Electronic supporting information for

"NMR-based quantitative studies of the conformational equilibrium between their square and folded forms of ascidiacyclamide and its analogues"

Akiko Asano*, Katsuhiko Minoura, Yuki Kojima, Taishi Yoshii, Ryoya Ito, Takeshi Yamada, Takuma Kato

and Mitsunobu Doi

Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka 569-1094, Japan.

Contents:

Synthesis and characterization of the peptides 8-12

General Experimental Methods

Pure products were obtained after liquid chromatography using Merck silica gel 60 (40-63 µm). Analytical thin-layer chromatography was carried out on Merck silica gel F_{254} plates with the following solvent system (v/v); chloroform : methanol : acetic acid (95 : 10 : 3). The plates were visualized with UV light (λ = 254 nm) and revealed with a 5 % solution of ninhydrin in ethanol. Melting points were determined on a Yanagimoto micro-melting point apparatus (YANAKO Measuring Instrument Trading Co., Kyoto, Japan). ^{1}H NMR spectra were recorded on an Agilent DD2 600-MHz NMR spectrometer (Agilent Technologies, California, USA). Peptide concentrations were about 5.0 mM in CD_3CN. Chemical shifts were measured relative to internal trimethylsilane at 0.00 ppm. The protons were assigned using two dimensional correlated spectroscopy (2D-COSY) and rotating-frame Overhauser effect spectroscopy (ROESY; mixing time = 500 ms). High-resolution mass spectra (HR-MS) were obtained using FAB mass spectrometry on a JMS-700 mass spectrometer (JEOL LTD., Tokyo, Japan).


Synthesis of Boc-D-Val(Thz)-OMe

Boc-D-Val(Thz)-OMe was prepared according to previous report (Y. Hamada *et. al.*, *J. Org. Chem.* 1987, **52**, 1252-1255) (Scheme S1). N-(*tert*-butoxycarbonyl)-D-valine (Boc-D-Val-OH) was first converted to the corresponding methyl ester by using methyl iodide in the presence of potassium hydrogen carbonate in N, N-dimethylformamide (DMF) at room temperature. The methyl ester was reduced with lithium chloride-sodium borohydride in tetrahydrofuran (THF) to give the amino alcohol derivative. Oxidation of the amino alcohol derivative was conveniently accomplished by the dimethyl sulfoxide (DMSO) oxidation using sulfur trioxide-pyridine complex ($Py \cdot SO_3$) in the presence of trimethylamine (Et_3N), giving the amino aldehyde derivative. Condensation of the amino aldehyde derivative with L-cysteine methyl ester (H-L-Cys-OMe) afforded the thiazolidine derivative as a mixture of C-2 epimers. Oxidation of the thiazolidine derivative to the Boc-D-Val(Thz)-OMe was performed with activated manganese dioxide (Sigma-Aldrich Co. Llc., St. Louis, USA) in benzene.
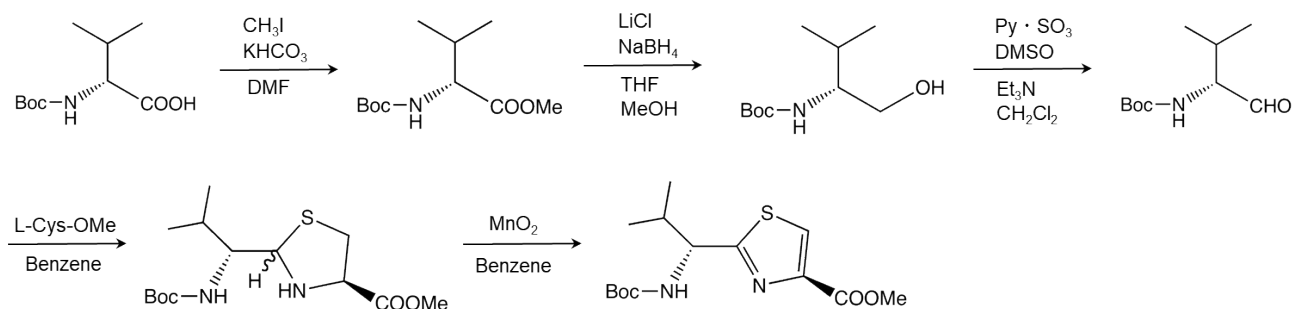
Scheme S1

General procedure for the condensation

Peptides were synthesized by a conventional liquid-phase method according to Scheme S2. The liner peptide were synthesized using 1-hydroxy-benzotiazole (HOBt) (Watanabe Chemical Ind. Ltd., Hiroshima, Japan) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl) (Watanabe Chemical Ind. Ltd., Hiroshima, Japan), and cyclization was conducted with benzotriazolyloxy-tris(pyrrolidino)-phosphonium hexafluorophosphate (PyBOP) (Watanabe Chemical Ind. Ltd., Hiroshima, Japan) in the presence of 4-dimethylaminopyridine (DMAP) (Nacalai tesque, Kyoto, Japan).
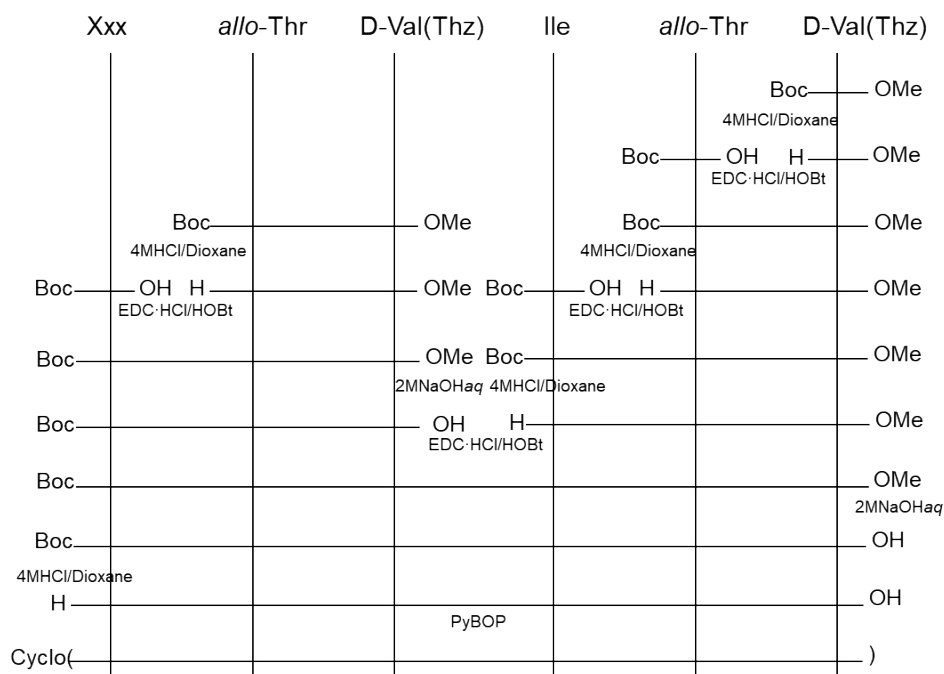

Xxx = Abu (**8**), Nva (**9**), Tbu (**10**), Chg (**11**), Tle (**12**)

Scheme S2

Synthesis of oxazoline rings

The oxazoline (Oxz) rings were formed by reacting the Ile–*allo*-Thr moiety with bis(2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor) (Fujifilm Wako Pure Chemical, Osaka, Japan) according to previous report (A. J. Phillips *et. al.*, *Org. Lett.* 2000, **2**, 1165-1168) (Scheme S3).

8: R = CH_2CH_3
9: R = $(CH_2)_2CH_3$
10: R = $CH_2C(CH_3)_3$
11: R = cyclohexane
12: R = $C(CH_3)_3$
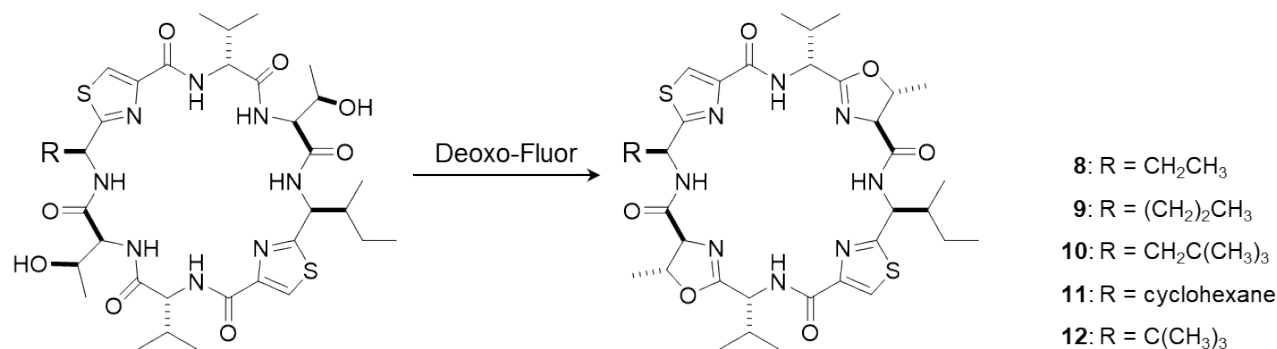
Scheme S3

Characterization of peptide 8

R_f = 0.72. Mp. 115–118 °C. HR-FAB MS (matrix: Glycerol) calcd for $[C_{34}H_{48}N_8O_6S_2 + H]^+$ = 729.3211, found *m/z* 729.3215. ^{1}H NMR (600 MHz, CD_3CN, 298 K) δ = 7.82 (d, 1H, NH Abu^1, J = 6.6 Hz); 7.75 (d, 1H, NH Ile^5, J = 7.8 Hz); 7.68 (s, 2H, H Thz^{4,8}); 7.22 (d, 1H, NH D-Val^3, J = 10.2 Hz); 7.14 (d, 1H, NH D-Val^7, J = 10.2); 5.16 (dd, 1H, $^\alpha$H D-Val^3, J = 10.2, 6.6 Hz); 5.13 (dd, 1H, $^\alpha$H D-Val^7, J = 10.2, 6.6 Hz); 4.87 (qd, 1H, $^\beta$H Oxz^6, J = 6.6, 4.8); 4.78 (qd, 1H, $^\beta$H Oxz^2, J = 6.0, 4.5); 4.71 (q, 1H, $^\alpha$H Abu^1, J = 6.6 Hz); 4.64 (t, 1H, $^\alpha$H Ile^5, J = 7.8 Hz); 4.30 (dd, 1H, $^\alpha$H Oxz^2, J = 4.5, 0.6 Hz); 4.29 (dd, 1H, $^\alpha$H Oxz^6, J = 4.8, 0.6 Hz); 2.34 (oct., 2H, $^\beta$H D-Val^{3,7}, J = 6.6 Hz); 2.05 (m, 1H, $^\beta$H Ile^5); 1.41 (d, 3H, $^\gamma$H Oxz^6, J = 6.6 Hz); 1.40 (d, 3H, $^\gamma$H Oxz^2, J = 6.0 Hz); 1.40 (m, 1H, $^{\gamma12}$H Ile^5); 1.20 (m, 1H, $^{\gamma13}$H Ile^5); 1.12 (d, 3H, $^{\gamma1}$H D-Val^3, J = 6.6 Hz); 1.11 (d, 3H, $^{\gamma1}$H D-Val^7, J = 6.6 Hz); 1.05 (d, 6H, $^{\gamma2}$H D-Val^{3,7}, J = 6.6 Hz); 0.83 (d, 3H, $^{\gamma2}$H Ile^5, J = 6.6 Hz); 0.78 (t, 3H, $^\gamma$H Abu^1, J = 7.2 Hz); 0.77 (t, 3H, $^\delta$H Ile^5, J = 7.2 Hz).

Characterization of peptide 9

R_f = 0.71. Mp. 201–202 ℃. HR-FAB MS (matrix: Glycerol) calcd for $[C_{35}H_{50}N_8O_6S_2 + H]^+$ = 743.3367, found m/z 743.3378. ^{1}H NMR (600 MHz, CD$_3$CN, 298 K) δ = 7.84 (d, 1H, NH Nva^1, J = 7.2 Hz); 7.79 (d, 1H, NH Ile^5, J = 7.8 Hz); 7.71 (s, 1H, H Thz^{4or8}); 7.70 (s, 1H, H Thz^{4or8}); 7.23 (d, 1H, NH D-Val^{3or7}, J = 10.2 Hz); 7.16 (d, 1H, NH D-Val^{3or7}, J = 10.2); 5.15 (dd, 1H, $^\alpha$H D-Val^{3or7}, J = 10.2, 5.4 Hz); 5.13 (dd, 1H, $^\alpha$H D-Val^{3or7}, J = 10.2, 5.4 Hz); 4.85 (qd, 1H, $^\beta$H Oxz^6, J = 6.6, 4.5); 4.80 (qd, 1H, $^\beta$H Oxz^2, J = 6.0, 4.5); 4.76 (q, 1H, $^\alpha$H Nva^1, J = 7.2 Hz); 4.65 (t, 1H, $^\alpha$H Ile^5, J = 7.8 Hz); 4.30 (d, 2H, $^\alpha$H Oxz^{2,6}, J = 4.5 Hz); 2.35 (m, 1H, $^\beta$H D-Val^{3or7}); 2.33 (m, 1H, $^\beta$H D-Val^{3or7}); 2.03 (m, 1H, $^\beta$H Ile^5); 1.92 (m, 1H, $^{\beta12}$H Nva^1); 1.72 (m, 1H, $^{\beta13}$H Nva^1); 1.42 (d, 3H, $^\gamma$H Oxz^6, J = 6.0 Hz); 1.40 (d, 3H, $^\gamma$H Oxz^2, J = 6.0 Hz); 1.40 (m, 3H, $^{\gamma12}$H Ile^5); 1.27 (m, 1H, $^{\gamma12}$H Nva^1); 1.19 (m, 1H, $^{\gamma13}$H Ile^5); 1.11 (d, 3H, $^{\gamma1}$H D-Val^{3or7}, J = 6.0 Hz); 1.10 (d, 3H, $^{\gamma2}$H D-Val^{3or7}, J = 6.0 Hz); 1.10 (m, 1H, $^{\gamma13}$H Nva^1); 1.04 (d, 6H, $^{\gamma2}$H D-Val^{3,7}, J = 6.0 Hz); 0.82 (d, 3H, $^{\gamma2}$H Ile^5, J = 6.6 Hz); 0.79 (t, 3H, $^\delta$H Nva^1, J = 6.6 Hz); 0.77 (t, 3H, $^\delta$H Ile^5, J = 7.2 Hz).

Characterization of peptide 10

R_f = 0.61. Mp. 205–208 ℃. HR-FAB MS (matrix: Glycerol) calcd for $[C_{37}H_{54}N_8O_6S_2 + H]^+$ = 771.3680, found m/z 771.3688. ^{1}H NMR (600 MHz, CD$_3$CN, 298 K) δ = 7.61 (d, 1H, NH Tbu^1, J = 7.2 Hz); 7.52 (d, 1H, NH Ile^5, J = 7.8 Hz); 7.53 (s, 2H, H Thz^{4,8}); 7.17 (d, 1H, NH D-Val^3, J = 10.8 Hz); 7.08 (d, 1H, NH D-Val^7, J = 10.2 Hz); 5.15 (dd, 1H, $^\alpha$H D-Val^3, J = 10.8, 3.6 Hz); 5.13 (dd, 1H, $^\alpha$H D-Val^7, J = 10.2, 3.6 Hz); 4.92 (qd, 1H, $^\beta$H Oxz^6, J = 6.6, 3.6); 4.89 (ddd, 1H, $^\alpha$H Tbu^1, J = 9.6, 7.2, 4.2 Hz); 4.81 (qd, 1H, $^\beta$H Oxz^2, J = 6.6, 3.6); 4.60 (dd, 1H, $^\alpha$H Ile^5, J = 10.8, 7.8 Hz); 4.32 (d, 1H, $^\alpha$H Oxz^6, J = 3.6 Hz); 4.31 (d, 1H, $^\alpha$H Oxz^2, J = 3.6 Hz); 2.37 (sept.d, 1H, $^\beta$H D-Val^3, J = 6.6, 3.6 Hz); 2.36 (sept.d, 1H, $^\beta$H D-Val^7, J = 6.6, 3.6 Hz); 2.23 (m, 1H, $^\beta$H Ile^5); 2.12 (dd, 1H, $^{\beta12}$H Tbu^1, J = 13.8, 9.6 Hz); 1.63 (dd, 1H, $^{\beta13}$H Tbu^1, J = 13.8, 4.2 Hz); 1.58 (m, 1H, $^{\gamma12}$H Ile^5); 1.44 (d, 3H, $^\gamma$H Oxz^6, J = 6.6 Hz); 1.41 (d, 3H, $^\gamma$H Oxz^2, J = 6.6 Hz); 1.32 (m, 1H, $^{\gamma13}$H Ile^5); 1.12 (d, 3H, $^{\gamma1}$H D-Val^3, J = 6.6 Hz); 1.09 (d, 9H, $^{\gamma1}$H D-Val^7, $^{\gamma2}$H D-Val^{3,7}, J = 6.6 Hz); 0.98 (d, 3H, $^{\gamma2}$H Ile^5, J = 5.4 Hz); 0.97 (s, 9H, $^\delta$H Tbu^1); 0.85 (t, 3H, $^\delta$H Ile^5, J = 7.2 Hz).

Characterization of peptide 11

R_f = 0.72. Mp. 283–284 ℃. HR-FAB MS (matrix: Glycerol) calcd for $[C_{38}H_{54}N_8O_6S_2 + H]^+$ = 783.3680, found m/z 783.3681. ^{1}H NMR (600 MHz, CD$_3$CN, 298 K) δ = 8.01 (d, 1H, NH Ile^5, J = 7.8 Hz); 7.92 (d, 1H, NH Chg^1, J = 7.8 Hz); 7.85 (s, 2H, H Thz^{4,8}); 7.26 (d, 1H, NH D-Val^{3or7}, J = 9.6 Hz); 7.25 (d, 1H, NH D-Val^{3or7}, J = 10.2 Hz); 5.15 (dd, 1H, $^\alpha$H D-Val^{3or7}, J = 9.6, 6.6 Hz); 5.14 (dd, 1H, $^\alpha$H D-Val^{3or7}, J = 10.2, 6.6 Hz); 4.81 (quint., 2H, $^\beta$H Oxz^{2,6}, J = 6.0); 4.69 (ddd, 1H, $^\alpha$H Ile^5, J = 7.8,

5.4, 1.2); 4.63 (ddd, 1H, $^\alpha$H Chg^1, J = 7.8, 5.7, 1.2 Hz); 4.28 (dd, 1H, $^\alpha$H Oxz^{2or6}, J = 6.0, 1.2 Hz); 4.27 (dd, 1H, $^\alpha$H Oxz^{2or6}, J = 6.0, 1.2 Hz); 2.30 (oct., 1H, $^\beta$H D-Val^{3or7}, J = 6.6 Hz); 1.94 (m, 1H, $^\beta$H Ile^5); 1.80 (m, 1H, $^\beta$H Chg^1);   1.43 (d, 3H, $^\gamma$H Oxz^{2or6}, J = 6.0 Hz); 1.41 (d, 3H, $^\gamma$H Oxz^{2or6}, J = 6.0 Hz); 1.35 (m, 1H, $^{\gamma12}$H Ile^5); 1.19 (m, 1H, $^{\gamma13}$H Ile^5); 1.10 (d, 6H, $^{\gamma1}$H D-Val^{3,7}, J = 6.6 Hz); 1.00 (d, 3H, $^{\gamma2}$H D-Val^{3or7}, J = 6.6 Hz); 0.99 (d, 3H, $^{\gamma2}$H D-Val^{3or7}, J = 6.6 Hz); 0.76 (t, 3H, $^\delta$H Ile^5, J = 7.2 Hz); 0.72 (d, 3H, $^{\gamma2}$H Ile^5, J = 7.2 Hz).

Characterization of peptide 12

R_f = 0.88. Mp. 252–253 ℃. HR-FAB MS (matrix: Glycerol) calcd for $[C_{36}H_{52}N_8O_6S_2 + H]^+$ = 757.3524, found m/z 757.3529. ^{1}H NMR (600 MHz, CD$_3$CN, 298 K) δ = 8.22 (d, 1H, NH Tle^1, J = 9.0 Hz); 8.14 (d, 1H, NH Ile^5, J = 7.8 Hz); 8.01 (s, 1H, H Thz^{4or8}); 8.00 (s, 1H, H Thz^{4or8}); 7.41 (d, 1H, NH D-Val^7, J = 10.2 Hz); 7.40 (d, 1H, NH D-Val^3, J = 9.6); 5.21 (dd, 1H, $^\alpha$H D-Val^7, J = 10.2, 7.2 Hz); 5.11 (dd, 1H, $^\alpha$H D-Val^3, J = 9.6, 7.8 Hz); 4.83 (quint., 1H, $^\beta$H Oxz^2, J = 6.0); 4.81 (quint., 1H, $^\beta$H Oxz^6, J = 6.0); 4.75 (ddd, 1H, $^\alpha$H Ile^5, J = 7.5, 3.6, 1.8 Hz); 4.48 (dd, 1H, $^\alpha$H Tle^1, J = 9.0, 1.8 Hz); 4.28 (dd, 1H, $^\alpha$H Oxz^6, J = 6.0, 1.8 Hz); 4.25 (dd, 1H, $^\alpha$H Oxz^2, J = 6.0, 1.8 Hz); 2.26 (m, 1H, $^\beta$H D-Val^3); 2.23 (m, 1H, $^\beta$H D-Val^7); 2.23 (m, 1H, $^\beta$H Ile^5); 1.82 (m, 1H, $^\beta$H Ile^5); 1.42 (d, 3H, $^\gamma$H Oxz^6, J = 6.0 Hz); 1.41 (d, 3H, $^\gamma$H Oxz^2, J = 6.0 Hz); 1.18 (m, 1H, $^{\gamma12}$H Ile^5); 1.10 (m, 1H, $^{\gamma13}$H Ile^5); 1.09 (d, 3H, $^{\gamma1}$H D-Val^3, J = 6.6 Hz); 1.08 (d, 3H, $^{\gamma1}$H D-Val^7, J = 6.6 Hz); 0.97 (d, 3H, $^{\gamma2}$H D-Val^7, J = 6.6 Hz); 0.94 (d, 3H, $^{\gamma2}$H D-Val^3, J = 6.6 Hz); 0.76 (s, 9H, $^\gamma$H Tle^1); 0.70 (d, 3H, $^{\gamma2}$H Ile^5, J = 6.6 Hz); 0.61 (t, 3H, $^\delta$H Ile^5, J = 7.2 Hz).

