SUPPLEMENTARY MATERIAL

Total Synthesis and Stereochemical Revision of (+)-Aeruginosin 298-A

Peter Wipf* and Joey-Lee Methot

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, U.S.A.

Experimental parts. ^{1}H and ^{13}C NMR spectra.

General: All reactions were performed in flame-dried or oven-dried glassware under a nitrogen atmosphere. THF and Et_2O were distilled over Na/benzophenone, while CH_2Cl_2, pyridine and diethylamine were distilled over CaH_2. Hexane and EtOAc were distilled prior to use. All other reagents and solvents were used as received unless otherwise noted. Analytical thin layer chromatography was performed on pre-coated silica gel 60 F-254 plates available from Merck. Flash chromatography was performed using silica gel 60 (230-400 mesh) available from Baker. NMR spectra were recorded in $CDCl_3$ (unless otherwise noted) at either 300 MHz (^{1}H NMR) or 75 MHz (^{13}C NMR) using Bruker Avance 300 with XWIN-NMR software. Chemical shifts (δ) are expressed relative to tetramethylsilane. IR spectra were obtained with a Nicolet Avatar 360 FT-IR, optical rotations were measured with a Perkin-Elmer 241 polarimeter, and mass spectra were obtained with a VG-70-70 HF.

(2*S*,7a*R*)-6-Oxo-2,3,5,6,7,7a-hexahydroindole-1,2-dicarboxylic Acid 1-benzyl ester 2-methyl ester (7). A solution of **4**[1] (1.36 g, 3.94 mmol) in 50 mL of CH_2Cl_2 and 3 mL of pyridine at -30 °C was treated with DMAP (48 mg, 0.39 mmol) and a solution of Ms_2O (1.37 g, 7.87 mmol) in 2 mL of CH_2Cl_2. The temperature was raised to 0 °C over 4 h, and the reaction mixture was stirred for an additional 12 h, washed with cold 10% HCl, ice-water, and dried (Na_2SO_4). Filtration and concentration provided the crude mesylate, which was redissolved in 50 mL of THF/AcOH (1:1). In a separate flask, a suspension of zinc[2] (2.58 g) in 5 mL of THF was treated with 50 µL of $BrCH_2CH_2Br$, and heated to reflux for 1 min. After cooling, 60 µL of TMSCl was added. After stirring for 15 min, the substrate solution was added and the mixture was stirred vigorously for 11 h, filtered, diluted with EtOAc, washed with excess water and saturated $NaHCO_3$, and dried ($MgSO_4$). Filtration, concentration and chromatography on SiO_2 (hexanes/EtOAc, 2:1) gave 1.22 g (94%) of **7**: R_f = 0.42 (EtOAc/hexanes, 1:1); $[\alpha]_D$ -100.5 (*c* 15.9, Et_2O); IR (neat) 3033, 3005, 2954, 2901, 2851, 1747, 1709, 1499, 1437, 1410, 1352, 1333, 1295, 1202, 1178, 1124, 1029, 1009, 973, 770, 755 cm^{-1}; ^{1}H NMR δ 7.31-7.28 (m, 5 H), 5.72 (br, 1 H), 5.18-4.93 (m, 2 H), 4.54 (br, 1 H), 4.49, 4.47 (2d, 1 H, *J* = 8.7, 6.3 Hz), 3.71, 3.44 (2s, 3 H), 3.58, 3.29 (2dd, 1 H, *J* = 15.5, 5.1 Hz), 3.0-2.65 (m, 4 H), 2.23, 2.18 (2d, 1 H, *J* = 11.0 Hz); ^{13}C NMR δ 207.9,

---

[1] (a) Wipf, P.; Kim, Y. *Tetrahedron Lett.* **1992**, *33*, 5477. (b) Wipf, P.; Kim, Y.; Goldstein, D.M. *J. Am. Chem. Soc.* **1995**, *117*, 11106.
[2] Knochel, P.; Yeh, M.C.P.; Berk, S.C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2392.

173.0, 172.7, 155.2, 154.5, 139.1, 138.4, 136.0, 128.7, 128.6, 128.4, 117.2, 117.1, 67.7, 67.3, 60.2, 59.9, 57.4, 56.5, 52.5, 52.3, 45.8, 45.0, 39.1, 38.9, 33.8, 33.4; MS (EI) *m/z* (rel intensity) 329 (M^+, 0.2), 287 (1), 270 (0.9), 243 (0.5), 226 (5), 194 (30), 184 (7), 91 (100), 65 (11); HRMS (EI) calculated for $C_{18}H_{19}NO_5$ 329.1263, found 329.1257.

(2*S*,3a*R*,7a*R*)-6-Oxo-2,3,3a,4,5,6,7,7a-octahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (8). A solution of **7** (73 mg, 0.22 mmol) in 2 mL of AcOH/EtOH (1:9) was treated with PtO_2 (5.0 mg, 0.022 mmol). The flask was evacuated and flushed with 1 atm of H_2 three times, then the mixture was stirred vigorously for 1 h at 0 °C under 1 atm of H_2. The suspension was diluted with EtOAc and was washed with water and saturated $NaHCO_3$, dried ($MgSO_4$), filtered through a plug of SiO_2 and concentrated, providing 68 mg (92%) of **8** with 25:1 facial selectivity[3]: R_f = 0.25 (EtOAc/hexanes, 1:1); $[\alpha]_D$ –37.6 (*c* 7.00, Et_2O); IR (neat) 2952, 2935, 1745, 1708, 1455, 1436, 1410, 1348, 1200, 1119 cm^{-1}; ^1H NMR (500 MHz, 380 K, DMSO-d_6) 7.37-7.29 (m, 5 H), 5.10, 5.05 (AB, 2 H, *J* = 12.6), 4.43 (dd, 1 H, *J* = 9.0, 1.4 Hz), 4.26 (td, 1 H, *J* = 8.8, 5.8 Hz), 3.61 (s, 3 H), 2.74-2.65 (m, 2 H), 2.53-2.5 (m, 1 H), 2.32-2.25 (m, 2 H), 2.21-2.15 (m, 1 H), 2.09-2.04 (m, 2 H), 1.79-1.72 (m, 1 H); ^{13}C NMR δ 210.3, 210.1, 173.1, 172.9, 154.8, 154.3, 136.3, 128.7, 128.5, 128.3, 128.1, 128.0, 67.5, 67.2, 59.6, 57.0, 56.4, 52.5, 52.3, 43.6, 42.5, 36.7, 35.0, 34.4, 34.0, 33.3, 24.1; MS (EI) m/z (rel intensity) 331 (M^+, 21), 305 (20), 272 (73), 262 (14), 228 (100), 224 (62), 196 (49), 143 (25), 98 (19), 91 (72); HRMS (EI) calculated for $C_{18}H_{21}NO_5$ 331.1420, found 331.1419.

(2*S*,3a*R*,6S,7a*R*)-6-Hydroxy-2,3,3a,4,5,6,7,7a-octahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (10). A solution of **8** (400 mg, 1.21 mmol) in 10 mL of THF was cooled to -78 °C and treated with a 1.0 M solution of L-selectride in THF (1.50 mL, 1.50 mmol). The mixture was stirred for 3 h and was quenched with 1 mL of 10% HCl before removing the cooling bath. The solution was diluted with water and extracted twice with 10 mL of EtOAc, then the combined organic layers were dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (EtOAc/hexanes, 1:1) gave 249 mg (62%) of **10**, along with the undesired diastereomer **9** (27 mg, 7%) and recovered **8** (113 mg, 28%): R_f = 0.13 (EtOAc/hexanes, 1:1); $[\alpha]_D$ –27.8 (*c* 0.41, CH_2Cl_2); IR (neat) 3434,

[3] Determined by integration of ^1H NMR methyl ester peaks.

2927, 2856, 1745, 1693, 1415, 1354, 1293, 1204, 1124 cm^{-1}; ^1H NMR δ 7.36-7.29 (m, 5 H), 5.29-4.94 (m, 2 H), 4.39-4.23 (m, 2 H), 4.03 (br, 1 H), 3.73, 3.52 (2s, 3 H), 2.6-2.4 (m, 1 H), 2.30-2.05 (m, 4 H), 1.86-1.79 (m, 1 H), 1.75-1.35 (m, 4 H); ^{13}C NMR δ 173.4, 173.2, 154.8, 154.0, 136.8, 136.5, 128.5, 128.4, 127.9 (2C), 67.0, 66.9, 65.9, 65.7, 58.6 (2C), 55.0, 53.7, 52.3, 52.1, 35.1, 34.7, 34.4, 34.0, 32.6, 31.2, 29.3, 27.8, 27.1, 20.6, 19.7; MS (EI) *m/z* (rel intensity) 333 (M^+, 6), 274 (68), 230 (95), 198 (45), 91 (100), 65 (17); HRMS (EI) calculated for $C_{18}H_{23}NO_5$ 333.1576, found 333.1579.

(2*R*,3a*R*,6*S*,7a*R*)-6-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,5,6,7,7a-octahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (D-3). A stirred solution of **10** (80 mg, 0.242 mmol) in 3 mL of CH_2Cl_2 was cooled to 0 °C and treated with pyridine (100 μL), and TBSOTf (100 μL, 0.435 mmol). After 4 h, the cooling bath was removed and stirring was continued for another 10 h. The mixture was poured into 10 mL of 10% HCl and extracted twice with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/EtOAc, 9:1) yielded 102 mg (94%) of the silylated alcohol: ^1H NMR δ 7.35-7.28 (m, 5 H), 5.20-5.03 (m, 2 H), 4.37, 4.34 (2d, 1 H, *J* = 9.2, 7.8 Hz), 4.3-4.2 (m, 1 H), 3.99 (br, 1 H), 3.74, 3.53 (2s, 3 H), 2.6-2.4 (m, 1 H), 2.3-2.1 (m, 3 H), 1.84-1.77 (m, 1 H), 1.5-1.3 (m, 3 H), 1.3-1.1 (m, 1H), 0.90, 0.84 (2s, 9 H), 0.10, 0.04, -0.02, -0.07 (4s, 6 H).

