Supporting Information

New archetypes in self-assembled Phe-Phe motif induced nanostructures from nucleoside conjugated-diphenylalanines

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CF= Carboxyfluorescein

Peptides:

1 = Boc-Phe-Phe-OH, **2** = Boc-Phe-Phe-Propyne, **4** = Boc-Leu-Leu-Propyne, **7** = Boc-Phe-Phe-*tz*-A$^{N(Boc)_2}$, **8** = Boc-Phe-Phe-*tz*-A^{NH_2}, **9** = H-Phe-Phe-*tz*-A^{NH_2}, **10** = Boc-Leu-Leu-*tz*-A$^{N(Boc)_2}$, **12 =** Boc-Phe-Phe-*am*-A$^{N(Boc)_2}$, **15** = Boc-Phe-Phe-*tz*-U, **16** = Boc-Phe-Phe-*tz*-T; **S7** = Fmoc-Phe-Phe-*tz*-A$^{N(Boc)_2}$

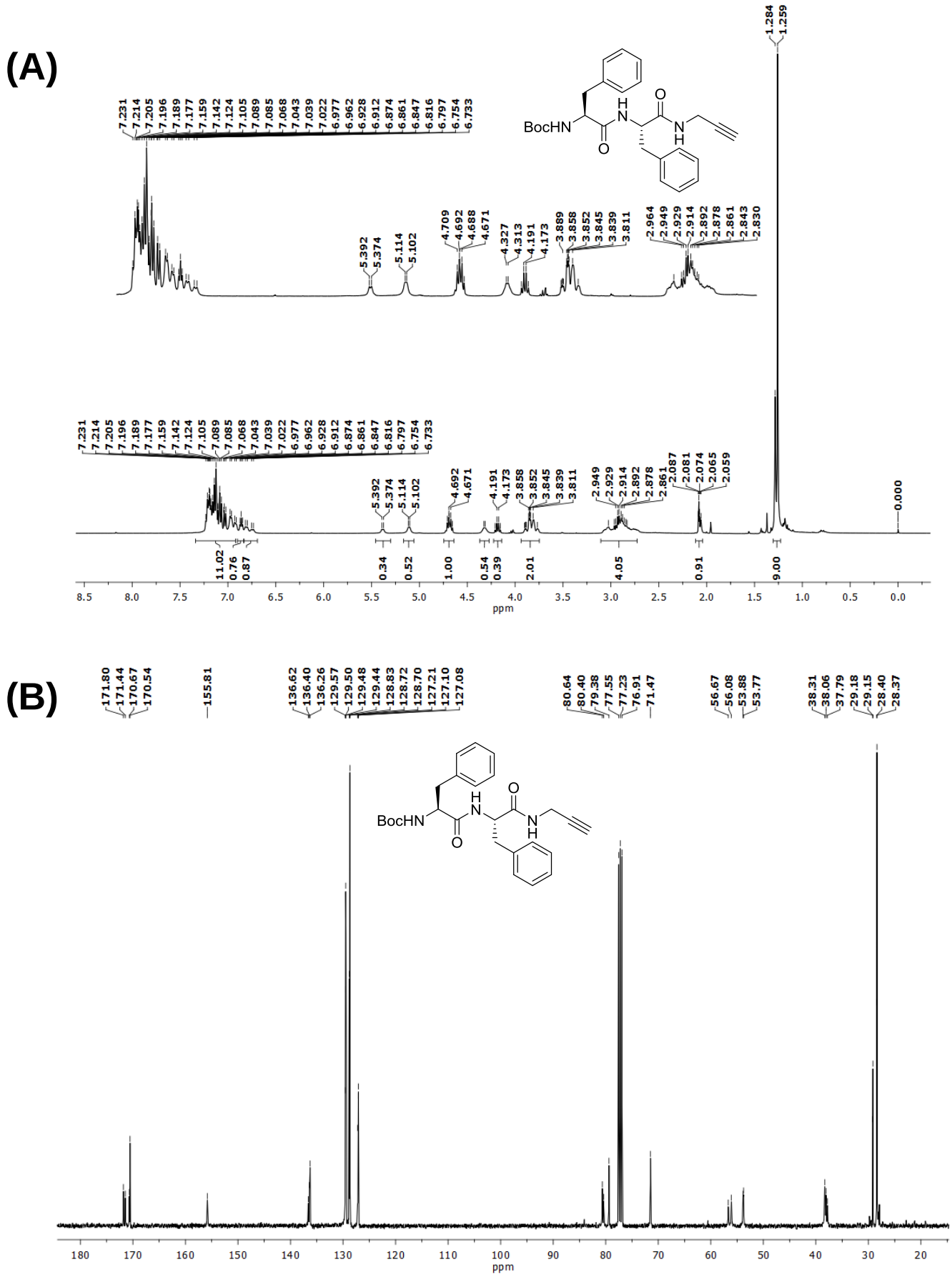


Figure S1: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of peptide **2** (Boc-Phe-Phe-Propyne).

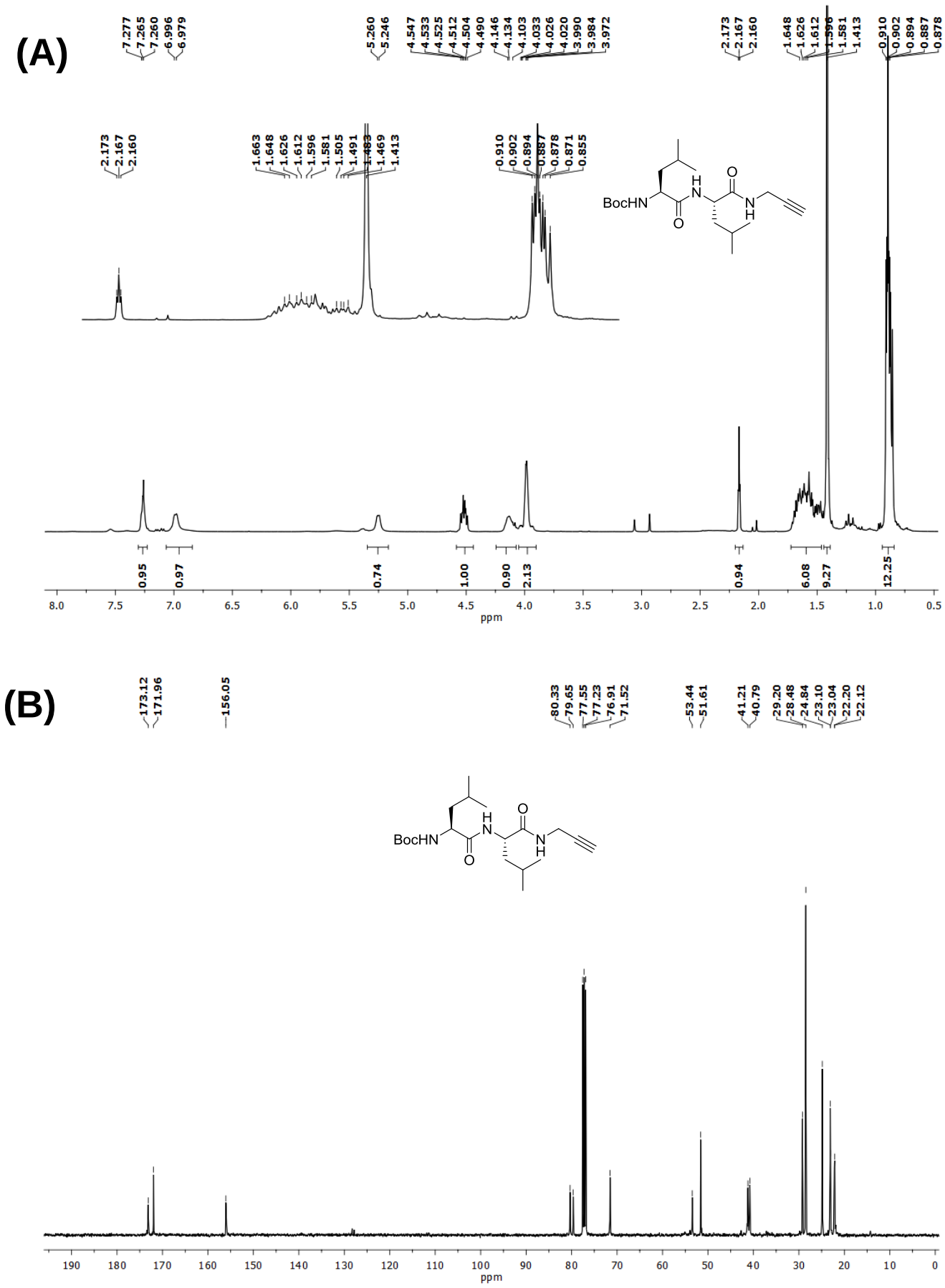


Figure S2: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **4** (Boc-Leu-Leu-Propyne).

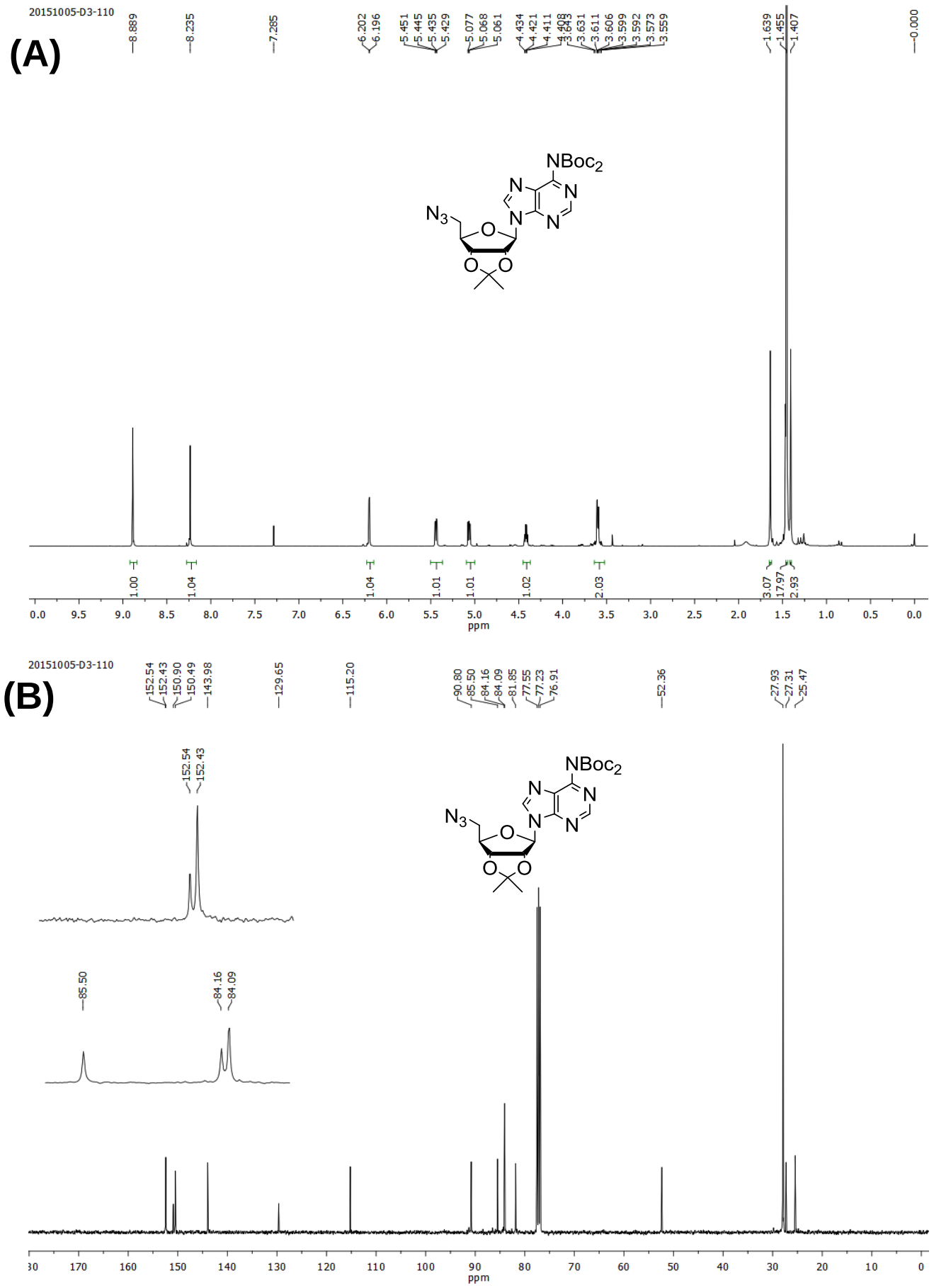


Figure S3: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of **5**.

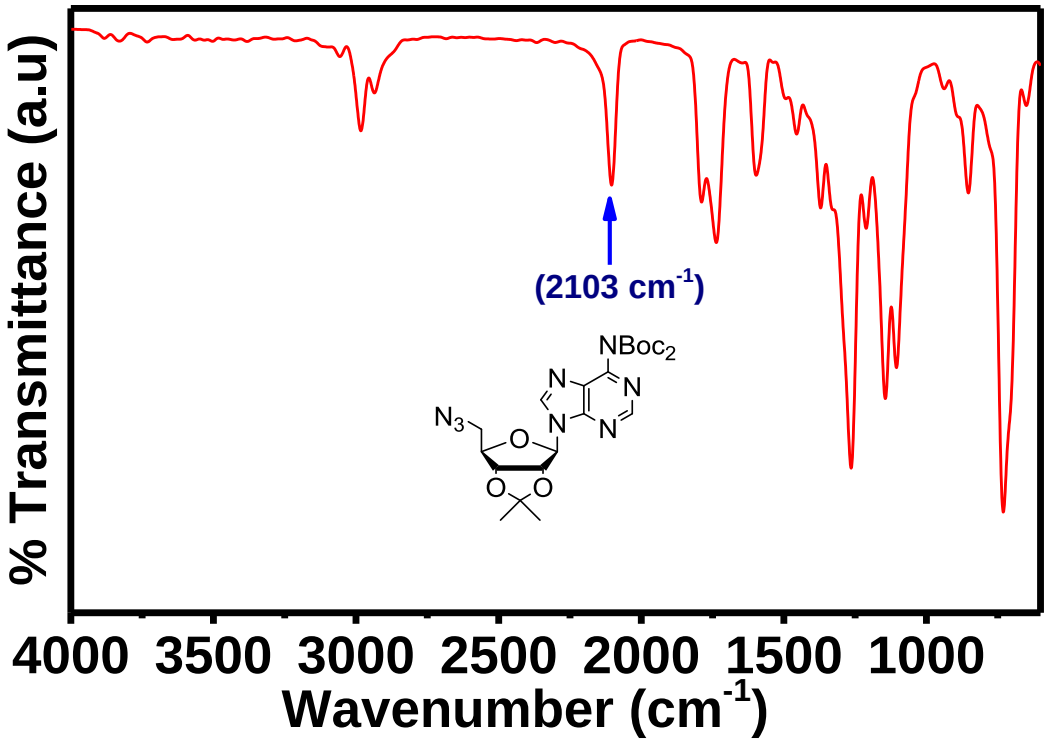


Figure S4: ATR-IR spectrum of **5**.

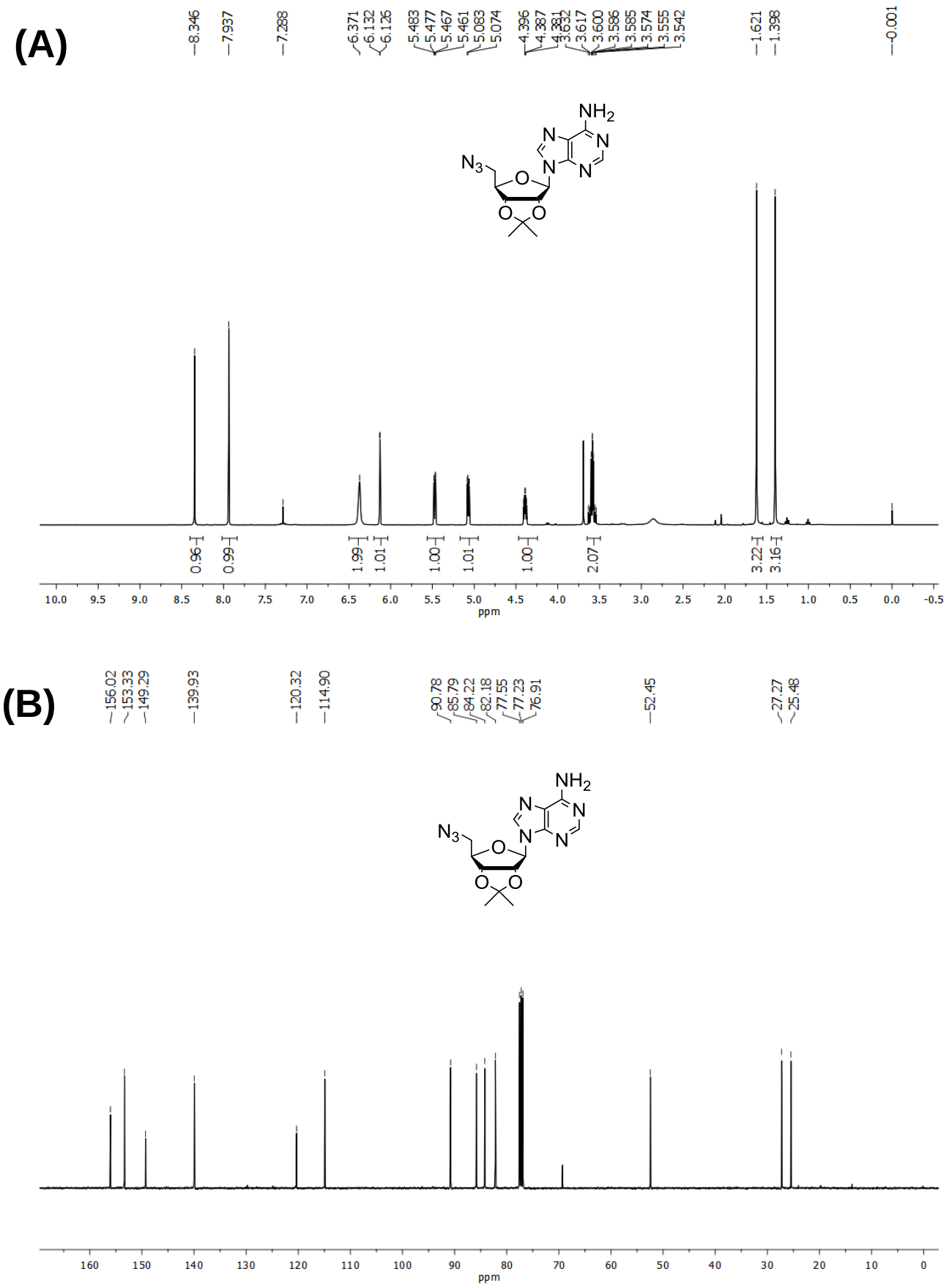


Figure S5: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR of spectra of **6**.

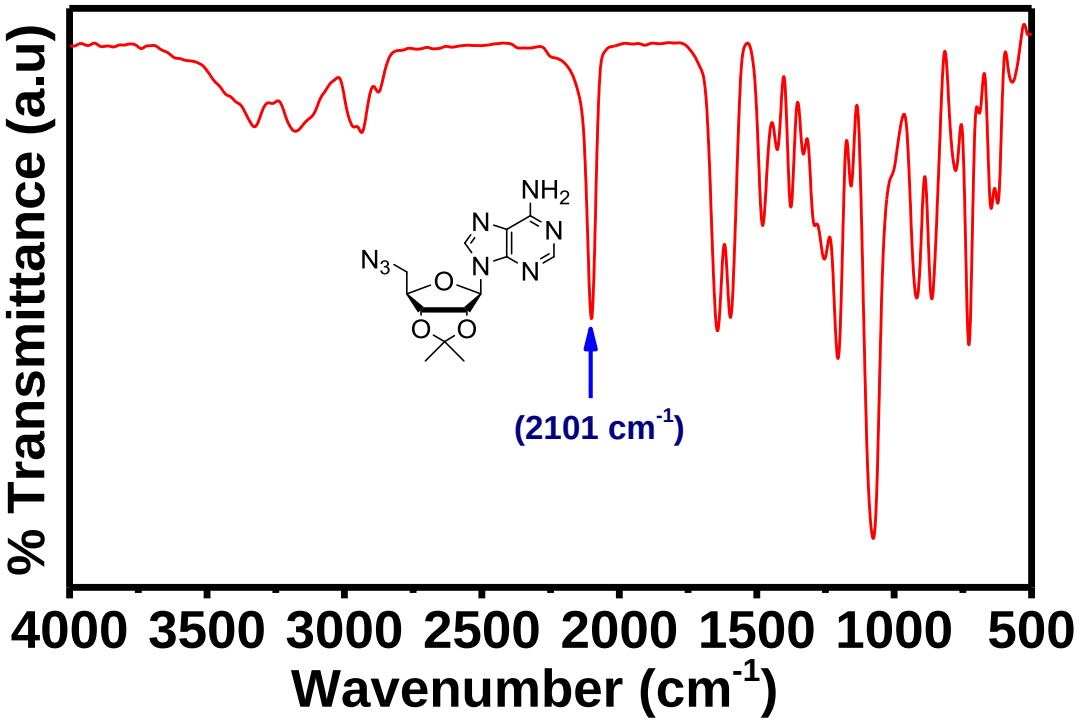


Figure S6: ATR-IR spectrum of crude **6**.

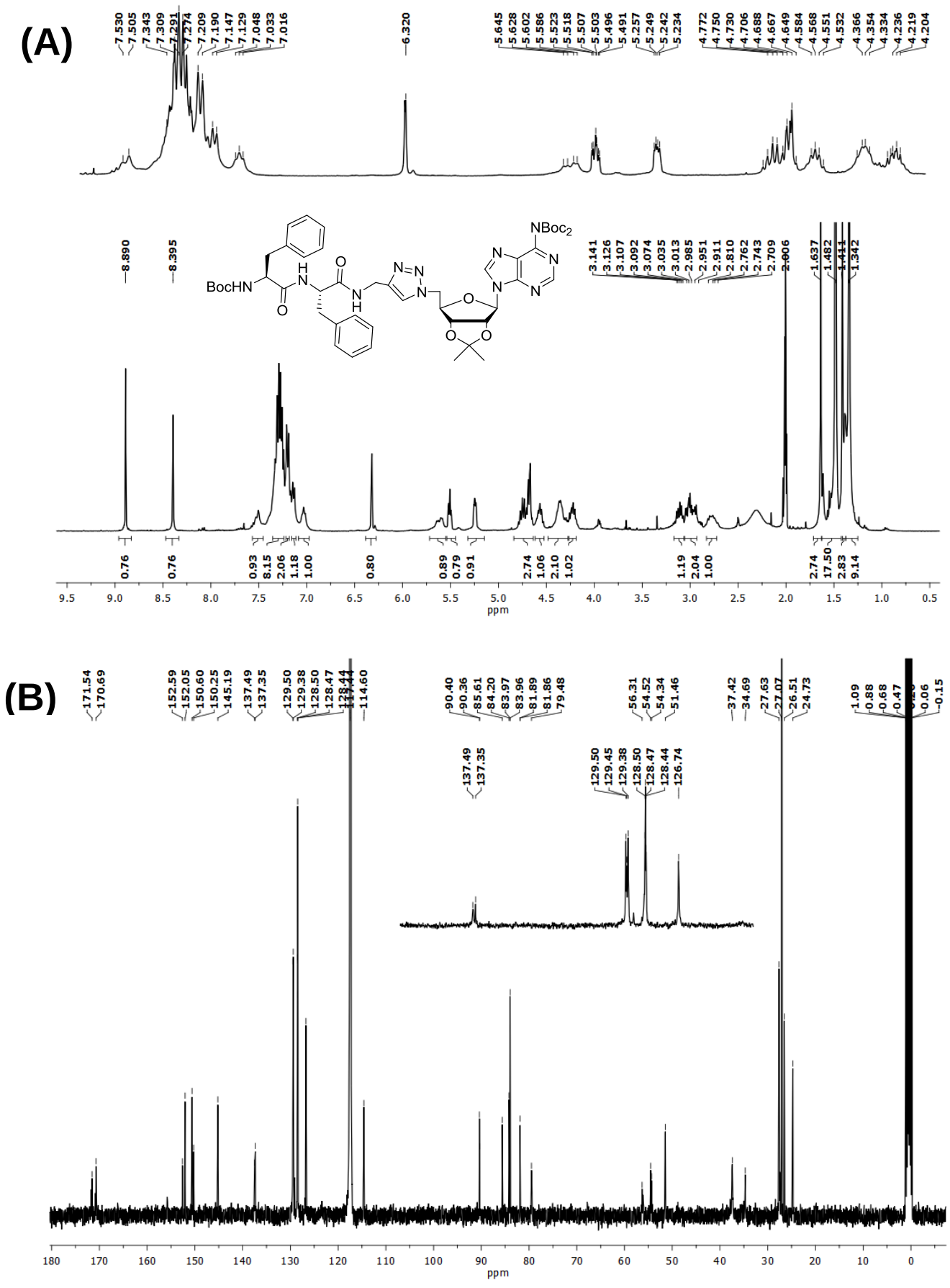


Figure S7: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **7** (Boc-Phe-Phe-*tz*-A$^{N(Boc)_2}$).

