Supporting Information

Twists or Turns: stabilising alpha vs beta turns in tetrapeptides

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1. General

Abbreviations: BOP, benzotriazol-1-yloxy-tris(dimethylamino)-phosphonium; DCM, dichloromethane; DIPEA, N,N-diisopropylethylamine; DMF, N,N-dimethylformamide; ESMS, electrospray mass spectrometry; HATU, 2-(1H-7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uranium hexafluorophosphate methanaminium; HBTU, benzotriazol-1-yl-1,1,3,3-tetramethyluronium; NMR, Nuclear Magnetic Resonance Spectroscopy; TFA, trifluoroacetic acid.

Fmoc-Asp(OPip)-OH was obtained from Bachem (Bubendorf, Switzerland). Fmoc-Lys(Mtt)-OH, other L-amino acids, Rink amide MBHA LL, and Rink Amide MBHA resins were obtained from Novabiochem (Melbourne, Australia). Benzotriazol-1-yl-1,1,3,3-tetramethyluronium (HBTU) and benzotriazol-1-yloxy-tris(dimethylamino)-phosphonium (BOP) were obtained from Iris Biotech (Germany). Dimethylformamide, diisopropylethylamine, trifluoroacetic acid other reagents were of peptide synthesis grade and obtained from Auspep (Melbourne, Australia).

2. Peptide Synthesis

2.1 Peptide assembly

Protected amino acids and resins were obtained from ChemImpex and Novabiochem . TFA, piperidine, DIPEA, DCM and DMF (peptide synthesis grade were reagent grade unless otherwise stated. Peptides were synthesized using Fmoc solid support chemistry on Rink amide resin (low loading 0.38 mmol/g; Novabiochem) at a 100 μM scale on a Symphony Multiplex Synthesizer. Amino acids (4 eq.) were activated using HCTU (4 eq.) and DIPEA (8 eq.) in DMF (2 × 20 min) prior to remove N-terminal Fmoc protecting group using 20% piperidine in DMF (2 × 5 min).

2.2 Cyclisation

Formation of lactam constraints was conducted on or off resin. For peptides **22-30** on resin cyclisation was used. Side-chain protecting groups of aspartic or glutamic acid and lysine, ornithine, diaminobutyric acid (Dab) or diaminopropionic acid (Dap) were first removed. Phenylisopropyl (OPip) esters and methyl trityl (Mtt) protecting groups were removed by allowing 5 × 10 mL portions of 3% TFA in DCM to drip through the resin. The resin was then wash with 2 × 10 mL portions of DCM, 2 × 10 mL portions of DMF and 2 × 10 mL portions of 5% DIPEA in DMF. For D-aspartate and D-glutamate containing peptides **28** and **29** Fmoc-D-Asp(OAllyl)-OH and Fmoc-D-Glu(OAllyl)-OH were used. Allyl esters were removed by treating the peptide resin with $Pd(PPh_3)_4$ (5 mol%) N,N-dimethylbarbituric acid (5eq) in DCM under argon for two hours, repeating the procedure a

second time. Cyclization was achieved on peptide-resin with BOP or PyBOP (2 eq), DIPEA (2 eq), HOAt (2eq) in DMF overnight at room temperature with periodic nitrogen bubbling to mix. For peptides 1-16, off resin cyclisation was used. Asp/Glu were protected with tBu esters and Lys/Orn/Dab/Dap were protected with Boc carbamates. After linear assembly, the tetrapeptides were cleaved normally. After lyophilisation, peptides were redissolved in DMF to a concentration of 0.1 M and treated with BOP (2 eq) and DIPEA (2eq) and heated at 60 ^{o}C overnight with stirring under nitrogen. DMF was then removed in vacuo and peptide residues redissolved in acetonitrile/water 1:1 and lyophilised for purification.

For isoaspartate cyclic peptides **31**-**32**, linear peptides were assembled incorporating Fmoc-Dap(Mtt)-OH and keeping the final Fmoc group on the N-terminus. Whilst still on resin, Mtt protecting groups were removed from Dap side chains and Fmoc-(L-or D-)-Asp(OAll)-OH was coupled onto the Dap side chain γ-amino through its α-carboxyl. Next, the β-carboxyl allyl ester was removed using the previously described conditions followed by simulataneous deprotection of the N-terminal Fmoc group and the aspartate Fmoc group with 20% piperidine in DMF. The peptide was then cyclised with BOP (2eq), DIPEA(2eq) and HOAt (2eq) overnight at room temperature. The peptide resin was then washed with DMF (2 × 10 mL) and treated with acetic anhydride (5eq), DIPEA (5eq) in DMF to acetylate the aspartate α-amino group. The isoaspartate cyclic tetrapeptide is formed selectively as cyclisation of the aspartate β-carboxyl onto the aspartate α-amino group would result in a highly unfavourable four membered lactam.

For succinate and glutarate cyclised peptides **33** and **34**, linear peptides were assembled incorporating Fmoc-Dap(Mtt)-OH and with removal of the final N-terminal Fmoc group. Succinic or glutaric anhydride (2eq) and DIPEA (2eq) were coupled onto the resin twice for 2 h at room temperature. The resin was washed with DMF (2 × 10 mL) and then treated twice with water (10 eq) and DIPEA (10 eq) in DMF for 1 h to hydrolyse any succinic or glutaric polyanhydrides formed during coupling. Then the Mtt group on the side chain of Dap was removed with the usual conditions, the resin was washed and cyclised as described previously.

2.3 Cleavage

Peptides were cleaved from the resin using TFA/TIPS/H_2O (95/2.5/2.5) for 2 h. Solutions were filtered from the resin and the cleavage mixture removed *in vacuo*. The resulting residues treated with ice-cold diethyl ether to precipitate the peptides. Ether was removed by decanting. The crude peptides were dried under nitrogen, dissolved in acetonitrile-water (1:1) and lyophilised. Crude peptides were purified by reverse-phase HPLC on Waters 486 system equipped with a Rheodyne semi-preparative injector with a 5 mL loop volume on a Phenomenex Luna C18 15 μm column, 250 mm x 22 mm, at

20 mL/min using linear gradient elution (solvent A is water and 0.1% TFA; solvent B is 90% MeCN, 10% water, and 0.1% TFA) and UV detection at 214 nm.

2.4 HPLC-MS Characterization

Purity of compounds assessed via analytical rpHPLC (Waters 996 on a Phenomenex Luna C18 5 μm column, 250 x 4 mm (**condition A**) or on a Varian Pursuit C8 5 μm column, PN A 3030-250x046 (**condition B**) or on a Agilent Technologies 1200 Seires on a Phenomenex Luna C8 5 μm column, 250 x 4.60 mm (**condition C**), at 1 mL/min by using a linear gradient 0-100%B over 20 mins), or analytical UHPLC-MS method: Schimadzu HPLC system Waters Acquity UPLC HSS T3 column, 1.8 μm, 2.1 mm × 50 mm – gradient 0-100% solvent B (H_2O/MeCN 10/90 with 0.05% TFA) in solvent A (H_2O with 0.05% TFA) over 6 min at 0.4 mL/min, (**condition D**) mass spectrometry, and NMR. The molecular weight of the peptides (1 mg/mL) was determined by electrospray mass spectrometry on a Micromass LCT mass spectrometer and by HRMS. Note different retention times between Waters and Agilent analytical HPLCs come from the different equilibration times used (10 min for Waters, 3 min for Agilent).

3. CD spectroscopy

CD measurements were performed using a Jasco model J-710 spectropolarimeter which was routinely calibrated with (1*S*)-(+)-10-camphorsulfonic acid. A stock solution of 1–5 mg of peptide was dissolved in 600 μL of 18 MΩ deionised water, 60 μL D_2O and 10 μL of 50 mM TSS was added as an internal standard. Accurate concentrations of these solutions were then determined using the PULCON method (Dreier, L. and G. Wider, *Concentration measurements by PULCON using X-filtered or 2D NMR spectra.* Magn Reson Chem, **2006**. 44 Spec No: p. S206-12.). 90° pulses were accurately determined and then 1D Spectra were acquired using the standard watergate sequence with a ns= 16, d1= 30s to ensure complete relaxation of proton signals. Integration of well resolved signals compared to the internal TSS standard were used to determine concentration of peptide solutions using the following equation:

$$[Peptide] = [DSS] \times \left(\frac{Integral_{Peptide} \times \#H_{DSS}}{Integral_{DSS} \times \#H_{peptide}} \right) \qquad (Eq.\ 1)$$

where [*Peptide*] is the peptide concentration, [*DSS*] is the concentration of DSS in the NMR tube (746 μM). *#H* is the number of protons corresponding to the *Integral* (in absolute units) for the peptide signal or DSS signal.

An appropriate amount of the NMR stock solutions was then used to prepare the CD solution making up the difference with 10 mM Phosphate Buffer (pH 7.4) and TFE. Spectra were recorded at room

temperature (298K), with a 0.1 cm Jasco quartz cell over the wavelength range 260-185 nm at 50 nm/min, with a bandwidth of 1.0 nm, response time of 1 s, resolution step width of 1 nm and sensitivity of 20-50 Mdeg. Each spectrum represents the average of 5 scans. Spectra were analysed using the spectral analysis software and smoothed using 'adaptive smoothing' function.

4. NMR Spectroscopy

1D and 2D ^{1}H-NMR spectra were recorded on a Bruker Avance III DRX-600 spectrometer with Cryo-Probe. 2D ^{1}H-spectra were recorded in phase-sensitive mode using time-proportional phase incrementation for quadrature detection in the *t*1 dimension. The 2D experiments included TOCSY (standard Bruker mlevgpph pulse program), ROESY (standard Bruker roesygpph pulse program), NOESY and dqfCOSY (standard Bruker dqfcosygpph pulse program). TOCSY spectra were acquired over 6887 Hz with 2048 complex data points in *F2*, 256 increments in *F1* and 8 scans per increment. ROESY and NOESY spectra were acquired over 6887 Hz with 4096 complex data points in *F2*, 512 increments in *F1* and 32 scans per increment. TOCSY, ROESY and NOESY spectra were acquired with several isotropic mixing times of 80 ms for TOCSY, 350 ms for ROESY. For all NMR experiments, water suppression was achieved using modified WATERGATE. For 1D ^{1}H NMR spectra acquired in H_2O/D_2O (9:1), the water resonance was suppressed by low power irradiation during the relaxation delay (1.5 to 3.0 s). The variable temperature NMR experiments were performed in 10^{o}C increments over the range of 278-318K. Spectra were processed using Topspin (Bruker, Germany). The *t*1 dimensions of all 2D spectra were zero-filled to 1024 real data points with 90˚ phase-shifted QSINE bell window functions applied in both dimensions followed by Fourier transformation and fifth order polynomial baseline correction. ^{1}H chemical shifts were referenced to DSS (δ 0.00 ppm) in water. $^{3}J_{NHCH\alpha}$ coupling constants were measured from 1D ^{1}H NMR and dqf-COSY spectra. Sparky NMR was used to analyse 2D spectra and determine ROE peak volumes.

5. Structure Calculations

Distance restraints used in calculating the structure for peptides in water were derived from ROESY (for peptides **5, 6, 7, 9, 13, 15, 17, 18, 21, 20, 21, 22, 23, 24**) spectra (recorded at 288K or 298K) using mixing time of 300ms. ROE cross-peak volumes obtained from SparkyNMR ensuring accurate gaussiuan peak fitting. Volumes were converted to distances using the relationship:

$$Distance = \log_6(constant \times Volume) \quad \text{(Eq. 2)}$$

The *constant* was first derived using the volume of two known vicinal protons e.g. two Hβ protons in Asp set at a distance of 2.24 Å. When the derived *constant* was applied to Eq. 2 to determine distances, the strongest ROEs gave a distance of 2.7 Å, which is equivalent to the standard manual

binning technique (i.e. setting strong ROEs with an upper distance limit of 2.7 Å). All weaker ROE volumes then scaled accordingly up to a maximum of ~6.5 Å. This standardised ROE intensities and removed human error associated with manual classification. Standard pseudoatom distance corrections were applied for non-stereospecifically assigned protons. To address the possibility of conformational averaging, intensities were classified conservatively and only upper distance limits were included in the calculations to allow the largest possible number of conformers to fit the experimental data. Backbone dihedral angle restraints were inferred from $^3J_{NH\text{-}CH\alpha}$ coupling constants in 1D spectra, ϕ was restrained to $-65 \pm 30°$ for $^3J_{NH\text{-}CH\alpha} \leq 6$Hz and to $-120 \pm 30°$ for $^3J_{NH\text{-}CH\alpha} \geq 8$Hz. There was clearly no evidence at all for *cis*-amides about peptide bonds (i.e. no CHα-CHα (*i*, *i+1*) ROEs) in the ROESY spectra so all ψ-angles were set to *trans* ($\psi = 180^\circ$). Starting structures with randomised ϕ and ψ angles and extended side chains were generated using an *ab initio* simulated annealing protocol. The calculations were performed using the standard forcefield parameter set (PARALLHDG5.2.PRO) and topology file (TOPALLHDG5.2.PRO) in XPLOR-NIH with in house modifications to generated lactam bridges Lys/Orn/Dab/Dap and Asp/Glu residues. Refinement of structures was achieved using the conjugate gradient Powell algorithm with 4000 cycles of energy minimisation and a refined forcefield based on the program CHARMm (Brooks, B. R.; Bruccoleri, R. E.; Olafson, B. D.; States, D. J.; Swaminathan, S.; Karplus, M. *J. Comput. Chem.* **1983**, *4,* 187). Structures were visualised with Pymol and analysed for distance (> 0.2Å) and dihedral angle (> 5°) violations using noe.inp files. Final structures contained no distance violations (> 0.2Å) or angle violations (> 5°).

6. Molecular Dynamics

All simulations were performed using Maetro simulation package. The force field topologies of the cyclic tetrapeptides were derived from the OPSL_2005 parameter set. The cyclic peptide was placed in a pre-equilibrated truncated octahedral box filled with 1038 SPC water molecules. The simulation was carried out at 298 K. After a steepest descent minimization step, the cyclic peptides were subjected to 100 ps of simulation with position restraints on the peptide to relax the solvent. The systems were subsequently equilibrated for 1 ns without restraints. The simulations were performed at constant temperature (298 K) and pressure (1 atm). This was achieved using a Berendsen thermostat with a coupling time of 0.1 ps and a Berendsen barostat with a coupling time of 0.5 ps. Nonbonded interactions were calculated using a twin-range cut-off. Interactions within the short-

range cut-off of 0.8 nm were updated every time step. Interactions within the longer-range cut-off of 1.4 nm were updated every 5 time steps together with the pairlist. All bonds were constrained using the SHAKE algorithm with a geometric tolerance of 0.0001. Initial velocities were taken from the Maxwell-Boltzmann distribution at 298 K and were acquired for 50 ns. Backbone (Cα) atom-positional RMSD values were calculated after translational superposition of centres of mass and least-squares rotational fitting of atomic positions.

Table S1. **ϕ, ψ angles for idealized α-turns.**

α-turn types	ϕ(*i*+1)°	ψ(*i*+1)°	ϕ(*i*+2)°	ψ(*i*+2)°	ϕ(*i*+3) °	ψ(*i*+3) °
0-α_{RS}[a]	-58	-47	-58	-47	-58	-47
0-α_{LS}[a]	58	47	58	47	58	47
$3_{10\text{-RS}}$	-60	-30	-60	-30	-60	-30
$3_{10\text{-LS}}$	60	30	60	30	60	30
I-α_{RS}	-60±11	-29±13	-72±14	-29±15	-96±20	-20±17
I-α_{LS}	48±22	42±14	67±9	33±14	70±11	32±12
II-α_{RS}	-59±10	129±15	88±15	-16±19	-91±22	-32±18
II-α_{LS}	53±15	-137±25	-95±12	81±23	57±5	38±8
I-α_{RU}	59±18	-157±31	-67±17	-29±20	-68±12	-39±12
I-α_{LU}	-61±12	158±15	64±17	37±21	62±12	39±8
II-α_{RU}	54±8	39±15	67±13	-5±31	-125±11	-34±32
II-α_{LU}	-65±15	-20±15	-90±17	16±44	86±18	37±27
I-α_{C}	-103±23	14±34	-85±8	2±6	-54±6	-39±9

[a] 0-α_{RS} and 0-α_{LS} are classical α-turns from α-helix; $3_{10\text{-RS}}$ and $3_{10\text{-LS}}$ are classical 3_{10}-turns from 3_{10}-helix; 9 other α-turn types [V. Pavone, G. Gaeta, A. Lombardi, F. Nastri, O. Maglio, C. Isernia, M. Saviano, *Biopolymers* **1996**, *38*, 705 - 721.]

Table S2. **ϕ, ψ angles for β-turns.**

β-turn types	ϕ(*i*+1)°	ψ(*i*+1)°	ϕ(*i*+2)°	ψ(*i*+2)°
β–I	-60	-30	-90	0
β–I’	60	30	90	0
β-II	-60	120	80	0
β-II’	-60	-120	-80	0
β-III	-60	-30	-60	-30
β-III’	60	30	60	30
β-VIa1	-60	120	-90	0
β-VIa2	-120	120	-60	0
β-VIb	-135	135	-75	160
β-VIII	-60	-30	-120	120
β-IV	-60	10	-50	20
γ-Classic	70 to 85	-60 to -70		
γ-Inverse	-70 to -85	60 to 70		

Table S3. Cyclic tetrapeptides examined in this study.

#	Peptide[a]	Ring Size
1	Ac-(cyclo-1,4)-[DapAAD]-NH_2	14
2	Ac-(cyclo-1,4)-[DabAAD]-NH_2	15
3	Ac-(cyclo-1,4)-[OAAD]-NH_2	16
4	Ac-(cyclo-1,4)-[KAAD]-NH_2	17
5	Ac-(cyclo-1,4)-[DAADap]-NH_2	14
6	Ac-(cyclo-1,4)-[DAADab]-NH_2	15
7	Ac-(cyclo-1,4)-[DAAO]-NH_2	16
8	Ac-(cyclo-1,4)-[DAAK]-NH_2	17
9	Ac-(cyclo-1,4)-[DapAAE]-NH_2	15
10	Ac-(cyclo-1,4)-[DabAAE]-NH_2	16
11	Ac-(cyclo-1,4)-[OAAE]-NH_2	17
12	Ac-(cyclo-1,4)-[KAAE]-NH_2	18
13	Ac-(cyclo-1,4)-[EAADap]-NH_2	15
14	Ac-(cyclo-1,4)-[EAADab]-NH_2	16
15	Ac-(cyclo-1,4)-[EAAO]-NH_2	17
16	Ac-(cyclo-1,4)-[EAAK]-NH_2	18
17	Ac-(cyclo-1,4)-[dAADap]-NH_2	14
18	Ac-(cyclo-1,4)-[eAADap]-NH_2	15
19	Ac-(cyclo-1,4)-[dAADab]-NH_2	15
20	Ac-(cyclo-1,4)-[dAAO]-NH_2	16
21	Ac-(cyclo-1,4)-[IsoDAADap]-NH_2	14
22	Ac-(cyclo-1,4)-[IsodAADap]-NH_2	14
23	(cyclo-1,4)-[SuccAADap]-NH_2	14
24	(cyclo-1,4)-[GlutAADap]-NH_2	15
25	Ac-(cyclo-1,5)-[KAAAD]-NH_2	20

[a] Dap = Diaminopropionic acid, Dab = Diaminobutyric acid, O = Ornithine, d = D-Asp, e = D-Glu, Isod = D-IsoAsp, Succ = Succinic acid, Glut = Glutaric acid.

Table S4. Peptide characterization data

#	Peptide	Formula	$[MH]^+$ calculated	$[M+XH]^+$ observed (HRMS)	R_t (min) / (Method)
1	Ac-(cyclo-1,4)-[DapAAD]-NH_2	$C_{15}H_{25}N_6O_6 + Na^+$	407.1650	407.1645	2.0 (D)
2	Ac-(cyclo-1,4)-[DabAAD]-NH_2	$C_{16}H_{27}N_6O_6^+$	399.1987	399.1987	11.7 (B)
3	Ac-(cyclo-1,4)-[OAAD]- NH_2	$C_{17}H_{29}N_6O_6^+$	413.2143	413.2147	11.9 (B)
4	Ac-(cyclo-1,4)-[KAAD]-NH_2	$C_{18}H_{31}N_6O_6^+$	427.2300	427.2303	12.1 (B)
5	Ac-(cyclo-1,4)-[DAADap]-NH_2	$C_{15}H_{25}N_6O_6 + Na^+$	407.1650	407.1649	2.1 (D)
6	Ac-(cyclo-1,4)-[DAADab]-NH_2	$C_{16}H_{27}N_6O_6^+$	399.1987	399.1986	12.1 (B)
7	Ac-(cyclo-1,4)-[DAAO]-NH_2	$C_{17}H_{29}N_6O_6^+$	413.2143	413.2147	12.2 (B)
8	Ac-(cyclo-1,4)-[DAAK]-NH_2	$C_{18}H_{31}N_6O_6^+$	427.2300	427.2300	7.7 (C)
9	Ac-(cyclo-1,4)-[DapAAE]-NH_2	$C_{16}H_{27}N_6O_6 + Na^+$	421.1806	421.1806	2.0 (D)
10	Ac-(cyclo-1,4)-[DabAAE]-NH_2	$C_{17}H_{29}N_6O_6^+$	413.2143	413.2142	12.0 (B)
11	Ac-(cyclo-1,4)-[OAAE]-NH_2	$C_{18}H_{31}N_6O_6^+$	427.2300	427.2307	6.8 (C)
12	Ac-(cyclo-1,4)-[KAAE]-NH_2	$C_{19}H_{33}N_6O_6^+$	441.2456	441.2453	7.1 (C)
13	Ac-(cyclo-1,4)-[EAADap]-NH_2	$C_{16}H_{27}N_6O_6^+$	399.1987	399.1987	2.1 (D)
14	Ac-(cyclo-1,4)-[EAADab]-NH_2	$C_{17}H_{29}N_6O_6^+$	413.2143	413.2143	12.0 (B)
15	Ac-(cyclo-1,4)-[EAAO]-NH_2	$C_{18}H_{31}N_6O_6^+$	427.2300	427.2300	5.9 (C)
16	Ac-(cyclo-1,4)-[EAAK]-NH_2	$C_{19}H_{33}N_6O_6^+$	441.2456	441.2456	12.2 (B)
17	Ac-(cyclo-1,4)-[dAADap]-NH_2	$C_{15}H_{25}N_6O_6 + Na^+$	407.1650	407.1650	2.1 (D)
18	Ac-(cyclo-1,4)-[eAADap]-NH_2	$C_{16}H_{27}N_6O_6 + Na^+$	421.1806	421.1807	2.2 (D)
19	Ac-(cyclo-1,4)-[dAADab]-NH_2	$C_{16}H_{27}N_6O_6 + Na^+$	421.1806	421.1808	2.1 (D)
20	Ac-(cyclo-1,4)-[dAAO]-NH_2	$C_{17}H_{29}N_6O_6^+$	413.2143	413.2140	2.0 (D)
21	Ac-(cyclo-1,4)-[IsoDAADap]-NH_2	$C_{15}H_{24}N_6O_6^+$	385.1830	385.1826	8.0 (C)
22	Ac-(cyclo-1,4)-[IsodAADap]-NH_2	$C_{15}H_{24}N_6O_6^+$	385.1830	385.1831	7.9 (C)
23	(cyclo-1,4)-[SuccAADap]-NH_2	$C_{13}H_{22}N_5O_5^+$	328.1621	328.1626	7.8 (C)
24	(cyclo-1,4)-[GlutAADap]-NH_2	$C_{14}H_{24}N_5O_5^+$	342.1772	342.1774	8.28 (C)

	Peptide	Formula	$[MH]^+$ calculated	$[M+XH]^+$ observed	R_t (min) / (Method)
27	Ac-(cyclo-1,4)-[DAADap](ARL)$_3$-NH_2	$C_{60}H_{111}N_{24}O_{15}^{3+}$	469.28	469.41 628.51	2.74 (D)
28	Ac-(cyclo-1,4)-[DAADab]](ARL)$_3$-NH_2	$C_{61}H_{113}N_{24}O_{15}^{3+}$	473.96	473.96 710.45	2.93 (D)
29	Ac-(cyclo-1,4)-[DAAO](ARL)$_3$-NH_2	$C_{62}H_{115}N_{24}O_{15}^{3+}$	478.63	478.21	2.78 (D)
30	Ac-(cyclo-1,4)-[DapAAE](ARL)$_3$-NH_2	$C_{61}H_{113}N_{24}O_{15}^{3+}$	474.24	474.21	2.74 (D)
31	Ac-(cyclo-1,4)-[EAADap](ARL)$_3$-NH_2	$C_{61}H_{113}N_{24}O_{15}^{3+}$	474.24	474.24	2.81 (D)
32	Ac-(cyclo-1,4)-[EAAO](ARL)$_3$-NH_2	$C_{63}H_{117}N_{24}O_{15}^{3+}$	483.30	483.81	2.80 (D)
33	Ac-(cyclo-1,4)-[dAADap](ARL)$_3$-NH_2	$C_{60}H_{111}N_{24}O_{15}^{3+}$	469.28	469.33 703.67	2.48 (D)
34	Ac-(cyclo-1,4)-[eAADap](ARL)$_3$-NH_2	$C_{61}H_{113}N_{24}O_{15}^{3+}$	474.24	474.32	2.71 (D)
35	Ac-(cyclo-1,4)-[dAAO](ARL)$_3$-NH_2	$C_{62}H_{115}N_{24}O_{15}^{3+}$	478.63	478.41	2.80 (D)
36	Ac-(cyclo-1,4)-[isoDAADap](ARL)$_3$-NH_2	$C_{60}H_{111}N_{24}O_{15}^{3+}$	469.28	469.32 703.67	2.55 (D)
37	Ac-(cyclo-1,4)-[isodAADap](ARL)$_3$-NH_2	$C_{60}H_{111}N_{24}O_{15}^{3+}$	469.28	469.30 703.78	2.59 (D)
38	Ac-(cyclo-1,4)-[Succ-AAD](ARL)$_3$-NH_2	$C_{58}H_{108}N_{23}O_{14}^{3+}$	450.28	450.28 674.78	2.74 (D)
39	Ac-(cyclo-1,4)-[Glut-AAD](ARL)$_3$-NH_2	$C_{59}H_{110}N_{23}O_{14}^{3+}$	448.95	448.70 682.02	2.59 (D)
40	Ac-(cyclo-1,4)-[KAAAD](ARL)$_3$-NH_2	$C_{66}H_{122}N_{25}O_{16}^{3+}$	506.98	506.31	2.67 (D)

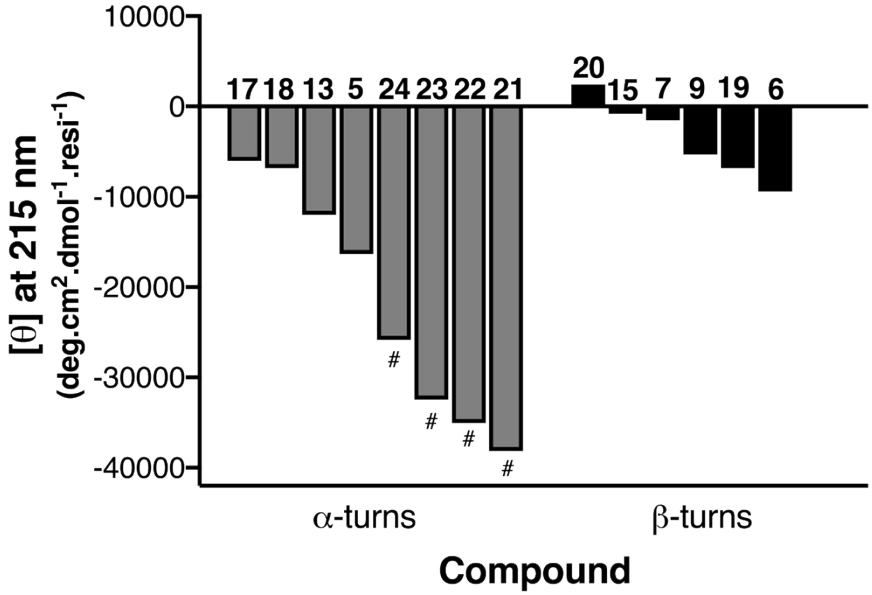

Figure S1. Molar ellipticity at λ = 215 nm for compounds mimicking alpha turns (**5**, **13**, **17**, **21**-**24**) versus beta turns (**6**, **7**, **9**, **15**, **19**, **20**) showing stronger circular dichroism absorbance for the alpha turn than the beta turn at 215 nm. (#) Compounds where the N-terminal acetyl-cap has been moved or removed.

