Electronic Supplementary Material (ESI) for RSC Advances.

ESI: In Silico Design of Mimosine Containing Peptides as New Efficient Chelators of Aluminum

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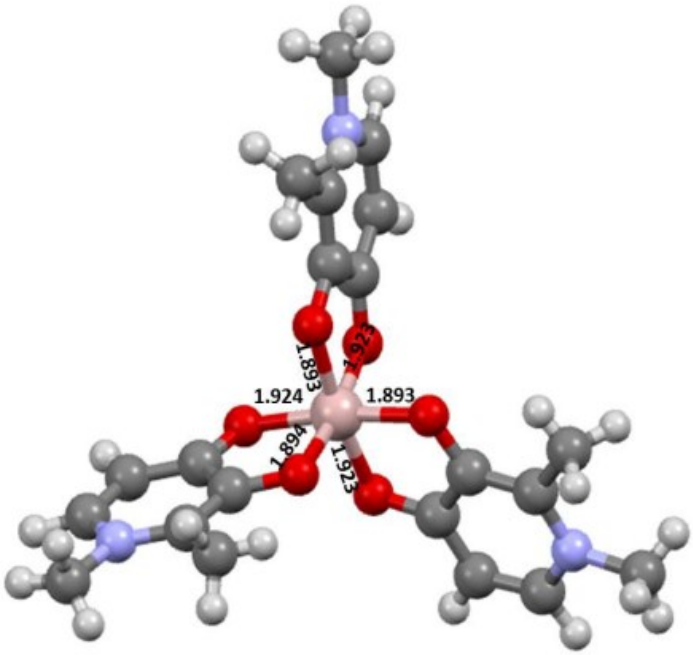

Figure S1. Crystal structure of Al(III)-DFP_3. Al-O distances (Å).

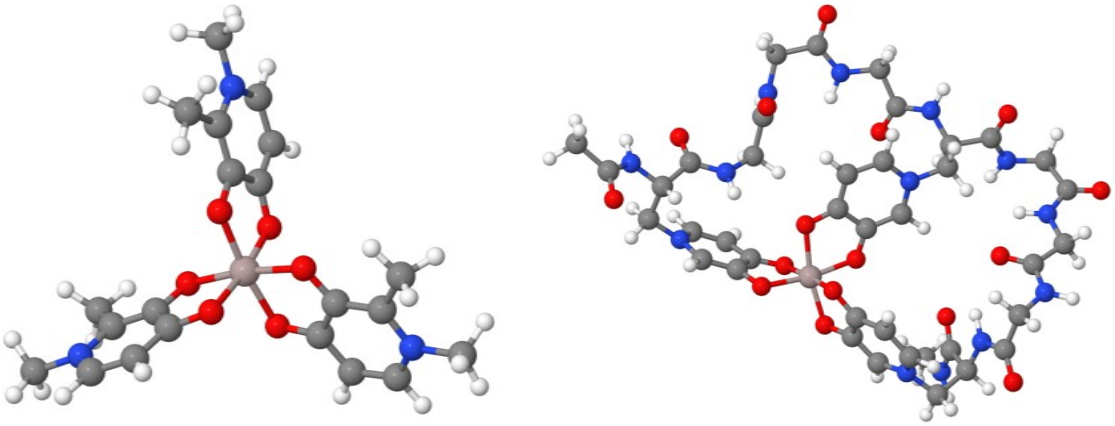

Figure S2. DFT structures of Al(III)-DFP_3 (left) and Al-$Pept^9_{3G}$ (right).

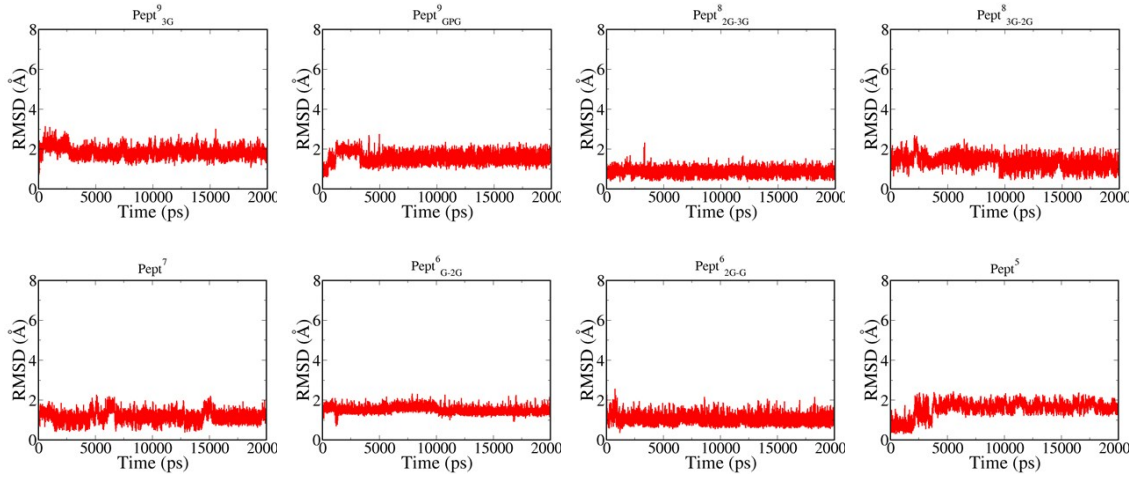

Figure S3. Root mean square deviations (RMSD, in Å) computed on the QM/MM MD simulations of the studied eight Al.Peptide complexes. From left to right, upper line: $Pept^{9}_{3G}$, $Pept^{9}_{GPG}$, $Pept^{8}_{2G\text{-}3G}$ and $Pept^{8}_{3G\text{-}2G}$; Bottom line: $Pept^{7}$, $Pept^{6}_{G\text{-}2G}$, $Pept^{6}_{2G\text{-}G}$ and $Pept^{5}$.

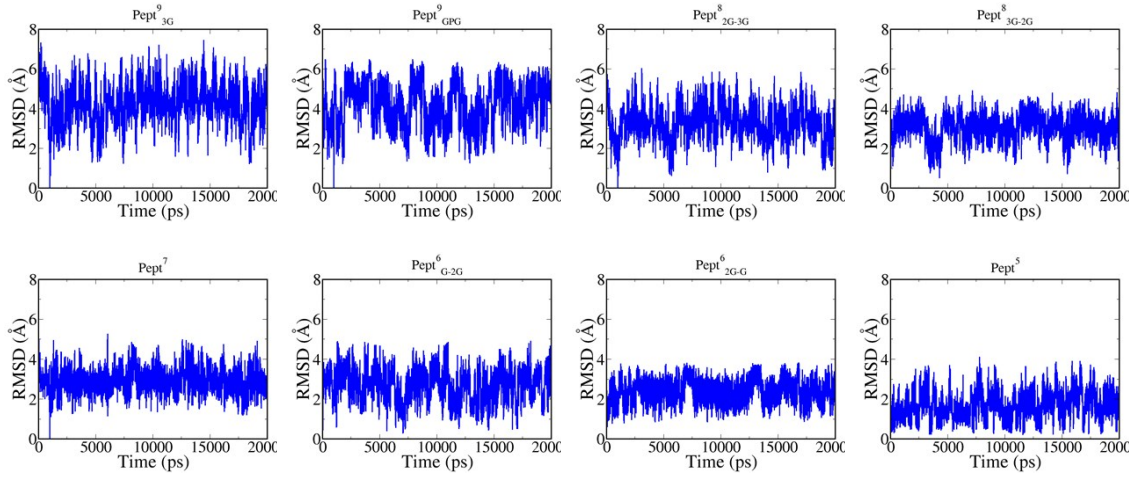

Figure S4. Root mean square deviations (RMSD, in Å) computed on the QM/MM MD simulations of the studied eight peptides in solution (their apoform). From left to right, upper line: $Pept^{9}_{3G}$, $Pept^{9}_{GPG}$, $Pept^{8}_{2G\text{-}3G}$ and $Pept^{8}_{3G\text{-}2G}$; Bottom line: $Pept^{7}$, $Pept^{6}_{G\text{-}2G}$, $Pept^{6}_{2G\text{-}G}$ and $Pept^{5}$.

