Conformational cooperativity between helical domains of differing geometry in oligoamide-oligoureac foldamer chimeras

Julien Maury, Bryden A. F. Le Bailly, James Raftery and Jonathan Clayden*

SUPPORTING INFORMATION

General Information .......................................................................................................................... S2
General Procedures............................................................................................................................ S3
Experimental Procedures and Characterisation Data ........................................................................ S5-34
Hydrogen Bonding of 2d, 7e and 8c ................................................................................................. S35
CD spectra ........................................................................................................................................ S36-38
VT-NMR $^{13}$C of 11 between -80 and 40°C ....................................................................................... S39-40
VT-NMR $^1$H of 11 between 5 and 38 °C ........................................................................................... S40
NMR Spectra ($^1$H, $^{13}$C, COSY, HSQC)......................................................................................... S41-108
General Information

All solvents were purchased from Sigma-Aldrich and used without purification except THF and CH₂Cl₂ which were obtained by distillation from sodium/benzophenone and calcium hydride respectively.

¹H NMR and ¹³C NMR spectra were recorded on a Bruker Ultrashield 400 or 500 MHz spectrometer. ¹H and ¹³C spectra were referenced relative to the solvent residual peaks and chemical shifts (δ) reported in ppm downfield of tetramethylsilane (CDCl₃ δ H: 7.26 ppm, δ C: 77.16 ppm; CD₃OD δ H: 3.31 ppm, δ C: 49.00 ppm). ¹H NMR splitting patterns with observed first-order coupling are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Coupling constants (J) are reported in hertz (Hz). In ¹H NMR spectra, amide NH signals that exchange with deuterated solvent are not reported.

Electrospray (ES) spectra were recorded on a Waters Platform II and high resolution mass spectra (HRMS) were recorded on a Thermo Finnigan MAT95XP and are accurate to ± 0.001 Da. Infrared spectra were recorded on a Thermo Scientific Nicolet iS5 FTIR spectrometer. Melting points were determined on a GallenKamp apparatus and are uncorrected.

Thin layer chromatography (TLC) was performed using commercially available pre-coated plates (Macherey-Nagel alugram. Sil G/UV254) and visualized under UV light at 254 nm and/or by staining with phosphomolybdic acid solution. Flash column chromatography was carried out on Fluorochem Davisil 40-63 µm 60 Å silica with the eluent quoted. Optical rotation measurements were taken on an AA-100 polarimeter using a cell with a path length of 0.25 dm at 24 °C with the solvent and concentration (g/100 mL) stated. Circular dichroism (CD) spectra were recorded on a Jasco J-815 spectrometer using a 1 mm cell at 20 °C with the solvent and concentration stated.
General Procedures

Activated chiral monomers C (a R= iBu; b R= Me; c R= iPr), activated achiral monomers M1 and M2, CBzGly-Aib₂-OtBu and GlyNH₂-Aib₂-NHBoc and azlactone A1, L-ValNH⁢Bu and H-PheNH⁢Bu were prepared using a previously described procedure.¹

![Scheme 1: Activated chiral monomers Ca,Cb and Cc](image)

![Scheme 2: Activated achiral monomers M1, M2 and M3](image)

![Scheme 3: Peptides CBzGly-Aib₂-OtBu and GlyNH₂-Aib₂-NHBoc](image)

![Scheme 4: Azlactone A1](image)

General Procedure A: CBzGly-Aib₂-OH (1.00 eq.) and 1-hydroxybenzotriazole hydrate (1.30 eq.) were dissolved in CH₂Cl₂ (60 mL/mmol) and the suspension cooled to 0 °C. N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide (1.1 eq.) was added and the reaction was allowed to warm to room temperature

and stirred until it was homogenous. The amine (1.5 or 2.5 eq.) and trimethylamine or DIPEA (1.5 or 2 eq.) were added and the reaction mixture was stirred for 72 hours. The solvent was removed in vacuo and EtOAc was added. The organic phase was washed with KHSO₄ (5%), NaHCO₃, brine, dried (MgSO₄), filtered and concentrated. The pure oligomer was isolated by column chromatography (CH₂Cl₂:MeOH, 90:10).

**General Procedure B** : Boc-protected oligomers (1.00 eq) were dissolved in a mixture CH₂Cl₂/TFA (3/1) and stirred for 2 hours. The reaction mixture was then concentrated under reduced pressure and the resulting residue was coevaporated 3 times with cyclohexane. The crude product was then dissolved in DMF. DIPEA (3.00 eq) was then added and the mixture was cooled to 0 °C prior to the dropwise addition of carbamate (1.00 eq) in DMF (0.3 M). The reaction mixture was left to stir at 0 °C for 30 minutes then was allowed to warm to room temperature and stirred for another 18 hours. The reaction mixture was then concentrated and purified by flash chromatography (CH₂Cl₂-MeOH, 90:10) to give the desired compound (If DIPEA remained after column chromatography, the mixture was dissolved in EtOH. CuSO₄·5H₂O was added and the reaction mixture was stirred for 3 hours. A filtration (CH₂Cl₂/MeOH, 90:10) over a short pad of silica gel gave the desired compound).

**General Procedure C** : The Boc-protected oligomer (1.00 eq) was dissolved in a mixture CH₂Cl₂/TFA (3/1) and stirred for 2 hours. The reaction mixture was then concentrated under reduced pressure and the resulting residue was coevaporated 3 times with cyclohexane. The crude product was then dissolved in DMF. DIPEA (3.00 eq) was then added and the mixture was cooled to 0 °C prior to the dropwise addition of isopropyl isocyanate (2.00 eq) dissolved in DMF. The reaction mixture was left to stir at 0 °C for 30 minutes, then was allowed to warm to room temperature and stirred for another 18 hours. The reaction mixture was then concentrated and purified by flash chromatography (CH₂Cl₂-MeOH, 90:10) to give the desired compound (If DIPEA remained after column chromatography, the mixture was dissolved in EtOH. CuSO₄·5H₂O was added and the reaction mixture was stirred for 3 hours. A filtration (CH₂Cl₂/MeOH, 90:10) over a short pad of silica gel gave the desired compound).

**General Procedure D** : Boc-protected oligourea (1.00 eq) and DIPEA (1.00 eq) were added to a solution of isopropyl amine (1.30 eq) in DMF (0.26 M). The reaction was stirred for 30 min, quenched with NaHCO₃ aqueous solution and EtOAc was added. The organic phase was washed with KHSO₄ (5%), NaHCO₃ (sat?), brine, dried (MgSO₄), filtered and concentrated.

---

2 From deprotection of Boc protected amine [CH₂Cl₂/TFA (3/1), 2h, r.t.]
Experimental Procedures and Characterisation Data

BocVal^u^-NH(CO)NH/Pr U1

U1 was prepared from Cc (1.00 g, 2.91 mmol), isopropylamine (310 μL, 3.78 mmol) and DIPEA (537 μL, 2.91 mmol) as described in the general procedure D. The pure oligomer U1 (794 mg, 95%) was isolated as a white solid. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta = 5.00-4.80\) (1H, m, NH), 4.79-4.64 (1H, m, NH), 4.54-4.35 (1H, m, NH), 3.81 (1H, oct, \(J = 6.9\), NCH\(_{\text{ipr}}\)), 3.51-3.38 (1H, m, NCH\(_{\text{val}}\)), 3.36-3.23 (1H, m, NCH\(_{\text{a}}\)H\(_{\text{val}}\)), 3.22-3.12 (1H, m, NCH\(_{\text{a}}\)H\(_{\text{val}}\)), 1.85-1.68 (1H, m, CH\(_{\text{val}}\)), 1.43 (9H, s, C(CH\(_3\))\(_3\)), 1.13 (6H, d, \(J = 6.5\), 2 x CH\(_{\text{ipr}}\)), 0.94 (3H, d, \(J = 6.8\), CH\(_{\text{3val}}\)), 0.92 (3H, d, \(J = 6.9\), CH\(_{\text{3val}}\)). \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta = 158.2\) (C=O), 157.3 (C=O), 79.6 (C(CH\(_3\))\(_3\)), 56.6 (NCH\(_{\text{val}}\)), 43.4 (NCH\(_{\text{ipr}}\)), 42.5 (NC \(_2\)H\(_{\text{val}}\)) and 30.7 (C\(_2\)H\(_{\text{val}}\)). \(\nu\)_max (film, cm\(^{-1}\)) \(= 3311, 2965, 2928, 2871, 1636, 1534;\) HRMS (ESI\(^+\)) \(m/z\) calcd for C\(_{24}\)H\(_{30}\)N\(_3\)O\(_3\) [M+H]\(^+\) 288.2287, found 288.2285.

BocAla^u^-NH(CO)NH/Pr U2\(^{1a}\)

U2 was prepared from Cb (1.50 g, 4.76 mmol), isopropylamine (506 μL, 6.18 mmol) and DIPEA (880 μL, 4.76 mmol) as described in the general procedure D. The pure oligomer U2 (1.16 g, 94.0%) was isolated as a white solid. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta = 5.17\) (1H, t, \(J = 4.5\), NH), 4.94 (1H, d, \(J = 7.5\), NH), 4.74 (1H, brs, NH), 3.82 (1H, oct, \(J = 6.7\), NCH\(_{\text{alb}}\)), 3.66 (1H, oct, \(J = 7.3\), NCH\(_{\text{ipr}}\)), 3.32-3.17 (1H, m, NCH\(_{\text{a}}\)H\(_{\text{a}}\)), 3.17-3.03 (1H, m, NCH\(_{\text{a}}\)H\(_{\text{a}}\)), 1.42 (9H, s, C(CH\(_3\))\(_3\)), 1.13 (9H, d, \(J = 6.5\), 2 x CH\(_{\text{ipr}}\) and CH\(_{\text{3alb}}\)). \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta = 158.3\) (C=O), 156.5 (C=O), 79.6 (C(CH\(_3\))\(_3\)), 47.6 (NCH\(_{\text{alb}}\)), 46.7 (NC \(_2\)H\(_{\text{alb}}\)) and 42.4 (NCH\(_{\text{ipr}}\)). \(\nu\)_max (film, cm\(^{-1}\)) \(= 3341, 2973, 2932, 2873, 1637, 1563;\) HRMS (ESI\(^+\)) \(m/z\) calcd for C\(_{14}\)H\(_{26}\)N\(_3\)O\(_3\) [M+H]\(^+\) 260.1974, found 260.1986.
**BocLeu"-NH(CO)NH/iPr U3**

U3 was prepared from Ca (2.00 g, 5.60 mmol), isopropylamine (600 μL, 7.27 mmol) and DIPEA (1.03 mL, 5.60 mmol) as described in the general procedure D. The pure oligomer U3 (1.58 g, 92.7%) was isolated as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ = 5.16-4.94 (1H, m, NH), 4.81-4.48 (2H, m, NH), 3.90-3.75 (1H, m, NCH$_{Leu}$), 3.70-3.59 (1H, m, NCH$_{iPr}$), 3.33-3.16 (1H, m, NCH$_4$H$_{Bleu}$), 3.16-3.02 (1H, m, NCH$_3$H$_{Bleu}$), 1.67 (1H, non, J = 6.9, CH$_{Leu}$), 1.42 (9H, s, C(CH$_3$)$_3$), 1.28 (2H, t, J = 7.3, CH$_{2Lae}$), 1.13 (6H, d, J = 6.5, CH$_{3iPr}$), 0.91 (3H, d, J = 6.5, CH$_{3iPr}$), 0.90 (3H, d, J = 6.5, CH$_{3Lae}$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 158.2 (C=O), 156.9 (C=O), 79.6 (C(CH$_3$)$_3$), 49.8 (NCH$_{iPr}$), 46.2 (NCH$_{H_{Bleu}}$), 42.4 (C$_{H_{2Lae}}$), 42.2 (NCH$_{iPr}$), 28.5 (C(CH$_3$)$_3$), 25.0 (CH$_{Leu}$), 23.6 (CH$_{iPr}$), 23.5 (CH$_{iPr}$), 23.2 (CH$_{3Lae}$), 22.2 (CH$_{3Lae}$). IR (film, cm$^{-1}$): ν$_{max}$ = 3341, 2964, 2931, 2870, 1636, 1526;

**BocVal"-Ala"-NH(CO)NH/iPr U4**

U4 was prepared from U2 (900 mg, 3.86 mmol), Cc (1.33 g, 3.86 mmol) and DIPEA (1.97 mL, 11.58 mmol) as described in the general procedure B2. The pure oligomer U4 (933 mg, 62.4% in two steps) was isolated as a white solid. $^1$H NMR (400 MHz, CD$_2$OH) δ = 6.39 (1H, d, J = 6.7, NH), 6.04-5.73 (4H, m, NH), 4.88-3.67 (2H, m, NCH$_{Ala}$ and NCH$_{iPr}$), 3.52-3.38 (1H, m, NCH$_{Vol}$), 3.37-3.15 (2H, m, NCH$_4$H$_{BVol}$ and NCH$_4$H$_{BAla}$), 3.01-2.82 (2H, m, NCH$_4$H$_{BVol}$ and NCH$_4$H$_{BAla}$), 1.70 (1H, oct, J = 6.6, CH$_{Val}$), 1.43 (9H, s, C(CH$_3$)$_3$), 1.11 (3H, d, J = 6.5, CH$_{3iPr}$), 1.10 (3H, d, J = 6.5, CH$_{3iPr}$), 1.07 (3H, d, J = 6.7, CH$_{3Ala}$), 0.93 (3H, d, J = 6.8, CH$_{3Val}$), 0.89 (3H, d, J = 6.8, CH$_{3Val}$). $^{13}$C NMR (100 MHz, CD$_2$OH) δ = 160.8 (C=O), 160.6 (C=O), 158.8 (C=O), 79.8 (C(CH$_3$)$_3$), 57.6 (NCH$_{Val}$), 47.6 (NCH$_{Ala}$), 46.9 (NCH$_{2Ala}$), 43.2 (NCH$_2$Val), 42.9 (NCH$_{iPr}$), 31.7 (CH$_{Val}$), 28.7 (C(CH$_3$)$_3$), 23.5 (CH$_{iPr}$), 23.4 (CH$_{iPr}$), 19.8 (CH$_{3Val}$), 19.0 (CH$_{3Ala}$), 18.3 (CH$_{3Val}$). IR (film, cm$^{-1}$): ν$_{max}$ = 3321, 2969, 2932, 2873, 1630, 1529; HRMS (ESI$^+$): m/z calcd for C$_{18}$H$_{38}$N$_2$O$_4$ [M+H]$^+$ 388.2924, found 388.2911.
BocAla<sup>u</sup>-Leu<sup>u</sup>-NH(CO)NH/Pr U5

U5 was prepared from U3 (1.30 g, 4.98 mmol), Cb (1.60 g, 4.98 mmol) and DIPEA (2.54 mL, 14.94 mmol) as described in the general procedure B2. The pure oligomer U5 (860 mg, 38.4% in two steps) was isolated as a white solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>OH) δ = 6.61-6.42 (1H, m, NH), 5.91-5.72 (4H, m, NH), 3.85-3.59 (1H, m, NCH<sub>Ala</sub>, NCH<sub>Leu</sub> and NCH<sub>IPr</sub>), 3.28-3.10 (2H, m, NCH<sub>Ala</sub>H<sub>Bleu</sub> and NCH<sub>Ala</sub>H<sub>Ala</sub>), 3.02-2.81 (2H, m, NCH<sub>Ala</sub>H<sub>Bleu</sub> and NCH<sub>Ala</sub>H<sub>Ala</sub>), 1.68 (1H, non, J = 6.9, CH<sub>Leu</sub>), 1.43 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>), 1.32-1.20 (2H, m, CH<sub>2</sub>Leu), 1.11 (3H, d, J = 6.5, CH<sub>3</sub>Pr), 1.10 (3H, d, J = 6.5, CH<sub>3</sub>Pr), 1.07 (3H, d, J = 6.7, CH<sub>3</sub>Ala), 0.92 (3H, d, J = 6.7, CH<sub>3</sub>Leu), 0.90 (3H, d, J = 6.6, CH<sub>3</sub>Leu).<sup>12</sup>C NMR (100 MHz, CD<sub>2</sub>OH) δ = 161.1 (C=O), 160.6 (C=O), 158.2 (C=O), 79.9 (C(CH<sub>3</sub>)<sub>3</sub>), 49.3 (NC<sub>IPr</sub>H<sub>Leu</sub>), 47.1(NC<sub>IPr</sub>H<sub>Ala</sub>), 46.5 (NC H<sub>2</sub>Leu), 46.3 (NC H<sub>2</sub>Leu), 43.1 (C H<sub>2</sub>Leu), 42.9 (NCH<sub>IPr</sub>), 28.7 (C(CH<sub>3</sub>)<sub>3</sub>), 25.9 (C,H<sub>Leu</sub>), 23.6 (CH<sub>IPr</sub>), 23.5 (CH<sub>IPr</sub>), 23.4 (CH<sub>3</sub>Leu), 22.3 (CH<sub>3</sub>Leu), 18.5 (C,H<sub>3</sub>Ala). IR (film, cm<sup>-1</sup>): ν<sub>max</sub> = 3331, 2968, 2932, 2872, 1636, 1536; HRMS (ESI<sup>+</sup>): m/z calcd for C<sub>19</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub>[M+Na]<sup>+</sup> 424.2900, found 424.2887.

BocVal<sup>u</sup>-Ala<sup>u</sup>-Leu<sup>u</sup>-NH(CO)NH/Pr U6

U6 was prepared from U5 (850 mg, 2.12 mmol), Cc (727 mg, 2.12 mmol) and DIPEA (1.08 mL, 6.35 mmol) as described in the general procedure B2. The pure oligomer U6 (728 mg, 64.9% in two steps) was isolated as a white solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>OH) δ = 6.53 (1H, d, J = 10.0, NH), 6.25 (1H, dd, J = 7.2 and 1.7, NH), 6.05 (1H, d, J = 7.9, NH), 5.96-5.86 (2H, m, NH), 5.83 (1H, d, J = 9.3, NH), 5.81-5.74 (1H, m, NH), 4.04-3.85 (2H, m, NCH<sub>Ala</sub> and NCH<sub>Leu</sub>), 3.77-3.68 (1H, oct, J = 7.6, NCH<sub>IPr</sub>), 3.59-3.39 (4H, m, NCH<sub>Vol</sub>, NCH<sub>β</sub>H<sub>Vol</sub>, NCH<sub>Ala</sub>H<sub>Bleu</sub> and NCH<sub>Ala</sub>H<sub>Ala</sub>), 2.74-2.34 (3H, m, NCH<sub>Ala</sub>H<sub>Bleu</sub> and NCH<sub>Ala</sub>H<sub>Ala</sub>), 1.76-1.58 (2H, m, CH<sub>Leu</sub> and CH<sub>Vol</sub>), 1.45 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>), 1.22 (2H, t, J = 7.1, CH<sub>2</sub>Leu), 1.11 (3H, d, J = 6.5, CH<sub>3</sub>Pr), 1.10 (3H, d, J = 6.5, CH<sub>3</sub>Pr), 1.04 (3H, d, J = 6.8, CH<sub>3</sub>Ala), 0.97-0.85 (12H, m, 2 x CH<sub>3</sub>Vol and 2 x CH<sub>3</sub>Leu).<sup>12</sup>C NMR (100 MHz, CD<sub>2</sub>OH) δ = 161.2 (C=O), 160.8 (C=O), 160.6 (C=O), 159.4 (C=O), 80.1 (C(CH<sub>3</sub>)<sub>3</sub>), 57.5 (NC<sub>IPr</sub>H<sub>Vol</sub>), 49.1 (NC<sub>IPr</sub>H<sub>Leu</sub>), 48.1 (NC H<sub>2</sub>Ala), 46.5 (NC<sub>IPr</sub>H<sub>Ala</sub>), 46.1 (NC H<sub>2</sub>Leu), 43.9 (NC H<sub>2</sub>Vol), 43.7 (C H<sub>2</sub>Leu), 42.8 (NCH<sub>IPr</sub>), 31.9 (C,H<sub>Vol</sub>), 28.7 (C(CH<sub>3</sub>)<sub>3</sub>), 25.9 (C,H<sub>Leu</sub>), 23.6 (2 x CH<sub>IPr</sub>),
23.5 (CH$_{3}$leu), 22.4 (CH$_{3}$leu), 20.0 (C$_6$H$_3$vol), 18.6 (C$_6$H$_3$ala), 18.4 (C$_6$H$_3$vol). IR (film, cm$^{-1}$): $\nu_{max} = 3319, 2963, 2931, 2872, 1628, 1567, 1530$; HRMS (ES$I$): m/z calcd for C$_{25}$H$_{52}$N$_7$O$_5$ [M+H]$^+$ 530.4030, found 530.4006.

