Supporting Information for:

Designing Well-Structured Cyclic Pentapeptides Based on Sequence–Structure Relationships

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SUPPLEMENTARY FIGURES

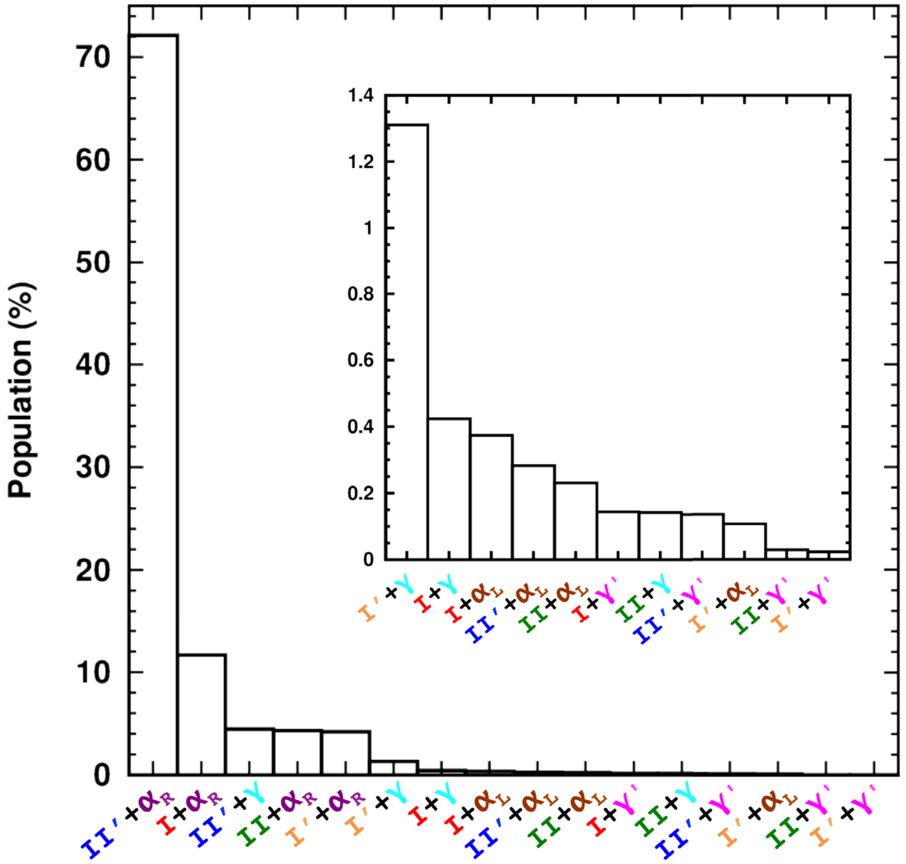

Figure S1. Populations of 16 turn combinations from simulations of cyclo-(X$_1$X$_2$AAA) of the S1 simulations. Results use cut-off turn analysis (see Materials and Methods for analysis details). Type I, I', II and II' β-turns are shown in red, orange, green and blue, respectively. Tight turns γ, γ', α_R, and α_L are shown in cyan, magenta, purple and brown, respectively.

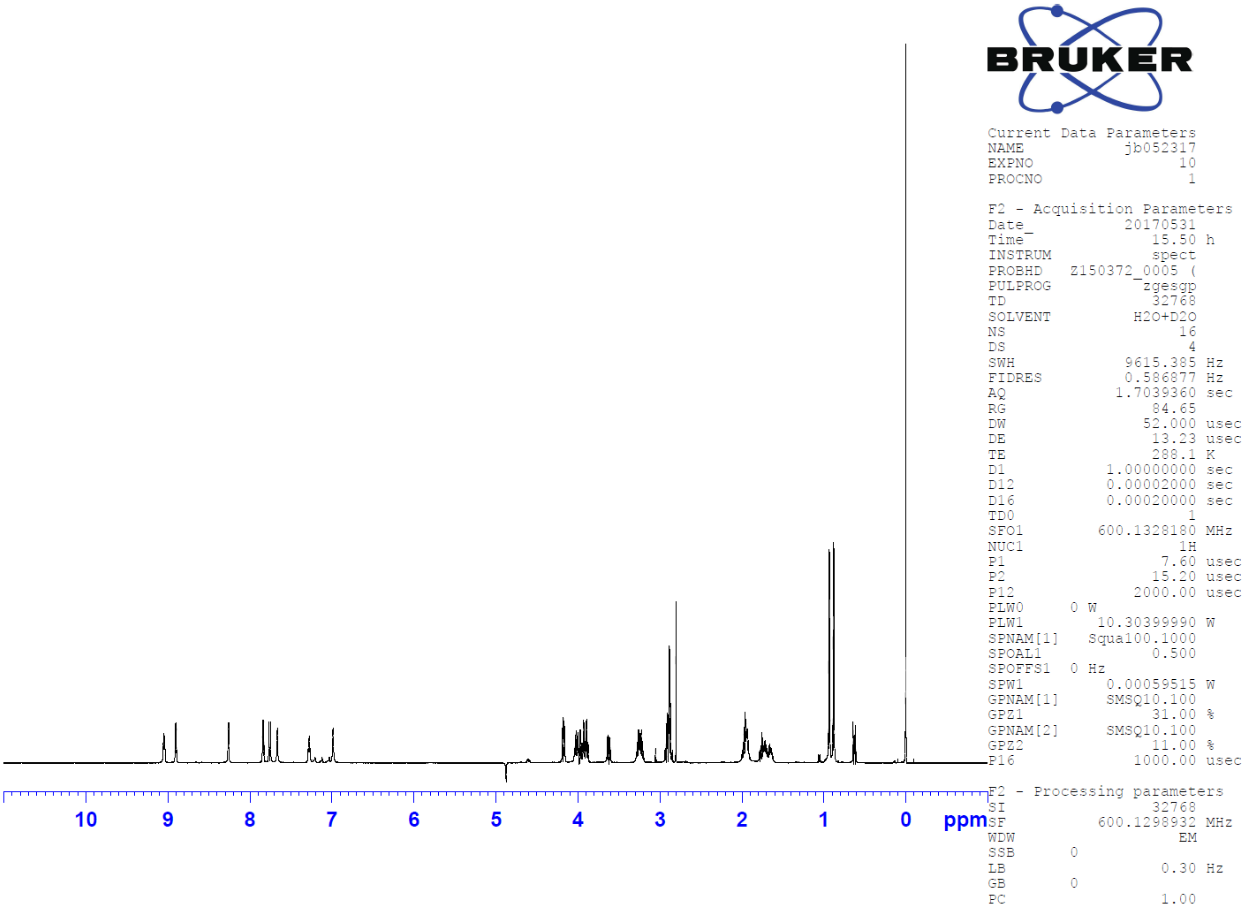

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Figure S2. ^{1}H NMR spectrum of cyclo-(GNSRV) in H_2O:D_2O (90:10) at 288 K.

