Synthesis of (+)-nojirimycin from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose

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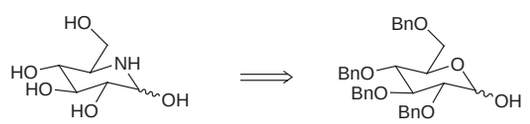
Synthesis of the antibiotic (+)-nojirimycin has been accomplished starting from commercially available 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **2**. This D-glucopyranose derivative was converted into the D-*xylo*-hexos-5-ulose dimethyl acetal **5** by thioacetalisation, C-5 oxidation and transacetalisation with methanol. Introduction of the 5-amino substituent with the correct D-*gluco*-stereochemistry was realised by conversion of ketone **5** into the corresponding oxime **6**, followed by diastereoselective reduction with lithium aluminium hydride. After protection of the resulting primary amine as its *tert*-butyl carbamate, the desired D-*gluco*-amine **7** could be separated from the unwanted L-*ido*-isomer **8**. Hydrogenolysis of **7** followed by treatment with aqueous sulfur dioxide yielded 1-deoxynojirimycin-1-sulfonic acid **9**, which was further transformed into (+)-nojirimycin **1**.

Introduction

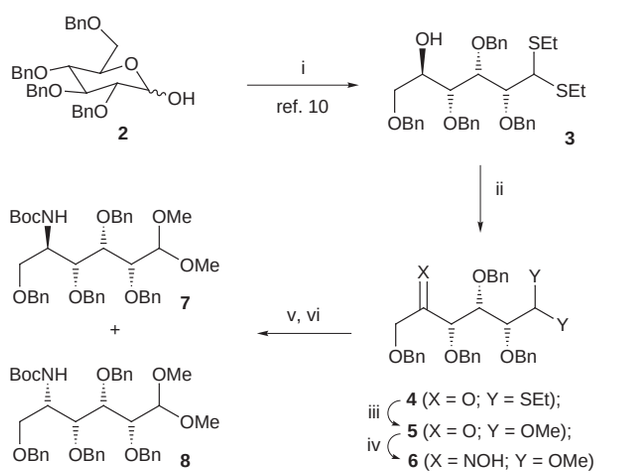
(+)-Nojirimycin **1**, isolated from several strains of *Streptomyces*[1] and *Bacillus*,[2] exhibits potent biological activity against drug-resistant strains of *Sarcina lutea*, *Shigella flexneri* and *Xanthomonas oryzae* (Scheme 1).[1a] Furthermore, (+)-nojirimycin **1** shows significant inhibitory activity against various glycosidases and glucoamylase.[3] As a result of its potent biological activity, there has been considerable interest in the development of synthetic approaches to (+)-nojirimycin **1** and related polyhydroxylated piperidines. To date, the chemical synthesis of nojirimycin has been realised starting from diethyl tartrate,[4] *myo*-inositol[5] and serine,[6] as well as from a variety of carbohydrate-based starting materials.[1b,7,8] Of the carbohydrate-based approaches, the vast majority of them involve elaboration of furanose-type systems.[1b,7] One exception is found in the work of Rajanikanth and Seshadri who reported an approach to (+)-nojirimycin **1** from a commercially available pyranose derivative, namely 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **2** (Scheme 1).[8] Unfortunately, this seemingly useful approach to (+)-nojirimycin **1** could not be reproduced in the hands of Fleet *et al.*,[9] and no further reports relating to this chemistry have been disclosed by the original authors. In this article, we describe an alternative approach to (+)-nojirimycin **1** from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **2** which, we believe, is competitive with previous synthetic approaches to this natural product.



