Electronic Supplementary Information (*ESI*)

Marked Difference in Self-assembly, Morphology, and Cell Viability of Positional Isomeric Dipeptides Generated by Reversal of Sequence

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Detail synthesis of Boc-Aib-*m*ABA-OMe (Peptide 2)

Synthesis of Boc-Aib-OH

The amino acid α-aminoisobutyric acid (5 g, 48.54 mmol) was suspended in a 1:1 tetrahydrofuran (THF) water mixture. Solid $NaHCO_3$ (12.23 g, 145.62mmol) was added and Boc-anhydride (11.63 mL, 53.39 mmol) was added to it. The reaction mixture was stirred at room temperature over night. After 24 h, the THF layer should be driven out with the help of vaccum pump. The aqueous layer was cooled in an icebath, acidified with 2M HCl and extracted with ethylacetate. The organic layer was washed with excess of water and dried over anhydrous Na_2SO_4 and evaporated in *vacuo* producing a white solid. Yield: 8.0 g (81.21%).

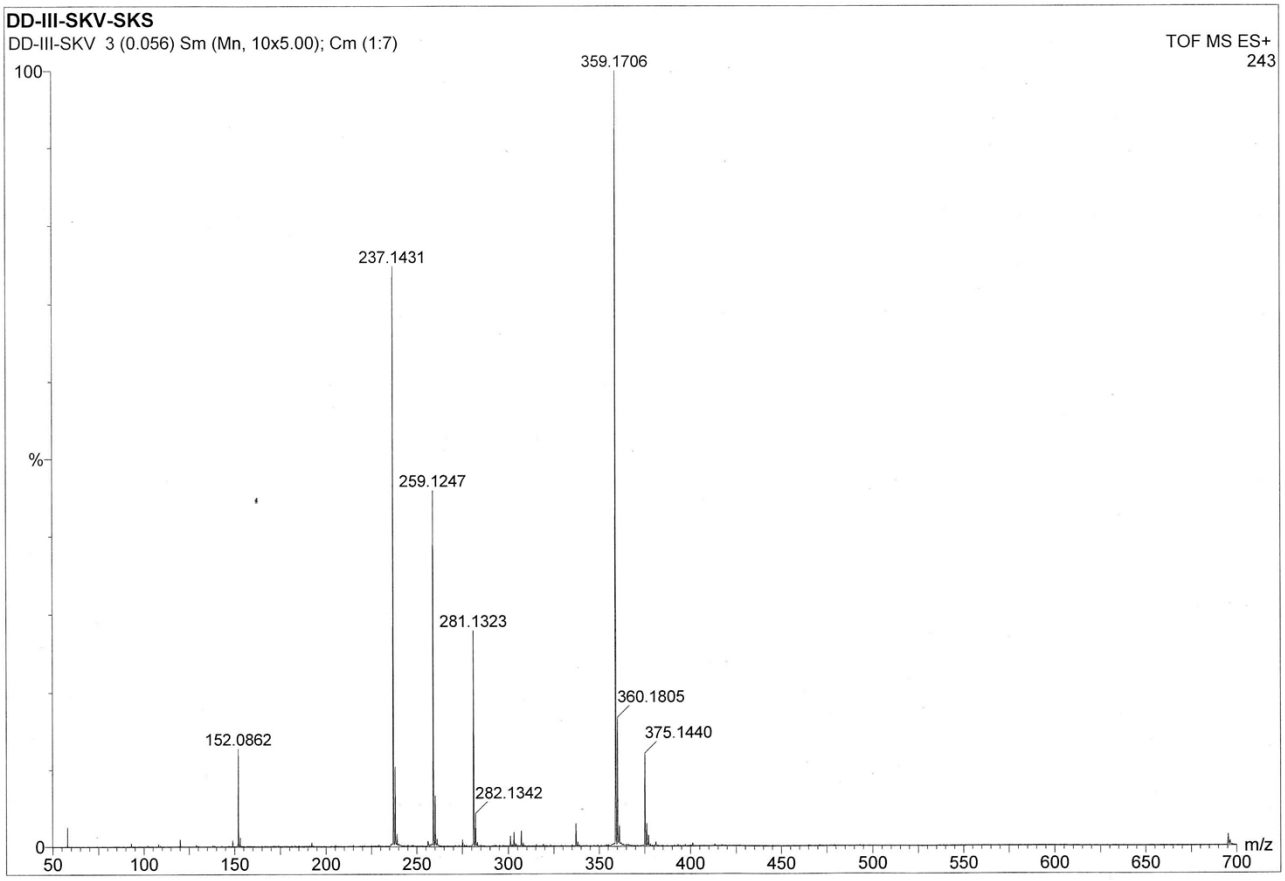
Synthesis of the peptide Boc-Aib-*m*ABA-OMe (Peptide 2)

