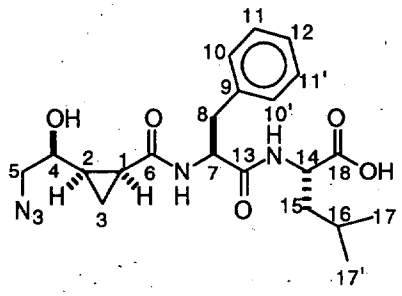
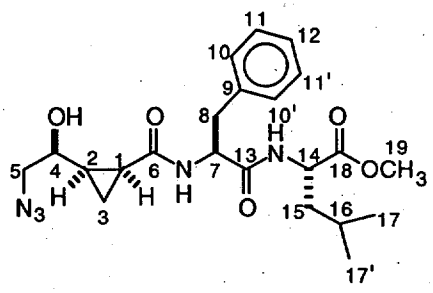
(*E*)-3-Phenyl-2-propenyldiazoacetate (27). Prepared from cinnamyl alcohol in 85% yield. The crude diazoacetate was purified by flash chromatography eluting with hexanes/EtOAc (15:1). This material was identical by ^1H and ^{13}C NMR spectroscopy as to the material reported by Doyle.[1]

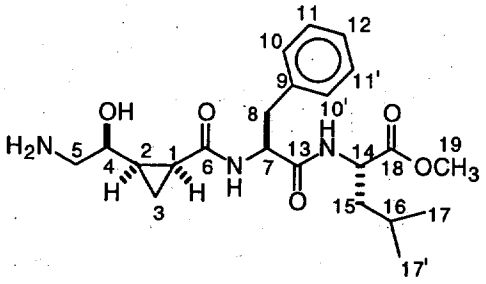


[1*S*,2*S*,2(1'*R*)]-2-(2'-Azido-1'-hydroxy)ethyl-cyclopropyl-1-carboxy-L-phenylalanyl-L-leucine. Prepared in 61% yield from **21** as a waxy white solid; CH_2Cl_2/MeOH (15:1); mp 146-148 °C; ^1H NMR (300 MHz, CD_3OD) δ 7.29-7.15 (comp, 5 H), 4.66-4.61 (m, 1 H), 4.49-4.42 (m, 1 H), 3.69-3.63 (m, 1 H), 3.20-3.09 (comp, 3 H), 2.85 (dd, *J* = 9.7, 13.9 Hz, 1 H), 1.79-1.59 (comp, 4 H), 1.29-1.23 (m, 1 H), 1.08-1.02 (m, 1 H), 1.00-0.95 (m, 1 H), 0.94 (d, *J* = 8.9 Hz, 3 H), 0.92 (d, *J* = 8.9 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.9, 173.7, 173.4, 138.4, 130.2 (2), 129.3 (2), 127.6, 70.3, 57.4, 56.0, 52.1, 41.8, 38.9, 25.8, 24.4, 23.3, 22.0, 20.0, 11.1; IR (nujol) ν 3290, 2095, 1635, 1540, 1060 cm^{-1}; mass spectrum (CI) *m/z* 432.2256 ($C_{21}H_{29}N_5O_5$+H requires 432.2247), 242 (base).

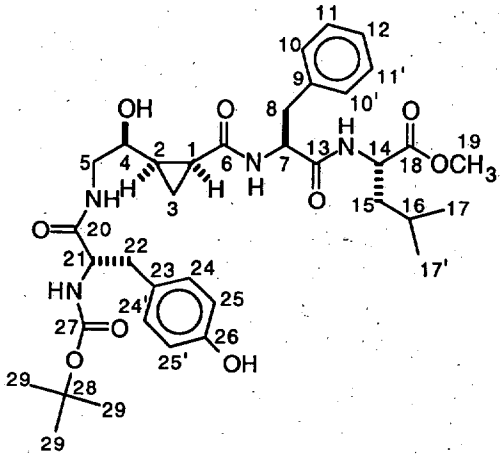


[1*S*,2*S*,2(1'*R*)]-2-(2'-Azido-1'-hydroxy)ethyl-cyclopropyl-1-carboxy-L-phenylalanyl-L-leucyl methyl ester. Prepared in 94% yield from requisite acid as a glassy solid; MeOH/CH_2Cl_2 (25:1); mp 156-158 °C; ^1H NMR (300 MHz, CD_3OD) δ 7.27-7.19 (comp, 5 H), 4.64 (dd, *J* = 5.5, 9.3 Hz, 1 H), 4.46 (dd, *J* = 6.3, 8.7 Hz, 1 H), 3.67 (s, 3 H) 3.66-3.63 (m, 1 H), 3.21 (dd, *J* = 3.5, 12.7 Hz, 1 H), 3.16 (dd, *J* = 6.9, 12.7 Hz, 1 H), 3.11 (dd, *J* = 5.6, 13.9 Hz, 1 H), 2.85 (dd, *J* = 9.7, 13.9 Hz, 1 H), 1.79-1.55 (comp, 4 H), 1.31-1.25 (m, 1 H), 1.10-1.00 (m, 1 H), 0.97 (dt, J = 6.3, 8.7 Hz, 1 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 0.90 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ

174.4, 173.7, 173.4, 138.4, 130.2 (2), 129.4 (2), 127.7, 70.4, 57.4, 56.0, 52.7, 52.1, 41.6, 38.9, 25.8, 24.5, 23.2, 22.0, 20.1, 11.1; IR (nujol) ν 3305, 2095, 1730, 1645 cm^{-1}; mass spectrum (CI) *m/z* 446.2387 ($C_{22}H_{31}N_5O_5$+H requires 446.2403), 212, 186.

