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Synthesis of 2-Acetamido-1,2,4-trideoxy-1,4-imino-D-galactitol and -D-glucitol for Evaluation as Glycosidase Inhibitors

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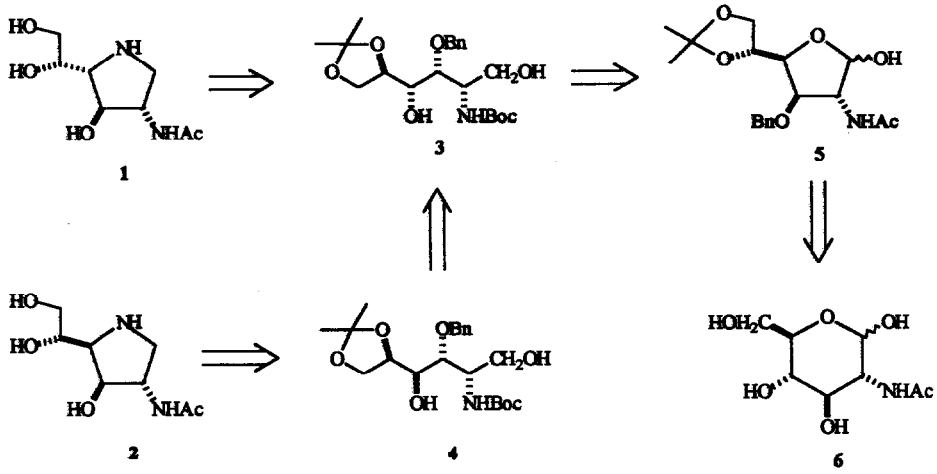
Abstract: The title compounds, galacto-**1** and gluco-**2**, were synthesised from *N*-acetyl-D-glucosamine via a common 1,4-diol intermediate that underwent transformations involving either a single or double inversion of stereochemistry at C-4, respectively. In the double inversion sequence, the first inversion involved participation by a *t*-butyloxycarbonylamino group in an intramolecular sulfonate displacement reaction with the formation of a novel cyclic carbamate.

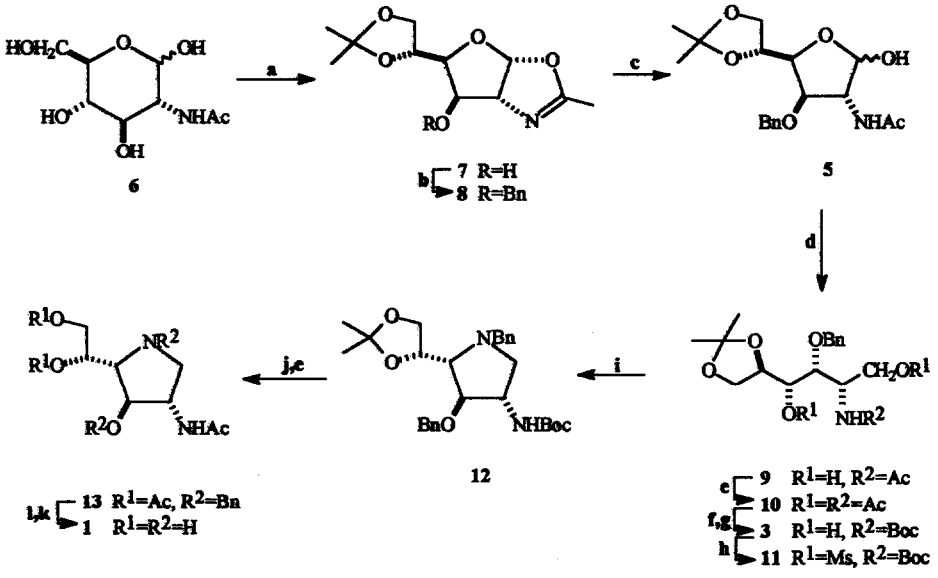
The processing of carbohydrates is essential for the normal growth and development of all organisms. Inhibitors of glycosidase enzymes, those enzymes responsible for the hydrolysis of glycosidic linkages, are important for the investigation, and potentially the treatment, of several diseases. The aza sugar class of glycosidase inhibitors, where the ring oxygen of a monosaccharide has been replaced by nitrogen, has received wide attention.[1,2] *N*-Acetyl-D-glucosamine and -D-galactosamine residues occur widely in many of the glycoconjugates which play important roles in a large number of biological processes. Hexosaminidase enzymes have therefore become targets for inhibition studies. As a general rule the aza sugar and the parent monosaccharide should be structurally similar for inhibition of the corresponding glycosidase. Therefore aza sugars bearing a 2-acetamido group are potential inhibitors of hexosaminidases and several have been prepared; so far, however, the focus has been on 1,5- rather than 1,4-imino-hexitols.[3-11] As part of our general interest in glycosidase inhibitors we wished to synthesise 2-acetamido-1,2,4-trideoxy-1,4-imino-D-galactitol[12,13] and -D-glucitol[14] for evaluation as hexosaminidase inhibitors.

We chose to prepare the title compounds using Fleet's methodology for the formation of imino-alditols[15] whereby the pyrrolidine ring is formed from a 1,5-diol by dimesylation then reaction with benzylamine in a double nucleophilic displacement reaction. As depicted in Scheme 1 our planned routes to both 1,4-imino-hexitols **1** and **2** incorporate diol **3** as a common intermediate. Diol **3** is a direct precursor of the galactitol **1** whereas inversion of stereochemistry at C4 prior to cyclisation gives the glucitol analogue **2**. The requisite diol **3** maybe obtained from *N*-acetyl-D-glucosamine **6** via the reduction of the glucofuranose derivative **5**.

The 5 step transformation of *N*-acetyl-D-glucosamine **6** to triacetate **10** (Scheme 2) could be conveniently carried out without purification of intermediates with an overall yield of 17%. Thus Lewis acid catalysed acetonation gave the oxazoline **7**[16] which was followed by protection of the C3 hydroxyl as its benzyl ether **8**. Treatment of **8** with aqueous acetic acid released the anomeric hydroxy group from the oxazoline ring to give **5** as a 4:1 mixture of anomers. Reduction of the mixture to diol **9** with sodium



Scheme 1



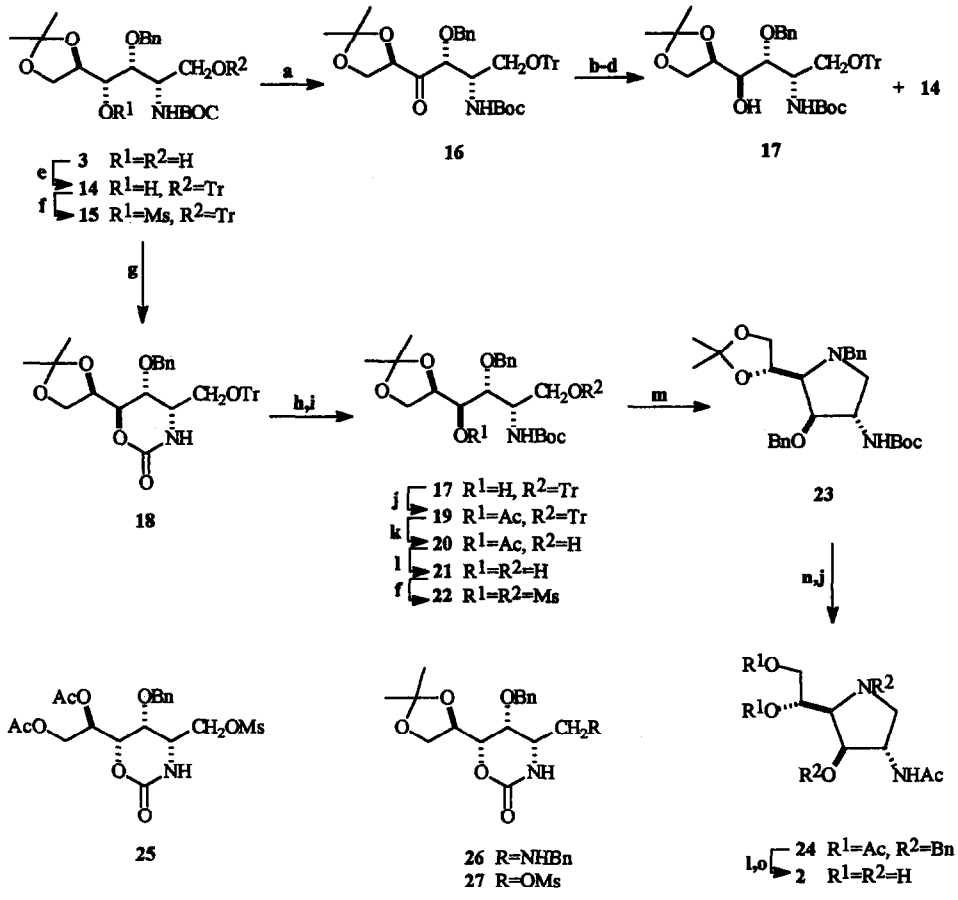
Scheme 2: a) $FeCl_3$, Me_2CO; b) NaH, BnBr, DMF; c) aq. HOAc, MeOH; d) $NaBH_4$, MeOH; e) Ac_2O, py; f) 1M NaOH, MeOH; g) $(Boc)_2O$, $KHCO_3$, dioxane, H_2O; h) MsCl, DMAP, py; i) $BnNH_2$; j) 1M HCl, MeOH; k) NaOMe, MeOH; l) H_2, 10% Pd-C, HCl, EtOH.

