Supplementary Material

Materials and Methods

Materials. β-[^{14}C-3]Alanine [250 μCi (1 Ci = 37 GBq), 55.5 × 10^7 dpm] was diluted with cold material as reported below for the synthesis of radiolabeled hydroxydestruxin B.

Synthesis of [^{14}C]Hydroxydestruxin B. The synthesis of [^{14}C]hydroxydestruxin B was carried out as described below, starting from oxazolidinone **8** (1), and summarized in Fig. 5.

(2'R, 4R, 5S)-(+)-4-methyl-5-phenyl-3-[4-methyl-(2-(phenylmethoxycarbonyloxy)-4-triethylsilyloxypentanoyl)-2-oxazolidinone (**9**). Benzyl chloroformate (0.15 mL, 1 mmol) and 4-(dimethylamino)pyridine (DMAP) (122 mg, 1 mmol) were added to a stirred solution of alcohol **8** (280 mg, 0.67 mmol) in CH_2Cl_2 (4 mL) at room temperature. After 2 h, additional benzyl chloroformate (0.075 mL, 0.5 mmol) and DMAP (61 mg, 0.50 mmol) were added and, after stirring for 2 h, the reaction mixture was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, concentrated, and fractionated by flash column chromatography (FCC) (50–75% CH_2Cl_2 in hexane) to give **9** as an oil (365 mg, 99%): $[\alpha]_D$ = +27 (*c* 1.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.35 (m, 10H), 6.22 (dd, *J* = 5.5, 6 Hz, 1H), 5.70 (d, *J* = 7 Hz, 1H), 5.18 (d, *J* = 12.5 Hz, 1H), 5.13 (d, *J* = 12.5 Hz, 1H), 4.73 (dq, *J* = 7, 6.5 Hz, 1H), 2.04 (m, 2H), 1.36 (s, 3H), 1.34 (s, 3H), 0.92 (m, 12H), 0.58 (q, *J* = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.9 (s), 154.8 (s), 152.3 (s), 135.3 (s), 133.3 (s), 129.1 (d), 129.0 (d ×2), 128.8 (d ×2), 128.7 (d), 128.4 (d ×2), 125.9 (d ×2), 79.7 (d), 73.9 (d), 72.7 (s), 70.1 (t), 55.5 (d), 45.1 (t), 31.4 (q), 30.4 (q), 14.2 (q), 7.3 (q ×3), 6.9 (t ×3); fast atom bombardment (FAB), *m/z* (relative intensity): 562 ($[M+7]^+$, 27), 540 (21), 91 (100); HR-FAB, *m/z* calcd. for $C_{30}H_{41}NO_7Si$: 562.2812 (M+Li); found: 562.2814; elemental analysis calcd. for $C_{30}H_{41}NO_7Si$: C, 64.84; H, 7.44; N, 2.52; found: C, 64.65; H, 7.22; N, 2.78; Fourier transform infrared (FTIR) ν_{max}: 2955, 1787, 1747, 1713, 1250 cm^{-1};

(2R)-2-(Phenylmethoxycarbonyloxy)-4-triethylsilyloxy-4-methylpentanoic acid [(2-OCbz,4-OTES)Dhmp] (**10**). Hydrogen peroxide (30%; 0.52 mL, 4.59 mmol) and LiOH (1 M in H_2O; 0.9

