Supporting Information

Supramolecular helix of an oligomeric azapeptide building block containing four β-turn structures

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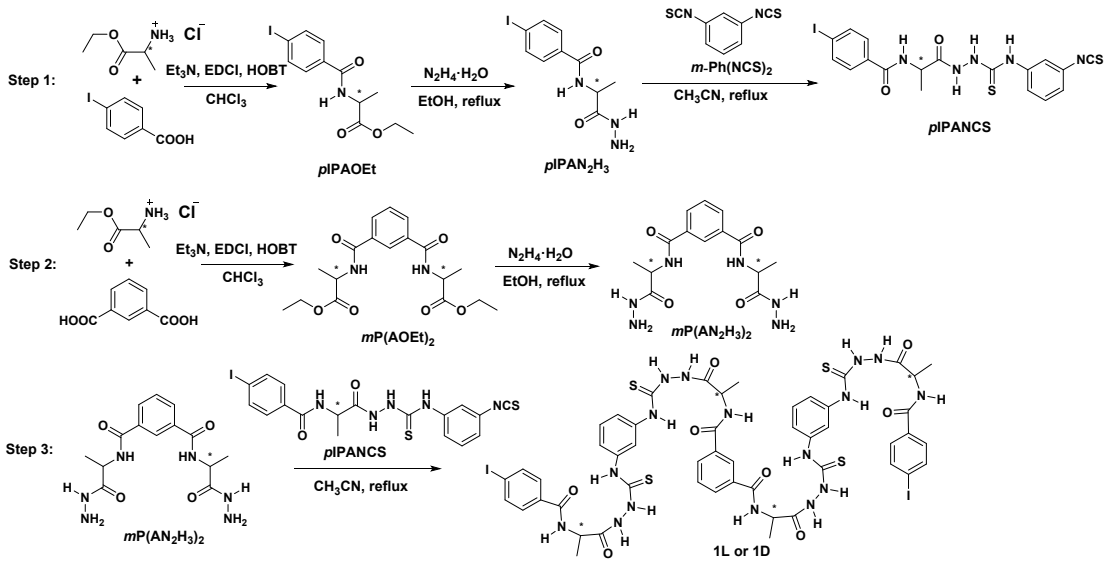
Content

1. General methods

^{1}H NMR, ^{13}C NMR and 2D NMR spectra were recorded on Bruker AV500 MHz, AV600 MHz or AV850 MHz spectrometer in dimethyl sulfoxide-D_6 (DMSO-d_6), acetonitrile-D_3 (CD_3CN) or their mixed solvents. High-resolution mass spectra (HR-MS) were obtained on a Bruker En Apex ultra 7.0 FT-MS. Absorption spectra were recorded on a Thermo Scientific Evolution 300 UV/Vis spectrophotometer. CD spectra were recorded with a JASCO J-1500 spectrometer. DLS data were collected on Malvern Zetasizer Nano-ZS90. SEM experiments were conducted on Hitachi S-4800 scanning electron microscope.

2. Syntheses and characterizations



Scheme S1. Syntheses of **1L** and **1D**.

***p*IPAN$_2$H$_3$:** *p*-Iodobenzoic acid (2.47 g, 10.0 mmol) was added to 60 mL $CHCl_3$, followed by the gradual addition of 1.5 mL Et_3N under the ice bath to obtain transparent solution. Then EDCI (2.11 g, 11.0 mmol) and HOBT (1.48 g, 11.0 mmol) were added and stirred for 30 min. L-or D-AOEt·HCl (1.50 g, 10.0 mmol) was added to the above solution. The reaction mixture was stirred at room temperature for 12 h. The solvent was removed by evaporated *in vacuo*, 20 mL ethyl acetate and 20 mL pure water were added in turn, and the organic phase was washed with dilute $NH_3·H_2O$ (0.1 M), dilute

HCl (0.1 M) and saturated NaCl solution for 3 times in turn, then was dried by anhydrous Na_2SO_4. The solvent was removed by evaporated *in vacuo* to afford white solid ***p*IPAOEt**. Next, excess $N_2H_4 \cdot H_2O$ (85%, 3.0 mL) was added to ***p*IPAOEt** in EtOH (50 mL) and the mixture was refluxed for 12 hours. Filtrating to remove the solvent, and the crude product was washed with EtOH and Et_2O several times to get white solid product ***p*IPAN$_2$H$_3$** (60% yield).

***p*IPANCS**: ***p*IPAN$_2$H$_3$** (0.333 g, 1.0 mmol) was gradually added to excess *m*-phenyldiisothiocyanate (0.384 g, 2.5 mmol) in CH_3CN (50 mL) and then refluxed for 24 h. The solvent was removed by filtration, and the crude product was washed with hot CH_3CN and Et_2O for several times, affording pure white solid product ***p*IPANCS** (50% yield).

***m*P(AN$_2$H$_3$)$_2$**: Isophthalic acid (1.67 g, 10.0 mmol) was added to 60 mL $CHCl_3$, and gradually add 3 mL Et_3N in the ice bat. Then EDCI (4.22 g, 22.0 mmol) and HOBT (2.97 g, 22.0 mmol) were added and stirred in the ice bath for 30 min. L-or D-AOEt·HCl (3.00 g, 10.0 mmol) was added to the above solution. The reaction mixture was stirred at room temperature for 12 h. The solvent was removed by evaporated *in vacuo*, 20 mL ethyl acetate and 20 mL pure water were added in turn, and the organic phase was washed with dilute $NH_3 \cdot H_2O$ (0.1 M), dilute HCl (0.1 M) and saturated NaCl solution for 3 times in turn, and was dried by anhydrous Na_2SO_4. The solvent was removed by evaporated *in vacuo*, affording a white solid ***m*P(AOEt)$_2$**. Excess $N_2H_4 \cdot H_2O$ (85%, 3.0 mL) was added to ***m*P(AOEt)$_2$** in EtOH (50 mL) and the mixture was refluxed for 12 hours. Filtrating to remove the solvent, and the crude product was washed with EtOH and Et_2O several times, producing white solid product ***m*P(AN$_2$H$_3$)$_2$** (60% yield).

1L: ***m*P(AN$_2$H$_3$)$_2$** (0.033 g, 0.1 mmol) was gradually added to ***p*IPANCS** (0.115 g, 0.22 mmol) dropwise in 30 mL CH_3CN and then refluxed for 48 h. The solvent was removed by filtration, and the crude product was washed with hot CH_3CN and Et_2O for several times, producing pure white solid product **1L** (67% yield). **1D** was similarly synthesized.

According to similar synthetic routes for **1L**, **2L-5L** (Fig. 1) were obtained. Replacing *p*-iodobenzoic acid with benzoic acid to generate **2L**; replacing the isophthalic acid with

terephthalic acid leads to **3L**; replacing *m*-phenyldiisothiocyanate with *p*-phenyldiisothiocyanate leads to **4L;** replacing isophthalic acid and *m*-phenyldiisothiocyanate with terephthalic acid and *p*-phenyldiisothiocyanate leads to **5L**.

1L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 10.40 (s, 1H), 9.73 (s, 1H), 9.25 (s, 1H), 8.99 (s, 1H), 7.89 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 5.8 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 7.16 (t, J = 7.1 Hz, 1H), 4.32 (s, 1H), 1.39 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) 180.19, 171.82, 166.93, 138.97, 137.24, 133.71, 132.66, 130.80, 129.75, 128.52, 127.70, 126.98, 121.35, 99.60, 49.25, 48.97, 16.92, 16.62. HRMS (ESI): calcd for $[C_{50}H_{52}I_2N_{16}O_8S_4Na]^+$: 1409.1018, found: 1409.1021.

1D: ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.40 (s, 4H), 9.75 (s, 4H), 9.31 (s, 4H), 8.97 (s, 4H), 8.41 (s, 1H), 8.03 (d, J = 6.5 Hz, 3H), 7.88 (d, J = 7.8 Hz, 4H), 7.71 (d, J = 7.0 Hz, 4H), 7.61 (s, 1H), 7.45 (s, 2H), 7.31 (s, 3H), 4.44 (s, 2H), 4.31 (s, 2H), 1.41 (d, J = 11.1 Hz, 11H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) 180.20, 171.83, 166.94, 138.98, 137.25, 133.71, 132.69, 130.82, 129.76, 128.53, 127.71, 127.00, 121.36, 99.59, 49.25, 16.93, 16.64. HRMS (ESI): calcd for $[C_{50}H_{52}I_2N_{16}O_8S_4Na]^+$: 1409.1018, found: 1409.1019.

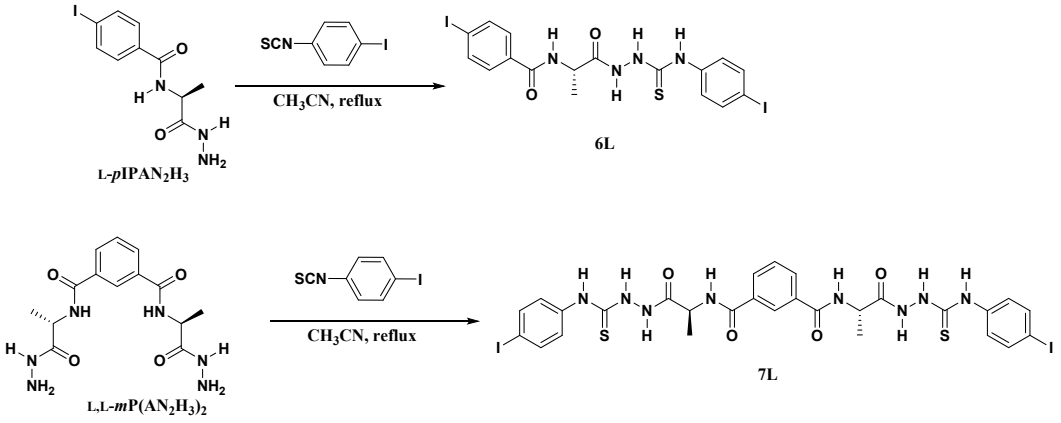
2L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 10.39 (s, 4H), 9.73 (s, 4H), 9.36 (s, 2H), 8.89 (s, 3H), 8.41 (s, 1H), 8.03 (d, J = 7.6 Hz, 3H), 7.92 (d, J = 7.4 Hz, 4H), 7.61 (d, J = 7.4 Hz, 1H), 7.53 (t, J = 7.2 Hz, 2H), 7.48 (t, J = 7.4 Hz, 4H), 7.42 (s, 2H), 7.31 (d, J = 6.9 Hz, 3H), 4.39 (d, J = 55.2 Hz, 4H), 1.41 (t, J = 8.1 Hz, 12H). ^{13}C NMR (214 MHz, DMSO-d_6) δ (ppm) 180.30, 171.81, 167.00, 138.91, 133.68, 133.19, 131.68, 130.78, 128.49, 128.32, 127.77, 126.95, 121.46, 48.91, 16.90, 16.59. HRMS (ESI): calcd for $[C_{50}H_{54}N_{16}O_8S_4Na]^+$: 1157.3086, found: 1157.3086.

3L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 10.40 (s, 4H), 9.73 (s, 4H), 9.28 (s, 4H), 8.98 (s, 4H), 7.97 (d, J = 9.5 Hz, 6H), 7.86 (dd, J = 8.0, 3.2 Hz, 4H), 7.67 (d, J = 8.0 Hz, 4H), 7.58 (s, 9H), 4.34 (s, 4H), 1.40 (d, J = 7.0 Hz, 12H). ^{13}C NMR (214 MHz, DMSO-d_6) δ (ppm) 180.20, 171.85, 166.84, 138.96, 137.23, 135.93, 132.62, 129.73, 127.68, 121.43, 99.59, 49.22, 16.68. HRMS (ESI): calcd for $[C_{50}H_{52}I_2N_{16}O_8S_4Na]^+$:

1409.1019, found: 1409.1019.

4L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 10.41 (s, 4H), 9.76 (s, 4H), 9.35 (s, 4H), 8.98 (s, 4H), 8.07 (s, 1H), 8.00 (s, 8H), 7.95 (s, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.31 (s, 6H), 4.38 (s, 4H), 1.41 (d, J = 5.7 Hz, 12H). ^{13}C NMR (214 MHz, DMSO-d_6) δ (ppm) 180.17, 171.83, 166.96, 137.21, 135.82, 133.88, 132.79, 130.65, 129.61, 128.34, 127.06, 124.35, 124.07, 99.56, 49.21, 16.89, 16.61. HRMS (ESI): calcd for $[C_{50}H_{52}I_2N_{16}O_8S_4Na]^+$: 1409.1019, found: 1409.1005.

