New access to 1-deoxynojirimycin derivatives via azide-alkene cycloaddition

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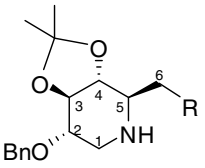
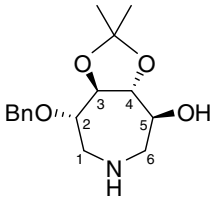
Supporting Information Section 1

Table S1: Selected ^{1}H-NMR spectroscopic data (δ)





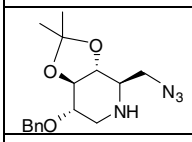
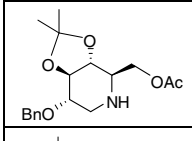
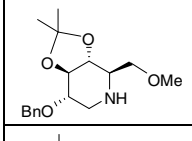
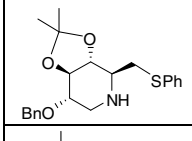
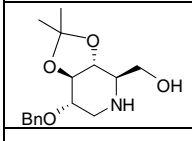
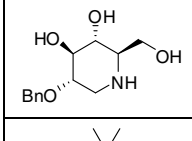
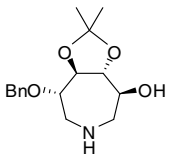
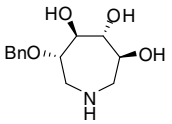
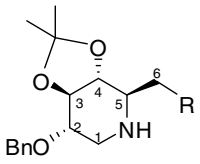
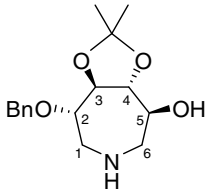
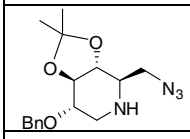
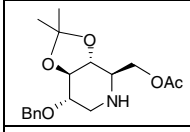
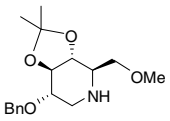
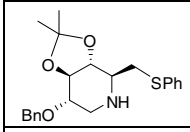
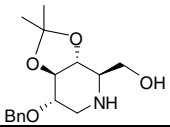
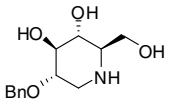
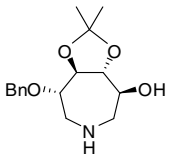
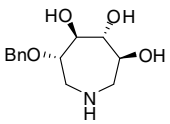
Compound	H1a (axial)	H1b (equatorial)	H2	H3	H4	H5	H6a	H6b
	2.50	3.27	3.59	3.50	3.11	2.88	3.63	3.47
	2.50	3.26	3.60	3.48	3.10	2.94	4.35	4.04
	2.49	3.26	3.59	3.47	3.17	2.83	3.59	3.46
	2.48	3.27	3.40	3.08	2.97	2.88	3.61	3.43
	2.52	3.29	3.62	3.51	3.17	2.84	3.83	3.68
	2.46	3.24	3.37	3.35	3.19	2.52	3.83	3.60
	2.88	3.13	3.56	4.11	3.76	3.77	3.23	2.62
	3.05	3.03	3.63	3.56	3.74	3.79	3.14	2.76

Table S2: ^{13}C-NMR spectroscopic data (δ)



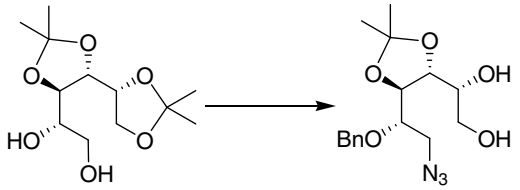


Compound	C1	C2	C3	C4	C5	C6
	48.5	77.1	83.3	76.4	57.0	52.7
	48.7	77.1	83.5	76.3	56.7	71.8
	48.6	77.3	83.6	76.0	57.6	72.5
	48.8	77.2	83.5	78.5	56.8	36.7
	48.5	77.0	83.4	76.5	58.9	63.1
	49.9	78.5	78.1	72.3	61.2	61.2
	54.1	79.3	81.2	81.0	73.6	55.0
	46.9	79.9	76.9	75.4	71.4	50.5

Experimental Section

General NMR spectra were recorded with a Varian 300 MHz, 400 MHz, 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 (δ 77.16) for ^{13}C. ^1H-NMR signals were assigned with the aid of COSY. ^{13}C signals were assigned with the aid of DEPT-135, HSQC and HMBC. Mass spectra were recorded on a Micromass LCT KC420 or Micromass Quattro instruments. IR spectra were recorded with a Varian IR using thin film on NaCl or Germanium plates. Optical rotations were determined with a Perkin-Elmer 343 model polarimeter at the sodium D line at 23 ºC. TLC was performed on aluminium sheets precoated with Silica Gel 60 (HF254, E. Merck) and spots visualized by UV and charring with 1:20 H_2SO_4-EtOH or with 1:1 $KMnO_4$ (1 % w/v solution)-$NaHCO_3$ (5 % w/v solution). Flash chromatography was generally employed and was carried out using 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, DCM (Riedel-deHaen), cyclohexane and MeOH (Sigma Aldrich). Anhydrous DMF and anhydrous toluene were used as purchased from Sigma-Aldrich. THF, CH_2Cl_2 and methanol were used as obtained from a Pure-Solv^{TM} solvent purification system.

