SUPPLEMENTARY MATERIAL

Syntheses of "Second Generation", 14-Membered Ring β-Turn Mimics

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This material consists of conformational analyses for:

- **1b**
- **2b**
- **3b**

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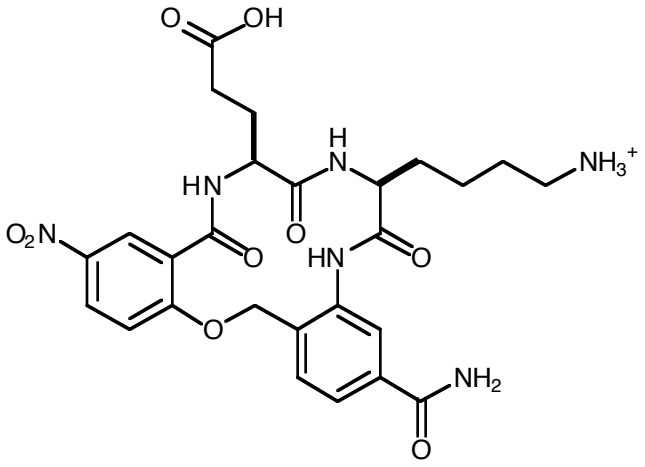
Conformational Studies of 1b



Key ROE contacts

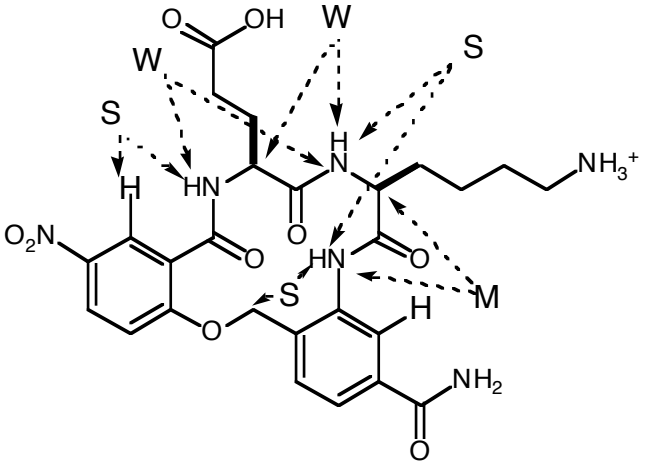
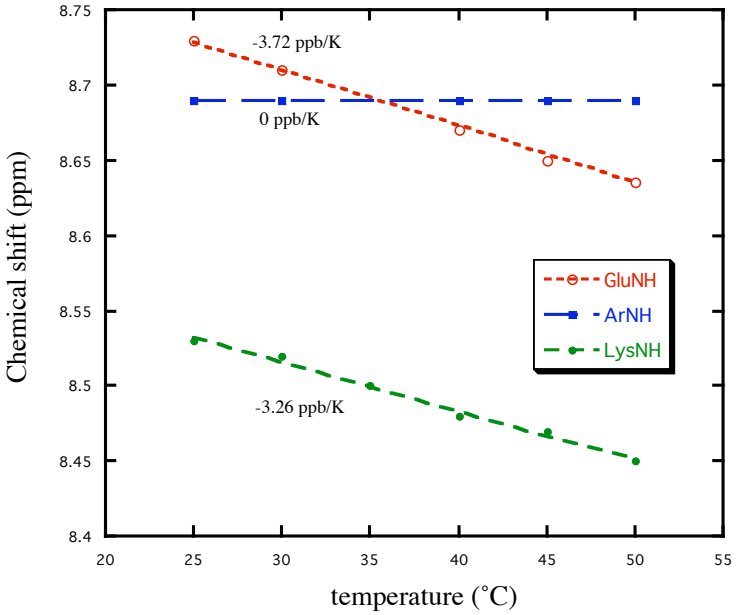


Table S1. Chemical Shift, Coupling Constants, and Temperature Coefficient Data for **1b**

sequence	proton	δ (ppm)	^3J (Hz)	temperature coefficient (ppb/K)
Glu	NH	8.73 (d)	7.0	-3.72
	α	4.28 (m)		
	β	2.00 (m)		
	γ	2.48 (m)		
	CO_2H	12.2 (bs)		
Lys	NH	8.53 (d)	8.5	-3.26
	α	4.48 (m)		
	β	1.93 (m)		
	γ	1.70 (m)		
	δ	1.35 (m)		
	ε	1.55 (m)		
	ζ	2.77 (m)		
	NHζ	7.66 (m)		
Ar1	NH	8.70 (s)		0
	δ2	8.37(d)	3.0	
	δ5	7.66 (s)		
	δ6	7.64 (d)	3.0	
$CONH_2$		8.00 (s)		
		7.40 (s)		
Ar1-CH_2	H	5.67 (d)	-12 (^2J)	
	H	5.23 (d)	-12 (^2J)	
Ar2	H2	8.41 (dd)	3.0, 9.0	
	H4	8.33 (d)	3.0	
	H5	7.68 (d)	9.0	

