Carbohydrate Research, 164 (1987) 141-148
Elsevier Science Publishers B.V., Amsterdam - Printed in The Netherlands

THE CHEMISTRY OF THE 1-DEOXYNOJIRIMYCIN SYSTEM. SYNTHESIS OF 2-ACETAMIDO-1,2-DIDEOXYNOJIRIMYCIN FROM 1-DEOXYNOJIRIMYCIN

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(Received September 15th, 1986; accepted for publication in revised form, October 20th, 1986)

ABSTRACT

The synthesis of 2-acetamido-1,2-dideoxynojirimycin (2-acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol) by a double inversion procedure starting from 1-deoxynojirimycin is reported. The key intermediates were the selectively protected *N*-benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-mannitol, the triflate ester *N*-benzyl-3-*O*-benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-2-*O*-(trifluoromethylsulfonyl)-D-mannitol, and 2-azido-*N*-benzyl-3-*O*-benzyl-1,2,5-trideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol, readily obtained in a sequence from 1-deoxynojirimycin. Thus 1-deoxynojirimycin served as a synthon compatible with the basic operations of carbohydrate chemistry.

INTRODUCTION

In the course of our research on inhibitors of intestinal α-glucosidases potentially useful for the control of diabetes mellitus, we noted the report of Kinast and Schedel[1] describing a short synthesis of the natural compound 1-deoxynojirimycin (**1**). This synthesis, starting from D-glucose and employing a combined chemical-microbiological reaction sequence, makes available the 1-deoxypiperidinose of the D-*gluco* configuration, which until then was accessible only by tedious synthetic routes[2]. More recently several additional papers have appeared dealing with the synthesis of polyhydroxy-substituted piperidines and pyrrolidines from carbohydrates[3]. We were therefore led to examine the extent to which well known methods in carbohydrate chemistry can be used to accomplish chemical modifications of the deoxynojirimycin system. Herein, we report the synthesis of 2-acetamido-1,2-dideoxynojirimycin (**2**) from 1-deoxynojirimycin. The product piperidinose **2** is an analogoue of *N*-acetyl-D-glucosamine, and hence potentially useful for inhibition studies of β-*N*-acetylhexosaminidases.

*Dedicated to my respected teacher Prof. Burckhardt Helferich on the occasion of his 100th anniversary.
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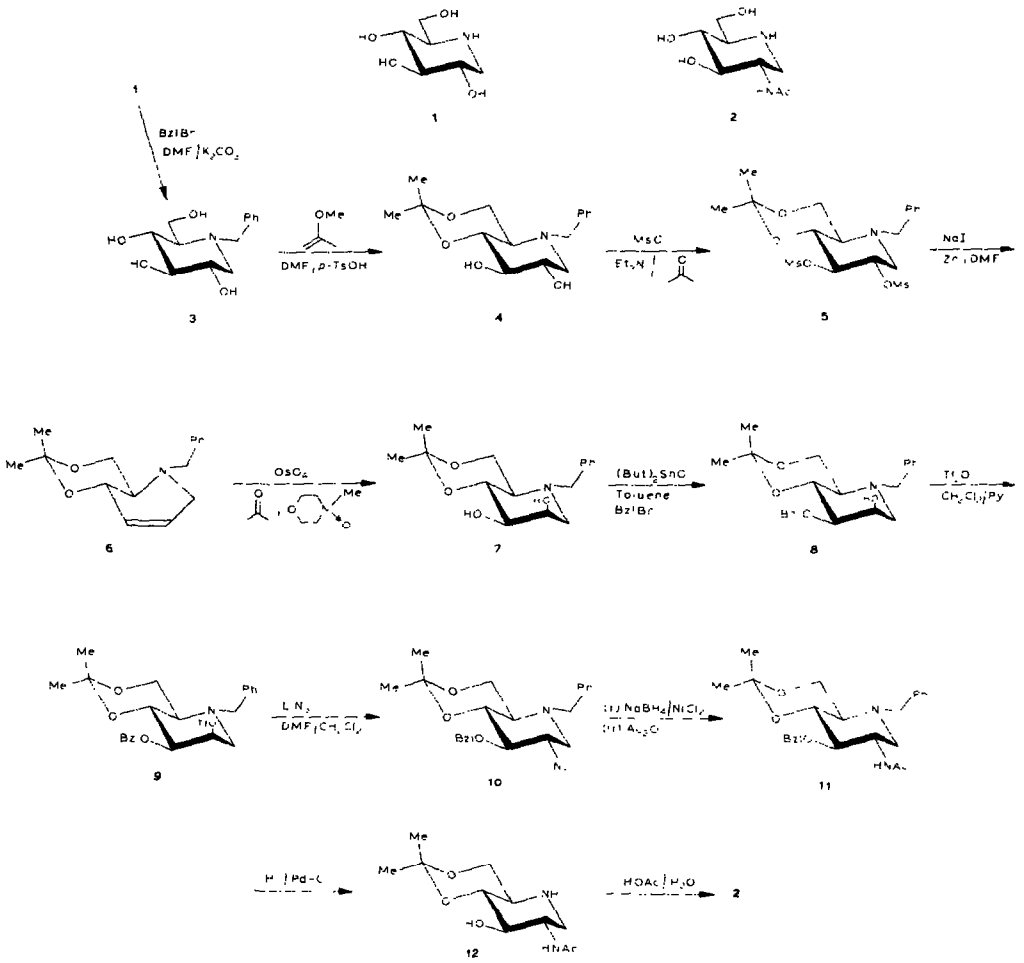
0008-6215/87/$ 03.50

