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SUPPORTING INFORMATION

Designed Peptides for Biomineral Polymorph Recognition: A Case Study for Calcium Carbonate

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Table S1. Selected sequences of peptides obtained from phage display selectiuon against vaterite. Characteristic for nearly all peptides is the presence of proline (black) and arginine (red). [a]Found in 80% of the sodium acetate selected phage clones in round 3. [b]Found in 70% of the EDTA selected phage clones in round 3. [c]Peptides synthesized by solid state peptide synthesis (SPPS).

Clone[a]	Selection round	Elution method	Sequence
Pep1	First	pH 2.2	TTDRPKY
Pep2	First	pH 2.2	SVPQRTP
Pep3	First	pH 2.2	VQTPARM[c]
Pep4	Second	pH 2.2	QPPRSTS
Pep5	Second	pH 2.2	VQTSSSY
Pep6	Second	pH 2.2	RCAPPCN
Pep7	Third	NaAc	HAPARVP
Pep8	Third	NaAc	ASTQPLR[a,c]
Pep9	Third	EDTA	EAPVRYF
Pep10	Third	EDTA	ATNPTDY[b,c]
Pep11	Third	EDTA	AITRSPA
Pep12	Third	EDTA	HAIYPRH
Pep13	Third	EDTA	TSFTWPR

Table S2. Details of the measurement and refinement of the X-ray diffraction data for the crystallization of $CaCO_3$ with Pep8 and gPep8.

	Pep8	gPep8
Diffractometer	Bruker D8 Discover, HiStar detector	
Measuring mode	Bragg-Brentano	
Wavelength	CuKα	
Measuring range	$13.7 \leq 2\Theta$ /° ≤ 80.22, $\Delta 2\Theta$/° = 0.02; 0.97 $\leq Q/Å^{-1} \leq 5.25$ Integration from (RJP) frames at individual scattering angles	
Temperature /K	298	
Profile Fit	Rietveld refinement according to reported crystal structure models	
Background / Parameters	Chebyshev / 42	Chebyshev / 18
Profile function	Fundamental Parameters Approach	
Program	TOPAS Academic V4.1	
Total No. of Parameters	54	24
R_{wp}	3.2	5.0
GoF	0.37	0.68
Phase I	**Calcite**	**Calcite**
Space group	*R*-3*c*	*R*-3*c*
Cell parameters /Å	a = 4.9(2) c = 17.062(9)	a = 4.984(1) c = 17.0275(6)
Crystallite size / nm	20(3)	68(1)
Fraction /%wt	2(3)	100(0)
Biso	Ca: 1, C, O: 1.5	Ca: 1, C, O: 1.5
Preferred Orientation (March-Dollse)	(002) / 0.18(8)	(002) / 0.232(2)
Phase II	**Vaterite, 6 layer model**	**-/-**
Space group	*C*-1	
Cell parameters /Å	a = 12.38(4) b= 7.15(2) c = 25.76(2) β = 99.3(2)°	
Crystallite size / nm	37(1)	
Fraction /%wt	98(3)	
Biso	Ca: 1, C, O: 1.5	

Table S3. Details of the measurement and refinement of the X-ray diffraction data for the incubation of vaterite nanocrystals with Pep8 and gPep8

	Pristine	After incubation
Diffractometer	Bruker D8 Discover, HiStar detector	
Measuring mode	Bragg-Brentano	
Wavelength	CuKα	
Measuring range	$6.7 \leq 2\Theta\ /° \leq 85.86$, $\Delta 2\Theta/° = 0.02$; $0.0477 \leq Q/Å^{-1} \leq 5.55$ Integration from (RJP) frames at individual scattering angles	
Temperature /K	298	
Profile Fit	Rietveld refinement according to reported crystal structure models	
Background / Parameters	Chebyshev / 20	
Profile function	Fundamental Parameters Approach	
Program	TOPAS Academic V4.1	
Total No. of Parameters	26	32
R_{wp}	8.2	4.1
GoF	0.69	0.51
Phase I	**Calcite**	**Calcite**
Space group	*R*-3*c*	*R*-3*c*
Cell parameters /Å	a = 4.9902(2) c = 17.0674(9)	a = 5.000(4) c = 17.01(1)
Crystallite size / nm	71.5(5)	53(1)
Fraction /%wt	100%	0.9(1)
Biso	Ca: 1, C, O: 1.5	Ca: 1, C, O: 1.5
Phase II	**-/-**	**Vaterite, 6 layer model**
Space group		*C*-1
Cell parameters /Å		a = 12.418(1) b= 7.1355(6) c = 25.766(1) β = 99.55(1)°
Crystallite size / nm		40(1)
Fraction /%wt		99.1(1)
Biso		Ca: 1, C, O: 1.5

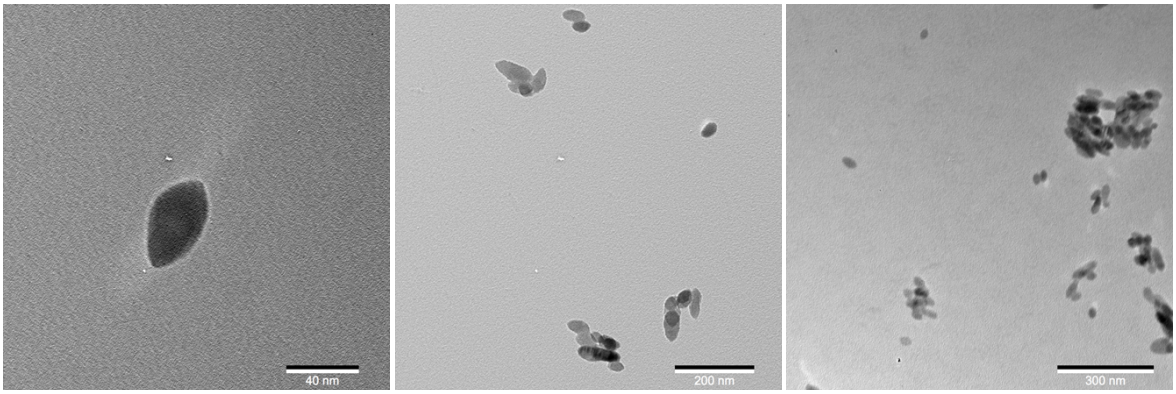


Fig. S1. Transmission electron microscopy images of vaterite nanoparticles used for the phage display.

