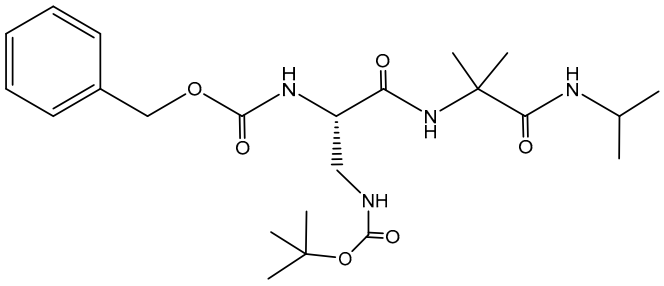
Supporting Information

Modulation of Ferrocene–Ferrocene Interactions by Varying Their Reciprocal Positions in L-Dap/Aib Helical Peptides

Annalisa Bisello [1], Barbara Biondi [2], Roberta Cardena [1], Renato Schiesari [1], Marco Crisma [2], Fernando Formaggio [1] and Saverio Santi [1,*]

[1] Department of Chemical Sciences, University of Padova, via Marzolo 1, 35131 Padova, Italy; roberta.cardena@unipd.it (R.C.); fernando.formaggio@unipd.it (F.F.)
[2] Institute of Biomolecular Chemistry, Padova Unit, Consiglio Nazionale delle Ricerche (CNR), via Marzolo 1, 35131 Padova, Italy; marco.crisma@unipd.it (M.C.)
* Correspondence: saverio.santi@unipd.it

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 CH_2Cl_2. 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, CH_2Cl_2 was evaporated under reduced pressure. The oily residue was dissolved in ethyl acetate (EtOAc) and washed with 5% $NaHCO_3$, 5% $KHSO_4$, 5% $NaHCO_3$ and saturated NaCl solution. The organic solution was dried on anhydrous Na_2SO_4 and after filtration the solvent was removed under vacuum to yield a white powder.

Yield, 78%;

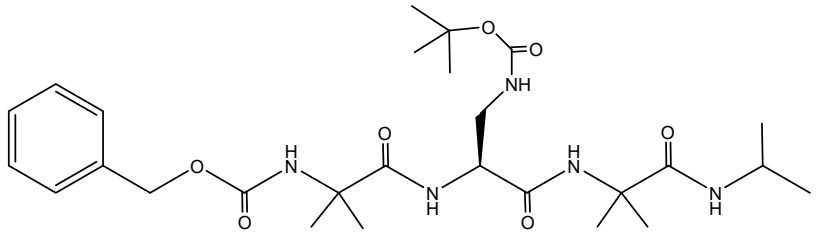
IR ($CDCl_3$, 1 mM) 3453, 3425, 3367, 1710, 1693, 1664, 1505 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.10 (m, 1H, CH Dap), 4.02 (m, 1H, CH *i*Pr), 3.48

(m, 2H, CH_2 Dap), 1.50 (s, 3H, CH_3Aib), 1.44 (s, 9H, CH_3Boc), 1.42 (s, 3H, CH_3Aib), 1.13 (dd, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{23}H_{36}N_4O_6$ $[M]^+$, 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.

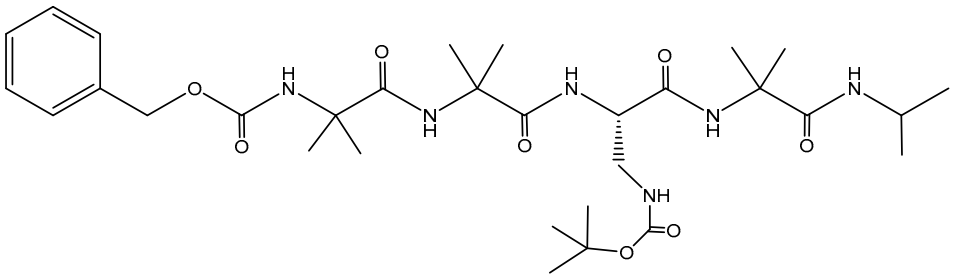
Yield, 89%;

IR ($CDCl_3$, 1 mM) 3453, 3433, 3345, 1716, 1677, 1525, 1505 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.13 (m, 1H, CH Dap), 4.02 (m, 1H, CH *i*Pr), 3.50 (m, 2H, CH_2 Dap), 1.54 (s, 3H, CH_3Aib), 1.51 (s, 3H, CH_3Aib), 1.48 (s, 3H, CH_3Aib), 1.44 (s, 9H, CH_3Boc), 1.43 (s, 3H, CH_3Aib), 1.15 (dd, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{43}N_5O_7$ $[M]^+$, 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.

