Supplementary Material (ESI) for Soft Matter

Supporting Information

Pentapeptide based organogels: the role of adjacently located phenylalanine residues in gel formation

Arijit Banerjee[b], *Goutam Palui*[b] *and Arindam Banerjee**[a,b]

a. *Indian Institute of Chemical Biology, Jadavpur, Kolkata- 700 032, India. Fax: 0091-33-2473-5197; Tel: +91-033-2473-3491; b. Department of Biological Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata- 700 032, India.*

Experimental Section:

1. Peptide synthesis.

The peptides were synthesized by conventional solution phase methods using racemization free fragment condensation strategy.[ref.S1] The Boc and Piv group were used for N-terminal protection and the C-terminus were protected as a methyl ester or ethyl ester. Synthesis of peptide **1** has already been discussed in our previous work.[26d] Couplings were mediated by dicyclohexylcarbodiimide-1-hydroxybenzotriazole (DCC / HOBt). All intermediates have been characterized by ^{1}H-NMR (300 MHz) and thin layer chromatography (TLC) on silica gel and used without further purification. The final products were purified by column chromatography using silica gel (100-200 mesh size) as stationary phase and ethyl acetate as eluent. Purified final compounds have been fully characterized by 300 MHz and 500 MHz ^{1}H -NMR spectroscopy.

1.1 Synthesis of peptide 2

(a) Boc-Leu-Leu-OMe **9**: 8.8 g (38 mmol) of Boc-Leu-OH was dissolved in a mixture of 40 mL dichloromethane (DCM) in an ice-water bath. H-Leu-OMe was isolated from 13.81 g (76 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentration (30 mL) and this was added to the reaction mixture, followed immediately by 10.3 g (50 mmol) of di-cyclohexaylcarbodiimide (DCC). The reaction mixture was allowed to come to room temperature and stirred for 24 h. DCM was evaporated, residue was taken in ethyl acetate (50 mL), and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 N HCl (3×50 mL), brine, then 1 M sodium carbonate (3×50 mL) and brine (2×50 mL) and dried over anhydrous sodium sulfate, and evaporated under *vacuum* to yield 12.25 g (34.2 mmol, 90%).

Anal. Calcd. for $C_{18}H_{34}N_2O_5$ (358): C, 60.34; H, 9.50; N, 7.82. Found: C, 60.31; H, 9.53; N, 7.83. MS (ESIMS) m/z 359.15 $(M+H)^+$, m/z 382.23 $(M+H+Na)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.47 (d, *J*= 7.2, NH, 1H), 4.86 (b, NH, 1H), 4.65-4.58 (m, CH, 1H), 4.11-4.09 (m, CH, 1H), 3.73 (s, OCH_3, 3H), 1.95-1.49 (m, CH_2, 4H), 1.44 (s, CH_3, 9H), 1.27-1.22 (m, CH, 2H), 0.96-0.47 (m, CH_3, 12H).

(b) Boc-Leu-Leu-OH **10**: To 11.47 g (32 mmol) of **9**, 80 mL MeOH and 40 mL of 2 N NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After 10 h methanol was removed under *vacuum*, the residue was taken in 80 mL of water, washed with diethyl ether (2×50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1 N 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 get the **10**.

Yield: 5.47 g (15.9 mmol, 75%)

Anal. Calcd. for $C_{17}H_{32}N_2O_5$ (344): C, 59.30; H, 9.30; N, 8.14. Found: C, 59.33; H, 9.26; N, 8.12. MS (ESIMS) m/z 344.12 $(M+H)^+$, m/z 383.10 $(M+H+K)^+$. 300 MHz ^{1}H NMR (DMSO-d_6) δ 12.46 (b, OH, 1H), 7.84 (d, *J*=7.9 Hz, NH, 1H), 6.76 (d, *J*=8.5 Hz, NH, 1H), 4.20-4.13 (m, CH, 1H), 3.94-3.87 (m, CH, 1H), 1.53-1.41 (m, CH and CH_2, 6H), 1.30 (s, CH_3, 9H), 0.82-0.75 (m, CH_3, 12H).

(c) Boc-Phe-Phe-OMe **11**: According to the process described for the preparation of 9, 11 was prepared from Boc-Phe-OH and H_2N-Phe-OMe.HCl as white solid (76%).

Yield: 10.7 g (25.0 m mol, 76%)

Anal. Calcd. for $C_{24}H_{30}N_2O_5$ (426): C, 67.61; H, 7.04; N, 6.57. Found: C, 67.63; H, 7.08; N, 6.54. MS (ESIMS) m/z 426.21 $(M)^+$, m/z 427.17 $(M+H)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.31-6.27 (m, ArH, 10H), 6.28 (d, *J*=6.9 Hz, NH, 1H), 4.93 (b, NH, 1H), 4.81-4.75 (m, CH, 1H), 4.36-4.31 (m, CH, 1H), 3.67 (s, OCH_3, 3H), 3.11-3.06 (m, CH_2, 4H), 1.40 (s, CH_3, 9H).

(d) Boc-Phe-Phe-OH **12**: Compound 12 was prepared as a white solid (84%) from 11 according to the procedure described for the preparation of 10.

Yield: 8.2 g (20.0 mmol, 80%)

Anal. Calcd. for $C_{23}H_{28}N_2O_5$ (412): C, 66.99; H, 6.8; N, 6.8. Found: C, 67.02; H, 6.79; N, 6.78. MS (ESIMS) m/z 414.19 $(M+2H)^+$, m/z 436.11 $(M+H+Na)^+$. 300 MHz ^{1}H NMR (DMSO-d_6) δ 12.50 (b, OH, 1H), 8.11 (d, *J*=7.8 Hz, NH, 1H), 7.27-7.14 (m, ArH, 10H), 6.85 (d, *J*=8.8 Hz, NH, 1H), 4.47-4.45 (m, CH, 1H), 4.02-4.00 (m, CH, 1H), 3.11-3.06 (m, CH_2, 2H), 2.93-9.86 (m, CH_2, 2H), 1.26 (s, CH_3, 9H).

(e) Boc-Phe-Phe-Ala-OMe **13**: According to the process described for the preparation of 9, 13 was prepared from 12 and H_2N-Ala-OMe.HCl as white solid (70%).

Yield: 7.0 g (14.0 mmol, 70 %)

Anal. Calcd. for $C_{27}H_{35}N_3O_6$ (497): C, 65.19; H, 7.04; N, 8.45. Found: C, 65.17; H, 7.01; N, 8.49. MS (ESIMS) m/z 498.23 $(M+H)^+$, m/z 520.11 $(M+H+Na)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.33-7.16 (m, ArH, 10H), 7.07 (d, *J*=6.8 Hz, NH, 1H), 6.44 (b, NH, 1H), 4.83 (d, *J*=5.1 Hz, NH, 1H), 4.67-4.60 (m, CH, 1H), 4.49-4.40 (m, CH, 1H), 4.33-4.27 (m, CH, 1H), 3.71 (s, OCH_3, 3H), 3.17-2.87 (m, CH_2, 4H), 1.34 (s, CH_3, 9H), 1.30 (m, CH_3, 3H).

(f) Boc-Leu-Leu-Phe-Phe-Ala-OMe **2**: To 5 mmol of Boc-Phe-Phe-Ala-OMe 13, 10 mL of 98% formic acid was added and the removal of Boc group was monitored by TLC. After 8h, the formic acid was removed under vacuum. This residue was taken in water (20 mL), washed with diethyl ether. The pH of the aqueous solution was adjuster to 8 with sodium bicarbonate and extracted with ethyl acetate (3x30 mL). The Organic extracts were pooled, washed with saturated brine, dried over sodium sulfate, concentrated to 5 mL that gives a positive

ninhydrine. The tripeptide free base was added to an ice-cold solution of Boc-Leu-Val-OH 11 (4.5 mmol) in 10 mL DMF, followed by 4.5 mmol DCC and 4.5 mmol HOBt. The reaction mixture was stirred for 3 days. The residue was taken in ethyl acetate and DCU was filtered off. The Organic Layer was washed 1N HCl (3x50 mL), 1N sodium carbonate (3x50 mL), brine (2x50 mL), dried over anhydrous sodium sulfate and evaporated under vacuum to yield peptide **1** as white solid

Yield: 2.28 g (3.15 mmol, 70%)

Anal. Calcd. for $C_{39}H_{57}N_5O_8$ (723): C, 64.73; H, 7.88; N, 9.68. Found: C, 64.76; H, 7.86; N, 9.66. MS (ESIMS) m/z 746.43 $(M+Na)^+$, m/z 747.46 $(M+H+Na)^+$. 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.24-7.03 (m, ArH, 10H), 6.90 (d, *J*=6.7 Hz, NH, 1H), 6.62 (d, *J*=5.5 Hz, NH, 1H), 6.58 (d, *J*=7.0 Hz, NH, 1H), 6.50 (b, NH, 1H), 5.49 (b, NH, 1H), 4.92-4.91 (m, CH, 1H), 4.58-4.44 (m, CH, 2H), 4.15-4.06 (m, CH, 2H), 3.71 (s, OCH_3, 3H), 3.11-3.04 (m, CH_2, 2H), 3.12-2.97 (m, CH_2, 2H), 1.92 (m, CH_2, 4H), 1.58 (m, CH_3, 3H), 1.44 (s, CH_3, 9H), 1.18-1.04 (m, CH, 2H), 0.96-0.84 (m, CH_3, 12H). ^{13}C NMR (75 MHz, RT, $(CD_3)_2SO$, δ ppm): 175.28, 172.38, 171.31, 170.95, 155.36, 136.98, 129.27, 128.83, 12870, 128.57, 128.42, 77.93, 53.19, 52.63, 47.53, 42.69, 33.37, 28.21, 23.31, 23.09, 22.63, 21.47. $[\alpha]_D$ 26.2 = -28.11 (C 1.97 $CHCl_3$).

1.2 Synthesis of peptide 3

(a) Boc-Leu-Ile-OMe **14**: According to the process described for the preparation of 9, 14 was prepared from Boc-Leu-OH and H_2N-Ile-OMe.HCl as white solid (74%).

Yield: 7.9 g (22.0 mmol, 74%)

Anal. Calcd. for $C_{18}H_{34}N_2O_5$ (358): C, 60.34; H, 9.50; N, 7.82. Found: C, 60.32; H, 9.52; N, 7.83. MS (ESIMS) m/z 359.16 $(M+H)^+$, m/z 382.28 $(M+H+Na)^+$. 300 MHz ^{1}H NMR (CDCl3) δ 6.61 (d, *J*=7.8 Hz, NH, 1H), 4.86 (b, NH, 1H), 4.65-4.58 (m, CH, 1H), 4.11-4.09 (m, CH, 1H), 3.73 (s, OCH_3, 3H), 1.92-1.88 (m, CH_2, 2H), 1.53-1.50 (m, CH, 1H), 1.45 (s, CH_3, 9H), 1.40-1.37 (m, CH, 1H), 1.25-1.22 (m, 2H), 0.96-0.89 (m, CH_3, 12H).

(b) Boc-Leu-Ile-OH **15**: Compound 15 was prepared (Yield = 83%) from 14 according to the procedure described for the preparation of 10.

Yield: 6.3 g (18.2 mmol, 83%)

Anal. Calcd. for $C_{17}H_{32}N_2O_5$ (344): C, 59.30; H, 9.30; N, 8.14. Found: C, 59.29; H, 9.33; N, 8.16. MS (ESIMS) m/z 345.01 $(M+H)^+$, m/z 367.14 $(M+H+Na)^+$. 300 MHz ^{1}H NMR (DMSO-d_6) δ 12.52 (b, OH, 1H), 7.84 (d, *J*=8.1 Hz, NH, 1H), 6.76 (d, *J*=8.3 Hz, NH, 1H), 4.20-4.13 (m, CH, 1H), 3.94-3.87 (m, CH, 1H), 1.53-1.41 (m, CH and CH_2, 6H), 1.30 (s, CH_3, 9H), 0.82-0.75 (m, CH_3, 12H).

