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Supporting Information

Designed Peptides with Homochiral and Heterochiral Diproline Templates as Conformational Constraints

Bhaswati Chatterjee,[a] Indranil Saha,[b] Srinivasarao Raghothama,[c] Subrayashastry Aravinda,[b] Rajkishor Rai,[a] Narayanaswamy Shamala*[b] and Padmanabhan Balaram*[a]

[a] Dr. B. Chatterjee, Dr. R. Rai, Prof. P. Balaram
Molecular Biophysics Unit, Indian Institute of Science
C.V. Raman Avenue, Bangalore-560012, India
Fax: (+) 91-80-23600683 / (+) 91-80-23600535
E-mail: pb@mbu.iisc.ernet.in

[b] I. Saha, Dr. S. Aravinda, Prof. N. Shamala
Department of Physics, Indian Institute of Science
C.V. Raman Avenue, Bangalore-560012, India
Fax: (+) 91-80-23602602 / (+) 91-80-23600683
E-mail: shamala@physics.iisc.ernet.in

[c] Dr. S. Raghothama
NMR Research Centre, Indian Institute of Science
C.V. Raman Avenue, Bangalore-560012, India

General Peptide Synthesis:

The general representative procedure for the synthesis of Piv-^{D}Pro-^{L}Pro-^{D}Ala-NHMe (**11**) is described in detail. The remaining compounds were prepared by following this general procedure except for the two cases, where the procedures for the synthesis of peptides Piv-^{D}Pro-^{L}Pro-NHMe (**1**) and Piv-^{D}Pro-^{L}Pro-GLy-NHMe (**9**) are described separately.

General Synthesis of Piv-^{D}Pro-^{L}Pro-^{D}Ala-NHMe (11):

Piv-^{D}Pro-OSu: 3.3 g (16.6 mmol) of Piv-^{D}Pro-OH was taken in 30 ml of ethyl acetate and cooled in an ice-bath. 3.6 g (17.6 mmol) of N,N'-dicyclohexylcarbodiimide (DCC), followed by 2.7 g (17.6 mmol) of N-hydroxysuccinimide (HOSu), was added and the reaction mixture was allowed to attain the room temperature. After 12 h, N,N'-dicyclohexylurea (DCU) was filtered off and the filtrate was washed with 1N HCl (3 x 20 ml), brine (3 x 20 ml) and 1M sodium carbonate (3 x 20 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated to yield a gum which solidified to yield white crystalline solid, Piv-^{D}Pro-OSu (4.7g, yield 95%).

Piv-^{D}Pro-^{L}Pro-OH: 4.7 g (15.9 mmol) of Piv-^{D}Pro-OSu was dissolved in 20 ml of tetrahydrofuran (THF), freshly passed through basic alumina, followed by addition of 20 ml of water containing 1.9 g (16.9 mmol) of H-^{L}Pro-OH and 2.0 ml of triethylamine (TEA). The reaction mixture was stirred for 12 h at room temperature. Tetrahydrofuran (THF) was evaporated; the residue was taken in 30 ml of water and washed with diethyl ether (3 x 20 ml). The aqueous layer was cooled; pH adjusted to ~2 by the addition of 1N HCl and extraction was carried out with ethyl acetate (3 x 20 ml). The pooled organic extracts were dried over anhydrous sodium sulfate and evaporated *in vacuo* to yield a gum, which solidified to yield white crystalline Piv-^{D}Pro-^{L}Pro-OH (4.2 g, yield 89%).

Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe: 1.0 g (3.4 mmol) of Piv-^{D}Pro-^{L}Pro-OH was dissolved in 3.0 ml of dimethylformamide (DMF) and cooled in an ice bath. H-^{D}Ala-OMe, isolated from 0.9 g (6.7 mmol) of its hydrochloride by neutralization; subsequent extraction with ethyl acetate and concentration to a volume of ~ 10 ml, was then added to the reaction mixture, followed immediately by 0.9g (4.4 mmol) of N,N'-dicyclohexylcarbodiimide (DCC) and 0.7g of 1-hydroxybenzotriazole (HOBT). The reaction mixture was allowed to attain room temperature and stirred for 24 h. Then N,N'-

dicyclohexylurea (DCU) was filtered off after addition of 20 ml of ethyl acetate to the reaction mixture. The organic layer was subsequently washed with 1N HCl (3 x 20 ml) followed by brine (3 x 20 ml), 1M sodium carbonate (3 x 20 ml) and finally again brine (3 x 30 ml). This layer was dried over anhydrous sodium sulfate and evaporated to yield Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe as white solid (1.1 g, yield 84.6%).

Piv-^{D}Pro-^{L}Pro-^{D}Ala-NHMe (11): 1.1 g (2.9 mmol) of compound Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe was dissolved in 20ml of dry methanol and saturated with methylamine gas. After 48 h, the absence of tripeptide methyl ester was detected by TLC. Methanol was evaporated *in vacuo* and a white solid was obtained (0.9g, yield 90%).

The compound was purified on a silica gel column (60-120 mesh) using 2% methanol in chloroform as the eluant. The column purified peptide was homogeneous on thin layer chromatography (TLC) and on analytical HPLC.

General Synthesis of Piv-^{D}Pro-^{L}Pro-NHMe (1):

Piv-^{D}Pro-^{L}Pro-OH (0.5g, 2mmol) was dissolved in 5 ml of dry tetrahydrofuran (THF) and cooled to 0^{o}C in an ice bath. Triethylamine (TEA), (0.3 ml, 2 mmol) was added to the reaction mixture, followed by ethyl chloroformate (0.26ml, 2 mmol). After 10 min, 10 ml of dry tetrahydrofuran (THF) saturated with methylamine gas was added to it. After 6 h, the reaction mixture was filtered and the filtrate evaporated under vacuum. This residue was dissolved in ethyl acetate and washed with 1N HCl (3 x 20 ml), brine (3 x 20 ml), 1M sodium carbonate (3 x 20 ml) and again brine (3 x 20 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated to yield Piv-^{D}Pro-^{L}Pro-NHMe (**1**) as white solid (0.5 g, yield 83%). The compound was purified on a silica gel column (60-120 mesh) using 2% methanol in chloroform as eluant. The purified peptide was recrystallized from mixture of petroleum ether and ethyl acetate.

General Synthesis of Piv-^{D}Pro-^{L}Pro-GLy-NHMe (9).

Piv-^{D}Pro-^{L}Pro-Gly-OMe: Glycine methyl ester hydrochloride (0.75 g, 6 mmol) was dissolved in 10 ml dimethylformamide (DMF) and cooled in an ice bath. Triethylamine (TEA) (0.9 ml, 6 mmol) was added to it and stirred for 10 min. Piv-^{D}Pro-^{L}Pro-OH (1.0 g, 3.4 mmol) was then

added to the reaction mixture followed by 0.9 g (4.4 mmol) of N,N'-dicyclohexylcarbodiimide (DCC) and 0.7 g (4.4 mmol) of 1-hydroxybenzotriazole (HOBT). The reaction mixture was allowed to attain room temperature and stirred for 24 h. The reaction was worked up as described for Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe to yield a gum (1.1 g, yield 92%).

Piv-^{D}Pro-^{L}Pro-Gly-NHMe (9): 1.1 g (3.0 mmol) of compound Piv-^{D}Pro-^{L}Pro-Gly-OMe was dissolved in 30 ml of dry methanol and saturated with methylamine gas. After 48 h, the absence of tripeptide methyl ester was detected by thin layer chromatography (T.L.C). Methanol was evaporated *in vacuo* and white solid was obtained (0.9g, yield 90%).

The compound was purified on a silica gel column (60-120 mesh) using 2% methanol in chloroform as the eluant. The purified peptide was homogeneous on TLC and on analytical HPLC.

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Table S1: M/Z values obtained in ESI-MS spectra (positive ion mode) for the peptides **1-23**.

	M_{calc}	M_{obs}				
		$M+H^+$	$M+Na^+$	$M+K^+$	$2M+Na^+$	$2M+K^+$
Piv-^{D}Pro-^{L}Pro-NHMe (**1**)	309	310.1	332.1	348.1	641.3	
Piv-^{D}Pro-^{L}Pro-^{L}Val-OMe (**2**)	409	410.2	432.2	448.1	841.4	857.4
Piv-^{D}Pro-^{L}Pro-^{L}Phe-OMe (**3**)	457	458.2	480.2	496.1	937.4	953.4
Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe (**4**)	381	382.1	404.1	420.1	785.3	
Piv-^{L}Pro-^{D}Pro-^{L}Ala-OMe (**5**)	381	382.1	404.1	420.1		
Piv-^{D}Pro-^{L}Pro-^{L}Val-NHMe (**6**)	408	409.3	431.2	447.2	839.4	855.4
Piv-^{D}Pro-^{L}Pro-^{L}Leu-NHMe (**7**)	422	423.3	445.3	461.2		
Piv-^{D}Pro-^{L}Pro-^{L}Phe-NHMe (**8**)	456	457.2	479.2	495.2		
Piv-^{D}Pro-^{L}Pro-Gly-NHMe (**9**)	366	367.3	389.2	405.1	755.4	
Piv-^{D}Pro-^{L}Pro-Aib-NHMe (**10**)	394	395.2	417.4	433.1		
Piv-^{D}Pro-^{L}Pro-^{D}Ala-NHMe (**11**)	380	381.2	403.2	419.2		
Piv-^{D}Pro-^{L}Pro-^{D}Val-NHMe (**12**)	408	409.2	431.3	447.2		
Piv-^{D}Pro-^{L}Pro-^{D}Leu-NHMe **13**)	422	423.2	445.2	461.2		
Piv-^{D}Pro-^{L}Pro-^{D}Phe-NHMe **14**)	456	457.2	479.2		935.5	
Piv-^{L}Pro-^{D}Pro-^{L}Val-OMe (**15**)	409	410.3	432.3	448.2		
Piv-^{L}Pro-^{L}Pro-^{L}Ala-OMe (**16**)	381	382.2	404.2	420.2		
Piv-^{L}Pro-^{L}Pro-^{L}Val-OMe (**17**)	409	410.2	432.2		841.4	
Piv-^{L}Pro-^{L}Pro-^{L}Phe-OMe (**18**)	457	458.2	480.2	496.1	937.4	
Piv-^{L}Pro-^{L}Pro-^{L}Ala-NHMe (**19**)	380	381.2	403.2	419.2		
Piv-^{L}Pro-^{L}Pro-^{L}Val-NHMe (**20**)	408	409.2	431.3			
Piv-^{L}Pro-^{L}Pro-^{L}Leu-NHMe (**21**)	422	423.3	445.3	461.2	867.5	
Piv-^{L}Pro-^{L}Pro-^{L}Phe-NHMe (**22**)	456	457.2	479.2	495.1		
Piv-^{L}Pro-^{L}Pro-Aib-NHMe (**23**)	394	395.2	417.2			

Note: The electrospray mass ionization (ESI)-MS data were obtained by using an Esquire 3000-plus mass spectrometer (Bruker Daltonics) and on a Hewlett Packard, HP 1100 MSD series spectrometer.

Table S2 : Crystal and diffraction parameters.

