Supplementary Information

Designer Pseudopeptides: Autofluorescent Polygonal Tubes via Phe-zipper and Triple Helix

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1. General Information

1.1 Materials

All solvents used were distilled before use. All amino acids were of L-configuration. Reactions were monitored by thin layer chromatography (TLC) using TLC plates purchased from Merck, India. Silica gel 100-200 mesh (SRL, India) was used for purification in column chromatography. ^{1}H NMR was recorded using Brucker-DPX-400 and 500 MHz spectrometers. Tetramethylsilane (TMS) was used as an internal standard. Coupling constants are recorded in Hz, and the ^{1}H NMR data are reported as s (singlet), d (doublet), br (broad), t (triplet) and m (multiplet), dd (double of doublet). IR spectra (KBr) pellets was recorded on Nicolet, Protégé 460 spectrometer. Bruker MicrO-TOF-QII model High-resolution mass spectrometer (HRMS) was used for characterization. AVIV Model 410 and BioLogic MOS-500 spectrometers were used for circular dichroism (CD) measurements. Quartz cell of 1mm path length was used for all measurements. A scan speed of 1 nm/min and averaged over 3 scans are employed. Shimadzu UV-2400 double beam spectrophotometer was used for recording UV-visible spectra measurements. FluoroMax-4 spectrofluorometer (HORIBA JOBIN YVON Scientific), was used for recording fluorescence spectra. A slit width of 2 nm excitation and collection were used for data collection. Samples were taken in 3 mL quartz cuvette. Fisher-Scientific melting point apparatus was used for recording melting points. X-ray diffraction analysis was done on a Bruker SMART APEX diffractometer fitted with CCD area detector. Structure solving, and refinement were carried out using the ShelXTL program. All spectroscopic experiments were done at room temperature.

1.2 Methods

1.2.1 Scanning Electron Microscopy (SEM)

Solutions of compounds were prepared by dissolving 1 mg of each compound in 1 mL of acetonitrile (ACN). A glass coverslip was attached to a stub using carbon tape. About 10 µL of the solution was drop-casted onto the coverslip and left to dry at room temperature. Further, it was coated with gold (~10 nm) and analyzed by ZEISS EVO 50 Scanning Electron Microscope. The images captured at room temperature were processed using Image J software.

1.2.2 Transmission Electron Microscopy (TEM)

Samples for TEM were prepared by dissolving the compound in ACN. About 5 µL aliquot of the sample solution was placed on a 200 mesh copper grid and allowed to dry at room temperature. Samples were viewed using a TECHNAI G2 (20S-TWIN) electron microscope and were processed using Image J software.

1.2.3 Atomic Force Microscopy (AFM)

Solutions of compounds were prepared by dissolving 1 mg of each compound in 1 mL of ACN. About 100 µL of the solution was drop-casted onto a glass slide and left to dry at room temperature. Further, it was analyzed by BRUKER Dimension Icon XR Atomic Force Microscope by tapping mode. The images captured at room temperature were processed using Image J software.

1.2.4 Field Emission Scanning Electron Microscopy (FESEM)

1mg of each compound was dissolved in 1 mL of ACN to make the corresponding solutions. Carbon tape was used to affix a glass coverslip to a stub. Approximately 10 microliters of the solution was drop-casted onto the coverslip, and allowed to air dry at room temperature. Then, a layer of gold (~10 nm) was applied to the sample, which

was then examined using a ZEISS EVO 18 Scanning Electron Microscope. The photos obtained at room temperature were analyzed using Image J program.

1.2.5 NMR titration study

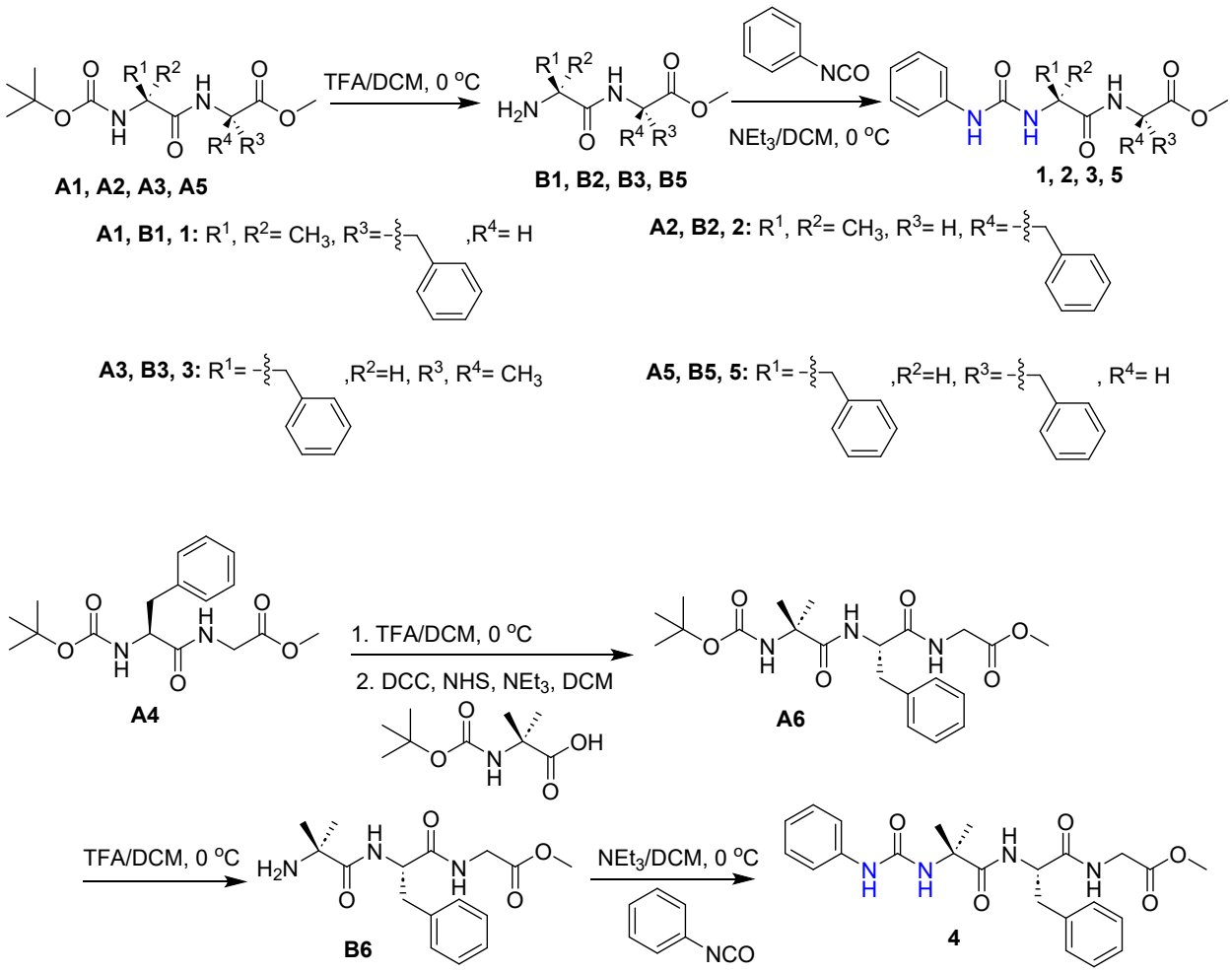
To 10 mM host solutions, small amounts of DMSO-d_6 were added and the NMR spectra were recorded.

1.2.6 Confocal Microscopy

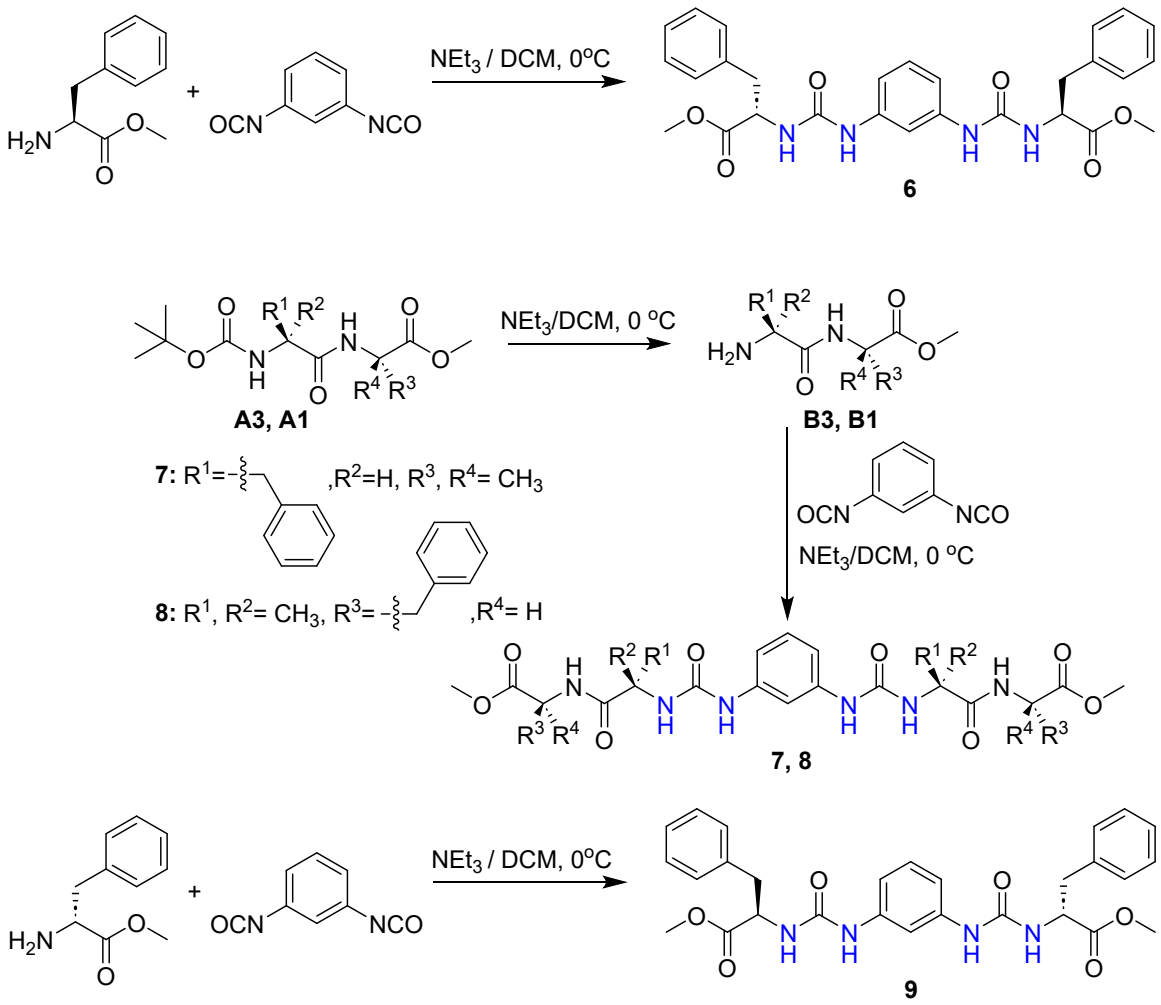
Solutions of compounds were prepared by dissolving 1 mg of each compound in 1 mL of ACN. About 10 µL of the solution was drop-casted onto a glass slide and left to dry at room temperature. Further, it was then covered with a cover slip and analyzed at room temperature by LEICA STELLARIS Stimulated Emission Depletion Microscope. The images captured at room temperature and Image J software was used for processing.

1.2.7 Job plot calculation

A series of solutions containing compounds (**6**, **7** and **8**) ($1x10^{-4}$ M) and anions ($1x10^{-4}$ M) were prepared in ACN. The mole fraction of the receptors was varied from 0.1 to 1 and the absorbance of each solution is measured at a suitable wavelength and a graph of the corrected absorbance versus mole fraction of X or P was plotted. Maximum absorbance is reached at the composition corresponding to the stoichiometry of the predominant complex.



Scheme S1: Synthesis of monourea-based peptides **1-5**.



Scheme S2: Synthesis of compounds **6-9**.

1.3 General Synthetic Procedure

1.3.1 Preparation of dipeptide A1

To an ice-cooled solution of Boc-Aib-OH, (600 mg, 2.95 mmol) in dry CH_2Cl_2 was added NHS (407 mg, 3.54 mmol) and DCC (730 mg, 3.54 mmol) and stirred. After 5 minutes, Phe-OMe.HCl (763 mg, 3.54 mmol) in ~50 mL dry CH_2Cl_2 and NEt_3 (0.49 mL, 3.54 mmol) were added stirred for 24 h. The reaction mixture was filtered, and the clear filtrate obtained was washed sequentially with 0.2N H_2SO_4, aq. $NaHCO_3$ solution and finally with water. The organic part was dried over anhydrous Na_2SO_4, evaporated,

and purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford about 86% yield of **A1**.

MP: 142-144 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 12H), 1.45 (s, 3H), 3.12 (m, 2H), 3.69 (s, 3H), 4.85 (m, 1H), 6.87 (s, 1H), 7.12 (d, *J* = 10 Hz, 2H), 7.16 – 7.30 (m, 4H).

^{13}C NMR ($CDCl_3$ 125 MHz) δ 25.4, 28.3, 38.1, 52.2, 53.3, 56.7, 80.2, 127.0, 128.5, 129.3, 136.1, 154.6, 172.0, 174.2.

IR (KBr): 3329, 2982, 1754, 1688, 1658, 1522, 1453, 1367, 1284, 1167, 1087 cm^{-1}.

HRMS: Calcd. for $C_{19}H_{28}N_2O_5Na$ m/z = 387.1896, found m/z = 387.1883.

1.3.2 Preparation of dipeptide A2

To an ice-cooled solution of Boc-Aib-OH, (300 mg, 1.48 mmol) in dry CH_2Cl_2 was added NHS (205 mg, 1.78 mmol) and DCC (367 mg, 1.78 mmol) and stirred. After 5 minutes, D-Phe-OMe.HCl (384 mg, 1.78 mmol) in ~50 mL dry CH_2Cl_2 and NEt_3 (0.25 mL, 1.78 mmol) were added stirred for 24 h. The reaction mixture was filtered, and the clear filtrate obtained was washed sequentially with 0.2N H_2SO_4, aq. $NaHCO_3$ solution and finally with water. The organic part was dried over anhydrous Na_2SO_4, evaporated, and purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford about 85% yield of **A2**.

MP: 142-144 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 12H), 1.45 (s, 3H), 3.12 (m, 2H), 3.70 (s, 3H), 4.85 (m, 1H), 6.86 (s, 1H), 7.12 (d, *J* = 10 Hz, 2H), 7.16 – 7.30 (m, 4H).

^{13}C NMR ($CDCl_3$ 125 MHz) δ 25.4, 28.3, 38.1, 52.2, 53.3, 56.7, 80.2, 127.0, 128.5, 129.3, 136.0, 154.5, 172.0, 174.2.

IR (KBr): 3329, 2983, 2935, 1752, 1687, 1656, 1525, 1452, 1366, 1284, 1167, 1082 cm^{-1}.

HRMS: Calcd. for $C_{19}H_{28}N_2O_5Na$ m/z = 387.1896, found m/z = 387.1897.

1.3.3 Preparation of dipeptide A3

To an ice-cooled solution of Boc-Phe-OH, (900 mg, 3.39 mmol) in dry CH_2Cl_2 was added NHS (468 mg, 4.07 mmol) and DCC (839 mg, 4.07 mmol) and stirred. After 5 minutes, Aib-OMe.HCl (625 mg, 4.07 mmol) in ~50 mL dry CH_2Cl_2 and NEt_3 (0.56 mL, 4.02 mmol) were added stirred for 24 h. The reaction mixture was filtered, and the clear filtrate obtained was washed sequentially with 0.2N H_2SO_4, aq. $NaHCO_3$ solution and finally with water. The organic part was dried over anhydrous Na_2SO_4, evaporated, and purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford about 92% yield of **A3**.

MP: 106-108 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ1.42 (s, 9H), 1.44 (d, *J* = 10.5 Hz, 6H), 3.01 (dd, *J* = 13.8, 7.3 Hz, 1H), 3.08 (dd, *J* = 13.3, 5.8 Hz, 1H), 3.71(s, 3H), 4.30 (m, 1H), 5.14 (br s, 1H), 6.36 (s, 1H), 7.21 – 7.25 (m, 3H), 7.27 – 7.32 (m, 2H).

^{13}C NMR ($CDCl_3$ 125 MHz) δ 24.5, 24.7, 28.3, 38.5, 52.6, 56.4, 80.1, 126.9, 128.6, 129.5, 136.8, 155.5, 170.3, 174.6.

IR (KBr): 3302, 2983, 1745, 1660, 1539, 1451, 1389, 1279, 1156, 1023 cm^{-1}.

HRMS: Calcd. for $C_{19}H_{28}N_2O_5Na$ m/z = 387.1896, found m/z = 387.1889.

1.3.4 Preparation of dipeptide A4

To an ice-cooled solution of Boc-Phe-OH, (600 mg, 2.26 mmol) in dry CH_2Cl_2 was added NHS (312 mg, 2.71 mmol) and DCC (559 mg, 2.71 mmol) and stirred. After 5 minutes, Gly-OMe.HCl (340 mg, 2.71 mmol) in ~50 mL dry CH_2Cl_2 and NEt_3 (0.38 mL, 2.71 mmol) were added stirred for 24 h. The reaction mixture was filtered, and the clear filtrate obtained was washed sequentially with 0.2N H_2SO_4, aq. $NaHCO_3$ solution and finally with water. The organic part was dried over anhydrous Na_2SO_4, evaporated,

and purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford about 81% yield of **A4**.

MP: 84-86 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.03-3.15 (m, 2H), 3.73 (s, 3H), 3.96-4.05 (m, 2H), 4.42 (m, 1H), 5.03 (br s, 1H), 6.46 (br s, 1H), 7.16-7.32 (m, 5H).

^{13}C NMR ($CDCl_3$ 125 MHz) δ 28.2, 38.3, 41.2, 52.4, 55.6, 80.3, 127.0, 128.7, 129.3, 136.5, 155.2, 169.9, 171.6.

IR (KBr): 3327, 2930, 2857, 1760, 1691, 1662, 1535, 1447, 1370, 1209, 1164, 1024 cm^{-1}.

HRMS: Calcd. for $C_{17}H_{24}N_2O_5Na$ m/z = 359.1583, found m/z = 359.1575.

1.3.5 Preparation of dipeptide A5

To an ice-cooled solution of Boc-Phe-OH, (300 mg, 1.13 mmol) in dry CH_2Cl_2 was added NHS (156 mg, 1.36 mmol) and DCC (281 mg, 1.36 mmol) and stirred. After 5 minutes, Phe-OMe.HCl (293 mg, 1.36 mmol) in ~50 mL dry CH_2Cl_2 and NEt_3 (0.19 mL, 1.36 mmol) were added stirred for 24 h. The reaction mixture was filtered, and the clear filtrate obtained was washed sequentially with 0.2N H_2SO_4, aq. $NaHCO_3$ solution and finally with water. The organic part was dried over anhydrous Na_2SO_4, evaporated, and purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford about 88% yield of **A5**.

MP: 114-116 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.00-3.22 (m, 4H), 3.67 (s, 3H), 4.33 (m, 1H), 4.78 (m, 1H), 4.91 (br s, 1H), 6.24 (d, *J*= 6.5 Hz, 1H), 6.96-7.31 (m, 10H).

^{13}C NMR ($CDCl_3$ 125 MHz) δ 28.2, 38.0, 38.2, 52.3, 53.3, 55.7, 80.2, 127.0, 127.1, 128.5, 128.7, 129.2, 129.4, 135.6, 136.5, 155.3, 170.8, 171.4.

IR (KBr): 3331, 3027, 2976, 2930, 1744, 1662, 1525, 1445, 1252, 1168, 1031 cm^{-1}.

HRMS: Calcd. for $C_{24}H_{30}N_2O_5Na$ m/z = 449.2052, found m/z = 449.2042.

1.3.6 Preparation of tripeptide A6

To an ice cold solution of **A4** (400 mg, 1.19 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 3 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap to afford N-deprotected derivative **B4**.

To an ice-cooled solution of Boc-Aib-OH, (291 mg, 1.43 mmol) in dry CH_2Cl_2 was added NHS (164 mg, 1.43 mmol) and DCC (285 mg, 1.43 mmol) and stirred. After 5 minutes, an ice cold solution of N-deprotected derivative **B4** (1.19 mmol) with NEt_3 (0.37 mL, 2.62 mmol) were added and stirred for 24 h. The reaction mixture was filtered, and the clear filtrate obtained was washed sequentially with 0.2N H_2SO_4, aq. $NaHCO_3$ solution and finally with water. The organic part was dried over anhydrous Na_2SO_4, evaporated, and purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford about 86% yield of **A6**.

MP: 126-128 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.35 (s, 9H), 1.42 (s, 3H), 3.18 (dd, *J*= 14.3, 7.8 Hz, 1H), 3.28 (dd, *J*= 14.4, 5.6 Hz, 1H), 3.71 (s, 3H), 3.79 (dd, *J*= 17.6, 5.3 Hz, 1H), 4.15 (dd, *J*= 17.6, 6.1 Hz, 1H), 4.74-4.83 (m, 2H), 6.42 (d, *J*= 9.1 Hz, 1H), 7.21-7.33 (m, 5H), 7.53 (br s, 1H)

^{13}C NMR ($CDCl_3$ 125 MHz) δ 24.0, 26.5, 28.2, 37.0, 41.2, 52.1, 53.4, 56.8, 81.0, 126.9, 128.7, 129.2, 136.7, 155.4, 170.0, 171.7, 173.9.

IR (KBr): 3320, 2928, 2853, 1758, 1694, 1659, 1512, 1453, 1367, 1288, 1166, 1079 cm^{-1}.

HRMS: Calcd. for $C_{21}H_{31}N_3O_6Na$ m/z = 444.2111, found m/z = 444.2098.

1.3.7 Preparation of 1

To an ice cold solution of **A1** (400 mg, 1.10 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 3 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap to afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B1** (1.10 mmol) with NEt_3 (0.15 mL, 1.10 mmol) in ~50 mL dry DCM was added phenylisocyanate (131 mg, 1.10 mmol) dropwise and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water. Dried over anhydrous Na_2SO_4 followed by evaporation. The obtained crude product was further purified by washing several times with EtOAc to afford 358 mg of pure product.

Yield: 85%

MP: 204-206 °C

$[\alpha]^{26}_D$: +16.

^{1}H NMR (500 MHz, CD_3CN) δ 1.30 (s, 3H), 1.32 (s, 3H), 2.94 (dd, 1H, *J* = 13.0, 7.5 Hz), 2.99 (dd, 1H, *J* = 14.0, 5.0 Hz), 3.56 (s, 3H), 4.57 (m, 1H), 5.51 (s, 1H), 6.91 (t, *J* = 7.0 Hz, 1H), 7.02 (d, *J* = 6.0 Hz, 1H), 7.08 (br s, 5H), 7.19 (t, *J* = 7 Hz, 3H), 7.31 (d, *J* = 7.5 Hz, 2H).

^{13}C NMR (DMSO-d_6, 125 MHz), δ 24.9, 25.2, 36.5, 51.8, 53.5, 55.5, 117.5, 121.0, 126.4, 128.1, 128.6, 129.2, 137.2, 140.4, 154.0, 171.8, 174.6.

IR (KBr): 3387, 3348, 3266, 3025, 1737, 1671, 1644, 1600, 1546, 1519, 1438, 1363, 1316, 1238 cm^{-1}.

HRMS: Calcd. for $C_{21}H_{25}N_3O_4Na$ m/z = 406.1743, found m/z = 406.1734.

1.3.8 Preparation of 2

To an ice cold solution of **A2** (400 mg, 1.10 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 3 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap to afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B2** (1.10 mmol) and NEt_3 (0.15 mL, 1.10 mmol) in dry DCM (~50 mL) was added phenylisocyanate (131 mg, 1.10 mmol) dropwise and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water. Dried over anhydrous Na_2SO_4 followed by evaporation. The obtained crude product was further purified by washing several time with EtOAc to afford 367 mg pure product.

Yield: 87%

MP: 204-206 °C

$[\alpha]^{26}_D$: -16°

^{1}H NMR (500 MHz, CD_3CN) δ 1.30 (s, 3H), 1.32 (s, 3H), 2.94 (dd, *J* = *13*.5, 7.0 Hz, 1H), 2.99 (dd, *J* = 14.0, 5.5 Hz, 1H), 3.56 (s, 3H), 4.57 (m, 1H), 5.54 (s, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.08 (br s, 6H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H).

^{13}C NMR ($CDCl_3$, 125 MHz), δ 25.5, 25.8, 37.8, 52.4, 53.3, 57.0, 120.7, 123.9, 127.1, 128.5, 129.2, 129.4, 135.8, 138.4, 154.6, 172.1, 174.8.

IR (KBr): 3385, 3352, 3270, 3013, 2987, 2947, 1737, 1668, 1647, 1597, 1547, 1518, 1439, 1390, 1362, 1316, 1263, 1241, 1216, 1108, 1019, 965, 883, 748, 696, 656, 585, 502 cm^{-1}.

HRMS: Calcd. for $C_{21}H_{25}N_3O_4Na$ m/z = 406.1743, found m/z = 406.1742.

1.3.9 Preparation of 3

To an ice cold solution of **A3** (500 mg, 1.37 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 3 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap and afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B3** (1.37 mmol) with NEt_3 (0.19 mL, 1.37 mmol) in ~50 mL dry DCM was added phenylisocyanate (163 mg, 1.37 mmol) dropwise and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water, dried over anhydrous Na_2SO_4 and evaporated. The obtained crude product further purified by column chromatography using EtOAc /hexane solvent and afford 483 mg product.

Yield: 91%

MP: 162-164 °C

$[\alpha]^{26}_D$: -8.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 6H), 2.92 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.11 (dd, *J* = 13.5, 5.5 Hz, 1H), 3.63 (s, 3H), 4.53 (m, 1H), 5.74 (d, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H), 7.24 (m, 4H), 7.32 (m, 5H), 7.40 (s, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz), δ 24.8, 24.9, 39.0, 52.4, 55.5, 56.2, 119.8, 122.5, 126.8, 128.4, 128.6, 129.5, 137.1, 139.0, 156.0, 173.3, 174.8.

IR (KBr): 3285, 3069, 2946, 1741, 1645, 1551, 1442, 1289, 1234, 1152 cm^{-1}.

HRMS: Calcd. for $C_{21}H_{25}N_3O_4Na$ m/z = 406.1743, found m/z = 406.1737.

1.3.10 Preparation of 4

To an ice cold solution of **A6** (400 mg, 0.95 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 3 h. The reaction was monitored by TLC and after

completion, the reaction mixture was evaporated under a high vacuum with a KOH trap to afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B6** (0.95 mmol) with NEt_3 (0.13 mL, 0.95 mmol) in dry DCM (~50 mL) was added phenylisocyanate (113 mg, 0.95 mmol) dropwise and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water. Dried over anhydrous Na_2SO_4 and evaporated. The obtained crude product was further purified by washing several time with EtOAc to afford 368 mg pure product.

