Design and Synthesis of Novel Scaffolds for Drug Discovery: Hybrids of β-D-Glucose with 1,2,3,4-Tetrahydro-benzo[*e*][1,4]diazepin-5-one, the Corresponding 1-Oxazepine, and 2- and 4-Pyridyldiazepines

SUPPORTING INFORMATION

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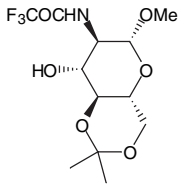
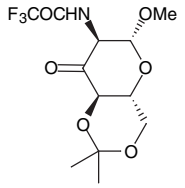


(-)-**10**

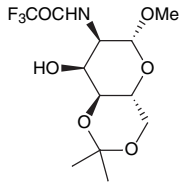
Methyl 2-deoxy-4,6-*O*-isopropylidene- *N*-(trifluoroacetamido) -β-D-glucosamine [(-)-10]. To a solution of triol (-)-**2** (12.1 g, 43.7 mmol) in dimethylformamide (435 mL) was added 2,2-dimethoxypropane (22.7 mL, 218.5 mmol) and *p*-toluenesulfonic acid (582 mg, 3.06 mmol) at room temperature and the reaction was stirred at room temperature for 48 h. After the mixture was neutralized with triethylamine, the solvent was removed by distillation under high vacuum. Flash chromatography (5% methanol/methylene chloride) gave(-)-**10** (12.2 g, 88% yield) as a white solid; $[\alpha]_D^{25}$ -4.4 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3600 (m), 3420 (s), 3000 (s), 2890 (m), 1730 (s), 1550 (s), 1390 (m), 1230 (m), 1170 (s), 1100 (s), 940 (m), 850 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.41 (bs, 1 H), 4.68 (d, *J* = 8.4 Hz, 1 H), 4.09 (ddd, *J* = 9.3, 9.3, 2.5 Hz, 1 H), 3.96 (dd, *J* = 10.5, 5.0 Hz, 1 H), 3.80 (t, *J* = 10.5 Hz, 1 H), 3.55 (t, *J* = 9.3 Hz, 1H), 3.50 (s, 3H), 3.47 (m, 1H), 3.33 (ddd, *J* = 9.6, 9.6, 5.4 Hz, 1H), 1.52 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 101.3, 100.2, 74.5, 70.6, 67.4, 62.1, 58.8, 57.4, 51.1, 31.1, 29.2, 19.3; high resolution mass spectrum (CI, NH_3) *m/z* 347.1428 [$(M+NH_4)^+$; calcd for $C_{12}H_{22}O_6N_2F_3$: 347.1430].



(-)-**21**

Methyl 2-deoxy-4,6-*O*-isopropylidene-*N*-(trifluoroacetamido)-β-D-*ribo*-hex-3-ulopyranoside [(-)-21]. Freshly distilled acetic anhydride (3.5 mL) was added in one portion, at room temperature, to a stirring solution of common intermediate alcohol (-)-**10** (100 mg, 0.25 mmol) in dimethylsulfoxide (7 mL). The reaction was covered in aluminum foil, stirred overnight then diluted with diethyl ether (150 mL) and

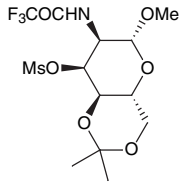
shaken with H_2O (100 mL). The aqueous layer was extracted with ether (2 x 100 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrate *in vacuo.* Residual dimethylsulfoxide was removed by distillation under high vacuum. Flash chromatography (from 2.5% methanol/methylene chloride) gave(-)-**21** (84 mg, 85% yield) as an off-white solid; $[\alpha]_D^{25}$ -25.5° (*c* 0.51, $CHCl_3$; IR ($CHCl_3$) 3400 (m), 3010 (s), 2900 (m), 1740 (s), 1540 (s), 1380 (s), 1240 (s), 1180 (m), 1130 (s), 1100 (s), 840 (m), 720 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, *J* = 7.9 Hz, 1 H), 4.76 (t, *J* = 8.3, 1 H), 4.50 (d, *J* = 7.9 Hz, 1 H), 4.70 (dd, *J* = 10.1, 1.4 Hz, 1 H), 4.13 (dd, *J* = 10.9, 5.3 Hz, 1 H), 4.00 (t, *J* = 10.5 Hz,1 H), 3.58 (s, 3H), 3.51 (m, 1 H), 1.56 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 158.9, 104.5, 100.3, 76.2, 67.9, 62.1, 60.5, 57.3, 30.1, 28.7, 19.0; high resolution mass spectrum (CI, NH_3) *m/z* 270.0977 [$(M)^+$; calcd for $C_{12}H_{16}N_6F_3$: 270.0967].



