Supporting Information

Metal Driven Folding and Assembly of Minimal β-sheet into 3D-Porous Honeycomb Framework

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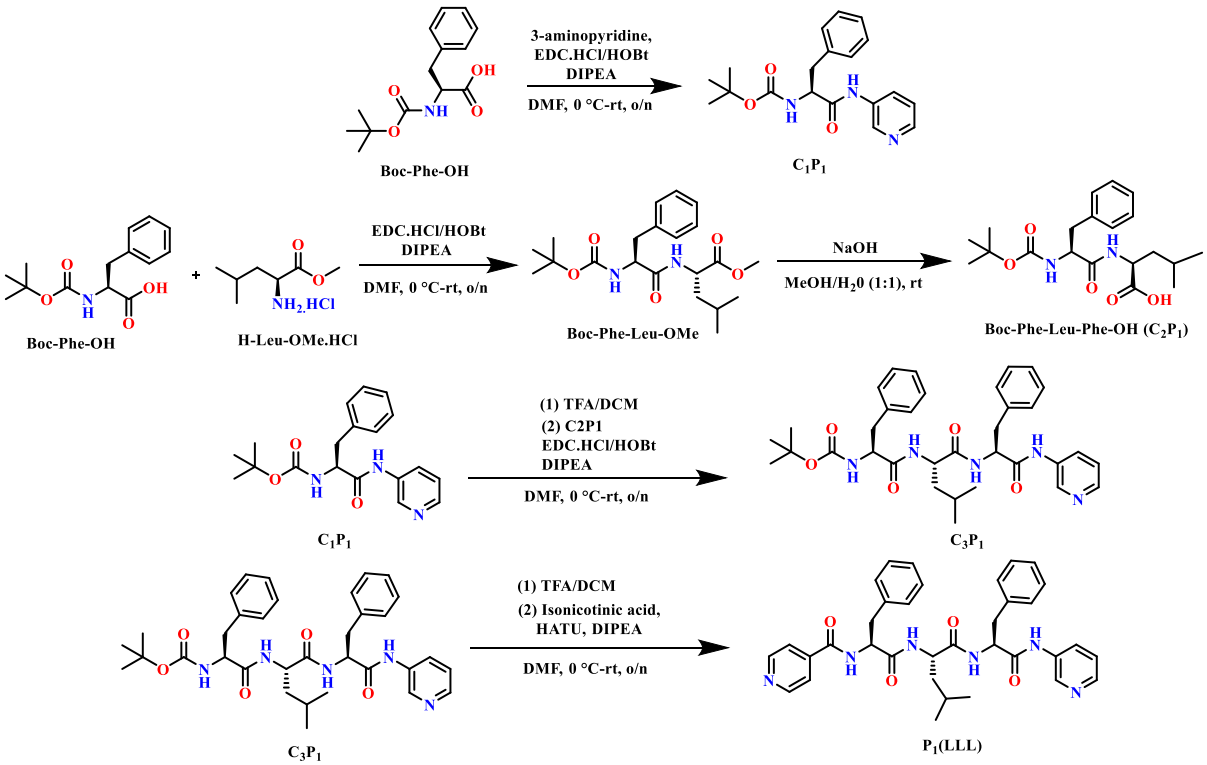
Materials and methods

Boc-L-Phenylalanine, Boc-D-Phenylalanine, Boc-L-leucine and Boc-D-leucine, H-Leucine, 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide hydrochloride (EDC.HCl), *N*,*N*,*N*′,*N*′-Tetramethyl-O-(1*H*-benzotriazol-1-yl) uronium hexafluorophosphate (HBTU), Isonicotinic acid, Nicotinic Acid were purchased from BLD Pharmatech Limited. 1-hydroxy-1H-benzotriazole monohydrate (HOBt•H_2O), Trifluoroacetic acid (TFA), *N*, *N*-Diisopropylethylamine (DIPEA), and Di-*tert*-butyl dicarbonate were purchased from Spectrochem, $AgBF_4$ and $AgTF_2N$ were purchased from TCI. Other reagents and solvents were purchased from TCI, and Spectrochem. All chemicals were of reagent grades and used without any further purification.

Peptide synthesis (P1)



Scheme S1. Synthesis of peptide **P1= 4Py-Phe-Leu-Phe-3Py**

Boc-L-Phe-3Py (C1P1)

Boc-L-Phenylalanine (1.2 equiv.) was dissolved in DMF to which coupling agent EDC.HCl (1.2 equiv.), HOBt.H_2O (1.2 equiv.) and DIPEA (2.5 equiv.) were added and stirred for 15 min at 0 °C under inert conditions. Further, 3-aminopyridine (1 equiv.) was added to the reaction mixture and stirred overnight at ambient temperature, the reaction progress was monitored by TLC. Upon completion of reaction, the reaction mixture was diluted with ethyl acetate and washed thrice successively with ice cold water, saturated sodium carbonate solution and brine. The organic layer was dried over a bed of anhydrous sodium sulphate and evaporated on a rotavapor to yield the crude product. The crude product was purified using column chromatography employing silica as stationary phase (EtOAc/Hexane=70:30). A white solid Boc-L-Phe-3Py (C1P1) was obtained with a 78% yield.

Boc-L-Phe-L-Leu-OH (C2P1)

Boc-L-Phenylalanine (1 equiv.) was dissolved in DMF to which coupling agent EDC.HCl (1 equiv.), HOBt.H_2O (1 equiv.) and DIPEA (3.5 equiv.) were added and stirred at 0 °C for 15 min under inert conditions. Further, L-Leucine methyl ester hydrochloride (1 equiv.) was added was added to the reaction mixture and stirred overnight at ambient temperature, the reaction

progress was monitored by TLC. Upon completion of reaction, the reaction mixture was diluted with ethyl acetate and washed thrice successively with ice cold water, 1N HCl, saturated sodium carbonate solution and brine respectively. The organic layer was dried over a bed of anhydrous sodium sulphate and evaporated on a rotavapor to yield white solid product of Boc-L-Phe-L-Leu-OMe.

Boc-L-Phe-L-Leu-OMe was dissolved in methanol to which an aqueous solution of NaOH (5 equiv.) was added and stirred at ambient temperature, the reaction progress was monitored by TLC. Upon completion of reaction, methanol was evaporated on a rotavapor and the resulting aqueous reaction mixture was acidified using 1N HCl till pH 2; the aqueous layer was then extracted with ethyl acetate. The ethyl acetate layer was further washed with brine and dried over a bed of anhydrous sodium sulphate. The organic layer was evaporated on a rotavapor to yield a white fluffy solid product of Boc-L-Phe-L-Leu-OH (C2P1) with a 70% yield.

Boc-L-Phe-L-Leu-L-Phe-3Py (C3P1)

C1P1 was subjected to Boc deprotection using TFA/DCM (1:1). The reaction mixture was stirred at room temperature and the reaction progress was monitored by TLC. Upon completion of deprotection reaction, DCM was evaporated on a rotavapor and successively washed five times with DCM.

C2P1 (1.2 equiv.) was dissolved in DMF to which coupling agent EDC.HCl (1.2 equiv.), HOBt.H_2O (1.2 equiv.) and DIPEA (3.5 equiv.) were added and stirred at 0 ^oC for 15 min under inert condition. Further, the Boc deprotected C1P1 (1 equiv.) was added and stirred overnight, the reaction progress was monitored by TLC. Upon completion of reaction, the reaction mixture was diluted with ethyl acetate and washed thrice successively with ice cold water, saturated sodium carbonate solution and brine. The organic layer was dried over a bed of anhydrous sodium sulphate and evaporated on a rotavapor to yield the crude product. The crude product was purified using column chromatography employing silica as stationary phase (EtOAc/Hexane=80:20). A white solid product Boc-L-Phe-L-Leu-L-Phe-3Py (C3P1) was obtained with a 75% yield.

4Py-L-Phe-L-Leu-L-Phe-3Py (P1)

C3P1 was subjected to Boc deprotection using TFA/DCM (1:1). The reaction mixture was stirred at room temperature and the reaction progress was monitored by TLC. Upon completion of deprotection reaction, DCM was evaporated on a rotavapor and successively washed five times with DCM.

Isonicotinic acid (1.2 equiv.) was dissolved in DMF to which coupling agent HATU (1.5 equiv.) and DIPEA (3.5 equiv.) were added and stirred at 0 ^oC under inert condition. Further, the Boc deprotected C3P1 was added and stirred overnight, the reaction progress was monitored by TLC. Upon completion of reaction, the reaction mixture was diluted with ethyl acetate and washed thrice successively with ice cold water, saturated sodium carbonate solution and brine. The organic layer was dried over a bed of anhydrous sodium sulphate and evaporated on a rotavapor to obtain peptide P1 with 70% yield

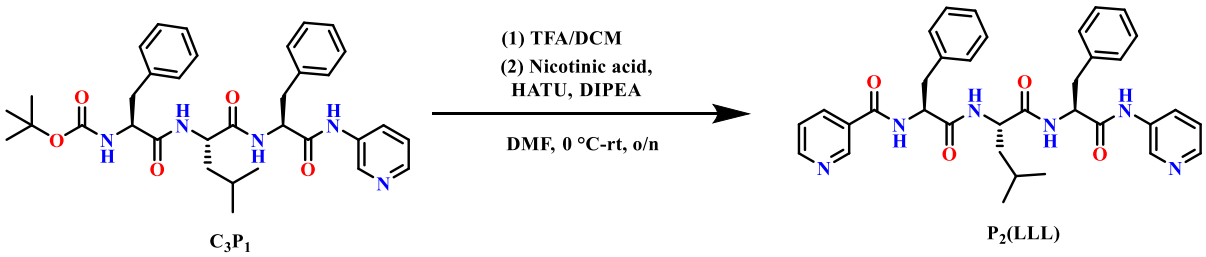
The synthesized peptide P1 was further subjected to Reverse Phase HPLC purification using a C-18 column employing Acetonitrile and Water as mobile phase and lyophilised.

