A terminally modified pseudopeptide (Gly-*m*-aminobenzoic acid) produces supramolecular helix, staircase and water-mediated β-sheet through self-assembly

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Abstract
The pseudopeptide Gly-*m*-ABA (*m*-ABA = *m*-amino benzoic acid) has been chosen to study the formation of supramolecular structures through self-assembly. Single crystal X-ray diffraction studies reveal that the pseudopeptide Boc-Gly-*m*-ABA-OMe (**1**), where both N- and C-terminus are protected, self-assembles to a supramolecular helical structure, whereas the pseudopeptide Boc-Gly-*m*-ABA-OH (**2**) with free $–CO_2H$ at the C-terminus produces molecular staircase through self-assembly. Again the terminally unprotected pseudopeptide $^{+}NH_3$-Gly-*m*-ABA-CO_2^- (**3**) aggregates to a water mediated supramolecular β-sheet structure stabilized by intermolecular hydrogen bonds and π-π interactions. The study reveals that the terminally modified Gly-*m*-ABA generates various kinds of self-assembling building blocks that can fabricate different types of supramolecular architectures such as helix, β-sheet and staircase.

Keywords: Pseudopeptide, supramolecular helix, staircase, β-sheet, self-assembly

Introduction

In nature various biological systems such as rigid biomineralized shells and bones,[1] high-strength spider silks,[2] tobacco mosaic virus (TMV),[3] collagen triple helix [4] and DNA double helix [5] are the results of molecular self-assembly. The design and synthesis of suitable molecular building blocks that can act as potential subunits for desired supramolecular architectures is an active area of current research. Creation of supramolecular helices [6] and β-sheets [7] through the self-assembly of small peptide building blocks have attracted considerable attention in the recent time because of their biological importance in various neurodegenerative diseases such as Alzheimer's disease,[8] Huntington's disease,[9] and prion-protein [10]. Moreover it has been observed that

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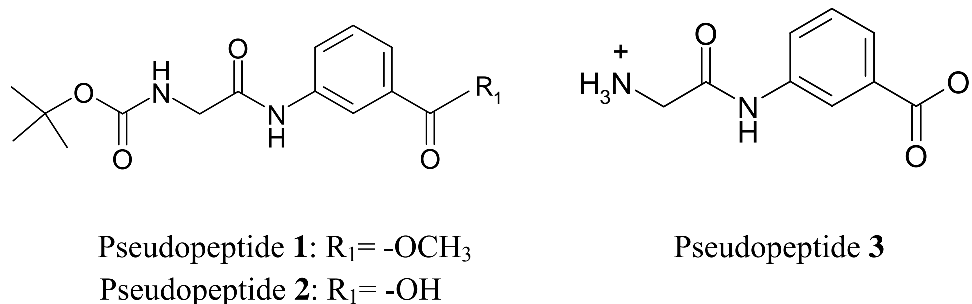
fabrication of various peptide based nanomaterials such as nanotubes, [11] nanorods, [12] and nanowires[13] can be achieved through molecular self-assembly.

Therefore developing easily modifiable molecular scaffolds that will self-assemble to various supramolecular structures is important. In this context we chose a pseudopeptide Gly-*m*-ABA (*m*-ABA = *m*-amino benzoic acid) which on modification at the terminal groups gives different self-assembling peptides such as Boc-Gly-*m*-ABA-OMe (**1**), Boc-Gly-*m*-ABA-OH (**2**) and $^{+}NH_3$-Gly-*m*-ABA-CO_2^-(**3**) (Figure 1). In **1** both N- and C-terminus are protected, whereas in **2** only N terminus is protected and in **3** both N- and C-terminus are free. The incorporation of *m*-aminobenzoic acid in **1**-**3** may help in self-assembly through π-stacking interactions. Moreover *m*-aminobenzoic acid which is considered as a substituted γ-amino butyric acid with an all *trans* extended configuration is expected to provide extended and semi-extended structure in the backbone of the pseudopeptides. It will be interesting to know how the modification of the terminal groups in the pseudopeptide influences the self-assembly in the solid state. The result will provide insights for engineering supramolecular architectures in crystal. The pseudopeptides **1-3** were synthesized by conventional solution phase methodology and their crystal structures were obtained by X-ray diffraction studies.



Pseudopeptide **1**: R_1= -OCH_3
Pseudopeptide **2**: R_1= -OH

Pseudopeptide **3**

Figure 1. Schematic diagram of pseudopeptides **1**-**3**.

Results and Discussion

The colorless orthorhombic crystals of pseudopeptide **1** were obtained from chloroform-petroleum ether mixture by slow evaporation. Pseudopeptide **1** crystallizes with two molecules in the unit cell designated as **1A** and **1B**. The SCHAKAL diagram of one of the isomers of **1** with atom numbering scheme is presented in Figure 2. The ϕ, ψ values of Gly in **1A** are 62.6 ^{o} and -130.6 ^{o} and that of in **1B** are -65.2 ^{o} and 138.0 ^{o}, respectively (Table 1). Therefore **1A** and **1B** are two enantiomeric structures with a bend around Gly residue. In the unit cell the isomers **1A** and **1B** are inter-linked in antiparallel fashion by two hydrogen bonds between N3A and O5B and between N3B and O5A with donor-acceptor distances of 2.840 and 2.957 Å, respectively, to form a molecular duplex -(**1A**-**1B)-** (Figure 3a and Table 2). The resulting 10-membered ring between **1A** and **1B** is nearly planar.