Compound	Peptide 1	Peptide 2	Peptide 3	Peptide 4	Peptide 5	Peptide 6	Peptide 7
Empirical formula	$C_{16}H_{27}N_3O_3$	$C_{21}H_{35}N_3O_5$. 0.08 H_2O	$C_{25}H_{35}N_3O_5$. H_2O	$C_{19}H_{31}N_3O_5$	$C_{19}H_{31}N_3O_5$	$C_{21}H_{36}N_4O_4$. H_2O	$C_{22}H_{38}N_4O_4$. 0.34H_2O
Crystal habit	Clear, Block	Clear, Rectangular	Clear , Plate	Clear , Block	Yellow colour, Block	Clear, Plate	Clear , Block
Crystal size (mm)	0.57 x 0.52 x 0.17	0.35 x 0.20 x 0.09	0.25 x 0.12 x 0.10	0.35 x 0.29 x 0.14	0.38 x 0.23 x 0.19	0.26 x 0.14 x 0.09	0.46 x 0.24 x 0.21
Crystallizing solvent	Ethylacetate/ petroleum ether	Ethylacetate / water	Ethylacetate / petroleum ether	Ethylacetate / petroleum ether	Ethylacetate/ petroleum ether	Ethylacetate / petroleum ether	Ethylacetate / petroleum ether
Space group	$P2_1$	$P2_12_12_1$	$P2_1$	$P2_1$	$P2_12_12_1$	$P2_1$	$P2_1$
a (Å)	10.785 (1)	10.676 (1)	9.538 (1)	11.269 (1)	9.043 (2)	9.386 (1)	9.231 (1)
b (Å)	15.037 (2)	16.608 (1)	10.3668 (8)	9.945 (1)	10.183 (2)	12.112(1)	17.558 (2)
c (Å)	11.335 (1)	39.886 (3)	13.102 (1)	18.550 (2)	23.371 (1)	10.736(1)	15.563 (1)
α (deg)	90.00	90.00	90.00	90.00	90.00	90.00	90.00
β (deg)	109.96 (1)	90.00	93.04 (1)	97.46 (1)	90.00	99.528 (2)	91.938 (2)
γ (deg)	90.00	90.00	90.00	90.00	90.00	90.00	90.00
Volume ($Å^3$)	1727.8 (1)	7072.0 (1)	1293.8 (2)	2061.2 (1)	2152.1 (1)	1203.6 (2)	2521.1(1)
Z	4	12	2	4	4	2	4
Molecules/asym. unit	2	3	1	2	1	1	2
Co-crystallized solvent	None	H_2O	H_2O	None	None	H_2O	H_2O
Molecular weight	309.41	410.87	473.56	381.47	381.47	424.54	428.04
Final R(%) / wR2 (%)	3.88 / 10.47	6.88 / 17.01	5.04 / 14.55	5.63 / 12.49	7.53 / 16.03	5.28 / 13.04	5.55 / 14.22
Goodness of fit (S)	1.075	1.128	1.102	1.122	1.242	1.171	1.088

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Compound	Peptide 8	Peptide 10	Peptide 11	Peptide 15	Peptide 18	Peptide 20	Peptide 23
Empirical formula	$C_{25}H_{36}N_4O_4 . H_2O$	$C_{20}H_{34}N_4O_4$	$C_{19}H_{32}N_4O_4$	$C_{21}H_{35}N_3O_5 . H_2O$	$C_{25}H_{35}N_3O_5 . 0.5\,H_2O$	$C_{21}H_{36}N_4O_4 . H_2O$	$C_{20}H_{34}N_4O_4 . H_2O$
Crystal habit	Clear , Plate	Clear, Rod	Translucent yellow, Plate	Clear, Rod	Clear, Rod	Clear, Block	Clear , Block
Crystal size (mm)	0.21 x 0.19 x 0.10	0.48 x 0.09 x 0.07	0.35 x 0.18 x 0.07	0.25 x 0.08 x 0.05	0.22 x 0.10 x 0.07	0.36 x 0.26 x 0.14	0.33 x 0.26 x 0.15
Crystallizing solvent	Methanol / water	Ethylacetate/petroleum ether	Ethylacetate/ petroleum ether	Ethylacetate / petroleum ether	Methanol / water	Ethylacetate / petroleum ether	Ethylacetate / petroleum ether
Space group	$P2_12_12_1$	$P2_12_12_1$	P1	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
a (Å)	10.473 (1)	10.571 (1)	5.964 (1)	8.784 (4)	10.199 (1)	9.454 (1)	6.271 (1)
b (Å)	15.980 (2)	11.063 (1)	9.354 (1)	11.587 (5)	20.702 (2)	11.119 (1)	14.011 (2)
c (Å)	15.994 (1)	18.536 (1)	9.961 (1)	23.328 (10)	23.970 (2)	23.021(2)	12.888 (2)
α (deg)	90.00	90.00	75.44 (1)	90.00	90.00	90.00	90.00
β (deg)	90.00	90.00	78.90 (1)	90.00	90.00	90.00	96.80 (1)
γ (deg)	90.00	90.00	77.04 (1)	90.00	90.00	90.00	90.00
Volume ($Å^3$)	2676.7 (1)	2167.8 (1)	518.6 (1)	2374.2 (2)	5060.9 (7)	2420.2 (3)	1124.5 (2)
Z	4	4	1	4	8	4	2
Molecules/asym. unit	1	1	1	1	2	1	1
Co-crystallized solvent	H_2O	None	None	H_2O	H_2O	H_2O	H_2O
Molecular weight	472.58	394.51	380.49	425.52	465.56	424.54	410.51
Final R(%) / wR2 (%)	6.20 / 18.26	5.78 / 12.56	7.28 / 15.28	8.88 / 14.65	7.16 / 17.60	5.51 / 14.92	4.64 / 12.44
Goodness of fit (S)	1.011	1.265	1.298	1.065	1.313	1.113	1.047

Table S3 : List of intramolecular and intermolecular hydrogen bonds in the crystal structures.

Donor	Acceptor	N / C / O…O Donor…Acceptor (Å)	H…O (Å)	C=O..H (deg)	C=O…N (deg)	O…H-N (deg)	C-H…O (deg)
Piv-^{D}Pro-^{L}Pro-NHMe (**1**)							
Intramolecular							
Molecule A							
4→1 N(3)	O(0)	2.903	2.133	133.57	137.08	164.55	
Molecule B							
4→1 N(6)	O(3)	2.926	2.124	135.27	136.23	161.38	
Piv-^{D}Pro-^{L}Pro-^{L}Val-OMe (**2**)							
Intramolecular							
Molecule A							
4→1 N(3)	O(0)	3.013	2.214	145.44	142.61	154.44	
Molecule B							
4→1 N(7)	O(4)	3.122	2.290	135.08	137.50	162.98	
Molecule C							
4→1 N(11)	O(8)	3.033	2.201	136.47	134.17	162.85	
Intermolecular							
O1w	O(1)	2.904					
O1w	O(3)	2.817					
Piv-^{D}Pro-^{L}Pro-^{L}Phe-OMe (**3**)							
Intramolecular							
4→1 N(3)	O(0)	3.052	2.235	139.88	138.14	158.57	
Intermolecular							
O1w	O(2)	2.965					
O1w	O(1)[a]	2.891					
Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe (**4**)							
Intramolecular							
Molecule A							
4→1 N(3)	O(0)	3.095	2.326	143.18	140.81	148.86	
Molecule B							
4→1 N(6)	O(00)	3.114	2.310	142.52	141.09	155.78	
Piv-^{L}Pro-^{D}Pro-^{L}Ala-OMe (**5**)							
Intramolecular							
4→1 N(3)	O(0)	3.147	2.307	137.05	137.57	166.64	
Piv-^{D}Pro-^{L}Pro-^{L}Val-NHMe (**6**)							
Intramolecular							
4→1 N(3)	O(0)	3.168	2.349	138.49	135.02	159.44	
4→1 N(4)	O(1)	3.148	2.307	118.97	119.99	165.99	
Intermolecular							
O1w	O(2)	3.068					
O1w	O(1)[b]	2.864					
Piv-^{D}Pro-^{L}Pro-^{L}Leu-NHMe (**7**)							
Intramolecular							
Molecule A							
4→1 N(3)	O(0)	3.024	2.238	137.55	132.65	151.79	
4→1 N(4)	O(1)	2.974	2.147	121.11	123.62	161.11	
Molecule B							
4→1 N(7)	O(4)	3.051	2.308	142.55	136.94	144.77	
4→1 N(8)	O(5)	3.019	2.256	119.44	123.75	163.72	
Intermolecular							
O1w	O(2)	2.982					
O1w	O(4)[c]	2.998					

Continued…

Donor	Acceptor	N / C / O…O Donor…Acceptor (Å)	H…O (Å)	C=O..H (deg)	C=O…N (deg)	O…H-N (deg)	C-H…O (deg)
Piv-^{D}Pro-^{L}Pro-^{L}Phe-NHMe (**8**)							
Intramolecular							
4→1 N(3)	O(0)	3.144	2.382	138.20	132.01	147.97	
4→1 N(4)	O(1)	3.109	2.285	120.93	126.06	160.37	
Intermolecular							
O1w	O2w[d]	2.930					
O1w	O(2)	2.731					
O2w	O(3)	3.148					
O1w	O2w	3.351					
Piv-^{D}Pro-^{L}Pro-Aib-NHMe (**10**)							
Intramolecular							
4→1 N(3)	O(0)	3.262	2.666	146.10	145.81	129.43	
4→1 N(4)	O(1)	3.445	2.770	113.66	117.20	139.71	
Piv-^{D}Pro-^{L}Pro-^{D}Ala-NHMe (**11**)							
Intramolecular							
4→1 N(3)	O(0)	3.291	2.580	126.75	134.18	147.50	
5→1 N(4)	O(0)	2.849	2.020	154.52	151.15	161.70	
Piv-^{D}Pro-^{L}Pro-^{D}Val-NHMe (**12**)							
Intermolecular							
N(3)	O1w	3.023	2.100			163.89	
N(4)	O2w	2.782	1.995			151.82	
O1w	O(0)[e]	2.940					
O1w	O(1)[f]	2.821					
O2w	O1w[g]	3.368					
Piv-^{D}Pro-^{L}Pro-^{D}Leu-NHMe (**13**)							
Intramolecular							
4→1 N(4)	O(1)	3.172	2.400	138.81	139.66	149.67	
Intermolecular							
N(3)	O1w	2.861	2.015			167.45	
O1w	O(0)[h]	2.769					
O1w	O(2)[h]	2.760					
Racemic mixture of Piv-^{L}Pro-^{D}Pro-^{L}Phe-NHMe + Piv-^{D}Pro-^{L}Pro-^{D}Phe-NHMe (**14**)							
Intermolecular							
O1w	O(1)	2.828					
O2w	O(0)	2.861					
O1w	O(1)[i]	2.863					
O1w	O2w[i]	2.937					
N(3)	O(3)[j]	2.785	1.961	132.49	138.26	160.06	
N(4)	O(2)[k]	2.883	2.036	132.88	136.14	168.29	
Piv-^{L}Pro-^{D}Pro-^{L}Val-OMe (**15**)							
Intermolecular							
N(3)	O1w	3.061	2.244			158.58	
O1w	O(1)[l]	2.814					
O1w	O(0)[m]	2.898					
Piv-^{L}Pro-^{L}Pro-^{L}Phe-OMe (**18**)							
Intramolecular							
Molecule A							
4→1 N(3)	O(0)	2.865	2.207	142.91	134.95	133.14	
Molecule B							
4→1 N(7)	O(4)	2.857	2.259	145.63	137.31	126.59	
Intermolecular							
O1w	O(1)	3.046					
O1w	O(5)B[n]	3.123					

Continued…

Donor	Acceptor	N / C / O…O Donor…Acceptor (Å)	H…O (Å)	C=O..H (deg)	C=O…N (deg)	O…H-N (deg)	C-H…O (deg)
Piv-^{L}Pro-^{L}Pro-^{L}Val-NHMe (**20**)							
Intermolecular							
O1w	O(1)	2.746					
O1w	O(3)[o]	2.775					
N(4)	O(0)[o]	2.904	2.081	130.59	134.80	159.99	
N(3)	O1w[p]	2.863	2.101			147.33	
Piv-^{L}Pro-^{L}Pro-Aib-NHMe (**23**)							
Intramolecular							
4→1 N(4)	O(1)	3.273	2.559	133.72	126.59	141.16	
Intermolecular							
O1w	O(1)	2.840					
N(3)[q]	O(3)	3.016	2.179	141.66	142.15	173.24	
O1w [r]	O(0)	2.899					

[a]Symmetry related by –x, y+1/2, -z+1.
[b]Symmetry related by –x, y+1/2, -z.
[c]Symmetry related by x, y,z-1.
[d]Symmetry related by x+1/2, -y+1/2+1, -z+1.
[e]Related by symmetry x+1/2, -y+1/2, -z.
[f]Related by symmetry x+1, y, z.
[g]Symmetry related by -x+1, y-1/2, -z+1/2+1.
[h]Related by symmetry –x, y-1/2, -z+1/2.
[i]Symmetry related by -x, -y+1,-z.
[j]Symmetry related by -x, -y+1,-z+1.
[k]Symmetry related by –x+1, -y+1,-z+1.
[l]Symmetry related by x+1,y,z.
[m]Symmetry related by x+1/2,-y+1/2,-z+2.
[n]Symmetry related by -x+1/2+1, -y+1, z+1/2.
[o]Symmetry related by –x,y-1/2,-z+1/2.
[p]Symmetry related by –x,y+1/2,-z+1/2.
[q]Symmetry related by x-1, y, z.
[r]Symmetry related by –x+1, y+1/2, -z+1.