Boc-Aib-OH (0.65 g, 3.25 mmol) was dissolved in dimethylformamide (DMF; 10 mL). *m*-ABA-OMe (1.40 g, 6.5 mmol) obtained from its hydrochloride was added followed by DC DCC (0.97 g, 4.87 mmol) and HOBT (0.42 g, 3.25 mmol). The reaction mixture was stirred at room temperature for 1 day. The precipitated dicyclohexylurea (DCU) was filtered and diluted with ethyl acetate (80 mL). The organic layer was washed with excess of water, 1M HCl (3 X 30 mL), 1M Na_2CO_3 solution (3 X 30 mL) and again with water. The solvent was then dried over anhydrous Na_2SO_4 and evaporated in *vacuo*, giving a light yellow gum. Purification was done using silica gel as stationary phase and an ethyl acetate-petroleum ether mixture as the eluent. Yield: 0.95 g (88.78%). M.p = 138^0C.

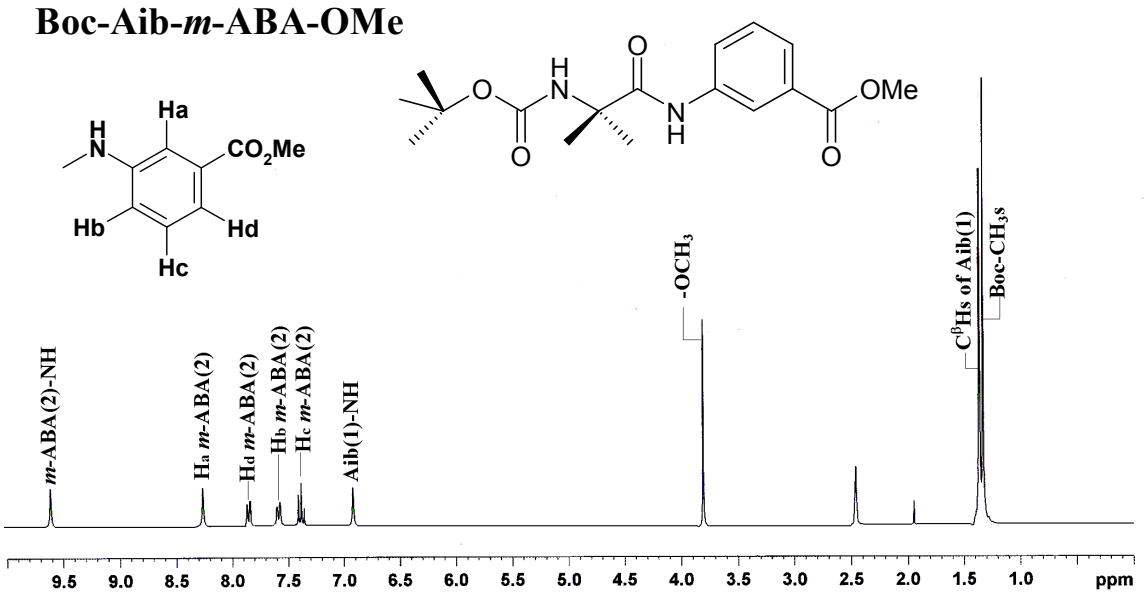
Single Crystal X-Ray Diffraction

Diffraction data for peptide **2** grown by slow evaporation of methanol was collected with MoKα radiation at 100 K using the Bruker SMART CCD diffractometer System. Data analyses were carried out with the Bruker SAINT program. The structures were solved using direct methods with the SHELXL-2013 program (Sheldrick, 2013). For peptide **1** and **2** the structures were refined on F^2 using SHELXL-2013 (Sheldrick, 2013) to R1=0.039; wR2 =0.103 for 4367 reflections with $I > 2\sigma(I)$ for peptide **1** (*Chem. Commun.*, **2014**, *50*, 2638-2641), and to R1=0.052; wR2 =0.097 for 2530 reflections with $I > 2\sigma(I)$ for peptide 2, respectively. Crystallographic details of peptide **1** and **2** have been deposited at the Cambridge Crystallographic Data Centre; reference CCDC no of peptide **1** is 949965 (*Chem. Commun.*, **2014**, *50*, 2638-2641) and that of peptide **2** is 992075. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

