Experimental Section

Materials and Methods. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Varian VXR-300 (300 MHz) or Varian VXR-500 (500 MHz) spectrometers. Chemical shifts are reported relative to internal tetramethylsilane (δ 0.00 ppm) or residual solvent signal. Infrared (IR) spectra were obtained on a Prospect MIDAC FT-IR spectrometer. Optical rotations were measured with a Jasco DIP-370 digital polarimeter in the solvent specified. Flash column chromatography was performed on ICN reagent 60 (60-200 mesh) silica gel. Analytical thin-layer chromatography was performed with precoated glass-backed plates (Whatman K6F 60è , F_{254}) and visualized by quenching of fluorescence and by charring after treatment with *p*-anisaldehyde or potassium permanganate stain. R_f values are obtained by elution in the stated solvent ratios (v/v). Combustion analysis was performed by M-H-W Laboratories, Phoenix, AZ.

Ether and THF were distilled from benzophenone and sodium metal. Methylene chloride and triethylamine were distilled from calcium hydride. Unless otherwise noted, solvents were reagent grade and were used without purification. Commercial reagents were used without purification unless otherwise noted. The ligand $(DHQ)_2$PHAL was purchased from Aldrich Chemical Co. Fox Chlor (St. Paul, MN) brand aqueous sodium hypochlorite solutions (5.25 %) were used. *tert*-Butyl hypochlorite was freshly prepared according to the *Organic Synthesis* procedure[1] and stored over anhydrous $CaCl_2$ at ~4 °C. Furfural was freshly distilled. *m*-Chloroperbenzoic acid (95%) was obtained from the commercially available material by recrystallization according to the procedure of Bortolini and co-workers.[2] Purity was determined by integration of its ^{1}H NMR spectra (500 MHz). Jones Reagent (chromic acid) was prepared by the method of Eisenbraun.[3]

Spectral Data for Amide Rotamers and Inseparable Pairs of Diasteriomers: In the ^{1}H and ^{13}C NMR data (δ values are in ppm) resonances associated with the major amide rotamer or diasteriomer are indicated with * and those for the minor amide rotamer or diasteriomer with **. Resonances comprising protons from both rotamers and/or both diasteriomers bear no asterisk.

The enantiomeric excesses of compounds **6** and **9** were determined by conversion of the alcohols to the corresponding Mosher esters and measured by analysis of the ^{19}F NMR.[4] Furthermore, the optical rotation of compound **21** was of opposite sign and of equal value within experimental error of its enantiomer reported in the literature,[5] which derived its chirality from a carbohydrate source.

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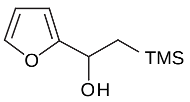
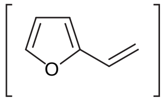
[1] Mintz, M. J.; Walling, C. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 183.
[2] Bortolini, O.; Campestrini, S.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1987**, *52*, 5093.
[3] Eisenbraun, E. J. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 310.
[4] Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143.
[5] Mocerino, M.; Stick, R. V. *Aust. J. Chem.* **1990**, *43*, 1183-1193.

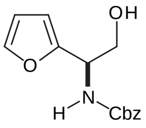




7

1-(2′-Furyl)-2-(trimethylsilyl)-ethanol. Magnesium turnings (10.1 g, 415 mmol) were placed in a 1 L 3-neck flask. A condenser and a pressure equalizing addition funnel were attached. The apparatus was flame dried and flushed with nitrogen gas (3 ×). Chloromethyltrimethylsilane (42.4 g, 346 mmol) and ether (200 mL) were slowly added to the dry magnesium. After the addition was complete, the solution was refluxed for 1 h. Freshly distilled furfural (25 mL, 300 mmol) and dry ether (300 mL) were slowly added to the Grignard reagent at 0 °C and the solution was stirred for 12 h. The reaction was quenched with satd aq NH_4Cl (200 mL) and was extracted with ether (3 × 100 mL). The organic layer was washed with satd aq $NaHCO_3$ (2 × 50 mL), brine (2 × 50 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give a yellow oil (not shown in the paper), (50.05 g, 272 mmol, 90% yield). R_f 0.58 (ether/hexane = 3:7); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (dd, J = 0.7, 1.8 Hz, 1H), 6.24 (dd, J = 1.8, 3.1 Hz, 1H), 6.13 (d, J = 3.3 Hz, 1H), 4.77 (dd, J = 6.9, 8.8 Hz, 1H), 3.13 (bs, 1H), 1.28 (dd, J = 14.1, 8.8 Hz, 1H), 1.23 (dd, J = 14.1, 6.8 Hz, 1H), -0.10 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 141.6, 110.1, 105.5, 65.6, 24.8, -1.4; IR (thin film) 3390, 2950, 2895, 1655, 1505, 1250, 1010, 860, 690 cm^{-1}; HRMS (CI, NH_3) accurate mass cald for $(C_9H_{16}O_2Si)^+$ requires *m/z* 184.0919, found *m/z* 184.0905.

2-Vinylfuran (7). 1-(2′-Furyl)-2-(trimethylsilyl)-ethanol (10.0 g, 54.2 mmol) and ether (20 mL) were added to a 100 mL flask followed by addition of aqueous HCl (1 M, 20 mL) with vigorous stirring for 1 h, at which time the starting material was absent as determined by TLC analysis. The phases were separated and the aqueous layer was extracted with ether (2 x 10 mL) and combined with the organic layer.



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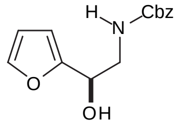

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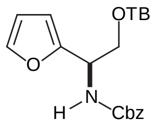
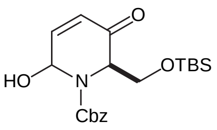


5a

(1*R*)-*N*-(Benzyloxycarbonyl)-1-(2-furyl)-2-*tert*-butyldimethylsilyloxy-ethylamine (5a): A 1 L flask was charged with benzyl carbamate (6.99 g, 46.2 mmol) and *tert*-BuOH (160 mL). To this stirred solution was added a freshly prepared aqueous solution of NaOH (1.77 g, 45.4 mmol in 160 mL water), followed by *tert*-butyl hypochlorite (4.93 g, 44.4 mmol). After 5 min a solution of $(DHQ)_2$PHAL (1.87 g, 2.4 mmol, 6 mol %) in *tert*-BuOH was added; the reaction became homogeneous at this point. 2-Vinylfuran (**7**) (5.65 g, 54.2 mmol, dissolved in 40 mL of ether) was added followed by OsO_4 (508 mg, 2.0 mmol, 5 mol %). The light green solution was stirred at 25 °C and became yellow after 1 h, indicating completion. The reaction was quenched by the addition of a satd aq sodium sulfite solution (120 mL) and stirred for 15 min. The two phases were separated, and the aqueous phase was extracted with ethyl acetate (3 x 50 mL). The combined organic phases were washed with water (100 mL), brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated to afford the crude mixture of regioisomers (**6**:**9** = 1:2). Flash chromatography (SiO_2, 5-40%

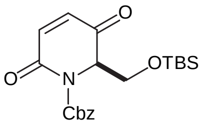
EtOAc/hexane gradient elution) provided a mixture of regioisomer **6** and **9** (10.1 g, 38.8 mmol, 84% yield by benzyl carbamate) as a waxy solid.