TABLE S4: Pyrrolidine ring puckering states in the crystal structures of the peptides.

	χ_1	χ_2	χ_3	χ_4	θ	Q^a	ϕ^a	Puckering Mode	χ_1	χ_2	χ_3	χ_4	θ	Q^a	ϕ^a	Puckering Mode
Peptide **1**																
Mol A (DL)	18.8	-32.5	33.5	-22.1	2.2	0.329	110.3	C^{γ}-exo	34.5	-34.6	20.5	1.8	-23.1	0.352	70.7	C^{β}-exo
Mol B (DL)	23.0	-36.5	35.3	-21.6	-0.9	0.362	105.5	C^{γ}-exo	34.1	-35.8	23.2	-1.5	-20.5	0.355	75.6	C^{β}-exo
Peptide **2**																
Mol A (DL)	16.8	-26.1	23.9	-11.9	-2.6	0.231	101.0	C^{γ}-exo	2.1	4.6	-9.2	10.2	-7.7	0.094	338.0	Planar
Mol B (DL)	15.8	-27.1	26.6	-16.2	0.7	0.254	107.9	C^{γ}-exo	35.7	-36.6	22.8	-0.2	-22.3	0.364	73.6	C^{β}-exo
Mol C (DL)	-3.8	6.0	-5.7	3.1	0.3	-	-	Planar	29.2	-28.6	15.8	4.0	-20.7	0.284	65.4	C^{β}-exo
Peptide **3**(DL)	23.4	-35.3	33.0	-18.8	-2.3	0.338	103.2	**C^{γ}-exo**	34.1	-37.8	26.0	-4.1	-19.0	0.369	78.5	C^{β}-exo
Peptide **4**																
Mol A (DL)	21.1	-33.6	32.9	-20.3	-0.4	0.331	106.1	C^{γ}-exo	34.7	-39.7	29.2	-7.4	-17.0	0.386	83.4	**C^{γ}-endo**
Mol B (DL)	23.4	-34.7	32.2	-18.1	-3.1	0.332	102.1	C^{γ}-exo	33.2	-39.4	29.6	-8.9	-15.1	0.377	85.4	**C^{γ}-endo**
Peptide **5** (LD)	28.2	-35.7	28.5	-10.5	-10.8	0.332	89.5	**C^{γ}-endo**	-34.9	38.8	-27.5	5.0	18.7	0.375	260.3	C^{β}-exo
Peptide **6** (DL)	27.9	-38.3	33.5	-16.7	-7.2	0.371	96.8	**C^{γ}-exo**	30.3	-37.5	29.6	-10.6	-12.0	0.356	89.0	**C^{γ}-endo**
Peptide **7**																
Mol A (DL)	-14.8	23.5	-22.0	11.5	1.8	0.211	282.6	C^{γ}-endo	29.4	-33.2	23.1	-3.9	-16.1	0.311	79.6	C^{β}-exo
Mol B (DL)	29.7	-40.0	35.2	-17.3	-7.6	0.392	96.6	**C^{γ}-exo**	-7.8	16.7	-18.5	13.5	-4.1	0.168	300.0	Planar
Peptide **8** (DL)	-26.0	36.6	-32.7	15.9	6.1	0.346	277.0	C^{γ}-endo	31.0	-38.8	31.1	-12.6	-11.0	0.376	91.5	**C^{γ}-endo**
Peptide**10** (DL)	-21.8	34.8	-34.2	20.6	0.6	0.342	286.0	C^{γ}-endo	29.2	-38.1	31.8	-14.1	-9.6	0.367	93.0	**C^{γ}-endo**
Peptide**11** (DL)	-27.9	37.4	-31.7	14.3	8.3	0.356	274.7	**C^{γ}-endo**	35.2	-39.7	28.5	-6.4	-17.9	0.386	81.8	C^{β}-exo
Peptide**12** (DL)	-10.8	13.2	-9.7	1.6	5.6	0.099	240.0	Planar	27.6	-33.4	25.6	-8.5	-12.1	0.332	87.1	**C^{γ}-endo**
Peptide**13** (DL)	-24.4	35.0	-31.7	16.1	4.9	0.336	279.2	C^{γ}-endo	23.9	-34.5	31.2	-16.7	-4.4	0.335	100.0	C^{γ}-endo
Peptide**14** (DL)	-22.1	29.4	-25.1	11.3	6.3	0.271	265.3	C^{γ}-endo	23.5	-33.4	28.9	-14.6	-5.7	0.304	82.6	C^{γ}-endo
Peptide**15** (LD)	-0.9	2.6	-3.1	2.4	-1.0	-	-	Planar	-26.4	32.0	-24.0	7.0	12.1	0.302	265.3	**C^{γ}-endo**
Peptide **18**																
Mol A (LL)	-27.4	37.1	-32.2	15.7	7.3	0.359	276.1	**C^{γ}-exo**	35.8	-40.8	29.7	-6.6	-18.3	0.399	81.8	C^{β}-exo
Mol B (LL)	-31.2	40.0	-32.6	13.1	11.7	0.383	270.7	**C^{γ}-exo**	36.8	-40.4	27.6	-3.7	-21.1	0.399	77.4	C^{β}-exo
Peptide**20** (LL)	2.1	4.0	-8.3	9.6	-7.2	0.086	338.0	Planar	-29.0	38.4	-32.5	14.9	7.9	0.369	275.1	**C^{γ}-exo**
Peptide**23** (LL)	37.8	-33.9	17.0	7.5	-28.5	0.370	62.7	C^{β}-exo	-22.4	35.6	-34.5	21.1	0.6	0.355	285.8	C^{γ}-exo

[a] **Q** and ϕ are Cremer & Pople Puckering Parameters.

Note : C^{γ}-exo refers to Twisted C^{γ}-exo-C^{β}-endo and **C^{γ}-endo** refers to Twisted C^{γ}-endo-C^{β}-exo pyrrolidine ring puckering state.

TABLE S5 : Pyrrolidine ring puckerings of acyclic peptides obtained from CSD and containing homochiral or heterochiral diproline segments.

CSD ID / Sequence	**Backbone torsion angles in degrees**			**Proline puckering parameters**							
	ϕ	**ψ**	**ω**	**χ_1**	**χ_2**	**χ_3**	**χ_4**	**θ**	**Q^a**	**ϕ^a**	**Puckering mode**
BCPPGA : t-Butyloxycarbonyl –L-prolyl-L-prolyl-glycine											
L-Pro	-60.9	156.3	-178.8	-22.2	32.9	-29.4	15.6	4.0	0.312	279.4	C^{γ}-exo
L-Pro	-64.9	-23.0	177.8	24.7	-37.9	35.8	-21.6	-1.9	0.380	104.1	C^{γ}-endo
BOCPRO : t-Butyloxycarbonyl -L-prolyl-proline											
L-Pro	-66.6	141.5	-175.8	26.7	-31.1	22.6	-5.3	-12.9	0.290	82.9	C^{β}-exo
L-Pro	-95.1	12.1	-	38.4	-35.7	18.9	5.9	-27.9	0.373	64.7	C^{β}-exo
BOCPRO01 : t-Butyloxycarbonyl prolylproline											
Molecule 1											
L-Pro	-71.3	149.0	169.1	25.8	-34.3	29.7	-13.3	-7.5	-	-	**C^{γ}-endo**
*L-Pro	-86.5	-176.9	-	24.6	-15.2	0.0	16.6	-25.8	-	-	-
Molecule 2											
L-Pro	-63.6	144.3	174.0	26.3	-33.8	27.1	-10.3	-9.7	-	-	**C^{γ}-endo**
*L-Pro	-83.2	-175.4	-	21.4	-13.9	0.2	14.4	-21.9	-	-	-
Molecule 3											
L-Pro	-62.9	148.0	175.7	12.7	-18.0	15.3	-6.3	-4.3	-	-	Planar
L-Pro	-87.5	-179.9	-	38.3	-41.8	28.1	-3.3	-21.2	-	-	C^{β}-exo
Molecule 4											
L-Pro	-64.3	142.5	-179.2	-25.4	36.9	-33.6	18.3	5.0	-	-	C^{γ}-exo
L-Pro	-80.7	168.6	-	30.7	-34.5	23.9	-4.1	-17.2	-	-	C^{β}-exo

Continued…

CSD ID / Sequence	Backbone torsion angles in degrees			Proline puckering parameters							
	ϕ	ψ	ω	χ_1	χ_2	χ_3	χ_4	θ	Q	ϕ	Puckering mode
BUFLIX : Pivaloyl-L-prolyl-D-proline-methyl ester											
L-Pro	-69.7	129.1	-19.1	-10.1	21.2	-23.1	17.1	-4.2	-	-	C^{γ}-exo
D-Pro	84.3	-169.0	179.6	-17.3	20.1	-14.1	2.5	8.6	-	-	Planar
BUHLEV10 : t-butoxycarbonyl-alpha-amino-isobutyryl-prolyl-N-methylamide trihydrate											
Molecule 1											
L-Pro	-67.0	154.5	170.2	26.7	-35.2	29.1	-12.0	-9.6	0.334	88.4	**C^{γ}-endo**
L-Pro	-57.4	152.8	172.1	-20.1	34.9	-35.1	23.7	-2.9	0.355	249.1	C^{γ}-exo
Molecule 2											
L-Pro	-71.3	158.1	178.8	13.8	-15.6	10.6	-0.6	-8.3	0.143	105.3	Planar
L-Pro	-71.9	148.6	179.4	32.4	-40.5	32.7	-13.1	-11.5	0.397	88.8	**C^{γ}-endo**
BZCPRO : Benzyloxycarbonyl-L-prolyl-L-proline											
L-Pro	-64.9	155.3	-179.6	-17.7	32.5	-33.9	23.5	-3.7	0.332	247.7	C^{γ}-exo
L-Pro	-52.6	141.2	-	-26.2	33.1	-26.1	9.3	10.4	0.309	271.4	**C^{γ}-exo**
DEGKIJ : t-butylcarbonyl-L-prolyl-L-proline-N-methylamide monohydrate											
L-Pro	-60.4	137.6	-170.5	-30.1	41.5	-36.6	18.3	7.5	0.408	277.1	**C^{γ}-exo**
L-Pro	-94.7	-6.8	-	35.8	-40.1	28.3	-5.6	-18.8	0.392	80.1	C^{β}-exo
DEGKOP : t-butylcarbonyl-L-prolyl-D-proline-N-methylamide											
Molecule 1											
L-Pro	-55.8	138.9	-178.5	-18.5	32.8	-34.4	23.4	-3.7	0.341	292.4	C^{γ}-exo
D-Pro	84.3	-13.9	-172.8	-34.4	35.5	-21.6	-0.8	22.3	0.358	252.5	C^{β}-exo