			Al-DFP$_3$		Al-Pept$^9{}_{3G}$
			X-ray	DFT	DFT
Atom1	**Atom2**		**Distances**		
Al	$O_C{}^A$		1.924	1.951	1.943
Al	$O_H{}^A$		1.894	1.916	1.903
Al	$O_C{}^B$		1.923	1.946	1.990
Al	$O_H{}^B$		1.893	1.914	1.913
Al	$O_C{}^C$		1.923	1.945	1.954
Al	$O_H{}^C$		1.893	1.918	1.908
Atom1	**Atom2**	**Atom3**	**Angles**		
Al	$O_C{}^A$	$C_C{}^A$	112.22	112.18	109.76
Al	$O_{OH}{}^A$	$C_{OH}{}^A$	111.97	112.85	109.81
Al	$O_C{}^B$	$C_C{}^B$	112.19	111.77	110.20
Al	$O_{OH}{}^B$	$C_{OH}{}^B$	112.22	112.32	111.66
Al	$O_C{}^C$	$C_C{}^C$	111.97	112.02	108.96
Al	$O_{OH}{}^C$	$C_{OH}{}^C$	112.00	112.44	108.87
$O_C{}^A$	Al	$O_{OH}{}^A$	84,23	83.57	83.90
$O_C{}^A$	Al	$O_C{}^B$	89,83	90.66	92.73
$O_C{}^A$	Al	$O_{OH}{}^B$	171,91	172.55	93.53
$O_C{}^A$	Al	$O_C{}^C$	89,79	94.12	175.22
$O_C{}^A$	Al	$O_{OH}{}^C$	95.65	90.05	95.10
$O_{OH}{}^A$	Al	$O_C{}^B$	95.73	94.45	88.59
$O_{OH}{}^A$	Al	$O_{OH}{}^B$	90,87	91.52	170.87
$O_{OH}{}^A$	Al	$O_C{}^C$	171,82	91.20	91.63
$O_{OH}{}^A$	Al	$O_{OH}{}^C$	90,84	171.69	100.96
$O_C{}^B$	Al	$O_{OH}{}^B$	84,25	84.12	82.77
$O_C{}^B$	Al	$O_C{}^C$	89,82	172.98	88.85
$O_C{}^B$	Al	$O_{OH}{}^C$	171,85	90.94	168.22
$O_{OH}{}^B$	Al	$O_C{}^C$	95,68	91.58	91.15
$O_{OH}{}^B$	Al	$O_{OH}{}^C$	90,83	95.33	87.98
$O_C{}^C$	Al	$O_{OH}{}^C$	84,19	83.92	84.05

Table S1. Distances (in Å) and angles (in degrees) computed on the crystal structure of Al(III)-DFP$_3$, and the DFT structures of Al(III)-DFP$_3$ and Al.Pept$^9{}_{3G}$.

	Apoform	Al(III)-Peptide
Pept$^{9}_{3G}$	7.68 (1.14)	6.78 (0.10)
Pept$^{9}_{GPG}$	7.04 (0.97)	7.05 (0.11)
Pept$^{8}_{2G-3G}$	7.15 (1.01)	6.56 (0.09)
Pept$^{8}_{3G-2G}$	7.12 (0.92)	6.43 (0.12)
Pept^{7}	6.49 (0.77)	6.25 (0.11)
Pept$^{6}_{G-2G}$	6.36 (0.69)	5.71 (0.15)
Pept$^{6}_{2G-G}$	6.43 (0.70)	5.89 (0.13)
Pept^{5}	5.90 (0.50)	5.32 (0.18)

Table S2 Average and standard deviation (in Å) radius of Gyration computed along the QM/MM MD simulation trajectories of the apoform of the peptides in solution and Al-Pept complexes.

	$Pept^{9}_{3G}$	$Pept^{9}_{GPG}$	$Pept^{8}_{2G-3G}$	$Pept^{8}_{3G-2G}$	$Pept^{7}$	$Pept^{6}_{G-2G}$	$Pept^{6}_{2G-G}$	$Pept^{5}$
O_C^A-Al-O_{OH}^A	88.1 (3.6)	87.8 (3.7)	87.6 (3.7)	87.2 (4.0)	88.3 (3.6)	88.8 (3.5)	89.0 (3.6)	88.2 (3.7)
O_C^A-Al-O_C^B	91.5 (8.1)	93.7 (7.9)	98.8 (8.1)	86.0 (7.8)	92.6 (16.5)	101.7 (27.1)	126.8 (9.2)	129.4 (25.7)
O_C^A-Al-O_{OH}^B	90.6 (8.6)	87.5 (8.3)	84.8 (7.6)	103.6 (25.5)	134.9 (35.0)	93.1 (8.4)	112.3 (10.6)	129.5 (16.8)
O_C^A-Al-O_C^C	168.2 (6.2)	167.3 (6.5)	166.5 (6.5)	156.5 (24.8)	92.5 (11.4)	89.7 (8.1)	84.6 (6.6)	84.6 (8.6)
O_C^A-Al-O_{OH}^C	89.1 (8.5)	85.9 (7.8)	84.9 (7.7)	95.0 (12.7)	122.8 (31.9)	165.4 (7.7)	128.9 (13.6)	116.2 (19.4)
O_{OH}^A-Al-O_C^B	85.9 (7.0)	82.3 (6.4)	80.7 (6.0)	114.8 (37.1)	107.5 (32.8)	121.3 (11.4)	120.5 (7.8)	111.2 (11.3)
O_{OH}^A-Al-O_{OH}^B	167.3 (6.3)	164.3 (7.2)	161.9 (6.9)	135.4 (35.4)	94.3 (14.7)	125.5 (8.9)	103.7 (9.0)	95.3 (12.1)
O_{OH}^A-Al-O_C^C	90.6 (8.1)	94.2 (8.5)	96.7 (8.2)	84.5 (7.5)	144.9 (30.4)	117.8 (10.6)	158.8 (11.4)	155.7 (24.9)
O_{OH}^A-Al-O_{OH}^C	100.7 (8.4)	101.1 (8.9)	103.5 (8.5)	107.3 (23.9)	89.6 (16.5)	83.4 (6.8)	83.5 (7.2)	94.1 (10.2)
O_C^B-Al-O_{OH}^B	87.3 (3.7)	86.8 (4.2)	86.9 (3.8)	84.5 (7.5)	72.4 (25.2)	29.9 (11.3)	26.2 (9.9)	28.4 (18.8)
O_C^B-Al-O_C^C	91.8 (9.4)	92.7 (9.0)	89.1 (8.5)	107.1 (25.8)	98.6 (17.3)	111.7 (17.2)	77.2 (10.7)	86.5 (23.8)
O_C^B-Al-O_{OH}^C	167.3 (6.2)	168.3 (6.3)	168.1 (6.1)	127.2 (42.8)	135.6 (36.1)	87.7 (25.4)	98.7 (9.4)	103.5 (12.5)
O_{OH}^B-Al-O_C^C	91.3 (7.9)	91.8 (7.9)	92.6 (8.0)	89.3 (8.9)	108.9 (32.8)	115.7 (9.3)	95.2 (9.7)	98.7 (14.9)
O_{OH}^B-Al-O_{OH}^C	86.5 (7.0)	90.1 (8.1)	89.6 (7.5)	110.3 (35.0)	94.6 (13.1)	96.7 (7.9)	117.6 (8.9)	112.6 (10.6)
O_C^C-Al-O_{OH}^C	87.9 (3.7)	88.0 (3.8)	87.3 (3.8)	88.3 (3.6)	88.0 (3.8)	89.5 (3.6)	88.9 (3.6)	85.2 (16.5)

