Biophysical Journal, Volume *116*

Supplemental Information

β-Branched Amino Acids Stabilize Specific Conformations of Cyclic Hexapeptides

Ashleigh E. Cummings, Jiayuan Miao, Diana P. Slough, Sean M. McHugh, Joshua A. Kritzer, and Yu-Shan Lin

I. Simulation data tables and figures

Table S1. Cumulative variance associated to the first three eigenvectors for the cyclic hexapeptides analyzed in the paper.

Name	Sequence	% Variance of the first 3 PC's
P7	VVGGVG	67.4%
P6	VVGVGG	60.9%
V1A	AVGGVG	70.3%
V2A	VAGGVG	64.0%
V5A	VVGGAG	68.5%
V1I	IVGGVG	66.9%
V1L	LVGGVG	72.3%
V1T	TVGGVG	68.0%
V1S	SVGGVG	68.5%

Table S2. Thermodynamic decomposition between cluster 1 and cluster 2 for P7, V1A, V1I, V1L; and between cluster 1 and cluster 3 for V1T, V1S. S1 and S2 are two sets of parallel simulations beginning with different initial structures. The error of ΔG is the standard error of the mean (SEM) estimated from the five neutral replicas in BE-META simulations. $-T\Delta S_{\mathrm{P}}^{\mathrm{conf}}$ is calculated using maximum information spanning tree (MIST) approach, which provides a tight estimation of the upper bound of the entropy. The error of $-T\Delta S$ is propagated from ΔG and ΔH according to the relation: $-T\Delta S = \Delta G - \Delta H$. The error of $-T\Delta S_{\mathrm{W}}$ is propagated from $-T\Delta S$ according to the relation: $-T\Delta S_{\mathrm{W}} = (-T\Delta S) - (-T\Delta S_{\mathrm{P}}^{\mathrm{conf}})$. The errors of the remaining quantities are SEM calculated from 60,000 frames sampled from the additional MD simulations.

S1

			ΔG	ΔH	$-T\Delta S$	$\Delta H_{\mathrm{P}}^{\mathrm{vac}}$	ΔH_{rest}	$-T\Delta S_{\mathrm{P}}^{\mathrm{conf}}$	$-T\Delta S_{\mathrm{W}}$	$\Delta H_{\mathrm{P}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{P}}^{\mathrm{EE(SR+1,4)}}$	$\Delta H_{\mathrm{P}}^{\mathrm{bond}}$	$\Delta H_{\mathrm{P}}^{\mathrm{angle}}$	$\Delta H_{\mathrm{P}}^{\mathrm{dih.}}$	$\Delta H_{\mathrm{P}}^{\mathrm{imp.}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(SR)}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(LR)}}$
P7	VVGGVG	75.3%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	VVGGVG	2.6%	8.38±0.14	12.17±1.29	-3.79±1.30	46.77±0.16	-34.60±1.28	-14.72	10.93±1.30	4.21±0.06	38.23±0.11	-0.25±0.07	0.20±0.11	4.42±0.05	-0.03±0.02	0.49±1.28	-22.93±2.01	-12.16±0.12
V1A	AVGGVG	47.2%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	AVGGVG	10.2%	3.84±0.13	2.09±1.31	1.75±1.32	49.99±0.15	-47.90±1.31	-6.00	7.75±1.32	-2.73±0.06	49.68±0.11	-0.15±0.07	1.72±0.10	1.82±0.05	-0.34±0.02	6.33±1.31	-24.30±2.05	-29.93±0.12
V1I	IVGGVG	77.8%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	IVGGVG	2.9%	8.22±0.06	10.67±1.23	-2.45±1.23	51.16±0.16	-40.49±1.23	-15.97	13.52±1.23	7.26±0.06	39.25±0.11	-0.03±0.07	0.55±0.11	4.20±0.05	-0.08±0.02	0.69±1.23	-25.62±1.92	-15.56±0.12
V1L	LVGGVG	32.4%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	LVGGVG	14.4%	2.03±0.07	1.81±1.22	0.22±1.23	62.74±0.17	-60.93±1.22	-9.15	9.37±1.23	5.61±0.06	60.33±0.12	-0.67±0.07	-3.18±0.11	0.51±0.06	0.13±0.02	-2.91±1.22	-21.26±1.91	-36.76±0.12
V1T	TVGGVG	63.8%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	TVGGVG	4.1%	6.87±0.05	5.71±1.23	1.16±1.23	61.27±0.16	-55.56±1.23	-12.71	13.87±1.23	-0.20±0.06	54.44±0.13	-0.01±0.07	1.60±0.11	5.50±0.05	-0.06±0.02	3.10±1.23	-29.01±1.92	-29.65±0.12
V1S	SVGGVG	44.2%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	SVGGVG	7.6%	4.40±0.10	1.08±1.23	3.32±1.23	53.70±0.17	-52.62±1.22	-5.75	9.07±1.23	-1.26±0.06	52.11±0.13	-0.07±0.07	1.65±0.10	1.49±0.05	-0.21±0.02	4.09±1.23	-28.95±1.92	-27.77±0.12

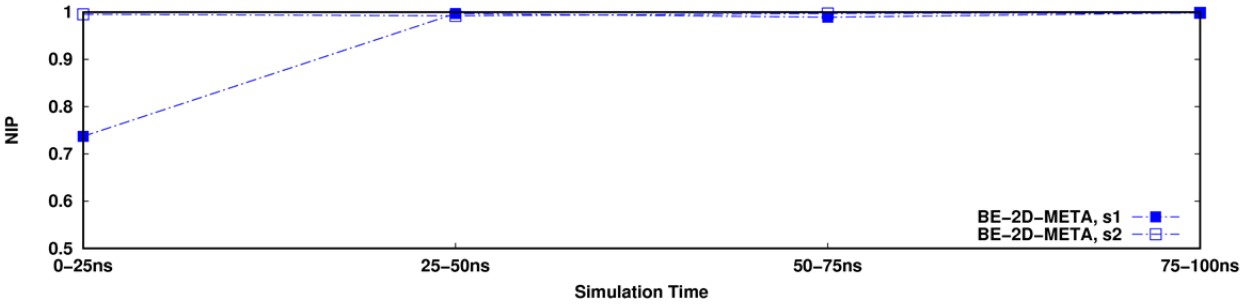
S2

			ΔG	ΔH	$-T\Delta S$	$\Delta H_{\mathrm{P}}^{\mathrm{vac}}$	ΔH_{rest}	$-T\Delta S_{\mathrm{P}}^{\mathrm{conf}}$	$-T\Delta S_{\mathrm{W}}$	$\Delta H_{\mathrm{P}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{P}}^{\mathrm{EE(SR+1,4)}}$	$\Delta H_{\mathrm{P}}^{\mathrm{bond}}$	$\Delta H_{\mathrm{P}}^{\mathrm{angle}}$	$\Delta H_{\mathrm{P}}^{\mathrm{dih.}}$	$\Delta H_{\mathrm{P}}^{\mathrm{imp.}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(SR)}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(LR)}}$
P7	VVGGVG	77.7%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	VVGGVG	1.4%	9.96±0.20	10.87±1.25	-0.91±1.26	47.15±0.16	-36.28±1.24	-15.54	14.64±1.26	3.71±0.06	37.80±0.12	-0.05±0.07	0.64±0.11	5.13±0.05	-0.08±0.02	0.78±1.24	-23.33±1.94	-13.72±0.12
V1A	AVGGVG	47.6%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	AVGGVG	8.3%	4.38±0.13	4.58±1.23	-0.20±1.23	50.40±0.15	-45.82±1.22	-5.91	5.72±1.23	-2.47±0.06	50.24±0.11	-0.07±0.07	1.66±0.10	1.39±0.05	-0.36±0.02	1.98±1.23	-18.14±1.92	-29.66±0.11
V1I	IVGGVG	81.1%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	IVGGVG	1.8%	9.46±0.16	8.87±1.24	0.59±1.25	50.85±0.16	-41.99±1.24	-15.33	15.92±1.25	7.63±0.06	39.20±0.11	0.02±0.07	0.22±0.11	3.86±0.05	-0.08±0.02	-0.21±1.24	-26.26±1.94	-15.52±0.12
V1L	LVGGVG	36.0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	LVGGVG	13.7%	2.40±0.05	2.10±1.27	0.30±1.27	62.29±0.16	-60.19±1.27	-8.68	8.98±1.27	6.30±0.06	60.04±0.12	-0.70±0.07	-3.93±0.11	0.48±0.05	0.10±0.02	-1.21±1.27	-23.26±1.99	-35.72±0.12
V1T	TVGGVG	64.1%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	TVGGVG	3.8%	7.06±0.10	5.02±1.24	2.04±1.24	60.96±0.16	-55.94±1.22	-12.78	14.81±1.24	-0.14±0.06	54.39±0.13	-0.27±0.07	1.53±0.11	5.51±0.05	-0.06±0.02	3.36±1.24	-29.99±1.94	-29.31±0.12
V1S	SVGGVG	45.1%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	SVGGVG	8.3%	4.21±0.03	0.84±1.25	3.36±1.25	53.20±0.17	-52.36±1.25	-5.59	8.95±1.25	-1.32±0.06	52.09±0.14	-0.12±0.07	0.88±0.10	1.88±0.05	-0.21±0.02	4.42±1.24	-27.77±1.94	-29.00±0.13

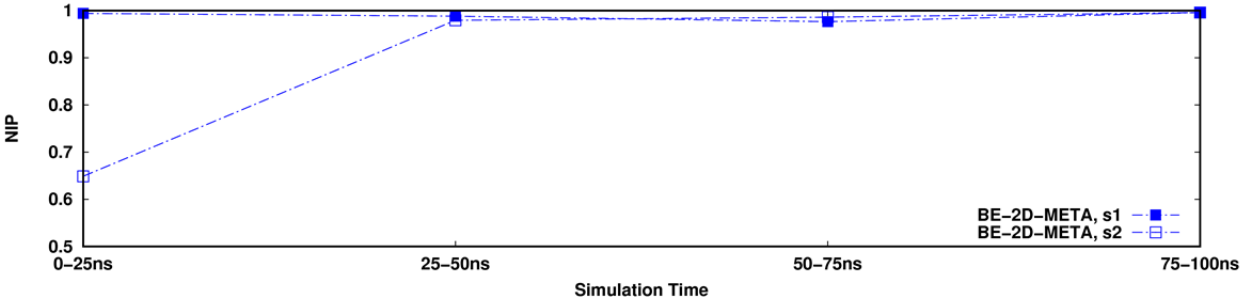
Table S3. The population percentages and structures of the top three clusters from BE-META simulations using the amber99sb force field. S1 and S2 are two sets of simulations beginning with different initial structures. Types I, II and II′ β turns are colored red, green and blue, respectively.

CP	VVGGVG		AVGGVG		IVGGVG		LVGGVG		TVGGVG		SVGGVG	
	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2
Cluster 1	VVGGVG 22.9%	VVGGVG 27.2%	AVGGVG 31.4%	AVGGVG 26.8%	IVGGVG 25.6%	IVGGVG 31.3%	LVGGVG 36.7%	LVGGVG 31.2%	TVGGVG 34.9%	TVGGVG 29.1%	SVGGVG 32.0%	SVGGVG 26.3%
Cluster 2	VVGGVG 12.6%	VVGGVG 9.7%	AVGGVG 9.9%	AVGGVG 12.6%	IVGGVG 25.5%	IVGGVG 14.1%	LVGGVG 9.9%	LVGGVG 11.1%	TVGGVG 10.5%	TVGGVG 9.7%	SVGGVG 8.7%	SVGGVG 12.6%
Cluster 3	VVGGVG 10.5%	VVGGVG 8.7%	AVGGVG 6.3%	AVGGVG 6.8%	IVGGVG 6.1%	IVGGVG 8.2%	LVGGVG 7.6%	LVGGVG 10.1%	TVGGVG 8.6%	TVGGVG 9.2%	SVGGVG 6.7%	SVGGVG 7.0%

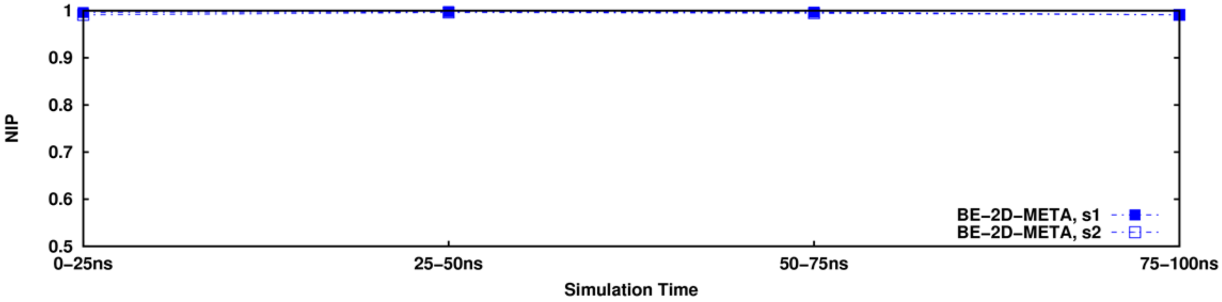
cyclo-(VVGGVG)



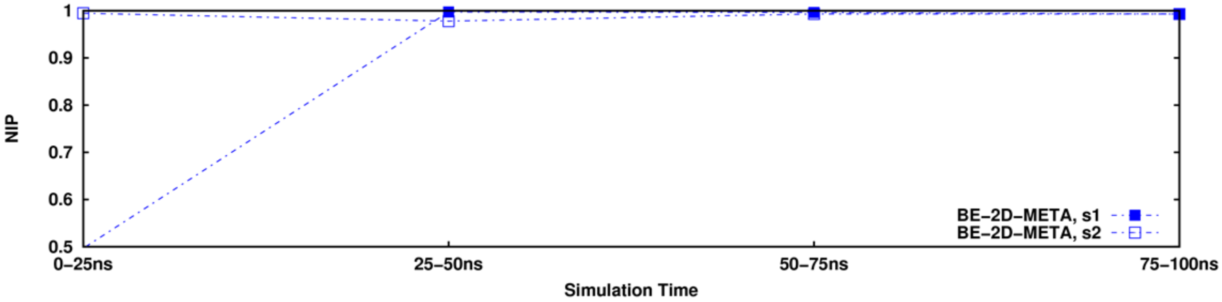
cyclo-(VVGVGG)

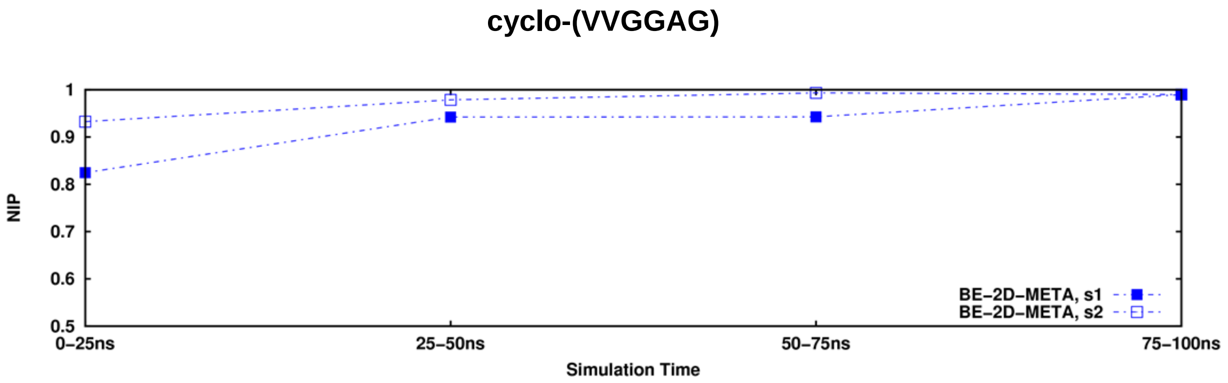


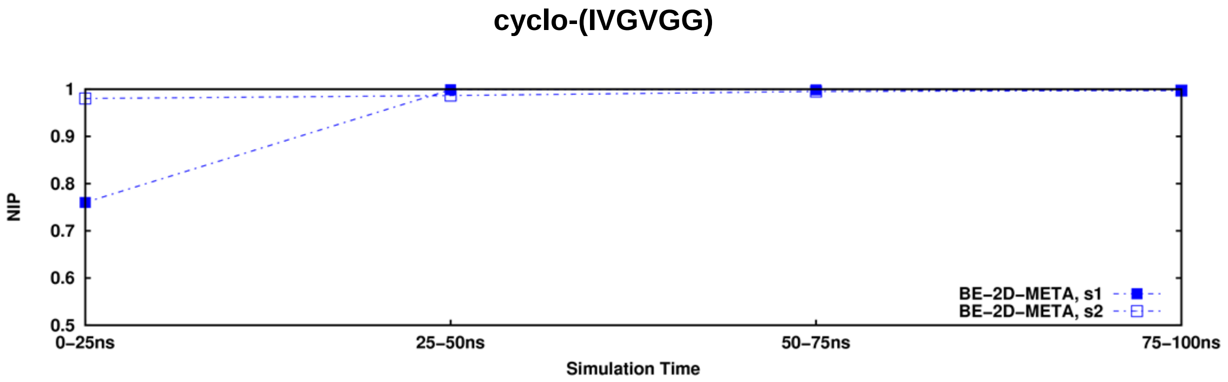
cyclo-(AVGGVG)

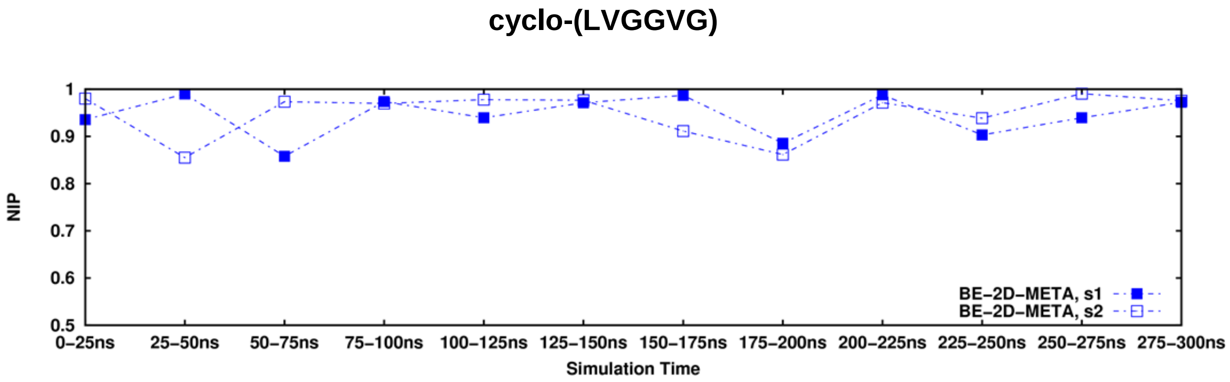


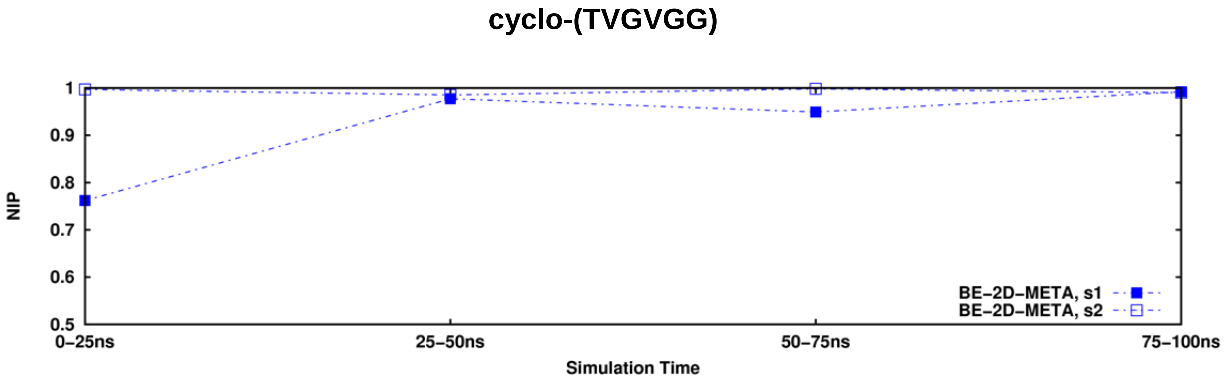
cyclo-(VAGGVG)




cyclo-(VVGGAG)


cyclo-(IVGVGG)


cyclo-(LVGGVG)


cyclo-(TVGVGG)

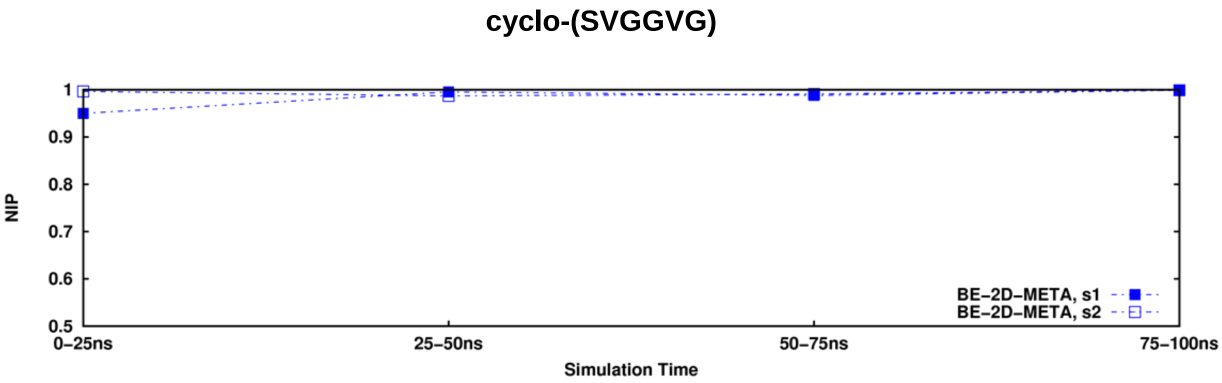


Figure S1. NIP figures of all cyclic hexapeptides analyzed in the paper.

P7

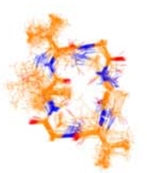
Simulated annealing starting from initial structure #1

Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
25	2	VAL	H	1	VAL	HB	3.7	0.0	3.869–4.432
11	3	GLY	H	2	VAL	HA	3.2	0.0	3.466–3.591
10	4	GLY	H	1	VAL	HG#	4.9	0.0	5.033–9.214
5	5	VAL	H	5	VAL	HB	3.8	0.0	3.804–3.929
5	2	VAL	H	2	VAL	HB	3.6	0.0	3.661–3.721
5	2	VAL	H	1	VAL	HA	3.5	0.0	3.568–3.598
3	6	GLY	H	5	VAL	HA	3.2	0.0	3.234–3.624
2	3	GLY	H	4	GLY	H	4.2	0.0	4.360–4.376

	Res #	Dihedral	Upper	Lower	Range of violations
45	5	VAL (ϕ)	−90.0	−150.0	−89.814 to −87.417
17	1	VAL (ϕ)	−90.0	−150.0	−150.980 to −150.079; −89.998 to −88.458
1	2	VAL (ϕ)	−30.0	−90.0	−90.784

Simulated annealing starting from initial structure #2

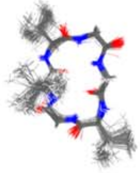


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
28	2	VAL	H	1	VAL	HB	3.7	0.0	3.785–4.638
20	4	GLY	H	1	VAL	HG#	4.9	0.0	5.138–8.182
19	2	VAL	H	1	VAL	HA	3.5	0.0	3.535–3.621
18	2	VAL	H	2	VAL	HB	3.6	0.0	3.655–3.760
12	3	GLY	H	2	VAL	HA	3.2	0.0	3.232–3.630
9	3	GLY	H	4	GLY	H	4.2	0.0	4.268–4.536
6	6	GLY	H	5	VAL	HA	3.2	0.0	3.437–3.568
4	5	VAL	H	5	VAL	HB	3.8	0.0	3.803–3.873

	Res #	Dihedral	Upper	Lower	Range of violations
57	5	VAL (ϕ)	−90.0	−150.0	−89.924 to −87.489
8	1	VAL (ϕ)	−90.0	−150.0	−151.061 to −150.220; −89.676 to −88.021
3	2	VAL (ϕ)	−30.0	−90.0	−90.586 to −90.279

Number of violations of the predicted top cluster

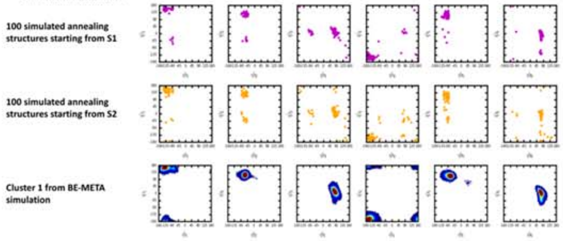


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
16	2	VAL	H	1	VAL	HB	3.7	0.0	3.890–4.302
3	2	VAL	H	2	VAL	HB	3.6	0.0	3.656–3.768
1	1	VAL	HA	1	VAL	HB	3.1	0.0	3.111
1	4	GLY	H	1	VAL	HG#	4.9	0.0	5.123

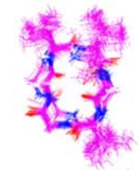
	Res #	Dihedral	Upper	Lower	Range of violations
88	5	VAL (ϕ)	−90.0	−150.0	−89.035 to −46.637
18	1	VAL (ϕ)	−90.0	−150.0	−173.824 to −150.002; −86.369 to −58.039
1	2	VAL (ϕ)	−30.0	−90.0	−5.599

*First column: # of the violations out of 100 structures



P6

Simulated annealing starting from initial structure #1

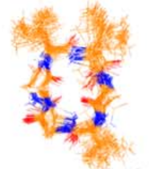


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
31	2	VAL	H	2	VAL	HB	3.8	0.0	3.809–3.987
28	3	GLY	H	2	VAL	HA	3.4	0.0	3.424–3.620
21	3	GLY	H	2	VAL	H	4.4	0.0	4.405–4.583
17	5	GLY	H	6	GLY	H	4.2	0.0	4.217–4.545
13	5	GLY	H	4	VAL	HA	3.4	0.0	3.417–3.578
13	4	VAL	H	4	VAL	HB	3.7	0.0	3.702–3.840
5	2	VAL	H	6	GLY	HA#	5.2	0.0	5.286–5.679
3	1	VAL	H	1	VAL	HB	3.8	0.0	3.804–3.913
1	1	VAL	H	2	VAL	H	4.0	0.0	4.508

	Res #	Dihedral	Upper	Lower	Range of violations
3	2	VAL (ϕ)	−90.0	−150.0	−150.299; −89.249, −89.120

Simulated annealing starting from initial structure #2



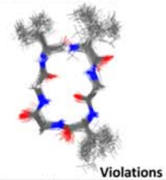
Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
33	2	VAL	H	2	VAL	HB	3.8	0.0	3.823–3.961
29	3	GLY	H	2	VAL	HA	3.4	0.0	3.457–3.610
28	3	GLY	H	2	VAL	H	4.4	0.0	4.400–4.658
22	5	GLY	H	6	GLY	H	4.2	0.0	4.280–4.725
21	5	GLY	H	4	VAL	HA	3.4	0.0	3.410–3.610
16	4	VAL	H	4	VAL	HB	3.7	0.0	3.700–3.932
10	1	VAL	H	1	VAL	HB	3.8	0.0	3.801–3.860
5	2	VAL	H	6	GLY	HA#	5.2	0.0	5.219–5.641
1	1	VAL	H	2	VAL	H	4.0	0.0	4.323

	Res #	Dihedral	Upper	Lower	Range of violations
2	2	VAL (ϕ)	−90.0	−150.0	−150.587; −89.932

Number of violations of the predicted top cluster

First cluster from BE-META simulation

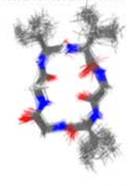


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
66	3	GLY	H	2	VAL	HA	3.4	0.0	3.410–3.749
27	2	VAL	H	2	VAL	HB	3.8	0.0	3.802–4.060
5	4	VAL	H	4	VAL	HB	3.7	0.0	3.702–3.844
4	1	VAL	H	1	VAL	HB	3.8	0.0	3.817–3.916
1	3	GLY	H	2	VAL	HB	4.7	0.0	4.716

	Res #	Dihedral	Upper	Lower	Range of violations
13	2	VAL (ϕ)	−90.0	−150.0	−88.873 to −68.875

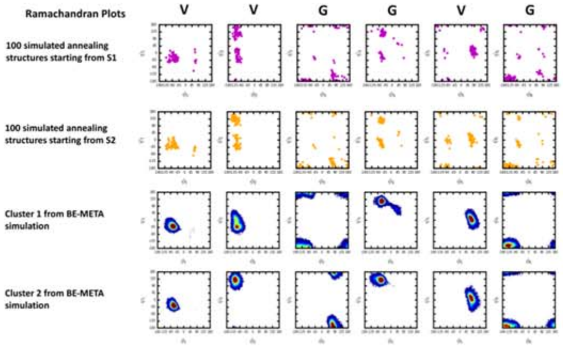
Second cluster from BE-META simulation



Violations

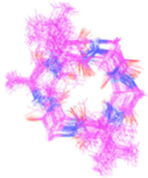
	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
29	3	GLY	H	2	VAL	H	4.4	0.0	4.402-4.663
6	4	VAL	H	4	VAL	HB	3.7	0.0	3.707-3.871
2	2	VAL	H	2	VAL	HB	3.8	0.0	3.957-3.999
2	1	VAL	H	1	VAL	HB	3.8	0.0	3.876-3.904

	Res #	Dihedral	Upper	Lower	Actual dihedral range
6	2	VAL (ϕ)	−90.0	−150.0	−88.329 to −80.327