Continued…

CSD ID / Sequence	Backbone torsion angles in degrees			Proline puckering parameters							
	ϕ	ψ	ω	χ_1	χ_2	χ_3	χ_4	θ	Q	ϕ	Puckering mode
Molecule 2											
L-Pro	-57.7	134.4	179.5	-24.5	38.2	-36.4	21.8	1.5	0.381	284.9	C^{γ}-exo
D-Pro	83.2	-6.4	-173.6	-32.8	35.5	-23.6	2.3	19.3	0.351	256.8	C^{β}-exo
EABXEK : N-t-Butyloxycarbonyl prolyl-(prolyl (2,N) ethanoglycinamide											
L-Pro	-61.0	138.9	173.0	-23.5	37.8	-36.7	22.9	0.3	0.381	286.0	C^{γ}-exo
L-Pro	-51.0	128.7	-179.3	-33.0	41.4	-32.7	12.4	12.9	0.400	270.4	**C^{γ}-exo**
JUQYEZ : (4'R-(4'alpha, 7'alp ha, 8'aalpha))-1-(((t-Butoxy carbon yl)-2(S)-pyrrolidinyl) carbonyl)- tetrahydro-6'-oxospiro (pyrroli dine-2',7'-(6' H)-pyrrolo (2,1-b) thiazine) -4'-carbox amide monohydrate											
L-Pro	-62.9	136.9	170.9	-9.6	22.3	-25.5	19.1	-6.3	0.230	238.7	C^{γ}-exo
L-Pro	-49.0	134.2	173.3	-29.5	38.4	-31.7	13.6	10.1	0.373	267.8	**C^{γ}-exo**
KOKRIL : (1S,4S,7S,10S)-12 -Acetyl-4-rboxy-3, 12-diazo-2-oxy-9-thiatricyclotridecane											
L-Pro	-81.0	-20.0	175.8	34.7	-41.1	31.1	-9.5	-15.9	-	-	**C^{γ}-endo**
L-Pro	-67.4	-28.8	-	29.0	-39.0	33.0	-15.4	-8.3	-	-	**C^{γ}-endo**
PVPALM : Pivaloyl-D-prolyl-L-prolyl-L-alanine-N-methylamide											
D-Pro	58.9	-135.8	-179.4	27.3	-38.2	34.0	-17.5	-6.4	-	-	C^{γ}-exo
L-Pro	-58.5	-23.7	-179.7	-25.1	36.4	-33.8	18.4	3.8	-	-	C^{γ}-exo
QILCIX : N-Ferrocenoylprolinyl-prolinyl-benzyl ester											
L-Pro	-66.2	136.3	170.0	32.7	-39.8	32.7	-12.4	-12.1	-	-	**C^{γ}-endo**
L-Pro	-70.9	-24.0	-172.8	31.0	-38.0	28.3	-6.2	-16.2	-	-	C^{β}-exo

Continued…

CSD ID / Sequence	Backbone torsion angles in degrees			Proline puckering parameters							
	ϕ	ψ	ω	χ_1	χ_2	χ_3	χ_4	θ	Q	ϕ	Puckering mode
QILDAQ : N-Ferrocenoylproli nyl-prolinyl-N-phenylalanine dichloromethane solvat											
L-Pro	-53.7	137.7	16.0	-33.2	38.7	-29.0	7.8	15.6	-	-	**C^{γ}-exo**
L-Pro	-93.1	11.0	161.5	36.0	-39.7	27.9	-4.9	-19.8	-	-	C^{β}-exo
ZAYSUN : Ehyl(1-(1-(4-phen- ylbutanoyl)-2(S)-indolinylcarbonyl)-2(S)-pyrrolidinyl)-2-oxoacetate											
L-Pro	-59.0	154.6	-177.1	2.6	-2.6	1.4	0.4	-2.0	-	-	Planar
L-Pro	-69.8	159.2	-9.3	32.0	-41.6	35.0	-15.8	-9.6	0.406	85.5	**C^{γ}-endo**
ZAYTAU : Benzyl 2-(2-(2-thia zolecarbonyl) pyrr-li dinecarbonyl) indoline-1-carboxylate											
L-Pro	-67.3	144.0	179.7	7.9	-6.0	1.3	4.5	-7.8	-	-	Planar
L-Pro	-74.1	150.0	-	28.7	-37.2	31.0	-14.4	-8.4	0.082	136.0	**C^{γ}-endo**
ZAYTEY : Benzyl 2-(2-(2-Benzothiazolecarbonyl) pyrrlidinecar- bonyl) pyrrolidine-1-carboxylate											
L-Pro	-65.3	150.1	176.1	0.1	10.8	-17.1	18.0	-11.6	-	-	Planar
L-Pro	-64.9	155.4	-	14.7	-21.6	19.0	-9.8	-2.5	0.197	100.0	Planar
AQEVEX : (2S)-1-((2R,3R)-1-(2,2-Dimethyl-pro- pionyl)-3-isopropyl pyrrolidin-2-ylcarbonyl)pyrrolidine-2-carboxylic acid methylamide											
D-Pro	67.8	-123.9	175.7	-33.0	39.4	-30.4	9.5	15.0			**C^{γ}-endo**
L-Pro	-73.8	-12.8	-177.2	35.2	-37.8	25.6	-3.3	-19.9			C^{β}-exo

[a] **Q** and ϕ are Cremer & Pople Puckering Parameters.

Note : C^{γ}-exo refers to Twisted C^{γ}-exo-C^{β}-endo and **C^{γ}-endo** refers to Twisted C^{γ}-endo-C^{β}-exo pyrrolidine ring puckering state.

TABLE S6: Grouping of the puckering states of the proline rings

A) Dataset comprising of the 17 crystal structures mentioned in Table S4

Serial no.	**χ_1**	**χ_2**	**χ_3**	**χ_4**	**θ**	**Q**	**ϕ**	**Puckering Mode**	**Serial no.**	**χ_1**	**χ_2**	**χ_3**	**χ_4**	**θ**	**Q**	**ϕ**	**Puckering Mode**
Pro1	-18.8	32.5	-33.5	22.1	-2.2	0.329	110.3	C^{γ}-exo	**Pro25**	14.8	-23.5	22.0	-11.5	-1.8	0.211	282.6	C^{γ}-endo
Pro2	-23.0	36.5	-35.3	21.6	0.9	0.362	105.5	C^{γ}-exo	**Pro26**	26.0	-36.6	32.7	-15.9	-6.1	0.346	277.0	C^{γ}-endo
Pro3	-16.8	26.1	-23.9	11.9	2.6	0.231	101.0	C^{γ}-exo	**Pro27**	21.8	-34.8	34.2	-20.6	-0.6	0.342	286.0	C^{γ}-endo
Pro4	-15.8	27.1	-26.6	16.2	-0.7	0.254	107.9	C^{γ}-exo	**Pro28**	24.4	-35.0	31.7	-16.1	-4.9	0.336	279.2	C^{γ}-endo
Pro5	-23.4	35.3	-33.0	18.8	2.3	0.338	103.2	C^{γ}-exo	**Pro29**	22.1	-29.4	25.1	-11.3	-6.3	0.271	265.3	C^{γ}-endo
Pro6	-21.1	33.6	-32.9	20.3	0.4	0.331	106.1	C^{γ}-exo	Pro30	23.9	-34.5	31.2	-16.7	-4.4	0.335	100.0	C^{γ}-endo
Pro7	-23.4	34.7	-32.2	18.1	3.1	0.332	102.1	C^{γ}-exo	Pro31	23.5	-33.4	28.9	-14.6	-5.7	0.304	82.6	C^{γ}-endo
Pro8	-22.4	35.6	-34.5	21.1	0.6	0.355	285.8	C^{γ}-exo									
Pro9	34.9	-38.8	27.5	-5.0	-18.7	0.375	260.3	C^{β}-exo	**Pro32**	26.4	-32.0	24.0	-7.0	-12.1	0.302	265.3	**C^{γ}-endo**
Pro10	34.5	-34.6	20.5	1.8	-23.1	0.352	70.7	C^{β}-exo	Pro33	34.7	-39.7	29.2	-7.4	-17.0	0.386	83.4	**C^{γ}-endo**
Pro11	34.1	-35.8	23.2	-1.5	-20.5	0.355	75.6	C^{β}-exo	Pro34	33.2	-39.4	29.6	-8.9	-15.1	0.377	85.4	**C^{γ}-endo**
Pro12	35.7	-36.6	22.8	-0.2	-22.3	0.364	73.6	C^{β}-exo	**Pro35**	27.9	-37.4	31.7	-14.3	-8.3	0.356	274.7	**C^{γ}-endo**
Pro13	29.2	-28.6	15.8	4.0	-20.7	0.284	65.4	C^{β}-exo	Pro36	30.3	-37.5	29.6	-10.6	-12.0	0.356	89.0	**C^{γ}-endo**
Pro14	34.1	-37.8	26.0	-4.1	-19.0	0.369	78.5	C^{β}-exo	Pro37	31.0	-38.8	31.1	-12.6	-11.0	0.376	91.5	**C^{γ}-endo**
Pro15	29.4	-33.2	23.1	-3.9	-16.1	0.311	79.6	C^{β}-exo	Pro38	27.6	-33.4	25.6	-8.5	-12.1	0.332	87.1	**C^{γ}-endo**
Pro16	35.2	-39.7	28.5	-6.4	-17.9	0.386	81.8	C^{β}-exo	Pro39	28.2	-35.7	28.5	-10.5	-10.8	0.332	89.5	**C^{γ}-endo**
Pro17	36.8	-40.4	27.6	-3.7	-21.1	0.398	77.4	C^{β}-exo	Pro40	29.2	-38.1	31.8	-14.1	-9.6	0.367	93.0	**C^{γ}-endo**
Pro18	35.8	-40.8	29.7	-6.6	-18.3	0.399	81.7	C^{β}-exo									
Pro19	37.8	-33.9	17.0	7.5	-28.5	0.370	62.7	C^{β}-exo									
									Pro41	3.8	-6.0	5.7	-3.1	-0.3	-	-	Planar
Pro20	-27.9	38.3	-33.5	16.7	7.2	0.371	96.8	**C^{γ}-exo**	**Pro42**	10.8	-13.2	9.7	-1.6	-5.6	0.099	240.0	Planar
Pro21	-29.7	40.0	-35.2	17.3	7.6	0.392	96.6	**C^{γ}-exo**	Pro43	0.9	-2.6	3.1	-2.4	1.0	-	-	Planar
Pro22	-27.4	37.1	-32.2	15.7	7.3	0.358	276.1	**C^{γ}-exo**	Pro44	2.1	4.6	-9.2	10.2	-7.7	0.094	338.0	Planar
Pro23	-31.2	40.0	-32.6	13.1	11.7	0.383	270.7	**C^{γ}-exo**	Pro45	-7.8	16.7	-18.5	13.5	-4.1	0.168	300.0	Planar
Pro24	-29.0	38.4	-32.5	14.9	7.9	0.369	275.1	**C^{γ}-exo**	Pro46	2.1	4.0	-8.3	9.6	-7.2	0.086	338.0	Planar