Yield: 88%

MP: 94-96 °C

$[\alpha]^{26}_D$: +82.

^{1}H NMR (500 MHz, CD_3CN) δ 0.99 (s, 3H), 1.26 (s, 3H), 2.79 (dd, 1H, *J* = 18, 14 Hz), 3.29 (dd, 1H, *J* = 17.5, 5.0 Hz), 3.51 (s, 3H), 3.74 (m, 2H), 4.49 (m, 1H), 5.60 (br s, 1H), 6.92-7.31 (m, 12H), 7.97 (t, *J* = 8 Hz, 1H).

^{13}C NMR (CD_3CN, 125 MHz), δ 23.9, 26.6, 36.6, 41.3, 52.1, 54.7, 56.9, 119.2, 123.0, 126.9, 128.8, 129.4, 129.7, 139.0, 140.0, 156.1, 170.6, 172.7, 175.4.

IR (KBr): 3531, 3435, 3326, 2929, 1748, 1675, 1648, 1600, 1547, 1312, 1211, 748, 697 cm^{-1}.

HRMS: Calcd. for $C_{23}H_{28}N_4O_5Na$ m/z = 463.1957, found m/z = 463.1967.

1.3.11 Preparation of 5

To an ice cold solution of **A5** (400 mg, 0.94 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 3 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap and afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B5** (0.94 mmol) with NEt_3 (0.13 mL, 0.94 mmol) in ~50 mL dry DCM was added phenylisocyanate (112 mg, 0.94 mmol) dropwise and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water. Dried over anhydrous Na_2SO_4 followed by evaporation. The obtained crude product was further purified by washing several time with EtOAc to afford 360 mg pure product.

Yield: 86%

MP: 208-210 °C

$[\alpha]^{26}_D$: -20°

^{1}H NMR (500 MHz, CD_3CN) δ 2.76 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.90 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.02 (m, 2H), 3.57 (s, 3H), 4.41 (m, 1H), 4.57 (m, 1H), 5.30 (d, *J* = 7.5 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.95 (t, *J*= 7.5 Hz, 1H), 6.99 (d, *J* = 7.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz), δ 37.8, 38.6, 52.3, 53.8, 55.1, 120.5, 121.1, 123.6, 124.2, 127.1, 128.6, 129.2, 129.4, 135.5, 136.6, 138.1, 138.4, 155.4, 171.3, 172.0

IR (KBr): 3333, 3076, 2930, 2857, 1743, 1646, 1603, 1556, 1497, 1443, 1374, 1318, 1214 cm^{-1}.

HRMS: Calcd. for $C_{26}H_{28}N_3O_4$ m/z = 446.2080, found m/z = 446.2100; for $C_{26}H_{27}N_3O_4Na$ m/z = 468.1899, found m/z = 468.1922, for $C_{26}H_{27}N_3O_4K$ m/z = 484.1639, found m/z = 484.1656.

1.3.12 Preparation of 6

To a stirred solution of Phe-OMe.HCl (500 mg, 2.32 mmol) and NEt_3 (0.32 mL, 2.32 mmol) in ~50 mL dry DCM under ice cold condition, 1,3-phenyldiisocyanate (185.8 mg 1.16 mmol) was added drop wise and stirred the reaction mixture for 12 h. After completion of reaction, reaction mixture was washed with 0.2N H_2SO_4, saturated

$NaHCO_3$ and finally with water. The organic part was dried over anhydrous Na_2SO_4 and evaporated. The obtained crude product was purified by column chromatography using EtOAc/hexane solvent and afford 350 mg product.

Yield: 68%

MP: 194-196 °C.

$[\alpha]^{26}_D$: +42.

^{1}H NMR (500 MHz, CD_3CN) δ 3.03 (dd, *J* = 14.0, 7.5 Hz, 2H), 3.14 (dd, *J* = 14.0, 5.5 Hz, 2H), 3.69 (s, 6H), 4.64 (m, 2H), 5.49 (d, *J* = 8.0 Hz, 2H), 6.95 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.25 (m, 6H), 7.35 (m, 6H), 7.53 (br s, *J* = 2.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz), δ 38.2, 52.3, 54.2, 111.2, 114.7, 127.1, 128.5, 129.2, 129.3, 136.2, 139.0, 155.4, 173.9.

IR (KBr): 3330, 3029, 2949, 1740, 1644, 1555, 1492, 1441, 1357, 1210, 1074, 1023 cm^{-1}.

HRMS: Calcd. for $C_{28}H_{30}N_4O_6Na$ m/z = 541.2063, found m/z = 541.2056.

1.3.13 Preparation of 7

To an ice cold solution of **A3** (500 mg, 1.37 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 4 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap to afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B3** (1.37 mmol) with NEt_3 (0.19 mL, 1.37mmol) in dry DCM was added a solution of 1,3-phenyldiisocyanate (110 mg, 0.68 mmol) drop wise and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water. Dried over anhydrous Na_2SO_4

followed by evaporation. The obtained crude product was further purified by column chromatography using ethylacetate /hexane solvent to afford 311 mg product.

Yield: 66%

MP: 166-168 °C.

$[\alpha]^{26}_{D}$: -20.

^{1}H NMR (500 MHz, CD_3CN) δ 1.48 (s+s, 12H), 2.86 (dd, *J* = 13.8, 9.2 Hz, 2H), 3.11 (dd, *J* = 14, 5.0 Hz, 2H), 3.60 (s, 6H), 4.58 (m, 2H), 6.81 (s, 2H), 7.22 (m, 5H), 7.28 (m, 9H), 7.39 – 7.71 (m, 2H).

^{13}C NMR (DMSO, 125 MHz), δ 24.7, 25.1, 51.9, 53.3, 55.1, 106.7, 110.6, 126.3, 128.0, 128.9, 129.5, 137.4, 140.7, 154.4, 170.9, 174.3.

IR (KBr): 3356, 3300, 3065, 2928, 1740, 1650, 1550, 1492, 1387, 1288, 1235, 1154 cm^{-1}.

HRMS: Calcd. for $C_{36}H_{44}N_6O_8Na$ m/z = 711.3118, found m/z = 711.3119.

1.3.14 Preparation of 8

To an ice cold solution of **A1** (500 mg, 1.37 mmol) in ~20 mL dry DCM was added TFA (8 mL) and kept stirred for 4 h. The reaction was monitored by TLC and after completion, the reaction mixture was evaporated under a high vacuum with a KOH trap to afford N-deprotected derivative.

To an ice cold solution of N-deprotected derivative **B1** (1.37 mmol) with NEt_3 (0.19 mL, 1.37 mmol) in dry DCM was added a solution of 1,3-phenyldiisocyanate (110 mg, 0.69 mmol) in DCM and the reaction mixture was kept stirred for 12 h. The reaction was monitored by TLC and after completion, the reaction mixture washed with 0.2 N H_2SO_4, saturated aqueous $NaHCO_3$, and water. Dried over anhydrous Na_2SO_4 followed by evaporation. The crude product was further purified by column chromatography using EtOAc/hexane solvent and afford 304 mg product.

Yield: 64%

MP: 112-114 °C.

$[\alpha]^{26}_{D}$: +5.

^{1}H NMR (500 MHz, CD_3CN) δ 1.40 (s+s, 12H), 3.1 (m, 4H), 3.65 (s, 19H), 4.67 (m, 2H), 5.58 (s, 2H), 7.05 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.18 (m, 13H), 7.33 (s, 2H), 7.64 (s, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz), δ 25.9, 37.9, 52.3, 53.6, 56.6, 127.1, 128.6, 129.5, 136.1, 139.9, 155.3, 172.2, 175.9.

IR (KBr): 3353, 2944, 1743, 1658, 1547, 1445, 1361, 1241, 1169, 1021 cm^{-1}.

HRMS: Calcd. for $C_{36}H_{44}N_6O_8Na$ m/z = 711.3118, found m/z = 711.3137.

1.3.15 Preparation of 9

To a stirred solution of D-Phe-OMe.HCl, (500 mg, 2.32 mmol) and NEt_3 (0.32 mL, 2.32 mmol) in dry DCM under ice cold condition, a solution of 1,3-phenyldiisocyanate (185.8 mg 1.16 mmol) in dry DCM was added dropwise and stirred the reaction mixture for 12 h. After completion of reaction, reaction mixture was washed with 0.2N H_2SO_4, saturated $NaHCO_3$ and finally with water. The organic part was dried over anhydrous Na_2SO_4 and evaporated. The crude product was purified by column chromatography using EtOAc/hexane solvent to afford 525 mg product.

Yield: 87%.

$[\alpha]^{26}_{D}$: -46.

^{1}H NMR (500 MHz, CD_3CN) δ 3.03 (dd, *J* = 14.0, 7.5 Hz, 2H), 3.14 (dd, *J* = 14.0, 5.5 Hz, 2H), 3.69 (s, 6H), 4.64 (m, 2H), 5.49 (d, *J* = 8.0 Hz, 2H), 6.95 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.25 (m, 6H), 7.35 (m, 6H), 7.53 (t, *J* = 2.5 Hz, 1H).

^{13}C NMR (CD_3CN, 125 MHz), δ 37.6, 51.7, 54.1, 108. 4, 112.2, 126.8, 128.4, 129.1, 129.4, 136.9, 140.2, 154.5, 172.7.

HRMS: Calcd. for $C_{28}H_{30}N_4O_6Na$ m/z = 541.2063, found m/z = 541.2056

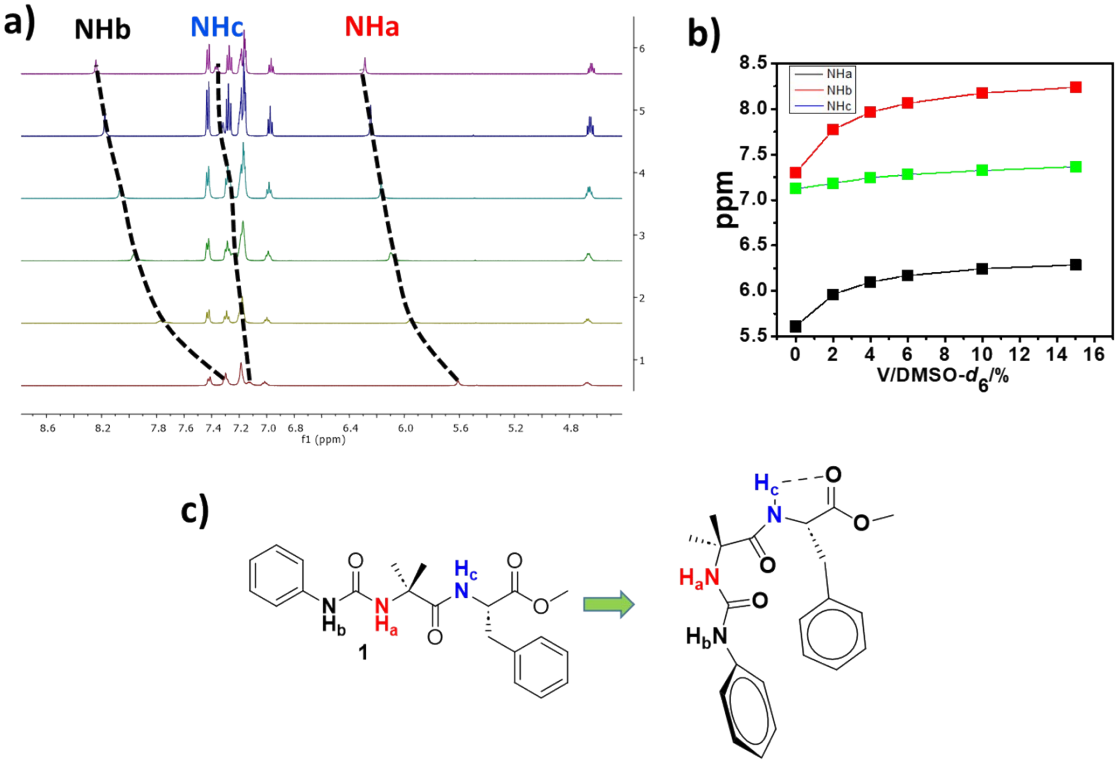


Figure S1: a) Partial ^{1}H NMR (500 MHz, CD_3CN) spectra of **1** upon the addition of various amounts of DMSO-d_6, b) Influence on NH protons of **1** in CD_3CN by the volume fraction of DMSO-d_6, c) Chemical structure of **1** showing β-turn.

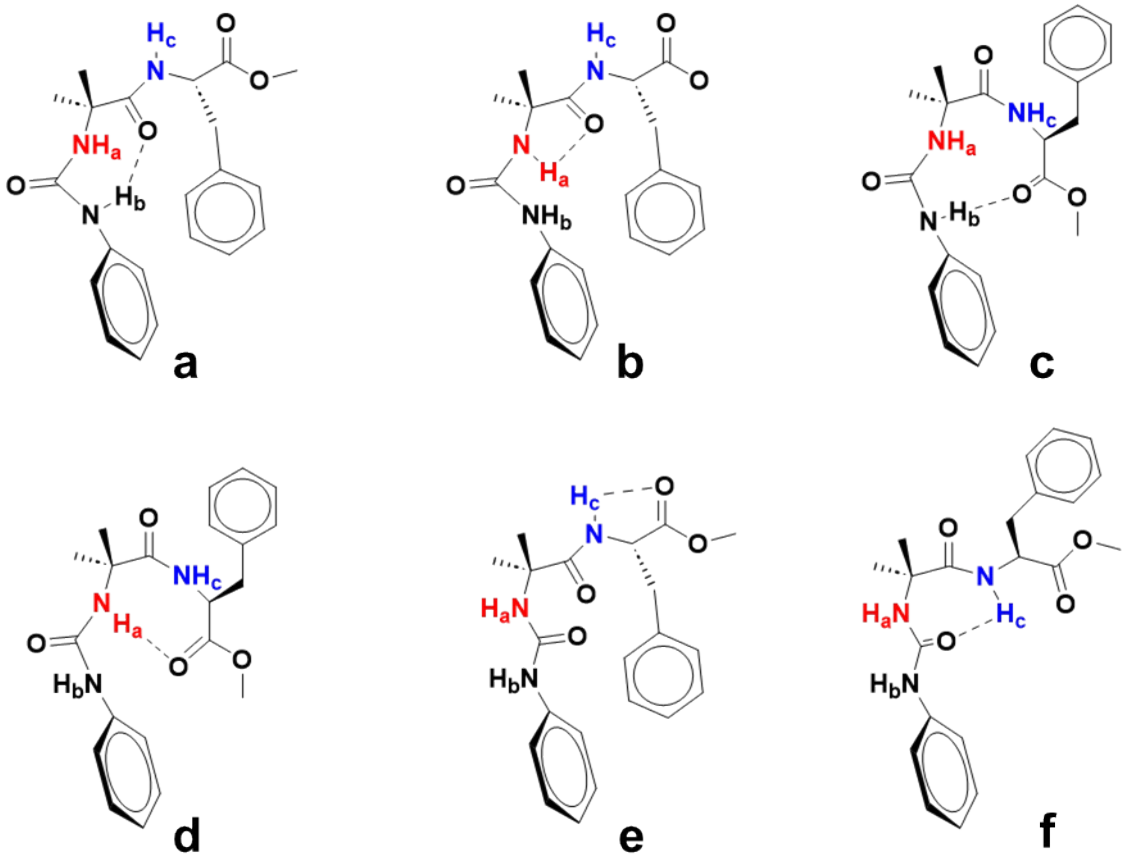


Figure S2: Possibilities of CO-NH hydrogen bonds in peptide **1**.

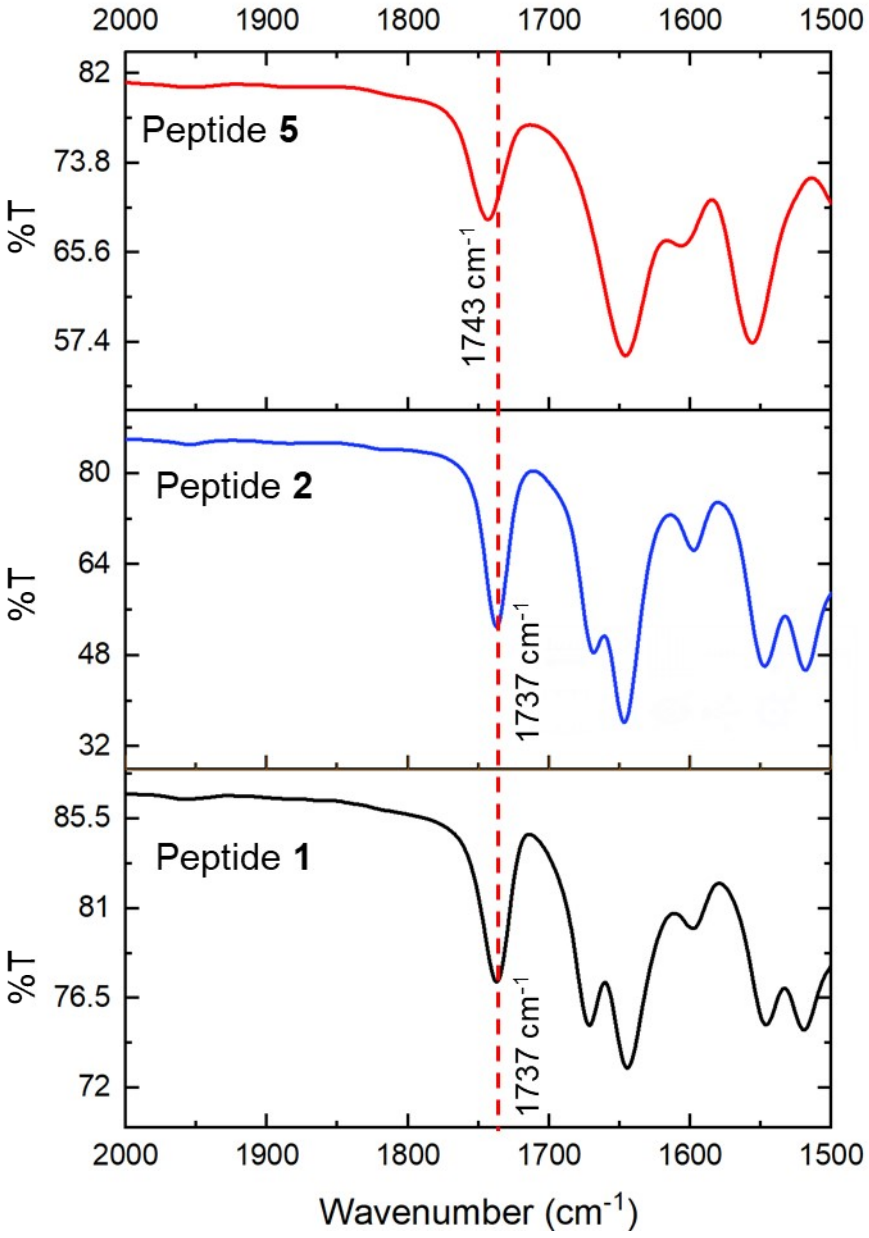


Figure S3: The infrared (IR) spectra comparison of peptide **1**, **2** and **5** showing stretching frequency of ester carbonyls in **1** and **2** at 1737 cm^{-1}, while that of peptide **5** at 1743 cm^{-1}.

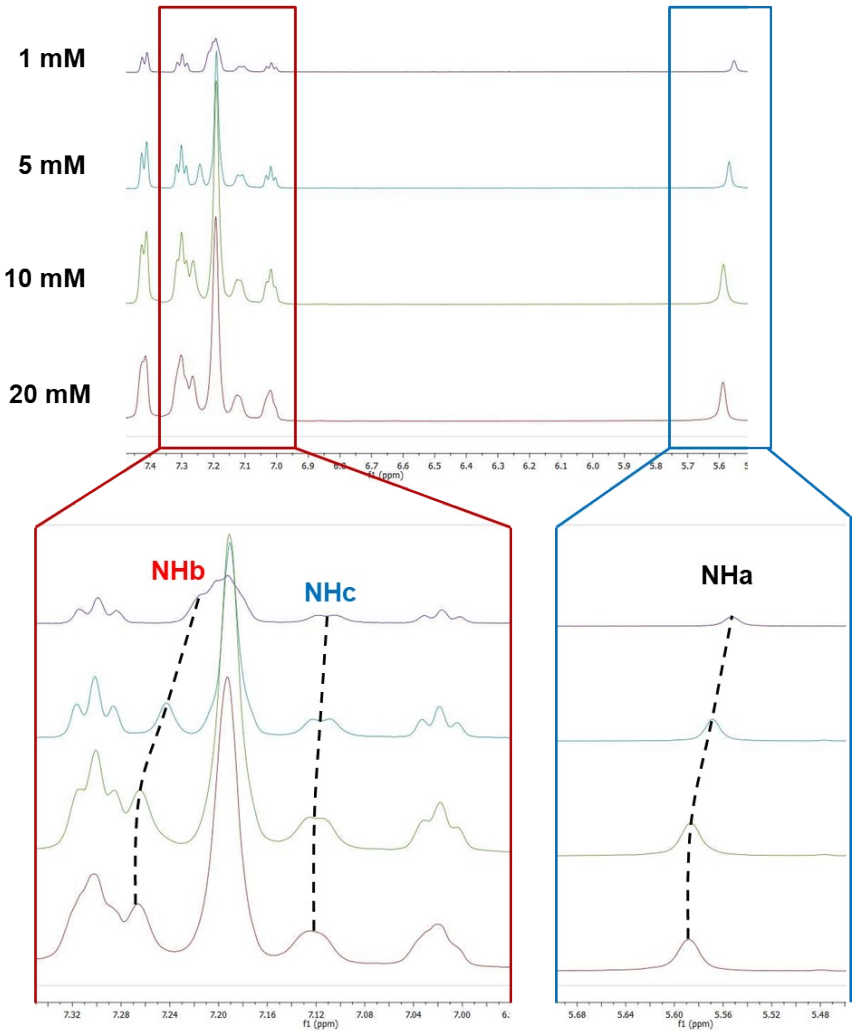


Figure S4. Partial ^{1}H NMR (500 MHz, CD_3CN) spectra of **1** at different concentrations.

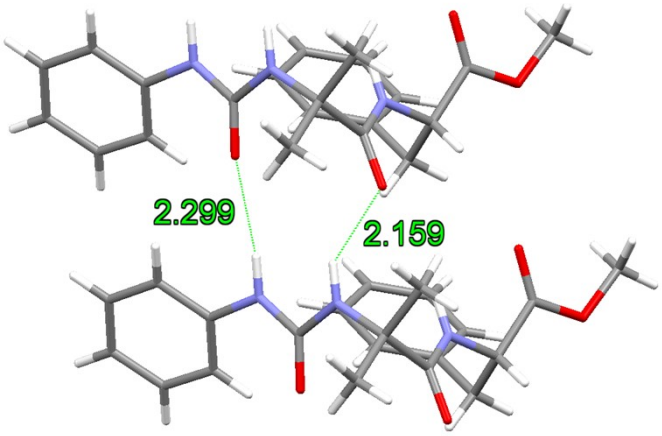


Figure S5: Crystal structure of peptide **1** showing N–H···O hydrogen bonds between Aib amide and urea carbonyls with urea NHs. The distances are 2.2 and 2.3 Å respectively.

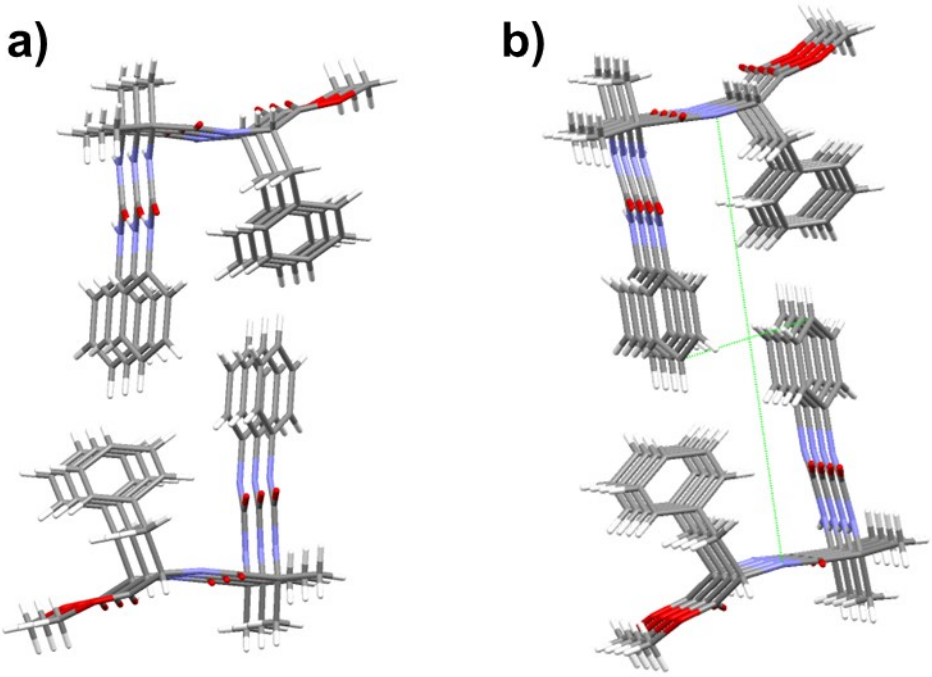


Figure S6: a) Association of peptide **1** through intermolecular π-π interactions and H-bonding to form the tubular structure, b) Intermolecular hydrogen bonded supramolecular tubular structure of peptide **1**, with dimensions of the cavity are 5 Å and 14 Å.

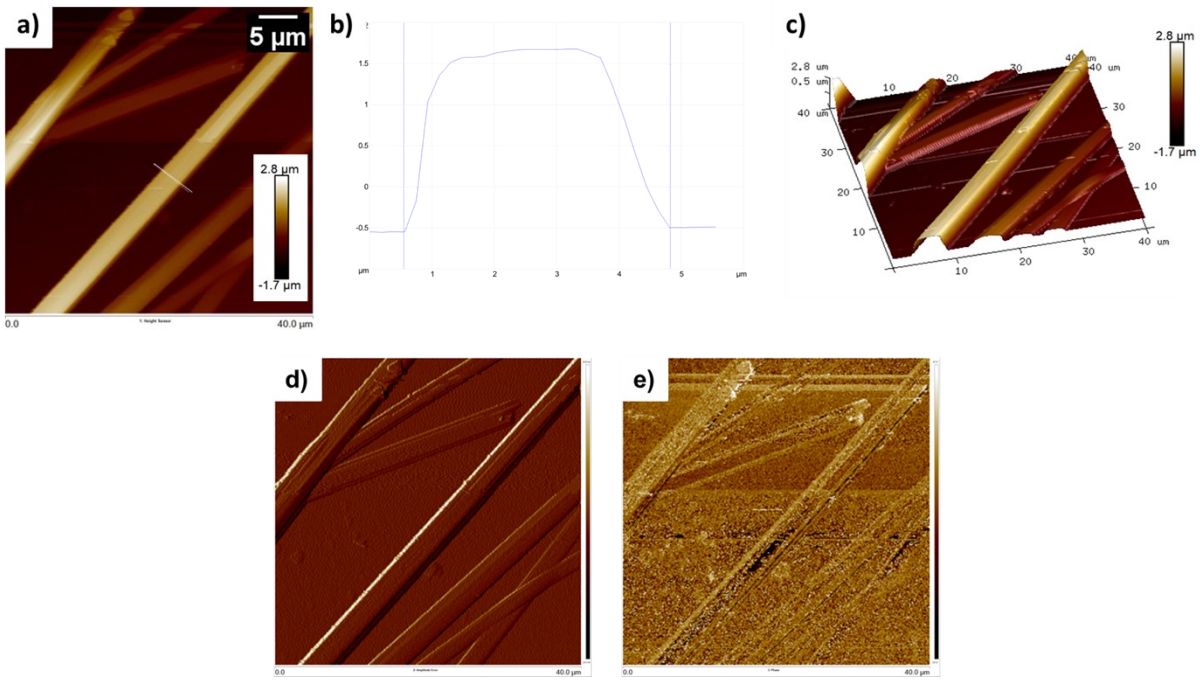


Figure S7: a) AFM topological image of **1** showing microtubular assembly, b) height analysis of a single microtube formed by self-assembly of **1**, c) 3D AFM topographical image of **1**, d) amplitude image and e) phase image of **1** showing tubular assembly.