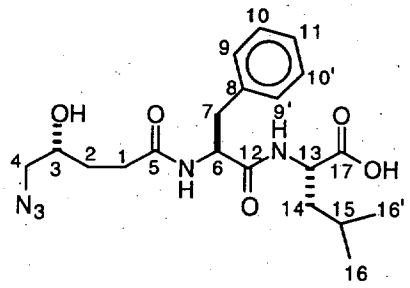


[1*S*,2*S*,2(1'*R*)]-2-(2'-Amino-1'-hydroxy)ethyl-cyclopropyl-1-carboxy-L-phenylalanyl-L-leucyl methyl ester (22). Prepared in 92% yield from the preseeding azide as pale yellow solid; mp 136-138 °C; ^1H NMR (300 MHz, CD_3OD) δ 7.30-7.18 (comp, 5 H), 4.65-4.61 (m, 1 H), 4.47-4.40 (m, 1 H), 3.67 (s, 3 H) 3.43-3.39 (m, 1 H), 3.15 (dd, *J* = 5.4, 13.9 Hz, 1 H), 2.86 (dd, *J* = 9.4, 13.9 Hz, 1 H), 2.70-2.56 (m, 2 H, C5-H), 1.80-1.56 (comp, 4 H), 1.30-1.21 (m, 1 H), 1.19-0.97 (comp, 2 H), 0.93 (d, *J* = 10.8 Hz, 3 H), 0.90 (d, *J* = 10.8 Hz, 3 H; ^{13}C NMR (75 MHz, CD_3OD) δ 174.3, 173.9, 173.8, 138.4, 130.3 (2), 129.4 (2), 127.7, 71.8, 56.2, 52.6, 52.1, 49.3, 41.5, 38.9, 25.8, 25.1, 23.3, 21.9, 20.3, 10.3; IR (nujol) ν 3298, 1735, 1640, 1534, 1096 cm^{-1}; mass spectrum (CI) *m/z* 420.2499 ($C_{22}H_{33}N_2O_5$+H requires 420.2498), 261, 212(base).

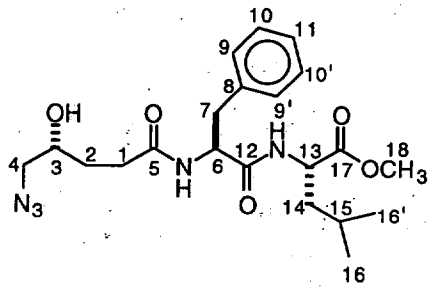


***N*-[1*S*,2*S*,2(1'*R*)]-2-[2'-(*N*-*tert*-Butoxycarbonyl-L-tyrosyl)amino-1'-hydroxy]ethyl-cyclopropyl-1-carboxy-L-phenylalanyl-L-leucyl methyl ester.** Prepared in 70% yield from **22** as a white solid; CH_2Cl_2/MeOH (25:1); mp 121-123 °C; ^1H NMR (300 MHz, CD_3OD) δ 7.30-7.17 (comp, 5 H), 7.06 (d, *J* = 8.5 Hz, 2 H), 6.70 (d, *J* = 8.5 Hz, 2 H), 4.61 (dd, *J* =

4.8, 10.4 Hz, 1 H), 4.56-4.50 (comp, 2 H), 3.72 (s, 3 H) 3.69-3.65 (m, 1 H), 3.37 (dt, *J* = 5.2, 9.6 Hz, 1 H), 3.14 (dd, *J* = 4.2, 14.3 Hz, 1 H), 2.90-2.84 (comp, 2 H), 2.81 (dd, *J* = 10.8, 14.3 Hz, 1 H), 2.71 (dd, J = 9.7, 13.7 Hz, 1 H), 1.76-1.60 (comp, 4 H), 1.37 (s, 9 H), 1.13-1.10 (m, 1 H), 1.07-1.03 (m, 1 H), 0.95 (d, *J* = 6.6 Hz, 3 H), 0.89 (d, *J* = 6.6 Hz, 3 H), 0.81-0.78 (m, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.5, 175.4, 174.6, 174.1, 158.3, 157.2, 138.6, 131.5 (2), 130.1 (2), 129.6 (2), 129.4, 127.7, 116.1 (2), 80.7, 69.0, 58.2, 57.1, 52.8, 52.1, 45.1, 41.7, 38.8, 38.5, 28.8, 25.7, 25.3, 23.5, 21.7, 21.0, 8.5; IR ($CHCl_3$) ν 3307, 2958, 1739, 1688, 1516, 1456, 1418, 1171 cm^{-1}; mass spectrum (CI) *m/z* 683.3664 ($C_{36}H_{50}N_4O_9$+H requires 683.3656), 583, 293 (base).