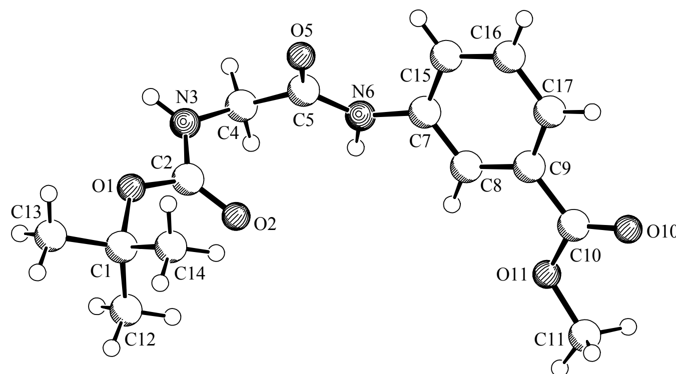


Figure 2. SCHAKAL diagram of pseudopeptide **1** with atom numbering scheme.

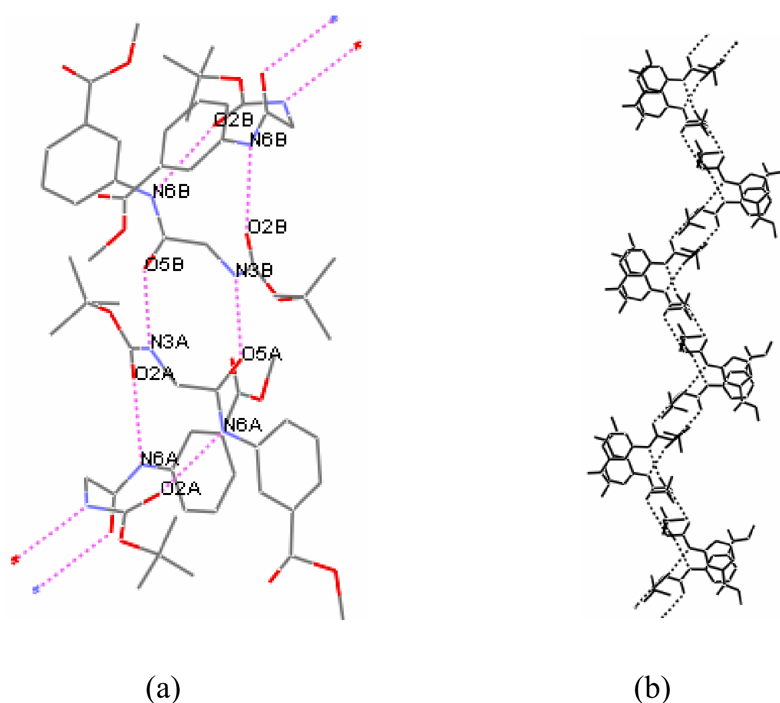


Figure 3. (a) Showing the packing of **1A** and **1B** through intermolecular hydrogen bonds (hydrogen atoms are omitted); (b) Showing the supramolecular helical assembly along the crystallographic *a* axis. Intermolecular hydrogen bonds are shown as dotted lines.

In the crystalline state the duplexes -(**1A-1B)-** are regularly inter-linked via intermolecular hydrogen bonds to form a supramolecular helix along the crystallographic *a* axis (Figure 3b). The pattern of self-assembly along the helix axis is found to be -(**1A-1B**)-(**1B-1A**)-(**1A-1B**)-(**1B-1A**)-. Two adjacent **1A** molecules are inter-connected in antiparallel fashion by two intermolecular hydrogen bonds between N6A and O2A with a donor-acceptor distance 2.866 Ǻ (Figure 3a, Table 2). Similarly two adjacent **1B** molecules are also connected through two intermolecular hydrogen bonds between N6B and O2B with a donor-acceptor distance of

2.896 Å. The resulting 14-membered rings between **1A** and **1A** and also between **1B** and **1B** are twisted. This twisted nature of hydrogen bonding incorporates helical sense in the self-assembly to produce supramolecular helical structure. The arrangement is further stabilized by π-π interactions between the phenyl rings of two adjacent **1A** and two adjacent **1B** molecules (Figure 3a,b). The result shows that the self-assembly of a small pseudopeptide can lead to a complex supramolecular architecture such as helix.

