**Electronic Supplementary Information :**

# Selective trihydroxyazepane NagZ inhibitors increase sensitivity of *Pseudomonas aeruginosa* to β-lactams‡

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## Chemical synthesis:

All reagents were used as purchased from commercial suppliers without further purification. Solvents (DMF, THF) were distilled under anhydrous conditions. TLC plates (Macherey-Nagel, ALUGRAM® SIL G/UV$_{254}$, 0.2 mm silica gel 60 Å) were visualized under 254 nm UV light and/or by dipping the TLC plate into a solution of 3 g of phosphomolybdic acid in 100 mL of ethanol followed by heating with a heat gun. Flash column chromatography was performed using Macherey-Nagel silica gel 60 (15-40 μm). NMR experiments were recorded with a Bruker Avance 400 spectrometer at 400 MHz for $^{1}$H nuclei and at 100 MHz for $^{13}$C nuclei. The chemical shifts are expressed in part per million (ppm) relative to TMS ($\delta$ = 0 ppm) and the coupling constant *J* in hertz (Hz). NMR multiplicities are reported using the following abbreviations: b = broad, s = singulet, d = doublet, t = triplet, q = quadruplet, m = multiplet. HRMS were obtained from the Mass Spectrometry Service, CRMPO, at the University of Rennes I, France, using a MICROMASS ZABSPEC-TOF spectrometer and a VARIAN MAT311 spectrometer.

### (3S,4R,5R,6R)-Benzyl 3,4,5-tris(benzyloxy)-6-hydroxyazepane-1-carboxylate 2

Triphenylphosphine polymer bound (1 g, 3.2 mmol.g$^{-1}$, 3.2 mmol) was added to a solution of azidolactol (1 g, 2.10 mmol) in anhydrous THF (30 mL). The reaction mixture was stirred at 40 °C overnight, then filtered on a Celite plug and the solvent removed under reduce pressure to give the crude (3*R*,4*S*,5*S*,6*R*,7*S*)-4,5,6-tris(benzyloxy)-8-oxa-1-aza-bicyclo[3.2.1]octane as a colorless oil (990 mg); $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.35-7.23 (m, 15H, ArH), 5.06 (s, 1H, H-7), 4.57-4.52 (m, 5H, 2 OC*H*$_2$Ph, H-3), 4.43 (br s, 2H, OC*H*$_2$Ph), 3.57 (br s, 1H, H-5), 3.31 (br s, 1H, H-6), 3.25 (br s, 1H, H-4), 3.08-2.98 (m, 2H, H-2); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.3, 138.2, 138.0 (Ar*C*), 128.6, 128.56, 128.52, 128.06, 128.00, 127.9, 127.8 (Ar*C*H), 88.7 (C-7), 77.7 (C-6), 77.3 (C-4), 75.9 (C-5), 73.9 (C-3), 72.1, 71.5, 71.01 (O*C*H$_2$Ph), 45.9 (C-2).

The crude bicyclic N,O-acetal (990 mg) was dissolved in AcOH (8 mL), $NaBH_3CN$ (173 mg, 2.74 mmol) was added and the mixture was stirred at room temperature for 14 h, quenched with a 1N NaOH aqueous solution and extracted with $CH_2Cl_2$. The organic layer was washed sequentially with water and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude (3*R*,4*R*,5*S*,6*S*)-4,5,6-tris(benzyloxy)azepan-3-ol as a colorless oil (822 mg, 1.90 mmol). $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 15H, ArH), 4,69-4,52 (m, 6H, 3 OC*H*$_2$Ph), 4.00 (dt, *J* = 5.6, 1.6 Hz, 1H, H-3), 3,93 (ddd, *J* = 6.1, 2.5, 0.8 Hz, 1H, H-5), 3,70 (dd, *J* = 6.1, 1.6 Hz, 1H, H-4), 3.54 (ddd, *J* = 6.0, 2.5, 0.8 Hz, 1H, H-6), 3.15 (dd, *J* = 15.2, 6.0 Hz, 1H, H-7a), 3.09 (dd, *J* = 14.4, 5.6 Hz, 1H, H-2a), 2.83 (dd, *J* = 15.2, 0.8 Hz, 1H, H-7b), 2.75 (dd, *J* = 14.4, 1.6 Hz, 1H, H-2b); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.3 (Ar*C*), 138.0 (Ar*C*), 137.0 (Ar*C*), 128.6-127.6 (9Ar*C*H), 86.3 (C-4), 82.7 (C-5), 78.0 (C-6), 73.1 (*C*H$_2$Ph), 72.4 (*C*H$_2$Ph), 71.7 (C-3), 71.6 (*C*H$_2$Ph), 52.0 (C-2), 46.7 (C-7).

To a cooled biphasic solution of the crude azepane (822 mg, 1.90 mmol) in EtOAc/water (50 mL:50 mL) at 0°C were added $K_2CO_3$ (1.9 g, 19 mmol) and benzyl chloroformate (0.8 mL, 5.64 mmol). The reaction mixture was stirred at room temperature for 18h, then extracted with EtOAc. The combinated organic layers were successively washed with a 1N HCl solution, water and brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (EtOAc/petroleum ether, 5 to 20%) afforded the corresponding azepane **2** (536 mg, 45% over 3 steps). $[\alpha]_D$= - 10 (*c* = 1, $CHCl_3$); $^{1}$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.30 (m, 20H, ArH), 5.11–5.02 (m, 2H, NCOOC*H*$_2$Ph, NCOOC*H*$_2$'Ph), 4.77-4.40 (m, 6H, 3 C*H*$_2$Ph, 3 C*H*$_2$'Ph), 4.18-4.05 (m, 1H, H-6, H-6'), 4.01–3.26 (m, 7H, 2H-2, H-3, H-4, H-5, 2H-7 and 2H-2', H-3', H-4', H-5', 2H-7'); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 155.8, 155.7 (2 C=O, Z), 140.9, 138.0, 137.9, 136.6 and 136.4 (Ar*C*), 128.6–126.9 (Ar*C*H), 82.9, 82.3 (C-5, C-5'), 80.2, 80.0, 79.8 and 77.9 (C-3, C-3', C-4, C-4'), 73.0, 72.9, 72.7, 72.6, 72.1, 71.9 (3 *C*H$_2$Ph, 3 *C*H$_2$'Ph), 68.7 and 68.6 (C-6, C-

6'), 67.5, 67.2 (NCOO*C*$H_2$Ph, NCOO*C*$H_2$'Ph,), 49.5, 49.3, 47.0, 46.4 (C-2, C-2', C-7, C-7'); HRMS (CIMS) *m/z*: [M+H]$^+$ calcd for $C_{35}H_{38}O_6N$: 568.2699; found: 568.2695.