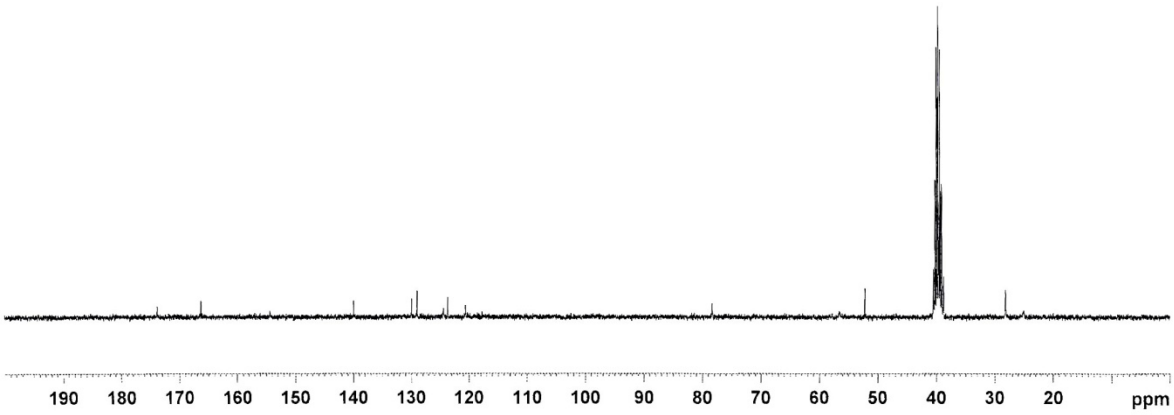
Detail characterization of Boc-Aib-*m*ABA-OMe (Peptide 2)



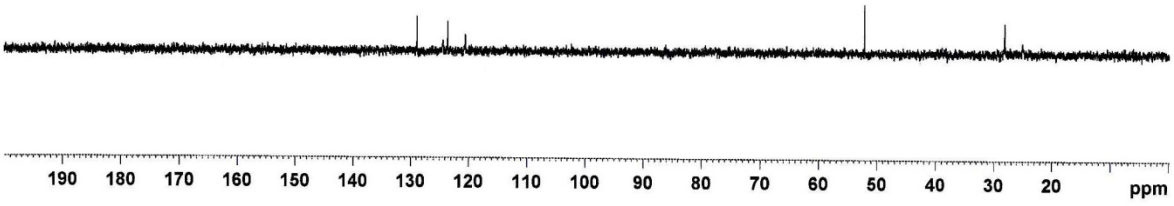
Mass spectrum of peptide **2**



^{1}H NMR spectrum of peptide **2** in DMSO-D6 (300 MHz)



^{13}C NMR spectrum of peptide **2** in DMSO-D6 (75MHz)



DEPT-135 spectrum of peptide **2** in DMSO-D6 (75MHz)

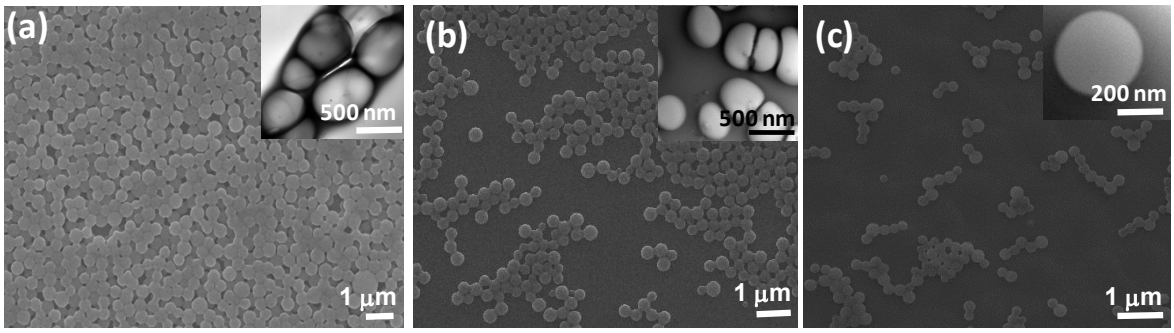


Fig. *S1* FE-SEM images of methanolic solutions of peptide at concentrations of: (a) 10 mM; (b) 5 mM, arrows indicate the fused spherical structures and (c) 1 mM solutions. In the insets of (a), (b) and (c) the TEM images show the hollow nature of the spherical structures

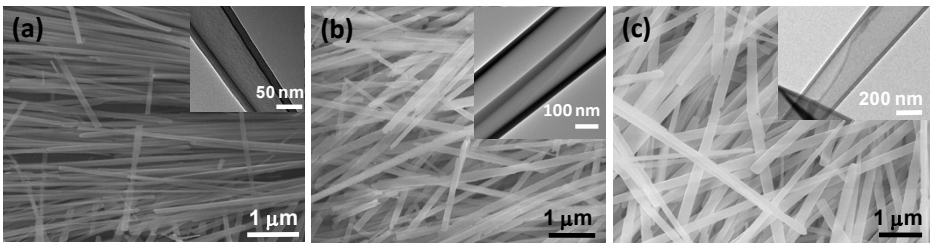


Fig. *S2* Different types of microscopic analysis showing the formation of tubular structures self-assembled from methanolic solutions. SEM images of peptide at concentrations of: (a) 1 mM, (b) 5 mM, and (c) 10 mM solutions. In the insets of (a), (b) and (c) the TEM images show the hollow nature of the nanotubes