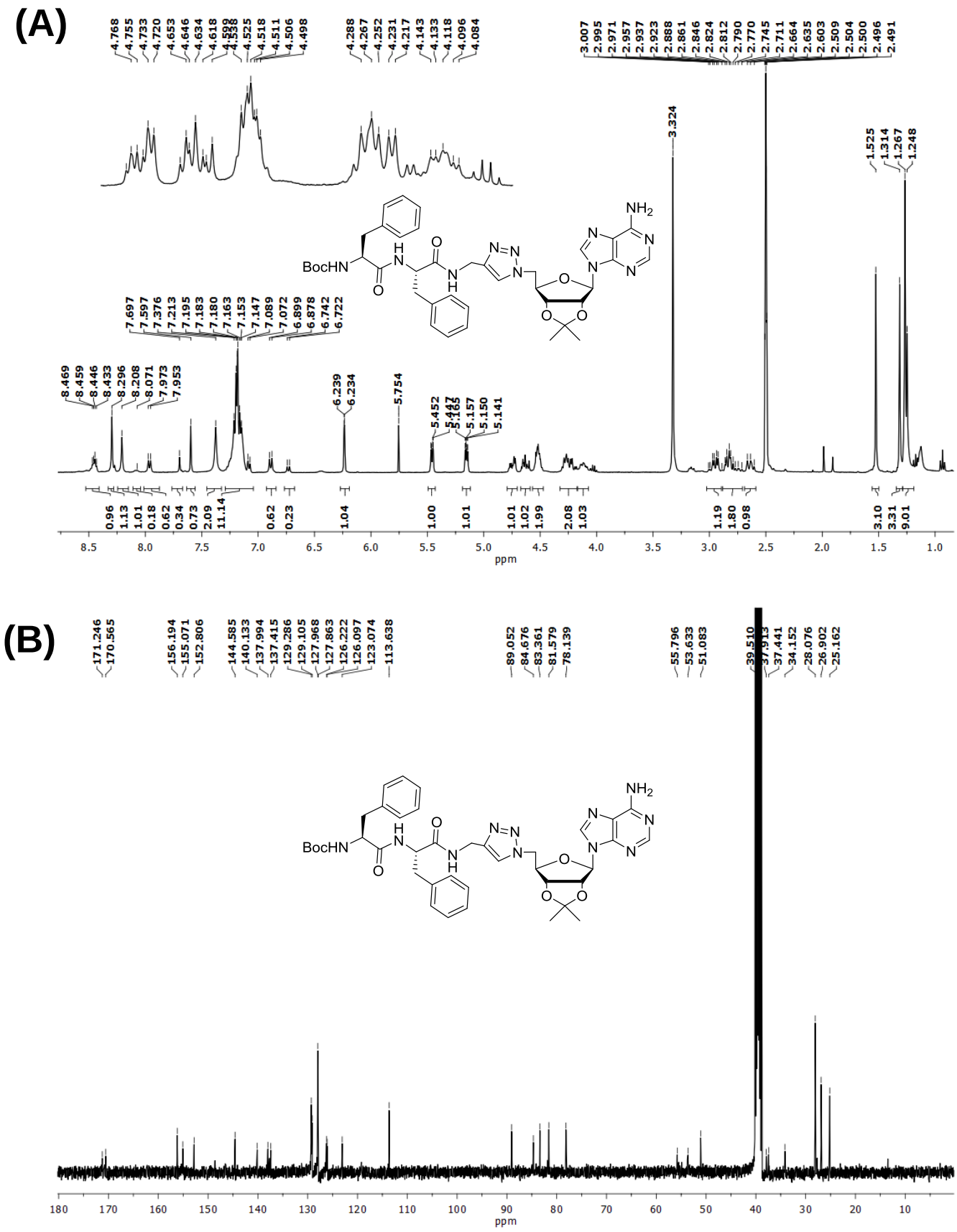


Figure S8: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}).

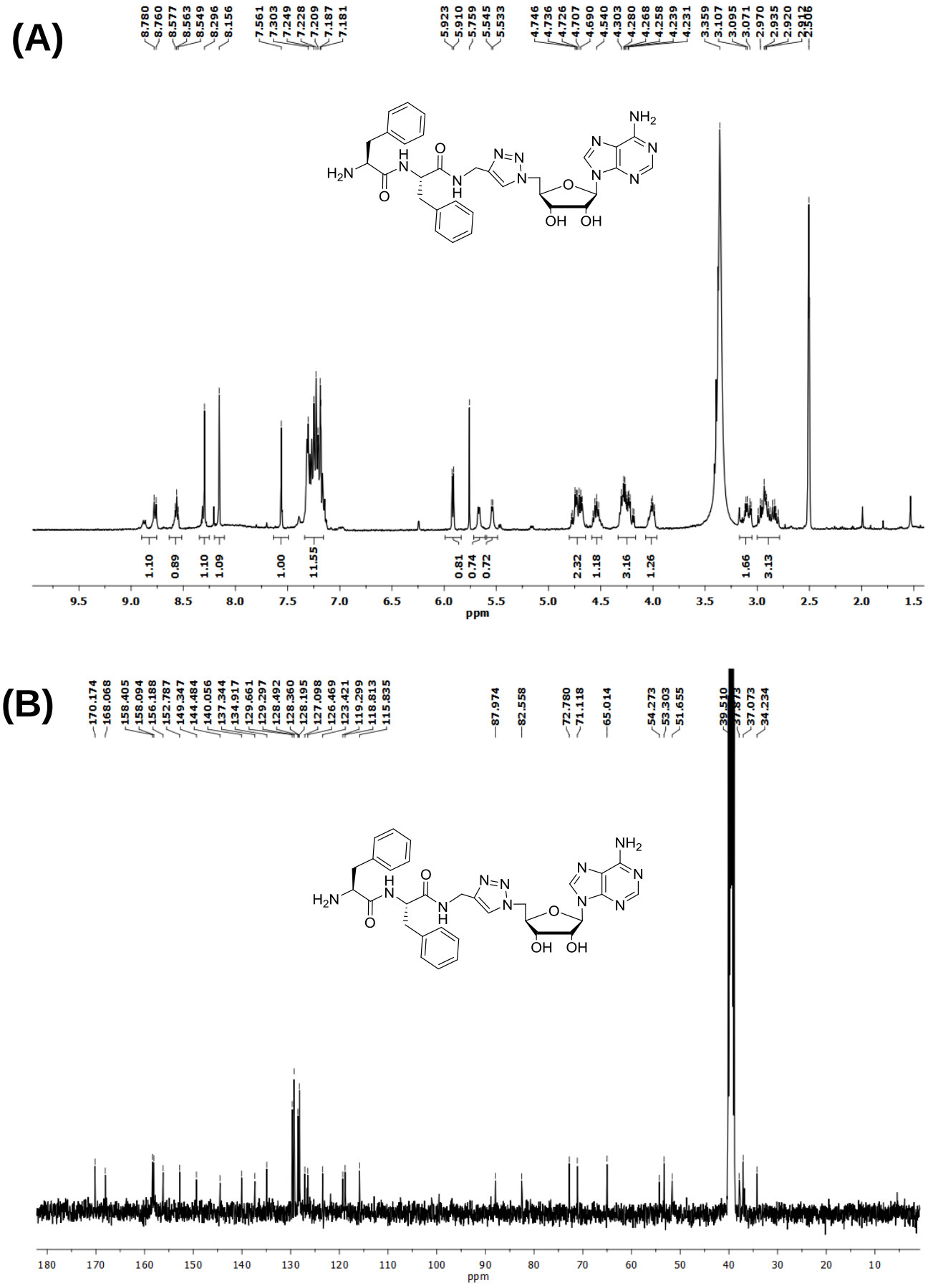


Figure S9: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}).

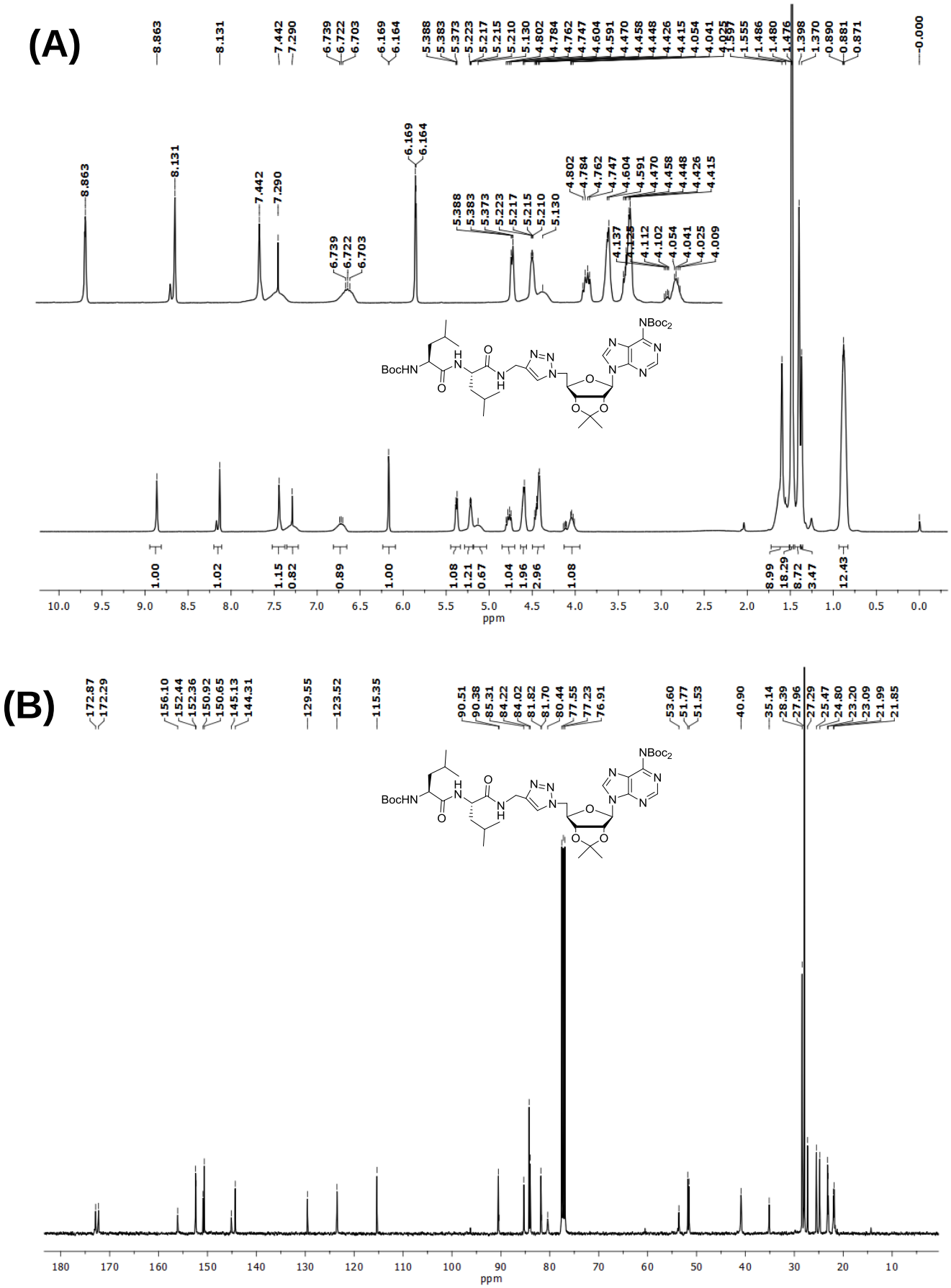


Figure S10: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **10** (Boc-Leu-Leu-*tz*-A$^{N(Boc)_2}$).

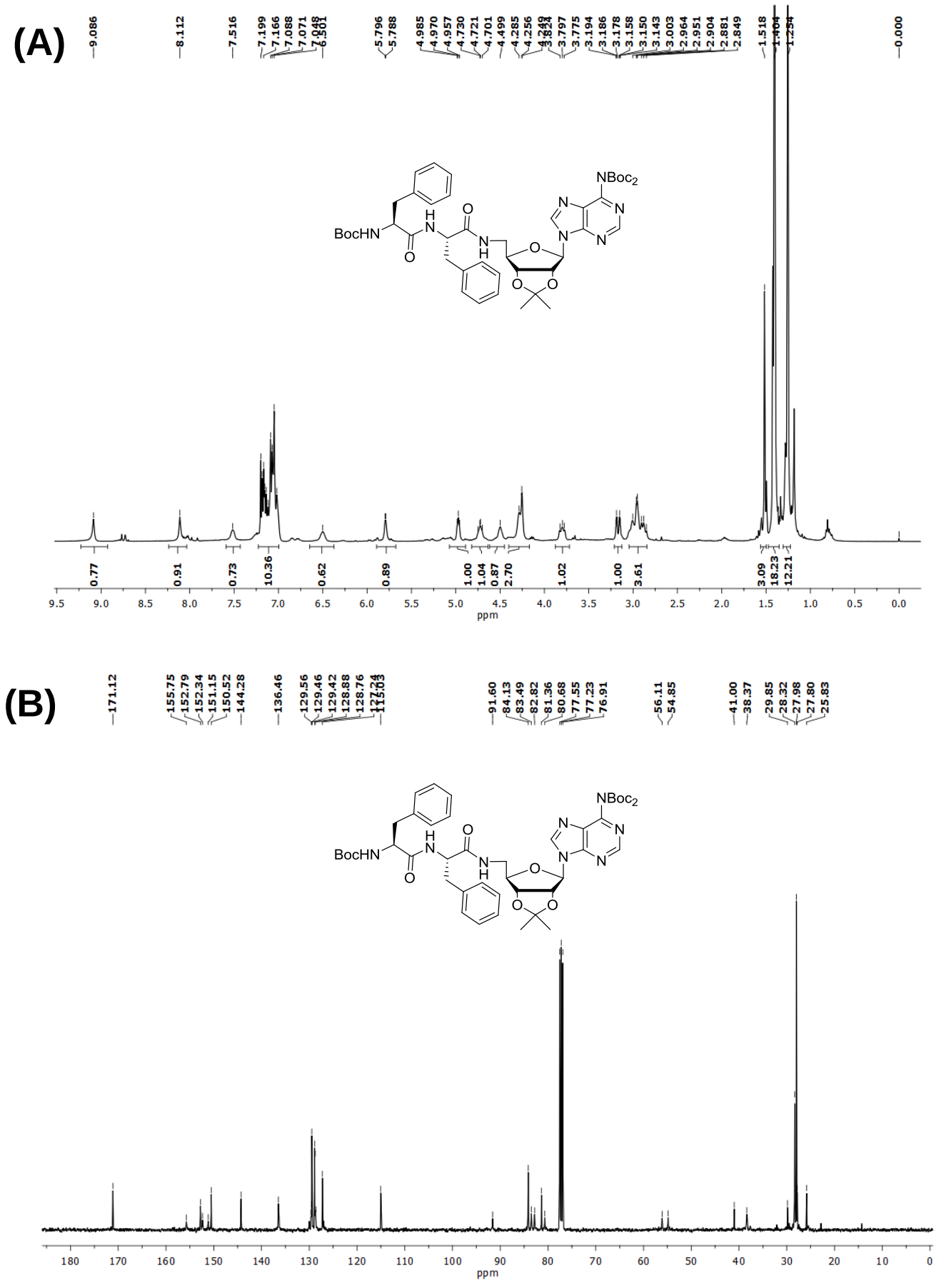


Figure S11: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **12** (Boc-Phe-Phe-*am*-A$^{N(Boc)_2}$).

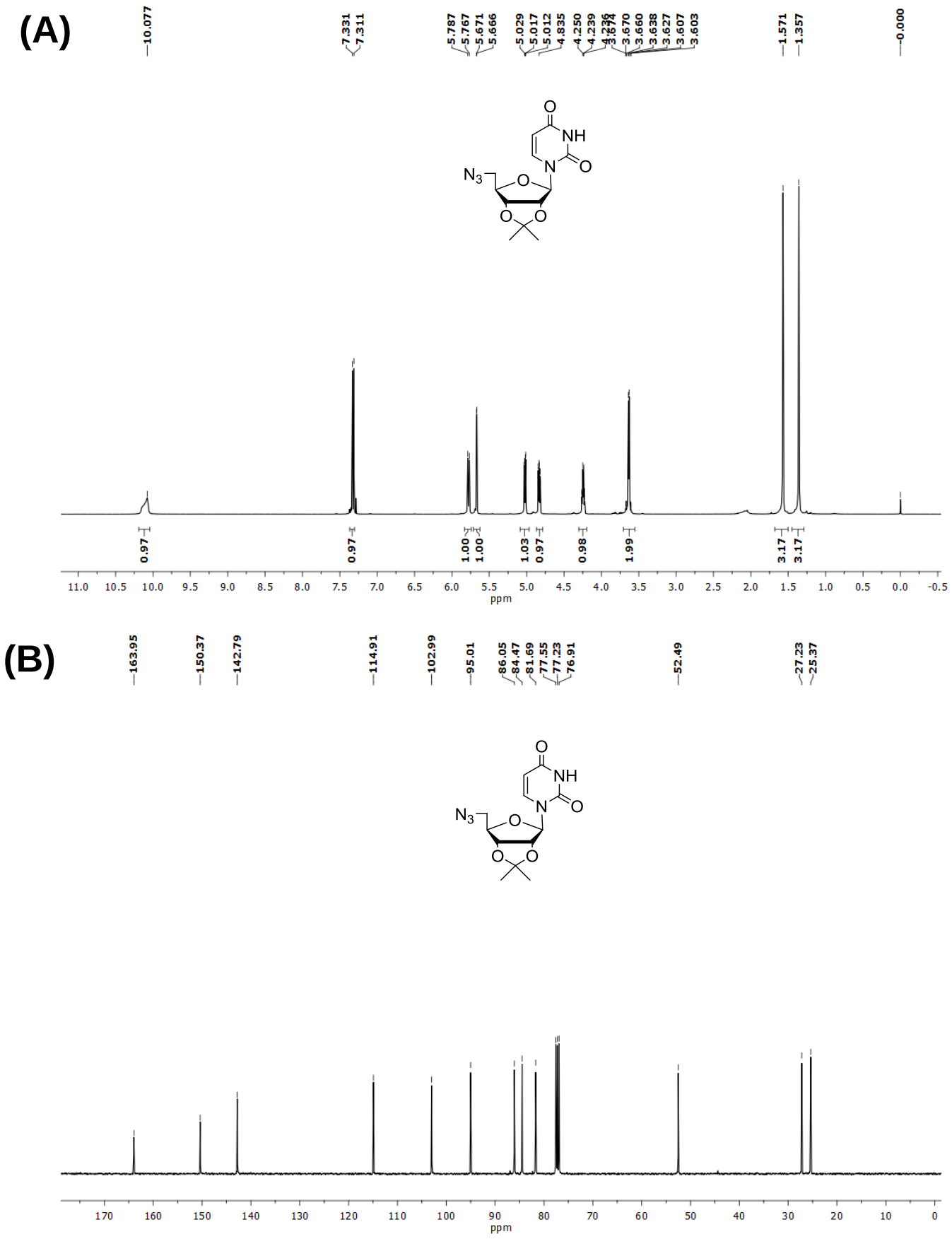


Figure S12: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of azide **13**.

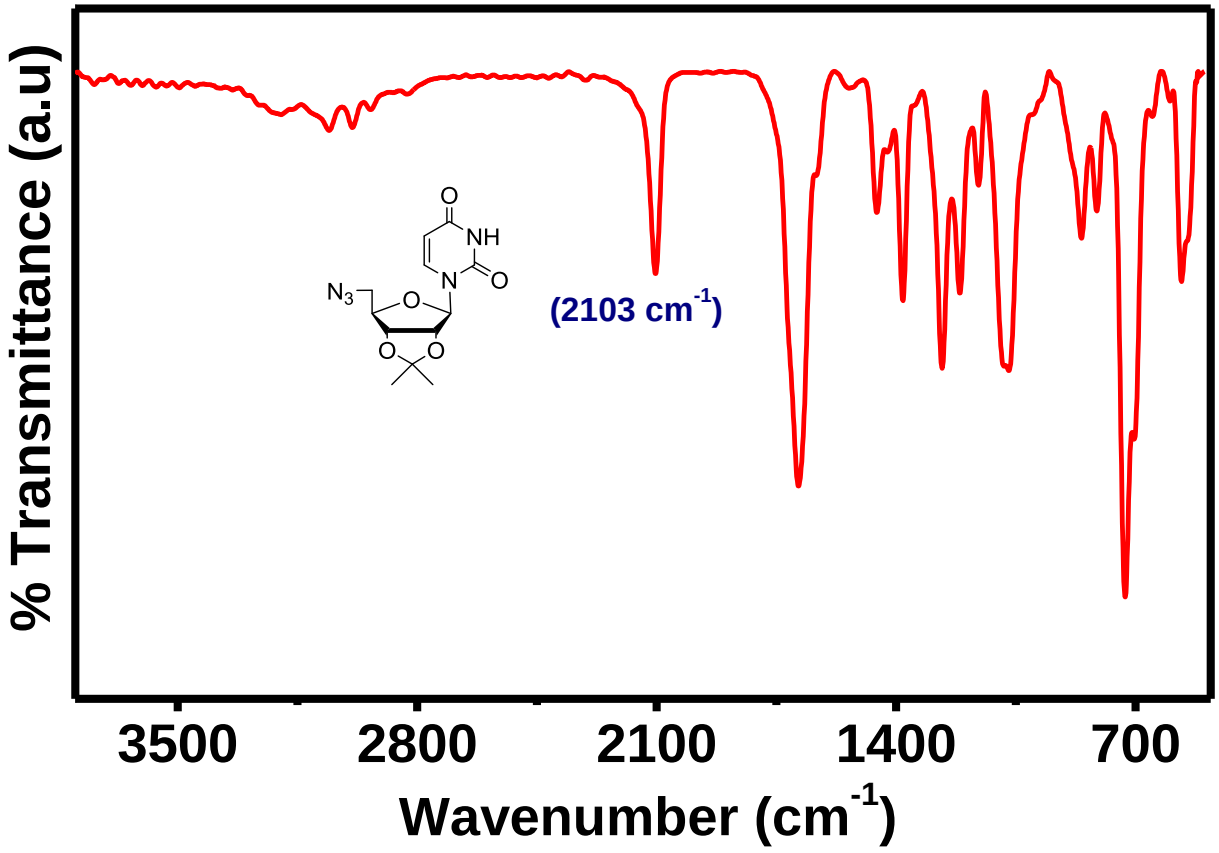


Figure S13: FTIR of azide **13**.