**(3*S*,4*R*,5*R*,6*S*)-Benzyl 3-azido-4,5,6-tris(benzyloxy)azepane-1-carboxylate 3**

Methanesulfonyl chloride (1.1 mL, 14.81 mmol) was added dropwise at 0°C under argon to a solution of alcohol **2** (2.80 g, 4.93 mmol) and a catalytic amount of DMAP in dry pyridine (30 mL). The ice bath was removed and the reaction mixture was stirred for 3 h at rt, co-evaporated with toluene and concentrated. The residue was dissolved in $CH_2Cl_2$ (100 mL) and washed with a 1M HCl aq. solution (50 mL), water (50 mL) and brine (50 mL). The organic layer was then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude mesylate was used directly without further purification. To a solution of crude mesylate in DMF (90 mL) was added $NaN_3$ (1.8 g, 27.62 mmol) and the reaction mixture was heated at 90 ºC for 96 h. The solvent was removed under reduced pressure and the residue was dissolved in AcOEt/toluene (2:1, 100 mL) and washed successively with aq. $NH_4Cl$ (50 mL), water (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent evaporated under reduced pressure. Purification by flash column chromatography (petroleum ether-EtOAc 10:1 then 10:2) afforded the azido azepane **3** (2.1 g, 72%) as an oil. $[\alpha]_D$= + 5.8 (*c* = 1, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.29-7.05 (m, 20H, Ar*H*), 5.14-5.01 (m, 2H, NCOOC*H*$_2$Ph, NCOOC*H*$_2$'Ph,), 4.71 (d, *J* = 12.0 Hz, 0.5H, C*H*Ph), 4.54-4.42 (m, 4.5H, 4.5 x C*H*Ph), 4.39 (d, *J* = 12.0 Hz, 0.5H, C*H*Ph), 4.34 (d, *J* = 12.0 Hz, 0.5H, CHPh), 3.91 (td, *J* = 8.0, 2.0 Hz, 0.5H, H-6), 3.85 (td, *J* = 7.6, 1.6 Hz, 0.5H, H-6'), 3.80-3.67 (m, 2.5H, H-2a, H-2'a, H-3', H-4, H-4'), 3.65-3.60 (m, 1.5H, H-7'a, H-7a, H-3), 3.58-3.55 (m, 1H, H-5, H-5'), 3.50-3.45 (m, 1.5H, H-2b, H-2'b, H-7b), 3.39 (dd, *J* = 14.8, 7.6 Hz, 0.5H, H-7'b); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.2, 156.1 (2 x C=O), 138.4, 138.1, 137.9, 137.8, 137.7, 137.6, 136.5, 136.4 (8 x Ar*C*), 128.6-127.4 (Ar*C*H), 83.0, 82.4 (C-5', C-5), 81.7, 81.1 (C-4, C-4'), 79.4, 78.5 (C-3, C-3'), 73.3, 73.1, 73.0, 72.9, 71.7, 71.6 (3*C*$H_2$Ph, 3*C*$H_2$'Ph), 67.8, 67.5 (NCOOC$H_2$Ph, NCOOC$H_2$'Ph), 64.0, 63.3 (C-6', C-6), 46.1, 46.0 (C-7, C-7'), 44.8, 44.4 (C-2', C-2); HRMS (CIMS) *m/z*: [M+H]$^+$ calcd for $C_{35}H_{37}O_5N_4$: 593.2764; found: 593.2763.

**(3S,4R,5R,6S)-Benzyl 3-Acetamido-4,5,6-tris(benzyloxy)azepane-1-carboxylate 4**

Triphenyl phosphine (342 mg, 1.30 mmol) was added to a solution of the azido azepane **3** (514 mg, 0.868 mmol) in a 3:1 mixture of THF/$H_2O$ (40 mL) under nitrogen. The reaction mixture was stirred at 50° C for 24 h, by which time TLC revealed no trace of starting material. The reaction mixture was concentrated under reduced pressure to afford the crude amine that was directly engaged in the next step. Acetic anhydride (2.5 mL) and a catalytic amount of DMAP were added to the solution of crude amine in anhydrous pyridine (5 mL). The reaction mixture was stirred at room temperature for 5 h, quenched with 1N HCl, extracted with $CH_2Cl_2$. The organic layer was washed with 1N HCl and brine, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/EtOAc, 80:20 then 70:30) afforded the corresponding acetamido azepane **4** (392 mg, 74%, 2 steps) as a white solid. Mp 147-148 °C; $[\alpha]_D$ = +5.9 (c 0.20, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.32–7.08 (m, 20H, Ar*H*), 6.60 and 6.50 (2d, *J* = 7.4 Hz, 1H, NH, NH'), 5.15–5.03 (m, 2H, NCOOC$H_2$Ph, NCOOC$H_2$'Ph), 4.79-3.72 (m, 12H, 3 C*H*$_2$Ph, H-2a, H-3, H-4, H-5, H-6, H-7a and 3 C*H*$_2$'Ph, H-2'a, H-3', H-4' H-5', H-6', H-7'a), 3.29–3.21 (m, 2H, H-2b, H-7b and H-2'b, H-7'b), 1.73 and 1.43 (2s, 3H, $CH_3CO$, $CH_3$'CO); $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 170.0, 169.7 (2 C=O, Ac), 156.5, 156.2 (2 C=O, Z), 138.2, 138.1, 137.7, 137.5, 137.4, 137.3, 136.6, 136.5 (8 Ar*C*), 128.6–127.6 (Ar*C*H), 83.7, 83.4 (C-5, C-5'), 81.3, 81.1 (C-6', C-6), 76.0, 75.8 (C-4, C-4'), 72.7, 72.5, 72.3, 71.9, 71.8 (6 $CH_2$Ph), 67.5, 67.2 (2 NCOOC$H_2$Ph), 51.9, 51.5 (C-3', C-3), 47.8, 47.7, 47.6, 46.8 (C-2, C-7 and C-2', C-7'), 22.8 ($CH_3CO$); HRMS (CIMS) m/z: [M+H]+ calcd for $C_{37}H_{41}N_2O_6$: 609.2965; found: 609.2961.

