Electronic supporting information for

"Electronic substituent effect on conformation of phenylalanine-incorporated cyclic peptide"

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Contents:

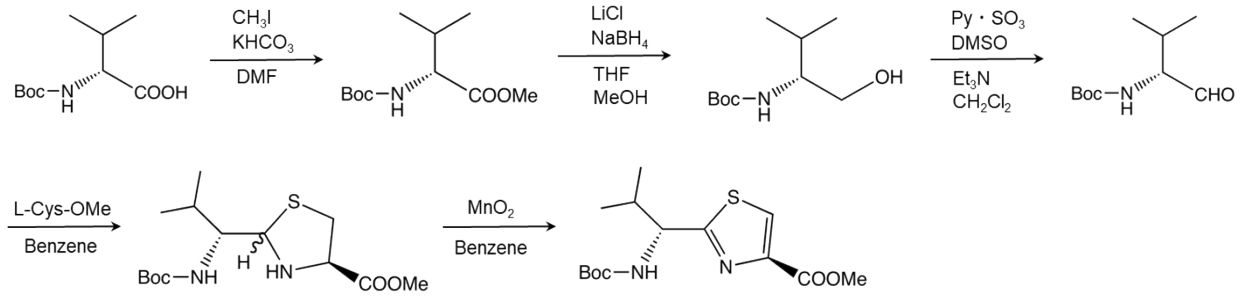
Synthesis and characterization of the peptides 1, 2, 3, 6, 7, 8, 9 and 10.

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. ^{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). Low-resolution mass spectra (LR-MS) were obtained by using matrix-assisted laser desorption ionization (MALDI-TOF) mass spectroscopy on a Bruker microflex LRF (Bruker, Massachusetts, USA).

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

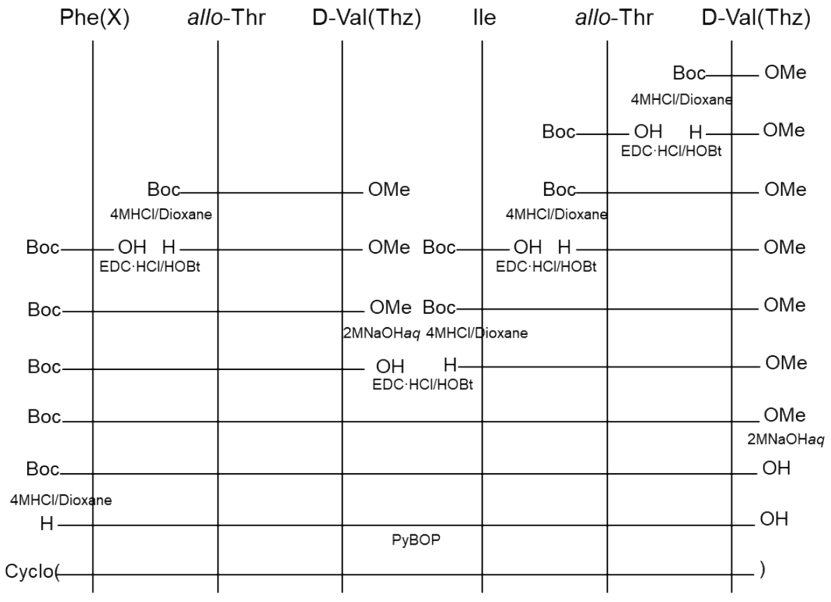
Boc-D-Val(Thz)-OMe was prepared according to previous report (Y. Hamada *et. al*., *J. Org. Chem*., 1987, **52**, 1252-1255) (Scheme S1). N-(*tert*-butoxycarbonyl)-D-valine (Boc-D-Val-OH) was first converted to the corresponding methyl ester by using methyl iodide in the presence of potassium hydrogen 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).

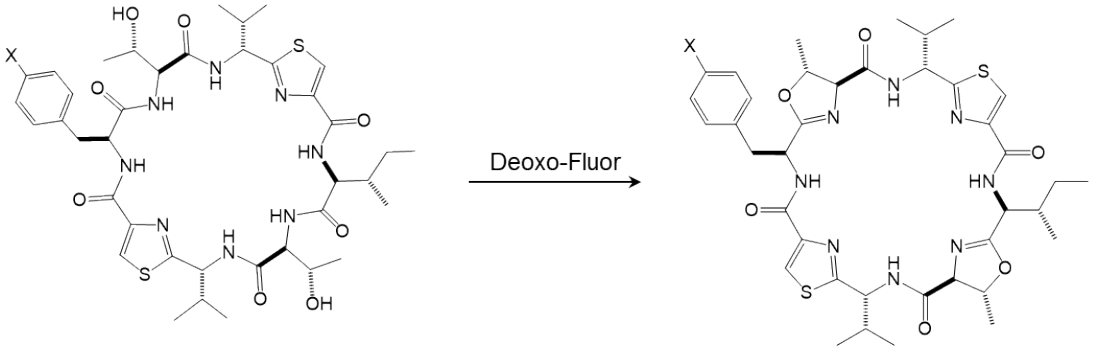


1; X=OCH_3, **2**; X=CH_3, **3**; X=$C(CH_3)_3$, **6**; X=I
7; X=Cl, **8**; X=Br, **9**; X=CF_3, **10**; X=NO_2

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).



1; X=OCH_3, **2**; X=CH_3, **3**; X=$C(CH_3)_3$, **6**; X=I
7; X=Cl, **8**; X=Br, **9**; X=CF_3, **10**; X=NO_2

Scheme S3

Table S1. MALDI-TOF Mass spectroscopic data for **1**, **2**, **3**, **6**, **7**, **8**, **9** and **10**.

Peptide	Mass type	Calculated mass	Observed mass
1	$[M+H]^+$	821.35	821.59
	$[M+Na]^+$	843.33	843.58
	$[M+K]^+$	859.30	ND
2	$[M+H]^+$	805.35	805.57
	$[M+Na]^+$	827.33	827.56
	$[M+K]^+$	843.31	ND
3	$[M+H]^+$	847.40	ND
	$[M+Na]^+$	869.38	869.69
	$[M+K]^+$	885.36	ND
6	$[M+H]^+$	917.23	917.54
	$[M+Na]^+$	939.22	939.54
	$[M+K]^+$	955.19	ND
7	$[M+H]^+$	825.30	825.53
	$[M+Na]^+$	847.28	847.52
	$[M+K]^+$	863.25	ND
8	$[M+H]^+$	869.55	869.53
	$[M+Na]^+$	891.23	891.51
	$[M+K]^+$	907.20	ND
9	$[M+H]^+$	859.32	859.66
	$[M+Na]^+$	881.31	881.65
	$[M+K]^+$	897.28	897.62
10	$[M+H]^+$	836.32	836.68
	$[M+Na]^+$	858.30	858.65
	$[M+K]^+$	874.28	874.63

^{1}H NMR spectra of peptides 1

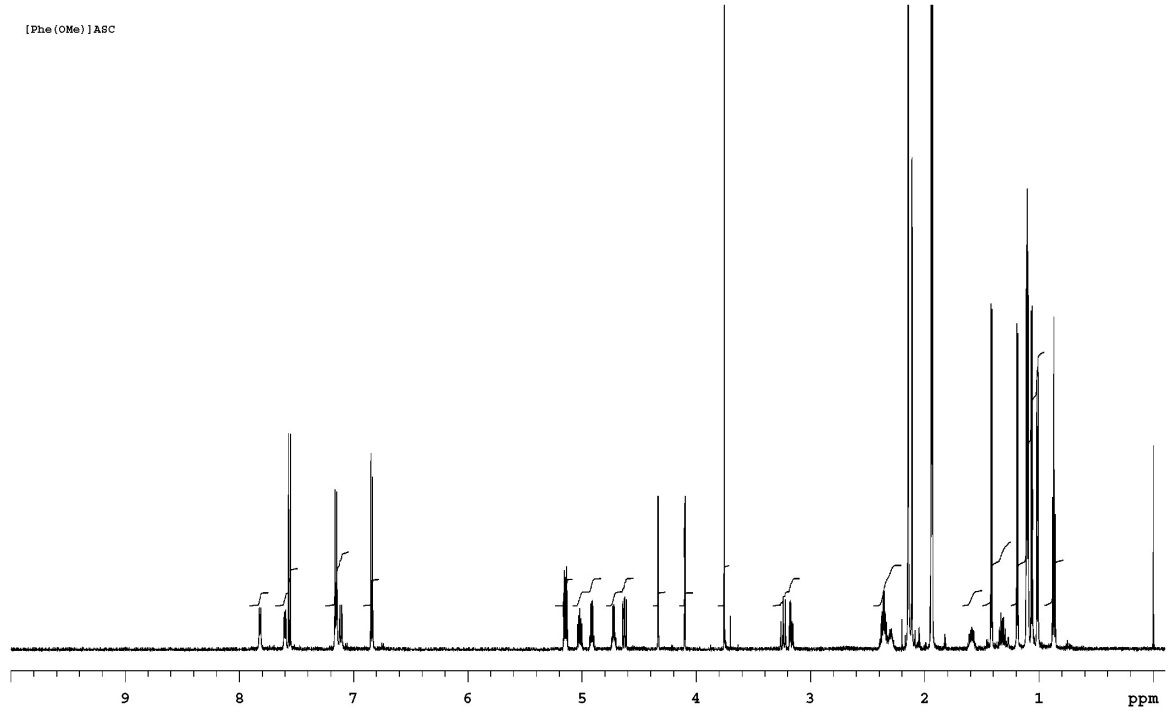


Fig. S1 1D ^{1}H NMR spectrum of peptide **1** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(OMe)[1]	7.82 d, *J* = 6.6	5.02 ddd, *J* = 11.4, 6.6, 5.4	γCH$_2$ 3.24, 3.17 dd, *J* = 13.2, 11.4, dd, *J* = 13.2, 5.4		7.16 d, *J* = 9.0	εH 6.84, OMe 3.74 d, *J* = 9.0, s
Oxz[2]		4.10 d, *J* = 3.6	4.73 qd, *J* = 6.0, 3.6	1.19 d, *J* = 6.0		
D-Val[3or7]	7.11 d, *J* = 10.2	5.15 dd, *J* = 10.2, 4.8	2.37 m	γCH$_3$ 1.11, γ'CH$_3$ 1.10 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.55 s
Ile[5]	7.60 d, *J* = 7.8	4.63 dd, *J* = 10.2, 7.8	2.30 m	γCH$_2$ 1.59, 1.32 γCH$_3$ 1.01 m, m d, *J* = 6.6	0.87 t, *J* = 7.2	
Oxz[6]		4.34 d, *J* = 4.2	4.92 qd, *J* = 6.6, 4.2	1.42 d, *J* = 6.6		
D-Va[3or7]	7.15 d, *J* = 10.2	5.14 dd, *J* = 10.2, 4.8	2.36 m	γCH$_3$ 1.10, γ'CH$_3$ 1.07 d, *J* = 7.2, d, *J* = 7.2		
Thz[4or8]						7.60 s

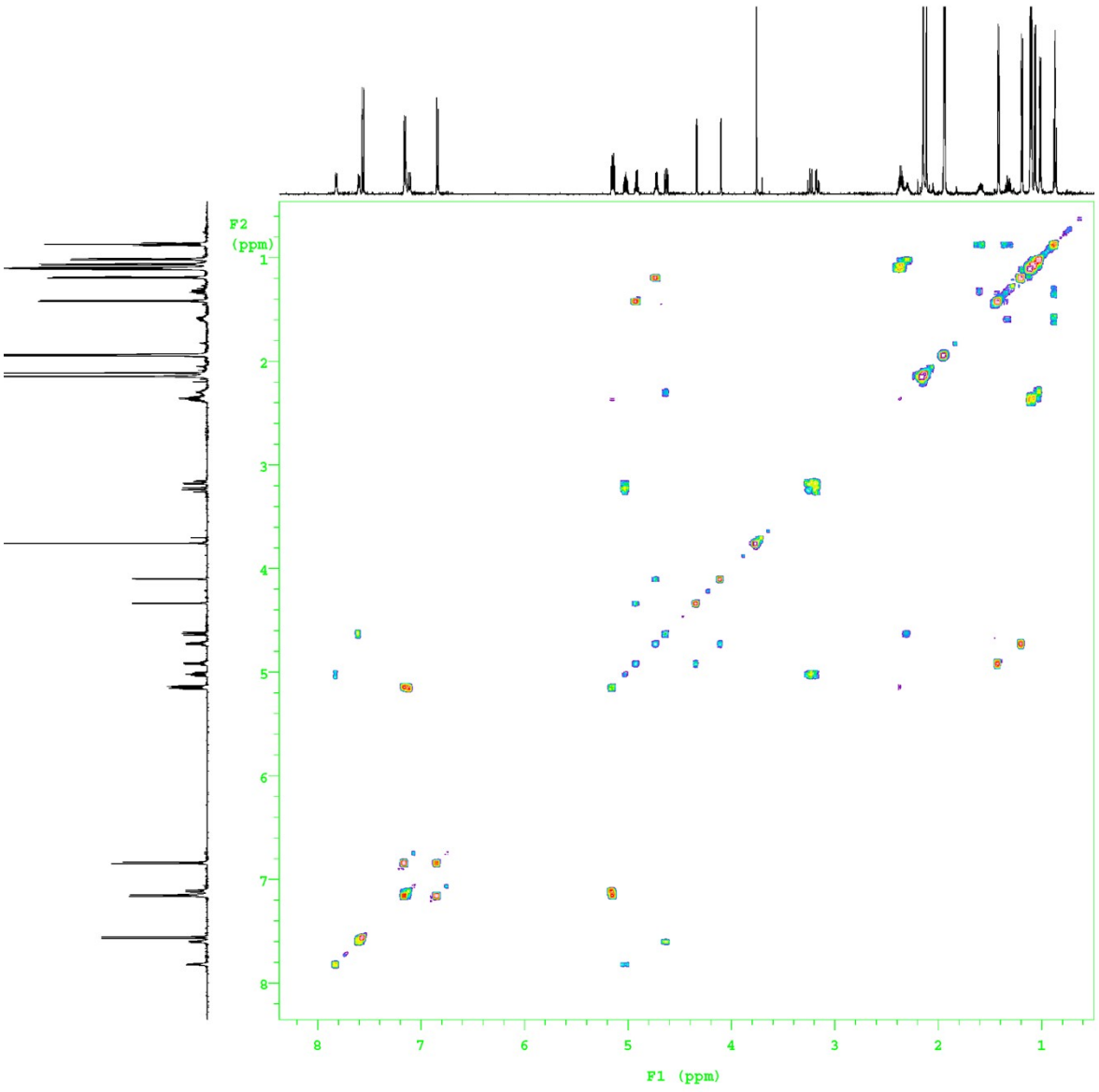


Fig. S2 2D ^{1}H-^{1}H COSY spectrum of peptide **1** in CD_3CN at 298 K.