AVGGVG

Simulated annealing starting from initial structure #1

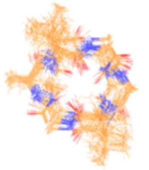


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
69	6	GLY	H	1	ALA	H	4.2	0.0	4.281–4.677
49	3	GLY	H	4	GLY	H	4.1	0.0	4.227–4.671
33	1	ALA	H	2	VAL	H	4.3	0.0	4.308–4.708
27	2	VAL	H	2	VAL	HB	3.7	0.0	3.705–3.981
22	6	GLY	H	5	VAL	HA	3.2	0.0	3.223–3.604
22	4	GLY	H	5	VAL	H	4.3	0.0	4.308–4.593
21	3	GLY	H	2	VAL	HA	3.2	0.0	3.213–3.574
5	3	GLY	H	2	VAL	HG#	4.3	0.0	4.465–4.865
2	6	GLY	H	5	VAL	HG#	4.3	0.0	4.537–4.670
1	2	VAL	H	1	ALA	HB#	4.1	0.0	4.115
1	1	ALA	H	6	GLY	HA#	3.6	0.0	3.808

	Res #	Dihedral	Upper	Lower	Range of violations
20	5	VAL (ϕ)	−90.0	−150.0	−89.886 to −87.434

Simulated annealing starting from initial structure #2

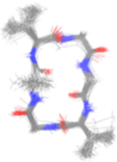


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
67	6	GLY	H	1	ALA	H	4.2	0.0	4.235–4.679
45	3	GLY	H	4	GLY	H	4.1	0.0	4.174–5.187
30	1	ALA	H	2	VAL	H	4.3	0.0	4.323–4.684
20	2	VAL	H	2	VAL	HB	3.7	0.0	3.701–3.999
19	4	GLY	H	5	VAL	H	4.3	0.0	4.310-4.670
16	6	GLY	H	5	VAL	HA	3.2	0.0	3.216–3.589
15	3	GLY	H	2	VAL	HA	3.2	0.0	3.261–3.604
9	6	GLY	H	5	VAL	HG#	4.3	0.0	4.314–4.699
2	2	VAL	H	1	ALA	HB#	4.1	0.0	4.166–4.207
1	3	GLY	H	2	VAL	HG#	4.3	0.0	4.684

	Res #	Dihedral	Upper	Lower	Range of violations
19	5	VAL (ϕ)	−90.0	−150.0	−89.999 to −87.426

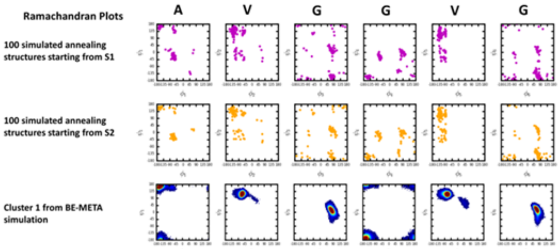
Number of violations of the predicted top cluster



Violations

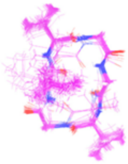
	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
90	1	ALA	H	2	VAL	H	4.3	0.0	4.302–4.775
64	4	GLY	H	5	VAL	H	4.3	0.0	4.312–4.622
2	6	GLY	H	5	VAL	HG#	4.3	0.0	4.541–4.576
1	3	GLY	H	2	VAL	HG#	4.3	0.0	4.301
1	2	VAL	H	2	VAL	HB	3.7	0.0	3.751

	Res #	Dihedral	Upper	Lower	Range of violations
90	5	VAL (ϕ)	−90.0	−150.0	−89.843 to −37.581



IVGGVG

Simulated annealing starting from initial structure #1

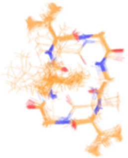


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
100	4	GLY	H	5	VAL	HA	4.3	0.0	4.379–5.358
93	1	ILE	H	1	ILE	HD#	4.3	0.0	4.356–5.689
77	1	ILE	HA	1	ILE	HD#	4.4	0.0	4.468–4.931
38	4	GLY	H	1	ILE	HD#	5.0	0.0	5.003–6.357
36	2	VAL	H	1	ILE	HD#	4.8	0.0	4.804–5.678
24	2	VAL	H	1	ILE	HB	3.7	0.0	3.773–4.165
13	3	GLY	H	2	VAL	HA	3.0	0.0	3.447–3.590
11	2	VAL	H	2	VAL	HB	3.5	0.0	3.670–3.724
7	4	GLY	HA#	1	ILE	HD#	5.5	0.0	5.504–6.998
7	4	GLY	H	1	ILE	HG#	4.4	0.0	4.422–5.980
5	5	VAL	H	5	VAL	HB	3.8	0.0	3.805–3.867
4	3	GLY	H	2	VAL	HG#	4.2	0.0	4.203–4.412
4	2	VAL	H	1	ILE	HA	3.4	0.0	3.501–3.604
4	1	ILE	HB	1	ILE	HD#	3.2	0.0	3.818–3.861
3	6	GLY	H	1	ILE	H	4.3	0.0	4.307–4.509
2	4	GLY	HA#	1	ILE	HG#	6.1	0.0	6.988–7.583

	Res #	Dihedral	Upper	Lower	Range of violations
8	1	VAL (ϕ)	−90.0	−150.0	−151.848 to −150.380; −89.813 to −89.552
41	5	VAL (ϕ)	−90.0	−150.0	-89.944 to −87.141

Simulated annealing starting from initial structure #2

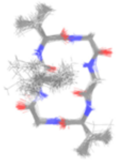


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
100	4	GLY	H	5	VAL	HA	4.3	0.0	4.521–5.187
88	1	ILE	H	1	ILE	HD#	4.3	0.0	4.305–5.700
81	1	ILE	HA	1	ILE	HD#	4.4	0.0	4.734–4.934
33	4	GLY	H	1	ILE	HD#	5.0	0.0	5.012–6.517
26	2	VAL	H	1	ILE	HD#	4.8	0.0	4.806–5.698
12	2	VAL	H	1	ILE	HB	3.7	0.0	3.961–4.530
9	3	GLY	H	2	VAL	HA	3.0	0.0	3.509–3.607
9	2	VAL	H	2	VAL	HB	3.5	0.0	3.670–3.795
8	4	GLY	HA#	1	ILE	HD#	5.5	0.0	5.613–6.991
8	4	GLY	H	1	ILE	HG#	4.4	0.0	4.842–6.922
4	2	VAL	H	1	ILE	HA	3.4	0.0	3.578–3.635
4	1	ILE	HB	1	ILE	HD#	3.2	0.0	3.811–3.841
3	5	VAL	H	5	VAL	HB	3.8	0.0	3.832–3.927
2	6	GLY	H	1	ILE	H	4.3	0.0	4.389–4.483
2	4	GLY	HA#	1	ILE	HG#	6.1	0.0	6.326–8.267

	Res #	Dihedral	Upper	Lower	Range of violations
9	1	VAL (ϕ)	−90.0	−150.0	−151.600 to −150.171; −89.502 to −88.596
52	5	VAL (ϕ)	−90.0	−150.0	−89.993 to −87.194

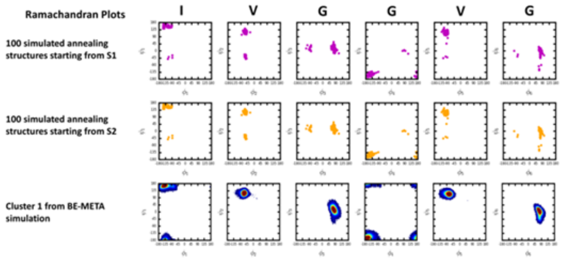
Number of violations of the predicted top cluster



Violations

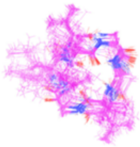
	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
100	4	GLY	H	5	VAL	HA	4.3	0.0	4.383–5.771
94	1	ILE	H	1	ILE	HD#	4.3	0.0	4.328–5.676
85	1	ILE	HA	1	ILE	HD#	4.4	0.0	4.439–5.214
21	4	GLY	H	1	ILE	HD#	5.0	0.0	5.052–7.607
21	2	VAL	H	1	ILE	HD#	4.8	0.0	4.814–5.350
13	4	GLY	HA#	1	ILE	HD#	5.5	0.0	5.785–8.763
13	2	VAL	H	1	ILE	HB	3.7	0.0	3.968–4.341
6	2	VAL	H	2	VAL	HB	3.5	0.0	3.604–3.771
5	4	GLY	H	1	ILE	HG#	4.4	0.0	4.532–6.129
3	3	GLY	H	2	VAL	HG#	4.2	0.0	4.246–4.421

	Res #	Dihedral	Upper	Lower	Range of violations
26	1	VAL (ϕ)	−90.0	−150.0	−176.793 to −150.696; −89.431 to −53.393
86	5	VAL (ϕ)	−90.0	−150.0	−89.874 to −41.442



LVGGVG

Simulated annealing starting from initial structure #1

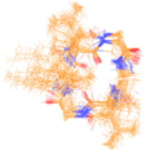


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
73	4	GLY	H	5	VAL	HA	5.0	0.0	5.000–5.587
68	5	VAL	H	6	GLY	HA#	5.2	0.0	5.213–5.757
68	2	VAL	H	3	GLY	HA#	5.4	0.0	5.406–6.132
58	4	GLY	HA#	1	LEU	HD#	5.3	0.0	5.387–9.911
43	1	LEU	H	2	VAL	H	4.0	0.0	4.100–4.647
39	4	GLY	H	5	VAL	H	4.1	0.0	4.102–4.355
37	1	LEU	H	1	LEU	HB#	3.5	0.0	3.515–3.768
29	6	GLY	H	1	LEU	H	4.4	0.0	4.428–4.667
28	4	GLY	H	2	VAL	HG#	5.4	0.0	5.400–6.117
22	1	LEU	H	1	LEU	HD#	4.4	0.0	4.416–5.007
21	1	LEU	H	2	VAL	HA	5.5	0.0	5.500–5.747
18	2	VAL	H	1	LEU	HB#	4.1	0.0	4.106–4.457
12	2	VAL	H	2	VAL	HB	3.6	0.0	3.648–3.834
9	3	GLY	H	4	GLY	H	4.0	0.0	4.201–4.616
7	6	GLY	H	5	VAL	HA	3.1	0.0	3.199–3.539
7	5	VAL	H	5	VAL	HB	3.8	0.0	3.801–3.961
7	3	GLY	H	2	VAL	HA	3.1	0.0	3.326–3.581
3	6	GLY	H	5	VAL	HG#	4.3	0.0	4.441–4.612
3	3	GLY	H	2	VAL	HG#	4.2	0.0	4.204–4.326
1	3	GLY	H	2	VAL	H	5.0	0.0	5.123

	Res #	Dihedral	Upper	Lower	Range of violations
25	5	VAL (ϕ)	−90.0	−150.0	−89.989 to −88.853

Simulated annealing starting from initial structure #2

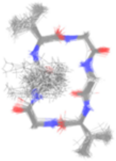


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
67	4	GLY	H	5	VAL	HA	5.0	0.0	5.005–5.490
66	5	VAL	H	6	GLY	HA#	5.2	0.0	5.209–5.720
64	2	VAL	H	3	GLY	HA#	5.4	0.0	5.407–6.098
56	1	LEU	H	2	VAL	H	4.0	0.0	4.016–4.673
54	4	GLY	HA#	1	LEU	HD#	5.3	0.0	5.337–8.356
42	4	GLY	H	5	VAL	H	4.1	0.0	4.122–4.408
29	6	GLY	H	1	LEU	H	4.4	0.0	4.403–4.658
28	1	LEU	H	1	LEU	HB#	3.5	0.0	3.524–3.793
27	4	GLY	H	2	VAL	HG#	5.4	0.0	5.402–6.399
23	1	LEU	H	1	LEU	HD#	4.4	0.0	4.412–4.992
20	2	VAL	H	1	LEU	HB#	4.1	0.0	4.101–4.475
20	1	LEU	H	2	VAL	HA	5.5	0.0	5.504–5.826
13	3	GLY	H	2	VAL	HA	3.1	0.0	3.237–3.603
13	2	VAL	H	2	VAL	HB	3.6	0.0	3.657–3.974
10	6	GLY	H	5	VAL	HA	3.1	0.0	3.358–3.582
7	3	GLY	H	4	GLY	H	4.0	0.0	4.153–4.642
6	6	GLY	H	5	VAL	HG#	4.3	0.0	4.322–4.743
6	5	VAL	H	5	VAL	HB	3.8	0.0	3.802–3.876
1	3	GLY	H	2	VAL	HG#	4.2	0.0	4.270
1	3	GLY	H	2	VAL	H	5.0	0.0	5.225
1	1	LEU	H	6	GLY	HA#	3.4	0.0	3.726

	Res #	Dihedral	Upper	Lower	Range of violations
23	5	VAL (ϕ)	−90.0	−150.0	−89.911 to −87.512

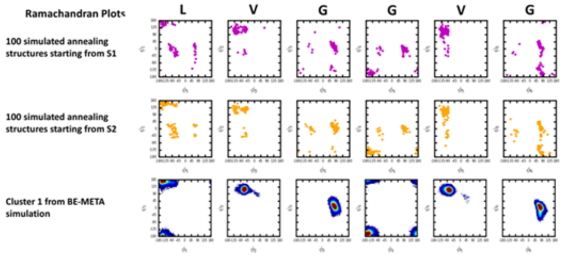
Number of violations of the predicted top cluster



Violations

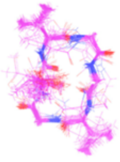
	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
99	1	LEU	H	2	VAL	H	4.0	0.0	4.096–4.751
98	5	VAL	H	6	GLY	HA#	5.2	0.0	5.201–6.103
92	2	VAL	H	3	GLY	HA#	5.4	0.0	5.409–6.161
91	4	GLY	H	5	VAL	H	4.1	0.0	4.103–4.738
68	4	GLY	H	5	VAL	HA	5.0	0.0	5.003–5.647
44	4	GLY	H	2	VAL	HG#	5.4	0.0	5.402–6.175
34	1	LEU	H	1	LEU	HB#	3.5	0.0	3.535–3.825
15	1	LEU	H	2	VAL	HA	5.5	0.0	5.503–5.858
8	1	LEU	H	1	LEU	HD#	4.4	0.0	4.658–5.075
6	4	GLY	HA#	1	LEU	HD#	5.3	0.0	5.477–6.596
4	3	GLY	H	2	VAL	HG#	4.2	0.0	4.215–4.593
4	2	VAL	H	2	VAL	HB	3.6	0.0	3.637–3.747
3	6	GLY	H	5	VAL	H	4.7	0.0	4.716–4.726
2	2	VAL	H	1	LEU	HB#	4.1	0.0	4.253–4.368
2	1	LEU	HA	1	LEU	HD#	4.3	0.0	4.328–4.342
2	1	LEU	H	6	GLY	HA#	3.4	0.0	3.422–3.449

	Res #	Dihedral	Upper	Lower	Range of violations
77	5	VAL (ϕ)	−90.0	−150.0	−89.705 to −50.748



TVGGVG

Simulated annealing starting from initial structure #1

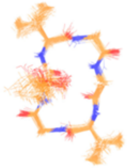


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
23	4	GLY	HA#	1	THR	HG#	5.6	0.0	5.631–8.020
21	2	VAL	H	1	THR	HB	3.6	0.0	3.790–4.462
16	2	VAL	H	2	VAL	HB	3.5	0.0	3.645–3.934
10	6	GLY	H	5	VAL	HA	3.4	0.0	3.536–3.624
9	5	VAL	H	5	VAL	HB	3.7	0.0	3.724–3.941
4	2	VAL	H	1	THR	HA	3.5	0.0	3.599–3.656
4	2	VAL	H	1	THR	H	4.6	0.0	4.609–4.646
3	3	GLY	H	2	VAL	HG#	4.2	0.0	4.319–4.396
3	1	THR	H	1	THR	HG#	4.1	0.0	4.392–4.660
2	3	GLY	H	4	GLY	H	3.8	0.0	4.385–4.444
1	6	GLY	H	5	VAL	HG#	4.6	0.0	4.608
1	5	VAL	H	4	GLY	HA#	3.5	0.0	3.572
1	5	VAL	H	4	GLY	H	4.7	0.0	4.819

	Res #	Dihedral	Upper	Lower	Range of violations
18	1	THR (ϕ)	−90.0	−150.0	−151.143 to −150.022; −89.061
67	5	VAL (ϕ)	−90.0	−150.0	−89.931 to −87.039

Simulated annealing starting from initial structure #2

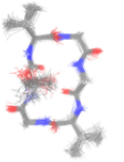


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
17	4	GLY	HA#	1	THR	HG#	5.6	0.0	5.646–6.744
17	2	VAL	H	1	THR	HB	3.6	0.0	3.707–4.044
11	6	GLY	H	5	VAL	HA	3.4	0.0	3.493–3.608
11	2	VAL	H	2	VAL	HB	3.5	0.0	3.641–3.830
6	5	VAL	H	5	VAL	HB	3.7	0.0	3.735–3.856
2	2	VAL	H	1	THR	H	4.6	0.0	4.621–4.627
1	3	GLY	H	4	GLY	H	3.8	0.0	4.308

	Res #	Dihedral	Upper	Lower	Range of violations
10	1	THR (ϕ)	−90.0	−150.0	−152.027 to −150.312; −89.718
65	5	VAL (ϕ)	−90.0	−150.0	−89.975 to −86.881

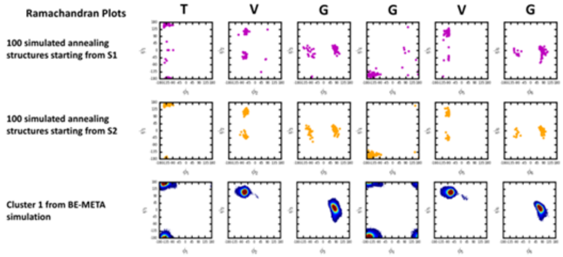
Number of violations of the predicted top cluster

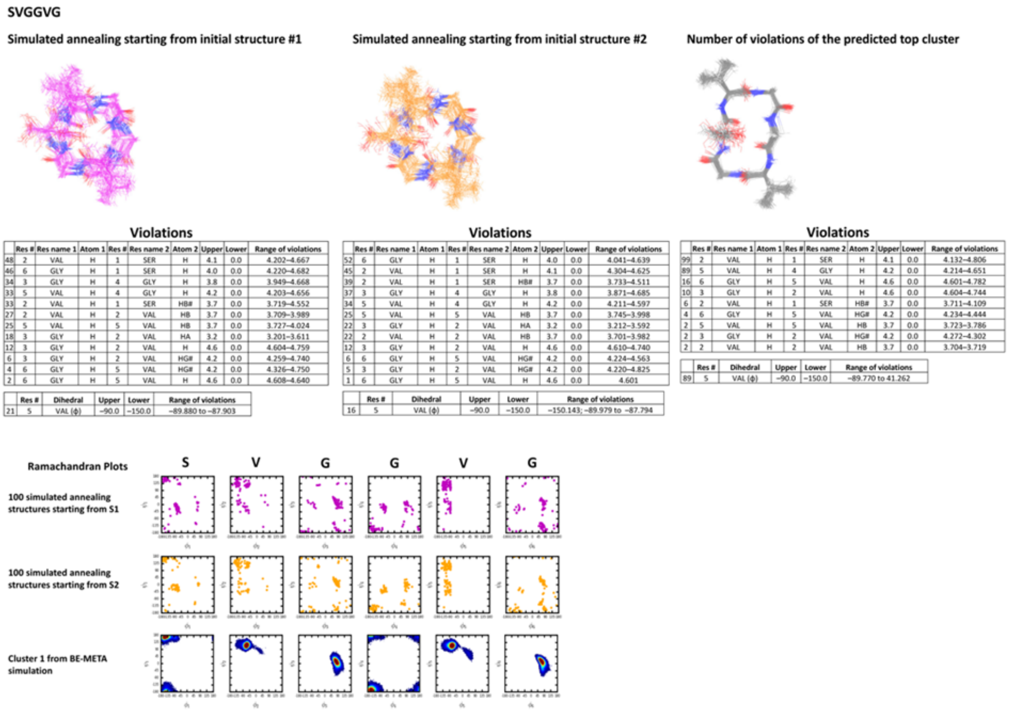


Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
53	2	VAL	H	1	THR	HB	3.6	0.0	3.601–4.164
10	4	GLY	HA#	1	THR	HG#	5.6	0.0	5.604–6.564
9	2	VAL	H	1	THR	H	4.6	0.0	4.609–4.777
1	3	GLY	H	2	VAL	HG#	4.2	0.0	4.319
1	2	VAL	H	2	VAL	HB	3.5	0.0	3.731
1	1	THR	H	1	THR	HG#	4.1	0.0	4.567

	Res #	Dihedral	Upper	Lower	Range of violations
37	1	THR (ϕ)	−90.0	−150.0	−175.136 to −150.161; −87.840
91	5	VAL (ϕ)	−90.0	−150.0	−87.369 to −42.814





SVGGVG

Simulated annealing starting from initial structure #1

Simulated annealing starting from initial structure #2

Number of violations of the predicted top cluster

Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
48	2	VAL	H	1	SER	H	4.1	0.0	4.202–4.667
46	6	GLY	H	1	SER	H	4.0	0.0	4.220–4.682
34	3	GLY	H	4	GLY	H	3.8	0.0	3.949–4.668
33	5	VAL	H	4	GLY	H	4.2	0.0	4.203–4.656
33	2	VAL	H	1	SER	HB#	3.7	0.0	3.719–4.552
27	2	VAL	H	2	VAL	HB	3.7	0.0	3.709–3.989
25	5	VAL	H	5	VAL	HB	3.7	0.0	3.727–4.024
18	3	GLY	H	2	VAL	HA	3.2	0.0	3.201–3.611
12	3	GLY	H	2	VAL	H	4.6	0.0	4.604–4.759
6	3	GLY	H	2	VAL	HG#	4.2	0.0	4.259–4.740
4	6	GLY	H	5	VAL	HG#	4.2	0.0	4.326–4.750
2	6	GLY	H	5	VAL	H	4.6	0.0	4.608–4.640

	Res #	Dihedral	Upper	Lower	Range of violations
21	5	VAL (ϕ)	−90.0	−150.0	−89.880 to −87.903

Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
52	6	GLY	H	1	SER	H	4.0	0.0	4.041–4.639
45	2	VAL	H	1	SER	H	4.1	0.0	4.304–4.625
39	2	VAL	H	1	SER	HB#	3.7	0.0	3.733–4.511
37	3	GLY	H	4	GLY	H	3.8	0.0	3.871–4.685
34	5	VAL	H	4	GLY	H	4.2	0.0	4.211–4.597
25	5	VAL	H	5	VAL	HB	3.7	0.0	3.745–3.998
22	3	GLY	H	2	VAL	HA	3.2	0.0	3.212–3.592
22	2	VAL	H	2	VAL	HB	3.7	0.0	3.701–3.982
12	3	GLY	H	2	VAL	H	4.6	0.0	4.610–4.740
6	6	GLY	H	5	VAL	HG#	4.2	0.0	4.224–4.563
5	3	GLY	H	2	VAL	HG#	4.2	0.0	4.220–4.825
1	6	GLY	H	5	VAL	H	4.6	0.0	4.601

	Res #	Dihedral	Upper	Lower	Range of violations
16	5	VAL (ϕ)	−90.0	−150.0	−150.143; −89.979 to −87.794

Violations

	Res #	Res name 1	Atom 1	Res #	Res name 2	Atom 2	Upper	Lower	Range of violations
99	2	VAL	H	1	SER	H	4.1	0.0	4.132–4.806
89	5	VAL	H	4	GLY	H	4.2	0.0	4.214–4.651
16	6	GLY	H	5	VAL	H	4.6	0.0	4.601–4.782
10	3	GLY	H	2	VAL	H	4.6	0.0	4.604–4.744
6	2	VAL	H	1	SER	HB#	3.7	0.0	3.711–4.109
4	6	GLY	H	5	VAL	HG#	4.2	0.0	4.234–4.444
2	5	VAL	H	5	VAL	HB	3.7	0.0	3.723–3.786
2	3	GLY	H	2	VAL	HG#	4.2	0.0	4.272–4.302
2	2	VAL	H	2	VAL	HB	3.7	0.0	3.704–3.719

	Res #	Dihedral	Upper	Lower	Range of violations
89	5	VAL (ϕ)	−90.0	−150.0	−89.770 to 41.262

Ramachandran Plots

100 simulated annealing structures starting from S1

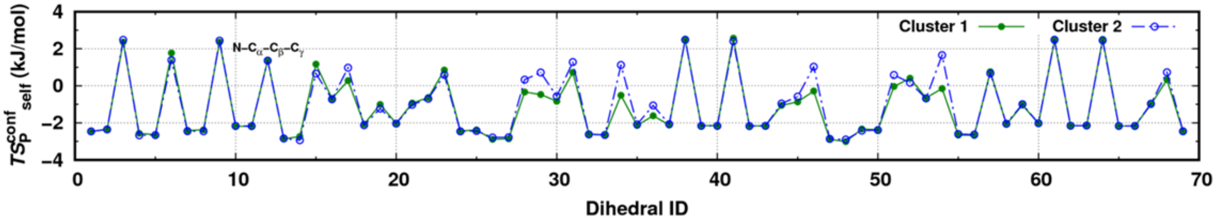
100 simulated annealing structures starting from S2

Cluster 1 from BE-META simulation

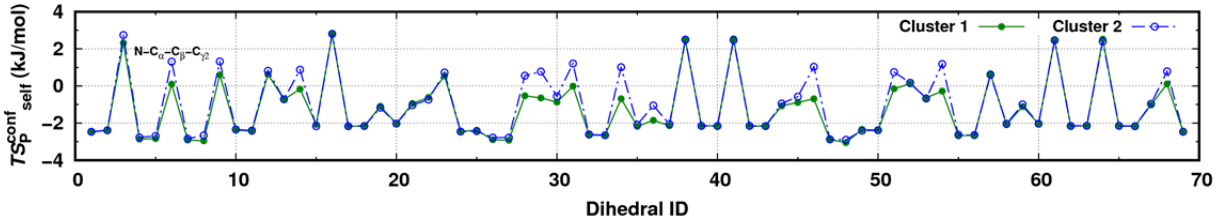
Figure S2. Simulated annealing results of P7, P6, V1A, V1I, V1L, V1T, and V1S using the distance and dihedral restraints derived from the experimental NOEs and *J*-couplings, along with the number of violations of the top clusters from the BE-META simulations. Throughout the simulated annealing protocol, NOE-based distance restraints (**Tables S6, S9, S12, S15, S18, S21, and S24**) were applied to the peptide with a force constant of 1,000 kJ/mol/rad^2 with the lower bounds changed to 0 Å. When there is degeneracy, the longer or shorter NOE-based distance restraints were kept in the simulated annealing simulations. From the *J*-coupling values, additional restraints are placed on the dihedral angles. For each CP, two different initial structures, S1 and S2, were first energy minimized in vacuum. Next, beginning with the minimized structure, 100 simulations were performed with different initial velocities and each replica was annealed from 300 K to 800 K in vacuum for 200 ps in an NVT ensemble. After annealing, each replica was solvated using pre-equilibrated water molecules. The box dimensions were chosen such that the minimum distance between the box walls and any atom of the CP was 1.0 nm. The entire system was then energy minimized using the steepest descent algorithm to remove any bad contacts. Next, the system underwent a 500 ps NVT equilibration at 300 K. Lastly, the system was annealed from 300 K to 500 K and then subsequently down to 5K over 1 ns in an NPT ensemble. The temperature was regulated using the v-rescale thermostat, with a coupling time constant of 0.1 ps. The pressure was regulated using the Berendsen barostat, with a time coupling constant of 2.0 ps and isothermal compressibility of 4.5×10^{-5} bar^{-1}. The leapfrog algorithm with an integration time step of 2 fs was used to evolve the dynamics of the system. The LINCS algorithm was used to constrain all peptide bonds containing hydrogen to their equilibration values. For vacuum simulation steps, all non-bonded (electrostatics and van der Waals) interaction cutoffs were set to 999.0 nm and the neighbor list was only constructed once and never updated. For simulation steps in solvent, all non-bonded interactions as well as neighbor searching were truncated at 1.0 nm. Long-range electrostatics beyond the 1.0 nm were calculated using the particle mesh Ewald (PME) method with a Fourier spacing of 0.12 nm and an interpolation order of 4. To account for truncation of the Lennard-Jones interactions, a long-range analytic dispersion correction was applied to both energy and pressure. After all simulation steps, the final frames from each of the 100 trajectories were used to calculate distance and dihedral violations.