^{1}H NMR spectra of peptides 8-12

Fig. S1 1D ^{1}H NMR spectrum of peptide **8** in CD$_3$CN at 298 K.

Fig. S2 2D ^{1}H-^{1}H COSY spectrum of peptide **8** in CD$_3$CN at 298 K.

Fig. S3 2D ^{1}H-^{1}H ROESY spectrum of peptide **8** in CD$_3$CN at 298 K.
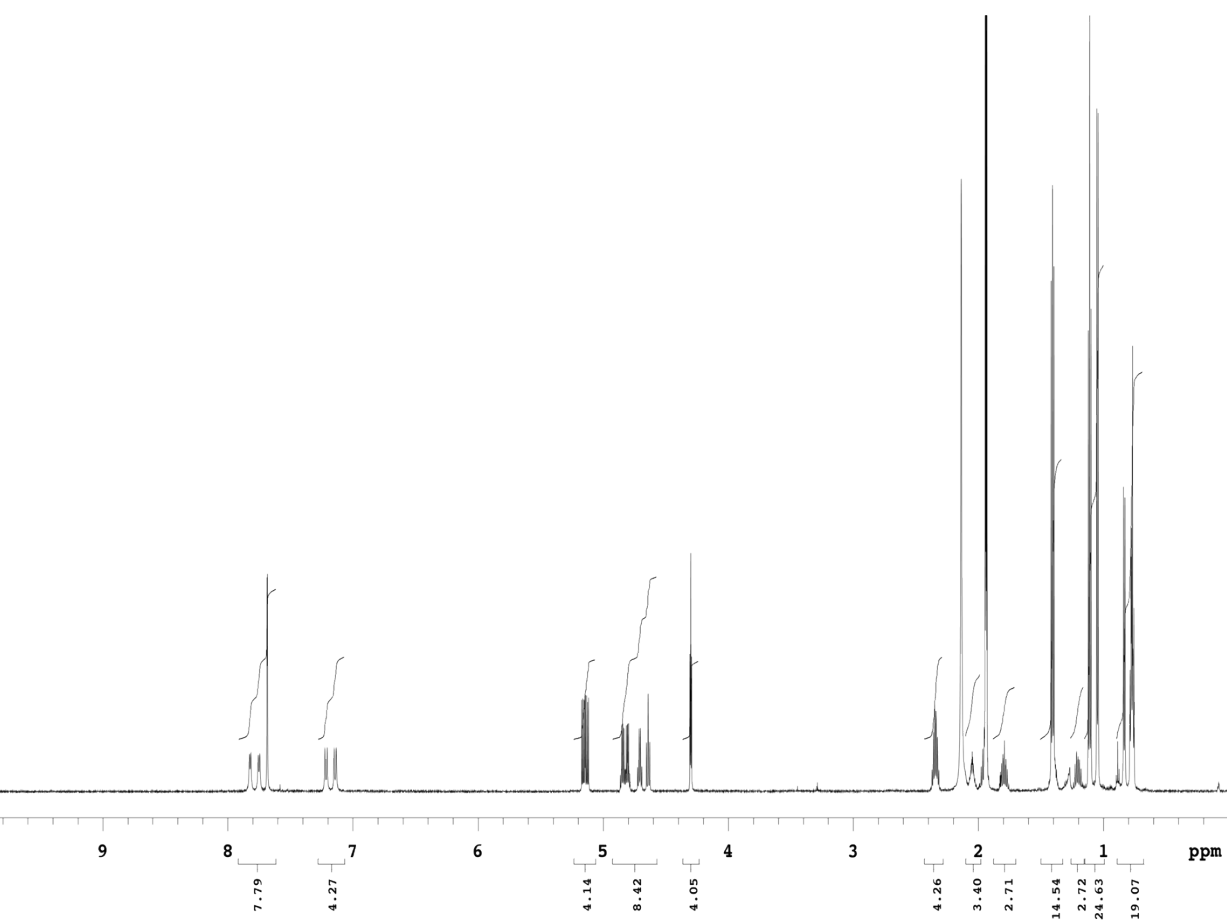
Fig. S4 1D ^{1}H NMR spectrum of peptide **9** in CD$_3$CN at 298 K.

Fig. S5 2D ^{1}H-^{1}H COSY spectrum of peptide **9** in CD$_3$CN at 298 K.