(R)-1-((4R,5R)-5-((S)-2-azido-1-(benzyloxy)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl) ethane-1,2-diol 9

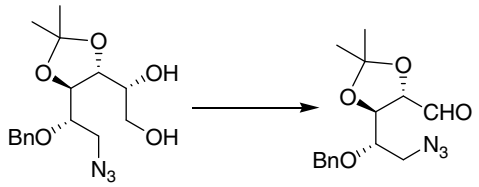


D-(+)-D-Glucono-δ-lactone **1** (20 g, 1.15 mol) was dissolved in acetone (12 mL), methanol (4 mL) and dimethoxypropane (40 mL). p-TsOH (300 mg, 1.55 mmol) was added and the mixture was stirred for 2 days at room temp. Satd $NaHCO_3$ (4 mL) was then added. The acetone and dimethoxypropane were removed under diminished pressure and the residue then dissolved in CH_2Cl_2 (100 mL) and washed with brine (100 mL). The aqueous layer was extracted with CH_2Cl_2 (2×50 mL) and the combined organic layers dried ($MgSO_4$). Filtration and removal of the solvent under diminished pressure gave the intermediate acetonide (32.0 g) as colourless oil, which was used in the next step without further purification. Sodium borohydride (5.0 g, 0.13 mol) was added to the acetonide (32.0 g, 0.11 mol) in ethanol (100 mL). The reaction mixture was heated at reflux, while stirring for 1h. Excess ethanol was removed under diminished pressure and the residue was dissolved in EtOAc (150 mL) and washed with water (150 mL). The aqueous layer was extracted with EtOAc (4 × 60 mL). The combined organic layer were dried ($MgSO_4$), filtered and the solvent removed to give **8**[1] (27.5 g) as a colourless oil, which was used in the next step

[1] Long, D. D.; Smith, M. D.; Martin, A.; Wheatley, J. R.; Watkin, D. G.; Müller, M.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1*, **2002**, 1982.

without further purification. 2,6-Lutidine (6.48 mL, 0.056 mol) and methanesulfonyl chloride (4.32 mL, 0.056 mol) were added to an ice-bath cooled solution of diol compound (12.2 g, 0.046 mol) in CH_2Cl_2 (150 mL) and the mixture was stirred at room temp for 15 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with satd $NaHCO_3$ (150 mL) and brine (150 mL), dried ($MgSO_4$), filtered and the solvent removed. Chromatography of the residue (EtOAc-cyclohexane, 1:2) gave the desired mesylate (11.7 g, 75%) as white solid; ^{1}H NMR ($CDCl_3$, 400MHz) δ 4.30 (d, 1 H, *J* = 2.1 Hz), 4.29 (s, 1 H), 4.14-4.11 (m, 1 H), 4.03 (m, 2 H), 3.96-3.90 (m, 3 H), 3.06 (s, 3 H), 1.40, 1.39, 1.35, 1.32 (s each, 3 H each); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 110.3 (C), 110.2 (C), 79.8 (CH), 77.4 (CH), 77.3 (CH), 71.4 (CH_2), 68.4 (CH), 68.1 (CH_2), 37.8 (CH_3), 27.3 (CH_3), 27.0 (CH_3), 26.9 (CH_3), 25.4 (CH_3); IR (cm^{-1}) ν_{max} = 3513, 2988, 2938, 2359, 1457, 1373, 1355, 1215, 1176, 1071, 964, 843; ESI/MS$^-$ (*m*/*z*): 363.1 (M+Na$^+$); ESI-HRMS: calcd for $C_{13}H_{25}O_8S$ [M+H$^+$]: 341.1270; Found: 341.1263. Sodium azide (767 mg, 11.8 mmol, 1.3 eq) was added to the mesylate (3.09 g, 9.08 mmol) in DMF (20 mL) and the mixture stirred at 100 °C for 3.5 h. The reaction mixture was cooled to room temp, diluted with EtOAc (100 mL), and then washed with water (80 mL). The aq layer was washed with EtOAc (3 × 50 mL) and the combined organic layer was dried ($MgSO_4$) to give the desired azide intermediate (2.71 g) as a colourless oil. To a stirred solution of this azide compound (2.71 g, 9.08 mmol) at 0 °C in THF (80 mL) was added NaH (1.18 g, 11.8 mmol, 60% dispersion in mineral oil). The suspension was stirred for 1h at room temperature. Then benzyl bromide (1.40 mL, 11.8 mmol) was added dropwise and the mixture was stirred overnight at room temp. The mixture was filtered through celite, concentrated and EtOAc (80 mL) was added. The organic layer was washed with water (80 mL) and dried ($MgSO_4$). Filtration and removal of solvent gave **9** (3.97 g) as a yellow oil, which was used next step directly. This benzylated intermediate compound (3.97 g, 9.08 mmol) was dissolved in aq AcOH (80 mL) and the mixture stirred at room temp for 15 h. The solvent was removed under vacuum and chromatography of the reside (EtOAc-cyclohexane, 1:2) gave **9** (2.15 g, yield for 3 steps = 79%) as a pale yellow oil; ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.36-7.33 (m, 5 H), 4.81 (d, 1H, *J* 11.4 Hz), 4.65 (d, 1 H, *J* 11.4 Hz), 4.02 (m, 1 H), 3.90 (t, 1 H, *J* 7.5 Hz), 3.82 (m, 1H), 3.74 (m, 1 H), 3.64-3.58 (m, 2 H), 3.53 (m, 2 H), 2.04 (OH), 1.39, 1.36 (s each, 3 H each); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.3 (C), 128.9 (CH), 128.6 (CH), 128.5 (CH), 109.7 (C), 79.8 (CH), 76.9 (CH), 76.7 (CH), 74.1 (CH_2), 73.0 (CH), 64.1 (CH_2), 51.8 (CH_2), 27.2 (CH_3), 27.0 (CH_3); IR (cm^{-1}) ν_{max} = 3423, 2987, 2935, 2879, 2103, 1455, 1372, 1252, 1215, 1074, 872, 738, 699; ESI/MS$^-$ (*m*/*z*): 360.1 (M+Na$^+$); ESI-HRMS: calcd for $C_{16}H_{24}N_3O_5$: 338.1716; Found: 338.1718.