(A)	$TS_{\mathrm{P}}{}^{\mathrm{conf}}{}_{\mathrm{self}}$ (kJ/mol)			$TS_{\mathrm{P}}{}^{\mathrm{conf}}{}_{\mathrm{mutual}}$ (kJ/mol)	$TS_{\mathrm{P}}{}^{\mathrm{conf}}$ (kJ/mol)
	Bond	Angle	Dihedral		
Cluster 1	–488.89	–257.90	–78.42	32.90	–858.11
Cluster 2	–488.86	–257.52	–70.37	32.21	–848.96

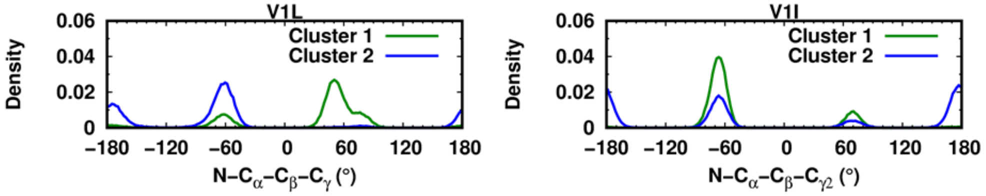
(B) V1L



(C) V1I



(D)



(E)

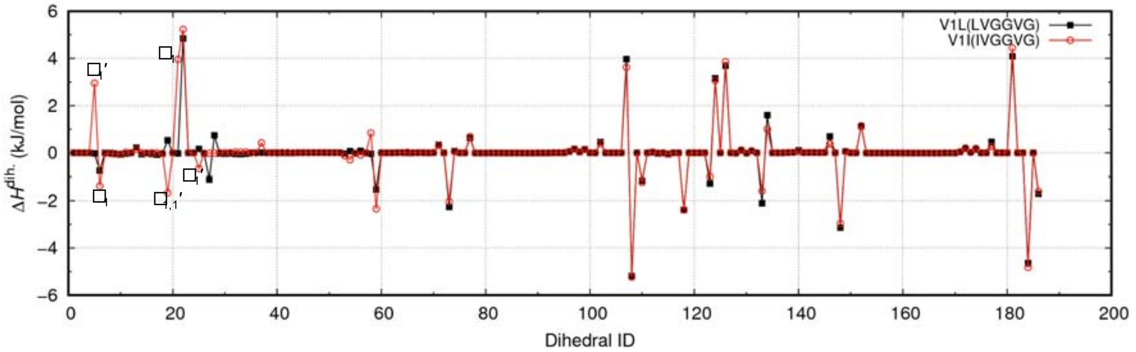


Figure S3. (A) The configurational entropy of V1L. $TS_{\mathrm{P}}{}^{\mathrm{conf}} = TS_{\mathrm{P}}{}^{\mathrm{conf}}{}_{\mathrm{self}} - TS_{\mathrm{P}}{}^{\mathrm{conf}}{}_{\mathrm{mutual}}$. **(B)** The configurational self-entropy for each dihedral degree of freedom of V1L. **(C)** The configurational self-entropy for each dihedral degree of freedom of V1I. Note that the dihedrals shown here were the chosen n–3 independent torsional degrees of freedom in the internal coordinate system of the molecule used in the PARENT program. **(D)** The distributions of the N-C$_{\alpha}$-C$_{\beta}$-C$_{\gamma}$ (χ_1) dihedral of the first residue for V1L (dihedral 12) and the distribution of N-C$_{\alpha}$-C$_{\beta}$-C$_{\gamma2}$ of the first residue for V1I (dihedral 6). **(E)** Decomposition of $\Delta H_{\mathrm{P}}{}^{\mathrm{dih.}}$ into contributions of each dihedral for V1L and V1I. The major contributions to $\Delta H_{\mathrm{P}}{}^{\mathrm{dih.}}$ come from dihedrals 5, 6, 19, 21, and 25, which are just the dihedrals ϕ', ϕ, χ_1', ψ, and ψ' of the first residue.

II. NMR data tables and spectra

Table S4. NOEs for P7, cyclo-(VVGGVG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
9.07	3Gly-NH	3.77	3Gly-Haa
9.07	3Gly-NH	4.14	3Gly-Hab
8.97	6Gly-NH	3.74	6Gly-Haa
8.97	6Gly-NH	4.13	6Gly-Hab
8.15	4Gly-NH	3.65	4Gly-Haa
8.65	5Val-NH	4.15	5Val-Ha
8.38	2Val-NH	3.90	2Val-Ha
8.15	4Gly-NH	4.34	4Gly-Hab
7.39	1Val-NH	4.47	1Val-Ha
8.66	5Val-NH	2.05	5Val-Hb
8.37	2Val-NH	1.98	2Val-Hb
7.39	1Val-NH	2.20	1Val-Hb
8.66	5Val-NH	0.96	5Val-Hga
8.37	2Val-NH	0.93	2Val-Hga
7.39	1Val-NH	0.69	1Val-Hga
7.39	1Val-NH	0.87	1Val-Hgb
8.37	2Val-NH	1.03	2Val-Hgb
4.47	1Val-Ha	2.19	1Val-Hb
4.15	5Val-Ha	2.05	5Val-Hb
3.90	2Val-Ha	1.98	2Val-Hb
3.90	2Val-Ha	0.93	2Val-Hga
3.90	2Val-Ha	1.03	2Val-Hgb
4.47	1Val-Ha	0.69	1Val-Hga
4.47	1Val-Ha	0.88	1Val-Hgb
4.15	5Val-Ha	0.94	5Val-Hga
9.07	3Gly-NH	3.90	2Val-Ha
8.15	4Gly-NH	4.14	3Gly-Hab
8.66	5Val-NH	3.64	4Gly-Haa
8.97	6Gly-NH	4.16	5Val-Ha
7.39	1Val-NH	4.13	6Gly-Hab
8.38	2Val-NH	4.47	1Val-Ha
8.15	4Gly-NH	3.77	3Gly-Haa
7.39	1Val-NH	3.73	6Gly-Haa
8.66	5Val-NH	4.34	4Gly-Hab
8.37	2Val-NH	2.20	1Val-Hb
8.37	2Val-NH	0.68	1Val-Hga
9.07	3Gly-NH	0.94	2Val-Hga
3.90	2Val-Ha	0.69	1Val-Hga
8.66	5Val-NH	4.33	4Gly-Hab
8.97	6Gly-NH	2.05	5Val-Hb
9.07	3Gly-NH	1.98	2Val-Hb
9.07	3Gly-NH	1.04	2Val-Hgb
8.97	6Gly-NH	7.39	1Val-NH
9.07	3Gly-NH	8.15	4Gly-NH
8.38	2Val-NH	7.39	1Val-NH
8.66	5Val-NH	8.15	4Gly-NH
8.15	4Gly-NH	0.69	1Val-Hga
8.15	4Gly-NH	3.91	2Val-Ha
8.66	5Val-NH	0.69	1Val-Hga

8.14	4Gly-NH	0.87	1Val-Hgb
3.64	4Gly-Haa	0.69	1Val-Hga
3.64	4Gly-Haa	0.88	1Val-Hgb

Table S5. *J*-coupling values and associated torsional restraints for P7, cyclo-(VVGGVG). If the coupling constant was ≤ 5 Hz, a dihedral restraint of –60° ± 30° was assigned; if the coupling constant was ≥ 8 Hz, a dihedral restraint of –120° ± 30° was assigned.

Residue	$^3J_{\mathrm{NHCH}\alpha}$ (Hz)	φ restraints (˚)
V_1	8.1	–120 ± 30
V_2	4.7	–60 ± 30
G_3	6.3	
G_4	7.3	
V_5	8.7	–120 ± 30
G_6	6.2	

Table S6. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for P7, cyclo-(VVGGVG). The list was generated using CNSsolve (1, 2). In the list of distance restraints, the first number was the distance value between the two atoms in Å, and the second and third numbers were subtracted and added from the first number to obtain the lower and upper bounds, respectively. In the list of dihedral restraints, the first number was the energy constant (1.0), the second the value of the dihedral in degrees, the third the range around the dihedral (±), and the last the exponent of the restraining function.

Distance constraints:

```
assign ( resid 1 and name HN ) ( resid 1 and name HA ) 3.6 0.7 0.7
assign ( resid 1 and name HN ) ( resid 1 and name HB ) 4.3 0.9 0.9
assign ( resid 1 and name HN ) ( resid 1 and name HG1# ) 3.7 0.7 0.7
assign ( resid 1 and name HN ) ( resid 1 and name HG2# ) 4.1 0.8 0.8
assign ( resid 1 and name HN ) ( resid 6 and name HA2 ) 3.5 0.7 0.7
assign ( resid 1 and name HN ) ( resid 6 and name HA1 ) 4.2 0.8 0.8
assign ( resid 1 and name HA ) ( resid 1 and name HG1# ) 3.3 0.7 0.7
assign ( resid 1 and name HA ) ( resid 1 and name HG2# ) 2.8 0.6 0.6
assign ( resid 1 and name HA ) ( resid 1 and name HB ) 2.6 0.5 0.5

assign ( resid 2 and name HN ) ( resid 2 and name HA ) 3.5 0.7 0.7
assign ( resid 2 and name HN ) ( resid 2 and name HB ) 3.0 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HG2# ) 4.1 0.8 0.8
assign ( resid 2 and name HN ) ( resid 2 and name HG1# ) 3.2 0.6 0.6
assign ( resid 2 and name HN ) ( resid 1 and name HA ) 2.9 0.6 0.6
assign ( resid 2 and name HN ) ( resid 1 and name HB ) 3.1 0.6 0.6
assign ( resid 2 and name HN ) ( resid 1 and name HG1# ) 4.1 0.8 0.8
assign ( resid 2 and name HN ) ( resid 1 and name HN ) 5.0 1.0 1.0
assign ( resid 2 and name HA ) ( resid 2 and name HG2# ) 2.9 0.6 0.6
assign ( resid 2 and name HA ) ( resid 2 and name HG1# ) 2.7 0.5 0.5
assign ( resid 2 and name HA ) ( resid 1 and name HG1# ) 5.0 1.0 1.0
assign ( resid 2 and name HA ) ( resid 2 and name HB ) 3.0 0.6 0.6

assign ( resid 3 and name HN ) ( resid 3 and name HA1 ) 2.9 0.6 0.6
assign ( resid 3 and name HN ) ( resid 3 and name HA2 ) 4.2 0.8 0.8
assign ( resid 3 and name HN ) ( resid 2 and name HA ) 2.7 0.5 0.5
assign ( resid 3 and name HN ) ( resid 2 and name HG2# ) 4.0 0.8 0.8
assign ( resid 3 and name HN ) ( resid 4 and name HN ) 3.5 0.7 0.7

assign ( resid 4 and name HN ) ( resid 4 and name HA1 ) 3.3 0.7 0.7
assign ( resid 4 and name HN ) ( resid 4 and name HA2 ) 3.5 0.7 0.7
```

```
assign ( resid 4 and name HN ) ( resid 3 and name HA2 ) 3.7 0.7 0.7
assign ( resid 4 and name HN ) ( resid 3 and name HA1 ) 3.9 0.8 0.8
assign ( resid 4 and name HN ) ( resid 1 and name HG1# ) 4.1 0.8 0.8

assign ( resid 5 and name HN ) ( resid 5 and name HA ) 3.6 0.7 0.7
assign ( resid 5 and name HN ) ( resid 5 and name HB ) 3.2 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HG1# ) 3.6 0.7 0.7
assign ( resid 5 and name HN ) ( resid 4 and name HA2 ) 2.9 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HN ) 5.1 1.0 1.0
assign ( resid 5 and name HA ) ( resid 5 and name HG1# ) 2.7 0.5 0.5
assign ( resid 5 and name HA ) ( resid 5 and name HB ) 3.2 0.6 0.6

assign ( resid 6 and name HN ) ( resid 6 and name HA1 ) 2.9 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA2 ) 2.7 0.5 0.5
assign ( resid 6 and name HN ) ( resid 5 and name HA ) 2.7 0.5 0.5
assign ( resid 6 and name HN ) ( resid 1 and name HN ) 3.8 0.8 0.8
```

Phi dihedral angle constraints:

```
assign ( resid 6 and name c ) ( resid 1 and name n )
       ( resid 1 and name ca ) ( resid 1 and name c ) 1.0 -120.0 30.0 2
assign ( resid 1 and name c ) ( resid 2 and name n )
       ( resid 2 and name ca ) ( resid 2 and name c ) 1.0 -60.0 30.0 2
assign ( resid 4 and name c ) ( resid 5 and name n )
       ( resid 5 and name ca ) ( resid 5 and name c ) 1.0 -120.0 30.0 2
```

Table S7. NOEs for P6, cyclo-(VVGVGG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
8.96	5Gly-NH	3.86	5Gly-Haa
8.96	5Gly-NH	4.07	5Gly-Hab
8.02	2Val-NH	4.18	2Val-Ha
7.80	6Gly-NH	3.91	6Gly-Haa
7.80	6Gly-NH	4.24	6Gly-Hab
8.34	4Val-NH	3.94	4Val-Ha
8.33	1Val-NH	4.00	1Val-Ha
8.29	3Gly-NH	3.85	3Gly-Haa
8.29	3Gly-NH	4.05	3Gly-Hab
8.28	3Gly-NH	2.09	2Val-Hb
8.96	5Gly-NH	0.94	4Val-Hga
8.97	5Gly-NH	2.05	4Val-Hb
8.34	4Val-NH	2.04	4Val-Hb
8.32	1Val-NH	2.11	1Val-Hb
8.02	2Val-NH	2.90	2Val-Hb
8.32	1Val-NH	1.00	1Val-Hga
8.02	2Val-NH	0.91	2Val-Hga
8.34	4Val-NH	0.94	4Val-Hga
4.17	2Val-Ha	2.08	2Val-Hb
4.00	1Val-Ha	2.12	1Val-Hb
3.94	4Val-Ha	2.05	4Val-Hb
4.17	2Val-Ha	0.92	2Val-Hga
4.00	1Val-Ha	1.00	1Val-Hga
3.94	4Val-Ha	1.00	4Val-Hgb
3.93	4Val-Ha	0.94	4Val-Hga
8.32	1Val-NH	4.24	6Gly-Hab
8.29	3Gly-NH	4.18	2Val-Ha

8.03	2Val-NH	4.01	1Val-Ha
7.80	6Gly-NH	4.07	5Gly-Hab
8.97	5Gly-NH	3.94	4Val-Ha
8.34	4Val-NH	3.85	3Gly-Haa
8.34	4Val-NH	4.05	3Gly-Hab
8.96	5Gly-NH	7.80	6Gly-NH
8.33	1Val-NH	7.80	6Gly-NH
8.32	1Val-NH	8.03	2Val-NH
8.96	5Gly-NH	8.34	4Val-NH
8.29	3Gly-NH	8.03	2Val-NH
8.02	2Val-NH	3.91	6Gly-Haa

Table S8. *J*-coupling values and associated torsional restraints for P6, cyclo-(VVGVGG).

Residue	$^{3}J_{\mathrm{NHCH}\alpha}$ (Hz)	φ restraints (˚)
V_1	7.9	
V_2	9.5	–120 ± 30
G_3	5.8	
V_4	6.5	
G_5	6.8	
G_6	–	

Table S9. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for P6, cyclo-(VVGVGG).

Distance constraints:

```
assign ( resid 1 and name HN ) ( resid 1 and name HA ) 3.5 0.7 0.7
assign ( resid 1 and name HN ) ( resid 1 and name HB ) 3.2 0.6 0.6
assign ( resid 1 and name HN ) ( resid 1 and name HG2# ) 3.0 0.6 0.6
assign ( resid 1 and name HA ) ( resid 1 and name HB ) 2.9 0.6 0.6
assign ( resid 1 and name HA ) ( resid 1 and name HG2# ) 2.6 0.5 0.5
assign ( resid 1 and name HN ) ( resid 6 and name HN ) 4.2 0.8 0.8
assign ( resid 1 and name HN ) ( resid 2 and name HN ) 3.3 0.7 0.7
assign ( resid 1 and name HN ) ( resid 6 and name HA1 ) 3.5 0.7 0.7

assign ( resid 2 and name HA ) ( resid 2 and name HB ) 3.0 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HA ) 3.3 0.7 0.7
assign ( resid 2 and name HN ) ( resid 2 and name HB ) 3.2 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HG1# ) 3.5 0.7 0.7
assign ( resid 2 and name HA ) ( resid 2 and name HG1# ) 2.7 0.5 0.5
assign ( resid 2 and name HN ) ( resid 6 and name HA2 ) 4.3 0.9 0.9
assign ( resid 2 and name HN ) ( resid 1 and name HA ) 3.6 0.7 0.7

assign ( resid 3 and name HN ) ( resid 3 and name HA1 ) 3.0 0.6 0.6
assign ( resid 3 and name HN ) ( resid 3 and name HA2 ) 3.4 0.7 0.7
assign ( resid 3 and name HN ) ( resid 2 and name HB ) 3.9 0.8 0.8
assign ( resid 3 and name HN ) ( resid 2 and name HN ) 3.7 0.7 0.7
assign ( resid 3 and name HN ) ( resid 2 and name HA ) 2.8 0.6 0.6

assign ( resid 4 and name HN ) ( resid 4 and name HA ) 3.2 0.6 0.6
assign ( resid 4 and name HN ) ( resid 4 and name HB ) 3.1 0.6 0.6
assign ( resid 4 and name HN ) ( resid 4 and name HG1# ) 3.9 0.8 0.8
assign ( resid 4 and name HA ) ( resid 4 and name HB ) 3.1 0.6 0.6
assign ( resid 4 and name HA ) ( resid 4 and name HG2# ) 2.8 0.6 0.6
assign ( resid 4 and name HA ) ( resid 4 and name HG1# ) 2.9 0.6 0.6
```

```
assign ( resid 4 and name HN ) ( resid 3 and name HA1 ) 3.2 0.6 0.6
assign ( resid 4 and name HN ) ( resid 3 and name HA2 ) 2.9 0.6 0.6

assign ( resid 5 and name HN ) ( resid 5 and name HA1 ) 3.1 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HA2 ) 3.6 0.7 0.7
assign ( resid 5 and name HN ) ( resid 6 and name HN ) 3.5 0.7 0.7
assign ( resid 5 and name HN ) ( resid 4 and name HN ) 4.1 0.8 0.8
assign ( resid 5 and name HN ) ( resid 4 and name HG1# ) 4.0 0.8 0.8
assign ( resid 5 and name HN ) ( resid 4 and name HB ) 4.9 1.0 1.0
assign ( resid 5 and name HN ) ( resid 4 and name HA ) 2.8 0.6 0.6

assign ( resid 6 and name HN ) ( resid 6 and name HA2 ) 3.0 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA1 ) 3.5 0.7 0.7
assign ( resid 6 and name HN ) ( resid 5 and name HA2 ) 3.7 0.7 0.7
```

Phi dihedral angle constraints:

```
assign ( resid 1 and name c ) ( resid 2 and name n )
         ( resid 2 and name ca ) ( resid 2 and name c ) 1.0 -120.0 30.0 2
```

Table S10. NOEs for V1I, cyclo-(IVGGVG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
9.00	3Gly-NH	3.77	3Gly-Haa
8.92	6Gly-NH	3.73	6Gly-Haa
8.56	5Val-NH	4.14	5Val-Ha
8.14	4Gly-NH	3.68	4Gly-Haa
8.14	4Gly-NH	4.30	4Gly-Hab
7.45	1Ile-NH	4.47	1Ile-Ha
8.99	3Gly-NH	4.13	3Gly-Hab
8.26	2Val-NH	3.94	2Val-Ha
8.92	6Gly-NH	4.11	6Gly-Hab
8.56	5Val-NH	2.05	5Val-Hb
8.56	5Val-NH	0.96	5Val-Hga
8.27	2Val-NH	1.99	2Val-Hb
8.27	2Val-NH	1.00	2Val-Hgb
8.27	2Val-NH	0.93	2Val-Hga
7.46	1Ile-NH	0.86	1Ile-Hd1
7.45	1Ile-NH	0.96	1Ile-Hg2
7.45	1Ile-NH	1.91	1Ile-Hb
7.45	1Ile-NH	1.14	1Ile-Hg1a
4.46	1Ile-Ha	0.86	1Ile-Hd1
4.46	1Ile-Ha	1.91	1Ile-Hb
4.46	1Ile-Ha	1.14	1Ile-Hg1a
4.15	5Val-Ha	2.06	5Val-Hb
1.91	1Ile-Hb	1.14	1Ile-Hg1a
1.99	2Val-Hb	1.03	2Val-Hgb
0.97	1Ile-Hb	1.15	1Ile-Hg1a
0.85	1Ile-Hg2	1.15	1Ile-Hg1a
4.15	5Val-Ha	0.97	5Val-Hga
3.93	2Val-Ha	0.93	2Val-Hga
3.93	2Val-Ha	1.03	2Val-Hgb
3.94	2Val-Ha	2.00	2Val-Hb
9.00	3Gly-NH	3.94	2Val-Ha
8.56	5Val-NH	3.68	4Gly-Haa
8.56	5Val-NH	4.30	4Gly-Hab

8.26	2Val-NH	4.47	1Ile-Ha
8.14	4Gly-NH	3.77	3Gly-Haa
8.14	4Gly-NH	4.13	3Gly-Hab
7.45	1Ile-NH	3.74	6Gly-Haa
7.45	1Ile-NH	4.11	6Gly-Hab
8.92	6Gly-NH	4.14	5Val-Ha
9.00	3Gly-NH	1.98	2Val-Hb
8.92	6Gly-NH	2.05	5Vla-Hb
9.00	3Gly-NH	1.02	2ValHgb
9.00	3Gly-NH	0.93	2Val-Hga
8.27	2Val-NH	1.14	1Ile-Hg1a
8.26	2Val-NH	0.84	1Ile-Hd1
8.26	2Val-NH	1.91	1Ile-Hb
1.91	2Val-Hb	0.85	1Ile-Hb
2.01	1Ile-Hd1	0.93	2Val-Hga
8.27	2Val-NH	7.45	1Ile-NH
9.00	3Gly-NH	8.14	4Gly-NH
8.56	5Val-NH	8.14	4Gly-NH
8.92	6Gly-NH	7.47	1Ile-NH
8.14	4Gly-NH	3.95	2Val-Ha
8.14	4Gly-NH	1.14	1Ile-Hg1a
8.13	4Gly-NH	0.85	1Ile-Hd1
3.67	4Gly-Haa	1.14	1Ile-Hg1a
3.67	4Gly-Haa	0.95	5Val-Hga
3.67	4Gly-Haa	0.85	1Ile-Hd1
2.06	2Val-Hb	0.94	5Val-Hga

Table S11. *J*-coupling values and associated torsional restraints for V1I, cyclo-(IVGGVG).

Residue	$^3J_{\text{NHCH}\alpha}$ (Hz)	φ restraints (˚)
I_1	8.0	–120 ± 30
V_2	5.1	
G_3	6.4	
G_4	7.3	
V_5	9.0	–120 ± 30
G_6	6.2	

Table S12. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for V1I, cyclo-(IVGGVG).

Distance constraints:

assign (resid 1 and name HN) (resid 1 and name HA) 4.6 0.9 0.9
assign (resid 1 and name HN) (resid 6 and name HA2) 4.2 0.8 0.8
assign (resid 1 and name HN) (resid 6 and name HA1) 3.5 0.7 0.7
assign (resid 1 and name HN) (resid 1 and name HD1#) 3.6 0.7 0.7
assign (resid 1 and name HN) (resid 1 and name HG2#) 3.6 0.7 0.7
assign (resid 1 and name HN) (resid 1 and name HB) 4.0 0.8 0.8
assign (resid 1 and name HN) (resid 1 and name HG13) 4.1 0.8 0.8
assign (resid 1 and name HA) (resid 1 and name HD1#) 3.7 0.7 0.7
assign (resid 1 and name HA) (resid 1 and name HB) 3.6 0.7 0.7
assign (resid 1 and name HA) (resid 1 and name HG13) 4.6 0.9 0.9
assign (resid 1 and name HB) (resid 1 and name HG13) 3.2 0.6 0.6
assign (resid 1 and name HB) (resid 1 and name HD1#) 2.7 0.5 0.5
assign (resid 1 and name HG2#) (resid 1 and name HG13) 2.6 0.5 0.5

```
assign ( resid 1 and name HD1# ) ( resid 1 and name HG13 ) 2.3 0.5 0.5

assign ( resid 2 and name HN ) ( resid 2 and name HA ) 3.2 0.6 0.6
assign ( resid 2 and name HN ) ( resid 1 and name HA ) 2.8 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HB ) 2.9 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HG2# ) 2.9 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HG1# ) 3.6 0.7 0.7
assign ( resid 2 and name HN ) ( resid 1 and name HG13 ) 3.9 0.8 0.8
assign ( resid 2 and name HN ) ( resid 1 and name HD1# ) 4.0 0.8 0.8
assign ( resid 2 and name HN ) ( resid 1 and name HB ) 3.1 0.6 0.6
assign ( resid 2 and name HA ) ( resid 2 and name HG1# ) 3.2 0.6 0.6
assign ( resid 2 and name HA ) ( resid 2 and name HG2# ) 3.0 0.6 0.6
assign ( resid 2 and name HA ) ( resid 2 and name HB ) 3.1 0.6 0.6
assign ( resid 2 and name HB ) ( resid 2 and name HG2# ) 2.9 0.6 0.6
assign ( resid 2 and name HB ) ( resid 2 and name HG1# ) 2.7 0.5 0.5
assign ( resid 2 and name HN ) ( resid 1 and name HN ) 4.3 0.9 0.9

assign ( resid 3 and name HN ) ( resid 3 and name HA2 ) 2.8 0.6 0.6
assign ( resid 3 and name HN ) ( resid 3 and name HA1 ) 4.5 0.9 0.9
assign ( resid 3 and name HN ) ( resid 2 and name HA ) 2.5 0.5 0.5
assign ( resid 3 and name HN ) ( resid 2 and name HB ) 4.4 0.9 0.9
assign ( resid 3 and name HN ) ( resid 2 and name HG2# ) 4.1 0.8 0.8
assign ( resid 3 and name HN ) ( resid 2 and name HG1# ) 3.5 0.7 0.7
assign ( resid 3 and name HN ) ( resid 4 and name HN ) 3.2 0.6 0.6

assign ( resid 4 and name HN ) ( resid 4 and name HA1 ) 3.2 0.6 0.6
assign ( resid 4 and name HN ) ( resid 4 and name HA2 ) 3.4 0.7 0.7
assign ( resid 4 and name HN ) ( resid 3 and name HA2 ) 3.8 0.8 0.8
assign ( resid 4 and name HN ) ( resid 2 and name HA ) 4.2 0.8 0.8
assign ( resid 4 and name HN ) ( resid 5 and name HA ) 3.6 0.7 0.7
assign ( resid 4 and name HN ) ( resid 1 and name HG13 ) 3.7 0.7 0.7
assign ( resid 4 and name HN ) ( resid 1 and name HD1# ) 4.2 0.8 0.8
assign ( resid 4 and name HA1 ) ( resid 1 and name HG13 ) 5.1 1.0 1.0
assign ( resid 4 and name HA1 ) ( resid 1 and name HG2# ) 6.3 1.3 1.3
assign ( resid 4 and name HA1 ) ( resid 1 and name HD1# ) 4.6 0.9 0.9

assign ( resid 5 and name HN ) ( resid 5 and name HA ) 3.2 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HA1 ) 3.0 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HA2 ) 4.1 0.8 0.8
assign ( resid 5 and name HN ) ( resid 5 and name HB ) 3.2 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HG1# ) 3.2 0.6 0.6
assign ( resid 5 and name HA ) ( resid 5 and name HG1# ) 3.3 0.7 0.7
assign ( resid 5 and name HA ) ( resid 5 and name HB ) 3.5 0.7 0.7
assign ( resid 5 and name HB ) ( resid 5 and name HG1# ) 3.0 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HN ) 4.7 0.9 0.9

assign ( resid 6 and name HN ) ( resid 6 and name HA2 ) 2.8 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA1 ) 3.0 0.6 0.6
assign ( resid 6 and name HN ) ( resid 5 and name HB ) 4.4 0.9 0.9
assign ( resid 6 and name HN ) ( resid 1 and name HN ) 3.6 0.7 0.7
```

Phi dihedral angle constraints:

```
assign ( resid 6 and name c ) ( resid 1 and name n )
        ( resid 1 and name ca ) ( resid 1 and name c ) 1.0 -120.0 30.0 2
assign ( resid 4 and name c ) ( resid 5 and name n )
        ( resid 5 and name ca ) ( resid 5 and name c ) 1.0 -120.0 30.0 2
```

Table S13. NOEs for V1L, cyclo-(LVGGVG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
8.81	3Gly-NH	3.08	3Gly-Haa
8.81	3Gly-NH	4.04	3Gly-Hab
8.71	6Gly-NH	3.75	6Gly-Haa
8.71	6Gly-NH	4.04	6Gly-Hab
8.42	4Gly-NH	3.97	4Gly-Haa
8.05	5Val-Ha	4.17	5Val-Ha
7.97	2Val-NH	4.16	2Val-Ha
8.32	1Leu-NH	4.34	1Leu-Ha
8.05	5Val-Ha	2.10	5Val-Hb
7.97	2Val-NH	2.03	2Val-Hb
8.32	1Leu-NH	1.65	1Leu-Hba
8.32	1Leu-NH	0.87	1Leu-Hda
7.97	2Val-NH	0.95	2Val-Hgb
8.05	5Val-Ha	0.91	5Val-Hga
4.33	1Leu-Ha	0.86	1Leu-Hda
4.34	1Leu-Ha	1.69	1Leu-Hba
4.18	5Val-Ha	2.11	5Val-Hb
4.16	2Val-Ha	2.04	2Val-Hb
2.04	2Val-Hb	0.93	2Val-Hgb
2.10	5Val-Hb	0.93	5Val-Hga
1.70	1Leu-Hba	0.87	1Leu-Hda
1.64	1Leu-Hbb	0.87	1Leu-Hda
7.97	2Val-NH	0.88	2Val-Hga
4.17	5Val-Ha	0.92	5Val-Hga
4.15	2Val-Ha	0.92	2Val-Hga
4.15	2Val-Ha	0.97	2Val-Hgb
8.81	3Gly-NH	4.16	2Val-Ha
8.71	6Gly-NH	4.17	5Val-Ha
8.42	4Gly-NH	3.80	3Gly-Haa
8.42	4Gly-NH	4.04	3Gly-Hab
8.31	1Leu-NH	3.75	6Gly-Haa
8.32	1Leu-NH	4.05	6Gly-Hab
7.97	2Val-NH	4.34	1Leu-Ha
8.05	5Val-NH	3.97	4Gly-Haa
7.97	2Val-NH	1.67	1Leu-Hba
8.81	3Gly-NH	2.03	2Val-Hb
8.72	6Gly-NH	2.10	5Val-Hb
8.81	3Gly-NH	0.92	2Val-Hgb
8.71	6Gly-NH	0.92	5Val-Hga
4.04	6Gly-Hab	0.92	5Val-Hga
3.97	4Gly-Haa	0.93	5Val-Hga
8.81	3Gly-NH	7.98	2Val-NH
8.71	6Gly-NH	8.05	5Val-NH
8.81	3Gly-NH	8.43	4Val-NH
8.71	6Gly-NH	8.32	1Leu-NH
8.43	4Gly-NH	8.06	5Val-NH
8.32	1Leu-NH	7.98	2Val-NH
8.42	4Gly-NH	0.89	2Val-Hga
3.96	4Gly-Haa	0.87	1Leu-Hda

Table S14. *J*-coupling values and associated torsional restraints for V1L, cyclo-(LVGGVG).