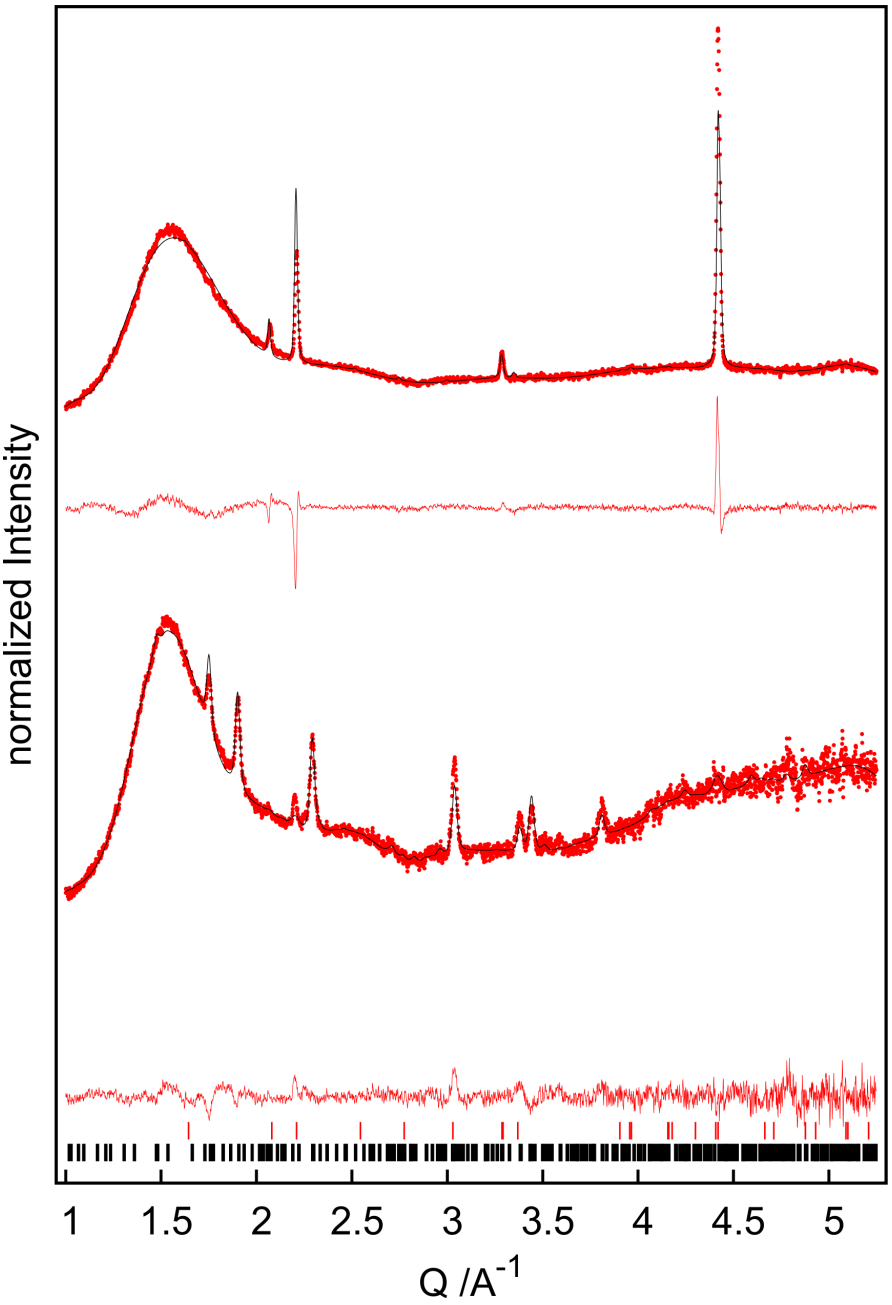


Fig. S2. XRD diffraction pattern of a bulk sample of calcium carbonate crystallized in the presence of Pep8 (bottom trace) and gPep8 (top trace). Crystallization in the presence of Pep8 lead to the formation of vaterite, whereas gPep8 induced the formation of calcite. Red dots: observed, black line: calculated, red line: difference, black ticks mark the reflection positions of the constituent phases.