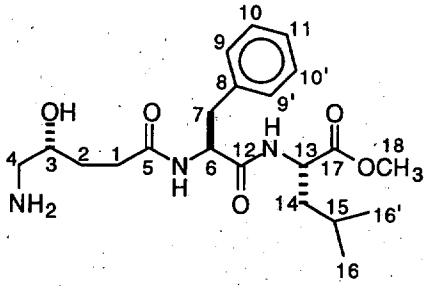


***N*-[1-(2'-Azido-1'*R*-hydroxy)butylcarboxy]-L-phenylalanyl-L-leucine.** Prepared in 73% yield from **40** as a waxy solid; CH_2Cl_2/MeOH (10:1); mp 56-58 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.29-7.16 (m, 5 H), 4.72-4.67 (m, 1 H), 4.45-4.41 (m, 1 H), 3.58-3.51 (m, 1H), 3.21-3.11 (comp, 3 H), 2.83 (dd, *J* = 4.0, 9.9 Hz, 1 H), 2.32-2.15 (m, 2 H), 1.72-1.55 (comp, 5 H), 0.95 (d, *J* = 6.2 Hz, 3 H), 0.91 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.4, 173.8 (2), 138.6, 130.3 (2), 129.4 (2), 127.7, 71.0, 57.6, 55.7, 52.3, 41.8, 38.8, 32.8, 31.2, 26.0, 23.4, 21.9; IR ($CHCl_3$) ν 3336, 2960, 2105, 1718, 1662, 1516 cm^{-1}; mass spectrum (CI) *m/z* 420.2247 ($C_{20}H_{29}N_5O_5$+H requires 420.2247), 391, 377, 120.

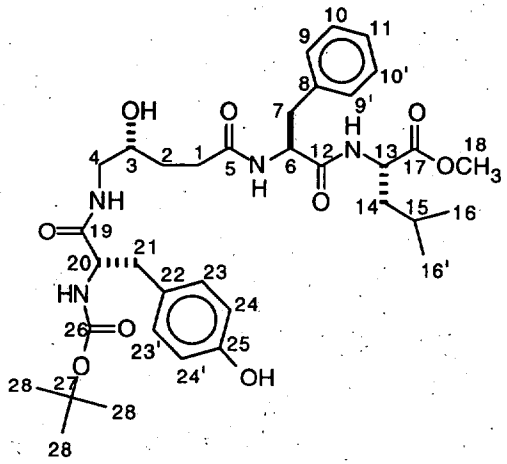


***N*-[1-(2'-Azido-1'*R*-hydroxy)butylcarboxy]-L-phenylanalyl-L-leucyl methyl ester (41).** Prepared in 95% yield from the requisite acid as a glassy solid; MeOH/CH_2Cl_2 (25:1); mp 99-101

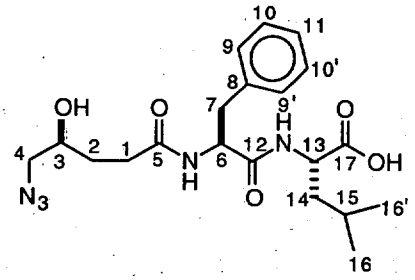
°C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.26-7.17 (comp, 5 H), 4.69 (dd, *J* = 5.3, 9.5 Hz, 1H), 4.46 (dd, *J* = 6.1, 8.7 Hz, 1 H), 3.67 (s, 3 H), 3.61-3.56 (m, 1 H), 3.18-3.11 (comp, 3 H), 2.84 (dd, *J* = 9.6, 13.9 Hz, 1 H), 2.25 (t, *J* = 7.5 Hz, 2 H), 1.70-1.54 (comp, 5 H), 0.94 (d, *J* = 6.2 Hz, 3 H), 0.90 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.3, 174.3, 173.9, 138.4, 130.3 (2), 129.4 (2), 127.7, 70.9, 57.6, 52.7, 52.1, 41.4, 38.8, 32.7, 31.1, 25.8, 23.3, 21.8; IR (nujol) ν 3280, 2096, 1745, 1654, 1624 cm^{-1}; mass spectrum (CI) *m/z* 434.2394 ($C_{21}H_{31}N_5O_5$+H requires 434.2403), 416, 391, 290.



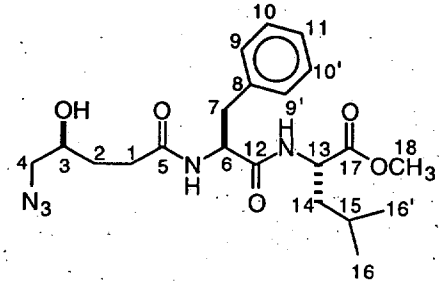
N-[1-(2'-Amino-1'*R*-hydroxy)butylcarboxy]-L-phenylanalyl-L-leucyl methyl ester. Prepared in 90% yield as a crystalline solid; mp 68-70 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.29-7.17 (comp, 5 H), 4.68 (dd, *J* = 5.2, 9.5 Hz, 1 H), 4.45 (dd, *J* = 6.1, 8.8 Hz, 1 H), 3.42-3.38 (m, 1 H), 3.15 (dd, *J* = 5.2, 14.0 Hz, 1 H), 2.84 (dd, *J* = 9.6, 14.0 Hz, 1 H), 2.57 (dd, *J* = 4.0, 13.1 Hz, 1 H), 2.45 (dd, *J* = 7.5, 13.1 Hz, 1 H), 2.27-2.23 (m, 2 H), 1.69-1.51 (comp, 5 H), 0.94 (d, *J* = 6.4 Hz, 3 H), 0.90 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.7, 174.3, 173.8, 138.5, 130.3 (2), 129.4 (2), 127.7, 72.8, 55.7, 52.7, 52.2, 49.3, 41.6, 38.8, 33.1, 31.5, 25.9, 23.2, 22.0; IR (nujol) ν 3292, 1745, 1644, 1565, 1105 cm^{-1}; mass spectrum (CI) *m/z* 408.2495 ($C_{21}H_{33}N_3O_5$+H requires 408.2498), 307, 298 (base), 261.