(c) Boc-Leu-Ile-Phe-Phe-Ala-OMe **3**: According to the process described for the preparation of 2 from 13 and 15 peptide 3 was obtained as gummy material.

Yield: 2.44 g (3.38 mmol, 75%)

Anal. Calcd. for $C_{39}H_{57}N_5O_8$ (723): C, 64.73; H, 7.88; N, 9.68. Found: C, 64.76; H, 7.86; N, 9.66. MS (ESIMS) m/z 746.40 $(M+Na)^+$, m/z 747.46 $(M+H+Na)^+$. 600 MHz ^{1}H NMR ($CDCl_3$) δ 7.21-7.09 (m, ArH, 10H), 7.10 (d, *J*=6.0 Hz, NH, 1H), 6.92 (d, *J*=6.6 Hz, NH, 1H), 6.85 (d, *J*=8.4 Hz, NH, 1H), 6.62 (d, *J*=5.8 Hz, NH, 1H), 5.69 (d, 7.2 Hz, NH, 1H), 4.91-4.88 (m, CH, 1H), 4.78-4.73 (m, CH, 1H), 4.65- 4.62 (m, CH, 1H), 4.53-4.51 (m, CH, 1H), 4.34-4.32 (m, CH, 1H), 3.72 (m, OCH_3, 3H), 3.49-3.48 (m, CH_2, 4H), 1.72-1.68 (m, CH_2, 2H), 1.65-1.58 (m, CH, 1H), 1.41 (s, CH_3, 9H), 1.39-1.36 (m, CH_3, 3H), 1.17-1.13 (m, CH, 1H), 0.98-0.78 (m, CH_3, 12H). ^{13}C NMR (75 MHz, RT, $(CD_3)_2SO$, δ ppm): 175.34, 172.38, 171.31, 170.95, 155.39, 129.18, 127.97, 126.21, 77.97, 53.20, 52.64, 47.55, 42.67, 33.39, 28.23, 24.56, 24.34, 23.34, 23.11, 22.63, 21.49, 10.12. $[\alpha]_D$ 26.1 = -30.59 (C 1.99 $CHCl_3$).

1.3 Synthesis of peptide 4

(a) Boc-Phe-Phe-Ala-OEt **16**: According to the process described for the preparation of 9, 16 was prepared from 12 and H_2N-Ala-OEt.HCl as white solid (78%).

Anal. Calcd. for $C_{28}H_{37}N_3O_6$ (511): C, 65.75; H, 7.24; N, 8.22. Found: C, 65.76; H, 7.26; N, 8.20. MS (ESIMS) m/z 534.33 $(M+Na)^+$, m/z 535.46 $(M+H+Na)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.33-7.16 (m, ArH, 10H), 7.07 (d, *J*=6.8, NH, 1H), 6.46 (b, NH, 1H), 4.84 (d, *J*=5.1, NH, 1H), 4.67-4.60 (m, CH, 1H), 4.45-4.40 (m, CH, 1H), 4.34-4.27 (m, CH, 1H), 4.16 (q, OCH_2CH_3, 2H), 3.16-2.88 (m, CH_2, 4H), 1.76 (m, OCH_2CH_3, 3H), 1.34 (s, CH_3, 9H), 1.31 (m, CH_3, 3H).

(b) Boc-Leu-Val-Phe-Phe-Ala-OEt **4**: According to the process described for the preparation of 2 from Boc-Leu-Val-OH and 16 peptide 4 was obtained as white solid.

Yield: 2.68 g (3.7 mmol, 82%)

Anal. Calcd. for $C_{38}H_{55}N_5O_8$ (723.87): C, 64.29; H, 7.81; N, 9.87. Found: C, 64.41; H, 7.86; N, 9.70. MS (ESIMS) m/z 746.5 $(M+Na)^+$, m/z 747.3 $(M+H+Na)^+$, m/z 748.5 $(M+Na+2H)^+$. 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.10-7.22 (m, ArH, 10H), 6.76 (d, *J*=6.4 Hz, NH, 1H), 6.67 (d, *J*=7.8 Hz, NH, 1H), 6.54 (d, *J*=7.1 Hz, NH, 1H), 6.43 (d, *J*=6.9 Hz, NH, 1H), 5.72 (b, NH, 1H), 5.12 (m, CH, 1H), 4.73-4.63 (m, 2H), 4.47- 4.42 (m, CH, 1H), 4.19-4.15 (m, OCH_2CH_3, 2H), 4.04 (m, CH, 1H), 3.05-2.99 (m, CH_2, 4H), 2.12-2.11 (m, CH, 1H), 1.94-1.92 (m, CH, 1H), 1.70-1.68 (m, OCH_2CH_3, 3H), 1.44 (s, CH_3, 9H), 1.29-1.25 (m, CH_3, 3H), 0.97-0.94 (m, CH_3, 6H), 0.93-0.83 (m, CH_3, 6H). ^{13}C NMR (75 MHz, RT, $(CD_3)_2SO$, δ ppm): 174.02, 172.89, 172.38, 171.31, 171.14, 155.41, 137.82, 137.73, 129.28, 129.22, 128.03, 127.99, 126.22, 77.99, 60.45, 58.80, 57.09, 53.97, 53.42, 47.78, 33.38, 31.35, 28.23, 23.09, 21.44, 17.79, 16.88, 14.04. $[\alpha]_D$ 25.6 = -32.17 (C 1.95 $CHCl_3$)

1.4 Synthesis of peptide 5

(a) Piv-Leu-Val-OMe **17**: According to the process described for the preparation of 9, 17 was prepared from Piv-Leu-OH and H_2N-Val-OMe.HCl as gummy material (76%).

Yield = 1.64 g (5.0 mmol, 76 %)

Anal. Calcd. for $C_{17}H_{32}N_2O_4$ (328): C, 62.20; H, 9.76; N, 8.54. Found: C, 62.23; H, 9.72; N, 8.53. MS (ESIMS) m/z 329.98 $(M+2H)^+$, m/z 367.10 $(M+H+K)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.69 (d, *J*= 8.7 Hz, NH, 1H), 6.00 (d, *J*= 7.8 Hz, NH, 1H), 4.52-4.43 (m, CH, 2H), 3.74 (s, OCH_3, 3H), 2.19-2.16 (m, CH, 1H), 1.74-1.51 (m, CH and CH_2, 3H), 1.20 (s, CH_3, 9H), 0.97-0.88 (m, CH_3, 12H).

(b) Piv-Leu-Val-OH **18**: Compound 18 was prepared as a white solid (80%) from 17 according to the procedure described for the preparation of 10.

Yield: 3.8 g (4.0 mmol, 80%)

Anal. Calcd. for $C_{16}H_{30}N_2O_4$ (314): C, 61.15; H, 9.55; N, 8.92. Found: C, 61.17; H, 9.52; N, 8.93. MS (ESIMS) m/z 315.11 $(M+H)^+$, m/z 337.08 $(M+H+Na)^+$. 300 MHz ^{1}H NMR (DMSO-d_6) δ 12.45 (b, OH, 1H), 7.64 (d, *J*= 8.8 Hz, NH, 1H), 7.48 (d, *J*= 7.7 Hz, NH, 1H), 4.38-4.11 (m, CH, 2H), 2.07-2.00 (m, CH, 1H), 1.64-1.42 (m, CH and CH_2, 3H), 1.11 (s, CH_3, 9H), 0.89-0.81 (m, CH_3, 12H).

(c) Piv-Leu-Val-Phe-Phe-Ala-OMe **5**: According to the process described for the preparation of 2 from 13 and 18 peptide 5 was obtained as white solid.

Yield = 2.43 g (3.5 mmol, 78 %)

Anal. Calcd. for $C_{38}H_{55}N_5O_7$ (693): C, 65.80; H, 7.94; N, 10.10. Found: C, 65.76; H, 7.96; N, 9.08. MS (ESIMS) m/z 716.3 $(M+Na)^+$, m/z 717.5 $(M+H+Na)^+$. 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.25-7.14 (m, ArH, 10H), 6.83 (d, *J*=8.5 Hz, NH, 1H), 6.24 (b, NH, 1H), 6.18 (b, NH, 1H), 6.05 (d, *J*=7.2 Hz, NH, 1H), 5.53 (b, NH, 1H), 4.54-4.41 (m, CH, 2H), 4.35-4.33 (m, CH, 1H), 4.29-4.26 (m, CH, 1H), 4.09-4.08 (m, CH, 1H), 3.71 (s, OCH_3, 3H), 3.09-3.03 (m, CH_2, 2H), 3.01-2.92 (m, CH_2, 2H), 2.88-2.83 (m, CH, 1H), 1.95-1.92 (m, CH_2, 2H), 1.61-1.59 (m, CH_3, 3H), 1.39-1.31 (m, 1H), 1.21 (s, CH_3, 9H), 1.17-1.09 (m, CH_3, 6H), 0.96-0.86 (m, CH_3, 6H). ^{13}C NMR (75 MHz, RT, $CDCl_3$, δ ppm): 174.02, 172.38, 171.10, 170.95, 170.59, 136.78, 129.31, 129.18, 128.64, 128.44, 128.35, 126.76, 126.61, 65.12, 59.06, 58.09, 54.06, 52.34, 52.02, 49.19, 48.08, 33.96, 27.48, 25.63, 24.96, 23.05, 22.06, 19.17, 17.97, 17.59. $[\alpha]_D$ 26.1= -30.90 (C 1.95 $CHCl_3$)

1.5 Synthesis of peptide 6

(a) Boc-Ala-Phe-OMe **19**: According to the process described for the preparation of 9, 19 was prepared from Boc-Ala-OH and H_2N-Phe-OMe.HCl as white solid (75%).

Yield = 2.9 g (8.3 mmol, 83%)

Anal.Calcd. for $C_{18}H_{26}N_2O_5$ (350): C, 61.71; N, 8.0; H, 7.43. Found: C, 61.69; N, 7.78; H, 7.46. MS (ESIMS) m/z 373.22 $(M+Na)^+$, m/z 374.10 $(M+H+Na)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.27-7.02 (m, ArH, 5H), 6.44 (d, *J*= 6.9 Hz, NH, 1H), 4.84 (d, *J*= 7.2 Hz, NH, 1H), 4.74-4.79 (m, CH, 1H), 4.04-4.06 (m, CH, 1H), 3.65 (s, OCH_3, 3H), 2.96-3.13 (m, 2H), 1.37 (s, CH_3, 9H), 1.23-1.25 (d, *J*= 5.9 Hz, CH_3, 3H).

(b) Boc-Ala-Phe-OH **20**: Compound 20 was prepared as a white solid (82%) from 19 according to the procedure described for the preparation of 10.

Yield = 2.05 g (6.1 mmol, 76%).

Anal.Calcd. for $C_{17}H_{24}N_2O_5$ (336): C, 60.71; N, 8.33; H, 7.14. Found: C, 60.73; N, 8.30; H, 7.16. MS (ESIMS) m/z 337.43 $(M+H)^+$, m/z 359.11 $(M+H+Na)^+$. 300 MHz ^{1}H NMR (DMSO-d_6) δ 12.61 (b, OH, 1H), 7.68 (d, *J* = 6.7 Hz, NH, 1H), 6.39 (d, *J* = 7.5 Hz, NH, 1H), 6.93-7.04 (m, ArH, 5H), 4.14-4.21 (m, CH, 1H), 3.81-3.87 (m, CH, 1H), 3.69-3.73 (m, CH_2, 2H), 1.12 (s, CH_3, 9H), 0.87 (d, *J* = 6.2 Hz, CH_3, 3H).

