Supporting Information

Effect of spatial folding of molecules on two-photon absorption and nonlinear refraction in foldamers

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S1.1 Synthesis scheme

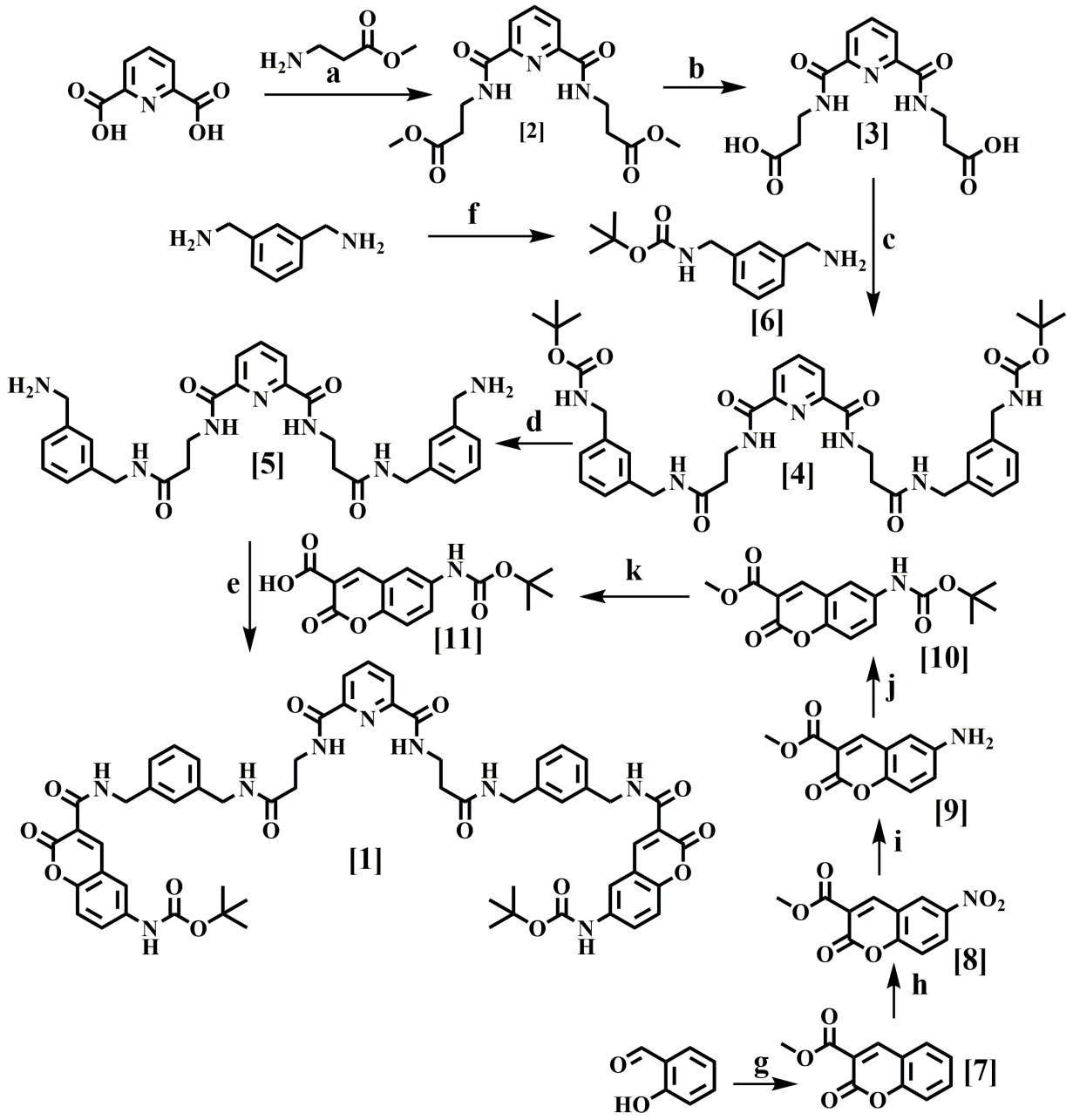


Fig. S1: Synthetic route of the foldamer F1 (1): Reaction conditions: (a) DCC, HOBt, 0°C, DCM, Et_3N, 48h; (b) MeOH, NaOH, 12h; (c) EDC, HOBt, 0°C, DCM, DIPEA, 48h; (d) DCM, TFA, Et_3N ; (e) EDC.HCl, HOBt, 0°C, DCM, DIPEA, 48h; (f) di-tert-butyldicarbonate, Dioxane, 48h; (g) piperidine, 80°C, 2h; (h) mixed acid, ice bath, 2h; (i) Fe, NH_4Cl, H_2O, 80°C, 2h; (j) di-tert-butyldicarbonate, Et_3N, Dioxane, 48h; (k) MeOH, NaOH, 12h.

The reported peptides were synthesized by conventional solution-phase methods using racemisation free fragment condensation strategy (Fig. S1). For N-terminal protection, Boc-anhydride was used and the C-terminal was protected as a methyl ester. Couplings were mediated by dicyclohexylcarbodiimide/1-hydroxybenzotriazole (DCC/HOBt). The product was purified by column chromatography using the silica gel (100-200-mesh size) as a stationary phase and n-hexane-ethyl acetate mixture as eluent. The final compounds were fully characterized by 400MHz and 500 MHz ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, mass spectrometry and Fourier-transform infrared (FT-IR) Spectroscopy.

S1.2 Synthesis of PDCBA (2)

1.67 g (10 mmol) 2,6-pyridinedicarboxylic acid (PDC) was dissolved in 30 mL of DCM and 5 mL of DMF in an ice-water bath. NH_2-β-Ala-OMe 2.58 g (25 mmol) was isolated from the corresponding methyl ester hydrochloride by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated under vacuum to 5 mL, then diluted with DCM to 30 mL. Then it was added to the reaction mixture, followed immediately by 5.16 g (25 mmol) of N,N-dicyclohexylcarbodiimide (DCC) and 3.38 g (25 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and then stirred for 48h. After that DCM was evaporated, the residue was taken in 30 mL ethyl acetate and N,N-dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2(M) HCL (3×50 mL), brine (2×50 mL), then 1 (M) sodium carbonate (3X30 mL) and brine (2×30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the compound 2 as a white solid. Purification was done by silica gel column (100-200 mesh size) with an ethyl acetate and hexane mixture 1:2 as the eluent.

Yield: 2.62 g (7.77 mmol, 77.65 %).

^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm): 8.50 (s, 2H, β-Ala NH); 8.30 (d, 2H, J = 7.64, Aromatic Proton); 8.00 (t, 1H, J = 7.99, Aromatic Proton); 3.78-3.73 (m, 4H, β-Ala CH_2); 3.71 (s, 6h, OMe); 2.70-2.67 (m, 4H, β-Ala CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ in ppm): 172.99, 163.58, 148.65, 139.10, 124.88, 51.98, 35.15, 33.76. ESI-MS (MeOH): m/z (Calc): $C_{15}H_{19}N_3O_6Na$ $[M+Na]^+$ 360.117; found: 360.074.

