Supporting information

Stereoconvergent synthesis of 1-deoxynojirimycin isomers by using the 3 component 4 centred Ugi reaction

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**General Information:** Reagent grade solvents were used for the extraction and flash chromatography. All the reagents and chemicals were purchased from Sigma–Aldrich Chemical Co., Lancaster and were used directly without further purification. The progress of reactions was checked by analytical thin-layer chromatography (TLC, Merck silica gel 60 F-254 plates). The plates were visualized first with UV illumination followed by charring with 10% H$_2$SO$_4$ in CH$_3$OH. Flash column chromatography was performed using silica gel (230-400 mesh). The solvent compositions reported for all chromatographic separations are on a volume/volume (v/v) basis. $^1$H-NMR spectra were recorded at either 200 or 300 MHz and are reported in parts per million (ppm) on the $\delta$ scale relative to tetramethylsilane as an internal standard. $^{13}$C-NMR spectra were recorded at either 50 or 75 MHz and are reported in parts per million (ppm) on the $\delta$ scale relative to CDCl$_3$ ($\delta$ 77.00). Mass spectra were obtained using JEOL SX-102 (ESI) instrument. Melting points were determined on a Mel Temp II melting point apparatus and are uncorrected.
2,3-O-Cyclohexylidene-β-ribose (20)

A mixture of β-ribose 12 (30.0 g, 0.2 mol) and p-toluenesulfonic acid (0.7 g, 3.7 mmol) was stirred in freshly distilled cyclohexanone (200 mL) under nitrogen. After 12 h, TLC (ethyl acetate) indicated complete consumption of starting material (Rf 0.1), and the formation of a major product (Rf 0.7). Ethyl acetate (500 ml) was added and the mixture washed with sodium bicarbonate solution (300 ml), and water (300 ml). The organic extracts were dried (Na₂SO₄), filtered, the solvent removed and the residue purified by dry flash chromatography (MeOH:CHCl₃ 5%) to yield 2.3-O-cyclohexylidene-β-ribose 98 (44.5 g, 97%) as a colourless oil; [α]²⁰ -20.8 (c, 1.1 in CHCl₃); IR (νmax, KBr, cm⁻¹): 3556, 2842, 2922, 1186, 1048, 718.; ¹H NMR (300 MHz, CDCl₃ + D₂O): δ 5.55 (s, 1H), 4.71 – 4.30 (m, 3H), 4.08 (s, 1H), 3.91 (s, 1H), 3.32 (s, 1H), 2.10 – 1.77 (m, 2H), 1.73 – 1.34 (m, 6H), 1.24 (s, 1H), 1.09 – 0.69 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 111.15, 102.1, 83.56, 81.19, 74.59, 62.1, 36.63, 34.27, 24.38, 23.84, 23.84; Anal. calcd for C₁₁H₁₈O₅ (230.12): C, 57.38; H, 7.88%; Found: C, 57.42; H, 7.76; ES-MS (M+H): 231.1 m/z.

5-Azido-2,3-O-cyclohexylidene-5-deoxy-α/β-β-ribofuranose (24)

p-Toluenesulfonyl chloride (9.45 g, 49.5 mmol) was added to a cooled (0 °C) and stirred solution of 98 (11.5 g, 50 mmol) in dry pyridine (250 mL). The mixture was allowed to warm to room temperature and stirring was continued for 16 h. Benzoyl chloride (14.5 mL, 125 mmol, 2.5 equiv) was added and after stirring for an additional 90 min the mixture was concentrated, taken up in ethyl acetate and subsequently washed with saturated aqueous NaHCO₃ (2x), saturated aqueous NH₄Cl and brine (2x). The organic layer was dried (Na₂SO₄) and concentrated to obtain a yellow oil, which was coevaporated with toluene and dissolved in 250 mL dry DMF. Sodium azide (16.25 g, 250 mmol, 5 equiv) was added and the resulting suspension was stirred for 12 h at 120°C. The mixture was concentrated, taken up in ethyl acetate and washed with saturated aqueous NaHCO₃ (2x) and brine (2x). The organic layer was dried (Na₂SO₄) and concentrated. The residue was dissolved in methanol (300 mL), brought to pH 9 with sodium methanolate and stirred for 14 h. After neutralization of the solution with amberlyte H⁺, the mixture was filtered and concentrated in vacuo yielding a yellow oil. The residue was taken up in ethyl acetate and washed with brine (3x), dried (Na₂SO₄) and concentrated. Purification by flash column chromatography (EtOAc:Hexane
20%) yielded compound 102 as a pale yellow oil (6.51 g, 25.5 mmol, 51%) as well as a minor fraction of the starting material 98 (2.26 g, 4.9 mmol, 9.8%). \( [\alpha]_{D}^{20} +40^\circ (0.1, \text{ACN}) \); IR (\( v_{\text{max}}, \text{Neat, cm}^{-1} \)): 3421, 2934, 2836, 2099, 1446, 1269, 1233, 1162, 1012, 1057, 999, 968, 937; \( ^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 5.65 - 5.46 (m, 1 H), 4.49 - 4.77 (m, 2 H), 4.28 - 4.49 (m, 1 H), 3.54 - 3.73 (m, 1 H), 3.30 - 3.54 (m, 1 H), 1.12 - 1.74 (m, 10 H); \( ^{13}\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 111.64, 104.59, 84.92, 82.02, 80.03, 55.52, 38.03, 35.67, 25.47, 25.09; Anal. Caled for C\(_{11}\)H\(_{17}\)N\(_3\)O\(_4\) (255.12): C, 51.76; H, 6.71; N, 16.46%; Found: C, 51.72; H, 6.72; N, 16.45; ES-MS (M+H): 256.2 m/z.