As the target compound **2** has the D-*gluco* configuration, a strategy employing **1** as a precursor necessitates a double inversion at position 2 of the molecule. This in turn requires the synthesis of a derivative of deoxynojirimycin having the D-*manno* configuration, and a pattern of protecting groups that allows for the simultaneous inversion and introduction of a nitrogen substituent at position 2.

RESULTS AND DISCUSSION



The key step in our synthesis of **2** is the displacement by the azide nucleophile of the trifluoromethanesulfonate (triflate) group in position 2 of the D-*manno* compound **9**. Compound **8**, the precursor of this triflateester was obtained in excellent yield from **1**. First, the *N*-alkylation of **1** with benzyl bromide and potassium carbonate in *N*,*N*-dimethylformamide led to the ring-nitrogen protected compound **3**.

The subsequent monoisopropylidenation of **3** was easily achieved with isopropenyl methyl ether–*p*-toluenesulfonic acid in *N*,*N*-dimethylformamide, giving the acetal **4** in 85% yield, crystalline after flash chromatography.

The reaction of **4** with methanesulfonyl chloride in acetone–triethylamine produced the crystalline dimesyl compound **5** in 97% yield. The mesylate **5** was then treated with sodium iodide–zinc in *N*,*N*-dimethylformamide under the conditions described by Tipson and Cohen[4] slightly modified. This reaction led smoothly to the olefin **6**, which was obtained in 70% yield after column chromatography, and proved to be a stable compound. The *cis*-hydroxylation of olefin **6** was accomplished with a catalytic amount of osmium (VIII) oxide, and *N*-methylmorpholine *N*-oxide as the oxygen source[5], to give the the D-*manno* compound **7** diastereoselectively. On short column chromatography **7** was isolated in 75% yield and in crystalline form, suitable for the following steps.

On reaction with dibutyltin oxide–benzyl bromide in toluene the equatorial hydroxyl group in position 3 was selectively protected[6]. Compound **8**, having an unprotected hydroxy group in position 2, was obtained in 73% yield. The esterification of **8** with triflic anhydride in dichloromethane–pyridine then gave triflic ester **9**. On reaction with lithium azide in dichloromethane–*N*,*N*-dimethylformamide, this highly reactive compound selectively formed the D-*gluco* 2-azido product **10** in 74% yield. Compound **10** was easily transformed into the amide **11** by the successive action of sodium borohydride–nickel chloride and acetic anhydride. Hydrogenation and acid hydrolysis of the isopropylidene acetal provided a quantitative yield of the title compound **2**.