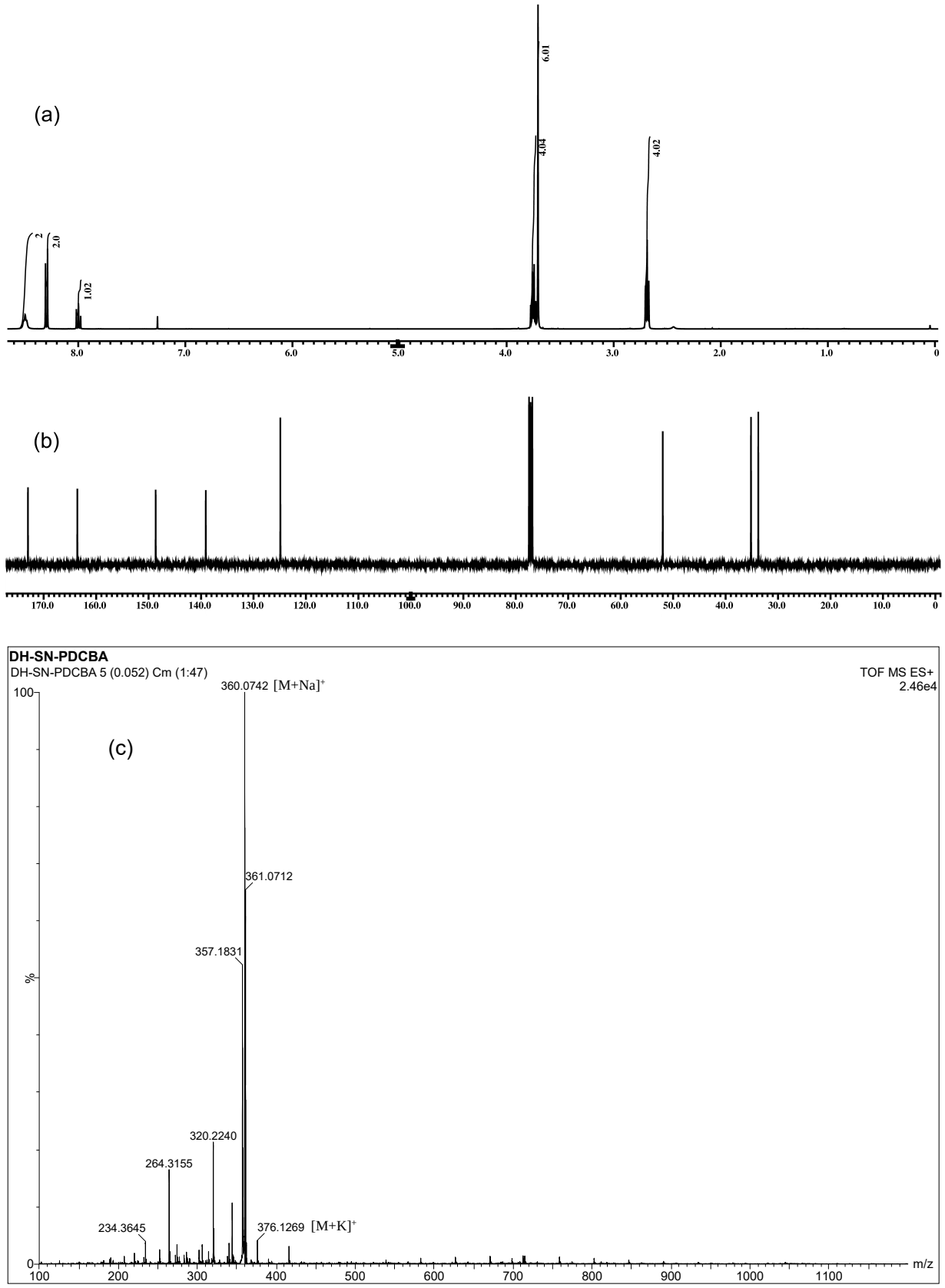


Fig. S2: (a) ^{1}H NMR (400 MHz) and (b) ^{13}C NMR (100 MHz) spectra ($CDCl_3$, δ in ppm, 295 K) and (c) mass spectrum of compound 2.

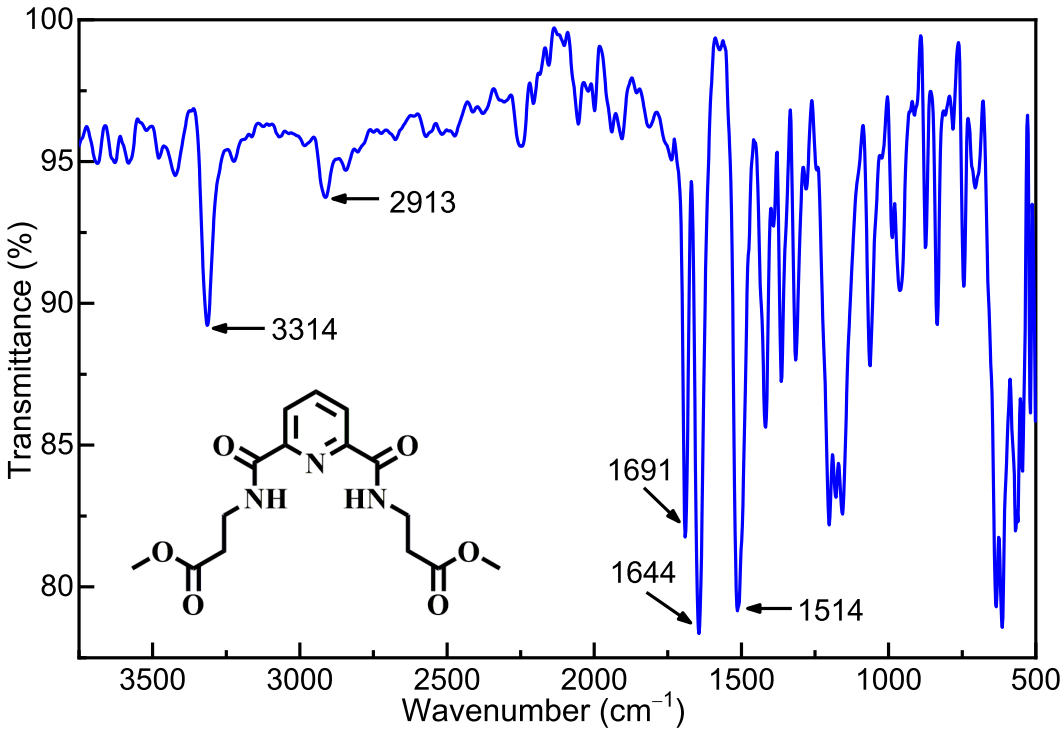


Fig. S3: FT-IR spectrum of compound 2 whose molecular structure is given in the inset.

S1.3 Synthesis of PDCBAOH (3)

To 2.36 g (7.0 mmol) of PDCBA (2), 50 mL MeOH and 2(M) 40 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After 10 h, methanol was removed under vacuum; the residue was dissolved in 25 mL of water and washed with diethyl ether (2×50mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3×50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a white solid.

Yield:1.91 g (6.15 mmol, 87.85 %).

^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 12.20 (bs, 2H, COOH); 9.38 (t, 2H, β-Ala NH); 8.19-5.15 (m, 3H, Aromatic Proton); 3.60-3.55 (m, 4H, β-Ala CH_2); 2.60-2.56 (m, 4H, β-Ala CH_2). ^{13}C NMR (100 MHz, DMSO-d_6, δ in ppm): 172.87, 163.30, 148.60, 139.57, 124.29, 35.34, 34.08. ESI-MS (MeOH): m/z (Calc): $C_{13}H_{15}N_3O_6Na$ $[M+Na]^+$ 332.086; found: 332.044.