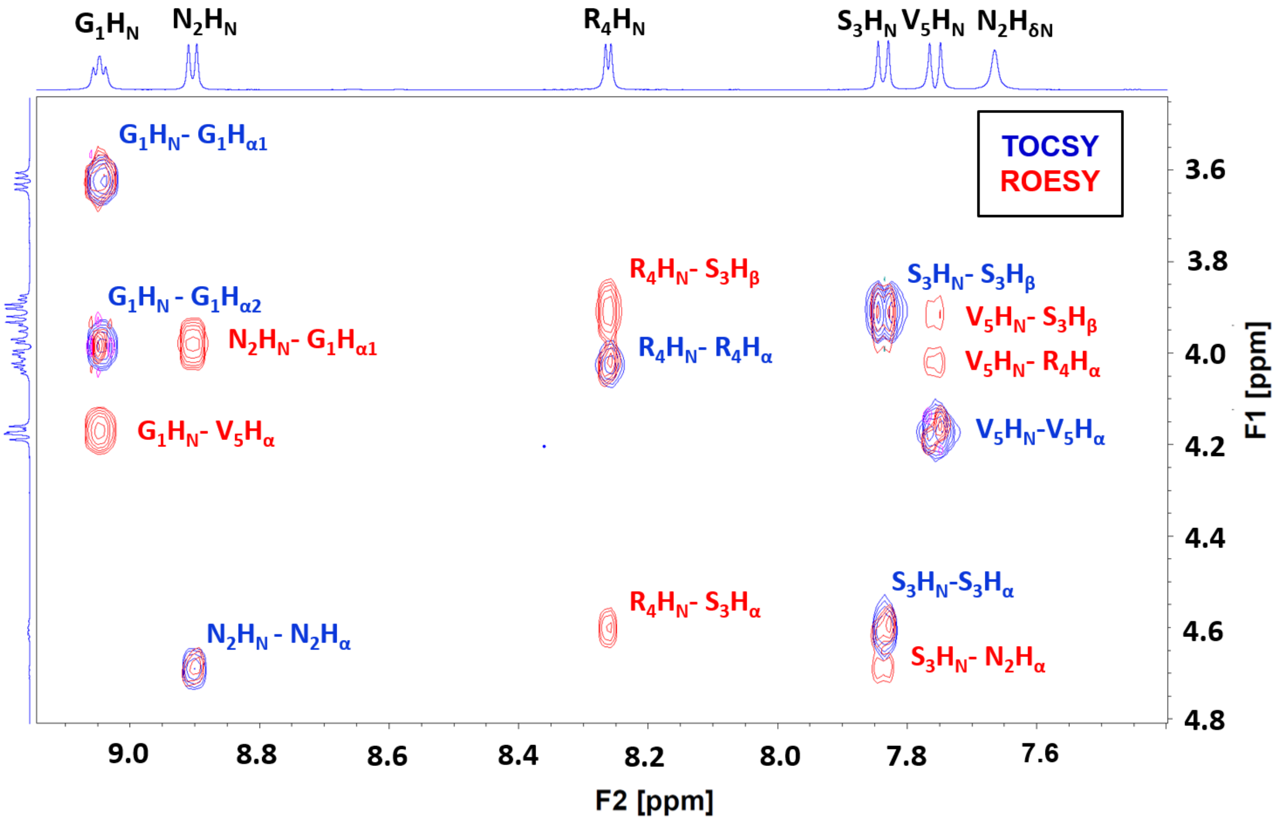
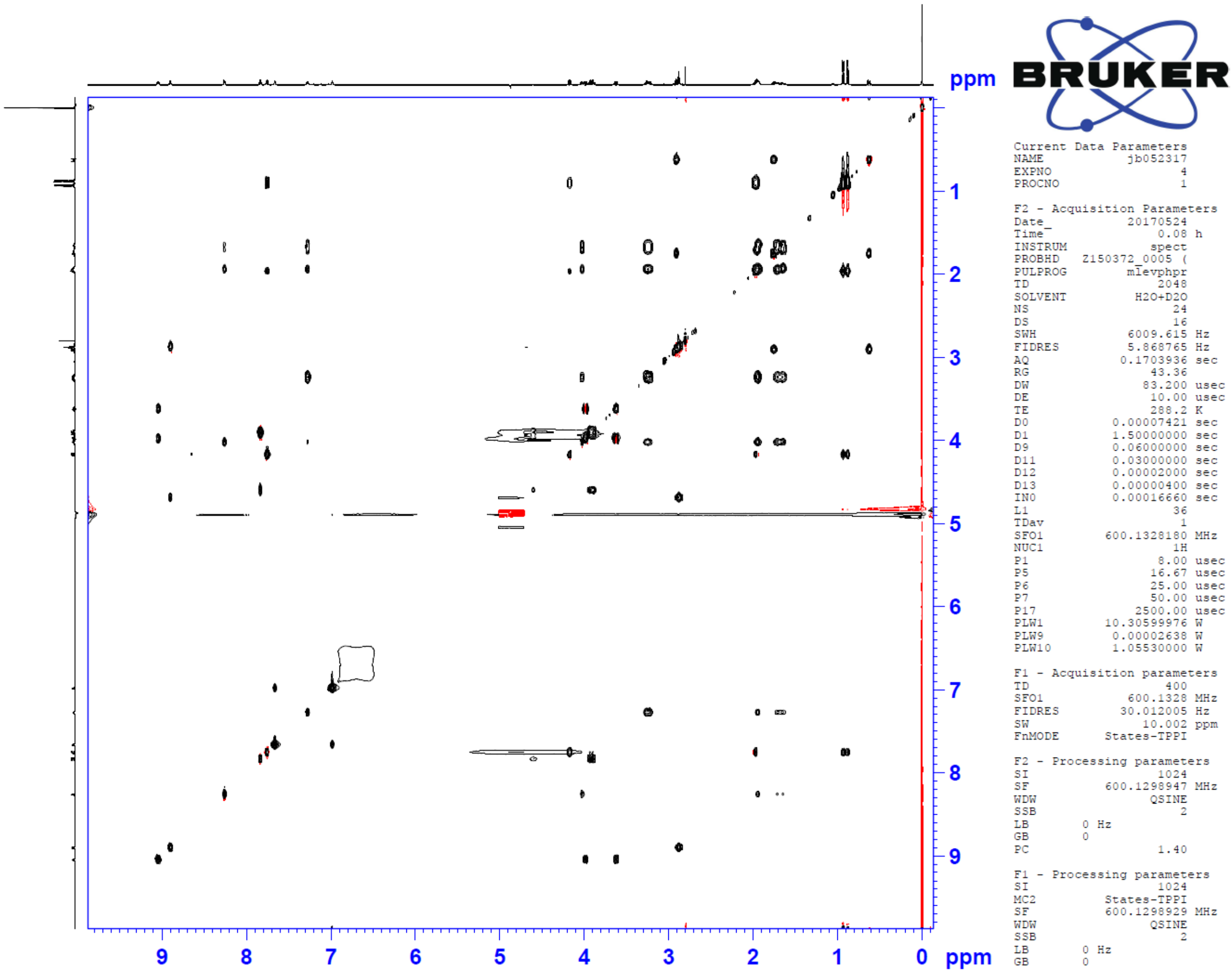


Figure S3. Fingerprint region of the 2D spectra for cyclo-(GNSRV). TOCSY peaks are shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (**top**) and the H_α region (**left side**). The peptide was dissolved in H_2O:D_2O (90:10) at a concentration of 3.5 mM at 288 K.



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SOLVENT            H2O+D2O
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DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
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TE                   288.2 K
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D1              1.50000000 sec
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D13             0.00000400 sec
IN0             0.00016660 sec
L1                      36
TDav                     1
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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

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SW                  10.002 ppm
FnMODE         States-TPPI

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GB         0
PC                    1.40

F1 - Processing parameters
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WDW                  QSINE
SSB                      2
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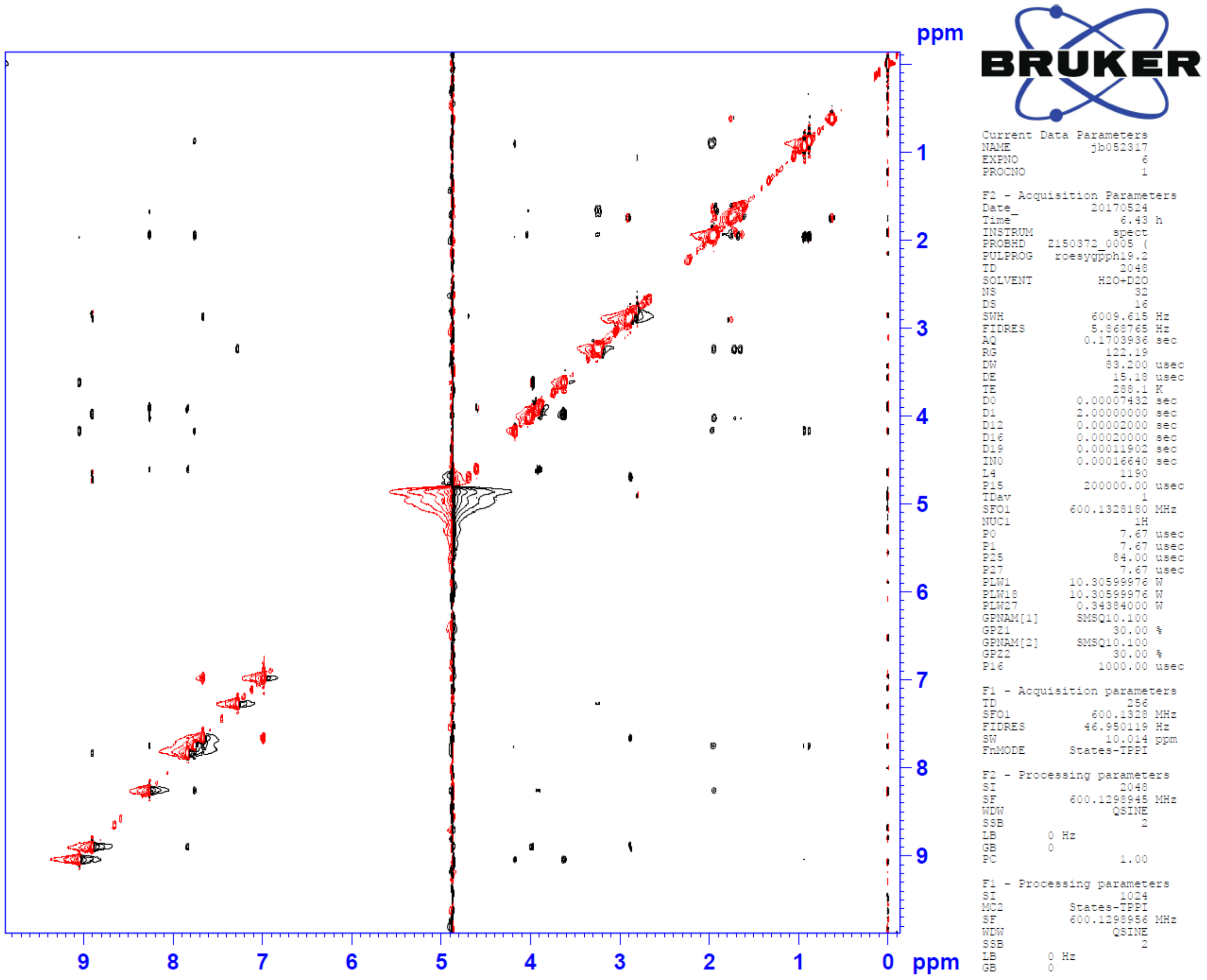
Figure S4. Full ^{1}H–^{1}H TOCSY spectrum of cyclo-(GNSRV) in H_2O:D_2O (90:10) at 288 K.