Table 1. Selected back-bone torsion angles (deg) in pseudopeptides **1-3**

Mol **1A**			
O1A-C2A-N3A-C4A	-177.5(1)	C5A-N6A-C7A-C8A	169.5(2)
C2A-N3A-C4A-C5A (φ)	62.6(2)	N6A-C7A-C8A-C9A	179.7(2)
N3A-C4A-C5A-N6A (ψ)	-130.6(2)	C7A-C8A-C9A-C10A	-178.4(1)
C4A-C5A-N6A-C7A	179.6 (2)	C8A-C9A-C10A-O11A	174.1(2)
Mol **1B**			
O1B-C2B-N3B-C4B	-179.6(1)	C5B-N6B-C7B-C8B	143.2(2)
C2B-N3B-C4B-C5B (φ)	-65.2(2)	N6B-C7B-C8B-C9B	-178.4(2)
N3B-C4B-C5B-N6B (ψ)	138.0(2)	C7B-C8B-C9B-C10B	177.8(2)
C4B-C5B-N6B-C7B	-176.2(2)	C8B-C9B-C10B-O11B	1.6(2)
2			
O1-C2-N3-C4	169.5(2)	C5-N6-C7-C8	-164.6(2)
C2-N3-C4-C5 (φ)	76.5(3)	N6-C7-C8-C9	178.2(2)
N3-C4-C5-N6 (ψ)	-171.4(2)	C7-C8-C9-C10	-177.4(2)
C4-C5-N6-C7	175.0(2)	C8-C9-C10-011	175.9(2)
3			
N1-C2-C3-N5	-175.9(1)	C6-C11-C10-C12	-177.3(1)
C2-C3-N5-C6	168.9(2)	C11-C10-C12-O13	-23.6(2)
C3-N5-C6-C11	153.1(2)	C11-C10-C12-O14	156.1(2)
N5-C6-C11-C10	171.9(1)		

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Table 2. Intermolecular hydrogen bonding parameters of pseudopeptides **1-3**

D-H---A	H---A/ Å	D---A/ Å	D-H---A/°
1			
N3A-H3A---O5B	1.98	2.840	178.8
N6A-H6A---O2A [a]	1.99	2.866	179.0
N3B-H3B---O5A	2.09	2.957	169.8
N6B-H6B---O2B [b]	1.98	2.896	174.8
2			
N6-H6---O10 [c]	2.17	3.006	171.1
O11-H11---O2 [d]	1.87	2.625	150.6
N3-H3---O5 [e]	2.08	2.921	174.7
3			
O15-H15A---O14 [f]	2.28	3.027	138.0
O15-H15B---O14 [g]	1.74	2.705	169.1
O15-H15A---O13	2.06	2.945	160.8
N1-H1B---O15	1.82	2.740	167.9
N1-H1C---O14 [h]	1.85	2.749	170.6
N1-H1A---O13 [i]	1.79	2.726	174.7
N5-H5---O4 [j]	2.02	2.882	159.9

Symmetry equivalents: [a]-x +1/2, -y + 3/2, z; [b] -x + 1/2, -y + 1/2, z; [c] -x + 1, -y + 1, -z + 1; [d]-x + 1, -y, -z + 1; [e] -x + 1/2, y + 1/2, -z + 1/2; [f] x + 1, -y + 1/2, z - 1/2; [g] -x + 1, -y, -z; [h] x, -y + 1/2, z - 1/2; [i] -x + 1, -y + 1, -z; [j] x - 1, y, z.

The hydrolysis of the methyl ester group at the C-terminus of peptide **1** affords peptide **2** (Figure 4). The single crystals of **2** are grown from ethyl acetate by slow evaporation. Peptide **2** crystallizes with one molecule in the asymmetric unit. The ϕ, ψ values at Gly (76.6°, -171.4°) and the backbone torsion angles at *m*-ABA indicate an extended structure in peptide **2** (Table 1, Figure 4). Due to the presence of free $–CO_2H$ at the C-terminus, peptide **2** shows a remarkable change in the self-assembly compared to peptide **1**. Two molecules of peptide **2** are inter-linked in antiparallel fashion through intermolecular hydrogen bonds between N6-H----O(10)=C to form molecular duplex (Figure 5a, Table 2). The duplexes are further inter-connected through hydrogen bonds between Boc C=O(2) and carboxylic H11-O11 to form supramolecular staircase running infinitely in the same direction (Figure 5b and Table 2). The formation of metal ion directed supramolecular straicase[14] and nanostaircase through self-assembly of conformationally rigid molecular scaffolds have been reported recently.[15] The present result shows that not only rigid molecular scaffolds but also flexible molecule like **2** can form supramolecular straicase through self-assembly.

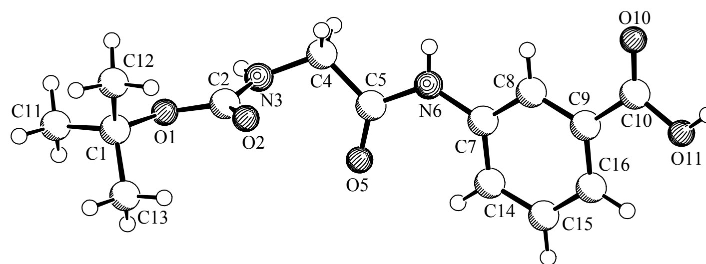

Figure 4. SCHAKAL diagram of pseudopeptide **2** with atom numbering scheme.

