

Arecoline Tripeptide Inhibitors of Proteasome

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Supporting Information

1,2,5,6-tetrahydropyridine-3-carbonyl-Leu-Leu-Leu-NH-Bzl (17). ^1H NMR (CDCl_3): δ 0.97-1.05 (m, 18H); 1.69-1.90 (m, 5H); 2.11 (m, 2H); 2.80-2.93 (m, 3H); 3.35 (s, 2H); 4.31-4.87 (m, 5H); 6.60 (d, 1H); 7.02-7.17 (m, 5H); 7.35-7.90 (m, 4H). HPLC: K' = 6.23. MS: $\text{M}+\text{H}^+$ = 556.8. Anal. Calcd for $\text{C}_{31}\text{H}_{49}\text{N}_5\text{O}_4$: C, 67.00; H, 8.89; N, 12.60; O, 11.52. Found: C, 67.13; H, 8.93; N, 12.45.

1,2,5,6-tetrahydropyridine-3-carbonyl-Val-Ser-Leu-NH-Bzl (18). ^1H NMR (CDCl_3): δ 0.99-1.06 (m, 12H); 1.75-2.07 (m, 5H); 2.66-2.88 (m, 4H); 3.30 (s, 2H); 4.01 (d, 2H); 4.44-4.61 (m, 6H); 6.75 (d, 1H); 6.93-7.20 (m, 5H); 7.28-7.77 (m, 4H). HPLC: K' = 7.71. MS: $\text{M}+\text{H}^+$ = 516.7. Anal. Calcd for $\text{C}_{27}\text{H}_{41}\text{N}_5\text{O}_5$: C, 62.89; H, 8.01; N, 13.58; O, 15.51. Found: C, 62.93; H, 7.95; N, 13.45.

1,2,5,6-tetrahydropyridine-3-carbonyl-Phe-Ser-Leu-NH-Bzl (19). ^1H NMR (CDCl_3): δ 0.97-1.08 (m, 6H); 1.70-1.81 (m, 3H); 2.09 (m, 2H); 2.53-3.07 (m, 5H); 3.31 (d, 2H); 4.02 (m, 2H); 4.41-4.87 (m, 6H); 6.37 (d, 1H); 6.69-7.20 (m, 10H); 7.35-8.04 (m, 4H). HPLC: K' = 5.95. MS: $\text{M}+\text{H}^+$ = 564.7. Anal. Calcd for $\text{C}_{31}\text{H}_{41}\text{N}_5\text{O}_5$: C, 66.05; H, 7.33; N, 12.42; O, 14.19. Found: C, 66.93; H, 7.45; N, 12.45.

Z-Leu-Leu-Leu-1,2,5,6-methyl-tetrahydropyridine-3-carboxylate (20). ^1H NMR (CDCl_3): δ 0.98-1.12 (m, 18H); 1.75-2.11 (m, 11H); 3.50 (t, 2H); 3.75 (s, 3H); 3.91 (s, 2H); 4.41-4.59 (m, 3H); 5.25 (s, 2H); 6.82 (t, 1H); 7.23 (m, 5H); 7.80-8.11 (m, 3H). HPLC: K' = 7.14. MS: $\text{M}+\text{H}^+$ = 589.7. Anal. Calcd for $\text{C}_{33}\text{H}_{50}\text{N}_4\text{O}_7$: C, 64.47; H, 8.20; N, 9.11; O, 18.22. Found: C, 65.02; H, 8.60; N, 9.05.

Fmoc-Leu-Leu-Leu-1,2,5,6-methyl-tetrahydropyridine-3-carboxylate (21). ^1H NMR (CDCl_3): δ 0.97-1.08 (m, 18H); 1.70-2.15 (m, 11H); 3.42 (t, 2H); 3.69 (s, 3H); 3.99 (s, 2H); 4.49-4.64 (m, 3H); 5.35 (s, 2H); 7.01 (t, 1H); 7.30-7.72 (m, 9H); 7.80-8.11 (m, 3H). HPLC: K' = 8.19. MS: $\text{M}+\text{H}^+$ = 703.8. Anal. Calcd for $\text{C}_{40}\text{H}_{54}\text{N}_4\text{O}_7$: C, 68.35; H, 7.74; N, 7.97; O, 15.93. Found: C, 68.02; H, 7.86; N, 7.35.