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TD                   2048
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DS                     16
SWH              6009.615 Hz
FIDRES           5.868765 Hz
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RG                 122.19
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DE                  15.18 usec
TE                  288.1 K
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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
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PLW18         10.30599976 W
PLW27          0.34384000 W
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GPZ1                30.00 %
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GPZ2                30.00 %
P16               1000.00 usec

F1 - Acquisition parameters
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FIDRES          46.950119 Hz
SW                 10.014 ppm
FnMODE        States-TPPI

F2 - Processing parameters
SI                   2048
SF            600.1298945 MHz
WDW                 QSINE
SSB                     2
LB       0 Hz
GB       0
PC                   1.00

F1 - Processing parameters
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WDW                 QSINE
SSB                     2
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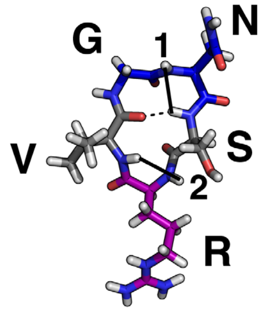
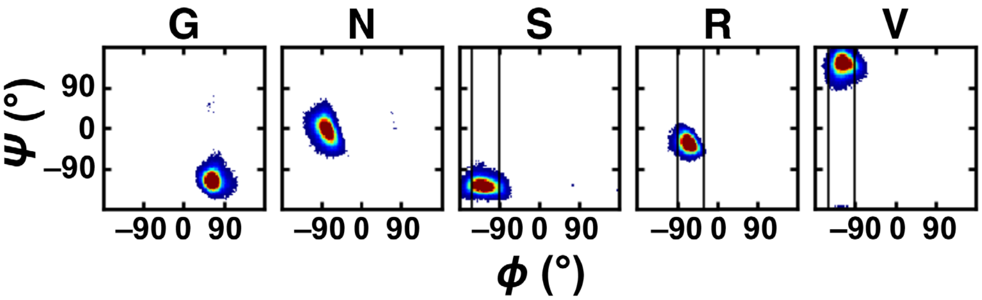
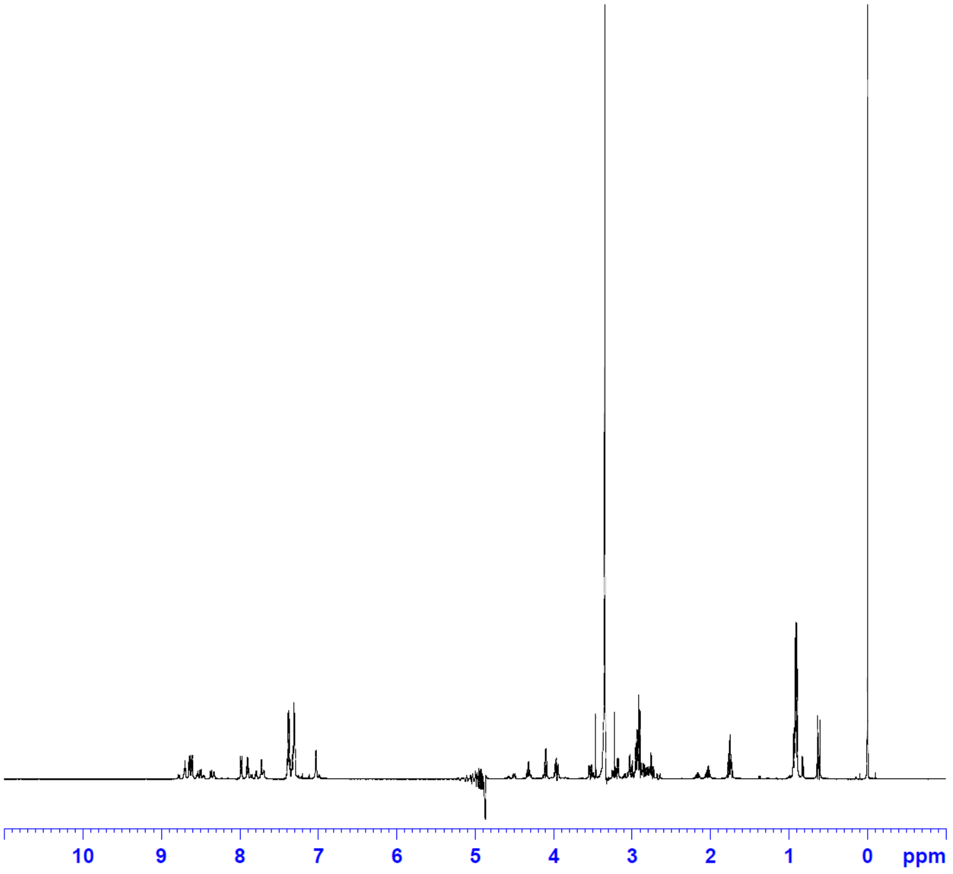
Figure S5. Full ^1H–^1H ROESY spectrum of cyclo-(GNSRV) in H_2O:D_2O (90:10) at 288 K.





Selected strong NOEs	
1	Asn^2(H$_N$)–Ser^3(H$_N$)
2	Arg^4(H$_N$)–Val^5(H$_N$)

Figure S6. Correlations between predicted structure and experimental data. Shown are a representative structure and Ramachandran plots for the most populated cluster from simulations of cyclo-(GNSRV). Type II' β-turns and α_R tight turns are shown in blue and purple, respectively. (**left**) Strong NOEs were observed between Asn^2(H$_N$) and Ser^3(H$_N$) and Arg^4(H$_N$) and Val^5(H$_N$). These are shown as black lines on the structure of cyclo-(GNSRV). (**right**) ϕ angles were estimated from *J*-values for Ser^3, Arg^4 and Val^5. These are shown as solid vertical lines on the Ramachandran plot and are in agreement with the predicted structure.



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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                  288.2 K
D1             1.00000000 sec
D12            0.00002000 sec
D16            0.00020000 sec
TD0                     1
SFO1          600.1328180 MHz
NUC1                   1H
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P2                  15.20 usec
P12               2000.00 usec
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GPZ2                11.00 %
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F2 - Processing parameters
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SSB       0
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PC                   1.00
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Figure S7. ^{1}H NMR spectrum of cyclo-(GFDNV) in H_2O:D_2O (90:10) at 288 K**.**

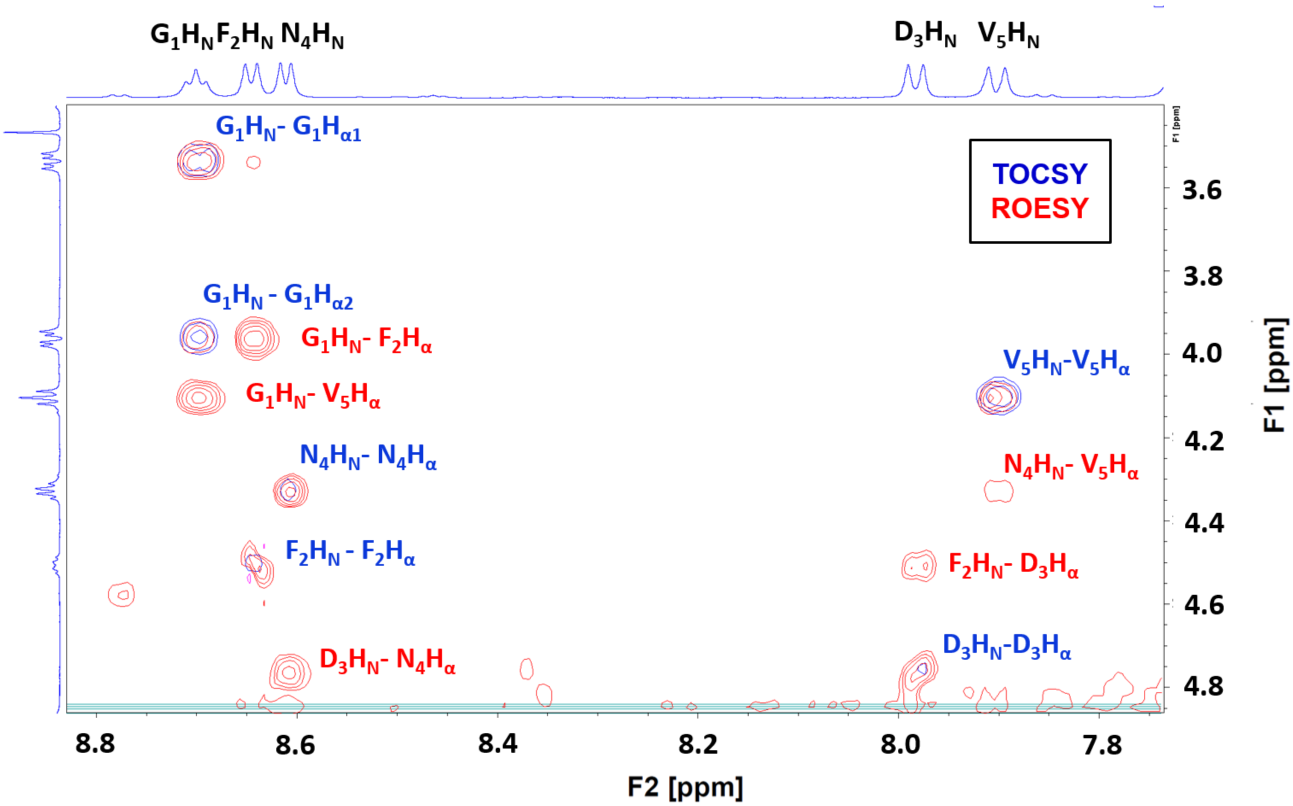
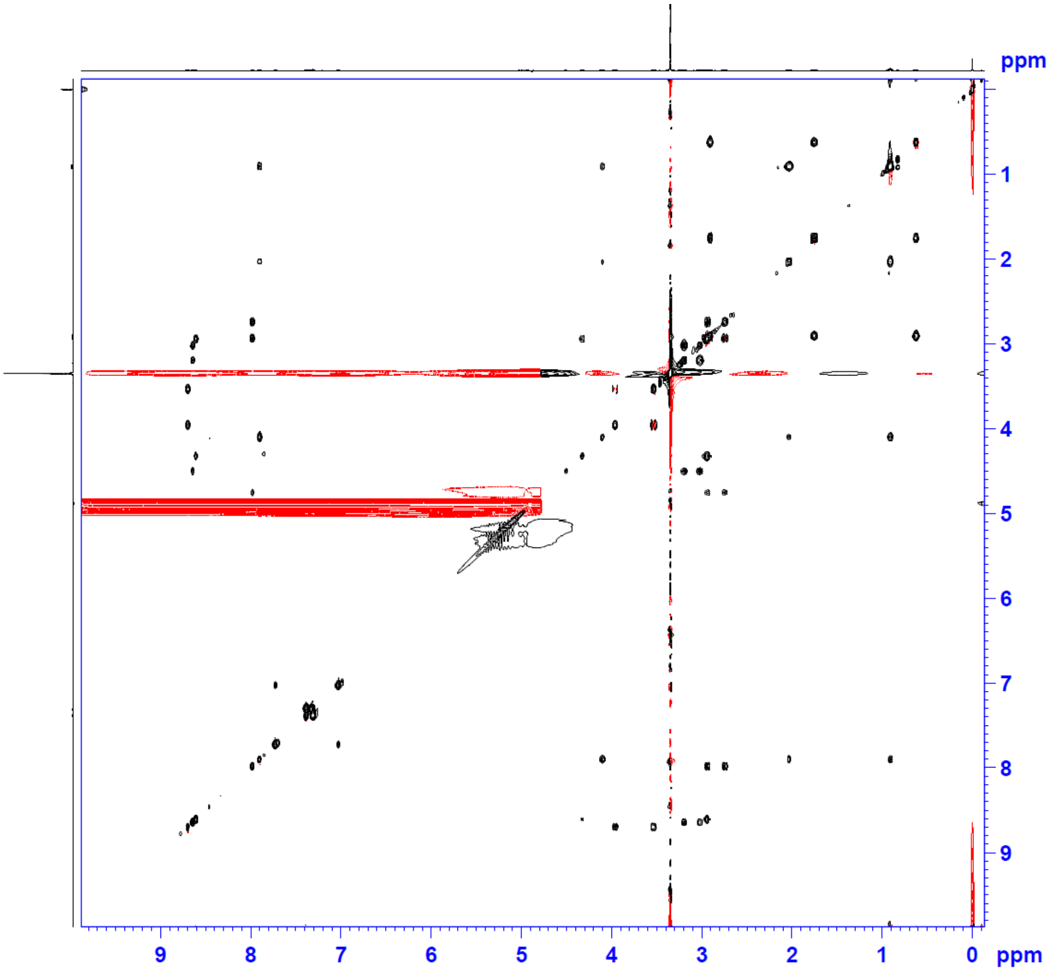