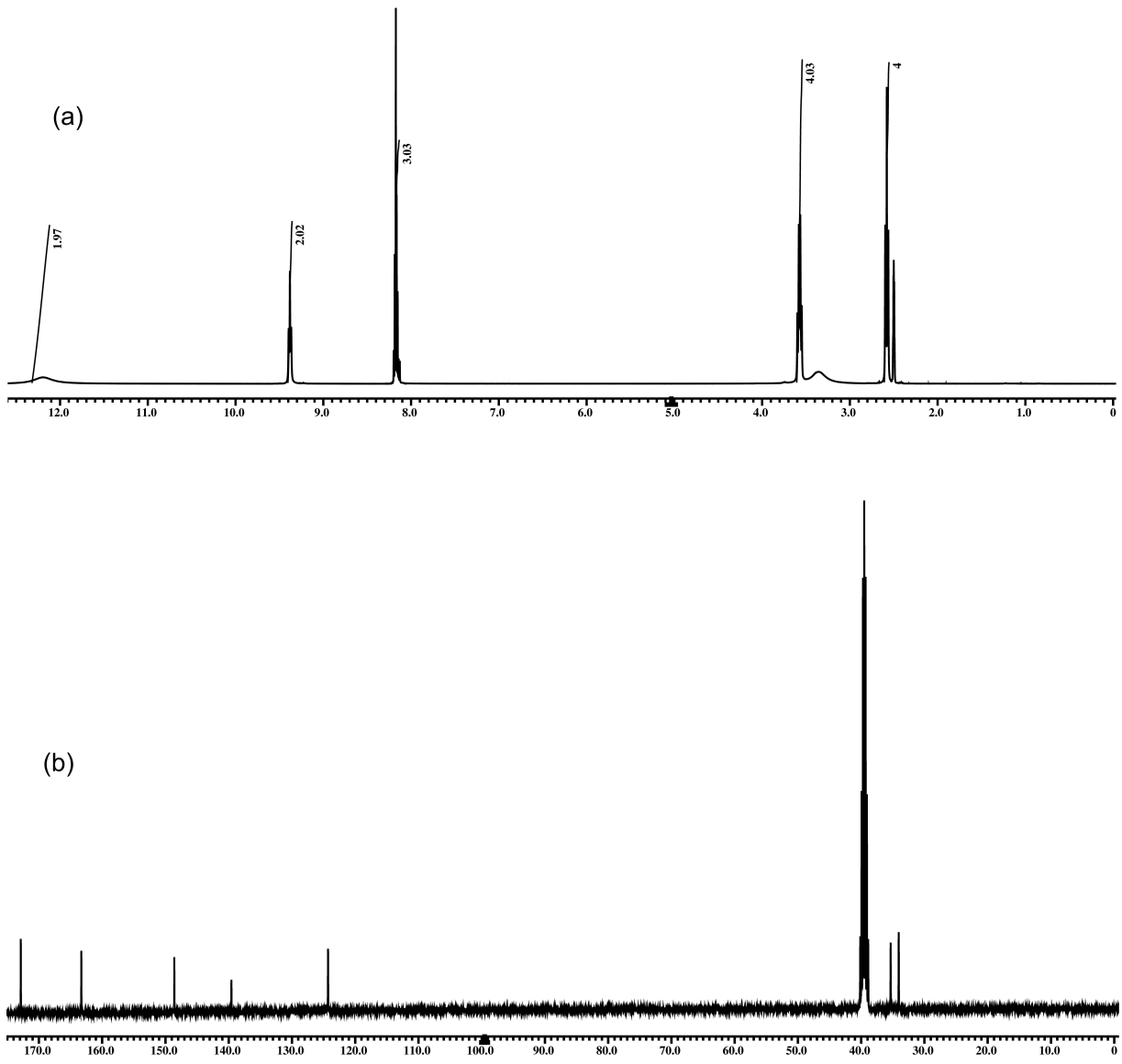


Fig. S4: (a) ^{1}H NMR (400 MHz) and (b) ^{13}C NMR (100 MHz) spectra (DMSO-d_6, δ in ppm, 295 K) of compound 3.

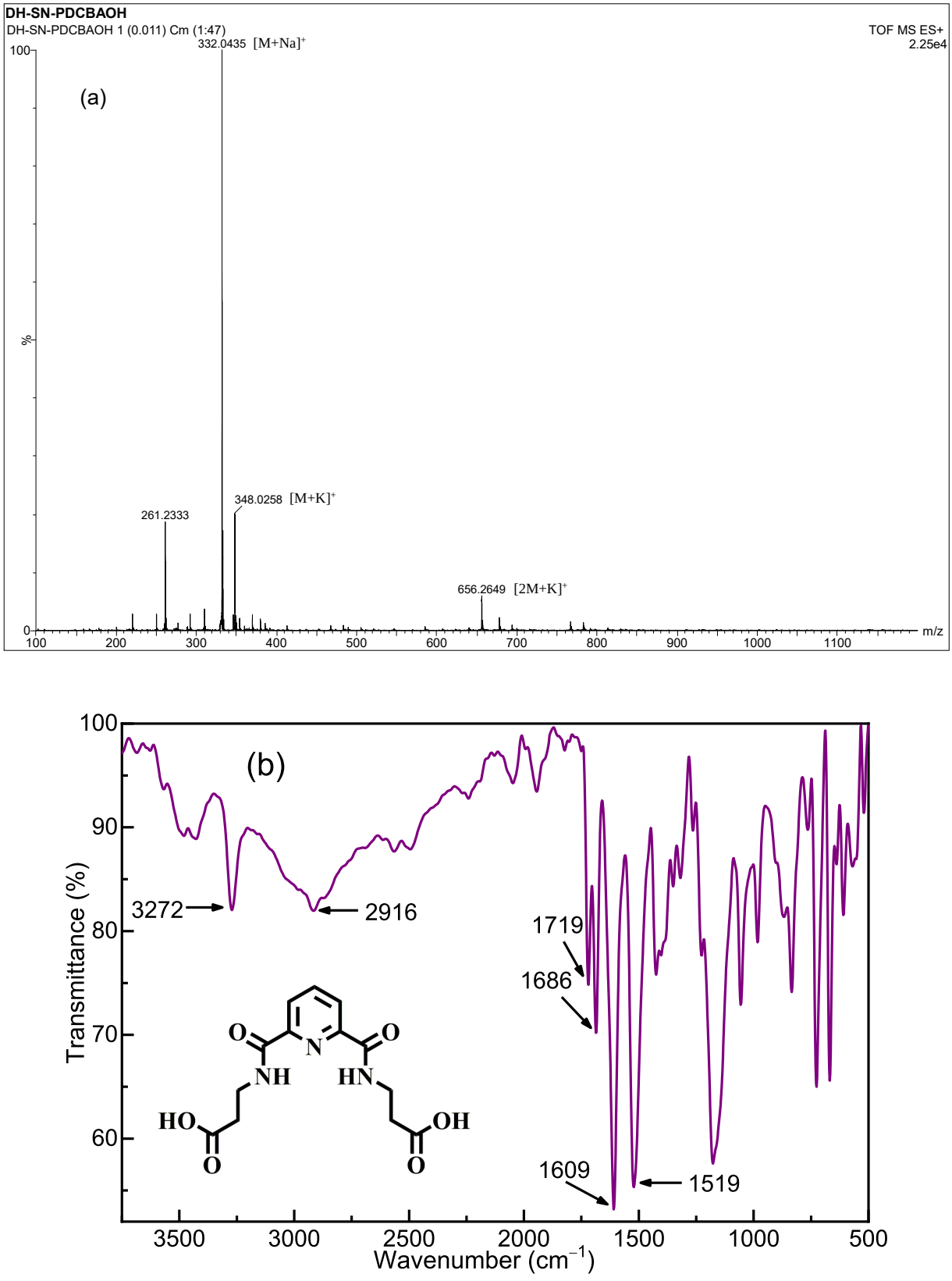


Fig. S5: (a) Mass spectrum and (b) FT-IR spectrum of compound 3 whose molecular structure is given in the inset of (b).

S1.4 Synthesis of PDCBAXYL (4)

1.55 g (5 mmol) of compound 3 (PDCBAOH) was dissolved in 25 mL of DCM and 5 mL of DMF in an ice-water bath. NH_2-Xyl-Boc 2.95 g (12.5 mmol) was pre-prepared from m-xylenediamineand dissolved in 5 mL of DMF and 15 mL of DCM. Then it was added to the pre-cooled reaction mixture, followed immediately by 2.40 g (12.5 mmol) of 1-ethyl-3-(dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl), 2.61 mL (15 mmol) of N,N-diisopropylethylamine (DIPEA) and 1.69 g (12.5 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and then stirred for 48h. After that DCM was evaporated, the residue was taken in 30 mL ethyl acetate. The organic layer was washed with 2(M) HCL (3×50 mL), brine (2×50 mL), then 1 (M) sodium carbonate (3×30 mL) and brine (2×30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the compound 4 as a white solid. Purification was done by silica gel column (100-200 mesh size) with an ethyl acetate and hexane mixture 2:1 as the eluent.

Yield: 2.72 g (3.64 mmol, 72.67 %).

^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm): 8.90 (s, 2H, Xyl-NH); 8.20 (d, 2H, J = 7.64, Aromatic Proton); 7.95 (t, 1H, J = 8.02, Aromatic Proton); 7.28 (s, 2H, Boc NH); 7.06-6.98 (m, 8H, Aromatic Proton); 5.28 (s, 2H, β-Ala NH); 4.27 (d, 4H, J = 5.36, Xyl CH_2); 4.13 (d, 4H, J = 5.36, Xyl CH_2); 3.66-3.62 (m, 4H, β-Ala CH_2); 2.51-2.48 (m, 4H, β-Ala CH_2); 1.41 (s, 18H, Boc CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ in ppm): 172.15, 163.68, 156.27, 148.45, 139.59, 139.08, 138.38, 128.89, 126.58, 126.47, 126.33, 124.50, 79.69, 44.35, 43.52, 36.22, 35.51, 28.50. ESI-MS (MeOH): m/z (Calc): $C_{39}H_{51}N_7O_8Na$ $[M+Na]^+$ 768.370; found: 768.368.

