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Selective protecting group manipulations on the 1-deoxynojirimycin scaffold

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Abstract—Iminosugars are inhibitors of glycoprocessing and are of interest as scaffolds for medicinal chemistry, as their successful application as peptide mimetics has shown. The synthesis of novel peptidomimetics based on 1-deoxynojirimycin (DNJ) requires practical strategies that allow introduction of amino acid side chains or pharmacophore groups at each of its hydroxyl groups or to the nitrogen atom. This paper describes one approach towards achieving selective protection and deprotection at the hydroxyl and amino groups of DNJ and a novel synthesis of DNJ from L-sorbose is included.

1. Introduction

Monosaccharides and their derivatives have been receiving increased attention as scaffolds for the synthesis of novel compounds. Such carbohydrate derivatives have been mainly designed to modulate protein–protein and peptide–protein interactions (peptidomimetics) although carbohydrate–protein (glycomimetics) and carbohydrate–nucleic acid interactions (aminoglycoside mimetics) have also been of interest. 1-Deoxynojirimycin (DNJ) **1**[1] is a naturally occurring member of the iminosugars, which constitute polyhydroxylated heterocycles containing an endocyclic nitrogen atom. The polyhydroxylated piperidines are true structural analogues of pyranosides and the substitution of the ring oxygen of the corresponding pyranose with a nitrogen atom renders these compounds stable to glucosidases, but does not prevent their recognition by glycosidases[2] and glycosyltransferases.[3] Consequently, derivatives of DNJ have found clinical application[4] and analogues are of interest for treatment of HIV infection, hepatitis C virus infection, diabetes and other metabolic disorders.[5] In addition, DNJ derivatives, which have pharmacophoric groups attached are potentially bioactive compounds,[6–8] and preliminary studies using iminosugar based scaffolds bioactive molecule synthesis indicate promise in this regard.[9] For example, the Lys-Trp mimetic **2**, based on 1-deoxymannojirimycin (DMJ) as a scaffold, is a ligand for somatostatin receptors.[10] In this compound, the amino acid side chains of lysine and tryptophan are grafted strategically to functional groups on the DMJ scaffold. The synthesis of molecules based on iminosugars thus requires practical strategies that allow introduction of substituents at each of the hydroxyl groups or to the nitrogen atom of iminosugars so that structure–activity relationships may be established. Such strategies would also facilitate the synthesis of novel analogues of iminosugars for investigation as glycosidase inhibitors or for other purposes.[11] Herein, we describe one approach towards

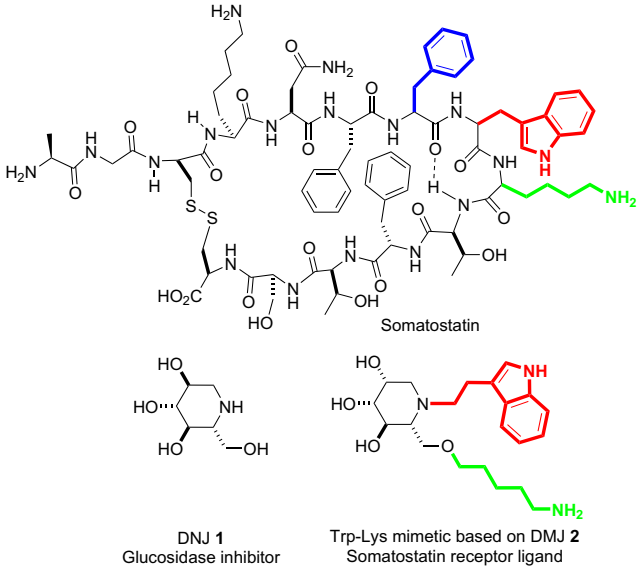

Chart 1.

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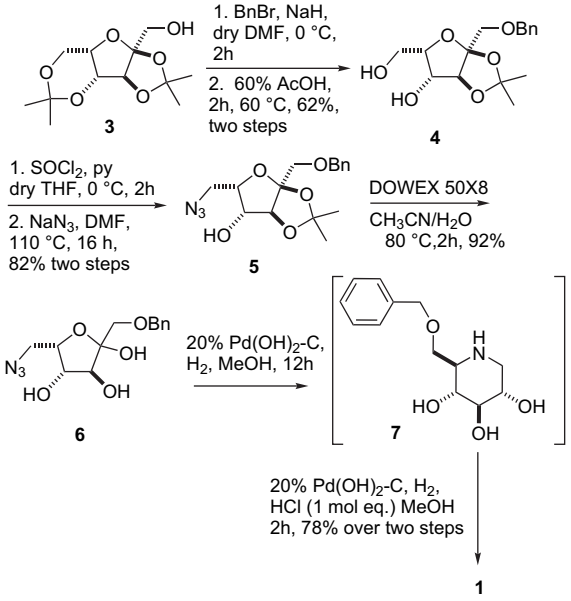
achieving selective protection and deprotection strategies for **1**[12] including an alternative preparation of **1** from L-sorbose.

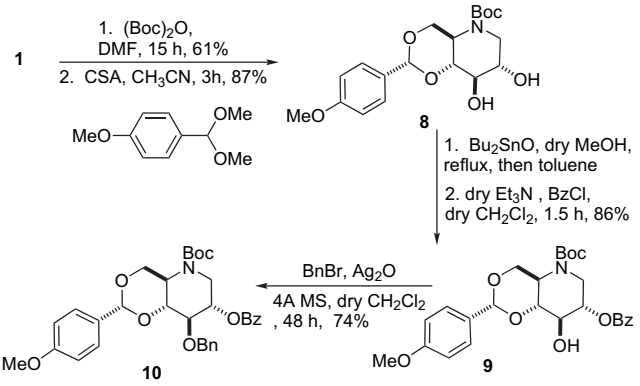
2. Results and discussion

Strategies where pharmacophoric groups can be introduced at the desired position of an iminosugar could involve introduction of the pharmacophoric group to a suitable precursor followed by formation of the piperidine ring, or the synthesis could begin from the iminosugar itself and involve both chemo- and regioselective reactions of the amine and hydroxyl groups. The work described herein focuses more on the latter approach and a practical synthesis of DNJ was thus first required.[13] Our group has developed a synthesis of DNJ from 6-deoxy-hex-5-enopyranosyl azides but scale-up of this route to provide multi-gram quantities of DNJ was not practical and thus a novel approach was developed from L-sorbose (Scheme 1). The bis-acetonide **3** was first prepared[14] and subsequent benzylation of the C-1 hydroxyl group and regioselective hydrolysis of one acetonide group gave the dihydroxylated derivative **4**. A cyclic sulfite was generated from the reaction of **4** with thionyl chloride and reaction of this sulfite with sodium azide at 110 °C in DMF gave, after aqueous work-up and purification, the 6-azido-L-sorbofuranose derivative **5**.[15] Hydrolysis of the acetonide located at C-2 and C-3 hydroxyl groups promoted by the acidic ion exchange resin Dowex-50-X8-100 (H^+)[16] gave the 6-azido-1-*O*-benzylated sorbofuranose derivative **6**. Catalytic hydrogenation using $Pd(OH)_2$ adsorbed on charcoal in methanol led to formation of the 6-*O*-benzylated derivative **7** without any loss of the benzyl group occurring in these conditions. Various attempts to convert **7** to **1** were investigated by catalytic hydrogenation; this included using different catalysts (Pd–C or $Pd(OH)_2$–C), pressures (100 psi and 90 bar) and temperatures (25–100 °C), but the benzyl group could not be removed. The addition of acetic acid to reaction mixtures led to degradation. Finally **7** was converted to **1** by catalytic hydrogenolysis in methanol in the presence of HCl (1.0–1.4 mol equiv), which facilitated removal of the benzyl group in less than 1 h at atmospheric pressure. The satisfactory purification of **1** was achieved by chromatography using an acid ion exchange resin (Dowex-50-X8) as the stationary phase, which unlike the use of silica gel as stationary phase, did not lead to loss of product. The overall yield of **1** using this sequence of reactions was 30% in seven steps from L-sorbose,[17] and the sequence is suitable for preparation of gram quantities of **1**. Also the sequence used herein, where selective alkylation of the 1-OH and 3-OH groups of sorbose and subsequent formation of the piperidine are possible, could, in principle, be used to regioselectively introduce pharmacophoric groups to **1**; however, this was not exploited during the course of this study.



