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A Galactopyranose Analogue of Hydantocidin

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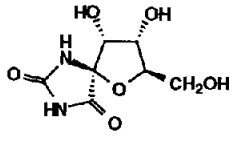
Abstract: The synthesis of (2R,3R,4S,5R,6S)-3,4,5-trihydroxy-2-hydroxymethyl-7,9-diaza-oxaspiro-[4,5]decane-8,10-dione, a galactopyranose analogue of the powerful herbicide hydantocidin, is described. The compound caused no inhibition of the activity of a number of glucosyl or galactosyl transferases, or of α- or β-galactosidases. An azidoester containing a galactopyranosyl moiety may be a useful intermediate for the generation of libraries of compounds of galactose mimics.

The chemical stability of carbohydrate mimics with both an N-acyl group and a carbonyl function at the anomeric carbon[1] has allowed the incorporation of such moieties, such as mannofuranose[2] and mannopyranose,[3] into oligopeptides. Such compounds contain an individual carbohydrate epitope but allow substantial chemical diversity to be introduced at the anomeric position of a sugar; an approach to the synthesis of combinatorial libraries containing rhamnofuranose recognition sites has been reported.[4] Hydantoins[5] and diketopiperazines[6] are chemical structures that feature in both natural and synthetic compounds with a range of biological activities; such structures may be introduced into the anomeric position of sugars. Interest was stimulated by the isolation of hydantocidin **1** from *Streptomyces*;[7,8] **1**, which shows potent herbicidal activity nearly equal to that of glyphosate[9] with no toxicity to micro-organisms or animals,[10] was the first example of a spirohydantoin at the anomeric position of a sugar. Syntheses of the natural product **1**[11] and of other furanoses containing anomeric spirohydantoins[12] have been reported; spirodiketopiperazines[13] and other spiro derivatives of furanoses[14,15] have been described. The potent inhibitor of glycogen phosphorylase **2** was the first reported spirohydantoin of a pyranose,[16] although the epimer **3** has very little effect on the enzyme. A spirodiketopiperazine of glucopyranose[17] has also been shown to be a specific inhibitor of phosphorylase. Some similar derivatives of rhamnose have been shown to interfere with mycobacterial cell growth and provide a mechanism based strategy for the chemotherapy of diseases such as tuberculosis and leprosy.[18] It is clear that analogous compounds of other sugars are also likely to have potential in highly specific binding to enzymes or receptors involving carbohydrates.



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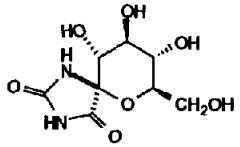

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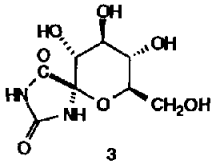

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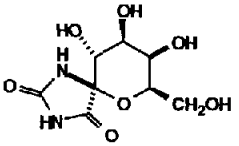
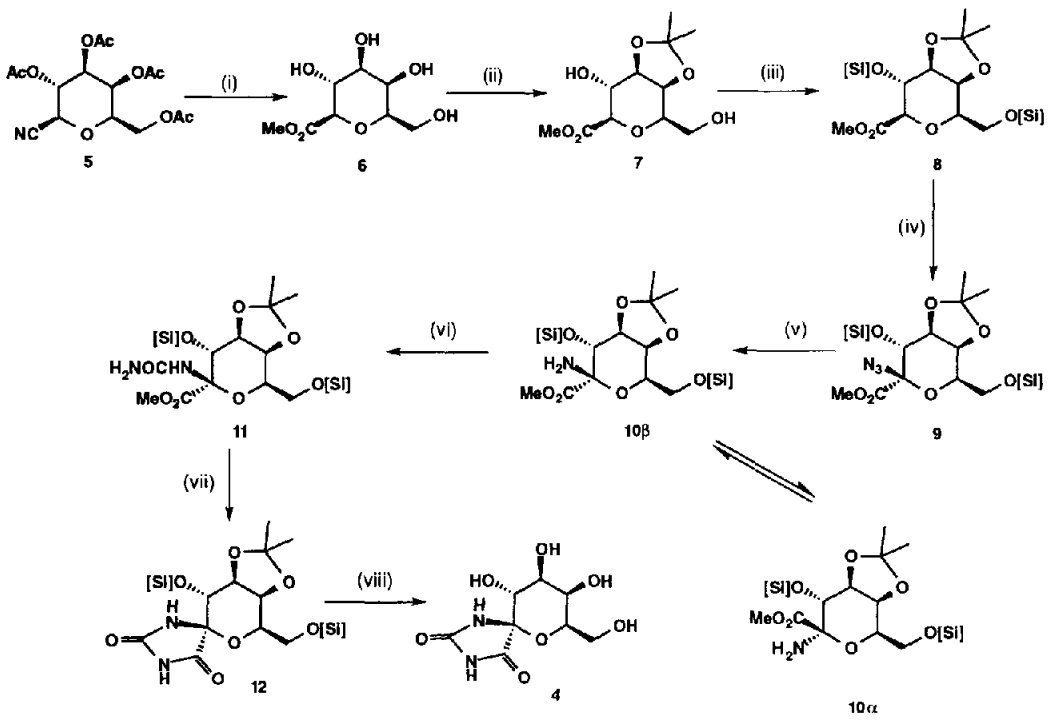


4

This paper reports the synthesis of the galactopyranose spirohydantoin **4** and its lack of effect on the activities of a number of galactosidases and galactosyl transferases; the azidoester **9** may be a useful intermediate for the utilisation of combinatorial techniques for the generation of libraries of compounds containing the galactopyranosyl mimic for high through-put screening of galactose mimics. In contrast to the potent and specific inhibition of glycogen phosphorylase by **2**, **4** shows no inhibition on the enzyme. Early stages of an alternative approach to the galactopyranose **4** have been reported by Dondoni.[19]

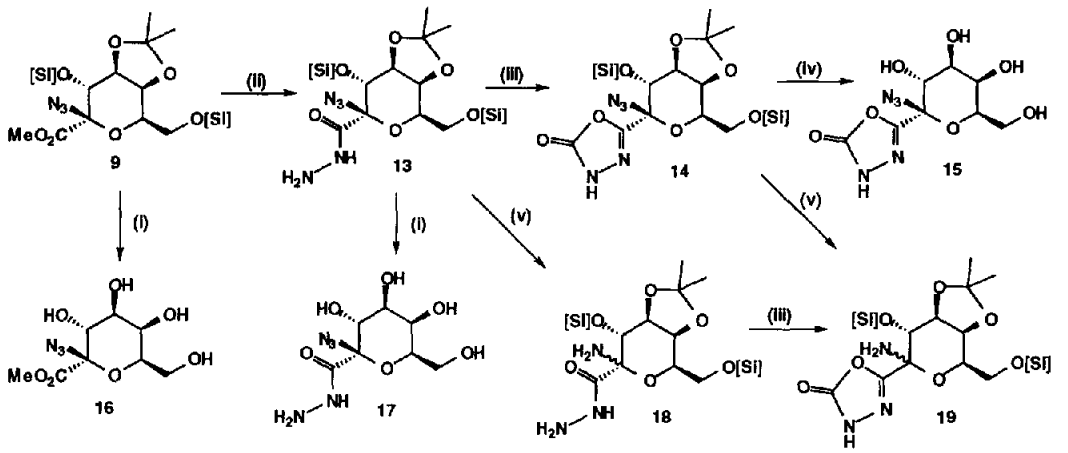


Scheme 1 (i) MeOH, HCl (ii) acetone, CSA (iii) TBDMSOTf, NEt_3 (iv) NBS, $(PhCO)_2O$, CCl_4; then NaN_3, DMF (v) H_2, Pd, MeOH (vi) KNCO, MeCOOH (vii) KOtBu, tetrahydrofuran (viii) dioxan / water / CF_3COOH 1:1:1

The synthesis of the hydantoin **4** required a one carbon chain extension, and the establishment of the correct level of oxidation, at the anomeric position of the galactose [Scheme 1]. Accordingly, nitromethane ascension of galactose with subsequent dehydration and acylation gave the protected nitrile **5** as previously described.[20] Reaction of **5** with methanolic hydrogen chloride gave the unprotected methyl ester[21] **6** which, with acetone in the presence of copper sulphate and camphor sulfonic acid, afforded the acetonide **7** [60% overall yield from **5**]. The remaining free hydroxyl groups in **7** were protected as *tert*-butyldimethylsilyl [TBDMS] ethers by treatment with TBDMS triflate and triethylamine in dichloromethane to give the fully protected equatorial ester **8** [quantitative yield], establishing the pyranose ring of galactose; the equatorial functional group at C-1 is likely to allow easy kinetic radical abstraction of an *axial* hydrogen,[22] permitting introduction of a bromine atom at the anomeric position. Radical bromination of **8** by N-bromosuccinimide in carbon tetrachloride with benzoyl peroxide[23] as initiator occurred regioselectively *via* the most stable captodative[24] radical to give an unstable bromide which, with sodium azide in dimethyl formamide, gave a single azide **10β** [65% overall yield from **8**].