All intermediates in the synthetic sequence were characterized by high field ^{1}H-n.m.r. spectroscopy, and mass spectra and analytical data confirmed the proposed structures. Except for the olefin **6** all the compounds adopt the $^4C_1$ conformation in solution. The ^{1}H-n.m.r. spectrum and melting point of **2** are in good agreement with the data recently presented by G.W.J. Fleet[7], who describes the synthesis of **2** starting from D-glucose.

EXPERIMENTAL

General methods. — Melting points were measured on a Büchi 520 apparatus and are corrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. N.m.r. spectra were recorded with Bruker WM-250 and WM-300 instruments. ^{1}H-Spectra taken in chloroform-*d* or benzene-d_6 solutions were referenced to internal tetramethylsilane. For spectra measured in D_2O, the HDO signal was the reference signal. First-order character was assumed in calculating coupling constants. Thin-layer chromatography was performed on Merck 5562 foil; for column chromatography we used silica gel 60, 230–400 mesh (Merck, Darmstadt, F.R.G.).

N-Benzyl-1,5-dideoxy-1,5-imino-D-glucitol (**3**). — First 163.2 g (1.0 mol) of deoxynojirimycin was suspended in 2.5 L of *N*,*N*-dimethylformamide, 76.0 g (0.55

mol) of potassium carbonate was added, and the suspension was cooled to 0°. Then 188.1 g (1.1 mol) of benzyl bromide was added dropwise over the course of 30 min. After about 120 min the starting material was completely consumed, as judged by t.l.c. in 4:3:1 $CHCl_3$–MeOH–aq. NH_3 (detection with $KMnO_4$). A small portion was withdrawn and purified, after removal of the solvent, by column chromatography on silica gel with 4:1 chloroform–methanol as eluent. The compound obtained was a crystalline solid, m.p. 181°, $[\alpha]_D^{20}$ −48.3° (*c* 1.0, methanol); m.s.: *m/z* 254 ($M + 1^+$); ^{1}H-n.m.r. (300 MHz, CD_3OD): δ 1.84 (dd, 1 H, $J_{1a,1e} = J_{1a,2}$ 10.7 Hz, H-1a), 2.09 (ddd, 1 H, $J_{5,6a}$ 2.2, $J_{5,6b}$ 3.1, $J_{5,4}$ 9.2 Hz, H-5), 2.81 (dd, 1 H, $J_{1e,2}$ 4.9 Hz, H-1e), 3.09 (dd, 1 H, $J_{2,3} = J_{3,4}$ 9.2 Hz, H-3), 3.21 (d, 1 H, J_{AB} 13.2 Hz, PhCH_2), 3.34 (ddd, 1 H, H-2), 3.37 (dd, 1 H, H-4), 3.89 (dd, 1 H, $J_{6a,6b}$ 11.9 Hz, H-6b), 4.05 (dd, 1 H, H-6a), and 4.20 (d, 1 H, PhCH_2).

Anal. Calc. for $C_{13}H_{19}NO_4$: C, 61.7; H, 7.6; N, 5.5. Found: C, 61.6; H, 7.5; N, 5.3.