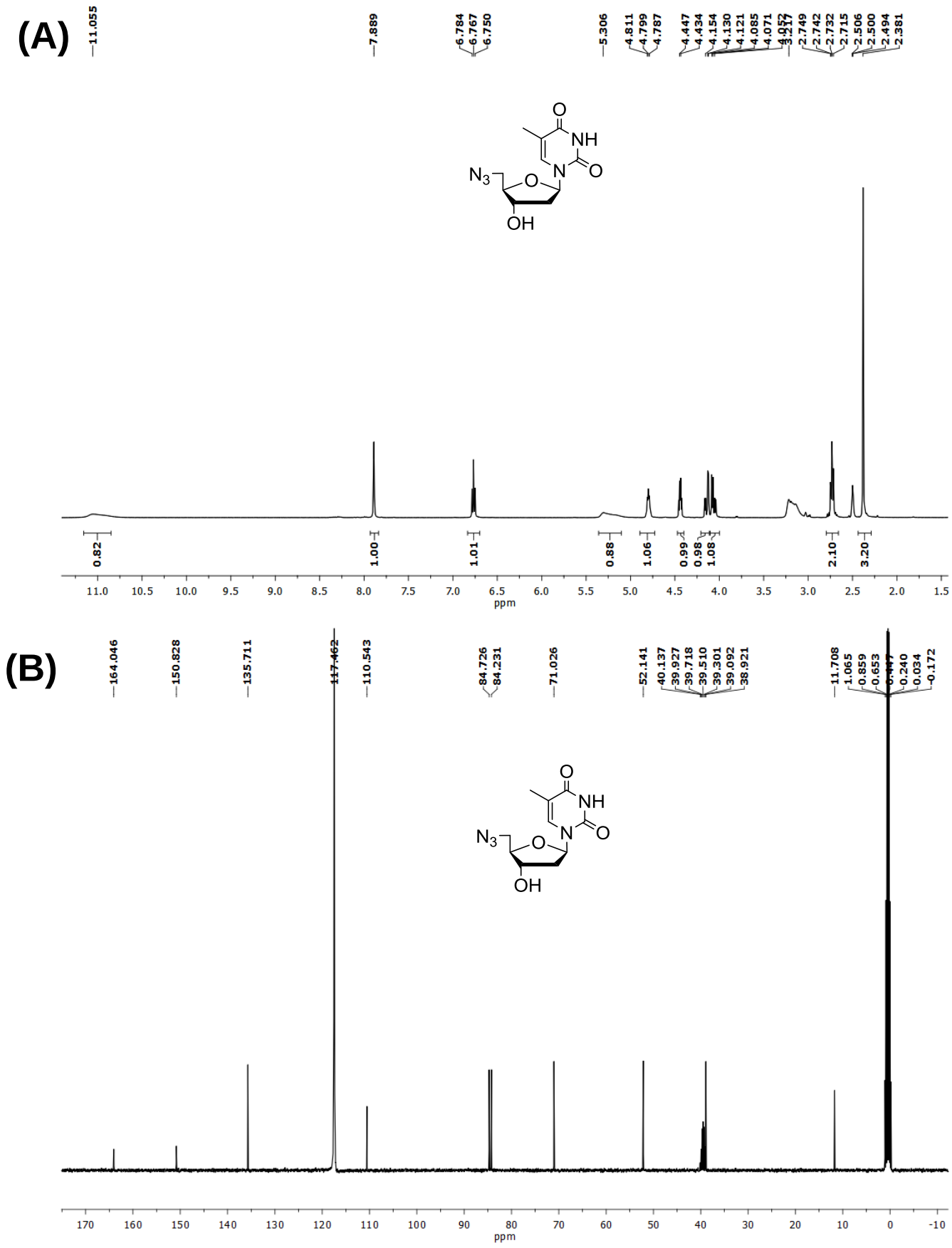


Figure S14: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of azide **14** [in ACN-d_3 + DMSO-d_6 (5:1)].

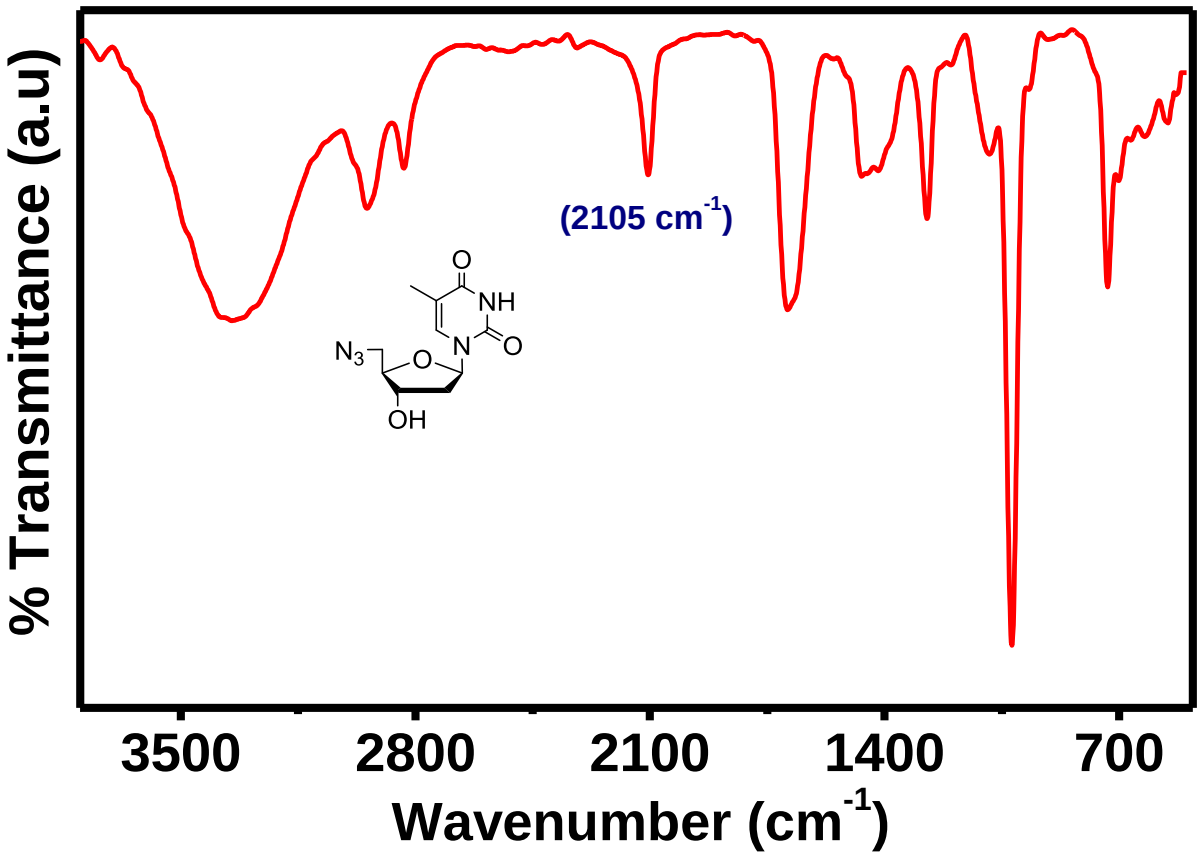


Figure S15: FTIR of azide **14**

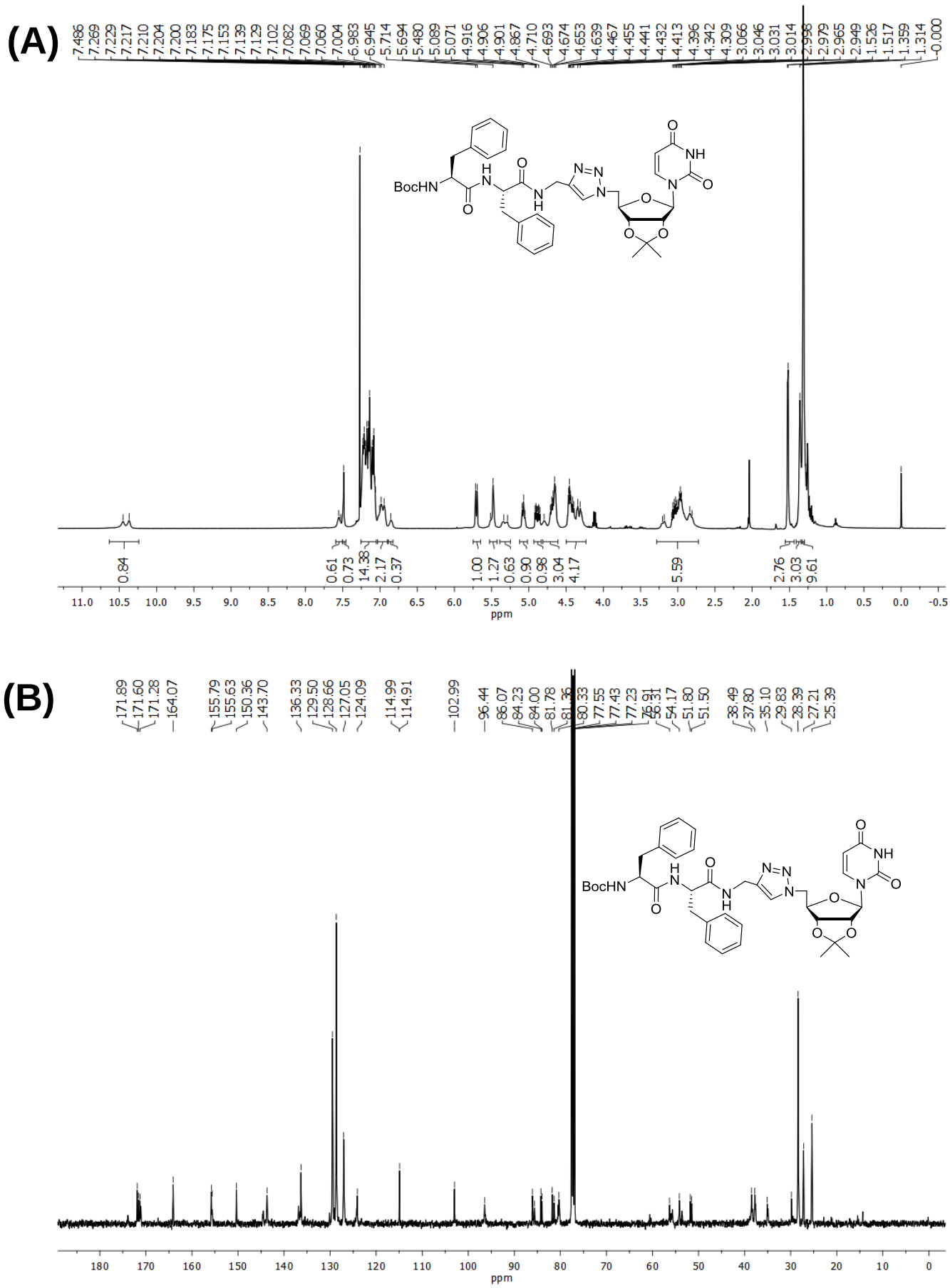


Figure S16: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **15** (Boc-Phe-Phe-*tz*-U).

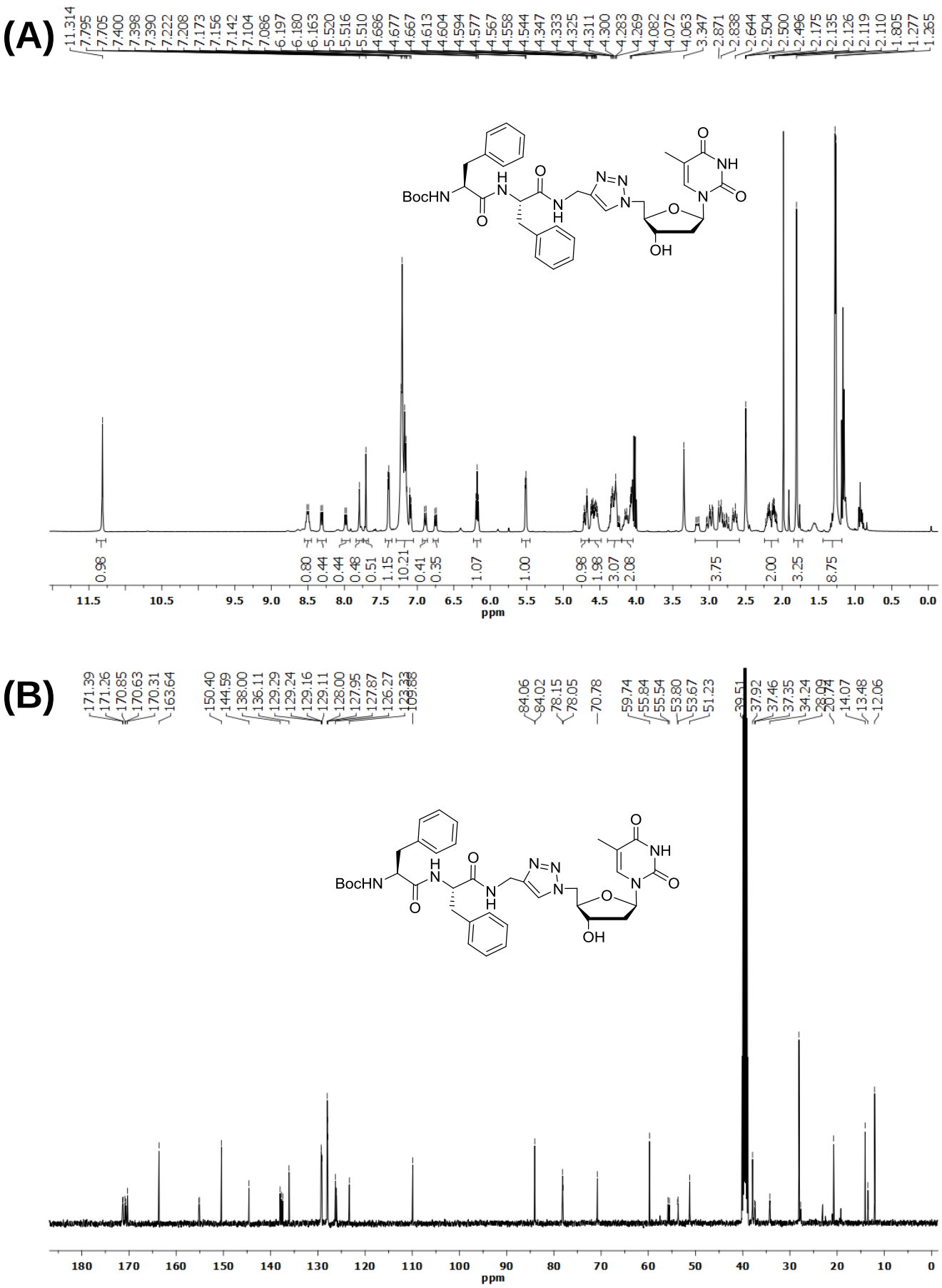


Figure S17: (A) ^{1}H-NMR **(B)** ^{13}C-NMR spectra of peptide **16** (Boc-Phe-Phe-*tz*-T).

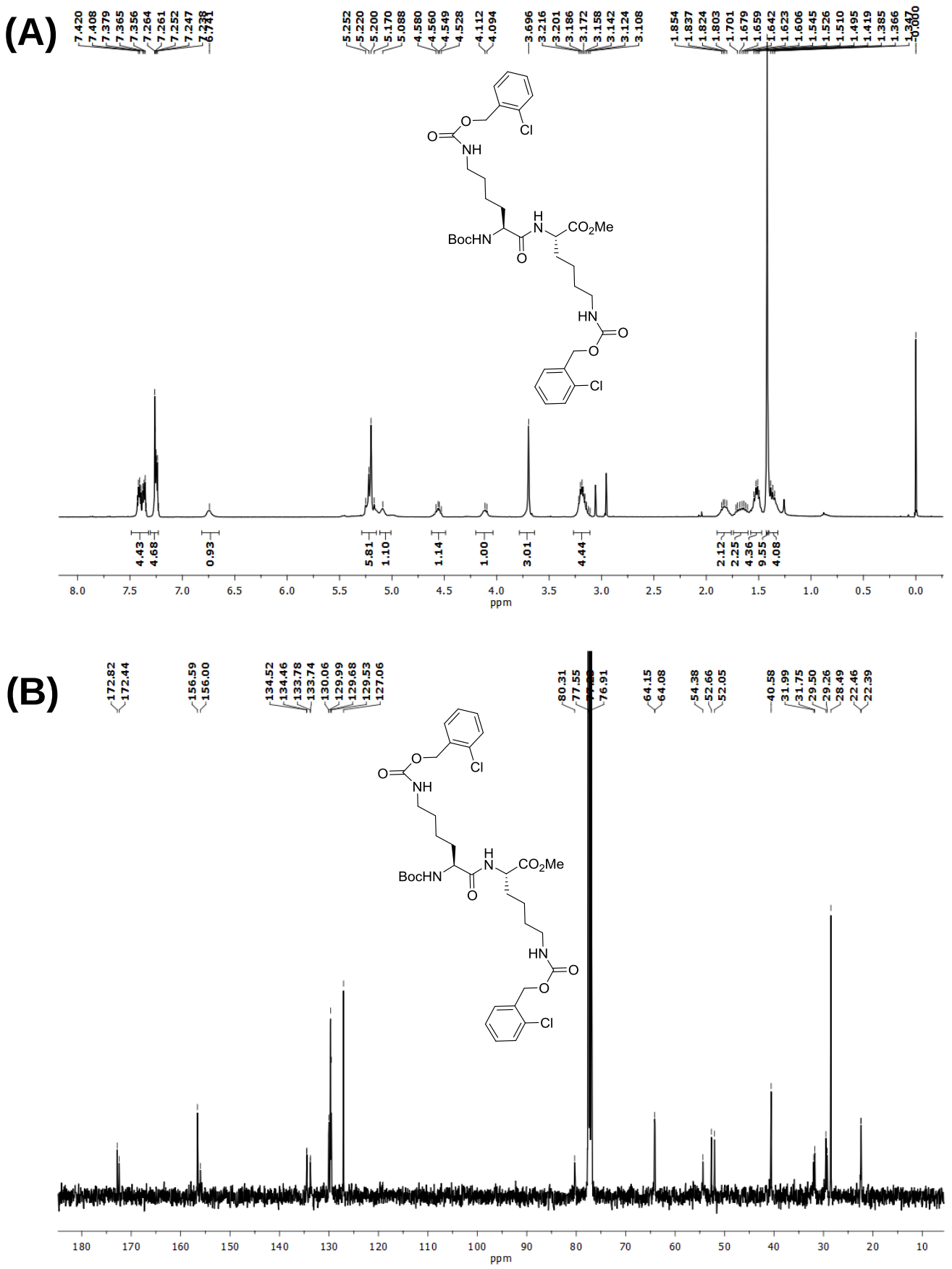


Figure S18: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Boc-Lys(Cl-Cbz)-Lys(Cl-Cbz)-OMe (**S3**).

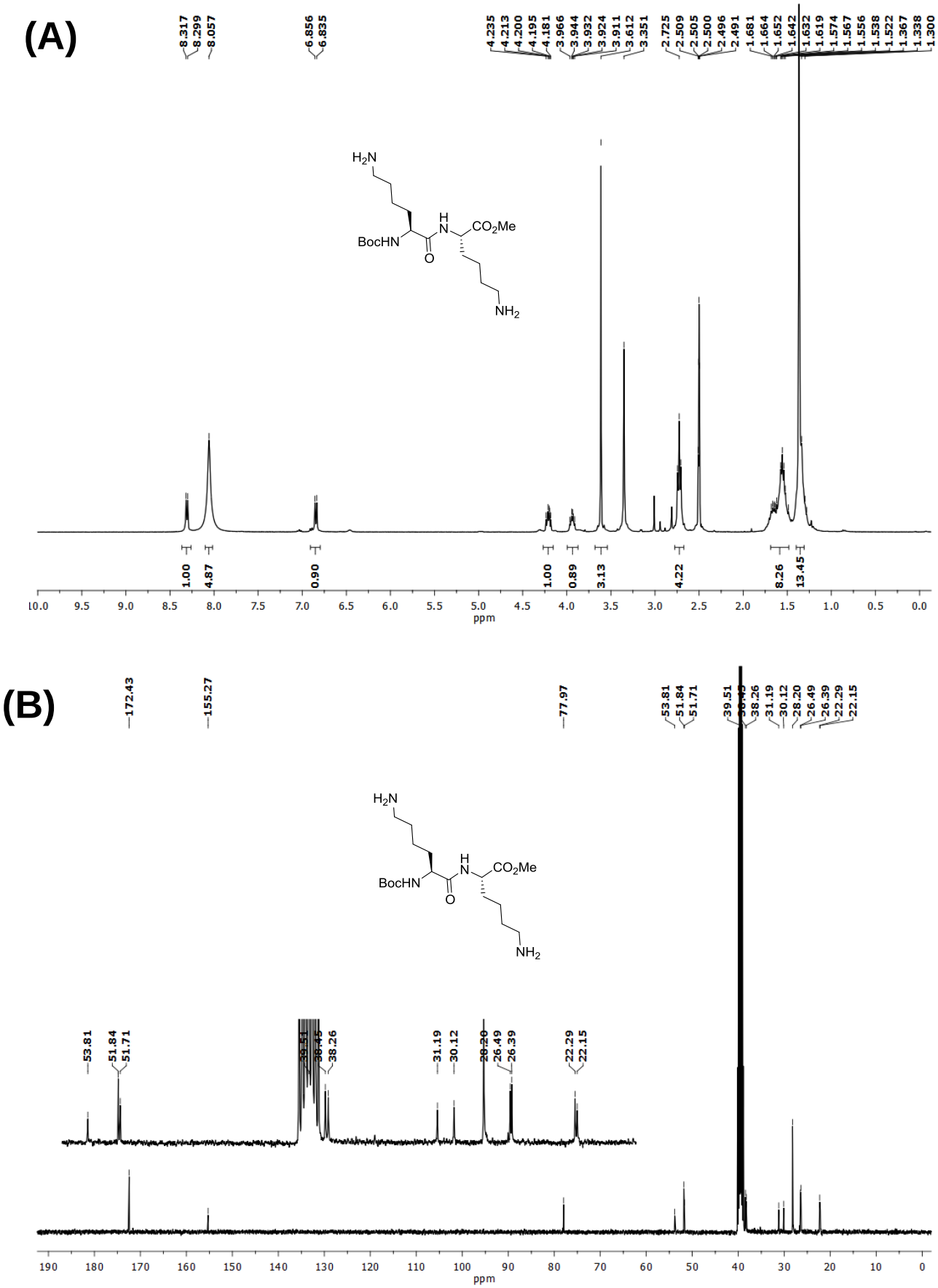
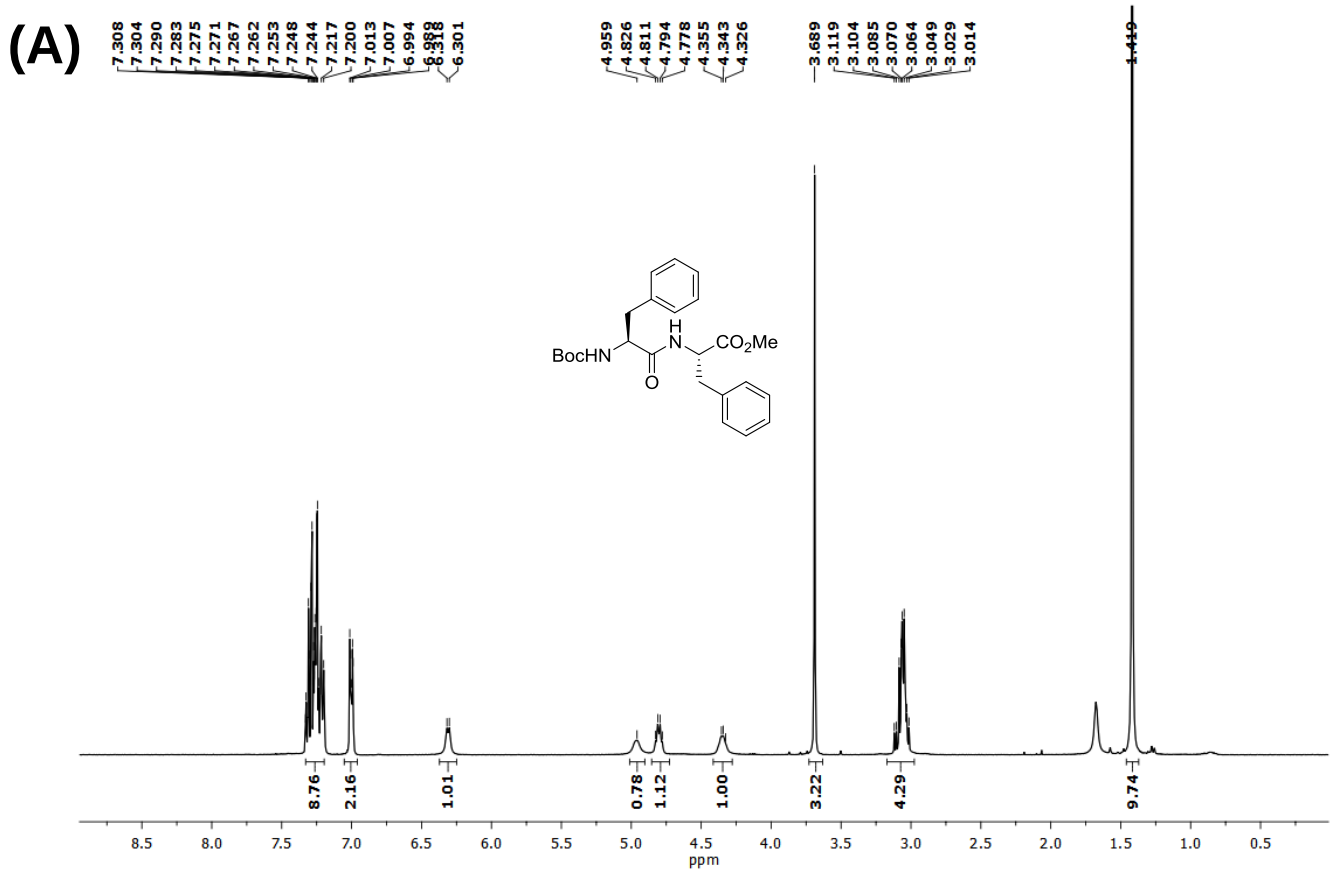


Figure S19: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Boc-Lys-Lys-OMe (**S4**).