Temperature Coefficients



Concentration Effect on Chemical Shifts of NH Protons

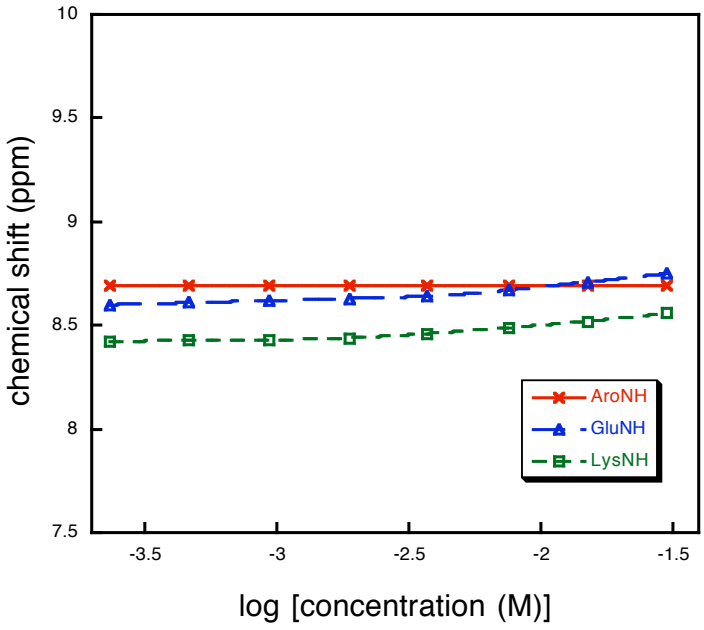
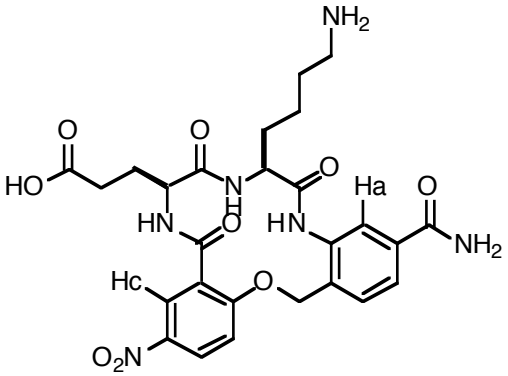


Table S2. QMD data (Cut-off energy = 2.82 - 7.82, RMS threshold = 0.7)



Residue	Dihedral angle (°)	Lowest energy conformers			
		Family 1	Family 2	Family 3	Family 4
E (Glu)	□	-66.62	-105.8	-67.58	-75.35
	□	-26.79	37.53	110.4	-36.60
K (Lys)	□	-75.28	-172.0	68.65	-141.4
	□	-22.70	-35.51	45.01	38.83
Number in family		90	6	12	5
Lowest energy (Kcal/mol)		2.82	6.25	6.54	6.94
Distance (A°) $C0_i$□ NH_{i+3}		2.51	3.64	2.42	3.06
Type of turn		□ III	X	X	X

Comparison of ROE with simulated distances

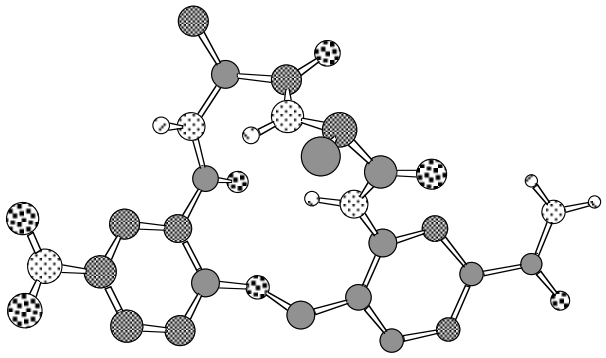
	ROE intensity	Distances for lowest energy conformers (A°)			
		Family 1	Family 2	Family 3	Family 4
(Aryl) N*H* - (Lys) N*H*	Strong	2.472	1.659	2.583	2.356
(Aryl^{l}) H_c - (Glu) N*H*	Strong	1.878	1.852	2.080	4.173
(Aryl) N*H* - (Benzyl) H_1	Strong	2.414	2.193	2.553	3.366
(Aryl) N*H* - (Lys) C□*H*	Medium	3.464	3.467	2.710	2.741
(Lys) N*H* - (Glu) C□*H*	Weak	3.433	2.662	2.073	3.479
(Aryl) N*H* - (Aryl) H_a	Weak	3.473	3.399	3.305	3.023
(Lys) N*H* - (Glu) N*H*	Weak	2.326	2.683	4.341	2.363
(Aryl) N*H* - (Benzyl) H_2	Weak	3.717	3.691	3.988	4.296