Synthesis of Peptide P2

C3P1 was subjected to Boc deprotection using TFA/DCM (1:1). The reaction mixture was stirred at room temperature and the reaction progress was monitored by TLC. Upon completion of deprotection reaction, DCM was evaporated on a rotavapor and successively washed five times with DCM.

Nicotinic acid (1.2 equiv.) was dissolved in DMF to which coupling agent HATU (1.5 equiv.) and DIPEA (3.5 equiv.) were added and stirred at 0 °C under inert condition. Further, the Boc deprotected C3P1 was added and stirred overnight, the reaction progress was monitored by TLC. Upon completion of reaction, the reaction mixture was diluted with ethyl acetate and washed thrice successively with ice cold water, saturated sodium carbonate solution and brine. The organic layer was dried over a bed of anhydrous sodium sulphate and evaporated on a rotavapor to obtain peptide P2 with 70% yield.

The synthesized peptide P2 was further subjected to Reverse Phase HPLC purification using a C-18 column employing Acetonitrile and Water as mobile phase and lyophilised.



Scheme S2. Synthesis of peptide **P2 = 3Py-Phe-Leu-Phe-3Py**

Crystallization of P1-$AgBF_4$ complex

Ligand **P1** (3.79 mg, 25 mM) in ethanol (250µL), and $AgBF_4$ (1.21 mg, 25 mM) in ethanol (250µL) were mixed in a capped microtube. The microtube was kept in dark at ambient temperature. After 7 days, white block crystals were obtained.

Gelation study on P2:

Peptide **P2** (3.79 mg, 25 mM) was dissolved in ethanol (250µL) and $AgBF_4$ (1.21 mg, 25 mM) in water (250 µL) in a glass vial. Sonicated for 1 min, resulting in instantaneous formation of stable gel as confirmed by vial inversion method.

Rheology:

Rheological measurements were carried out using an Anton Parr MCR302 rheometer using a parallel plate geometry. The frequency sweep experiments were conducted in 200 µL samples of pregelated hydrogel disks in the frequency range of 0.1-100 Hz at a constant strain of 0.1%. The strain sweep experiments were also performed in 200 µL samples of pre-gelated hydrogel disks by increasing the strain from 0.01-100% at a constant frequency of 1 Hz.

FTIR Spectroscopy:

Dried lyophilized metallogel powder were placed in dimond crystal of IRTracer-100 instrument (Shimadzu, japan) and spectra were recorded in the range of 4000–400 cm^{-1}

Transmission electron microscopy:

A 5 µL aliquot of the dilute metallogel was placed on a 400 mesh copper grids. After 1 min, excess fluid was removed and the sample was left to dry at room temperature. Samples were viewed using a FEI Tecnai (G2 F20) electron microscope operating at 120 keV

Powder X-ray Diffraction

Powder X-ray diffraction experiments for dried lyophilized metallogel were collected into a Rigaku smart lab diffractometer (Rigaku, Tokyo, Japan) using Cu Kα radiation (λ = 1.5406 Å). The voltage of the tube was set at 40 kV, and the current of the tube was set at 75 mA. X-ray diffraction patterns were recorded over a 2θ range of 2–50° with the step size being 0.01° with a rate of 10°/min.

Thermogravimetric Analysis (TGA):

Thermogravimetric analysis of the MOF crystals was done using a TGA-8000 instrument (PerkinElmer). The samples (less than 5 mg) were placed into a ceramic crucible and were heated from 30 to 500 °C at a constant heating rate of 10 °C/min while continuously purging nitrogen gas at a flow rate of 20 mL/min.

Gas Sorption Measurement:

All the gas sorption isotherms were recorded using an ASAP 2020 (micromeritics) instrument employing ultra-high pure N_2 and CO_2 gas. Prior to the isotherm measurement, the sample (~50 mg) was activated at 50°C under vacuum for ~8 hours. The temperature was maintained using a liquid nitrogen bath or a chiller.