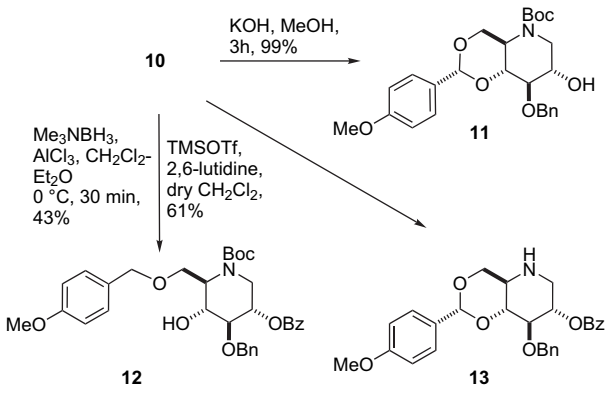
Scheme 1.

With gram quantities of **1** in hand, our attention turned to an investigation of its selective protection and deprotection reactions. Firstly a Boc protecting group was introduced onto the nitrogen atom of **1** and subsequent reaction of the product with the dimethylacetal of anisaldehyde in acetonitrile in the presence of a catalytic amount of camphorsulfonic acid gave the benzylidene derivative **8** in good yield. Next a variety of reactions to differentiate the two secondary hydroxyl groups of **8** were investigated. The most satisfactory of these approaches was a regioselective benzoylation, which gave **9** via reaction of the dibutyltin ketal derivative obtained from **8** with benzoyl chloride. The main product, the 2-*O*-benzoylated derivative **9**, was separated from a minor amount of the 3-*O*-benzoylated isomer (2-OBz–3-OBz 10:1) by chromatography. Other attempts at obtaining highly regioselective reactions were less successful. For example, the benzylation of **8** using dibutyltin oxide and benzyl bromide (1.1 equiv)[18] gave a mixture of the two mono-benzylated ethers with low regioselectivity (2-OBn–3-OBn, 1.4:1). The reaction of **8** with pivaloyl chloride (1 equiv) in presence of pyridine gave a mixture of mono- and di-*O*-pivaloylated products,[19] whereas the reaction of **8** with TIPSOTf in presence of 2,6-lutidine gave either recovery of substantial amounts of unreacted **8** (using 1.0 equiv TIPSOTf) or gave a mixture of mono- and di-*O*-silylated products (using 1.5 equiv TIPSOTf). Reaction of **9** was next investigated, given that benzoylation was the most satisfactory approach and benzylation using benzyl bromide in presence of silver oxide gave **10** in 74% yield (Scheme 2).



Scheme 2.

Reactions of **10** were investigated (Scheme 3). The benzoyl ester of **10** was hydrolysed selectively using potassium hydroxide in methanol to give **11** in high yield. Attempts to



Scheme 3.

effect selective cleavage of the methoxybenzylidene group of **10** using DIBAL-H were investigated but reductive hydrolysis of the benzoyl ester was a competing reaction. The reductive cleavage of the methoxybenzylidene group of **10**, to give the 6-*O*-methoxyphenylmethyl derivative **12**, was achieved in moderate yield using borane–trimethyl amine complex in presence of aluminium trichloride at 0 °C in dichloromethane–ether.[20] The structure of this regioisomer was assigned using COSY, which showed correlation between the proton of the 4-hydroxyl group and the proton at C-4. A selective deprotection of the Boc group of **10** using TMSOTf and 2,6-lutidine[21] gave amine **13**, proving to be useful for the chemoselective removal of the Boc group in presence of the acid sensitive methoxybenzylidene group (Scheme 3).

The allylation of **11** with sodium hydride and allyl bromide gave **14** (Scheme 4). The chemoselective deprotection of the Boc group of **14** using TMSOTf and 2,6-lutidine gave amine **15**. The reaction of **11** with TIPSOTf in presence of 2,6-lutidine gave **16** (53%) when the TIPSOTf was added portionwise (total added was 4.5 equiv) during the course of reaction (20 h). If all the TIPSOTf (4.0 equiv), which was required to ensure the complete conversion of **11** (TLC analysis) to product, were added in one portion at the beginning of the reaction then the exchange of the *tert*-butyl group for TIPS was observed and the silyl carbamate **17** was isolated.[22]

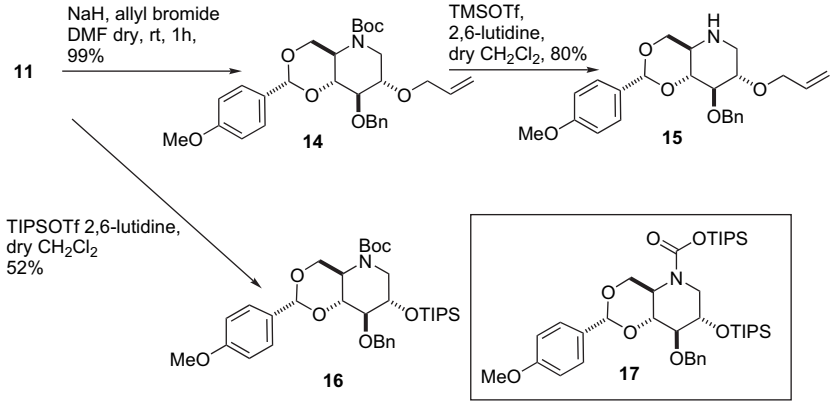
In summary, an alternative synthesis of DNJ in 30% overall yield is described from L-sorbose that also offers the opportunity for strategic grafting of pharmacophoric groups at selected hydroxyl groups of DNJ. In addition, a series of orthogonally protected DNJ derivatives are described and conditions for the selective manipulation of three protecting groups (*N*-Boc, methoxybenzylidene and Bz) are provided. The approach has potential for synthesis of pharmacologically interesting structures, including glycosidase inhibitors and peptidomimetics based on DNJ.