borohydride gave a crude product which was acetylated in acetic anhydride and pyridine to the diacetate **10** in order to facilitate purification. We had anticipated the preparation of a dimesylate from diol **9** would be facile, but under standard conditions (methanesulfonyl chloride/pyridine) this reaction gave a complex mixture. We reasoned its failure was due to participation of the acetamido function and oxazoline ring formation. The acetamide of **10** was therefore converted to the less nucleophilic *t*-butyl carbamate by base hydrolysis followed by reaction with di-*t*-butyl dicarbonate to give the diol **3** (87% yield). Mesylation now proceeded smoothly to afford dimesylate **11** (82%). The key cyclisation reaction occurred in benzylamine at 70° overnight to give the protected 1,4-imino-D-galactitol **12** (66%). Acid catalysed hydrolysis of the acetonide and carbamate moieties was followed by peracetylation to give the triacetate **13** (96%). De-*O*-acetylation and hydrogenolytic removal of the benzyl groups over palladium in ethanol containing dilute hydrochloric acid provided 2-acetamido-1,2,4-trideoxy-1,4-imino-D-galactitol **1** (90%) as its hydrochloride salt.

Encouraged by the successful synthesis of the galactitol analogue **1** we returned to diol **3** to investigate methods for the inversion of stereochemistry at C4. Implementation of the chemistry described above would then give the glucitol analogue **2**. Firstly we focused on the stereoselective reduction of a ketone as a method to effect the desired inversion, however these attempts failed to give a satisfactory yield of the required epimer. The primary alcohol of diol **3** was protected as its trityl ether to give alcohol **14** (85%) (Scheme 3) then pyridinium dichromate oxidation afforded ketone **16** in high yield (91%). Sodium borohydride reduction gave a mixture of alcohols **17** and **14** with the approximate ratio 70:30 in favour of the desired epimer **17** as determined by ^{1}H and ^{13}C NMR but these epimers were difficult to separate chromatographically. Reduction with L-Selectride gave only alcohol **14** and when this reaction was carried out in the presence of zinc chloride a 75:25 mixture favouring alcohol **14** was produced.

At the same time we were investigating the nucleophilic displacement of a leaving group at C4 of alcohol **14**. Thus mesylation gave **15** (85%) which was then treated with tetrabutylammonium nitrite in dimethylformamide. No reaction was observed at 60° however, after several hours at 120°, a polar product was isolated which was not the expected alcohol **17**. ^{1}H and ^{13}C NMR spectra showed the absence of *t*-butyl and mesyl signals and the appearance of a high field carbonyl signal (δ_C 152.8) consistent with the cyclic carbamate **18**. We subsequently found that this intramolecular nucleophilic substitution did not require the presence of tetrabutylammonium nitrite but occurred simply upon heating. Furthermore an improved yield (94%) resulted when triethylamine was added to the reaction mixture presumably by eliminating any decomposition due to acidic byproducts. Having achieved inversion of configuration at C4 the cyclic carbamate was hydrolysed with aqueous sodium hydroxide in dioxane and the resulting amine reprotected as its *t*-butyl carbamate **17** (95%).

We now required removal of the trityl protecting group. Under a variety of acidic reaction conditions,[17] however, both alcohol **17** and acetate **19** gave either no reaction or competitive removal of the acetonide group. A satisfactory yield for the formation of alcohol **20** (67%) was eventually obtained by employing the standard conditions for acetonide formation from a diol (*p*-toluenesulfonic acid, dimethoxypropane, acetone) thus preserving the acetonide moiety while removing the trityl group. Deacetylation to **21** (91% yield) was followed by mesylation to give dimesylate **22** (83%), precursor for the key cyclisation reaction. At this point we became aware of the markedly different behaviour of dimesylate **22** relative to its C4 epimer **11**. In contrast to the stable dimesylate **11** we found **22** to decompose on standing to a polar mixture from which



Scheme 3: a) PDC, CH_2Cl_2, mol. sieves; b) $NaBH_4$, EtOH, -78°; c) L-Selectride, THF, -78°; d) L-Selectride, $ZnCl_2$,THF, -78°; e) TrCl, DMAP, py; f) MsCl, DMAP, py; g) Et_3N, DMF 120°; h) 1M NaOH, dioxane; i) $(Boc)_2O$, $KHCO_3$, dioxane, H_2O; j) Ac_2O, py; k) TsOH, $Me_2C(OMe)_2$, Me_2CO; l) NaOMe, MeOH; m) $BnNH_2$, 50°; n) 10% HCl, MeOH; o) H_2, 10% Pd-C, HOAc, EtOH.

one compound was purified subsequent to acetylation of the mixture. ^1H and ^{13}C NMR spectra showed the loss of the *t*-butyl carbamate and the acetonide groups but the primary mesylate to be intact along with a carbamate-like carbonyl (δ_C 159.3). This compound was assigned the cyclic carbamate structure **25** resulting from spontaneous intramolecular substitution of the secondary mesylate by the *t*-butyl carbamate and cleavage of the acetonide. The decomposition was, however, slow enough to allow chromatographic purification of the dimesylate **22** and treatment with benzylamine. This gave the required cyclic amine **23** but in poor yield (13%). Also isolated were the benzylamine **26** (11%) and the mesylate **27** (19%) resulting from

intramolecular displacement of the C1 mesyloxy group by benzylamine and the C4 mesyloxy group by the carbamate. Other products were observed by TLC but were either not isolated or were unable to be assigned structures. Amine **23** was transformed to triacetate **24** (70%) by acid hydrolysis followed by peracetylation. De-*O*-acetylation and hydrogenolytic removal of the benzyl groups gave the target 2-acetamido-1,2,4-trideoxy-1,4-imino-D-glucitol **2**.

Results of the evaluation of **1** and **2** as hexosaminidase inhibitors will be reported elsewhere.

EXPERIMENTAL

Melting points were recorded on a Reichert hot stage microscope and are uncorrected. Optical rotations were measured using a Perkin-Elmer 241 polarimeter. Infrared spectra were recorded as thin films or KBr discs on a Perkin-Elmer 1605 FTIR. ^{1}H and ^{13}C NMR were recorded on Bruker AC300 or (where indicated) Varian Unity 500 spectrometers and assignments were made with the assistance of DEPT and COSY experiments. Mass spectra were recorded at the Institute of Environmental Science and Research Limited, Lower Hutt, on a VG70-250S double-focusing mass spectrometer under positive EI or ammonia CI conditions. Elemental analyses were performed by the Campbell Microanalytical Laboratory, University of Otago, Dunedin. Thin layer chromatography was carried out on 60 PF_{254} silica gel coated aluminium sheets. Column chromatography was performed using Sorbsil C60-H (40-60) silica gel. Radial chromatography was performed using a Harrison Research Chromatotron and 60 PF_{254} silica gel (Merck 7749) plates of 1, 2 or 4 mm thickness. Solvents were dried and purified before use according to standard procedures. Petrol refers to the fraction of petroleum ether boiling between 60-80°.