**General method for the synthesis of 26a-l and 27**

The azide 102 was dissolved in MeCN (15 mL), BF\(_3\)·OEt\(_2\) (1.0 equiv), NaI (50 mol%) was added at -10°C. The reaction mixture was stirred then 40–50 min, after that the mixture was again cooled to -20 to -15°C, carboxylic acid (2 mmol) and isocyanide (2 mmol) were added and stirring was continued for 12h at rt. The mixture was concentrated and the reductive cyclized followed by Ugi products were isolated by flash column chromatography (MeOH:CHCl\(_3\), 20%).

**(3a’S,4’R,7’R,7a’R)-5’-benzoyl-N-cyclohexyl-7’-hydroxyhexahydrospiro[cyclohexane-1,2’-[1,3]dioxolo[4,5-c]pyridine]-4’-carboxamide (26a)**

Yield 43%; white solid; \( [\alpha]_{D}^{25} +42.8 \) (c 1.0, CHCl\(_3\)); IR (\( v_{\text{max}}, \text{Neat, cm}^{-1} \)): 3456, 3445, 3326, 1642, 1532, 1312, 1266, 1099; \( ^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.75 - 8.04 (m, 1 H), 7.34 - 7.54 (m, 3 H), 6.29 (br. s., 1 H), 4.43 - 4.73 (m, 3 H), 4.22 - 4.43 (m, 2 H), 3.95 - 4.12 (m, 1 H), 3.74 - 3.93 (m, 1 H), 3.14 - 3.35 (m, 1 H), 1.33 - 1.72 (m, 20 H); \( ^{13}\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 170.56, 168.44, 134.96, 130.69, 128.94, 126.43, 110.86, 81.93, 79.02, 62.9, 58.99, 45.6, 45.43, 37.51, 35.87, 32.59, 25.2, 24.54, 24.37, 23.36; Anal. Caled for C\(_{25}\)H\(_{34}\)N\(_2\)O\(_5\) (442.25): C, 67.85; H, 7.74; N, 6.33%; Found: C, 67.79; H, 7.72; N, 6.34; ES-MS (M+H): 443.3 m/z.

**(3a’S,4’R,7’R,7a’R)-N-cyclohexyl-7’-hydroxy-5’-(4-methylpentanoyl)hexahydrospiro[cyclohexane-1,2’-[1,3]dioxolo[4,5-c]pyridine]-4’-carboxamide (26b)**

Yield 52%; white solid; \( [\alpha]_{D}^{25} = -61.2 \) (c 1.4, CHCl\(_3\)); IR (\( v_{\text{max}}, \text{Neat, cm}^{-1} \)): 3454, 3446, 3322, 2875, 1642, 1532, 1266, 1099, 726; \( ^1\)H
NMR (300 MHz, CDCl₃): δ 6.29 (br. s., 1 H), 4.37 - 4.66 (m, 2 H), 4.18 - 4.31 (m, 1 H), 3.81 - 4.04 (m, 3 H), 2.90 (t, J=9.90 Hz, 2 H), 2.20 - 2.42 (m, 1 H), 1.21 - 1.62 (m, 23 H), 0.79 - 1.01 (m, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ 173.24, 169.33, 110.31, 82.62, 77.45, 62.6, 61.76, 48.03, 44.33, 36.69, 35.07, 32.99, 31.62, 30.83, 25.19, 24.74, 24.51, 24.33, 22.37, 22.08; Anal. Calcd for C₂₄H₄₀N₂O₅ (436.29): C, 66.03; H, 9.24; N, 6.42%; Found: C, 66.06; H, 9.21; N, 6.41; ES-MS (M+Na): 459.3 m/z.

(3a'S,4'R,7'R,7a'R)-5'-butyryl-N-cyclohexyl-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine]-4'-carboxamide (26c)

Yield 66%; white solid; [α]²⁵ = -14.7 (c 1.4, CHCl₃); IR (ν max, Neat, cm⁻¹): 3461, 3446, 3327, 2877, 1617, 1528, , 1261, 1103, 727; ¹H NMR (300 MHz, CDCl₃): δ 6.26 (br. s., 1 H), 4.30 - 4.68 (m, 3 H), 4.13 - 4.30 (m, 1 H), 3.81 - 4.03 (m, 3 H), 2.75 - 2.95 (m, 1 H), 2.52 - 2.75 (m, 2 H), 1.25 - 1.78 (m, 22 H), 0.87 - 1.11 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 173.14, 169.45, 110.3, 81.73, 76.91, 62.36, 61.77, 48.00, 44.10, 36.68, 35.78, 35.03, 32.97, 25.15, 24.49, 24.3, 22.34, 18.33, 13.74; Anal. calcd for C₂₂H₃₆N₂O₅ (408.26): C, 64.68; H, 8.88; N, 6.86%; Found: C, 64.70; H, 8.90; N, 6.85; ES-MS (M+H): 409.2 m/z.

benzyl (2S)-1-(((3a'S,4'R,7'R,7a'R)-4'-(cyclohexylcarbamoyl)-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine]-6'-yl)-3-methyl-1-oxobutan-2-yl)carbamate (26d)