Comparison of Coupling constants

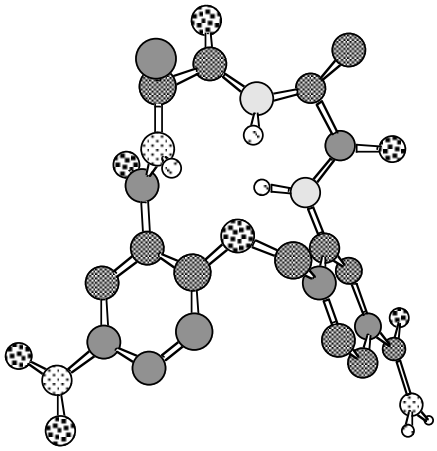
Residue	$^3J_{obs}$ (Hz)	$^3J_{calc}$ (Hz) (*from Family 1)*
Glu-NH	7.0	5.0
Lys-NH	8.5	6.1

Figure S1. Backbone conformation of the lowest energy structures

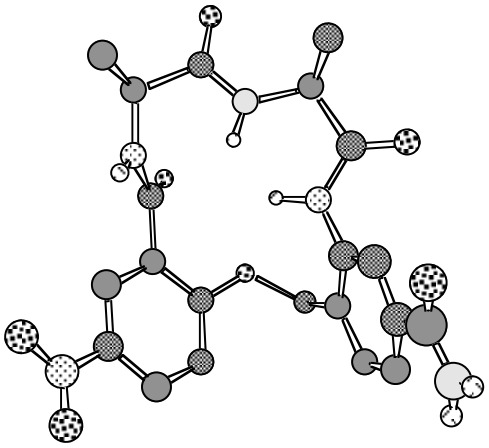
family 1



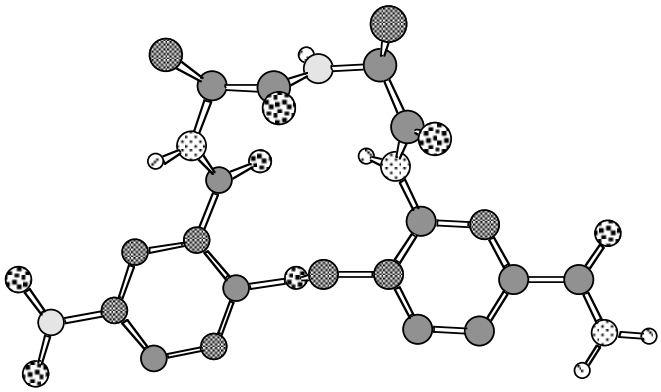
family 2