Residue	$^{3}J_{\mathrm{NHCH}\alpha}$ (Hz)	φ restraints (˚)
L_1	7.0	
V_2	7.6	
G_3	5.9	
G_4	5.6	
V_5	9.3	–120 ± 30
G_6	6.1	

Table S15. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for V1L, cyclo-(LVGGVG).

Distance constraints:
assign (resid 1 and name HN) (resid 1 and name HA) 3.7 0.7 0.7
assign (resid 1 and name HN) (resid 6 and name HA1) 4.0 0.8 0.8
assign (resid 1 and name HN) (resid 6 and name HA2) 2.8 0.6 0.6
assign (resid 1 and name HN) (resid 2 and name HA) 4.6 0.9 0.9
assign (resid 1 and name HN) (resid 1 and name HB2) 2.9 0.6 0.6
assign (resid 1 and name HN) (resid 1 and name HD1#) 3.7 0.7 0.7
assign (resid 1 and name HN) (resid 2 and name HN) 3.3 0.7 0.7
assign (resid 1 and name HA) (resid 1 and name HD1#) 3.6 0.7 0.7
assign (resid 1 and name HA) (resid 1 and name HB2) 4.8 1.0 1.0
assign (resid 1 and name HB1) (resid 1 and name HD1#) 3.0 0.6 0.6
assign (resid 1 and name HB2) (resid 1 and name HD1#) 2.5 0.5 0.5

assign (resid 2 and name HN) (resid 2 and name HA) 3.4 0.7 0.7
assign (resid 2 and name HN) (resid 1 and name HA) 3.1 0.6 0.6
assign (resid 2 and name HN) (resid 3 and name HA2) 4.5 0.9 0.9
assign (resid 2 and name HN) (resid 2 and name HB) 3.0 0.6 0.6
assign (resid 2 and name HN) (resid 1 and name HB2) 3.4 0.7 0.7
assign (resid 2 and name HN) (resid 2 and name HG2#) 3.0 0.6 0.6
assign (resid 2 and name HA) (resid 2 and name HB) 3.9 0.8 0.8
assign (resid 2 and name HB) (resid 2 and name HG2#) 2.9 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HG1#) 4.0 0.8 0.8
assign (resid 2 and name HA) (resid 2 and name HG1#) 2.9 0.6 0.6
assign (resid 2 and name HA) (resid 2 and name HG2#) 3.5 0.7 0.7

assign (resid 3 and name HN) (resid 3 and name HA1) 2.8 0.6 0.6
assign (resid 3 and name HN) (resid 3 and name HA2) 3.4 0.7 0.7
assign (resid 3 and name HN) (resid 2 and name HA) 2.6 0.5 0.5
assign (resid 3 and name HN) (resid 2 and name HG2#) 3.5 0.7 0.7
assign (resid 3 and name HN) (resid 2 and name HN) 4.2 0.8 0.8
assign (resid 3 and name HN) (resid 4 and name HN) 3.3 0.7 0.7
assign (resid 3 and name HN) (resid 2 and name HB) 4.1 0.8 0.8

assign (resid 4 and name HN) (resid 4 and name HA1) 2.6 0.5 0.5
assign (resid 4 and name HN) (resid 3 and name HA1) 3.5 0.7 0.7
assign (resid 4 and name HN) (resid 3 and name HA2) 3.2 0.6 0.6
assign (resid 4 and name HN) (resid 5 and name HA) 4.2 0.8 0.8
assign (resid 4 and name HN) (resid 2 and name HG1#) 4.5 0.9 0.9
assign (resid 4 and name HN) (resid 5 and name HN) 3.4 0.7 0.7
assign (resid 4 and name HA1) (resid 5 and name HG2#) 4.4 0.9 0.9
assign (resid 4 and name HA1) (resid 1 and name HD1#) 4.4 0.9 0.9

assign (resid 5 and name HN) (resid 5 and name HA) 4.1 0.8 0.8
assign (resid 5 and name HN) (resid 4 and name HA1) 2.9 0.6 0.6
assign (resid 5 and name HN) (resid 6 and name HA2) 4.3 0.9 0.9

```
assign ( resid 5 and name HN ) ( resid 5 and name HB ) 3.2 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HG2# ) 3.1 0.6 0.6
assign ( resid 5 and name HA ) ( resid 5 and name HB ) 3.6 0.7 0.7
assign ( resid 5 and name HB ) ( resid 5 and name HG2# ) 3.0 0.6 0.6
assign ( resid 5 and name HA ) ( resid 5 and name HG2# ) 3.1 0.6 0.6

assign ( resid 6 and name HN ) ( resid 6 and name HA1 ) 2.8 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA2 ) 3.3 0.7 0.7
assign ( resid 6 and name HN ) ( resid 5 and name HA ) 2.6 0.5 0.5
assign ( resid 6 and name HN ) ( resid 5 and name HB ) 4.2 0.8 0.8
assign ( resid 6 and name HN ) ( resid 5 and name HG2# ) 3.6 0.7 0.7
assign ( resid 6 and name HN ) ( resid 5 and name HN ) 3.9 0.8 0.8
assign ( resid 6 and name HN ) ( resid 1 and name HN ) 3.7 0.7 0.7
assign ( resid 6 and name HA2 ) ( resid 5 and name HG2# ) 8.0 1.6 0.0
```

Phi dihedral angle constraints:

```
assign ( resid 4 and name c ) ( resid 5 and name n )
        ( resid 5 and name ca ) ( resid 5 and name c ) 1.0 -120.0 30.0 2
```

Table S16. NOEs for V1T, cyclo-(TVGGVG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
8.97	6Gly-NH	3.80	6Gly-Haa
8.97	6Gly-NH	4.10	6Gly-Hab
8.90	3Gly-NH	3.87	3GLy-Haa
8.90	3Gly-NH	4.03	3GLy-Hab
8.42	5Val-NH	4.07	5Val-Ha
8.14	2Val-NH	4.01	2Val-Ha
7.96	4Gly-NH	3.74	4GLy-Haa
7.96	4Gly-NH	4.22	4GLy-Hab
7.74	1Thr-NH	4.52	1Thr-Ha
7.74	1Thr-NH	4.26	1THr-Hb
8.14	2Val-NH	2.03	2Val-Hb
8.43	5Val-NH	2.04	5Val-Hb
7.74	1Thr-NH	1.06	1Thr-Hg1
8.15	2Val-NH	1.01	2Val-Hgb
8.15	2Val-NH	0.93	2Val-Hga
8.43	5Val-NH	0.97	5Val-Hgb
8.43	5Val-NH	0.92	5Val-Hga
4.51	1Thr-Ha	1.06	1Thr-Hg1
4.25	1Thr-Hb	1.06	1Thr-Hg1
4.07	5Val-Ha	0.98	5Val-Hgb
4.07	5Val-Ha	0.93	5Val-Hga
4.02	2Val-Ha	1.01	2Val-Hgb
4.02	2Val-Ha	0.93	2Val-Hga
4.03	2Val-Ha	2.02	2Val-Ha
4.07	5Val-Ha	2.04	5Val-Hb
4.21	4Gly-Hab	3.74	4Gly-Haa
4.51	1Thr-Ha	4.26	1Thr-Hb
4.10	6Gly-Hab	3.80	6Gly-Haa
8.43	5Val-NH	3.74	4Gly-Haa
8.43	5Val-NH	4.23	4Gly-Hab
8.14	2Val-NH	4.26	1Thr-Hb
8.14	2Val-NH	4.51	1Thr-Ha
7.96	4Gly-NH	3.87	3Gly-Haa

7.96	4Gly-NH	4.04	3GLy-Hab
7.74	1Thr-NH	3.80	6Gly-Haa
7.75	1Thr-NH	4.10	6Gly-Hab
8.96	6Gly-NH	4.06	5Val-Ha
8.90	3Gly-NH	2.03	2Val-Hb
8.97	6Gly-NH	2.04	5Val-Hb
8.97	6Gly-NH	0.92	5Val-Hga
8.90	3Gly-NH	0.94	2Val-Hga
8.90	3Gly-NH	1.00	2Val-Hgb
3.74	4Gly-Haa	0.95	5Val-Hga
3.87	3Gly-Haa	0.93	2Val-Hga
8.97	6Gly-NH	7.75	1Thr-NH
8.90	3Gly-NH	7.96	4Gly-NH
8.90	3Gly-NH	8.15	2Val-NH
8.97	6Gly-NH	8.44	5Val-NH
8.42	5Val-NH	7.96	4Gly-NH
8.15	2Val-NH	7.74	1Thr-NH
3.74	4Gly-Haa	1.06	1Thr-Hg1

Table S17. *J*-coupling values and associated torsional restraints for V1T, cyclo-(TVGGVG).

Residue	$^{3}J_{\mathrm{NHCH}\alpha}$ (Hz)	φ restraints (˚)
T_1	8.1	–120 ± 30
V_2	6.1	
G_3	6.1	
G_4	6.8	
V_5	8.0	–120 ± 30
G_6	6.4	

Table S18. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for V1T, cyclo-(TVGGVG).

Distance constraints:
assign (resid 1 and name HN) (resid 1 and name HA) 3.2 0.6 0.6
assign (resid 1 and name HN) (resid 1 and name HB) 4.0 0.8 0.8
assign (resid 1 and name HN) (resid 6 and name HA2) 3.9 0.8 0.8
assign (resid 1 and name HN) (resid 6 and name HA1) 3.3 0.7 0.7
assign (resid 1 and name HN) (resid 1 and name HG1) 3.4 0.7 0.7
assign (resid 1 and name HA) (resid 1 and name HG1) 4.1 0.8 0.8
assign (resid 1 and name HB) (resid 1 and name HG1) 4.4 0.9 0.9
assign (resid 1 and name HA) (resid 1 and name HB) 3.9 0.8 0.8

assign (resid 2 and name HN) (resid 2 and name HA) 3.5 0.7 0.7
assign (resid 2 and name HN) (resid 1 and name HB) 3.0 0.6 0.6
assign (resid 2 and name HN) (resid 1 and name HA) 2.9 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HB) 2.9 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HG1#) 3.0 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HG2#) 3.4 0.7 0.7
assign (resid 2 and name HA) (resid 2 and name HG1#) 3.2 0.6 0.6
assign (resid 2 and name HA) (resid 2 and name HG2#) 3.2 0.6 0.6
assign (resid 2 and name HA) (resid 2 and name HB) 3.3 0.7 0.7
assign (resid 2 and name HN) (resid 1 and name HN) 3.8 0.8 0.8

assign (resid 3 and name HN) (resid 3 and name HA2) 2.9 0.6 0.6
assign (resid 3 and name HN) (resid 3 and name HA1) 2.6 0.5 0.5
assign (resid 3 and name HN) (resid 2 and name HB) 4.1 0.8 0.8

```
assign ( resid 3 and name HN ) ( resid 2 and name HG2# ) 3.5 0.7 0.7
assign ( resid 3 and name HN ) ( resid 2 and name HG1# ) 4.1 0.8 0.8
assign ( resid 3 and name HN ) ( resid 4 and name HN ) 3.2 0.6 0.6
assign ( resid 3 and name HN ) ( resid 2 and name HN ) 4.1 0.8 0.8

assign ( resid 4 and name HN ) ( resid 4 and name HA1 ) 3.3 0.7 0.7
assign ( resid 4 and name HN ) ( resid 4 and name HA2 ) 3.4 0.7 0.7
assign ( resid 4 and name HN ) ( resid 3 and name HA2 ) 3.8 0.8 0.8
assign ( resid 4 and name HN ) ( resid 3 and name HA1 ) 3.5 0.7 0.7
assign ( resid 4 and name HA1 ) ( resid 1 and name HG1 ) 4.7 0.9 0.9
assign ( resid 4 and name HA2 ) ( resid 4 and name HA1 ) 2.3 0.5 0.5

assign ( resid 5 and name HN ) ( resid 5 and name HA ) 3.2 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HA1 ) 2.9 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HA2 ) 3.6 0.7 0.7
assign ( resid 5 and name HN ) ( resid 5 and name HB ) 3.1 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HG1# ) 3.1 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HG2# ) 3.7 0.7 0.7
assign ( resid 5 and name HA ) ( resid 5 and name HG1# ) 3.5 0.7 0.7
assign ( resid 5 and name HA ) ( resid 5 and name HG2# ) 3.4 0.7 0.7
assign ( resid 5 and name HA ) ( resid 5 and name HB ) 3.3 0.7 0.7
assign ( resid 5 and name HN ) ( resid 4 and name HN ) 3.9 0.8 0.8

assign ( resid 6 and name HN ) ( resid 6 and name HA2 ) 2.9 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA1 ) 3.2 0.6 0.6
assign ( resid 6 and name HN ) ( resid 5 and name HA ) 2.8 0.6 0.6
assign ( resid 6 and name HN ) ( resid 5 and name HB ) 4.2 0.8 0.8
assign ( resid 6 and name HN ) ( resid 5 and name HG2# ) 3.8 0.8 0.8
assign ( resid 6 and name HA1 ) ( resid 6 and name HA2 ) 3.0 0.6 0.6
assign ( resid 6 and name HN ) ( resid 1 and name HN ) 3.3 0.7 0.7
assign ( resid 6 and name HN ) ( resid 5 and name HN ) 4.0 0.8 0.8
```

Phi dihedral angle constraints:

```
assign ( resid 6 and name c ) ( resid 1 and name n )
        ( resid 1 and name ca ) ( resid 1 and name c ) 1.0 -120.0 30.0 2
assign ( resid 4 and name c ) ( resid 5 and name n )
        ( resid 5 and name ca ) ( resid 5 and name c ) 1.0 -120.0 30.0 2
```

Table S19. NOEs for V1S, cyclo-(SVGGVG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
8.93	6Gly-NH	3.82	6Gly-Haa
8.93	6Gly-NH	4.08	6Gly-Hab
8.83	3Gly-NH	3.88	3Gly-Haa
8.83	3Gly-NH	4.01	3Gly-Hab
8.29	5Val-NH	4.10	5Val-Ha
8.19	2Val-NH	4.08	2Val-NH
8.09	4Gly-NH	3.84	4Gly-Haa
8.10	1Ser-NH	4.54	1Ser-Ha
8.09	4Gly-NH	4.13	4Gly-Hab
8.10	1Ser-NH	3.92	1Ser-Hbb
8.29	5Val-NH	2.05	5Val-Hb
8.19	2Val-NH	2.05	2Val-Hgb
8.19	2Val-NH	0.99	2Val-Hgb
8.19	2Val-NH	0.93	2Val-Hga
8.29	5Val-NH	0.97	5Val-Hgb

8.29	5Val-NH	0.93	5Val-Hgb
2.05	5Val-Hb	0.95	5Val-Hga
4.08	2Val-Ha	0.98	2Val-Hgb
4.10	5Val-Ha	2.06	5Val-Hb
4.08	2Val-Ha	0.93	2Val-Hga
4.10	5Val-Ha	0.93	5Val-Hga
3.93	1Ser-Hbb	4.54	1Ser-Ha
3.83	1Ser-Hba	4.54	1Ser-Hba
2.04	2Val-Hb	1.00	2Val-Hb
8.83	3Gly-NH	4.08	2Val-Ha
8.29	5Val-NH	3.84	4Gly-Haa
8.09	1Ser-NH	4.08	6Gly-Hab
8.09	4Gly-NH	4.00	3Gly-Hab
8.19	2Val-NH	4.53	1Ser-Ha
8.19	2Val-NH	3.88	3Gly-Haa
8.19	2Val-NH	3.92	1Ser-Hbb
8.82	3Gly-NH	0.92	2Val-Hga
8.83	3Gly-NH	0.98	2Val-Hgb
8.93	6Gly-NH	0.92	5Val-Hga
8.83	3Gly-NH	2.04	2Val-Hga
8.93	6Gly-NH	2.06	5Val-Hb
8.93	6Gly-NH	8.10	1Ser-NH
8.82	3Gly-NH	8.09	4Gly-NH
8.82	3Gly-NH	8.20	2Val-NH
8.93	6Gly-NH	8.30	5Val-NH
8.28	5Val-NH	8.09	4Gly-NH
8.19	2Val-NH	8.09	1Ser-NH

Table S20. *J*-coupling values and associated torsional restraints for V1S, cyclo-(SVGGVG).

Residue	$^3J_{\mathrm{NHCH\alpha}}$ (Hz)	φ restraints (˚)
S$_1$	–	
V$_2$	6.2	
G$_3$	6.3	
G$_4$	–	
V$_5$	8.3	–120 ± 30
G$_6$	6.0	

Table S21. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for V1S, cyclo-(SVGGVG).

Distance constraints:
assign (resid 1 and name HN) (resid 1 and name HA) 3.2 0.6 0.6
assign (resid 1 and name HN) (resid 1 and name HB1) 3.7 0.7 0.7
assign (resid 1 and name HN) (resid 6 and name HA2) 3.0 0.6 0.6
assign (resid 1 and name HB1) (resid 1 and name HA) 3.4 0.7 0.7
assign (resid 1 and name HB2) (resid 1 and name HA) 3.6 0.7 0.7

assign (resid 2 and name HN) (resid 2 and name HA) 3.4 0.7 0.7
assign (resid 2 and name HN) (resid 1 and name HB1) 3.1 0.6 0.6
assign (resid 2 and name HN) (resid 1 and name HA) 3.1 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HB) 3.1 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HG2#) 3.1 0.6 0.6
assign (resid 2 and name HN) (resid 2 and name HG1#) 3.4 0.7 0.7
assign (resid 2 and name HA) (resid 2 and name HG2#) 3.2 0.6 0.6

```
assign ( resid 2 and name HA ) ( resid 2 and name HG1#) 3.0 0.6 0.6
assign ( resid 2 and name HN ) ( resid 1 and name HN) 3.4 0.7 0.7
assign ( resid 2 and name HB ) ( resid 2 and name HG2# ) 3.3 0.7 0.7

assign ( resid 3 and name HN ) ( resid 3 and name HA1 ) 2.9 0.6 0.6
assign ( resid 3 and name HN ) ( resid 3 and name HA2 ) 3.6 0.7 0.7
assign ( resid 3 and name HN ) ( resid 2 and name HA ) 2.7 0.5 0.5
assign ( resid 3 and name HN ) ( resid 2 and name HB ) 4.0 0.8 0.8
assign ( resid 3 and name HN ) ( resid 2 and name HG1# ) 3.5 0.7 0.7
assign ( resid 3 and name HN ) ( resid 2 and name HG2# ) 3.9 0.8 0.8
assign ( resid 3 and name HN ) ( resid 4 and name HN) 3.2 0.6 0.6
assign ( resid 3 and name HN ) ( resid 2 and name HN) 3.8 0.8 0.8

assign ( resid 4 and name HN ) ( resid 4 and name HA2 ) 2.9 0.6 0.6
assign ( resid 4 and name HN ) ( resid 4 and name HA1) 3.3 0.7 0.7
assign ( resid 4 and name HN ) ( resid 3 and name HA2) 3.6 0.7 0.7

assign ( resid 5 and name HN ) ( resid 5 and name HA ) 3.3 0.7 0.7
assign ( resid 5 and name HN ) ( resid 4 and name HA2) 3.0 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HB) 3.1 0.6 0.6
assign ( resid 5 and name HN ) ( resid 5 and name HG2# ) 3.3 0.7 0.7
assign ( resid 5 and name HN ) ( resid 5 and name HG1#) 3.2 0.6 0.6
assign ( resid 5 and name HB ) ( resid 5 and name HG1# ) 2.8 0.6 0.6
assign ( resid 5 and name HA ) ( resid 5 and name HB ) 3.2 0.6 0.6
assign ( resid 5 and name HA ) ( resid 5 and name HG1# ) 3.1 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HN) 3.5 0.7 0.7

assign ( resid 6 and name HN ) ( resid 6 and name HA2) 2.9 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA1) 2.6 0.5 0.5
assign ( resid 6 and name HN ) ( resid 5 and name HB ) 4.2 0.8 0.8
assign ( resid 6 and name HN ) ( resid 5 and name HG1#) 3.5 0.7 0.7
assign ( resid 6 and name HN ) ( resid 1 and name HN) 3.3 0.7 0.7
assign ( resid 6 and name HN ) ( resid 5 and name HN) 3.8 0.8 0.8
```

Phi dihedral angle constraints:

```
assign ( resid 4 and name c ) ( resid 5 and name n )
        ( resid 5 and name ca ) ( resid 5 and name c ) 1.0 -120.0 30.0 2
```

Table S22. NOEs for V1A, cyclo-(AVGGVG).

Coordinate 1	Assignment 1	Coordinate 2	Assignment 2
8.85	3Gly-NH	4.05	3Gly-Hab
8.85	3Gly-NH	3.81	3Gly-Haa
8.78	6Gly-NH	3.78	6Gly-Haa
8.78	6Gly-NH	3.99	6Gly-Hab
8.31	4Gly-NH	3.95	4Gly-Haa
8.31	4Gly-NH	4.04	4Gly-Hab
8.15	5Val-NH	4.13	5Val-Ha
8.05	2Val-NH	4.10	2Val-Ha
8.20	1Ala-NH	4.36	1Ala-Ha
8.15	5Val-NH	2.07	5Val-Hb
8.05	2Val-NH	2.02	2Val-Hb
8.20	1Ala-NH	1.37	1Ala-Hb
8.05	2Val-NH	0.97	2Val-Hgb
8.15	5Val-NH	0.93	5Val-Hga
8.05	2Val-NH	0.93	2Val-Hga

4.36	1Ala-Ha	1.38	1Ala-Hb
4.13	5Val-Ha	0.93	5Val-Hga
4.10	2Val-Ha	0.93	2Val-Hga
4.09	2Val-Ha	0.97	2Val-Hgb
4.14	5Val-Ha	2.08	5Val-Hb
4.11	2Val-Ha	2.03	2Val-Hb
2.07	5Val-Hb	0.91	5Val-Hga
2.00	2Val-Hb	0.92	2Val-Hga
2.00	2Val-Hb	0.97	2Val-Hgb
8.85	3Gly-NH	4.10	2Val-Ha
8.79	6Gly-NH	4.13	5Val-Ha
8.05	2Val-NH	4.36	1Ala-Ha
8.15	5Val-NH	3.95	4Gly-Haa
8.21	1Ala-NH	3.99	6Gly-Hab
8.31	4Gly-NH	3.82	3Gly-Haa
8.21	1Ala-NH	3.79	6Gly-Haa
8.15	5Val-NH	4.03	4Gly-Hab
8.05	2Val-NH	1.38	1Ala-Hb
8.78	6Gly-NH	0.92	5Val-Hga
8.85	3Gly-NH	0.93	2Val-Hga
8.85	3Gly-NH	8.31	4Gly-NH
8.78	6Gly-NH	8.20	1Ala-NH
8.31	4Gly-NH	8.16	5Val-NH
8.20	1Ala-NH	8.06	2Val-NH
8.85	3Gly-NH	8.05	2Val-NH
8.78	6Gly-NH	8.15	5Val-NH

Table S23. *J*-coupling values and associated torsional restraints for V1A, cyclo-(AVGGVG).

Residue	$^3J_{NHCH\alpha}$ (Hz)	φ restraints (˚)
A_1	6.4	
V_2	7.0	
G_3	5.8	
G_4	5.4	
V_5	8.8	–120 ± 30
G_6	5.8	

Table S24. List of NOE-derived distance restraints and *J*-coupling-derived dihedral angle restraints for V1A, cyclo-(AVGGVG).

Distance constraints:

```
assign ( resid 1 and name HN ) ( resid 1 and name HA ) 3.6 0.7 0.7
assign ( resid 1 and name HN ) ( resid 1 and name HB# ) 3.0 0.6 0.6
assign ( resid 1 and name HN ) ( resid 6 and name HA1 ) 3.0 0.6 0.6
assign ( resid 1 and name HN ) ( resid 6 and name HA2 ) 3.9 0.8 0.8
assign ( resid 1 and name HA ) ( resid 1 and name HB# ) 3.2 0.6 0.6
assign ( resid 1 and name HN ) ( resid 2 and name HN ) 3.6 0.7 0.7

assign ( resid 2 and name HN ) ( resid 2 and name HA ) 3.6 0.7 0.7
assign ( resid 2 and name HN ) ( resid 2 and name HB ) 3.1 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HG1# ) 3.1 0.6 0.6
assign ( resid 2 and name HN ) ( resid 1 and name HA ) 3.2 0.6 0.6
assign ( resid 2 and name HN ) ( resid 2 and name HG2# ) 3.4 0.7 0.7
assign ( resid 2 and name HA ) ( resid 2 and name HG2# ) 3.3 0.7 0.7
assign ( resid 2 and name HA ) ( resid 2 and name HG1#) 3.3 0.7 0.7
```

```
assign ( resid 2 and name HA ) ( resid 2 and name HB ) 3.4 0.7 0.7
assign ( resid 2 and name HB ) ( resid 2 and name HG2# ) 3.0 0.6 0.6
assign ( resid 2 and name HB ) ( resid 2 and name HG1# ) 3.3 0.7 0.7
assign ( resid 2 and name HN ) ( resid 1 and name HB# ) 3.4 0.7 0.7

assign ( resid 3 and name HN ) ( resid 3 and name HA2 ) 3.6 0.7 0.7
assign ( resid 3 and name HN ) ( resid 3 and name HA1) 2.9 0.6 0.6
assign ( resid 3 and name HN ) ( resid 2 and name HA) 2.7 0.5 0.5
assign ( resid 3 and name HN ) ( resid 2 and name HG2# ) 3.6 0.7 0.7
assign ( resid 3 and name HN ) ( resid 4 and name HN ) 3.4 0.7 0.7

assign ( resid 4 and name HN ) ( resid 4 and name HA2 ) 4.5 0.9 0.9
assign ( resid 4 and name HN ) ( resid 4 and name HA1 ) 2.7 0.5 0.5
assign ( resid 4 and name HN ) ( resid 3 and name HA1 ) 3.6 0.7 0.7
assign ( resid 4 and name HN ) ( resid 5 and name HN ) 3.6 0.7 0.7

assign ( resid 5 and name HN ) ( resid 5 and name HA) 4.0 0.8 0.8
assign ( resid 5 and name HN ) ( resid 5 and name HB) 3.3 0.7 0.7
assign ( resid 5 and name HN ) ( resid 5 and name HG1#) 3.1 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HA2 ) 3.2 0.6 0.6
assign ( resid 5 and name HN ) ( resid 4 and name HA1 ) 3.6 0.7 0.7
assign ( resid 5 and name HA ) ( resid 5 and name HG1# ) 3.0 0.6 0.6
assign ( resid 5 and name HA ) ( resid 5 and name HB ) 3.5 0.7 0.7
assign ( resid 5 and name HB ) ( resid 5 and name HG1#) 2.9 0.6 0.6

assign ( resid 6 and name HN ) ( resid 6 and name HA2 ) 2.9 0.6 0.6
assign ( resid 6 and name HN ) ( resid 6 and name HA1 ) 3.6 0.7 0.7
assign ( resid 6 and name HN ) ( resid 5 and name HA ) 2.7 0.5 0.5
assign ( resid 6 and name HN ) ( resid 5 and name HG1# ) 3.6 0.7 0.7
assign ( resid 6 and name HN ) ( resid 1 and name HN ) 3.5 0.7 0.7
```

Phi dihedral angle constraints:

```
assign ( resid 4 and name c ) ( resid 5 and name n )
        ( resid 5 and name ca ) ( resid 5 and name c ) 1.0 -120.0 30.0 2
```