(-)-**22**

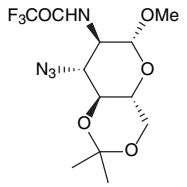
Methyl 2-deoxy-4,6-*O*-isopropylidene-*N*-(trifluoroacetamido)-β-D-allosamine [(-)-22]. To alcohol (-)-**21** (1.60 g, 6.86 mmol) in methylene chloride (40 mL) at 0 °C was added triethylamine (0.96 mL, 6.86 mmol) and trifluoroacetic anhydride (0.96 mL, 6.86 mmol), and the reaction allowed to warm to room temperature slowly over 2 h. Stirring was continued for 24 h. The reaction was diluted with methylene chloride (75 mL), washed with brine (50 mL), and the aqeuous layer extracted with methylene chloride (2 x 75 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (5% methanol/methylene chloride) gave (-)-**22** (2.05 g, 92% yield) as white solid: m.p. 118-120 °C; $[\alpha]_D^{25}$ -73.4° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3600 (m), 3600-3200 (br m), 3430 (s), 3000 (s), 2910 (m), 1745 (s), 1545 (s), 1380 (s), 1180 (s), 875 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.81 (br t, 1 H), 4.60 (d, *J* = 8.1 Hz, 1 H), 4.14 (m, 2 H), 3.99 (m, 1 H), 3.82 (m, 2 H), 3.71 (m, 1 H), 3.50 (s, 3 H), 2.55 (br m, 1 H), 1.53 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9 (q, *J* =

37 Hz, C-F), 100.8, 99.9, 71.2, 68.4, 64.3, 62.2, 57.1, 52.5, 28.9, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 347.1441 [$(M+NH_4)^+$; calcd for $C_{12}H_{18}NO_6F_3$: 347.1430].



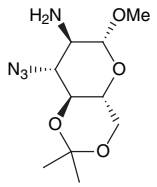
(-)-**23**

Methyl 2-deoxy-3-*O*-(methanesulfonyl)- 4,6-*O*-isopropylidene-*N*-(trifluoroacetamido)-β-D-allosamine [(-)-23]. To alcohol (-)-**22** (0.95 g, 2.9 mmol) in methylene chloride (50 mL) at 0 °C was added triethylamine (0.80 mL, 5.8 mmol) and methanesulfonyl chloride (0.45 mL, 5.8 mmol). After stirring for 2 h at 0 °C, the reaction was allowed to warm to room temperature and stirring continued for 18 h. The reaction was diluted with methylene chloride (50 mL), shaken with 5% aqueous HCl (50 mL), and water (50 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (40% ethyl acetate/hexane) gave (-)-**23** (1.07 g, 91% yield) as white solid: m.p. 160 °C (dec.); $[\alpha]_D^{25}$ -108.9° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3700-3200 (br w), 3010 (m), 1735 (s), 1550 (s), 1375 (s), 1180 (s), 930 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.62 (br d, 1 H), 5.14 (t, *J* = 2.5 Hz, 1 H), 4.65 (d, *J* = 8.5 Hz, 1 H), 4.20 (ddd, *J* = 8.5, 2.8 Hz, 1 H), 4.03 (apparent dd, *J* = 9.9, 4.3 Hz, 1 H), 3.83 (m, 3 H), 3.53 (s, 3 H), 3.16 (s, 3 H), 1.55 (s, 3 H), 1.44 (s, 3 H); ^{13}C NMR (125 MHz, MeOD) δ 159.1 (q, *J* = 37 Hz, C-F), 101.4, 100.5, 79.0, 70.8, 66.1, 63.2, 57.2, 54.5, 39.3, 29.2, 19.3; high resolution mass spectrum (CI, NH_3) *m/z* 425.1208 [$(M+NH_4)^+$; calcd for: $C_{13}H_{20}NO_8SF_3$: 425.1205]. Anal. Calcd. for $C_{13}H_{20}NO_8SF_3$: C 38.33; H 4.95; N 3.44. Found: C 38.63; H 4.71; N 3.32.