BocAib$^{\alpha}$-Val$^{\beta}$-Ala$^{\gamma}$-Leu$^{\delta}$-NH(CO)NHiPr U7

![Chemical Structure](image)

**U7** was prepared from **U6** (150 mg, 0.28 mmol), **M2** (93 mg, 0.28 mmol) and DIPEA (145 $\mu$L, 0.85 mmol) as described in the general procedure B2. The pure oligomer **U7** (50 mg, 27.4% in two steps) was isolated as a white solid. $^1$H NMR (500 MHz, CD$_3$OD) $\delta = 6.87$ (1H, t, $J = 6.9$, NH), 6.40 (1H, d, $J = 9.4$, NH), 6.13 (1H, d, $J = 9.4$, NH), 5.93 (1H, d, $J = 9.4$, NH), 5.79 (1H, s, NH), 5.77 (1H, d, $J = 10.0$, NH), 5.61 (1H, d, $J = 9.8$, NH), 4.09-3.96 (1H, m, NCH$_{ala}$), 3.94-3.85 (1H, m, NCH$_{ala}$), 3.77-3.68 (1H, m, NCH$_{vol}$ and NCH$_{ipr}$), 3.67-3.44 (4H, m, NCH$_{ala}$H$_{B}$, NCH$_{ala}$H$_{B}$, NCH$_{ala}$H$_{B}$, NCH$_{ala}$H$_{B}$ and NCH$_{ala}$H$_{B}$), 2.87-2.76 (1H, m, NCH$_{ala}$H$_{B}$), 2.70-2.57 (1H, m, NCH$_{ala}$H$_{B}$), 2.53-2.32 (2H, m, NCH$_{ala}$H$_{B}$ and NCH$_{ala}$), 1.69 (1H, non, $J = 6.8$, CH$_{ala}$), 1.62 (1H, oct, $J = 6.7$, CH$_{ala}$), 1.46 (9H, s, C(CH$_3$)$_3$), 1.37 (3H, s, CH$_3$), 1.22 (2H, t, $J = 7.2$, CH$_{2ala}$), 1.14 (3H, s, CH$_3$), 1.13 (3H, d, $J = 6.5$, CH$_{3ipr}$), 1.12 (3H, d, $J = 6.5$, CH$_{3ipr}$), 1.04 (3H, d, $J = 6.8$, CH$_{3ala}$), 0.95-0.86 (12H, m, 2 x CH$_{3vol}$ and 2 x CH$_{3leu}$). $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta = 161.6$ (C=O), 161.5 (C=O), 160.7 (C=O), 160.5 (C=O), 159.1 (C=O), 80.1 (C(CH$_3$)$_3$), 56.0 (NC$_{B}$H$_{vol}$), 54.8 (C), 49.3 (NC$_{ala}$H$_{ala}$), 47.9 (NCH$_{ala}$), 47.5 (NC$_{ala}$H$_{ala}$), 46.5 (NC$_{ala}$H$_{ala}$), 46.0 (NC$_{ala}$H$_{ala}$), 44.5 (NC$_{ala}$H$_{ala}$), 43.8 (C$_{ala}$H$_{2ala}$), 42.8 (NCH$_{ala}$), 31.8 (C$_{ala}$H$_{vol}$), 28.9 (C(CH$_3$)$_3$), 26.6 (CH$_3$), 26.0 (CH$_3$), 25.9 (C$_{ala}$H$_{ala}$), 23.7 (CH$_{ala}$), 23.7 (CH$_{ala}$), 23.6 (CH$_{3ala}$), 22.6 (CH$_{3ala}$), 20.3 (C$_{ala}$H$_{vol}$), 18.8 (C$_{ala}$H$_{ala}$), 18.6 (C$_{ala}$H$_{ala}$). IR (film, cm$^{-1}$): $\nu_{max} = 3300, 2970, 1656, 1527$; HRMS (ES$I$): m/z calcd for C$_{25}$H$_{52}$N$_7$O$_5$ [M+H]$^+$ 644.4823, found 644.4826.

BocEDA-Val$^{\alpha}$-Ala$^{\beta}$-Leu$^{\delta}$-NH(CO)NHiPr U8

![Chemical Structure](image)

**U8** was prepared from **U6** (100mg, 0.16 mmol), **M3** (47 mg, 0.16 mmol) and DIPEA (79 $\mu$L, 0.46 mmol) as described in the general procedure B2. The pure oligomer **U8** (50 mg, 52.4% in two steps)
was isolated as a white solid. $^1$H NMR (400 MHz, CD$_3$OH) $\delta$ = 6.78-6.66 (1H, m, NH), 6.34-6.20 (2H, m, NH), 6.17-6.04 (2H, m, NH), 5.97 (1H, d, $J$ = 9.3, NH), 5.91-5.78 (3H, m, NH), 4.06-3.94 (1H, m, NCH$_{\text{Ala}}$), 3.93-3.85 (1H, m, NCH$_{\text{Leu}}$), 3.84-3.73 (1H, m, NCH$_{\text{Val}}$), 3.66-3.42 (4H, m, NCH$_{\text{Val}}$ NCH$_{\text{Val}}$ NCH$_{\text{Bleu}}$ and NCH$_{\text{Val}}$ NCH$_{\text{Bleu}}$), 3.41-3.26 (2H, m, 2 x NCH$_{\text{Ala}}$ NCH$_{\text{Ala}}$), 3.07-2.89 (2H, m, 2 x NCH$_{\text{Ala}}$ NCH$_{\text{Ala}}$), 2.75-2.37 (3H, m, NCH$_{\text{Bleu}}$ NCH$_{\text{Bleu}}$ and NCH$_{\text{Ala}}$ NCH$_{\text{Ala}}$), 1.75-1.57 (2H, m, CH$_{\text{Leu}}$ and CH$_{\text{Val}}$), 1.45 (9H, s, C(CH$_{3}$)$_{3}$), 1.33-1.16 (2H, m, CH$_{\text{Leu}}$), 1.12 (3H, d, $J$ = 6.5, CH$_{\text{Bleu}}$), 1.11 (3H, d, $J$ = 6.5, CH$_{\text{Bleu}}$), 1.04 (3H, d, $J$ = 6.7, CH$_{\text{Val}}$), 0.97-0.85 (12H, m, 2 x CH$_{3\text{Leu}}$ and 2 x CH$_{3\text{Val}}$). $^{13}$C NMR (100 MHz, CD$_3$OH) $\delta$ = 161.5 (C=O), 161.4 (C=O), 160.6 (C=O), 160.6 (C=O), 159.0 (C=O), 80.2 (C(CH$_{3}$)$_{3}$), 56.5 (NC$_{\text{HVal}}$), 49.4 (NC$_{\text{HLeu}}$), 48.0 (NC$_{\text{HVal}}$ NCH$_{\text{Val}}$ and NCH$_{\text{Val}}$), 46.4 (NC$_{\text{HVal}}$), 46.1 (NC$_{\text{HVal}}$), 44.5 (NC$_{\text{HVal}}$), 43.8 (C$_{\text{HVal}}$), 42.8 (NCH$_{\text{Val}}$), 41.6 (NCH$_{\text{Val}}$), 41.5 (NCH$_{\text{Val}}$), 31.8 (C$_{\text{HVal}}$), 28.7 (C(CH$_{3}$)$_{3}$), 25.8 (C$_{\text{HVal}}$), 23.7 (C$_{\text{HVal}}$), 23.6 (C$_{\text{HVal}}$), 23.5 (C$_{\text{HVal}}$), 22.5 (C$_{\text{HVal}}$), 20.2 (C$_{\text{HVal}}$), 18.7 (C$_{\text{HVal}}$), 18.6 (C$_{\text{HVal}}$). IR (film, cm$^{-1}$): $\nu_{\text{max}}$ = 3310, 2936, 1651, 1538; Mp: >200°C; HRMS (ESI$^+$): m/z calcd for C$_{28}$H$_{57}$N$_{9}$O$_{5}$Na [M+Na]$^+$ 638.4330, found 638.4324.

U9 was prepared from U4 (583 mg, 0.99 mmol), Ca (355 mg, 0.99 mmol) and DIPEA (506 µL, 2.98 mmol) as described in the general procedure B2. The pure oligomer U9 (450 mg, 85.8% in two steps) was isolated as a white solid. $^1$H NMR (400 MHz, CD$_3$OH) $\delta$ = 6.59 (1H, d, $J$ = 9.6, NH), 6.23-6.14 (1H, m, NH), 6.12-6.02 (1H, m, NH), 6.02-5.87 (2H, m, NH), 5.83 (2H, d, $J$ = 9.1, NH), 3.95-3.76 (3H, m, NCH$_{\text{Ala}}$, NCH$_{\text{Leu}}$ and NCH$_{\text{Val}}$), 3.62-3.55 (2H, m, NCH$_{\text{Val}}$ and NCH$_{\text{Val}}$), 3.55-3.45 (1H, m, NCH$_{\text{Bleu}}$), 3.45-3.36 (1H, m, NCH$_{\text{Val}}$), 2.80-2.68 (1H, m, NCH$_{\text{Val}}$), 2.67-2.58 (1H, m, NCH$_{\text{Val}}$), 2.57-2.44 (1H, m, NCH$_{\text{Val}}$), 1.79-1.60 (2H, m, CH$_{\text{Leu}}$ and CH$_{\text{Val}}$), 1.48 (9H, s, C(CH$_{3}$)$_{3}$), 1.34-1.18 (2H, m, CH$_{2\text{Val}}$), 1.14 (6H, d, $J$ = 6.5, 2 x CH$_{3\text{Val}}$), 1.07 (3H, d, $J$ = 6.7, CH$_{3\text{Ala}}$), 1.01-0.87 (12H, m, 2 x CH$_{3\text{Val}}$ and 2 x CH$_{3\text{Leu}}$).

$^{13}$C NMR (100 MHz, CD$_3$OH) $\delta$ = 161.4 (C=O), 161.1 (C=O), 160.6 (C=O), 159.1 (C=O), 80.1 (C(CH$_{3}$)$_{3}$), 56.4 (NC$_{\text{HVal}}$), 50.0 (NC$_{\text{HVal}}$), 47.1 (NC$_{\text{HAla}}$), 46.7 (NC$_{\text{HAla}}$), 46.5 (NC$_{\text{HVal}}$), 44.5 (NC$_{\text{HVal}}$), 42.8 (NCH$_{\text{Val}}$), 42.4 (C$_{\text{HVal}}$), 31.9 (C$_{\text{HVal}}$), 28.9 (C(CH$_{3}$)$_{3}$), 26.2 (C$_{\text{HVal}}$), 23.8 (C$_{\text{HVal}}$), 23.7 (2 x CH$_{\text{Val}}$), 22.5 (C$_{\text{HVal}}$), 20.1 (C$_{\text{HVal}}$), 19.4 (C$_{\text{HVal}}$), 18.5 (C$_{\text{HVal}}$). IR (film, cm$^{-1}$): $\nu_{\text{max}}$ = 3339, 2936, 2931, 2871, 1636, 1567; [α]$_D^{19}$ = +58.8 (c = 1.00, MeOH); Mp: 194-196°C; HRMS (ESI$^+$): m/z calcd for C$_{28}$H$_{52}$N$_{9}$O$_{5}$ [M+H]$^+$ 530.4030, found 530.4006.
Boc-protected oligourepa U10 (87 mg, 0.16 mmol) was dissolved in TFA (870 μl) and stirred for 45 min. The reaction mixture was then concentrated under reduced pressure and a crude product was obtained. Triethylamine (36 μL, 0.26 mmol) and an azlactone (85 mg, 0.23 mmol) were added to the crude product in acetonitrile (0.58 mL). The reaction stirred at reflux for 3 d. The solvents were removed under reduced pressure and purification by column chromatography (Silica; CH₂Cl₂:MeOH; 99:1→90:10) gave the title compound as a white solid (34 mg, 36.8%).

\[ \text{H} \text{NMR (400 MHz, CD₃OH)} \delta = 7.73 (1H, s, NH), 7.27 (1H, d, J = 9.8, NH), 6.10 (1H, d, J = 9.3, NH), 5.97 (1H, d, J = 9.8, NH), 5.79-5.68 (1H, m, NH), 5.60 (1H, d, J = 10.0, NH), 4.28-4.10 (1H, m, NCH₂leu), 3.99-3.87 (1H, m, NCH₃abo), 3.86-3.77 (1H, m, NCH₃ipr), 3.74-3.48 (4H, m, NCH₃val, NCH₃hVal, NCH₃hVal, NCH₃hVal, NCH₃hVal and NCH₃hVal), 2.77-2.60 (1H, m, NCH₃hVal and NCH₃hVal), 2.46 (1H, dd, J = 13.8 and 11.8, NCH₂hVal), 1.73-1.58 (2H, m, CH₆leu and CH₃val), 1.48-1.37 (1H, m, CH₆hVal), 1.56 (3H, s, CH₃), 1.53 (9H, s, 3 x CH₃), 1.47 (3H, s, CH₃), 1.45 (3H, s, CH₃), 1.43 (3H, s, CH₃), 1.39 (3H, s, CH₃), 1.27-1.17 (1H, m, CH₆hVal), 1.14 (6H, d, J = 6.5, 2 x CH₃fH₁), 1.06 (3H, d, J = 6.7, CH₃abo), 0.99-0.83 (12H, m, 2 x CH₃fH₁ and 2 x CH₃fH₁).

\[ \text{C} \text{NMR (100 MHz, CD₃OH)} \delta = 178.2 (C=O), 176.7 (C=O), 175.0 (C=O), 161.7 (C=O), 161.3 (C=O), 160.7 (C=O), 160.7 (C=O), 164.8 (CN₃), 58.4 (C), 57.9 (C), 57.8 (C), 57.8 (C), 56.4 (NC₂H₁Val), 48.7 (NC₂H₁Leu), 48.7 (NC₂H₁Abu), 46.7 (NC₂H₂Ala), 58.2 (NC₂H₂leu), 44.4 (NC₂H₂leu), 42.8 (NC₂H₁ipr), 42.3 (C₂H₂leu), 32.2 (C₂H₁Val), 28.1 (CH₁), 27.4 (CH₃), 26.3 (CH₃), 26.3 (CH₃), 25.9 (CH₃), 24.6 (C₆H₁Leu), 24.5 (CH₃), 23.8 (CH₁ipr), 23.8 (CH₁ipr), 23.7 (CH₃leu), 23.6 (CH₃), 23.4 (CH₃), 23.1 (CH₃), 22.4 (CH₃leu), 20.1 (C₆H₁Val), 19.5 (C₂H₂ab), 18.5 (C₂H₂val).

\[ \text{GlyNH₂-Aib₂-(Val)ᵣ₋ᵣ}⁻₃⁻\text{NHBOc} \text{ 2a}

\[ \text C₂H₅N₃O₂ \text M = 642.78 \text{ g mol}^{-1}

\[ \text{2a} \text{ was prepared from GlyNH₂-Aib₂-NH₃ (547 mg, 1.32 mmol), Cc (453 mg, 1.32 mmol) and DIPEA (673 μL, 3.96 mmol) as described in the general procedure B. The pure oligomer 2a (500 mg, 58.9%) was isolated as a white solid.} \text{H} \text{NMR (500 MHz, CD₃OH)} \delta = 8.60 (1H, s, NH), 8.14 (1H, t, J = 6.3, NH₃ipr), 8.07 (1H, s, NH), 7.95 (1H, s, NH), 7.43 (1H, s, NH₃val), 7.22 (1H, s, NH), 6.38 (1H, s, NH), 6.32
(1H, d, J = 9.5, NH$_{val}$), 5.99 (1H, t, J = 7.0, NH$_{val}$), 3.94 (1H, dd, J = 17.5 and 7.0, NCH$_2$CH$_{Boc}$), 3.72 (1H, dd, J = 17.5 and 5.7, NCH$_2$CH$_{Boc}$), 1.69 (1H, oct, J = 6.9, CH$_{val}$), 1.50 (3H, s, CH$_3$), 1.50 (3H, s, CH$_3$), 1.47-1.40 (24H, m, C(CH$_3$)$_3$ and 5 x CH$_3$), 1.34 (3H, s, CH$_3$), 0.94 (3H, d, J = 6.9, CH$_3$)$_3$, 0.91 (3H, d, J = 6.9, CH$_3$)$_3$. $^{13}$C NMR (125 MHz, CD$_3$OD) δ = 178.3 (C=O), 178.1 (C=O), 178.0 (C=O), 175.4 (C=O), 160.2 (C=O), 158.5 (C=O), 79.7 (C=O), 58.1 (C), 58.0 (C), 57.8 (C), 57.6 (C), 57.0 (NC$_2$H$_{val}$), 43.7 (NCH$_2$Gly), 43.4 (NC H$_{2val}$), 31.5 (NC$_2$H$_{val}$), 28.8 (C(CH$_3$)$_3$), 26.7 (CH$_3$), 26.5 (CH$_3$), 24.8 (CH$_3$), 24.6 (CH$_3$), 24.3 (CH$_3$). IR (film, cm$^{-1}$): ν$_{max}$ = 3306, 2981, 2935, 1651, 1543; [α]$_D^2$ = +24.8 (c = 1.00; MeOH); Mp: 88-90 °C; HRMS (ESI$^+$): m/z calcd for C$_{29}$H$_{55}$N$_4$O$_8$ [M+H]$^+$ 643.4137, found 643.4118.