3. Experimental section

3.1. General

NMR spectra were recorded with a Varian 300, 400, 500 or 600 MHz spectrometers. Chemical shifts are reported relative to internal Me_4Si in $CDCl_3$ (δ 0.0) or HOD for D_2O (δ 4.79) for ^1H and D_2O (δ 77.16) for ^{13}C. ^{13}C signals were assigned with the aid of DEPT-135. ^1H NMR signals were assigned with the aid of COSY. Mass spectra were recorded on a Micromass LCT KC420 or Micromass Quattro. TLC was performed on aluminium sheets precoated with Silica Gel 60 (HF254, E. Merck) and spots visualised by UV and charring with 1:20 H_2SO_4–EtOH. Chromatography was carried out with Silica Gel 60 (0.040–0.630 mm, E. Merck) and employed a stepwise solvent polarity gradient correlated with the TLC mobility. Chromatography solvents used were EtOAc (Riedel de Haen), cyclohexane and MeOH (Sigma–Aldrich). Anhydrous DMF was used as purchased from Sigma–Aldrich. THF, dichloromethane and methanol were used as obtained from a Pure-Solv™ solvent purification system.

3.1.1. 1-*O*-Benzyl-2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose. To **3** (35.92 g, 138 mmol) in dry DMF (508 mL), NaH (60% dispersion in mineral oil, 11.06 g, 276 mmol) was added slowly at 0 °C. Then benzyl bromide (32.9 mL, 276 mmol) was added dropwise and the reaction was allowed to stir at 0 °C for 2 h. The mixture was then poured into ice and the aqueous phase extracted with diethyl ether (3×400 mL). The organic extracts were combined and dried ($MgSO_4$), filtered, the solvent was removed in vacuo and the residue was purified by chromatography (EtOAc–cyclohexane, 1:15, R_f 0.12) to afford the title compound as a colourless syrup (35.2 g, 73%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 4H, aromatic H), 7.27 (m, 1H, aromatic H), 4.72 (d, 1H, J −12.3 Hz, CH_2Ph), 4.59 (d, 1H,



Scheme 4.

J −12.3 Hz, CH_2Ph), 4.51 (s, 1H, H-3), 4.31 (d, 1H, $J_{4,5}$ 2.2 Hz, H-4), 4.08 (m, 1H, H-5), 4.05 (dd, 1H, $J_{6a,6b}$ −13.4 Hz, $J_{6a,5}$ 2.3 Hz, H-6a), 3.99 (d, 1H, $J_{6a,6b}$ −13.4 Hz, H-6b), 3.80 (d, 1H, $J_{1a,1b}$ −10.9 Hz, H-1a), 3.73 (d, 1H, $J_{1b,1a}$ −10.9 Hz, H-1b), 1.52 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (aromatic C), 128.5 (3×C, aromatic CH), 127.8 (2×d, aromatic CH), 114.3 (C), 112.5 (C), 97.5 (C), 84.5 (CH), 73.8 (CH_2), 73.5 (CH), 72.3 (CH), 70.1 (CH_2), 60.5 (CH_2), 29.1 (C), 27.8 (CH_3), 26.7 (CH_3), 18.8 (CH_3); ESI-HRMS: Calcd for $C_{19}H_{27}O_6$ 351.1808; found m/z 351.1797 $[M+H]^+$.

3.1.2. 1-*O*-Benzyl-2,3-*O*-isopropylidene-α-L-sorbofuranose 4. To 1-*O*-benzyl-2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (35.15 g, 100.3 mmol), aqueous AcOH (60%, 576 mL) was added. The mixture was stirred at 60 °C for 2 h. The solvent was then removed under diminished pressure and the residue purified by column chromatography (EtOAc–cyclohexane, 2:3, R_f 0.23) to afford **4** as a white solid (26.64 g, 85%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40–7.31 (m, 5H, aromatic H), 4.68 (d, 1H, J −11.6 Hz, CH_2Ph), 4.60 (d, 1H, J −11.6 Hz, CH_2Ph), 4.43 (s, 1H, H-3), 4.36 (dt, 1H, $J_{5,4}$ 2.9 Hz, $J_{5,6a}$ 5.2 Hz, $J_{5,4}$ 5.2 Hz, H-5), 4.17 (dd, 1H, $J_{4,5}$ 2.9 Hz, $J_{4,OH}$ 10.9 Hz, H-4), 3.93 (m, 2H, H-6), 3.84 (d, 1H, $J_{1a,1b}$ −10.0 Hz, H-1a), 3.73 (d, 1H, $J_{OH,4}$ 10.9 Hz, OH), 3.64 (d, 1H, $J_{1a,1b}$ 10.0 Hz, H-1b), 1.51 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.8 (C), 128.9 (2C), 128.5 (CH), 128.2 (2CH), 112.8 (C), 112.6 (C), 87.1 (CH), 82.0 (CH), 75.7 (CH), 74.3 (CH_2), 71.7 (CH_2), 61.6 (CH_2), 27.4 (CH_3), 26.3 (CH_3); ESI-HRMS: Calcd for $C_{16}H_{22}O_6Na$ 333.1314, found m/z 333.1328 $[M+Na]^+$.

3.1.3. 6-Azido-6-deoxy-1-*O*-benzyl-2,3-*O*-isopropylidene-α-L-sorbofuranose 5. To **4** (16.8 g, 54.2 mmol) in dry THF (180 mL) was added dry pyridine (10.5 mL, 130 mmol). The reaction mixture was stirred at 0 °C, and $SOCl_2$ (4.73 mL, 65.0 mmol) in dry THF (23 mL) was added dropwise and then the reaction mixture was stirred at 0 °C for 2 h. The solution was then filtered through Celite and washed with cold THF. The solvent was removed under diminished pressure and the crude product was dissolved in dichloromethane (300 mL) and washed with H_2O (300 mL×3). The organic layer was then dried ($MgSO_4$), filtered and the solvent was removed under diminished pressure, whilst keeping the temperature of the water bath below 35 °C, and the residue dissolved in DMF (300 mL). Sodium azide (10.6 g, 163 mmol) was then added and the reaction mixture was stirred at 110 °C overnight. The DMF was removed under diminished pressure and the residue dissolved in Et_2O (200 mL), washed with water (150 mL×3) and the organic layer was dried ($MgSO_4$), filtered, and the solvent was then removed under diminished pressure. The residue was purified by column chromatography (EtOAc–cyclohexane, 1:5, R_f 0.17) to afford **5** as a white solid (15 g, 82%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39–7.38 (m, 2H, aromatic H), 7.37–7.31 (m, 3H, aromatic H), 4.67 (d, 1H, J −11.8 Hz, CH_2Ph), 4.60 (d, 1H, J −11.8 Hz, CH_2Ph), 4.43 (s, 1H, H-3), 4.35 (ddd, 1H, $J_{5,4}$ 2.5 Hz, $J_{5,6a}$ 6.1 Hz, $J_{5,6b}$ 7.1 Hz, H-5), 4.07 (dd, 1H, $J_{4,5}$ 2.5 Hz, $J_{4,OH}$ 11.9 Hz, H-4), 3.83 (d, 1H, $J_{1a,1b}$ −9.9 Hz, H-1a), 3.61 (d, 1H, $J_{1a,1b}$ −9.9 Hz, H-1b), 3.55 (d, 1H, $J_{OH,4}$ −11.9 Hz, OH), 3.53 (dd, 1H, $J_{6a,5}$ 6.1 Hz, $J_{6a,6b}$ −12.8 Hz, H-6a), 3.49 (dd, 1H, $J_{6b,5}$ 7.1 Hz, $J_{6b,6a}$ −12.8 Hz, H-6b), 1.51 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.4 (C), 129.0 (2×CH), 128.6 (CH), 128.2 (2×CH), 112.8 (2×C), 86.8 (CH), 80.9 (CH), 74.7 (CH), 74.3 (CH_2), 71.6 (CH_2), 49.9 (CH_2), 27.3 (CH_3), 26.2 (CH_3); ESI-HRMS: Calcd for $C_{16}H_{21}N_3O_5Na$ 358.1379, found m/z 358.1387 $[M+Na]^+$.