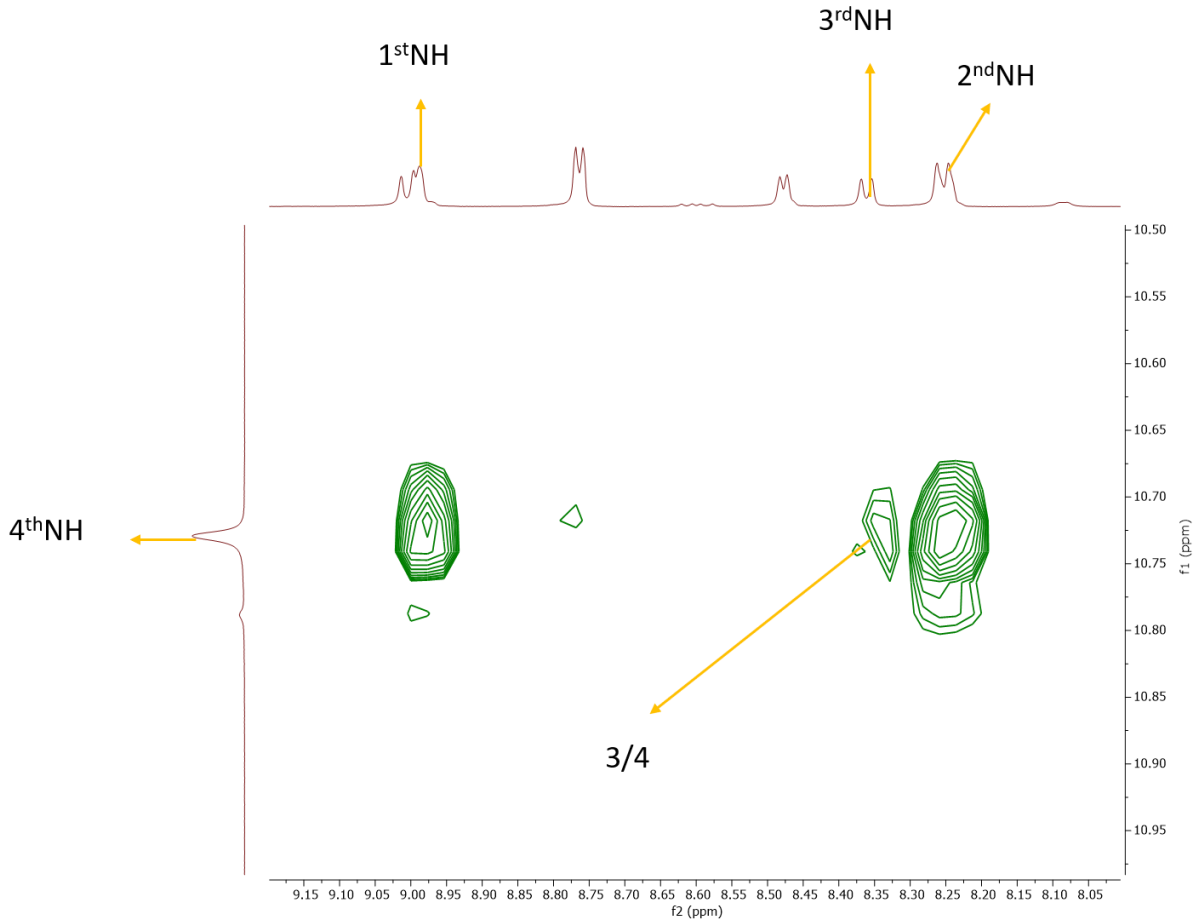


Figure S1: Partial ROESY spectra of **P1** showing very weak NH ↔NH NOEs

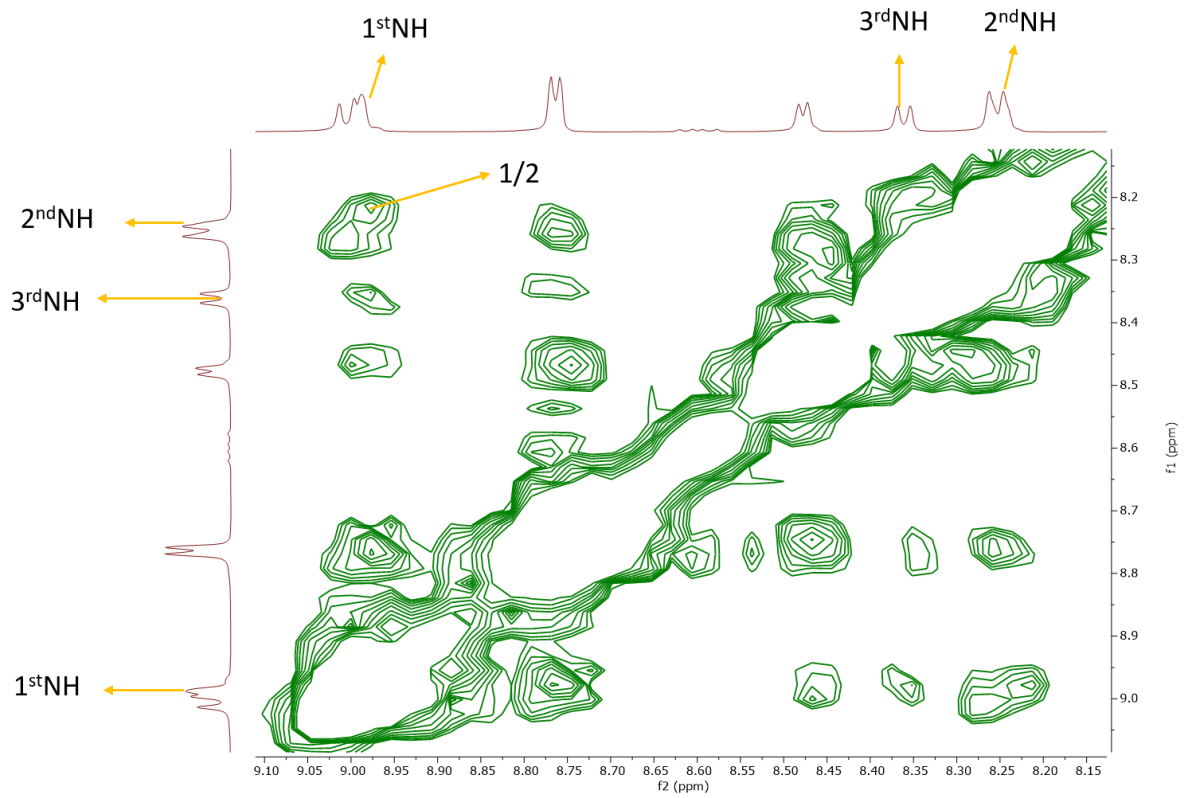


Figure S2: Partial ROESY spectra of **P1** showing very weak NH ↔NH NOEs

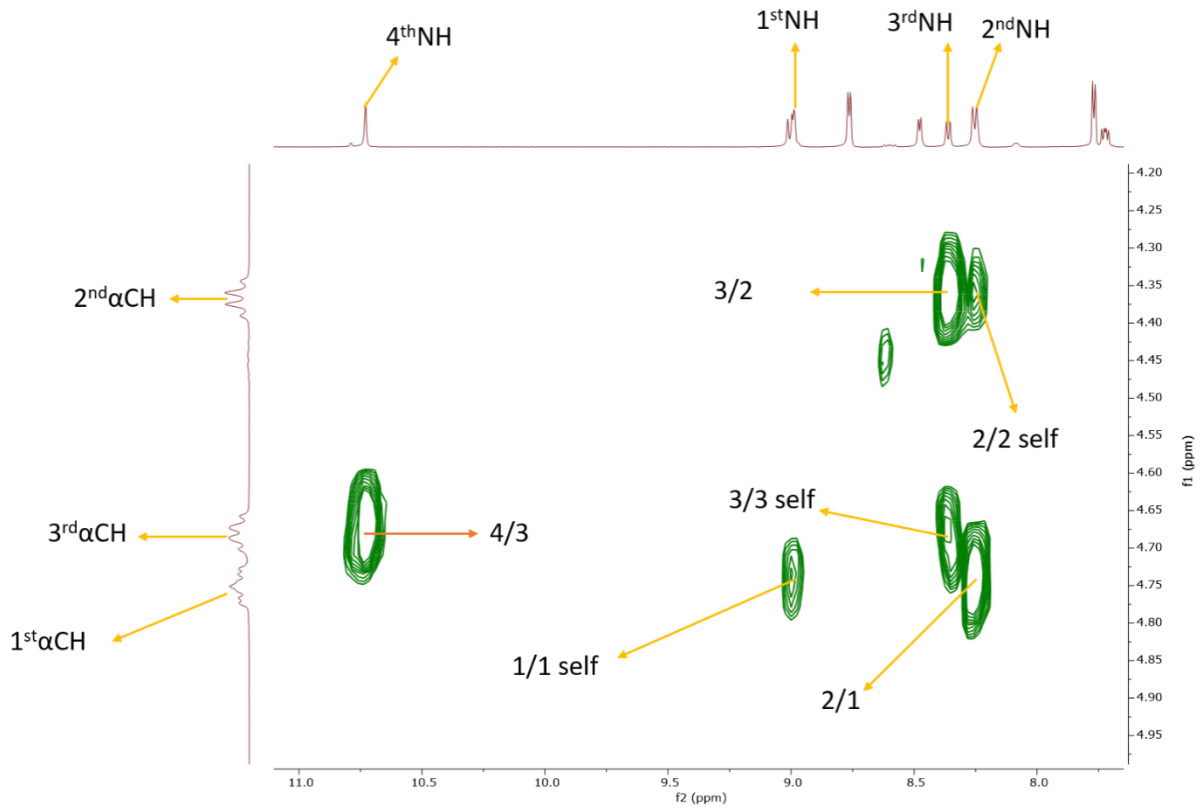


Figure S3: Partial ROESY spectra of **P1** showing very strong NH ↔CαH NOEs

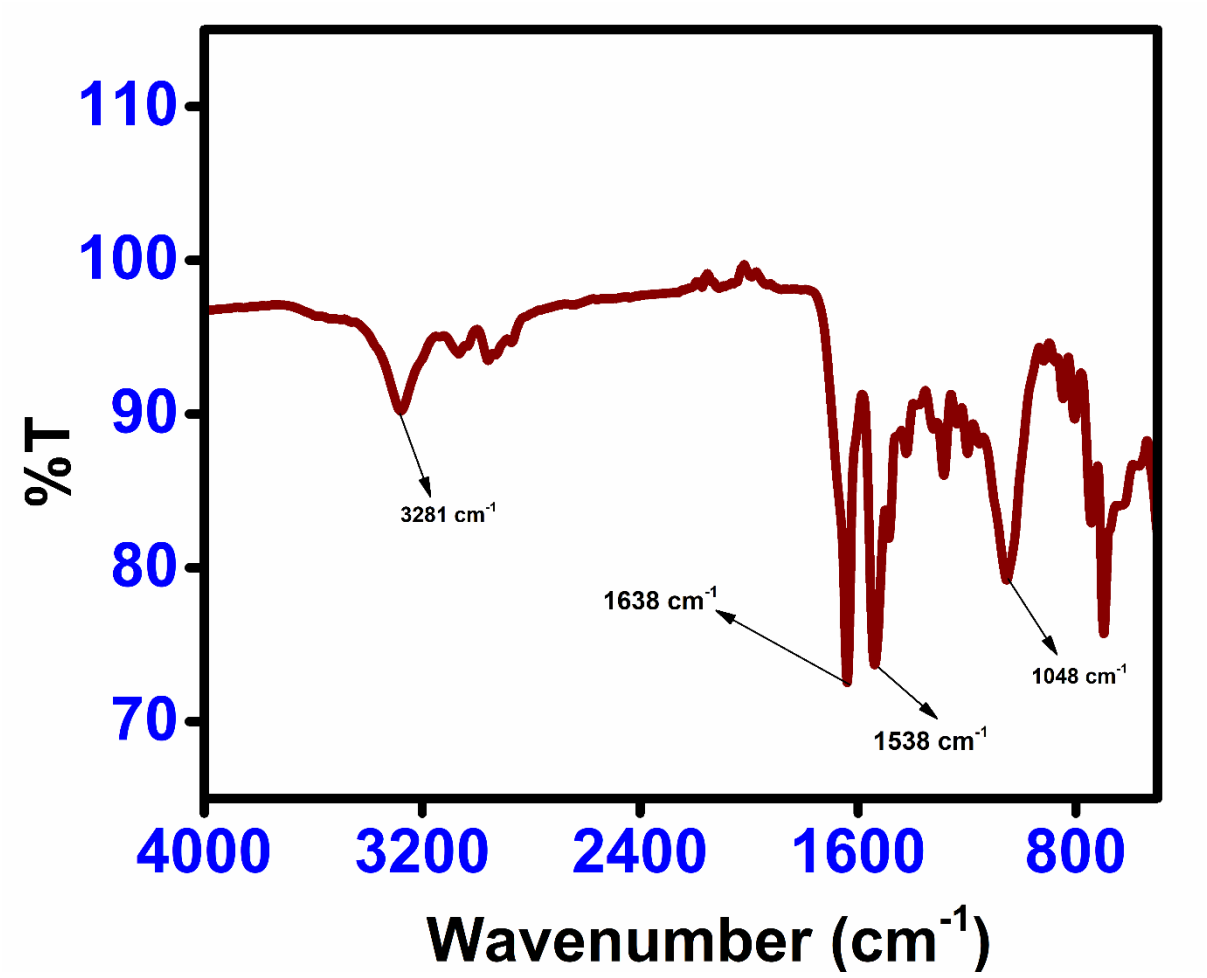


Figure S4: FTIR spectra of P1-$AgBF_4$ complex.

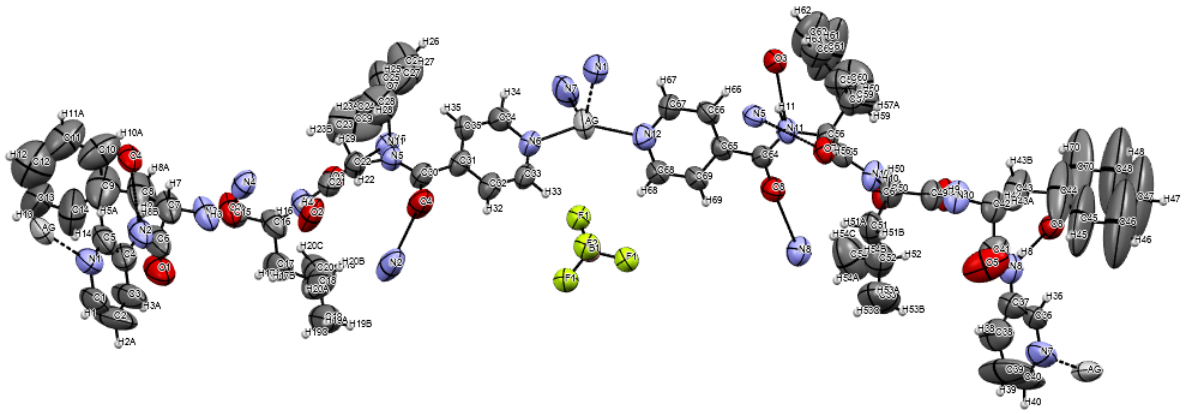


Figure S5: ORTEP diagram of with 50% probability of P1-$AgBF_4$ complex.