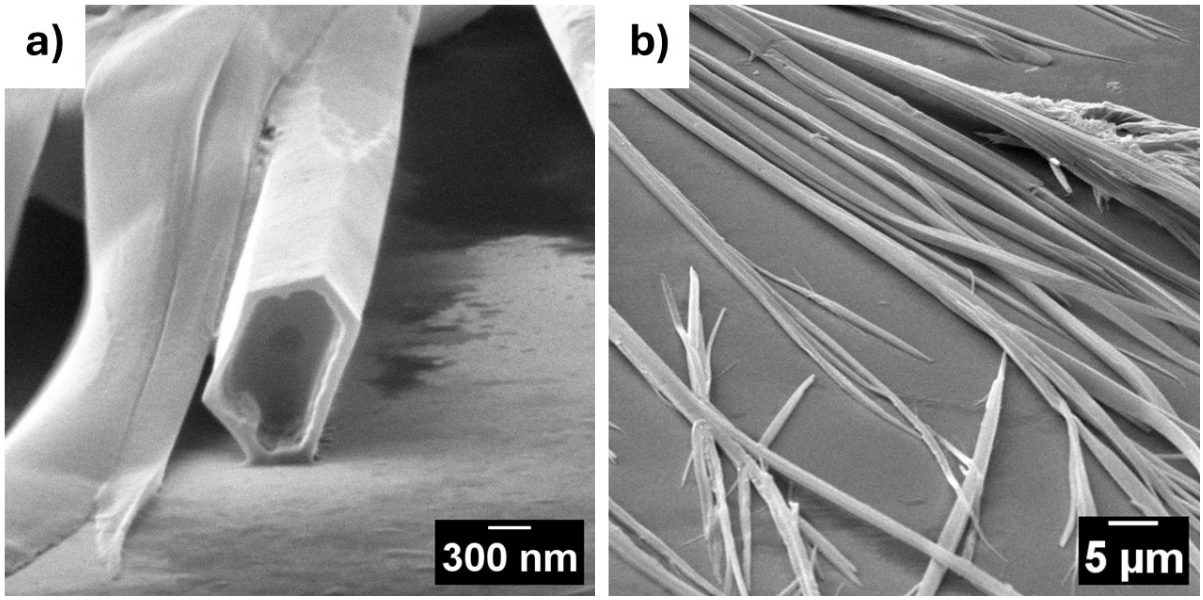


Figure S8: a) FESEM images of **2** taken at an angle of 10° from the surface showing the open end of the microtubular assembly.

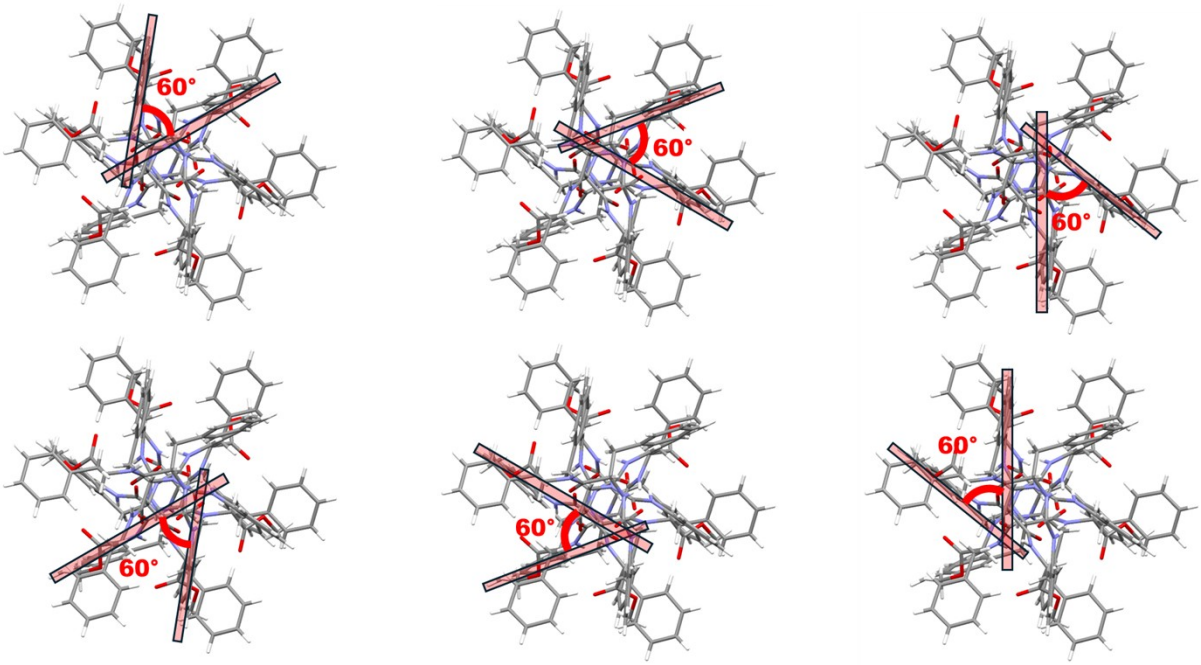


Figure S9: The interplanar angle between the aromatic rings of consecutive molecules were found to be 60 °.

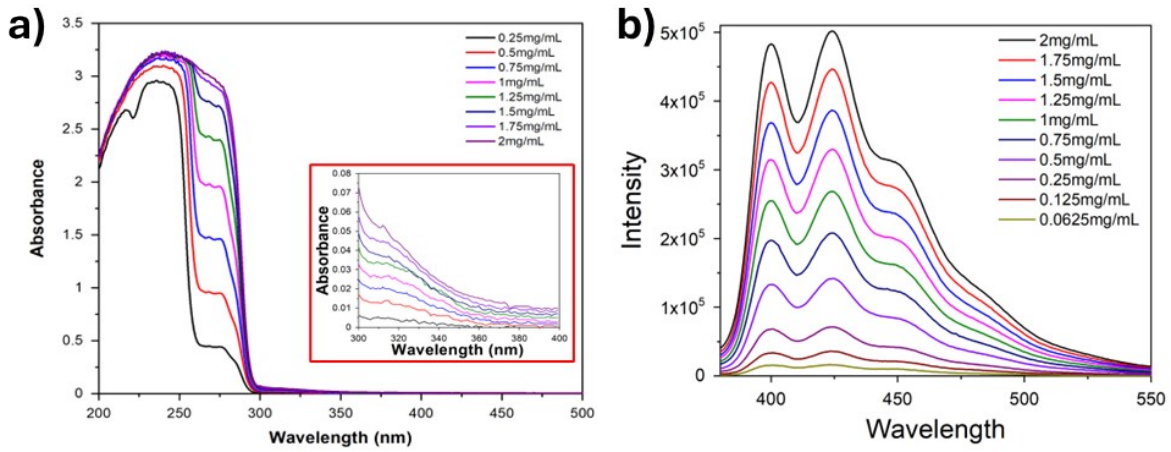


Figure S10: a) UV-visible absorption spectra of **1** at different concentrations. The inset shows partial absorption spectra indicating absorption at higher wavelengths, b) Fluorescence emission spectra for different concentrations of **1** upon excitation at 365 nm.

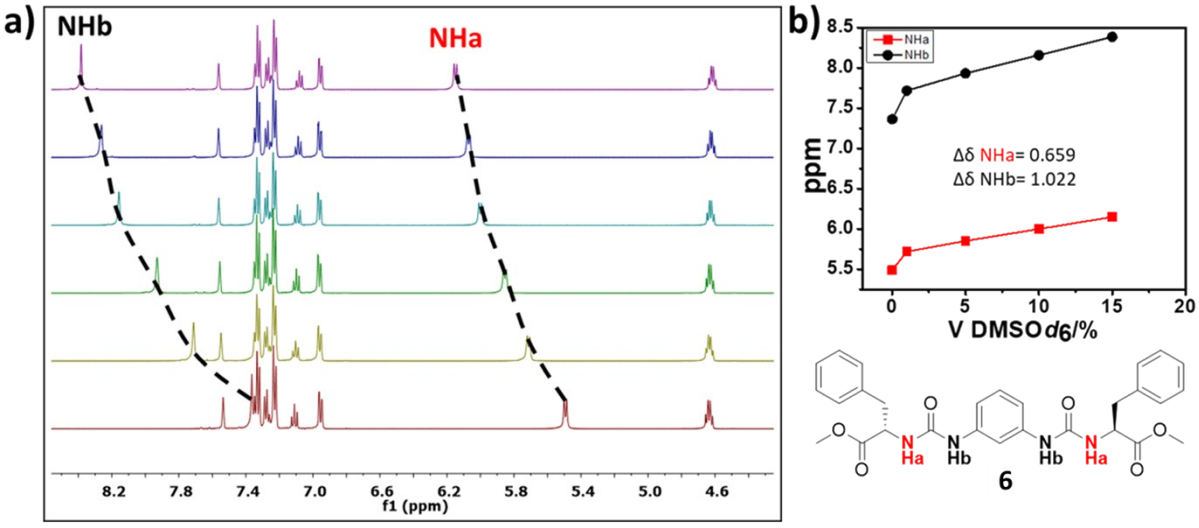


Figure S11: Partial ^{1}H NMR (500 MHz, CD_3CN) spectra of **6** upon the addition of various amounts of DMSO-d_6.

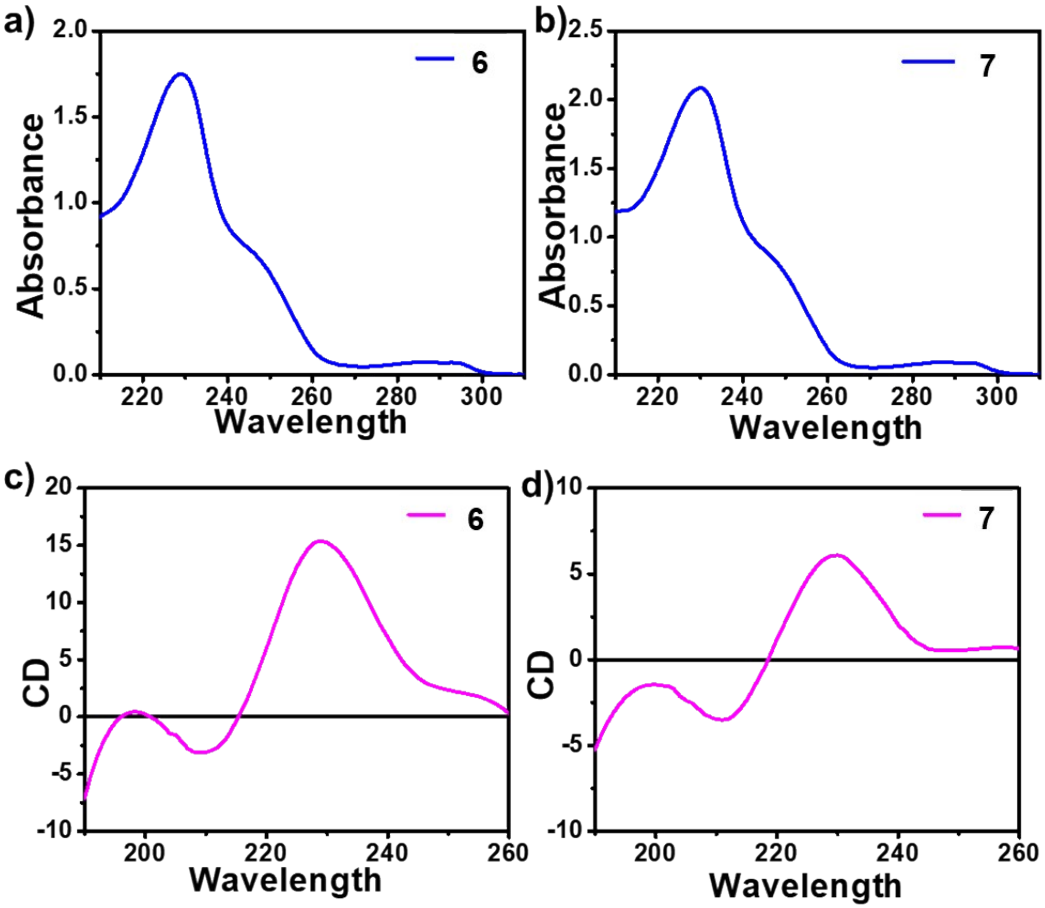


Figure S12: UV-vis spectra of a) **6** and b) **7**, and CD spectra of c) **6** and d) **7**.

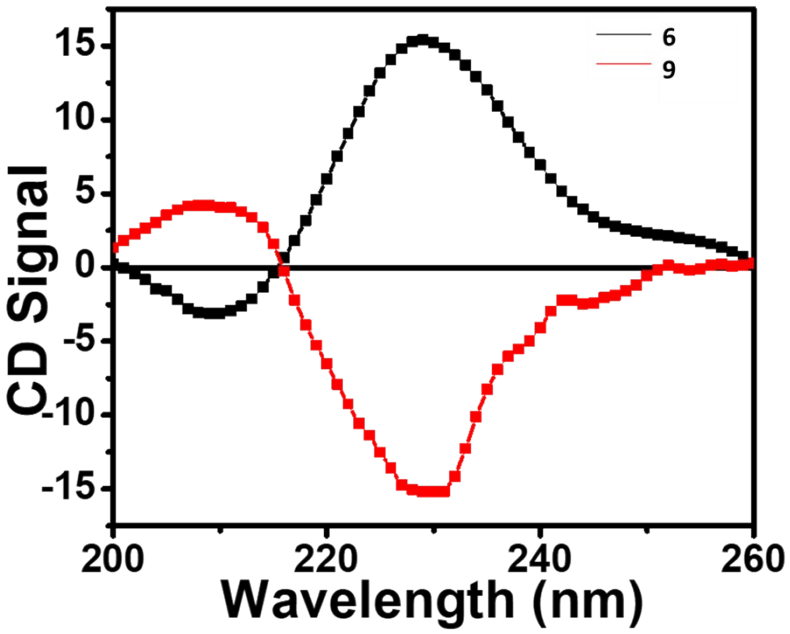


Figure S13: CD spectra of **6** and **9** in acetonitrile.

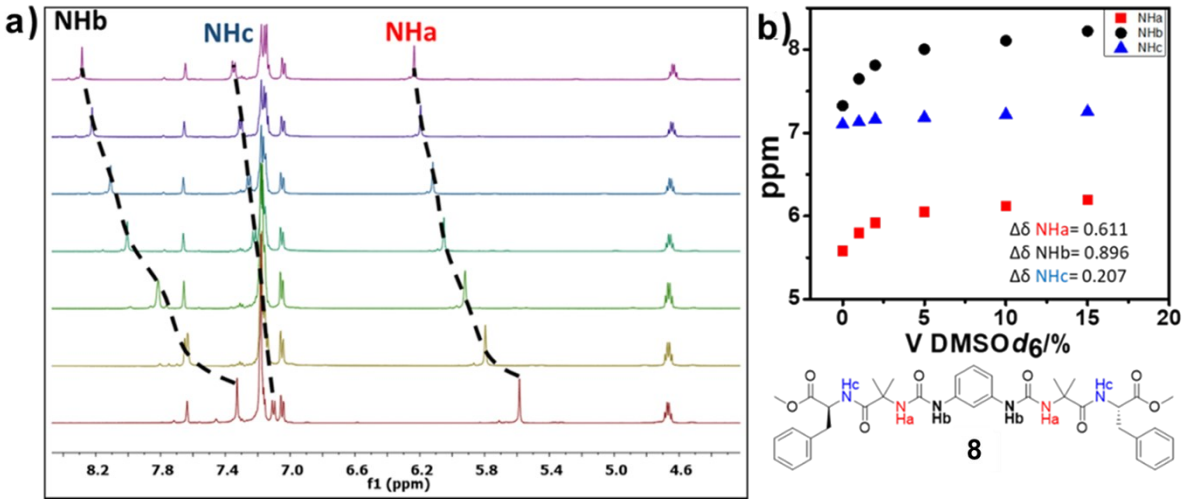


Figure S14: a) Partial ^{1}H NMR (500 MHz, CD_3CN) spectra of **8** upon the addition of various amounts of DMSO-d_6. b) Change in the chemical shift of NH proton with the addition of DMSO-d_6.

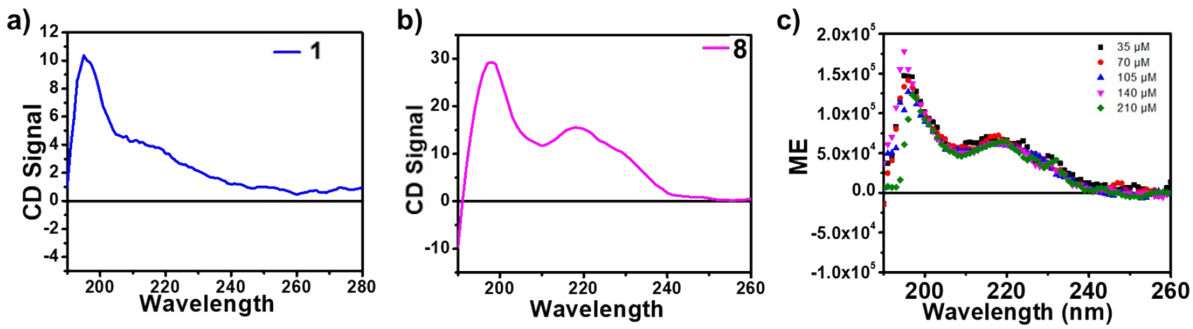


Figure S15: CD spectra of a) **1** and b) **8**, c) Concentration-dependent CD spectra of **8**.

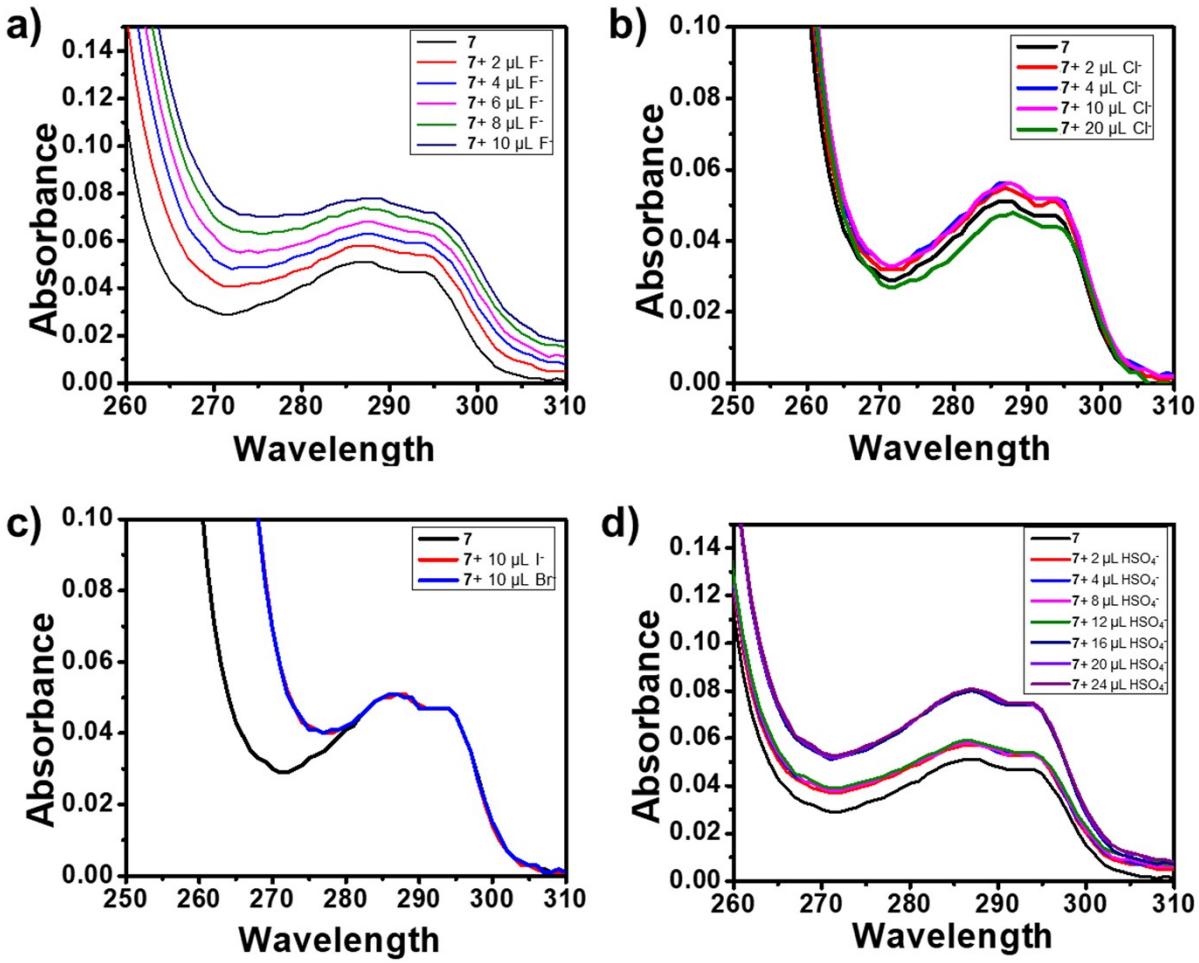


Figure S16: UV-vis spectra of **7** on addition of a) F^-, b) Cl^-, c) I^- and Br^-, and d) HSO_4^-.

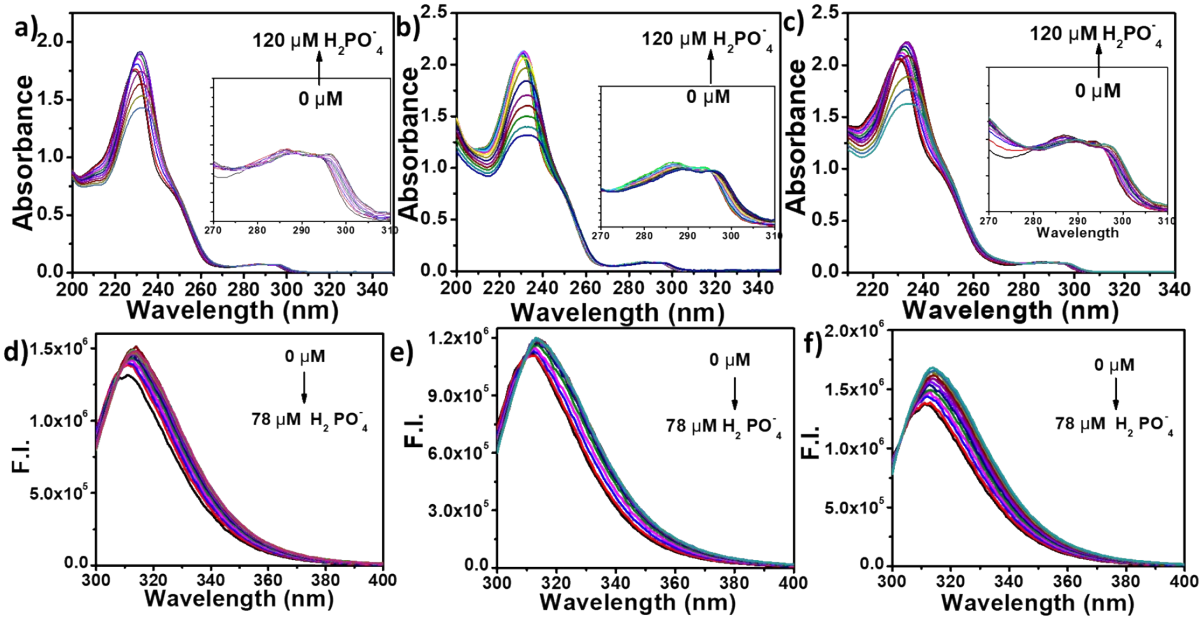


Figure S17: UV-vis spectra of a) **6,** b) **7** and c) **8** on addition of $H_2PO_4^-$ (inset showing the band at 270-300 nm) and fluorescence spectra of d) **6**, e) **7** and f) **8** on addition of $H_2PO_4^-$ (λ_{ex} =290 nm).

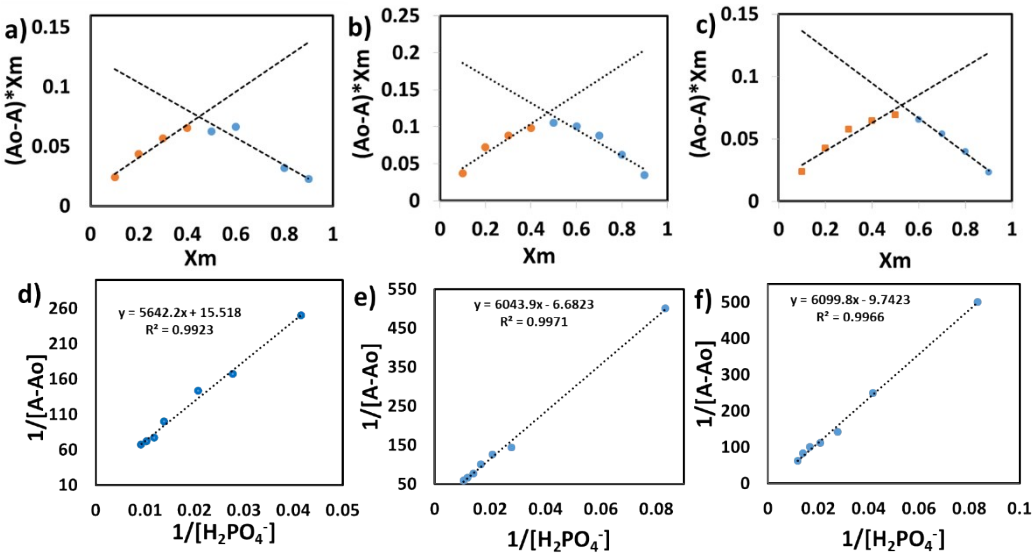


Figure S18: Job Plots: a) **6**, b) **7** and c) **8** and BH plot of a) **6**, b) **7** and c) **8** upon addition of $H_2PO_4^-$.