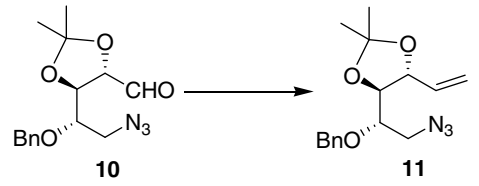
(4S,5R)-5-[(S)-2-Azido-1-(benzyloxy)ethyl]-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde 10



9 **10**

Diol **9** (3.75 g, 0.011 mol) was dissolved in CH_2Cl_2 (50 mL) and water (50 mL). The reaction mixture was cooled to 0 °C and then $NaIO_4$ (3.09 g, 0.014 mol) was added and stirring was continued for 2 h allowing the mixture to attain room temperature. Water (20 mL) was then added, and then the organic layer was separated and the aq layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layer was dried ($MgSO_4$), filtered and the solvent was removed under diminished pressure. Chromatography of the residue (EtOAc-cyclohexane, 1:4) gave **10** (2.758 g, 82%) as a colourless oil; ^{1}H NMR ($CDCl_3$, 400MHz) δ 9.73 (d, 1 H, *J* 1.5 Hz), 7.37-7.30 (m, 5 H), 4.75 (d, 1 H, *J* 11.5 Hz), 4.69 (d, 1 H, *J* 11.5 Hz), 4.29 (dd, 1 H, *J* 1.5 Hz, *J* 7.1Hz), 4. 24 (dd, 1 H, *J* 4.2 Hz, *J* 7.1 Hz), 3.70 (td, 1H, *J* 6.2 Hz, *J* 5.1 Hz), 3.47 (brs, 1 H), 3.46 (d, 1 H, *J* 2.2 Hz), 1.48, 1.39 (s each, 3 H each); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.3 (CH), 137.6 (C), 128.8 (CH), 128.3 (CH), 111.9 (C), 81.1 (CH), 77.1 (CH), 77.0 (CH), 73.8 (CH_2), 51.5 (CH_2), 26.7 (CH_3), 26.3 (CH_3); IR (cm^{-1}) ν_{max} = 3428, 2988, 2935, 2103, 1732, 1455, 1372, 1254, 1215, 11646, 1081, 870, 737, 698; ESI/MS$^-$ (*m*/*z*): 328.1 (M+Na$^+$).

(4S,5R)-4-((S)-2-Azido-1-(benzyloxy)ethyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane 11

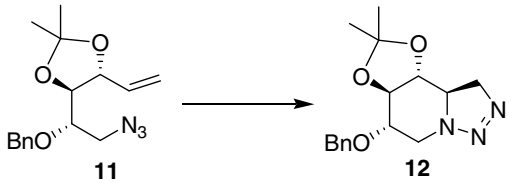


10 **11**

To a cooled solution of Ph_3PCH_2I (2.458 g, 6.08 mmol) in THF (70 mL) at -78 °C was added 1.0 M NaHMDS solution (6.08 mL, 6.08 mmol) dropwise and stirring was continued at -78 °C for 25 min followed by 15 min at O °C and a further 30 min at room temperature. The mixture was cooled again to -78 °C and **10** (1.419 g, 4.68 mmol), which had been pre-dissolved in anhyd. THF (40 mL), was then added dropwise via syringe. The reaction was then stirred at -78 °C for 10 min and stirring was continued at room temp for a further 2 h. The reaction was quenched by the addition of water (100 mL). The aq layer was extracted with EtOAc (3 x 100 mL) and the combined organic layer dried ($MgSO_4$), filtered and the solvent was removed. Chromatography of the residue (EtOAc-cyclohexane, 1:25) gave the title compound **11** (950 mg, 67%) as a colourless oil; ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.37-7.31 (m, 5 H), 5.77 (m, 1H), 5.23 (dd, 1 H, *J* 1.8 Hz, 2.0 Hz), 5.20 (m, 1 H), 4.77 (d, 1 H, *J* 11.7 Hz), 4.66 (d, 1 H, *J* 11.7 Hz), 4.31 (t, 1 H, *J* 7.9 Hz), 3.83 (dd, 1 H, *J* 8.4 Hz, *J* 4.0 Hz), 3.59 (dt, 1 H, *J* 5.8 Hz, *J* 4.1 Hz), 3.46 (br s, 1 H), 3.44 (br s, 1 H), 1.43, 1.42

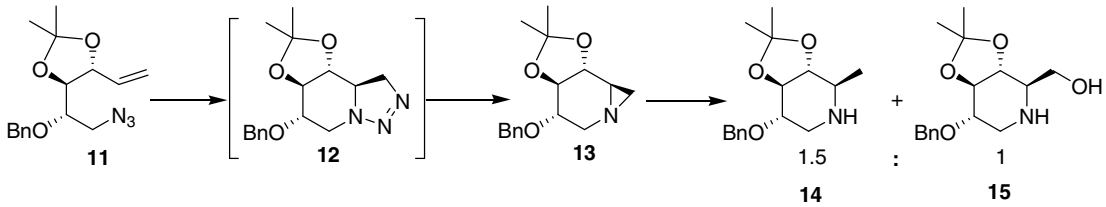
(each s, each 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.6 (C), 135.2 (CH), 128.5 (CH), 128.2 (CH), 128.0 (CH), 119.3 (CH_2), 109.4 (C), 80.7 (CH), 78.3 (CH), 76.1 (CH), 73.3 (CH_2), 51.7 (CH_2), 26.9 (CH_3), 26.8 (CH_3); IR (cm^{-1}) ν_{max} = 2987, 2934, 2874, 2101, 1496, 1371, 1244, 1216, 1067, 876, 737, 698; ESI-HRMS-ESI: calcd for $C_{16}H_{22}N_3O_3$ [M+H$^+$] 304.1661; Found: 304.1658.