Fig. S6 2D ^{1}H-^{1}H ROESY spectrum of peptide **9** in CD$_3$CN at 298 K.
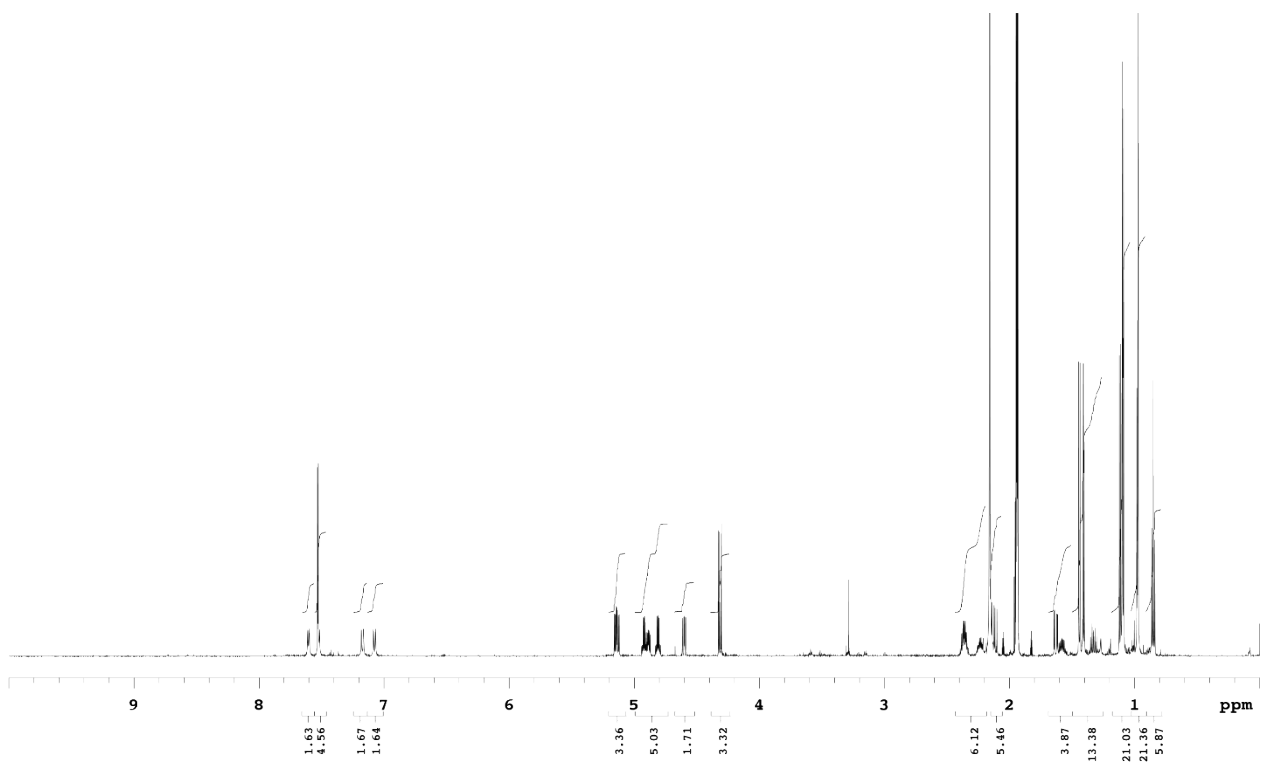
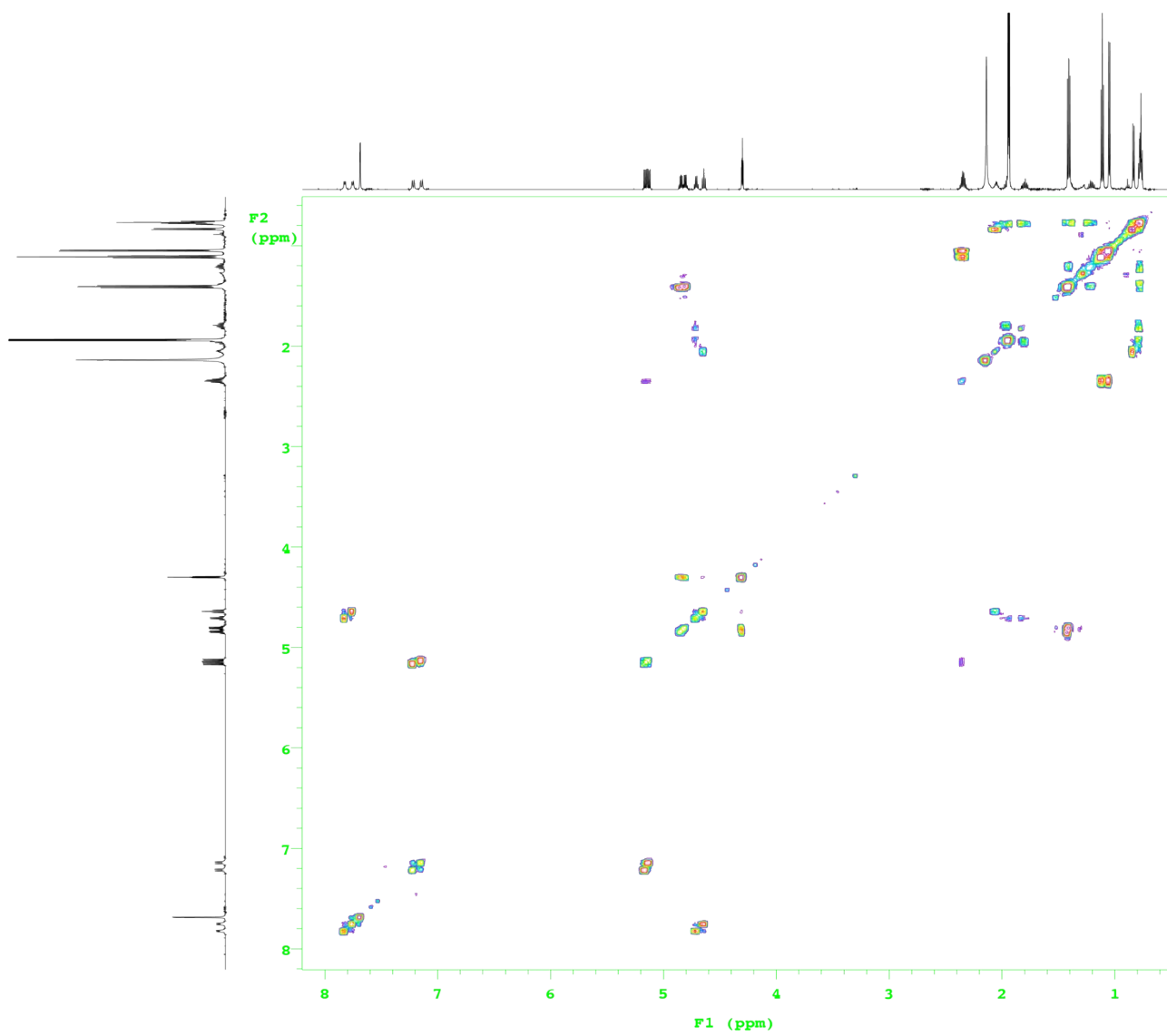**Fig. S7** 1D ^{1}H NMR spectrum of peptide **10** in CD$_3$CN at 298 K.
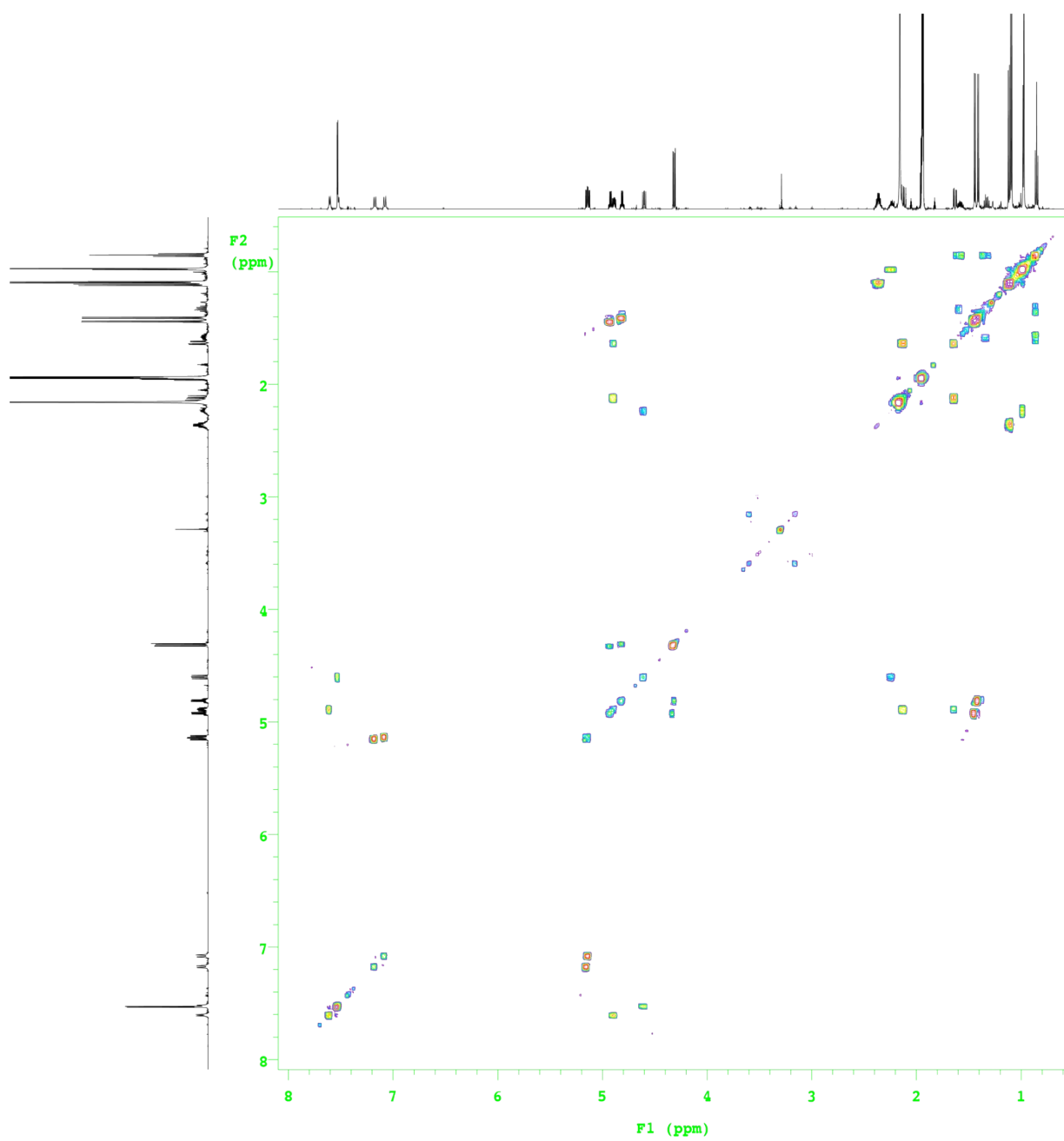
Fig. S8 2D ^{1}H-^{1}H COSY spectrum of peptide **10** in CD$_3$CN at 298 K.
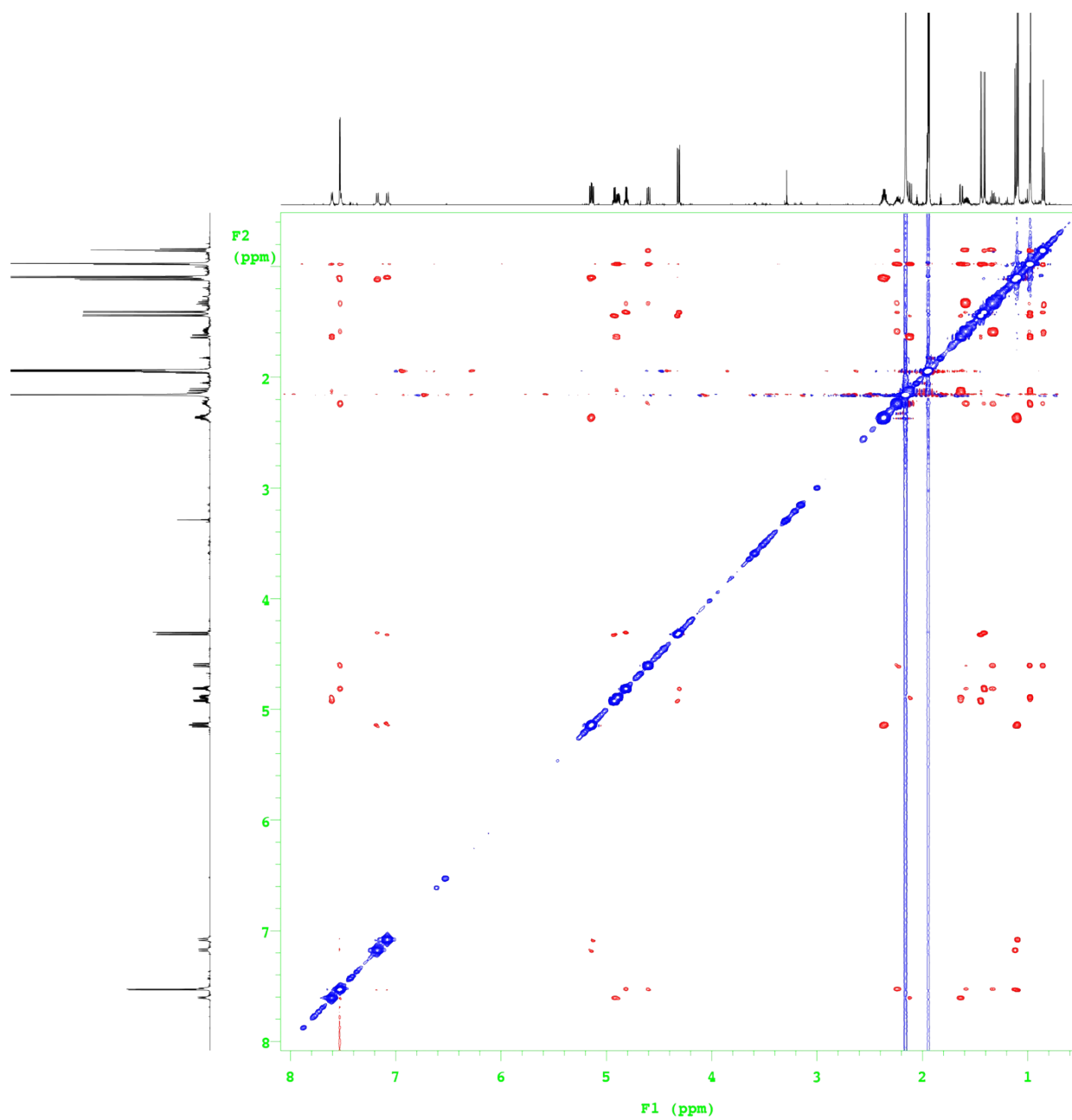
Fig. S9 2D ^{1}H-^{1}H ROESY spectrum of peptide **10** in CD$_3$CN at 298 K.
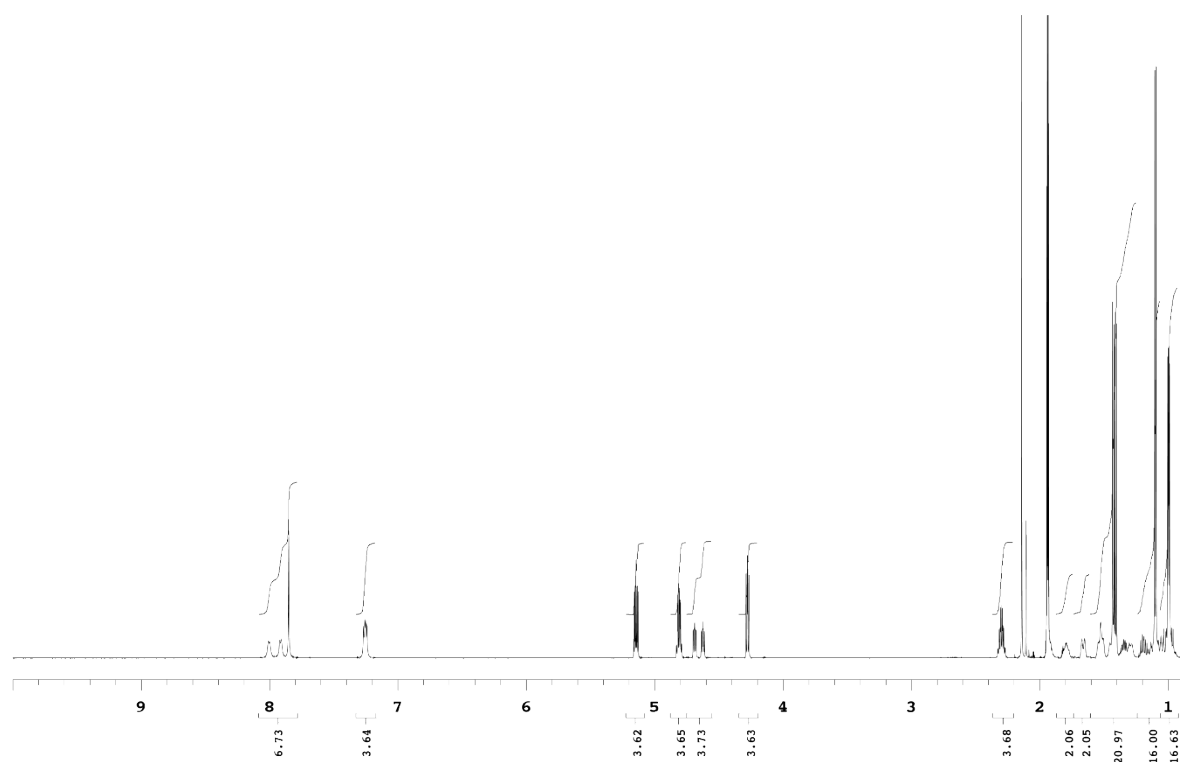
Fig. S10 1D ^{1}H NMR spectrum of peptide **11** in CD$_3$CN at 298 K.
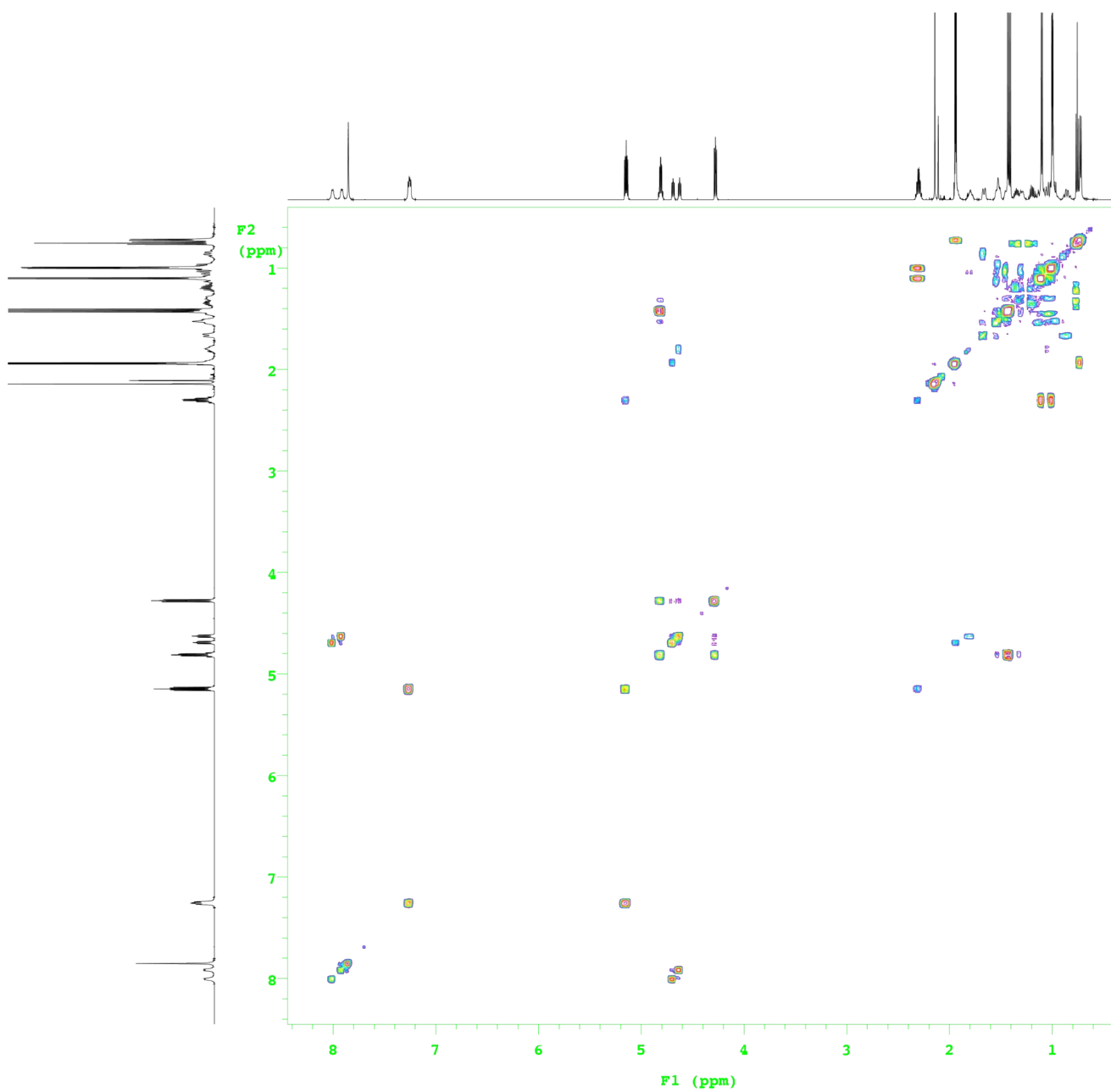
Fig. S11 2D ^{1}H-^{1}H COSY spectrum of peptide **11** in CD$_3$CN at 298 K.
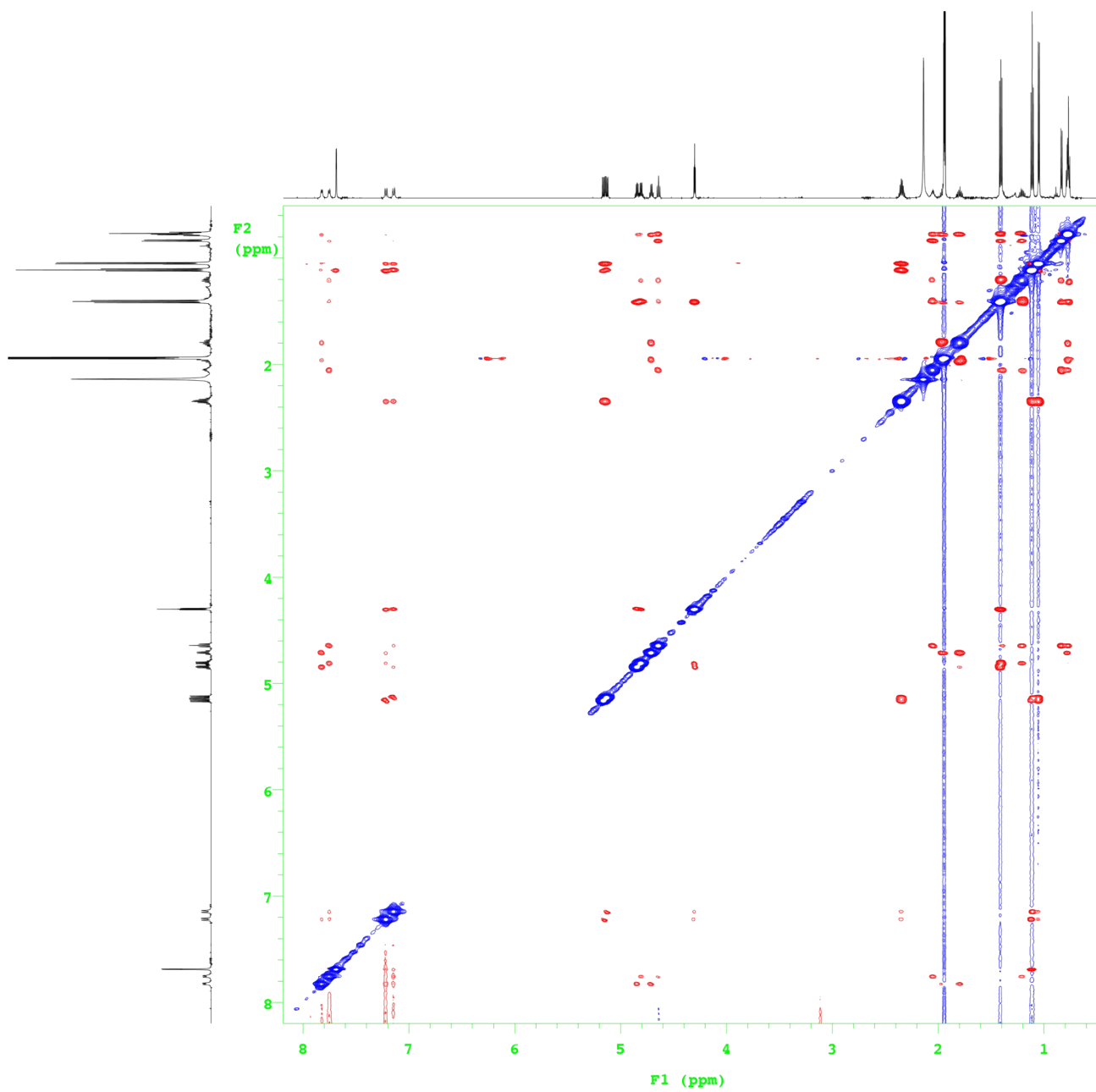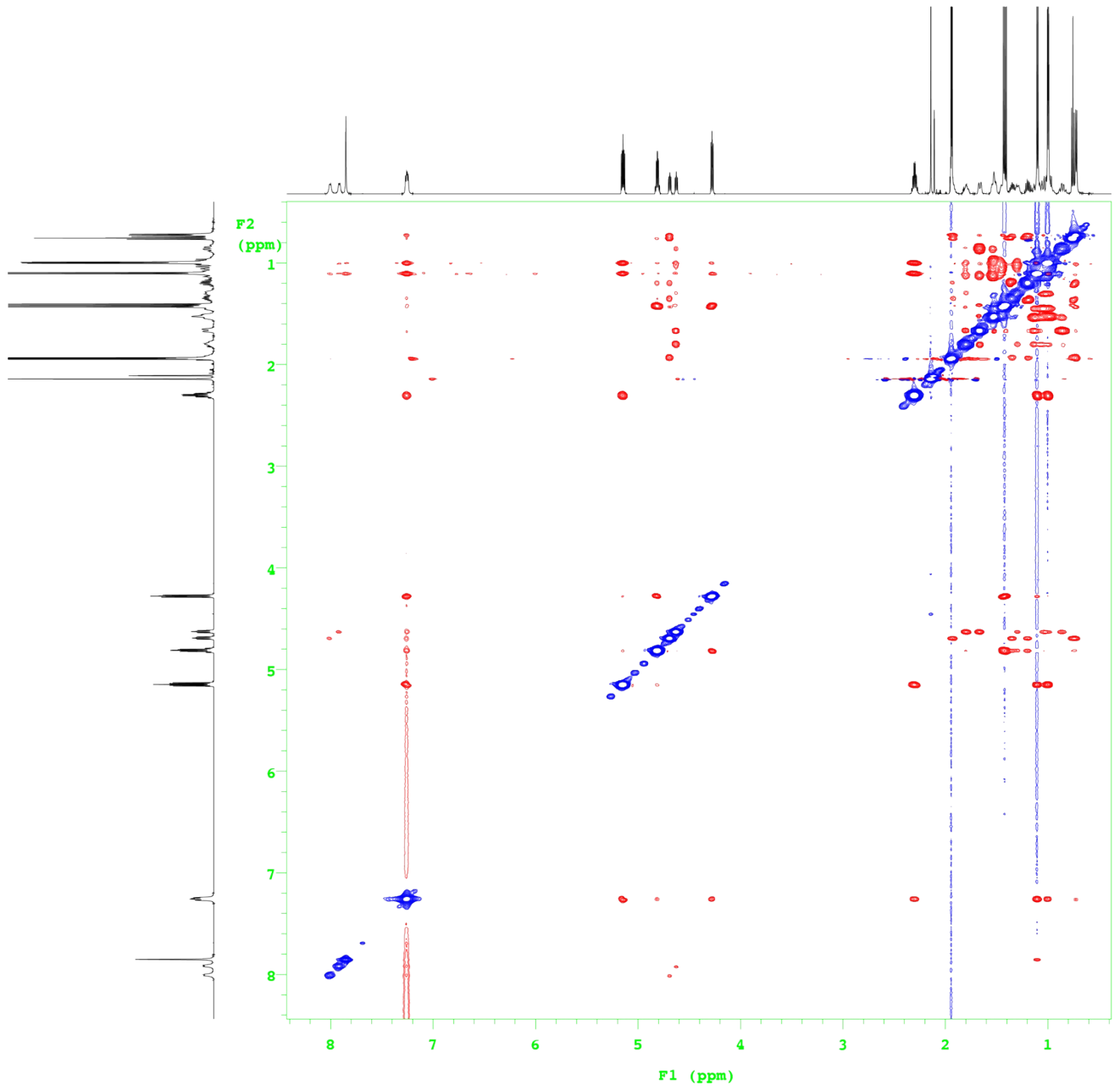
Fig. S12 2D ^{1}H-^{1}H ROESY spectrum of peptide **11** in CD$_3$CN at 298 K.
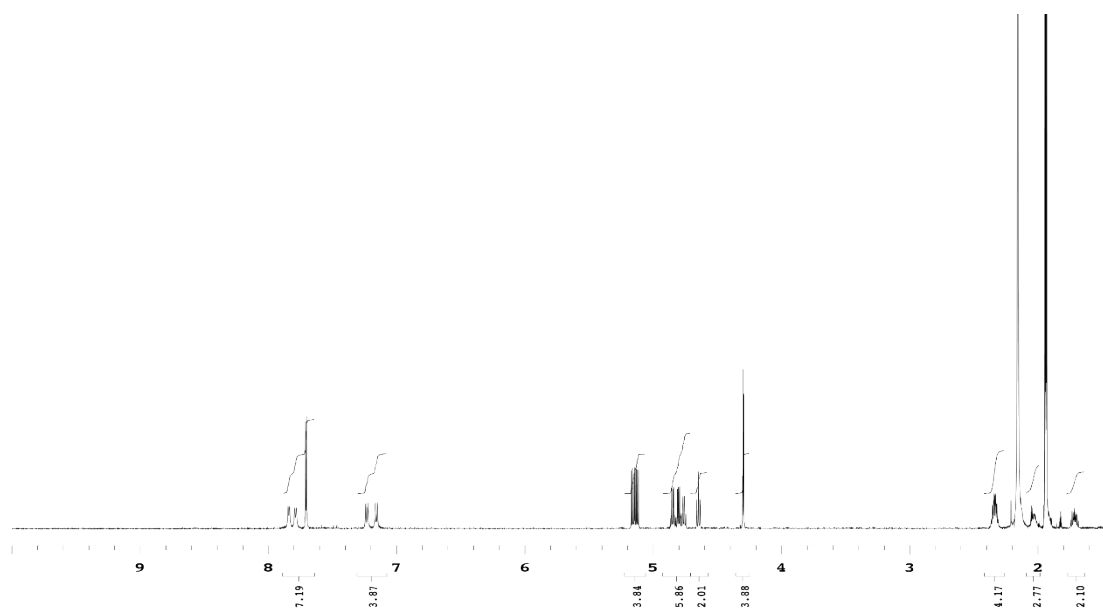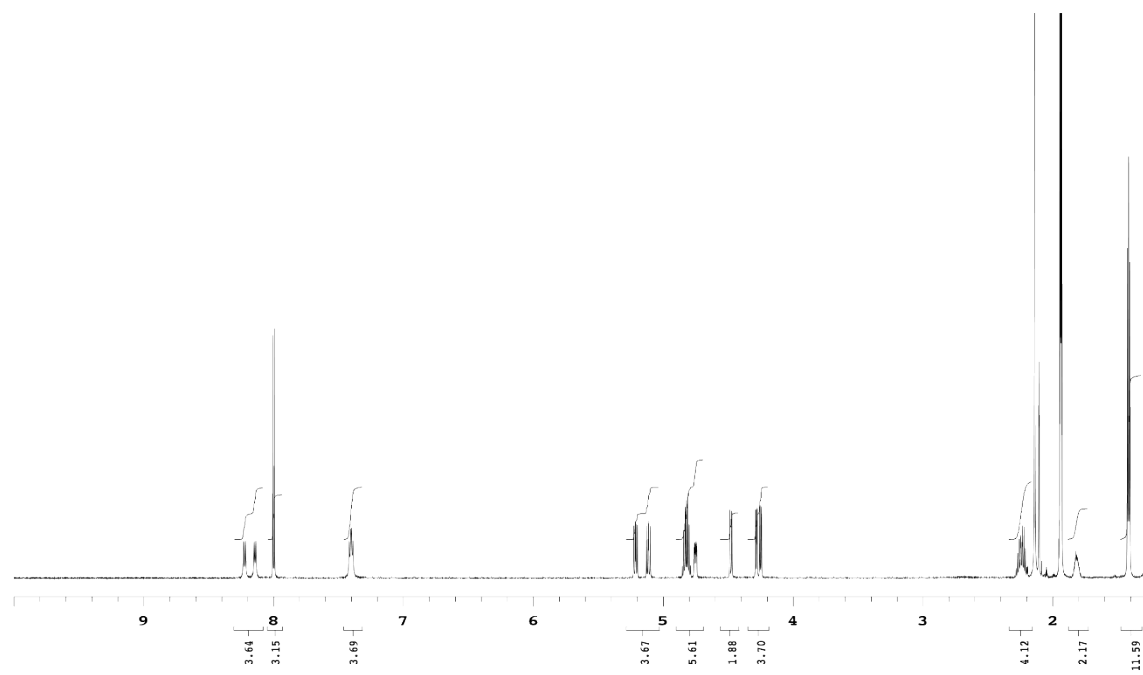
Fig. S13 1D ^{1}H NMR spectrum of peptide **12** in CD$_3$CN at 298 K.
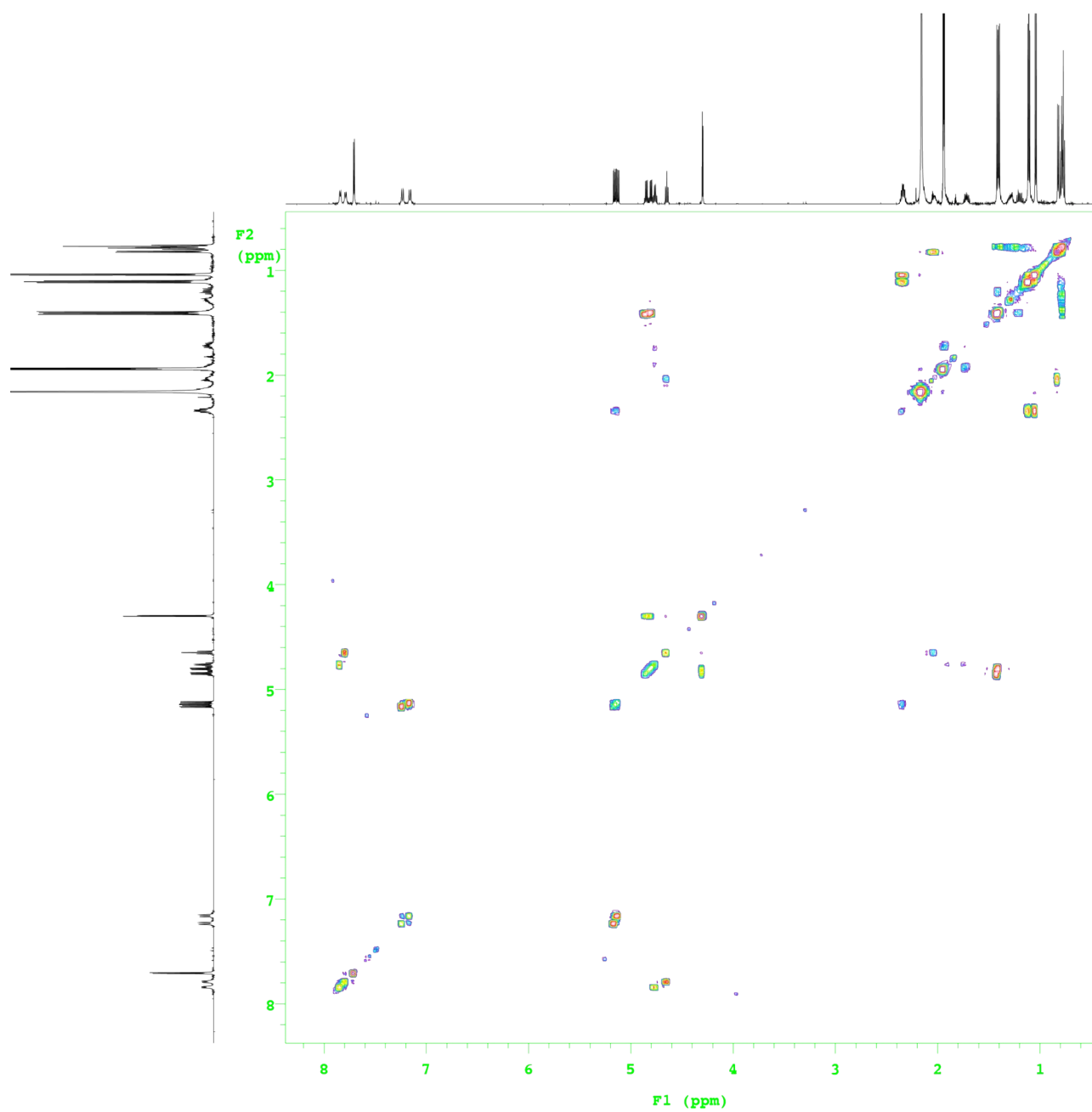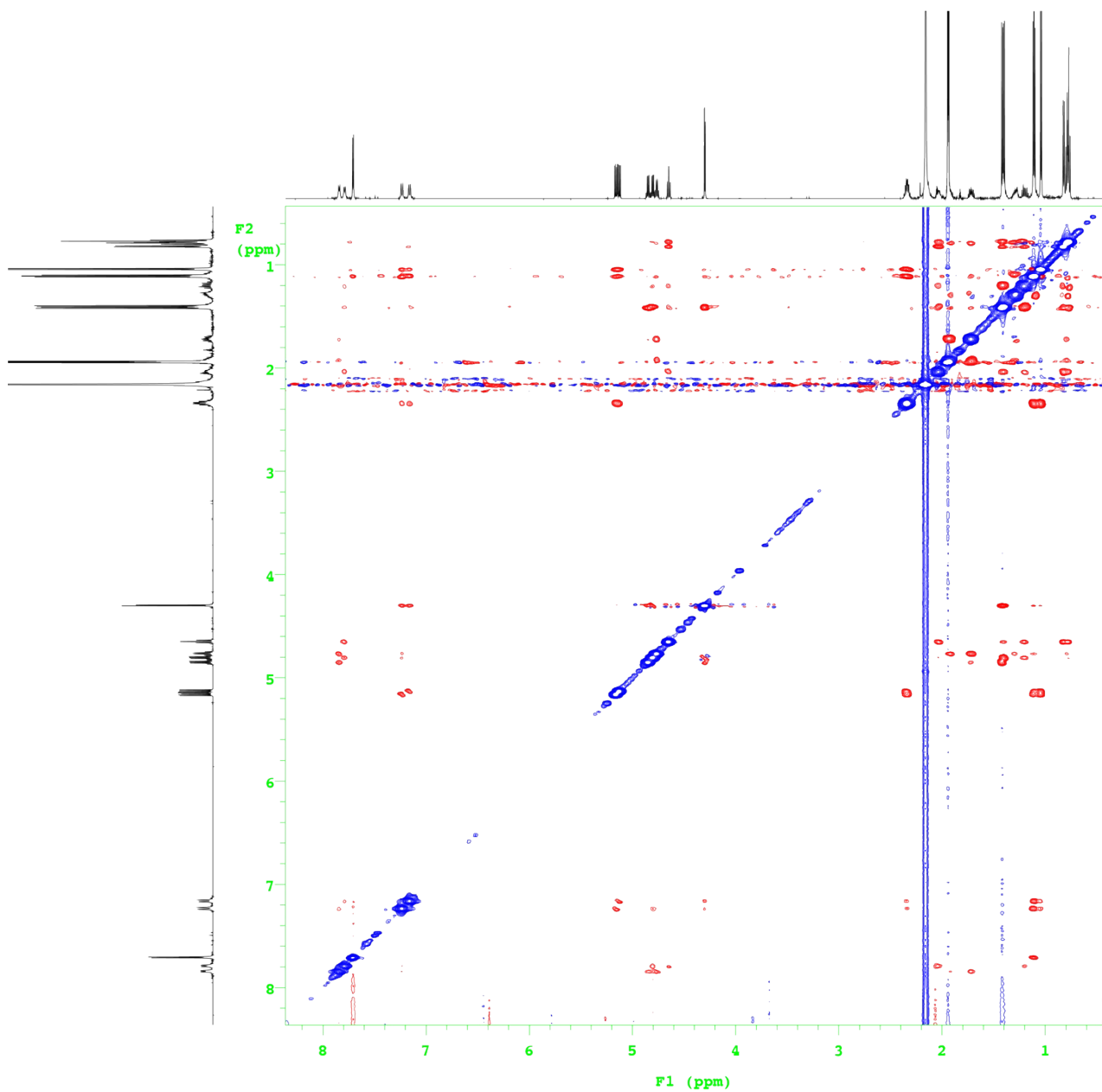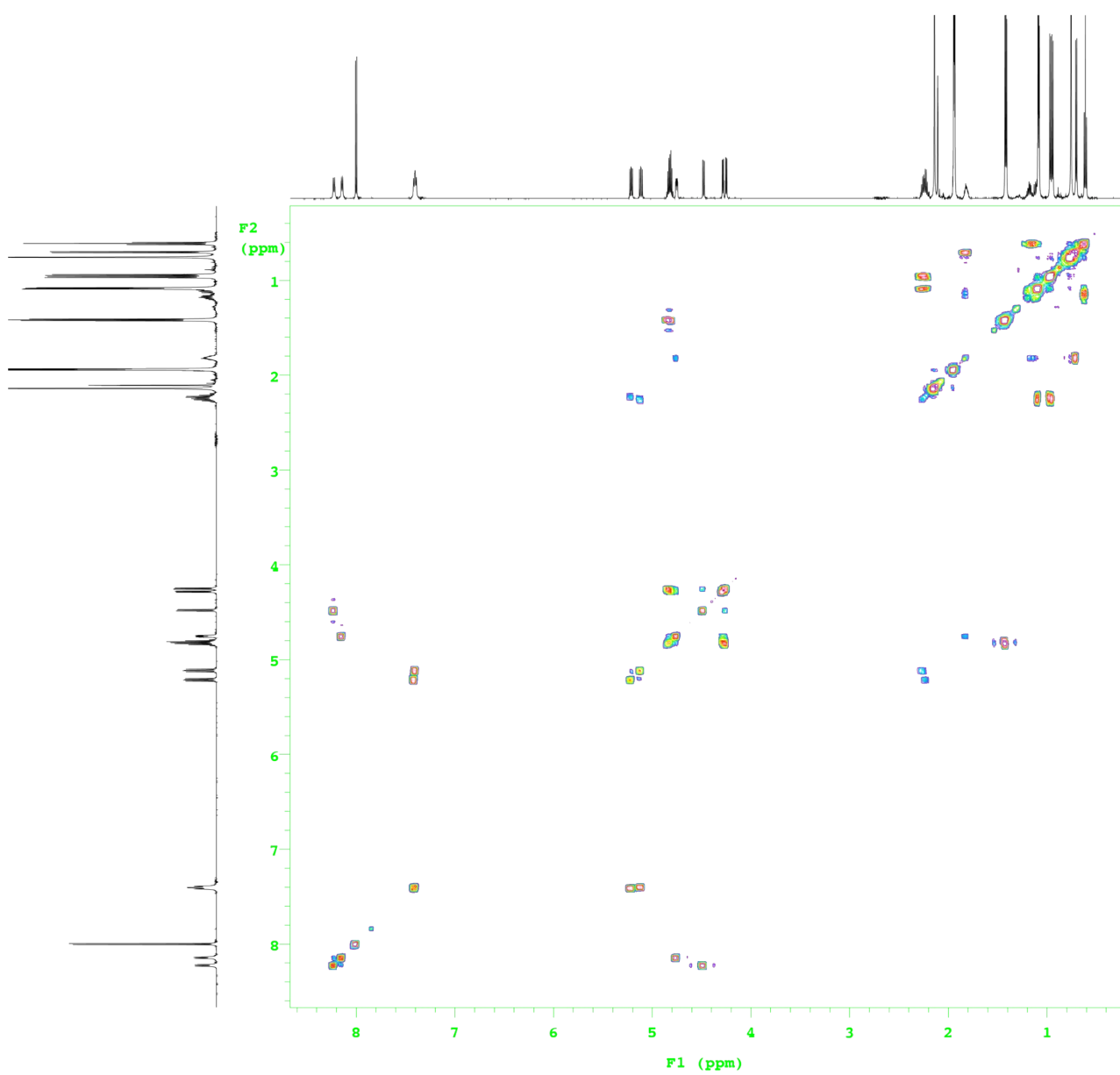
Fig. S14 2D ^{1}H-^{1}H COSY spectrum of peptide **12** in CD$_3$CN at 298 K.
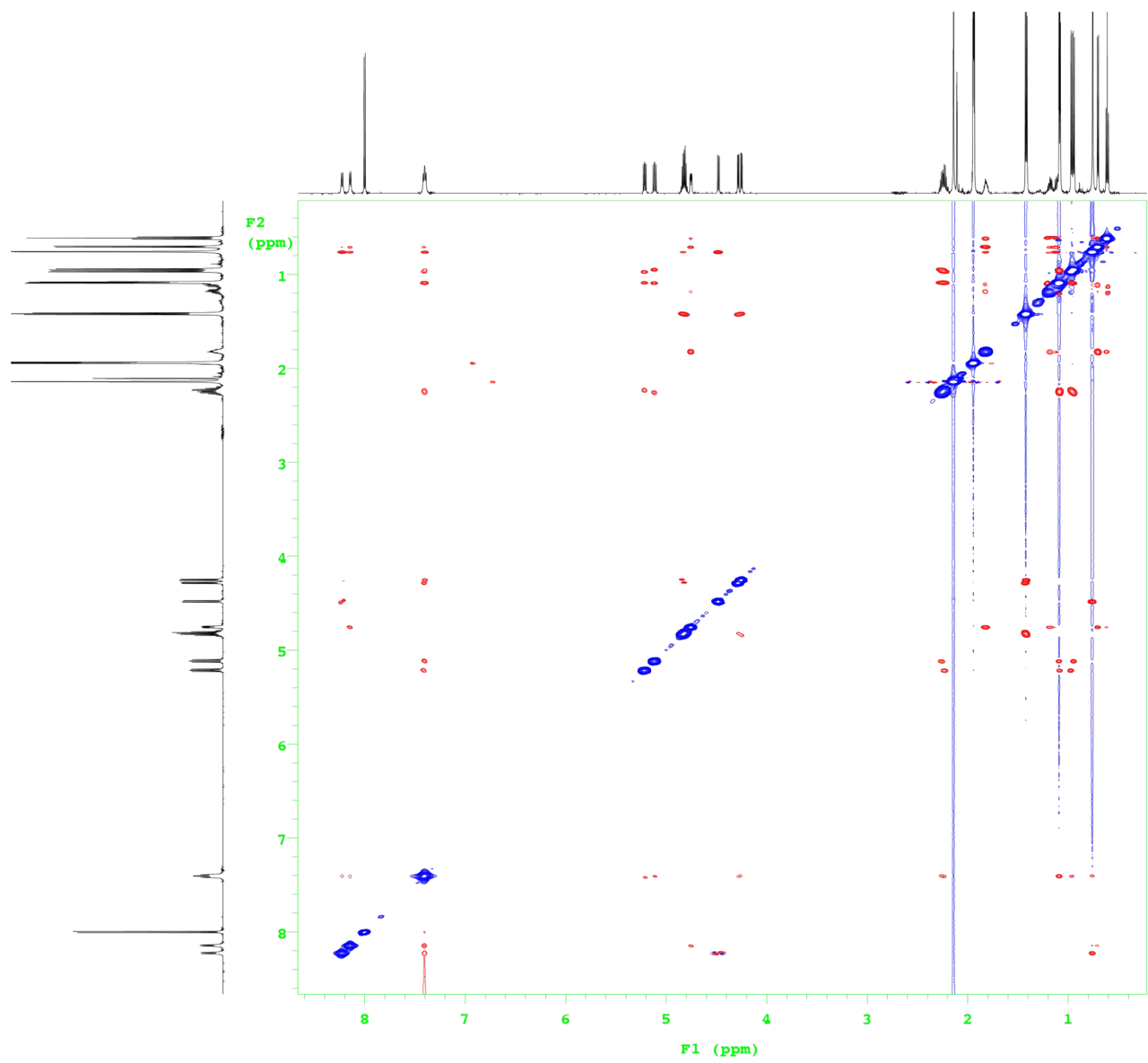
Fig. S15 2D ^{1}H-^{1}H ROESY spectrum of peptide **12** in CD$_3$CN at 298 K.