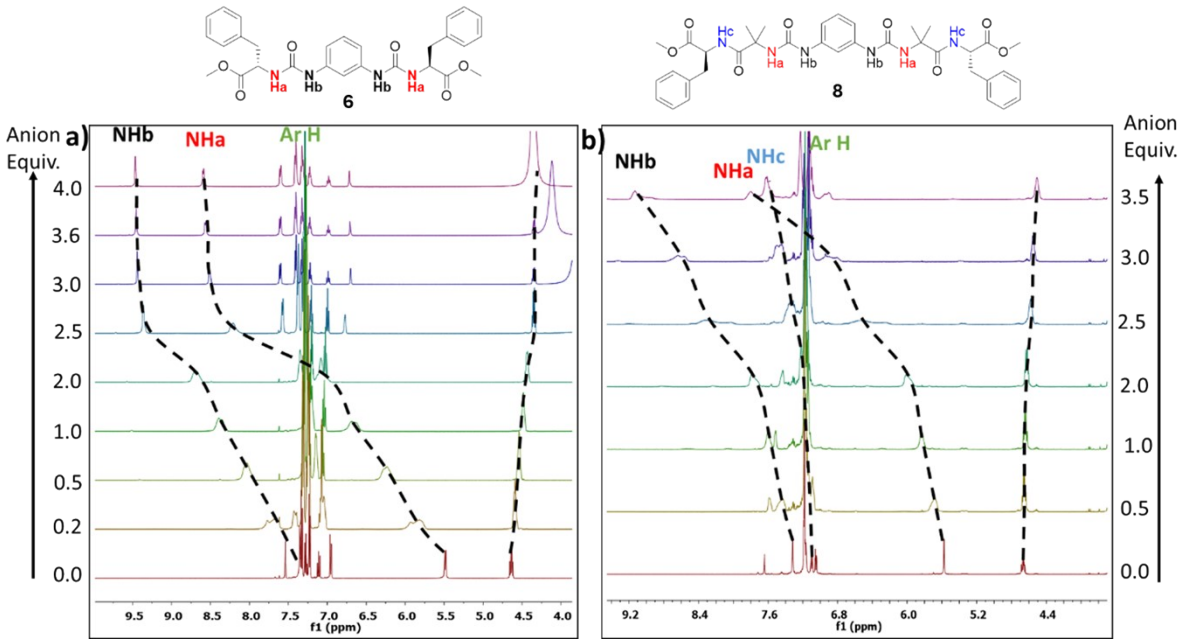


Figure S19: Partial ^{1}H NMR (500 MHz, CD_3CN) spectra of a) **6** and b) **8** at increasing concentration of $H_2PO_4^-$ ions.

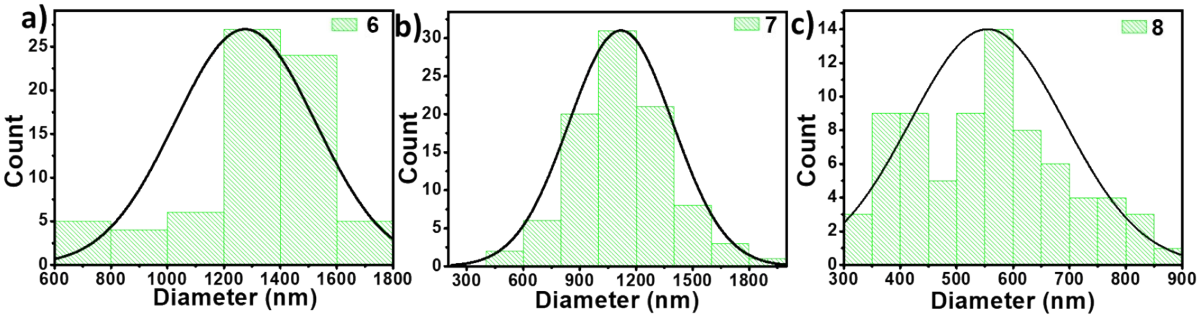


Figure S20: Histograms are based on SEM images. Diameters of vesicles obtained from a) **6**, b) **7** and c) **8**.

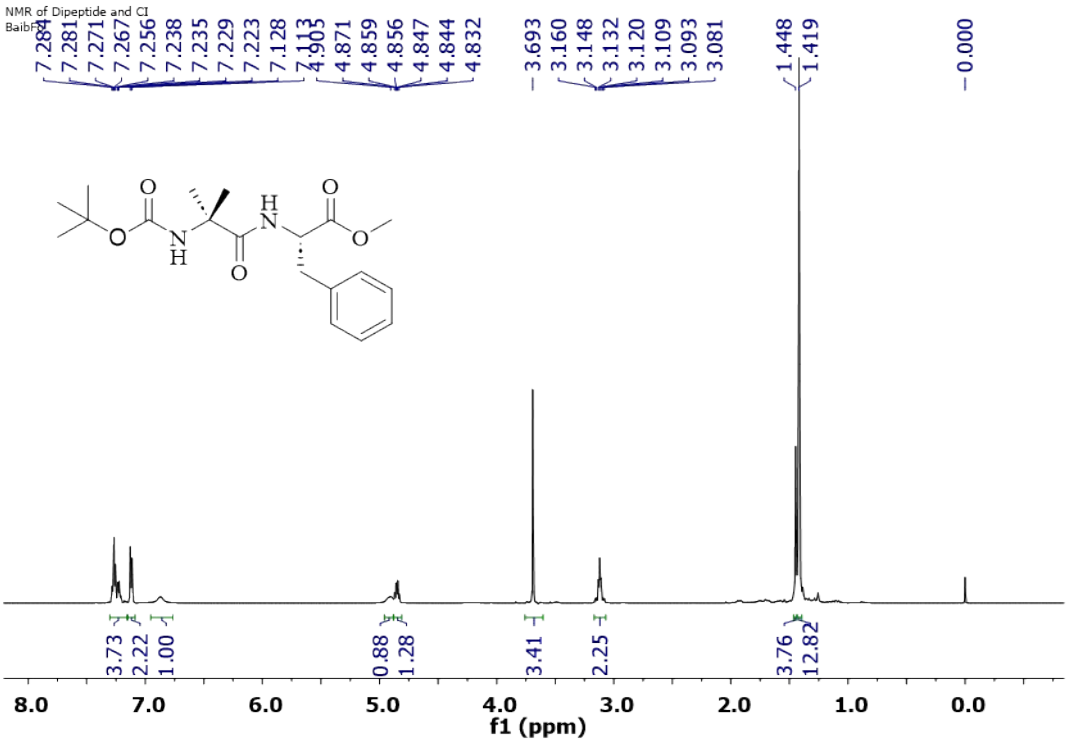


Figure S21: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **A1**.

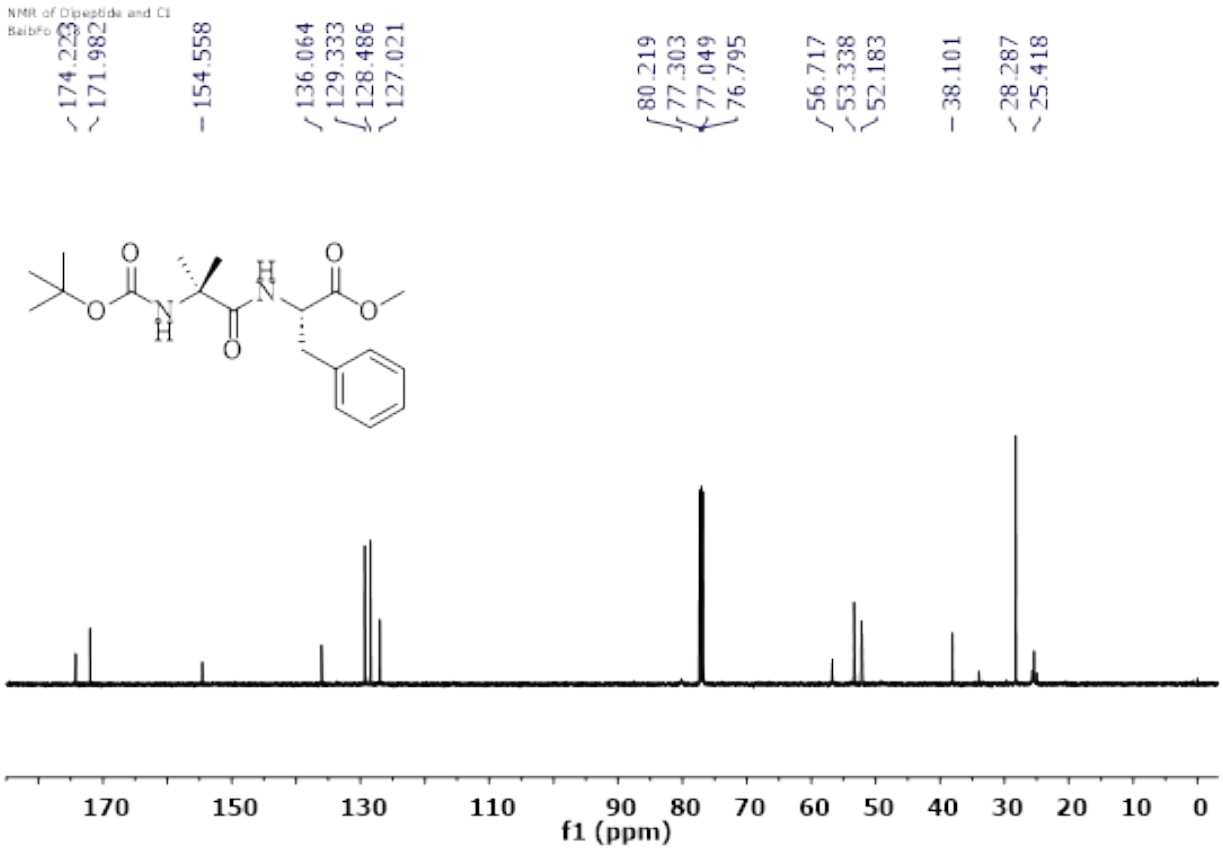


Figure S22: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **A1**.

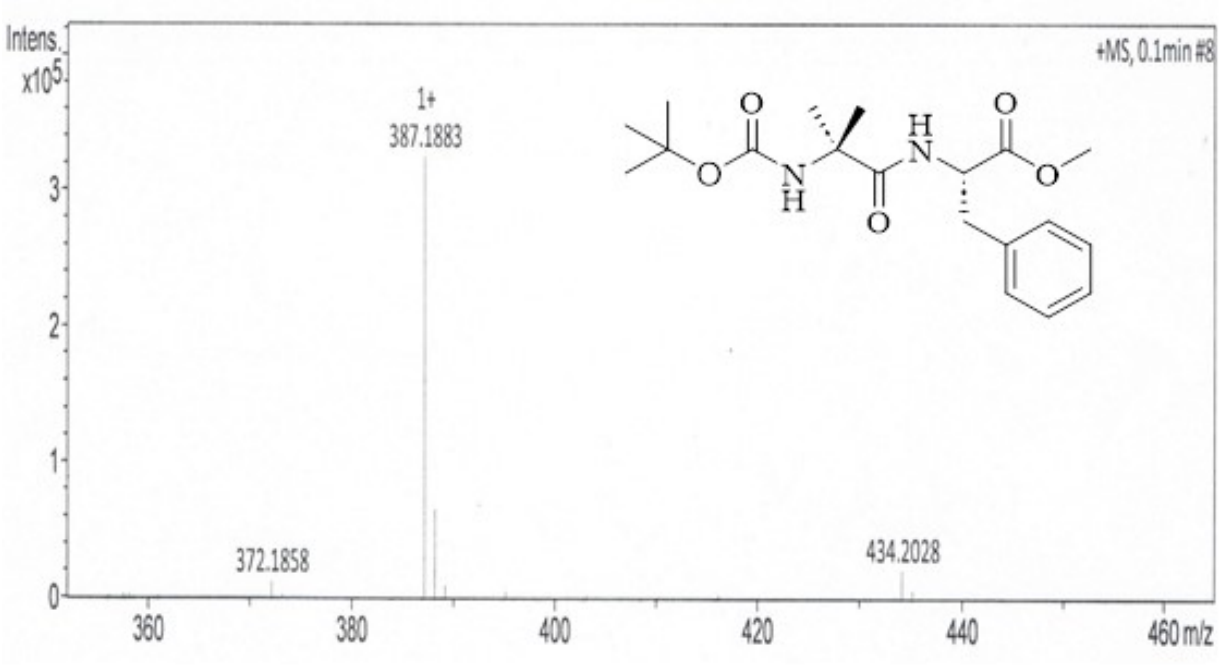


Figure S23: ESI-Mass spectrum of **A1**.

Figure S24: ^{1}H NMR (500 MHz, $CDCl_3$) of **A2.**

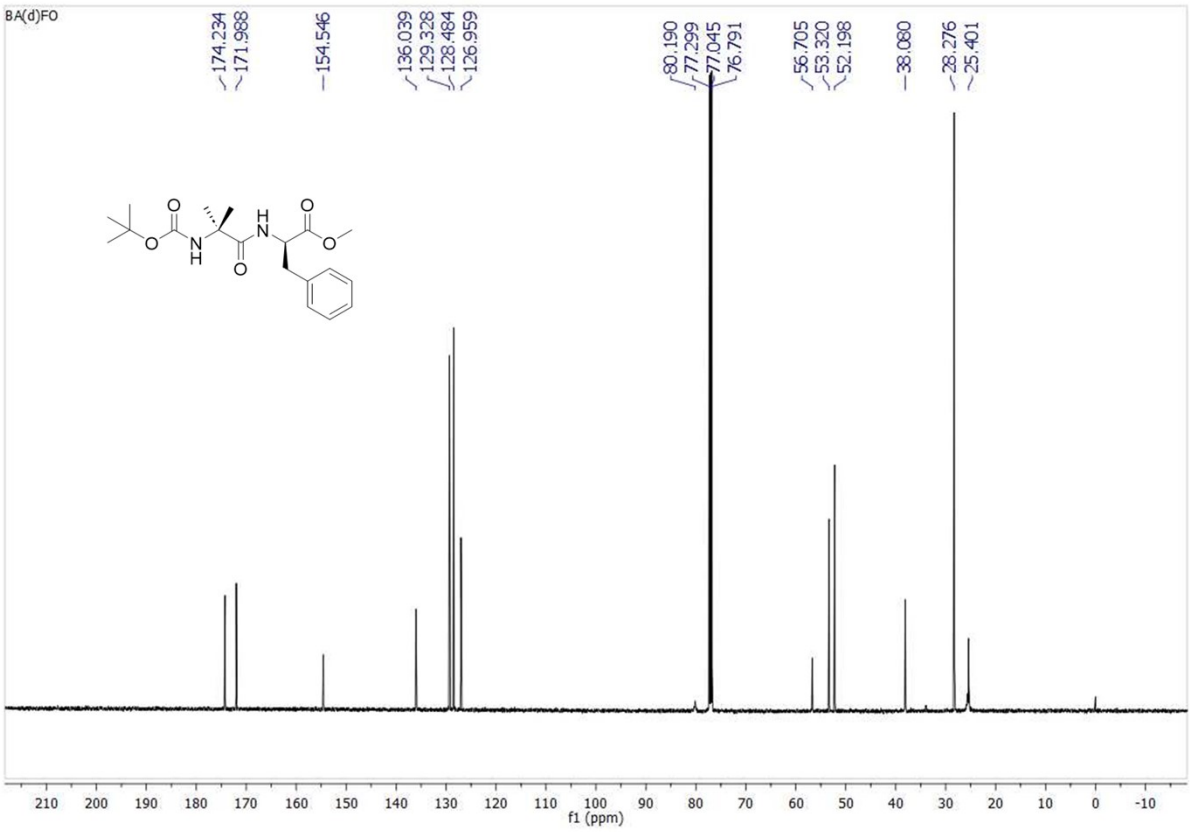


Figure S25: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **A2**.

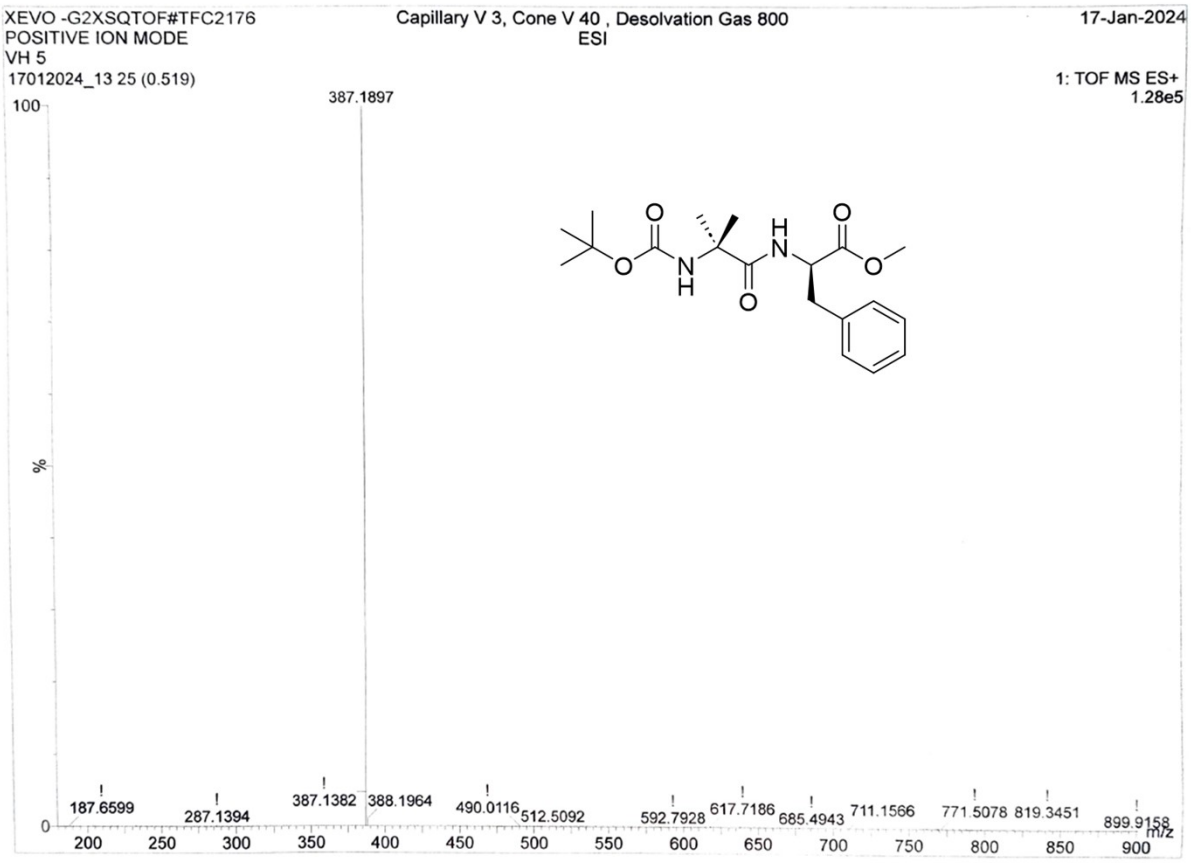


Figure S26: ESI-Mass spectrum of **A2**.

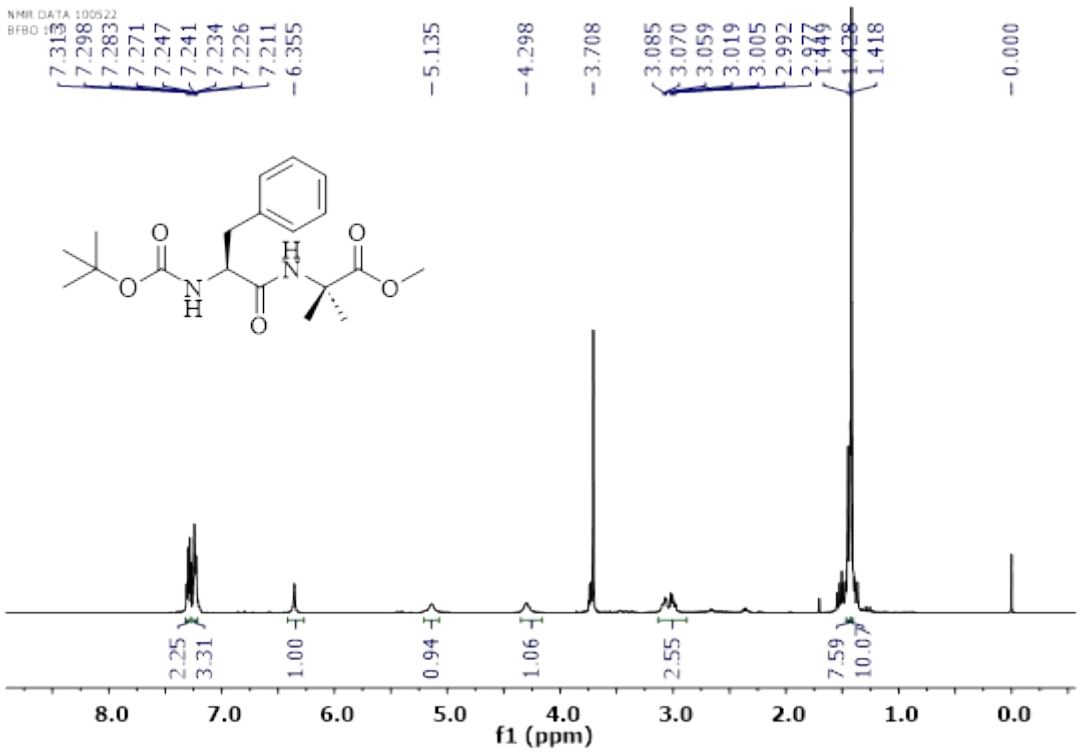


Figure S27: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **A3**.

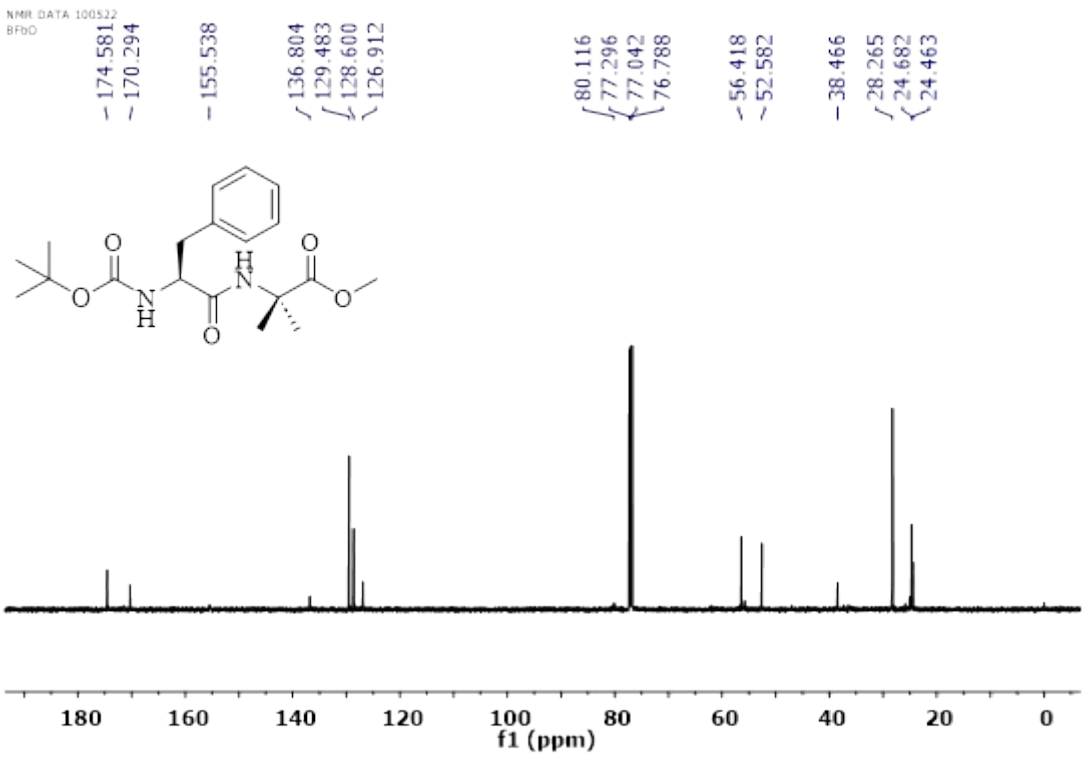


Figure S28: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **A3**.

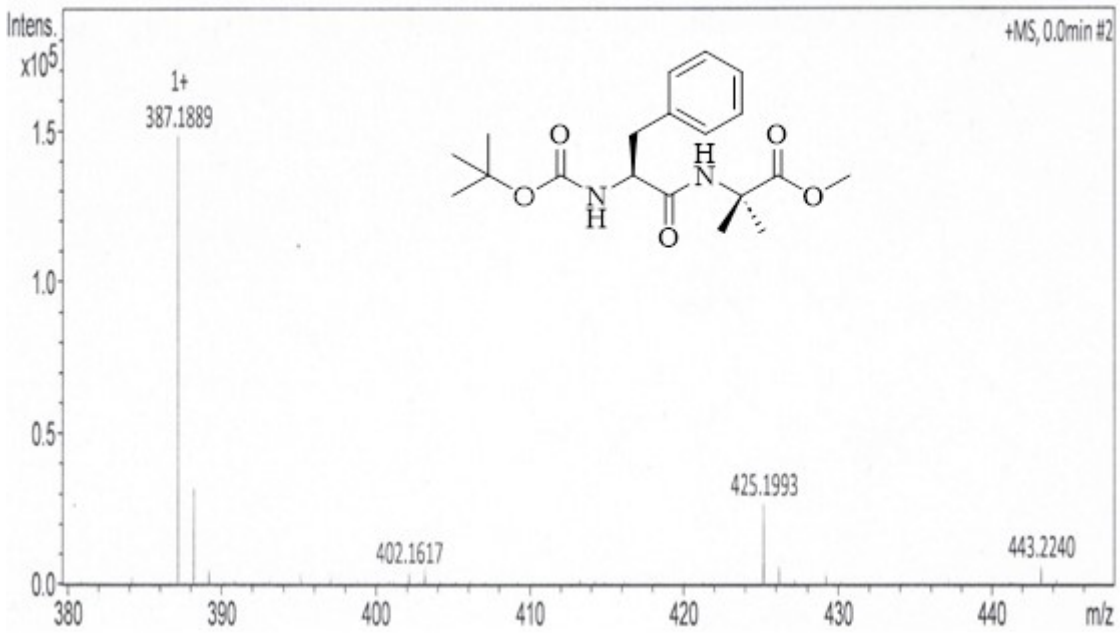


Figure S29: ESI-Mass spectrum of **A3**.