3.1.4. 6-Azido-6-deoxy-1-*O*-benzyl-α-L-sorbofuranose 6. To **5** (5.0 g, 14.9 mmol) in CH_3CN–H_2O (1:4, 500 mL) was added Dowex-50-X8-100 (H^+) (29 g) and the mixture was stirred whilst heating at reflux for 3 h. The solvent was then evaporated under diminished pressure and the residue was purified by column chromatography (EtOAc–cyclohexane, 3:7 then 1:1, R_f =0.28) to afford **6** as a white solid (4.1 g, 92%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38–7.31 (m, 5H, aromatic H), 4.63 (2×d, 2H, J −11.8 Hz, CH_2Ph), 4.35 (dd, 1H, $J_{5,6a}$ 5.0 Hz, $J_{5,6b}$ 5.9 Hz, $J_{5,4}$ 10.7 Hz, H-5), 4.12 (m, 1H, H-4), 4.04 (s, 1H, H-3), 3.67 (d, 1H, $J_{1a,1b}$ −9.9 Hz, H-1a), 3.61 (d, 1H, $J_{1b,1a}$ −9.9 Hz, H-1b), 3.51 (dd, 1H, $J_{6a,5}$ 5.1 Hz, $J_{6a,6b}$ −12.9 Hz, H-6a), 3.46 (dd, 1H, $J_{6b,5}$ 6.0 Hz, $J_{6b,6a}$ −12.9 Hz, H-6b), 3.42 (d, 1H, $J_{OH,4}$ 9.6 Hz, OH), 2.82 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.5 (C), 128.5 (2×CH), 128.1 (CH), 127.9 (2×CH), 102.3 (C), 78.2 (CH), 78.1 (CH), 76.7 (CH), 72.4 (CH_2), 73.8 (CH_2), 50.2 (CH_2). ESI-HRMS: Calcd for $C_{13}H_{17}N_3O_5Na$ 318.1066, found m/z 318.1060 $[M+Na]^+$.

3.1.5. 1,5-Dideoxy-1,5-imino-D-glucitol 1. Sorbose derivative **6** (2.78 g, 9.41 mmol) was dissolved in MeOH (110 mL), and $Pd(OH)_2$–C 20% (670 mg) was added; the reaction mixture was stirred under an atmosphere of hydrogen (1 atm) at room temperature for 12 h. Filtration and removal of solvent gave a residue containing 6-*O*-benzyl-1,5-dideoxy-1,5-imino-D-glucitol. The residue was then dissolved in MeOH (110 mL) and a 1.2 M methanolic solution of HCl (11.2 mL) was then added and the resulting mixture was stirred at room temperature under hydrogen (1 atm) for 2 h. The reaction mixture was then filtered through Celite and evaporated in vacuo. The residue was dissolved in 1.0 M methanolic solution of HCl (28 mL) and the solvent was evaporated. The residue, dissolved in H_2O, was introduced to a Dowex-50W-X8-100 (H^+) packed ion-exchange column (pre-washed with MeOH and H_2O), washed with water (200 mL) and MeOH (100 mL) and then the product was eluted with 0.6 M aqueous solution of NH_4OH. The combined pure fractions were evaporated in vacuo to give **1** (1.28 g, 84%) as a pale orange solid. The NMR data of the free amine **1** were in excellent agreement to those reported in literature;[23] ^{1}H NMR (D_2O, 400 MHz) δ 3.70 (dd, 1H, $J_{6a,5}$ 2.9 Hz, $J_{6a,6}$ −11.6 Hz, H-6a), 3.50 (dd, 1H, $J_{6b,5}$ 6.3 Hz, $J_{6a,6b}$ −11.6 Hz, H-6b), 3.36 (ddd, 1H, $J_{2,1b}$ 5.2 Hz, $J_{2,3}$ 9.1 Hz, $J_{2,1a}$ 10.8 Hz, H-2), 3.19 (t, 1H, $J_{3,4}$ 9.0 Hz, $J_{3,2}$ 9.1 Hz, H-3), 3.10 (dd, 1H, $J_{4,3}$ 9.5 Hz, $J_{4,5}$ 9.4 Hz, H-4), 2.98 (dd, 1H, $J_{1b,2}$ 5.2 Hz, $J_{1b,1a}$ −12.3 Hz, H-1b), 2.41 (ddd, 1H, $J_{5,6a}$ 2.9 Hz, $J_{5,6b}$ 6.3 Hz, $J_{5,4}$ 9.4 Hz, H-5), 2.33 (dd, 1H, $J_{1a,2}$ 10.8 Hz, $J_{1a,1b}$ −12.3 Hz, H-1a); ^{13}C NMR (D_2O, 100 MHz) δ 79.4, 72.7, 72.1 (each CH), 62.8 (CH_2), 61.9 (CH), 50.4 (CH_2).

3.1.6. *N*-(*tert*-Butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol. To **1** (306 mg, 1.9 mmol) in DMF (4.5 mL), Boc_2O (495 mg, 2.27 mmol) was added and the mixture

was stirred at room temperature overnight. The solvent was then evaporated under diminished pressure and the residue was purified by flash column chromatography (CH_2Cl_2–MeOH, 14:1) to give the title compound (303 mg, 61%) as a white solid; ^{1}H NMR (CD_3OD, 600 MHz) δ 4.10 (dd, 1H, $J_{5,6b}$ 5.6 Hz, $J_{5,6b}$ 9.3 Hz, H-5), 3.90 (d, 1H, $J_{1a,1b}$ −13.9 Hz, H-1a), 3.80 (dd, 1H, $J_{6a,5}$ 9.3 Hz, $J_{6a,6b}$ −11.4 Hz, H-6a), 3.77 (dd, 1H, $J_{6b,5}$ 5.6 Hz, $J_{6b,6a}$ −11.4 Hz, H-6b), 3.75 (m, 1H, H-4), 3.66 (m, 2H, H-2, H-3), 3.38 (dd, 1H, $J_{1b,2}$ 1.8 Hz, $J_{1b,1a}$ −13.9 Hz, H-1b), 1.47 (s, 9H, ^{t}Bu); ^{13}C NMR (CD_3OD, 150 MHz) δ 158.2 (C), 81.4 (C), 72.4, 71.5, 70.6 (each CH), 61.3 (CH_2), 61.2 (CH), 44.3 (CH_2), 28.8 (3×CH_3). ESI-HRMS: Calcd for $C_{11}H_{20}NO_6$ 262.1291, found *m/z* 262.1280 $[M-H]^-$.

