Supplementary Information

Retro Diels-Alder-triggered self-assembly of a polymerizable macrocyclic diacetylene

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Contents

1. Instruments. Raman spectra were recorded on a LabRAM HR Evolution Raman spectrometer (Horiba Scientific, 785 nm laser source). UV absorption spectra and transmittance spectra were recorded on Scinco Mega-800 and USB 2000 Miniature Fiber Optic Spectrometer (Ocean Optics). IR spectra were recorded on a Thermo Nicolet iS50 FTIR using an ATR accessory (Thermo Fisher Scientific, Inc.). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unitylnova (600 MHz) spectrometer at 298 K in $CDCl_3$. High-resolution mass spectra (HRMS) were recorded on a SYNAPT G2 (water, U.K.) using a time-of-flight (TOF) analyzer. DLS data were obtained using Malvern Instruments, ZEN3600. Optical microscopic images were obtained by Olympus BX 51 W/DP74. Scanning electron microscope (SEM) images were obtained using a HORIBA EX-250 operated at a beam energy of 15 kV.

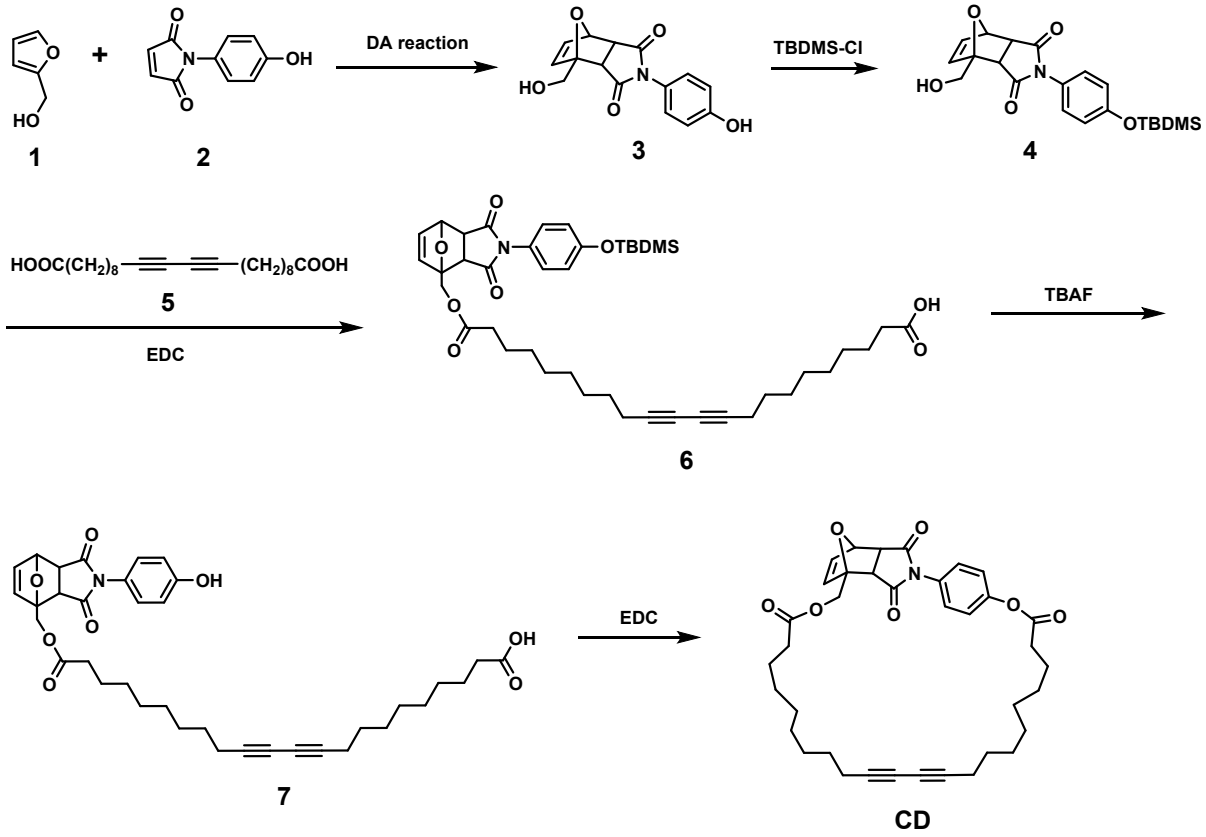
2. Materials. The intermediates Diels-Alder adduct **3** in Scheme S1 was synthesized according to the literature procedures.[1] Docosa-10,12-diynedioic acid (DCDDA) was obtained from GFS Chemicals (Powell, OH). Furfuryl alcohol was purchased form Sigma Aldrich (Korea). N-(4-Hydroxy phenyl) maleimide was purchased from Alfa-Aesar. tert-Butyldimethylsilyl chloride, 1-(3-Dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride, and 4-dimethylaminopyridine were purchased from Tokyo Chemical Industry (Korea). Triethylamine was purchased from Daejung Co (Korea). All chemicals were used as received without purification.

