5), 4.65 (1H, d, H-2, $J_{2,3}$ 6.0 Hz), 4.72 (1H, dd, H-3), 5.48 (1H, s, H-1); δ_C ($CDCl_3$): 24.5, 25.2, 25.8, 26.6 (4 x q, 4 x MeC), 66.0 (t, C-6), 75.5, 79.8, 82.2, 85.6 (4 x d, C-2, C-3, C-4, C-5), 101.4 (d, C-1), 109.9, 113.0 (2 x s, 2 x CMe_2); *m/z* (NH_3, DCI): 278 (M+NH_4^+, 4%), 261 (M+H$^+$, 15%), 203 (M+H$^+$-acetone, 100%).(Found: C, 55.20; H, 8.05. $C_{12}H_{20}O_6$ requires: C, 55.37; H, 7.74%).

3,4:6,7-Di-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone,(8) and 3,4:6,7-Di-*O*-isopropylidene-**D**-*glycero*-**L**-*galacto*-heptono-1,5-lactone (9). A mixture of 2,3:5,6-di-*O*-isopropylidene-**D**-gulonofuranose (7) (9.04 g, 35 mmol) and sodium cyanide (2.04 g, 1.2 equiv) was stirred in water (75 ml) at room temperature for 10 min. The resulting solid mass was heated at 100°C for 3 hours at which time no cyanide remained and t.l.c. (ether : hexane, 7 : 3) showed predominantly a baseline spot. The reaction mixture was cooled to room temperature and extracted with dichloromethane (4 x 50 ml) to remove unreacted starting material. The combined dichloromethane extracts were dried (magnesium sulphate) and the solvent removed under reduced pressure to yield recovered starting material (1.12 g, 4.3 mmol, 12%). The aqueous layer was acidified to pH 3 by careful, dropwise addition of concentrated sulphuric acid and extracted with ethyl acetate (2 x 50 ml). After further acidification to pH 1 the aqueous layer was again extracted with ethyl acetate (2 x 50 ml). The combined organic extracts were washed with brine (15 ml), dried (magnesium sulphate) and evaporated. Allowing the resulting crude residue to stand for 3 days gave a mixture of two product lactones (R_f 0.6 and R_f 0.3 in ethyl acetate : hexane, 2 : 1). The lactones were purified by flash column chromatography (hexane : ethyl acetate, 2 : 1, increasing polarity to hexane : ethyl acetate, 1 : 2) to yield *3,4;6,7-di-O-isopropylidene-D-glycero-L-galacto-heptono-1,5-lactone* (9) (931 mg, 3.23 mmol, 11.5% based on recovered starting material) as the minor product (R_f 0.6 in ethyl acetate : hexane, 2 : 1), m.p.134-136°C; $[\alpha]_D^{20}$ -92.4 (*c*, 1.0 in $CHCl_3$); υ_{max} (KBr): 3338 (br, OH), 1763 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.34 (3H, s, Me), 1.41 (3H, s, Me), 1.43 (3H, s, Me), 1.46 (3H, s, Me), 3.84 (1H, t, H-7', $J_{6,7'}$ 7.3 Hz, $J_{7,7'}$ 7.3 Hz), 4.19 (1H, dd, H-7, $J_{6,7}$ 7.3 Hz), 4.41 (1H, dd, H-5, $J_{4,5}$ 2.9 Hz, $J_{5,6}$ 7.5 Hz), 4.46 (1H, d, H-2, $J_{2,3}$ 2.1 Hz), 4.47 (1H, q, H-6), 4.59 (1H, dd, H-4, $J_{3,4}$ 8.0 Hz), 4.82 (1H, dd, H-3); δ_C ($CDCl_3$): 23.9, 25.4, 25.7, 26.4 (4 x q, 4 x MeC), 65.3 (t, C-7), 68.9, 71.5, 75.0, 75.5, 78.2 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.4, 110.9 (2 x s, 2 x CMe_2), 169.8 (s, C-1); *m/z* (NH_3, DCI): 306 (M+NH_4^+, 37%), 289 (M+H$^+$, 100%), 231 (M+H$^+$-acetone, 36%). (Found:

