Supporting Information

Synthesis of an α-Helix Mimetic Library Targeting Protein–Protein Interactions

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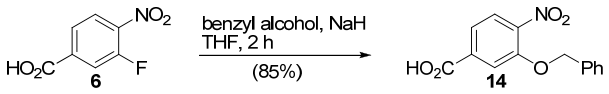
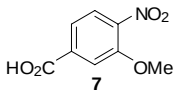
Experimental Section

Sources 1-Hydroxy-7-azabenzotriazole (HOAt) was obtained from CS BiO (Menlo Park, CA). Amino acids were obtained from Chem-Impex International (Wood Dale, IL). Sulfonyl chloride polystyrene resin was obtained from EMD Biosciences (San Diego, CA). All other reagents were obtained from Aldrich Chemical (Milwaukee, WI) or Acros Organics (Morris Plains, NJ) and used without further purification. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl.

General Procedure for the Preparation of the Aryl Monomers

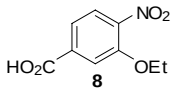


Sodium hydride (60%, 0.50 g, 12.4 mmol) was suspended in THF (10 mL) and benzyl alcohol (0.67 mL, 6.48 mmol) was added dropwise at 0 °C. The mixture was stirred at 0 °C for 15 min under an atmosphere of argon before fluoride **6** (1.0 g, 5.4 mmol) was added. The mixture was stirred at 0 °C for 5 min and room temperature for 2 h, quenched with saturated aqueous NH_4Cl, diluted with EtOAc, and extracted with aqueous HCl (0.1 M, × 2). The organic layer was collected, concentrated, and the product purified by chromatography (SiO_2, 3:2:0.1 hexanes/Et_2O/HOAc) to give **14** as a solid (1.26 g, 85%). R_f = 0.30 (1:1:0.04 hexanes/Et_2O/HOAc); ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 13.66 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.87 (s, 1H), 7.66 (d, J = 10.0 Hz, 1H), 7.41 (m, 5H), 5.39 (s, 2H); HRMS-ESI (*m/z*) calcd for $[C_{14}H_{11}NO_5+Na]^+$ 296.0529; found: 296.0532.



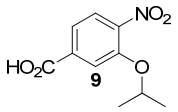
7. ^{1}H NMR (400 MHz, acetone-d_6, 25°C) δ 9.94 (s, 1H) 7.93 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 1.4 Hz, 1H), 7.77 (dd, J = 8.3, 1.5 Hz, 1H), 4.08 (s, 3H); HRMS-ESI (*m/z*) calcd for $[C_8H_7NO_5+H]^+$ 198.0397;

found: 198.0395.



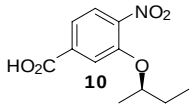
8

8. ^{1}H NMR (400 MHz, acetone-d_6, 25°C) δ 11.75 (s, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.81 (d, J = 1.5 Hz, 1H), 7.72 (dd, J = 8.3, 1.6 Hz, 1H), 4.32 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_9H_9NO_5+H]^+$ 212.0553; found: 212.0553.



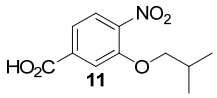
9

9. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 9.71 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.84 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 4.92 (septet, J = 6.0 Hz, 1H), 1.37 (d, J = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{10}H_{11}NO_5+Na]^+$ 248.0529; found: 248.0528.



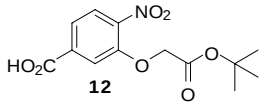
10

10. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.76 (s, 1H), 7.85 (d, J = 8.3 Hz, 1H), 7.82 (d, J = 1.5 Hz, 1H), 7.70 (dd, J = 8.3, 1.6 Hz, 1H), 4.73 (sextet, J = 6.0 Hz, 1H), 1.80-1.64 (m, 2H), 1.33 (d, J = 6.1 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{11}H_{13}NO_5+H]^+$ 240.0866; found: 240.0873.



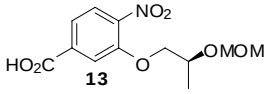
11

11. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 10.80 (s, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.83 (d, J = 1.5 Hz, 1H), 7.74 (dd, J = 8.3, 1.6 Hz, 1H), 4.07 (d, J = 6.4 Hz, 2H), 2.13 (septet, J = 6.6 Hz, 1H), 1.06 (d, J = 6.7 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{11}H_{13}NO_5-H]^-$ 238.0721; found: 238.0720.



12

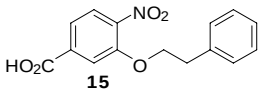
12. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.82 (s, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.77 (dd, J = 8.3, 1.4 Hz, 1H), 7.73 (d, J = 1.5 Hz, 1H), 4.92 (s, 2H), 1.43 (s, 9H); HRMS-ESI (*m/z*) calcd for $[C_{13}H_{15}NO_7+Na]^+$ 320.0741; found: 320.0739.



13

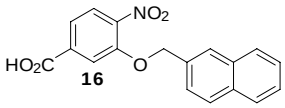
13. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.82 (s, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.87 (d, J = 1.5

Hz, 1H), 7.76 (dd, *J* = 8.3, 1.6 Hz, 1H), 4.70 (q, *J* = 6.8 Hz, 2H), 4.27 (d, *J* = 5.2 Hz, 2H), 4.17-4.08 (m, 1H), 3.32 (s, 3H), 1.30 (d, *J* = 6.4 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{12}H_{15}NO_7+Na]^+$ 308.0741; found: 308.0740.



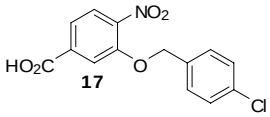
15

15. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.78 (s, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 1.5 Hz, 1H), 7.74 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.40-7.19 (m, 5H), 4.50 (t, *J* = 6.6 Hz, 2H), 3.15 (t, *J* = 6.6 Hz, 2H); HRMS-ESI (*m/z*) calcd for $[C_{15}H_{13}NO_5+H]^+$ 288.0866; found: 288.0864.



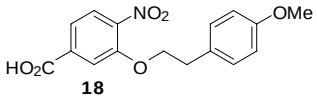
16

16. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) δ 13.63 (s, 1H), 8.03-7.89 (m, 6H), 7.67 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.59 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.57-7.52 (m, 2H), 5.56 (s, 2H); HRMS-ESI (*m/z*) calcd for $[C_{19}H_{15}NO_5+H]^+$ 338.1023; found: 337.1043.



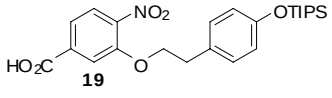
17

17. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.84 (s, 1H), 7.98-7.94 (m, 2H), 7.79 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.49-7.44 (m, 2H), 5.45 (s, 2H); HRMS-ESI (*m/z*) calcd for $[C_{14}H_{10}ClNO_5+Na]^+$ 330.014; found: 330.0137.



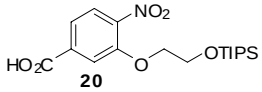
18

18. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.78 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 1.5 Hz, 1H), 7.73 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.44 (t, *J* = 6.7 Hz, 2H), 3.76 (s, 3H), 3.08 (t, *J* = 6.6 Hz, 2H); HRMS-ESI (*m/z*) calcd for $[C_{16}H_{15}NO_6+Na]^+$ 340.0792; found: 340.0789.



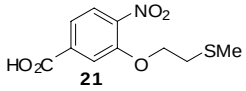
19

19. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.78 (s, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 1.52 Hz, 1H), 7.73 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.45 (t, *J* = 6.7 Hz, 2H), 3.08 (t, *J* = 6.7 Hz, 2H), 1.34-1.22 (m, 3H), 1.11 (d, *J* = 7.2 Hz, 18H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{33}NO_6Si+Na]^+$ 482.1969; found: 482.1964.



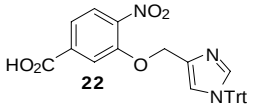
20

20. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.79 (s, 1H), 7.94 (d, J = 1.5 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 7.75 (dd, J = 8.3, 1.6 Hz, 1H), 4.43 (t, J = 4.6 Hz, 2H), 4.15 (t, J = 4.6 Hz, 2H), 1.24-0.95 (m, 21H); HRMS-ESI (*m/z*) calcd for $[C_{18}H_{29}NO_6Si+H]^+$ 384.1837; found: 384.1838.



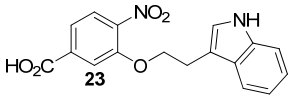
21

21. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.81 (s, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 1.5 Hz, 1H), 7.77 (dd, J = 8.3, 1.6 Hz, 1H), 4.49 (t, J = 6.6 Hz, 2H), 2.94 (t, J = 6.5 Hz, 2H), 2.21 (s, 3H); HRMS-ESI (*m/z*) calcd for $[C_{10}H_{11}NO_5S+Na]^+$ 280.025; found: 280.0253.



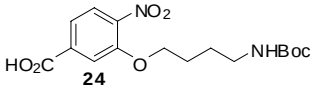
22

22. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) δ 13.58 (s, 1H), 7.99 (s, 1H), 7.93-7.87 (m, 2H), 7.62 (d, J = 8.4 Hz, 1H), 7.40-7.33 (m, 10H), 7.23 (s, 1H), 7.08-7.00 (m, 6H), 5.28 (s, 2H); HRMS-ESI (*m/z*) calcd for $[C_{30}H_{23}N_3O_5+H]^+$ 506.1710; found: 506.1705.



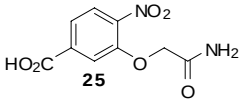
23

23. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.91 (s, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.77 (s, 1H), 7.60 (t, J = 9.0 Hz, 2H), 7.34 (d, J = 7.8 Hz, 1H), 7.23 (s, 1H), 7.07 (t, J = 7.2 Hz, 1H), 6.98 (t, J = 7.2 Hz, 1H), 4.44 (t, J = 6.6 Hz, 2H). 3.17 (t, J = 6.0 Hz, 2H); HRMS-MALDI (*m/z*) calcd for $[C_{17}H_{14}N_2O_5+Na]^+$ 349.0795; found: 349.0787.



24

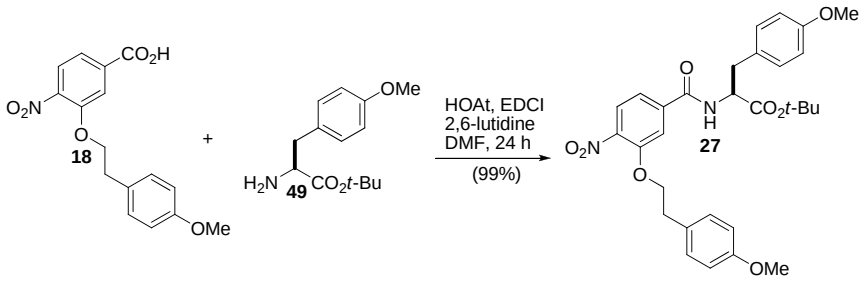
24. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 11.78 (s, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.81 (d, J = 1.4 Hz, 1H), 7.71 (dd, J = 8.3, 1.6 Hz, 1H), 5.97 (s, 1H), 4.29 (t, J = 6.3 Hz, 2H), 3.12 (q, J = 6.7 Hz, 2H), 1.88-1.80 (m, 2H), 1.70-1.61 (m, 2H), 1.36 (s, 9H); HRMS-ESI (*m/z*) calcd for $[C_{16}H_{22}N_2O_7+H]^+$ 355.15; found: 355.1500.



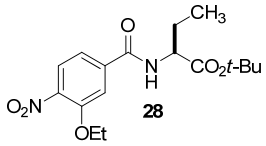
25

25. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) δ 13.65 (s, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.69-7.63 (m, 2H), 7.47 (d, J = 6.1 Hz, 2H), 4.76 (s, 2H); HRMS-ESI (*m/z*) calcd for $[C_9H_8N_2O_6+H]^+$ 241.0455; found: 241.0453.

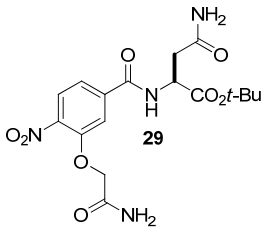
General Procedure for the Preparation of Dimers



27. Monomer **18** (95 mg, 0.30 mmol) was combined with amine **49** (88 mg, 0.35 mmol) in DMF (0.75 mL) in a 0.5 dram vial. HOAt (61 mg, 0.45 mmol), EDCI (69 mg, 0.36 mmol), and 2,6-lutidine (0.17 mL, 1.5 mmol) were added. The mixture was agitated on a titer plate shaker for 24 h, diluted with EtOAc/Et_2O, extracted with aqueous HCl (0.1 M, × 2) and saturated aqueous $NaHCO_3$ (× 1). The organic layer was collected, dried (Na_2SO_4), and concentrated to give **27** as a solid (163 mg, 99%) that was homogeneous by TLC analysis. R_f = 0.33 (7:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.67 (d, *J* = 8.3 Hz, 1H), 7.38 (d, *J* = 1.4 Hz, 1H), 7.14 (m, 6H), 6.82 (m, 4H), 4.87 (q, *J* = 6.2 Hz, 1H), 4.18 (t, *J* = 6.7 Hz, 2H), 3.75 (s, 3H), 3.73 (s, 3H), 3.20 (dd, *J* = 6.1, 14.0 Hz, 1H), 3.10 (dd, *J* = 6.3, 14.0 Hz, 1H), 3.02 (t, *J* = 6.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.9, 164.5, 158.5, 158.2, 151.8, 141.0, 138.7, 130.2, 130.0, 129.3, 127.7, 125.2, 117.7, 113.7, 113.4, 82.6, 70.5, 55.0, 54.3, 36.6, 34.3, 27.8; HRMS-ESI (*m/z*) calcd for $[C_{30}H_{34}N_2O_8+H]^+$ 551.2388; found: 551.2382.

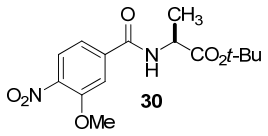


28. The product was obtained as a solid (96%) that was homogeneous by TLC analysis. R_f = 0.25 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.75 (d, *J* = 8.3 Hz, 1H), 7.52 (s, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.25 (d, *J* = 7.4 Hz, 1H), 4.64 (m, 1H), 4.19 (q, *J* = 6.8 Hz, 2H), 2.01 (m, 1H), 1.82 (m, 1H), 1.52 (s, 9H), 1.46 (t, *J* = 7.0 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 172.1, 164.8, 152.0, 141.4, 138.6, 125.2, 117.7, 113.8, 82.6, 65.5, 54.4, 27.9, 25.4, 14.4, 9.5; HRMS-ESI (*m/z*) calcd for $[C_{17}H_{24}N_2O_6+H]^+$ 353.1707; found: 353.1708.



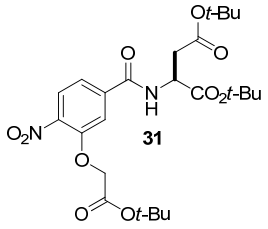
29. The product was obtained as a solid (77%) that was homogeneous by TLC analysis. R_f = 0.33 (10:1

CH_2Cl_2/MeOH); ^{1}H NMR (300 MHz, CD_3OD, 25 °C) δ 8.02 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 1.6 Hz, 1H), 7.58 (dd, *J* = 1.6, 8.4 Hz, 1H), 4.83 (dd, *J* = 5.7, 7.1 Hz, 1H), 4.78 (s, 2H), 2.85 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD, 25 °C) δ 174.9, 172.3, 171.4, 167.5, 152.1, 142.6, 141.0, 127.2, 121.6, 115.7, 83.4, 69.0, 52.2, 37.5, 28.2; HRMS-ESI (*m/z*) calcd for $[C_{17}H_{22}N_4O_8+H]^+$ 411.1510; found: 411.1505.



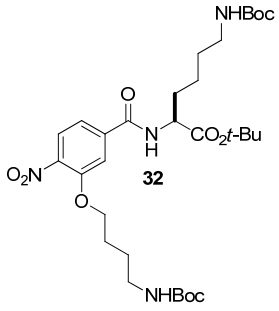
30

30. The product was obtained as a solid (95%) that was homogeneous by TLC analysis. R_f = 0.36 (3:2 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.80 (d, *J* = 8.3 Hz, 1H), 7.56 (d, *J* = 1.5 Hz, 1H), 7.32 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 1H), 4.65 (p, *J* = 7.1 Hz, 1H), 3.97 (s, 3H), 1.49 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 172.8, 164.7, 153.1, 141.5, 139.3, 125.8, 118.2, 113.3, 83.0, 57.0, 49.5, 28.2, 18.7; HRMS-ESI (*m/z*) calcd for $[C_{15}H_{20}N_2O_6+H]^+$ 325.1394; found: 325.1391.