Continued…

B) Dataset comprising of the crystal structures mentioned in Table S5

Serial no.	χ_1	χ_2	χ_3	χ_4	θ	**Q**	ϕ	**Puckering Mode**	**Serial no.**	χ_1	χ_2	χ_3	χ_4	θ	**Q**	ϕ	**Puckering Mode**
Pro47	-22.2	32.9	-29.4	15.6	4.0	0.312	279.4	C^{γ}-exo	Pro68	24.7	-37.9	35.8	-21.6	-1.9	0.380	104.1	C^{γ}-endo
Pro48	-10.1	21.2	-23.1	17.1	-4.2	-	-	C^{γ}-exo									
Pro49	-20.1	34.9	-35.1	23.7	-2.9	0.355	249.1	C^{γ}-exo	Pro69	28.7	-37.2	31.0	-14.4	-8.4	0.082	136.0	**C^{γ}-endo**
Pro50	-17.7	32.5	-33.9	23.5	-3.7	0.332	247.7	C^{γ}-exo	Pro70	32.0	-41.6	35.0	-15.8	-9.6	0.406	85.5	**C^{γ}-endo**
Pro51	-18.5	32.8	-34.4	23.4	-3.7	0.341	292.4	C^{γ}-exo	Pro71	32.7	-39.8	32.7	-12.4	-12.1	-	-	**C^{γ}-endo**
Pro52	-24.5	38.2	-36.4	21.8	1.5	0.381	284.9	C^{γ}-exo	Pro72	26.7	-35.2	29.1	-12.0	-9.6	0.334	88.4	**C^{γ}-endo**
Pro53	-23.5	37.8	-36.7	22.9	0.3	0.381	286.0	C^{γ}-exo	Pro73	32.4	-40.5	32.7	-13.1	-11.5	0.397	88.8	**C^{γ}-endo**
Pro54	-9.6	22.3	-25.5	19.1	-6.3	0.230	238.7	C^{γ}-exo	Pro74	34.7	-41.1	31.1	-9.5	-15.9	-	-	**C^{γ}-endo**
Pro55	-25.1	36.4	-33.8	18.4	3.8	-	-	C^{γ}-exo	Pro75	29.0	-39.0	33.0	-15.4	-8.3	-	-	**C^{γ}-endo**
Pro56	-25.4	36.9	-33.6	18.3	5.0	-	-	C^{γ}-exo	**Pro76**	33.0	-39.4	30.4	-9.5	-15.0	-	-	**C^{γ}-endo**
Pro57	-27.3	38.2	-34.0	17.5	6.4	-	-	C^{γ}-exo									
									Pro77	-33.2	38.7	-29.0	7.8	15.6	-	-	**C^{γ}-exo**
									Pro78	-29.5	38.4	-31.7	13.6	10.1	0.373	267.8	**C^{γ}-exo**
									Pro79	-26.2	33.1	-26.1	9.3	10.4	0.309	271.4	**C^{γ}-exo**
Pro58	26.7	-31.1	22.6	-5.3	-12.9	0.290	82.9	C^{β}-exo	Pro80	-33.0	41.4	-32.7	12.4	12.9	0.400	270.4	**C^{γ}-exo**
Pro59	38.4	-35.7	18.9	5.9	-27.9	0.373	64.7	C^{β}-exo	Pro81	-30.1	41.5	-36.6	18.3	7.5	0.408	277.1	**C^{γ}-exo**
Pro60	35.8	-40.1	28.3	-5.6	-18.8	0.392	80.1	C^{β}-exo									
Pro61	31.0	-38.0	28.3	-6.2	-16.2	-	-	C^{β}-exo	**Pro82**	17.3	-20.1	14.1	-2.5	-8.6	-	-	Planar
Pro62	36.0	-39.7	27.9	-4.9	-19.8	-	-	C^{β}-exo	Pro83	12.7	-18.0	15.3	-6.3	-4.3	-	-	Planar
Pro63	38.3	-41.8	28.1	-3.3	-21.2	-	-	C^{β}-exo	Pro84	13.8	-15.6	10.6	-0.6	-8.3	0.143	105.3	Planar
Pro64	30.7	-34.5	23.9	-4.1	-17.2	-	-	C^{β}-exo	Pro85	2.6	-2.6	1.4	0.4	-2.0	-	-	Planar
Pro65	35.2	-37.8	25.6	-3.3	-19.9	-	-	C^{β}-exo	Pro86	7.9	-6.0	1.3	4.5	-7.8	-	-	Planar
Pro66	34.4	-35.5	21.6	0.8	-22.3	0.358	252.5	C^{β}-exo	Pro87	0.1	10.8	-17.1	18.0	-11.6	-	-	Planar
Pro67	32.8	-35.5	23.6	-2.3	-19.3	0.351	256.8	C^{β}-exo	Pro88	14.7	-21.6	19.0	-9.8	-2.5	0.197	100.0	Planar

Note : 1) C^{γ}-exo refers to Twisted C^{γ}-exo-C^{β}-endo and **C^{γ}-endo** refers to Twisted C^{γ}-endo-C^{β}-exo pyrrolidine ring puckering state.

2) Pro residues which are highlighted in bold font have the D-configuration (^{D}Pro). In order to facilitate assignment of ring conformational states by comparison with ^{L}Pro residues, all the values in the cases of ^{D}Pro residues have been inverted in sign.

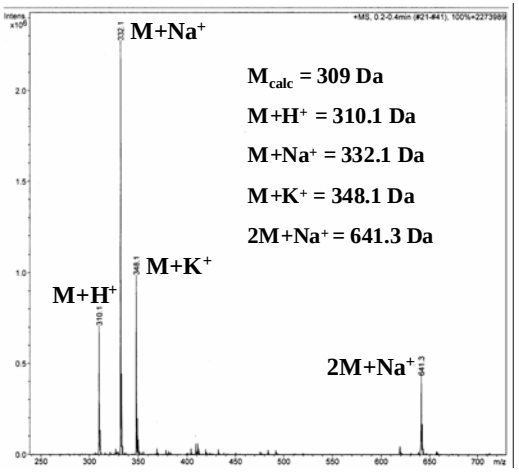
Table S7: ^{13}C chemical shifts for the peptides Piv-^{L}Pro-^{L}Pro-^{L}Xxx-NHMe in $CDCl_3$

		Chemical shifts (ppm)				
Conformers	**Residues**	**C^{α}**	**C^{δ}**	**C^{β}**	**C^{γ}**	**$\Delta\delta(C^{\beta}-C^{\gamma})$**
		Piv-^{L}Pro-^{L}Pro-^{L}Ala-NHMe (19)				
	^{L}Pro (1)	60.22	48.74	26.86	26.45	0.41
trans	^{L}Pro(2)	61.04	47.53	29.34	24.23	5.11
	^{L}Ala (3)	48.98	-	16.87	-	-
		Piv-^{L}Pro-^{L}Pro-^{L}Phe-NHMe (22)				
	^{L}Pro (1)	60.53	48.41	27.05	26.05	1
trans	^{L}Pro (2)	61.04	47.24	28.16	25.23	2.93
	^{L}Phe (3)	53.52	-	37.02	-	-
	^{L}Pro (1)	60.95	48.78	26.9	25.97	0.93
cis	^{L}Pro (2)	60.91	46.62	31.68	21.22	10.46
	^{L}Phe (3)	56.3	-	37.93	-	

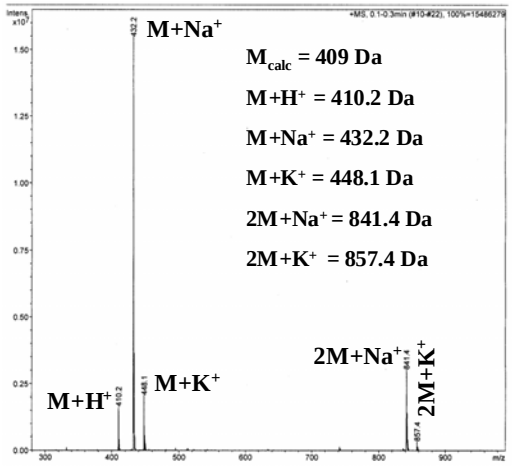
Figure Legends:

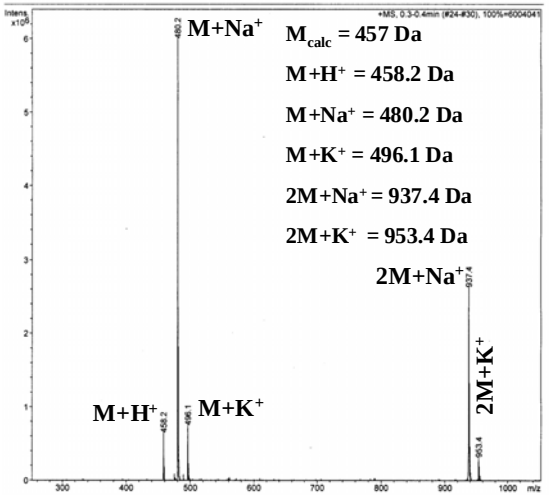
Figure S1.

Piv-^{D}Pro-^{L}Pro-NHMe (1)

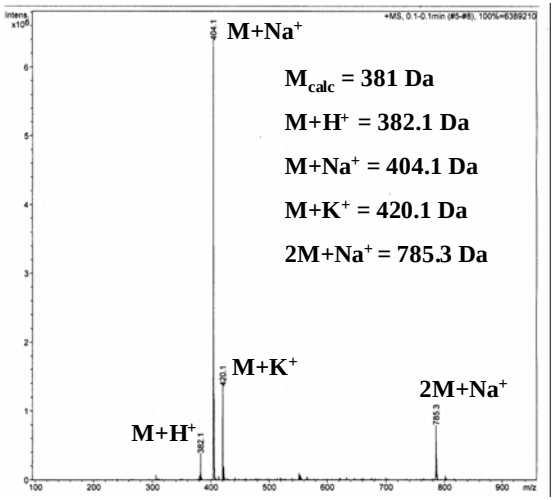


Piv-^{D}Pro-^{L}Pro-^{L}Val-OMe (2)





Piv-^{D}Pro-^{L}Pro-^{L}Phe-OMe (3)



Piv-^{D}Pro-^{L}Pro-^{D}Ala-OMe (4)

Figure S2.

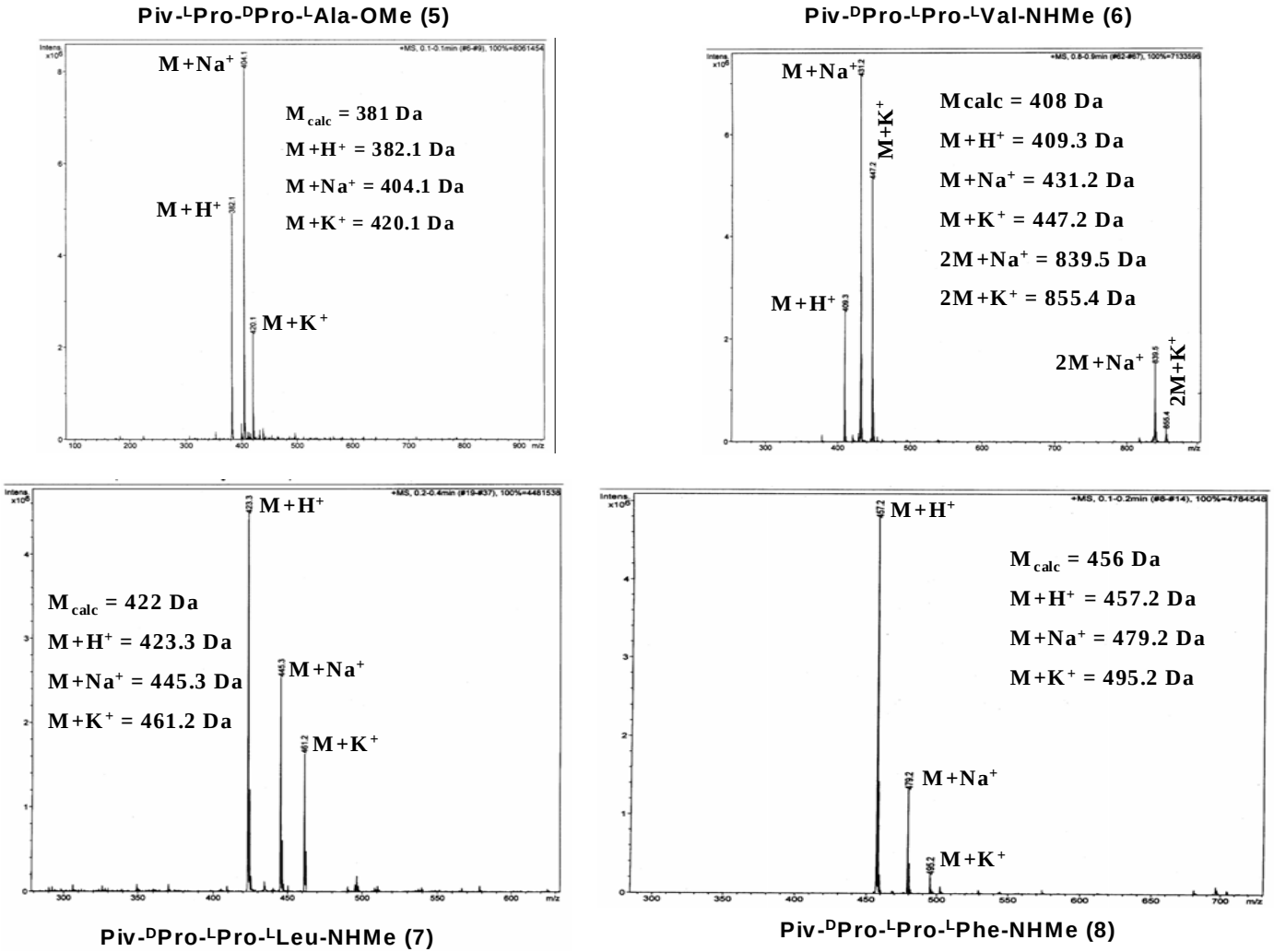
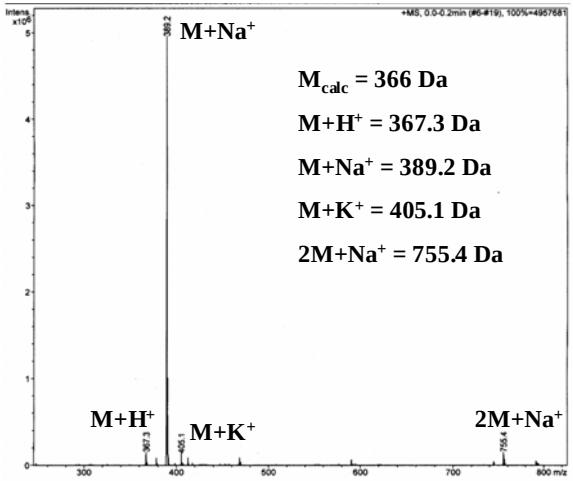
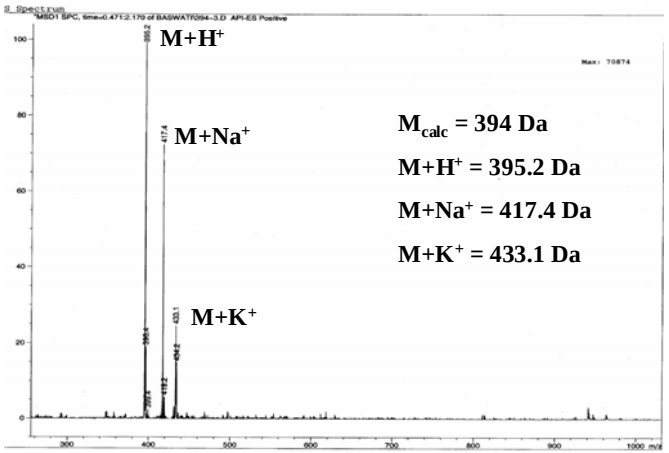