3. retro Diels-Alder reaction, Self-assembly and Polymerization of CD. A **CD** solution in DMF-d_7 (10 mM) was heated at 85 ^{o}C for 30 min on a hot plate, placed in a freezer (-10 ^{o}C) for 10 min and allowed to cool back to room temperature. 100 µL of the resulting solution was drop-casted on a filter paper (diameter: 1 cm). Polymerization was conducted by irradiation with a common hand-held laboratory UV lamp (254 nm, 1 mW/cm^2) for 1 min.

4. In-situ rDA-promoted Self-assembly and Polymerization of CD. A solution of **CD** in DMF (10 mM) was mixed with Di-water (2.5:1, v/v) and heated at 85 ^{o}C for 30 min, cooled in a freezer (-10 ^{o}C) for 10 min and allowed to stabilize at room temperature. A white suspension was formed and to the suspention was irradiated with UV (254 nm, 1 mW/cm^2) for 1 min. Appearance of an intense blue color was monitored, confirming polydiacetylene formation.

5. Thiol-promoted color change of polydiacetylene. Blue-colored polydiacetylene-coated filter papers that were prepared by a sequential rDA reaction (85 ^{o}C, 30 min), drop casting and photopolymerization (254 nm, 1 mW/cm^2, 1 min) were exposed to 10 mM of various compounds in hexane-EtOH mixture (2:1, v/v) for 2 h.

For ^{1}H NMR monitoring, heat treated (85 ^{o}C, 30 min) **CD** solution in DMF was dried and resulted powder was dispersed in 10 mM of thiol solution in hexane-EtOH (2:1, v/v) and stirred at room temperature for 2 h. After exposure, the precipitation was collected by filtration and dissolved in $CDCl_3$.



Scheme S1. Synthetic routes for **CD**.

6. Synthesis of Cyclic Diacetylene CD. The macrocyclic diacetylene, CD, was prepared according to the protocols shown in **Scheme S1**. The intermediate DA adduct **3** was prepared according to the literature methods.[1] N-(p-Hydroxyphenyl)-maleimide (4.0 g, 21.2 mmol, 1.0 equiv.) and fufuryl alcohol (2.5 g, 25.3 mmol, 1.2 equiv.) were dissolved in anhydrous acetonitrile (35 mL) under a nitrogen atmosphere in a flame-dried flask equipped with a magnetic stirring bar. The reaction mixture was stirred at 35 °C for 18 h. When TLC indicated there was no longer starting material present, the solvent was removed, and the reaction mixture was concentrated under reduced pressure for 1 h. The residue was subjected to a silica gel column chromatography (6:4 to 4:6, hexanes:ethyl acetate) to afford a mixture of exo and endo adduct **3** (1:4 exo: endo)). ^{1}H NMR (600 MHz, DMSO-d_6): 9.72 (s, 1H), 6.89 (d, J = 9.4 Hz, 2H), 6.79 (d, J = 9.4 Hz, 2H), 6.58~6.55 (m, 2H), 5.32~5.31 (m, 1H), 3.74 (t, J = 5.4 Hz, 1H), 3.52 (d, J = 6.0 Hz, 1H), 3.15 (d, J = 6.0 Hz, 1H), 2.98 (d, J = 6.0 Hz, 1H). The exo-endo stereoisomers were used for the preparation of intermediate **4** without further purification.