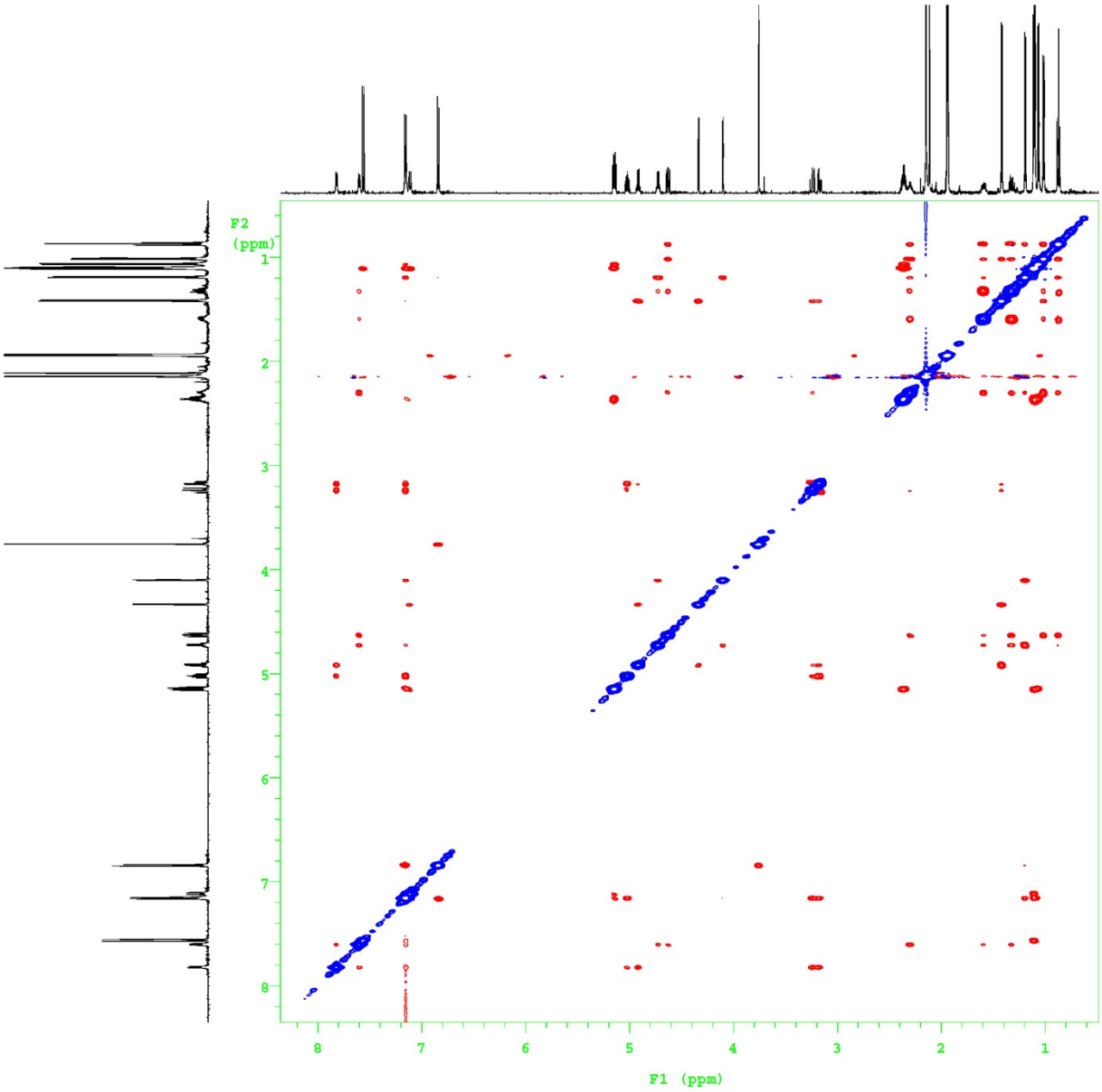


Fig. S3 2D ^{1}H-^{1}H ROESY spectrum of peptide **1** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 2

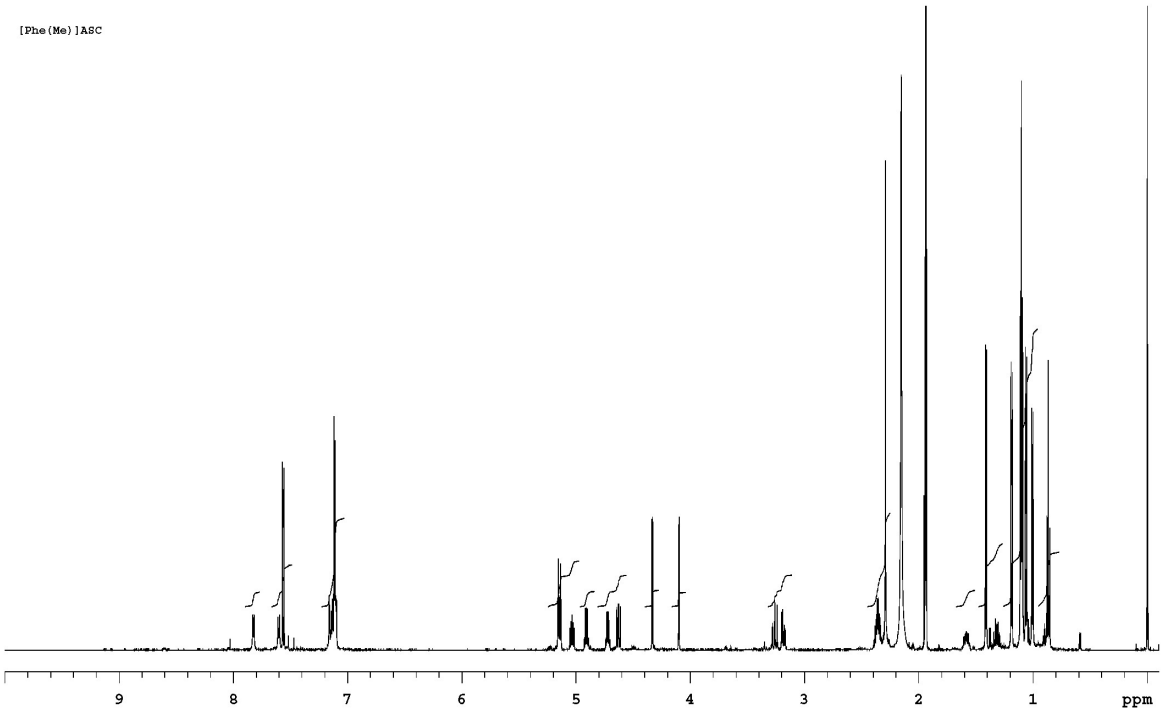


Fig. S4 1D ^{1}H NMR spectrum of peptide **2** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(Me)[1]	7.83 d, *J* = 6.6	5.04 ddd, *J* = 11.4, 6.6, 5.4	γCH$_2$ 3.26, 3.19 dd, *J* = 13.2, 11.4, dd, *J* = 13.2, 5.4		7.13 d, *J* = 8.4	εH7.10, Me 2.29 d, *J* =7.8, s
Oxz[2]		4.10 d, *J* = 3.6	4.72 qd, *J* = 6.0, 3.6	1.19 d, *J* = 6.6		
D-Val[3]	7.15 d, *J* = 10.2	5.14 dd, *J* = 10.2, 3.6	2.33 sept. d, *J* = 6.6, 3.6	γCH$_3$ 1.10, γ'CH$_3$ 1.06 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.56 s
Ile[5]	7.60 d, *J* = 7.8	4.63 dd, *J* = 10.2, 7.8	2.28 m	γCH$_2$ 1.59, 1.38 γCH$_3$ 1.01 m, m d, *J* = 7.2	0.87 t, *J* = 7.2	
Oxz[6]		4.33 d, *J* = 4.2	4.91 qd, *J* = 6.6, 3.6	1.41 d, *J* = 6.6		
D-Va[7]	7.10 d, *J* = 10.2	5.15 dd, *J* = 10.2, 3.6	2.36 sept. d, *J* = 6.6, 3.6	γCH$_3$ 1.11, γ'CH$_3$ 1.10 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.57 s

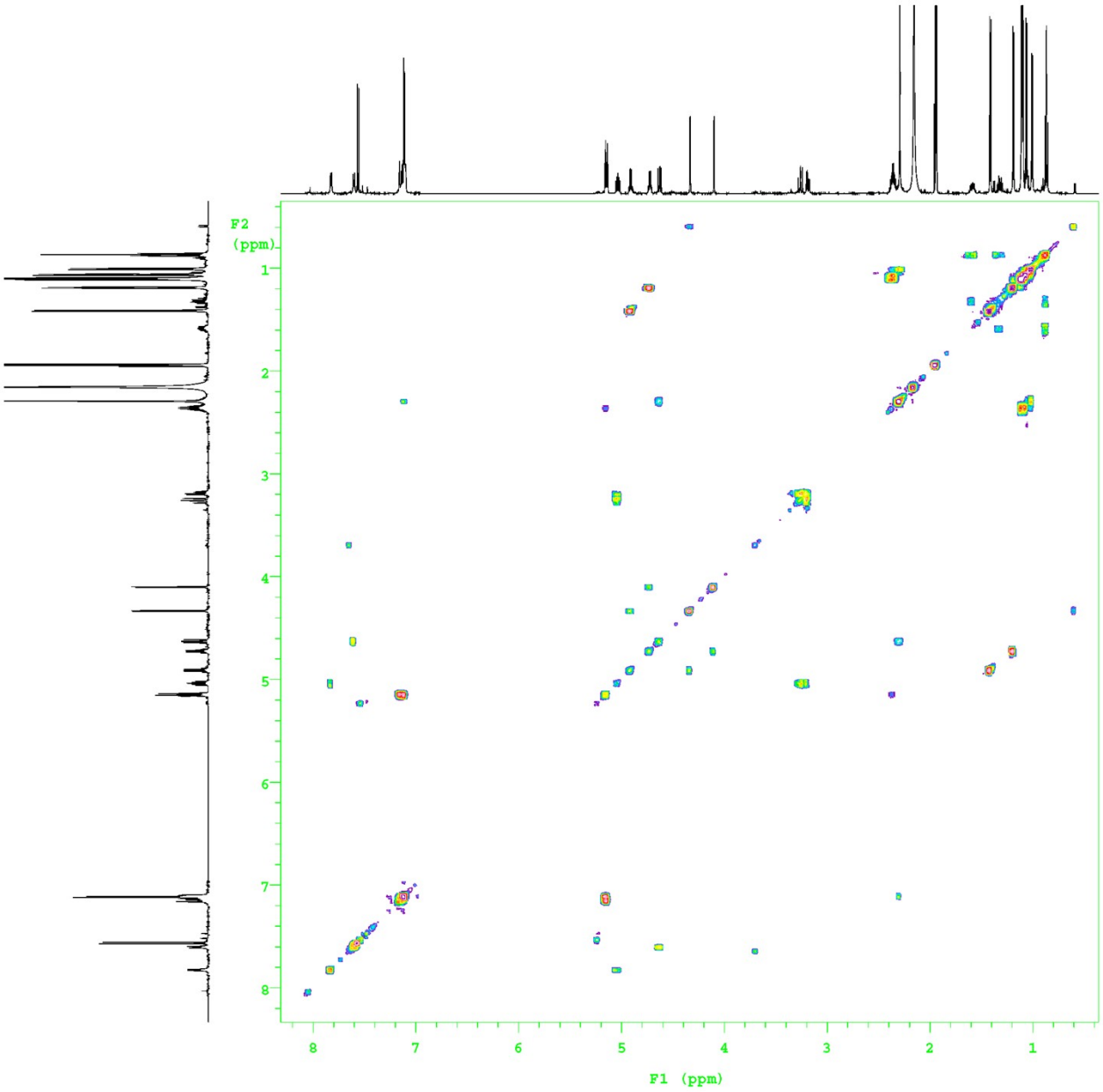


Fig. S5 2D ^{1}H-^{1}H COSY spectrum of peptide **2** in CD_3CN at 298 K.

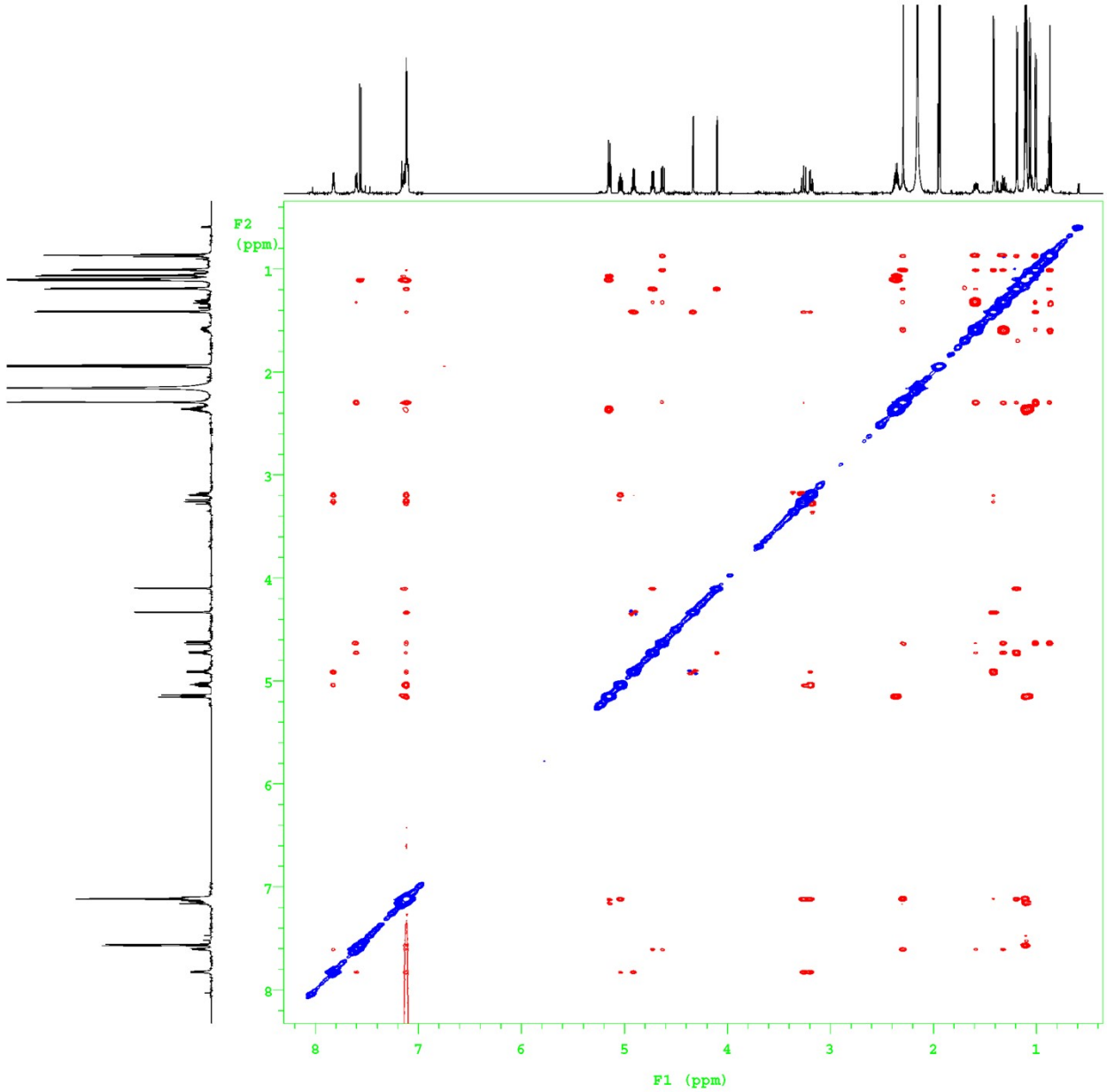


Fig. S6 2D ^{1}H-^{1}H ROESY spectrum of peptide **2** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 3

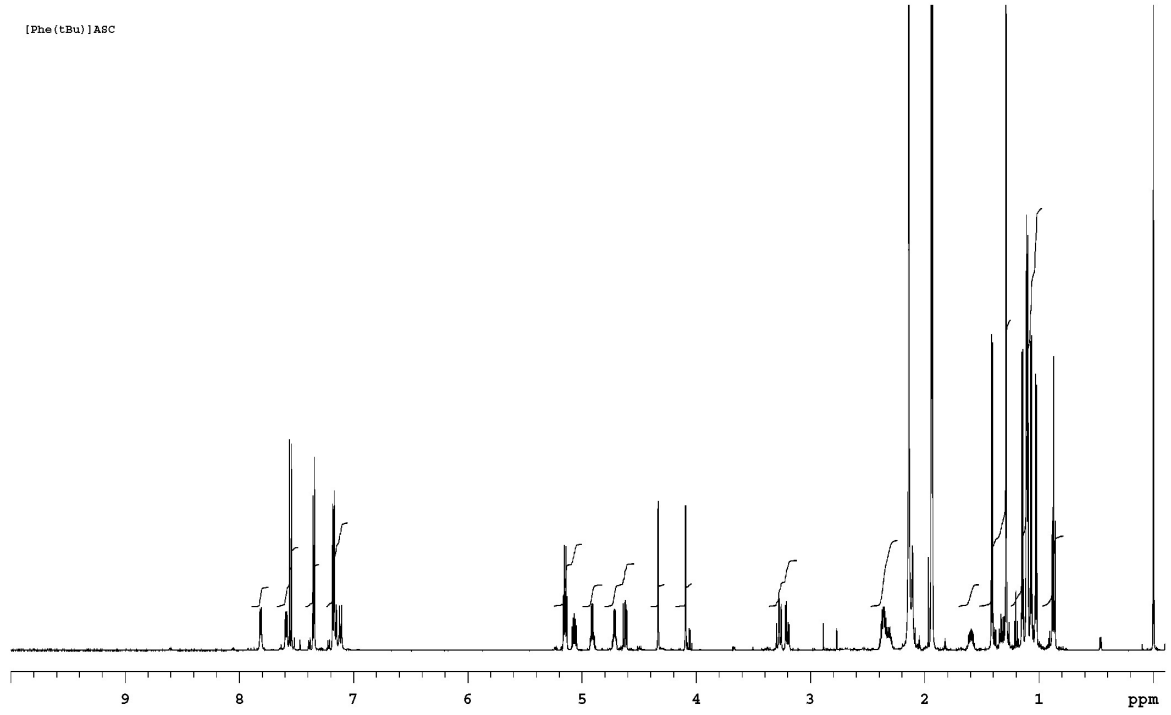


Fig. S7 1D ^{1}H NMR spectrum of peptide **3** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(tBu)[1]	7.81 d, *J* = 6.6	5.07 ddd, *J* = 11.4, 6.6, 5.4	γCH$_2$ 3.28, 3.20 dd, *J* = 13.2, 11.4, dd, *J* = 13.2, 5.4		7.18 d, *J* = 8.4	εH 7.35, tBu 1.29 d, *J* = 8.4, s
Oxz[2]		4.10 d, *J* = 3.6	4.72 qd, *J* = 6.0, 3.6	1.15 d, *J* = 6.0		
D-Val[3]	7.16 d, *J* = 10.2	5.14 dd, *J* = 10.2, 6.6	2.36 m	γCH$_3$ 1.11, γ'CH$_3$ 1.07 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.55 s
Ile[5]	7.59 d, *J* = 7.8	4.63 dd, *J* = 10.8, 7.8	2.32 m	γCH$_2$ 1.45, 1.31 γCH$_3$ 1.03 m, m d, *J* = 7.2	0.87 t, *J* = 7.8	
Oxz[6]		4.34 d, *J* = 4.2	4.91 qd, *J* = 6.6, 4.2	1.41 d, *J* = 6.6		
D-Va[7]	7.11 d, *J* = 10.2	5.15 dd, *J* = 10.2, 6.6	2.36 m	γCH$_3$ 1.11, γ'CH$_3$ 1.10 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.56 s