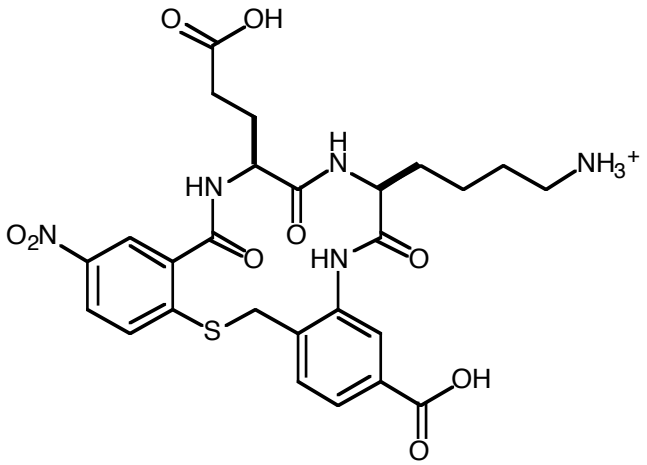
family 3



family 4



Conformational Studies of 2b



Key ROE contacts

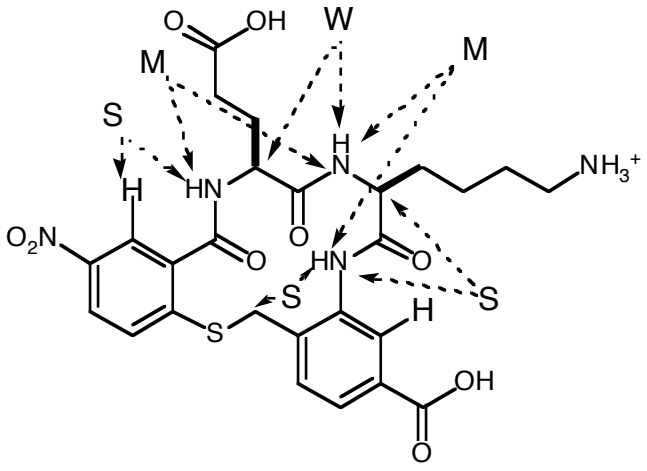
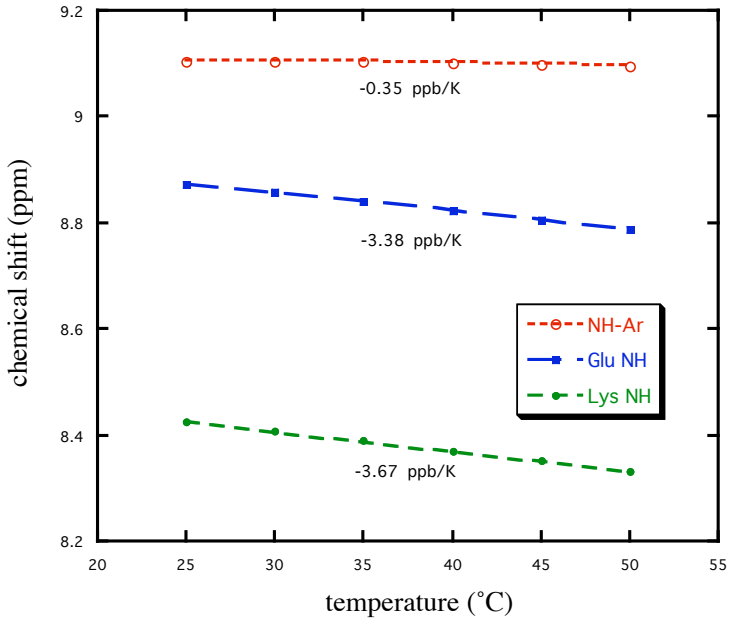
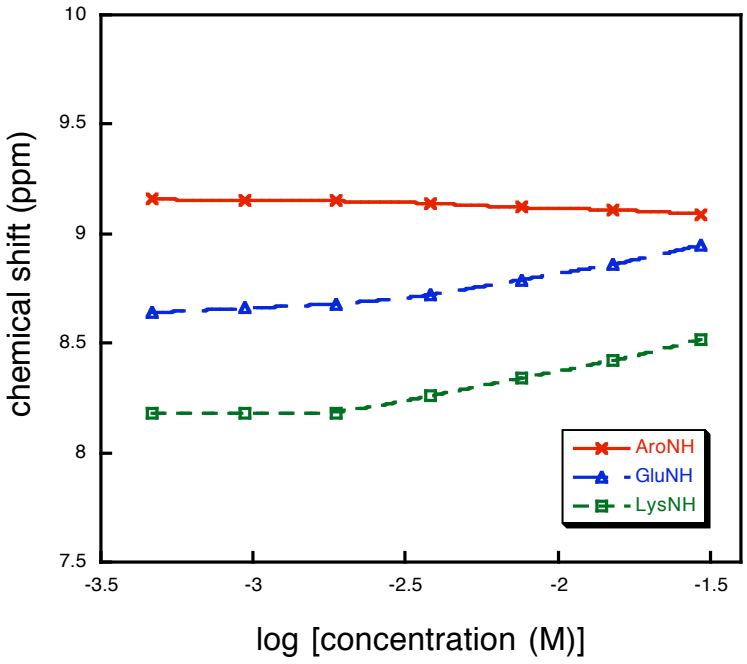


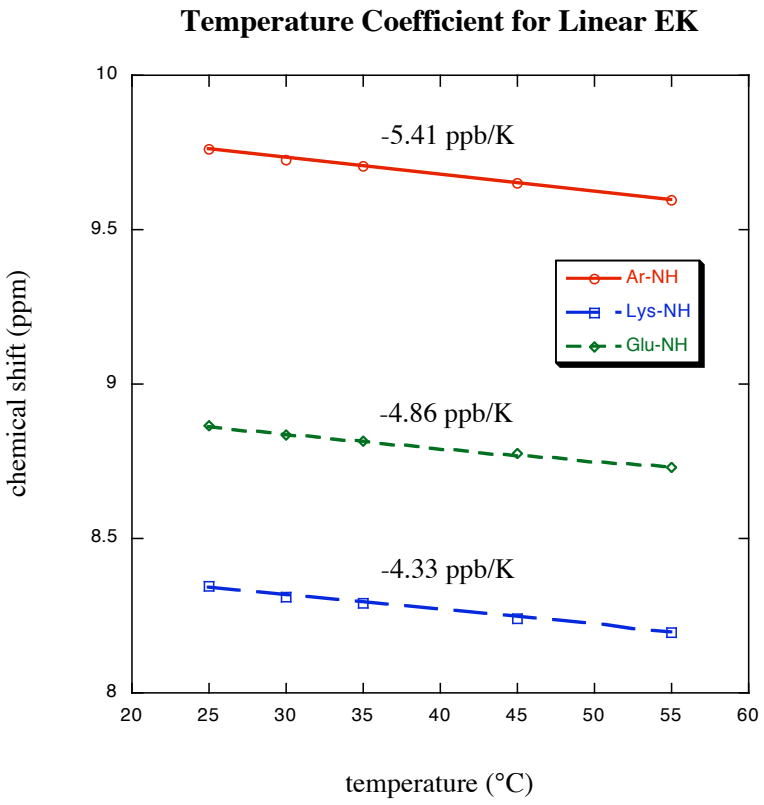
Table S3. Chemical Shift, Coupling Constants, and Temperature Coefficient Data for **2b**