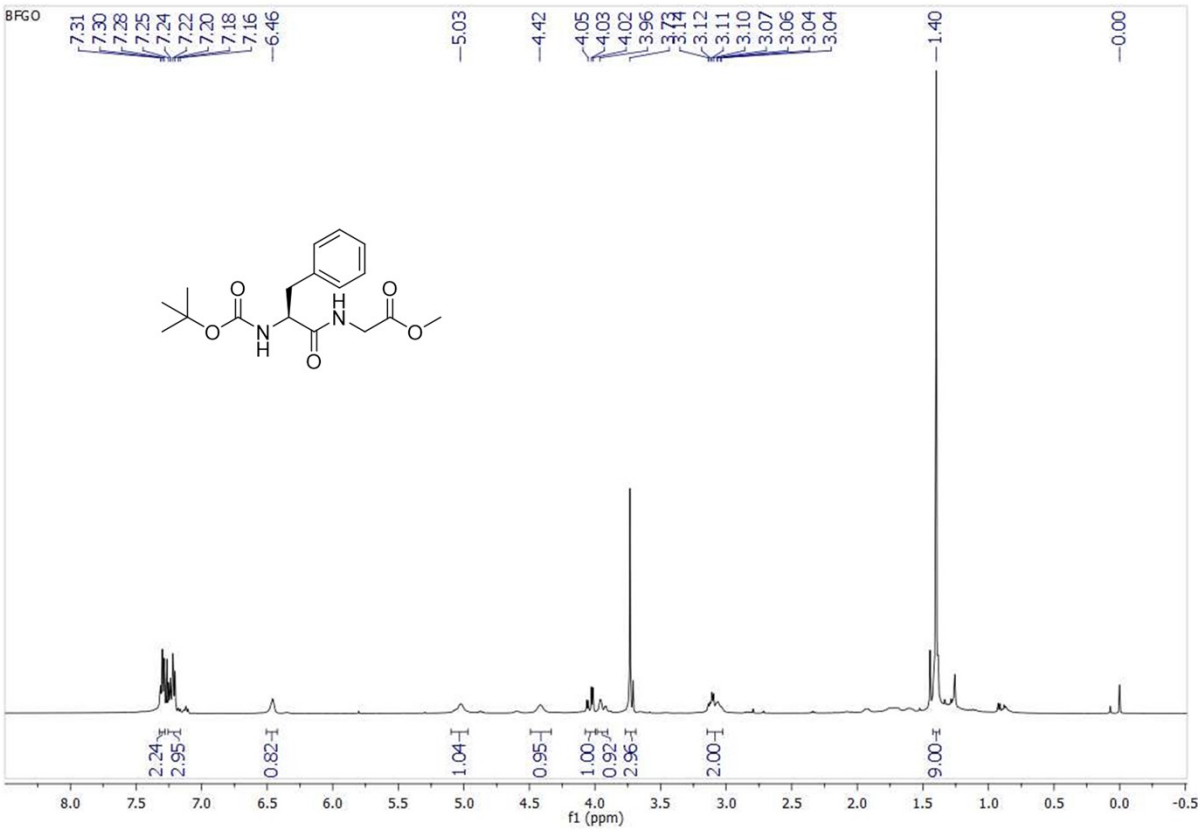


Figure S30: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **A4**.

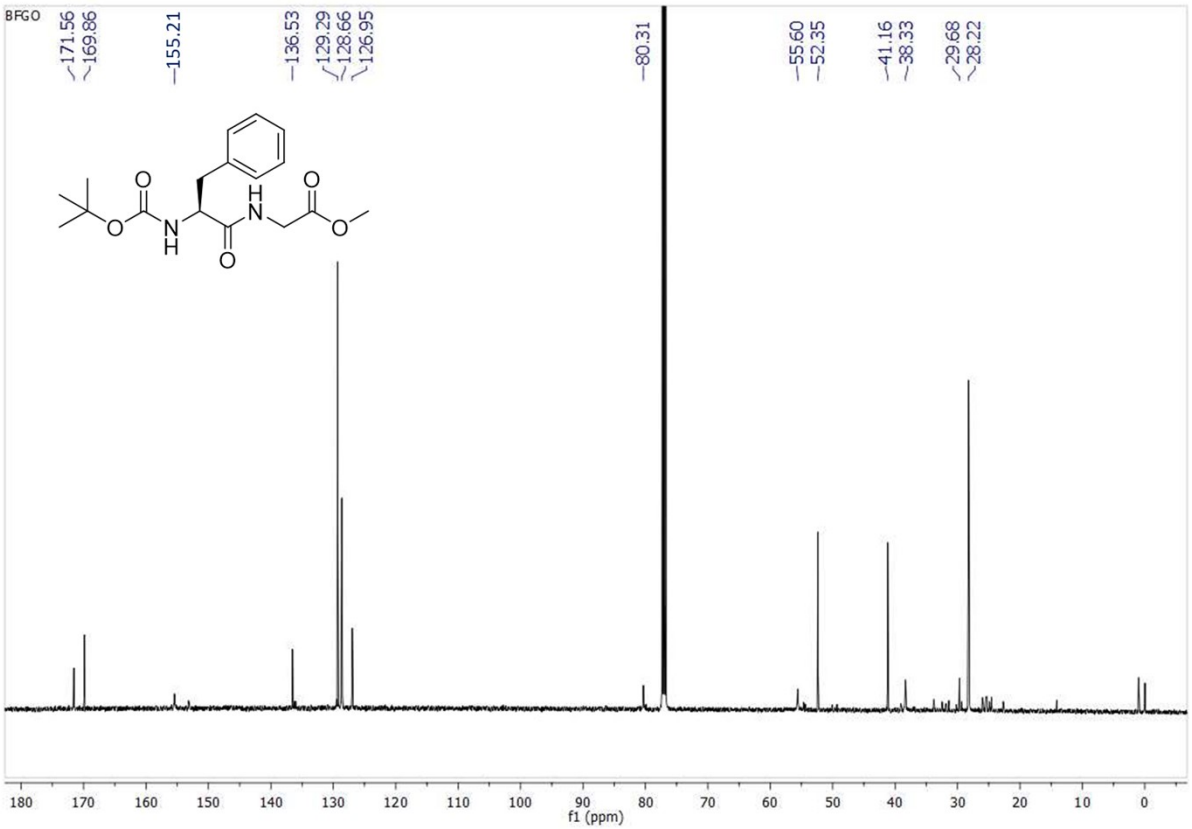


Figure S31: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **A4**.

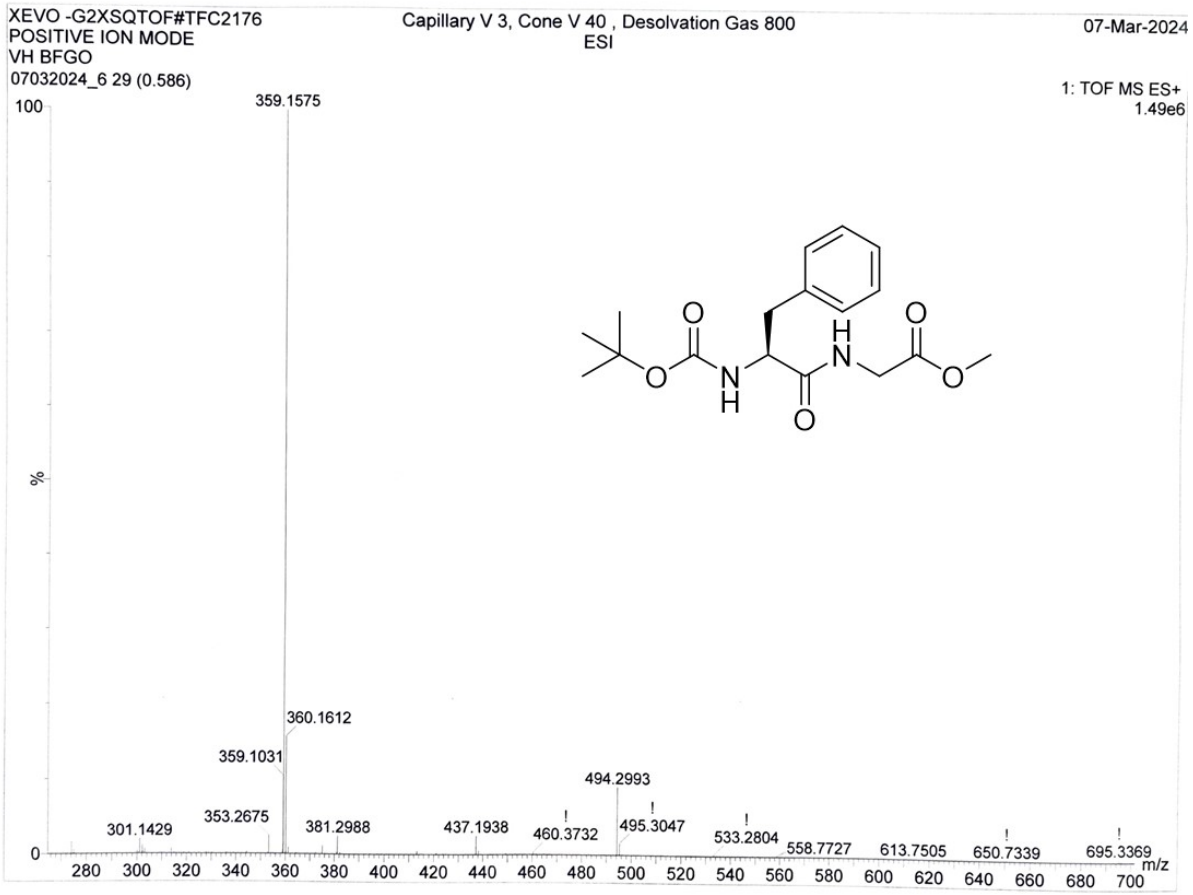


Figure S32: ESI-Mass spectrum of **A4**.

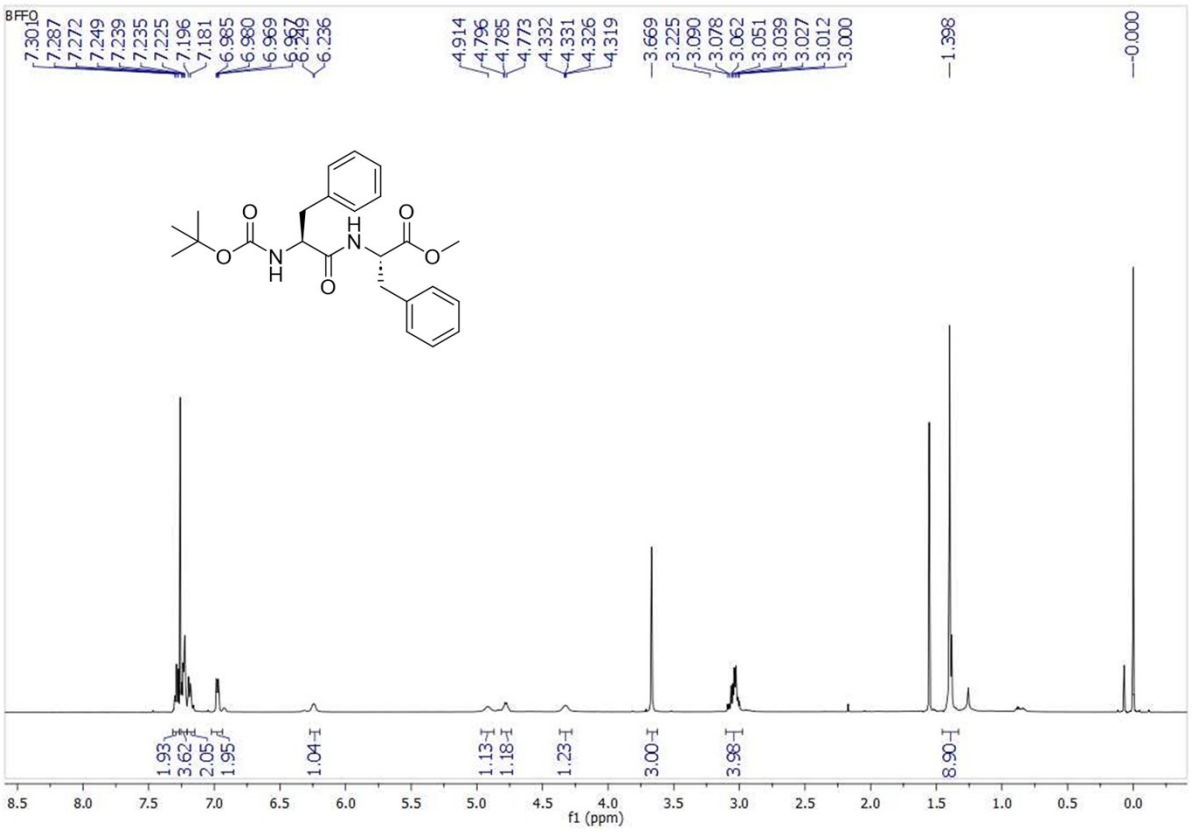


Figure S33: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **A5**.

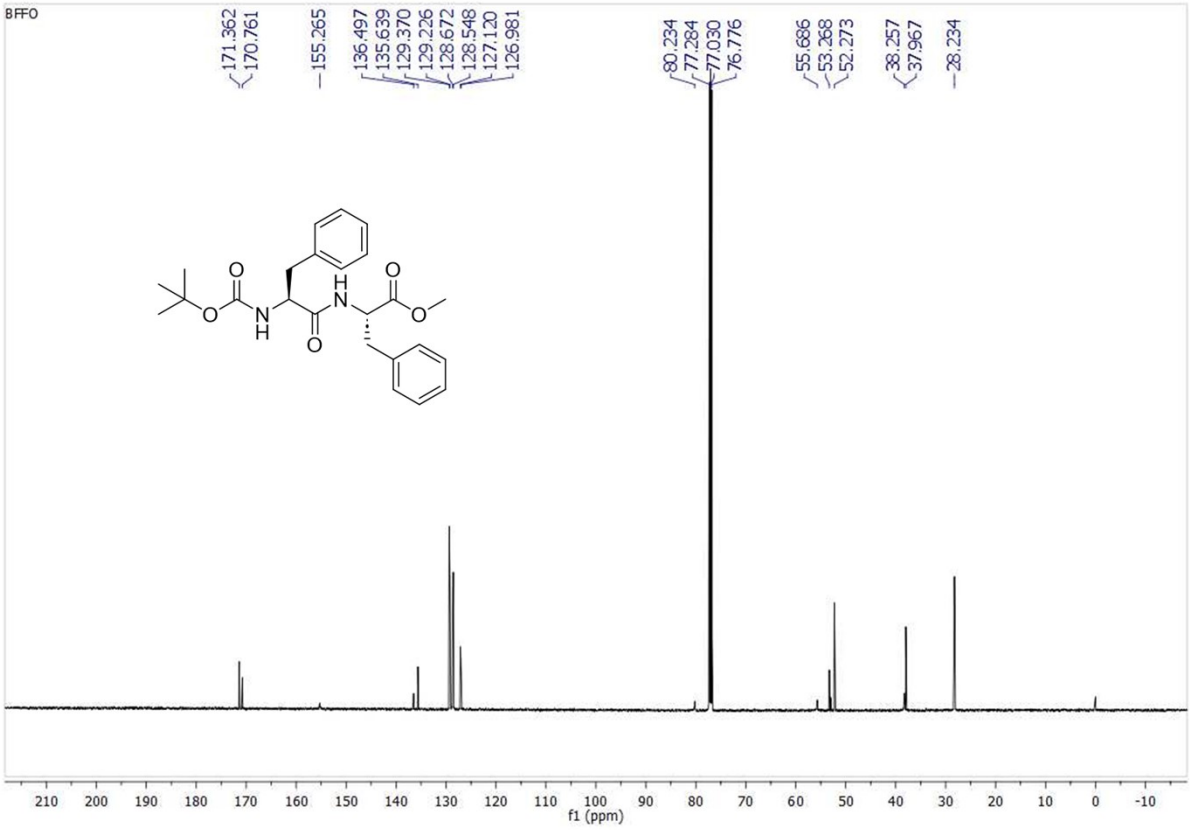


Figure S34: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **A5**.

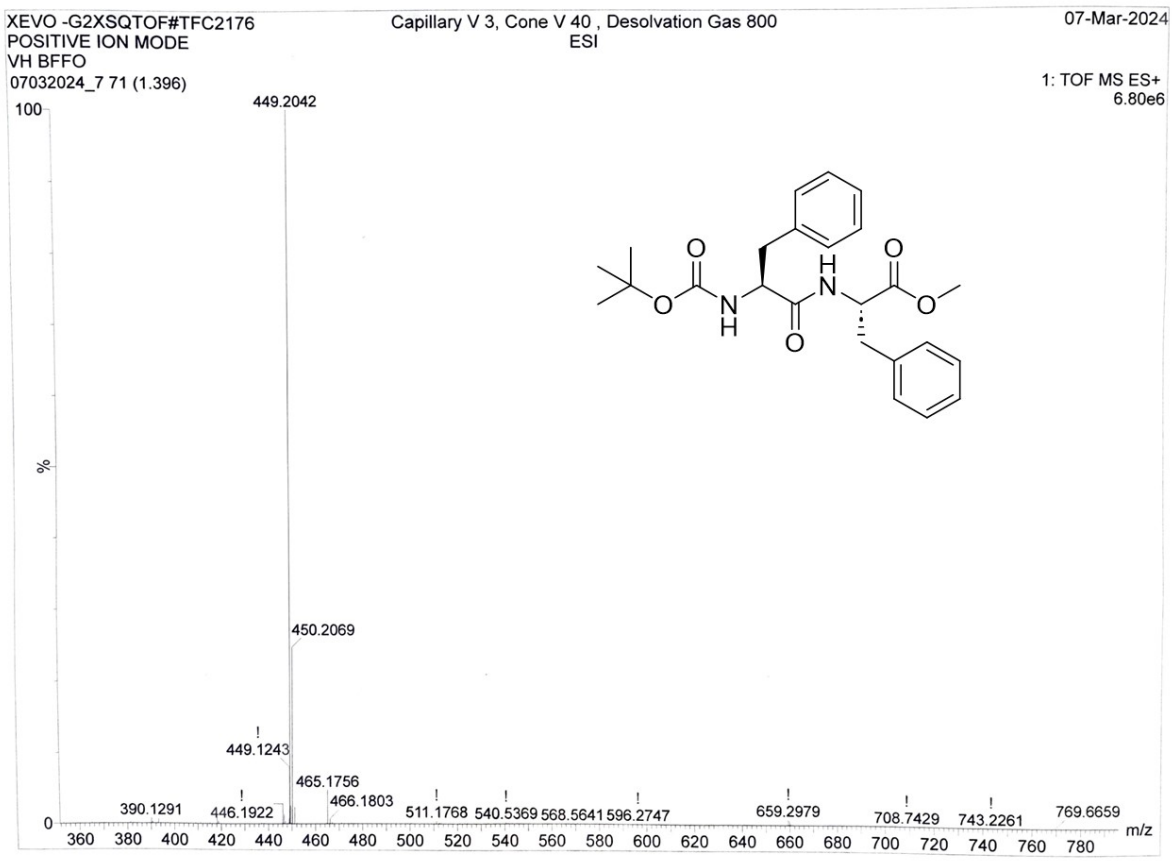


Figure S35: ESI-Mass spectrum of **A5**.

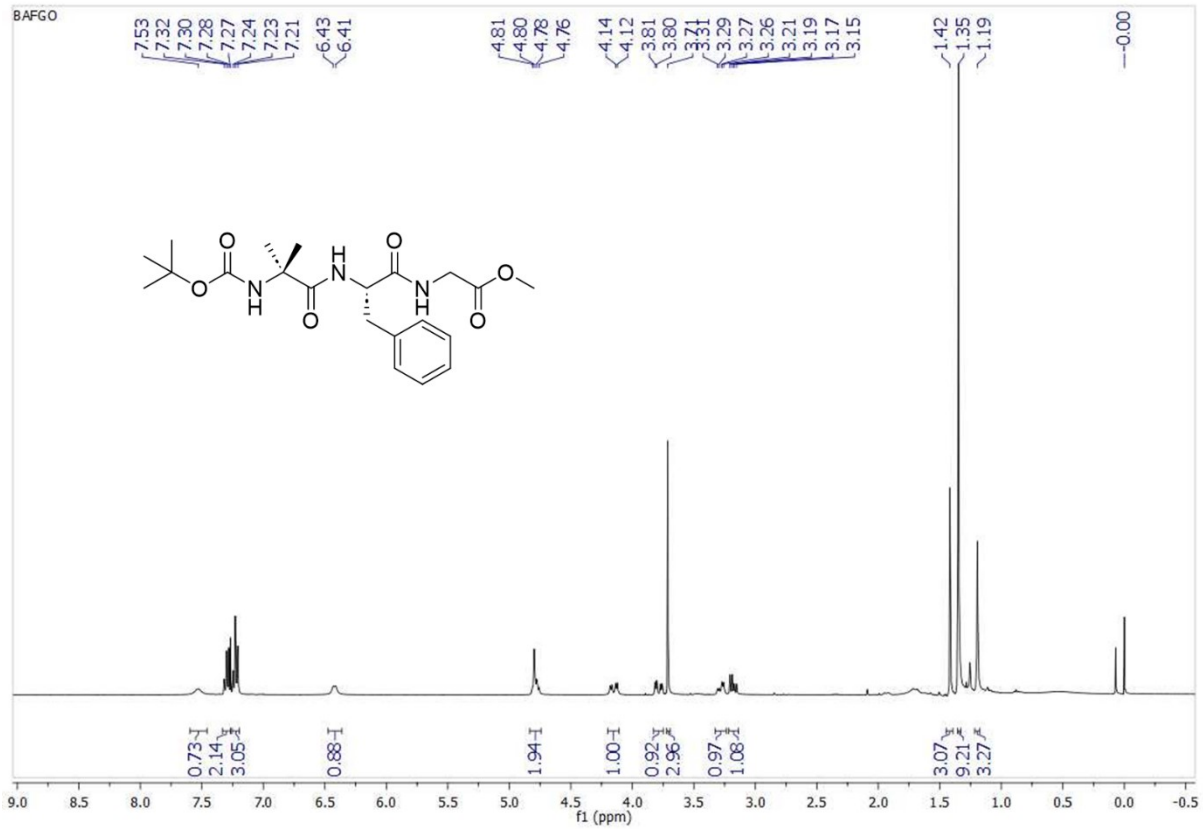


Figure S36: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **A6**.

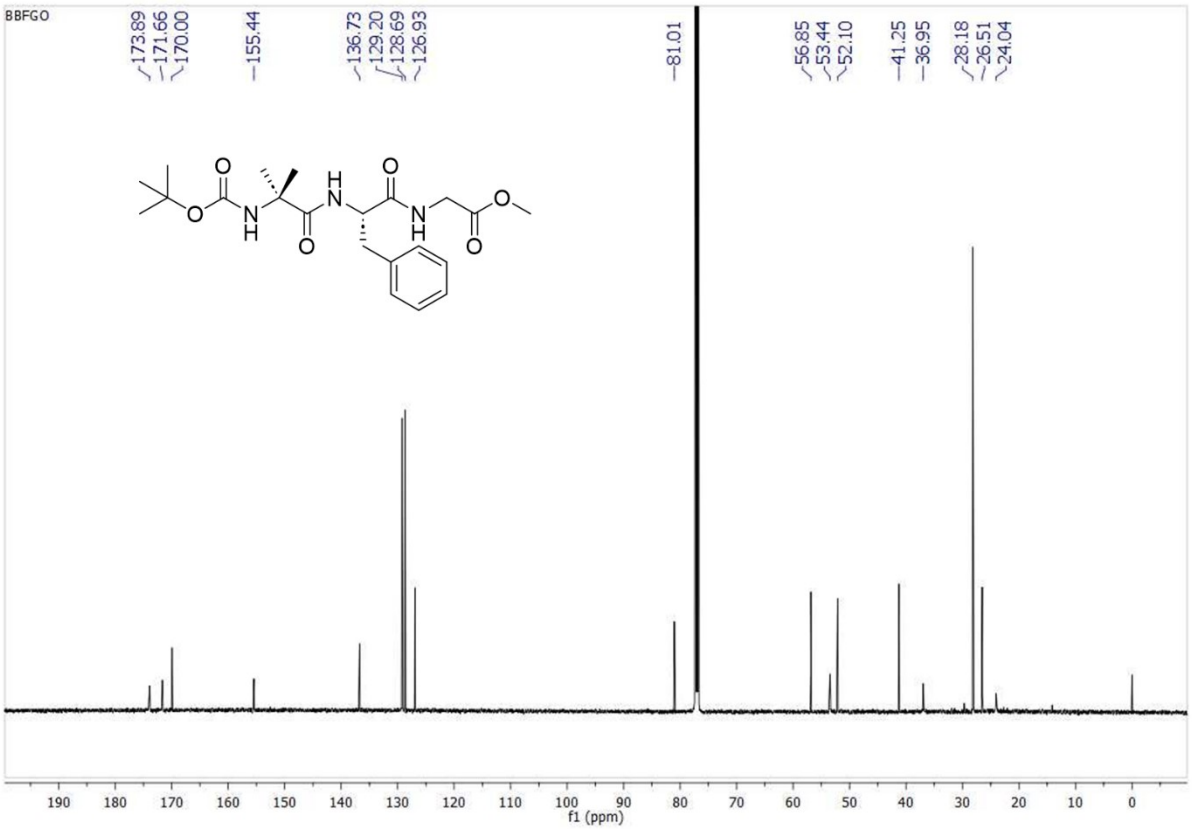


Figure S37: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **A6**.

