

Supporting Information

Analysis of Designed β -Hairpin Peptides: Molecular Conformation and Packing in Crystals†

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The list of the peptide sequences.

Boc-Leu-Phe-Val-^D**Pro**-^L**Pro**-Leu-Phe-Val-OMe (**1**)

Boc-Leu-Tyr-Val-^D**Pro**-^L**Pro**-Leu-Phe-Val-OMe (**2**, polymorphic forms labeled as **2a** and **2b**)

Boc-Leu-Val-Val-^D**Pro**-^L**Pro**-Leu-Val-Val-OMe (**3**)

Boc-Leu-Phe-Val-^D**Pro**-**Aib**-Leu-Phe-Val-OMe (**4**, polymorphic forms labeled as **4a** and **4b**)

Boc-Leu-Phe-Val-^D**Pro**-**Ac₆C**-Leu-Phe-Val-OMe (**5**)

Boc-Leu-Phe-Val-^D**Pro**-**Ala**-Leu-Phe-Val-OMe (**6**)

Table S1. Main Chain Conformation (deg) of the amino acid residues in Peptides **1-3**.

Residue	Torsion	1		2a		2b		3	
		Mol A	Mol B	Mol A	Mol B	Mol A	Mol B	Mol A	Mol B
Leu(1)	ϕ	-133.4	-117.2	-124.6	-120.9	-134.9	-127.3	-104.9	-95.7
	ψ	132.3	124.7	136.6	135.8	133.3	122.3	-58.3	-61.9
	ω	-171.9	-173.0	-166.9	173.7	-172.0	-167.6	-174.8	-176.1
Phe(2)/ Tyr(2)/ Val(2)	ϕ	-137.3	-130.2	-130.3	-131.6	-138.9	-130.4	-121.4	-122.7
	ψ	143.9	145.5	143.3	133.3	149.2	144.8	110.4	127.6
	ω	162.7	164.0	160.3	166.5	164.1	161.7	-172.3	-177.1
Val(3)	ϕ	-111.2	-111.5	-116.1	-99.3	-112.8	-108.7	-121.4	-126.5
	ψ	94.0	94.7	99.0	74.5	94.4	93.3	99.5	82.9
	ω	-173.3	-165.7	-174.7	-166.7	-174.4	-165.4	-165.7	-171.0
^D Pro(4)	ϕ	59.2	51.2	58.3	65.7	56.3	50.1	55.6	66.5
	ψ	-125.6	-126.4	-136.4	-122.3	-129.8	-124.4	-134.9	-135.7
	ω	-178.4	-178.7	-177.8	176.0	178.2	177.5	-178.1	-179.4
Pro(5)	ϕ	-82.9	-77.9	-77.7	-81.3	-77.5	-79.0	-82.9	-80.2
	ψ	-6.1	-14.8	-2.3	-13.3	-6.7	-12.2	-2.5	-7.3
	ω	-176.0	-177.6	-177.4	-174.9	-178.8	176.2	177.9	-177.4
Leu(6)	ϕ	-85.7	-78.7	-89.9	-88.0	-79.9	-81.6	-81.9	-86.6
	ψ	117.8	120.1	125.1	121.6	119.6	114.9	134.0	134.5
	ω	174.5	175.9	172.7	-174.4	170.7	179.4	174.9	176.0
Phe(7)/ Val(7)	ϕ	-84.2	-83.2	-79.7	-85.8	-89.1	-80.2	-108.6	-123.0
	ψ	117.8	129.0	140.8	121.0	129.5	123.7	113.9	125.1
	ω	-169.0	-175.6	-171.3	174.3	-166.6	-170.2	-174.1	-179.9
Val(8)	ϕ	-125.4	-125.5	-111.0	-131.5	-134.1	-131.7	-89.4	-88.8
	ψ	171.1	-3.3	-25.5	-177.0	170.6	18.2	137.7	145.6
	ω	176.5	176.5	143.5	-173.3	-176.6	175.7	167.7	178.1

The standard deviation in torsion angles are ~ 0.8 deg, 0.9 deg, 1.2 deg and 1.0 deg for peptides **1**, **2a**, **2b** and **3** respectively.

Table S2. Main Chain Conformation (deg) of the amino acid residues in Peptides **4-6**.

Residue	Torsion	4a		4b		5		6	
		Mol A	Mol B	Mol A	Mol B	Mol A	Mol B	Mol A	Mol B
Leu(1)	ϕ	-126.2	-137.2	-118.4	-129.9	-122.4	-124.0	-79.0	-160.5
	ψ	129.9	132.2	132.2	136.5	129.4	148.4	149.4	160.5
	ω	180.0	-174.5	-174.7	-173.6	-168.0	-173.3	-163.6	-178.7
Phe(2)	ϕ	-124.4	-129.8	-123.8	-132.4	-129.0	-132.1	-128.4	-117.2
	ψ	143.9	142.1	143.0	142.4	148.9	143.7	130.7	143.7
	ω	168.5	171.7	166.1	163.7	164.2	169.1	-176.6	165.9
Val(3)	ϕ	-112.0	-112.3	-113.0	-111.1	-122.9	-115.0	-129.7	-109.1
	ψ	96.8	91.1	95.8	94.5	101.1	97.4	80.9	96.4
	ω	-166.8	-161.9	-165.9	-163.3	-163.9	-160.9	169.3	-168.2
^D Pro(4)	ϕ	60.5	58.3	53.3	51.8	58.9	55.6	84.6	57.1
	ψ	-139.7	-131.2	-139.0	-136.5	-138.7	-137.9	-73.5	-132.3
	ω	-176.1	-174.3	-175.1	-177.6	176.6	-178.6	175.8	178.8
Aib(5)/ Ac ₆ C(5)/ Ala(5)	ϕ	-74.8	-66.0	-64.9	-72.3	-70.1	-76.5	-138.3	-83.2
	ψ	-12.0	-18.0	-20.5	-9.2	-10.1	-8.3	-13.8	4.0
	ω	-176.0	-167.1	-172.8	-176.2	-170.0	179.1	-175.6	-179.5
Leu(6)	ϕ	-79.9	-88.8	-77.9	-84.4	-93.0	-75.3	-96.0	-93.8
	ψ	119.1	120.2	120.3	124.1	125.2	119.2	145.7	125.8
	ω	171.6	178.4	174.7	178.0	-176.7	171.6	171.3	178.8
Phe(7)	ϕ	-82.2	-86.8	-82.8	-85.5	-88.6	-78.7	-107.2	-89.7
	ψ	129.5	121.3	128.8	119.3	122.6	117.9	129.0	131.2
	ω	-174.2	-176.4	-177.4	-178.0	-176.8	-174.9	-177.8	-179.3
Val(8)	ϕ	-113.1	-125.7	-113.1	-121.3	-127.6	-92.0	-133.9	-108.3
	ψ	-58.7	4.1	-60.2	0.9	5.6	-63.6	175.2	116.1
	ω	170.9	178.9	175.4	177.6	179.7	177.8	-175.1	178.9

The standard deviation in torsion angles are ~ 1.0 deg, 0.9 deg, 1.2 deg and 1.2 deg for peptides **4a**, **4b**, **5** and **6** respectively.

Table S3. Side Chain Conformation (deg) of the amino acid residues in Peptides **1-3**.