Z-Val-Ser-Leu-1,2,5,6-methyl-tetrahydropyridine-3-carboxylate (22). ^1H NMR (CDCl_3): δ 1.00-1.52 (m, 12H); 1.73-2.01 (m, 5H); 2.64 (m, 1H); 3.40 (d, 2H); 3.68 (s, 3H); 3.90 (s, 2H); 4.10 (m, 2H); 4.42 (t, 1H); 4.58-4.69 (m, 3H); 5.28 (s, 2H); 6.85 (t, 1H); 7.15 (m, 5H); 7.70-8.04 (m, 3H). HPLC: K' = 6.27. MS: $\text{M}+\text{H}^+$ = 575.7. Anal. Calcd for $\text{C}_{29}\text{H}_{42}\text{N}_4\text{O}_8$: C, 60.61; H, 7.37; N, 9.75; O, 22.27. Found: C, 60.82; H, 7.60; N, 9.55.

Fmoc-Val-Ser-Leu-1,2,5,6-methyl-tetrahydropyridine-3-carboxylate (23). ^1H NMR (CDCl_3): δ 0.90-1.12 (m, 12H); 1.63-1.87 (m, 5H); 2.44 (m, 1H); 3.09 (d, 2H); 3.45 (s, 3H); 3.79 (s, 2H); 4.00 (m, 2H); 4.37 (t, 1H); 4.52-4.68 (m, 3H); 5.15 (s, 2H); 6.72 (t, 1H); 7.28-8.10 (m, 12H). HPLC: K' = 7.52. MS: $\text{M}+\text{H}^+$ = 663.8. Anal. Calcd for $\text{C}_{36}\text{H}_{46}\text{N}_4\text{O}_8$: C, 65.24; H, 7.00; N, 8.45; O, 19.31. Found: C, 65.62; H, 7.37; N, 8.48.

Z-Phe-Ser-Leu-1,2,5,6-methyl-tetrahydropyridine-3-carboxylate (24). ^1H NMR (CDCl_3): δ 1.07 (m, 16H); 1.75-2.07 (m, 5H); 3.03 (m, 2H); 3.52 (t, 2H); 3.69 (s, 3H); 4.04 (s, 2H); 4.23-4.71 (m, 6H); 5.43 (s, 2H); 6.82 (t, 1H); 7.08-7.24 (m, 10H); 7.84-8.23 (m, 3H). HPLC: K' = 6.85. MS: $\text{M}+\text{H}^+$ = 623.7. Anal. Calcd for $\text{C}_{33}\text{H}_{42}\text{N}_4\text{O}_8$: C, 63.65; H, 6.80; N, 9.00; O, 20.55. Found: C, 64.12; H, 6.99; N, 9.05.

Fmoc-Phe-Ser-Leu-1,2,5,6-methyl-tetrahydropyridine-3-carboxylate (25). ^1H NMR (CDCl_3): δ 1.15 (m, 16H); 1.79-2.02 (m, 5H); 3.20 (m, 2H); 3.55 (t, 2H); 3.91 (s, 3H); 4.15 (s, 2H); 4.38-4.97 (m, 6H); 5.77 (s, 2H); 6.76 (t, 1H); 7.24-8.30 (m, 17H). HPLC: K' = 7.89. MS: $\text{M}+\text{H}^+$ = 711.8. Anal. Calcd for $\text{C}_{40}\text{H}_{46}\text{N}_4\text{O}_8$: C, 67.59; H, 6.52; N, 7.88; O, 18.01. Found: C, 67.32; H, 6.29; N, 7.43.