mL, 0.9 mmol) were added to a stirred solution of *N*-acyloxazolidinone **9** (170 mg, 0.31 mmol) in tetrahydrofuran (THF) (3.2 mL) at 0°C under argon. After 75 min, 10% aqueous Na_2SO_3 (10 mL) was added and the mixture stirred at room temperature for 20 min. The reaction mixture was diluted with EtOAc, washed sequentially with citric acid (0.75 M) and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (eluting first with hexane-CH_2Cl_2-^{i}PrOH-NH_4OH, 45:45:9:1, and then with 15% CH_3OH in CH_2Cl_2) to give the oxazolidinone (50 mg, 92%) and carboxylic acid **10** (110 mg, 91%): $[\alpha]_D$ = +52 (*c* 0.89, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.45–7.95 (br s, 1H), 7.31 (m, 5H), 5.20 (d, *J* = 12 Hz, 1H), 5.12–5.06 (m, 1H), 5.07 (d, *J* = 12 Hz, 1H), 2.09 (d, *J* = 14.5 Hz, 1H), 1.90 (dd, *J* = 9, 14.5 Hz, 1H), 1.22 (s, 6H), 0.88 (t, *J* = 8 Hz, 9H), 0.54 (q, *J* = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 177.4 (s), 155.5 (s), 135.8 (s), 128.7 (d ×2), 128.5 (d ×3), 76.0 (d), 72.7 (s), 69.8 (t), 45.8 (t), 31.2 (q), 30.2 (q), 7.3 (q ×3), 6.8 (t ×3); FAB, *m/z* (relative intensity): 403 ($[M+7]^+$, 18), 265 (11), 91 (100); HR-FAB *m/z* calcd. for $C_{20}H_{32}O_6Si$: 403.2128 (M+Li); found: 403.2141; FTIR ν_{max}: 2500–3500 (br), 2954, 1749, 1731, 1456, 1597, 1265 cm^{-1}.

(2-O-*Cbz,4*-O-*TES)Dhmp-Pro-OAll* (**12**). *N,N'*-dicyclohexylcarbodiimide (DCC) (149.3 mg, 0.68 mmol) was added to a stirred solution of **10** (206 mg, 0.52 mmol), Pro-O-allyl (All) (**11**; 121 mg, 0.78 mmol) and 1-hydroxybenzotriazole (HOBt) hydrate (103 mg, 0.68 mmol) in CH_2Cl_2 (3 mL) at 0°C. The mixture was stirred at 0°C for 1 h and at room temperature for 20 h and then was diluted with EtOAc and the precipitated DCU was filtered off. The combined filtrate and washings were washed sequentially with 0.5 M aqueous citric acid and saturated aqueous $NaHCO_3$, dried over $MgSO_4$, concentrated, and fractionated by FCC (20% EtOAc in hexane) to give **12** as an oil (221 mg, 80%): $[\alpha]_D$ = –22 (*c* 1.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.27 (m, 5H), 5.84 (m, 1H), 5.36 (d, *J* = 8 Hz, 1H), 5.25 (d, *J* = 17.5 Hz, 1H), 5.15–5.01 (m, 3H), 4.54 (m, 2H), 4.42 (dd, *J* = 3, 8 Hz, 1H), 3.85–3.50 (m, 2H), 2.26–1.70 (m, 6H), 1.22 (s, 6H), 0.88 (t, *J* = 7.5 Hz, 9H), 0.51 (q, *J* = 7.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.4 (s), 169.3 (s), 154.5 (s), 135.5 (s), 132.3 (d), 128.6 (d ×2), 128.5 (d), 128.2 (d ×2), 118.3 (t), 72.7 (s), 72.6 (d), 69.8 (t), 65.8 (t), 59.5 (d), 46.5 (t), 45.8 (t), 31.8 (q), 29.2 (q), 29.1 (t), 24.8

(t), 7.2 (q ×3), 6.7 (t ×3); FAB, *m/z* (relative intensity): 534 ($[M+1]^+$, 30), 504 (27), 402 (64), 250 (66), 91 (100); HR-FAB, *m/z* calcd. for $C_{28}H_{43}NO_7Si$: 534.2887 (M+H); found: 534.2887; FTIR ν_{max}: 2955, 1747, 1668, 1437, 1266, 743 cm^{-1}.

