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Supporting Information

# Synthesis and characterization of water-soluble macrocyclic peptides stabilizing protein α-turn

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HPLC chromatograms of peptides 1-8a (AA<sub>1</sub> = AA<sub>3</sub> = Gly).

See the experimental section for details. Gradient conditions: 30-100% B in 30 min for **1-7** and 15-50% B in 30 min for **8a**.



\*Denotes a non-peptide side product.

## HPLC chromatograms of peptides 9a, 10a, 10b and 10c.

See the experimental section for details. Gradient conditions: 30-100% in 30 min for **9a**, **10b** and **10c**; 15-50% B in 30 min for **10a**.



A and **B** are crude chromatograms of cyclization reactions of 10 mM solutions of 7 and 8 respectively. d: dimer; t: trimer.

CD spectra of peptides **10a** and **11** in 10 mM phosphate buffer pH 7.4 without (blue and black) and with (red and green) 30% TFE, at 293 K.





COSY spectrum of peptide 9a (<sup>1</sup>H, 400 MHz, *d6*-DMSO).



ROESY spectrum of peptide 9a (<sup>1</sup>H, 400 MHz, *d6*-DMSO).

	NH	Hα	$\mathbf{H}_{\boldsymbol{\beta}}$	Harom	Cter-NH <sub>2</sub>	1,1'	2,2'	3,3'
G1 (o-Ns)	-	3.66 4.05	-	7.86 7.91 8.00 8.14	-	-	-	-
A2	8.72	4.50	1.20	-	-	-	-	-
G3	8.58	3.41 4.35	-	-	-	-	-	-
A4	-	3.92	1.22	-	-	2.89 3.28	1.55 1.74	2.95 3.02
F5	7.64	4.26	2.88 3.06	7.13-7.26	7.09	-	-	-

Attribution table for peptide **9a** (chemical shifts extracted from the ROESY spectrum).









TOCSY spectrum of peptide 10a (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).



NOESY spectrum of peptide 10a (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).

	NH	Hα	$\mathbf{H}_{\boldsymbol{\beta}}$	Harom	Cter-NH <sub>2</sub>	1,1'	2,2'	3,3'
G1	-	3.60 3.89	-	-	-	-	-	-
A2	9.09	4.31	1.30	-	-	-	-	-
G3	8.47	3.84	-	-	-	-	-	-
A4	-	3.89	1.29	-	-	2.85- 3.25	1.75 1.86	2.95- 3.15
F5	7.71	4.48	2.91 3.16	7.21- 7.33	7.04 7.42	-	-	-

Attribution table for peptide **10a** (major rotamer, chemical shifts extracted from the NOESY spectrum).



NMR spectra of peptide 10b.



<sup>1</sup>H NMR spectrum of peptide **10b** (400 MHz,  $H_2O/D_2O$  9:1).



TOCSY spectrum of peptide 10b ( $^{1}$ H, 400 MHz, H<sub>2</sub>O /D<sub>2</sub>O 9:1).



NOESY spectrum of peptide **10b** (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).

	NH	Hα	$\mathbf{H}_{\boldsymbol{\beta}}$	$\mathbf{H}_{\gamma}$	Hδ	Harom	Cter-NH <sub>2</sub>	1,1'	2,2'	3,3'
<b>G1</b>	-	3.58 3.88	-	-	-	-	-	-	-	-
A2	8.84	4.09	1.33	-	-	-	-	-	-	-
L3	7.56	4.47	1.39	1.27	0.78	-	-	-	-	-
A4	-	3.83	1.30	-	-	-	-	2.14 ?	1.81 2.03	2.88- 3.36
F5	7.89	4.36	3.01 3.09	-	-	7.21- 7.34	7.02 7.59	-	-	-

Attribution table for peptide 10b (major rotamer, chemical shifts extracted from the NOESY spectrum).







TOCSY spectrum of peptide 10c (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).



NOESY spectrum of peptide **10c** (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).

	NH	Hα	$\mathbf{H}_{\boldsymbol{\beta}}$	$\mathbf{H}_{\gamma}$	$\mathbf{H}_{\delta}$	Harom	Cter-NH <sub>2</sub>	1,1'	2,2'	3,3'
L1	-	4.05	1.66 1.75	?	0.94	-	-	-	-	-
A2	8.30	4.24	1.47	-	-	-	-	-	-	-
L3	8.67	4.58	1.57 1.63	1.46	0.88	-	-	-	-	-
A4	-	4.01	1.33	-	-	-	-	3.10 4.05	1.84 2.10	2.38 2.85
F5	7.78	4.58	3.02 3.24	-	-		7.34 7.52	-	-	-

Attribution table for peptide **10c** (major rotamer, chemical shifts extracted from the NOESY spectrum).



NMR spectra of peptide 11.



<sup>1</sup>H NMR spectrum of peptide **11** (400 MHz,  $H_2O/D_2O$  9:1).



TOCSY spectrum of peptide 11 (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).



NOESY spectrum of peptide 11 (<sup>1</sup>H, 400 MHz, H<sub>2</sub>O/D<sub>2</sub>O 9:1).

Attribution table for peptide 11, Ac-GAGAF- $NH_2$  (chemical shifts extracted from the NOESY spectrum).

	NH	Ηα	$\mathbf{H}_{\boldsymbol{\beta}}$	Harom	Cter-NH <sub>2</sub>	N <sub>ter</sub> -Ac
<b>G1</b>	8.18	3.85	-	-	-	1.96
A2	8.30	4.24	1.32	-	-	-
G3	8.34	3.80	-	-	-	-
A4	7.99	4.13	1.13	-	-	-
F5	8.03	4.50	2.93 3.12	7.20-7.31	7.01	-



Variable temperature <sup>1</sup>H NMR data for peptides **10a-c** and **11**.

Amide region of the <sup>1</sup>H NMR spectra of peptide **10a** at the indicated temperatures (400 MHz,  $H_2O/D_2O$  9:1).



Amide region of the <sup>1</sup>H NMR spectra of peptide **11** at the indicated temperatures (400 MHz,  $H_2O/D_2O$  9:1).



Amide region of the <sup>1</sup>H NMR spectra of peptide **10b** at the indicated temperatures (400 MHz,  $H_2O/D_2O$  9:1).



Amide region of the <sup>1</sup>H NMR spectra of peptide **10c** at the indicated temperatures (400 MHz,  $H_2O/D_2O$  9:1).

Graphical representation of the dependence of amide protons chemical shifts on temperature for peptides **11** (left) and **10a** (right, major rotamer only).