Scheme 1

Results and discussion

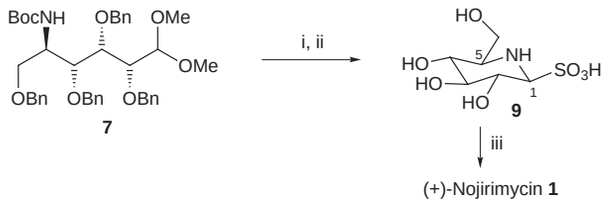
Our approach to (+)-nojirimycin **1** employed commercially available 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **2** as the starting material. Opening of the pyranose ring with concurrent protection of the aldehyde functionality was accomplished according to the published procedure.[10] The resulting alcohol **3** was oxidised to the corresponding ketone **4** using the tetrapropylammonium perruthenate (TPAP) method of Ley *et al.* (Scheme 2).[11] It is notable that none of the desired ketone was produced using the Swern oxidation method.[12] At this juncture, transacetalisation of the thioacetal group within **4** to the more acid-labile dimethyl acetal was effected by treatment with mercury(II) salts in the presence of methanol. The resulting ketone **5** was further converted into oxime **6**, as an essentially 1:1 mixture of geometric isomers as judged by ^{1}H NMR spectroscopy, by treatment with hydroxylamine hydrochloride in the presence of pyridine. Treatment of this oxime mixture with lithium aluminium hydride effected reduction of the C=N bond and simultaneous cleavage of the N–O bond to give a diastereomeric mixture of amines. The diastereoselectivity of this reduction was determined to be 2:1 by integration of the resolved methyl singlets at δ 3.30 (minor) and δ 3.22 (major) in the ^{1}H NMR spectrum of the crude product. At this point, it was not possible to readily separate the D-*gluco*-isomer from the unwanted L-*ido*-isomer using silica gel chromatography although some diastereomeric enrichment could be accomplished by repeated chromatography. Fortunately, reaction of the amine mixture with di-*tert*-butyl dicarbonate furnished the readily separable urethanes **7** and **8** in 65% and 15% overall yields respectively from oxime **6**.[13] The stereochemistry of the major compound **7** was tentatively assigned as having the



Scheme 2 *Reagents and conditions (yields)*: (i) EtSH, HCl, 1,4-dioxane (56%); (ii) TPAP, NMO, CH_2Cl_2 (81%); (iii) HgO, $HgCl_2$, MeOH (81%); (iv) $NH_2OH{\cdot}HCl$, pyridine, EtOH (90%); (v) $LiAlH_4$, Et_2O; (vi) $(Boc)_2O$, Et_3N, MeCN, **7** (65% from **6**), **8** (15% from **6**).

D-*gluco*-stereochemistry by NMR comparisons with related structures.[14] This assignment was subsequently confirmed by conversion of compound **7** into (+)-nojirimycin **1** and the more readily characterisable 1-deoxynojirimycin-1-sulfonic acid **9**.

The final steps in our approach to (+)-nojirimycin **1** involved exhaustive deprotection of amine **7** (Scheme 3). First, hydro-



Scheme 3 *Reagents and conditions (yield)*: (i) $Pd(OH)_2$, H_2, EtOH; (ii) SO_2, H_2O (80% over 2 steps); (iii) Dowex 1-X2 (HO^-), H_2O (quantitative).

genolysis of the benzyl ethers was effected using Pearlman's catalyst in ethanol. After removal of the catalyst by filtration and of the solvent by evaporation, the resulting crude tetraol was dissolved in water and treated with an excess of gaseous sulfur dioxide. These acidic conditions effected cleavage of the urethane and the dimethyl acetal, which upon further *in situ* reaction with the sulfur dioxide yielded 1-deoxynojirimycin-1-sulfonic acid **9** in 80% isolated yield from urethane **7**. All spectral and analytical data were in full agreement with those reported in the literature for 1-deoxynojirimycin-1-sulfonic acid **9** derived from natural (+)-nojirimycin **1**.[1b,4] Additional support for the D-*gluco*-stereochemistry of sulfonic acid **9** came from NMR experiments performed after the proton assignments had been established using correlation spectroscopy. Large vicinal coupling constants were observed in sulfonic acid **9** ($J_{1,2}$ = 10.5 Hz; $J_{2,3}$ = 9.0 Hz; $J_{3,4}$ = 9.0 Hz; $J_{4,5}$ = 10.5 Hz) suggesting the ring hydrogens adopt axial positions within a $^4C_1$ chair conformation of the piperidine ring. This supposition is further supported by nuclear Overhauser enhancement (NOE) experiments involving irradition of H-5, which produced strong enhancements of both H-1 (11.5%) and H-3 (9.3%) along with much smaller enhancements of H-4 (2.4%) and one of the H-6 (4.4%) hydrogens.

Further conversion of our synthetic sulfonic acid **9** into (+)-nojirimycin **1** was accomplished by treatment with Dowex 1-X2 (HO^-) in accordance with a literature method.[7d] Gratifyingly, the optical rotation, $[\alpha]_D^{15}$ +70 (*c* 0.4, H_2O, 24 h), and melting point, mp 122–130 °C (decomp.), of our synthetic material were in good agreement with the published values for natural (+)-nojirimycin {$[\alpha]_D^5$ +73.5 (H_2O, 20 h); mp 126–130 °C (decomp.)}.[1b] In summary, our approach produces (+)-nojirimycin **1** *via* a 9-step sequence in 17% overall yield from a commercially available D-glucopyranose derivative, namely 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose.