Residue	Torsion	1		2a		2b		3	
		Mol A	Mol B	Mol A	Mol B	Mol A	Mol B	Mol A	Mol B
Leu(1)	χ^1	-175.0	-164.2	176.4	-71.6	-176.9	-158.0	-70.9	173.8
	χ^2	63.2,	67.3,	87.3,	64.4,	-171.8,	158.0,	-92.5,	71.2,
		179.9	171.9	-163.5	176.6	69.8	35.6	174.5	166.5
Phe(2)/ Tyr(2)/ Val(2)	χ^1	-68.5	-70.9	-70.9	-57.7	-57.8	-76.8	-50.1,	-172.8,
								-172.4	62.1
Val(3)	χ^2	84.8,	88.8,	84.3,	81.8,	-98.4,	98.3,		
		-94.0	-88.6	-97.7	-100.8	75.6	-82.4		
	χ^1	-62.8,	-58.0,	-40.4,	-41.9,	-60.6,	-57.6,	-55.6,	-47.5,
^D Pro(4)		-179.6	174.5	-178.4	180.0	177.2	-177.6	-178.2	-176.1
	χ^1	22.5	18.0	14.3	11.7	27.0	19.4	12.5	-39.1
	χ^2	-35.4	-33.7	-26.9	-28.8	-42.1	-37.2	-24.5	50.8
	χ^3	33.2	35.7	30.2	31.9	38.4	39.1	23.1	-39.1
	χ^4	-20.2	-25.4	-20.4	-21.2	-21.7	-27.6	-17.3	13.8
	θ	-1.0	4.2	5.1	5.7	-3.2	7.3	5.0	15.5
	χ^1	35.9	31.3	32.4	33.7	32.4	34.9	50.7	-2.8
Pro(5)/ Aib(5)/	χ^2	-41.0	-34.4	-37.6	-42.8	-36.2	-37.6	-51.8	14.0
	χ^3	28.6	24.0	26.3	31.0	24.7	25.6	28.6	-19.4
	χ^4	-4.6	-3.7	-4.3	-11.0	-2.9	-0.8	1.0	18.4
	θ	-19.7	-16.8	-16.8	-11.1	-18.1	-21.5	-29.9	-11.2
	χ^1	-66.3	180.0	-176.0	-171.8	-67.2	-173.2	166.5	158.1
Leu(6)	χ^2	-62.9,	-166.0,	178.5,	-159.9,	-52.2,	-171.6,	-178.1,	-178.7,
		178.5	74.7	49.1	74.5	177.8	71.4	79.0	70.5
	χ^1	-174.8	178.9	-171.6	-174.9	-175.6	-179.7	-44.4,	-63.4,
Phe(7)/ Val(7)								169.4	-178.4
	χ^2	42.2,	78.0,	62.7,	36.1,	-139.7,	81.6,		
Val(8)		-145.0	-103.7	-98.8	-139.7	36.5	-97.5		
	χ^1	59.8,	75.5,	-52.6,	66.9,	54.6,	66.8,	-56.8,	-67.6,
		-66.7	-78.7	176.1	-47.0	-69.2	-78.0	-179.3	174.1

The standard deviation in side chain torsion angles are ~ 0.8 deg, 0.9 deg, 1.2 deg and 1.0 deg for peptides **1**, **2a**, **2b** and **3** respectively

Table S4. Side Chain Conformation (deg) of the amino acid residues in Peptides **4-6**.

Residue	Torsion	4a		4b		5		6	
		Mol A	Mol B	Mol A	Mol B	Mol A	Mol B	Mol A	Mol B
Leu(1)	χ^1	-175.1	-118.2	-172.8	-64.0	-65.6	-67.1	-47.9	112.1
	χ^2	75.8, 154.6	-18.8, -175.6	65.6, -176.2	165.3, 64.9	160.2, -75.6	170.4, -74.3	-60.3, 175.4	0.4, 175.6
Phe(2)/ Val(2)	χ^1	-76.3	-66.8	-72.6	-68.5	-70.8	-65.5	178.5	-64.7
	χ^2	89.0, -96.6	76.5, -101.1	82.6, -95.1	-96.8, 82.3	-104.1, 76.8	-98.9, 78.4	55.3, -130.6	86.9, -96.7
Val(3)	χ^1	-61.6, 177.5	-62.2, 173.9	-59.6, 176.1	-59.8, 176.7	-173.2, -53.7	179.8, -57.6	-50.0, -175.4	-51.6, -173.4
	χ^1	22.9	13.7	22.1	14.9	12.9	8.3	-24.4	-12.1
^D Pro(4)	χ^2	-38.4	-31.2	-33.3	-33.3	-22.9	-21.6	36.7	16.0
	χ^3	34.1	34.2	31.6	37.7	22.6	25.5	-32.0	-12.3
	χ^4	-20.1	-26.4	-22.2	-29.4	-12.7	-19.8	14.6	3.7
	θ	-2.1	10.6	0.0	9.3	1.0	7.5	6.4	4.3
Leu(6)	χ^1	179.6	-171.8	177.3	-175.3	-60.8	170.9	-65.2	-170.2
	χ^2	-170.5, 63.9	-170.9, 67.5	-168.6, 69.4	-169.7, 71.3	175.1, -63.8	-174.6, 63.9	166.7, -87.4	-167.0, 87.3
Phe(7)/ Val(7)	χ^1	178.8	-176.8	177.9	-175.2	-174.6	-179.6	-64.0	-177.2
	χ^2	65.4, -114.3	48.4, -137.9	68.1, -116.6	49.9, -141.8	39.5, -144.8	60.6, -121.3	90.9, -88.9	68.7, -106.1
Val(8)	χ^1	-57.6, -176.4	59.2, -64.0	62.2, -73.0	62.8, -64.0	67.4, -58.2	177.0, -59.0	64.5, -65.2	-58.8, 178.9

The standard deviation in side chain torsion angles are ~ 1.0 deg, 0.9 deg, 1.2 deg and 1.2 deg for peptides **4a**, **4b**, **5** and **6** respectively

Table S5. Hydrogen bond parameters in Peptides **1**, **2a** and **2b**.

Donor (D)	Acceptor (A)	D⋯A (Å)			H⋯A (Å)			∠C=D⋯H (deg)			∠C=D⋯A (deg)			∠A⋯H-D (deg)		
		1	2a	2b	1	2a	2b	1	2a	2b	1	2a	2b	1	2a	2b
Intramolecular																
N13	O16	2.901	2.869	2.913	2.079	2.027	2.077	152.8	152.9	158.0	154.2	153.9	159.6	159.6	165.9	164.0
N16	O13	2.969	2.958	2.964	2.148	2.133	2.146	133.5	136.0	137.6	131.2	132.4	133.1	159.4	160.8	158.8
N18	O11	2.878	2.809	2.898	2.019	2.031	2.045	151.5	161.2	152.4	152.4	154.1	152.5	176.7	150.1	171.3
N23	O26	2.796	2.937	2.792	1.956	2.118	1.947	150.0	146.1	154.9	151.6	144.7	154.2	165.1	159.0	167.3
N26	O23	2.957	3.021	2.953	2.175	2.201	2.172	137.6	135.6	138.2	131.3	130.8	133.8	150.9	159.5	150.9
N28	O21	2.931	2.976	2.898	2.075	2.133	2.057	152.3	143.4	157.2	152.1	146.8	156.8	173.4	166.3	165.6
Intermolecular																
N12	O22	2.897	2.907	2.885	2.133	2.127	2.128	147.0	152.9	145.3	155.3	160.0	153.7	147.9	150.7	146.6
N22	O12	2.928	2.939	2.904	2.109	2.111	2.083	147.5	152.4	151.5	153.0	156.7	157.4	158.9	161.4	159.4
N27	O17 ^a	2.816		2.838	1.972		2.006	173.0		169.8	174.2		175.1	166.8		162.2
N17	O27 ^b		2.903			2.069			170.6			168.1			163.2	
Peptide-Solvent/Solvent-solvent																
O25	O1W	2.741		2.637							151.2		153.9			
N17 ^a	O1W	3.052									169.9					
O15 ^a	O1W	3.339		2.982							126.6		138.2			
O15	O2W ^b		2.665									167.3				
O1T	O1W		3.107													
O1T	O2W ^c			2.705												
O2T	O3W		3.030	3.005												
N27	O2W		3.022			2.166									174.5	
O1W	O2W		2.792													
O24	O2W			2.783									123.2			
O1W	O3W			3.035												

^a symmetry related by (x, y+1, z); ^b symmetry related by (1+x, y, z); ^c symmetry-related by (-x, 1/2+y, 1-z).