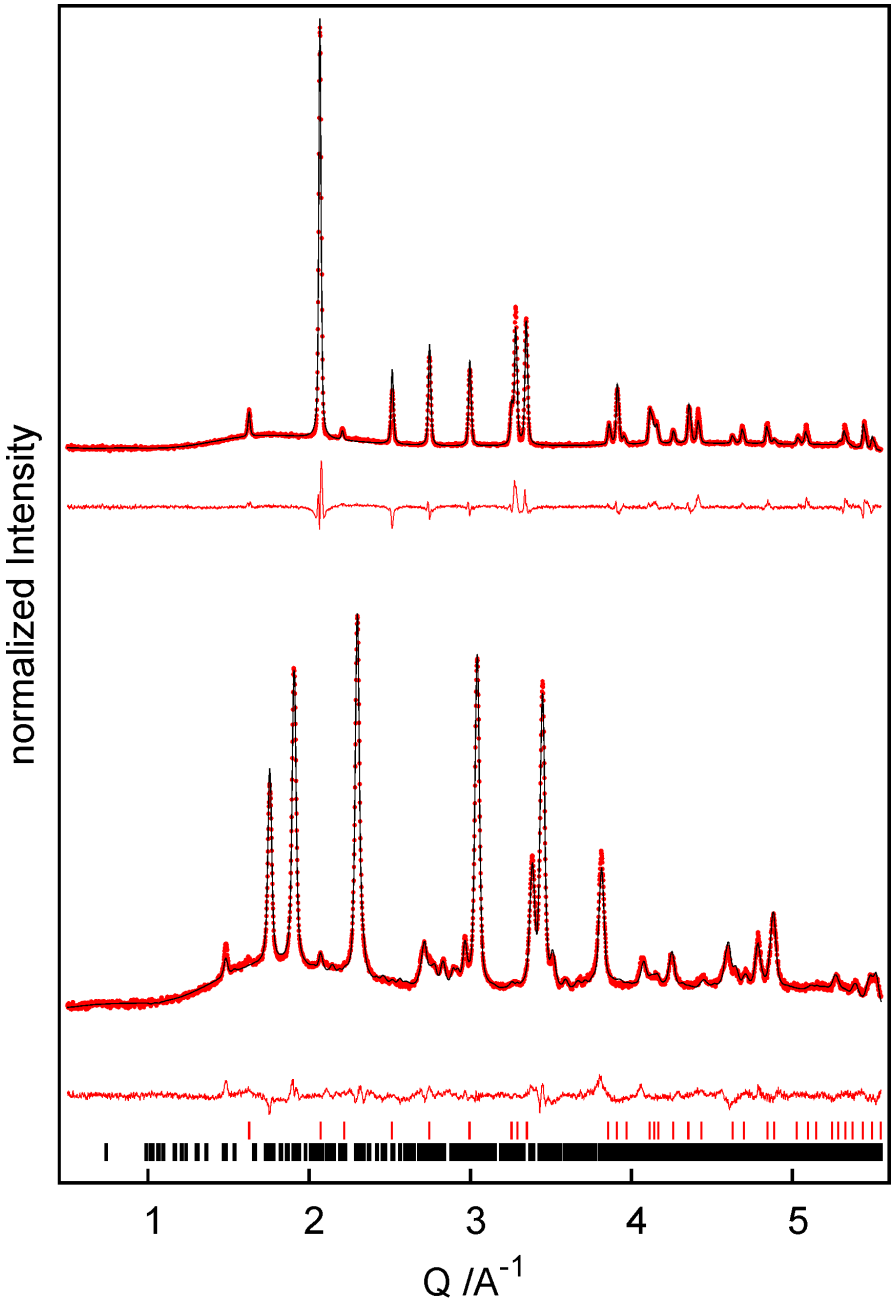


Fig. S3. XRD diffraction pattern of a bulk sample of vaterite nanoparticles incubated at ambient temperature with Pep8 (bottom trace) and gPep8 (top trace). Incubation with gPep8 triggered a phase transition from vaterite to calcite, whereas vaterite remained stable in the presence of Pep8. Red dots: observed, black line: calculated, red line: difference, black ticks mark the reflection positions of the constituent phases..

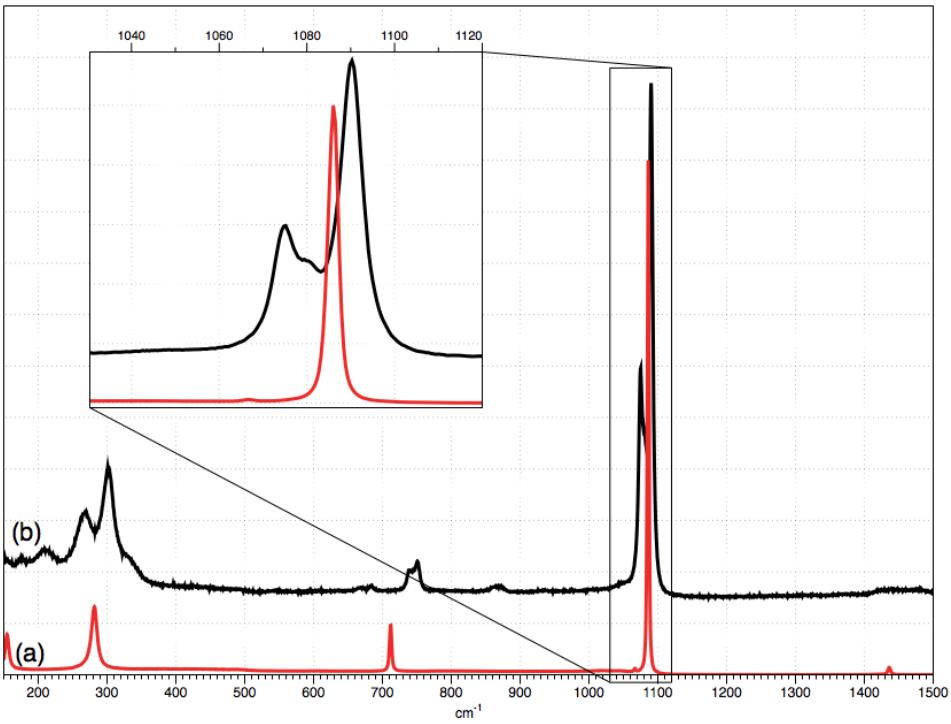
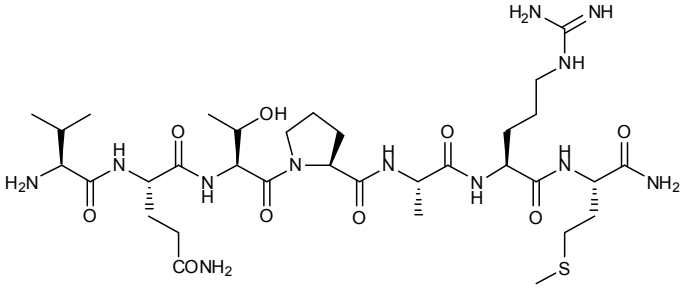


Figure S4. Raman spectra of calcium carbonate precipitated in the presence of 1 mg·mL^{-1} Pep8 (a) and gPep8 (b).