A solution of diethylamine (0.200 mL, 1.93 mmol) in THF (5 mL) at 0 °C was treated with 1.3 M BuLi/hexane (1.40 mL, 1.82 mmol) and stirred for 20 min. A portion of this solution (0.5 mL, ca. 0.142 mmol of $LiNEt_2$) was transferred to another flask and cooled to -78 °C. HMPA (0.1 mL) and a solution of the substrate (16 mg, 0.036 mmol) in THF (1 mL) were added and the mixture was stirred for 20 min before quenching with 0.1 mL of *t*-BuOH, followed immediately by saturated NH_4Cl. The mixture was extracted into Et_2O and the organic phase was washed with 10% HCl, saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (EtOAc/hexanes, 1:9) provided an inseparable mixture of diastereomers (11 mg, 69%, 12:1[4]): $[\alpha]_D$ +32.3 (*c* 0.49, CH_2Cl_2); Major diastereomer (**D-3**): ^1H NMR (500 MHz, DMSO-d_6,, 380 K) δ 7.36-7.29 (m, 5 H), 5.04 (s, 2 H), 4.29 (dd, 1 H, *J* = 8.7, 8.6 Hz), 4.14 (dt, 1 H, *J* = 10.5, 6.4 Hz), 4.09 (m, 1 H), 3.62 (s, 3 H), 2.38-2.31 (m, 1 H), 2.20 (dt, 1 H, *J* = 12.3, 7.6 Hz), 2.07-

[4] Determined by integration of ^1H NMR methyl ester peaks.

1.98 (m, 2 H), 1.90 (td, 1 H, *J* = 12.3, 9.3 Hz), 1.62 (ddd, 1 H, *J* = 13.3, 10.6, 2.3 Hz), 1.6-1.4 (m, 3 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR δ 174.1, 173.9, 154.8, 136.7, 128.7, 128.1, 127.9, 67.2, 67.0, 66.7, 59.4, 54.9, 54.4, 52.5, 52.3, 36.8, 36.2, 34.5, 34.0, 32.8, 31.8, 27.6, 27.4, 26.0, 25.9, 19.6, 18.2, -4.8, -4.9.

(2*S*,3a*R*,7a*R*)-3a-(Benzoyloxy)-6-oxo-2,3,3a,6,7,7a-hexahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (11).[1b] A solution of **4** (6.72 g, 19.5 mmol) in 20 mL of CH_2Cl_2 and 8.00 mL of pyridine (98.9 mmol) were treated with Bz_2O (7.50 g, 32.9 mmol) and DMAP (250 mg, 2.05 mmol), and stirred at 40 °C for 50 h. Upon cooling the mixture was diluted with CH_2Cl_2 and washed with 10% HCl, saturated $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. Chromatography on SiO_2 (EtOAc/hexanes, 1:9 to 2:3) gave 7.87 g (90%) of **11** as a colorless foam: R_f = 0.25 (hexanes/ether, 1:3); ^{1}H NMR (500 MHz, 373 K, DMSO-d_6) δ 7.88 (d, 2 H, *J* = 8.1 Hz), 7.66 (t, 1 H, *J* = 7.5 Hz), 7.52 (dd, 2 H, *J* = 7.9, 7.7 Hz), 7.35-7.30 (m, 5 H), 7.11 (d, 1 H, *J* = 10.5 Hz), 6.07 (d, 1 H, *J* = 10.3 Hz), 5.15-5.05 (m, 2 H), 4.94 (dd, 1 H, *J* = 10.1, 7.4 Hz), 4.71 (dd, 1 H, *J* = 9.1, 2.4 Hz) 3.50 (s, 3 H), 3.1-2.9 (m, 3 H), 2.76 (dd, 1 H, *J* = 16.4, 10.0 Hz).

(2*S*,3a*S*,7a*S*)-3a-(Benzoyloxy)-6-oxo-2,3,3a,6,7,7a-hexahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (12). A solution of **11** (1.51 g, 3.36 mmol) and $NaHCO_3$ (280 mg, 3.33 mmol) in DMSO (10 mL) was stirred at 90 °C for 1 h. The suspension was cooled, diluted with EtOAc, washed with 10% HCl, 2 N NaOH, and water, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (ether/hexanes, 1:1) provided 863 mg of **12** and 556 mg of **11**. The recovered starting **11** was resubjected to the same reaction and work-up conditions to provide an additional 314 mg of **12** and 189 mg of recovered **11**. A total of 1.18 g (78%) of **12** was isolated as a white foam: R_f = 0.33 (hexanes/ether, 1:3); $[\alpha]_D$ +74.7 (*c* 1.50, CH_2Cl_2); IR (neat) 3063, 3032, 2954, 2913, 1749, 1713, 1452, 1414 cm^{-1}; ^{1}H NMR (500 MHz, 363 K, DMSO-d_6) δ 7.95 (d, 2 H, *J* = 7.8 Hz), 7.67 (t, 1 H, *J* = 7.4 Hz), 7.52 (t, 2 H, *J* = 7.8 Hz), 7.28-7.23 (m, 5 H), 7.14 (d, 1 H, *J* = 10.4 Hz), 6.05 (d, 1 H, *J* = 10.5 Hz), 5.10, 5.06 (AB, 2 H, *J* = 12.7 Hz), 4.95 (dd, 1 H, *J* = 9.2, 6.9 Hz), 4.69 (t, 1 H, *J* = 8.5 Hz) 3.65 (s, 3 H), 3.2-3.1 (m, 1 H), 3.0-2.82 (m**,** 2 H), 2.61 (dd, 1 H, *J* = 14.1, 8.9 Hz); ^{13}C NMR δ 195.2, 172.1, 172.0, 165.4, 154.3, 153.6, 144.9, 144.5, 135.9, 133.9, 129.9, 129.8, 129.4, 129.3, 128.7, 128.6, 128.5, 128.3, 127.9, 127.8, 84.1, 83.3,

67.7, 62.5, 61.9, 59.1, 58.8, 52.8, 52.6, 42.6, 41.8, 40.0, 39.3, 31.0; MS (EI) 327 ($[M-C_7H_6O_2]^+$, 3), 283 (8), 224 (10), 105 (19), 91 (100), 77 (14); HRMS (EI) calculated for $C_{18}H_{17}NO_5$ [M-$C_7H_6O_2$] 327.1107, found 327.1104.

(2*S*,7a*S*)-6-Oxo-2,3,5,6,7,7a-hexahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (13).

By reduction with Zn: A suspension of zinc dust (930 mg, 14.2 mmol) in 2 mL of THF was treated with $BrCH_2CH_2Br$ (20 μL) and heated at reflux for 1 min. After cooling to room temperature, the suspension was treated with TMSCl (25 μL) vigorously stirred for 15 min. Finally, a solution of **12** (640 mg, 1.42 mmol) in THF/AcOH (1:1, 20 mL) was added and the reaction mixture was stirred at 65 °C for 9 h, filtered, diluted with Et_2O, washed with water and saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (EtOAc/hexanes, 1:2) provided 351 mg (75%) of enone **13**.

By reduction with SmI_2: A flame-dried flask was charged with Sm powder (2.06 g, 13.7 mmol) and the metal was covered with THF. Dropwise addition of CH_2I_2 (1.00 mL, 12.4 mmol) was accompanied by color changes from green to brown, then to blue, after which 120 mL of THF was added. After stirring at room temperature for 1 h, the mixture was warmed to reflux and a solution of **12** (2.187 g, 4.866 mmol) in THF/AcOH (1:1, 10 mL) was added dropwise. The reaction mixture was immediately placed over ice and diluted with EtOAc, washed with 10% HCl, 2 N NaOH, and water, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (ether/hexanes, 3:7 to 1:1) provided 1.01 g (63%) of enone **13**: ^{1}H NMR δ 7.35-7.31 (m, 5 H), 5.78 (br, 1 H), 5.25-5.11 (m, 2 H), 4.75, 4.67 (2d, 1 H, *J* = 9.6, 9.7 Hz), 4.6-4.4 (m, 1 H), 3.73, 3.68 (2s, 3 H), 3.45, 3.22 (2dd, 1 H, *J* = 15.1, 5.0 Hz and *J'* = 15.2, 5.1 Hz), 3.1-2.5 (m, 5 H).

(2*S*,3a*S*,7a*S*)-6-Oxo-2,3,3a,4,5,6,7,7a-octahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (14). A solution of **13** (622 mg, 1.89 mmol) in 10 mL of AcOH/EtOH (1:9) was treated with 9.1 mg (0.040 mmol) of PtO_2. The flask was evacuated and flushed with 1 atm of H_2 several times, then the mixture was stirred vigorously for 1 h at 0 °C under 1 atm of H_2. EtOAc was added and the solution was washed with water and saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated, providing 594 mg (95%) of **14** with >98:2 facial selectivity (^{1}H NMR): R_f = 0.30 (EtOAc/hexanes, 1:1); $[\alpha]_D$ +18.1 (*c* 1.15, CH_2Cl_2); IR (neat) 3063, 3034, 2958, 2928, 1740, 1709, 1692, 1453, 1420 cm^{-1}; ^{1}H NMR

(500 MHz, 360 K, DMSO-d_6) δ 7.37-7.29 (m, 5 H), 5.08, 5.06 (AB, 2 H, *J* = 12.7 Hz), 4.39 (t, 1 H, *J* = 8.3 Hz), 4.27-4.22 (m, 1 H), 3.63 (s, 3 H), 2.68-2.57 (m, 3 H), 2.50-2.44 (m, 1 H), 2.39-2.33 (m, 1 H), 2.14-2.08 (m, 1 H), 2.01-1.95 (m, 2 H), 1.85-1.78 (m, 1 H); ^{13}C NMR δ 209.7, 173.4, 154.2, 153.7, 136.3, 128.6, 128.1, 127.9, 67.4, 67.2, 59.8, 59.5, 58.0, 57.6, 52.5, 52.4, 43.8, 43.0, 36.6, 35.7, 34.3, 33.1, 24.4; MS (EI) 331 (M^+, 10), 272 (16), 228 (52), 196 (7), 138 (5), 91 (100); HRMS (EI) calculated for $C_{18}H_{21}NO_5$ 331.1420, found 331.1414.