Table S6. Hydrogen bond parameters in Peptides **3**, **4a** and **4b**.

Donor (D)	Acceptor (A)	D...A (Å)			H...A (Å)			$\angle$ C=D...H (deg)			$\angle$ C=D...A (deg)			$\angle$ A...H-D (deg)		
		3	4a	4b	3	4a	4b	3	4a	4b	3	4a	4b	3	4a	4b
Intramolecular																
N13	O16	2.901	2.911	2.862	2.053	2.076	2.025	147.8	152.5	151.1	151.0	154.6	153.2	168.5	163.7	164.1
N16	O13	2.942	3.097	3.018	2.162	2.302	2.260	137.0	133.6	132.1	133.6	130.6	129.1	150.6	154.1	147.0
N18	O11	2.890	2.953	2.890	2.036	2.102	2.036	152.3	160.9	161.0	152.8	159.4	158.6	171.8	170.4	171.7
N23	O26	2.915	2.912	2.861	2.059	2.072	2.031	154.2	157.4	153.5	155.5	158.8	154.5	173.9	165.9	161.9
N26	O23	3.094	3.172	2.988	2.313	2.415	2.200	130.0	126.7	136.2	127.3	129.1	134.0	151.1	147.3	152.1
N28	O21	2.940	2.953	2.894	2.081	2.095	2.041	151.1	154.2	154.0	152.1	154.3	155.2	176.3	175.0	171.4
Intermolecular																
N12	O22		2.952	2.927		2.126	2.114		148.3	147.9		153.0	153.6		160.8	157.6
N22	O12		3.017	2.920		2.213	2.146		148.3	147.4		154.4	154.6		155.7	149.5
N17	O27 ^a		2.955	2.908		2.103	2.055		168.4	165.9		167.7	165.6		170.4	170.9
N11	O17 ^a	2.865			2.014			154.5			155.3			170.3		
N12	O17 ^a	3.207			2.362			140.8			144.0			167.7		
N17 ^a	O12	3.060			2.026			169.5			167.3			171.8		
N21	O27 ^b	2.942			2.120			145.6			150.9			160.2		
N22	O27 ^b	3.189			2.350			148.6			152.6			165.2		
N27 ^b	O22	3.156			2.302			156.2			158.4			171.6		
Peptide-Solvent/Solvent-solvent																
N15	O1S		2.829			2.003									160.9	
N25 ^c	O2S		3.026			2.194									162.8	
O15	O1w			2.725									155.3			
N27	O1w ^c			2.922			2.066									174.3
N27	O2w		2.993			2.138									173.0	
O24	O2w															
O25	O1w															
O2t	O3w															

^a symmetry related by (1+x, y, z); ^b symmetry related by (-1+x, y, z); ^c symmetry related by (1+x, y, 1+z).

Table S7. Hydrogen bond parameters in Peptides 5 and 6.

Donor (D)	Acceptor (A)	D...A (Å)		H...A (Å)		$\angle$ C=D...H (deg)		$\angle$ C=D...A (deg)		$\angle$ A...H-D (deg)	
		5	6	5	6	5	6	5	6	5	6
Intramolecular											
N11	O18		3.092		2.401		163.9		154.4		137.8
N13	O16	2.897	2.816	2.052	1.983	153.1	160.6	156.2	163.8	167.3	162.5
N15	O13		2.770		2.079		110.5		98.5		136.8
N16	O13	2.978	3.144	2.158	2.294	136.1	121.7	136.2	119.3	159.1	169.9
N18	O11	2.928	2.846	2.073	2.008	153.5	141.1	153.8	145.8	172.8	164.2
N23	O26	2.957	2.824	2.128	1.987	150.6	154.2	153.2	154.1	161.7	164.0
N26	O23	2.985	2.965	2.211	2.129	137.0	134.2	134.1	133.8	149.5	164.1
N28	O21	2.890	2.845	2.044	1.999	162.2	175.5	161.1	173.2	167.5	167.6
Intermolecular											
N12	O22	2.904	2.893	2.153	2.088	141.7	146.7	149.1	149.7	145.7	165.2
N22	O12	2.917	2.867	2.218	2.057	142.4	149.4	151.2	154.3	138.3	156.5
N27	O17 ^a	2.956	2.782	2.100	1.926	154.5	168.1	153.6	166.4	173.5	173.8
Peptide-Solvent/Solvent-solvent											
N17	O1W	3.002	2.953	2.148	2.094					172.3	178.0
N25	O2W	2.941	2.999	2.087	2.142					172.2	172.8
O2W	O18 ^b	2.964									
O3Wa *	O15	2.652									
O15	O1W		2.935						149.8		
O3W *	O17	3.132									
O1W	O3Wa *	2.798									
O1W	O25 ^{c, d}	2.865	2.783						147.9		
O2W	O27 ^e	3.040	2.934						133.0		
O2W	O28 ^e	3.145									
O3W *	O25 ^f	2.856									

^a symmetry related by (x+1, y, z); ^b symmetry related by (-x+1, y+1/2, -z+1/2); ^c symmetry related by (x-1, y, z); ^d symmetry related by (-x, 1/2+y, 3/2-z); ^e symmetry related by (-x+2, y+1/2, -z+1/2); ^f symmetry related by (x-1, y, z). * O3w in 5 is disordered over two positions (O3w and O3wa with occupancy of 0.42 and 0.58 respectively)

Table S8. Twist of the individual hairpin molecules in the peptides **1-6** and the angle between the two molecules in the asymmetric unit.

Peptide	Twist of the β -strands in the β -hairpin molecules (deg)		Angle between the β -hairpin molecules in the asymmetric unit (deg)
	Molecule A	Molecule B	
1	-11.58	-13.45	73.47
2a	-18.18	-10.56	76.88
2b	-9.78	-14.36	74.44
3	-19.74	-15.15	37.17
4a	-17.47	-10.51	68.59
4b	-15.13	-17.92	66.34
5	-19.62	-21.38	51.84
6	-18.40	-26.76	85.83

Table S9. Aromatic-aromatic interactions observed in the peptides **1-6**.^a

Peptide	Molecule	R _{cen} (Å)	R _{clo} (Å)	γ (deg)	Geometry
1	A	4.975	3.475	66.33	T-shaped
	B	5.431	3.661	22.69	Inclined
2a	A	5.498	3.851	72.74	T-shaped
	B	5.009	3.464	28.72	Inclined
2b	A	4.898	3.475	20.15	Inclined
	B	5.563	3.942	71.88	T-shaped
4a	A	5.391	3.751	58.22	T-shaped
	B	5.227	3.695	35.39	Inclined
4b	A	5.317	3.823	55.08	T-shaped
	B	5.045	3.699	33.08	Inclined
5	A	5.042	3.641	26.77	Inclined
	B	5.177	3.529	46.87	T-shaped
6	A	4.765	3.553	24.62	Inclined
	B	5.129	3.721	61.29	T-shaped

^aFor definition of R_{cen}, R_{clo}, and γ see reference: S. Aravinda, N. Shamala, C. Das, A. Sriranjini, I. L. Karle and P. Balaram, *J. Am. Chem. Soc.*, 2003, **125**, 5308.