Experimental

General

Reactions requiring anhydrous conditions were performed using oven-dried glassware and conducted under a positive pressure of nitrogen. Anhydrous solvents were prepared in accordance with standard protocols, or alternatively purchased from Aldrich in Sure/Seal™ bottles. IR spectra were recorded (4000–600 cm^{-1}) on a Nicolet Magna-550 FT-IR spectrometer with internal calibration. Spectra were recorded as thin films or Nujol® mulls. NMR spectra were recorded on Bruker ACF-300 and DRX 400 spectrometers with either TMS or residual protic solvent as internal reference; *J*-values are given in Hz. Elemental analyses were carried out on a Perkin-Elmer 2400 CHN elemental analyser. Mass spectra and accurate masses were recorded under EI^+ or CI^+ conditions on a VG Analytical ZAB-E instrument at the EPSRC Mass Spectrometry Centre, University College, Swansea or under EI^+ conditions on a Kratos Profile HV-3 mass spectrometer. Optical rotations were determined on the sodium D-line (589.3 nm) using an AA-1000 polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Light petroleum refers to the fraction with distillation range 40–60 °C.

2,3,4,6-Tetra-*O*-benzyl-D-*xylo*-hexos-5-ulose diethyl dithioacetal 4

Solid TPAP (68 mg, 0.19 mmol) was added portionwise to a stirred mixture of dithioacetal **3**[10] (2.49 g, 3.85 mmol), 4-methylmorpholine *N*-oxide (NMO) (676 mg, 5.77 mmol) and powdered 4 Å molecular sieves (2 g) in dry CH_2Cl_2 (8 ml) at 0 °C under nitrogen. The mixture was stirred for 45 min at room temperature, filtered through a short pad of silica and eluted with ethyl acetate. The filtrate was concentrated *in vacuo* to give a yellow oil. Column chromatography (light petroleum : ethyl acetate 6 : 1) provided ketone **4** (2.00 g, 81%) as a colourless oil; $[\alpha]_D^{20}$ −7 (*c* 0.92, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1731 (C=O), 1449, 1111, 738, 697; δ_H(300 MHz; $CDCl_3$) 7.43–7.18 (20H, m, ArH), 4.82 (1H, d, *J* 11.0, CH_2Ph), 4.74 (1H, d, *J* 11.0, CH_2Ph), 4.70 (1H, d, *J* 11.0, CH_2Ph), 4.69 (1H, d, *J* 11.0, CH_2Ph), 4.52 (1H, d, *J* 11.0, CH_2Ph), 4.41–4.33 (4H, m, 3 × CH_2Ph, H-3), 4.24 (1H, d, $J_{6,6'}$ 18.0, H-6), 4.16 (1H, d, $J_{3,4}$ 4.0, H-4), 4.12 (1H, d, $J_{6,6'}$ 18.0, H′-6), 4.04 (1H, dd, $J_{2,3}$ 6.0, $J_{1,2}$ 4.5, H-2), 3.75 (1H, d, $J_{1,2}$ 4.5, H-1), 2.64 (2H, m, SC$H_2$$CH_3$), 2.56 (2H, m, SC$H_2$$CH_3$), 1.19 (3H, t, *J* 7.5, SCH_2CH_3), 1.18 (3H, t, *J* 7.5, SCH_2CH_3); δ_C(75.4 MHz; $CDCl_3$) 206.5 (C=O), 138.3 (ArC), 137.7 (ArC), 137.3 (ArC), 136.8 (ArC), 128.6 (ArCH), 128.46 (ArCH), 128.43 (ArCH), 128.38 (ArCH), 128.35 (ArCH), 128.25 (ArCH), 128.21 (ArCH), 127.9 (ArCH), 127.87 (ArCH), 127.85 (ArCH), 127.5 (ArCH), 81.6 (CH), 81.4 (CH), 80.7 (CH), 75.2 (CH_2), 75.1 (CH_2), 74.3 (CH_2), 73.34 (CH_2), 73.31 (CH_2), 53.3 (CH), 25.2 (CH_2), 14.4 (CH_3); *m*/*z* 645 (MH^+), 583, 477, 369 (Found: MH^+, 645.2704. $C_{38}H_{45}O_5S_2$ requires *m*/*z*, 645.2708).