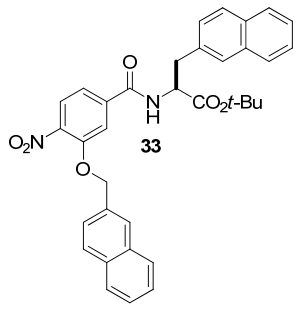
31

31. The product was obtained as a solid (95%) that was homogeneous by TLC analysis. R_f = 0.35 (7:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.89 (d, *J* = 8.3 Hz, 1H), 7.52 (s, 1H), 7.41 (d, *J* = 8.4, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 4.84 (m, 1H), 4.74 (s, 2H), 2.99 (dd, *J* = 3.6, 17.1 Hz, 1H), 2.84 (dd, *J* = 3.7, 17.2 Hz, 1H), 1.47 (m, 27 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.9, 164.9, 151.5, 142.4, 138.9, 125.3, 117.1, 115.2, 82.6, 77.6, 57.2, 38.3, 28.9, 28.0, 25.5,18.9, 15.3, 11.7, 9.4; HRMS-ESI (*m/z*) calcd for $[C_{25}H_{36}N_2O_{10}+H]^+$ 525.2443; found: 525.2444.

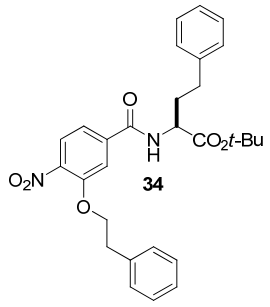


32

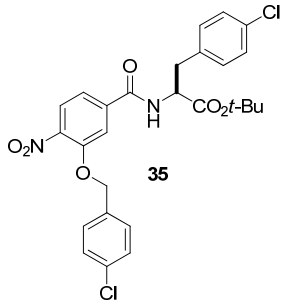
32. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.37 (1:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.79 (d, *J* = 8.3 Hz, 1H), 7.56 (d, *J* = 1.1 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 4.84 (t, *J* = 5.1 Hz, 1H), 4.75 (t, *J* = 5.5 Hz, 1H), 4.63 (q, *J* = 7.2 Hz, 1H), 4.16 (t, *J* = 6.0 Hz, 2H), 3.14 (m, 4H), 1.87 (m, 4H), 1.69 (m, 4H), 1.55 (m, 2H), 1.50 (s, 9H), 1.44 (s, 9H), 1.39 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 171.7, 165.0, 156. 0, 152.0, 141.2, 138.9, 125.3, 118.1, 113.8, 82.5, 78.9, 69.2, 53.3, 39.8, 31.6, 29.6, 28.3, 28.2, 27.9, 26.4, 26.0, 22.4; HRMS-ESI (*m/z*) calcd for $[C_{31}H_{50}N_4O_{10}+H]^+$ 639.3600; found: 639.3597.



33. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.22 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.71 (m, 8 H), 7.62 (s, 1H), 7.49 (s, 1H), 7.41 (m, 5 H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 7.3 Hz, 1H), 5.18 (m, 2 H), 5.01 (q, *J* = 6.0 Hz, 1H), 3.38 (m, 2H), 1.45 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.7, 164.6, 151.6, 141.5, 138.8, 133.4, 133.2, 133.0, 132.3, 128.4, 128.1, 128.0, 127.6, 127.4, 127.3, 126.2, 125.7, 125.5, 124.6, 118.1, 114.1, 83.0, 71.1, 54.2, 37.7, 27.9; HRMS-ESI (*m/z*) calcd for $[C_{35}H_{32}N_2O_6+H]^+$ 577.2333; found: 577.2325.

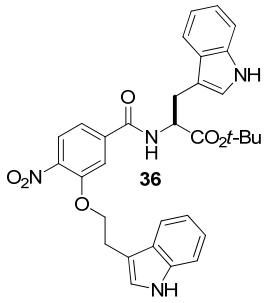


34. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.31 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.69 (d, *J* = 8.3 Hz, 1H), 7.41 (d, *J* = 1.5 Hz, 1H), 7.21 (m, 12H), 4.74 (m, 1H), 4.25 (m, 2 H), 3.10 (t, *J* = 6.7 Hz, 2H), 2.72 (t, *J* = 7.0 Hz, 2H), 2.26 (m, 1 H), 2.11 (m, 1 H), 1.50 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 171.8, 164.6, 151.9, 141.2, 140.6, 138.5, 137.3, 129.1, 128.5, 128.4, 128.2, 126.6, 126.2, 125.2, 117.8, 113.6, 82.8, 70.4, 53.3, 35.4, 33.7, 31.8, 27.9; HRMS-ESI (*m/z*) calcd for $[C_{29}H_{32}N_2O_6+H]^+$ 505.2333; found: 505.2330.



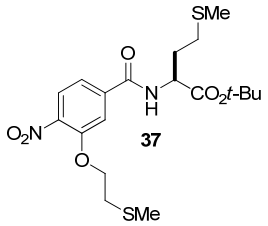
35. The product was obtained as a solid (99%) that was homogeneous by TLC analysis. R_f = 0.33 (1:1 hexanes/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.80 (d, *J* = 8.3 Hz, 1H), 7.52 (s, 1H), 7.35 (m, 4H), 7.25 (m, 3H), 7.12 (m, 2H), 6.96 (d, *J* = 7.3 Hz, 1H), 5.17 (s, 2H), 4.90 (q, *J* = 6.0 Hz, 1H), 3.25

(dd, J = 6.2, 14.0 Hz, 1H), 3.15 (dd, J = 5.8, 13.9 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.6, 164.4, 151.5, 141.6, 138.7, 134.4, 134.1, 133.4, 133.0, 130.7, 128.8, 128.5, 128.4, 125.7, 118.2, 114.2, 83.3, 70.4, 54.1, 37.0, 27.9; HRMS-ESI (*m/z*) calcd for $[C_{27}H_{26}Cl_2N_2O_6+H]^+$ 545.1241; found: 545.1246.



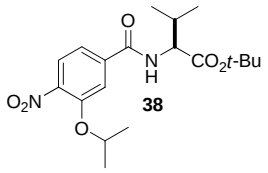
36

36. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.46 (1:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.29 (m, 2H), 7.48 (m, 3H), 7.06 (m, 10H), 6.64 (d, J = 7.6 Hz, 1H), 4.94 (q, J = 5.5 Hz, 1H), 3.95 (m, 2H), 3.39 (dd, J = 5.6, 14.9 Hz, 1H), 3.27 (dd, J = 5.6, 14.9 Hz, 1H), 3.06 (t, J = 6.5 Hz, 2H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.9, 165.1, 151.9, 140.9, 138.7, 135.9, 127.6, 127.1, 125.2, 122.9, 122.8, 122.1, 121.8, 119.6, 119.2, 118.4, 118.3, 117.9, 113.2, 111.3, 111.2, 111.1, 109.6, 82.7, 69.6, 54.1, 27.9, 27.1, 24.6; HRMS-ESI (*m/z*) calcd for $[C_{32}H_{32}N_4O_6+H]^+$ 569.2394; found: 569.2386.



37

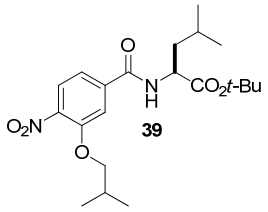
37. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.35 (7:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.81 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 1.5 Hz, 1H), 7.38 (dd, J = 1.6, 8.3 Hz, 1H), 7.30 (d, J = 7.6 Hz, 1H), 4.80 (m, 1H), 4.33 (t, J = 6.6 Hz, 2H), 2.93 (t, J = 6.7 Hz, 2H), 2.60 (t, J = 7.8 Hz, 2H), 2.25 (m, 1H), 2.23 (s, 3H), 2.13 (s, 3H), 2.09 (m, 1H), 1.52 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 171.1, 164.7, 151.7, 141.5, 138.7, 125.5, 118.2, 114.0, 83.0, 69.7, 52.9, 32.5, 31.4, 30.1, 27.9, 16.3, 15.5; HRMS-ESI (*m/z*) calcd for $[C_{19}H_{28}N_2O_6S_2+H]^+$ 445.1461; found: 445.1465.



38

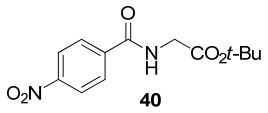
38. The product was obtained as a solid (96%) that was homogeneous by TLC analysis. R_f = 0.34 (7:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.77 (d, J = 8.3 Hz, 1H), 7.61 (s, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.89 (d, J = 8.3 Hz, 1H), 4.77 (m, 1H), 4.65 (dd, J = 4.6, 8.4 Hz, 1H), 2.30 (m, 1H), 1.51 (s, 9H), 1.40 (d, J = 6.0 Hz, 6H), 1.02 (d, J = 5.7 Hz, 3H), 1.00 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz,

$CDCl_3$, 25 °C) δ 171.1, 165.2, 151.2, 142.5, 138.8, 125.2, 117.3, 115.5, 82.5, 72.8, 58.0, 31.6, 28.0, 21.7, 18.9, 17.8; HRMS-ESI (*m/z*) calcd for $[C_{19}H_{28}N_2O_6+H]^+$ 381.2020; found: 381.2018.



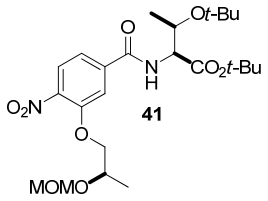
39

39. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.32 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.70 (d, *J* = 8.3 Hz, 1H), 7.44 (d, *J* = 1.5 Hz, 1H), 7.42 (s, 1H), 7.30 (dd, *J* = 1.6, 8.4 Hz, 1H), 4.73 (m, 1H), 3.83 (m, 2H), 2.12 (m, 1H), 1.73 (m, 3H), 1.54 (s, 9H), 1.04 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.2 Hz, 3H), 0.98 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 173.3, 164.7, 152.2, 141.2, 138.3, 125.1, 117.4, 113.7, 82.6, 75.7, 52.0, 41.2, 28.1, 28.0, 25.0, 22.7, 21.8, 18.9, 18.8; HRMS-ESI (*m/z*) calcd for $[C_{21}H_{32}N_2O_6+H]^+$ 409.2333; found: 409.2327.



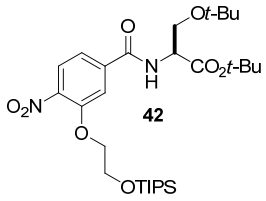
40

40. The product was obtained as a solid (95%) that was homogeneous by TLC analysis. R_f = 0.40 (1:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.28 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.8 Hz, 2H), 6.93 (s, 1H), 4.15 (d, *J* = 5.0 Hz, 2H), 1.51 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 168.9, 165.2, 149.6, 139.3, 128.2, 123.8, 83.0, 42.6, 28.0; HRMS-ESI (*m/z*) calcd for $[C_{13}H_{16}N_2O_5+Na]^+$ 303.0951; found: 303.0953.

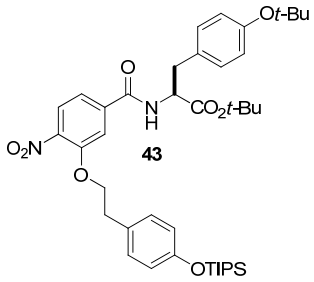


41

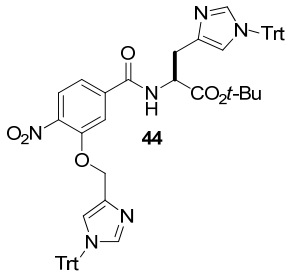
41. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.38 (7:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.90 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 1.5 Hz, 1H), 7.40 (dd, *J* = 1.6, 8.3 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 1H), 4.78 (d, *J* = 6.9 Hz, 1H), 4.74 (d, *J* = 6.9 Hz, 1H), 4.56 (dd, *J* = 2.0, 9.0 Hz, 1H), 4.32 (qd, *J* = 2.0, 6.2 Hz, 1H), 4.15 (m, 3H), 3.39 (s, 3H), 1.50 (s, 9H), 1.33 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.3 Hz, 3H), 1.21 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 169.4, 165.5, 152.1, 141.3, 139.4, 125.6, 118.0, 114.1, 95.5, 82.2, 74.0, 73.3, 70.8, 67.2, 58.9, 55.3, 28.6, 28.0, 21.1, 17.2; HRMS-ESI (*m/z*) calcd for $[C_{24}H_{38}N_2O_9+H]^+$ 499.2650; found: 499.2646.



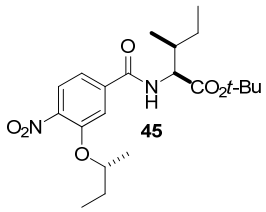
42. The product was obtained as a solid (97%) that was homogeneous by TLC analysis. R_f = 0.33 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.83 (d, *J* = 8.3 Hz, 1H), 7.67 (s, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 4.78 (dt, *J* = 2.6, 8.1 Hz, 1H), 4.29 (t, *J* = 5.2 Hz, 2H), 4.10 (t, *J* = 5.1 Hz, 2H), 3.89 (dd, *J* = 2.6, 8.9 Hz, 1H), 3.68 (dd, *J* = 2.8, 8.9 Hz, 1H), 1.51 (s, 9H), 1.17 (s, 9H), 1.08 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 169.2, 164.9, 152.3, 141.6, 139.2, 125.4, 118.0, 114.4, 82.3, 73.2, 71.2, 62.0, 61.7, 53.8, 28.0, 27.3, 17.8, 11.8; HRMS-ESI (*m/z*) calcd for $[C_{29}H_{50}N_2O_8Si+H]^+$ 583.3409; found: 583.3401.



43. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.36 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.75 (d, *J* = 8.3 Hz, 1H), 7.46 (s, 1H), 7.12 (m, 5H), 6.87 (m, 5H), 4.88 (q, *J* = 6.1 Hz, 1H), 4.24 (t, *J* = 6.9 Hz, 2H), 3.17 (dd, *J* = 2.6, 6.2 Hz, 2H), 3.05 (t, *J* = 6.7 Hz, 2H), 1.44 (s, 9H), 1.31 (s, 9H), 1.24 (m, 3H), 1.09 (d, *J* = 7.0 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.7, 164.5, 154.7, 154.4, 152.1, 141.3, 138.8, 130.6, 130.0, 129.8, 129.5, 125.4, 124.1, 119.8, 117.6, 113.7, 82.8, 78.3, 70.8, 54.2, 37.1, 34.6, 28.7, 27.9, 17.8, 12.5; HRMS-ESI (*m/z*) calcd for $[C_{41}H_{58}N_2O_8Si+H]^+$ 735.4035; found: 735.4024.

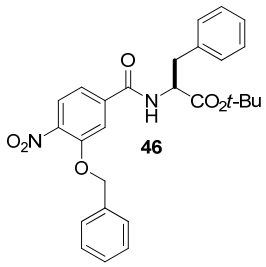


44. The product was obtained as a solid (91%) that was homogeneous by TLC analysis. R_f = 0.25 (5:0.1 CH_2Cl_2/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.94 (d, *J* = 1.2 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.51 (dd, *J* = 1.3, 8.4 Hz, 1H), 7.43 (m, 2H), 7.30 (m, 19H), 7.11 (m, 12H), 7.00 (m, 1H), 6.64 (s, 1H), 5.21 (m, 2H), 4.85 (m, 1H), 3.08 (m, 2H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 169.8, 164.6, 151.7, 142.0, 141.4, 139.1, 138.9, 138.6, 136.3, 135.4, 129.5, 127.9, 125.3, 121.2, 119.3, 118.7, 115.2, 81.4, 75.3, 75.1, 66.2, 53.2, 29.2, 27.9; HRMS-ESI (*m/z*) calcd for $[C_{59}H_{52}N_6O_6+H]^+$ 941.4021; found: 941.3996.



45

45. The product was obtained as a solid (100%) that was homogeneous by TLC analysis. R_f = 0.40 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.77 (d, *J* = 8.3 Hz, 1H), 7.60 (d, *J* = 1.2 Hz, 1H), 7.29 (dd, *J* = 1.6, 8.3 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 4.68 (dd, *J* = 4.5, 8.1 Hz, 1H), 4.56 (m, 1H), 2.02 (m, 1H), 1.75 (m, 2H), 1.56 (m, 1H), 1.51 (s, 9H), 1.35 (d, *J* = 6.1 Hz, 3H), 1.28 (m, 1H), 0.99 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.9, 164.9, 151.5, 142.4, 138.9, 125.3, 117.1, 115.2, 82.6, 77.6, 57.2, 38.3, 28.9, 28.0, 25.5, 18.9, 15.3, 11.7, 9.4; HRMS-ESI (*m/z*) calcd for $[C_{21}H_{32}N_2O_6+H]^+$ 409.2333; found: 409.2334.