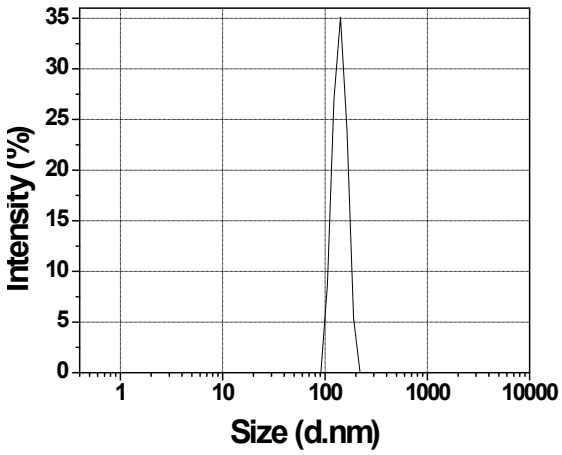


Fig. *S3* Size distribution profile in DLS study of peptide **2** showing hydrodynamic diameter, 122.58 nm, with polydispersity index, 1.00

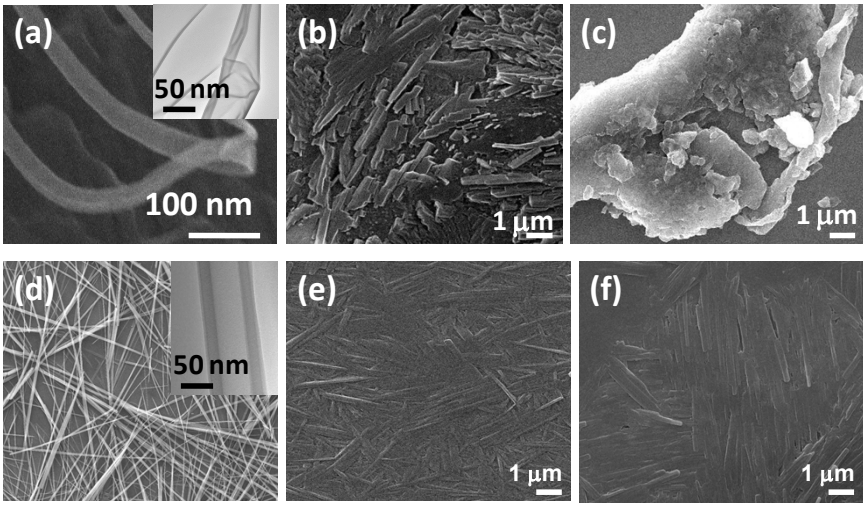


Fig. *S4* FE-SEM images of peptides **1** and **2**, obtained after thermal treatment for 1hr in a convection oven at a constant temperature of 50°C [(a) peptide **1** and (d) peptide **2**], 170°C [(b) peptide **1** and (e) peptide **2**] and 200°C [(c) peptide **1** and (f) peptide **2**]

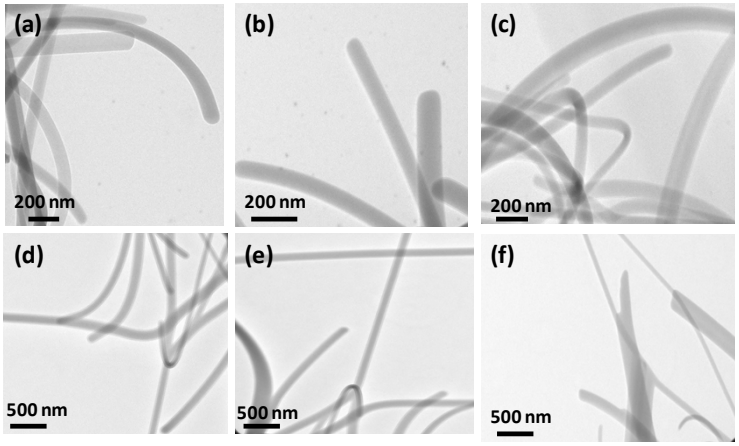


Fig. *S5* TEM images of peptide **2** forming nano tubes from (a) chloroform-methanol (1:1 v/v), (b) toluene, (c) from ethyl-acetate, (d) $CHCl_3$-Petroleum ether (1:1 v/v), (e) acetone and (f) dimethylformamide solvent.