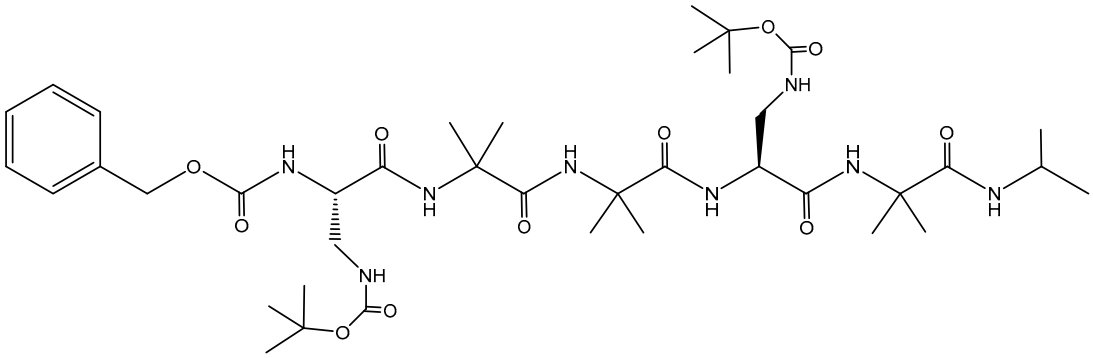
Yield, 75%;

IR ($CDCl_3$, 1 mM) 3450, 3424, 3349, 1709, 1678, 1529, 1505 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.06 (m, 1H, CH Dap), 4.03 (m, 1H, CH *i*Pr), 3.63, 3.47 (m, 2H, CH_2 Dap), 1.55 (s, 3H, CH_3Aib), 1.51 (s, 3H, CH_3Aib), 1.50 (s, 3H, CH_3Aib), 1.47 (s, 3H, CH_3Aib), 1.46 (s, 3H, CH_3Aib), 1.40 (s, 9H, CH_3Boc), 1.36 (s, 3H, CH_3Aib), 1.14 (t, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{31}H_{50}N_6O_8$ $[M]^+$, 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.

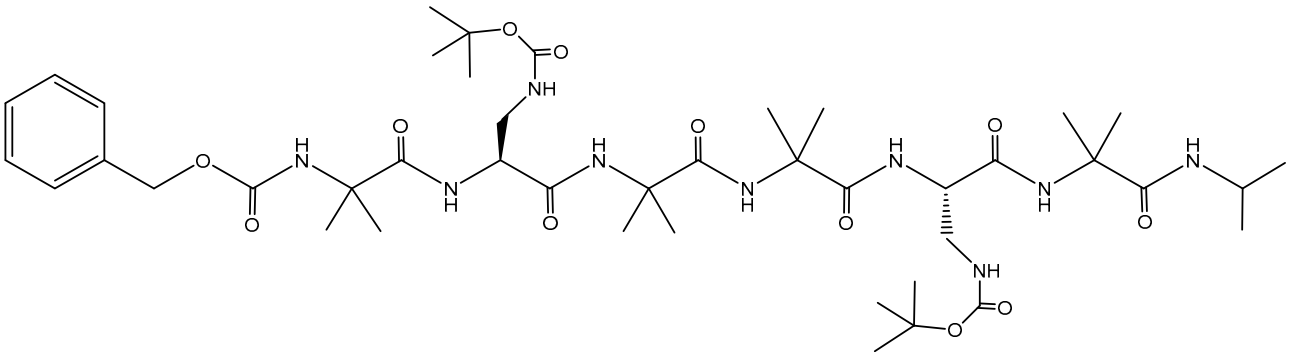
Yield, 80%;

IR ($CDCl_3$, 1 mM) 3450, 3407, 3342, 1707, 1673, 1514 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.20 (m, 2H, CH Dap), 4.03 (m, 1H, CH *i*Pr), 3.70, 3.59, 3.51 (m, 4H, CH_2 Dap), 1.55 (s, 3H, CH_3Aib), 1.52 (s, 3H, CH_3Aib), 1.51 (s, 3H, CH_3Aib), 1.46 (s, 21H, CH_3Boc and CH_3Aib), 1.44 (s, 3H, CH_3Aib), 1.29 (s, 3H, CH_3Aib), 1.10 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{39}H_{64}N_8O_{11}$ $[M]^+$, 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%;