C, 53.93; H, 7.09; $C_{13}H_{20}O_7$ requires: C, 54.16; H, 6.99%), and *3,4:6,7-di-O-isopropylidene-**D**-glycero-**L**-talo-heptono-1,5-lactone* (8), (1.29 g, 4.47 mmol, 16% yield based on recovered starting material) as the major product (R_f 0.3 in ethyl acetate : hexane, 2 : 1), m.p.174-176°C; $[\alpha]_D^{20}$ -66.4 (*c*, 0.5 in acetone); υ_{max} (KBr): 3420, 3385 (br,OH), 1755 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.35 (3H, s, Me), 1.41 (3H, s, Me), 1.46 (6H, s, Me_2C), 3.83 (1H, dd, H-7', $J_{6,7'}$ 7.1 Hz, $J_{7,7'}$ 8.5 Hz), 4.17 (1H, dd, H-5, $J_{4,5}$ 1.7 Hz, $J_{5,6}$ 7 8 Hz), 4.20 (1H, dd, H-7, $J_{6,7}$ 6.4 Hz), 4.35 (1H, d, H-2, $J_{2,3}$ 3.4 Hz), 4.45 (1H, dd, H-4, $J_{3,4}$ 7.6 Hz), 4.50 (1H, q, H-6), 4.81 (1H, dd, H-3); δ_C ($CDCl_3$): 24.2, 25.2, 25.7, 26.5 (4 x q, 4 x MeC), 65.2 (t, C-7), 68.4, 72.8, 74.6, 74.8, 78.3 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.5, 111.5 (2 x s, 2 x CMe_2), 171.3 (s, C-1); *m/z* (NH_3, DCI): 306 ($M+NH_4^+$, 84%), 289 ($M+H^+$, 87%), 248 ($M+NH_4^+$- acetone, 10%), 231 ($M+H^+$-acetone, 100%). (Found: C, 54.25; H, 7.25. $C_{13}H_{20}O_7$ requires: C, 54.16; H, 6.99%).

3,4-*O*-Isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (10). The diacetonide (2) (962 mg, 3.34 mmol) in 80% aqueous acetic acid (20 ml) was stirred at 50°C for 3h when t.l.c. (ethyl acetate) showed complete consumption of starting material (R_f 0.8) and a single product (R_f 0.2). The solvent was removed and the product was recrystallised from ethanol/ethyl acetate to give *3,4-O-isopropylidene-D-glycero-D-talo-heptono-1,5-lactone* (10) (796 mg, 96%), as colourless crystals, m.p. 188-190°C (EtOH/EtOAc); $[\alpha]_D^{20}$+97.5 (*c*, 1.09 in MeOH); υ_{max} (KBr): 3350 (OH), 3510 (OH), 1745 (C=O) cm^{-1}; δ_H (CD_3OD): 1.36 (3H, s, Me), 1.38 (3H, s, Me), 3.66 (1H, dd, H-7, $J_{6,7}$ 4.4 Hz, $J_{7,7'}$ 11.8 Hz), 3.76 (1H, dd, H-7', $J_{6,7'}$ 2.5 Hz), 3.87 (1H, ddd, H-6, $J_{5,6}$ 9.2 Hz), 4.25 (1H, d, H-5), 4.51 (1H, br d, H-2, J 2.0 Hz), 4.78 (2H, d, H-3, H-4, J 2.3 Hz), 4.87 (3H, br s, 3 x OH); δ_C[$(CD_3)_2SO$]: 25.4, 27.2 (2 x q, 2 x MeC), 63.7 (t, C-7), 69.3, 69.6, 73.6, 75.6, 76.7 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.0 (s, CMe_2), 173.0 (s, C-1); *m/z* (NH_3, DCI): 266 ($M + NH_4^+$, 100%). (Found: C, 48.33; H, 6.80. $C_{10}H_{16}O_7$ requires: C, 48.39; H, 6.50%).

Reaction of 3,4-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (10) with acetone and acid. The monoacetonide (10) (114 mg, 0.46 mmol) was stirred with 4-camphor sulphonic acid (5 mg, 0.02 mmol) in acetone (5 ml) at room temperature. After 3 h the reaction was complete; the solution was neutralised by the addition of anhydrous sodium carbonate and the solvent removed. The residue was taken up in ethyl acetate (20 ml), filtered through Celite and washed with water (5 ml). The solution was dried (sodium sulphate) and the solvent removed to give 3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (2) (110 mg, 83 %) identical in all respects to the material prepared above.