7. NMR Data

7.1 1H NMR Spectra in H_2O:D_2O (9:1).

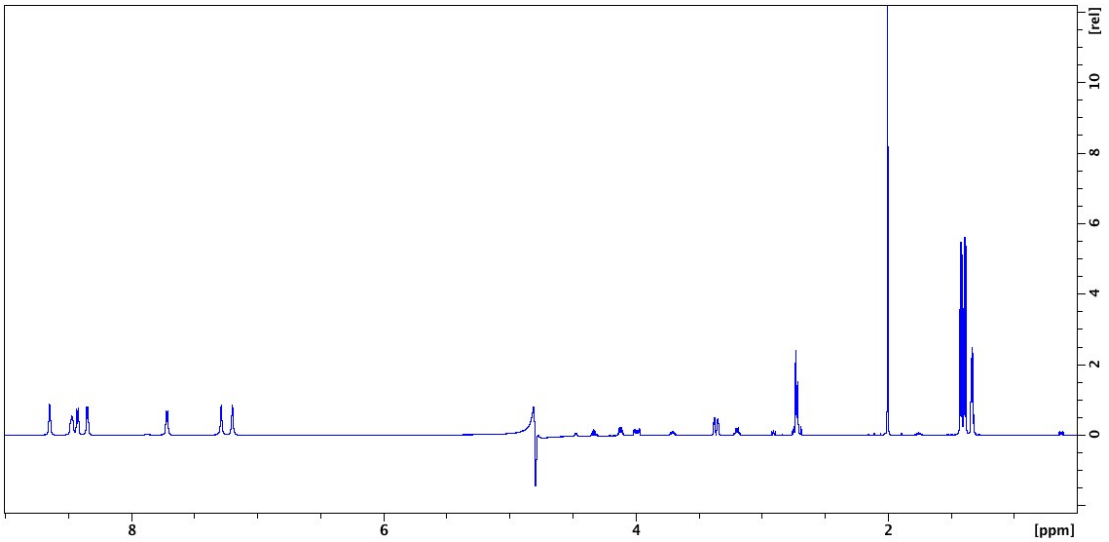

Figure 1. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DapAAD]-NH_2 **(1).**

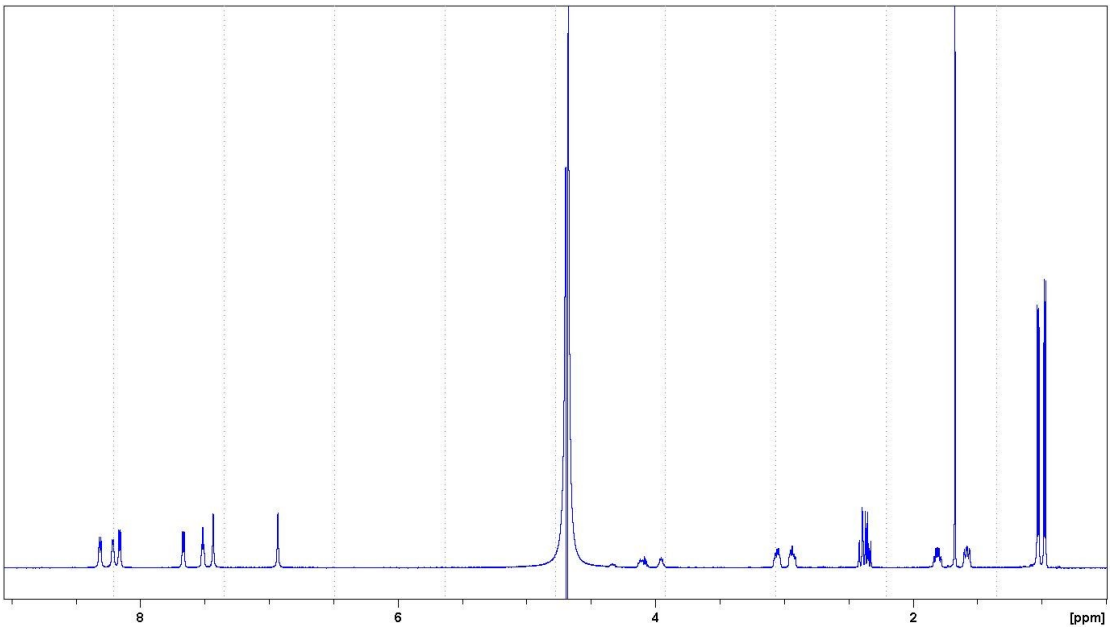

Figure 2. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DabAAD]-NH_2 **(2).**

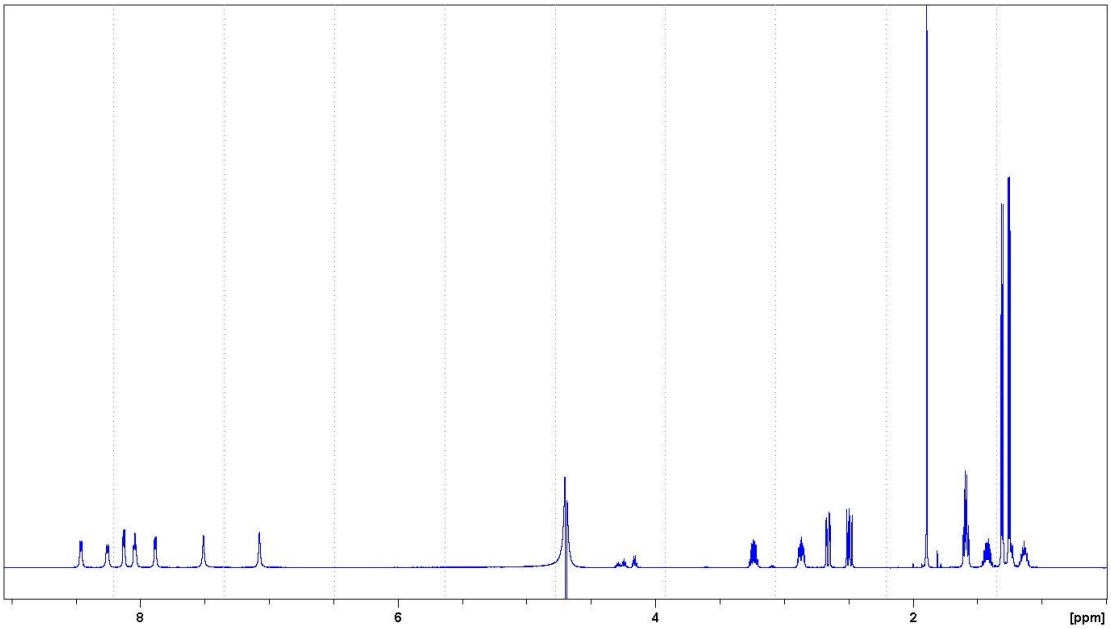

Figure 3. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[OAAD]-NH_2 **(3).**

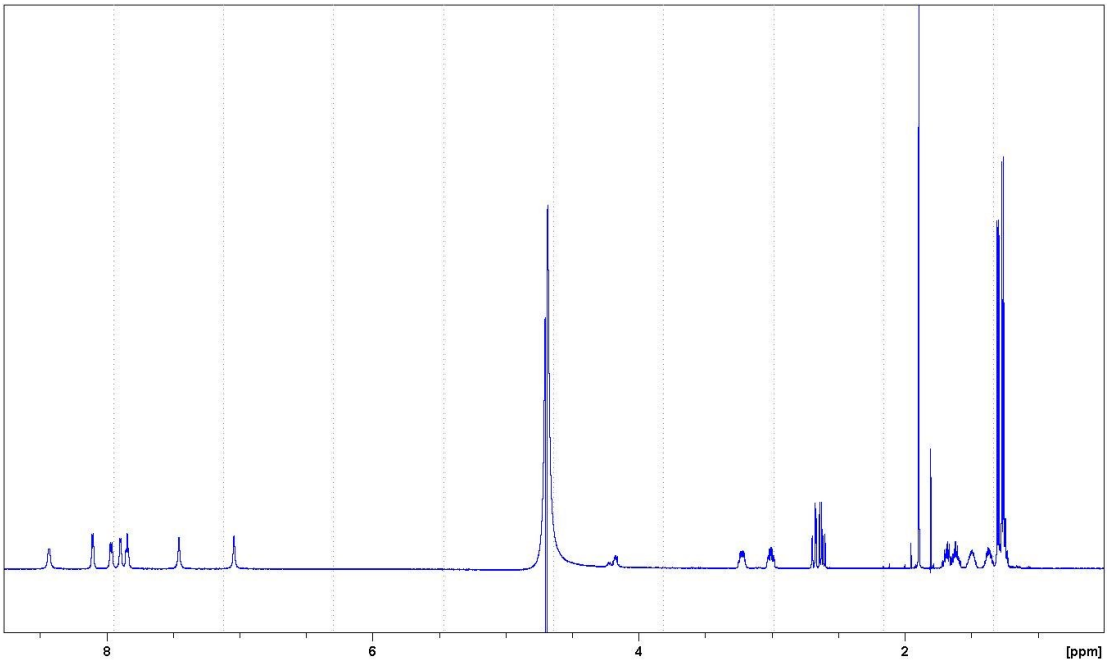

Figure 4. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[KAAD]-NH_2 (**4**).

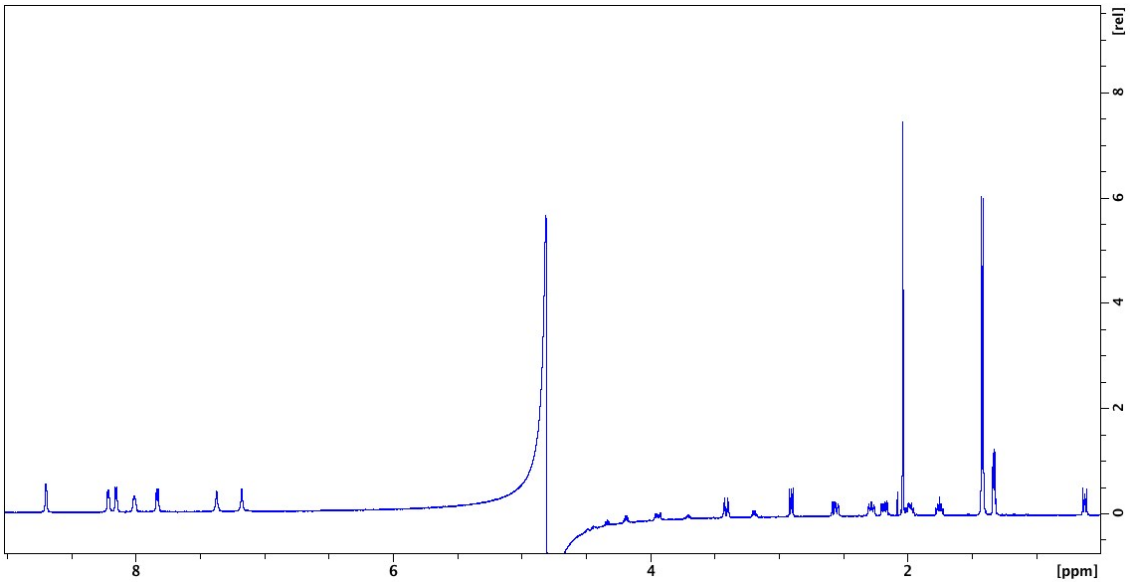

Figure 5. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DAADap]-NH_2 (**5**).

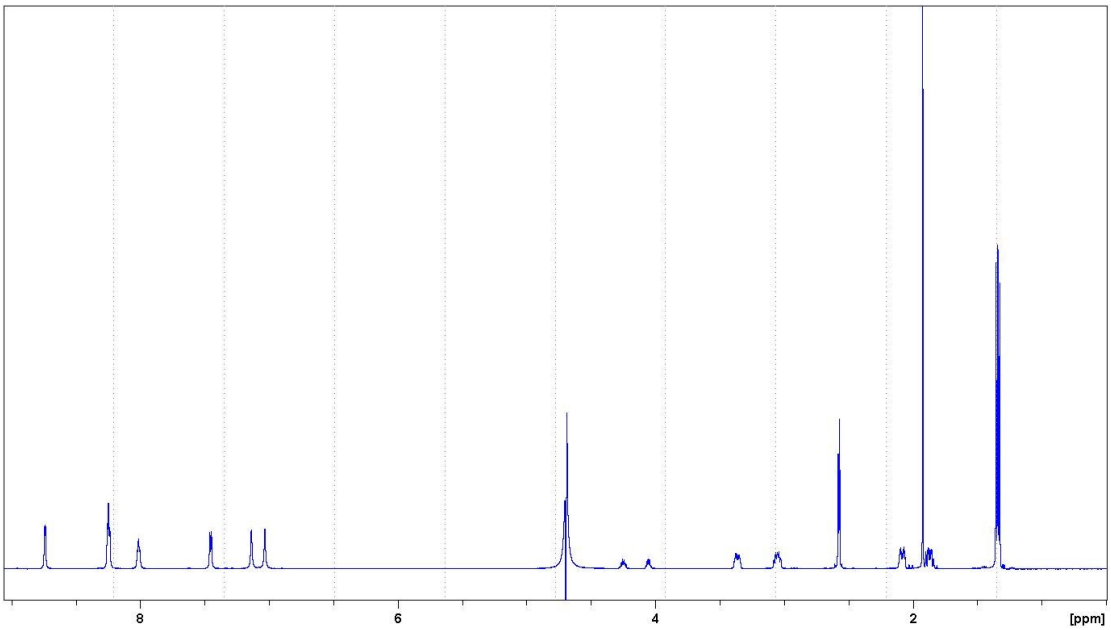

Figure 6. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DAADab]-NH_2 (**6**).

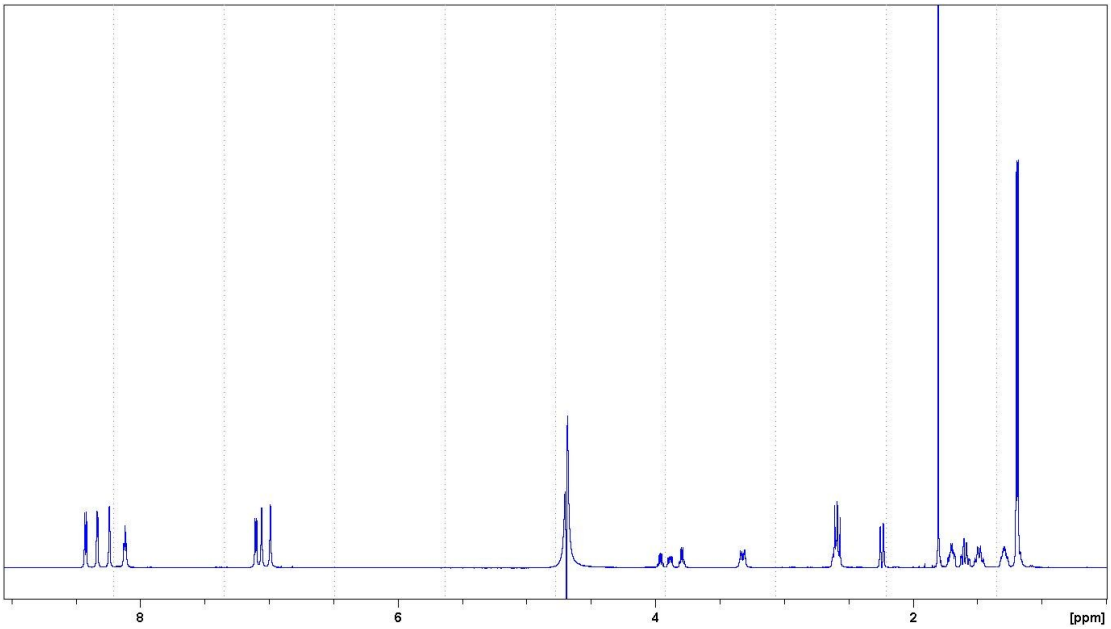

Figure 7. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DAAO]-NH_2 (**7**).

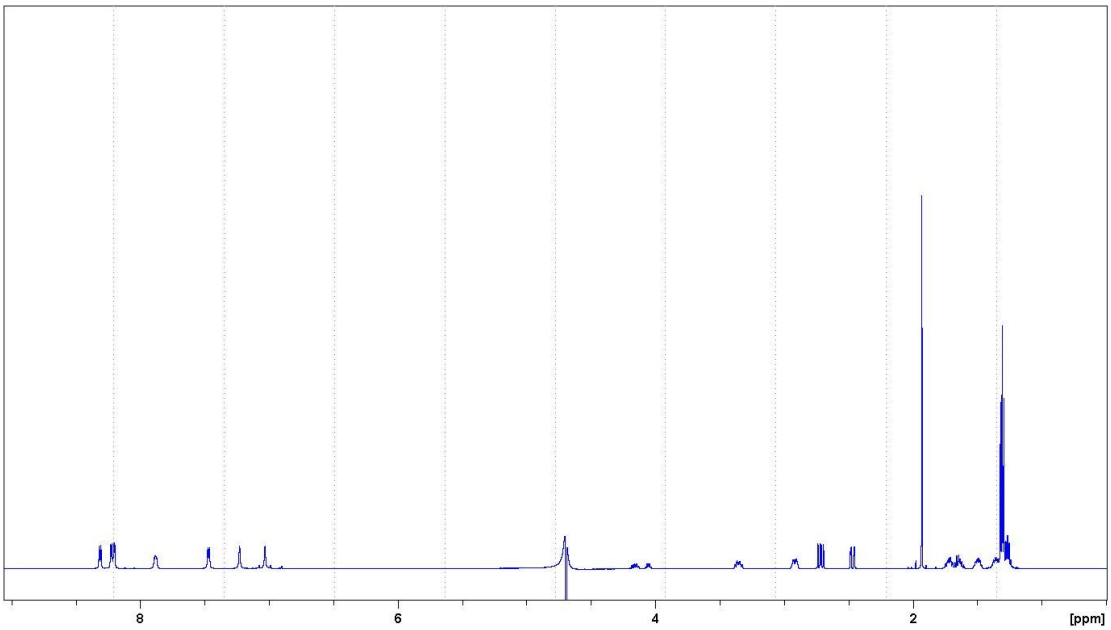

Figure 8. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DAAK]-NH_2 (**8**).

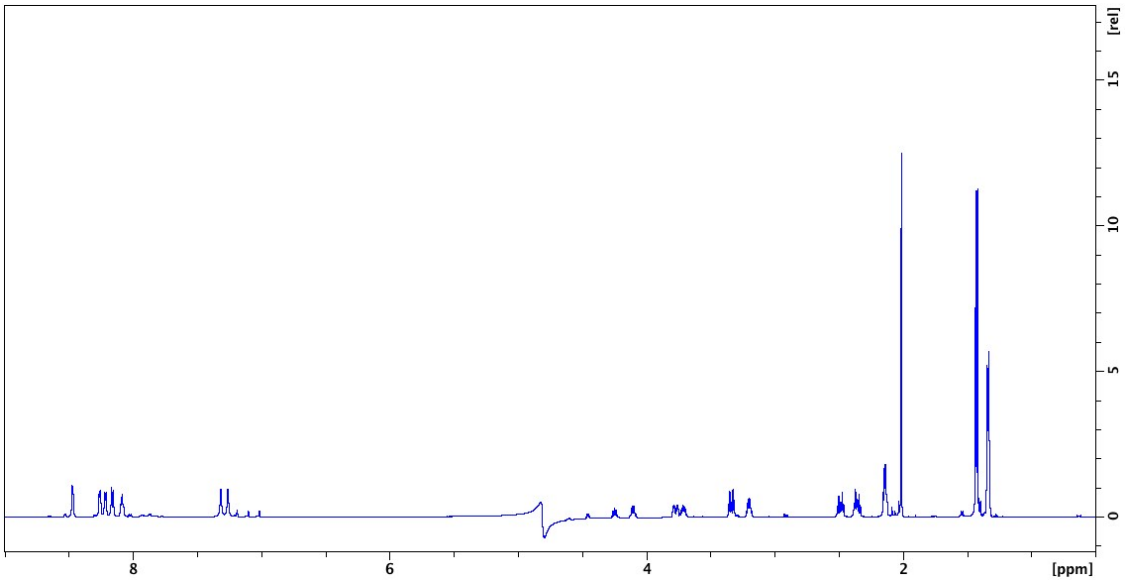

Figure 9. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DapAAE]-NH_2 (**9**).

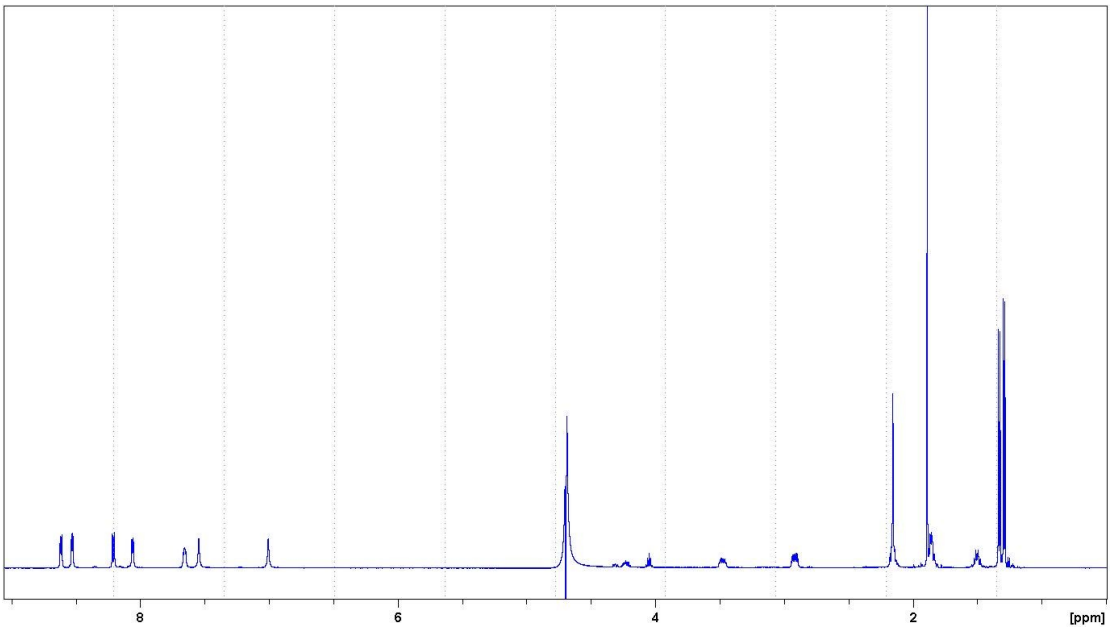

Figure 10. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[DabAAE]-NH_2 (**10**).