A 500 mL flask was charged with a mixture of alcohols **6** and **9** (10.1 g, 38.8 mmol), methylene chloride (200 mL), triethylamine (3.62 mL, 26.0 mmol), DMAP (79 mg, 0.65 mmol, 5 mol %) and *tert*-butyldimethylsilylchloride (2.94 g, 19.5 mmol). The reaction mixture was allowed to stir at 23 °C for 3 h, at which time the reaction was complete as judged by TLC analysis. The reaction mixture was diluted with ether (100 mL), silica gel (15 g) was added and the solvent was removed *in vacuo*. The mixture adsorbed onto silca gel was directly submitted to flash chromatography (SiO_2, 5-40% EtOAc/hexane gradient elution) provided furan **5a** as a colorless oil (3.71 g, 9.87 mmol, 21% from benzyl carbamate). For **5a**: R_f 0.33 (EtOAc/hexane = 1:19), $[\alpha]^{25}_{D}$ +13.1 (*c* 1.15, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 7.36-7.30 (m, 6H), 6.31 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.23 (d, *J* = 3.3 Hz, 1H), 5.11 (s, 2H), 5.04 (t, *J* = 3.9 Hz, 1H), 4.82 (t, *J* = 6.0 Hz, 1H), 3.51 (ddd, *J* = 27.2, 13.6, 6.0 Hz, 1H), 0.87 (s, 9H), 0.06 (s, 3H), -0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.3, 154.4, 131.9, 136.5, 128.5, 128.1, 110.1, 107.0, 67.3, 66.7, 46.1, 25.7, 18.1, -5.1, -5.2, missing 1 ipso carbon; IR (thin film) 3452, 3331, 2929, 2856, 1725, 1499, 1249, 1111, 837 cm^{-1}; HRMS (CI, NH_3) accurate mass cald for $(C_{20}H_{30}NO_4Si + H)^+$ requires *m/z* 376.1944, found *m/z* 376.1948. Anal. Calcd for $C_{20}H_{29}NO_4Si$: C, 63.97; H, 7.79. Found: C, 64.14; H 7.82.
For **(1*R*)-*N*- (Benzyloxycarbonyl)-1-(2-furyl)-2-hydroxy-ethylamine (9):** a white crystalline solid (4.85 g, 18.5 mmol, 40% from benzyl carbamate, 14 % ee), mp 49.5-50.0 °C; $[\alpha]^{25}_{D}$ +2.9 (*c* 2.85, CH_2Cl_2); R_f 0.2 (EtOAc/hexane = 3:7); ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.33 (m, 6H), 6.32 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.28 (d, *J* = 3.3 Hz, 1H), 5.60 (dd, *J* = 5.1, 5.1 Hz, 1H), 5.09 (s, 2H), 4.79 (m, 1H), 3.98 (br s, 1H, OH), 3.55 (ddd, *J* = 12.0, 7.2, 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.0, 154.0, 142.2, 137.3, 128.4, 128.1, 128.0, 110.2, 109.2, 67.0, 66.9, 45.4; IR (thin film) 3384, 3032, 2941, 1700, 1526, 1451, 1255, 1147, 735 cm^{-1}; HRMS (CI, NH_3) accurate mass cald for $(C_{14}H_{16}NO_4 + H)^+$ requires *m/z* 262.1079, found *m/z* 262.1078. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.34; H, 5.79. Found: C, 64.52; H 5.83.



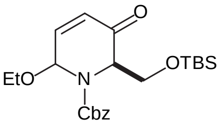
4a

(2*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-hydroxy-3-oxo-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (4a): In a 100 mL flask, furan **5a** (2.28 g, 6.07 mmol) was dissolved in CH_2Cl_2 (12 mL). The flask was cooled to 0 °C and (95% pure) *m*-CPBA (2.09 g, 12.14 mmol) dissolved in 6 mL CH_2Cl_2 was added in small portions. After 3 h the reaction was judged complete by TLC analysis. The white precipitate (chlorobenzoic acid) was removed by vacuum filtration and the filtrate was diluted with ether (12 mL) and washed with satd aqueous $NaHCO_3$. The phases were separated, the aqueous layer was extracted with ether (3 × 10 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* and flash chromatography (EtOAc/hexanes = 3:17) yielded **4a** (2.06 g, 5.25 mmol, 87% yield) as a white solid: mp 72-74 °C, $[\alpha]^{25}_{D}$ +4.30 (*c* 1.12, CH_2Cl_2); R_f 0.33 (EtOAc/hexanes = 3:17); ^1H NMR (300 MHz, $CDCl_3$) as a mixture of C-1 diasteriomers (1:1.6 ratio), δ 7.41-7.29 (m, 5 H), 7.05** (dd, *J* = 10.2, 5.1 Hz, 1H), 6.92* (dd, J = 10.2, 5.1 Hz, 1H), 6.24** (d, J = 10.2 Hz, 1H), 6.15* (d, J = 10.2 Hz, 1H), 6.06** (dd, J = 11.4, 4.8 Hz, 1H), 5.96* (ddd, J = 11.4, 4.8, 0.6 Hz, 1H), [5.32** (d, J = 12 Hz, 1H), 4.87** (d, J = 12 Hz, 1H), 5.21* (d, J = 10 Hz, 1H), 5.18* (d, J = 10 Hz, 1H)], 4.76* (dd, J = 2.1, 2.1 Hz, 1H), 4.66** (dd, J = 2.1, 2.1 Hz, 1H), 4.08* (dd, J = 10.5, 2.1 Hz, 1H), 4.05** (dd, J = 10.5, 2.1 Hz, 1H), 3.87* (J = 10.5, 2.1 Hz, 1H), 3.76** (J = 10.5, 2.1 Hz, 1H), 0.83* (s, 9H), 0.82** (s, 9H), 0.04* (s, 3H), 0.02** (s, 3H), 0.01* (s, 3H), -0.1** (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 194.1*, 194.0**, 154.5, 146.7, 146.1, 135.8*, 135.5**, 128.6**, 128.5*, 128.2, 128.1*, 127.9**, 70.6*, 70.4**, 68.1**, 68.0*, 65.4**, 64.8*, 62.0**, 61.7*, 25.8, 18.2, -5.8; IR (thin film): 3385, 2953, 2935, 2861, 1704, 1695, 1418, 1306, 1254 cm^{-1}; HRMS (CI, NH$_3$) accurate mass calcd for $(C_{20}H_{29}NO_5Si - H_2O + NH_4)^+$ requires m/z 374.1788, found m/z 374.1784. Anal. Calcd for $C_{20}H_{29}NO_5Si$: C, 61.35; H, 7.47. Found C, 61.14; H, 7.24.