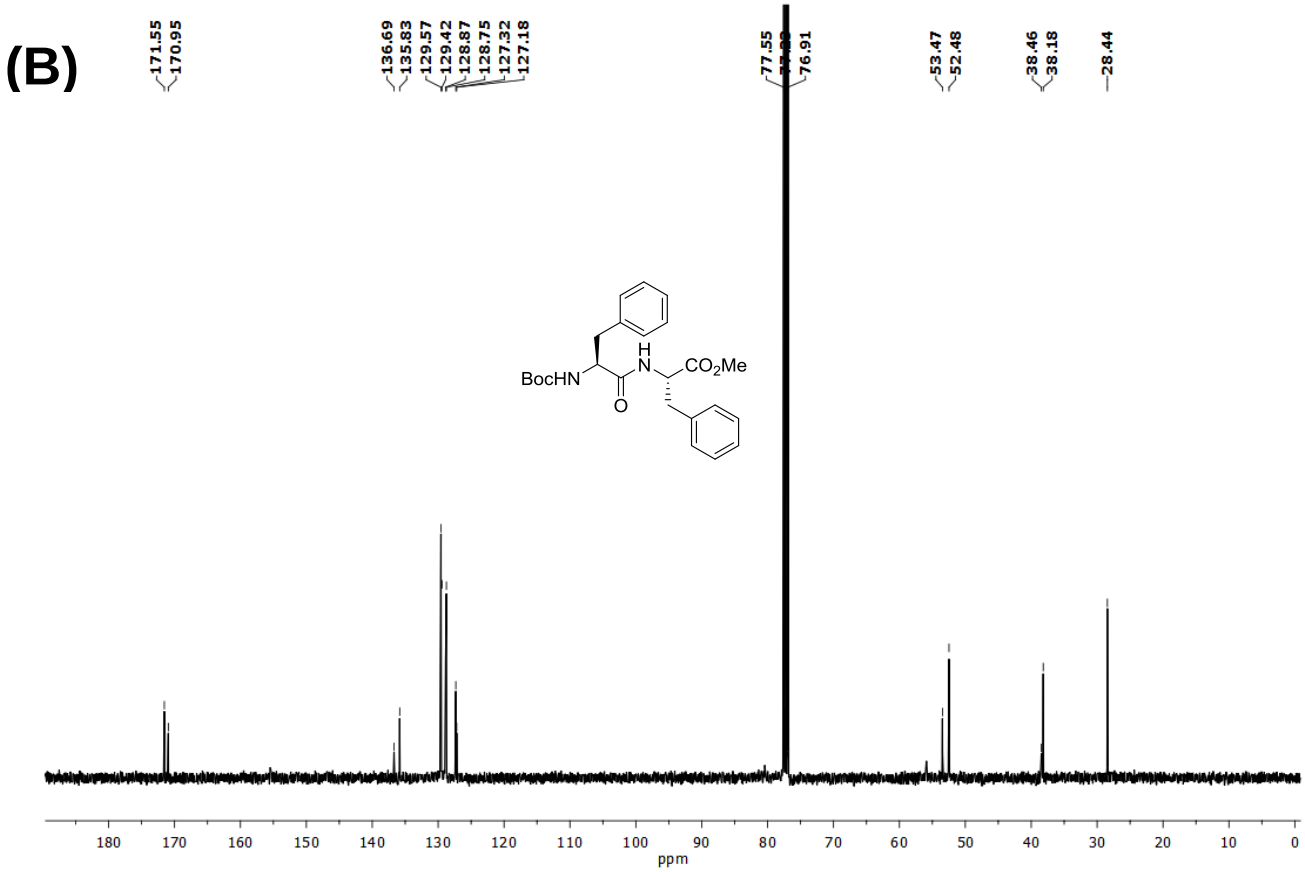


Figure S20: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Boc-Phe-Phe-OMe.

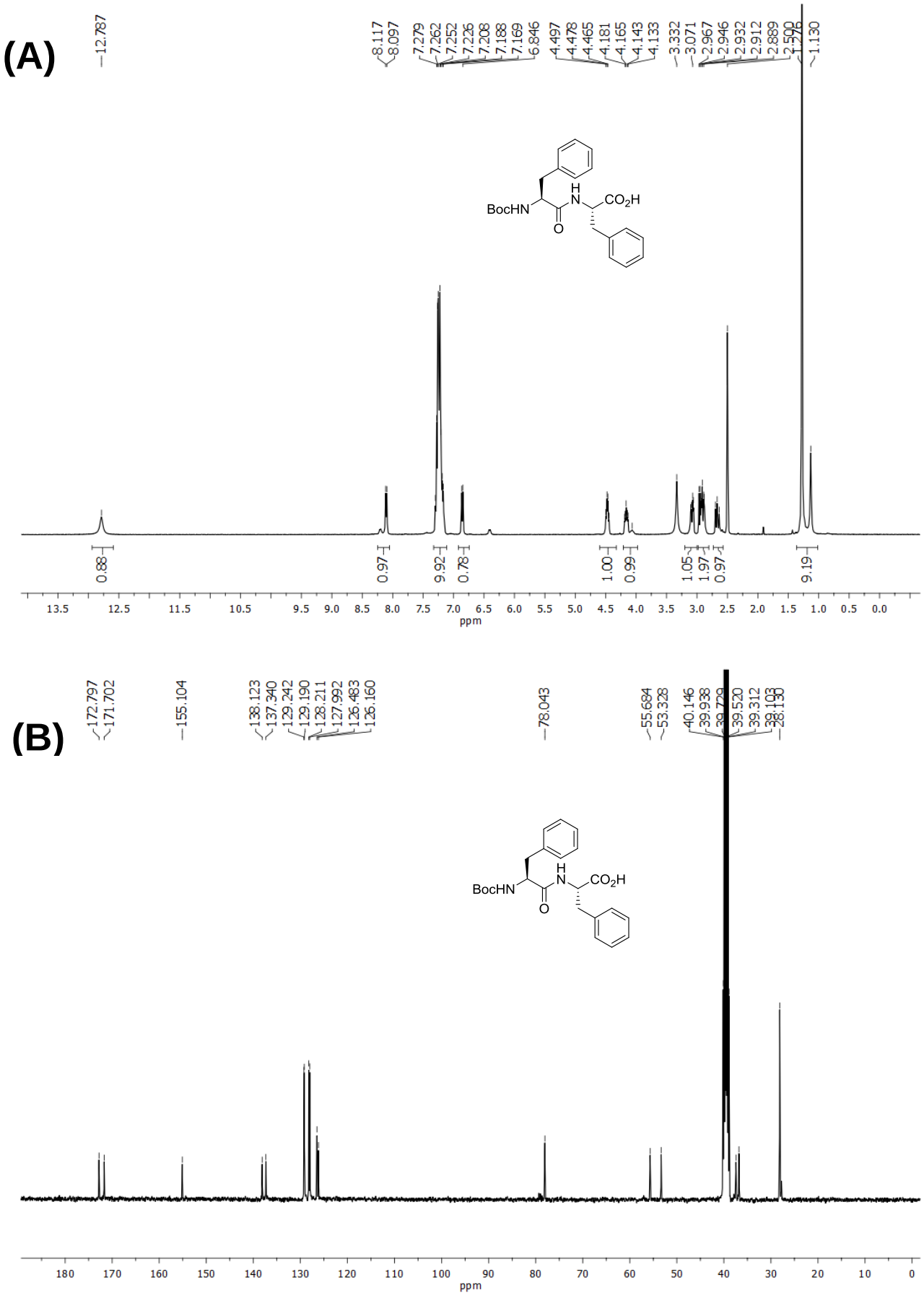


Figure S21: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Boc-Phe-Phe-OH (**1**).

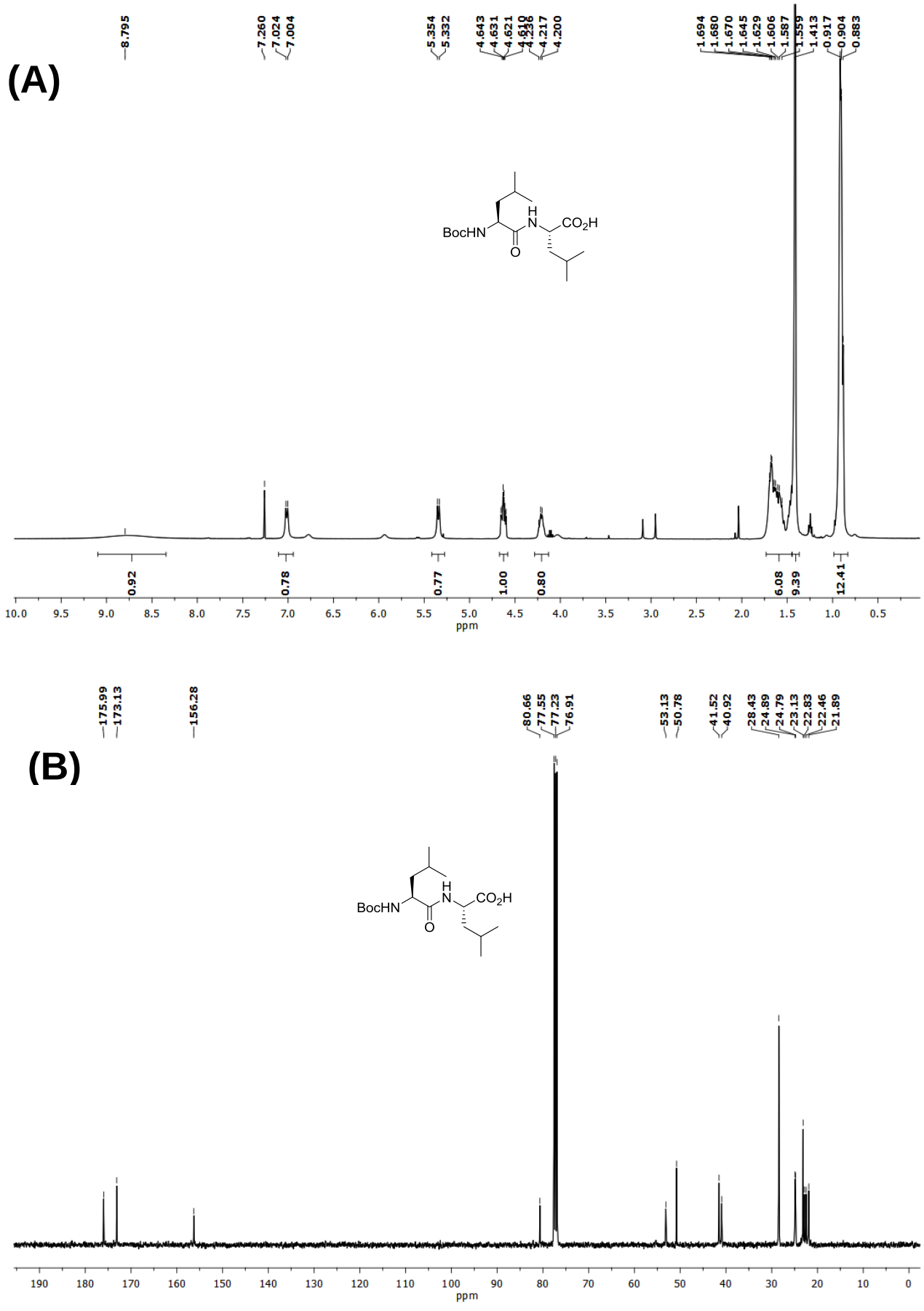


Figure S22: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Boc-Leu- Leu-OH (**2**).

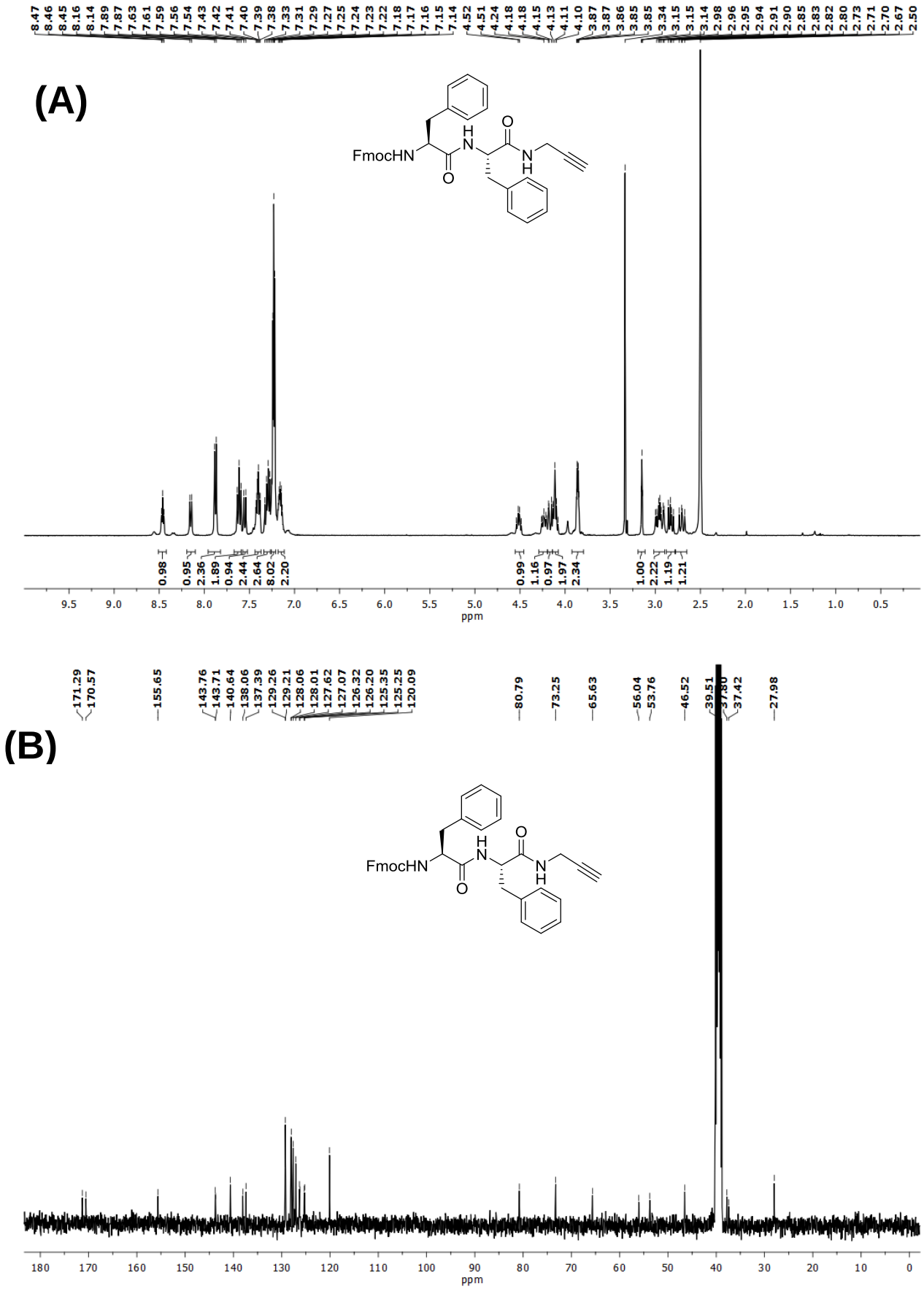


Figure S23: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Fmoc-Phe-Phe-Propyne (**S5**).

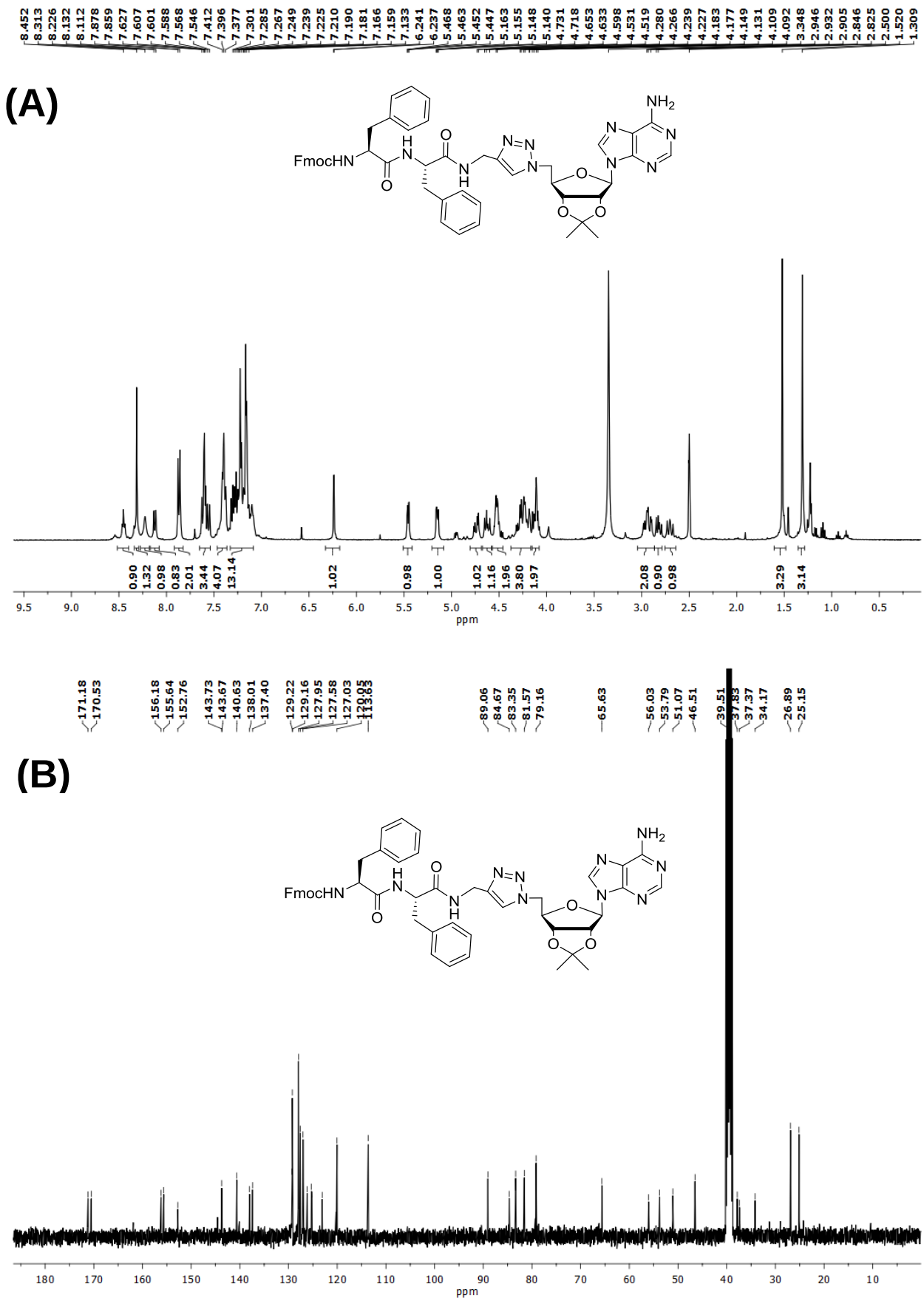


Figure S24: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Fmoc-Phe-Phe-*tz*-A^{NH_2} (**S6**).

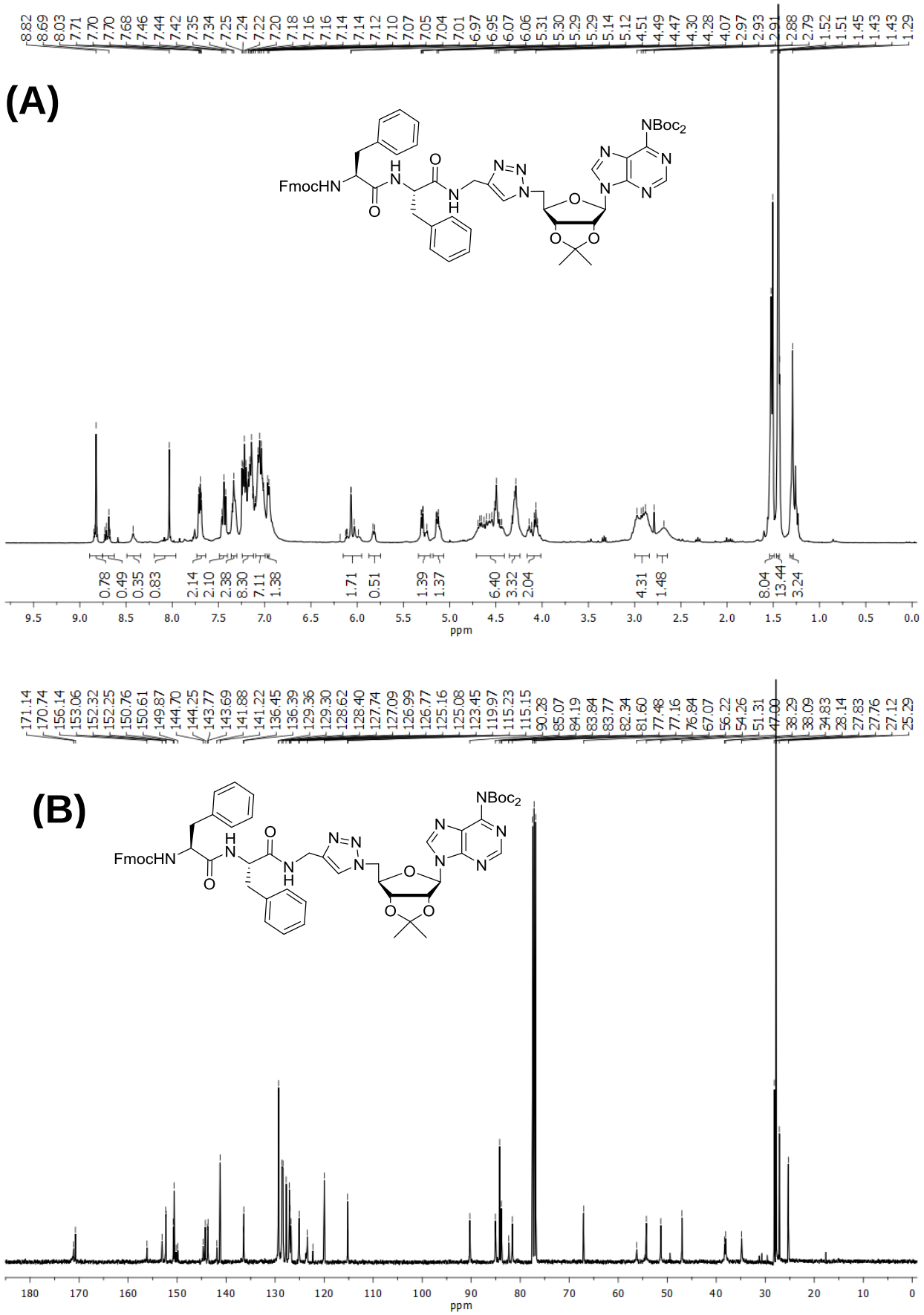


Figure S25: (A) ^{1}H-NMR and **(B)** ^{13}C-NMR spectra of Fmoc-Phe-Phe-*tz*-A$^{N(Boc)_2}$ (**S7**).