(c) Boc-Ala-Phe-Ala-OMe **21**: According to the process described for the preparation of 9, 21 was prepared from 20 and H_2N-Ala-OMe.HCl as white solid (85%).

Yield = 2.15 g (5.1 mmol, 85%).

Anal.Calcd. for $C_{21}H_{31}N_3O_6$ (421): C, 59.86; N, 9.98; H, 7.36. Found: C, 59.89; N, 9.94; H, 7.38. MS (ESIMS) m/z 422.31 $(M+H)^+$, m/z 445.12 $(M+H+Na)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.33-7.20 (m, ArH, 5H), 6.60 (d, *J* = 7.8 Hz, NH, 1H), 6.47 (d, *J* = 11.2 Hz, NH, 1H), 4.81 (d, *J* = 8.9 Hz, NH, 1H), 4.62-4.69 (m, CH, 1H), 4.33-4.53 (m, CH, 1H), 4.01-4.11 (m, CH, 1H), 3.71 (s, OCH_3, 3H), 3.02-3.20 (m, CH_2, 2H), 1.40 (s, CH_3, 9H), 1.32-1.35 (d, *J* = 5.9 Hz, CH_3, 3H), 1.27-1.31 (d, *J* = 5.6 Hz, CH_3, 3H).

(d) Boc-Leu-Val-Ala-Phe-Ala-OMe **6**: According to the process described for the preparation of 2 from Boc-Leu-Val-OH and 21 peptide 6 was obtained as white solid.

Yield = 1.71 g (2.7 mmol, 60%)

Anal. Calcd. for $C_{32}H_{51}N_5O_8$ (633): C, 60.66; H, 8.06; N, 11.06. Found: C, 60.64; H, 8.03; N, 11.08. MS (ESIMS) m/z 656.3 $(M+Na)^+$, m/z 657.3 $(M+H+Na)^+$, m/z 658.5 $(M+Na+2H)^+$. 300 MHZ ^{1}H NMR ($CDCl_3$) δ 7.43-7.22 (m, ArH, 5H), 7.04 (d, *J*=7.1 Hz, NH, 1H), 7.33 (d, *J*=5.7 Hz, NH, 1H), 7.11 (d, *J*=5.5 Hz, NH, 1H), 6.59 (d, *J*=5.4 Hz, NH, 1H), 5.01 (b, NH, 1H), 4.76-4.68 (m, CH, 1H), 4.58-4.48 (m, CH, 1H), 4.29-4.22 (m, CH, 1H), 4.06-3.97 (m, CH, 2H), 3.72 (s, OCH_3, 3H), 3.00-2.92 (m, CH_2, 2H), 2.34-2.30 (m, CH, 1H), 1.95-1.91 (m, CH_2, 2H), 1.76-1.71 (m, CH, 1H), 1.62 (s, CH_3, 9H), 1.47-1.42 (m, CH_3, 6H), 1.00-0.86 (m, CH_3, 12H). ^{13}C NMR (75 MHz, RT, $(CD_3)_2SO$, δ ppm): 172.84, 172.37, 171.81, 170.74, 170.38, 155.35, 137.57, 129.18, 127.97, 126.21, 78.15, 56.90, 53.42, 53.14, 51.87, 47.57, 37.35, 33.35, 30.99, 28.15, 24.47, 24.28, 22.99, 21.49, 19.15, 18.06, 17.81, 16.88. $[\alpha]_D$ 25.8 = -27.90 (C 2.02 CHCl3)

1.6 Synthesis of peptide 7

(a) Boc-Ile-Phe-OMe **22**: According to the process described for the preparation of 9, 22 was prepared from Boc-Ile-OH and H_2N-Phe-OMe.HCl as white solid (75%).

Yield: 3.4 g (8.6 mmol, 75%)

Anal. Calcd. for $C_{21}H_{32}N_2O_5$ (392): C, 64.29; H, 8.16; N, 7.14. Found: C, 64.32; H, 8.14; N, 7.12. MS (ESIMS) m/z 393.21 $(M+H)^+$, m/z 432.11 $(M+H+K)^+$. 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.34-7.12 (m, ArH, 5H), 6.34 (d, *J*= 7.02 Hz, NH, 1H), 5.01 (d, *J*= 7.6 Hz, NH, 1H), 4.93-4.86 (m, CH, 1H), 3.97-3.92 (m, CH, 1H), 3.73 (s, OCH_3, 3H), 2.20-3.09 (m, CH_2, 2H), 1.89-1.80 (m, CH, 1H), 1.46 (s, CH_3, 9H), 1.11-1.09 (m, CH_2, 2H), 0.91-0.82 (m, CH_3, 6H).

(b) Boc-Ile-Phe-OH **23**: Compound 23 was prepared as a white solid (84%) from 22 according to the procedure described for the preparation of 10.

Yield: 2.5 g (6.7 mmol, 84%)

Anal. Calcd. for $C_{20}H_{30}N_2O_5$ (378): C, 63.49; H, 7.94; N, 7.41. Found: C, 63.53; H, 7.96; N, 7.43. MS (ESIMS) m/z 379.17 $(M+H)^+$, m/z 402.11 $(M+H+Na)^+$. 300 MHz ^{1}H NMR (DMSO-d_6) δ 12.46 (b, OH, 1H), 8.04 (d, *J*= 7.9 Hz, NH, 1H), 7.27-7.18 (m, ArH, 5H), 6.59 (d, *J*= 9.1 Hz, NH, 1H], 4.48-4.41 (m, CH, 1H), 3.82-3.76 (m, CH, 1H), 3.08-2.84 (m, CH_2, 2H), 1.57-1.59 (m, CH, 1H), 1.23 (s, CH_3, 9H), 1.05-0.98 (m, CH_2, 1H), 0.98-0.61 (m, CH_3, 6H).

(c) Boc-Ile-Phe-Ala-OMe **24**: According to the process described for the preparation of 9, 24 was prepared from 23 and H_2N-Ala-OMe.HCl as white solid (70%).

Yield: 2.2 g (4.8 mmol, 70%)

Anal. Calcd. for $C_{24}H_{37}N_3O_6$ (463): C, 62.20; H, 7.99; N, 9.07. Found: C, 62.17; H, 7.10; N, 9.09. MS (ESIMS) m/z 464.39 $(M+H)^+$, m/z 467.15 $(M+H+Na)^+$. 300 MHZ 1H NMR ($CDCl_3$) δ δ 7.44-7.14 (m, ArH, 5H), 6.34 (d, *J*= 7.02 Hz, NH, 1H), 5.01 (d, *J*= 7.6 Hz, NH, 1H), 4.96-4.82 (m, CH, 1H), 4.10-3.98 (m, CH, 1H), 3.95-3.92 (m, CH and CH_2, 1H), 3.74 (s, OCH_3, 3H), 2.23-3.19 (m, 2H), 1.89-1.86 (m, CH, 1H), 1.61 (m, CH_3, 3H), 1.41 (s, CH_3, 9H), 1.12-1.09 (m, CH_2, 2H), 0.89-0.80 (m, CH_3, 6H).

(d) Boc-Leu-Val-Ile-Phe-Ala-OMe **7**: According to the process described for the preparation of 2 from Boc-Leu-Val-OH and 24 peptide 7 was obtained as white solid.

Yield: 1.96 g (2.9 mmol, 65%)

Anal. Calcd. for $C_{35}H_{57}N_5O_8$ (675): C, 62.22; H, 8.44; N, 10.37. Found: C, 62.25; H, 8.42; N, 10.35. MS (ESIMS) m/z 698.5 $(M+Na)^+$, m/z 699.3 $(M+H+Na)^+$, m/z 700.5 $(M+Na+2H)^+$. 500 MHZ ^{1}H NMR ($CDCl_3$) δ 7.23-7.20 (m, ArH, 5H), 7.18-7.06 (m, NH, 4H), 6.67 (d, *J*=5.1 Hz, NH, 1H), 4.81-4.77 (m, CH, 1H), 4.23-4.20

(m, CH, 1H), 4.14-4.10 (m, CH, 1H), 4.05-4.02 (m, CH, 2H), 3.72 (s, OCH_3, 3H), 3.49-3.45 (m, CH_2, 2H), 1.88 (b, CH_2, 2H), 1.71-1.68 (m, CH_3, 3H), 1.62-1.58 (m, 3H), 1.41 (s, CH_3, 9H), 1.25-1.23 (m, CH_2, 2H), 1.18-1.11 (m, CH_3, 6H), 0.95-0.87 (m, CH_3, 14H). ^{13}C NMR (75 MHz, RT, $(CD_3)_2SO$, δ ppm): 172.80, 171.53, 171.18, 170.79, 170.54, 155.36, 137.59, 120.06, 127.96, 126.17, 77.96, 59.85, 56.72, 53.15, 51.85, 50.72, 47.57, 37.40, 36.67, 33.35, 28.13, 25.32, 24.47, 23.93, 23.12, 21.56, 19.20, 18.21, 16.87, 15.07, 10.87. $[\alpha]_D$ 25.4 = -26.48 (C 2.05 $CHCl_3$)

1.7 Synthesis of peptide 8

(a) Boc-Phe-Ile-OMe **25**: According to the process described for the preparation of 9, 25 was prepared from Boc-Phe-OH and H_2N-Ile-OMe.HCl as white solid (82%).

Yield: 10.2 g (26.0 mmol, 82%)

Anal. Calcd. for $C_{21}H_{32}N_2O_5$ (392): C, 64.29; H, 8.16; N, 7.14. Found: C, 64.33; H, 8.12; N, 7.16. MS (ESIMS) m/z 393.22 $(M+H)^+$, m/z 432.21 $(M+H+K)^+$. 300 MHz ^1H NMR ($CDCl_3$) δ 7.32-7.16 (m, ArH, 5H), 6.41 (d, *J*=8.4 Hz, NH, 1H), 5.03 (b, NH, 1H), 4.52-4.48 (m, CH, 1H), 3.35-3.34 (m, CH, 1H), 3.69 (s, OCH_3, 3H), 3.08-3.06 (m, CH_2, 2H), 1.85-1.80 (m, CH, 1H), 1.42 (s, CH_3, 9H), 1.14-1.05 (m, CH_2, 1H), 0.91-0.82 (m, CH_3, 6H).

(b) Boc-Phe-Ile-OH **26**: Compound 26 was prepared as a white solid (84%) from 25 according to the procedure described for the preparation of 10.

Yield: 7.9 g (21.0 mmol, 84%)

Anal. Calcd. for $C_{20}H_{30}N_2O_5$ (378): C, 63.49; H, 7.94; N, 7.41. Found: C, 63.45; H, 7.97; N, 7.44. MS (ESIMS) m/z 401.14 $(M+Na)^+$, m/z 402.23 $(M+H+Na)^+$. 300 MHz ^1H NMR (DMSO-d_6) δ12.01 (b, OH, 1H), 7.88 (d, *J*=8.4 Hz, NH, 1H), 7.27-7.18 (m, ArH, 5H), 6.95 (d, *J*=8.6 Hz, NH, 1H), 4.24-4.20 (m, CH, 2H), 3.04-2.93 (m, CH_2, 2H), 1.86-1.80 (m, CH, 1H), 1.50-1.37 (m, CH_2, 1H), 1.30 (s, CH_3, 9H), 0.86-0.84 (m, CH_3, 6H).

(c) Boc-Phe-Ile-Ala-OMe **27**: According to the process described for the preparation of 9, 27 was prepared from 26 and H_2N-Ala-OMe.HCl as white solid (70%).