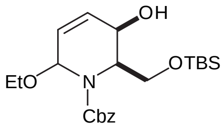
12

(2*R*)-2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3,6-dioxo-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (12): A 25 mL flask was charged with hemi-aminal **4a** (60 mg, 0.15 mmol), acetone (1.5 mL), and a stir bar. The mixture was cooled in an ice bath and Jones Reagent[3] (2.5 M, 0.12 mL) was slowly added via syringe. The solution turned from colorless to orange to green. After 2 h of stirring, the reaction was judged complete by TLC analysis. The reaction was quenched with 2-propanol (1 mL) and was allowed to stir for 15 min. The mixture was filtered through diatomaceous earth and concentrated *in vacuo* to give a crude white solid (65 mg). Purification by flash chromatography (SiO$_2$; EtOAc/hexanes = 3:17) afforded **12** (47 mg, 0.12 mmol, 80% yield) as a white solid: mp 76.5-78.5 °C; $[\alpha]^{25}_{D}$ -14.6 (c 1.5, CH$_2$Cl$_2$); R_f 0.30 (EtOAc / hexanes = 3:17); ^{1}H NMR: (500 MHz, CDCl$_3$) δ 7.45-7.32 (m, 5H), 6.88 (d, J = 10.0 Hz, 1H), 6.67 (d, J = 10.0 Hz, 1H), 5.34 (s, 2H), 4.76 (dd, J = 2.5, 2.5 Hz, 1H), 4.04 (dd, J = 10.0, 3.0 Hz, 1H), 3.97 (dd, J = 10.0, 1.5 Hz, 1H), 0.78 (s, 9H), -0.07 (s, 3H), -0.08 (s, 3H); ^{13}C NMR: (75 MHz, CDCl$_3$) δ 193.7, 161.3, 152.5, 141.4, 136.9, 134.8, 128.6, 128.5, 128.1, 69.0, 66.4, 65.8, 25.6, 18.0, -5.9, -6.0; IR (thin film): 2953, 2929, 2829, 2850, 1774, 1719, 1695, 1267 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{20}H_{27}NO_5Si + H)^+$ requires m/z 390.1737, found m/z 390.1751. Anal. Calcd for $C_{20}H_{27}NO_5Si$: C, 61.67; H, 6.99. Found C, 61.69; H, 6.89.



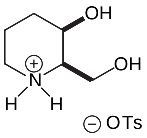
13

(2*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-ethoxy-3-oxo-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (13): A 50 mL flask was charged with a stir bar, aminal **2a** (1.09 g, 2.60 mmol), CH$_2$Cl$_2$ (5 mL), followed by the addition of triethyl orthoformate (1.73 mL, 10.4 mmol) and p-toluene sulfonic acid monohydrate (49 mg, 0.26 mmol, 10 mol %). The reaction was allowed to stir for 24 h, at which time it was judged complete by TLC analysis. The reaction mixture was diluted with ether (10 mL) and was washed with satd aqueous $NaHCO_3$. The phases were separated, the aqueous layer was extracted with ether (3×) and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* and flash chromatography (EtOAc/hexanes = 1:9) afforded **13** (798 mg, 1.90 mmol, 87% yield) as a colorless oil: $[\alpha]^{25}_{D}$ +35.9 (*c* 1.30, CH_2Cl_2); R_f 0.35 (EtOAc/hexanes = 3:17); ^1H NMR (300 MHz, $CDCl_3$) as a mixture of C-1 diasteriomers (1:2 ratio), δ 7.40-7.28 (m, 5 H), 6.96* (dd, *J* =10.2, 4.8 Hz, 1H), 6.86** (dd, *J* = 10.4, 4.8 Hz, 1H), 6.07 (d, *J* = 10.4 Hz, 1H), [6.03* (d, *J* = 4.8 Hz, 1H, major), 5.86** (d, *J* = 4.8 Hz, 1H, minor), [5.26* (d, *J* = 12 Hz, 1H, major), 5.25** (d, *J* = 12 Hz, 1H, minor), 5.14** (d, *J* = 12 Hz, 1H), 5.06* (d, *J* = 12 Hz, 1H), 4.89 (dd, *J* = 9.0, 5.4 Hz, 1H), 3.94* (dd, *J* = 19.2, 9.6 Hz, 2H), 3.88** (m, 2H), 3.74* (m, 2H), 3.52** (m, 2H), 1.22* (t, *J* = 6.9 Hz, 3H), 1.13** (t, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.07** (s, 3H), 0.04* (s, 3H), 0.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 144.3, 143.4, 135.7, 128.6, [128.3**, 128.2*], [127.5**, 127.3*], 77.1, 68.0, [65.0*, 64.9**], [64.6*, 64.1**], 25.7, 18.1, 15.2, -5.6, -5.7; IR (thin film): 2960, 2938, 2887, 2862, 1706, 1695, 1420, 1320, 1258, 1111 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{22}H_{33}NO_5Si + Na)^+$ requires *m/z* 442.2026, found *m/z* 442.2033. Anal. Calcd for $C_{22}H_{33}NO_5Si$: C, 62.98; H, 7.93. Found C, 63.15; H, 8.04.



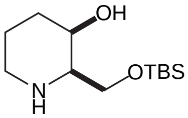
14

(2*R*,3*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-ethoxy-3-hydroxy-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (14): A 100 mL flask was charged with enone **13** (555 mg, 1.32 mmol), a magnetic stir bar and CH_2Cl_2 (6 mL). The mixture was cooled to - 78 °C in a dry ice/acetone bath under a nitrogen atmosphere. To this solution was added a 0.4 M solution of $CeCl_3$ in methanol (10 mL). After additional stirring and continued cooling, $NaBH_4$ (75 mg, 1.98 mmol, 1.5 eq) was added. The reaction was allowed to stir (2 h) at - 78 °C until only alcohol was visible by TLC. The reaction was diluted with ether (15 mL) and was quenched at - 78 °C by the addition of 1 M $NaHSO_4$ (4 mL). This mixture was allowed to stir for 20 min and the phases were separated. The aqueous layer was extracted with ether (4 × 10 mL) and the combined organic layers were washed with brine and dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography provided pure alcohol **14** (477 mg, 1.13 mmol, 86% yield) as a colorless oil: R_f 0.36 (EtOAc /hexanes = 1:4); $[\alpha]^{25}_{D}$ +3.5 (*c* 0.95, CH_2Cl_2); ^1H NMR: (300 MHz, C_6D_6, 78 °C) as a mixture of anomers, δ 7.2-7.0 (m, 5H); 5.74 (d, *J* = 9.6 Hz, 1H), 6.45 (d, *J* = 9.6 Hz, 1H), 5.06 (s, 2H), 4.81 (br s, 1H), 4.37 (q, *J* = 5.7 Hz, 2H), 3.90 (dd, *J* = 10.5, 5.7 Hz, 1H), 3.65-3.30 (m, 3H), 1.00 (t, *J* = 6.9 Hz, 3H), 0.84 (s, 9H), -0.02 (s, 3H), -0.04 (s, 3H); ^{13}C NMR: (75 MHz, C_6D_6, 78 °C) δ 156.3, 137.4, 132.8, 129.1, 128.8, (missing 1 ipso carbon), 79.2, 68.2, 67.9, 63.1, 53.6, 26.4, 18.7, 15.9, -5.1, -5.2; IR (thin film): 3458, 3032, 2960, 2935, 2856, 1713, 1493, 1409, 1263, 1079 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{22}H_{35}NO_5Si + Na)^+$ requires *m/z* 444.2182, found *m/z* 444.2158. Anal. Calcd for $C_{22}H_{35}NO_5Si$: C, 62.67; H, 8.37. Found C, 62.81; H, 8.22.