Yield 55%; light yellow solid; [α]²⁵ = +26.3 (c 1.0, CHCl₃); IR (ν max, Neat, cm⁻¹): 3433, 3423, 3323, 2827, 1619, 1529, 1262, 1105, 689, 727; ¹H NMR (300 MHz, CDCl₃): δ 7.19 - 7.38 (m, 5 H), 6.29 (br. s., 1 H), 5.98 (br. s., 1 H), 5.52 (br. s., 1 H), 5.04 (s, 2 H), 4.61 - 4.80 (m, 2 H), 4.40 - 4.61 (m, 1 H), 3.94 - 4.10 (m, 1 H), 3.63 - 3.79 (m, 2 H), 3.48 - 3.62 (m, 1 H), 2.57 (br. s., 1 H), 1.21 - 1.75 (m, 20 H), 0.94 - 1.11 (m, 3 H), 0.70 - 0.86 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 168.69, 155.76, 135.75, 128.37, 128.2, 128, 110.12, 82.02, 76.99, 70.67, 66.81, 66.44, 65.88, 61.91, 48.87, 36.7, 35.07, 32.89, 29.9, 25.2, 24.5, 24.36, 23.26, 19.01, 16.33; Anal. calcd. for C₃₁H₄₅N₅O₅ (571.33): C, 65.13; H, 7.93; N, 7.35%; Found: C, 65.15; H, 7.92; N, 7.34; ES-MS (M+H): 572.4 m/z.
benzyl (2S)-1-((3a'S,4'R,7'R,7a'R)-4'-(cyclohexylcarbamoyl)-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridin]-6'-yl)-1-oxopropan-2-yl)carbamate (26e)

Yield 52%; light yellow solid; $[\alpha]_{D}^{25} = -38.3$ (c 1.0, CHCl$_3$); IR ($\nu_{max}$, Neat, cm$^{-1}$): 3451, 3433, 3331, 2829, 1621, 1531, 1263, 1112, 691, 728; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.21 - 7.37 (m, 5 H), 6.29 (br. s., 1 H), 5.98 (br. s., 1 H), 5.46 (br. s., 1 H), 4.98 - 5.12 (m, 2 H), 4.41 - 4.79 (m, 1 H), 3.63 - 3.89 (m, 1 H), 3.44 - 3.63 (m, 1 H), 2.57 (br. s., 1 H), 1.20 -1.70 (m, 23 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 168.89, 155.85, 135.95, 128.36, 128.23, 128.03, 110.12, 81.43, 77.01, 71.16, 66.94, 65.26, 62.07, 54.09, 48.89, 36.71, 35.06, 32.88, 25.18, 24.51, 24.34, 23.25, 17.88; Anal. calcd. for C$_{29}$H$_{41}$N$_3$O$_7$ (543.29): C, 64.07; H, 7.60; N, 7.73%; Found: C, 64.09; H, 7.63; N, 7.74; ES-MS (M+H): 544.3 m/z.

benzyl (2S)-1-((3a'S,4'R,7'R,7a'R)-4'-(cyclohexylcarbamoyl)-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridin]-6'-yl)-1-oxo-3-phenylpropan-2-yl)carbamate (26f)

Yield 50%; white solid; $[\alpha]_{D}^{25} = +12.4$ (c 1.1, CHCl$_3$); IR ($\nu_{max}$, Neat, cm$^{-1}$): 3459, 3238, 3194, 2833, 1673, 1334, 1266, 1104, 634; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.10 - 7.33 (m, 10 H), 6.28 (br. s., 1 H), 5.98 (br. s., 1 H), 5.57 (br. s., 1 H), 4.96 - 5.12 (m, 2 H), 4.58 - 4.76 (m, 2 H), 4.41 - 4.58 (m, 1 H), 3.62 - 3.90 (m, 2 H), 3.46 - 3.62 (m, 1 H), 3.04 - 3.21 (m, 1 H), 2.85 - 3.04 (m, 1 H), 2.39 - 2.70 (m, 1 H), 1.29 - 1.70 (m, 20 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 169.41, 156.09, 136.94, 136.01, 130.94, 128.96, 128.58, 128.5, 128.37, 128.15, 127.18, 110.26, 80.79, 76.54, 70.73, 67.17, 65.55, 61.95, 59.74, 49.01, 38.74, 36.82, 35.18, 33.02, 25.31, 24.61, 24.45, 23.37; Anal. calcd. for C$_{35}$H$_{45}$N$_3$O$_7$ (619.33): C, 67.83; H, 7.32; N, 6.78%; Found: C, 67.85; H, 7.31; N, 6.74; ES-MS (M+H): 620.4 m/z.

(3a'S,4'R,7'R,7a'R)-5'-benzoyl-N-((tert-butyl)-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine]-4'-carboxamide (26g)