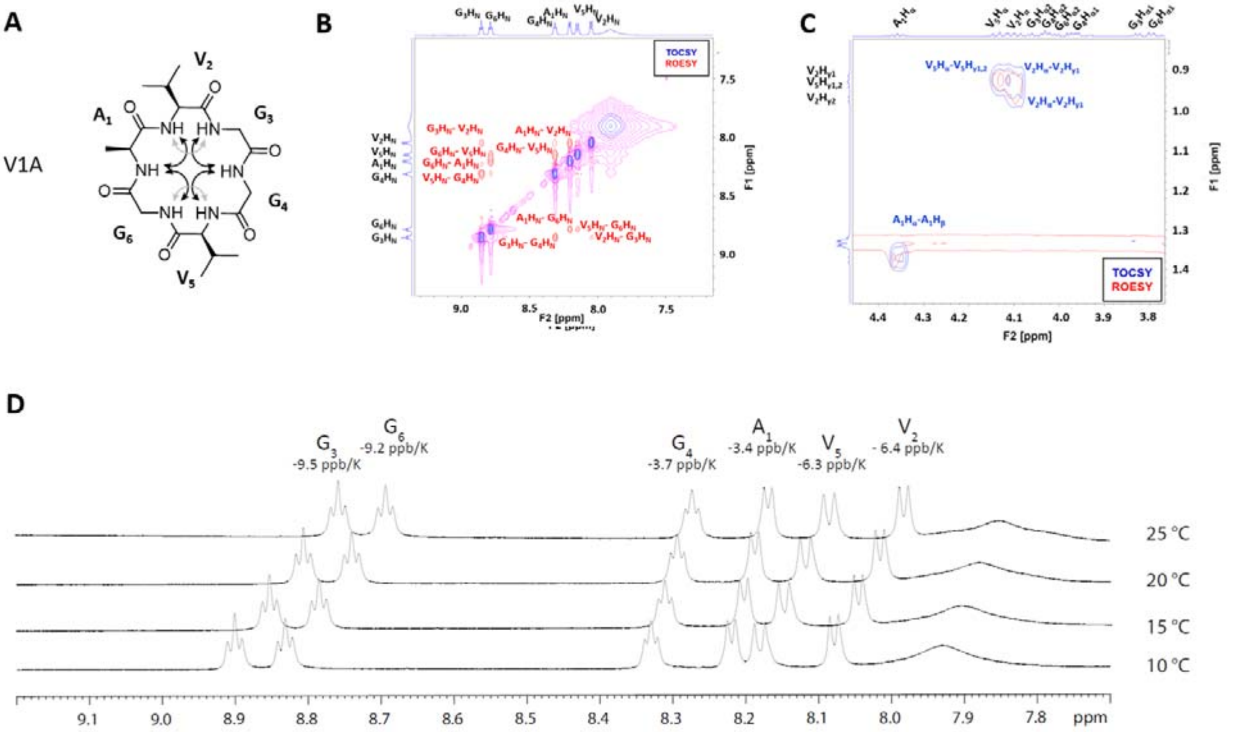
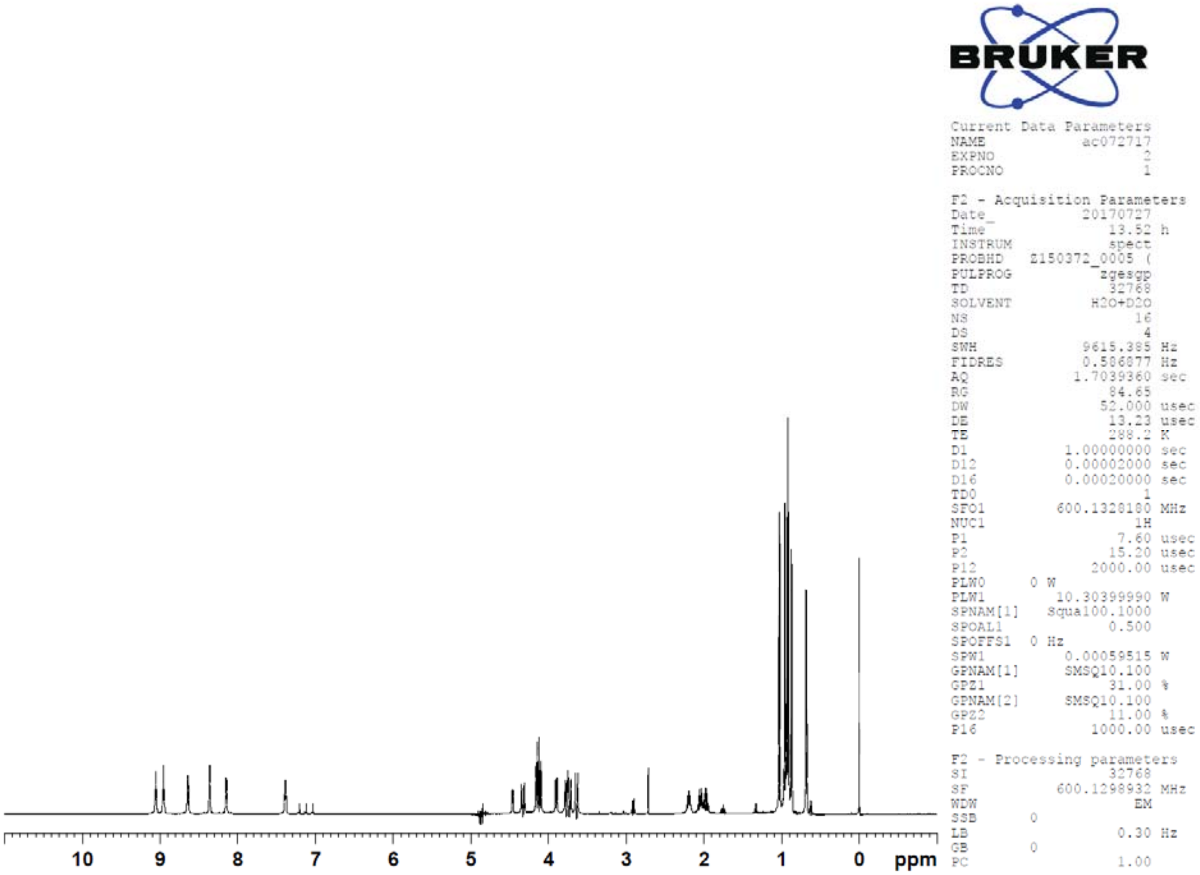


Figure S4. 2D-NMR data for peptide V1A (cyclo-AVGGVG) in water. (A) Visual depiction of the strong (black) and weak (grey) NOEs from the ROESY spectra for V1A. (B) Amide-to-amide proton region of the TOCSY and ROESY spectra for V1A. NOE cross-peaks are expected for positions at which beta-turns predominate in the solution ensemble. (C) Alpha-to-methyl proton region of the TOCSY and ROESY spectra for V1A. (D) Temperature dependence of amide proton chemical shifts. Stacked spectra show the amide regions of ^{1}H NMR experiments at the indicated temperature. Solvent-exposed amide protons typically have chemical shifts that shift upfield with temperature by more than 4.5 ppb/K (temperature coefficient between –4.5 and –16 ppb/K). Temperature coefficients between 2.0 and –4.5 ppb/K indicate protection from solvent, as occurs when an amide proton is involved in a hydrogen bond. Despite apparent > 99 % purity via HPLC and LC-MS, unidentified resonances were observed at 1.33 ppm and 7.93 ppm (visible in panels C and D, respectively). This did not interfere with analysis of the structural ensemble of V1A.



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PROCNO                  1

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PULPROG            zgesgp
TD                  32768
SOLVENT           H2O+D2O
NS                     16
DS                      4
SWH              9615.385 Hz
FIDRES           0.586877 Hz
AQ              1.7039360 sec
RG                  84.65
DW                 52.000 usec
DE                  13.23 usec
TE                  288.2 K
D1             1.00000000 sec
D12            0.00002000 sec
D16            0.00020000 sec
TD0                     1
SFO1          600.1328180 MHz
NUC1                   1H
P1                   7.60 usec
P2                  15.20 usec
P12               2000.00 usec
PLW0      0 W
PLW1          10.30399990 W
SPNAM[1]    Squa100.1000
SPOAL1              0.500
SPOFFS1   0 Hz
SPW1           0.00059515 W
GPNAM[1]       SMSQ10.100
GPZ1                31.00 %
GPNAM[2]       SMSQ10.100
GPZ2                11.00 %
P16               1000.00 usec

F2 - Processing parameters
SI                  32768
SF            600.1298932 MHz
WDW                    EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
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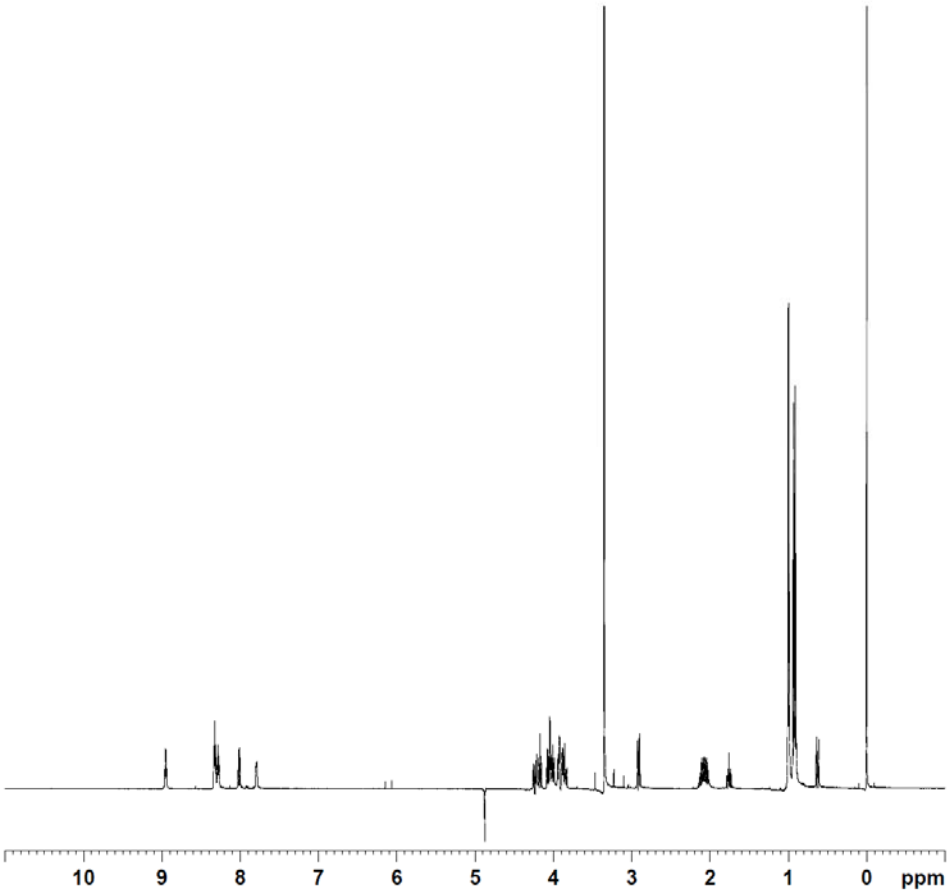
Figure S5. Complete ^{1}H NMR spectrum of P7 in 90:10 H_2O:D_2O at 288 K.



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EXPNO                   3
PROCNO                  1

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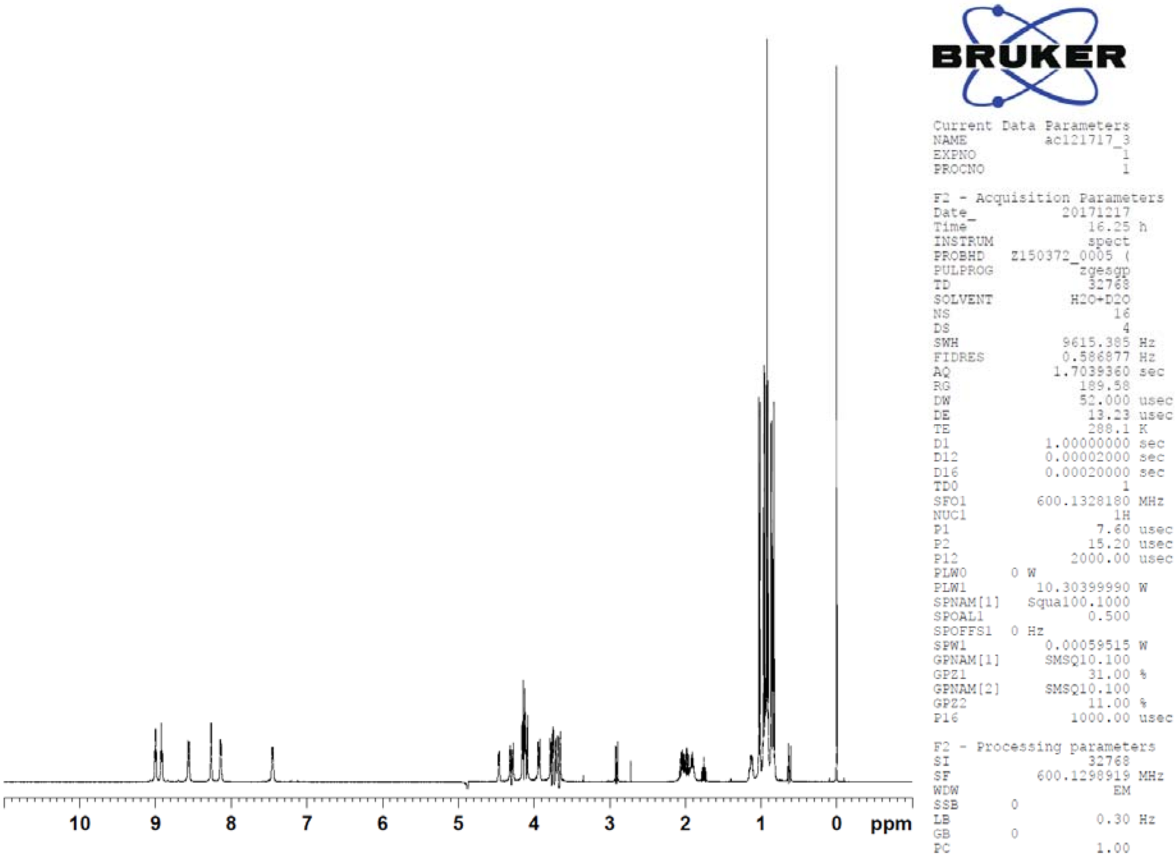
PULPROG            zgesgp
TD                  32768
SOLVENT           H2O+D2O
NS                     16
DS                      4
SWH              9615.385 Hz
FIDRES           0.586877 Hz
AQ              1.7039360 sec
RG                 189.58
DW                 52.000 usec
DE                  13.23 usec
TE                  288.1 K
D1             1.00000000 sec
D12            0.00002000 sec
D16            0.00020000 sec
TD0                     1
SFO1          600.1328180 MHz
NUC1                   1H
P1                   7.60 usec
P2                  15.20 usec
P12               2000.00 usec
PLW0      0 W
PLW1          10.30399990 W
SPNAM[1]    Squa100.1000
SPOAL1              0.500
SPOFFS1   0 Hz
SPW1           0.00059515 W
GPNAM[1]       SMSQ10.100
GPZ1                31.00 %
GPNAM[2]       SMSQ10.100
GPZ2                11.00 %
P16               1000.00 usec