*2-Acetamido-1,4-di-*O*-acetyl-3-*O*-benzyl-2-deoxy-5,6-*O*-isopropylidene-*D*-glucitol* ***10***

2-Acetamido-2-deoxy-D-glucoyranose **6** (20.0 g, 0.90 mol) and anhydrous iron(III) chloride (30.0 g, 0.18 mol) were heated under reflux in freshly distilled acetone (300 ml) for 30 min. After cooling to 0° a solution of triethylamine (40 ml) in acetone (100 ml) was added with swirling. Na_2CO_3 (30 g) in H_2O (200 ml) was added slowly followed by reduction of solvent *in vacuo* while maintaining the temperature below 30°. After filtration of solid material, the filtrate was exhaustively extracted with EtOAc (8 x 100 ml). The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated to a yellow-orange oil. The crude oxazoline **7**[11,16] was judged by ^{1}H NMR to be sufficiently pure for use in the next step. The product was dissolved in DMF (60 ml) and cooled to 0°. Sodium hydride (80% disp. in oil, 2.5 g, 0.83 mol) was added portionwise followed by benzyl bromide (10.0 ml, 0.84 mol). The mixture was stirred at r.t. overnight then quenched with H_2O and extracted with EtOAc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated to an orange-brown oil. After dissolution in MeOH (50 ml), aqueous HOAc (10%, 50 ml) was added and the mixture stirred at r.t. TLC (EtOAc) showed the reaction was complete after 7 h. The mixture was diluted with H_2O, extracted with EtOAc (3 x), and the combined extracts were dried ($MgSO_4$), filtered and concentrated. ^{1}H NMR showed a ~4:1 mixture of anomers **5**. The crude mixture was taken up in MeOH (50 ml) and treated with excess sodium borohydride (2.0 g). After stirring at r.t. for 1 h the mixture was diluted with H_2O, acidified (10% HCl) then extracted with

EtOAc (3 x). The combined extracts were dried ($MgSO_4$), filtered and concentrated to an oil. A small quantity was purified by column chromatography (70% EtOAc/petrol to 10% MeOH/EtOAc) to give clean 2-acetamido-3-*O*-benzyl-2-deoxy-5,6-*O*-isopropylidene-D-glucitol **9**. δ_H ($CDCl_3$) 1.30, 1.36, 1.95 (3 x 3H, s, Me), 3.49-3.59 (2H, m, H1,3), 3.92-4.09 (5H, m, H1,4,5,6,6), 4.15-4.22 (1H, m, H2), 4.70 (2H, AB, J 11.2 Hz, O*CH*$_2$Ph), 6.46 (1H, d, J 7.6 Hz, NH), 7.31-7.35 (5H, m, Ar). δ_C ($CDCl_3$) 23.0q (Ac), 25.2q and 26.8q (C*Me*$_2$), 50.6d (C2), 59.8t (C1), 66.9t (C6), 70.7d (C3), 73.7t (O*CH*$_2$Ph), 75.4d and 75.5d (C4,5), 109.2s (*C*Me$_2$), 128.0d, 128.1d, 128.4d and 137.5s (Ar), 170.2s (C=O). *m/z* calculated for $C_{18}H_{28}NO_6$ (MH^+) 354.1919, found 354.1919. The remaining crude oil was dissolved in acetic anhydride and pyridine (1:1, 40 ml) and stirred at r.t. overnight. After dilution with H_2O and acidification with 10% HCl the mixture was extracted with EtOAc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. Column chromatography (50-70% petrol/EtOAc) gave the triacetate **10** (6.83 g, 17% from **6**), $[\alpha]_D^{25}$ +16.2° (*c*1.2, $CHCl_3$), (Found: C, 60.27; H, 7.29; N, 3.12%. $C_{22}H_{31}NO_8$ requires C, 60.40; H, 7.14; N, 3.20%). ν_{max} (film) 1743, 1655, 1534, 1372, 1229, 1049 cm^{-1}. δ_H ($CDCl_3$) 1.35, 1.41 (2 x 3H, s, CMe_2), 1.97, 1.99, 2.06 (3 x 3H, s, Ac), 3.79-3.84 (2H, m, H3,6), 3.99-4.04 (3H, m, H1,1,6), 4.24 (1H, q, J 6.3 Hz, H5), 4.40 (1H, ddd, J 9.2, 6.8, 2.5 Hz, H2), 4.60, 4.73 (2H, AB, J 11.2 Hz, O*CH*$_2$Ph), 5.15 (1H, t, J 5.9 Hz, H4), 6.02 (1H, d, J 8.6 Hz, NH), 7.29-7.39 (5H, m, Ar). δ_C ($CDCl_3$) 20.6q, 20.9q and 23.1q (Ac), 25.2q and 26.3q (C*Me*$_2$), 48.7d (C2), 62.7t (C1), 66.2t (C6), 72.5t (C4), 74.4t (O*CH*$_2$Ph), 74.5d (C5), 75.4d (C3), 109.6s (*C*Me$_2$), 128.2d, 128.5d and 137.2s (Ar), 169.8s, 170.1s and 170.4s (C=O). *m/z* calculated for $C_{22}H_{32}NO_8$ (MH^+) 438.2128, found 438.2131.

3-O-Benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-D-glucitol ***3***

The triacetate **10** (6.38 g, 14.6 mmol) was dissolved in MeOH (75 ml), aqueous NaOH (1M, 75 ml) was added and the solution was heated under gentle reflux for 7 h. The MeOH content was then reduced *in vacuo*, and the solution was diluted with H_2O and extracted with EtOAc (3 x). The combined extracts were dried ($MgSO_4$), filtered and concentrated to an oil, the ^1H NMR spectrum of which showed no acetate signals. The product was taken up in dioxane (100 ml) and di-*t*-butyl dicarbonate (3.40 g, 15.6 mmol) added followed by potassium hydrogen carbonate (1.5 g, 15.0 mmol) in H_2O (50 ml). After stirring at r.t. overnight the reaction was diluted with H_2O and extracted with EtOAc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (70% EtOAc/petrol) gave the carbamate **3** (5.23 g, 87%), $[\alpha]_D^{25}$ -35.9° (*c*1.1, $CHCl_3$), (Found: C, 61.20; H, 7.92; N, 3.30%. $C_{21}H_{33}NO_7$ requires C, 61.29; H, 8.08; N, 3.40%). ν_{max} (film) 3410, 1692, 1249, 1216, 1167, 1067, 1028 cm^{-1}. δ_H ($CDCl_3$) 1.31, 1.37 (2 x 3H, s, CMe_2), 1.43 (9H, s, *t*-Bu), 3.36 (2H, br s, OH), 3.53 (1H, dd, J 11.5, 3.9 Hz, H1), 3.59 (1H, d, J 6.6 Hz, H4 or 5), 3.91-4.04 (6H, m, H1,2,3,4 or 5, 6), 4.65, 4.73 (2H, AB, J 11.1 Hz, O*CH*$_2$Ph), 5.38 (1H, d, J 6.3 Hz, NH), 7.27-7.34 (5H, m, Ar). δ_C ($CDCl_3$) 25.2q and 26.9q (C*Me*$_2$), 28.2q (*t*-Bu), 51.2d, (C2), 59.7t (C1), 67.1t (C6), 70.3d (C4), 73.6t (O*CH*$_2$Ph), 75.4d (C5), 75.9d (C3), 79.5s (*t*-Bu), 109.2s (*C*Me$_2$), 127.9d, 127.9d, 128.3d and 137.7s (Ar), 155.6s (C=O). *m/z* calculated for $C_{21}H_{34}NO_7$ (MH^+) 412.2335, found 412.2330.