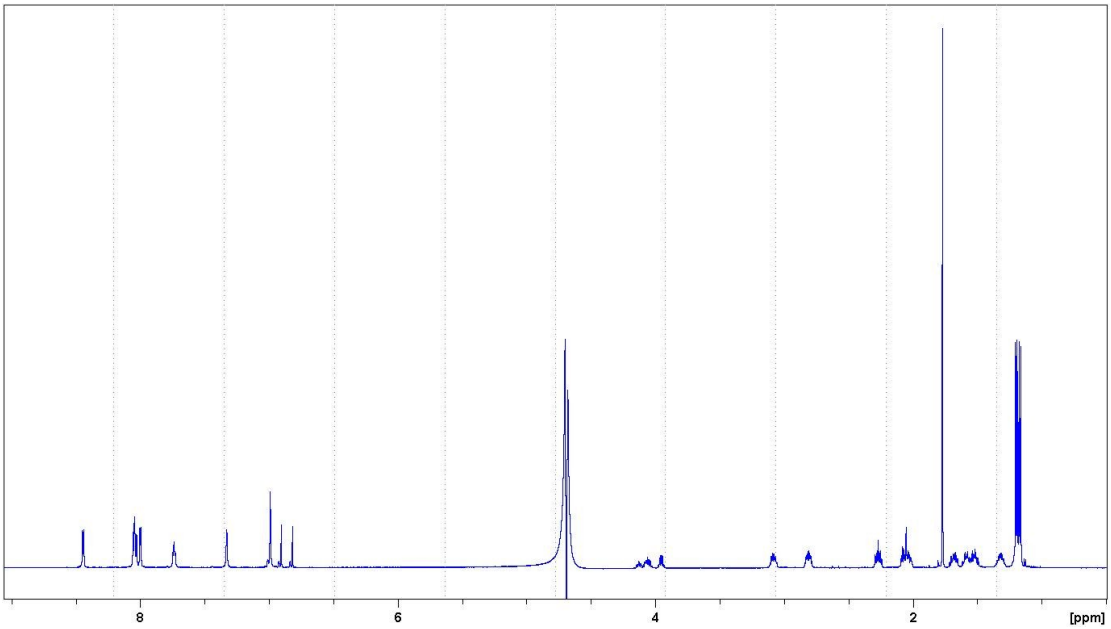

Figure 11. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[OAAE]-NH_2 (**11**).

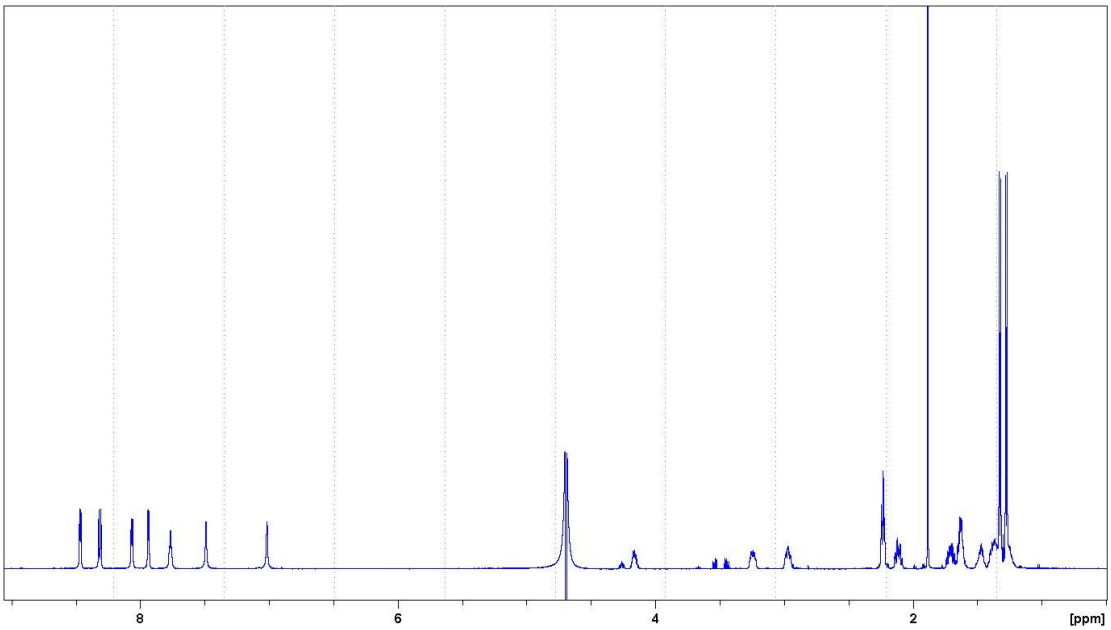

Figure 12. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[KAAE]-NH_2 (**12**).

Figure 13. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[EAADab]-NH_2 (**13**).

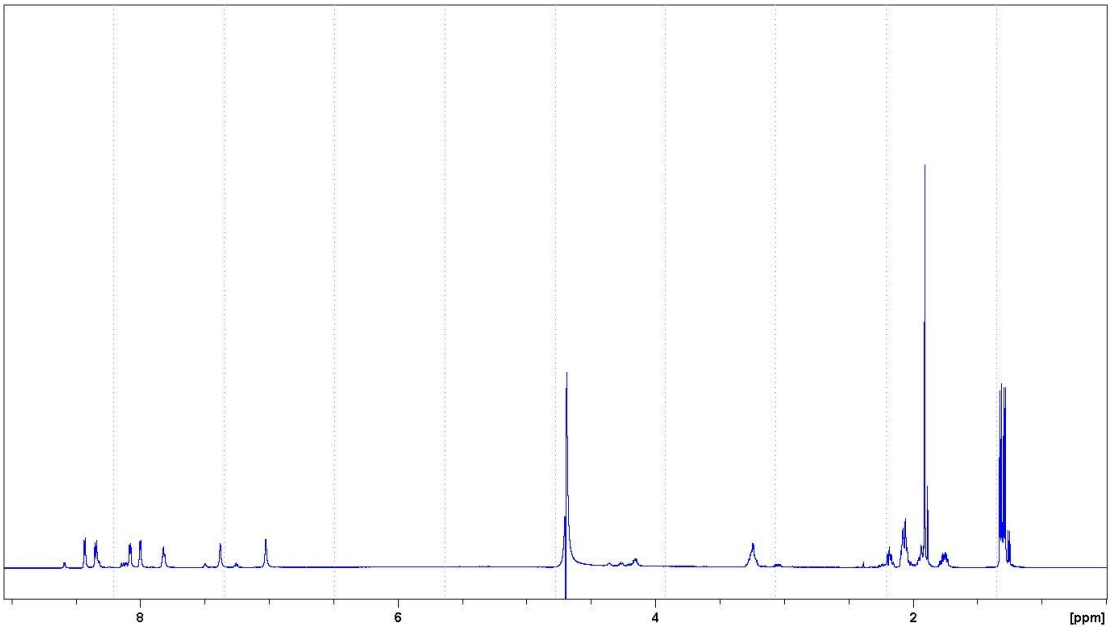

Figure 14. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[EAADab]-NH_2 (**14**).

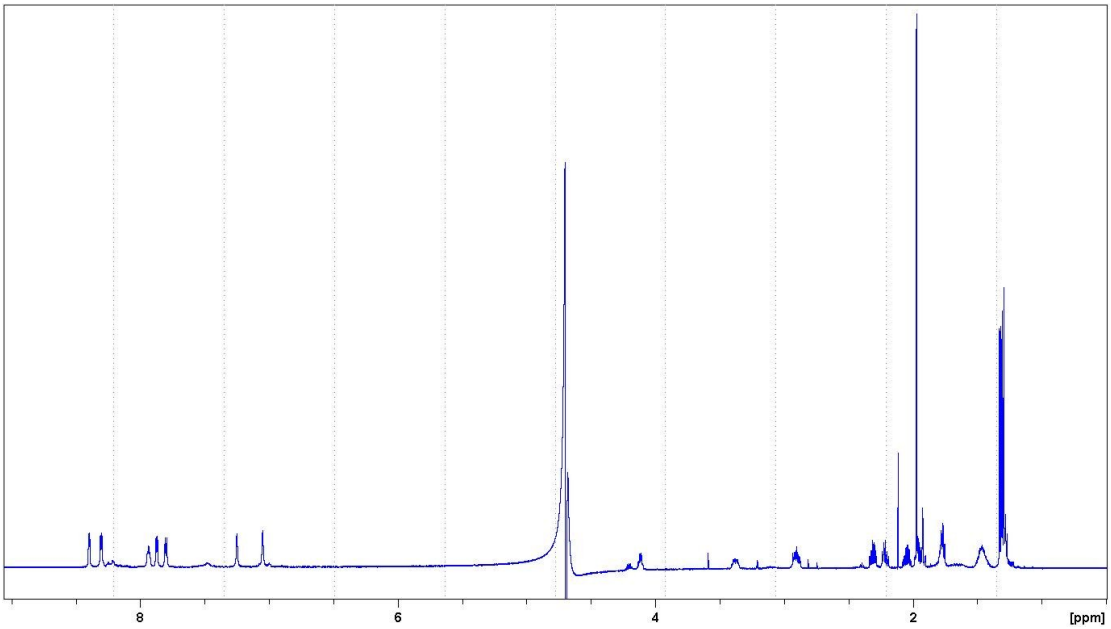

Figure 15. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[EAAO]-NH_2 (**15**).

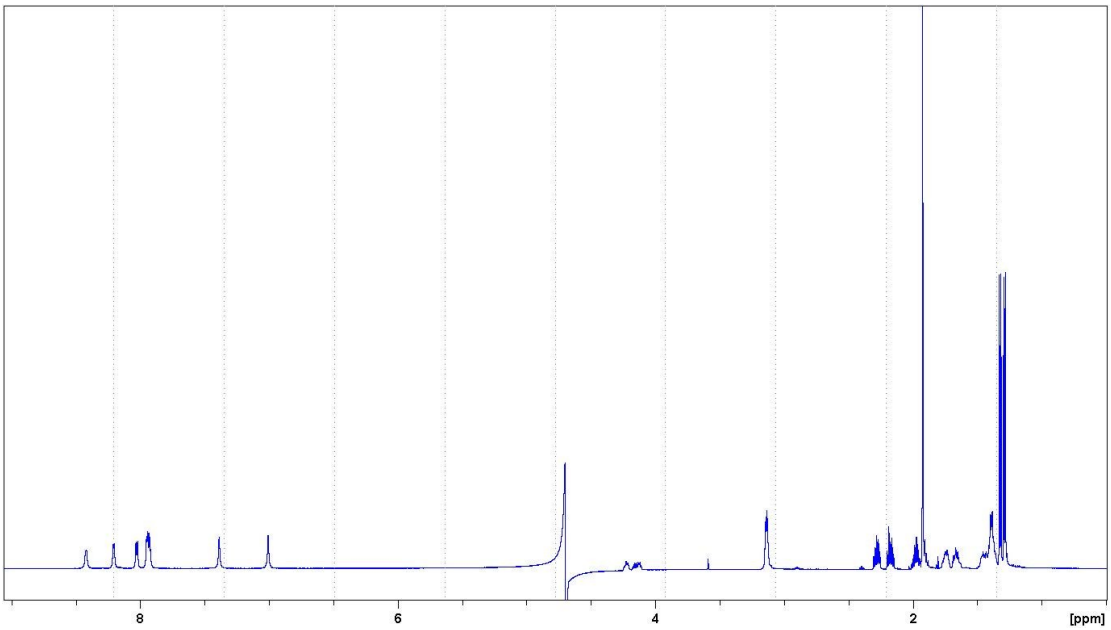

Figure 16. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[EAAK]-NH_2 (**16**).

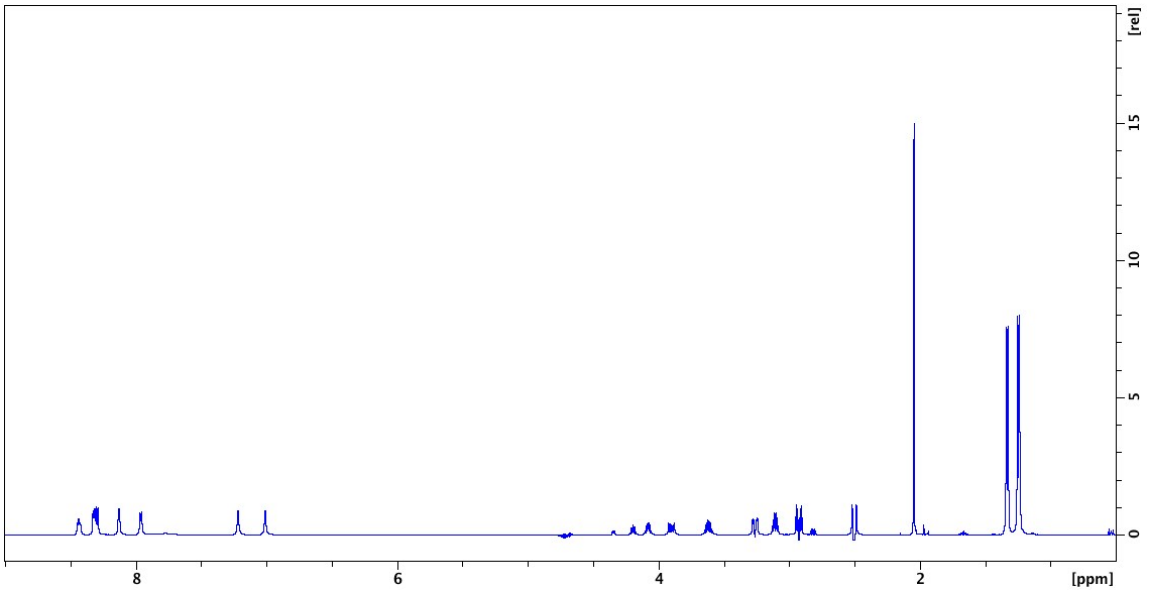

Figure 17. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[dAADap]-NH_2 (**17**).

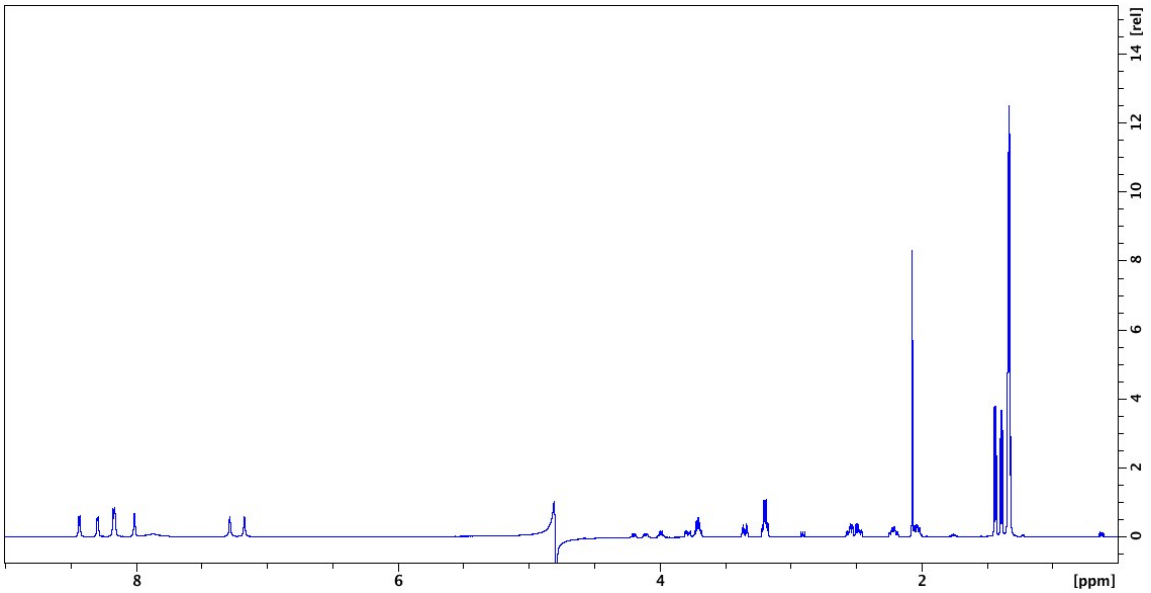

Figure 18. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[eAADap]-NH_2 (**18**).

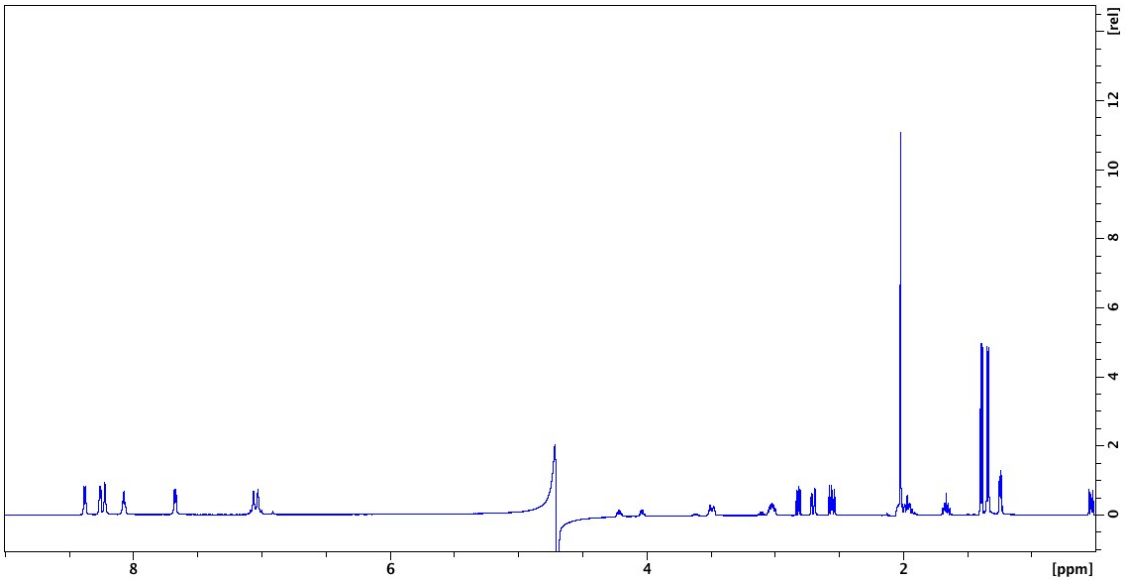

Figure 19. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[dAADab]-NH_2 (**19**).

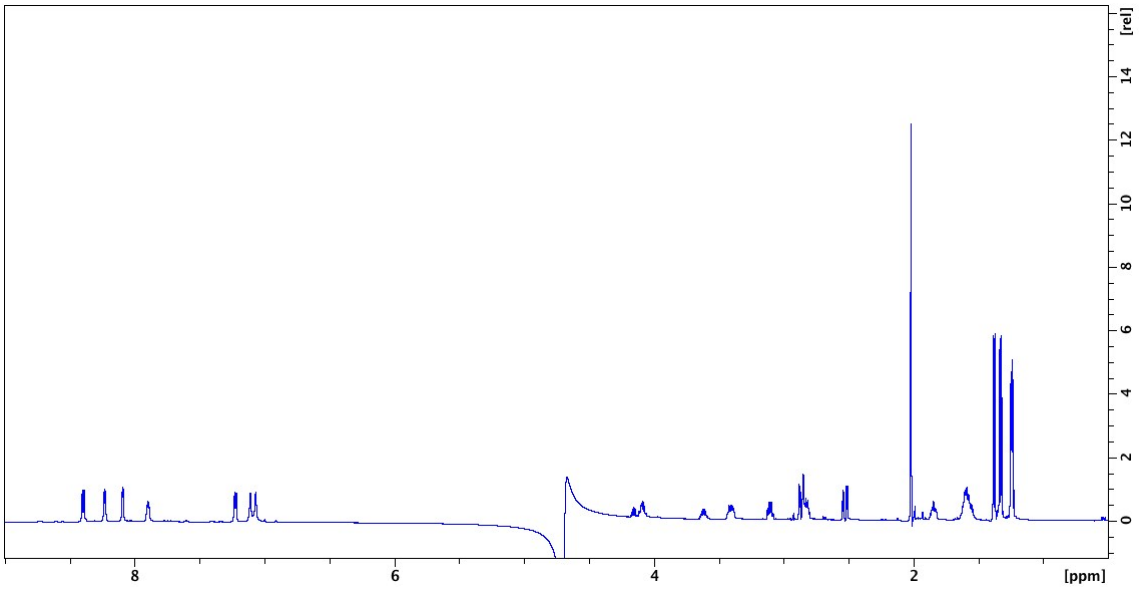

Figure 20. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[dAAO]-NH_2 (**20**).

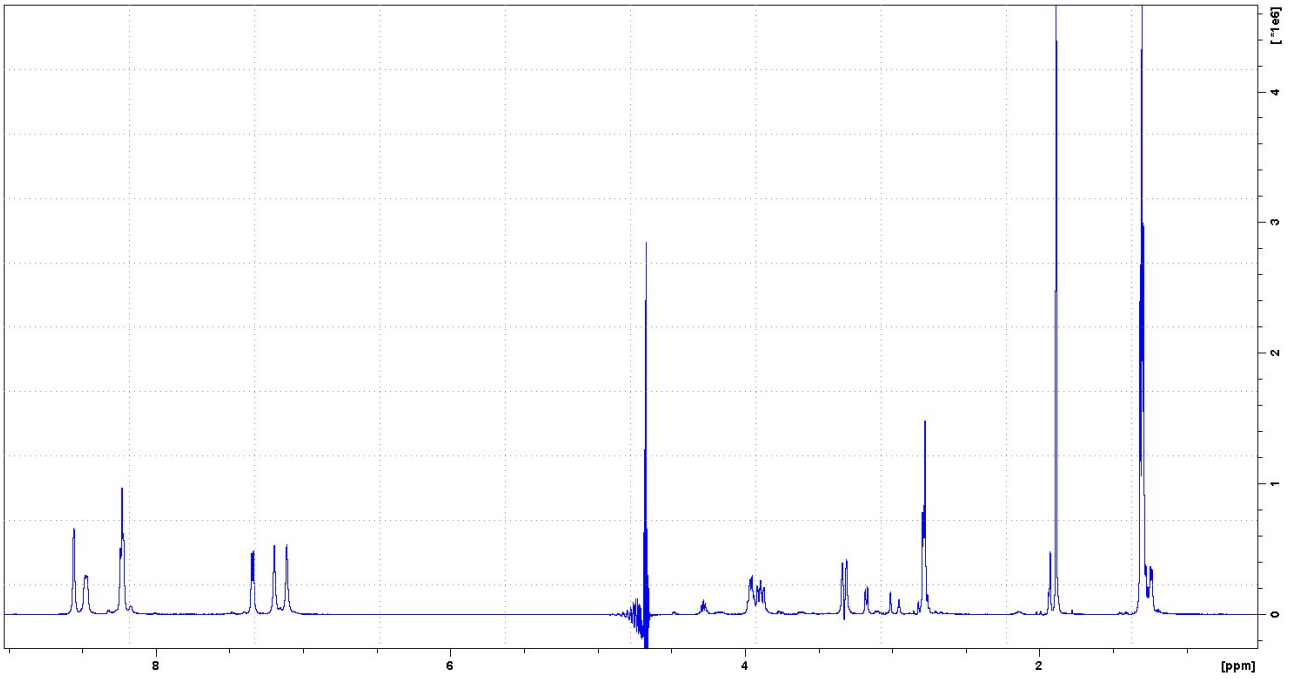

Figure 21. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[IsoDAADap]-NH_2 (**21**) .

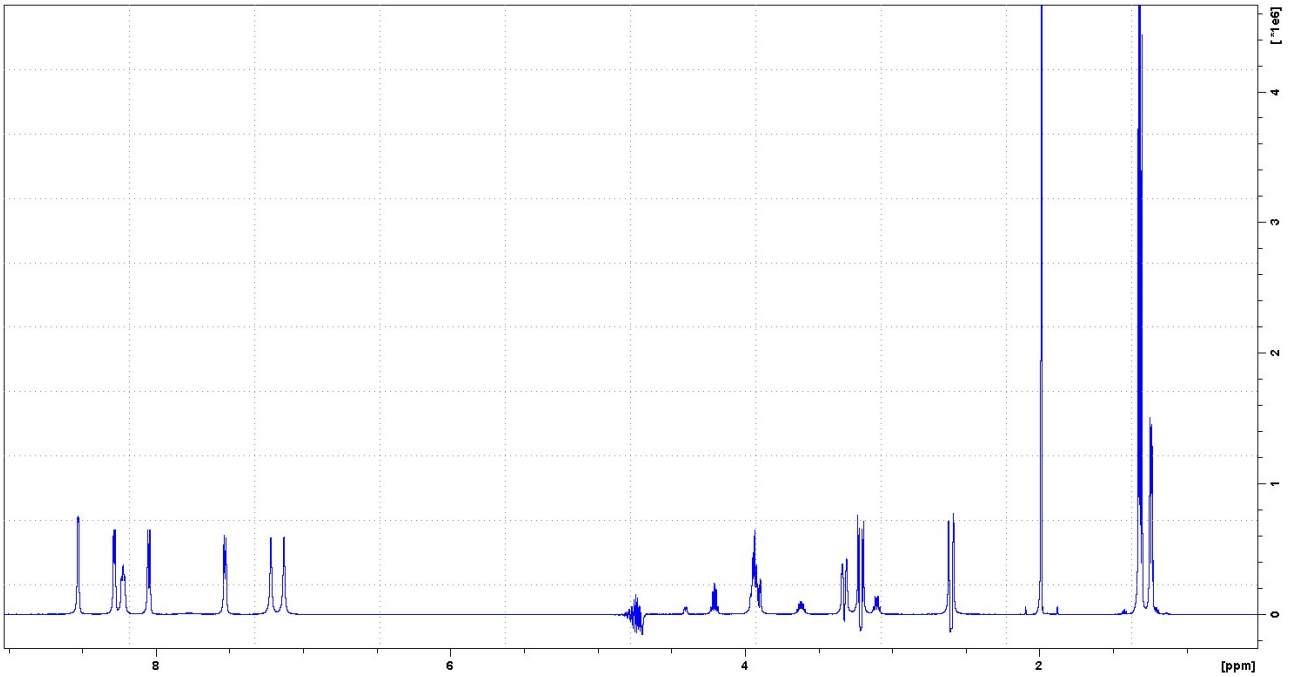

Figure 22. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[IsodAADap]-NH_2 (**22**).