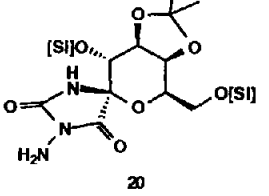
Hydrogenation of the azide **9** in methanol in the presence of palladium on carbon gave the corresponding amine **10β** initially, which equilibrated on standing to an anomeric mixture in which the apparently more stable axial amine **10α** predominated; it was possible to isolate pure samples of **10α** but not to isolate **10β** in a pure form. However, when the mixture of amines was treated with potassium cyanate in

acetic acid, a single urea **11** was isolated (60% yield); as expected, although the anomeric amines interconvert readily, there is no evidence of equilibration of N-acylated derivatives. A possible explanation for the formation of **11** is that the axial amine **10α** is too hindered to act as an effective nucleophile, so that the urea formed is that derived from the less hindered, less stable, but more nucleophilic equatorial amine **10β**. Treatment of the urea **11** with potassium *tert*-butoxide induced cyclisation to give a single spirohydantoin **12** in 88% yield. Both the silyl and ketal protecting groups were removed from **12** by hydrolysis with trifluoroacetic acid in aqueous dioxan to give the unprotected galactopyranose analogue of hydantocidin in 86% yield. The anomeric configurations of the compounds in this sequence were determined by equilibrium NOE studies described below.

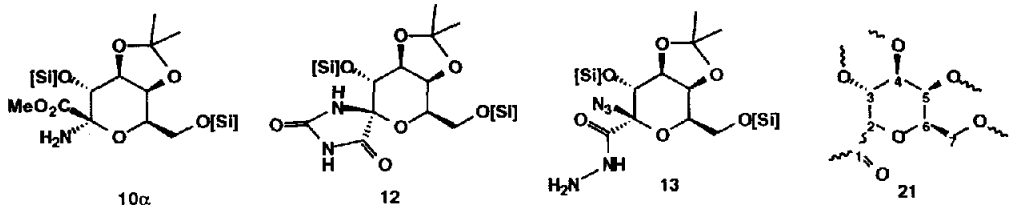


Scheme 2 (i) MeOH, CF_3COOH 1:1 (ii) NH_2NH_2, MeOH (iii) Im_2CO, THF (iv) H_2O, dioxan, CF_3COOH (v) H_2, Pd, EtOAc

Some other transformations [Scheme 2] were performed on the azidoester **9** in order to provide evidence for the configuration at the anomeric position and also to broaden the range of galactose mimics. Thus, trifluoroacetic acid in methanol caused removal of all the protecting groups from **9** to give the azidoester **16** in 77% yield. Reaction of **9** with hydrazine hydrate in methanol gave the acyl hydrazide **13** [81% yield] from which the protecting groups were removed by acid methanolysis to give **17** [100% yield]. Treatment of the hydrazide **13** with carbonyldiimidazole on tetrahydrofuran gave the protected oxadiazole **14** [95% yield] from which the protecting groups were removed by acid hydrolysis to afford **15** [quantitative yield]. Attempts were made to use the hydrazide **13** to prepare a spirohydantoin: accordingly, hydrogenation of **13** in methanol in the presence of palladium on carbon gave an anomeric amine **18** [68% yield] which was treated with carbonyldiimidazole in the anticipation that the amine group would be acylated, allowing the development of an N-aminospirohydantoin ring **20**.



Nonetheless, the only product isolated from the reaction was the oxadiazole **19** [83% yield], identical to material produced by hydrogenation of the azide **14**. Several alternative, but unsuccessful, strategies towards the construction of **20** were investigated; however, because none of the materials generated in these syntheses had any effect on any enzymes studied, further efforts to synthesise aminohydantoins by this route were abandoned.



The anomeric configurations at C1 of the compounds in the above sequences were established by NMR studies on the aminoester **10α**, the protected spirohydantoin **12** and the azidohydrazide **13**. The numbering of carbons for all the compounds in the NMR data is shown in **21**. In all cases, the carbon backbone could be followed unambiguously. The only remaining ambiguities in assignments were to the two NH groups in compound **12** (dealt with below) and in the stereo-specific assignments of the CH_2 resonances and the protecting group methyl resonances. Phase-sensitive 2D NOESY spectra for all three compounds were recorded with mixing times of 200 and 400 ms without any random variation. Inter-proton distances were determined from the NOE cross-peak volumes using the two-spin approximation as previously described.[25]

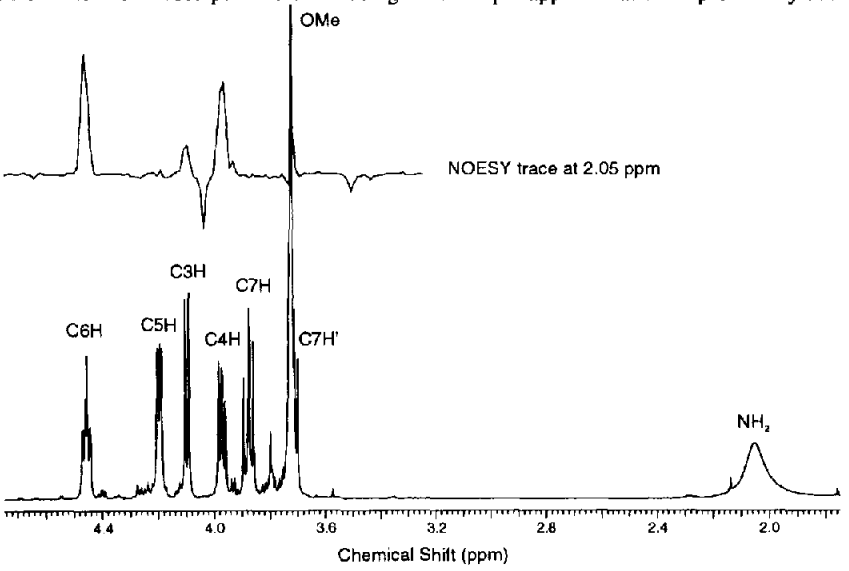


Figure 1: *Lower trace*: 1D ^{1}H NMR spectrum of compound amino ester **10α**, showing the resonance assignments. *Upper trace*: a trace through the phase-sensitive 2D NOESY spectrum, 400 ms mixing time, at 2.05 ppm (corresponding to the NH_2 protons).

From inspection of the 1D NMR spectrum in figure 1, the amine **10α** consists of a single major component (at least 95 % pure). NOEs are observed from the NH_2 resonance to both the C4H and C6H resonances, the latter stronger than the former, and a much weaker NOE to the C3H. Table 1 gives the theoretical average distances between the NH_2 protons and the ring protons for the two possible anomeric configurations (axial and equatorial C1), determined by molecular modelling. The observed pattern of NOEs is only consistent with an equatorial C1 configuration. Because of the large line-width of the NH_2 resonance, the NOE cross-peaks are too broad to allow accurate quantitation.