2,3,4,6-Tetra-*O*-benzyl-D-*xylo*-hexos-5-ulose dimethyl acetal 5

Mercuric oxide (HgO; yellow) (1.06 g, 4.90 mmol) was added to a solution of ketone **4** (790 mg, 1.22 mmol) in boiling MeOH (33 ml). The hot solution was stirred vigorously while a solution of $HgCl_2$ (1.00 g, 3.67 mmol) in dry MeOH (4 ml) was added over a period of 1 min, and stirring was continued while the suspension was refluxed for 15 min. The hot solution was filtered, the solid matter washed with MeOH, and the combined solutions concentrated *in vacuo* to give a syrup, which was dissolved in CH_2Cl_2 (25 ml). A white solid was filtered off and the filtrate washed successively with water, 10% aqueous KI (2×) and water (3×). The solution was dried over $MgSO_4$ and the solvent removed *in vacuo* to give an oil. Column chromatography (light petroleum : ethyl acetate 5 : 1 containing 1% Et_3N) provided ketone **5** (579 mg, 81%) as a colourless oil; $[\alpha]_D^{19}$ −22 (*c* 1.10, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1731 (C=O), 1449, 1086, 738, 697; δ_H(300 MHz; $CDCl_3$) 7.50–7.15 (20H, m, ArH), 4.72 (1H, d, *J* 11.0, CH_2Ph), 4.64 (1H, d, *J* 12.0, CH_2Ph), 4.62 (1H, d, *J* 11.0, CH_2Ph), 4.53 (2H, m, 2 × CH_2Ph), 4.46 (1H, d, *J* 12.0, CH_2Ph), 4.43 (1H, d, $J_{3,4}$ 6.3, H-4), 4.37 (1H, d, *J* 12.0, CH_2Ph), 4.31 (1H, d, *J* 12.0, CH_2Ph), 4.21 (2H, s, 2 × H-6), 4.15 (1H, d, $J_{1,2}$ 4.7, H-1), 4.00 (1H, dd, $J_{2,3}$ 4.5, $J_{1,2}$ 4.7, H-2), 3.73 (1H, dd, $J_{2,3}$ 4.5, $J_{3,4}$ 6.3, H-3), 3.40 (3H, s, OCH_3), 3.31 (3H, s, OCH_3); δ_C(75.4 MHz; $CDCl_3$) 206.3, 138.4, 137.7, 137.6, 137.3, 128.5, 128.45, 128.43, 128.39, 128.36, 128.2, 128.0, 127.8, 127.7, 127.5, 105.4, 80.8, 79.9, 77.6, 74.7, 74.3, 74.2, 73.3, 73.2, 56.0, 54.7; *m*/*z* 602 (M + NH_4^+), 496, 362, 106 (Found: M + NH_4^+, 602.3111. $C_{36}H_{44}NO_7$ requires *m*/*z*, 602.3118).

2,3,4,6-Tetra-*O*-benzyl-5-deoxy-5-hydroxyimino-D-*xylo*-hexose dimethyl acetal 6

A stirred solution of ketone **5** (592 mg, 1.01 mmol), hydroxyl-

amine hydrochloride (211 mg, 3.03 mmol), pyridine (327 μl, 4.05 mmol) and EtOH (2.5 ml) was heated at 60 °C for 20 min. The solvent was removed *in vacuo* and the residue taken up in Et_2O and washed with water. The organic layer was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Column chromatography (light petroleum : ethyl acetate 3 : 1 containing 1% Et_3N) provided oxime **6** (546 mg, 90%) as a colourless oil and as a 1 : 1 mixture of *Z* and *E* isomers; ν_{max}(thin film)/cm^{-1} 3334, 3037 (OH), 1501, 1449, 1086, 732, 697; δ_H(300 MHz; $CDCl_3$) 8.59 (0.5H, d, *J* 4.0, OH), 8.56 (0.5H, br s, OH), 7.50–7.10 (20H, m, ArH), 5.19 (0.5H, d, *J* 5.5), 4.87 (0.5H, d, *J* 11.0, CH_2Ph), 4.77 (0.5H, d, *J* 11.0, CH_2Ph), 4.76 (0.5H, d, *J* 11.0, CH_2Ph), 4.72–4.38 (8H, m), 4.28–4.08 (3H, m), 3.69 (0.5H, m), 3.61 (0.5H, m), 3.36 (1.5H, s, OCH_3), 3.31 (1.5H, s, OCH_3), 3.21 (1.5H, s, OCH_3), 3.16 (1.5H, s, OCH_3); δ_C(75.4 MHz; $CDCl_3$) 139.1, 138.6, 137.8, 129.1, 128.37, 128.35, 128.29, 128.25, 128.19, 128.17, 128.11, 128.02, 127.96, 127.87, 127.80, 127.71, 127.53, 127.48, 127.35, 127.28, 125.3, 105.4, 80.5, 79.7, 79.2, 79.1, 78.7, 75.7, 75.2, 74.5, 74.3, 74.2, 73.7, 73.0, 72.6, 72.2, 68.0, 62.1, 55.9, 55.7, 55.1, 53.9; *m*/*z* 600 (MH^+), 599 (M^+), 461, 91 (Found: M^+, 599.2886. $C_{36}H_{41}NO_7$ requires *m*/*z*, 599.2883).