5L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) δ 10.39 (s, 4H), 9.72 (s, 4H), 9.31 (s, 4H), 8.98 (s, 4H), 8.41 (s, 2H), 8.02 (s, 3H), 7.85 (d, J = 8.3 Hz, 3H), 7.67 (d, J = 6.9 Hz, 4H), 7.58 (s, 11H), 4.43 (s, 4H), 1.41 (dd, J = 13.2, 7.8 Hz, 12H). ^{13}C NMR (214 MHz, DMSO-d_6) δ (ppm) 180.17, 171.84, 166.82, 137.20, 135.79, 132.81, 129.59, 127.59, 124.06, 99.54, 49.18, 16.63. HRMS (ESI): calcd for $[C_{50}H_{52}I_2N_{16}O_8S_4Na]^+$: 1409.1019, found: 1409.1014.



Scheme S2. Syntheses of **6L** and **7L**.

6L: L-***p*IPAN$_2$H$_3$** (0.333 g, 1.0 mmol) was gradually added to 4-iodophenyl isothiocyanate (0.261 g, 1 mmol) dropwise in 50 mL CH_3CN and then refluxed for 12 h. The solvent was removed by filtration, and the crude product was washed with hot CH_3CN and Et_2O for several times to afford pure white solid product **6L** (81% yield).

7L: L,L-***m*P(AN$_2$H$_3$)$_2$** (0.336 g, 1.0 mmol) was gradually added to 4-iodophenyl isothiocyanate (0.574 g, 2.2 mmol) dropwise in 50 mL CH_3CN and then refluxed for

12 h. The solvent was removed by filtration, and the crude product was washed with hot CH_3CN and Et_2O for several times to afford pure white solid product **7L** (88% yield).

6L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 10.41 (s, 1H), 9.83 (s, 1H), 9.28 (s, 1H), 9.00 (s, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.69 (t, J = 7.6 Hz, 4H), 7.54 (s, 2H), 4.30 (s, 1H), 1.39 (d, J = 7.0 Hz, 3H). ^{13}C NMR (214 MHz, DMSO-d_6) δ (ppm) 179.95, 171.80, 166.99, 138.94, 137.22, 136.85, 132.63, 129.58, 126.02, 99.59, 89.23, 49.25, 16.48. HRMS (ESI): calcd for $[C_{17}H_{16}I_2N_4O_2SNa]^+$: 616.8970, found: 616.8962.

7L: ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 10.44 (s, 2H), 9.85 (s, 2H), 9.32 (s, 2H), 9.06 (s, 2H), 8.41 (s, 1H), 8.06 (d, J = 6.5 Hz, 2H), 7.65 (t, J = 11.6 Hz, 6H), 7.56 (s, 4H), 4.38 (s, 2H), 1.42 (d, J = 5.0 Hz, 6H). ^{13}C NMR (214 MHz, DMSO-d_6) δ (ppm) 180.18, 171.87, 167.09, 139.03, 133.74, 130.61, 128.31, 128.17, 127.24, 124.86, 124.20, 49.10, 16.72. HRMS (ESI): calcd for $[C_{28}H_{28}I_2N_8O_4S_2Na]^+$: 880.9657, found: 8880.9637.

3. Experimental data

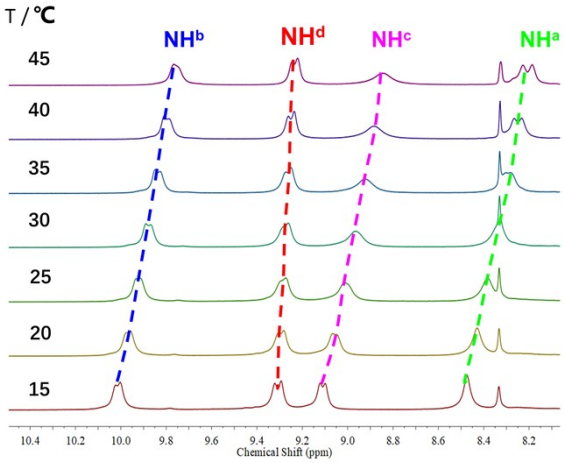


Figure S1. Temperature-dependent partial ^{1}H NMR spectra of -NH protons of **1L** in 90:10 (v/v) CD_3CN/DMSO-d_6 mixture. [**1L**] = 2 mM.

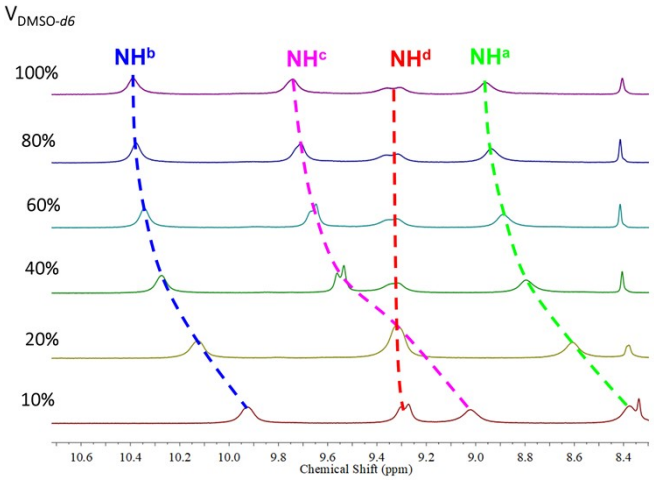


Figure S2. Partial ^{1}H NMR spectra of -NH protons of **1L** in CD_3CN/DMSO-d_6 mixtures of varying volume fraction of DMSO-d_6 (500 MHz, 298 K). [**1L**] = 2 mM.

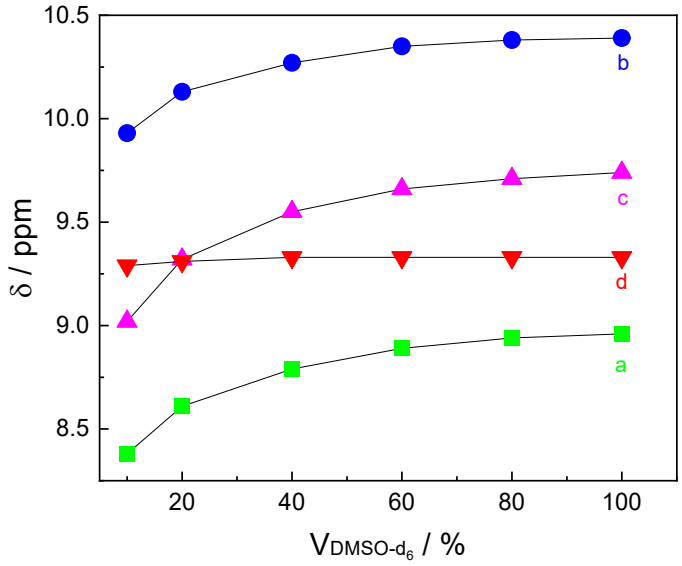


Figure S3. Influence on resonances of -NH protons of **1L** in CD_3CN/DMSO-d_6 mixture by volume fraction of DMSO-d_6 (500 MHz, 298 K). [**1L**] = 2 mM.

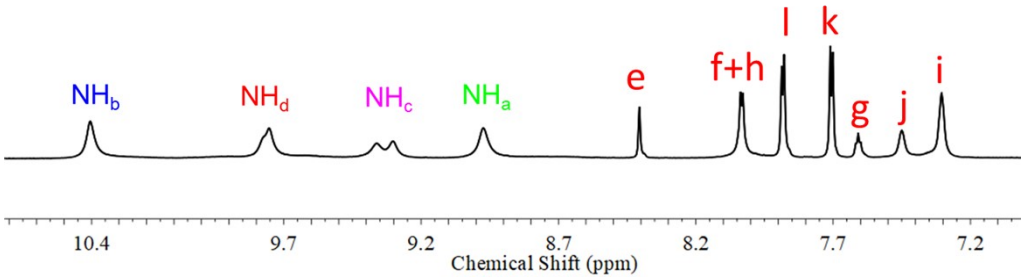


Figure S4. Partial ^{1}H NMR spectrum of **1L** in DMSO-d_6. [**1L**] = 2 mM.

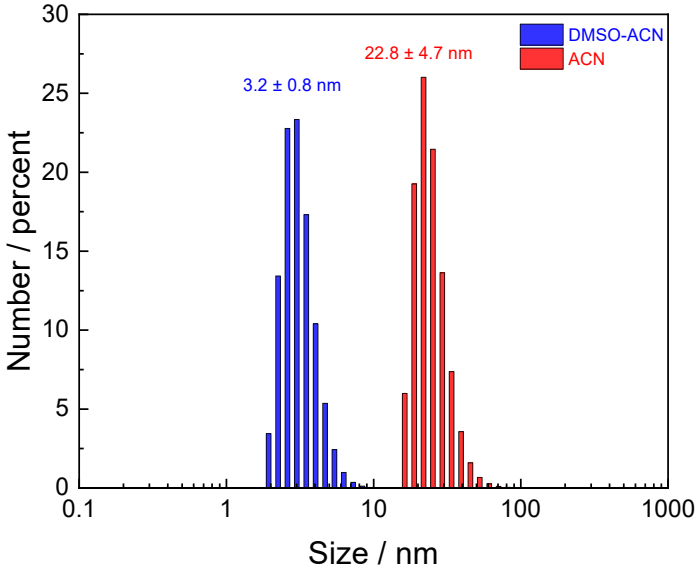


Figure S5. Hydrodynamic diameters of **1L** in 1:199 (v/v) DMSO/CH_3CN and in CH_3CN measured by dynamic light scattering. [**1L**] = 5 μM.

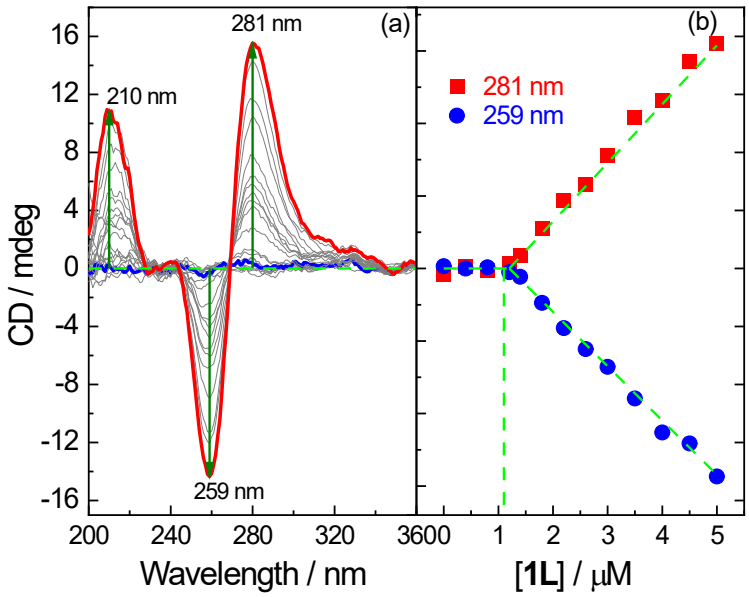


Figure S6. (a) Concentration-dependent CD spectra of **1L** in CH_3CN and (b) plots of CD signals at 259 nm and 280 nm versus concentration of **1L** over 0 to 5 μM.

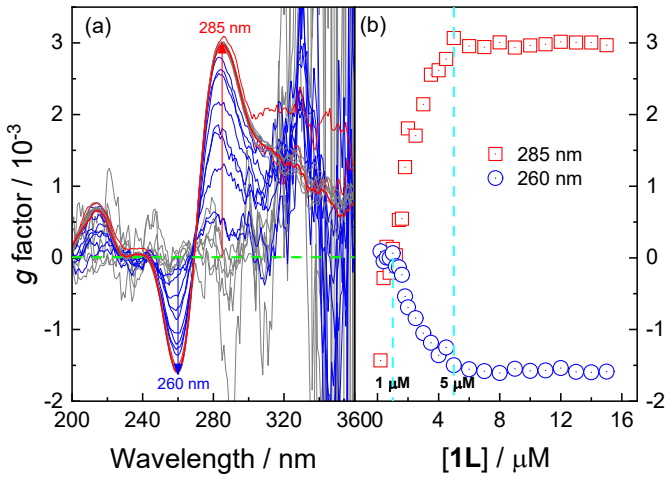


Figure S7. (a) Wavelength profiles of *g* factor of **1L** of increasing concentration in CH_3CN and (b) plots of *g* factors at 285 nm and 260 nm versus concentration of **1L** over 0 to 15 μM.