Anomer		*Average distance (Å)*				
		C3H	C4H	C5H	C6H	C7H/H'
Axial C1	NH_2	**2.77**	4.62	5.59	4.42	4.96
Equatorial C1	NH_2	3.68	3.11	4.35	**2.83**	4.60

Table 1 -- Theoretical average distances between the NH_2 protons and the ring protons for the two possible configurations at C2 (axial C1 and equatorial C1) of amine 10α, determined by molecular modelling. The numbers in bold indicate proton pairs that would be predicted to give strong NOE cross-peaks (less than 3 Å).

From analysis of the 1D (figure 2) and 2D COSY spectra of the spirohydantoin **12**, all the ring proton assignments can be made but ambiguity remains over the assignment of the two NH resonances at 8.14 ppm and 5.88 ppm. An NOE is observed from the NH resonance at 5.88 ppm to the C3H resonance, but not to any other ring resonances (figure 2). The NH resonance at 8.14 ppm does not give an NOE to any ring resonance.

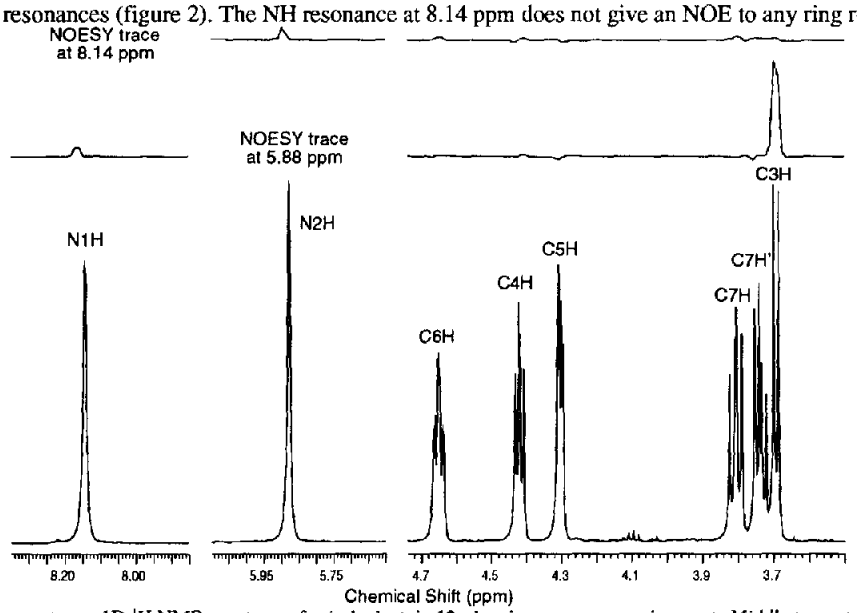


Figure 2: *Lower trace*: 1D ^{1}H NMR spectrum of spirohydantoin **12**, showing resonance assignments.*Middle trace*: trace through the phase-sensitive 2D NOESY spectrum, 400 ms mixing time, at 5.88 ppm (corresponding to the N2H proton). *Upper trace*:- a trace through the phase-sensitive 2D NOESY spectrum, 400 ms mixing time, at 8.14 ppm (corresponding to the N1H proton).

Anomer		Distance (Å)				
		C3H	C4H	C5H	C6H	C7H/H'
Axial C1	N1H	5.22	5.19	6.52	4.74	6.04
	N2H	**2.86**	5.08	5.78	4.63	4.80
Equatorial C1	N1H	4.70	5.97	7.21	5.63	6.30
	N2H	3.98	**2.85**	4.14	**2.71**	4.79

Table 2: Theoretical distances between the N1H and N2H protons and the ring protons for the two possible configurations at C2 (axial C1 and equatorial C1) of spirohydantoin **12**, determined by molecular modelling. The numbers in bold indicate proton pairs that would be predicted to give strong NOE cross-peaks (less than 3 Å).

Table 2 gives the theoretical distances between the N1H and N2H protons and the ring protons for the two possible anomeric configurations (axial or equatorial C1) in **12**, determined from molecular modelling. The absence of any NOEs to ring protons allows the assignment of the resonance at 8.14 ppm to N1H. The presence of an NOE to C3H but not to any other ring proton confirms the assignment of the resonance at 5.88 ppm to N2H and allows the configuration at C2 to be determined as having C1 axial.

Proton pair	NOE distance (Å)	Calibration distance (Å)	Calculated distance (Å)	Model distance (Å)
C5H -- C6H	0.270	2.37	--	2.37
C3H -- C4H	0.033	--	3.36	3.07
C3H -- N2H	0.124	--	2.70	2.86

Table 3: Calculated inter-proton distances based on the NOE cross-peak intensity for spriohydantoin 12. The C5H-C6H distance, determined from molecular modelling, is used as an internal calibration. The model distances given for comparison are those for the axial C1 configuration.

This can be confirmed by a quantitative analysis of the NOE intensities, shown in Table 3. By using the C5H-C6H distance of 2.37 Å as an internal calibration, the distance from N2H to C3H can be calculated as 2.70 Å. This compares to theoretical distances of 2.86 Å for an axial C1 configuration and 3.98 Å for an equatorial C1 configuration (Table 3). Further confirmation is provided by the observation of a stronger NOE between N1H and the protecting group on O3 than between N2H and the same protecting group, indicating that N1 is on the same side of the ring as O3.

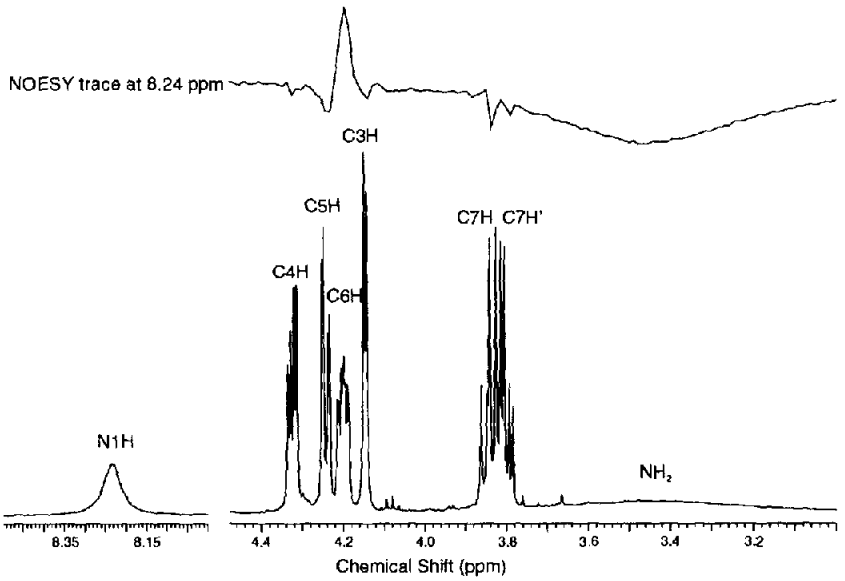
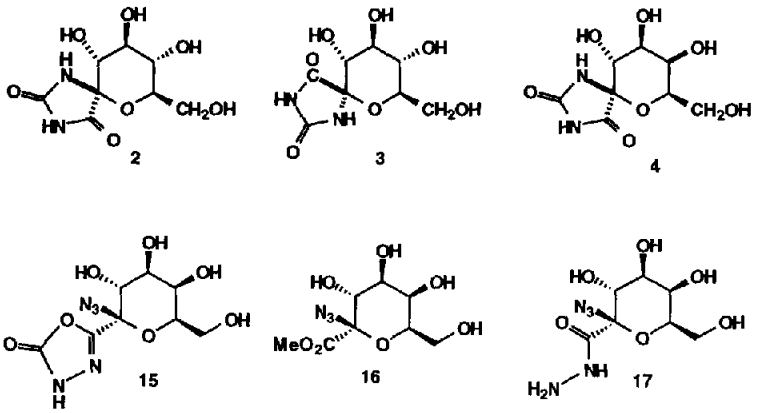


Figure 3: *Lower trace*: 1D ^{1}H NMR spectrum of hydrazide **13**, showing the resonance assignments. *Upper trace*: a trace through the phase-sensitive 2D NOESY spectrum, 400 ms mixing time, at 8.24 ppm (corresponding to the N1H proton). The very broad, negative peak at 3.48 ppm is due to direct chemical exchange between the N1H and NH_2 protons.

