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Synthesis of 1-deoxy-L-*gulo*nojirimycin (L-*gulo*DNJ) and 1-deoxy-D-*talo*nojirimycin (D-*talo*DNJ)

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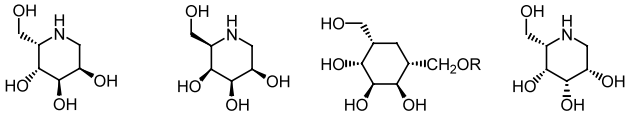
Abstract

Carbohydrate based syntheses of azasugars with unusual configurations viz. 1,5-dideoxy-1,5-imino-L-gulitol (L-*gulo*DNJ) and 1,5-dideoxy-1,5-imino-L-talitol (L-*talo*DNJ) are reported, from D-mannose and D-fructose, respectively. The key steps in both syntheses involved reductive aminative cyclizations. Thus, L-*gulo*DNJ was obtained by reduction of 2,3;4,6-di-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-D-mannononitrile with $LiAlH_4$ in DME to give the protected azasugar which upon hydrolysis with HCl afforded crystalline L-*gulo*DNJ as the HCl salt in 29% overall yield. Reduction of 6-azido-1-*O*-*tert*-butyldimethylsilyl-2,3-*O*-isopropylidene-β-D-*ribo*hexulofuranose obtained from D-fructose in six steps, followed by treatment with HCl, afforded L-*talo*DNJ as an HCl salt in ~10% overall yield.

Keywords: Azasugars; Iminosugars; Glycosidase inhibitors; L-*gulo*DNJ; D-*talo*DNJ

1. Introduction

Azasugars (also termed imino sugars) are an important class of inhibitors of glycosidases and glycosyl processing enzymes which continue to attract considerable attention.[1] Many of them are excellent agents for HIV/AIDS, cancer, and diabetes therapy.[1,2] Many syntheses of azasugars have been focused on derivatives with D-*gluco* or D-*manno* configurations.[1,2] The syntheses of L-*gulo*DNJ (**1**) and D-*talo*DNJ (**2**) are among the least of those reported. The biological activity of **1** has not yet been fully established. It is a constituent entity of a novel disaccharide **3**, a potent α-glycosidase inhibitor.[3] It is thought that L-*gulo*DNJ (**1**) could also be a potent glycosidase inhibitor and further efforts need to be made to find alternative syntheses and to evaluate its biological activities. Compound **4**, the L isomer of **2**, has also been shown to be a potent α-glucosidase and α-L-fucosidase inhibitor.[4]



1 **2** **3** R = β-D-glucopyranosyl **4**

Compound **1** has been obtained[5] during degradative analysis of a capsular polysaccharide. It was isolated as an amorphous hydroacetate. A synthesis has also been described[6] from D-mannose in eight steps; the product required separation from an enantiomer. It has been obtained in admixture with 1,5-dideoxy-1,5-mannojirimycin (DMJ) and D-*manno*-azepane derivatives from D-mannitol[7] and more recently, via an aza-Achmatowicz reaction as a peracetate.[8]

The earlier syntheses of compound **2** utilized a chemo-enzymatic approach.[9a,9b] It has also been obtained via a *syn*-aldol condensation of a protected D-erythrose derivative with stannous salts of substituted dimethoxydihydropyrazine derivatives.[10] As part of a programme to devise simplified routes to a number of azasugar derivatives, alternative syntheses of **1** and **2** from D-mannose and D-fructose, respectively, using readily available reagents, are reported.

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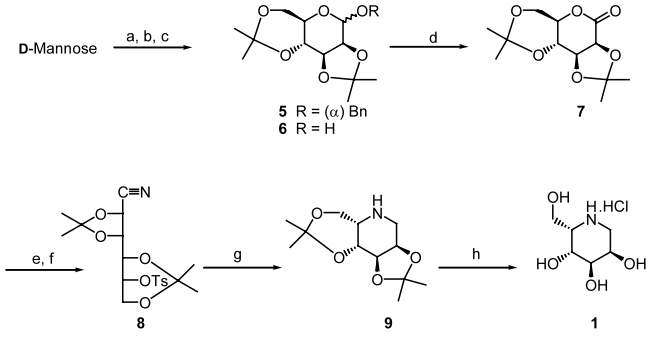
2. Results and discussion