N-*Benzyl-1,5-dideoxy-1,5-imino-4,6-O-isopropylidene*-D-*glucitol* (**4**). — After the solids had been removed by filtration from the reaction mixture containing crude **3**, sufficient *p*-toluenesulfonic acid was added to adjust the pH to 1.5. Then a mixture of 2.2-dimethoxypropane (208 g, 2 mol) and 2-methoxypropene (144 g, 2 mol) was added. After a reaction time of 2 hours at 30°, thin-layer chromatography in 3:1 toluene–ethanol established that the reaction was complete. For workup the mixture was stirred for several hours with a suspension of sodium hydrogencarbonate (210 g) in water (100 mL), then the solvent was removed by evaporation, the residue digested with chloroform, and the chloroform phase washed, dried over sodium sulphate, and evaporated. After crystallization from ethyl acetate–petroleum ether, the yield of **4** was 249.3 g (85% from **1**). The compound had m.p. 117°, $[\alpha]_D^{20}$ −100.3° (*c* 1.0, methanol); ^{1}H-n.m.r. (300 MHz, C_6D_6): δ 1.34, 1.52 (2 s, 6 H, CCH_3), 1.97 (dd, 1 H, $J_{1a,1e}$ 11.1, $J_{1a,2}$ 10.0 Hz, H-1a), 2.22 (ddd, 1 H, $J_{5,6a}$ 4.6, $J_{5,6b}$ 2.5, $J_{4,5}$ 10.1 Hz, H-5), 2.12 (d, 1 H, J_{AB} 13.5 Hz, PhCH_2), 3.01 (dd, 1 H, $J_{1e,2}$ 4.9 Hz, H-1e), 3.45 (d, 1 H, PhCH_2), 3.47–3.70 (m, 3 H, H-3,4,6b), 3.77 (ddd, 1 H, H-2), and 3.93 (dd, 1 H, $J_{6a,6b}$ 10.8 Hz, H-6a).

Anal. Calc. for $C_{16}H_{23}NO_4$: C, 65.5; H, 7.9; N, 4.8. Found: C, 66.3; H, 8.0; N, 4.7.

N-*Benzyl-1,5-dideoxy-1,5-imino-4,6-O-isopropylidene-2,3-di-O-(methylsulfonyl)*-D-*glucitol* (**5**). — The product **4** (240g, 0.81 mol) was dissolved in a mixture of acetone (2000 mL) and triethylamine (300 mL, 2.1 mol). To this mixture, cooled in ice, was slowly added a solution of methanesulfonyl chloride (138 mL, 1.8 mol) in acetone (600 mL). Then the cooling bath was removed, and the mixture was stirred at room temperature. After 6 h the reaction was complete (t.l.c. 4:1 toluene–acetone). The precipitated salts were removed by filtration, the excess mesyl chloride in the filtrate was hydrolyzed by the addition of a little ice, and the solvent was removed in a rotary evaporator. The crystalline residue was taken up in methylene chloride, and the organic phase was washed with water, dried over Na_2SO_4, and evaporated. The product was pure enough for use in the next step, but it could be

recrystallized from ethyl acetate–petroleum ether. The yield was 354 g (97%); m.p. 162°, $[\alpha]_D^{20}$ −44.8° (*c* 1.0, $CHCl_3$); ^{1}H-n.m.r. (300 MHz, $CDCl_3$): δ 1.40, 1.48 (2 s, 6 H, CCH_3), 2.32 (dd, 1 H, $J_{1a,1e} = J_{1a,2} = 11.4$ Hz, H-1a), 2.37 (ddd, 1 H, $J_{4,5}$ 9.3, $J_{5,6a}$ 4.6, $J_{5,6b}$ 11.0 Hz, H-5), 3.09, 3.10 (2 s, 6 H, 2 CH_3SO_2), 3.24 (dd, 1 H, $J_{1e,2}$ 5.5 Hz, H-1e), 3.34 (d, 1 H, J_{AB} 13.8 Hz, PhCH_2), 3.69 (dd, 1 H, $J_{6a,6b}$ 11.0 Hz, H-6b), 3.76 (d, 1 H, PhCH_2), 3.82 (dd, 1 H, $J_{3,4}$ 9.3 Hz, H-4), 4.12 (dd, 1 H, H-6a), 4.52 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-3), 4.63 (ddd, 1 H, H-2), and 7.20–7.40 (m, 5 H, Ph–H).

Anal. Calc. for $C_{18}H_{27}NO_8S_2$: C, 48.1; H, 6.1; N, 3.1. Found: C, 47.9; H, 6.2; N, 3.0.