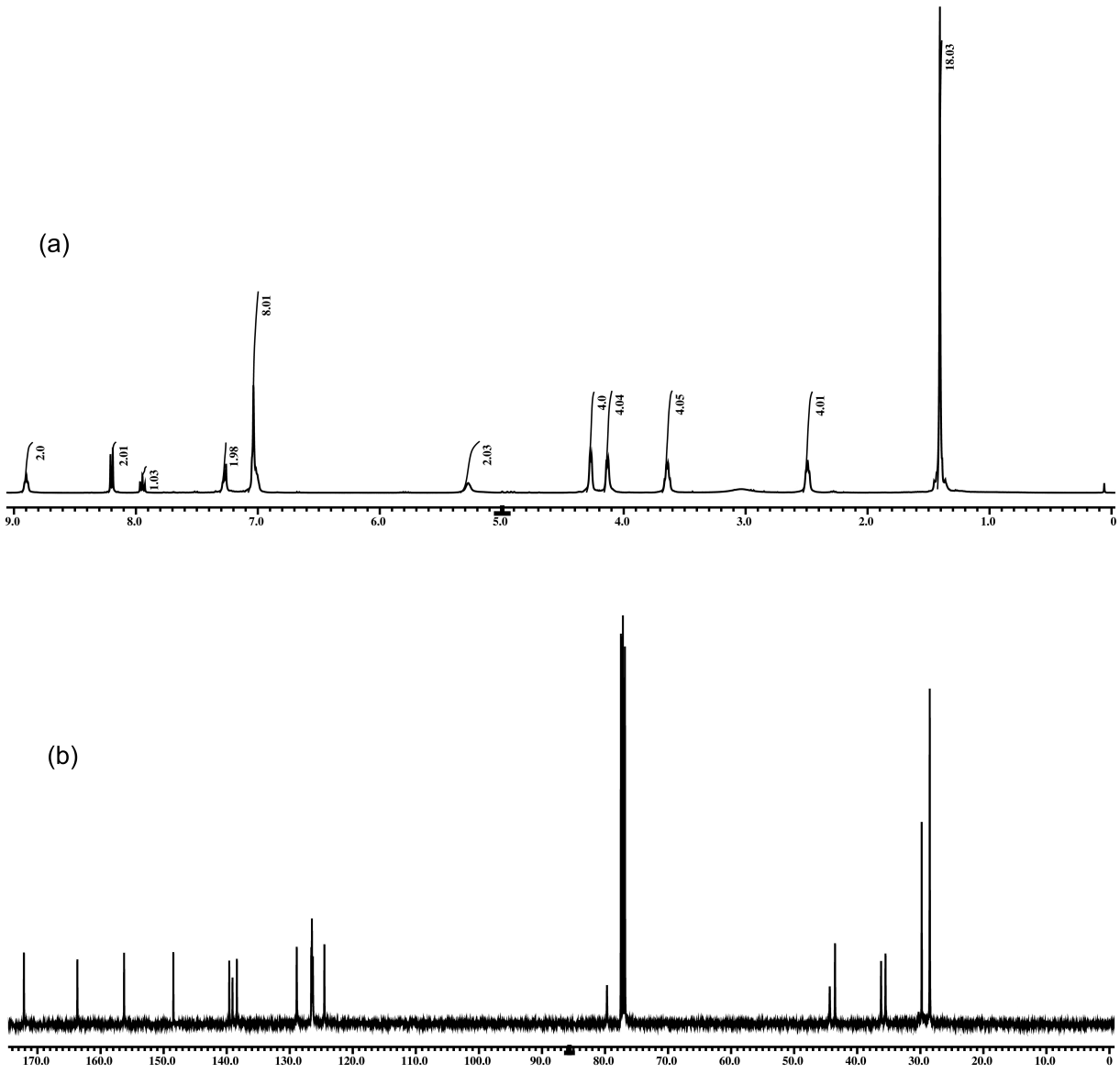
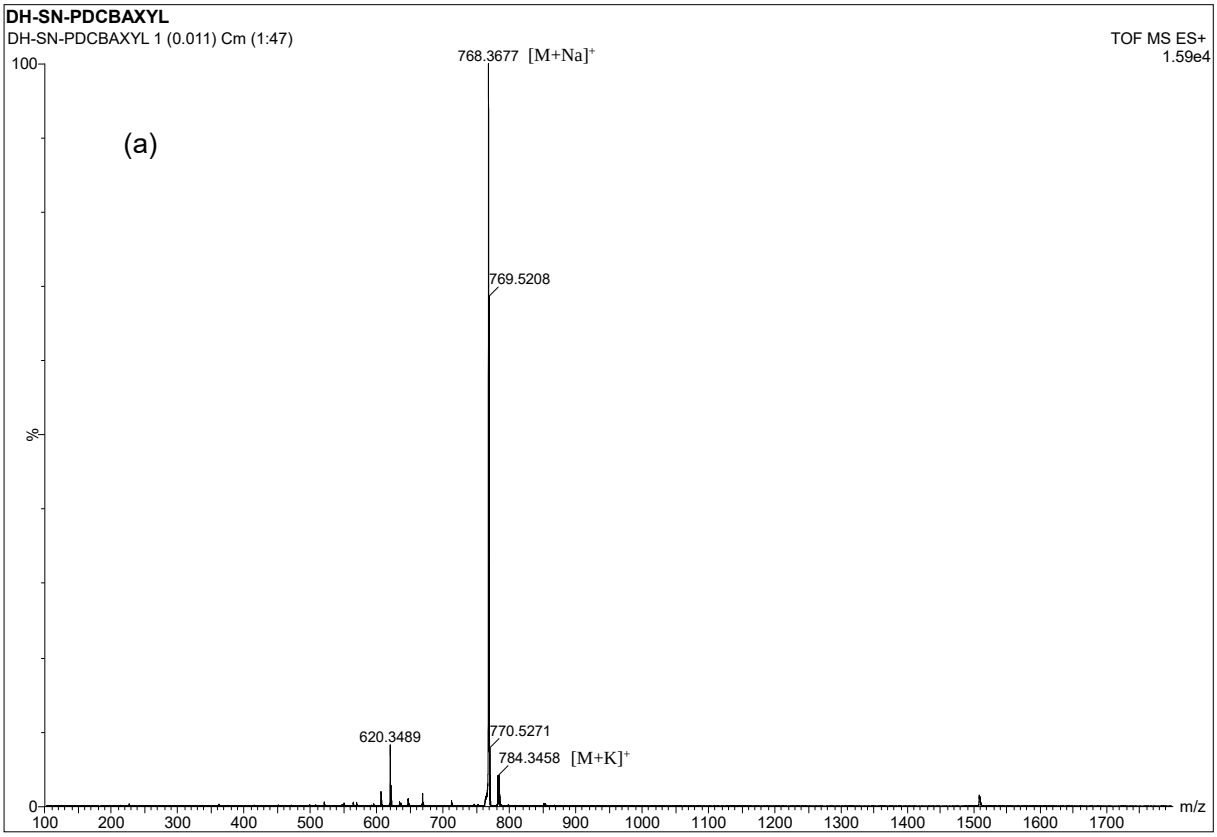


Fig. S6: (a) ^{1}H NMR (400 MHz) and (b) ^{13}C NMR (100 MHz) spectra ($CDCl_3$, δ in ppm, 295 K) of compound 4.