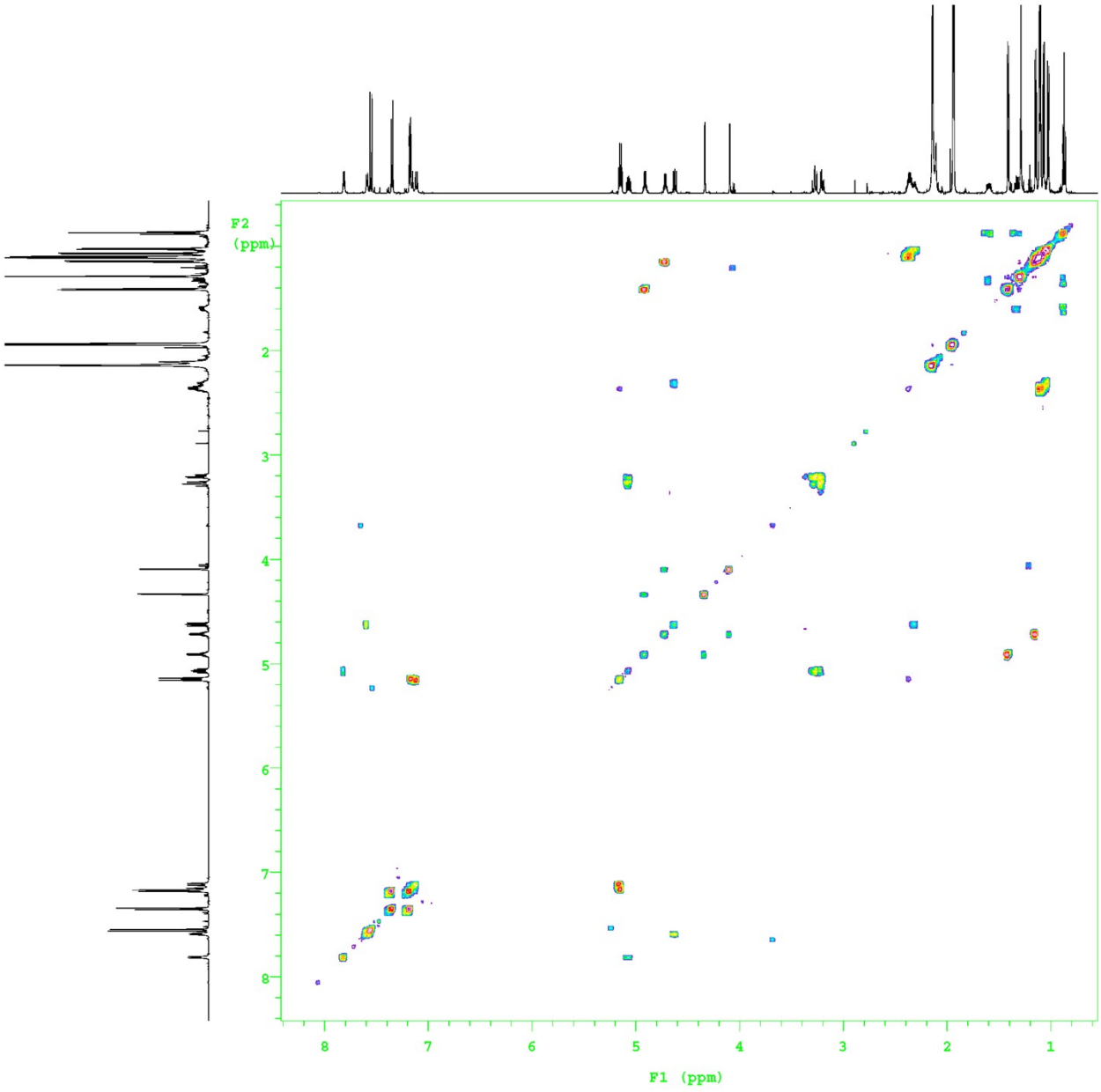


Fig. S8 2D ^{1}H-^{1}H COSY spectrum of peptide **3** in CD_3CN at 298 K.

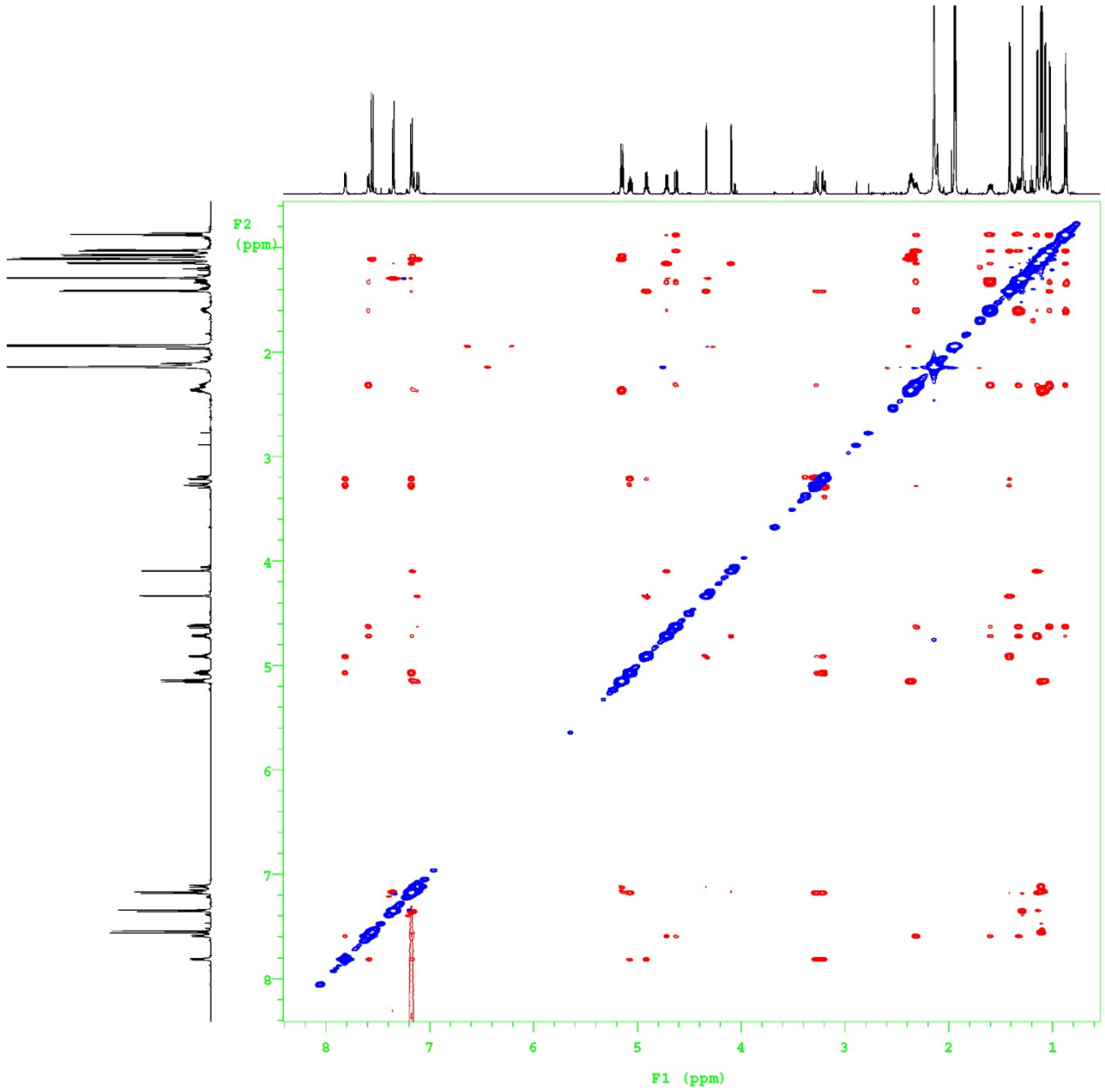


Fig. S9 2D ^{1}H-^{1}H ROESY spectrum of peptide **3** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 6

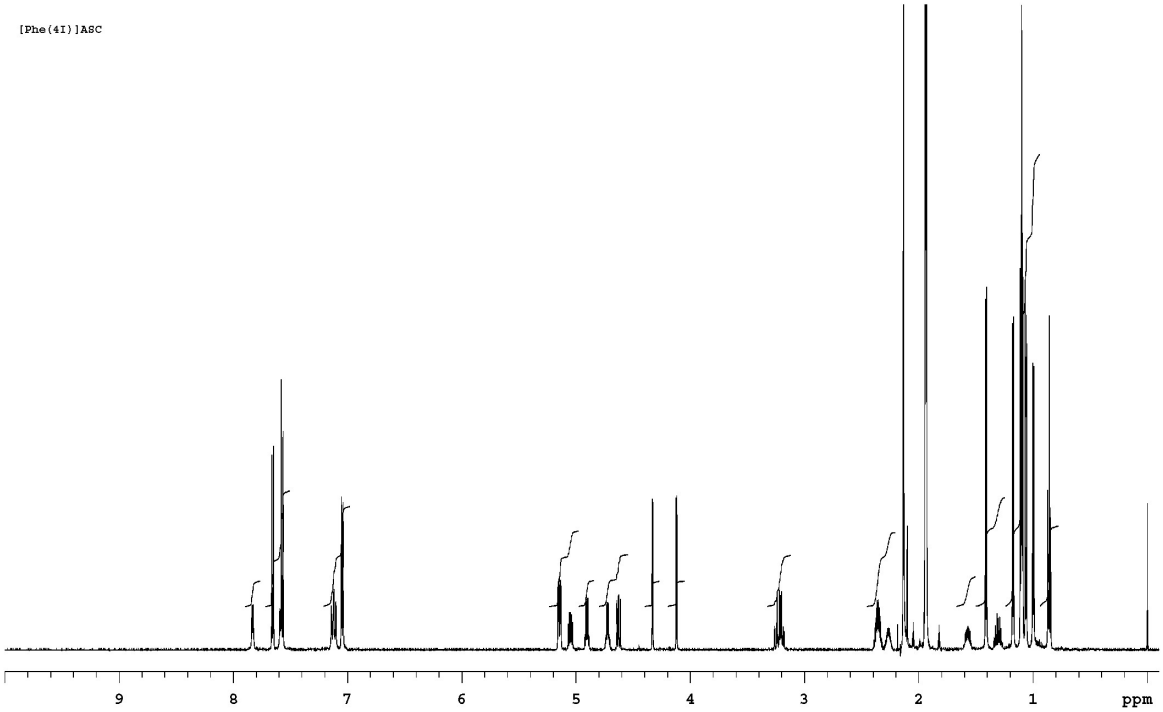


Fig. S10 1D ^{1}H NMR spectrum of peptide **6** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(4I)[1]	7.83 d, *J* = 7.2	5.05 ddd, *J* = 11.4, 7.2, 6.6	γCH$_2$ 3.24, 3.20 dd, *J* = 13.5, 11.4, dd, *J* = 13.5, 6.6		7.05 d, *J* = 8.4	εH 7.66 d, *J* = 8.4
Oxz[2]		4.12 d, *J* = 3.6	4.73 qd, *J* = 6.6, 3.6	1.18 d, *J* = 6.6		
D-Val[3]	7.13 d, *J* = 10.8	5.14 dd, *J* = 10.8, 4.2	2.35 hept. d, *J* = 6.6, 4.2	γCH$_3$ 1.10, γ'CH$_3$ 1.06 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.57 s
Ile[5]	7.59 d, *J* = 7.2	4.63 dd, *J* = 10.2, 7.2	2.27 m	γCH$_2$ 1.58, 1.31 m, m γCH$_3$ 1.00 d, *J* = 7.2	0.86 t, *J* = 7.8	
Oxz[6]		4.33 d, *J* = 3.6	4.91 qd, *J* = 6.6, 3.6	1.41 d, *J* = 6.6		
D-Va[7]	7.11 d, *J* = 10.8	5.15 dd, *J* = 10.8, 4.2	2.37 hept. d, *J* = 6.6, 4.2	γCH$_3$ 1.11, γ'CH$_3$ 1.10 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.58 s

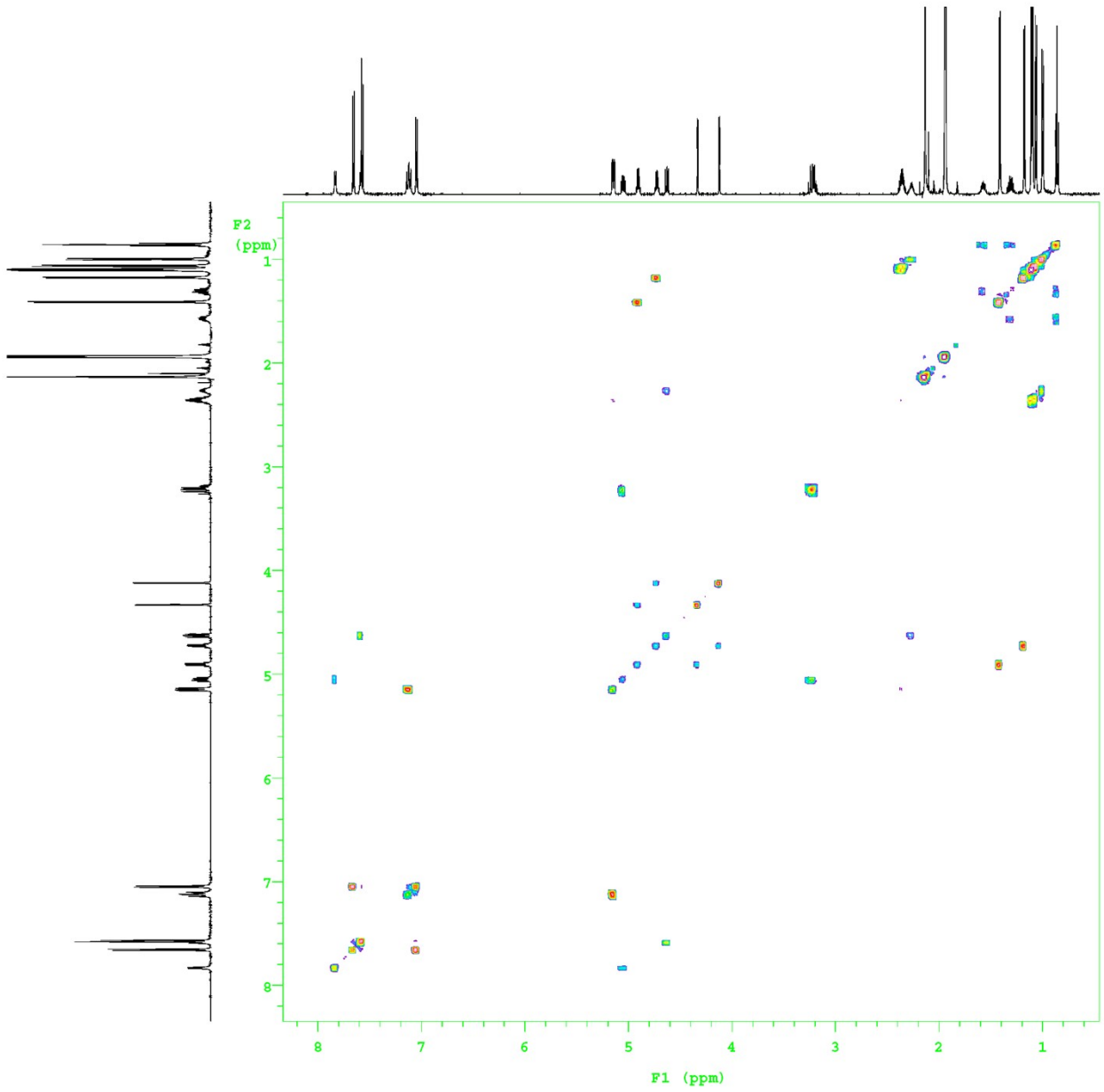


Fig. S11 2D ^{1}H-^{1}H COSY spectrum of peptide **6** in CD_3CN at 298 K.