3.1.7. *N*-*tert*-Butoxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-[4-methoxybenzylidene]-D-glucitol 8. *N*-*tert*-Butoxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (200 mg, 0.76 mmol), camphorsulfonic acid (4.2 mg) and anisaldehyde dimethylacetal (258 μL, 1.5 mmol) in MeCN (4 mL) were stirred for 2 h at room temperature. Triethylamine (4 μL) was added and the solution was stirred for a further 30 min, the solvent was removed under diminished pressure and the residue purified by flash column chromatography (EtOAc–cyclohexane, 1:1) to give **8** (251 mg, 87%) as a white solid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41 (d, 2H, *J* 8.7 Hz, aromatic H), 6.90 (d, 2H, $J_{3,2}$ 8.7 Hz, aromatic H), 5.51 (s, 1H, benzylidene CH), 4.77 (dd, 1H, $J_{6a,5}$ 4.6 Hz, $J_{6a,6b}$ −11.5 Hz, H-6a), 4.40 (dd, 1H, $J_{6b,5}$ 10.8 Hz, $J_{6b,6a}$ −11.2 Hz, H-6b), 4.28 (dd, 1H, $J_{1,2}$ 4.9 Hz, $J_{1a,1b}$ −13.4 Hz, H-1a), 3.81 (s, 3H, OMe), 3.65 (m, 1H, H-2), 3.56 (m, 2H, H-3, H-4), 3.19 (ddd, 1H, $J_{5,6a}$ 4.6 Hz, $J_{5,6b}$ 10.2 Hz, $J_{5,4}$ 9.8 Hz, H-5), 2.73 (br s, 1H, OH), 2.69 (dd, 1H, $J_{1b,2}$ 10.5 Hz, $J_{1b,1a}$ −13.4 Hz, H-1b), 2.46 (br s, 1H, OH), 1.46 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.4, 154.4, 130.1 (each C), 127.9 (2×CH), 113.9 (2×CH), 101.7 (CH), 81.4 (C), 80.4 (CH), 77.2 (CH), 69.9 (CH_2), 69.7 (CH), 55.5 (CH_3), 55.0 (CH), 49.5 (CH_2), 28.6 (3×CH_3). ESI-HRMS: Calcd for $C_{19}H_{28}NO_7$ 382.1866, found *m/z* 382.1884 $[M+H]^+$.

3.1.8. 2-*O*-Benzoyl-*N*-*tert*-butoxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-(4-methoxybenzylidene)-D-glucitol 9. Benzylidene **8** and Bu_2SnO were pre-dried under vacuum over KOH overnight. Then to a mixture of **8** (700 mg, 1.8 mmol) and Bu_2SnO (914 mg, 3.7 mmol), under a nitrogen atmosphere, was added MeOH (7 mL, pre-dried over 4Å molecular sieves) and the mixture was heated at reflux overnight. The volatile materials were then evaporated and toluene was evaporated from the residue (×2). The residue was dissolved in anhydrous CH_2Cl_2 (7 mL) and placed under a nitrogen atmosphere. Dry Et_3N (291 μL, 2.09 mmol) and BzCl (213 μL, 1.836 mmol) were then added and the mixture was stirred for 1.5 h at room temperature. Aqueous $NaHCO_3$ was then added, the organic layer washed with brine, dried ($MgSO_4$), filtered and the solvent removed under diminished pressure. Chromatography of the residue (EtOAc–cyclohexane, 1:6) gave **9** (770 mg, 86%) as a white solid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.03 (d, 2H, *J* 8.5 Hz, aromatic H), 7.57 (t, 1H, *J* 7.5 Hz, aromatic H), 7.44 (dd, 2H, *J* 7.9, 8.5 Hz, aromatic H), 7.43 (d, 2H, *J* 8.5 Hz, aromatic H), 6.86 (d, 2H, *J* 8.5 Hz, aromatic H), 5.56 (s, 1H, benzylidene H), 5.05 (m, 1H, H-2), 4.79 (dd, 1H, $J_{6a,5}$ 4.5 Hz, $J_{6a,6b}$ −11.1 Hz, H-6a), 4.13 (dd, 1H, $J_{6a,6b}$ −11.1 Hz, $J_{6b,5}$ 10.6 Hz, H-6b), 4.00–3.95 (m, 2H, H-1a, H-3), 3.83 (d, 1H, $J_{4,5}$ 10.2 Hz, H-4), 3.80 (s, 3H, CH_3), 3.49 (dd, 1H, $J_{1b,2}$ 7.9 Hz, $J_{1b,1a}$ −14.5 Hz, H-1b), 3.44 (dt, 1H, $J_{5,6a}$ 4.6 Hz, $J_{5,4}$ 10.2 Hz, $J_{5,6b}$ 10.4 Hz, H-5), 2.82 (br s, 1H, OH), 1.44 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.2, 165.8, 160.3, 155.0 (each C), 133.4 (CH), 129.8 (2×CH), 129.6 (C), 128.4 (2×CH), 127.6 (2×CH), 113.7 (2×CH), 101.9 (CH), 81.2 (C), 80.1, 74.2, 73.9 (each CH), 69.8 (CH_2), 55.3 (CH_3), 52.6 (CH), 44.8 (CH_2), 28.3 (3×CH_3); ESI-HRMS: Calcd for $C_{26}H_{32}NO_8$ 486.2128, found *m/z* 486.2133 $[M+H]^+$.