2-*O*-*tert*-Butyldimethylsilyl-3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone (11). A solution of *tert*-butyldimethylsilyl chloride (877 mg, 5.8 mmol, 2 equiv) in dry dimethylformamide (10 ml) was added to a stirred solution of 3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone (8) (839 mg, 2.91 mmol) and imidazole (793 mg, 11.6 mmol, 4 equiv) in dry dimethylformamide at room temperature. The solution was stirred for 3.5 h by which time t.l.c. (ethyl acetate : hexane, 2 : 1) showed no starting material (R_f 0.2) and one product (R_f 0.7). The reaction was quenched by addition of water (8 ml) and the solvent removed *in vacuo*. To the crude residue was added a further portion of water (15 ml), and the mixture extracted with ethyl acetate (4 x 50 ml). The combined ethyl acetate extracts were washed with brine (10 ml), dried (magnesium sulphate) and evaporated. Purification by flash column chromatography (hexane, increasing polarity to hexane : ethyl acetate, 4 : 1) yielded *2-O-tert-butyldimethylsilyl-3,4:6,7-di-O-isopropylidene-**D**-glycero-**L**-talo-heptono-1,5-lactone* (11) as a white solid, (964 mg, 82%), m.p. 122-124°C; $[\alpha]_D^{20}$ -33.4 (*c*,

1.0 in $CHCl_3$); υ_{max} (KBr): 1761 (C=O) cm^{-1}; δ_H ($CDCl_3$): 0.14 (3H, s, MeSi), 0.24 (3H, s, MeSi), 0.94 (9H, s, Bu^t), 1.34 (3H, s, Me), 1.40 (3H, s, Me), 1.46 (3H, s, Me),1.47 (3H, s, Me), 3.78 (1H, t, H-7, $J_{6,7}$ 6.8 Hz, $J_{7,7'}$ 8.2 Hz), 4.12 (1H, dd, H-5, $J_{4,5}$ 1.9 Hz, $J_{5,6}$ 7.5 Hz), 4.20 (1H, dd, H-7', $J_{6,7'}$ 7.6 Hz), 4.37 (1H, d, H-2, $J_{2,3}$ 3.0 Hz), 4.40 (1H, dd, H-4, $J_{3,4}$ 7.7 Hz), 4.47 (1H, q, H-6), 4.67 (1H, dd, H-3); δ_C ($CDCl_3$): -5.7, -4.6 (2 x q, 2 x MeSi), 18.4 (s, SiCMe3), 25,7 (q, Bu^t), 24.4, 25.3, 25.8, 26.5 (4 x q, 4 x MeC), 65.2 (t, C-7), 70.0, 73.2, 74.9, 76.6, 78.1 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.3, 111.4 (2 x s, 2 x CMe_2), 168.8 (s, C-1); *m/z* (NH_3, DCI): 420 ($M+NH_4^+$, 12%). (Found: C, 56.32; H, 8.70. $C_{19}H_{34}O_7Si$ requires: C, 56.68; H, 8.53%).

2-*O*-*tert*-Butyldimethylsilyl-3,4-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone (12). 2-*O*-*tert*-Butyldimethylsilyl-3,4:6,7-di-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone (11) (892 mg, 2.22 mmol) was stirred in a solution of acetic acid (48 ml), dioxan (30 ml) and water (12 ml). After 14 h, t.l.c. (ethyl acetate : hexane, 2 : 1) showed no starting material (R_f 0.8) and one product (R_f 0.2). The solvents were removed *in vacuo* and the residue purified by flash column chromatography (ethyl acetate : hexane, 7 : 3) to yield *2-O-tert-butyldimethylsilyl-3,4-O-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone* (12), (660 mg, 1.82 mmol, 82%), as a white crystalline solid, m.p. 105-107°C; $[\alpha]_D^{20}$ -35.6 (*c*, 1.0 in $CHCl_3$); υ_{max} (KBr): 3369 (OH), 1767 (C=O) cm^{-1}; δ_H ($CDCl_3$): 0.14 (3H, s, MeSi), 0.24 (3H, s, MeSi), 0.95 (9H, s, Bu^t), 1.36 (3H, s, Me), 1.47 (3H, s, Me), 2.26, 2.92 (2 x 1H, 2 x br s, 2 x OH, D_2O exchange), 3.81 (1H, dd, H-7', $J_{6,7'}$ 3.4 Hz, $J_{7,7'}$ 12.2 Hz), 3.89 (1H, dd, H-7, $J_{6,7}$ 3.4 Hz), 4.07 (1H, dt, H-6, $J_{5,6}$ 7.3 Hz), 4.27 (1H, dd, H-5, $J_{4,5}$ 1.6 Hz), 4.41 (1H, d, H-2, $J_{2,3}$ 2.9 Hz), 4.62 (1H, dd, H-4, $J_{3,4}$ 7.7 Hz), 4.68 (1H, dd, H-3); δ_C ($CDCl_3$): -5.6, -4.6 (2 x q, 2 x MeSi), 18.4 (s, SiCMe3), 25.7 (q, Bu^t), 24.2, 25.8 (2 x q, 2 x MeC), 62.1 (t, C-7), 70.1, 70.8, 72.9, 76.6, 77.2 (5 x d, C-2, C-3, C-4, C-5, C-6), 110.9 (s, CMe_2), 170.3 (s, C-1); *m/z* (NH_3, DCI): 380 ($M+NH_4^+$, 13%), 363 ($M+H^+$, 100%), 305 ($M+H^+$-acetone, 87%). (Found: C, 53.03; H, 8.04. $C_{16}H_{30}O_7Si$ requires: C, 53.04; H, 8.29%).