Synthesis of **4**

To a solution of **3** (5.0 g, 17.4 mmol, 1.0 equiv.) in dry CH_2Cl_2 (200 mL) was slowly added *tert*-butyldimethylsilyl chloride (6.3 g, 41.8 mmol, 2.4 equiv.) solution in dry CH_2Cl_2 (100 mL) followed by trimethylamine (6.3 mL, 45.3 mmol, 2.6 equiv.). The resulting homogeneous solution was stirred at room temperature for 18 h. The solvent was evaporated under reduced pressure and the crude material was purified by a silica gel column chromatography with chloroform/methanol to afford the desired product **4** (4.9 g, 70%). m.p: 114-116 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): 6.96 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.40~5.39 (m, 1H), 4.32 (d, J = 12.6 Hz, 1H), 4.21 (d, J = 12.6 Hz, 1H), 3.79 (m, 1H), 3.56 (d, J = 7.8 Hz, 1H), 0.97 (s, 9 H), 0.19 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): 175.3, 174.9, 156.7, 136.5, 135.7, 128.3, 128.2, 125.2, 121.2, 93.1, 80.6, 62.3, 48.7, 46.8, 26.4, 18.9, -3.7; IR (ATR) vcm^{-1}: 3493, 2953, 2930, 2855, 1701, 1604, 1510, 1381, 1254, 1169, 1043, 908, 887, 833, 780, 740, 699,

660, 633; HRMS (ESI, m/z): exact mass calculated for $C_{21}H_{27}NO_5NaSi$ required 424.1556 $[M+Na]^+$, found 424.1558.

Synthesis of **6**

To a solution of 10,12-docosadiyndioic acid (DCDDA) (4.5 g, 11.2 mmol, 1.0 equiv.), the TBDMS protected intermediate **4** (4.1 g, 11.2 mmol, 1.0 equiv.) in dry tetrahydrofuran (300 mL), 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (2.4 g, 12.3 mmol, 1.1 equiv.) and 4-dimethylaminopyridine (1.5g, 12.3 mmol, 1.1 equiv.) were added at 0 °C and stirred at room temperature for 2 days. After the reaction, the solvent was evaporated *in vacuo*. The mixture was extracted with $NaHCO_3$ and the organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to a silica gel column chromatography ($CHCl_3$ and MeOH) to afford the desired product **6** (4.0 g, 48%). m.p: 119-121 °C; ^{1}H NMR (600 MHz, $CDCl_3$): 6.95 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 6.58 (d, J = 5.4 Hz, 1H), 6.45 (d, J = 5.4 Hz, 1H), 5.40 (d, J = 7.2 Hz, 1H), 4.90 (d, J = 12.6 Hz, 1H), 4.62 (d, J = 12.6 Hz, 1H), 3.80~3.78 (m, 1H), 3.52 (d, J = 7.8 Hz, 1H), 2.38 (t, J = 7.8 Hz, 2H), 2.33 (t, J = 7.2 Hz, 2H), 2.23 (t, J = 7.2 Hz, 4H), 1.65~1.59 (m, 4H), 1.52~1.47 (m, 4H), 1.39~1.24 (m, 16H), 0.96 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): 180.3, 174.6, 174.4, 174.0, 156.7, 136.5, 135.4, 128.1, 125.1, 121.2, 90.8, 80.7, 78.2, 78.1, 66.0, 62.5, 48.4, 47.3, 34.7, 34.7, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.53 29.0, 26.3, 25.5, 25.4, 19.9, 18.9, -3.7; IR (ATR) vcm^{-1}: 3493, 2930, 2856, 1702, 1510, 1465, 1382, 1254, 1171, 1043, 908, 882, 836, 823, 780, 738; HRMS (ESI, m/z): exact mass calculated for $C_{43}H_{59}NO_8NaSi$ required 768.3908 $[M+Na]^+$, found 768.3910.