3.1.9. 2-*O*-Benzoyl-3-*O*-benzyl-*N*-*tert*-butoxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-(4-methoxybenzylidene)-D-glucitol 10. To **9** (338 mg, 0.7 mmol) in dry CH_2Cl_2 (3.5 mL), in the presence of 4Å molecular sieves and under a nitrogen atmosphere, was added Ag_2O (480 mg, 2.1 mmol) and benzyl bromide (166 μL, 1.4 mmol) dropwise. The mixture was stirred at room temperature for 48 h and was then filtered through Celite and the solvent was evaporated under diminished pressure and chromatography of the residue (EtOAc–cyclohexane, 1:7) gave **10** as a white solid (295 mg, 74%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.98 (d, 2H, *J* 8.0 Hz, aromatic H), 7.57 (t, 1H, *J* 7.3 Hz, aromatic H), 7.43 (d, 2H, *J* 8.8 Hz, aromatic H), 7.42 (dd, 2H, *J* 7.4, 8.1 Hz, aromatic H), 7.32 (m, 2H, aromatic H), 7.25–7.23 (m, 3H, aromatic H), 6.91 (d, 2H, *J* 8.8 Hz, aromatic H), 5.59 (s, 1H, benzylidene H), 5.20 (ddd, 1H, $J_{2,1b}$ 3.0 Hz, $J_{2,1a}$ 3.5 Hz, $J_{2,3}$ 6.0 Hz, H-2), 4.85 (dd, 1H, $J_{6a,5}$ 4.3 Hz, $J_{6a,6b}$ −10.4 Hz, H-6a), 4.82 (s, 2H, CH_2Ph), 4.03 (dd, 1H, $J_{4,3}$ 8.5 Hz, $J_{4,5}$ 10.5 Hz, H-4), 3.96 (t, 1H, $J_{6b,5}$ 10.2 Hz, $J_{6b,6a}$ −10.4 Hz, H-6b), 3.82 (s, 3H, OMe), 3.80–3.76 (m, 2H, H-1a, H-3), 3.72 (dd, 1H, $J_{1b,2}$ 3.0 Hz, $J_{1b,1a}$ −14.2 Hz, H-1b), 3.54 (ddd, 1H, $J_{5,6a}$ 4.3 Hz, $J_{5,6b}$ 10.2 Hz, $J_{5,4}$ 10.5 Hz, H-5), 1.40 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.2, 160.0, 155.7, 137.9 (each C), 133.3 (CH), 130.1 (C), 129.8 (2×CH), 129.6 (C), 128.4 (2×CH), 128.3 (2×CH), 128.0 (2×CH), 127.7 (CH), 127.4 (2×CH), 113.6 (2×CH), 101.4 (CH), 81.1 (C), 80.3 (CH), 79.8 (CH), 73.1 (CH_2), 72.5 (CH), 70.3 (CH_2), 55.3 (CH_3), 51.3 (CH), 43.9 (CH_2), 28.2 (3×CH_3). ESI-HRMS: Calcd for $C_{33}H_{38}NO_8$ 576.2597, found *m/z* 576.2584 $[M+H]^+$.

3.1.10. 3-*O*-Benzyl-*N*-*tert*-butoxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-[4-methoxybenzylidene]-D-glucitol 11. To **10** (150 mg, 0.26 mmol) in MeOH (4.0 mL), was added KOH in MeOH (40 mg in 4.3 mL, 0.71 mmol) and the mixture was stirred at room temperature for 3 h. Amberlite IR-120 (H^+) was then added until the solution was neutral. The mixture was then filtered and the solvent evaporated. The residue was purified by chromatography (EtOAc–cyclohexane, 1:3 then 1:1) to give **11** (123 mg, 99%) as a white solid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.43 (d, 2H, *J* 8.7 Hz, aromatic H), 7.35 (m, 4H, aromatic H), 7.32 (m, 1H, aromatic H), 6.92 (d, 2H, *J* 8.7 Hz, aromatic H), 5.58 (s, 1H, benzylidene H), 5.00 (d, 1H, *J* −11.6 Hz, C*H*$_2$Ph), 4.76 (dd, 1H, $J_{6a,5}$ 4.5 Hz, $J_{6a,6b}$ −11.1 Hz, H-6a), 4.71 (d, 1H, *J* −11.6 Hz, C*H*$_2$Ph), 4.44 (dd, 1H, $J_{6b,5}$ 10.5 Hz, $J_{6b,6a}$ −11.1 Hz, H-6b), 4.19 (dd, 1H, $J_{1a,2}$ 4.8 Hz, $J_{1a,1b}$ −13.4 Hz, H-1a), 3.83 (s, 3H, OMe), 3.84–3.80 (m, 1H, H-4), 3.66 (m, 1H, H-2), 3.48 (dd, 1H, $J_{3,2}$ 8.1 Hz, $J_{3,4}$ 8.3 Hz, H-3), 3.26 (ddd, 1H, $J_{5,6a}$ 4.5 Hz, $J_{5,6b}$ 10.5 Hz,

$J_{5,4}$ 10.1 Hz, H-5), 2.79 (dd, 1H, $J_{1b,2}$ 10.1 Hz, $J_{1b,1a}$ −13.4 Hz, H-1b), 2.29 (br s, 1H, OH), 1.47 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.3, 154.6, 138.6, 130.4 (each s), 128.8 (2×CH), 128.3 (2×CH), 128.2 (CH), 127.5 (2×CH), 113.9 (2×CH), 101.2 (CH), 84.6 (CH), 81.3 (CH), 81.2 (C), 75.0 (CH_2), 70.0 (C), 69.6 (CH), 55.5 (CH), 55.3 (C), 49.3 (CH_2), 28.6 (3×CH_3); ESI-HRMS: Calcd for $C_{26}H_{34}NO_7$ 472.2335, found *m/z* 472.2354 $[M+H]^+$.

3.1.11. 2-*O*-Benzoyl-3-*O*-benzyl-*N*-*tert*-butoxycarbonyl-1,5-dideoxy-1,5-imino-6-*O*-[4-methoxybenzyl]-D-glucitol 12. A suspension of $AlCl_3$ (185 mg, 1.39 mmol) in ether (2.1 mL) was added, over 15 min, to a stirred mixture of **10** (200 mg, 0.35 mmol), Me_3NBH_3 (152 mg, 2.1 mmol) and 4Å molecular sieves in CH_2Cl_2 (7 mL) and ether (1.4 mL) at 0 °C. The mixture was then stirred for 30 min at 0 °C and then filtered through Celite and washed with aqueous $NaHCO_3$ and water. The organic phase was dried ($MgSO_4$) and the solvent was removed under diminished pressure and the residue purified by column chromatography (EtOAc–cyclohexane, 1:5) to give **12** as a colourless oil (86 mg, 43%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (d, 2H, *J* 8.2 Hz, aromatic H), 7.57 (t, 1H, *J* 7.5 Hz, aromatic H), 7.43 (dd, 2H, *J* 7.5, 8.2 Hz aromatic H), 7.33–7.28 (m, 5H, aromatic H), 7.22 (d, 2H, *J* 8.6 Hz, aromatic H), 6.86 (d, 2H, *J* 8.6 Hz, aromatic H), 5.14 (m, 1H, H-2), 4.70 (d, 1H, *J* −11.7 Hz, C*H*(H)$_2$Ar), 4.64 (d, 1H, *J* −11.7 Hz, CH(*H*)Ar), 4.49 (d, 1H, *J* −11.6 Hz, C(H)*H*Ar), 4.43 (d, 1H, *J* −11.6 Hz, C*H*(H)$_2$Ar), 4.34 (dd, 1H, $J_{5,4}$ 11.2 Hz, $J_{5,6b}$ 5.8 Hz, H-5), 4.25 (d, 1H, $J_{1a,1b}$ −15.1 Hz, H-1a), 4.07 (dd, 1H, $J_{4,OH}$ 6.0 Hz, $J_{4,5}$ 11.2 Hz, H-4), 3.80 (s, 3H, CH_3), 3.81–3.77 (overlapping of signals, 2H, H-6a, H-3), 3.70 (dd, 1H, $J_{6b,5}$ 5.8 Hz, $J_{6b,6a}$ −10.0 Hz, H-6b), 3.36 (dd, 1H, $J_{1b,2}$ 2.6 Hz, $J_{1b,1a}$ −15.1 Hz, H-1b), 2.66 (d, 1H, $J_{OH,4}$ 6.0 Hz, OH), 1.29 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.4, 158.2, 154.3, 136.5 (each C), 132.4 (CH), 129.2 (2×C), 128.7 (2×CH), 128.2 (2×CH), 127.5 (2×CH), 127.5 (2×CH), 126.9 (C), 126.7 (2×CH), 112.8 (2×CH), 79.1 (C), 77.1 (CH_2), 71.7 (2×CH_2), 71.6 (CH), 66.6 (CH), 66.2 (CH), 55.6 (CH), 54.2 (CH_3), 40.2 (CH_2), 27.1 (3×CH_3). ESI-HRMS: Calcd for $C_{33}H_{40}NO_8$ 578.2754, found *m/z* 578.2759 $[M+H]^+$.