Corresponding slope values with standard errors:

Peptide 11	Slope (ppb/K)
G1	$-7.6 \pm 0.2$
A2	$-8.4 \pm 0.2$
G3	$-7.6 \pm 0.2$
A4	$-6.8 \pm 0.2$
F5	$-7.4 \pm 0.2$
Cter-NH <sub>2</sub>	$-5.7 \pm 0.2$

Peptide 10a	Slope (ppb/K)
A2	$-7.6 \pm 0.2$
G3	$-8.4 \pm 0.2$
F5	$-7.4 \pm 0.3$
Cter-NH <sub>2</sub>	$-6.0 \pm 0.1$

NOE derived distance restraints used for calculating the solution structure of the major rotamer of **10a**. Values were calculated using the CcpNmr software.<sup>[1]</sup>

GAGAF_RS5modif_run4A1		Distances (lower and upper
		distance errors)
4ha	4hg1	3.5 1.0 0.7
4ha	4hd1	3.3 0.8 0.7
4ha	4he1	4.2 0.8 0.8
4ha	4hd2	3.2 0.6 0.6
4ha	4hb#	3.4 0.7 0.7
1ha2	1ha1	3.3 1.4 0.7
5hn	4ha	3.1 0.6 0.6
4ha	4hg2	3.3 0.7 0.7
4ha	4he2	4.1 0.8 0.8
5hb1	5hb2	2.2 0.4 0.4
5hn	5hb2	3.0 0.6 0.6
5h1	5hb2	2.7 0.2 2.3
5hb2	4hd1	3.9 0.8 1.1
5hb2	4hd2	4.4 0.9 0.9
5hn	5hb1	3.5 0.7 0.7
5hb1	4hd1	4.3 0.9 0.9
5h1	5hb1	2.7 0.2 2.3
5hb1	4hd2	3.9 0.8 1.1
5h1	5ha	2.8 0.6 0.6
5hn	5ha	3.1 0.6 0.6
5h2	5ha	3.2 0.7 1.8
4hd2	4hb#	4.4 0.9 0.9
5hn	4hb#	3.3 0.7 0.7
4hd1	4hb#	4.4 0.9 0.9
5hn	5h2	3.8 0.8 1.2
5hn	5h1	3.5 0.7 0.7
1ha1	4hd1	4.6 0.9 0.9
4hg1	4hd1	4.5 1.8 0.9
3hn	4hd1	3.8 0.8 0.8
4hg2	4hd1	4.7 2.0 0.9
4hg1	4hd2	2.8 0.6 0.6
1ha1	4hd2	5.1 1.0 0.9
4hg2	4hd2	3.6 0.7 0.7
1ha1	4he2	4.2 0.8 0.8
3hn	4he2	4.6 0.9 0.9
5hn	2hb#	4.1 0.7 0.7
3hn	4hg2	4.0 0.8 0.8
3hn	4hg1	3.7 0.8 0.8
2hn	1ha2	3.4 0.7 0.7
2hn	2hb#	3.2 0.7 0.7
2hn	2ha	3.3.0.7.0.7
2hn	1ha1	290606
2hn	3hn	341007
3hn	2ha	340707
JIII	2110	J.4 U.7 U.7

2ha	2hb#	3.5 0.8 0.8
3hn	2hb#	4.1 0.8 0.8
3hn	3ha*	3.5 0.7 0.7
3ha2	4hg2	1.8 0.0 0.0 <sup>\$</sup>

# Methyl groups with degenerated protons.

\* Not stereospecifically assigned protons.

<sup>\$</sup> The analysis of structures indicated the presence of a steric clash between these hydrogen atoms. Therefore, a distance of 1.8 Å was imposed for the final calculation.

Numbering of the hydrogen atoms of the covalent linker for XPLOR-NIH calculations:



NOE derived distance restraints used for calculating the solution structure of the major rotamer of **10a**. Values were set according to the NOE intensity as strong (2.6 Å), medium (3.5 Å), weak (5.0 Å) and very weak (6.0 Å).

