Supplementary Material (ESI) for Chemical Communications

Supporting Information

A short water-soluble self-assembling peptide forms amyloid-like fibrils

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Synthesis of peptides 1 and 2

Peptides **1** and **2** employed in this report were synthesized by conventional solution phase methods using racemization free fragment condensation strategy. Couplings were mediated by dicyclohexylcarbodiimide/1-hydroxybenzotriazole (DCC-HOBt). The final compounds were fully characterized by IR spectroscopy, ^{1}H-NMR spectroscopy and mass spectrometry.

Synthesis of peptide **1**:

Boc-Val-OH 3. A solution of valine 2.34 g (20 mmol) in a mixture of dioxane (40 mL), water (20 mL) and 1 M NaOH (20 mL) was stirred and cooled in an ice-water bath. Di-t*ert*-butylpyrocarbonate 4.8 g (22 mmol) was added and stirring was continued at room temperature for 6 h. Then the solution was concentrated in *vacuo* to about 15 to 20 mL, cooled in an ice water bath, covered with a layer of ethyl acetate (about 30 mL) and acidified with a dilute solution of $KHSO_4$ to pH 2-3 (Congo red). The aqueous phase was extracted with ethyl acetate and this operation was done repeatedly. The ethyl acetate extracts were pooled, washed with water and dried over anhydrous Na_2SO_4 and evaporated in *vacuo*. The pure material was obtained as a white solid.

Yield = 4.0 g (18.43 mmol, 93%). (Found: C, 55.27; H, 8.76; N, 6.47%. $C_{10}H_{19}NO_4$ (217) requires C, 55.29; H, 8.75; N, 6.45%).

Boc-Val(1)-Ile(2)-OMe 4. 3.25 g (15 mmol) of Boc-Val-OH was dissolved in a mixture of 5 mL of DMF and cooled in an ice-water bath. H-Ile-OMe was isolated from 5.45 g (30 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentration to 10 mL. Then this was added to the reaction mixture, followed immediately by 3.09 g (15 mmol) of di-

cyclohexylcarbodiimide (DCC) and 2.02 g (15 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and stirred for 48 h. The residue was taken in ethyl acetate (60 mL), and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCl (3 × 50 mL), brine (2 × 50 mL) then 1 M sodium carbonate (3 × 50 mL) and brine (2 × 50 mL) respectively. Then dried over anhydrous sodium sulfate, and evaporated in *vacuo* to yield **4** as a white solid.

Yield = 4.12 g (11.97 mmol, 79.84%). (Found: C, 59.29; H, 9.21; N, 8.15%. $C_{17}H_{32}N_2O_5$ (344) requires: C, 59.30; H, 9.30; N, 8.13%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.36 (1H, d, J = 6 Hz); 5.02 (1H, d, J = 6Hz); 4.58 (1H, m); 3.89 (1H, m); 3.73 (3H, s); 2.11-2.03 (1H, m); 1.90 (1H, m); 1.44 (9H, s); 1.41-1.37 (2H, m); 0.98-0.93 (6H, m); 0.92-0.89 (6H, m).

Boc-Val(1)-Ile(2)-OH 5. To 3.5 g (10.17 mmol) of Boc-Val(1)-Ile(2)-OMe **4**, 10 mL MeOH and 5 mL of 2 M NaOH were added. The reaction mixture was stirred and the progress of saponification was monitored by thin layer chromatography (TLC). After 10 h methanol was removed under *vacuo*, the residue was taken in 20 mL of water, washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1 M HCl and it was extracted with ethyl acetate (3 × 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated in *vacuo* to yield **5** as a solid material.

Yield = 2.64 g (8 mmol, 78.8%). (Found: C, 58.15; H, 7.10; N, 8.22%. $C_{16}H_{30}N_2O_5$ (330) requires: C, 58.18; H, 9.09, N, 8.48%);

^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 12.56 (1H, b); 7.77 (1H, d, J = 9Hz); 6.76 (1H, d, J = 9 Hz); 4.15 (1H, m); 3.81 (1H, m); 2.48 (1H, m); 1.91 (1H, m); 1.75 (5H, m); 1.35 (9H, s); 1.22-1.03 (3H, m); 0.84-0.78 (6H, m).

Boc-Val(1)-Ile(2)-Ala(3)-OMe 6. 2.31 g (7 mmol) of Boc-Val(1)-Ile(2)-OH **5** in 10 mL of DMF was cooled in an ice-water bath and H-Ala-OMe was isolated from 1.95 g (14 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentration to 10 mL. Then it was added to the reaction mixture, followed immediately by 1.44 g (7 mmol) DCC and 0.945 g (7 mmol) of HOBt. The reaction mixture was stirred for three days. The residue was taken in ethyl acetate (60 mL) and the DCU was filtered off .The organic layer was washed with 2 M HCl (3 × 50 mL), brine (2 × 50 mL), 1 M sodium carbonate (3 × 50 mL) and brine (2 × 50 mL) respectively. Then dried over anhydrous sodium sulfate and evaporated in *vacuo* to yield **6** as a white solid. Purification was done by silica gel column (100-200 mesh) using 3:1 ethyl acetate-toluene as eluent.