Figure S8. Fingerprint region of the 2D spectra for cyclo-(GFDNV). TOCSY peaks are shown in blue and ROESY peaks shown in red. 1D spectra correspond to the H_N region (**top**) and the $H_α$ region (**left side**). The peptide was dissolved in H_2O:D_2O (90:10) at a concentration of 3.5 mM at 288 K.



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TD                    2048
SOLVENT            H2O+D2O
NS                      24
DS                      16
SWH               6009.615 Hz
FIDRES            5.868765 Hz
AQ               0.1703936 sec
RG                   19.62
DW                  83.200 usec
DE                   10.00 usec
TE                   288.1 K
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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
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FIDRES           30.012005 Hz
SW                  10.002 ppm
FnMODE         States-TPPI

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WDW                  QSINE
SSB                      2
LB         0 Hz
GB         0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2            States-TPPI
SF             600.1298929 MHz
WDW                  QSINE
SSB                      2
LB         0 Hz
GB         0
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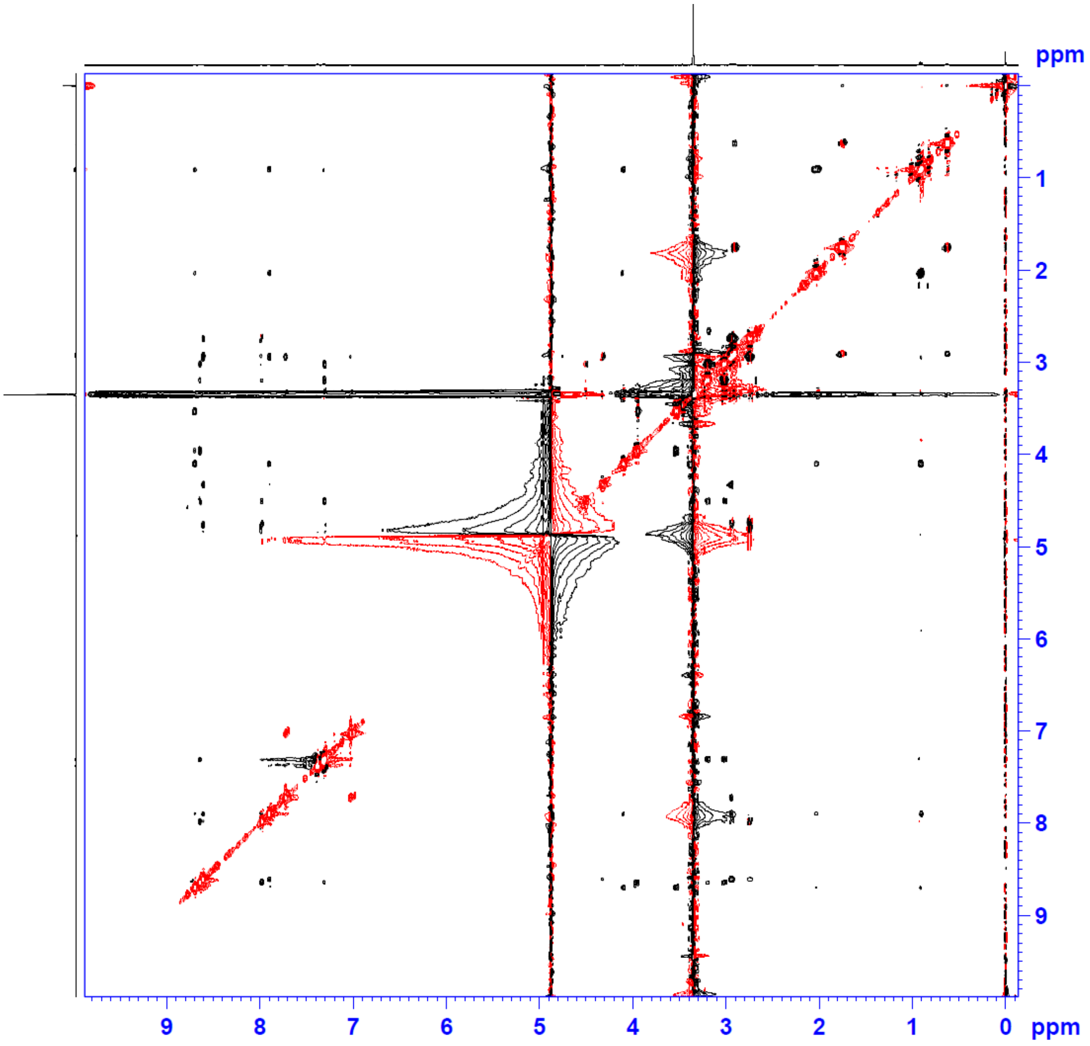
Figure S9. Full ^{1}H–^{1}H TOCSY spectrum of cyclo-(GFDNV) in H2O:D2O (90:10) at 288 K.



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PROCNO                   1

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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
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GPZ1                 30.00 %
GPNAM[2]       SMSQ10.100
GPZ2                 30.00 %
P16                1000.00 usec

F1 - Acquisition parameters
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FIDRES           46.950119 Hz
SW                  10.014 ppm
FnMODE         States-TPPI

F2 - Processing parameters
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SF             600.1298941 MHz
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SSB                      2
LB         0 Hz
GB         0
PC                    1.00

F1 - Processing parameters
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WDW                  QSINE
SSB                      2
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GB         0
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Figure S10. Full ^1H–^1H ROESY spectrum of cyclo-(GFDNV) in H_2O:D_2O (90:10) at 288 K.

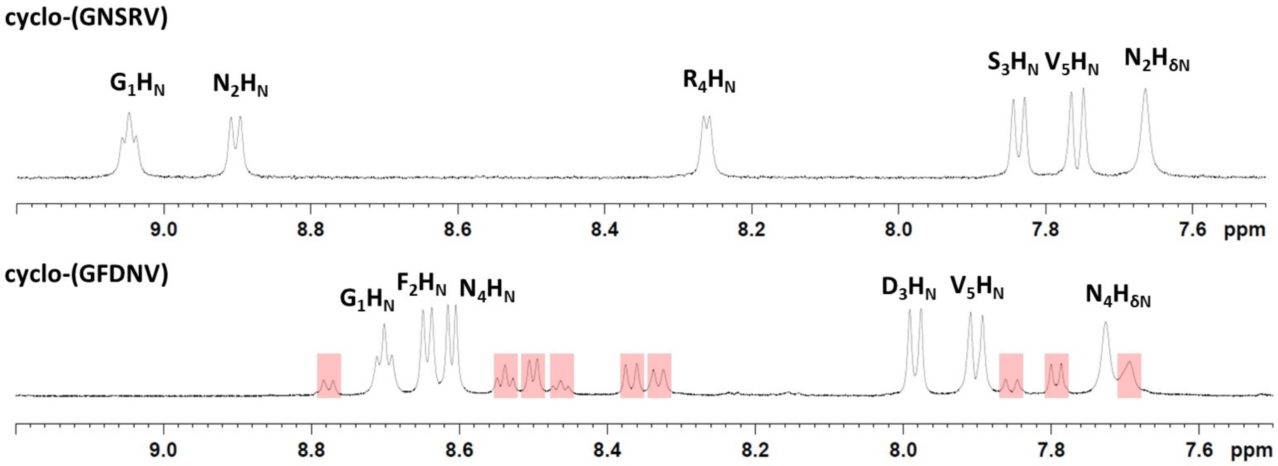
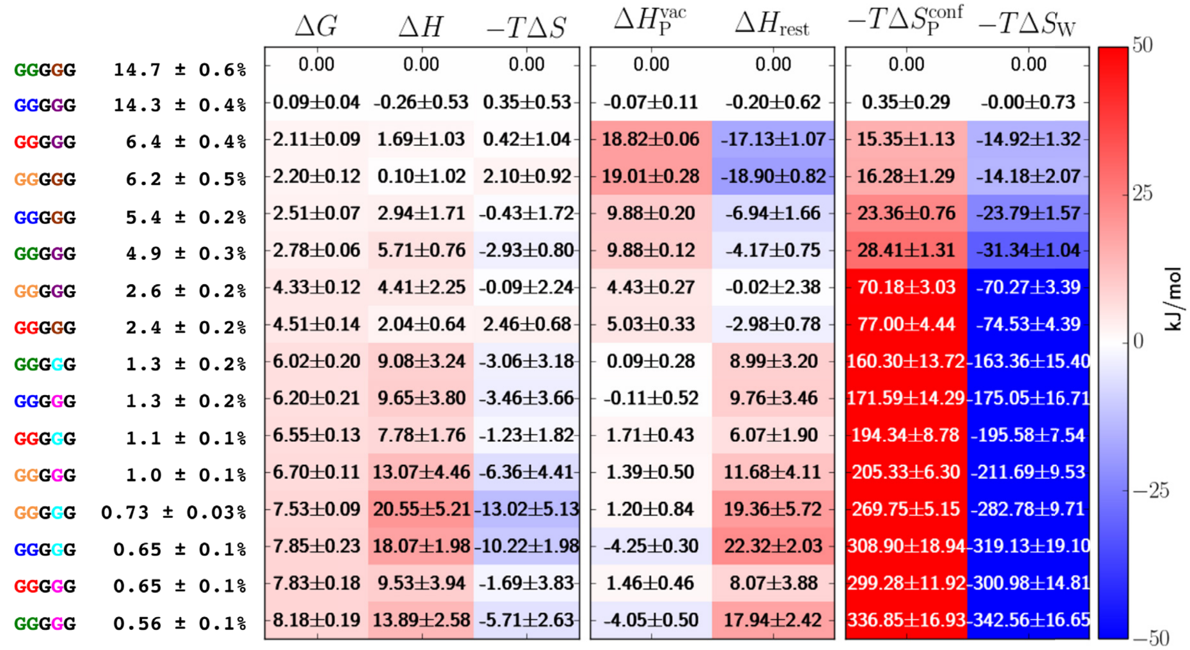