Yield 47%; light yellow solid; $[\alpha]_{D}^{25} = -48.6$ (c 1.1, CHCl$_3$); IR ($\nu_{max}$, Neat, cm$^{-1}$): 3561, 3356, 3276, 2873, 1633, 1208, 1088, 725; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.36 - 8.05 (m, 5 H), 6.48 (br. s., 1 H), 4.96 - 5.12 (m, 2 H), 4.58 - 4.76 (m, 2 H), 4.41 - 4.58 (m, 1 H), 4.06 - 4.22 (m, 1 H), 3.62 - 3.90 (m, 2 H), 3.46 - 3.62 (m, 1 H), 3.04 - 3.21 (m, 1 H), 2.85 - 3.04 (m, 1 H), 2.39 - 2.70 (m, 1 H), 1.27 - 1.70 (m, 20 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 169.41, 156.09, 136.94, 136.01, 130.94, 128.96, 128.58, 128.5, 128.37, 128.15, 127.18, 110.26, 80.79, 76.54, 70.73, 67.17, 65.55, 61.95, 59.74, 49.01, 38.74, 36.82, 35.18, 33.02, 25.31, 24.61, 24.45, 23.37; Anal. calcd. for C$_{35}$H$_{45}$N$_3$O$_7$ (619.33): C, 67.83; H, 7.32; N, 6.78%; Found: C, 67.85; H, 7.31; N, 6.74; ES-MS (M+H): 620.4 m/z.
(m, 3 H), 4.19 - 4.41 (m, 2 H), 3.89 - 4.12 (m, 1 H), 3.10 - 3.31 (m, 1 H), 1.23 - 1.71 (m, 20 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 170.92, 168.88, 134.74, 130.62, 128.89, 126.35, 110.25, 81.29, 79.22, 62.85, 60.65, 50.72, 45.06, 37.48, 35.83, 27.61, 24.52, 24.34; Anal. calcd for C\(_{23}\)H\(_{32}\)N\(_2\)O\(_5\) (416.23): C, 66.32; H, 7.74; N, 6.73%; Found: C, 66.30; H, 7.76; N, 6.74; ES-MS (M+H): 417.3 m/z.

(3a'S,4'R,7'R,7a'R)-N-(tert-butyl)-7'-hydroxy-5'-4-methylpentanoylhexahydrospiro
cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine-4'-carboxamide
(26h)
Yield 44%; white solid; \([\alpha]^{25}_{D} = 122.6\) (c 1.0, CHCl\(_3\)); IR (\(\nu_{max}\), Neat, cm\(^{-1}\)): 3562, 3293, 3275, 228, 1637, 1287, 1104, 957, 712; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 6.48 (br. s., 2 H), 4.35 - 4.74 (m, 3 H), 4.17 - 4.35 (m, 1 H), 3.78 - 4.08 (m, 2 H), 2.71 - 2.96 (m, 1 H), 2.14 - 2.41 (m, 2 H), 1.18 - 1.75 (m, 22 H), 0.80 - 1.02 (m, 6 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 173.77, 169.18, 168.18, 109.75, 82.04, 77.69, 64.32, 61.76, 53.14, 43.82, 36.7, 35.07, 31.72, 30.82, 28.62, 24.73, 24.52, 24.35, 22.08; Anal. calcd for C\(_{23}\)H\(_{32}\)N\(_2\)O\(_5\) (410.28): C, 64.36; H, 9.33; N, 6.82%; Found: C, 64.33; H, 9.36; N, 6.84; ES-MS (M+Na): 405.3 m/z.

(3a'S,4'R,7'R,7a'R)-N-(tert-butyl)-5'-butyryl-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-
[1,3]dioxolo[4,5-c]pyridine]-4'-carboxamide
(26i)
Yield 44%; white solid; \([\alpha]^{25}_{D} = +17.7\) (c 1.2, CHCl\(_3\)); IR (\(\nu_{max}\), Neat, cm\(^{-1}\)): 356, 3487, 3238, 2287, 1673, 1276, 1108, 943, 782, 692; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 6.48 (br. s., 3 H), 4.31 - 4.67 (m, 8 H), 4.17 - 4.29 (m, 3 H), 3.83 - 4.04 (m, 6 H), 2.73 - 2.91 (m, 3 H), 2.46 - 2.69 (m, 6 H), 1.18 - 1.83 (m, 63 H), 0.99 (quin, J=6.98 Hz, 9 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 173.65, 169.29, 109.73, 82.15, 77.17, 77.12, 64.12, 61.83, 53.13, 43.6, 36.71, 35.93, 35.05, 28.63, 24.51, 24.34, 18.37, 13.77; Anal. Calcd for C\(_{22}\)H\(_{34}\)N\(_2\)O\(_5\) (382.25): C, 62.80; H, 8.96; N, 7.32%; Found: C, 62.83; H, 8.94; N, 7.31; ES-MS (M+Na): 405.3 m/z.

benzyl ((2S)-1-((3a'S,4'R,7'R,7a'R)-4'-tert-butylcarbamoyl)-7'-hydroxyhexahydrospiro
cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine-6'-yl)-3-methyl-1-oxobutan-2-yl)
carbamate
(26j)
Yield 54%; yellow solid; \([\alpha]^{25}_{D} = -26.2\) (c 1.0, CHCl\(_3\)); IR (\(\nu_{max}\), Neat, cm\(^{-1}\)): 382, 3376, 3238, 2287, 1673, 1294, 2207, 966, 782; \(^1\)H
NMR (300 MHz, CDCl₃): δ 7.26 (s, 5 H), 6.66 (br. s., 1 H), 5.93 (br. s., 1 H), 5.49 - 5.61 (m, 1 H), 5.00 (s, 2 H), 4.72-4.65 (br. s., 2 H), 4.43 - 4.60 (m, 1 H), 3.98 - 4.14 (m, 1 H), 3.52 - 3.76 (m, 1 H), 1.49 - 1.77 (m, 5 H), 1.17 - 1.49 (m, 15 H), 0.94 - 1.11 (m, 3 H), 0.68 - 0.90 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 169.98, 155.73, 135.71, 128.38, 128.32, 128.16, 127.96, 109.51, 81.35, 77.18, 70.6, 66.74, 66.38, 65.34, 64.56, 50.06, 36.62, 35.00, 29.82, 28.62, 24.42, 24.28, 18.93, 16.24; Anal. calcd for C_{29}H_{43}N_{3}O_{7}: C, 63.83; H, 7.94; N, 7.70%; Found: C, 63.81; H, 7.92; N, 7.72; ES-MS (M+H): 546.3 m/z.