HPLC analyses for peptides 8-12

HPLC analyses for peptides **8-12** were performed using analytical reverse HPLC system (2000 Series, JASCO LTD., Tokyo, Japan), equipped with PU-2089 HPLC pump, a 2077-UV intelligent UV/Vis detector, and COSMOSIL $5C_{18}$-MS-II packed column (4.6 x 150 mm, 5 μm particle size, Nacalai tesque, Kyoto, Japan). Ctehromatographies were carried out by a flow rate of 1 mL/min and monitored at 245 nm. Elution solvents used acetonitrile/water + 0.1 % formic acid from 50 to 100% in 18 min. HPLC profiles of peptides **8-12** were shown in Fig. S16.
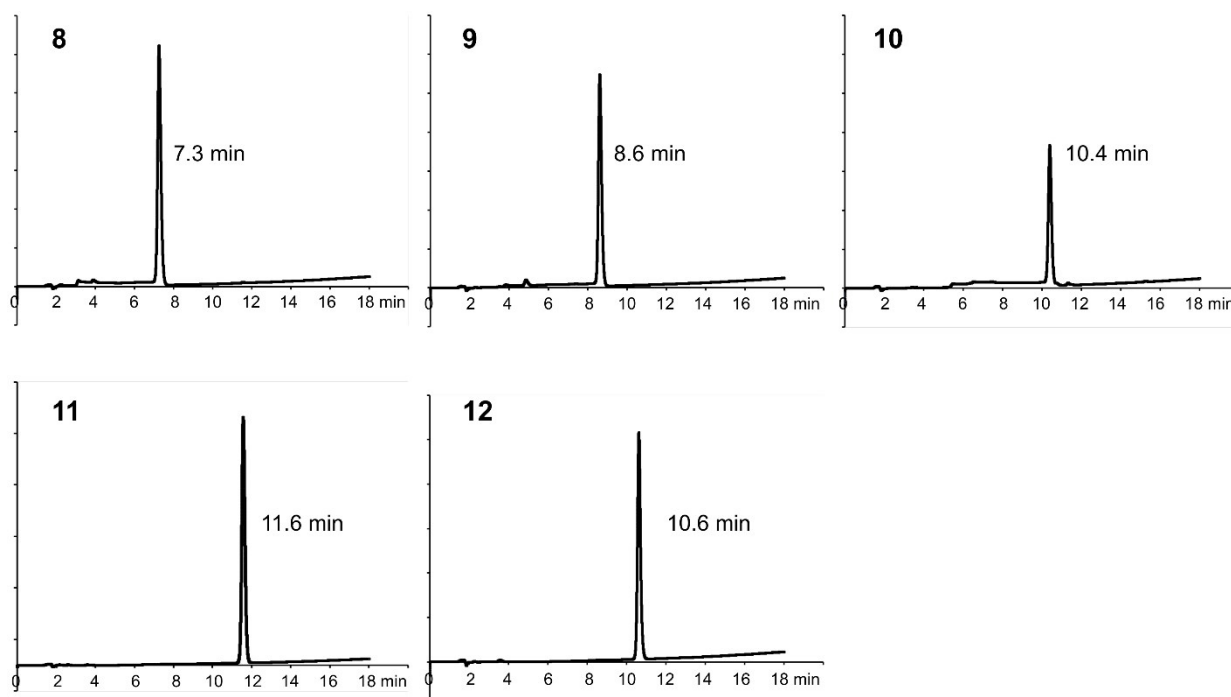
Fig. S16 HPLC profiles of peptides **8-12**.

Crystallographic data for peptides 10-12

Table S1. Crystal and experimental data for peptides **10-12**.

Peptide	10	11	12
Formula	$C_{37}H_{54}N_8O_6S_2$	$C_{38}H_{54}N_8O_6S_2$	$C_{36}H_{52}N_8O_6S_2$
	$2(C_3H_7NO)$	$2(C_4H_9NO)\ H_2O$	$2(C_3H_7NO)$
Formula Weight	917.20	975.27	903.17
Cell System	monoclinic	tetragonal	monoclinic
Space Group	$P2_1$	$P4_1$	$C2$
a, Å	12.9799(6)	12.9682(9)	15.917(3)
b, Å	12.1900(7)	12.9682(9)	12.1964(19)
c, Å	15.9375(8)	30.798(3)	12.962(2)
α, deg	90.0	90.0	90.0
β, deg	102.703(5)	90.0	102.303(2)
γ, deg	90.0	90.0	90.0
Volume, Å^3	2460.0(2)	5179.4(7)	2458.5(7)
Z	2	4	2
Dc, g cm^{-3}	1.238	1.251	1.220
$F(000)$	984	2096	968
μ, mm^{-1}	1.464 (Cu Kα)	0.164 (Mo Kα)	0.166 (Mo Kα)
Wavelength, Å	1.54178	0.71073	0.71073
No. of reflections (obs)	13264	47663	9560
R_{INT}	0.0321	0.0370	0.0366
θ_{max}, deg	67.729	27.87	26.37
No. of reflections ($I>2\sigma(I)$)	5358	10492	4460
Flack parameter	0.38(2)	0.09(11)	0.1(2)
$R1$	0.0993	0.0799	0.0962
wR	0.2545	0.2149	0.2606
Goodness of fit	0.858	1.034	1.153
$(\Delta/\sigma)_{max}$	0.064	0.011	0.007
Fraction for θ_{max}	0.999	0.999	0.994
$\Delta\rho_{max}$, e Å^{-3}	0.605	1.637	0.613
$\Delta\rho_{min}$, e Å^{-3}	–0.453	–0.560	–0.238
CCDC Number	2007056	2007057	2007058

VT-NMR data for peptide 1

Table S2. ^{1}H NMR chemical shifts of peptide **1** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)		δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Ile[1]	7.93 d, J = 8.4	4.72 ddd, J = 8.4, 5.4, 1.2	1.91 m	γCH₂ 1.23, 1.12 m, m	γCH₃ 0.76 d, J = 6.6	0.68 t, J = 7.2	
Oxz[2]		4.28 dd, J = 6.0, 1.2	4.80 quint. J = 6.0	1.42 d, J = 6.0			
D-Val[3]	7.26 d, J = 10.2	5.15 dd, J = 10.2, 6.6	2.30 oct. J = 6.6	γCH₃ 1.10, γ'CH₃ 1.00 d, J = 6.6, d, J = 6.6			
Thz[4]							7.87 s
Ile[5]	7.93 d, J = 8.4	4.72 ddd, J = 8.4, 5.4, 1.2	1.91 m	γCH₂ 1.23, 1.12 m, m	γCH₃ 0.76 d, J = 6.6	0.68 t, J = 7.2	
Oxz[6]		4.28 dd, J = 6.0, 1.2	4.80 quint. J = 6.0	1.42 d, J = 6.0			
D-Val[7]	7.26 d, J = 10.2	5.15 dd, J = 10.2, 6.6	2.30 oct. J = 6.6	γCH₃ 1.10, γ'CH₃ 1.00 d, J = 6.6, d, J = 6.6			
Thz[8]							7.87 s

Table S3. Chemical shifts of amide and Thz protons of peptide **1** at various temperatures and their temperature coefficients.

T (K)	δ Ile[1,5] HN (ppm)	δ D-Val[3,7] HN (ppm)	δ Thz[4,8] H (ppm)
273	7.88	7.28	7.82
283	7.90	7.27	7.84
293	7.92	7.27	7.86
303	7.94	7.27	7.88
313	7.97	7.28	7.90
323	7.98	7.28	7.92
333	8.00	7.28	7.93
Δδ/ΔT (ppb/K)	2.0	0.0	1.9

Fig. S17 Diagrams of the amide and Thz protons temperature coefficients of peptide **1**.

VT-NMR data for peptide 2

Table S4. ^{1}H NMR chemical shifts of peptide **2** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)	δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Ala[1]	7.78 d, J = 7.2	4.84 quint. J =7.2	1.48 d, J = 7.2			
Oxz[2]		4.29 dd, J =4.5, 0.6	4.78 qd, J = 6.0, 4.5	1.40 d, J = 6.0		
D-Val[3]	7.13 d, J = 10.2	5.13 dd, J = 10.2, 4.8	2.34 m	γCH3 1.10, γ′CH3 1.06 d, J = 6.6, d, J = 6.6		
Thz[4]						7.64 s
Ile[5]	7.69 d, J = 7.8	4.65 t, J = 7.8	2.12 m	γCH2 1.43, 1.24 γCH3 0.92 m, m d, J = 7.2	0.79 t, J = 7.2	
Oxz[6]		4.30 dd, J = 4.8, 0.6	4.87 qd, J = 6.6, 4.8	1.42 d, J = 6.6		
D-Val[7]	7.23 d, J = 10.2	5.17 dd, J = 10.2, 4.8	2.33 m	γCH3 1.11, γ′CH3 1.06 d, J = 6.6, d, J = 6.6		
Thz[8]						7.64 s

Table S5. Chemical shifts of amide and Thz protons of peptide **2** at various temperatures and their temperature coefficients.

T (K)	δ Ala[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4,8] H (ppm)
273	7.74	7.09	7.64	7.21	7.55
283	7.75	7.10	7.66	7.22	7.58
293	7.77	7.12	7.67	7.23	7.62
303	7.79	7.14	7.71	7.24	7.66
313	7.81	7.15	7.72	7.25	7.70
323	7.84	7.17	7.75	7.26	7.74
333	7.86	7.18	7.78	7.26	7.78
Δδ/ΔT (ppb/K)	2.0	1.6	2.2	1.0	3.9

Ala[1] HN: y = 0.0020 x + 7.19 (R^2 = 0.981)
D-Val[3] HN: y = 0.0016 x + 6.64 (R^2 = 0.991)
Ile[5] HN: y = 0.0022 x + 7.04 (R^2 = 0.975)
D-Val[7] HN: y = 0.0010 x + 6.93 (R^2 = 1.00)
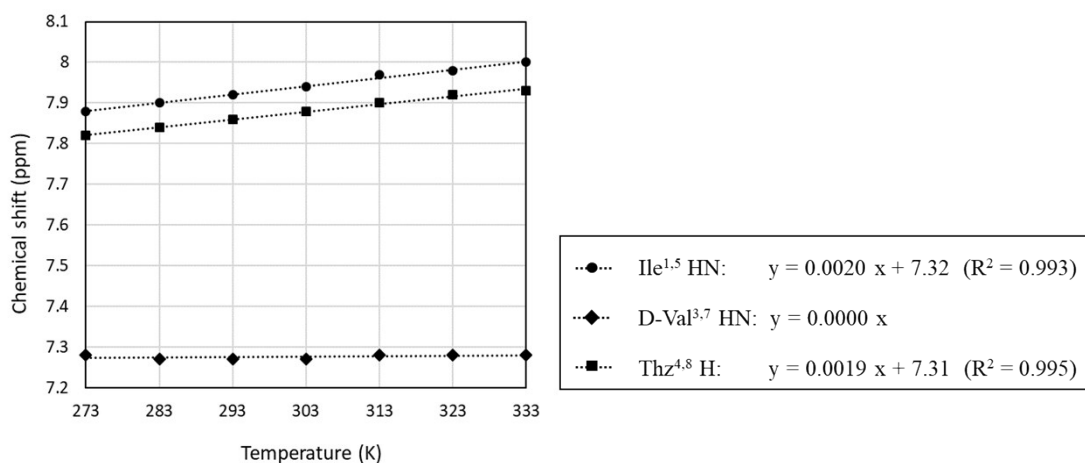Thz[4,8] H: y = 0.0039 x + 6.49 (R^2 = 0.998)

Fig. S18 Diagrams of the amide and Thz protons temperature coefficients of peptide **2**.

VT-NMR data for peptide 3

Table S6. ^{1}H NMR chemical shifts of peptide **3** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)	δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Val[1]	7.85 d, J = 7.2	4.59 t, J = 7.2	2.15 m	γCH₃ 0.85, γ'CH₃ 0.75 d, J = 6.6, d, J = 6.6		
Oxz[2]		4.29 dd, J =4.2, 1.2	4.83 qd, J = 6.6, 4.2	1.41 d, J = 6.6		
D-Val[3]	7.21 d, J = 10.2	5.14 dd, J = 10.2, 6.6	2.33 oct. J = 6.6	γCH₃ 1.11, γ'CH₃ 1.02 d, J = 6.6, d, J = 6.6		
Thz[4or8]						7.78 s
Ile[5]	7.86 d, J = 6.6	4.68 t, J = 6.6	1.99 m	γCH₂ 1.31, 1.19 m, m ‖ γCH₃ 0.80 d, J = 7.2	0.72 t, J = 7.2	
Oxz[6]		4.30 dd, J = 4.5, 1.2	4.82 qd, J = 6.0, 4.5	1.42 d, J = 6.0		
D-Val[7]	7.23 d, J = 10.2	5.15 dd, J = 10.2, 6.6	2.31 oct. J = 6.6	γCH₃ 1.10, γ'CH₃ 1.02 d, J = 6.6, d, J = 6.6		
Thz[4or8]						7.79 s

The chemical shifts of Thz[4]H and Thz[8]H were indistinguishable.