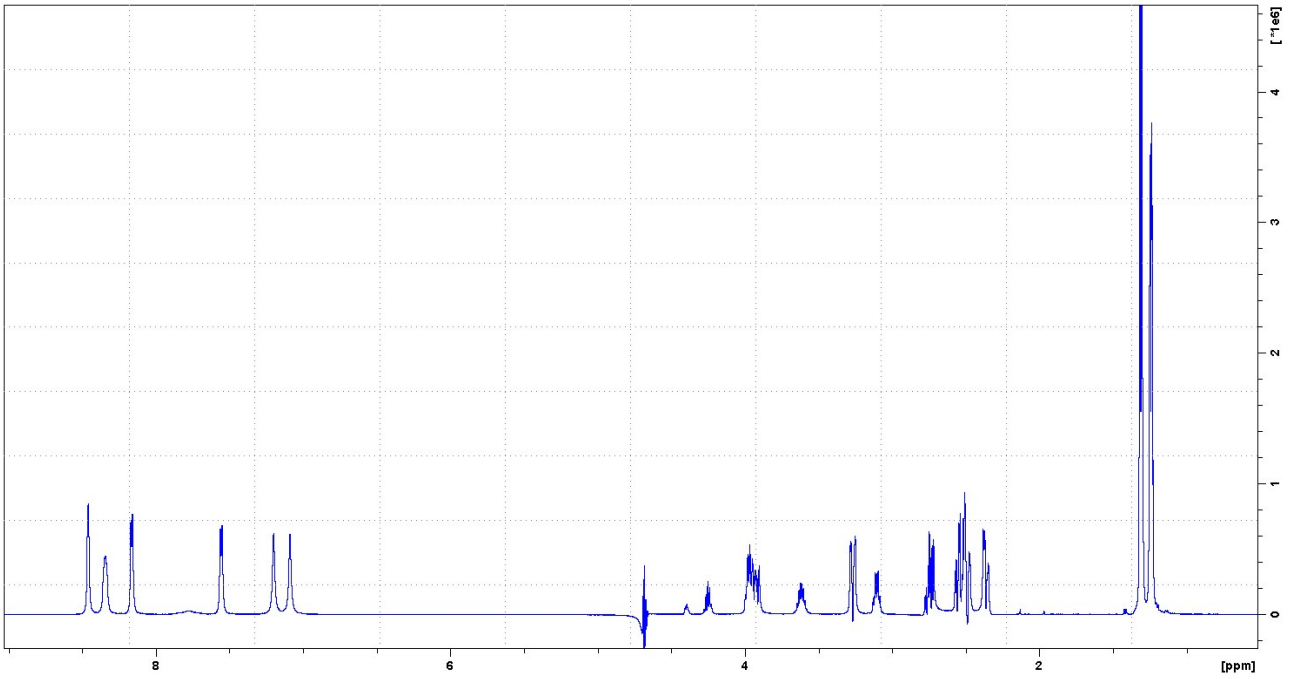

Figure 23. 600 MHz ^{1}H NMR spectrum of cyclo-(1,4)-[SuccAADap]-NH_2 (**23**).

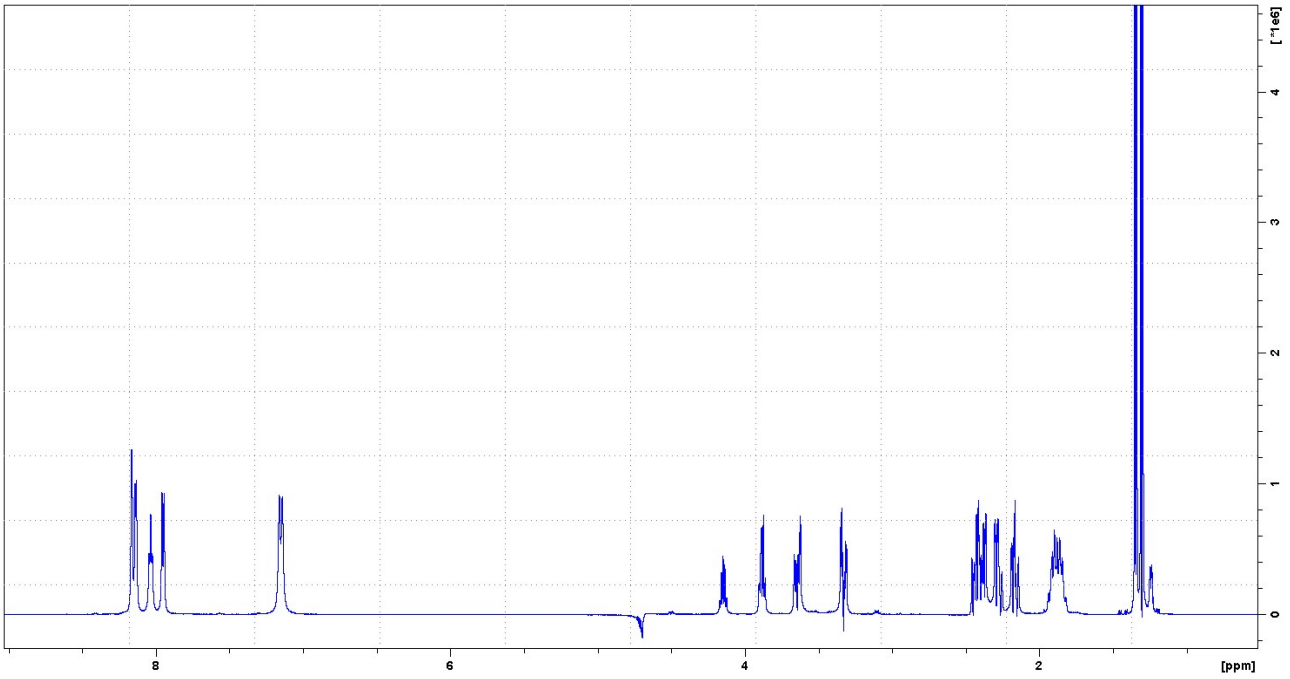

Figure 24. 600 MHz ^{1}H NMR spectrum of cyclo-(1,4)-[GlutAADap]-NH_2 (**24**).

Table S5. Amide proton coupling constants (Hz) of **1–24** in H_2O:D_2O (9:1).

#		X	A	A	Z	
1	**Dap**	6.8	6.3	7.7	8.9	**D**
2	**Dab**	7	6.1	7.9	7.7	**D**
3	**O**	6.3	7.3	6.6	8.1	**D**
4	**K**	5.8	6	4.9	7.9	**D**
5	**D**	8	4.2	6.3	7.3	**Dap**
6	**D**	7.4	4.1	6.3	7.2	**Dab**
7	**D**	7.9	3.1	5.0	7.5	**O**
8	**D**	7.5	4.6	5.8	7.3	**K**
9	**Dap**	6.4	4.3	6.8	8.1	**E**
10	**Dab**	6.2	5.5	6.7	8.8	**E**
11	**O**	6.2	5.9	4.4	8.1	**E**
12	**K**	6	5.3	4.8	8.8	**E**
13	**E**	6.1	4.4	5.6	7.8	**Dap**
14	**E**	6	5.8	5.1	7.8	**Dab**
15	**E**	5.9	4.5	6.0	7.1	**O**
16	**E**	5.3	5.3	4.5	7.6	**K**
17	**d**	8.7	4.5	5.9	6.7	**Dap**
18	**e**	6.0	3.8	4.9	8.4	**Dap**
19	**d**	7.5	3.7	5.7	7	**Dab**
20	**d**	8.1	4.3	5.6	7.6	**O**
21	**IsoD**	3.1	7.0	8.1	7.5	**Dap**
22	**Isod**	2.8	6.1	7.5	8.8	**Dap**
23	**Succ**	n/a	2.5	6.4	7.2	**Dap**
24	**Glut**	n/a	1.9	5.3	8.6	**Dap**

Yellow > 8 Hz (β-strand), Green < 6 Hz (α-helix)

Table S6. Amide proton temperature coefficients (ppb/K) for **1–24** in H_2O:D_2O (9:1).

#		X	A	A	Z		S.C. NH	CtermH1	CtermH2
1	**Dap**	6.3	7.1	7.3	5.9	**D**	6.2	5	5.4
2	**Dab**	7.6	8	7.8	6.9	**D**	6.7	5.9	6.5
3	**O**	8.5	7.2	6.4	5.5	**D**	7.9	5.8	6.1
4	**K**	7.4	7.3	7.5	6.2	**D**	6.6	4.9	5.2
5	**D**	7.5	6.4	8.6	3.9	**Dap**	9.1	1.4	5.2
6	**D**	6.5	9.4	8	2.8	**Dab**	7.6	2.6	7.2
7	**D**	8.4	7.3	8.3	2.7	**O**	9.3	2.2	7.6
8	**D**	4.1	5.5	5	8	**K**	4.4	4.9	7.8
9	**Dap**	6.2	6.9	6.5	3.9	**E**	6.2	3.1	6.3
10	**Dab**	8.2	9.7	10.8	8.1	**E**	6.7	6.3	6.5
11	**O**	9.3	8.2	3.9	5.9	**E**	7.9	4.9	7.2
12	**K**	7.5	7.6	6.8	8.2	**E**	6.6	5.7	5.8
13	**E**	6.9	6	8	4.4	**Dap**	7.9	0.6	6.3
14	**E**	8	7.2	8.1	7.9	**Dab**	7.8	6	6.7
15	**E**	8.5	7.4	4	3.6	**O**	9.2	2.9	7.2
16	**E**	7.9	7.9	8.2	8.8	**K**	7.3	6.5	7.2
17	**d**	5.8	9.3	5.1	5.6	**Dap**	8.0	0.9	6.4
18	**e**	7.1	5.5	9.5	4.2	**Dap**	7.9	0.3	6.3
19	**d**	8.0	6.9	8.2	1.4	**Dab**	6.4	2.2	7.2
20	**d**	7.9	8.8	6.7	2.8	**O**	7.2	2.0	7.0
21	**IsoD**	7.4	8.54	2.55	7.60	**Dap**	8.5	1.9	6.2
22	**Isod**	6.09	9.19	3.57	5.49	**Dap**	7.9	2.1	5.6
23	**Succ**	n/a	6.97	8.85	3.37	**Dap**	8.8	1.3	14.7
24	**Glut**	n/a	6.61	8.03	2.54	**Dap**	7.6	0.4	5.8

Cyan = < 4 ppb/K (likely H-bond). S.C. = side chain.

Table S7. Proton NMR chemical shifts (ppm) of **1**–**24** in H_2O:D_2O (9:1).

Peptide	Residue	NH	Hα	Hβ	Other
5	Ac-		2.00		
	Asp1	8.42	4.91	2.72	
	Ala2	8.64	4.12	1.42	
	Ala3	8.34	4.33	1.39	
	Dap4	7.72	4.48	3.36, 3,99	NHγ 8.47
	-NH_2	7.20, 7.28			
6	Ac-		2.03		
	Asp1	8.41	4.76	2.68	
	Ala2	8.93	4.15	1.44	
	Ala3	8.43	4.35	1.45	
	Dab4	7.59	4.35	1.98	Hγ = 3.14, 3.29, NHδ = 8.19
	-NH_2	7.22, 7.27			
7	Ac-		2.03		
	Asp1	8.64	4.84	2.47 2.81	
	Ala2	8.46	4.02	1.42	
	Ala3	8.56	4.19	1.42	
	Orn4	8.64	4.12	1.71, 1.82	Hγ = 1.52, 1.93 Hδ = 2.82, 3.55 NHε = 8.33
	-NH_2	7.22, 7.28			
9	Ac-		2.04		
	Dap1	8.22	4.50	3.43, 3.94	NHγ = 8.02
	Ala2	8.70	4.21	1.42	
	Ala3	8.16	4.34	1.42	
	Glu4	7.84	4.45	2.00, 2.29	Hγ = 2.57
	-NH_2	7.18, 7.38			
13	Ac-		2.01		
	Glu1	8.21	4.45	2.14	Hγ = 2.36, 2.48
	Ala2	8.46	4.10	1.42	
	Ala3	8.25	4.24	1.42	
	Dap4	8.15	4.60	3.33, 3.77	NHγ = 8.08
	-NH_2	7.26, 7.31			
15	Ac-				
	Glu1	8.40	4.22	2.07, 2.14	Hγ = 2.32, 2.41
	Ala2	8.50	4.22	1.43	
	Ala3	7.97	4.31	1.41	
	Orn4	7.90	4.22	1.88	Hγ = 1.57 Hδ = 3.00, 3.48 NHε = 8.03
	-NH_2	7.14, 7.35			
17	Ac-		2.13		
	D-Asp1	2.13	4.83	2.59, 2.99	
	Ala2	8.27	4.16	1.42	
	Ala3	8.50	4.27	1.42	
	Dap4	8.10	4.42	3.01, 3.99	NHγ = 8.60
	-NH_2	7.11, 7.37			
18	Ac-		2.07		
	D-Glu1	8.50	4.10	2.02, 2.23	Hγ = 2.48, 2.55
	Ala2	8.06	3.98	1.39	
	Ala3	8.38	4.18	1.45	
	Dap4	8.21	4.56	3.35, 3.78	NHγ = 8.23
	-NH_2	7.17, 7.34			
19	Ac-	2.11			
	D-Asp1	8.47	4.72		
	Ala2	8.31	4.13	1.43	
	Ala3	8.35	4.31	1.48	

	Dab4	7.77	4.30	2.06, 2.10	Hγ = 3.11, 3.57 NHδ = 8.17
	-NH_2	7.12, 7.15			
20	Ac-		2.11		
	D-Asp1	8.49	4.74	2.62, 2.95	
	Ala2	8.18	4.17	1.41	
	Ala3	8.32	4.24	1.47	
	Orn4	7.32	4.19	1.68	Hγ = 1.94 Hδ = 2.92, 3.49 NHε = 7.99
	-NH_2	7.16, 7.20			
21	isoD1	8.24	4.67	2.78 (2H)	Ac-cap 1.89
	A2	8.56	3.96	1.31	
	A3	8.23	4.29	1.30	
	Dap4-NH_2	7.34	4.48	3.90, 3.33	T1 7.20 , T2 7.11
22	Isod	8.05	4.68	3.22, 2.60	Ac-cap 1.99
	A1	8.53	3.94	1.31	
	A2	8.28	4.21	1.32	
	Dap3-NH_2	7.53	4.40	3.92, 3.33	T1 7.22, T2 7.13; side NH 8.22
23	Succ1				2.75 1H; 2.58-2.46 2H; 2.37 1H;
	A2	8.46	3.98	1.31	
	A3	8.17	4.25	1.31	
	Dap4-NH_2	7.46	4.40	3.93, 3.27	T1 7.20, T2 7.09;
24	Glut1				2.46-2.37 2H; 2.29 1H; 2.17 1H; 1.94-1.84 2H;
	A2	8.16	3.89	1.31	
	A3	8.14	4.15	1.35	
	Dap4-NH_2	7.95	4.51	3.65, 3.33	T1, 7.16, T2 7.14;

7.2 Phi, Psi Angle Analysis

Table S8. ϕ, ψ, χ1 (degree) angles for **5**–**7**, **9**, **13**, **15**, **17**–**20**.

#	ϕ_i	ψ_i	ϕ_{i+1}	ψ_{i+1}	ϕ_{i+2}	ψ_{i+2}	ϕ_{i+3}	ψ_{i+3}	χ^1_{i+3}
5	-114	69	-62	-36	-73	-46	-68	-39	58
6	-101	117	-57	-40	-54	-35	-85	-6	-28
7	-86	-35	-60	-39	-56	-32	-85	12	-59
9	-122	122	-58	-41	-56	-34	-114	21	30
13	-151	128	-62	-35	-70	-9	16	-49	54
15	-69	27	-57	31	-6	-5	-18	12	-77
17	148	-41	-63	-44	-65	-49	-66	-40	59
18	109	45	-90	-42	-52	-45	-91	-33	41
19	69	-3	-56	-39	-54	-36	-87	0	-23
20	123	-47	-58	-30	-51	-39	-77	-13	-66

7.4 ROE restraints

Table S9. Restraints used to calculate the structure of **5** Ac-[DAADap]-NH_2 H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	ASP2	HN	3.95	weak
2	ACE1	HA	ALA3	HN	5.60	very weak
3	ASP2	HA	ASP2	HN	4.06	weak
4	ASP2	HA	ALA3	HN	3.55	weak
5	ASP2	HA	ALA4	HN	3.70	weak
6	ASP2	HA	DAP5	HN	3.66	weak
7	ASP2	HB	ASP2	HN	4.01	weak
8	ASP2	HB	ALA3	HA	5.63	very weak
9	ASP2	HB	ALA3	HN	5.57	very weak
10	ASP2	HB	DAP5	H1	5.92	very weak
11	ASP2	HB	DAP5	H2	6.24	very weak
12	ASP2	HB	DAP5	HB	4.99	weak
13	ASP2	HB	DAP5	HG1	3.60	weak
14	ASP2	HB	DAP5	HN	5.40	very weak
15	ALA3	HA	ALA3	HN	4.38	weak
16	ALA3	HA	ALA4	HN	4.71	weak
17	ALA3	HA	DAP5	H1	5.58	very weak
18	ALA3	HA	DAP5	H2	6.09	very weak
19	ALA3	HA	DAP5	HN	5.44	very weak
20	ALA3	HB	ALA3	HN	4.22	weak
21	ALA4	HA	ALA3	HN	6.68	very weak
22	ALA4	HA	DAP5	H1	5.47	very weak
23	ALA4	HA	DAP5	H2	6.02	very weak
24	ALA4	HA	DAP5	HN	4.43	weak
25	ALA4	HB	ALA4	HN	3.95	weak
26	ALA4	HB	DAP5	H1	6.03	very weak
27	ALA4	HB	DAP5	HN	4.84	weak
28	ALA4	HN	ALA3	HN	4.47	weak
29	DAP5	H1	DAP5	HG1	5.48	very weak
30	DAP5	H1	DAP5	HN	4.60	weak
31	DAP5	H2	DAP5	HG1	5.71	very weak
32	DAP5	H2	DAP5	HN	5.34	very weak
33	DAP5	HA	ALA4	HN	5.77	very weak
34	DAP5	HA	DAP5	H1	4.57	weak
35	DAP5	HA	DAP5	H2	5.11	very weak
36	DAP5	HA	DAP5	HG1	5.19	very weak
37	DAP5	HA	DAP5	HN	4.27	weak

38	DAP5	HB	ALA4	HN	5.41	very weak
39	DAP5	HB	DAP5	H1	5.90	very weak
40	DAP5	HB	DAP5	H2	6.12	very weak
41	DAP5	HB	DAP5	HG1	3.74	weak
42	DAP5	HB	DAP5	HN	4.22	weak
43	DAP5	HB	DAP5	HN	5.32	very weak
44	DAP5	HN	ALA3	HN	4.80	weak
45	DAP5	HN	ALA4	HN	4.29	weak
46	DAP5	HN	DAP5	HG1	5.15	very weak

Figure S10. Restraints used to calculate the structure of **6** Ac-[DAADab]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	ASP2	HN	4.18	weak
2	ASP2	HA	ASP2	HN	4.14	weak
3	ASP2	HA	ALA3	HN	3.57	weak
4	ASP2	HA	DAB5	HD1	5.24	very weak
5	ASP2	HB	ASP2	HN	4.32	weak
6	ASP2	HB	DAB5	HD1	3.81	weak
7	ASP2	HB	DAB5	HN	4.94	weak
8	ALA3	HA	ALA3	HN	4.06	weak
9	ALA3	HA	ALA4	HN	4.56	weak
10	ALA3	HA	DAB5	H1	5.56	very weak
11	ALA3	HA	DAB5	HN	5.12	very weak
12	ALA3	HB	ALA3	HN	4.56	weak
13	ALA4	HA	ALA4	HN	4.16	weak
14	ALA4	HB	ALA4	HN	4.30	weak
15	ALA4	HB	DAB5	HN	5.18	very weak
16	ALA4	HN	ALA3	HN	4.51	weak
17	DAB5	H1	DAB5	HN	4.69	weak
18	DAB5	H2	DAB5	HN	5.66	very weak
19	DAB5	HA	DAB5	H1	4.35	weak
20	DAB5	HA	DAB5	H2	5.15	very weak
21	DAB5	HA	DAB5	HD1	5.11	very weak
22	DAB5	HA	DAB5	HN	4.11	weak
23	DAB5	HB	DAB5	H1	5.30	very weak
24	DAB5	HB	DAB5	HD1	4.84	weak
25	DAB5	HB	DAB5	HN	4.37	weak
26	DAB5	HG	DAB5	HD1	4.27	weak
27	DAB5	HG	DAB5	HD1	4.13	weak
28	DAB5	HG	DAB5	HN	4.65	weak
29	DAB5	HN	ALA4	HN	4.42	weak
30	DAB5	HN	DAB5	HD1	4.72	weak
31	ASP2	O	DAB5	HN	1.6-2.2	H-bond
32	ASP2	O	DAB5	N	2.6-3.2	H-bond
33	ALA3	O	DAB5	H1	1.6-2.2	H-bond
34	ALA3	O	DAB5	NT	2.6-3.2	H-bond

Table S11. Restraints used to calculate the structure of **7** Ac-[DAAO]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	ASP2	HN	4.42	weak
2	ACE1	HA	ALA3	HN	5.84	very weak
3	ASP2	HA	ASP2	HN	4.04	weak
4	ASP2	HA	ALA3	HN	3.93	weak
5	ASP2	HA	ALA4	HN	3.58	weak
6	ASP2	HA	ORN5	HD	4.65	weak
7	ASP2	HA	ORN5	HN	3.73	weak
8	ASP2	HA	ORN5	NE	3.77	weak
9	ASP2	HB	ASP2	HN	4.82	weak
10	ASP2	HB	ASP2	HN	4.82	weak
11	ASP2	HB	ORN5	NE	5.17	very weak
12	ASP2	HN	ALA4	HN	4.66	weak
13	ASP2	HN	ORN5	NE	5.30	very weak
14	ALA3	HA	ASP2	HN	5.96	very weak
15	ALA3	HA	ALA4	HN	4.83	weak
16	ALA3	HA	ORN5	H1	5.34	very weak
17	ALA3	HA	ORN5	H2	4.80	weak
18	ALA3	HA	ORN5	HN	5.06	very weak
19	ALA3	HB	ALA3	HN	4.70	weak
20	ALA3	HB	ORN5	HN	5.27	very weak
21	ALA4	HA	ORN5	H1	5.44	very weak
22	ALA4	HA	ORN5	HN	3.73	weak
23	ALA4	HB	ALA4	HN	4.57	weak
24	ALA4	HN	ALA3	HN	4.46	weak
25	ALA4	HN	ORN5	NE	4.78	weak
26	ALA4	HN	ORN5	NE	4.80	weak
27	ORN5	HA	ORN5	H1	4.68	weak
28	ORN5	HA	ORN5	H2	3.94	weak
29	ORN5	HB	ORN5	H1	4.84	weak
30	ORN5	HB	ORN5	HN	4.30	weak
31	ORN5	HB	ORN5	HN	4.53	weak
32	ORN5	HB	ORN5	NE	5.75	very weak
33	ORN5	HB	ORN5	NE	4.78	weak
34	ORN5	HD	ORN5	HN	6.00	very weak
35	ORN5	HD	ORN5	HN	5.54	very weak
36	ORN5	HD	ORN5	NE	3.65	weak
37	ORN5	HG	ORN5	H1	5.25	very weak
38	ORN5	HG	ORN5	HN	5.96	very weak
39	ORN5	HG	ORN5	HN	5.89	very weak
40	ORN5	HG	ORN5	NE	5.93	very weak
41	ORN5	HG	ORN5	NE	5.89	very weak
42	ORN5	HN	ALA3	HN	4.28	weak
43	ORN5	HN	ALA4	HN	4.61	weak
44	ORN5	HN	ORN5	NE	4.82	weak
45	ASP2	O	ORN5	HN	1.6-2.2	H-bond
46	ASP2	O	ORN5	N	2.6-3.2	H-bond
47	ALA3	O	ORN5	H1	1.6-2.2	H-bond
48	ALA3	O	ORN5	NT	2.6-3.2	H-bond

Table S12. Restraints used to calculate the structure of **9** Ac-[DapAAE]-NH_2 H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	DAP2	HN	4.30	weak
2	DAP2	HA	DAP2	HG	4.89	weak

3	DAP2	HA	DAP2	HN	4.28	weak
4	DAP2	HA	ALA3	HN	3.60	weak
5	DAP2	HB	DAP2	HN	5.04	very weak
6	DAP2	HB	DAP2	HG	4.26	weak
7	DAP2	HB	DAP2	HG	4.15	weak
8	DAP2	HB	DAP2	HN	4.52	weak
9	DAP2	HB	ALA3	HN	4.65	weak
10	DAP2	HB	ALA4	HN	4.83	weak
11	DAP2	HB	GLU5	HN	5.44	very weak
12	DAP2	HG	DAP2	HN	4.47	weak
13	DAP2	HG	ALA3	HN	5.49	very weak
14	ALA3	HA	ALA4	HN	4.21	weak
15	ALA3	HA	GLU5	H1	5.52	very weak
16	ALA3	HA	GLU5	HN	5.07	very weak
17	ALA3	HB	ALA3	HN	4.70	weak
18	ALA3	HA	ALA3	HN	4.43	weak
19	ALA4	HA	ALA4	HN	3.98	weak
20	ALA4	HA	GLU5	H1	4.20	weak
21	ALA4	HA	GLU5	H2	5.91	very weak
22	ALA4	HA	GLU5	HN	4.34	weak
23	ALA4	HB	ALA4	HN	5.10	very weak
24	ALA4	HB	GLU5	HN	5.39	very weak
25	ALA4	HN	ALA3	HN	4.70	weak
26	GLU5	H1	GLU5	HN	4.77	weak
27	GLU5	H2	GLU5	HN	5.44	very weak
28	GLU5	HA	GLU5	H1	4.45	weak
29	GLU5	HA	GLU5	H2	5.29	very weak
30	GLU5	HA	GLU5	HN	4.31	weak
31	GLU5	HB	DAP2	HG	4.75	weak
32	GLU5	HB	GLU5	H1	5.51	very weak
33	GLU5	HB	GLU5	H1	5.66	very weak
34	GLU5	HB	GLU5	H2	5.96	very weak
35	GLU5	HB	GLU5	H2	5.86	very weak
36	GLU5	HB	GLU5	HN	4.65	weak
37	GLU5	HB	GLU5	HN	5.26	very weak
38	GLU5	HG	DAP2	HG	4.84	weak
39	GLU5	HG	DAP2	HG	4.10	weak
40	GLU5	HG	GLU5	H1	5.88	very weak
41	GLU5	HG	GLU5	H2	6.1	very weak
42	GLU5	HG	GLU5	HN	5.26	very weak
43	GLU5	HG	GLU5	HN	5.20	very weak
44	GLU5	HN	ALA3	HN	6.07	very weak
45	GLU5	HN	ALA4	HN	4.39	weak
46	DAP2	O	GLU5	HN	1.6-2.2	H-bond
47	DAP2	O	GLU5	N	2.6-3.2	H-bond
48	ALA3	O	GLU5	H1	1.6-2.2	H-bond
49	ALA3	O	GLU5	NT	2.6-3.2	H-bond

