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Influence of Amino Acid Side Chains on the Formation of Two Component Self-Assembling Nanofibrous Hydrogels

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Supporting Information

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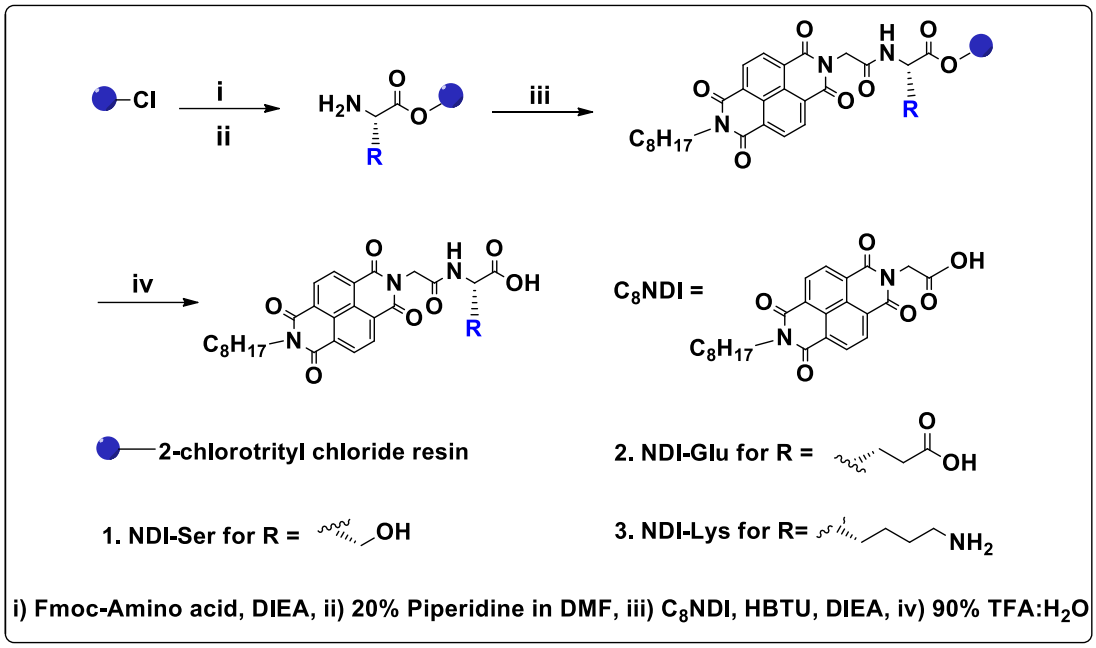
1. Synthetic routes for compounds 1-3:



Scheme S1. Schematic representation of the synthetic route for the preparation of NDI derivatives.

2. Experimental Section

Synthesis of (7-Octyl-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1H benzo[lmn][3,8] phenanthrolin-2-yl) acetic acid (C_8NDI)

A solution of 1,4,5,8-Naphthalenetetracarboxylic dianhydride (NDA) (2.68 g, 10.0 mmol), n-octylamine (1.30 g, 20.0 mmol), and glycine (0.62 g, 20.0 mmol) in DMF (40 mL) was stirred at 120^{o}C for 4 h. After the mixture had cooled to room temperature, the insoluble solid was filtered off and the solution was poured into water (100 mL) The precipitate was filtered, washed with water (15 mL), methanol (15 mL), and CH_2Cl_2 (15 mL). Compound C_8NDI was obtained as a pink solid (1.33 g, 29%) ^{1}H NMR (300 MHz, d_6-DMSO, 25 ^{o}C): δ=0.80-0.95 (m, 3H; CH_3), 1.25-1.50 (m, 10H; CH_2), 1.60-1.80 (m, 2H; CH_2), 4.09 (t, *J*=7.35 Hz, 2H; CH_2), 4.75-4.85 (s, 2H; CH_2), 8.65-8.85 (m, 4H; CH).[S1]