(+)-**24**

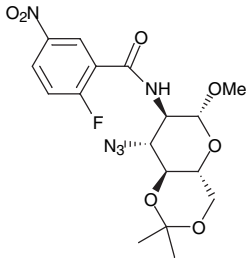
Methyl 2,3-deoxy-3-(azido)- 4,6-*O*-isopropylidene-*N*-(trifluoroacetamido)-β-D-glucosamine [(+)-24]. To mesylate (-)-**23** (2.26 g, 5.5 mmol) in DMF (25 mL) was added sodium azide (1.44 g, 22 mmol) and tetrabutylammonium hydrogen sulfate (100 mg, catalytic). The reaction mixture was heated at 100 °C for 36 h. The reaction was cooled, diluted with ethyl acetate (100 mL), washed with water (75 mL), and the aqueous layer further extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (33% ethyl acetate/hexane) gave (+)-**24** (1.74 g, 92% yield) as white solid: m.p. 218-220 °C; $[\alpha]_D^{25}$ +1.3° (c 0.46, $CHCl_3$); IR ($CHCl_3$) 3450 (w), 2110 (s), 1735 (s), 1550 (m), 1090 (s), 850 (m) cm^{-1} ;^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (br d, 1 H), 4.77 (d, J = 8.2 Hz, 1 H), 4.10 (d, J = 10.8, 9.6 Hz, 1 H), 3.99 (dd, J = 10.9, 5.3 Hz, 1 H), 3.82 (t, J = 10.7 Hz, 1 H), 3.65 (t, J = 9.5 Hz, 1 H), 3.51 (s, 3 H), 3.42 (ddd, J = 9.8, 5.3 Hz, 1 H), 3.34 (dt, J = 10.9, 8.1 Hz, 1 H), 1.55 (s, 3 H), 1.47 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5 (q, J = 37 Hz, C-F), 100.6, 100.1, 73.7, 68.1, 62.1, 60.9, 57.3, 56.8, 28.9, 19.0; high resolution mass spectrum (CI, NH_3) m/z 372.1499 [$(M+NH_4)^+$; calcd for $C_{12}H_{17}N_4O_5F_3$: 372.1495].



(+)-**1**

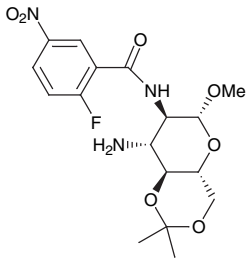
Methyl 2,3-deoxy-3-(azido)-4,6-*O*-isopropylidene-β-D-glucosamine [(+)-1]. To azide (+)-**24** (0.60 g, 1.75 mmol) in methanol (10 mL) was added 5 M KOH (1 mL) and the reaction mixture was heated at reflux for 24 h. The reaction was cooled, concentrated *in vacuo*, and purified via flash chromatography (33% ethyl acetate/hexane) to give (+)-**1** (0.44 g, 99% yield) as yellow oil: $[\alpha]_D^{25}$ +2.9° (*c* 0.65, $CHCl_3$); IR ($CHCl_3$) 3400 (br w), 3005 (m), 2895 (m), 2120 (s), 1375 (m), 1270 (s), 1100 (s), 850 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.19 (d, *J* = 7.8 Hz, 1 H), 3.96 (dd, *J* = 9.9, 5.3 Hz, 1 H), 3.82 (t, *J* = 10.5 Hz, 1 H), 3.69 (t, *J* = 9.5 Hz, 1 H), 3.55 (s, 3 H), 3.35 (m, 2 H), 2.67 (dd, *J* = 10.1, 7.8 Hz, 1 H), 1.57 (br s, 2 H), 1.55 (s, 3 H), 1.46 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 105.7, 100.0, 73.3, 68.4, 65.3, 62.3, 57.4, 56.4, 29.0,