3-O-Benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-1,4-di-O-methanesulfonyl-D-glucitol 11

Methanesulfonyl chloride (2.0 ml, 25.8 mmol) was added to diol **3** (1.84 g, 4.5 mmol) in pyridine (10 ml) and the solution stirred under Ar overnight. After dilution with 10% HCl the mixture was extracted with EtOAc (3 x). The combined extracts were washed with 10% HCl and brine then dried ($MgSO_4$), filtered and concentrated. Column chromatography (30% EtOAc/petrol) gave dimesylate **11** (2.09 g, 82%), $[\alpha]_D^{25}$ +21.7° (*c*0.9, $CHCl_3$). ν_{max} (film) 1711, 1358, 1175, 1054, 944 cm^{-1}. δ_H ($CDCl_3$) 1.36, 1.44 (2 x 3H, s, C*Me*$_2$), 1.44 (9H, s, *t*-Bu), 2.98, 3.06 (2 x 3H, s, OMs), 3.93-4.22 (6H, m, H1,2,3,6), 4.33 (1H, br d, J 5.4 Hz, H5), 4.63, 4.84 (2H, AB, J 10.8 Hz, O*CH*$_2$Ph), 4.91 (1H, t, J 5.1 Hz, H4), 5.10 (1H, br s, NH), 7.32-7.37 (5H, m, Ar). δ_C ($CDCl_3$) 25.0q and 26.4q (C*Me*$_2$), 28.4q (*t*-Bu), 37.6q and 39.1q (Ms), 49.9d (C2), 65.6t (C6), 67.3t (C1), 74.1d (C5), 75.1t (O*CH*$_2$Ph), 75.7d (C3), 79.4d (C4), 80.6s (*t*-Bu), 109.7s (*C*Me$_2$), 128.6d, 128.7d, 128.8d and 136.9s (Ar), 155.2s (C=O).

3-O-Benzyl-1,4-(N-benzylimino)-2-t-butyloxycarbonylamino-1,2,4-trideoxy-5,6-O-isopropylidene-D-glucitol 12

The dimesylate **11** (1.90 g, 3.4 mmol) was dissolved in freshly distilled benzylamine (10 ml) and stirred at 70° overnight. The mixture was diluted with H_2O and extracted with CH_2Cl_2 (3 x). The combined extracts were dried ($MgSO_4$), filtered and concentrated using high vacuum to remove most of the benzylamine. Radial chromatography (10% EtOAc/petrol) gave the cyclic amine **12** (1.06 g, 66%) as white crystals, mp 99-101°, $[\alpha]_D^{25}$ -36.7° (*c*1.05, $CHCl_3$), (Found: C, 69.78; H, 7.89; N, 5.83%. $C_{28}H_{38}N_2O_5$ requires C, 69.68; H, 7.94; N, 5.81%). ν_{max} (KBr) 1711, 1257, 1214, 1154, 1093, 1067, 848 cm^{-1}. δ_H ($CDCl_3$) 1.34, 1.39 (2 x 3H, s, C*Me*$_2$), 1.46 (9H, s, *t*-Bu), 2.61-2.72 (3H, m, H1,4), 3.35 (1H, d, J 13.2 Hz, N*CH*$_2$Ph), 3.45 (1H, br s, H3), 3.63 (1H, t, J 8.0 Hz, H6), 3.95 (1H, q, J 3.7 Hz, H2), 4.13 (1H, q, J 7.1 Hz, H5), 4.36 (1H, d, J 13.2 Hz, N*CH*$_2$Ph), 4.55, 4.75 (2H, AB, J 11.8 Hz, O*CH*$_2$Ph), 5.03 (1H, d, J 7.8 Hz, NH), 7.21-7.38 (10H, m, Ar). δ_C ($CDCl_3$) 25.8q and 26.7q (C*Me*$_2$), 28.5q (*t*-Bu), 53.7d (C2), 57.5t (C1), 59.5t (N*CH*$_2$Ph), 66.7t (C6), 71.3t (O*CH*$_2$Ph), 72.0d (C4), 79.0d (C5), 79.6s (*t*-Bu), 86.6d (C3), 109.5s (*C*Me$_2$), 127.1d, 127.9d, 128.4d, 128.7d, 129.0d, 137.8s and 139.1s (Ar), 155.2s (C=O). *m/z* calculated for $C_{28}H_{39}N_2O_5$ (MH^+) 483.2859, found 483.2856.

2-Acetamido-5,6-di-O-acetyl-3-O-benzyl-1,4-(N-benzylimino)-1,2,4-trideoxy-D-galactitol 13

Cyclic amine **12** (0.90 g, 1.9 mmol) was dissolved in MeOH (10 ml), aqueous HCl (10%, 10 ml) added and the solution stirred at r.t. for 24 h. After evaporation to dryness the residue was dissolved in acetic anhydride and pyridine (1:1, 20 ml) and stirred at r.t. overnight. The reaction mixture was diluted with H_2O and extracted with EtOAc (3 x). The combined extracts were dried ($MgSO_4$), filtered and evaporated. Pyridine was removed by codistillation with toluene (3 x). Radial chromatography (50% EtOAc/petrol) provided the triacetate **13** (0.84 g, 96%), $[\alpha]_D^{25}$ -34.9° (*c*1.3, $CHCl_3$), (Found: C, 66.66; H, 7.17; N, 6.03%. $C_{26}H_{32}N_2O_6$ requires C, 66.64; H, 6.88; N, 5.98%). ν_{max} (film) 1741, 1655, 1529, 1372, 1228, 1047 cm^{-1}. δ_H ($CDCl_3$, 500 MHz) 1.99, 2.01, 2.02 (3 x 3H, s, Ac), 2.67 (1H, dd, J 10.1, 4.6 Hz, H1), 2.72 (1H, d, J 10.1 Hz, H1),

2.82 (1H, dd, J 8.2 , 1.8 Hz, H4), 3.45, 4.12 (2H, AX, J 13.4 Hz, NCH_2Ph), 3.76 (1H, s, H3), 3.96 (1H, dd, J 12.2, 7.3 Hz, H6), 4.29-4.34 (2H, m, H2,6), 4.59, 4.78 (2H, AB, J 12.0 Hz, OCH_2Ph), 5.18 (1H, td, J 7.6, 2.7 Hz, H5), 6.31 (1H, d, J 7.6 Hz, NH), 7.25-7.35 (10H, H, Ar). δ_C ($CDCl_3$) 20.9q, 21.3q and 23.3q (Ac), 52.8d (C2), 56.3t (C1), 60.2t (NCH_2Ph), 63.4t (C6), 69.4d (C4), 71.5t (OCH_2Ph), 71.9d (C5), 85.7d (C3), 127.4d, 128.0d, 128.4d, 128.5d, 128.7d, 138.1s and 138.4s (Ar), 170.1s, 170.8s, 171.2s (C=O). *m/z* calculated for $C_{26}H_{33}N_2O_6$ (MH^+) 469.2338, found 469.2339.

*2-Acetamido-1,2,4-trideoxy-1,4-imino-*D*-galactitol hydrochloride 1*

The triacetate **13** (0.77 g, 1.6 mmol) was dissolved in MeOH (20 ml) containing a catalytic amount of sodium methoxide. After stirring at r.t. for 5 h the solvent was evaporated and the residue dissolved in EtOH (20 ml). Palladium on charcoal (10%, 0.20 g) and aqueous HCl (10%, 2 ml) were added and the mixture stirred under a H_2 atmosphere overnight. After filtration through celite and evaporation of the solvent the residue was recrystallised from EtOH to give the title imino-D-galactitol **1** as its hydrochloride salt (0.34 g, 90%), mp 168°, $[\alpha]_D^{20}$ -6.4° (*c*1.2, H_2O), (Found: C, 39.83; H, 6.85; N, 11.43%. $C_8H_{17}N_2O_4Cl$ requires C, 39.92; H, 7.12; N, 11.64%). ν_{max} (KBr) 3430-2900, 1630, 1575, 1281, 1110, 1037, 936, 852, 819 cm^{-1}. δ_H (D_2O, 500 MHz)[18] 2.02 (3H, s, Ac), 3.23 (1H, dd, J 12.2, 7.5 Hz, H1), 3.58 (1H, dd, J 7.8, 4.4 Hz, H4), 3.68 (1H, dd, J 12.0, 4.9 Hz, H6), 3.74 (1H, dd, J 12.5, 7.8 Hz, H1), 3.77 (1H, dd, J 12.0, 3.8 Hz, H6), 4.05 (1H, q, J 4.4 Hz, H5), 4.26-4.32 (2H, m, H2,3). δ_C (D_2O) 24.8q (Ac), 49.1t (C1), 57.1d (C2), 66.1t (C6), 67.0d (C4), 70.4d (C5), 76.8d (C3), 177.7s (C=O). *m/z* calulated for $C_8H_{17}N_2O_4$ (MH^+) 205.1188, found 205.1186.