*2.1. Preparation of compounds (**1-3**)*

All the NDI-capped peptide derivatives were prepared using solid phase peptide synthesis (SPPS). Firstly, 1.2 g of resin was swollen with anhydrous dichloromethane (DCM) for 30 min under nitrogen atmosphere. Corresponding Fmoc protected amino acid (2 mmol) i.e., O-tert-Butyl-L-serine (2 mmol) or Fmoc-L-Glutamic acid 5-tert-butyl ester or *N*-alpha-Fmoc-Nepsilon-BOC-L-Lysine in anhydrous *N, N*-Dimethlyformamide (DMF) and *N, N*-Diisopropylethylamine (DIEA) (0.830 mL, 5

mmol) were added in to the resin solution and stirred for 1 h at room temperature. After 30 min, the block solution (DCM: MeOH: DIEA) was added followed by the addition of 20% of piperidine for the deprotection of Fmoc group for 30 min and repeated for every 2 min twice. Then, the 7-octyl naphthalene diimide (C8NDI) (0.4365 g, 1 mmol) was coupled to the free amino group using O-(benzotriazol-1-yl)-*N, N, N', N'*,-tetramethyluroniumhexafluorophospate (HBTU) (0.759 g, 2 mmol) and *N, N*-Diisopropylethylamine (DIEA) (0.83 mL, 5 mmol) as the coupling reagent. The reaction mixture was stirred overnight, followed by the treatment with 90 % trifluoroaceticacid (TFA) in water for 3 h for the cleavage of resin from the peptide derivative. The resultant solution was collected and solid product was precipitated by adding ice cold diethyl ether. The product obtained was dried under the vacuum to remove the residual solvents.

2.1.1.(*S*)-3-hydroxy-2-(2-(7-octyl-1,3,6,8-tetraoxo-7,8-dihydrobenzo[lmn][3,8]phenanthrolin-2(1H,3H,6H)-yl)acetamido)propanoic acid (**1**).

Dark red solid: 0.281 g .^{1}H NMR (300 MHz, d_6-DMSO, 25^{o}C): δ=0.85-0.95 (t, *J*=7.5 Hz 3H; CH_3), 1.20-1.45 (m, 10H; CH_2), 1.60-1.80 (m, 2H; CH_2), 3.60-3.70 (m, 1H; CH_2), 3.70-3.80 (m, 1H; CH_2), 4.05-4.15 (t, *J*=9.6 Hz, 2H; CH_2), 4.30-4.40 (m, 1H; CH), 4.75-4.90 (s, 2H; CH_2), 8.55-8.65 (d, *J*=10.4 Hz, 1H; NH), 8.65-8.75 (m, 3H; CH), 8.75-8.80 (m, 1H; CH). ^{13}C NMR (75 MHz, d_6-DMSO, 25^{o}C): δ=14.0, 22.1,

26.5, 27.3, 28.6, 28.7, 31.3, 42.4, 54.8, 61.5, 125.7, 126.0, 126.1, 126.2, 126.5, 130.4, 130.7, 130.8, 162.3, 162.4, 166.3, 171.8. MS [ESI$^-$]: m/z (%): Calculated: 523.20, observed: 522.4 [*M*-H]$^-$.

2.1.2. (*S*)-2-(2-(7-octyl-1,3,6,8-tetraoxo-7,8-dihydrobenzo[lmn][3,8]phenanthrolin 2(1H,3H,6H)-yl)acetamido)pentanedioic acid (**2**).