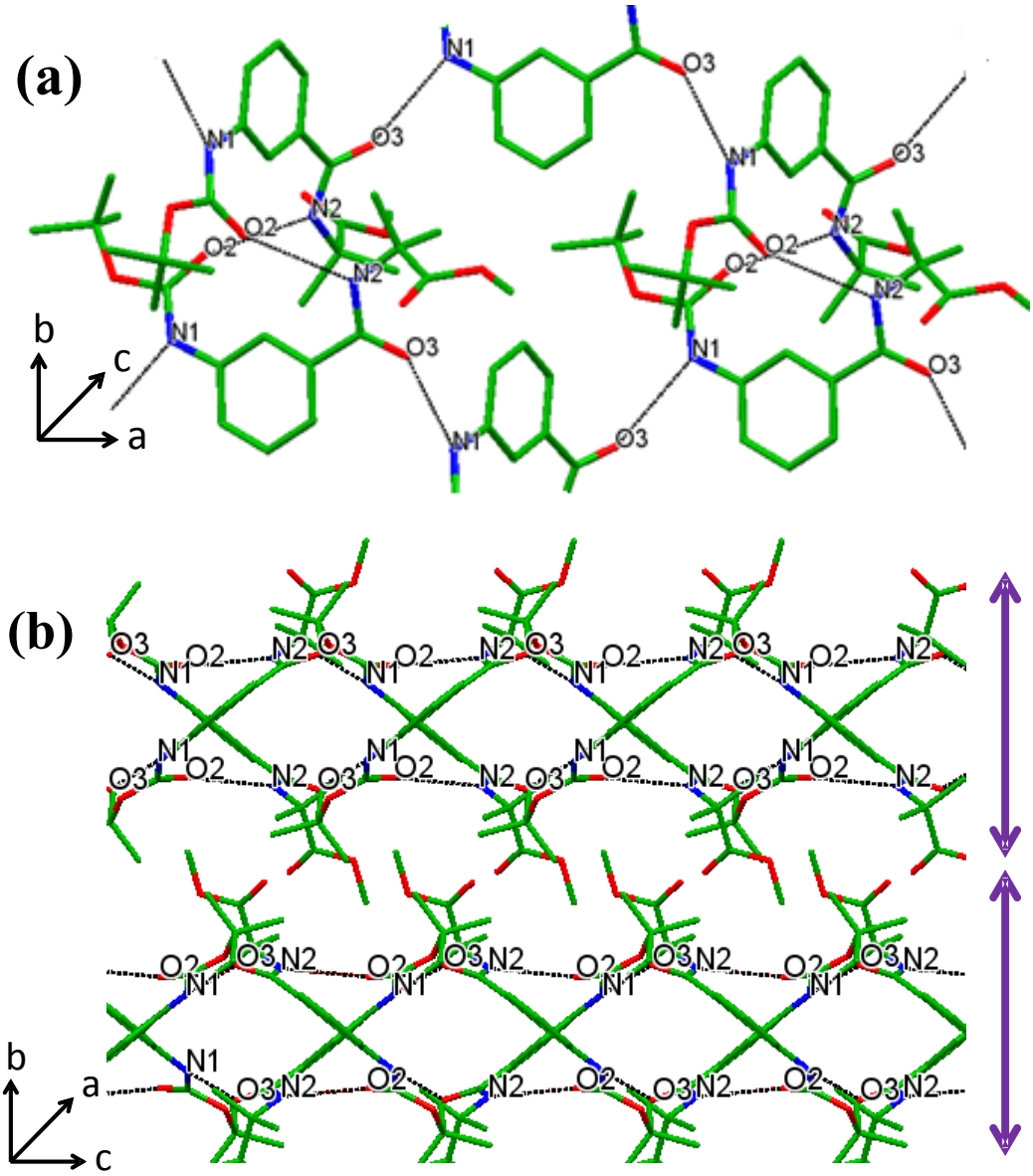


Fig. *S6* X-ray crystallographic structure of peptide **1**; (a) peptide molecules self-assemble to form β-sheet like structure in *ab* plane; (b) β-sheet like structures are stacking layer by layer in *bc* plane (Taken from Chem. Commun. 2014, 50, 2638-2641)