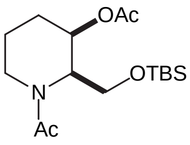
15

(2*R*, 3*R*)-2-Hydroxymethylpiperidin-3-ol tosic acid salt (15): A 15 mL flask was charged with piperidine **14** (44 mg, 0.104 mmol), methanol (1 mL), and 10% palladium on carbon (5 mg). The headspace was flushed with hydrogen gas and a hydrogen balloon was added to the flask via a needle through septum. The mixture was stirred for 12 h at which time the starting material was absent by TLC analysis. Filtration through diatomaceous earth and concentration *in vacuo* afforded the free amine as a colorless oil (25 mg, 0.102 mmol, 98% yield). The free amine was dissolved in methanol (2 mL) and tosic acid monohydrate was added (20.7 mg, 0.109 mmol) with stirring. After 12 h the mixture was concentrated to dryness and was rinsed sequentially with dry ether (2 mL), dry THF (2 mL), and $CHCl_3$ (2 mL). The salt was then dried under high vacuum to yield pure salt **15** (30 mg, 0.100 mmol, 96% yield from piperidine **14**) as a colorless solid: mp 218 °C; $[\alpha]^{25}_{D}$ –2.8 (*c* 1.2, MeOH); ^{1}H NMR (300 MHz, CD_3OD), δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 3.98 (br s, 1H), 3.73 (d, *J* = 7.2 Hz, 1H), 3.52 (dd, *J* = 6.6, 6.6 Hz, 1H), 3.27 (m, 1H), 3.13 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.92 (ddd, *J* = 13.2, 13.2, 3.3 Hz, 1H), 2.35 (s, 3H), 2.07 (dddd, *J* = 14.4, 14.4, 4.2, 4.2 Hz, 1H), 1.90-1.85 (m, 1H), 1.71-1.61 (m, 1H), 1.49 (ddd, *J* = 14.4, 6.6, 3.3 Hz, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 143.9, 141.9, 130.0, 127.1, 63.8, 62.6, 61.7, 45.7, 30.7, 21.5, 18.2; IR (thin film): 3391, 3052, 3021, 2925, 1491 cm^{-1}; HRMS (CI, NH_3) accurate mass calcd for $(C_6H_{13}NO_2 + H)^+$ requires *m/z* 132.1025, found *m/z* 132.1025.



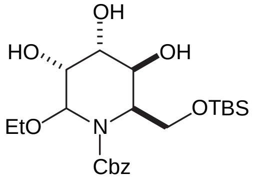
14

(2*R*,3*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-piperidin-3-ol (14): A 25 mL flask was charged with allyl alcohol **12** (85 mg, 0.021 mmol), MeOH (2 mL), a magnetic stir bar, and 10% palladium on carbon (9 mg). The flask headspace was flushed with hydrogen gas and the reaction mixture was stirred rapidly for 12 h, at which time no starting material remained by TLC analysis. The reaction mixture was filtered through a pad of diatomaceous earth and was concentrated *in vacuo* and dried under high vacuum to yield free amine **8** (48 mg, 0.20 mmol, 97% yield) as clear syrup: $[\alpha]^{25}_{D}$ –3.0 (*c* 1.1, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80-3.70 (m, 2H), 3.07 (ddd, *J* = 12, 6.0, 2.1 Hz, 1H), 2.97-2.73 (m, 2H), 2.64 (dd, *J* = 7.5, 4.5 Hz, 1H), 2.63 (dddd, *J* = 15, 9.0, 7.5, 3.0 Hz, 1H), 1.87 (m, 1H), 1.79 (ddd, *J* = 12, 4.5, 4.5 Hz, 1H), 1.53-1.37 (m, 1H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 66.3, 65.9, 60.9, 31.6, 25.8, 20.3, 18.2, -5.5; IR (thin film): 3318, 2936, 2861, 1462, 1255, 1091 cm^{-1}; HRMS (CI, NH_3) accurate mass calcd for $(C_{12}H_{27}NO_2Si + H)^+$ requires *m/z* 246.1889, found *m/z* 246.1911.



15

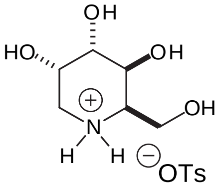
Acetic acid (2*R*,3*R*)-1-acetyl-2-(*tert*-butyldimethylsilyloxymethyl)-piperidin-3-yl ester (15): A 25 mL flask was charged with free amine **14** (40 mg, 0.16 mmol), a magnetic stir bar, pyridine (1.6 mL), CH_2Cl_2 (0.5 mL), acetic anhydride (45 υL, 48 mmol, 3 eq), DMAP (19 mg, 0.16 mmol), and was stirred for 12 h, at which time the reaction was judged complete by TLC analysis. The reaction was diluted with water (4 mL) and the phases were separated. The aqueous phase was extracted with $CHCl_3$ (4 × 5 mL). The combined organic phases were dried over Na_2SO_4, concentrated *in vacuo* and dried under high vacuum to yield crude diacetate **15** (68 mg). Flash chromatography (SiO_2; 2% MeOH in ether) afforded pure diacetate **15** (42 mg, 0.127 mmol, 80% yield) as a clear solid: mp 43-45 °C; $[\alpha]^{25}_{D}$ +4.7 (*c* 1.3, CH_2Cl_2); R_f 0.32 (EtOAc /hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$), δ 4.87 (ddd, *J* = 12.3, 10.8, 5.4 Hz, 1H), 4.56** (br d, *J* = 3.0 Hz, 1H), 4.51* (br d, *J* = 3.0 Hz, 1H), 4.24 (ddd, *J* = 9.3, 4.2, 4.2 Hz, 1 H), 3.92 (dd, *J* = 10.5, 10.5 Hz, 1 H), 3.73 (dd, 10.5, 3.6 Hz, 1H), 2.55 (ddd, *J* = 13.2, 13.2, 3.0 Hz, 1H), 2.14* (s, 3 H), 2.10** (s, 3H), 2.08* (s, 3H), 2.05** (s, 3H), 1.92-1.84 (m, 1H), 1.79-1.73 (m, 1H), 1.64-1.47 (m, 2H), 0.86 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 71.3, 61.1, 58.3, 57.8, 35.6, 26.3, 24.0, 22.2, 20.9, 18.7, -5.1; IR (thin film): 2954, 2929, 1742, 1652, 1429, 1368, 1243 cm^{-1}; HRMS (CI, NH_3) accurate mass calcd for $(C_{16}H_{31}NO_9 + H)^+$ requires *m/z* 330.2101, found *m/z* 330.2127.