Yield = 2 g (4.81 mmol, 68.96%). (Found: C, 57.84; H, 8.89; N, 10.14%. $C_{20}H_{37}N_3O_6$ (415) requires: C, 57.83; H, 8.91; N, 10.12%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (1H, d); 7.27 (1H, d, J = 9 Hz); 5.67 (1H, d, J = 6 Hz); 4.48 (1H, m); 4.31 (1H, m); 3.94 (1H, m); 3.70 (3H, s); 2.11-2.05 (1H, m); 1.89-1.87 (1H, m); 1.43 (9H, s); 1.39-1.37 (3H, d, J = 6 Hz) 1.25-1.07 (5H, m); 0.95-0.88 (3H, m); (6H, m); ESI-MS $(M+Na)^+$ = 438.3, M_{calcd} = 415; $[\alpha]_D^{20}$ - 71.8 (*c* 0.71, CH_3OH).

Boc-Val(1)-Ile(2)-Ala(3)-OH 7. To 1.78 g (4.3 mmol) of Boc-Val(1)-Ile(2)-Ala-OMe, 10 mL MeOH and 5 mL of 2 M NaOH were added. The reaction mixture was stirred and the progress of saponification was monitored by thin layer chromatography (TLC). After 10 h methanol was removed under *vacuo*, the residue was taken in 20 mL of water, washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1 M HCl and it was extracted with ethyl acetate (3 × 50 mL). The extracts were

pooled, dried over anhydrous sodium sulfate, and evaporated in *vacuo* to yield **7** as a white solid compound.

Yield = 1.2 g (2.99 mmol, 68.96%). (Found: C, 56.86; H, 8.74; N, 10.52%; $C_{19}H_{35}N_3O_6$ (401) requires: C, 56.85, H, 8.72; N, 10.47%); ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 12.25 (1H, b); 8.24 (1H, d, *J* = 9 Hz); 7.59 (1H, d, *J* = 9 Hz); 6.87 (1H, d, *J* = 9 Hz); 4.23 (1H, m); 4.14 (1H, m); 3.76 (1H, m); 1.93-1.90 (1H, m); 1.71-1.69 (6H, m); 1.37 (9H, s); 1.24 (3H, d, *J* = 6 Hz); 1.11-1.04 (3H, m); 0.86-0.79 (6H, m); HRMS $(M+Na)^+$ = 424.0908, M_{calcd} = 401.2525.

Peptide 1. To 1.12 gm (2.8 mmol) of Boc-Val(1)-Ile(2)-Ala(3)-OH, 2 mL TFA (Trifluoroacetic acid) was added. The reaction mixture was stirred and the progress of deprotection of Boc-group was monitored by thin layer chromatography (TLC). After 2 hours TFA was removed under *vacuo* and the residue was taken in 10 mL of water, washed with diethyl ether (2 × 50 mL). The aqueous part is then dried under *vacuo* to yield **1** as a white solid.

Yield = 0.6 g (2 mmol, 71.25%). (Found: C, 55.82; H, 8.95; N, 13.98%. $C_{14}H_{27}N_3O_4$ (301) requires: C, 55.81, H, 8.97; N, 13.95%); ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 8.35 (1H, d, *J* = 9 Hz); 8.27 (1H, d, *J* = 9 Hz); 4.25 (1H, m); 4.16 (1H, m); 3.39 (1H, m); 2.05-1.98 (1H, m); 1.73-1.71 (1H, m); 1.54-1.47 (5H, m); 1.26-1.24 (3H, d, *J* = 6 Hz); 1.13-1.03 (3H, m); 0.91-0.81 (6H, m). $[\alpha]_D^{20}$ - 35.6 (*c* 0.77, H_2O); HRMS $(M+Na)^+$ = 324.1211; $(2M+Na)^+$ = 625.2397, M_{calcd} = 301.2001.

Synthesis of peptide **2**:

Boc-Ala-OH 8. A solution of alanine 2.22 g (25 mmol) in a mixture of dioxan (50 mL), water (25 mL) and 1 M NaOH (25 mL) was stirred and cooled in an ice-water bath. Di-t*ert*-butylpyrocarbonate 6.6 g (27.5 mmol) was added and stirring was continued at room temperature for 6 h. Then the solution was concentrated in *vacuo* to about 15 to 20 mL, cooled in an ice water bath, covered with a layer of ethyl acetate (about 30 mL) and acidified with a dilute solution of $KHSO_4$ to pH 2-3 (Congo red). The aqueous phase was extracted with ethyl acetate and this operation was done repeatedly. The ethyl acetate extracts were pooled, washed with water and dried over anhydrous Na_2SO_4 and evaporated in *vacuo*. The pure material was obtained as a white solid.

Yield = 4.1 g (21.7 mmol, 86.77%). (Found: C, 50.75; H, 7.95; N, 7.41%. $C_8H_{15}NO_4$ (189) requires C, 50.79; H, 7.93; N, 7.40%).

Boc-Ala(1)-Val(2)-OMe 9. 3.78 g (20 mmol) of Boc-Ala-OH was dissolved in a mixture of 5 mL of DMF and cooled in an ice-water bath. H-Val-OMe was isolated from 6.7 g (40 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentration to 10 mL. Then this was added to the reaction mixture, followed immediately by 4.12 g (20 mmol) of di-cyclohexylcarbodiimide (DCC) and 2.70 g (20 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and stirred for 48 h. The residue was taken in ethyl acetate (60 mL), and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCl (3 × 50 mL), brine (2 × 50 mL) then 1 M sodium carbonate (3 × 50 mL) and brine (2 × 50 mL) respectively. Then dried over anhydrous sodium sulfate, and evaporated in *vacuo* to yield **9** as a white solid.