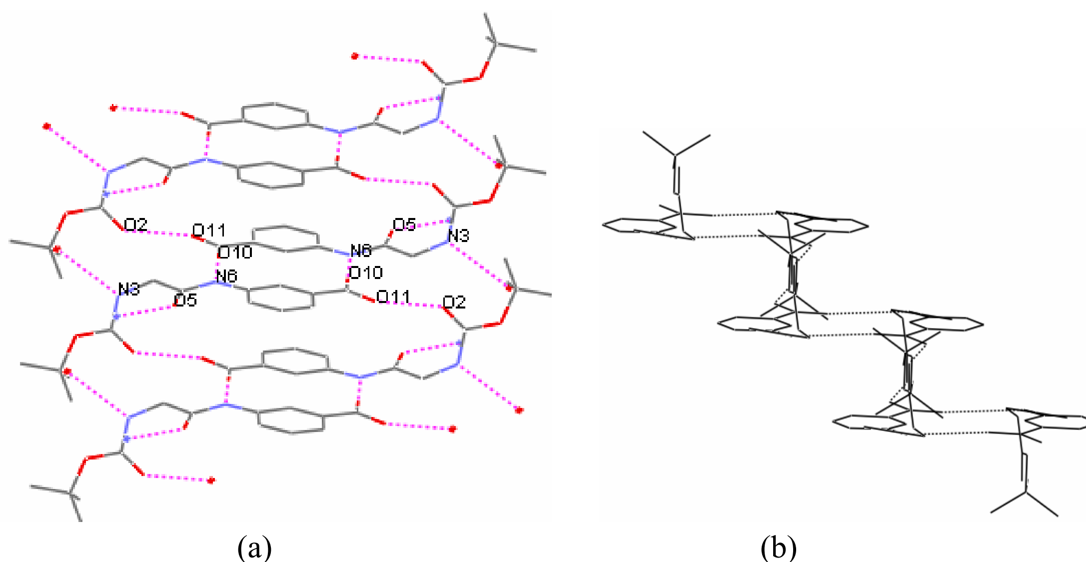

Figure 5. (a) Crystal packing of **2** illustrating the formation of supramolecular staircase (hydrogen atoms are omitted); (b) A lateral view of the same supramolecular staircase structure. Intermolecular hydrogen bonds are shown as dotted lines.

The removal of Boc group from the N-terminus of peptide **2** by acid catalysis produces water soluble peptide **3**. The colorless monoclinic crystals of peptide **3** are obtained from water by slow evaporation. In the solid state the peptide remains in the zwitterionic form (Figure 6). The backbone torsion angles of **3**, that characterize an extended conformation, include N1-C2-C3-N5 = -175.9 ^{o}, C2-C3-N5-C6 = 168.9 ^{o}, C3-N5-C6-C11 = 153.1 ^{o}, N5-C6-C11-C10 = 171.9 ^{o}, C6-C11-C10-C12 = -177.3 ^{o} and C11-C10-C12-O14 = 156.1 ^{o} (Figure 6 and Table 1). The incorporation of *m*-ABA helps to attain a fully extended conformation, which is necessary for β-sheet formation.

In the crystalline state peptide **3** are inter-linked in head-to-tail fashion along the crystallographic *a* axis through intermolecular hydrogen bonds N1-H1C---O14 between –CO_2^- and H_3^+N- (Figure 7, Table 2). The arrays of molecules are further inter-linked along the crystallographic *b* axis to form layers of peptides stabilized by the hydrogen bond between O4 and N5 with a donor-acceptor distance of 2.882 Å (Figure 7, Table 2). The arrangement is

further stabilized by π-π interactions between the phenyl rings and water mediated hydrogen bonds O15-H15A--O14, O15-H15A--O13 and N1-H1B--O15 between $–CO_2^-$ and H_3^+N- (Figure 7, Table 2). Several such layers are cross-linked along the crystallographic ***c*** axis through water mediated hydrogen bond O15-H15B--O14 and direct hydrogen bonds N1-H1A--O13 between $–CO_2^-$ and H_3^+N- to form supramolecular β-sheet structure (Figure 8, Table 2). It is well documented that π-π interactions[16] and β-sheet cross-linking[17] play significant roles in amyloid fibril formation. Supramolecular β-sheets also have many potential applications in material[18] as well as in biological sciences.[19]

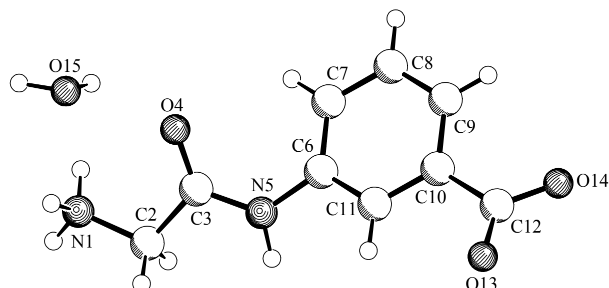

Figure 6. SCHAKAL diagrams of pseudopeptide **3** with atom numbering scheme.