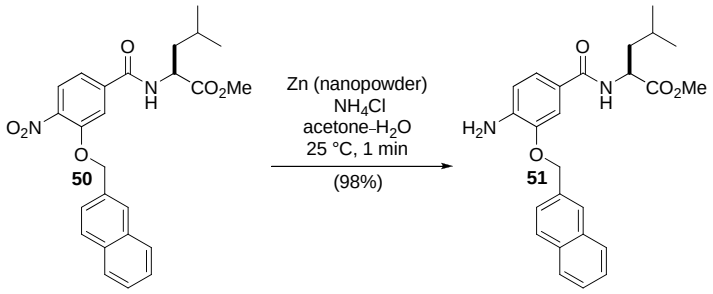
46

46. The product was obtained as a solid (99%) that was homogeneous by TLC analysis. R_f = 0.37 (4:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.77 (d, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 1.4 Hz, 1H), 7.30 (m, 11H), 6.91 (d, *J* = 7.5 Hz, 1H), 5.19 (s, 2H), 4.92 (q, *J* = 6.0 Hz, 1H), 3.23 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 170.7, 164.5, 151.7, 141.6, 138.8, 135.8, 134.9, 129.4, 128.6, 128.4, 128.3, 127.1, 125.5, 118.1, 114.3, 82.9, 71.1, 54.1, 37.7, 27.9; HRMS-ESI (*m/z*) calcd for $[C_{27}H_{28}N_2O_6+H]^+$ 477.2020; found: 477.2014.

	[PheCl]	[Ala]	[Phe]	[Trp]	[Asp]	[Gly]	[TyrMe]	[Thr]	[Val]	[Ser]	[Tyr]	[Met]	[His]	[Leu]	[Ile]	[Lys]	[Abu]	[Asn]	[Nap]	[HoPhe]
PheCl	162mg 99%	105mg 100%	154mg 100%	145mg 100%	159mg 99%	124mg 100%	162mg 97%	159mg 100%	115mg 100%	130mg 96%	210mg 100%	120mg 100%	175mg 100%	144mg 100%	122mg 100%	178mg 100%	133mg 99%	120mg 100%	167mg 99%	157mg 100%
Ala	125mg 96%	92mg 95%	111mg 92%	137mg 100%	140mg 100%	87mg 99%	248mg 93%	113mg 91%	104mg 98%	135mg 96%	153mg 94%	121mg 100%	177mg 93%	105mg 96%	99mg 90%	145mg 100%	100mg 99%	102mg 93%	127mg 94%	119mg 96%
Phe	152mg 99%	114mg 95%	142mg 99%	162mg 100%	156mg 100%	114mg 100%	315mg 100%	145mg 99%	119mg 93%	168mg 100%	190mg 100%	137mg 99%	191mg 90%	129mg 97%	120mg 90%	167mg 100%	120mg 97%	127mg 95%	154mg 97%	145mg 99%
Trp	172mg 100%	146mg 100%	160mg 100%	176mg 100%	173mg 100%	132mg 100%	339mg 100%	165mg 100%	130mg 93%	159mg 91%	172mg 87%	155mg 100%	240mg 100%	149mg 100%	147mg 100%	191mg 100%	143mg 100%	152mg 100%	178mg 100%	164mg 100%
Asp	163mg 100%	132mg 100%	142mg 95%	170mg 100%	150mg 95%	122mg 100%	330mg 100%	160mg 100%	144mg 100%	178mg 100%	168mg 87%	155mg 100%	196mg 89%	138mg 99%	146mg 100%	177mg 100%	128mg 97%	129mg 92%	165mg 100%	147mg 95%
Gly	109mg 86%	82mg 88%	103mg 89%	124mg 94%	101mg 82%	80mg 95%	246mg 95%	111mg 93%	88mg 87%	116mg 85%	147mg 92%	100mg 90%	148mg 80%	95mg 90%	100mg 95%	118mg 84%	83mg 85%	86mg 81%	107mg 82%	107mg 89%
TyrMe	161mg 99%	130mg 100%	159mg 100%	173mg 100%	162mg 100%	124mg 100%	163mg 99%	158mg 100%	133mg 97%	184mg 99%	209mg 100%	147mg 100%	217mg 98%	138mg 97%	143mg 100%	181mg 100%	134mg 100%	143mg 100%	164mg 98%	162mg 100%
Thr	158mg 100%	126mg 100%	149mg 100%	166mg 100%	156mg 100%	118mg 100%	160mg 100%	152mg 100%	135mg 100%	180mg 100%	203mg 100%	142mg 100%	194mg 90%	137mg 100%	139mg 100%	173mg 100%	131mg 100%	137mg 100%	165mg 100%	154mg 100%
Val	136mg 98%	107mg 100%	125mg 97%	150mg 100%	138mg 100%	98mg 100%	286mg 100%	135mg 100%	109mg 96%	163mg 1005	188mg 100%	122mg 99%	176mg 89%	117mg 99%	120mg 100%	156mg 100%	108mg 98%	124mg 100%	146mg 100%	135mg 100%
Ser	150mg 99%	121mg 100%	140mg 99%	161mg 100%	148mg 99%	112mg 100%	157mg 100%	146g 100%	117mg 92%	169mg 97%	203mg 100%	136mg 99%	195mg 92%	131mg 100%	129mg 98%	170mg 100%	117mg 95%	134mg 100%	156mg 100%	143mg 98%
Tyr	172mg 98%	138mg 97%	158mg 96%	179mg 99%	174mg 100%	134mg 100%	179mg 100%	162mg 96%	148mg 99%	195mg 99%	222mg 100%	158mg 99%	236mg 100%	155mg 100%	152mg 98%	188mg 100%	147mg 100%	152mg 98%	173mg 96%	169mg 100%
Met	147mg 99%	110mg 95%	138mg 100%	148mg 96%	147mg 100%	109mg 100%	153mg 100%	144mg 100%	122mg 99%	171mg 100%	191mg 98%	133mg 100%	192mg 92%	124mg 97%	122mg 100%	151mg 93%	118mg 99%	123g 96%	156mg 100%	142mg 100%
His	223mg 100%	195mg 100%	214mg 100%	227mg 99%	221mg 100%	184mg 100%	227mg 100%	218mg 100%	180mg 91%	242mg 98%	214mg 80%	209mg 100%	258mg 91%	199mg 98%	205mg 100%	235mg 99%	196mg 100%	202mg 100%	221mg 97%	215mg 99%
Leu	144mg 100%	107mg 97%	132mg 99%	147mg 99%	141mg 100%	103mg 100%	296mg 100%	138mg 100%	117mg 99%	166mg 100%	191mg 100%	130mg 99%	204mg 100%	124mg 100%	121mg 99%	159mg 100%	113mg 99%	125mg 100%	148mg 100%	135mg 99%
Ile	137mg 96%	107mg 97%	131mg 99%	150mg 100%	139mg 99%	105mg 100%	147mg 100%	139mg 100%	119mg 100%	168mg 100%	190mg 100%	133mg 100%	191mg 94%	121mg 99%	123mg 100%	161mg 100%	111mg 97%	127mg 100%	148mg 100%	136mg 99%
Lys	175mg 99%	145mg 100%	169mg 100%	185mg 100%	176mg 100%	136mg 100%	185mg 100%	173mg 100%	152mg 99%	199mg 99%	223mg 100%	164mg 100%	239mg 100%	158mg 100%	158mg 100%	193mg 100%	150mg 100%	155mg 98%	184mg 100%	170mg 99%
Abu	133mg 99%	98mg 97%	123mg 99%	142mg 100%	132mg 100%	95mg 100%	136mg 99%	129mg 100%	112mg 100%	158mg 100%	180mg 100%	123mg 100%	183mg 94%	115mg 100%	116mg 100%	150mg 100%	102mg 96%	115mg 100%	140mg 100%	129mg 100%
Asn	143mg 100%	102mg 93%	133mg 100%	150mg 100%	140mg 100%	100mg 99%	143mg 98%	138mg 100%	115mg 97%	167mg 100%	190mg 100%	127mg 99%	193mg 95%	124mg 100%	122mg 99%	158mg 100%	109mg 95%	95mg 77%	149mg 100%	135mg 98%
Nap	169mg 100%	136mg 100%	160mg 100%	174mg 100%	139mg 84%	130mg 100%	173mg 100%	165mg 100%	145mg 100%	192mg 100%	219mg 100%	157mg 100%	229mg 100%	149mg 100%	150mg 100%	183mg 100%	140mg 100%	149mg 100%	174mg 100%	164mg 100%
HoPhe	159mg 100%	125mg 100%	148mg 100%	164mg 100%	155mg 100%	116mg 100%	165mg 100%	152mg 100%	134mg 100%	181mg 100%	204mg 100%	143mg 100%	218mg 100%	137mg 99%	136mg 99%	173mg 100%	127mg 99%	138mg 100%	163mg 100%	152mg 100%
	[PheCl]	[Ala]	[Phe]	[Trp]	[Asp]	[Gly]	[TyrMe]	[Thr]	[Val]	[Ser]	[Tyr]	[Met]	[His]	[Leu]	[Ile]	[Lys]	[Abu]	[Asn]	[Nap]	[HoPhe]

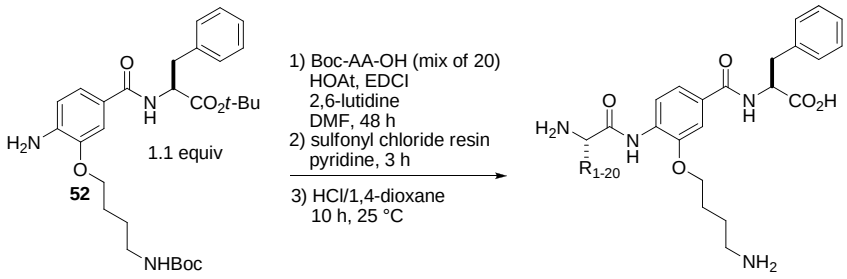
Figure S1. Synthesized 400 dimers with coupling yields and product amounts.

General Procedure for the Reduction of Aryl Nitro Group with Zinc Nanopowder



A solution of nitro dimer **50** (45 mg, 0.10 mmol) in acetone/water (5:1, 1.8 mL) in a 1 dram vial was treated with activated zinc nanopowder (65 mg, 0.10 mmol) and ammonium chloride (80 mg, 1.5 mmol). The mixture was vigorously shaken at room temperature for 1 min and filtered. The filtrate was diluted with EtOAc/Et_2O and extracted saturated aqueous $NaHCO_3$ (× 1). The organic layer was collected, dried (Na_2SO_4), and concentrated to give **51** as a solid (41 mg, 98%) that was homogeneous by TLC analysis. R_f = 0.20 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 7.85 (m, 4H), 7.50 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 8.0 Hz, 1H), 5.21 (s, 2H), 4.85 (m, 1H), 4.20 (s, 2H), 3.74 (s, 3H), 1.68 (m, 3H), 0.97 (t, *J* = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{25}H_{28}N_2O_4+H]^+$ 421.2122; found: 421.2126.

General Procedure for the Preparation of the Library Trimers as 20 Compound Mixtures



Aniline dimer **52** (41 mg, 0.0771 mmol, 1.1 equiv) was placed in a 0.5 dram vial and treated with the prepared 0.10 M stock solution of a mixture of 20 Boc-AA-OH in DMF (0.70 mL, 0.070 mmol). HOAt (20 mg, 0.147 mmol), EDCI (16.1 mg, 0.084 mmol), and 2,6-lutidine (50 mL, 0.43 mmol) were added. The mixture was agitated on a titer plate shaker for 48 h, diluted with EtOAc/Et_2O, extracted with aqueous HCl (0.1 M, × 2) and saturated aqueous $NaHCO_3$ (× 2). The organic layer was collected, dried (Na_2SO_4), and concentrated. The product mixture was then transferred into a 1 dram vial, treated with sulfonyl chloride polystyrene resin (100 mg, loading level 2.4 mmol/g), pyridine (2.0 mL), and agitated on a titer plate shaker for 5 h. The resin was drained and washed with Et_2O, EtOAc, and CH_2Cl_2. All the washes were combined with the original filtrate, diluted with EtOAc/Et_2O, extracted with aqueous HCl (0.2 M, × 3). The organic layer was collected, dried (Na_2SO_4), and concentrated. The product mixture was again transferred into a 1 dram vial, treated with 4.0 M solution of HCl in 1,4-dioxane (2.0 mL), and agitated on a titer plate shaker for 10 h. The solvent was evaporated with a stream of nitrogen. The product mixture was dried under vacuum and dissolved in DMSO (1.40 mL) to prepare a 50 mM stock solution for screening dispensing.

Preparation of a Stock Solution of a Mixture of 20 Boc-Protected Amino Acids

Twenty Boc-AA-OH (Figure S2) were combined to generate 0.10 M stock solution in DMF (0.50 mmol of each amino acid in 100.0 mL of DMF).

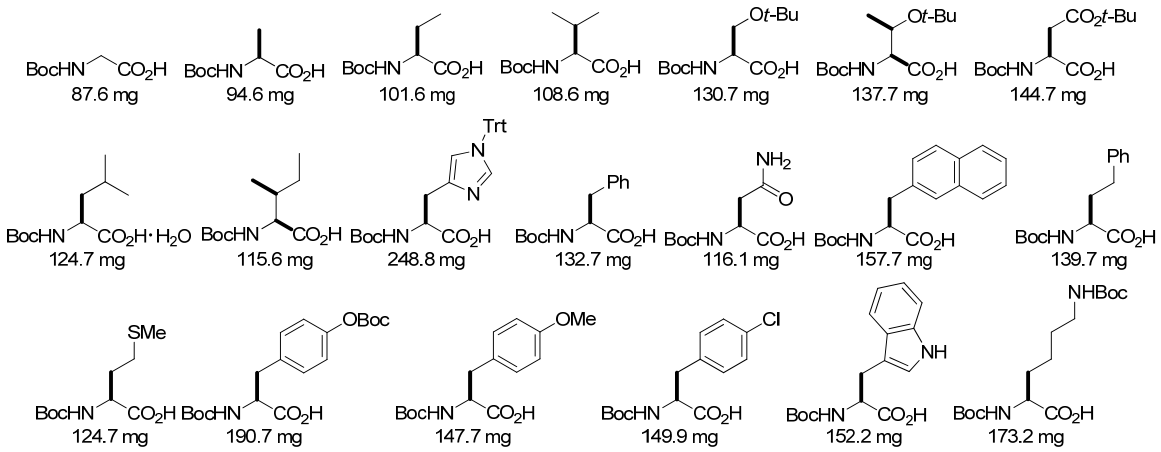
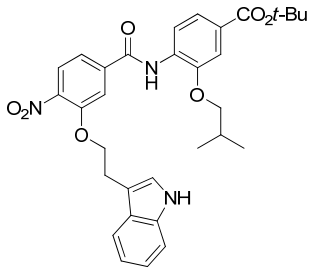
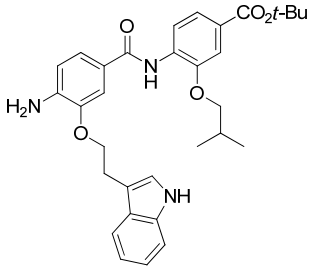


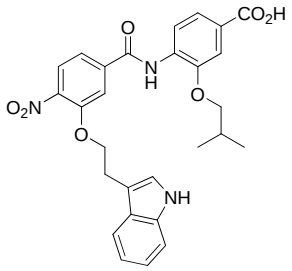
Figure S2. Boc-protected amino acids used to generate a stock solution



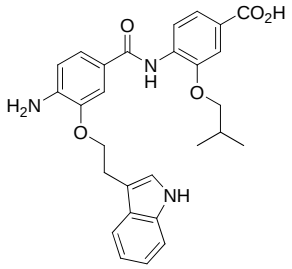
O_2N-[Trp]-[Leu]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.73 (s, 1H), 8.54 (d, *J* = 8.5 Hz, 1H), 8.12 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.66 (m, 3H), 7.55 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.21 (m, 2H), 7.14 (t, *J* = 7.0 Hz, 1H), 4.44 (t, *J* = 7.0 Hz, 2H), 3.90 (d, *J* = 6.5 Hz, 2H), 3.35 (t, *J* = 7.0 Hz, 2H), 2.14 (m, 1H), 1.62 (s, 9H), 1.03 (d, *J* = 7.0 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{32}H_{35}N_3O_7+H]^+$ 574.2548; found: 574.2532.