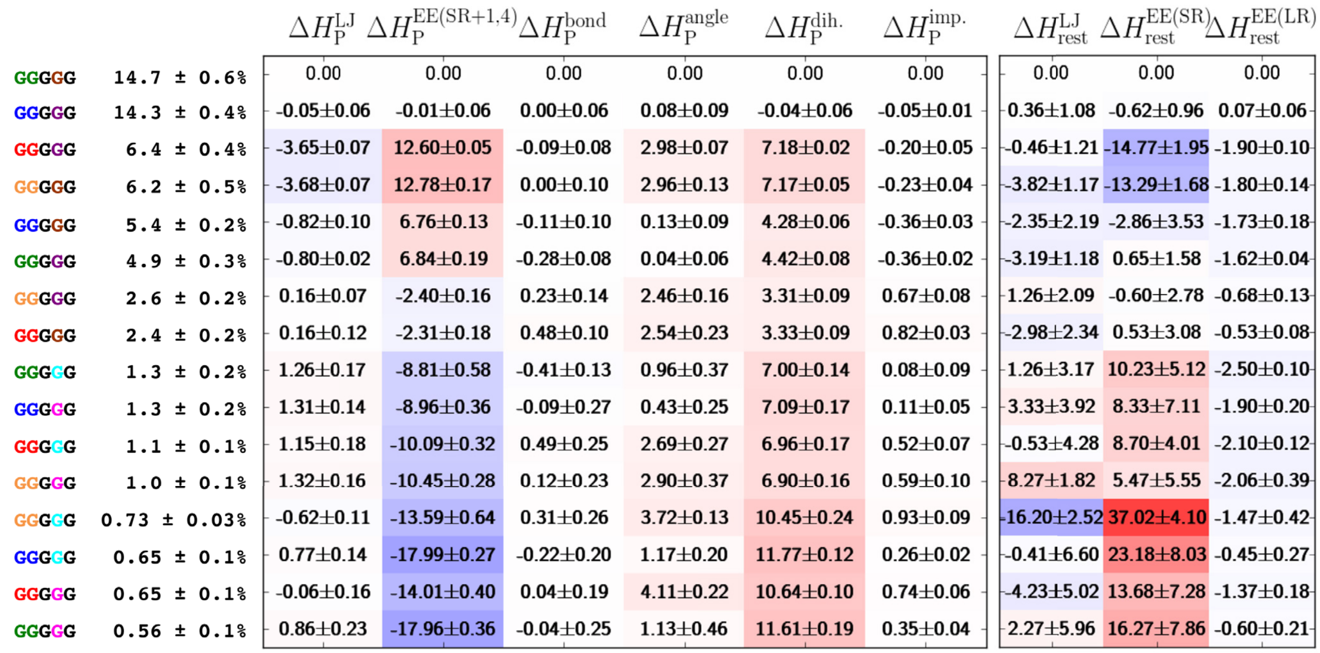
Figure S11. ^{1}H NMR spectra of H_N region for cyclo-(GNSRV) (**top**) and cyclo-(GFDNV) (**bottom**) in H_2O:D_2O (90:10) at 288 K after NMR samples were incubated at room temperature for 6 weeks or longer. The spectrum for cyclo-(GFDNV) exhibits additional H_N peaks, which are highlighted in red boxes. These increased in volume over time before saturating at the peak volumes shown. The total volume of the highlighted peaks represents roughly 33% of the total peak volume in the amide region.

SUPPLEMENTARY TABLES

Table S1. Thermodynamics decomposition for cyclo-(GGGGG). Results use cut-off turn analysis (see Materials and Methods for analysis details). Type I, I', II and II' β-turns are shown in red, orange, green and blue, respectively. Tight turns γ, γ', α_R, and α_L are shown in cyan, magenta, purple and brown, respectively. All thermodynamic terms are defined in the Materials and Methods. Populations and standard error of mean were calculated from the five neutral replicas of the S1 simulation.

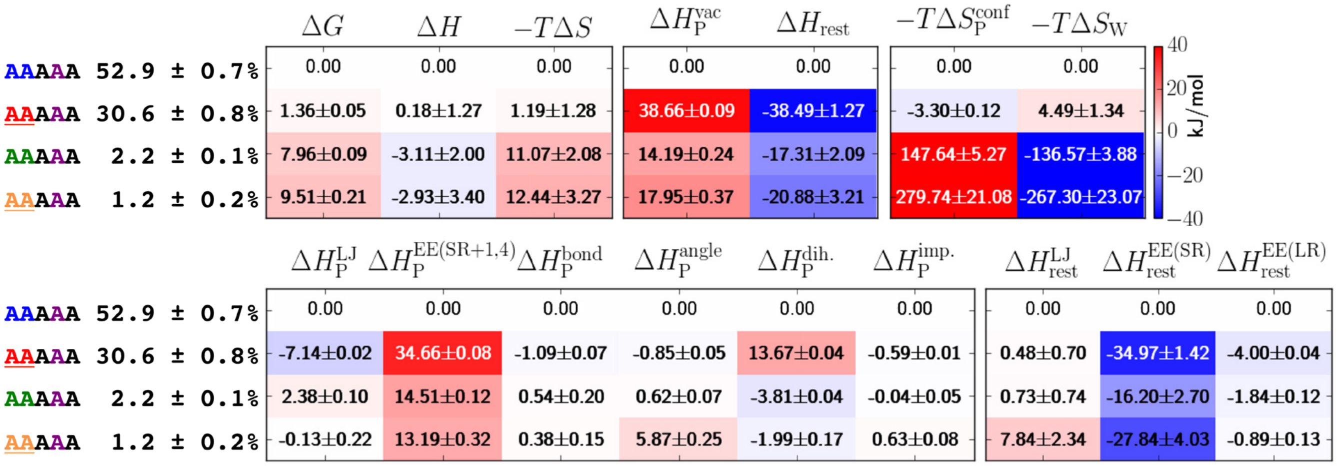


		ΔG	ΔH	$-T\Delta S$	$\Delta H_{\mathrm{P}}^{\mathrm{vac}}$	ΔH_{rest}	$-T\Delta S_{\mathrm{P}}^{\mathrm{conf}}$	$-T\Delta S_{\mathrm{W}}$
GGGGG	14.7 ± 0.6%	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GGGGG	14.3 ± 0.4%	0.09±0.04	-0.26±0.53	0.35±0.53	-0.07±0.11	-0.20±0.62	0.35±0.29	-0.00±0.73
GGGGG	6.4 ± 0.4%	2.11±0.09	1.69±1.03	0.42±1.04	18.82±0.06	-17.13±1.07	15.35±1.13	-14.92±1.32
GGGGG	6.2 ± 0.5%	2.20±0.12	0.10±1.02	2.10±0.92	19.01±0.28	-18.90±0.82	16.28±1.29	-14.18±2.07
GGGGG	5.4 ± 0.2%	2.51±0.07	2.94±1.71	-0.43±1.72	9.88±0.20	-6.94±1.66	23.36±0.76	-23.79±1.57
GGGGG	4.9 ± 0.3%	2.78±0.06	5.71±0.76	-2.93±0.80	9.88±0.12	-4.17±0.75	28.41±1.31	-31.34±1.04
GGGGG	2.6 ± 0.2%	4.33±0.12	4.41±2.25	-0.09±2.24	4.43±0.27	-0.02±2.38	70.18±3.03	-70.27±3.39
GGGGG	2.4 ± 0.2%	4.51±0.14	2.04±0.64	2.46±0.68	5.03±0.33	-2.98±0.78	77.00±4.44	-74.53±4.39
GGGGG	1.3 ± 0.2%	6.02±0.20	9.08±3.24	-3.06±3.18	0.09±0.28	8.99±3.20	160.30±13.72	-163.36±15.40
GGGGG	1.3 ± 0.2%	6.20±0.21	9.65±3.80	-3.46±3.66	-0.11±0.52	9.76±3.46	171.59±14.29	-175.05±16.71
GGGGG	1.1 ± 0.1%	6.55±0.13	7.78±1.76	-1.23±1.82	1.71±0.43	6.07±1.90	194.34±8.78	-195.58±7.54
GGGGG	1.0 ± 0.1%	6.70±0.11	13.07±4.46	-6.36±4.41	1.39±0.50	11.68±4.11	205.33±6.30	-211.69±9.53
GGGGG	0.73 ± 0.03%	7.53±0.09	20.55±5.21	-13.02±5.13	1.20±0.84	19.36±5.72	269.75±5.15	-282.78±9.71
GGGGG	0.65 ± 0.1%	7.85±0.23	18.07±1.98	-10.22±1.98	-4.25±0.30	22.32±2.03	308.90±18.94	-319.13±19.10
GGGGG	0.65 ± 0.1%	7.83±0.18	9.53±3.94	-1.69±3.83	1.46±0.46	8.07±3.88	299.28±11.92	-300.98±14.81
GGGGG	0.56 ± 0.1%	8.18±0.19	13.89±2.58	-5.71±2.63	-4.05±0.50	17.94±2.42	336.85±16.93	-342.56±16.65