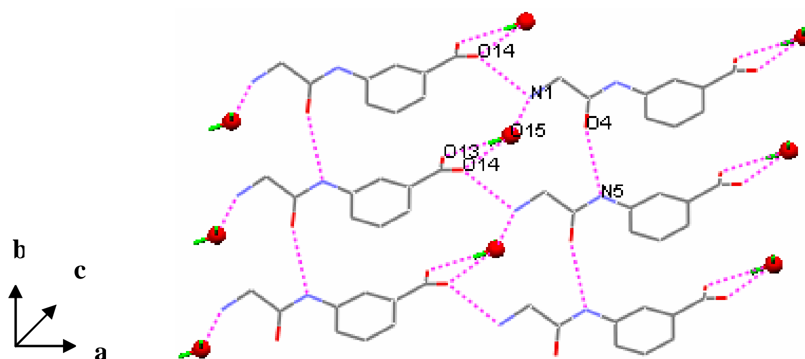

Figure 7. Packing diagram of **3** shows the formation layer of pseudopeptides along the crystallographic ***b*** axis.

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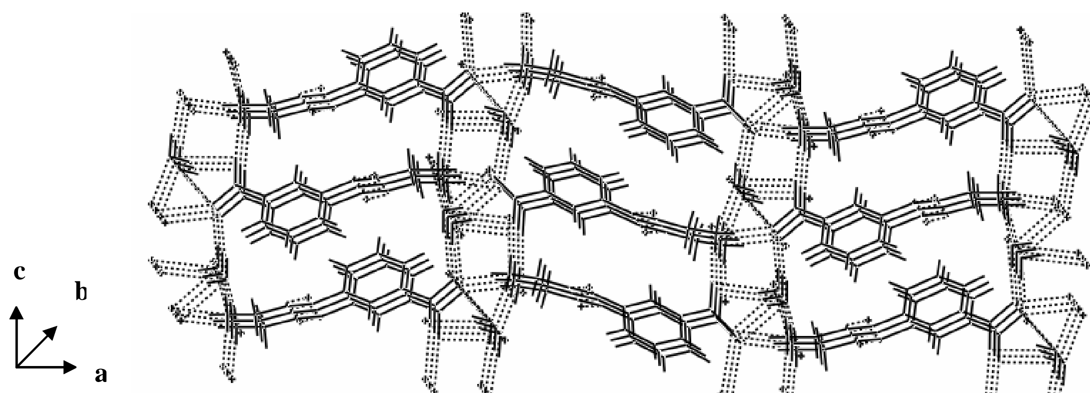

Figure 8. Showing the cross-linking between the pseudopeptide **3** layers along the crystallographic ***c*** axis to form supramolecular β-sheet through higher order self-assembly.

Conclusions

The present study shows that the terminally modified pseudopeptide Gly-*m*-ABA generates various kinds of building blocks that can self-assemble to different types of supramolecular architectures such as helix, β-sheet and staircase. The protection and deprotection of the N- and C-terminal groups of the pseudopeptide influence the pattern of self-assembly significantly. The gradual removal of protecting groups from **1** to **3** produces more number of donor and acceptor groups which can participate in fabricating supramolecular structures through hydrogen bond mediated self-assembly. The study provides valuable insights for engineering supramolecular architectures in crystal.

Experimental Section

Synthesis of peptides. The peptides **1-3** were synthesized by conventional solution phase methods.[20] The Boc group was used for N-terminal protection, and the C-terminus was protected as a methyl ester. Deprotection of N- and C-terminus were performed by using CF_3COOH and saponification, respectively. Couplings were mediated by dicyclohexylcarbodiimide (DCC). All peptides were characterized by thin layer chromatography on silica gel and purified by column chromatography using silica gel (100-200 mesh) as the stationary phase. The reported peptides **1-3** were fully characterized by X-ray crystallography, NMR and IR spectroscopy.

Peptide Boc-Gly-*m*-ABA-OMe (1). Boc-Gly-OH (2.0 g, 11.4 mmol) was dissolved in dichloromethane (DCM, 10 ml) in an ice-water bath. *m*-ABA-OMe obtained from its hydrochloride[13, 14] (4.3 g, 22.9 mmol) was added to it, followed by DCC (3.5 g, 17.2 mmol). The reaction mixture was stirred at room temperature for 1 day. The precipitated dicyclohexylurea

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(DCU) was filtered. The organic layer was washed with 1 M HCl (3 x 30 mL), 1 M Na_2CO_3 solution (3 x 30 mL) and water. The solvent was then dried over anhydrous Na_2SO_4 and evaporated in *vacuo,* giving a light yellow gum. Yield: 3.2 g (90.9%). Purification was done using silica gel as stationary phase and ethyl acetate-petroleum ether mixture as the eluent. Single crystals were grown from chloroform-petroleum ether mixture by slow evaporation and were stable at room temp. Mp = 105-107°C; Elemental analysis calcd for $C_{15}H_{20}N_2O_5$ (308.33): C, 58.43; H, 6.54; N, 9.09 %; Found: C, 58.37; H, 6.62; N, 9.15 %. IR (KBr): 3306, 2978, 1727, 1674, 1612, 1556, 1490, 1430, 1298, 1238, 1203, 1165 cm^{-1}. ^1H NMR 300 MHz ($CDCl_3$, δ ppm): 8.89 (*m*-ABA-NH, 1H, *s*), 8.06 [Ha (*m*-ABA), 1H, *s*], 7.82 [Hd (*m*-ABA), 1H, *d*, *J* = 7.8 Hz], 7.73 [Hb (*m*-ABA), 1H, *d*, *J* = 7.8 Hz], 7.33 [Hc (*m*-ABA), 1H, *t*, *J* = 8.1 Hz], 5.69 (Gly-NH, 1H, *t*, *J* = 5.2 Hz), 3.99 (C^{α}Hs of Gly, 2H, *d*, *J* = 5.2 Hz), 3.86 (-OCH_3, 3H, *s*), 1.44 (CH_3s Boc, 9H, *s*); ^{13}C NMR 75 MHz ($CDCl_3$, δ ppm): 168.3, 166.7, 156.5, 137.8, 130.7, 129.0, 125.4, 124.5, 120.9, 80.5, 52.2, 45.2, 28.3.