3.1.12. 2-*O*-Benzoyl-3-*O*-benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-[4-methoxybenzylidene]-D-glucitol 13. To **10** (50 mg, 0.09 mmol) in CH_2Cl_2 (1 mL) were added, under a nitrogen atmosphere and at 0 °C, 2,6-lutidine (60 μL, 0.54 mmol) and, dropwise, TMSOTf (36 μL, 0.2 mmol). The mixture was allowed to attain room temperature and was stirred for 12 h and then poured into aqueous $NaHCO_3$ and then extracted with CH_2Cl_2 (×2). The combined organic layers were washed with brine, dried ($MgSO_4$) and the solvent was evaporated under diminished pressure. The residue was purified by column chromatography (EtOAc–cyclohexane, 1:3) to give **13** (25 mg, 61%) as a white solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.97 (d, 2H, *J* 7.8 Hz, aromatic H), 7.58 (t, 1H, *J* 7.2 Hz, aromatic H), 7.45 (d, 2H, *J* 8.8 Hz, aromatic H), 7.44 (dd, 2H, *J* 6.8, 8.2 Hz, aromatic H), 7.25–7.14 (m, 5H, aromatic H), 6.92 (d, 2H, *J* 8.8 Hz, aromatic H), 5.59 (s, 1H, benzylidene H), 5.15 (ddd, 1H, $J_{2,1a}$ 5.5 Hz, $J_{2,3}$ 10.4 Hz, $J_{2,1b}$ 10.8 Hz, H-2), 4.88 (d, 1H, *J* −11.8 Hz, C(*H*)HPh), 4.77 (d, 1H, *J* −11.8 Hz, C(H)*H*Ph), 4.32 (dd, 1H, $J_{6a,5}$ 4.4 Hz, $J_{6a,6b}$ −10.4 Hz, H-6a), 3.87–3.80 (m, 1H, H-3), 3.83 (s, 3H, OMe), 3.73–3.67 (overlapping of signals, 2H, H-4 and H-6b), 3.50 (dd, 1H, $J_{1a,2}$ 5.3 Hz, $J_{1a,1b}$ −13.6 Hz, H-1a), 2.88 (dt, 1H, $J_{5,6a}$ 4.4 Hz, *J* 9.2, 9.2 Hz, H-5), 2.72 (dd, 1H, $J_{1b,2}$ 10.8 Hz, $J_{1b,1a}$ −12.0 Hz, H-1b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 160.2, 138.4 (each CH), 133.4 (CH), 130.3 (C), 130.0 (2×CH), 128.6 (2×CH), 128.4 (2×CH), 128.3 (2×CH), 127.8 (CH), 127.5 (2×CH), 113.8 (2×CH), 101.5 (CH), 83.9 (CH), 80.1 (CH), 76.7 (C), 74.8 (CH_2), 73.3 (CH), 69.8 (CH_2), 55.5 (CH_3), 54.1 (CH), 48.0 (CH_2). ESI-HRMS: Calcd for $C_{28}H_{30}NO_6$ 476.1995, found *m/z* 476.2579 $[M+H]^+$.

3.1.13. 2-*O*-Allyl-3-*O*-benzyl-*N*-*tert*-butoxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-[4-methoxybenzylidene]-D-glucitol 14. To **11** (150 mg, 0.32 mmol) in dry DMF (10 mL) was added portionwise, at 0 °C, sodium hydride (60% mineral oil, 25 mg, 0.64 mmol) and the mixture was stirred for a few minutes and then allyl bromide (41 μL, 0.48 mmol) was added dropwise. The mixture was allowed to attain room temperature and was then stirred under a nitrogen atmosphere for 1 h. A few drops of methanol were added and the solvent was evaporated under diminished pressure and the residue purified by column chromatography (EtOAc–cyclohexane, 1:4) to give **14** (163 mg, >99%) as a colourless oil; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42 (d, 2H, *J* 8.7 Hz, aromatic H), 7.35 (d, 2H, *J* 7.0 Hz, aromatic H), 7.32–7.28 (m, 3H, aromatic H), 6.90 (d, 2H, *J* 8.7 Hz, aromatic H), 5.89 (ddt, 1H, *J* 5.5, 5.5, 10.5, 16 Hz, allyl CH), 5.54 (s, 1H, benzylidene H), 5.28 (dd, 1H, *J* 1.4, 16.0 Hz, allyl C*H*(H)), 5.17 (dd, 1H, *J* 1.4, 10.5 Hz, allyl CH(*H*)), 4.82 (d, 1H, *J* −11.5 Hz, C(*H*)HPh), 4.75 (d, 1H, *J* −11.5 Hz, C(H)*H*Ph), 4.74 (dd, 1H, $J_{6a,5}$ 4.5 Hz, $J_{6a,6b}$ −11.0 Hz, H-6a), 4.12 (dd, 1H, *J* 5.5, −12.5 Hz, allyl C(*H*)HO), 4.06 (dd, 1H, $J_{6b,5}$ 10.5 Hz, $J_{6b,6a}$ −11.0 Hz, H-6b), 4.31 (dd, 1H, *J* 5.5, 12.5 Hz, allyl C(H)*H*O), 3.84 (dd, 1H, $J_{4,3}$ 8.5 Hz, $J_{4,5}$ 10.5 Hz, H-4), 3.81 (s, 3H, OMe), 3.73 (dd, 1H, $J_{1a,2}$ 3.0 Hz, $J_{1a,1b}$ −14.0 Hz, H-1a), 3.61 (dd, 1H, $J_{3,2}$ 5.0 Hz, $J_{3,4}$ 8.5 Hz, H-3), 3.51 (m, 1H, H-2), 3.36 (dt, 1H, $J_{5,6a}$ 4.5 Hz, $J_{5,4}$ 10.5 Hz, $J_{5,6b}$ 10.5 Hz, H-5), 3.35 (d, 1H, $J_{1b,1a}$ −13.8 Hz, H-1b), 1.46 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.9, 154.2 (each C), 137.4 (CH), 133.5 (C), 129.2 (C), 127.3 (2×CH), 126.9 (2×CH), 126.6 (CH), 126.3 (2×CH), 116.0 (CH_2), 112.5 (2×CH), 100.1 (CH), 81.2 (CH), 79.8 (CH), 79.7 (C), 76.3 (CH), 72.9 (CH_2), 69.5 (CH_2), 69.1 (CH_2), 54.2 (CH_3), 51.4 (CH), 43.7 (CH_2), 27.3 (3×CH_3); ESI-HRMS: Calcd for $C_{29}H_{38}NO_7$ 512.2648, found *m/z* 512.2628 $[M+H]^+$.