19.0; high resolution mass spectrum (CI, NH_3) *m/z* 259.1406 [$(M+H)^+$; calcd for $C_{10}H_{18}N_4O_4$: 259.1402]. Anal. Calcd for $C_{10}H_{18}N_4O_4$: C 46.48; H 7.03; N 21.69. Found: C 46.51; H 6.94; N 21.42.



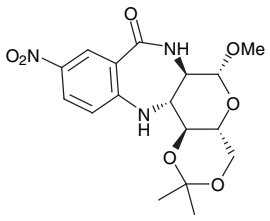
(+)-**25**

Methyl 2,3-deoxy-3-(azido)- 4,6-*O*-isopropylidene-*N*-(2-fluoro-5-nitro-benzamido)-β-D-glucopyranoside [(+)-25]. To a suspension of amine (+)-**1** (101.8 mg, 0.39 mmol) and 2-fluoro-5-nitro-benzoic acid **3** (X=NO_2) (135 mg, 0.47 mmol) in methylene chloride (4 mL) at 0 °C was added a solution of EDAC (105 mg, 0.51 mmol) in methylene chloride (1.0 mL total) via cannula, after which time the reaction mixture became homogeneous. After stirring at 0 °C for 45 min, the reaction was allowed to warm to room temperature then diluted with methylene chloride (25 mL), washed with water (25 mL), and the aqueous layer further extracted with methylene chloride (3 x 25 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (2% methanol/methylene chloride) gave (+)-**25** (160 mg, 95% yield) as a white solid: m.p. 211-213 °C (decomp); $[\alpha]_D^{25}$ +6.1° (*c* 0.59, $CHCl_3$; IR ($CHCl_3$) 3460 (m), 3005 (m), 2110 (s), 1685 (s), 1635 (m), 1535 (s), 1480 (m), 1355 (s), 1095 (s), 855 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.96 (dd, *J* = 6.5, 2.9 Hz, 1 H), 8.40 (ddd, *J* = 7.3, 4.3, 3.0 Hz, 1 H), 7.35 (dd, *J* = 10.3, 9.1 Hz, 1 H), 6.89 (dd, *J* = 11.4, 8.1 Hz, 1 H), 4.91 (d, *J* = 8.2 Hz, 1 H), 4.21 (dd, *J* = 10.7, 9.5 Hz, 1 H), 4.00 (dd, *J* = 10.9, 5.4 Hz, 1 H), 3.84 (t, *J* = 10.5 Hz, 1 H), 3.67 (t, *J* = 9.5 Hz, 1 H), 3.55 (m, 1 H), 3.51 (s, 3 H), 1.56 (s, 3 H), 1.47 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3 (d, *J* = 257 Hz, C-F), 161.4, 144.8, 128.7 (d, *J* = 11.4 Hz, C-F), 128.2 (d, *J* = 3.9 Hz, C-F), 122.3 (d, *J* = 14.7 Hz, C-F), 117.7 (d, *J* = 27.6 Hz, C-F), 101.3, 100.0, 73.6, 68.1, 62.2, 61.6, 57.2, 57.2, 28.9, 19.0; high resolution mass spectrum (CI, NH_3) *m/z* 425.1429 [$(M+H)^+$; calcd for $C_{17}H_{20}N_5O_7F$: 425.1425].