Table S3 Average values (and their standard deviations) of all possible O^{Mim}-Al-O^{Mim} angles computed along the standard MD simulation trajectories of the Al-Pept complexes. Since the indexes of the three Mimosine residues differ on the systems, they are referred to as A, B and C for the first, central and last Mimosine in the corresponding sequence shown in Figure 1.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
GLY_3@O	GLY_5@H	GLY_5@N	215	0.0108	2.8785	146.3374
GLY_7@O	GLY_9@H	GLY_9@N	212	0.0107	2.8822	146.6055
MIH_2@O	GLY_4@H	GLY_4@N	115	0.0058	2.9048	144.1116
GLY_3@O	GLY_7@H	GLY_7@N	108	0.0054	2.8808	155.7838
MIH_6@O	GLY_8@H	GLY_8@N	108	0.0054	2.9069	145.295
GLY_4@O	GLY_8@H	GLY_8@N	105	0.0053	2.8992	148.6666
GLY_7@O	NME_11@H	NME_11@N	103	0.0052	2.9102	158.7487
GLY_5@O	GLY_8@H	GLY_8@N	88	0.0044	2.9053	151.2934
MIH_6@O	GLY_9@H	GLY_9@N	83	0.0042	2.9332	149.4445
MIH_2@O	GLY_5@H	GLY_5@N	79	0.004	2.9273	150.6268
GLY_8@O	GLY_5@H	GLY_5@N	76	0.0038	2.8772	152.9991
GLY_8@O	MIH_10@H	MIH_10@N	74	0.0037	2.8827	143.9258
GLY_3@O	MIH_6@H	MIH_6@N	70	0.0035	2.9301	153.4352
GLY_4@O	MIH_6@H	MIH_6@N	67	0.0034	2.8916	143.8881
GLY_7@O	MIH_10@H	MIH_10@N	65	0.0033	2.9414	155.0316
ACE_1@O	GLY_4@H	GLY_4@N	61	0.0031	2.9071	151.0677
GLY_3@O	GLY_8@H	GLY_8@N	57	0.0029	2.8701	147.764
GLY_4@O	GLY_9@H	GLY_9@N	47	0.0024	2.8802	150.0839
GLY_9@O	NME_11@H	NME_11@N	40	0.002	2.9071	142.9866
GLY_5@O	GLY_7@H	GLY_7@N	38	0.0019	2.9128	143.2313
GLY_5@O	GLY_9@H	GLY_9@N	36	0.0018	2.8748	154.2794
ACE_1@O	GLY_8@H	GLY_8@N	35	0.0018	2.8871	155.9333
GLY_9@O	GLY_4@H	GLY_4@N	33	0.0017	2.8694	154.1742
ACE_1@O	GLY_3@H	GLY_3@N	32	0.0016	2.9065	145.3006
GLY_3@O	GLY_9@H	GLY_9@N	30	0.0015	2.885	148.2627
GLY_3@O	NME_11@H	NME_11@N	25	0.0013	2.9134	159.6403
GLY_9@O	GLY_5@H	GLY_5@N	23	0.0012	2.8768	153.1714
GLY_4@O	GLY_7@H	GLY_7@N	19	0.001	2.9105	151.6243
GLY_9@O	GLY_3@H	GLY_3@N	18	0.0009	2.8835	152.2386

GLY_8@O	GLY_4@H	GLY_4@N	18	0.0009	2.8916	153.0775
ACE_1@O	GLY_5@H	GLY_5@N	18	0.0009	2.8945	153.0308
MIH_6@O	MIH_2@H	MIH_2@N	18	0.0009	2.9474	155.769
ACE_1@O	GLY_7@H	GLY_7@N	16	0.0008	2.8653	156.489
GLY_7@O	GLY_4@H	GLY_4@N	16	0.0008	2.91	160.0729
GLY_8@O	GLY_3@H	GLY_3@N	14	0.0007	2.8735	154.0044
ACE_1@O	GLY_9@H	GLY_9@N	10	0.0005	2.8745	155.7919
ACE_1@O	NME_11@H	NME_11@N	10	0.0005	2.8876	164.7855
GLY_8@O	NME_11@H	NME_11@N	9	0.0005	2.8826	161.073
GLY_5@O	MIH_2@H	MIH_2@N	9	0.0005	2.9112	159.5201
GLY_7@O	GLY_3@H	GLY_3@N	9	0.0005	2.9287	147.5528
GLY_9@O	MIH_6@H	MIH_6@N	9	0.0005	2.9326	161.5631
GLY_5@O	NME_11@H	NME_11@N	8	0.0004	2.9105	152.8098
MIH_6@O	MIH_10@H	MIH_10@N	8	0.0004	2.9398	149.5473
MIH_6@O	GLY_3@H	GLY_3@N	7	0.0004	2.908	156.0943
MIH_2@O	MIH_10@H	MIH_10@N	7	0.0004	2.9193	154.3373
ACE_1@O	MIH_10@H	MIH_10@N	7	0.0004	2.9381	155.7219
MIH_10@O	GLY_7@H	GLY_7@N	7	0.0004	2.9427	153.8193
MIH_10@O	GLY_4@H	GLY_4@N	6	0.0003	2.8829	150.1012
GLY_4@O	MIH_10@H	MIH_10@N	5	0.0003	2.8669	158.2397
MIH_10@O	MIH_6@H	MIH_6@N	4	0.0002	2.8581	154.516
GLY_4@O	NME_11@H	NME_11@N	4	0.0002	2.8599	164.25
GLY_8@O	MIH_6@H	MIH_6@N	4	0.0002	2.9029	147.6096
MIH_2@O	NME_11@H	NME_11@N	4	0.0002	2.9237	146.8696
MIH_10@O	GLY_5@H	GLY_5@N	3	0.0002	2.861	147.852
MIH_2@O	GLY_8@H	GLY_8@N	3	0.0002	2.8987	143.7901
ACE_1@O	MIH_6@H	MIH_6@N	3	0.0002	2.9012	158.9874
MIH_2@O	MIH_6@H	MIH_6@N	3	0.0002	2.929	145.2159
MIH_2@O	GLY_7@H	GLY_7@N	3	0.0002	2.9306	151.2682
GLY_7@O	GLY_5@H	GLY_5@N	3	0.0002	2.9482	164.0803

GLY_8@O	MIH_2@H	MIH_2@N	3	0.0002	2.9585	151.8144
GLY_7@O	MIH_2@H	MIH_2@N	2	0.0001	2.8744	145.217
GLY_4@O	MIH_2@H	MIH_2@N	2	0.0001	2.9244	148.2908
GLY_3@O	MIH_10@H	MIH_10@N	2	0.0001	2.9429	170.6483
MIH_10@O	MIH_2@H	MIH_2@N	2	0.0001	2.9467	164.2435
MIH_10@O	GLY_3@H	GLY_3@N	1	0.0001	2.9103	137.865
GLY_9@O	MIH_2@H	MIH_2@N	1	0.0001	2.9395	144.758
MIH_6@O	NME_11@H	NME_11@N	1	0.0001	2.9558	173.4173
			Total	**11.79**		

Table S4 List of all hydrogen bonds identified during the QM/MM MD simulation of the $Pept^{9}_{3G}$ apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 11 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
GLY_3@O	GLY_7@H	GLY_7@N	1958	0.1018	2.88	158.3044
GLY_3@O	MIH_6@H	MIH_6@N	645	0.0335	2.9143	153.7117
GLY_7@O	NME_11@H	NME_11@N	511	0.0266	2.8869	155.9729
GLY_7@O	MIH_10@H	MIH_10@N	346	0.018	2.9199	155.4973
PRO_4@O	GLY_9@H	GLY_9@N	174	0.009	2.8823	146.9834
GLY_7@O	GLY_9@H	GLY_9@N	111	0.0058	2.8501	144.9871
PRO_4@O	MIH_6@H	MIH_6@N	87	0.0045	2.8943	144.1337
PRO_8@O	MIH_10@H	MIH_10@N	70	0.0036	2.8935	143.1248
GLY_3@O	GLY_5@H	GLY_5@N	62	0.0032	2.8747	145.3162
GLY_3@O	NME_11@H	NME_11@N	44	0.0023	2.8821	158.9585
GLY_7@O	GLY_3@H	GLY_3@N	43	0.0022	2.9058	159.7418
MIH_10@O	GLY_5@H	GLY_5@N	33	0.0017	2.9146	154.8955
MIH_6@O	GLY_9@H	GLY_9@N	33	0.0017	2.9287	147.7181
GLY_9@O	GLY_3@H	GLY_3@N	31	0.0016	2.8865	158.5505
ACE_1@O	GLY_9@H	GLY_9@N	27	0.0014	2.868	151.8591
MIH_2@O	GLY_9@H	GLY_9@N	27	0.0014	2.9029	153.7497
PRO_4@O	GLY_7@H	GLY_7@N	26	0.0014	2.9099	150.8733
GLY_9@O	NME_11@H	NME_11@N	25	0.0013	2.9142	142.2446
ACE_1@O	GLY_3@H	GLY_3@N	24	0.0012	2.933	143.2126
MIH_2@O	MIH_10@H	MIH_10@N	21	0.0011	2.9393	148.7389
GLY_7@O	GLY_5@H	GLY_5@N	20	0.001	2.8781	151.2832
MIH_10@O	GLY_7@H	GLY_7@N	17	0.0009	2.8736	154.7412
GLY_9@O	GLY_5@H	GLY_5@N	15	0.0008	2.895	157.5342
GLY_7@O	MIH_2@H	MIH_2@N	15	0.0008	2.8985	157.9786
PRO_8@O	NME_11@H	NME_11@N	13	0.0007	2.8961	153.712
GLY_5@O	GLY_7@H	GLY_7@N	13	0.0007	2.9011	144.3597
PRO_4@O	NME_11@H	NME_11@N	12	0.0006	2.9109	158.0943
MIH_2@O	GLY_5@H	GLY_5@N	12	0.0006	2.9299	147.889
MIH_6@O	GLY_3@H	GLY_3@N	12	0.0006	2.936	152.2779
PRO_4@O	MIH_10@H	MIH_10@N	11	0.0006	2.9064	155.0446
MIH_10@O	GLY_3@H	GLY_3@N	11	0.0006	2.907	149.9275
GLY_3@O	GLY_9@H	GLY_9@N	11	0.0006	2.9311	148.8482
MIH_10@O	MIH_2@H	MIH_2@N	10	0.0005	2.9149	151.3628
GLY_3@O	MIH_10@H	MIH_10@N	8	0.0004	2.9028	151.6664
MIH_10@O	MIH_6@H	MIH_6@N	8	0.0004	2.9356	156.3425