(3aR,4S,9bR)-4-(Benzyloxy)-2,2-dimethyl-3a,4,5,9,9a,9b-hexahydro-[1,3]dioxolo [4,5-c][1,2,3]triazolo[1,5-a]pyridine 12



A solution of compound **11** (67 mg, 0.22 mmol) in DMF (7 mL) was stirred at 110 °C for 8 h. Water (10 mL) was added and the laters were separated. The aq layer was extracted with Et_2O (3×20 mL) and the combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed. Chromatography of the residue (EtOAc-cyclohexane, 1:3) gave the title compound **12** (35 mg, yield: 52%): ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.37-7.26 (m, 5 H), 4.83 (d, 1 H, *J* 11.9 Hz), 4.68 (dd, 1 H, *J* 5.7, 14.4 Hz), 4.65 (d, 1 H, *J* 11.9 Hz), 4.52 (dd, 1 H, *J* 2.0 Hz, *J* 16.1 Hz), 3.94 (dd, 1 H, *J* 9.6 Hz, *J* 16.1 Hz), 3.62 (m, 2 H), 3.52 (t, 1 H, *J* 9.2 Hz), 3.20 (dd, 1 H, *J* 9.6 Hz, *J* 14.4 Hz), 2.77 (dd, 1 H, *J* 10.2 Hz, *J* 9.2 Hz), 1.44, 1.41 (s each, 3 H each); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.9 (C), 128.5 (CH), 127.9 (CH), 127.8 (CH), 111.2 (C), 81.4 (CH), 75.8 (CH), 73.3 (CH), 72.2 (CH_2), 67.9 (CH_2), 56.9 (CH), 49.2 (CH_2), 26.8 (CH_3), 26.7 (CH_3); IR (cm^{-1}) ν_{max} = 2985, 2931, 2871, 1494, 1372, 1232, 1087, 986, 839, 694; ESI/MS$^-$ (*m*/*z*): 304.1 (M+H$^+$).

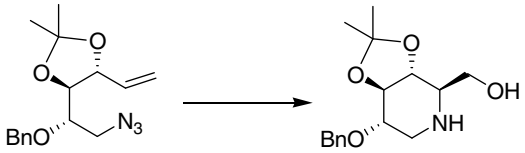
(3aR,4R,7S,7aR)-7-(benzyloxy)-2,2,4-trimethylhexahydro-[1,3]dioxolo [4,5-c]pyridine 14 and (3aR,4R,7S,7aR)-7-(benzyloxy)-2,2-dimethylhexahydro-[1,3]dioxolo [4,5-c]pyridin-4-yl)methanol 15



Azide **11** (60 mg, 0.2 mmol) in toluene (6 mL) was stirred whilst heating at reflux for 1h, and the solution was then cooled to room temperature. Silica gel (600 mg, 10% w/w) was added and stirring was continued for overnight at room temp. The mixture was filtered through celite and removal of solvent and subsequent chromatography of the residue (EtOAc-cyclohexane, 2:1) aziridine **13** (24 mg, 33%); LRESI-MS (*m*/*z*): 276.2; [M+H$^+$]; HRMS-ESI: calcd for $C_{16}H_{22}NO_3$ [M+H$^+$] 276.1600; Found: 276.1605. The aziridine **13** (24 mg, 0.09 mmol) was dissolved in EtOAc (3 mL) and

by 10% Pd-C (12 mg) was added and the mixture stirred under H_2. Filtration, removal of solvent and chromatography of the residue gave a 1.5:1 mixture of **14** and **15** (19 mg); ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.36-7.26 (m, 12.5 H, ArH), 4.83 (d, 1 H, *J* 12.0 Hz, H7a, **15**), 4.75 (d, 1.5 H, *J* 12.1 Hz, H7a, **14**), 4.66 (d, 1.5 H, *J* 11.6 Hz, H7b, **14**), 4.64 (d, 1 H, *J* 11.0 Hz, H7b, **15**), 4.06 (dd, 1.5 H, *J* 5.6 Hz, *J* 12.0 Hz, H3, **14**), 4.03 (dd, 1.5 H, *J* 2.4 Hz, *J* 5.4 Hz, H4, **14**), 3.81 (dd, 1 H, *J* 3.8 Hz, *J* 11.0 Hz, H6a, **15**), 3.68 (dd, 1 H, *J* 5.5 Hz, *J* 11.0 Hz, H6b, **15**), 3.60 (dt, 1 H, *J* 4.9 Hz, *J* 9.4 Hz, H2, **15**), 3.50 (t, 1 H, *J* 9.1 Hz, H3, **15**), 3.45 (ddd, 1.5 H, *J* 5.4 Hz, *J* 6.5 Hz, *J* 10.4 Hz, H2, **14**), 3.28 (dd, 1 H, *J* 4.9 Hz, *J* 13.1 Hz, H1a, **15**), 3.17 (dd, 1.5 H, *J* 5.3 Hz, *J* 13.1 Hz, H1a, **14**), 3.16 (t, 1 H, *J* 9.4 Hz, H4, **15**), 3.04 (dq, 1.5 H, *J* 2.3 Hz, *J* 6.7 Hz, H5, **14**), 2.82 (m, 1 H, H5, **15**), 2.49 (m, 2.5 H, H1b, **14** and **15**), 2.13 (brs, 3.5 H, -NH, -OH), 1.45 (s, 6 H, 2 -CCH_3, **15**), 1.44 (s, 4.5 H, -CCH_3, **14**), 1.37 (s, 4.5 H, -CCH_3, **14**), 1.25 (d, 4.5 H, J 6.8 Hz, CH_3, **14**); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.4 (2C), 128.3 (CH), 128.2 (CH), 127.0 (CH), 127.6 (CH), 127.5 (CH), 110.2 (C), 108.8 (C), 83.4 (CH), 79.4 (CH), 77.4 (CH), 76.9 (CH), 76.6 (CH), 76.5 (CH), 71.8 (CH2), 71.7 (CH2), 63.1 (CH_2), 58.9 (CH), 51.4 (CH), 48.5 (CH_2), 46.8 (CH_2), 28.1 (CH_3), 27.0 (CH_3), 26.7 (CH_3), 26.3 (CH_3), 17.6 (CH_3); ESI/MS- (*m*/*z*): 278.2 [M**14**+H^+] and 294.2 [M**15**+H^+].