(2-O-*Cbz, 4*-O-*TES)Dhmp-Pro* (**13**). $(Ph_3P)_4Pd$ (65 mg, 0.056 mmol) was added to a stirred solution of **12** (200 mg, 0.38 mmol) in dry THF (3 mL) at room temperature under argon. Morpholine (0.33 mL, 3.80 mmol) was added dropwise to the resulting yellow solution. After 1 h, the mixture was concentrated, taken up in EtOAc, washed sequentially with 1M citric acid and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (eluting first with CH_2Cl_2-hexane-^{i}PrOH-NH_4OH, 45:45:9:1, and then with 25% CH_3OH in CH_2Cl_2) to give the acid **13** (182 mg, 99%): $[\alpha]_D$ = –15 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.30 (m, 5H), 7.01 (br s, 1H), 5.30 (d, *J* = 8.5 Hz, 1H), 5.21 (d, *J* = 12.5 Hz, 1H), 5.10 (d, *J* = 12.5 Hz, 1H), 4.35 (m, 1H), 3.74–3.60 (m, 1H), 3.60–3.45 (m, 1H), 2.28–1.65 (m, 6H), 1.22 (s, 3H), 1.21 (s, 3H), 0.89 (t, *J* = 7.5 Hz, 9H), 0.54 (q, *J* = 7.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 178.4 (s), 169.1 (s), 154.9 (s), 135.8 (s), 128.6 (d ×3), 128.4 (d ×2), 73.1 (s), 72.6 (d), 70.2 (t), 62.2 (d), 46.9 (t), 45.9 (t), 31.8 (q), 29.5 (t), 29.1 (q), 24.7 (t), 7.2 (q ×3), 6.7 (t ×3); FAB, *m/z* (relative intensity): 500 ($[M+7]^+$, 43), 354 (18), 173 (42), 91 (100); HR-FAB, *m/z* calcd. for $C_{25}H_{39}NO_7Si$: 500.2656 (M+Li); found: 500.2663; FTIR ν_{max}: 3300–2500 (br), 2955, 1747, 1664, 1649, 1266 cm^{-1}.

(2-O-*Cbz, 4*-O-*TES)Dhmp-Pro-Ile-MeVal-MeAla-NHNHBoc* (**16**). Ten percent Pd/C (*ca*. 25 mg) was added to a solution of the tripeptide **15** (2) (94 mg, 0.16 mmol) in MeOH (3 mL) at room temperature and the resulting suspension was vigorously stirred under hydrogen (balloon pressure). After 2 h, the mixture was filtered through Celite and the combined filtrate and washings were concentrated. Residual methanol was removed by concentration from CH_2Cl_2 (×2) and drying under high vacuum. The residue was taken up in CH_2Cl_2 (1.2 mL) and **13** (80 mg, 0.16 mmol), HOBt (32 mg, 0.21 mmol), and DCC (43 mg, 0.21 mmol), were sequentially added to the stirred solution. After 45 h, the reaction mixture was diluted with EtOAc (*ca*. 5 mL) and filtered. The combined filtrate and washings were washed sequentially with 0.5 M aqueous citric acid and sat. aqueous $NaHCO_3$, dried over Na_2SO_4, concentrated, and fractionated by FCC

(40–80% EtOAc in hexane) to give the pentadepsipeptide **16** (122 mg, 82%): [α]= –138 (*c* 0.93, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ: (a 1:1 mixture of rotamers) 9.10 and 7.80 (s ×2, 1H), 7.42–7.28 (m, 5H), 5.32–5.05 (m, 5H), 4.72–4.54 (m, 2H), 3.84–3.70 (m, 1H), 3.70–3.56 (m, 1H), 3.31 (s, 1.5H), 3.05 (s, 1.5H), 2.97 (s, 1.5H), 2.82 (s, 1.5H), 2.45–1.45 (m, 9H), 1.44 (s, 9H), 1.37 (s, 6H), 1.28–1.23 (m, 3H), 1.20–1.08 (m, 1H), 0.98–0.78 (m, 21H), 0.56 (q, *J* = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 174.5, 172.3, 170.8, 170.1, 169.1, 155.3 (br), 135.4, 128.7, 128.3, 128.1, 81.6, 72.8, 72.5, 70.2, 60.3, 58.2, 57.7, 54.3, 53.8, 53.5, 50.7, 46.7, 45.5, 36.9, 36.1, 31.9, 31.3, 31.0, 30.6, 29.2, 28.3, 27.3, 24.5, 19.7, 19.0, 18.3, 15.6, 15.0, 13.5, 11.2, 10.9, 7.2, 6.7; FAB, *m/z* (relative intensity): 925 ($[M+7]^+$, 100), 826 (43), 160 (33); HR-FAB, *m/z* calcd. for $C_{46}H_{78}N_6O_{11}Si$: 925.5658 (M+Li); found: 925.5660; elemental analysis calcd. for $C_{46}H_{78}N_6O_{11}Si$: C, 60.10; H, 8.55; N, 9.14; found: C, 60.09; H, 8.69; N, 9.38; FTIR ν_{max}: 3293, 2962, 1745, 1727, 1650, 1623, 1266, 745 cm^{-1}.