2,7-Di-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone (13). A solution of *tert*-butyldimethylsilyl chloride (109 mg, 0.73 mmol, 1.3 equiv) in dimethylformamide was added to a stirred solution of 2-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-**D**-*glycero*-**L**-*talo*-heptono-1,5-lactone (12) (202 mg, 0.56 mmol) and imidazole (114 mg, 1.7 mmol, 3 equiv) in dimethylformamide at -35°C. The reaction mixture was allowed to warm to -20°C and stirring was continued for 5.5 h at which time t.l.c (ethyl acetate : hexane, 1 : 2) showed no starting material (Rf 0.0) and one major product (Rf 0.6). The reaction was quenched by addition of water (3 ml) and the solvents removed *in vacuo*. To the crude residue was added a further portion of water (5 ml), and the mixture extracted with ethyl acetate (4 x 20 ml). The combined organic extracts were washed with brine (5 ml), dried (magnesium sulphate) and evaporated. Purification by flash column chromatography (ethyl acetate : hexane, 1 : 1) yielded *2,7-di-O-tert-butyldimethylsilyl-3,4-isopropylidene-D-glycero-L-talo-heptono-1,5-lactone* (13), (188 mg, 70%) as a colourless solid, m.p.75-77°C ; $[\alpha]_D^{20}$ -44.4 (*c*, 0.25 in $CHCl_3$); υ_{max} (KBr): 3514 (OH), 1780 (C=O) cm^{-1}; δ_H ($CDCl_3$): 0.10 (6H, s, Me_2Si), 0.14 (3H, s, MeSi), 0.24 (3H, s, MeSi), 0.95 (9H, s, Bu^t), 1.36 (3H, s, Me), 1.48 (3H, s, Me), 3.81 (2H, d, H-7, H-7', $J_{6,7}$ 5.1 Hz, $J_{6,7'}$ 5.1 Hz), 4.04 (1H, q, H-6, $J_{5,6}$ 5.2 Hz), 4.23 (1H, dd, H-5, $J_{4,5}$ 1.6 Hz), 4.38 (1H, d, H-2, $J_{2,3}$ 2.9 Hz), 4.61 (1H, dd, H-4, $J_{3,4}$ 7.8 Hz), 4.68 (1H, dd, H-3); δ_C ($CDCl_3$): -5.7, -4.6 (2 x q, 2 x MeSi), 18.1, 18.4 (2 x s, 2 x SiCMe3), 24.3, 25.7 (2 x q, 2 x MeC), 25.7 (q, Bu^t), 62.7 (t, C-7), 70.3, 71.2, 74.3, 75.6, 76.7 (C-2, C-3, C-4, C-5, C-6), 111.1 (s, CMe_2), 169.7 (s, C-1); *m/z*

(NH_3, DCI): 494 ($M+NH_4^+$, 15%), 477 ($M+H^+$, 100%), 419 ($M+H^+$-acetone, 35%). (Found: C, 55.27; H, 9.56; $C_{22}H_{44}O_7Si_2$ requires: C, 55.41; H, 9.32%).