Yield: 4.6 g (10.0 mmol, 70%)

Anal. Calcd. for $C_{24}H_{37}N_3O_6$ (463): C, 62.20; H, 7.99; N, 9.07. Found: C, 62.16; H, 7.11; N, 9.09. MS (ESIMS) m/z 464.2 $(M+H)^+$, m/z 487.12 $(M+H+Na)^+$. 300 MHz ^1H NMR ($CDCl_3$) δ 7.32-7.19 (m, ArH, 5H), 6.50 (d, *J*=8.7 Hz, NH, 1H), 6.45 (d, *J*=8.7 Hz, NH, 1H), 4.96 (b, NH, 1H), 4.54-4.47 (m, CH, 1H), 4.36-4.4 (m, CH, 1H), 4.26-4.21 (m, CH, 1H), 3.75 (s, OCH_3, 3H), 3.10-3.03 (m, CH_2, 2H), 1.89-1.93 (m, CH, 1H), 1.41 (s, CH_3, 9H), 1.30 (d, *J*=7.2 Hz, CH_3, 3H), 1.01-0.99 (m, CH_2, 1H), 0.90-0.85 (m, CH_3, 6H).

(d) Boc-Leu-Val-Phe-Ile-Ala-OMe **8**: According to the process described for the preparation of 2 from Boc-Leu-Val-OH and 27 peptide 8 was obtained as white solid.

Yield = 2.59 g (3.83 mmol, 85 %)

Anal. Calcd. for $C_{35}H_{57}N_5O_8$ (675): C, 62.22; H, 8.44; N, 10.37. Found: C, 62.26; H, 8.42; N, 10.34. MS (ESIMS) m/z 698.5 $(M+Na)^+$, m/z 699.3 $(M+H+Na)^+$. 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.25-7.13 (m, ArH, 5H), 6.98 (d, *J*=7.2 Hz, NH, 1H), 6.94 (d, *J*=8.3 Hz, NH, 1H), 6.87 (d, *J*=7.6 Hz, NH, 1H), 6.61 (b, NH, 1H), 5.12 (d, *J*=7.7 Hz, NH, 1H), 4.56-4.51 (m, CH, 1H), 4.34-4.29 (m, CH, 1H), 4.18 (m, CH, 1H), 4.12 (m, CH, 1H), 4.91-4.88 (m, CH, 1H), 3.75 (s, OCH_3, 3H), 3.42-3.38 (m, CH_2, 2H), 2.27-2.21 (m, CH, 1H), 1.93-1.90 (m, CH, 1H), 1.52-1.46 (m, CH_2, 4H), 1.44 (s, CH_3, 9H), 1.38-1.30 (m, CH_3, 3H), 0.92-0.84 (m, CH_3, 18H). ^{13}C NMR (75 MHz, RT, $CDCl_3$, δ ppm): 174.39, 174.23, 172.83, 171.21, 170.73, 155.88, 136.12, 129.35, 128.58, 128.55, 129.06, 127.96, 126.26, 78.96, 58.01, 57.92, 57.15, 49.43, 48.10, 40.82, 33.71, 31.19, 28.30, 24.85, 24.80, 24.69, 22.95, 22.12, 19.28, 19.02, 17.56, 15.15, 11.12. $[\alpha]_D$ 26.0 = -26.31 (C 1.98 $CHCl_3$).

^{1}H NMR spectroscopy

All NMR studies were carried out on a Brüker DPX 300 MHz, DRX 500 MHz and AVANCE 600 MHz spectrometer at 300K in $CDCl_3$, C_6D_6 or $(CD_3)_2SO$. Either TMS was used as internal reference or the solvent $CDCl_3$ resonance was fixed at 7.26 ppm as reference. Peptide concentrations were generally used in the range 5-10 mM.

FT-IR spectroscopy

The FT-IR spectra were taken using a Shimadzu (Japan) model FT-IR spectrophotometer with a sample-shuttle device, averaging over 40 scans. Solvent (DCB) spectra were obtained under the same conditions using a cuvette with 1 mm path length. A Nicolet FT-IR instrument [Magna IR-750 spectrophotometer Series II)] was used to obtain the solid state and the gel state FT-IR spectra. For the solid-state measurements the KBr disk technique was used. The solvent spectrum was subtracted from the gel spectra to obtain pentapeptide **1** spectra in the gel state.

Mass spectrometry

The mass spectra of the peptides were recorded on a Micromass Zabspec Hybrid Sector-TOF by positive mode electronspray ionization using a 1 % solution of acetic acid in methanol/water as liquid carrier.

Optical and Polarization microscopy

The reported peptides were strained with Congo red and their binding capacity with the dye was examined under optical microscope. The gel slices were placed on microscopic slides and dried in vacuum at room temperature. An alkaline saturated Congo red solution was prepared by dissolving Congo red in a solution (80% methanol / 20% glass distilled water) containing 10 μL of 1% NaOH. The sample slides containing a slice of peptide gel

were stained by this alkaline stain solution for 2 minutes, then the excess stain (Congo red solution) was removed by rinsing the sample coated slide with 80% methanol / 20% glass distilled water solution for several times. The stain sample was dried under vacuum at room temperature for 24 hours, then visualized at 40× or 100× magnification and birefringence was observed between crossed polarizers.

Scanning Electron Microscopic Studies

Morphologies of all reported dendritic gels were investigated using field emission scanning electron microscopy (FE-SEM). For SEM study, a piece of the gel material was placed on a glass cover slip and then dried under a vaccumand and then gold coated sample was placed to observe the morphology. Micrographs were taken in a SEM apparatus (Jeol Scanning Microscope-JSM-6700F).

Transmission Electron Microscopic Studies

Transmission electron microscopy measurements were carried out to observe finer morphological details. Transmission electron microscopic studies were done by placing a small amount of gel (at its minimum gelation concentration) of the corresponding compounds on carbon-coated copper grids (300 mesh) and dried by slow evaporation. The grid was then allowed to dry in vacuum at 30^0C for 2 days. Images were taken by JEM-2010 electron microscope and FEI (Tecnai spirit) instrument.

Wide Angle X-ray Diffraction Study

The WAXS patterns were made on the tripeptide gel of 5 % (w/v) peptide 1 in benzene. The experiment was carried out in a Seifert X-ray diffractometer (C 3000) with a parallel beam optics attachment. The instrument was operated at a 35 KV voltage and 30 mA current and was calibrated with a standard silicon sample. The sample was scanned from 2° to 50° 2θ at the step scan mode (step size 0.03°, preset time 2 s) and the diffraction pattern was recorded using a scintillation scan detector.

Polarimeter

Optical rotations were measured by PerkinElmer instrument. Model 341 LC Polarimeter.

Tables:

Table S1: Major peaks in FTIR spectra obtained from peptide **1** to **8** in their solid states[a].

Peptide	C=O stretch / NH bending (cm^{-1})		NH stretch (cm^{-1})
	Amide I	Amide II	
Boc-L-V-F-F-A-OMe **1**	1628(st)	1554(st)	3295(st)
Boc-L-L-F-F-A-OMe **2**	1652(st), 1685(st)	1552(m)	3320(st)
Boc-L-I-F-F-A-OMe **3**	1631(st), 1695(st)	1576(m)	3278(w), 3327 (st)
Boc-L-V-F-F-A-OEt **4**	1641(st), 1691(m)	1540(m)	3283(st), 3417(w)
Piv-L-V-F-F-A-OMe **5**	16369st)	1534(m)	3322(st)
Boc-L-V-A-F-A-OMe **6**	1631(st)	1526(m)	3284(st), 3322(st)
Boc-L-V-I-F-A-OMe **7**	1635(st), 1695(w)	1572(m)	3282(st), 3325(st), 3460(w)
Boc-L-V-F-I-A-OMe **8**	1641(st), 1692(m)	1534(m)	3285(st), 3417(vw)

[a]st = strong, m = medium, w = weak, vw = very weak

Table S2: Major Peaks in the XRD Pattern for Compound **2**

Peptide **2**	d-spacing (A^o)	
	Bulk solid:	9.83, 6.97, 5.89, 5.60, 5.24, 4.98, 4.14, 3.90, 3.64, 3.16, 2.72, 2.41, 1.94
	Wet gel:	12.58, 9.49, 8.58, 5.17, 4.69, 4.36
	Dried gel:	11.82, 9.75, 8.79, 6.93, 6.39,5.82, 5.21, 4.95, 4.43, 4.20, 4.10, 3.81, 3.60, 3.15, 2.88, 2.71

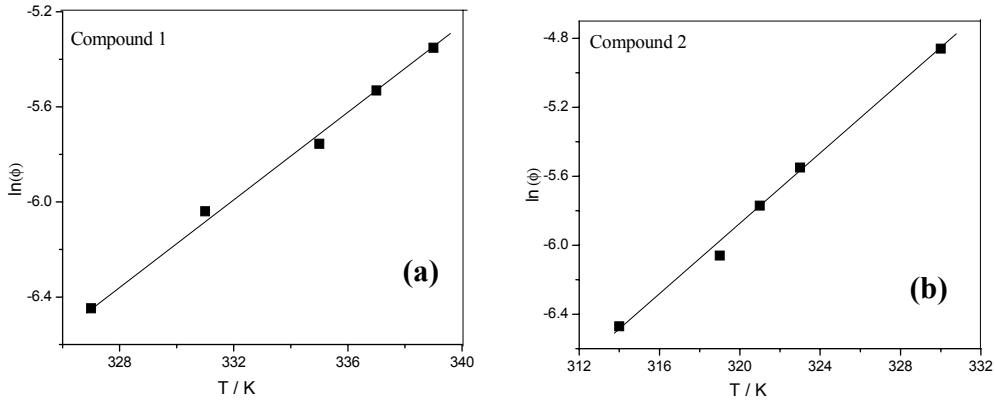

Fig. S1: (a) Concentration-temperature phase diagrams ln(ϕag) vs. T of peptide **1** in different solvents, (b) Concentration-temperature phase diagrams ln(ϕag) vs. T of peptide **2** in different solvents.