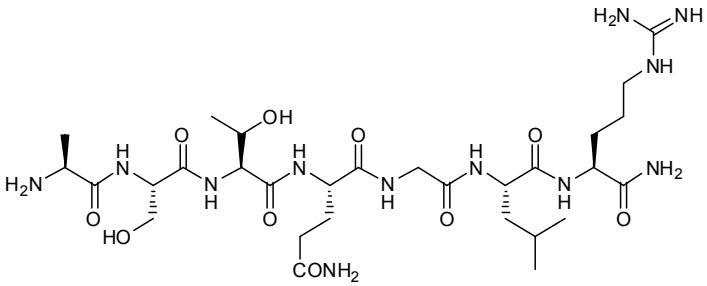
Peptide Analysis

***L*-Valyl-*L*-glutamyl-*L*-threonyl-*L*-prolyl-*L*-alanyl-*L*-arginyl-*L*-methionylamide (Pep3)**



417 mg (0.1 mmol, loading: 0.24 mmol/g) of Fmoc-*L*-Met-*RAM-Tentagel-S* resin were used in the synthesis as described above to yield 84 mg of crude peptide. The crude peptide was purified by *semi-preparative HPLC* (R_t = 21.9 min, JUPITER, methanol/water, grad. (5:95)→(20:80), 20 min; 5 min constant; λ = 214 nm) to yield 49 mg (61 µmol, 61%) as a colourless, amorphous solid. *Analytical HPLC*: R_t = 13.8 min (JUPITER, methanol/water, grad. (5:95)→(20:80), 20 min; →(100:0), 10 min; λ = 214 nm); $[\alpha]_D^{23}$ (MeOH/H_2O (1:1), c = 1.04) = -65.88 °; *ESI-MS* (positive ion mode) *m/z*: 401.22 ($[M+2H]^{2+}$, calcd.: 401.23); 801.41 ($[M+H]^+$, calcd.: 801.44); *HR-ESI-MS* (positive ion mode) *m/z*: calcd. for $C_{33}H_{61}N_{12}O_9S$: 801.4405, found: 801.4377 $[M+H]^+$; *^{1}H-NMR* (400 MHz, DMSO, *^{1}H*, *COSY*, *TOCSY*), δ (ppm) = 8.59 (d, $J_{QNH,Q\alpha}$ = 7.4 Hz, 1H, Q^{NH}); 8.23 (d, $J_{ANH,Aa}$ = 6.0 Hz, 1H, A^{NH}); 8.11 (d, $J_{TNH,Ta}$ = 7.0 Hz, 1H, T^{NH}); 7.98 (d, $J_{RNH,Ra}$ = 6.8 Hz, 1H, R^{NH}); 7.92-7.83 (m, 2H, M^{NH} {7.89}, $R^{\varepsilon NH}$ {7.87}); 7.33 (s, 1H, $Q^{\delta CONH2a}$); 7.30 (s, 1H, M^{CONH2a}); 7.11 (s, 1H, M^{CONH2b}); 6.82 (s, 1H, $Q^{\delta CONH2b}$); 4.88 (s, 1H, T^{OH}); 4.46-4.36 (m, 2H, Q^{α} {4.41}, T^{α} {4.40}); 4.36-4.29 (m, 1H, P^{α}); 4.28-4.10 (m, 3H, M^{α} {4.24}, R^{α} {4.18}, A^{α} {4.15}); 3.91-3.80 (m, 1H, T^{β}); 3.79-3.69 (m, 1H, $P^{\delta a}$); 3.69-3.57 (m, 2H, $P^{\delta b}$ {3.65}, V^{α} {3.62}); 3.14-3.01 (m, 2H, R^{δ}); 2.48-2.32 (m, 2H, M^{γ}); 2.21-1.64 (m, 15H, Q^{γ} {2.12}, $P^{\beta a}$ {2.08}, V^{β} {2.05}, M^{ε} {2.01}, $M^{\beta a}$ {1.91}, P^{γ} {1.86}, $Q^{\beta a}$ {1.83}, $R^{\beta a}$ {1.83}, $P^{\beta b}$ {1.81}, $M^{\beta b}$ {1.77}, $Q^{\beta b}$ {1.72}); 1.63-1.40 (m, 3H, $R^{\beta b}$ {1.57}, R^{γ} {1.47}); 1.21 (d, $J_{A\beta,A\alpha}$ = 7.1 Hz, 3H, A^{β}); 1.10 (d, $J_{T\gamma,T\beta}$ = 6.2 Hz, 3H, T^{γ}); 0.96-0.85 (m, 6H, V^{γ} {0.92}, $V^{\gamma`}$ {0.90}); *^{13}C-NMR* (100.6 MHz, DMSO, *^{13}C*, *HSQC*, *HMBC*), δ (ppm) = 174.0 ($Q^{\varepsilon CONH2}$); 173.2 (M^{CONH2}); 172.8 (A^{CO}); 171.8 (P^{CO}); 171.3 (R^{CO}); 171.0 (Q^{CO}); 169.1 (T^{CO}); 168.0 (V^{CO}); 156.9 (R^{ξ}); 66.8 (T^{β}); 59.5 (P^{α}); 57.4 (V^{α}); 56.7 (T^{α}); 52.5 (R^{α}); 52.1 (Q^{α}); 51.8 (M^{α}); 48.9 (A^{α}); 47.5 (P^{δ}); 40.4 (R^{δ}); 31.7 (M^{β}); 31.4 (Q^{γ}); 30.0 (V^{β}); 29.7 (M^{γ}); 29.1 (P^{β}); 28.7 (R^{β}); 28.4 (Q^{β}); 24.9 (R^{γ}); 24.7 (P^{γ}); 19.3 (T^{γ}); 18.4, 17.7 (V^{γ},$V^{\gamma`}$); 17.5 (A^{β}); 14.7 (M^{ε}).

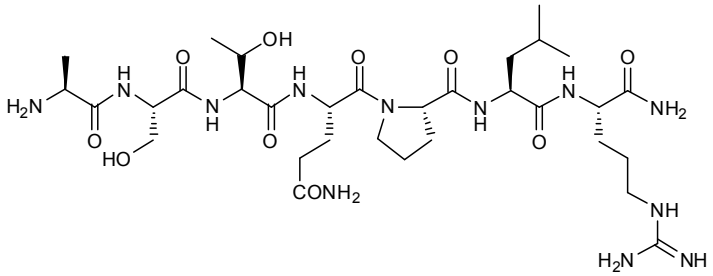
***L*-Alanyl-*L*-seryl-*L*-threonyl-*L*-glutaminyl-glycyl-*L*-leucyl-*L*-arginylamide (gPep8)**



476 mg (0.1 mmol, loading: 0.21 mmol/g) of Fmoc-*L*-Arg(Pbf)-*RAM-Tentagel-S* resin were used in the synthesis as described above to yield 79 mg of crude peptide. The crude peptide was purified by *semi-preparative HPLC* (R_t = 25.2 min, JUPITER, methanol + 0.1% TFA/water + 0.1% TFA, grad. (5:95)→(20:80), 20 min; 5 min