**benzyl ((2S)-1-((3a'S,4'R,7'R,7a'R)-4'-(tert-butylcarbamoyl)-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridin]-6'-yl)-1-oxopropan-2-yl)carbamate (26k)**

Yield 48%; white solid; [α]D²⁵ = -86.4 (c 1.5, CHCl₃); IR (νmax, Neat, cm⁻¹): 3523, 3376, 3277, 2895, 1654, 1287, 1105, 954, 753; ¹H NMR (300 MHz, CDCl₃): δ 7.18 - 7.42 (m, 5 H), 6.70 (br. s., 1 H), 5.96 (br. s., 1 H), 5.49 (br. s., 1 H), 4.96 - 5.15 (m, 2 H), 4.39 - 4.81 (m, 3 H), 4.04 - 4.27 (m, 1 H), 3.58 - 3.89 (m, 2 H), 3.04 - 3.21 (m, 1 H), 2.84 - 3.04 (m, 1 H), 2.58 (br. s., 1 H), 1.21 - 1.72 (m, 19 H), 1.15 - 1.75 (m, 23 H); ¹³C NMR (75 MHz, CDCl₃): δ 170.2, 155.85, 135.95, 128.36, 128.23, 109.56, 80.85, 77.26, 71.16, 66.94, 64.78, 54.09, 50.15, 36.71, 35.06, 28.68, 24.51, 24.34, 17.88; Anal. Calcd for C_{27}H_{39}N_{3}O_{7}: C, 62.65; H, 7.59; N, 8.12%; Found: C, 62.61; H, 7.52; N, 8.11; ES-MS (M+H): 518.2 m/z.

**benzyl ((2S)-1-((3a'S,4'R,7'R,7a'R)-4'-(tert-butylcarbamoyl)-7'-hydroxyhexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridin]-6'-yl)-1-oxo-3-phenylpropan-2-yl)carbamate (26l)**

Yield 46%; white solid; [α]D²⁵ = +32.6 (c 1.6, CHCl₃); IR (νmax, Neat, cm⁻¹): 3576, 5476, 3364, 2863, 1063, 973, 812, 783; ¹H NMR (300 MHz, CDCl₃): δ 7.10 - 7.36 (m, 10 H), 6.70 (br. s., 1 H), 5.98 (br. s., 1 H), 5.49 (br. s., 1 H), 4.96 - 5.15 (m, 2 H), 4.39 - 4.81 (m, 3 H), 4.04 - 4.27 (m, 1 H), 3.58 - 3.89 (m, 2 H), 3.04 - 3.21 (m, 1 H), 2.84 - 3.04 (m, 1 H), 2.58 (br. s., 1 H), 1.21 - 1.72 (m, 19 H), 1.15 - 1.75 (m, 23 H); ¹³C NMR (75 MHz, CDCl₃): δ 170.57, 155.93, 136.05, 135.86, 130.78, 128.81, 128.35, 128.21, 128.11, 127.03, 109.55, 80.06, 76.65, 70.62, 67.04, 64.96, 64.52, 59.61, 50.15, 38.62, 36.71, 35.06, 28.68, 24.51, 24.33; Anal. Calcd for C_{33}H_{43}N_{3}O_{7}: C, 66.76; H, 7.30; N, 7.08%; Found: C, 66.75; H, 7.29; N, 7.32; ES-MS (M+H): 594.4 m/z.
(3a'S,4'R,7'R,7a'R)-N-benzyl-7'-hydroxy-5'-(pent-4-enoyl)hexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine]-4'-carboxamide (27)

Yield 59%; white solid; [α]D25 = -52.7 (c 1.0, CHCl3); IR (νmax, Neat, cm⁻¹): 3487, 3396, 3289, 1276, 1202, 1108, 973, 723; ¹H NMR (300 MHz, CDCl3): δ 8.34 (br. s., 1 H), 7.18 - 7.39 (m, 5 H), 5.54 - 5.79 (m, 1 H), 5.08 (d, J=16.80 Hz, 1 H), 4.81 (d, J=10.80 Hz, 1 H), 4.37 - 4.65 (m, 3 H), 4.19 - 4.37 (m, 3 H), 3.76 - 4.03 (m, 2 H), 2.81 (dd, J=9.75 Hz, 1 H), 2.40 - 2.52 (m, 1 H), 2.23 - 2.40 (m, 2 H), 1.18 - 1.74 (m, 10 H); ¹³C NMR (75 MHz, CDCl3): δ 174.42, 169.07, 139.42, 135.33, 128.49, 127.84, 126.65, 115.23, 109.09, 80.45, 78.05, 62.76, 61.86, 43.81, 41.97, 36.66, 35.02, 34.1, 26.81, 24.45, 24.3; Anal. Caled for C₃₃H₄₃N₃O₇ (428.23): C, 67.27; H, 7.53; N, 6.54%; Found: C, 67.25; H, 7.58; N, 6.52; ES-MS (M+H): 429.3 m/z.