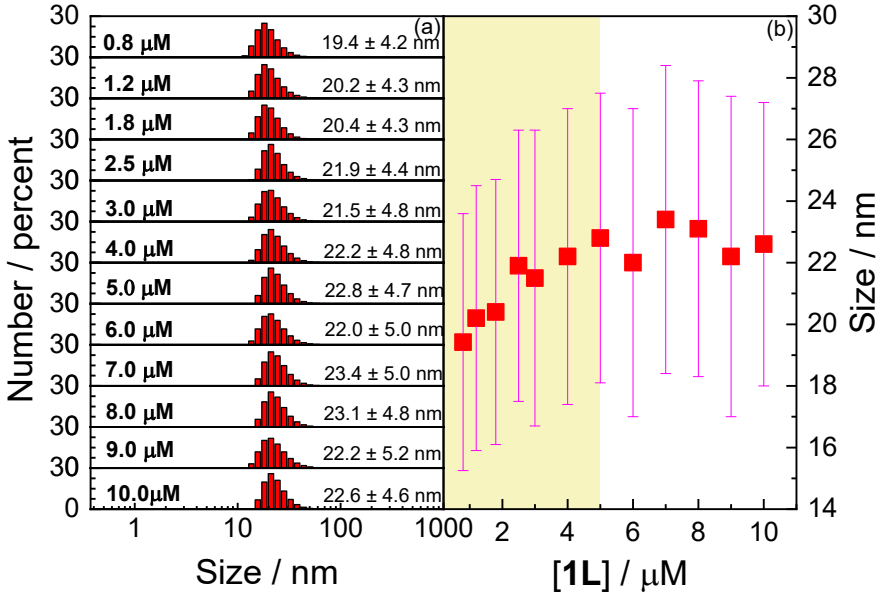


Figure S8. (a) DLS hydrodynamic diameters of **1L** of increasing concentration in CH_3CN and (b) plots of hydrodynamic diameter versus concentration of **1L**. [**1L**] = 0 - 10 μM.

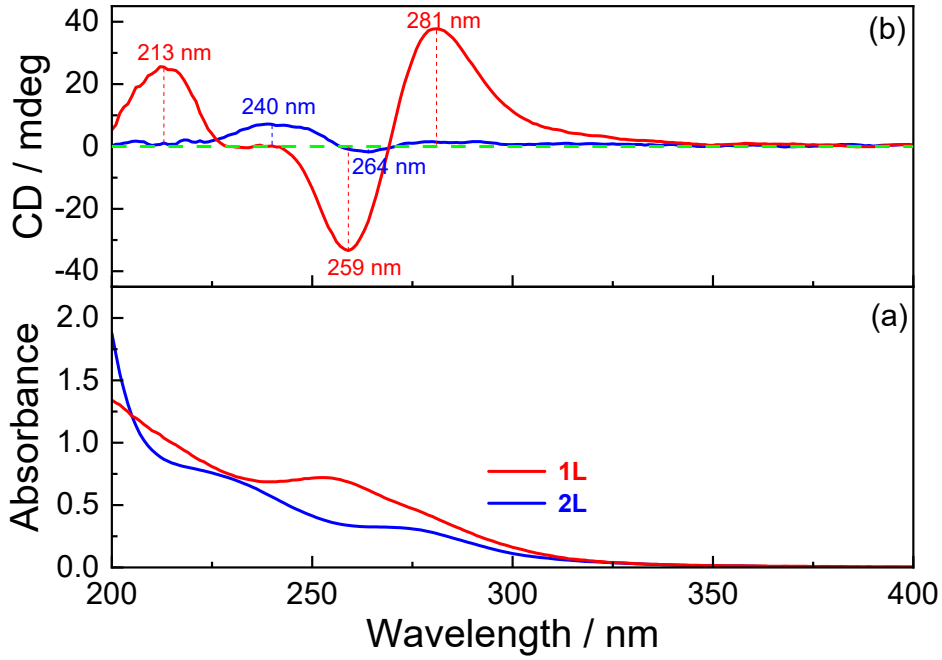


Figure S9. Absorption (a) and CD (b) spectra of **1L** (red line) and **2L** (blue line) in CH_3CN. [**1L**] = [**2L**] =10 μM.

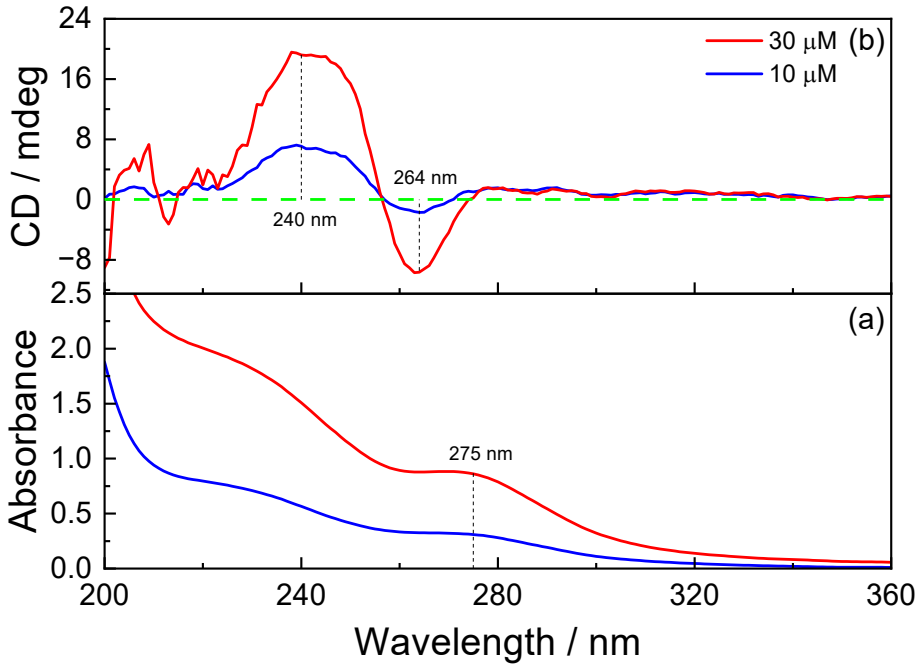


Figure S10. Absorption (a) and CD (b) spectra of **2L** of 10 and 30 μM in CH_3CN.

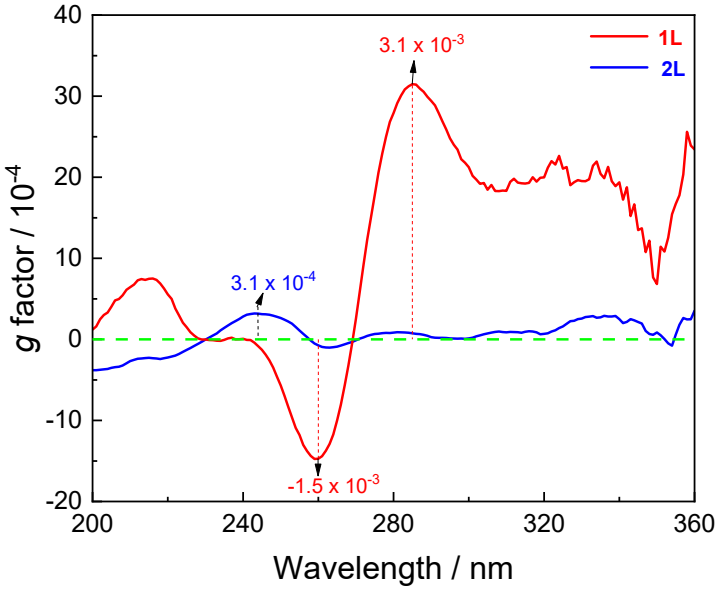


Figure S11. Wavelength profiles of *g* factors of **1L** (red line) and **2L** (blue line) in CH_3CN. [**1L**] = [**2L**] = 10 μM.

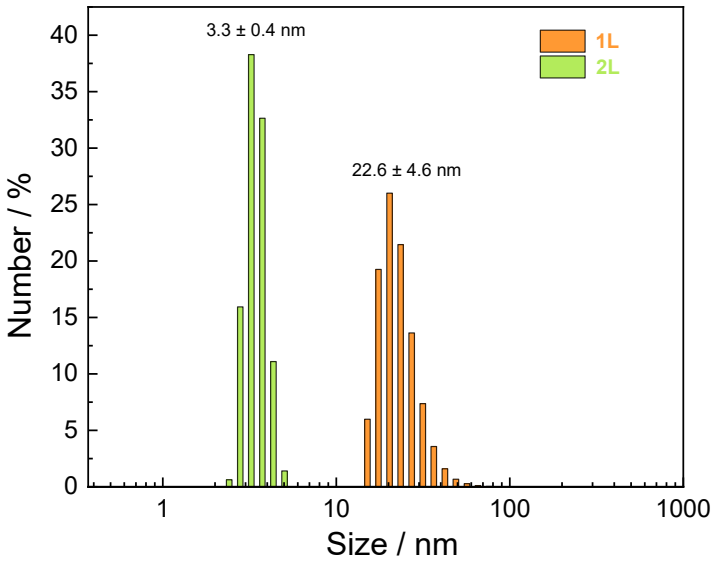


Figure S12. Hydrodynamic diameters of **1L** and **2L** in CH_3CN measured by dynamic light scattering. [**1L**] = [**2L**] =10 μM.

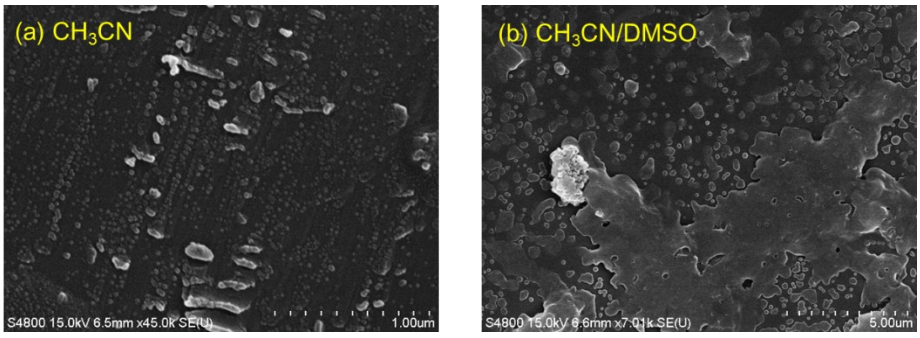


Figure S13. SEM images of air-dried samples of **2L** in CH_3CN and 1:199 (v/v) DMSO/CH_3CN on platinum coated silicon wafers. [**2L**] = 10 μM.

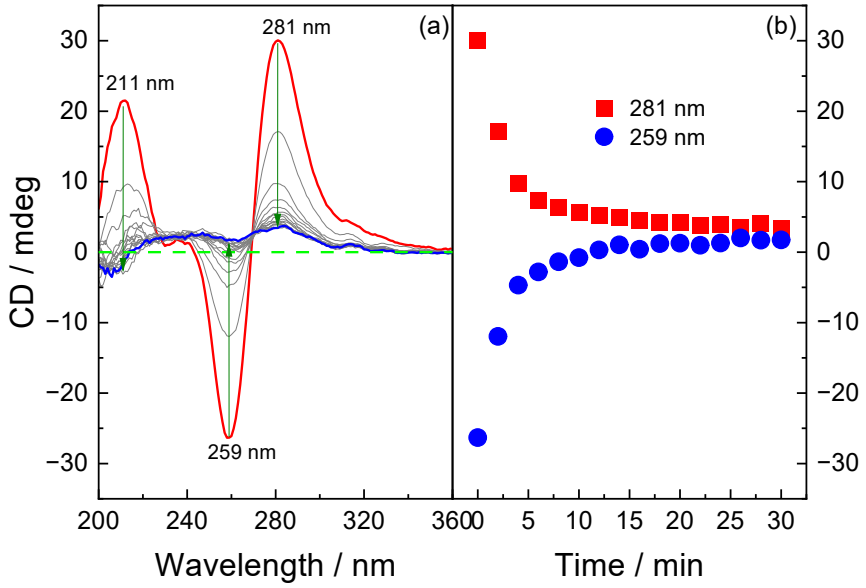


Figure S14. (a) Time-dependent CD spectra and (b) CD signals at 281 nm and 259 nm of **1L** in CH_3CN with 20% by volume H_2O. [**1L**] = 8 μM.

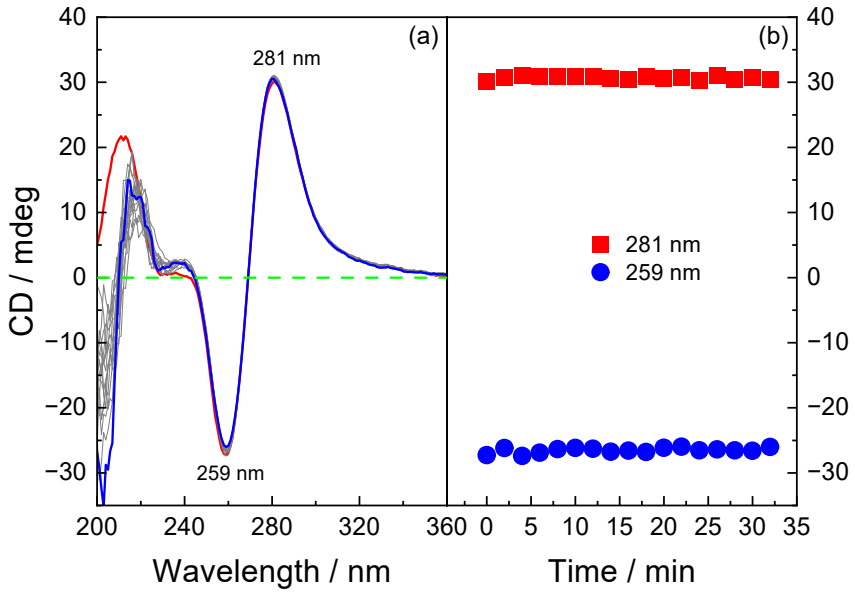


Figure S15. (a) Time-dependent CD spectra and (b) CD signals at 281 nm and 259 nm of **1L** in CH_3CN with 20% by volume THF. [**1L**] = 8 μM.