2,3,4,6-Tetra-*O*-benzyl-5-[*N*-(*tert*-butoxycarbonyl)amino]-5-deoxy-D-glucose dimethyl acetal 7 and 2,3,4,6-tetra-*O*-benzyl-5-[*N*-(*tert*-butoxycarbonyl)amino]-5-deoxy-L-idose dimethyl acetal 8

A solution of oxime **7** (542 mg, 0.90 mmol) in dry Et_2O (2.5 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (103 mg, 2.70 mmol) in dry Et_2O (2.5 ml). The mixture was stirred overnight at room temperature. Ethyl acetate was added slowly to decompose the excess of lithium aluminium hydride, followed by an aqueous solution of 5 M NaOH. The resulting cloudy suspension was filtered through a pad of Celite and washed thoroughly with Et_2O. The filtrate was washed with saturated $NaHCO_3$ solution and then dried over $MgSO_4$. The solvent was removed *in vacuo* and subsequent column chromatography (CH_2Cl_2 : MeOH 30 : 1 containing 0.5% Et_3N) provided a mixture of the two diastereomeric amines (444 mg) as a colourless oil. The diastereomeric ratio of the reduction was determined to be 2 : 1 prior to chromatography (see Results and discussion section).

To a stirred solution of a portion of this mixture (363 mg, 0.62 mmol) and Et_3N (95 μl, 0.68 mmol) in CH_3CN (1.5 ml) was added di-*tert*-butyl dicarbonate (162 mg, 0.74 mmol) and the solution stirred for 10 min at room temperature. The mixture was diluted with water and extracted with Et_2O. The organic phase was washed successively with a saturated solution of $NaHCO_3$, and brine, and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* to give a yellow oil. Column chromatography (light petroleum : ethyl acetate 8 : 1 containing 0.5% Et_3N) provided the less polar amine **8** (77 mg, 15% from oxime **6**) as a colourless oil; ν_{max}(thin film)/cm^{-1} 3447, 3313 (NH), 1705 (C=O), 1490, 1157, 1086, 727, 697; δ_H(300 MHz; $CDCl_3$) 7.40–7.10 (20H, m, ArH), 4.96–4.78 (4H, m), 4.72–4.55 (3H, m), 4.48 (1H, d, *J* 11.0, CH_2Ph), 4.38 (2H, dd, *J* 11.0, CH_2Ph), 4.20 (1H, d, *J* 8.8), 4.05 (1H, m), 3.80 (2H, m), 3.45 (1H, m), 3.44 (3H, s, OCH_3), 3.35 (1H, t, *J* 8.8), 3.20 (3H, s, OCH_3), 1.40 (9H, s, ^{t}Bu); δ_C(75.4 MHz; $CDCl_3$) 155.6 (C=O), 139.0 (ArC), 138.8 (ArC), 138.6 (ArC), 138.1 (ArC), 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.4, 104.4, 80.7, 79.5, 78.3, 77.8, 75.4, 75.3, 74.6, 72.9, 69.5, 55.0, 52.2, 50.3, 28.4; *m*/*z* 686 (MH^+), 622, 106 (Found: MH^+, 686.3720. $C_{41}H_{52}NO_8$ requires *m*/*z*, 686.3693).