The synthesis of L-*gulo*DNJ (**1**) from D-mannose required an aminative-cyclization process between C-1 and C-5, with inversion of configuration at C-5. This was achieved using the known[11] lactone **7**, readily obtainable by oxidation of the diacetal **6**. The direct isopropylidenation of D-mannose with 2-methoxypropene under carefully controlled conditions to give compound **6** has been described.[12] Difficulties were experienced in obtaining consistent yields using this procedure. We decided to investigate a modified approach for preparing **6**. Thus, D-mannose was reacted with benzyl alcohol in the presence of BF_3–methanol complex (50–52%, BF_3) and the crude material obtained was treated with a mixture of 2,2-dimethoxypropane and acetone containing *p*-toluenesulfonic acid. Catalytic hydrogenolysis of the product **5** in the presence of palladized charcoal (10%) gave the known diacetal **6** in 67.5% overall yield. Standard Swern oxidation[13] of **6** gave the lactone **7**. Treatment of **7** in 1:1 ammoniacal methanol solution with ammonia gas at 0 °C followed by reaction of the crude product with excess *p*-toluenesulfonyl chloride in anhydrous pyridine gave the activated nitrile derivative **8**. Reduction of **8** with $LiAlH_4$ in 1,2-dimethoxyethane at 0 °C occurred with concomitant cyclization to give the protected azasugar **9** which on hydrolysis with HCl afforded crystalline L-*gulo*DNJ (**1**) as its HCl salt in 29% overall yield. The route compares favorably with preexisting ones and could be used to produce **1** in considerable quantities if required (Scheme 1).

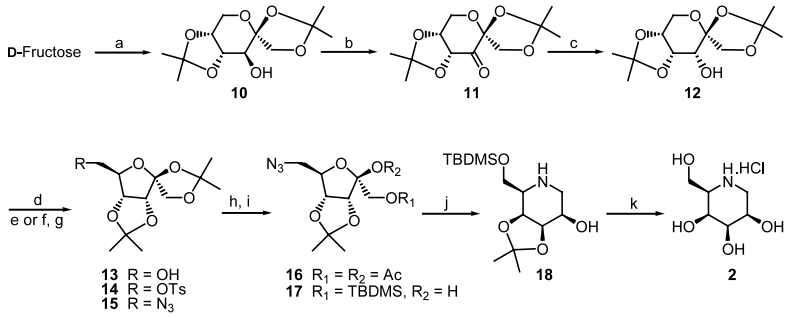
The envisaged route to compound **2** was from D-fructose via 1,2;4,5-di-*O*-isopropylidene-β-D-*ribo*hexulofuranose (**13**). The use of D-fructose for the synthesis of azasugars is rather limited. It has been used in a simple synthesis of 1-deoxymannojirimycin.[14] Treatment of D-fructose with acetone in the presence of a catalytic amount of elemental iodine at room temperature gave the kinetically favored 1,2;4,5-di-*O*-isopropylidene-β-D-fructopyranose (**10**).[15] Compound **12** was obtained from pure **10**, via the diulose **11** using a known[16] oxidation-selective reduction sequence. Treatment of **12** with 2,2-dimethoxypropane in acetone, in the presence of a catalytic quantity of 70% perchloric acid, gave the thermodynamically more stable re-arrangement product **13** (92.5%). The C-6 primary hydroxyl group of compound **13** was converted into the corresponding azido derivative, 6-azido-6-deoxy-1,2;4,5-di-*O*-isopropylidene-β-D-*ribo*hexulofuranose (**15**) using two different procedures. The first method,[17] which is a one-pot reaction sequence, involved treatment of compound **13** with 1-methyl-2-fluoropyridinium tosylate followed by reaction with LiN_3[18] in 1-methyl-2-pyrrolidinone to give compound **15** (>80%). The second procedure involved treatment of **13** with *p*-toluenesulfonyl chloride–pyridine in the usual manner,[19] to give the tosylate derivative **14**, followed by reaction with LiN_3[18] in DMF at ~40 °C to afford **15** in 76% yield, for the two-stage process. The beneficial use of LiN_3 in nucleophilic displacement reactions has been reviewed.[20] The following step in the projected synthesis of **2** required removal of the 1,2-*O*-isopropylidene group from **15**. Acid hydrolysis of 1,2-*O*-acetal groups of ketose derivatives is sometimes problematical[21] leading to considerable decomposition. Mild acetolysis of the 1,2-*O*-isopropylidene group of compound **15** by treatment with acetic anhydride in the presence of a catalytic quantity of BF_3–etherate gave the diacetate **16**. Deacetylation (Zemplén) of **16** followed by reaction with *tert*-butyldimethylsilylchloride–imidazole gave the selectively protected compound **17**. It was noteworthy that the 3,4-*O*-isopropylidene group of **15** remained unaffected by this treatment, which indicated the stability of the cis-fused 5:5 bicyclic ring system. Catalytic hydrogenation (Pd–C) of **17** in EtOH afforded 6-*O*-*tert*-butyldimethylsilyl-1-deoxy-3,4-*O*-isopropylidene-D-*talo*nojirimycin (**18**). Treatment of compound **18** with HCl in MeOH gave D-*talo*DNJ (**2**), as the HCl salt in ~10% overall yield. Efforts were made to crystallize the free azasugar or the HCl salt from various solvent mixtures. These were mainly unsuccessful, but the compound eventually crystallized well from MeOH–ether, but attempts to dry the resulting material proved to be extremely difficult as the crystals were highly deliquescent (Scheme 2).