GlyNH$_2$-Aib$_4$-(Val$^a$)$_{15}$-(Ala$^a$)$_{15}$-NH$_{Boc}$ 2b

2b was prepared from 2a (400 mg, 0.62 mmol), Cb (196 mg, 0.62 mmol) and DIPEA (318 µL, 1.87 mmol) as described in the general procedure B. The pure oligomer 2b (100 mg, 21.6%) was isolated as a white solid. $^1$H NMR (500 MHz, CD$_3$OD) δ = 8.57 (1H, s, NH), 8.48 (1H, s, NH), 8.15 (1H, t, J = 6.2, NH$_{Gly}$), 7.96 (1H, s, NH), 6.60 (1H, s, NH$_{Ala}$), 6.59 (1H, s, NH), 6.04 (1H, t, J = 5.9, NH$_{Ala}$), 5.95 (1H, d, J = 5.9, NH$_{Val}$), 5.78 (1H, d, J = 9.1, NH$_{val}$), 3.97 (1H, dd, J = 17.6 and 7.1, NCH$_2$H$_{Boc}$), 3.94-3.83 (1H, m, NCH$_{val}$), 3.69 (2H, dd, J = 17.6 and 5.7, NCH$_2$CH$_{Boc}$), 3.66-3.53 (2H, m, NCH$_{Ala}$ and NCH$_2$H$_{Boc}$), 2.77-2.65 (1H, m, NCH$_2$H$_{val}$), 2.59-2.44 (1H, m, NCH$_{2 Ala}$), 2.65 (1H, oct, J = 6.7, CH$_{val}$), 1.51 (3H, s, CH$_3$), 1.50 (3H, s, CH$_3$), 1.47-1.40 (24H, m, C(CH$_3$)$_3$ and 5 x CH$_3$), 1.34 (3H, s, CH$_3$), 1.08 (3H, d, J = 6.9, CH$_{3 Ala}$), 0.94 (3H, d, J = 6.9, CH$_{3 val}$), 0.91 (3H, d, J = 6.9, CH$_{3 val}$). $^{13}$C NMR (125 MHz, CD$_3$OD) δ = 178.5 (C=O), 178.2 (C=O), 178.1 (C=O), 178.1 (C=O), 175.4 (C=O), 158.7 (C=O), 158.0 (C=O), 80.1 (C=O), 58.1 (C), 57.9 (C), 57.8 (C), 56.9 (C), 56.5 (NC$_2$H$_{val}$), 47.6 (NC H$_{2 Ala}$), 47.3 (NC$_2$H$_{Ala}$), 44.7 (NCH$_2$Gly), 43.8 (NC H$_{2val}$), 31.6 (NC$_2$H$_{val}$), 28.7 (C(CH$_3$)$_3$), 27.1 (CH$_3$), 27.0 (CH$_3$), 26.9 (CH$_3$), 26.7 (CH$_3$), 24.7 (CH$_3$), 24.3 (CH$_3$), 23.9 (CH$_3$), 23.8 (CH$_3$), 20.1 (C$_{H3 val}$), 18.8 (C$_{H3 val}$), 18.4 (C$_{H3 val}$). IR (film, cm$^{-1}$): ν$_{max}$ = 3282, 2981, 2935, 1649, 1544; [α]$_D^2$ = +8.0 (c = 1.00; MeOH); Mp: 100-105 °C; HRMS (ESI$^+$): m/z calcd for C$_{33}$H$_{62}$N$_{10}$O$_{8}$Na[M+H]$^+$ 765.4599, found 765.4586.
GlyNH₂-Aib₂-(Val⁺).<sub>rev</sub>-(Ala⁺).<sub>rev</sub>-(Leu⁺).<sub>rev</sub>–NHBOc 2c

2c was prepared from 2b (90 mg, 0.12 mmol), Ca (43 mg, 0.12 mmol) and DIPEA (21 μL, 0.36 mmol) as described in the general procedure B. The pure oligomer 2c (80 mg, 74.7%) was isolated as a white solid. <sup>1</sup>HNMR (500 MHz, CD₃OD) δ = 8.57 (1H, s, NH), 8.46 (1H, s, NH), 8.16 (1H, d, J = 6.7, NH₂), 7.94 (1H, s, NH), 7.42 (1H, s, NH), 7.22 (1H, s, NH), 6.88 (1H, d, J = 6.7, NH₂), 6.61 (1H, d, J = 10.0, NH₂), 6.44 (1H, brd, J = 9.5, NH₂), 6.08 (1H, t, J = 6.7, NH₂), 5.88 (1H, dd, J = 9.4 and 3.4, NH₂), 5.84 (1H, d, J = 9.9, NH₂), 5.76 (1H, d, J = 10.4, NH₂), 4.13-4.02 (1H, m, NCH₂), 3.98 (1H, dd, J = 17.5 and 7.2, NCH₂), 3.89-3.76 (1H, m, NCH₂), 3.68 (1H, d, J = 17.5 and 5.5, NCH₂), 3.74-3.54 (3H, m, NCH₂), 2.98 (3H, s, NCH₂), 2.46-2.13 (2H, m, NCH₂) and 1.51 (3H, s, CH₃), 1.50 (3H, s, CH₃), 1.48-1.42 (24H, m, 5 x CH₃ and C(CH₃)₃), 1.34 (3H, m, CH₃), 1.31-1.14 (2H, m, CH₂), 1.06 (3H, d, J = 7.0, CH₃), 0.94 (3H, d, J = 6.7, CH₃), 0.93 (3H, d, J = 6.9, CH₃), 0.90 (3H, d, J = 6.6, CH₃), 0.89 (3H, d, J = 6.8, CH₃). <sup>13</sup>C NMR (125 MHz, CD₃OD) δ = 178.6 (C=O), 178.3 (C=O), 178.2 (C=O), 178.1 (C=O), 175.4 (C=O), 161.4 (C=O), 160.9 (C=O), 160.7 (C=O), 159.2 (C=O), 80.1 (C=O), 58.1 (C), 57.9 (C), 57.9 (C), 56.9 (C), 55.8 (NC₃H₂), 50.0 (NC₃H₂), 48.5 (NC₃H₂), 46.8 (NC₃H₂), 46.6 (NC₃H₂), 44.5 (NC₃H₂), 43.8 (NC₃H₂), 42.3 (C₃H₂), 31.9 (C₃H₂), 28.8 (C₃H₂), 27.4 (CH₂), 27.2 (CH₃), 27.1 (CH₃), 26.8 (CH₂), 26.2 (CH₂), 24.5 (CH₂), 24.3 (CH₂), 23.8 (CH₂), 23.7 (CH₂), 23.5 (CH₂), 22.6 (CH₂), 21.4 (CH₂), 18.6 (C₃H₂), 18.4 (C₃H₂) IR (film, cm⁻¹): νmax = 3297, 2975, 1659, 1537; [α]₂⁰0 = + 30.0 (c = 1.00; MeOH); Mp: 138-140 °C; HRMS (ESI⁺): m/z calcd for C₄₉H₇₁O₁₅N₁₂[+M+H⁺]⁺ 885.5880, found 885.5880.

GlyNH₂-Aib₂-(Val⁺).<sub>rev</sub>-(Ala⁺).<sub>rev</sub>-(Leu⁺).<sub>rev</sub>–NH(CO)NH/Pr 2d

2d was prepared from 2c (60 mg, 0.07 mmol), isopropyl isocyanate (13.3 μL, 0.14 mmol) and DIPEA (28 μL, 0.20 mmol) as described in the general procedure C. The pure oligomer 2d (56 mg, 94.9%) was isolated as a white solid. <sup>1</sup>HNMR (500 MHz, CD₃OD) δ = 8.58 (1H, s, NH), 8.44 (1H, s, NH), 8.18
found 629.3974. 6.06 (1H, d, J = 6.7, NH$_{Val}$), 5.95 (1H, d, J = 5.73 (1H, d, J = 5.57 (1H, d, J = 4.09-3.90 (2H, m, NCH$_{Aib}$ and NCH$_{Val}$), 3.96 (1H, dd, J = and, NCH$_{Val}$), 3.80 (1H, oct, J = NH$_{Pr}$), 3.70 (1H, dd, J = and, NCH$_{Aib}$), 3.67-3.58 (2H, m, NCH$_{Val}$ and NCH$_{Val}$), 3.57-3.47 (1H, m, NCH$_{Aib}$), 3.44-3.35 (1H, m, NCH$_{Val}$), 2.64-2.48 (2H, m, NCH$_{Val}$ and NCH$_{Val}$), 2.47-2.38 (1H, m, NCH$_{Aib}$), 1.76-1.55 (2H, m, CH$_{Val}$ and CH$_{Val}$), 1.51 (3H, s, CH$_{3}$), 1.50 (3H, s, CH$_{3}$), 1.48-1.42 (24H, m, 5 x CH$_{3}$ and C(CH$_{3}$)$_{3}$), 1.34 (3H, s, CH$_{3}$), 1.26-1.18 (2H, m, CH$_{2Val}$), 1.13 (6H, d, J =, CH$_{3})$, 1.06 (3H, d, J =, CH$_{3Val}$), 0.93 (6H, d, J = 6.9, CH$_{3Val}$). $^{13}$C NMR (125 MHz, CD$_{3}$OH) $\delta$ = 178.6 (C=O), 178.4 (C=O), 178.2 (C=O), 175.5 (C=O), 163.1 (C=O), 162.8 (C=O), 161.8 (C=O), 161.0 (C=O), 160.5 (C=O), 58.1 (C), 57.9 (C), 57.8 (C), 56.9 (C), 56.0 (NC$_{Val}$), 48.7 (NC$_{Val}$), 48.2 (NC$_{H_{Val}}$), 47.2 (NC$_{H_{Val}}$), 46.8 (NC$_{H_{Aib}}$), 44.3 (NC$_{H_{Aib}}$), 43.7 (NCH$_{Val}$), 43.0 (NCH$_{Val}$), 43.0 (C$_{H_{Val}}$), 31.9 (C$_{Val}$), 27.2 (CH$_{3}$), 27.0 (CH$_{3}$), 26.9 (CH$_{3}$), 26.7 (CH$_{3}$), 26.2 (C$_{H_{Val}}$), 24.6 (CH$_{3}$), 24.4 (CH$_{3}$), 23.9 (CH$_{3}$), 23.8 (CH$_{3}$), 23.6 (CH$_{3Val}$), 23.5 (CH$_{3Val}$), 23.4 (CH$_{3Val}$), 22.5 (CH$_{3Val}$), 20.0 (C$_{H_{Val}}$), 18.8 (C$_{H_{Val}}$), 18.5 (C$_{H_{Aib}}$). IR (film, cm$^{-1}$): $\nu_{max}$ = 3325, 2965, 1648, 1555; $[\alpha]$$_D^{28}$ = +28 (c = 1.00; MeOH); M$: > 200 °C; HRMS (ESI$^-$): m/z calcd for C$_{25}$H$_{39}$O$_{5}$N$_{13}$ [M+H]$^+$ 870.5883, found 870.5873.

GlyNH$_2$-Aib$_{2}$-Aib$_{3}$-NHBOC 3

3 was prepared from GlyNH$_2$Aib$_{2}$NHBOC (650 mg, 1.57 mmol), M2 (517 mg, 1.57 mmol) and DIPEA (800 µL, 4.70 mmol) as described in the general procedure B. The pure oligomer 3 (200 mg, 20.3%) was isolated as a white solid. $^1$H NMR (500 MHz, CD$_{3}$OH) $\delta$ = 8.81 (1H, s, NH), 8.20 (1H, s, NH), 8.15 (1H, t, J = 5.8, NH$_{Gly}$), 7.98 (1H, s, NH), 7.44 (1H, s, NH), 7.27 (1H, s, NH), 6.65 (1H, t, J = 5.9, NH$_{Aib}$), 6.06 (1H, s, NH), 5.75 (1H, s, NH), 3.83 (2H, brd, J = 17.5 and 7.0, NCH$_{Gly}$), 3.25 (2H, brd, J = 4.5, NCH$_{2Aib}$), 1.50 (6H, s, CH$_{3}$), 1.45 (15H, m, C(CH$_{3}$)$_{2}$ and 2 x CH$_{3}$), 1.43 (6H, s, CH$_{3}$), 1.35 (6H, s, CH$_{3}$), 1.25 (6H, s, CH$_{3}$). $^{13}$C NMR (125 MHz, CD$_{3}$OH) $\delta$ = 178.4 (C=O), 178.2 (2 x C=O), 178.1 (C=O), 175.4 (C=O), 159.2 (C=O), 158.3 (C=O), 97.9 (C=O), 58.1 (C), 58.1 (C), 57.8 (C), 56.8 (C), 54.6 (C), 48.8 (NCH$_{2Aib}$), 43.7 (NCH$_{2Gly}$), 28.7 (C(CH$_{3}$)$_{2}$), 26.0 (2 x CH$_{3}$), 25.8 (2 x CH$_{3}$), 25.5 (6 x CH$_{3}$). IR (film, cm$^{-1}$): $\nu_{max}$ = 3343, 2982, 29341, 1650, 1542; M$: 103-105 °C; HRMS (ESI$^-$): m/z calcd for C$_{25}$H$_{35}$O$_{8}$N$_{13}$ [M+H]$^+$ 629.3981, found 629.3974.
GlyNH₂-Aib₂-Aib⁻{(Val)₃}_{rev}⁻NHBoc 3a

3a was prepared from 3 (200 mg, 0.32 mmol), Cc (109 mg, 0.32 mmol) and DIPEA (162 µL, 0.95 mmol) as described in the general procedure B. The pure oligomer 3a (150 mg, 62.3%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ = 8.74 (1H, s, NH), 8.46 (1H, s, NH), 8.15 (1H, t, J = 6.1, NH₂(C₆)), 7.91 (1H, s, NH), 7.45 (1H, s, NH), 7.23 (1H, s, NH), 6.45 (1H, d, J = 9.8, NH₂(C₆)), 6.38 (1H, s, NH), 6.13 (1H, t, J = 6.0, NH₂(C₆)), 6.00 (1H, t, J = 5.9, NH₂(C₆)), 5.58 (1H, s, NH), 3.91 (1H, dd, J = 17.4 and 6.6, NCH₂CH₃(CH₃)), 3.75 (1H, dd, J = 17.3 and 5.7, NCH₂CH₂(CH₃)), 3.71-3.59 (1H, m, NCH₂(CH₂(Boc))), 3.58-3.50 (1H, m, NCH₂(CH₃)), 3.49-3.39 (1H, m, NCH₂(CH₂(Boc))), 2.95-2.88 (1H, m, NCH₂(CH₂(Boc))), 2.79 (1H, ddd, J = 6.9, NCH₂(CH₂(Boc))), 1.68 (1H, oct, J = 6.8, CH₃), 1.50 (6H, s, 2 x CH₃), 1.46 (6H, s, 2 x CH₃), 1.45 (9H, s, C(CH₃)3), 1.42 (6H, s, 2 x CH₃), 1.40 (3H, s, CH₃), 1.35 (6H, s, 2 x CH₃), 1.15 (3H, s, CH₃), 0.97 (3H, d, J = 6.7, CH₃(CH₃)), 0.92 (3H, d, J = 6.8, CH₃(CH₃)). ¹³C NMR (125 MHz, CD₃OH) δ = 178.6 (C=O), 178.5 (C=O), 178.2 (C=O), 178.1 (C=O), 175.4 (C=O), 160.7 (C=O), 159.3 (C=O), 159.1 (C=O), 79.9 (C-O), 58.1 (C), 58.0 (C), 57.8 (C), 57.5 (NC₃(CH₃)), 56.8 (C), 55.0 (C), 48.5 (NCH₂(CH₂(Boc))), 43.8 (NCH₂(CH₂(Boc))), 43.4 (NC₃(CH₃)), 32.0 (NCH₂(CH₃)), 28.8 (C(CH₃)₃), 26.8 (CH₃), 26.3 (3 x CH₃), 26.2 (CH₃), 25.5 (CH₃), 25.0 (CH₃), 24.9 (CH₃), 24.6 (2 x CH₃), 19.9 (CH₃(CH₃)), 18.8 (CH₃(CH₃)). IR (film, cm⁻¹): vₘₐₓ = 3295, 2976, 2941, 1654, 1555; [α]₀²⁰ = +29.0 (c = 1.00; MeOH); Mp: 115-117 °C; HRMS (ESI⁺): m/z calcd for C₃₅H₅₆O₉N₁₀Na [M+Na]^⁺ 779.4755, found 779.4684.

GlyNH₂-Aib₂-Aib⁻{(Val)₃}_{rev}⁻{(Ala)₃}_{rev}⁻NHBoc 3b

3b was prepared from 3a (115 mg, 0.15 mmol), Cb (48 mg, 0.15 mmol) and DIPEA (78 µL, 0.46 mmol) as described in the general procedure B. The pure oligomer 3b (58 mg, 44.5%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ = 8.74 (1H, s, NH), 8.45 (1H, s, NH), 8.16 (1H, t, J = 6.3, NH₂(C₆)), 7.98 (1H, s, NH), 7.47 (1H, s, NH), 7.25 (1H, s, NH), 6.56 (1H, d, J = 8.8, NH₂(C₆)), 6.47 (1H, s, NH), 6.15-6.05 (2H, m, NH₃(CH₃) and NH₃(CH₃)), 6.04-5.97 (1H, m, NH₂(C₆)), 5.87 (1H, d, J = 9.4, NH₂(C₆)), 5.78 (1H, s, NH), 3.92 (1H, dd, J = 17.5 and 6.8, NCH₂CH₃(CH₃)), 3.75 (1H, dd, J = 17.2 and 5.7, NCH₂CH₂(CH₃)), 3.83-3.64 (3H, m, NCH₂(CH₂(Boc)), NCH₂(CH₂(Boc)), 3.61-3.48 (1H, m, NCH₂(CH₂(Boc)), 3.29-3.22 (1H, m, NCH₂(CH₂(Boc)), S14
2.95-2.78 (2H, m, NCH₃H₉BAiB and NCH₃H₉BAiB), 2.69-2.55 (1H, m, NCH₃H₉BAiB), 1.67 (1H, oct, J = 6.9, CH₂), 1.50 (6H, s, 2 x CH₃), 1.46 (6H, s, 2 x CH₃), 1.44 (9H, s, C(CH₃)₃), 1.43 (6H, s, 2 x CH₃), 1.40 (3H, s, CH₃), 1.35 (6H, s, 2 x CH₃), 1.17 (3H, s, CH₃), 1.07 (3H, d, J = 6.8, CH₃₈ₙ), 0.97 (3H, d, J = 6.9, CH₃₈ₙ), 0.93 (3H, d, J = 6.9, CH₃₈ₙ).