2,3;6,7-Di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (15). 3,4:6,7-Di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (2) (4.51 g, 15.6 mmol) was stirred at 40°C in 40% aqueous trifluoroacetic acid (20 ml). T.l.c (ethyl acetate) showed immediate consumption of the starting material (R_f 0.7), formation of a major product (R_f 0.3), identified as 3,4-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,5-lactone (10) and also a minor product (R_f 0.1). After 8 h, t.l.c. (ethyl acetate) showed a major product (R_f 0.1). The solvent was removed and the residue co-evaporated with toluene (2 x 10 ml). A small amount of material was purified by flash chromatography (ethyl acetate, increasing polarity to ethyl acetate : ethanol, 9 : 1) and recrystallised from ethanol/ethyl acetate to give **D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (14) as a white crystalline solid, m.p. 132-134°C [Lit. 130°C,[16] 131-132°C,[17] 152°C[18]], $[\alpha]_D^{20}$ -35.7 (*c*, 1.00 in H_2O) [Lit. -35.7 (*c*, 4 in H_2O),[16] -34.9 (*c*, 0.6 in H_2O),[17] +35.3 (*c*, 0.2 in H_2O)[18]]; υ_{max} (KBr): 3500-3200 (br, OH), 1770 (C=O) cm^{-1}; δ_H (D_2O): 3.50 (3H, m), 3.70 (3H, m), 4.34 (1H, d, H-2, $J_{2,3}$, 5.8 Hz); δ_C (D_2O): 63.7 (t, C-7), 69.5, 70.6, 71.0, 71.1 (4 x d, C-3, C-4, C-5, C-6), 86.6 (d, C-2), 179.8 (s, C-1); *m/z* (NH_3, DCI): 226 ($M+NH_4^+$, 100%) , 209 ($M+H^+$, 90%). (Found: C, 40.45 ; H, 5.82. $C_7H_{12}O_7$ requires: C, 40.39, H, 5.81%). The crude product (14) was dissolved in dry acetone (30 ml). 2,2-Dimethoxypropane (9 ml, 5 equiv) and camphor sulphonic acid (360 mg, 10%) were added and the mixture stirred at room temperature for 24 h when t.l.c (ethyl acetate : hexane , 1 : 1) showed formation of a major product (R_f 0.5). The solvent was removed and the residue purified by flash chromatography (ethyl acetate : hexane, 1 : 3) to give *2,3;6,7-di-O-isopropylidene-D-glycero-D-talo-heptono-1,4-lactone* (15), (3.10 g, 69% over two steps), as a colourless viscous oil, $[\alpha]_D^{20}$ +29.53 (*c*, 1.07 in $CHCl_3$); υ_{max} (film): 3470 (OH), 1773 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.36 (3H, s, Me), 1.39 (3H, s, Me), 1.41 (3H, s, Me), 1.47 (3H, s, Me), 2.84 (1H, br, OH), 3.87 (1H, br m, H-5), 3.95 (1H, dd, H-7, $J_{6,7}$ 5.8 Hz, $J_{7,7'}$ 8.8 Hz), 4.09 (1H, dd, H-7', $J_{6,7'}$ 6.1 Hz), 4.18 (1H, m, H-6), 4.76 (1H, s, H-4), 4.79 (1H, d, H-3, $J_{2,3}$ 5.6 Hz), 4.84 (1H, d, H-2); δ_C ($CDCl_3$): 24.90, 25.29, 26.55, 28.09 (4 x q, 4 x MeC), 66.09 (t, C-7), 71.59, 74.95, 75.24, 78.82, 82.37 (5 x d, C-2, C-3, C-4, C-5, C-6), 109.5, 113.2 (2 x s, 2 x CMe_2), 175.73 (s, C-1); *m/z* (NH_3, DCI): 306 ($M+NH_4^+$, 100%), 289 ($M+H^+$, 90%). This diacetonide (15) was relatively unstable as the terminal acetonide was extremely susceptible to hydrolysis.