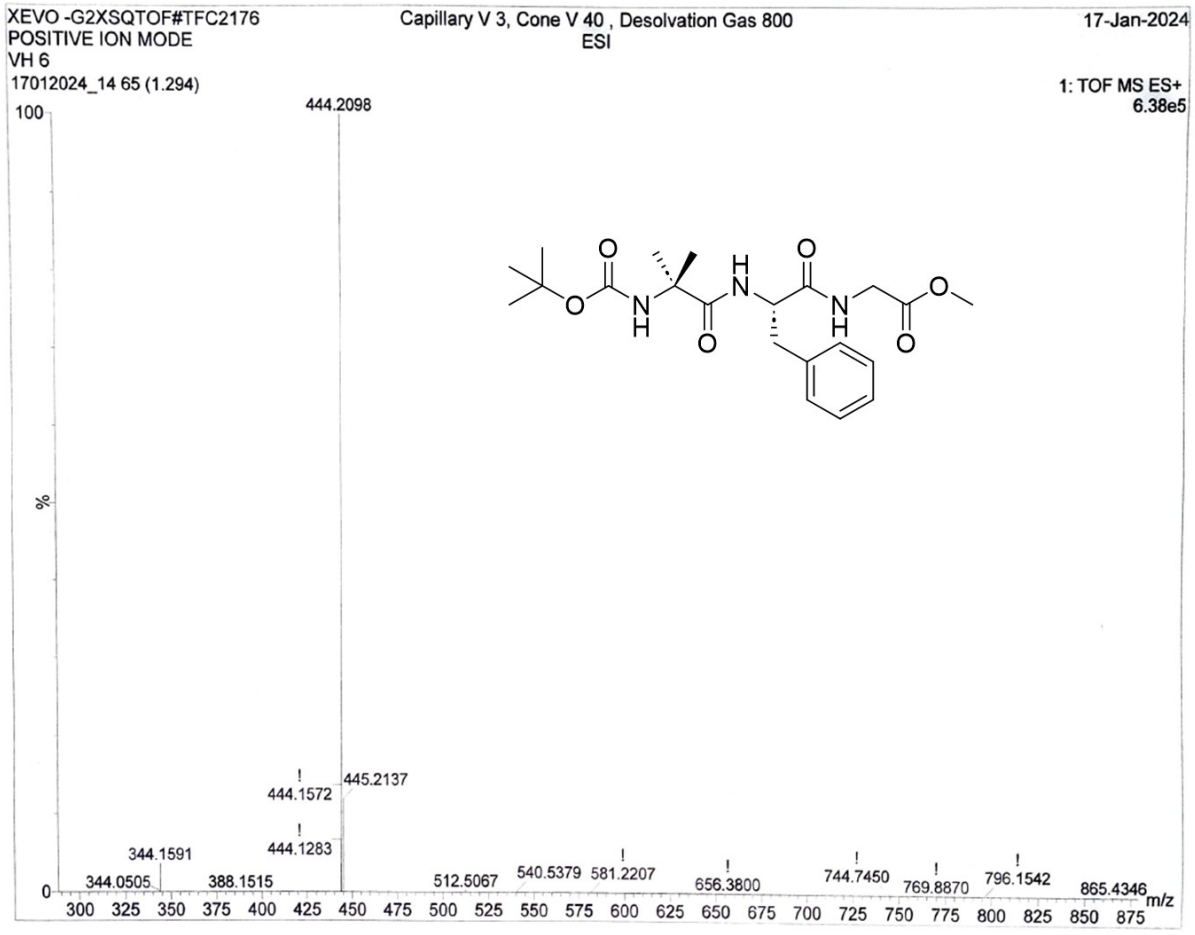


Figure S38: ESI-Mass spectrum of **A6**.

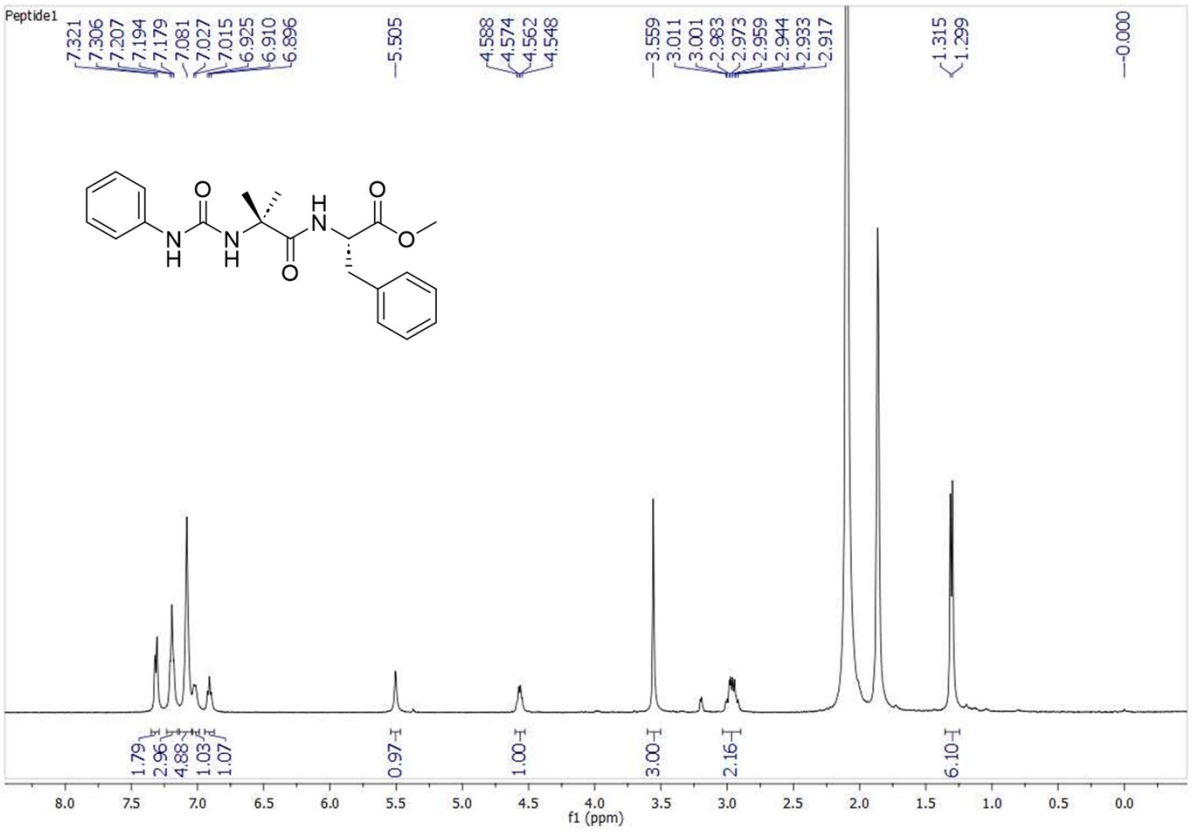


Figure S39: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **1**.

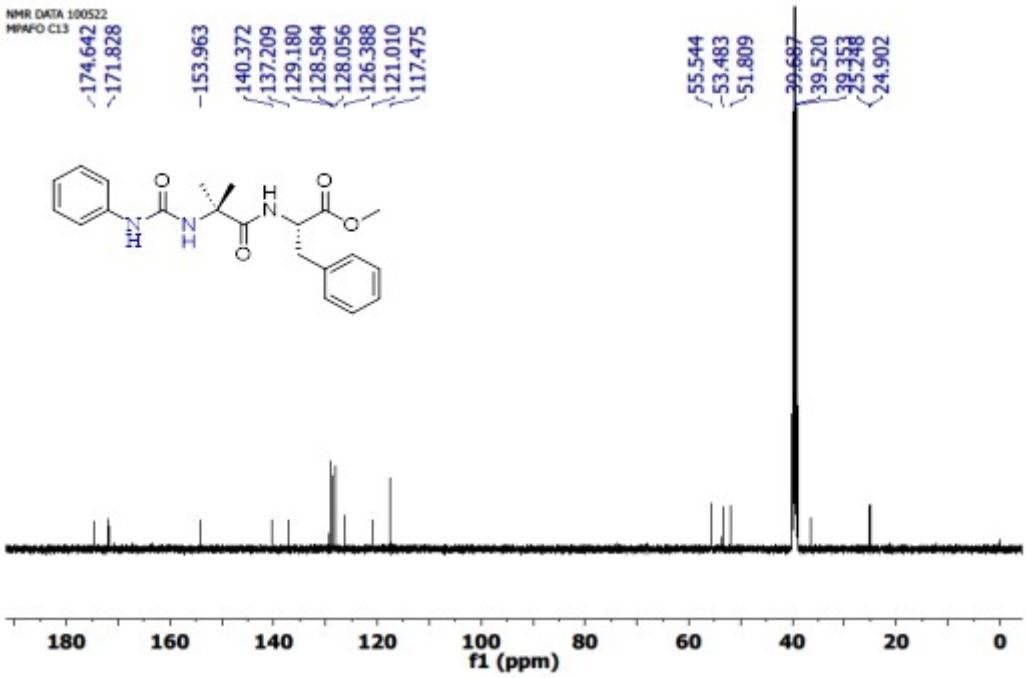


Figure S40: ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of **1**.

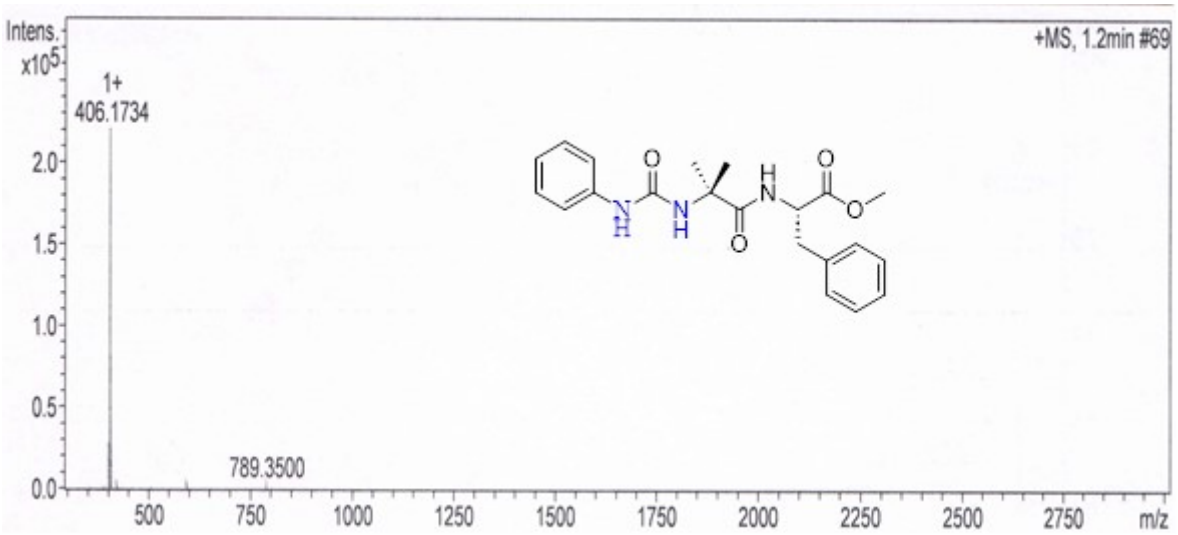


Figure S41: ESI-Mass spectrum of **1**.

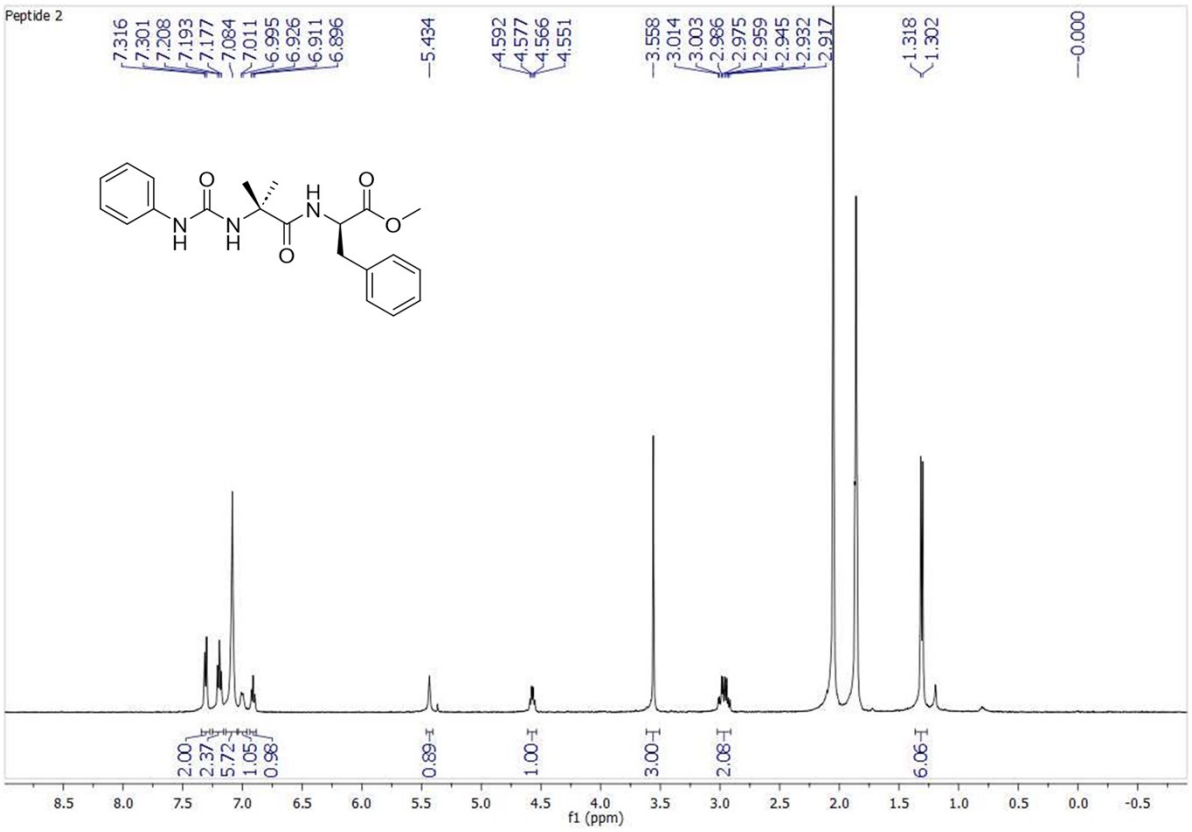


Figure S42: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **2**.

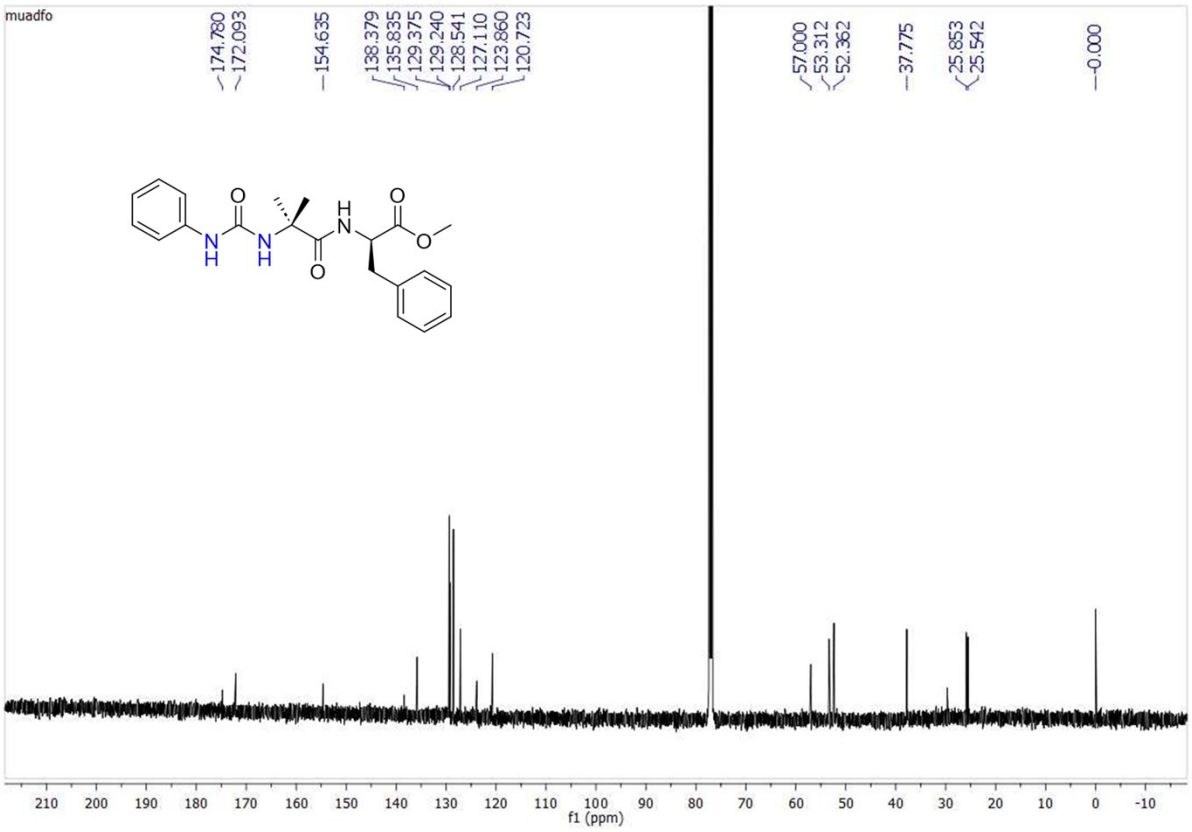


Figure S43: ^{13}C NMR (500 MHz, $CDCl_3$) spectrum of **2**.

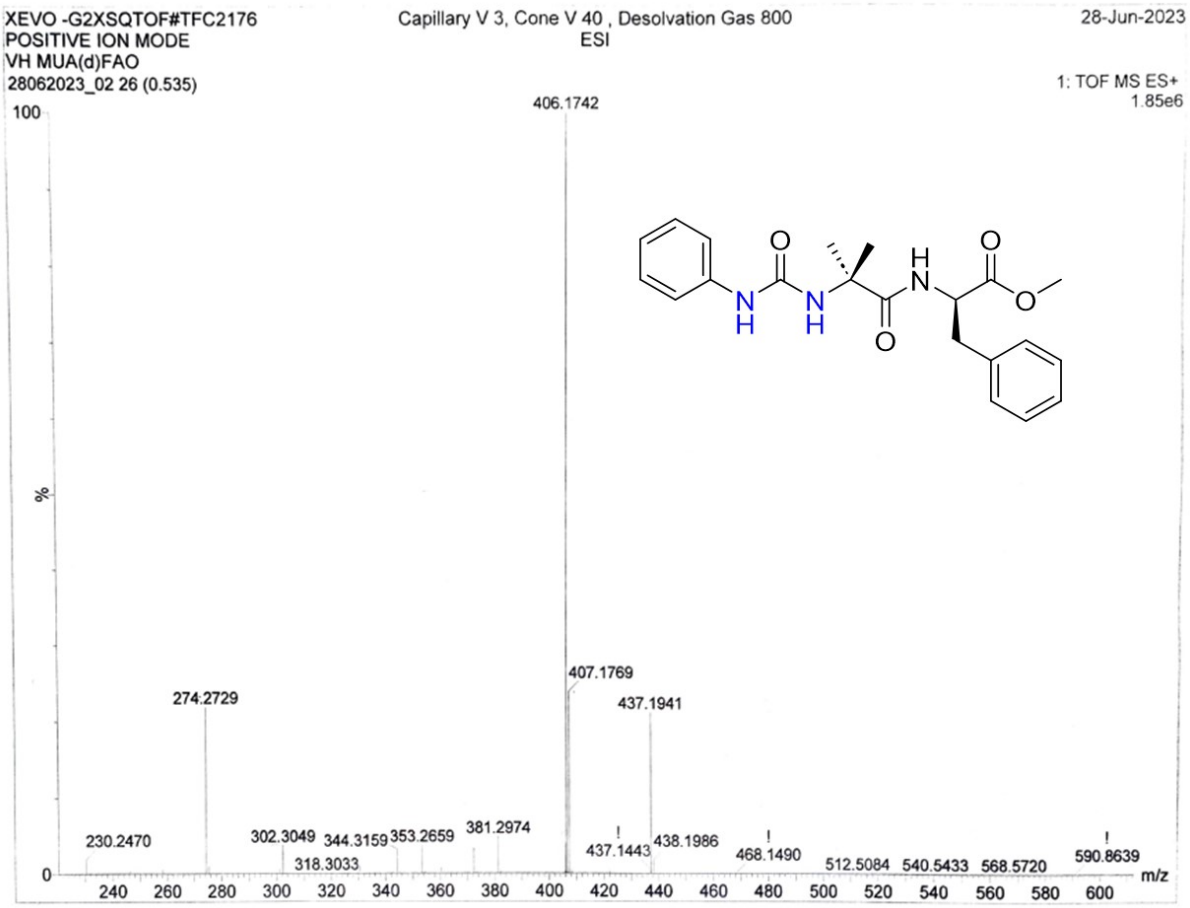


Figure S44: ESI-Mass spectrum of **2**.

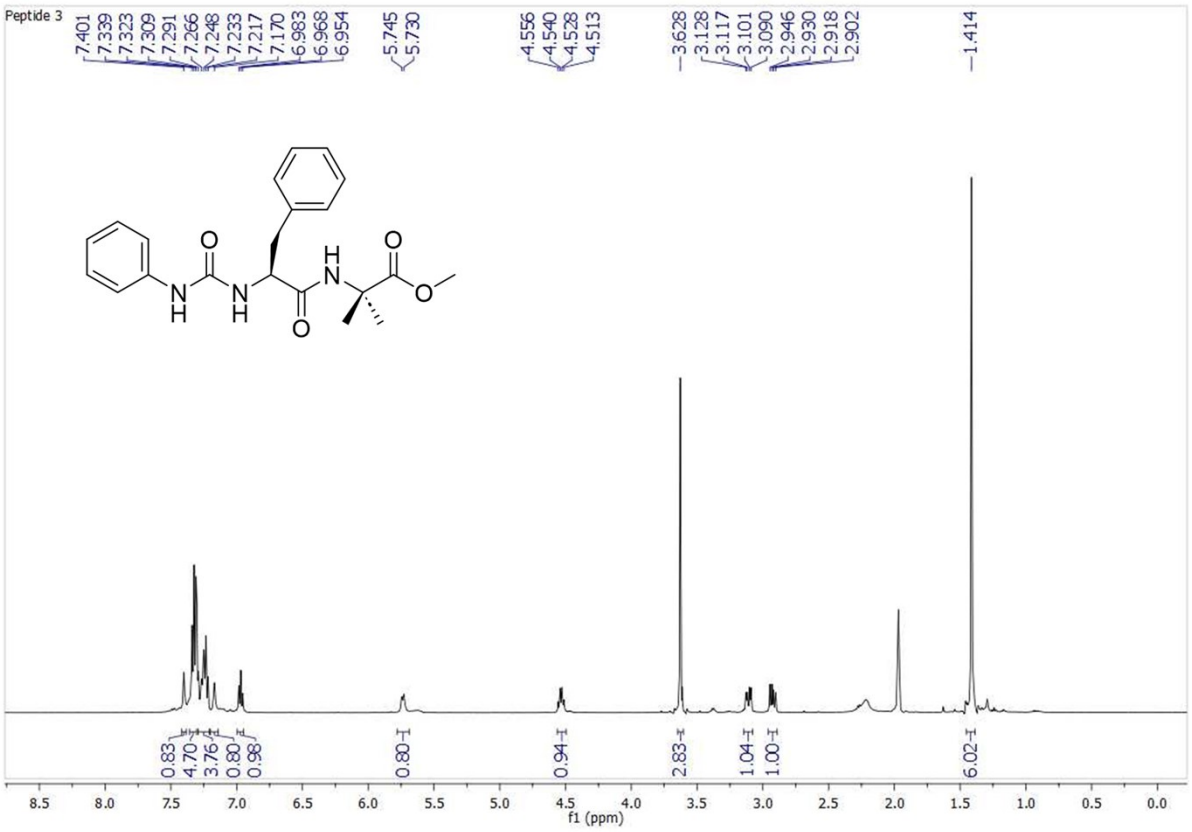


Figure S45: ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3**.

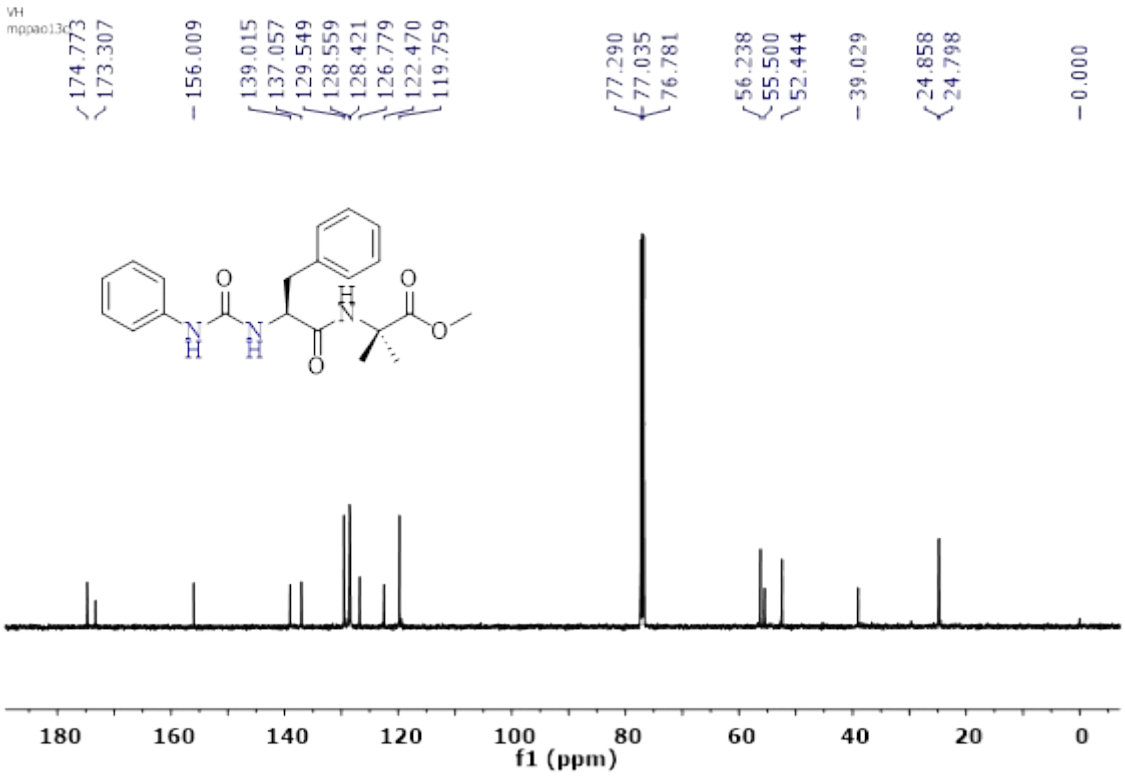


Figure S46: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3**.

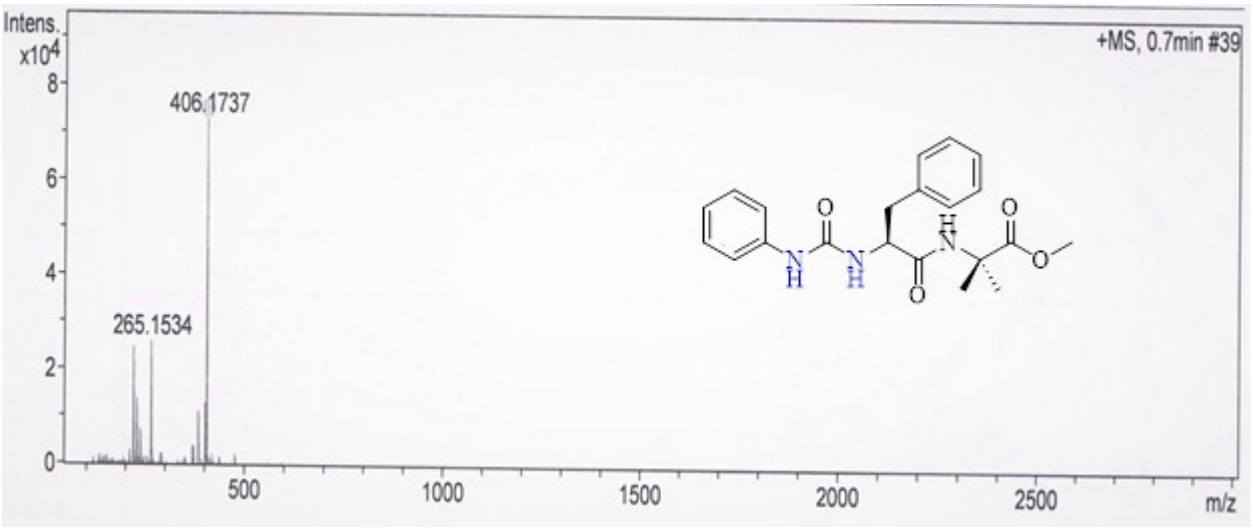


Figure S47: ESI-Mass spectrum of **3**.