**¹³C NMR** (125 MHz, CD₃OH) δ = 178.6 (2 x C=O), 178.2 (C=O), 178.2 (C=O), 175.5 (C=O), 161.5 (C=O), 159.0 (C=O), 158.4 (C=O), 150.0 (C), 58.1 (C), 58.0 (C), 57.8 (C), 56.8 (NC₆H₅), 56.4 (C), 54.8 (C), 48.5 (NCH₂BAiB), 48.0 (NC₆H₂₈ₙ), 46.8 (NC₆H₂₈ₙ), 44.3 (NC₂H₂₈ₙ), 43.8 (NCH₂₂₈ₙ), 31.9 (NCH₂₈ₙ), 28.7 (C(CH₃)₃), 26.9 (CH₃), 26.4 (2 x CH₃), 26.3 (CH₃), 26.2 (CH₃), 25.6 (CH₃), 24.9 (2 x CH₃), 24.5 (2 x CH₃), 20.0 (CH₃₈ₙ), 18.7 (CH₃₈ₙ), 18.5 (CH₃₈ₙ), 178.6 (2 x C=O), 178.2 (C=O), 175.5 (C=O), 161.5 (C=O), 159.0 (C=O), 158.4 (C=O), 80.0 (C-O), 73.2 (2H, m, NCH₂), 3.75 (1H, s, NCH₂₂₈ₙ), 0.97 (1H, d, J = 6.4, NH₃₂₈ₙ), 3.75 (1H, d, dd, J = 6.7 and 3.6, NH₃₂₈ₙ), 2.89 (1H, dd, J = 14.4 and 3.3, NCH₃₈₉₈ₙ), 2.63-2.55 (1H, m, NCH₃₂₈ₙ), 2.53-2.44 (1H, m, NCH₃₂₈ₙ), 2.40-2.30 (1H, m, NCH₃₂₈ₙ), 1.75-1.59 (2H, m, CH₃CH₂ and CH₃CH₂), 1.52 (6H, s, 2 x CH₃), 1.48 (15H, s, 2 x CH₃ and C(CH₃)₃), 1.45 (6H, s, 2 x CH₃), 1.42 (3H, s, CH₃), 1.39 (3H, s, CH₃), 1.36 (3H, s, CH₃), 1.32-1.09 (2H, m, CH₂CH₂), 1.21 (3H, s, CH₃), 1.05 (3H, d, J = 6.9, CH₃₂₈ₙ), 0.97 (3H, d, J = 6.9, CH₃₂₈ₙ), 0.94 (3H, d, J = 7.1, CH₂₈ₙ), 0.93 (3H, d, J = 7.3, CH₃₂₈ₙ), 0.90 (3H, d, J = 6.7, CH₂₈ₙ).

S15
\((\text{C}_2\text{H}_3\text{Leu})\), 22.5 \((\text{C}_2\text{H}_3\text{Val})\), 19.8 \((\text{C}_2\text{H}_3\text{Val})\), 18.7 \((\text{C}_2\text{H}_3\text{Val})\), 18.5 \((\text{C}_2\text{H}_3\text{Ala})\) \text{IR} \text{ (film, cm}^{-1}\): \(\nu_{\text{max}} = 3287, 2970, 1636, 1549; \ [\alpha]^2_0 = +34.0 \text{ (c = 1.00; MeOH); MP: 154-156 °C; HRMS (ESI\(^+\)): m/z calcd for C\(_{45}\)H\(_{80}\)O\(_{11}\)N\(_{14}\) \([\text{M+H}]^+ = 999.6673, \text{found 999.6655.}\)

\text{GlyNH}_2\text{-Aib}_2\text{-Aib}^\text{\text{- (Val)\text{- (Ala)\text{- (Leu)\text{- (NHCO)NHPr}}}} 3d

\includegraphics{image}

\textbf{3d} was prepared from 3c (40 mg, 0.04 mmol), isopropyl isocyanate (7.9 \(\mu\text{L}, 0.08 \text{mmol}) and DIPEA (17 \(\mu\text{L}, 0.12 \text{mmol}) as described in the general procedure C. The pure oligomer \textbf{3d} (35 mg, 88.9%) was isolated as a white solid. \textbf{\textsuperscript{1}H NMR} \(500 \text{MHz, CD}_2\text{OD}\) \(\delta = 8.75 \text{ (1H, s, NH), 8.40 \text{ (1H, s, NH), 8.16 \text{ (1H, t, J = 6.3, NH}\_\text{Val})}, 7.99 \text{ (1H, s, NH), 7.45 \text{ (1H, s, NH), 7.23 \text{ (1H, s, NH), 6.52 \text{ (1H, s, NH), 6.45-6.34 \text{ (2H, m, NH}\_\text{Val and NH}\_\text{Ala}), 6.28 \text{ (1H, dd, J = 9.4 and 3.2, NH}\_\text{Ala}), 6.24 \text{ (1H, d, J = 10.3, NH}\_\text{Val}, 5.95 \text{ (1H, t, J = 7.1, NH}\_\text{Leu), 5.85 \text{ (1H, d, J = 9.7, NH}\_\text{Ala}), 5.75 \text{ (1H, s, NH), 5.68 \text{ (1H, d, J = 7.9, NH}\_\text{Ipr}, 5.50 \text{ (1H, d, J = 9.5, NH}\_\text{Leu), 4.08-3.96 \text{ (2H, m, NCH}\_\text{Leu and NCH}\_\text{Ala), 3.93 \text{ (1H, dd, J = 17.6 and 7.0, NCH}\_\text{CH}\_\text{BO}_{\text{2}}\text{H}, 3.80 \text{ (1H, oct, J = 6.7, NCH}\_\text{Ipr), 3.77-3.68 \text{ (2H, m, NCH}\_\text{H}_{\text{BAib}^\text{- (Val)\text{- (Ala)\text{- (Leu)\text{- (NHCO)NHPr}}}} \text{NMR} \(125 \text{MHz, CD}_2\text{OD}\) \(\delta = 178.6 \text{ (2x C=O), 178.2 \text{ (C=O), 178.1 \text{ (C=O), 175.4 \text{ (C=O), 162.1 \text{(C=O), 161.1 \text{(C=O), 160.8 \text{(C=O), 160.5 \text{(C=O), 159.4 \text{(C=O), 58.1 \text{(C), 58.0 \text{(C), 57.7 \text{(C), 56.8 \text{(C), 56.1 \text{(NC}\_\text{Ipr)\text{- (Val)\text{- (Ala)\text{- (Leu)\text{- (NHCO)NHPr}} \text{IR} \text{ (film, cm}^{-1}\): \(\nu_{\text{max}} = 3297, 2966, 2930, 2872, 1638, 1546; \ [\alpha]^2_0 = +64.8 \text{ (c = 1.00; MeOH); MP: 166-168°C; HRMS (ESI\(^+\)): m/z calcd for C\(_{44}\)H\(_{86}\)O\(_{11}\)N\(_{15}\) \([\text{M+H}]^+ = 984.6677, \text{found 984.6677.}}\)
GlyNH₂-Aib₂-{Aib²}₇-NHBoc 4

4 was prepared from GlyNH₂-Aib₂-NHBoc (518 mg, 1.25 mmol), M1 (4.12 mg, 1.25 mmol) and DIPEA (638 μL, 3.75 mmol) as described in the general procedure B. The pure oligomer 4 (521 mg, 82.9%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ = 8.56 (1H, s, NH), 8.15 (1H, t, J = 6.2, NH₂Gly), 8.03 (1H, s, NH), 8.01 (1H, s, NH), 7.44 (1H, s, NH), 7.27 (1H, s, NH), 6.48 (2H, s, NH), 6.26 (1H, t, J = 6.3, NH₂Aib), 3.83 (2H, brd, J = 6.2, NCH₂Gly), 3.28 (2H, brd, J = 6.2, NCH₂Aib), 1.49 (6H, s, 2 x CH₃), 1.46 (6H, s, 2 x CH₃), 1.40 (9H, s, C(CH₃)₃), 1.39 (6H, s, 2 x CH₃), 1.23 (6H, s, 2 x CH₃). ¹³C NMR (125 MHz, CD₃OH) δ = 178.2 (C=O), 178.1 (C=O), 178.1 (C=O), 177.9 (C=O), 175.4 (C=O), 160.5 (C=O), 156.8 (C=O), 79.8 (C=O), 58.1 (C), 58.0 (C), 57.5 (C), 57.1 (C), 54.8 (C), 49.5 (NCH₂Aib), 43.7 (NCH₂Gly), 28.7 (C(CH₃)₃), 25.6 (4 x CH₃), 25.2 (2 x CH₃), 25.2 (2 x CH₃). IR (film, cm⁻¹): νmax = 3304, 2982, 2934, 1642, 1539; HRMS (ESI⁺): m/z calcd for C₇₉H₁₂₃O₇N₈ [M+H]⁺ 629.3981, found 629.3971.

GlyNH₂-Aib₂-{Aib²}₇-{Val⁷}₇-NHBoc 4a

4a was prepared from 4 (474 mg, 0.75 mmol), Cc (259 mg, 0.75 mmol) and DIPEA (418 μL, 2.26 mmol) as described in the general procedure B. The pure oligomer 4a (281 mg, 49.2%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ = 8.50 (1H, s, NH), 8.14 (1H, t, J = 6.3, NH₂Gly), 7.97 (2H, s, NH), 7.46 (1H, s, NH), 7.24 (1H, s, NH), 6.41 (1H, s, NH), 6.36 (1H, d, J = 9.8, NH₂Val), 6.15 (1H, t, J = 6.4, NH₂Aib), 5.84 (1H, s, NH), 5.75 (1H, t, J = 5.7, NH₂Val), 3.85 (1H, dd, J = 17.5 and 6.4, NCH₆CH₂Gly), 3.80 (1H, dd, J = 17.4 and 6.2, NCH₆CH₂Gly), 3.49 (1H, dd, J = 13.5 and 5.8, NCH₆H₂BAIb), 3.45-3.39 (1H, m, NH₂Val), 3.39-3.33 (2H, m, NCH₆H₂BAIb and NCH₆H₂BAIb), 2.88 (1H, ddd, J = 14.8, 9.9 and 5.7, NCH₆H₂BAIb), 1.70 (1H, oct, J = 6.8, CH₂Val), 1.50 (6H, s, 2 x CH₃), 1.45 (15H, s, C(CH₃)₃ and 2 x CH₃), 1.39 (12H, s, 4 x CH₃), 1.25 (3H, s, CH₃), 1.19 (3H, s, CH₃), 0.94 (3H, d, J = 6.9, CH₃Val), 0.90 (3H, d, J = 6.9, CH₃Val). ¹³C NMR (125 MHz, CD₃OH) δ = 178.2 (C=O), 178.1 (C=O), 178.1 (C=O), 178.0 (C=O), 175.5 (C=O), 160.4 (C=O), 160.1 (C=O), 158.8 (C=O), 79.8 (C=O), 58.1 (C), 58.0 (C), 57.6 (C), 57.5 (NC₆H₂Val), 57.0 (C), 54.4 (C), 49.2 (NCH₂Aib), 43.7 (NCH₂Gly), 42.7 (NC₁H₂Val), 31.9 (NC₁H₂Val), 28.8 (C(CH₃)₃), 26.5
(CH₃), 25.9 (CH₃), 25.7 (CH₃), 25.5 (2 x CH₃), 25.4 (2 x CH₃), 25.1 (2 x CH₃), 25.0 (CH₃), 19.8 (C₆H₃Val), 18.4 (C₆H₃Val). IR (film, cm⁻¹): v_max = 3283, 2962, 2938, 1648, 1537; [α]D²⁰ = + 26.0 (c = 1.00; MeOH); Mp: 116-118 °C; HRMS (ESI⁺): m/z calcd for C₃₄H₄₅O₈N₁₀ [M+H]⁺ 757.4930, found 757.4928.

**GlyNH₂-Aib₂-(Aib⁴)rev-(Val⁴)rev-(Ala⁴)rev—NHBOc 4b**

4b was prepared from 4a (280 mg, 0.37 mmol), Cb (117 mg, 0.37 mmol) and DIPEA (205 μL, 1.11 mmol) as described in the general procedure B. The pure oligomer 4b (260 mg, 82.0%) was isolated as a white solid. **¹H NMR** (500 MHz, CD₃OH) δ = 8.43 (1H, s, NH), 8.14 (1H, t, J = 6.3, NH₃Val), 8.00 (1H, s, NH), 7.96 (1H, s, NH), 7.43 (1H, s, NH), 7.22 (1H, s, NH), 6.65 (1H, d, J = 9.3, NH₃Ala), 6.54 (1H, s, NH), 6.38-6.33 (1H, dd, J = 7.4 and 2.2, NH₃Aib), 6.13 (1H, t, J = 6.0, NH₃Ala), 6.00 (1H, s, NH), 5.83 (1H, d, J = 10.1, NH₃Val), 5.78 (1H, dd, J = 8.6 and 3.6, NH₃Val), 3.95-3.71 (1H, m, NCH₃Val), 3.88 (1H, dd, J = 17.4 and 6.7, NCH₃CH₂BGly), 3.77 (1H, dd, J = 17.4 and 6.0, NCH₃CH₂BGly), 3.71-3.50 (3H, m, NCH₃H₃Aib, NCH₃H₃Val and NCH₃Val), 3.42-3.33 (2H, m, NCH₃H₃Val and NCH₃H₃Aib), 2.78-2.68 (1H, m, NCH₃H₃Val), 2.54-2.43 (1H, m, NCH₃H₃Val), 1.76-1.59 (1H, m, CH₃Val), 1.50 (6H, s, 2 x CH₃), 1.46 (18H, s, 3 x CH₃ and C(CH₃)₃), 1.40 (3H, s, CH₃), 1.39 (3H, s, CH₃), 1.38 (3H, s, CH₃), 1.29 (3H, s, CH₃), 1.10 (3H, s, CH₃), 1.10 (3H, d, J = 7.0, CH₃Val), 0.96 (3H, d, J = 6.9, CH₃Val), 0.92 (3H, d, J = 6.9, CH₃Val). **¹³C NMR** (125 MHz, CD₃OH) δ = 178.1 (C=O), 178.1 (C=O), 178.1 (C=O), 178.0 (C=O), 175.4 (C=O), 161.6 (C=O), 160.3 (C=O), 160.2 (C=O), 158.6 (C=O), 80.2 (C=O), 58.1 (C), 58.0 (C), 57.5 (C), 57.0 (NCH₃Val), 56.2 (C), 54.7 (C), 48.0 (NCH₃Val), 47.7 (NC₃H₃Ala), 47.5 (NC₃H₃Ala), 44.2 (NC₃H₃Val), 43.7 (NCH₃Val), 31.8 (NCH₃Val), 28.7 (C(CH₃)₃), 26.9 (CH₃), 26.4 (2 x CH₃), 26.0 (CH₃), 25.9 (CH₃), 25.8 (CH₃), 25.5 (CH₃), 25.0 (CH₃), 24.6 (CH₃), 24.5 (CH₃), 19.9 (C₆H₃Val), 18.7 (C₆H₃Val), 18.5 (C₆H₃Val). IR (film, cm⁻¹): v_max = 3312, 2974, 2944, 1649, 1540; [α]D²⁰ = + 33.0 (c = 1.00; MeOH); Mp: 128-130 °C; HRMS (ESI⁺): m/z calcd for C₃₈H₄₇O₁₇N₁₂ [M+H]⁺ 857.5567, found 857.5559.
GlyNH₂-Aib₄-{Aib}₄-{Val}₄-{Ala}₄-{Leu}₄-NH-Boc 4c

4c was prepared from 4b (240 mg, 0.28 mmol), Ca (100 mg, 0.28 mmol) and DIPEA (109 µL, 0.84 mmol) as described in the general procedure B. The pure oligomer 4c (215 mg, 76.8%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ = 8.38 (1H, s, NH), 8.14 (1H, t, J = 5.2, NH₂), 8.04 (1H, s, NH), 7.96 (1H, s, NH), 7.46 (1H, s, NH), 7.24 (1H, s, NH), 6.65 (1H, s, NH), 6.62 (1H, d, J = 10.0, NH₂), 6.43-6.21 (3H, m, NH, NH₂ and NH), 6.11 (1H, brs, NH₂), 6.03 (1H, d, J = 8.5, NH₂), 5.89 (1H, s, NH), 5.87 (1H, s, NH₂), 4.03-3.94 (1H, m, NCH₂), 3.92-3.69 (2H, m, NCH₂ and NCH₂), 3.89 (1H, dd, J = 17.6 and 6.4, NCH₂CH₂), 3.75 (1H, dd, J = 16.6 and 4.5, NCH₂CH₂), 3.69-3.62 (1H, m, NCH₂H₂), 3.62-3.50 (2H, m, NCH₂H₂ and NCH₂H₂), 3.49-3.37 (1H, m, NCH₂H₂), 2.30-2.31 (1H, m, NCH₂H₂), 2.50-2.43 (2H, m, NCH₂H₂ and NCH₂H₂), 2.42-2.33 (1H, m, NCH₂H₂), 1.73-1.57 (2H, m, CH₂ and CH₂), 1.50 (6H, s, 2 x CH₃), 1.46 (12H, s, 1 x CH₃ and 2(CH₃)₂), 1.44 (6H, s, 2 x CH₃), 1.39 (3H, s, CH₃), 1.38 (3H, s, CH₃), 1.37 (3H, s, CH₃), 1.30 (3H, s, CH₃), 1.28-1.15 (2H, m, CH₂), 1.08 (3H, s, CH₃), 1.06 (3H, d, J = 7.0, CH₂), 0.94 (3H, d, J = 10.3, CH₂), 0.93 (3H, d, J = 6.8, CH₂), 0.89 (3H, d, J = 6.6, CH₂), 0.88 (3H, d, J = 7.0, CH₂). ¹³C NMR (125 MHz, CD₃OH) δ = 178.1 (3 x C=O), 178.0 (2 x C=O), 162.3 (C=O), 160.6 (C=O), 160.5 (C=O), 160.2 (C=O), 159.3 (C=O), 80.1 (C=O), 58.1 (C), 58.0 (C), 57.5 (C), 56.9 (C), 55.5 (NCH₂), 53.8 (C), 49.7 (NCH₂), 48.5 (NCH₂), 47.9 (NCH₂), 46.8 (NCH₂), 46.8 (NCH₂), 43.9 (NCH₂), 43.8 (NCH₂), 42.1 (NCH₂), 31.8 (NCH₂), 29.8 (C(CH₃)₂), 31.9 (C(CH₃)₂), 27.0 (CH₃), 26.6 (C₄H₉), 26.2 (3 x CH₃), 26.2 (CH₃), 26.2 (CH₃), 25.7 (CH₃), 25.7 (CH₃), 24.8 (CH₃), 24.4 (CH₃), 24.2 (CH₃), 23.5 (C₄H₉), 22.6 (C₄H₉), 19.9 (C₄H₉), 18.6 (C₄H₉), 18.2 (C₄H₉), 18.1 (C₄H₉). IR (film, cm⁻¹): vₕax = 3290, 2961, 2938, 1635, 1351; [α]₀ᵇ = + 8.0 (c = 1.00; MeOH); Mp: 144-146 °C; HRMS (ESI⁺): m/z calcd for C₄₅H₆₈O₁₁N₁₄ [M+H]⁺ 999.6673, found 999.6657.