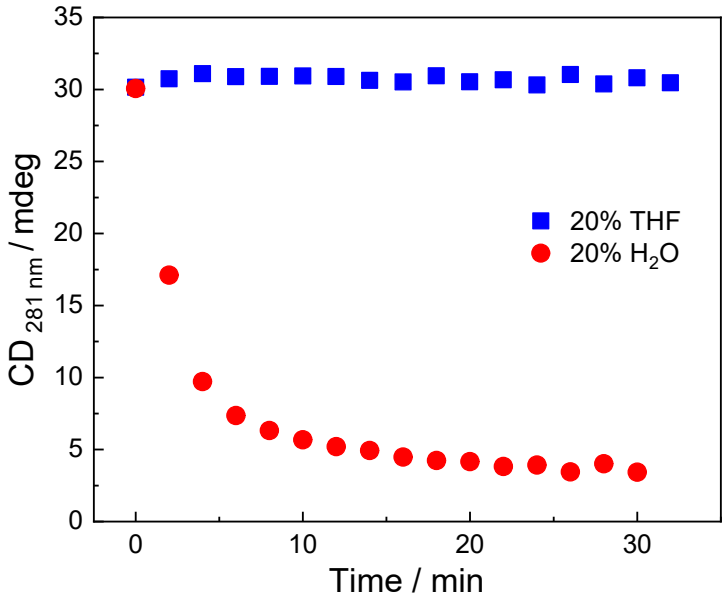


Figure S16. Time profiles of CD signal at 281 nm of **1L** in CH_3CN with 20% volume fraction of THF and H_2O. [**1L**] = 8 μM.

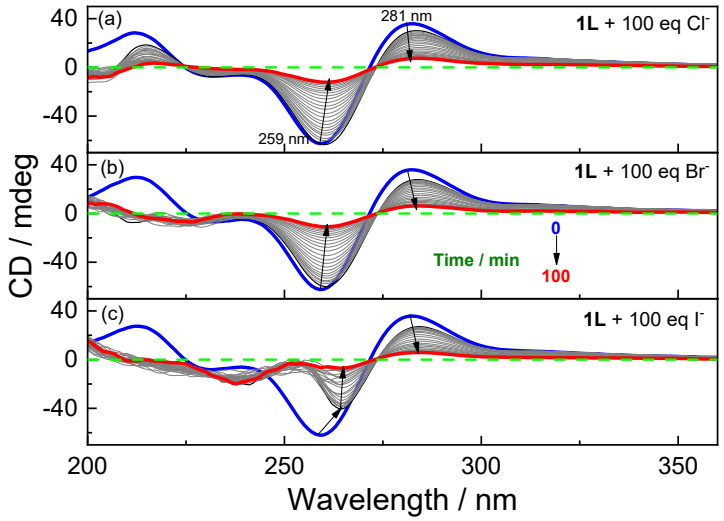


Figure S17. Time-dependent CD spectra of **1L** in the presence of 100 eq of Cl^- (a), Br^- (b) and I^- (c) in CH_3CN. [**1L**] = 10 μM, [I^-] = [Br^-] = [Cl^-] = 1000 μM. I^-, Br^- and Cl^- exist as their *n*-Bu_4N^+ salts.

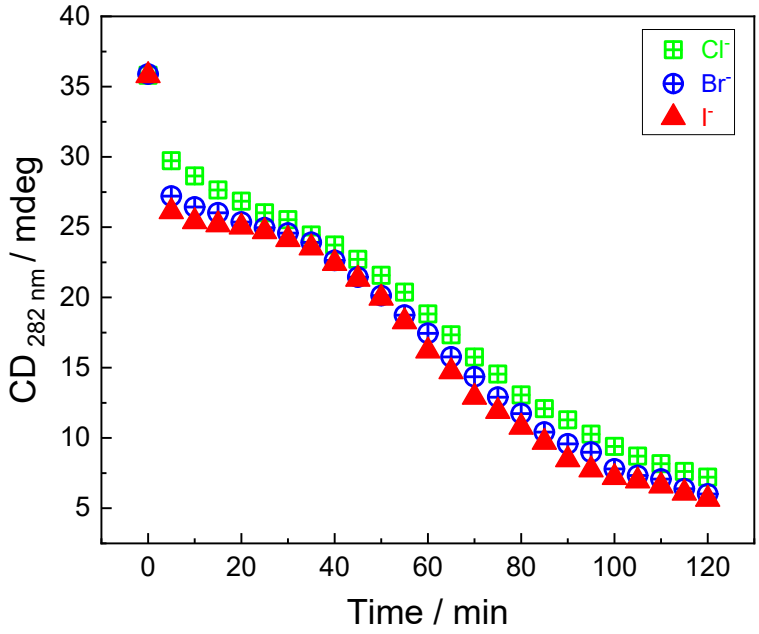


Figure S18. Time profiles of CD signal at 282 nm of **1L** in the presence of 100 eq I^-, Br^- and Cl^- in CH_3CN. [**1L**] = 10 μM, [I^-] = [Br^-] = [Cl^-] = 1000 μM. I^-, Br^- and Cl^- exist as their $(n\text{-Bu})_4N^+$ salts.

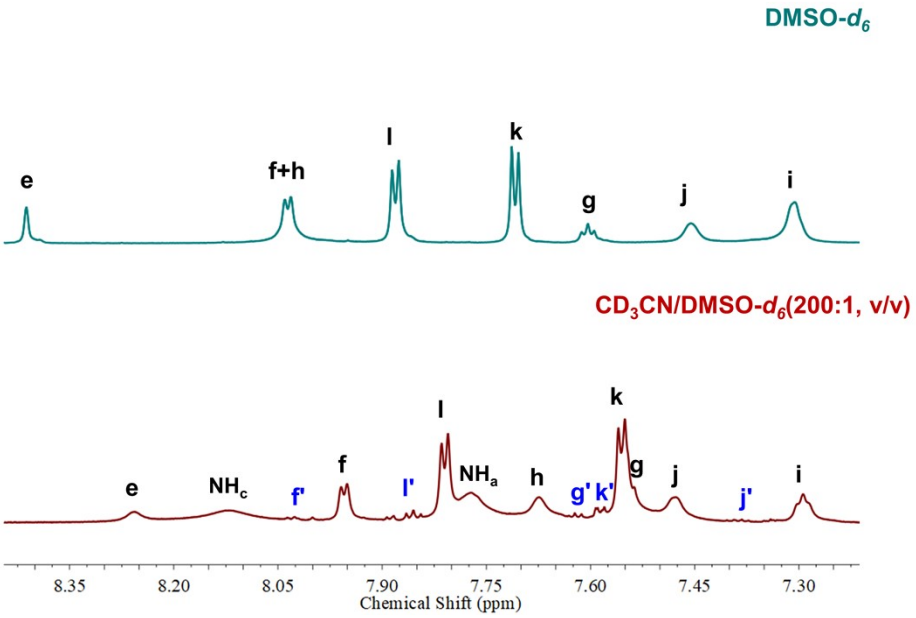


Figure S19. Partial ^1H NMR spectra of **1L** in DMSO-d_6 and in 200:1 (v/v) CD_3CN/DMSO-d_6 mixture (850 MHz, 25 °C). $H^{f'}$, $H^{l'}$, $H^{g'}$, $H^{k'}$ and $H^{j'}$ are those from the oligomers of **1L**. Numbering of protons is shown in Figure 1a. [**1L**] = 200 μM.

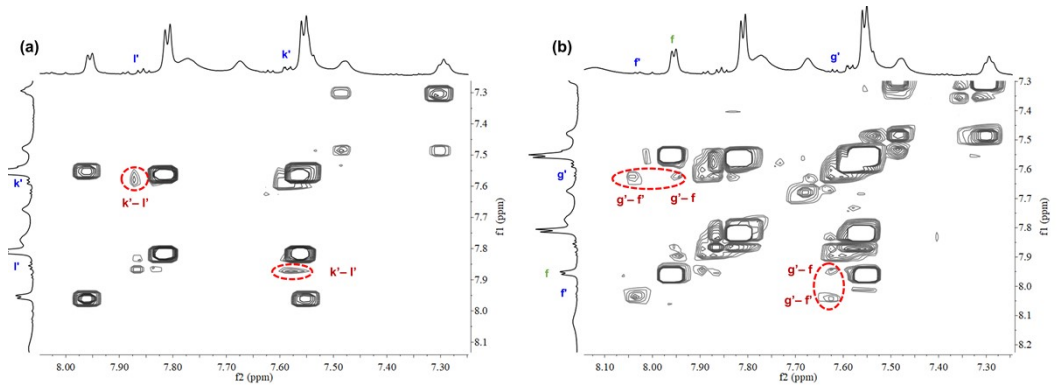


Figure S20. Expanded 2D COSY spectra of couplings between protons in phenyl rings in **1L** in 200:1 (v/v) CD_3CN/DMSO-d_6 mixture (850 MHz, 25 °C). Numbering of protons is given in Figure 1a. [**1L**] = 200 μM.

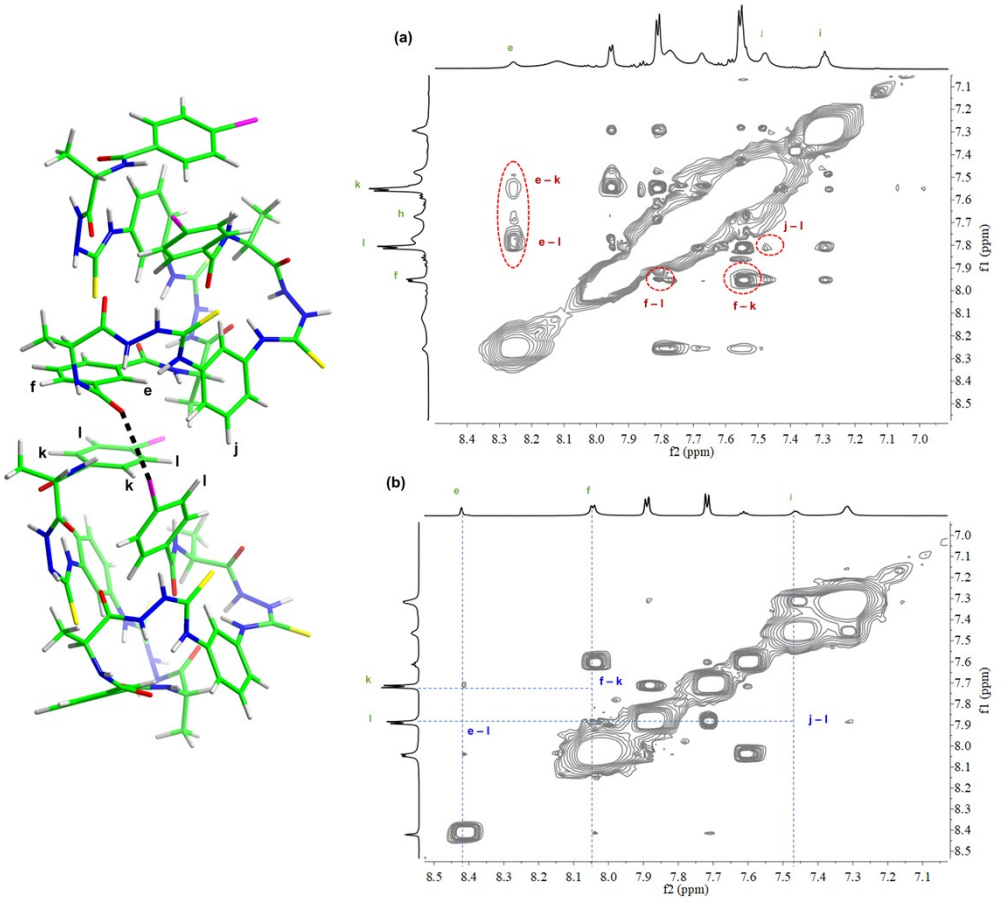


Figure S21. Expanded 2D NOESY spectra of **1L** in (a) 200:1 (v/v) CD_3CN/DMSO-d_6 mixture and (b) DMSO-d_6 (850 MHz, 25 °C). [**1L**] = 200 μM. The proposed structure of the dimer of **1L** shows that two molecules are connected by C-I···O halogen bonding (dashed black line), allowing couplings of H^e-H^k, H^e-H^l, H^f-H^k, H^f-H^l and H^j-H^l.