*3-*O*-Benzyl-2-*t*-butyloxycarbonylamino-2-deoxy-5,6-*O*-isopropylidene-1-*O*-triphenylmethyl-*D*-glucitol 14*

Trityl chloride (5.0 g, 17.9 mmol) and a catalytic amount of 4-dimethylaminopyridine were added to a solution of diol **3** (5.34 g, 13.0 mmol) in pyridine (20 ml). After stirring at r.t. overnight the reaction was diluted with H_2O, acidified (10% HCl) and extracted with EtOAc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography (30% EtOAc/petrol) gave the trityl ether **14** (7.25 g, 85%), $[\alpha]_D^{25}$ +4.8° (*c*1.08, $CHCl_3$), (Found: C, 73.13; H, 7.09; N, 2.23%. $C_{40}H_{47}NO_7$ requires C,73.48; H, 7.25; N, 2.14%). ν_{max} (film) 1712, 1249, 1216, 1163, 1068 cm^{-1}. δ_H ($CDCl_3$) 1.36, 1.39 (2 x 3H, s, CMe_2), 1.42 (9H, s, *t*-Bu), 2.49 (1H, br s, OH), 3.16 (1H, br t, J 7.3 Hz, H1), 3.30 (1H, dd, J 9.2, 5.4 Hz, H1), 3.52-3.58 (1H, m, H4), 3.92 (1H, dd, J 7.0, 4.8 Hz, H6), 3.98-4.18 (4H, m, H2,3,5,6), 4.45, 4.60 (2H, AB, J 10.7 Hz, OCH_2Ph), 4.79 (1H, br d, J 8.2 Hz, NH), 7.14-7.31 (15H, m, Ar), 7.40-7.48 (5H, m, Ar). δ_C ($CDCl_3$) 25.4q and 26.8q (CMe_2), 28.4q (*t*-Bu), 52.5d (C2), 63.0t (C1), 67.2t (C6), 73.1d (C4), 74.9t (OCH_2Ph), 75.9d (C3), 77.2d (C5), 86.8s (*t*-Bu), 109.3s (CMe_2), 127.1d, 127.3d, 127.9d, 128.2d, 128.4d, 128.7d, 137.9s and 143.7s (Ar), 155.6s (C=O).

*4-*O*-Benzyl-5-*t*-butyloxycarbonylamino-5-deoxy-1,2-*O*-isopropylidene-6-*O*-triphenylmethyl-*L*-xylo-hex-3-ulose 16*

The alcohol **3** (0.34 g, 0.52 mmol) in CH_2Cl_2 (50 ml) was heated under reflux with pyridinium dichromate (0.97 g, 2.6 mmol) and ground 4Å molecular sieves (0.5 g) for 4 h. After cooling, the mixture was filtered

through a plug of silica then radially chromatographed (20% EtOAc/petrol) to give the ketone **16** (0.31 g, 91%), ν_{max} (film) 1714, 1249, 1221, 1164, 1086 cm^{-1}. δ_H ($CDCl_3$) 1.37 (9H, s, *t*-Bu), 1.42, 1.59 (2 x 3H, s, C*Me*$_2$), 3.08 (1H, t, J 8.6 Hz, H6), 3.30 (1H, dd, J 8.4, 5.6 Hz, H6), 3.97 (1H, t, J 7.7 Hz, H1), 4.19 (1H, t, J 8.1 Hz, H1), 4.25, 4.49 (2H, AB, J 10.9 Hz, O*CH*$_2$Ph), 4.54-4.65 (2H, m, H2,5), 4.82 (1H, s, H4), 4.83 (1H, d, J 8.9 Hz, NH), 7.09-7.45 (15H, m, Ar). δ_C ($CDCl_3$) 25.3q and 26.2q (C*Me*$_2$), 28.2q (*t*-Bu), 50.8d (C5), 62.4t (C6), 66.3t (C1), 73.1t (O*CH*$_2$Ph), 79.4d (C2), 79.6s (*t*-Bu), 80.0d (C4), 86.8s (*C*Ph$_3$), 111.0s (*C*Me$_2$), 127.1d, 127.9d, 128.0d, 128.1d, 128.3d, 128.6d, 137.1s and 143.7s (Ar), 155.1s and 207.3s (C=O). *m/z* calculated for $C_{40}H_{46}NO_7$ (MH^+) 652.3274, found 652.3262.

3-O-Benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-4-O-methanesulfonyl-1-O-triphenylmethyl-D-glucitol ***15***

Alcohol **14** (4.61 g, 7.05 mmol) in pyridine (20 ml) was stirred with methanesulfonyl chloride (1.0 ml, 12.9 mmol) and a catalytic amount of 4-dimethylaminopyridine at r.t. overnight. The mixture was diluted with H_2O, acidified (10% HCl) and extracted with EtAOc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography (30% EtOAc/petrol) gave the mesylate **15** (5.02 g, 97%), $[\alpha]_D^{25}$ +33.2° (*c*1.3, $CHCl_3$), (Found: C, 67.00; H, 6.73; N, 1.91%. $C_{41}H_{49}NO_9S$ requires C, 67.28; H, 6.75; N, 1.91%). ν_{max} (film) 1712, 1367, 1246, 1221, 1176, 1071, 943, 911 cm^{-1}. δ_H ($CDCl_3$) 1.38, 1.46 (2 x 3H, s, C*Me*$_2$), 1.40 (9H, s, *t*-Bu), 2.99 (3H, s, OMs), 2.97-3.05 (1H, m, H1), 3.36 (1H, dd, J 8.3, 5.9 Hz, H1), 3.97-4.11 (4H, m, H2,3,6), 4.20 (1H, d, J 10.4 Hz, O*CH*$_2$Ph), 4.39-4.45 (1H, m, H5), 4.66 (1H, d, J 10.4 Hz, O*CH*$_2$Ph), 4.80 (1H, d, J 9.6 Hz, NH), 4.90-4.92 (1H, m, H4), 7.04-7.43 (20H, m, Ar). δ_C ($CDCl_3$) 25.0q and 26.3q (C*Me*$_2$), 28.3q (*t*-Bu), 39.0q (Ms), 51.0d (C2), 62.8t (C1), 64.9t (C6), 74.0d (C5), 75.1t (O*CH*$_2$Ph), 77.2d (C3), 79.8s (*t*-Bu), 80.5d (C4), 86.9s (*C*Ph$_3$), 109.4s (*C*Me$_2$), 127.2d, 127.9d, 128.0d, 128.3d, 128.4d, 128.6d, 137.1s and 143.6s (Ar), 155.2s (C=O). *m/z* 597 (1%), 581 (3), 580 (6), 451 (15), 390 (18), 355 (33), 338 (100).

*2-Amino-3-O-benzyl-2,4-*N,O*-carbonyl-2-deoxy-5,6-O-isopropylidene-1-O-triphenylmethyl-D-galactitol* ***18***

The mesylate **15** (3.69 g, 5.0 mmol) was dissolved in DMF (30 ml), triethylamine (1.5 ml, 10.8 mmol) added and the solution stirred at 120° for 40 h. The mixture was diluted with H_2O, acidified (10% HCl) and extracted with EtOAc (3 x). The combined extracts were washed with 10% HCl and brine then dried ($MgSO_4$), filtered and the solvent evaporated. Column chromatography (50% EtOAc/petrol) gave the cyclic carbamate **18** (2.76 g, 94%) as a clear oil, $[\alpha]_D^{25}$ -41.9° (*c*1.1, $CHCl_3$), (Found: C, 74.41; H, 6.44; N, 2.48%. $C_{36}H_{37}NO_6$ requires C, 74.59; H, 6.43; N, 2.42%). ν_{max} (film) 1713, 1262, 1219, 1152, 1100, 1075 cm^{-1}. δ_H ($CDCl_3$) 1.38, 1.43 (2 x 3H, s, C*Me*$_2$), 3.36 (2H, d, J 5.4 Hz, H1), 3.73-3.81 (2H, m, H2,3), 4.00-4.04 (2H, m, H6), 4.14 (1H, dd, J 7.3, 1.9 Hz, H5), 4.27 (1H, dd, J 5.3, 1.6 Hz, H4), 4.35, 4.51 (2H, AB, J 11.5 Hz, O*CH*$_2$Ph), 5.57 (1H, br s, NH), 7.05-7.41 (20H, m, Ar). δ_C ($CDCl_3$) 25.8q and 25.9q (C*Me*$_2$), 51.6d (C2), 63.0t (C1), 65.1t (C6), 70.0d (C3), 72.0t (O*CH*$_2$Ph), 74.1d (C5), 74.8d (C4), 87.3s (*C*Ph$_3$), 110.2s (*C*Me$_2$), 127.1d, 127.7d, 127.8d, 127.9d, 128.3d, 128.4d, 136.6s and 143.3s (Ar), 152.5s (C=O). *m/z* calculated for $C_{36}H_{38}NO_6$ (MH^+) 580.2699, found 580.2690.