		$\Delta H_{\mathrm{P}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{P}}^{\mathrm{EE(SR+1,4)}}$	$\Delta H_{\mathrm{P}}^{\mathrm{bond}}$	$\Delta H_{\mathrm{P}}^{\mathrm{angle}}$	$\Delta H_{\mathrm{P}}^{\mathrm{dih.}}$	$\Delta H_{\mathrm{P}}^{\mathrm{imp.}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(SR)}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(LR)}}$
GGGGG	14.7 ± 0.6%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GGGGG	14.3 ± 0.4%	-0.05±0.06	-0.01±0.06	0.00±0.06	0.08±0.09	-0.04±0.06	-0.05±0.01	0.36±1.08	-0.62±0.96	0.07±0.06
GGGGG	6.4 ± 0.4%	-3.65±0.07	12.60±0.05	-0.09±0.08	2.98±0.07	7.18±0.02	-0.20±0.05	-0.46±1.21	-14.77±1.95	-1.90±0.10
GGGGG	6.2 ± 0.5%	-3.68±0.07	12.78±0.17	0.00±0.10	2.96±0.13	7.17±0.05	-0.23±0.04	-3.82±1.17	-13.29±1.68	-1.80±0.14
GGGGG	5.4 ± 0.2%	-0.82±0.10	6.76±0.13	-0.11±0.10	0.13±0.09	4.28±0.06	-0.36±0.03	-2.35±2.19	-2.86±3.53	-1.73±0.18
GGGGG	4.9 ± 0.3%	-0.80±0.02	6.84±0.19	-0.28±0.08	0.04±0.06	4.42±0.08	-0.36±0.02	-3.19±1.18	0.65±1.58	-1.62±0.04
GGGGG	2.6 ± 0.2%	0.16±0.07	-2.40±0.16	0.23±0.14	2.46±0.16	3.31±0.09	0.67±0.08	1.26±2.09	-0.60±2.78	-0.68±0.13
GGGGG	2.4 ± 0.2%	0.16±0.12	-2.31±0.18	0.48±0.10	2.54±0.23	3.33±0.09	0.82±0.03	-2.98±2.34	0.53±3.08	-0.53±0.08
GGGGG	1.3 ± 0.2%	1.26±0.17	-8.81±0.58	-0.41±0.13	0.96±0.37	7.00±0.14	0.08±0.09	1.26±3.17	10.23±5.12	-2.50±0.10
GGGGG	1.3 ± 0.2%	1.31±0.14	-8.96±0.36	-0.09±0.27	0.43±0.25	7.09±0.17	0.11±0.05	3.33±3.92	8.33±7.11	-1.90±0.20
GGGGG	1.1 ± 0.1%	1.15±0.18	-10.09±0.32	0.49±0.25	2.69±0.27	6.96±0.17	0.52±0.07	-0.53±4.28	8.70±4.01	-2.10±0.12
GGGGG	1.0 ± 0.1%	1.32±0.16	-10.45±0.28	0.12±0.23	2.90±0.37	6.90±0.16	0.59±0.10	8.27±1.82	5.47±5.55	-2.06±0.39
GGGGG	0.73 ± 0.03%	-0.62±0.11	-13.59±0.64	0.31±0.26	3.72±0.13	10.45±0.24	0.93±0.09	-16.20±2.52	37.02±4.10	-1.47±0.42
GGGGG	0.65 ± 0.1%	0.77±0.14	-17.99±0.27	-0.22±0.20	1.17±0.20	11.77±0.12	0.26±0.02	-0.41±6.60	23.18±8.03	-0.45±0.27
GGGGG	0.65 ± 0.1%	-0.06±0.16	-14.01±0.40	0.04±0.19	4.11±0.22	10.64±0.10	0.74±0.06	-4.23±5.02	13.68±7.28	-1.37±0.18
GGGGG	0.56 ± 0.1%	0.86±0.23	-17.96±0.36	-0.04±0.25	1.13±0.46	11.61±0.19	0.35±0.04	2.27±5.96	16.27±7.86	-0.60±0.21

Table S2. Thermodynamics decomposition for cyclo-(AAAAA). Type I, I', II and II' β-turns are shown in red, orange, green and blue, respectively and distorted β-turns are underlined. The tight turn α_R is shown in purple. All thermodynamic terms are defined in the Materials and Methods. Populations and standard error of mean were calculated from the five neutral replicas of the S1 simulation.



	ΔG	ΔH	$-T\Delta S$	$\Delta H_{\mathrm{P}}^{\mathrm{vac}}$	ΔH_{rest}	$-T\Delta S_{\mathrm{P}}^{\mathrm{conf}}$	$-T\Delta S_{\mathrm{W}}$
AAAAA 52.9 ± 0.7%	0.00	0.00	0.00	0.00	0.00	0.00	0.00
AAAAA 30.6 ± 0.8%	1.36±0.05	0.18±1.27	1.19±1.28	38.66±0.09	-38.49±1.27	-3.30±0.12	4.49±1.34
AAAAA 2.2 ± 0.1%	7.96±0.09	-3.11±2.00	11.07±2.08	14.19±0.24	-17.31±2.09	147.64±5.27	-136.57±3.88
AAAAA 1.2 ± 0.2%	9.51±0.21	-2.93±3.40	12.44±3.27	17.95±0.37	-20.88±3.21	279.74±21.08	-267.30±23.07

	$\Delta H_{\mathrm{P}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{P}}^{\mathrm{EE(SR+1,4)}}$	$\Delta H_{\mathrm{P}}^{\mathrm{bond}}$	$\Delta H_{\mathrm{P}}^{\mathrm{angle}}$	$\Delta H_{\mathrm{P}}^{\mathrm{dih.}}$	$\Delta H_{\mathrm{P}}^{\mathrm{imp.}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{LJ}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(SR)}}$	$\Delta H_{\mathrm{rest}}^{\mathrm{EE(LR)}}$
AAAAA 52.9 ± 0.7%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
AAAAA 30.6 ± 0.8%	-7.14±0.02	34.66±0.08	-1.09±0.07	-0.85±0.05	13.67±0.04	-0.59±0.01	0.48±0.70	-34.97±1.42	-4.00±0.04
AAAAA 2.2 ± 0.1%	2.38±0.10	14.51±0.12	0.54±0.20	0.62±0.07	-3.81±0.04	-0.04±0.05	0.73±0.74	-16.20±2.70	-1.84±0.12
AAAAA 1.2 ± 0.2%	-0.13±0.22	13.19±0.32	0.38±0.15	5.87±0.25	-1.99±0.17	0.63±0.08	7.84±2.34	-27.84±4.03	-0.89±0.13

Table S3. Population and turn combination for the top three most populated clusters of cyclo-(X_1AAAA) of the S1 simulations. Type I, I', II and II' β-turns are shown in red, orange, green and blue, respectively and distorted β-turns are underlined. The tight turn α_R is shown in purple.

AAAAA		CAAAA		DAAAA		EAAAA		FAAAA	
53%	AAAAA	18%	CAAAA	20%	DAAAA	14%	EAAAA	18%	FAAAA
31%	AAAAA	13%	CAAAA	11%	DAAAA	11%	EAAAA	15%	FAAAA
2%	AAAAA	10%	CAAAA	9%	DAAAA	10%	EAAAA	10%	FAAAA

GAAAA		HAAAA		IAAAA		KAAAA		LAAAA	
30%	GAAAA	23%	HAAAA	30%	IAAAA	13%	KAAAA	12%	LAAAA
11%	GAAAA	21%	HAAAA	16%	IAAAA	13%	KAAAA	10%	LAAAA
5%	GAAAA	16%	HAAAA	10%	IAAAA	10%	KAAAA	9%	LAAAA

MAAAA		NAAAA		PAAAA		QAAAA		RAAAA	
20%	MAAAA	17%	NAAAA	32%	PAAAA	23%	QAAAA	17%	RAAAA
15%	MAAAA	13%	NAAAA	18%	PAAAA	15%	QAAAA	10%	RAAAA
11%	MAAAA	8%	NAAAA	9%	PAAAA	7%	QAAAA	9%	RAAAA

SAAAA		TAAAA		VAAAA		WAAAA		YAAAA	
19%	SAAAA	12%	TAAAA	36%	VAAAA	19%	WAAAA	23%	YAAAA
13%	SAAAA	10%	TAAAA	11%	VAAAA	10%	WAAAA	10%	YAAAA
12%	SAAAA	10%	TAAAA	8%	VAAAA	9%	WAAAA	10%	YAAAA

Table S4. Population and turn combination for the top three most populated clusters of cyclo-(X_1X_2AAA) of the S1 simulations. Type I, I', II and II' β-turns are shown in red, orange, green and blue, respectively and distorted β-turns are underlined. The tight turns γ and α_R are shown in cyan and purple, respectively.