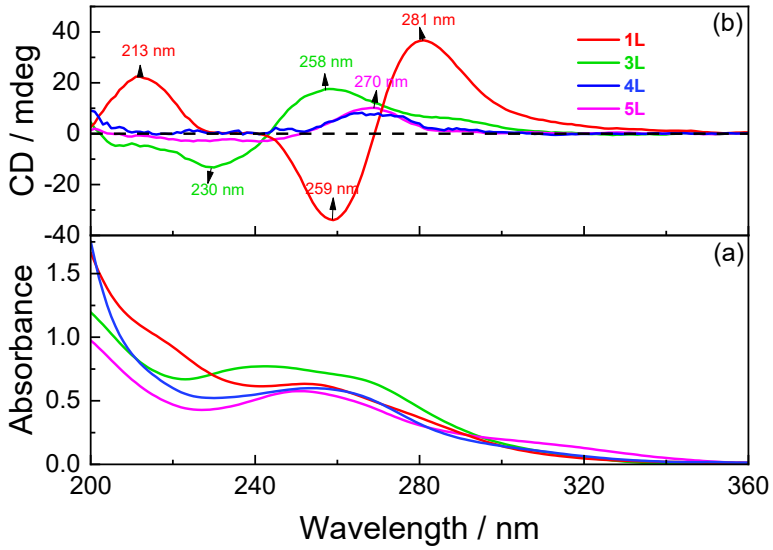


Figure S22. Absorption (a) and CD (b) spectra of **1L**, **3L**, **4L** and **5L** in CH_3CN. [**1L**] = [**3L**] = [**4L**] = [**5L**] = 10 μM.

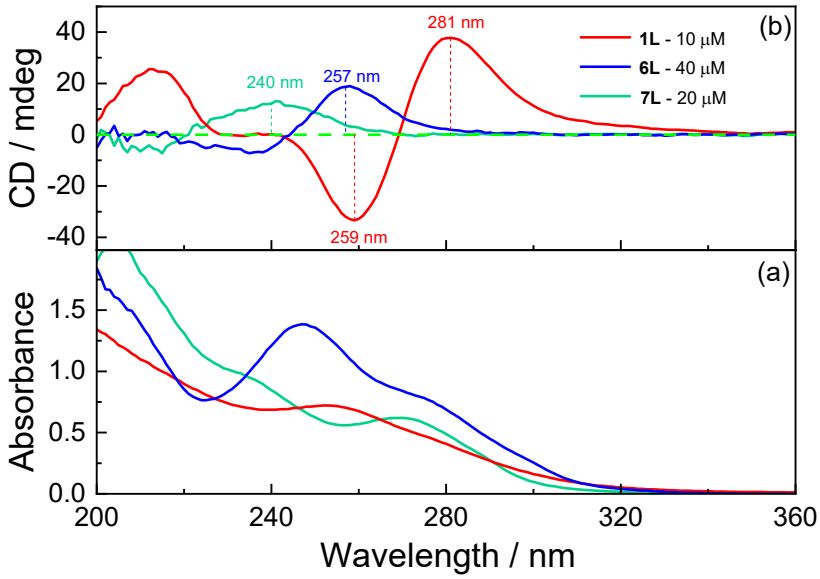


Figure S23. Absorption (a) and CD (b) spectra of **1L**, **6L** and **7L** in CH_3CN. [**1L**] = 10 μM, [**6L**] = 40 μM and [**7L**] = 20 μM.

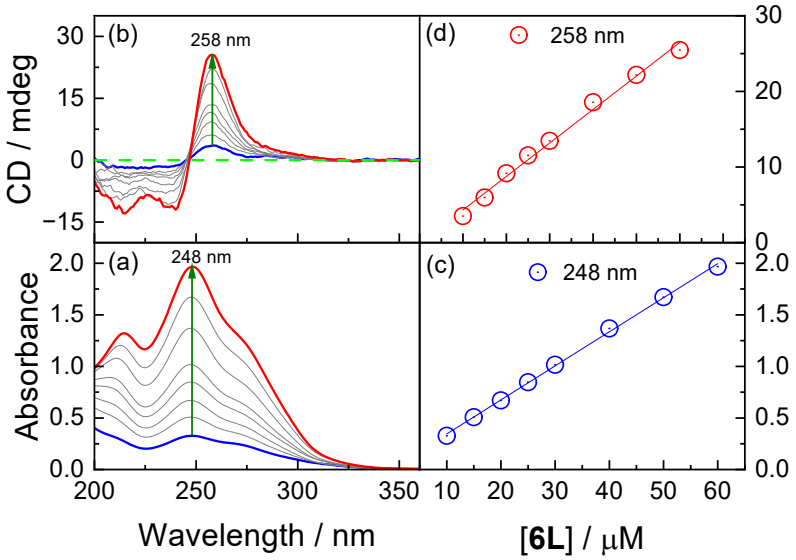


Figure S24. Concentration-dependent absorption (a) and CD (b) spectra of **6L** in CH_3CN and plots of absorbance at 248 nm (c) and CD signal at 258 nm (d) versus concentration of **6L** over 10 to 60 μM.

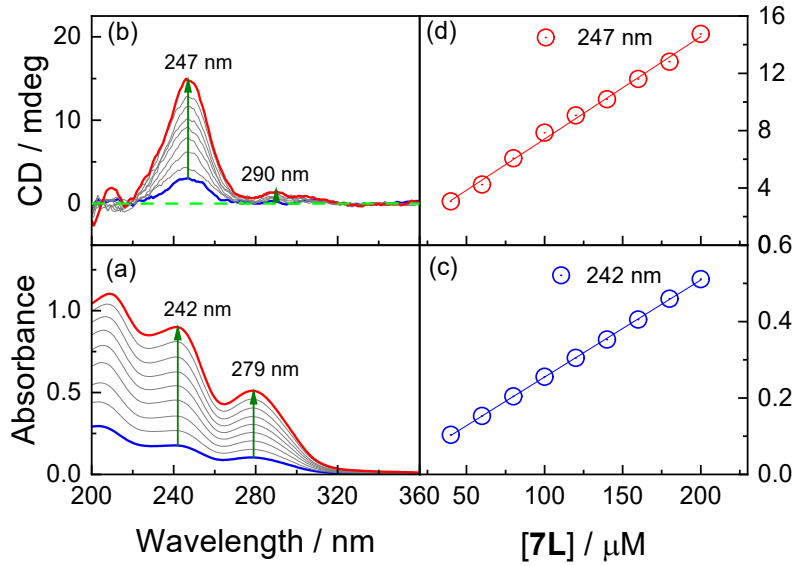


Figure S25. Concentration-dependent absorption (a) and CD (b) spectra of **7L** in CH_3CN and plots of absorbance at 242 nm (c) and CD signal at 247 nm (d) versus concentration of **7L** over 40 to 200 μM.

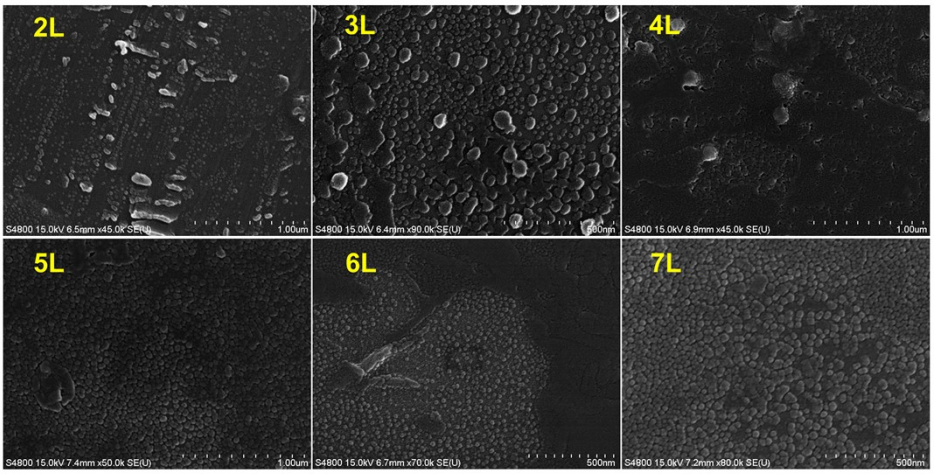


Figure S26. SEM images of air-dried samples of **2L, 3L**, **4L**, **5L**, **6L** and **7L** in CH_3CN on platinum coated silicon wafers. Concentrations of **2L-7L** are 10 μM.

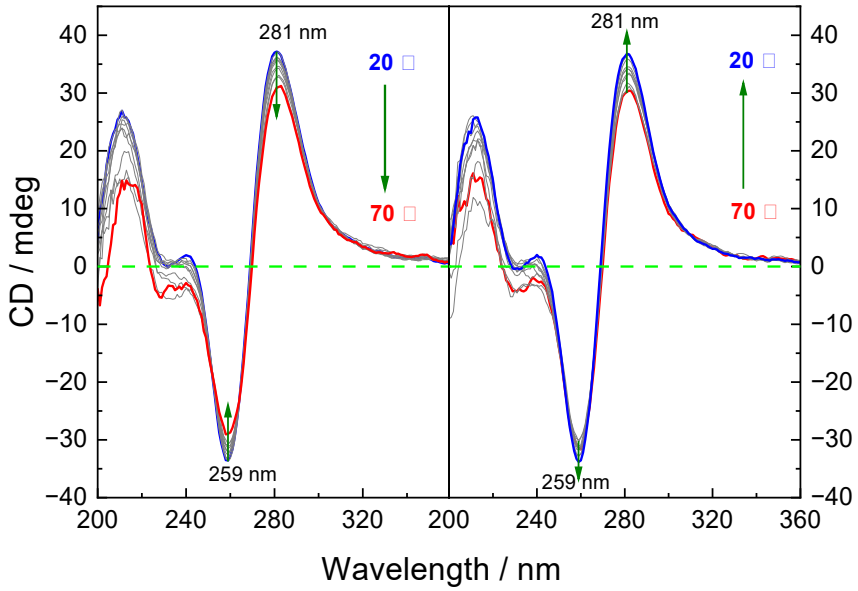


Figure S27. Temperature-dependent CD spectra of **1L** in CH_3CN. [**1L**] = 10 μM.

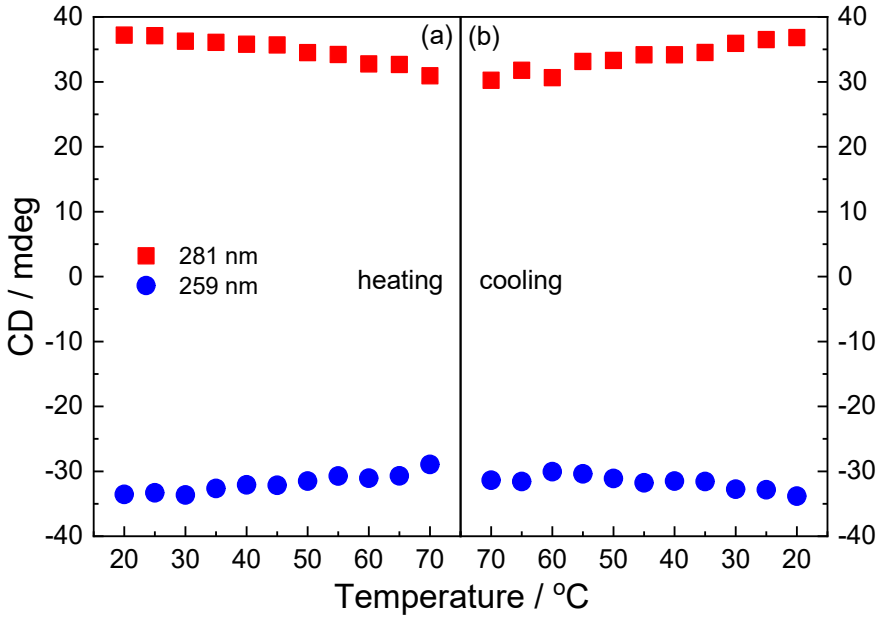


Figure S28. Temperature-dependent CD signals at 259 nm and 281 nm of **1L** in CH_3CN in the heating (a) and next cooling (b) processes. [**1L**] = 10 μM.