sequence	proton	δ (ppm)	^3J (Hz)	temperature coefficient (ppb/K)
Glu	NH	8.86 (d)	8.0	-3.38
	α	4.45 (m)		
	β	1.95 (m)		
	γ	2.04 (m)		
	δ	2.54 (m)		
	CO_2H	12.6 (bs)		
Lys	NH	8.42 (d)	9.0	-3.67
	α	4.53 (m)		
	β	1.64 (m)		
	γ	1.87 (m)		
	δ	1.30 (m)		
	ε	1.54 (m)		
	ζ	2.75 (m)		
	NHζ	7.68 (m)		
Ar1	NH	9.10 (s)		-0.35
	δ2	8.54 (d)	1.5	
	δ5	7.71 (dd)	1.5, 8.0	
	δ6	7.67 (d)	8.0	
Ar1-CH_2	H	4.77 (d)	-10.5 (^2J)	
	H	4.46 (d)	-10.5 (^2J)	
Ar2	H2	8.33 (dd)	2.5, 8.5	
	H4	8.31 (d)	2.5	
	H5	8.13 (d)	8.5	

Temperature Coefficients






Temperature Coefficient for Linear EK
chemical shift (ppm)
temperature (°C)
-5.41 ppb/K
-4.86 ppb/K
-4.33 ppb/K
Ar-NH
Lys-NH
Glu-NH
10
9.5
9
8.5
8
20
25
30
35
40
45
50
55
60

Concentration Effect on Chemical Shifts of NH Protons

UV absorbance (@ 410 nm) vs. concentration of trityl cation

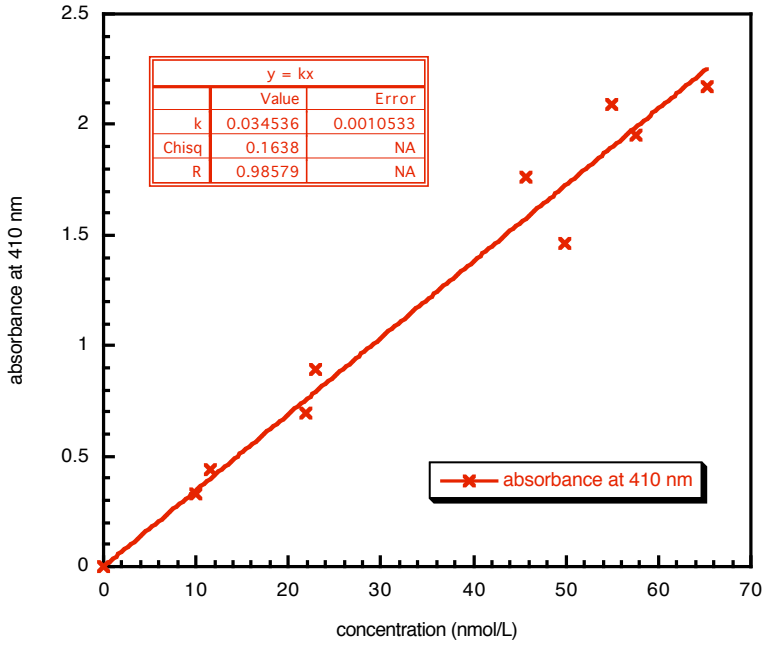
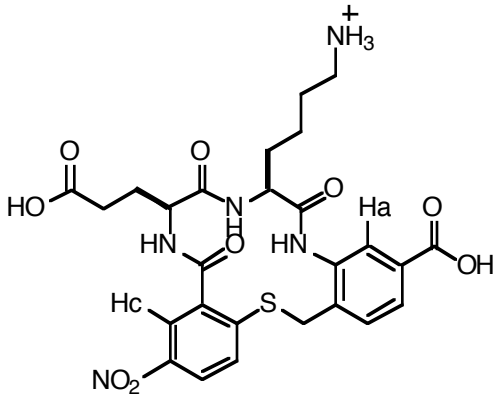


Table S4. QMD data (Cut-off energy = 2.71 - 8.71, RMS threshold = 0.7)