Scheme 1. Reagents and conditions: (a) BnOH–BF_3, MeOH (b) DMP–Me_2CO, TsOH (c) H_2, Pd–C (d) Me_2SO–TFAA, CH_2Cl_2 (e) NH_3–NH_4OH, MeOH (f) TsCl, Py (g) H_2, $LiAlH_4$, DME, 0 °C (h) HCl.

3. Experimental

Melting points were determined using a Reichert thermopan microscope equipped with cross polarizers and are uncorrected. IR spectra were determined on a Perkin–Elmer 298 spectrophotometer. Optical rotations were determined with a Perkin–Elmer automatic polarimeter model 241 MC on 1% solutions in the



Scheme 2. Reagents and conditions: (a) $Me_2CO–I_2$ (b) TFAA–Me_2SO, CH_2Cl_2 (c) $NaBH_4$–EtOH (d) DMP–Me_2CO, $HClO_4$ (e) 1-methyl-2-fluoropyridinium toluenesulfonate, LiN_3–1-methyl-2-pyrollidinone or (f) TsCl–Py, (g) LiN_3–DMF (h) $Ac_2O–BF_3{\cdot}OEt_2$ (i) NaOMe–MeOH, TBDMSCl–DMF, imidazole (j) H_2, Pd–C, EtOH (k) HCl–MeOH.

solvents indicated. Column chromatography was performed using Silica Gel (E. Merck) using the eluents indicated. Thin-layer chromatography (TLC) on precoated plates of Silica Gel GF_{254} (E. Merck) was conducted in the solvent mixtures given. Compounds were detected by spraying with 3% H_2SO_4 in EtOH followed by heating at 140 °C. ^1H and ^{13}C NMR were recorded on Brucker AC 100 (100 MHz), AC 300 (300 MHz) and Varian AM 400 (400 MHz) spectrometers at rt on solutions in $CDCl_3$ (internal Me_4Si) or D_2O (external 1,4-dioxane, 76.8 ppm). 1-Methyl-2-fluoropyridinium tosylate was purchased from Aldrich.

2,3;4,6-Di-O-*isopropylidene*-D-*mannopyranose* (**6**).—A stirred suspension of D-mannose (10 g) in benzyl alcohol (200 mL) was treated with $BF_3{\cdot}MeOH$ complex (50–52%, BF_3; 1.4 mL) and the mixture was maintained overnight at ca. 75 °C. The cooled mixture was neutralized with solid $NaHCO_3$ (pH paper), filtered, and concentrated in vacuo to give an oil which was dissolved in water (200 mL), extracted with ether (2 × 150 mL), and the aqueous layer was decolorized by treatment with charcoal, concentrated in vacuo and EtOAc (2 × 50 mL), and distilled from the residue to give a pale brown syrup. A stirred solution of the resultant material in acetone (70 mL) and 2,2-dimethoxypropane (70 mL) was treated with *p*-toluenesulfonic acid monohydrate (40 mg) and set aside at rt for 4 h, when analysis (TLC; 3:2 1,2-dimethoxyethane–cyclohexane) indicated completeness of reaction. The mixture was neutralized ($NaHCO_3$), filtered, concentrated in vacuo, and a solution of the crude product in EtOH (40 mL) was hydrogenated (1 atm) in the presence of palladium charcoal (10%, 600 mg) for 48 h. The mixture was filtered through Celite, the inorganic material washed with EtOH and the combined filtrate and washings concentrated in vacuo. Column chromatography (3:1 hexane–EtOAc) of the residue gave pure **6** (9.7 g, 67.5%): mp 137–140 °C (petroleum ether, 80–100 °C), lit.[12] mp 139–141 °C; $[\alpha]_D$ −33.2° ($CHCl_3$), lit.[12] $[\alpha]_D$ −39° ($CHCl_3$).