4. ^{1}H NMR and ^{13}C NMR spectra

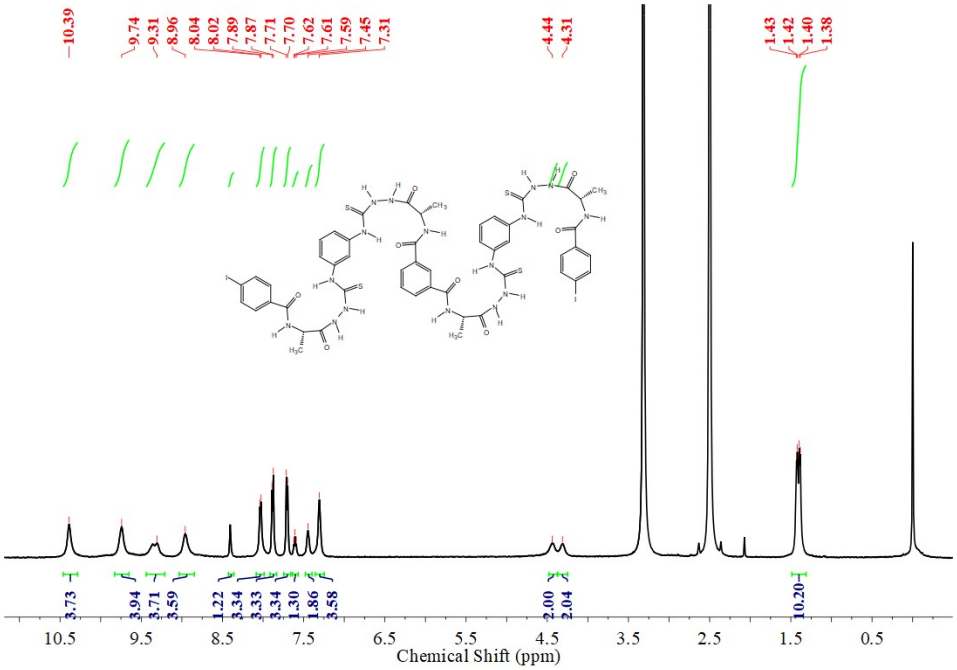


Figure S29. 500 MHz ^{1}H NMR spectrum of **1L** in DMSO-d_6.

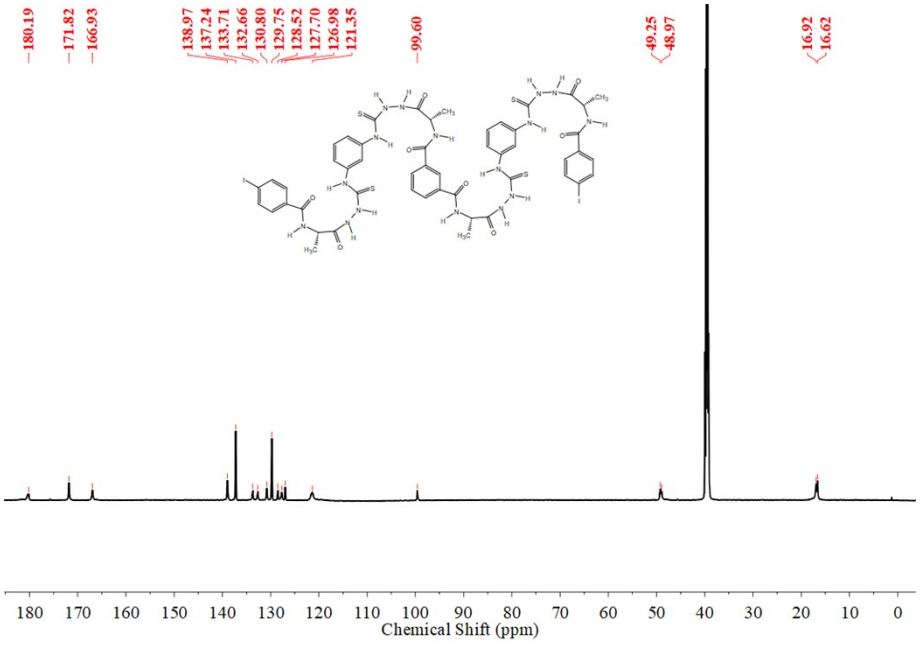


Figure S30. 214 MHz ^{13}C NMR spectrum of **1L** in DMSO-d_6.

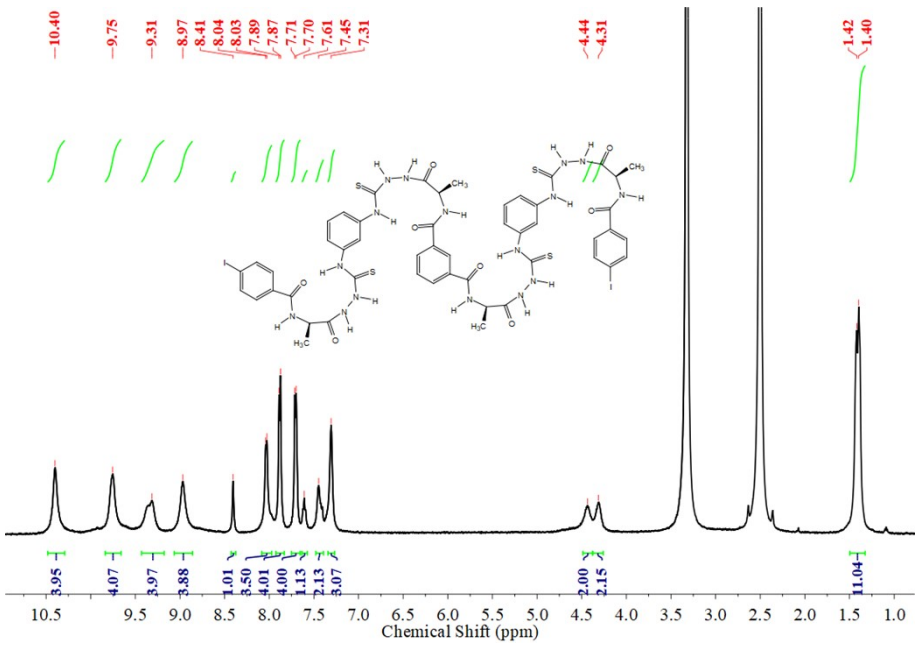


Figure S31. 500 MHz ^{1}H NMR spectrum of **1D** in DMSO-d_6.

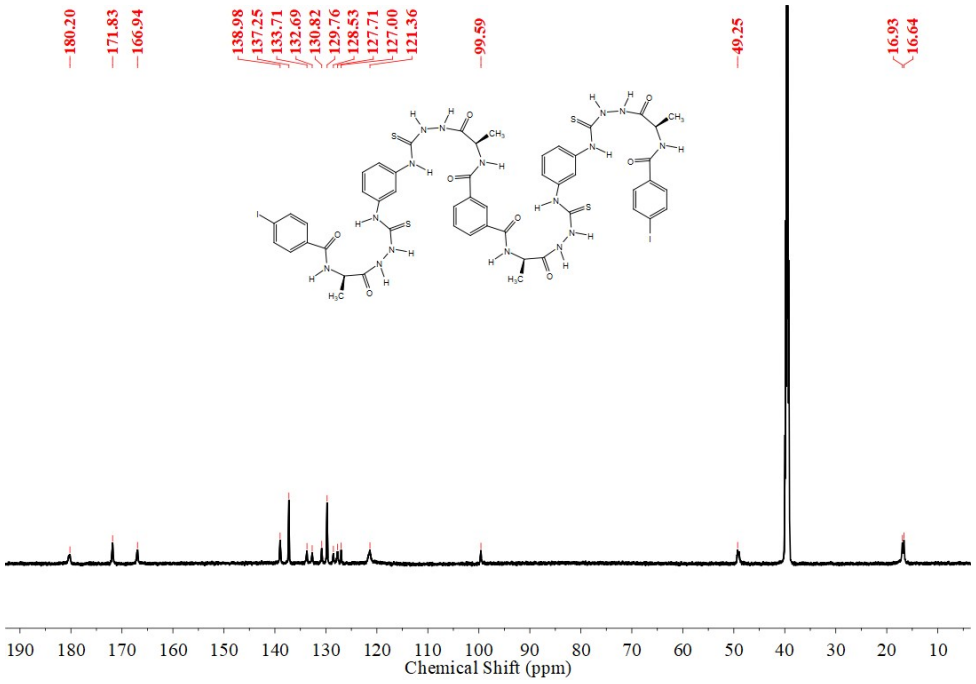


Figure S32. 214 MHz ^{13}C NMR spectrum of **1D** in DMSO-d_6.

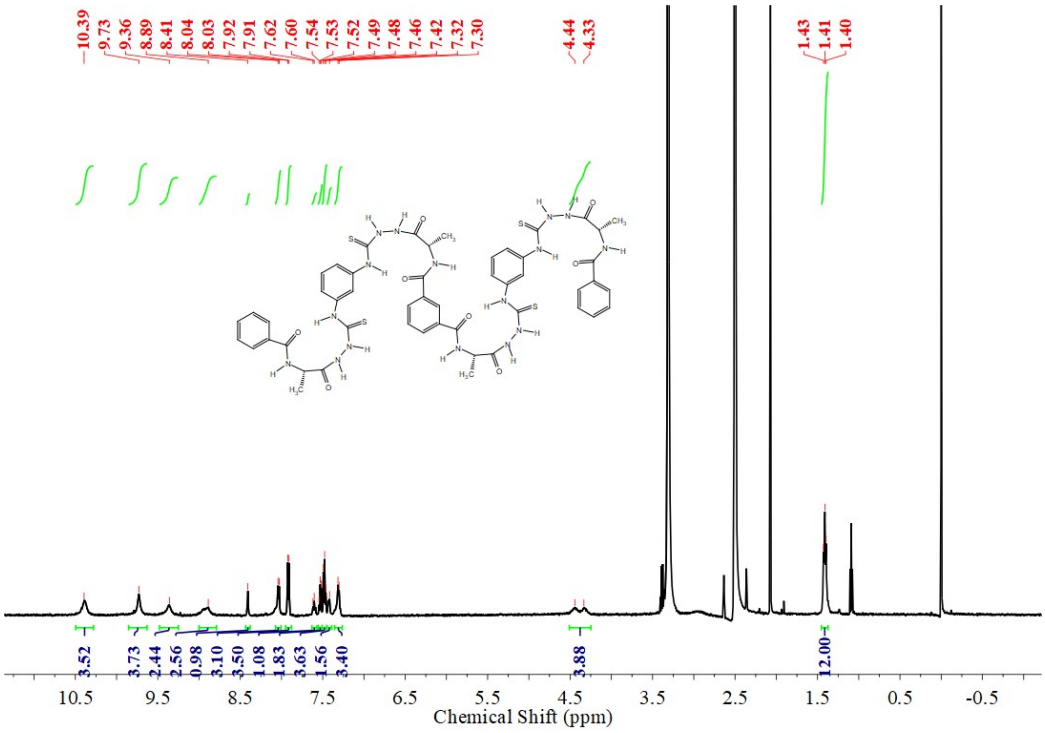


Figure S33. 500 MHz ^{1}H NMR spectrum of **2L** in DMSO-d_6.

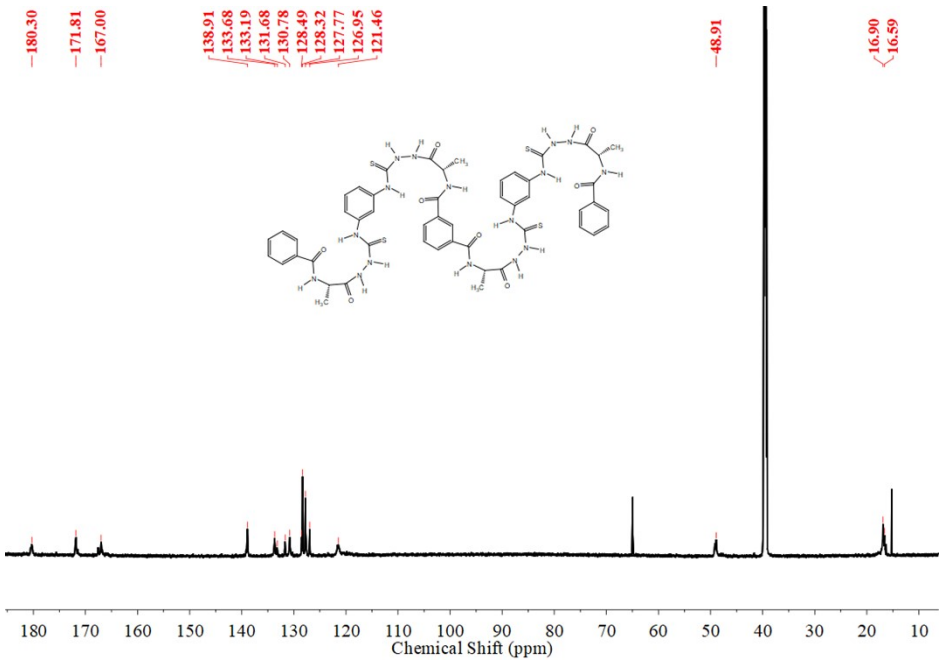


Figure S34. 214 MHz ^{13}C NMR spectrum of **2L** in DMSO-d_6.