Table S13. Restraints used to calculate the structure of **13** Ac-[EAADap]-NH_2 H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	GLU2	HN	4.79	weak
2	ACE1	HA	ALA3	HN	5.97	very weak
3	ACE1	HA	DAP5	H1	6.28	very weak
4	ACE1	HA	DAP5	H2	6.93	very weak
5	ACE1	HN	DAP5	H1	3.77	weak
6	GLU2	HA	ALA3	HN	3.87	weak
7	GLU2	HA	ALA4	HN	4.03	weak

8	GLU2	HA	DAP5	HG	6.41	very weak
9	GLU2	HB	GLU2	HN	5.15	very weak
10	GLU2	HB	ALA3	HN	5.95	very weak
11	GLU2	HB	ALA4	HN	5.87	very weak
12	GLU2	HB	DAP5	HG	5.99	very weak
13	GLU2	HB	DAP5	HN	6.31	very weak
14	GLU2	HG2	GLU2	HN	5.06	very weak
15	GLU2	HG2	DAP5	HG	4.38	weak
16	GLU2	HG3	GLU2	HN	5.53	very weak
17	GLU2	HG3	ALA3	HN	5.92	very weak
18	GLU2	HG3	DAP5	HG	5.28	very weak
19	GLU2	HN	ALA3	HN	5.13	very weak
20	ALA3	HA	ACE1	HN	5.74	very weak
21	ALA3	HA	ALA4	HN	4.96	weak
22	ALA3	HA	DAP5	H1	5.91	very weak
23	ALA3	HA	DAP5	H2	6.33	very weak
24	ALA3	HA	DAP5	HN	5.56	very weak
25	ALA3	HB	ALA3	HN	5.28	very weak
26	ALA4	HA	DAP5	H1	5.92	very weak
27	ALA4	HA	DAP5	H2	6.86	very weak
28	ALA4	HA	DAP5	HG	6.31	very weak
29	ALA4	HA	DAP5	HN	4.52	weak
30	ALA4	HB	ALA4	HN	4.97	weak
31	ALA4	HB	DAP5	HN	5.69	very weak
32	ALA4	HN	DAP5	H1	6.57	very weak
33	DAP5	HA	DAP5	H1	4.87	weak
34	DAP5	HA	DAP5	H2	5.44	very weak
35	DAP5	HA	DAP5	HG	5.30	very weak
36	DAP5	HB2	DAP5	H1	5.83	very weak
37	DAP5	HB2	DAP5	H2	5.73	very weak
38	DAP5	HB2	DAP5	HN	4.89	weak
39	DAP5	HB3	DAP5	H1	5.97	very weak
40	DAP5	HB3	DAP5	H2	6.23	very weak
41	DAP5	HB3	DAP5	HN	5.18	very weak
42	DAP5	HG	DAP5	H1	6.27	very weak
43	DAP5	HN	DAP5	H1	5.12	very weak
44	DAP5	HN	DAP5	H2	5.77	very weak
45	GLU2	O	DAP5	H1	1.6-2.2	H-bond
46	GLU2	O	DAP5	NT	2.6-3.2	H-bond

Table S14. Restraints used to calculate the structure of **15** Ac-[EAAO]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	GLU2	HA	GLU2	HN	4.28	weak
2	GLU2	HB	GLU2	HN	3.99	weak
3	GLU2	HB	GLU2	HN	4.75	weak
4	GLU2	HB	ALA3	HN	5.10	very weak
5	GLU2	HB	ALA3	HN	5.52	very weak
6	GLU2	HB	ORN5	HE1	4.84	weak
7	GLU2	HG	GLU2	HN	5.14	very weak
8	GLU2	HG	GLU2	HN	5.60	very weak
9	GLU2	HG	ALA3	HN	5.92	very weak
10	GLU2	HG	ALA3	HN	5.46	very weak
11	GLU2	HG	ALA4	HN	5.91	very weak
12	GLU2	HG	ALA4	HN	5.88	very weak
13	GLU2	HG	ORN5	HE1	4.57	weak
14	GLU2	HG	ORN5	HE1	4.18	weak
15	ALA3	HA	ALA3	HN	3.75	weak
16	ALA3	HA	ALA4	HN	4.25	weak
17	ALA3	HB	ALA3	HN	4.43	weak

18	ALA3	HN	ALA4	HN	4.62	weak
19	ALA4	HA	ALA4	HN	4.25	weak
20	ALA4	HA	ORN5	H1	5.73	very weak
21	ALA4	HA	ORN5	H2	6.23	very weak
22	ALA4	HA	ORN5	HN	4.06	weak
23	ALA4	HB	ALA4	HN	4.19	weak
24	ALA4	HB	ORN5	H1	6.37	very weak
25	ALA4	HB	ORN5	H2	7.12	very weak
26	ALA4	HB	ORN5	HN	5.25	very weak
27	ORN5	HA	ORN5	H1	4.40	weak
28	ORN5	HA	ORN5	H2	5.05	very weak
29	ORN5	HA	ORN5	HE1	4.86	weak
30	ORN5	HA	ORN5	HN	4.16	weak
31	ORN5	HB	ORN5	H1	5.22	very weak
32	ORN5	HB	ORN5	H2	5.57	very weak
33	ORN5	HB	ORN5	HE1	4.57	weak
34	ORN5	HB	ORN5	HN	4.36	weak
35	ORN5	HD	ORN5	HE	4.24	weak
36	ORN5	HD	ORN5	HE1	4.58	weak
37	ORN5	HG	ORN5	H1	5.98	very weak
38	ORN5	HG	ORN5	H2	6.17	very weak
39	ORN5	HG	ORN5	HE1	4.98	weak
40	ORN5	HG	ORN5	HN	4.61	weak
41	ORN5	HN	ORN5	H1	4.87	weak
42	ORN5	HN	ORN5	H2	5.35	very weak
43	GLU2	O	ORN5	HN	1.6-2.2	H-bond
44	GLU2	O	ORN5	N	2.6-3.2	H-bond
45	ALA3	O	ORN5	H1	1.6-2.2	H-bond
46	ALA3	O	ORN5	NT	2.6-3.2	H-bond

Table S15. Restraints used to calculate the structure of **17** Ac-[dAADap]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	dASP2	HN	4.00	weak
2	ACE1	HA	ALA3	HN	5.41	very weak
3	ACE1	HA	ALA4	HN	6.20	very weak
4	dASP2	HA	dASP2	HN	4.07	weak
5	dASP2	HA	ALA3	HN	4.29	weak
6	dASP2	HB	dASP2	HN	5.67	very weak
7	dASP2	HB	dASP2	HN	4.56	weak
8	dASP2	HB	ALA3	HN	5.79	very weak
9	dASP2	HB	ALA4	HN	6.15	very weak
10	dASP2	HB	DAP5	H2	6.35	very weak
11	dASP2	HB	DAP5	HG1	3.82	weak
12	dASP2	HB	DAP5	HG1	5.22	very weak
13	dASP2	HB	DAP5	HN	5.00	weak
14	ALA3	HA	dASP2	HN	6.17	very weak
15	ALA3	HA	ALA3	HN	4.46	weak
16	ALA3	HA	ALA4	HN	4.91	weak
17	ALA3	HA	DAP5	H1	5.50	very weak
18	ALA3	HA	DAP5	H2	5.99	very weak
19	ALA3	HA	DAP5	HN	5.53	very weak
20	ALA3	HB	dASP2	HN	5.86	very weak
21	ALA3	HB	ALA3	HN	4.40	weak
22	ALA3	HN	dASP2	HN	4.39	weak
23	ALA3	HN	ALA4	HN	4.68	weak
24	ALA4	HA	dASP2	HN	6.17	very weak
25	ALA4	HA	ALA3	HN	6.57	very weak
26	ALA4	HA	ALA4	HN	4.34	weak

27	ALA4	HA	DAP5	H1	5.65	very weak
28	ALA4	HA	DAP5	HN	4.63	weak
29	ALA4	HB	ALA4	HN	4.29	weak
30	ALA4	HB	DAP5	H1	6.25	very weak
31	ALA4	HB	DAP5	HN	5.00	weak
32	DAP5	H1	ALA4	HN	5.83	very weak
33	DAP5	H1	DAP5	H2	3.87	weak
34	DAP5	H1	DAP5	HG1	5.50	very weak
35	DAP5	H1	DAP5	HN	4.65	weak
36	DAP5	H2	DAP5	HG1	5.91	very weak
37	DAP5	HA	ALA4	HN	6.23	very weak
38	DAP5	HA	DAP5	H1	4.65	weak
39	DAP5	HA	DAP5	H2	5.53	very weak
40	DAP5	HA	DAP5	HG1	5.45	very weak
41	DAP5	HA	DAP5	HN	4.18	weak
42	DAP5	HB	dASP2	HN	6.00	very weak
43	DAP5	HB	ALA4	HN	5.99	very weak
44	DAP5	HB	DAP5	H1	6.07	very weak
45	DAP5	HB	DAP5	H1	5.20	very weak
46	DAP5	HB	DAP5	H1	5.99	very weak
47	DAP5	HB	DAP5	H2	6.18	very weak
48	DAP5	HB	DAP5	HG1	4.65	weak
49	DAP5	HB	DAP5	HG1	3.95	weak
50	DAP5	HB	DAP5	HN	5.83	very weak
51	DAP5	HB	DAP5	HN	4.29	weak
52	DAP5	HN	ALA4	HN	4.45	weak
53	DAP5	HN	DAP5	HG1	5.44	very weak

Table S16. Restraints used to calculate the structure of **18** Ac-[eAADap]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	dGLU2	HN	4.07	weak
2	ACE1	HA	ALA3	HN	5.31	very weak
3	ACE1	HA	ALA4	HN	6.64	very weak
4	dGLU2	HA	dGLU2	HN	4.50	weak
5	dGLU2	HA	ALA3	HN	4.81	weak
6	dGLU2	HA	ALA4	HN	5.30	very weak
7	dGLU2	HA	DAP5	H1	6.05	very weak
8	dGLU2	HA	DAP5	H2	6.74	very weak
9	dGLU2	HA	DAP5	HG1	5.07	very weak
10	dGLU2	HA	DAP5	HN	5.75	very weak
11	dGLU2	HB	dGLU2	HN	4.50	weak
12	dGLU2	HB	dGLU2	HN	4.66	weak
13	dGLU2	HB	ALA3	HN	5.15	very weak
14	dGLU2	HB	ALA4	HN	5.42	very weak
15	dGLU2	HB	DAP5	HG1	6.23	very weak
16	dGLU2	HB	DAP5	HN	5.96	very weak
17	dGLU2	HG	dGLU2	HN	6.78	very weak
18	dGLU2	HG	dGLU2	HN	5.78	very weak
19	dGLU2	HG	ALA3	HN	5.39	very weak
20	dGLU2	HG	ALA3	HN	7.26	very weak
21	dGLU2	HG	ALA4	HN	6.45	very weak
22	dGLU2	HG	ALA4	HN	8.04	very weak
23	dGLU2	HG	DAP5	H1	6.14	very weak
24	dGLU2	HG	DAP5	HG1	3.99	weak
25	dGLU2	HG	DAP5	HG1	4.72	weak
26	dGLU2	HG	DAP5	HN	6.17	very weak
27	dGLU2	HG	DAP5	HN	6.05	very weak
28	ALA3	HA	dGLU2	HN	5.88	very weak

29	ALA3	HA	ALA3	HN	4.31	weak
30	ALA3	HA	ALA4	HN	4.89	weak
31	ALA3	HA	DAP5	H1	5.30	very weak
32	ALA3	HA	DAP5	H2	5.53	very weak
33	ALA3	HA	DAP5	HN	5.42	very weak
34	ALA3	HB	ALA3	HN	4.35	weak
35	ALA3	HB	ALA4	HN	4.98	weak
36	ALA3	HN	dGLU2	HN	4.50	weak
37	ALA3	HN	ALA4	HN	4.60	weak
38	ALA4	HA	ALA3	HN	6.27	very weak
39	ALA4	HA	ALA4	HN	4.34	weak
40	ALA4	HA	DAP5	H1	5.74	very weak
41	ALA4	HA	DAP5	H2	6.91	very weak
42	ALA4	HA	DAP5	HG1	6.26	very weak
43	ALA4	HA	DAP5	HN	4.39	weak
44	ALA4	HB	ALA3	HN	4.76	weak
45	ALA4	HB	ALA4	HN	4.41	weak
46	ALA4	HB	DAP5	H1	6.42	very weak
47	ALA4	HB	DAP5	HN	5.03	very weak
48	DAP5	H1	DAP5	H2	3.94	weak
49	DAP5	H1	DAP5	HG1	5.49	very weak
50	DAP5	H1	DAP5	HN	4.63	weak
51	DAP5	H2	DAP5	HG1	6.40	very weak
52	DAP5	H2	DAP5	HN	5.82	very weak
53	DAP5	HA	ALA3	HN	6.60	very weak
54	DAP5	HA	ALA4	HN	6.35	very weak
55	DAP5	HA	DAP5	H1	4.61	weak
56	DAP5	HA	DAP5	H2	5.45	very weak
57	DAP5	HA	DAP5	HG1	5.85	very weak
58	DAP5	HA	DAP5	HN	4.08	weak
59	DAP5	HB	ALA4	HN	6.50	very weak
60	DAP5	HB	DAP5	H1	5.58	very weak
61	DAP5	HB	DAP5	H1	5.72	very weak
62	DAP5	HB	DAP5	H2	6.37	very weak
63	DAP5	HB	DAP5	H2	6.21	very weak
64	DAP5	HB	DAP5	HG1	5.28	very weak
65	DAP5	HB	DAP5	HG1	3.85	weak
66	DAP5	HB	DAP5	HN	4.36	weak
67	DAP5	HB	DAP5	HN	5.06	very weak
68	DAP5	HN	ALA4	HN	4.55	weak
69	dGLU2	O	DAP5	H1	1.6-2.2	H-bond
70	DAP5	O	ALA4	NT	2.6-3.2	H-bond

Table S17. Restraints used to calculate the structure of **19** Ac-[dAADab]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	dASP2	HN	4.31	weak
2	ACE1	HA	ALA3	HN	5.51	very weak
3	dASP2	HA	dASP2	HN	4.19	weak
4	dASP2	HA	ALA3	HN	4.78	weak
5	dASP2	HB	dASP2	HN	4.73	weak
6	dASP2	HB	dASP2	HN	4.61	weak
7	dASP2	HB	ALA3	HN	5.91	very weak
8	dASP2	HB	ALA4	HN	5.28	very weak
9	dASP2	HB	DAB5	HD1	4.00	weak
10	dASP2	HB	DAB5	HD1	4.75	weak
11	dASP2	HB	DAB5	HN	5.34	very weak
12	ALA3	HA	ALA3	HN	4.44	weak
13	ALA3	HA	ALA4	HN	4.98	weak

14	ALA3	HA	DAB5	H1	5.62	very weak
15	ALA3	HA	DAB5	H2	5.88	very weak
16	ALA3	HA	DAB5	HN	5.30	very weak
17	ALA3	HB	ALA3	HN	4.68	weak
18	ALA3	HB	ALA4	HN	5.21	very weak
19	ALA3	HN	dASP2	HN	4.61	weak
20	ALA4	HA	ALA4	HN	4.42	weak
21	ALA4	HB	ALA4	HN	4.63	weak
22	ALA4	HB	DAB5	HN	5.29	very weak
23	DAB5	H1	DAB5	HN	4.89	weak
24	DAB5	HA	DAB5	H1	4.66	weak
25	DAB5	HA	DAB5	H2	5.05	very weak
26	DAB5	HA	DAB5	HD1	5.26	very weak
27	DAB5	HA	DAB5	HN	4.13	weak
28	DAB5	HB	DAB5	H1	5.25	very weak
29	DAB5	HB	DAB5	H1	6.01	very weak
30	DAB5	HB	DAB5	H2	5.87	very weak
31	DAB5	HB	DAB5	HD1	5.30	very weak
32	DAB5	HB	DAB5	HD1	5.32	very weak
33	DAB5	HB	DAB5	HN	5.76	very weak
34	DAB5	HB	DAB5	HN	4.68	weak
35	DAB5	HG	DAB5	HD1	4.11	weak
36	DAB5	HG	DAB5	HD1	4.14	weak
37	DAB5	HG	DAB5	HN	4.85	weak
38	DAB5	HN	ALA4	HN	4.53	weak
39	DAB5	HN	DAB5	HD1	4.86	weak
40	dASP2	O	DAB5	HN	1.6-2.2	H-bond
41	dASP2	O	DAB5	N	2.6-3.2	H-bond
42	ALA3	O	DAB5	H1	1.6-2.2	H-bond
43	ALA3	O	DAB5	NT	2.6-3.2	H-bond

Table S18. Restraints used to calculate the structure of **20** Ac-[dAAO]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	dASP2	HN	4.39	weak
2	ACE1	HA	ALA3	HN	5.77	very weak
3	ACE1	HA	ALA4	HN	6.35	very weak
4	dASP2	HA	dASP2	HN	4.87	weak
5	dASP2	HA	ALA3	HN	5.45	very weak
6	dASP2	HA	ALA4	HN	4.41	weak
7	dASP2	HA	ORN5	HN	5.63	very weak
8	dASP2	HB	dASP2	HN	5.37	very weak
9	dASP2	HB	dASP2	HN	4.91	weak
10	dASP2	HB	ALA3	HN	4.71	weak
11	dASP2	HB	ALA3	HN	5.96	very weak
12	dASP2	HB	ALA4	HN	6.26	very weak
13	dASP2	HB	ORN5	HE1	4.23	weak
14	dASP2	HB	ORN5	HN	6.63	very weak
15	ALA3	HA	ALA3	HN	4.50	weak
16	ALA3	HA	ALA4	HN	4.74	weak
17	ALA3	HB	ALA3	HN	4.74	weak
18	ALA3	HB	ALA4	HN	5.46	very weak
19	ALA3	HN	dASP2	HN	4.53	weak
20	ALA3	HN	ALA4	HN	4.75	weak
21	ALA4	HA	ALA3	HN	6.63	very weak
22	ALA4	HA	ALA4	HN	4.40	weak
23	ALA4	HA	ORN5	H1	5.69	very weak
24	ALA4	HA	ORN5	H2	5.58	very weak
25	ALA4	HA	ORN5	HN	4.66	weak

26	ALA4	HB	ALA3	HN	6.63	very weak
27	ALA4	HB	ALA4	HN	4.79	weak
28	ALA4	HB	ORN5	HN	5.51	very weak
29	ALA4	HN	dASP2	HN	4.96	weak
30	ORN5	H1	ORN5	HN	5.13	very weak
31	ORN5	HA	ORN5	H1	4.80	weak
32	ORN5	HA	ORN5	H2	5.19	very weak
33	ORN5	HA	ORN5	HN	4.40	weak
34	ORN5	HB	ALA3	HN	7.02	very weak
35	ORN5	HB	ALA4	HN	6.18	very weak
36	ORN5	HB	ORN5	HE1	4.68	weak
37	ORN5	HB	ORN5	H1	6.02	very weak
38	ORN5	HB	ORN5	H2	6.10	very weak
39	ORN5	HB	ORN5	HN	4.32	weak
40	ORN5	HD	dASP2	HN	6.42	very weak
41	ORN5	HD	ALA4	HN	6.13	very weak
42	ORN5	HD	ORN5	HE1	4.75	weak
43	ORN5	HD	ORN5	HE1	4.35	weak
44	ORN5	HD	ORN5	HN	4.94	weak
45	ORN5	HG	ORN5	HE1	5.64	very weak
46	ORN5	HG	ORN5	H1	6.04	very weak
47	ORN5	HG	ORN5	H2	6.18	very weak
48	ORN5	HG	ORN5	HN	6.50	very weak
49	ORN5	HN	ALA3	HN	6.02	very weak
50	ORN5	HN	ALA4	HN	4.69	weak
51	ORN5	HN	ORN5	HE1	6.21	very weak
52	dASP2	O	ORN5	HN	1.6-2.2	H-bond
53	dASP2	O	ORN5	N	2.6-3.2	H-bond
54	ALA3	O	ORN5	H1	1.6-2.2	H-bond
55	ALA3	O	ORN5	NT	2.6-3.2	H-bond

Table S19. Restraints used to calculate the structure of **21** Ac-[IsoDAADap]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	dASP2	HN	4.2	weak
2	ASP2	HB	ALA3	HN	3.7	medium
3	ALA3	HA	ALA4	HN	5.0	weak
4	ALA3	HA	DAP5	HN	6.0	Very weak
5	ALA3	HA	DAP5	H1	6.0	Very weak
6	ALA3	HN	ALA4	HN	5.0	weak
7	ALA4	HA	DAP5	HN	3.5	medium
8	ALA4	HA	DAP5	H1	6.0	Very weak
9	ALA4	HB*	DAP5	HN	4.5	weak
10	ALA4	HN	DAP5	HN	2.7	strong
11	DAP5	HA	DAP5	H2	6.0	very weak
12	DAP5	HA	DAP5	H1	3.5	medium
13	DAP5	HB2	DAP5	H1	5.0	weak
14	DAP5	HN	ASP2	HB*	7.0	Very weak
15	DAP5	HG	DAP5	H1	6.0	very weak
16	DAP5	HN	DAP5	H1	3.5	medium

Table S20. Restraints used to calculate the structure of **22** Ac-[IsodAADap]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	ACE1	HA	dASP2	HN	4.2	weak
2	ACE1	HA	DAP5	HN	6.5	Very weak
3	ASP2	HB	ALA3	HN	3.7	medium

4	ASP2	HB11	ALA3	HN	2.7	Strong
5	ASP2	HB11	ALA4	HN	5.0	Weak
6	ASP2	HB11	DAP5	HG	6.0	Very weak
7	ASP2	HB12	ALA3	HN	3.5	Medium
8	ASP2	HN	DAP5	HG	3.5	Medium
9	ASP2	HN	DAP5	H1	6.0	Weak
10	ALA3	HA	ALA4	HN	3.5	Medium
11	ALA3	HA	dASP2	HN	6.0	Very weak
12	ALA3	HA	DAP5	H2	6.0	Very weak
13	ALA3	HN	ALA4	HN	3.5	Medium
14	ALA3	HA	DAP5	H1	5.0	Weak
15	ALA3	HN	DAP5	HN	6.0	Very weak
16	ALA3	HA	dASP	HB12	6.0	Very weak
17	ALA4	HA	DAP5	HN	3.5	medium
18	ALA4	HA	DAP5	H1	6.0	Very weak
19	ALA4	HB	DAP5	HN	4.5	weak
20	ALA4	HN	DAP5	HN	2.7	strong
21	DAP5	HA	DAP5	H2	5.0	weak
22	DAP5	HA	DAP5	H1	3.5	medium
23	DAP5	HB2	DAP5	H1	5.0	weak
24	DAP5	HB2	DAP5	H2	6.0	Very weak
25	DAP5	HN	ASP2	H2	5.0	weak
26	DAP5	HG	DAP5	H1	6.0	very weak
27	DAP5	HG	DAP5	H2	5.0	Weak
28	DAP5	HN	DAP5	H1	3.5	medium

Table S21. Restraints used to calculate the structure of **23** [SuccAADap]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	SUCC1	HZ1	ALA2	HN	2.7	Strong
2	SUCC1	HE21	ALA2	HN	5.0	weak
3	SUCC1	HZ2	ALA2	HN	5.0	weak
4	SUCC1	HE21	DAP4	HG	2.7	Strong
5	SUCC1	HZ1	DAP4	HN	6.0	Very weak
6	SUCC1	HE21	DAP4	HN	6.0	Very weak
7	SUCC1	HE22	DAP4	HG	5.0	Weak
8	ALA2	HN	ALA3	HN	2.7	Strong
9	ALA2	HN	DAP4	HN	5.0	Weak
10	ALA2	HA	ALA3	HN	5.0	Weak
11	ALA2	HA	DAP4	H2	6.0	Very weak
12	ALA2	HA	DAP4	H1	5.0	Weak
13	ALA2	HA	DAP4	HN	6.0	Very weak
14	ALA3	HA	DAP4	HN	5.0	Weak
15	ALA3	HN	DAP4	HN	2.7	Strong
16	ALA3	HN	DAP4	HB1	6.0	Very weak
17	ALA3	HN	SUCC1	HZ1	6.0	Very weak
18	DAP4	HA	ALA3	HN	6.0	Very weak
19	DAP4	HA	DAP4	H2	5.0	weak
20	DAP4	HA	DAP4	H1	3.5	Medium
21	DAP4	HB1	DAP4	H1	6.0	Very weak
22	DAP4	HB1	DAP4	H2	6.0	Very weak
23	DAP4	HB2	DAP4	H1	5.0	weak
24	DAP4	HB2	DAP4	H2	6.0	Very weak
25	DAP4	HN	DAP4	H2	5.0	weak
26	DAP4	HN	DAP4	H1	3.5	Medium

27	DAP4	HG	DAP4	H2	6.0	Very Weak
28	DAP4	HG	DAP4	H1	5.0	Weak
29	DAP4	HN	ALA3	HB	6.0	Very weak

Table S22. Restraints used to calculate the structure of **24** Ac-[GlutAADap]-NH_2 in H_2O:D_2O (9:1).