**(3S,4R,5R,6*S*)-Benzyl 3,4,5-tris(benzyloxy)-6-(propionamido)azepane-1-carboxylate 5**

Triphenyl phosphine (200 mg, 0.762 mmol) was added to a solution of the azepane **3** (301 mg, 0.508 mmol) in a 3:1 mixture of THF/$H_2O$ (15:5 mL) under nitrogen. The reaction mixture was stirred at 50° C for 12 h by which time TLC revealed no trace of starting material. The reaction mixture was concentrated under reduced pressure to afford the crude amine that was directly engaged in the next step. The crude amine was dissolved in anhydrous pyridine (3 mL) in presence of a catalytic amount of DMAP and propionyl chloride (90 µL, 1.02 mmol) was added under nitrogen at 0 °C. The reaction mixture was left to stand at 10 °C overnight, extracted with $CH_2Cl_2$, washed with 1N HCl and brine. Purification by flash chromatography (PE/EA, 85:15 to 70:30) afforded the corresponding azepane **5** (145 mg, 45%, 2 steps) as a white solid. Mp 137.5-138 °C; $[\alpha]_D$ = +25 (c 0.21, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.39–7.14 (m, 20H, ArH), 6.60 and 6.51 (2d, 1H, *J* = 7.4 Hz, 1H, NH, NH'), 5.17–5.04 (m, 2H, NCOOC*H*$_2$Ph, NCOOC*H*$_2$'Ph), 4.80-4.17 (m, 9H, 3 $CH_2$Ph, H-2a, H-6, H-7a and 3 $CH_2$'Ph, H-2'a, H-6', H-7'a), 4.07–3.77 (m, 3H, H-3, H-4, H-5 and H-3', H-4', H-5'), 3.36–3.28 (m, 2H, H-2b, H-7b and H-2'b, H-7'b), 1.98 and 1.71 (qd, *J* = 7.6 and 2.5 Hz and q, *J* = 7.6 Hz, 2H, C*H*$_2$ and C*H*$_2$'), 0.94 and 0.76 (2t, *J* = 7.6 Hz, 3H, C*H*$_3$ and C*H*$_3$'); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 173.5, 173.2 (2 C=O), 156.3, 156.2 (2 C=O, Z), 138.2, 138.1, 137.7, 137.5, 137.4, 137.3, 136.5, 136.4 (8 Ar*C*), 128.5–126.9 (Ar*C*H), 83.7, 83.5 (C-4, C-4'), 81.6, 81.4 (C-3, C-3'), 76.1, 75.9 (C-5, C-5'), 72.8, 72.6, 72.4, 72.2, 71.8, 71.6 (3 *C*$H_2$Ph, 3 *C*$H_2$'Ph), 67.4, 67.2 (NCOO*C*$H_2$Ph, NCOO*C*$H_2$'), 51.5, 51.2 (C-6, C-6'), 47.6, 47.4, 47.2 and 46.5 (C-2, C-7 and C-2', C-7'), 29.7, 29.4 (*C*$H_2$ and *C*$H_2$'), 9.4, 9,3 (*C*$H_3$ and *C*$H_3$'); HRMS (CIMS) m/z: [M+H]+ calcd for $C_{38}H_{43}N_2O_6$: 623.3115; found: 623.3102.

**(3S,4R,5R,6*S*)-Benzyl 3,4,5-tris(benzyloxy)-6-(butyramido)azepane-1-carboxylate 6**

Triphenyl phosphine (175 mg, 0.666 mmol) was added to a solution of the azido azepane **3** (263 mg, 0.444 mmol) in a 3:1 mixture of THF–$H_2O$ (20 mL) under nitrogen. The reaction mixture was stirred at 40° C for 15 h, by which time TLC revealed no trace of starting material. The reaction mixture was concentrated under reduced pressure to afford the crude amine that was directly engaged in the next step. The crude amine was dissolved in anhydrous pyridine (3 mL) in presence of a catalytic amount of DMAP and butyryl chloride (92 µL, 0.888 mmol) was added under nitrogen at 0 °C. The reaction mixture was left to stand at 10 °C overnight, extracted with $CH_2Cl_2$, washed with 1N HCl and brine. Purification by flash chromatography (Petroleum ether/EtOAc, 85:15 to 70:30) afforded the corresponding azepane **6** (198 mg, 70%) as a white solid. mp 117 °C. $[\alpha]_D$ = +27 (c 0.2, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.40–7.15 (m, 20H, ArH), 6.60 and 6.51 (2d, 1H, *J* = 7.4 Hz, 1H, NH, NH'), 5.18–5.04 (m, 2H NCOOC$H_2$Ph, NCOOC$H_2$'Ph), 4.81-4.18 (m, 9H, 3 C*H*$_2$Ph, H-2a, H-6, H-7a and 3 C*H*$_2$'Ph, H-6', H-2'a, H-7'a), 4.07–3.77 (m, 3H, H-3, H-4, H-5 and H-3', H-4', H-5'), 3.37–3.23 (m, 2H, H-2b, H-7b and H-2'b, H-7'b), 1.94-1.21 (4m, 2 $CH_2$, 2 $CH_2$'), 0.81 and 0.69 (2t, *J* = 7.6 Hz, 3H, C*H*$_3$ and C*H*$_3$'); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 172.7, 172.6 (2 C=O), 156.3, 156.2 (2 C=O, Z), 138.2, 138.1, 137.7, 137.5, 137.4, 137.3, 136.5, 136.4 (8 Ar*C*), 128.5–127.6 (Ar*C*H), 83.7, 83.5 (C-4, C-4'), 81.6, 81.4 (C-3', C-3), 76.1, 75.9 (C-5, C-5'), 72.7, 72.6, 72.4, 72.2, 71.7, 71.6 (6 $CH_2$Ph), 67.4, 67.1 (2 NCOOC$H_2$Ph), 51.4, 51.1 (C-6', C-6), 47.5 (C-7' or C-2'), 47.4 (C-2' or C-7'), 47.2 (C-2 or C-7), 46.5 (C-2 or C-7), 38.7, 38.4 (2 $CH_2$), 18.7, 18.6 (2 $CH_2$), 13.7, 13.6 (2 $CH_3$); HRMS (ESI) m/z: [M+H]+ calcd for $C_{39}H_{44}N_2O_6Na$: 659.3091; found: 659.3093.