The 1D NMR spectrum of hydrazide **13** is shown in figure 3. An NOE is observed from the N1H resonance to the C6H resonance, but not to any other ring protons (figure 3). Molecular modelling shows that the N1H to C6H distance can vary (due to potential rotation around the C1-C2 bond) between van der Waal's contact and 4.8 Å for the axial C1 configuration and between 3.9 Å and 5.3 Å for the equatorial C1 configuration. The equatorial C1 configuration would also result in a short N1H to C3H distance. Thus, the observation of an NOE from N1H to C6H but not to C3H is only consistent with an axial C1 configuration.



Biological assays. The glucohydantoin **2** is among the most potent inhibitors of glycogen phosphorylase yet discovered, although the epimer **3** has essentially no inhibitory effect on the enzyme;[16] the galactohydantoin **4** also showed no inhibition of glycogen phosphorylase at 10 mM, showing that phosphorylase is very demanding in respect of the stereochemical features required for the binding of potential inhibitors.[26]

The galactohydantoin **4** and the unprotected galactose derivatives **15**, **16** and **17** were also assayed at 2mM concentrations against UDP-Glc:ceramide glucosyl transferase, UDP-Gal:ceramide galactosyl transferase, UDP-Gal:GlcNAc galactosyl transferase and ceramide β-galactosidase, and at 1mM concentrations against coffee bean α-galactosidase jack bean β-galactosidase.[27] None of the galactose analogues showed any inhibitory effect on any of the transferases or galactosidases.

While the lack of any biological activity of any of the unprotected galactose mimics is disappointing, it is clear that the protected azidoester **9** would be a candidate for the incorporation of galactopyranose into a novel set of N-linked glycopeptides. The generation of libraries of such materials by combinatorial technology and subsequent screening may discover galactose mimics with highly specific biological activity.[28]

Experimental: Melting points were recorded on a Kofler hot block and are corrected. Proton nuclear magnetic resonance (δ_H) spectra were recorded on a Bruker AC 200 (200 MHz) or a Bruker AM 500 (500 MHz) spectrometer. ^{13}C Nuclear magnetic resonance (δ_C) spectra were recorded on a Varian Gemini 200 (50 MHz), a Bruker AC 200 (50 MHz) or a Bruker AM 500 (125 MHz) spectrometer and multiplicities were assigned using DEPT sequence. All chemical shifts are quoted on the δ-scale. The following abbreviations were used to explain multiplicities: s, singulett; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad, app, apperent. Infra-red spectra were recorded on a Perkin-Elmer 1750 FT spectrophotometer. Mass spectra were recorded on Masslab 20-250, Trio-1 GCMS (DPX-5 column), BIO-Q or Platform spectrometers using desorption chemical ionisation (NH_3, DCI), chemical ionisation (CI), electron impact (EI) or electrospray, 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. ^1H NMR spectra on compounds **10α**, **12** and **13** in $CDCl_3$ were recorded on a Varian Unity 500, with a probe temperature of 30°C. Resonance assignments were obtained from the 1D and phase-sensitive 2D COSY spectra, referenced to the residual solvent signal at 7.24 ppm. Molecular modelling was performed on a Silicon Graphics Personal Iris 4D/35 using the InsightII and Discover software (Biosym Tech. Inc.). 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. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptononitrile **5** was prepared as previously described.[20]

Methyl 2,6-anhydro-4,5-O-isopropylidene-D-glycero-L-manno-heptonate **7** A solution of 3,4,5,7-tetra-O-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptononitrile **5**[20] (5.52 g, 15.45 mmol) in methanolic hydrogen chloride [prepared by addition of acetyl chloride (4.2 ml) to dry methanol (25 ml) at 0°C] was heated to 60°C for 72 hours, when t.l.c. (n-BuOH:EtOH:water 5:1:4) showed no starting material (R_f 0.5) and the formation of one major product (R_f 0.3). The solvent was removed under reduced pressure to give crude methyl 2,6-anhydro-D-*glycero*-L-*manno*-heptonate **6**[21] (4.3 g) which was suspended in dry acetone (70 ml). Camphor sulfonic acid (500 mg, 2.15 mmol) and anhydrous copper sulfate (560 mg, 3.5 mmol) were added and the reaction mixture was stirred for 24 hours at room temperature. The reaction was quenched by addition of sodium bicarbonate (220 mg, 2.60 mmol), filtered through Celite, the solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (EtOAc) to give *the title compound* **7** (2.45 g, 60%) as a colourless oil. (Found: C, 49.98; H, 7.21%. $C_9H_{16}N_4O_4$ requires C, 50.38; H, 6.92%). $[\alpha]_D^{25}$ +32.4 (c, 1.0 in acetone). ν_{max} (film) 3428 cm^{-1} (br, OH), 1745 cm^{-1} (C=O). m/z (CI NH_3): 280 ($M+NH_4^+$, 14%), 263 (MH^+, 23%), 208 (100%). δ_H (500 MHz, $CDCl_3$): 1.36, 1.52 (2 s, 2 x 3 H, CMe_2), 2.60 (br s, 2 H, OH), 3.76 (d, J = 9.6 Hz, 1 H, H-2), 3.82 (dd, J = 4.1, 11.7 Hz, 1 H, H-7), 3.83 (s, 3 H, OMe), 3.89 - 3.93 (m, 2 H, H-3, H-6), 3.99 (dd, J = 7.1, 11.7 Hz, 1 H, H-7'), 4.14 (dd, J = 5.7, 6.8 Hz, 1 H, H-4), 4.22 (dd, J = 2.3, 5.7 Hz, 1 H, H-5). δ_C (50 MHz, $CDCl_3$): 26.1, 27.8 (2 q, $C\underline{Me}_2$), 52.7 (q, OMe), 62.4 (t, C-7), 70.7, 73.5, 76.8, 76.9, 78.6 (5 d, C-2, C-3, C-4, C-5, C-6), 110.5 (s, $\underline{C}Me_2$), 170.3 (s, C-1).

Methyl 2,6-anhydro-3,7-di-O-tert-butyldimethylsilyl-4,5-O-isopropylidene-D-glycero-L-manno-heptonate **8** Triethylamine (7.80 ml, 56.0 mmol) was added to a solution of the diol **7** (2.45 g, 9.36 mmol) in dry dichloromethane (25 ml), which was cooled to 0°C. *Tert*-butyldimethylsilyl trifluoromethanesulfonate (7.15 ml, 23.5 mmol) was added and the reaction mixture was stirred at 0°C for one hour, when t.l.c. (EtOAc / hexane 1:3) showed no starting material (R_f 0.0) and the formation of one product (R_f 0.8). The mixture was diluted with dichloromethane (30 ml), washed with 1 M aqueous HCl (20 ml) and pH-7 buffer (20 ml); the organic layer was dried ($MgSO_4$), filtered and the solvent removed under reduced pressure to give a residue which was purified by flash chromatography (diethyl ether / hexane 1:20) to afford *the title compound* **8** (4.54 g, 100%) as a white solid, m.p. 34-35°C. (Found: C, 56.48; H, 9.38%. $C_{23}H_{46}O_7Si_2$ requires C, 56.29; H, 9.45%). $[\alpha]_D^{22}$ +13.8 (c, 1.0 in $CHCl_3$). ν_{max} (film) 1757 cm^{-1} (C=O). m/z (CI NH_3): 508 ($M+NH_4^+$, 11%), 491 (MH^+, 31%), 94 (100%). δ_H (500 MHz, $CDCl_3$): 0.06, 0.07, 0.08, 0.15 (4 s, 4 x 3 H, SiMe), 0.87, 0.89 (2 s, 2 x 9 H, Si^tBu), 1.34, 1.52 (2 s, 2 x 3 H, CMe_2), 3.75 (s, 3 H, OMe), 3.78 (d, J = 7.8 Hz, 1 H, H-2), 3.80 - 3.90 (m, 3 H, H-6, H-7, H-7'), 4.00 (dd, J = 6.4, 7.8 Hz, 1 H, H-3), 4.03 (app t, J = 6.0 Hz, 1 H, H-4), 4.25 (dd, J = 1.6, 5.7 Hz, 1 H, H-5). δ_C (50 MHz, $CDCl_3$): -5.5, -4.4, -3.0 (3 q, SiMe), 17.8, 18.2 (2 s, $Si\underline{C}Me_3$), 25.6, 25.7, 26.1, 27.8 (4 q, $SiC\underline{Me}_3$, $C\underline{Me}_2$), 52.0 (q, OMe), 61.8 (t, C-7), 71.7, 72.7, 76.4, 78.8 (4 d, C-2, C-3, C-4, C-5, C-6), 109.5 (s, $\underline{C}Me_2$), 169.5 (s, C-1).