Light brown solid: 0.3280 g. ^{1}H NMR (300 MHz, d_6-DMSO, 25^{o}C): δ=0.85-0.95 (m, 3H; CH_3), 1.20-1.45 (m, 10H; CH_2), 1.60-1.80 (m, 2H; CH_2),1.75-2.05 (m, 2H; CH_2), 2.30-2.40 (t, *J*=7.35 Hz 2H; CH_2), 4.05-4.15 (t, *J*=7.2 Hz 2H; CH_2), 4.25-4.35 (m, 1H; CH), 4.75-4.85 (s, 2H; CH_2), 8.60-8.80 (m, 4H; CH). ^{13}C NMR (75 MHz, d_6-DMSO, 25^{o}C): δ=14.9, 23.1, 27.5, 27.6, 28.3, 29.5, 29.7, 30.9, 32.2, 43.4, 52.2, 126.7, 127.0, 127.1, 127.4, 131.4, 131.6, 163.3, 163.4, 167.4, 174.0, 174.7. MS [ESI$^-$]: m/z (%): calculated: 565.21, observed: 564.5 [*M*-H]$^-$.

2.1.3.(*S*)-6-amino-2-(2-(7-octyl-1,3,6,8-tetraoxo-7,8-dihydrobenzo[lmn][3,8]phenanth rolin-2(1H,3H,6H)-yl)acetamido)hexanoic acid (**3**).

Light brown solid: 0.422 g. ^{1}H NMR (300 MHz, d_6-DMSO, 25^{o}C): δ=0.85-0.95 (m, 3H; CH_3), 1.25-1.45 (m, 12H; CH_2), 1.55-1.90 (m, 6H; CH_2), 2.80-2.90 (t, *J*=10.0 Hz, 2H; CH_2), 4.05-4.15 (t, *J*=9.6 Hz, 1H; CH_2), 4. 25-4.35 (m, 1H; CH) 4.75-4.85 (s, 2H; CH_2), 7.70-7.80 (d, *J*=7.6 Hz, 1H; NH), 8.60-8.70 (d, *J*=10.8 Hz, 1H; CH), 8.70-8.75 (m, 2H; CH), 8.75-8.80 (m, 1H; CH). ^{13}C NMR (75 MHz, d_6-DMSO, 25^{o}C): δ=14.0,

22.1, 22.4, 26.5, 26.6, 27.4, 28.6, 28.7, 30.6, 31.3, 35.9, 42.5, 51.9, 125.6, 125.87, 125.90, 126.1, 126.3, 130.4, 130.7, 162.2, 162.3, 166.4, 173.3. MS [ESI^+]: m/z (%): calculated: 564.26, observed: 565.2 [M+H]$^-$.