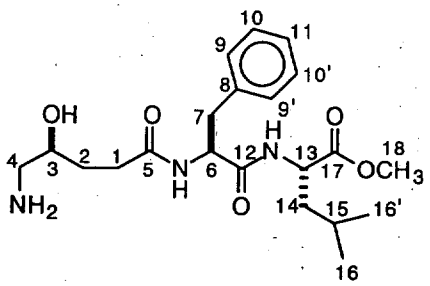
***N*-[1-(2'[*N*-*tert*-Butoxycarbonyl-L-tyrosyl]amino-1'(*R*)-hydroxy)butylcarboxy]-L-phenylanalyl-L-leucyl methyl ester.** Prepared in 74% yield as an off-white solid; CH_2Cl_2/MeOH (25:1); mp 100-102 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.32-7.16 (comp, 5 H), 7.02 (d, *J* = 8.3 Hz, 2 H), 6.68 (d, *J* = 8.3 Hz, 2 H), 4.67 (dd, J = 5.4, 9.5 Hz, 1 H), 4.45 (dd, J = 6.0, 9.0 Hz, 1 H), 4.21-4.16 (m, 1 H), 3.67 (s, 3 H), 3.49-3.43 (m, 1 H), 3.18-3.05 (comp, 3 H), 2.96 (dd, *J* = 6.0, 13.8 Hz, 1 H), 2.84 (dd, *J* = 8.9, 14.0 Hz, 1 H), 2.72 (dd, *J* = 8.9, 13.8 Hz, 1 H), 2.24 (app t, *J* = 7.6 Hz, 2 H), 1.69-1.41 (comp, 5 H), 1.36 (s, 9 H), 0.94 (d, *J* = 6.3 Hz, 3 H), 0.89 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.6, 174.7, 174.3, 173.9, 156.9, 156.2, 138.5, 131.4, 130.3, 129.4, 129.3, 127.7, 116.2, 80.7, 70.5, 57.8, 55.7, 52.7, 52.2, 46.1, 41.5, 38.9, 38.6, 32.8, 31.3, 28.7, 25.9, 23.3, 21.9; IR (nujol) ν 3280, 1730, 1655, 1516, 1396, 1176, 1060 cm^{-1}; mass spectrum (CI) *m/z* 671.3644 ($C_{35}H_{50}N_4O_4$+H requires 671.3656), 571, 305 (base), 279.



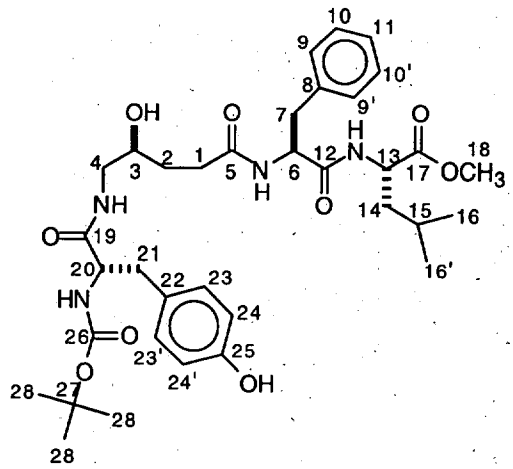
***N*-[1-(2'-Azido-1'(*S*)-hydroxy)butylcarboxy]-L-phenylalanyl-L-leucine.** Prepared in 70% yield from **40** as a waxy solid; CH_2Cl_2/MeOH (10:1); mp 58-60 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.29-7.16 (comp, 5 H), 4.72-4.67 (m, 1 H), 4.45-4.41 (m, 1 H), 3.58-3.51 (m, 1H), 3.21-3.11 (comp, 3 H), 2.83 (dd, *J* = 4.0, 9.9 Hz, 1 H), 2.32-2.15 (m, 2 H), 1.72-1.55 (comp, 5 H), 0.95 (d, *J* = 6.2 Hz, 3 H), 0.91 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.5, 173.7 (2), 138.6, 130.3 (2), 129.4 (2), 127.7, 71.2, 57.6, 55.6, 52.3, 41.8, 38.8, 32.9, 31.2, 25.9, 23.4, 21.9; IR ($CHCl_3$) ν 3340, 2960, 2105, 1720, 1662, 1522 cm^{-1}; mass spectrum (CI) *m/z* 420.2234 ($C_{20}H_{29}N_5O_5$+H requires 420.2247), 403, 345, 116.