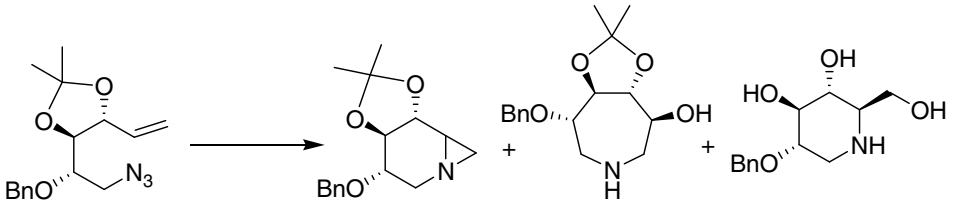
((3aR,4R,7S,7aR)-7-(Benzyloxy)-2,2-dimethylhexahydro-[1,3]dioxolo[4,5-c]pyridin-4-yl) methanol 15



11 **15**

A solution of azide **11** (40 mg, 0.14 mmol) in toluene (3 mL) was stirred whilst heating at reflux for 1 h and then cooled to room temperature. Then water (3 mL) was added and the mixture was stirred under reflux for 15 h. TLC showed that the intermediate triazoline was consumed. The mixture was then cooled to room temperature, and extracted with EtOAc (3×5 mL) and combined organic layers were dried ($MgSO_4$), filtered and the solvent removed. Chromatography of the residue (EtOAc-cyclohexane, 1:3 and MeCN) gave the title compound **15** (8 mg, 19%): ^{1}H NMR ($CDCl_3$, 600MHz) δ 7.35 (m, 5 H), 4.82 (d, 1 H, *J* 12.0 Hz), 4.64 (d, 1 H, *J* 12.0 Hz), 3.83 (dd, 1 H, *J* 3.8 Hz, *J* 11.0 Hz), 3.68 (dd, 1 H, *J* 5.5 Hz, *J* 11.0 Hz), 3.62 (dt, 1 H, *J* 9.5 Hz, *J* 5.0 Hz), 3.51 (t, 1 H, *J* 9.1 Hz), 3.29 (dd, 1 H, *J* 5.0 Hz, *J* 13.1 Hz), 3.17 (t, 1 H, *J* 9.4 Hz), 2.84 (ddd, 1 H, *J* 9.5 Hz, *J* 5.2 Hz, *J* 4.0 Hz), 2.52 (dd, 1 H, *J* 9.7 Hz, *J* 13.1 Hz), 1.45 (s, 6 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.4 (C), 128.4 (CH), 127.8 (CH), 127.6 (CH), 110.3 (C), 83.4 (CH), 77.0 (CH), 76.5 (CH), 71.9 (CH_2), 63.1 (CH_2), 58.9 (CH), 48.5 (CH_2), 27.0 (CH_3), 26.7 (CH_3); IR (cm^{-1}) ν_{max} = 3313 (br), 2984, 2929, 2877, 1642, 1454, 1381, 1371, 1229, 1098, 1068, 843, 737, 698; HRMS-ESI: calcd for $C_{16}H_{24}NO_4$ [M+H^+]: 294.1705; Found: 294.1694.

(3aR,4S,8S,8aR)-8-(Benzyloxy)-2,2-dimethylhexahydro-3aH-[1,3]dioxolo[4,5-d]azepin-4-ol 16 and (2R,3R,4S,5S)-5-(Benzyloxy)-2-(hydroxymethyl)piperidine-3,4-diol 17

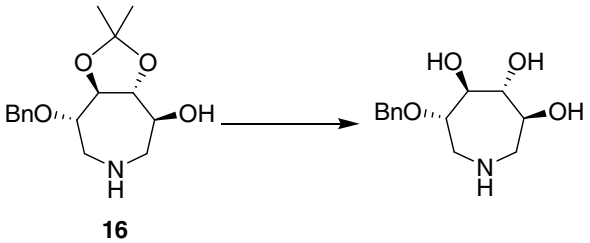


Compound **11** (106 mg, 0.35 mmol) was dissolved in 70% acetic acid (20 mL). The mixture was stirred at room temperature for 15 h, and then concentrated. Chromatography of the residue (EtOAc-cyclohexane, 3:1 to 5:1 gradient elution) gave aziridine **13** (7.9 mg, 15%), **16** (33.8 mg, 33%) as a pale yellow oil and the title compound **17** (12.4 mg, 14%) as a pale yellow oil.