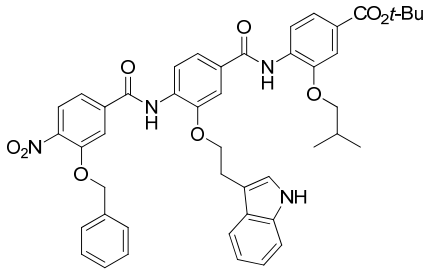
H_2N-[Trp]-[Leu]-OtBu. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 10.90 (s, 1H), 8.98 (s, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.45 (s, 1H), 7.34 (m, 4H), 7.08 (t, *J* = 7.0 Hz, 1H), 6.99 (t, *J* = 7.0 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.47 (s, 2H), 4.23 (t, *J* = 7.0 Hz, 2H), 3.85 (d, *J* = 6.5 Hz, 2H), 3.23 (t, *J* = 7.0 Hz, 2H), 2.01 (m, 1H), 1.54 (s, 9H), 0.91 (d, *J* = 7.0 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{32}H_{37}N_3O_5+H]^+$ 544.2806; found: 544.2792.



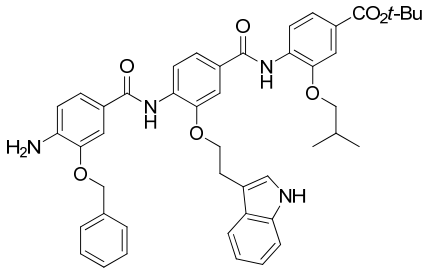
O_2N-[Trp]-[Leu]-OH. ^{1}H NMR (500 MHz, acetone-d_6, 25 °C) δ 11.20 (s, 1H), 10.13 (s, 1H), 9.15 (s, 1H), 8.48 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.85 (s, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.66 (d, J = 6.5 Hz, 2H), 7.62 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.33 (s, 1H), 7.10 (t, J = 8.0 Hz, 1H), 7.03 (t, J = 8.0 Hz, 1H), 4.57 (t, J = 7.0 Hz, 2H), 3.94 (d, J = 6.5 Hz, 2H), 3.34 (t, J = 7.0 Hz, 2H), 2.12 (m, 1H), 0.99 (d, J = 7.0 Hz, 6H); HRMS-MALDI (*m/z*) calcd for$[C_{28}H_{27}N_3O_7+H]^+$ 518.1922; found: 518.1918.



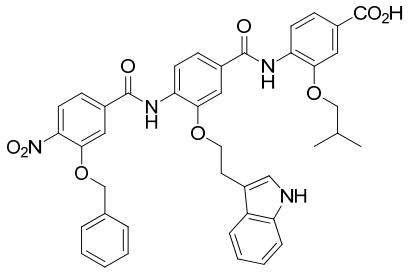
H_2N-[Trp]-[Leu]-OH. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 12.83 (s, 1H), 10.90 (s, 1H), 8.99 (s, 1H), 8.20 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.50 (s, 1H), 7.34 (m, 4H), 7.08 (t, J = 7.0 Hz, 1H), 6.99 (t, J = 7.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.52 (s, 2H), 4.24 (t, J = 7.0 Hz, 2H), 3.85 (d, J = 6.0 Hz, 2H), 3.23 (t, J = 7.0 Hz, 2H), 2.01 (m, 1H), 0.91 (d, J = 6.5 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{28}H_{29}N_3O_5+H]^+$ 488.2180; found: 488.2173.



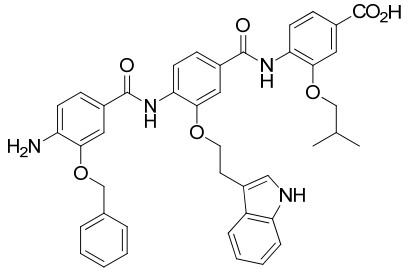
O_2N-[Phe]-[Trp]-[Leu]-OtBu. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.90 (s, 1H), 9.75 (s, 1H), 9.49 (s, 1H), 8.05 (m, 3H), 7.95 (s, 1H), 7.69 (s, 1H), 7.59 (m, 4H), 7.45 (m, 5H), 7.34 (m, 2H), 7.25 (s, 1H), 7.03 (t, J = 7.2 Hz, 1H), 6.86 (t, J = 7.2 Hz, 1H), 5.40 (s, 2H), 4.41 (t, J = 6.6 Hz, 2H), 3.86 (d, J = 6.0 Hz, 2H), 3.26 (t, J = 6.6 Hz, 2H), 2.02 (m, 1H), 1.55 (s, 9H), 0.92 (d, J = 6.6 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{46}H_{46}N_4O_9+H]^+$ 799.3337; found: 799.3319.



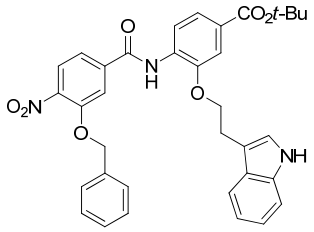
H_2N-[Phe]-[Trp]-[Leu]-OtBu. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.85 (s, 1H), 8.64 (m, 3H), 7.98 (s, 1H), 7.66 (m, 3H), 7.55 (s, 1H), 7.51 (s, 1H), 7.40 (m, 7H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.12 (t, *J* = 7.0 Hz, 1H), 7.07 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.54 (d, *J* = 8.5 Hz, 1H), 5.10 (s, 2 H), 4.56 (t, *J* = 6.5 Hz, 2H), 4.24 (s, 2H), 3.93 (d, *J* = 6.0 Hz, 2H), 3.37 (t, *J* = 6.5 Hz, 2H), 2.19 (m, 1H), 1.62 (s, 9H), 1.09 (d, *J* = 6.5 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{46}H_{48}N_4O_7+H]^+$ 769.3596; found: 769.3572.



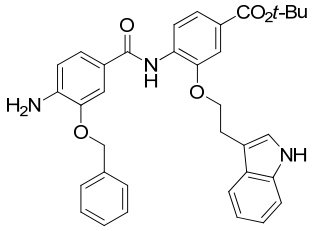
O_2N-[Phe]-[Trp]-[Leu]-OH. ^1H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.92 (s, 1H), 10.89 (s, 1H), 9.75 (s, 1H), 9.47 (s, 1H), 8.05 (m, 3H), 7.95 (s, 1H), 7.69 (s, 1H), 7.58 (m, 5H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.25 (s, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 6.86 (t, *J* = 7.2 Hz, 1H), 5.40 (s, 2H), 4.41 (t, *J* = 6.6 Hz, 2H), 3.86 (d, *J* = 6.0 Hz, 2H), 3.26 (t, *J* = 6.6 Hz, 2H), 2.03 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{42}H_{38}N_4O_9+H]^+$ 743.2711; found: 743.2711.



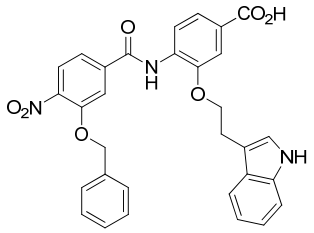
H_2N-[Phe]-[Trp]-[Leu]-OH. ^1H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.90 (s, 1H), 10.91 (s, 1H), 9.39 (s, 1H), 8.99 (s, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.64 (s, 1H), 7.59 (m, 3H), 7.51 (m, 4H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 8.4 Hz, 2H), 7.27 (m, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.90 (t, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 5.57 (s, 2H), 5.18 (s, 2H), 4.42 (t, *J* = 6.6 Hz, 2H), 3.86 (d, *J* = 6.0 Hz, 2H), 2.03 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 6H); HRMS-MALDI (*m/z*) calcd for $[C_{42}H_{40}N_4O_7+H]^+$ 713.2970; found: 713.2963.



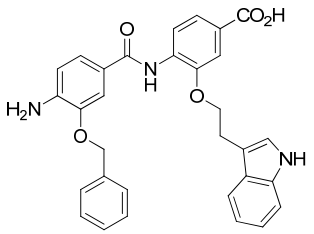
O_2N-[Phe]-[Trp]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.53 (s, 1H), 8.50 (d, *J* = 8.5 Hz, 1H), 8.24 (s, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.65 (s, 1H), 7.61 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.39 (m, 4H), 7.33 (d, *J* = 7.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 5.15 (s, 2H), 4.53 (t, *J* = 6.5 Hz, 2H), 3.29 (t, *J* = 6.5 Hz, 2H), 1.63 (s, 9H); HRMS-ESI (*m/z*) calcd for $[C_{35}H_{33}N_3O_7+H]^+$ 608.2391; found: 608.2392.



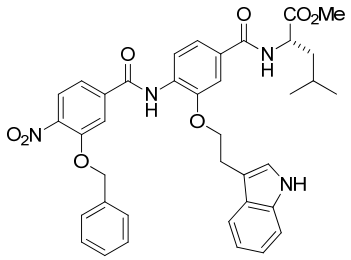
H_2N-[Phe]-[Trp]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.61 (s, 1H), 8.57 (d, *J* = 8.5 Hz, 1H), 8.02 (s, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.60 (s, 1H), 7.49 (s, 1H), 7.37 (m, 6H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.03 (s, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 5.06 (s, 2H), 4.50 (t, *J* = 6.5 Hz, 2H), 4.21 (s, 2H), 3.33 (t, *J* = 6.5 Hz, 2H), 1.60 (s, 9H); HRMS-ESI (*m/z*) calcd for $[C_{35}H_{35}N_3O_5+H]^+$ 578.2649; found: 578.2650.



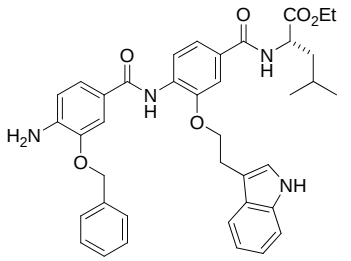
O_2N-[Phe]-[Trp]-OH. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) δ 12.99 (s, 1H), 10.88 (s, 1H), 9.66 (s, 1H), 8.03 (m, 2H), 7.92 (s, 1H), 7.63 (m, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.43 (m, 4H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.25 (s, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 5.38 (s, 2H), 4.40 (t, *J* = 6.8 Hz, 2H), 3.23 (t, *J* = 6.8 Hz, 2H); HRMS-ESI (*m/z*) calcd for $[C_{31}H_{25}N_3O_7+H]^+$ 552.1765; found: 552.1769.



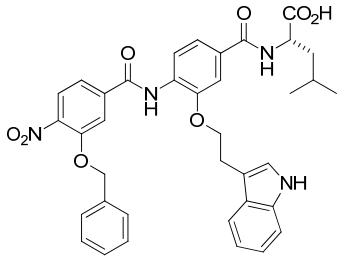
H_2N-[Phe]-[Trp]-OH. ^1H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.81 (s, 1H), 10.90 (s, 1H), 8.94 (s, 1H), 8.24 (d, J = 8.4Hz, 1H), 7.59 (m, 3H), 7.47 (m, 4H), 7.32 (m, 6H), 7.20 (d, J = 8.4 Hz, 1H), 7.05 (t, J = 7.2 Hz, 1H), 6.89 (t, J = 7.2 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 5.16 (s, 2H), 4.42 (t, J = 6.6 Hz, 2H), 3.28 (t, J = 6.6 Hz, 2H); HRMS-ESI (*m/z*) calcd for $[C_{31}H_{28}N_3O_5+H]^+$ 522.2029; found: 522.2012.



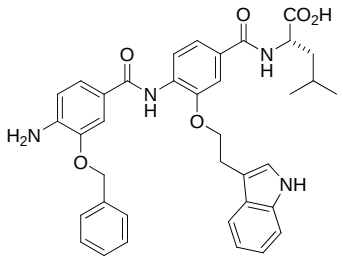
O_2N-[Phe]-[Trp]-Leu-OMe. ^1H NMR (600 MHz, $CDCl_3$, 25 °C) δ 8.48 (s, 1H), 8.44 (d, J = 8.4 Hz, 1H), 8.30 (s, 1H), 7.60 (s, 1H), 7.53 (m, 3H), 7.45 (m, 7H), 7.15 (t, J = 7.2 Hz, 1H), 7.04 (t, J = 7.2 Hz, 1H), 6.94 (s, 1H), 6.75 (d, J = 7.8 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 5.15 (s, 2H), 4.86 (m, 1H), 4.45 (m, 2H), 3.77 (s, 3H), 3.23 (t, J = 6.0 Hz, 2H), 1.75 (m, 3H), 1.00 (t, J = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{38}H_{38}N_4O_8+H]^+$ 679.2762; found: 679.2754.



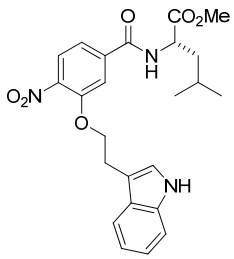
H_2N-[Phe]-[Trp]-Leu-OEt. ^1H NMR (600 MHz, $CDCl_3$, 25 °C) δ 8.58 (m, 2H), 8.05 (s, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.55 (s, 1H), 7.49 (s, 1H), 7.37 (m, 7H), 7.20 (t, J = 7.2 Hz, 1H), 7.11 (t, J = 7.2 Hz, 1H), 7.03 (s, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.51 (d, J = 8.4 Hz, 1H), 5.07 (s, 2H), 4.84 (m, 1H), 4.50 (t, J = 6.0 Hz, 2H), 4.24 (m, 4H), 3.32 (t, J = 6.0 Hz, 2H), 1.73 (m, 3H), 1.31 (t, J = 6.6 Hz, 3H), 1.01 (d. J = 5.4 Hz, 3H), 0.99 (d, J = 5.4 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{39}H_{42}N_4O_6+H]^+$ 663.3177; found: 663.3181.



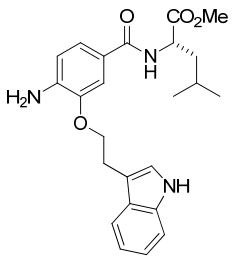
O_2N-[Phe]-[Trp]-Leu-OH. ^1H NMR (600 MHz, $CDCl_3$, 25 °C) δ 8.43 (s, 1H), 8.38 (d, J = 7.2 Hz, 1H), 8.17 (s, 1H), 7.39 (m, 11H), 7.13 (t, J = 7.2 Hz, 1H), 7.01 (t, J = 7.2 Hz, 1H), 6.95 (s, 1H), 6.85 (s, 1H), 6.64 (s, 1H), 5.10 (s, 2H), 4.80 (s, 1H), 4.37 (s, 2H), 3.16 (s, 2H), 1.79 (m, 3H), 0.99 (d, J = 4.2 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{37}H_{36}N_4O_8+H]^+$ 665.2606; found: 665.2596.



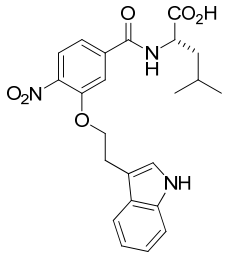
H_2N-[Phe]-[Trp]-Leu-OH. ^1H NMR (500 MHz, CD_2Cl_2-CD_3OD (1:1), 25 °C) δ 8.43 (s, 1H), 7.85 (m, 2H), 7.67 (m, 9H), 7.37 (m, 2H), 7.25 (m, 2H), 5.34 (s, 2H), 4.95 (m, 1H), 4.81 (t, J = 6.0 Hz, 2H), 3.60 (t, J = 6.0 Hz, 2H), 2.02 (m, 3H), 1.23 (t, J = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{37}H_{38}N_4O_6+H]^+$ 635.2864; found: 635.2871.



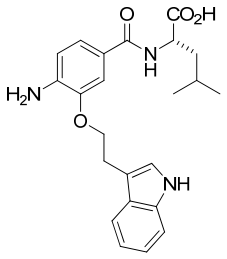
O_2N-[Trp]-Leu-OMe. ^1H NMR (600 MHz, $CDCl_3$, 25 °C) δ 8.20 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.49 (s, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 7.16 (m, 3H), 6.76 (s, 1H), 4.83 (m, 1H), 4.34 (t, J = 6.6 Hz, 2H), 3.75 (s, 3H), 3.29 (t, J = 6.6 Hz, 2H), 1.71 (m, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.97 (d, J = 6.6 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{27}N_3O_6+H]^+$ 454.1973; found: 454.1962.



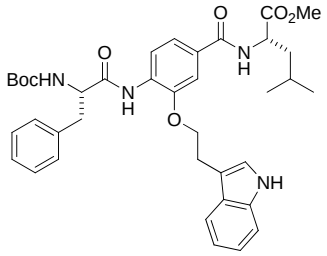
H_2N-[Trp]-Leu-OMe. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.30 (s, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.36 (m, 2H), 7.20 (m, 2H), 7.14 (t, J = 7.5 Hz, 1 H), 7.04 (s, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.44 (s, 1H), 4.85 (m, 1H), 4.28 (t, J = 6.5 Hz, 2H), 4.08 (s, 2H), 3.74 (s, 3H), 3.25 (t, J = 6.5 Hz, 2H), 1.70 (m, 3H), 0.98 (d, J = 6.0 Hz, 3H), 0.96 (d, J = 6.0 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{29}N_3O_4+H]^+$ 424.2231; found: 424.2220.