***N*-[1-(2'-Azido-1'(*S*)-hydroxy)butylcarboxy]-L-phenylalanyl-L-leucyl methyl ester.** Prepared in 92% yield from the requisite acid as a glassy solid; MeOH/CH_2Cl_2 (25:1); mp 142-144 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.29-7.17 (comp, 5 H), 4.70-4.65 (m, 1 H), 4.48-4.43 (m, 1 H), 3.67 (s, 3 H), 3.60-3.54 (m, 1 H), 3.20-3.12 (comp, 3 H), 2.83 (dd, *J* = 4.0, 9.8 Hz, 1 H), 2.32-2.18 (m, 2 H), 1.69-1.54 (comp, 5 H), 0.94 (d, *J* = 6.1 Hz, 3 H), 0.90 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.5, 174.3, 173.8, 138.5, 130.3 (2), 129.4 (2), 127.7, 71.2, 57.6, 55.6, 52.7, 41.3, 38.9, 32.9, 31.2, 25.8, 23.3, 21.8; IR (nujol) ν 2094, 1745, 1654, 1615, 1100 cm^{-1}; mass spectrum (CI) *m/z* 434.2395 ($C_{21}H_{31}N_5O_5$+H requires 434.2403), 359 (base), 219.



***N*-[1-(2'-Amino-1'(*S*)-hydroxy)butylcarboxy]-L-phenylalanyl-L-leucyl methyl ester.** Prepared in 90% yield as a crystalline solid; mp 60-62 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.29-7.17 (comp, 5 H), 4.67 (dd, *J* = 5.5, 9.4 Hz, 1 H), 4.44 (dd, *J* = 6.1, 8.7 Hz, 1 H), 3.67 (s, 3 H), 3.40-3.34 (m, 1 H), 3.15 (dd, *J* = 5.5, 14.0 Hz, 1 H), 2.84 (dd, *J* = 9.5, 14.0 Hz, 1 H), 2.58 (dd, *J* = 3.9, 13.0 Hz, 1 H), 2.45 (dd, *J* = 7.7, 13.0 Hz, 1 H), 2.30-2.20 (m, 2 H), 1.69-1.52 (comp, 5 H), 0.94 (d, *J* = 6.3 Hz, 3 H), 0.90 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.7, 174.3, 173.7, 138.4, 130.3 (2), 129.4 (2), 127.7, 72.9, 55.6, 52.7, 52.2, 49.2, 41.5, 38.9, 33.1, 31.5, 25.9, 23.2, 21.9; IR (nujol) ν 3291, 1744, 1642, 1550, 1104 cm^{-1}; mass spectrum (CI) *m/z* 408.2493 ($C_{21}H_{33}N_3O_5$+H requires 408.2498), 359, 261 (base).



***N*-[1-(2'[*N-tert*-Butoxycarbonyl-L-tyrosyl]amino-1'(*S*)-hydroxy)butylcarboxy]-L-phenylanalyl-L-leucyl methyl ester.** Prepared in 73% yield as a pale yellow solid; CH_2Cl_2/MeOH (25:1); mp 102-104 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.26-7.16 (comp, 5 H), 7.02 (d, *J* = 8.3 Hz, 2 H), 6.68 (d, *J* = 8.3 Hz, 2 H), 4.67 (dd, *J* = 5.3, 9.1 Hz, 1 H), 4.45 (dd, *J* = 6.1, 8.9 Hz, 1 H), 4.20-4.05 (m, 1 H), 3.67 (s, 3 H), 3.46-3.43 (m, 1 H), 3.19-3.07 (comp, 3 H), 2.95 (dd, *J* = 6.2, 13.8 Hz, 1 H), 2.85 (dd, *J* = 9.4, 13.8 Hz, 1 H), 2.73 (dd, *J* = 8.6, 13.6 Hz, 1 H), 2.29-2.18 (comp, 2 H), 1.66-1.41 (comp, 5 H), 1.36 (s, 9 H), 0.93 (d, *J* = 6.1 Hz, 3 H), 0.89 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.7, 174.7, 174.3, 173.8, 157.6, 157.2, 138.4, 131.4, 130.3, 129.4, 129.2, 127.7, 116.2, 80.7, 70.5, 57.8, 55.7, 52.7, 52.1, 46.1, 41.5, 38.9, 38.6, 32.9, 31.3, 28.7, 25.9, 23.3, 21.9; IR (nujol) ν 3301, 1746, 1655, 1562, 1052 cm^{-1}; mass spectrum (CI) *m/z* 671.3650 ($C_{35}H_{50}N_4O_9$+H requires 671.3656), 572, 463, 293 (base).

2(*S*)-Methyl-(*R*)-(-)-γ-trityloxymethyl-γ-butyrolactone (43) and 2(*R*)-Methyl-(*R*)-(-)-γ-trityloxymethyl-γ-butyrolactone (44). To a solution of *i*-Pr_2NH (1.3 mL, 9.6 mmol) in THF (25 mL) at -78 °C was added *n*-BuLi (2.5 M, 3.6 mL) dropwise, and the reaction mixture was stirred at -78 °C for 15 min, 0 °C for 15 min, and then recooled to -78 °C. To this solution was added dropwise a solution **42**[2] (2.7 g, 7.4 mmol) in THF (35 mL), and the mixture was stirred for 30 min at -78 °C; MeI (0.55 mL, 8.9 mmol) was then added. After 30 min, the reaction mixture was warmed to -40 °C and stirred for 3 h. Saturated aqueous NH_4Cl (15 mL) was added, and the mixture was warmed to rt. The reaction mixture was diluted with Et_2O (30 mL) and H_2O (5 mL), and the layers were separated. The aqueous layer was extracted with Et_2O (2 x 20 mL), and the organic layers were combined, washed with

brine (2 x 20 mL), dried (Na_2SO_4), and concentrated under reduced pressure to yield an orange solid as an (8:1) mixture of **43** to **44** by ^1H NMR. The crude oil was taken on crude to the next step.