Analytical data for Compound 16: ^{1}H NMR ($CDCl_3$, 600MHz): δ 7.34 (m, 5 H), 4.78 (d, 1 H, *J* 12.2 Hz), 4.62 (d, 1 H, *J* 12.2 Hz), 4.11 (dd, 1 H, *J* 8.9 Hz, *J* 7.1 Hz), 3.76 (m, 2 H), 3.56 (dt, 1 H, *J* 7.4 Hz, *J* 3.3 Hz), 3.23 (dd, 1 H, *J* 13.6 Hz, *J* 5.3 Hz), 3.13 (dd, 1 H, *J* 14.8 Hz, *J* 3.2 Hz), 2.88 (dd, 1 H, *J* 14.8 Hz, *J* 4.8 Hz), 2.62 (dd, 1 H, *J* 13.6 Hz, *J* 7.5 Hz), 1.44, 1.43 (s each, 3 H each); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.7 (C), 128.3 (CH), 127.8 (CH), 127.5 (CH), 109.6 (C), 81.2 (CH), 81.0 (CH), 79.3 (CH), 73.6 (CH), 71.6 (CH_2), 55.0 (CH_2), 54.1 (CH_2), 27.2 (CH_3), 27.1 (CH_3); IR (cm^{-1}): ν_{max} = 3364, 2924, 2857, 1734, 1638, 1454, 1374, 1234, 1068, 739, 698; HRMS-ESI: calcd for $C_{16}H_{24}NO_4$ [M+H$^+$] 294.1705; Found: 294.1694.

Analytical data for Compound 17: ^{1}H-NMR (CD_3OD, 400MHz): δ 7.39 (m, 5 H), 4.73 (d, 1 H, *J* 11.7 Hz), 4.65 (d, 1 H, *J* 11.7 Hz), 3.83 (dd, 1 H, *J* 10.9 Hz, *J* 1.8 Hz), 3.60 (dd, 1 H, *J* 10.9 Hz, *J* 6.3 Hz), 3.35 (m, 2 H), 3.24 (dd, 1 H, *J* 9.2 Hz, *J* 3.1 Hz), 3.19 (m, 1 H), 2.48 (m, 2 H); ^{13}C NMR (CD_3OD, 100MHz) δ 138.6 (C), 127.9 (CH), 127.6 (CH), 127.2 (CH), 78.5 (CH), 78.1 (CH), 72.3 (CH_2), 71.5 (CH), 61.2 (CH, CH_2), 49.9 (CH_2); IR (cm^{-1}) ν_{max} = 3318 (br), 2922, 1565, 1454, 1413, 1099, 746, 699; HRMS-ESI: calcd for $C_{16}H_{24}NO_4$ [M+H$^+$] 294.1705; Found: 294.1698.

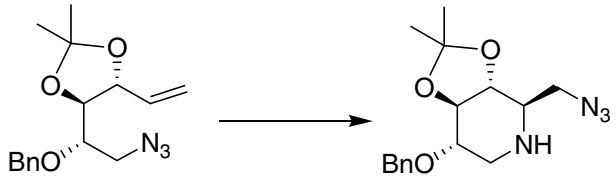
(3S,4R,5S,6S)-6-(Benzyloxy)azepane-3,4,5-triol



Compound **16** (34 mg, 1.18 mmol) was dissolved in the 70% acetic acid (5 mL) and the mixture was stirred at 70 °C for 3h. The reaction mixture was cooled to room temperature, and concentrated, and chromatography of the residue (EtOAc-cyclohexane, 1:10 to 1:3 gradient elution) gave the title compound (9.5 mg, 33%) as a colourless oil: ^{1}H NMR (CD_3OD, 400MHz): δ 7.40-7.25 (m, 5 H), 4.71 (d,

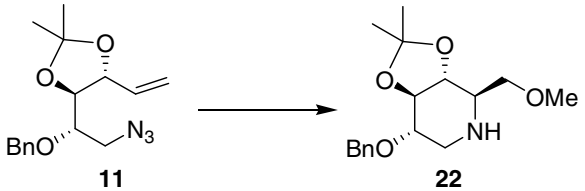
1 H, *J* 11.7 Hz), 4.63 (d, 1 H, *J* 11.7 Hz), 3.79 (t, 1 H, *J* 6.2 Hz), 3.74 (dd, 1 H, *J* 8.1 Hz, *J* 3.0 Hz), 3.63 (dd, 1 H, *J* 8.7 Hz, *J* 5.6 Hz), 3.56 (dd, 1 H, *J* 7.7 Hz, *J* 6.4 Hz), 3.14 (dd, 1 H, *J* 13.6 Hz, *J* 2.2 Hz), 3.03 (m, 2 H), 2.76 (dd, 1 H, *J* 13.6 Hz, *J* 8.5 Hz); ^{13}C NMR (CD_3OD, 100MHz) δ 138.3 (C), 127.9 (CH), 127.6 (CH), 127.3 (CH), 79.9 (CH), 76.9 (CH), 75.4 (CH), 71.7 (CH_2), 71.4 (CH), 50.5 (CH_2), 46.9 (CH_2); IR (cm^{-1}) ν_{max} = 3300 (br), 2922, 1570, 1453, 1412, 1053, 742, 698; ESI/MS$^-$ (*m*/*z*): 254.2 ($M+H^+$); HRMS-ESI: calcd for $C_{13}H_{20}NO_4$: 254.1392; Found: 254.1399.