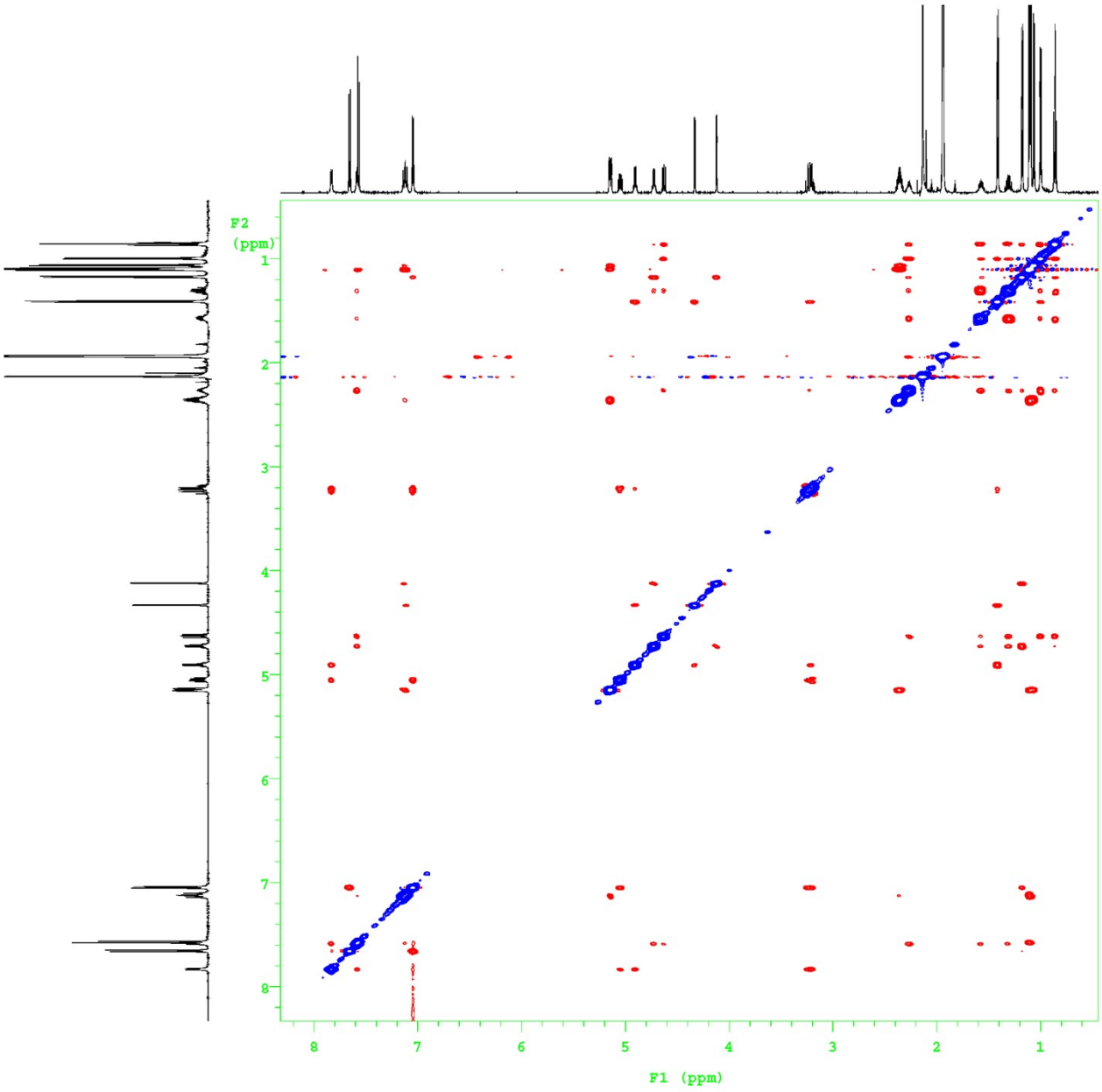


Fig. S12 2D ^{1}H-^{1}H ROESY spectrum of peptide **6** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 7

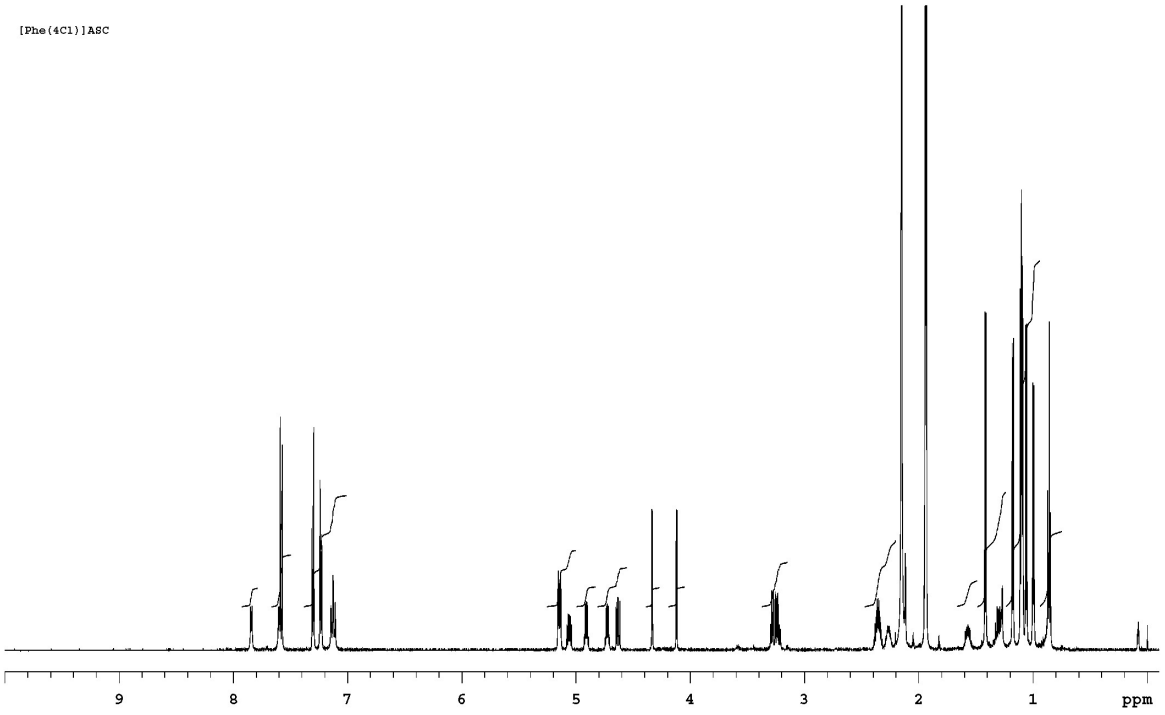


Fig. S13 1D ^{1}H NMR spectrum of peptide **7** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(4Cl)[1]	7.84 d, *J* = 6.6	5.06 ddd, *J* = 10.8, 6.6, 6.0	γCH$_2$ 3.28, 3.23 dd, *J* = 13.2, 10.8, dd, *J* = 13.2, 6.0		7.24 d, *J* = 8.4	εH 7.30 d, *J* = 8.4
Oxz[2]		4.12 d, *J* = 3.6	4.73 qd, *J* = 6.6, 3.6	1.18 d, *J* = 6.6		
D-Val[3]	7.14 d, *J* = 10.2	5.14 dd, *J* = 10.2, 4.2	2.35 hept. d, *J* = 6.6, 4.2	γCH$_3$ 1.10, γ'CH$_3$ 1.06 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.57 s
Ile[5]	7.60 d, *J* = 9.6	4.63 dd, *J* = 9.6, 7.8	2.27 m	γCH$_2$ 1.57, 1.31 γCH$_3$ 1.00 m, m d, *J* = 7.2	0.86 t, *J* = 7.8	
Oxz[6]		4.34 d, *J* = 3.6	4.91 qd, *J* = 6.0, 3.6	1.42 d, *J* = 6.0		
D-Va[7]	7.12 d, *J* = 10.2	5.15 dd, *J* = 10.2, 4.2	2.37 hept. d, *J* = 6.6, 4.2	γCH$_3$ 1.11, γ'CH$_3$ 1.09 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.59 s

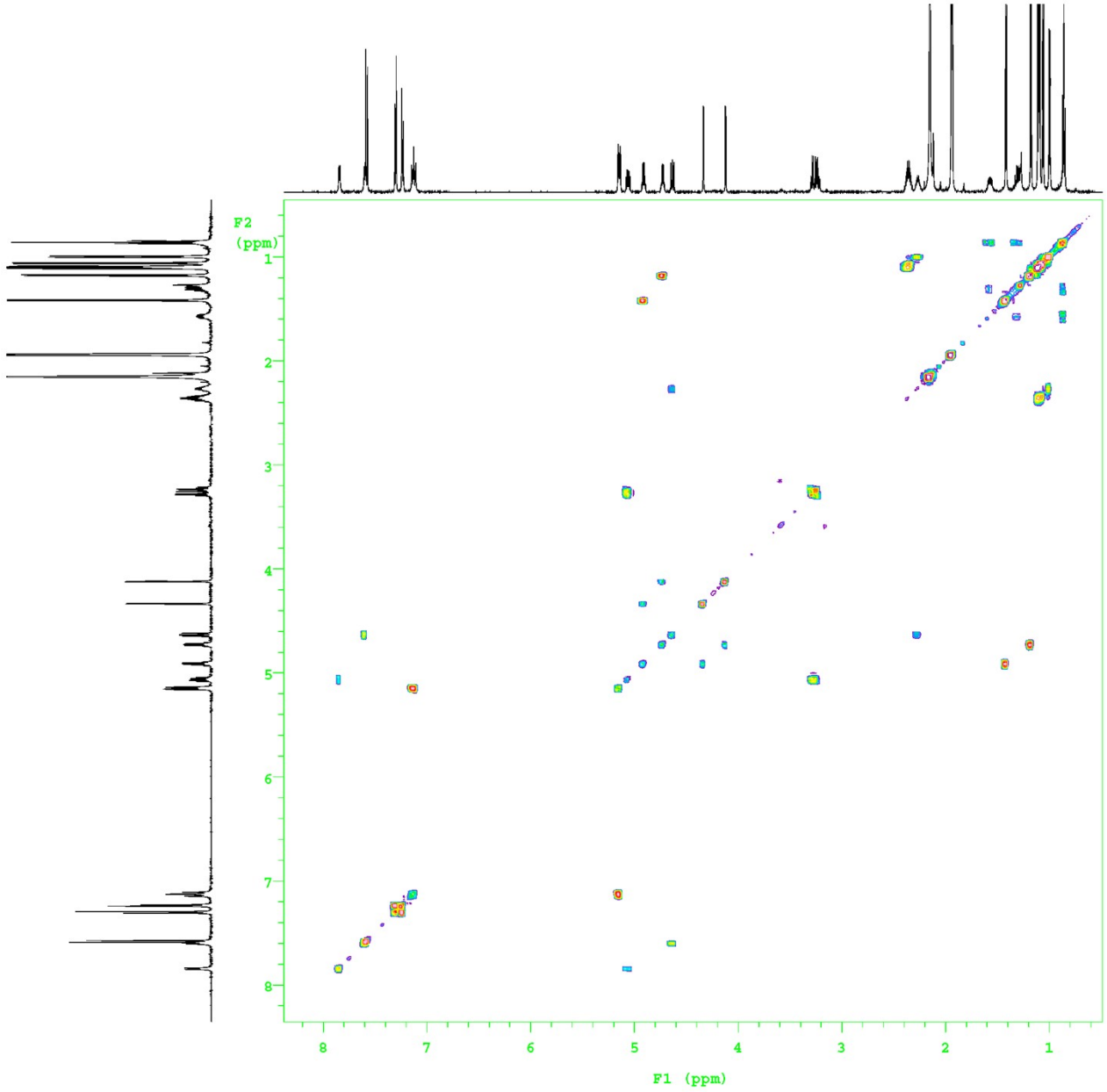


Fig. S14 2D ^{1}H-^{1}H COSY spectrum of peptide **7** in CD_3CN at 298 K.

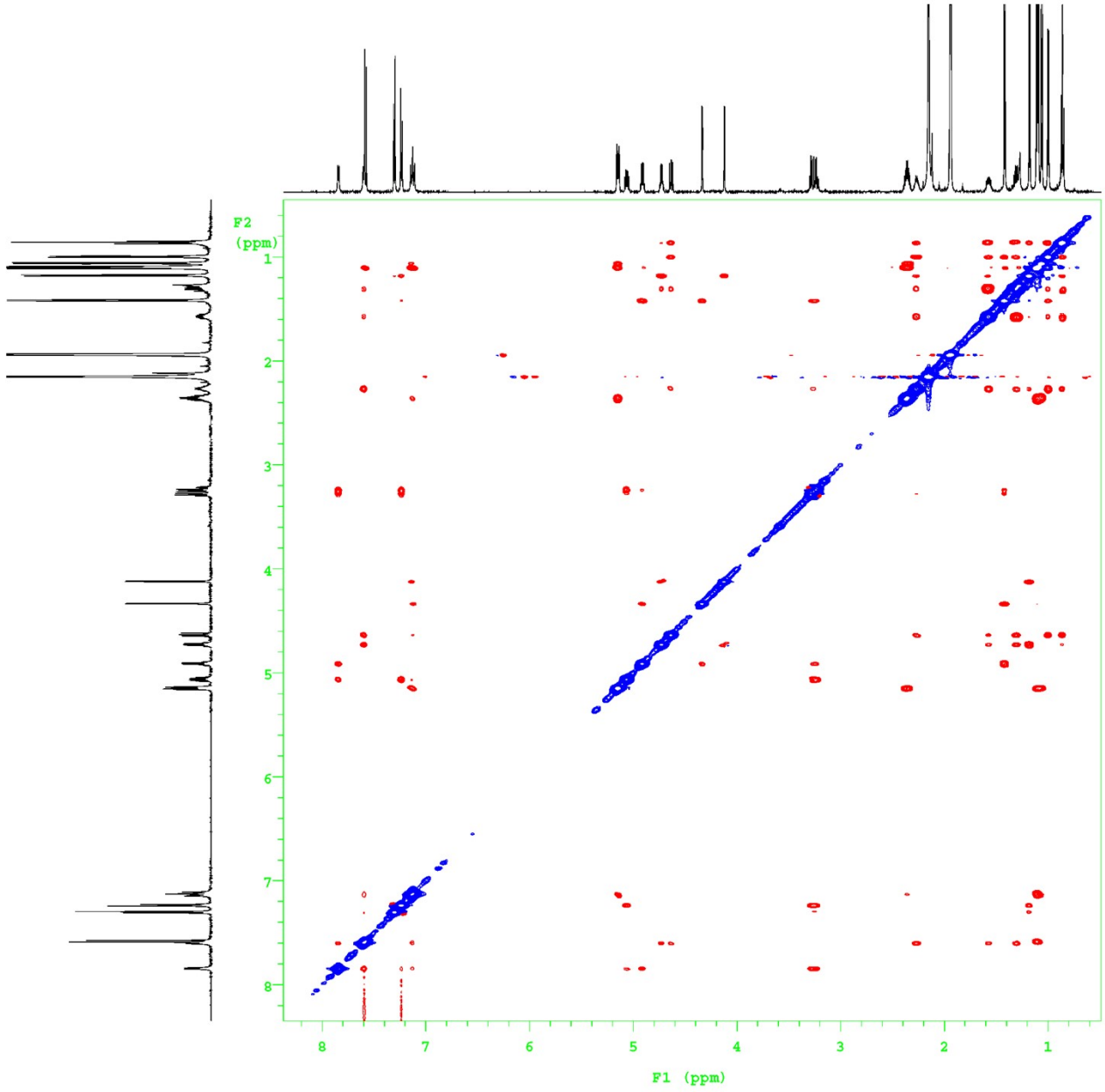


Fig. S15 2D ^{1}H-^{1}H ROESY spectrum of peptide **7** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 8