(4-O-*TES)Dhmp-Pro-Ile-MeVal-MeAla-NHNHBoc* (**17**). Ten percent Pd/C (*ca*. 25 mg) was added to a vigorously stirred solution of the **16** (54 mg, 0.059 mmol) and ammonium formate (16 mg, 0.25 mmol) in CH_3OH (2 mL) at room temperature under argon. After 15 min, the reaction mixture was filtered through Celite and the combined filtrate and washings were concentrated. The residue was dissolved in EtOAc and washed with water and brine, dried over Na_2SO_4, and concentrated to give the alcohol **17** (46 mg, 99%): $[\alpha]_D$ = –164 (*c* 1.7, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ: (a 1.5:1 mixture of rotamers) 9.15–6.20 (several signals, 3H), 5.28–5.05 (m, 2H), 4.69 (q, *J* = 8 Hz, 1H), 4.60–4.42 (m, 2H), 3.71–3.49 (m, 2H), 3.27 (s, 1.2H), 3.04 (s, 1.8H), 3.03 (s, 1.8H), 2.82 (s, 1.2H), 2.45–1.45 (m, 9H), 1.42 (s, 12H), 1.36 (s, 3H), 1.30–1.25 (m, 3H), 1.20–1.05 (m, 1H), 0.98–0.76 (m, 21H), 0.58 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 178.7, 174.3, 172.6, 171.8, 170.9, 170.4, 168.8, 154.8 (br), 81.6, 73.7, 67.6, 60.1, 58.1, 57.8, 54.1, 53.5, 50.5, 49.2, 46.6, 37.6, 37.3, 30.9, 30.5, 29.3, 28.1, 27.5, 27.0, 24.7, 24.3, 19.6, 19.1, 18.1, 15.5, 14.9, 13.1, 11.2, 11.0, 7.0, 6.6; FAB, *m/z* (relative intensity): 791 ($[M+7]^+$, 100), 692 (39), 160 (25); HR-FAB, *m/z* calcd. for $C_{38}H_{72}N_6O_9Si$: 791.5290 (M+Li); found: 791.5266; FTIR ν_{max}: 3431, 3298, 2963, 1663, 1645, 1627, 1530, 1460, 743 cm^{-1}.