N-*Benzyl-1,2,3,5-tetradeoxy-1,5-imino-4,6-*O*-isopropylidene*-D-erythro-*2-hexenitol* (**6**). — To a solution of compound **5** (90 g, 0.2 mol) in *N,N*-dimethylformamide (1600 mL) were added NaI (149.9 g, 1.0 mol) and Zn powder (130.8 g, 2.0 mol). The mixture was stirred for 3 h at 135°, when t.l.c. in 3:1 toluene–ethyl acetate showed the reaction to be complete. After cooling, the salts were removed by filtration with suction, and the filtrate was evaporated to dryness. The residue was taken up in CH_2Cl_2, and the solution was washed several times with water. The organic phase was dried over Na_2SO_4 and evaporated, and the residual syrup was filtered through silica gel (230–400 mesh; mobile phase toluene → 30:1 toluene–acetone). The yield was 36.3 g (70%); $[\alpha]_D^{20}$ −51.4° (*c* 0.9, $CHCl_3$); ^{1}H-n.m.r. (300 MHz, C_6D_6): δ 1.30, 1.52 (2 s, 6 H, CCH_3), 2.42 (dm, 1 H, $J_{1a,1e}$ 17.2 Hz, H-1a), 2.51 (m, 1 H, H-5), 2.78 (d, 1 H, J_{AB} 13.0 Hz, PhCH_2), 2.95 (dm, 1 H, H-1e), 3.52 (d, 1 H, PhCH_2), 3.64 (dd, 1 H, $J_{6a,6b} = J_{5,6b} = 10.6$ Hz, H-6b), 3.97 (dd, 1 H, $J_{5,6a}$ 4.3 Hz, H-6a), 4.49 (m, 1 H, H-4), 5.32 (dm, 1 H, H-2), and 5.78 (dm, 1 H, $J_{3,2}$ 10.0 Hz, H-3).

Anal. Calc. for $C_{16}H_{21}NO_2$: C, 74.1; H, 8.2; N, 5.4. Found: C, 73.7; H, 8.0; N, 5.3.

N-*Benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene*-D-*mannitol* (**7**). — First the product **6** (40 g, 0.154 mol) was dissolved in a mixture of acetone (1200 mL), H_2O (300 mL), and *tert*-butyl alcohol (100 mL), then *N*-methylmorpholine *N*-oxide hydrate (27.0 g, 0.2 mol) and OsO_4 (400 mg) were added, and the mixture was stirred until the reaction was complete (t.l.c., 1:1 toluene–acetone). Then cyclohexene (10 mL) was added to the reaction mixture, and stirring was continued for 2 hours (black coloration). The solution was then filtered through Celite and evaporated. The syrupy residue was taken up in CH_2Cl_2, and the organic phase was washed several times with water, dried over Na_2SO_4, and again evaporated. The residue was purified by flash chromatography on silica gel (mobile phase 1:1→1:3 toluene–ethyl acetate) and crystallized from ethyl acetate–petroleum ether. The yield was 33.9 g (75%) m.p. 123–125°, $[\alpha]_D^{20}$ −128° (*c* 1.1, $CHCl_3$)

Anal. Calc. for $C_{16}H_{23}NO_4$: C, 65.5; H, 7.9; N, 4.8. Found: C, 66.0; H, 7.8; N, 4.8.

The di-*O*-acetyl derivative gave the following ^{1}H-n.m.r spectrum (250 MHz, C_6D_6): δ 1.32, 1.47 (2 s, 6 H, CCH_3), 1.69 (dd, 1 H, $J_{1a,1b}$ 13.7, $J_{1b,2}$ 1.7 Hz, H-1b), 1.76, 1.77 (2 s, 6 H, CH_3CO), 2.21 (ddd, 1 H, $J_{4,5}$ 9.9, $J_{5,6a}$ 4.6, $J_{5,6b}$ 10.2 Hz, H-5),

2.63 (d, 1 H, J_{AB} 13.7 Hz, PhCH_2), 2.64 (dd, 1 H, $J_{1a,2}$ 3.1 Hz, H-1a), 3.39 (d, 1 H, PhCH_2), 3.65 (dd, 1 H, $J_{6a,6b}$10.9 Hz, H-6b), 3.91 (dd, 1 H, H-6a), 4.38 (dd, 1 H, $J_{3,4}$ 9.9 Hz, H-4), 5.13 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-3), and 5.42 (ddd, 1 H, H-2).