**(3S,4R,5R,6*S*)-Benzyl 3,4,5-tris(benzyloxy)-6-(pentanamido)azepane-1-carboxylate 7**

Triphenyl phosphine (281 mg, 1.07 mmol) was added to a solution of the azido azepane **3** (424 mg, 0.716 mmol) in a 3:1 mixture of THF–$H_2O$ (28 mL) under nitrogen. The reaction mixture was stirred at 50° C for 15 h, by which time TLC revealed no trace of starting material. The reaction mixture was concentrated under reduced pressure and the crude amine was directly engaged in the next step. The crude amine was dissolved in anhydrous pyridine (4 mL) in presence of a catalytic amount of DMAP and valeroyl chloride (0.16 mL, 1.39 mmol) was added under nitrogen at 0 °C. The reaction mixture was left to stand at 10 °C overnight, extracted with $CH_2Cl_2$, washed with 1N HCl and brine. Purification by flash chromatography (Petroleum ether/EtOAc, 85:15 then 80:20) afforded the corresponding azepane **7** (290 mg, 62%) as a white solid. Mp 110-115 °C. $[\alpha]_D$ = +36 (c 0.22, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.40–7.28 (m, Ar*C*H), 6.61 (d, *J* = 7.0 Hz, NH), 6.52 (d, *J* = 7.2 Hz, NH'), 5.17–5.03 (m, $NCOOCH_2Ph$, $NCOOCH_2$'Ph), 4.81-4.17 (m, 3 $CH_2Ph$, 3 $CH_2$'Ph, H-6, H-6', H-2a, H-2'a, H-7a, H-7'a), 4.02–3.76 (m, H-4, H-4', H-5, H-5', H-3, H-3'), 3.37–3.28 (m, H-2b, H-2'b, H-7b, H-7'b), 1.98-1.06 (5m, 3$CH_2$, 3$CH_2$'), 0.81 (t, *J* = 7.3 Hz, $CH_3$'), 0.74 (t, *J* = 7.3 Hz, $CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 172.8, 172.7 (2 C=O), 156.3, 156.2 (2 C=O, Z), 138.2, 138.1, 137.7, 137.5, 137.4, 137.3, 136.5, 136.4 (8 Ar*C*), 128.5–127.6 (Ar*C*H), 83.7, 83.5 (C-5, C-5'), 81.7, 81.5 (C-6', C-6), 76.1, 75.9 (C-4, C-4'), 72.8, 72.7, 72.4, 72.2, 71.8, 71.7 (6 $CH_2Ph$), 67.5, 67.1 (2 $NCOOCH_2Ph$), 51.4, 51.1 (C-3', C-3), 47.5 (C-7' or C-2'), 47.4 (C-2' or C-7'), 47.2 (C-2 or C-7), 46.5 (C-2 or C-7), 36.4, 36.2 (2 $CH_2$), 27.3, 27.2 (2 $CH_2$), 22.3, 22.2 (2 $CH_2$), 13.7, 13.6 (2 $CH_3$); HRMS (ESI) m/z: [M+H]+ calcd for $C_{40}H_{47}N_2O_6$: 651.3428; found: 651.3423.

**(3S,4R,5R,6*S*)-Benzyl 3-(2-ethylbutanamido)-4,5,6-tris(benzyloxy)azepane-1-carboxylate 8**

Triphenyl phosphine (195 mg, 0.742 mmol) was added to a solution of the azido azepane **3** (293 mg, 0.495 mmol) in a 3:1 mixture of THF–$H_2O$ (20 mL) under nitrogen. The reaction mixture was stirred at 50° C for 15 h, by which time TLC revealed no trace of starting material. The reaction mixture was concentrated under reduced pressure and the crude amine was directly engaged in the next step. The crude amine was dissolved in anhydrous pyridine (3 mL) in presence of a catalytic amount of DMAP and 2-ethylbutyryl chloride (0.13 mL, 0.99 mmol) was added under nitrogen at 0 °C. The reaction mixture was left to stand at 10 °C overnight, extracted with $CH_2Cl_2$, washed with 1N HCl and brine. Purification by flash chromatography (Petroleum ether/EtOAc, 85:15) afforded the corresponding azepane **8** (178 mg, 54%) as a white solid. Mp 135 °C. $[\alpha]_D$ = +33 (c 0.20, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ (presence of 2 rotamers) 7.39–7.15 (m, Ar*C*H), 6.54 (d, *J* = 7.0 Hz, NH), 6.51 (d, *J* = 7.2 Hz, NH'), 5.27 and 4.91 (2d, *J* = 12.5 Hz, $NCOOCH_2Ph$), 5.16 and 5.07 (2d, *J* = 12.2 Hz, $NCOOCH_2$'Ph), 4.80 and 4.66 (2d, *J* = 11.7 Hz, $CH_2Ph$), 4.61-4.37 (m, 2 $CH_2Ph$, 3 $CH_2$'Ph, H-3, H-3'), 4.31-4.16 (m, H-2a, H-2'a, H-7a, H-7'a), 4.05–3.76 (m, H-4, H-4', H-5, H-5', H-6, H-6'), 3.39–3.30 (m, H-2b, H-2'b, H-7b, H-7'b), 1.65-1.30 (m, 2$CH_2$, 2$CH_2$', 1CH, 1CH'), 0.83-067 (m, 2$CH_3$, 2$CH_3$'); $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 175.4 (C=O), 156.3, 156.2 (2 C=O, Z), 138.2, 138.1, 137.7, 137.5, 137.4, 137.3, 136.6, 136.5 (8 Ar*C*), 128.6–127.6 (Ar*C*H), 83.6, 83.5 (C-5, C-5'), 81.8, 81.7 (C-6', C-6), 76.9, 76.7 (C-4, C-4'), 72.9, 72.7, 72.4, 72.2, 71.6 (6 $CH_2Ph$), 67.4, 67.1 (2 $NCOOCH_2Ph$), 51.1, 51.0, 50.81, 50.80 (C-3', C-3, CH, CH'), 47.3 (C-7' or C-2'), 47.0 (C-2' or C-7'), 46.5 (C-2 or C-7), 46.3 (C-2 or C-7), 25.1, 25.0, 24.85, 24.84 (2 $CH_2$, 2 $CH_2$'), 11.9, 11.8, 11.7 (3 $CH_3$); HRMS (ESI) m/z: [M+H]+ calcd for $C_{41}H_{49}N_2O_6$: 665.3594; found: 665.3594.