GlyNH₂-Aib₄-{Aib}₄-{Val}₄-{Ala}₄-{Leu}₄-NH-(CO)NHPr 4d

4d was prepared from 4c (107 mg, 0.11 mmol), isopropyl isocyanate (21 µL, 0.21 mmol) and DIPEA (44.8 µL, 0.32 mmol) as described in the general procedure C. The pure oligomer 4d (71 mg, 67.4%)
was isolated as a white solid. $^1$H NMR (500 MHz, CD$_3$OD) $\delta$ = 8.38 (1H, s, NH), 8.14 (1H, t, J = 6.2, NH$_{ Gly}$), 8.05 (1H, s, NH), 7.96 (1H, s, NH), 7.43 (1H, s, NH), 7.23 (1H, brs, NH), 6.69 (1H, s, NH), 6.50-6.40 (2H, m, NH$_{Val}$ and NH$_{Abu}$), 6.35 (1H, dd, J = 9.2 and 2.0, NH$_{Ala}$), 6.32-6.22 (2H, m, NH$_{Val}$), 5.96 (1H, t, J = 6.7, NH$_{Ceu}$), 5.86 (1H, d, J = 9.9, NH$_{Ala}$), 5.69 (1H, d, J = 7.8, NH$_{Phe}$), 5.49 (1H, d, J = 9.5, NH$_{Ceu}$), 4.10-3.94 (2H, m, NCH$_{Ceu}$ and NCH$_{Ala}$), 3.91 (1H, dd, J = 17.5 and 6.7, NCH$_{3}$CH$_{2}$BN), 3.78 (1H, oct, J = 6.9, NCH$_{Phe}$), 3.77-3.72 (1H, m, NCH$_{Val}$), 3.74 (1H, dd, J = 17.2 and 5.5, NCH$_{3}$CH$_{2}$BN), 3.70-3.64 (1H, m, NCH$_{H_{Abu}}$), 3.63-3.52 (2H, m, NCH$_{3}$H$_{Val}$ and NCH$_{3}$H$_{Abu}$), 3.45 (1H, ddd, J = 13.6, 7.4 and 3.4, NCH$_{3}$H$_{Ala}$), 3.30-3.25 (1H, m, NCH$_{3}$H$_{Abu}$), 2.56-2.33 (3H, m, NCH$_{3}$H$_{Val}$, NCH$_{3}$H$_{leu}$ and NCH$_{3}$H$_{Ala}$), 1.68 (1H, non, J = 6.9, CH$_{Ceu}$), 1.61 (1H, oct, J = 6.7, CH$_{Val}$), 1.50 (6H, s, 2 x CH$_{3}$), 1.46 (3H, s, CH$_{3}$), 1.45 (6H, s, 2 x CH$_{3}$), 1.41 (3H, s, CH$_{3}$), 1.39 (3H, s, CH$_{3}$), 1.38 (3H, s, CH$_{3}$), 1.32 (3H, s, CH$_{3}$), 1.21 (2H, t, J = 7.4, CH$_{3leu}$), 1.13 (6H, d, J = 6.6, CH$_{3phe}$), 1.09 (3H, s, CH$_{3}$), 1.06 (3H, d, J = 6.9, CH$_{3ala}$), 0.95 (3H, d, J = 8.1, CH$_{3val}$), 0.93 (3H, d, J = 7.2, CH$_{3leu}$), 0.89 (6H, d, J = 6.8, CH$_{3val}$ and CH$_{3leu}$). $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta$ = 178.2 (C=O), 178.1 (C=O), 178.1 (C=O), 178.0 (C=O), 175.4 (C=O), 162.8 (C=O), 160.8 (C=O), 160.5 (C=O), 160.5 (C=O), 160.2 (C=O), 158.1 (C), 58.0 (C), 58.0 (C), 57.5 (C), 56.9 (C), 56.5 (NC$_{3}$H$_{Val}$), 53.8 (C), 48.5 (NC$_{3}$H$_{ala}$), 48.5 (NC H$_{ala}$), 47.8 (NCH$_{2}$Val), 47.4 (NC H$_{leu}$), 46.9 (NC$_{3}$H$_{ala}$), 43.8 (NC H$_{2val}$), 43.8 (NCH$_{2}$Val), 43.1 (NCH$_{Phe}$), 42.9 (C H$_{leu}$), 31.9 (NC$_{3}$H$_{Val}$), 27.0 (CH$_{3}$), 26.7 (2 x CH$_{3}$), 26.3 (CH$_{2}$Ceu), 26.2 (2 x CH$_{3}$), 25.7 (CH$_{3}$), 25.4 (CH$_{3}$), 24.8 (CH$_{3}$), 24.3 (CH$_{3}$), 24.1 (CH$_{3}$), 23.6 (C$_{3}$H$_{3leu}$), 23.5 (C$_{3}$H$_{leu}$), 23.5 (C$_{3}$H$_{ala}$), 22.5 (C$_{3}$H$_{ala}$), 19.9 (C$_{3}$H$_{Val}$), 18.9 (C$_{3}$H$_{ala}$), 18.4 (C$_{3}$H$_{ala}$). IR (film, cm$^{-1}$): $\nu_{max}$ = 3310, 2972, 1640, 1563; [a]$_D^{20}$ = + 28 (c = 1.00; MeOH); Mp: >200 °C; HRMS (ESI$^+$): m/z calcd for C$_{44}$H$_{60}$O$_{10}$N$_{15}$ [M+H]$^+$ 984.6677, found 984.6661.

Cbz-GlyAib$_3$ValOMe 6a

Cbz-GlyAib$_3$OH (71 mg, 0.13 mmol) and HOBT hydrate (27 mg, 0.16 mmol) were dissolved in CH$_2$Cl$_2$ (6 mL) and the solution cooled to 0 °C. EDC (22 µL, 0.13 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 2 h. L-Valine methyl ester hydrochloride (169 mg, 1.01 mmol) and NEt$_3$ (0.20 mL, 1.46 mmol) were added and the solution stirred for 48 h. The solution was then diluted with CH$_2$Cl$_2$ (15 mL) and the organic phase washed with HCl (1 M, 2 x 10 mL), NaHCO$_3$ (sat., 2 x 10 mL) and brine (1 x 10 mL). The organic phase was then dried (MgSO$_4$), filtered and concentrated to give a white solid, which was purified by column chromatography (1-5% MeOH in CH$_2$Cl$_2$) to give the pure peptide (56 mg, 73%) as a white solid. $^1$H-NMR (500 MHz, CD$_3$OD) $\delta$H: 7.83 (1H, br s, NH), 7.75 (1H, br s, NH), 7.74 (1H, br s, NH), 7.73 (1H, br s, NH), 7.72 (1H, br s, NH), 7.36 (5H, m, ArCH x5), 5.13 (1H, d, J=12.5, CH$_2$O, H$^\alpha$ of AB system).
5.10 (1H, d, J=12.5, CH₂O, H² of AB system), 4.22 (1H, m, CH), 3.77 (1H, d, J=17.0 Hz, CH₂-NH, H⁴ of AB system), 3.70 (1H, d, J=18.0, CH₂-NH, H⁵ of AB system), 3.68 (3H, s, OCH₃), 2.26 (1H, dqq, J=7.0, 7.0, 7.0 Hz, CH-(CH₃)₂), 1.50 (3H, s, CH₃), 1.48 (3H, s, CH₃), 1.43 (3H, s, CH₃), 1.42 (3H, s, CH₃), 1.42 (3H, s, CH₃), 1.40 (3H, s, CH₃), 1.40 (3H, s, CH₃), 1.39 (3H, s, CH₃), 1.02 (3H, d, J=7.0, CH₃-CH), 0.97 (3H, d, J=7.0, CH₃-CH). ¹³C-NMR (126 MHz, CD₂OD) δC 178.0 (CO), 177.1 (CO), 176.8 (CO), 176.6 (CO), 172.3 (CO), 159.5 (CO (Cbz)), 138.2 (ArC) 129.7 (ArCH), 128.9 (ArCH), 67.9 (CH₂O), 60.3 (CH-NH), 58.2 (C), 57.97 (C), 58.02 (C), 57.7 (C), 52.4 (OCH₃), 45.4 (CH₂-NH), 31.6 (CH), 27.0 (CH₃), 26.1 (CH₃), 25.8 (CH₃), 25.1 (CH₃), 24.9 (CH₃), 24.8 (CH₃), 19.8 (CH₃-CH), 19.4 (CH₃-CH). IR (neat) νmax/cm⁻¹ = 3324, 2985, 2476, 1658. [α]⁺²⁰ = -23.6 (c 1.0, MeOH). Mp 209-210 °C. HRMS (ES⁺, MeOH) Calc. for C₃₂H₃₆N₃O₈ ([M+H]+) = 663.3718, found 663.3701.

Cbz-GlyAib₄ValNH'Bu 6b

Cbz-Gly-Aib₄-OH (43 mg, 0.078 mmol) and HOBt hydrate (18 mg, 0.104 mmol) were dissolved in CH₂Cl₂ (4 mL) and the solution cooled to 0 °C. EDC (14 µL, 0.08 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. L-ValNH’Bu (35 mg, 0.2 mmol) in CH₂Cl₂ (1 mL) and NEt₃ (42 µL, 0.3 mmol) were added and the solution stirred for 48 h. The solution was then diluted with CH₂Cl₂ (15 mL) and the organic phase washed with KHSO₄ (5%, 2 x 10 mL), NaHCO₃ (sat., 2 x 10 mL) and brine (1 x 10 mL). The organic phase was then dried (MgSO₄), filtered and concentrated and the crude residue was purified by column chromatography (5% MeOH in CH₂Cl₂) to give the pure peptide (18 mg, 33%) as a white solid. ¹H-NMR (500 MHz, CD₂OD) δH 7.29-7.37 (5H, m, ArCH x5), 7.08 (1H, br s, NH), 5.14 (1H, d, J=12.5, CH₂O, H⁴ of AB system), 5.09 (1H, d, J=12.5, CH₂O, H⁵ of AB system), 3.99 (1H, d, J=6.0, CH), 3.80 (1H, d, J=18.0, CH₂-NH, H⁶ of AB system), 3.68 (1H, d, J=17.0, CH₂-NH, H⁷ of AB system), 2.33 (1H, dqq, J=7.0, 7.0, 6.5, CH-(CH₃)₂), 1.49 (6H, s, AibCH x3), 1.44 (3H, s, CH₃), 1.41 (9H, m, CH₃ x3), 1.39 (6H, s, AibCH x2), 1.37 (9H, s, C(CH₃)₃). ¹³C-NMR (126 MHz, CD₂OD) δC 178.1 (CO), 177.2 (CO), 177.1 (CO), 176.7 (CO), 173.5 (CO), 172.3 (CO), 159.6 (CO (Cbz)), 138.3 (Arc), 129.7 (ArCH), 129.3 (ArCH), 128.9 (ArCH), 68.0 (CH₂O), 62.0 (CH-NH), 58.1 (-C), 57.92 (-C), 57.88 (-C) 57.7 (C), 52.6 (CMe₃), 45.5 (CH₂-NH), 31.0 (CH-(CH₃)₂), 29.2 (C(CH₃)₃), 28.0 (CH₃), 27.2 (CH₃), 26.9 (CH₃), 26.4 (CH₃), 24.3 (CH₃), 24.2 (CH₃), 24.1 (CH₃), 19.9 (CH₃-CH), 18.5 (CH₃-CH). IR (neat) νmax/cm⁻¹ = 3305, 2976, 2474, 1644. [α]⁺²⁰ = +14.1 (c 0.5, MeOH). Mp 124-126 °C. HRMS (ES⁺, MeOH) Calc. for C₃₅H₄₁N₅O₈ ([M+Na]+) = 726.4166, found 726.4164.
Cbz-GlyAib₄PheO'Bu 6c

Cbz-Gly-Aib₄-OH (62 mg, 0.113 mmol) and HOBt hydrate (26 mg, 0.147 mmol) were dissolved in CH₂Cl₂ (5 mL) and the solution cooled to 0 °C. EDC (20 µL, 0.113 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. L-PheO'Bu.HCl (117 mg, 0.45 mmol) and NEt₃ (95 µL, 0.88 mmol) were added and the solution stirred for 48 h. The solution was diluted with CH₂Cl₂ (15 mL) and the organic phase washed with KHSO₄ (5%, 2 x 10 mL), NaHCO₃ (sat., 2 x 10 mL), brine (1 x 10 mL). The organic phase was then dried (MgSO₄), filtered and concentrated and the crude residue purified by column chromatography (5% MeOH in CH₂Cl₂) to give the pure peptide (58 mg, 68%) as a white solid.

¹H-NMR (500 MHz, CD₃OD) δ H 7.29 (10H, m, ArCHₓ₁₀), 5.13 (1H, d, J=12.5, CH₂O, Hᵣ of AB system), 5.10 (1H, d, J=12.5, CH₂O, Hᵣ of AB system), 4.44 (1H, dd, J=7.5, 7.5 Hz, CH), 3.77 (1H, d, J=16.5, C(CH₃)₂-NH, Hᵣ of AB system), 3.70 (1H, d, J=16.5, CH₂-NH, Hᵣ of AB system), 3.15 (1H, dd, J=14.0, 7.5, CH₂-Ph), 3.09 (1H, dd, J=14.0, 7.0, CH₂-Ph) 1.50 (3H, s, CH₃), 1.46 (3H, s, CH₃), 1.44 (3H, s, CH₃), 1.43 (3H, s, CH₃), 1.42 (3H, s, CH₃), 1.41 (3H, s, CH₃), 1.41 (3H, s, CH₃), 1.40 (3H, s, CH₃), 1.35 (9H, s, C(CH₃)₃). ¹³C-NMR (126 MHz, CD₃OD) δ C 177.6 (CO), 177.2 (CO), 176.9 (CO), 176.5 (CO), 172.4 (CO), 172.3 (CO), 159.5 (CO (Cbz)), 139.0 (ArC), 138.3 (ArC), 130.7 (ArCH), 129.7 (ArCH), 129.4 (ArCH), 129.3 (ArCH), 128.9 (ArCH), 127.7 (ArCH), 82.5 (CMe₃), 67.9 (CH₂O), 58.14 (C), 58.10 (C), 57.9 (C), 57.7 (C), 56.9 (C), 45.4 (CH₂-NH), 38.6 (CH₂-Ph), 28.3 (C(CH₃)₃), 27.0 (CH₃), 26.6 (CH₃), 26.1 (CH₃), 25.8 (CH₃), 25.0 (CH₃), 24.9 (CH₃), 24.8 (CH₃). IR (neat) ν_max/cm⁻¹ = 3306, 2982, 2934, 1709, 1651. [α]D²⁰ −12.0 (c 1.0, MeOH). Mp 200-202 °C. HRMS (ES⁺, MeOH) Calc. for C₃₉H₅₇N₆O₉Na ([M+Na⁺]⁺) = 753.4182, found 753.4178.

Cbz-GlyAib₄PheNH'Bu 6d

Cbz-Gly-Aib₄-OH (75 mg, 0.136 mmol) and HOBt hydrate (31 mg, 0.177 mmol) were dissolved in CH₂Cl₂ (5 mL) and the solution cooled to 0 °C. EDC (24 µL, 0.136 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. H-PheNH'Bu (75 mg, 0.34 mmol) and NEt₃ (71 µL, 0.51 mmol) were added and the solution stirred for 48 h. The solution was diluted with CH₂Cl₂ (15 mL) and the organic phase washed with KHSO₄ (5%, 2 x 10 mL), NaHCO₃ (sat., 2 x 10 mL), brine (1 x 10 mL). The organic phase was then dried (MgSO₄), filtered and concentrated.
The crude residue was purified by column chromatography (2-5% MeOH in CH₂Cl₂) to give the pure peptide (89 mg, 87%) as a white solid. ¹H-NMR (500 MHz, CD₃OD) δ H: 7.13-7.38 (10H, m, ArCH x10), 5.14 (1H, d, J=12.5, CH₂O, H² of AB system), 5.09 (1H, d, J=12.5, CH₂O, H⁸ of AB system), 4.37 (1H, dd, J=11.5, 3.0, CH-NH), 3.80 (1H, d, J=16.5, CH₂-NH, H² of AB system), 3.69 (1H, d, J=16.5, CH₂-NH, H⁸ of AB system), 3.41 (1H, m, CH₂-Ph), 2.92 (1H, m, CH₂-Ph), 1.37-1.46 (30H, m, CH₃ x7 and C(CH₃)₃), 1.18 (3H, s, CH₃). ¹³C-NMR (126 MHz, CD₃OD) δ C: 177.8 (CO), 177.6 (CO), 177.4 (CO), 176.6 (CO), 173.4 (CO), 172.3 (CO), 159.6 (CO (Cbz)), 140.0 (ArC), 138.8 (ArC), 130.3 (ArCH), 129.7 (ArCH), 129.4 (ArCH), 129.3 (ArCH), 128.9 (ArCH), 127.6 (ArCH), 68.0 (CH₂O), 58.1 (C), 57.9 (C), 57.6 (C), 57.5 (CH-NH), 52.8 (CMe₃), 45.4 (CH₂-NH), 38.2 (CH₂-Ph), 29.2 (C(CH₃)₃), 27.4 (CH₃), 27.2 (CH₃), 26.9 (CH₃), 26.4 (CH₃), 24.3 (CH₃), 23.9 (CH₃). IR (neat) ν max/cm⁻¹ = 3303, 2983, 2936, 1729, 1651, 1530, 1455. [α]D²⁰ +12.0 (c 1.0, MeOH). Mp 122-124 °C. HRMS (ES⁺, MeOH) Calc. for C₃₅H₅₇N₂O₉Na [(M+Na)⁺] = 751.4269, found 751.4277.