To a solution of *i*-Pr_2NH (0.56 mL, 4.3 mmol) in THF (15 ml) at -78 °C was added *n*-BuLi (2.3 M, 1.7 mL) dropwise, and the reaction mixture was stirred for 15 min. The reaction mixture was warmed to 0 °C and stirred for 15 min, and then recooled to -78 °C. To this solution was then added dropwise a solution of **43** and **44** (1.2 g, 3.3 mmol) in THF (12 mL). The reaction mixture was stirred for 1 h at -78 °C, saturated aqueous Na_2SO_4 (10 mL) was added, and the mixture was warmed to rt. Water (10 mL) and Et_2O (20 mL) were added, and the layers separated. The aqueous layer was extracted with Et_2O (2 x 20 mL). The organic layers were combined, washed with brine (2 x 20 mL), dried (Na_2SO_4), and concentrated under reduced pressure to yield 1.20 g of a yellow solid that was purified by flash chromatography eluting with hexane/EtOAc/Et_3N (80/19/1) to yield 0.90 g (70%) of **44** together with 0.21 g (19%) of **43**.

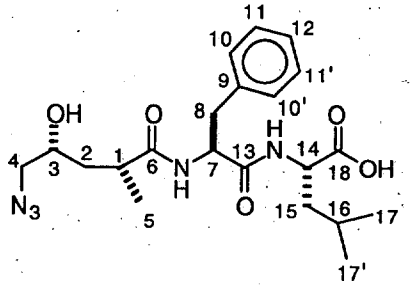
2(*R*)-Methyl-(*R*)-(-)-γ-trityloxymethyl-γ-butyrolactone (44). Isolated as a white solid; mp 113-115 °C; ^1H NMR (300 MHz) δ 7.45 (d, J = 7.0 Hz, 6 H), 7.32-7.20 (comp, 9 H), 4.54-4.45 (m, 1 H), 3.31-3.20 (m, 2 H), 2.70-2.58 (m, 1 H), 2.37-2.28 (m, 1 H), 1.66 (q, J = 11.8 Hz, 1 H), 1.25 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz) δ 179.3, 143.4, 128.5, 127.8, 127.1, 86.6, 64.9, 35.2, 32.9, 15.2; IR ($CHCl_3$) ν 3018, 1765, 1491, 1449, 1172, 1035 cm^{-1}; mass spectrum (CI) *m/z* 372.1723 ($C_{25}H_{24}O_3$ requires 372.1725), 271, 243 (base).

(*R*)-(-)-γ-Hydroxymethyl-[2(*R*)-methyl]-γ-butyrolactone. To a solution of **44** (0.33 g, 0.89 mmol) in MeOH (10 mL) at rt were added 6 drops of conc HCl. The mixture was stirred for 2 h at rt, whereupon saturated aqueous $NaHCO_3$ was added until pH=8 was reached. The mixture was concentrated under reduced pressure, and the resulting aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a light yellow oil. The crude product was purified by flash chromatography eluting with CH_2Cl_2/MeOH to yield 0.10 g (87%) of alcohol as a light yellow oil. ^1H NMR (300 MHz) δ 4.54-4.46 (m, 1 H), 3.92 (dd, J = 2.7, 12.5 Hz, 1 H), 3.63 (dd, J = 5.0, 12.5 Hz, 1 H), 2.79-2.67 (m, 1 H), 2.44-2.35 (m, 1 H), 1.86-1.74 (m, 1 H), 1.30 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz) δ 179.3, 78.5, 63.7,

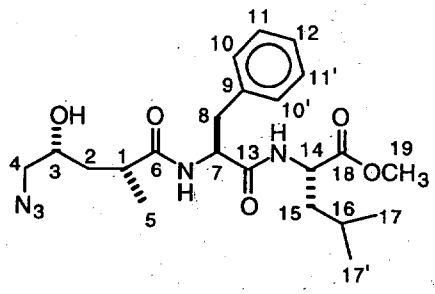
35.6, 31.6, 15.1; IR ($CHCl_3$) ν 3407, 1768, 1455, 1168, 1090 cm^{-1}; mass spectrum (CI) *m/z* 131.0705 ($C_6H_{10}O_3$+H requires 131.0708), 113, 85.