MIH_6@O	MIH_2@H	MIH_2@N	7	0.0004	2.9368	152.4178
MIH_2@O	NME_11@H	NME_11@N	7	0.0004	2.9508	145.2459
ACE_1@O	NME_11@H	NME_11@N	6	0.0003	2.9075	159.0805
GLY_5@O	NME_11@H	NME_11@N	6	0.0003	2.9109	152.9593
GLY_9@O	MIH_2@H	MIH_2@N	4	0.0002	2.9145	150.8553
PRO_8@O	MIH_2@H	MIH_2@N	3	0.0002	2.9136	160.2622
GLY_9@O	MIH_6@H	MIH_6@N	3	0.0002	2.9233	157.5447
MIH_2@O	MIH_6@H	MIH_6@N	3	0.0002	2.95	155.0058
ACE_1@O	GLY_7@H	GLY_7@N	1	0.0001	2.7774	145.0489
ACE_1@O	MIH_10@H	MIH_10@N	1	0.0001	2.8831	159.7035
MIH_2@O	GLY_7@H	GLY_7@N	1	0.0001	2.9581	142.4575
PRO_4@O	MIH_2@H	MIH_2@N	1	0.0001	2.9693	136.4532
GLY_7@O	MIH_6@H	MIH_6@N	1	0.0001	2.9836	144.6059
MIH_6@O	MIH_10@H	MIH_10@N	1	0.0001	2.9965	166.3753
			Total	**23.59**		

Table S5 List of all hydrogen bonds identified during the QM/MM MD simulation of the $Pept^{9}_{GPG}$ apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 11 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
GLY_6@O	GLY_8@H	GLY_8@N	248	0.0128	2.8873	145.1479
GLY_6@O	NME_10@H	NME_10@N	210	0.0108	2.889	159.8586
GLY_3@O	GLY_7@H	GLY_7@N	187	0.0096	2.8841	150.9704
GLY_3@O	GLY_8@H	GLY_8@N	171	0.0088	2.8873	151.8764
MIH_2@O	GLY_4@H	GLY_4@N	107	0.0055	2.9141	144.1075
GLY_3@O	MIH_5@H	MIH_5@N	96	0.0049	2.9002	143.7966
MIH_5@O	GLY_8@H	GLY_8@N	95	0.0049	2.9182	150.0832
MIH_5@O	GLY_7@H	GLY_7@N	93	0.0048	2.8982	144.9737
GLY_6@O	MIH_9@H	MIH_9@N	82	0.0042	2.9048	152.6675
GLY_7@O	MIH_9@H	MIH_9@N	78	0.004	2.8999	144.4584
GLY_4@O	GLY_7@H	GLY_7@N	66	0.0034	2.9005	148.7571
MIH_2@O	MIH_5@H	MIH_5@N	66	0.0034	2.9291	154.457
GLY_3@O	GLY_6@H	GLY_6@N	53	0.0027	2.9116	148.7328
ACE_1@O	GLY_4@H	GLY_4@N	45	0.0023	2.8944	151.9484
GLY_6@O	GLY_3@H	GLY_3@N	44	0.0023	2.891	158.822
MIH_2@O	GLY_6@H	GLY_6@N	36	0.0019	2.9259	152.5658
GLY_8@O	NME_10@H	NME_10@N	30	0.0015	2.9277	143.0043
GLY_4@O	GLY_6@H	GLY_6@N	28	0.0014	2.904	145.7611
ACE_1@O	GLY_3@H	GLY_3@N	27	0.0014	2.925	144.2819
ACE_1@O	GLY_8@H	GLY_8@N	21	0.0011	2.9	157.7117
GLY_7@O	GLY_4@H	GLY_4@N	18	0.0009	2.9207	151.1105
GLY_4@O	GLY_8@H	GLY_8@N	17	0.0009	2.8906	153.0675
MIH_2@O	GLY_7@H	GLY_7@N	16	0.0008	2.898	146.4786
GLY_7@O	GLY_3@H	GLY_3@N	14	0.0007	2.8657	155.8258
GLY_3@O	MIH_9@H	MIH_9@N	14	0.0007	2.9133	152.3677
GLY_3@O	NME_10@H	NME_10@N	14	0.0007	2.9288	162.9838
GLY_7@O	MIH_2@H	MIH_2@N	12	0.0006	2.8819	165.9856
GLY_8@O	GLY_3@H	GLY_3@N	11	0.0006	2.8759	155.5976
GLY_8@O	GLY_4@H	GLY_4@N	11	0.0006	2.8935	156.9359
MIH_5@O	MIH_2@H	MIH_2@N	11	0.0006	2.9488	155.4122
GLY_4@O	MIH_9@H	MIH_9@N	10	0.0005	2.8999	154.341
GLY_7@O	NME_10@H	NME_10@N	10	0.0005	2.9141	147.8452
MIH_9@O	GLY_6@H	GLY_6@N	9	0.0005	2.9176	146.6791
ACE_1@O	GLY_6@H	GLY_6@N	7	0.0004	2.8864	163.9489
GLY_4@O	NME_10@H	NME_10@N	7	0.0004	2.8937	158.9534
ACE_1@O	GLY_7@H	GLY_7@N	6	0.0003	2.8577	149.7698

MIH_5@O	MIH_9@H	MIH_9@N	6	0.0003	2.8958	152.0844
MIH_2@O	GLY_8@H	GLY_8@N	6	0.0003	2.9162	141.6467
MIH_9@O	GLY_3@H	GLY_3@N	5	0.0003	2.9291	145.9894
MIH_9@O	MIH_5@H	MIH_5@N	5	0.0003	2.9515	157.0493
GLY_8@O	MIH_2@H	MIH_2@N	4	0.0002	2.8319	158.1465
GLY_8@O	MIH_5@H	MIH_5@N	4	0.0002	2.8552	156.8847
ACE_1@O	NME_10@H	NME_10@N	4	0.0002	2.8561	154.8016
GLY_8@O	GLY_6@H	GLY_6@N	4	0.0002	2.9012	159.6242
MIH_9@O	GLY_4@H	GLY_4@N	4	0.0002	2.9171	146.3207
MIH_2@O	NME_10@H	NME_10@N	4	0.0002	2.9184	143.9855
MIH_2@O	MIH_9@H	MIH_9@N	4	0.0002	2.933	160.2773
ACE_1@O	MIH_9@H	MIH_9@N	3	0.0002	2.836	153.5137
MIH_5@O	NME_10@H	NME_10@N	3	0.0002	2.9165	147.2706
ACE_1@O	MIH_5@H	MIH_5@N	3	0.0002	2.9632	140.0127
MIH_5@O	GLY_3@H	GLY_3@N	2	0.0001	2.7482	141.7097
GLY_4@O	MIH_2@H	MIH_2@N	2	0.0001	2.9692	159.8182
GLY_6@O	GLY_4@H	GLY_4@N	1	0.0001	2.9701	137.0208
MIH_9@O	MIH_2@H	MIH_2@N	1	0.0001	2.9742	151.3305
			Total	**10.5**		