2,3;4,6-Di-O-*isopropylidene*-D-*mannono*-*1,5*-*lactone* (**7**).—Treatment of **6** under standard Swern oxidation[13] conditions gave pure **7** (3.3 g, 82.8%) as fine fiber-like crystals: mp 200–201 °C (petroleum ether, 80–100 °C), lit.[11] mp 202 °C; $[\alpha]_D$ +46.4° ($CHCl_3$), lit.[11] $[\alpha]_D$ +43.5°.

2,3;4,6-Di-O-*isopropylidene*-*5*-O-p-*toluenesulfonyl*-D-*mannononitrile* (**8**).—A stirred cooled solution of the lactone **7** (3 g, 11.58 mmol) in a mixture of MeOH (30 mL) and 25% aq ammonia solution (30 mL) was treated with ammonia gas for 10 min and then left to stir at rt for 30 min. The mixture was concentrated in vacuo to give a colorless foam which was dissolved in anhyd pyridine (30 mL), cooled to 0 °C, treated with tosyl chloride (8.83 g, 46.33 mmol, 4 equiv), and after a further 1 h at this temperature, was set aside at ca. 5 °C for 5 days. The mixture was poured into ice water (200 mL) and the resultant white solid was collected by filtration and recrystallized (MeOH) to give the nitrile **8** (3.4 g, 71.4%): mp 129–131 °C; $[\alpha]_D$ −11.06° ($CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84, 7.34 (ABq, 4 H, aromatic H), 4.8 (d, 1 H, $J_{2,3}$ 4.72 Hz, H-2), 4.75 (t, 1 H, $J_{4,3}$ 9.2, $J_{4,5}$ 9.0 Hz, H-4), 4.28 (ddd, 2 H, $J_{6,5}$ 6.8, $J_{6a,6b}$ 12.7 Hz, H-6a, H-6b), 4.2 (t, 1 H, $J_{3,2}$ 4.9, $J_{3,4}$ 9.0 Hz, H-3), 4.10 (m, 1 H, H-5), 2.4 (s, 3 H, tosyl Me), 1.48, 1.35, 1.14, 1.30 (4s, each 3 H, CMe_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.90, 133.62,129.33, 128.65, (C_{arom}), 116.59 (C≡N), 111.42 and 111.336 (2qC), 80.27 (C-2), 77.48 (C-3), 74.34 (C-4), 67.95 (C-6), 66.48 (C-5), 26.38, 25.67, 25.58, 25.45 (2 × CMe_2) and 21.60 (tosyl Me). Anal. Calcd for $C_{19}H_{25}NSO_7$: C, 55.46; H, 6.12; N, 3.40; S, 7.79. Found: C, 55.32; H, 6.07; N, 3.47; S, 7.92.

1-Deoxy-2,3;4,6-di-O-*isopropylidene*-L-*gulonojirimycin* (**9**).—A solution of the nitrile **8** (1.75 g, 4.26 mmol) in dry 1,2-dimethoxyethane (20 mL) was added dropwise over 10 min to a stirred, cooled (0 °C) suspension of $LiAlH_4$ (0.647 g, 17.03 mmol, 4 equiv) in 1,2-dimethoxyethane (20 mL) maintained under nitrogen. The mixture was set aside for 4 h, diluted with 1,2-dimethoxyethane (40 mL), treated dropwise over 15