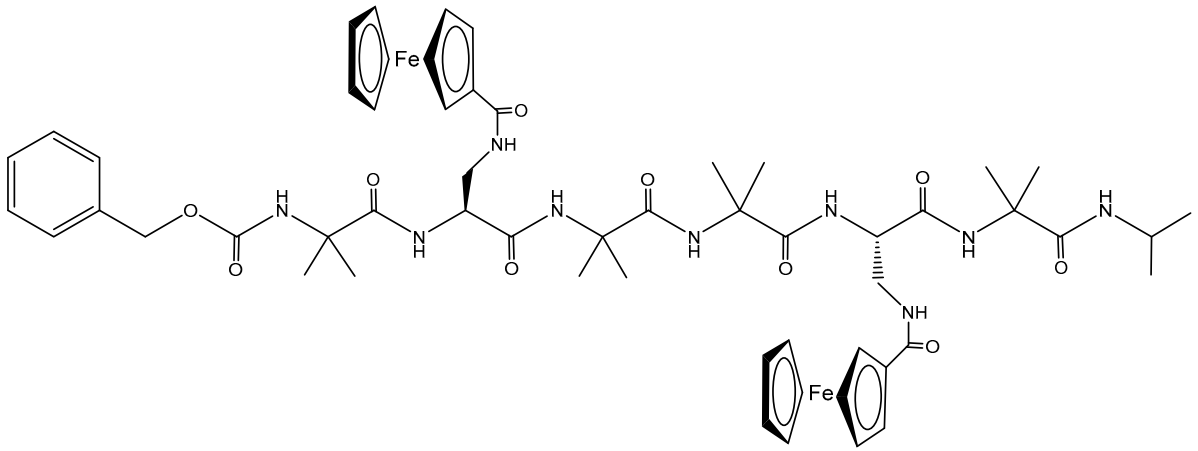
IR ($CDCl_3$, 1 mM) 3444, 3431, 3323, 1708, 1670, 1532, 1506 cm^{-1}.

^1H NMR (400.13 MHz, DMSO-d_6): 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, CH_2 Z), 4.04 (m, 1H, CH Dap), 4.00 (m, 1H, CH Dap), 3.79 (m, 1H, CH *i*Pr), 3.48 (m, 2H, CH_2 Dap), 3.26 (m, 1H, CH_2 Dap), 3.20 (m, 1H, CH_2 Dap), 1.38 (s, 18H, CH_3Boc), 1.36 (s, 12H, CH_3Aib), 1.33 (s, 6H, CH_3Aib), 1.32 (s, 6H, CH_3Aib), 1.01 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{43}H_{71}N_9O_{12}$ $[M]^+$, 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 CH_2Cl_2. 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% $NaHCO_3$, 5% $KHSO_4$, 5% $NaHCO_3$ and saturated NaCl solution. The organic solution was dried on anhydrous Na_2SO_4 and after filtration evaporated to dryness yielding an orange powder. The crude product was purified by flash chromatography (CH_2Cl_2/EtOH, 10%).

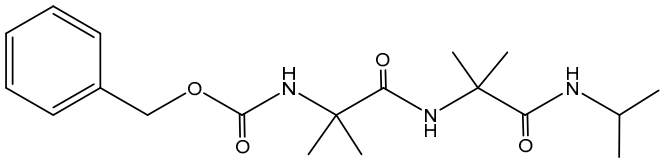
Yield: 34%;

IR ($CDCl_3$, 1 mM) 3429, 3310, 1710, 1664, 1523 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$, 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, CH_2 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, CH_2 Dap), 3.76 (m, 1H, CH_2 Dap), 3.67 (m, 2H, CH_2 Dap), 1.63 (s, 3H, CH_3Aib), 1.56 (s, 3H, CH_3Aib), 1.50 (s, 3H, CH_3Aib), 1.48 (s, 3H, CH_3Aib), 1.44 (s, 3H, CH_3Aib), 1.42 (s, 6H, CH_3Aib), 1.39 (s, 3H, CH_3Aib), 1.18 (m, 6H, NH-*i*Pr).

HRMS (ESI+)*:* m/z calcd for $C_{55}H_{71}Fe_2N_9O_{10}$, $[M]^+$ 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.

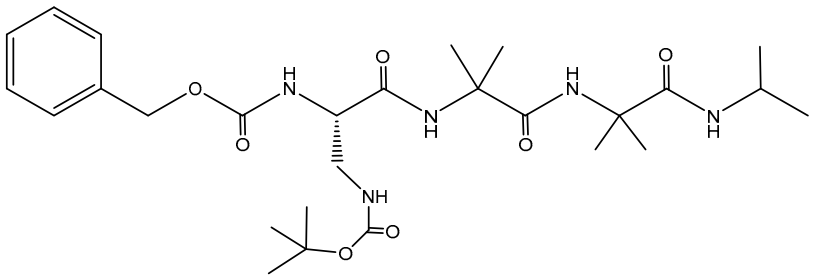
Yield, 66%;

IR ($CDCl_3$, 1 mM) 3430, 3373, 1720, 1687, 1658, 1499 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.02 (m, 1H, CH *i*Pr), 1.47 (s, 6H, CH_3Aib), 1.41 (s, 6H, CH_3Aib), 1.14 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{19}H_{29}N_3O_4$ $[M]^+$, 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.