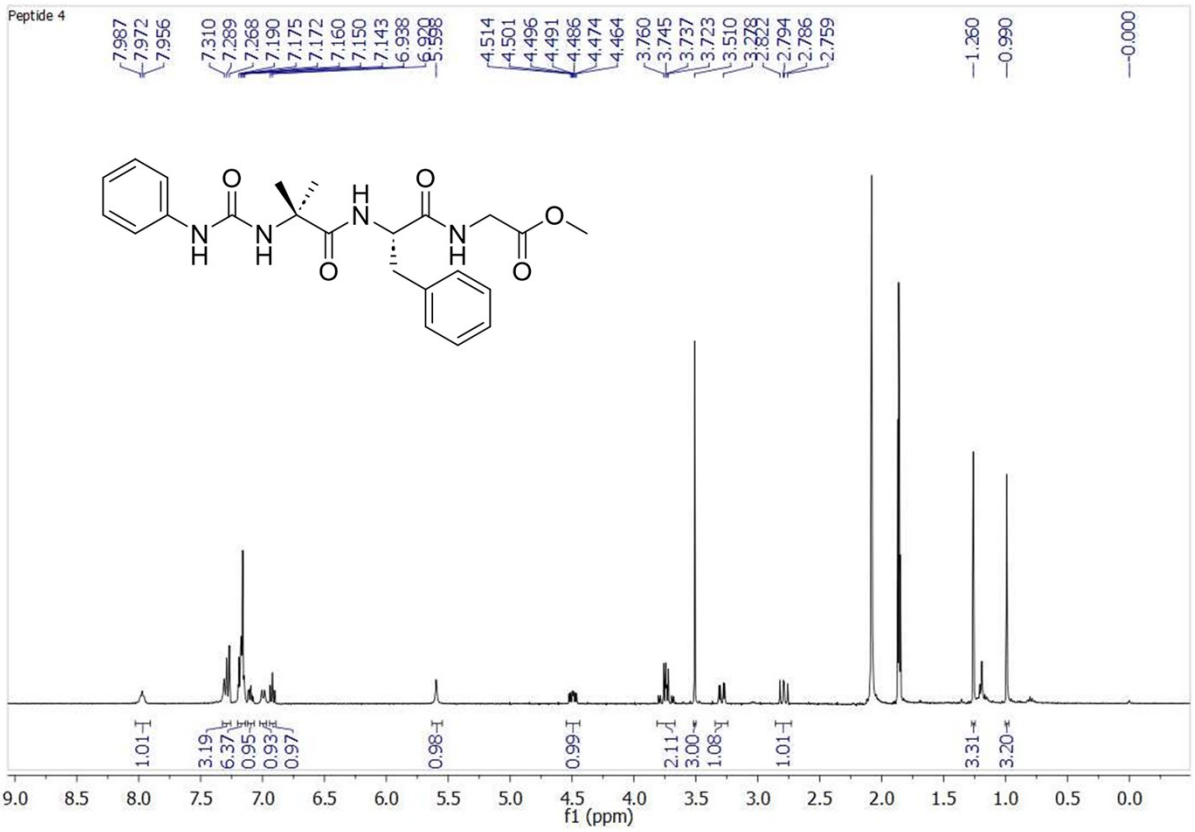


Figure S48: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **4**.

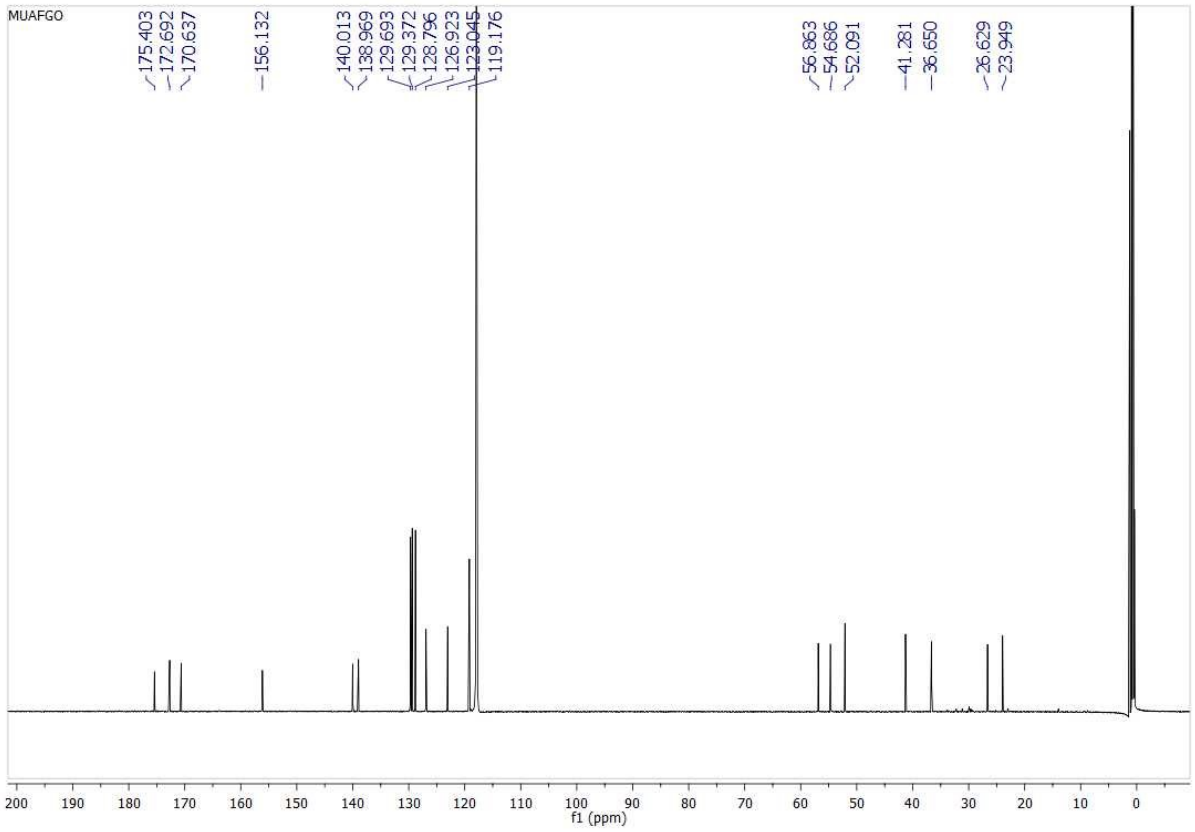


Figure S49: ^{13}C NMR (125 MHz, CD_3CN) spectrum of **4**.

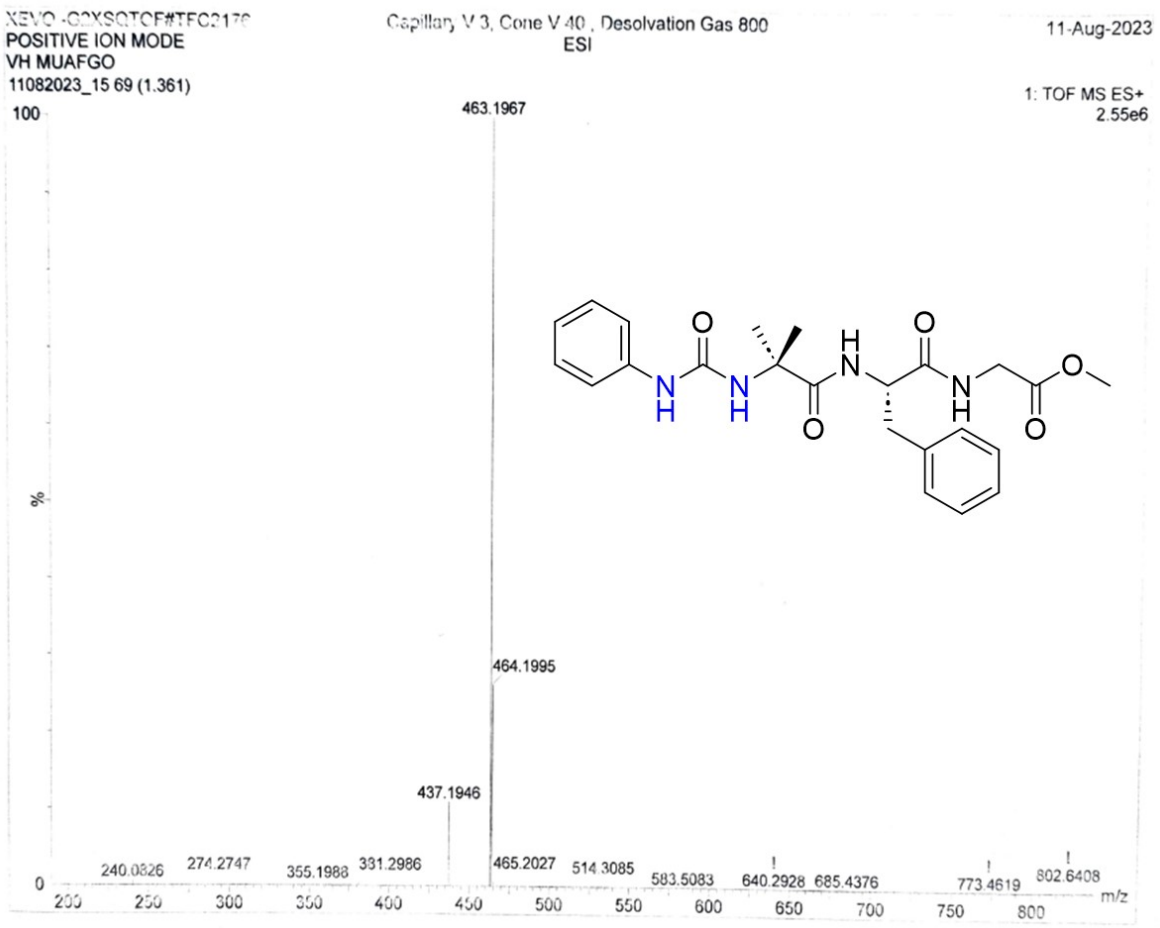


Figure S50: ESI-Mass spectrum of **4**.

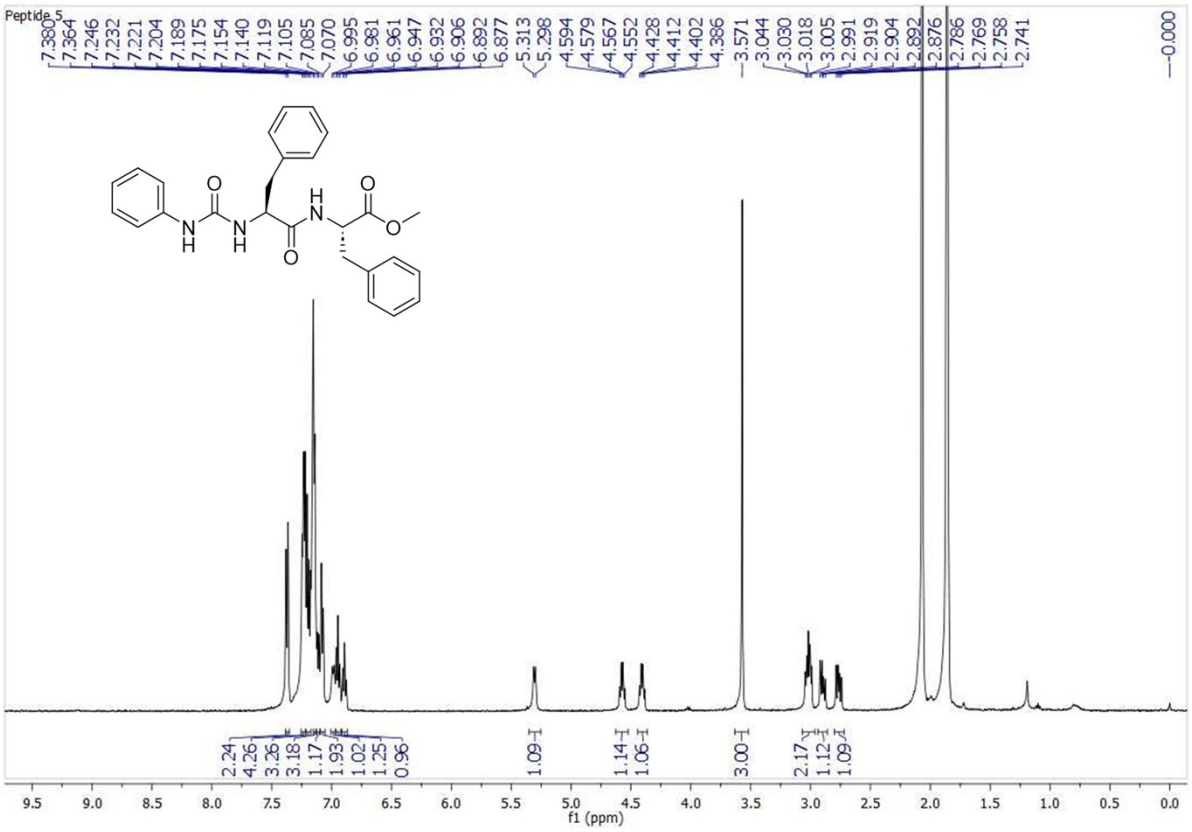


Figure S51: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **5**.

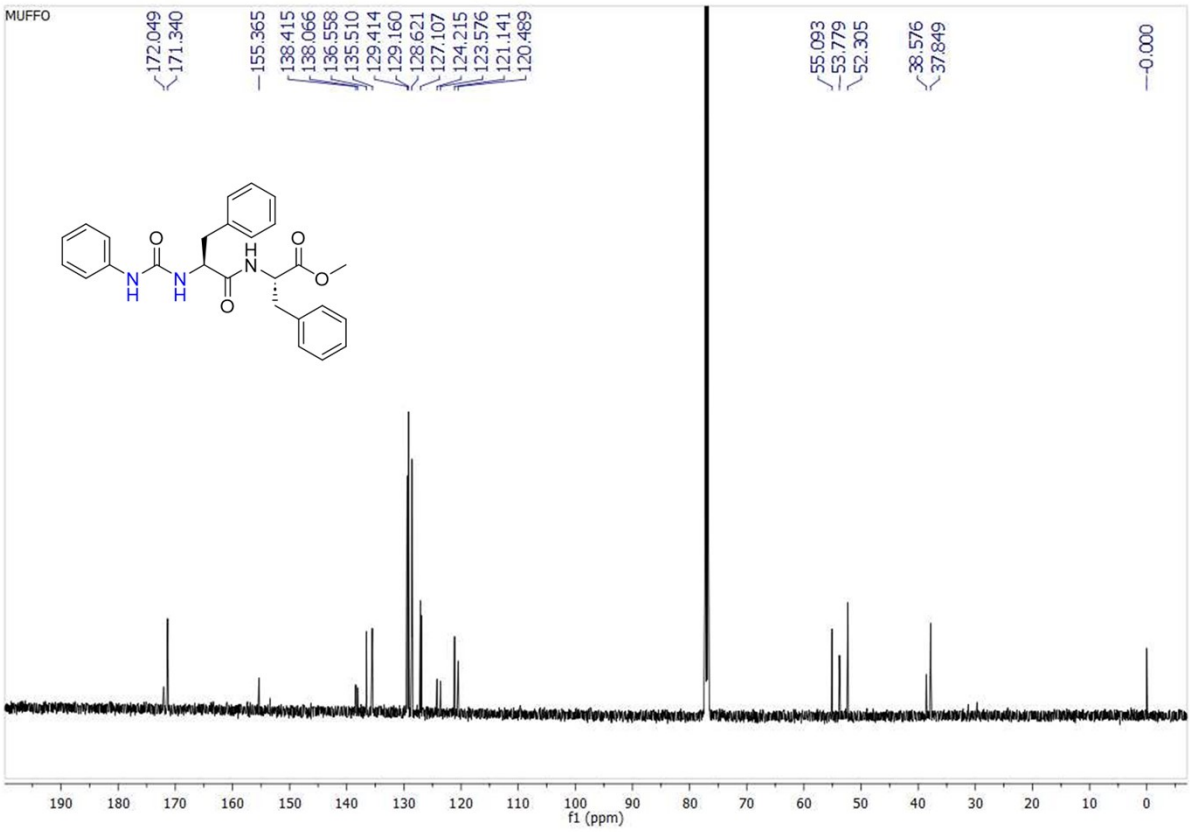


Figure S52: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **5**.

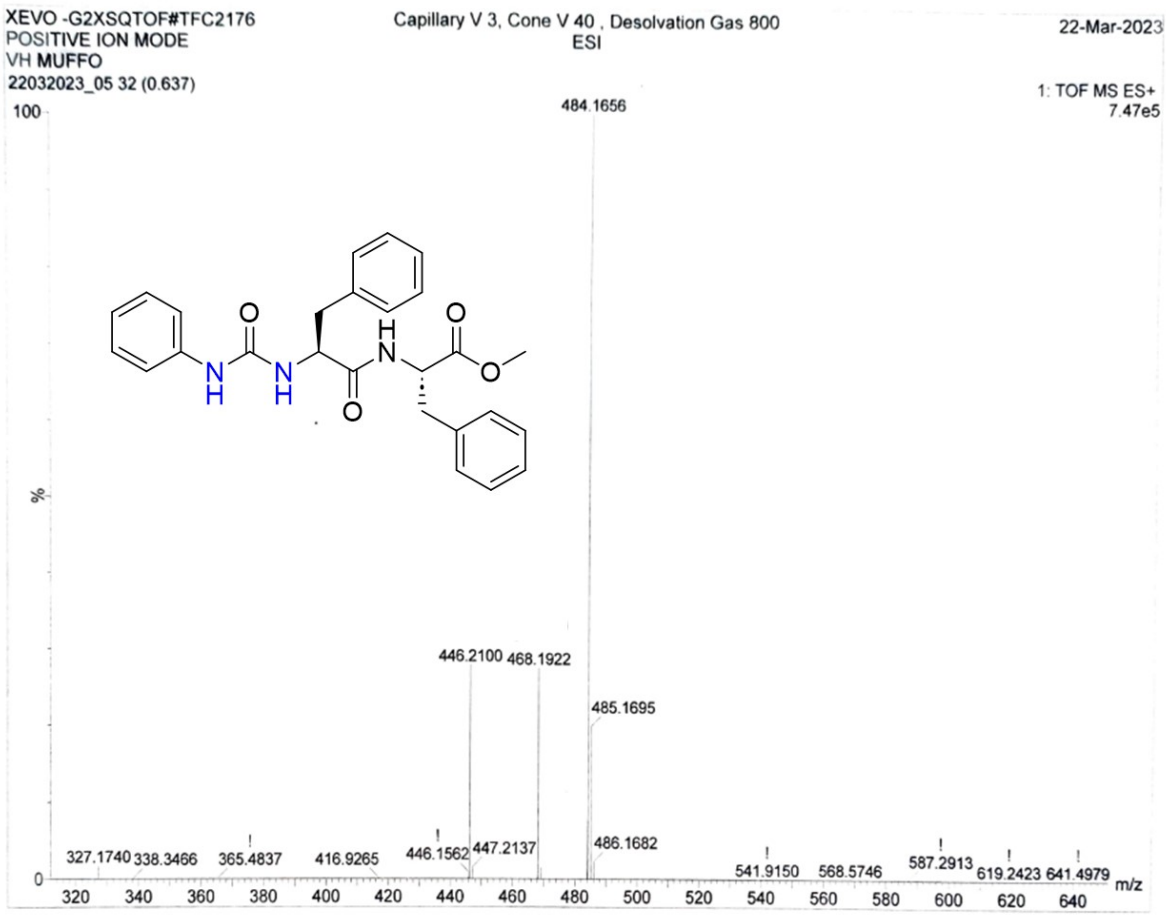


Figure S53: ESI-Mass spectrum of **5**.

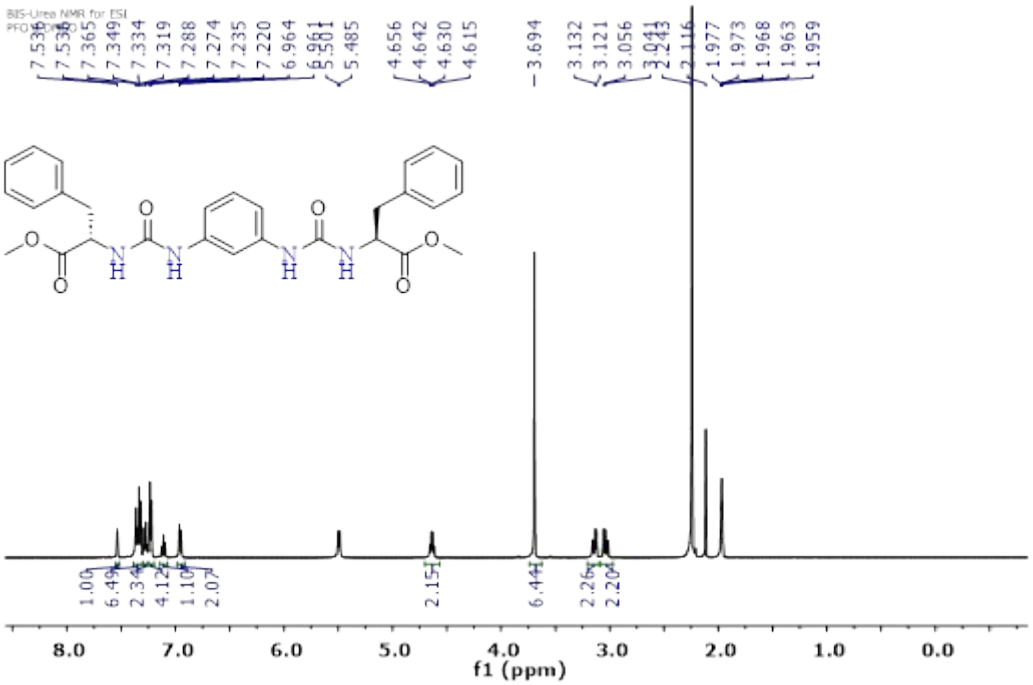


Figure S54: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **6**.

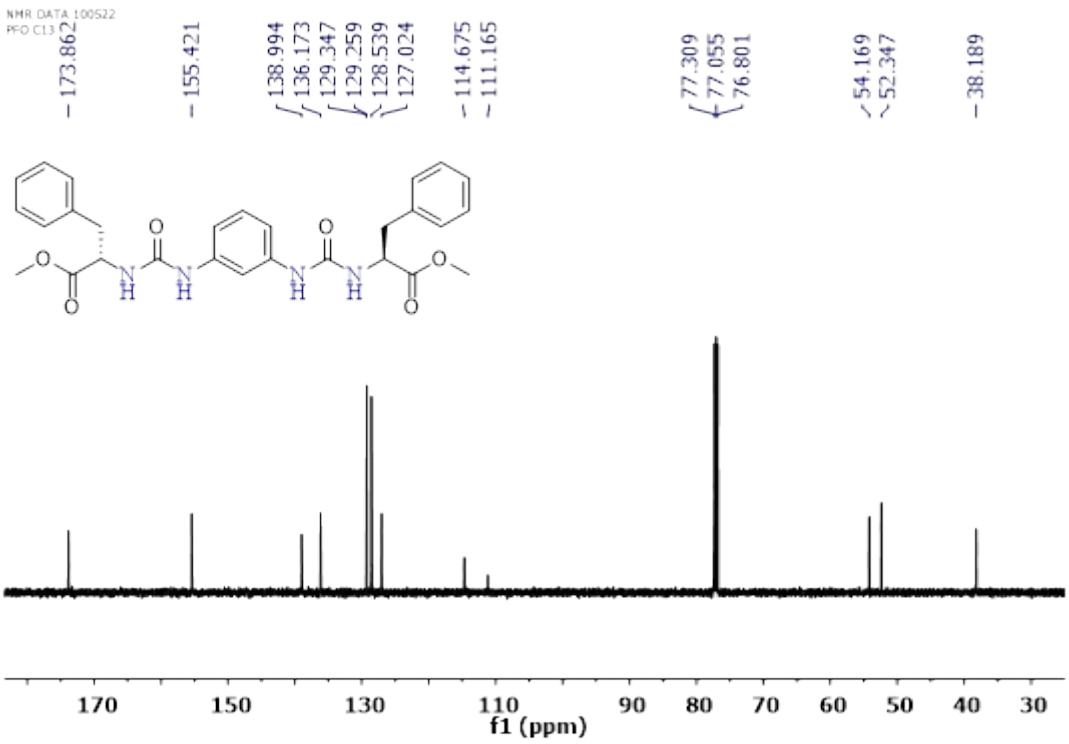


Figure S55: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **6**.

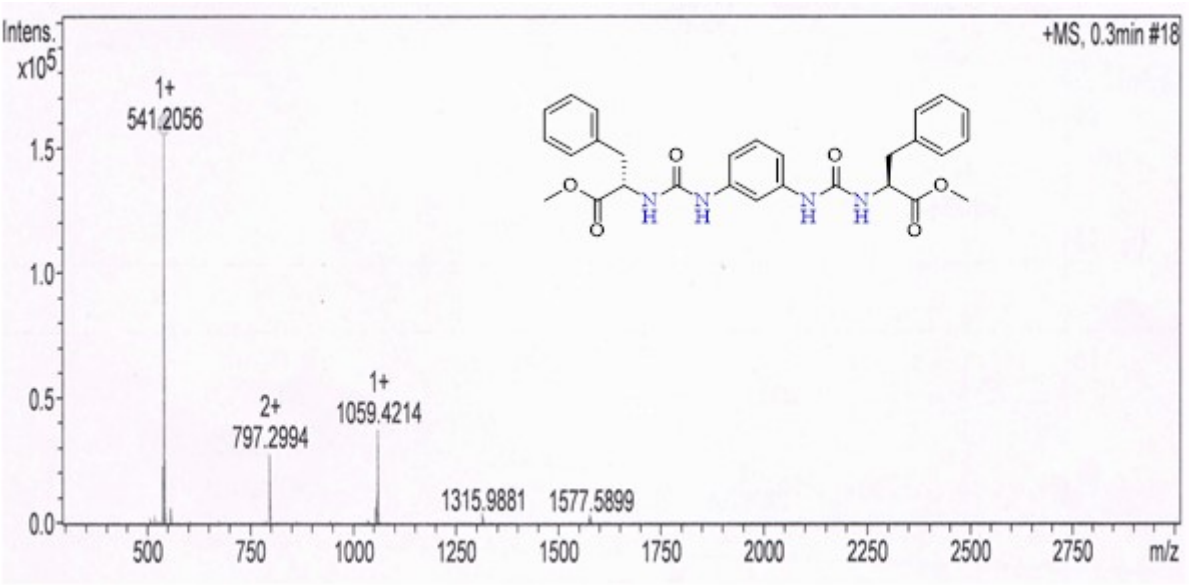


Figure S56: ESI-Mass spectrum of **6**.