β-*[^{14}C-3]Ala hydroxydestruxin B* (**3**). A solution of β-[^{14}C-3]alanine (0.250 mCi, 46.1 mCi/mmol) in 2% aqueous EtOH (2.5 mL) was added to a stirred solution of β-alanine (6 mg, 0.007 mmol) in *tert*-butyl (^{t}Bu) alcohol (1 mL). The solution was cooled to 0°C (ice bath) and NaOH (1 M, 0.074 mL, 0.074 mmol) and a solution of $(Boc)_2O$ (15 mg, 0.081 mmol) in *tert*-butyl alcohol (1.5 mL) were added. After stirring for 22 h at room temperature, the reaction mixture was concentrated to ca. 0.5 mL and diluted with aqueous $KHSO_4$ (0.2 M, 1 mL). The mixture was saturated with NaCl and extracted with EtOAc (1 mL, ×6). The combined organic layers were dried over Na_2SO_4, concentrated, and dried under high vacuum for 30 min to give *tert*-butoxycarbonyl (Boc)-β-[^{14}C-3]Ala (9.6 mg) as a white solid. DCC (16 mg, 0.078 mmol) and DMAP (0.9 mg, 0.007 mmol) were added to a stirred solution of Boc-β-[^{14}C-3]Ala (9.6 mg) and **17** (44 mg, 0.057 mmol) in CH_2Cl_2 (0.5 mL) at 0°C under argon. After 1 h at 0°C and 21 h at room temperature, the mixture was filtered through Celite and the combined filtrate and washings were concentrated and filtered through a plug of SiO_2 eluting first with 50% EtOAc in hexane to remove DCU and then with 80% EtOAc in hexane to obtain the hexadepsipeptide (40 mg). Trifluoroacetic acid (TFA) (0.35 mL) was added to a solution of the hexadepsipeptide (40 mg) in CH_2Cl_2 (0.35 mL) and after 20 min, the mixture was concentrated to dryness. Water (1 mL) was added to the residue and, after cooling the solution to 0 to –5°C (ice-salt bath), HCl (1 M, 0.084 mL, 0.084 mmol) and $NaNO_2$ (6 mg, 0.087 mmol) were added sequentially to the stirred solution. After 20 min, ice cold saturated aqueous $NaHCO_3$ (0.9 mL) and ice cold CH_2Cl_2 (7.5 mL) were added and the biphasic mixture was stirred vigorously at ambient temperature for 20 h. The aqueous layer was saturated with NaCl and extracted with CH_2Cl_2 (×3) and the combined organic layers were dried over Na_2SO_4, concentrated, and fractionated by FCC (60% acetone in hexane) to give β-[^{14}C-3]Ala hydroxydestruxin B (**3**; 9.1 mg, 0.044 mCi).

Synthesis of α− (6) and β−D−Glucosyl Hydroxydestruxin B (5).

*[(4-*O*-(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranos-1-yl))Dhmp]hydroxydestruxin B*. Oven dried powdered 3A molecular seives (80 mg) were added to a stirred solution of hydroxydestruxin B (108 mg, 0.18 mmol) and phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-D-