Synthesis of **7**

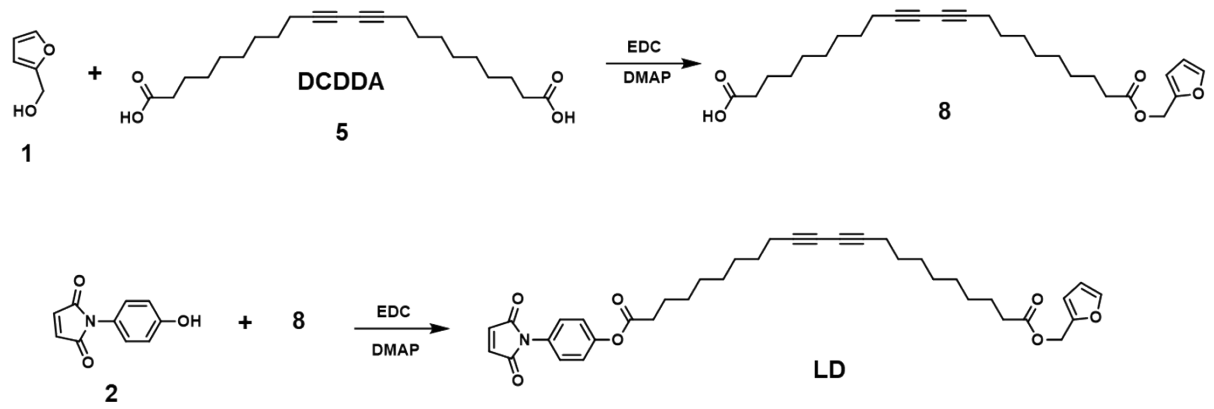
To a solution of **6** (4.0 g, 5.36 mmol, 1.0 equiv.) in dry tetrahydrofuran, tetrabutylammonium fluoride 1 M solution (5.9 mL, 5.9 mmol, 1.1 equiv.) in tetrahydrofuran was added. The reaction mixture was then stirred at room temperature overnight. After the reaction was completed, the solution was washed with brine (2x). The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude was purified by a column chromatography (0–10% MeOH/dichloromethane) to provide **7** (2.7 g, 79%). m.p: 105-107 °C; ^{1}H NMR (600 MHz, $CDCl_3$): 6.88 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 9.0 Hz, 2H), 6.59 (d, J = 6.0 Hz, 1H), 6.46 (d, J = 6.0 Hz, 1H), 5.40 (d, J = 6.0 Hz, 1H), 4.90 (d, J = 12.6 Hz, 1H), 4.63 (d, J = 11.4 Hz, 1H), 3.81~3.78 (m, 1H), 3.52 (d, J = 7.8 Hz, 1H), 2.39 (t, J = 7.8Hz, 2H), 2.34 (t, J = 7.2 Hz, 2H), 2.23 (t, J = 7.2 Hz, 4H), 1.65~1.59 (m, 4H), 1.52~1.47 (m, 4H), 1.39~1.24 (m, 16H); ^{13}C NMR (150 MHz, $CDCl_3$): 179.1, 174.3, 174.1, 173.5, 156.4, 135.2, 134.6, 127.7, 123.0, 117.7, 90.1, 79.3, 77.5, 77.4, 65.3, 61.8, 47.6, 46.6, 34.0, 33.9, 29.0, 28.9, 28.8, 28.7, 28.6, 28.5, 28.4, 24.7, 24.6, 19.1; IR (ATR) vcm^{-1}: 3495, 3402, 2932, 2855, 1698, 1515, 1468, 1395, 1323, 1252, 1167, 1099, 1028, 993, 965, 910, 884, 834, 780, 717, 632; HRMS (ESI, m/z): exact mass calculated for $C_{37}H_{45}NO_8Na$ required 654.3043 $[M+Na]^+$, found 654.3042.