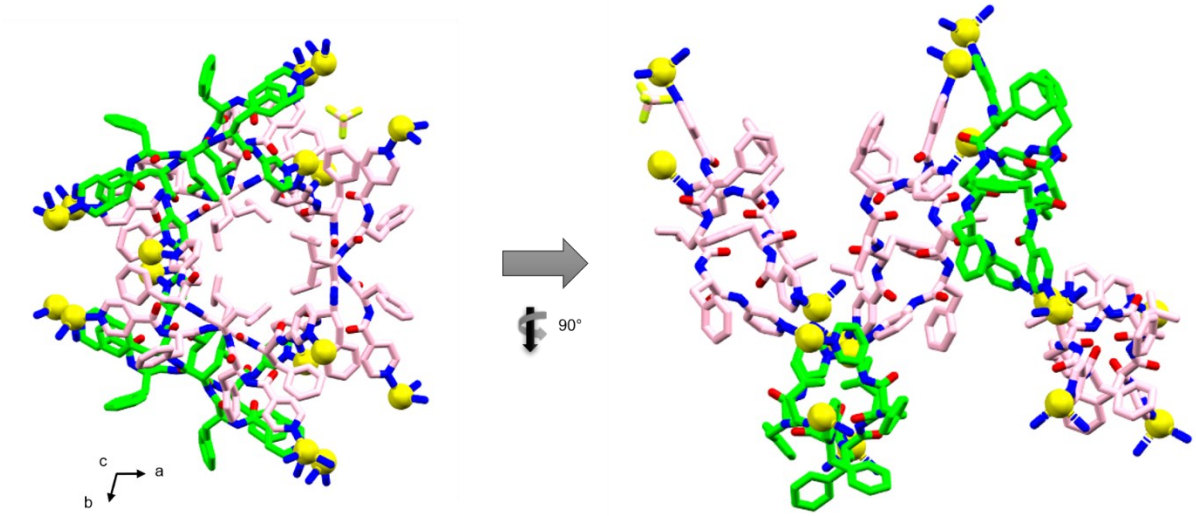


Figure S6: Interaction of adjacent β-sheets through 3Py-Ag-3Py coordination to produce supramolecular helical structural arrangement with Leu2 residues extended towards the central cavity. The top view (left) and side view (right) of the structural pattern.

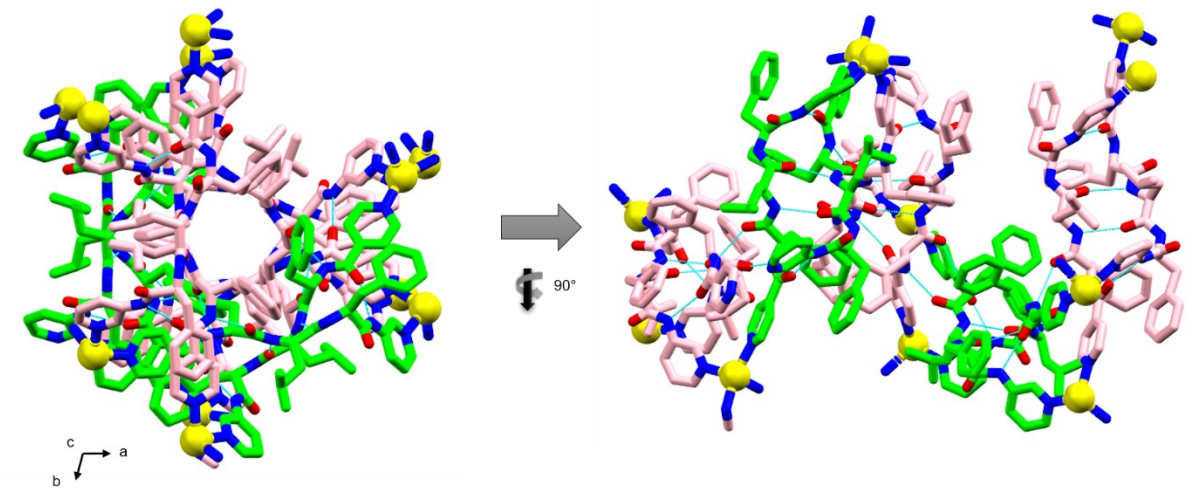


Figure S7: H-bonding and metal coordination (3Py-Ag-4Py and 4Py-Ag-3Py) driven self-assembly of β-sheets into supramolecular helical structure. The top view (left) showing the formation of large hydrophilic cavity and side view (right) represents the growth of helical structure along the crystallographic *a*-direction.

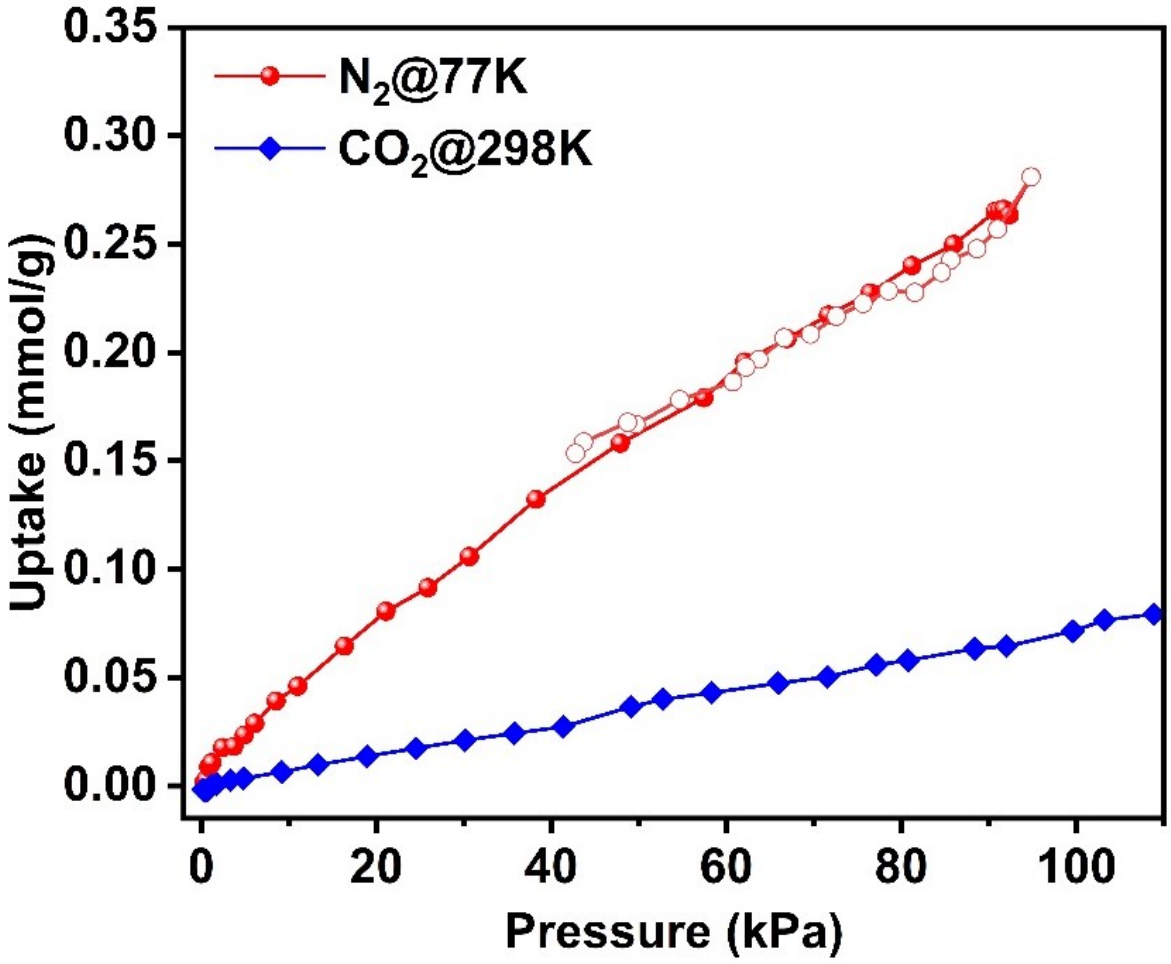


Figure S8: N_2 and CO_2 isotherm collected at 77K and 298K respectively

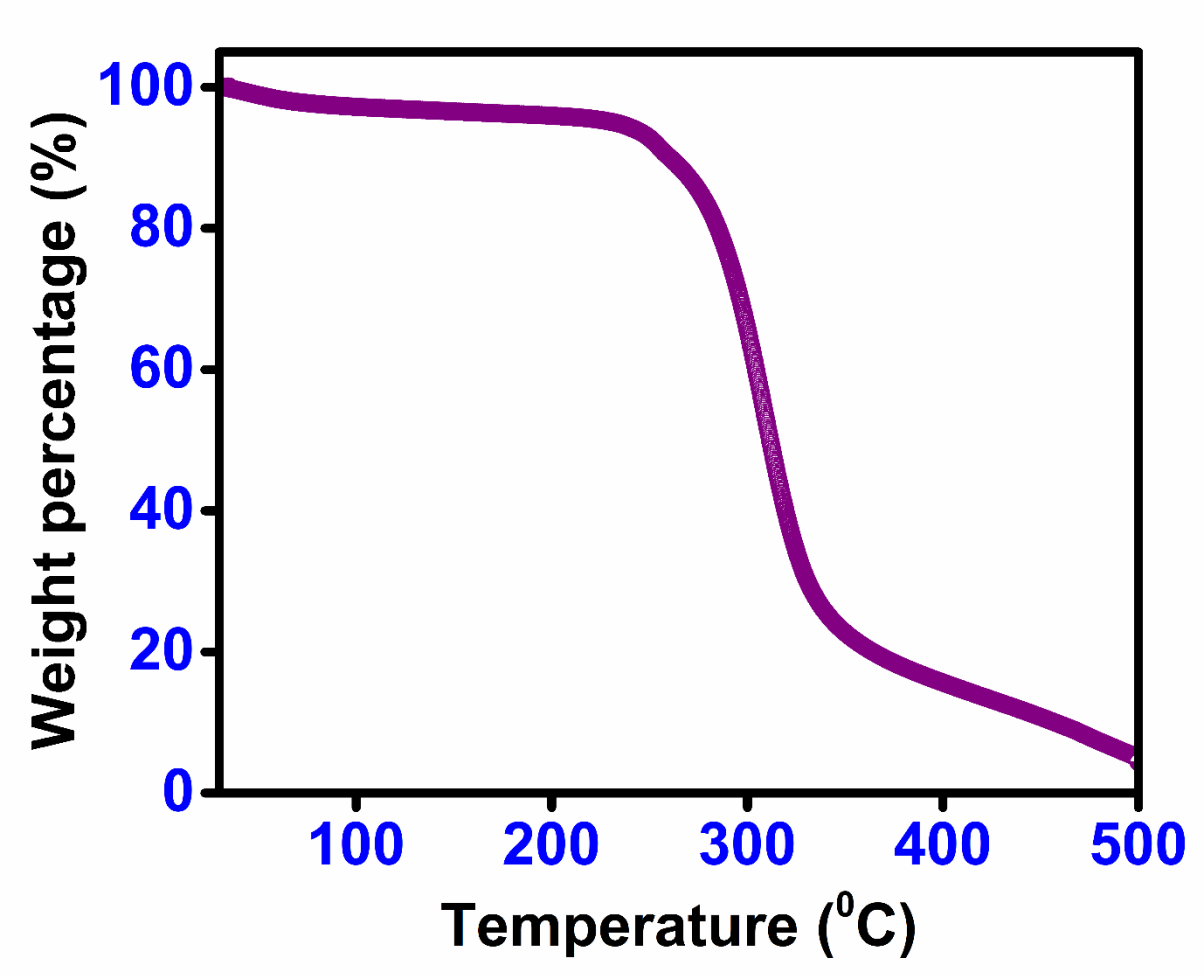


Figure S9: Thermogravimetric thermograms of peptide P1-$AgBF_4$ complex.