Table S7. Chemical shifts of amide and Thz protons of peptide **3** at various temperatures and their temperature coefficients.

T (K)	δ Val[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4or8] H (ppm)	δ Thz[4or8] H (ppm)
273	7.79	7.20	7.79	7.20	7.70	7.70
283	7.82	7.20	7.82	7.22	7.73	7.74
293	7.84	7.21	7.84	7.23	7.76	7.78
303	7.86	7.21	7.88	7.23	7.80	7.81
313	7.89	7.22	7.91	7.25	7.82	7.84
323	7.91	7.23	7.93	7.25	7.85	7.86
333	7.93	7.23	7.96	7.26	7.87	7.89
Δδ/ΔT (ppb/K)	2.3	0.6	2.9	0.9	2.9	3.1

Ala[1] HN: y = 0.0023 x + 7.16 (R² = 0.997)
D-Val[3] HN: y = 0.0006 x + 7.04 (R² = 0.941)
Ile[5] HN: y = 0.0029 x + 7.01 (R² = 0.995)
D-Val[7] HN: y = 0.0009 x + 6.95 (R² = 0.939)
Thz[4or8] H: y = 0.0029 x + 6.91 (R² = 0.993)
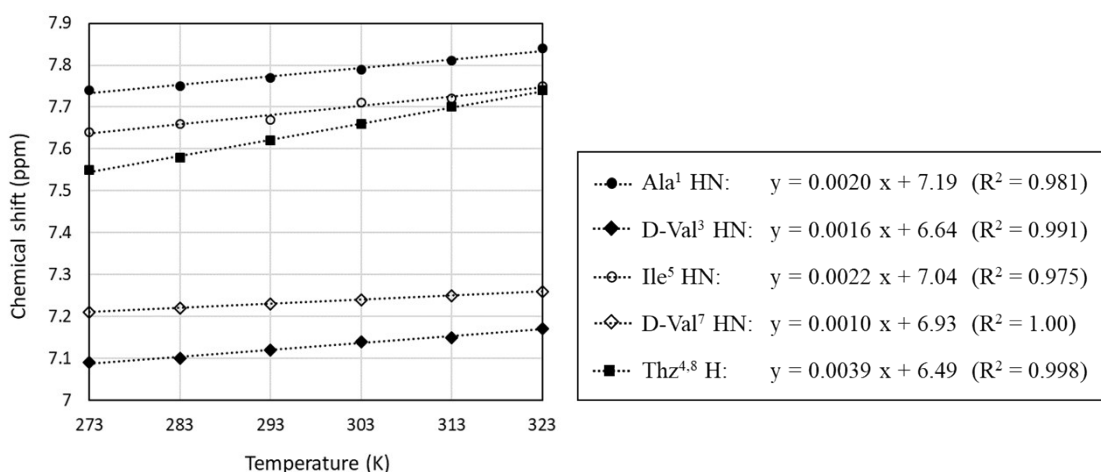Thz[4or8] H: y = 0.0031 x + 6.86 (R² = 0.989)

Fig. S19 Diagrams of the amide and Thz protons temperature coefficients of peptide **3**.

VT-NMR data for peptide 4

Table S8. ^{1}H NMR chemical shifts of peptide **4** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)		δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Leu[1]	7.71 d, J = 6.6	4.81 m	γCH$_2$ 2.02, 1.55 m, m	1.58 m		δCH$_3$ 0.93, δ'CH$_3$ 0.88 d, J = 6.6, d, J = 6.6	
Oxz[2]		4.30 d, J = 3.0	4.81 m	1.39 d, J = 6.0			
D-Val[3]	7.20 d, J = 10.2	5.16 dd, J = 10.2, 4.8	2.35 m	γCH$_3$ 1.12, γ'CH$_3$ 1.07 d, J = 7.2, d, J = 7.2			
Thz[4]							7.60 s
Ile[5]	7.67 d, J = 7.8	4.61 dd, J = 9.3, 7.8	2.14 m	γCH$_2$ 1.52, 1.27 m, m	γCH$_3$ 0.91 d, J = 7.2	0.82 t, J = 7.2	
Oxz[6]		4.31 d, J = 4.2	4.87 qd, J = 6.0, 4.2	1.43 d, J = 6.0			
D-Val[7]	7.11 d, J = 10.2	5.14 dd, J = 10.2, 4.8	2.35 m	γCH$_3$ 1.10, γ'CH$_3$ 1.07 d, J = 7.2, d, J = 7.2			
Thz[8]							7.60 s

Table S9. Chemical shifts of amide and Thz protons of peptide **4** at various temperatures and their temperature coefficients.

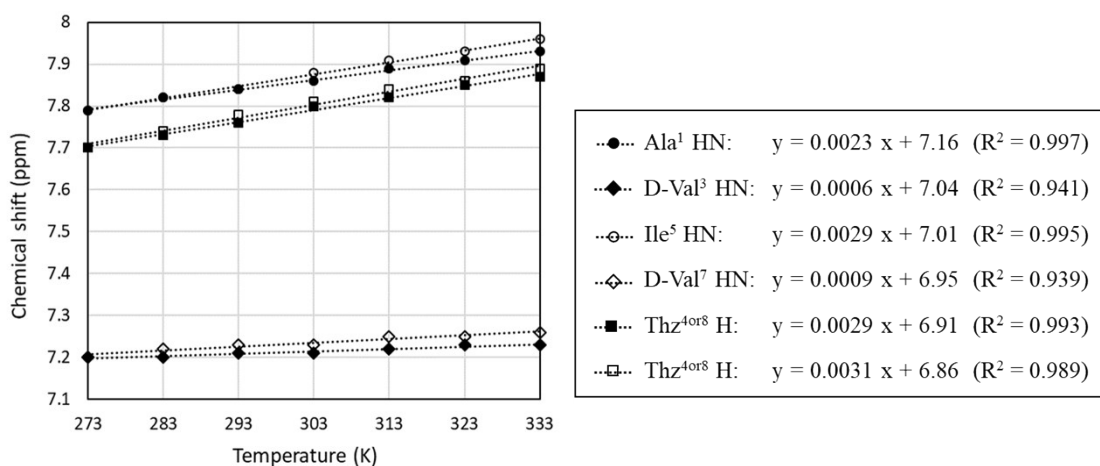| T (K)	δ Leu[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4,8] H (ppm)
273	7.67	7.19	7.62	7.08	7.53
283	7.68	7.19	7.64	7.09	7.56
293	7.70	7.20	7.66	7.11	7.59
303	7.72	7.21	7.68	7.12	7.62
313	7.74	7.21	7.71	7.14	7.66
323	7.76	7.22	7.74	7.15	7.69
333		7.23		7.17	7.73
Δδ/ΔT (ppb/K)	1.9	0.7	2.4	1.5	3.3

Fig. S20 Diagrams of the amide and Thz protons temperature coefficients of peptide **4**.

VT-NMR data for peptide 5

Table S10. ^{1}H NMR chemical shifts of peptide **5** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) ^{3}J (Hz)	δ Hα (ppm) ^{3}J (Hz)	δ Hβ (ppm) ^{3}J (Hz)	δ Hγ (ppm) ^{3}J (Hz)	δ Hδ (ppm) ^{3}J (Hz)	δ Other protons (ppm) ^{3}J (Hz)
Phe^1	7.85 d, J = 6.6	5.07 ddd, J = 10.8, 6.6, 5.4	γCH$_2$ 3.31, 3.25 dd, J = 13.2, 10.8, dd, J = 13.2, 5.4			Ar 7.28-7.25, 7.23-7.19
Oxz^2		4.10 d, J = 3.6	4.73 qd, J = 6.6, 3.6	1.18 d, J = 6.6		
D-Val^3	7.12 d, J = 10.2	5.14 dd, J = 10.2, 4.2	2.35 m	γCH$_3$ 1.10, γ'CH$_3$ 1.05 d, J = 6.6, d, J = 6.6		
Thz^{4or8}						7.59 s
Ile^5	7.63 d, J = 7.8	4.64 dd, J = 9.9, 7.8	2.29 m	γCH$_2$ 1.58, 1.31 γCH$_3$ 0.98 m, m d, J = 7.2	0.87 t, J = 7.2	
Oxz^6		4.33 d, J = 3.6	4.92 qd, J = 6.6, 3.6	1.42 d, J = 6.6		
D-Val^7	7.11 d, J = 10.2	5.15 dd, J = 10.2, 4.2	2.35 m	γCH$_3$ 1.10, γ'CH$_3$ 1.09 d, J = 6.6, d, J = 6.6		
Thz^{4or8}						7.60 s

The chemical shifts of Thz^{4}H and Thz^{8}H were indistinguishable.

Table S11. Chemical shifts of amide and Thz protons of peptide **5** at various temperatures and their temperature coefficients.

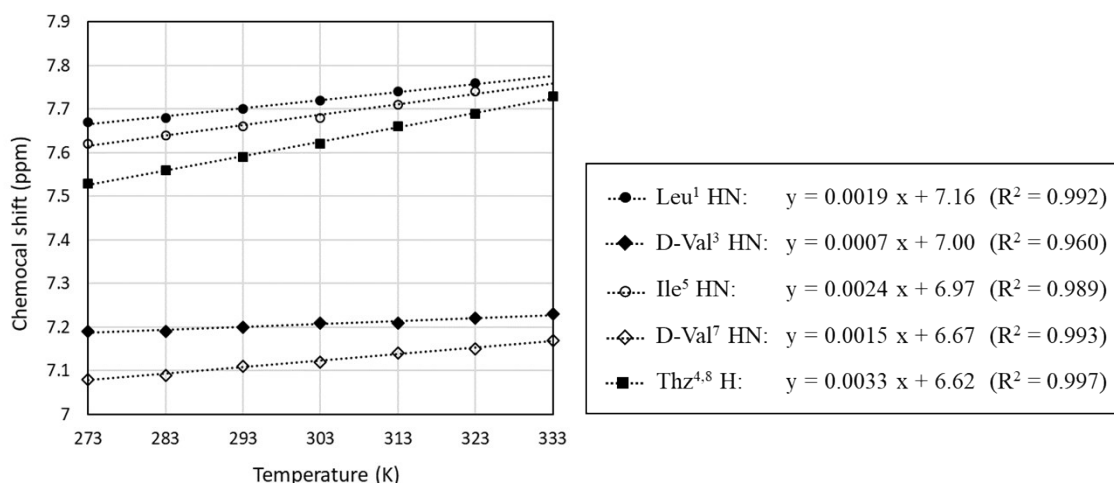| T (K)	δ Phe^1 HN (ppm)	δ D-Val^3 HN (ppm)	δ Ile^5 HN (ppm)	δ D-Val^7 HN (ppm)	δ Thz^{4or8} H (ppm)	δ Thz^{4or8} H (ppm)
273	7.83	7.11	7.59	7.09	7.52	7.54
283	7.84	7.12	7.61	7.1	7.55	7.56
293	7.85	7.12	7.62	7.11	7.58	7.59
303	7.86	7.13	7.64	7.12	7.61	7.62
313	7.87	7.14	7.66	7.13	7.65	7.66
323	7.88		7.69		7.69	7.69
333	7.90		7.72		7.73	7.73
Δδ/ΔT (ppb/K)	1.1	0.7	2.1	1.0	3.5	3.2

Fig. S21 Diagrams of the amide and Thz protons temperature coefficients of peptide **5**.

VT-NMR data for peptide 6

Table S12. ^{1}H NMR chemical shifts of peptide **6** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)		δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Cha[1]	7.68 d, J = 6.6	4.83 m	1.98, 1.61 m, m				1.67-0.82 (10H, cyclohexyl CH$_2$) m
Oxz[2]		4.30 d, J = 3.6	4.81 qd, J = 6.6, 3.6	1.40 d, J = 6.6			
D-Val[3]	7.20 d, J = 10.2	5.16 dd, J = 10.2, 4.8	2.34 m	γCH$_3$ 1.11, γ'CH$_3$ 1.07 d, J = 6.6, d, J = 6.6			
Thz[4]							7.60 s
Ile[5]	7.66 d, J = 7.8	4.61 dd, J = 9.3, 7.8	2.12 m	γCH$_2$ 1.54, 1.28 m, m	γCH$_3$ 0.92 d, J = 7.2	0.82 t, J = 7.2	
Oxz[6]		4.31 d, J = 4.2	4.87 qd, J = 6.6, 4.2	1.42 d, J = 6.6, d, J = 6.6			
D-Val[7]	7.12 d, J = 10.2	5.14 dd, J = 10.2, 4.8	2.34 m	γCH$_3$ 1.10, γ'CH$_3$ 1.07 d, J = 6.6, d, J = 6.6			
Thz[8]							7.60 s

Table S13. Chemical shifts of amide and Thz protons of peptide **6** at various temperatures and their temperature coefficients.

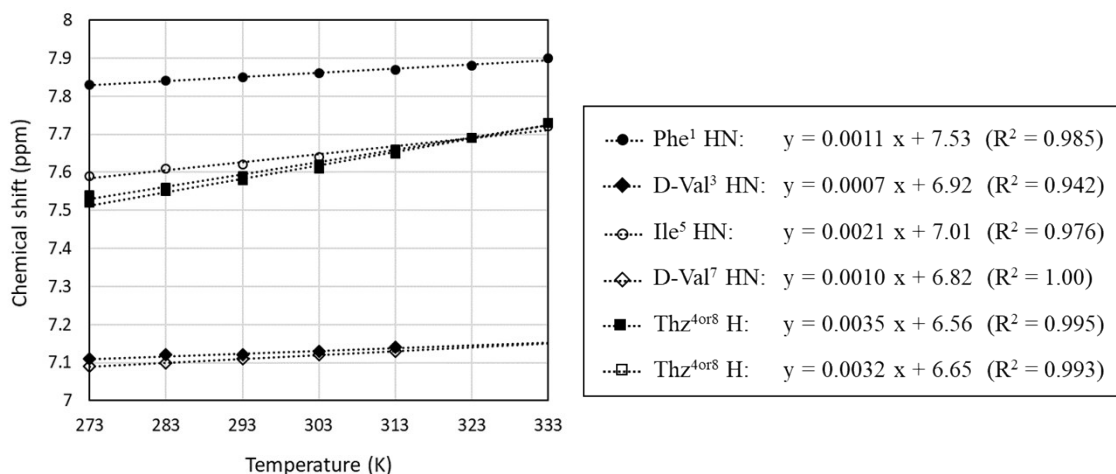| T (K)	δ Cha[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4,8] H (ppm)
273	7.65	7.19	7.61	7.09	7.52
283	7.66	7.19	7.63	7.10	7.55
293	7.67	7.20	7.65	7.12	7.58
303	7.69	7.21	7.67	7.13	7.62
313	7.71	7.22	7.70	7.15	7.65
323	7.74	7.23	7.73	7.16	7.69
333	7.77	7.24	7.76	7.18	7.73
Δδ/ΔT (ppb/K)	2.0	0.9	2.5	1.5	3.5

Fig. S22 Diagrams of the amide and Thz protons temperature coefficients of peptide **6**.

VT-NMR data for peptide 7

Table S14. ^{1}H NMR chemical shifts of peptide **7** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)	δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Phg[1]	8.55 d, J = 8.4	5.80 dd, J = 8.4, 1.2				Ar 7.20-7.16, 7.05-7.03
Oxz[2]		4.39 dd, J = 6.6, 1.2	4.68 m	1.42 d, J = 6.6, d, J = 6.6		
D-Val[3]	7.58 d, J = 9.6	5.20 dd, J = 9.6, 1.2	2.31 oct. J = 6.6	γCH₃ 1.15, γ'CH₃ 0.98 d, J = 6.6, d, J = 6.6		
Thz[4or8]						8.12 s
Ile[5]	8.09 d, J = 7.8	4.69 m	1.45 m	γCH₂ 0.68, 0.98 γCH₃ 0.18 m, m d, J = 6.6	0.37 t, J = 7.2	
Oxz[6]		4.24 dd, J = 6.6, 1.8	4.69 m	1.34 d, J = 6.6		
D-Val[7]	7.31 d, J = 10.2	5.09 dd, J = 10.2, 6.6	2.32 oct. J = 6.6	γCH₃ 1.12, γ'CH₃ 0.95 d, J = 6.6, d, J = 6.6		
Thz[4or8]						7.98 s

The chemical shifts of Thz[4]H and Thz[8]H were indistinguishable.

Table S15. Chemical shifts of amide and Thz protons of peptide **7** at various temperatures and their

temperature coefficients.

T (K)	δ Phg[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4or8] H (ppm)	δ Thz[4or8] H (ppm)
273	8.58	7.65	8.12	7.37	8.12	7.97
283	8.56	7.62	8.11	7.34	8.12	7.98
293	8.56	7.59	8.10	7.32	8.12	7.98
303	8.55	7.57	8.09	7.31	8.12	7.98
313	8.54	7.55	8.08	7.30	8.12	7.99
323	8.54	7.53	8.08	7.29	8.12	7.99
333	8.54	7.52	8.08	7.28	8.12	7.99
Δδ/ΔT (ppb/K)	—*	-2.2	-0.7	-1.4	0.0	—*

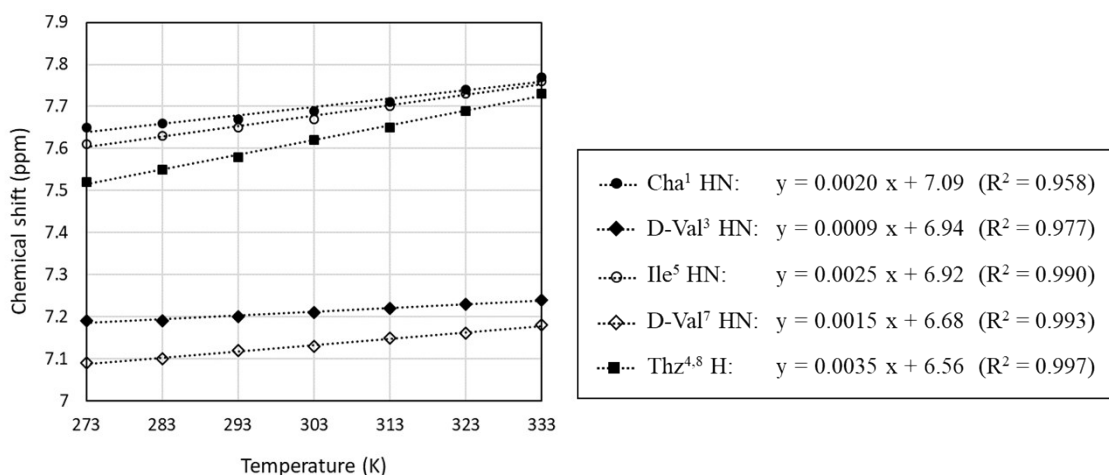*The correlation coefficients were less than 0.9.

Fig. S23 Diagrams of the amide and Thz protons temperature coefficients of peptide **7**.

VT-NMR data for peptide 8

Table S16. ^{1}H NMR chemical shifts of peptide **8** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) ^{3}J (Hz)	δ Hα (ppm) ^{3}J (Hz)	δ Hβ (ppm) ^{3}J (Hz)	δ Hγ (ppm) ^{3}J (Hz)	δ Hδ (ppm) ^{3}J (Hz)	δ Other protons (ppm) ^{3}J (Hz)
Abu[1]	7.82 d, J = 6.6	4.71 q, J =6.6	βCH$_2$ 1.95, 1.79 m, m	0.78 t, J = 7.2		
Oxz[2]		4.30 dd, J =4.5, 0.6	4.78 qd, J = 6.0, 4.5	1.40 d, J = 6.0		
D-Val[3]	7.22 d, J = 10.2	5.16 dd, J = 10.2, 6.6	2.34 oct. J = 6.6	γCH$_3$ 1.12, γ'CH$_3$ 1.05 d, J = 6.6, d, J = 6.6		
Thz[4]						7.68 s
Ile[5]	7.75 d, J = 7.8	4.64 t, J = 7.8	2.05 m	γCH$_2$ 1.40, 1.20 γCH$_3$ 0.83 m, m d, J = 6.6	0.77 t, J = 7.2	
Oxz[6]		4.29 dd, J = 4.8, 0.6	4.87 qd, J = 6.6, 4.8	1.41 d, J = 6.6		
D-Val[7]	7.14 d, J = 10.2	5.13 dd, J = 10.2, 6.6	2.34 oct. J = 6.6	γCH$_3$ 1.11, γ'CH$_3$ 1.05 d, J = 6.6, d, J = 6.6		
Thz[8]						7.68 s

Table S17. Chemical shifts of amide and Thz protons of peptide **8** at various temperatures and their temperature coefficients.

T (K)	δ Abu[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4,8] H (ppm)
273	7.78	7.22	7.70	7.13	7.61
283	7.80	7.22	7.72	7.14	7.64
293	7.82	7.22	7.75	7.15	7.67
303	7.84	7.23	7.77	7.16	7.71
313	7.87	7.23	7.80	7.17	7.74
323	7.89	7.24	7.83	7.18	7.77
333	7.91	7.24	7.86	7.19	7.81
Δδ/ΔT (ppb/K)	2.2	—*	2.7	1.0	3.3

*The correlation coefficient was less than 0.9.