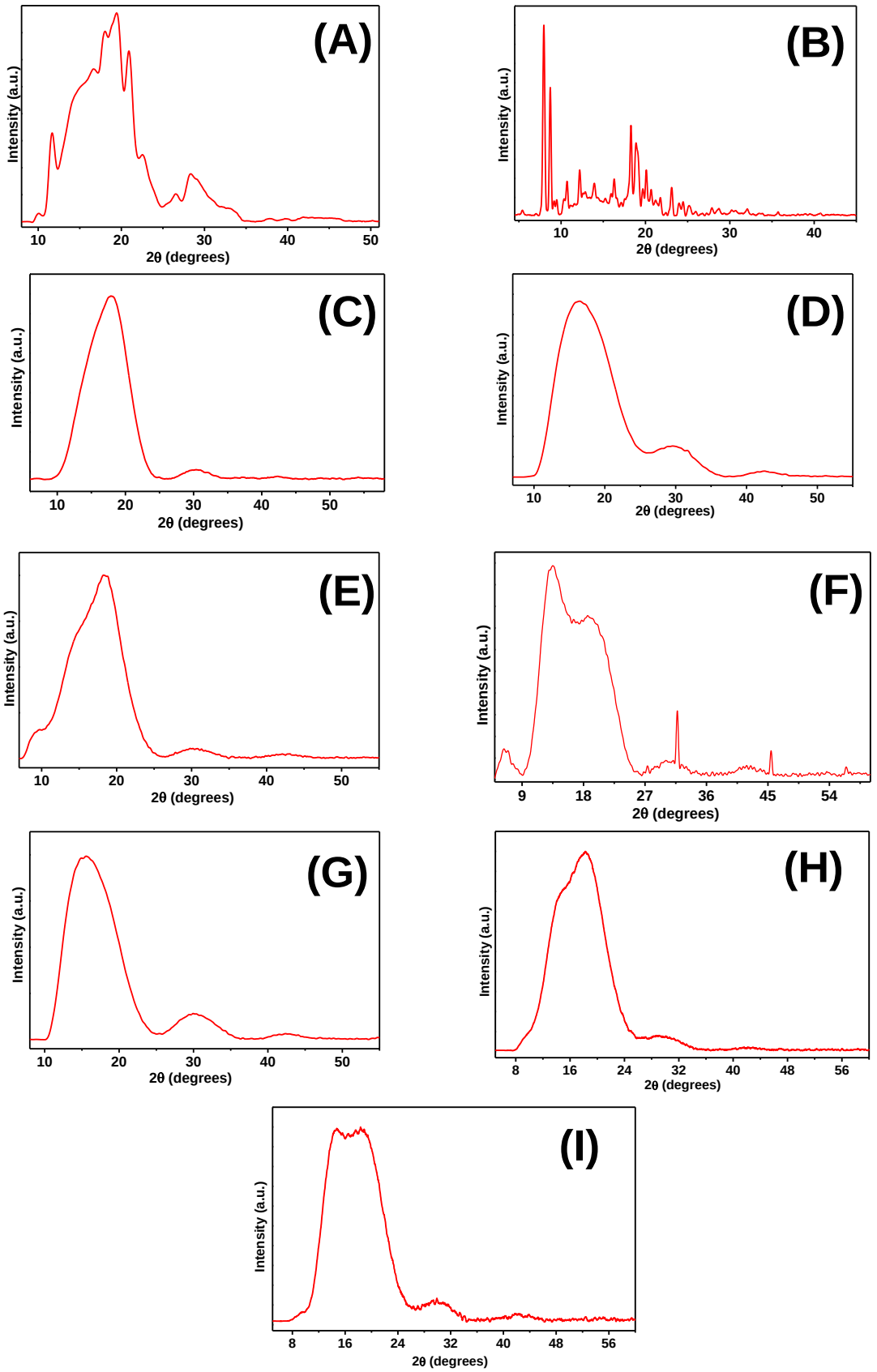


Figure S26: PXRD patterns of (A) peptide **2** (Boc-Phe-Phe-Propyne), (B) peptide **4** (Boc-Leu-Leu-Propyne), (C) peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), (D) peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}), (E) peptide **10** (Boc-Leu-Leu-*tz*-$A^{N(Boc)_2}$), (F) peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}), (G) peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$), (H) peptide **15** (Boc-Phe-Phe-*tz*-U) and (I) peptide **16** (Boc-Phe-Phe-*tz*-T).

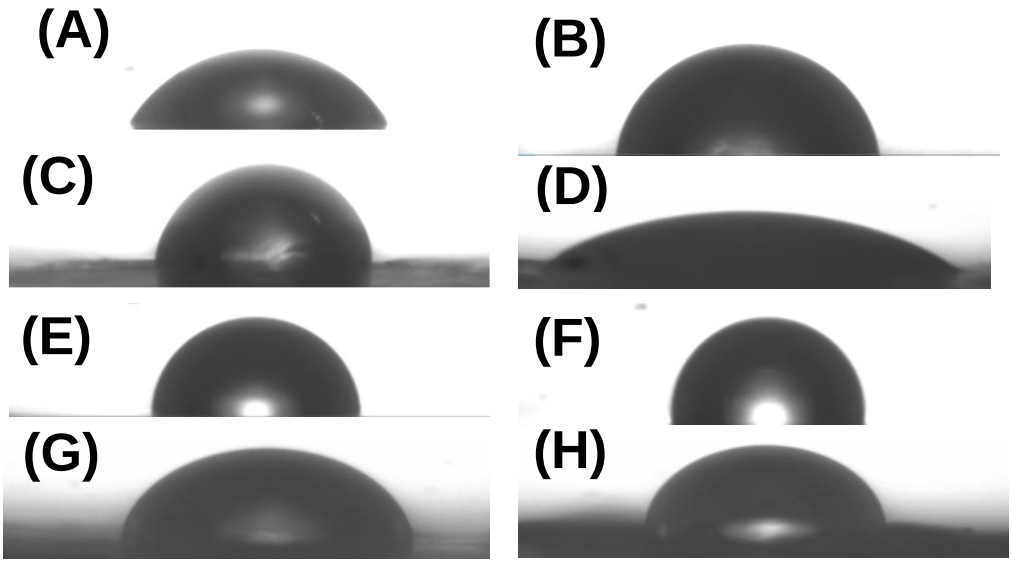


Figure S27: Images taken for contact angle measurement of (A) bare glass, (B) peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), (C) peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}), (D) peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}), (E) peptide **10** (Boc-Leu-Leu-*tz*-$A^{N(Boc)_2}$), (F) peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$), (G) peptide **15** (Boc-Phe-Phe-*tz*-U) and (H) peptide **16** (Boc-Phe-Phe-*tz*-T).

Table S1: Contact angle (CA) measured for peptides on glass surface

Sample/Surface	**Contact angle (CA in degree)[a]**	**ΔCA (in degree)**
Bare glass	60 ± 2	-
Peptide **7** Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$	84 ± 2	+24
Peptide **8** Boc-Phe-Phe-*tz*-A^{NH_2}	81 ± 1	+21
Peptide **9** H-Phe-Phe-*tz*-A^{NH_2}	32 ± 2	−28
Peptide **10** Boc-Leu-Leu-*tz*-$A^{N(Boc)_2}$	83 ± 2	+23
Peptide **12** Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$	93 ± 1	+33
Peptide **15** Boc-Phe-Phe-*tz*-U	73 ± 2	+13
Peptide **16** Boc-Phe-Phe-*tz*-T	75 ± 2	+15

[a] Data are the mean ± SD (n=4)

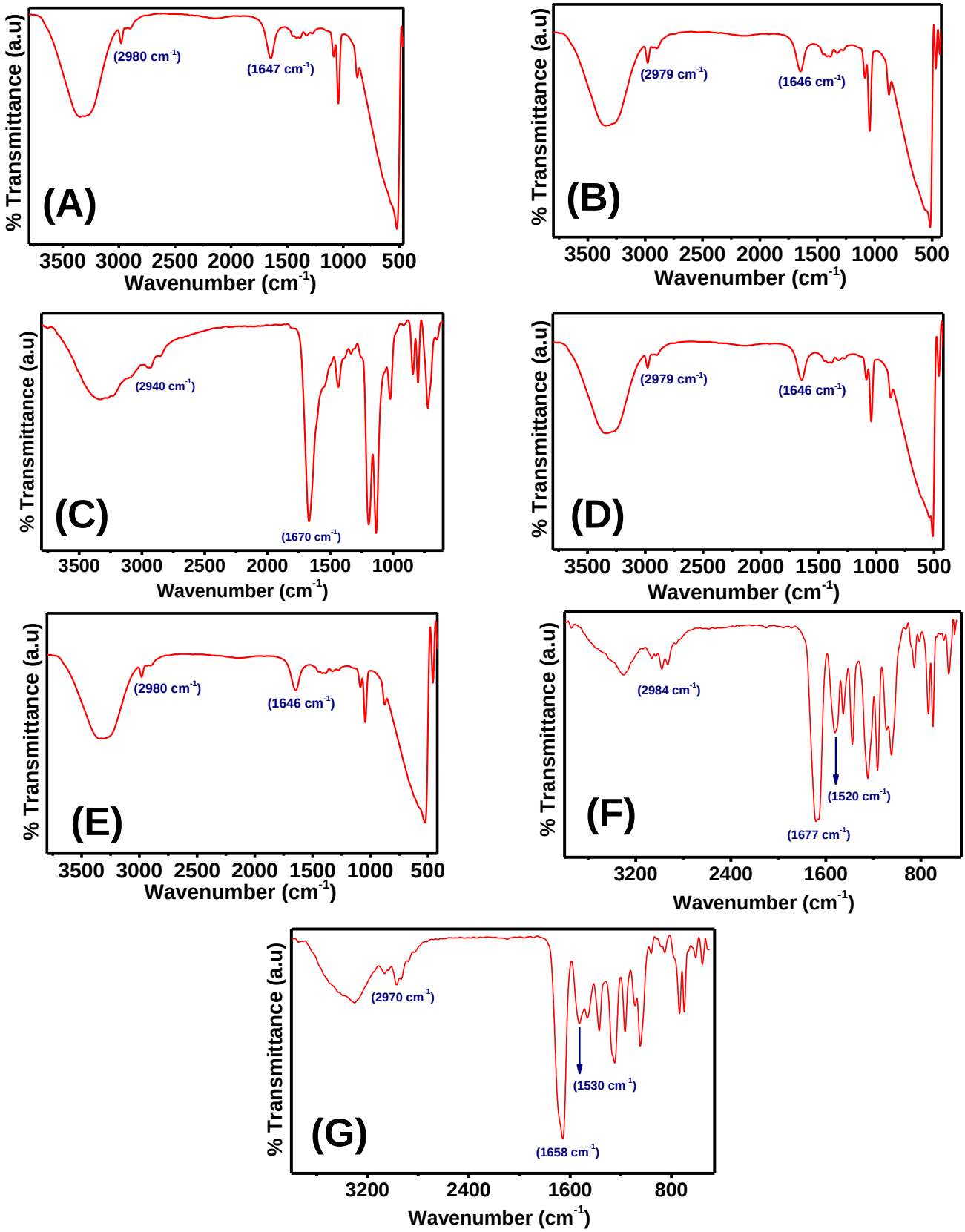
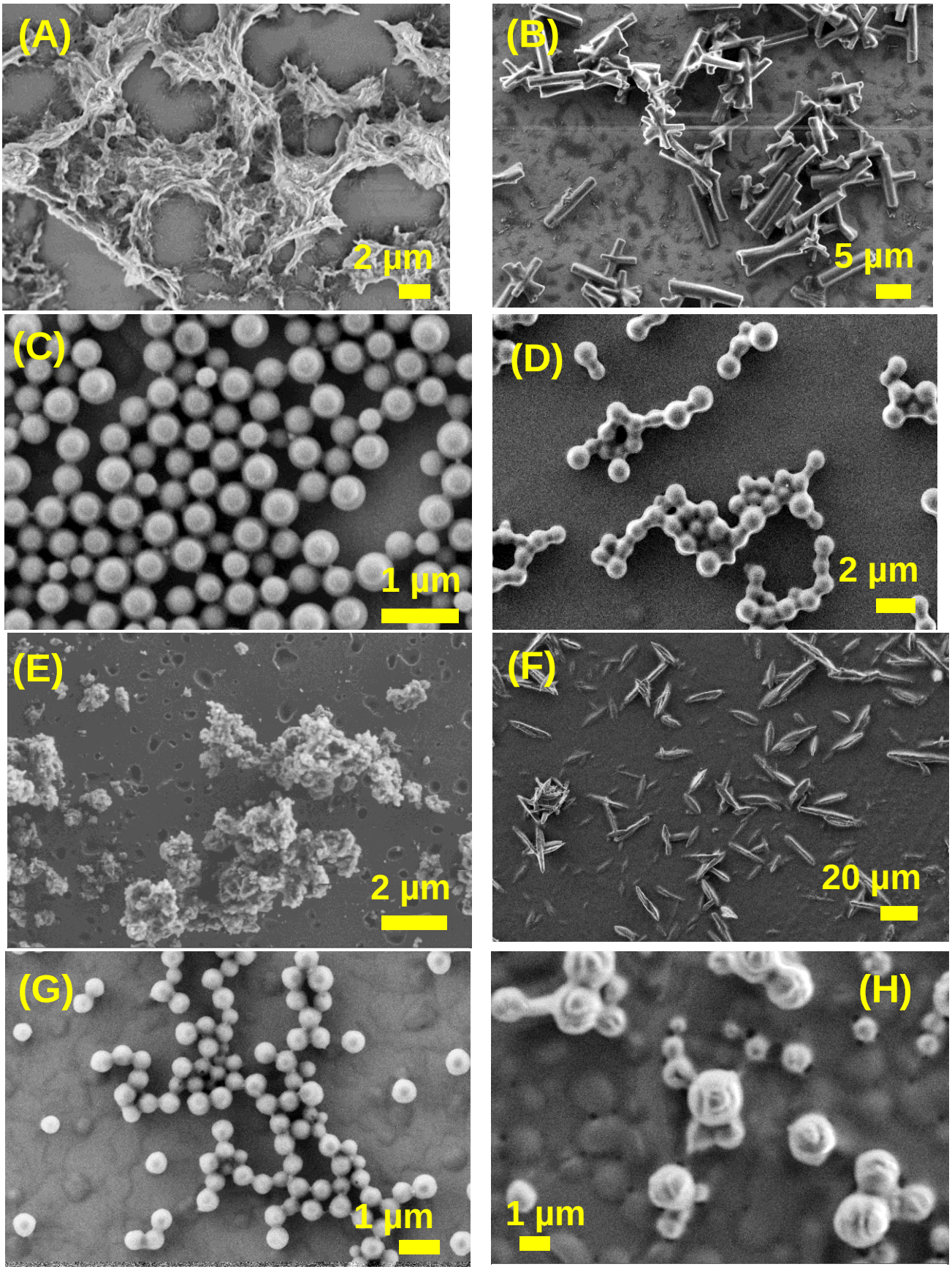


Figure S28: FTIR spectra of (A) peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), (B) peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}), (C) peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}), (D) peptide **10** (Boc-Leu-Leu-*tz*-$A^{N(Boc)_2}$), (E) peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$), (F) peptide **15** (Boc-Phe-Phe-*tz*-U) and (G) peptide **16** (Boc-Phe-Phe-*tz*-T).


(A)
2 μm
(B)
5 μm
(C)
1 μm
(D)
2 μm
(E)
2 μm
(F)
20 μm
(G)
1 μm
(H)
1 μm

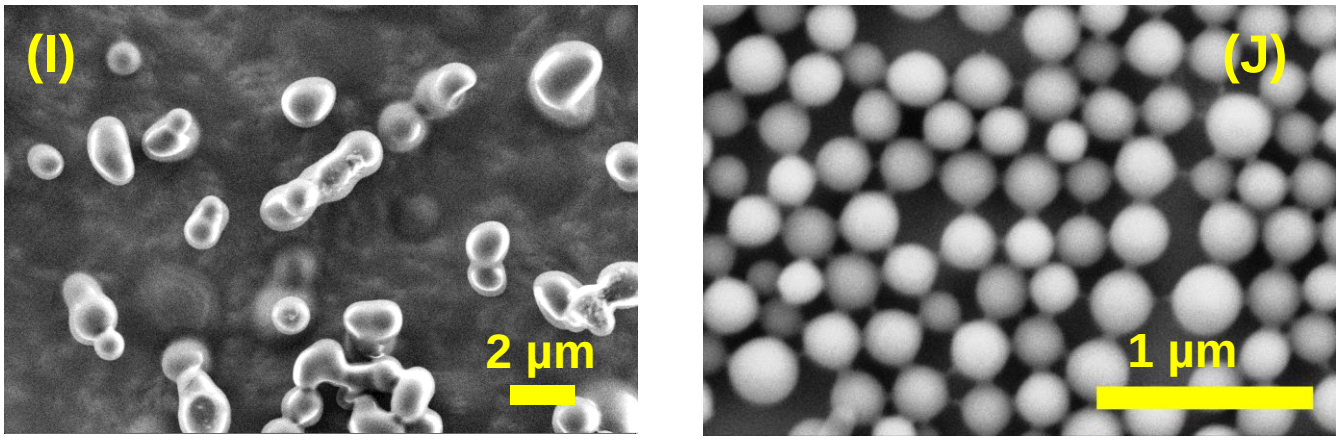


Figure S29: SEM images of (A) peptide **2** (Boc-Phe-Phe-Propyne), (B) peptide **4** (Boc-Leu-Leu-Propyne), (C) peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), (D) peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}), (E) peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}), (F) peptide **10** (Boc-Leu-Leu-*tz*-$A^{N(Boc)_2}$) (G) peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$), (H) peptide **15** (Boc-Phe-Phe-*tz*-T), (I) peptide **16** (Boc-Phe-Phe-*tz*-T) and (J) peptide **S7** (Fmoc-Phe-Phe-*tz*-$A^{N(Boc)_2}$).

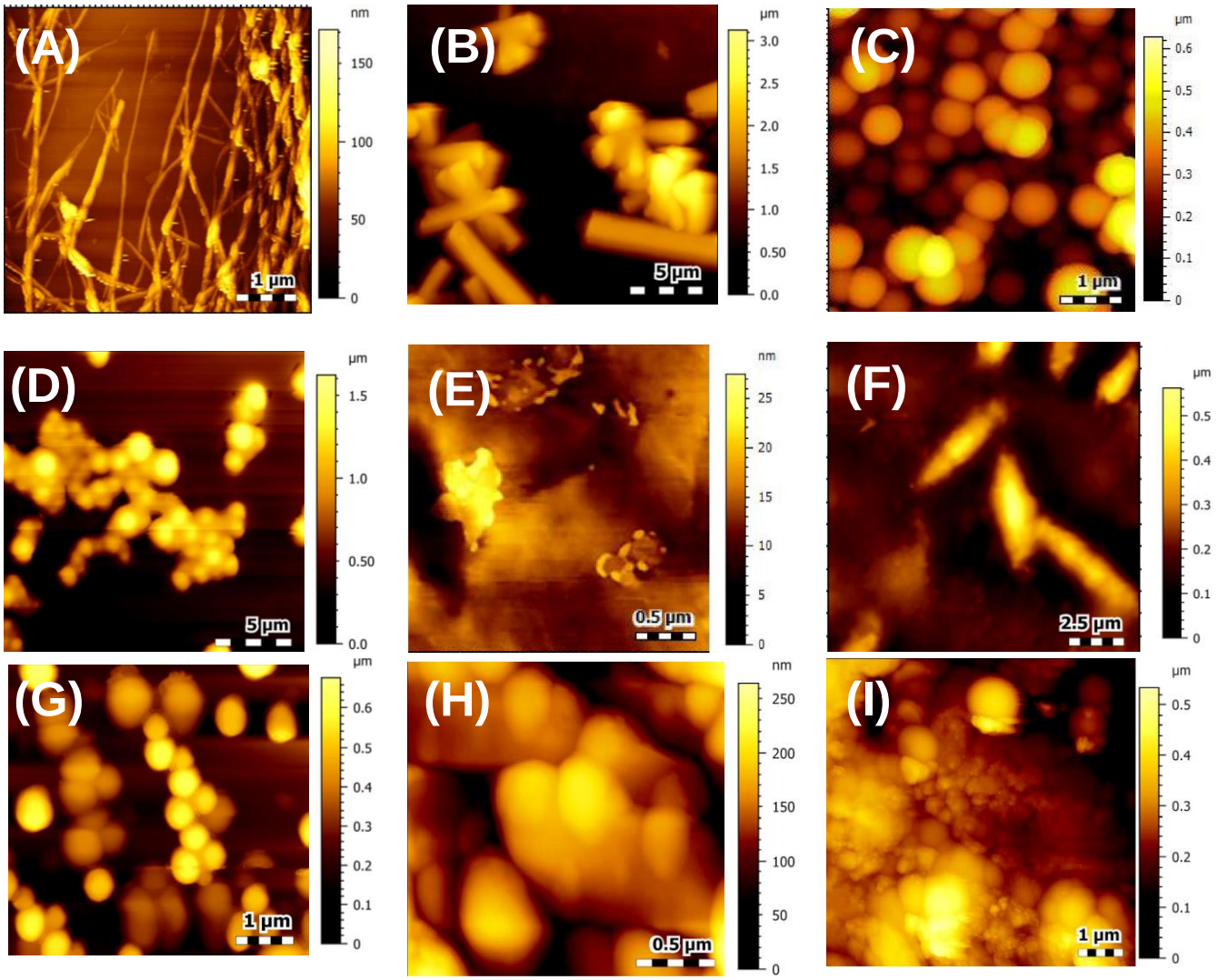


Figure S30: AFM topography images of (A) fibrous dipeptide **2** (Boc-Phe-Phe-Propyne), (B) rod-like dipeptide **4** (Boc-Leu-Leu-Propyne), (C) perfect spheres of peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), (D) agglomerated spheres of peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}), (E) fully deprotected peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}), (F) spindle like peptide **10** (Boc-Leu-Leu-*tz*-$A^{N(Boc)_2}$), (G) spherical peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$), (H) peptide **15** (Boc-Phe-Phe-*tz*-T) and (I) peptide **16** (Boc-Phe-Phe-*tz*-T).