3. Transmission Electron Microscopy (TEM):

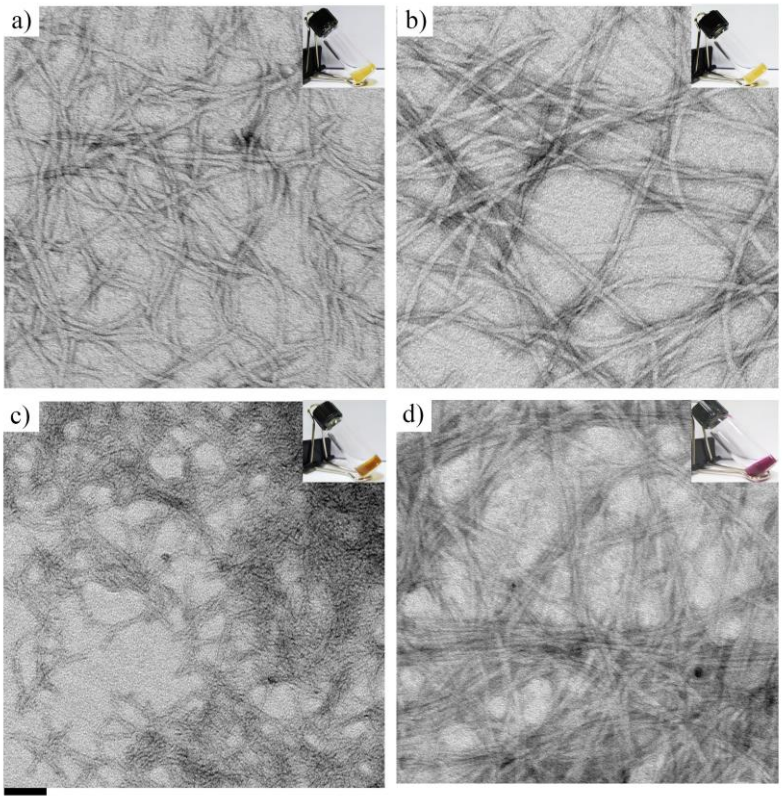


Fig S1. TEM images of the corresponding gels (a) **1**, (b) **2**, (c) **3** and (d) **2+4** at 1 wt% respectively. The inset represents the optical images of their corresponding gels. The scale bar indicates 50 nm.

4. UV-Vis absorption Spectra:

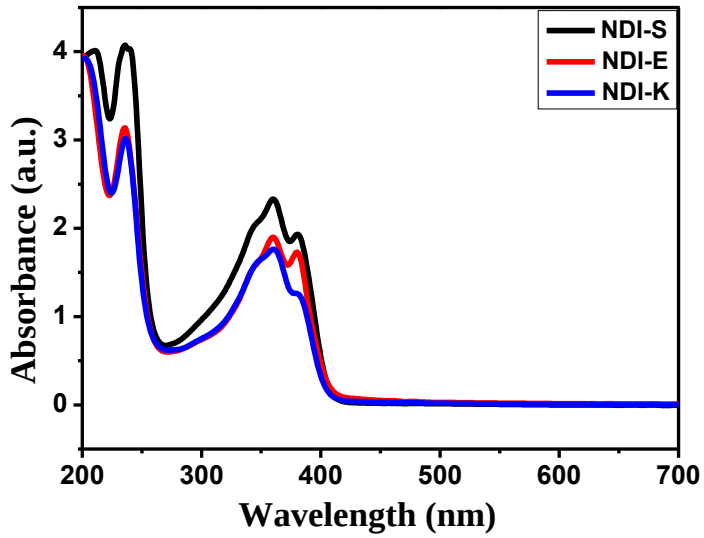


Fig. S2 UV-Vis absorption spectra of single components **1** (black), **2** (red) and **3** (blue) at 2000 µM concentration in aqueous media.

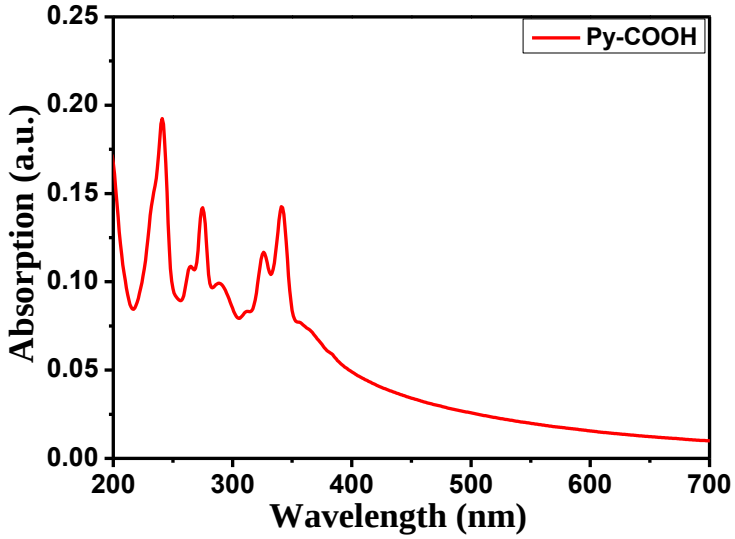


Fig. S3 UV-Vis absorption spectra of compound **4** at 100 µM concentration in aqueous media.