(3a'S,4'R,7'S,7a'R)-N-benzyl-7'-hydroxy-5'-(pent-4-enoyl)hexahydrospiro[cyclohexane-1,2'-[1,3]dioxolo[4,5-c]pyridine]-4'-carboxamide (32)

A 50 mL round bottom flask was charged with picolinic acid (494.44 mg, 4 mmol), 106 (428.53 mg, 1 mmol), and triphenylphosphine (1.049 g, 4 mmol). The flask was flushed with nitrogen, and THF (1 mL, freshly distilled) was added, and the solution cooled to -20°C for 10-15 min. Diisopropyl azodicarboxylate (DIAD, 808.84 mg, 4 mmol) was then added dropwise to the solution over 5 min. The temperature of the bath was maintained at -20 to -25°C for 6 h and the cold bath allowed to slowly warm to ambient temperature and allowed to stir overnight. The reaction mixture was then concentrated at reduced pressure, and the products were purified by flash chromatography (EtOAc:Hexane 15%) to provide the picolinate ester of 106 in 82% (437.57 mg, ) yield. The ester so formed was then subjected to hydrolysis. A 50 mL round bottom flask was charged with CHCl₃ (20 mL), ester (808.84 mg, 0.82 mmol), methanol (280μL, 6.56 mmol) and Cu(OAc)₂ (69 mg, 0.41 mmol). The reaction was allowed to stir for 6 h at which point it was judged by TLC. The reaction was diluted with hexanes (5 mL) and washed with disodium EDTA (5mL of a 0.1 M solution). The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure to white coloured solid. Flash chromatography (MeOH:CHCl₃ 20%) provided the 111 in 85% yield (298 mg) mp 112-113°C; [α]D25 = +63.5 (c 1.0, CHCl3); IR (νmax, Neat, cm⁻¹): 3486, 3393, 3291, 1266, 1212, 1106, 975, 726; ¹H NMR (300 MHz, CDCl₃): δ 8.35 (br. s., 1 H), 7.07 - 7.53 (m, 5 H), 5.51 - 5.79 (m, 1 H), 5.08 (d, J=16.80 Hz, 1 H), 4.81 (d, J=10.50 Hz, 1 H), 4.35 - 4.66 (m, 3 H), 4.29 (s, 3 H), 3.87 - 4.11 (m, 1 H), 3.62 - 3.85 (m, 1 H), 2.84 (dd, J=7.48 Hz, 1 H),
2.40 - 2.58 (m, 2 H), 2.19 - 2.40 (m, 2 H), 1.22 - 1.73 (m, 10 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)):
\(\delta\) 174.41, 169.08, 139.41, 135.32, 128.47, 127.85, 126.63, 115.25, 109.11, 80.43, 78.07, 62.75, 61.89, 43.82, 41.98, 36.64, 35.05, 34.12, 26.79, 24.44, 24.31; Anal. calcd for C\(_{33}\)H\(_{43}\)N\(_3\)O\(_7\) (428.23): C, 67.27; H, 7.53; N, 6.54%; Found: C, 67.29; H, 7.51; N, 6.53; ES-MS (M+H): 429.3 m/z.

**General method for the synthesis of 28 and 33**

To a solution ketal (1 mmol) in acetonitrile (3 ml) in a polypropylene vessel was added, Pyridinium poly(hydrogen fluoride) PPHF ( 3 mmol) at room temperature and the mixture was stirred at the same temperature for 15 min. After addition of an adequate quantity of solid NaHCO\(_3\) (slightly exothermic) to neutralize briefly, the mixture was stirred for about 5 minutes and transferred into a separatory funnel using ethyl ether. The resultant organic layer was treated successively with a saturated NaHCO\(_3\) solution, H\(_2\)O, and a saturated NaCl solution, dried over Na\(_2\)SO\(_4\), and concentrated to give diol in excellent yield. The diols were directly subjected to benylation without purification. To a cooled (0°C) hexane-washed suspension of NaH (2.1 mmol, 60% suspension in oil) was dropwise added substrate (1 mmol) in THF (15 mL). After bringing the mixture to room temperature and stirring for 10 min, the mixture was cooled to 0°C, and BnBr (2.4 mmol) and Bu\(_4\)NI (cat.) were added. The mixture was brought to room temperature and stirred for an additional 5 h. The reaction was quenched with aqueous saturated NH\(_4\)Cl, and the mixture was concentrated in vacuo and extracted with EtOAc. The organic extract was washed with water and brine and then dried. Solvent removal followed by column chromatography (silica gel, 5% EtOAc/hexane) of the residue furnished benzylated product 107 and 112.

**(2R,3S,4R,5S)-N-benzyl-3,4,5-tris(benzyloxy)-1-(pent-4-enoyl)piperidine-2-carboxamide (28)**

Yield 81%; glassy liquid; \([\alpha]\)\(^{25}\) = -14.2 (c 1.2, CHCl\(_3\)); IR (\(\nu_{\text{max}}\), Neat, cm\(^{-1}\)): 3439, 3336, 1679, 1625, 1277, 1095, 965, 732; \(^{1}\)H NMR (300 MHz, CDCl\(_3\)):
\(\delta\) 8.34 (br. s., 1 H), 7.15 - 7.39 (m, 20 H), 5.49 - 5.83 (m, 1 H), 5.01 - 5.19 (m, 1 H), 4.70 - 4.86 (m, 2 H), 4.22 - 4.69 (m, 9 H), 3.92 - 4.15 (m, 2 H), 3.75 (br. s., 1 H), 2.66 - 2.86 (m, 1 H), 2.38 - 2.54 (m, 2 H), 2.21 - 2.38 (m, 2 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)):
\(\delta\) 178.00, 171.83, 141.43, 140.23, 139.36, 137.34, 130.57, 130.5, 130.43, 130.3, 129.85, 129.79, 129.72, 129.59, 128.68, 117.23, 78.69, 78.06, 76.62, 75.97, 73.69, 73.58, 65.11, 44.22, 43.98, 35.74, 28.83; Anal. calcd for
C₃₀H₄₂N₂O₅ (618.31): C, 75.70; H, 6.84; N, 4.53%; Found: C, 75.73; H, 6.82; N, 4.51; ES-MS (M+H): 619.3 m/z.