Peptide Boc-Gly-*m*-ABA–OH (2). Peptide **1** (3.2 g, 10.4 mmol) was dissolved in methanol (25 mL) and 2 M NaOH (7 mL) was added to it. The reaction mixture was stirred for 24 hr at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction methanol was evaporated. The residue was dissolved in water and washed with diethyl ether. The aqueous layer was cooled in ice-bath, neutralized with 2 M HCl and extracted with ethyl acetate. The solvent was evaporated in *vacuo* to give a white solid. Yield: 2.75 g (90.1%). Purification was done using silica gel as stationary phase and ethyl acetate-petroleum ether mixture as the eluent. Single crystals were grown from ethyl acetate by slow evaporation and were stable at room temp. Mp = 195-197°C; Elemental analysis calcd for $C_{14}H_{18}N_2O_5$ (294.30): C, 57.13; H, 6.16; N, 9.53 %; Found: C, 57.21; H, 6.23; N, 9.61 %. IR (KBr): 3319, 3059, 2975, 2927, 1690, 1666, 1548, 1482, 1422, 1373, 1299, 1248, 1153 cm^{-1}. ^1H NMR 300 MHz (DMSO-d_6, δ ppm): 10.12 (*m*-ABA-NH, 1H, *s*), 8.22 [Ha (*m*-ABA), 1H, *s*], 7.76 [Hd (*m*-ABA), 1H, *d*, *J* = 7.7 Hz], 7.62 [Hb (*m*-ABA), 1H, *d*, *J* = 7.7 Hz], 7.42 [Hc (*m*-ABA), 1H, *t*, *J* = 8.1 Hz], 7.01 (Gly-NH, 1H, *t*), 4.00 (C^{α}Hs of Gly, 2H, *d*, *J* = 5.4 Hz), 1.38 (CH_3s Boc, 9H, *s*). ^{13}C NMR 75 MHz (DMSO-d_6, δ ppm): 169.1, 167.7, 156.5, 139.5, 131.7, 129.5, 124.6, 123.8, 120.4, 78.8, 44.2, 28.6.

Peptide $^+NH_3$-Gly-*m*-ABA-CO_2^-(3). Peptide **2** (2.75 g, 9.4 mmol) was dissolved in trifluoroacetic acid (6 mL) at 0°C. Then the reaction mixture was stirred at room temperature and the progress of deprotection was monitored by TLC. After 6 hr of stirring trifluoroacetic acid was removed under *vacuo* and the residue was taken in 15 ml of distilled water, washed with diethyl ether (2x15ml). The aqueous part was then dried under *vacuo* to yield white solid. Yield: 1.5 g (82.6%). Purification was done using silica gel as stationary phase and chloroform-methanol mixture as the eluent. Single crystals were grown from water by slow evaporation and were stable at room temp. Mp = 231-233°C. Elemental analysis calcd for $C_9H_{10}N_2O_2.H_2O$ (212.20): C, 50.94; H, 5.70; N, 13.20 %; Found: C, 50.86; H, 5.64; N, 13.15 %. IR (KBr): 3401, 3286, 2921, 2670, 2370, 1675, 1544, 1383, 1298, 1119 cm^{-1}. ^1H NMR 300 MHz (DMSO-d_6, δ ppm): 10.70 (*m*-ABA-NH, 1H, *s*), 8.26 [Ha (*m*-ABA), 1H, *s*], 7.78 [Hd (*m*-ABA), 1H, *d*, *J*

= 7.8 Hz], 7.67 [Hb (*m*-ABA), 1H, *d*, J = 7.8 Hz], 7.47 [Hc (*m*-ABA), 1H, *t*, J = 8.1 Hz], 4.00 (C^{α}Hs of Gly, 2H, br. *s*). ^{13}C NMR 75 MHz (DMSO-d_6, δ ppm): 167.5, 165.5, 138.8, 132.1, 129.7, 125.2, 123.8, 120.4, 41.5.

Single crystal X-ray diffraction study

Data sets were collected with Nonius KappaCCD diffractometers using Mo-radiation equipped with a rotating anode generator (Table 3). Programs used: data collection COLLECT,[21] data reduction Denzo-SMN, [22] absorption correction SORTAV [23] and Denzo, [24] structure solution SHELXS-97, [25] structure refinement SHELXL-97, [26] graphics SCHAKAL. [27]

CCDC 658984(**1**), 658985(**2**), and 658986(**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internet.) +44(1223)336-033, E-mail: deposit@ccdc.cam.ac.uk].