(2*S*,3a*S*,6*R*,7a*S*)-6-Hydroxy-2,3,3a,4,5,6,7,7a-octahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (16). A solution of **14** (612 mg, 1.85 mmol) in THF (5 mL) at -78 °C was treated dropwise with 1.0 M L-selectride/THF (2.00 mL, 2.00 mmol) over a 2 h period. After stirring for an additional 1 h, the reaction mixture was quenched with AcOH and warmed to ambient temperature. The mixture was poured into EtOAc and washed with 10% HCl, 2 N NaOH, brine, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (EtOAc/hexanes, 1:1) provided 110 mg (18%) of **15** and 419 mg (68%) of **16**: R_f = 0.11 (EtOAc/hexanes, 1:1); $[\alpha]_D$ -23.1 (*c* 0.620, CH_2Cl_2); ^{1}H NMR (373 K, DMSO-d_6) δ 7.38-7.28 (m, 5 H), 5.07, 5.05 (AB, 2 H, *J* = 13.1 Hz), 4.29 (t, 1 H, *J* = 8.6 Hz), 4.14 (dt, 1 H, *J* = 10.4, 6.4 Hz) 3.93-3.88 (m, 1 H), 3.61 (s, 3 H), 2.35-2.26 (m, 1 H), 2.23-2.14 (m, 1 H), 2.1-1.95 (m, 2 H), 1.89 (td, 1 H, *J* = 12.1, 9.2 Hz), 1.61 (ddd, 1 H, *J* = 13.5, 10.5, 2.7 Hz), 1.53-1.35 (m, 4 H); ^{13}C NMR δ 173.9, 154.9, 154.1, 137.0, 136.7, 128.6, 128.1, 128.0, 67.1, 66.2, 66.0, 59.5, 59.3, 54.6, 54.0, 52.5, 52.3, 36.7, 36.1, 33.9, 33.6, 32.8, 31.7, 26.6, 19.7, 19.6; MS (EI) 333 (M^+, 6), 274 (17), 230 (28), 149 (14), 140 (25), 91 (100); HRMS (EI) calculated for $C_{18}H_{23}NO_5$ 333.1576, found 333.1585.

Minor diastereomer **15**: R_f = 0.06 (EtOAc/hexanes, 1:1; ^{1}H NMR (373 K, DMSO-d_6) 7.36-7.29 (m, 5 H), 5.06 (s, 2 H), 4.29 (dd, 1 H, *J* = 9.6, 7.9 Hz), 3.92 (dt, 1 H, *J* = 11.3, 6.4 Hz), 3.62 (s, 3 H), 3.36 (tt, 1 H, *J* = 11.5, 3.7 Hz), 2.3-2.2 (m, 1 H), 2.2-2.1 (m, 2 H), 1.90 (td, 1 H, *J* = 12.5, 9.8 Hz), 1.7-1.6 (m, 4 H), 1.36 (q, 1 H, *J* = 11.8 Hz), 1.3-1.2 (m, 1 H).

(2*S*,3a*S*,6*R*,7a*S*)-6-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,5,6,7,7a-octahydroindole-1,2-dicarboxylic acid 1-benzyl ester 2-methyl ester (L-3). A solution of **16** (254 mg, 0.763 mmol) in 4 mL of CH_2Cl_2 was cooled to 0 °C and treated with imidazole (162 mg, 2.38 mmol) followed by TBSOTf (350 μL, 1.52 mmol). After stirring for 16 h at room temperature, the mixture was diluted with

EtOAc, washed with 10% HCl and saturated $NaHCO_3$ dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/ether, 9:1) provided 297 mg (87%) of **L-3**: R_f = 0.83 (EtOAc/hexanes, 1:1); $[\alpha]_D$ -42 (*c* 0.42, CH_2Cl_2); IR (neat) 2952, 2930, 2890, 2860, 1761, 1708, 1462, 1416, 1355 cm^{-1}; ^1H NMR (500 MHz, 373 K, DMSO-d_6) δ 7.36-7.28 (m, 5 H), 5.04 (s, 2 H), 4.28 (dd, 1 H, *J* = 9.2, 8.2 Hz), 4.12 (dt, 1 H, *J* = 10.7, 6.3 Hz), 4.08 (br, 1 H), 3.62 (s, 3 H), 2.38-2.31 (m, 1 H), 2.19 (dt, 1 H, *J* = 12.4, 7.5, Hz), 2.06-1.98 (m, 2 H), 1.89 (td, 1 H, *J* = 12.4, 9.5 Hz), 1.60 (ddd, 1 H, *J* = 13.2, 10.7, 2.2 Hz), 1.6-1.4 (m, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR δ 173.8, 173.6, 154.5, 153.7, 136.6, 128.4, 128.1, 127.9, 127.7, 67.0, 66.8, 66.6, 59.2, 59.1, 54.7, 54.2, 52.2, 52.0, 36.6, 36.0, 34.4, 33.8, 32.7, 31.7, 27.4, 27.3, 25.9, 25.8, 19.5, 18.0, -4.8, -5.0; MS (EI) 432 ($[M-CH_3]^+$, 0.3), 390 (27), 346 (20), 270 (3), 196 (4), 120 (6), 91 (100); HRMS (EI) calculated for $C_{23}H_{34}NO_5Si$ [M-CH_3] 432.2206, found 432.2192.

Alloc-Argol(Cbz)-OH (17). A solution of L-Arg•HCl (10.0 g, 47.4 mmol) and NaOH (4.70 g, 143 mmol) in 100 mL of water at 0 °C was treated dropwise with allyl chloroformate (5.00 mL, 47.1 mmol) over 3 h. After stirring overnight, the reaction mixture was neutralized to pH 4 with 10% HCl and concentrated to ca. 25 mL. The suspension was filtered, washed with cold water and air-dried to provide 9.66 g (79%) of Alloc-L-Arg-OH: ^1H NMR (DMSO-d_6) δ 9.07 (br, 1 H), 8.0-7.3 (br, 4 H), 6.57 (d, 1 H, *J* = 7.3 Hz), 5.92-5.79 (m, 1 H), 5.23 (d, 1 H, *J* = 17.1 Hz), 5.11 (d, 1 H, *J* = 10.5 Hz), 4.39 (d, 2 H, *J* = 4.6 Hz), 3.70-3.60 (m, 1 H), 3.05-2.95 (br, 2 H), 1.75-1.25 (m, 4 H).

A solution of Alloc-L-Arg-OH (8.80 g, 34.1 mmol) and NaOH (2.75 g, 68.8 mmol) in 35 mL of water and 10 mL of THF was treated simultaneously in a dropwise fashion with 5.00 mL (35.0 mmol) of benzyl chloroformate and a solution of NaOH (4.10 g, 103 mmol) in 5 mL of H_2O. After 12 h, the solution was washed with EtOAc, acidified with 10% HCl to pH 4, and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$), filtered and concentrated to give 8.42 g (63%) of the acid as a white foam: ^1H NMR (DMSO-d_6) δ 8.23 (br, 1 H), 7.46 (d, 1 H, *J* = 7.7 Hz), 7.35-7.2 (m, 5 H), 7.15-7.11 (m, 1 H), 6.57 (br, 1 H), 5.93-5.80 (m, 1 H), 5.25 (d, 1 H, *J* = 17.1 Hz), 5.13 (d, 1 H, *J* = 10.5 Hz), 4.94 (s, 2 H), 4.43 (d, 2 H, *J* = 5.0 Hz), 3.90-3.80 (m, 1 H), 3.06 (br, 2 H), 1.75-1.6 (m, 1 H), 1.6-1.4 (m, 3 H).

A solution of Alloc-L-Arg(Cbz)-OH (2.277 g, 5.80 mmol) and NMM (700 μL, 6.31 mmol) in DMF (10 mL) at -20 °C was treated with isobutyl chloroformate (800 μL, 5.88 mmol), stirred for 1 min, and treated with a solution of $NaBH_4$ (779

mg, 20.6 mmol) in water (5 mL). The mixture was slowly warmed to room temperature, diluted with EtOAc, washed with 10% HCl, 2 N NaOH, dried ($MgSO_4$), filtered, and concentrated to give **17** as a colorless oil (1.577 g, 72%): $[\alpha]_D$ -6.31 (*c* 0.745, EtOAc); IR (neat) 3388, 3320, 3089, 3061, 3033, 2945, 2876, 1699, 1632, 1596, 1539 cm^{-1}; ^1H NMR δ 7.34-7.22 (m, 5 H), 7.16 (d, 1 H, *J* = 7.5 Hz), 5.90-5.79 (m, 1 H), 5.59 (br d, 1 H, *J* = 5.7 Hz), 5.25 (d, 1 H, *J* = 17.1 Hz), 5.17 (d, 1 H, *J* = 10.4 Hz), 5.04 (s, 2 H), 4.55-4.40 (m, 2 H), 3.6-3.4 (m, 3 H), 3.09 (br, 1 H), 2.96 (br, 1 H), 1.45 (br, 2 H), 1.30 (br, 2 H); ^{13}C NMR δ 163.4, 161.6, 157.2, 137.3, 132.8, 128.6, 128.4, 128.1, 117.9, 66.4, 65.8, 64.6, 52.1, 40.7, 28.8, 25.4.