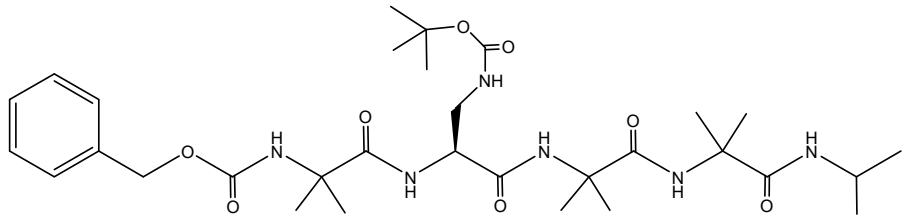
Yield, 70%;

IR ($CDCl_3$, 1 mM) 3453, 3419, 3367, 1705, 1689, 1506 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.04 (m, 1H, CH Dap), 4.00 (m, 1H, CH *i*Pr), 3.48 (m, 2H, CH_2 Dap), 1.46 (s, 6H, CH_3Aib), 1.44 (s, 12H, CH_3Boc, CH_3Aib), 1.34 (s, 3H, CH_3Aib), 1.13 (d, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{27}H_{43}N_5O_7$ $[M]^+$, 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.

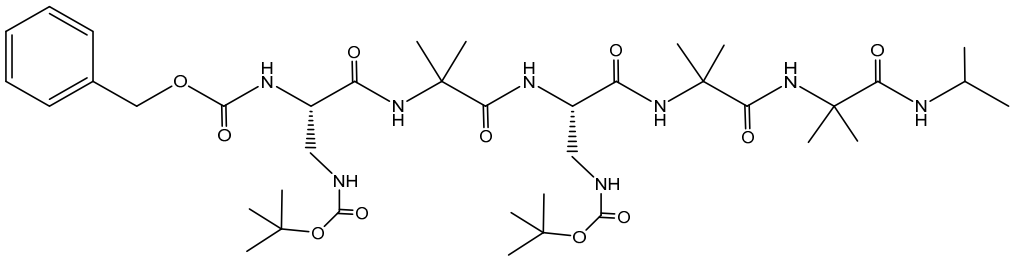
Yield, 85%;

IR ($CDCl_3$, 1 mM) 3453, 3433, 3341, 1714, 1676, 1528, 1505 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.05 (m, 1H, CH Dap), 4.01 (m, 1H, CH *i*Pr), 3.50 (m, 2H, CH_2 Dap), 1.52 (s, 3H, CH_3Aib), 1.50 (s, 3H, CH_3Aib), 1.46 (s, 3H, CH_3Aib), 1.45 (s, 3H, CH_3Aib), 1.44 (s, 9H, CH_3Boc), 1.40 (s, 6H, CH_3Aib), 1.14 (dd, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{31}H_{50}N_6O_8$ $[M]^+$, 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.

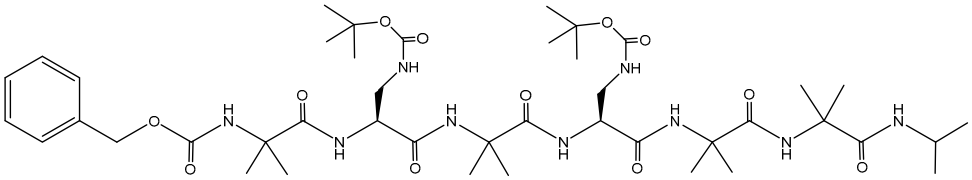
Yield, 90%;

IR ($CDCl_3$, 1 mM) 3454, 3416, 3346, 1687, 1676, 1525, 1509 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): 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, CH_2 Z), 4.15 (m, 1H, CH Dap), 4.03 (m, 1H, CH Dap), 4.00 (m, 1H, CH *i*Pr), 3.50 (m, 4H, CH_2 Dap), 1.49 (s, 6H, CH_3Aib), 1.47 (s, 6H, CH_3Aib), 1.45 (s, 9H, CH_3Boc), 1.43 (s, 9H, CH_3Boc), 1.41 (s, 6H, CH_3Aib), 1.15 (m, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{39}H_{64}N_8O_{11}$ $[M]^+$, 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.