Table S6 List of all hydrogen bonds identified during the QM/MM MD simulation of the $Pept^{8}_{2G\text{-}3G}$ apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 10 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
GLY_3@O	GLY_7@H	GLY_7@N	754	0.0371	2.8779	158.0234
GLY_3@O	GLY_8@H	GLY_8@N	373	0.0184	2.8862	152.1049
GLY_3@O	MIH_6@H	MIH_6@N	275	0.0135	2.9169	153.2689
GLY_3@O	GLY_5@H	GLY_5@N	188	0.0093	2.8767	146.7852
GLY_4@O	GLY_8@H	GLY_8@N	132	0.0065	2.8929	148.0462
MIH_2@O	GLY_4@H	GLY_4@N	115	0.0057	2.9064	145.7169
MIH_6@O	GLY_8@H	GLY_8@N	108	0.0053	2.9102	144.6828
GLY_5@O	GLY_8@H	GLY_8@N	89	0.0044	2.8939	152.3736
MIH_2@O	GLY_5@H	GLY_5@N	89	0.0044	2.9253	150.4109
GLY_7@O	MIH_9@H	MIH_9@N	70	0.0034	2.8882	144.4823
GLY_4@O	MIH_6@H	MIH_6@N	66	0.0032	2.8969	143.983
MIH_6@O	MIH_9@H	MIH_9@N	63	0.0031	2.9374	153.1904
GLY_4@O	MIH_9@H	MIH_9@N	53	0.0026	2.9069	151.0583
GLY_8@O	GLY_5@H	GLY_5@N	51	0.0025	2.8768	157.1594
ACE_1@O	GLY_4@H	GLY_4@N	40	0.002	2.9045	150.4863
GLY_5@O	GLY_7@H	GLY_7@N	39	0.0019	2.9054	142.3242
GLY_8@O	NME_10@H	NME_10@N	38	0.0019	2.8974	142.5205
GLY_4@O	NME_10@H	NME_10@N	32	0.0016	2.8986	156.9252
GLY_8@O	GLY_4@H	GLY_4@N	31	0.0015	2.8739	156.8424
ACE_1@O	GLY_3@H	GLY_3@N	30	0.0015	2.9048	141.9304
GLY_7@O	GLY_4@H	GLY_4@N	23	0.0011	2.8877	157.1277
GLY_4@O	GLY_7@H	GLY_7@N	23	0.0011	2.9003	153.5001
GLY_3@O	NME_10@H	NME_10@N	19	0.0009	2.9168	161.7408
GLY_3@O	MIH_9@H	MIH_9@N	18	0.0009	2.8883	150.0677
MIH_2@O	MIH_9@H	MIH_9@N	15	0.0007	2.9102	152.5233
ACE_1@O	GLY_8@H	GLY_8@N	12	0.0006	2.8828	162.1359
MIH_9@O	GLY_4@H	GLY_4@N	12	0.0006	2.9078	146.3489
MIH_6@O	NME_10@H	NME_10@N	11	0.0005	2.9035	157.8823
MIH_6@O	GLY_3@H	GLY_3@N	11	0.0005	2.9111	152.5976
GLY_8@O	GLY_3@H	GLY_3@N	10	0.0005	2.8566	156.4978
ACE_1@O	NME_10@H	NME_10@N	10	0.0005	2.8869	157.5946
MIH_9@O	MIH_2@H	MIH_2@N	10	0.0005	2.93	157.4721
MIH_2@O	NME_10@H	NME_10@N	9	0.0004	2.9107	155.7627
MIH_9@O	MIH_6@H	MIH_6@N	9	0.0004	2.9145	155.2164
MIH_9@O	GLY_5@H	GLY_5@N	8	0.0004	2.8747	149.6254
GLY_8@O	MIH_2@H	MIH_2@N	8	0.0004	2.8939	161.4626

MIH_2@O	MIH_6@H	MIH_6@N	7	0.0003	2.9287	151.2034
ACE_1@O	GLY_5@H	GLY_5@N	6	0.0003	2.8594	149.8754
GLY_7@O	NME_10@H	NME_10@N	6	0.0003	2.9096	154.6404
GLY_5@O	MIH_2@H	MIH_2@N	5	0.0002	2.8755	147.8595
MIH_9@O	GLY_3@H	GLY_3@N	5	0.0002	2.917	148.1186
GLY_7@O	MIH_2@H	MIH_2@N	5	0.0002	2.927	154.0848
ACE_1@O	MIH_9@H	MIH_9@N	4	0.0002	2.8645	158.72
MIH_2@O	GLY_8@H	GLY_8@N	4	0.0002	2.9498	163.5209
MIH_2@O	GLY_7@H	GLY_7@N	3	0.0001	2.9018	143.1263
ACE_1@O	MIH_6@H	MIH_6@N	3	0.0001	2.9166	154.1501
GLY_8@O	MIH_6@H	MIH_6@N	3	0.0001	2.9461	144.9694
GLY_7@O	GLY_3@H	GLY_3@N	2	0.0001	2.8768	148.5593
MIH_6@O	MIH_2@H	MIH_2@N	2	0.0001	2.9286	155.9171
ACE_1@O	GLY_7@H	GLY_7@N	2	0.0001	2.931	161.2361
GLY_7@O	GLY_5@H	GLY_5@N	2	0.0001	2.9482	161.8298
GLY_5@O	MIH_9@H	MIH_9@N	1	0	2.9257	163.0251
GLY_5@O	NME_10@H	NME_10@N	1	0	2.9809	163.5218
			Total	**14.24**		

Table S7 List of all hydrogen bonds identified during the QM/MM MD simulation of the $Pept^{8}_{2G\text{-}3G}$ apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 10 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
GLY_3@O	GLY_7@H	GLY_7@N	170	0.0092	2.8977	148.9097
MIH_5@O	GLY_7@H	GLY_7@N	124	0.0067	2.9076	144.4154
MIH_5@O	MIH_8@H	MIH_8@N	98	0.0053	2.9312	151.6136
GLY_3@O	MIH_5@H	MIH_5@N	81	0.0044	2.899	144.4622
MIH_2@O	GLY_4@H	GLY_4@N	81	0.0044	2.9005	145.4876
GLY_6@O	MIH_8@H	MIH_8@N	76	0.0041	2.892	143.8784
MIH_2@O	MIH_5@H	MIH_5@N	76	0.0041	2.9325	153.2701
GLY_4@O	GLY_7@H	GLY_7@N	67	0.0036	2.9203	150.902
ACE_1@O	GLY_4@H	GLY_4@N	59	0.0032	2.8874	149.5484
GLY_3@O	MIH_8@H	MIH_8@N	57	0.0031	2.9194	151.9448
MIH_2@O	GLY_6@H	GLY_6@N	42	0.0023	2.9079	156.0776
GLY_4@O	GLY_6@H	GLY_6@N	34	0.0018	2.9045	144.2805
GLY_3@O	GLY_6@H	GLY_6@N	32	0.0017	2.9055	148.7617
GLY_7@O	NME_9@H	NME_9@N	32	0.0017	2.921	142.9699
MIH_5@O	NME_9@H	NME_9@N	28	0.0015	2.9225	156.9073
ACE_1@O	GLY_3@H	GLY_3@N	26	0.0014	2.9162	142.4152
GLY_3@O	NME_9@H	NME_9@N	23	0.0012	2.9045	160.4789
MIH_8@O	GLY_4@H	GLY_4@N	13	0.0007	2.8836	147.0329
MIH_8@O	MIH_2@H	MIH_2@N	13	0.0007	2.9253	158.122
MIH_8@O	GLY_3@H	GLY_3@N	11	0.0006	2.8877	148.3853
GLY_6@O	NME_9@H	NME_9@N	11	0.0006	2.9268	153.3033
ACE_1@O	NME_9@H	NME_9@N	10	0.0005	2.9177	160.3734
ACE_1@O	GLY_7@H	GLY_7@N	9	0.0005	2.8705	157.9581
GLY_7@O	GLY_3@H	GLY_3@N	9	0.0005	2.9412	155.5651
GLY_4@O	MIH_8@H	MIH_8@N	8	0.0004	2.8788	153.2212
MIH_5@O	MIH_2@H	MIH_2@N	8	0.0004	2.9329	160.2779
MIH_2@O	NME_9@H	NME_9@N	7	0.0004	2.9017	153.7408
MIH_8@O	MIH_5@H	MIH_5@N	7	0.0004	2.9077	147.7103
MIH_2@O	GLY_7@H	GLY_7@N	7	0.0004	2.9253	145.9651
GLY_4@O	NME_9@H	NME_9@N	6	0.0003	2.8417	147.9796
GLY_7@O	MIH_2@H	MIH_2@N	6	0.0003	2.9405	153.85
ACE_1@O	MIH_8@H	MIH_8@N	4	0.0002	2.8922	149.3166
GLY_6@O	GLY_3@H	GLY_3@N	4	0.0002	2.9107	157.9424
GLY_7@O	MIH_5@H	MIH_5@N	3	0.0002	2.9077	150.4977
GLY_7@O	GLY_4@H	GLY_4@N	2	0.0001	2.8335	142.8448
ACE_1@O	MIH_5@H	MIH_5@N	1	0.0001	2.7792	139.917

GLY_4@O	MIH_2@H	MIH_2@N	1	0.0001	2.9069	172.5264
ACE_1@O	GLY_6@H	GLY_6@N	1	0.0001	2.9183	149.7025
GLY_6@O	GLY_4@H	GLY_4@N	1	0.0001	2.9631	157.5588
			Total	**6.75**		