distance errors)           4ha         4hg1         5.0 3.2 0.0           4ha         4hd1         5.0 3.2 0.0           4ha         4he1         5.0 3.2 0.0           4ha         4hd2         5.0 3.2 0.0           4ha         4hd2         5.0 3.2 0.0           4ha         4hd2         5.0 3.2 0.0           1ha2         1ha1         5.0 3.2 0.0           5hn         4ha         4hg2           4ha         4hg2         5.0 3.2 0.0           4ha         4hg2         5.0 3.2 0.0           5hn         4ha         4he2           5.0 3.2 0.0         5hb1         5hb2           5hb1         5hb2         5.0 3.2 0.0           5hb1         5hb2         5.0 3.2 0.0           5hb1         5hb2         5.0 3.2 0.0           5hb1         5hb1         5.0 3.2 0.0           5hb1         4hd1         6.0 4.2 0.0           5h1         5.0 3.2 0.0         5hb1           5h1         5.0 3.2 0.0         5hb1           4hd2         5.0 3.2 0.0         5hb1           5h1         5.0 3.2 0.0         5hb1           5ha         5.0 3.2 0.0         5hn <th>GAGAF RS5modif run4A1</th> <th></th> <th>Distances (lower and upper</th>	GAGAF RS5modif run4A1		Distances (lower and upper
4ha       4hg1       5.0 3.2 0.0         4ha       4hd1       5.0 3.2 0.0         4ha       4hd1       5.0 3.2 0.0         4ha       4hd2       5.0 3.2 0.0         4ha       4hd2       5.0 3.2 0.0         4ha       4hd2       5.0 3.2 0.0         1ha       5.0 3.2 0.0       1ha         4ha       4hg2       5.0 3.2 0.0         4ha       4hg2       5.0 3.2 0.0         4ha       4hg2       5.0 3.2 0.0         5hn       4ha       4hg2         5hn       5.0 3.2 0.0         5hn       5hb2       5.0 3.2 0.0         5hn       5hb2       5.0 3.2 0.0         5h1       5hb2       5.0 3.2 0.0         5hb1       5hb2       4hd2       6.0 4.2 0.0         5hb1       5hb1       5.0 3.2 0.0         5h1       5ha       5.0 3.2 0.0         5h1       5ha       5.0 3.2 0.0         5hn       5ha       5.0 3.2 0.0         5hn       5ha       5.0 3.2 0.0			distance errors)
Aha         Ahd1         5.03.20.0           Aha         Ahe1         5.03.20.0           Aha         Ahb4         5.03.20.0           Aha         Ahb#         5.03.20.0           Iha2         Iha1         5.03.20.0           Son 20.0         Son 20.0         Son 20.0           Son 4         Ana         5.03.20.0           Aha         Ahg2         5.03.20.0           Aha         Ahg2         5.03.20.0           Aha         Ahg2         5.03.20.0           Aha         Ahg2         5.03.20.0           Shb1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Shb1         S.03.20.0         Shb2           Shn         Shb1         S.03.20.0           Shb1         S.03.20.0         Shb1           Shb1         S.03.20.0         Shb1           Shb1         S.03.20.0         Shb1           Sha         3.51.70.0         Shn           Sha         S.03.20.0         Shh           Sha         S.03.20.0         Shn           Sha         S.03.20.0         Shn </td <td>4ha</td> <td>4hg1</td> <td>5.0 3.2 0.0</td>	4ha	4hg1	5.0 3.2 0.0
Aha         Ahe1         5.03.20.0           Aha         Ahd2         5.03.20.0           Aha         Ahb#         5.03.20.0           Iha2         Iha1         5.03.20.0           Shn         Aha         4.02           Aha         4.02         5.03.20.0           Shn         Aha         4.02           Aha         Ahe2         5.03.20.0           Shb1         Shb2         5.03.20.0           Shb1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Shb2         Ahd1         5.03.20.0           Shb2         Ahd1         5.03.20.0           Shb1         Shb1         S.03.20.0           Sh1         S.03.20.0         Sh1           Sh1         S.03.20.0         Sh1           Sh1         Sh1         S.03.20.0           Sh1         Sh3         S.03.20.0           Sh1         Sh3         S.03.20.0           Sh1         Sha         S.03.20.0           Sh1         Sha         S.03.20.0	4ha	4hd1	5.0 3.2 0.0
Aha         Ahd2         5.03.20.0           Aha         Ahb#         5.03.20.0           Iha2         Iha1         5.03.20.0           Shn         Aha         5.03.20.0           Aha         4ha         5.03.20.0           Aha         Aha         5.03.20.0           Aha         Aha2         5.03.20.0           Aha         Ahe2         5.03.20.0           Shb1         Shb2         5.03.20.0           Shn         Shb2         5.03.20.0           Shn         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Shn         Shb1         5.03.20.0           Shn         Shb1         5.03.20.0           Shn         Shb1         5.03.20.0           Sh1         Sha3         5.17.0           Sh1         Sha3         3.51.70           Sh1         Sha         3.51.70           Shn         Sha         5.03.20.0           Shn         Sha         S.03.20.0           Ahd2         Sha         S.03.20.0           Shn         Shb1         S.03.20.0	4ha	4he1	5.0 3.2 0.0
Aha         Ahb#         5.03.20.0           1ha2         1ha1         5.03.20.0           Shn         4ha         5.03.20.0           Aha         4hg2         5.03.20.0           Aha         4hg2         5.03.20.0           Aha         4hg2         5.03.20.0           Shu         5hb2         2.60.80.0           Shn         5hb2         5.03.20.0           Shb1         5.03.20.0         5hb2           Sh1         5hb2         5.03.20.0           Shb2         4hd1         5.03.20.0           Shb2         4hd1         5.03.20.0           Shb1         5.03.20.0         5hb1           Shb1         5.03.20.0         5hb1           Sh1         5.03.20.0         5hb1           Sh1         5.03.20.0         5h1           Sh1         5.03.20.0         5h1           Sh1         5.03.20.0         5h1           Sh1         5.03.20.0         5h1           Sh1         5.03.20.0         5h2           Sh1         5.03.20.0         5h1           Sh1         5.03.20.0         5h1           Sh1         5.03.20.0         5h1	4ha	4hd2	5.0 3.2 0.0
1ha2         1ha1         5.0 3.2 0.0           Shn         4ha         5.0 3.2 0.0           4ha         4hg2         5.0 3.2 0.0           4ha         4hg2         5.0 3.2 0.0           Shb1         Shb2         2.6 0.8 0.0           Shn         Shb2         5.0 3.2 0.0           Sh1         Shb2         5.0 3.2 0.0           Sh1         Shb2         5.0 3.2 0.0           Sh1         Shb2         4.0           Sol 3.2 0.0         Shb1         5.0 3.2 0.0           Shb2         4.01         S.0 3.2 0.0           Shb1         Shb1         S.0 3.2 0.0           Shn         Shb1         S.0 3.2 0.0           Sh1         Shb1         S.0 3.2 0.0           Sh1         Shb1         S.0 3.2 0.0           Sh1         Sha         3.5 1.7 0.0           Sh1         Sha         S.0 3.2 0.0           Sh1         Sha         S.0 3.2 0.0           Sh1         Sha         S.0 3.2 0.0           Shn         Sha         S.0 3.2 0.0           Shn         Sha         S.0 3.2 0.0           Shn         Sh1         S.0 3.2 0.0           Shn         Sh1<	4ha	4hb#	5.0 3.2 0.0