F2 - Processing parameters
SI                  32768
SF            600.1298915 MHz
WDW                    EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
```

Figure S6. Complete ^{1}H NMR spectrum of P6 in 90:10 H_2O:D_2O at 288 K.



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EXPNO                     1
PROCNO                    1

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INSTRUM               spect
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PULPROG             zgesgp
TD                    32768
SOLVENT             H2O+D2O
NS                       16
DS                        4
SWH                9615.385 Hz
FIDRES             0.586877 Hz
AQ                1.7039360 sec
RG                   189.58
DW                   52.000 usec
DE                    13.23 usec
TE                    288.1 K
D1               1.00000000 sec
D12              0.00002000 sec
D16              0.00020000 sec
TD0                       1
SFO1            600.1328180 MHz
NUC1                     1H
P1                     7.60 usec
P2                    15.20 usec
P12                 2000.00 usec
PLW0      0 W
PLW1            10.30399990 W
SPNAM[1]     Squa100.1000
SPOAL1                0.500
SPOFFS1   0 Hz
SPW1             0.00059515 W
GPNAM[1]         SMSQ10.100
GPZ1                  31.00 %
GPNAM[2]         SMSQ10.100
GPZ2                  11.00 %
P16                 1000.00 usec

F2 - Processing parameters
SI                    32768
SF              600.1298919 MHz
WDW                      EM
SSB       0
LB                     0.30 Hz
GB        0
PC                     1.00
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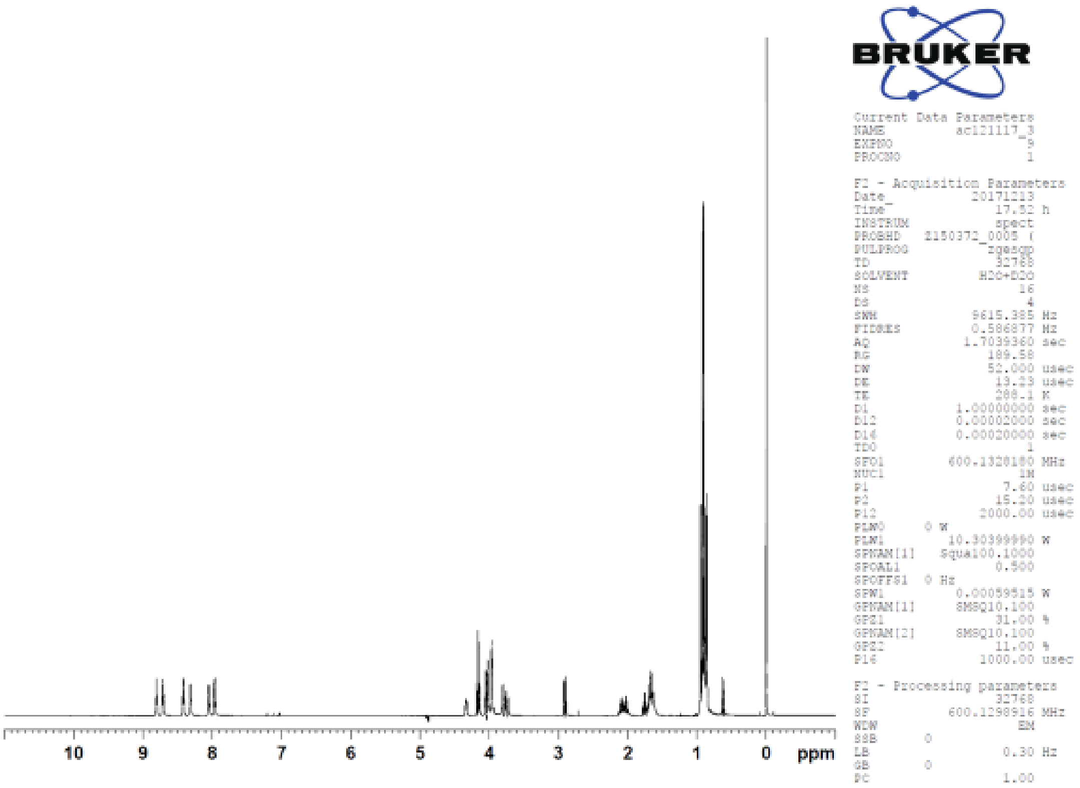
Figure S7. Complete ^{1}H NMR spectrum of V1I in 90:10 H_2O:D_2O at 288 K.



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DS                     4
SWH             9615.385 Hz
FIDRES          0.586877 Hz
AQ             1.7039360 sec
RG                189.58
DW                52.000 usec
DE                 13.23 usec
TE                 288.1 K
D1            1.00000000 sec
D12           0.00002000 sec
D14           0.00020000 sec
TD0                    1
SFO1         600.1328180 MHz
NUC1                  1H
P1                  7.60 usec
P2                 15.20 usec
P12              2000.00 usec
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PLW1         10.30399990 W
SPNAM[1]    Squa100.1000
SPOAL1             0.500
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SPW1          0.00059515 W
GPNAM[1]      SMSQ10.100
GPZ1               31.00 %
GPNAM[2]      SMSQ10.100
GPZ2               11.00 %
P16              1000.00 usec

F2 - Processing parameters
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SF           600.1298916 MHz
WDW                   EM
SSB       0
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GB        0
PC                  1.00
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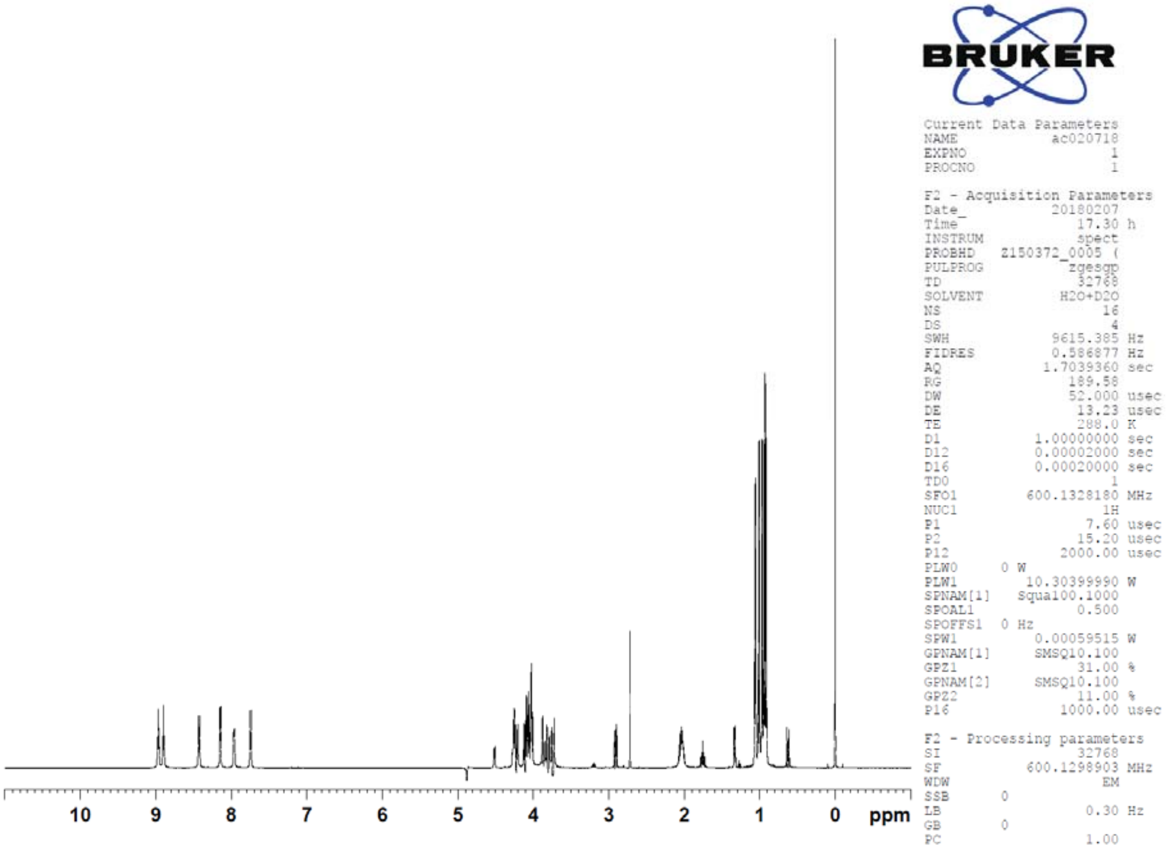
Figure S8. Complete ^{1}H NMR spectrum of V1L in 90:10 H_2O:D_2O at 288 K..



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PROCNO                 1

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PULPROG           zgesgp
TD                 32768
SOLVENT          H2O+D2O
NS                    16
DS                     4
SWH             9615.385 Hz
FIDRES          0.586877 Hz
AQ             1.7039360 sec
RG                189.58
DW                52.000 usec
DE                 13.23 usec
TE                 288.0 K
D1            1.00000000 sec
D12           0.00002000 sec
D16           0.00020000 sec
TD0                    1
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NUC1                  1H
P1                  7.60 usec
P2                 15.20 usec
P12              2000.00 usec
PLW0      0 W
PLW1         10.30399990 W
SPNAM[1]   Squa100.1000
SPOAL1             0.500
SPOFFS1   0 Hz
SPW1          0.00059515 W
GPNAM[1]      SMSQ10.100
GPZ1               31.00 %
GPNAM[2]      SMSQ10.100
GPZ2               11.00 %
P16              1000.00 usec

F2 - Processing parameters
SI                 32768
SF           600.1298903 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
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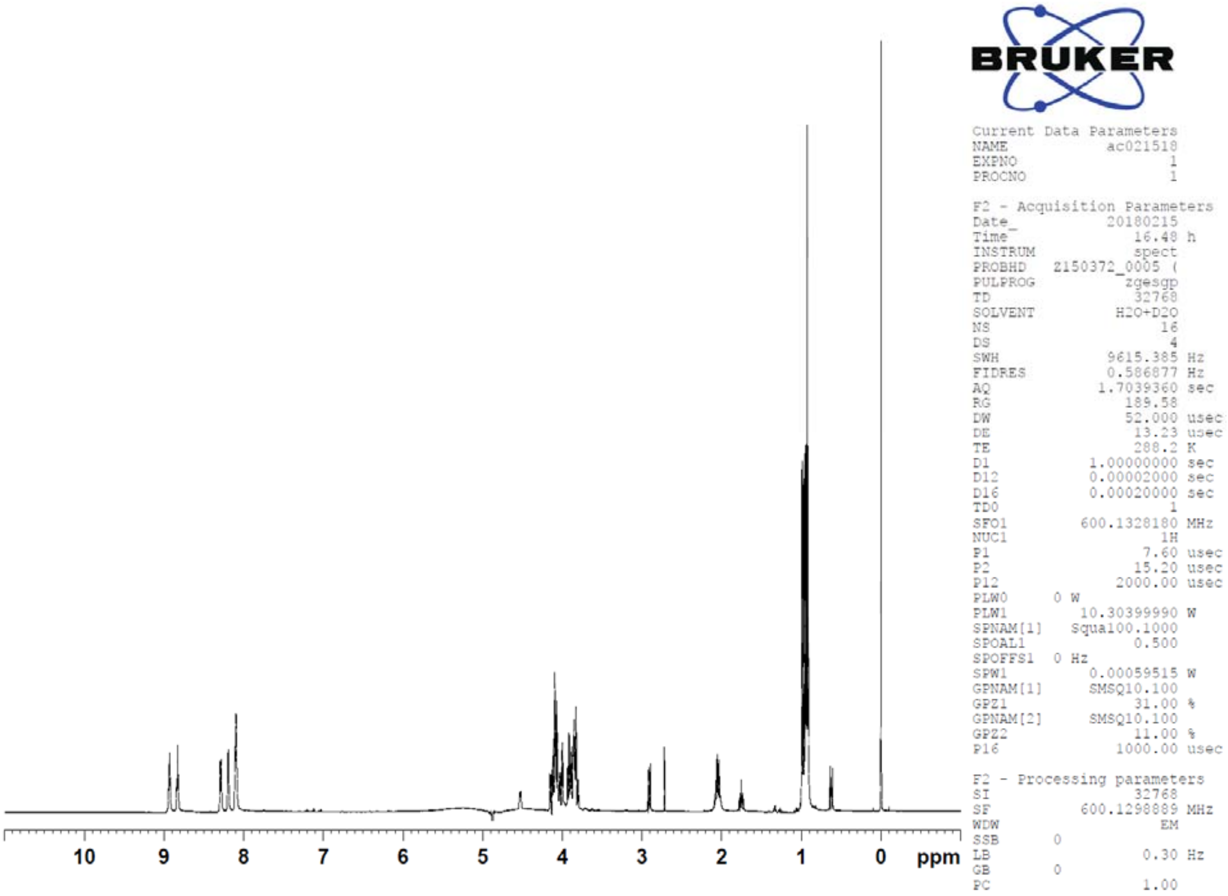
Figure S9. Complete ^1H NMR spectrum of V1T in 90:10 $H_2O:D_2O$ at 288 K.



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PROCNO                   1

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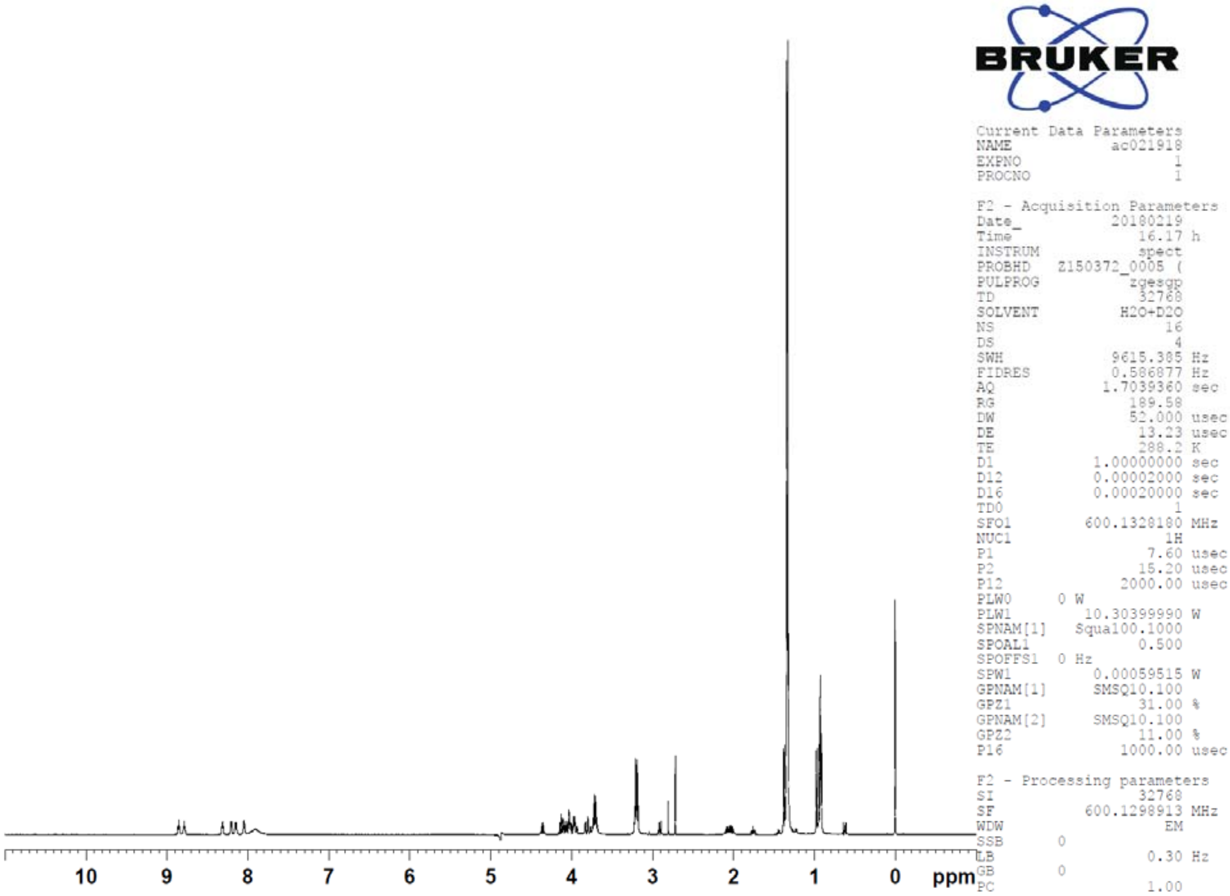
PULPROG            zgesgp
TD                   32768
SOLVENT          H2O+D2O
NS                      16
DS                       4
SWH               9615.385 Hz
FIDRES            0.586877 Hz
AQ               1.7039360 sec
RG                  189.58
DW                  52.000 usec
DE                   13.23 usec
TE                   288.2 K
D1              1.00000000 sec
D12             0.00002000 sec
D16             0.00020000 sec
TD0                      1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    7.60 usec
P2                   15.20 usec
P12                2000.00 usec
PLW0      0 W
PLW1           10.30399990 W
SPNAM[1]    Squa100.1000
SPOAL1               0.500
SPOFFS1   0 Hz
SPW1            0.00059515 W
GPNAM[1]       SMSQ10.100
GPZ1                 31.00 %
GPNAM[2]       SMSQ10.100
GPZ2                 11.00 %
P16                1000.00 usec

F2 - Processing parameters
SI                   32768
SF             600.1298889 MHz
WDW                     EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

Figure S10. Complete ^{1}H NMR spectrum of V1S in 90:10 H_2O:D_2O at 288 K.



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EXPNO                     1
PROCNO                    1

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PULPROG              zgesgp
TD                    32768
SOLVENT             H2O+D2O
NS                       16
DS                        4
SWH                9615.385 Hz
FIDRES             0.586877 Hz
AQ                1.7039360 sec
RG                   189.58
DW                   52.000 usec
DE                    13.23 usec
TE                    288.2 K
D1               1.00000000 sec
D12              0.00002000 sec
D16              0.00020000 sec
TD0                       1
SFO1            600.1328180 MHz
NUC1                     1H
P1                     7.60 usec
P2                    15.20 usec
P12                 2000.00 usec
PLW0         0 W
PLW1            10.30399990 W
SPNAM[1]       Squa100.1000
SPOAL1                0.500
SPOFFS1  0 Hz
SPW1             0.00059515 W
GPNAM[1]         SMSQ10.100
GPZ1                  31.00 %
GPNAM[2]         SMSQ10.100
GPZ2                  11.00 %
P16                 1000.00 usec

F2 - Processing parameters
SI                    32768
SF              600.1298913 MHz
WDW                      EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

Figure S11. Complete ^{1}H NMR spectrum of V1A in 90:10 H_2O:D_2O at 288 K. Despite apparent > 99 % purity via HPLC and LC-MS, unidentified resonances were observed at 1.33 ppm and 7.93 ppm. This did not interfere with analysis of the structural ensemble of V1A.

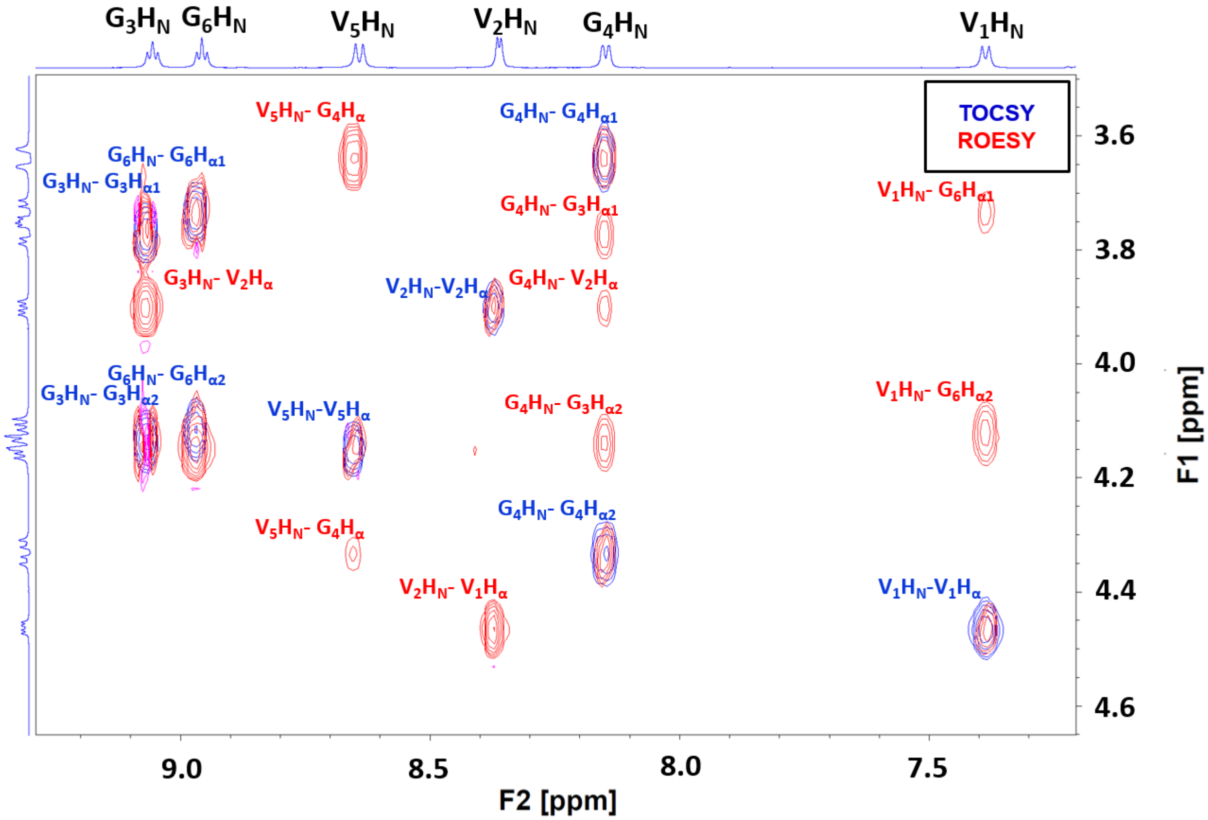


Figure S12. Fingerprint region of the 2D spectra for P7 at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.

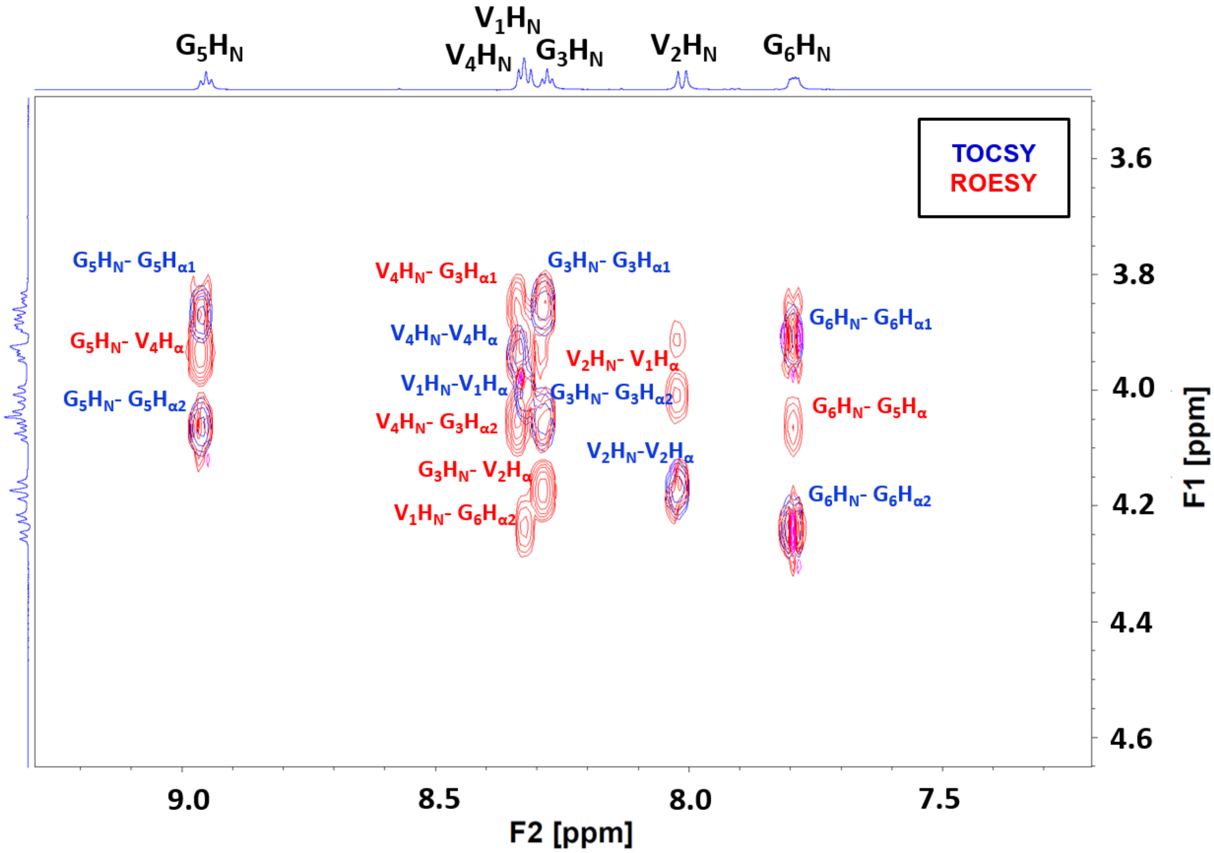


Figure S13. Fingerprint region of the 2D spectra for P6 at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.

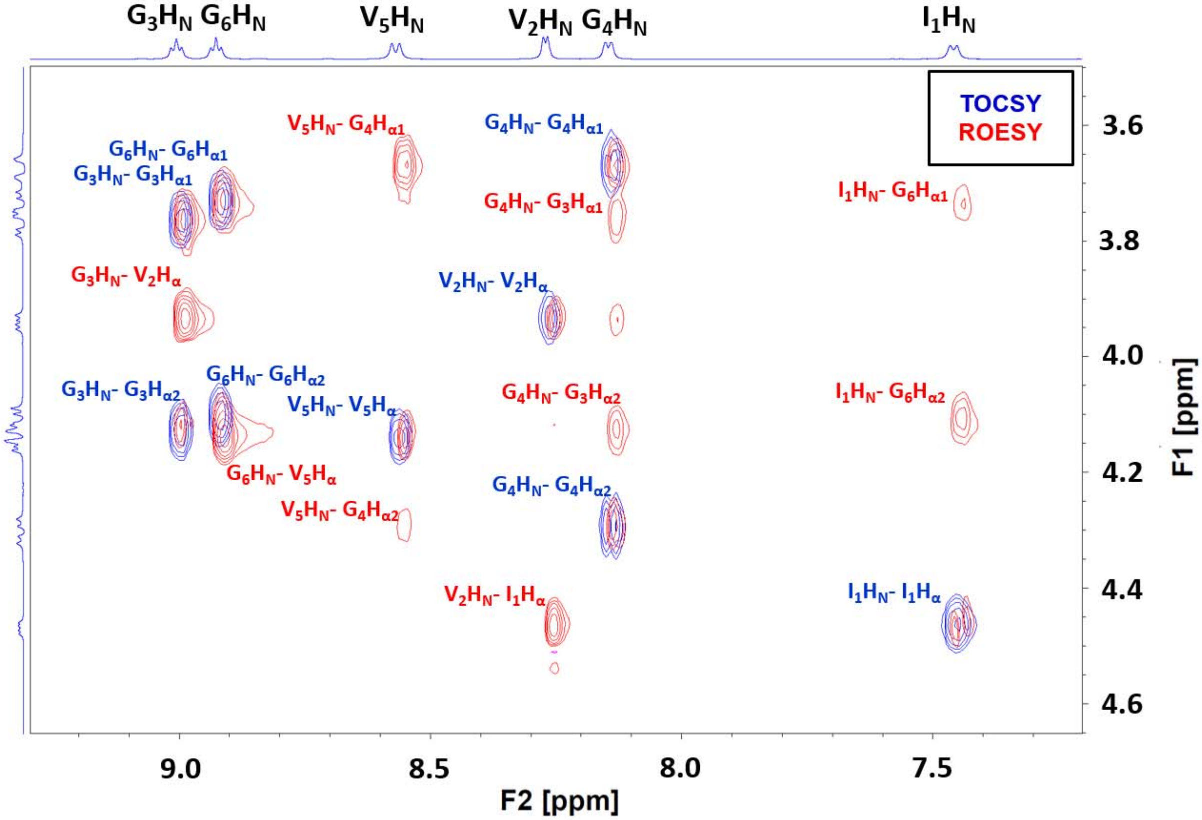


Figure S14. Fingerprint region of the 2D spectra for V1I at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.

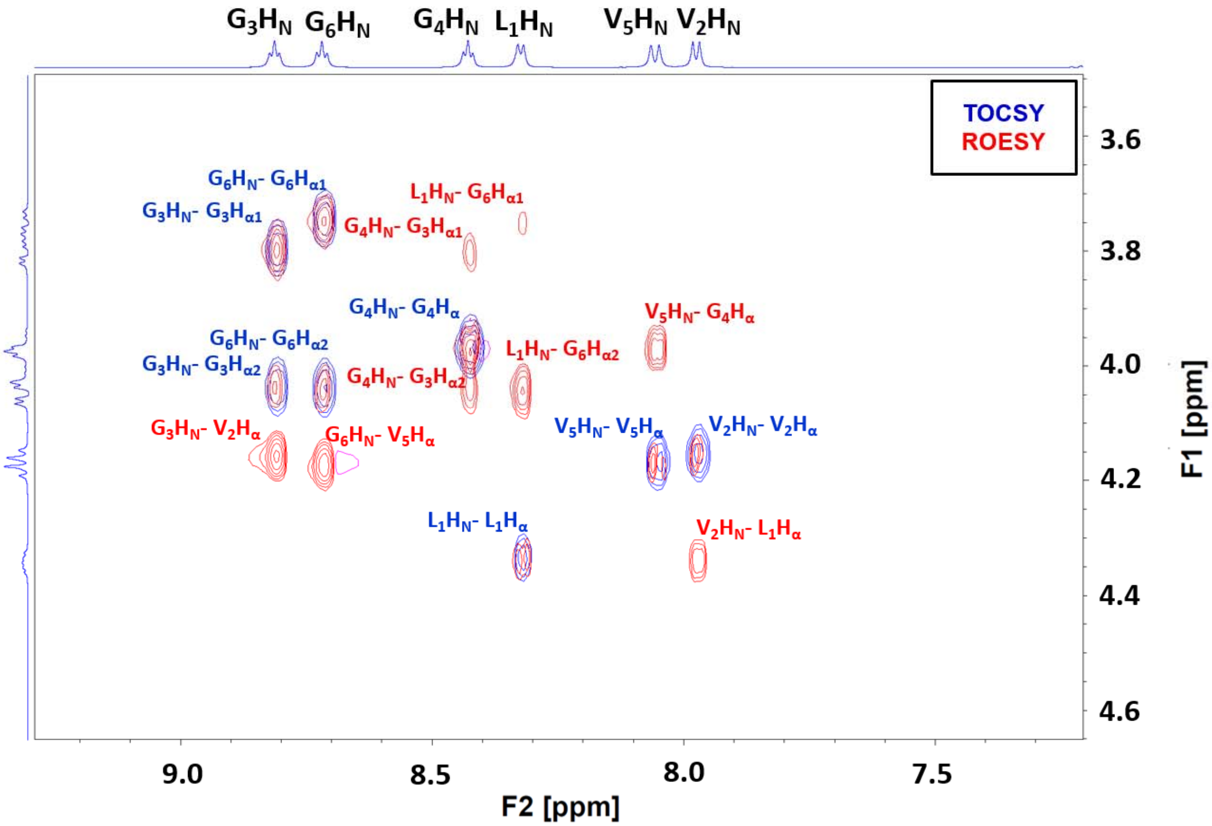


Figure S15. Fingerprint region of the 2D spectra for V1L at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.

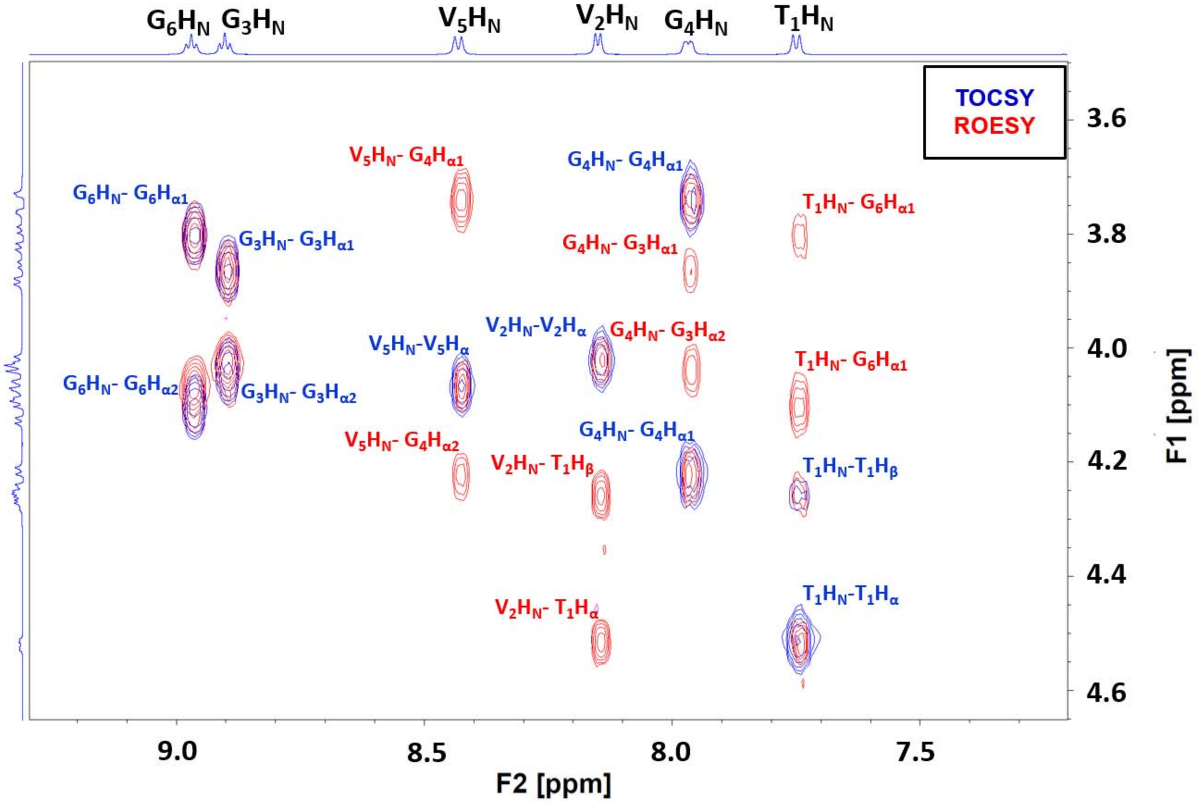


Figure S16. Fingerprint region of the 2D spectra for V1T at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.

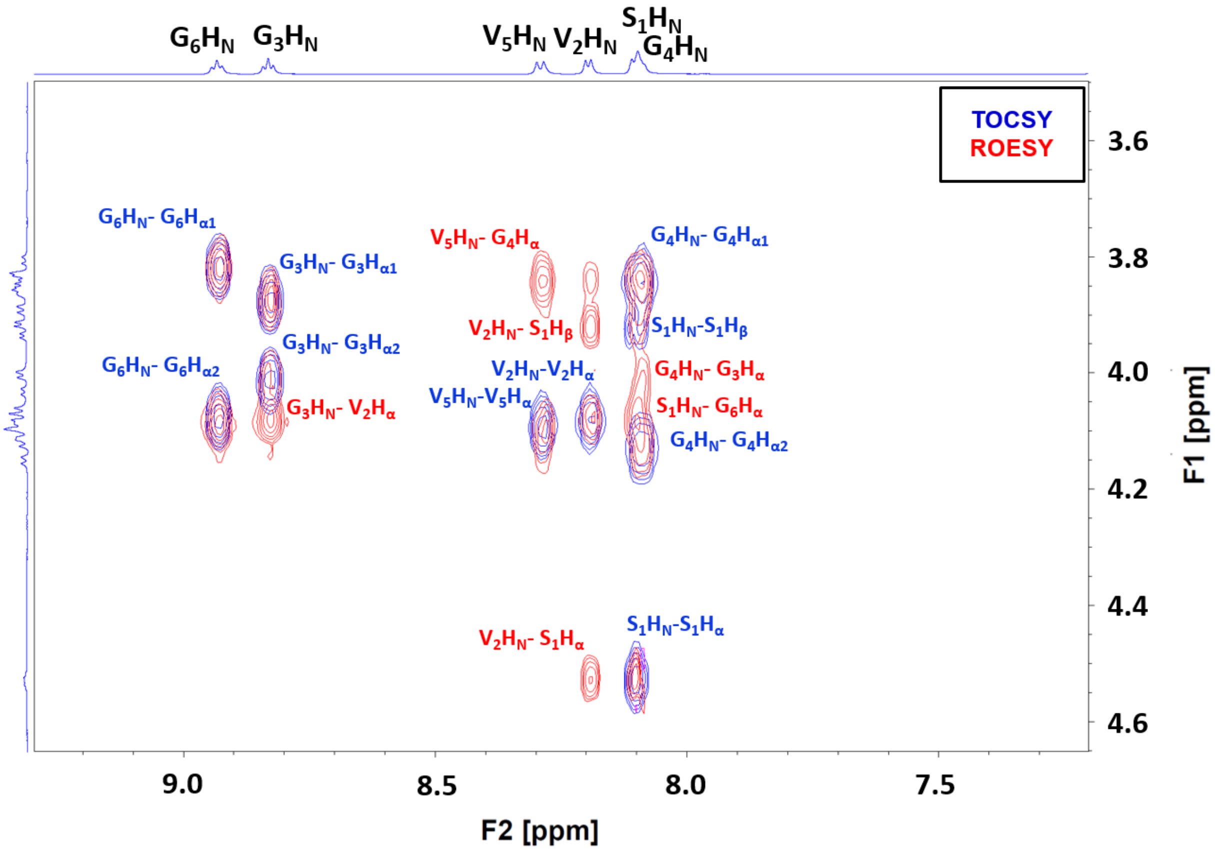


Figure S17. Fingerprint region of the 2D spectra for V1S at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.

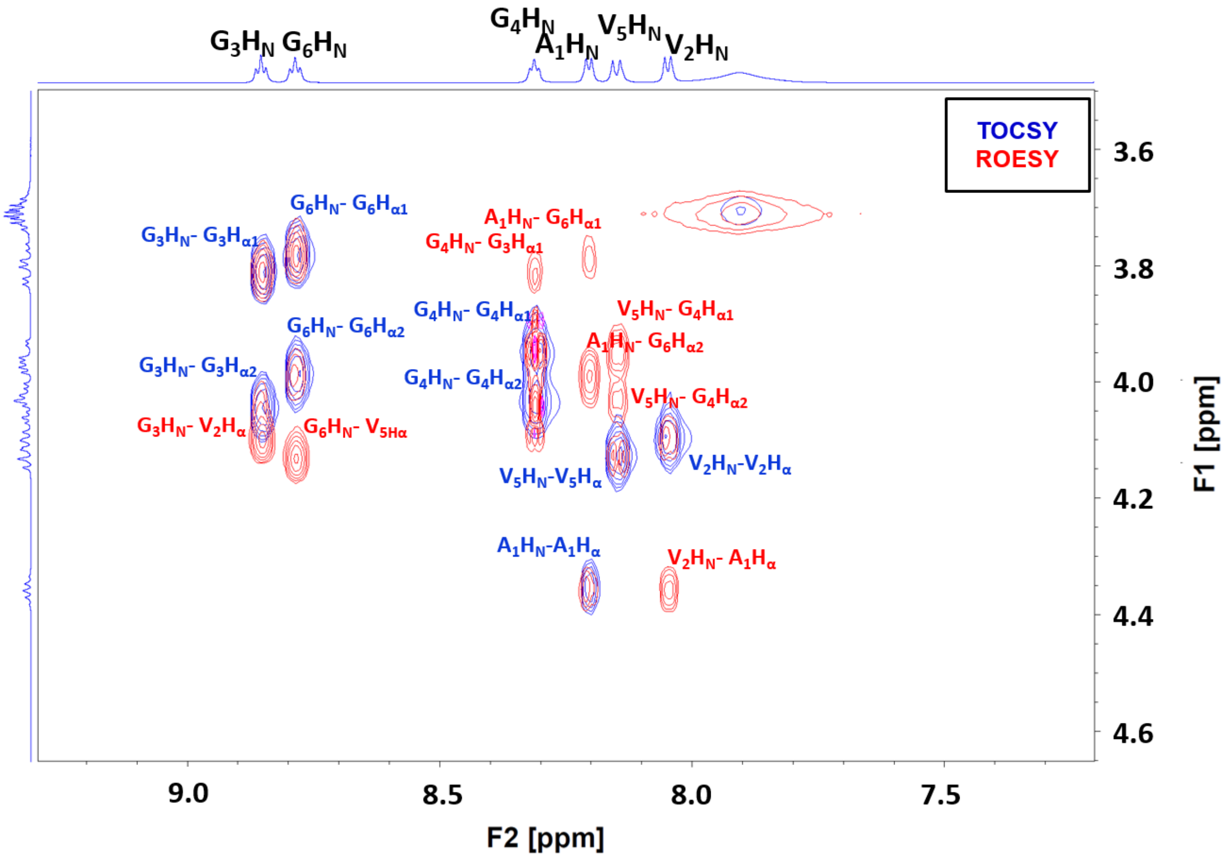
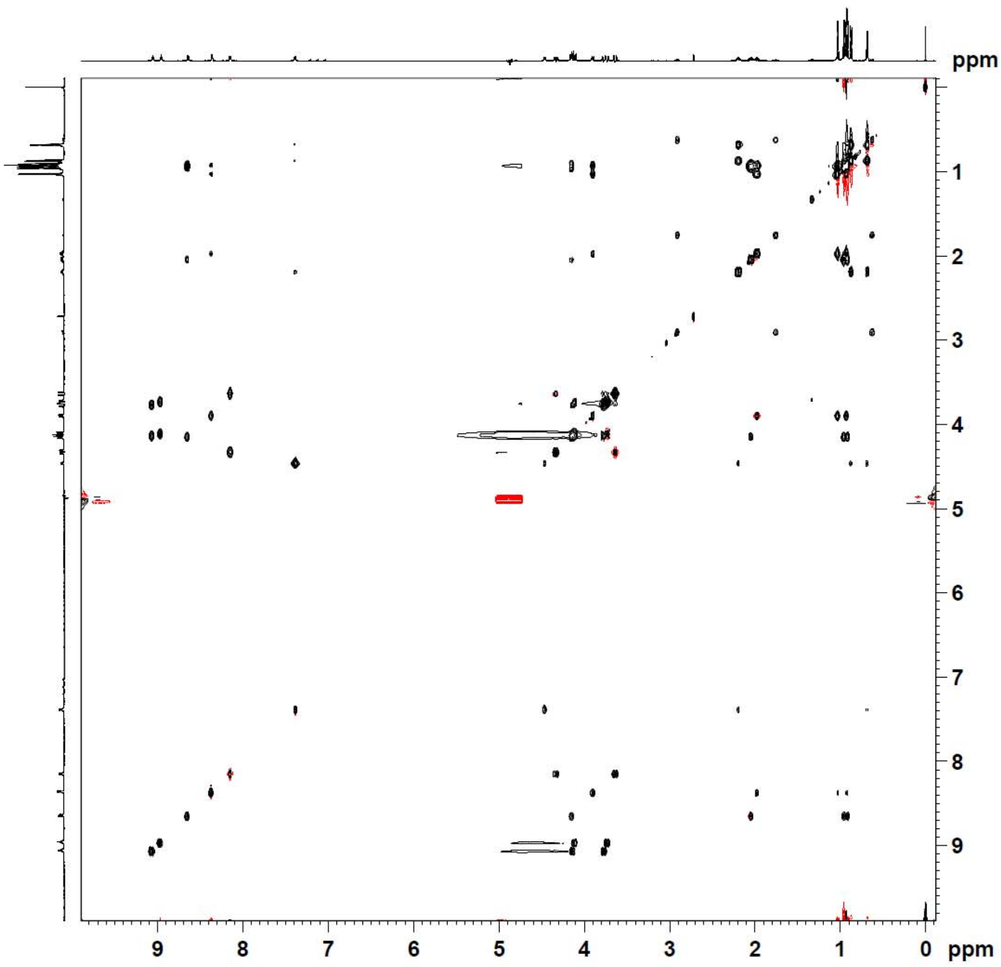


Figure S18. Fingerprint region of the 2D spectra for V1A at 288K, with TOCSY peaks shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (top) and the H_α region (side). The peptide was dissolved in 90:10 H_2O:D_2O at a concentration of roughly 3.0 mM.



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PROCNO                   1

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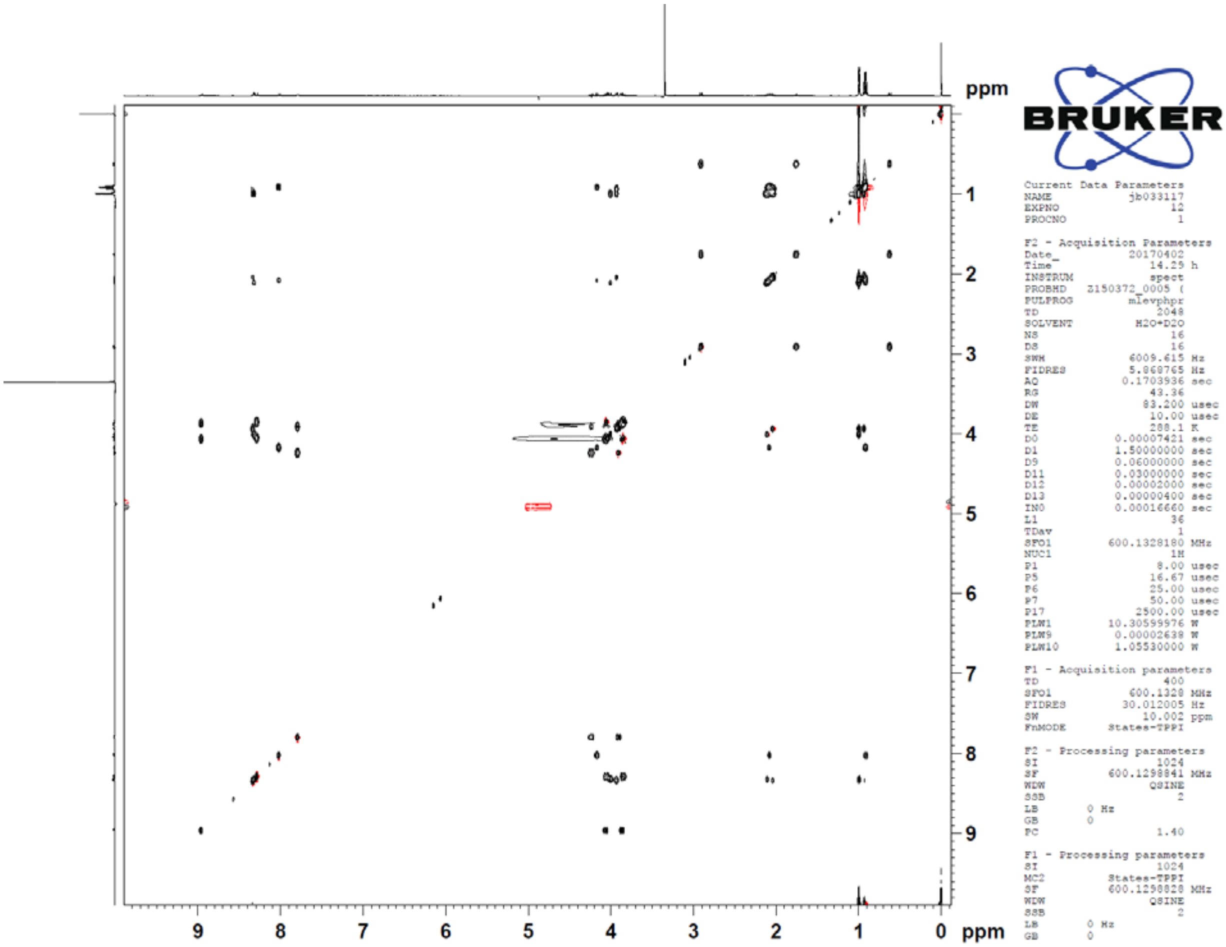
PULPROG           mlevphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      16
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   35.31
DW                  83.200 usec
DE                   10.00 usec
TE                   288.2 K
D0              0.00007421 sec
D1              1.50000000 sec
D9              0.06000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P5                   16.67 usec
P6                   25.00 usec
P7                   50.00 usec
P17                2500.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW10           1.05530000 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298841 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298828 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
```

Figure S19. Complete ^1H–^1H TOCSY NMR spectrum of P7 in 90:10 H_2O:D_2O at 288 K.