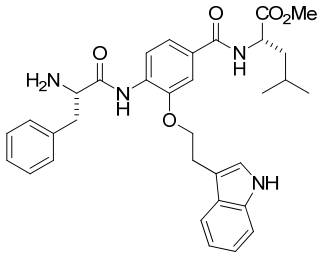
O_2N-[Trp]-Leu-OH. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 8.17 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.41 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.13 (m, 4H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.77 (m, 1H), 4.25 (t, *J* = 6.8 Hz, 2H), 3.21 (t, *J* = 6.4 Hz, 2H), 1.74 (m, 3H), 0.97 (d, *J* = 5.2 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{23}H_{25}N_3O_6+H]^+$ 440.1816; found: 440.1820.



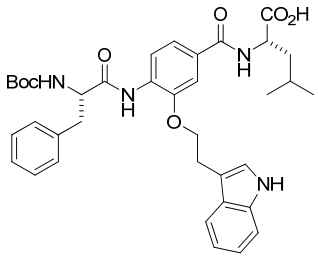
H_2N-[Trp]-Leu-OH. ^{1}H NMR (500 MHz, acetone-d_6, 25 °C) δ 10.07 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.47 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.30 (s, 1H), 7.10 (t, *J* = 7.0 Hz, 1H), 7.03 (t, *J* = 7.0 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 4.68 (m, 1H), 4.27 (t, *J* = 7.0 Hz, 2H), 3.27 (t, *J* = 7.0 Hz, 2H), 1.75 (m, 3H), 0.93 (d, *J* = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{23}H_{27}N_3O_4+H]^+$ 410.2074; found: 410.2074.



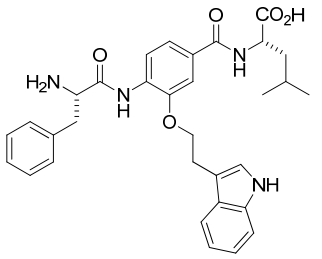
Boc-Phe-[Trp]-Leu-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.67 (s, 1H), 8.33 (s, 1H), 8.18 (s, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.40 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.24 (m, 3H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.13 (m, 3H), 7.00 (s, 1H), 6.94 (s, 1H), 5.19 (s, 1H), 4.87 (m, 1H), 4.48 (s, 1H), 4.17 (m, 2H), 3.74 (s, 3H), 3.14 (t, *J* = 6.5 Hz, 2H), 3.09 (s, 1H), 2.97 (s, 1H), 1.74 (m, 3H), 1.44 (s, 9H), 0.98 (t, *J* = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{38}H_{46}N_4O_7+H]^+$ 671.3439; found: 671.3443.



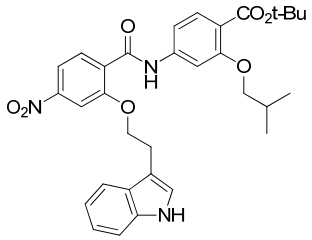
H_2N-Phe-[Trp]-Leu-OMe. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 10.95 (s, 1H), 9.68 (s, 1H), 8.68 (d, J = 8.0 Hz, 1H), 8.37 (s, 3H), 7.99 (d, J = 8.5 Hz, 1H), 7.56 (m, 3H), 7.30 (m, 7H), 7.08 (t, J = 7.5 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 4.50 (m, 2H), 4.32 (m, 2H), 3.63 (s, 3H), 3.16 (m, 4H), 1.67 (m, 3H), 0.91 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{33}H_{38}N_4O_5+H]^+$ 571.2915; found: 571.2916.



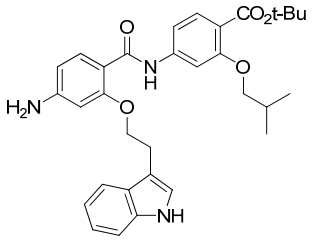
Boc-Phe-[Trp]-Leu-OH. ^{1}H NMR (500 MHz, acetone-d_6, 25 °C) δ 10.09 (s, 1H), 9.09 (s, 1H), 8.44 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.61 (s, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 8.5 Hz, 1H), 7.36 (s, 1H), 7.30 (m, 4H), 7.21 (m, 1H), 7.11 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.51 (d, J = 7.5 Hz, 1H), 4.73 (m, 1H), 4.57 (s, 1H), 4.34 (t, J = 7.5 Hz, 2H), 3.33 (m, 3H), 2.99 (m, 1H), 1.74 (m, 3H), 1.37 (s, 9H), 0.94 (d, J = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{37}H_{44}N_4O_7+H]^+$ 657.3283; found: 657.3282.



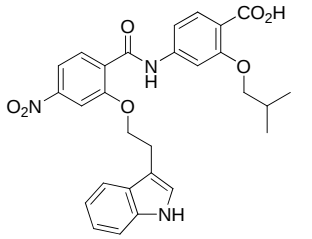
H_2N-Phe-[Trp]-Leu-OH. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 12.57 (s, 1H), 10.94 (s, 1H), 9.67 (s, 1H), 8.55 (d, J = 8.0 Hz, 1H), 8.33 (s, 3H), 7.99 (d, J = 8.5 Hz, 1H), 7.57 (m, 3H), 7.30 (m, 7H), 7.08 (t, J = 8.0 Hz, 1H), 7.00 (t, J = 8.0 Hz, 1H), 4.47 (m, 2H), 4.32 (m, 2H), 3.21 (t, J = 7.5 Hz, 2H), 3.14 (m, 2H), 1.66 (m, 3H), 0.91 (d, J = 6.0 Hz, 3H), 0.86 (d, J = 6.0 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{32}H_{36}N_4O_5+H]^+$ 557.2758; found: 557.2758.



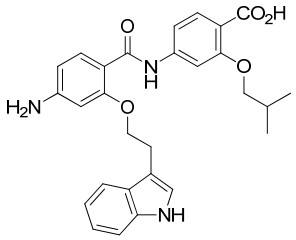
O_2N-{Trp}-{Leu}-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 9.77 (s, 1H), 8.44 (d, *J* = 9.0 Hz, 1H), 8.11 (s, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.95 (s, 1H), 7.69 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.07 (s, 1H), 6.10 (d, *J* = 8.0 Hz, 1H), 4.73 (t, *J* = 6.5 Hz, 2H), 3.71 (d, *J* = 6.5 Hz, 2H), 3.51 (t, *J* = 6.5 Hz, 2H), 2.11 (m, 1H), 1.59 (s, 9H), 1.03 (d, *J* = 7.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{32}H_{35}N_3O_7+H]^+$ 574.2548; found: 574.2546.



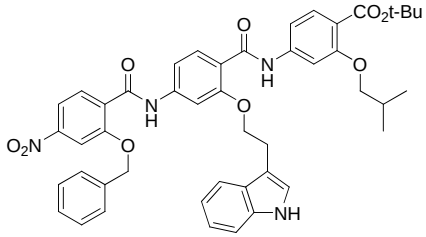
H_2N-{Trp}-{Leu}-OtBu. ^{1}H NMR (400 MHz, $CDCl_3$–CD_3OD (1:1), 25 °C) δ 10.03 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.42 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 7.07 (m, 2H), 6.36 (m, 2H), 6.10 (d, *J* = 8.4 Hz, 1H), 4.54 (t, *J* = 6.4 Hz, 2H), 3.55 (d, *J* = 6.4 Hz, 2H), 3.39 (t, *J* = 6.0 Hz, 2H), 2.01 (m, 1H), 1.53 (s, 9H), 0.95 (d. *J* = 6.8 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{32}H_{37}N_3O_5+H]^+$ 544.2806; found: 544.2805.



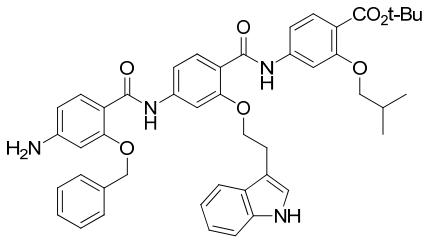
O_2N-{Trp}-{Leu}-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.31 (s, 1H), 10.86 (s, 1H), 10.55 (s, 1H), 7.95 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.58 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.20 (m, 2H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 4.48 (t, *J* = 6.6 Hz, 2H), 3.75 (d, *J* = 6.6 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.05 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{28}H_{27}N_3O_7+H]^+$ 518.1922; found: 518.1924.



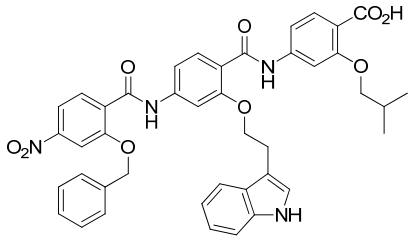
H_2N-{Trp}-{Leu}-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.14 (s, 1H), 10.88 (s, 1H), 9.98 (s, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.53 (s, 1H), 7.44 (m, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.22 (s, 1H), 7.10 (t, J = 7.8 Hz, 1H), 7.00 (t, J = 7.8 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 6.36 (s, 1H), 6.27 (d, J = 7.8 Hz, 1H), 5.92 (s, 2H), 4.42 (t, J = 6.6 Hz, 2H), 3.62 (d, J = 6.0 Hz, 2H), 3.36 (t, J = 6.6 Hz, 2H, partially overlapped with H_2O peak in DMSO), 1.97 (m, 1H), 0.95 (d, J = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{28}H_{29}N_3O_5+H]^+$ 488.2180; found: 418.2185.



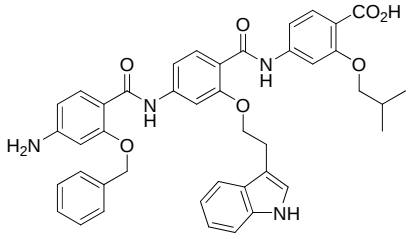
O_2N-{Phe}-{Trp}-{Leu}-OtBu. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.90 (s, 1H), 10.68 (s, 1H), 10.19 (s, 1H), 8.06 (s, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.60 (s, 2H), 7.51 (d, J = 7.2 Hz, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.35 (m, 2H), 7.29 (t, J = 7.2 Hz, 2H), 7.23 (m, 2H), 7.08 (t, J = 7.8 Hz, 1H), 6.97 (t, J = 7.8 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 5.36 (s, 2H), 4.25 (m, 2H), 3.67 (d, J = 5.4 Hz, 2H), 3.33 (2H, overlapped with H_2O peak in DMSO), 2.02 (m, 1H), 1.51 (s, 9H), 0.99 (d, J = 6.6 Hz, 6H); HRMS-ESI (*m/z*) $[MH]^+$ calcd for $[C_{46}H_{46}N_4O_9+H]^+$ 799.3337; found: 799.3324.



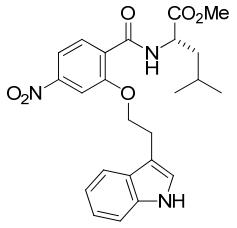
H_2N-{Phe}-{Trp}-{Leu}-OtBu. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 10.91 (s, 1H), 10.13 (s, 1H), 9.99 (s, 1H), 7.67 (m, 3H), 7.59 (m, 3H), 7.44 (d, J = 8.5 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 7.5 Hz, 2H), 7.21 (m, 3H), 7.10 (t, J = 7.5 Hz, 1H), 7.00 (m, 2H), 6.87 (d, J = 8.5 Hz, 1H), 6.42 (s, 1H), 6.29 (d, J = 8.5 Hz, 1H), 6.00 (s, 2H), 5.17 (s, 2H), 4.21 (t, J = 6.5 Hz, 2H), 3.66 (d, J = 6.0 Hz, 2H), 3.33 (2H, overlapped with H_2O peak in DMSO), 2.01 (m, 1H), 1.50 (s, 9H), 0.98 (d, J = 7.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{46}H_{48}N_4O_7+H]^+$ 769.3596; found: 769.3589.



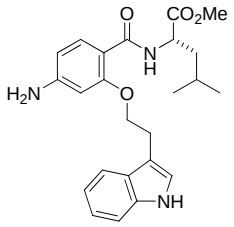
O_2N-{Phe}-{Trp}-{Leu}-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.23 (s, 1H), 10.89 (s, 1H), 10.66 (s, 1H), 10.19 (s, 1H), 8.06 (s, 1H), 7.96 (d, J = 7.0 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.61 (m, 4H), 7.51 (d, J = 7.2 Hz, 2H), 7.36 (d, J = 7.8 Hz, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 7.23 (m, 2H), 7.08 (t, J = 7.8 Hz, 1H), 6.95 (m, 2H), 5.36 (s, 2H), 4.36 (m, 2H), 3.70 (d, J = 6.0 Hz, 2H), 3.32 (2H, overlapped with H_2O peak in DMSO), 2.01 (m, 1H), 0.98 (d, J = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{42}H_{38}N_4O_9+H]^+$ 743.2711; found: 743.2721.



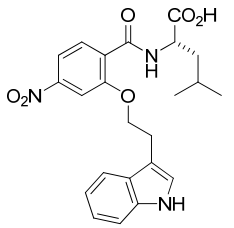
H_2N-{Phe}-{Trp}-{Leu}-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.24 (s, 1H), 10.92 (s, 1H), 10.13 (s, 1H), 9.99 (s, 1H), 7.67 (m, 3H), 7.60 (m, 3H), 7.55 (d, J = 7.2 Hz, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.21 (m, 3H), 7.10 (m, 1H), 6.99 (m, 2H), 6.89 (d, J = 7.2 Hz, 1H), 6.42 (s, 1H), 6.29 (d, J = 7.8 Hz, 1H), 6.00 (s, 2H), 5.17 (s, 2H), 4.21 (m, 2H), 3.69 (d, J = 6.0 Hz, 2H), 3.30 (2H, overlapped with H_2O peak in DMSO), 2.01 (m, 1H), 0.97 (d, J = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{42}H_{40}N_4O_7+H]^+$ 713.2970; found: 713.2970.



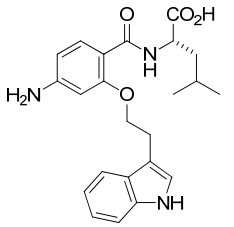
O_2N-{Trp}-Leu-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.38 (d, J = 9.0 Hz, 1H), 8.32 (d, J = 7.0 Hz, 1H), 8.16 (s, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.87 (s, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.18 (m, 2H), 4.77 (m, 1H), 4.61 (m, 2H), 3.76 (s, 3H), 3.47 (t, J = 7.0 Hz, 2H), 1.57 (m, 2H), 1.30 (m, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.83 (d, J = 6.0 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{27}N_3O_6+H]^+$ 454.1973; found: 454.1968.



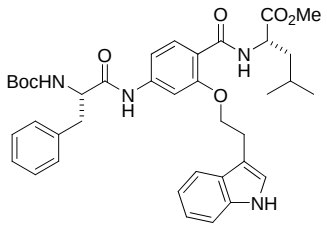
H_2N-{Trp}-Leu-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.76 (s, 1H), 8.29 (d, *J* = 7.0 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.99 (s, 1H), 6.23 (d, *J* = 8.0 Hz, 1H), 6.11 (s, 1H), 4.72 (m, 1H), 4.31 (m, 1H), 4.24 (m, 1H), 4.13 (s, 2H), 3.68 (s, 3H), 3.30 (t, *J* = 6.5 Hz, 2H), 1.59 (m, 1H), 1.50 (m, 1H), 1.29 (m, 1H), 0.82 (d, *J* = 6.5 Hz, 3H). 0.79 (d, *J* = 7.0 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{29}N_3O_4+H]^+$ 424.2231; found: 424.2227.



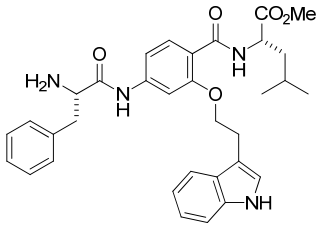
O_2N-{Trp}-Leu-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.86 (s, 1H), 10.91 (s, 1H), 8.60 (d, *J* = 7.8 Hz, 1H), 7.92 (s, 1H), 7.88 (s, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.99 (t, *J* = 7.8 Hz, 1H), 4.49 (m, 3H), 3.25 (m, 2H), 1.70 (m, 1H), 1.54 (t, *J* = 6.6 Hz, 2H), 0.85 (d, *J* = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{23}H_{25}N_3O_6+Na]^+$ 462.1635; found: 462.1631.