Piv-LPro-DPro-LAla-OMe (5)
M+Na+
M+H+
M+K+
Mcalc = 381 Da
M+H+ = 382.1 Da
M+Na+ = 404.1 Da
M+K+ = 420.1 Da
Piv-DPro-LPro-LVal-NHMe (6)
M+Na+
M+K+
M+H+
2M+Na+
2M+K+
Mcalc = 408 Da
M+H+ = 409.3 Da
M+Na+ = 431.2 Da
M+K+ = 447.2 Da
2M+Na+ = 839.5 Da
2M+K+ = 855.4 Da
Piv-DPro-LPro-LLeu-NHMe (7)
M+H+
M+Na+
M+K+
Mcalc = 422 Da
M+H+ = 423.3 Da
M+Na+ = 445.3 Da
M+K+ = 461.2 Da
Piv-DPro-LPro-LPhe-NHMe (8)
M+H+
M+Na+
M+K+
Mcalc = 456 Da
M+H+ = 457.2 Da
M+Na+ = 479.2 Da
M+K+ = 495.2 Da

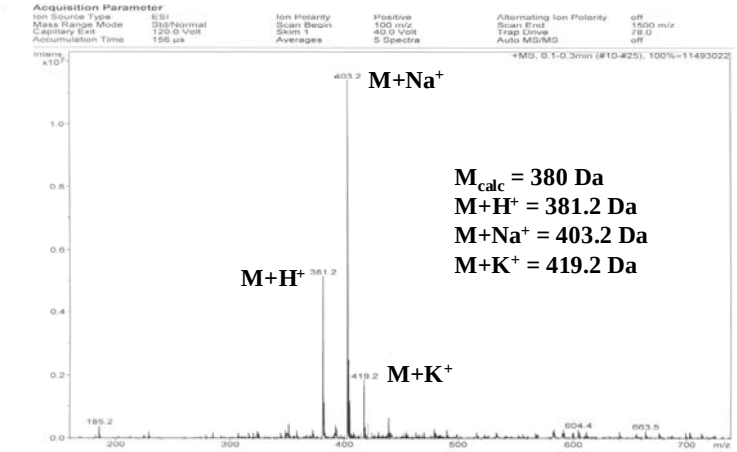
Figure S3.

Piv-^{D}Pro-^{L}Pro-Gly-NHMe (9)

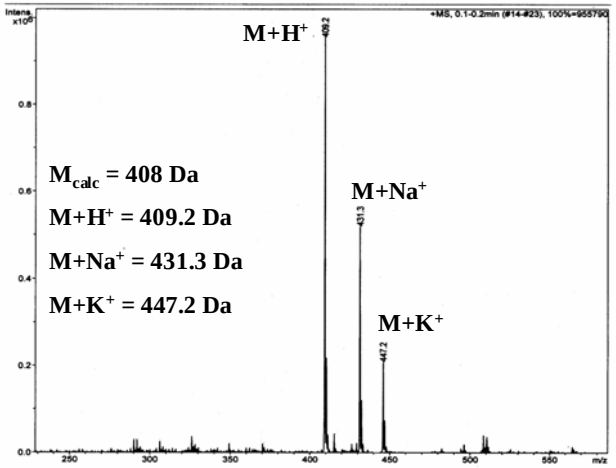


Piv-^{D}Pro-^{L}Pro-Aib-NHMe (10)





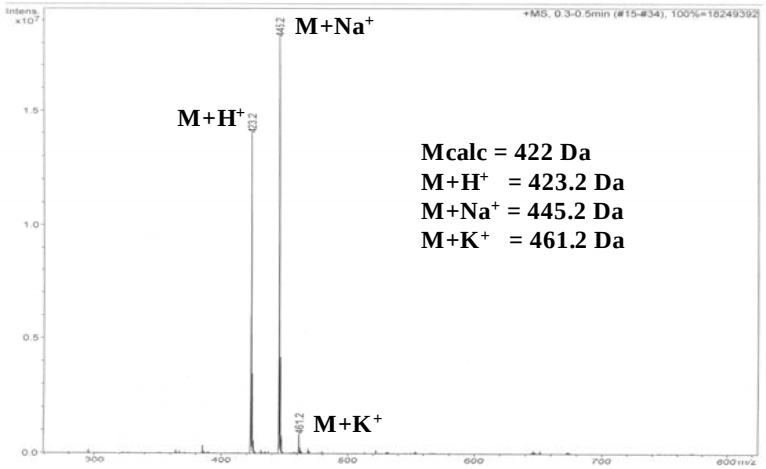
Piv-^{D}Pro-^{L}Pro-^{D}Ala-NHMe (11)



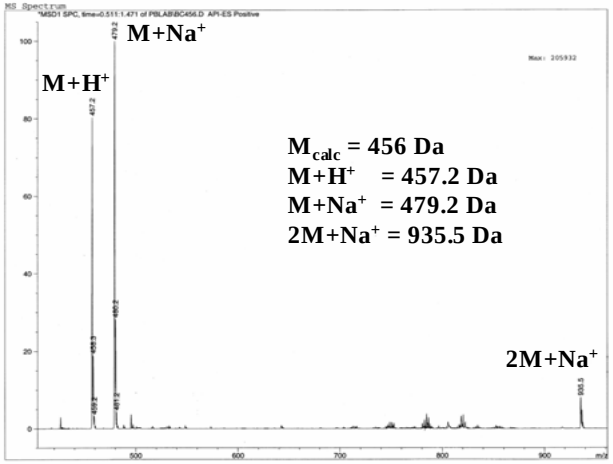
Piv-^{D}Pro-^{L}Pro-^{D}Val-NHMe (12)

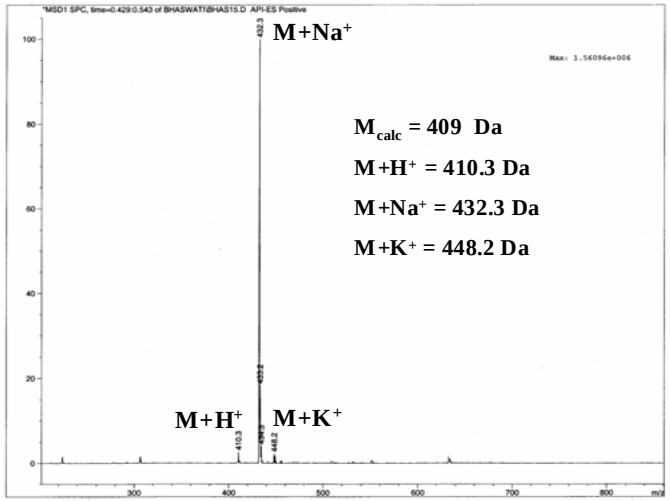
Figure S4.

Piv-^{D}Pro-^{L}Pro-^{D}Leu-NHMe (13)

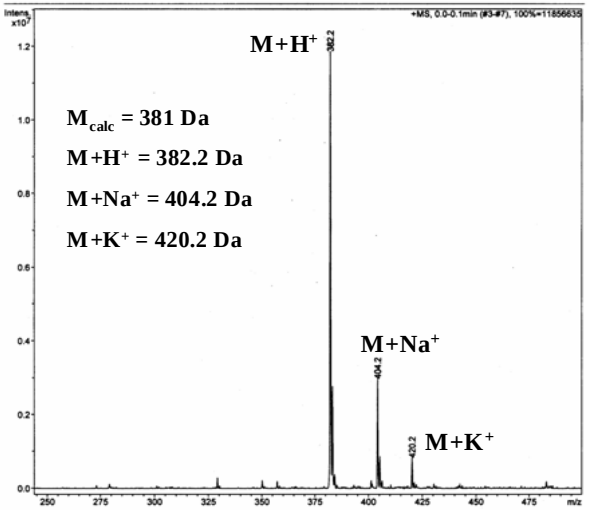


Piv-^{D}Pro-^{L}Pro-^{D}Phe-NHMe (14)





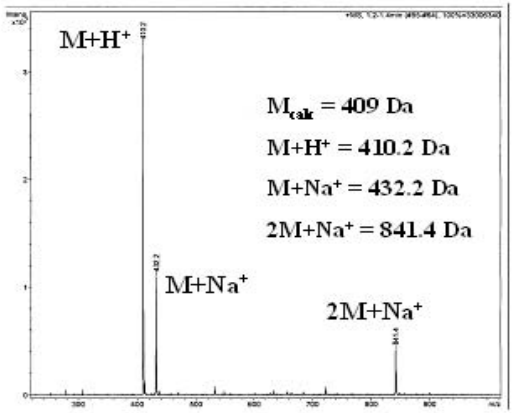
Piv-^{L}Pro-^{D}Pro-^{L}Val-OMe (15)



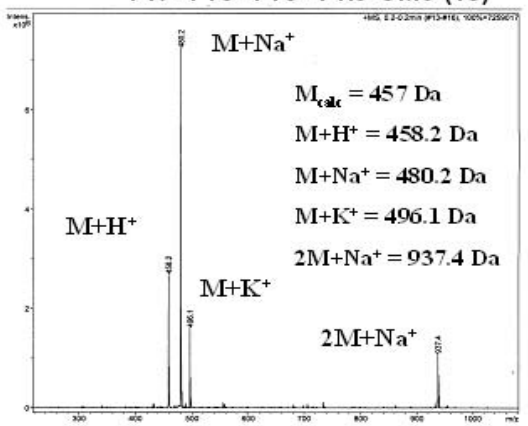
Piv-^{L}Pro-^{L}Pro-^{L}Ala-OMe (16)

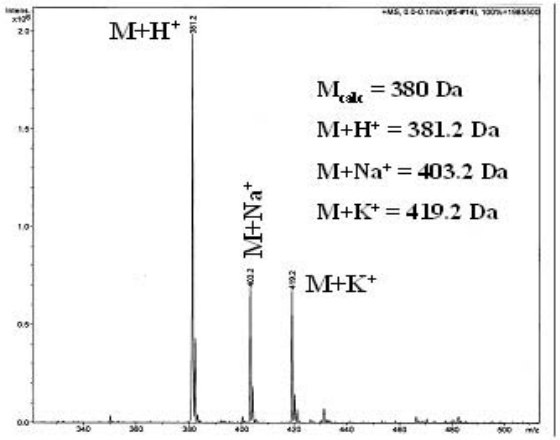
Figure S5.