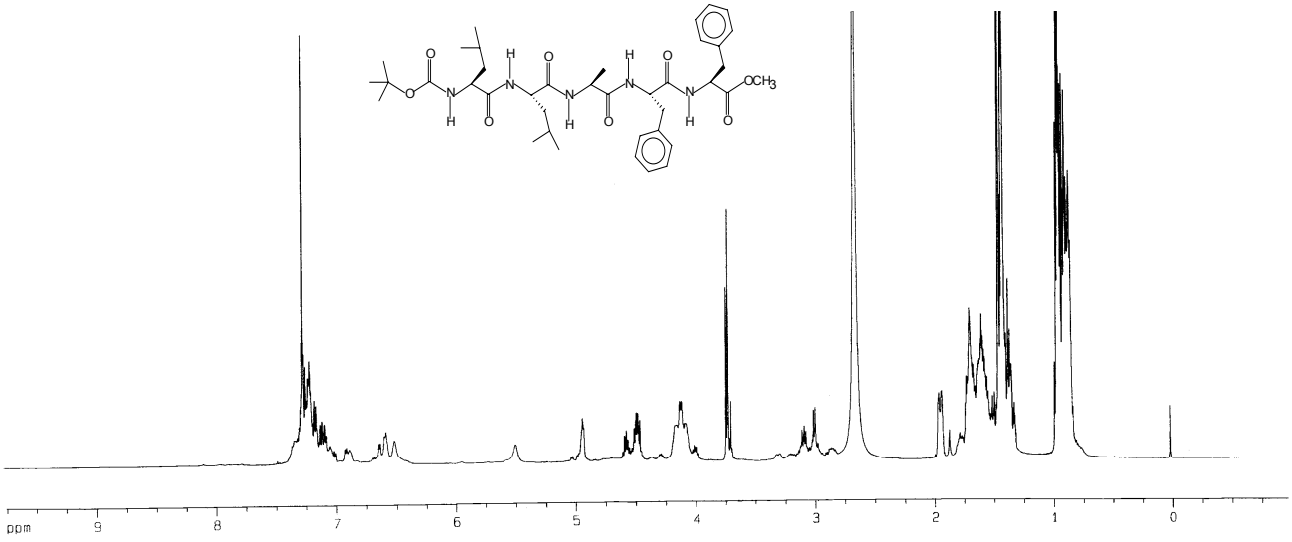

Fig. S2: 500 MHz NMR Spectra of Peptide **2**

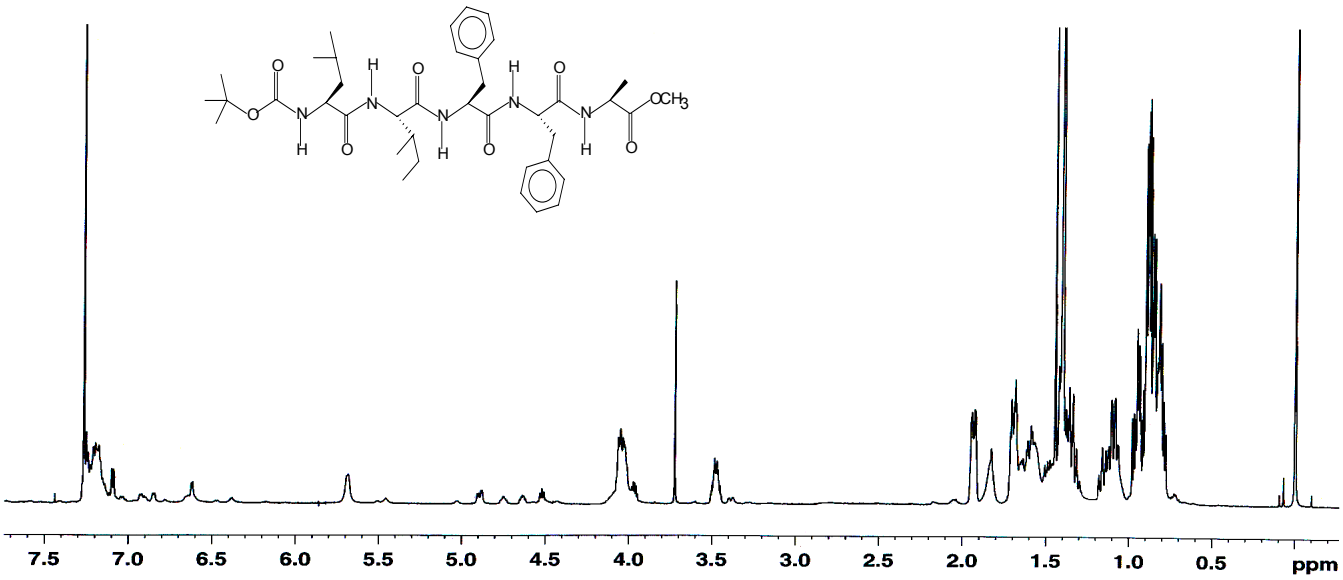

Fig. S3: 600 MHz NMR Spectra of Peptide **3**

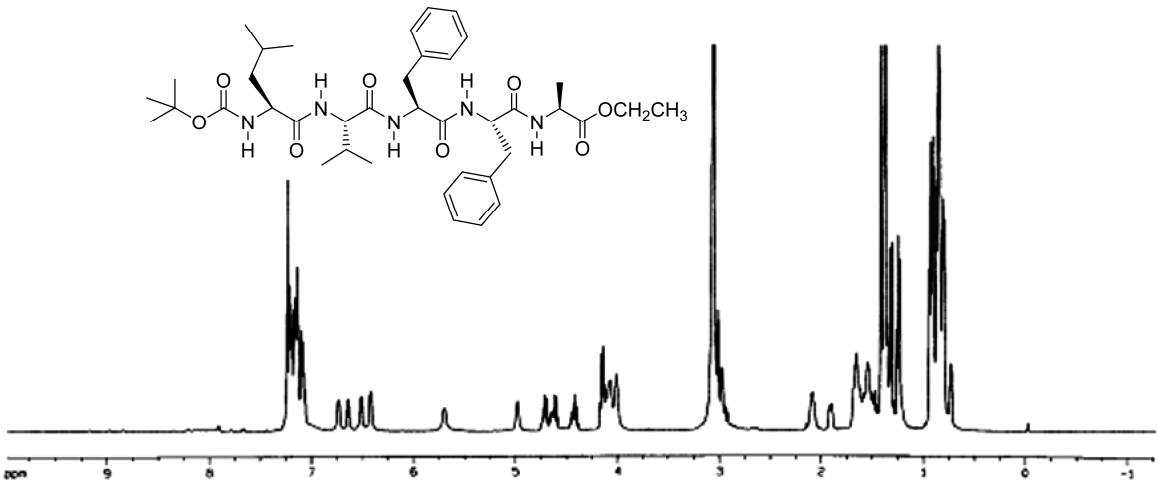

Fig. S4: 500 MHz NMR Spectra of Peptide **4**

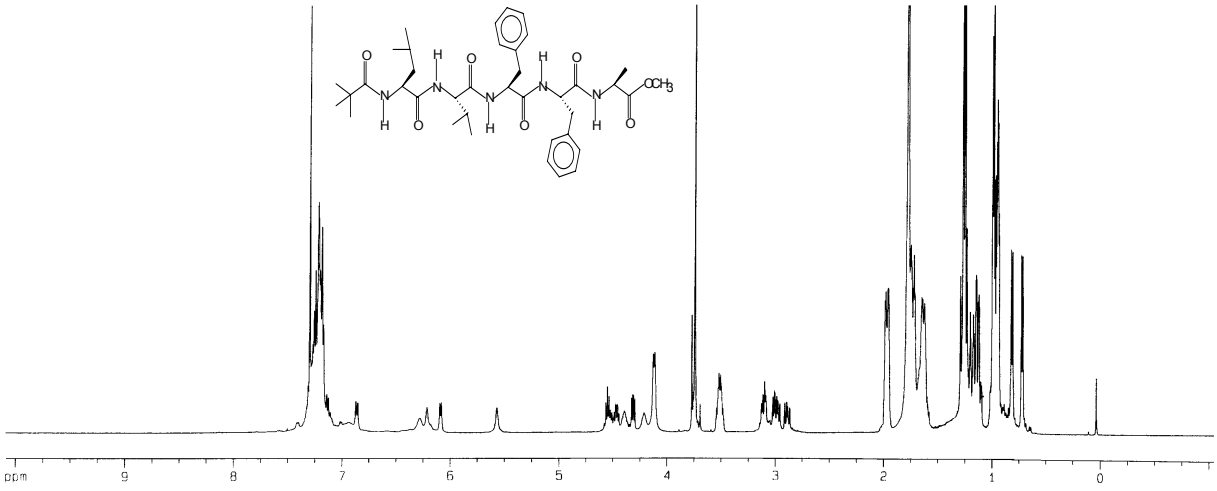

Fig. S5: 500 MHz NMR Spectra of Peptide **5**

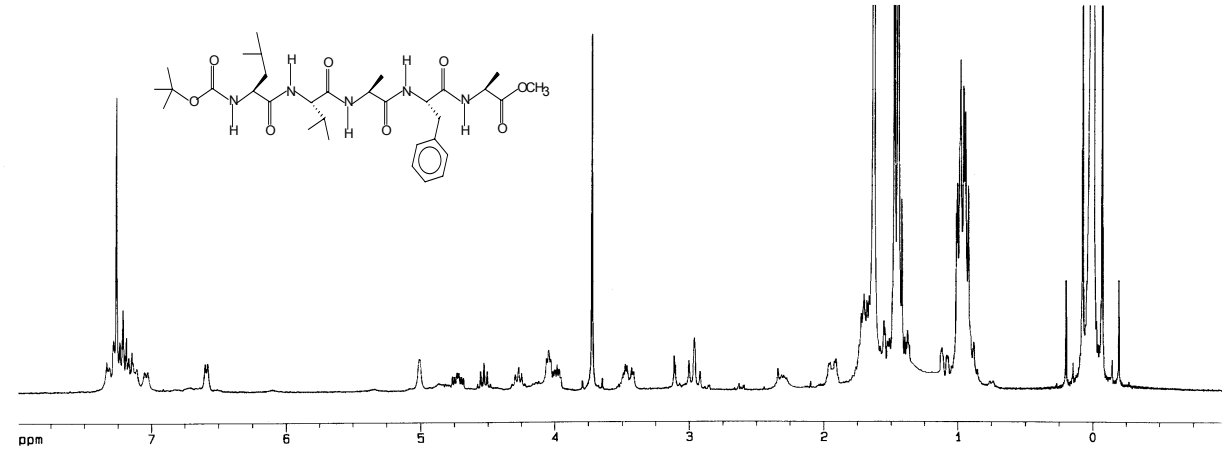

Fig. S6: 300 MHz NMR Spectra of Peptide **6**

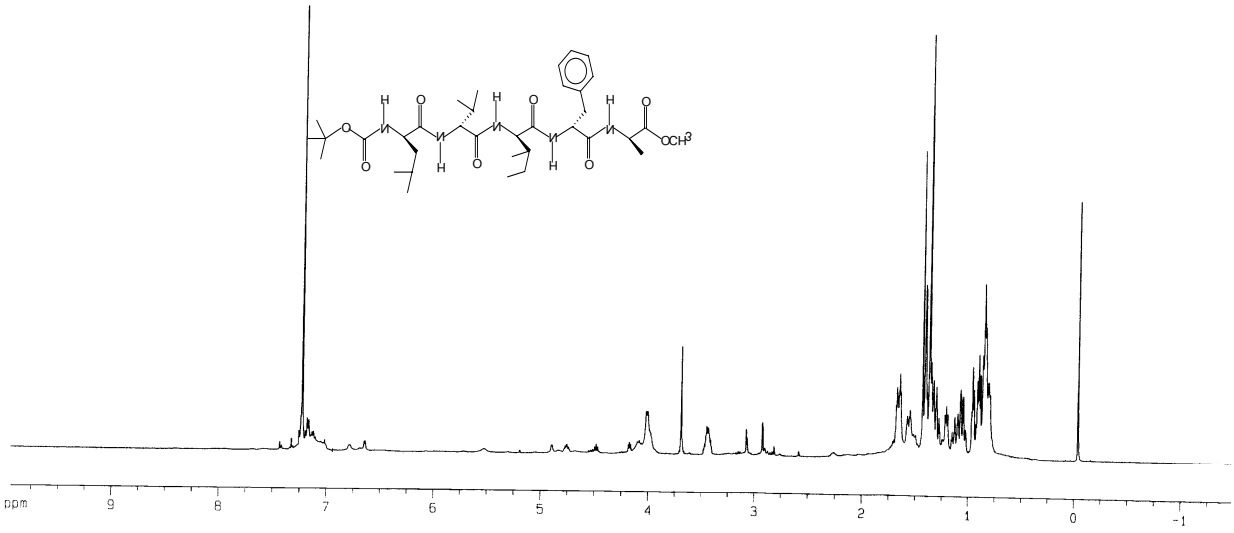