(2R,3S,4R,5S)-N-benzyl-3,4,5-tris(benzyloxy)-1-(pent-4-enoyl)piperidine-2-carboxamide (33)

Yield 84%; glassy liquid; [α]25D = -58.6 (c 1.2, CHCl₃); IR (ν max, Neat, cm⁻¹): 3441, 3337, 1681, 1627, 1094, 964, 731; 1H NMR (300 MHz, CDCl₃): δ 8.34 (br. s., 1 H), 7.12 - 7.45 (m, 20 H), 5.54 - 5.81 (m, 1 H), 5.08 (d, J= 16.48 Hz, 1 H), 4.69 - 4.90 (m, 2 H), 4.54 - 4.69 (m, 1 H), 4.22 - 4.54 (m, 7 H), 3.94 - 4.11 (m, 2 H), 3.58 - 3.76 (m, 1 H), 2.68 - 2.89 (m, 1 H), 2.38 - 2.57 (m, 2 H), 2.17 - 2.38 (m, 2 H); 13C NMR (75 MHz, CDCl₃): δ 178.03, 171.82, 141.42, 140.26, 139.39, 137.32, 130.56, 130.53, 130.41, 130.29, 129.86, 129.81, 129.69, 129.62, 128.67, 117.26, 78.72, 78.12, 76.60, 75.96, 73.70, 73.57, 65.15, 44.21, 43.96, 35.77, 28.88; Anal. Calcd for C₃₉H₄₂N₂O₅ (618.31): C, 75.70; H, 6.84; N, 4.53%; Found: C, 75.74; H, 6.88; N, 4.50; ES-MS (M+H): 619.3 m/z.

General method for the synthesis of 29 and 34

The bis amide (1 mmol) was dissolved in THF (4 mL), and an equal volume of H₂O (4 mL) was added subsequently, resulting in a cloudy suspension. Additional organic solvent (THF) was then added slowly until the turbid solution became clear. The reaction mixture was treated with I₂ (3 mmol) and allowed to stir until completion which was monitored by tlc. The reaction was quenched with solid Na₂S₂O₃ (disappearance of brown color) and the mixture concentrated. The crude material was dissolved in CHCl₃ (10mL) and washed with brine. The organic phase was dried (Na₂SO₄), filtered, concentrated, and chromatographed (MeOH: CHCl₃ 20%) to afford the desired mono amide.

(2R,3S,4R,5R)-N-benzyl-3,4,5-tris(benzyloxy)piperidine-2-carboxamide (29)

Yield 76%; light yellow viscous oil; [α]25D = +22.4 (c 0.8, CHCl₃); IR (ν max, Neat, cm⁻¹): 3412, 3325, 3198, 2863, 1645, 1610, 1298, 974, 763; 1H NMR (300 MHz, CDCl₃): δ 7.73 (br., s, 1 H), 7.18 - 7.40 (m, 20 H), 4.35 - 4.71 (m, 8 H), 3.67 - 3.88 (m, 3 H), 3.44 - 3.58 (m, 1 H), 3.25 - 3.39 (m, 1 H), 2.84 - 3.03 (m, 1 H), 2.70 (br. s., 1 H); 13C NMR (75 MHz, CDCl₃): δ 171.72, 138.21, 137.97, 137.82, 137.13, 128.54, 128.46, 128.39, 128.27, 127.76, 127.68, 127.55, 127.47, 126.64, 76.77, 76.36, 74.39, 72.36, 71.9, 61.08, 48.09, 43.22; Anal. calcd for
C₃₄H₃₆N₂O₄ (536.27): C, 76.09; H, 6.76; N, 5.22%; Found: C, 76.11; H, 6.78; N, 5.23; ES-MS (M+H): 537.4 m/z.

(2R,3S,4R,5S)-N-benzyl-3,4,5-tris(benzyloxy)piperidine-2-carboxamide (34)

Yield 78%; light yellow viscous oil; [α]D²⁵ = -112.6 (c 0.8, CHCl₃); IR (νmax, Neat, cm⁻¹): 3414, 3326, 3203, 2868, 1649, 1613, 1292, 976, 765; ¹H NMR (300 MHz, CDCl₃): δ 7.74 (br. s., 1 H), 7.15 - 7.43 (m, 20 H), 4.56 - 4.73 (m, 2H), 4.37 - 4.56 (m, 6 H), 3.77 - 4.03 (m, 1 H), 3.70 (dd, J=4.05, 1.35 Hz, 1 H), 3.45 - 3.65 (m, 2 H), 3.25 - 3.39 (m, 1 H), 2.86 - 3.02 (m, 1 H), 2.68 (br. s., 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 171.74, 138.20, 137.96, 137.79, 137.17, 128.52, 128.44, 128.32, 128.29, 127.81, 127.56, 127.45, 127.39, 126.71, 76.76, 76.41, 74.36, 72.32, 71.98, 61.15, 48.11, 43.21; Anal. calcd for C₃₄H₃₆N₂O₄ (536.27): C, 76.09; H, 6.76; N, 5.22%; Found: C, 76.08; H, 6.77; N, 5.23; ES-MS (M+H): 537.4 m/z.