*CbZGly-Aib₂-{Val⁹}rev-NHBoc 7a*

7a was prepared from CbzGly-Aib-OH (480 mg, 0.87 mmol), HOBT (173 mg, 1.13 mmol), EDC (169 µL, 0.96 mmol), DIPEA (223 µL, 1.31 mmol) and an amine (265 mg, 1.31 mmol) as described in the general procedure A. The pure oligomer 7a (422 mg, 70%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ H: 7.86 (1H, m, NH), 7.76 (1H, d, CH₃), 7.70 (1H, s, NH), 7.61 (1H, s, NH), 7.50 (1H, s, NH), 7.38-7.24 (5H, m, 5 x =CH₂), 6.62 (1H, d, J = 10.1, NH), 6.05 (1H, d, J = 8.2, NH), 5.11 (2H, s, OCH₂), 3.75 (1H, d, J = 17.8, A part of AB pattern, NH₂H₂O₅), 3.72 (1H, d, J = 17.1, B part of AB pattern, NH₂H₂O₅), 3.63-3.52 (1H, m, NCH₂H₂O₅), 3.48-3.39 (1H, m, NCH₂H₂O₅), 3.17-3.06 (1H, m, NCH₂H₂O₅), 1.85 (1H, oct, J = 7.5, CH₂), 1.51-1.31 (33H, m, 8 x CH₃ and C(CH₃)₃), 0.90 (3H, d, J = 7.0, CH₃), 0.89 (3H, d, J = 7.1, CH₃). ¹³C NMR (125 MHz, CD₃OH) δ C: 177.8 (C=O), 177.6 (C=O), 176.6 (C=O), 176.4 (C=O), 172.1 (C=O), 159.3 (C=O), 158.1 (C=O), 138.1 (C₉H), 129.4 (2 x =CH₂), 129.0 (2 x =CH₂), 128.6 (2 x =CH₂), 79.7 (C=O), 67.7 (OCH₃), 58.3 (C), 58.0 (C), 57.8 (C), 57.5 (C), 57.1 (NCH₂O₅), 45.2 (NCH₂O₅), 42.5 (NC-CH₂), 30.4 (NC-CH₂), 28.7 (C(CH₃)₃), 26.2 (CH₃), 25.6 (CH₃), 25.5 (CH₃), 25.2 (2 x CH₃), 24.9 (CH₃), 19.9 (C₉H₂O₅), 19.2 (C₉H₂O₅). IR (film, cm⁻¹): ν max = 3344, 2965, 2930, 2907, 1632, 1571; [α]D²⁰ = -76 (c = 1.00, MeOH); Mp: 89-91 °C; HRMS (ES⁺): m/z calcd for C₃₆H₅₈N₂O₉ [M+H]⁺ 734.4447, found 734.4446.
CbzGly-Aib₄-(Val)₃rev-(Ala)₃rev-NHBoc 7b

7b was prepared from 7a (385 mg, 0.52 mmol), Cb (164 mg, 0.52 mmol) and DIPEA (172 µL, 1.57 mmol) as described in the general procedure B. The pure oligomer 7b (300 mg, 69.2%) was isolated as a white solid. ¹H NMR (500 MHz, CD₂OH) δ = 7.79 (1H, s, NH), 7.74 (1H, s, NH), 7.72 (1H, s, NH), 7.47 (1H, t, J = 5.4, NH₃val), 7.38-7.26 (5H, m, 5 × CH₃), 6.46 (1H, d, J = 7.0, NH₃Ala), 5.94-5.87 (2H, m, NH₃val and NH₃Ala), 5.10 (2H, s, OCH₃), 3.75 (1H, d, J = 17.0, A part of AB pattern, NCH₃H₃BO₂), 3.72 (1H, d, J = 17.3, B part of AB pattern, NCH₃H₃BO₂), 3.67-3.52 (2H, m, NCH₃Val and NCH₃Ala), 3.41-3.33 (1H, m, NCH₃H₃BO₂, 3.32-3.23 (1H, m, NCH₃H₃BO₂), 3.17-3.05 (2H, m, NCH₃2Ala), 1.88 (1H, oct, J = 6.7, CH₂Val), 1.50-1.35 (33H, m, 8 × CH₃ and C(CH₃)₃), 1.07 (3H, d, J = 6.7, CH₃Ala), 0.93 (3H, d, J = 6.8, CH₃Val), 0.90 (3H, d, J = 6.9, CH₃Val). ¹³C NMR (125 MHz, CD₂OH) δ = 177.8 (C=O), 177.4 (C=O), 176.8 (C=O), 176.5 (C=O), 172.1 (C=O), 161.0 (C=O), 159.3 (C=O), 157.9 (C=O), 138.0 (C=Ala), 129.4 (2 × CH₂Val), 129.0 (CH₃Val), 128.6 (2 × CH₃Val), 79.8 (C=O), 67.7 (OCH₃), 58.2 (C), 57.3 (C), 57.8 (C), 57.6 (C), 56.2 (NCH₃Val), 48.5 (NCH₃Ala), 46.0 (NC H₂Ala), 45.2 (NCH₃Val), 42.4 (NC H₂Val), 30.4 (NCH₃Val), 28.7 (C(CH₃)₂), 26.2 (CH₃Val), 25.6 (CH₃Val), 25.4 (CH₃Val), 25.2 (2 × CH₃), 25.0 (CH₃Val), 20.1 (CH₃Val), 18.6 (CH₃Val), 18.5 (C₂H₃Ala). IR (film, cm⁻¹): νₚₓₓ = 3309, 2977, 2938, 1656, 1537; [α]₀° = -124 (c = 1.00; MeOH); Mp: 129-131 °C; HRMS (ESI⁺): m/z calc for C₄₀H₆₈N₉O₁₀ [M+H]⁺ 834.5084, found 834.5083.

CbzGly-Aib₄-(Val)₃rev-(Ala)₃rev-(Leu)₃rev-NHBoc 7c

7c was prepared from 7b (250 mg, 0.30 mmol), Ca (107 mg, 0.30 mmol) and DIPEA (153 µL, 0.90 mmol) as described in the general procedure B. The pure oligomer 7c (249 mg, 85.1%) was isolated as a white solid. ¹H NMR (500 MHz, CD₂OH) δ = 8.34 (1H, s, NH), 7.77 (1H, s, NH), 7.74 (1H, s, NH), 7.52 (1H, t, J = 5.4, NH₃Val), 7.42 (1H, s, NH), 7.37-7.26 (5H, m, 5 × CH₃), 6.36 (1H, d, J = 6.8, NH₃Leu), 5.98-5.87 (3H, m, NH₃Leu, NH₃Ala and NH₃Ala), 5.81 (1H, d, J = 6.8, NH₃Val), 5.10 (2H, s, OCH₃), 3.76 (1H, d, J = 15.4, A part of AB pattern, NCH₃H₃BO₂), 3.71 (1H, d, J = 16.9, B part of AB pattern, NCH₃H₃BO₂), 3.77-3.68 (1H, m, NCH₃Ala), 3.66-3.52 (2H, m, NCH₃Val and NCH₃Leu), 3.51-3.39 (1H, m, NCH₃H₃BO₂), 3.32-3.22 (2H, m, NCH₃H₃BO₂ and NCH₃H₃BO₂), 3.20-3.16 (1H, m, NCH₃H₃BO₂), 3.07-2.97 (2H, m, NCH₃H₃BO₂ and
NCH$_3$H$_{3}$Boc, 1.90 (1H, oct, $J = 7.0$, CH$_{3}$ole), 1.65 (1H, non, $J = 7.1$, CH$_{2}$Leu), 1.50-1.35 (33H, m, 8 x CH$_3$ and C(CH$_3$)$_3$), 1.34-1.28 (1H, m, CH$_3$Boc), 1.24-1.19 (1H, m, CH$_3$Boc), 1.08 (3H, d, $J = 6.8$, CH$_{3}$ole), 0.93 (3H, d, $J = 6.8$, CH$_{3}$ole); 0.92 (3H, d, $J = 7.2$, CH$_{3}$Leu), 0.90 (3H, d, $J = 7.6$, CH$_{3}$Leu), 0.89 (3H, d, $J = 6.8$, CH$_{3}$ole). $^1$C NMR (125 MHz, CD$_3$OD) δ = 177.9 (C=O), 177.3 (C=O), 176.9 (C=O), 176.5 (C=O), 172.2 (C=O), 161.0 (C=O), 160.8 (C=O), 159.3 (C=O), 158.2 (C=O), 138.0 (C=O), 129.4 (2 x CH$_3$), 129.0 (2 x CH$_3$), 128.6 (2 x CH$_3$), 79.7 (C=O), 67.7 (OCH$_2$), 58.2 (C), 57.9 (C), 57.8 (C), 57.6 (C), 56.3 (NC$_3$H$_{3}$Val), 50.5 (NC$_3$H$_{3}$Leu), 47.5 (NC$_3$H$_{3}$Ala), 46.3 (NC$_3$H$_{3}$Ala), 45.5 (NC$_3$H$_{2}$Val), 45.9 (NC$_3$H$_{2}$Val), 42.6 (HC$_{2}$Leu), 41.9 (HC$_{2}$Val), 40.0 (HC$_{2}$Val), 28.7 (C(CH$_3$)$_3$), 26.5 (CH$_3$), 25.9 (CH$_3$), 26.5 (CH$_3$), 25.4 (CH$_3$), 25.0 (CH$_3$), 24.9 (2 x CH$_3$), 23.5 (CH$_3$Leu), 22.4 (CH$_3$Leu), 20.2 (CH$_3$), 19.0 (CH$_3$), 18.6 (CH$_3$). IR (film, cm$^{-1}$): $\nu_{max} = 3304, 2932, 2873, 1655, 1536; [\alpha]^{20}_D = -14$ (c = 1.00; MeOH); Mp: 135-136 °C; HRMS (ESI$^+$): m/z calcd for C$_{47}$H$_{82}$N$_{11}$O$_{11}$ [M+H]$^+$ 976.6190, found 976.6189.

7d was prepared from 7c (150 mg, 0.15 mmol), Cc (53 mg, 0.15 mmol) and DIPEA (79 µL, 0.46 mmol) as described in the general procedure B. The pure oligomer 7d (40 mg, 21.6%) was isolated as a white solid. $^1$H NMR (500 MHz, CD$_3$OD) δ = 8.35 (1H, s, NH), 7.80-7.70 (3H, m, NH), 7.62 (1H, t, $J = 5.4$, NH$_{3}$Val), 7.52 (1H, s, NH), 7.43 (1H, t, $J = 5.4$, NH$_{3}$Val), 7.42 (1H, s, NH), 7.39-7.28 (5H, m, 5 x CH$_3$), 6.44 (1H, d, $J = 6.8$, NH$_{3}$Leu), 6.27 (1H, s, NH$_{3}$Lys), 6.10-5.75 (4H, m, NH$_{3}$Val, NH$_{3}$Leu, NH$_{3}$Val and NH$_{3}$Lys), 5.12 (2H, s, OCH$_2$), 3.96-3.37 (8H, m, NCH$_{3}$Val, NCH$_{3}$Leu, NCH$_{3}$Ala, NCH$_{3}$Boc, NCH$_{3}$Val, NCH$_{3}$Leu, NCH$_{3}$Boc, and NCH$_{3}$Boc) 3.78 (1H, d, $J = 19.4$, A part of AB pattern, NCH$_{3}$Boc), 3.78 (1H, d, $J = 19.8$, B part of AB pattern, NCH$_{3}$Boc), 3.28-3.11 (1H, m, NCH$_{3}$Boc), 2.99-2.47 (3H, m, NCH$_{3}$Boc, NCH$_{3}$Boc and NCH$_{3}$Boc), 1.95 (1H, oct, $J = 7.0$, CH$_{3}$ole), 1.75-1.62 (2H, m, CH$_{3}$ole and CH$_{3}$ole), 1.52-1.35 (35H, m, 8 x CH$_3$ and C(CH$_3$)$_3$ and CH$_{3}$Leu), 1.09 (3H, d, $J = 6.8$, CH$_{3}$ole), 0.98-0.86 (18H, m, 4 x CH$_{3}$ole and 2 x CH$_{3}$ole). $^{13}$C NMR (125 MHz, CD$_3$OD) δ = 178.0 (C=O), 177.3 (C=O), 177.0 (C=O), 176.6 (C=O), 175.0 (C=O), 172.3 (C=O), 161.1 (C=O), 161.0 (C=O), 159.4 (C=O), 159.1 (C=O), 138.2 (C=O), 129.6 (2 x CH$_3$), 129.1 (2 x CH$_3$), 128.8 (2 x CH$_3$), 80.0 (C=O), 67.8 (OCH$_2$), 58.3 (C), 58.0 (C), 57.9 (C), 57.7 (C and NC$_3$H$_{3}$Val), 56.1 (NC$_3$H$_{3}$Val), 49.5 (NC$_3$H$_{3}$Leu), 47.4 (NC$_3$H$_{3}$Ala), 46.6 (NC$_3$H$_{3}$Val), 46.5 (NC$_3$H$_{3}$Val), 45.4 (NC$_3$H$_{3}$Val), 43.4 (NC$_3$H$_{3}$Val), 43.0 (C$_{2}$), 42.3 (NC$_3$H$_{3}$Val), 31.9 (C$_3$H$_{3}$), 29.7 (C$_3$H$_{3}$), 28.9 (C(CH$_3$)$_3$), 26.6 (CH$_3$), 26.1 (CH$_3$), 26.0 (CH$_3$), 25.6 (CH$_3$), 25.5 (CH$_3$), 25.1 (2 x CH$_3$), 23.8 (CH$_{3}$ole), 22.6 (CH$_{3}$ole), 20.6 (CH$_{3}$ole), 20.1 (CH$_{3}$ole).
19.2 (C₆H₃Al), 18.8 (C₆H₃Val), 18.1 (C₆H₃Val). IR (film, cm⁻¹): νmax = 3312, 2945, 1649, 1528; [α]D²⁰ = -16 (c = 1.00; MeOH); Mp: 159-161 °C; HRMS (ES⁺): m/z calcld for C₅₅H₄₉N₃9O₁₂Na [M+Na]⁺ 1126.99.

CbzGly-Aib₄-{Val"}₆rev-{Ala"}₆rev-{Leu"}₆rev-{Val"}₆rev-NH(CO)NH₂Pr 7e

7e was prepared from 7d (36 mg, 0.03 mmol), isopropyl isocyanate (6.4 µL, 0.07 mmol) and DIPEA (13.6 µL, 0.10 mmol) as described in the general procedure C. The pure oligomer 7e (32 mg, 89.8%) was isolated as a white solid. 

¹H NMR (500 MHz, CDCl₃) δ = 8.34 (1H, s, NH), 7.80-7.70 (3H, m, NH), 7.57 (1H, t, J = 6.5, NHVal), 7.40-7.24 (5H, m, 5 x =C₆H₃), 6.16 (1H, s, NHLeu), 6.07 (1H, d, J = 8.8, NHLeu), 6.03-5.96 (1H, d, J = 3.9, NHα), 5.96-5.78 (4H, m, NHVal, NHα, NHVal and NHAla), 5.69 (1H, d, J = 9.7, NHVal), 5.11 (2H, s, OCH₂), 3.90-3.66 (3H, m, NCH₃Val, NCH₃Leu, NCH₃Val) 3.76 (1H, d, J = 16.6, A part of AB pattern, NCH₃Val), 3.71 (1H, d, J = 16.6, B part of AB pattern, NCH₃Val), 3.64-3.38 (6H, m, NCH₃Val, NCH₃Val, NCH₃Val, NCH₃Val, NCH₃Val, NCH₃Val), 3.22-3.11 (1H, m, NCH₃Val), 2.99-2.88 (1H, m, NCH₃Val), 2.87-2.77 (1H, m, NCH₃Val), 2.76-2.65 (1H, m, NCH₃Val), 1.93 (1H, oct, J = 6.9, CH₃Val), 1.77-1.59 (2H, m, CH₃Val and CH₃Val), 1.49 (3H, s, CH₃), 1.48 (3H, s, CH₃), 1.47-1.33 (18H, m, 6 x CH₃ and C(CH₃)₃), 1.33-1.14 (2H, m, CH₃Val), 1.11 (6H, d, J = 7.5, NHVal), 1.07 (3H, d, J = 6.9, C₆H₃Al), 0.7-0.86 (18H, m, 4 x CH₃Val and 2 x CH₃Val). 

¹³C NMR (125 MHz, CDCl₃) δ = 177.9 (C=O), 177.1 (C=O), 176.9 (C=O), 176.5 (C=O), 175.9 (C=O), 175.7 (C=O), 172.2 (C=O), 161.1 (C=O), 161.0 (C=O), 160.7 (C=O), 159.3 (C=O), 138.1 (C₆H₃), 129.4 (2 x =CH₃), 129.0 (CH₃), 128.6 (2 x =CH₃), 67.7 (OCH₃), 58.2 (C), 57.9 (C), 57.8 (C), 57.6 (C), 56.3 (NC₃Val), 49.9 (NC₃Val), 47.3 (NC₃Val), 45.9 (NC H₂Val), 45.7 (NCH₃Val), 45.3 (NC H₂Val), 43.3 (NCH₃Val), 42.8 (NC H₂Val), 42.7 (C H₂Val), 41.9 (NC H₂Val), 31.7 (C₆H₃Val), 29.7 (C₆H₃Val), 26.6 (CH₃), 25.9 (C₆H₃Val), 25.6 (CH₃), 25.4 (CH₃), 25.3 (CH₃), 25.0 (CH₃), 24.8 (CH₃), 23.6 (CH₃Val), 23.5 (2 x CH₃Val), 23.5 (CH₃Val), 20.4 (C₆H₃Val), 20.0 (C₆H₃Val), 18.9 (C₆H₃Ala), 18.6 (C₆H₃Val), 18.4 (C₆H₃Val). IR (film, cm⁻¹): νmax = 3316, 2971, 2871, 1643, 1549; [α]D²⁰ = +49.6 (c = 1.00; MeOH); Mp: 190-192 °C; HRMS (ES⁺): m/z calcld for C₅₅H₄₉N₃9O₁₂Na [M+H]⁺ 1111.8.
CbzGly-Aib₂-(Val₁₁)-NH(CO)NH/Pr 8a

8a was prepared from CBzGly-Aib-OH (200 mg, 0.36 mmol), HOBt (72 mg, 0.47 mmol), EDC.HCl (76 mg, 0.40 mmol), DIPEA (92 μL, 0.55 mmol) and U1 (250 mg, 0.55 mmol) as described in the general procedure A. The pure oligomer 8a (176 mg, 68%) was isolated as a white solid. ¹H NMR (500 MHz, CD₂OH) δ = 7.82-7.59 (5H, m, NH), 7.40-7.26 (5H, m, 5 x =CH₂), 7.24 (1H, d, J = 9.7, CHNH₂Val), 5.59 (1H, d, J = 12.6, A part of AB pattern, OCH₂H₈), 5.08 (1H, d, J = 12.6, B part of AB pattern, OCH₃H₈), 3.80 (1H, d, J = 16.5, A part of AB pattern, NCH₃H₈), 3.67 (1H, d, J = 16.8, B part of AB pattern, NCH₃H₈), 3.83-3.56 (3H, m, NCH₂Pr, NCH₃H₈val and NCH₃Val), 1.75 (1H, oct, J = 6.94, Val₂Val), 1.54-1.47 (6H, m, 2 x CH₃), 1.46-1.30 (18H, m, 6 x CH₃), 1.12 (3H, d, J = 6.7, CH₃Pr), 1.10 (3H, d, J = 6.8, CH₃Pr), 0.95 (3H, d, J = 6.9, CH₃Val), 0.92 (3H, d, J = 6.9, CH₂₃Val). ¹³C NMR (125 MHz, CD₂OH) δ = 177.7 (C=O), 177.5 (C=O), 177.3 (C=O), 176.6 (C=O), 172.2 (C=O), 160.4 (C=O), 159.3 (C=O), 158.0 (=CH₂), 129.4 (2 x =CH₂), 129.0 (=CH₂), 128.6 (2 x =CH₂), 67.7 (OCH₂), 58.4 (C), 57.8 (C), 57.7 (C), 57.6 (C), 56.7 (NC₃H₈), 45.3 (NCH₂Gly), 42.9 (NCH₂Pr), 42.5 (NC₃H₂Val), 32.1 (NC₃H₈), 27.2 (CH₃), 26.9 (CH₃), 26.5 (CH₃), 26.2 (CH₃), 25.1 (CH₃), 24.0 (CH₃), 23.9 (CH₃), 23.7 (CH₃), 23.5 (CH₂Pr), 23.4 (CH₂Pr), 19.9 (C₃H₃Val), 19.0 (C₃H₃Val). IR (film, cm⁻¹): νmax = 3304, 2975, 2937, 2873, 1645, 1530; [α]D²⁰ = +27.6 (c = 1.00; MeOH); Mp: 120-122 °C; HRMS (ESI⁺): m/z calc'd for C₃₅H₅₃N₆O₉ [M+H]⁺ 719.4456, found 719.4427.