(-)-**26**

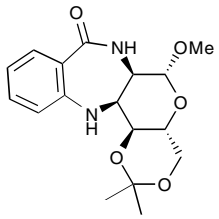
Methyl 2,3-deoxy-3-(amino)-4,6-*O*-isopropylidene-*N*-(2-fluoro-5-nitro-benzamido)-β-D-glucopyranoside [(-)-26]. To a solution of azide (+)-**25** (153 mg, 0.36 mmol) in tetrahydrofuran (10 mL) was added water (100 μL) followed by triphenylphosphine (141 mg, 0.54 mmol) and the reaction heated at 55 °C for 48 h. The mixture was concentrated *in vacuo* and purified directly by flash chromatography (2.5% methanol/methylene chloride then 5% methanol/methylene chloride) to give (-)-**26** (106.7 mg, 74% yield) as a yellow solid: m.p. 166-168 °C; $[\alpha]_D^{25}$ -21.0° (*c* 0.31, $CHCl_3$); IR ($CHCl_3$) 3460 (m), 3005 (s), 1680 (s), 1635 (m), 1535 (s), 1355 (s), 1200 (m), 1095 (s), 860 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.00 (dd, *J* = 6.5, 2.9 Hz, 1 H), 8.39 (ddd, *J* = 9.0, 4.1, 3.1 Hz, 1 H), 7.34 (dd, *J* = 10.4, 9.2 Hz, 1 H), 6.66 (br t, *J* = 9.4 Hz, 1 H), 3.97 (dd, *J* = 11.0, 5.7 Hz, 1 H), 3.83 (t, *J* = 10.6 Hz, 1 H), 3.81 (m, 1 H), 3.52 (s, 3 H), 3.51-3.38 (m, 2 H), 3.25 (dd, *J* = 10.4, 9.1 Hz, 1 H), 1.58 (br s, 2 H), 1.55 (s, 3 H), 1.46 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3 (d, *J* = 257 Hz, C-F), 161.4, 144.8, 128.5, 128.5, 122.7 (d, *J* = 14.9 Hz, C-F), 117.6 (d, *J* = 27.9 Hz, C-F), 102.3, 99.8, 75.1, 68.6, 62.2, 58.4, 56.9, 54.8, 29.1, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 400.1533 [$(M+H)^+$; calcd for $C_{17}H_{22}N_3O_7F$: 400.1520].



(+)-**4**

Trans-Fused Benzodiazepine-Sugar [(+)-4]. A solution of acylated amine (-)-**26** (86.8 mg, 0.20 mmol) in acetonitrile (80 mL, 0.0025M) was heated at 80 °C for 48 h. The mixture was concentrated *in*

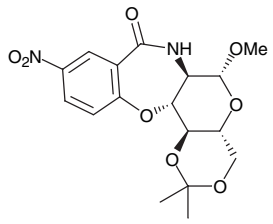
vacuo and purified directly by flash chromatography (50% ethyl acetate/hexane) to give (+)-**4** (34.5 mg, 70% yield) as crystalline yellow solid: m.p. 150-152 °C; $[\alpha]_D^{25}$ +29.3° (*c* 0.45, $CHCl_3$); IR ($CHCl_3$) 3405 (m), 3005 (m), 1665 (s), 1620 (s), 1535 (s), 1515 (s), 1345 (s), 1130 (s), 1100 (s), 860 (m) cm^{-1}; UV (ε_{356} = 14,762); ^1H NMR (500 MHz, $CDCl_3$) δ 9.08 (d, *J* = 2.7 Hz, 1 H), 8.09 (dd, *J* = 9.1, 2.7 Hz, 1 H), 7.29 (br s, 1 H), 6.69 (d, *J* = 9.1 Hz, 1 H), 5.26 (br s, 1 H), 4.49 (d, *J* = 7.8 Hz, 1 H), 4.03 (dd, *J* = 11.0, 5.5 Hz, 1 H), 3.85 (t, *J* = 10.5 Hz, 1 H), 3.69 (t, *J* = 9.4 Hz, 1 H), 3.66 (s, 3 H), 3.58 (t, *J* = 9.3 Hz, 1 H), 3.51 (m, 2 H), 1.60 (s, 3 H), 1.50 (s, 3 H);^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 149.6, 139.5, 131.4, 127.7, 118.8, 115.4, 102.5, 100.6, 72.1, 68.0, 61.7, 59.8, 57.6, 56.7, 29.0, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 397.1727 $[(M+NH_4)^+$; calcd for $C_{17}H_{21}N_3O_7$: 397.1723].