16

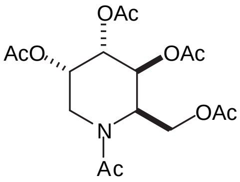
(2*R*,3*S*,4*R*,5*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-ethoxy-3,4,5-trihydroxy-piperidine-1-carboxylic acid benzyl ester (16): A 50 mL flask was charged with a stir bar, allyl alcohol **12** (350 mg, 0.830 mmol), and CH_2Cl_2 (4 mL). A solution of (50% w/v) *N*-methyl morpholine *N*-oxide/water (292 mg, 3 eq) was added and the mixture was cooled to 0 °C. Crystalline OsO_4 (4.2 mg, 0.017 mmol, 2 mol %) was added and the reaction was allowed to stir for 12 h, at which time all starting material had been consumed as judged by TLC. The reaction mixture was pipetted directly on to a silica gel column (4 cm × 3.5 cm). A small amount (1 mL) of CH_2Cl_2 was used in two portions to rinse the reaction mixture onto the column. Impurities were eluted with ether and the product was eluted with MeOH/ether (1:99). Pure fractions were combined and concentrated to afford triol **16** (360 mg, 0.790 mmol, 95% yield) as a clear solid: mp 80-81.5 °C; $[\alpha]^{25}_{D}$ –4.2 (*c* 0.45, CH_2Cl_2); R_f 0.32 (diethyl ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.29 (m, 5H), 5.59* (s, 1H), 5.45** (s, 1H), 5.16 (m, 2H), 4.79* (dd, *J* = 9.0, 3.6 Hz, 1H), 4.66 (dd, *J* = 9.0, 3.6 Hz, 1H), 4.23 (ddd, *J* = 6.0, 5.7, 3.6 Hz, 1H), 4.10-3.98 (m, 2H), 3.71* (ddd, *J* = 9.6, 6.0, 3.6 Hz, 1H), 3.60** (ddd, *J* = 10.2, 6.0, 4.2 Hz, 1H), 3.49* (ddd, 13.2, 8.4, 4.2 Hz, 1H), 3.32** (ddd, *J* = 8.4, 5.4, 4.2

Hz, 1H), 1.14* (t, *J* = 4.2 Hz, 3H), 1.06** (t, *J* = 4.2 Hz, 3H), 0.89** (s, 9H), 0.84* (s, 9H), 0.12** (s, 3H), 0.10* (s, 3H), 0.0* (s, 3H), -0.01** (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8,* 156.1,** 135.9,* 135.8,** 128.5, 128.2, 128.0, 84.6,* 84.4,** 70.4,* 70.2,** 69.4,** 69.3,* 68.9,* 68.8,** 68.0, 63.9,** 63.3,* 63.0,* 62.9,** 54.5,* 53.8,** 25.7, 18.0, 15.0, -5.7; IR (thin film): 3422, 2929, 2856, 1689 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{22}H_{37}NO_7Si + Na)^+$ requires *m/z* 478.2237, found *m/z* 478.2242.



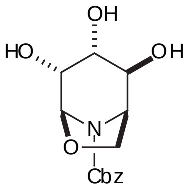
17

(+)-Deoxygulonojirimycin • TsOH salt (**17**): A 25 mL flask was charged with triol **16** (280 mg, 0.61 mmol), methanol (3 mL), a magnetic stir bar, and 10% palladium on carbon (28 mg). The flask headspace was flushed with hydrogen gas and the reaction mixture was stirred rapidly for 12 h, at which time no starting material remained by TLC analysis. The reaction mixture was filtered through a pad of diatomaceous earth and was concentrated *in vacuo* and dried under high vacuum to yield the free amine DGJ as clear soft glass (153 mg, 90% yield). A portion of this material (140 mg, 0.50 mmol) was taken up in MeOH and was stirred with *p*-toluene sulfonic acid monohydrate (119 mg, 0.625 mmol) for 3 h. The reaction mixture was then concentrated, dried under high vacuum, and then rinsed with $CHCl_3$ to remove impurities, and then concentrated and dried under high vacuum again to yield **17 (**170 mg, 0.50 mmol, 99% yield**)** as a clear solid: mp 98-99 °C; $[\alpha]^{25}_D$ +1.5 (*c* 1.0, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 3.99 (ddd, *J* = 11.4, 5.7, 2.4 Hz, 1H), 3.78-3.71 (m, 2H), 3.64-3.58 (m, 2H), 3.24 (dd, *J* = 7.5, 7.5 Hz, 1H), 2.97-2.82 (m, 2H), 2.19 (s, 3H); ^{13}C NMR: (75 MHz, CD_3OD) δ 143.3, 142.0, 130.0, 127.0, 70.4, 68.8, 64.0, 60.7, 57.2, 44.2, 21.5; IR (thin film): 3373, 3063, 3027, 1602, 1451 cm^{-1}; HRMS (FAB) accurate mass cald for $(C_6H_{13}NO_4 + H)^+$ requires *m/z* 164.0923, found *m/z* 164.0927.