N-*Benzyl-3*-O-*benzyl-1,5-dideoxy-1,5-imino-4,6*-O-*isopropylidene*-D-*mannitol* (**8**). — To a solution of compound **7** (15 g, 51 mmol) in absolute toluene (300 mL) was added dibutyltin oxide (14 g, 56 mmol), and the suspension was heated to reflux under a nitrogen atmosphere in a flask equipped with a water separator. When the separation of water was complete the temperature was lowered to 100°, and tetrabutylammonium bromide (1.64 g, 5.1 mmol) was added under continued nitrogen flow. Then benzyl bromide (9.58 g, 56 mmol) was run in over the course of 1 h. After 8 h t.l.c. (5:1 toluene–acetone) showed that the starting material was almost completely consumed. For workup the solvent was removed by evaporation, the residue was taken up in chloroform, and the solution was washed with saturated aqueous sodium hydrogencarbonate. Precipitated tin salts were removed by centrifugation, the supernatant then being dried over Na_2SO_4 and finally evaporated to dryness. The residue was purified by chromatography with 40:1 toluene–acetone as the eluent. The yield was 14.3 g (37 mmol, 73%), $[\alpha]_D^{20}$ −55° (*c* 0.9, ethanol).

Anal. Calc. for $C_{23}H_{29}NO_4$: C, 72.0; H, 7.6; N, 3.7. Found: C, 72.9; H, 7.3; N, 3.5.

The *O*-acetyl derivative gave the following ^{1}H-n.m.r. spectrum (200 MHz, $CDCl_3$): δ 1.45, 1.55 (2 s, 6 H, CCH_3), 2.13 (s, 3 H, CH_3CO), 2.16 (dd, 1 H, $J_{1e,1a}$ 13.3, $J_{1e,2}$ 2.6 Hz, H-1e), 2.26 (ddd, 1 H, $J_{4,5}$ 9.1, $J_{5,6a}$ 4.8, $J_{5,6b}$ 11.8 Hz, H-5), 2.90 (dd, 1 H, $J_{1a,2}$ 3.3 Hz, H-1a), 3.19 (d, 1 H, J_{AB} 13.3 Hz, N-CH_2Ph), 3.38 (dd, 1 H, $J_{2,3}$ 4.0, $J_{3,4}$ 9.1 Hz, H-3), 3.78 (d, 1 H, N-CH_2Ph), 3.83 (dd, 1 H, $J_{6a,6b}$ 11.8 Hz, H-6b), 4.13 (dd, 1 H, H-6a), 4.16 (dd, 1 H, H-4), 4.68 (s, 2 H, O-CH_2Ph), and 5.25 (bs, 1 H, H-2).

2-*Azido*-N-*benzyl-3*-O-*benzyl-1,2,5-trideoxy-1,5-imino-4,6*-O-*isopropylidene*-D-*glucitol* (**10**). — To a solution of compound **8** (14 g, 37 mmol) in absolute dichloromethane (140 mL) was added pyridine (6.9 g, 88 mmol), and the mixture was cooled to −20° under an inert atmosphere. A solution of trifluoromethanesulfonic anhydride (10.4 g, 37 mmol in 60 mL CH_2Cl_2) was then added dropwise over 60 min. After a further hour the starting material had been converted into a product having R_F 0.3 in 10:1 toluene–acetone. For workup the reaction mixture was vigorously stirred with saturated aqueous $NaHCO_3$ (50 mL) for 30 min at 0°, then the organic phase was separated and dried over sodium sulphate. Evaporation furnished *N*-benzyl-3-*O*-benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-2-*O*-(trifluoro-methyl)sulfonyl-D-*mannitol* (**9**; 18.1 g, 35 mmol, 95%).