Shn         4ha         5.0 3.2 0.0           4ha         4hg2         5.0 3.2 0.0           4ha         4he2         5.0 3.2 0.0           Shb1         Shb2         2.6 0.8 0.0           Shn         Shb2         5.0 3.2 0.0           Shn         Shb2         2.6 0.8 0.0           Shn         Shb2         5.0 3.2 0.0           Shb1         Shb2         4.0           Shb2         4.0         5.0 3.2 0.0           Shb2         4.0         6.0 4.2 0.0           Shn         Shb1         5.0 3.2 0.0           Shb1         5.0 3.2 0.0         Shb1           Shb1         Shb1         S.0 3.2 0.0           Shb1         Shb1         S.0 3.2 0.0           Sh1         Sha         3.5 1.7 0.0           Shn         Sha         S.0 3.2 0.0           Sh1         Sha         S.0 3.2 0.0           Sh1         Sha         S.0 3.2 0.0           Sh1         Sha         S.0 3.2 0.0           Shn         Sha         S.0 3.2 0.0           Shn         Sh2         So 3.2 0.0           Shn         Sh1         S.0 3.2 0.0           Shn         Sh2	1ha2	1ha1	5.0 3.2 0.0
4ha         4hg2         5.03.20.0           4ha         4he2         5.03.20.0           Shb1         Shb2         2.60.80.0           Shn         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Shb2         4hd1         5.03.20.0           Shb2         4hd2         6.04.20.0           Shn         Shb1         5.03.20.0           Shb1         4hd2         6.04.20.0           Shn         Shb1         5.03.20.0           Sh1         Shb1         5.03.20.0           Sh1         Shb1         5.03.20.0           Sh1         Sha         3.51.70.0           Shn         Sha         S.03.20.0           Sh1         Sha         S.03.20.0           Sh1         Sha         S.03.20.0           Sha         S.03.20.0         Sha           Sha         S.03.20.0         Shn           Shn         Sh2         Sha           Sha         S.03.20.0         Shn           Shn         Sh1         S.03.20.0           Shn         Sh1         S.03.20.0      S	5hn	4ha	5.0 3.2 0.0
4ha         4he2         5.03.20.0           Shb1         Shb2         2.60.80.0           Shn         Shb2         5.03.20.0           Sh1         Shb2         5.03.20.0           Shb2         4hd1         5.03.20.0           Shb2         4hd1         5.03.20.0           Shb2         4hd1         6.04.20.0           Shn         Shb1         5.03.20.0           Shb1         4hd2         6.04.20.0           Sh1         Shb1         5.03.20.0           Sh1         Shb1         4.4d2         5.03.20.0           Sh1         Shb1         4.4d2         5.03.20.0           Sh1         Sha         3.51.70.0         Shn           Shn         Sha         S.03.20.0         Sh1           Shn         Sha         S.03.20.0         Sh1           Shn         Sha         S.03.20.0         Sh1           Shn         Sha         S.03.20.0         Sh1           Shn         Sh2         So.3.20.0         Sh1           Shn         Sh1         So.3.20.0         Sh1           Shn         Sh2         So.3.20.0         Sh1           Sha         So.3.20.0 </td <td>4ha</td> <td>4hg2</td> <td>5.0 3.2 0.0</td>	4ha	4hg2	5.0 3.2 0.0
Shb1         Shb2         2.6 0.8 0.0           Shn         Shb2         S.0 3.2 0.0           Sh1         Shb2         4.01           Shb2         4.01         S.0 3.2 0.0           Shb2         4.01         S.0 3.2 0.0           Shb2         4.02         6.0 4.2 0.0           Shn         Shb1         S.0 3.2 0.0           Shb1         4.02         S.0 3.2 0.0           Shb1         4.041         6.0 4.2 0.0           Sh1         Shb1         S.0 3.2 0.0           Sh1         Shb1         Sh0         S.0 3.2 0.0           Sh1         Sha         3.5 1.7 0.0           Sh1         Sha         S.0 3.2 0.0           Shn         Sh1         S.0 3.2 0.0           Shn	4ha	4he2	5.0 3.2 0.0
Shn         Shb2         5.0.3.2.0.0           Sh1         Shb2         4.01         5.0.3.2.0.0           Shb2         4.01         5.0.3.2.0.0           Shb2         4.02         6.0.4.2.0.0           Shn         Shb1         5.0.3.2.0.0           Shn         Shb1         5.0.3.2.0.0           Shn         Shb1         6.0.4.2.0.0           Sh1         Shb1         6.0.4.2.0.0           Sh1         Shb1         4.02         5.0.3.2.0.0           Sh1         Shb1         4.042         5.0.3.2.0.0           Sh1         Sha         3.5.1.7.0.0         5.0.3.2.0.0           Sh1         Sha         S.0.3.2.0.0         5.0.3.2.0.0           Sh1         Sha         S.0.3.2.0.0         5.0.3.2.0.0           Shn         Sha         S.0.3.2.0.0         5.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0         5.0.3.2.0.0           Shn         Sh2         S.0.3.2.0.0         5.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0         5.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0         5.0.3.2.0.0           Shn         Ahd1         6.0.4.2.0.0         4.02	5hb1	5hb2	2.6 0.8 0.0
Sh1         Shb2         5.0.3.2.0.0           Shb2         4hd1         5.0.3.2.0.0           Shb2         4hd2         6.0.4.2.0.0           Shn         Shb1         5.0.3.2.0.0           Shb1         4hd1         6.0.4.2.0.0           Shn         Shb1         5.0.3.2.0.0           Shb1         4hd1         6.0.4.2.0.0           Sh1         Shb1         5.0.3.2.0.0           Sh1         Shb1         4hd2           Sh1         Sha         3.5.1.7.0.0           Shn         Sha         5.0.3.2.0.0           Sh1         Sha         S.0.3.2.0.0           Sh1         Sha         S.0.3.2.0.0           Sh1         Sha         S.0.3.2.0.0           Sh1         Sha         S.0.3.2.0.0           Ahb#         6.0.4.2.0.0         Shn           Shn         Sh1         S.0.3.2.0.0           Shn         4hd1         6.0.4.2.0.0           Ahg1         Ahd2	5hn	5hb2	5.0 3.2 0.0
Shb2         4hd1         5.03.20.0           Shb2         4hd2         6.04.20.0           Shn         Shb1         5.03.20.0           Shb1         4hd1         6.04.20.0           Shb1         4hd1         6.04.20.0           Shb1         Shb1         5.03.20.0           Shb1         Shb1         5.03.20.0           Sh1         Sha         3.51.70.0           Shn         Sha         5.03.20.0           Sh1         Sha         5.03.20.0           Sh1         Sha         5.03.20.0           Shn         Sha         5.03.20.0           Shn         Sha         5.03.20.0           Shn         Sha         5.03.20.0           Ahd2         4hb#         6.04.20.0           Shn         Abb#         5.03.20.0           Ahd1         4hb#         6.04.20.0           Shn         Sh1         5.03.20.0           Shn         Sh1         5.03.20.0           Shn         Sh1         6.04.20.0           Ahg1         4hd1         6.04.20.0           Ahg1         4hd1         6.04.20.0           Ahg1         4hd2         5.03.20.0 </td <td>5h1</td> <td>5hb2</td> <td>5.0 3.2 0.0</td>	5h1	5hb2	5.0 3.2 0.0