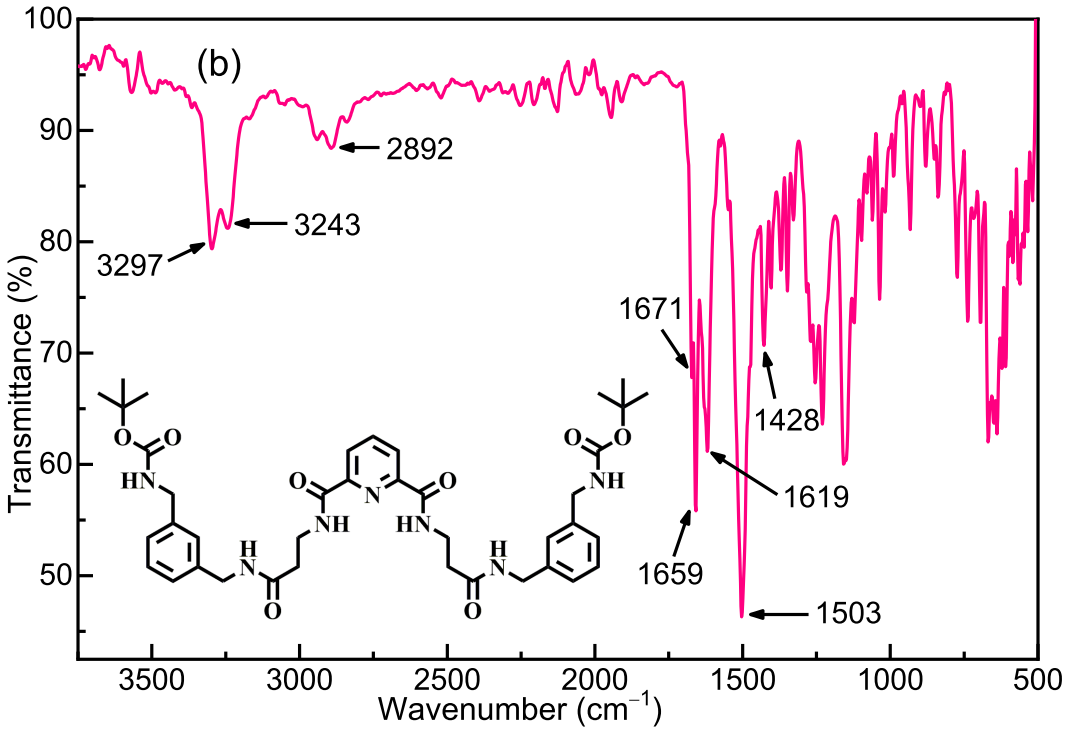


Fig. S7: (a) Mass spectrum and (b) FT-IR spectrum of compound 4 whose molecular structure is given in the inset.

S1.5 Synthesis of PDCBAXYLCOU (1)

1.53 g (5 mmol) of compound 11(Boc-CouOH) was dissolved in 25 mL of DCM and 5 mL of DMF in an ice-water bath. NH_2-PDCBAXYL (compound 5) 1.09 g (2 mmol) was isolated from the corresponding amine-TFA salt by neutralization and subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated under vacuum to 5 mL, then diluted with 20 mL DCM. It was then added to the pre-cooled reaction mixture, followed immediately by 1.0 g (5.2 mmol) of 1-ethyl-3-(dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl), 1.05 mL (6 mmol) of N,N-diisopropylethylamine (DIPEA) and 0.70 g (5.2 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and then stirred for 48h. After that DCM was evaporated, the residue was taken in 30 mL ethyl acetate. The organic layer was washed with 2(M) HCL (3×50 mL), brine (2×50 mL), then 1 (M) sodium carbonate (3×30 mL) and brine (2×30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the compound 4 as a white solid. Purification was done by silica gel column (100-200 mesh size) with an ethyl acetate and hexane mixture 4:1 as the eluent.

Yield: 1.47 g (1.31 mmol, 65.42 %).

^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 9.61 (s, 2H, Boc NH); 9.41 (bs, 2H, Xyl-NH); 9.10 (t, 2H, $J = 6.1$ Aromatic Proton); 8.75 (s, 2H, Cou proton); 8.48 (t, 2H, $J = 5.74$, Aromatic Proton); 8.13-8.09 (m, 3H, Aromatic Proton); 7.99 (s, 2H, Xyl-NH); 7.66-7.63 (m, 2H, β-Ala NH); 7.37 (d, 2H, $J = 9.16$, Aromatic Proton); 7.20-7.18 (m, 6H, Aromatic Proton); 7.13-7.10 (m, 2H, Aromatic Proton); 4.48 (d, 4H, $J = 6.12$, Xyl CH_2); 4.26 (d, 4H, $J = 5.36$, Xyl CH_2); 3.60-3.55 (m, 4H, β-Ala CH_2); 3.40-3.34 (m, 4H, β-Ala CH_2); 1.48 (s, 18H, Boc CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, δ in ppm): 170.26, 163.13, 161.24, 160.42, 152.79, 149.17, 148.54, 147.58, 139.66, 139.22, 138.94, 136.52, 128.30, 126.11, 125.81, 124.68, 124.01, 119.10, 118.34, 117.51, 116.43, 79.53, 42.67, 41.97, 35.98, 35.63, 28.09. ESI-MS (MeOH): m/z (Calc): $C_{59}H_{61}N_9O_{14}Na$ $[M+Na]^+$ 1142.424; found: 1142.415.

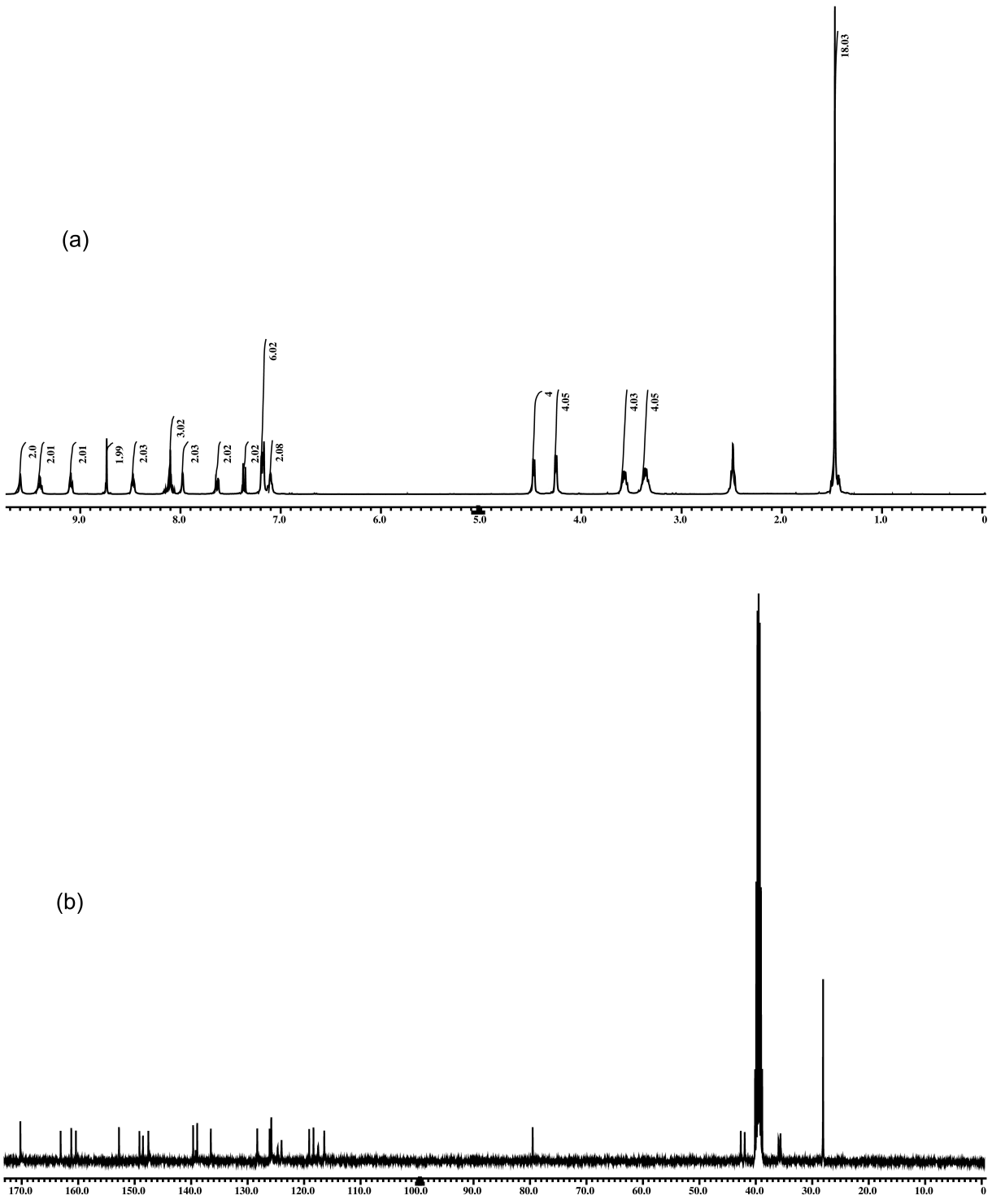
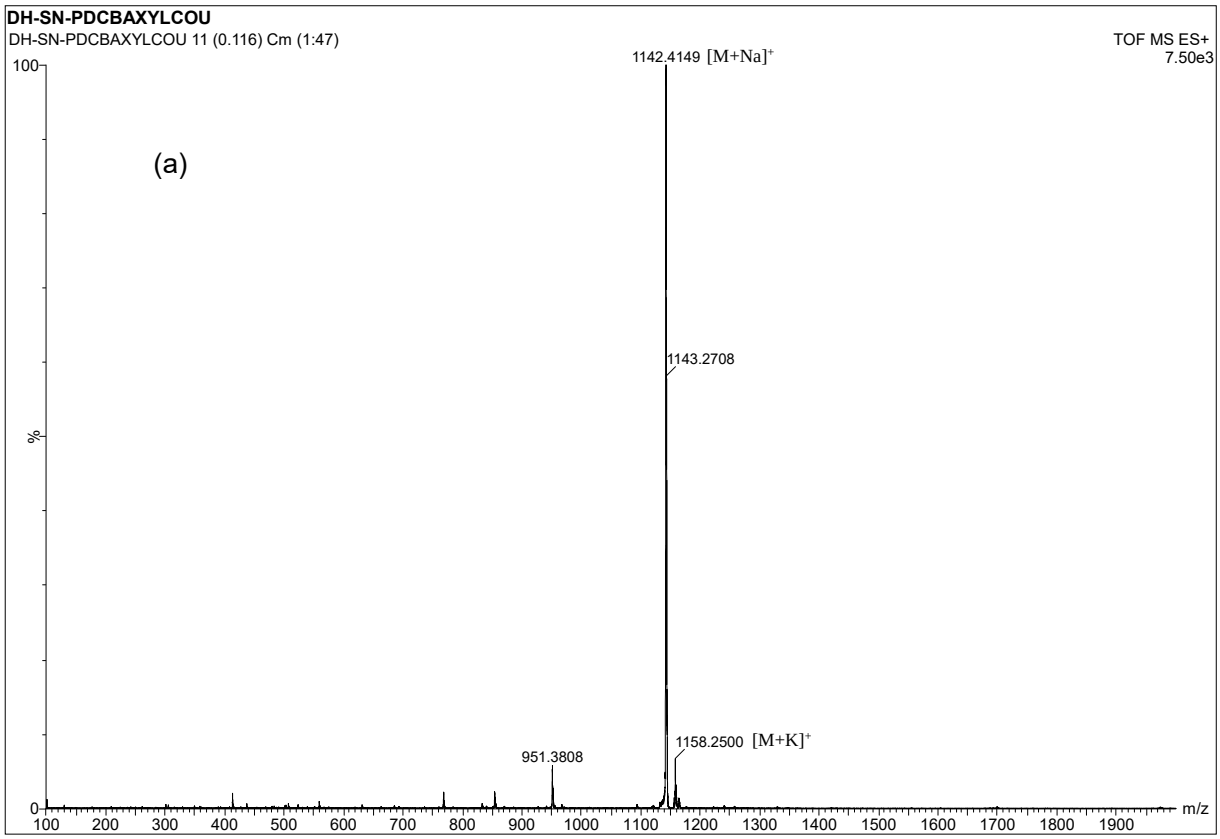