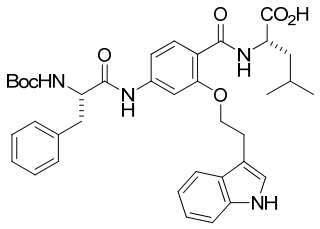
H_2N-{Trp}-Leu-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.91 (s, 1H), 8.12 (d, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.24 (s, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.99 (t, *J* = 7.2 Hz, 1H), 6.30 (s, 1H), 6.20 (d, *J* = 9.0 Hz, 1H), 5.74 (s, 2H), 4.41 (m, 1H), 4.32 (m, 2H), 3.26 (m, 2H), 1.57 (m, 1H), 1.47 (m, 1H), 1.36 (m, 1H), 0.80 (t, *J* = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{23}H_{27}N_3O_4+Na]^+$ 432.1894; found: 432.1897.



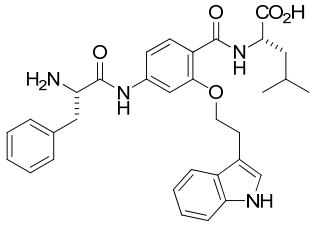
Boc-Phe-{Trp}-Leu-OMe. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 8.28 (m, 3H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.62 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.26 (m, 6H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.02 (s, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 5.16 (s, 1H), 4.69 (m, 1H), 4.45 (m, 3H), 3.71 (s, 3H), 3.34 (t, *J* = 6.4 Hz, 2H), 3.14 (m, 2H), 1.53 (m, 1H), 1.41 (s, 10H), 1.17 (m, 1H), 0.80 (d, *J* = 6.4 Hz, 3H), 0.76 (d, *J* = 6.4 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{38}H_{46}N_4O_7+H]^+$ 671.3439; found: 671.3433.



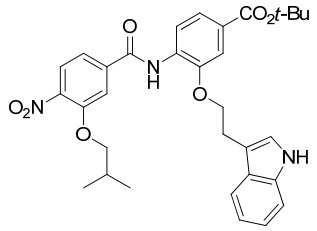
H_2N-Phe-{Trp}-Leu-OMe. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.94 (s, 1H), 10.71 (s, 1H), 8.31 (s, 3H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.45 (s, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.27 (m, 7H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 7.2 Hz, 1H), 4.48 (m, 1H), 4.37 (m, 2H), 4.16 (s, 1H), 3.65 (s, 3H), 3.30 (m, 2H), 3.17 (m, 1H), 3.09 (m, 1H), 1.57 (m, 1H), 1.41 (m, 2H), 0.80 (d, *J* = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{33}H_{38}N_4O_5+H]^+$ 571.2915; found: 571.2894.



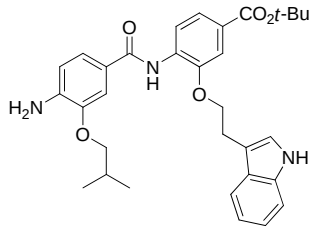
Boc-Phe-{Trp}-Leu-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.79 (s, 1H), 10.92 (s, 1H), 10.25 (s, 1H), 8.32 (d, *J* = 6.6 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.50 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.28 (m, 5H), 7.18 (m, 2H), 7.08 (t, *J* = 7.8 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 4.37 (m, 4H), 3.30 (m, 2H), 2.98 (m, 1H), 2.82 (m, 1H), 1.61 (m, 1H), 1.51 (m, 1H), 1.43 (m, 1H), 1.30 (s, 9H), 0.82 (t, *J* = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{37}H_{44}N_4O_7+H]^+$ 657.3283; found: 657.3281.



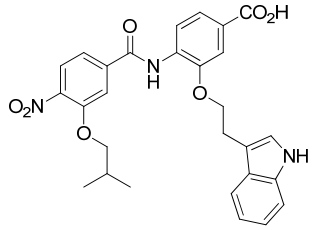
H_2N-Phe-{Trp}-Leu-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.91 (s, 1H), 8.36 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.60 (m, 2H), 7.23 (m, 9H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 7.2 Hz, 1H), 4.36 (m, 3H), 3.57 (m, 1H), 3.00 (m, 3H), 2.71 (m, 1H), 1.52 (m, 3H), 0.83 (t, *J* = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{32}H_{36}N_4O_5+H]^+$ 557.2758; found: 557.2751.



O_2N-[Leu]-[Trp]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.57 (s, 1H), 8.51 (d, J = 8.5 Hz, 1H), 8.02 (s, 1H), 7.70 (dd, J = 8.5, 1.5 Hz, 1H), 7.66 (d, J = 1.8 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.56 (d, J = 1.5 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.5 Hz, 1H), 7.22 (t, J = 7.4 Hz, 1H), 7.11 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 2.2 Hz, 1H), 6.71 (dd, J = 8.5, 1.5 Hz, 1H), 4.57 (t, J = 6.6 Hz, 2H), 3.87 (d, J = 6.6 Hz, 2H), 3.33 (t, J = 6.6 Hz, 2H), 2.14 (septet, J = 6.6 Hz, 1H), 1.62 (s, 9H), 1.04 (d, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ 165.5, 163.2, 152.8, 147.0, 141.7, 139.7, 136.5, 131.6, 128.1, 127.6, 125.8, 123.6, 122.8, 121.9, 120.0, 118.9, 118.7, 117.0, 114.3, 112.5, 112.2, 111.6, 81.5, 76.2, 68.8, 28.5, 28.4, 25.5, 19.2; MALDI-FTMS (*m/z*) calcd for $[C_{32}H_{35}N_3O_7+Na]^+$ 596.2367; found: 596.2346.

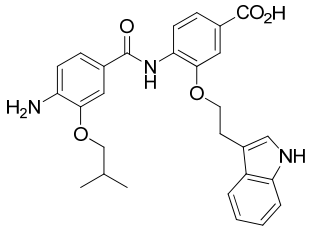


H_2N-[Leu]-[Trp]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.62 (s, 1H), 8.56 (d, J = 8.5 Hz, 1H), 8.16 (s, 1H), 7.68 (dd, J = 8.5, 1.5 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.60 (d, J = 1.5 Hz, 1H), 7.40 (d, J = 1.5 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 7.12 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 1.9 Hz, 1H), 6.88 (dd, J = 8.4, 1.5 Hz, 1H), 6.66 (d, J = 8.1 Hz, 2H), 4.49 (t, J = 6.6 Hz, 2H), 3.79 (d, J = 6.6 Hz, 2H), 3.33 (t, J = 6.6 Hz, 2H), 2.13 (septet, J = 6.6 Hz, 1H), 1.61 (s, 9H), 1.01 (d, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ 165.8, 164.9, 146.8, 136.5, 132.4, 127.4, 127.0, 123.6, 122.4, 122.3, 119.8, 119.3, 118.7, 118.5, 112.2, 112.0, 111.6, 111.3, 81.2, 75.3, 68.6, 28.5, 28.4, 25.7, 19.5; MALDI-FTMS (*m/z*) calcd for $[C_{32}H_{37}N_3O_5+H]^+$ 544.2806; found: 544.2806.

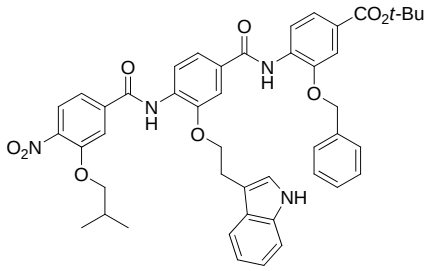


O_2N-[Leu]-[Trp]-OH. ^{1}H NMR (500 MHz, acetone-d_6, 25 °C) δ 8.50 (d, J = 8.8 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.73 (m, 3H), 7.65 (d, J = 8.1 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.32 (s, 1H), 7.27 (dd, J = 8.5, 1.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.96 (t, J = 7.3 Hz, 1H), 4.60 (t, J = 6.6 Hz, 2H), 4.02 (d, J = 6.6 Hz, 2H), 3.38 (t, J = 6.6 Hz, 2H), 2.10 (septet, J = 6.6 Hz, 1H), 1.03 (d, J = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, acetone-d_6, 25 °C) δ 167.2, 164.1, 152.9, 148.7, 142.9, 140.6, 137.6, 133.0, 128.6, 127.2, 126.2, 124.0, 123.7, 122.4, 120.0, 119.7, 119.3, 119.2, 114.8, 113.5, 112.3, 112.1, 76.6, 70.0, 29.0, 25.9,

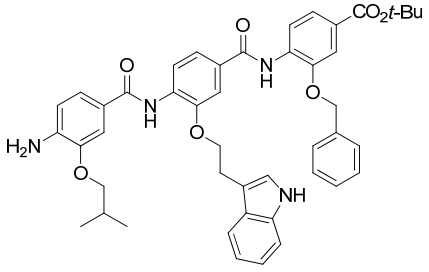
19.3; MALDI-FTMS (*m/z*) calcd for $[C_{28}H_{27}N_3O_7+Na]^+$ 540.1741; found: 540.1753.



H_2N-[Leu]-[Trp]-OH. ^1H NMR (500 MHz, CD_3OD, 25 °C) δ 8.30 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 1.5 Hz, 1H), 7.71 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H) 7.51 (d, *J* = 1.9 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 8.1 Hz, 1H), 7.10 (m, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 4.54 (t, *J* = 6.6 Hz, 2H), 3.85 (t, *J* = 6.6 Hz, 2H), 3.31 (d, *J* = 6.6 Hz, 2H), 2.14 (septet, *J* = 6.6 Hz, 1H), 1.05 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, CD_3OD, 25 °C) δ 169.5, 166.5, 152.8, 149.9, 138.2, 133.2, 129.0, 128.3, 124.2, 123.7, 123.4, 122.6, 121.7, 120.9, 120.0, 119.4, 114.1, 112.9, 112.5, 112.4, 76.7, 70.5, 29.5, 26.2, 19.6; ESI-TOFMS (*m/z*) calcd for $[C_{28}H_{29}N_3O_5+H]^+$ 488.2180; found: 488.2174.

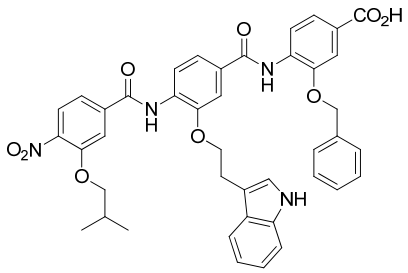


O_2N-[Leu]-[Trp]-[Phe]-OtBu. ^1H NMR (500 MHz, CD_3OD, 25 °C) δ 8.83 (s, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 8.55 (s, 1H), 8.51 (d, *J* = 8.5 Hz, 1H), 8.02 (s, 1H), 7.73 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.69 (d, *J* = 1.5 Hz, 1H), 7.62 (d, *J* = 1.9 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 1.5 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.46 (m, 4H), 7.40 (d, *J* = 7.3 Hz, 1H), 7.36 (m, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 2.2 Hz, 1H), 6.67 (dd, *J* = 8.4, 1.9 Hz, 1H), 5.23 (s, 2H), 4.52 (t, *J* = 6.2 Hz, 2H), 3.88 (d, *J* = 6.6 Hz, 2H), 3.32 (t, *J* = 6.2 Hz, 2H), 2.15 (septet, *J* = 6.6 Hz, 1H), 1.62 (s, 9H), 1.05 (d, *J* = 6.6 Hz, 6H); ESI-TOFMS (*m/z*) calcd for $[C_{46}H_{46}N_4O_9+H]^+$ 799.3337; found: 799.3345.

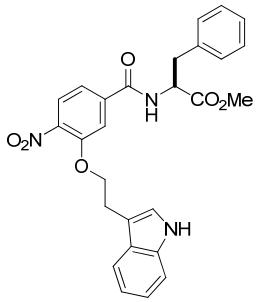


H_2N-[Leu]-[Trp]-[Phe]-OtBu. ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 8.83 (s, 1H), 8.63 (d, *J* = 8.2 Hz, 1H), 8.62 (s, 1H), 8.57 (d, *J* = 8.5 Hz, 1H), 8.04 (s, 1H), 7.72 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.68 (d, *J* = 1.4 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 1.5 Hz, 1H), 7.42 (m, 7H), 7.31 (d, *J* = 8.5, 1.5 Hz, 1H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 7.03 (d, *J* = 1.8 Hz, 1H), 6.87 (dd, *J* = 8.2, 1.5 Hz, 1H), 6.49 (d, *J* = 7.9, 1.9 Hz, 1H), 5.21 (s, 2H), 4.46 (t, *J* = 6.4 Hz, 2H), 3.79 (d, *J* = 6.7 Hz, 2H), 3.33 (t, *J* =

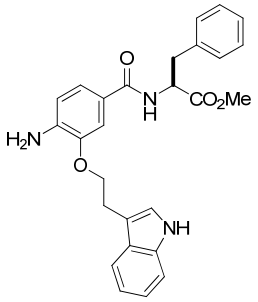
6.4 Hz, 2H), 2.12 (septet, *J* = 6.7 Hz, 1H), 1.62 (s, 9H), 1.03 (d, *J* = 6.8 Hz, 6H); ESI-TOFMS (*m/z*) calcd for $[C_{46}H_{48}N_4O_7+H]^+$ 769.3596; found: 769.3581.



O_2N-[Leu]-[Trp]-[Phe]-OH. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 10.13 (s, 1H), 9.10 (s, 1H), 9.00 (s, 1H), 8.58 (dd, *J* = 6.5, 1.8 Hz, 1H), 8.50 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.88 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.77 (dd, *J* = 10.0, 1.6 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.68 (d, *J* = 1.8 Hz, 1H), 7.64 (m, 3H), 7.59 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.36 (m, 2H), 7.33 (m, 1H), 7.28 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.96 (td, *J* = 7.5, 0.9 Hz, 1H), 5.36 (s, 2H), 4.54 (t, *J* = 6.1 Hz, 2H), 4.03 (d, *J* = 6.3 Hz, 2H), 3.38 (t, *J* = 6.1 Hz, 2H), 1.03 (d, *J* = 6.8 Hz, 6H); ESI-TOFMS (*m/z*) calcd for $[C_{42}H_{38}N_4O_9+H]^+$ 743.2711; found: 743.2708.

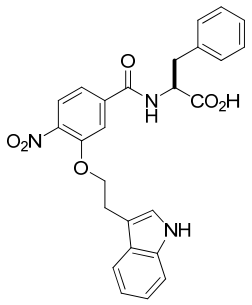


O_2N-[Trp]-Phe-OMe. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 8.11 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.43 (s, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.19 (m, 6H), 7.08 (d, *J* = 7.3 Hz, 2H), 6.50 (d, *J* = 7.4 Hz, 1H), 5.04 (m, 1H), 4.38 (t, *J* = 6.5 Hz, 2H), 3.80 (s, 3H), 3.33 (t, *J* = 6.5 Hz, 2H), 3.25 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ 172.0, 165.1, 152.5, 141.7, 139.0, 136.2, 135.7, 129.4, 128.9, 127.6, 127.4, 125.8, 123.2, 122.3, 119.7, 118.6, 118.0, 114.0, 111.6, 111.4, 70.2, 53.8, 52.9, 37.8, 25.1; ESI-TOFMS (*m/z*) calcd for $[C_{27}H_{25}N_3O_6+H]^+$ 488.1816; found: 488.1815.

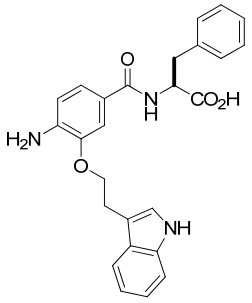


H_2N-[Trp]-Phe-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.15 (s, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 1.5 Hz, 1H), 7.22 (m, 4H), 7.12 (m, 5H), 6.64 (s, 1H), 6.44 (d, *J* = 7.7 Hz, 1H), 5.06 (m, 1H), 4.30 (t, *J* = 6.6 Hz, 2H), 3.75 (s, 3H), 3.28 (t, *J* = 6.6 Hz, 2H), 3.23 (m, 2H); ^{13}C

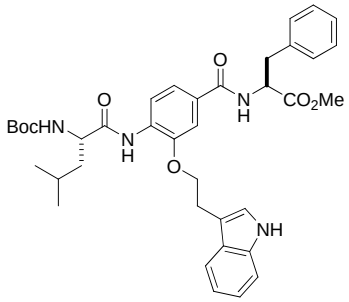
NMR (125 MHz, $CDCl_3$, 25 °C) δ 172.6, 167.0, 146.2, 140.2, 136.4, 136.2, 129.5, 128.8, 127.8, 127.3, 123.5, 122.3, 122.2, 120.3, 119.6, 118.8, 113.6, 112.6, 111.5, 110.9, 68.9, 53.6, 52.6, 38.2, 25.5; ESI-TOFMS (*m/z*) calcd for $[C_{27}H_{25}N_3O_6+H]^+$ 458.2074; found: 458.2075.