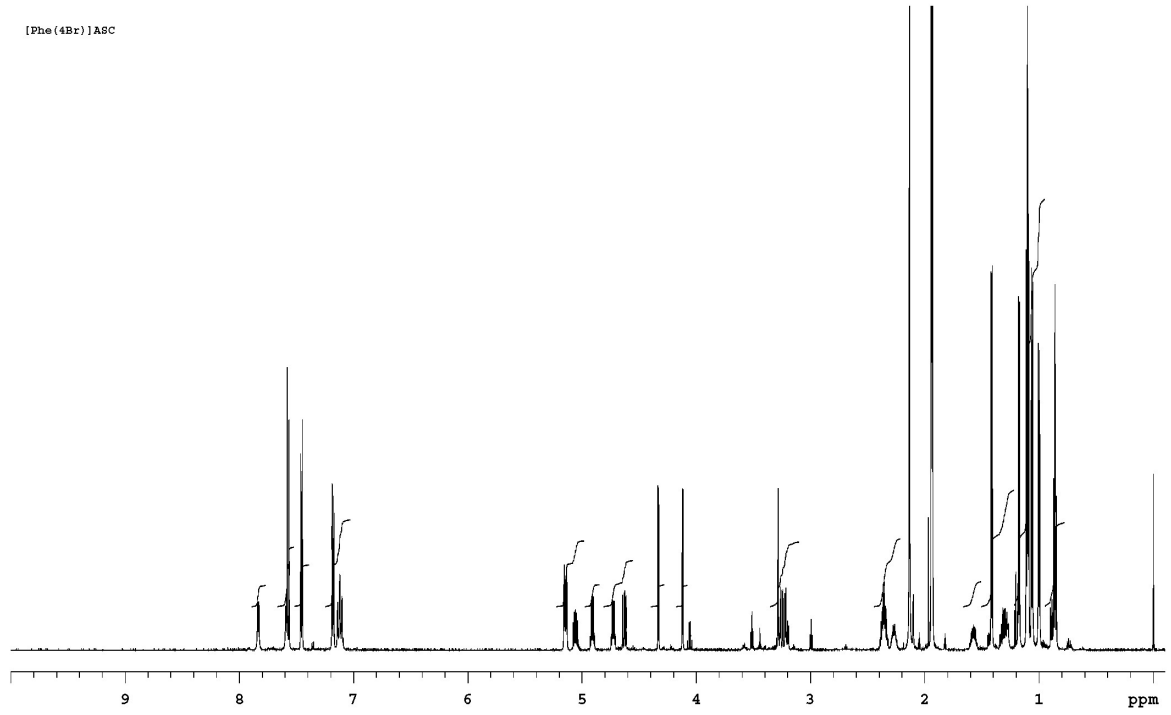


Fig. S16 1D ^{1}H NMR spectrum of peptide **8** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(4Br)[1]	7.84 d, *J* = 7.2	5.06 ddd, *J* = 11.4, 7.2, 5.4	γCH$_2$ 3.21, 3.26 dd, *J* = 13.2, 11.4, dd, *J* = 13.2, 5.4		7.18 d, *J* = 8.4	εH 7.46 d, *J* = 8.4
Oxz[2]		4.12 d, *J* = 3.6	4.73 qd, *J* = 6.0, 3.6	1.18 d, *J* = 6.0		
D-Val[3]	7.13 d, *J* = 10.2	5.14 dd, *J* = 10.2, 3.6	2.35 hept. d, *J* = 6.6, 3.6	γCH$_3$ 1.10, γ'CH$_3$ 1.06 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.57 s
Ile[5]	7.59 d, *J* = 7.2	4.63 dd, *J* = 10.2, 7.2	2.27 m	γCH$_2$ 1.58, 1.31 m, m γCH$_3$ 1.00 d, *J* = 7.2	0.86 t, *J* = 7.8	
Oxz[6]		4.33 d, *J* = 3.6	4.91 qd, *J* = 6.0, 3.6	1.42 d, *J* = 6.0		
D-Va[7]	7.11 d, *J* = 10.2	5.15 dd, *J* = 10.2, 3.6	2.37 hept. d, *J* = 7.2, 3.6	γCH$_3$ 1.11, γ'CH$_3$ 1.10 d, *J* = 7.2, d, *J* = 7.2		
Thz[4or8]						7.58 s

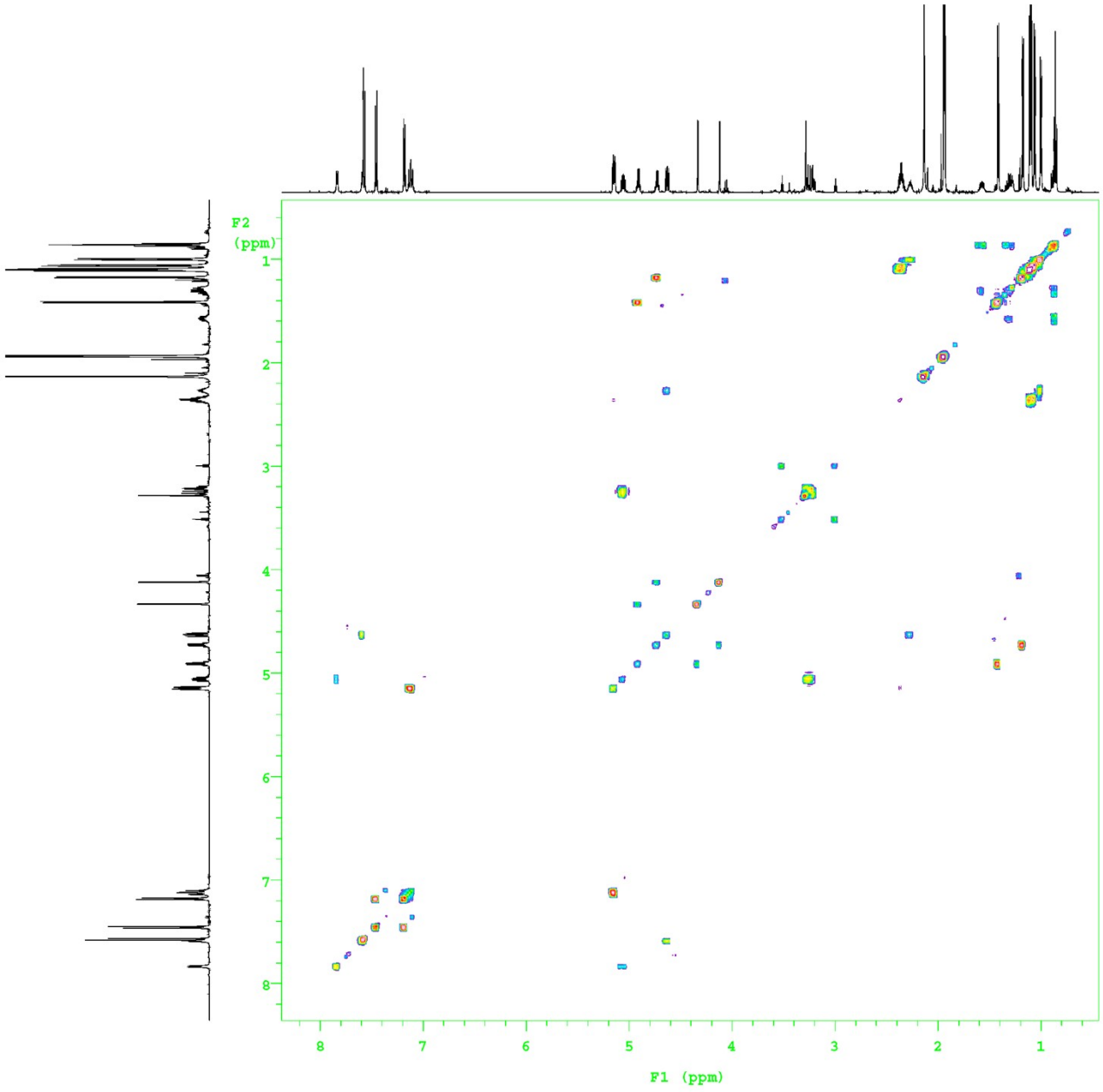


Fig. S17 2D ^{1}H-^{1}H COSY spectrum of peptide **8** in CD_3CN at 298 K.

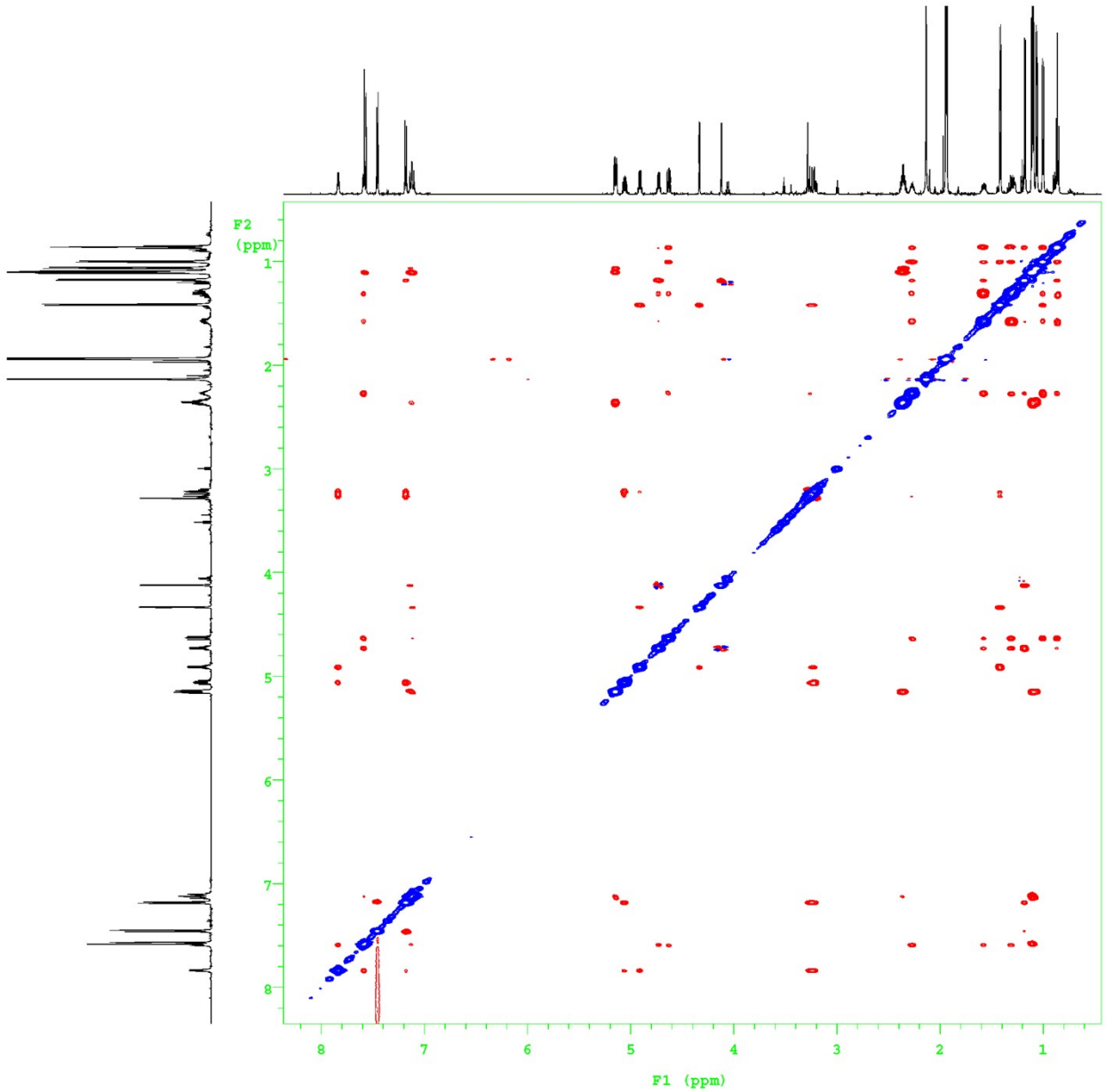


Fig. S18 2D ^{1}H-^{1}H ROESY spectrum of peptide **8** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 9

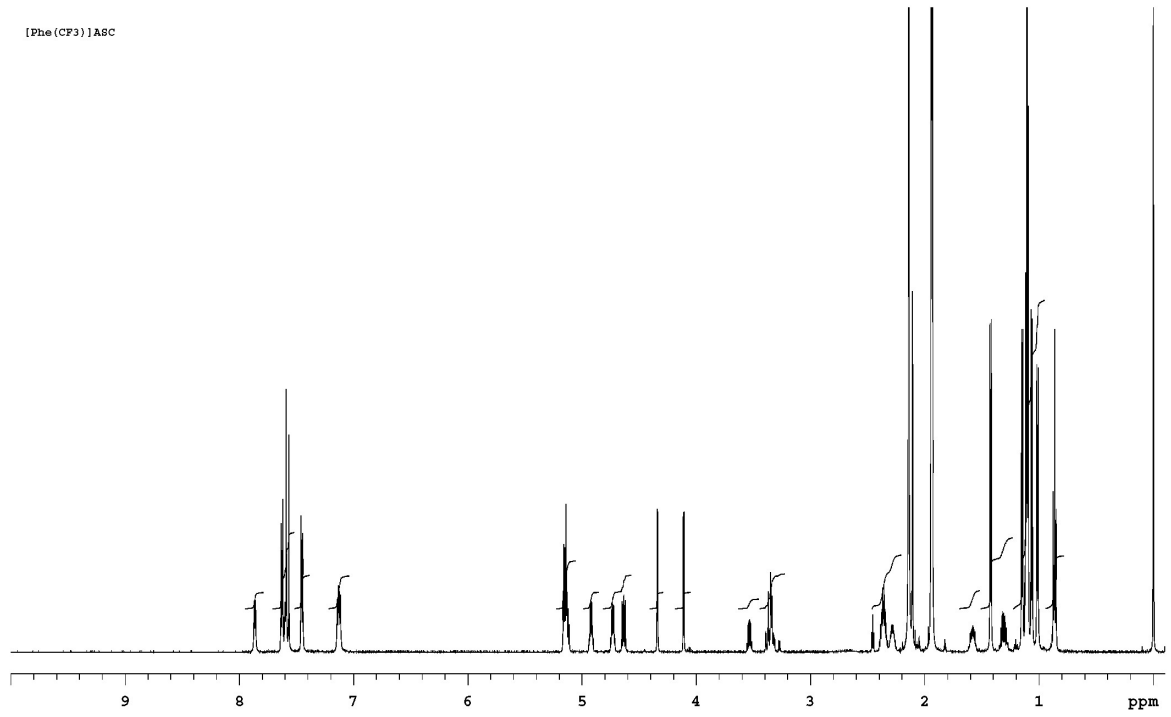


Fig. S19 1D ^{1}H NMR spectrum of peptide **9** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(CF3)[1]	7.87 d, *J* = 6.6	5.13 dt, *J* = 10.8, 6.6	γCH$_2$ 3.37, 3.33 dd, *J* = 13.2, 10.8, dd, *J* = 13.2, 6.6		7.45 d, *J* = 8.4	εH 7.63 d, *J* = 8.4
Oxz[2]		4.11 d, *J* = 3.6	4.73 qd, *J* = 6.0, 3.6	1.15 d, *J* = 6.0		
D-Val[3]	7.14 d, *J* = 10.2	5.15 dd, *J* = 10.2, 4.8	2.36 m	γCH$_3$ 1.11, γ'CH$_3$ 1.07 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.57 s
Ile[5]	7.60 d, *J* = 7.8	4.64 dd, *J* = 10.8, 7.8	2.29 m	γCH$_2$ 1.58, 1.31 m, m γCH$_3$ 1.01 d, *J* = 6.6	0.86 t, *J* = 7.8	
Oxz[6]		4.34 d, *J* = 4.2	4.92 qd, *J* = 6.0, 4.2	1.43 d, *J* = 6.0		
D-Va[7]	7.12 d, *J* = 10.2	5.16 dd, *J* = 10.2, 4.8	2.37 m	γCH$_3$ 1.11, γ'CH$_3$ 1.10 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.59 s

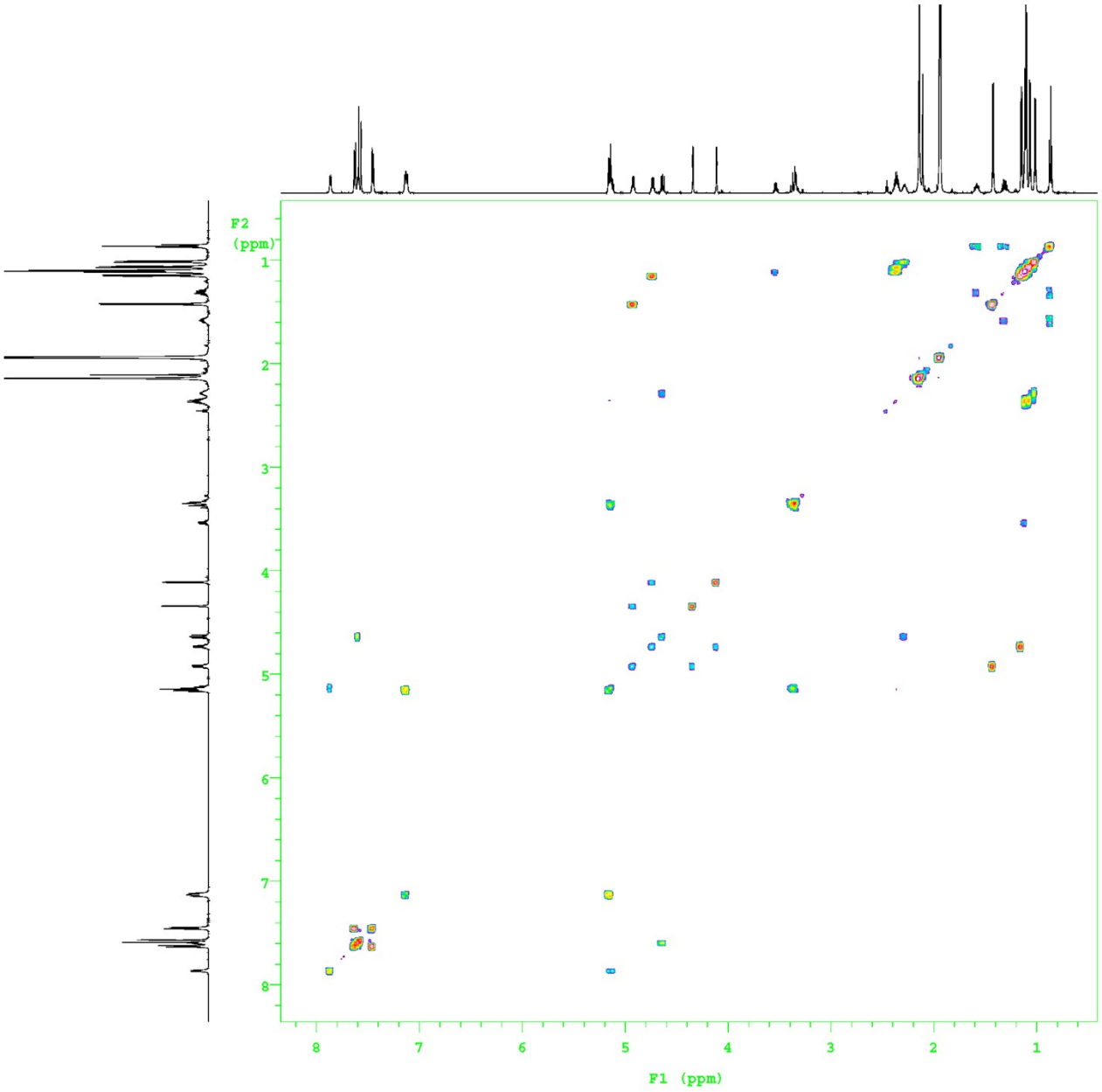


Fig. S20 2D ^{1}H-^{1}H COSY spectrum of peptide **9** in CD_3CN at 298 K.