Fig. S8: (a) ^{1}H NMR (400 MHz) and (b) ^{13}C NMR (100 MHz) spectra (DMSO-d_6, δ in ppm, 295 K) of compound 1.



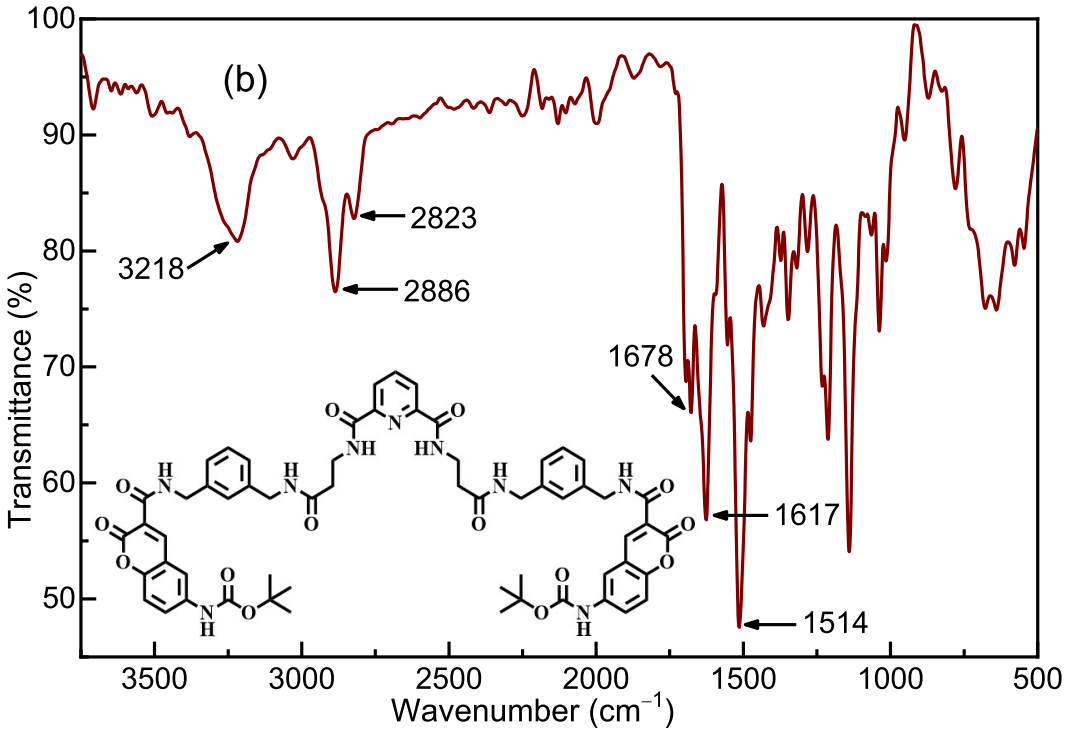


Fig. S9: (a) Mass spectrum and (b) FT-IR spectrum of compound 1 whose molecular structure is given in the inset.

S1.6 Synthesis of Xylmb (6)

3.25 g (30 mmol) m-xylenediamine was dissolved in 300 mL of dioxane and was cooled in ice bath. A solution of di-tert-butyldicarbonate (7.5 mmol, 1.65g) in dioxane (200 mL) was added drop-wise to the precooled diamine solution over a period of 1 hrs. After stirring for 48 h, the dioxane was evaporated in vacuum. The resulting mixture was dissolved in ethyl acetate and washed with brine (4×100 ml) and water (1×100 ml). Then it was dried over anhydrous Na_2SO_4 and concentrated in vacuum to afford a yellow viscous oily liquid. Now it was purified by column chromatography to obtain 4.2 gm (90 %) of tert-Butyl 3-aminomethyl benzylcarbamate, (xylmb) as colourless viscous oil.

Yield: 1.52g (6.43 mmol, 85.75 %).

^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm, 295 K): 7.41 (s, 1H, Xyl NH); 7.27-7.23 (m, 3H, aromatic proton); 7.13 (d, 1H, $J = 6.88$, aromatic proton), 5.50 (bs, 2H, Xyl-NH_2); 4.13 (d, 2H, $J = 6.12$, Xyl-CH_2), 3.78 (s, 2H, Xyl-CH_2); 1.41 (s, 9H, BOC CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, δ in ppm, 295 K): 155.83, 140.96, 140.11, 128.15, 126.26, 125.91, 125.41, 77.75, 44.42, 43.43, 28.27). ESI-MS (MeOH): m/z (Calc): $C_{13}H_{20}N_2O_2Na$ $[M+Na]^+$ 259.142; found: 259.137.