NH_2-Argol(Cbz_2)-OTBS (18). A solution of alcohol **17** (238 mg, 0.630 mmol) in CH_2Cl_2 (5 mL) was treated with imidazole (130 mg, 1.91 mmol) and TBSOTf (450 μL, 1.96 mmol), stirred for 9 h, and diluted with EtOAc, washed with 10% HCl, 2 N NaOH, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (EtOAc) provided 251 mg (81%) of the silyl ether as a colorless oil: R_f = 0.54 (MeOH/EtOAc, 1:9); $[\alpha]_D$ -12.9 (*c* 0.665, EtOAc); IR (neat) 3401, 3317, 3089, 3062, 3032, 2953, 2930, 2857, 1704, 1634, 1594, 1538, 1510 cm^{-1}; ^1H NMR δ 7.35-7.21 (m, 5 H), 5.93-5.82 (m, 1 H), 5.28 (dd, 1 H, *J* = 17.4, 1.4 Hz), 5.20 (dd, 1 H, *J* = 10.5, 0.8 Hz), 5.04 (s, 2 H), 4.51 (d, 2 H, *J* = 5.5 Hz), 3.65-3.5 (m, 2 H), 3.45 (d, 1 H, *J* = 6.8 Hz), 3.25-3.15 (m, 1 H), 2.94 (br, 1 H), 1.55-1.35 (br, 3 H), 1.15-1.05 (br, 1 H), 0.88 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR δ 163.6, 161.8, 156.9, 137.7, 132.8, 128.4, 128.0, 127.7, 117.9, 66.1, 65.8, 65.6, 50.9, 40.4, 29.5, 26.0, 25.3, 18.4, -5.4; FABMS ($[M+H]^+$, 100), 449 (10), 385 (30), 359 (70); HRMS (FAB) calculated for $C_{24}H_{41}N_4O_5Si$ (M+H) 493.2846, found 493.2854.

A solution of this silyl ether (147 mg, 0.298 mmol) in 5 mL of DMF was treated with K_2CO_3 (208 mg, 1.51 mmol), DMAP (1.9 mg, 0.016 mmol), and finally in a dropwise fashion, benzyl chloroformate (100 μL, 0.700 mmol). The mixture was stirred for 21 h and partitioned between ether and 10% HCl. The organic layer was washed with saturated $NaHCO_3$, dried ($MgSO_4$), and filtered. Concentration followed by chromatography on SiO_2 (EtOAc/hexanes, 1:9-3:7) gave 161 mg (86%) of the bis-protected compound: R_f = 0.46 (EtOAc/hexanes, 3:7); ^1H NMR δ 11.76 (s, 1 H), 8.35 (br, 1 H), 7.41-7.30 (m, 10 H), 5.97-5.86 (m, 1 H), 5.30 (d, 1 H, *J* = 17.2 Hz), 5.21 (d, 1 H, *J* = 10.4 Hz), 5.17 (s, 2 H), 5.13 (s, 2 H), 5.02 (d, 1 H, *J* = 8.8 Hz), 4.56 (d, 2 H, *J* = 4.9 Hz), 3.7-3.6 (br m, 1 H), 3.60 (br m, 2 H), 3.5-3.4 (m, 2 H), 1.7-1.5 (m, 4 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR δ 163.9,

156.2, 156.1, 154.0, 137.0, 134.8, 133.2, 129.0, 128.9, 128.6 (2C), 128.3, 128.1, 117.8, 68.3, 67.3, 65.6, 64.9, 52.3, 41.1, 29.1, 26.0, 18.4, -5.3.

A solution of this tetraprotected arginine derivative (249 mg, 0.397 mmol) in CH_2Cl_2 (5 mL) was treated at 0 °C with AcOH (50 μL, 0.87 mmol) and $Pd(PPh_3)_4$ (23 mg, 0.020 mmol). The flask was evacuated and purged with nitrogen 3 times, then treated with Bu_3SnH (170 μL, 0.632 mmol). After stirring for 1 h, the solution was partitioned between Et_2O and saturated $NaHCO_3$, the Et_2O layer was dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (MeOH/EtOAc, 0% to 10%) provided 190 mg (88%) of the desired oily **18**: R_f = 0.44 (MeOH/EtOAc, 1:9); ^{1}H NMR δ 8.39 (br, 1 H), 7.41-7.29 (m, 10 H), 5.18 (s, 2 H), 5.14-5.12 (m, 2 H), 3.55 (dd, 1 H, *J* = 9.7, 4.1 Hz), 3.5-3.4 (m, 2 H), 3.34 (dd, 1 H, *J* = 9.7, 7.2 Hz), 2.85-2.75 (m, 1 H), 1.75-1.6 (m, 2 H), 1.5-1.4 (m, 2 H), 0.90 (s, 9 H), 0.06 (s, 6 H).

(*R*)-(-)-Benzylglycidol[5]. A solution of *S*-(-)-glycidol (1.00 mL, 15.1 mmol), *n*Bu_4NI (230 mg, 0.623 mmol), and BnBr (1.50 mL, 12.6 mmol) in DMF (30 mL) was treated at 0 °C with 700 mg (17.5 mmol) of a 60% suspension of NaH in mineral oil. After 1 h the mixture was warmed to room temperature and stirred for another 13 h, poured into Et_2O, washed with 10% HCl, saturated $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. Chromatography on SiO_2 (ether/hexanes, 1:4) gave 997 mg (48%) of (*R*)-(-)-benzylglycidol: ^{1}H NMR δ 7.43-7.29 (m, 5 H), 4.63, 4.58 (AB, 2 H, *J* = 11.9 Hz), 3.79 (dd, 1 H, *J* = 11.4, 3.0 Hz), 3.46 (dd, 1 H, *J* = 11.3, 5.8 Hz), 3.24-3.18 (m, 1 H), 2.82 (dd, 1 H, *J* = 4.8, 4.4 Hz), 2.64 (dd, 1 H, *J* = 4.9, 2.7 Hz).

1-Benzyloxy-3-(4-triisopropylsilanyloxy-phenyl)-propan-2-(*R*)-ol (19). A solution of 4-bromophenol (1.33 g, 7.69 mmol), imidazole (1.30 g, 19.1 mmol), and TIPSCl (1.76 g, 9.13 mmol) in THF (25 mL) was stirred at room temperature for 36 h. The suspension was poured into EtOAc and washed with 10% HCl, saturated $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. Chromatography on SiO_2 (ether/hexanes, 1:19) provided 2.22 g (88%) of the silyl ether: ^{1}H NMR δ 7.31 (d, 2 H, *J* = 8.6 Hz), 6.77 (d, 2 H, *J* = 8.6 Hz), 1.30-1.18 (m, 3 H), 1.10 (d, 18 H, *J* = 7.0 Hz).

A solution of *O*-(triisopropylsilyl)-4-bromophenol (1.91 g, 5.79 mmol) in THF (10 mL) was treated dropwise at -78 °C with 1.7 M *t*-BuLi in pentane (3.40 mL, 5.78 mmol). After 10 min, $CuBr \bullet SMe_2$ (595 mg, 2.89 mmol) was added and the

[5] Chong, J. M.; Sokoll, K. K. *Org. Prep. Proced. Int.*; **1993**, 25, 639.

suspension was warmed to -45 °C. When the solution became homogeneous, (*R*)-(-)-benzylglycidol (241 mg, 1.47 mmol in 1 mL of THF) and $BF_3 \bullet OEt_2$ (10 μL, 0.079 mmol) were added. The reaction was slowly warmed to -20 °C over 3 h, then poured into Et_2O, washed with 10% HCl and saturated $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. Chromatography on SiO_2 (EtOAc/hexanes, 1:9 to 3:7) gave 504 mg (83%) of adduct **19**: R_f = 0.40 (hexanes/ether, 1:1); $[\alpha]_D$ -8.50 (*c* 1.07, CH_2Cl_2); IR (neat) 3437, 2944, 2894, 2866, 1657, 1651, 1644, 1611, 1510 cm^{-1}; ^1H NMR δ 7.41-7.32 (m, 5 H), 7.07 (d, 2 H, *J* = 8.3 Hz), 6.84 (d, 2 H, *J* = 8.3 Hz), 4.56 (s, 2 H), 4.07-3.99 (m, 1 H), 3.51, 3.40 (AB of ABX, 2 H, J_{AB} = 9.4, J_{AX} = 3.3, J_{BX} = 7.0 Hz), 2.79, 2.75 (AB of ABX, 2 H, J_{AB} = 13.7, J_{AX} = 6.9, J_{BX} = 6.5 Hz), 2.38 (br, 1 H), 1.34-1.21 (m, 3 H), 1.13 (d, 18 H, *J* = 7.0 Hz); ^{13}C NMR δ 154.7, 138.1, 130.3, 128.5, 127.9, 119.9, 73.5, 73.4, 71.6, 39.2, 18.0, 12.7; MS (EI) 414 (M^+, 20), 371 (16), 311 (12), 283 (9), 263 (9), 221 (9), 164 (10), 107 (12), 91 (100); HRMS (EI) calculated for $C_{25}H_{38}O_3Si$ 414.2590, found 414.2576.

2-(*R*)-(*tert*-Butyldimethylsilanoxy)-3-(4-triisopropylsilanyloxy-phenyl)-propan-1-ol (20). A solution of **19** (297 mg, 0.717 mmol), imidazole (241 mg, 3.54 mmol), and TBSOTf (0.330 mL, 1.437 mmol) in CH_2Cl_2 (2 mL) was stirred at room temperature for 11 h. The mixture was diluted with EtOAc, washed with 10% HCl and 2 N NaOH, dried ($MgSO_4$), filtered and concentrated. A solution of the resulting oil in EtOAc (10 mL) was treated with 10% Pd/C (77 mg, 0.0726 mmol), placed under vacuum and flushed with H_2. The reaction mixture was shaken in a Parr hydrogenator for 50 h under 3 atm of H_2. Filtration and concentration gave an oil which was chromatographed on SiO_2 (ether/hexanes, 1:4) to provide primary alcohol **20** (289 mg, 92%): ^1H NMR δ 7.02 (d, 2 H, *J* = 8.3 Hz), 6.80 (d, 2 H, *J* = 8.3 Hz), 3.90-3.85 (m, 1 H), 3.53, 3.45 (AB of ABX, 2 H, J_{AB} = 11.0, J_{AX} = 3.5, J_{BX} = 4.3 Hz), 2.73 (d, 1 H, *J* = 6.8 Hz), 1.91 (br, 1 H), 1.3-1.2 (m, 3 H), 1.10 (d, 18 H, *J* = 6.9 Hz), 0.89 (s, 9 H), 0.22 (s, 3 H), -0.09 (s, 3 H).