Shb2         4hd2         6.0.4.2.0.0           Shn         Shb1         5.0.3.2.0.0           Shb1         4hd1         6.0.4.2.0.0           Sh1         Shb1         5.0.3.2.0.0           Sh1         Shb1         4hd2         5.0.3.2.0.0           Sh1         Sha         3.5.1.7.0.0           Sh1         Sha         3.5.1.70.0           Sh1         Sha         5.0.3.2.0.0           Ahd2         Ahb#         6.0.4.2.0.0           Shn         Sh2         S.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0           Shn         Sh2         S.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0           Shn         S.0.3.2.0.0         Sh1           Abd1         6.0.4.2.0.0         Sh1           Abd2         S.0.3.2.0.0           Ahd1         A.0.4.2.0.	5hb2	4hd1	5.0 3.2 0.0
Shn         Shb1         5.0 3.2 0.0           Shb1         4hd1         6.0 4.2 0.0           Sh1         Shb1         5.0 3.2 0.0           Shb1         4hd2         5.0 3.2 0.0           Sh1         Sha         3.5 1.7 0.0           Shn         Sha         3.5 1.7 0.0           Shn         Sha         5.0 3.2 0.0           Sh1         Sha         5.0 3.2 0.0           Add2         Abb#         6.0 4.2 0.0           Shn         Sha         5.0 3.2 0.0           Ahd2         Abb#         6.0 4.2 0.0           Shn         Sh1         S.0 3.2 0.0           Shn         Sh2         S.0 3.2 0.0           Shn         Sh1         S.0 3.2 0.0           Ahd1         6.0 4.2 0.0         Ahd1           Ahd1         S.0 3.2 0.0         Ahd1           Ahd2         S.0 3.2 0.0         Ahd2           Ahd1         Ahd2         S.0 3.2 0.0           Ahg2         Ahd2         S.0 3.2 0.0           Ahg2         A	5hb2	4hd2	6.0 4.2 0.0
Shb1         4hd1         6.0 4.2 0.0           Sh1         Shb1         S.0 3.2 0.0           Shb1         4hd2         S.0 3.2 0.0           Sh1         Sha         3.5 1.7 0.0           Shn         Sha         S.0 3.2 0.0           Sh2         Sha         S.0 3.2 0.0           Sh2         Sha         S.0 3.2 0.0           Sh2         Sha         S.0 3.2 0.0           Ahd2         Ahb#         6.0 4.2 0.0           Shn         Sh2 0.0         Ahb#           Shn         Sh2 0.0         Ahb#           Shn         Sh2 0.0         Shn           Shn         Sh1         S.0 3.2 0.0           Shn         Sh2         S.0 3.2 0.0           Shn         Sh2         S.0 3.2 0.0           Shn         Sh1         S.0 3.2 0.0           Iha1         4hd1         6.0 4.2 0.0           Ahg1         4hd1         S.0 3.2 0.0           Jhn         4hd1         S.0 3.2 0.0           Ahg1         4hd2         S.0 3.2 0.0           Jha1         4hd2         S.0 3.2 0.0           Jha1         4hd2         S.0 3.2 0.0           Jhn         Ahd2	5hn	5hb1	5.0 3.2 0.0
Sh1         Shb1         S.0.3.2.0.0           Shb1         4hd2         S.0.3.2.0.0           Sh1         Sha         3.5.1.7.0.0           Shn         Sha         S.0.3.2.0.0           Sh2         Sha         S.0.3.2.0.0           4hd2         4hb#         6.0.4.2.0.0           Shn         4hb#         S.0.3.2.0.0           4hd1         4hb#         S.0.3.2.0.0           4hd1         4hb#         S.0.3.2.0.0           4hd1         4hb#         S.0.3.2.0.0           5hn         Sh1         S.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0           Shn         Sh1         S.0.3.2.0.0           1ha1         4hd1         6.0.4.2.0.0           3hn         Sh1         S.0.3.2.0.0           4hg1         4hd1         6.0.4.2.0.0           4hg2         4hd1         6.0.4.2.0.0           4hg1         4hd2         3.5.1.7.0.0           1ha1         4hd2         S.0.3.2.0.0           1ha1         4hd2         S.0.3.2.0.0           3hn         4he2         S.0.3.2.0.0           3hn         4he2         S.0.3.2.0.0           3hn	5hb1	4hd1	6.0 4.2 0.0
Shb1       4hd2       5.0 3.2 0.0         Sh1       Sha       3.5 1.7 0.0         Shn       Sha       5.0 3.2 0.0         Sh2       Sha       5.0 3.2 0.0         4hd2       4hb#       6.0 4.2 0.0         Shn       4hb#       5.0 3.2 0.0         4hd1       4hb#       6.0 4.2 0.0         Shn       4hb#       6.0 4.2 0.0         Shn       Sh2       5.0 3.2 0.0         4hd1       4hb#       6.0 4.2 0.0         Shn       Sh1       5.0 3.2 0.0         Ha1       4hd1       6.0 4.2 0.0         4hg1       4hd1       5.0 3.2 0.0         3hn       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4hd2       6.0 4.2 0.0         3hn       4hd2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0     <	5h1	5hb1	5.0 3.2 0.0
Sh1       Sha       3.5 1.7 0.0         Shn       Sha       5.0 3.2 0.0         Sh2       Sha       5.0 3.2 0.0         4hd2       4hb#       6.0 4.2 0.0         Shn       4hb#       5.0 3.2 0.0         4hd1       4hb#       5.0 3.2 0.0         4hd1       4hb#       6.0 4.2 0.0         Shn       Sh2       S.0 3.2 0.0         Shn       Sh2       S.0 3.2 0.0         Shn       Sh1       S.0 3.2 0.0         Iha1       4hd1       6.0 4.2 0.0         4hg1       4hd1       6.0 4.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg2       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       S.0 3.2 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       S.0 3.2 0.0         3hn       4he2       S.0 3.2 0.0         3hn       4hg2       S.0 3.2 0.0         3hn       4hg2       S.0 3.2 0.0	5hb1	4hd2	5.0 3.2 0.0
Shn         Sha         5.0 3.2 0.0           Sh2         Sha         5.0 3.2 0.0           4hd2         4hb#         6.0 4.2 0.0           Shn         4hb#         5.0 3.2 0.0           4hd1         4hb#         6.0 4.2 0.0           Shn         4hb#         6.0 4.2 0.0           Shn         Sh2         5.0 3.2 0.0           4hd1         4hb#         6.0 4.2 0.0           Shn         Sh1         5.0 3.2 0.0           Shn         Sh1         5.0 3.2 0.0           1ha1         4hd1         6.0 4.2 0.0           4hg1         4hd1         6.0 4.2 0.0           3hn         4hd1         5.0 3.2 0.0           4hg2         4hd1         6.0 4.2 0.0           4hg1         4hd2         3.5 1.7 0.0           1ha1         4hd2         5.0 3.2 0.0           1ha1         4hd2         5.0 3.2 0.0           1ha1         4he2         5.0 3.2 0.0           3hn         4he2         5.0 3.2 0.0           3hn         4he2         5.0 3.2 0.0           3hn         4hg1         5.0 3.2 0.0           3hn         4hg1         5.0 3.2 0.0           3hn	5h1	5ha	3.5 1.7 0.0