min with water (6 mL), set aside for 30 min, filtered through a layer (~ 1 cm) of $MgSO_4$, and the inorganic material was washed with 1,2-dimethoxyethane (10 mL). The combined filtrate and washings were concentrated in vacuo to yield a colorless syrup (1.12 g), which crystallized on standing. Recystallization (diisopropyl ether) gave **9** (0.860 g, 83%): mp 55–57 °C; $[\alpha]_D$ −23.8° ($CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.75–4.71 (m, 1 H, H-2), 4.50 (dd, 1 H, H-4), 4.05 (m, 2 H, H-6a, H-6b), 3.85 (t, 1 H, H-5), 3.15 (dd, 1 H, H-3), 3.06 (t, 2 H, H-1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 111.50 and 109.34 (2 × qC), 83.93 (C-2), 82.130 (C-3), 75.90 (C-4), 66.80 (C-5), 66.76 (C-6), 53.08 (C-1), 26.42, 25.28, and 24.14 (CMe_2). Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.00; H, 8.57; N, 5.64.

1-Deoxy-L-*gulonojirimycin.HCl* (**1**).—A stirred solution of a portion of the foregoing product (100 mg) in MeOH (20 mL) containing concd HCl (5 drops) was maintained at rt for 18 h, when charcoal (20 mg) was added. The mixture was heated under reflux for 20 min, cooled, filtered, the residue washed with MeOH (10 mL), and the combined filtrate and washings were concentrated in vacuo to give a colorless gum. The crude gum was crystallized from MeOH–ether to give **1**·HCl salt (103 mg, 90%): mp 143 °C, lit.[2] (free base) mp 150–151 °C; $[\alpha]_D$ −45.0° (MeOH), lit.[2] (free base) $[\alpha]_{578}$ −21° (water); ^{1}H NMR (D_2O, 300 MHz): δ 4.31 (m, 1 H, H-2), 4.21 (dd, 1 H, H-4), 3.80–3.75 (m, 1 H, H-3), 3.66–3.61 (m, 1 H, H-5), 3.56–3.49 (m, 1 H, H-6a, H-6b), 3.21–3.15 (m, 1 H, H-6a, H-6b), 3.04–3.00 (m, 1 H, H-1a, H-1b), 2.87–2.82 (m, 1 H, H-1a, H-1b). ^{13}C NMR (D_2O, 75 MHz): δ 74.57(C-5), 71.69/70.19 (C-3, C-4), 65.82 (C-1), 64.19 (C-2), 52.29 (C-6). Anal. Calcd for $C_6H_{14}ClNO_4$: C, 36.10; H, 7.07; N, 7.02. Found: C, 35.92; H, 6.98; N, 6.91.

6-Azido-6-deoxy-1,2;3,4-di-O-*isopropylidene-β*-D-ribo*hexulofuranose* (**15**)

Method A. Compound **13**[16,19] (5.12 g, 19.69 mmol) was added to a stirred suspension of 1-methyl-2-fluoropyridinium toluenesulfonate (6.13 g, 21.66 mmol, 1.1 equiv) in $CHCl_3$ (200 mL) containing triethylamine (3 mL). The mixture was stirred for 1 h and then concentrated in vacuo to give a yellowish–orange syrup which was dissolved in 1-methyl-2-pyrrolidinone (50 mL) treated with LiN_3[18] (4.82 g, 98.46 mmol, 5 equiv) and maintained at 80 °C for 2 h. The cooled mixture was poured into ice-water (150 mL), extracted with ether (2 × 150 mL), and the combined ether extracts washed with brine (60 mL), dried (Na_2SO_4), and concentrated in vacuo. Column chromatography (1:1 hexane–EtOAc) of the residue gave **15** as a colorless syrup (4.6 g, 82%): $[\alpha]_D$ +4.0° ($CHCl_3$); IR(neat) ν_{max} 2100 (–N=N=N) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.6 (dd, 2 H, $J_{1a,1b}$ 6.3, $J_{1a,1b}$ 12.2 Hz, H-1a, H-1b), 4.33 (d, 1 H, $J_{3,4}$ 9.8 Hz, H-3, H-4), 4.20 (t, 1 H, $J_{5,6}$ 7.10 Hz, H-5), 4.06 (d, 1 H, $J_{4,3}$ 9.8 Hz, H-4, H-3), 3.54 (dd, 1 H, $J_{6,5}$ 7.56, $J_{6a,6b}$ 12.5 Hz, H-6a, H-6b), 3.30 (dd, 1 H, $J_{6,5}$ 7.13, $J_{6b,a}$ 12.8 Hz, H-6b, H-6a), 1.44, 1.43, 1.34, 1.32 (4s, each 3 H, CMe_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 113.8 (C-2), 112.92, 111.92 (2 × qC), 85.19 (C-5), 84.08, 82.32 (C-3, C-4), 53.22 (C-6), 26.4, 26.36, 26.20, 25.10 (4 × CMe_2).