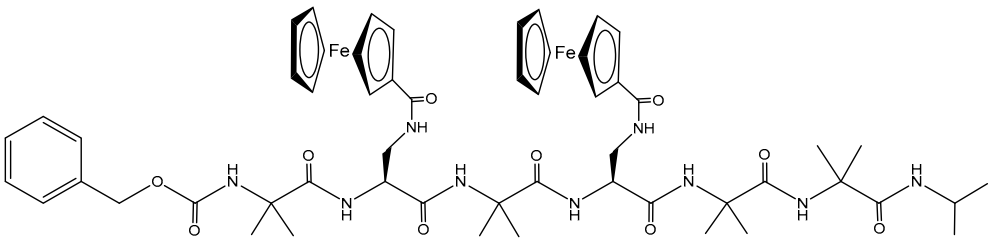
Yield, 70%;

IR ($CDCl_3$, 1 Mm) 3452, 3429, 3333, 1711, 1667, 1532, 1506 cm^{-1}.

^1H NMR (400.13 MHz, DMSO-d_6): 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, CH_2 Z), 4.09 (m, 2H, 2 CH Dap), 3.76 (m, 1H, CH *i*Pr), 3.42 (m, 1H, CH_2 Dap), 3.39 (m, 1H, CH_2 Dap), 3.32 (m, 1H, CH_2 Dap), 3.30 (m, 1H, CH_2 Dap), 1.33 (m, 42H, CH_3Aib, CH_3Boc), 1.03 (m, 6H, NH-*i*Pr).

HRMS (ESI+): *m*/*z* calcd for $C_{43}H_{71}N_9O_{12}$ $[M]^+$, 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 (CH_2Cl_2/EtOH, 10%).

Yield: 35%;

IR ($CDCl_3$, 1 mM) 3429, 3318, 1708, 1666, 1523 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$, 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, CH_2 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, CH_2 Dap), 3.69 (m, 2H, CH_2 Dap), 3.57 (m, 1H, CH_2 Dap), 1.54 - 1.47 (m, 24H, CH_3Aib), 1.23 (m, 6H, NH-*i*Pr).

HRMS (ESI+)*:* m/z calcd for $C_{55}H_{71}Fe_2N_9O_{10}$, $[M]^+$ 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	$C_{27}H_{43}N_5O_7$	
Formula weight	549.66	
Temperature	293(2) K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 11.85134(8) Å	α= 90°.
	b = 15.53512(13) Å	β= 90°.
	c = 17.02931(13) Å	γ = 90°.
Volume	3135.30(4) Å^3	
Z	4	
Density (calculated)	1.164 Mg/m^3	
Absorption coefficient	0.695 mm^{-1}	
F(000)	1184	
Crystal size	0.300 x 0.200 x 0.100 mm^3	
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 F^2	
Data / restraints / parameters	6231 / 0 / 361	
Goodness-of-fit on F^2	1.037	
Final R indices [I>2sigma(I)]	R_1 = 0.0363, wR_2 = 0.1011	
R indices (all data)	R_1 = 0.0378, wR_2 = 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.

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)

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

Symmetry transformations used to generate equivalent atoms:

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

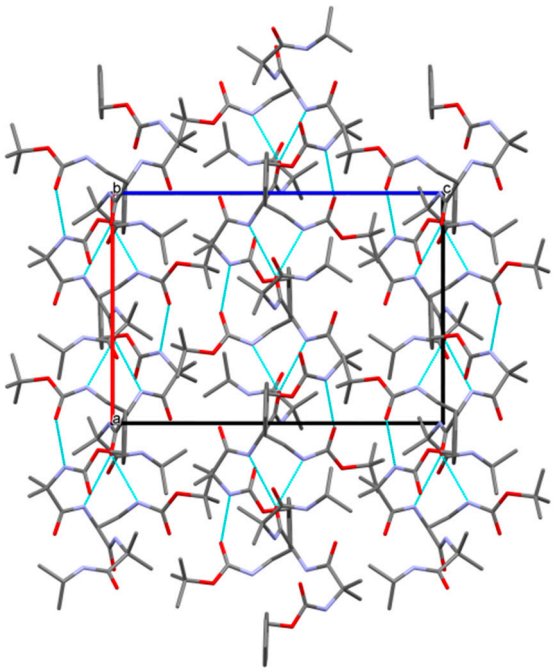


Figure S1. Packing mode of Z-Aib-L-Dap(Boc)-Aib-NH*i*Pr as viewed down the b axis. Intermolecular N-H…O=C H-bonds are indicated by dashed lines.