glucopyranoside (3) (93 mg, 0.15 mmol) in dry CH_3CN (3.5 mL). After 10 min, *N*-bromosuccinimide (recrystallized; 39 mg, 0.22 mmol) was added (4). After 20 min, the mixture was diluted with CH_2Cl_2 and filtered through Celite. The combined filtrate and washings were washed sequentially with 10% $NaHSO_3$ and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (20–60% acetone in hexane) to give recovered hydroxydestruxin B (42 mg, 31%) and a 1.4:1 mixture of β:α glucosides (100 mg, 59%). The glucosides were fractionated by PTLC (80% EtOAc in hexane, ×5) to give the β-glucoside (51 mg) and α-glucoside (36 mg) and a mixture of glucosides (7 mg). Spectroscopic data of the β-glucoside: $[\alpha]_D$ = –90 (*c* 0.96, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.16 (br d, *J* = 9 Hz, 1H), 7.35–7.17 (m, 20H), 7.13 (d, *J* = 9 Hz, 1H), 5.22–5.11 (m, 2H), 4.95–4.73 (m, 6H), 4.63–4.42 (m, 5H), 3.98–3.85 (m, 1H), 3.78–3.26 (m, 8H), 3.21 (s, 3H), 2.94 (dd, *J* = 11.5, 13 Hz, 1H), 2.71 (s, 3H), 2.55 (dd, *J* = 10.5, 18 Hz, 1H), 2.35–2.27 (m, 2H), 2.22 (dd, *J* = 4.5, 18 Hz, 1H), 2.08–1.80 (m, 6H), 1.45–1.23 (m, 3H), 1.34 (s, 3H), 1.31 (s, 3H), 1.28 (d, *J* = 6.5 Hz, 3H), 0.80 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 173.8 (s), 173.6 (s), 171.27 (s), 171.29 (s), 169.9 (s), 169.8 (s), 138.5 (s), 138.4 (s), 138.2 (s), 138.1 (s), 128.7 (d ×6), 128.6 (d ×2), 128.1 (d ×4), 128.0 (d), 127.9 (d ×2), 127.8 (d), 127.7 (d ×2), 127.5 (d ×2), 98.1 (d), 85.4 (d), 82.6 (d), 78.1 (d), 76.7 (s), 76.1 (t), 75.1 (t), 74.8 (t), 74.6 (d), 73.4 (t ×2), 70.7 (d), 69.2 (t), 60.9 (d), 58.3 (d), 55.7 (d), 53.8 (d), 46.4 (t), 43.3 (t), 37.7 (d), 34.6 (t), 33.4 (t), 31.1 (d), 29.1 (t), 28.3 (q), 27.5 (q ×2), 26.8 (q), 24.7 (t), 24.1 (t), 20.3 (q), 19.9 (q), 15.7 (q), 15.5 (q), 11.7 (q); FAB, *m/z* (relative intensity): 1133 ($[M+1]^+$, 15), 592 (23), 154 (100); HR-FAB, *m/z* calcd. for $C_{64}H_{85}N_5O_{13}$: 1132.6222 (M+H); found: 1132.6216; FTIR ν_{max}: 3385, 3294, 2965, 1730, 1671, 1633, 1452, 1069, 737 cm^{-1}. Spectroscopic data of the α-glucoside: $[\alpha]_D$ = –115 (*c* 1.2, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.16 (br d, *J* = 9 Hz, 1H), 7.41–7.09 (m, 21H), 5.24 (d, *J* = 3.5 Hz, 1H), 5.19–5.12 (m, 2H), 4.95–4.70 (m, 5H), 4.70–4.53 (m, 3H), 4.48–4.42 (m, 2H), 4.02–3.90 (m, 1H), 3.88–3.55 (m, 8H), 3.20 (s, 3H), 3. 02 (dd, *J* = 12, 13 Hz, 1H), 2.71 (s, 3H), 2.62 (dd, *J* = 11, 18 Hz, 1H), 2.47 (dd, *J* = 4, 18 Hz, 1H), 2.35–2.25 (m, 2H), 2.12 (dd, *J* = 9, 15 Hz, 1H), 1.96–1.84 (m, 2H), 1.74–1.56 (m, 4H), 1.41–1.20 (m, 3H), 1.33 (s, 3H), 1.29 (s, 3H), 1.28 (d, *J* = 6 Hz, 3H), 0.87 (m, 12H); ^{13}C NMR (75 MHz,

$CDCl_3$) δ: 173.8 (s), 173.6 (s), 171.3 (s), 171.2 (s), 169.9 (s), 169.8 (s), 138.7 (s), 138.2 (s), 138.1 (s), 138.0 (s), 128.76 (d ×2), 128.72 (d ×2), 128.68 (d ×2), 128.63 (d ×2), 128.34 (d), 128.27 (d ×2), 128.19 (d ×2), 128.1 (d ×3), 128.0 (d ×2), 127.9 (d ×2), 91.7 (d), 82.5 (d), 80.5 (d), 78.1 (d), 76.0 (s), 75.8 (t), 75.5 (t), 75.2 (t ×2), 70.7 (d), 70.5 (d), 68.8 (t), 60.9 (d), 58.3 (d), 55.7 (d), 53.8 (d), 46.8 (t), 44.1 (t), 37.6 (d), 34.8 (t), 33.4 (t), 31.1 (d), 29.1 (t), 28.3 (q), 27.5 (q), 27.0 (q), 26.4 (q), 24.0 (t), 23.2 (t), 20.3 (q), 19.9 (q), 15.7 (q), 15.5 (q), 11.6 (q); FAB, *m/z* (relative intensity): 1133 ($[M+1]^+$, 7), 592 (7), 154 (100); HR-FAB, *m/z* calcd. for $C_{64}H_{85}N_5O_{13}$: 1132.6222 (M+H); found: 1132.6226; FTIR ν_{max}: 3387, 3296, 2965, 1730, 1672, 1632, 1452, 1089, 736 cm^{-1}.