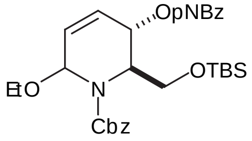
18

Acetic acid (2*R*,3*S*,4*S*,5*S*)-4,5-diacetoxy-2-acetoxymethyl-1-acetyl-piperidin-3-yl ester (18): A 25 mL flask was charged with tetrol salt **17** (105 mg, 0.313 mmol), a magnetic stir bar, pyridine (1.5 mL), CH_2Cl_2 (1.5 mL), acetic anhydride (222 µL, 2.35 mmol, 7.5 eq), 4-DMAP (38 mg, 0.313 mmol), and was stirred for 12 h, at which time the reaction was judged complete by TLC analysis. The reaction was diluted with water (4 mL) and the phases were separated. The aqueous phase was extracted with $CHCl_3$ (4 × 5 mL). The combined organic phases were dried over Na_2SO_4, concentrated *in vacuo* and dried under high vacuum to yield crude pentaacetate **18** as a yellow oil (97 mg). Flash chromatography (MeOH /ether = 1:49) yielded pure pentaacetate **18** (86 mg, 0.23 mmol, 74%) as a colorless oil which became a solid white foam upon drying under vacuum (1 mm Hg): mp 52-54 °C; $[\alpha]^{25}_{D}$ +20.5 (*c* 1.10, CH_2Cl_2); R_f 0.25 (MeOH /ether = 1:49); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.43 (ddd, *J* = 8.5, 3.0, 1.5 Hz, 1H), 5.36-5.32 (m, 2H), 5.30 (dd, *J* = 8.5, 8.5 Hz, 1H), 5.28 (dd, *J* = 15.5, 7.0 Hz, 1H), 5.21 (dd, *J* = 11, 3.0 Hz, 1H), 5.17 (dd, *J* = 11, 3.0 Hz, 1H), 4.80** (dd, *J* = 3.0, 1.5 Hz, 1H), 4.77* (dd, *J* = 3.0, 1.5 Hz, 1H), 4.62 (ddd, *J* = 15.5, 9.0, 4.0 Hz, 1H), 4.55-4.47 (m, 2H), 4.17 (dd, *J* = 3.5, 3.5 Hz, 1H), 4.14 (dd, *J* = 3.5, 3.5 Hz, 1H), 3.88** (dd, *J* = 3.5, 1.5 Hz, 1H), 3.85* (dd, *J* = 3.5, 1.5 Hz, 1H), 3.67* (d, *J* = 3.5 Hz, 1H), 3.64** (dd, *J* = 1.5 Hz, 1H), 2.17 (s, 3H), 2.10** (s, 3H), 2.09* (s, 3H, major), 2.06 (s, 3H), 2.05** (s, 3H), 2.04** (s, 3H), 2.00* (s, 3H), 1.99** (s, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 170.0, 69.9, 69.1, 68.6,* 68.4,** 66.9, 60.3,* 59.4,** 54.9, 49.7, 44.6, 39.0, 21.7,* 21.4,** 20.6,* 20.4**; IR (thin film) : 2972, 2941, 1746, 1658, 1428, 1372, 1230, 1056 cm^{-1}. HRMS (CI, NH_3) accurate mass calcd for $(C_{16}H_{23}NO_9 + H)^+$ requires *m/z* 374.1451, found *m/z* 374.1467.



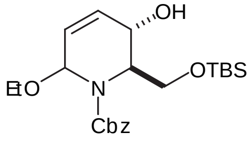
19

(1*R*,2*R*,3*R*,4*S*,5*R*)-2,3,4-Trihydroxy-6-oxa-8-aza-bicyclo[3.2.1]octane-8-carboxylic acid benzyl ester (19): To a solution of triol **16** (65 mg, 0.14 mmol) in benzene (0.7 mL) was added tosic acid monohydrate (2.6 mg, 0.014 mmol). The solution was stirred for 4 h and was quenched with triethylamine (2.9 μL, 0.021 mmol). The mixture was concentrated and purified on silica gel by elution with 10% methanol in CH_2Cl_2 to yield a colorless oil, which formed white crystalline needles after being dissolved in $CHCl_3$. Filtration yielded pure **19** (30 mg, 0.10 mmol, 73% yield) as white crystalline needles: mp 150 °C; $[\alpha]^{25}_{D}$ +16.5 (*c* 1.3, MeOH); R_f 0.30 (MeOH /CH_2Cl_2 = 1:9); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.39-7.30 (m, 5H), 5.43 (d, *J* = 3.5 Hz, 1H), 5.22 (d, *J* = 4.5 Hz, 1H, OH), 5.10 (s, 2H), 4.83 (d, *J* = 5.0 Hz, 1H, OH), 4.56 (d, *J* = 7.0 Hz, 1H, OH), 4.20 (dd, *J* = 4.0, 4.0 Hz, 1H), 3.81 (d, *J* = 7.5 Hz, 1H), 3.65 (ddd, *J* = 5.0, 5.0, 3.5 Hz, 1H), 3.58 (ddd, *J* = 12.5, 4.5, 4.0 Hz, 1H), 3.40 (dd, *J* = 7.5, 4.0 Hz, 1H), 3.36 (ddd, *J* = 12.5, 7.0, 5.0 Hz, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 158.7**, 158.0*, 138.3, 129.9, 129.3**, 129.2*, 129.0**, 128.9*, 89.0, 71.9*, 71.8**, 68.9**, 68.7*, 68.5**, 68.4*, 62.3**, 62.1*, 58.9**, 58.4*, 56.8**, 56.6*; IR (thin film) : 3368, 3232, 3055, 2979, 1689, 1424, 1265, 735 cm^{-1}; HRMS (CI, NH_3) accurate mass calcd for $(C_{14}H_{17}NO_6 + H)^+$ requires *m/z* 296.1134, found *m/z* 296.1141.



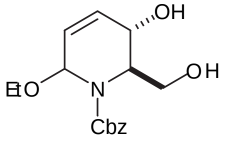
20a

(2*R*,3*S*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-ethoxy-3-(4-nitro-benzoyloxy)-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (20a): A 25 mL flask was charged with alcohol **12** (325 mg, 0.77 mmol), THF (4 mL) and was cooled to 0° C. Triphenylphosphine (404 mg, 1.54 mmol), diethylazodicarboxylate (0.24 mL, 1.54 mmol) and then *p*-nitrobenzoic acid (257 mg, 1.54 mmol) were added with stirring. The reaction was monitored by TLC and was found to be complete after 30 min. The reaction mixture was diluted with ether (4 mL) and was quenched with satd sodium bicarbonate (10 mL). The phases were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were washed with brine, dried over sodium sulfate and concentrated in vacuo to yield a crude mass of 1.23 g. The crude mass was purified by column chromatography to yield **20a** as a colorless oil (370 mg, 0.65 mmol, 84% yield). $[\alpha]^{25}_{D}$ +206 (*c* 1.1, CH_2Cl_2); R_f 0.33 (EtOAc / hexanes = 1: 9); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.21** (d, *J* = 8.7 Hz, 1H), 8.13* (d, *J* = 8.7 Hz, 1H), 8.08** (d, *J* = 8.7 Hz, 1H), 7.96* (d, *J* = 8.7 Hz, 1H), 7.37-7.24 (m, 5H), 6.17-6.05 (m, 2H), 5.78* (d, *J* = 3.3 Hz, 1H), 5.64** (d, *J* = 3.3 Hz, 1H), 5.56** (d, *J* = 5.4 Hz, 1H), 5.49* (d, *J* = 5.4 Hz, 1H), 5.34-5.02 (m, 2H), 4.86** (dd, *J* = 10.2, 5.4 Hz, 1H), 4.75* (dd, *J* = 9.3, 6.3 Hz, 1H), 3.88-3.44 (m, 4H), 1.19* (t, J = 7.2 Hz, 3H), 1.12** * (t, J = 7.2 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 163.8**, 163.7*, 156.4*, 155.7**, 150.3, 136.0, 135.4**, 135.2*, 131.3**, 130.9*, 130.6*, 130.5**, 128.6**, 128.5*, 128.3**, 128.2*, 128.1**, 128.0*, 123.4, 122.6**, 122.1*, 77.2**, 77.1*, 67.9**, 67.6*, 66.2**, 66.1*, 64.2*, 63.5**, 62.3*, 61.9**, 55.3*, 54.6**, 25.8, 18.2, 15.3**, 15.2*, -5.4, -5.5; IR (thin film): 2954, 2930, 2885, 2858, 1724, 1707, 1530, 1268, 1100 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{29}H_{38}N_2O_8Si + Na)^+$ requires *m/z* 593.2295, found *m/z* 593.2339. Anal. Calcd for $C_{29}H_{38}N_2O_8Si$: C, 61.03; H, 6.71. Found C, 60.85; H, 6.59.