2(*R*)-Methyl-(*R*)-(-)-γ-[(4-methylphenyl)sulfonyl]-γ-butyrolactone. To a solution of the alcohol from the preceeding experiment (0.10 g, 0.77 mmol) at rt in CH_2Cl_2 (3 mL) was added TsCl (0.16 g, 0.85 mmol), Et_3N (0.13 ml, 0.92 mmol), and DMAP (0.10 g, 0.85 mmol). The mixture was stirred for 14 h at rt and concentrated under reduced pressure to yield a pale yellow solid. The crude solid was purified by flash chromatography eluting with hexane/EtOAc (2:1) to yield 0.20 g (91%) of mesylate as a white solid; mp 118-120 °C (dec); ^1H NMR (300 MHz) δ 7.80 (d, *J* = 8.0 Hz, 2 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 4.57-4.52 (m, 1 H), 4.22 (dd, *J* = 3.5, 11.1 Hz, 1 H), 4.11 (dd, *J* = 5.0, 11.1 Hz, 1 H), 2.73-2.64 (m, 1 H), 2.50-2.43 (m, 1 H), 2.46 (s, 3 H), 1.76-1.65 (m, 1 H), 1.27 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz) δ 178.2, 145.2, 132.1, 129.9, 127.8, 74.4, 69.4, 34.9, 31.9, 21.5, 14.9; IR ($CHCl_3$) ν 2940, 1779, 1600, 1368, 1177 cm^{-1}; mass spectrum (CI) *m/z* 285.0793 ($C_{13}H_{16}O_5S$+H requires 285.0797), 113.

(*R*)-(-)-γ-Azidomethyl-[2(*R*)-methyl]-γ-butyrolactone (45). To a solution of the mesylate from the preceeding experiment (0.20 g, 0.70 mmol) in DMF (3 mL) was added NaN_3 (0.23 g, 3.5 mmol) in one portion. The mixture was heated to 65 °C and stirred for 5 h and cooled to rt. The mixture was diluted with Et_2O (5 mL) and the resulting organic solution was washed with water (2 x 2 mL) and brine (2 x 2 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure to yield a yellow oil. The crude oil was purified by flash chromatography eluting with hexane/EtOAc (3:1) to yield 89 mg (82%) of **45** as a light yellow oil. ^1H NMR (300 MHz) δ 4.55-4.46 (m, 1 H), 3.58 (dd, *J* = 3.9, 13.4 Hz, 1 H), 3.43 (dd, *J* = 5.4, 13.4 Hz, 1 H), 2.76-2.64 (m, 1 H), 2.50-2.41 (m, 1 H), 1.77-1.65 (m, 1 H), 1.29 (d, *J* = 8.1 Hz, 3 H); ^{13}C NMR (75 MHz) δ 178.4, 76.1, 53.6, 35.3, 33.4, 15.1; IR ($CHCl_3$) ν 2936, 2109, 1775, 1164, 1035 cm^{-1}; mass spectrum (CI) *m/z* 156.0777 ($C_6H_9N_3O_2$+H requires 156.0773), 154, 136.

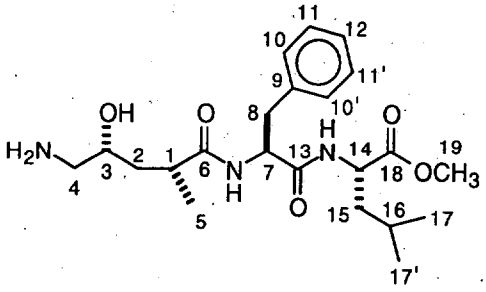


***N*-[1-(2'-Azido-1'(*R*)-hydroxy-1(*R*)-methyl)butylcarboxy]-L-phenylalanyl-L-leucine.** Prepared in 70% yield from **45** as a white solid; CH_2Cl_2/MeOH (20:1); mp 63-65 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 8.27 (d, *J* = 8.2 Hz, 1 H), 8.03 (d, *J* = 8.4 Hz, 1 H), 7.30-7.16 (comp, 5 H), 4.69 (ddd, *J* = 5.0, 10.2, 13.4 Hz, 1 H), 4.48-4.40 (m, 1 H), 3.51-3.44 (m, 1 H), 3.20 (dd, *J* = 4.6, 14.1 Hz, 1 H), 3.09 (dd, *J* = 3.6, 12.7 Hz, 1 H), 3.00 (dd, *J* = 6.1, 12.7 Hz, 1 H), 2.85 (dd, *J* = 10.2, 14.1 Hz, 1 H), 2.40 (q, *J* = 6.8 Hz, 1 H), 1.76-1.42 (comp, 3 H), 1.37-1.28 (comp, 2 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.95 (d, *J* = 6.4 Hz, 3 H), 0.92 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 178.9, 175.7, 173.7, 138.7, 130.3 (2), 129.4 (2), 127.7, 69.4, 57.7, 55.4, 52.1, 41.8, 39.1, 38.6, 38.2, 25.9, 23.3, 21.9, 17.8; IR ($CHCl_3$) ν 3336, 2961, 2105, 1722, 1661, 1513, 1286, 1093 cm^{-1}; mass spectrum (CI) *m/z* 434.2408 ($C_{21}H_{31}N_5O_5$+H requires 434.2403), 279 (base).