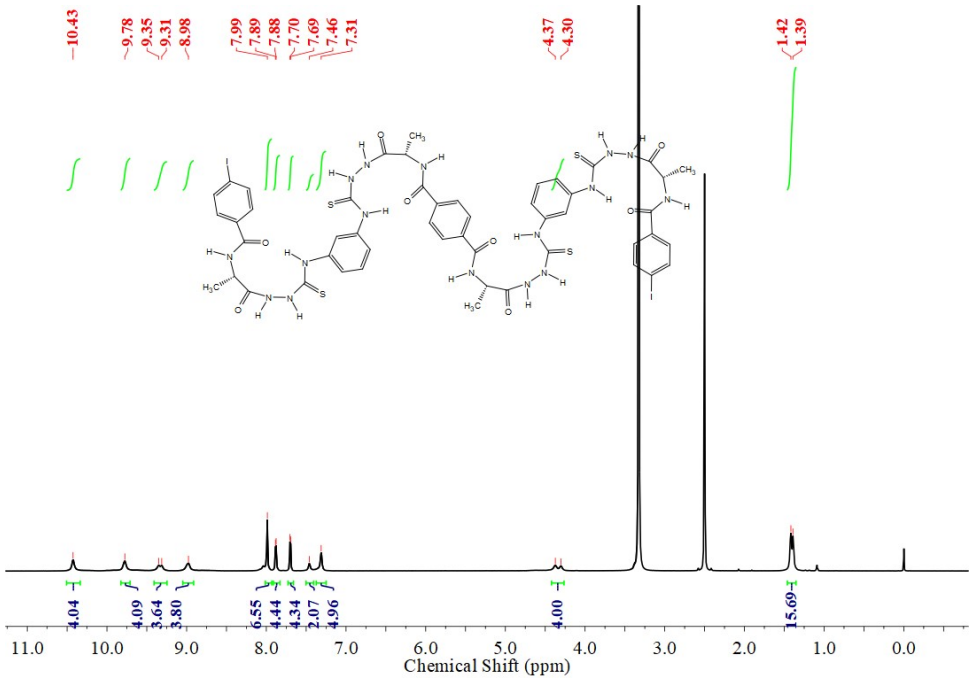


Figure S35. 500 MHz ^{1}H NMR spectrum of **3L** in DMSO-d_6.

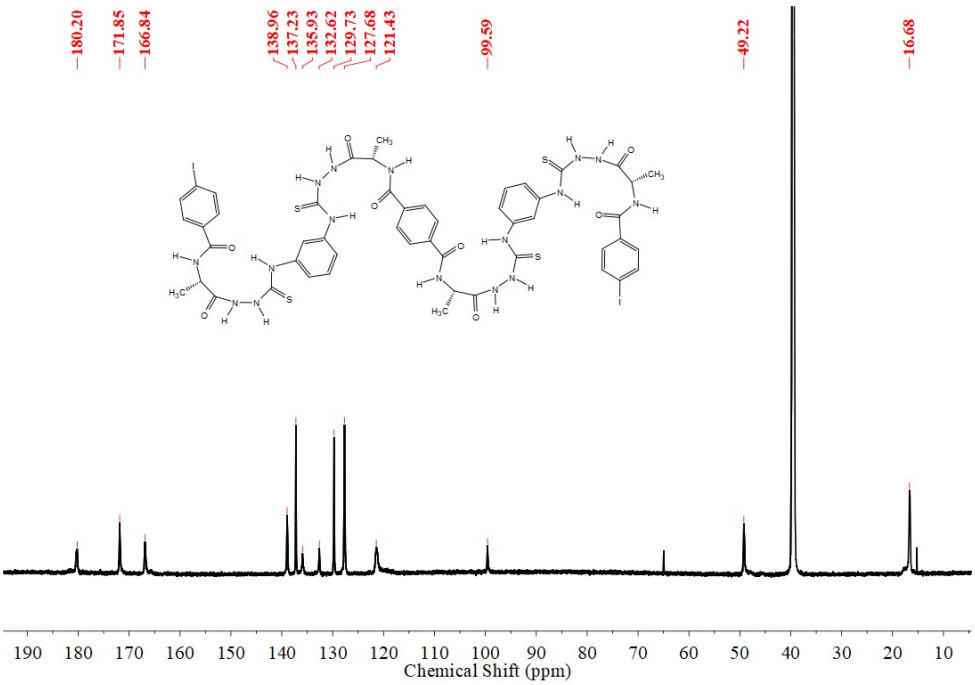


Figure S36. 214 MHz ^{13}C NMR spectrum of **3L** in DMSO-d_6.

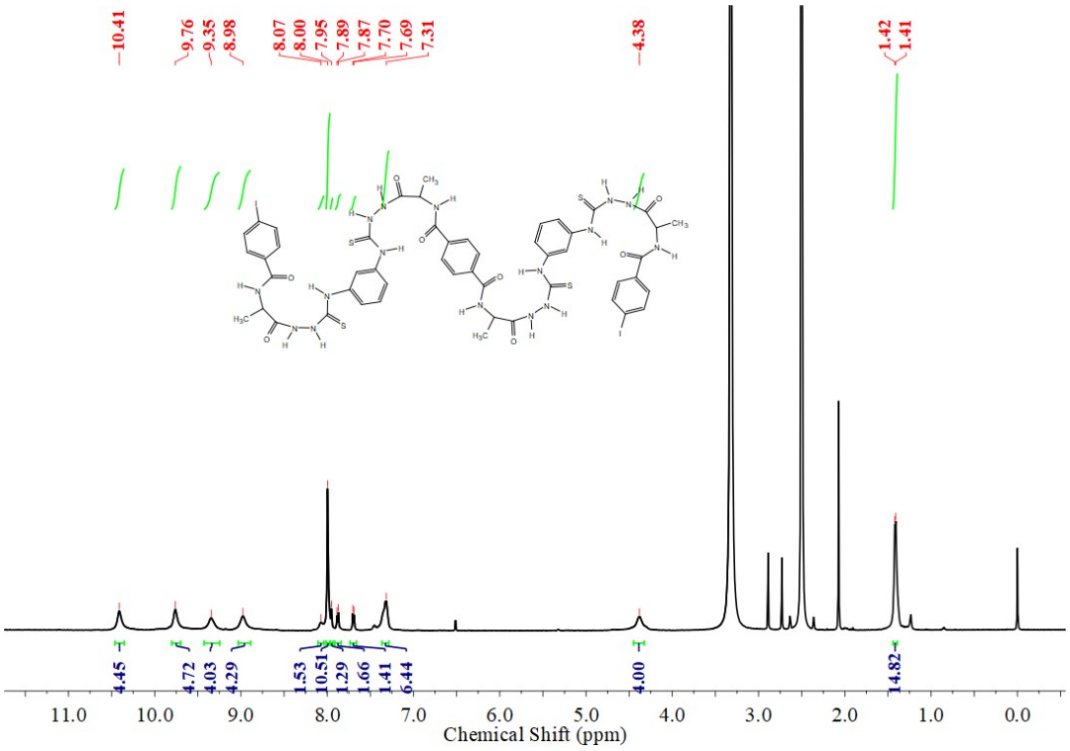


Figure S37. 500 MHz ^{1}H NMR spectrum of **4L** in DMSO-d_6.

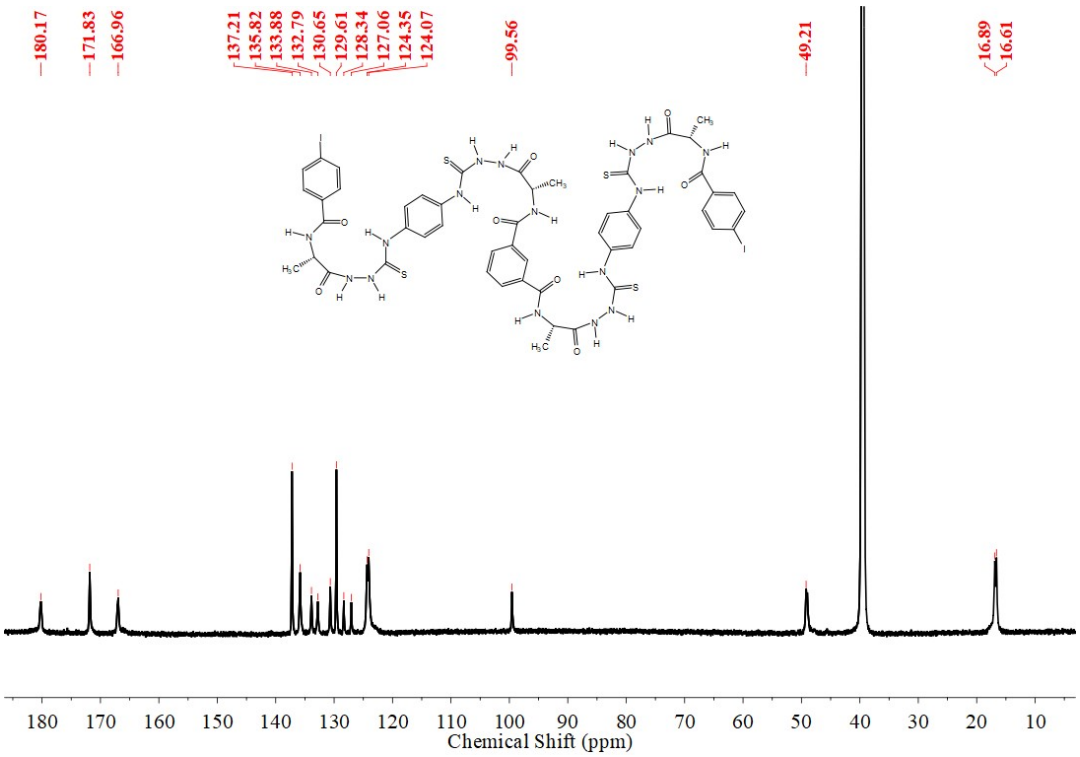


Figure S38. 214 MHz ^{13}C NMR spectrum of **4L** in DMSO-d_6.

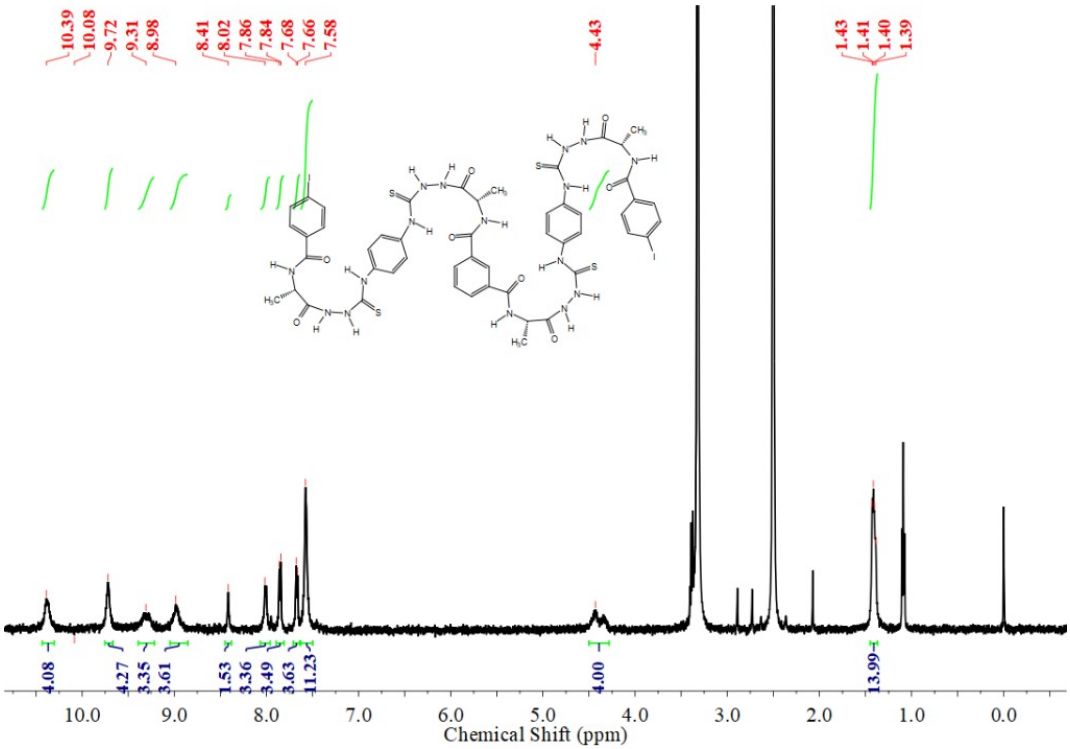


Figure S39. 500 MHz ^{1}H NMR spectrum of **5L** in DMSO-d_6.