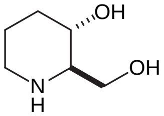
20

(2*R*,3*S*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-ethoxy-3-hydroxy-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (20): A V-shaped vial was charged with ester **20a** (14.0 mg, 0.024 mmol), methanol (0.5 mL), and triethylamine (10 µL, 0.072 mmol) and was stirred for 8 h at which time the reaction was complete by TLC analysis. The reaction was concentrated *in vacuo* and was purified by column chromatography to yield pure alcohol **20** (9.5 mg, 0.0225 mmol, 94% yield) as a colorless oil: $[\alpha]^{25}_{D}$ +81.7 (*c* 1.3, CH_2Cl_2); R_f 0.22 (EtOAc / hexanes = 3:17); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 6.02 (dd, J = 10.0, 5.0 Hz, 1H), 5.98-5.88 m, 1H), 5.67* (br s, 1H), 5.53** (br s, 1H), 5.23-5.16 (m, 2H), 4.61** (br s, 1H), 4.55* (br s, 1H), 4.28** (br s, 1H), 4.18 (br s, 1H), 3.71-3.39 (m, 2H), 3.67** (br q, *J* = 5.0, 2H), 3.60* (q, *J* = 5.0, 2H), 1.15* (t, *J* = 5.0, 3H), 1.07 (t, *J* = 5.0, 3H), 0.87 (s, 9H), 0.03 (s, 3H), -0.01 (s, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 156.8, 136.2, 132.2, 130.2, 128.5, 128.2*, 127.8**, 126.8, 77.1, 67.6, 64.2, 62.9**, 62.8*, 64.4, 58.6*, 58.0**, 25.8, 18.2, 15.3, -5.4, -5.6; IR (thin film): 3450, 3047, 2959, 2929, 2856, 1701 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{22}H_{35}NO_5Si + Na)^+$ requires *m/z* 444.2182, found *m/z* 444.2189. Anal. Calcd for $C_{22}H_{35}NO_5Si$: C, 62.67; H, 8.37. Found C, 62.46; H, 8.17.



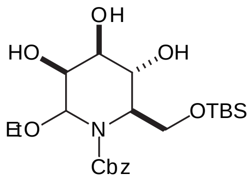
20b

(2*R*,3*S*)-6-Ethoxy-3-hydroxy-2-hydroxymethyl-3,6-dihydro-2*H*-pyridine-1-carboxylic acid benzyl ester (20b): A 15 mL flask was charged with silyl ether **20** (25 mg, 0.059 mmol), a magnetic stir bar and THF (0.5 mL), followed by tetrabutylammonium fluoride (1M in THF, 0.09 mL, 0.09 mmol). The mixture was stirred for 4 h at which time no starting material was visible by TLC analysis. The reaction mixture was concentrated under reduced pressure. Flash chromatography provided pure diol **20b** (17 mg, 0.055 mmol, 93% yield) as a colorless oil: $[\alpha]^{25}_{D}$ +140 (*c* 1.0, MeOH); R_f 0.35 (ether). ^{1}H NMR: (300 MHz, $CDCl_3$) δ 7.38-7.33 (m, 5H), 6.08 (dd, *J* = 9.6, 5.4 Hz, 1H), 6.00-5.88 (m, 1H), 5.75* (br s, 1H), 5.61** (br s, 1H), 5.29-5.09 (m, 2H), 4.68-4.59 (m, 1H), 4.16** (br s, 1H), 4.05* (br s, 1H), 3.80-3.49 (m, 4H), 3.10 (br s, 1H, OH), 1.20* (t, *J* = 6.6 Hz, 3H), 1.11 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 155.1, 132.0, 128.6, 128.4, 128.2, 127.7, 126.8, 76.8, 67.8, 63.7,** 63.4,* 58.3, 30.3,* 29.7,** 15.3; IR (thin film): 3434, 2930, 2856, 1701, 1421, 1306 cm^{-1}; HRMS (CI, NH_3) accurate mass calcd for $(C_{16}H_{21}NO_5 + Na)^+$ requires *m/z* 330.1317, found *m/z* 330.1334.



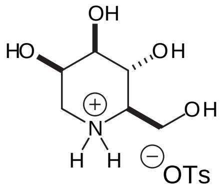
21

(2*R*,3*S*)-2-Hydroxymethylpiperidin-3-ol (21): A 15 mL flask was charged with diol **20b** (23 mg, 0.07 mmol), methanol (1.4 mL), and 10% palladium on carbon (2.5 mg). The headspace was flushed with hydrogen gas and a hydrogen balloon was added to the flask via a needle through septum. The mixture was stirred for 12 h at which time the starting material was absent as judged by TLC analysis. Filtration through diatomaceous earth and concentration *in vacuo* yielded free amine **21 (**9.5 mg, 0.7 mmol, 95% yield**)** as a colorless oil: $[\alpha]^{25}_{D}$ +52.7 (*c* 0.75, MeOH); R_f 0.32 (methanol); ^{1}H NMR (300 MHz, CD_3OD), δ 3.88 (dd, *J* = 10.8, 3.3 Hz; 1H), 3.54 (dd, *J* = 10.8, 6.9 Hz; 1H), 3.32-3.25 (m, 1H), 2.95 (dddd, *J* = 12, 4.2, 2.4, 1.8 Hz; 1H), 2.51 (ddd, *J* = 12.3, 12.3, 3.0 Hz; 1H), 2.38 (ddd, *J* = 10.8, 6.6, 3.0 Hz; 1H), 2.02 (ddddd, *J* = 12.0, 4.5, 3.0, 3.0, 1.5 Hz; 1H), 1.73 (ddddd, *J* = 13.5, 7.5, 3.0, 3.0, 3.0 Hz; 1H), 1.52 (ddddd, *J* = 13.5, 13.2, 9.9, 4.2, 4.2 Hz; 1H), 1.38-1.28 (m, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 68.2, 63.7, 62.3, 45.0, 33.5, 24.7; IR (thin film): 3306, 2930, 2868, 1647, 1443 cm^{-1}; HRMS (CI, NH_3) accurate mass calcd for $(C_6H_{13}NO_2 + H)^+$ requires *m/z* 132.1025, found *m/z* 132.1028.