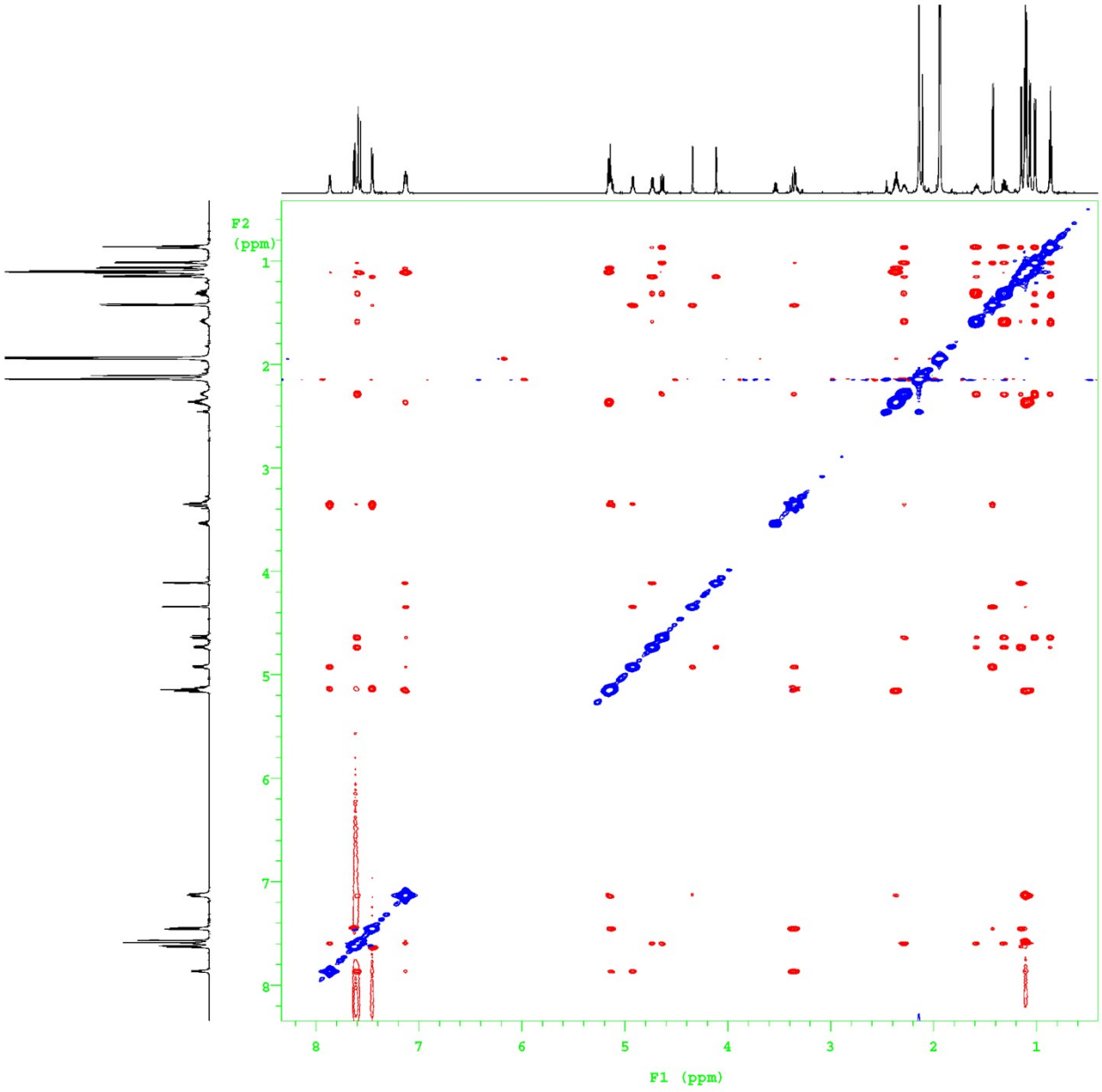


Fig. S21 2D ^{1}H-^{1}H ROESY spectrum of peptide **9** in CD_3CN at 298 K.

^{1}H NMR spectra of peptides 10

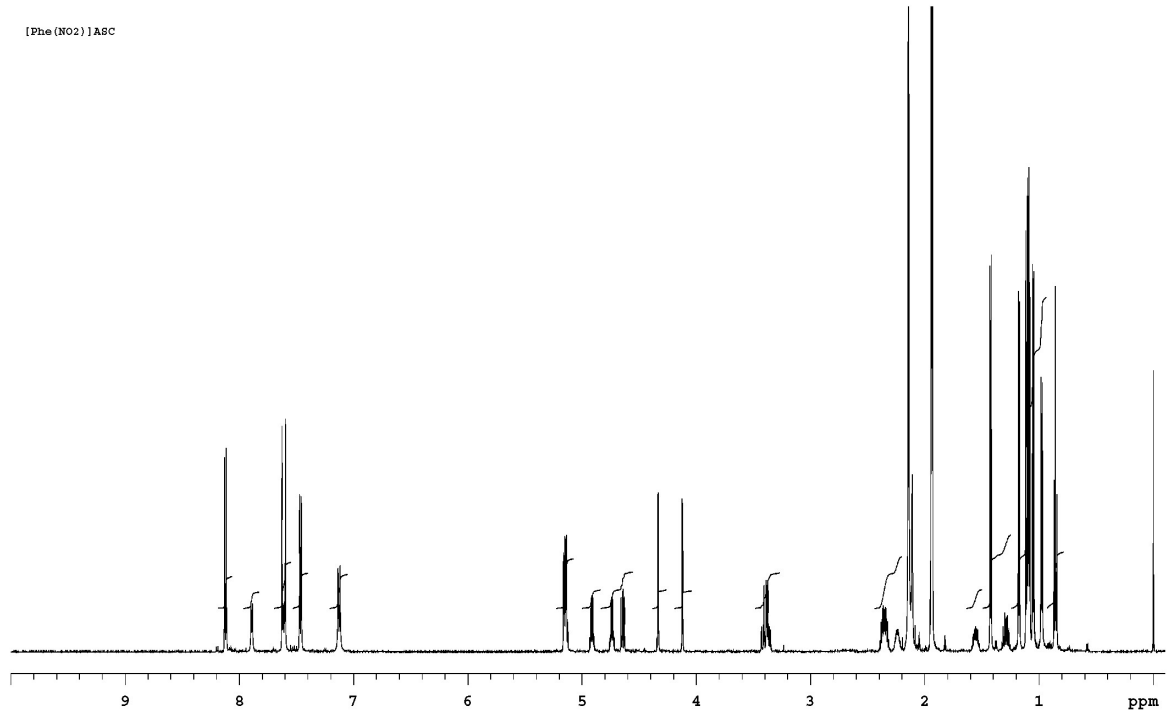


Fig. S22 1D ^{1}H NMR spectrum of peptide **10** in CD_3CN at 298 K.

Residue	δ HN (ppm) ^3J (Hz)	δ Hα (ppm) ^3J (Hz)	δ Hβ (ppm) ^3J (Hz)	δ Hγ (ppm) ^3J (Hz)	δ Hδ (ppm) ^3J (Hz)	δ Other protons (ppm) ^3J (Hz)
Phe(NO2)[1]	7.89 d, *J* = 6.6	5.15 m	γCH$_2$ 3.41, 3.37 dd, *J* = 13.5, 10.8, dd, *J* = 13.5, 6.6		7.47 d, *J* = 8.4	εH 8.12 d, *J* = 8.4
Oxz[2]		4.12 d, *J* = 3.6	4.74 qd, *J* = 6.0, 3.6	1.18 d, *J* = 6.0		
D-Val[3or7]	7.13 d, *J* = 10.2	5.15 dd, *J* = 10.2, 6.6	2.36 m	γCH$_3$ 1.11, γ'CH$_3$ 1.09 d, *J* = 7.2, d, *J* = 7.2		
Thz[4or8]						7.60 s
Ile[5]	7.61 d, *J* = 7.8	4.64 dd, *J* = 9.9, 7.8	2.24 m	γCH$_2$ 1.56, 1.29 γCH$_3$ 0.98 m, m d, *J* = 7.2	0.86 t, *J* = 7.8	
Oxz[6]		4.34 d, *J* = 4.2	4.92 qd, *J* = 6.6, 4.2	1.43 d, *J* = 6.6		
D-Va[3or7]	7.13 d, *J* = 10.2	5.15 dd, *J* = 10.2, 6.6	2.36 m	γCH$_3$ 1.10, γ'CH$_3$ 1.05 d, *J* = 6.6, d, *J* = 6.6		
Thz[4or8]						7.63 s

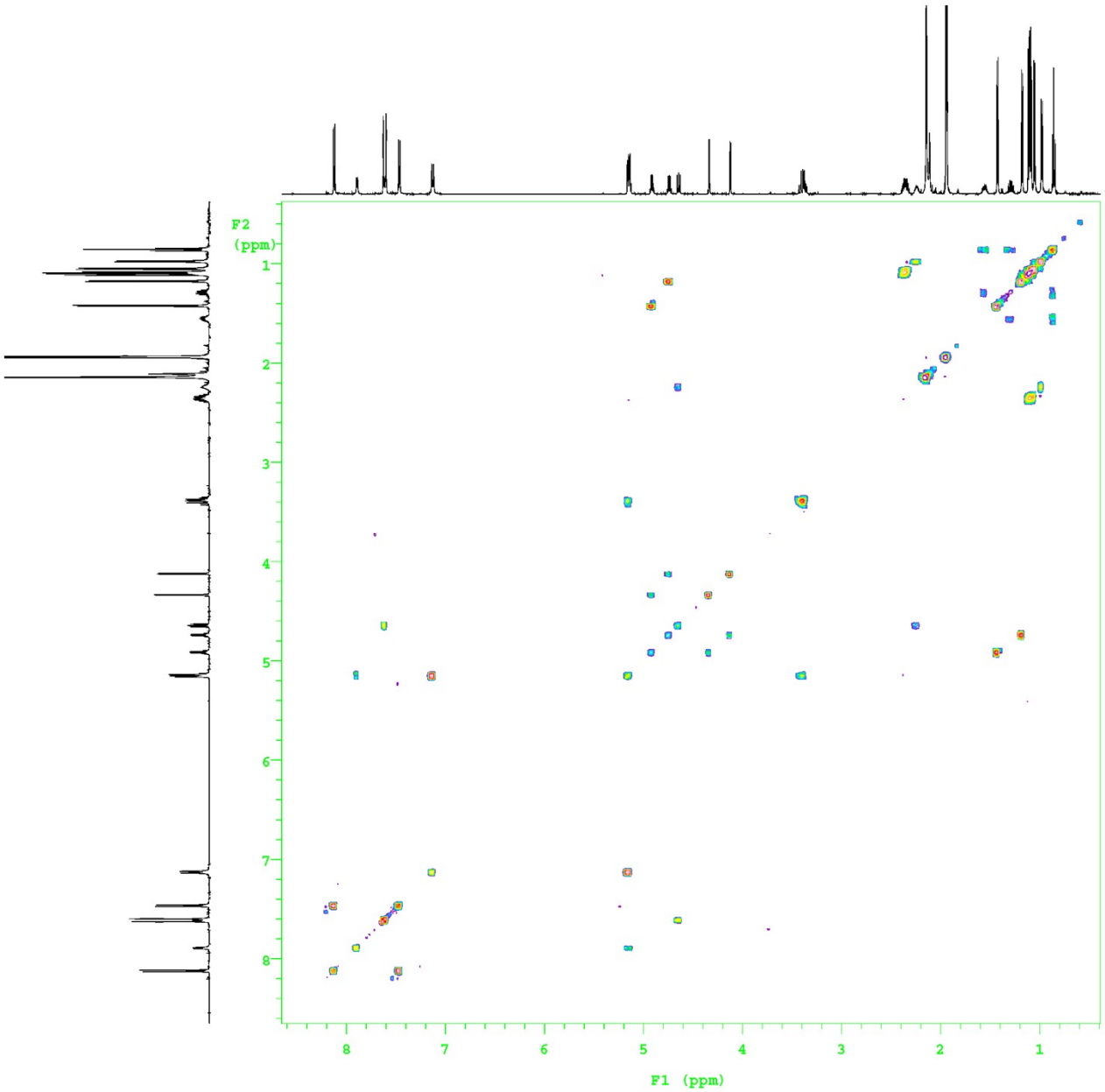


Fig. S23 2D ^{1}H-^{1}H COSY spectrum of peptide **10** in CD_3CN at 298 K.

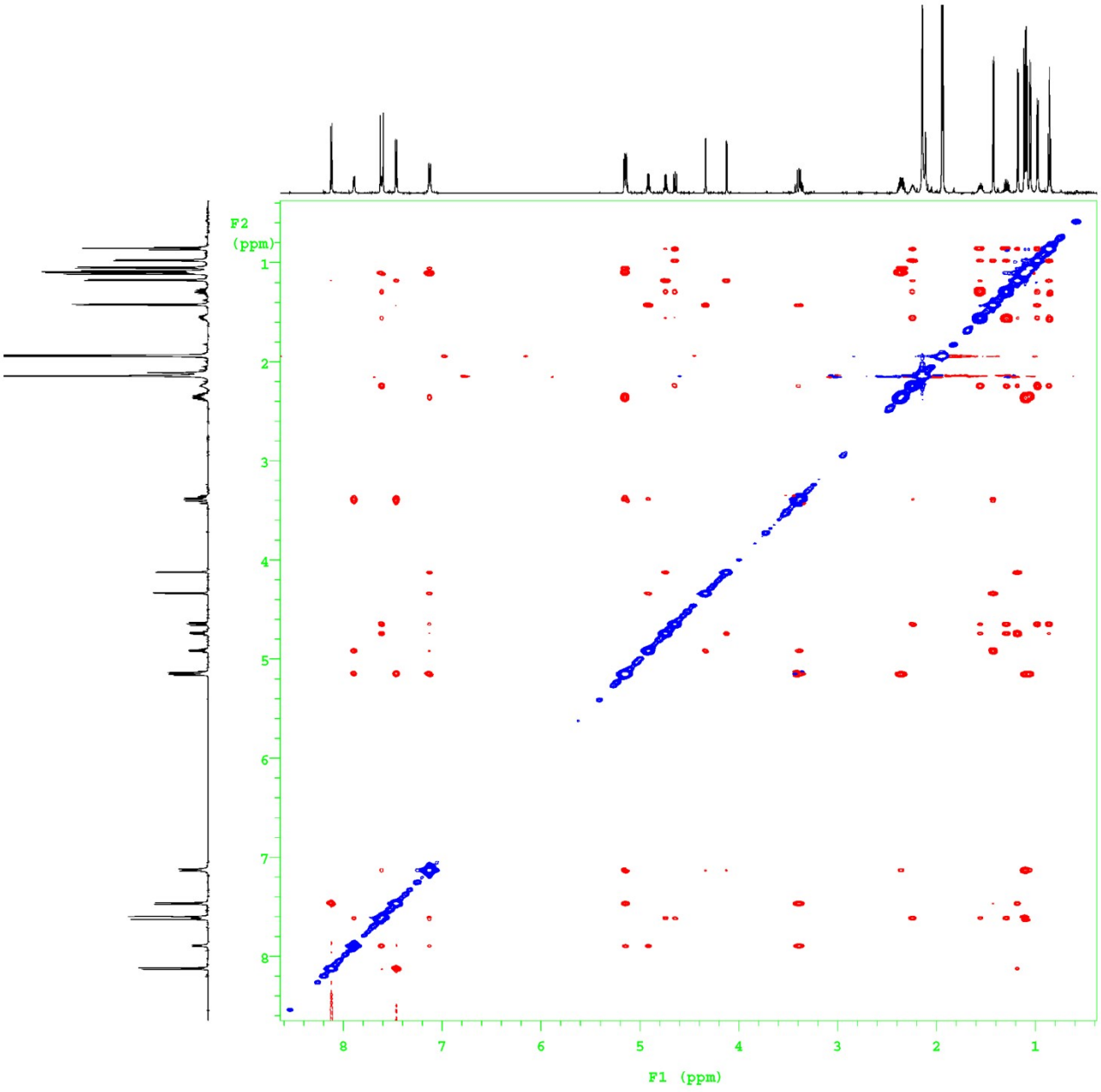


Fig. S24 2D ^{1}H-^{1}H ROESY spectrum of peptide **10** in CD_3CN at 298 K.