CbzGly-Aib₂-Val₁₁-Ala₈₁-NH(CO)NH/Pr 8b

8b was prepared from CBzGly-Aib-OH (200 mg, 0.36 mmol), HOBt (72 mg, 0.47 mmol), EDC.HCl (76 mg, 0.40 mmol), DIPEA (92 μL, 0.55 mmol) and U4 (300 mg, 0.55 mmol) as described in the general procedure A. The pure oligomer 8b (177 mg, 60%) was isolated as a white solid. ¹H NMR (500 MHz, CD₂OH) δ = 7.82 (2H, s, NH), 7.80 (2H, s, NH), 7.78 (1H, brs, NH), 7.42-7.25 (5H, m, 5 x =CH₂), 7.16 (1H, d, J = 10.1, NH₂Val), 6.07 (1H, d, J = 7.9, NH₂Ile), 5.88 (1H, dd, J = 7.9 and 3.4, NH₃Ala), 5.61 (1H, s, NH₃Ala), 5.59 (1H, s, NH₂Val), 5.15 (1H, d, J = 12.6, A part of AB pattern, OCH₃H₈), 5.08 (1H, d, J = 12.5, B part of AB pattern, OCH₃H₈), 3.98-3.76 (3H, m, NCH₂Pr, NH₂Val and NH₃Ala), 3.81 (1H, d, J = 16.7, A part
of AB pattern, NCH₂H₉Gly), 3.67 (1H, d, J = 16.3, B part of AB pattern, NCH₂H₉Gly), 3.72-3.59 (1H, m, NCH₂H₅Val), 3.47 (1H, ddd, J = 13.2, 8.1 and 4.1, NCH₂H₆Ala), 2.84 (1H, ddd, J = 14.2, 11.3 and 3.2, NCH₂H₅Val), 2.70 (1H, ddd, J = 13.4, 9.4 and 3.6, NCH₂H₆Ala), 1.73 (1H, oct, J = 6.9, CH₃Val), 1.52 (3H, m, CH₃), 1.50 (3H, m, CH₃), 1.47-1.32 (18H, m, 6 x CH₃), 1.13 (3H, d, J = 6.6, CH₃ipr), 1.11 (3H, d, J = 6.6, CH₃ipr), 1.07 (3H, d, J = 6.8, CH₃Ab), 0.96 (3H, d, J = 6.9, CH₃Val), 0.91 (3H, d, J = 6.9, CH₃Val). ¹³C NMR (125 MHz, CD₃OH) δ = 178.1 (C=O), 177.9 (C=O), 177.4 (C=O), 176.6 (C=O), 172.2 (C=O), 160.8 (C=O), 160.6 (C=O), 159.3 (C=O), 138.0 (=Cδ), 129.4 (2 x =Cδ), 129.0 (=Cδ), 128.6 (2 x =Cδ), 67.7 (OCH₂), 58.3 (C), 57.7 (C), 57.6 (C), 57.5 (C), 56.2 (NC₆H₅Val), 47.2 (NC₆H₅Ala), 46.7 (NC₆H₅Val), 45.2 (NCH₂Gly), 43.0 (NC₆H₅Val), 42.8 (NCH₂ipr), 32.0 (NC₆H₅Val), 28.1 (CH₂), 27.2 (CH₃), 26.8 (CH₃), 26.4 (CH₃), 25.0 (CH₃), 23.8 (CH₃), 23.6 (CH₂ipr), 23.5 (CH₂ipr), 23.4 (CH₃), 23.3 (CH₃), 20.0 (C₆H₅Val), 19.2 (C₆H₅Ab), 19.0 (C₆H₅Val). IR (film, cm⁻¹): v_max = 3309, 2961, 2871, 1640, 1538; [α]D30 = +57.2 (c = 1.00; MeOH); Mp: 135-137 °C; HRMS (ESI⁺): m/z calcd for C₃₉H₆₇N₅O₉ [M+H]⁺ 819.5092, found 819.5108.

CbzGly-Aib₄-Val⁵-Ala⁶-Leu⁷-NH(CO)NHPr 8c

8c was prepared from CBzGly-Aib-OH (200 mg, 0.36 mmol), HOBt (72 mg, 0.47 mmol), EDC.HCl (76 mg, 0.40 mmol), DIPEA (92 µL, 0.55 mmol) and U6 (350 mg, 0.55 mmol) as described in the general procedure A. The pure oligomer 8c (170 mg, 49.1%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OH) δ = 7.80-7.48 (5H, m, NH), 7.46-7.25 (5H, m, 5 x =CH₆), 7.15 (1H, d, J = 10.1, NH₃Val), 6.31 (1H, d, J = 8.2, NH₆Leu), 6.21 (1H, d, J = 7.9, NH₆ipr), 6.04 (1H, d, J = 9.7, NH₅Leu), 5.95 (1H, dd, J = 9.0 and 3.6, NH₆Ala), 5.72 (1H, dd, J = 9.1 and 2.9, NH₃Val), 5.45 (1H, d, J = 10.2, NH₅Ab), 5.15 (1H, d, J = 12.6, A part of AB pattern, OCH₂H₂), 5.07 (1H, d, J = 12.4, B part of AB pattern, OCH₂H₂), 4.18-4.02 (1H, m, NCH₆Ab), 4.01-3.89 (1H, m, NCH₅Leu), 3.82 (1H, d, J = 16.3, A part of AB pattern, NCH₆H₅Gly), 3.88-3.75 (2H, m, NCH₅ipr and NCH₅Val), 3.67 (1H, d, J = 16.3, B part of AB pattern, NCH₆H₅Gly), 3.73-3.65 (1H, m, NCH₆H₇Val), 3.60 (1H, ddd, J = 13.3, 9.5 and 3.7, NCH₇H₅Leu), 3.53 (1H, ddd, J = 13.6, 9.4 and 3.2, NCH₇H₇Ala), 2.80 (1H, d, J = 14.8, 12.4 and 3.4, NCH₇H₅Val), 2.64 (1H, ddd, J = 12.6, 10.4 and 1.5, NCH₇H₇Leu), 2.39 (1H, ddd, J = 14.3, 11.9 and 3.4, NCH₇H₇Ab), 1.78-1.61 (2H, m, CH₃Val and CH₃Leu), 1.54 (3H, s, CH₃), 1.50 (3H, s, CH₃), 1.44 (6H, s, 2 x CH₃), 1.41 (6H, s, 2 x CH₃), 1.40 (6H, s, 2 x CH₃), 1.39 (6H, s, 2 x CH₃), 1.31-1.16 (2H, m, CH₂Leu), 1.12 (3H, d, J = 6.6, CH₃ipr), 1.11 (3H, d, J = 6.6, CH₃ipr), 1.05 (3H, d, J = 6.9, CH₃Ab), 0.98-0.82 (12H, m, 2 x CH₃Val and 2 x CH₃Leu). ¹³C NMR (125 MHz, CD₃OH) δ = 178.5 (C=O), 178.0 (C=O), 177.6 (C=O), 176.6 (C=O), 172.2 (C=O), 161.1 (2 x C=O), 160.6 (C=O), 159.3 (C=O), 138.0 (=Cδ), 129.4
(2 x =CH₂), 129.0 (=CH₃), 128.6 (2 x =CH₂), 67.7 (OCH₃), 58.2 (C), 57.7 (C), 57.6 (C), 57.5 (C), 56.2 (NC≡CH₂), 49.4 (NC=NCH₃), 48.1 (NC,H₂), 47.5 (NC=NCH₃), 46.1 (NC,NCH₃), 45.3 (NCH₂), 44.0 (C,H₂), 42.9 (NC=CH₂), 42.7 (NCH₃), 32.2 (CH₂), 28.3 (CH₃), 27.3 (CH₃), 26.9 (CH₃), 26.5 (CH₃), 25.9 (C,H₂), 23.8 (CH₃), 23.7 (CH₃), 23.6 (CH₃), 23.5 (CH₃), 23.3 (CH₃), 23.2 (CH₃), 23.1 (CH₃), 22.5 (CH₃), 20.1 (C,H₂), 19.1 (C,H₂), 18.7 (C,H₂).

IR (film, cm⁻¹): v max = 3309, 2962, 2932, 2871, 1641, 1544; [a]D²⁰ = +64.4 (c = 1.00; MeOH); Mp: 151-153°C; HRMS (ESI⁺): m/z calcd for C₆₈H₇₈O₁₀ [M+H]+ 960.6120, found 976.6189.

CbzGly-Aib²-(Aib³)², Val⁵-Ala⁶-Leu⁷-NH(CO)NHPr 9c

9c was prepared from CBzGly-Aib-OH (33 mg, 0.06 mmol), HOBT (12 mg, 0.08 mmol), EDC.HCl (13 mg, 0.07 mmol), DIPEA (16 μL, 0.09 mmol) and U7 (50 mg, 0.08 mmol) as described in the general procedure A. The pure oligomer 9c (50 mg, 77.9%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OD) δ = 8.37 (1H, s, NH), 7.88-7.68 (3H, m, NH), 7.55-7.40 (2H, m, NH₂, and NH), 7.40-7.24 (5H, m, 5 x =CH₂), 6.40 (1H, dd, J = 9.5 and 3.2, NH₃), 6.36 (1H, d, J = 9.7, NH₂), 6.32 (1H, dd, J = 9.4 and 2.2, NH₂), 6.27 (1H, d, J = 8.4, NH₃), 6.20 (1H, d, J = 7.9, NH₂), 5.79 (1H, d, J = 10.1, NH₂), 5.61 (1H, d, J = 10.0, NH₂), 5.56 (1H, s, NH), 5.13 (1H, d, J = 12.7, A part of AB pattern, OCH₃), 5.09 (1H, d, J = 12.5, B part of AB pattern, OCH₃), 4.14 (1H, dd, J = 13.7 and 7.6, NCH₃), 4.09-3.97 (1H, m, NCH₃), 3.96-3.86 (1H, m, NCH₃), 3.86-3.63 (4H, m, NCH₃, NCH₃, NCH₃, and NCH₃). 3.63-3.45 (3H, m, NCH₃ and NCH₃, and NCH₃, and NCH₃), 2.72 (1H, dd, J = 13.5 and 3.6, NCH₃), 2.54-2.51 (1H, m, NCH₃, and NCH₃), 2.51-2.31 (2H, m, NCH₃, NCH₃, and NCH₃), 1.77-1.65 (1H, m, CH₃), 1.63-1.52 (1H, m, CH₃), 1.52 (3H, s, CH₃), 1.50 (3H, s, CH₃), 1.45 (3H, s, CH₃), 1.42-1.35 (18H, m, 6 x CH₃), 1.25 (3H, s, CH₃), 1.24-1.17 (2H, m, CH₃), 1.12 (3H, d, J = 6.6, CH₃), 1.11 (3H, d, J = 6.6, CH₃), 1.03 (3H, d, J = 6.9, CH₃), 0.97-0.85 (12H, m, 2 x CH₃ and 2 x CH₃). ¹³C NMR (125 MHz, CD₃OD) δ = 177.8 (C=O), 177.3 (C=O), 177.1 (C=O), 176.6 (C=O), 172.2 (C=O), 161.8 (C=O), 161.5 (C=O), 160.6 (C=O), 160.3 (C=O), 159.3 (C=O), 138.0 (C=O), 129.4 (2 x =CH₂), 129.0 (2 x =CH₂), 128.6 (2 x =CH₂), 67.7 (OCH₃), 58.2 (C), 57.8 (C), 57.7 (C), 57.5 (C), 55.9 (NC=NCH₃), 53.7 (C), 49.2 (NC,NCH₃), 48.4 (NCH₂), 47.8 (NC=CH₂), 46.5 (NC=NCH₃), 46.2 (NC=CH₂), 45.2 (NCH₂), 44.6 (NC=NCH₃), 43.9 (C,H₂), 42.7 (NCH₃), 32.0 (C,H₂), 27.5 (CH₃), 27.2 (CH₃), 26.1 (CH₃), 25.9 (2 x CH₃), 25.6 (C,H₂), 25.0 (CH₃), 24.8 (CH₃), 24.6 (CH₃), 23.6 (CH₃), 23.6 (CH₃), 23.5 (CH₃), 22.5 (CH₃), 20.1 (C,H₂), 18.8 (C,H₂), 18.6 (C,H₂).
IR (film, cm\(^{-1}\)):\(\nu_{\text{max}} = 3326, 2970, 2871, 1642, 1551; [\alpha]^0_D = +50.4\) (c = 1.00; MeOH); \(M_p > 200^\circ\text{C}\); MS (ES\(^+\)): m/z calcd for C\(_{51}\)H\(_{87}\)N\(_6\)O\(_{11}\) [M+H]\(^+\) 1076.3.

\textbf{CbzGly-Aib\(_4\)-Val\(_6\)-Ala\(_2\)-Leu\(_2\)-NH(CO)NH\textit{Pr} 10c}

10c was prepared from CBzGly-Aib-OH (34 mg, 0.06 mmol), HOBt (12 mg, 0.08 mmol), EDCl (13 mg, 0.07 mmol), DIPEA (16 \(\mu\)L, 0.09 mmol) and U8 (50 mg, 0.08 mmol) as described in the general procedure A. The pure oligomer 10c (53 mg, 81.0%) was isolated as a white solid. \(^1\)H NMR (500 MHz, CD\(_2\)OD) \(\delta = 8.41\) (1H, s, NH), 7.83 (1H, s, NH), 7.79 (1H, s, NH), 7.76 (1H, s, NH), 7.51-7.42 (1H, m, NH\(_{\text{GB}}\)), 7.39-7.27 (6H, m, 5 x =CH\(_{2}\) and NH\(_{\text{EDA}}\)), 6.37 (1H, d, \(J = 8.3\), NH\(_{\text{Leu}}\)), 6.30 (1H, d, \(J = 6.7\), NH\(_{\text{Ala}}\)), 6.18 (1H, d, \(J = 7.9\), NH\(_{\text{Pr}}\)), 6.07 (1H, d, \(J = 8.6\), NH\(_{\text{Val}}\)), 6.02 (1H, d, \(J = 9.8\), NH\(_{\text{Leu}}\)), 5.99-5.88 (2H, m, NH\(_{\text{EDA}}\) and NH\(_{\text{Ala}}\)), 5.63 (1H, d, \(J = 10.2\), NH\(_{\text{Val}}\)), 5.15 (1H, d, \(J = 12.6\), A part of AB pattern, OCH\(_3\)H\(_2\)), 5.09 (1H, d, \(J = 12.5\), B part of AB pattern, OCH\(_3\)H\(_2\)), 4.14-3.99 (1H, m, NCH\(_{\text{Leu}}\)), 3.98-3.86 (1H, m, NCH\(_{\text{Leu}}\)), 3.86-3.73 (3H, m, NCH\(_{\text{Hedral}}\) NCH\(_{\text{Hgly}}\) and NCH\(_{\text{Pr}}\)), 3.72-3.43 (6H, m, NCH\(_{\text{Val}}\) NCH\(_{\text{Hedral}}\) NCH\(_{\text{Hgly}}\) NCH\(_{\text{Hedral}}\)) CbzH\(_{\text{Hgly}}\) NCH\(_{\text{Herald}}\) and NCH\(_{\text{Hgly}}\) 3.11-2.98 (1H, m, NCH\(_{\text{Hedral}}\)), 2.95-2.80 (1H, m, NCH\(_{\text{Hedral}}\)), 2.70-2.56 (1H, m, NCH\(_{\text{HDala}}\)), 2.56-2.40 (2H, m, NCH\(_{\text{HDala}}\) and NCH\(_{\text{Hdal}}\)) 1.76-1.65 (1H, m, CH\(_{\text{Leu}}\)), 1.64-1.55 (1H, m, CH\(_{\text{Val}}\)), 1.51 (6H, m, 2 x CH\(_3\)), 1.47-1.36 (18H, m, 6 x CH\(_3\)), 1.28-1.17 (2H, m, CH\(_{\text{HDala}}\)), 1.12 (3H, d, \(J = 6.6\), CH\(_{\text{3P}}\)), 1.11 (3H, d, \(J = 6.6\), CH\(_{\text{3P}}\)), 1.06 (3H, d, \(J = 6.9\), CH\(_{\text{3Ala}}\)), 0.97-0.85 (12H, m, 2 x CH\(_{\text{3leu}}\) and 2 x CH\(_{\text{3val}}\)). \(^{13}\)C NMR (125 MHz, CD\(_2\)OD) \(\delta = 178.4\) (C\(_{\text{O}}\)), 177.7 (C\(_{\text{O}}\)), 176.8 (C\(_{\text{O}}\)), 172.2 (C\(_{\text{O}}\)), 161.7 (C\(_{\text{O}}\)), 161.4 (C\(_{\text{O}}\)), 161.3 (C\(_{\text{O}}\)), 160.6 (C\(_{\text{O}}\)), 160.6 (C\(_{\text{O}}\)), 159.4 (C\(_{\text{O}}\)), 138.0 (=C\(_{\alpha}\)), 129.5 (2 x =CH\(_{2}\)), 129.0 (=CH\(_{2}\)), 128.6 (2 x =CH\(_{2}\)), 67.7 (OCH\(_3\)), 58.0 (C), 57.8 (C), 57.6 (C), 56.4 (NC\(_{\text{Oval}}\)), 49.3 (NC\(_{\text{OHala}}\)), 48.1 (NC\(_{\text{Hala}}\)), 46.3 (NC\(_{\text{Hala}}\)), 46.2 (NC\(_{\text{Hala}}\)), 45.3 (NC\(_{\text{Hala}}\)), 44.6 (NC\(_{\text{Hala}}\)), 44.0 (C\(_{\text{Hala}}\)), 42.8 (NC\(_{\text{Pr}}\)), 40.3 (NCH\(_{2}\)), 40.2 (NCH\(_{2}\)), 32.0 (C\(_{\text{Val}}\)), 27.6 (CH\(_3\)), 27.0 (CH\(_3\)), 26.5 (CH\(_3\)), 26.1 (CH\(_3\)), 25.8 (CH\(_3\)), 24.2 (CH\(_3\)), 23.8 (CH\(_3\)), 23.7 (CH\(_3\)), 23.7 (CH\(_{3P}\)), 23.6 (CH\(_{3P}\)), 23.6 (CH\(_{3P}\)), 22.5 (CH\(_{3P}\)), 20.2 (CH\(_{3P}\)), 18.7 (CH\(_{3P}\)), 18.6 (CH\(_{3P}\)). IR (film, cm\(^{-1}\)):\(\nu_{\text{max}} = 3338, 2960, 2934, 2872, 1639, 1549; [\alpha]^0_D = +55.2\) (c = 1.00; MeOH); \(M_p\) 162-164 °C; MS (ES\(^+\)): m/z calcd for C\(_{49}\)H\(_{78}\)N\(_{16}\)O\(_{11}\) [M+H]\(^+\) 1047.9.
Cbz-Aib*-Aib*-(AibO)-re-Val-Val*-Leu*-NH(CO)NHPr 11