(3aR,4R,7S,7aR)-4-(azidomethyl)-7-(benzyloxy)-2,2-dimethylhexahydro-[1,3]dio xolo[4,5-c] pyridine 21



A solution of azide **11** (56 mg, 0.18 mmol) in toluene (5 mL) was stirred whilst heating at reflux for 1 h and then cooled to room temperature. Then NaN_3 (60 mg, 0.92 mmol) and AcOH (16 μL, 0.28 mmol) was added. The mixture was heated at reflux, whilst stirring for 15 h. The reaction mixture was cooled to room temperature and diluted with EtOAc, washed with water (1×20 mL) and then the aqueous layer was extracted with EtOAc (3×10 mL). The organic layers were combined and dried ($MgSO_4$), filtered and the solvent was removed. Chromatography of the residue (EtOAc-cyclohexane, 1:3 followed by MeCN) gave the title compound **21** (20 mg, yield: 35%): ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.36-7.26 (m, 5 H), 4.81 (d, 1 H, *J* 12.0 Hz), 4.62 (d, 1 H, *J* 12.0 Hz), 3.63 (dd, 1 H, *J* 12.5 Hz, *J* 3.1 Hz), 3.59 (dd, 1 H, *J* 9.5 Hz, *J* 5.0 Hz), 3.50 (dd, 1 H, *J* 12.5 Hz, *J* 6.0 Hz), 3.47 (t, 1 H, *J* 9.2 Hz), 3.27 (dd, 1 H, *J* 13.1 Hz, *J* 5.0 Hz), 3.11 (t, 1 H, *J* 9.3 Hz), 2.88 (ddd, 1 H, *J* 9.3 Hz, *J* 6.0 Hz, *J* 3.0 Hz), 2.50 (dd, 1 H, *J* 13.1 Hz, *J* 9.6 Hz), 1.45 (s, 3H), 1.44 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.3 (C), 128.4 (CH), 127.8 (CH), 127.6 (CH), 110.3 (C), 83.3 (CH), 77.1 (CH), 76.4 (CH), 71.9 (CH_2), 57.0 (CH), 52.7 (CH_2), 48.5 (CH_2), 26.9 (CH_3), 26.6 (CH_3); IR (cm^{-1}): ν_{max} = 2923, 2875, 2359, 2338, 2103, 1453, 1375, 1230, 1096, 787; HRMS-ESI: calcd for $C_{16}H_{23}N_4O_3$ [$M+H^+$] 319.1770; Found: 319.1781.

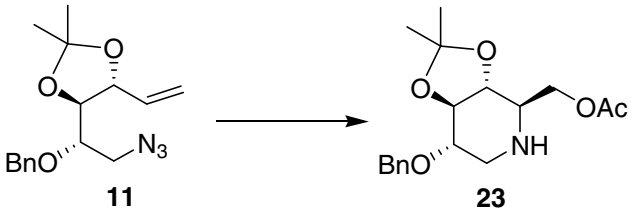
(3aR,4R,7S,7aR)-7-(Benzyloxy)-4-(methoxymethyl)-2,2-dimethylhexahydro-[1,3] dioxolo[4,5-c]pyridine 22



A solution of azide **11** (38.7 mg, 0.13 mmol, 1.0 eq) in toluene (3 mL) was stirred whilst heating at reflux for 1 h and then cooled to room temperature. The toluene was evaporated and then MeOH (3 mL) was added. The mixture was heated at reflux

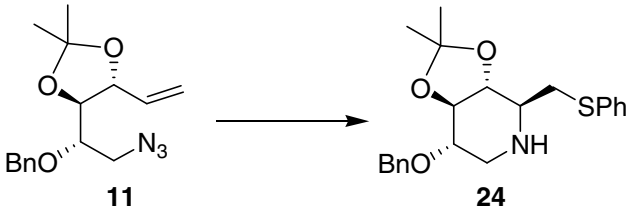
whilst stirring for another 1 h, then cooled to room temperature and the MeOH was removed. Chromatography of the residue (EtOAc-cyclohexane, 1:3) gave the title compound **22** (8 mg, yield: 20%): ^{1}H NMR ($CDCl_3$, 600MHz) δ 7.35 (m, 5 H), 4.82 (d, 1 H, *J* 12.0 Hz), 4.63 (d, 1 H, *J* 12.0 Hz), 3.59 (m, 2 H), 3.47 (t, 1 H, *J* 9.1 Hz), 3.46 (dd, 1 H, *J* 5.6 Hz, *J* 9.6 Hz), 3.35 (s, 3 H), 3.26 (dd, 1 H, *J* 5.0 Hz, *J* 13.0 Hz), 3.17 (t, 1 H, *J* 9.4 Hz), 2.83 (ddd, 1 H, *J* 2.7 Hz, *J* 5.6 Hz, *J* 9.5 Hz), 2.49 (dd, 1 H, *J* 9.7 Hz, *J* 13.0 Hz), 1.45 (s, 6 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.5 (C), 128.3 (CH), 127.8 (CH), 127.6 (CH), 110.0 (C), 83.6 (CH), 77.3 (CH), 76.0 (CH), 72.5 (CH_2), 71.8 (CH_2), 59.3 (CH_3), 57.6 (CH_2), 48.6 (CH_2), 27.0 (CH_3), 26.8 (CH_3); IR (cm^{-1}) ν_{max} = 2984, 2922, 2888, 1454, 1380, 1371, 1097, 1063, 843, 736, 698; 308.2; HRMS-ESI: calcd for $C_{17}H_{26}NO_4$ [M+H$^+$] 308.1862; Found: 308.1855.