	RES1	**ATOM1**	**RES2**	**ATOM2**	**DISTANCE** (Å)	**CLASS**
1	GLUT1	HH1	ALA2	HN	2.7	Strong
2	GLUT1	HZ1	ALA2	HN	6.0	Very weak
3	GLUT1	HH2	ALA2	HN	3.5	Medium
4	GLUT1	HE21	DAP4	HG	5.0	weak
5	GLUT1	HE22	DAP4	HG	6.0	Very weak
6	GLUT1	HH2	DAP4	HG	6.0	Very weak
7	GLUT1	HZ1	DAP4	HN	6.0	Very weak
8	ALA2	HN	ALA3	HN	2.7	Strong
9	ALA2	HN	DAP4	HE22	5.0	weak
10	ALA2	HA	ALA3	HN	3.5	Medium
11	ALA2	HA	DAP4	HN	5.0	weak
12	ALA2	HA	DAP4	H1	5.0	weak
13	ALA2	HA	DAP4	H2	5.0	weak
14	ALA3	HA	DAP4	H1	5.0	weak
15	ALA3	HA	DAP4	H2	6.0	Very weak
16	ALA3	HA	DAP4	HN	3.5	Medium
17	ALA3	HN	GLUT1	HH1	5.0	weak
18	ALA3	HN	GLUT1	HE22	6.0	Very weak
19	ALA3	HN	DAP4	HN	2.7	Strong
20	ALA3	HN	DAP4	H1	6.0	Very weak
21	DAP4	HN	ALA3	HB	6.0	Very weak
22	DAP4	HA	DAP4	H2	5.0	weak
23	DAP4	HA	DAP4	H1	3.5	Medium
24	DAP4	HB1	DAP4	H1	6.0	Very weak
25	DAP4	HB1	DAP4	H2	6.0	Very weak
26	DAP4	HB2	DAP4	H1	5.0	weak
27	DAP4	HB2	DAP4	H2	6.0	Very weak
28	DAP4	HN	GLUT1	HE21	6.0	Very weak
29	DAP4	HN	ALA2	HB	7.5	Medium
30	DAP4	HG	GLUT1	HZ2	5.0	weak
31	DAP4	HG	GLUT1	HZ1	2.7	Strong
32	DAP4	HN	GLUT1	HZ2	6.0	Very weak
33	DAP4	HG	DAP4	H1	5.0	weak
34	DAP4	HN	DAP4	H1	2.7	Strong

7.5 Molecular Dynamics Simulations

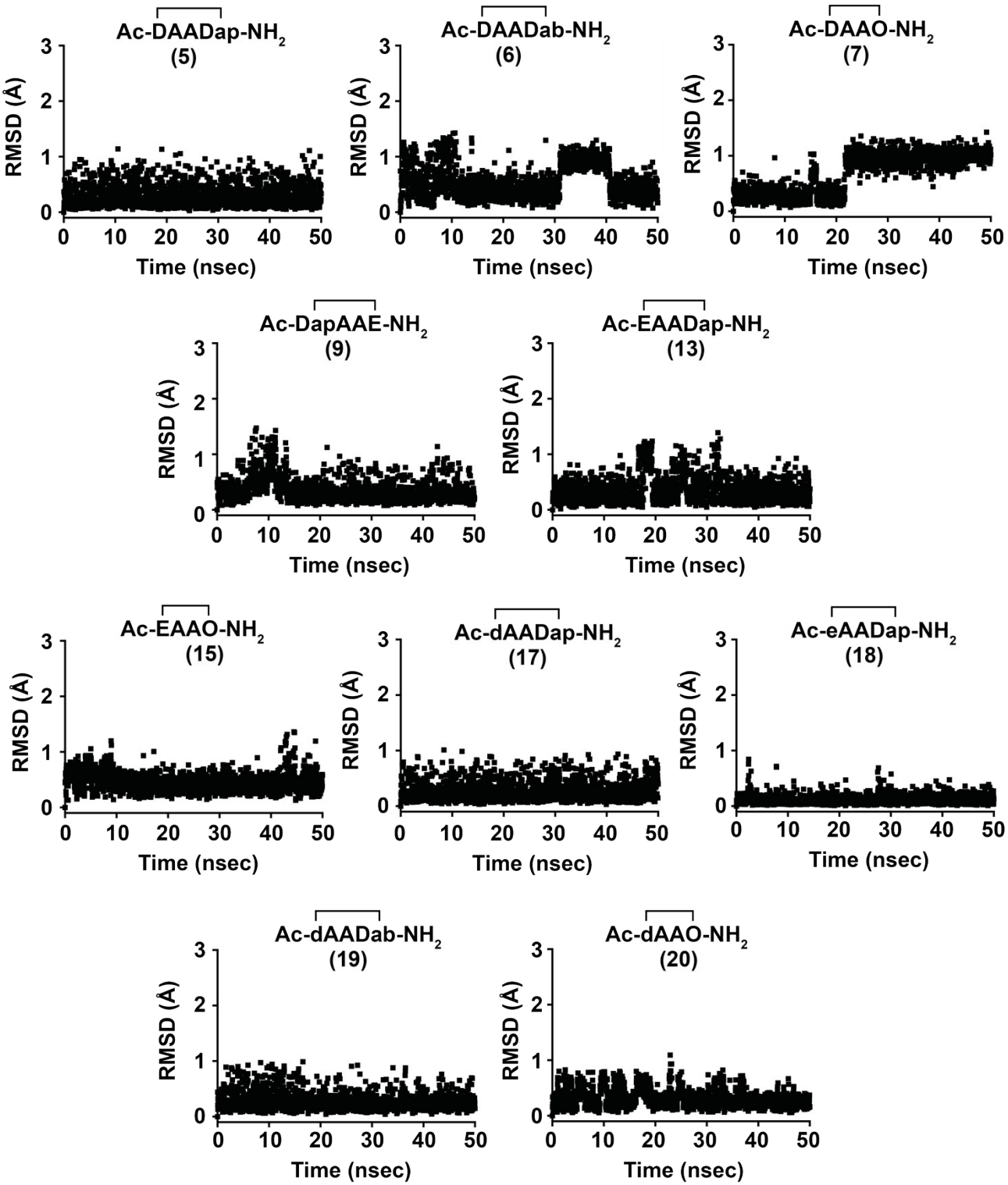

Figure S25. Molecular dynamics simulations (50 ns) of NMR structures (RMSD variations of backbones) in a water box model (TIP3P) at 300 K for peptides **5**–**7**, **9**, **13**, **15**, **17**–**20**.

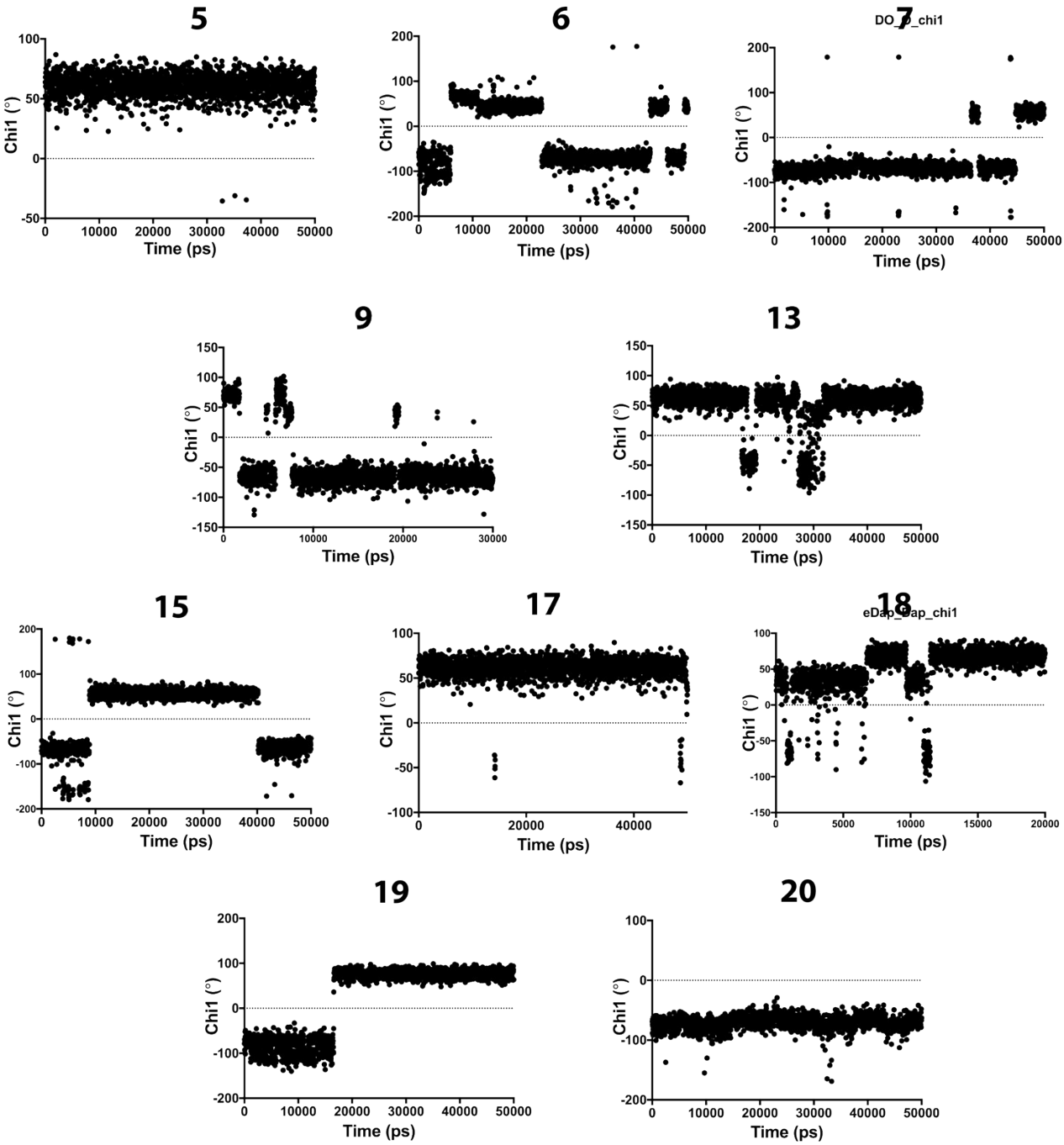

Figure S26. Molecular dynamics simulations (50 ns) of NMR structures (Chi1 angle for the 4th residue (Z)) in a water box model (TIP3P) at 300 K for peptides **5**–**7**, **9**, **13**, **15**, **17**–**20**.

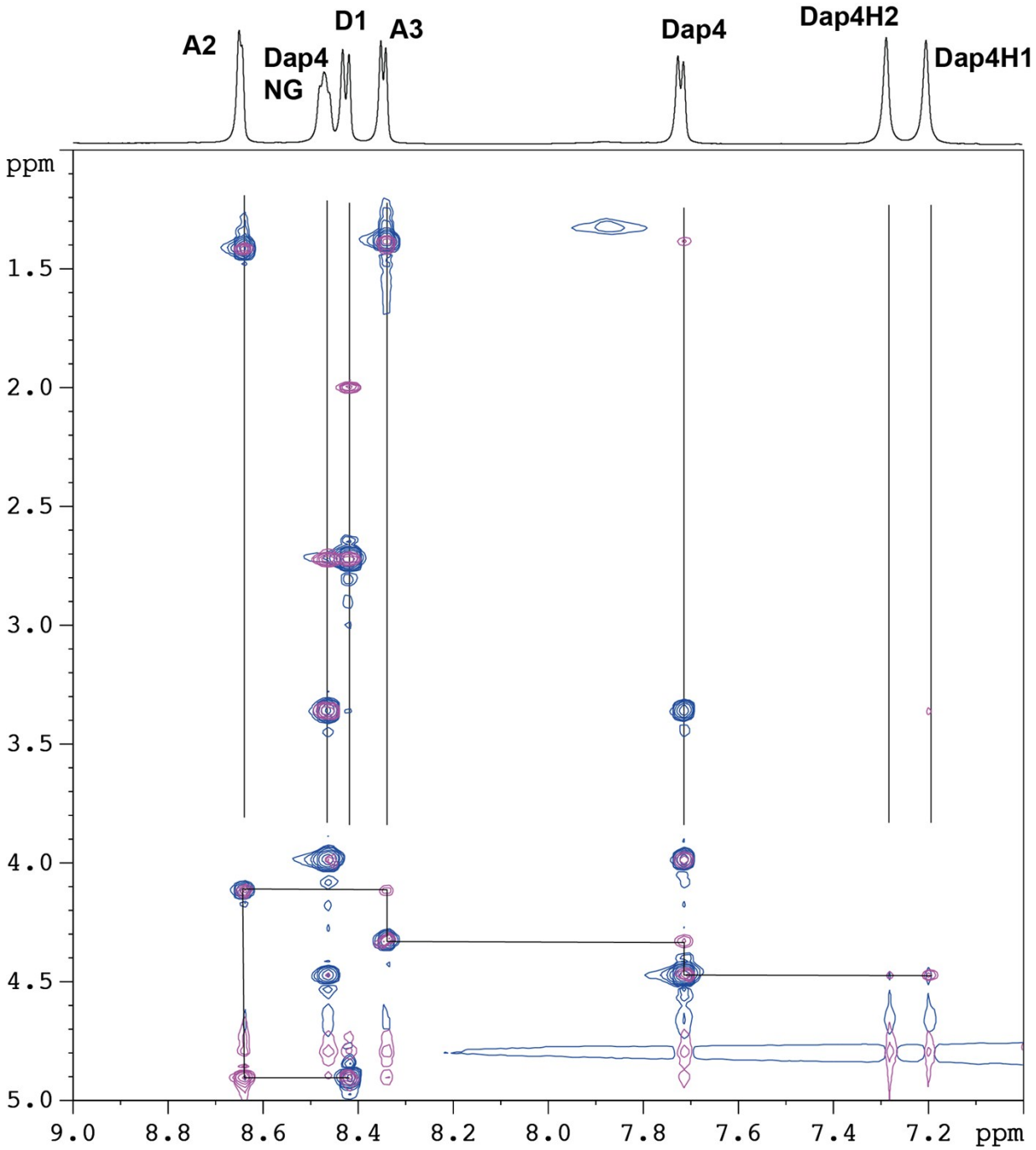

Figure S27. Skewers and sequential ROE walk for Ac-[DAADap]-NH_2 (**5**). (Blue = TOCSY spectrum, Red = ROESY spectrum).

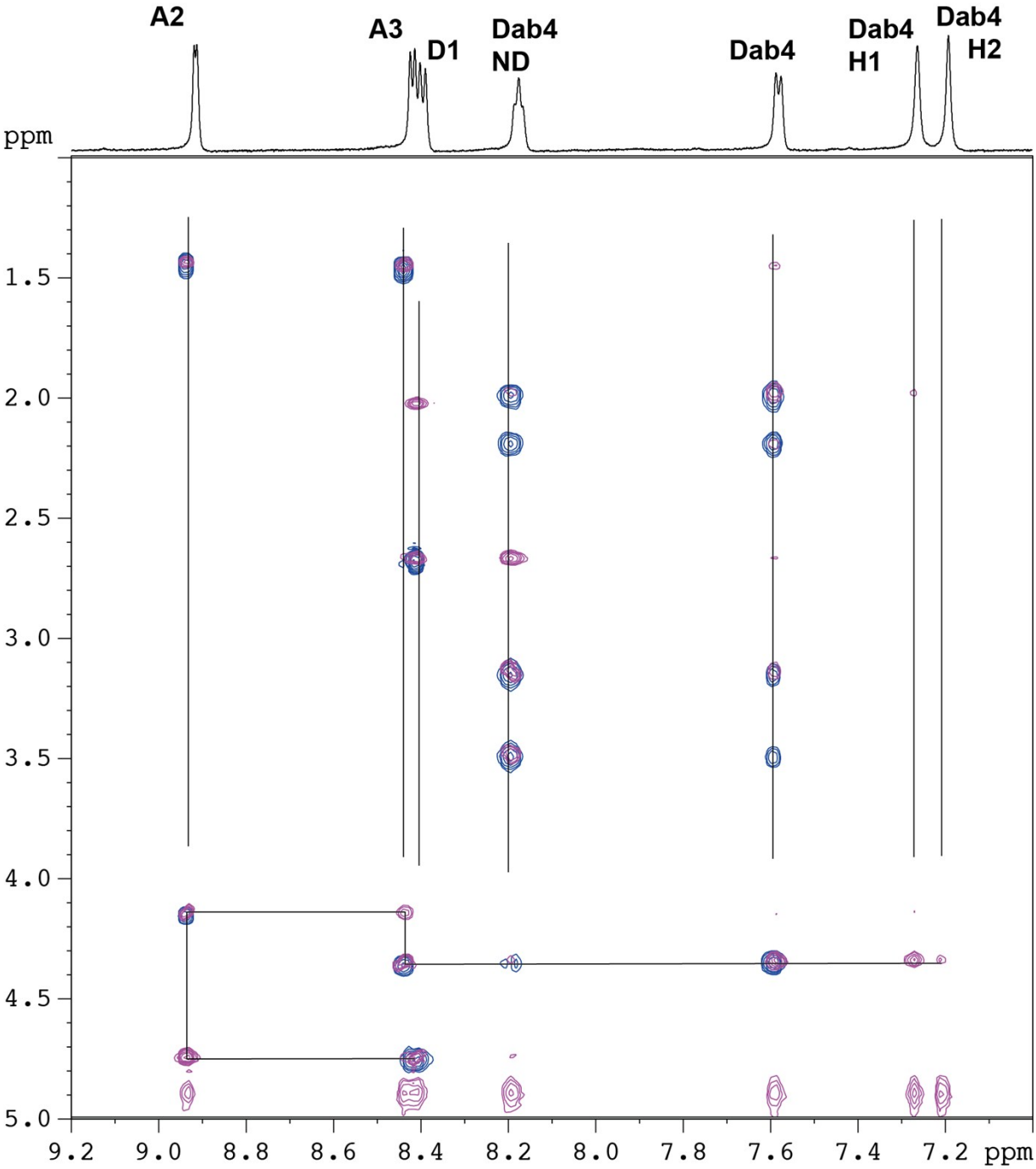

Figure S28. Skewers and sequential ROE walk for Ac-[DAADab]-NH_2 (**6**). (Blue = TOCSY spectrum, Red = ROESY spectrum).

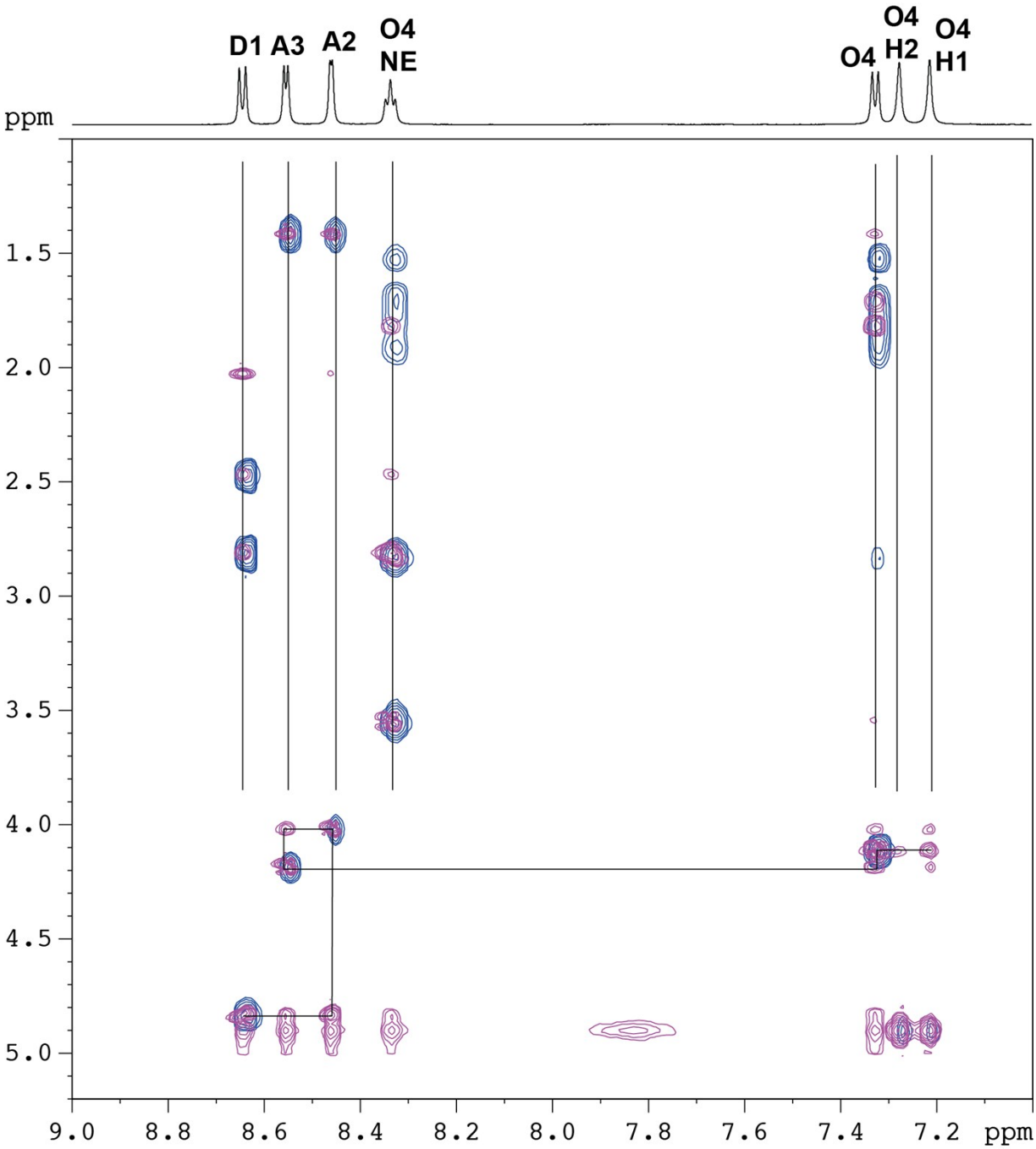

Figure S29. Skewers and sequential ROE walk for Ac-[DAAO]-NH_2 (**7**). (Blue = TOCSY spectrum, Red = ROESY spectrum).

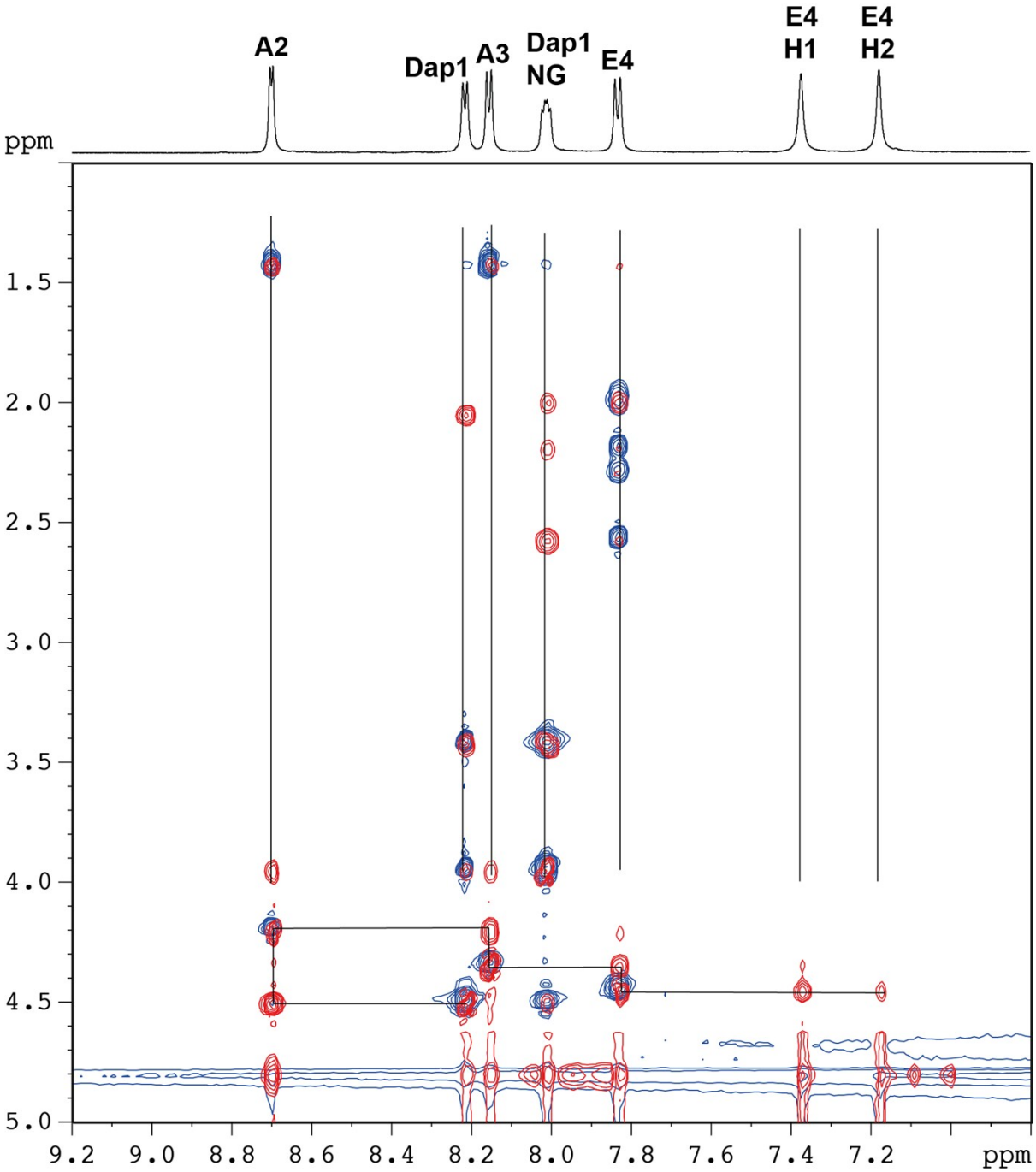

Figure S30. Skewers and sequential ROE walk for Ac-[DapAAE]-NH_2 (**9**). (Blue = TOCSY spectrum, Red = ROESY spectrum).