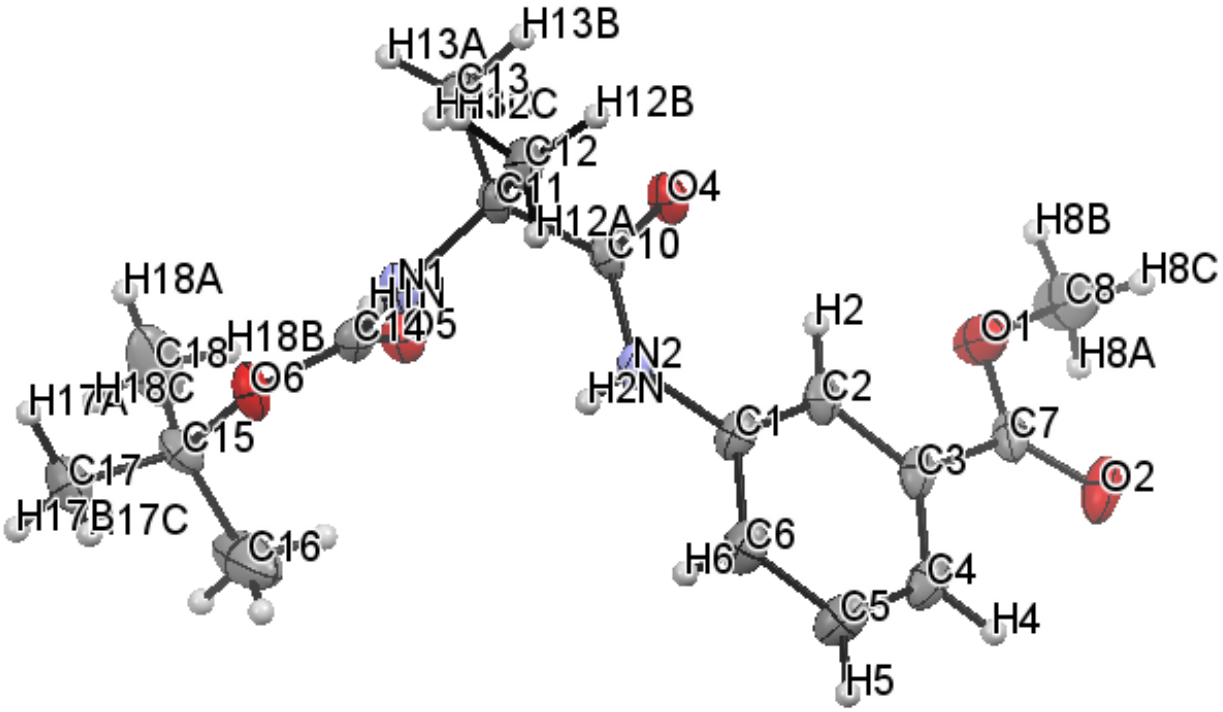
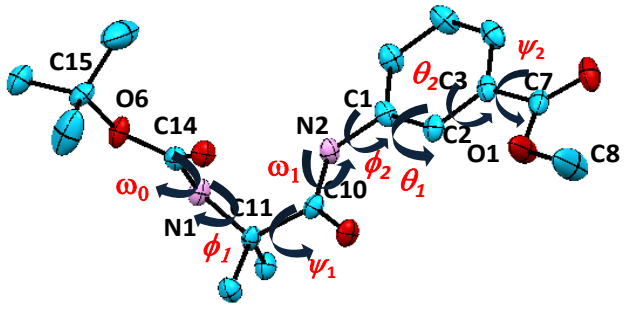


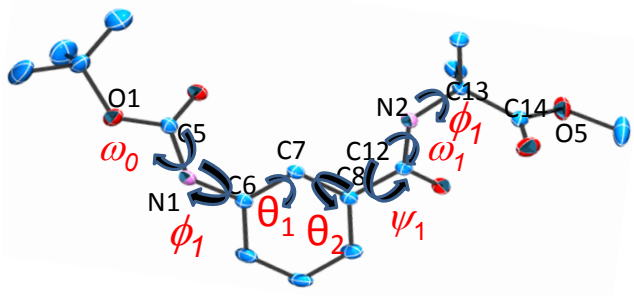
Fig. *S7* ORTEP diagram of peptide **2**. Percentage probability of the ellipsoids is 50 %

Table *S1* Selected backbone torsion angles (°) for peptides **1** and **2**



Selected backbone torsion angles (°) for peptide **2**

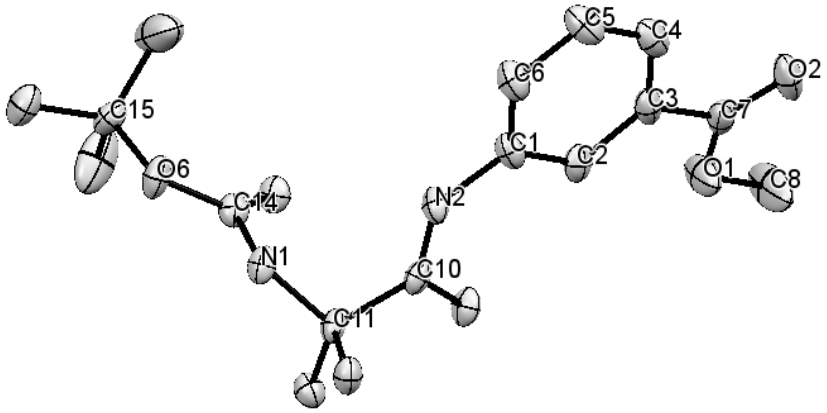
N1-C14-O6-C15	178.2(3)	C2-C1-N2-C10 (ϕ_2)	-2.4(6)
C11-N1-C14-O6 (w_0)	-164.3(3)	C3-C2-C1-N2 (θ_1)	-179.9(4)
C10-C11-N1-C14(ϕ_1)	-61.2(4)	C7-C3-C2-C1 (θ_2)	178.9(3)
N2-C10-C11-N1 (ψ_1)	-42.2(4)	O1-C7-C3-C2 (ψ_2)	-10.3(5)
C1-N2-C10-C11 (w_1)	176.2(3)		