Table S8 List of all hydrogen bonds identified during the QM/MM MD simulation of the Pept[7] apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 9 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
MIH_4@O	GLY_6@H	GLY_6@N	151	0.0074	2.9008	143.0568
MIH_2@O	MIH_4@H	MIH_4@N	131	0.0064	2.9108	142.9848
GLY_3@O	GLY_6@H	GLY_6@N	110	0.0054	2.9042	151.6088
MIH_4@O	MIH_7@H	MIH_7@N	88	0.0043	2.9415	153.682
GLY_5@O	MIH_7@H	MIH_7@N	74	0.0036	2.9013	144.1374
MIH_4@O	NME_8@H	NME_8@N	54	0.0027	2.9221	151.3264
GLY_3@O	GLY_5@H	GLY_5@N	47	0.0023	2.8913	144.0601
MIH_7@O	MIH_2@H	MIH_2@N	33	0.0016	2.9228	153.792
MIH_2@O	GLY_6@H	GLY_6@N	32	0.0016	2.9318	145.408
ACE_1@O	GLY_3@H	GLY_3@N	28	0.0014	2.8948	144.0492
GLY_6@O	NME_8@H	NME_8@N	26	0.0013	2.9062	145.2781
GLY_6@O	MIH_2@H	MIH_2@N	24	0.0012	2.9325	159.1319
MIH_7@O	MIH_4@H	MIH_4@N	20	0.001	2.9205	157.7276
GLY_5@O	MIH_2@H	MIH_2@N	16	0.0008	2.9169	155.0697
ACE_1@O	GLY_5@H	GLY_5@N	13	0.0006	2.8988	153.3561
GLY_6@O	GLY_3@H	GLY_3@N	11	0.0005	2.9025	153.1315
GLY_3@O	MIH_7@H	MIH_7@N	10	0.0005	2.9396	152.6466
MIH_7@O	GLY_3@H	GLY_3@N	8	0.0004	2.8474	152.7994
GLY_6@O	MIH_4@H	MIH_4@N	8	0.0004	2.9232	155.8506
GLY_5@O	NME_8@H	NME_8@N	8	0.0004	2.9491	150.2356
MIH_2@O	GLY_5@H	GLY_5@N	6	0.0003	2.9148	144.6319
ACE_1@O	MIH_4@H	MIH_4@N	6	0.0003	2.9418	155.3531
MIH_4@O	MIH_2@H	MIH_2@N	5	0.0002	2.902	160.4888
MIH_2@O	NME_8@H	NME_8@N	5	0.0002	2.9102	145.793
MIH_2@O	MIH_7@H	MIH_7@N	5	0.0002	2.9584	148.6413
GLY_3@O	NME_8@H	NME_8@N	1	0	2.8016	169.7221
ACE_1@O	NME_8@H	NME_8@N	1	0	2.9319	141.9541
MIH_7@O	GLY_5@H	GLY_5@N	1	0	2.9348	142.3034
ACE_1@O	GLY_6@H	GLY_6@N	1	0	2.9541	147.8889
			Total	**4.5**		

Table S9 List of all hydrogen bonds identified during the QM/MM MD simulation of the $Pept^{6}_{G\text{-}2G}$ apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 8 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
MIH_5@O	MIH_7@H	MIH_7@N	127	0.0063	2.9082	144.9952
MIH_7@O	GLY_4@H	GLY_4@N	124	0.0061	2.9123	147.5652
MIH_2@O	GLY_4@H	GLY_4@N	121	0.006	2.9068	144.2411
GLY_3@O	MIH_5@H	MIH_5@N	82	0.004	2.9095	143.6877
MIH_2@O	GLY_6@H	GLY_6@N	82	0.004	2.9252	154.9145
MIH_2@O	MIH_5@H	MIH_5@N	62	0.0031	2.9261	154.3665
ACE_1@O	GLY_4@H	GLY_4@N	52	0.0026	2.9231	153.6765
GLY_3@O	NME_8@H	NME_8@N	49	0.0024	2.8967	157.6187
GLY_4@O	GLY_6@H	GLY_6@N	31	0.0015	2.9201	143.0025
ACE_1@O	GLY_3@H	GLY_3@N	27	0.0013	2.9142	145.4752
GLY_3@O	MIH_7@H	MIH_7@N	24	0.0012	2.9199	151.945
MIH_7@O	GLY_3@H	GLY_3@N	21	0.001	2.9201	147.0023
GLY_4@O	MIH_7@H	MIH_7@N	19	0.0009	2.9069	150.5797
GLY_6@O	NME_8@H	NME_8@N	19	0.0009	2.9244	143.367
GLY_3@O	GLY_6@H	GLY_6@N	16	0.0008	2.8923	149.3829
MIH_5@O	MIH_2@H	MIH_2@N	13	0.0006	2.8781	152.0273
MIH_5@O	NME_8@H	NME_8@N	9	0.0004	2.9257	146.0922
ACE_1@O	GLY_6@H	GLY_6@N	9	0.0004	2.9469	152.4124
ACE_1@O	MIH_5@H	MIH_5@N	7	0.0003	2.9539	158.3778
MIH_7@O	MIH_5@H	MIH_5@N	6	0.0003	2.9163	156.5813
GLY_4@O	NME_8@H	NME_8@N	6	0.0003	2.9287	157.2526
MIH_7@O	MIH_2@H	MIH_2@N	5	0.0002	2.8991	151.8919
ACE_1@O	NME_8@H	NME_8@N	3	0.0001	2.8847	154.2694
MIH_2@O	MIH_7@H	MIH_7@N	2	0.0001	2.9162	157.6013
GLY_4@O	MIH_2@H	MIH_2@N	2	0.0001	2.934	149.0547
GLY_6@O	GLY_4@H	GLY_4@N	1	0	2.9444	137.7786
			Total	**4.49**		

Table S10 List of all hydrogen bonds identified during the QM/MM MD simulation of the $Pept^{6}_{2G\text{-}G}$ apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom,

hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 8 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
MIH_6@O	MIH_2@H	MIH_2@N	158	0.0079	2.9189	156.8119
MIH_4@O	MIH_6@H	MIH_6@N	136	0.0068	2.9137	144.2391
MIH_2@O	MIH_4@H	MIH_4@N	120	0.006	2.9172	143.5579
MIH_6@O	GLY_3@H	GLY_3@N	101	0.0051	2.9067	148.0095
GLY_5@O	NME_7@H	NME_7@N	31	0.0016	2.9042	144.3577
GLY_5@O	MIH_2@H	MIH_2@N	29	0.0015	2.8944	153.3918
ACE_1@O	GLY_5@H	GLY_5@N	25	0.0013	2.891	155.3835
GLY_3@O	GLY_5@H	GLY_5@N	23	0.0012	2.9244	143.6728
ACE_1@O	GLY_3@H	GLY_3@N	20	0.001	2.9083	145.2975
ACE_1@O	MIH_4@H	MIH_4@N	14	0.0007	2.9484	154.6062
MIH_4@O	MIH_2@H	MIH_2@N	13	0.0007	2.9373	145.0839
GLY_3@O	MIH_6@H	MIH_6@N	8	0.0004	2.9423	161.4659
MIH_6@O	MIH_4@H	MIH_4@N	6	0.0003	2.9324	151.7514
MIH_2@O	NME_7@H	NME_7@N	5	0.0003	2.9603	138.5456
MIH_2@O	MIH_6@H	MIH_6@N	2	0.0001	2.863	142.462
MIH_2@O	GLY_5@H	GLY_5@N	2	0.0001	2.9528	164.4862
GLY_3@O	NME_7@H	NME_7@N	2	0.0001	2.9804	154.6807
MIH_4@O	NME_7@H	NME_7@N	2	0.0001	2.9916	154.4958
			Total	**3.52**		

Table S11 List of all hydrogen bonds identified during the QM/MM MD simulation of the Pept^5 apoform with implicit solvent. From left to right, the columns refer to: hydrogen bond acceptor atom, hydrogen bond donor hydrogen atom, donor heavy atom, number of frames in which a given hydrogen bond was detected (note the total number of frames is approximately 20000), fraction of time (from 0 to 1) in which a given hydrogen bond was detected, average donor-acceptor distance (in Å), and average donor-H-acceptor angle (in degrees). Note the accumulated lifetime is given at the end of the table. Note as well residue numbers 1 (residue ACE) and 7 (residue NME) correspond to the two terminal methyl groups, and therefore the residue IDs are +1 with respect to the residue IDs discussed in the main manuscript.