constant; →(5:95), 10 min; λ = 214 nm) to yield 60 mg (82 µmol, 82%) as a colourless, amorphous solid. *Analytical HPLC*: R_t = 13.8 (JUPITER, methanol + 0.1% TFA/water + 0.1% TFA, grad. (5:95)→(20:80), 20 min; →(100:0), 10 min; λ = 214 nm); $[\alpha]_D^{26}$(c = 0.98, MeOH) = -22.93 °; *ESI-MS* (positive ion mode) *m/z*: 731.45 ([M+H]$^+$, calcd.: 731.42); *HR-ESI-MS* (positive ion mode) *m/z*: calcd. for $C_{29}H_{55}N_{12}O_{10}$: 731.4164, found) 731.4150 [M+H]$^+$; *^{1}H-NMR* (400 MHz, DMSO, *^{1}H*, *COSY*, *TOCSY*), δ (ppm) = 8.67 (d, $J_{SNH,S\alpha}$ = 7.7 Hz, 1H, S^{NH}); 8.22-8.09 (m, 3H; G^{NH} {8.17}, A^{NH2} {8.15}); 8.02-7.92 (m, 3H, Q^{NH} {7.99}, R^{NH} {7.97}, L^{NH} {7.96}); 7.86 (d, $J_{TNH,T\alpha}$ = 8.1 Hz, 1H, T^{NH}); 7.76 (t, $J_{R\varepsilon NH,R\delta}$ = 5.6 Hz, 1H, $R^{\varepsilon NH}$); 7.29 (s, 1H, $Q^{\delta CONH2a}$); 7.26 (s, 1H, R^{CONH2a}); 7.06 (s, 1H, R^{CONH2b}); 6.83 (s, 1H, $Q^{\delta CONH2b}$); 4.49 (dd, J = 6.0 Hz, J = 13.5 Hz, 1H, S^{α}); 4.31-4.05 (m, 5H, L^{α} {4.27}, T^{α} {4.21}, Q^{α} {4.21}, R^{α} {4.21}, T^{β} {4.07}); 3.97-3.88 (m, 1H, A^{α}); 3.76-3.57 (m, 4H, G^{α} {3.72}, $S^{\beta a}$ {3.69}, $S^{\beta b}$ {3.61}); 3.09 (dd, $J_{R\delta,R\gamma}$ = 12.6 Hz, $J_{R\delta,R\varepsilon NH}$ = 6.5 Hz, 2H, R^{δ}); 2.11 (t, $J_{Q\gamma,Q\beta}$ = 7.9 Hz, 2H, Q^{γ}); 1.95-1.82 (m, 1H, $Q^{\beta a}$); 1.80-1.64 (m, 2H, $Q^{\beta b}$ {1.74}, $R^{\beta a}$ {1.68}); 1.63-1.39 (m, 6H, L^{γ} {1.58}, $R^{\beta b}$ {1.53}, R^{γ} {1.45}, L^{β} {1.45}); 1.35 (d, $J_{A\beta,A\alpha}$ = 6.9 Hz, 3H, A^{β}); 1.03 (d, $J_{T\gamma,T\beta}$ = 6.3 Hz, 3H, T^{γ}); 0.86 (d, $J_{L\delta,L\delta'}$ = 6.5 Hz, 3H, L^{δ}); 0.82 (d, $J_{L\delta',L\gamma}$ = 6.5 Hz, 3H, $L^{\delta'}$); *^{13}C-NMR* (100.6 MHz, DMSO, *^{13}C*, *HSQC*, *HMBC*), δ (ppm) = 174.1 ($Q^{\delta CONH2}$); 173.4 (R^{CONH2}); 172.0 (L^{CO}); 171.8 (Q^{CO}); 170.1 (T^{CO}); 170.0 (S^{CO}); 169.8 (A^{CO}); 168.8 (G^{CO}); 156.9 (R^{ξ}); 66.3 (T^{β}); 61.7 (S^{β}); 58.3 (T^{α}); 55.0 (S^{α}); 52.6 (Q^{α}); 52.2 (R^{α}); 51.3 (L^{α}); 48.1 (A^{α}); 42.1 (G^{α}); 40.7 (L^{β}); 40.4 (R^{δ}); 31.4 (Q^{γ}); 29.0 (R^{β}); 27.8 (Q^{β}); 25.3 (R^{γ}); 24.2 (L^{γ}); 23.1 (L^{δ}); 21.6 ($L^{\delta'}$); 19.8 (T^{γ}); 17.4 (A^{β}).

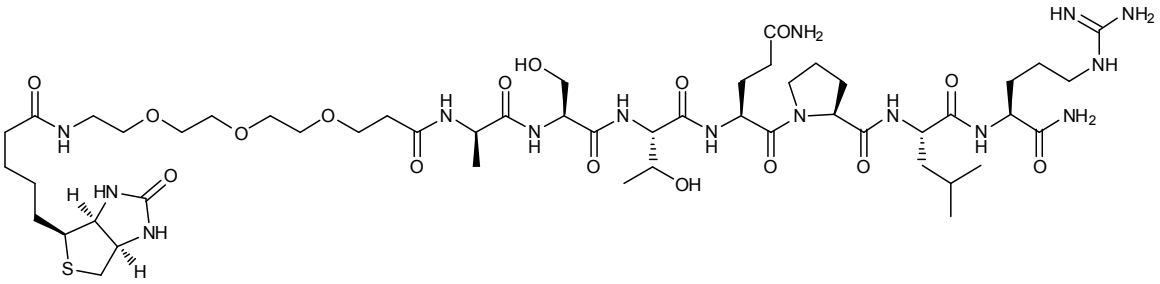
_L_-Alanyl-_L_-seryl-_L_-threonyl-_L_-glutamyl-_L_-prolyl-_L_-leucyl-_L_-arginylamide(Pep8)



476 mg (0.1 mmol, loading: 0.21 mmol/g) of Fmoc-*L*-Arg(Pbf)-*RAM-Tentagel-S* resin were used in the synthesis as described above to yield 75 mg of crude peptide. The crude peptide was purified by *semi-preparative HPLC* (R_t = 27.5 min, JUPITER, methanol + 0.1% TFA/water + 0.1% TFA, grad. (5:95)→(20:80), 20 min; 5 min constant; →(5:95), 10 min; λ = 214 nm) to yield 47 mg (61 µmol, 61%) as a colourless, amorphous solid. *Analytical HPLC*: R_t = 12.7 min (JUPITER, methanol + 0.1% TFA/water + 0.1% TFA, grad. (5:95)→(20:80), 20 min; →(100:0), 10 min; λ = 214 nm); $[\alpha]_D^{27}$ (c = 1.02; MeOH/H_2O (1:1)) = -74.41 °; *ESI-MS* (positive ion mode) *m/z*: 771.48 ([M+H]$^+$, calcd.: 771.45); *HR-ESI-MS* (positive ion mode) *m/z*: calcd. for $C_{32}H_{59}N_{12}O_{10}$: 771.4477, found: 771.4471 [M+H]$^+$,); *^{1}H-NMR* (400 MHz, DMSO, *^{1}H*, *COSY*, *TOCSY*), δ (ppm) = 8.63 (d, $J_{SNH,S\alpha}$ = 7.7 Hz, 1H, S^{NH}) 8.16-8.05 (m, 3H, A^{NH2} {8.11}, L^{NH} {8.09}); 7.97 (d, $J_{QNH,Q\alpha}$ = 7.8 Hz, 1H, Q^{NH}); 7.80 (d, $J_{TNH,T\alpha}$ = 8.3 Hz, 1H, T^{NH}); 7.74 (d, $J_{RNH,R\alpha}$ = 8.1 Hz, 1H, R^{NH}); 7.70 (t, $J_{R\varepsilon NH,R\delta}$ = 5.7 Hz, 1H, $R^{\varepsilon NH}$); 7.29 (s, 1H, $Q^{\delta CONH2a}$); 7.25 (s, 1H, R^{CONH2a}); 7.11 (s, 1H, R^{CONH2b}); 6.88 (s, 1H, $Q^{\delta CONH2b}$); 4.55-4.43 (m, 2H, Q^{α} {4.51}, S^{α} {4.48}); 4.34-4.27 (m, 1H, P^{α}); 4.23-4.10 (m, 3H, T^{α} {4.20}, L^{α} {4.18}, R^{α} {4.15}); 4.08-4.00 (m, 1H, T^{β}); 3.96-3.87 (m, 1H, A^{α}); 3.69-3.42 (m, 4H, $S^{\beta a}$ {3.65}, P^{δ} {3.60}, $S^{\beta b}$ {3.58}); 3.08 (dd, $J_{R\delta,R\gamma}$ = 12.7 Hz, $J_{R\delta,R\varepsilon NH}$ = 6.6 Hz, 2H, R^{δ}); 2.12 (t, $J_{Q\gamma,Q\beta}$ = 7.5 Hz, 2H Q^{γ}); 2.08-1.97 (m, 1H, $P^{\beta a}$); 1.93-1.76 (m, 4H, $Q^{\beta a}$ {1.88}, $P^{\beta b}$ {1.83}, P^{γ} {1.83}); 1.75-1.57 (m, 3H, $R^{\beta a}$ {1.69}, $Q^{\beta b}$ {1.67}, L^{γ} {1.60}); 1.57-1.39 (m, 5H, $R^{\beta b}$ {1.50}, L^{β}