Table S2. Crystal and experimental data for **2**, **3** and **6**.

Peptide	**2**	**3**	**6**
Formula	$C_{40}H_{52}N_8O_6S_2$, C_2H_3N	$C_{43}H_{58}N_8O_6S_2$, C_2H_3N, H_2O	$2(C_{39}H_{48}IN_8O_6S_2)$, C_4H_9NO
Formula Weight	846.07	906.16	1919.88
Cell System	orthorhombic	triclinic	monoclinic
Space Group	$P2_12_12_1$	P1	$P2_1$
a, Å	15.6599(13)	9.38850(10)	13.7742(6)
b, Å	16.5029(14)	10.0778(2)	21.7130(16)
c, Å	17.2608(14)	13.0183(2)	15.1389(6)
α, deg	90.0	82.6590(10)	90.0
β, deg	90.0	86.0780(10)	91.337(4)
γ, deg	90.0	80.1310(10)	90.0
Volume, Å^3	4460.8(6)	1202.20(3)	4526.5(4)
Z	4	1	2
Dc, g cm^{-3}	1.260	1.252	1.409
F(000)	1800	484	1982
μ, mm^{-1}	0.175 (Mo Kα)	1.473 (Cu Kα)	6.876 (Cu Kα)
Wavelength, Å	0.71073	1.54184	1.54184
No. of reflections (obs)	36244	20933	26294
R_{INT}	0.0397	0.0307	0.0779
θ_{max}, deg	26.37	66.559	68.251
No. of reflections (I>2σ(I))	8537	7368	9911
Flack parameter	–0.02(9)	0.010(7)	0.000(10)
*R*1	0.0681	0.0462	0.1093
wR	0.1719	0.1315	0.2930
Goodness of fit	1.096	1.047	1.170
$(\Delta/\sigma)_{max}$	0.002	0.008	0.000
Fraction for θ_{max}	1.000	0.996	0.999
$\Delta\rho_{max}$, e Å^{-3}	0.532	0.860	4.104
$\Delta\rho_{min}$, e Å^{-3}	–0.177	–0.439	–2.411
CCDC Number	2289960	2289964	2289961

Table S3. Crystal and experimental data for **7**, **8** and **9**.

Peptide	**7**	**8**	**9**
Formula	$C_{39}H_{49}ClN_8O_6S_2$, $0.5(C_2H_3N)$	$2(C_{39}H_{49}BrN_8O_6S_2)$, C_2H_3N	$C_{40}H_{47}F_3N_8O_6S_2$, C_3H_6O
Formula Weight	845.96	1780.82	915.05
Cell System	monoclinic	monoclinic	triclinic
Space Group	$P2_1$	$P2_1$	P1
a, Å	15.6272(2)	15.64800(10)	9.4424(4)
b, Å	16.6962(2)	16.8169(2)	9.8919(4)
c, Å	16.1368(2)	16.1537(2)	12.9370(6)
α, deg	90.0	90.0	80.097(4)
β, deg	95.4400(10)	95.6830(10)	80.867(4)
γ, deg	90.0	90.0	84.776(4)
Volume, Å^3	4191.37(9)	4229.97(8)	1172.74(9)
Z	4	2	1
Dc, g cm^{-3}	1.341	1.398	1.296
F(000)	1788	1860	482
μ, mm^{-1}	2.205 (Cu Kα)	2.711 (Cu Kα)	1.607 (Cu Kα)
Wavelength, Å	1.54184	1.54184	1.54184
No. of reflections (obs)	46819	33721	17517
R_{INT}	0.0287	0.0838	0.0439
θ_{max}, deg	74.452	68.247	63.685
No. of reflections (I>2σ(I))	16132	12539	4779
Flack parameter	0.019(4)	–0.010(12)	0.023(15)
*R*1	0.0428	0.0719	0.1268
wR	0.1329	0.1901	0.3550
Goodness of fit	0.718	1.069	1.500
$(\Delta/\sigma)_{max}$	0.001	0.000	0.005
Fraction for θ_{max}	0.986	0.983	0.995
$\Delta\rho_{max}$, e Å^{-3}	0.769	1.929	0.749
$\Delta\rho_{min}$, e Å^{-3}	–0.354	–0.899	–0.429
CCDC Number	2289963	2289962	2289965

Table S4. Hydrogen bonds in the crystal structures of **2**, **3**, **6**, **7**, **8** and **9**.

	Donor	Acceptor	Distance (Å)	Angle (˚)
Peptide	D–H	A	D…A	D–H…A
2	N[Phe(CH_3)^1]–H	O$^\gamma$(Oxz^6)	3.371	155.5
	N(D-Val^3)–H	O(Thz^8)	3.180	139.8
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.229	159.3
	N(D-Val^7)–H	O(Thz^4)	3.225	133.8
3	W–H	N(Oxz^2)	2.994	150.7
	W–H	N(Oxz^6)	3.004	153.6
	N[Phe(C(CH_3)$_3$)^1]–H	W	2.981	146.8
	N(Ile^5)–H	W	2.964	146.9
6 (molecule A)	N[Phe(I)^1]–H	O$^\gamma$(Oxz^6)	3.056	153.9
	N(D-Val^3)–H	O(Thz^8)	3.077	147.0
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.196	124.1
	N(D-Val^7)–H	O(Thz^4)	3.491	155.4
6 (molecule B)	N[Phe(I)^1]–H	O$^\gamma$(Oxz^6)	3.089	152.7
	N(D-Val^3)–H	O(Thz^8)	3.099	145.6
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.321	155.0
	N(D-Val^7)–H	O(Thz^4)	3.201	129.0
7 (molecule A)	N[Phe(Cl)^1]–H	O$^\gamma$(Oxz^6)	3.200	159.6
	N(D-Val^3)–H	O(Thz^8)	3.067	140.9
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.325	161.0
	N(D-Val^7)–H	O(Thz^4)	3.149	131.1
7 (molecule B)	N[Phe(Cl)^1]–H	O$^\gamma$(Oxz^6)	3.225	157.1
	N(D-Val^3)–H	O(Thz^8)	3.160	148.3
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.241	158.1
	N(D-Val^7)–H	O(Thz^4)	3.165	135.6
8 (molecule A)	N[Phe(Br)^1]–H	O$^\gamma$(Oxz^6)	3.194	158.1
	N(D-Val^3)–H	O(Thz^8)	3.066	142.4
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.312	160.7
	N(D-Val^7)–H	O(Thz^4)	3.158	130.5
8 (molecule B)	N[Phe(Br)^1]–H	O$^\gamma$(Oxz^6)	3.280	155.3
	N(D-Val^3)–H	O(Thz^8)	3.154	149.6
	N(Ile^5)–H	O$^\gamma$(Oxz^2)	3.282	157.7
	N(D-Val^7)–H	O(Thz^4)	3.181	136.8
9	N[Phe(CF_3)^1]–H	O(Ac_2O)	3.122	153.0
	N(Ile^5)–H	O(Ac_2O)	3.054	162.6

A letter of W represents the oxygen atom of water.

The CH···π contacts within the folded forms of 2 and 4.

The distances between the γH atoms of Oxz^2 side chains to the π-orbital of $Phe(X)^1$ in folded forms were estimated by surveying the CH···π contacts for the six-membered π-system, as described by Umezawa *et al*. (Y. Umezawa *et al*., *Bull*. *Chem*. *Soc*. *Jpn*., 1998, **71**, 1207-1213) (Fig. S25). The distance between a C-H hydrogen atom and the π-plane, the distance between H and the line C^1-C^2, and the H/C^1 interatomic distance are defined as D_{pln}, D_{lin} and D_{atm}, respectively. These distance parameters (D_{pln}, D_{lin} and D_{atm}) correspond to regions 1, 2 and 3, respectively. A C-H hydrogen atom is positioned above the π-plane in region 1 or at a position where it is able to contact the π-orbital in regions 2 and 3. An alkyl group can interact with the π-group in regions where the hydrogen atom is above the π-plane but slightly offset, outside the ring. The dihedral angles determined by the π-plane, plane H-C^1-C^2 and angle ∠H-X-C^1 (X=C, O, etc.) are defined as ω and θ, respectively. The distances from the γH atoms of Oxz^2 to the π-orbital of the $Phe(X)^1$ residue in the crystal structures of peptides are listed in Table S5.

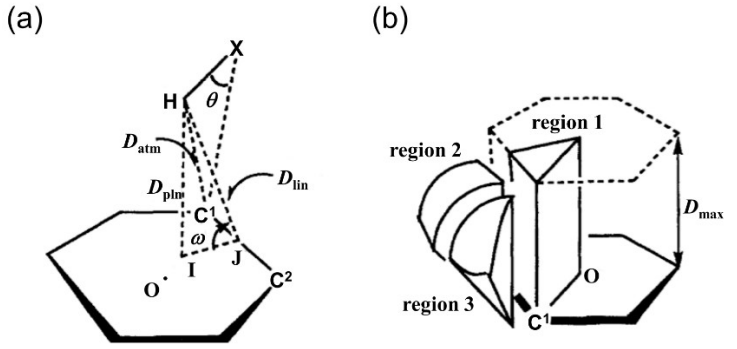


Fig. S25 Method for surveying CH···π contacts in a six-membered π-system (Y. Umezawa *et al*., *Bull*. *Chem*. *Soc*. *Jpn*., 1998, **71**, 1207-1213). (a) O: center of the plane. C^1 and C^2: nearest and second nearest sp^2-carbons to H. ω: dihedral angle defined by the C^1OC^2 and HC^1C^2 planes. θ: ∠HXC^1. D_{pln}: H/π-plane distance (H/I). D_{atm}: interatomic distance (H/C^1). D_{lin}: distance between H and line C^1C^2 (H/J). (b) 1: region where H is above the aromatic ring. 2 and 3: regions where H is outside region 1 but may interact with the π-orbitals. $D_{pln} < D_{max}$, $\theta < 60^\circ$, $|\omega| < 90^\circ$ for region 1; $D_{lin} > D_{max}$, $\theta < 60^\circ$, $90^\circ < |\omega| < 130^\circ$ for region 2; and $D_{atm} < D_{max}$, $\theta < 60^\circ$, $50^\circ < \phi < 90^\circ$ for region 3 (ϕ: HC^1I). (θ should be smaller than 60° to avoid contact of atom X with C^1). D_{max}: cutoff value in every region.

Table S5. The distances from the γH atoms of Oxz[2] side chains to the π-orbital of the Phe(X)[1] residue and angle parameters (θ and ω) within the crystal structures of peptides were estimated by surveying the CH···π contacts in a six-membered π-system.

	2	**4**
θ (°)	35.10	40.69
ω (°)	96.54	72.89
Region	2	1
Distance (Å)	3.233[a]	2.893 [b]

[a] These distance parameters determined as D_{lin} correspond to region 2.

[b] This distance parameter determined as D_{pln} corresponds to region 1.

Thermodynamic parameters and van't Hoff plots for peptides 1, 2, 3, 5, 6, 7, 8, 9 and 10.

Table S6. Equilibrium parameters of peptide **1**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.50	3.901	-3089
283	7.52	3.265	-2784
293	7.55	2.709	-2428
303	7.58	2.253	-2046
313	7.61	1.835	-1580
323	7.64	1.513	-1112
333	7.68	1.236	-586

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^o = -RT\ln K$

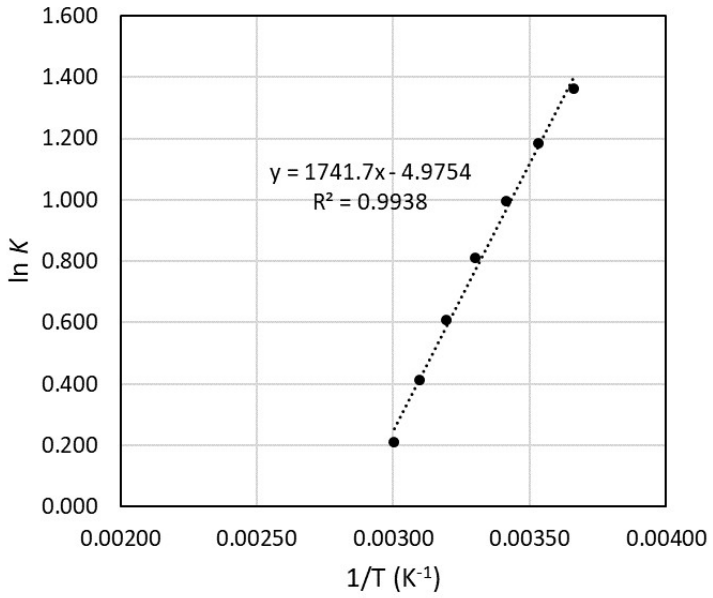


Fig. S26 van't Hoff plot of peptide **1**.

Table S7. Thermodynamic parameters of peptide **1**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-14.48	-41.37	-2.15

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

Table S8. Equilibrium parameters of peptide **2**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.511	3.596	-2905
283	7.533	3.044	-2619
293	7.558	2.558	-2288
303	7.588	2.109	-1880
313	7.620	1.741	-1442
323	7.653	1.442	-983
333	7.688	1.189	-480

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^{o} = -RT\ln K$

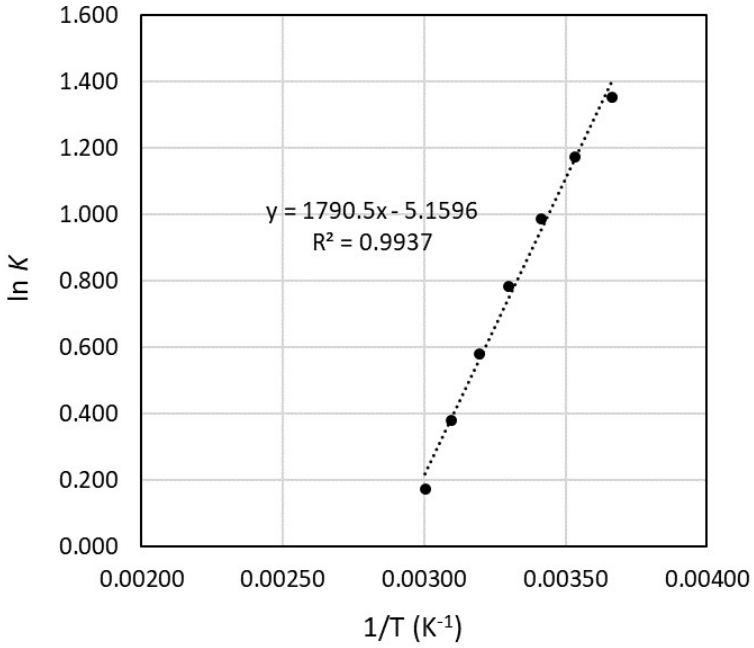


Fig. S27 van't Hoff plot of peptide **2**.