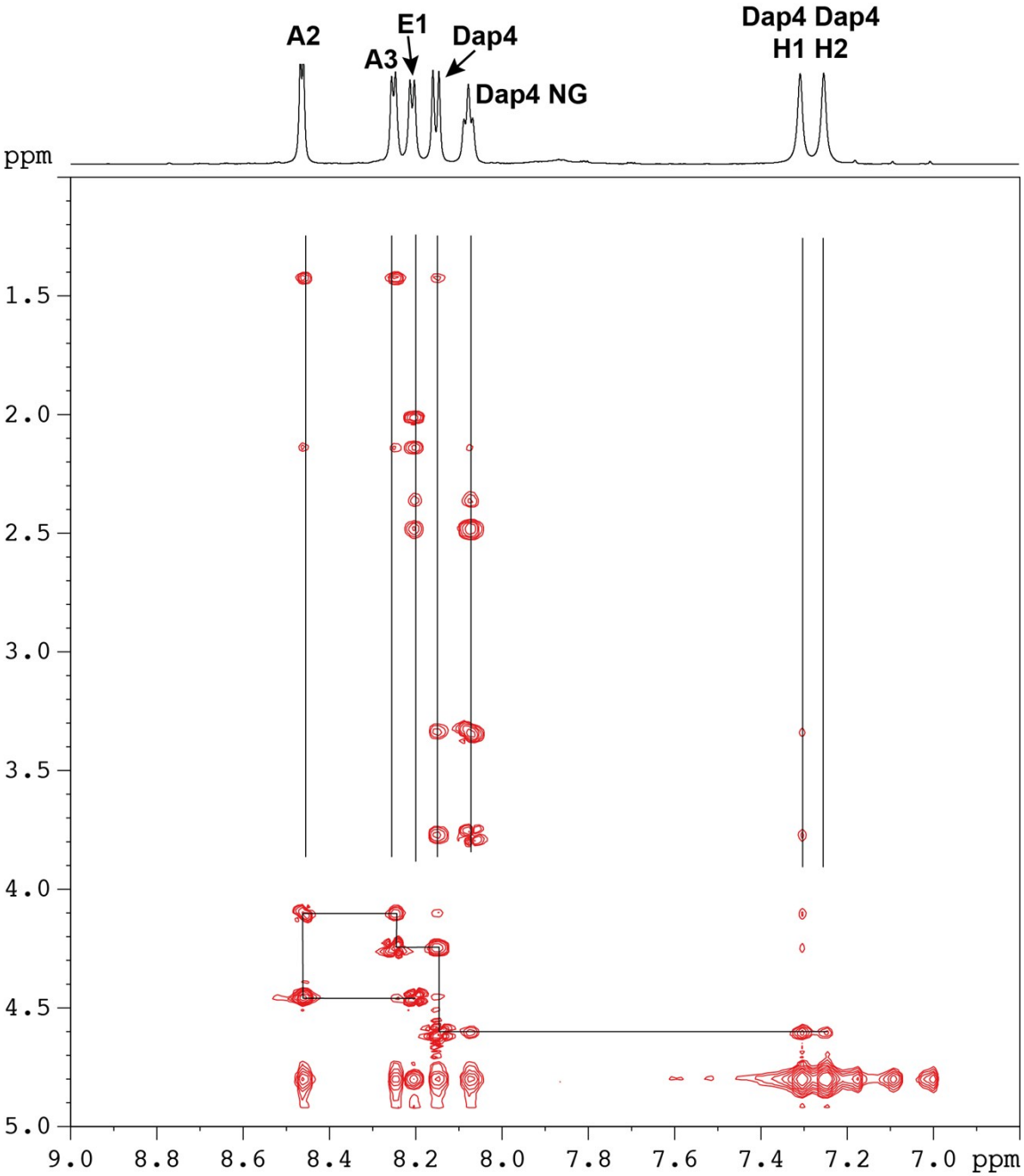

Figure S31. Skewers and sequential ROE walk for Ac-[EAADap]-NH_2 (**13**). (Blue = TOCSY spectrum, Red = ROESY spectrum).

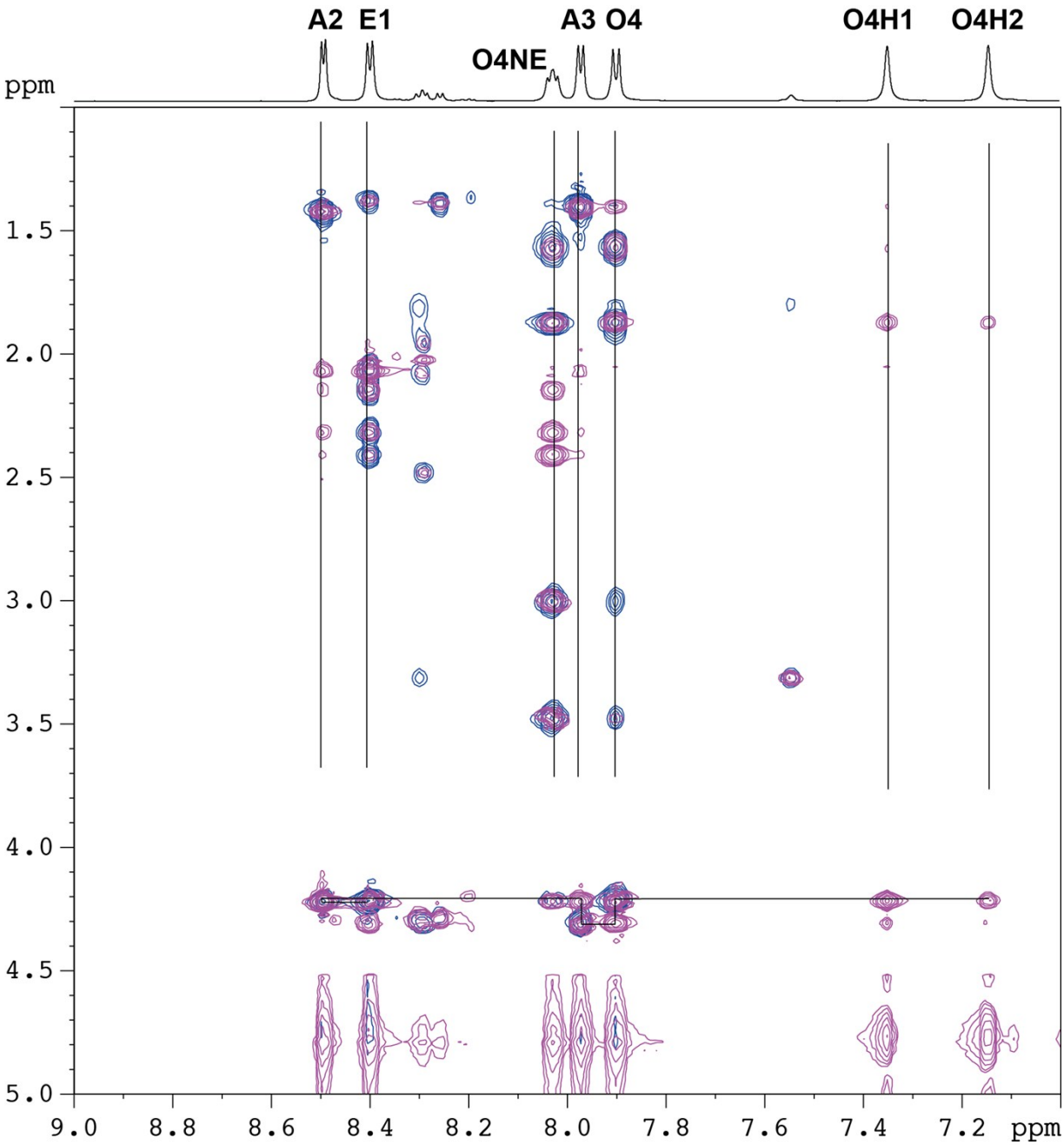

Figure S32. Skewers and sequential ROE walk for Ac-[EAAO]-NH_2 (**15**). (Blue = TOCSY spectrum, Red = ROESY spectrum).

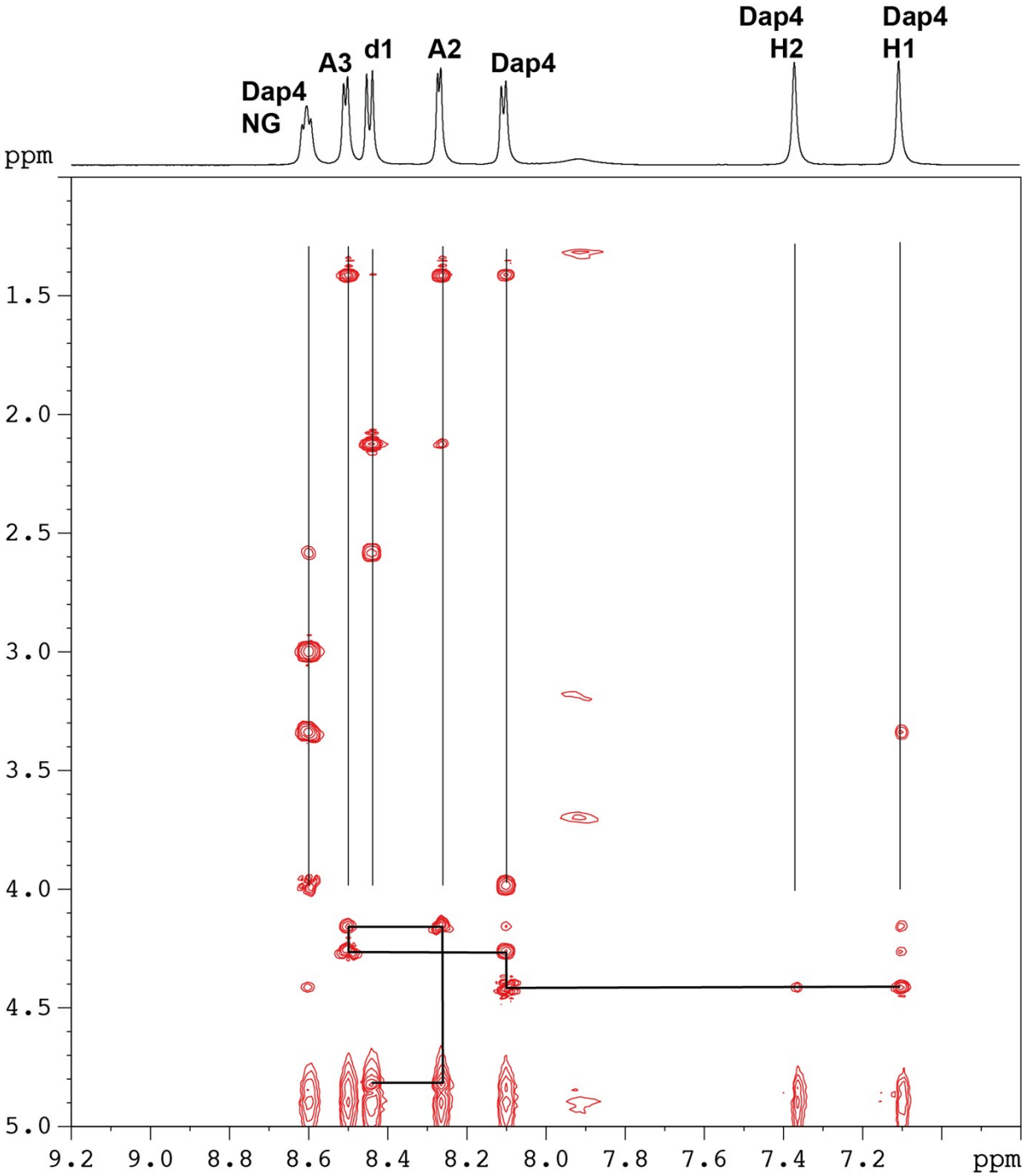

Figure S33. Skewers and sequential ROE walk for Ac-[dAADap]-NH_2 (**17**). (Red = ROESY spectrum).

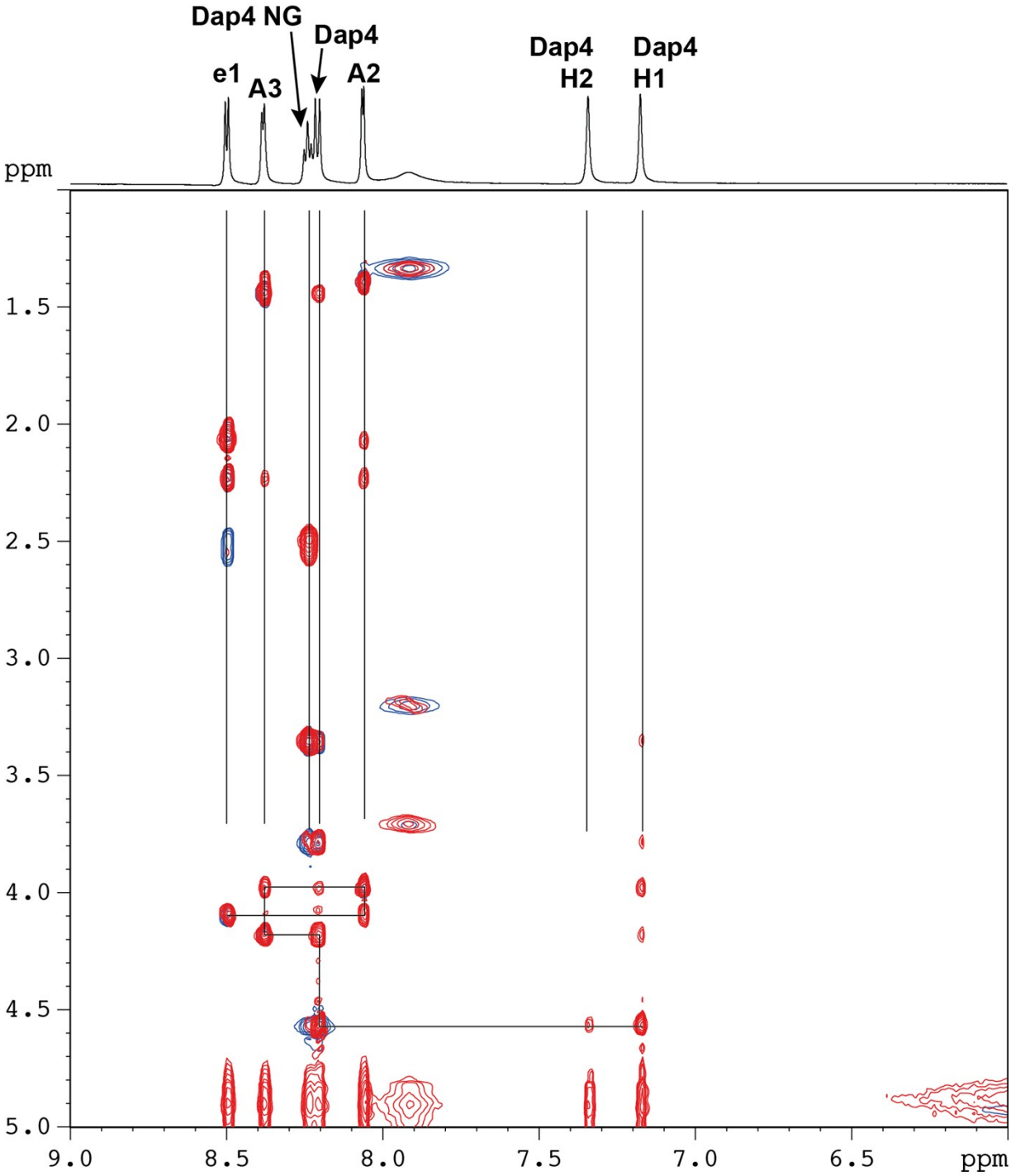

Figure S34. Skewers and sequential ROE walk for Ac-[eAADap]-NH_2 (**18**). (Blue = TOCSY spectrum. Red = ROESY spectrum).

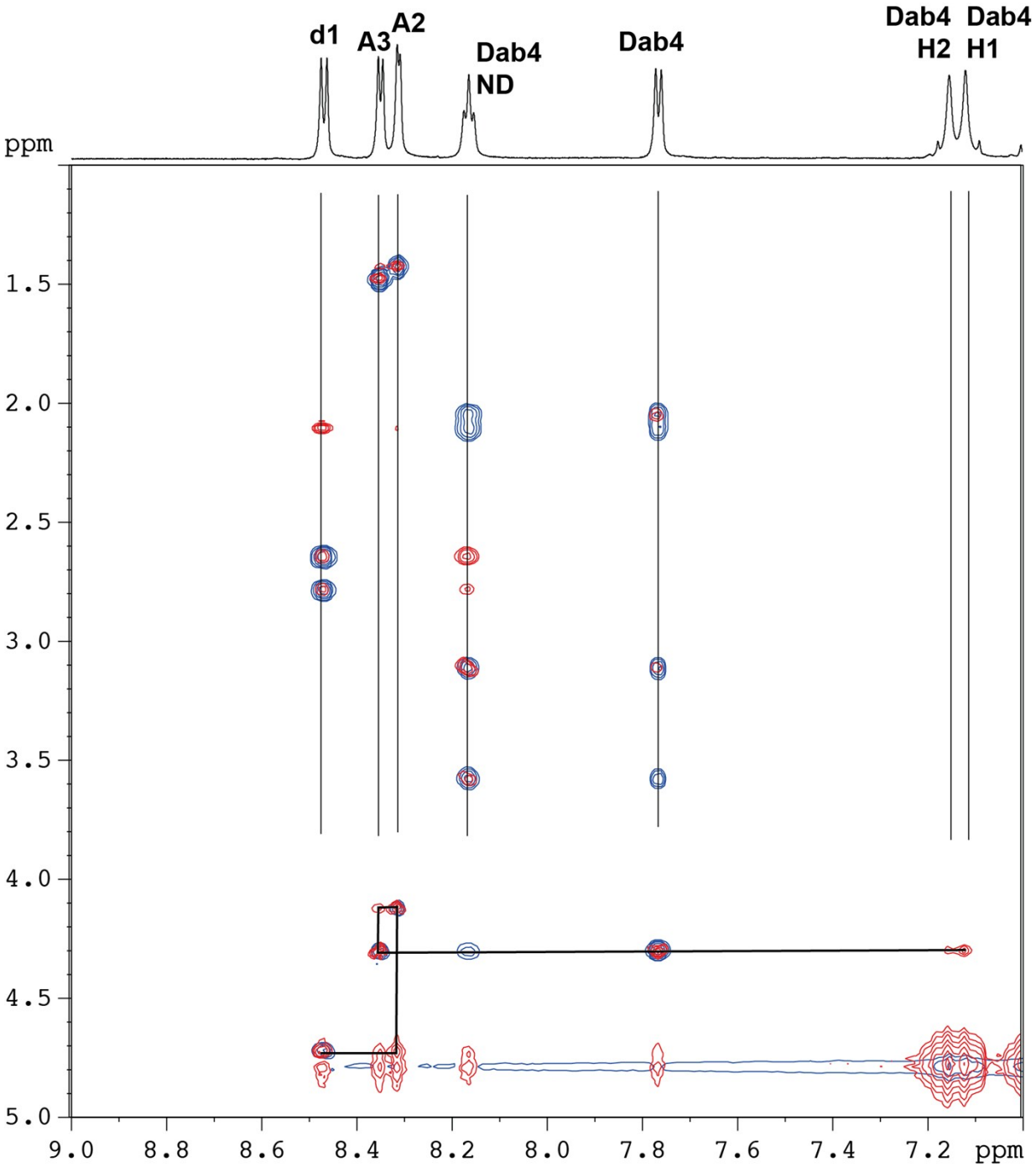

Figure S35. Skewers and sequential ROE walk for Ac-[dAADab]-NH_2 (**19**). (Blue = TOCSY spectrum. Red = ROESY spectrum).

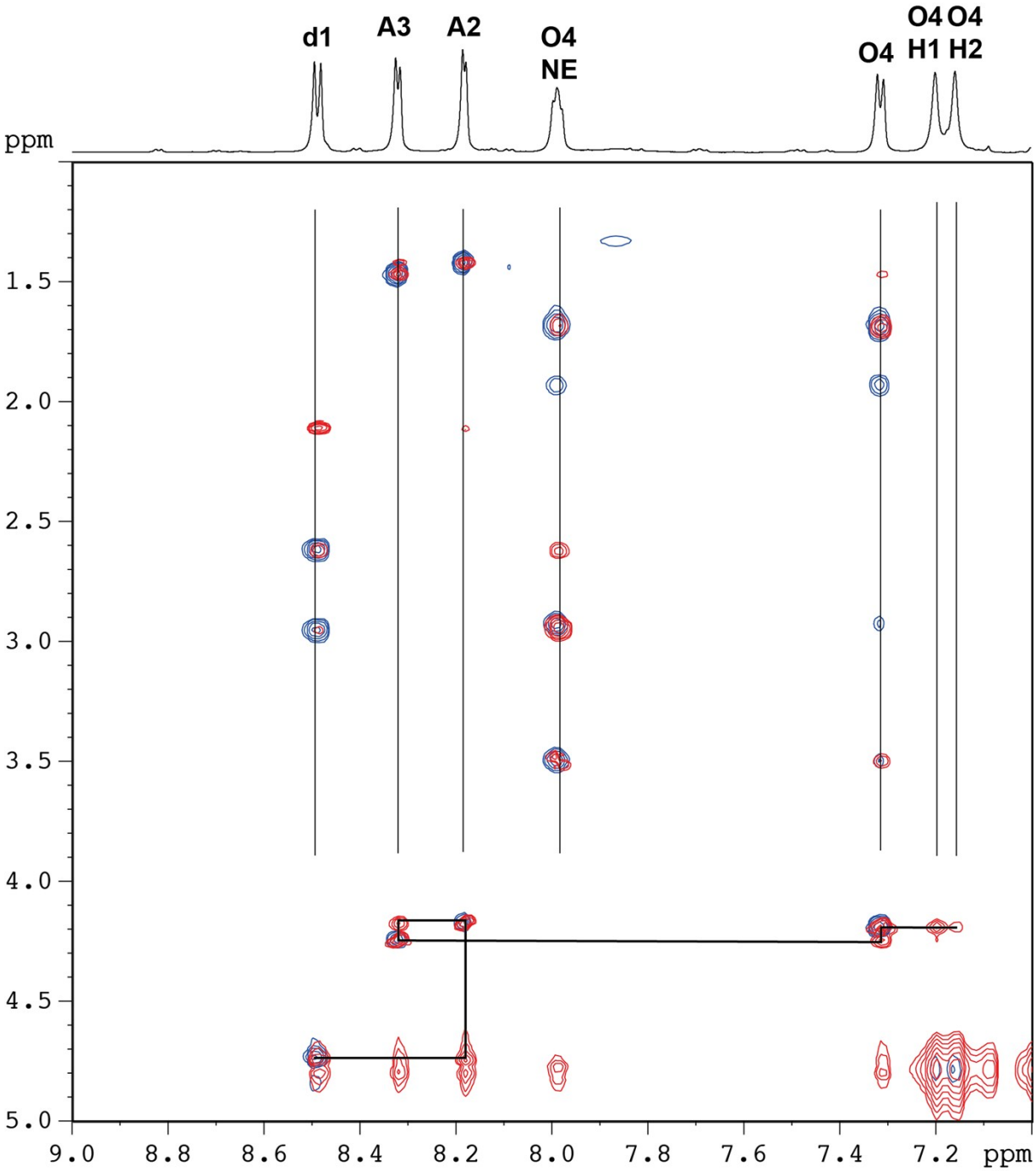

Figure S36. Skewers and sequential ROE walk for Ac-[dAAO]-NH_2 (**20**). (Blue = TOCSY spectrum. Red = ROESY spectrum).