{1.46}, R^{γ} {1.44}); 1.34 (d, $J_{A\beta,A\alpha}$ = 6.9 Hz, 3H, A^{β}); 1.03 (d, $J_{T\beta,T\alpha}$ = 6.3 Hz, 3H, T^{β}); 0.88 (d, $J_{L\delta,L\gamma}$ = 6.6 Hz, 3H, L^{δ}); 0.82 (d, $J_{L\delta',L\gamma}$ = 6.5 Hz, 3H, $L^{\delta'}$); *^{13}C-NMR* (100.6 MHz, DMSO, *^{13}C*, *HSQC*, *HMBC*), δ (ppm) = 174.2 ($Q^{\delta CONNH2}$); 173.3 (R^{CONH2}); 171.9 (L^{CO}), 171.9 (P^{CO}); 170.0 (S^{CO}); 169.9 (T^{CO}), 169.8 (Q^{CO}); 169.7 (A^{CO}); 156.8 (R^{ξ}); 66.4 (T^{β}); 61.6 (S^{β}); 59.5 (P^{α}); 58.1 (T^{α}); 54.9 (S^{α}); 51.9 (R^{α}); 51.6 (L^{α}); 50.0 (Q^{α}); 48.1 (A^{α}); 46.9 (P^{δ}); 40.3 (R^{δ}); 40.1 (L^{β} (under the signal of DMSO)); 30.9 (Q^{γ}); 29.2 (P^{β}); 29.1 (R^{β}); 27.3 (Q^{β}); 25.1 (R^{γ}); 24.5 (P^{γ}); 24.2 (L^{γ}); 23.1 (L^{δ}); 21.5 ($L^{\delta'}$); 19.9 (T^{γ}); 17.3 (A^{β}).

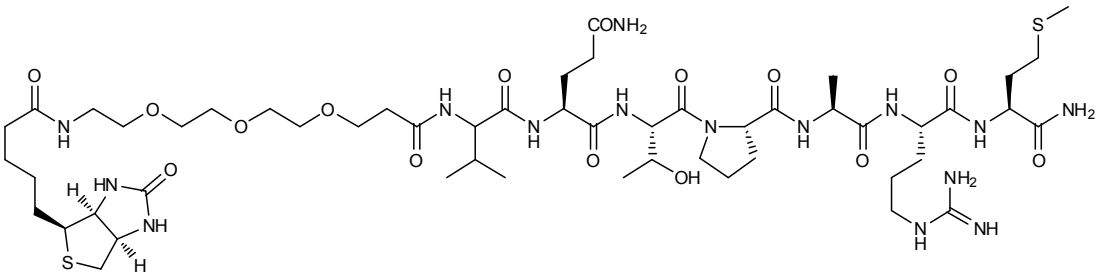
_N_-Biotinyl-12-amido-4,7,10-trioxa-dodecanoylamido-_L_-alanyl-_L_-seryl-_L_-threonyl-_L_-glutaminyl-_L_-prolyl-_L_-leucyl-_L_-arginylamide (Biotin-Pep8)