Method B. A stirred solution of **14**[19] (2.0 g, 4.83 mmol) in DMF (10 mL) containing LiN_3 (0.71 g, 14.5 mmol) was maintained at 40 °C for 6 days. The mixture was poured into a mixture of ice-water (30 mL) and ether (30 mL). The separated aqueous layer was extracted with ether (3 × 30 mL) and the combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and concentrated in vacuo. Column chromatography (3:2 1,2-dimethoxyethane–cyclohexane) of the resultant material gave **15** (1.05 g, 76%) as an oil: $[\alpha]_D$ +38° ($CHCl_3$). The spectral characteristics were identical to those given above.

1,2-Di-O-*acetyl-3,4*-O-*isopropylidene-6-azido-6-deoxy-β*-D-ribo*hexulofuranose* (**16**).—A stirred, cooled (0 °C) solution of the azide **15** (4.3 g, 15.08 mmol) in Ac_2O (74 mL) containing BF_3·OEt_2 (0.37 mL) was set aside for 2 h. The mixture was then poured into ice cold satd aq $NaHCO_3$ solution with vigorous stirring and left to stand at rt until effervescence had ceased. The mixture was extracted with CH_2Cl_2 (2 × 100 mL) and the combined organic extracts dried (Na_2SO_4) and concentrated in vacuo to give a crude syrup. Column chromatography (3:1 hexane–EtOAc) of the crude material gave compound **16** as a colorless syrup (4.8 g, 94.7%): $[\alpha]_D$ +16.4° ($CHCl_3$); IR(neat) ν_{max} 2100 (N=N=N), 1740 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.95 (d, 1 H, $J_{3,4}$ 6.07 Hz, H-3), 4.76 (dd, 1 H, $J_{4,5}$ 2.35 Hz, H-4), 4.65 (d, 1 H, $J_{1a,1b}$ 11.94 Hz, H-1a), 4.58 (d, 1 H, H-1b), 4.36 (td, 1 H, H-5), 3.55 (dd, 1 H, $J_{6a,5}$ 6.98, $J_{6a,6b}$ 12.71 Hz, H-6a), 3.35 (dd, 1 H, $J_{6b,5}$ 6.24 Hz, H-6b), 2.1, 2.08 (s, 6 H, 2 × CH_3CO), 1.51, 1.33 (2s, each 3 H, CMe_2). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 170.0, 169.20 (2 × CH_3CO), 114.14 (C-2), 110.64 (qC-acetal), 86.41 (C-5), 85.30, 82.02 (C-3, C-4), 62.43 (C-1), 52.74 (C-6), 26.44, 25.00 ($C(CH_3)_2$ acetal), 21.91, 20.78 (2 × CH_3CO).

6-Azido-1-O-tert-*butyldimethylsilyl-3,4*-O-*isopropylidene-β*-D-ribo*hexulofuranose* (**17**).—A stirred solution of compound **16** in MeOH (60 mL) was treated with 0.5% methanolic NaOMe (17 mL) and after a period of 5 min was neutralized with Amberlite IR-120 ion-exchange resin (H^+ form), filtered and the filtrate concentrated in vacuo. Column chromatography (1:1 hexane–EtOAc) of the brown residue gave a colorless syrup (2.35 g) which was dissolved in DMF (10 mL), cooled to 0 °C, treated with a mixture of *tert*-butyldimethylsilylchloride (5.06 g, 33.57 mmol) and imidazole (6.52 g, 96.0 mmol) and, after 5 min, was set aside at rt for a further 30 min. Ether (200 mL) was

