Supporting Information

Modulation of ferrocene-ferrocene interactions by varying their reciprocal positions in Dap/Aib helical peptides

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**Synthesis and characterization of Z-L-Dap(Boc)-Aib-NH*i*Pr**



Z-L-Dap(Boc)-OH (2.40 g, 7.09 mmol) was dissolved in anhydrous CH2Cl2. Then, HOBt (1.30 g, 8.51 mmol), EDC·HCl (1.55 g, 1.63 mmol), and H-Aib-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-Aib-NH*i*Pr(1.99 g, 7.15 mmol) and DIEA (1.85 mL, 10.64 mmol) were added to the solution. After stirring the solution at room temperature for 24 h, CH2Cl2 was evaporated under reduced pressure. The oily residue was dissolved in ethyl acetate (EtOAc) and washed with 5% NaHCO3, 5% KHSO4, 5% NaHCO3 and saturated NaCl solution. The organic solution was dried on anhydrous Na2SO4 and after filtration the solvent was removed under vacuum to yield a white powder.

Yield, 78%;

IR (CDCl3, 1 mM) 3453, 3425, 3367, 1710, 1693, 1664, 1505 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 7.35 (m, 5H, Z), 6.64 (s, 1H, NH-Aib), 6.40 (s, 1H, NH-Dap), 6.35 (s, 1H, NH-*i*Pr), 5.14 (m, 3H, NH Boc, CH2 Z), 4.10 (m, 1H, CH Dap), 4.02 (m, 1H, CH *i*Pr), 3.48 (m, 2H, CH2 Dap), 1.50 (s, 3H, CH3Aib), 1.44 (s, 9H, CH3Boc), 1.42 (s, 3H, CH3Aib), 1.13 (dd, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C23H36N4O6 [M]+, 464.26; found, 487 [M+Na]+.

**Synthesis and characterization of Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr**



This compound was obtained from Z-Aib-OH (1.00 g, 3.59 mmol) and H-L-Dap(Boc)-Aib-NH*i*Pr, obtained by catalytic hydrogenolysis of Z- L-Dap(Boc)-Aib-NH*i*Pr (1.67 g, 3.59 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 89%;

IR (CDCl3, 1 mM) 3453, 3433, 3345, 1716, 1677, 1525, 1505 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 8.35 (d, 1H, NH-Dap),7.34 (m, 5H, Z), 7.31 (s, 1H, NH-Aib), 6.60 (d, 1H, NH-*i*Pr), 5.26 (s, 1H, NH-Aib), 5.18 (m, 1H, NH Boc), 5.11, 5.04 (q AB, 2H, CH2 Z), 4.13 (m, 1H, CH Dap), 4.02 (m, 1H, CH *i*Pr), 3.50 (m, 2H, CH2 Dap), 1.54 (s, 3H, CH3Aib), 1.51 (s, 3H, CH3Aib), 1.48 (s, 3H, CH3Aib), 1.44 (s, 9H, CH3Boc), 1.43 (s, 3H, CH3Aib), 1.15 (dd, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C27H43N5O7 [M]+, 549.32; found, 572.3 [M+Na]+.

**Synthesis and characterization of Z-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr**



This compound was obtained from Z-Aib-OH (1.00 g, 3.59 mmol) and H-Aib-L-Dap(Boc)-Aib-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr (1.97 g, 3.59 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 75%;