*3-O-Benzyl-2-t-butyloxycarbonylamino-deoxy-5,6-O-isopropylidene-1-O-triphenylmethyl-*D*-galactitol* ***17***

The cyclic carbamate **18** (3.50 g, 6.0 mmol) was heated under reflux in aqueous NaOH (1M)/dioxane (1:1, 150 ml) for 15 h. After cooling, the mixture was diluted with H_2O and extracted with EtOAc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$) and filtered. The filtrate was concentrated then dissolved in dioxane (20 ml). Di-*t*-butyl dicarbonate (1.58 g, 7.2 mmol), potassium hydrogen carbonate (0.72 g, 7.2 mmol) and H_2O (20 ml) were added and the reaction stirred at r.t. overnight. After dilution with H_2O and acidification (10% HCl) the mixture was extracted with EtOAc (3 x). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated. Column chromatography (30% EtOAc/petrol) gave the alcohol **17** (3.75 g, 95%), $[\alpha]_D^{25}$ -15.6° (*c*1.2, $CHCl_3$), (Found: C, 73.28; H, 6.99; N, 2.24%. $C_{40}H_{47}NO_7$ requires C, 73.48; H, 7.25; N, 2.14%). ν_{max} (film) 3439, 1713, 1696, 1255, 1219, 1165, 1078, 1043 cm^{-1}. δ_H ($CDCl_3$) 1.38, 1.47 (2 x 3H, s, C*Me*$_2$), 1.43 (9H, s, *t*-Bu), 3.15, 3.31 (2 x 1H, t, J 7.9 Hz, H1), 3.42 (1H, br d, J 8.2 Hz, H3), 3.76 (1H, d, J 8.7 Hz, H4), 3.97 (2H, d, J 6.8 Hz, H6), 4.27, 4.46 (2H, AB, J 10.6 Hz, O*CH*$_2$Ph), 4.32 (1H, dd, J 7.0, 2.3 Hz, H5), 4.38-4.45 (1H, m, H2), 4.75 (1H, d, J 9.7 Hz, NH), 6.98-7.47 (20H, m, Ar). δ_C ($CDCl_3$) 25.5q and 26.3q (C*Me*$_2$), 28.3q (*t*-Bu), 50.9d (C2), 63.0t (C1), 65.9t (C6), 69.1d (C3), 74.2t (O*CH*$_2$Ph), 75.0d (C5), 78.8d (C4), 79.7s (*t*-Bu), 86.7s (*C*Ph$_3$), 109.0s (*C*Me$_2$), 127.0d, 127.8d, 128.0d, 128.2d, 128.6d, 129.4d, 137.5s and 143.7s (Ar), 156.5s (C=O). *m/z* 580 (1%), 554 (1), 412 (2), 312 (14), 243 (CPh$_3$, 100).

*4-O-Acetyl-3-O-benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-1-O-triphenylmethyl-*D*-galactitol* ***19***

Alcohol **17** (2.78 g, 4.25 mmol) was dissolved in acetic anhydride and pyridine (1:1, 20 ml) and stirred at r.t. for 4 h. The reaction was diluted with H_2O, acidified (10% HCl) and extracted with EtOAc (3 x). The combined extracts were washed with saturated aqueous $NaHCO_3$ (3 x) and then with brine. After drying over $MgSO_4$ the solution was filtered and concentrated. Column chromatography (20% EtOAc/petrol) gave the acetate **19** (2.96 g, 100%) as white crystals, mp 159°, $[\alpha]_D^{25}$ +4.5° (*c*1.0, $CHCl_3$), (Found: C, 72.73; H, 6.98; N, 2.03%. $C_{42}H_{49}NO_8$ requires C, 72.49; H, 7.10; N, 2.01%). ν_{max} (KBr) 1743, 1711, 1500, 1243, 1225, 1173, 1156, 1098, 1079, 1040 cm^{-1}. δ_H ($CDCl_3$) 1.36, 1.48 (2 x 3H, s, C*Me*$_2$), 1.40 (9H, s, *t*-Bu), 2.16 (3H, s, OAc), 3.05 (1H, t, J 8.2 Hz, H1), 3.31 (1H, t, J 7.7 Hz, H1), 3.72 (1H, dd, J 8.4, 6.4 Hz, H6), 3.98 (1H, t, J 7.6 Hz, H6), 4.14 (1H, d, J 9.3 Hz, H3), 4.19-4.27 (1H, m, H2), 4.20, 4.52 (2H, AB, J 10.5 Hz, O*CH*$_2$Ph), 4.39 (1H, td, J 6.3, 2.1 Hz, H5), 4.67 (1H, d, J 10.1 Hz, NH), 4.98 (1H, d, J 9.2 Hz, H4), 6.97-7.46 (20H, m, Ar). δ_C ($CDCl_3$) 21.1q (Ac), 25.7q and 26.2q (C*Me*$_2$), 28.4q (*t*-Bu), 50.2d (C2), 63.4t (C1), 65.7t (C6), 69.7d (C4), 74.3d (C5), 74.6t (O*CH*$_2$Ph), 76.6d (C3), 79.3s (*t*-Bu), 86.8s (*C*Ph$_3$), 109.2s (*C*Me$_2$), 125.3d, 127.1d, 127.9d, 128.0d, 128.2d, 128.3d, 128.7d, 129.0d, 137.6s and 143.8s (Ar), 155.2s and 170.5s (C=O). *m/z* 578 (1%), 454(1), 415 (1), 354 (6), 243 (CPh$_3$, 100).

*4-O-Acetyl-3-O-benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-*D*-galactitol* ***20***

The trityl ether **19** (1.09 g, 1.57 mmol) was dissolved in dry acetone (20 ml) and stirred with *p*-

toluenesulfonic acid (0.20 g, 1.05 mmol) and dimethoxypropane (1.0 ml, 8.1 mmol) at r.t. for 6 h. Saturated aqueous $NaHCO_3$ (10 ml) was added and stirring continued for 10 min. The mixture was then diluted with H_2O and extracted with EtOAc (3 x). The combined extracts were dried ($MgSO_4$), filtered and concentrated. Radial chromatography (20, 50% EtOAc/petrol) gave the alcohol **20** (0.48 g, 67%). ν_{max} (film) 3448, 1746, 1697, 1500, 1369, 1227, 1167, 1063 cm^{-1}. δ_H ($CDCl_3$) 1.36, 1.44 (2 x 3H, s, C*Me*$_2$), 1.41 (9H, s, *t*-Bu), 2.12 (3H, s, Ac), 3.56 (1H, dd, J 10.6, 7.8 Hz, H1), 3.64-3.72 (2H, m, H1,6), 3.88-3.96 (1H, m, H2), 4.00 (1H, dd, J 8.6, 6.6 Hz, H6), 4.10 (1H, d, J 9.0 Hz, H3), 4.42 (1H, td, J 6.4, 2.0 Hz, H5), 4.65, 4.76 (2H, AB, J 11.0 Hz, O*CH*$_2$Ph), 4.87 (1H, d, J 9.6 Hz, NH), 5.00 (1H, d, J 9.0 Hz, H4), 7.12-7.39 (5H, m, Ar). δ_C ($CDCl_3$) 20.7q (Ac), 25.5q and 26.0q (C*Me*$_2$), 28.1q (*t*-Bu), 51.8d (C2), 62.9t (C1), 65.5t (C6), 69.4d (C4), 74.0d (C5), 74.5t (O*CH*$_2$Ph), 75.7d (C3), 79.6s (*t*-Bu), 109.1s (*C*Me$_2$), 127.9d, 128.4d, 128.8d and 137.4s (Ar), 155.8s and 170.2s (C=O). *m/z* calculated for $C_{23}H_{36}NO_8$ (MH^+) 454.2441, found 454.2446.