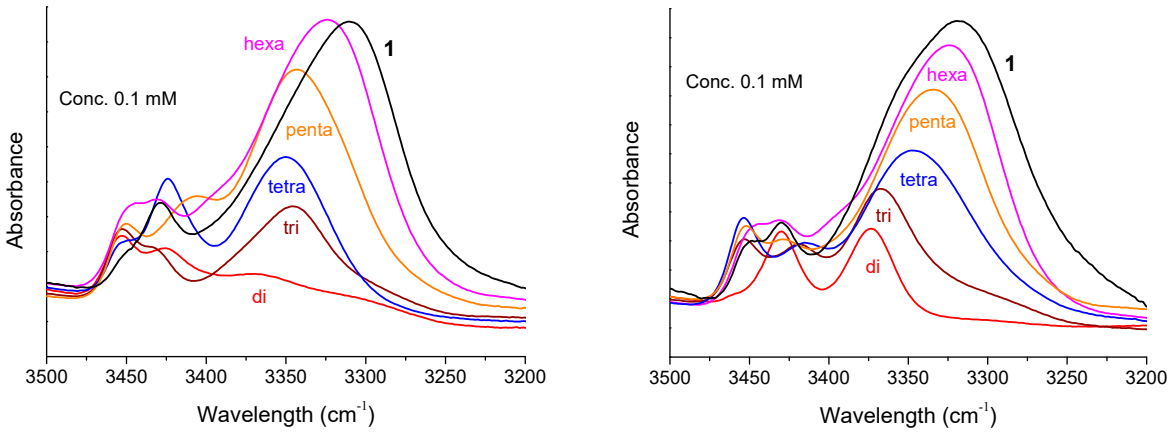


Figure S2. FT-IR spectra in the amide A region of the Fc-hexapeptides **1** (left) and **2** (right) and of their shorter intermediates, from the dipeptide to the hexapeptide. Peptide concentration: 0.1 mM in $CDCl_3$.

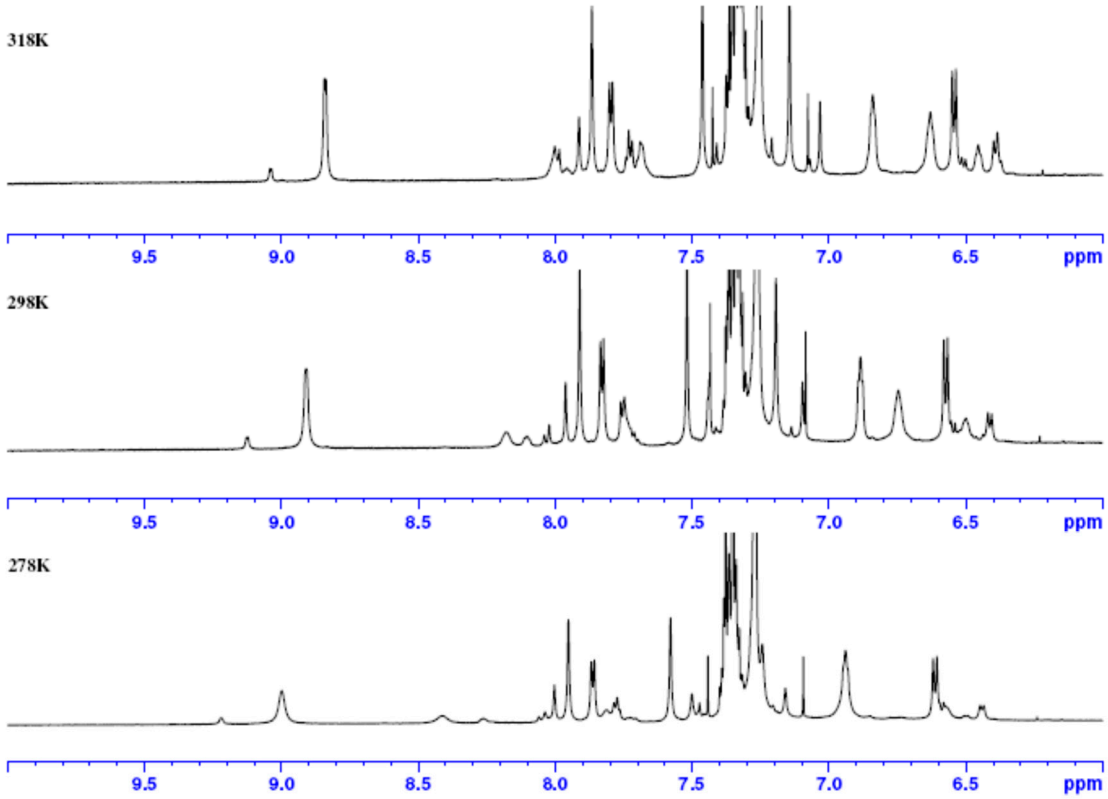


Figure S3. ^{1}H-NMR spectra of the **1** in the NH region at different temperatures. Peptide concentration: 0.1 mM in $CDCl_3$.