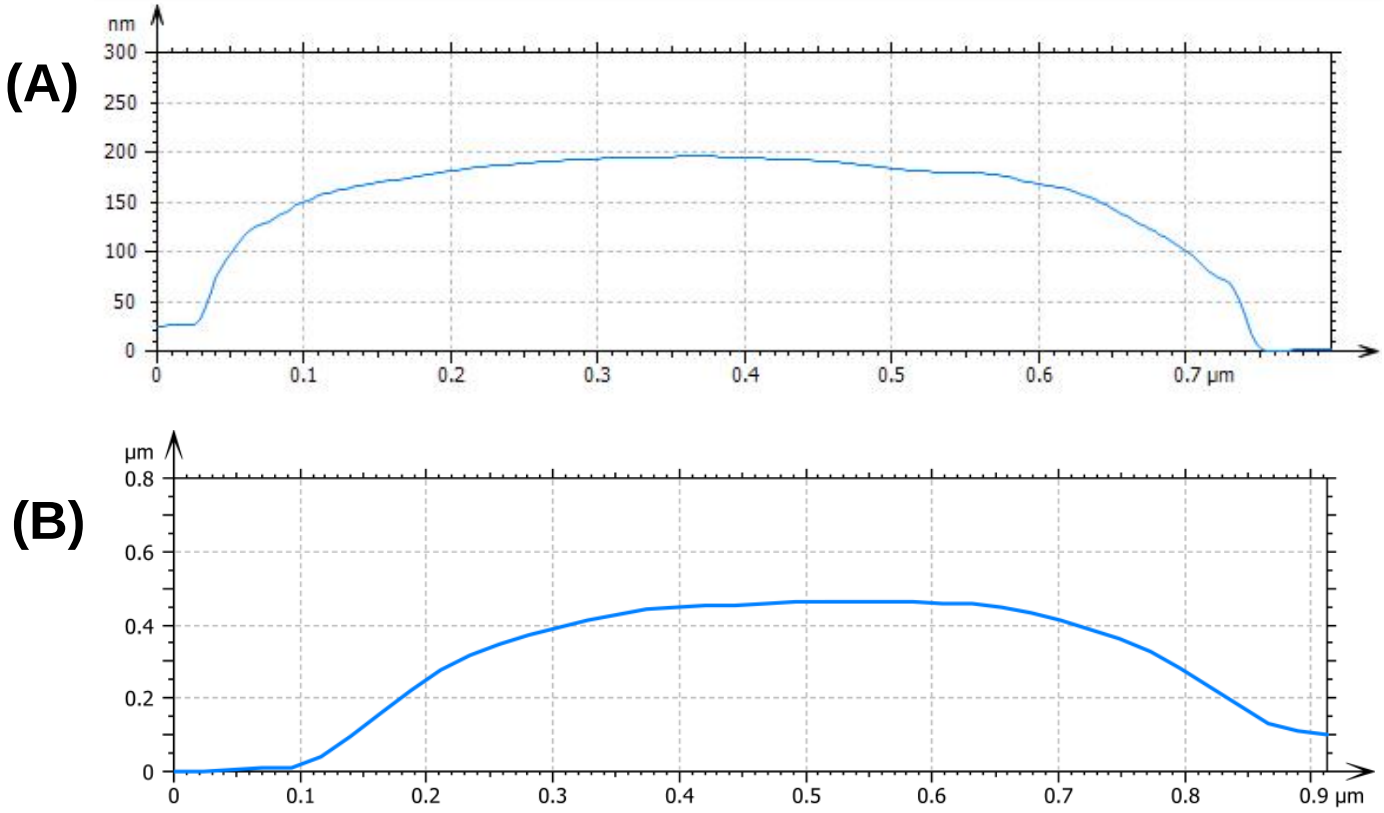


Figure S31: Height profiles diagrams of perfect spheres of **(A)** peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), **(B)** peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$) obtained from AFM.

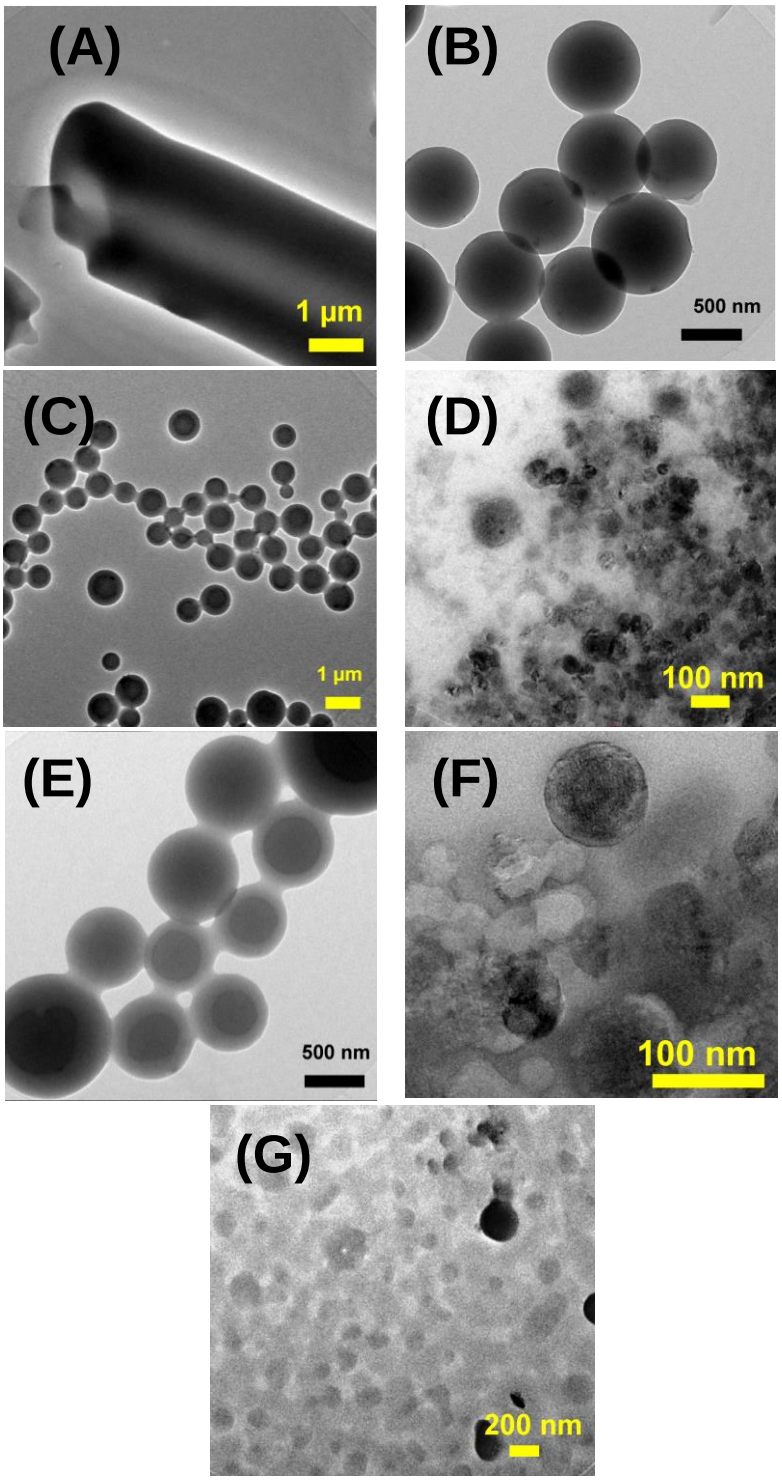


Figure S32: HRTEM images of (A) dipeptide **4** (Boc-Leu-Leu-Propyne) showing hollow tubular stucture**,** (B) solid spheres of peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), (C) interlinked spheres of peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}), (D) fully deprotected peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}), (E) interlinked spherical peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$), (F) peptide **15** (Boc-Phe-Phe-*tz*-U) and (G) peptide **16** (Boc-Phe-Phe-*tz*-T).

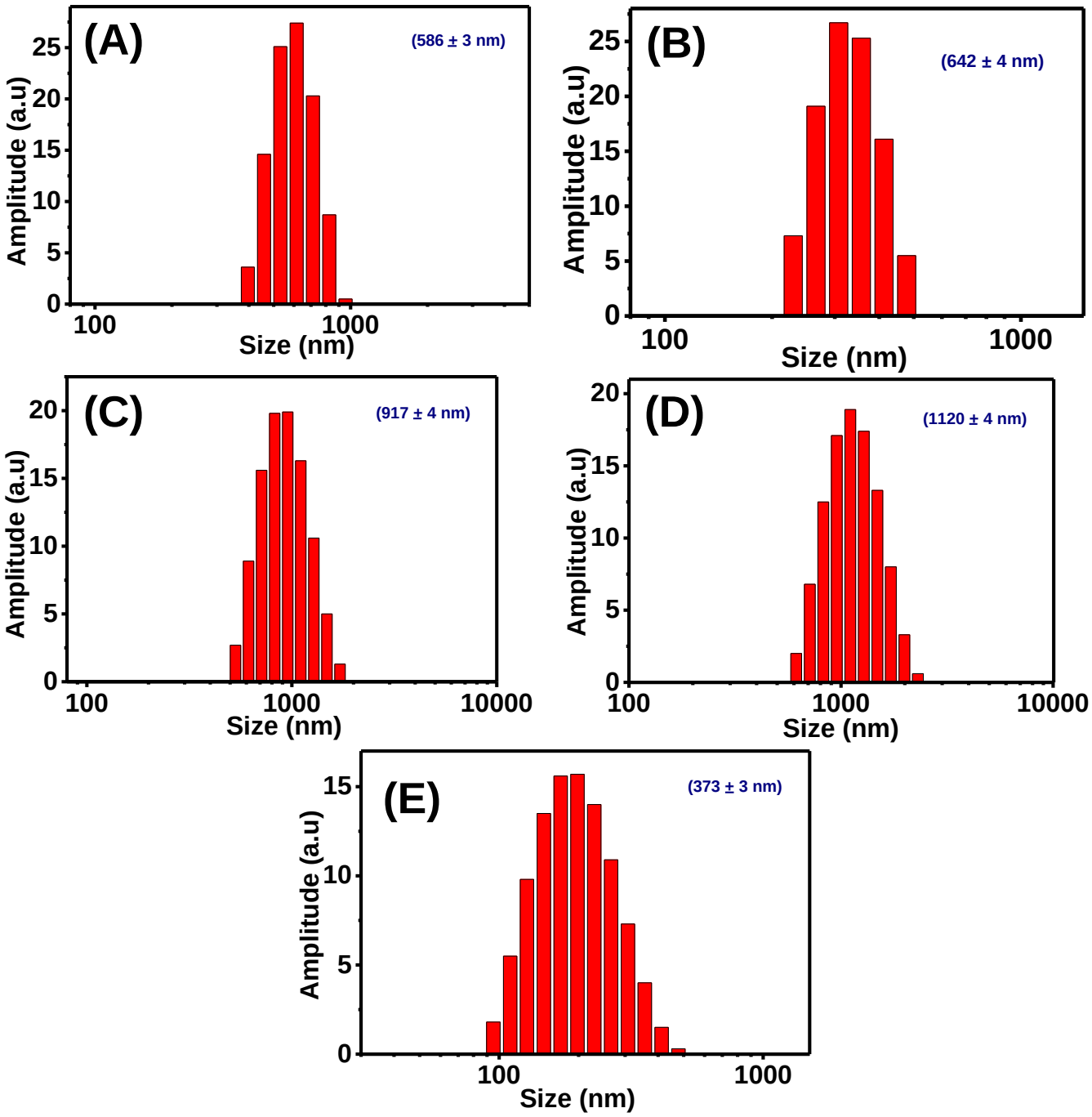


Figure S33: DLS spectra of (A) peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$) without lyophilization (PDI = 0.015), (B) peptide **7** after lyophilization (PDI = 0.012), (C) peptide **7** with higher concentration (4 mg/mL, PDI = 0.142), (D) peptide **7** after 10 days of incubation (PDI = 0.224), (E) peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$) (PDI = 0.168).

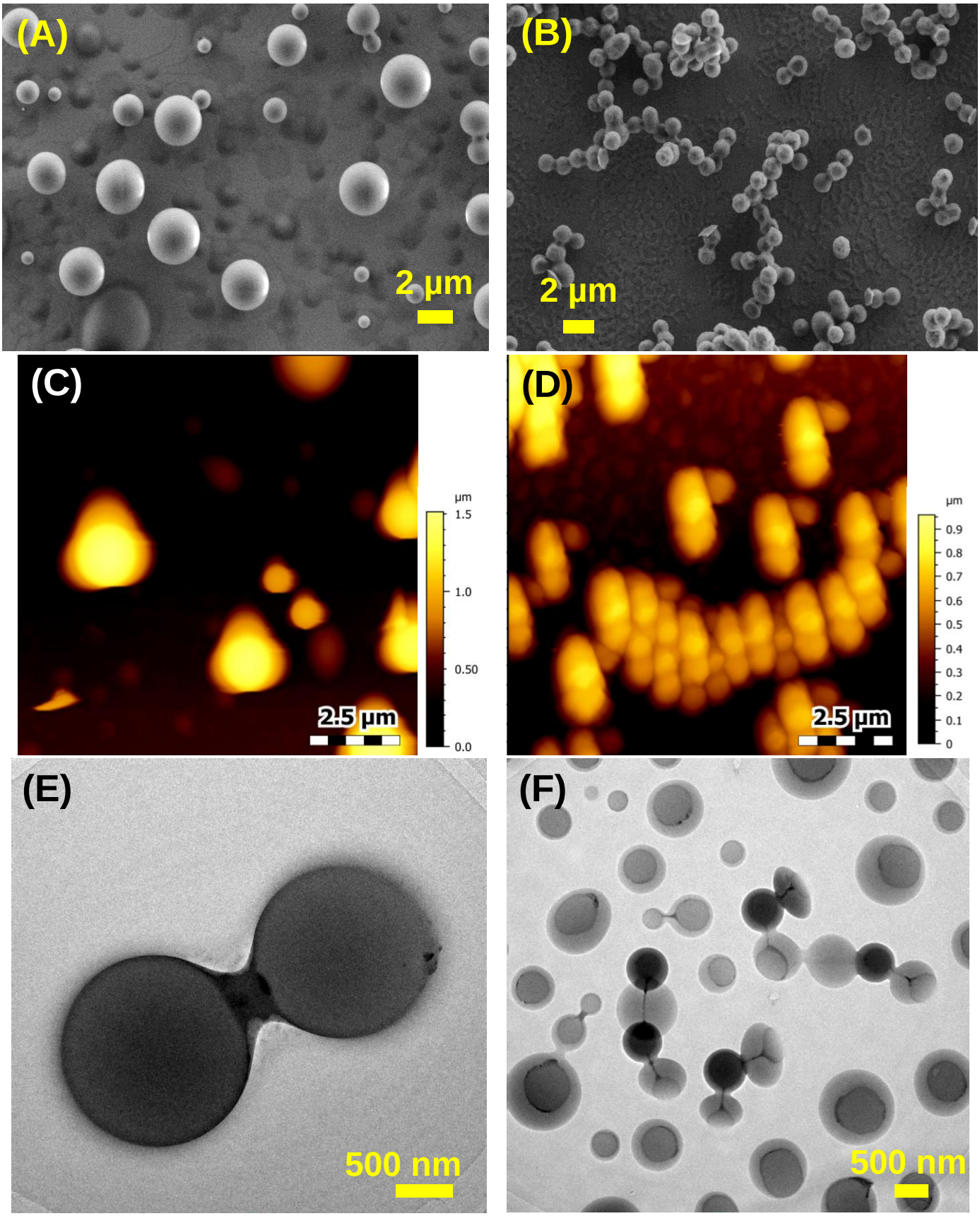


Figure S34: SEM (A), AFM (C) and HRTEM (E) images of peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$) with higher concentration (4 mg / mL) and SEM (B), AFM (D) and HRTEM (F) images of peptide **7** after 10 days of incubation respectively. Necklace formations are evident from SEM, AFM and HRTEM (Figure S24:B,D and F).

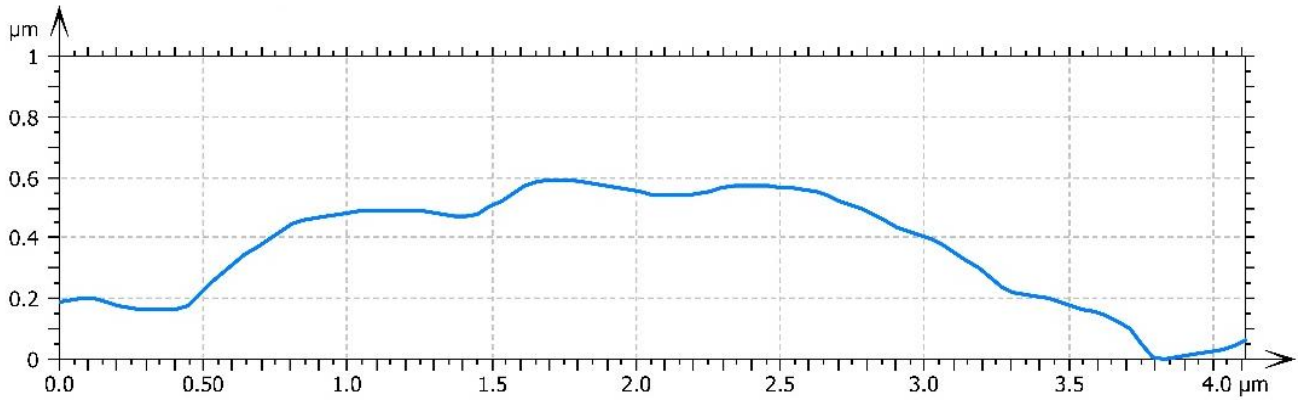


Figure S35: Height profiles diagrams of **(B)** aggregated peptide **7** (Boc-Phe-Phe-*tz*-A$^{N(Boc)_2}$) after 10 days of incubation obtained from AFM.

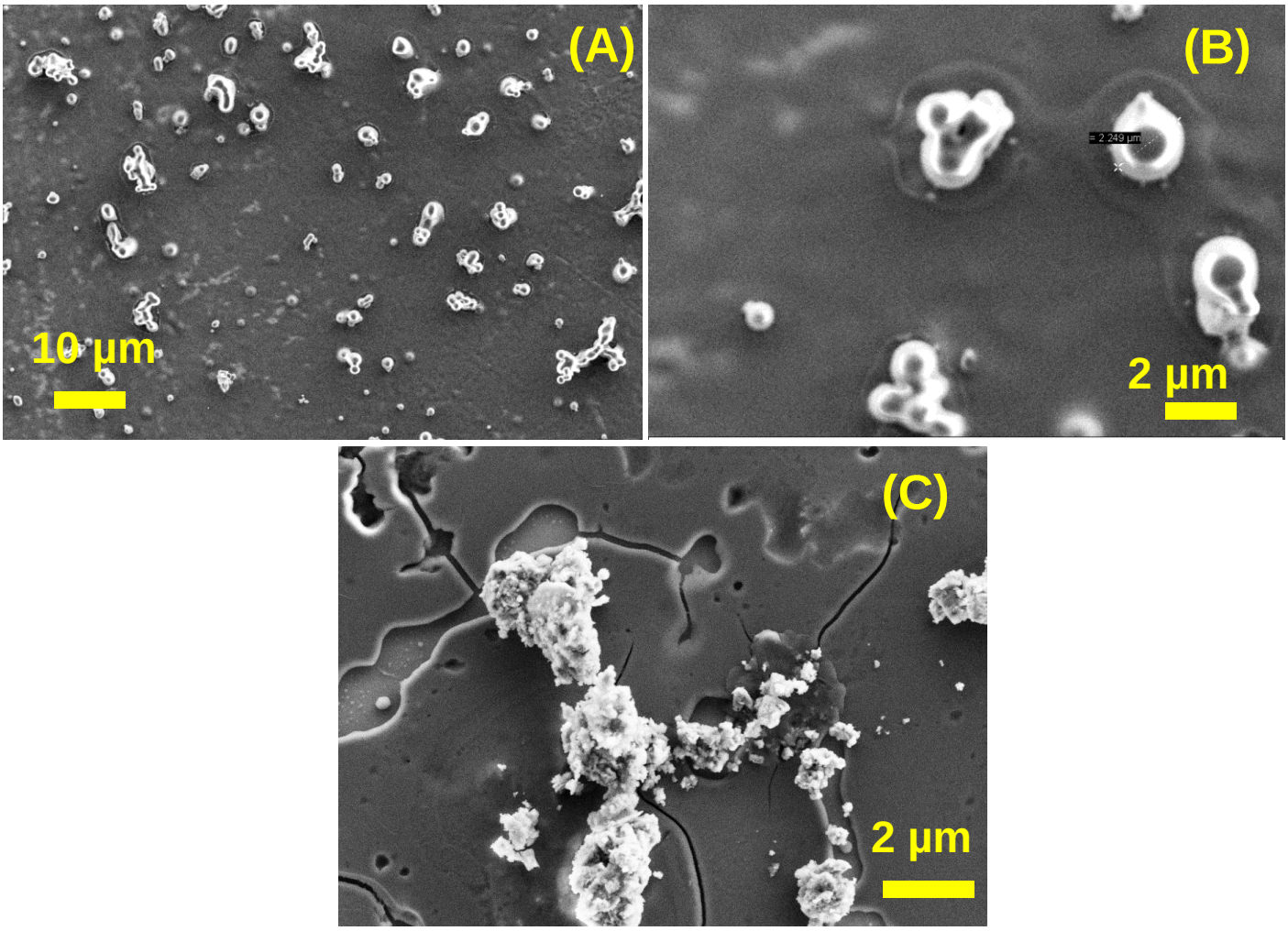


Figure S36: SEM images of (A), (B) peptide **8** (Boc-Phe-Phe-*tz*-A^{NH_2}) and (C) peptide **9** (H-Phe-Phe-*tz*-A^{NH_2}) with higher concentration (4 mg / mL)

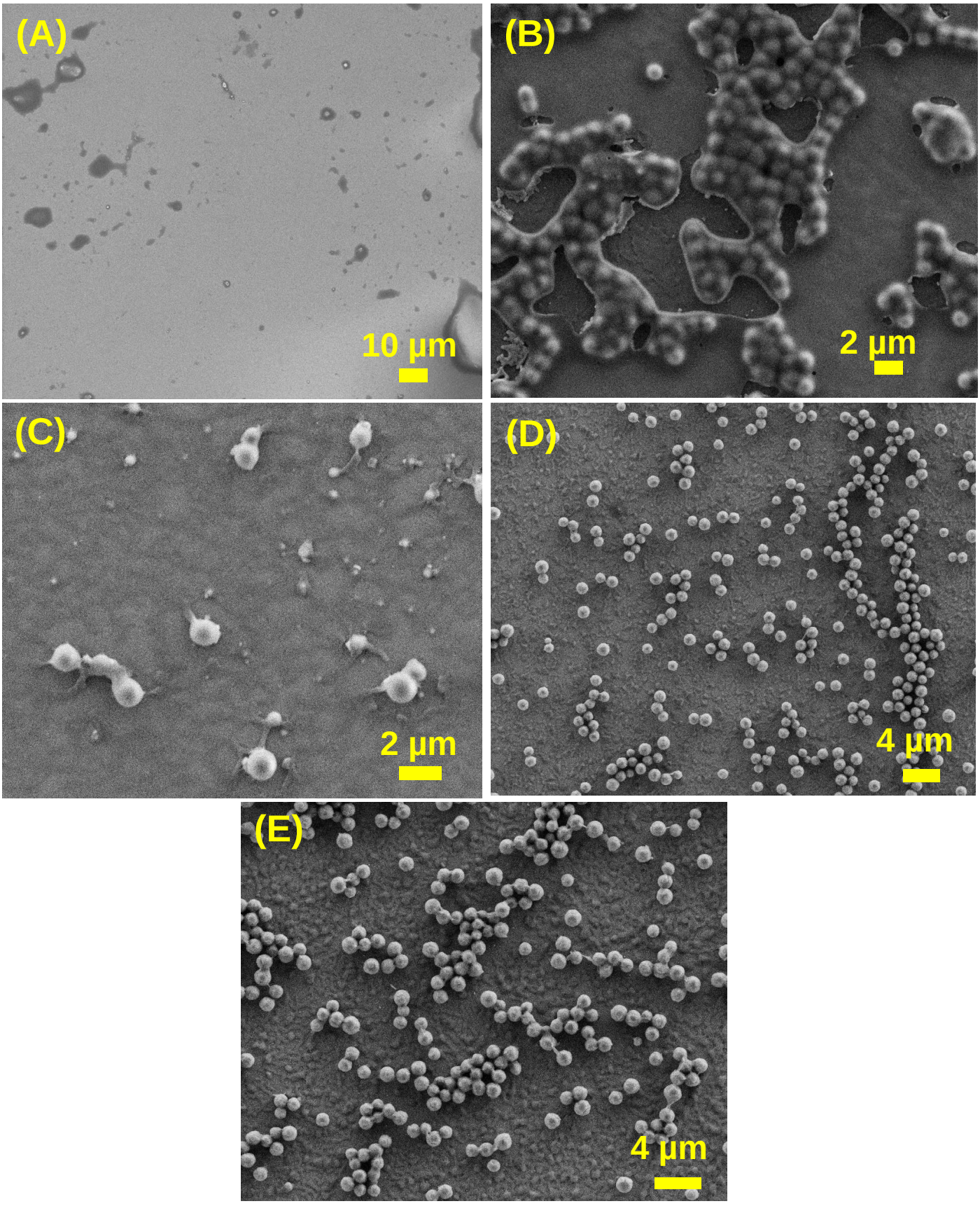


Figure S37: SEM images of peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$) (A) at pH 2, (B) at pH 6, (C) at pH 10, (D) after heating at 100 ^{o}C, (E) after heating at 200 ^{o}C