Residue	Dihedral angle (°)	Lowest energy conformers			
		Family 1	Family 2	Family 3	Family 4
E (Glu)	□	-72.69	-71.9	82.5	-71.3
	□	-22.13	-36.6	-65.7	-35.2
K (Lys)	□	-70.63	-135.5	-149.6	-130.1
	□	-22.27	28.3	-24.2	29.3
Number in family		95	27	31	4
Lowest energy (Kcal/mol)		0.3698	2.8796	3.0141	3.7996
Distance (A°) C0$_i$□ NH_{i+3}		2.373	2.797	2.541	2.591
Type of turn		None fits any turn type			

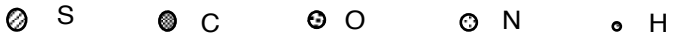
Comparison of ROE with simulated distances

	ROE intensity	Distances for lowest energy conformers (A°)			
		Family 1	Family 2	Family 3	Family 4
(Aryl^{l}) H_c - (Glu) N*H*	Strong	1.778	1.782	1.854	4.227
(Aryl) N*H* - (Benzyl) H_1	Strong	2.095	2.101	2.354	3.539
(Aryl) N*H* - (Lys) C□*H*	Strong	3.439	2.822	3.445	2.844
(Lys) N*H* - (Glu) N*H*	Medium	2.344	2.331	3.612	2.426
(Aryl) N*H* - (Lys) N*H*	Medium	2.472	2.195	1.595	2.327
(Lys) N*H* - (Glu) C□*H*	Weak	3.439	3.492	3.547	3.480
(Aryl) N*H* - (Aryl) H_a	Weak	3.489	3.465	3.406	2.883
(Aryl) N*H* - (Benzyl) H_2	Weak	3.634	3.609	3.798	4.440

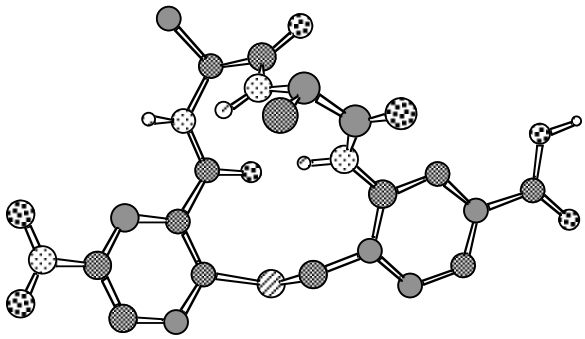
Comparison of Coupling constants

Residue	$^3J_{obs}$ (Hz)	$^3J_{calc}$ (Hz) (*from Family 1)*
Glu-NH	8.0	5.8
Lys-NH	9.0	5.5

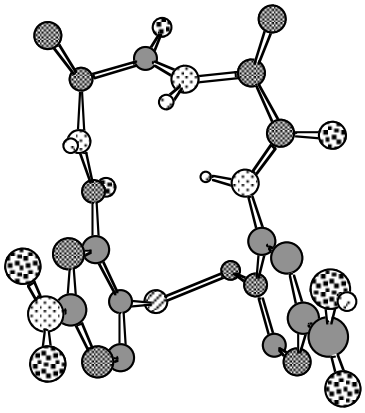
Figure S2. Backbone conformation of the lowest energy structures