Further elution (light petroleum : ethyl acetate 8 : 1, containing 0.5% Et_3N) then gave amine **7** (330 mg, 65% from oxime **6**) as a colourless oil; $[a]_D^{20}$ +6 (*c* 1.00, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 3416, 3324 (NH), 1710 (C=O), 1496, 1449, 1163, 737, 697; δ_H(300 MHz; $CDCl_3$) 7.40–7.10 (20H, m, ArH), 5.20 (1H, d, $J_{5,NH}$ 8.8, NH), 4.85–4.55 (6H, m, 3 × CH_2Ph), 4.50 (2H, s, CH_2Ph), 4.37 (1H, d, $J_{1,2}$ 5.0, H-1), 4.20 (1H, m, H-5), 3.99 (1H, t, $J_{2,3} = J_{3,4}$ = 5.0, H-3), 3.85 (1H, t, $J_{3,4} = J_{4,5}$ = 5.0, H-4), 3.76 (1H, t, $J_{2,3} = J_{1,2}$ = 5.0, H-2), 3.62–3.43 (2H, m, 2 × H-6), 3.35 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 1.40 (9H, s, ^{t}Bu); δ_C(75.4 MHz; $CDCl_3$) 155.6 (C=O), 138.7 (ArC), 138.5 (ArC), 138.4 (ArC), 138.2 (ArC), 128.4, 128.33, 128.30, 128.2, 127.8, 127.7, 127.6, 127.5, 127.4, 105.6, 79.3, 79.1, 79.0, 77.6, 75.0, 74.7, 73.2, 72.9, 69.4, 55.5, 55.0, 50.3, 28.4; *m*/*z* 686 (MH^+), 622, 106 (Found: MH^+, 686.3669. $C_{41}H_{52}NO_8$ requires *m*/*z*, 686.3693).

1-Deoxynojirimycin-1-sulfonic acid 9

A solution of amine **7** (234 mg, 0.34 mmol) in EtOH (2.4 ml) was hydrogenated in the presence of 20% $Pd(OH)_2$ on carbon (50 mg) at room temperature under one atmospheric pressure of hydrogen for 4 h. The catalyst was removed by filtration and the filtrate was concentrated *in vacuo* to give a white solid. This solid (96 mg) was dissolved in water (1.5 ml) then the solution saturated with sulfur dioxide at room temperature and stirred at 40 °C for 2 days. The resulting white precipitate was collected by filtration, washed with MeOH and dried under vacuum to give **9** (66 mg, 80% over 2 steps) as a white solid, mp 140–143 °C (decomp.) (lit.,[1b] 145–147 °C decomp.); ν_{max}(Nujol)/cm^{-1} 3355, 3124, 1583; δ_H(400 MHz; D_2O) 4.15 (1H, d, $J_{1,2}$ 10.5, H-1), 3.98 (1H, dd, $J_{5,6}$ 3.0, $J_{6,6'}$ 12.0, H-6), 3.90 (1H, dd, $J_{5,6'}$ 4.5, $J_{6,6'}$ 12.0, H′-6), 3.89 (1H, dd, $J_{2,3}$ 9.0, $J_{1,2}$ 10.5, H-2), 3.67 (1H, dd, $J_{3,4}$ 9.0, $J_{4,5}$ 10.5, H-4), 3.56 (1H, t, $J_{2,3} = J_{3,4}$ = 9.0, H-3), 3.25 (1H, m, H-5); δ_C(100.6 MHz; D_2O) 75.9 (C-3), 70.4 (C-1), 69.4 (C-2), 67.2 (C-4), 60.4 (C-5), 57.5 (C-6); *m*/*z* 242 ($M - H)^-$ (Found: C, 27.55; H, 5.70; N, 5.07. $C_6H_{13}NO_7S{\cdot}H_2O$ requires C, 27.58; H, 5.79; N, 5.36%). Selected NOE data: irradiation of H-5 enhances H-3 (9.3%), H-4 (2.4%), H-6 (4.4%) and H-1 (11.5%).

(+)-Nojirimycin 1

A mixture of 1-deoxynojirimycin-1-sulfonic acid **9** (27 mg, 0.11 mmol), Dowex 1-X2 (HO^-) (0.5 ml) and water (0.5 ml) was stirred for 45 min at room temperature. The mixture was placed on a column of resin Dowex 1-X2 (HO^-) (3.5 ml) and eluted with water (115 ml). The filtrate was freeze-dried to provide **1** (20 mg, quantitative) as a white solid, mp 122–130 °C (decomp.) {lit.,[1b] 126–130 °C decomp.}; $[a]_D^{25}$ +62 (*c* 0.4, H_2O, 5 min), $[a]_D^{15}$ +70 (*c* 0.4, H_2O, 24 h) {lit.,[1b] $[a]_D^{5}$ +73.5 (H_2O, 20 h)}.

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