IR (CDCl3, 1 mM) 3450, 3424, 3349, 1709, 1678, 1529, 1505 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 7.69 (d, 1H, NH-Dap), 7.37 (m, 5H, Z), 7.23 (s, 1H, NH-Aib), 6.68 (d, 1H, NH-*i*Pr), 6.53 (s, 1H, NH-Aib), 5.42 (s, 1H, NH-Aib), 5.40 (m, 1H, NH Boc), 5.20, 5.12 (q AB, 2H, CH2 Z), 4.06 (m, 1H, CH Dap), 4.03 (m, 1H, CH *i*Pr), 3.63, 3.47 (m, 2H, CH2 Dap), 1.55 (s, 3H, CH3Aib), 1.51 (s, 3H, CH3Aib), 1.50 (s, 3H, CH3Aib), 1.47 (s, 3H, CH3Aib), 1.46 (s, 3H, CH3Aib), 1.40 (s, 9H, CH3Boc), 1.36 (s, 3H, CH3Aib), 1.14 (t, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C31H50N6O8 [M]+, 634.37; found, 657.4 [M+Na]+.

**Synthesis and characterization of Z-L-Dap(Boc)-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr**



This compound was obtained from Z-L-Dap(Boc)-OH (0.85 g, 2.52 mmol) and H-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr (1.60 g, 2.52 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 80%;

IR (CDCl3, 1 mM) 3450, 3407, 3342, 1707, 1673, 1514 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 7.48 (d, 1H, NH-Dap), 7.35 (m, 5H, Z), 7.31 (s, 1H, NH-Aib), 7.19 (s, 1H, NH-Aib), 6.96 (s, 1H, NH-Dap), 6.68 (s, 1H, NH-Aib), 6.57 (d, 1H, NH-*i*Pr), 5.31 (m, 2H, NH Boc), 5.13, 5.09 (q AB, 2H, CH2 Z), 4.20 (m, 2H, CH Dap), 4.03 (m, 1H, CH *i*Pr), 3.70, 3.59, 3.51 (m, 4H, CH2 Dap), 1.55 (s, 3H, CH3Aib), 1.52 (s, 3H, CH3Aib), 1.51 (s, 3H, CH3Aib), 1.46 (s, 21H, CH3Boc and CH3Aib), 1.44 (s, 3H, CH3Aib), 1.29 (s, 3H, CH3Aib), 1.10 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C39H64N8O11 [M]+, 820.47; found, 843.4 [M+Na]+.

**Synthesis and characterization of Z-Aib-L-Dap(Boc)-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr**



This compound was obtained from Z-Aib-OH (0.45 g, 1.88 mmol) and H-L-Dap(Boc)-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-L-Dap(Boc)-(Aib)2-L-Dap(Boc)-Aib-NH*i*Pr (1.54 g, 1.88 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 65%;

IR (CDCl3, 1 mM) 3444, 3431, 3323, 1708, 1670, 1532, 1506 cm-1.

1H NMR (400.13 MHz, DMSO-d6): δ 8.21 (s, 1H, NH-Aib), 8.06 (s, 1H, NH-Dap), 7.98 (s, 1H, NH-Aib), 7.63 (s, 1H, NH-Aib), 7.38 (m, 7H, Z, NH-Aib), 7.07 (m, 2H, NH Boc), 6.79 (d, 1H, NH-*i*Pr), 6.72 (m, 2H, NH Boc), 5.16, 5.01 (q AB, 2H, CH2 Z), 4.04 (m, 1H, CH Dap), 4.00 (m, 1H, CH Dap), 3.79 (m, 1H, CH *i*Pr), 3.48 (m, 2H, CH2 Dap), 3.26 (m, 1H, CH2 Dap), 3.20 (m, 1H, CH2 Dap), 1.38 (s, 18H, CH3Boc), 1.36 (s, 12H, CH3Aib), 1.33 (s, 6H, CH3Aib), 1.32 (s, 6H, CH3Aib), 1.01 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C43H71N9O12 [M]+, 905.52; found, 928.5 [M+Na]+.