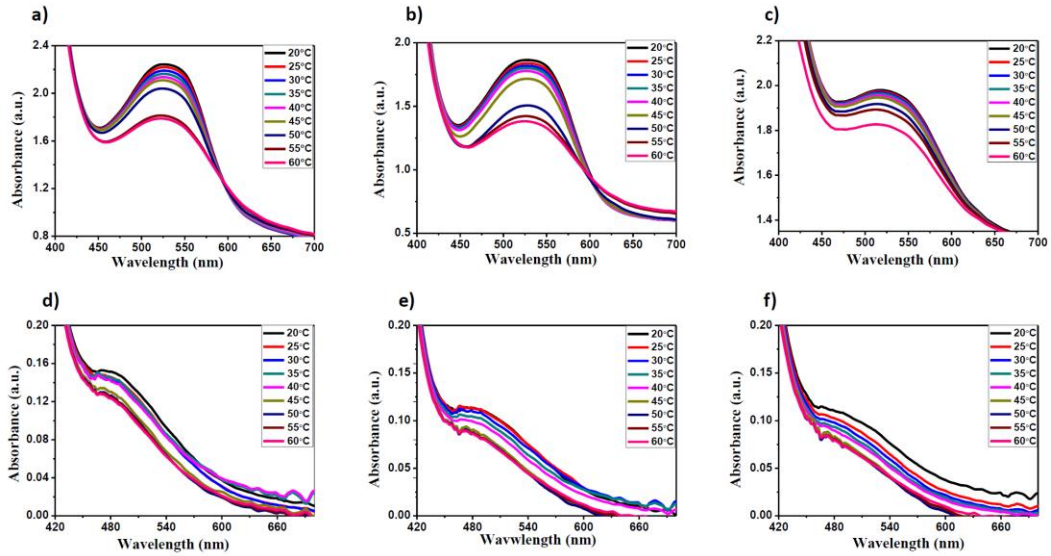


Fig. S4 Variable temperature dependent UV-Vis absorption spectra of the 1:1 blend of a) **1+4**, b) **2+4**, as well as c) **3+4** at 20000 µM concentration in H_2O and (d, e, f) in DMSO.

5. CD Spectra:

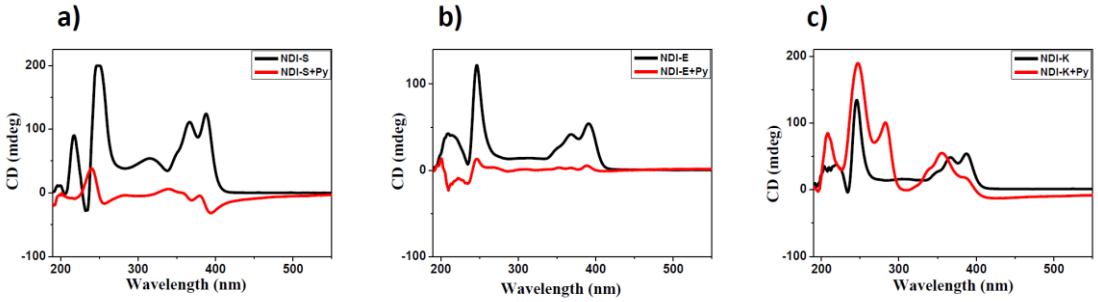


Fig. S5 CD spectrum of single components **1-3** in black and mixed components **1+4**, **2+4**, **3+4** in red at 2000 µM concentration in water.