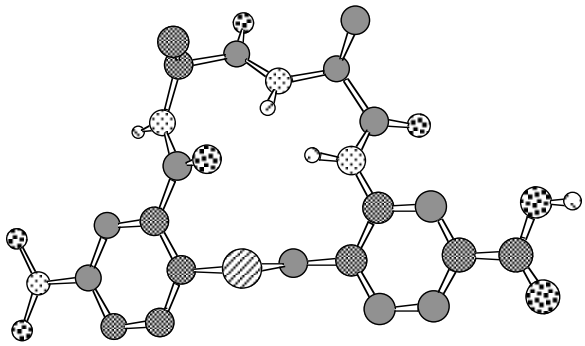
family 1



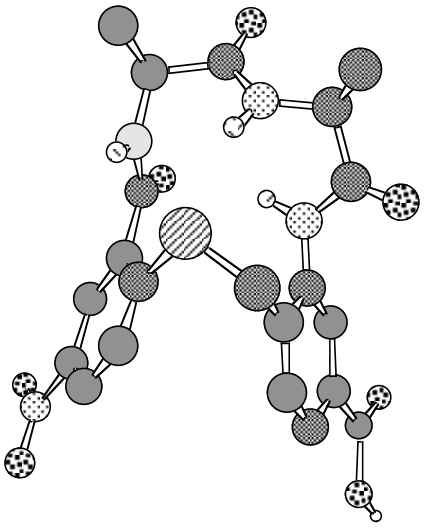
family 2



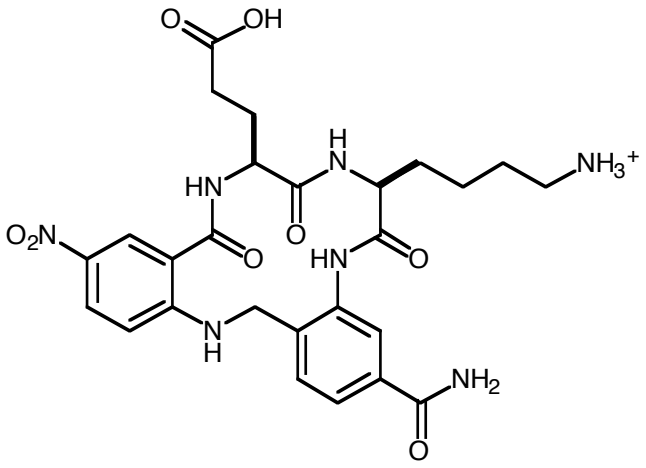
family 3



family 4



Conformational Studies of 3b



ROE Contacts

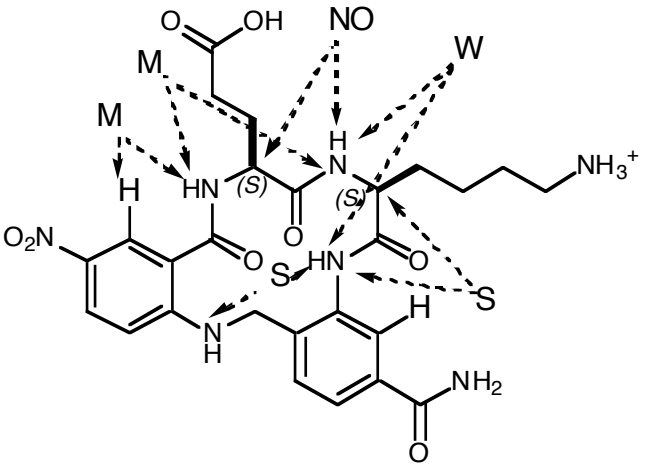
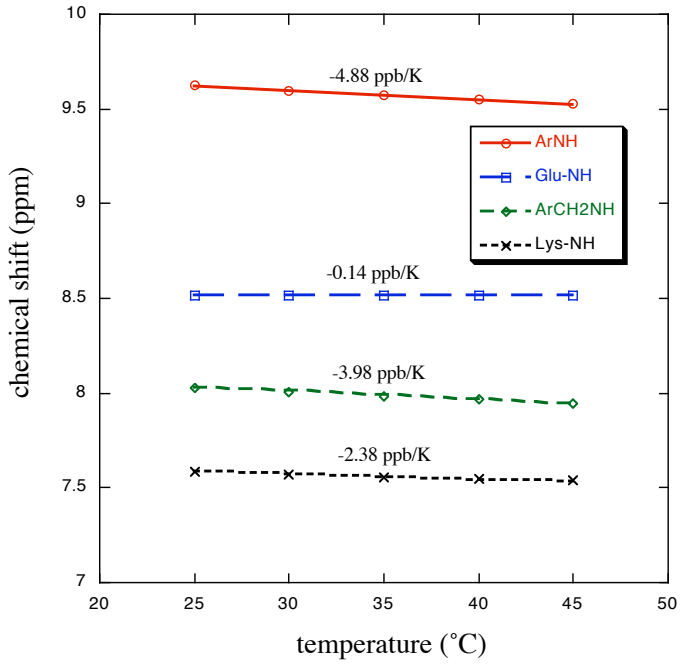


Table S5. Chemical Shifts, Coupling Constants and Temperature Coefficients for **3c**

sequence	proton	δ (ppm)	^3J (Hz)	temperature coefficient (ppb/K)
Glu	NH	8.507 (d)	7.0	-0.14
	α	4.110 (m)		
	β	1.965 (m)		
	γ	1.882 (m)		
	δ	2.462 (m)		
	OH	12.11 (b)		
Lys	NH	7.578 (d)	7.0	-2.38
	α	4.312 (m)		
	β	1.780 (m)		
	γ	1.641 (m)		
	δ	1.335 (m)		
	ε	1.597 (m)		
	ζ	2.816(m)		
	NHζ	7.677 (b)		
Ar1	NH	9.623 (s)		-4.88
	α	8.265 (m)		
	β	7.639-7.693 (m)		
	γ	7.639-7.693 (m)		
Ar1-CH_2	H	4.928 (dd)	-16(^2J), 7.5	
	H	4.456 (dd)	-16(^2J), 4.5	
Ar1CH2N<u>H</u>		8.031 (m)		-3.98
Ar2	H	8.265 (m)		
	H	8.052 (m)		
	H	6.768 (d)	9.5	
C termini	NH	7.942 (s)		
	NH	7.369 (s)		