3-O-Benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-D-galactitol ***21***

The acetate **20** (1.06 g, 2.34 mmol) was dissolved in MeOH (20 ml) containing a catalytic amount of sodium methoxide and the solution stirred at r.t. for 3.5 h. After removal of the solvent *in vacuo* radial chromatography (50% EtOAc/petrol) gave the diol **21** (0.88 g, 91%), $[\alpha]_D^{25}$ -50.3° (*c*1.1, $CHCl_3$), (Found: C, 61.09; H, 7.86; N, 3.24%. $C_{21}H_{33}NO_7$ requires C, 61.29; H, 8.08; N, 3.40%). ν_{max} (film) 3440, 1692, 1499, 1250, 1217, 1166, 1062 cm^{-1}. δ_H ($CDCl_3$) 1.39, 1.47 (2 x 3H, s, C*Me*$_2$), 1.42 (9H, s, *t*-Bu), 3.48 (1H, dd, J 9.2, 2.2 Hz, H4), 3.62 (1H, dd, J 10.9, 7.2 Hz, H1), 3.74 (1H, dd, J 11.0, 6.0 Hz, H1), 3.78 (1H, d, J 7.9 Hz, H3), 3.94-4.03 (2H, m, H6), 4.14 (1H, br d, J 8.6 Hz, H2), 4.35 (1H, td, J 7.0, 2.4 Hz, H5), 4.65, 4.69 (2H, AB, J 10.9 Hz, O*CH*$_2$Ph), 5.12 (1H, d, J 9.4 Hz, NH), 7.16-7.38 (5H, m, Ar). δ_C ($CDCl_3$) 25.5q and 26.3q (C*Me*$_2$), 28.3q (*t*-Bu), 52.4d (C2), 62.8t (C1), 66.0t (C6), 69.2d (C4), 74.5t (O*CH*$_2$Ph), 75.0d (C5), 78.9d (C3), 80.1s (*t*-Bu), 109.2s (*C*Me$_2$), 128.2d, 128.6d, 129.0d and 137.5s (Ar), 157.0s (C=O). *m/z* calculated for $C_{21}H_{34}NO_7$ (MH^+) 412.2335, found 412.2335.

3-O-Benzyl-2-t-butyloxycarbonylamino-2-deoxy-5,6-O-isopropylidene-1,4-di-O-methanesulfonyl-D-galactitol ***22*** *and 5,6-di-O-acetyl-2-amino-3-O-benzyl-2,4-N,O-carbonyl-2-deoxy-1-O-methanesulfonyl-D-glucitol* ***25***

The diol **21** (0.82 g, 1.99 mmol) was dissolved in pyridine (10 ml) and stirred with methanesulfonyl chloride (1.0 ml, 12.9 mmol) and a catalytic amount of 4-dimethylaminopyridine at r.t. overnight. The reaction was diluted with H_2O, acidified (10% HCl) and extracted with EtOAc (3 x). The combined extracts were washed with 10% HCl and brine then dried ($MgSO_4$), filtered and concentrated. Radial chromatography (30% EtOAc/petrol) gave the dimesylate **22** (0.94 g, 83 %). ν_{max} (film) 1710, 1358, 1249, 1226, 1174, 1104, 1060, 978, 943 cm^{-1}. δ_H ($CDCl_3$) 1.39, 1.47 (2 x 3H, s, C*Me*$_2$), 1.43 (9H, s, *t*-Bu), 3.02, 3.15 (2 x 3H, s, OMs), 3.89 (1H, d, J 6.1 Hz, H3), 3.99 (1H, dd, J 8.9, 6.7 Hz, H6), 4.08 (1H, dd, J 8.9, 6.6 Hz, H6), 4.16, 4.21 (2H, AB, J 9.2 Hz, H1), 4.19-4.28 (1H, m, H2), 4.37 (1H, td, J 6.6, 3.7 Hz, H5), 4.62, 4.82 (2H, AB, J 10.7 Hz, O*CH*$_2$Ph), 4.84 (1H, t, J 5.0 Hz, H4), 5.07 (1H, d, J 8.6 Hz, NH), 7.33-7.38 (5H, m, Ar). δ_C ($CDCl_3$) 25.5q and 25.9q (C*Me*$_2$), 28.1q (*t*-Bu), 37.3q and 38.8q (Ms), 49.5d (C2), 65.5t (C6), 67.0t (C1), 73.9d (C5), 74.1t (O*CH*$_2$Ph), 74.8d (C3), 78.6d (C4), 80.1s (*t*-Bu), 109.8s (*C*Me$_2$), 128.3d, 128.5d and 136.4s (Ar), 155.0s (C=O). Dimesylate **22** (0.20 g, 0.35 mmol) decomposed on standing to a polar mixture which was acetylated

(acetic anhydride/pyridine) and worked up in the usual manner. Radial chromatography (70% EtOAc/petrol) gave the cyclic carbamate **25** (0.12 g, 74%). ν_{max} (film) 1747, 1370, 1346, 1223, 1175, 1092, 1050, 942, 916, 734 cm^{-1}. δ_H ($CDCl_3$) 2.07, 2.11 (2 x 3H, s, Ac), 3.09 (3H, s, Ms), 3.60 (1H, t, J 3.6 Hz, H3), 4.07-4.12 (3H, m, H1,2,6), 4.32 (1H, dd, J 12.1, 4.7 Hz, H6), 4.43 (1H, t, J 10.0 Hz, H1), 4.58, 4.77 (2H, AB, J 11.0 Hz, O*CH*$_2$Ph), 5.05 (1H, t, J 4.6 Hz, H4), 5.53 (1H, q, J 5.3 Hz, H5), 5.85 (1H, br s, NH), 7.33-7.38 (5H, m, Ar). δ_C ($CDCl_3$) 20.7q and 20.9q (Ac), 39.0q (Ms), 53.0d (C2), 62.0t (C6), 67.3t (C1), 68.6d (C5), 74.1t (O*CH*$_2$Ph), 77.9d (C4), 78.0d (C3), 128.6d, 128.7d, 128.9d and 136.2s (Ar), 159.3s, 170.1s and 170.4s (C=O). *m/z* calculated for $C_{19}H_{29}N_2O_{10}S$ (MNH_4^+) 477.1542, found 477.1540.

*3-*O*-Benzyl-1,4-(*N*-benzylimino)-2-t-butyloxycarbonylamino-5,6-*O*-isopropylidene-1,2,4-trideoxy-*D*-glucitol* **23**, *1,2-diamino-1,3-di-*N,O*-benzyl-2,4-*N,O*-carbonyl-1,2-deoxy-5,6-*O*-isopropylidene-*D*-glucitol* **26** *and 2-amino-3-*O*-benzyl-2,4-*N,O*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-1-*O*-methanesulfonyl-*D*-glucitol* **27**

The dimesylate **22** (0.37 g, 0.65 mmol) was dissolved in benzylamine (10 ml) and stirred at 50° for 17 h. The mixture was diluted with H_2O and extracted with CH_2Cl_2 (3 x). The combined extracts were dried ($MgSO_4$), filtered and concentrated using high vacuum to remove most of the benzylamine. Radial chromatography (20, 50% EtOAc/petrol) gave the cyclic amine **23** (0.040 g, 13%) and the cyclic carbamate **26** (0.032 g, 11%). Further chromatography (70% CH_2Cl_2/EtOAc then EtOAc) gave cyclic carbamate **27** (0.051 g, 19%) and a fourth unknown product.