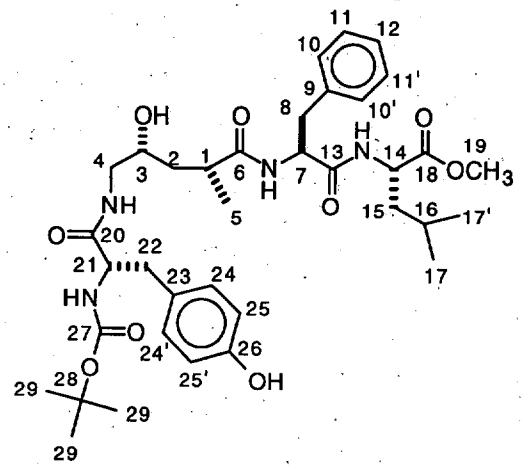


***N*-[1-(2'-Azido-1'(*R*)-hydroxy-1(*R*)-methyl)butylcarboxy]-L-phenylalanyl-L-leucyl methyl ester (46).** Prepared in 93% yield from the requisite acid as a white solid; MeOH/CH_2Cl_2 (25:1); mp 117-119 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 7.30-7.17 (comp, 5 H), 4.73-4.67 (m, 1 H), 4.50-4.44 (m, 1 H), 3.68 (s, 3 H), 3.53-3.47 (m, 1 H), 3.21-3.07 (comp, 2 H), 3.01 (dd, *J* = 6.2, 12.8 Hz, 1 H), 2.85 (dd, *J* = 10.0, 14.1 Hz, 1 H), 2.41 (q, *J* = 7.1 Hz, 1 H), 1.69-1.54 (comp, 3 H), 1.39-1.31 (comp, 2 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.4 Hz, 3 H), 0.89 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 178.9, 174.4, 173.9, 138.6, 130.3 (2), 129.4 (2), 127.7, 69.4, 57.5, 55.4, 52.7, 52.1, 41.1, 39.0, 38.7, 38.1, 25.8, 23.3, 21.8, 17.8; IR ($CHCl_3$) ν 3418, 2960,

2105, 1740, 1668, 1510, 1439 cm^{-1}; mass spectrum *m/z* (CI) 448.2554 ($C_{22}H_{33}N_5O_5$+H requires 448.2560), 373 (base), 293.



***N*-[1-(2'-Amino-1'(*R*)-hydroxy-1(*R*)-methyl)butylcarboxy]-L-phenylalanyl-L-leucyl methyl ester.** Prepared in 90% yield from **46** as a glassy solid; mp 98-100 °C; ^1H NMR (300 MHz, CD_3OD) δ 7.27-7.19 (comp, 5 H), 4.68 (dd, *J* = 5.5, 9.8 Hz, 1 H), 4.46 (dd, *J* = 6.1, 8.9 Hz, 1 H), 3.68 (s, 3 H), 3.35-3.31 (m, 1 H), 3.17 (dd, *J* = 5.2, 13.9 Hz, 1 H), 2.86 (dd, *J* = 9.8, 13.9 Hz, 1 H), 2.50 (dd, *J* = 3.6, 13.2 Hz, 1 H), 2.45-2.33 (comp, 2 H), 1.68-1.46 (comp, 3 H), 1.36-1.28 (comp, 2 H), 1.04 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 6.4 Hz, 3 H), 0.90 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 179.3, 174.4, 173.8, 138.7, 130.4 (2), 129.4 (2), 127.7, 71.2, 55.4, 52.6, 50.1, 41.6, 39.5, 38.6, 38.3, 25.8, 23.2, 21.9, 17.8; IR ($CHCl_3$) ν 3304, 2954, 1742, 1665, 1602, 1502 cm^{-1}; mass spectrum (CI) *m/z* 422.2645 ($C_{22}H_{35}N_3O_5$+H requires 422.2655), 293, 130.



***N*-[1-(2'[*N*-*tert*-Butoxycarbonyl-L-tyrosyl]amino-1'(*R*)-hydroxy-1(*R*)-methyl)butylcarboxy]-L-phenylanalyl-L-leucyl methyl ester.** Prepared in 72% yield as an off-white solid; CH_2Cl_2/MeOH (25:1); mp. 114-116 °C; ^1H NMR (300 MHz, CD_3OD) δ 7.26-7.18 (comp, 5 H), 7.02 (d, *J* = 8.3 Hz, 2 H), 6.69 (d, *J* = 8.3 Hz, 2 H), 4.67 (dd, *J* = 5.5, 9.8 Hz, 1 H), 4.45 (dd, *J* = 6.0, 8.9 Hz, 1 H), 4.18 (app t, *J* = 5.7 Hz, 1 H), 3.67 (s, 3 H), 3.40-3.30 (m, 1 H), 3.16 (dd, *J* = 5.2,

14.1 Hz, 1 H), 3.07 (dd, J = 6.2, 13.4 Hz, 1 H), 3.00-2.94 (comp, 2 H), 2.86 (dd, J = 9.6, 14.1 Hz, 1 H), 2.75-2.68 (m, 1 H), 2.42 (q, J = 7.0 Hz, 1 H), 1.65-1.48 (comp, 3 H), 1.36 (d, 9 H), 1.01 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.1 Hz, 3 H), 0.90 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, CD_3OD) δ 179.2, 174.8, 174.4, 173.8, 158.2, 155.8, 138.6, 131.3, 130.4, 129.5, 129.3, 127.7, 116.2, 79.9, 68.8, 55.5, 52.7, 52.1, 45.2, 41.5, 39.2, 38.7, 38.2, 28.7, 25.8, 23.3, 21.8, 18.0; IR ($CHCl_3$) ν 3450, 2928, 1732, 1665, 1375, 1265 cm^{-1}; mass spectrum (CI) *m/z* 685.3811 ($C_{36}H_{52}N_4O_9$+H requires 685.3813).

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2. Takano, S.; Yonaga, M.; Ogasawara, K. *Synthesis* **1981**, 265-266.