Methyl 2-azido-3,7-di-O-tert-butyldimethylsilyl-2-deoxy-4,5-O-isopropylidene-β-D-galacto-2-heptulopyranosonate ***9*** N-Bromosuccinimide (1.32 g, 7.38 mmol) and benzoyl peroxide (70 mg, 0.28 mmol) were added to a solution of the ester **8** (2.79 g, 5.68 mmol) in carbon tetrachloride (70 ml) and the mixture heated to 80°C for 45 minutes under an atmosphere of dry nitrogen. After cooling to room temperature, the reaction mixture was filtered and the solvent was removed under reduced pressure to give the unstable anomeric bromide, which was dissolved in dry DMF (10 ml) and treated with sodium azide (1.10 g, 17.0 mmol); the resulting mixture was stirred at room temperature for 18 hours in the dark. The solvent was then removed under reduced pressure and the residue dissolved in diethyl ether (50 ml). After washing with pH-7-buffer (20 ml) the organic layer was dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The resulting residue was purified by flash chromatography (diethyl ether / hexane 1:20) to give *the title compound* ***9*** (1.96 g, 65%) as a white solid, m.p. 69-71°C. (Found: C, 52.27; H, 8.90; N, 8.01%. $C_{23}H_{45}N_3O_7Si_2$ requires C, 51.95; H, 8.53; N, 7.90%). $[\alpha]_D^{22}$ +3.6 (c, 1.0 in $CHCl_3$). ν_{max} (film) 2128 cm^{-1} (N_3), 1746 cm^{-1} (C=O). m/z (CI NH_3): 549 ($M+NH_4^+$, 5%), 504 (MH^+ - N_2, 11%), 489 (MH^+ - HN_3, 16%), 90 (100%). δ_H (500 MHz, $CDCl_3$): 0.09 (s, 3 H, SiMe), 0.10 (s, 6 H, SiMe), 0.14 (s, 3 H, SiMe), 0.86, 0.91 (2 s, 2 x 9 H, Si^{t}Bu), 1.35, 1.53 (2 s, 2 x 3 H, CMe_2), 3.80 (s, 3 H, OMe), 3.87 (dd, J = 6.2, 10.1 Hz, 1 H, H-7), 3.88 (d, J = 4.7 Hz, 1 H, H-3), 3.90 (dd, J = 7.0, 10.1 Hz, 1 H, H-7'), 4.25 (app dt, J = 2.1, 6.5 Hz, 1 H, H-6), 4.32 (dd, J = 2.1, 6.7 Hz, 1 H, H-5), 4.37 (dd, J = 4.7, 6.7 Hz, 1 H, H-4). δ_C (50 MHz, $CDCl_3$): -5.5, -5.4, -5.3, -4.5 (4 q, SiMe), 17.8, 18.2 (2 s, $SiCMe_3$), 25.2, 25.5, 26.7, 28.8 (4 q, $SiC\underline{Me}_3$, $C\underline{Me}_2$), 52.6 (q, OMe), 61.8 (t, C-7), 71.5, 72.1, 72.8, 75.6 (4 d, C-3, C-4, C-5, C-6), 91.0 (s, C-2), 109.4 (s, $\underline{C}Me_2$), 167.3 (s, C-1).

Methyl 2-amino-3,7-di-O-tert-butyldimethylsilyl-2-deoxy-4,5-O-isopropylidene-α-D-galacto-2-heptulopyranosonate ***10*** Hydrogen was preabsorbed on palladium on carbon (10 mg) in methanol (2 ml). A solution of azide **9** (50 mg, 0.094 mmol) in methanol (2 ml) was added and the mixture was stirred at room temperature for 2.5 hours under an atmosphere of hydrogen, when t.l.c. (EtOAc / hexane 1:4) showed no starting material (R_f 0.7) and the formation of two products (R_f 0.6 and 0.2). The mixture was filtered through Celite, the solvent removed under reduced pressure and the resulting residue purified by flash chromatography (EtOAc / hexane 1:4) to give *the title compound* ***10α*** (R_f 0.6, 22 mg, 46%) as a colourless oil. (Found: C, 54.95; H, 9.22; N, 3.01%. $C_{23}H_{47}NO_7Si_2$ requires C, 54.62; H, 9.37; N, 2.77%). $[\alpha]_D^{22}$ +32.5 (c, 1.0 in $CHCl_3$). ν_{max} (film) 3400 cm^{-1} (br, NH_2), 1751 cm^{-1} (C=O). m/z (CI NH_3): 506 (MH^+, 100%). δ_H (500 MHz, $CDCl_3$): 0.04, 0.05, 0.06, 0.16 (4 s, 4 x 3 H, SiMe), 0.84, 0.89 (2 s, 2 x 9 H, Si^{t}Bu), 1.33, 1.54 (2 s, 2 x 3 H, CMe_2), 2.05 (br s, 2 H, NH_2), 3.75 (dd, J = 5.9, 9.7 Hz, 1 H, H-7), 3.76 (s, 3 H, OMe), 3.91 (dd, J = 8.0, 9.7 Hz, 1 H, H-7'), 4.01 (dd, J = 5.5, 7.1 Hz, 1 H, H-4), 4.13 (d, J = 7.1 Hz, 1 H, H-3), 4.23 (dd, J = 2.5, 5.5 Hz, 1 H, H-5), 4.49 (ddd, J = 2.5, 5.5, 8.0 Hz, 1 H, H-6). δ_C (50 MHz, $CDCl_3$): -5.8, -5.5, -5.4, -4.2 (4 q, SiMe), 17.8, 18.2 (2 s, $SiCMe_3$), 25.6, 25.8, 26.3, 28.2 (4 q, $SiC\underline{Me}_3$, $C\underline{Me}_2$), 52.8 (q, OMe), 61.9 (t, C-7), 68.5, 72.4, 72.9, 77.7 (4 d, C-3, C-4, C-5, C-6), 87.6 (s, C-2), 108.6 (s, $\underline{C}Me_2$), 171.8 (s, C-1).

A further 20 mg (42%) of a mixture of anomers was isolated. The other epimer **10β** could not be isolated and characterised because it underwent fast epimerisation. The crude mixture of anomers was used for all following experiments.