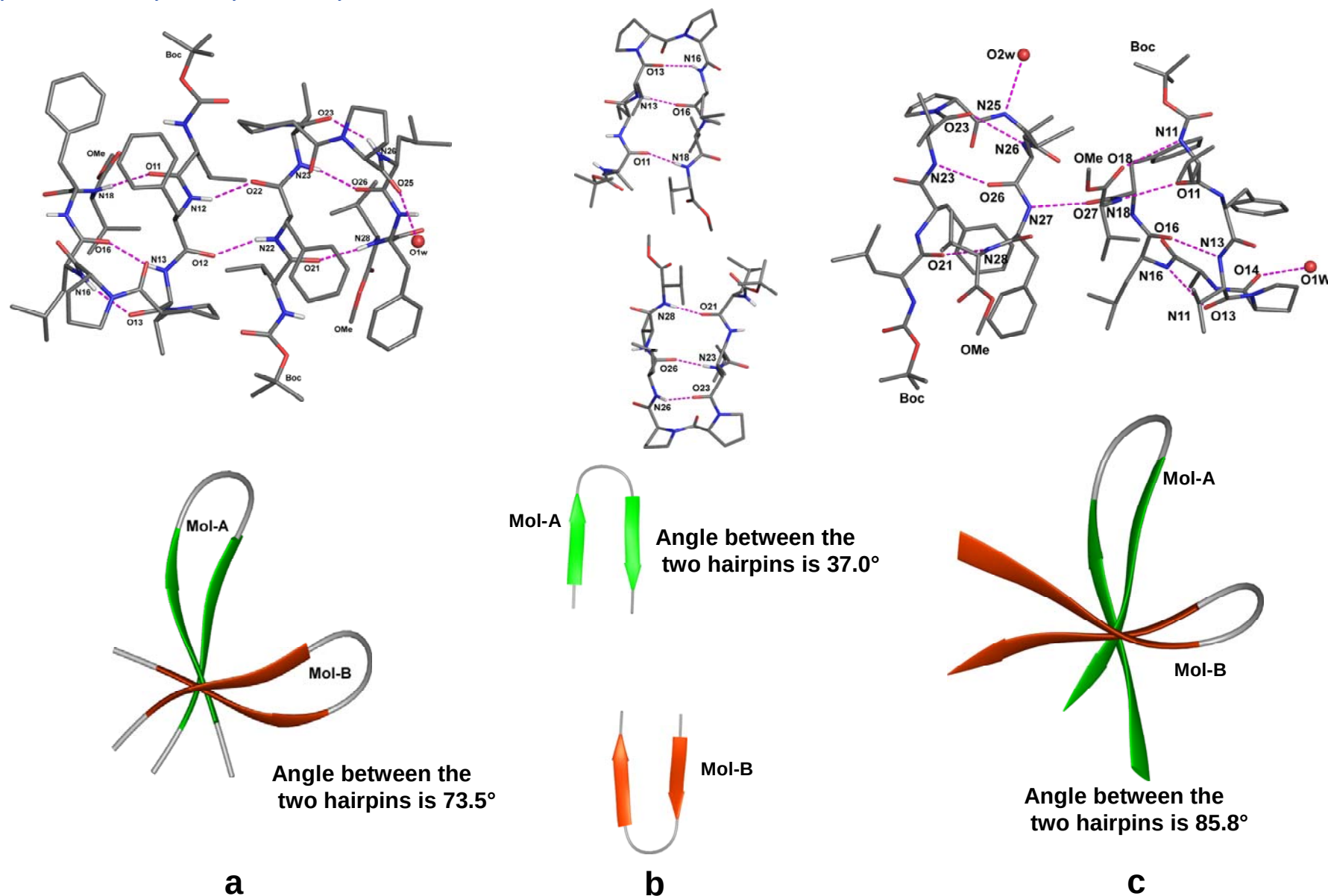


Figure S1. Asymmetric unit of the octapeptide (a) Boc-Leu-Phe-Val-^DPro-Pro-Leu-Phe-Val-OMe (1), (b) Boc-Leu-Val-Val-^DPro-Pro-Leu-Val-Val-OMe (3) (c) Boc-Leu-Phe-Val-^DPro-Ala-Leu-Phe-Val-OMe (6). Top: Peptide molecules shown as sticks. Hydrogen bonds and solvent-peptide hydrogen bonds are shown as dashed lines (magenta). Bottom: Schematic showing the "orthogonal" packing of the sheets, resulting in a "ribbon" structure. Molecule A in green and Molecule B in orange.

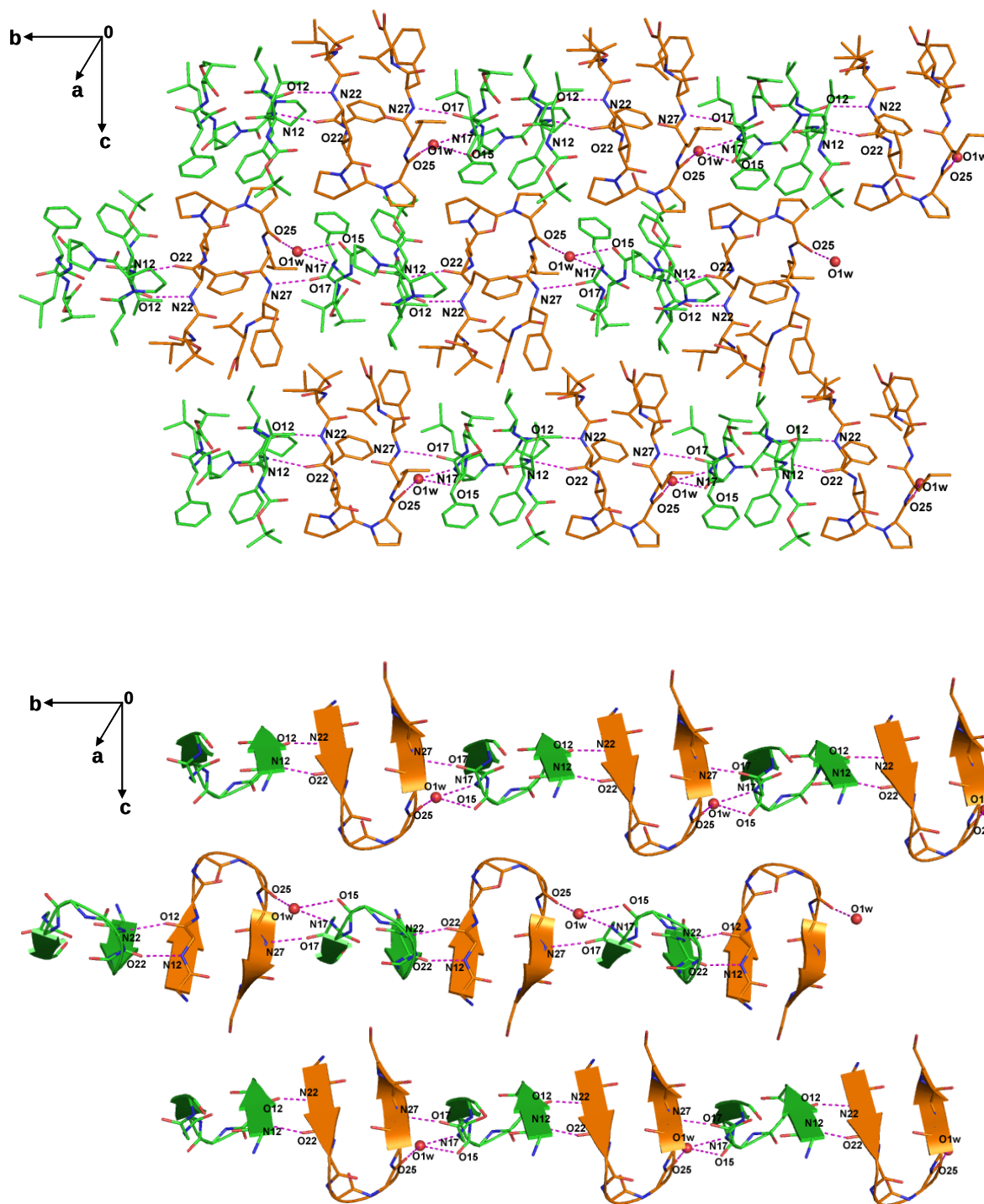


Figure S2. Molecular packing of the octapeptide Boc-Leu-Phe-Val-^DPro-Pro-Leu-Phe-Val-OMe (1). Top: Peptide molecules shown as sticks. Intermolecular hydrogen bonds and solvent-peptide hydrogen bonds are shown as dashed lines (magenta). Bottom: Schematic showing the “orthogonal” packing of the sheets, resulting in a “ribbon” structure. Molecule A in green and Molecule B in orange.