Selected backbone torsion angles (°) for peptide**1** (Taken from Chem. Commun. 2014, 50, 2638-2641)

N1-C5-O1-C4	-179.25(10)	N2-C12-C8-C7 (ψ_1)	22.87(13)
C6-N1-C5-O1 (w_0)	-177.19(9)	C13-N2-C12-C8 (w_1)	-178.94(8)
C7-C6-N1-C5(ϕ_1)	24.31(15)	C14-C13-N2-C12 (ϕ_2)	-55.80(11)
C8-C7-C6-N1 (θ_1)	177.31(8)	O5-C14-C13-N2 (ψ_2)	145.55(8)
C12-C8-C7-C6 (θ_2)	177.78(8)		

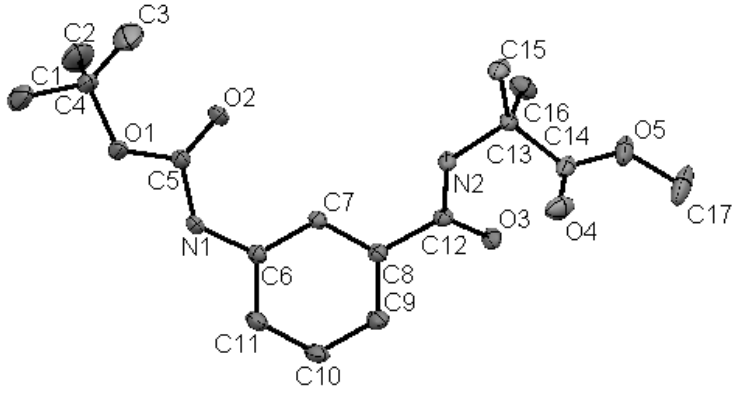
Table *S2* Intermolecular hydrogen bonds parameters for peptides **1** and **2**



Peptide 2

Type	N....O/(Å)	H....O/(Å)	O....H-N/(°)
N(1)-H(1)...O(5)[a]	2.915(4)	2.06(4)	164(3)
N(2)-H(2)...O(4)[a]	2.846(5)	2.13(4)	143(3)

Symmetry elements: [a] 1.5-x, y, ½+z, [b] 1.5-x, y, ½+z



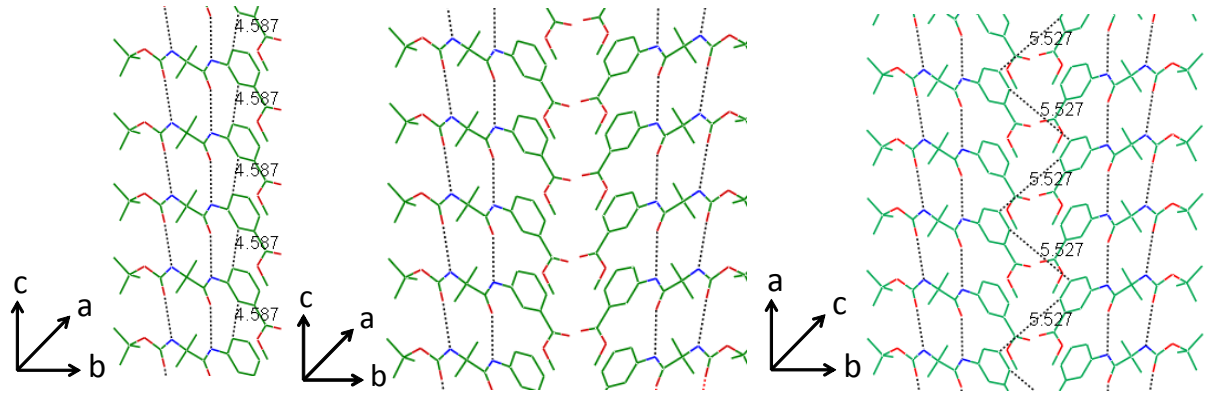
Peptide 1

Type	N....O/(Å)	H....O/(Å)	O....H-N/(°)
N(2)-H(2)...O(2)[a]	2.943(1)	2.08(2)	176(1)
N(1)-H(1)...O(3)[b]	2.934(1)	2.10(2)	160(1)