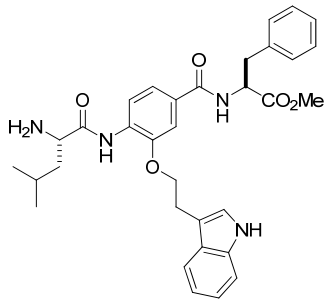
O_2N-[Trp]-Phe-OH. ^1H NMR (500 MHz, acetone-d_6, 25 °C) δ 10.12 (s, 1H), 8.07 (d, J = 7.7 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.1 Hz, 1H), 7.65 (s, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.31 (m, 3H), 7.21 (t, J = 7.7 Hz, 1H), 7.11 (q, J = 7.3 Hz, 2H), 7.04 (t, J = 7.7 Hz, 1H), 4.88 (m, 1H), 4.43 (t, J = 7.0 Hz, 2H), 3.31 (m, 1H), 3.29 (t, J = 7.0 Hz, 2H), 3.09 (m, 1H); ^{13}C NMR (125 MHz, acetone-d_6, 25 °C) δ 173.6, 166.3, 152.9, 140.8, 139.1, 138.2, 130.7, 129.8, 129.1, 128.0, 126.3, 124.8, 122.8, 120.6, 120.2, 119.8, 115.2, 112.8, 112.0, 71.5, 55.7, 38.4, 26.2; ESI-TOFMS (*m/z*) calcd for $[C_{26}H_{23}N_3O_6+H]^+$ 474.1660; found: 474.1653.



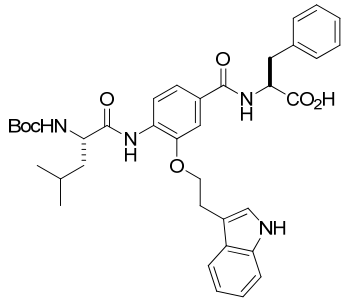
H_2N-[Trp]-Phe-OH. ^1H NMR (500 MHz, CD_3OD, 25 °C) δ 7.62 (d, J = 8.1 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.20 (m, 7H), 7.09 (q, J = 7.4 Hz, 2H), 7.03 (t, J = 7.4 Hz, 1H), 6.66 (d, J = 8.1 Hz, 1H), 4.77 (m, 1H), 4.26 (m, 2H), 3.31 (m, 1H), 3.27 (t, J = 6.6 Hz, 2H), 3.10 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD, 25 °C) δ 147.1, 142.9, 139.0, 138.3, 130.5, 129.5, 129.2, 127.8, 123.9, 123.7, 122.5(2C), 119.9, 119.4, 114.6, 112.6, 112.4, 111.8, 70.5, 56.0, 38.5, 26.5; ESI-TOFMS (*m/z*) calcd for $[C_{26}H_{25}N_3O_4+H]^+$ 444.1918; found: 444.1913.



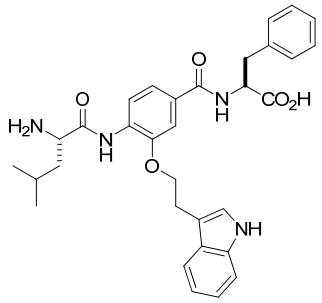
Boc-Leu-[Trp]-Phe-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.62 (s, 1H), 8.37 (s, 1H), 8.35 (s, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.43 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.23 (m, 6H), 7.12 (t, *J* = 7.1 Hz, 3H), 6.51 (d, *J* = 7.7 Hz, 1H), 5.05 (m, 1H), 4.44 (m, 1H), 4.36 (m, 1H), 4.21 (m, 1H), 3.77 (s, 3H), 3.31 (m, 2H), 3.24 (m, 2H), 1.66 (m, 2H), 1.59 (m, 1H), 1.50 (s, 9H), 0.94 (dd, *J* = 6.1, 2.4 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ 172.3, 171.0, 166.3, 155.9, 147.4, 136.6, 136.0, 131.2, 129.5, 129.2, 128.9, 127.5, 122.7, 122.4, 119.7, 119.5, 118.9, 118.7, 112.1, 111.7, 111.2, 68.8, 54.3, 53.7, 52.7, 42.0, 38.1, 28.6, 25.5, 25.0, 23.1, 22.2; ESI-TOFMS (*m/z*) calcd for $[C_{38}H_{46}N_4O_7+H]^+$ 671.3439; found: 671.3428.



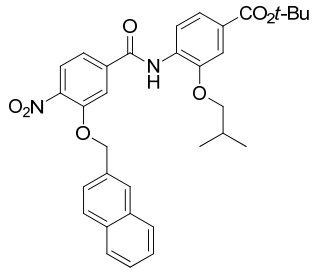
H_2N-Leu-[Trp]-Phe-OMe. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 10.04 (s, 1H), 8.45 (d, *J* = 8.2 Hz, 1H), 8.13 (s, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 1.8 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.23 (s, 5H), 7.13 (m, 4H), 6.53 (d, *J* = 7.6 Hz, 1H), 5.06 (m, 1H), 4.40 (td, *J* = 6.7, 1.8 Hz, 2H), 3.77 (s, 3H), 3.44 (m, 1H), 3.31 (t, *J* = 6.7 Hz, 2H), 3.24 (m, 2H), 1.76 (m, 3H), 1.26 (s, 6H), 0.97 (dd, *J* = 11.6, 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 174.4, 172.3, 166.6, 147.8, 136.4, 136.0, 131.4, 129.5, 128.9, 128.8, 127.7, 122.5, 122.4, 119.7, 119.5, 118.9, 118.7, 112.3, 111.4, 110.8, 69.0, 54.5, 53.7, 52.6, 44.1, 38.1, 29.9, 25.4, 25.2, 23.6, 21.5; ESI-TOFMS (*m/z*) calcd for $[C_{33}H_{38}N_4O_5+H]^+$ 571.2915; found: 571.2912.



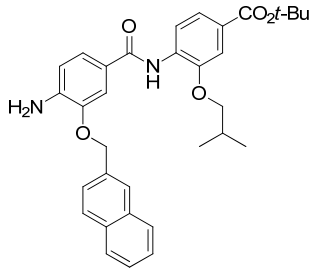
Boc-Leu-[Trp]-Phe-OH. ^{1}H NMR (500 MHz, acetone-d_6, 25 °C) δ 10.12 (s, 1H), 9.10 (s, 1H), 8.42 (d, *J* = 8.5 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 1.5 Hz, 1H), 7.45 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.38 (d, *J* = 2.2 Hz, 1H), 7.32 (d, *J* = 7.0 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.13 (m, 2H), 7.06 (t, *J* = 7.0 Hz, 1H), 6.50 (m, 1H), 4.87 (m, 1H), 4.36 (m, 1H), 4.28 (m, 1H), 3.37 (t, *J* = 7.1 Hz, 2H), 3.29 (m, 1H), 3.09 (m, 1H), 1.74 (m, 2H), 1.64 (m, 1H), 1.45 (s, 9H), 0.95 (t, *J* = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, acetone-d_6, 25 °C) δ 173.3, 172.0, 166.9, 148.1, 138.7, 137.8, 131.9, 130.2, 129.2, 128.6, 127.5, 124.2, 122.3, 121.1, 119.8, 119.2, 119.1, 112.4, 111.6, 111.4, 70.1, 55.2, 55.0, 41.1, 38.0, 28.7, 26.2, 25.7, 23.5, 21.9; ESI-TOFMS (*m/z*) calcd for $[C_{37}H_{44}N_4O_7+H]^+$ 657.3283; found: 657.3282.



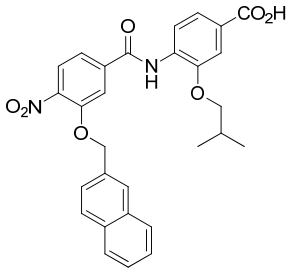
H_2N-Leu-[Trp]-Phe-OH. ^{1}H NMR (400 MHz, CD_3OD, 25 °C) δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 1.5 Hz, 1H), 7.36 (m, 1H), 7.35 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.25 (d, *J* = 7.0 Hz, 2H), 7.10 (m, 6H), 4.82 (m, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 3.98 (m, 1H), 3.34 (t, *J* = 6.7 Hz, 2H), 3.09 (dd, *J* = 13.8, 9.7 Hz, 1H), 1.68 (m, 3H), 0.94 (t, *J* = 2.9 Hz, 6H); ^{13}C NMR (100 MHz, CD_3OD, 25 °C) δ 169.6, 150.4, 138.9, 138.3, 132.6, 130.8, 130.4, 129.6, 129.1, 127.9, 123.9, 122.7, 120.0, 119.3, 112.6, 112.0, 70.7, 38.3, 30.9, 26.3, 23.1, 22.5; ESI-TOFMS (*m/z*) calcd for $[C_{32}H_{36}N_4O_5+H]^+$ 557.2758; found: 557.2754.



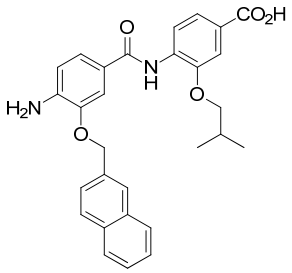
O_2N-[Nap]-[Leu]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.77 (s, 1H), 8.55 (d, *J* = 8.5Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.95 (s, 1H), 7.87 (m, 4H), 7.68 (d, *J* = 7.0Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.55 (s, 1H), 7.51 (m, 2H), 7.41 (d, *J* = 7.0 Hz, 1H), 5.49 (s, 2H), 3.92 (d, *J* = 6.5 Hz, 2H), 2.18 (m, 1H), 1.61 (s, 9H), 1.08 (d, *J* = 7.0 Hz); HRMS-ESI (*m/z*) calcd for $[C_{33}H_{34}N_2O_7+H]^+$ 571.2439; found: 571.2431.



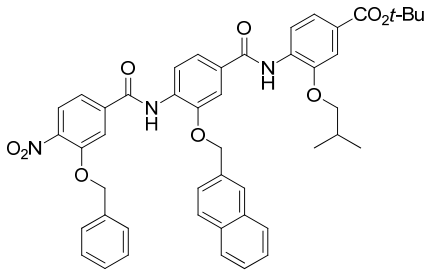
H_2N-[Nap]-[Leu]-OtBu. ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C) δ 8.70 (s, 1H), 8.59 (d, *J* = 8.4 Hz, 1H), 7.98 (s, 1H), 7.89 (m, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.72 (s, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H), 7.53 (m, 3H), 7.40 (m, 2H), 7.18 (s, 2H), 5.24 (s, 2H), 3.92 (d, *J* = 6.6 Hz, 2H), 2.18 (m, 1H), 1.61 (s, 9H), 1.08 (d, *J* = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{33}H_{36}N_2O_5+H]^+$ 541.2697; found: 541.2688.



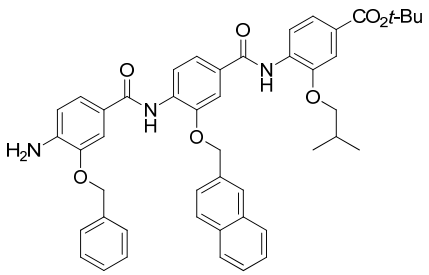
O_2N-[Nap]-[Leu]-OH. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C) δ 12.92 (s, 1H), 9.84 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.96 (m, 6H), 7.67 (d, J = 8.5 Hz, 1H), 7.58 (m, 5H), 5.58 (s, 2H), 3.87 (d, J = 6.0 Hz, 2H), 2.05 (m, 1H), 0.96 (d, J = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{29}H_{26}N_2O_7+H]^+$ 515.1813; found: 515.1816.



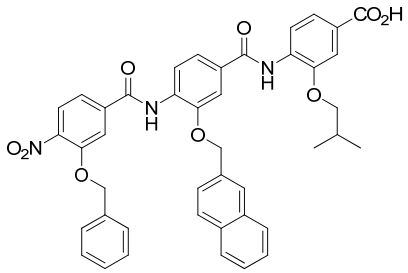
H_2N-[Nap]-[Leu]-OH. ^{1}H NMR (600 MHz, CD_2Cl_2-CD_3OD (1:1), 25 °C) δ 8.55 (s, 1H), 7.93 (m, 12H), 5.67 (s, 2H), 4.10 (m, 2H), 2.36 (m, 1H), 1.24 (m, 6H); HRMS-ESI (*m/z*) calcd for $[C_{29}H_{28}N_2O_5+H]^+$ 485.2071; found: 485.2075.



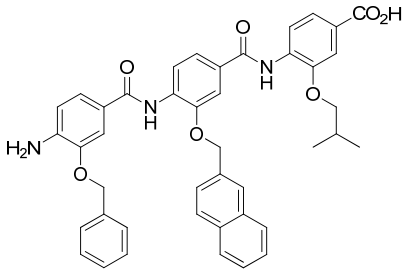
O_2N-[Phe]-[Nap]-[Leu]-OtBu. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.85 (s, 1H), 8.77 (s, 1H), 8.65 (d, J = 8.5 Hz, 1H), 8.59 (d, J = 8.5 Hz, 1H), 7.89 (s, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.81 (m, 3H), 7.73 (d, J = 8.5 Hz, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.63 (s, 1H), 7.51 (m, 5H), 7.35 (m, 5H), 7.25 (m, 1H), 5.37 (s, 2H), 5.10 (s, 2H), 3.92 (d, J = 6.5 Hz, 2H), 2.21 (m, 1H), 1.61 (s, 9H), 1.12 (d, J = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{47}H_{45}N_3O_9+H]^+$ 796.3228; found: 796.3222.



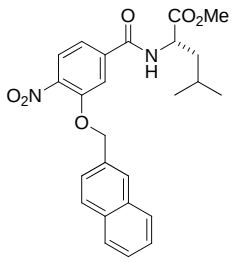
H_2N-[Phe]-[Nap]-[Leu]-OtBu. ^1H NMR (500 MHz, CD_2Cl_2-CD_3OD (1:1), 25 °C) δ 8.79 (d, J = 8.5 Hz, 1H), 8.67 (d, J = 8.5 Hz, 1H), 8.20 (s, 1H), 8.09 (m, 2H), 7.99 (m, 2H), 7.86 (t, J = 7.0 Hz, 2H), 7.77 (m, 2H), 7.70 (m, 2H), 7.62 (s, 1H), 7.56 (m, 6H), 7.07 (d, J = 8.5 Hz, 1H), 5.67 (s, 2H), 5.17 (s, 2H), 4.17 (d, J = 6.5 Hz, 2H), 2.44 (m, 1H), 1.82 (s, 9H), 1.34 (d, J = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{47}H_{47}N_3O_7+H]^+$ 766.3487; found: 766.3479.



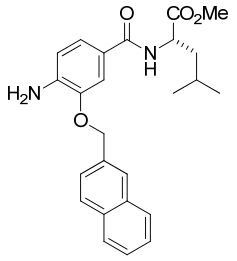
O_2N-[Phe]-[Nap]-[Leu]-OH. ^1H NMR (500 MHz, DMSO-d_6, 25 °C) δ 12.93 (s, 1H), 10.08 (s, 1H), 9.51 (s, 1H), 8.04 (m, 3H), 7.97 (m, 2H), 7.91 (d, J = 8.5 Hz), 7.86 (m, 1H), 7.81 (m, 2H), 7.66 (m, 4H), 7.57 (s, 1H), 7.48 (m, 2H), 7.37 (m, 5H), 5.48 (s, 2H), 5.33 (s, 2H), 3.90 (d, J = 6.5 Hz, 2H), 2.09 (m, 1H), 0.99 (d, J = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{43}H_{37}N_3O_9+Na]^+$ 762.2422; found: 762.2419.



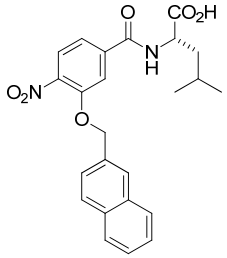
H_2N-[Phe]-[Nap]-[Leu]-OH. ^1H NMR (600 MHz, CD_2Cl_2-CD_3OD (1:1), 25 °C) δ 8.72 (d, J = 7.2 Hz, 1H), 8.67 (d, J = 7.8 Hz, 1H), 8.18 (s, 1H), 8.05 (m, 2H), 7.97 (s, 2H), 7.91 (d, J = 7.8 Hz, 1H), 7.67 (m, 10H), 7.43 (s, 1H), 5.66 (s, 2H), 5.25 (s, 2H), 4.15 (d, J = 5.4 Hz, 2H), 2.41 (m, 1H), 1.31 (d, J = 6.6 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{43}H_{39}N_3O_7+H]^+$ 710.2861; found: 710.2855.