**Synthesis and characterization of Z-Aib-L-Dap(Fc)-(Aib)2-L-Dap(Fc)-Aib-NH*i*Pr (1)**



Fc-COOH (82 mg, 0.36 mmol) was dissolved in anhydrous in CH2Cl2. Then, HOBt (64 mg, 0.42 mmol), EDC∙HCl (82 mg, 0.43 mmol), Z-Aib-L-Dap-(Aib)2-L-Dap-Aib-NH*i*Pr (106 mg, 0.15 mmol), obtained removing the Boc group from the side chain of the Dap unit, and DIEA (66 µL, 0.38 mmol) were added to the solution. After stirring at room temperature for 24 h, the solvent was evaporated under reduced pressure. The oily residue was dissolved in EtOAc and washed with 5% NaHCO3, 5% KHSO4, 5% NaHCO3 and saturated NaCl solution. The organic solution was dried on anhydrous Na2SO4 and after filtration evaporated to dryness yielding an orange powder. The crude product was purified by flash chromatography (CH2Cl2/EtOH, 10%).

Yield: 34%;

IR (CDCl3, 1 mM) 3429, 3310, 1710, 1664, 1523 cm-1.

1H NMR (600 MHz, CDCl3, 25°C, TMS): δ 8.92 (s, 1H, NH-Dap), 7.91 (s, 1H, NH-Aib), 7.83 (d, 1H, NH-Dap), 7.52 (s, 1H, NH-Aib), 7.36 (s, 1H, NH-Aib), 7.33 (m, 5H, Z), 7.19 (s, 1H, NH-Aib), 6.89 (m, 1H, NH Dap), 6.81 (m, 1H, NH Dap), 6.57 (d, 1H, NH-*i*Pr), 5.07, 4.97 (q AB, 2H, CH2 Z), 4.75 (m, 1H, Fc), 4.71 (m, 2H, Fc), 4.69 (m, 1H, Fc), 4.40 (m, 1H, Fc), 4.39 (m, 1H, Fc), 4.32 (m, 3H, CH Dap, Fc), 4.20 (s, 5H, Fc), 4.19 (s, 5H, Fc), 4.18 (m, 1H, CH Dap), 4.08 (m, 1H, CH *i*Pr), 3.76 (m, 1H, CH2 Dap), 3.76 (m, 1H, CH2 Dap), 3.67 (m, 2H, CH2 Dap), 1.63 (s, 3H, CH3Aib), 1.56 (s, 3H, CH3Aib), 1.50 (s, 3H, CH3Aib), 1.48 (s, 3H, CH3Aib), 1.44 (s, 3H, CH3Aib), 1.42 (s, 6H, CH3Aib), 1.39 (s, 3H, CH3Aib), 1.18 (m, 6H, NH-*i*Pr).

HRMS (ESI+)*:* m/z calcd for C55H71Fe2N9O10, [M]+ 1129.40;found, 1130.3 [M+H]+.

**Synthesis and characterization of Z-(Aib)2-NH*i*Pr**



This compound was obtained from Z-Aib-OH (1.50 g, 5.39 mmol) and H-Aib-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-Aib-NH*i*Pr (1.28 g, 5.39 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 66%;

IR (CDCl3, 1 mM) 3430, 3373, 1720, 1687, 1658, 1499 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 7.35 (m, 5H, Z), 6.81 (s, 1H, NH-*i*Pr), 6.28 (s, 1H, NH-Aib), 5.19 (s, 1H, NH-Aib), 5.12 (m, 2H, CH2 Z), 4.02 (m, 1H, CH *i*Pr), 1.47 (s, 6H, CH3Aib), 1.41 (s, 6H, CH3Aib), 1.14 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C19H29N3O4 [M]+, 363.22; found, 386.40 [M+Na]+.