6. FT-IR spectra:

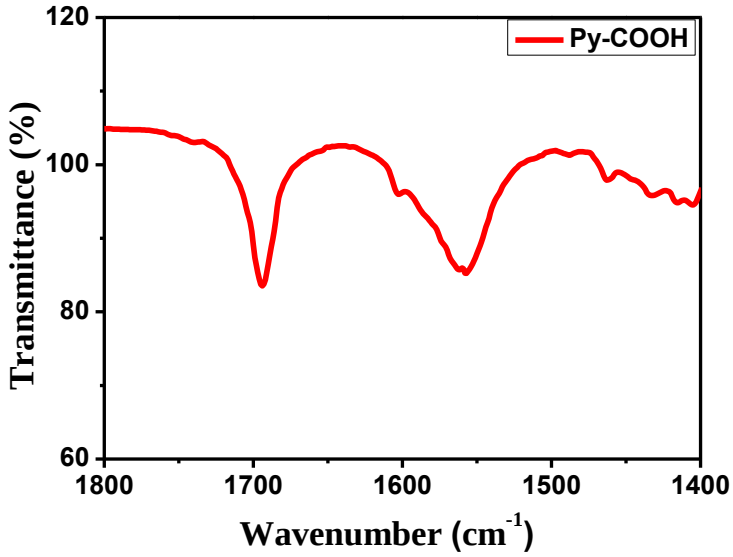


Fig. S6 FT-IR spectra of Pyrene butyric acid (**4**) in aqueous media.

7. Optimized Geometry of Dimers:

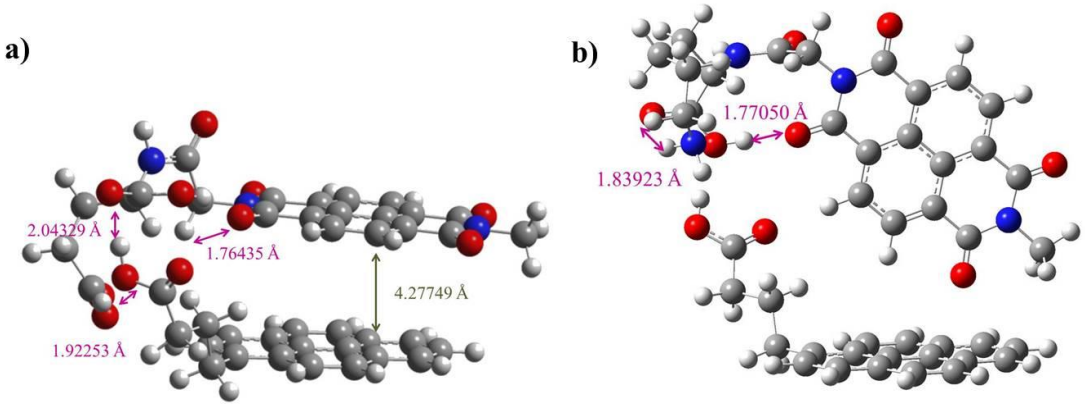


Fig. S7 The optimized dimer structures of **2**+**4** (left) and **3**+**4** (right) which were calculated at DFT/B3LYP/6-31G* level of theory.