Note: *The thermal stability of the* **P1**-*$AgBF_4$ porous framework was evaluated using thermogravimetric analysis (TGA), revealing no significant mass change up to 300 °C, indicative of its good thermal stability.*

Table S1: Important backbone torsion angles of peptide ligand **P1** as observed in the complex.

P1A

Residue	ϕ (deg)	Ψ (deg)
Phe1	-86	152
Leu2	-152	158
Phe3	-86	124

P1B

Residue	ϕ (deg)	Ψ (deg)
Phe1	-113	155
Leu2	-129	149
Phe3	-69	132

Table S2: H-bonding distance between the strands P1A strand 1.

Donor (D)	Acceptor (A)	D…. A (Å)	DH…. A (Å)	NH…. O (deg)
N10	O6	2.89	2.06	158
N8	O8	2.81	1.98	170

Table S3: H-bonding distance between P1A antiparallel strand 2.

Donor (D)	Acceptor (A)	D…. A (Å)	DH…. A (Å)	NH…. O (deg)
N10	O6	2.89	2.06	158
N8	O8	2.81	1.98	170

Table S4: Inter sheet H-bond distance:

Donor (D)	Acceptor (A)	D…. A (Å)	DH…. A (Å)	NH…. O (deg)
N11	O3	2.88	2.048	158
N5	O7	2.91	2.10	152

Table S5: H-bonding distance between the strands P1B strand 1

Donor (D)	Acceptor (A)	D…. A (Å)	DH…. A (Å)	NH…. O (deg)
N4	O2	2.85	1.99	165
N2	O4	2.81	1.94	166

Table S6: H-bonding distance between the strands P1B antiparallel strand 2

Donor (D)	Acceptor (A)	D…. A (Å)	DH…. A (Å)	NH…. O (deg)
N4	O2	2.85	1.99	165
N2	O4	2.81	1.94	166

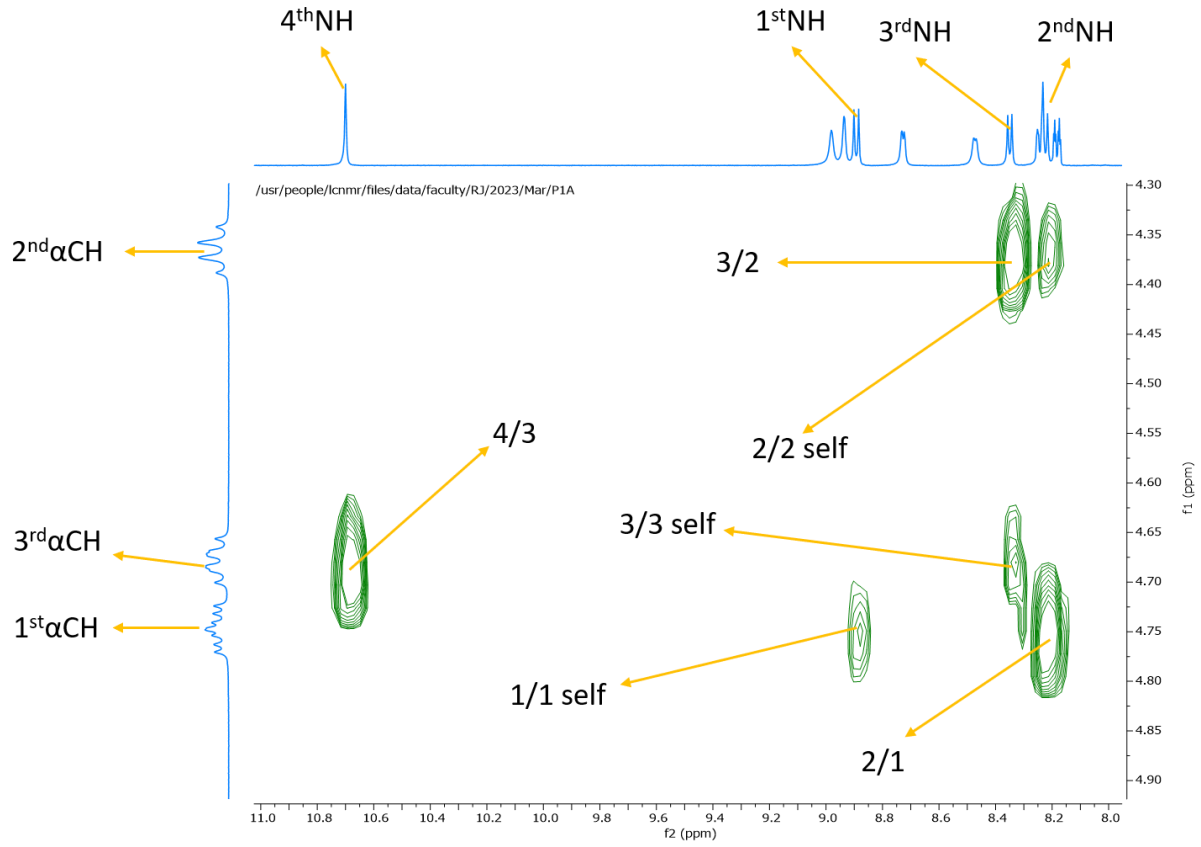


Figure S10: Partial ROESY spectra of **P2** showing very strong NH ↔CαH NOEs.

Supplementary Note on Metal Binding Study:

*It is noteworthy to mention that our different extensive attempts to crystallize the [(AgBF$_4$)·**P2**]$_n$ complex were not successful. This could be due to the natural tendency of* **P2** *to form a linear complex with di-coordinated Ag instead of forming the tetra-coordinated Ag in the [(AgBF$_4$)·**P1**]$_n$ complex. In addition, we investigated the metal binding properties of the same peptide sequences terminated at both the sides with 4 pyridyl groups as well as C terminal*

4-pyridyl and N terminal 3-pyridyl groups. However, we did not observe any crystal formation or gelation in ethanol. This clearly indicates the fact that the presence of the 3- and 4-pyridyl binding sites in the C and N terminals of the peptide sequence is crucial to isolate the crystalline 3D framework materials.

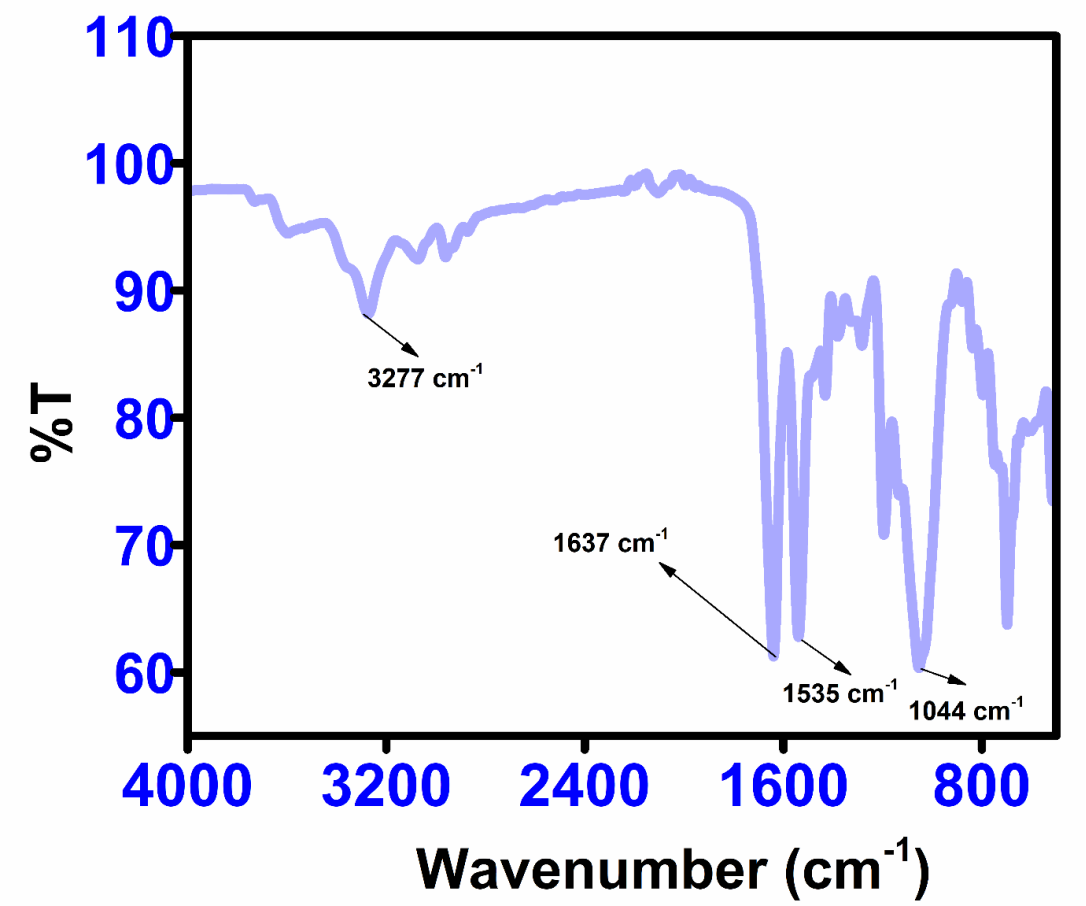


Figure S11: IR spectra of dried **P2** silver metallogel.