Table 3. Crystallographic data for pseudopeptides **1-3**

	1	**2**	**3**
Formula	$C_{15}H_{20}N_2O_5$	$C_{14}H_{18}N_2O_5$	$C_9H_{10}N_2O_3$ * H_2O
Formula weight	308.33	294.30	212.21
Crystallising solvent	Chloroform	Ethyl acetate	Water
Crystal colour	Colourless	Colourless	Colourless
Crystal system	Orthorhombic	Monoclinic	Monoclinic
Space group	*P*ccn	*C*2/c	*P*2$_1$/c
a (Å)	20.0442(3)	28.4205(6)	4.7455(1)
b (Å)	16.8270(2)	5.4632(1)	8.9043(1)
c (Å)	20.0430(2)	20.6704(5)	23.0044(1)
α (^{0})	90.000	90.000	90.000
β (^{0})	90.000	115.767(2)	94.551(1)
γ (^{0})	90.000	90.000	90.000
Z	16	8	4
V (Å^3)	6760.18(15)	2890.31(11)	968.99(2)
Temperature (^{0}C)	-75	-50	-50
μ (cm^{-1})	9.20	8.68	9.82
$D_{calculated}$ (g cm^{-3})	1.212	1.353	1.455
R (int)	0.070	0.073	0.052
No of independent reflections	8060	2514	1744
Reflections with I> 2σ (I)	4324	1912	1646
R_1 (I> 2σ (I))	0.051	0.049	0.049
wR_2 (I> 2σ(I))	0.124	0.109	0.137

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References and Notes

1. (a) Mann, S. *Biomineralization: Principles and Concepts in Bioinorganic Materials Chemistry;* Oxford University Press: Oxford, 2001. (b) Vincent J. F.; Currey, J. D. *The Mechanical Properties of Biological Materials*; Eds.; Cambridge University Press: Cambridge, 1980.
2. Vincent J. F.; Currey, J. D. *The Mechanical Properties of Biological Materials*; Eds; Cambridge University Press: Cambridge, 1980**.**
3. Franklin, R. E. *Nature* **1955**, *175*, 379.
4. Ramachandran, G. N.; Kartha, G. *Nature* **1955**, *176*, 593.
5. Watson, J. D.; Crick, F. C. H. *Nature* **1953**, *171*, 737.
6. (a) Haldar, D.; Drew, M. G. B.; Banerjee, A. *Tetrahedron* **2006**, *62,* 6370. (b) Das, A. K.; Banerjee, A.; Drew, M. G. B.; Ray, S.; Haldar, D.; Banerjee, A. *Tetrahedron* **2005**, *61*, 5027. (c) Görbitz, C. H. *Chem.-Eur. J.* **2007**, *13*, 1022. (d) Guha, S.; Drew, M. G. B.; Banerjee, A. *Org. Lett.* **2007**, *9*, 1347. (e) Parthasarathy, R.; Chaturvedi, S.; Go, K. *Proc. Natl. Acad. Sci. USA* **1990**, *87*, 871. (f) Guha, S.; Drew, M. G. B.; Banerjee, A. *Tetrahedron Lett.* **2006**, *47*, 7951.
7. (a) Dutt, A.; Drew, M. G. B.; Pramanik, A. *Org. Biomol. Chem*. **2005**, *3*, 2250. (b) Kundu, S. K.; Mazumdar, P. A.; Das, A. K.; Bertolasi, V.; Pramanik, A. *J. Chem. Soc. Perkin Trans. 2* **2002**, 1602. (c) Maji, S. K.; Haldar, D.; Drew, M. G. B.; Banerjee, A.; Das, A. K.; Banerjee, A. *Tetrahedron* **2004**, *60***,** 3251. (d) Banerjee, A.; Das, A. K.; Drew, M. G. B.; Banerjee, A. *Tetrahedron* **2005**, *61***,** 5906. (e) Ray, S.; Das, A. K.; Drew, M. G. B.; Banerjee, A. *Chem. Commun*. **2006**, *40*, 4230. (f) Ray, S.; Drew, M. G. B.; Das, A. K.; Banerjee, A. *Supramolecular Chemistry* **2006**, *18*, 455.
8. (a) Taubes, G.; *Science* **1996**, *271*, 1493. (b) Lansbury, P. T. Jr. *Acc. Chem. Res*. **1996**, *29*, 317. (c) Rochet, J. C.; Lansbury, P. T. Jr. *Curr. Opin. Struct. Biol*. **2000**, *10*, 60.
9. (a) Goedert, M.; Spillntini, M. G.; Davies, S. W. *Curr. Opin. Neurobiol*. **1998**, *8*, 619. (b) Spillantini, M. G.; Crowther, R. A.; Jakes, R.; Hasegawa, M.; Goedert, M. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 6469.
10. (a) Pan, K. M.; Baldwin, M.; Nguyen, J.; Gasset, M.; Serban, A.; Groth, D.; Mehlhorn, I.; Huang, Z.; Fletterick, R. J.; Cohen, F. E. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 10962. (b) Prusiner, S. B. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 13363.