General method for the synthesis of 30 and 35

To a 50-mL round-bottom flask equipped with a septum was added the amide (2.0 mmol, 1.0 equiv). The amide was diluted with 8 mL of anhydrous dichloromethane (0.25M) and 2-fluoropyridine (2.2 mmol) was added to the solution. The solution was then cooled to −78°C and stirred for 5 min. Trifluoromethanesulfonic (triflic) anhydride (Tf₂O) (2.1 mmol) was added dropwise via a syringe at −78°C and the reaction was stirred for 10 min. The solution was heated at 0°C using a water/ice bath and the reaction was stirred for 10 min. Trifluoromethanesulfonic (triflic) anhydride (Tf₂O) (2.1 mmol) was added dropwise via a syringe at −78°C and the reaction was stirred for 10 min. The solution was heated at 0°C using a water/ice bath and the reaction was stirred for 10 min. Triethylsilane (Et₃SiH, 2.2 mmol) was added dropwise at 0°C and the reaction was stirred for 10 min. The solution was heated to room temperature and stirred for 5 h. Then, the septum was removed and 8 mL of an aqueous solution of citric acid [0.08M] and 8 mL of THF were added to the flask. A reflux condenser was installed on the flask and the reaction was then heated to 45 °C and stirred for 2 h. The biphasic mixture was transferred to a separation funnel and the layers were separated. The aqueous layer was extracted with dichloromethane (2x) and the organic layers were combined. The organic layer was dried over anhydrous sodium sulphate (Na₂SO₄), filtered over a sintered funnel and evaporated to dryness to give crude aldehyde. The obtained crude aldehyde was then subjected to hydrogenation without purification.

General method for the synthesis of 31 and 36
A solution of aldehyde (1 mmol) and 10% Pd/C (0.0625 g) in MeOH (20 mL) was stirred under an H₂ atmosphere at 100 psi for 10 h at 25 °C. The catalyst was filtered through a pad of Celite 545. Solvent evaporation afforded isomers of DNJ.

(2S,3S,4R,5S)-2-(hydroxymethyl)piperidine-3,4,5-triol (1,5-dideoxy-1,5-imino-\(\alpha\)-altritol) (\emph{altro-DNJ, 88})

Yield 95%; semisolid; \([\alpha]^{25}_D = -7.2\) (c 0.5, MeOH); IR (v max, Neat, cm\(^{-1}\)): 3515, 1046, 715; \(^1\)H NMR (400 MHz, D\(_2\)O): \(\delta\) 3.69 - 3.98 (m, 1 H), 3.40 - 3.69 (m, 3 H), 3.14 (br. s., 1 H), 2.75-3.00 (2s, 1 H), 2.40-2.70 (2 s, 2 H); \(^{13}\)C NMR (75 MHz, D2O+CDCl\(_3\)): \(\delta\) 79.38, 72.45, 70.89, 63.51, 60.80, 50.75; Anal. Calcd for C\(_6\)H\(_{13}\)NO\(_4\) (163.08): C, 44.17; H, 8.03; N, 8.58%; Found: C, 44.19; H, 8.02; N, 8.61; ES-MS (M+Na): 186.1 m/z.

(2S,3S,4R,5R)-2-(hydroxymethyl)piperidine-3,4,5-triol (1,5-dideoxy-1,5-imino-\(\beta\)-allitol) (\emph{allo-DNJ, 90})

Yield 96%; semisolid; \([\alpha]^{25}_D = +34.5.0\) (c = 1, H\(_2\)O); IR (v max, Neat, cm\(^{-1}\)): 3518, 1052, 718; \(^1\)H NMR (400 MHz, D2O): \(\delta\) 3.71 - 4.06 (m, 1 H), 3.49 - 3.71 (m, 2 H), 3.31 - 3.49 (m, 1 H), 3.14 (br. s., 1 H), 2.89 (d, J=9.20 Hz, 1 H), 2.42 - 2.71 (m, 2 H); \(^{13}\)C NMR (75 MHz, D2O+CDCl\(_3\)): \(\delta\) 78.96, 72.47, 70.44, 63.54, 60.83, 50.78; Anal. Calcd for C\(_6\)H\(_{13}\)NO\(_4\) (163.08): C, 44.17; H, 8.03; N, 8.58%; Found: C, 44.18; H, 8.05; N, 8.59; ES-MS (M+Na): 186.1 m/z.
$^1$H and $^{13}$C NMR Spectra of 24
$^1$H and $^{13}$C NMR Spectra of 26a
$^1$H and $^{13}$C NMR Spectra of 26c
$^1$H and $^{13}$C NMR Spectra of 26f
$^1$H and $^{13}$C NMR Spectra of 26j
\(^1\text{H}\) and \(^{13}\text{C}\) NMR Spectra of 28
$^1\text{H}$ and $^{13}\text{C}$ NMR Spectra of 29
$^1$H and $^{13}$C NMR spectra of altro-DNJ (36)
\(^1\text{H}\) and \(^{13}\text{C}\) NMR spectra of \textit{allo}-DNJ (31)