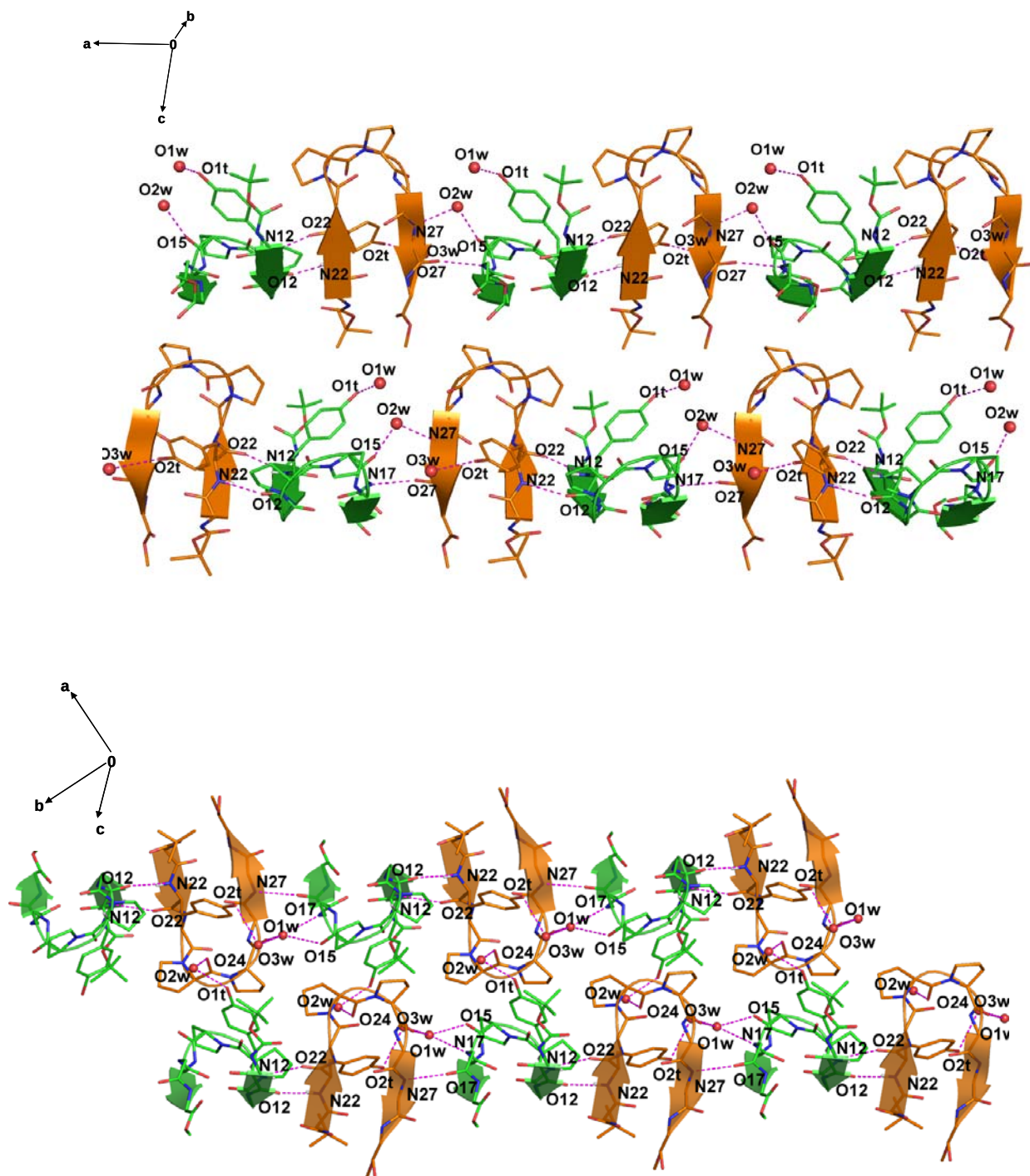


Figure S3 Comparison of the packing of molecules in the crystals of peptide Boc-Leu-Tyr-Val-^DPro-Leu-Phe-Val-OMe (2). **2a** (top) and **2b** (bottom). Backbone atoms have been shown for all the residues for ease of visualization, Boc, Tyr(2), OMe and β -turn residues have been shown as sticks. Molecule-A in green and Molecule-B in orange.

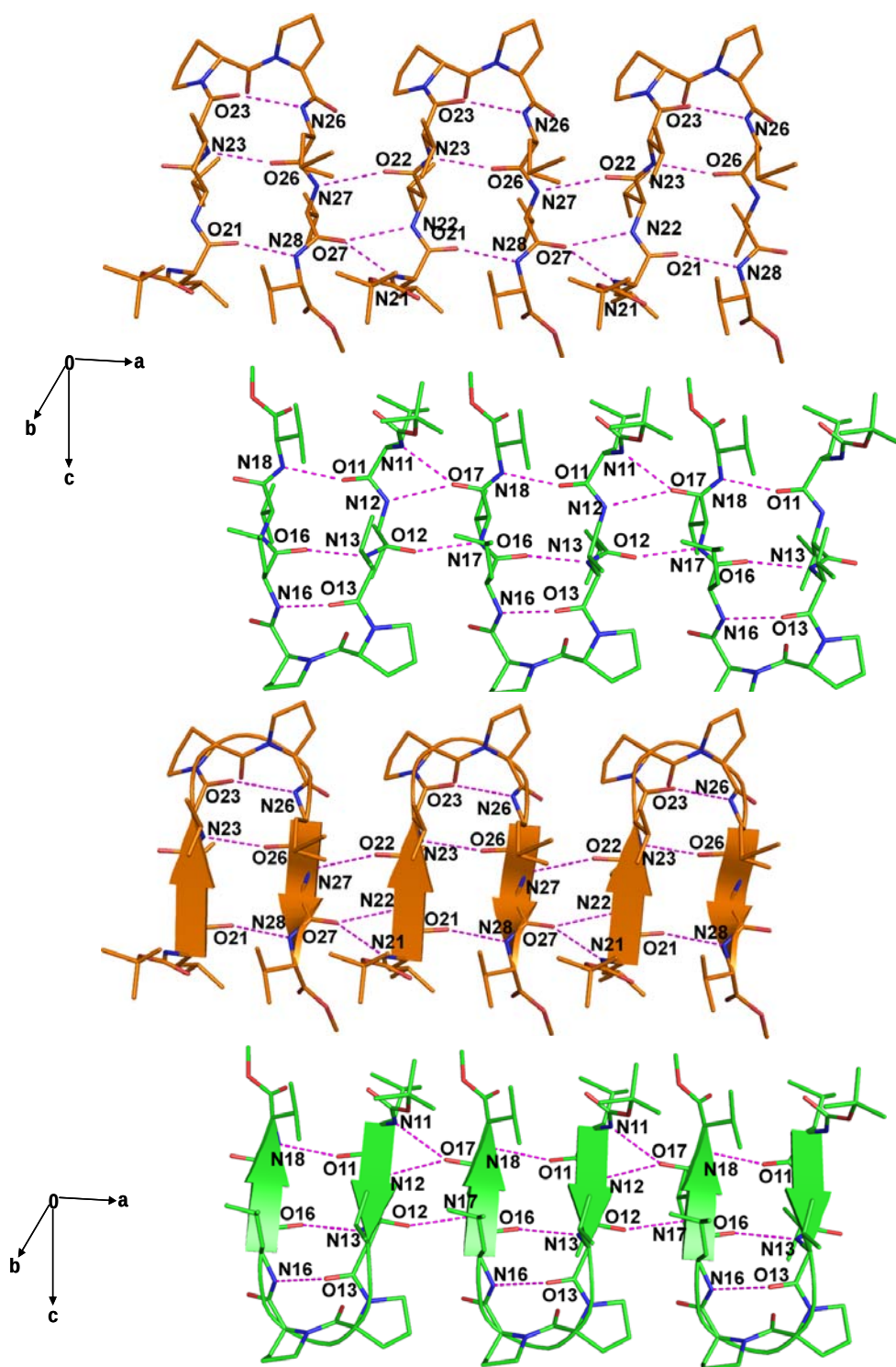


Figure S4 Molecular packing of the octapeptide Boc-Leu-Val-Val-^DPro-Pro-Leu-Val-Val-OMe (**3**). Top: All peptides are shown as sticks. Bottom: Schematic showing the propagation of separate sheets of the two molecules, by translation. Intramolecular and intermolecular hydrogen bonds are shown as dashed lines (magenta). Molecule A in green and Molecule B in orange.