Methyl 3,7-di-O-tert-butyldimethylsilyl-2-deoxy-4,5-O-isopropylidene-2-ureido-β-D-galacto-2-heptulopyranosonate ***11*** Hydrogen was preabsorbed on palladium on carbon (80 mg) in methanol (5 ml). A solution of azide **9** (405 mg, 0.76 mmol) in methanol (7 ml) was added and the mixture was stirred at room temperature for 2.5 hours under an atmosphere of hydrogen, when t.l.c. (EtOAc / hexane 1:4) showed no starting material

(R_f 0.7) and the formation of two products (R_f 0.6 and 0.2). The mixture was filtered through Celite and the solvent was removed under reduced pressure. The residue was dissolved in acetic acid (5 ml), potassium cyanate (309 mg, 3.81 mmol) was added and the mixture was stirred at room temperature for 1.5 h, when t.l.c. (EtOAc / hexane 1:1) showed no starting material and the formation of one major product (R_f 0.2). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (EtOAc / hexane 1:3→1:2→1:1→EtOAc) to give *the urea* ***11*** (252 mg, 60%) as a white solid, m.p. 149-155°C (phase change), 220-223°C. (Found: C, 52.56; H, 9.13; N, 4.96%. $C_{24}H_{48}N_2O_8Si_2$ requires C, 52.52; H, 8.82; N, 5.10%). $[\alpha]_D^{22}$ -46.9 (c, 1.0 in MeOH). ν_{max} (film) 3461, 3318 cm^{-1} (br, NH), 1766, 1664 cm^{-1} (C=O). m/z (CI NH_3): 566 ($M+NH_4^+$, 54%), 549 (MH^+, 100%). δ_H (500 MHz, MeCN): 0.08 (s, 3 H, SiMe), 0.09 (s, 6 H, SiMe), 0.15 (s, 3 H, SiMe), 0.86, 0.90 (2 s, 2 x 9 H, Si^{t}Bu), 1.36, 1.48 (2 s, 2 x 3 H, CMe_2), 3.65 (s, 3 H, OMe), 3.69 (dd, J = 5.6, 9.7 Hz, 1 H, H-7), 3.72 (dd, J = 8.4, 9.7 Hz, 1 H, H-7'), 4.20 (ddd, J = 1.7, 5.6, 8.4 Hz, 1 H, H-6), 4.24 (d, J = 3.4 Hz, 1 H, H-3), 4.37 (dd, J = 1.7, 7.8 Hz, 1 H, H-5), 4.48 (dd, J = 3.4, 7.8 Hz, 1 H, H-4), 4.91 (s, 2 H, NH_2), 6.06 (s, 1 H, NH). δ_C (50 MHz, MeOD): -5.2, -5.1, -4.4 (3 q, SiMe), 18.7, 19.2 (2 s, $SiCMe_3$), 25.4, 26.2, 26.4 (3 q, $SiCMe_3$, CMe_2), 53.0 (q, OMe), 62.1 (t, C-7), 71.4, 72.0, 73.3, 75.8 (4 d, C-3, C-4, C-5, C-6), 87.4 (s, C-2), 111.8 (s, CMe_2), 159.8 (s, urea), 171.1 (s, C-1).

(2R,3R,4S,5R,6S)-5-O-tert-Butyldimethylsilyl-2-tert-butyldimethylsilyloxymethyl-3,4-O-isopropylidene-7,9-diaza-oxaspiro-[4,5]decane-3,4,5-triol-8,10-dione ***12*** Potasium *tert*-butoxide (71 mg, 0.63 mmol) was added to a solution of urea **11** (290 mg, 0.53 mmol) in dry tetrahydrofuran (5 ml) and the mixture was stirred for 20 minutes at room temperature under an atmosphere of nitrogen, when t.l.c. (EtOAc / hexane 1:1) showed no starting material (R_f 0.2) and the formation of one product (R_f 0.8). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (EtOAc / hexane 1:4) to give *the title compound* ***12*** (239 mg, 88%) as a white solid, m.p. 223-224°C. (Found: C, 53.69; H, 8.36; N, 5.18%. $C_{23}H_{44}N_2O_7Si_2$ requires C, 53.46; H, 8.58; N, 5.42%). $[\alpha]_D^{22}$ + 35.3 (c, 1.0 in $CHCl_3$). ν_{max} (film) 3305 cm^{-1} (br, NH), 1780, 1734 cm^{-1} (C=O). m/z (CI NH_3): 534 ($M+NH_4^+$, 93%), 517 (MH^+, 100%). δ_H (500 MHz, $CDCl_3$): 0.07 (s, 6 H, SiMe), 0.09, 0.15 (2 s, 2 x 3 H, SiMe), 0.86, 0.89 (2 s, 2 x 9 H, Si^{t}Bu), 1.36, 1.53 (2 s, 2 x 3 H, CMe_2), 3.71 (d, J = 6.9 Hz, 1 H, H-3), 3.77 (dd, J = 6.1, 9.9 Hz, 1 H, H-7), 3.84 (dd, J = 7.2, 9.9 Hz, 1 H, H-7'), 4.33 (dd, J = 2.4, 5.4 Hz, 1 H, H-5), 4.45 (dd, J = 5.4, 6.9 Hz, 1 H, H-4), 4.67 (app dt, J = 2.4, 6.5 Hz, 1 H, H-6), 5.88 (s, 1 H, NH), 8.14 (s, 1 H, NH). δ_C (50 MHz, $CDCl_3$): -5.5, -5.4, -5.2, -4.4 (4 q, SiMe), 17.8, 18.2 (2 s, $SiCMe_3$), 25.6, 25.7, 26.3, 28.3 (4 q, $SiCMe_3$, CMe_2), 61.8 (t, C-7), 71.4, 72.8, 73.5, 77.6 (4 d, C-3, C-4, C-5, C-6), 88.3 (s, C-2), 109.2 (s, CMe_2), 156.5, 170.7 (2 s, C=O).

(2R, 3R, 4S, 5R, 6S) 3,4,5-Trihydroxy-2-hydroxymethyl-7,9-diaza-oxaspiro-[4,5]decane-8,10-dione ***4*** The protected hydantoin **12** (165 mg, 0.32 mmol) was dissolved in dioxan / water / trifluoroacetic acid 1:1:1 (6 ml) and stirred at room temperature for 94 hours, when t.l.c. showed no starting material (R_f 0.8 EtOAc / hexane 1:1) and the formation of one major product (R_f 0.2, EtOAc / MeOH 9:1). The solvent was removed under reduced pressure and the residue was purified by recrystallisation (EtOH) to give *the title compound* ***4*** (68 mg, 86%) as a white solid, m.p. 238-240°C. (Found: C, 38.45; H, 5.08; N, 10.91%. $C_8H_{12}N_2O_7$ requires C, 38.72; H, 4.87; N, 11.29%). $[\alpha]_D^{22}$ +84.4 (c, 1.0 in MeOH). ν_{max} (KBr) 3385 cm^{-1} (br, NH, OH), 1782, 1733, 1677 cm^{-1} (C=O). m/z (electrospray): 271 ($M+Na^+$, 93%), 266 ($M+NH_4^+$, 100%), 259 (MH^+, 7%). δ_H (500 MHz, D_2O): 3.69 (dd, J = 7.2, 11.8 Hz, 1 H, H-7), 3.71 (dd, J = 4.8, 11.8 Hz, 1 H, H-7'), 3.89 (d, J = 10.2 Hz, 1 H, H-3), 4.03 (d, J = 3.3 Hz, 1 H, H-5), 4.27 (dd, J = 3.3, 10.2 Hz, 1 H,

H-4), 4.48 - 4.51 (m, 1 H, H-6). δ_C (125 MHz, D_2O): 61.7 (t, C-7), 69.0, 69.7, 70.1, 75.1 (4 d, C-3, C-4, C-5, C-6), 89.1 (s, C-2), 158.9, 173.7 (2 s, C=O).

Methyl 2-azido-2-deoxy-β-D-galacto-2-heptulopyranosonate ***16*** Ester **9** (42 mg, 0.079 mmol) was dissolved in methanol / trifluoroacetic acid 1:1 (2 ml) and stirred at room temperature for 96 hours, when t.l.c. showed no starting material (R_f 0.9, EtOAc / hexane 1:4) and the formation of one major product (R_f 0.1, EtOAc). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (EtOAc / methanol 19:1) to give *the title compound* ***16*** (16 mg, 77%) as a colourless gum. (Found: C, 36.29; H, 5.20; N, 15.68%. $C_8H_{13}N_3O_7$ requires C, 36.51; H, 4.98; N, 15.96%). $[\alpha]_D^{24}$ + 75.7 (c, 1.0 in MeOH). ν_{max} (film) 3366 cm^{-1} (br, OH), 2132 cm^{-1} (N_3), 1739, 1681 cm^{-1} (C=O). m/z (CI NH_3): 281 ($M+NH_4^+$, 24%), 238 ($M+NH_4^+$ - HN_3, 21%), 118 (100%). δ_H (500 MHz, MeOD): 3.71 (d, J = 9.9 Hz, 1 H, H-3), 3.73 (d, J = 5.7 Hz, 2 H, H-7, H-7'), 3.82 (s, 3 H, OMe), 3.94 (dd, J = 0.9, 3.3 Hz, 1 H, H-5), 4.05 (dd, J = 3.3, 9.9 Hz, 1 H, H-4), 4.08 (app dt, J = 0.9, 5.7 Hz, 1 H, H-6). δ_C (125 MHz, MeOD): 62.7 (t, C-7), 70.0, 71.9, 73.1, 78.1 (4 d, C-3, C-4, C-5, C-6), 94.4 (s, C-2), 169.0 (s, C=O).