Synthesis of **CD**

To a solution of **7** (1.0 g, 1.58 mmol, 1.0 equiv.) in dry tetrahydrofuran (60 mL), 1-(3-Dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (0.36 g, 1.90 mmol, 1.2 equiv.) and 4-dimethylaminopyridine (0.23 g, 1.90 mmol, 1.2 equiv.) were added at 0 °C and stirred at room temperature for 3 days. After the reaction, the solvent was evaporated under a vacuum. The mixture was extracted with $NaHCO_3$ and the organic layer was dried over Na_2SO_4. The crude was purified by column chromatography (hexane and ethyl acetate) to afford the desired product **CD** (0.1 g, 10%). m.p: 99-101 °C; ^{1}H NMR (600 MHz, $CDCl_3$): 7.17~7.14 (m, 4H), 6.60 (d, J = 6.0 Hz, 1H), 6.51 (d, J = 6.0 Hz, 1H), 5.41 (d, J = 5.4 Hz, 1H), 4.89 (d, J = 12.6 Hz, 1H), 4.55 (d, J = 12.6 Hz, 1H), 3.82~3.79 (m, 1H), 3.51 (d, J = 8.4 Hz, 1H), 2.56 (t, J = 7.8 Hz, 2H), 2.42 (t, J = 7.2 Hz, 2H), 2.24~2.20 (m, 4H), 1.78~1.73 (m, 2H), 1.68~1.62 (m, 2H), 1.50~1.46 (m, 4H), 1.43~1.26 (m, 16H); ^{13}C NMR (150 MHz, $CDCl_3$): 173.4, 173.3, 172.7, 171.8, 150.7, 135.5, 135.1, 129.8, 127.4, 123.5, 90.0, 79.8, 77.5, 77.4, 65.4, 65.3, 62.5, 47.7, 47.6, 34.2, 34.1, 29.1, 29.0, 28.9, 28.7, 28.6, 28.5, 28.3, 28.1, 28.0, 24.9, 19.2, 18.9; IR (ATR) vcm^{-1}: 3493, 2930, 2856, 1702, 1510, 1465, 1382,

1254, 1171, 1043, 908, 882, 836, 823, 780, 738; HRMS (ESI, m/z): exact mass calculated for $C_{37}H_{43}NO_7Na$ required 636.2937 $[M+Na]^+$, found 636.2938.

7. Synthesis of Linear Diacetylene LD. The linear diacetylene, **LD**, was prepared according to the protocols shown in **Scheme S2**.



Scheme S2. Synthetic routes for **LD**.

Synthesis of **8**

To a solution of furfuryl alcohol (1.0 g, 10.2 mmol, 1.0 equiv.), 10,12-docosadiyndioic acid (DCDDA) (11.1 g, 30.6 mmol, 3.0 equiv.) in dry tetrahydrofuran (300 mL), 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (2.2 g, 11.2 mmol, 1.1 equiv.) and 4-dimethylaminopyridine (1.4 g, 11.2 mmol, 1.1 equiv.) were added at 0 °C and stirred at room temperature for 2 days. After the reaction, the solvent was evaporated *in vacuo*. The mixture was extracted with $NaHCO_3$ and the organic layer was dried over Na_2SO_4. The crude residue was subjected to a silica gel column chromatography ($CHCl_3$ and MeOH) to afford the desired product **8** (3.4 g, 76%). m.p: 45-47 °C; ^{1}H NMR (600 MHz, $CDCl_3$): 7.42 (d, J = 1.8 Hz, 1H), 6.39 (d, J = 3.0 Hz, 1H), 6.36 (t, J = 3.0 Hz, 1H), 5.06 (s, 2H), 2.35~2.31 (m, 4H), 2.25~2.22 (m, 4H), 1.65~1.59 (m, 4H), 1.51~1.47 (m, 4H), 1.39~1.25 (m, 16H); ^{13}C NMR (150 MHz, $CDCl_3$): 179.7, 173.5, 149.6, 143.2, 110.5, 110.4, 77.5, 77.4, 65.3, 65.3, 57.9, 34.1, 33.9, 29.1, 29.0, 28.9, 28.8, 28.7, 28.6, 28.5, 28.3, 28.2, 24.8, 24.6, 19.2; IR (ATR) vcm-1: 3074, 2918, 2850, 1732, 1699, 1467, 1432, 1418, 1343, 1318, 1284, 1250, 1222, 1208, 1168, 1095, 1017, 986, 944, 916, 737, 724; HRMS (ESI, m/z): exact mass calculated for $C_{27}H_{38}NO_5Na$ required 465.2617 $[M+Na]^+$, found 465.2617.