			Al-Pept$^{9}_{3G}$		Al-Pept$^{9}_{GPG}$		Al-Pept$^{8}_{2G-3G}$		Al-Pept$^{8}_{3G-2G}$	
			DFT	**PM6**	**DFT**	**PM6**	**DFT**	**PM6**	**DFT**	**PM6**
	Atom1	**Atom2**	**Distances**							
	Al	O_C^A	1.952	1.950	1.951	1.956	1.952	1.958	1.963	1.951
	Al	O_{OH}^A	1.911	1.906	1.912	1.909	1.921	1.912	1.921	1.920
	Al	O_C^B	1.970	1.951	1.973	1.957	1.965	1.957	1.959	1.957
	Al	O_{OH}^B	1.919	1.926	1.922	1.926	1.927	1.931	1.929	1.917
	Al	O_C^C	1.949	1.946	1.950	1.942	1.951	1.941	1.948	1.947
	Al	O_{OH}^C	1.914	1.916	1.911	1.911	1.911	1.907	1.902	1.905
Atom1	**Atom2**	**Atom3**	**Angles**							
Al	O_C^A	C_C^A	111.7	107.4	111.2	107.1	111.3	107.2	109.5	106.5
Al	O_{OH}^A	C_{OH}^A	111.9	107.6	111.1	106.9	110.7	106.8	110.0	106.8
Al	O_C^B	C_C^B	112.1	108.3	112.2	108.4	112.2	108.4	112.0	108.3
Al	O_{OH}^B	C_{OH}^B	112.8	108.4	112.7	108.5	112.3	108.1	112.6	108.9
Al	O_C^C	C_C^C	110.0	106.7	109.8	106.6	110.2	106.7	111.1	106.7
Al	O_{OH}^C	C_{OH}^C	110.0	106.5	110.0	106.5	110.5	106.6	111.5	106.9
O_C^A	Al	O_{OH}^A	83.8	88.7	83.8	88.1	83.5	87.9	83.2	88.1
O_C^A	Al	O_C^B	92.7	92.1	93.3	96.0	95.2	98.9	88.8	83.4
O_C^A	Al	O_{OH}^B	90.9	87.5	90.1	85.1	88.4	81.0	92.7	98.0
O_C^A	Al	O_C^C	174.4	178.1	174.1	174.2	173.9	172.0	172.9	171.6
O_C^A	Al	O_{OH}^C	92.2	89.9	91.3	86.4	90.9	87.0	93.9	91.7
O_{OH}^A	Al	O_C^B	89.0	86.4	87.4	81.4	86.2	79.9	87.5	85.5
O_{OH}^A	Al	O_{OH}^B	170.3	173.1	168.2	166.4	165.8	161.7	169.8	170.4
O_{OH}^A	Al	O_C^C	92.8	92.3	94.0	95.0	95.1	99.2	90.2	83.5
O_{OH}^A	Al	O_{OH}^C	99.8	100.0	100.9	102.3	101.3	101.1	99.4	100.5
O_C^B	Al	O_{OH}^B	83.2	88.0	82.9	87.6	83.0	87.4	83.1	87.8
O_C^B	Al	O_C^C	91.7	89.6	92.1	89.3	90.6	86.0	93.5	96.1
O_C^B	Al	O_{OH}^C	170.4	173.3	170.9	175.7	170.9	174.1	172.7	172.2
O_{OH}^B	Al	O_C^C	93.0	91.6	93.0	92.8	94.1	93.0	94.3	90.4

$O_{OH}{}^{B}$	Al	$O_{OH}{}^{C}$	88.5	85.7	89.2	89.1	90.4	92.9	90.1	86.8
$O_{C}{}^{C}$	Al	$O_{OH}{}^{C}$	83.9	88.3	83.8	88.2	83.6	88.1	84.5	89.6

Table S12. Distances (in Å) and angles (in degrees) computed on the Al.Pept$^{9}{}_{3G}$, Al.Pept$^{9}{}_{GPG}$, Al.Pept$^{9}{}_{2G-3G}$ and Al.Pept$^{9}{}_{3G-2G}$ complexes characterized at two level of theories: B3LYP/6-31+G(d,p) and PM6.

			Al-Pept$^{7}_{hexa}$		Al-Pept$^{7}_{penta}$		Al-Pept$^{6}_{G\text{-}2G}$		Al-Pept$^{6}_{2G\text{-}G}$		Al-Pept^{5}	
			DFT	**PM6**	**DFT**	**PM6**	**DFT**	**PM6**	**DFT**	**PM6**	**DFT**	**PM6**
	Atom1	**Atom2**	**Distances**									
	Al	O_C^A	1.936	1.920	1.916	1.884	1.919	1.914	1.888	1.915	1.890	1.883
	Al	O_{OH}^A	1.917	1.932	1.866	1.914	1.880	1.888	1.887	1.885	1.891	1.908
	Al	O_C^B	1.990	1.963	4.394	3.950	4.525	4.335	4.490	4.325	4.435	4.136
	Al	O_{OH}^B	1.919	1.936	1.793	1.820	1.809	1.827	1.806	1.822	1.809	1.822
	Al	O_C^C	1.954	1.935	1.896	1.940	1.877	1.887	1.918	1.894	1.925	1.927
	Al	O_{OH}^C	1.912	1.917	1.886	1.873	1.897	1.916	1.867	1.918	1.865	1.896
Atom1	**Atom2**	**Atom3**	**Angles**									
Al	O_C^A	C_C^A	110.9	107.5	111.8	108.4	112.4	108.0	112.5	107.9	110.8	107.0
Al	O_{OH}^A	C_{OH}^A	111.1	107.1	112.6	107.3	112.8	108.0	112.1	108.3	110.0	106.1
Al	O_C^B	C_C^B	110.3	106.9	-	-	-	-	-	-	-	-
Al	O_{OH}^B	C_{OH}^B	111.3	106.7	134.0	108.2	124.8	110.6	129.2	110.1	122.7	107.1
Al	O_C^C	C_C^C	108.3	106.1	112.0	107.0	112.7	108.1	111.1	108.5	110.8	107.7
Al	O_{OH}^C	C_{OH}^C	108.5	106.0	111.6	107.3	111.6	107.4	112.0	107.2	111.5	107.8
O_C^A	Al	O_{OH}^A	84.1	89.2	84.9	89.8	84.5	89.4	85.0	89.5	84.7	89.9
O_C^A	Al	O_C^B	87.6	84.3	-	-	-	-	-	-	-	-
O_C^A	Al	O_{OH}^B	169.1	170.7	98.9	119.4	96.6	99.7	107.2	97.7	133.1	124.8
O_C^A	Al	O_C^C	93.9	92.3	88.1	80.5	89.6	83.5	89.0	82.1	88.9	87.0
O_C^A	Al	O_{OH}^C	100.9	101.5	158.9	122.9	164.1	158.0	143.4	157.3	114.1	115.4
O_{OH}^A	Al	O_C^B	91.4	88.7	111.8	101.5	116.7	118.3	103.5	115.1	94.7	96.4
O_{OH}^A	Al	O_{OH}^B	90.9	91.9	-	-	-	-	-		-	-
O_{OH}^A	Al	O_C^C	175.0	173.4	143.3	166.8	130.8	132.4	159.2	132.3	172.3	169.7
O_{OH}^A	Al	O_{OH}^C	92.3	85.2	88.6	87.8	87.5	80.1	88.1	81.0	92.9	83.3
O_C^B	Al	O_{OH}^B	82.8	86.6	-	-	-	-	-	-	-	-
O_C^B	Al	O_C^C	93.2	97.8	-	-	-	-	-	-	-	-
O_C^B	Al	O_{OH}^C	171.0	171.5	-	-	-	-	-	-	-	-
O_{OH}^B	Al	O_C^C	91.7	87.5	104.9	91.1	112.5	109.3	97.3	112.6	92.8	93.4

O_{OH}^{B}	Al	O_{OH}^{C}	89.0	87.7	102.1	117.0	99.3	102.3	109.4	104.9	112.8	119.8
O_{C}^{C}	Al	O_{OH}^{C}	83.5	88.3	85.1	90.1	85.3	89.3	84.9	89.1	85.8	89.2

Table S13. Distances (in Å) and angles (in degrees) computed on the Al.Pept^{7}, Al.Pept$^{6}_{G\text{-}2G}$, Al.Pept$^{6}_{2G\text{-}G}$ and Al.Pept^{5} complexes characterized at two level of theories: B3LYP/6-31+G(d,p) and PM6.