GXAAA

GGAAA		GAAAA		GVAAA		GFAAA		GRAAA		GDAAA		GNAAA		GSAAA	
24%	GGAAA	30%	GAAAA	23%	GVAAA	26%	GFAAA	41%	GRAAA	32%	GDAAA	40%	GNAAA	31%	GSAAA
11%	GGAAA	11%	GAAAA	7%	GVAAA	10%	GFAAA	8%	GRAAA	6%	GDAAA	11%	GNAAA	20%	GSAAA
8%	GGAAA	5%	GAAAA	6%	GVAAA	6%	GFAAA	6%	GRAAA	6%	GDAAA	2%	GNAAA	4%	GSAAA

VXAAA

VGAAA		VAAAA		VVAAA		VFAAA		VRAAA		VDAAA		VNAAA		VSAAA	
58%	VGAAA	36%	VAAAA	21%	VVAAA	18%	VFAAA	18%	VRAAA	49%	VDAAA	38%	VNAAA	53%	VSAAA
4%	VGAAA	11%	VAAAA	13%	VVAAA	18%	VFAAA	13%	VRAAA	21%	VDAAA	8%	VNAAA	7%	VSAAA
3%	VGAAA	8%	VAAAA	9%	VVAAA	14%	VFAAA	8%	VRAAA	2%	VDAAA	5%	VNAAA	6%	VSAAA

FXAAA

FGAAA		FAAAA		FVAAA		FFAAA		FRAAA		FDAAA		FNAAA		FSAAA	
37%	FGAAA	18%	FAAAA	20%	FVAAA	23%	FFAAA	17%	FRAAA	31%	FDAAA	24%	FNAAA	31%	FSAAA
10%	FGAAA	15%	FAAAA	11%	FVAAA	14%	FFAAA	9%	FRAAA	20%	FDAAA	17%	FNAAA	12%	FSAAA
6%	FGAAA	10%	FAAAA	9%	FVAAA	12%	FFAAA	9%	FRAAA	7%	FDAAA	7%	FNAAA	11%	FSAAA

RXAAA

RGAAA		RAAAA		RVAAA		RFAAA		RRAAA		RDAAA		RNAAA		RSAAA	
33%	RGAAA	17%	RAAAA	26%	RVAAA	15%	RFAAA	11%	RRAAA	22%	RDAAA	25%	RNAAA	35%	RSAAA
6%	RGAAA	10%	RAAAA	11%	RVAAA	11%	RFAAA	10%	RRAAA	21%	RDAAA	12%	RNAAA	14%	RSAAA
5%	RGAAA	9%	RAAAA	7%	RVAAA	11%	RFAAA	9%	RRAAA	6%	RDAAA	7%	RNAAA	7%	RSAAA

DXAAA

DGAAA		DAAAA		DVAAA		DFAAA		DRAAA		DDAAA		DNAAA		DSAAA	
12%	DGAAA	20%	DAAAA	19%	DVAAA	24%	DFAAA	21%	DRAAA	19%	DDAAA	31%	DNAAA	15%	DSAAA
12%	DGAAA	11%	DAAAA	14%	DVAAA	11%	DFAAA	20%	DRAAA	15%	DDAAA	6%	DNAAA	13%	DSAAA
11%	DGAAA	9%	DAAAA	11%	DVAAA	9%	DFAAA	7%	DRAAA	14%	DDAAA	5%	DNAAA	13%	DSAAA

NXAAA

NGAAA		NAAAA		NVAAA		NFAAA		NRAAA		NDAAA		NNAAA		NSAAA	
22%	NGAAA	17%	NAAAA	15%	NVAAA	18%	NFAAA	21%	NRAAA	18%	NDAAA	20%	NNAAA	20%	NSAAA
16%	NGAAA	13%	NAAAA	12%	NVAAA	9%	NFAAA	8%	NRAAA	17%	NDAAA	18%	NNAAA	18%	NSAAA
7%	NGAAA	8%	NAAAA	8%	NVAAA	8%	NFAAA	8%	NRAAA	12%	NDAAA	7%	NNAAA	12%	NSAAA

SXAAA

SGAAA		SAAAA		SVAAA		SFAAA		SRAAA		SDAAA		SNAAA		SSAAA	
29%	SGAAA	19%	SAAAA	15%	SVAAA	21%	SFAAA	28%	SRAAA	20%	SDAAA	31%	SNAAA	22%	SSAAA
10%	SGAAA	13%	SAAAA	15%	SVAAA	13%	SFAAA	10%	SRAAA	13%	SDAAA	10%	SNAAA	20%	SSAAA
7%	SGAAA	12%	SAAAA	10%	SVAAA	8%	SFAAA	7%	SRAAA	11%	SDAAA	8%	SNAAA	14%	SSAAA

Table S5. Highest scoring sequences from neighbor analysis of simulations of cyclo-(X_1X_2AAA), where X_1/X_2 = G, V, F, R, D, N or S, for the $\beta_{II'}$+α_R turn combination.

Rank	CP	Score	Rank	CP	Score
1	GNSRV	1.287	11	GRSDV	1.191
2	GRSRV	1.265	12	GRSFV	1.188
3	GNSVV	1.235	13	SNSRV	1.184
4	GSSRV	1.226	14	GNRVV	1.178
5	GNRRV	1.220	15	GRRRV	1.177
6	GDSRV	1.215	16	GRNRV	1.175
7	GRSVV	1.213	17	GSSVV	1.174
8	GNSDV	1.213	18	GNFRV	1.165
9	GNNRV	1.211	19	GDSVV	1.163
10	GNSFV	1.210	20	GNGRV	1.162

Table S6. Thermodynamics decomposition for (**A**) cyclo-(GNSRV), (**B**) cyclo-(GNAAA), (**C**) cyclo-(ANSAA), (**D**) cyclo-(AASRA), (**E**) cyclo-(AAARV) and (**F**) cyclo-(GAAAV). Type I, I' and II' β-turns are shown in red, orange and blue, respectively and distorted β-turns are underlined. The tight turns γ and α_R are shown in cyan and purple, respectively. In B–F, arrows indicate the turn combination that is at same location as in cyclo-(GNSRV). For A–B and E–F, boxes indicate factors that stabilize the most populated conformation. In C–D, the factors that stabilize the most populated conformation over others is undetermined as the error is larger than the average. All thermodynamic terms are defined in the Materials and Methods. Populations and standard error of mean were calculated from the five neutral replicas of the S1 simulations.

(A)

		ΔG	ΔH	$-T\Delta S$	ΔH_P^{vac}	ΔH_{rest}	$-T\Delta S_P^{conf}$	$-T\Delta S_W$	ΔH_P^{LJ}	$\Delta H_P^{EE(SR+1,4)}$	ΔH_P^{bond}	ΔH_P^{angle}	$\Delta H_P^{dih.}$	$\Delta H_P^{imp.}$	ΔH_{rest}^{LJ}	$\Delta H_{rest}^{EE(SR)}$	$\Delta H_{rest}^{EE(LR)}$
GNSRV	67.4%	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
GNSRV	7.6%	5.43±0.08	3.36±1.33	2.07±1.29	-29.34±0.65	32.70±1.26	51.15±1.58	-49.08±2.44	-5.40±0.19	-39.91±0.76	0.98±0.08	3.59±0.10	11.43±0.17	-0.03±0.04	7.19±2.37	19.37±3.11	6.14±0.65
GNSRV	4.9%	6.57±0.13	5.21±2.57	1.36±2.56	11.91±1.04	-6.71±2.87	82.00±4.92	-80.64±5.76	0.66±0.19	-6.71±0.83	-0.23±0.10	2.77±0.10	15.16±0.19	0.26±0.07	3.97±2.51	-1.69±3.96	-8.99±0.87

(B)

		ΔG	ΔH	$-T\Delta S$	ΔH_P^{vac}	ΔH_{rest}	$-T\Delta S_P^{conf}$	$-T\Delta S_W$	ΔH_P^{LJ}	$\Delta H_P^{EE(SR+1,4)}$	ΔH_P^{bond}	ΔH_P^{angle}	$\Delta H_P^{dih.}$	$\Delta H_P^{imp.}$	ΔH_{rest}^{LJ}	$\Delta H_{rest}^{EE(SR)}$	$\Delta H_{rest}^{EE(LR)}$
→ GNAAA	40.4%	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
GNAAA	11.0%	3.25±0.10	3.95±1.78	-0.69±1.75	-1.43±0.42	5.38±2.06	16.68±0.74	-17.38±2.01	0.07±0.06	-7.01±0.41	0.73±0.07	5.67±0.12	-1.12±0.04	0.22±0.03	0.14±1.15	2.98±2.69	2.25±0.33
GN<u>AA</u>A	2.3%	7.11±0.09	11.36±1.63	-4.25±1.66	-55.41±1.34	66.77±2.41	131.08±5.37	-135.33±4.82	-5.84±0.27	-60.92±1.23	0.67±0.13	1.07±0.14	8.98±0.27	0.63±0.07	5.02±2.61	26.71±3.28	35.04±0.65

(C)

		ΔG	ΔH	$-T\Delta S$	ΔH_P^{vac}	ΔH_{rest}	$-T\Delta S_P^{conf}$	$-T\Delta S_W$	ΔH_P^{LJ}	$\Delta H_P^{EE(SR+1,4)}$	ΔH_P^{bond}	ΔH_P^{angle}	$\Delta H_P^{dih.}$	$\Delta H_P^{imp.}$	ΔH_{rest}^{LJ}	$\Delta H_{rest}^{EE(SR)}$	$\Delta H_{rest}^{EE(LR)}$
ANSAA	19.9%	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
ANSAA	18.1%	0.23±0.03	0.86±0.85	-0.63±0.87	-12.28±0.54	13.14±0.81	-1.37±0.29	0.74±0.73	-0.26±0.07	-9.35±0.67	-0.28±0.07	0.62±0.14	-2.91±0.15	-0.10±0.04	-3.33±0.86	6.88±0.92	9.59±0.75
→ ANSAA	12.1%	1.25±0.06	0.34±1.28	0.91±1.27	-16.29±0.94	16.63±1.88	7.79±0.66	-6.88±1.52	1.22±0.08	-15.77±0.86	0.07±0.05	1.91±0.07	-3.75±0.06	0.04±0.03	0.05±0.95	6.77±1.96	9.80±0.83

(D)