2-(*R*)-(*tert*-Butyldimethylsilanoxy)-3-(4-triisopropylsilanyloxy-phenyl)-propionic acid (21). A solution of **21** (144 mg, 0.328 mmol) and the Dess-Martin periodinone[6] (208 mg, 0.491 mmol) in CH_2Cl_2 (3 mL) was stirred at 0 °C for 45 min. The mixture was quenched with saturated $Na_2S_2O_3$ solution, stirred

[6] Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277. Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

for 10 min, and diluted with 5 mL of Et_2O. The organic layer was washed with 10% HCl, 2 N NaOH, brine, dried ($MgSO_4$), and concentrated to give a colorless oil. Chromatography on SiO_2 (ether/hexanes, 1:9) gave 120 mg (84%) of aldehyde: R_f = 0.40 (hexanes/ether, 4:1); $[\alpha]_D$ +44.9 (*c* 0.305, CH_2Cl_2); IR (neat) 3419, 2948, 2865, 1738, 1642, 1610, 1511 cm^{-1}; ^1H NMR δ 9.65 (s, 1 H), 7.06 (d, 2 H, *J* = 8.3 Hz), 6.82 (d, 2 H, *J* = 8.3 Hz), 4.09 (dd, 1 H, *J* = 9.2, 3.6 Hz), 2.93, 2.71 (AB of ABX, 2 H, J_{AB} = 13.7, J_{AX} = 3.7, J_{BX} = 9.2 Hz), 1.31-1.19 (m, 3 H), 1.11 (d, 18 H, *J* = 7.0 Hz), 0.85 (s, 9 H), -0.10 (s, 3 H), -0.21 (s, 3 H); ^{13}C NMR δ 203.9, 155.0, 130.8, 129.2, 119.8, 79.3, 38.4, 25.8, 18.0, 12.7, -5.0, -5.2; MS (CI) 437 (M^+, 13), 419 (3), 379 (5), 305 (5), 263 (18).

A solution of this aldehyde (82 mg, 0.188 mmol) in 2 mL of *t*-BuOH/water (1:1) was treated at 0 °C with 2-methyl-2-butene (1 mL), $NaH_2PO_4 \bullet H_2O$ (161 mg, 1.78 mmol), and $NaClO_2$ (172 mg, 1.24 mmol). The mixture was stirred for 1 h, quenched with 1 mL of saturated $Na_2S_2O_3$, and diluted with 3 mL of EtOAc. The organic layer was washed with 10% HCl, water, dried ($MgSO_4$), filtered and concentrated to give 79 mg (93%) of acid **21**: ^1H NMR δ 7.07 (d, 2 H, *J* = 8.3 Hz), 6.82 (d, 2 H, *J* = 8.3 Hz), 4.36 (dd, 1 H, *J* = 8.5, 3.4 Hz), 3.07, 2.87 (AB of ABX, 2 H, J_{AB} = 13.7, J_{AX} = 3.3, J_{BX} = 8.6 Hz), 1.32-1.19 (m, 3 H), 1.11 (d, 18 H, *J* = 6.9 Hz), 0.85 (s, 9 H), -0.07 (s, 3 H), -0.15 (s, 3 H).

D-Hpla(TIPS,TBS)-L-Leu-OH (L^{Leu}-22). A solution of **21** (168 mg, 0.371 mmol) in 5 mL of CH_2Cl_2 was treated with *i*Pr_2NEt (400 µL, 2.30 mmol), cooled to –30 °C, and then diethyl cyanophospinate (100 µL, 0.659 mmol) was added. The reaction was warmed to –20 °C over a 20 min period, a solution of $HCl \bullet NH_2$-L-Leu-OBn[7] (282 mg, 1.09 mmol) in 1 mL of CH_2Cl_2 was added and stirring was continued for another 2 h. The solution was partitioned between Et_2O and 10% HCl, and the organic layer was washed with 2 N NaOH, water, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/EtOAc, 9:1) provided 178 mg (73%) of the desired oily benzyl ester: R_f = 0.22 (hexanes/EtOAc, 9:1); $[\alpha]_D$ +33.4 (*c* 1.35, CH_2Cl_2); ^1H NMR δ 7.4-7.3 (m, 5 H), 7.05 (d, 2 H, *J* = 8.4 Hz), 6.96 (d, 1 H, *J* = 8.6 Hz), 6.79 (d, 2 H, *J* = 8.5 Hz), 5.16 (s, 2 H), 4.67 (td, 1 H, *J* = 8.7, 4.8 Hz), 4.22 (dd, 1 H, *J* = 9.1, 2.8 Hz), 3.07 (dd, 1 H, *J* = 13.7, 2.6 Hz), 2.69 (dd, 1 H, 13.7, 9.1 Hz), 1.7-1.5 (m, 3 H), 1.31-1.21 (m, 3 H), 1.11 (d, 18 H, *J* = 6.9 Hz), 0.96 (d, 3 H, *J* = 5.8 Hz), 0.92 (d, 3 H, *J* = 6.0 Hz), 0.86 (s, 9 H), -0.14 (s, 3 H), -

[7] Wakamiya, T.; Kamata, M.; Kusumoto, S.; Kobayashi, H.; Sai, Y. *Bull. Soc. Chem. Jpn.* **1998**, *71*, 699.

0.35 (s, 3 H); ^{13}C NMR δ 173.3, 172.3, 154.8, 135.4, 131.1, 130.0, 128.6, 128.4, 128.3, 119.6, 75.3, 67.1, 50.4, 42.0, 41.2, 25.7, 24.9, 22.8, 21.8, 18.0, 12.7, -5.4, -5.6; MS (EI) 656 (M^+, 4), 640 (4), 598 (73), 523 (45), 508 (65), 303 (65), 263 (100); HRMS (EI) calculated for $C_{33}H_{52}NO_5Si$ (M-C_4H_8) 598.3384, found 598.3386.

A solution of D-Hpla(TIPS,TBS)-L-Leu-OBn (120 mg, 0.183 mmol) in EtOH (2 mL) was treated with 10% Pd/C (19 mg), placed under vacuum and purged with H_2 several times. The reaction mixture was vigorously stirred under a H_2 atmosphere for 2 h. The suspension was filtered and concentrated to give 96.1 mg (93%) of D-Hpla(TIPS,TBS)-L-Leu-OH (**L^{Leu}-22**): ^{1}H NMR δ 7.05 (d, 2 H, *J* = 8.4 Hz), 6.89 (d, 1 H, *J* = 6.9 Hz), 6.80 (d, 2 H, *J* = 8.5 Hz), 4.55 (td, 1 H, *J* = 9.0, 5.0 Hz), 4.25 (dd, 1 H, *J* = 8.7, 3.0 Hz), 3.08 (dd, 1 H, *J* = 13.7, 2.8 Hz), 2.74 (dd, 1 H, *J* = 13.7, 8.8 Hz), 1.6-1.8 (m, 2 H), 1.6-1.5 (m, 1 H), 1.29-1.18 (m, 3 H), 1.10 (d, 18 H, *J* = 7.0 Hz), 0.97 (d, 3 H, *J* = 6.3 Hz), 0.96 (d, 3 H, *J* = 6.3 Hz), 0.87 (s, 9 H), -0.12 (s, 6 H), -0.32 (s, 6 H).

Alloc-Choi(TBS)-Argol(Cbz$_2$)-OTBS (23). A solution of **L-3** (397 mg, 0.884 mmol) in 10 mL of EtOH was treated with 10% Pd/C (90 mg) and sequentially evacuated and flushed with H_2 several times. The reaction mixture was vigorously stirred for 1 h under 1 atm of H_2, filtered and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL) and treated with pyridine (0.500 mL, 6.18 mmol) followed by allyl chloroformate (0.200 mL, 1.88 mmol). The solution was stirred for 2 h, washed with 10% HCl, saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/EtOAc, 9:1) gave 321 mg (91%) of the desired Alloc-protected bicycle: ^{1}H NMR (DMSO-d_6, 340 K) δ 5.92-5.81 (m, 1 H), 5.29-5.14 (m, 2 H), 4.48 (m, 2 H), 4.26 (dd, 1 H, *J* = 9.3, 8.2 Hz), 4.15-4.05 (m, 2 H), 3.65 (s, 3 H), 2.40-2.25 (m, 1 H), 2.23-2.14 (m, 1 H), 2.08-1.95 (m, 2 H), 1.94-1.83 (m, 1 H), 1.65-1.35 (m, 4 H), 0.91 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H).

A solution of this bicycle (202 mg, 0.509 mmol) and LiOH•H_2O (32 mg, 1.5 eq.) in 2 mL of THF/H_2O (1:1), was stirred at 35 °C for 14 h, partitioned between CH_2Cl_2 and 10% HCl. The organic layer was washed with water, dried (Na_2SO_4), filtered and concentrated to give crude oily acid, which was dissolved in 2 mL of CH_2Cl_2. A solution of argol amine **18** (385 mg, 0.709 mmol) in 1 mL of CH_2Cl_2 was added followed by *i*Pr_2NEt (0.200 mL, 1.13 mmol) and FDPP (300 mg, 0.781

mmol). The reaction mixture was stirred for 2 d, partitioned between CH_2Cl_2 and 10% HCl, and the organic layer was washed with 2 N NaOH, dried ($MgSO_4$), filtered, and concentrated. Chromatography on SiO_2 (hexanes/EtOAc, 9:1) gave 319 mg (0.351 mmol) of the desired dipeptide **23**: R_f = 0.65 (EtOAc/hexanes, 1:1); $[\alpha]_D$ –24 (*c* 0.50, CH_2Cl_2); IR (neat) 2952, 2928, 2856, 1731, 1693, 1643, 1462, 1427 cm^{-1}; ^1H NMR (500 MHz) δ 11.75 (s, 1 H), 8.34 (t, 1 H, *J* = 5.1 Hz), 7.40-7.32 (m, 10 H), 7.30 (d, 1 H, *J* = 8.5 Hz); 5.91-5.84 (m, 1 H), 5.28 (d, 1 H, *J* = 17.2 Hz), 5.19-5.15 (s, 2 H), 5.17 (m, 1 H), 5.12 (s, 2 H), 4.55 (d, 2 H, *J* = 5.2 Hz), 4.27 (b, 1 H), 4.21 (dd, 1 H, *J* = 8.7, 8.4 Hz), 4.07 (br s, 1 H), 4.0-3.93 (m, 1 H), 3.60, 3.55 (AB of ABX, 2 H, J_{AB} = 10.0, J_{AX} = 2.7, J_{BX} = 3.7 Hz), 3.55-3.35 (m, 2 H), 2.26-2.20 (m, 1 H), 2.15-2.0 (m, 3 H), 1.68-1.43 (m, 9 H), 0.88 (s, 9 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.04 (s, 9 H); ^{13}C NMR δ 172.0, 163.8, 156.1, 153.8, 136.8, 134.7, 132.8, 128.8, 128.7, 128.5, 128.4, 128.2, 128.0, 117.2, 68.1, 67.1, 66.7, 65.9, 64.6, 61.1, 55.0, 50.2, 41.0, 36.2, 34.7, 34.0, 29.7, 28.6, 27.3, 25.9, 25.8, 25.7, 25.0, 19.6, 18.2, 18.1, 13.7, -4.9 (2C), -5.5 (2C); FABMS 908 (M^+, 62), 850 (15), 774 (30), 338 (100).