Temperature Coefficient



Concentration Effect on Chemical Shifts of NH Protons

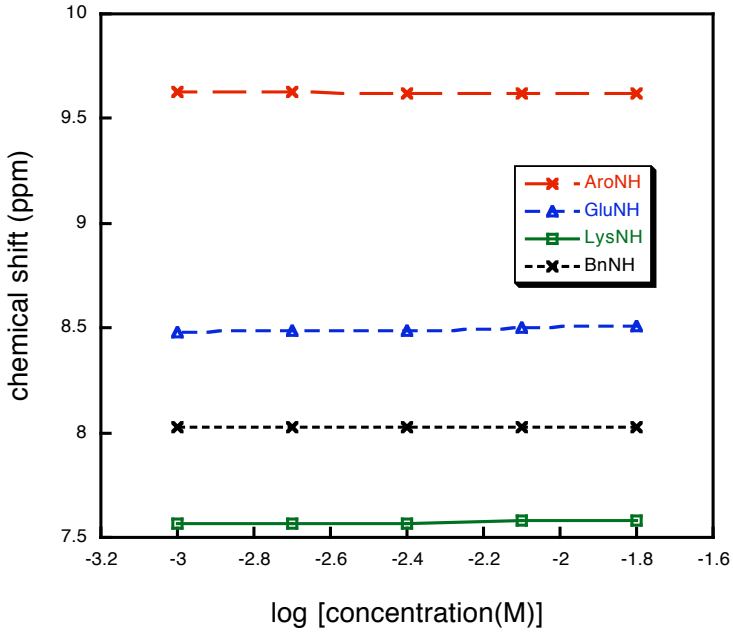
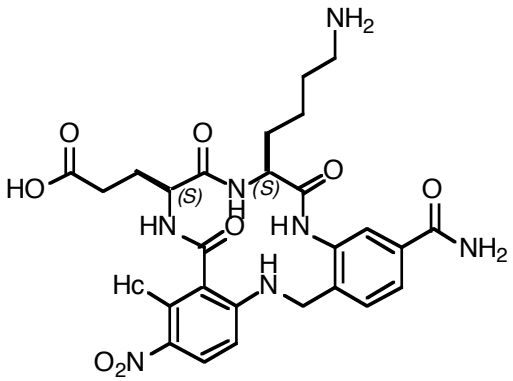


Table S6. QMD data (Cut-off energy = 2.33 - 7.33, RMS threshold = 0.8)



Residue	Dihedral angle (°)	Lowest energy conformers		
		Family 1	Family 2	Family 3
E (Glu)	□	-69.62	-73.61	-78.63
	□	-29.99	-26.94	-64.55
K (Lys)	□	-93.16	-140.4	-83.22
	□	39.56	13.73	-13.11
Number in family		93	40	3
Lowest energy (Kcal/mol)		0.4241	1.033	2.6537
Distance (A°) $C0_i$□ NH_{i+3}		2.565	3.007	3.481
Type of turn		None fits any turn type		

Comparison of ROE with simulated distances

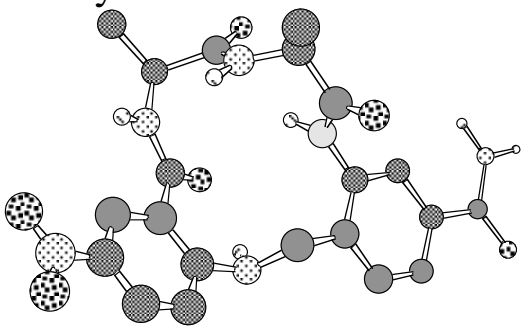
	ROE intensity	Distances for lowest energy conformers (A°)		
		Family 1	Family 2	Family 3
(Aryl) N*H* - (Lys) C□*H*	Strong	2.795	3.071	3.377
(Aryl) *Hc* – (Glu) N*H*	Medium	1.870	1.796	4.264
(Lys) N*H* - (Glu) N*H*	Medium	2.368	2.336	2.671
(Aryl) N*H* - (Lys) N*H*	Weak	3.051	1.881	2.180
(Lys) N*H* - (Glu) C□*H*	Not Observed	3.454	3.463	3.530

Comparison of Coupling constants

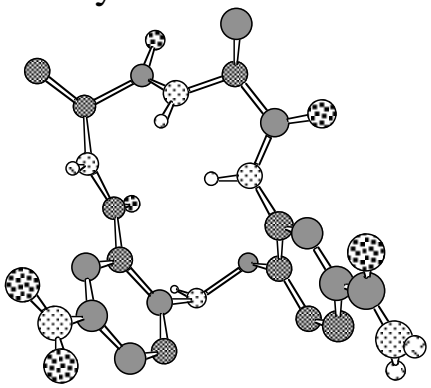
Residue	$^3J_{obs}$ (Hz)	$^3J_{calc}$ (Hz) (*from Family 1)*
Glu-NH	7.0	5.4
Lys-NH	7.0	8.2

Figure S3. Backbone conformation of the lowest energy structures

family 1



family 2



family 3