***N*-[(3S,4R,5R,6*S*)-4,5,6-Trihydroxyazepan-3-yl]acetamide 1**

To a solution of the protected acetamido azepane **4** (18 mg, 0.030 mmol) in $CH_3OH$ (3 mL) was added 10% Pd/C (20 mg) and a 1 M HCl aq solution (30 µL). The solution was degassed three times and air was replaced by $H_2$. After stirring for 7 h at rt, the reaction mixture was filtered, filter eluted with $CH_3OH$, and concentrated to afford the acetamido azepane **1** (6.1 mg, quantitative yield) as its hydrochloride salt. $[\alpha]_D$ = +14.8 (c 0.4, $CH_3OH$); $^1H$ NMR (400 MHz, $CD_3OD$): δ = 4.21 (td, *J* = 9.0 and 3.4 Hz, 1H, H-3), 4.05 (dd, *J* = 5.9 and 5.0 Hz, 1H, H-6), 3.87 (dd, *J* = 5.9 and 3.7 Hz, 1H, H-5), 3.65 (dd, 9.0 and 3.7 Hz, 1H, H-4), 3.31–3.11 (m, 4H, 2H-2, 2H-7), 1.90 (s, 3H, $CH_3CO$); $^{13}C$ NMR (100 MHz, $D_2O$): δ =174.0 (CO), 75.9 (C-5), 74.8 (C-4), 67.6 (C-6), 49.4 (C-3), 46.5 (C-2 or C-7), 46.1 (C-2 or C-7), 21.9 ($COCH_3$); HRMS (CIMS) (as free amine) m/z: [M+H]+ calcd for $C_8H_{17}N_2O_4$: 205.1188; found: 205.1183.

### *N*-[(3S,4R,5R,6S)-4,5,6-Trihydroxyazepan-3-yl]propionamide 9

To a solution of the protected azepane **5** (21.5 mg, 0.345 mmol) in $CH_3OH$ (7 mL) was added 10% Pd/C (13 mg), Pd black (12 mg) and a 1 M HCl aq solution (70 µL, 0.070 mmol). The solution was purged with $N_2$ then with $H_2$. After stirring for 20 h at rt, the reaction mixture was filtered on celite, filter eluted with $CH_3OH$, and concentrated at reduce pressure without heating, to afford the azepane **9** as its hydrochloride (8.8 mg, quantitative yield). $[\alpha]_D$ = +96 (c 0.06, $CH_3OH$); $^1H$ NMR (400 MHz, $CD_3OD$): δ = 4.31 (m, 1H, H-3), 4.15 (t, *J* = 5.8 Hz, 1H, H-6), 3.96 (dd, *J* = 5.8 and 3.8 Hz, 1H, H-5), 3.65 (dd, 8.9 and 3.8 Hz, 1H, H-4), 3.43–3.24 (m, 4H, 2H-2, 2H-7), 2.26 (q, *J* = 7.5 Hz, 2H, $CH_2$), 1.13 (t, *J* = 7.5 Hz, 3H, $CH_3$); $^{13}C$ NMR (100 MHz, $CD_3OD$): δ =175.3 (CO), 77.5 (C-4), 76.7 (C-5), 69.7 (C-6), 52.3 (C-3), 47.8 (C-2 or C-7), 47.1 (C-2 or C-7), 30.1 ($CH_2$), 10.2 ($CH_3$); HRMS (CIMS) (as free amine) m/z: [M+H]+ calcd for $C_9H_{19}N_2O_4$: 219.1344; found: 219.1345.

### *N*-[(3S,4R,5R,6S)-4,5,6-Trihydroxyazepan-3-yl]butyramide 10

To a solution of the protected azepane **6** (33 mg, 0.0518 mmol) in $CH_3OH$ (8 mL) was added 10% Pd/C (17 mg), Pd black (16 mg) and a 1 M HCl aq solution (54 µL, 0.054 mmol). The solution was purged with $N_2$ then with $H_2$. After stirring for 4 h at rt, the reaction mixture was filtered, filter eluted with $CH_3OH$, and concentrated at reduce pressure without heating, to afford the azepane **10** (13.9 mg, quantitative yield) as its hydrochloride. $[\alpha]_D$ = +87 (c 0.12, $CH_3OH$); $^1H$ NMR (400 MHz, $CD_3OD$): δ = 4.21 (dt, *J* = 9.0 and 6 Hz, 1H, H-3), 4.05 (t, *J* = 5.7 Hz, 1H, H-6), 3.87 (dd, *J* = 5.7 and 3.8 Hz, 1H, H-5), 3.65 (dd, 9.0 and 3.8 Hz, 1H, H-4), 3.31–3.11 (m, 4H, 2H-2, 2H-7), 2.12 (t, *J* = 7.1 Hz, 2H, $CH_2$), 1.55 (sext, *J* = 7.1 Hz, 2H, $CH_2$), 0.86 (t, *J* = 7.1 Hz, 3H, $CH_3$); $^{13}C$ NMR (100 MHz, $CD_3OD$): δ =176.3 (CO), 77.6 (C-4), 76.7 (C-5), 69.7 (C-6), 52.3 (C-3), 47.9 (C-2 or C-7), 47.3 (C-2 or C-7), 38.9 ($CH_2$), 20.3 ($CH_2$), 14.0 ($CH_3$); HRMS (CIMS) (as free amine) m/z: [M+H]+ calcd for $C_{10}H_{21}N_2O_4$: 233.1501 ; found: 233.1502 .

### *N*-[(3S,4R,5R,6S)-4,5,6-Trihydroxyazepan-3-yl]pentanamide 11

Azepane **7** (11.2 mg, 0.0172 mmol) was deprotected as described for compound **1** to afford compound **11** as its hydrochloride salt (4.3 mg, 88%).