Sh2       Sha       5.0 3.2 0.0         4hd2       4hb#       6.0 4.2 0.0         Shn       4hb#       5.0 3.2 0.0         4hd1       4hb#       6.0 4.2 0.0         Shn       Sh2       5.0 3.2 0.0         Shn       Sh1       5.0 3.2 0.0         Shn       Sh1       5.0 3.2 0.0         Shn       Sh1       5.0 3.2 0.0         Iha1       4hd1       6.0 4.2 0.0         4hg1       4hd1       6.0 4.2 0.0         3hn       4hd1       6.0 4.2 0.0         3hn       4hd1       6.0 4.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       5.0 3.2 0.0         4hg2       4hd2       5.0 3.2 0.0         4hg2       4hd2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       2ha       5.0 3.2 0.0	5hn	5ha	5.0 3.2 0.0
4hd2 $4hb#$ $6.04.20.0$ $5hn$ $4hb#$ $5.03.20.0$ $4hd1$ $4hb#$ $6.04.20.0$ $5hn$ $5h2$ $5.03.20.0$ $5hn$ $5h1$ $5.03.20.0$ $1ha1$ $4hd1$ $6.04.20.0$ $4hg1$ $4hd1$ $6.04.20.0$ $3hn$ $4hd1$ $6.04.20.0$ $4hg2$ $4hd1$ $6.04.20.0$ $4hg2$ $4hd1$ $6.04.20.0$ $4hg2$ $4hd2$ $3.51.70.0$ $1ha1$ $4hd2$ $5.03.20.0$ $4hg2$ $4hd2$ $5.03.20.0$ $3hn$ $4he2$ $5.03.20.0$ $3hn$ $4he2$ $5.03.20.0$ $3hn$ $4hg2$ $5.03.20.0$ $3hn$ $4hg2$ $5.03.20.0$ $3hn$ $4hg1$ $5.03.20.0$ $3hn$ $4hg1$ $5.03.20.0$ $3hn$ $4hg1$ $5.03.20.0$ $2hn$ $2hb#$ $5.03.20.0$ $2hn$ $2hb#$ $5.03.20.0$	5h2	5ha	5.0 3.2 0.0
Shn       4hb#       5.0 3.2 0.0         4hd1       4hb#       6.0 4.2 0.0         Shn       5h2       5.0 3.2 0.0         Shn       Sh1       5.0 3.2 0.0         1ha1       4hd1       6.0 4.2 0.0         4hg1       4hd1       6.0 4.2 0.0         3hn       4hd1       6.0 4.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       2hb#       5.0 3.2 0.0	4hd2	4hb#	6.0 4.2 0.0
4hd1       4hb#       6.0 4.2 0.0         5hn       5h2       5.0 3.2 0.0         5hn       5h1       5.0 3.2 0.0         1ha1       4hd1       6.0 4.2 0.0         4hg1       4hd1       6.0 4.2 0.0         3hn       4hd1       5.0 3.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       5.0 3.2 0.0         1ha1       4hd2       5.0 3.2 0.0         1ha1       4hd2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0<	5hn	4hb#	5.0 3.2 0.0
Shn         Sh2         5.0 3.2 0.0           Shn         Sh1         5.0 3.2 0.0           1ha1         4hd1         6.0 4.2 0.0           4hg1         4hd1         6.0 4.2 0.0           3hn         4hd1         5.0 3.2 0.0           4hg2         4hd1         6.0 4.2 0.0           4hg2         4hd1         6.0 4.2 0.0           4hg2         4hd1         6.0 4.2 0.0           4hg1         4hd2         3.5 1.7 0.0           1ha1         4hd2         6.0 4.2 0.0           4hg2         4hd2         3.5 1.7 0.0           1ha1         4hd2         5.0 3.2 0.0           1ha1         4hd2         5.0 3.2 0.0           1ha1         4he2         5.0 3.2 0.0           3hn         4he2         5.0 3.2 0.0           3hn         4hg2         5.0 3.2 0.0           3hn         4hg1         5.0 3.2 0.0           2hn         1ha2         5.0 3.2 0.0           2hn         2ha         5.0 3.2 0.0	4hd1	4hb#	6.0 4.2 0.0
Shn         5h1         5.0 3.2 0.0           1ha1         4hd1         6.0 4.2 0.0           4hg1         4hd1         6.0 4.2 0.0           3hn         4hd1         5.0 3.2 0.0           4hg2         4hd1         6.0 4.2 0.0           4hg1         4hd1         5.0 3.2 0.0           4hg2         4hd1         6.0 4.2 0.0           4hg1         4hd2         3.5 1.7 0.0           1ha1         4hd2         6.0 4.2 0.0           4hg2         4hd2         5.0 3.2 0.0           1ha1         4hd2         5.0 3.2 0.0           3hn         4he2         5.0 3.2 0.0           3hn         4he2         5.0 3.2 0.0           3hn         4hg2         5.0 3.2 0.0           3hn         4hg1         5.0 3.2 0.0           3hn         4hg1         5.0 3.2 0.0           3hn         4hg1         5.0 3.2 0.0           2hn         1ha2         5.0 3.2 0.0           2hn         2hb#         5.0 3.2 0.0	5hn	5h2	5.0 3.2 0.0
1ha1       4hd1       6.0 4.2 0.0         4hg1       4hd1       6.0 4.2 0.0         3hn       4hd1       5.0 3.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg1       6.0 4.2 0.0       4hg2         4hg1       6.0 4.2 0.0       4hg1         4hg2       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2ha       5.0 3.2 0.0	5hn	5h1	5.0 3.2 0.0
4hg1       4hd1       6.0 4.2 0.0         3hn       4hd1       5.0 3.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	1ha1	4hd1	6.0 4.2 0.0
3hn       4hd1       5.0 3.2 0.0         4hg2       4hd1       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2ha       5.0 3.2 0.0	4hg1	4hd1	6.0 4.2 0.0
4hg2       4hd1       6.0 4.2 0.0         4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         1ha1       4he2       6.0 4.2 0.0         3hn       4he2       6.0 4.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	3hn	4hd1	5.0 3.2 0.0
4hg1       4hd2       3.5 1.7 0.0         1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         3hn       4he2       6.0 4.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	4hg2	4hd1	6.0 4.2 0.0
1ha1       4hd2       6.0 4.2 0.0         4hg2       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         3hn       4he2       6.0 4.2 0.0         3hn       4he2       6.0 4.2 0.0         3hn       4he2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2ha       5.0 3.2 0.0	4hg1	4hd2	3.5 1.7 0.0
4hg2       4hd2       5.0 3.2 0.0         1ha1       4he2       5.0 3.2 0.0         3hn       4he2       6.0 4.2 0.0         5hn       2hb#       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	1ha1	4hd2	6.0 4.2 0.0
1ha1       4he2       5.0 3.2 0.0         3hn       4he2       6.0 4.2 0.0         5hn       2hb#       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	4hg2	4hd2	5.0 3.2 0.0
3hn       4he2       6.0 4.2 0.0         5hn       2hb#       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	1ha1	4he2	5.0 3.2 0.0
5hn       2hb#       5.0 3.2 0.0         3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0	3hn	4he2	6.0 4.2 0.0
3hn       4hg2       5.0 3.2 0.0         3hn       4hg1       5.0 3.2 0.0         2hn       1ha2       5.0 3.2 0.0         2hn       2hb#       5.0 3.2 0.0         2hn       2ha       5.0 3.2 0.0	5hn	2hb#	5.0 3.2 0.0
3hn     4hg1     5.0 3.2 0.0       2hn     1ha2     5.0 3.2 0.0       2hn     2hb#     5.0 3.2 0.0       2hn     2hb#     5.0 3.2 0.0       2hn     2ha     5.0 3.2 0.0       2hn     2ha     5.0 3.2 0.0	3hn	4hg2	5.0 3.2 0.0
2hn     1ha2     5.0 3.2 0.0       2hn     2hb#     5.0 3.2 0.0       2hn     2hb#     5.0 3.2 0.0       2hn     2ha     5.0 3.2 0.0       2hn     2ha     5.0 3.2 0.0	3hn	4hg1	5.0 3.2 0.0
2hn         2hb#         5.0 3.2 0.0           2hn         2ha         5.0 3.2 0.0           2hn         2ha         5.0 3.2 0.0	2hn	1ha2	5.0 3.2 0.0
2hn         2ha         5.0 3.2 0.0           2hn         1ha1         3.5 1 7 0.0	2hn	2hb#	5.0 3.2 0.0
2 5 1 7 0 0	2hn	2ha	5.0 3.2 0.0
2         1  d1     3.3 1.7 U.U	2hn	1ha1	3.5 1.7 0.0