Synthesis of **LD**

To a solution of **8** (1.0 g, 2.26 mmol, 1.0 equiv.), N-(4-hydroxyphenyl)maleimide (0.47 mg, 2.49 mmol, 1.1 equiv.) in dry tetrahydrofuran (30 mL), 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (0.48 mg, 2.49 mmol, 1.1 equiv.) and 4-dimethylaminopyridine (0.31 mg, 2.49 mmol, 1.1 equiv.) were added at 0 °C and stirred at room temperature for 1 day. After the reaction, the solvent was evaporated *in vacuo*. The mixture was extracted with $NaHCO_3$ and the organic layer was dried over Na_2SO_4. The crude residue was subjected to a siliga gel column chromatography (hexane and ethyl acetate) to afford the desired product **LD** (580 mg, 42%). m.p: 58-60 °C; ^{1}H NMR (600 MHz, $CDCl_3$): 7.42 (m, 1H), 7.37 (m, 2H) , 7.18 (m, 2H), 6.85 (s, 2H), 6.39 (d, J = 3.0 Hz, 1H), 6.36 (m, 1H), 5.06 (s, 2H), 2.56 (t, J = 7.2 Hz, 2H), 2.32 (t, J = 7.2 Hz, 2H), 2.24 (m, 4H), 1.75 (quint, J = 7.2 Hz, 2H), 1.61 (quint, J = 7.2 Hz, 2H), 1.51 (m, 4H), 1.41~1.26 (m, 16H); ^{13}C NMR (150 MHz, $CDCl_3$): 173.4, 171.8, 169.3, 149.9, 149.6, 143.2, 134.2, 128.6, 126.9, 122.3, 110.5, 110.4, 77.5, 77.4, 65.3, 65.2, 57.8, 34.3, 34.1, 29.1, 29.0, 28.9, 28.8, 28.7, 28.6, 28.5, 28.4, 28.3, 24.8, 24.7, 19.2, 19.1; IR (ATR) vcm^{-1}: 2915, 2849, 1758, 1733, 1701, 1510, 1464, 1407, 1393, 1376, 1344, 1315, 1284, 1245, 1213, 1157, 1134, 1095, 1015, 924, 833, 743, 709, 686; HRMS

(ESI, m/z): exact mass calculated for $C_{37}H_{43}NO_7Na$ required 636.2937 $[M+Na]^+$, found 636.2939.

References

1. J. Park, J.-M. Heo, S. Seong, J. Noh and J.-M. Kim, *Nat. Commun.*, 2021, **12**, 4207.

8. ^{1}H and ^{13}C NMR spectra of Intermediates, CD and LD (Figure S1-6).