(-)-**13**

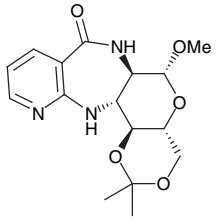
Cis-Fused Benzodiazepine-Sugar [(-)-13]. *N*-benzyloxycarbonyl (Cbz) protected anilino-ketone precursor (-)-**12** (89 mg, 0.18 mmol) in tetrahydrofuran (18 mL) was placed under argon atmosphere. The flask was first evacuated and charged with argon, a procedure which was repeated three times, then followed by addition of 5% Pd/C (catalytic). The flask was again evacuated and charged this time with hydrogen, a procedure which was also repeated three times. The reaction was stirred for 24 h, filtered through celite, concentrated and purified via preparative thin layer chromatography (500 mm, 5% methanol/methylene chloride) to afford (-)-**13** (12 mg, 20% yield) as a beige solid. $[\alpha]_D^{25}$ -48.7° (*c* 0.115, $CHCl_3$); IR ($CHCl_3$) 3300 (m), 2900 (m), 2850 (m), 1620 (s), 1480 (s), 1200 (m), 990 (s), 850 (m), 740 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 2.7 Hz, 1 H), 7.29 (m, 1 H), 6.92 (t, *J* = 7.2 Hz, 1 H), 6.25 (d, *J* = 8.0 Hz, 1 H), 6.40 (br s, 1 H), 4.67 (d, *J* = 8.0 Hz, 1 H), 4.58 (br s, 1 H), 3.89 (m, 5 H), 3.52 (s, 3 H), 3.32 (m, 1 H), 1.60 (s, 3 H), 1.50 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 148.2, 134.0, 132.9, 119.9,

118.5, 117.6, 102.3, 100.0, 70.6, 65.3, 62.5, 58.3, 57.5, 55.6, 30.8, 28.9, 19.1; high resolution mass spectrum (CI, NH_3) *m/z* 334.1521 [$(M+NH_4)^+$; calcd for $C_{17}H_{21}N_2O_5$: 334.1528].



(-)-**14**

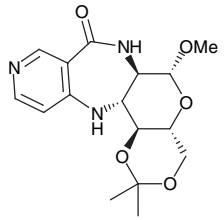
Oxazepine-Sugar [(-)-14]. Cesium fluoride (79 mg, 0.52 mmol) was added to a stirring solution of alcohol (-)-**27** (140 mg, 0.35 mmol) in dimethylformamide (10 mL) and the mixture heated at 85 °C for 24 h. The solvent was evaporated *in vacuo* and the residue directly purified by flash chromatography (5% methanol/methylene chloride) to give (-)-**14** (73 mg, 55% yield); $[\alpha]_D^{25}$ -113.4° (*c* 0.686, $CHCl_3$); IR ($CHCl_3$) 2920 (m), 2840 (m), 1650 (s), 1620 (s), 1520 (s), 1350 (s), 1250 (m), 990 (s), 850 (m) cm^{-1}; UV (ε_{289} = 10,431); ^1H NMR (500 MHz, $CDCl_3$) δ 9.16 (d, *J* = 2.9 Hz, 1H), 8.25 (dd, *J* = 9.0 Hz, 2.9 Hz, 1 H), 7.24 (s, 1 H), 7.18 (d, *J* = 9.0 Hz, 1 H), 4.94 (d, *J* = 7.9 Hz, 1 H), 4.18 (t, *J* = 8.8 Hz 1 H), 4.02 (dd, *J* = 10.9 Hz, 5.3 Hz, 1 H), 3.93 (t, *J* = 9.4 Hz, 1 H), 3.87 (t, *J* = 10.5 Hz, 1 H), 3.60 (m, 1 H), 3.41 (ddd, *J* = 10.0 Hz, 10.0 Hz, 5.3 Hz, 1 H), 1.58 (s, 3 H), 1.45 (s, 3H); ^{13}CNMR (125 MHz, $CDCl_3$) δ 164.2, 160.9, 142.9, 130.1, 128.2, 122.1, 120.7, 102.6, 100.3, 81.8, 71.5, 67.5, 61.8, 58.2, 57.6, 28.9, 19.0; high resolution mass spectrum (CI, NH_3) *m/z* 381.1293 [$(M+H)^+$; calcd for $C_{17}H_{21}N_2O_8$: 381.1297].