Abu[1] HN: y = 0.0022 x + 7.17 (R^2 = 0.997)
D-Val[3] HN: y = 0.0004 x + 7.11 (R^2 = 0.889)
Ile[5] HN: y = 0.0027 x + 6.96 (R^2 = 0.996)
D-Val[7] HN: y = 0.0010 x + 6.86 (R^2 = 1.00)
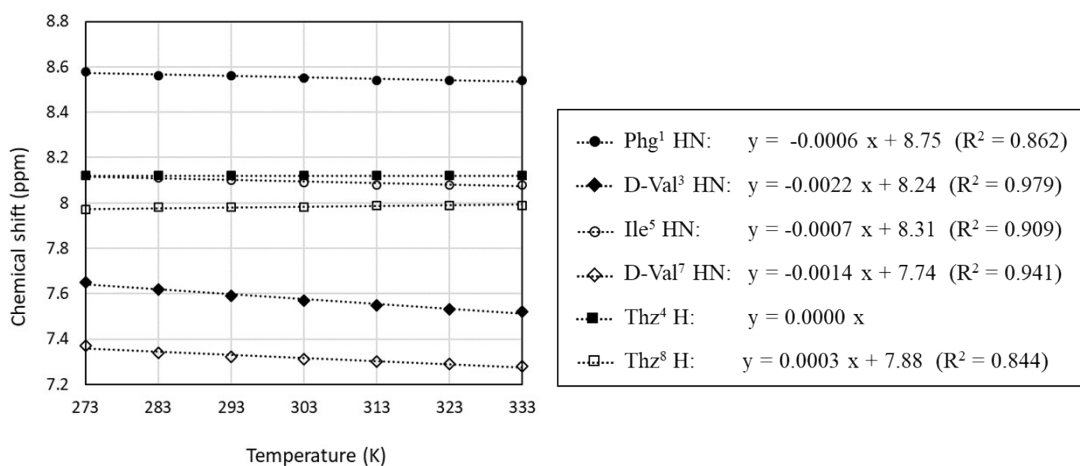Thz[4,8] H: y = 0.0033 x + 6.71 (R^2 = 0.998)

Fig. S24 Diagrams of the amide and Thz protons temperature coefficients of peptide **8**.

VT-NMR data for peptide 9

Table S18. ^{1}H NMR chemical shifts of peptide **9** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) ^{3}J (Hz)	δ Hα (ppm) ^{3}J (Hz)	δ Hβ (ppm) ^{3}J (Hz)	δ Hγ (ppm) ^{3}J (Hz)	δ Hδ (ppm) ^{3}J (Hz)	δ Other protons (ppm) ^{3}J (Hz)
Nva[1]	7.84 d, J = 7.2	4.76 q, J = 7.2	βCH$_2$ 1.92, 1.72 m, m	γCH$_2$ 1.27, 1.10 m, m	0.79 t, J = 6.6	
Oxz[2]		4.30 d, J =4.5	4.80 qd, J = 6.0, 4.5	1.40 d, J = 6.0		
D-Val[3or7]	7.23 d, J = 10.2	5.15 dd, J = 10.2, 5.4	2.33 m	γCH$_3$ 1.11, γ'CH$_3$ 1.04 d, J = 6.0, d, J = 6.0		
Thz[4or8]						7.70 s
Ile[5]	7.79 d, J = 7.8	4.65 t, J = 7.8	2.03 m	γCH$_2$ 1.40, 1.19 γCH$_3$ 0.82 m, m d, J = 6.6	0.77 t, J = 7.2	
Oxz[6]		4.30 d, J = 4.5	4.85 qd, J = 6.0, 4.5	1.42 d, J = 6.0		
D-Val[3or7]	7.16 d, J = 10.2	5.13 dd, J = 10.2, 5.4	2.35 m	γCH$_3$ 1.10, γ'CH$_3$ 1.04 d, J = 6.0, d, J = 6.0		
Thz[4or8]						7.71 s

The chemical shifts of Thz[4]H and Thz[8]H were indistinguishable.

The chemical shifts of D-Val[3] and D-Val[7] were indistinguishable.

Table S19. Chemical shifts of amide and Thz protons of peptide **9** at various temperatures and their temperature coefficients.

T (K)	δ Nva[1] HN (ppm)	δ D-Val[3or7] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[3or7] HN (ppm)	δ Thz[4or8] H (ppm)	δ Thz[4or8] H (ppm)
273	7.79	7.23	7.73	7.14	7.63	7.63
283	7.81	7.23	7.75	7.15	7.66	7.66
293	7.83	7.23	7.78	7.16	7.69	7.70
303	7.85	7.24	7.80	7.17	7.72	7.73
313	7.87	7.24	7.83	7.18	7.75	7.76
323	7.89	7.24	7.85	7.18	7.78	7.79
333	7.91	7.25	7.88	7.20	7.81	7.82
Δδ/ΔT (ppb/K)	2.0	—*	2.5	0.9	3.0	3.2

*The correlation coefficient was less than 0.9.

Nva[1] HN: $y = 0.0020\ x + 7.24$ ($R^2 = 1.00$)
D-Val[3or7] HN: $y = 0.0003\ x + 7.14$ ($R^2 = 0.844$)
Ile[5] HN: $y = 0.0025\ x + 7.05$ ($R^2 = 0.998$)
D-Val[3or7] HN: $y = 0.0009\ x + 6.89$ ($R^2 = 0.971$)
Thz[4or8] H: $y = 0.0030\ x + 6.81$ ($R^2 = 1.00$)
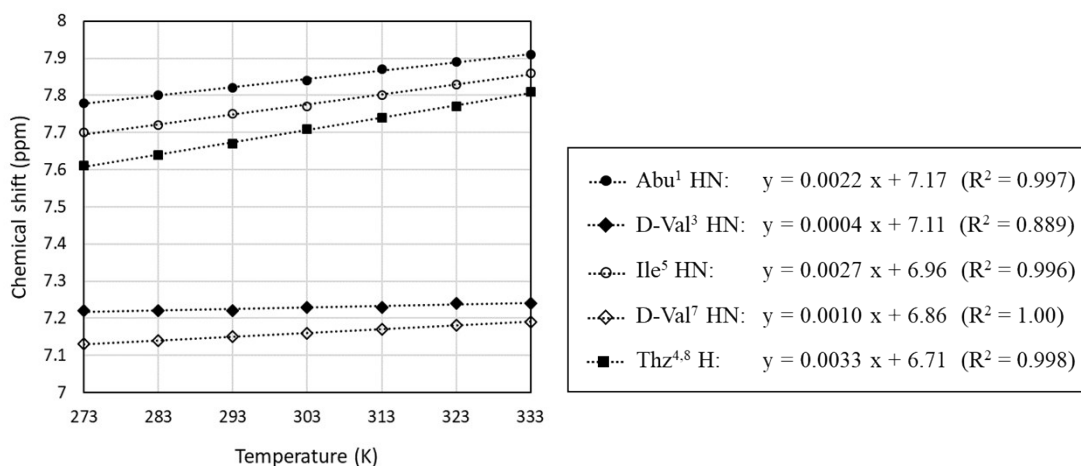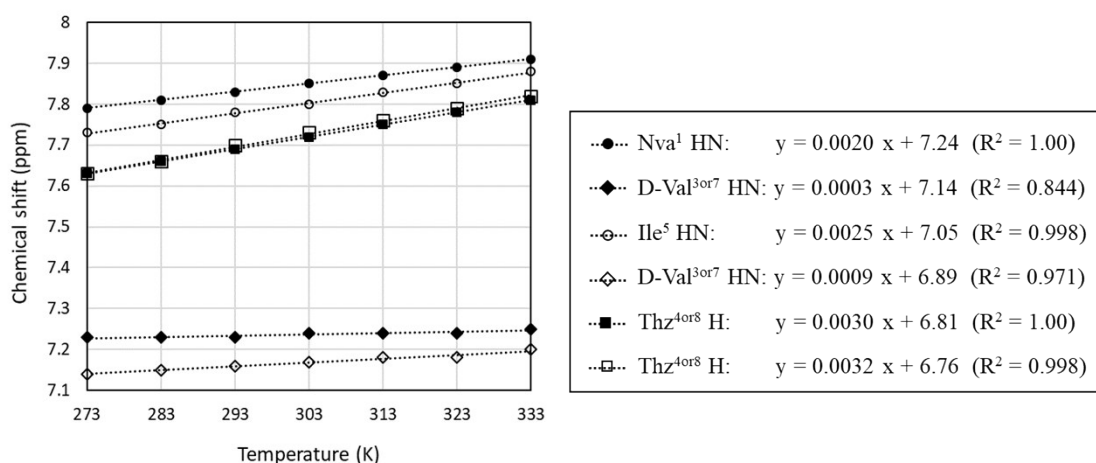Thz[4or8] H: $y = 0.0032\ x + 6.76$ ($R^2 = 0.998$)

Fig. S25 Diagrams of the amide and Thz protons temperature coefficients of peptide **9**.

VT-NMR data for peptide 10

Table S20. ^{1}H NMR chemical shifts of peptide **10** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)		δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Tbu[1]	7.61 d, J = 7.2	4.89 ddd, J = 9.6, 7.2, 4.2	βCH₂ 2.12, 1.63 dd, J = 13.8, 9.6, dd, J = 13.8, 4.2			0.97 s	
Oxz[2]		4.31 d, J = 3.6	4.81 qd, J = 6.6, 3.6	1.41 d, J = 6.6			
D-Val[3]	7.17 d, J = 10.8	5.15 dd, J = 10.8, 3.6	2.37 sept.d, J = 6.6, 3.6	γCH₃ 1.12, γ'CH₃ 1.09 d, J = 6.6, d, J = 6.6			
Thz[4]							7.53 s
Ile[5]	7.52 d, J = 7.8	4.60 dd, J = 10.8, 7.8	2.23 m	γCH₂ 1.58, 1.32 m, m	γCH₃ 0.98 d, J = 5.4	0.85 t, J = 7.2	
Oxz[6]		4.32 d, J = 3.6	4.92 qd, J = 6.6, 3.6	1.44 d, J = 6.6			
D-Val[7]	7.08 d, J = 10.2	5.13 dd, J = 10.2, 3.6	2.36 sept.d, J = 6.6, 3.6	γCH₃ 1.09, γ'CH₃ 1.09 d, J = 6.6, d, J = 6.6			
Thz[8]							7.53 s

Table S21. Chemical shifts of amide and Thz protons of peptide **10** at various temperatures and their temperature coefficients.

T (K)	δ Tbu[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4or8] H (ppm)	δ Thz[4or8] H (ppm)
273	7.60	7.16	7.49	7.05	7.48	7.48
283	7.60	7.17	7.5	7.06	7.50	7.50
293	7.60	7.17	7.52	7.07	7.52	7.52
303	7.61	7.18	7.53	7.08	7.54	7.55
313	7.62	7.18	7.56	7.10	7.57	7.58
323	7.63	7.19	7.58	7.12	7.60	7.61
333	7.65	7.20	7.61	7.13	7.63	7.64
Δδ/ΔT (ppb/K)	—*	0.6	2.0	1.4	2.5	2.7

*The correlation coefficient was less than 0.9.

Tbu[1] HN: $y = 0.0008\,x + 7.37$ ($R^2 = 0.870$)

D-Val[3] HN: $y = 0.0006\,x + 6.88$ ($R^2 = 0.951$)

Ile[5] HN: $y = 0.0020\,x + 6.94$ ($R^2 = 0.975$)

D-Val[7] HN: $y = 0.0014\,x + 6.66$ ($R^2 = 0.980$)

Thz[4or8] H: $y = 0.0025\,x + 6.79$ ($R^2 = 0.989$)

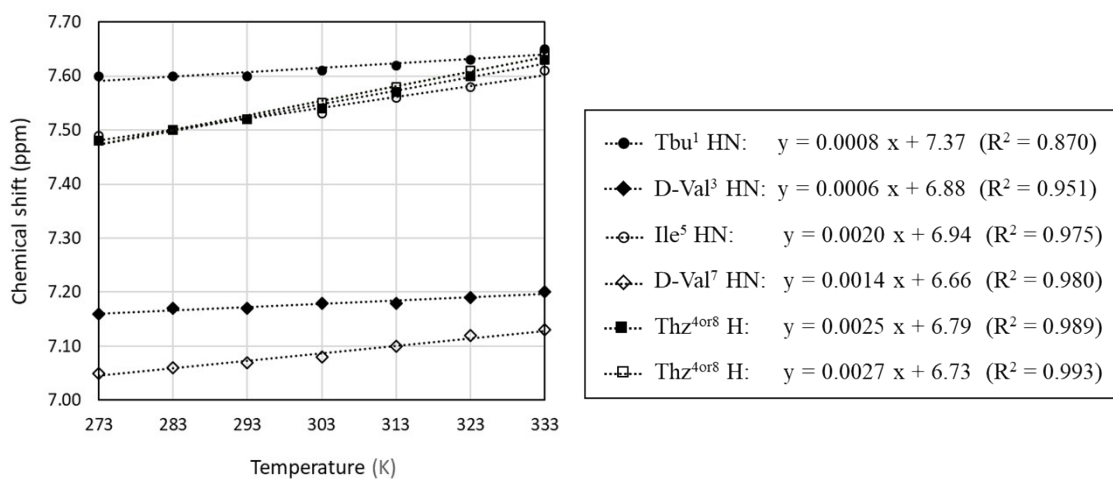Thz[4or8] H: $y = 0.0027\,x + 6.73$ ($R^2 = 0.993$)

Fig. S26 Diagrams of the amide and Thz protons temperature coefficients of peptide **10**.

VT-NMR data for peptide 11

Table S22. ^{1}H NMR chemical shifts of peptide **11** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) ^{3}J (Hz)	δ Hα (ppm) ^{3}J (Hz)	δ Hβ (ppm) ^{3}J (Hz)	δ Hγ (ppm) ^{3}J (Hz)	δ Hδ (ppm) ^{3}J (Hz)	δ Other protons (ppm) ^{3}J (Hz)
Chg^1	7.92 d, J = 7.8	4.63 ddd, J = 7.8,5.7, 1.2	1.80 m			1.67-0.82 (10H, cyclohexyl CH$_2$) m
Oxz^{2or6}		4.27 dd, J =6.0, 1.2	4.81 quint. J = 6.0	1.41 d, J = 6.0		
D-Val^{3or7}	7.25 d, J = 10.2	5.14 dd, J = 10.2, 6.6	2.30 oct. J = 6.6	γCH$_3$ 1.10, γ'CH$_3$ 0.99 d, J = 6.6, d, J = 6.6		
Thz^4						7.85 s
Ile^5	8.01 d, J = 7.8	4.69 ddd, J = 7.8, 5.4, 1.2	1.94 m	γCH$_2$ 1.35, 1.19 γCH$_3$ 0.72 m, m d, J = 7.2	0.76 t, J = 7.2	
Oxz^{2or6}		4.28 dd, J = 6.0, 1.2	4.81 quint. J = 6.0	1.43 d, J = 6.0		
D-Val^{3or7}	7.26 d, J = 9.6	5.15 dd, J = 9.6, 6.6	2.30 oct. J = 6.6	γCH$_3$ 1.10, γ'CH$_3$ 1.00 d, J = 6.6, d, J = 6.6		
Thz^8						7.85 s

The chemical shifts of Oxz^2 and Oxz^6 were indistinguishable.

The chemical shifts of D-Val^3 and D-Val^7 were indistinguishable.

Table S23. Chemical shifts of amide and Thz protons of peptide **11** at various temperatures and their temperature coefficients.

T (K)	δ Chg^1 HN (ppm)	δ D-Val^{3or7} HN (ppm)	δ Ile^5 HN (ppm)	δ D-Val^{3or7} HN (ppm)	δ Thz^{4,8} H (ppm)
273		7.25	7.95	7.25	7.80
283	7.87	7.25	7.97	7.25	7.82
293	7.90	7.25	8.00	7.26	7.84
303	7.93	7.25	8.02	7.26	7.87
313	7.95	7.26	8.04	7.27	7.89
323	7.98	7.26	8.06	7.27	7.90
333	7.99	7.26	8.07	7.28	7.92
Δδ/ΔT (ppb/K)	2.5	—*	2.1	0.5	2.0

*The correlation coefficient was less than 0.9.

Chg^1 HN: y = 0.0025 x + 7.18 (R^2 = 0.984)

D-Val^{3or7} HN: y = 0.0002 x + 7.19 (R^2 = 0.750)

Ile^5 HN: y = 0.0021 x + 7.39 (R^2 = 0.987)

D-Val^{3or7} HN: y = 0.0005 x + 7.11 (R^2 = 0.942)

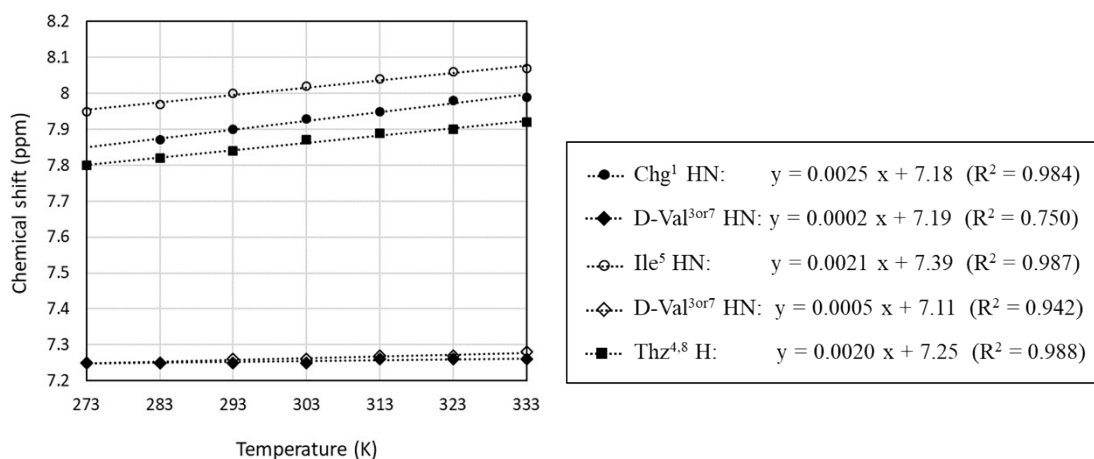Thz^{4,8} H: y = 0.0020 x + 7.25 (R^2 = 0.988)

Fig. S27 Diagrams of the amide and Thz protons temperature coefficients of peptide **11**.

VT-NMR data for peptide 12

Table S24. ^{1}H NMR chemical shifts of peptide **12** (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)	δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Tle[1]	8.22 d, J = 9.0	4.48 dd. J =9.0, 1.8		0.76 s		
Oxz[2]		4.25 dd, J = 6.0, 1.8	4.83 quint. J = 6.0	1.41 d, J = 6.0		
D-Val[3]	7.40 d, J = 9.6	5.11 dd, J = 9.6, 7.8	2.26 m	γCH₃ 1.09, γ'CH₃ 0.94 d, J = 6.6, d, J = 6.6		
Thz[4or8]						8.00 s
Ile[5]	8.14 d, J = 7.8	4.75 ddd, J = 7.8, 3.6, 1.8	1.82 m	γCH₂ 1.18, 1.10 γCH₃ 0.70 m, m d, J = 6.6	0.61 t, J = 7.2	
Oxz[6]		4.28 dd, J = 6.0, 1.8	4.81 quint. J = 6.0	1.42 d, J = 6.0		
D-Val[7]	7.41 d, J = 10.2	5.21 dd, J = 10.2, 7.2	2.23 m	γCH₃ 1.08, γ'CH₃ 0.97 d, J = 6.6, d, J = 6.6		
Thz[4or8]						8.01 s

The chemical shifts of Thz[4]H and Thz[8]H were indistinguishable.

Table S25. Chemical shifts of amide and Thz protons of peptide **12** at various temperatures and their temperature coefficients.

T (K)	Tle[1] HN (ppm)	D-Val[3] HN (ppm)	Ile[5] HN (ppm)	D-Val[7] HN (ppm)	Thz[4,8] H (ppm)	Thz[4,8] H (ppm)
273	8.22	7.44	8.14	7.42	7.99	8.01
283	8.22	7.42	8.14	7.41	8.00	8.01
293	8.23	7.41	8.14	7.40	8.00	8.01
303	8.23	7.41	8.14	7.39	8.00	8.01
313	8.23	7.40	8.15	7.39	8.00	8.01
323	8.23	7.40	8.15	7.38	8.00	8.01
333	8.23	7.40	8.15	7.39	8.00	8.02
Δδ/ΔT (ppb/K)	0.0	—*	0.0	—*	0.0	0.0

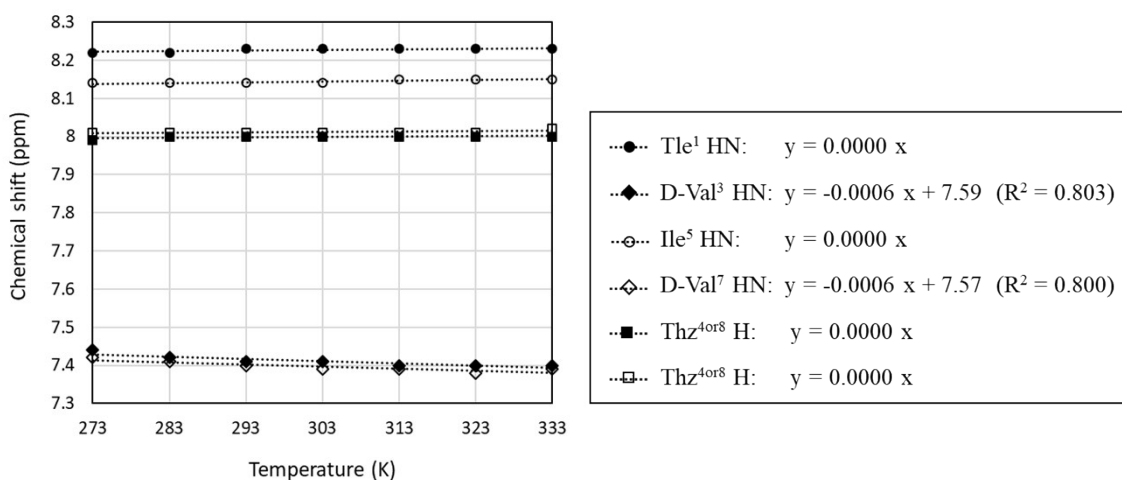*The correlation coefficients were less than 0.9.

Fig. S28 Diagrams of the amide and Thz protons temperature coefficients of peptide **12**.