$[\alpha]_D$ = +41 (c 0.1, $CH_3OH$); $^1H$ NMR (400 MHz, $CD_3OD$): δ = 4.33 (dt, *J* = 8.9 and 5.8 Hz, 1H, H-3), 4.16 (t, *J* = 5.8 Hz, 1H, H-6), 3.97 (dd, *J* = 5.8 and 3.8 Hz, 1H, H-5), 3.77 (dd, *J* = 9.0 and 3.8 Hz, 1H, H-4), 3.40–3.20 (m, 4H, 2H-2, 2H-7), 2.24 (t, *J* = 7.1 Hz, 2H, $CH_2$), 1.60 (quint, *J* = 7.1 Hz, 2H, $CH_2$), 1.37 (sext, *J* = 7.1 Hz, 2H, $CH_2$), 0.93 (t, *J* = 7.1 Hz, 3H, $CH_3$); $^{13}C$ NMR (100 MHz, $CD_3OD$): δ

=176.5 (CO), 77.6 (C-4), 76.6 (C-5), 69.7 (C-6), 52.3 (C-3), 47.9 (C-2 or C-7), 47.2 (C-2 or C-7), 36.7 ($CH_2$), 28.9 ($CH_2$), 23.4 ($CH_2$), 14.1 ($CH_3$); HRMS (CIMS) (as free amine) m/z: [M+H]+ calcd for $C_{11}H_{23}N_2O_4$: 247.1657 ; found: 247.1542.

**2-Ethyl-*N*-[(3S,4R,5R,6S)-4,5,6-Trihydroxyazepan-3-yl]butanamide 12**

Azepane **8** (11.8 mg, 0.0178 mmol) was deprotected as described for compound **1** to afford compound **12** as its hydrochloride salt (5.1 mg, 97%).

$[\alpha]_D$ = +61 (c 0.1, $CH_3OH$); $^1H$ NMR (400 MHz, $CD_3OD$): δ = 8.23 (d, *J* = 4 Hz), 4.36 (td, *J* = 9.2 and 2.5 Hz, 1H, H-3), 4.17 (t, *J* = 5.5 Hz, 1H, H-6), 3.98 (dd, *J* = 5.5 and 3.8 Hz, 1H, H-5), 3.77 (dd, 9.2 and 3.8 Hz, 1H, H-4), 3.43–3.21 (m, 4H, 2H-2, 2H-7), 2.10 (m, 1H, CH), 1.60-1.45 (m, 4H, $2CH_2$), 0.93 and 0.91 (2t, *J* = 7.5 Hz, 3H, $CH_3$); $^{13}C$ NMR (100 MHz, $CD_3OD$): δ =179.0 (CO), 77.9 (C-4), 76.6 (C-5), 69.5 (C-6), 52.4 (C-3), 51.6 (CH), 48.3 (C-2 or C-7), 47.2 (C-2 or C-7), 26.8 ($CH_2$), 12.4 ($CH_3$); HRMS (CIMS) (as free amine) m/z: [M+H]+ calcd for $C_{12}H_{25}N_2O_4$: 261.1814; found: 261.1811.

***N*-[(3S,4R,5R,6S)-4,5,6-Tris(benzyloxy)azepan-3-yl]acetamide 4'**

To a solution of the protected acetamido azepane **4** (98 mg, 0.161 mmol) and $Et_3N$ (11.2 μL, 0.080 mmol) in $CH_3OH$ (10 mL) was added 5% $Pd/CaCO_3$ (98 mg). The solution was degassed three times and air was replaced by $H_2$. After stirring for 2 h at RT, the reaction mixture was filtered, eluted with $CH_3OH$, and concentrated to afford the acetamido azepane **4'** as a colorless oil (76.4 mg, quantitative yield), used without purification in the next step. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.33–7.30 (m, 15H), 6.51 (d, *J* = 6.3 Hz, NH), 4.62 (s, 4H, $2CH_2Ph$), 4.56 (s, 2H, $1CH_2Ph$), 4.27 (m, 1H, H-3), 3.91 (m, 2H, H-4, H-5), 3.69 (m, 1H, H-6), 3.17 (dd, *J* = 13 .4 and 1.9 Hz, H-2a), 3.11 (dd, *J* = 13 .5 and 3.0 Hz, H-7a), 3.00 (dd, *J* = 13 .5 and 9.3 Hz, H-7b), 2.87 (dd, *J* = 13.4 and 4.9 Hz, H-2b), 1.85 (s, 3H, $CH_3CO$); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 169.8 (CO), 138.4, 138.1, 138.0 (3 Cipso), 128.47–127.55 (aromatic CH), 85.4 (C-5), 85.1 (C-6), 78.1 (C-4), 73.1 ($CH_2Ph$), 72.1 ($CH_2Ph$), 51.4 (C-3), 49.1 (C-7), 48.3 (C-2), 23.4 ($CH_3CO$).

***N*-[(3S,4R,5R,6S)-4,5,6-Tris(benzyloxy)-1-butylazepan-3-yl]acetamide 13**

Potassium carbonate (84 mg, 0.608 mmol) was added to a stirred solution of azepane **4'** (57.7 mg, 0.121 mmol) and n-butyl bromide (26 μL, 0.312 mmol) in a 8:1 mixture of EtOAc/$H_2O$ (3.4 mL) under nitrogen. The reaction mixture was stirred at 80° C for 48h, by which time TLC revealed no trace of starting material. The reaction mixture was diluted with EtOAc, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by preparative TLC chromatography (EtOAc/MeOH, 95:5) afforded the corresponding azepane **13** (52 mg, 80%) as a white solid. Mp 115 °C. $[\alpha]_D$ = +3 (c 0.16, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 15H), 6.46 (d, *J* = 7.3 Hz, NH), 4.70-4.58 (m, 6H, 3 x $CH_2Ph$), 4.25 (m, 1H, H-3), 3.98 (m, 1H, H-4), 3.77 (dd, *J* = 7.3 and 3.6 Hz, 1H, H-5), 3.66 (m, 1H, H-6), 2.85 (m, 2H, H-2a, H-7a), 2.64 (m, 2H, H-2b, H-7b), 2.49 (t, *J* = 7.2 Hz, $CH_2$), 1.75 (s, 3H, $CH_3CO$), 1.40 (m, 2H, $CH_2$), 1.28 (quint, *J* = 7.1 Hz, 2H, $CH_2$), 0.91 (t, *J* = 7.1 Hz, 3H, $CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 169.6 (CO), 138.5, 138.4, 138.3 (Ar*C*), 128.36–127.56 (Ar*C*H), 86.4 (C-5), 82.8 (C-6), 78.2 (C-4), 73.5 ($CH_2Ph$), 72.6 ($CH_2Ph$), 72.0 ($CH_2Ph$), 59.2 ($CH_2$), 56.7 and 53.9 (C-2, C-7), 49.5 (C-3), 29.3 (*C*$H_2$), 23.4 (*C*$H_3CO$), 20.4 (*C*$H_2$), 14.0 (*C*$H_3$); HRMS (CIMS) m/z: [M+H]+ calcd for $C_{33}H_{43}N_2O_4$: 531.3217; found: 531.3217.