3.1.14. 2-*O*-Allyl-3-*O*-benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-[4-methoxybenzylidene]-D-glucitol 15. To **14** (313 mg, 0.618 mmol) in dry CH_2Cl_2 (15 mL), under a nitrogen atmosphere at 0 °C, were added 2,6-lutidine (423 μL, 3.65 mmol) and TMSOTf (232 μL, 1.24 mmol) dropwise. The mixture was stirred at room temperature overnight and was then poured into aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with brine, dried ($MgSO_4$) and the solvent was removed under diminished pressure. The crude was purified by column chromatography (EtOAc–cyclohexane, 1:2 then 3:1), to give **15** (204 mg, 80%) as a colourless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.42 (d, 2H, *J* 8.4 Hz, aromatic H), 7.38 (d, 2H, *J* 7.4 Hz, aromatic H), 7.30 (dd, 2H, *J* 6.6, 7.7 Hz, aromatic H), 7.27–7.24 (m, 1H, aromatic H), 6.9 (d, 2H, *J* 8.4 Hz,

aromatic H), 5.92 (ddt, 1H, *J* 6.0, 6.0, 10.6, 16.2 Hz, allyl CH), 5.53 (s, 1H, benzylidene H), 5.29 (dd, 1H, *J* 1.2, 16.8 Hz, allyl C(*H*)H), 5.18 (dd, 1H, *J* 1.2, 10.4 Hz, allyl CH(*H*)), 4.91 (d, 1H, *J* −11.4 Hz, C(*H*)HPh), 4.81 (d, 1H, *J* −11.4 Hz, C*H*(H)Ph), 4.24 (dd, 1H, $J_{6a,5}$ 4.2 Hz, $J_{6a,6b}$ −10.8 Hz, H-6a), 4.23 (dd, 1H, *J* 6.0, −12.6 Hz, allyl OCH(*H*)), 4.16 (dd, 1H, *J* 6.0, −12.6 Hz, allyl OC*H*(H)), 3.82 (s, 3H, OMe), 3.61 (dd, 1H, $J_{6b,5}$ 10.2 Hz, $J_{6b,6a}$ −10.8 Hz, H-6b), 3.60 (dd, 1H, $J_{3,2}$ 7.2 Hz, $J_{3,4}$ 7.8 Hz, H-3), 3.50 (dd, 1H, $J_{4,3}$ 8.7 Hz, $J_{4,5}$ 9.0 Hz, H-4), 3.46 (ddd, 1H, $J_{2,1a}$ 5.4 Hz, $J_{2,3}$ 8.3 Hz, $J_{2,1b}$ 10.8 Hz, H-2), 3.30 (dd, 1H, $J_{1a,2}$ 5.4 Hz, $J_{1a,1b}$ −12.0 Hz, H-1a), 2.75 (ddd, 1H, $J_{5,6a}$ 4.2 Hz, $J_{5,4}$ 9.6 Hz, $J_{5,6b}$ 11.8 Hz, H-5), 2.60 (dd, 1H, $J_{1b,2}$ 10.8 Hz, $J_{1b,1a}$ −12.0 Hz, H-1b), 1.61 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.2, 139.1, 135.2 (each C), 135.2 (CH), 130.6 (C), 128.5 (2×CH), 128.2 (2×CH), 127.7 (CH), 127.5 (2×CH), 117.2 (CH_2), 113.8 (CH), 101.4 (CH), 83.7 (CH), 83.5 (CH), 79.4 (CH), 75.4 (CH_2), 72.5 (CH_2), 70.1 (CH_2), 55.5 (CH_3), 54.2 (CH), 49.2 (CH_2). ESI-HRMS: Calcd for $C_{24}H_{30}NO_5$ 412.2124, found *m*/*z* 412.2138 $[M+H]^+$.

3.1.15. 3-*O*-Benzyl-*N*-*tert*-butoxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-[4-methoxybenzylidene]-2-*O*-triisopropylsilyloxy-1-D-glucitol 16. To **11** (53 mg, 0.11 mmol) and 2,6-lutidine (39 μL, 0.34 mmol) in anhydrous CH_2Cl_2 at 0 °C, was added TIPSOTf (46 μL, 0.17 mmol) dropwise under a nitrogen atmosphere. The mixture was stirred at room temperature under a nitrogen atmosphere with the same amount of 2,6-lutidine and TIPSOTf being again added at 4 and 8 h and stirring continued overnight. The reaction mixture was washed with 5% NH_4Cl and water and the organic phase was dried ($MgSO_4$) and the solvent removed. The residue was purified by column chromatography (EtOAc–cyclohexane, 1:15) to give **16** (37 mg, 52%) as a colourless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40 (d, 2H, *J* 8.8 Hz, aromatic H), 7.34–7.25 (m, 5H, aromatic H), 6.89 (d, 2H, *J* 8.8 Hz, aromatic H), 5.54 (s, 1H, benzylidene H), 4.88 (d, 1H, *J* −11.2 Hz, C*H*(H)Ph), 4.86 (dd, 1H, $J_{6a,5}$ 4.4 Hz, $J_{6a,6b}$ −10.8 Hz, H-6a), 4.72 (d, 1H, *J* −11.2 Hz, CH(*H*)Ph), 4.06 (dd, 1H, $J_{6b,5}$ 10.4 Hz, $J_{6a,6b}$ −10.8 Hz, H-6b), 3.93 (m, 1H, H-2), 3.86 (dd, 1H, $J_{4,3}$ 8.5 Hz, $J_{4,5}$ 10.4 Hz, H-4), 3.80 (s, 3H, OMe), 3.71 (dd, 1H, $J_{1a,2}$ 2.8 Hz, $J_{1a,1b}$ −13.3 Hz, H-1a), 3.56 (dd, 1H, $J_{3,2}$ 4.4 Hz, $J_{3,4}$ 8.6 Hz, H-3), 3.41 (dt, 1H, $J_{5,6a}$ 4.4 Hz, $J_{5,6b}$ 10.4 Hz, $J_{5,4}$ 10.4 Hz, H-5), 3.33 (dd, 1H, $J_{1b,2}$ 7.2 Hz, $J_{1b,1a}$ −13.3 Hz, H-1b), 1.45 (s, 9H, ^{t}Bu), 1.07 (s, 18H, TIPS), 1.02 (m, 3H, TIPS); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.9, 154.1, 137.5, 129.3 (each C), 127.2 (2×CH), 126.9 (2×CH), 126.5 (CH), 126.3 (2×CH), 112.5 (2×CH), 100.1 (CH), 82.9 (CH), 80.8 (CH), 79.6 (C), 73.2 (CH_2), 70.5 (CH_3), 69.4 (CH_2), 54.3 (CH), 50.9 (CH), 47.2 (CH_2), 27.3 (3×CH_3), 17.0 (6×CH_3), 11.3 (3×C). ESI-HRMS: Calcd for $C_{35}H_{54}NO_7Si$ 628.3670, found *m*/*z* 628.4121 $[M+H]^+$.

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Supplementary data

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