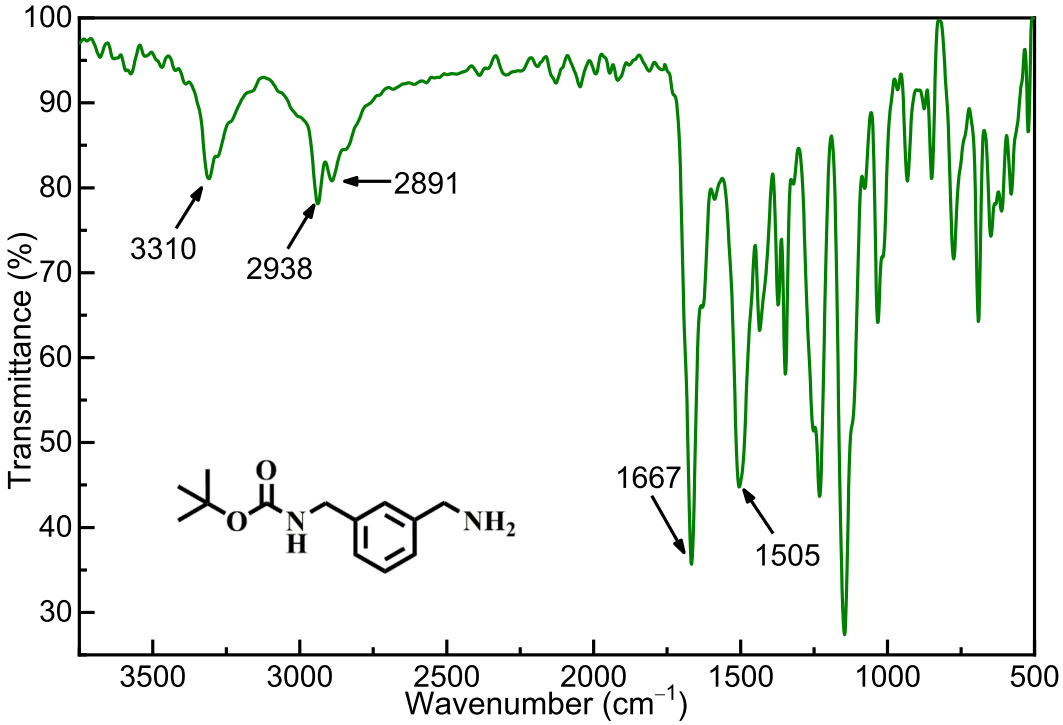


Fig. S10: FT-IR spectrum of compound 6 whose molecular structure is given in the inset.

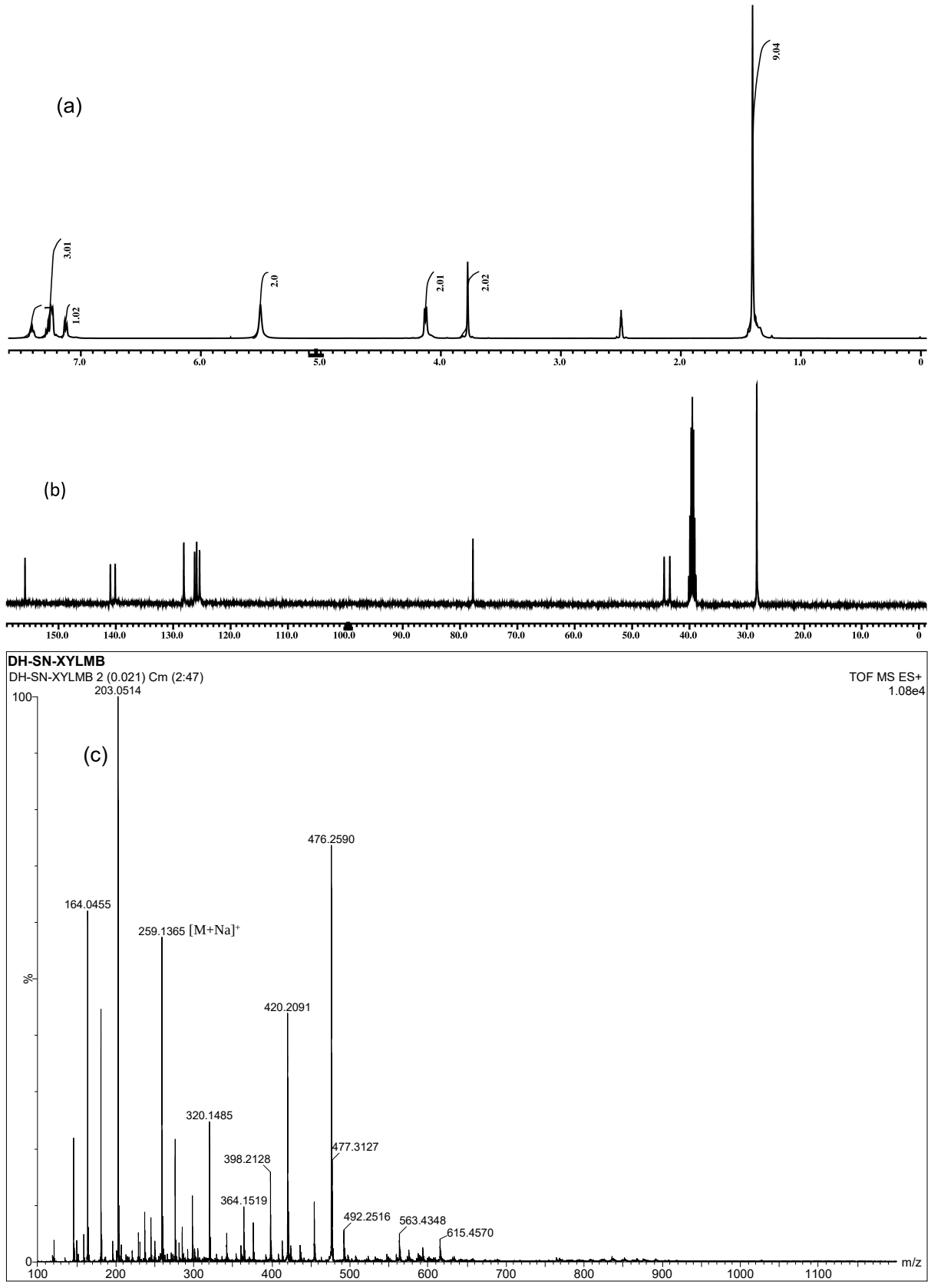


Fig. S11: (a) ^{1}H NMR (400 MHz) and (b) ^{13}C NMR (100 MHz) spectra (100 MHz, DMSO-d_6, δ in ppm, 295 K), and (c) mass spectrum of compound 6.

S2 Absorption and photoluminescence spectra

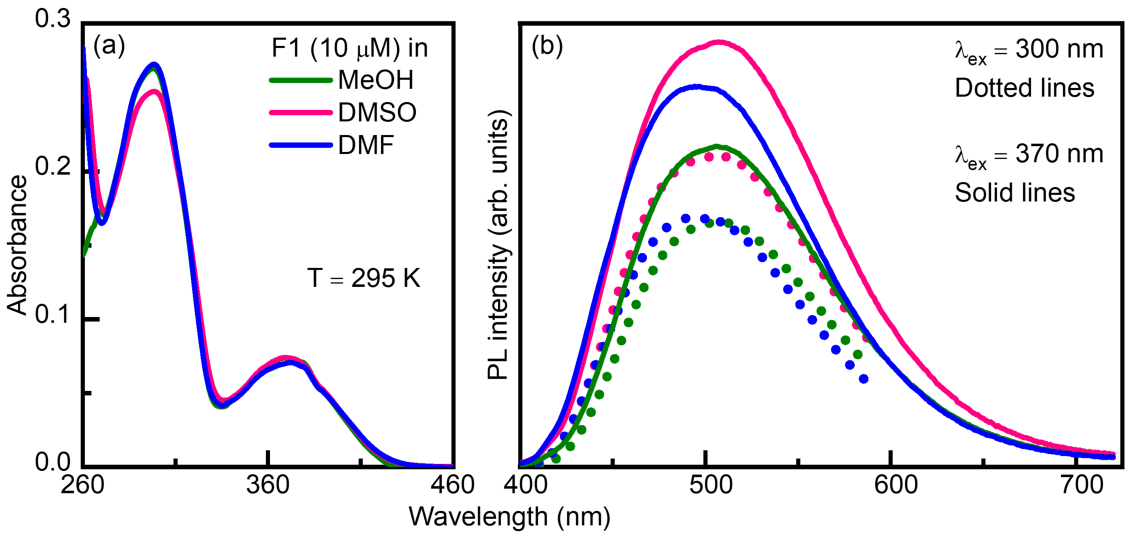


Fig. S12: (a) Absorption and (b) PL spectra of 10 μM solutions of F1 in MeOH, DMSO, and DMF. Color codes are same in (a) and (b). PL spectra measured for excitation wavelengths λ_{ex} = 300 nm (recorded up to 590 nm to avoid detection of second order diffraction of excitation light) and 370 nm, were scaled by the absorbance at the respective λ_{ex}.