Piv-L-Pro-L-Pro-L-Val-OMe (17)

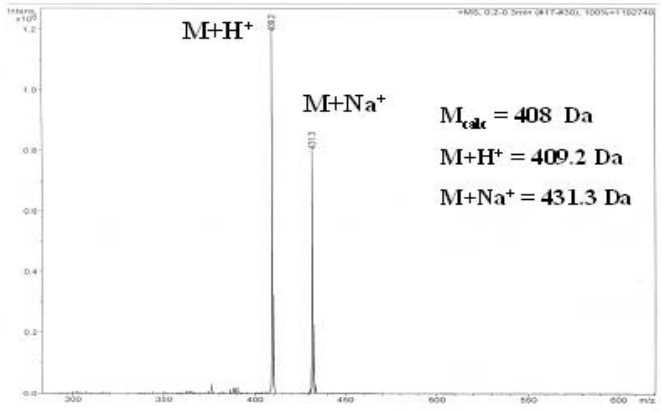


Piv-L-Pro-L-Pro-L-Phe-OMe (18)





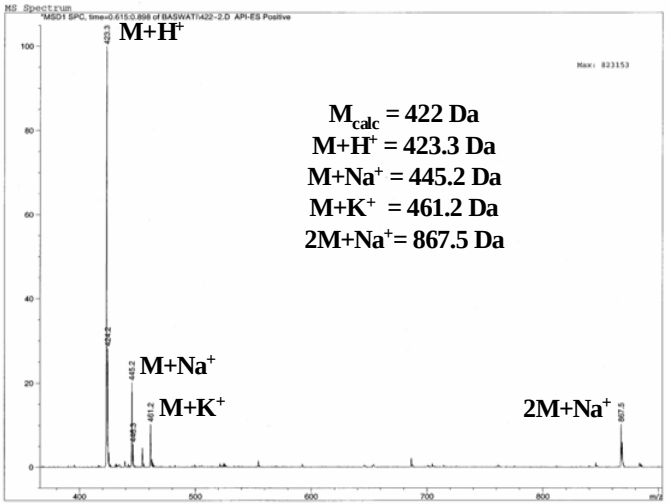
Piv-L-Pro-L-Pro-L-Ala-NHMe (19)



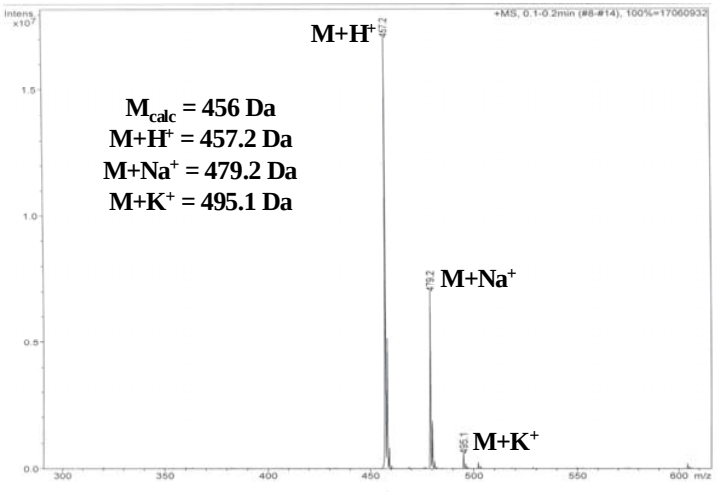
Piv-L-Pro-L-Pro-L-Val-NHMe (20)

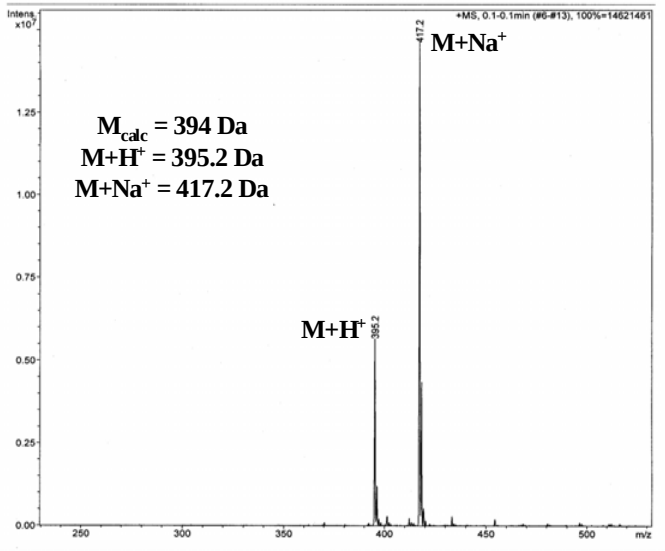
Figure S6.

Piv-^{L}Pro-^{L}Pro-^{L}Leu-NHMe (21)



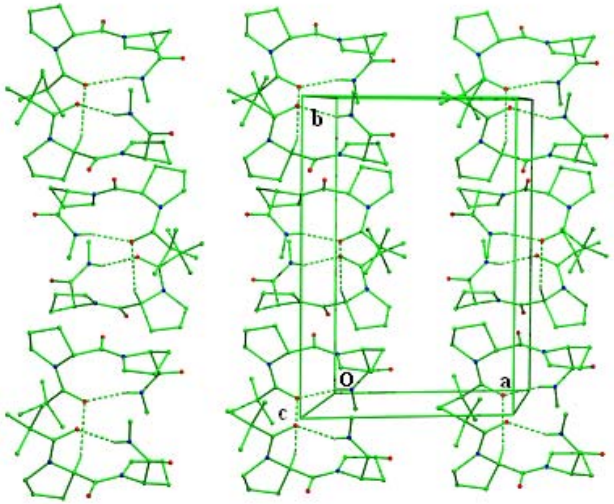
Piv-^{L}Pro-^{L}Pro-^{L}Phe-NHMe (22)



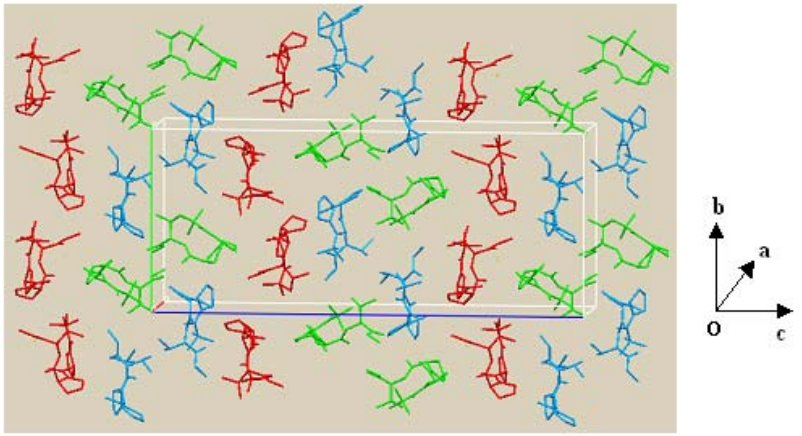


Piv-^{L}Pro-^{L}Pro-Aib-NHMe (23)

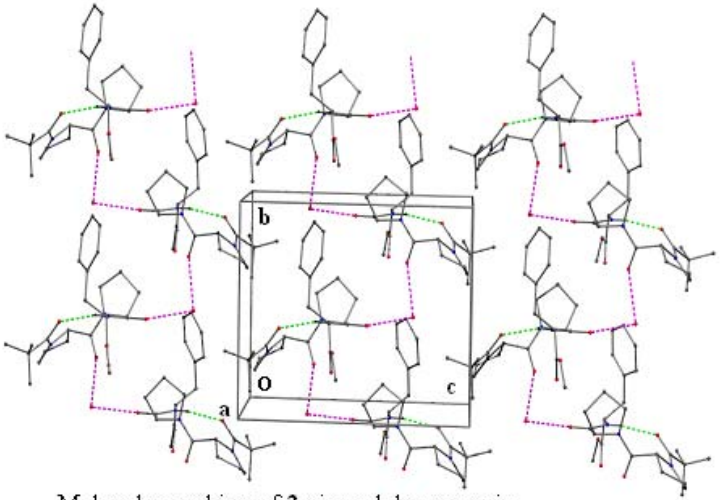
Figure S7.



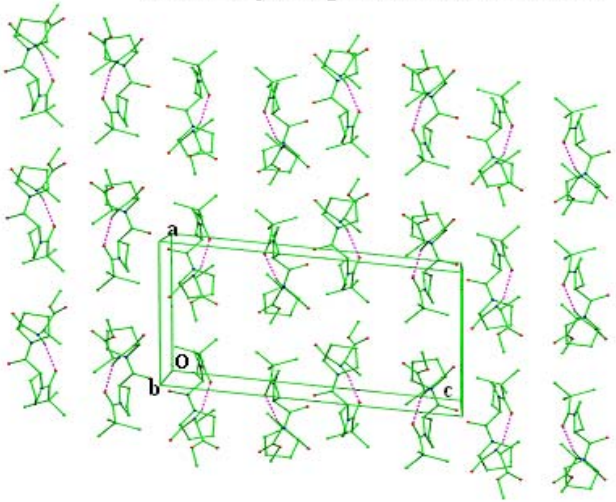
Molecular packing of **1** viewed down c-axis



Molecular packing of **2** viewed down a-axis

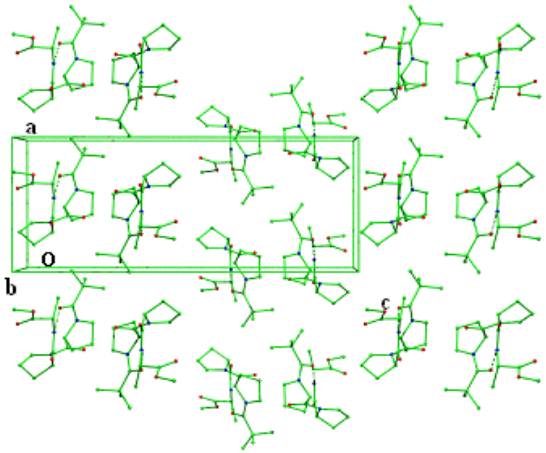


Molecular packing of **3** viewed down a-axis

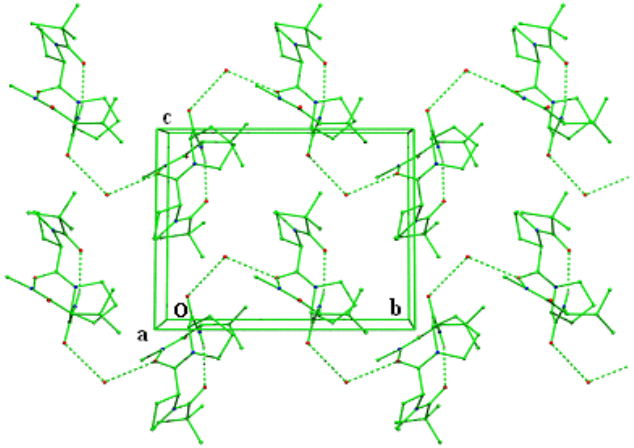


Molecular packing of **4** viewed down b-axis

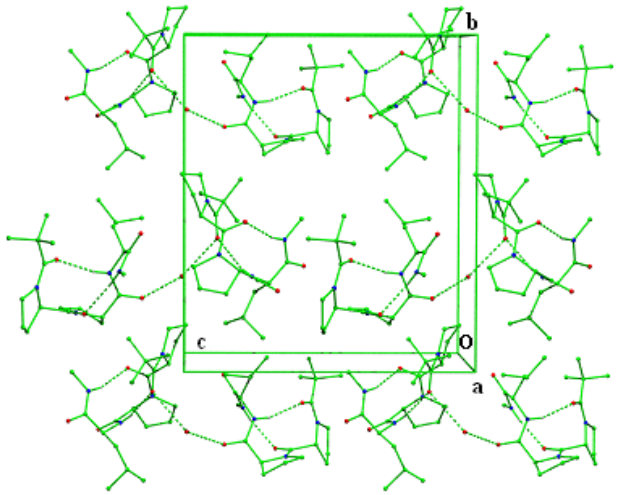
Figure S8.