476 mg (0.1 mmol, loading: 0.21 mmol/g) of Fmoc-*L*-Arg(Pbf)-*RAM-Tentagel-S* resin were used in the synthesis as described above to yield 113 mg of crude peptide. The crude peptide was purified by *semi-preparative HPLC* (R_t = 23.5 min, JUPITER, methanol/water, grad. (5:95)→(40:60), 20 min; 10 min constant; λ = 214 nm) to yield 57 mg (47.5 µmol, 47%) as a colourless, amorphous solid. *Analyticyl HPLC*: R_t = 16.8 min (Phenomenex JUPITER, methanol/water, grad.: (5:95)→(40:60), 20 min; →(100:0), 10 min; λ = 214 nm); $[\alpha]_D^{20}$ (c = 0.93, MeOH/H_2O (1:1)) = -37.69 °; *ESI-MS* (positive ion mode) *m/z*: 600.83 ($[M+2H]^{2+}$, calcd.: 600.83); 611.81 ($[M+H+Na]^{2+}$, calcd.: 611.82); 619.80 ($[M+H+K]^{2+}$, calcd.: 619.81); 1200.65 ($[M+H]^{+}$, calcd.:
00.64); *HR-ESI-MS* (positive ion mode) *m/z*: calcd. for $C_{51}H_{90}N_{15}O_{16}S$: 1200.6411, found: 1200.6407 $[M+H]^{+}$; *^{1}H-NMR* (600 MHz, DMSO, *^{1}H*, COSY, TOCSY), δ (ppm) = 8.17-8.09 (m, 2H, A^{NH} {8.14}, L^{NH} {8.12}); 8.05 (d, $J_{SNH,S\alpha}$ = 7.4 Hz, 1H, S^{NH}); 7.93 (d, $J_{QNH,Q\alpha}$ = 7.7 Hz, 1H, Q^{NH}); 7.88 (t, $J_{SpacerNH,Spacer-H12}$ = 5.7 Hz, 1H, Spacer-NH); 7.77 (d, $J_{RNH,R\alpha}$ = 8.1 Hz, 1H, R^{NH}); 7.65 (d, $J_{TNH,T\alpha}$ = 8.4 Hz, 1H, T^{NH}); 7.31 (s, 1H, $Q^{\delta CONH2a}$); 7.23 (s, 1H, R^{CONH2a}); 7.12 (s, 1H, R^{CONH2b}); 6.88 (s, 1H, $Q^{\delta CONH2b}$); 6.46 (s, 1H, Biotine-NH3); 6.39 (s, 1H, Biotine-NH1); 5.16 (t, $J_{SOH,S\beta}$ = 5.5 Hz, 1H, S^{OH}); 4.89 (d, $J_{TOH,T\beta}$ = 5.4 Hz, 1H, T^{OH}); 4.48 (pq, J = 7.5 Hz, 1H, Q^{α}); 4.36-4.27 (m, 4H, S^{α} {4.33}, A^{α} {4.32}, Biotine-H8 {4.30}, P^{α} {4.29}); 4.19-4.10 (m, 4H, T^{α} {4.17}, L^{α} {4.16}, Biotine-H4 {4.12}, R^{α} {4.12}); 4.03 (dq, $J_{T\beta,T\alpha}$ = 9.6 Hz, $J_{T\beta,T\gamma}$ = 5.9 Hz, 1H, T^{β}); 3.64-3.52 (m, 6H, $S^{\beta a}$ {3.62}, P^{δ} {3.60}, Spacer-H3 {3.57}, $S^{\beta b}$ {3.54}); 3.50-3.45 (m, 8H, 4x Spacer-CH_2O); 3.38 (t, $J_{Spacer-H11,Spacer-H12b}$ = 5.9 Hz, 2H, Spacer-H11); 3.17 (pq, J = 5.8 Hz, 2H, Spacer-H12); 3.11-3.04 (m, 3H, Biotine-H5 {3.08}, R^{δ} {3.07}); 2.81 (dd, $J_{Biotine-H7a,Biotine-H7b}$ = 12.5 Hz, $J_{Biotine-H7a,Biotine-H8}$ = 5.1 Hz, 1H, Biotine-H7a); 2.57 (pd, $J_{Biotine-H7b,BiotineH7a}$ = 12.4 Hz, 1H, Biotine-H7b); 2.41-2.32 (m, 2H, Spacer-H2); 2.12 (t, $J_{Q\gamma,Q\beta a/b}$ = 7.7 Hz, 2H Q^{γ}); 2.10-2.00 (m, 3H, $P^{\beta a}$ {2.05}, Biotine-H12 {2.05}); 1.92-1.75 (m, 4H, $Q^{\beta a}$ {1.89}, P^{γ} {1.83}, $P^{\beta b}$ {1.80}); 1.74-1.56 (m, 4H, $R^{\beta a}$ {1.70}, $Q^{\beta b}$ {1.69}, L^{γ} {1.63}, Biotine-H9a {1.58}); 1.56-1.38 (m, 8H, $R^{\beta b}$ {1.52}, Biotine-H11 {1.51}, L^{β} {1.47}, Biotine-H9b {1.44}, R^{γ} {1.42}); 1.35-1.22 (m, 2H, Biotine-H10); 1.19 (d, $J_{A\beta,A\alpha}$ = 7.1 Hz, 3H, A^{β}); 1.02 (d, $J_{T\gamma,T\beta}$ = 6.3 Hz, 3H, T^{γ}); 0.88 (d, $J_{L\delta,L\gamma}$ = 6.5 Hz, 3H, L^{δ}); 0.82 (d, $J_{L\delta',L\gamma}$ = 6.5 Hz, 3H $L^{\delta'}$); *^{13}C-NMR* (150.9 MHz, DMSO, *13C*, *HSQC*, *HMBC*), δ (ppm) = 174.4 ($Q^{\delta CONH2}$); 173.4 (R^{CONH2}); 172.7 (A^{CO}); 173.4 (Biotine-

CO); 2x 172.1 (P^{CO}, L^{CO}); 170.3 (S^{CO}); 170.2 (Spacer-CO); 2x 170.0 (T^{CO}, Q^{CO}); 162.9 (Biotine-C2); 156.8 (R^{ξ}); 2x 69.8, 69.7, 69.6 (4x Spacer-*C*H_2O); 69.3 (Spacer-C11); 66.8 (Spacer-C3); 66.5 (T^{β}); 61.6 (S^{β}); 61.2 (Biotine-C4); 59.7 (P^{α}); 59.3 (Biotine-C8); 58.2 (T^{α}); 55.6 (Biotine-C5); 55.0 (S^{α}); 52.0 (R^{α}); 51.7 (L^{α}); 50.2 (Q^{α}); 48.2 (A^{α}); 47.0 (P^{δ}); 40.4 (R^{δ}); 40.1 (L^{β}); 40.0 (Biotine-C7); 38.6 (Spacer-C12); 35.9 (Spacer-C2); 35.2 (Biotine-C12); 31.0 (Q^{γ}); 29.3 (P^{β}); 29.1 (R^{β}); 28.3 (Biotine-C10); 28.1 (Biotine-C9); 27.2 (Q^{β}); 25.4 (Biotine-C11); 25.1 (R^{γ}); 24.6 (P^{χ}); 24.3 (L^{γ}); 23.2 (L^{δ}); 21.6 ($L^{\delta`}$); 20.0 (T^{γ}); 18.4 (A^{β}).