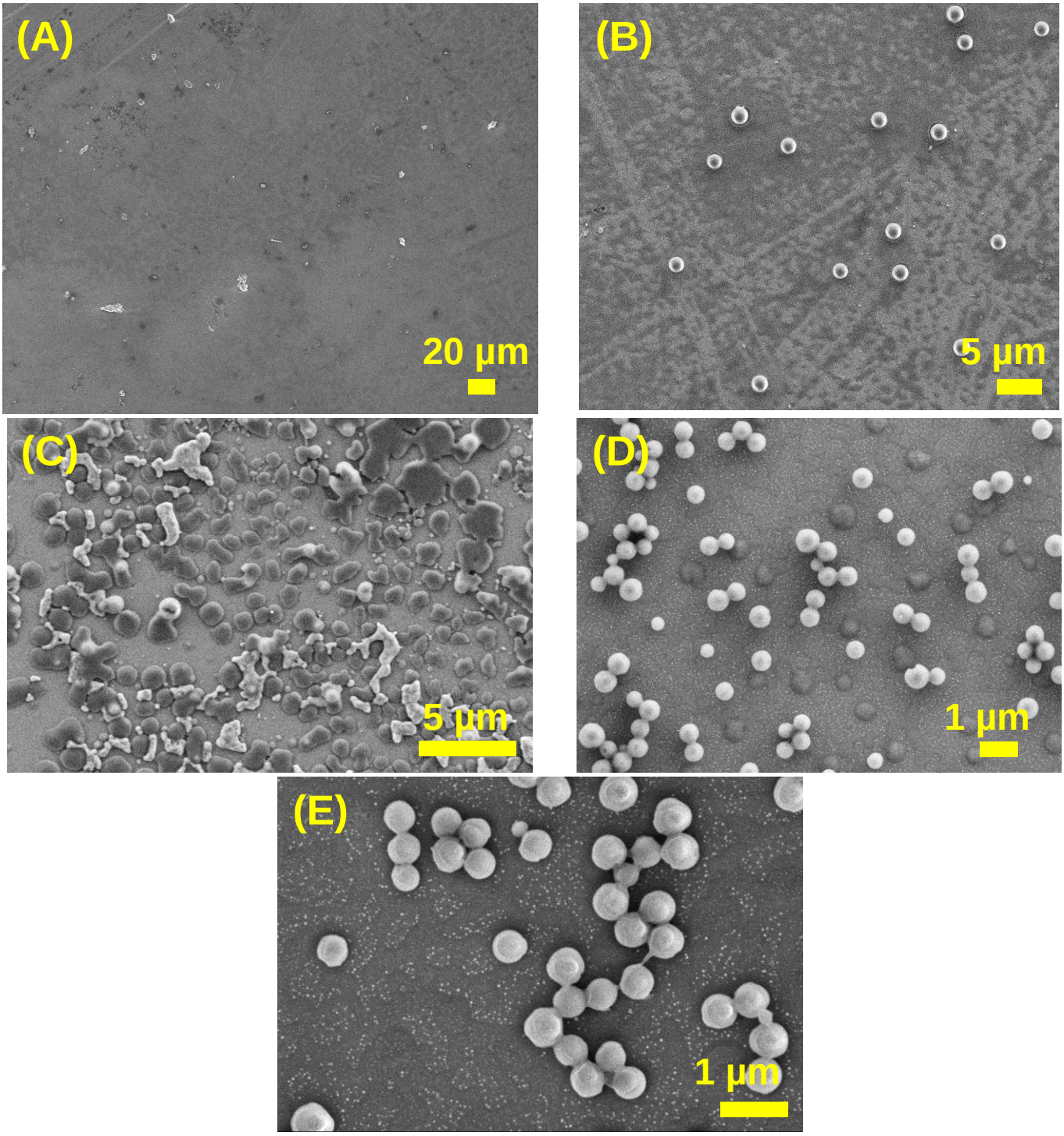


Figure S38: SEM images of peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$) (A) at pH 2, (B) at pH 6, (C) at pH 10, (D) after heating at 100 ^{o}C, (E) after heating at 200 ^{o}C.

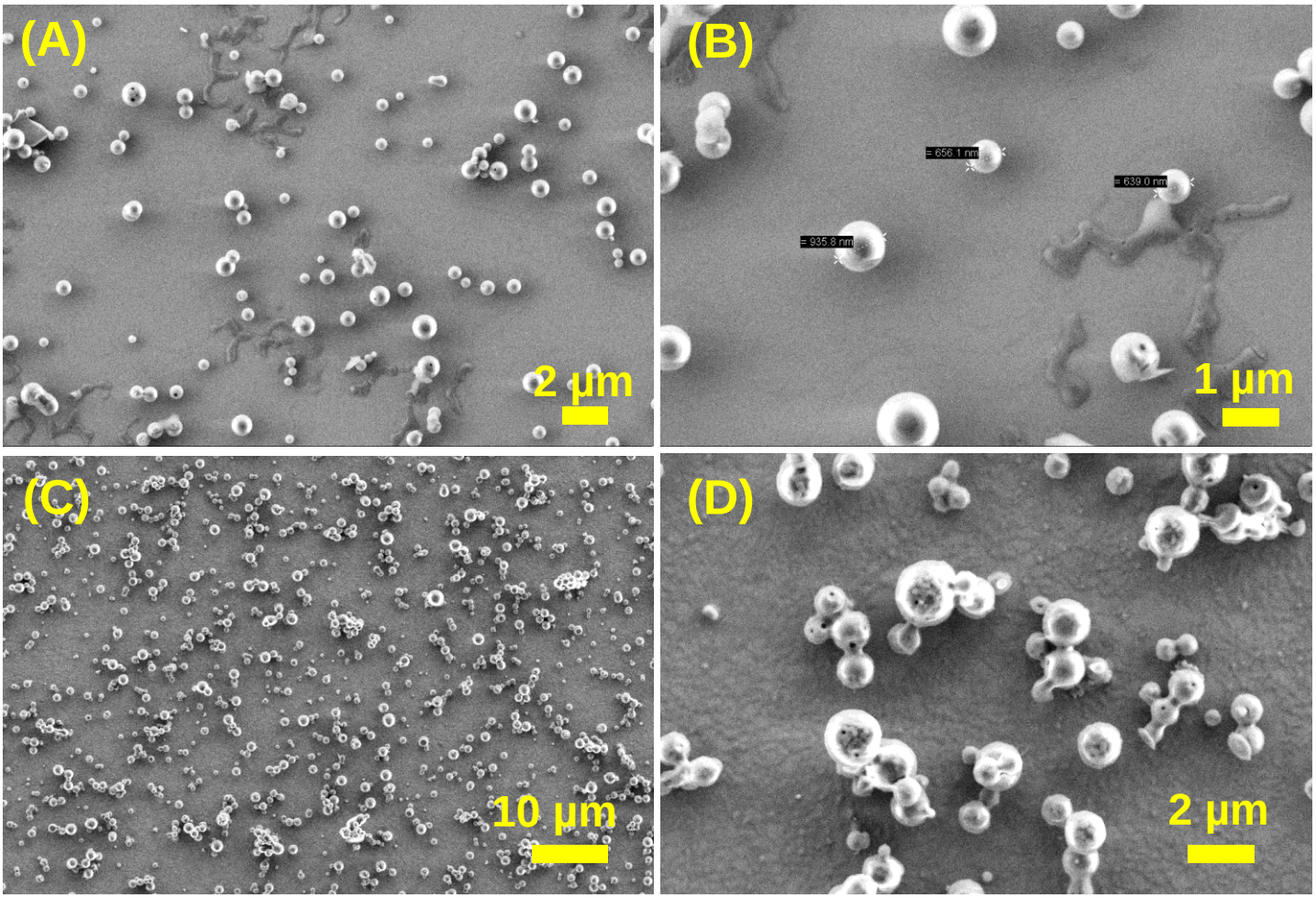


Figure S39: SEM images of peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$) (A), (B) after addition of 1.0 equiv. of $Zn(NO_3)_2$ and (C), (D) after addition of 1.0 equiv. of $Cu(NO_3)_2$.

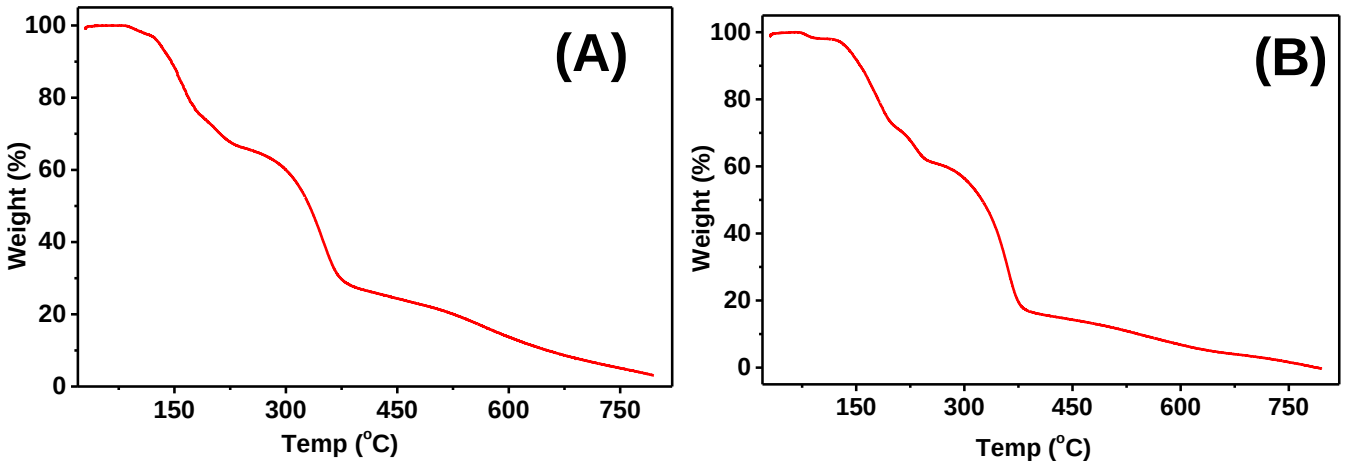


Figure S40: TGA of (A) peptide **7** (Boc-Phe-Phe-*tz*-A$^{N(Boc)_2}$) and (B) peptide **12** (Boc-Phe-Phe-*am*-A$^{N(Boc)_2}$).

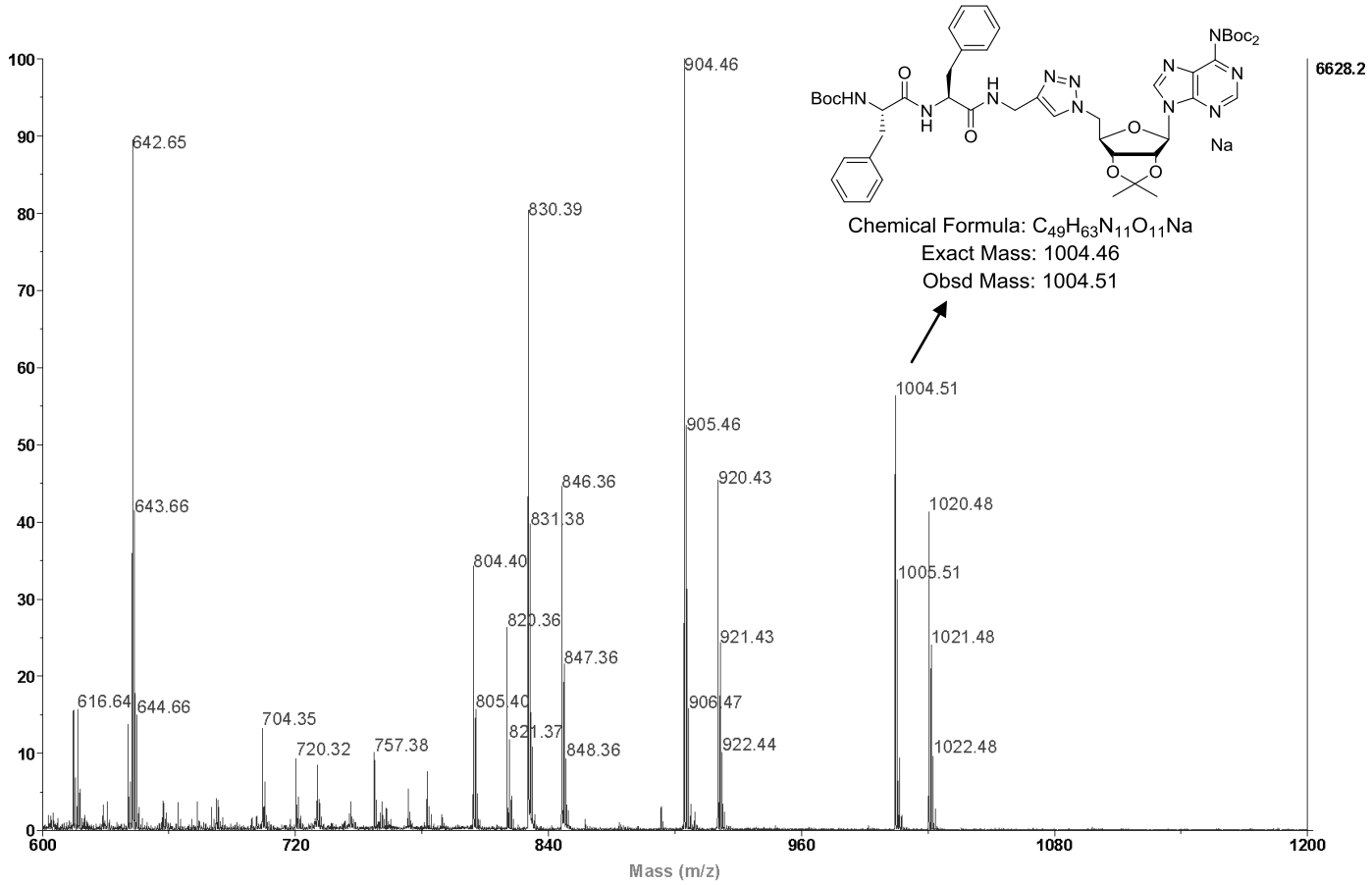


Figure S41: MALDI spectrum after thermal stability experiment of peptide **7** (Boc-Phe-Phe-*tz*-A$^{N(Boc)_2}$)

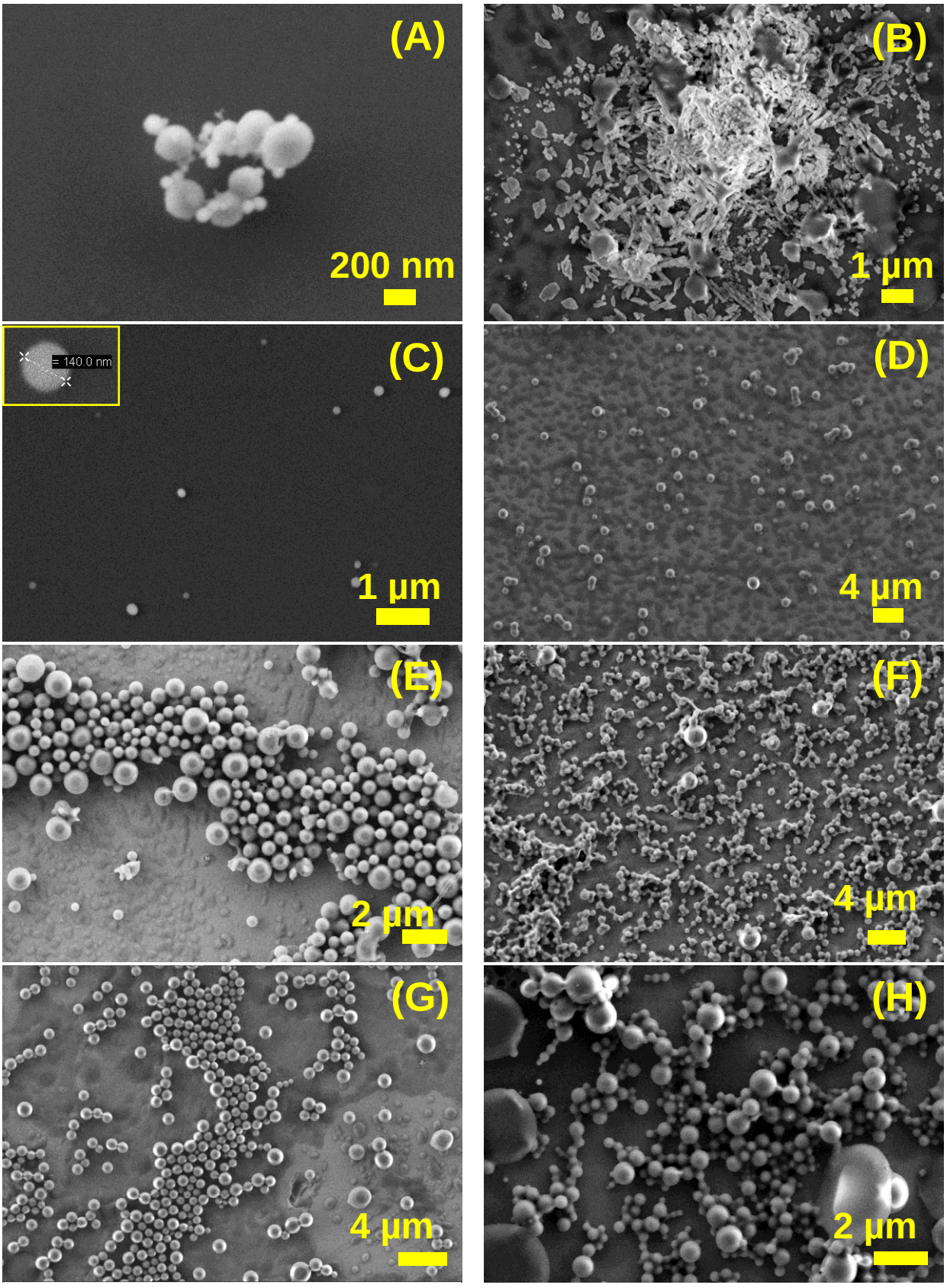


Figure S42: Solvent dependent morphology in SEM images of peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$): (A) in toluene, (B) in isopropyl alcohol, (C) in HFIP, (D) in ethanol, (E) in 7:1 MeOH and water, (F) in 1:1 MeOH and water, (G) in 1:1 $CHCl_3$ and MeOH, and (H) in 1:1 THF and water.

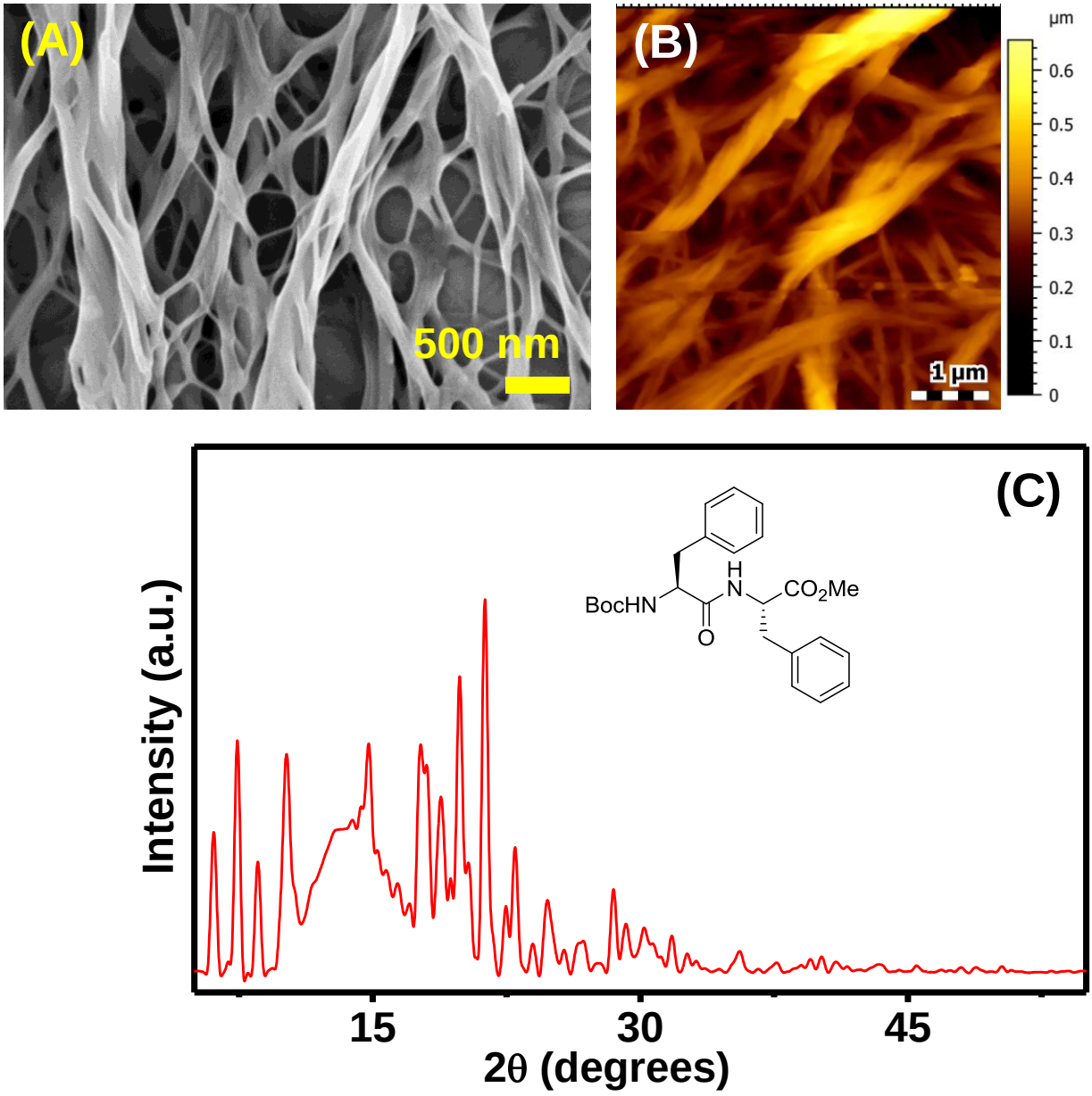


Figure S43: SEM image (A), AFM image (B) and PXRD pattern (C) of BocPhePheOMe in 1:1 ethanol and water after lyophilization in HFIP.

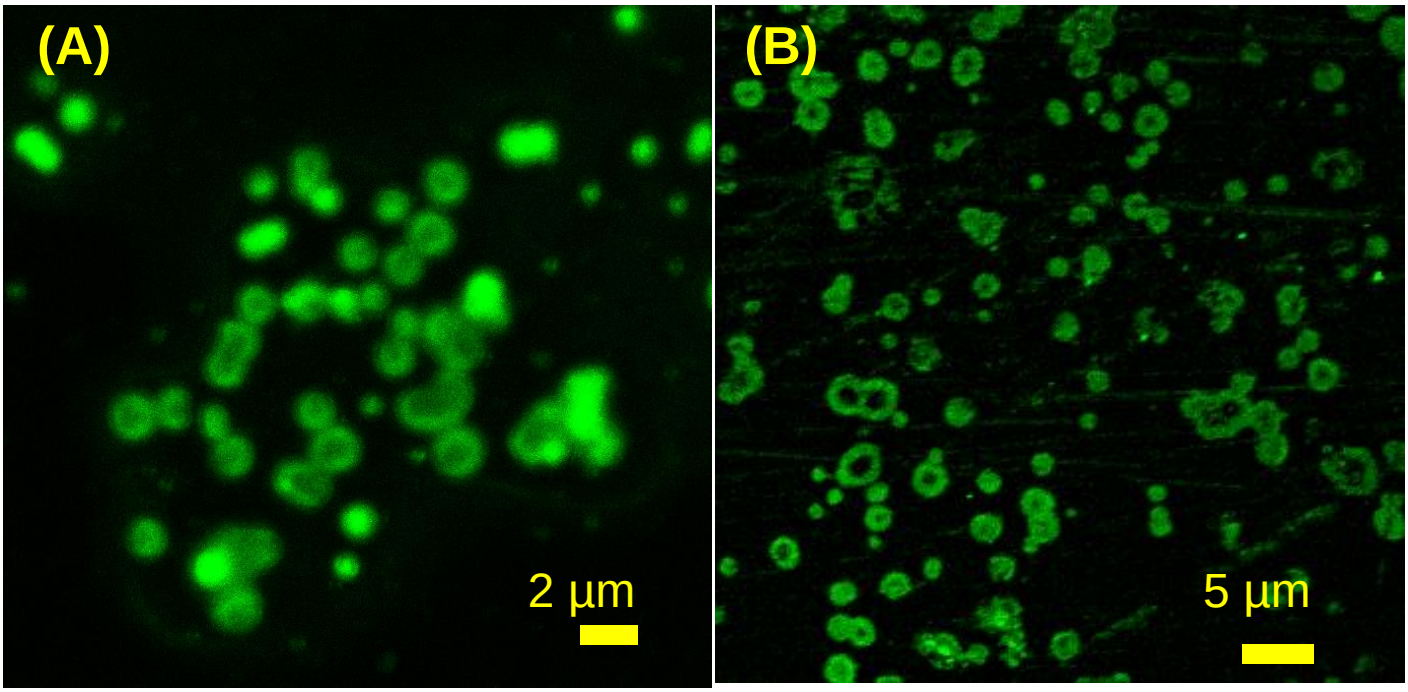


Figure S44: Confocal microscope images of fluorescent dye encapsulated (A, B) peptide **7 (**Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$).