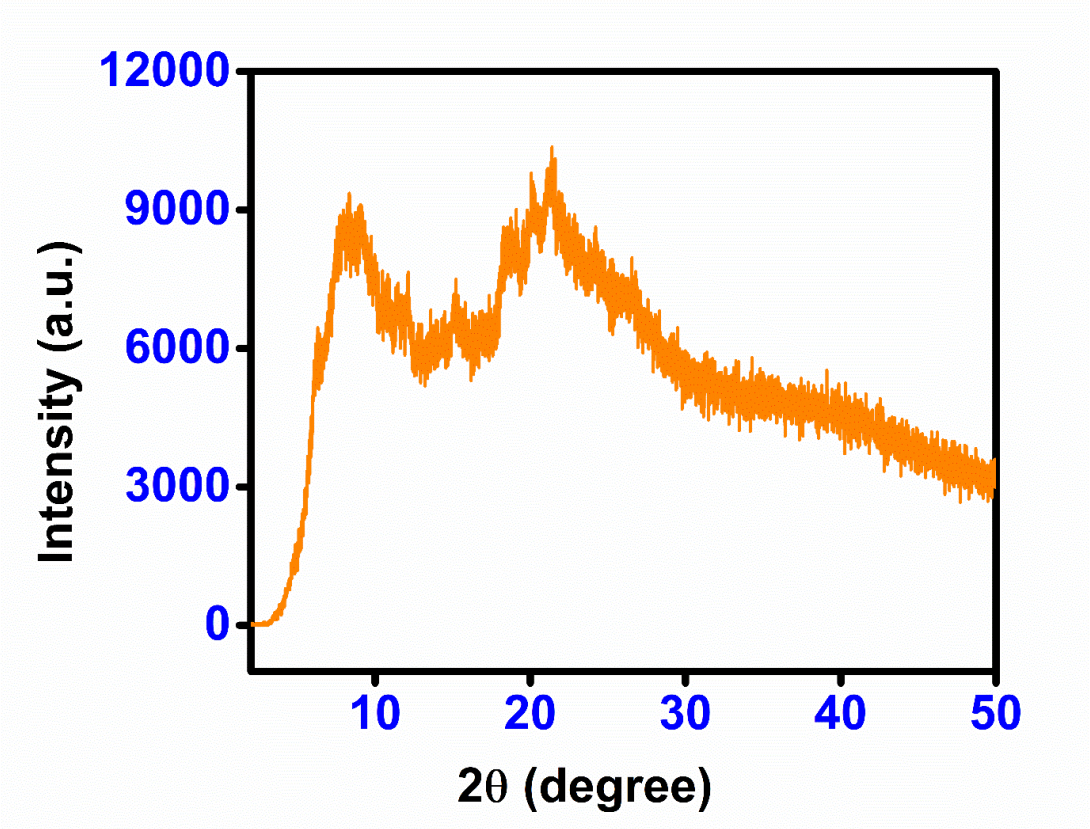


Figure S12: PXRD pattern of lyophilized **P2** silver metallogel.

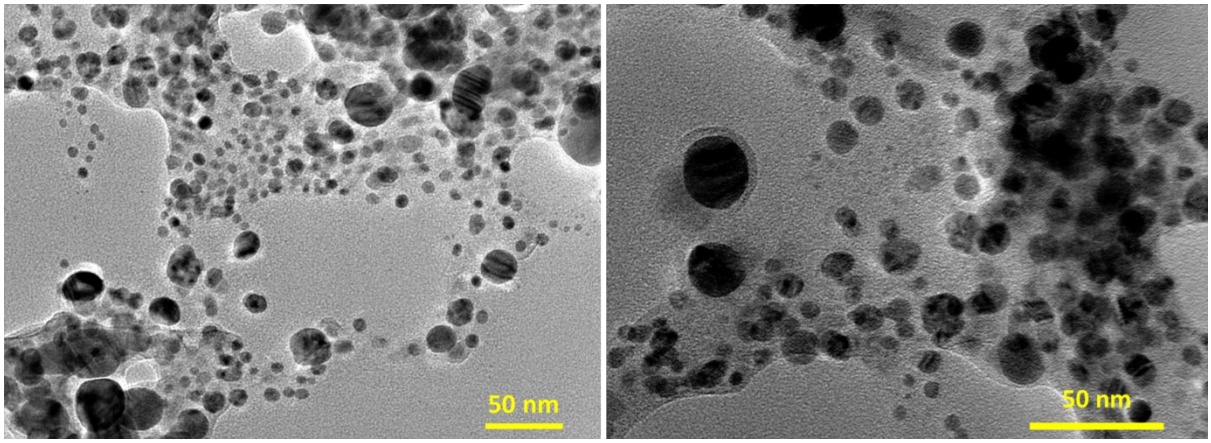


Figure S13: TEM micrograph of in *situ* silver nanoparticles formation in the **P2** metallogel matrix.

Crystallization and Structure Determination:

Folding and assembly of peptide ligand **P1** upon coordination to $AgBF_4$ was carried out in the following way: a solution of ligand **P1** (30 mM, 250 μL) in ethanol, along with a solution of $AgBF_4$ (30 mM, 250 μL) in either ethanol or methanol, were added together and leftundisturbed for a duration of 7 days at ambient temperature. Peptide-$AgBF_4$ complex was isolated as single crystals. For data collection, crystals were coated in paratone oil (Hampton Research), mounted on a MiTeGen cryo-loop and flash-frozen in liquid nitrogen. Diffraction data for **P1** were collected at 100 K on a Rigaku XtaLAB Synergy R, HyPix-Arc 150 using CuKα radiation at λ = 1.54184 Å. Data were processed and reduced with CrysAlisPro. The structures were solved by direct methods using SHELXT-2018[2] as implemented in Olex2 and refined by full matrix least squares against F2 with SHELXL-2013. All non-hydrogen atoms were refined with anisotropic temperature factors. Hydrogen atoms were placed in calculated positions and refined in the riding mode. The crystallographic data are given for peptide **P1** in Table S1. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition number CCDC 2290690.

Table S7: Refinement statics data for peptide **P1**

CCDC number	2290690
Crystal description	Colourless plate
Diffractometer	Rigaku XtaLab Synergy R Hy-Pix150
Empirical formula	C_{70} H_{76} Ag B0.33 F1.33 N_{12} O_8
Formula weight (g/mol)	1350.23
Temperature (K)	100 (2)
Wavelength (Å)	1.54184
Crystal system	Trigonal
Space group	*R 3 2*
a, Å	38.1751(4)
b, Å	38.1751(4)
c, Å	37.5163(6)
α°	90
β°	90
γ°	120
Volume (Å3)	47349.0(12)
Z	18
dcalc (mg/cm^3)	0.852
μ (mm^{-1})	1.890
F(000)	12684

Theta range for data collection (°)	3.466to 67.244
Reflections collected (unique)	142720
Rint	0.0314
Completeness %	99.9
Data/restraints/parameters	15129/696/755
Final R [I > 2 σ (I)]	R1=0.0620 wR2=0.1941
R (all data)	R1=0.0652 wR2=0.1977
Goodness of Fit	1.078
Largest diff. peak and hole ($e \cdot Å^{-3}$)	0.329, -0.471