_N_-Biotinyl-12-amido-4,7,10-trioxa-dodecanoylamido-_L_-valyl-_L_-glutaminyl-_L_-threonyl-_L_-prolyl-_L_-alanyl-_L_-arginyl-_L_-methionylamide (Biotine-Pep3)



417 mg (0.1 mmol, loading: 0.24 mmol/g) of Fmoc-*L*-Met-*RAM-Tentagel-S* resin were used in the synthesis as described above to yield 122 mg of crude peptide. The crude peptide was purified by *semi-preparative HPLC* (R_t = 25.4 min, JUPITER, methanol/water, grad. (5:95)→(40:60), 20 min; 20 min constant; λ = 214 nm) to yield 72 mg (58.5 µmol, 59%) as a colourless, amorphous solid. *Analytical HPLC*: R_t = 18.7 min (Phenomenex JUPITER, methanol/water, grad.: (5:95)→(40:60), 20 min; →(100:0), 10 min; λ = 214 nm); $[\alpha]_D^{21}$ (c = 0.99, MeOH/H_2O (1:1)) = -42.40 °; *ESI-MS* (positive ion mode) *m/z*: 423.52 ($[M+2H+K]^{3+}$, calcd.: 423.54); 615.82 ($[M+2H]^{2+}$, calcd.: 615.82); 626.81 ($[M+H+Na]^{2+}$, calcd.: 626.81); 634.79 ($[M+H+K]^{2+}$, calcd.: 634.80); 1230.59 ($[M+H]^{+}$, calcd.: 1230.63); *HR-ESI-MS* (positive ion mode) *m/z*: calcd. for $C_{52}H_{92}N_{15}O_{15}S_2$: 1230.6339, found:, 1230.6366 $[M+H]^{+}$; *^{1}H-NMR* (600 MHz, DMSO, *^{1}H*, *COSY*, *TOCSY*), δ (ppm) = 8.11 (d, $J_{ANH,A\alpha}$ = 6.6 Hz, 1H, A^{NH}); 8.08 (d, $J_{QNH,Q\alpha}$ = 7.7 Hz, 1H, Q^{NH}); 7.95-7.88 (m, 2H, R^{NH} {7.91}, V^{NH} {7.91}); 7.89-7.84 (m, 3H, Spacer-NH {7.87}, T^{NH} {7.86}, M^{NH} {7.86}); 7.58 (t, $J_{R\varepsilon NH,R\delta}$ = 5.8 Hz, 1H, $R^{\varepsilon NH}$); 7.31 (s, 1H, M^{CONH2a}); 7.27 (s, 1H, $Q^{\delta CONH2a}$); 7.11 (s, 1H, M^{CONH2b}); 6.79 (s, 1H, $Q^{\delta CONH2b}$); 6.47 (s, 1H, Biotine-NH3); 4.39 (pt, J = 6.9 Hz, 1H, T^{α}); 4.35-4.10 (m, 8H, P^{α} {4.31}, Biotine-H8 {4.31}, Q^{α} {4.28}, M^{α} {4.24}, R^{α} {4.19}, V^{α} {4.16}, A^{α} {4.15}, Biotine-H4 {4.12}); 3.88-3.79 (m, 1H, T^{β}); 3.75-3.68 (m, 1H, $P^{\delta a}$); 3.67-3.59 (m, 1H, $P^{\delta b}$); 3.60-3.53 (m, 2H, Spacer-H3); 3.51-3.45 (m, 8H, 4x Spacer-CH_2O); 3.38 (t, $J_{Spacer\text{-}H11,Spacer\text{-}H12}$ = 5.9 Hz, 2H, Spacer-H11); 3.17 (pq, J = 5.8 Hz, 2H, Spacer-H12); 3.11-3.05 (m, 3H, Biotine-H5 {3.08}, R^{δ} {3.07}); 2.81 (dd, $J_{Biotine\text{-}H7a,Biotine\text{-}H7b}$ = 12.5 Hz, $J_{Biotine\text{-}H7a,Biotine\text{-}H8}$ = 5.1 Hz, 1H, Biotine-H7a); 2.57 (pd, $J_{Biotine\text{-}H7b,Biotine\text{-}H7a}$ = 12.4 Hz, 1H, Biotine-H7b); 2.49-2.31 (m, 4H, Spacer-H2 {2.40}, M^{γ} {2.40}); 2.12-1.99 (m, 8H, Q^{γ} {2.07}, Biotin-H12 {2.06}, $P^{\beta a}$ {2.03}, M^{ε} {2.02}); 1.97-1.64 (m, 9H, $M^{\beta a}$ {1.99}, V^{β} {1.93}, P^{γ} {1.85}, $Q^{\beta a}$ {1.84}, $P^{\beta b}$ {1.80}, $M^{\beta b}$ {1.77}, $R^{\beta a}$ {1.70}, $Q^{\beta b}$ {1.67}); 1.64-1.40 (m, 7H, Biotine-H9a {1.60}, $R^{\beta b}$ {1.54}, Biotine-H11 {1.49}, R^{γ} {1.45}, Biotine-H9b {1.43}); 1.35-1.17 (m, 5H, Biotine-H10 {1.28} A^{β} {1.20}); 1.09 (d, $J_{T\gamma,T\beta}$ = 6.3 Hz, 3H, T^{γ}); 0.83 (d, $J_{V\gamma,V\beta}$ = 6.7 Hz, 3H, V^{γ}); 0.81 (d, $J_{V\gamma`,V\beta}$ = 6.8 Hz, 3H, $V^{\gamma`}$); *^{13}C-NMR* (150.9 MHz, DMSO, *13C*, *HSQC*, *HMBC*), δ (ppm) = 174.0 ($Q^{\delta CONH2}$); 173.1 (M^{CONH2}); 172.6 (A^{CO}); 172.3 (Biotine-CO); 171.8 (P^{CO}); 171.4 (Q^{CO}); 2x 171.2 (R^{CO}, V^{CO}); 170.5 (Spacer-CO); 169.1 (T^{CO}); 162.9 (Biotine-C2); 156.8 (R^{ξ}); 2x 69.8, 69.6, 69.5 (4x Spacer-*C*H_2O); 69.2 (Spacer-C11); 67.0 (Spacer-C3); 66.9 (T^{β}); 61.2 (Biotine-C4); 59.5 (P^{α}); 59.3 (Biotine-C8); 57.7 (V^{α}); 56.6

(T^{α}); 55.6 (Biotine-C5); 52.4 (R^{α}); 52.0 (Q^{α}); 51.8 (M^{α}); 48.8 (A^{α}); 47.5 (P^{δ}); 40.5 (R^{δ}); 40.1 (Biotine-C7); 38.6 (Spacer-C12); 36.0 (Spacer-C2); 35.2 (Biotine-C12); 31.8 (M^{β}); 31.5 (Q^{γ}); 30.6 (V^{β}); 29.7 (M^{γ}); 29.2 (P^{β}); 28.8 (R^{β}); 28.3 (Biotine-C10); 28.1 (Biotine-C9); 28.0 (Q^{β}); 25.4 (Biotine-C11); 25.0 (R^{γ}); 24.6 (P^{γ}); 19.4 (V^{γ}); 19.3 (T^{γ}); 18.2 ($V^{\gamma`}$); 17,6 (A^{β}); 14.7 (M^{ε}).