**Synthesis and characterization of Z-L-Dap(Boc)-(Aib)2-NH*i*Pr**



This compound was obtained from Z-L-Dap(Boc)-OH (1.30 g, 3.85 mmol) and H-(Aib)2-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-(Aib)2-NH*i*Pr (1.40 g, 3.85 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 70%;

IR (CDCl3, 1 mM) 3453, 3419, 3367, 1705, 1689, 1506 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 7.34 (m, 6H, Z, NH-Aib ), 6.84 (s, 1H, NH-*i*Pr), 6.79 (s, 1H, NH-Aib), 6.65 (s, 1H, NH-Aib), 5.48 (m, 1H, NH Boc), 5.10 (m, 2H, CH2 Z), 4.04 (m, 1H, CH Dap), 4.00 (m, 1H, CH *i*Pr), 3.48 (m, 2H, CH2 Dap), 1.46 (s, 6H, CH3Aib), 1.44 (s, 12H, CH3Boc, CH3Aib), 1.34 (s, 3H, CH3Aib), 1.13 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C27H43N5O7 [M]+, 549.32; found, 572.3 [M+Na]+.

**Synthesis and characterization of Z-Aib-L-Dap(Boc)-(Aib)2-NH*i*Pr**



This compound was obtained from Z-Aib-OH (0.36 g, 1.51 mmol) and H-L-Dap(Boc)-(Aib)2-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-L-Dap(Boc)-(Aib)2-NH*i*Pr (0.83 g, 1.51 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 85%;

IR (CDCl3, 1 mM) 3453, 3433, 3341, 1714, 1676, 1528, 1505 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 8.45 (d, 1H, NH-Dap), 7.59 (s, 1H, NH-Aib), 7.35 (m, 5H, Z), 6.93 (d, 1H, NH-*i*Pr), 6.89 (s, 1H, NH-Aib), 5.57 (s, 1H, NH-Aib), 5.40 (m, 1H, NH Boc), 5.11, 5.07 (q AB, 2H, CH2 Z), 4.05 (m, 1H, CH Dap), 4.01 (m, 1H, CH *i*Pr), 3.50 (m, 2H, CH2 Dap), 1.52 (s, 3H, CH3Aib), 1.50 (s, 3H, CH3Aib), 1.46 (s, 3H, CH3Aib), 1.45 (s, 3H, CH3Aib), 1.44 (s, 9H, CH3Boc), 1.40 (s, 6H, CH3Aib), 1.14 (dd, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C31H50N6O8 [M]+, 634.37; found, 657.3 [M+Na]+.

**Synthesis and characterization of Z-L-Dap(Boc)-Aib-L-Dap(Boc)-(Aib)2-NH*i*Pr**



This compound was obtained from Z-L-Dap(Boc)-OH (0.47 g, 1.39 mmol) and H-Aib-L-Dap(Boc)-(Aib)2-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-Aib-L-Dap(Boc)-(Aib)2-NH*i*Pr (0.88 g, 1.39 mmol) as described for Z-L-Dap(Boc)-Aib-NH*i*Pr.

Yield, 90%;

IR (CDCl3, 1 mM) 3454, 3416, 3346, 1687, 1676, 1525, 1509 cm-1.

1H NMR (400.13 MHz, CDCl3): δ 7.99 (s, 1H, NH-Dap), 7.50 (s, 1H, NH-Aib), 7.36 (m, 5H, Z), 7.12 (s, 1H, NH-Aib), 6.96 (d, 1H, NH-*i*Pr), 6.91 (s, 1H, NH-Aib), 6.58 (s, 1H, NH-Dap), 5.46 (m, 1H, NH Boc), 5.34 (m, 1H, NH Boc), 5.14 (m, 2H, CH2 Z), 4.15 (m, 1H, CH Dap), 4.03 (m, 1H, CH Dap), 4.00 (m, 1H, CH *i*Pr), 3.50 (m, 4H, CH2 Dap), 1.49 (s, 6H, CH3Aib), 1.47 (s, 6H, CH3Aib), 1.45 (s, 9H, CH3Boc), 1.43 (s, 9H, CH3Boc), 1.41 (s, 6H, CH3Aib), 1.15 (m, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C39H64N8O11 [M]+, 820.47; found, 843.5 [M+Na]+.