2-Azido-3,7-di-O-tert-butyldimethylsilyl-2-deoxy-4,5-O-isopropylidene-β-D-galacto-2-heptulopyranosonic hydrazide ***13*** Hydrazine hydrate (5 ml) was added to a solution of ester **9** (506 mg, 0.95 mmol) in methanol (5 ml) and dioxane (5 ml). The mixture was stirred for 8 hours at room temperature, when t.l.c. (EtOAc / hexane 1:4) showed no starting material (R_f 0.7) and the formation of one product (R_f 0.2). The solvent was removed under reduced pressure and the resulting residue was dissolved in EtOAc (50 ml). The solution was washed with water (40 ml), dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The resulting residue was purified by flash chromatography (EtOAc / hexane 1:4) to give *the hydrazide* ***13*** (409 mg, 81%) as a white solid, m.p. 94-96°C. (Found: C, 49.46; H, 8.93; N, 12.89%. $C_{22}H_{45}N_5O_6Si_2$ requires C, 49.69; H, 8.53; N, 13.17%). $[\alpha]_D^{22}$ -27.3 (c, 1.0 in $CHCl_3$). ν_{max} (film) 3333 cm^{-1} (br, NH), 2123 cm^{-1} (N_3), 1691 cm^{-1} (C=O). m/z (electrospray): 554 ($M+Na^+$, 9%), 532 (MH^+, 100%), 489 (MH^+ - HN_3, 41%). δ_H (500 MHz, $CDCl_3$): 0.12 (s, 3 H, SiMe), 0.15 (s, 9 H, SiMe), 0.85, 0.93 (2 s, 2 x 9 H, Si^{t}Bu), 1.34, 1.54 (2 s, 2 x 3 H, CMe_2), 3.48 (br s, 2 H, NH_2), 3.83 (dd, J = 4.5, 10.6 Hz, 1 H, H-7), 3.88 (d, J = 7.7, 10.6, 1 H, H-7'), 4.18 (d, J = 3.5 Hz, 1 H, H-3), 4.23 (ddd, J = 1.8, 4.5, 7.7 Hz, 1 H, H-6), 4.28 (dd, J = 1.8, 7.5 Hz, 1 H, H-5), 4.36 (dd, J = 3.5, 7.5 Hz, 1 H, H-4), 8.24 (br s, 1 H, NH). δ_C (50 MHz, $CDCl_3$): -5.6, -5.4, -4.8 (3 q, SiMe), 17.7, 18.2 (2 s, Si<u>C</u>Me_3), 24.3, 25.5, 25.7 (3 q, SiC<u>Me</u>$_3$, C<u>Me</u>$_2$), 62.5 (t, C-7), 69.4, 71.2, 72.3, 74.4 (4 d, C-3, C-4, C-5, C-6), 89.6 (s, C-2), 110.1 (s, <u>C</u>Me_2), 167.2 (s, C-1).

2-Azido-2-deoxy-β-D-galacto-2-heptulopyranosonic hydrazide ***17*** Hydrazide **13** (30 mg, 0.056 mmol) was dissolved in methanol / trifluoroacetic acid 1:1 (2 ml) and stirred at room temperature for 68 hours, when t.l.c. showed no starting material (R_f 0.2 EtOAc / hexane 1:4) and the formation of one major product (R_f 0.2, EtOAc / MeOH 4:1). The solvent was removed under reduced pressure and the residue was coevaporated with methanol to give *the hydrazide* ***17*** (15 mg, 100%) as a colourless gum. (Found: C, 31.68; H, 5.21; N, 26.39%. $C_7H_{13}N_5O_6$ requires C, 31.94; H, 4.98; N, 26.61%). $[\alpha]_D^{24}$ + 70.0 (c, 1.0 in MeOH). ν_{max} (film) 3348 cm^{-1} (br, NH, OH), 2130 cm^{-1} (N_3), 1676 cm^{-1} (C=O). m/z (electrospray): 264 (MH^+, 100%), 221 (MH^+ - HN_3, 63%). δ_H (500 MHz, D_2O): 3.75 (dd, J = 4.4, 11.9 Hz, 1 H, H-7), 3.80 (dd, J = 7.5, 11.9 Hz, 1 H, H-7'), 3.94 (d, J = 10.3 Hz, 1 H, H-3), 4.03 (br d, J = 3.3 Hz, 1 H, H-5), 4.10 (dd, J = 3.3, 10.3 Hz, 1 H, H-4), 4.17 (ddd, J = 0.7, 4.4, 7.5 Hz, 1 H, H-6). δ_C (125 MHz, MeOD): 62.6 (t, C-7), 70.0, 72.1, 72.6, 78.4 (4 d, C-3, C-4, C-5, C-6), 92.2 (s, C-2), 168.2 (s, C=O).

2-(1-Azido-2,6-di-O-tert-butyldimethylsilyl-3,4-O-isopropylidene-α-D-galactopyranosyl)-4,5-dihydro-1,3,4-oxadiazol-5-one ***14*** A solution of hydrazide **13** (33 mg, 0.62 mmol) in tetrahydrofuran (1 ml) was added dropwise to a solution of carbonyldiimidazole (12 mg, 0.075 mmol) in tetrahydrofuran (1 ml) and the mixture was stirred for one hour under an atmosphere of nitrogen, when t.l.c. (EtOAc / hexane 1:4) showed no starting material (R_f 0.4) and the formation of one product (R_f 0.5). The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (EtOAc / hexane 1:4) to give *the title compound* ***14*** (33 mg, 95%) as a colourless oil. (Found: C, 49.31; H, 7.93; N, 12.35%. $C_{22}H_{45}N_5O_6Si_2$ requires C, 49.53; H, 7.77; N, 12.56%). $[\alpha]_D^{25}$ +31.7 (c, 1.0 in $CHCl_3$). ν_{max} (film) 3271 cm^{-1} (br, NH), 2126 cm^{-1} (N_3), 1822, 1785 cm^{-1} (C=O). m/z (DCI NH_3): 575 ($M+NH_4^+$, 6%), 515 (MH^+ - HN_3, 92%), 73 (100%). δ_H (500 MHz, d-6 benzene): 0.05, 0.07, 0.09, 0.10 (4 s, 4 x 3 H, SiMe), 0.90, 0.94 (2 s, 2 x 9 H, Si^{t}Bu), 1.16, 1.44 (2 s, 2 x 3 H, CMe_2), 3.96 (d, J = 6.4 Hz, 2 H, H-7, H-7'), 4.01 (d, J = 5.6 Hz, 1 H, H-3), 4.10 (dd, J = 2.2, 6.4 Hz, 1 H, H-5), 4.23 (dt, J = 2.2, 6.4 Hz, 1 H, H-6), 4.35 (app t, J = 6.0 Hz, 1 H, H-4), 7.55 (br s, 1 H, NH). δ_C (50 MHz, $CDCl_3$): -5.5, -5.4, -5.3, -4.6 (4 q, SiMe), 17.7, 18.3 (2 s, Si$\underline{C}$Me$_3$), 25.0, 25.4, 25.8, 26.6 (4 q, SiC$\underline{Me}_3$, C$\underline{Me}_2$), 61.7 (t, C-7), 71.4, 72.1, 73.0, 75.2 (4 d, C-3, C-4, C-5, C-6), 88.5 (s, C-2), 109.9 (s, $\underline{C}Me_2$), 154.0, 154.2 (2 s, C=O, C=N).