2hn	3hn	5.0 3.2 0.0
3hn	2ha	5.0 3.2 0.0
2ha	2hb#	5.0 3.2 0.0
3hn	2hb#	5.0 3.2 0.0
3hn	3ha*	5.0 3.2 0.0

# Methyl groups with degenerated protons.

\* Not stereospecifically assigned protons.

NOE derived distance restraints used for calculating the solution structure of the major rotamer of **10c**. Values were calculated using the CcpNmr software.<sup>[1]</sup>

LALAF_R1_run7A4		Distances (lower and upper		
		distance errors)		
4hg2	4he1	2.8 0.6 0.6		
4hg2	4hd2	2.6 0.5 0.5		
4hg2	4hd1	2.6 0.5 0.5		
4hg2	4hg1	2.8 1.0 0.6		
4he1	4hg1	3.2 0.6 0.6		
1ht2	1ha or 4he1	2.9 0.6 0.6		
1ha	1hd#*	2.5 0.5 0.5		
4hd1	1hd#*	2.3 0.5 0.7		
1hb2	1hd#*	2.3 0.5 0.7		
1hb1	1hd#*	2.3 0.2 1.7		
5hb2	5ha	2.4 0.5 0.5		
5hn	5hb2	2.2 0.4 2.5		
5hb1	5hb2	1.8 0.0 0.4		
5h1	5hb2	2.1 0.3 0.4		
1ha	1hb2	2.5 0.5 0.5		
1ha	1hb1	2.0 0.2 0.4		
2hb#	5ha	2.1 0.3 0.4		
5hn	5ha	2.3 0.5 0.5		
5hb1	5ha	2.6 0.5 0.5		
5h1	5hb1	1.9 0.1 0.4		
5hb1	2hb#	4.0 0.7 0.7		
5hn	5hb1	2.5 0.5 2.0		
5h2	5hb1	2.9 0.6 0.6		
3hb1	3ha	2.4 0.5 0.5		
3hn	3hb1	2.8 0.6 1.1		
4hd2	4hd1	2.3 0.5 0.5		
4he2	4hd2	2.9 0.6 0.6		
4he1	4hd2	2.5 0.5 0.5		
2hn	1ha	3.2 0.6 0.6		
2hn	2ha	2.8 0.6 0.6		
2hn	2hb#	2.3 0.5 0.5		
3hn	2hn	3.0 0.6 0.6		
2ha	2hb#	2.7 0.5 0.5		
5hn	2hb#	2.8 0.6 0.6		
3hb2	3hg	2.0 0.2 0.4		
3hb2	3ha	2.4 0.5 0.5		
5hn	5h2	3.1 0.6 0.6		
5hn	4hb#	2.3 0.5 0.5		
5hn	5h1	2.1 0.3 0.4		
3hn	3hg	2.5 0.5 0.5		
3hn	3ha	3.0 0.6 0.6		
3hg	3ha	2.0 0.2 0.4		
	3ha	2.0 0.2 0.4		
4he2	4he1	1.8 0.0 0.4		

4he1	4hd1	2.5 0.4 0.4
4he2	4hd1	2.5 0.4 0.4
5h2	5h1	1.9 0.1 0.4
4ha	4hb#	2.7 0.5 0.5
4he1	2hn	2.0 0.2 0.2 <sup>\$</sup>
4he2	3hn	2.0 0.2 0.2 <sup>\$</sup>
1n	1hd22	2.0 0.2 0.2 <sup>\$</sup>
4hg2	3ha	2.0 0.2 0.2 <sup>\$</sup>
4he1	1hd21	2.0 0.2 0.2 <sup>\$</sup>

# Methyl groups with degenerated protons.

\* Not stereospecifically assigned methyl groups.

<sup>s</sup> The analysis of structures indicated the presence of steric clashes between these hydrogen atoms. Therefore, distances of  $2.0 \pm 0.2$  Å were imposed for the final calculation.

Numbering of the hydrogen atoms of the covalent linker for XPLOR-NIH calculations:



NOE derived distance restraints used for calculating the solution structure of the major rotamer of **10c**. Values were set according to the NOE intensity as strong (2.7 Å), medium (3.5 Å), weak (5.0 Å) and very weak (6.0 Å).