11 was prepared from CBzAib*-Aib-OH (50 mg, 0.09 mmol), HOEt (17 mg, 0.11 mmol), EDC.HCl (18 mg, 0.1 mmol), DIPEA (22 μL, 0.13 mmol) and U6 (75 mg, 0.11 mmol) as described in the general procedure A. The pure oligomer 11 (70 mg, 82.7%) was isolated as a white solid. ¹H NMR (500 MHz, CD₃OD) δ = 8.11 (1H, s, NH), 7.97 (1H, s, NH), 7.73 (1H, s, NH), 7.72 (1H, s, NH), 7.61 (1H, s, NH), 7.44-7.25 (5H, m, 5 x =CH₂), 1.75 (1H, d, J = 10.1, NHVal), 6.31 (1H, d, J = 7.6, NHLeu), 6.22 (1H, d, J = 7.9, NHVal), 6.04 (1H, d, J = 9.7, NHVal), 5.95 (1H, dd, J = 9.1 and 3.8, NHAla), 5.70 (1H, dd, J = 9.4 and 3.4, NHVal), 5.46 (1H, d, J = 10.2, NHAla), 5.22 (1H, d, J = 12.9, A part of AB pattern, OCH₃), 5.04 (1H, d, J = 12.7, B part of AB pattern, OCH₃), 4.18-4.03 (1H, m, NCH₂Ala), 4.01-3.88 (1H, m, NCH₃Val), 3.88-3.75 (2H, m, NCH₃Val and NCH₃Val), 3.68 (1H, ddd, J = 13.9, 9.6 and 3.8, NCH₃Val), 3.61 (1H, ddd, J = 13.2, 9.6 and 3.6, NCH₃Val), 3.53 (1H, ddd, J = 13.7, 9.5 and 3.3, NCH₃Val), 2.80 (1H, ddd, J = 14.9, 12.4 and 3.6, NCH₃Val), 2.64 (1H, ddd, J = 12.5, 10.0 and 1.3, NCH₃Val), 2.39 (1H, ddd, J = 14.4, 11.7 and 3.6, NCH₃Val), 1.77-1.62 (2H, m, CH₃Val and CH₃Val), 1.56-1.18 (32H, m, 10 x CH₃ and CH₃Val), 1.12 (3H, d, J = 6.6, CH₃Val), 1.11 (3H, d, J = 6.6, CH₃Val), 1.05 (3H, d, J = 6.9, CH₃Val), 0.96-0.86 (12H, m, 2 x CH₃Val and 2 x CH₃Val). ¹³C NMR (125 MHz, CD₃OD) δ = 178.5 (C=O), 178.0 (C=O), 177.9 (C=O), 177.2 (C=O), 177.0 (C=O), 161.1 (2 x C=O), 160.6 (C=O), 157.9 (C=O), 138.6 (=C=O), 129.5 (2 x =CH₂), 128.9 (=CH=), 128.4 (2 x =CH=), 67.5 (OCH₃), 58.2 (C), 57.8 (d, ¹H, ¹C = 39, ¹³C₃C), 57.7 (C), 57.6 (C), 57.5 (C), 56.2 (NC₃Val), 49.4 (NC₃Val), 48.1 (NC₃Val), 46.2 (NC₃Val), 46.1 (NC₃Val), 44.0 (C HVal), 43.0 (NC HVal), 42.7 (NCH₃Val), 32.2 (CH₃Val), 28.3 (CH₃), 27.4 (CH₃), 27.0 (CH₃), 26.8 (CH₃), 26.2 (¹HCH₃Val), 25.8 (CH₃Val), 24.4 (CH₃), 24.1 (¹CH₃Val), 23.7 (CH₃Val), 23.6 (CH₃Val), 23.5 (CH₃Val), 23.3 (CH₃), 23.2 (CH₃), 23.1 (CH₃), 22.5 (CH₃Val), 20.1 (CH₃Val), 19.1 (CH₃Val), 18.7 (CH₃Val). IR (film, cm⁻¹): v max = 3316, 2971, 2871, 1645, 1536; [α]D = +62.4 (c = 1.00; MeOH); Mp: 148-150 °C; HRMS (ESI⁺): m/z calcd for C₄₇H₈₅N₂O₁₀ [M+H]+ 990.6545, found 990.6538.
Ac²Phe-Alb²-Leu²⁻Val²⁻Ala²⁻NH(CO)NHPr 12

To a stirred solution of H-Alb²-Leu²⁻Val²⁻Ala²⁻NH(CO)NHPr (34 mg, 0.43 mmol; obtained in quantitative yield by hydrogenolysis of N₂-Alb²-Leu²⁻Val²⁻Ala²⁻NH(CO)NHPr) and Et₃N (9 µL, 0.06 mmol) in DMF (214 µL) was added A1 (15 mg, 0.08 mmol) and the reaction stirred at reflux for 5 d. The solvents were removed under reduced pressure and purification by column chromatography (SiO₂; CH₂Cl₂:MeOH; 99:1→90:10) gave the title compound as a white solid (13 mg, 31.8%).

1H NMR (400 MHz, CD₃OH) δ = 7.95-7.89 (1H, m, NH), 7.61-7.53 (2H, m, 2 x =CH₂), 7.50-7.43 (2H, m, 2 x =CH₂), 7.40-7.34 (1H, m, =CH₂), 7.33-7.22 (1H, m, NH), 6.90 (1H, s, =CH), 5.89-5.80 (1H, m, NH), 5.62 (1H, d, J = 10.1, NH), 4.32-4.15 (1H, m, NCH₂), 4.01-3.90 (1H, m, NCH₃), 3.89-3.81 (1H, m, NCH₃), 3.77-3.47 (4H, m, NCH₃), NCH₃H₁₈Val, NCH₃H₁₈Val, NCH₃H₁₈Val and NCH₃H₂₈Val, 2.83-2.62 (2H, m, NCH₃H₂₈Ala and NCH₃H₂₈Ala), 2.57-2.40 (1H, m, NCH₃H₁₈Val), 2.18 (3H, s, CH₃), 1.76-1.61 (2H, m, CH₂Val and CH₃Val), 1.60-1.47 (24H, m, 8 x CH₃), 1.46-1.36 (1H, m, CH₃H₁₈Val), 1.31-1.19 (1H, m, CH₃H₁₈Val), 1.16 (6H, d, J = 6.5, 2 x CH₃Pr), 1.09 (3H, d, J = 6.7, CH₃Ala), 1.03-0.84 (12H, m, 2 x CH₃Val and 2 x CH₃Val).

13C NMR (100 MHz, CD₃OH) δ = 178.2 (C=O), 178.1 (C=O), 176.8 (C=O), 176.9 (C=O), 173.1 (C=O), 161.7 (C=O), 161.3 (C=O), 161.3 (C=O), 160.7 (C=O), 153.1 (=C), 131.5 (=C), 130.6 (2 x =CH), 130.0 (=CH), 129.9 (2 x =CH), 127.3 (=CH), 58.4 (C), 58.2 (C), 58.0 (C), 57.7 (C), 56.3 (NC₃H₁₈Val), 48.7 (NC₃H₁₈Val), 47.0 (NC₃H₃Ala), 46.7 (NC H₂₈Ala), 45.8 (NC H₁₈Val), 44.4 (NC H₂₈Val), 42.8 (NCH₃Pr), 42.3 (C₃H₂₈Val), 32.2 (C₃H₂₈Val), 28.3 (CH₃), 27.5 (CH₃), 26.9 (CH₃), 26.8 (CH₃), 26.3 (CH₃), 23.9 (CH₃H₁₈Val), 23.8 (CH₃Pr), 23.7 (CH₃Pr), 23.7 (CH₃Val), 23.5 (CH₃), 23.2 (CH₃), 23.2 (CH₃), 22.8 (CH₃), 22.4 (CH₃Val), 20.2 (C₃H₃Ala), 19.6 (C₃H₃Ala), 18.5 (C₃H₃Val).

3435, 2972, 2949, 1625, 1493; [α]₂⁰° = + 41.0 (c = 1.00; MeOH); Mp: >200 °C; HRMS (ESI⁺): m/z calcd for C₄₁H₅₀N₁₂O₉Na [M+Na⁺] 979.6069, found 979.6024.

AcPhAla-Alb²-Leu²⁻Val²⁻Ala²⁻NH(CO)NHPr 13

A round-bottomed flask was charged with a solution of 12 (12 mg, 0.013 mmol) in EtOH (200 µL) and 10% m. of Pd/C was added carefully. The mixture was stirred under H₂ atmosphere (balloon) for 48 h.
Upon completion, the mixture was filtered through a celite pad and washed with EtOH. The mixture was then concentrated under reduced pressure to give compounds 13a and 13b (11 mg, 91.5%, diastereoselective ratio 1/3). $^1$H NMR (400 MHz, CD$_3$OD) δ = 7.39-7.16 (5H, m, =CH$_2$), 4.45 (0.25H, t, J = 7.7, AcNCH), 4.35 (0.75H, t, J = 8.0, AcNCH), 4.27-4.10 (1H, m, NCH$_{Leu}$), 3.99-3.77 (2H, m, NCH$_{Ala}$ and NCH$_{Ipr}$), 3.75-3.48 (4H, m, NCH$_{Vol}$, NCH$_{H_{BVal}}$, NCH$_{H_{BLeu}}$, NCH$_{H_{AVal}}$, NCH$_{A_{BAla}}$), 3.18-2.90 (2H, m, CH$_2$), 2.76-2.38 (3H, m, NCH$_{H_{BLeu}}$, NCH$_{A_{Val}}$ and NCH$_{A_{Ala}}$), 1.97 (3H, s, CH$_3$), 1.73-1.58 (2H, m, CH$_{Leu}$ and CH$_{Vol}$), 1.57-1.17 (26H, m, 8 x CH$_3$ and CH$_{2_{Leu}}$), 1.13 (6H, d, J = 6.6, 2 x CH$_{3_{Ipr}}$), 1.06 (3H, d, J = 6.7, CH$_{3_{Ala}}$), 1.0-0.81 (12H, m, 2 x CH$_{3_{Vol}}$ and 2 x CH$_{3_{Leu}}$).

$^{13}$C NMR (100 MHz, CD$_3$OD) δ = 178.1 (C=O), 178.1 (C=O), 177.7 (C=O), 176.8 (C=O), 174.3 (C=O), 173.8 (C=O), 173.6 (C=O), 161.7 (C=O), 161.3 (C=O), 160.7 (C=O), 138.1 (=C), 137.8 (=C), 130.5 (2 x =CH), 130.4 (=CH), 129.5 (2 x =CH), 128.0 (3 x =CH), 127.9 (2 x =CH), 58.3 (C), 58.2 (C), 57.8 (C), 57.7 (C), 57.6 (C), 57.5 (C), 57.3 (C), 57.1 (NC$_2$H$_{Vol}$), 56.2 (NCH), 48.7 (NC$_{H_{Leu}}$), 47.0 (NC$_{H_{Ala}}$), 46.7 (NC$_{H_{2_{Ala}}}$), 45.8 (NC$_{H_{2_{Leu}}}$), 44.4 (NC$_{H_{2_{Vol}}}$), 42.8 (NCH$_{Ipr}$), 42.3 (C$_{H_{2_{Leu}}}$), 38.1 (NCH), 38.0 (NCH), 32.2 (C$_{H_{Vol}}$), 28.3 (CH$_3$), 27.7 (CH$_3$), 27.3 (CH$_3$), 26.8 (CH$_3$), 26.3 (CH$_3$), 24.2 (C$_{H_{Leu}}$), 23.8 (CH$_{Ipr}$), 23.8 (CH$_{Ipr}$), 23.7 (CH$_{3_{Leu}}$), 23.4 (CH$_3$), 23.2 (CH$_3$), 23.2 (CH$_3$), 22.4 (CH$_3$), 22.4 (CH$_{3_{Leu}}$), 20.2 (C$_{H_{3_{Vol}}}$), 19.5 (C$_{H_{3_{Ala}}}$), 18.5 (C$_{H_{3_{Vol}}}$). IR (film, cm$^{-1}$): ν$_{max}$ = 3334, 2930, 1632, 1574, 1472; HRMS (ESI$^+$): m/z calcd for C$_{47}$H$_{82}$O$_{12}$N$_5$Na [M+Na]$^+$ 981.6225, found 981.6191.

Ac$^6$Phe-Leu$^5$-Val$^4$-Ala$^3$-NH(CO)NH$^2$IPr 14

Boc-protected oligourea U9 (80 mg, 0.15 mmol) was dissolved in TFA (800 μl) and stirred for 45 min.

The reaction mixture was then concentrated under reduced pressure. Triethylamine (14 μL, 0.14 mmol) and an A1 (25 mg, 0.13 mmol) were added to the crude product was then dissolved in acetonitrile.

The reaction stirred at reflux for 5 d. The solvents were removed under reduced pressure and purification by column chromatography (SiO$_2$; CH$_3$Cl$_2$:MeOH; 99:1→90:10) gave the title compound as a white solid (50 mg, 87%). $^1$H NMR (400 MHz, CD$_3$OD) δ = 7.60-7.51 (2H, m, =CH$_2$), 7.47-7.38 (2H, m, =CH$_2$), 7.38-7.29 (1H, m, =CH$_2$), 6.89 (1H, s, =CH), 4.37-4.23 (1H, m, NCH$_{Leu}$), 3.95-3.87 (1H, m, NCH$_{Ala}$), 3.86-3.70 (1H, m, NCH$_{Ipr}$), 3.70-3.56 (3H, m, NCH$_{Vol}$, NCH$_{H_{BVal}}$ and NCH$_{A_{BAla}}$), 3.55-3.44 (1H, m, NCH$_{H_{BLeu}}$), 2.70 (1H, dd, J = 13.2 and 9.5, NCH$_{H_{BLeu}}$), 2.62 (1H, t, J = 12.2, NCH$_{H_{BAla}}$), 2.50 (1H, t, J = 12.4, NCH$_{H_{BVal}}$), 2.13 (3H, s, CH$_3$), 1.81-1.69 (1H, m, CH$_{Leu}$), 1.65 (1H, oct, J =, CH$_{Vol}$), 1.44 (1H, ddd, J = 7.1, CH$_{H_{BLeu}}$), 1.26 (1H, ddd, J = 7.1, CH$_{H_{BLeu}}$), 1.14 (6H, d, J = 6.5, 2 x CH$_{3_{Ipr}}$), 1.04 (3H, d, J = 6.8,
CH₃AlO), 1.01-0.86 (12H, m, 2 x CH₂Val and 2 x CH₃Leu). ¹³C NMR (100 MHz, CD₂OH) δ = 173.5 (C=O), 168.9 (C=O), 161.6 (C=O), 161.2 (C=O), 160.6 (C=O), 135.1 (=C), 131.7 (=C), 130.5 (2 x =CH), 130.0 (=CH), 129.9 (2 x =CH), 127.9 (=CH), 56.3 (NC₅HVal), 49.7 (NC₅HVal), 47.0 (NC₅HAla), 46.7 (NC H₂Ala), 46.3 (NC H₂Leu), 44.1 (NC H₂Val), 42.8 (NCCH₃Val), 42.0 (C H₂Leu), 32.1 (CH₂Val), 26.5 (CH₂Leu), 23.8 (CH₃Leu), 23.7 (2 x CH₃), 22.7 (CH₃ and CH₃Leu), 20.1 (CH₃Val), 19.4 (CH₃Ala), 18.5 (CH₃Val). IR (film, cm⁻¹): νmax = 3428, 2962, 2929, 2872, 1619, 1480; [α]D²⁰ = +72 (c = 1.00; MeOH); Mp: 145-146 °C; HRMS (ESI⁺): m/z calcd for C₃₁H₅₂O₅N₅Na [M+Na]⁺ 639.3958, found 639.3965.

AcPhAla-Leu⁵⁻Val⁵⁻Ala⁵⁻NH(CO)NHPr 15

![Chemical structure](image)

C₅₇H₇₅O₅N₁₅ M = 618.80 g.mol⁻¹

A round-bottomed flask was charged with a solution of 14 (6 mg, 0.01 mmol) in EtOH (200 μL) and 10% m. of Pd/C was added carefully. The mixture was stirred under H₂ atmosphere (balloon) for 48 h. Upon completion, the mixture was filtered through a celite pad and washed with EtOH. The mixture was then concentrated under reduced pressure to give compounds 15a and 15b (5 mg, 83%, diastereoselective ratio 1/1.3). ¹H NMR (400 MHz, CD₂OH) δ = 7.38-7.12 (5H, m, =CH₃), 4.56 (0.42H, dd, J = 9.5 and 5.5, AcNCH), 4.56 (0.58H, t, J = 7.9, AcNCH), 4.20-4.03 (1H, m, NCH₃), 3.94-3.75 (2H, m, NCH₃Ala and NCH₃Pr), 3.67-3.39 (4H, m, NCH₂Val, NCH₂H₂Val, NCH₂H₂Leu, NCH₂H₂Ala), 3.15 (0.43H, dd, J = 14.2 and 5.6, CH₂CH₃), 3.00 (1.18H, d, J = 7.9, CH₂), 2.94 (0.43H, dd, J = 14.1 and 9.5, CH₃CH₂), 2.76-2.36 (3H, m, NCH₃H₂Leu, NCH₃H₂Val and NCH₃H₂Ala), 1.97 (1.65H, s, CH₃), 1.93 (1.27H, s, CH₃), 1.70-1.57 (2H, m, CH₃Leu and CH₃Val), 1.41-1.32 (1H, m, CH₃H₃Val), 1.26-1.17 (1H, m, CH₃H₃Leu), 1.16-0.70 (21H, m, 2 x CH₃Pr, 3CH₃Ala, 2 x CH₂Val and 2 x CH₃Leu). ¹³C NMR (100 MHz, CD₂OH) δ = 174.3 (C=O), 174.2 (C=O), 173.7 (C=O), 173.6 (C=O), 162.7 (C=O), 161.4 (C=O), 161.3 (C=O), 161.2 (C=O), 161.2 (C=O), 160.6 (C=O), 138.6 (=C), 137.9 (=C), 130.3 (2 x =CH), 130.2 (2 x =CH), 129.6 (2 x =CH), 129.5 (2 x =CH), 128.0 (=CH), 127.9 (=CH), 64.3 (NC₅HVal), 57.7 (NCH), 56.9 (NC₅HVal), 56.2 (NCH), 49.2 (NC₅HAla), 49.0 (NC₅HLeu), 47.3 (NC₅HAla), 47.2 (NC₅HAla), 46.7 (NC H₂Ala), 46.6 (NC H₂Ala), 46.2 (NC H₂Leu), 46.1 (NC H₂Leu), 44.4 (NC H₂Val), 42.8 (NCCH₃Pr), 42.8 (NCCH₃Pr), 41.9 (C H₂Leu), 38.8 (CH₂), 38.7 (CH₂), 32.0 (CH₂Val), 31.9 (C₃H₇Val), 26.0 (C₃H₇Leu), 25.5 (C₃H₇Leu), 24.2 (CH₃Leu), 23.8 (CH₃Leu), 23.7 (CH₃Leu), 23.6 (2 x CH₃Pr), 22.5 (CH₃), 22.5 (CH₃), 22.4 (CH₃Leu), 22.4 (CH₃Leu), 20.1 (CH₃Val), 20.1 (CH₃Val), 19.5 (CH₃Val), 19.4 (CH₃Val), 18.6 (CH₃Val), 18.4 (CH₃Val). IR (film, cm⁻¹): νmax = 3350, 2962, 2929, 1625, 1574, 1480; HRMS (ESI⁺): m/z calcd for C₃₁H₅₂O₅N₅Na [M+Na]⁺ 641.4115, found 641.4101.
Hydrogen Bonding of 2d, 7e and 8c
CD spectra

[Graphs showing CD spectra for compounds 2a, 2b, 2c, and 2d, 3a, 3b, 3c, and 3d, 4a, 4b, 4c, and 4d, with wavelength (λ) on the x-axis and optical rotation ([θ]_M) on the y-axis, in units of degrees cm^2 dmol^-1.]
VT-NMR $^{13}$C of 11 between -80 and 40°C

[Graph showing VT-NMR spectra for temperatures ranging from -80°C to +40°C]
VT-NMR $^1$H of 11 between 5 and 38 °C
NMR spectra (1H, 13C, COSY, HSQC)
CbzHN\[\text{\undertilde{\text{\textbackslash H}}\text{\_N}}\text{\_N}O
\]

\[8c\]