22

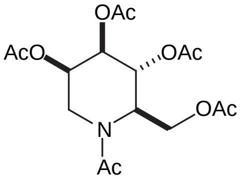
(2*R*,3*R*,4*S*,5*S*)-2-(*tert*-Butyldimethylsilyloxymethyl)-6-ethoxy-3,4,5-trihydroxy-piperidine-1-carboxylic acid benzyl ester (22): A 25 mL flask was charged with alkene **20** (38 mg, 0.09 mmol), CH_2Cl_2 (1 mL), *N*-Methyl morpholine-*N*-oxide (50% in water, w/v; 63 mg, 0.27 mmol), and was cooled to 0 °C. After cooling, OsO_4 was added to the stirring mixture (1.2 mg, 4.5 μmol) and the reaction was stirred at 0 °C for 12 h. The reaction was judged complete by TLC analysis and was concentrated by a stream of N_2 gas. This crude reaction mixture was dissolved in EtOAc/hexanes (2:3, 1 mL) and pipetted onto a silica gel column. The product triol **22** (41 mg, 0.09 mmol, 92% yield) was isolated as a colorless oil: $[\alpha]^{25}_D$ –9.4 (*c* 1.5, CH_2Cl_2); R_f 0.18 (EtOAc / hexanes = 2:3); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 5.67* (d, *J* = 1.5 Hz, 1H), 5.56** d, *J* = 1.5 Hz, 1H), 5.27-5.07 (m, 2H), 4.65* (dd, *J* = 9.3, 5.7 Hz, 1H), 4.56** (dd, *J* = 9.3, 5.7 Hz), 4.28-4.22** (m, 1H), 4.20-4.12* (m, 1H), 4.22-3.87 (m, 2H), 3.74 (dd, *J* = 10.2, 10.2 Hz, 1H), 3.63-3.26 (m, 3H), 1.12* (t, *J* = 6.9 Hz, 3H), 1.05** (t, *J* = 6.9 Hz, 3H), 0.88** (s, 9H), 0.84* (s, 9H), 0.07* (s, 3H), 0.06** (s, 3H), -0.03 (s, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 157.6**, 156.8*, 136.0, 128.5, 128.1, 128.0**, 127.8*, 85.5**, 85.4*, 71.6, 69.2, 67.9, 63.9, 63.3, 62.4*, 62.0**, 60.4*, 59.9**, 25.8, 18.2, 15.0, .5.6; IR (thin film): 3419, 2954, 2928, 1709, 1408, 1251, 1086 cm^{-1}; HRMS (FAB, Na) accurate mass calcd for $(C_{22}H_{37}NO_7Si + Na)^+$ requires *m/z* 478.2237, found *m/z* 478.2253.



23

Deoxymannojirimycin • TsOH salt (23): A 5 mL flask was charged with carbamate **22** (20 mg, 0.58 mmol), MeOH (0.5 mL), a magnetic stir bar, and 10% palladium on carbon (2 mg). The flask headspace was flushed with hydrogen gas and the reaction mixture was stirred rapidly for 12 h, at which time no starting material remained as judged by TLC analysis. The reaction mixture was filtered through a pad of diatomaceous earth and was concentrated *in vacuo* and dried under high vacuum to yield free amine **1** as a clear syrup (9.0 mg, 0.055 mmol, 95% yield). A portion of this material was dissolved in methanol (0.5 mL). A slight excess of tosic acid monohydrate was added (9.1 mg, 0.048 mmol) was added followed by the addition of ether (1 mL). The mixture was stirred for 12 hours and concentrated *in vacuo*, followed by drying under high vacuum. The residue was washed with small portions of dry ether, CH_2Cl_2 and $CHCl_3$ to leave the pure tosic acid salt **23** (15.3 mg, 0.0455 mmol, 99%): $[\alpha]^{25}_D$ +13.3 (*c* 0.90, MeOH); ^1H NMR (300 MHz, CD_3OD) δ 7.73 (d, *J* = 8.1

Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 3.98 (br s, 1H), 4.00 (t, *J* = 2.5 Hz, 1H), 3.86 (dd, *J* = 12.0, 3.0 Hz, 1H), 3.80 (ddd, *J* = 11.0, 6.0, 2.5 Hz, 1H), 3.78 (dd, *J* = 12.0, 5.5 Hz, 1H), 3.22 (ddd, *J* = 9.0, 5.5, 3.5 Hz, 1H), 3.06 (dd, *J* = 11.4, 7.2 Hz, 1H), 3.04 (dd, *J* = 7.2, 3.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR: (75 MHz, CD_3OD) δ 144.1, 142.1, 130.2, 127.8, 71.9, 67.3, 66.5, 59.1, 56.6, 43.5, 21.4; IR (thin film): 3368, 2943, 2828, 1659, 1450. 1180 cm^{-1}; HRMS (CI, NH_3) accurate mass cald for $(C_6H_{13}NO_4 + H)^+$ requires *m/z* 164.0923, found *m/z* 164.0917.



23a

Acetic acid (2*R*,3*R*,4*R*,5*R*)-4,5-diacetoxy-2-acetoxymethyl-1-acetyl-piperidin-3-yl ester (24): A 2 mL V-shaped vial was charged with amine salt **23** (10.6 mg, 0.0316 mmol), a magnetic stir bar, pyridine (0.15 mL), CH_2Cl_2 (0.15 mL), acetic anhydride (22.4 µL, 0.237 mmol), DMAP (3.9 mg, 0.0316 mmol), and was stirred for 12 h, at which time the reaction was judged complete by TLC analysis. The reaction was diluted with satd $NaHCO_3$ (2 mL) and $CHCl_3$ (2 mL) and the phases were separated. The aqueous phase was extracted with $CHCl_3$ (4 × 3 mL). The combined organic phases were dried over Na_2SO_4, concentrated *in vacuo* and dried under high vacuum to yield crude pentaacetate **24** as a yellow oil (12 mg). Flash chromatography (SiO_2; EtOAc) afforded pure pentaacetate **24 (**8.4 mg, 0.0225 mmol, 71% yield**)** as a colorless oil: $[\alpha]^{25}_{D}$ –7.0 (*c* 0.8, CH_2Cl_2); R_f 0.37 (EtOAc); ^{1}H NMR (300 MHz, C_5D_5N, 95 °C) δ 5.70 (dd, *J* = 3.0, 3.0 Hz, 1H), 5.62 (dd, *J* = 3.6, 3.6 Hz, 1H), 5.56 (dd, *J* = 5.7, 3.0 Hz, 1H), 4.66 (dd, *J* = 11.7, 7.5 Hz, 1H), 4.18 (br m, 2H), 3.62 (br m, 1H), 2.26 (s, 3H), 2.16 (s, 6H), 2.05 (s, 6H); IR (thin film): 2929, 2856, 1737, 1654, 1434, 1376, 1226 cm^{-1}; HRMS (FAB) accurate mass calcd for $(C_{16}H_{23}NO_9 + H)^+$ requires *m/z* 374.1451, found *m/z* 374.1432. [6]

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[6] Spectral data matches literature values of Hardick, D. J.; Hutchinson, D. W.; Trew, S. J.; Wellington, E. M. H. *Tetrahedron* **1992**, *48*(30), 6285.