Fig. S7: 500 MHz NMR Spectra of Peptide **7**

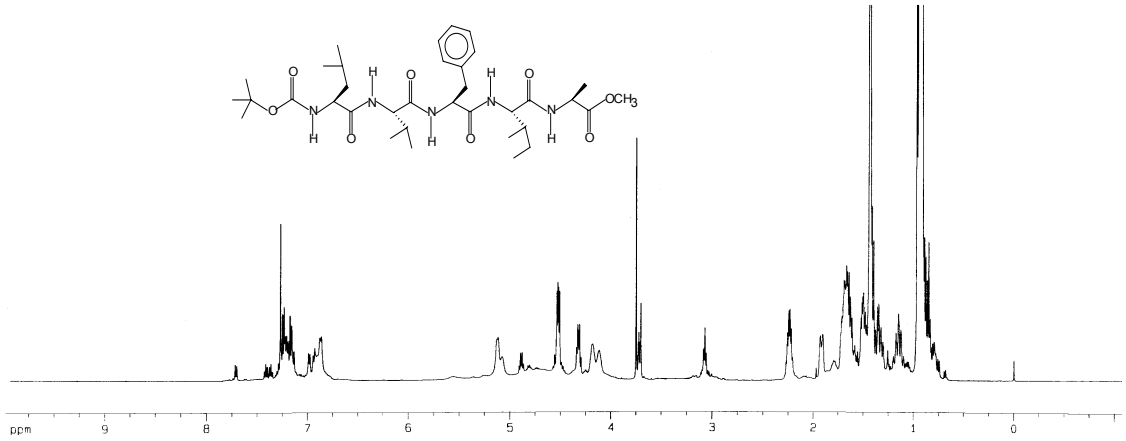

Fig. S8: 500 MHz NMR Spectra of Peptide **8**

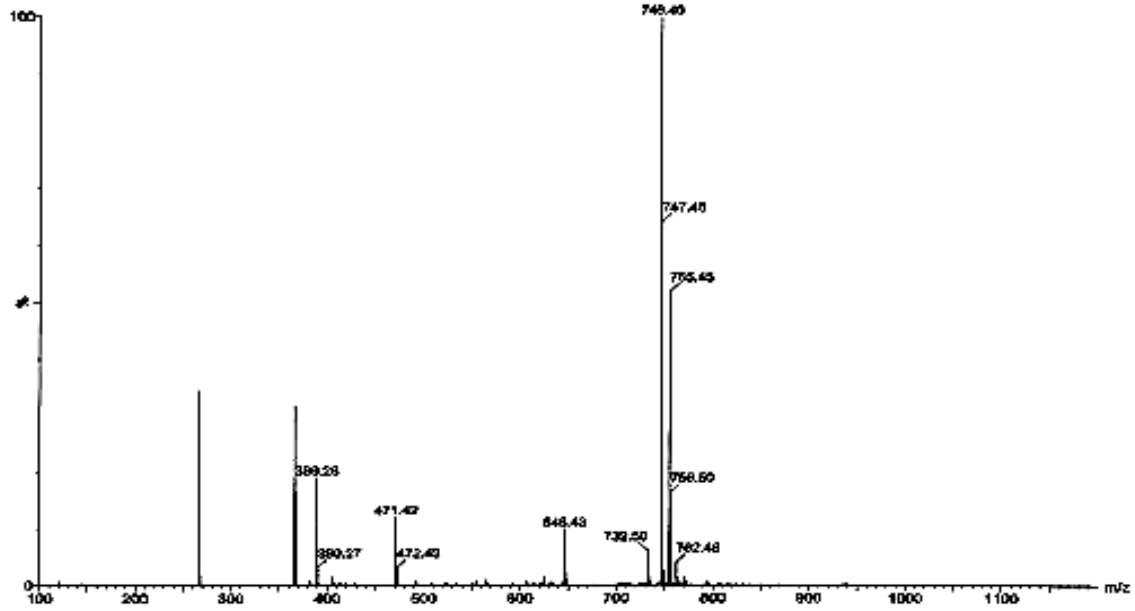

Fig. S9: ESI-MS Spectra of Peptide **2**

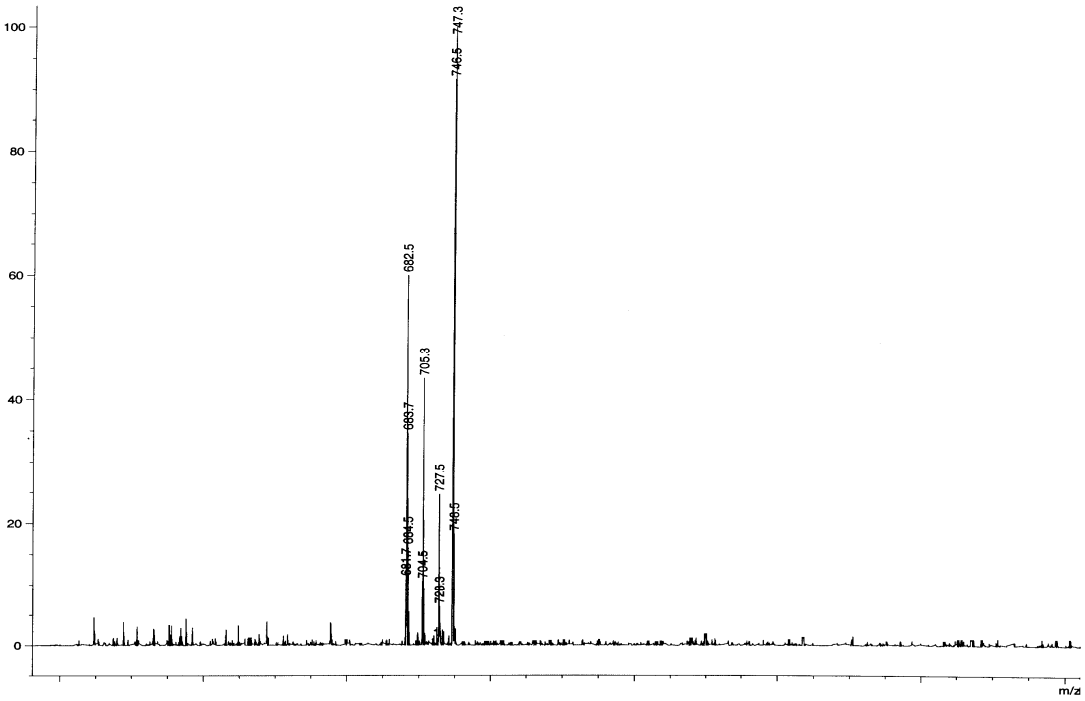

Fig. S10: ESI-MS Spectra of Peptide **3**

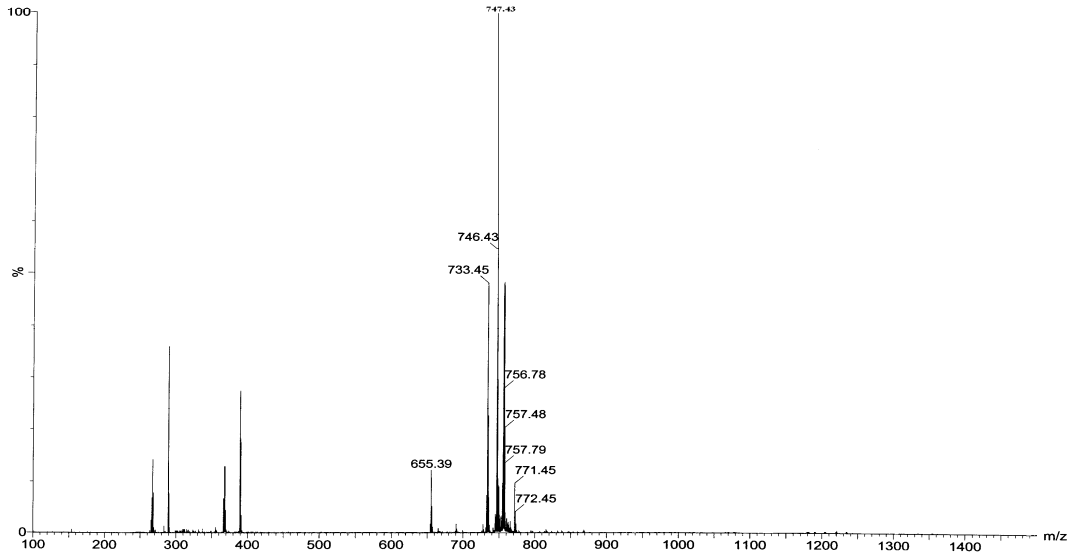

Fig. S11: ESI-MS Spectra of Peptide **4**

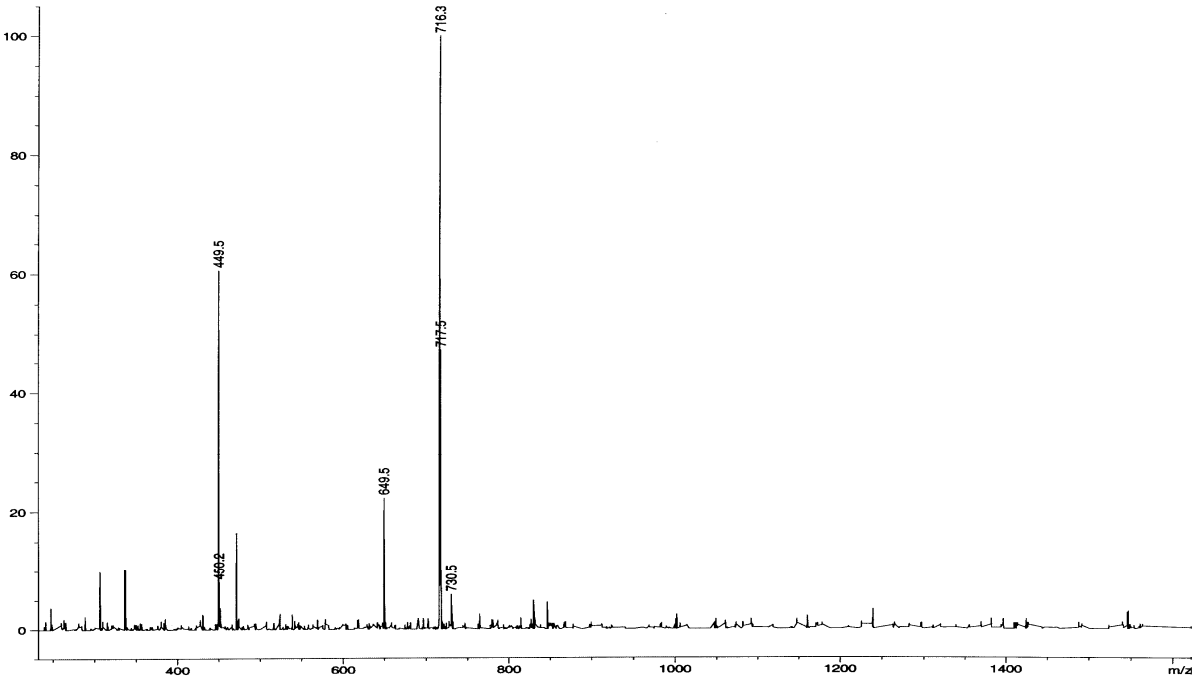

Fig. S12: ESI-MS Spectra of Peptide **5**