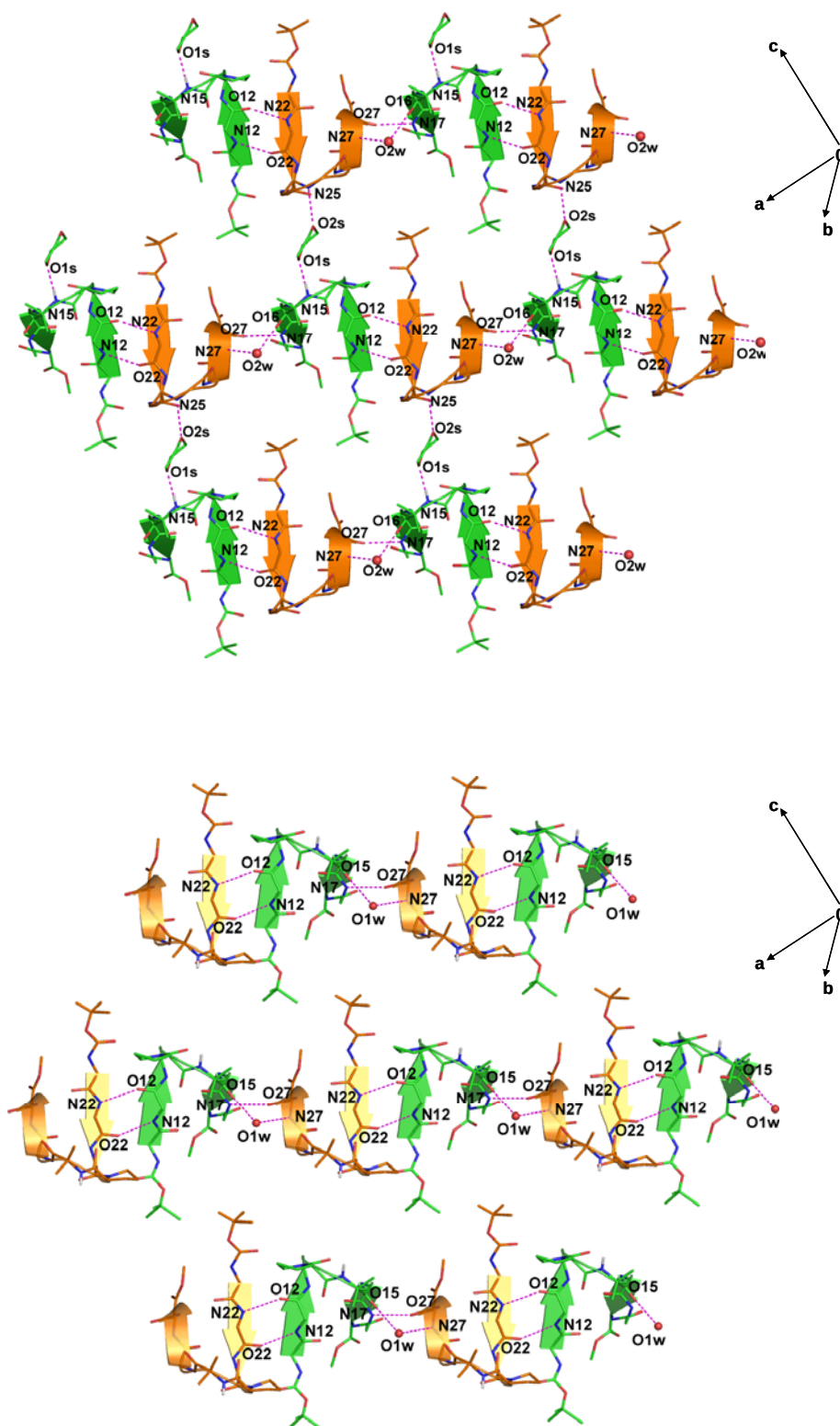
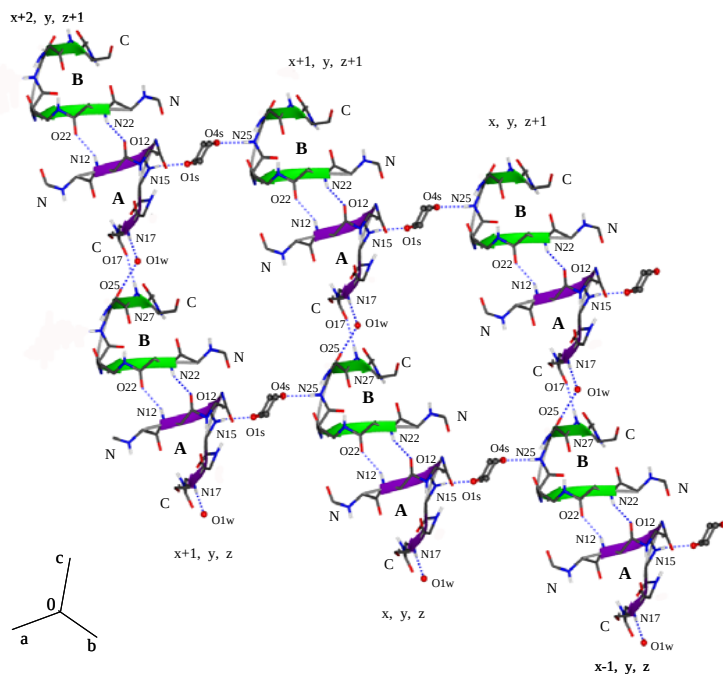
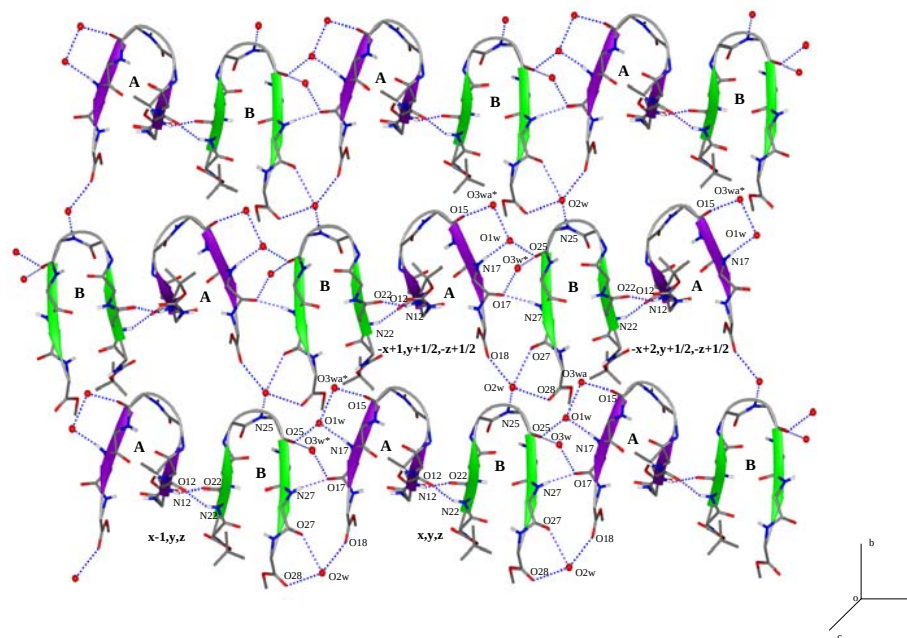