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11. (a) Reches, M.; Gazit, E. *Nano Lett.* **2004**, *4*, 581. (b) Ghadiri, M. R.; Granja, J. R.; Buehler, L. K. *Nature* **1994**, *369*, 301. (c) Guha, S.; Drew, M. G. B.; Banerjee, A. *Chem. Mater.* **2008**, *20*, 2282. (d) Ray, S.; Drew, M. G. B.; Das, A. K.; Banerjee, A. *Tetrahedron* **2006**, *62*, 7274.
12. Haldar, D.; Banerjee, A.; Drew, M. G. B.; Das, A. K.; Banerjee, A. *Chem. Commun*. **2003**, 1406.
13. Reches, M.; Gazit, E. *Science* **2003**, *300*, 625.
14. (a) Ghosh, S, K.; Bharadwaj, P. K. *Eur. J. Inorg. Chem.* **2005**, 4886. (b) Gabbai, F. P.; Schier, A.; Riede, J. *Angew. Chem., Int. Ed.* **1998**, *37*, 622. (c) Fortin, D; Drouin, M.; Harvey, P. D. *J. Am. Chem. Soc.* **1998**, *120*, 5351. (d) Nagata, N.; Kugimiya, S.; Fujiwara, E.; Kobuke, Y. *New J. Chem.* **2003**, *27*, 743. (e) Ren, C, -X.; Zhu, H, -L.; Yang, G.; Chen, X. –M. *J. Chem. Soc.; Dalton Trans.* **2001**, 85. (f) Alexakis, A.; Tomassini, A.; Chouillet, C.; Roland, S.; Mangeney, P.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 4093.
15. Ray, S.; Hegde, R. P.; Das, A. K.; Shamala, N.; Banerjee, A. *Tetrahedron* **2006**, *62***,** 9603.
16. Gazit, E. *FASEB J*. **2002**, *16*, 77.
17. (a) Makin O. S.; Serpell, L. C. *J. Mol. Biol*. **2004**, *335*, 1279. (b) Bond, J. P.; Deverin, S. P.; Inouye, H.; El-Agnaf, O. M. A.; Teeter, M. M.; Krischner, D. A. *J. Struc. Biol*. **2003**, *141*, 156. (c) Sundae, M.; Serpell, L. C.; Bartlam, M.; Fraser, P. E.; Pepys, M. B.; Blake, C. C. *J. Mol. Biol*. **1997,** *273*, 729. (d) Sundae, M.; Blake, C. *Adv. Protein. Chem*. **1997**, *50*, 123. (e) Damas, A. M.; Saraiva, M. J. *J. Struc. Biol*. **2000**, *130*, 290.
18. (a) Rathore, O.; Sogah, D. Y. *J. Am. Chem. Soc.* **2001**, *123*, 5231. (b) Krejchi, M. T.; Atkins, E. D.T.; Waddon, A. J.; Fournier, M. J.; Mason, T. L.; Tirrell, D. A. *Science* **1994**, *265*, 1427. (c) Caplan, M. R.; Moore, P. N.; Zhang, S.; Kamm, R. D.; Lauffenburger, D. A. *Biomacromolecules* **2000**, *1*, 627. (d) Vauthey, S.; Santoso, S.; Gong, H.; Watson, N.; Zhang, S. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 5355.
19. (a) Antzutkin, O. N.; Balbach, J. J.; Leapman, R. D.; Rizzo, N. W.; Reed, J.; Tycko, R. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 13045. (b) Tjernberg, L. O.; Callaway, D. J. E.; Tjernberg, A.; Hahne, S.; Lilliehook, C.; Terenius, L.; Thyberg, J.; Nordstedt, C. *J. Biol. Chem*. **1999**, *274*, 12619. (c) Benzinger, T. L. S.; Gregory, D. M.; Burkoth, T. S.; Miller-Auer, H.; Lynn, D. G.; Botto, R. E.; Meredith, S. C. *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 13407. (d) Wang, W.; Hecht, M. H. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 2760.
20. Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*; Springer-Verlag: New York, 1984; pp 1-282.
21. Hooft, R. Collect - Data Collection Software, 1998, Nonius B.V., The Netherlands.
22. Otwinowski, Z.; Minor, W. *Methods in Enzymology* **1997**, *276*, 307.
23. (a) Blessing, R. H. *Acta Cryst.* **1995**, *A51*, 33. (b) Blessing, R. H. *J. Appl. Cryst.* **1997**, *30*, 421.
24. Otwinowski, Z.; Borek, D.; Majewski, W.; Minor, W. *Acta Cryst.* **2003**, *A59*, 228.
25. Sheldrick, G. M. *Acta Cryst.* **1990**, A46, 467.
26. Sheldrick, G. M. *Acta Cryst.* **2008**, A64, 112.

27. Keller, E. SCHAKAL – *A computer program for the graphic representation of molecular and crystallographic models*, 1997, University Freiburg, Germany.

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