Yield = 5.12 g (16.9 mmol, 84.76%). (Found: C, 54.63; H, 8.58; N, 9.29%. $C_{14}H_{26}N_2O_5$ (302) requires C, 55.62; H, 8.60; N, 9.27%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59 (1H, d, *J* = 9 Hz); 4.9 (1H, d, *J* = 6 Hz); 4.45 (1H, m); 4.07 (1H, m); 3.66 (3H, s); 2.09 (1H, m); 1.38 (9H, s); 1.30-1.27 (1H, m); 0.87-0.82 (6H, m).

Boc-Ala(1)-Val(2)-OH 10. To 4.53 g (15 mmol) of Boc-Ala(1)-Val(2)-OMe **9**, 10 mL MeOH and 5 mL of 2 M NaOH were added. The reaction mixture was stirred and the progress of saponification was monitored by thin layer chromatography (TLC). After 10 h methanol was removed under *vacuo*, the residue was taken in 20 mL of water, washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1 M HCl and it was extracted with ethyl acetate (3 × 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated in *vacuo* to yield **10** as a solid material.

Yield = 3.45 g (12 mmol, 79.86%). (Found: C, 54.15; H, 8.35; N, 9.74%. $C_{13}H_{24}N_2O_5$ (288) requires C, 54.16; H, 8.33, N, 9.72%); ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 12.64 (1H, b); 7.68 (1H, d, *J* = 9 Hz); 6.96 (1H, d, *J* = 6 Hz); 4.13 (1H, m); 4.02 (1H, m); 2.08-1.97 (1H, m); 1.35 (9H, s); 1.14 (1H, *J* = 7.1 Hz); 0.86-0.84 (6H, m).

Boc-Ala(1)-Val(2)-Ile(3)-OMe 11. 2.88 g (10 mmol) of Boc-Ala(1)-Val(2)-OH in 10 mL of DMF was cooled in an ice-water bath and H-Ile-OMe was isolated from 3.63 g (20 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentration to 10 mL. Then it was added to the reaction mixture, followed immediately by 2.06 g (10 mmol) DCC and 1.35 g (10 mmol) of HOBt. The reaction mixture was stirred for three days. The residue was taken in ethyl

acetate (60 mL) and the DCU was filtered off .The organic layer was washed with 2 M HCl (3 × 50 mL), brine (2 × 50 mL), 1 M sodium carbonate (3 × 50 mL) and brine (2 × 50 mL) respectively. Then dried over anhydrous sodium sulfate and evaporated in *vacuo* to yield **11** as a white solid. Purification was done by silica gel column (100-200 mesh) using 3:1 ethyl acetate-toluene as eluent.

Yield = 3.32 g (8 mmol, 80%). (Found: C, 57.82; H, 8.90; N, 10.15%. $C_{20}H_{37}N_3O_6$ (415) requires C, 57.83; H, 8.91; N, 10.12%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (1H, d, J = 9 Hz); 6.56 (1H, d, J = 9 Hz); 5.06 (1H, d, J = 6 Hz); 4.56 (1H, m); 4.27 (1H, m); 4.18 (1H, m); 3.73 (3H, s); 2.19-2.12 (1H, m); 1.92-1.89 (1H, m); 1.44 (9H, s); 1.36-1.34 (3H, d, J = 6 Hz); 0.96-0.88 (14H, m); HRMS $(M+Na)^+$ = 438.1009, M_{calcd} = 415; $[\alpha]_D^{20}$ – 50.5 (*c* 0.56, CH_3OH).

Boc-Ala(1)-Val(2)-Ile(3)-OH 12. To 2.9 g (7 mmol) of Boc-Ala(1)-Val(2)-Ile(3)-OMe, 10 mL MeOH and 5 mL of 2 M NaOH were added. The reaction mixture was stirred and the progress of saponification was monitored by thin layer chromatography (TLC). After 10 h methanol was removed under *vacuo*, the residue was taken in 20 mL of water, washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1 M HCl and it was extracted with ethyl acetate (3 × 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated in *vacuo* to yield **12** as a white compound.

Yield = 2.0 g (5 mmol, 71.4%). (Found: C, 56.87; H, 8.82; N, 10.23%. $C_{19}H_{35}N_3O_6$ (401) requires C, 56.85; H, 8.72; N, 10.47%); ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 12.40 (1H, b); 7.93 (1H, d, J = 9 Hz); 7.43 (1H, d, J = 9 Hz); 7.00 (1H, d, J = 6 Hz); 4.21 (1H, m); 4.07

(1H, m); 3.94 (1H, m); 2.43 (1H, m); 1.91-1.83 (1H, m); 1.70 (5H, m); 1.30 (9H, s); 1.10-1.07 (3H, d); 0.79-0.74 (9H, m); HRMS $(M+Na)^+$ = 423.9803, M_{calcd} = 401.2525.

Peptide 2. To 1.8 g (4.5 mmol) Boc-Ala(1)-Val(2)-Ile(3)-OH **12**, 2 mL TFA (Trifluoroacetic acid) was added. The reaction mixture was stirred and the progress of deprotection of *Boc*-group was monitored by thin layer chromatography (TLC). After 2 h TFA was removed under *vacuo* and the residue was taken in 10 mL of water, washed with diethyl ether (2 × 50 mL). The aqueous part is then dried under vacuum to yield **2** as white solid.