D-Hpla(TIPS,TBS)-L-Leu-Choi(TBS)-Argol(Cbz_2)-OTBS (L^{Leu}-24). A solution of **23** (100 mg, 0.110 mmol) in 2 mL of CH_2Cl_2 was treated at 0 °C with AcOH (15 μL, 0.26 mmol), $Pd(PPh_3)_4$ (13 mg, 0.011 mmol), and Bu_3SnH (60 μL, 0.22 mmol). After stirring for 30 min, the mixture was partitioned between EtOAc and 2N NaOH and the organic layer was dried ($MgSO_4$), filtered and concentrated. A solution of **L^{Leu}-22** (96.1 mg) in 1 mL of CH_2Cl_2 was added, followed by *i*Pr_2NEt (150 μL, 0.861 mmol) and DEPBT[8] (100 mg, 0.334 mmol). The reaction mixture was stirred overnight, diluted with EtOAc, washed with 10% HCl, saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/Et_2O, 4:1) provided 95 mg (63%) of the desired **L^{Leu}-24**: R_f = 0.42 (ether/hexanes, 1:1); $[\alpha]_D$ –6.6 (*c* 0.50, CH_2Cl_2); ^1H NMR (500 MHz) δ 11.76 (br, 1 H), 8.31 (t, 1 H, *J* = 5.3 Hz), 7.40-7.32 (m, 10 H), 7.29 (d, 1 H, *J* = 7.2 Hz), 7.05-7.02 (m, 4 H), 6.77 (d, 2 H, *J* = 8.4 Hz), 5.16 (2s, 2 H), 5.12 (s, 2 H), 4.82-4.77 (m, 1 H), 4.48 (t, 1 H, *J* = 8.7 Hz), 4.48-4.43 (m, 1 H), 4.18 (dd, 1 H, *J* = 9.6, 2.5 Hz), 4.10 (br, 1 H), 3.97-3.93 (m, 1 H), 3.60, 3.55 (AB of ABX, 2 H, J_{AB} = 10.1 Hz, J_{AX} = 3.4 Hz, J_{BX} = 4.6 Hz), 3.46-3.42 (m, 2 H), 3.06 (dd, 1 H, *J* = 13.7, 2.5 Hz), 2.64 (dd, 1 H, *J* = 13.7, 9.6 Hz), 2.44 (td, 1 H, *J* = 13.0,

[8] DEPBT: 3-(Diethoxyphosphoryloxy)-1,2,3-benzotriazin-4(3H)-one; Li, H.; Jiang, X.; Ye, Y.; Fan, C.; Romoff, T.; Goodman, M. *Org. Lett.* **1999**, *1*, 91.

9.2 Hz), 2.36-2.28 (m, 1 H), 2.20-2.12 (m, 1 H), 1.92-1.85 (m, 2 H), 1.75-1.45 (m, 10 H), 1.41-1.35 (m, 1 H), 1.3-1.2 (m, 3 H), 1.10 (d, 18 H, *J* = 7.3 Hz), 1.01 (d, 3 H, *J* = 6.4 Hz), 0.92 (s, 9 H), 0.90 (s, 9 H), 0.90-0.88 (m, 3 H), 0.86 (s, 9 H), 0.07-0.05 (m, 12 H), -0.17 (s, 3 H), -0.41 (s, 3 H); ^{13}C NMR δ 173.1, 172.0, 171.0, 163.8, 156.1, 154.8, 153.8, 136.8, 134.6, 130.9, 130.3, 128.8, 128.7, 128.5, 128.4, 128.2, 127.9, 119.5, 75.5, 68.1, 67.1, 66.7, 64.7, 59.5, 55.9, 50.5, 48.2, 43.6, 41.2, 41.1, 36.8, 34.9, 31.6, 28.6, 28.2, 26.5, 26.0, 25.9, 25.8, 25.6, 24.9, 23.4, 22.7, 21.8, 19.3, 18.3, 18.1, 18.0, 14.2, 12.7, -4.9, -5.0, -5.4 (2C), -5.5, -5.6; FABMS 1373 ([M+1]$^+$, 38), 1314 (12), 1238 (21), 716 (6), 407 (100).

L-Leucine Aeruginosin 298-A (L^{Leu}-1). A solution of **L^{Leu}-24** (20 mg, 0.015 mmol) in 1 mL of HF(aq)/MeCN (1:9) was stirred at room temperature for 1 h, then poured into 2 N NaOH (1 mL). Repeated extraction with CH_2Cl_2 and EtOAc gave a bisCbz intermediate [R_f = 0.33 (MeOH/EtOAc, 1:9)] upon drying (Na_2SO_4), filtration and concentration. The amorphous solid was dissolved in 1 mL of EtOH containing 5 μL of TFA[9] and treated with 10% Pd/C (1.5 mg). The reaction mixture was sequentially evacuated and purged H_2 three times, and vigorously stirred for 2 h under a H_2 atmosphere (1 atm). Filtration and concentration (<20 °C) provided 4.4 mg (42%) of **L^{Leu}-1** as a colorless amorphous solid: $[\alpha]_D$ –18 (*c* 0.25, H_2O); ^{1}H NMR (500 MHz, DMSO-d_6)[10] δ 9.11 (s, 1 H), 7.70 (d, 1 H, *J* = 8.6 Hz), 7.60 (d, 1 H, *J* = 8.2 Hz), 7.33 (m, 1 H), 6.95 (d, 2 H, *J* = 8.4 Hz), 6.61 (d, 2 H, *J* = 8.3 Hz), 5.38 (d, 1 H, *J* = 6.3 Hz), 4.69 (br, 1 H), 4.53-4.49 (m, 2 H), 4.43-4.39 (m, 1 H), 4.23 (dd, 1 H, *J* = 9.3 Hz, 8.5 Hz), 4.00 (dd, 1 H, *J* = 12.8, 7.6 Hz), 3.91 (br, 1 H), 3.69-3.63 (m, 1 H), 3.27-3.21 (m, 1 H), 3.08-3.02 (m, 2 H), 2.79 (dd, 1 H, *J* = 13.7, 4.3 Hz), 2.54 (dd, 1 H, *J* = 13.7, 8.1 Hz), 2.25-2.15 (m, 2 H), 2.08-2.00 (m, 1 H), 2.0-1.94 (m, 2 H), 1.87-1.8 (m, 2 H), 1.76-1.70 (m, 1 H), 1.6-1.45 (m, 6 H), 1.3-1.2 (m, 2 H), 0.85 (2d, 6 H, *J* = 6.0 Hz, *J'* = 6.2 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 173.0, 171.3, 170.4, 156.6, 155.6, 130.2, 128.3, 114.7, 72.2, 64.0, 63.4, 59.6, 54.4, 50.0, 48.1, 41.5, 40.8, 36.5, 33.4, 30.3, 28.2, 26.0, 25.0, 24.1, 23.5, 21.6, 19.1; FABMS 605 ([M+1]$^+$, 100), 551 (48), 549 (48), 537 (44), 523 (46), 391 (66), 369 (60); HRFABMS calculated for $C_{30}H_{49}N_6O_7$ (M+H) 605.3663, found 605.3672.

---

[9] TFA was added to mimic the natural product isolation procedure.
[10] The presence of TFA does not appear to alter the ^{1}H NMR spectrum of **L^{Leu}-1**.

D-Hpla(TIPS,TBS)-D-Leu-OH (D^{Leu}-22). A solution of **21** (245 mg, 0.540 mmol) in 5 mL of CH_2Cl_2 was treated with *i*Pr_2NEt (400 μL, 2.30 mmol), cooled to –20 °C, and then diethyl cyanophosphinate (150 μL, 0.659 mmol) was added. After 20 min, a solution of HCl•NH_2-L-Leu-OBn[11] (300 mg, 1.17 mmol) in 1 mL of CH_2Cl_2 was added. The reaction mixture was stirred for 2 h, partitioned between Et_2O and 10% HCl, and the organic layer was washed with 2 N NaOH and water, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/EtOAc, 9:1) provided 241 mg (68%) of oily benzyl ester: R_f = 0.13 (hexanes/EtOAc, 9:1); $[\alpha]_D$ +39.6 (*c* 0.500, CH_2Cl_2); IR (neat) 2928, 2867, 1742, 1681, 1609, 1510, 1463, 1264 cm^{-1}; ^1H NMR δ 7.4-7.3 (m, 5 H), 7.07 (d, 2 H, *J* = 8.3 Hz), 6.86 (d, 1 H, *J* = 8.7 Hz), 6.78 (d, 2 H, *J* = 8.2 Hz), 5.17, 5.14 (AB, 2 H, *J* = 16.6, 12.3 Hz), 4.67-4.60 (m, 1 H), 4.27 (dd, 1 H, *J* = 6.8, 3.1 Hz), 3.03 (dd, 1 H, *J* = 13.7, 3.0 Hz), 2.84 (dd, 1 H, 13.7, 7.0 Hz), 1.6-1.5 (m, 1 H), 1.5-1.35 (m, 2 H), 1.3-1.2 (m, 3 H), 1.11 (d, 18 H, *J* = 7.0 Hz), 0.90-0.87 (m, 15 H), -0.04 (s, 3 H), -0.19 (s, 3 H); ^{13}C NMR δ 172.7, 172.4, 154.9, 135.4, 131.1, 129.5, 128.6, 128.4 (2C), 119.5, 74.6, 67.0, 50.2, 41.8, 40.8, 25.8, 24.7, 22.8, 22.0, 18.0, 12.7, -5.3, -5.5; MS (EI) 598 ($[M-C_4H_8]^+$, 21), 533 (9), 303 (5), 263 (10); HRMS (EI) calculated for $C_{33}H_{52}NO_5Si$ (M-C_4H_8) 598.3384, found 598.3376.