VT-NMR data for T3ASC

Table S26. ^{1}H NMR chemical shifts of T3ASC (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)		δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Ile[1]	8.05 d, J = 9.0	4.86 ddd, J = 9.0, 3.3, 1.8	1.87 m	γCH$_2$ 1.18, 1.13 m, m	γCH$_3$ 0.86 d, J = 6.6	0.66 t, J = 7.2	
Oxz[2]		4.23 dd, J = 6.6, 1.8	4.71 quint. J = 6.6	1.45 d, J = 6.6			
D-Val[3]	7.20 d, J = 10.2	5.08 dd, J = 10.2, 8.4	2.19 m	γCH$_3$ 1.02, γ'CH$_3$ 0.81 d, J = 6.6, d, J = 6.6			
Thz[4]							8.09 s
Ile[5]	8.14 d, J = 7.8	5.38 dd, J = 7.8, 6.6	2.01 m	γCH$_2$ 1.53, 1.17 m, m	γCH$_3$ 0.73 d, J = 6.6	0.92 t, J = 7.2	
Thz[6]		4.28 dd, J = 6.0, 1.2	4.80 quint. J = 6.0	1.42 d, J = 6.0			8.08 s
D-Val[7]	8.23 d, J = 9.0	5.35 dd, J = 9.0, 6.6	2.29 oct. J = 6.6	γCH$_3$ 1.09, γ'CH$_3$ 1.02 d, J = 6.6, d, J = 6.6			8.09
Thz[8]							7.87 s

Table S27. Chemical shifts of amide and Thz protons of T3ASC at various temperatures and their temperature coefficients.

T (K)	δ Ile[1] HN (ppm)	δ D-Val[3] HN (ppm)	δ Ile[5] HN (ppm)	δ D-Val[7] HN (ppm)	δ Thz[4,8] H (ppm)	δ Thz[6] H (ppm)
273	8.06	7.23	8.14	8.27	8.09	8.08
283	8.06	7.22	8.14	8.25	8.09	8.08
293	8.05	7.21	8.14	8.23	8.09	8.08
303	8.05	7.21	8.14	8.24	8.09	8.08
313	8.05	7.20	8.14	8.22	8.09	8.08
323	8.05	7.20	8.14	8.21	8.09	8.08
333	8.05	7.21	8.13	8.21	8.09	8.08
Δδ/ΔT (ppb/K)	0.0	—*	0.0	—*	0.0	0.0

*The correlation coefficients were less than 0.9.
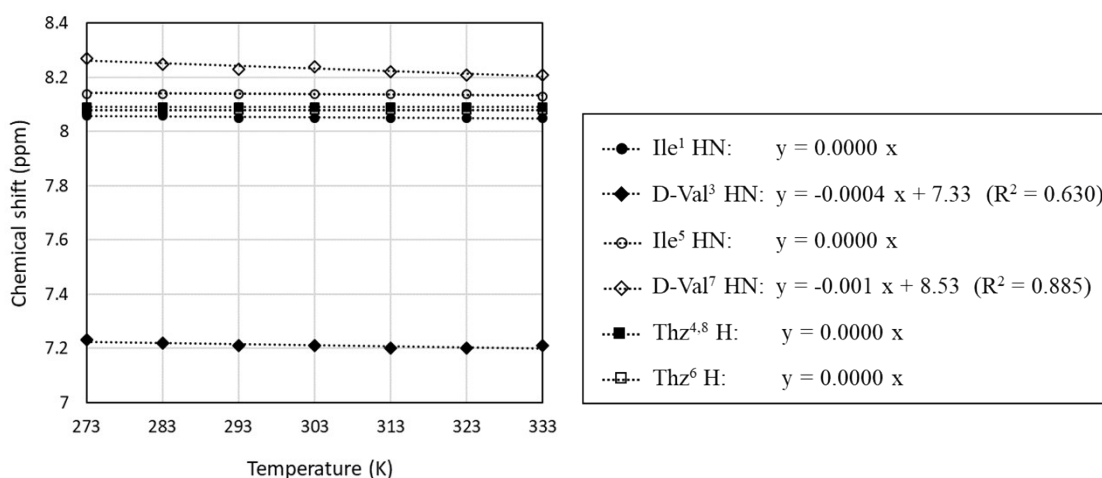

Fig. S29 Diagrams of the amide and Thz protons temperature coefficients of T3ASC.

VT-NMR data for *d*ASC

Table S28. ^{1}H NMR chemical shifts of *d*ASC (ca. 5mM) in acetonitrile-d_3 at 298 K.

Residue	δ HN (ppm) [3]J (Hz)	δ Hα (ppm) [3]J (Hz)	δ Hβ (ppm) [3]J (Hz)	δ Hγ (ppm) [3]J (Hz)		δ Hδ (ppm) [3]J (Hz)	δ Other protons (ppm) [3]J (Hz)
Ile[1]	9.25 d, J = 5.4	3.83 dd, J = 10.8, 5.4	2.34 m	γCH$_2$ 1.72, 1.16 m, m	γCH$_3$ 0.98 d, J = 7.2	0.88 t, J = 7.2	
aThr[2]	7.76 d, J = 7.2	3.49 t, J = 7.2	4.66 quint. J = 7.2	1.17 d, J = 7.2			
D-Val[3]	7.82 d, J = 9.6	5.33 t, J = 9.6	2.37 m	γCH$_3$ 1.14, γ'CH$_3$ 1.08 d, J = 6.0, d, J = 6.0			
Thz[4]							7.37 s
Ile[5]	9.25 d, J = 5.4	3.83 dd, J = 10.8, 5.4	2.34 m	γCH$_2$ 1.72, 1.16 m, m	γCH$_3$ 0.98 d, J = 7.2	0.88 t, J = 7.2	
aThr[6]	7.76 d, J = 7.2	3.49 t, J = 7.2	4.66 quint. J = 7.2	1.17 d, J = 7.2			
D-Val[7]	7.82 d, J = 9.6	5.33 t, J = 9.6	2.37 m	γCH$_3$ 1.14, γ'CH$_3$ 1.08 d, J = 6.0, d, J = 6.0			
Thz[8]							7.37 s

Table S29. Chemical shifts of amide and Thz protons of *d*ASC at various temperatures and their temperature coefficients.

T (K)	δ Ile[1,5] HN (ppm)	δ aThr[2,6] HN (ppm)	δ D-Val[3,7] HN (ppm)	δ Thz[4,8] H (ppm)
273	9.27	7.85	7.85	7.35
283	9.26	7.82	7.84	7.36
293	9.25	7.80	7.83	7.37
303	9.24	7.78	7.81	7.38
313	9.23	7.75	7.80	7.39
323	9.22	7.73	7.79	7.41
333	9.20	7.71	7.77	7.43
Δδ/ΔT (ppb/K)	-1.1	-2.3	-1.3	1.3

Ile[1,5] HN: y = -0.0011 x + 9.57 (R^2 = 0.985)
aThr[2,6] HN: y = -0.0023 x + 8.48 (R^2 = 0.997)
D-Val[3,7] HN: y = -0.0013 x + 8.21 (R^2 = 0.989)
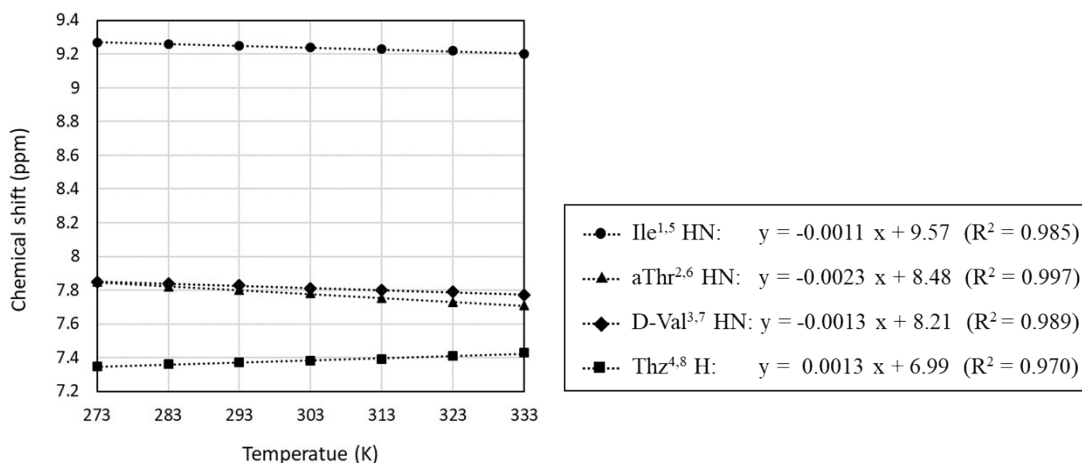Thz[4,8] H: y = 0.0013 x + 6.99 (R^2 = 0.970)

Fig. S30 Diagrams of the amide and Thz protons temperature coefficients of *d*ASC.

Thermodynamic parameters and van't Hoff plot of peptide 1

Table S30. Equilibrium parameters of peptide **1**.

T (K)	δ_{obs} Thz^{4,8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.82	0.574	1258
283	7.84	0.510	1583
293	7.86	0.451	1940
303	7.88	0.396	2332
313	7.90	0.345	2766
323	7.92	0.298	3249
333	7.93	0.276	3566

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
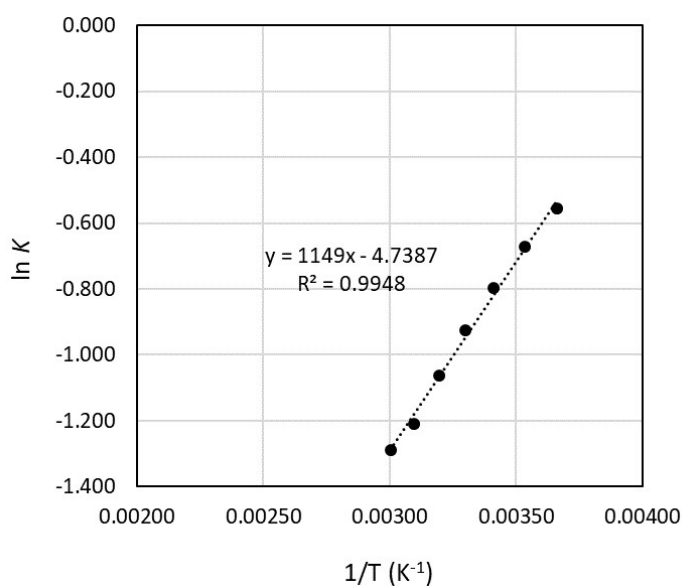
**$\Delta G^{\circ} = - RT\ln K$

Fig. S31 van't Hoff plot of peptide **1**.

Table S31. Thermodynamic parameters of peptide **1**.

ΔH° (kJ•mol^{-1})	ΔS^0 (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-9.55	-39.40	2.19

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plot of peptide 2

Table S32. Equilibrium parameters of peptide **2**.

T (K)	δ_{obs} Thz^{4,8} H (ppm)	K^*	ΔG° (J•mol^{-1})**
273	7.55	2.700	-2254
283	7.58	2.217	-1874
293	7.62	1.741	-1350
303	7.66	1.387	-824
313	7.70	1.114	-282
323	7.74	0.897	291
333	7.78	0.721	906

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
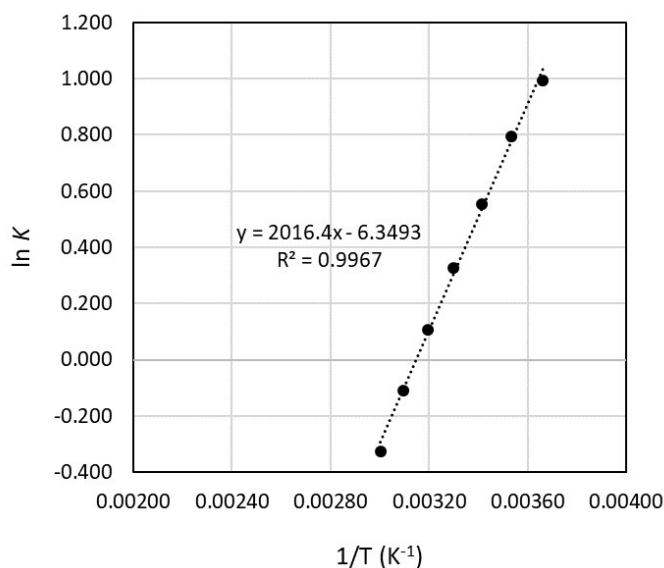
**$\Delta G^{\circ} = -$ RTln$K$

Fig. S32 van't Hoff plot of peptide **2**.

Table S33. Thermodynamic parameters of peptide **2**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-16.76	-52.79	-1.03

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plots of peptide 3

Table S34. Equilibrium parameters of peptide **3**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K^*	ΔG° (J•mol^{-1})**	T (K)	δ_{obs} Thz^{4or8} H (ppm)	K^*	ΔG° (J•mol^{-1})**
273	7.70	1.114	-246	273	7.70	1.114	-246
283	7.73	0.947	127	283	7.74	0.897	255
293	7.76	0.805	529	293	7.78	0.721	797
303	7.80	0.644	1107	303	7.81	0.609	1251
313	7.82	0.574	1442	313	7.84	0.510	1751
323	7.85	0.480	1971	323	7.86	0.451	2138
333	7.87	0.423	2382	333	7.89	0.370	2750

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of *d*ASC at 273 K.
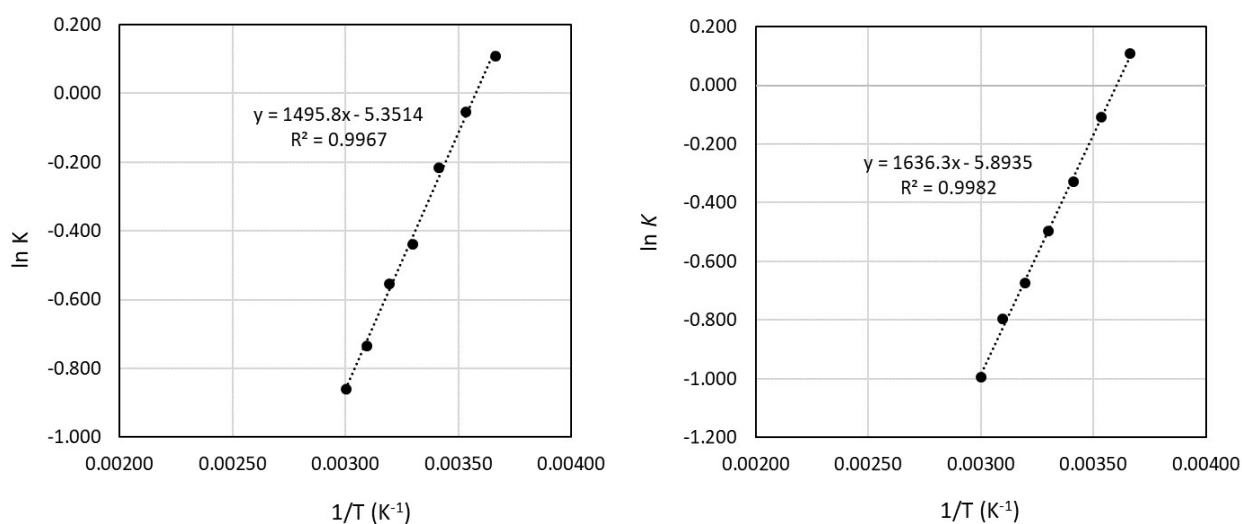
**$\Delta G^\circ = -$ RTln$K$

Fig. S33 van't Hoff plots of peptide **3**.

Table S35. Thermodynamic parameters of peptide **3**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*	ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-12.44	-44.49	0.82	-13.60	-49.00	1.00

*$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

Thermodynamic parameters and van't Hoff plot of peptide 4

Table S36. Equilibrium parameters of peptide **4**.

T (K)	δ_{obs} Thz^{4,8} H (ppm)	K^*	ΔG° (J$\bullet$mol^{-1})**
273	7.53	3.111	-2576
283	7.56	2.524	-2178
293	7.59	2.083	-1788
303	7.62	1.741	-1396
313	7.66	1.387	-852
323	7.69	1.176	-436
333	7.73	0.947	150

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
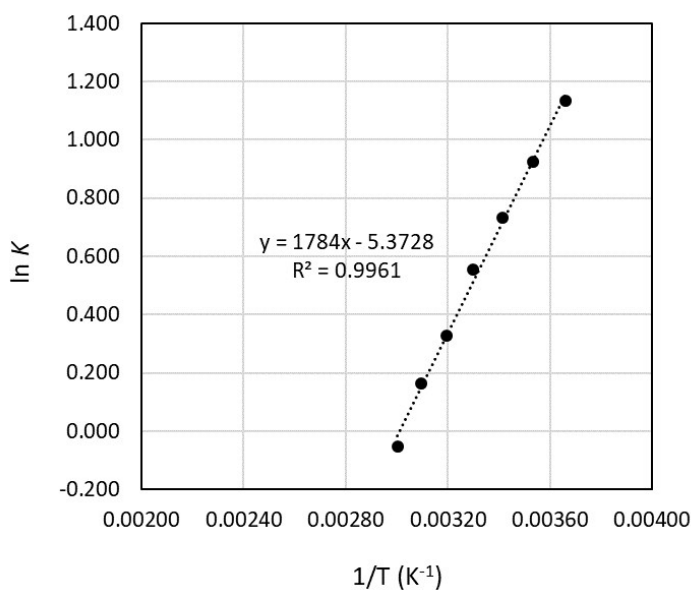
**$\Delta G^{\circ} = -$ RTln$K$

Fig. S34 van't Hoff plot of peptide **4**.

Table S37. Thermodynamic parameters of peptide **4**.

ΔH° (kJ$\bullet$mol^{-1})	ΔS° (J$\bullet$mol^{-1})	ΔG°_{298K} (kJ$\bullet$mol^{-1})*
-14.83	-44.67	-1.52

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plots of peptide 5

Table S38. Equilibrium parameters of peptide **5**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K^*	ΔG° (J·mol^{-1})**	T (K)	δ_{obs} Thz^{4or8} H (ppm)	K^*	ΔG° (J·mol^{-1})**
273	7.52	3.353	-2746	273	7.54	2.895	-2412
283	7.55	2.700	-2337	283	7.56	2.524	-2178
293	7.58	2.217	-1940	293	7.59	2.083	-1788
303	7.61	1.846	-1544	303	7.62	1.741	-1396
313	7.65	1.467	-997	313	7.66	1.387	-852
323	7.69	1.176	-436	323	7.69	1.176	-436
333	7.73	0.947	150	333	7.73	0.947	150

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of *d*ASC at 273 K.
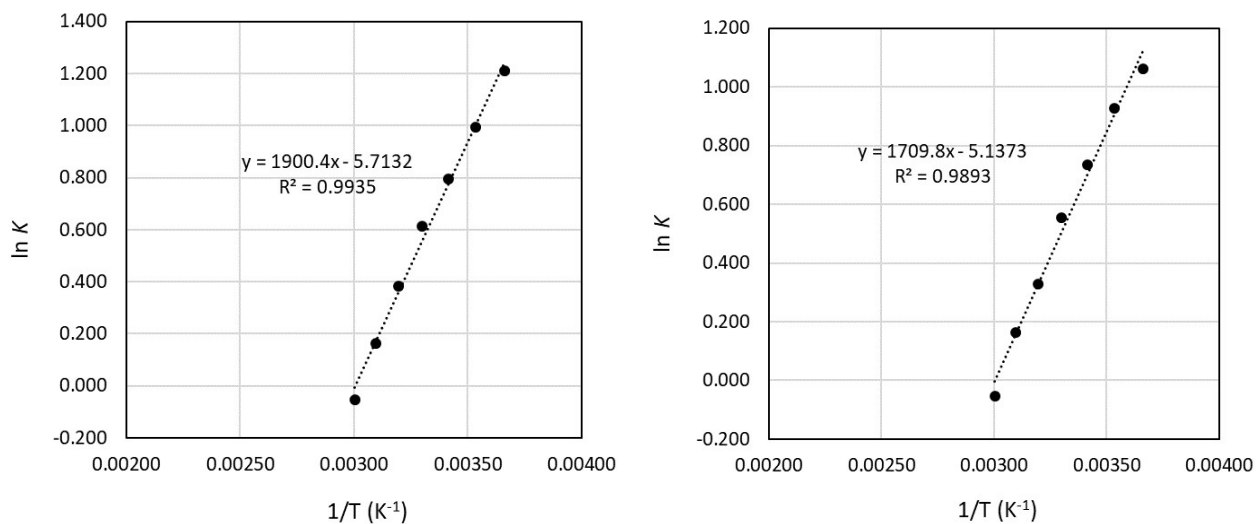
**$\Delta G^{\circ} = -$ RTln$K$

Fig. S35 van't Hoff plots of peptide **5**.

Table S39. Thermodynamic parameters of peptide **5**.

ΔH° (kJ·mol^{-1})	ΔS° (J·mol^{-1})	ΔG°_{298K} (kJ·mol^{-1})*	ΔH° (kJ·mol^{-1})	ΔS° (J·mol^{-1})	ΔG°_{298K} (kJ·mol^{-1})*
-15.80	-47.50	-1.64	-14.22	-42.71	-1.49

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plot of peptide 6

Table S40. Equilibrium parameters of peptide **6**.

T (K)	δ_{obs} Thz^{4,8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.52	3.353	-2746
283	7.55	2.700	-2337
293	7.58	2.217	-1940
303	7.62	1.741	-1396
313	7.65	1.467	-997
323	7.69	1.176	-436
333	7.73	0.947	150

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
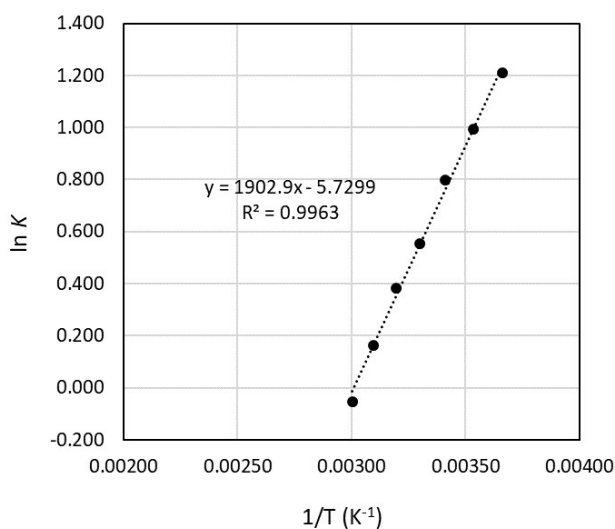
**$\Delta G^{\circ} = -$ RTln$K$

Fig. S36 van't Hoff plot of peptide **6**.