LALAF_R1_run7B3		Distances (lower and upper		
		distance errors)		
4hg2	4he1	3.5 1.7 0.0		
4hg2	4hd2	3.5 1.7 0.0		
4hg2	4hd1	3.5 1.7 0.0		
4hg2	4hg1	3.5 1.7 0.0		
4he1	4hg1	5.0 3.2 0.0		
1ht2	1ha or 4he1	3.5 1.7 0.0		
1ha	1hd#*	3.5 1.7 0.0		
4hd1	1hd#*	3.5 1.7 0.0		
1hb2	1hd#*	5.0 3.2 0.0		
1hb1	1hd#*	5.0 3.2 0.0		
5hb2	5ha	3.5 1.7 0.0		
5hn	5hb2	5.0 3.2 0.0		
5hb1	5hb2	2.7 0.9 0.0		
5h1	5hb2	2.7 0.9 0.0		
1ha	1hb2	3.5 1.7 0.0		
1ha	1hb1	2.7 0.9 0.0		
2hb#	5ha	2.7 0.9 0.0		
5hn	5ha	3.5 1.7 0.0		
5hb1	5ha	3.5 1.7 0.0		
5h1	5hb1	2.7 0.9 0.0		
5hb1	2hb#	5.0 3.2 0.0		
5hn	5hb1	5.0 3.2 0.0		
5h2	5hb1	3.5 1.7 0.0		
3hb1	3ha	3.5 1.7 0.0		
3hn	3hb1	5.0 3.2 0.0		
4hd2	4hd1	3.5 1.7 0.0		
4he2	4hd2	3.5 1.7 0.0		
4he1	4hd2	3.5 1.7 0.0		
2hn	1ha	5.0 3.2 0.0		
2hn	2ha	3.5 1.7 0.0		
2hn	2hb#	3.5 1.7 0.0		
3hn	2hn	5.0 3.2 0.0		
2ha	2hb#	3.5 1.7 0.0		
5hn	2hb#	3.5 1.7 0.0		
3hb2	3hg	2.7 0.9 0.0		
3hb2	3ha	3.5 1.7 0.0		
5hn	5h2	5.0 3.2 0.0		
5hn	4hb#	3.5 1.7 0.0		
5hn	5h1	2.7 0.9 0.0		
3hn	3hg	3.5 1.7 0.0		
3hn	3ha	5.0 3.2 0.0		
3hg	3ha	2.7 0.9 0.0		
3hd1# ou 3hd2#	3ha	2.7 0.9 0.0		

4he2	4he1	2.7 0.9 0.0
4he1	4hd1	3.5 1.7 0.0
4he2	4hd1	3.5 1.7 0.0
5h2	5h1	2.7 0.9 0.0
4ha	4hb#	3.5 1.7 0.0
4he1	2hn	1.8 0.0 0.0 <sup>\$</sup>
4he2	3hn	1.8 0.0 0.0 <sup>\$</sup>
1n	1hd22	2.0 0.2 0.2 <sup>\$</sup>

# Methyl groups with degenerated protons.

\* Not stereospecifically assigned methyl groups.

<sup>§</sup> The analysis of structures indicated the presence of steric clashes between these hydrogen atoms.

Therefore, distances of 1.8 Å and  $2.0 \pm 0.2$  Å were imposed for the final calculation.



Comparison of the sequential and short-range NOE connectivity and chemical shift indexes (CSI) of the major rotamers of the two cyclic peptides **10a** (left) and **10c** (right).



Overlap of backbone heavy atoms of the center member of cluster I of **10c\_down** with the NMR structure of **10c**. A RMSD of 0.55 Å was calculated. Only the 14 heavy atoms constituting the turn, used for superposition and RMSD calculation, are shown.

#### Catalyst parameter input for conformational search:

```
// Catalyst parameter file
confAnalysis.best.max.successive.failures=1000
confAnalysis.best.torsion.factor=10
sysSearch.sp3sp3SearchOffset=10
sysSearch.sp3sp2SearchIncrement=10
sysSearch.sp3sp2SearchIncrement=10
confAnalysis.fast.systematic.upperbound=10000
confAnalysis.fast.random.nAttempt=1000
confAnalysis.systematicFlipAxialEquatorialMaxRingSize=50
```



Molecular modeling of **10a-c\_cis** isomers.

RMSD (Å) versus the first conformation of 10,000 conformations from 100 ns molecular dynamic simulations for macrocyclic peptides **10a-c\_cis**.

Dihedral angles measured in center members of clusters of macrocyclic peptides <b>10a-c_cis</b> .								
	Cluster <sup>[a]</sup>	${\pmb \phi}_{i+1}$	$\psi_{_{i+1}}$	${\pmb \Phi}_{i+2}$	$\Psi_{\text{i+2}}$	${\pmb \phi}_{{\sf i}+3}$	$\psi_{\text{i+3}}$	<i>d</i> (Å) <sup>[b]</sup>
10a	l (71)	157	-153	-68	-47	-81	-136	4.5
	<b>II</b> (17)	117	-127	-71	-48	-81	-147	4.8
	<b>III</b> (12)	152	-127	-66	-63	-96	-176	4.8
10b	l (66)	71	-155	-68	-64	-95	134	5.1
	<b>II</b> (16)	93	-175	-65	-46	-94	141	4.9
	<b>III</b> (9)	72	-153	-55	-38	-133	111	5.2
	<b>IV</b> (3)	99	160	-61	-39	-107	121	4.7
	<b>V</b> (2)	77	-172	-69	-44	-114	151	4.7
	<b>VI</b> (2)	72	-152	-64	-61	-122	106	5.4
10c	<b>I</b> (51)	-55	-91	-81	-60	-87	136	5.2
	<b>II</b> (25)	-97	-98	-50	-52	-99	140	5.1
	<b>III</b> (9)	74	-132	-71	-64	-102	113	5.6
	<b>IV</b> (3)	67	-146	-64	-77	-91	125	5.4
	<b>V</b> (3)	-75	-87	-66	-64	-82	141	5.3
	<b>VI</b> (2)	45	-92	-74	-106	-74	126	5.9

[a] The cluster size in % is given in parenthesis; [b] d: distance from  $C\alpha_{i+1}$  to  $C\alpha_{i+3}.$ 



Conformations of the center members of the two major clusters of **10a-c\_cis** identified by molecular dynamic simulations. Cluster sizes are given in %. For clarity, only polar hydrogen atoms are shown, and the phenylalanine 5 amino acid is not represented.

[1] W. F. Vranken, W. Boucher, T. J. Stevens, R. H. Fogh, A. Pajon, M. Llinas, E. L. Ulrich, J. L. Markley, J. Ionides and E. D. Laue, *Proteins* **2005**, *59*, 687-696.