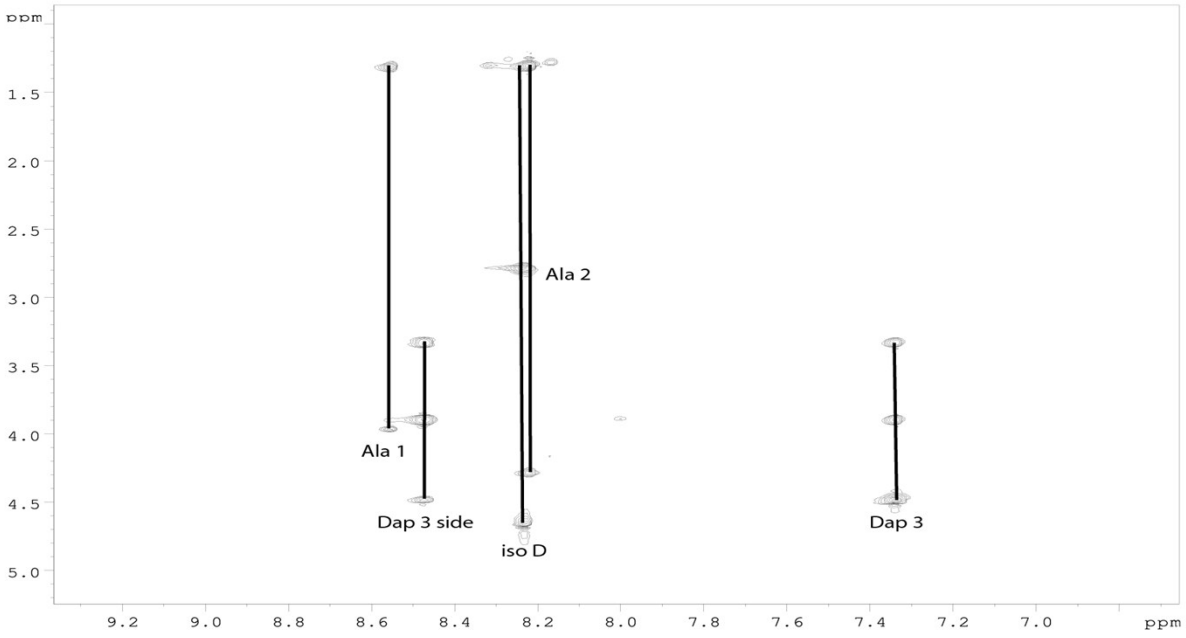

Figure S37. TOCSY spectrum for Ac-[IsoDAADap]-NH_2 **(21).**

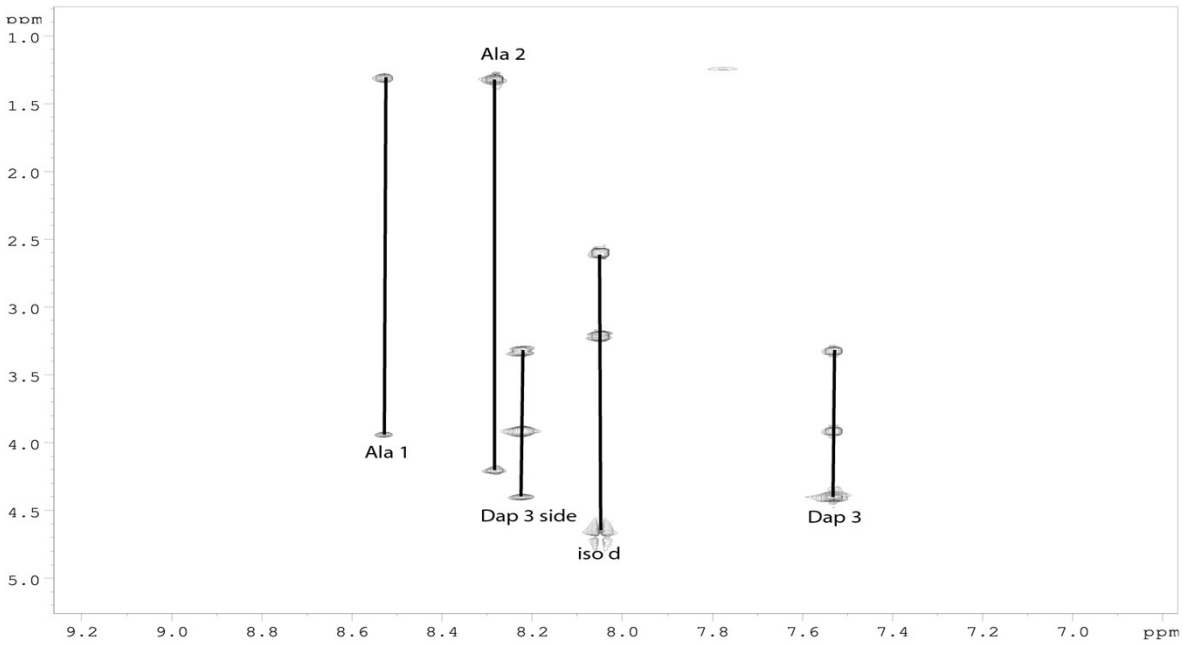

Figure S38. TOCSY spectrum for Ac-[IsodAADap]-NH_2 **(22).**

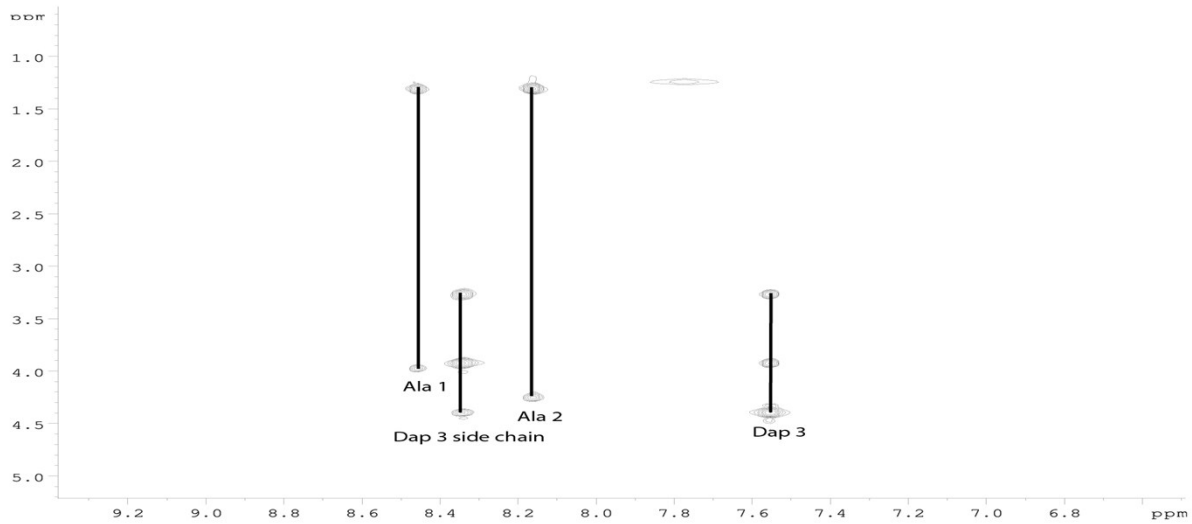

Figure S39. TOCSY spectrum for [SuccAADap]-NH_2 **(23).**

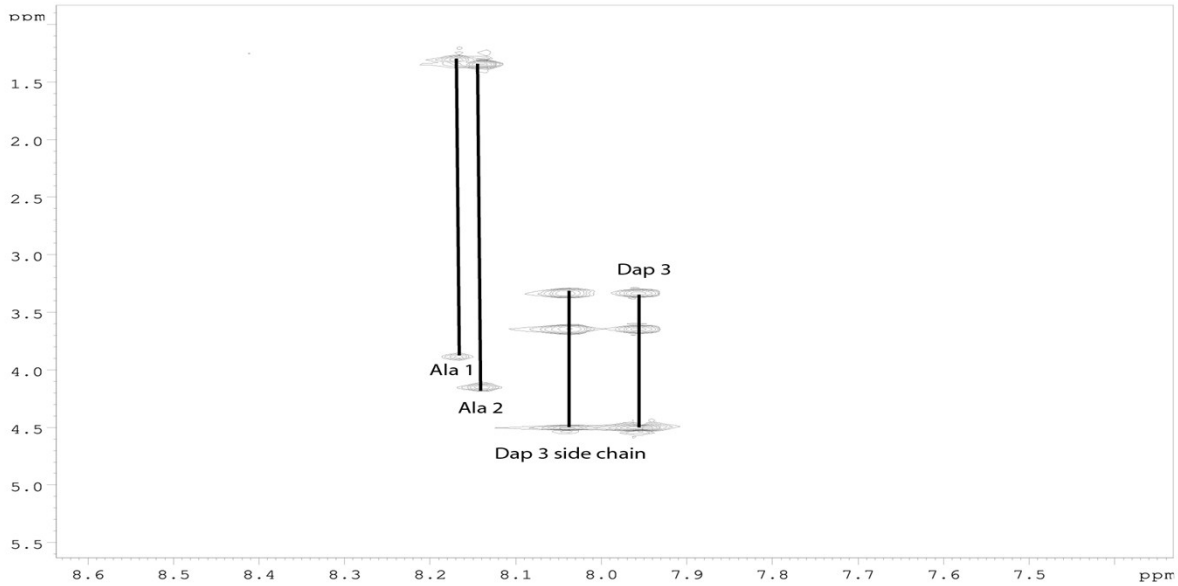

Figure S40. TOCSY spectrum for [GlutAADap]-NH_2 **(24).**

7.6 NMR spectra of N-capped peptides in H_2O:D_2O (9:1).

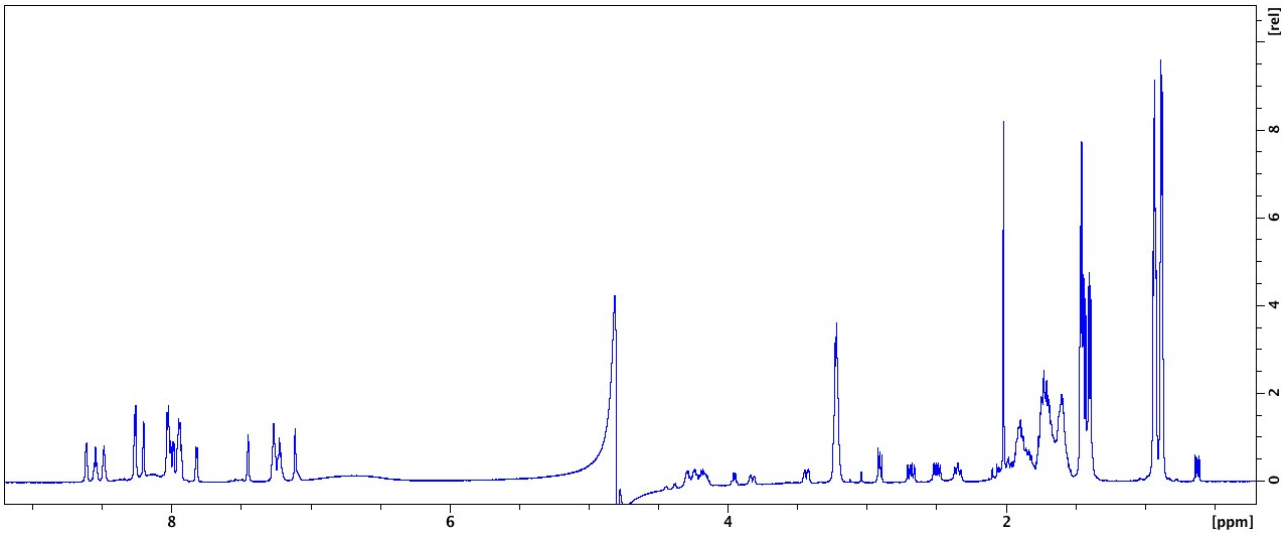

Figure S41. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[EAADap](ARL)$_3$-NH_2 (**31**).

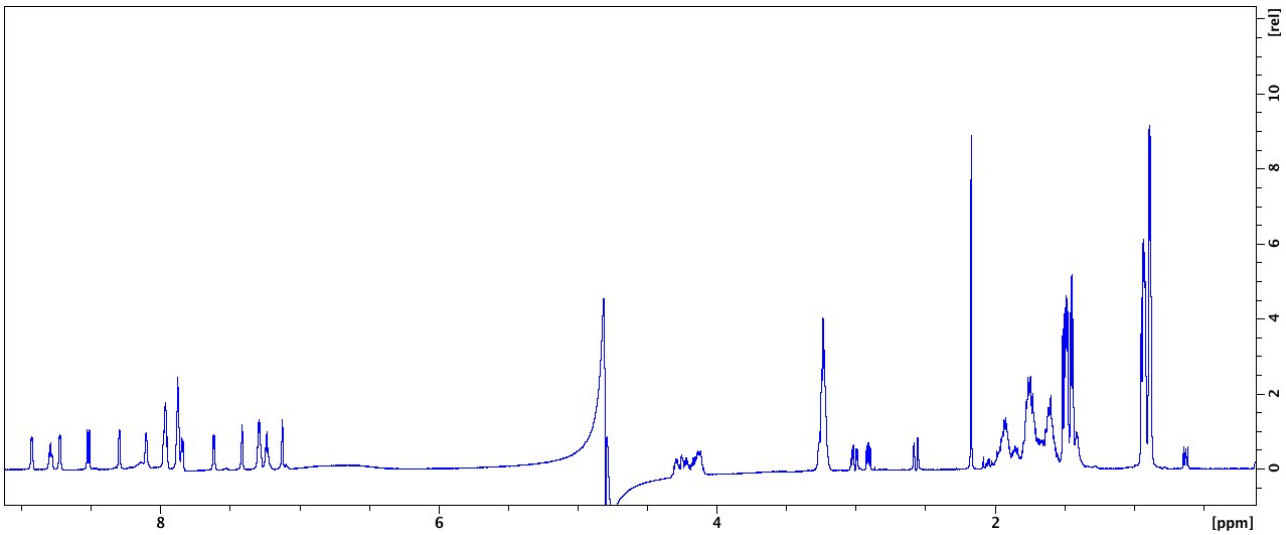

Figure S42. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[dAADap](ARL)$_3$-NH_2 (**33**).

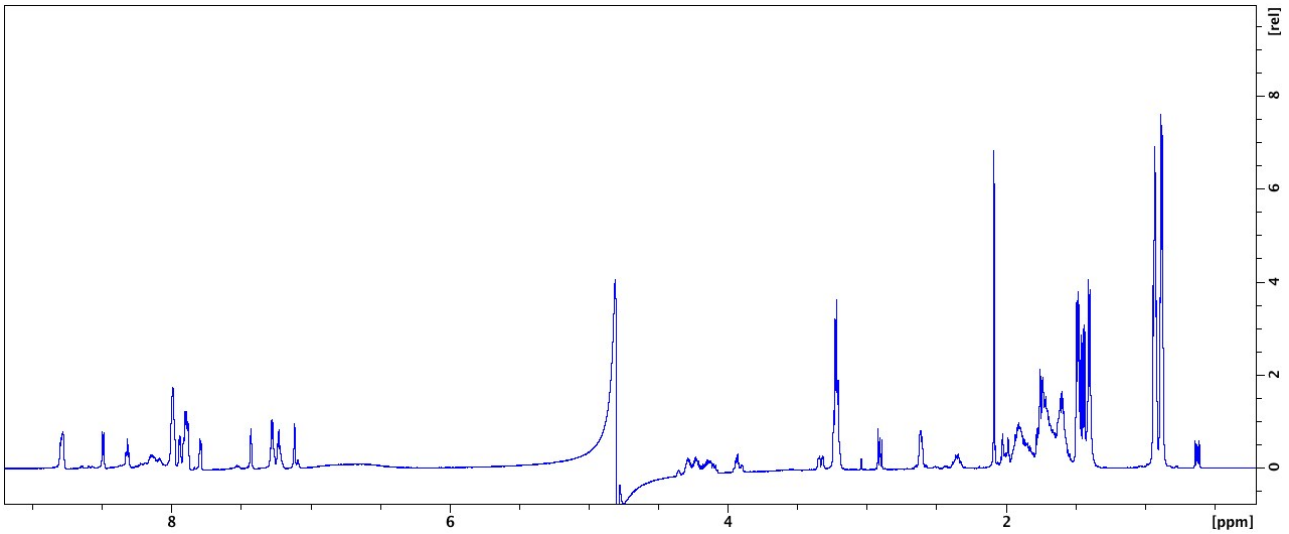

Figure S43. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[eAADap](ARL)$_3$-NH$_2$ (**34**).

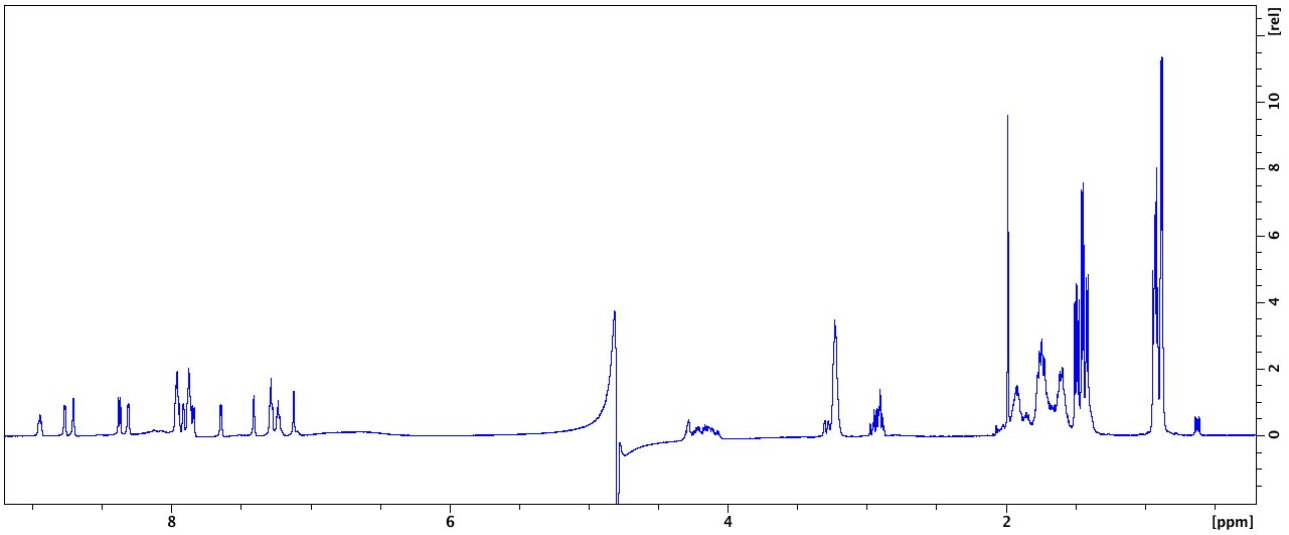

Figure S44. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[isoDAADap](ARL)$_3$-NH$_2$ (**36**).

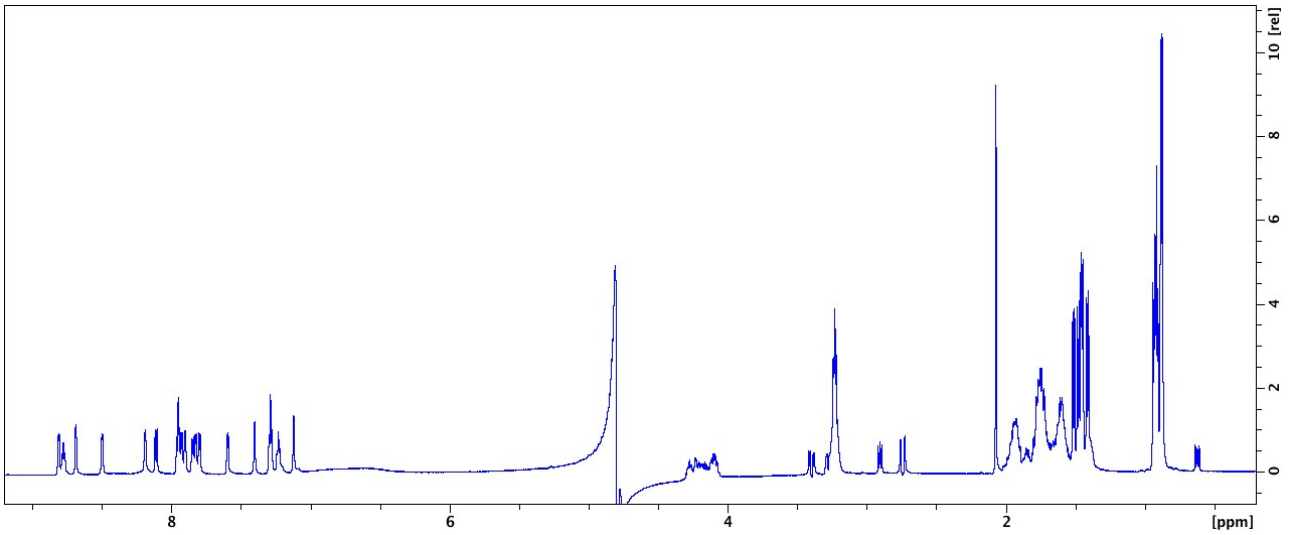

Figure S45. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,4)-[isodAADap](ARL)$_3$-NH$_2$ (**37**).

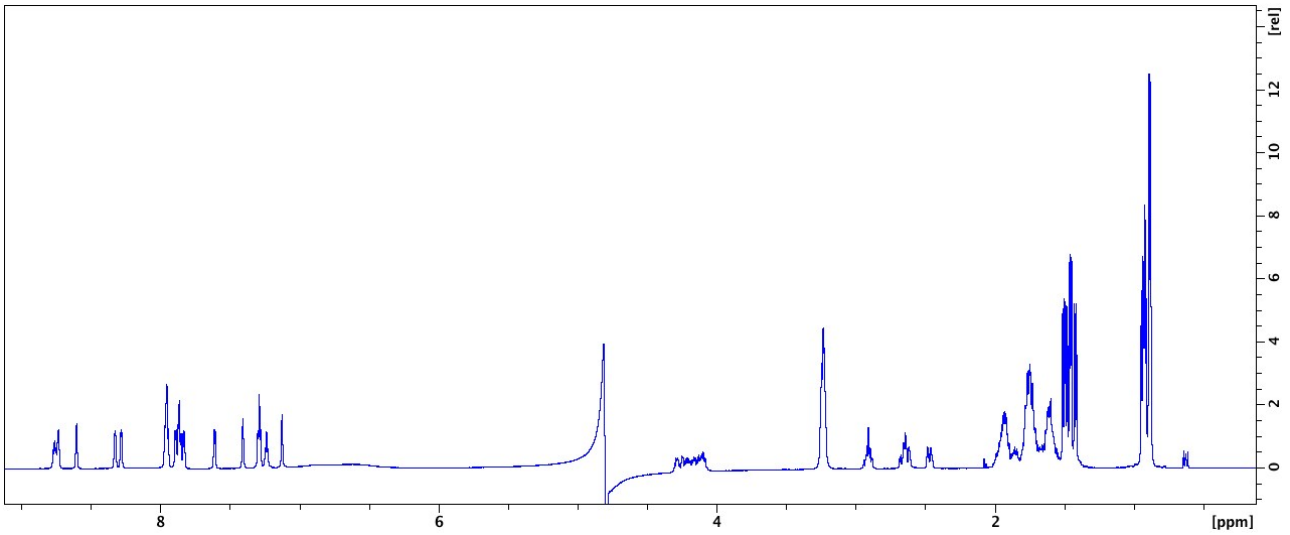

Figure S46. 600 MHz ^{1}H NMR spectrum of cyclo-(1,4)-[SuccAADap](ARL)$_3$-NH$_2$ (**38**).

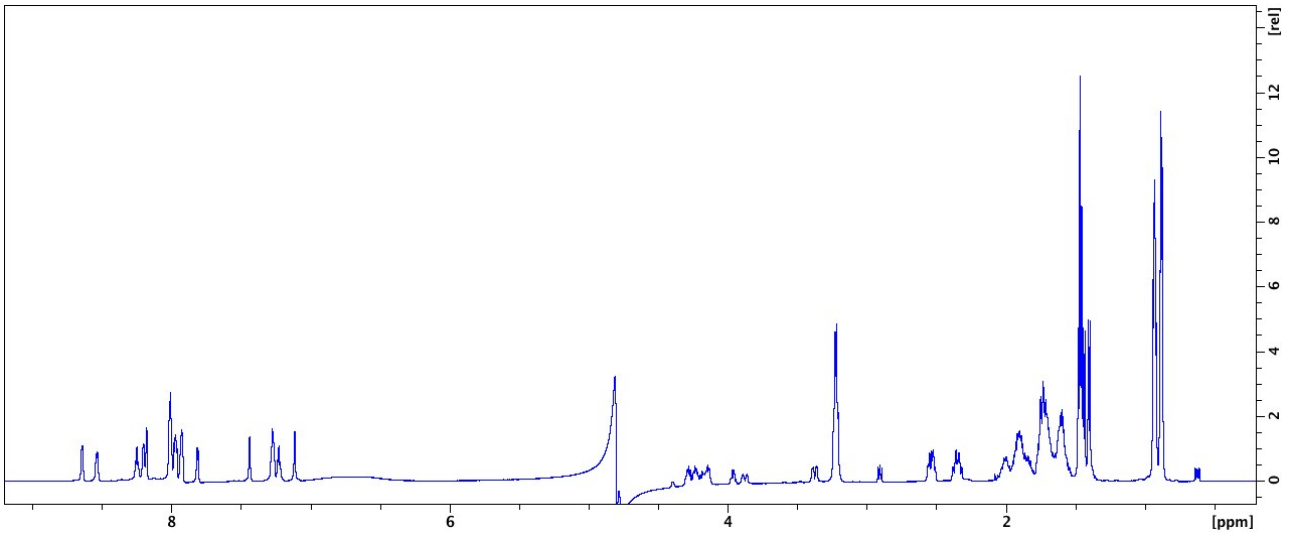

Figure S47. 600 MHz ^{1}H NMR spectrum of cyclo-(1,4)-[GlutAADap](ARL)$_3$-NH$_2$ (**39**).

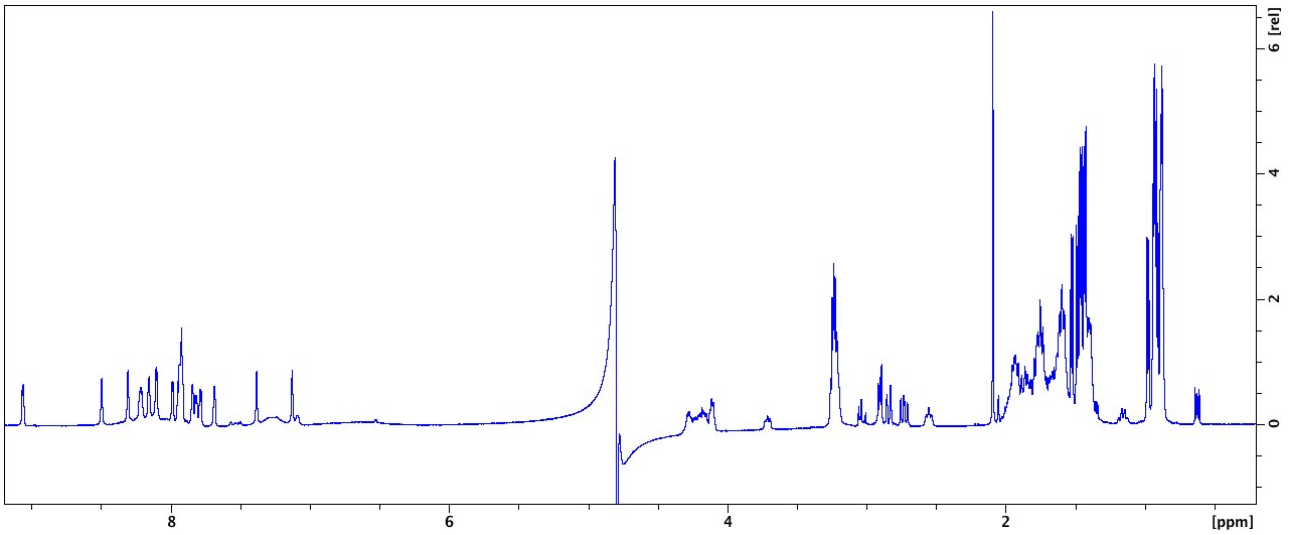

Figure S48. 600 MHz ^{1}H NMR spectrum of Ac-cyclo-(1,5)-[KAAAD](ARL)$_3$-NH$_2$ (**40**).