Yield = 0.9 g (3 mmol, 66.66%). (Found: C, 55.8; H, 8.96; N, 13.97%. $C_{14}H_{27}N_3O_4$ (301) requires C, 55.81; H, 8.97; N, 13.95%); ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 12.48 (1H, b); 8.29 (1H, d, *J* = 9 Hz); 8.01 (1H, d, *J* = 9 Hz); 4.25 (1H, m); 4.08 (1H, m); 3.85 (1H, m); 2.43-2.42 (1H, m); 1.94-1.88 (1H, m); 1.71 (5H, m); 1.24-1.21 (3H, d, *J* = 9 Hz); 1.16-1.07 (3H, m); 0.84-0.74 (6H, m); HRMS $(M+Na)^+$ = 324.1253; $(2M+Na)^+$ = 625.2567, M_{calcd} = 301.2001. $[\alpha]_D^{20}$ - 32.8 (*c* 0.68, H_2O).

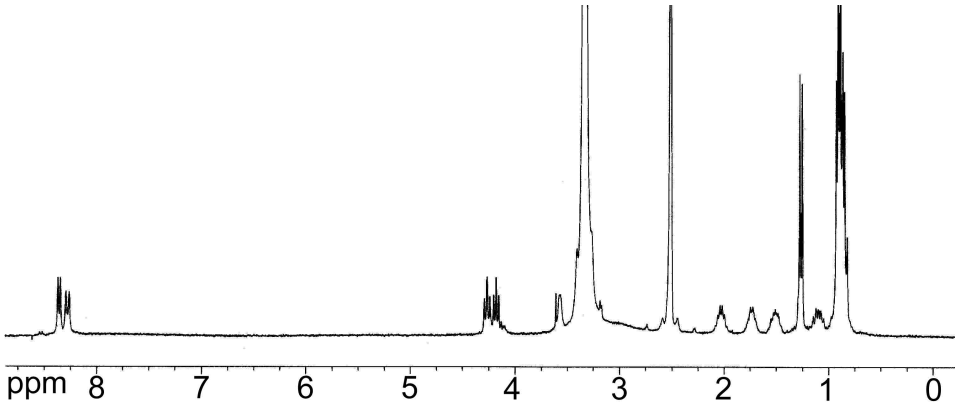


Figure S1. 300 MHz ^{1}H NMR spectra of peptide **1** in $(CD_3)_2SO$.

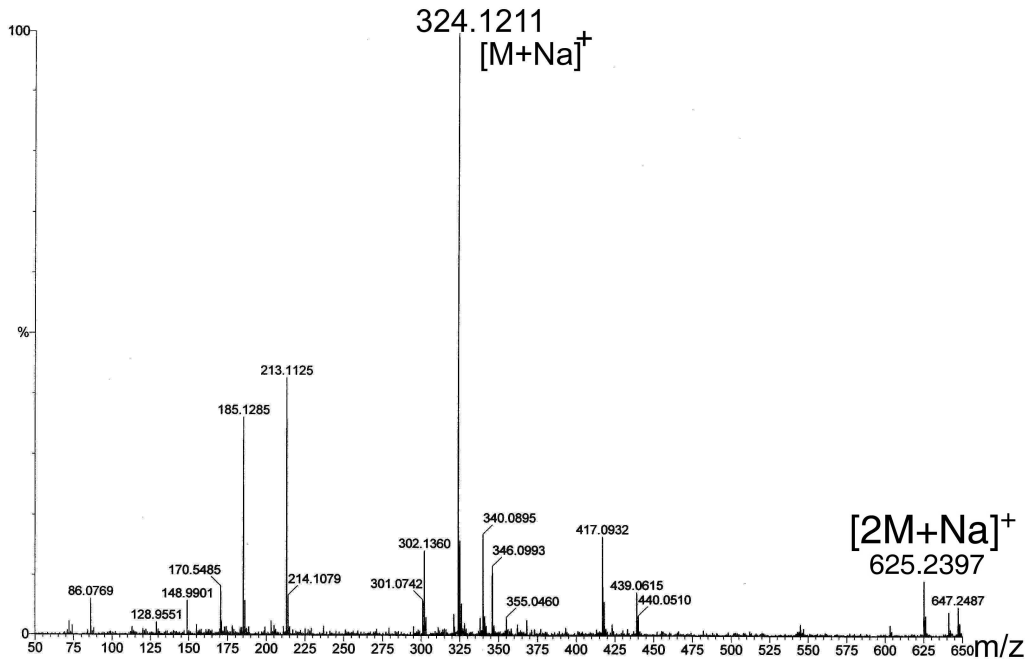


Figure S2. Typical mass spectrum (HRMS) of peptide **1**.

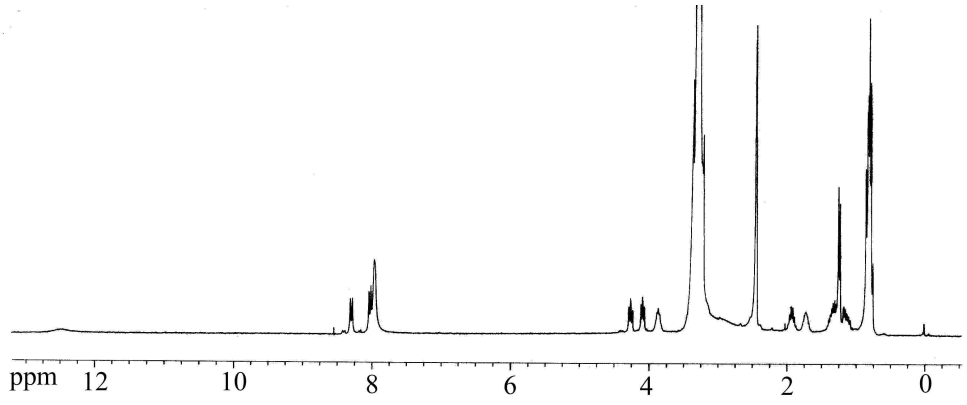


Figure S3. 300 MHz ^{1}H NMR spectra of peptide **2** in $(CD_3)_2SO$.