2,3-*O*-Isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (16). 2,3;5,6-Di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (15) (839 mg, 2.91 mmol), was dissolved in 50% aqueous acetic acid (20 ml), and stirred at room temperature. After 18 h, t.l.c. (ethyl acetate) indicated that no starting material remained (R_f 0.8), and a major product had formed (R_f 0.3). The solvent was removed, and the residue purified by flash chromatography (ethyl acetate : hexane, 9 : 1) to yield *2,3-O-isopropylidene-D-glycero-D-talo-heptono-1,4-lactone* (16) (566 mg, 78%) as a white crystalline solid, m.p. 129-130°C; $[\alpha]_D^{20}$ +19.8 (*c*, 1.00 in MeOH), υ_{max} (KBr): 3400 (br, OH), 1800, 1765 (C=O) cm^{-1}; δ_H [$(CD_3)_2SO$]: 1.29 (3H, s, Me), 1.33 (3H, s, Me), 3.28-3.40 (2H, m), 3.53-3.67 (2H, m), 4.69-4.76 (3H, m); δ_C (CD_3OD): 24.98, 26.46 (2 x q, 2 x MeC), 63.92 (t, C-7), 71.19, 71.30, 76.24, 80.22, 83.34 (5 x d, C-2, C-3, C-4, C-5, C-6), 113.4 (s, CMe_2), 176.96 (s, C-1); *m/z* (NH_3, DCI): 266 ($M+NH_4^+$, 100%), 249 ($M+H^+$, 10%). (Found: C, 48.39; H, 6.46. $C_{10}H_{16}O_7$ requires: C, 48.39: H, 6.50%).

7-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (17). 2,3-*O*-Isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (16) (441 mg, 1.78 mmol) and imidazole (226 mg, 2.2 equiv) were dissolved in dry dimethylformamide (5 ml) and stirred at 0°C under nitrogen. *tert*-Butylchlorodiphenylsilane (0.51 ml, 1.2 equiv) was added dropwise and the mixture allowed to warm to room temperature. After 2h t.l.c. (ethyl acetate : hexane , 1 : 1) indicated the formation of a single product (R_f 0.8). The solvent was removed and the crude reaction mixture shaken with water (20 ml) and ether (10 ml). The aqueous layer was further extracted with ether (3 x 10 ml), the combined organic extracts were then dried with magnesium sulphate, filtered and the solvent removed. The residue purified by flash column chromatography (ethyl acetate : hexane, 1 : 3), yielding *7-O-tert-butyldiphenylsilyl-2,3-O-isopropylidene-D-glycero-D-talo-heptono-1,4-lactone* (17) (794 mg, 92%) as a white solid, m.p. 40-44°C (glassy transition); $[\alpha]_D^{20}$ -7.44 (*c*, 1.07 in $CHCl_3$); υ_{max} ($CHCl_3$): 3450 (br, OH), 1790 (C=O) cm^{-1}; δ_H ($CDCl_3$) : 1.07 (9H, s, Bu^t), 1.40 (3H, s, Me), 1.48 (3H, s, Me), 2.38 (1H, br, s, OH), 3.04 (1H, br, s, OH), 3.84 (4H, m), 4.76, 4.83 (2 x 1H, 2 x d, H-2, H-3, $J_{2,3}$ 5.6 Hz), 4.91 (1H, s, H-4), 7.4-7.6 (12H, m, 2 x Ph); δ_C ($CDCl_3$): 18.99 ($SiCMe_3$), 25.38, 26.60 (2 x q, 2 x MeC), 26.68 (q, Bu^t), 65.84 (t, C-7), 69.26, 73.27, 75.32, 78.94, 82.00 (5 x d, C-2, C-3, C-4, C-5, C-6), 113.1 (s, CMe_2), 127.96, 128.14, 130.31 (3 x d, ArC), 132.38 (s, ArC), 175.40 (s, C-1); *m/z* (NH_3, DCI): 504 ($M+NH_4^+$, 100%). (Found: C, 64.40; H, 7.28. $C_{26}H_{34}O_7Si$ requires: C, 64.17; H, 7.04%).