NMR and mass spectroscopic data for BocPhe-3Py

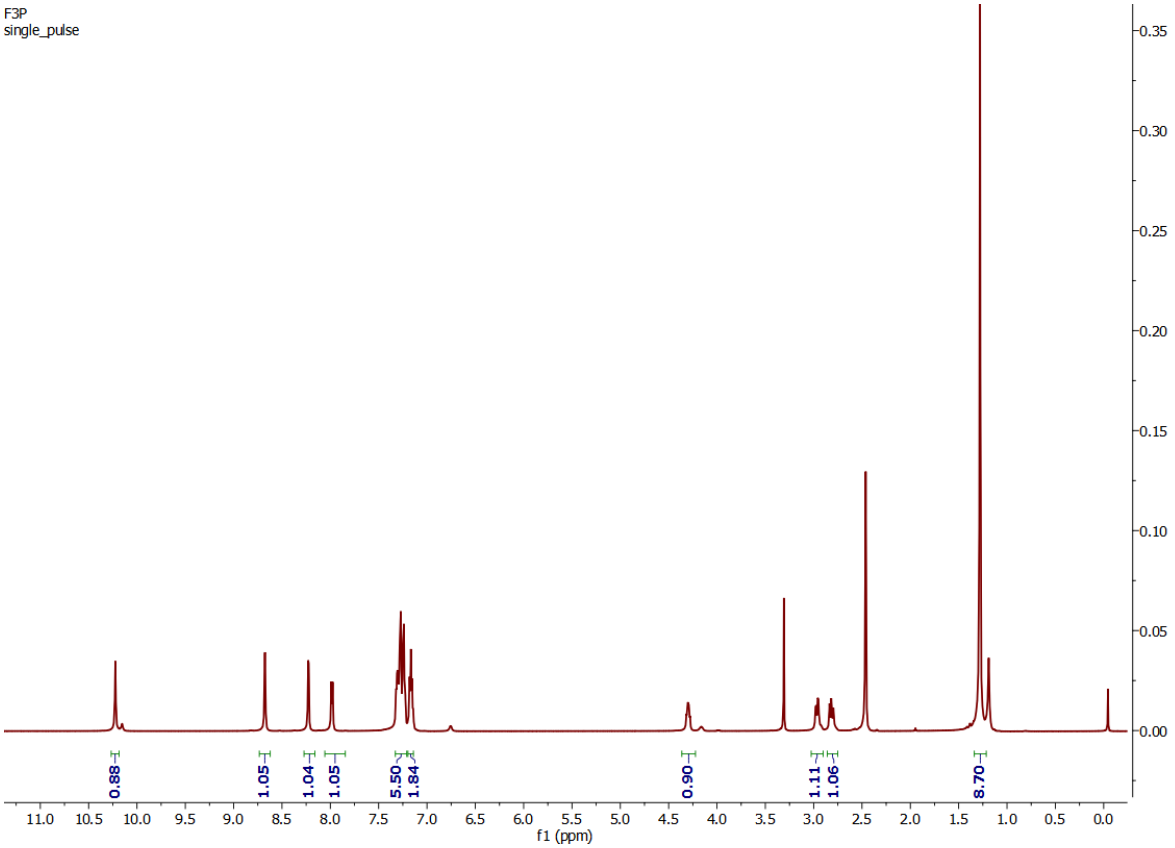


Figure S14: ^{1}H NMR spectra of peptide BocPhe-3Py

Exact mass ($M+H^+$): 342.17
Observed mass ($M+H^+$): 342.18

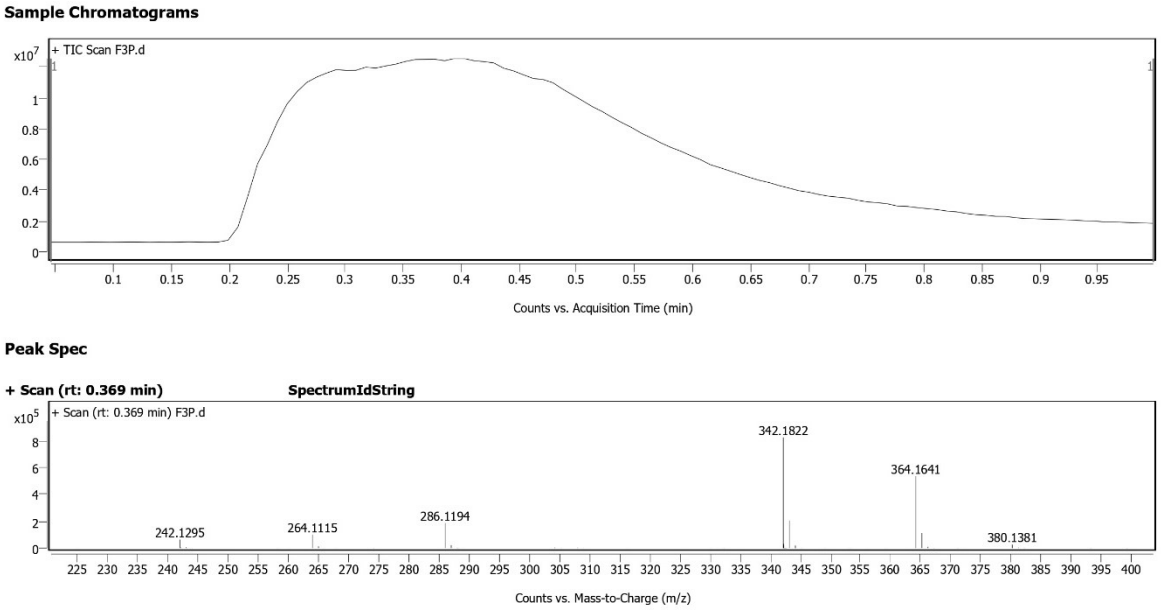


Figure S15: Mass spectra of peptide BocPhe-3Py

NMR and mass spectroscopic data for BocPhe-Leu-OH

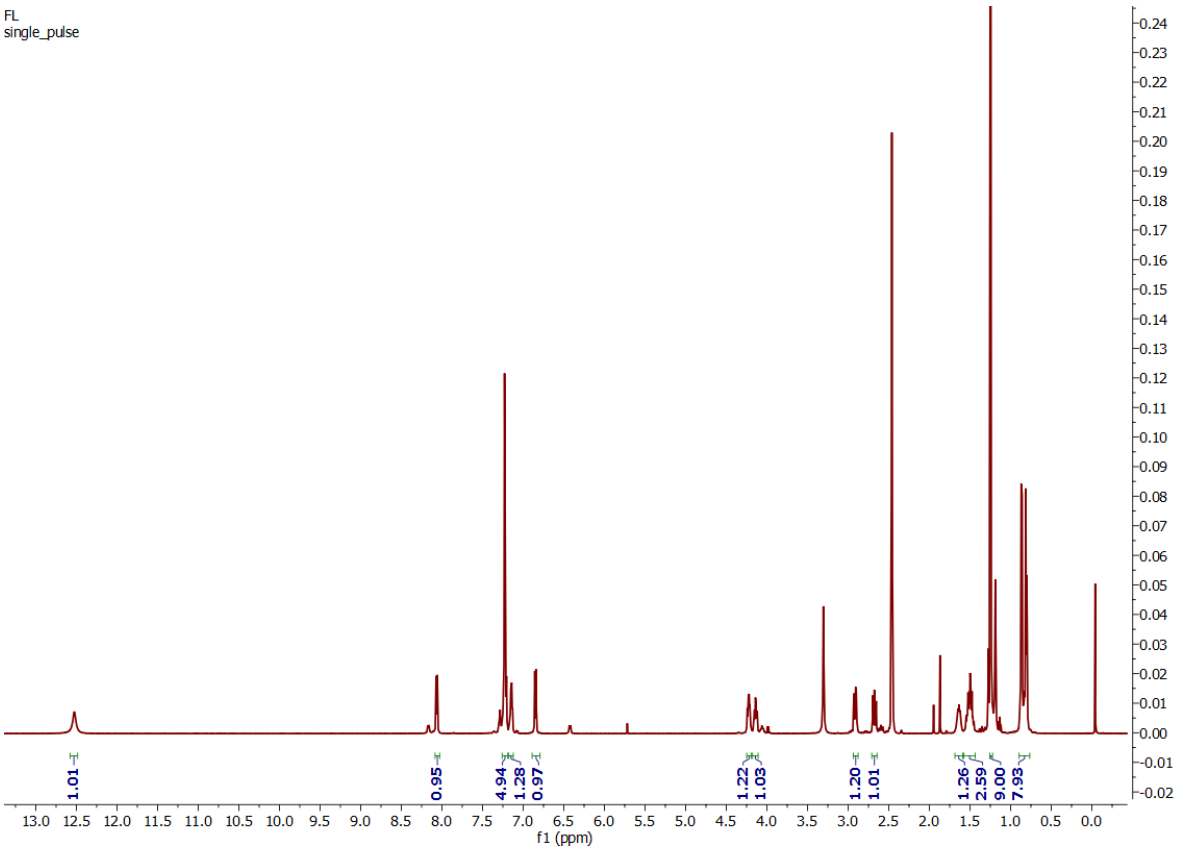


Figure S16: ^{1}H NMR spectra of peptide BocPhe-Leu-OH

Exact mass ($M+H^+$): 378.22

Observed mass ($M+Na^+$): 401.20

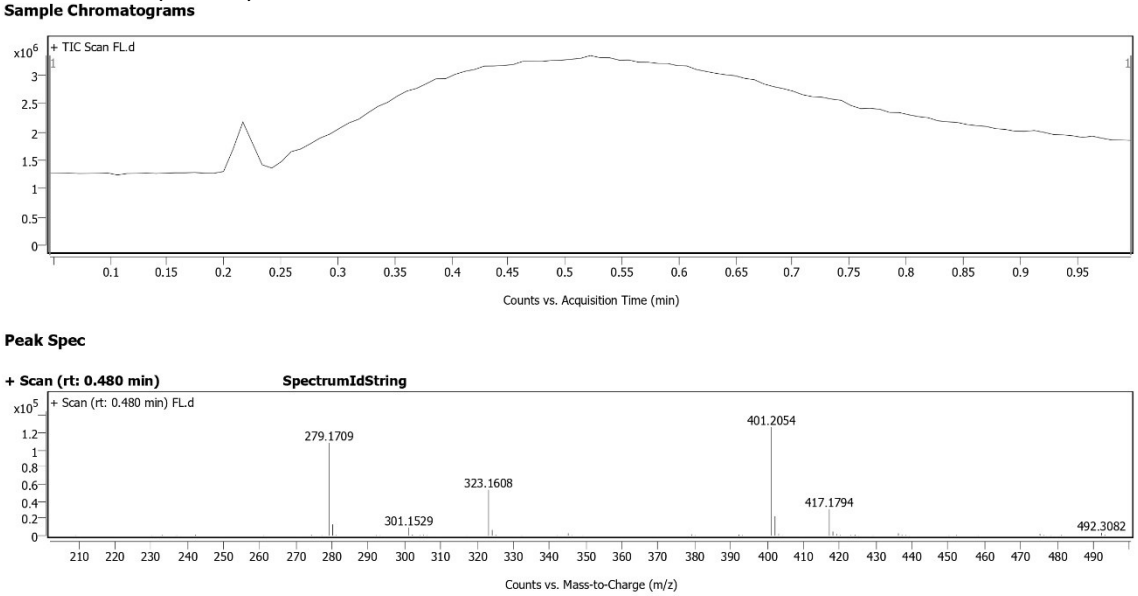


Figure S17: HRMS data of peptide BocPhe-Leu-OH