23: mp 150-2°, $[\alpha]_D^{25}$ -49.3° (*c*0.5, $CHCl_3$). ν_{max} (KBr) 1686, 1526, 1240, 1170, 1158, 1096, 1038 cm^{-1}. δ_H ($CDCl_3$) 1.33, 1.40 (2 x 3H, s, C*Me*$_2$), 1.43 (9H, s, *t*-Bu), 1.98 (1H, dd, J 10.0, 7.3 Hz, H1), 3.27-3.34 (3H, m, H1,4,N*CH*$_2$Ph), 3.79 (1H, dd, J 6.7, 3.9 Hz, H3), 3.96 (1H, br m, H2), 4.05 (1H, t, J 7.0 Hz, H6), 4.28-4.42 (4H, m, H5,6,N*CH*$_2$Ph,NH), 4.54, 4.70 (2H, AB, J 12.0 Hz, O*CH*$_2$Ph), 7.20-7.35 (10H, m, Ar). δ_C ($CDCl_3$) 24.2q and 26.3q (C*Me*$_2$), 28.3q (*t*-Bu), 54.7d (C2), 57.3t (C1), 60.1t (N*CH*$_2$Ph), 65.0d (C4), 65.9t (C6), 71.5t (O*CH*$_2$Ph), 76.4d (C5), 79.6s (*t*-Bu), 84.1d (C3), 107.4s (*C*Me$_2$), 126.9d, 127.7d, 127.9d, 128.2d, 128.3d, 128.7d, 128.8d, 138.1s and 138.9s (Ar), 154.9s (C=O). *m/z* calculated for $C_{28}H_{39}N_2O_5$ (MH^+) 483.2860, found 483.2844.

26: ν_{max} (film) 3340, 1634, 1565, 1255, 1214, 1159, 1121, 1068 cm^{-1}. δ_H ($CDCl_3$) 1.27, 1.37 (2 x 3H, s, C*Me*$_2$), 3.62 (1H, dd, J 9.5, 0.5 Hz, N*CH*$_2$Ph), 3.87 (1H, dd, J 8.5, 6.6 Hz, H6), 3.98-4.09 (4H, m, H3,4,6,N*CH*$_2$Ph), 4.24-4.33 (4H, m, H1,1,2,5), 4.62, 4.78 (2H, AB, J 11.9 Hz, O*CH*$_2$Ph), 5.05 (1H, d, J 6.3 Hz, NHCO), 5.59 (1H, t, J 5.7 Hz, N*H*CH$_2$Ph), 7.23-7.33 (10H, m, Ar). δ_C ($CDCl_3$) 25.2q and 26.5q (C*Me*$_2$), 44.4t (C1), 55.9d (C2), 66.2t (C6), 71.9t (N*CH*$_2$Ph), 72.0t (O*CH*$_2$Ph), 74.3d (C5), 80.7d and 83.3d (C3,4), 108.4s (*C*Me$_2$), 127.4d, 127.7d, 128.3d, 128.7d, 138.1s and 139.0s (Ar), 157.6s (C=O). *m/z* calculated for $C_{24}H_{31}N_2O_5$ (MH^+) 427.2233, found 427.2239.

27: δ_H ($CDCl_3$) 1.36, 1.45 (2 x 3H, s, C*Me*$_2$), 3.12 (3H, s, Ms), 3.55 (1H, dd, J 5.3, 3.9 Hz, H3), 3.97 (1H, dd, J 8.9, 6.1 Hz, H6), 4.08 (1H, d, J 6.9 Hz, H6), 4.10 (1H, dd, J 8.7, 3.6 Hz, H1), 4.23-4.29 (2H, m, H2,5), 4.43 (1H, t, J 8.7 Hz, H1), 4.62, 4.80 (2H, AB, J 11.3 Hz, O*CH*$_2$Ph), 4.82 (1H, dd, J 5.3, 2.7 Hz, H5), 5.53 (1H, br s, NH), 7.32-7.38 (5H, m, Ar). δ_C ($CDCl_3$) 25.4q and 26.0q (C*Me*$_2$), 39.1q (Ms), 53.2d (C2), 65.9t (C6), 67.4t (C1), 74.1t (O*CH*$_2$Ph), 74.1d (C5), 78.6d (C3), 79.0d (C4), 110.4s (*C*Me$_2$), 128.3d, 128.6d, 128.8d and 136.2s (Ar), 159.3s (C=O). *m/z* calculated for $C_{18}H_{26}NO_8S$ (MH^+) 416.1379, found 416.1355.

2-Acetamido-5,6-di-O-acetyl-3-O-benzyl-1,4-(N-benzylimino)-1,2,4-trideoxy-D-glucitol **24**

Cyclic amine **23** (0.053 g, 0.11 mmol) was dissolved in MeOH:10% aq. HCl (1:1, 10 ml) and the solution stirred at r.t. overnight. After concentration to dryness the residue was dissolved in acetic anhydride and pyridine (1:1, 2 ml) and stirred at r.t. overnight. The mixture was diluted with H_2O, acidified (10% HCl) and extracted with EtOAc (3 x). The combined extracts were dried ($MgSO_4$), filtered and concentrated. Radial chromatography (60% EtOAc/petrol) gave the triacetate **24** (0.036 g, 70%). δ_H ($CDCl_3$) 1.79, 2.03, 2.06 (3 x 3H, s, Ac), 3.18 (1H, dd, J 7.4, 2.3 Hz, H1), 3.25 (1H, dd, J 10.0, 6.8 Hz), 3.33, 4.21 (2H, AX, J 13.4 Hz, NCH_2Ph), 3.91 (1H, dd, J 7.3, 5.1 Hz, H1), 4.16-4.25 (1H, m), 4.51 (1H, dd, J 12.2, 8.0 Hz, H6), 5.09 (1H, br s), 5.44 (1H, dt, J 7.9, 2.4 Hz, H5), 7.27-7.34 (10H, m, Ar). δ_C ($CDCl_3$) 20.7q, 21.2q and 23.3q (Ac), 54.2d (C2), 55.6t (C1), 59.5t (NCH_2Ph), 64.5t (C6), 65.4d (C4), 72.1t (OCH_2Ph), 72.5d (C5), 83.0d (C3), 127.4d, 127.8d, 127.9d, 128.4d, 128.5d, 128.8d, 137.8s and 137.9s (Ar), 169.5s, 170.4s and 170.7s (C=O). *m/z* calculated for $C_{26}H_{33}N_2O_6$ (MH^+) 469.2339, found 469.2346.

2-Acetamido-1,2,4-trideoxy-1,4-imino-D-glucitol hydrochloride **2**

The triacetate **24** (0.036 g, 0.077 mmol) was dissolved in MeOH (1.0 ml) containing a catalytic amount of sodium methoxide and stirred at r.t. for 3 h. After evaporation of the solvent, EtOH (4 ml) and HOAc (1 ml) were added followed by Pd-C (10%, 0.3 g). The mixture was stirred under H_2 for 3 h then filtered through celite and the filtrate concentrated. 10% HCl (1 ml) was evaporated from the residue (2 x) to give the target 1,4-imino-glucitol hydrochloride **2** as a hygroscopic solid. δ_H (D_2O, 500 MHz)[18] 2.01 (3H, s, Ac), 3.41 (1H, dd, J 13.1, 2.4 Hz, H1), 3.71 (1H, dd, J 8.2, 3.4 Hz, H4), 3.76 (2H, ABX, $J_{6,6'}$ 12.0, $J_{6,5}$ 5.3, $J_{6',5}$ 4.9 Hz, H6), 3.90 (1H, dd, J 13.1, 7.0 Hz, H1), 4.15 (1H, dt, J 8.2, 5.0 Hz, H5), 4.31 (1H, br d, J 6.1 Hz, H2), 4.48 (1H, dd, J 3.4, 1.2 Hz, H3). δ_C ($CDCl_3$) 24.7q (Ac), 51.6t (C1), 58.3d (C2), 65.6d (C4), 66.0t (C6), 69.7d (C5), 76.4d (C3), 177.0s (C=O). *m/z* calculated for $C_8H_{17}N_2O_4$ (M^+) 205.1188, found 205.1181.

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17. For example: TsOH, MeOH; $BF_3.Et_2O$, CH_2Cl_2; Amberlyst 15-H, MeOH, CH_2Cl_2; $ZnCl_2$, CH_2Cl_2; 10% HCl, MeOH; HOAc, CH_2Cl_2; HCl, Et_2O; TsOH, acetone; $CuSO_4$, CH_2Cl_2; $ZnCl_2$, $BF_3.Et_2O$, CH_2Cl_2; HCO_2H, Et_2O.
18. Referenced to acetone as an internal standard at δ 2.217.

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