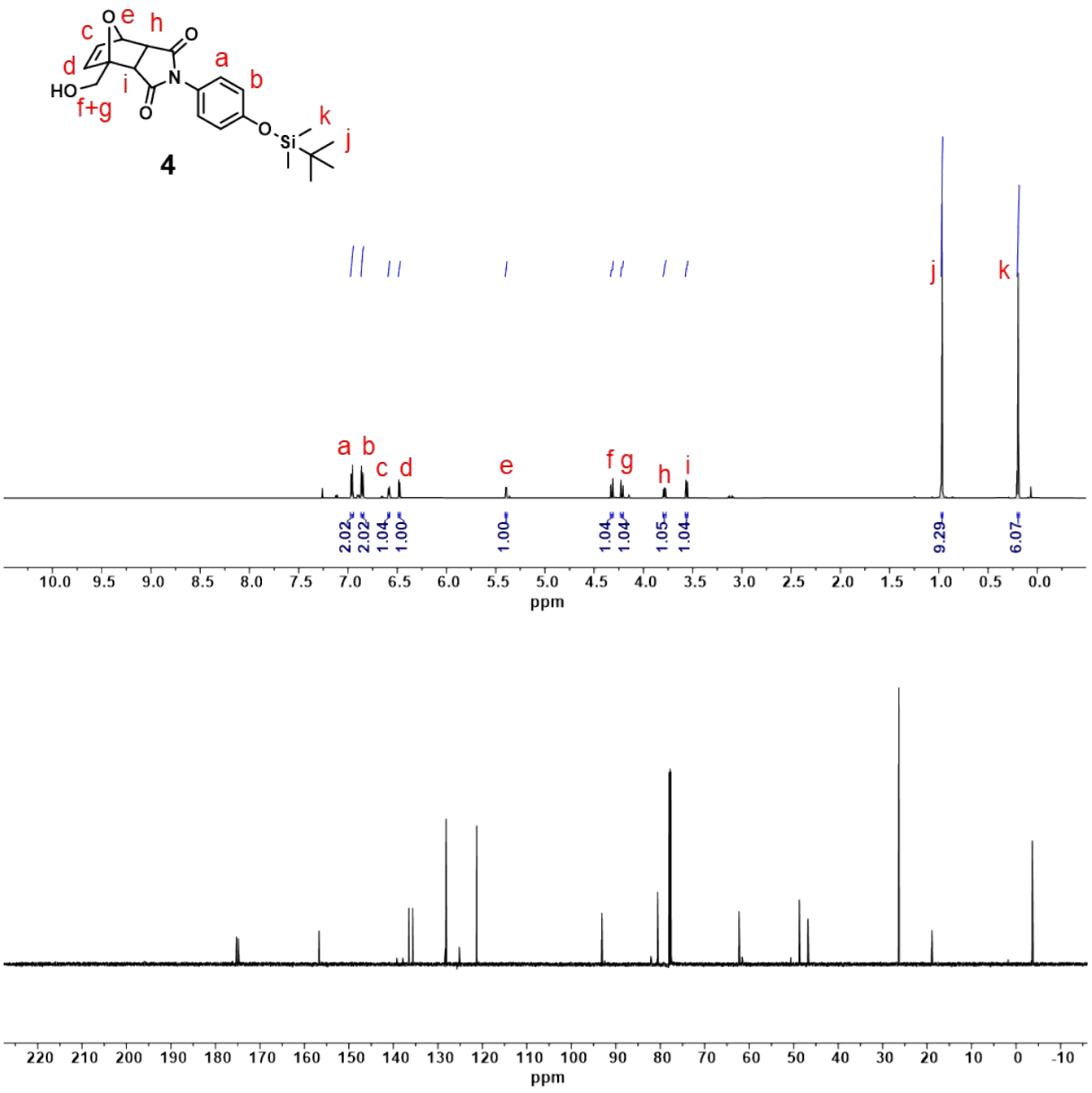


Figure S1. ^{1}H (top, 600 MHz) and ^{13}C (bottom, 150 MHz) NMR spectra of **4** in $CDCl_3$.