NMR and mass spectroscopic data for peptide P1

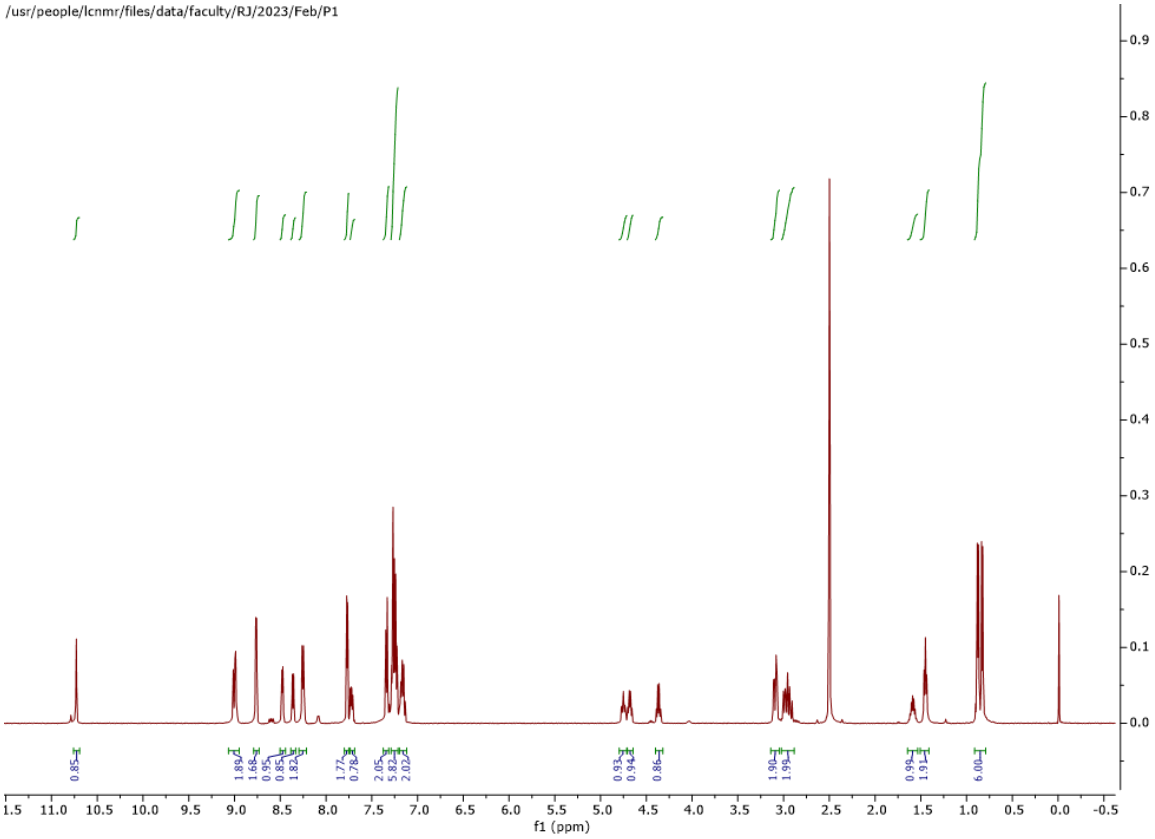


Figure S18: 1H NMR spectra of peptide P1

Mass spec of peptide P1:

Exact mass ($M+H^+$): 606.7345
Observed mass ($M+H^+$): 607.7360

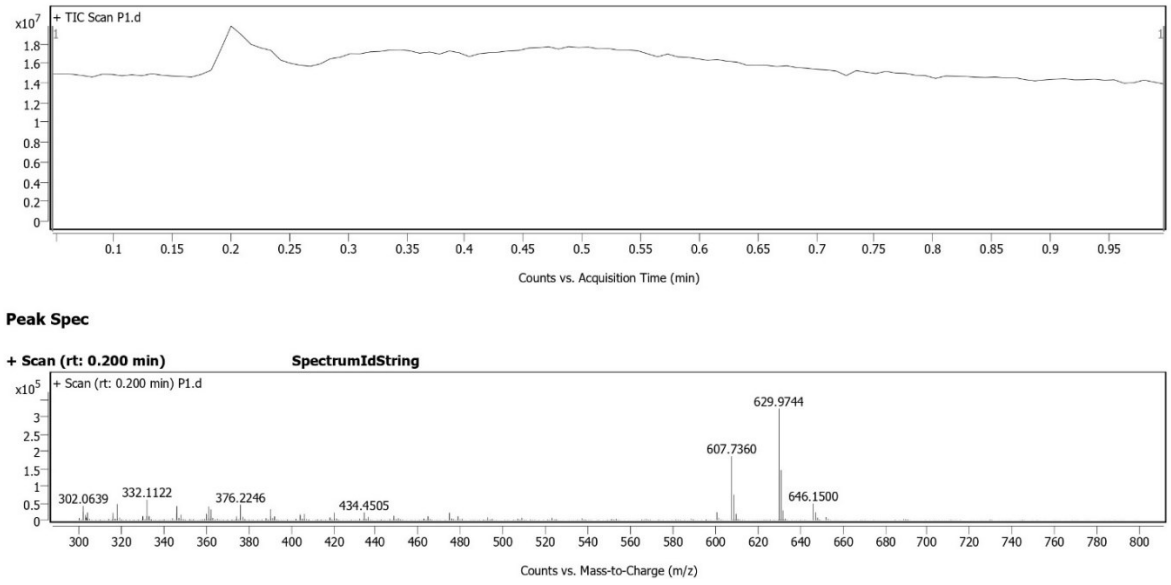


Figure S19: HRMS data of peptide P1

NMR and mass spectroscopic data for peptide P2

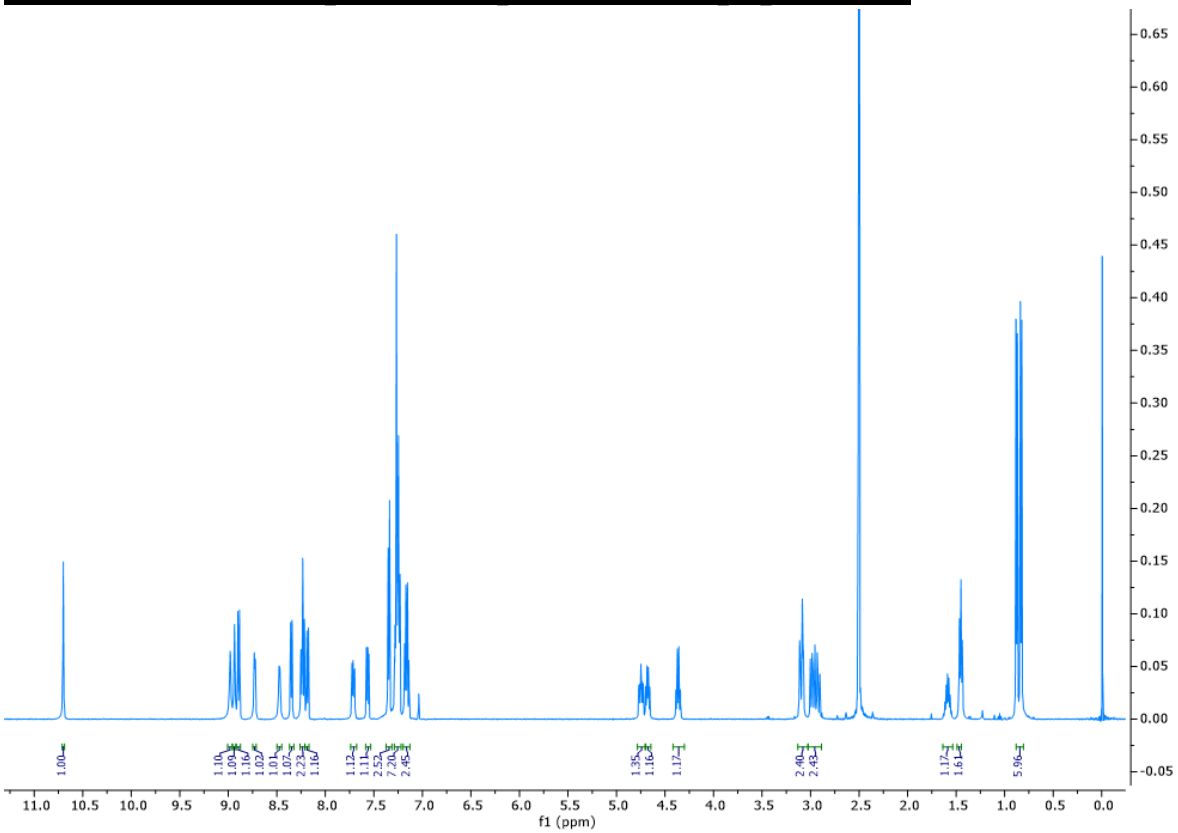


Figure S20: ^{1}H NMR spectra of peptide P2

Mass spec of peptide P2:

Exact mass ($M+H^{+}$): 606.7345
Observed mass ($M+H^{+}$): 607.7369

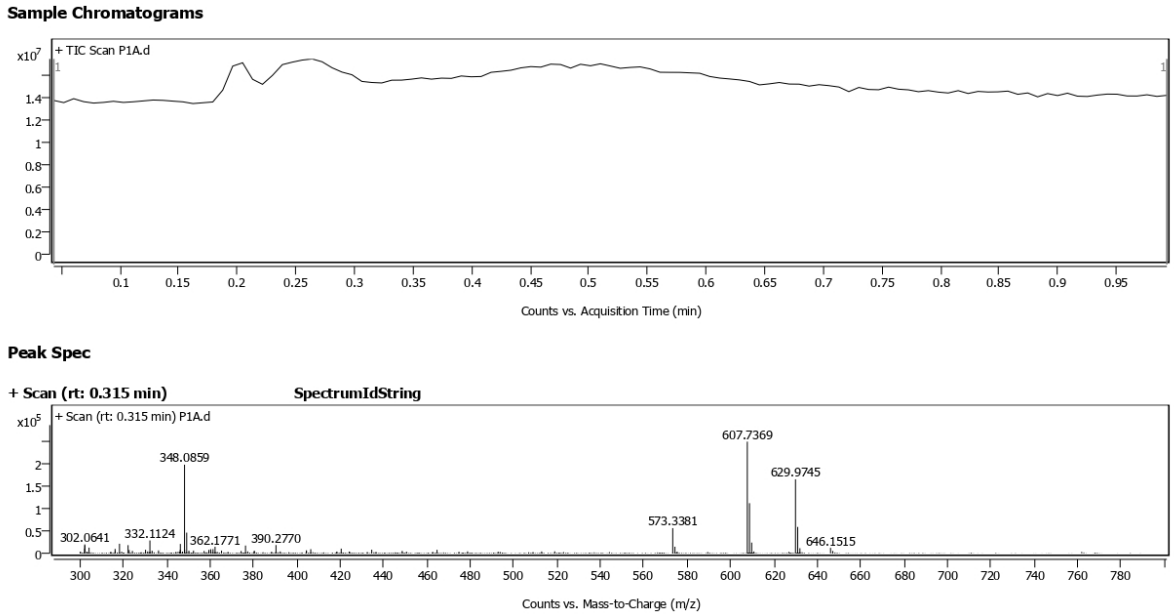


Figure S21: HRMS data of peptide P2