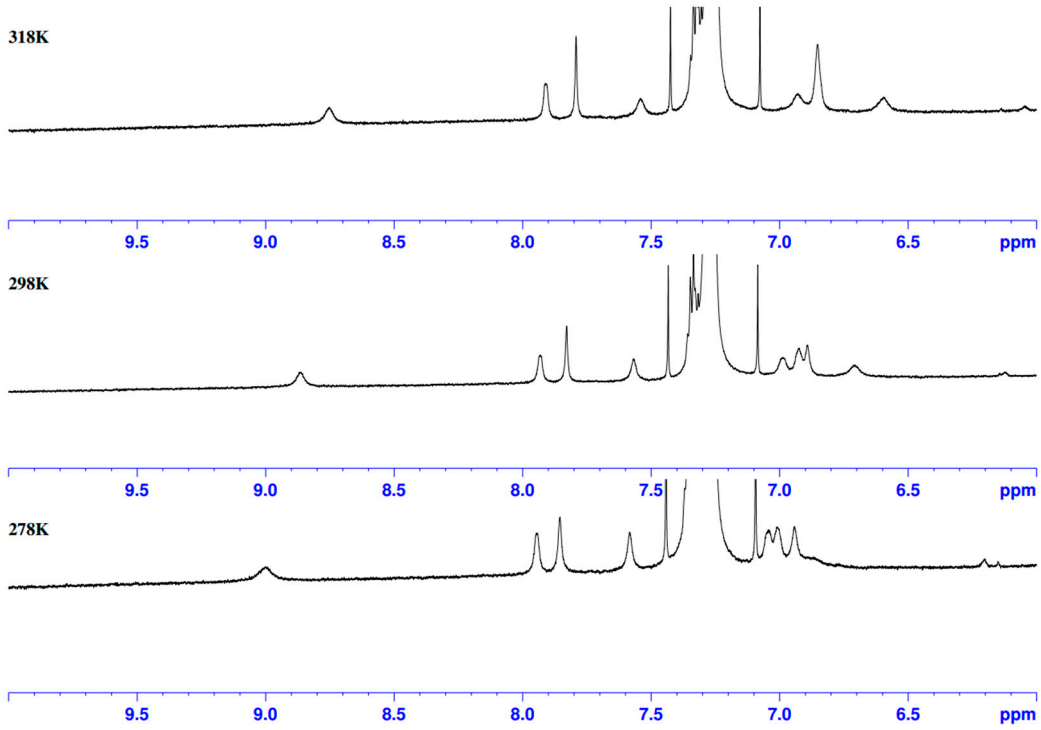


Figure S4. ^{1}H-NMR spectra of the **2** in the NH region at different temperatures. Peptide concentration: 0.1 mM in $CDCl_3$.

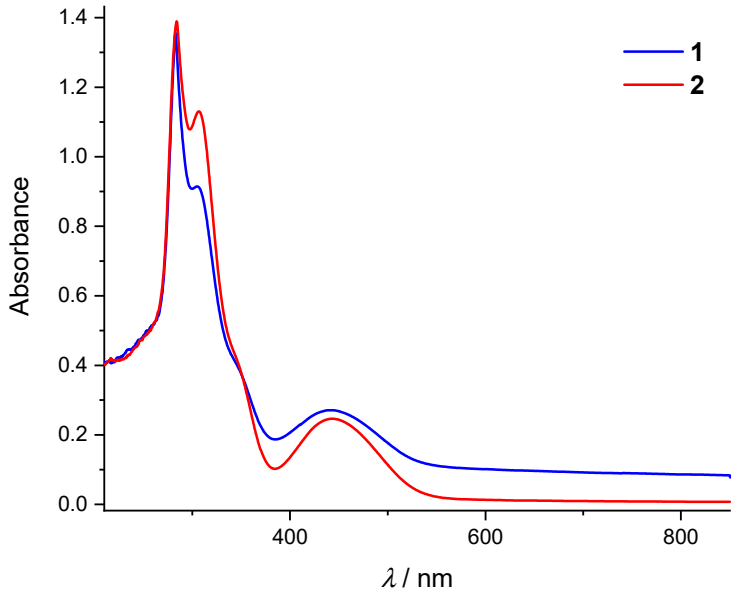


Figure S5. UV-vis spectra of **1** and **2** in CH_2Cl_2/0.1 M nBu$_4$B(C$_6$F$_5$)$_4$. Peptide concentration: 3.6 mM.