For the next step this material was dissolved in absolute dichloromethane (40 mL), the solution was cooled to −40° under a protective atmosphere, and absolute *N*,*N*-dimethylformamide (100 mL), as well as lithium azide (8.6 g, 0.175 mol) were added. The mixture was stirred for ~8 h at −40° (inert gas), until compound **9** was no longer observable by t.l.c (detection with naphthoresorcinol). The mixture was evaporated at 30° (bath temperature) under high vacuum to about one-quarter of its

initial volume, then diluted with toluene and washed several times with dilute aqueous NaCl. After drying over sodium sulphate, the solution was evaporated to dryness and the residue was purified by column chromatography, with 50:1 toluene–ethyl acetate as eluent. The pure product (10.6 g, 26.5 mmol, 74%) had $[\alpha]_D^{20}$ −78.9°, (*c* 1.2, $CHCl_3$); ^{1}H-n.m.r. (300 MHz, $CDCl_3$): δ 1.44, 1.49 (2 s, 6 H, CCH_3), 1.85 (dd, 1 H, $J_{1a,1e} = J_{1a,2}$ = 11.3 Hz, H-1a), 2.29 (ddd, 1 H, $J_{4,5}$ 9.1, $J_{5,6a}$ 4.5, $J_{5,6b}$ 10.9 Hz, H-5) 2.85 (dd, 1 H, $J_{1e,2}$ 4.9 Hz, H-1e), 3.12 (d, 1 H, J_{AB} 13.4 Hz, N-CH_2Ph), 3.36 (dd, 1 H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 3.49 (ddd, 1 H, H-2), 3.72 (dd, 1 H, $J_{6a,6b}$ 10.9, H-6b), 3.77 (d, 1 H, N-CH_2Ph), 3.81 (dd, 1 H, H-4), 4.11 (dd, 1 H, H-6a), 4.74 (d, 1 H, J_{AB} 11.0, O-CH_2Ph), 4.89 (d, 1 H, O-CH_2Ph), and 7.15–7.45 (m, 10 H, Ph-H).

Anal. Calc. for $C_{23}H_{28}N_4O_3$: C, 67.8; H, 6.9; N, 13.7. Found: C, 67.1; H, 6.9; N, 13.7.

2-*Acetamido*-N-*benzyl*-3-O-*benzyl*-1,2,5-*trideoxy*-1,5-*imino*-4,6-O-*isopropylidene*-D-*glucitol* (**11**). — To a 4% ethanolic $NiCl_2$ solution (100 mL) containing **10**, (10.6 g, 26 mmol) and stirred at 0°, saturated ethanolic $NaBH_4$ was added until the initially reversible black coloration persisted. T.l.c. in 10:1 toluene–ethanol showed that **10** had been completely converted into an amino compound (red coloration with ninhydrin). The solvent was removed in a rotary evaporator at 30° (bath temperature) under high vacuum, and the residue was treated with 1:2 acetic anhydride–pyridine (50 mL). After 2 h at 40°, a sample no longer gave a red color with ninhydrin. The mixture was again evaporated to dryness under high vacuum, and the residue was taken up in toluene–H_2O, and extracted several times with nearly saturated NaCl solution to remove nickel and boron compounds. The toluene phase was dried over sodium sulphate and evaporated, and the product was chromatographed on silica gel with 60:1 toluene–ethanol as eluent. The yield of **11** was 9.6 g (87%), m.p. 40°, $[\alpha]_D^{20}$ −3.3° (*c* 0.5, $CHCl_3$); ^{1}H-n.m.r. (300 MHz, C_6D_6): δ 1.28, 1.46, 1.52 (3 s, 9 H, 3 CH_3), 1.69 (dd, 1 H, $J_{1a,1e}$ 11.0, $J_{1a,2}$ 11.0 Hz, H-1a), 2.28 (ddd, 1 H, $J_{4,5}$ 9.0, $J_{5,6a}$ 4.6, $J_{5,6b}$ 10.8 Hz, H-5), 2.92 (d, 1 H, J_{AB} 13.9 Hz, N-CH_2Ph), 3.07 (dd, 1 H, $J_{1e,2}$ 4.9 Hz, H-1e), 3.25 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 9.0 Hz, H-3), 3.41 (d, 1 H, N-CH_2Ph), 3.55 (dd, 1 H, $J_{6a,6b}$ 10.8 Hz, H-6b), 3.89 (dd, 1 H, H-4), 3.97 (dd, 1 H, H-6a), 4.19 (ddd, 1 H, H-2), 4.58 (d, 1 H, $J_{NH,2}$ 7.3 Hz, N*H*), 4.66 (d, 1 H, J_{AB} 12.3 Hz, O-CH_2Ph), and 4.93 (d, 1 H, O-CH_2Ph).