added to the mixture which was then washed successively with water (3×50 mL), brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give compound **17** (2.80, 81.0%) as a colorless syrup: $[\alpha]_D$ −12.7° ($CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 4.62 (m, 2 H, H-6), 4.25 (t, 1 H, $J_{5,6}$ 7.43, 7.02 Hz, H-5), 4.12 (br s, OH), 3.80 (dd, 1 H, $J_{1a,1b}$ 10.54 Hz, H-1a, H-1b), 3.63 (m, 1 H, $J_{1b,1a}$ 9.2 Hz, H-1b, H-1b), 3.42 (d, 1 H, $J_{3,4}$ 5.1 Hz, H-3, H-4), 3.20 (dd, 1 H, $J_{4,3}$ 6.6 Hz, H-4, H-3), 1.46, 1.31 (2s, each 3 H, CMe_2), 0.92, 0.91 (2s, 9 H, CMe_3), 0.12, 0.09 (s, 6 H, 2 $SiMe_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 112.74 (C-2), 105.98 (qC-acetal), 85.35 (C-1), 84.89, 82.69 (C-3, C-4), 64.61 (C-5), 53.42 (C-6), 26.52, 26.31 ($2 \times CMe_2$), 25.73, 25.14, 24.95 ($3 \times CMe_3$-*tert*-butyl), 2×18.22 ($2 \times SiMe_2$).

6-O-tert-*Butyldimethylsilyl-1-deoxy-3,4*-O-*isopropylidene*-D-talo*nojirimycin* (**18**).—A solution of compound **17** (2.0 g, 5.57 mmol) in EtOH (20 mL) was treated with palladized charcoal (10%, 0.2 g) and then hydrogenated (1 atm) at rt for 18 h. The mixture was filtered through a layer of Celite, and the inorganic material was washed with EtOH (10 mL) and the combined filtrate and washings concentrated in vacuo. Column chromatography (4:1 CH_2Cl_2–MeOH) of the material gave pure **19** (1.52 g, 86.1%) as white crystals: mp 69–70 °C; $[\alpha]_D$ +16.0° ($CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 4.15 (dd, 1 H, $J_{3,2}$ 3.03 Hz, H-3), 4.04 (t, 1 H, $J_{5,6}$ 5.60 Hz, H-5), 3.69 (t, 2 H, $J_{6,5}$ 1.5, $J_{6a,6b,}$ 5.9 Hz, H-6a, H-6b), 3.68 (s, 1 H, H-4), 3.12 (dd, 1 H, $J_{1,2}$ 3.93, $J_{1a,1b}$ 9.1 Hz, H-1a), 2.93 (m, 1 H, H-2), 2.6 (dd, 1 H, $J_{1b,2}$ 1.42, $J_{1b,1a}$ 11.6 Hz, H-1b), 1.55, 1.33 (2s, each 3 H, CMe_2), 0.87 (3s, each 3 H, CMe_3), 0.05 (2s, each 3 H, $SiMe_2$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 109.10 (qC-acetal), 74.42 (C-3), 71.68 (C-2), 64.49 (C-6), 63.57 (C-4), 57.65 (C-5), 48.34 (C-1), 25.84, 25.42 ($2 \times CMe_2$). Anal. Calcd for $C_{15}H_{31}NSiO_4$: C, 56.75; H, 9.84; N, 4.41. Found: C, 56.33; H, 9.48; N, 4.40.

1-Deoxy-D-talo*nojirimycin·HCl* (**2**).—A stirred solution of a portion of the foregoing compound **18** (100 mg) in MeOH (10 mL) containing HCl (5 drops) was kept at rt for 18 h, treated with activated charcoal (20 mg), heated under reflux for ~20 min, filtered, and the filtrate concentrated in vacuo to give a colorless gum which crystallized from 3:1 MeOH–ether to give **2** as very hygroscopic white crystals: $[\alpha]_D$ −20.96° (MeOH), lit.[4] $[\alpha]_D$ −22.4° (MeOH); ^1H NMR (D_2O, 300 MHz): δ 4.18 (m, 1 H, H-3), 4.10 (m, 1 H, H-5), 3.83 (s, 1 H, H-4), 3.79 (t, 2 H, H-6), 3.45 (dd, 1 H, H-1a), 3.34 (ddd, 1 H, H-2) 3.20 (dd, 1 H, H-1b). ^{13}C NMR (D_2O, 75 MHz): δ 70.03 (C-3), 69.53 (C-4), 69.04 (C-2), 62.80 (C-6), 61.56 (C-5), 50.73 (C-1).

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