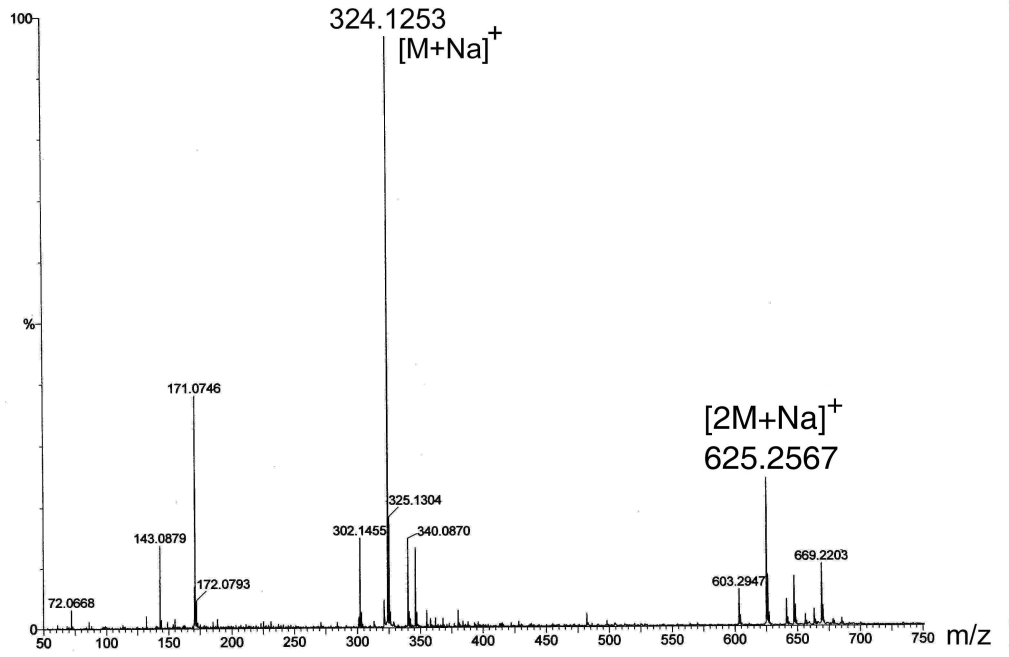


Figure S4. Typical mass spectrum (HRMS) of peptide **2**.

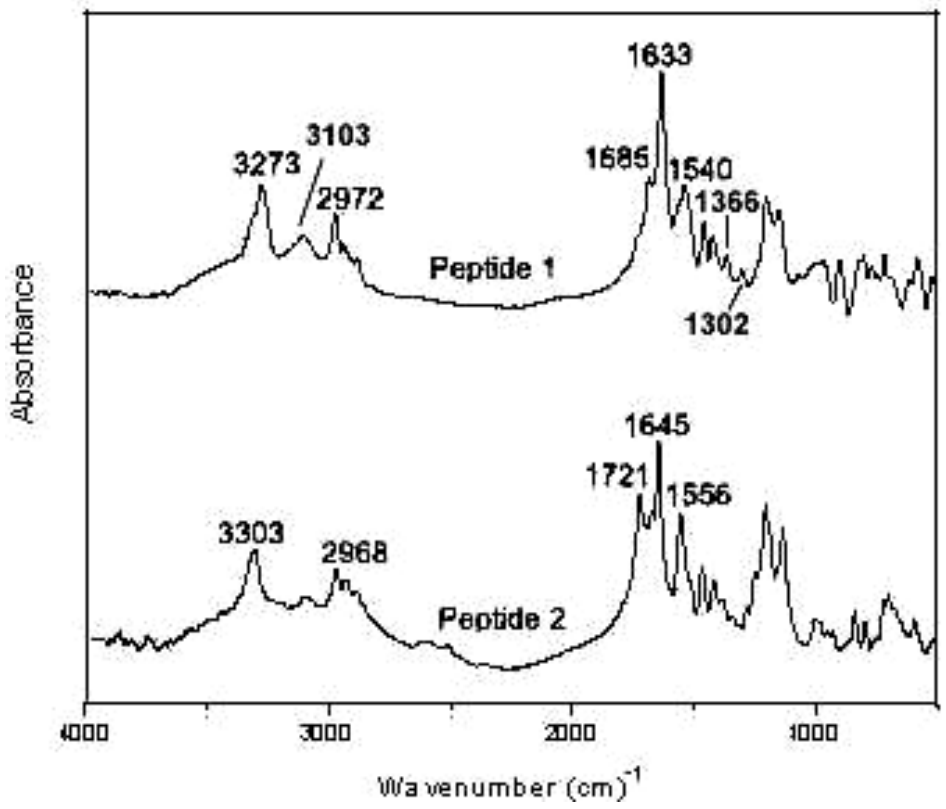


Figure S5. FT-IR spectra of peptides **1** and **2** in the solid state.