Anal. Calc. for $C_{25}H_{32}N_2O_4$: C, 70.7; H, 7.6; N, 6.6. Found: C, 70.3; H. 7.6; N, 6.6.

2-Acetamido-1,3,5-trideoxy-1,5-imino-D-*glucitol (2-acetamido-1,2-dideoxynojirimycin* (**2**). — An amount of **11** (2 g, 15 mmol) was dissolved in methanol (50 mL), glacial acetic acid (2 mL) and 10% palladium-on-charcol (5 g) were added, and the suspension was hydrogenated under a pressure of 300 kPa for 24 h. The resulting acetate salt of 2-acetamido-1,2,5-trideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (**12**) was subjected to several additions and evaporations of triethylamine to yield 1.1 g (quantitative) of the free base. The acetate salt had m.p. 166–169° (dec.), $[\alpha]_D^{20}$ −4.25° (*c* 0.58, pyridine).

Without further purification **12** (1.1 g) was dissolved in 3:2 glacial acetic acid–H_2O (20 mL), the solution was heated for 8 hours 60°, and then evaporated to dryness. The addition and evaporation of several portions of methanol–triethylamine gave the dry final product **2** in quantitative yield. The compound had m.p. 227–228°, $[\alpha]_D^{20}$ +16.4° (*c* 1.0, H_2O). The ^{1}H-n.m.r. (300 MHz, D_2O) of the free base showed δ 1.92 (s, 3 H, CH_3CO) 2.35 (dd, 1 H, $J_{1a,1e}$ 12.4, $J_{1a,2}$ 12.4 Hz, H-1a), 2.46 (ddd, 1 H, $J_{4,5}$ 9.1, $J_{5,6a}$ 3.0, $J_{5,6b}$ 5.9 Hz, H-5), 2.98 (dd, 1 H, $J_{1e,2}$ 5.0 Hz, H-1e), 3.22 (dd, 1 H, $J_{3,4}$ 9.1 Hz, H-4), 3.31 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-3), 3.58 (dd, 1 H, $J_{6b,6a}$ 11.5 Hz, H-6b), 3.64 (ddd, 1 H, H-2), and 3.74 (dd, 1 H, H-6a); that of the hydrochloride salt had δ 2.05 (s, 3 H, CH_3CO), 2.99 (dd, 1 H, $J_{1a,1e} = J_{1a,2} = 12.6$ Hz, H-1a), 3.24 (ddd, 1 H, H-5), 3.51 (dd, 1 H, $J_{1e,2}$ 5.0 Hz, H-1e), 3.63 (dd, 1 H, $J_{2,3}$ 9.1, $J_{3,4}$ 9.1 Hz, H-3), 3.69 (dd, 1 H, $J_{4,5}$ 9.1 Hz, H-4), 3.86–4.01 (m, 2 H, H-6a, H-6b), and 4.08 (ddd, 1 H, H-2).

Anal. Calc. for $C_8H_{16}N_2O_4$: C, 47.0; H, 7.9; N, 13.7. Found: C, 46.5; H. 7.8; N, 13.4.

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