Symmetry elements: [a]-x, y, -z+1/2; [b] -x+1/2, y-1/2, -z+1/2

Table *S3* Crystallographic refinement details for peptide **2**

Crystallographic refinement details	**Peptide 2**
Crystal Colour	Colourless
Chemical Formula	$C_{17}H_{24}N_2O_5$
Formula Weight (g)	336.37
Crystal System	orthorhombic
Space group	P c a 2_1
Z	4
a (Å)	16.161(2)
b (Å)	12.5161(16)
c (Å)	9.3110(12)
α(°)	90.00
β (°)	90.00
γ(°)	90.00
V (Å^3)	1883.3(4)
density (gcm^{-3})	1.186
Temperature (K)	100
Unique reflections	3973
reflections I>2σ(I)	2530
Nº Parameters	228
GoF	0.977
R_1 [I>2σ(I)], all	0.0526, 0.1044
wR_2[I>2σ(I)], all	0.0985, 0.1172
residual electron density (e/Å^3)	0.264 and -0.232



(a) **(b)** **(c)**

Fig. *S8* X-ray crystallographic structure of peptide **2**; (a) peptide molecules self-assemble in *bc* plane to form a β-sheet structure. The closest π-stacking distance between two aromatic rings is 4.587 Å (b) Peptide molecules again self-assemble in *ab* plane to form another zipper like structure; and (c) the closest π-stacking distance between two diagonally situated aromatic rings is 5.527 Å

In case of peptide **1** the formation of nanovesicles by peptide **1** may be envisaged by considering the wrapping of the β-sheet-like layers in two different directions simultaneously (Fig. *S9*). We assumed in our previous study, that thermal treatment or interaction with -CH_3 functional group on different SAM surfaces or in presence of different solvents, like acetone, ethyl acetate, DMF and chloroform-petroleum ether (1:1 v/v), the two-ways wrapping of β-sheet layers opens up and they are arranged side by side to form the fibrils/ribbons (Fig. *S9*). Again in chloroform-methanol solvent mixture (1:1 v/v) and aromatic solvent like toluene β-sheet-like layers may fold in only one direction to form the nano-tubes (Fig. *S9*). But under all the variable conditions peptide **2** maintains the one way wrapping of the sheet-like structures.

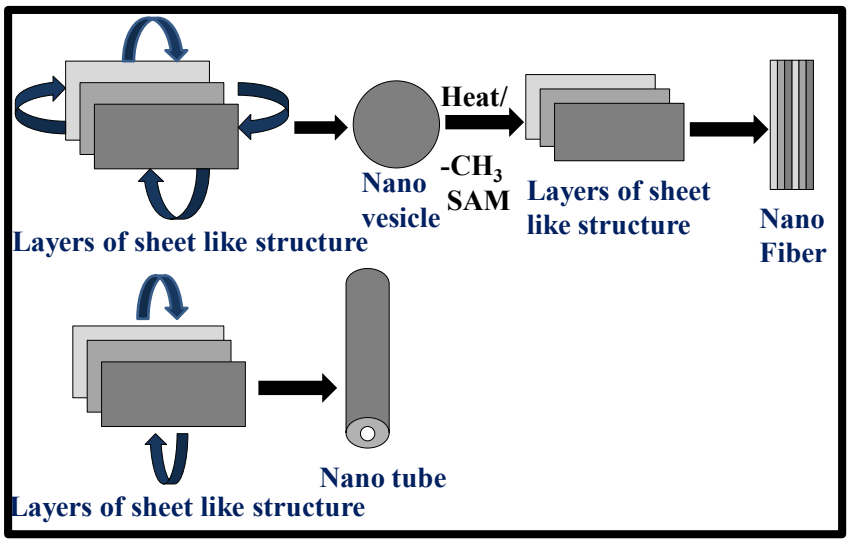


Fig. *S9* Schematic representation of formation of different nano-structures

Table *S4* Solid state FT-IR spectral analysis of as synthesized peptide **2** and its tubular form

	N–H stretching vibration &overtone of the N–H bending vibration (cm^{-1})	C=O stretching vibration in ester group (cm^{-1})	C=O stretching vibrations of the peptide urethane,amide I, and bending peaks of amide II (cm^{-1})
As-synthesized peptide	3319.54, 3210.78	1724.44	1679.82, 1594.81, 1549.03, 1523.79
Tube formation from methanol solvent	3324.88, 3211.46	1724.29	1684.81, 1595.23, 1552.57, 1524.63