**Synthesis and characterization of Z-Aib-L-Dap(Boc)-Aib-L-Dap(Boc)-(Aib)2-Nh*i*Pr**



This compound was obtained from Z-Aib-OH (0.27 g, 1.88 mmol) and H-L-Dap(Boc)-Aib-L-Dap(Boc)-(Aib)2-NH*i*Pr, obtained by catalytic hydrogenolysis of Z-L-Dap(Boc)-Aib-L-Dap(Boc)-(Aib)2-Nh*i*Pr (0.95 g, 1.15 mmol) as described for Z-L-Dap(Boc)-Aib-Nh*i*Pr.

Yield, 70%;

IR (CDCl3, 1 Mm) 3452, 3429, 3333, 1711, 1667, 1532, 1506 cm-1.

1H NMR (400.13 MHz, DMSO-d6): δ 8.01 (d, 1H, NH-Dap), 7.98 (s, 1H, NH-Aib), 7.94 (s, 1H, NH-Aib), 7.84 (d, 1H, NH-Dap), 7.75 (s, 1H, NH-Aib), 7.37 (m, 5H, Z), 7.13 (s, 1H, NH-Aib), 6.98 (d, 1H, NH-*i*Pr), 6.94 (t, 1H, NH Boc), 6.69 (t, 1H, NH Boc), 5.12, 4.98 (q AB, 2H, CH2 Z), 4.09 (m, 2H, 2 CH Dap), 3.76 (m, 1H, CH *i*Pr), 3.42 (m, 1H, CH2 Dap), 3.39 (m, 1H, CH2 Dap), 3.32 (m, 1H, CH2 Dap), 3.30 (m, 1H, CH2 Dap), 1.33 (m, 42H, CH3Aib, CH3Boc), 1.03 (m, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for C43H71N9O12 [M]+, 905.52; found, 928.5 [M+Na]+.

**Synthesis and characterization of Z-Aib-L-Dap(Fc)-Aib-L-Dap(Fc)-(Aib)2-NH*i*Pr (2)**



This compound was obtained from Fc-COOH (58 mg, 0.25 mmol) and Z-Aib-L-Dap-Aib-L-Dap-(Aib)2-NH*i*Pr (78 mg, 0.11 mmol), obtained removing the Boc group from the side chain of the Dap unit, as described for Z-Aib-L-Dap(Fc)-(Aib)2-L-Dap(Fc)-Aib-NH*i*Pr. The crude product was purified by flash chromatography (CH2Cl2/EtOH, 10%).

Yield: 35%;

IR (CDCl3, 1 mM) 3429, 3318, 1708, 1666, 1523 cm-1.

1H NMR (600 MHz, CDCl3, 25°C, TMS): δ 9.00 (s, 1H, NH-Dap), 7.88 (s, 1H, NH-Dap), 7.81(s, 1H, NH-Aib), 7.50 (s, 1H, NH-Aib), 7.33 (m, 5H, Z), 6.99 (m, 3H, NH Dap, NH-*i*Pr), 5.04 (m, 2H, CH2 Z), 4.78 (s, 1H, Fc), 4.76 (s, 1H, Fc), 4.72 (s, 1H, Fc), 4.63 (s, 1H, Fc), 4.41 (s, 1H, Fc), 4.38 (s, 1H, Fc), 4.34 (s, 1H, Fc), 4.32 (s, 1H, Fc), 4.20 (s, 6H, CH Dap, Fc,), 4.17 (s, 5H, Fc), 4.14 (m, 1H, CH Dap), 4.07 (m, 1H, CH *i*Pr), 3.81 (m, 1H, CH2 Dap), 3.69 (m, 2H, CH2 Dap), 3.57 (m, 1H, CH2 Dap), 1.54 - 1.47 (m, 24H, CH3Aib), 1.23 (m, 6H, NH-*i*Pr).