Figure S5. Comparison of the packing of molecules in the crystals of Boc-Leu-Phe-Val-^DPro-Aib-Leu-Phe-Val-OMe (**4**). **4a** (top) and **4b** (bottom). Backbone atoms have been shown for all the residues for ease of visualization, Boc, OMe and β -turn residues have been shown as sticks. Molecule-A in green and Molecule-B in orange.



a



b

Figure S6. Comparison of the packing of molecules in the crystals of Boc-Leu-Phe-Val-^DPro-Ac₆c-Leu-Phe-Val-OMe (**5**)
(a) In monoclinic form (Ref: Harini, V. V.; Aravinda, S.; Rai, R.; Shamala, N.; Balaram, P. *Chem. Eur. J.* **2005**, *11*, 3609)
(b) in orthorhombic form. Side chain atoms are omitted for clarity. Molecule-A in violet and Molecule-B in green

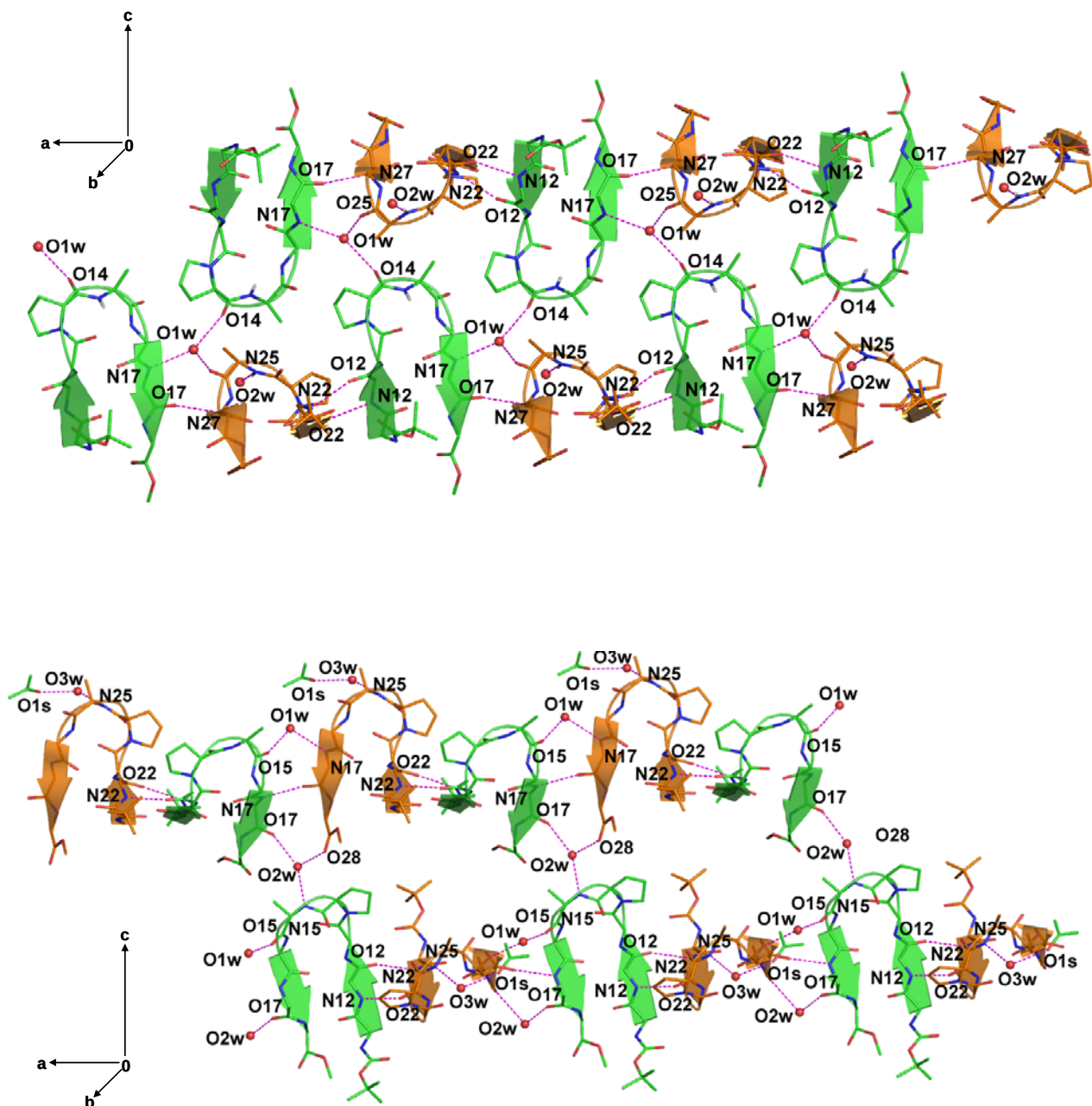


Figure S7. Comparison of the packing of molecules in the crystals of Boc-Leu-Phe-Val-^DPro-Ala-Leu-Phe-Val-OMe (**6**, top) and the polymorphs which determined earlier (bottom, Ref: Aravinda, S.; Harini, V. V.; Shamala, N.; Das, C.; Balaram, P. *Biochemistry* **2004**, 43, 1832). Backbone atoms have been shown for all the residues for ease of visualization, Boc, OMe and β -turn residues have been shown as sticks. Molecule-A in green and Molecule-B in orange.

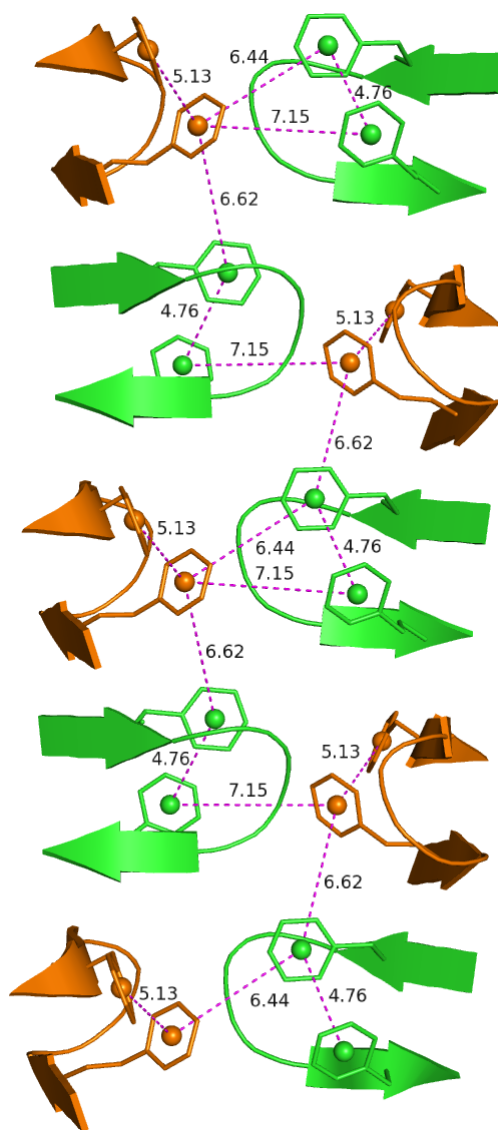


Figure S8. Schematic view of the ladder of aromatic (Phe-Phe) interactions observed in Boc-Leu-Phe-Val-^DPro-Ala-Leu-Phe-Val-OMe (**6**). Centroid to centroid distances (Å) between proximal aromatic rings are marked. Solvent and all the side chains, except Phe(2) and Phe(7) have been omitted for clarity. Molecule-A in green and Molecule-B in orange.