		ΔG	ΔH	$-T\Delta S$	ΔH_P^{vac}	ΔH_{rest}	$-T\Delta S_P^{conf}$	$-T\Delta S_W$	ΔH_P^{LJ}	$\Delta H_P^{EE(SR+1,4)}$	ΔH_P^{bond}	ΔH_P^{angle}	$\Delta H_P^{dih.}$	$\Delta H_P^{imp.}$	ΔH_{rest}^{LJ}	$\Delta H_{rest}^{EE(SR)}$	$\Delta H_{rest}^{EE(LR)}$
AASRA	28.1%	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
→ AASRA	10.3%	2.50±0.07	0.48±2.15	2.03±2.15	3.11±0.40	-2.63±2.15	21.63±0.66	-19.60±2.30	0.03±0.08	1.14±0.41	0.10±0.16	0.85±0.17	0.80±0.08	0.18±0.03	2.80±1.51	-4.19±3.44	-1.24±0.38
AASRA	6.7%	3.60±0.08	1.09±1.42	2.50±1.47	17.10±0.61	-16.01±1.12	44.10±1.95	-41.59±1.54	-1.36±0.12	15.66±0.23	-0.41±0.15	-1.61±0.21	4.81±0.21	-0.00±0.04	0.65±1.69	-8.41±2.18	-8.24±0.27

(E)

		ΔG	ΔH	$-T\Delta S$	ΔH_P^{vac}	ΔH_{rest}	$-T\Delta S_P^{conf}$	$-T\Delta S_W$	ΔH_P^{LJ}	$\Delta H_P^{EE(SR+1,4)}$	ΔH_P^{bond}	ΔH_P^{angle}	$\Delta H_P^{dih.}$	$\Delta H_P^{imp.}$	ΔH_{rest}^{LJ}	$\Delta H_{rest}^{EE(SR)}$	$\Delta H_{rest}^{EE(LR)}$
→ AAARV	25.8%	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
AAARV	11.1%	2.11±0.07	9.65±1.39	-7.54±1.46	-5.78±0.20	15.43±1.44	18.46±0.81	-26.01±0.78	2.61±0.10	-17.01±0.22	0.35±0.14	4.14±0.11	3.77±0.06	0.36±0.04	3.92±0.99	12.66±2.31	-1.15±0.18
AAA<u>RV</u>	6.9%	3.29±0.06	2.12±0.65	1.16±0.65	41.94±0.29	-39.81±0.72	35.14±1.14	-33.97±1.62	-6.05±0.15	34.55±0.33	-0.31±0.12	-0.76±0.11	15.29±0.07	-0.79±0.03	3.93±0.85	-41.76±1.30	-1.98±0.36

(F)

		ΔG	ΔH	$-T\Delta S$	ΔH_P^{vac}	ΔH_{rest}	$-T\Delta S_P^{conf}$	$-T\Delta S_W$	ΔH_P^{LJ}	$\Delta H_P^{EE(SR+1,4)}$	ΔH_P^{bond}	ΔH_P^{angle}	$\Delta H_P^{dih.}$	$\Delta H_P^{imp.}$	ΔH_{rest}^{LJ}	$\Delta H_{rest}^{EE(SR)}$	$\Delta H_{rest}^{EE(LR)}$
→ GAAAV	58.0%	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
GAAAV	4.1%	6.63±0.08	12.37±2.50	-5.74±2.53	0.09±0.30	12.27±2.74	68.30±3.09	-74.04±3.21	2.59±0.16	-11.34±0.32	-0.21±0.08	2.91±0.21	5.63±0.12	0.50±0.07	-0.94±2.10	12.13±3.18	1.07±0.20
GAAAV	3.5%	7.03±0.03	7.10±1.80	-0.08±1.80	-0.78±0.39	7.88±1.59	88.28±1.30	-88.36±1.79	2.42±0.12	-11.43±0.19	0.59±0.10	1.96±0.14	5.49±0.05	0.17±0.01	-2.89±2.46	2.01±3.14	8.76±0.21

Table S7. Observed NOEs for cyclo-(GNSRV).

Coordinate 1	Assignment1	Coordinate 2	Assignment 2	Strength
9.05	1Gly-NH	3.63	1Gly-Haa	strong
9.05	1Gly-NH	3.97	1Gly-Hab	strong
8.91	2Asn-NH	4.70	2Asn-Ha	strong
8.26	4Arg-NH	4.03	4Arg-Ha	strong
7.84	3Ser-NH	4.61	3Ser-Ha	strong
7.84	3Ser-NH	3.90	3Ser-Hb	strong
7.76	5Val-NH	4.18	5Val-Ha	strong
9.05	1Gly-NH	4.17	5Val-Ha	strong
8.91	2Asn-NH	3.98	1Gly-Hab	strong
8.26	4Arg-NH	3.91	3Ser-Hb	weak
8.26	4Arg-NH	4.61	3Ser-Ha	strong
7.28	4Arg-NHe	4.02	4Arg-Ha	weak
7.27	4Arg-NHe	3.25	4Arg-Hd	strong
8.90	2Asn-NH	2.88	2Asn-Hb	strong
8.27	4Arg-NH	1.95	4Arg-Hba	strong
8.27	4Arg-NH	1.71	4Arg-Hbb	weak
8.27	4Arg-NH	1.64	4Arg-Hg	weak
7.76	5Val-NH	1.96	5Val-Hb	strong
7.76	5Val-NH	0.93	5Val-Hga	strong
7.76	5Val-NH	0.86	5Val-Hgb	strong
7.28	4Arg-NHe	1.96	4Arg-Hba	weak
7.27	4Arg-NHe	1.73	4Arg-Hbb	strong
7.27	4Arg-NHe	1.65	4Arg-Hg	strong
8.90	2Asn-NH	7.83	3Ser-NH	strong
8.27	4Arg-NH	7.75	5Val-NH	strong
4.60	3Ser-Ha	3.91	3Ser-Hb	strong
4.70	2Asn-Ha	2.86	2Asn-Hb	strong
3.98	1Gly-Hab	3.63	1Gly-Haa	strong
4.03	4Arg-Ha	3.25	4Arg-Hd	strong
4.18	5Val-Ha	1.95	5Val-Hb	strong
4.03	4Arg-Ha	1.95	4Arg-Hba	strong
4.03	4Arg-Ha	1.17	4Arg-Hbb	strong
4.03	4Arg-Ha	1.66	4Arg-Hg	strong
4.18	5Val-Ha	0.92	5Val-Hga	strong
4.18	5Val-Ha	0.88	5Val-Hgb	strong
3.25	4Arg-Hd	1.95	4Arg-Hbb	strong
3.25	4Arg-Hd	1.69	4Arg-Hg	strong
1.95	4Arg-Hba	1.71	4Arg-Hbb	strong
1.94	4Arg-Hba	1.65	4Arg-Hg	strong

1.97	5Val-Hb	0.93	5Val-Hga	strong
1.97	5Val-Hb	0.88	5Val-Hgb	strong

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

Residue	$^3J_{\text{NH-CH}\alpha}$ (Hz)	ϕ restraints
G_1	5.3	–
N_2	7.7	–
S_3	9.1	–120 ± 30°
R_4	4.8	–60 ± 30°
V_5	9.3	–120 ± 30°

Table S9. Observed NOEs for cyclo-(GFDNV).

Coordinate1	Assignment1	Coordinate 2	Assignment 2	Strength
8.70	1Gly-NH	7.90	5Val-NH	weak
8.61	4Asn-NH	7.90	5Val-NH	strong
8.64	2Phe-NH	7.99	3Asp-NH	strong
8.61	4Asn-NH	7.99	3Asp-NH	weak
8.61	4Asn-NH	2.75	3Asp-Hba	strong
7.98	3Asp-NH	3.20	2Phe-Hbb	weak
7.98	3Asp-NH	3.03	2Phe-Hba	weak
7.90	5Val-NH	2.93	3Asp-Hbb	strong
8.70	1Gly-NH	2.04	5Val-Hb	weak
8.70	1Gly-NH	0.91	5Val-Hga	strong
7.32	2Phe-Hd	0.92	5Val-Hgb	weak
8.70	1Gly-NH	4.11	5Val-Ha	strong
8.64	2Phe-NH	3.95	1Gly-Hab	strong
7.90	5Val-NH	4.33	4Asn-Ha	weak
7.98	3Asp-NH	4.51	2Phe-Ha	strong
8.61	4Asn-NH	4.77	3Asp-Ha	strong
8.65	2Phe-NH	3.19	2Phe-Hbb	strong
8.64	2Phe-NH	3.03	2Phe-Hba	strong
8.61	4Asn-NH	2.94	4Asn-Hba	strong
7.98	3Asp-NH	2.93	3Asp-Hbb	strong
7.98	3Asp-NH	2.74	3Asp-Hba	strong
8.64	2Phe-NH	7.31	2Phe-Hd	strong
7.31	2Phe-Hd	3.20	2Phe-Hbb	strong
7.30	2Phe-Hd	3.03	2Phe-Hba	strong
7.90	5Val-NH	0.91	5Val-Hga	strong
7.90	5Val-NH	2.04	5Val-Hb	strong
3.96	1Gly-Hab	3.54	1Gly-Haa	strong

4.50	2Phe-Ha	3.21	2Phe-Hbb	strong
4.51	2Phe-Ha	3.03	2Phe-Hba	strong
4.33	4Asn-Ha	2.95	4Asn-Hba	strong
4.11	5Val-Ha	2.04	5Val-Hb	strong
4.10	5Val-Ha	0.92	5Val-Hga	strong
3.20	2Phe-Hbb	3.02	2Phe-Hba	strong
2.04	5Val-Hb	0.91	5Val-Hga	strong
2.94	3Asp-Hbb	2.75	3Asp-Hba	strong

Table S10. *J*-coupling values and associated torsional restraints for cyclo-(GFDNV).

Residue	**$^3J_{\mathrm{NH\text{-}CH\alpha}}$ (Hz)**	**ϕ restraints**
G_1	6.1	–
F_2	7.0	–
D_3	8.9	–120 ± 30°
N_4	6.5	–
V_5	9.7	–120 ± 30°