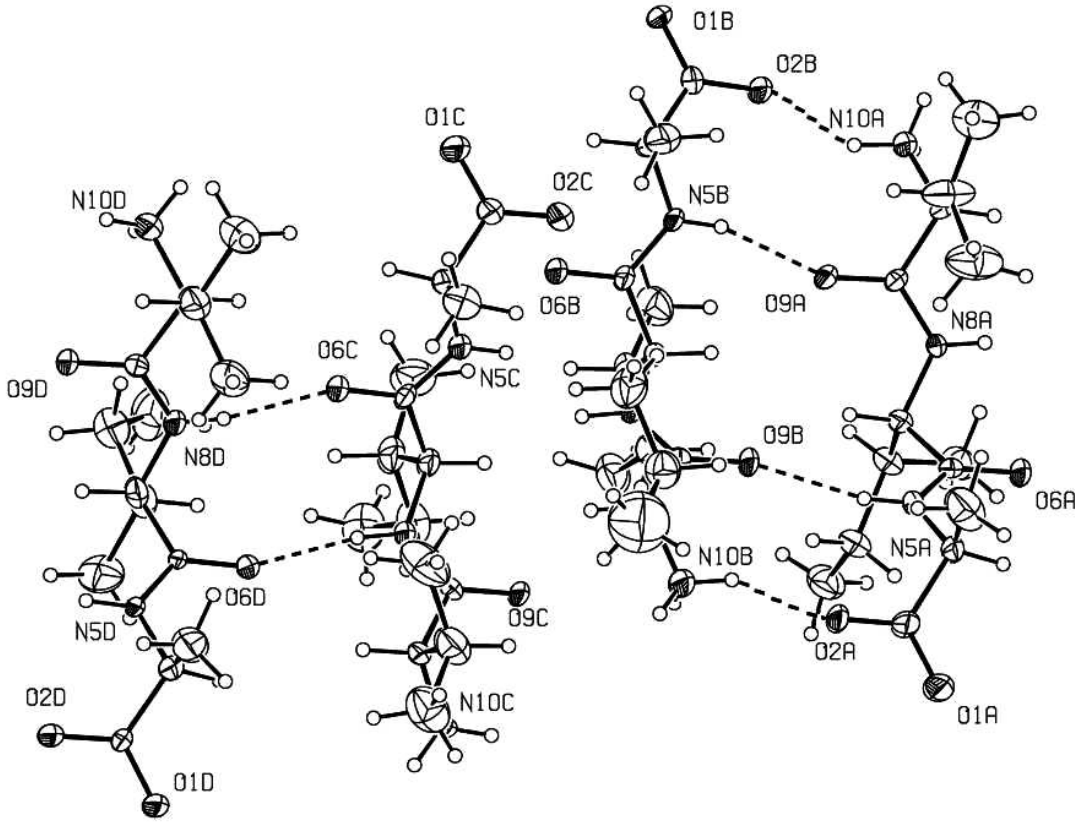
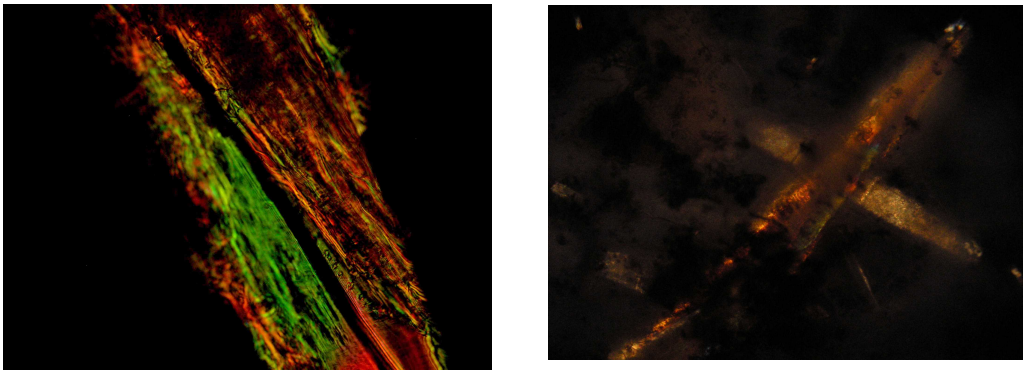
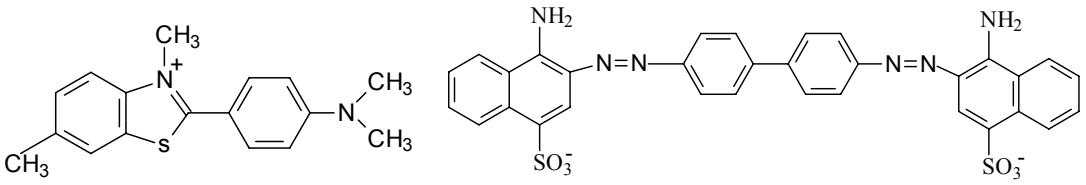


Figure S6. ORTEP diagram of peptide **1** with the atomic numbering scheme. Ellipsoids at 30% probability. Intermolecular hydrogen bonds are shown as dotted lines. Only nitrogen and oxygen atoms are labeled due to clarity. Co-solvents such as ethanol and trifluoroacetic acid are omitted due to clarity.



(a) (b)

Figure S7. Optical microscopic images of (a) peptide **1** (Aβ40-42) fibrils stained with a Congo red dye showing a green-gold birefringence, a characteristic feature of amyloid fibrils and (b) peptide **2** stained with a Congo red dye does not show any birefringence observed at 100 X magnification between crossed polarizers.