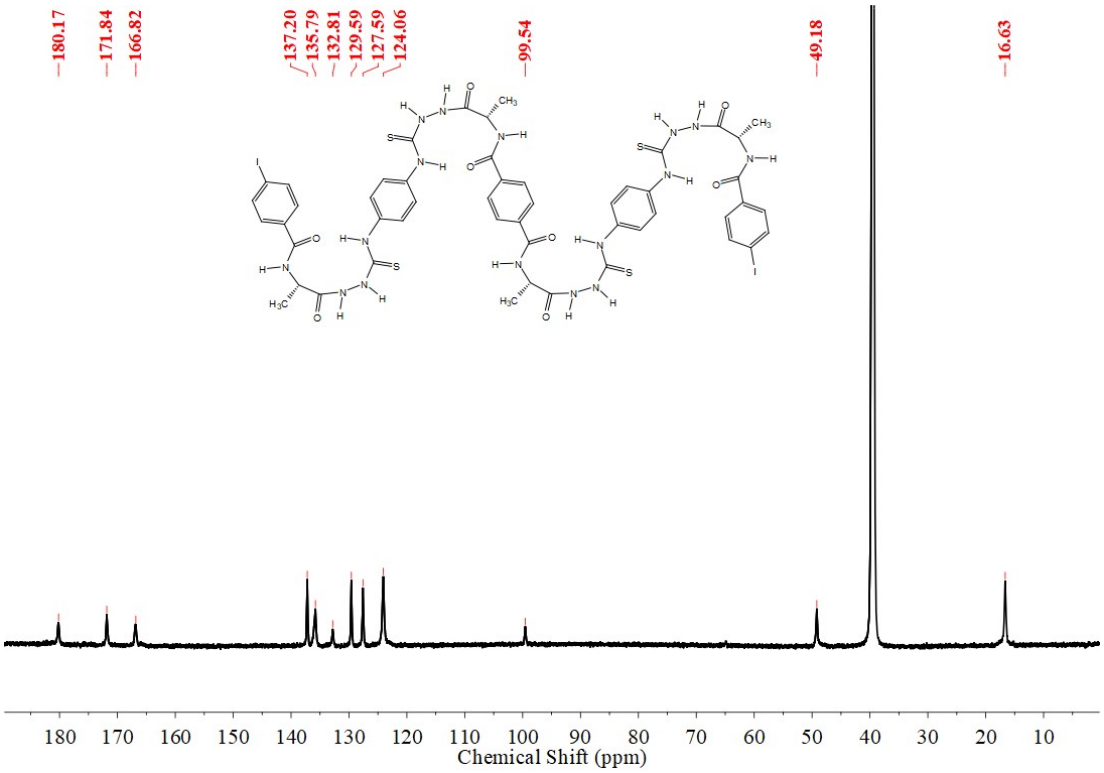


Figure S40. 214 MHz ^{13}C NMR spectrum of **5L** in DMSO-d_6.

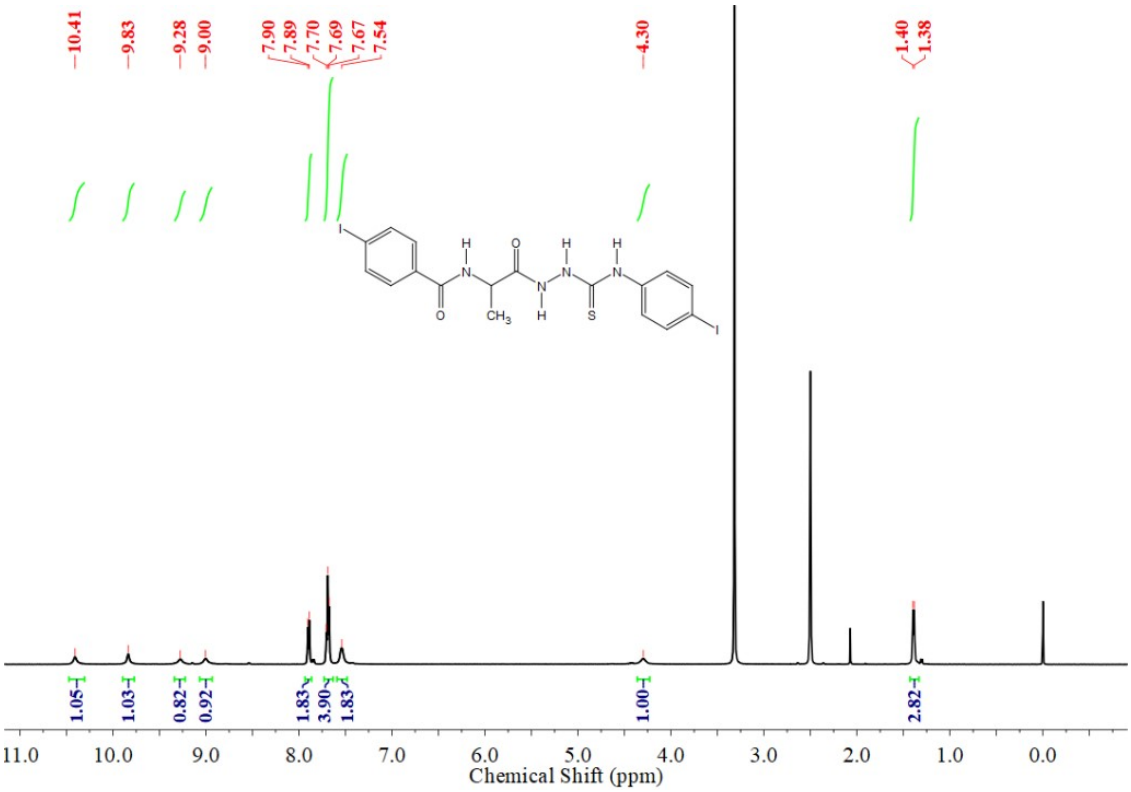


Figure S41. 500 MHz ^{1}H NMR spectrum of **6L** in DMSO-d_6.

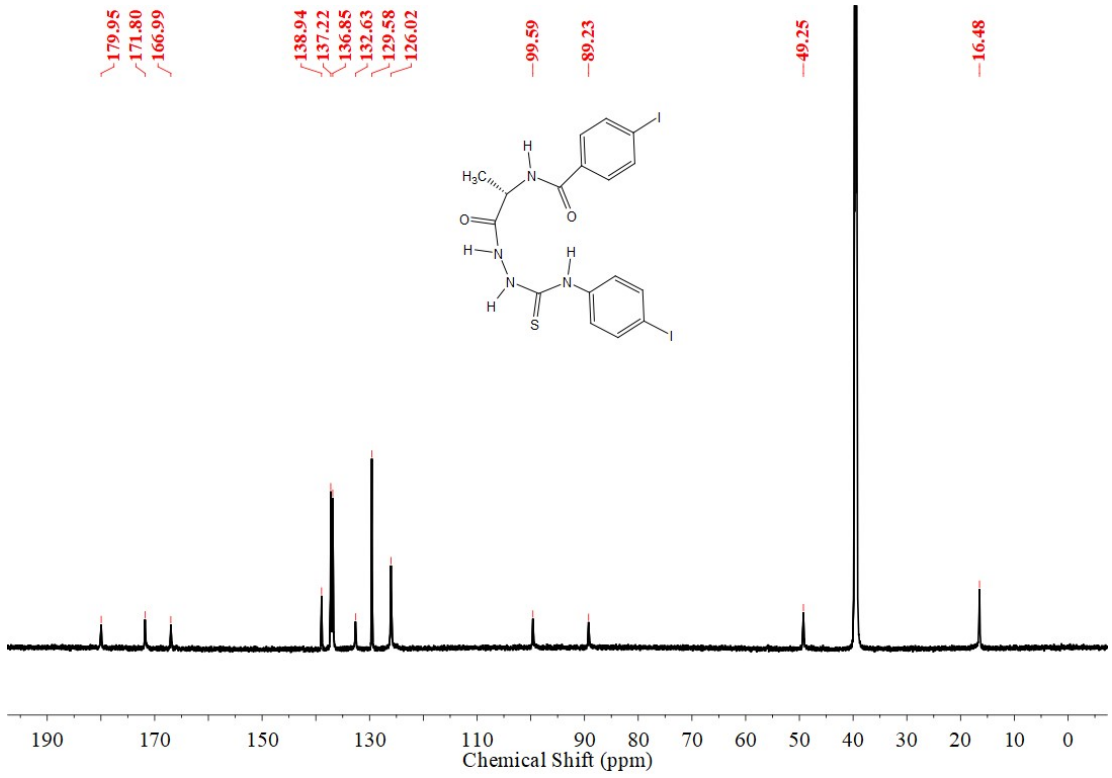


Figure S42. 214 MHz ^{13}C NMR spectrum of **6L** in DMSO-d_6.

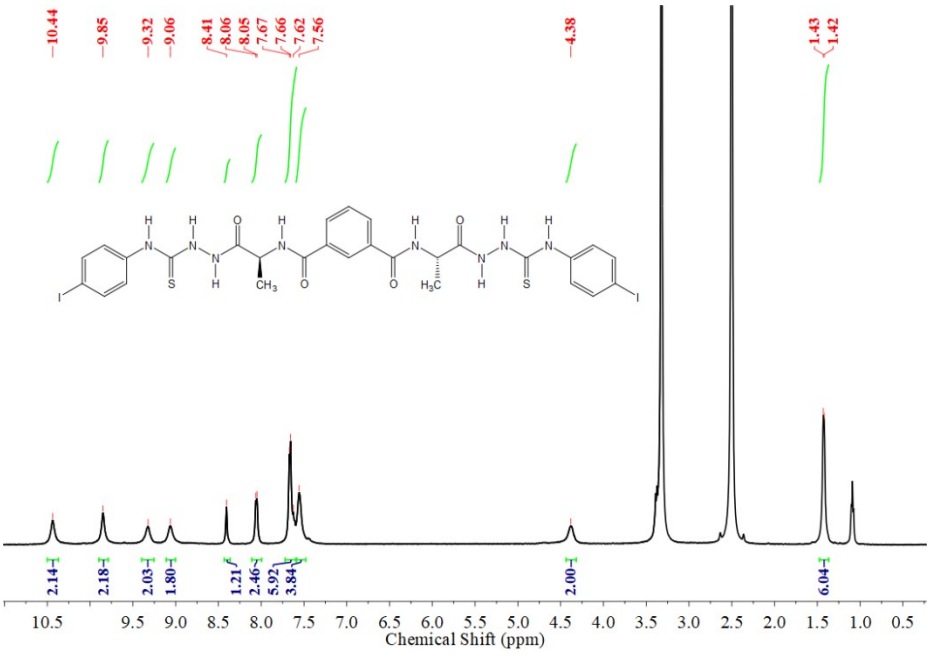


Figure S43. 500 MHz ^{1}H NMR spectrum of **7L** in DMSO-d_6.

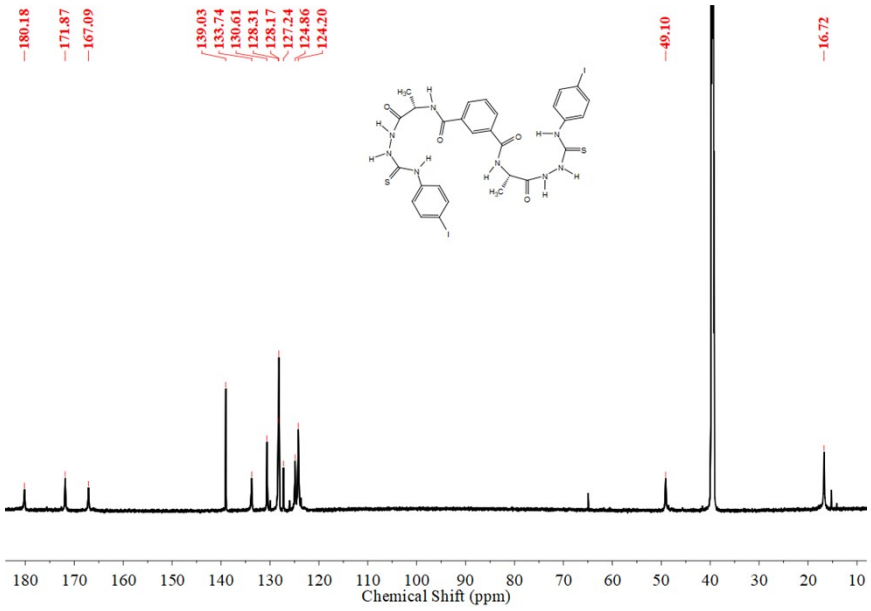


Figure S44. 214 MHz ^{13}C NMR spectrum of **7L** in DMSO-d_6.