Table S41. Thermodynamic parameters of peptide **6**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-15.8	-47.6	-1.62

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plot of peptide 8

Table S42. Equilibrium parameters of peptide **8**.

T (K)	δ_{obs} Thz^{4,8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.61	1.846	-1392
283	7.64	1.552	-1034
293	7.67	1.313	-662
303	7.71	1.056	-136
313	7.74	0.897	282
323	7.77	0.762	730
333	7.81	0.609	1374

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
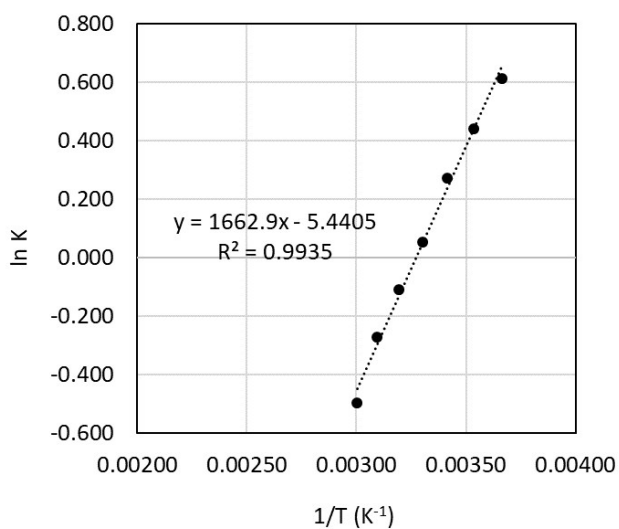
**$\Delta G^{\circ} = - RT\ln K$

Fig. S37 van't Hoff plot of peptide **8**.

Table S43. Thermodynamic parameters of peptide **8**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-13.83	-45.23	-0.35

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plots of peptide 9

Table S44. Equilibrium parameters of peptide **9**.

T (K)	Thz^{4or8} H (ppm)	K^*	ΔG° (J•mol^{-1})**	T (K)	Thz^{4or8} H (ppm)	K^{a*}	ΔG° (J•mol^{-1})**
273	7.63	1.643	-1127	273	7.63	1.643	-1127
283	7.66	1.387	-770	283	7.66	1.387	-770
293	7.69	1.176	-396	293	7.70	1.114	-264
303	7.72	1.000	0	303	7.73	0.947	136
313	7.75	0.850	423	313	7.76	0.805	565
323	7.78	0.721	879	323	7.79	0.682	1028
333	7.81	0.609	1374	333	7.82	0.574	1535

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
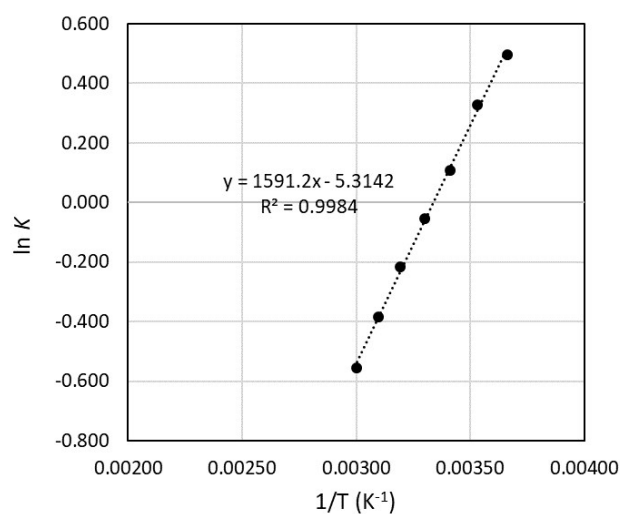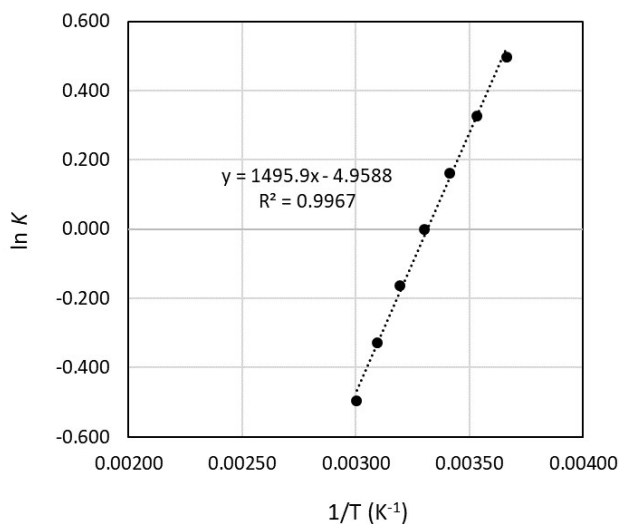
**$\Delta G^\circ = -$ RTln$K$

Fig. S38 van't Hoff plots of peptide **9**.

Table S45. Thermodynamic parameters of peptide **9**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*	ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-12.44	-41.23	-0.15	-13.23	-44.18	-0.06

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plots of peptide 10

Table S46. Equilibrium parameters of peptide **10**.

T (K)	Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**	T (K)	Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.48	4.692	-3509	273	7.48	4.692	-3509
283	7.50	3.933	-3222	283	7.50	3.933	-3222
293	7.52	3.353	-2947	293	7.52	3.353	-2947
303	7.54	2.895	-2678	303	7.55	2.700	-2502
313	7.57	2.364	-2238	313	7.58	2.217	-2072
323	7.60	1.960	-1807	323	7.61	1.846	-1646
333	7.63	1.643	-1374	333	7.64	1.552	-1216

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
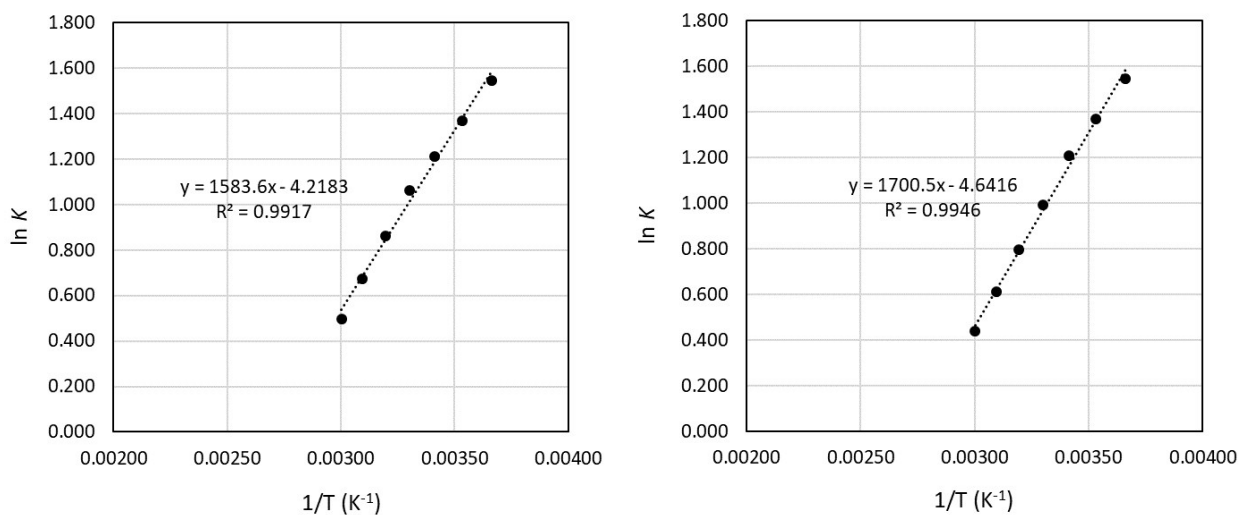
**$\Delta G^{\circ} = - RTlnK$

Fig. S39 van't Hoff plots of peptide **10**.

Table S47. Thermodynamic parameters of peptide **10**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*	ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-13.17	-35.07	-2.71	-14.14	-38.59	-2.64

*$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

Thermodynamic parameters and van't Hoff plot of peptide 11

Table S48. Equilibrium parameters of peptide **11**.

T (K)	Thz^{4,8} H (ppm)	K^*	ΔG° (J•mol^{-1})**
273	7.80	0.644	997
283	7.82	0.574	1304
293	7.84	0.510	1639
303	7.87	0.423	2167
313	7.89	0.370	2585
323	7.90	0.345	2854
333	7.92	0.298	3350

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.
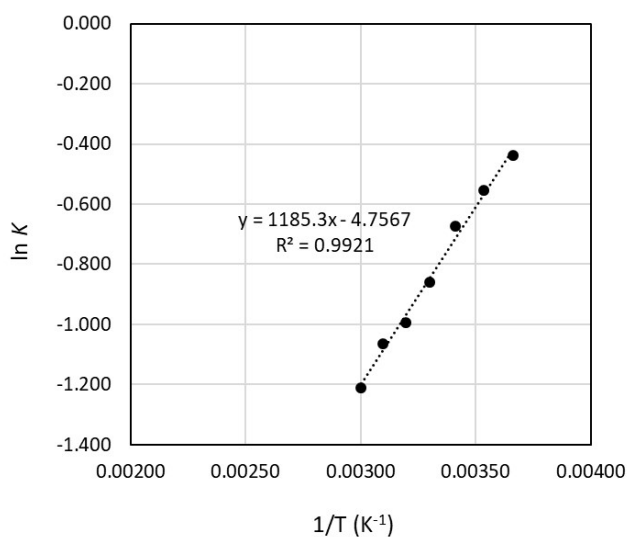
**$\Delta G^\circ = - RT\ln K$

Fig. S40 van't Hoff plot of peptide **11**.

Table S49. Thermodynamic parameters of peptide **11**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-9.85	-39.55	1.93

*$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

Thermodynamic parameters of peptide 7

Table S50. Equilibrium parameters of peptide **7**.

T (K)	Thz^{4,8} H (ppm)	$K*$	ΔG° (J·mol^{-1})**
273	7.97	0.194	3727
283	7.98	0.175	4106
293	7.98	0.175	4251
298	7.98	0.175	4324
303	7.98	0.175	4397
313	7.99	0.156	4831
323	7.99	0.156	4985
333	7.99	0.156	5139

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.

**$\Delta G^\circ = -$ RTln$K$

Thermodynamic parameters of peptide 12

Table S51. Equilibrium parameters of peptide **12**.

T (K)	Thz^{4or8} H (ppm)	$K*$	ΔG° (J·mol^{-1})**	T (K)	Thz^{4or8} H (ppm)	$K*$	ΔG° (J·mol^{-1})**
273	7.99	0.156	4213	273	8.01	0.121	4790
283	8.00	0.138	4652	283	8.01	0.121	4965
293	8.00	0.138	4816	293	8.01	0.121	5140
298	8.00	0.138	4907	303	8.01	0.121	5316
303	8.00	0.138	4981	313	8.01	0.121	5491
313	8.00	0.138	5145	323	8.01	0.121	5667
323	8.00	0.138	5310	333	8.02	0.104	6254
333	8.00	0.138	5474				

*Equilibrium constants were calculated from the values of the chemical shifts of Thz^4 and Thz^8 protons: $K = (\delta_s - \delta_{obs}) / (\delta_{obs} - \delta_f)$. δ_s (8.09 ppm) is the chemical shift for Thz proton of T3ASC. δ_f (7.35 ppm) is chemical shift for Thz proton of dASC at 273 K.

**$\Delta G^\circ = -$ RTln$K$

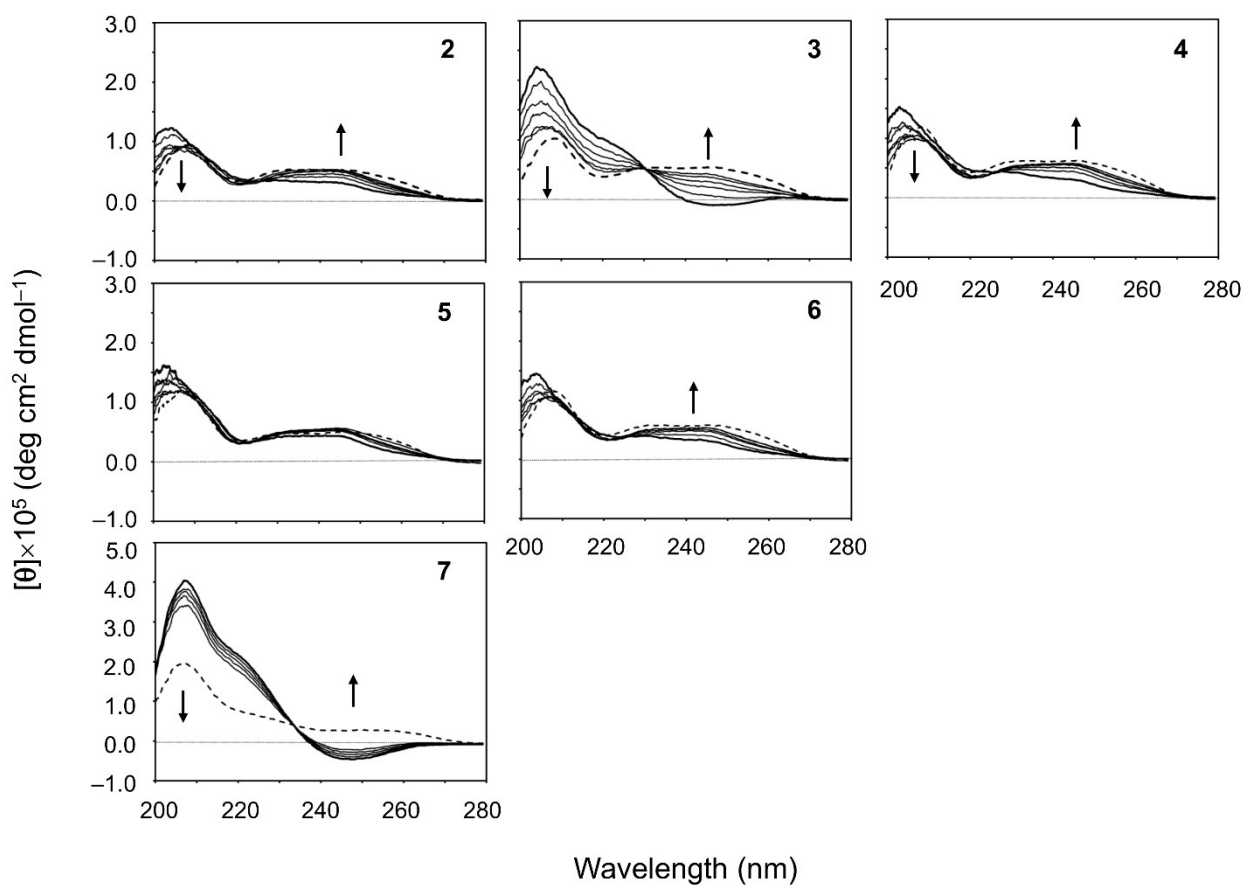**CD spectral changes by TFE titration for 2-7**

Fig. S41 CD spectral changes elicited by titration of TFE for peptides **2-7**. The spectra were measured in CH$_3$CN solution while changing the TFE concentration (10%, 20%, 30%, 40%, 50% and 100%). The spectra in 100% CH$_3$CN and 100% TFE solution are drawn in bold and dashed lines, respectively. The spectra for **2-5** are taken from previous report (A. Asano *et. al.*, *J. Peptide Res.*, 2002, **60**, 10-22). The spectra for **6** is taken from previous report (A. Asano *et. al.*, *Acta Cryst.*, 2003, **C59**, o488-o490). The spectra for **7** is taken from previous report (A. Asano *et. al.*, *Bioorg. Med. Chem.*, 2011, **19**, 3372-3377).

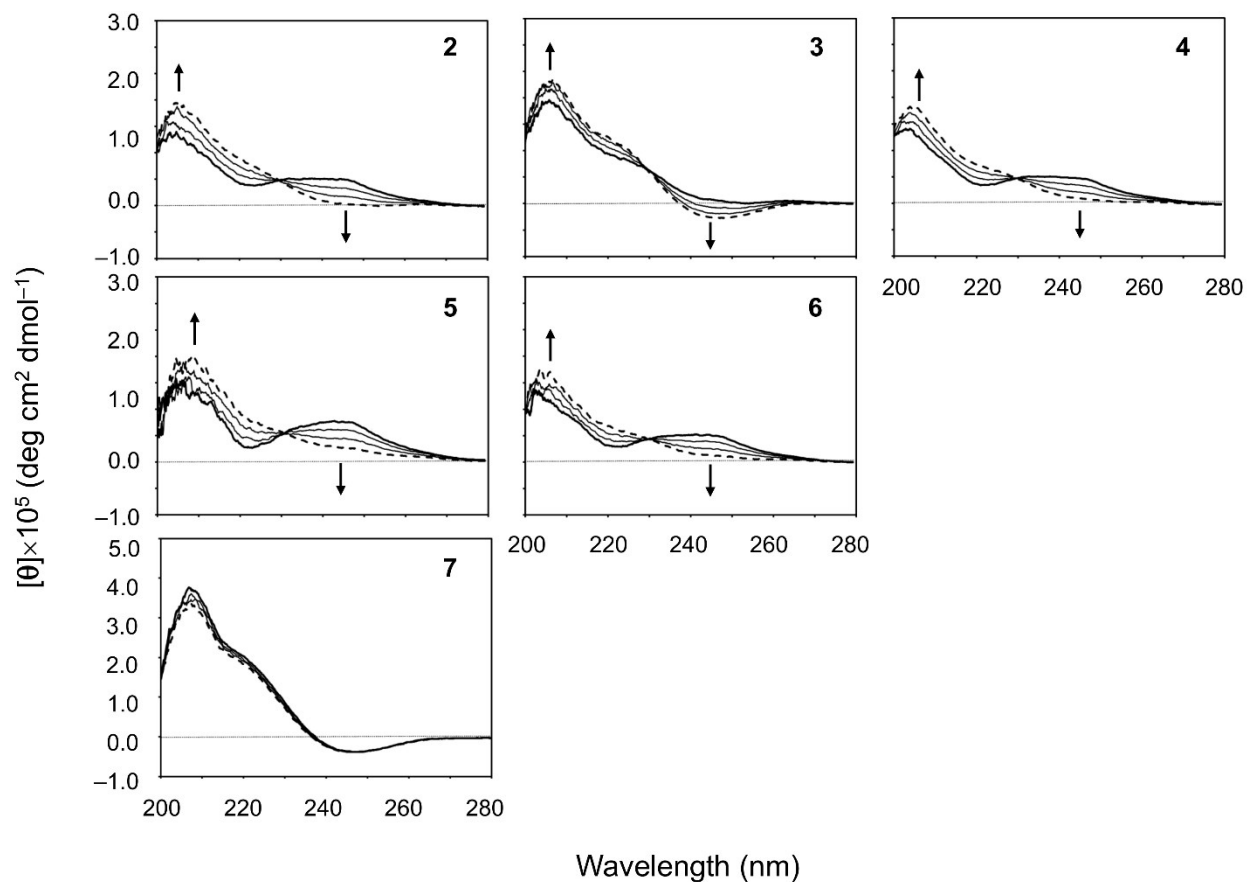**CD spectral changes by increasing temperature for 2-7**

Fig. S42 Temperature dependence of the CD spectra for peptides **2-7**. The spectra were measured every 20 K in CH$_3$CN solution at 273-333 K. The CD spectra at 273 and 333 K are drawn in bold and dashed lines, respectively. The spectra for **7** is taken from previous report (A. Asano *et. al.*, *Bioorg. Med. Chem.*, 2011, **19**, 3372-3377).

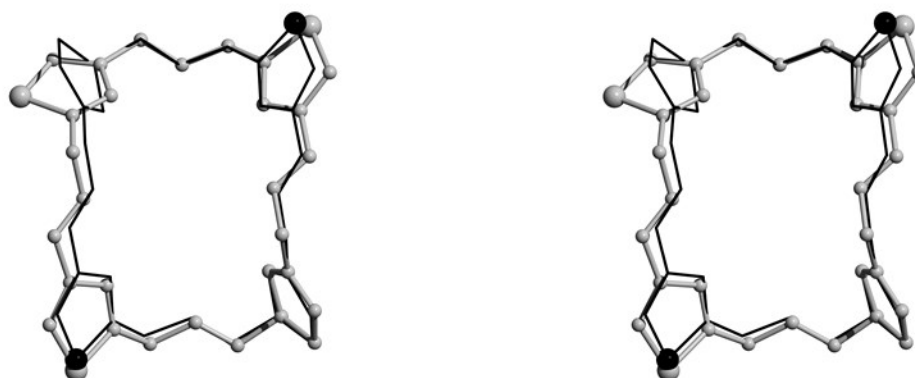**Superimposition of the X-ray structures of 1and T3ASC**

Fig. S43 Superimpositions of the crystal structures peptide **1** and T3ASC. Side chains and hydrogen atoms are omitted for clarity. Thin lines (black) represent the peptide ring of peptide **1**, and the sulfur atoms are represented by balls. This figure is taken from previous report (A. Asano *et*. *al*., *J. Pept. Sci*., 2018, e3120).

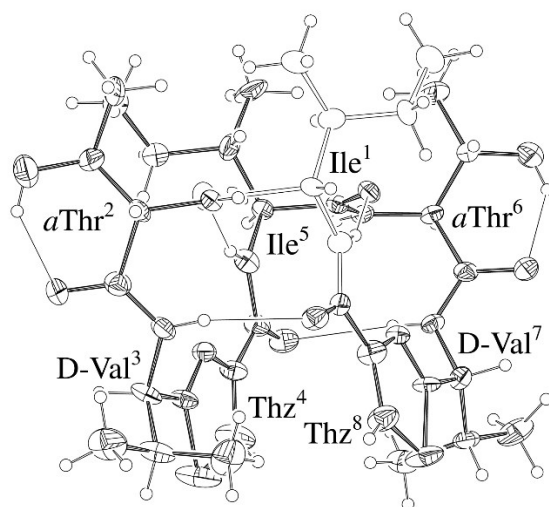**The X-ray structure of *d*ASC**

Fig. S44 The crystal structure of *d*ASC. Thin lines represent hydrogen bonds. This figure is taken from previous report (A. Asano *et. al.*, *Biopolymers* 2001, **58**, 295-304).