[(4-O-β-*D-glucopyranos-1-yl)Dhmp]hydroxydestruxin B* (**5**). A suspension of the tetrabenzyl-β-glucoside (65 mg, 0.057 mmol) and 10% Pd/C in CH_3OH (3 mL) was vigorously stirred under H_2 (balloon). After 1 h, the mixture was filtered. The combined filtrate and washings (CH_2Cl_2) were concentrated and fractionated by FCC (15% CH_3OH in CH_2Cl_2) to provide the product (43 mg, 97%) which was identical (NMR, TLC, HPLC) to the isolated metabolite **5**: $[\alpha]_D^{25}$ = −131 (*c* 0.48, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J* = 9 Hz, 1H), 7.10 (d, *J* = 9 Hz, 1H), 5.13 (m, 2H), 4.97 (d, *J* = 11 Hz, 1H), 4.85 (dd, *J* = 8.5, 6.5 Hz, 1H), 4.62 (d, *J* = 6.5 Hz, 1H), 4.53 (d, *J* = 7 Hz, 1H), 3.99 (m, 2H), 3.77 (m, 3H), 3.49 (m, 2H), 3.22 (m, 2H), 3.22 (s, 3H), 3.08 (br t, *J* = 12 Hz, 1H), 2.70 (s, 3H), 2.67–2.53 (m, 2H), 2.33–2.29 (m, 3H), 2.09–1.90 (m, 5H), 1.41 (m, 1H), 1.34 (s, 3H), 1.33 (s, 3H), 1.30 (d, *J* = 6.5 Hz, 3H), 1.26 (m, 1H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 7 Hz, 3H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.85 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 173.9 (s), 173.7 (s), 171.8 (s), 171.3 (s), 170.6 (s), 170.1 (s), 97.5 (d), 76.9 (d), 76.4 (s), 75.8 (d), 74.2 (d), 71.1 (d), 70.1 (d), 61.8 (t), 61.2 (d), 58.2 (d), 55.8 (d), 53.8 (d), 47.1 (t), 43.7 (t), 37.5 (d), 34.9 (t), 33.5 (t), 31.1 (q), 29.8 (t), 28.4 (q), 27.4 (d), 27.3 (q), 27.2 (q), 24.6 (t), 24.2 (t), 20.2 (q), 19.8 (q), 15.6 (q), 15.4 (q), 11.6 (q); FAB, *m/z* (relative intensity): 772 ($[M+1]^+$, 100), 592 (23), 86 (87); HR-FAB *m/z* calcd. for $C_{36}H_{62}N_5O_{13}$ (772.4344), found 772.4340; FTIR ν_{max}: 3380, 2966, 1730, 1635, 1446, 1176, 1079 cm^{-1}.

[(4-O-α-*D-glucopyranos-1-yl)Dhmp]hydroxydestruxin B* (**6**). Hydrogenolysis of the tetrabenzyl-α-glucoside (34 mg, 0.03 mmol) as above gave **6** (22 mg, 95%): $[\alpha]_D$= –146 (*c* 1.8,

CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, *J* = 9 Hz, 1H), 7.08 (d, *J* = 9 Hz, 1H), 5.17 (q, *J* = 7 Hz, 1H), 5.12 (d, *J* = 3.5 Hz, 1H), 5.08 (dd, *J* = 9.5, 2 Hz, 1H), 4.92 (d, *J* = 11 Hz, 1H), 4.82 (dd, *J* = 9, 7 Hz, 1H), 4.62 (d, *J* = 7 Hz, 1H), 3.96 (m, 2H), 3.74 (m, 3H), 3.54 (m, 4H), 3.20 (s, 3H), 3.05 (br t, *J* = 12 Hz, 1H), 2.69 (s, 3H), 2.66 (m, 2H), 2.40 (m, 1H), 2.26 (m, 3H), 1.97 (m, 5H), 1.34 (s, 3H), 1.33 (s, 3H), 1.30 (d, *J* = 6.5 Hz, 3H), 1.26 (m, 1H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 7 Hz, 3H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.85 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 173.8 (s ×2), 171.4 (s ×2), 170.4 (s), 170.1 (s), 93.3 (d), 76.4 (d), 74.7 (s), 72.1 (d), 71.9 (d), 71.0 (d), 70.5 (d), 62.1 (t), 61.1 (d), 58.4 (d), 55.7 (d), 54.0 (d), 47.1 (t), 42.8 (t), 37.5 (d), 34.7 (t), 33.7 (t), 31.1 (q), 29.4 (t), 28.4 (q), 27.9 (d), 27.5 (q), 25.6 (q), 24.7 (t), 24.3 (t), 20.2 (q), 19.8 (q), 15.6 (q), 15.4 (q), 11.5 (q); FAB, *m/z* (relative intensity): 772 ($[M+1]^+$, 100), 592 (19), 86 (49); HR-FAB, *m/z* calcd. for $C_{36}H_{62}N_5O_{13}$ (772.4344), found 772.4330; FTIR ν_{max}: 3384, 2966, 1730, 1631, 1444, 1174, 1025 cm^{-1}.