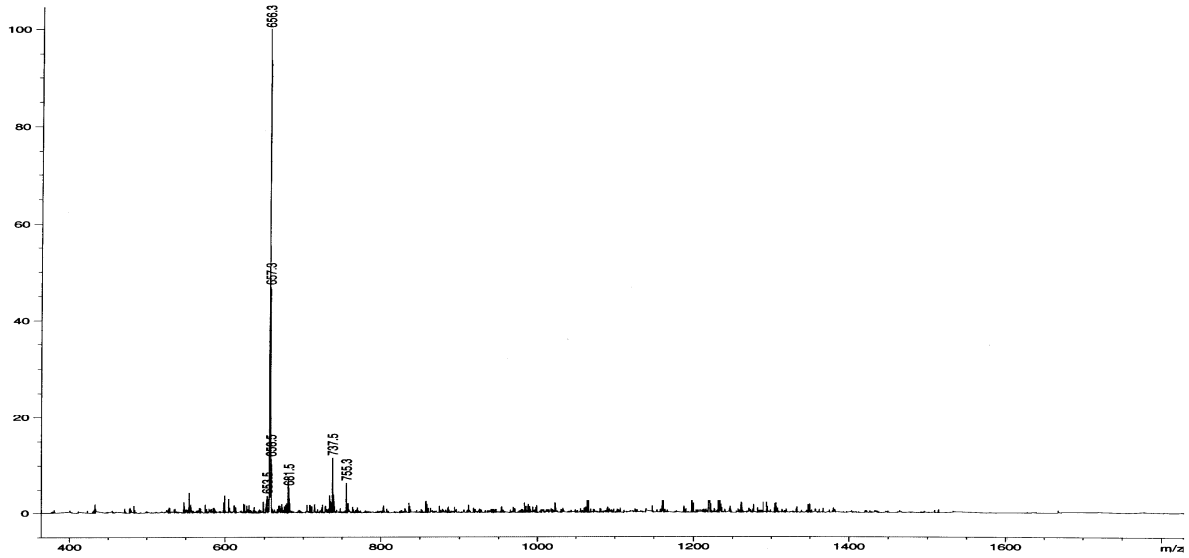

Fig. S13: ESI-MS Spectra of Peptide **6**

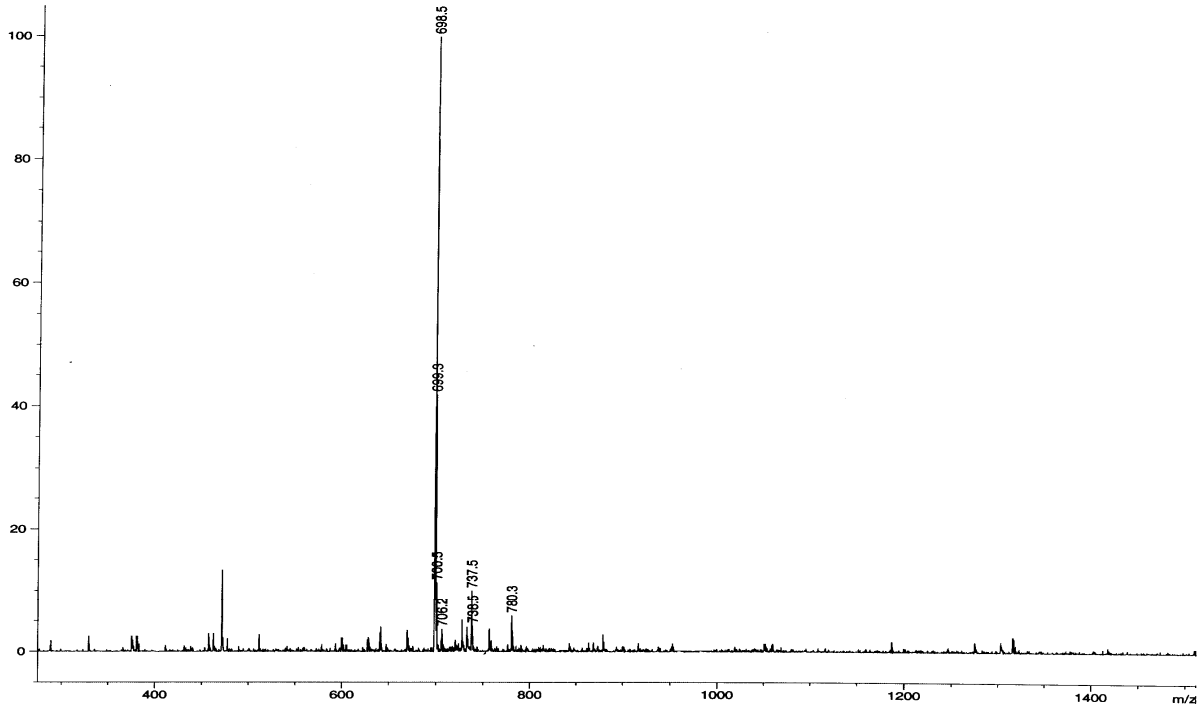

Fig. S14: ESI-MS Spectra of Peptide **7**

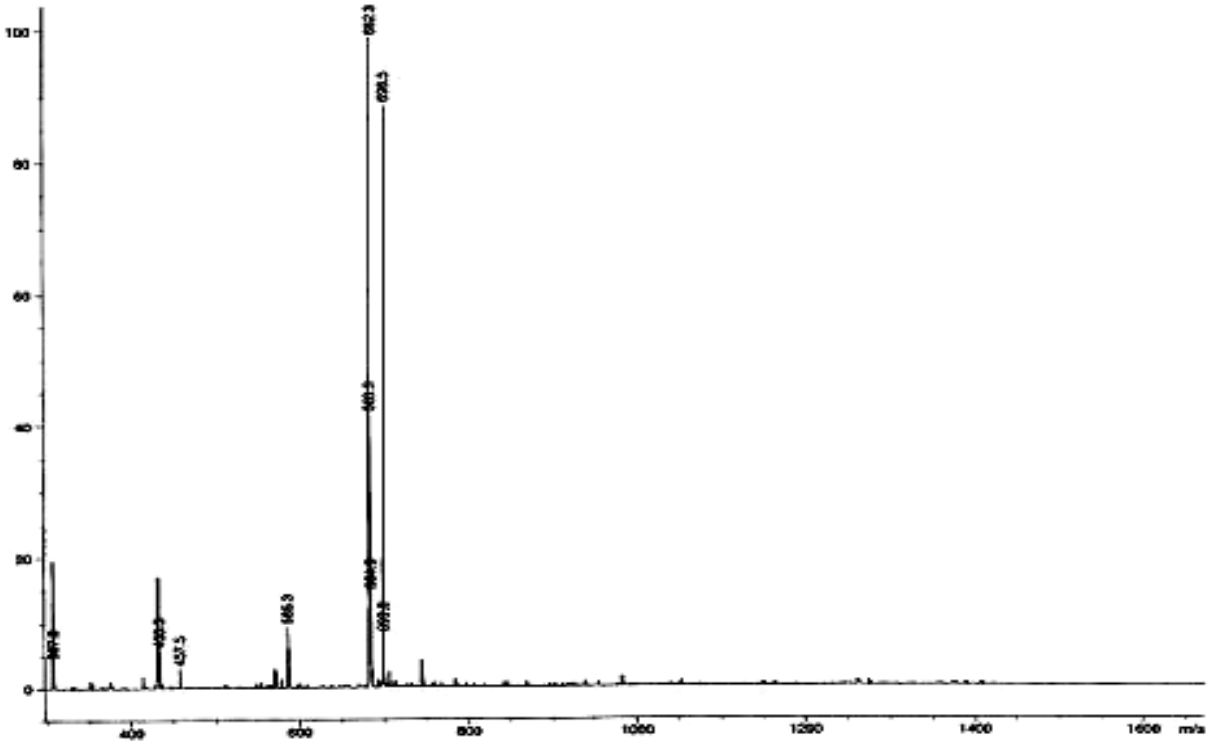

Fig. S15: ESI-MS Spectra of Peptide **8**

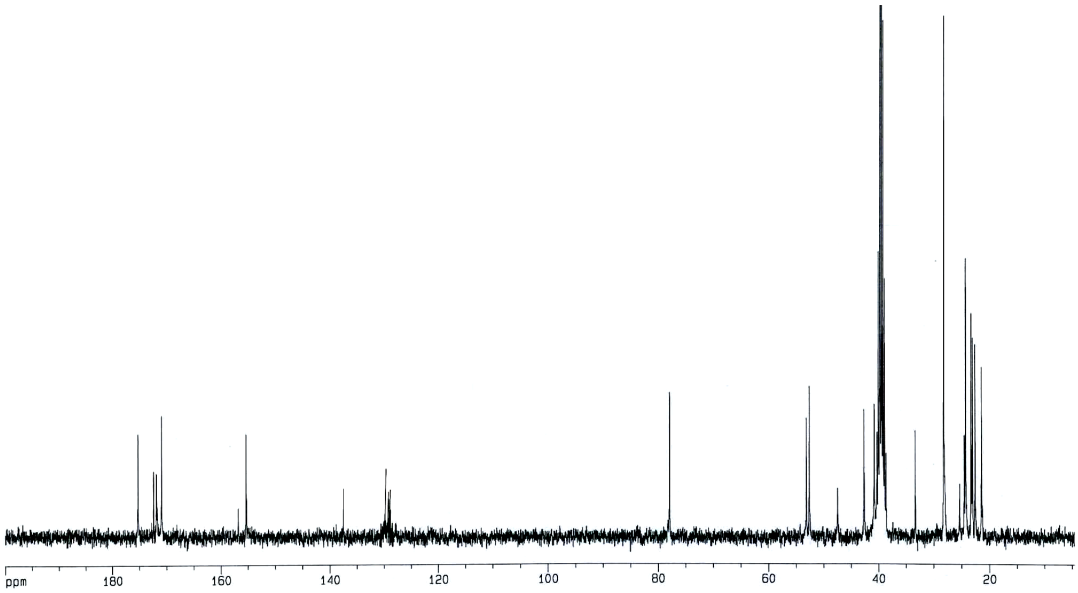

Fig. S16: ^{13}C NMR Spectra of Peptide **2**

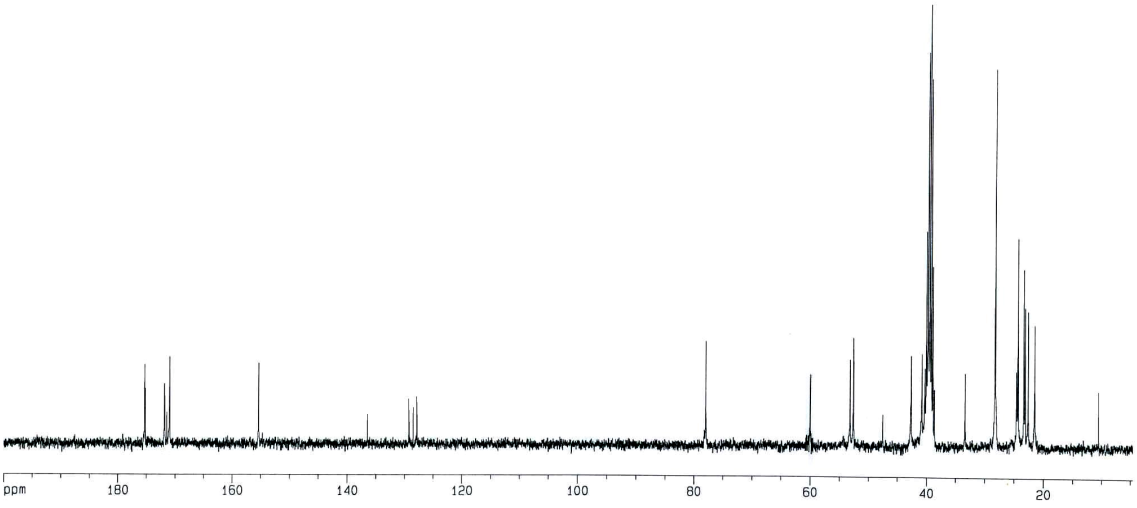

Fig. S17: ^{13}C NMR Spectra of Peptide **3**

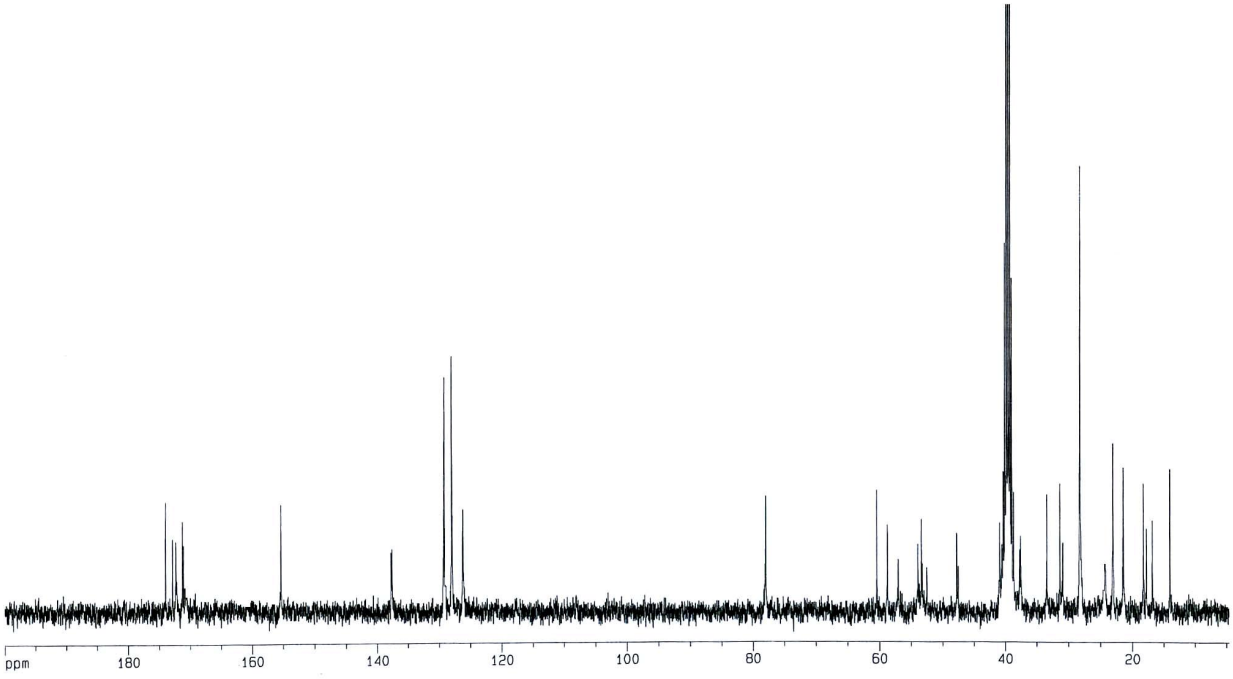