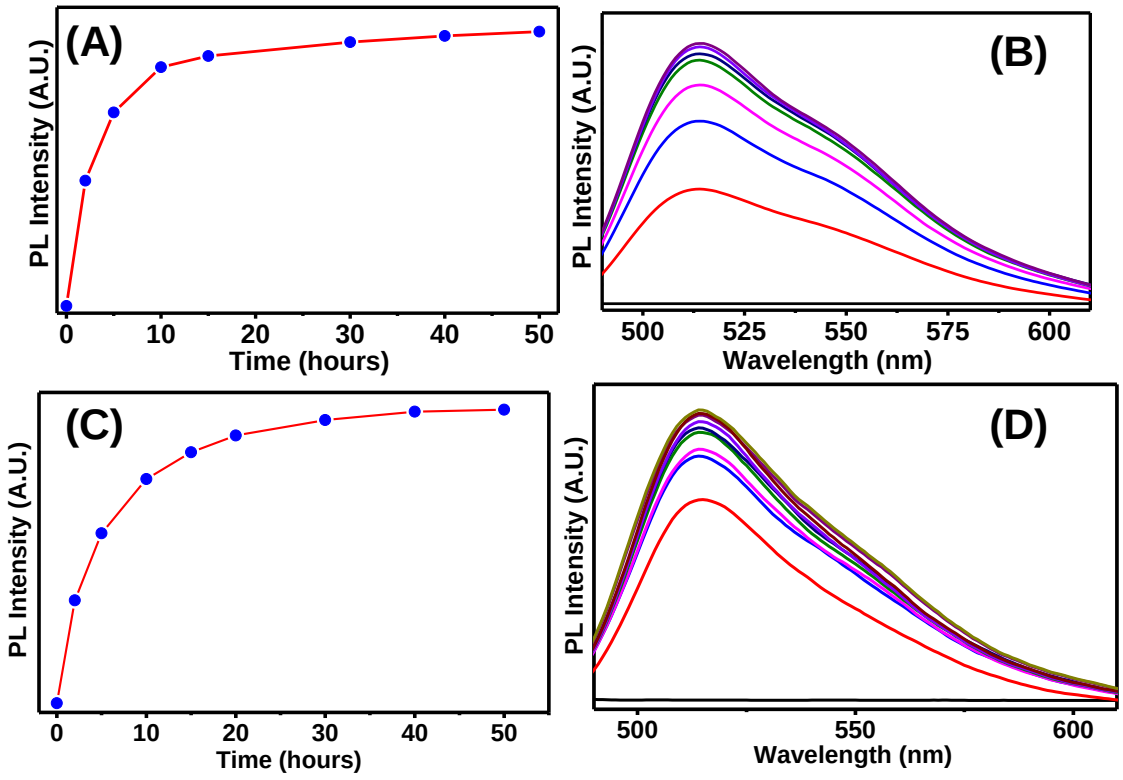
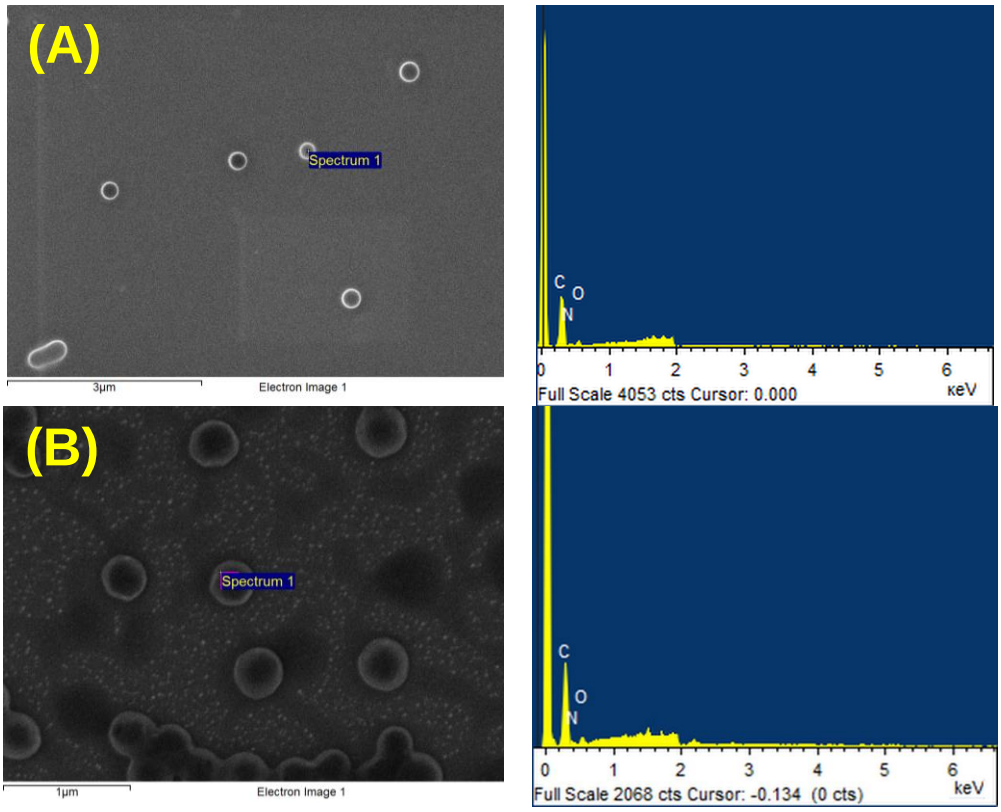


Figure S45: The increasing fluorescence intensity of the solution outside the dialysis tube containing **CF** encapsulated peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), after the addition of 3 eq. of (A) dicationic peptide (BocLysLysOMe) and (C) arginine into dialysis tube (λ_{ex} = 417nm). Fluorescence emission spectra of carboxyfluorescein (at 517 nm) showing increasing intensity after the addition of (B) dicationic peptide and (D) arginine into **CF** encapsulated peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$).

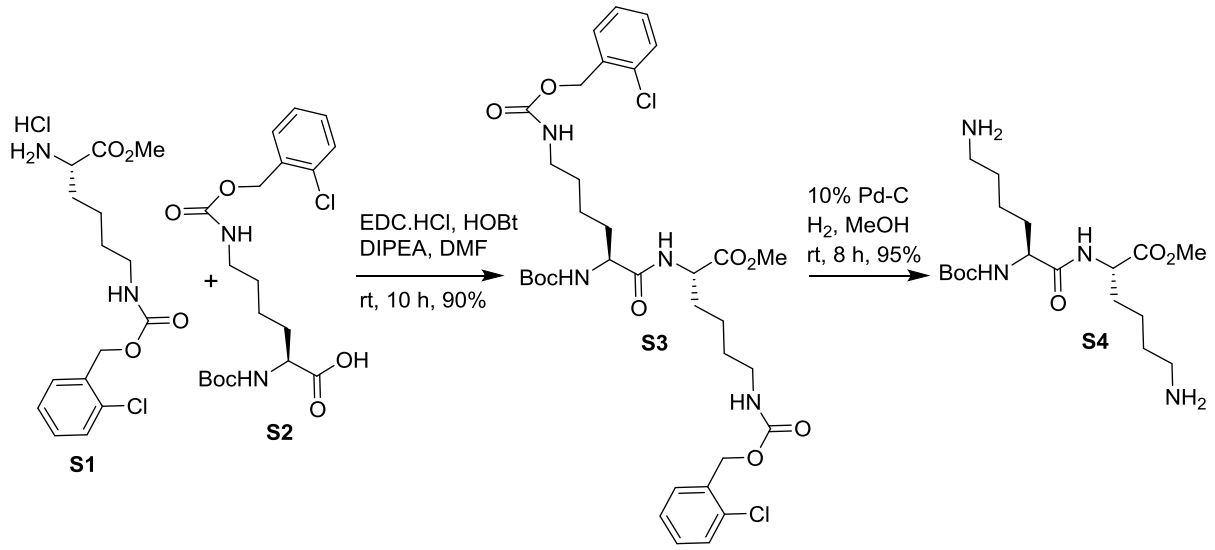


C K	49.74	54.83
N K	30.51	28.83
O K	19.75	16.34
Totals	100.00	

C K	49.51	54.35
N K	34.46	32.44
O K	16.03	13.21
Totals	100.00	

Figure S46: EDX images of (A) peptide **7** (Boc-Phe-Phe-*tz*-$A^{N(Boc)_2}$), and (B) peptide **12** (Boc-Phe-Phe-*am*-$A^{N(Boc)_2}$).

Synthesis of dicationic peptide Boc-(L)-Lys-(L)-Lys-OMe:



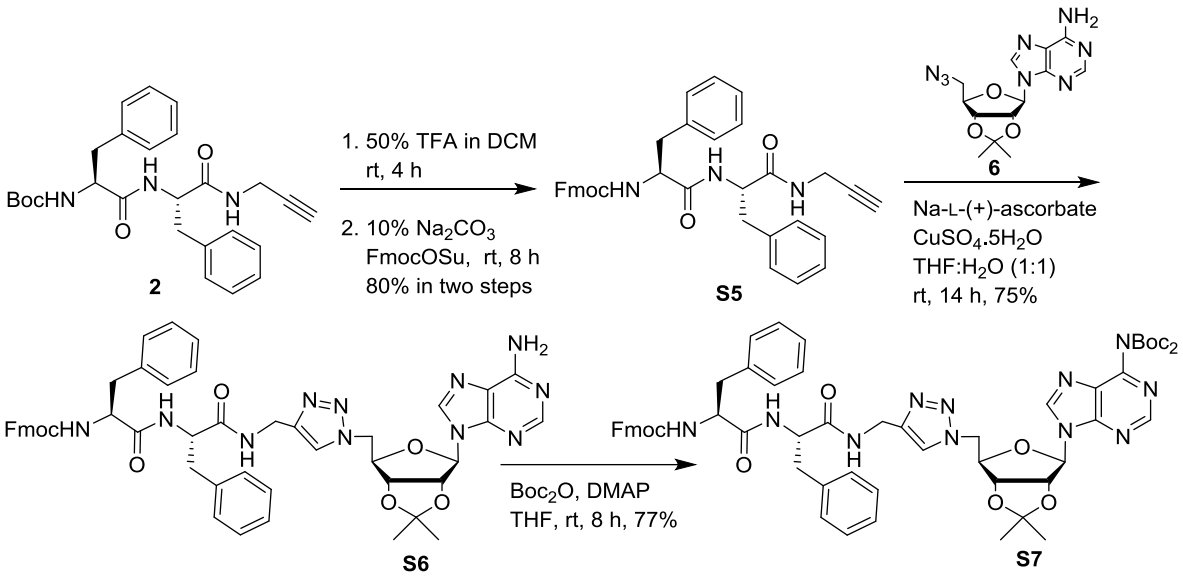
Scheme S1: Synthesis of dicationic peptide **S4**

Dicationic peptide **S4** [Boc-(L)-Lys-(L)-Lys-OMe] was synthesized after minor modification of the known procedure.[1,2] Commercially available (L)-Lys(*O*-Cl-Cbz)-OMe.HCl (**S1**; 0.44 gm, 1.20 mmol) and Boc-(L)-Lys(*O*-Cl-Cbz)-OH (**S2**; 0.50 gm, 1.20 mmol) were dissolved in dry DMF (10 mL). Diisopropylethylamine (DIPEA) (0.41 mL, 3.00 mmol) was added to the mixture and cooled to 0 °C in an ice bath. HOBt (0.16 gm, 1.20 mmol) and EDC.HCl (0.22 gm, 1.20 mmol) were added in portions into the reaction mixture and the reaction mixture was stirred for 1 h at 0 °C and kept at room temperature for overnight. EtOAc (100 mL) was added in to the reaction mixture. The organic layer was then washed successively with H_2O (100 mL), 10% aqueous solution of $NaHCO_3$ (100 mL), 10% aqueous solution of citric acid (100mL), and with brine (300 mL). The organic layer was dried over anhyd Na_2SO_4 and then evaporated under reduced pressure to give **S3** as a colorless viscous compound which was purified by flash column chromatography. The spectral data (NMR and HRMS) corresponded to the desired protected dipeptide **S3** (0.79 gm, 90% with respect to **S2**). ^{1}H NMR, 400 MHz ($CDCl_3$, 25°C, TMS): δ = 7.42-7.36 (m, 4H), 7.26-7.24 (m, 4H), 6.74 (brs, 1H), 5.25-5.17 (m, 5H), 5.09 (brs, 1H), 4.58-4.53 (m, 1H), 4.11-4.09 (m, 1H), 3.70 (s, 3H), 3.22-3.11 (m, 4H), 1.85-1.80 (m, 2H), 1.70-1.66 (m, 2H), 1.64-1.60 (m, 4H), 1.54-1.35 ppm (m, 13H); ^{13}C NMR, 100 MHz ($CDCl_3$, 25°C, TMS) δ = 172.8, 172.4, 156.6, 156.0, 134.5, 134.4, 133.8, 133.7, 130.1, 130.0, 129.7, 129.5, 127.1, 80.3, 64.1, 54.4, 52.7, 52.0, 40.6, 32.0, 31.7, 29.5, 29.3, 28.5, 22.4 ppm. HRMS (ESI^+), m/z calculated for $(M+H)^+$ $C_{34}H_{47}Cl_2N_4O_9$: 725.2720, found: 725.2719.

To a mixture of **S3** (0.50 gm, 0.69 mmol) in MeOH (10 mL), Pd/C (10%) (50 mg) was added into a flask. The mixture was stirred under H_2 atmosphere for 8 h, filtered through Celite-545 and evaporated under reduced pressure. The residue was then co-evaporated with CCl_4 and dried under high vacuum to afford peptide **S4** as a white solid (0.254 gm, 95%). Mp 226-228 °C (decomposes); ^{1}H NMR 400 MHz (DMSO-d_6, 25°C) δ =

8.31 (d, *J* = 7.3 Hz, 1H), 8.06 (s, 4H), 6.85 (d, *J* = 8.1 Hz, 1H), 4.23-4.14 (m, 1H), 4.02-3.86 (m, 1H), 3.61 (s, 3H), 2.79-2.66 (m, 4H), 1.68-1.43 (m, 8H), 1.37-1.28 ppm(m, 13H); ^{13}C NMR, 100 MHz (DMSO-d_6, 25°C): δ = 172.4, 155.3, 77.8, 53.8, 51.8, 51.7, 38.4, 38.3, 31.2, 30.1, 28.2, 26.5, 26.4, 23.2, 22.3, 22.1 ppm. HRMS (ESI$^+$), m/z calculated for $(M+H)^+$ $C_{18}H_{37}N_4O_5$: 389.2764, found: 389.2756.

Synthesis of Fmoc-Phe-Phe-*tz*-A$^{N(Boc)_2}$ (S7):



Scheme S2: Synthesis of Fmoc-Phe-Phe-*tz*-A$^{N(Boc)_2}$ (**S7**)

Compound **2** (1.0 g, 2.23 mmol) was stirred with trifluoroacetic acid (TFA) in DCM (20%, 10 mL) at room temperature. After 4 h, the volatile matters were evaporated to dryness under reduced pressure and residual liquid was co-evaporated with toluene (2x5 mL). The residue, thus obtained was subjected for next reaction without further purification. HRMS (ESI$^+$), m/z calculated for $(M+H)^+$ $C_{21}H_{24}N_3O_2$: 350.1868, found: 350.1869.

To a mixture of 10% Na_2CO_3 solution (15 mL) and the crude residue, FmocOSu (0.83 gm, 2.45 mmol) was added slowly in portions at 0 °C and then kept at room temperature for 8 h. The reaction mixture was then acidified with satd $KHSO_4$ solution to adjust the pH between 4-5. The resulting aq solution was washed with EtOAc (20 X 3 mL). The combined organic layer was then washed successively with H_2O (50 X 2 mL) and with brine (30 X 3 mL). Organic layer was dried over anhyd Na_2SO_4 and then evaporated under reduced pressure to give **S3** as a white compound which was purified by column chromatography to obtain compound **S5** (1.02 g, 80% with respect to **2**) [Eluent: 0-5% of MeOH in DCM] as hygroscopic solid; ^{1}H NMR 400 MHz (DMSO-d_6, 25°C) δ = 8.46 (t, *J* = 5.4 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.40 (td, *J* = 7.4, 3.2 Hz, 2H), 7.33 – 7.26 (m, 2H), 7.24 – 7.22 (m, 8H), 7.19 – 7.13 (m, 2H), 4.51 (dd, *J* = 13.6, 8.3 Hz, 1H), 4.28 – 4.19 (m, 1H), 4.16 (dd, *J* = 14.4, 3.5 Hz, 1H), 4.13 – 4.07 (m, 2H), 3.93 – 3.80 (m, 2H), 3.15 (t, *J* = 2.5 Hz, 1H), 3.01 – 2.88 (m, 2H), 2.83 (dd, *J* = 13.7, 8.8 Hz, 1H), 2.70

ppm (dd, J = 13.7, 10.7 Hz, 1H); ^{13}C NMR, 100 MHz (DMSO-d_6, 25°C): δ = 171.3, 170.6, 155.6, 143.8, 143.7, 140.64, 138.1, 137.4, 129.3, 129.2, 128.1, 128.0, 127.6, 127.1, 126.3, 126.2, 125.3, 125.2, 120.1, 80.8, 73.2, 65.6, 56.0, 53.8, 46.5, 39.5, 37.8, 37.4, 28.0 ppm. HRMS (ESI$^+$), m/z calculated for $(M+H)^+$ $C_{36}H_{34}N_3O_4$: 572.2549, found: 572.2549.

A mixture of **S5** (0.57 g, 1.00 mmol), $CuSO_4.5H_2O$ (12 mg, 0.05 mmol) and sodium ascorbate (0.10 g, 0.5 mmol) were stirred in THF (6.0 mL). To the resulting suspension, azide **6** (0.36 g, 1.10 mmol) dissolved in THF (6.0 mL) was added. 10 mL distilled water was added to the reaction mixture and stirred at room temperature. After 12 h, EtOAc (20 mL) was added into it and aq layer was further washed with EtOAc (3 x 20 mL). Organic layer was separated, dried over anhyd Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The crude mass thus obtained, was purified by column chromatography [Eluent: 0-5% MeOH in DCM] to afford compound **S6** as white solid (0.69 g, 77% with respect to **S5**). Mp 130-133 °C; ^{1}H NMR 400 MHz (DMSO-d_6, 25°C) δ = 8.45 (t, J = 5.4 Hz, 1H), 8.33 (s, 1H), 8.23 (s, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.87 (d, J = 7.5 Hz, 2H), 7.59 (dt, J = 22.0, 8.4 Hz, 3H), 7.39 (t, J = 7.0 Hz, 4H), 7.34 – 7.08 (m, 13H), 6.24 (d, J = 1.8 Hz, 1H), 5.46 (dd, J = 6.3, 2.0 Hz, 1H), 5.15 (dd, J = 6.2, 3.3 Hz, 1H), 4.74 (dd, J = 14.0, 5.1 Hz, 1H), 4.63 (dd, J = 13.9, 7.8 Hz, 1H), 4.56 – 4.48 (m, 2H), 4.34 – 4.16 (m, 4H), 4.10 (dd, J = 14.4, 7.5 Hz, 2H), 2.94 (td, J = 14.3, 4.7 Hz, 2H), 2.82 (dd, J = 13.7, 8.4 Hz, 1H), 2.75 – 2.66 (m, 1H), 1.52 (s, 3H), 1.31 ppm (s, 3H); ^{13}C NMR, 100 MHz (DMSO-d_6, 25°C): δ = 171.2, 170.5, 156.2, 155.6, 152.8, 143.7, 143.7, 140.6, 138.0, 137.4, 129.3, 129.2, 129.2, 127.9, 127.6, 127.0, 126.2, 125.3, 125.2, 123.1, 120.0, 113.6, 89.1, 84.7, 83.3, 81.6, 79.2, 65.6, 56.0, 53.8, 51.1, 46.5, 39.5, 37.8, 37.4, 34.2, 26.9, 25.1 ppm. HRMS (ESI$^+$), m/z calculated for $(M+H)^+$ $C_{49}H_{50}N_{11}O_7$: 904.3894, found: 904.3903.

Fmoc-Phe-Phe-*tz*-A$^{N(Boc)_2}$ (S7): To a mixture of **S6** (0.63 g, 0.69 mmol) in dry THF (50 mL), DMAP (8 mg, 0.07 mmol) was added. To the stirred suspension was added Boc_2O (0.36 g, 1.66 mmol) under an Ar atmosphere. The reaction mixture was stirred for 8 h at room temperature, at which point TLC analysis indicated completion of the reaction. The excess amount of THF was evaporated under reduced pressure. The residue thus obtained was purified by column chromatography [Eluent: 20-70% EtOAc in hexane] to afford peptide **S7** as white solid (0.59 g, 77%). Mp 114-117 °C; ^{1}H NMR, 400 MHz ($CDCl_3$, 25°C) δ = 8.82 (s, 1H), 8.69 (t, J = 8.1 Hz, 0.5H), 8.42 (s, 0.5H), 8.03 (s, 1H), 7.81 – 7.62 (m, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.34 (d, J = 7.5 Hz, 2H), 7.26 – 7.13 (m, 7H), 7.04 (dd, J = 15.5, 8.3 Hz, 6H), 6.96 (d, J = 6.4 Hz, 1H), 6.13 – 5.95 (m, 2H), 5.82 (d, J = 7.2 Hz, 1H), 5.34 – 5.23 (m, 1H), 5.14 (dd, J = 6.4, 3.6 Hz, 1H), 4.73 – 4.41 (m, 6H), 4.36 – 4.22 (m, 3H), 4.17 – 3.99 (m, 2H), 2.97 – 2.88 (m, 4H), 2.68 (s, 1H), 1.52 – 1.51 (m, 8H), 1.47 – 1.37 (m, 13H), 1.29 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.1, 170.7, 156.1, 153.1, 152.3, 152.2, 150.8, 150.6, 150.2, 149.9, 144.7, 144.2, 143.8, 143.7, 141.9, 141.2, 136.4, 136.4, 129.4, 129.3, 128.6, 128.4, 127.7, 127.1, 127.0,

126.8, 125.2, 125.1, 123.4, 122.3, 120.0, 115.2, 115.1, 90.3, 85.1, 84.2, 83.8, 83.8, 82.3, 81.6, 77.5, 77.2, 76.8, 67.1, 56.2, 54.3, 51.3, 47.00, 38.3, 38.1, 34.8, 28.1, 27.8, 27.8, 27.1, 25.3 ppm. . HRMS (ESI^+), m/z calculated for $(M+H)^+$ $C_{59}H_{66}N_{11}O_{11}$: 1104.4940, found: 1104.4924.

References:

1. (a) H. Xu and D. M. Rudkevich, *Chem. Eur. J.*, 2004, **10**, 5432-5442; (b) D. M. Rudkevich, G. A. Woldemariam and H. Xu, *Polym. Prepr.*, 2005, **6**, 1162-1163.

2. V. Stastny, A. Anderson and D. M. Rudkevich, *J. Org. Chem.*, 2006, **71**, 8696-8705.