	DFT				PM6			
	ΔH_{aq}	ΔG_{aq}	$\Delta\Delta H_{aq}$	$\Delta\Delta G_{aq}$	ΔH_{aq}	ΔG_{aq}	$\Delta\Delta H_{aq}$	$\Delta\Delta G_{aq}$
Al.Pept$^{9}_{3G}$	-25.9	-97.0	0.0	0.0	-6.9	-92.4	0.0	0.0
Al.Pept$^{9}_{GPG}$	6.5	-70.3	32.4	26.6	14.0	-73.4	20.9	18.9
Al.Pept$^{8}_{2G\text{-}3G}$	-8.8	-80.2	17.1	16.7	-5.0	-87.7	2.0	4.7
Al.Pept$^{8}_{3G\text{-}2G}$	-21.7	-90.3	4.2	6.6	-6.7	-86.6	0.2	5.7
Al.Pept^{7} (C.N.=6)	-3.0	-72.6	23.0	24.4	5.6	-80.1	12.6	12.3
Al.Pept^{7} (C.N.=5)	-1.0	-73.2	25.0	23.7	-3.8	-87.6	3.1	4.8
Al.Pept$^{6}_{G\text{-}2G}$	14.9	-59.6	40.8	37.4	-3.4	-83.7	3.5	8.7
Al.Pept$^{6}_{2G\text{-}G}$	1.8	-70.2	27.7	26.8	-5.6	-85.9	1.4	6.5
Al.Pept^{5}	-8.2	-73.8	17.8	23.2	-4.5	-83.5	2.5	8.9

Table S14. Enthalpies (ΔH_{aq}) and Gibbs free energies (ΔG_{aq}) in solution (in kcal/mol) of the eight Al.Peptide complexes computed according to reaction 3 at two level of theories: PM6 and B3LYP/6-311++G(3df,2p)//B3LYP/6-31+G(d) (DFT). The relative $\Delta\Delta H_{aq}$ and $\Delta\Delta G_{aq}$ values, taking Pepti$^{9}_{3G}$ as reference, are also shown.

Electron Delocalization Indices

Electron delocalization indices (DIs) were calculated on the most representative structures (shown in Figure 2). These indices are a measure of the covariance between the population of two atoms A and B and, consequently, a measure of the number of electrons simultaneously fluctuating between these atoms:

$$\delta(A,B)=\int_A\int_B d1d2\rho xc(1,2)=cov(NA,NB)$$

where ρxc(1,2) is the exchange-correlation density and it can be taken as the number of electron pairs shared between atoms A and B, i. e., the bond order.[1,2] The AIMAll v17.11.14 program[3] was used to carry out the QTAIM analysis[4] (what includes the characterization of DIs) on the previously optimized structures. Densities for QTAIM analysis were obtained at the B3LYP/6-311++g(3df,2p) level of theory using the IEFPCM solvation model.

Delocalization indices (D.I.) are a measure of the electron sharing between two atoms. Although Al-O bonds are mainly electrostatic in nature, there are also important dative interactions from the lone pair of the oxygens to the formally vacant 3s and 3p orbitals of Al(III).[5] Therefore, the higher the D. I. value, the stronger the covalent character of the bond between the two atoms. The D.I. were computed at the bonds formed by Al(III) and the six oxygen atoms of the three Mimosine residues in all Al-Pept complexes (Table S15).

Starting from the Al.Pept^9 complex, it can be observed that the D.I. values are ca 0.02 a.u. higher at Al-O_{OH} (ca 0.17 a.u.) than at Al-O_C (ca 0.15 a.u.). This is in agreement with the shorter bond distances of the formers (Table 1): the shorter the distance, the higher the D.I. value. However, a closer analysis of the values indicates that the values are about 0.005 a.u. smaller at the central Mimosine residues. Even if the difference is small, it suggests that the interaction with the central Mimosine is the weakest one among the three Mimosine residues (note this residue weakens its interaction with Al(III) with the shortest peptides). The total electron delocalization computed for the six Al-O bonds is 0.9590 a.u. These trends and values are maintained by Pept^8 and Pept^9 peptides, in which Al(III) is hexacoordinated, and in all of them the accumulated D.I. value is maintained in a narrow range between 0.9579-0.9590 a.u. We also add in Table S15 the values for the Al-DFP_3 complex, which demonstrates that the electronic structure of the Al.Pept^9 complex resembles the one of Al.DFP_3. In this sense, the D.I. for Al-O_{OH} bonds are larger than for Al-O_C and the accumulative D.I. is 0.9580. That is, the four Al.Pept^9 and Al.Pept^8 complexes have adopted the optimum interaction with respect to the three mimosine residues, and in this sense, an efficient

	L.. I.			D. I.				
Complex	Al	Al-O_C	Al-O_{OH}	Al-O_C	Al-O_{OH}	Al-O_C	Al-O_{OH}	Total
Pept$^9{}_{3G}$	9.9493	0.1520	0.1722	0.1472	0.1641	0.1546	0.1689	0.9590
Pept$^9{}_{GPG}$	9.9494	0.1516	0.1720	0.1462	0.1632	0.1550	0.1704	0.9584
Pept$^8{}_{2G\text{-}3G}$	9.9498	0.1513	0.1694	0.1481	0.1627	0.1550	0.1714	0.9579
Pept$^8{}_{3G\text{-}2G}$	9.9496	0.1493	0.1665	0.1486	0.1648	0.1544	0.1749	0.9586
Pept^7 (hexa)	9.9498	0.1626	0.1659	0.1418	0.1628	0.1550	0.1700	0.9581
Pept^7 (penta)	9.9459	0.1744	0.2036	0.0005	0.2228	0.1875	0.1881	0.9769
Pept$^6{}_{G\text{-}2G}$	9.9475	0.1714	0.1999	0.0006	0.2290	0.1989	0.1798	0.9796
Pept$^6{}_{2G\text{-}G}$	9.9466	0.1924	0.1876	0.0005	0.2220	0.1734	0.2029	0.9789
Pept^5	9.9474	0.1973	0.1823	0.0006	0.2283	0.1666	0.2011	0.9761
Al.DFP_3		0.1540	0.1657	0.1522	0.1665	0.1531	0.1665	0.9580

Table S15. Electron localization index (L.I.) for the aluminum atom and electron delocalization indices (D. I.) for the aluminum-Mimosine oxygen bonds (a. u.). All structures were optimized in solution and refined at the B3LYP-D3(BJ)/6-311++G(3df,2p) level of theory (see Methodology).

chelation of the aluminum ion is expected for these polypeptides.

For the Al.Pept^{7} complex two coordination modes were observed during the MD simulation of this complex and therefore two distinct structures were selected, with Al(III) hexa- or pentacoordinated. For Al(III) hexacoordinated structure, the D. I. values of Mim^{4} and Mim^{7} are very similar to the ones observed for the Pept^{8} and Pept^{9} peptides (again, the D.I. values are slightly smaller in the central Mimosine), while the two D.I. values computed on the first Mimosine residue are now almost the same (0.16 a.u.), although the accumulated D.I. maintains in 0.958 a.u.

A different scenario emerges when Al(III) is pentacoordinated by Pept^{7}. The D.I. value of Al-O_C^4 is almost vanished (0.0005 a.u.), since the O_C^4 atom is not present in the first coordination shell of the cation. Interestingly, the loss of O_C^4 atom interaction has strengthened the other five Al-O interactions, when comparing with the Al-Pept$^{7}_{hexa}$ structure. For instance, the D.I. value of the Al(III)- O_{OH}^4 bond increased to 0.2228 a.u, 0.06 a.u. higher than the same bond in the hexacoordinated complex. The indices of the other Al-O bonds have also incremented, namely 0.04 a. u. at Al-O_{OH}^1, 0.03 a.u. at Al-O_C^7, ca 0.1 at Al-O_C^1 and 0.1 a.u. at Al-O_{OH}^7. As a consequence, the accumulated D.I. is equal to 0.9769 a.u., 0.02 a.u. higher than in its counterpair with a hexacoordinated Al(III). This pattern is maintained by the three shortest peptides, in which Al(III) is pentacoordinated: the loss of one Al-O interaction has enlarged the indices of the other Al-O bond, and the accumulated D. I. value is ca. 0.98 in all of them.

In summary, the computed delocalization indices show that the reduction in the Al(III) coordination mode (from six to five) leads to an increment on the total dative interactions between Al(III) and the ligands. Nevertheless, note that this increment corresponds to the covalent part of the Al(III)-O bonds, and as we show in the next section this slightly enhanced covalent interactions between aluminum and mimosine can not compensated the loss of one Al-O electrostatic interaction in the first coordination shell when shifting from coordination number six to five.

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