Linear absorption and photoluminescence (PL) spectra measured at room-temperature (T = 295 K) on 10 μM solutions of F1 in MeOH, DMSO, and DMF are presented in Fig. S12a,b. Absorption spectra of F1 in MeOH, DMSO, and DMF are nearly identical (Fig. S12a), i.e., solvent effect on linear absorption is negligible. The absorption peaks at about 300 and 370 nm may be attributed, respectively, to the π to $\pi^\star$ and n to $\pi^\star$ transitions. The rise in absorbance below 270 nm for F1 in DMSO and DMF are due to the respective solvents. The solvent peak for MeOH appears at around 205 nm (not shown). Linear absorption for F1 is negligible for wavelengths longer than 430 nm. PL spectra (Fig. S12b) of F1 in MeOH, DMSO, and DMF, measured for excitation at wavelengths λ_{ex} = 300 and 370 nm, corresponding to the two absorption peaks, are plotted after scaling by the absorbance at the respective λ_{ex}. Spectral shape of the PL appears to be nearly independent of the λ_{ex} as well as the solvent used. However, the PL efficiency for a given solvent for λ_{ex} = 300 nm is nearly 30 % smaller than that for λ_{ex} = 370 nm. On the other hand, the PL efficiency for a given λ_{ex} for MeOH (DMF) is about 25 % (15 %) smaller than that for DMSO. Lower PL efficiency for F1 in MeOH as compared to that in DMSO indicates higher nonradiative-recombination in MeOH. The difference in PL efficiency for

different solvents at a given λ_{ex} may be on account of the difference in H-bonding pattern between F1 and these solvents.

S3 Instrument specifications

- **NMR study**

  All NMR experiments were performed on a Jeol 400 MHz and a Bruker 500 MHz spectrometer at room-temperature (T = 295 K). Compound concentrations were in the range of 1–10 mM.

- **FT-IR spectroscopy**

  Solid-state FT-IR spectra following ATR technique were measured in a Perkin Elmer Spectrum RX1 spectrophotometer at T = 295 K.

- **Mass spectrometry**

  Mass spectra of the compounds were recorded on a Q-Tof Micro YA263 high-resolution (Waters Corporation) mass spectrometer by positive-mode electrospray ionization.

- **Absorption spectroscopy**

  The absorption spectra were recorded on a Perkin Elmer Lambda 35 UV-Visible spectrophotometer at T = 295 K.

- **Photoluminescence spectroscopy**

  Photoluminescence (PL) spectra were recorded at T = 295 K on a Jasco 3 Fluorescence spectrometer using 1 cm path length quartz cell. Slit widths of 2.5 nm / 2.5 nm were used.

- **Circular dichroism spectroscopy**

  Circular dichroism (CD) spectra of foldamer F1 in DMSO, methanol, and DMF have been recorded in a JASCO J-815-150S CD spectrometer at room-temperature (T = 295 K).

S4 Additional data

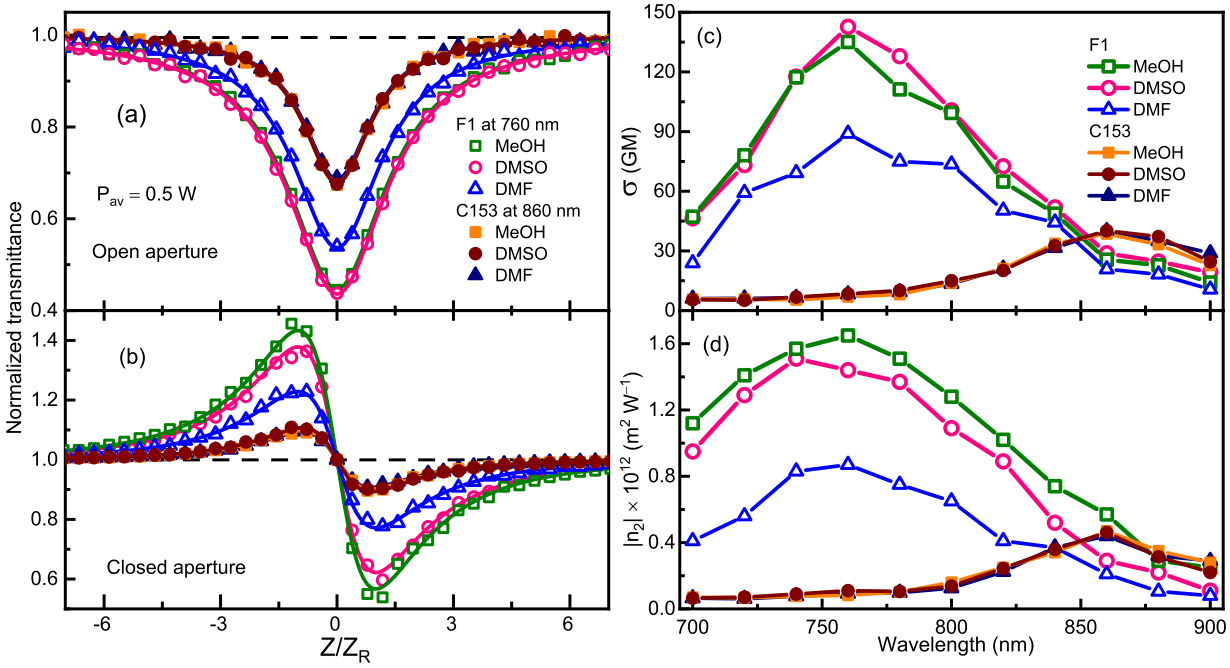


Fig. S13: (a) OAZS and (b) CAZS data for F1 and C153 in different solvents for $P_{\rm av} = 0.5$ W. Solid lines are theoretical fits. Wavelength-dependence of (c) TPA cross-section σ and (d) magnitude of nonlinear refractive index $|n_2|$, estimated, respectively, from OAZS and CAZS data. Plot legend are common for (a,b) and (c,d).

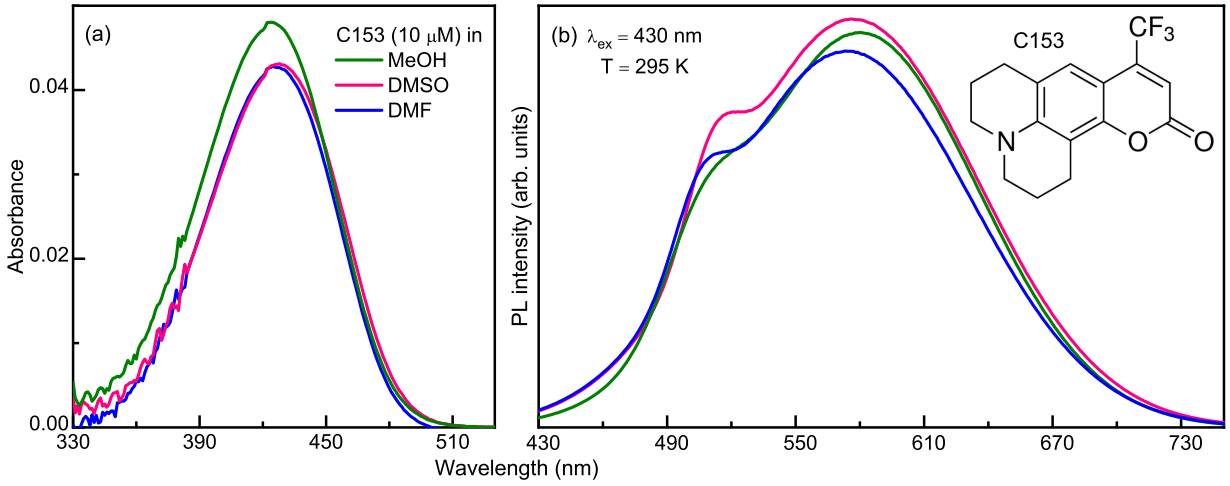


Fig. S14: (a) Absorption and (b) PL spectra (excitation at 430 nm) of C153 in MeOH, DMSO, and DMF, measured at room temperature. Color codes are same in (a) and (b). Inset of (b): Molecular structure of C153.