HRMS (ESI+)*:* m/z calcd for C55H71Fe2N9O10, [M]+ 1129.40;found, 1129.3 [M]+.

**Table S1**. Crystal data and structure refinement for Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr.

Identification code mc314

Empirical formula C27H43N5O7

Formula weight 549.66

Temperature 293(2) K

Wavelength 1.54184 Å

Crystal system Orthorhombic

Space group P212121

Unit cell dimensions a = 11.85134(8) Å = 90°.

b = 15.53512(13) Å = 90°.

c = 17.02931(13) Å  = 90°.

Volume 3135.30(4) Å3

Z 4

Density (calculated) 1.164 Mg/m3

Absorption coefficient 0.695 mm-1

F(000) 1184

Crystal size 0.300 x 0.200 x 0.100 mm3

Theta range for data collection 3.852 to 72.729°.

Index ranges -12<=h<=14, -19<=k<=19, -21<=l<=21

Reflections collected 31364

Independent reflections 6231 [R(int) = 0.0189]

Completeness to theta = 67.684° 100.0 %

Absorption correction Semi-empirical from equivalents

Max. and min. transmission 1.00000 and 0.53302

Refinement method Full-matrix least-squares on F2

Data / restraints / parameters 6231 / 0 / 361

Goodness-of-fit on F2 1.037

Final R indices [I>2sigma(I)] R1 = 0.0363, wR2 = 0.1011

R indices (all data) R1 = 0.0378, wR2 = 0.1032

Absolute structure parameter -0.07(4)

Extinction coefficient n/a

Largest diff. peak and hole 0.162 and -0.155 e.Å-3

**Table S2**. Selected torsion angles [°] for Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr.

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C02-C01-C07-OU 104.1(3)

C06-C01-C07-OU -78.3(3)

C01-C07-OU-C0 -106.7(3)

C07-OU-C0-N1 -165.05(19)

OU-C0-N1-C1A -178.84(17)

C0-N1-C1A-C1 -51.5(2)

N1-C1A-C1-N2 -37.7(2)

C1A-C1-N2-C2A -173.35(16)

C1-N2-C2A-C2 -64.3(2)

N2-C2A-C2B-N2G 62.8(2)

C2A-C2B-N2G-C201 107.0(2)

C2B-N2G-C201-O202 175.26(17)

N2G-C201-O202-C202 -173.1(2)

C201-O202-C202-C205 -67.9(3)

C201-O202-C202-C204 58.2(4)

C201-O202-C202-C203 174.5(2)

N2-C2A-C2-N3 -26.2(2)

C2A-C2-N3-C3A -178.35(17)

C2-N3-C3A-C3 -77.9(2)

N3-C3A-C3-NT -15.9(3)

C3A-C3-NT-CT1 -172.2(2)

C3-NT-CT1-CT3 151.8(3)

C3-NT-CT1-CT2 -81.1(3)

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**Table S3**. Hydrogen bonds for Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr [Å and °].

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

D-H...A d(D-H) d(H...A) d(D...A) <(DHA)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

N3-H3...O0 0.86 2.25 3.028(2) 149.8

NT-HT...O1 0.86 2.37 3.202(3) 163.6

N1-H1...O201#1 0.86 2.14 2.982(2) 166.4

N2-H2...O2#1 0.86 2.32 3.151(2) 162.7

N2G-H2G...O2#1 0.86 2.09 2.840(2) 145.7

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Symmetry transformations used to generate equivalent atoms:

#1 x-1/2, -y+3/2, -z

mc314_pack_down_b.tif

**Figure S1.** Packing mode of Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr as viewed down the b axis. Intermolecular N-H…O=C H-bonds are indicated by dashed lines.



**Figure S2**. FT-IR spectra in the amide A region of the Fc-hexapeptides **1** (left) and **2** (right) and of their shorter intermediates, from the dipeptide to the hexapeptide. Peptide concentration: 0.1 mM in CDCl3.