**_N_-[(3S,4R,5R,6S)-4,5,6- Tris(benzyloxy)-1-(4-phenylbutyl)azepan-3-yl]acetamide 14**

Reaction of azepane **4'** (74.8 mg, 0.158 mmol) with 1-bromo-4-phenylbutane afforded compound **15** as a white solid (62 mg, 64%) as described for compound **13.** Mp 197-108 °C; $[\alpha]_D$ = +1 (c 0.9, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.14 (m, 20H), 6.41 (d, *J* = 7.5 Hz, NH), 4.68-4.57 (m, 6H, $3CH_2Ph$), 4.25 (m, 1H, H-3), 3.97 (dd, *J* = 5.0 and 3.7 Hz, 1H, H-4), 3.76 (dd, *J* = 7.2 and 3.7 Hz, 1H, H-5), 3.64 (ddd, *J* = 10.0, 7.2 and 2.9 Hz, 1H, H-6), 2.87-2.80 (m, 2H, H-2a, H-7a), 2.68-2.59 (m, 4H, H-2b, H-7b, $CH_2$), 2.51 (t, *J* = 7.2 Hz, $NCH_2$), 1.83 (s, 3H, $CH_3CO$), 1.62 (quint, *J* = 7.2 Hz 2H, $CH_2$), 1.49 (m, 2H, $CH_2$); $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 169.6 (CO), 142.3, 138.5, 138.4, 138.3 (4 Ar*C*), 128.37–125.8 (Ar*C*H), 86.36 (C-5), 82.9 (C-6), 78.1 (C-4), 73.4 ($CH_2Ph$), 72.5 ($CH_2Ph$), 72.0 ($CH_2Ph$), 59.3 ($NCH_2$), 56.7 (C-7), 54.0 (C-2), 49.5 (C-3), 35.7 ($CH_2$), 29.2 ($CH_2$), 26.9 ($CH_2$), 23.4 ($CH_3CO$); HRMS (ESI) m/z: [M+H]+ calcd for $C_{39}H_{47}N_2O_4$: 607.3530; found: 607.3529.

**_N_-[(3S,4R,5R,6S)-1-Butyl-4,5,6-trihydroxyazepan-3-yl]acetamide 15**

To a solution of the protected azepane **13** (20 mg, 0.0341 mmol) in $CH_3OH$ (3 mL) was added 10% Pd/C (12 mg), Pd black (12 mg) and a 1 M HCl aq solution (35 µL, 0.035 mmol). The solution was purged with $N_2$ then with $H_2$. After stirring for 7 h at rt, the reaction mixture was filtered, eluted with $CH_3OH$, and concentrated under reduced pressure at rt, to afford the azepane **15** as a white solid (8.8 mg, quant yield). Mp 75-82 °C; $[\alpha]_D$ = +67 (c 0.2, $CH_3OH$); $^1$H NMR (400 MHz, $CD_3OD$): δ = 4.40 (td, 1H, J = 9.6 and 1.5 Hz, H-3), 4.16 (m, 1H, H-6), 3.97 (dd, *J* = 5.8, 3.2 Hz, 1H, H-5), 3.72 (dd, *J* = 9.6, 3.2 Hz, 1H, H-4), 3.47-3.31 (m, 4H, 2H-2, 2H-7), 3.25 (m, 2H, $CH_2$), 1.98 (s, 3H, $CH_3CO$), 1.72 (m, 2H, $CH_2$), 1.40 (sext, *J* = 7.2 Hz, 2H, $CH_2$), 0.99 (t, *J* = 7.2 Hz, 3H, $CH_3$); $^{13}$C NMR (100 MHz, $CD_3OD$): δ = 171.9 (CO), 77.9 (C-4), 76.4 (C-5), 69.4 (C-6), 60.2 ($CH_2$), 57.4 and 55.0 (C-2, C-7), 51.8 (C-3), 27.3 ($CH_2$), 23.1 ($CH_3CO$), 21.2 ($CH_2$), 14.9 ($CH_3$); HRMS (ESI) m/z: [M+H]+ calcd for $C_{12}H_{25}N_2O_4$: 261.1814; found: 261.1817.

**_N_-[(3S,4R,5R,6S)-4,5,6-Trihydroxy-1-(4-phenylbutyl)azepan-3-yl]acetamide 16**

Azepane **14** (11 mg, 0.018 mmol) was deprotected as described for compound **13** (one night at RT) to afford compound **16** as a white solid (6 mg, quant. yield). Amorphous solid; $[\alpha]_D$ = +38 (c 0.17, $CH_3OH$); $^1$H NMR (400 MHz, $CD_3OD$): δ = 7.27-7.17 (m, 5 Harom), 4.41 (td, 1H, *J* = 9.6, 1.3 Hz, H-3), 4.18 (m, 1H, H-6), 3.98 (dd, *J* = 5.8, 3.1 Hz, 1H, H-5), 3.74 (dd, *J* = 9.6, 3.1 Hz, 1H, H-4), 3.45-3.15 (m, 6H, 2H-2, 2H-7, $CH_2$), 2.70 (like t, *J* = 7.4 and 6.6 Hz, 2H, $CH_2$), 2.01 (s, 3H, $CH_3CO$), 1.78-1.65 (m, 4H, $2CH_2$); $^3$C NMR (100 MHz, $CD_3OD$): δ = 173.6 (CO), 142.8, (C), 129.5 (CH), 127.1 (CH), 77.9 (C-4), 76.3 (C-5), 69.3 (C-6), 59.8 ($NCH_2$), 57.0 (C-7), 54.9 (C-2), 49.9 (C-3), 36.1 ($CH_2$), 29.4 ($CH_2$), 24.6 ($CH_2$), 22.6 ($CH_3CO$); HRMS (ESI) m/z: [M+H]+ calcd for $C_{18}H_{29}N_2O_4$: 337.2127; found: 337.2128.