(a) (b)

Figure S8. Amyloid-binding and inhibiting reagents. (a) Chemical structure of Thioflavin T, an amyloid specific dye and (b) Chemical structure of Congo red (CR) dye, an amyloid-specific dye and amyloid formation inhibitor.

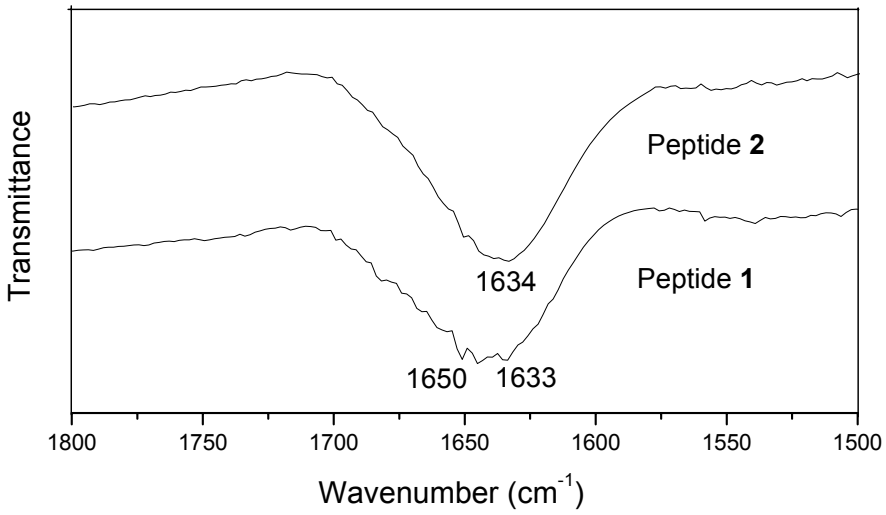


Figure S9. FT-IR spectra of aged peptide fibrils for peptides **1** and **2**.

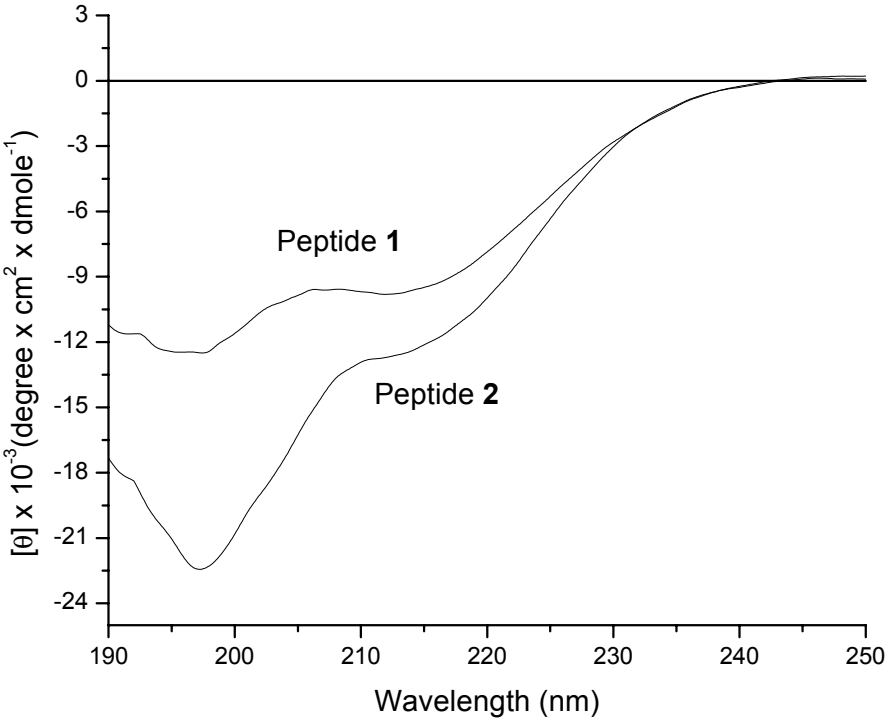


Figure S10. Circular dichroism (CD) spectra of aged peptide fibrils obtained from peptides **1** and **2**.

Experimental Procedures

NMR experiments

All NMR studies were carried out on a Brüker DPX 300 MHz spectrometer at 300 K. Peptide concentrations were in the range 1-10 mM in $CDCl_3$ and DMSO-d_6.

FT-IR spectroscopy

The FT-IR spectra were taken using Shimadzu (Japan) model FT-IR spectrophotometer. The solid-state FT-IR measurements were performed using the KBr disk technique. Aged peptide solutions were suspended on a CaF_2 plate and dried by vacuum. The peptide deposits were resuspended with D_2O and subsequently dried to form thin films and spectra were collected at 25°C.

Congo red binding assay

A solution of peptides in 10 mmol phosphate buffer (Tris buffer), pH 7.2 (aged for 4 days), was allowed to dry on a glass microscope slide. An alkaline saturated Congo red solution was prepared. The peptide fibrils were stained by the addition of a solution of 1 mmol Congo red in 10 mmol phosphate buffer, pH 7.2 for 2 minutes and then the excess stain (Congo red) was removed by rinsing the stained fibril with glass distilled water for several times. The stained fibrils were dried in vacuum at room temperature for 24 hours, then visualized at 100× magnification and birefringence was observed between crossed polarizers.