A solution of D-Hpla(TIPS,TBS)-D-Leu-OBn (63 mg, 0.096 mmol) in EtOH (2 mL) was treated with 10% Pd/C (10 mg, 0.1 eq.), and the suspension sequentially evacuated and purged H_2, stirred vigorously for 2 h under 1 atm of H_2, filtered and concentrated to give 51.5 mg (95%) of D-Hpla(TIPS,TBS)-L-Leu-OH (D^{Leu}-**22**).

D-Hpla(TIPS,TBS)-D-Leu-Choi(TBS)-Argol(Cbz_2)-OTBS (D^{Leu}-24). A solution of **23** (46.0 mg, 0.0507 mmol) in 1 mL of CH_2Cl_2 was treated at 0 °C with AcOH (10 μL), $Pd(PPh_3)_4$ (5.0 mg, 0.0043 mmol), and Bu_3SnH (25 μL, 0.095 mmol). After stirring for 1 h, the mixture was partitioned between CH_2Cl_2 and 2 N NaOH, and the organic layer was dried ($MgSO_4$), filtered and concentrated. A solution of D^{Leu}-**22** (51.5 mg) in 1 mL of CH_2Cl_2 was added, followed by *i*Pr_2NEt (40 μL, 0.23 mmol) and DEPBT (23 mg, 0.077 mmol). The reaction was stirred for 21 h, diluted with CH_2Cl_2, washed with 10% HCl, and 2 N NaOH, dried ($MgSO_4$), filtered and concentrated. Chromatography on SiO_2 (hexanes/Et_2O, 1:1) provided 41 mg (59%) of the desired tetrapeptide: R_f = 0.11 (ether/hexanes, 1:1); $[\alpha]_D$ –6.7

[11] Wakamiya, T.; Kamata, M.; Kusumoto, S.; Kobayashi, H.; Sai, Y. *Bull. Soc. Chem. Jpn.* **1998**, *71*, 699.

(*c* 0.38, CH_2Cl_2); ^{1}H NMR (500 MHz) δ 11.76 (br, 1 H), 8.40 (t, 1 H, *J* = 4.8 Hz), 7.39-7.31 (m, 10 H), 7.28 (d, 1 H, *J* = 7.0 Hz), 7.03 (d, 2 H, *J* = 8.3 Hz), 6.90 (d, 1 H, *J* = 8.9 Hz), 6.84 (d, 1 H, *J* = 7.0 Hz), 6.76 (d, 2 H, *J* = 8.2 Hz), 5.16 (s, 2 H), 5.12 (2s, 2 H), 4.45-4.40 (m, 1 H), 4.39 (dd, 1 H, *J* = 9.1, 8.4 Hz), 4.16-4.10 (m, 2 H), 3.93-3.88 (m, 1 H), 3.60-3.55 (m, 2 H), 3.45-3.40 (m, 1 H), 3.35 (dd, 1 H, *J* = 9.6, 7.3 Hz), 2.99 (dd, 1 H, *J* = 13.8, 3.3 Hz), 2.83 (dd, 1 H, *J* = 13.7, 6.9 Hz), 2.25-2.05 (m, 4 H), 1.8-1.7 (m, 1 H), 1.7-1.55 (m, 5 H), 1.55-1.45 (m, 3 H), 1.4-1.35 (m, 1 H), 1.3-1.2 (m, 5 H), 1.10 (d, 18 H, *J* = 7.4 Hz), 0.91 (s, 9 H), 0.88 (2s, 18 H), 0.91-0.85 (m, 6 H), 0.12 (s, 3 H), 0.07 (s, 3 H), 0.04 (s, 6 H), 0.02 (s, 3 H), -0.21 (s, 3 H); ^{13}C NMR δ 173.1, 171.6, 171.2, 163.9, 156.3, 154.9, 153.9, 137.0, 134.8, 131.2, 129.8, 128.9 (2C), 128.6 (2C), 128.3, 128.1, 119.5, 74.7, 68.2, 67.2, 66.7, 64.9, 60.3, 55.4, 50.9, 49.4, 41.9, 41.2, 40.8, 36.8, 34.3, 30.5, 30.1, 28.1, 26.8, 26.1, 25.9, 24.8, 23.6, 23.0, 22.2, 19.5, 18.4, 18.3, 18.1, 14.2, 12.8, -4.4, -4.9, -5.1, -5.2, -5.3; FABMS 1373 ($[M+1]^+$, 50), 1314 (14), 1238 (16).

D-Leucine Aeruginosin 298-A (D^{Leu}-1). A solution of **D^{Leu}-24** (29 mg, 0.021 mmol) in 1 mL of HF(aq)/MeCN (1:9) was stirred at room temperature for 2 h, then quenched with 2 N NaOH (to pH 5). Repeated extraction with CH_2Cl_2 and EtOAc gave the bis-Cbz intermediate [R_f = 0.20 (MeOH/EtOAc, 1:9)] upon drying (Na_2SO_4), filtration and concentration. This amorphous solid was dissolved in 1 mL of EtOH and treated with 10% Pd/C (1.5 mg). The suspension was sequentially evacuated and purged with H_2, stirred for 2 h under a hydrogen atmosphere (1 atm, filtered and concentrated. A solid-liquid extraction of the residue with *i*PrOH and concentration provided 4.3 mg (34%) of **D^{Leu}-1** as a colorless amorphous solid: $[\alpha]_D$ +16 (*c* 0.17, H_2O); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.12 (s, 1 H), 7.57 (d, 1 H, *J* = 8.6 Hz), 7.46 (d, 1 H, *J* = 8.1 Hz), 7.41 (br, 1 H), 6.98 (d, 2 H, *J* = 8.1 Hz), 6.63 (d, 2 H, *J* = 8.1 Hz), 5.71 (br d, 1 H, *J* = 4.8 Hz), 4.64 (br, 1 H), 4.51 (br, 1 H), 4.16 (t, 1 H, *J* = 9.0 Hz), 4.09-4.01 (m, 2 H), 3.92 (br, 1 H), 3.67-3.61 (m, 1 H), 3.25-3.19 (m, 1 H), 3.10-3.03 (m, 2 H), 2.85 (dd, 1 H, *J* = 13.8, 2.6 Hz), 2.64 (dd, 1 H, *J* = 13.8, 7.8 Hz), 2.29-2.23 (m, 1 H), 2.05-1.95 (m, 3 H), 1.85-1.78 (m, 1 H), 1.68-1.60 (m, 1 H), 1.6-1.15 (m, 10 H), 0.87 (d, 3 H, *J* = 6.2 Hz), 0.82 (d, 3 H, *J* = 6.3 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.8, 171.3, 169.7, 156.6, 155.7, 130.4, 128.1, 114.6, 72.1, 63.8, 63.3, 59.8, 54.0, 50.1, 48.0, 41.8, 40.8, 36.0, 33.4, 30.7, 28.0, 26.0, 25.0, 23.9, 23.4, 21.3, 19.0; FABMS 605 ($[M+1]^+$, 100), 577 (45), 551 (73), 549 (57), 538 (53), 523 (52), 369 (53); HRFABMS calculated for $C_{30}H_{49}N_6O_7$ (M+H) 605.3663, found 605.3670.

Marfey's analysis of $\mathbf{L^{Leu}}$-1 and $\mathbf{D^{Leu}}$-1:[12]

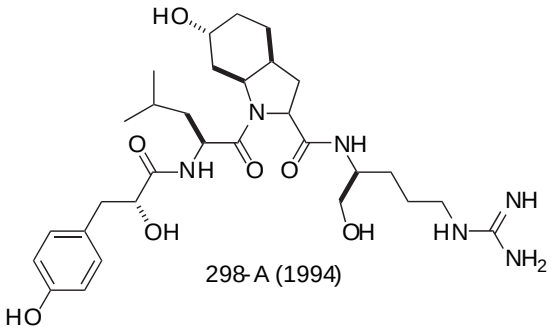
I. A solution of 1.0 mg of **$\mathbf{L^{Leu}}$-1** in 0.5 mL of water was treated with 0.5 mL of 12 N HCl and stirred at 90 °C in a sealed tube for 30 h. After concentration to dryness, 1.0 mL of 10 mM 1-fluoro-2,4-dinitrophenyl-5-L-alanine (L-FDAA) in acetone was added, followed by 1.0 mL of 1 N $NaHCO_3$. The reaction mixture was stirred at 40 °C for 1 h, allowed to cool, and acidified with 1.0 mL of 1 N HCl.

II. A solution of 0.6 mg of **$\mathbf{D^{Leu}}$-1** in 0.5 mL of water was treated with 0.5 mL of 12 N HCl and stirred at 90 °C in a sealed tube for 22 h. After concentration to dryness, 0.60 mL of 10 mM 1-fluoro-2,4-dinitrophenyl-5-L-alanine (L-FDAA) in acetone was added, followed by 0.60 mL of 1 N $NaHCO_3$. The reaction mixture was stirred at 40 °C for 1 h, allowed to cool, and acidified with 0.60 mL of 1 N HCl.