((3aR,4R,7S,7aR)-7-(Benzyloxy)-2,2-dimethylhexahydro-[1,3]dioxolo[4,5-c]pyridin-4-yl) methyl acetate 23



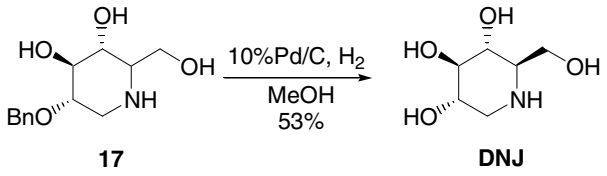
The azide **11** (37 mg, 0.12 mmol) in toluene (4 mL) was stirred whilst heating at reflux for 1 h and the mixture was then cooled to 50 °C. Then AcOH (35μL, 0.61 mmol) was added and the mixture was heated at reflux for another 1 h. The solution was then cooled to room temperature and concentrated. Chromatography of the residue (EtOAc-cyclohexane, 1:2) gave the title compound **23** (18 mg, 44%):^{1}H NMR ($CDCl_3$, 500MHz): δ 7.35 (m, 5 H), 4.82 (d, 1 H, *J* 12.0 Hz), 4.63 (d, 1 H, *J* 12.0 Hz), 4.35 (dd, 1 H, *J* 2.9 Hz, *J* 11.5 Hz), 4.04 (dd, 1 H, *J* 6.7 Hz, *J* 11.5 Hz), 3.60 (dt, 1 H, *J* 9.5 Hz, *J* 5.0 Hz), 3.48 (t, 1 H, *J* 9.1 Hz), 3.26 (dd, 1 H, *J* 5.0 Hz, *J* 13.0 Hz), 3.10 (t, 1 H, *J* 9.3 Hz), 2.94 (ddd, 1 H, *J* 9.6 Hz, *J* 6.7 Hz, *J* 2.9 Hz), 2.50 (dd, 1 H, *J* 9.6 Hz, *J* 13.0 Hz), 2.07 (s, 3 H), 1.44, 1.43 (s each, 3 H each); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.7 (C), 138.4 (C), 128.3 (CH), 127.8 (CH), 127.6 (CH), 110.2 (C), 83.5 (CH), 77.1 (CH), 76.3 (CH), 71.8 (CH_2), 64.8 (CH_2), 56.7 (CH), 48.7 (CH_2), 26.9 (CH_3), 26.7 (CH_3), 20.8 (CH_3); IR (cm^{-1}): ν_{max} = 2985, 2933, 2881, 1742, 1454, 1381, 1371, 1235, 1100, 1068, 842, 739, 699; HRMS-ESI: calcd for $C_{18}H_{26}NO_5$ [M+H$^+$] 336.1811; Found: 336.1806.

(3aR,4S,7S,7aR)-7-(benzyloxy)-2,2-dimethyl-4-(phenylthiomethyl)hexahydro-[1,3]dioxolo[4,5-c]pyridine 24



A solution of azide **11** (43 mg, 0.14 mmol) in toluene (4 mL) was stirred whilst heating at reflux for 1 h and then cooled to room temperature. Evaporated to remove toluene and then PhSH (1 mL) was added. The mixture was stirred at room temperature for overnight. TLC showed that the intermediate triazoline was consumed. Cooled to room temperature, and concentrated. Chromatography of the residue (EtOAc-cyclohexane, 1:3) gave the title compound **24** (30 mg, yield: 57%): ^{1}H NMR ($CDCl_3$, 600MHz) δ 7.39-7.20 (m, 10 H), 4.80 (d, 1 H, *J* 12.0 Hz), 4.61 (d, 1 H, *J* 12.0 Hz), 3.61 (dt, 1 H, *J* 5.0 Hz, *J* 9.5 Hz), 3.43 (t, 1 H, *J* 9.1 Hz), 3.40 (dd, 1 H, *J* 2.9 Hz, *J* 13.6 Hz), 3.27 (dd, 1 H, *J* 5.0 Hz, *J* 12.8 Hz), 3.08 (t, 1 H, *J* 9.1 Hz), 2.97 (dd, 1 H, *J* 7.9 Hz, *J* 13.6 Hz), 2.88 (ddd, 1 H, *J* 2.9 Hz, 8.0 Hz, *J* 9.4 Hz), 2.48 (dd, 1 H, *J* 9.6 Hz, *J* 12.8 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.5 (C), 135.9 (C), 129.4 (CH), 129.0 (CH), 128.4 (CH), 127.8 (CH), 127.6 (CH), 126.3 (CH), 110.1 (C), 83.5 (CH), 78.5 (CH), 77.2 (CH), 71.8 (CH_2), 56.8 (CH), 48.8 (CH_2), 36.7 (CH_2), 26.8 (CH_3), 26.7 (CH_3); IR (cm^{-1}) ν_{max} = 2984, 2925, 2876, 1481, 1454, 1439, 1381, 1371, 1229, 1092, 844, 738, 696; ESI/MS$^-$ (*m/z*): 386.2 ($M+H^+$); HRMS-ESI: calcd for $C_{22}H_{28}NO_3S$: 386.1790; Found: 386.1795.

1-Deoxynojirimycin



DNJ derivative **17** (12.4 mg, 0.05 mmol) was dissolved in MeOH (3 mL). And then 10% Pd-C (10 mg) was added and the mixture was stirred overnight under an atmosphere of H_2 at room temp. The mixture was then filtered through celite and the solvent was removed under diminished pressure. Chromatography of the residue (H_2O-MeOH-H_2O) gave DNJ (4.3 mg, 53%) as a pale-yellow solid. ^{1}H-NMR (CD_3OD, 400MHz) δ 3.85 (dd, 1H, *J* 3.1 Hz, *J* 11.2 Hz), 3.65 (dd, 1 H, *J* 6.2 Hz, *J* 11.2 Hz), 3.47 (m, 1 H), 3.23 (m, 2 H), 3.15 (dd, 1 H, *J* 5.2 Hz, 12.2 Hz), 2.60 (ddd, 1 H, *J* 8.99 Hz, *J* 5.82 Hz, *J* 3.16 Hz), 2.54 (t, 1 H, *J* 11.5 Hz); ESI/MS$^-$ (*m/z*): 164.2 ($M+H^+$).