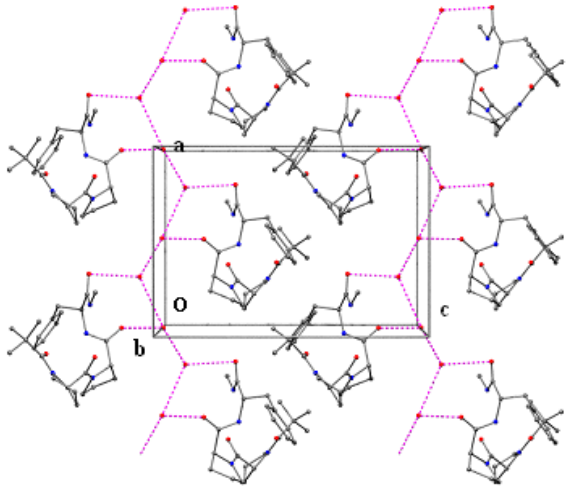
Molecular packing of **5** viewed down b-axis



Molecular packing of **6** viewed down a-axis

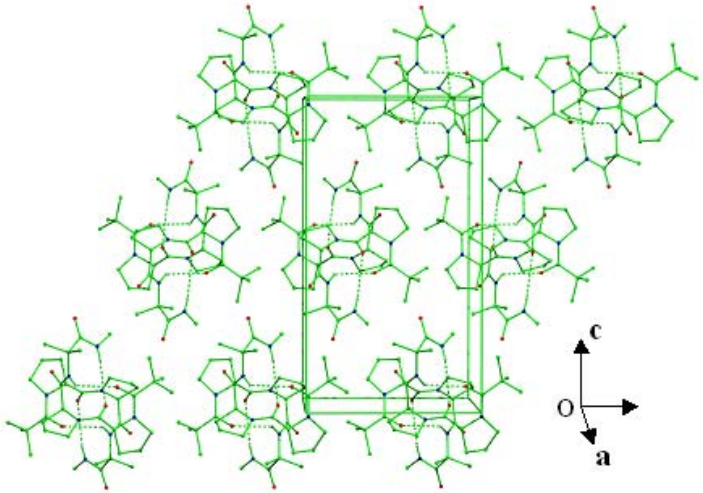


Molecular packing of 7 viewed down a-axis

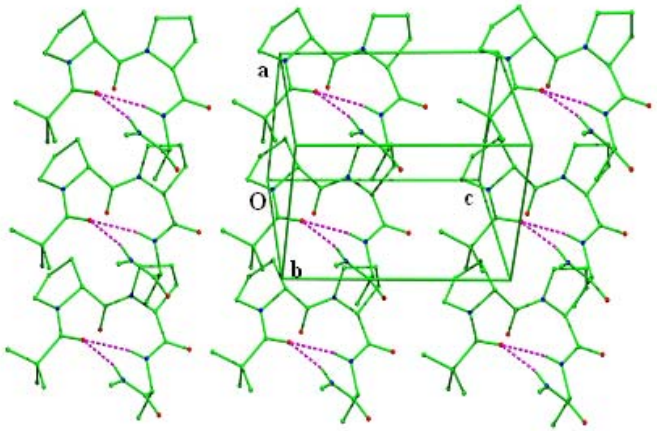


Molecular packing of **8** viewed down b-axis

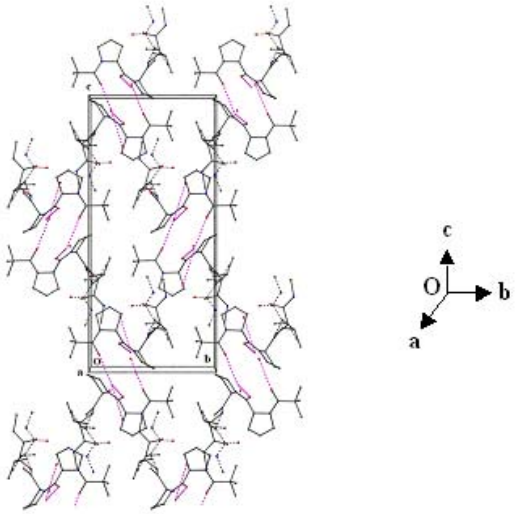
Figure S9.



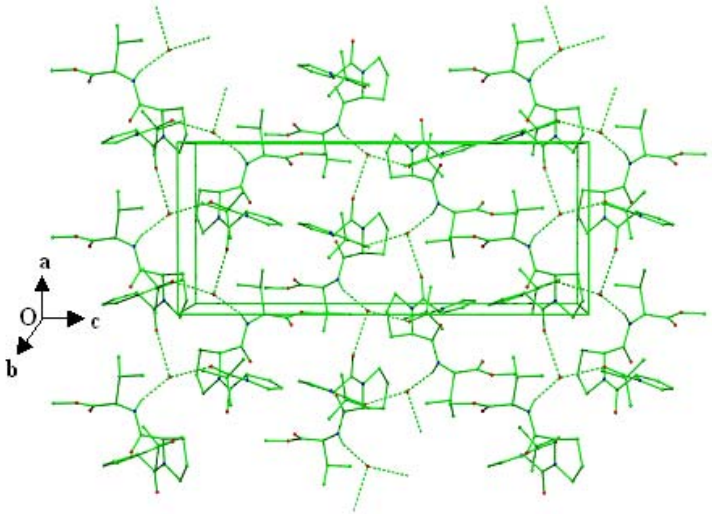
Molecular packing of **10** viewed down a-axis



Molecular packing of **11** viewed down b-axis

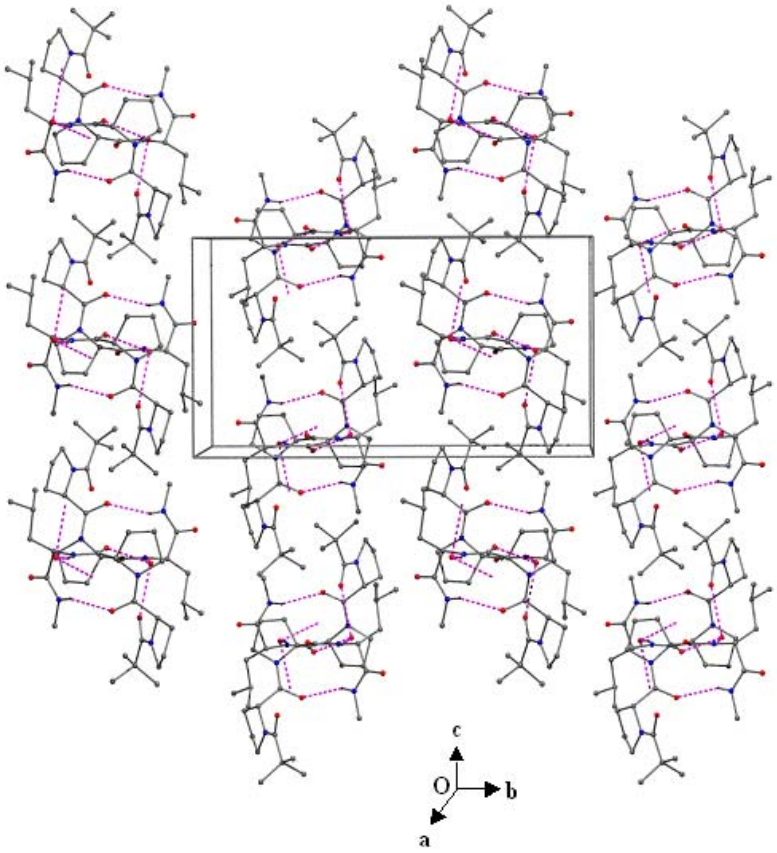


Molecular packing of **12** viewed down a-axis

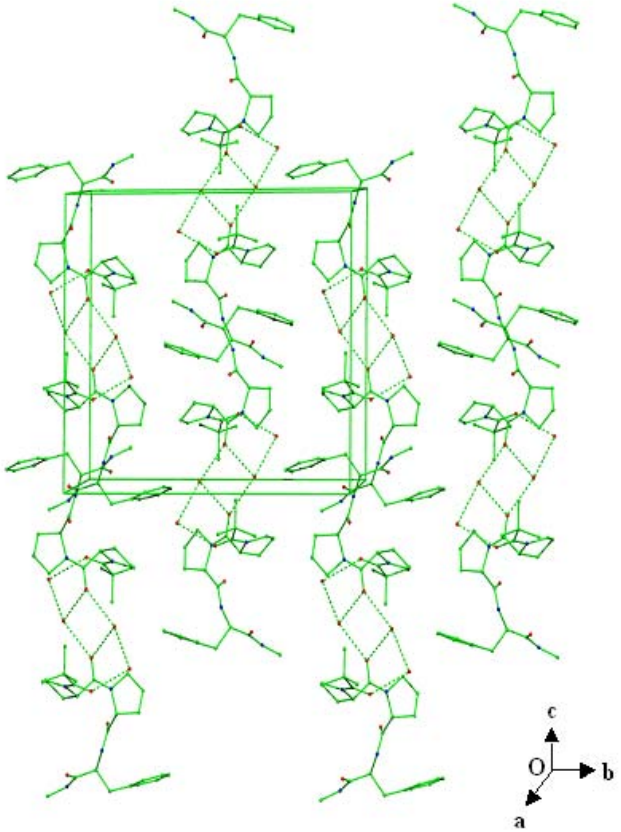


Molecular packing of **15** viewed down b-axis

Figure S10.

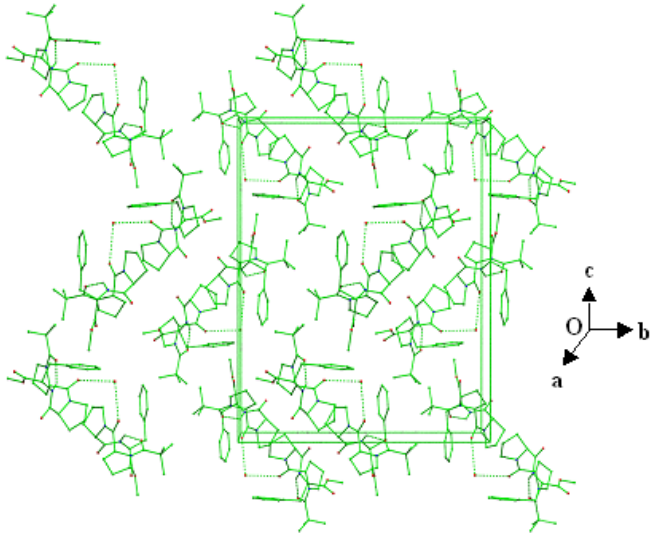


Molecular packing of **13** viewed down a-axis

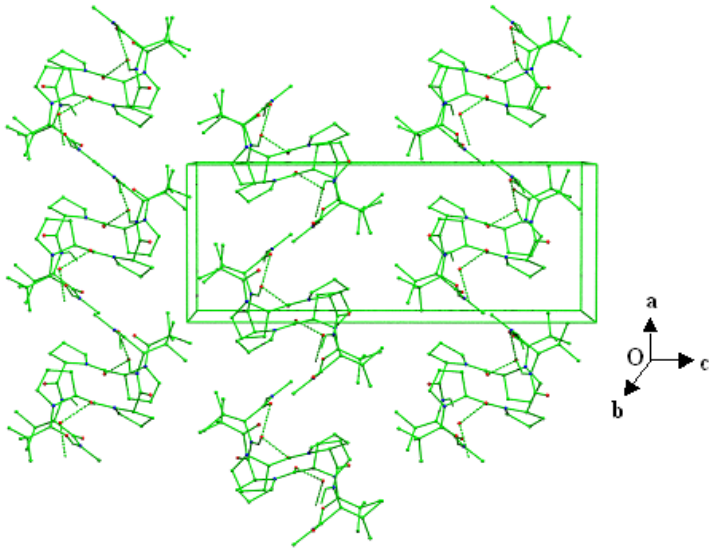


Molecular packing of **14** viewed down a-axis

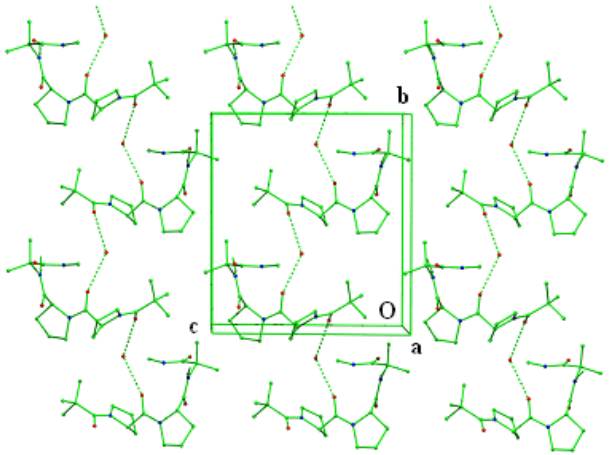
Figure S11.



Molecular packing of **18** viewed down a-axis



Molecular packing of **20** viewed down b-axis



Molecular packing of **23** viewed down a-axis