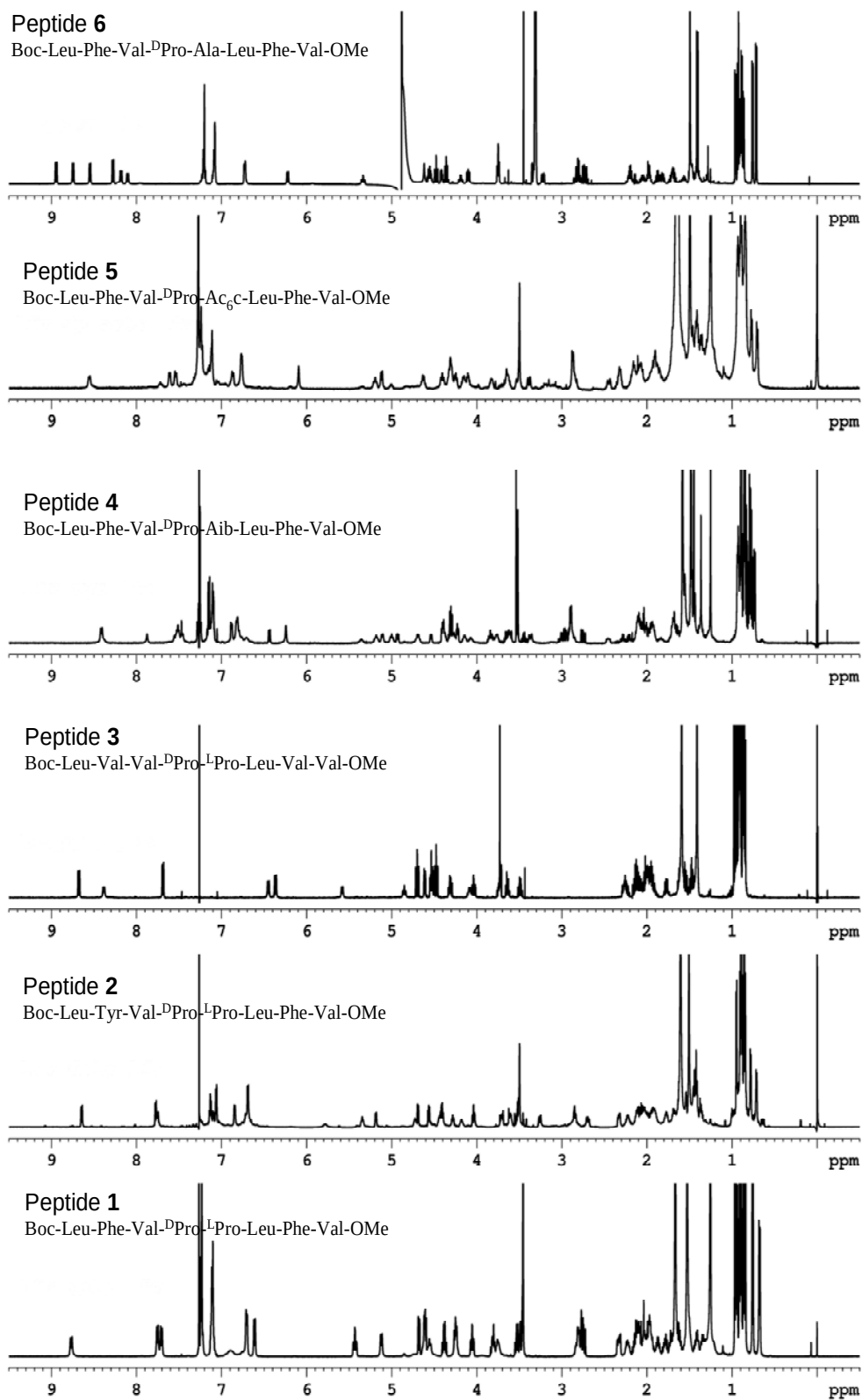


Figure S9: ¹H NMR spectra of peptides **1** to **6**. All the spectra recorded in CDCl₃ except peptide **6** which is recorded in MeOD

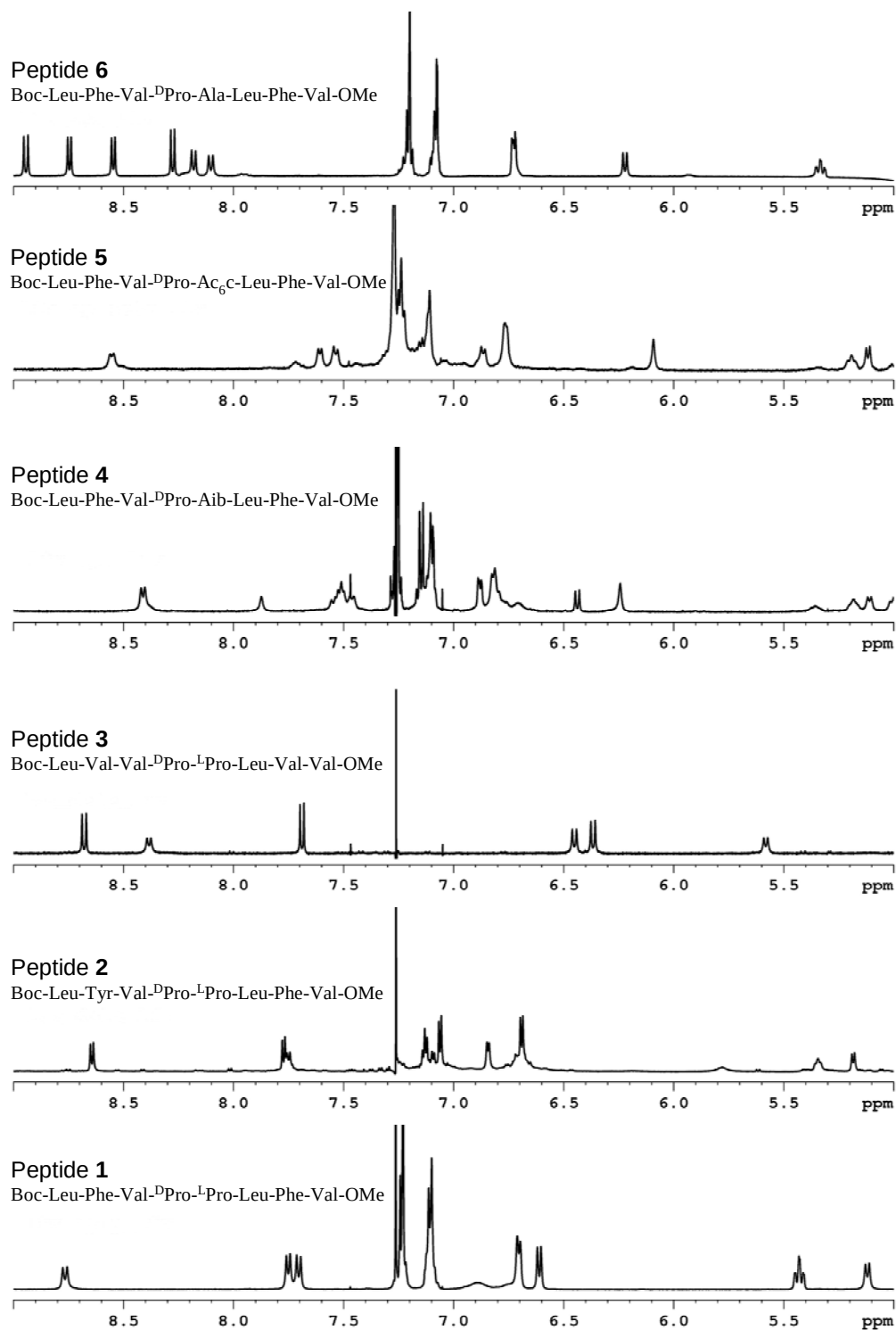


Figure S10: Expansion of NH region of peptides **1** to **6**. All the spectra recorded in CDCl₃ except peptide **6** which is recorded in MeOD