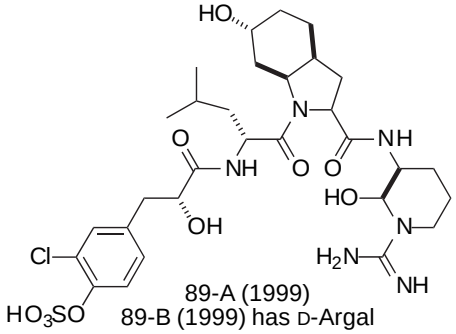
III. HPLC analysis of the hydrolysates was conducted using a Varian Microsorb 100 Å C18 column (150 X 4.6 mm), with 340 nm detection, and a 100:0 to 40:60 0.1% TFA(aq):MeCN gradient at 1 mL/min over a 1 h period. Retention times: L-Leu-L-FDAA, 42.8 min; D-Leu-L-FDAA, 46.9 min; observed for **$\mathbf{L^{Leu}}$-1**, 42.6 min; observed for **$\mathbf{D^{Leu}}$-1**, 47.7 min.

[12] For a procedure and standard application, see: Adamson, J. G.; Hoang, T.; Crivici, A.; Lajoie, G. A. *Anal. Biochem.* **1992**, *202*, 210.

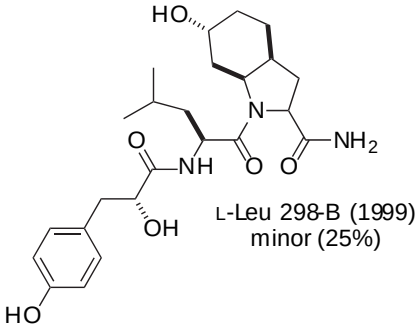
Selected Members of the Aeruginosin Family[13]



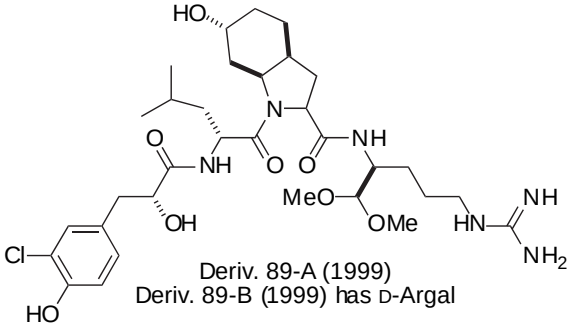
298-A (1994)



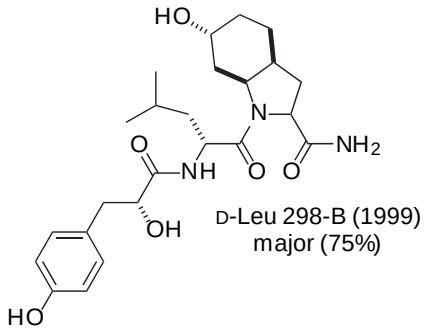
89-A (1999)
89-B (1999) has D-Argal



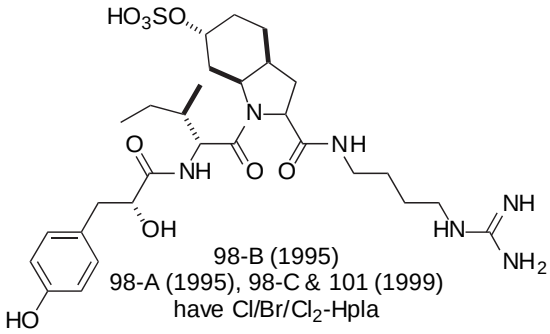
L-Leu 298-B (1999)
minor (25%)



Deriv. 89-A (1999)
Deriv. 89-B (1999) has D-Argal



D-Leu 298-B (1999)
major (75%)



98-B (1995)
98-A (1995), 98-C & 101 (1999)
have Cl/Br/Cl_2-Hpla

[13] Ishida, K.; Okita, Y.; Matsuda, H.; Okino, T.; Murakami, M. *Tetrahedron* **1999**, *55*, 10971.

^{1}H NMR Data of Selected Aeruginosins in DMSO-d_6

		298-A (L-Leu)	298-B (L-Leu)	298-B (D-Leu)	89-A (D-Leu)	Deriv. 89-A (D-Leu)	Deriv. 89-B (D-Leu)	98-B (D-allolle)	L^{Leu}-**1**[14]	D^{Leu}-**1**[15]
Hpla										
	2	4.04	4.00	4.01	4.10	4.09	4.06	4.05	4.00	4.04
	3	2.64	2.61	2.63	2.70	2.70	2.68	2.62	2.54	2.64
		2.85	2.81	2.84	2.92	2.84	2.84	2.87	2.79	2.85
	5	6.94	6.95	6.98	7.20	7.13	7.13	7.00	6.95	6.98
	6	6.60	6.60	6.62				6.63	6.61	6.63
	8	6.60	6.60	6.62	7.46	6.83	6.83	6.63	6.61	6.63
	9	6.94	6.95	6.98	7.05	6.94	6.94	7.00	6.95	6.98
	2-OH	5.69				5.80			5.38	5.71
	7-OH	9.12				9.80			9.11	9.12
Leu										
→	2	4.51	4.19	4.53	4.57	4.55	4.48	4.45	4.52	4.51
	3	1.20	1.24	1.20	1.23	1.17	1.21	1.55		
		1.40	1.41	1.33	1.39	1.36	1.37			
	4	1.35	1.28	1.32	1.35	1.24	1.29	1.18		
								0.98		
→	5	0.82	0.76	0.80	0.82	0.79	0.80	0.68	0.85	0.82
→	6	0.88	0.71	0.87	0.88	0.86	0.86	0.87	0.85	0.87
	NH	7.45	7.33	7.40	7.45	7.38	7.45	7.33	7.70	7.46
Choi										
→	2	4.16	4.64	4.12	4.28	4.20	4.22	4.17	4.23	4.16
	3	1.80	1.85	1.80	1.87	1.82	1.79	1.76		1.81
→		2.00	2.22	1.98	1.97	1.97	2.03	2.02		2.0
	3a	2.27	2.22	2.25	2.29	2.27	2.27	2.27	2.21	2.27
	4	1.43	1.45	1.41	1.43	1.42	1.42	1.42		
		2.02	2.02	2.02	2.06	2.04	2.04	1.98	2.04	2.0
→	5	1.43	1.39	1.42	1.44	1.43	1.43	1.33		
→		1.43	1.98	1.42	1.44	1.43	1.43	1.87		
→	6	3.92	3.84	3.92	3.91	3.93	3.93	4.35	3.91	3.92
→	7	1.65	1.43	1.65	1.66	1.64	1.64	1.68		1.65
→		2.02	1.85	2.00	2.03	2.03	2.03	2.28		2.0
→	7a	4.04	4.27	4.02	4.06	4.05	4.05	4.03	4.41	4.04
Arg										
	1	3.21			5.21	4.14	4.20		3.24	3.22
		3.31							(H_2O)	(H_2O)
	2	3.64			3.70	3.77	3.77	3.04	3.68	3.63
	3	1.30			1.57	1.30	1.32	1.39		
		1.60			1.72			1.39		
	4	1.50			1.49	1.43	1.32	1.46		
						1.55	1.43			
	5	3.07			3.11	3.05	3.03	3.08	3.06	3.07
					3.46					
	2-NH	7.54			7.70	7.74	7.50	7.78	7.60	7.57
	5-NH	7.52				7.38	7.46	7.46	7.33	7.41

[14] Assignments are tentative. Unassigned signals: 2.25-2.15 (m, 1 H), 2.08-2.00 (m, 1 H), 2.0-1.94 (m, 2 H), 1.87-1.8 (m, 2 H), 1.76-1.70 (m, 1 H), 1.6-1.45 (m, 6 H), 1.3-1.2 (m, 2 H).

[15] Assignments are tentative. Unassigned signals: 1.6-1.15 (m, 10 H).

^{13}C NMR Data of Selected Aeruginosins in DMSO-d_6

Carbon		298-A (L-Leu)	298-B (L-Leu)	298-B (D-Leu)	89-A (D-Leu)	Deriv. 89-A (D-Leu)	Deriv. 89-B (D-Leu)	98-B (D-allolle)
Hpla	1	172.8	172.3	172.3	172.1	172.0	172.3	172.8
	2	72.1	72.0	71.8	71.6	70.8	71.6	72.1
	3	39.3	39.0	39.0	39.0	38.8	38.8	38.7
	4	128.1	125.2	127.9	133.9	129.6	129.6	128.1
	5	130.4	130.0	130.0	130.3	130.6	130.6	130.4
	5’	130.4	130.0	130.0	128.5	129.1	129.1	130.4
	6	114.7	114.4	114.4	123.6	118.9	118.9	114.7
	6’	114.7	114.4	114.4	121.0	116.0	116.0	114.7
	7	155.7	155.4	155.4	147.8	151.4	151.4	155.6
Leu	1	169.8	169.8	169.4	169.5	169.7	169.7	169.1
	2	48.1	46.9	47.4	47.8	47.8	48.2	52.7
	3	41.8	41.7	41.8	42.0	42.2	41.6	37.4
	4	23.9	23.7	23.6	24.0	23.9	23.9	25.8
	5	23.3	23.0	23.0	23.3	23.2	23.4	13.9
	5’	21.4	21.3	21.4	21.4	21.3	21.3	11.8
Choi	1	171.3	173.3	173.0	170.8	171.4	171.4	171.5
	2	59.9	59.1	59.4	59.4	59.6	59.7	59.9
	3	30.7	30.1	30.1	30.2	30.3	30.6	30.6
	3a	36.0	35.9	35.8	36.0	35.9	36.0	35.9
	4	19.0	18.7	18.8	19.0	19.0	19.0	19.4
	5	26.0	25.9	25.9	26.0	26.0	26.0	23.4
	6	63.9	63.7	63.7	63.8	63.8	63.8	70.9
	7	33.4	33.4	33.2	33.5	33.3	33.3	31.6
	7a	54.0	53.9	53.6	53.9	54.0	54.0	54.0
Arg	1	63.3			76.2	105.3	105.3	
	2	50.2			49.0	49.9	49.8	37.9
	3	28.0			23.3	25.7	25.4	25.8
	4	25.0			23.4	25.0	25.4	26.2
	5	40.8			39.5	40.7	40.6	40.3
	C=N	156.7			156.6	156.6	156.6	156.6

Comparison of Synthetic and Natural Aeruginosin 298-A ^{13}C NMR Data