***Bc*NagZ expression, purification and crystallization:**

The open reading from for BcNagZ (UniProtKB B4EA43) was amplified by PCR from *Burkholderia cenocepacia* J2315 genomic DNA (provided by Dr. Silvia Cardona, Microbiology, University of Manitoba) as template and the following oligonucleotide primers: 5'-GATATACATATGGCGCATCACCATCACCATCACATGAAAACGACTCCCGGCCC-3' and 5'-GATATAGGATCCTTACGCCAGCGCGCTGCTCAACAGCGC-3'. The resulting PCR amplicon was restricted with NdeI and BamHI and ligated into a version of a pET28

plasmid (Novagen) containing a reduced multicloning site (Nde1/Spe1/BamH1). The resulting plasmid (pBCNagZ) was used to transform *E. coli* BL21 (DE3) GOLD cells. Transformants were selected on Luria broth (LB) agar supplemented with 50 mg/ml kanamycin. The resulting expression plasmid pBCNagZ was isolated from single kanamycin-resistant transformant and confirmed by DNA sequencing.

Expression of recombinant *Bc*NagZ was induced in *E. coli* BL21 (DE3) GOLD cells using IPTG. Cell culture pellets were lysed by French press in 25 mM HEPES pH 7, 500 mM NaCl, 5% glycerol and 1 mM PMSF. The His-tagged protein was purified using a nickel gravity column after being subjected to washes with wash buffer (25 mM HEPES pH 7, 500 mM NaCl and 5% glycerol) supplemented with 0, 10 and 20 mM imidazole, and eluted using wash buffer containing 250 mM imidazole. *Bc*NagZ crystals were grown at room temperature using the hanging drop vapour-diffusion method by mixing equal volumes of reservoir buffer (28-32% PEG8000, 0.1M MES pH 6.2-6.8) with protein solution (35-15 mg/ml). A single droplet containing several *Bc*NagZ crystals in reservoir buffer was soaked for 24 hours in MM-124 at a final concentration of 1 mM to obtain the protein-inhibitor complex. Prior to screening, crystals were cryo-protected in 30% PEG3500, 15% PEG8000 and 0.1M MES pH 6.6, and flash-cooled in liquid nitrogen. X-ray data were collected using a Rigaku R-AXIS IV++ detector and 007HF Microfocus X-ray generator at the University of Manitoba. The X-ray data were indexed using Mosflm[1], then scaled and averaged using SCALA.[2] The BcNagZ:**11** complex was determined by molecular replacement using PHASER (from within the PHENIX package[3]) and a structure of *Bc*NagZ (PDB ID: 4GNV) from which GlcNAc and solvent had been removed prior to use as the search model. The MR model was subsequently rebuilt using PHENIX.AUTOBUILD[3]. The ligand restraint file for **11** was generated using PHENIX eLBOW (Adams et al., 2010) and a model of the inhibitor was manually fit into its electron density. Subsequent refinement of the complex and addition of solvent was carried out using PHENIX.REFINE[3] and COOT[4]. Crystallographic and refinement statistics are presented in Table S1.

**Minimum inhibitory concentration assay (MIC):**

MICs were performed in triplicate using the broth microdilution method (Clinical and Laboratory Standards Institute) in a 96-well plate with appropriate serial dilutions of ceftazidime in 100 µl of cation-adjusted Mueller-Hinton broth (MHB). Addition of 50 µl MM-124 to a final concentration of 1 mM was followed by inoculation with 50 µl of ~$10^4$ cells of *P. aeruginosa* Δ*dacB* grown to an optical density ($OD_{600}$) of ~0.5. As a control, 50 µl of MHB was used in place of MM-124 in the above assay. MICs were determined after incubation of the cells for 18 h at 37 °C in a shaker incubator.

**TABLE S1:** Crystallographic and refinement statistic for *Bc*NagZ bound to **1**.

| **Data collection** | |
|---|---|
| **Space group** | P $2_1$ |
| **Cell dimensions** | |
| ***a, b, c* (Å)** | 48.76, 87.58, 67.21 |
| **α, β, γ (°)** | 90, 92.1, 90 |
| **Resolution (Å)** | 29.59-1.80 |
| $R_{merge}$ | 0.09 (0.55)* |
| **I / σI** | 9.3 (2.0) |
| **Completeness (%)** | 98.0 (96.2) |
| **Redundancy** | 3.2 (3.1) |
| **Refinement** | |
| $R_{work}$ / $R_{free}$ | 0.14/ 0.19 |
| **B-factor (Å²)** | |
| **Protein** | 19.4 |
| **MM-124 ligands** | 16.6 |
| **Water** | 31.0 |
| **R.m.s. deviations** | |
| **Bond lengths (Å)** | 0.01 |
| **Bond angles (°)** | 1.34 |

* Values in parentheses refer to the high-resolution shell (1.9 – 1.8 Å)

**Table S2:** Inhibition of *Salmonella typhyrium* NagZ, OGA, and HexA by azepanes **1**, **9-16**

| *Compound* | ***1*** | ***9*** | ***10*** | ***11*** | ***12*** | ***15*** | ***16*** |
|---|---|---|---|---|---|---|---|
| OGA $K_i$ (μM) | 0.7±0.1 | 2.2±0.2 | 47±3 | 190±20 | NI | 22±1 | 2.0±0.1 |
| NagZ $K_i$ (μM) | 0.4±0.2 | 0.4±0.2 | 7.4±0.5 | 27±2 | NI | NI | NI |
| HexA $K_i$ (μM) | *3.6*±0.9 | NI | NI | NI | NI | *51*±4 | *14*±3 |
| ($K_i$ OGA/$K_i$ NagZ) | 1.8 | 5.5 | 6.7 | 7.1 | NA | NA | NA |
| ($K_i$ HexA/$K_i$ NagZ) | 2.1 | + | + | + | NA | NA | NA |

NI: No significant inhibition at 500 μM, NA: not applicable, italic numbers $K_i$ by Dixon analysis, +: estimated to be at least >1000.

**Table S3:** Susceptibility of PAΔ*dacB* to CAZ in the presence or absence of 1 mM Azepane

| | CAZ MIC[a] (μg/ml) | | |
|---|---|---|---|
| Strain | - Azepane | + Azepane **1** | + Azepane **10** |
| PAΔ*dacB* | 24 | 12 | 8 |

[a] MICs were determined by the broth microdilution method using cation adjusted Mueller Hinton media according to CLSI guidelines.[5] Measurements were performed in triplicate.

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