7-*O*-*tert*-Butyldiphenylsilyl-2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (18). 7-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (17) (635 mg, 1.31 mmol) and camphor sulphonic acid (30 mg, 10%) were dissolved in dry acetone (20 ml) and stirred at 50°C. 2,2-Dimethoxypropane (671 mg, 5 equiv) was then added and after 20 min t.l.c. (ethyl acetate : hexane, 1 : 3) indicated the formation of a single product (R_f 0.7). The reaction mixture was cooled, neutralised with sodium hydrogen carbonate, filtered, the solvent removed and purified by flash column chromatography (ethyl acetate : hexane, 1 : 5) to yield *7-O-tert-butyldiphenylsilyl-2,3:5,6-di-O-isopropylidene-D-glycero-D-talo-heptono-1,4-lactone* (18), (627 mg, 91%), a white crystalline solid, m.p. 129-132°C; $[\alpha]_D^{20}$ -25.1 (*c*, 1.05 in $CHCl_3$); υ_{max} ($CHCl_3$): 1790 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.08 (9H, s, Bu^t), 1.30 (3H, s, Me), 1.34 (3H, s, Me), 1.39 (3H, s, Me), 1.49 (3H, s, Me), 4.00 (1H, dd, H-7, $J_{6,7}$ 5.6 Hz, $J_{7,7'}$ 10.3 Hz), 4.07 (1H, dd, H-7', $J_{6,7'}$ 8.3 Hz), 4.20 (1H, d, H-5, $J_{5,6}$ 7.3 Hz), 4.42 (1H, ddd, H-6), 4.70, 4.76 (2 x 1H, 2 x d, H-2, H-3, $J_{2,3}$ 5.6 Hz), 4.90 (1H, s, H-4), 7.4-7.6 (12H, m, 2 x Ph); δ_C ($CDCl_3$): 19.07 ($SiCMe_3$), 24.36, 25.47, 25.70, 26.63 (4 x q, 4 x MeC), 26.76 (q, Bu^t), 62.47 (t, C-7), 75.22, 76.33, 76.76, 79.17, 79.96 (5 x d, C-2, C-3, C-4, C-5, C-6), 109.8, 113.2 (2 x s, 2 x CMe_2), 127.98, 130.07, 135.67 (3 x d, ArC), 174.6 (s, C-1); *m/z* (NH_3, DCI): 544 ($M+NH_4^+$, 100%). (Found: C, 66.02; H, 7.45. $C_{29}H_{38}O_7Si$ requires: C, 66.13; H, 7.27%).

2,3:5,6-Di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (19). 7-*O*-*tert*-Butyldiphenylsilyl-2,3:5,6-di-*O*-isopropylidene-**D**-*glycero*-**D**-*talo*-heptono-1,4-lactone (18) (431 mg, 0.82 mmol) was dissolved in dry tetrahydrofuran and stirred at 0°C under nitrogen. Tetra-n-butylammonium fluoride (0.98 ml, 1M solution in tetrahydrofuran, 1.2 equiv) was added dropwise, and after 90 min, t.l.c. (ethyl acetate : hexane, 1 : 1) indicated the formation of a single product (R_f 0.3, not UV active). Evaporation of the solvent produced a yellow oil which was purified by flash chromatography (ethyl acetate : hexane, 1 : 2) yielding *2,3:5,6-di-O-isopropylidene-D-glycero-D-talo-heptono-1,4-lactone* (19), (172 mg, 73%), as a white crystalline solid, m.p.

107-109°C; $[\alpha]_D^{20}$ -4.8 (*c*, 1.05 in $CHCl_3$); υ_{max} ($CHCl_3$): 3600 (OH), 1790 (C=O) cm^{-1}; δ_H ($CDCl_3$): 1.34 (3H, s, Me), 1.37 (3H, s, Me), 1.40 (3H, s, Me), 1.47 (3H, s, Me), 3.86 (1H, dd, H-7, $J_{6,7}$ 5.6 Hz, $J_{7,7'}$ 11.1 Hz), 4.01 (1H, dd, H-7', $J_{6,7'}$ 7.0 Hz), 4.30 (1H, d, H-5, $J_{5,6}$ 7.4 Hz), 4.46 (1H, ddd, H-6), 4.69, 4.76 (2 x 1H, 2 x d, H-2, H-3, $J_{2,3}$ 5.5 Hz), 4.70 (1H, s, H-4); δ_C ($CDCl_3$): 24.11, 25.08, 25.66, 26.50 (4 x q, 4 x MeC), 61.30 (t, C-7) 76.12, 76.87, 78.05, 80.08, 80.99 (5 x d, C-2, C-3, C-4, C-5, C-6), 109.9, 113.3 (2 x s, 2 x $\underline{C}Me_2$), 174.54 (s, C-1); *m/z* (NH_3, DCI): 306 ($M+NH_4^+$, 100%) , 289 ($M+H^+$, 50%). (Found: C, 54.17; H, 7.26. $C_{13}H_{20}O_7$ requires: C, 54.16; H, 6.99%).

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