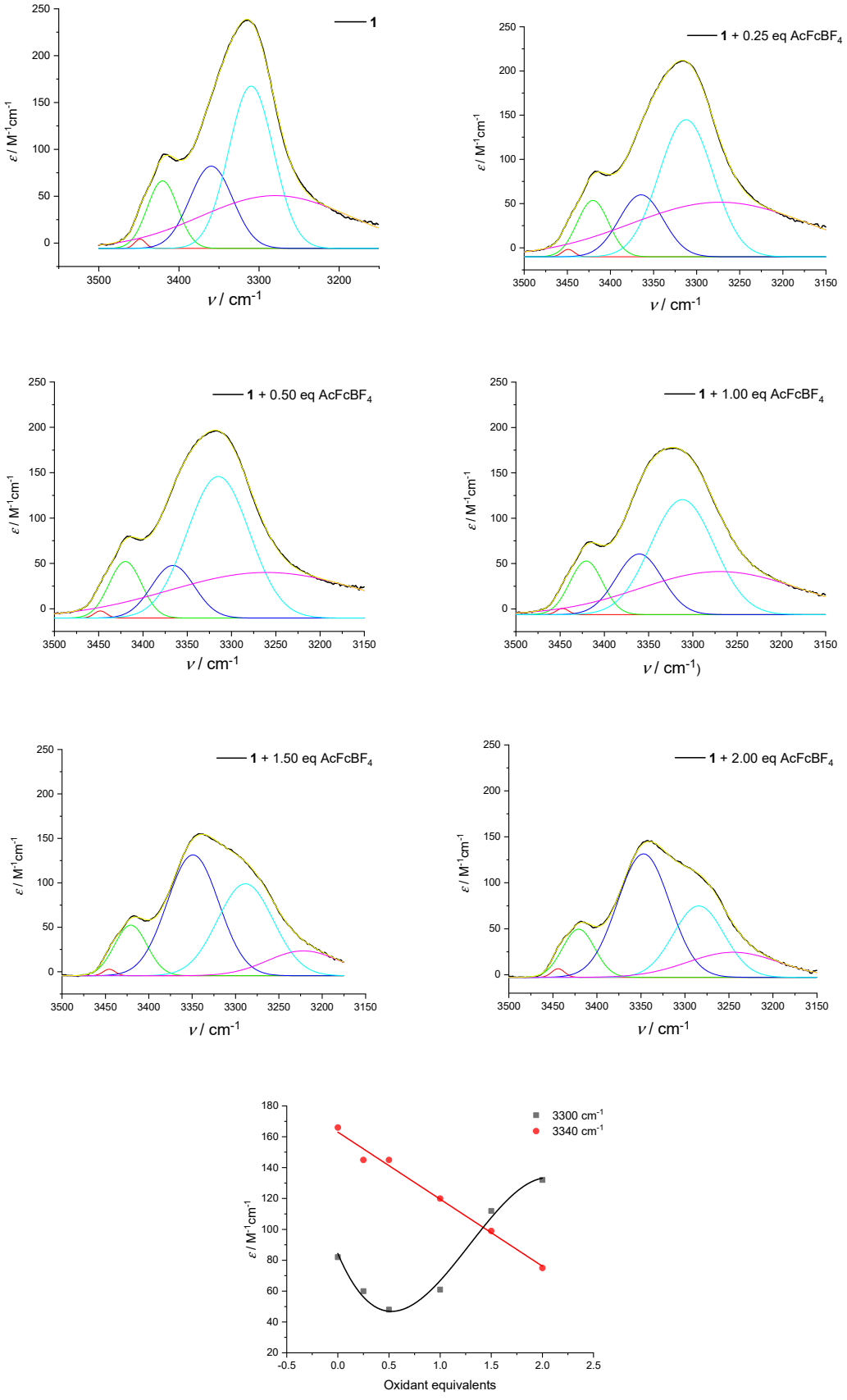


Figure S6. Fitting of MIR spectra of **1** in CH_2Cl_2/0.1 M nBu$_4$B(C_6F_5)$_4$ and behavior of absorption intensities of band at around 3350 and 3300 cm^{-1} as a function of oxidant addition.