Thioflavin T assay

The peptides were incubated for one week at a concentration of 0.4 mg/mL in 20 mmol phosphate buffer (pH 6.0) at room temperature. An aliquot of this sample and an aliquot of a highly concentrated solution of ThT were added to a solution of 20 mmol phosphate

buffer (pH 6.0). In final condition, after mixing, concentrations of present substances were 0.4 mg/mL peptide, 250 μM ThT and 20 mmol phosphate buffer (pH 6.0) at 25°C. The fluorescence spectra were obtained using a Perkin-Elmer spectrofluorimeter and excitation and emission wavelengths of 450 and 484 nm respectively.

Transmission Electron Microscopic study

The morphologies of the reported compounds were investigated using transmission electron microscope (TEM). A solution of peptides (1 mg in 1 mL glass distilled water) was incubated overnight at room temperature. The transmission electron microscopic studies of all the peptides were done using a small amount of the solution of the corresponding compounds on carbon-coated copper grids (300 mesh) by slow evaporation and allowed to dry in vacuum at 30 °C for two days. Images were taken at an accelerating voltage of 200 kV. TEM was done by a JEM-2010 electron microscope.

Mass spectrometry

Mass spectra were recorded on a HEWLETT PACKARD Series 1100MSD and Micromass Qtof Micro YA263 mass spectrometers by positive mode electrospray ionization. The dimerization of peptides **1** and **2** is evident from mass spectra (HRMS) analysis. A peak at 324.1211 $(M+Na)^+$, corresponding to the monomeric peptide **1**, was observed, and a peak attributed to the dimeric form of peptide **1** was also found at 625.2397 $(2M+Na)^+$. In case of peptide **2**, a peak at 324.1253 $(M+Na)^+$ corresponds to the monomeric form of peptide **2**, and a peak found at 625.2567 $(2M+Na)^+$ attributes the dimeric nature of peptide **2**.

Circular Dichroism Spectroscopy

CD Spectra were recorded at 25 ºC between 190 and 250 nm, with 0.1 nm intervals and a 3 s averaging time and having a scan speed of 20 nm/min, using a Jasco(J 720) spectrometer equipped with a 0.1 cm path length cuvette. Final scan values represent subtraction of baseline (water for all the cases). Stock solutions of the peptides were prepared by dissolving the respective compounds in double distilled water to a concentration of 0.6 mg/mL. After a 5 min sonication, the stock solution was dilutted in double-distilled water in the experiment cuvette to a final concentration of 100 μM.

The secondary structure of the aged solutions of peptide **1** and peptide **2** fibrils was investigated by CD spectroscopy (Figure S10). The CD spectrum at room temperature revealed a clear negative ellipticity with distinct double maxima at 197 and 215 nm for peptide **1**. Similar type of CD spectrum is observed for peptide **2** having a clear negative ellipticity with distinct double maxima at 195 and 214 nm for peptide **2.** These CD data are suggesting the presence of some random structure along with some definite β-sheet structures. From this CD spectral data it may be concluded that aged solution of peptide **2** fibrils is dominated by some type of unstructured or random structure than that of aged solution of peptide **1** fibrils at room temperature.

Table 1: Selected torsional angles for peptide **1**.

Residue	Molecule	ϕ	ψ	ω
Val(1)	A		140.3(6)	163.9(6)
	B		140.0(6)	169.9(6)
	C		134.9(7)	171.5(7)
	D		135.0(7)	175.2(7)
Ile(2)	A	-129.0(6)	129.8(6)	-179.9(6)
	B	-123.3(7)	129.1(7)	-179.3(7)
	C	-125.7(8)	123.8(8)	-176.4(8)
	D	-123.8(7)	123.4(7)	-178.1(7)
Ala(3)	A	-137.2(7)	127.7(9)	
	B	-145.3(7)	154.5(8)	
	C	-142.7(8)	123.0(9)	
	D	-143.8(7)	147.2(8)	

Table 2: Intermolecular hydrogen-bonding parameters for peptide **1**.

D-H…A	H…A/Å	D…A/Å	D-H…A/°
N5A-H…O9B	2.11	2.952(8)	166
N8A-H…O6B[a]	2.10	2.936(7)	166
N10A-H…O2D[b]	2.06	2.903(9)	157
N10A-H…O2B	2.02	2.813(8)	148
N10A-H…O1D[b]	2.57	3.170(9)	125
N5B-H…O9A	2.13	2.961(8)	163
N8B-H…O6A[c]	2.07	2.906(8)	165
N10B-H…O2A	1.96	2.796(10)	155
N10B-H…O2C[d]	2.09	2.911(12)	154
N10B-H…O1C[d]	2.42	3.151(11)	140
N5C-H…O9D[a]	2.10	2.932(9)	163
N8C-H…O6D	2.03	2.882(8)	170
N10C-H…O1B[e]	2.35	3.132(9)	146
N10C-H…O2B[e]	2.05	2.877(11)	155
N10C-H…2D[a]	1.91	2.788(9)	167
N5D-H…O9C[c]	2.09	2.923(7)	165
N8D-H…O6C	2.05	2.894(8)	167
N10D-H…O2A[f]	2.00	2.843(12)	158
N10D-H…O1A[f]	2.48	3.237(10)	143
N10D-H…O2C[c]	1.91	2.776(9)	165

Symmetry equivalent [a] x - 1, y, z; [b] x - 1, y, 1 + z; [c] 1 + x, y, z; [d] x, 1 + y, z; [e] x, y, z – 1; [f] x + 1, y-1, z