Fig. S18: ^{13}C NMR Spectra of Peptide **4**

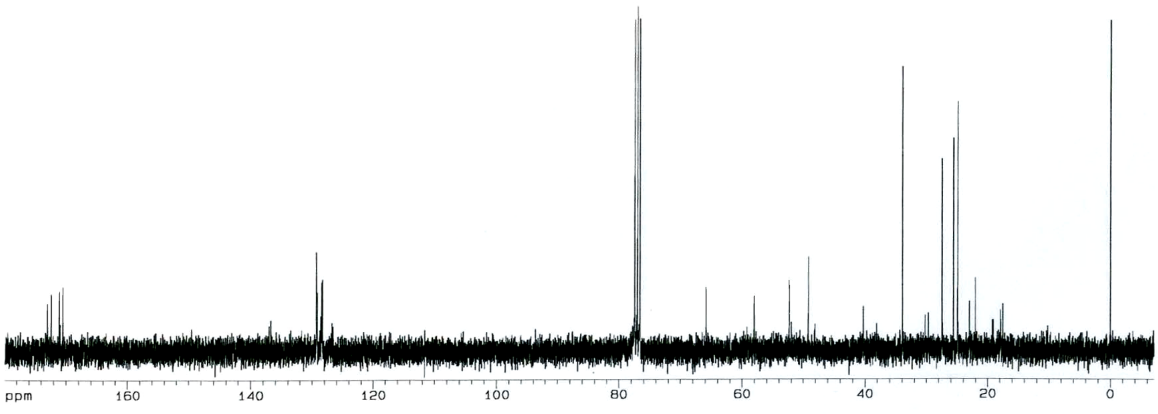

Fig. S19: ^{13}C NMR Spectra of Peptide **5**

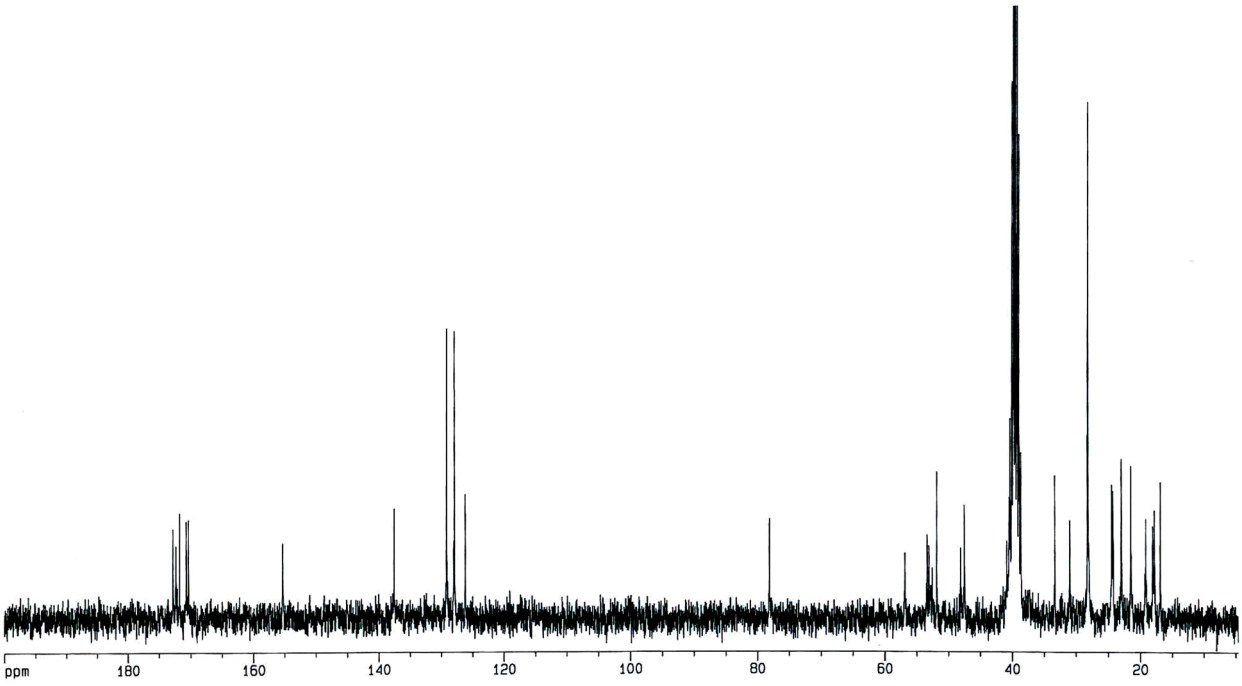

Fig. S20: ^{13}C NMR Spectra of Peptide **6**

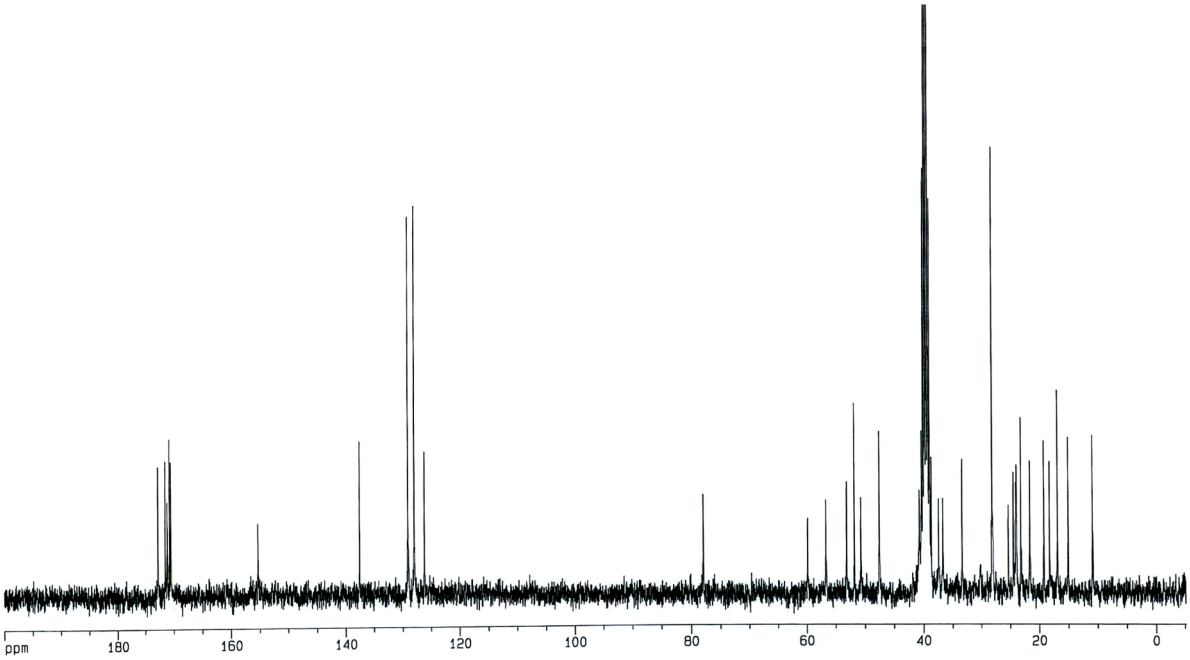

Fig. S21: ^{13}C NMR Spectra of Peptide **7**

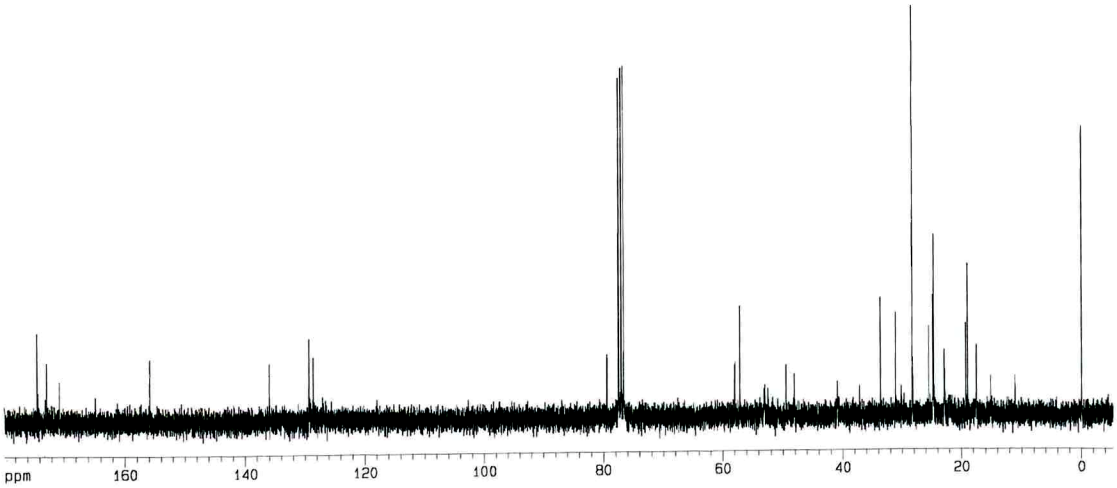

Fig. S22: ^{13}C NMR Spectra of Peptide **8**

Ref. S1. M. Bodanszky, A. *The practice of peptide synthesis. Springer: New York,* **1984**; pp 1–282.