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Current Data Parameters
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EXPNO                   12
PROCNO                   1

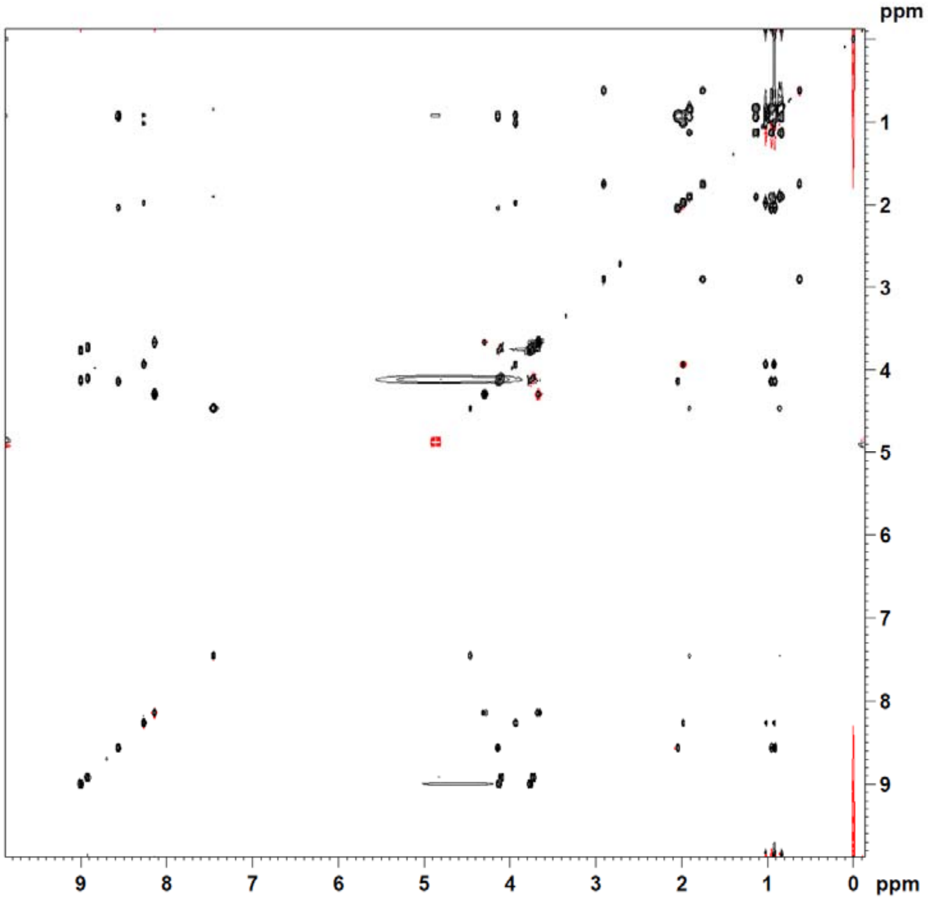
F2 - Acquisition Parameters
Date_             20170402
Time                 14.25 h
INSTRUM              spect
PROBHD   Z150372_0005 (
PULPROG          mlevphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      16
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   43.36
DW                  83.200 usec
DE                   10.00 usec
TE                   288.1 K
D0              0.00007421 sec
D1              1.50000000 sec
D9              0.06000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P5                   16.67 usec
P6                   25.00 usec
P7                   50.00 usec
P17                2500.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW10           1.05530000 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298841 MHz
WDW                  QSINE
SSB                      2
LB       0 Hz
GB       0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298828 MHz
WDW                  QSINE
SSB                      2
LB       0 Hz
GB       0
```

Figure S20. Complete ^1H–^1H TOCSY NMR spectrum of P6 in 90:10 H_2O:D_2O at 288 K.



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EXPNO                      3
PROCNO                     1

F2 - Acquisition Parameters
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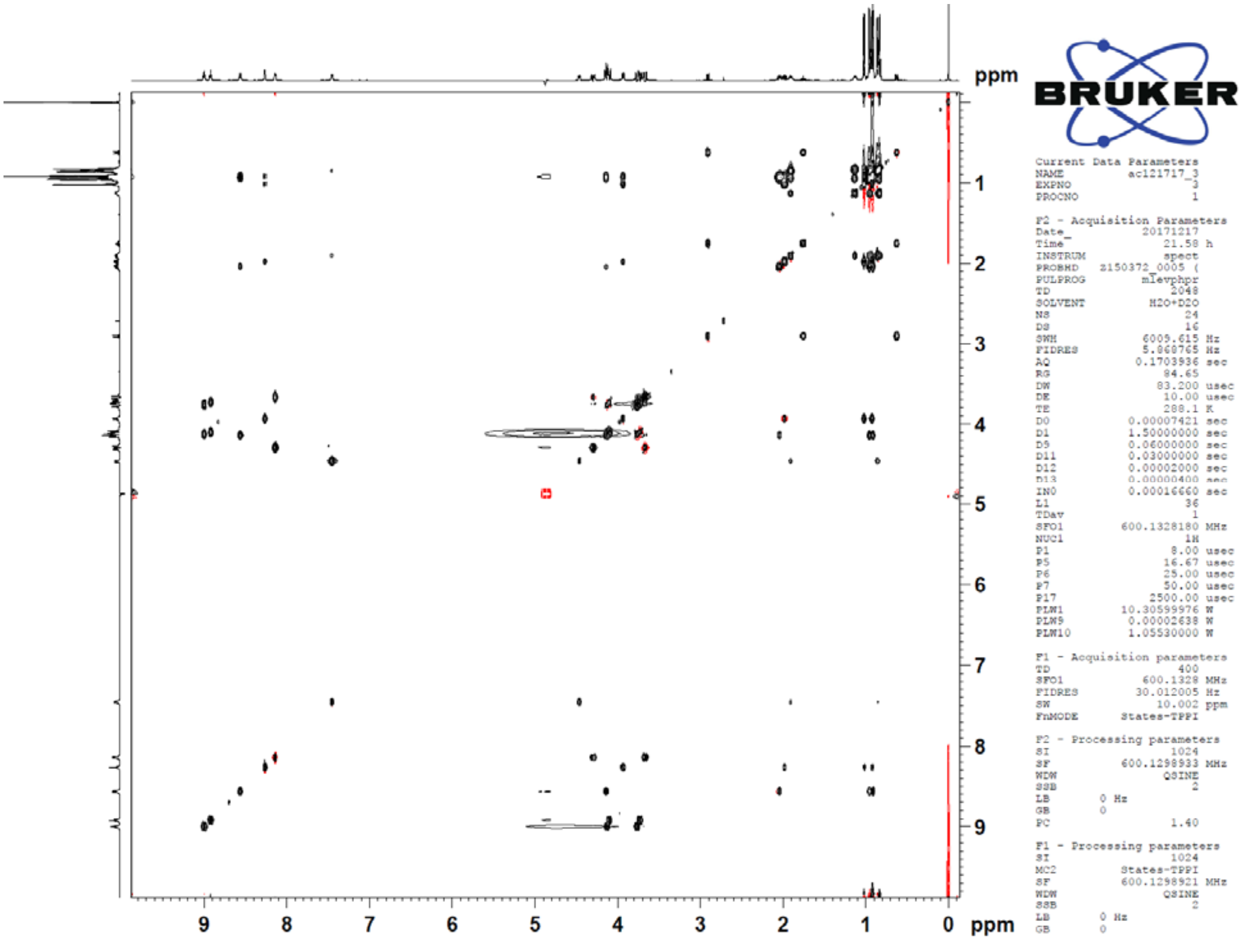
Time                   21.58 h
INSTRUM                spect
PROBHD   Z150372_0005 (
PULPROG             mlevphpr
TD                      2048
SOLVENT              H2O+D2O
NS                        24
DS                        16
SWH                 6009.615 Hz
FIDRES              5.868765 Hz
AQ                 0.1703936 sec
RG                     84.65
DW                    83.200 usec
DE                     10.00 usec
TE                     288.1 K
D0                0.00007421 sec
D1                1.50000000 sec
D9                0.06000000 sec
D11               0.03000000 sec
D12               0.00002000 sec
D13               0.00000400 sec
IN0               0.00016660 sec
L1                        36
TDav                       1
SFO1             600.1328180 MHz
NUC1                      1H
P1                      8.00 usec
P5                     16.67 usec
P6                     25.00 usec
P7                     50.00 usec
P17                  2500.00 usec
PLW1             10.30599976 W
PLW9              0.00002638 W
PLW10             1.05530000 W

F1 - Acquisition parameters
TD                       400
SFO1                600.1328 MHz
FIDRES             30.012005 Hz
SW                    10.002 ppm
FnMODE           States-TPPI

F2 - Processing parameters
SI                      1024
SF               600.1298933 MHz
WDW                    QSINE
SSB                        2
LB            0 Hz
GB            0
PC                      1.40

F1 - Processing parameters
SI                      1024
MC2              States-TPPI
SF               600.1298921 MHz
WDW                    QSINE
SSB                        2
LB            0 Hz
GB            0
```

Figure S21. Complete ^1H–^1H TOCSY NMR spectrum of V1I in 90:10 H_2O:D_2O at 288 K.



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EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
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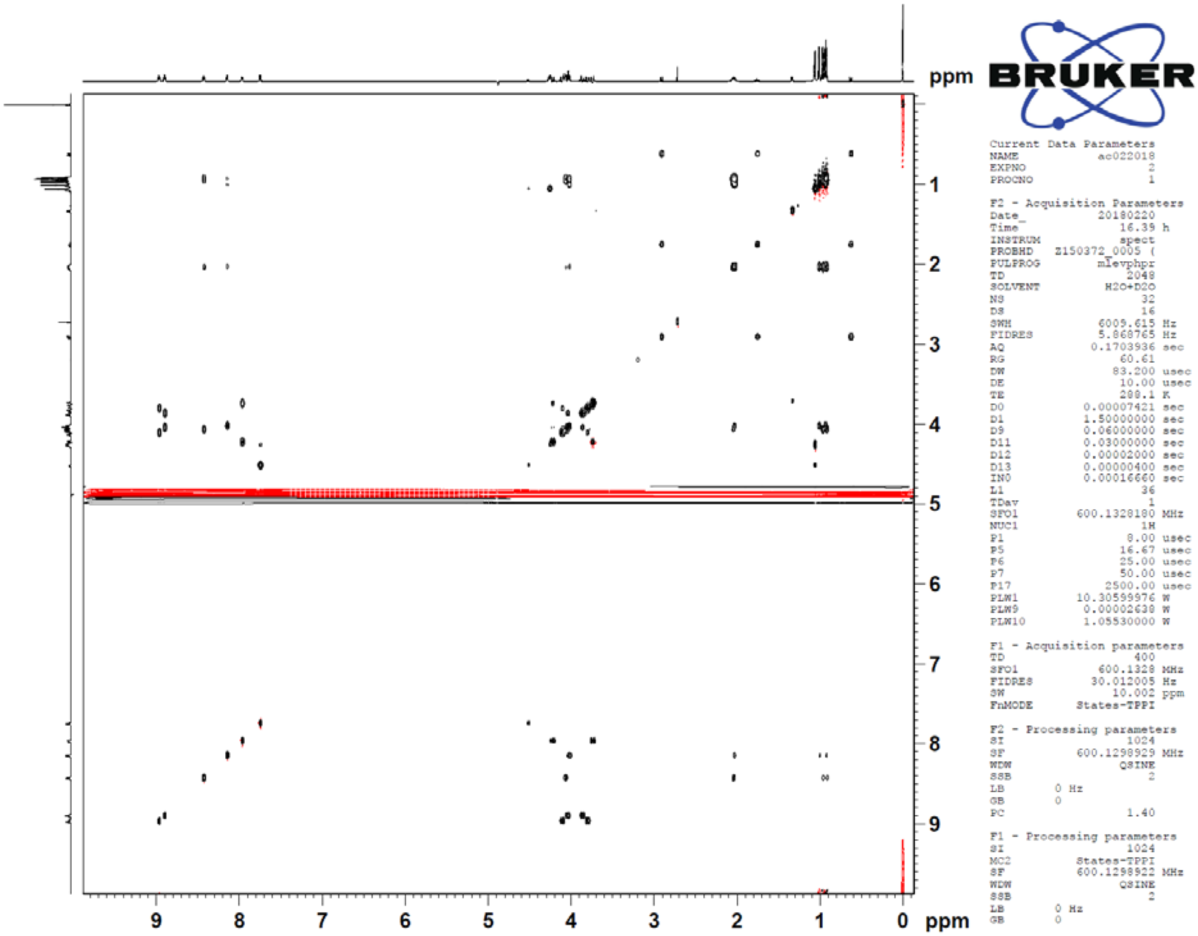
Time                 21.58 h
INSTRUM              spect
PROBHD   Z150372_0005 (
PULPROG           mlevphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      24
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   84.65
DW                  83.200 usec
DE                   10.00 usec
TE                   288.1 K
D0              0.00007421 sec
D1              1.50000000 sec
D9              0.06000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P5                   16.67 usec
P6                   25.00 usec
P7                   50.00 usec
P17                2500.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW10           1.05530000 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298933 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298921 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
```

Figure S22. Complete ^1H–^1H TOCSY NMR spectrum of V1L in 90:10 H_2O:D_2O at 288 K.



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EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
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Time                 16.39 h
INSTRUM              spect
PROBHD   Z150372_0005 (
PULPROG           mlevphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      32
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   60.61
DW                  83.200 usec
DE                   10.00 usec
TE                   288.1 K
D0              0.00007421 sec
D1              1.50000000 sec
D9              0.06000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P5                   16.67 usec
P6                   25.00 usec
P7                   50.00 usec
P17                2500.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW10           1.05530000 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298929 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298922 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
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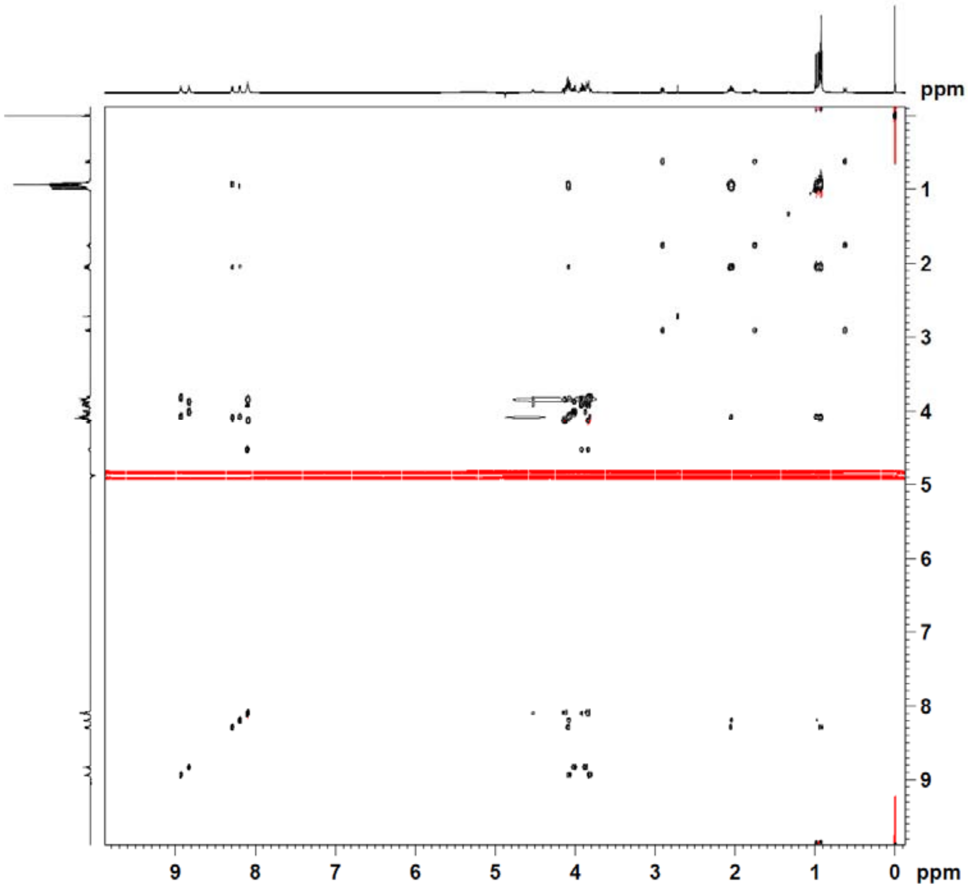
Figure S23. Complete ^1H–^1H TOCSY NMR spectrum of V1T in 90:10 H_2O:D_2O at 288 K.



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EXPNO                    4
PROCNO                   1

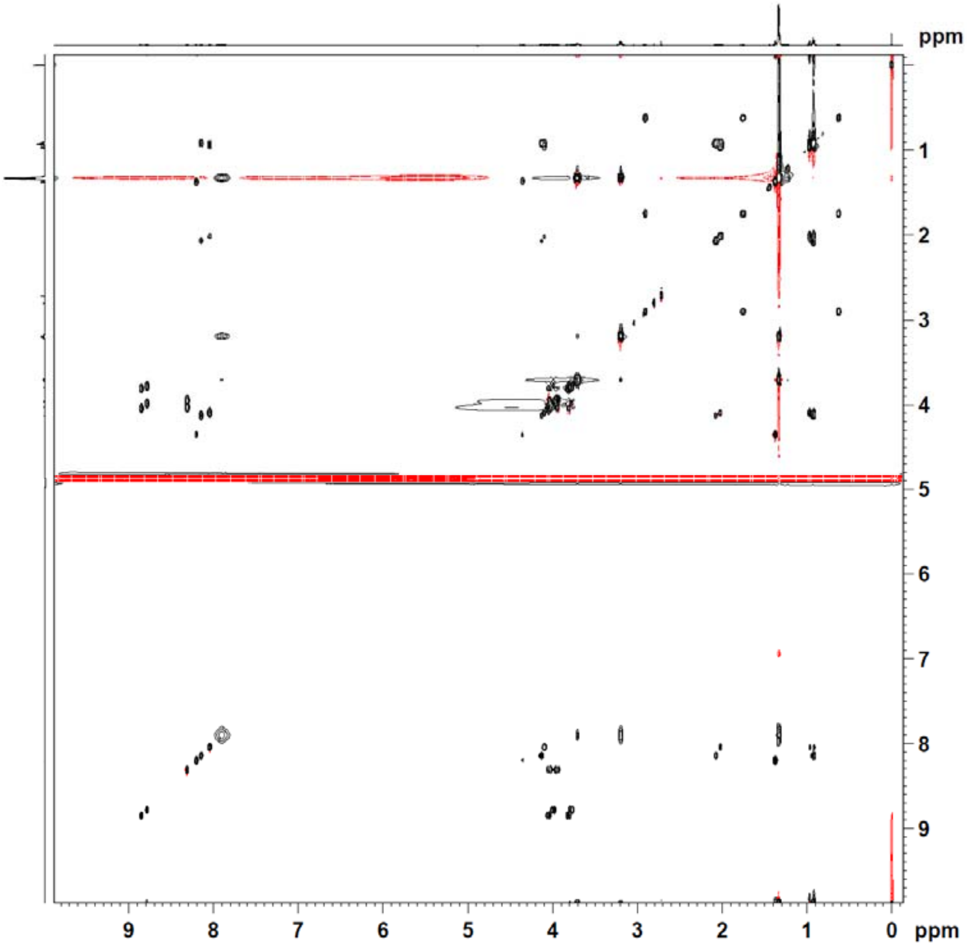
F2 - Acquisition Parameters
Date_             20180215
Time                 21.39 h
INSTRUM              spect
PROBHD    Z150372_0005 (
PULPROG           mlevphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      32
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   60.61
DW                  83.200 usec
DE                   10.00 usec
TE                   288.2 K
D0              0.00007421 sec
D1              1.50000000 sec
D9              0.06000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P5                   16.67 usec
P6                   25.00 usec
P7                   50.00 usec
P17                2500.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW10           1.05530000 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298908 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298892 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
```

Figure S24. Complete ^{1}H–^{1}H TOCSY NMR spectrum of V1S in 90:10 H_2O:D_2O at 288 K.



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Current Data Parameters
NAME              ac021918
EXPNO                    2
PROCNO                   1

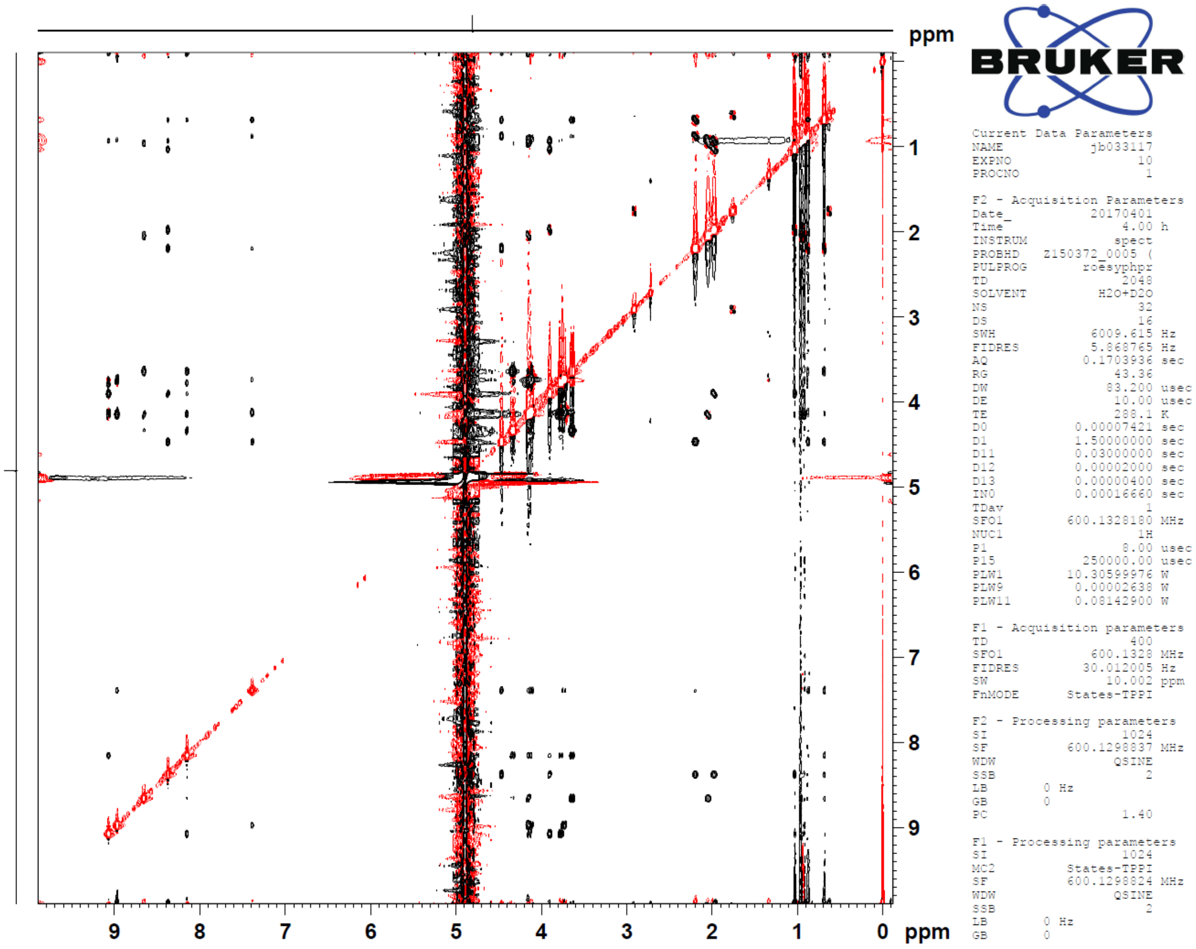
F2 - Acquisition Parameters
Date_             20180215
Time                 16.22 h
INSTRUM              spect
PROBHD   Z150372_0005 (
PULPROG           mlevphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      32
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   137.1
DW                  83.200 usec
DE                   10.00 usec
TE                   288.2 K
D0              0.00007421 sec
D1              1.50000000 sec
D9              0.06000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P5                   16.67 usec
P6                   25.00 usec
P7                   50.00 usec
P17                2500.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW10           1.05530000 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298927 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298934 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
```

Figure S25. Complete ^1H–^1H TOCSY NMR spectrum of V1A in 90:10 H_2O:D_2O at 288 K.



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PROCNO                  1

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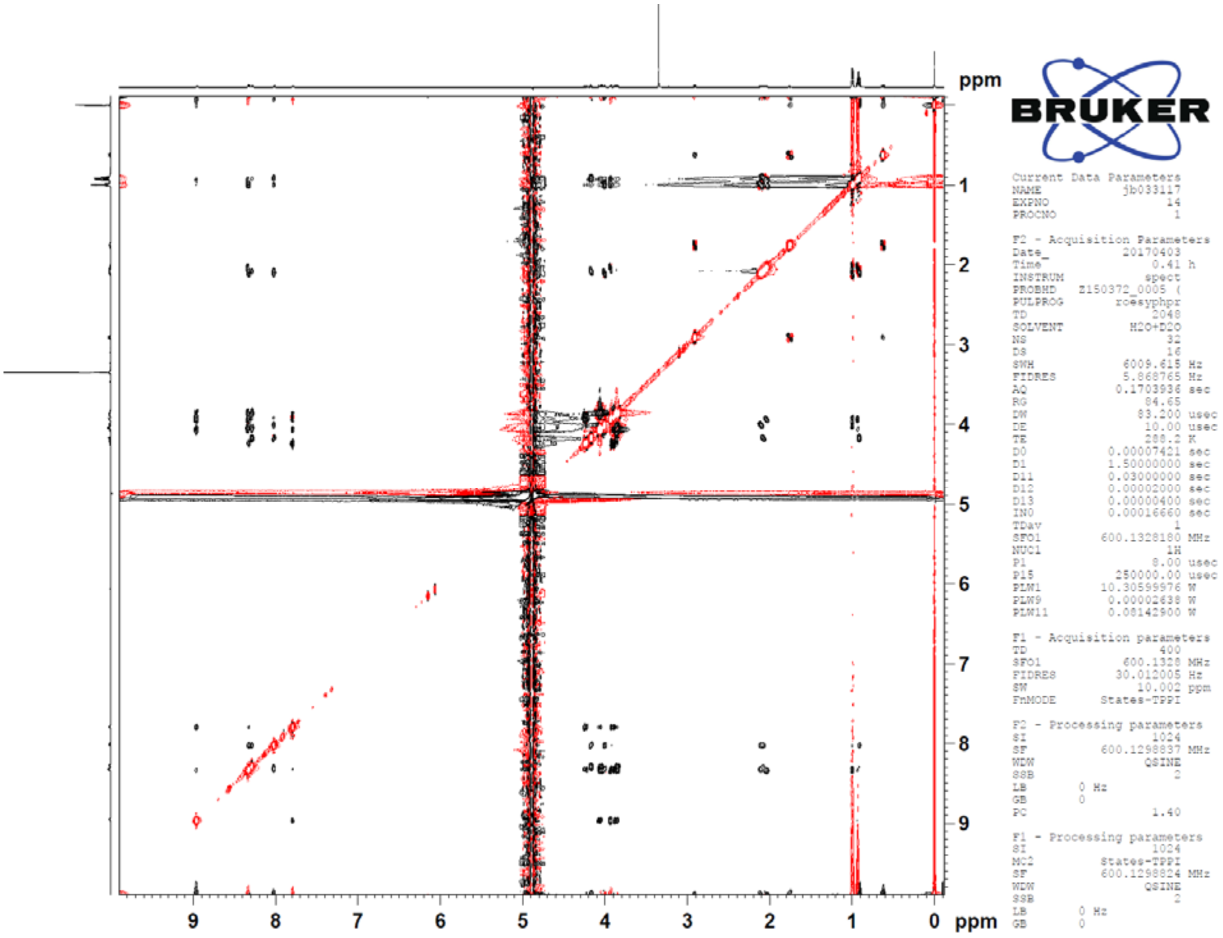
INSTRUM             spect
PROBHD   Z150372_0005 (
PULPROG        roesyphpr
TD                   2048
SOLVENT           H2O+D2O
NS                     32
DS                     16
SWH              6009.615 Hz
FIDRES           5.868765 Hz
AQ              0.1703936 sec
RG                  43.36
DW                 83.200 usec
DE                  10.00 usec
TE                  288.1 K
D0             0.00007421 sec
D1             1.50000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
D13            0.00000400 sec
IN0            0.00016660 sec
TDav                    1
SFO1          600.1328180 MHz
NUC1                   1H
P1                   8.00 usec
P15             250000.00 usec
PLW1          10.30599976 W
PLW9           0.00002638 W
PLW11          0.08142900 W

F1 - Acquisition parameters
TD                    400
SFO1             600.1328 MHz
FIDRES          30.012005 Hz
SW                 10.002 ppm
FnMODE        States-TPPI

F2 - Processing parameters
SI                   1024
SF            600.1298837 MHz
WDW                 QSINE
SSB                     2
LB         0 Hz
GB         0
PC                   1.40

F1 - Processing parameters
SI                   1024
MC2           States-TPPI
SF            600.1298824 MHz
WDW                 QSINE
SSB                     2
LB         0 Hz
GB         0
```

Figure S26. Complete ^{1}H–^{1}H ROESY NMR spectrum of P7 in 90:10 H_2O:D_2O at 288 K.