Synthesis of β−D−Tetracetylglucosyl Hydroxydestruxin B (7). Acetic anhydride (4 drops) was added to a stirred solution of **5** (5.5 mg, 0.0071 mmol) in pyridine (8 drops) at ambient temperature. After 17 h, toluene was added and reaction mixture and evaporated to dryness. The residue was fractionated by FCC (50% acetone in hexane) to give product **7** (6 mg, 90%): ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 9 Hz, 1H), 5.23 (t, *J* = 9.5 Hz, 1H), 5.18 (br q, *J* = 7 Hz, 1H), 5.08 (dd, *J* = 10, 2 Hz, 1H), 5.01 (dd, *J* = 9.5, 9.5 Hz, 1H), 4.96 (dd, *J* = 9.5, 8 Hz, 1H), 4.93 (d, *J* = 11 Hz, 1H), 4.86 (dd, *J* = 9, 7 Hz, 1H), 4.70 (d, *J* = 8 Hz, 1H), 4.62 (d, *J* = 7 Hz, 1H), 4.26 (dd, *J* = 12, 6 Hz, 1H), 4.05 (m, 2H), 3.86 (br t, *J* = 8.5 Hz, 1H), 3.72 (ddd, *J* = 10, 6, 2 Hz, 1H), 3.59 (m, 1H), 3.22 (s, 3H), 3.07 (t, *J* = 12.5 Hz, 1H), 2.72 (s, 3H), 2.67 (ddd, *J* = 18, 11.5, 1.5 Hz, 1H), 2.50 (dd, *J* = 18, 4.5 Hz, 1H), 2.44 (m, 1H), 2.31 (m, 1H), 2.09–1.92 (m, 6H), 2.06 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 1.97 (s, 3H), 1.44 (m, 1H), 1.33–1.26 (m, 1H), 1.31 (s, 3H), 1.30 (d, *J* = 6 Hz, 3H), 1.26 (s, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.86 (t, *J* = 7.5 Hz, 3H), 0.86 (d, *J* = 7 Hz, 3H); FAB, *m/z* (relative intensity): 940 ($[M+1]^+$, 100), 592 (10), 169 (27); HR-FAB, *m/z* calcd. for $C_{44}H_{70}N_5O_{17}$ (940.4767), found 940.4778; FTIR ν_{max}: 3296, 2966, 1755, 1668, 1630, 1224, 1037 cm^{-1}.

Abbreviations: All, allyl; Boc, *tert*-butoxycarbonyl; Cbz, benzyloxycarbonyl; DCC, *N,N'*-dicyclohexylcarbodiimide; Dhmp, (*2R*)-2,4-dihydroxy-4-methylpentanoic acid; DMAP, 4-(dimethylamino)pyridine; FAB, fast atom bombardment; FCC, flash column chromatography; FTIR, Fourier transform infrared; HOBt, 1-hydroxybenzotriazole; LSC, liquid scintillation counting; PTLC, preparative TLC; ^{t}Bu, *tert*-butyl; TES, triethylsilyl; TFA, trifluoroacetic acid.

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