8. ^{1}H NMR spectra

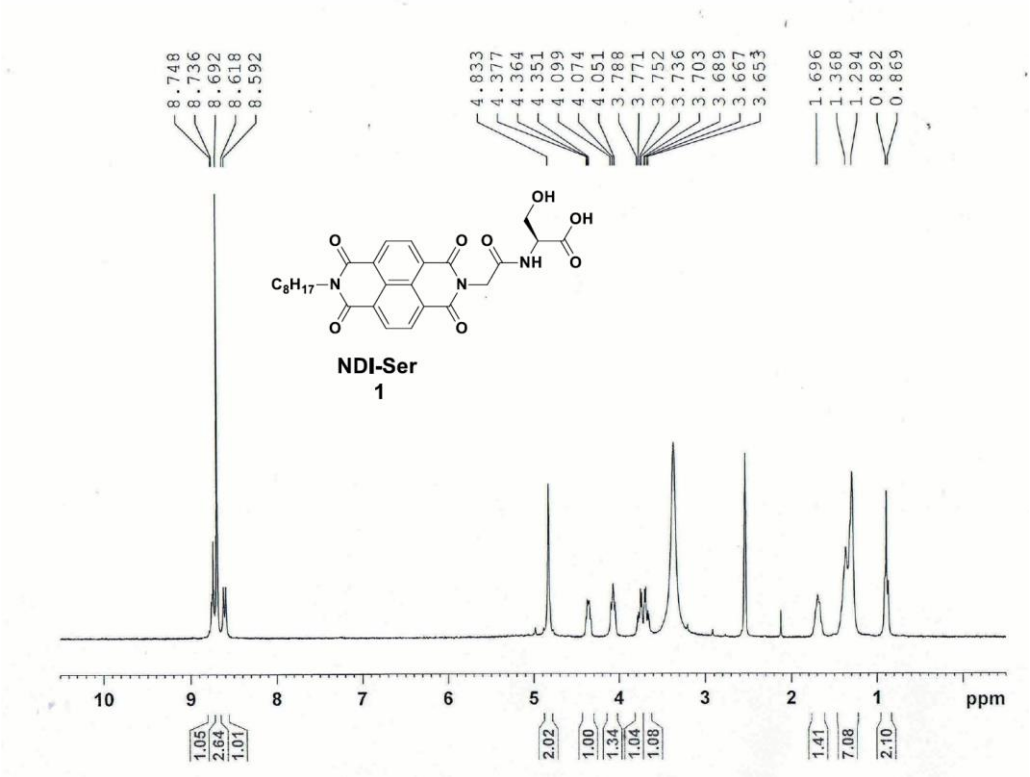


Fig. S8 ^{1}H-NMR spectrum of **1** in d_6-DMSO.

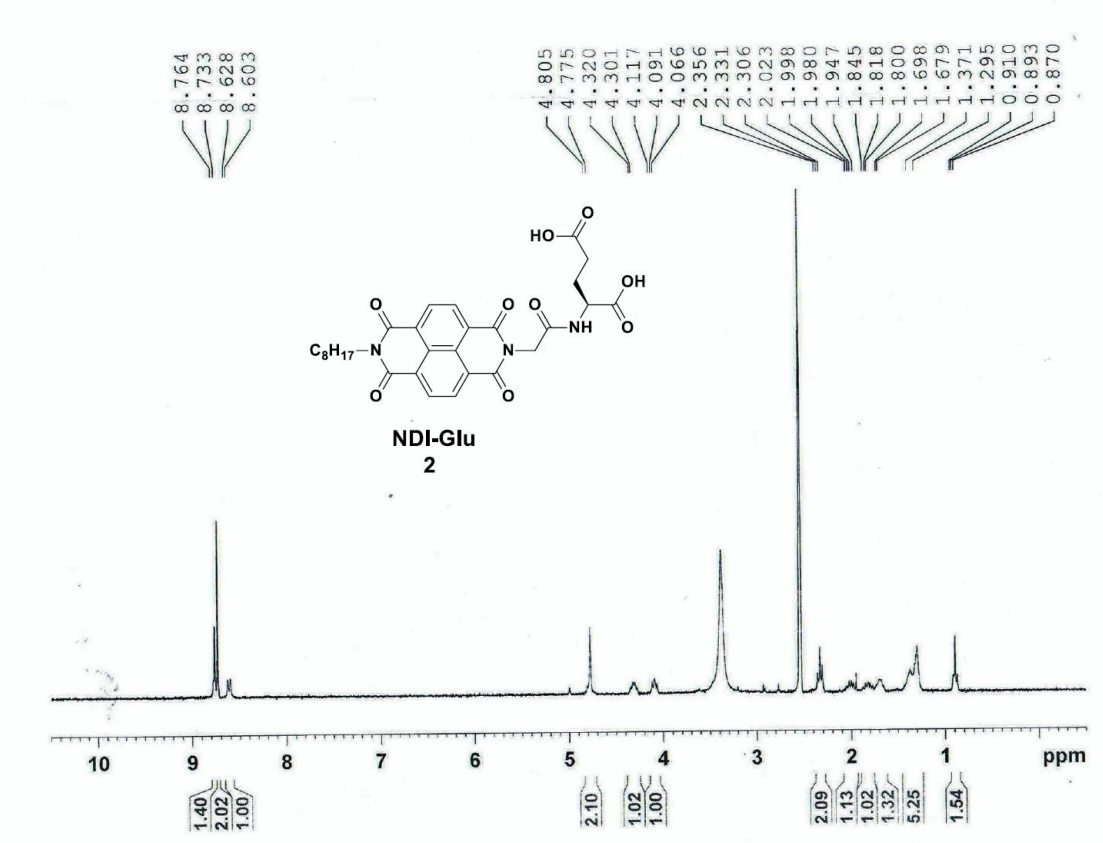


Fig. S9 ^{1}H-NMR spectrum of **2** in d_6-DMSO.