2-(1-Azido-α-D-galactopyranosyl)-4,5-dihydro-1,3,4-oxadiazol-5-one ***15*** Oxadiazolidinone **14** (30 mg, 0.054 mmol) was dissolved in dioxan / water / trifluoroacetic acid 1:1:1 (3 ml) and stirred at room temperature for 40 hours, when t.l.c. showed no starting material (R_f 0.5 EtOAc / hexane 1:4) and the formation of one major product (R_f 0.2, EtOAc / MeOH 19:1). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (EtOAc / MeOH 97:3) to give *the title compound* ***15*** (15 mg, 100%) as a colourless gum. (Found: C, 33.01; H, 4.03; N, 23.98%. $C_8H_{11}N_5O_7$ requires C, 33.22; H, 3.83; N, 24.22%). $[\alpha]_D^{26}$ + 98.2 (c, 1.0 in MeOH). ν_{max} (film) 3320 cm^{-1} (br, NH, OH), 2129 cm^{-1} (N_3), 1815 (shoulder), 1779 cm^{-1} (C=O). δ_H (500 MHz, MeOD): 3.74 (dd, J = 5.4, 11.5 Hz, 1 H, H-7), 3.77 (dd, J = 6.2, 11.5 Hz, 1 H, H-7'), 3.91 (d, J = 10.2 Hz, 1 H, H-3), 3.92 - 3.96 (m, 1 H, H-6), 3.97 (dd, J = 0.8, 3.3 Hz, 1 H, H-5), 4.04 (dd, J = 3.3, 10.2 Hz, 1 H, H-4). δ_C (125 MHz, MeOD): 62.5 (t, C-7), 70.0, 71.7, 73.3, 78.0 (4 d, C-3, C-4, C-5, C-6), 91.1 (s, C-2), 154.3, 156.1 (2 s, C=O, C=N).

2-Amino-3,7-di-O-tert-butyldimethylsilyl-2-deoxy-4,5-O-isopropylidene-D-galacto-2-heptulopyranosonic hydrazide ***18*** Hydrogen was preabsorbed on palladium on carbon (25 mg) in methanol (3 ml). A solution of azide **13** (56 mg, 0.11 mmol) in methanol (3 ml) was added and the mixture was stirred at room temperature for two hours under an atmosphere of hydrogen, when t.l.c. (EtOAc / hexane 1:2) showed no starting material (R_f 0.7) and the formation of one major product (R_f 0.1). The mixture was filtered through Celite and the solvent was removed under reduced pressure. The resulting residue was purified by flash chromatography (EtOAc / hexane 3:1) to give *the amine* ***18*** (435 mg, 68%) as a white solid, m.p. 156°C. (Found: C, 52.42; H, 9.52; N, 8.09%. $C_{22}H_{47}N_3O_6Si_2$ requires C, 52.24; H, 9.37; N, 8.31%). $[\alpha]_D^{22}$ -45.6 (c, 1.0 in $CHCl_3$). ν_{max} (film) 3375, 3332, 3231 cm^{-1} (br, NH), 1678 cm^{-1} (C=O). m/z (electrospray): 506 (MH^+, 100%), 489 (95%). δ_H (200 MHz, $CDCl_3$): 0.11, 0.12 (2 s, 2 x 6 H, SiMe), 0.83, 0.92 (2 s, 2 x 9 H, Si^{t}Bu), 1.32, 1.51 (2 s, 2 x 3 H, CMe_2), 2.31 (br s, 2 H, NH_2), 3.60-3.85 (m, 4 H, HNN$\underline{H}_2$, H-7, H-7'), 4.15-4.25 (m, 2 H, H-5, H-6), 4.31 (d, J = 3.6 Hz, 1 H, H-3), 4.43 (dd, J = 3.6, 7.5 Hz, 1 H, H-4), 8.48 (s, 1 H, NH). δ_C (50 MHz, $CDCl_3$): -5.5, -5.3, -4.7 (3 q, SiMe), 17.7, 18.4 (2 s, Si$\underline{C}$Me$_3$), 24.5, 25.5, 25.9, 26.0 (4 q, SiC$\underline{Me}_3$, C$\underline{Me}_2$), 63.2 (t, C-7), 70.7, 72.4, 72.8, 75.2 (4 d, C-3, C-4, C-5, C-6), 89.4 (s, C-2), 110.7 (s, $\underline{C}Me_2$), 170.6 (s, C-1).

2-(1-Amino-2,6-di-O-tert-butyldimethylsilyl-3,4-O-isopropylidene-α-D-galactopyranosyl)-4,5-dihydro-1,3,4-oxadiazol-5-one ***19*** *Method 1 (from hydrazide* ***13****)*: Hydrazide **13** (29 mg, 0.055 mmol) in dry tetrahydrofuran (1 ml) was added dropwise to a solution of carbonyldiimidazole (11 mg, 0.068 mmol) in dry tetrahydrofuran (1 ml) and the mixture was stirred for one hour under an atmosphere of nitrogen, when t.l.c. (EtOAc / hexane 1:4) showed no starting material (R_f 0.4) and the formation of one product (R_f 0.5). The solvent was removed under reduced pressure and the resulting residue was dissolved in ethyl acetate (1 ml). This solution was added to a suspension of reduced palladium black in ethyl acetate (2 ml) and the mixture was stirred for 1.5 hours at room temperature under an atmosphere of hydrogen, when t.l.c. (EtOAc / hexane 1:4) showed no **14** (R_f 0.5) and the formation of one major product (R_f 0.1), which interconverts on silica to another product (R_f 0.4). The mixture was filtered through Celite, the solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (EtOAc / hexane 1:4) to give *the hydrazide* ***19*** (25 mg, 85%) as a white solid, mp 171-172°C. (Found: C, 51.92; H, 8.70; N, 7.65%. $C_{23}H_{45}N_3O_7Si_2$ requires C, 51.95; H, 8.53; N, 7.90%). $[\alpha]_D^{22}$ +31.5 (c, 1.0 in $CHCl_3$). ν_{max} (film) 3404, 3268 cm^{-1} (br, NH), 1821, 1785 cm^{-1} (C=O). m/z (electrospray): 532 (MH^+, 100%), 515 (MH^+ - NH_3, 60%). δ_H (500 MHz, $CDCl_3$): 0.01, 0.07, 0.08, 0.16 (4 s, 4 x 3 H, SiMe), 0.81, 0.90 (2 s, 2 x 9 H, Si^{t}Bu), 1.34, 1.54 (2 s, 2 x 3 H, CMe_2), 2.13 (br s, 2 H, NH_2), 3.80 (dd, J = 6.3, 10.0 Hz, 1 H, H-7), 3.92 (dd, J = 7.2, 10.0 Hz, 1 H, H-7'), 3.99 (d, J = 7.0 Hz, 1 H, H-3), 4.10 (dd, J = 5.5, 7.0 Hz, 1 H, H-4), 4.25 (dd, J = 2.6, 5.5 Hz, 1 H, H-5), 4.54 (app dt, J = 2.6, 6.7 Hz, 1 H, H-6), 8.64 (br s, 1 H, NH). δ_C (125 MHz, $CDCl_3$): -5.7, -5.4, -5.3, -4.2 (4 q, SiMe), 17.8, 18.4 (2 s, Si$\underline{C}$Me$_3$), 25.6, 25.9, 26.3, 28.2 (4 q, SiC$\underline{Me}_3$, C$\underline{Me}_2$), 64.4 (t, C-7), 69.0, 72.4, 73.0, 77.6 (4 d, C-3, C-4, C-5, C-6), 84.3 (s, C-2), 109.1 (s, $\underline{C}$Me$_2$), 154.7, 158.0 (2 s, C=O, C=N).

Method 2 (from hydrazide ***18****)*: Hydrazide **18** (32 mg, 0.063 mmol) was dissolved in dry tetrahydrofuran (5 ml). Carbonyldiimidazole (11 mg, 0.068 mmol) was added and the mixture was stirred at room temperature for 1.5 hours, when t.l.c. (EtOAc / hexane 1:2) showed no starting material (R_f 0.1) and the formation of one major product (R_f 0.8). The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (EtOAc / hexane 1:4) to give *the title compound* (28 mg, 83%) as a white solid, identical to that reported above.

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