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EXPNO                   14
PROCNO                   1

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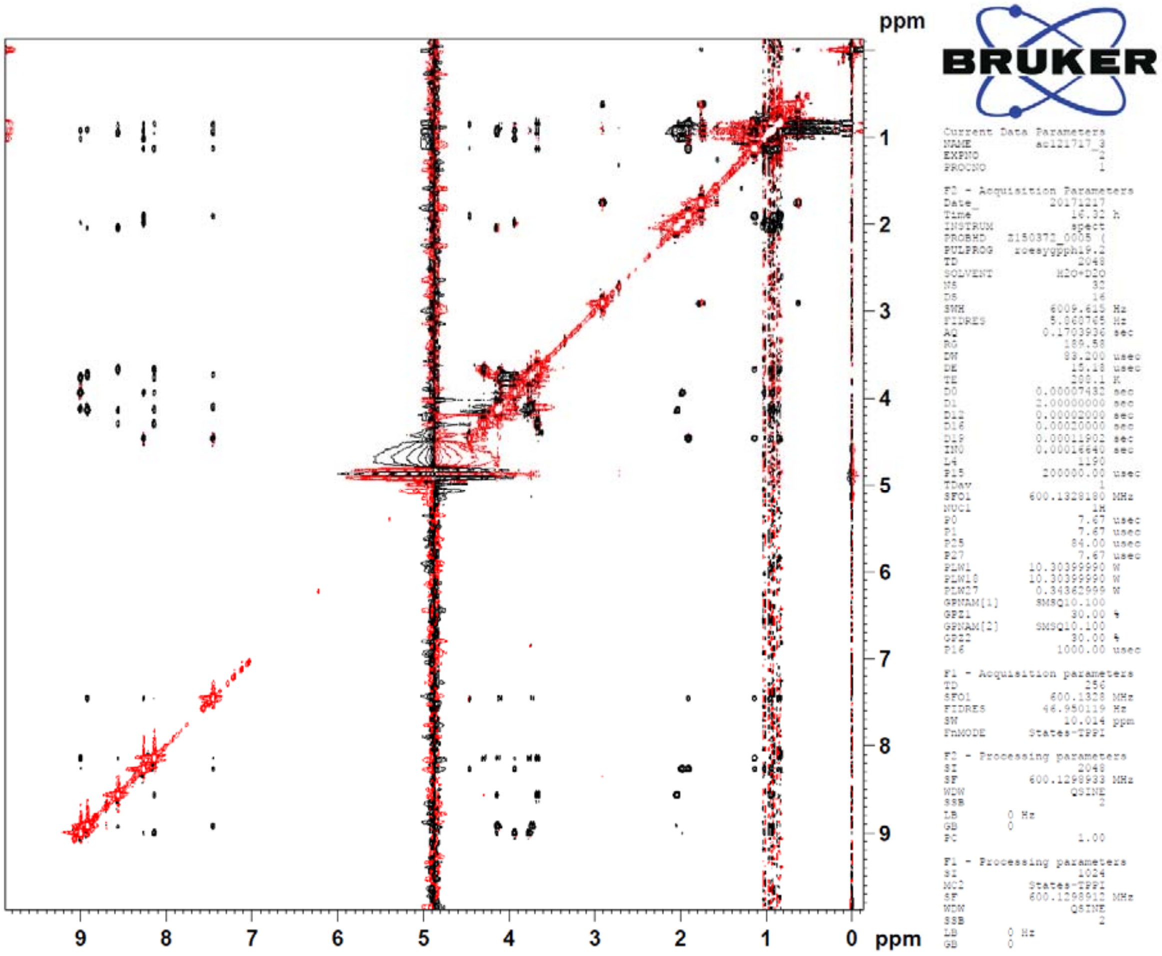
PULPROG         roesyphpr
TD                    2048
SOLVENT            H2O+D2O
NS                      32
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   84.65
DW                  83.200 usec
DE                   10.00 usec
TE                   288.2 K
D0              0.00007421 sec
D1              1.50000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
IN0             0.00016660 sec
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P1                    8.00 usec
P15              250000.00 usec
PLW1           10.30599976 W
PLW9            0.00002638 W
PLW11           0.08142900 W

F1 - Acquisition parameters
TD                     400
SFO1              600.1328 MHz
FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    1024
SF             600.1298837 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298824 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
```

Figure S27. Complete $^1H–^1H$ ROESY NMR spectrum of P6 in 90:10 $H_2O:D_2O$ at 288 K.



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Current Data Parameters
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EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20171217
Time                 16.32 h
INSTRUM              spect
PROBHD   Z150372_0005 (
PULPROG     roesygpph19.2
TD                    2048
SOLVENT            H2O+D2O
NS                      32
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                  189.58
DW                  83.200 usec
DE                   15.18 usec
TE                   288.1 K
D0              0.00007432 sec
D1              2.00000000 sec
D12             0.00002000 sec
D16             0.00020000 sec
D19             0.00011902 sec
IN0             0.00016640 sec
L4                    1190
P15              200000.00 usec
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P0                    7.67 usec
P1                    7.67 usec
P25                  84.00 usec
P27                   7.67 usec
PLW1           10.30399990 W
PLW18          10.30399990 W
PLW27           0.34362999 W
GPNAM[1]       SMSQ10.100
GPZ1                 30.00 %
GPNAM[2]       SMSQ10.100
GPZ2                 30.00 %
P16                1000.00 usec

F1 - Acquisition parameters
TD                     256
SFO1              600.1328 MHz
FIDRES           46.950119 Hz
SW                  10.014 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    2048
SF             600.1298933 MHz
WDW                  QSINE
SSB                      2
LB             0 Hz
GB             0
PC                    1.00

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298912 MHz
WDW                  QSINE
SSB                      2
LB             0 Hz
GB             0
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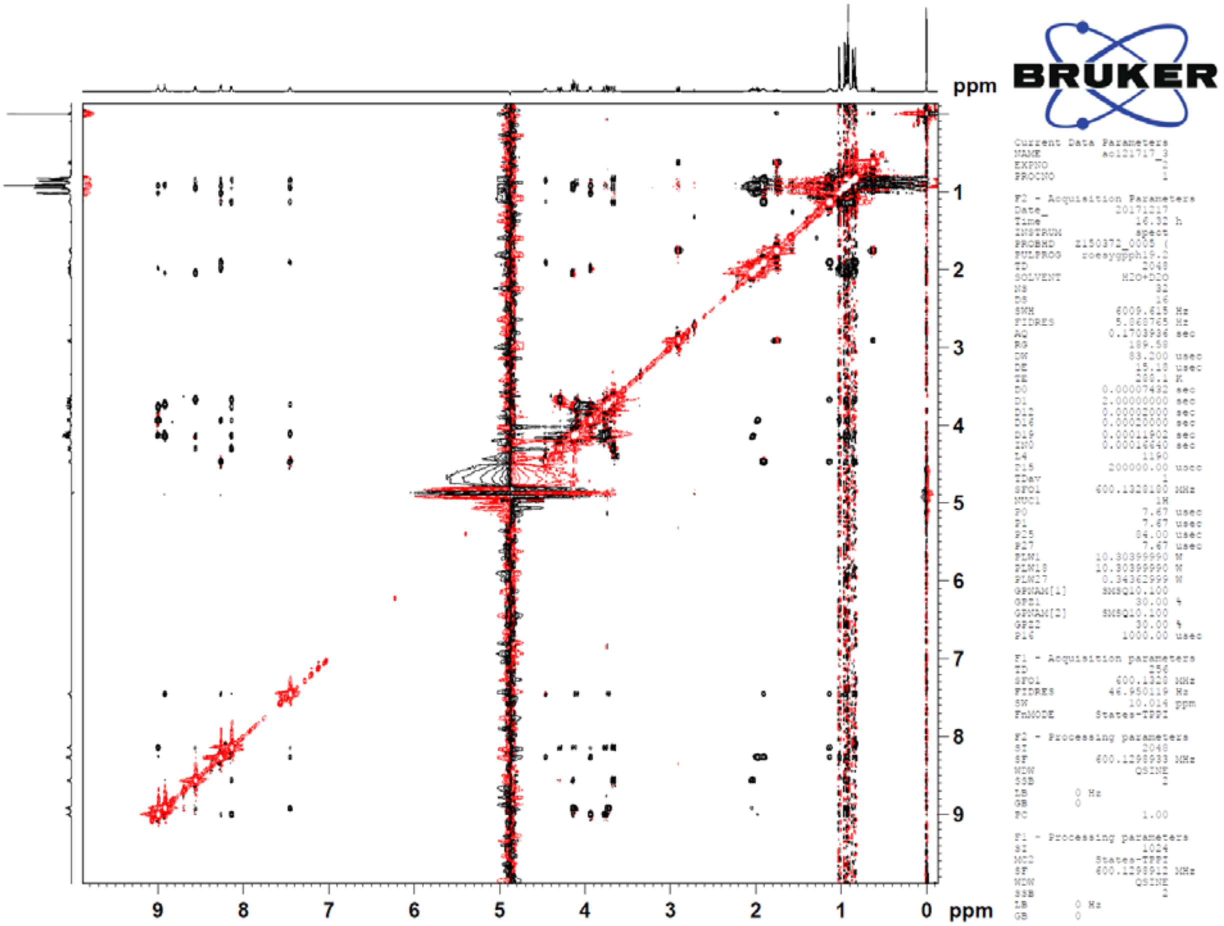
Figure S28. Complete ^1H–^1H ROESY NMR spectrum of V1I in 90:10 H_2O:D_2O at 288 K.



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Current Data Parameters
NAME             ac121717_3
EXPNO                     2
PROCNO                    1

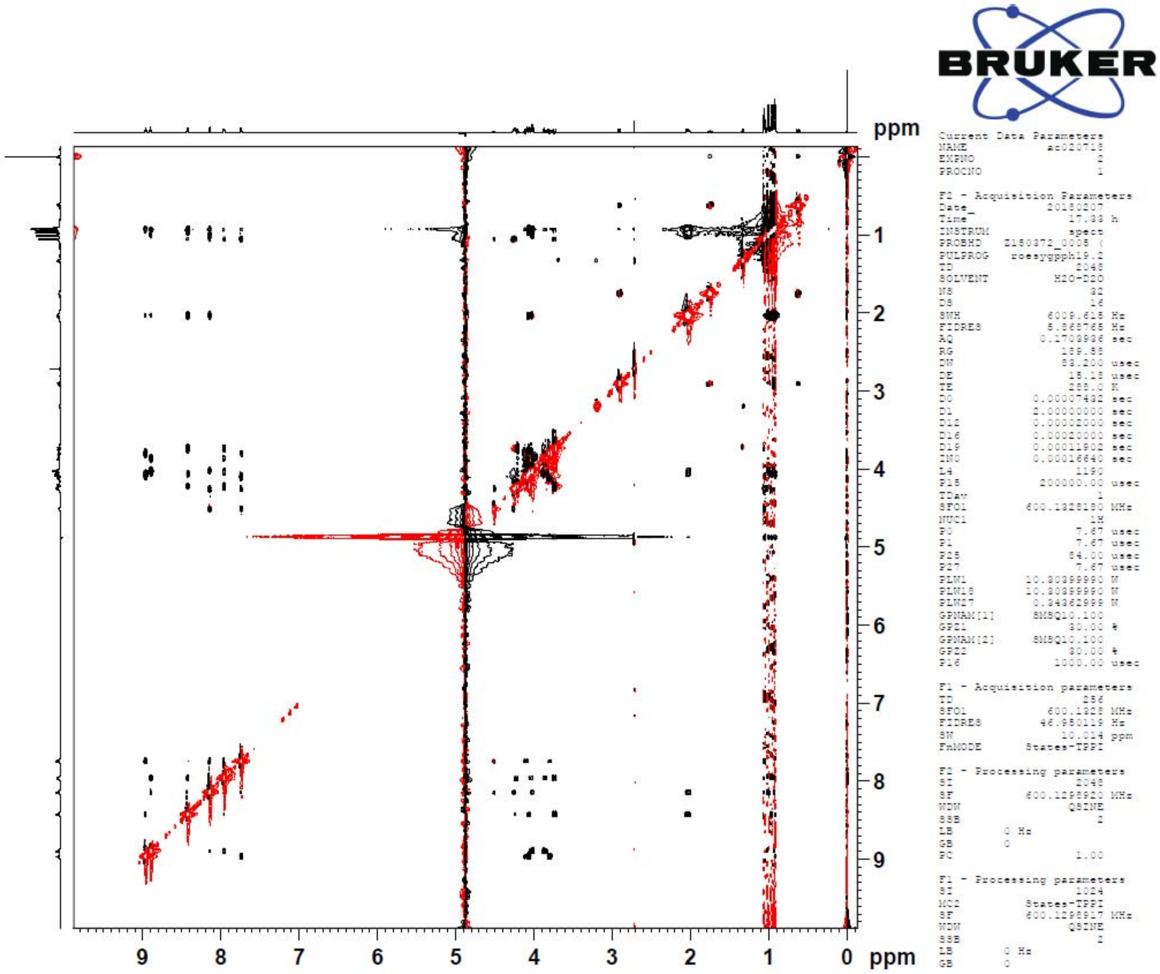
F2 - Acquisition Parameters
Date_              20171217
Time                  16.32 h
INSTRUM               spect
PROBHD   Z150372_0005 (
PULPROG    roesygpph19.2
TD                     2048
SOLVENT             H2O+D2O
NS                       32
DS                       16
SWH                6009.615 Hz
FIDRES             5.868765 Hz
AQ                0.1703936 sec
RG                   189.58
DW                   83.200 usec
DE                    15.18 usec
TE                    288.1 K
D0               0.00007432 sec
D1               2.00000000 sec
D12              0.00002000 sec
D16              0.00020000 sec
D19              0.00011902 sec
IN0              0.00016640 sec
L4                     1190
P15               200000.00 usec
TDav                      1
SFO1            600.1328180 MHz
NUC1                     1H
P0                     7.67 usec
P1                     7.67 usec
P25                   84.00 usec
P27                    7.67 usec
PLW1            10.30399990 W
PLW18           10.30399990 W
PLW27            0.34362999 W
GPNAM[1]        SMSQ10.100
GPZ1                  30.00 %
GPNAM[2]        SMSQ10.100
GPZ2                  30.00 %
P16                 1000.00 usec

F1 - Acquisition parameters
TD                      256
SFO1               600.1328 MHz
FIDRES            46.950119 Hz
SW                   10.014 ppm
FnMODE          States-TPPI

F2 - Processing parameters
SI                     2048
SF              600.1298933 MHz
WDW                   QSINE
SSB                       2
LB             0 Hz
GB             0
PC                     1.00

F1 - Processing parameters
SI                     1024
MC2             States-TPPI
SF              600.1298912 MHz
WDW                   QSINE
SSB                       2
LB             0 Hz
GB             0
```

Figure S29. Complete ^1H–^1H ROESY NMR spectrum of V1L in 90:10 H_2O:D_2O at 288 K.



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Current Data Parameters
NAME               ac020718
EXPNO                     2
PROCNO                    1

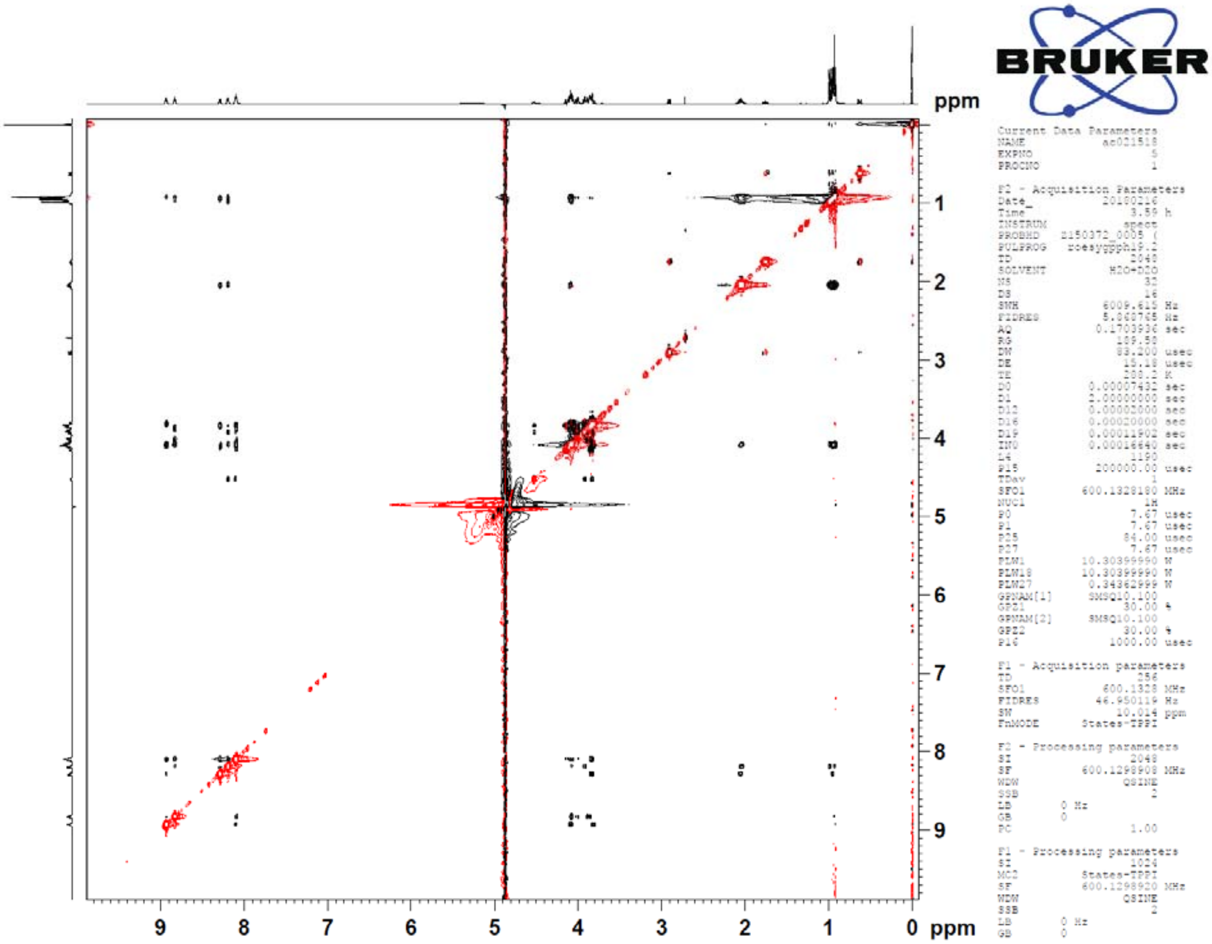
F2 - Acquisition Parameters
Date_              20180207
Time                  17.33 h
INSTRUM               spect
PROBHD   Z150372_0005 (
PULPROG   roesygpph19.2
TD                     2048
SOLVENT             H2O+D2O
NS                       32
DS                       16
SWH                6009.615 Hz
FIDRES             5.868765 Hz
AQ                0.1703936 sec
RG                   189.58
DW                   83.200 usec
DE                    15.18 usec
TE                    288.0 K
D0               0.00007432 sec
D1               2.00000000 sec
D12              0.00002000 sec
D16              0.00020000 sec
D19              0.00011902 sec
IN0              0.00016640 sec
L4                     1190
P15               200000.00 usec
TDav                      1
SFO1            600.1328180 MHz
NUC1                     1H
P0                     7.67 usec
P1                     7.67 usec
P25                   84.00 usec
P27                    7.67 usec
PLW1            10.80399990 W
PLW18           10.80399990 W
PLW27            0.34362999 W
GPNAM[1]        SMSQ10.100
GPZ1                  30.00 %
GPNAM[2]        SMSQ10.100
GPZ2                  30.00 %
P16                 1000.00 usec

F1 - Acquisition parameters
TD                      256
SFO1               600.1328 MHz
FIDRES            46.950119 Hz
SW                   10.014 ppm
FnMODE          States-TPPI

F2 - Processing parameters
SI                     2048
SF              600.1298920 MHz
WDW                   QSINE
SSB                       2
LB             0 Hz
GB             0
PC                     1.00

F1 - Processing parameters
SI                     1024
MC2             States-TPPI
SF              600.1298917 MHz
WDW                   QSINE
SSB                       2
LB             0 Hz
GB             0
```

Figure S30. Complete ^{1}H–^{1}H ROESY NMR spectrum of V1T in 90:10 H_2O:D_2O at 288 K.



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Current Data Parameters
NAME             ac021518
EXPNO                   5
PROCNO                  1

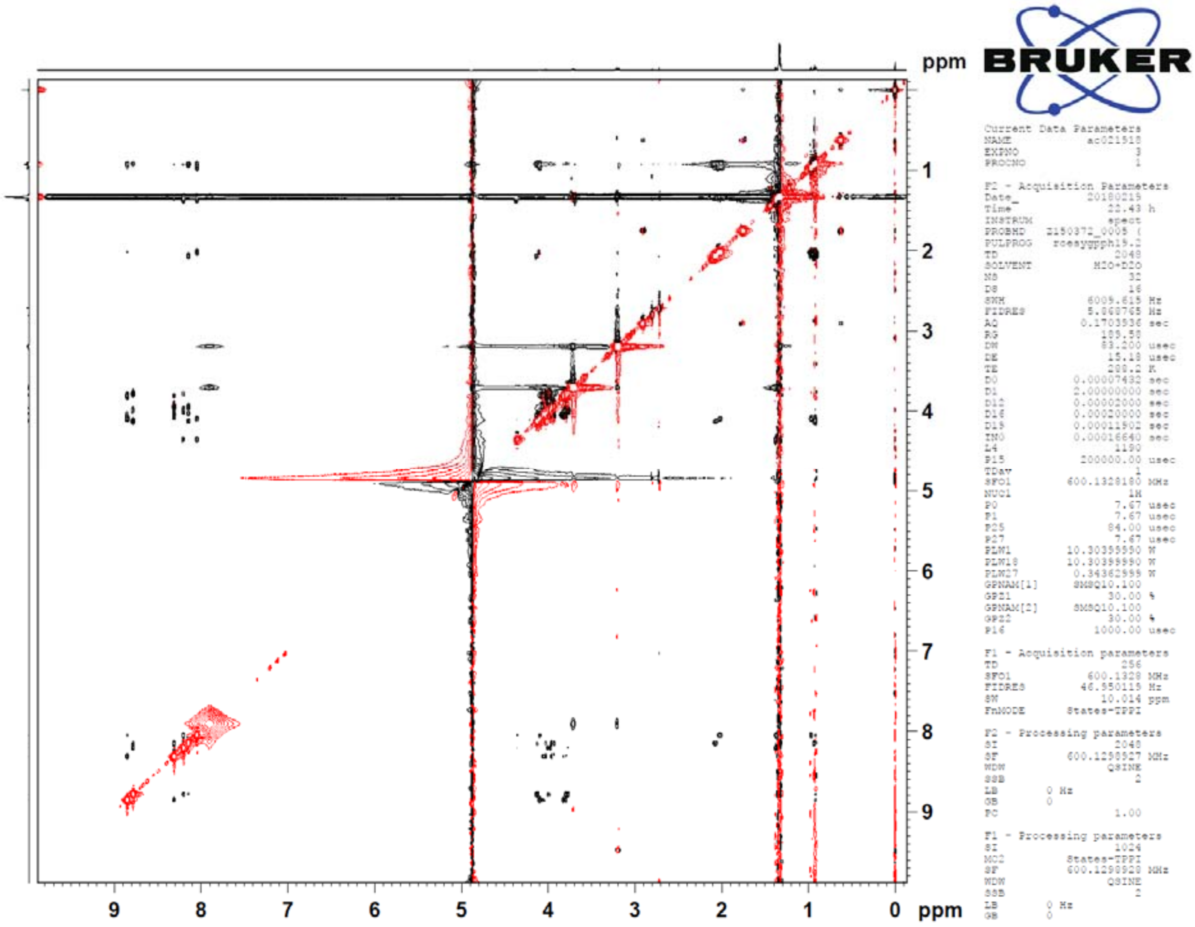
F2 - Acquisition Parameters
Date_            20180216
Time                 3.59 h
INSTRUM             spect
PROBHD   Z150372_0005 (
PULPROG   roesygpph19.2
TD                   2048
SOLVENT           H2O+D2O
NS                     32
DS                     16
SWH              6009.615 Hz
FIDRES           5.868765 Hz
AQ              0.1703936 sec
RG                 189.58
DW                 83.200 usec
DE                  15.18 usec
TE                  288.2 K
D0             0.00007432 sec
D1             2.00000000 sec
D12            0.00002000 sec
D16            0.00020000 sec
D19            0.00011902 sec
IN0            0.00016640 sec
L4                   1190
P15             200000.00 usec
TDav                    1
SFO1          600.1328180 MHz
NUC1                   1H
P0                   7.67 usec
P1                   7.67 usec
P25                 84.00 usec
P27                  7.67 usec
PLW1          10.30399990 W
PLW18         10.30399990 W
PLW27          0.34362999 W
GPNAM[1]       SMSQ10.100
GPZ1                30.00 %
GPNAM[2]       SMSQ10.100
GPZ2                30.00 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                    256
SFO1             600.1328 MHz
FIDRES          46.950119 Hz
SW                 10.014 ppm
FnMODE        States-TPPI

F2 - Processing parameters
SI                   2048
SF            600.1298908 MHz
WDW                 QSINE
SSB                     2
LB             0 Hz
GB             0
PC                   1.00

F1 - Processing parameters
SI                   1024
MC2           States-TPPI
SF            600.1298920 MHz
WDW                 QSINE
SSB                     2
LB             0 Hz
GB             0
```

Figure S31. Complete ^1H–^1H ROESY NMR spectrum of V1S in 90:10 H_2O:D_2O at 288 K.



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Current Data Parameters
NAME              ac021518
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_             20180215
Time                 22.43 h
INSTRUM              spect
PROBHD    Z150372_0005 (
PULPROG     roesygpph19.2
TD                    2048
SOLVENT            H2O+D2O
NS                      32
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                  189.58
DW                  83.200 usec
DE                   15.18 usec
TE                   288.2 K
D0              0.00007432 sec
D1              2.00000000 sec
D12             0.00002000 sec
D16             0.00020000 sec
D19             0.00011502 sec
IN0             0.00016640 sec
L4                    1190
P15              200000.00 usec
TDav                     1
SFO1           600.1328180 MHz
NUC1                    1H
P0                    7.67 usec
P1                    7.67 usec
P25                  84.00 usec
P27                   7.67 usec
PLW1           10.30399990 W
PLW18          10.30399990 W
PLW27           0.34362999 W
GPNAM[1]        SMSQ10.100
GPZ1                 30.00 %
GPNAM[2]        SMSQ10.100
GPZ2                 30.00 %
P16                1000.00 usec

F1 - Acquisition parameters
TD                     256
SFO1              600.1328 MHz
FIDRES           46.950115 Hz
SW                  10.014 ppm
FnMODE         States-TPPI

F2 - Processing parameters
SI                    2048
SF             600.1298527 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
PC                    1.00

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298920 MHz
WDW                  QSINE
SSB                      2
LB          0 Hz
GB          0
```

Figure S32. Complete ^1H–^1H ROESY NMR spectrum of V1A in 90:10 H_2O:D_2O at 288 K.

References

1. Brünger, A. T., P. D. Adams, G. M. Clore, W. L. DeLano, P. Gros, R. W. Grosse-Kunstleve, J. S. Jiang, J. Kuszewski, M. Nilges, N. S. Pannu, R. J. Read, L. M. Rice, T. Simonson, G. L. Warren. 1998. A new software suite for macromolecular structure determination. *Acta Cryst. D* 54:905-921.
2. Brunger, A. T. 2007. Version 1.2 of the crystallography and NMR system. *Nat. Protoc.* 2:2728-2733.