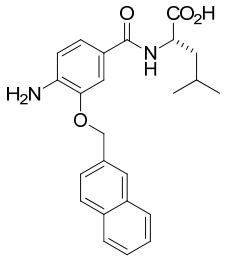
O_2N-[Nap]-Leu-OMe. ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 7.87 (s, 1H), 7.79 (m, 4H), 7.63 (s, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.45 (m, 2H), 7.34 (d, J = 7.2 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 5.32 (m, 2H), 4.84 (m, 1H), 3.79 (s, 3H), 1.71 (m, 3H), 0.97 (d, J = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{25}H_{26}N_2O_6+H]^+$ 451.1864; found: 451.1851.



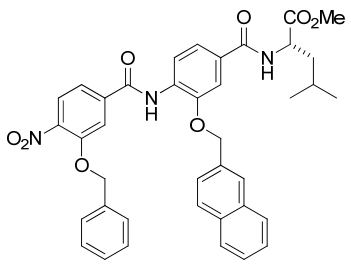
H_2N-[Nap]-Leu-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 7.85 (m, 4H), 7.50 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 8.0 Hz, 1H), 5.21 (s, 2H), 4.85 (m, 1H), 4.20 (s, 2H), 3.74 (s, 3H), 1.68 (m, 3H), 0.97 (t, *J* = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{25}H_{28}N_2O_4+H]^+$ 421.2122; found: 421.2126.



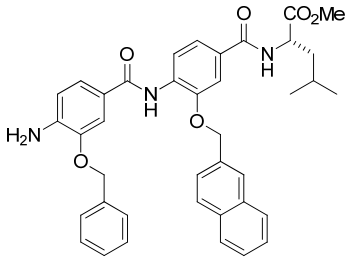
O_2N-[Nap]-Leu-OH. ^{1}H NMR (400 MHz, acetone-d_6, 25 °C) δ 8.12 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 7.94 (m, 5H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.54 (m, 2H), 5.57 (s, 2H), 4.74 (m, 1H), 1.79 (m, 3H), 0.97 (t, *J* = 6.0 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{24}N_2O_6-H]^-$ 435.1562; found: 435.1553.



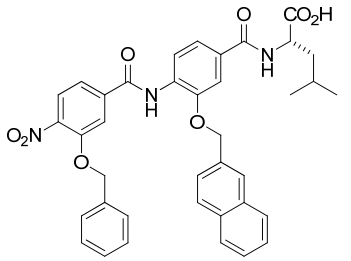
H_2N-[Nap]-Leu-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.52 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 8.07 (s, 1H), 7.94 (m, 3H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.53 (m, 3H), 7.37 (d, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.32 (s, 2H), 4.41 (m, 1H), 3.17 (s, 2H), 1.75 (m, 1H), 1.67 (m, 1H), 1.56 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{24}H_{26}N_2O_4+H]^+$ 407.1965; found: 407.1974.



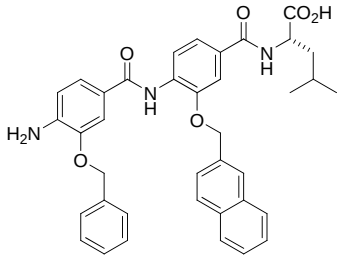
O_2N-[Phe]-[Nap]-Leu-OMe. ^1H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.70 (s, 1H), 8.52 (d, J = 8.0 Hz, 1H), 7.82 (m, 2H), 7.77 (m, 2H), 7.67 (s, 2H), 7.59 (s, 1H), 7.48 (m, 3H), 7.42 (d, J = 8.5 Hz, 1H), 7.34 (m, 5H), 7.19 (d, J = 8.0 Hz, 1H), 6.87 (s, 1H), 5.29 (s, 2H), 5.06 (s, 2H), 4.88 (m, 1H), 3.79 (s, 3H), 1.75 (m, 3H), 1.01 (t, J = 5.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{39}H_{37}N_3O_8+H]^+$ 676.2653; found: 676.2630.



H_2N-[Phe]-[Nap]-Leu-OMe. ^1H NMR (500 MHz, DMSO-d_6, 25 °C) δ 9.19 (s, 1H), 8.68 (d, J = 7.5 Hz, 1H), 8.11 (m, 2H), 7.91 (d, J = 8.0 Hz, 1H), 7.86 (m, 2H), 7.72 (s, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.50 (m, 3H), 7.39 (m, 5H), 7.32 (d, J = 7.0 Hz, 1H), 6.69 (d, J = 8.5 Hz, 1H), 5.52 (s, 2H), 5.45 (s, 2H), 5.07 (s, 2H), 4.51 (m, 1H), 3.65 (s, 3H), 1.80 (m, 1H), 1.69 (m, 1H), 1.60 (m, 1H), 0.94 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 6.5 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{39}H_{39}N_3O_6+H]^+$ 646.2911; found: 646.2904.

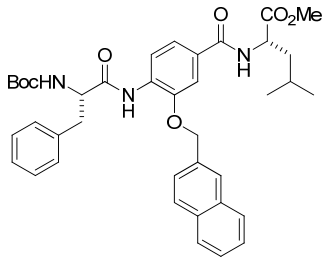


O_2N-[Phe]-[Nap]-Leu-OH. ^1H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.59 (s, 1H), 10.02 (s, 1H), 8.62 (d, J = 7.8 Hz, 1H), 8.04 (m, 2H), 7.96 (s, 1H), 7.87 (m, 3H), 7.79 (m, 1H), 7.75 (s, 1H), 7.70 (d, J = 9.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.48 (m, 2H), 7.40 (m, 4H), 7.35 (m, 1H), 5.45 (s, 2H), 5.32 (s, 2H), 4.46 (m, 1H), 1.79 (m, 1H), 1.70 (m, 1H), 1.61 (m, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{38}H_{35}N_3O_8+H]^+$ 662.2497; found: 662.2494.

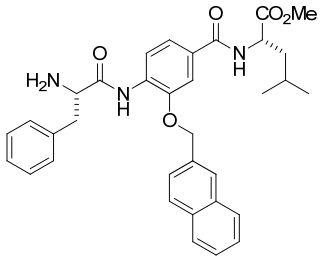


H_2N-[Phe]-[Nap]-Leu-OH. ^1H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.57 (s, 1H), 9.18 (s, 1H), 8.55 (d, J = 7.8 Hz, 1H), 8.11 (m, 2H), 7.91 (d, J = 8.4 Hz, 1H), 7.86 (m, 2H), 7.72 (m, 2H), 7.59 (d, J = 8.4 Hz, 1H), 7.50 (m, 2H), 7.47 (s, 1H), 7.39 (m, 5H), 7.32 (d, J = 7.2 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 5.51 (s, 2H), 5.45 (s, 2H), 5.07 (s, 2H), 4.46 (m, 1H), 1.79 (m, 1H), 1.71 (m, 1H), 1.61 (m, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{38}H_{37}N_3O_6+H]^+$ 632.2755;

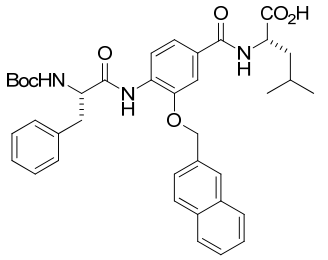
found: 632.2757.



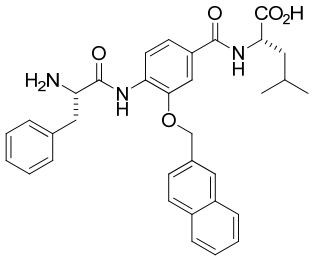
Boc-Phe-[Nap]-Leu-OMe. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 8.51 (s, 1H), 8.39 (d, J = 7.5 Hz, 1H), 7.85 (m, 3H), 7.80 (s, 1H), 7.53 (s, 1H), 7.50 (m, 2H), 7.41 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H), 7.17 (m, 5H), 6.91 (s, 1H), 5.16 (m, 2H), 5.05 (s, 1H), 4.85 (m, 1H), 4.54 (s, 1H), 3.60 (s, 3H), 3.13 (m, 1H), 3.04 (m, 1H), 1.70 (m, 3H), 1.28 (s, 9H), 0.95 (d, J = 6.0 Hz, 3H), 0.94 (d, J = 6.0 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{39}H_{45}N_3O_7+H]^+$ 668.3330; found: 668.3308.



H_2N-Phe-[Nap]-Leu-OMe. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 9.97 (s, 1H), 8.68 (d, J = 7.8 Hz, 1H), 8.35 (s, 2H), 8.04 (s, 1H), 7.93 (m, 2H), 7.87 (m, 1H), 7.66 (s, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.53 (m, 2H), 7.29 (m, 5H), 5.46 (m, 2H), 4.49 (m, 2H), 3.63 (s, 3H), 3.37 (3H, overlapped with H_2O peak in DMSO), 3.19 (m, 1H), 3.10 (m, 1H), 1.78 (m, 1H), 1.65 (m, 1H), 1.58 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{34}H_{37}N_3O_5+H]^+$ 568.2806; found: 568.2805.



Boc-Phe-[Nap]-Leu-OH. ^{1}H NMR (500 MHz, acetone-d_6, 25 °C) δ 9.17 (s, 1H), 8.48 (d, J = 8.5 Hz, 1H), 8.05 (s, 1H), 7.93 (m, 3H), 7.83 (d, J = 8.5 Hz, 1H), 7.75 (s, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.52 (m, 2H), 7.27 (m, 4H), 7.20 (d, J = 7.0 Hz, 1H), 6.48 (s, 1H), 5.41 (s, 2H), 4.74 (m, 1H), 4.55 (s, 1H), 3.32 (m, 1H), 3.03 (m, 1H), 1.83 (m, 3H), 1.21 (s, 9H), 0.96 (t, J = 6.5 Hz, 6H); HRMS-ESI (*m/z*) calcd for $[C_{38}H_{43}N_3O_7+H]^+$ 654.3174; found: 654.3188.



H_2N-Phe-[Nap]-Leu-OH. ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 12.56 (s, 1H), 9.93 (s, 1H), 8.52 (d, J = 7.8 Hz, 1H), 8.31 (s, 2H), 8.02 (s, 1H), 7.91 (m, 2H), 7.85 (m, 1H), 7.65 (s, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.51 (m, 2H), 7.27 (m, 5H), 5.44 (m, 2H), 4.49 (s, 1H), 4.40 (m, 1H), 3.36 (3H, overlapped with H_2O peak in DMSO), 3.17 (m, 1H), 3.07 (m, 1H), 1.74 (m, 1H), 1.63 (m, 1H), 1.56 (m, 1H), 0.89 (d, J = 6.0 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H); HRMS-ESI (*m/z*) calcd for $[C_{33}H_{35}N_3O_5+H]^+$ 554.2649; found: 554.2642.

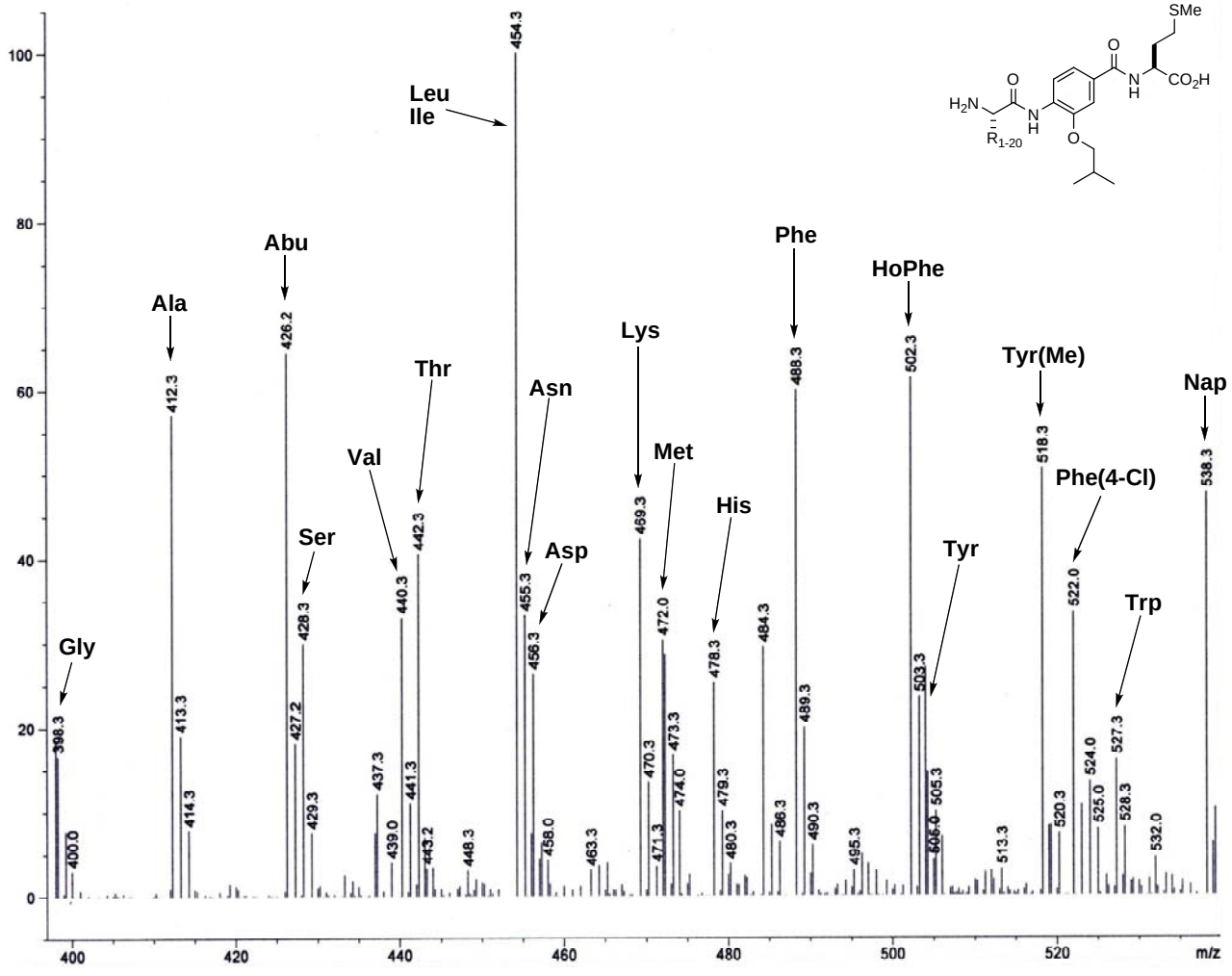


Figure S3. MS detection of all 20 compounds in a mixture of 20 trimers.

MDM2/p53 Binding Assay A streptavidin-coated 96 well plate (ReactiBind™ Streptavidin High Binding Capacity coated plate, Pierce) was rinsed with wash buffer (PBS + 0.05% Tween-20, 3x) and incubated with 100 μL per well of biotinylated SGSG-p53 peptide (17–27, 50 nM in wash buffer) at 4 °C for 1 h. Unbound peptide was then removed by rinsing with wash buffer (3x). In a separate 96 well polypropylene plate (Pierce), 50 μL of MDM2 (4 nM, EMD Bioscience) was incubated with 50 μL of inhibitor (a range of concentrations) at 4 °C for 30 min in a Wallac assay buffer (Perkin Elmer, Product No. 1244-111). The MDM2/inhibitor mixtures (100 μL) were then transferred to a well in the streptavidin-coated plate and then left to incubate at 4 °C for 1 h. The wells were then washed with wash buffer (5x), followed by the addition of 100 μL of anti-MDM2 [(Ab-6) mouse mAb(5B10C)] (EMD Bioscience), diluted 500-fold with a dilution buffer (PBS + 0.05% Tween-20 + 1% bovine serum albumin). After 2 h at 4 °C, the wells were washed with wash buffer (5x) and a solution of anti-mouse IgG horseradish peroxidase conjugate (Jackson Immunochemical), diluted in dilution buffer (1 μg/mL), was added. The wells were incubated at 4 °C for 1 h before being washed with wash buffer (5x). A 100 μL solution of peroxidase substrate, 3,3',5',5-tetramethylbenzidine (Sigma-Aldrich), was added and the reaction was allowed to incubate at room temperature for 30 min to develop a blue product. Quenching the reaction with 100 μL of aqueous HCl (0.15 N) produces a yellow color which can be read at 450 nm. The percentage of p53/MDM2 binding was calculated from which the IC50 values for the analogues were determined. The assay was performed in triplicate using a blank which does not contain SGSG-p53 peptide as a negative control.

Full citation for references 21c and 21f:

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