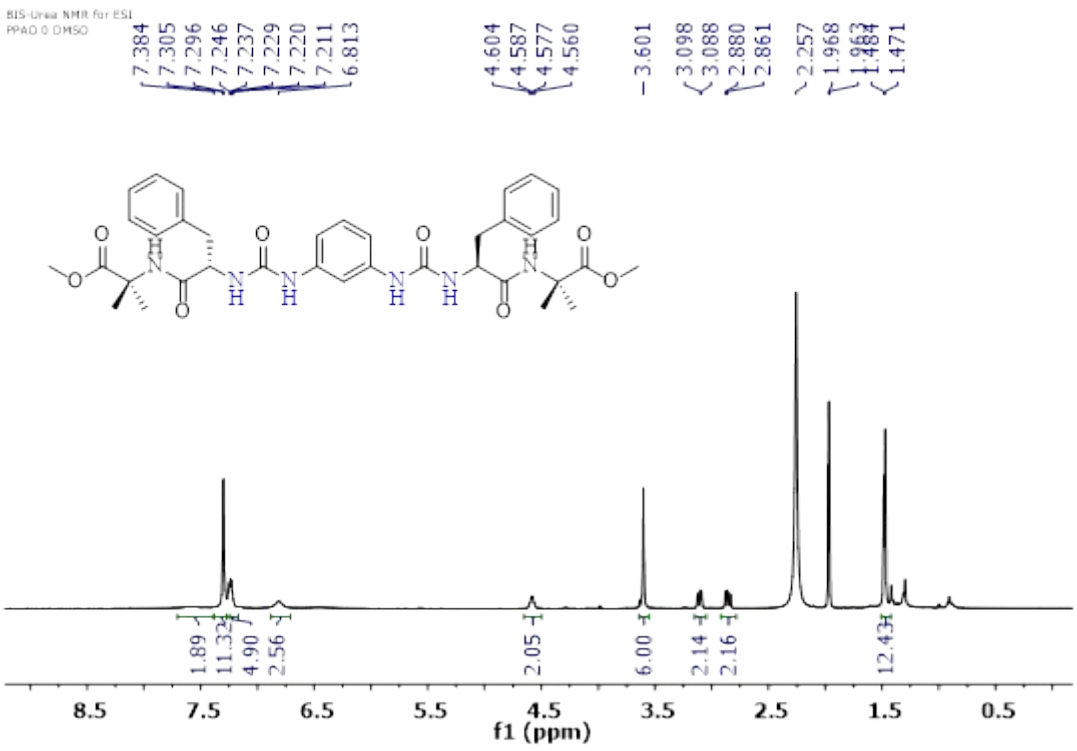


Figure S57: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **7**.

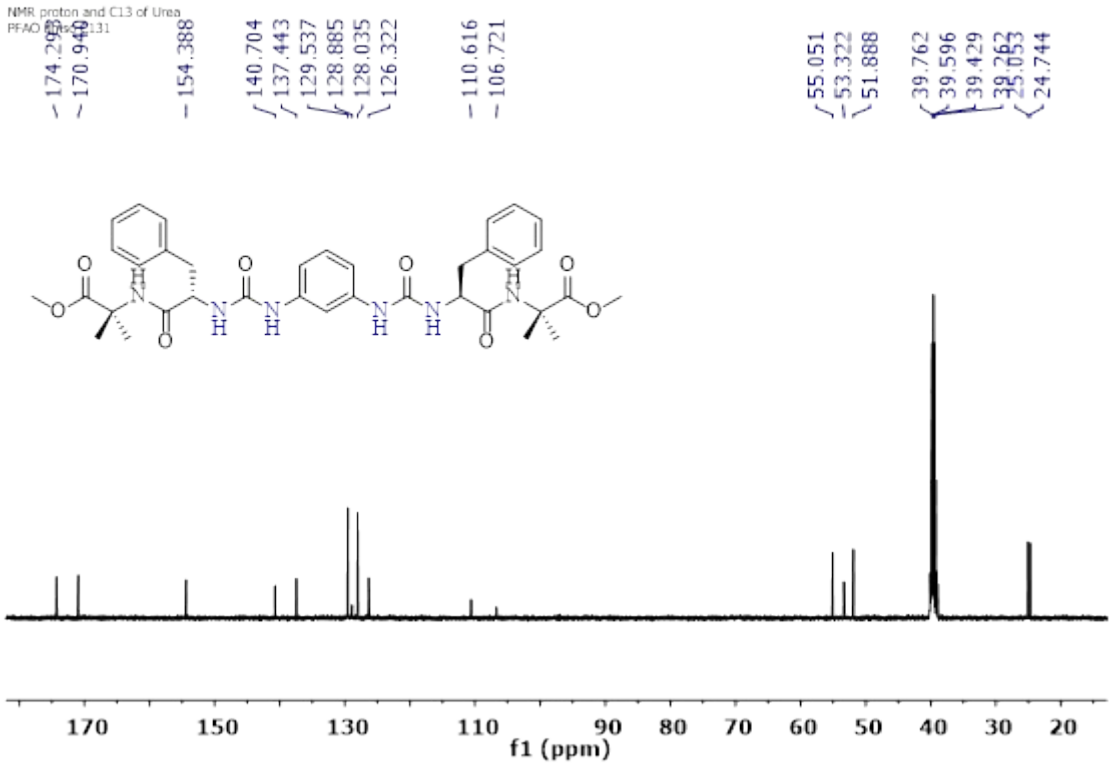


Figure S58: ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of **7**.

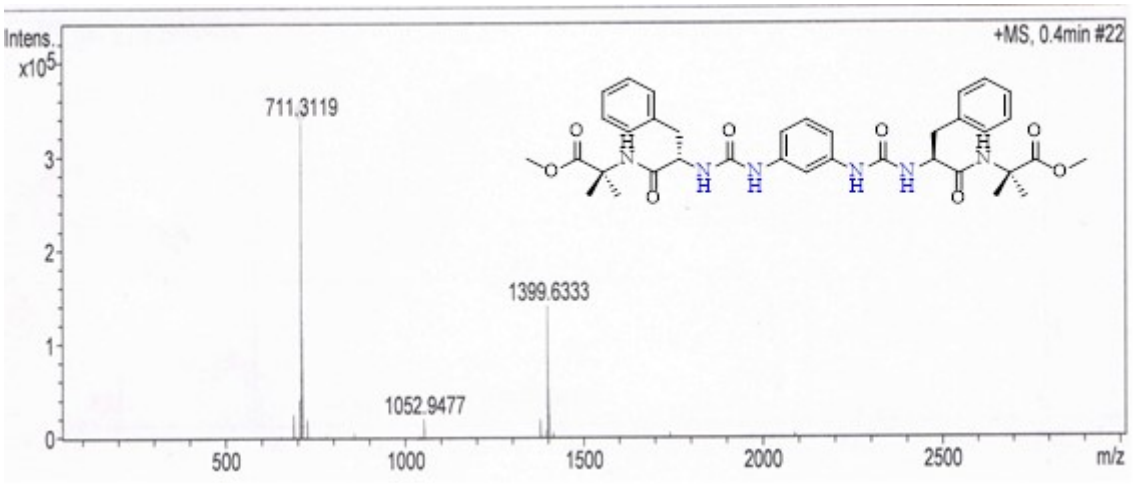


Figure S59: ESI-Mass spectrum of **7**.

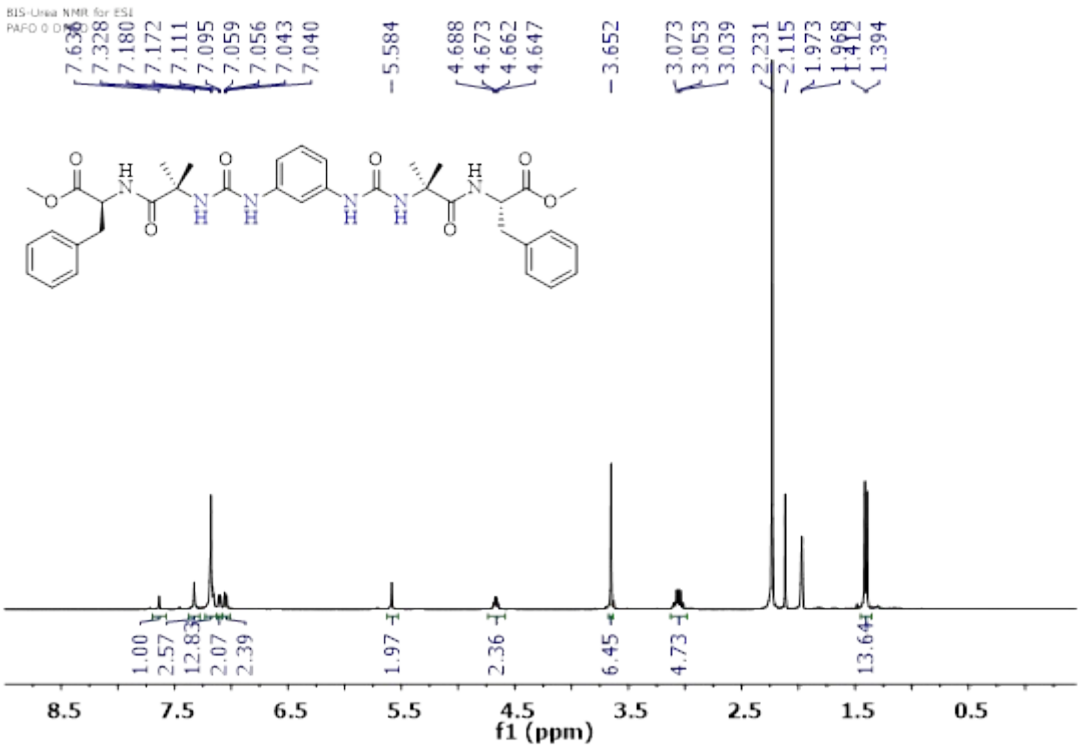


Figure S60: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **8**.

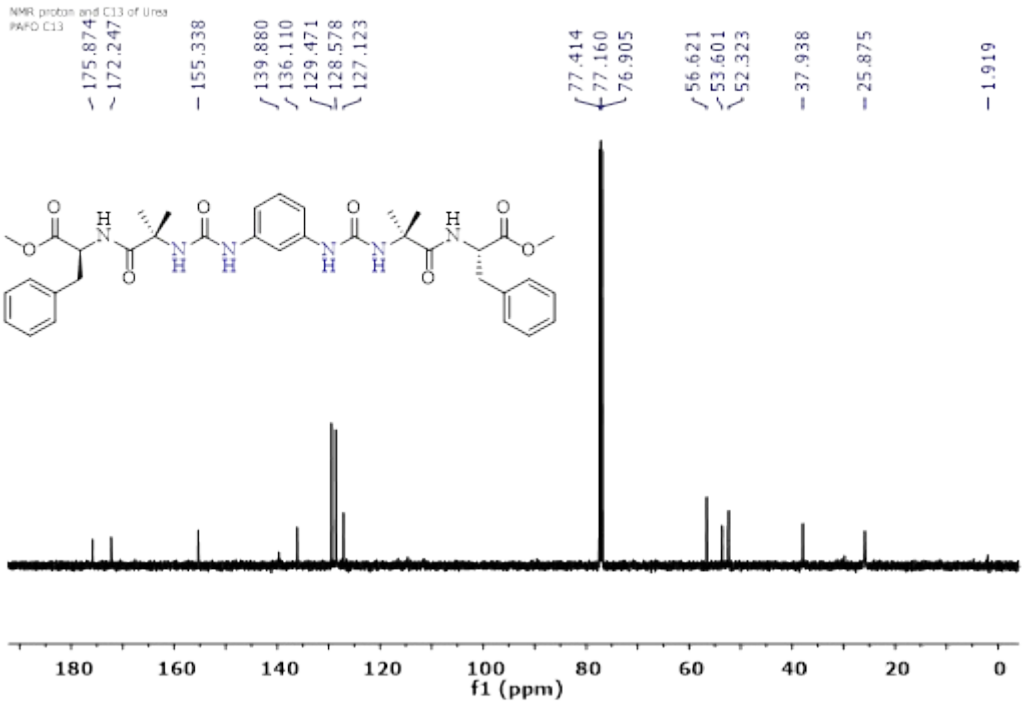


Figure S61: ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **8**.

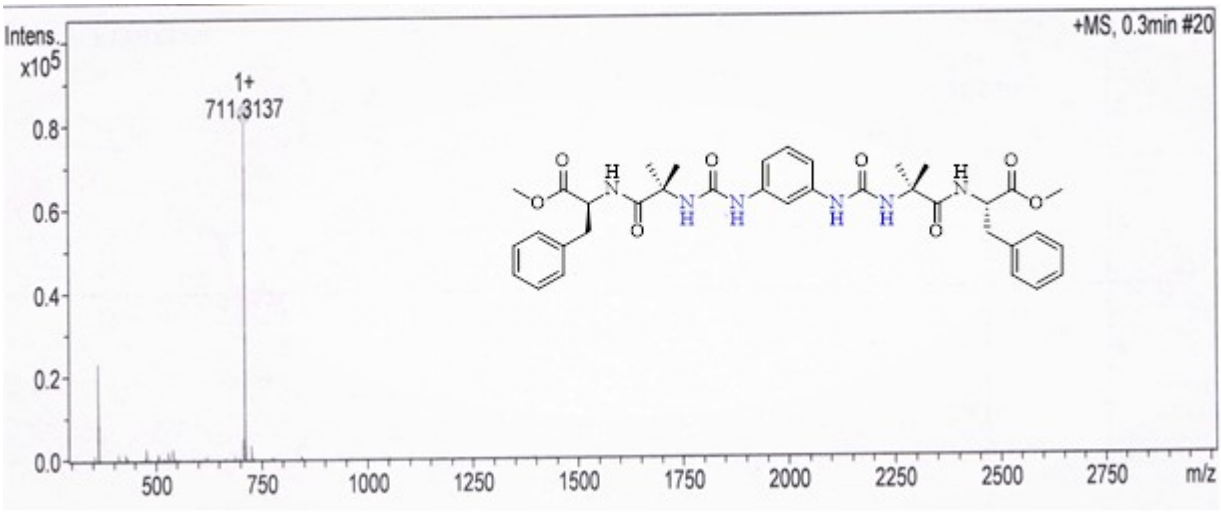


Figure 62: ESI-Mass spectrum of **8**.

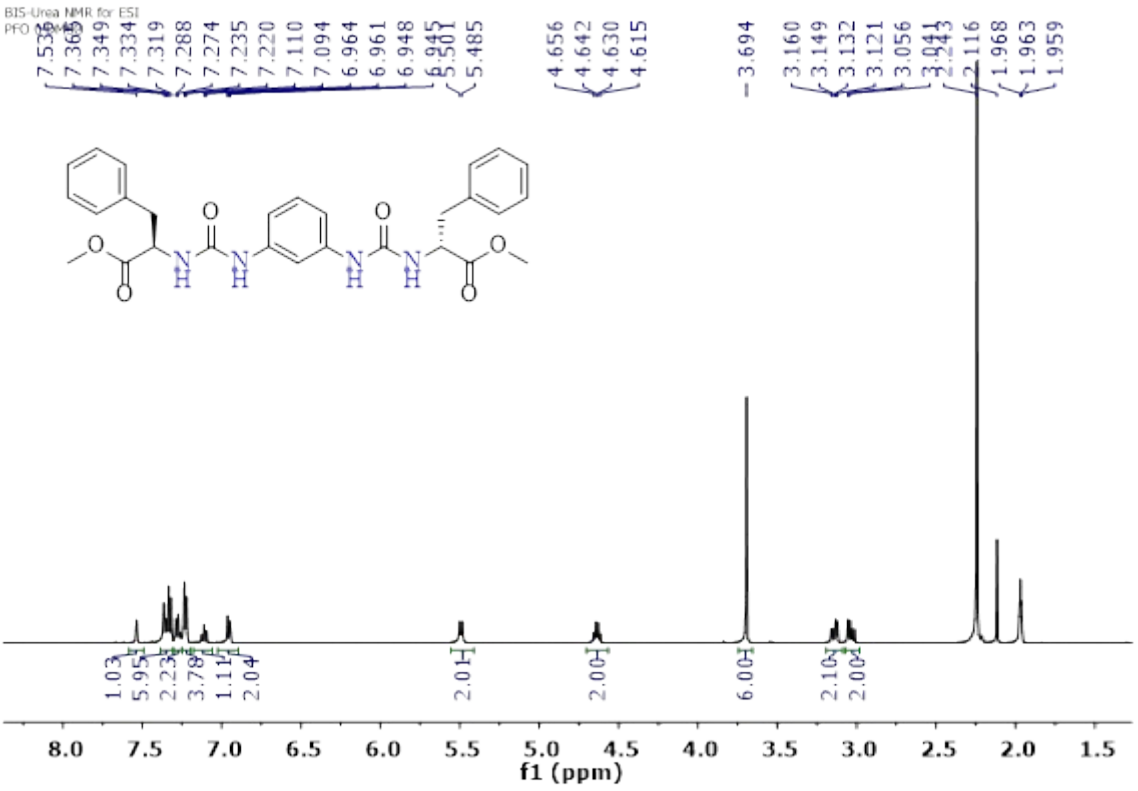


Figure S63: ^{1}H NMR (500 MHz, CD_3CN) spectrum of **9**.

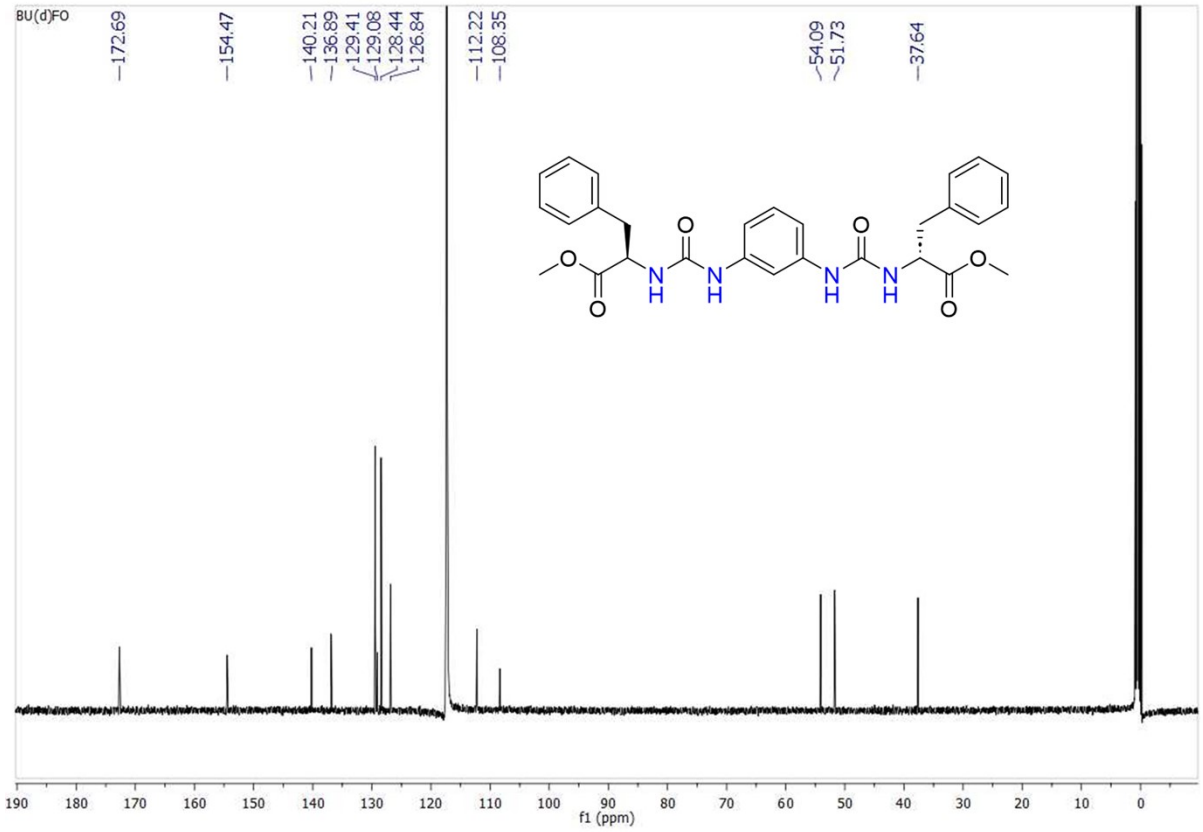


Figure S64: ^{13}C NMR (125 MHz, CD_3CN) spectrum of **9**.

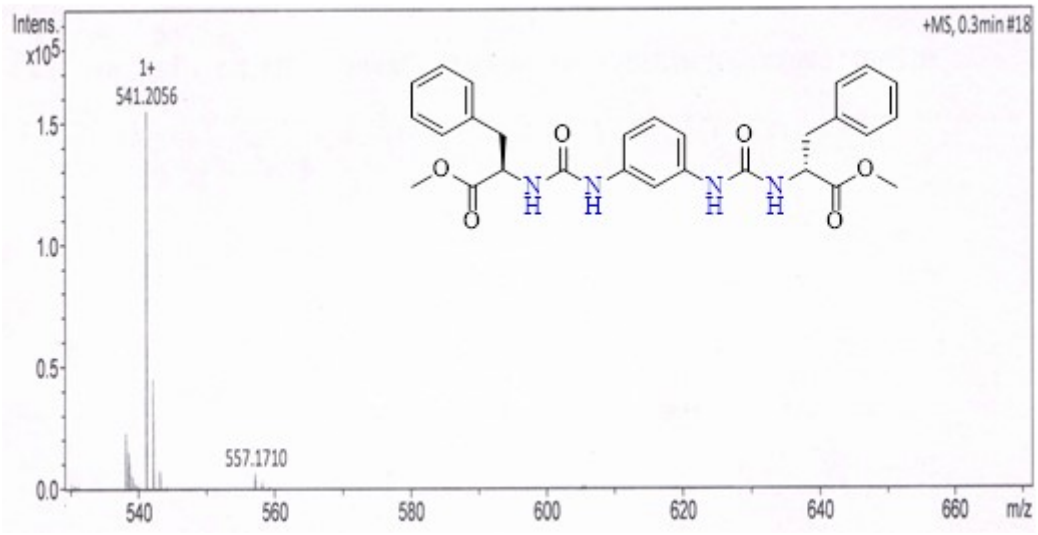


Figure S65: ESI-Mass spectrum of **9**.

Table S1. Crystal data and structure refinement for peptide 1 (CCDC 2354491).

Identification code	AibFurea
Empirical formula	$C_{21}H_{25}N_3O_4$
Formula weight	383.450
Temperature/K	304.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	5.3552(6)
b/Å	11.2241(13)
c/Å	33.850(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2034.6(4)
Z	4
ρ_{calc}g/cm^3	1.252
μ/mm^{-1}	0.088
F(000)	902.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.354 to 56.666
Index ranges	-7 ≤ h ≤ 5, -14 ≤ k ≤ 14, -45 ≤ l ≤ 43
Reflections collected	18534
Independent reflections	5035 [R_{int} = 0.0667, R_{sigma} = 0.0689]
Data/restraints/parameters	5035/0/262
Goodness-of-fit on F^2	1.017
Final R indexes [I>=2σ (I)]	R_1 = 0.0532, wR_2 = 0.1078
Final R indexes [all data]	R_1 = 0.1051, wR_2 = 0.1260
Largest diff. peak/hole / e Å^{-3}	0.17/-0.21
Flack parameter	0.2(10)

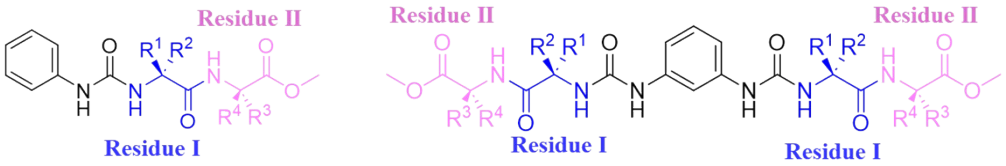
Table S2. Crystal data and structure refinement for peptide 2 (CCDC 2354492).

Identification code	dFAibUrea
Empirical formula	$C_{21}H_{25}N_3O_4$
Formula weight	383.1845
Temperature/K	302.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	5.3547(2)
b/Å	11.2231(4)
c/Å	33.8405(11)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2033.69(12)
Z	4
ρ_{calc}g/cm^3	1.252
μ/mm^{-1}	0.088
F(000)	816.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.356 to 56.51
Index ranges	-7 ≤ h ≤ 7, -13 ≤ k ≤ 14, -45 ≤ l ≤ 43
Reflections collected	19171
Independent reflections	5027 [R_{int} = 0.0630, R_{sigma} = 0.0691]
Data/restraints/parameters	5027/0/256
Goodness-of-fit on F^2	1.000
Final R indexes [I>=2σ (I)]	R_1 = 0.0508, wR_2 = 0.0994
Final R indexes [all data]	R_1 = 0.1112, wR_2 = 0.1207
Largest diff. peak/hole / e Å^{-3}	0.17/-0.18
Flack parameter	0.7(9)

Table S3. Crystal data and structure refinement for peptide 5 (CCDC 2354493).

Identification code	FFUrea
Empirical formula	$C_{26}H_{27}N_3O_4$
Formula weight	445.51
Temperature/K	150(2)
Crystal system	hexagonal
Space group	$P6_5$
a/Å	12.7958(3)
b/Å	12.7958(3)
c/Å	26.2968(12)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	3728.8(2)
Z	6
ρ_{calc}g/cm^3	1.190
μ/mm^{-1}	0.081
F(000)	1416.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.988 to 52.768
Index ranges	-16 ≤ h ≤ 16, -16 ≤ k ≤ 16, -32 ≤ l ≤ 32
Reflections collected	166845
Independent reflections	5074 [R_{int} = 0.0811, R_{sigma} = 0.0216]
Data/restraints/parameters	5074/1/299
Goodness-of-fit on F^2	1.057
Final R indexes [I>=2σ (I)]	R_1 = 0.0331, wR_2 = 0.0791
Final R indexes [all data]	R_1 = 0.0385, wR_2 = 0.0830
Largest diff. peak/hole / e Å^{-3}	0.23/-0.15
Flack parameter	0.1(3)

Table S4. Table showing CSI values of peptide 1, 2 and 8



Compounds	δ (obs)		Reference δ	Residue II Δ δ	Chemical Shift Index
	Residue I $C_\alpha H$	Residue II $C_\alpha H$			
Peptide 1	X*	4.57	4.66 ± 0.10	0.09	0
Peptide 2	X	4.57	4.66 ± 0.10	0.09	0
Peptide 8	X	4.67	4.66 ± 0.10	0.01	0

* 'X' denotes residue doesn't contain $C_\alpha H$.

Table S5. H-bonding distances (Å) and angles (°) present in peptide 1

Donor (D)	H Label (H)	Acceptor (A)	DH•••A (Å)	D•••A (Å)	<D•••H•••A angle (°)
N1	H1	O1	2.299	3.142	157.34
N2	H2	O3	2.159	2.825	134.01
N3	H3	O4	2.343	2.675	103.92