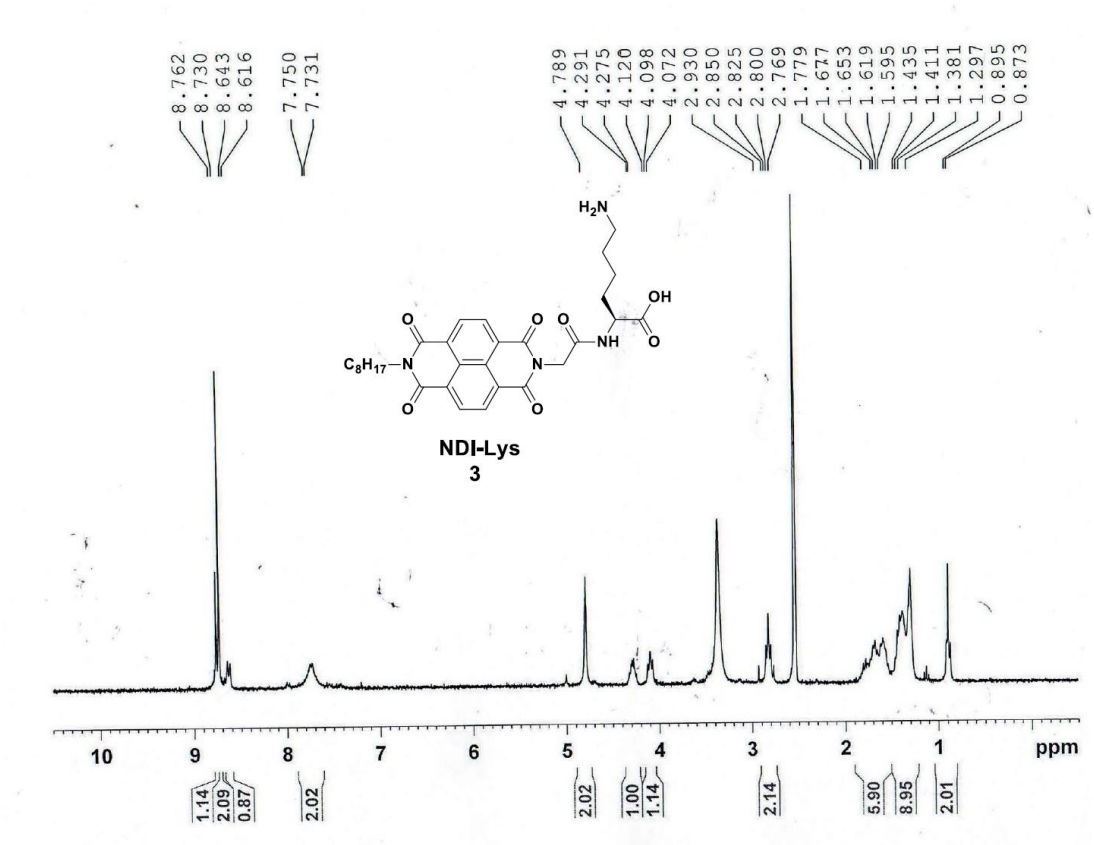


Fig. S10 ^{1}H-NMR spectrum of **3** in d_6-DMSO.

Reference:

[S1] X.-Z. Wang, X-Q Li, X.-B. Shao, X. Zhao, P. Deng, X.-K. Jiang, Z.-T. Li, Y.-Q. Chen, *Chem. Eur. J.* 2003, **9**, 2904 – 2913.