(-)-**19**

2-Pyridyldiazepine-Sugar [(-)-19]. Cesium fluoride (39.1 mg, 0.11 mmol) was added to a stirring solution of amine (-)-**17** (21.9 mg, 0.11 mmol) in dimethylformamide (10 mL) and the mixture was heated at 85 °C for 5 days. The solution was poured into sodium bicarbonate (5 mL) and extracted with

$CHCl_3$ (3 x 20 mL). The combined organic extracts were dried over sodium sulfate and potassium carbonate, filtered, and concentrated *in vacuo.* Preparatory thin layer chromatography (500 mm, 10% methanol/methylene chloride) provided (-)-**19** (12.0 mg, 36% yield) as white solid: $[\alpha]_D^{25}$ -57.6° (*c* 0.76, $CHCl_3$); IR ($CHCl_3$) 3386 (m), 3017 (m), 1636 (s), 1590 (s), 1510 (s), 1450 (s), 1380 (s), 1210 (s), 1090 (s), 920 (m), 850 (m), 764 (bw) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.48 (*J*= 1.8, 9 Hz, 1H), 8.22 (dd, *J* = 1.8 Hz, 2.8 Hz, 1 H), 6.81 (s, 1 H), 5.67 (s, 1 H), 4.38 (d, *J* = 7.4 Hz, 1 H), 3.95 (q, *J* = 5.4 Hz, 1 H), 3.82 (t, *J* = 10.6 Hz, 1 H), 3.71 (d, *J* = 9.3 Hz, 1 H), 3.58 (s, 3 H), 3.49 (m, 1 H), 3.46 (m, 2 H), 1.55 (s, 3 H), 1.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 156.4, 152.5, 143.3, 114.9, 110.7, 102.7, 100.5, 71.8, 68.3, 61.8, 57.9, 57.8, 57.4, 28.9, 19.0; high resolution mass spectrum (FAB) *m/z* 336.1548 $[(M+H)^+$; calcd for $C_{16}H_{22}O_5N_3$: 335.1481].



(-)-**20**

4-Pyridyldiazepine-Sugar [(-)-20]. Cesium fluoride (16 mg, 0.045 mmol) was added to a stirring solution of amine (-)-**18** (3.2 mg, 0.009 mmol) in dimethylformamide (0.9 mL) and the mixture was heated at 75 °C for 12 h under argon. The solvent was removed *in vacuo*, and flash chromatography (10% methanol/methylene chloride) provided (-)-**20** (2.0 mg, 71% yield) as white solid: $[\alpha]_D^{25}$ -36.0 (*c* 0.40 $CHCl_3$); IR ($CHCl_3$) 3360 (m), 3010 (m), 1636 (s), 1590 (s), 1509 (s), 1456 (s), 1370 (s), 1215 (s), 1089, 852, (s), 764 (bw) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.27 (d, *J* = 5.8 Hz, 1 H), 6.48 (d, *J*= 5.8 Hz, 1 H), 6.21 (s, 1 H), 4.99 (s, 1 H), 4.38 (d, *J* = 7.6 Hz, 1 H), 4.00 (q, *J* = 5.5 Hz, 1 H), 3.82 (t, *J* = 10.6 Hz, 1 H), 3.65 (t, *J* = 9.4 Hz, 1 H), 3.58 (s, 3 H), 3.47 (m, 2 H), 3.42 (dd, *J* = 7.4, 1.3 Hz, 3 H), 1.56 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 155.9, 151.4, 111.8, 102.6, 100.5, 71.9, 70.5, 68.0, 61.7, 58.9, 57.3, 56.6, 29.6, 28.9, 19.2; high resolution mass spectrum (FAB) *m/z* 336.1564 $[(M+H)^+$; calcd for $C_{16}H_{22}O_5N_3$: 335.1481].