Table S9. Thermodynamic parameters of peptide **2**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-14.89	-42.90	-2.10

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

Table S10. Equilibrium parameters of peptide **3**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	*K**	ΔG° (J•mol^{-1})**
273	7.51	3.540	-2869
283	7.53	3.077	-2645
293	7.56	2.601	-2329
303	7.58	2.197	-1982
313	7.61	1.841	-1588
323	7.64	1.517	-1119
333	7.68	1.256	-631

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^{o} = -RT\ln K$

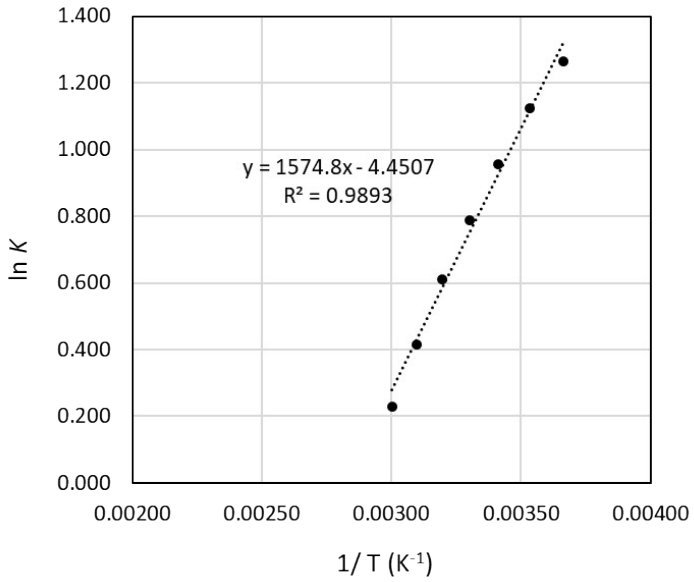


Fig. S28 van't Hoff plot of peptide **3**.

Table S11. Thermodynamic parameters of peptide **3**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-13.09	-37.00	-2.07

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

Table S12. Equilibrium parameters of peptide **5**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	*K**	ΔG° (J•mol^{-1})**
273	7.52	3.485	-2834
283	7.54	2.895	-2501
293	7.57	2.387	-2119
303	7.60	1.931	-1657
313	7.64	1.565	-1166
323	7.68	1.260	-620
333	7.72	1.005	-15

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^o = -RT\ln K$

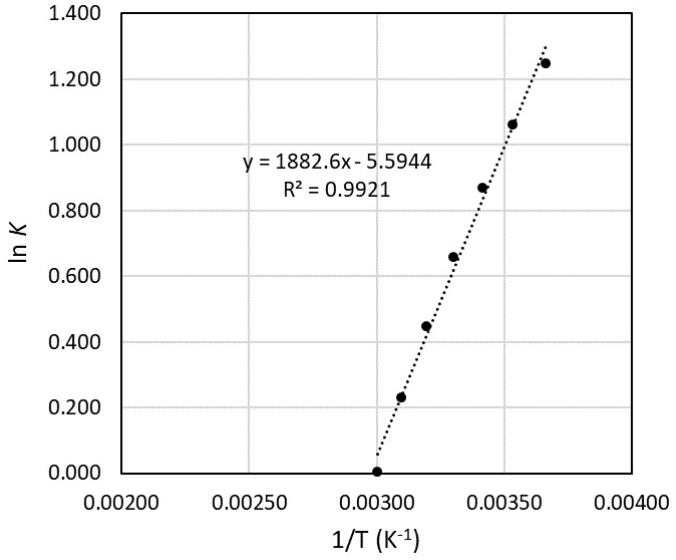


Fig. S29 van't Hoff plot of peptide **5**.

Table S13. Thermodynamic parameters of peptide **5**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-15.65	-46.51	-1.79

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

Table S14. Equilibrium parameters of peptide **6**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.50	3.805	-3033
283	7.53	3.134	-2688
293	7.56	2.575	-2304
303	7.59	2.083	-1849
313	7.62	1.701	-1382
323	7.66	1.360	-827
333	7.70	1.102	-270

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^{o} = -RT\ln K$

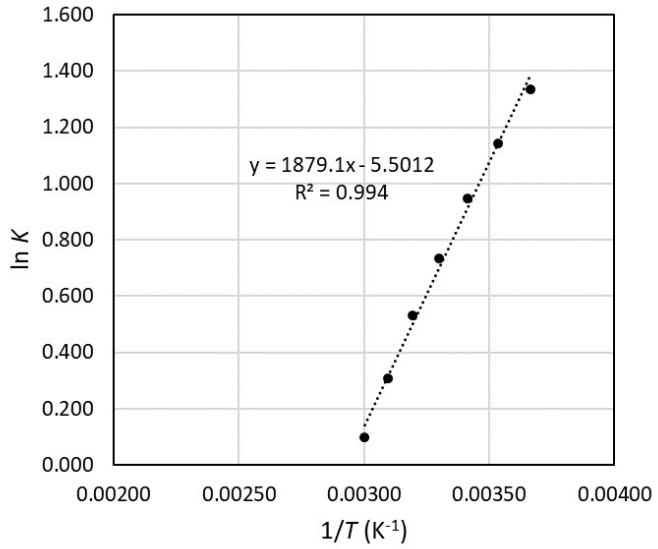


Fig. S30 van't Hoff plot of peptide **6**.

Table S15. Thermodynamic parameters of peptide **6**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-15.62	-45.74	-1.99

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

Table S16. Equilibrium parameters of peptide **7**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.51	3.512	-2851
283	7.54	2.915	-2518
293	7.57	2.410	-2143
303	7.60	1.937	-1665
313	7.64	1.578	-1188
323	7.68	1.266	-634
333	7.72	1.005	-15

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^{o} = -RT\ln K$

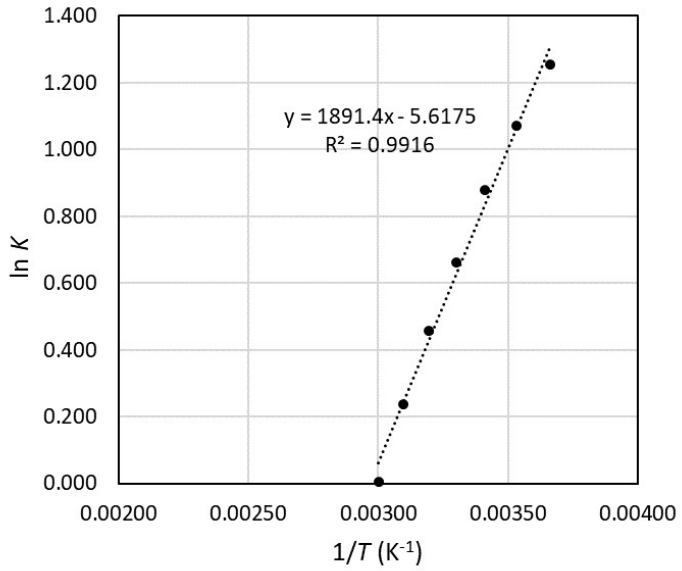


Fig. S31 van't Hoff plot of peptide **7**.

Table S17. Thermodynamic parameters of peptide **7**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-15.73	-46.70	-1.81

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

Table S18. Equilibrium parameters of peptide **8**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.52	3.485	-2834
283	7.54	2.936	-2534
293	7.57	2.418	-2151
303	7.60	1.960	-1695
313	7.64	1.578	-1188
323	7.68	1.266	-634
333	7.72	1.011	-30

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^o = -RT\ln K$

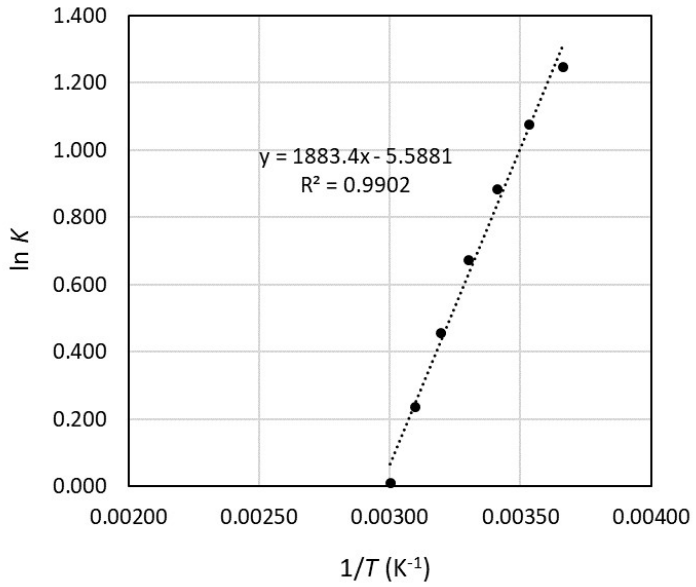


Fig. S32 van't Hoff plot of peptide **8**.

Table S19. Thermodynamic parameters of peptide **8**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-15.66	-46.46	-1.81

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

Table S20. Equilibrium parameters of peptide **9**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	K*	ΔG° (J•mol^{-1})**
273	7.53	3.111	-2576
283	7.55	2.645	-2289
293	7.58	2.210	-1932
303	7.61	1.841	-1537
313	7.64	1.513	-1077
323	7.68	1.236	-568
333	7.72	1.000	0

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^{o} = -RT\ln K$

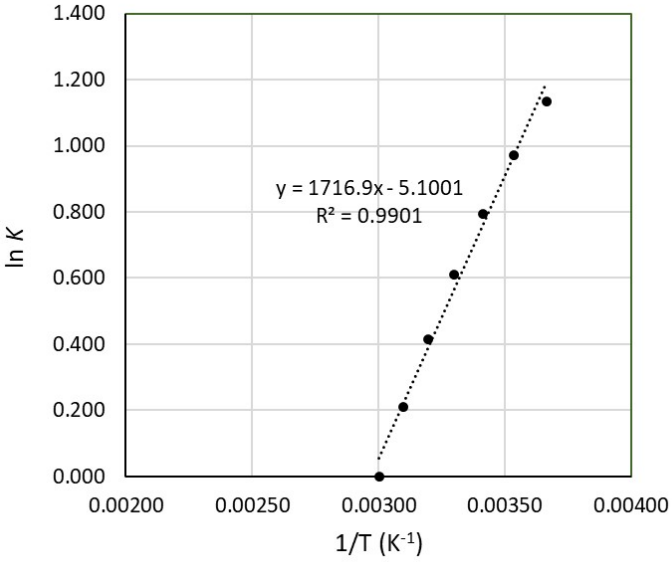


Fig. S33 van't Hoff plot of peptide **9**.

Table S21. Thermodynamic parameters of peptide **9**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-14.27	-42.40	-1.64

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

Table S22. Equilibrium parameters of peptide **10**.

T (K)	δ_{obs} Thz^{4or8} H (ppm)	*K**	ΔG° (J•mol^{-1})**
273	7.54	2.957	-2461
283	7.57	2.442	-2101
293	7.60	2.002	-1691
303	7.63	1.629	-1229
313	7.67	1.313	-708
323	7.71	1.058	-152
333	7.75	0.852	442

*Equilibrium constants were calculated from the average value 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 the chemical shift for Thz proton of *d*ASC at 273 K.

**$\Delta G^{o} = -RT\ln K$

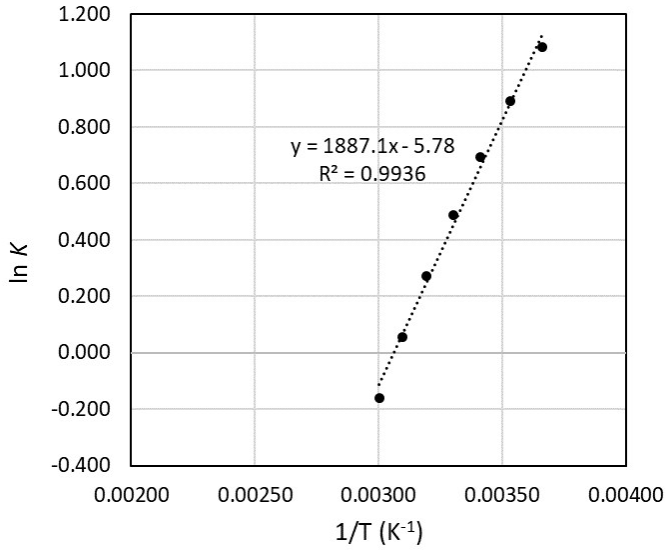


Fig. S34 van't Hoff plot of peptide **10**.

Table S23. Thermodynamic parameters of peptide **10**.

ΔH° (kJ•mol^{-1})	ΔS° (J•mol^{-1})	ΔG°_{298K} (kJ•mol^{-1})*
-15.69	-48.05	-1.37

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

Coupling constants ($^2J_{\beta1\beta2}$, $^3J_{\alpha\beta1}$ and $^3J_{\alpha\beta2}$) of Phe(X) residue at 273-333 K.

Peptide **1** (X=OCH_3)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	13.2
283	13.2	5.4	13.2
293	13.2	5.4	13.2
303	13.2	5.4	11.4
313	13.2	6.0	11.4
323	13.2	6.0	10.8
333	13.2	6.6	10.8

Peptide **2** (X=CH_3)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	4.8	12.6
283	13.2	5.4	11.4
293	13.2	5.4	11.4
303	13.2	5.4	10.8
313	13.2	5.4	10.8
323	13.2	5.4	10.8
333	13.2	6.0	10.2

Peptide **3** [X=$C(CH_3)_3$]

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	13.2
283	13.2	5.4	12.0
293	13.2	5.4	12.0
303	13.2	6.0	11.4
313	13.2	6.0	11.4
323	13.2	6.6	10.2
333		7.8	7.8

Peptide **4** (X=H)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	4.8	13.2
283	13.2	5.4	13.2
293	13.2	5.4	11.4
303	13.2	5.4	10.8
313	13.5	5.4	10.8
323	13.5	6.0	10.2
333	13.5	6.0	10.2

Peptide **5** (X=F)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	12.9	5.4	12.6
283	13.2	5.4	11.4
293	13.5	5.4	11.4
303	13.2	5.4	10.8
313	13.2	5.4	10.8
323	13.8	5.4	10.2
333	13.8	6.0	9.6

Peptide **6** (X=I)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	12.0
283	13.2	6.0	12.0
293	13.2	6.0	11.4
303	13.2	6.0	10.8
313	13.2	6.0	10.2
323	13.2	6.0	9.6
333		7.8	7.8

Peptide **7** (X=Cl)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	12.0
283	13.2	5.4	11.4
293	13.2	5.4	10.8
303	13.2	5.4	10.8
313	13.2	7.2	10.8
323	13.2	7.2	9.6
333	13.2	7.8	7.8

Peptide **8** (X=Br)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	12.0
283	13.2	5.4	11.4
293	13.2	5.4	11.4
303	13.2	5.4	11.4
313	13.2	6.6	9.6
323	13.2	6.6	9.6
333		7.8	7.8

Peptide **9** (X=CF_3)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	12.0
283	13.5	6.0	12.0
293	13.8	6.6	11.4
303	13.2	6.6	10.2
313	13.2	7.2	9.6
323		8.4	8.4
333	13.5	9.6	6.6

Peptide **10** (X=NO_2)

T (K)	$^2J_{\beta1\beta2}$	$^3J_{\alpha\beta1}$	$^3J_{\alpha\beta2}$
273	13.2	5.4	12.0
283	13.8	5.4	11.4
293	13.5	5.4	11.4
303	13.8	6.0	10.8
313	13.5	6.0	10.2
323	13.2	6.6	9.6
333		7.8	7.8

Chemical structures of *d*ASC and T3ASC as reference peptides.

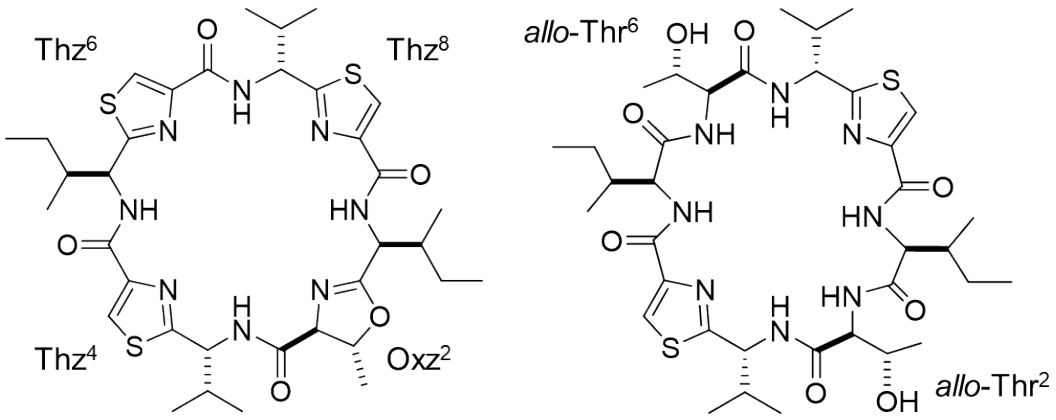


Fig. S35 Chemical structures of T3ASC (A. Asano *et al*., *J. Pept. Sci*., 2018, e3120) and *d*ASC (A. Asano *et al*., *Biopolymers*, 2001, **58**, 295–304). T3ASC and *d*ASC were used as reference peptides to provide reference chemical shifts for the fully square and folded forms, respectively.