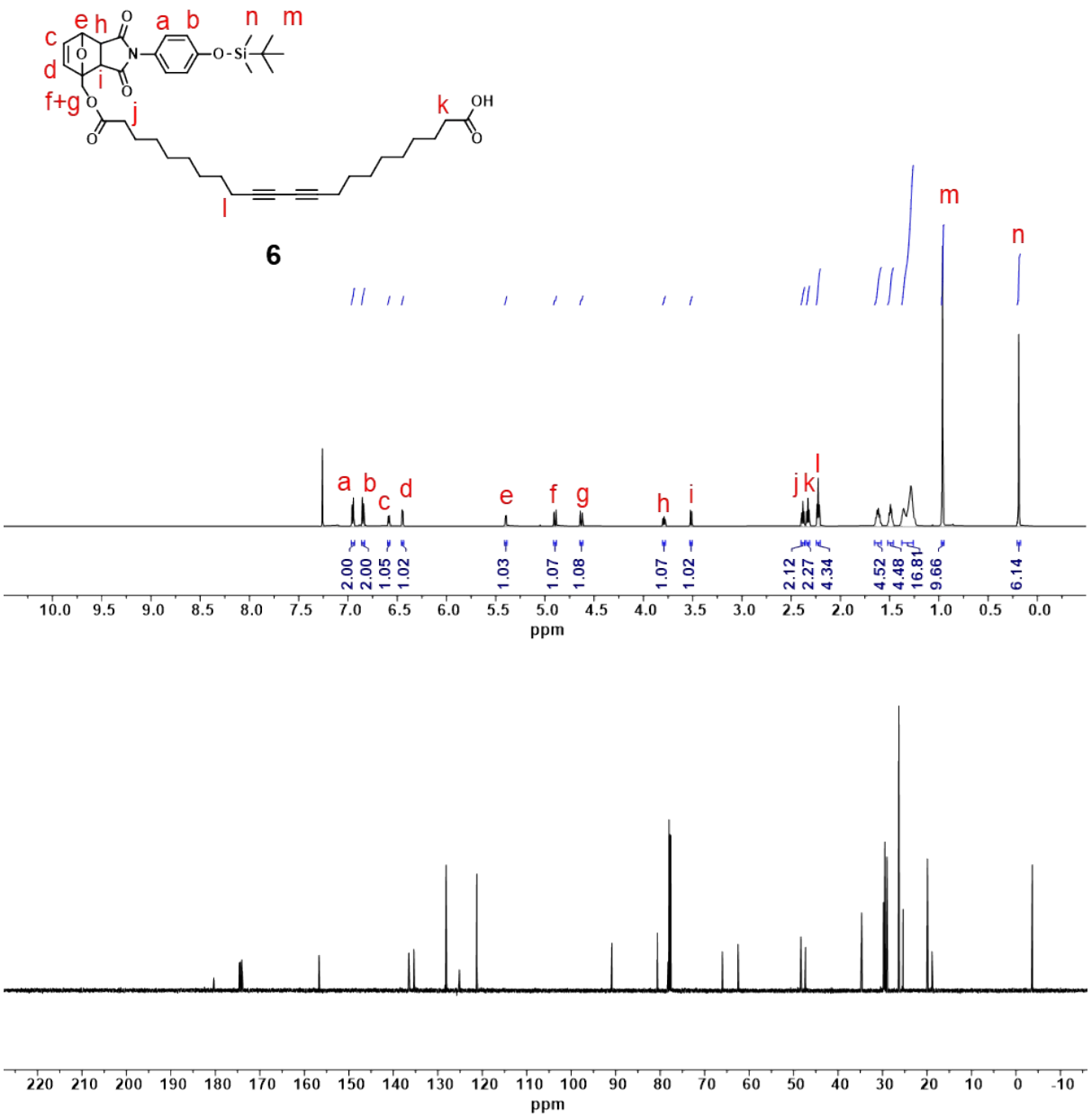


Figure S2. ^{1}H (top, 600 MHz) and ^{13}C (bottom, 150 MHz) NMR spectra of **6** in $CDCl_3$.

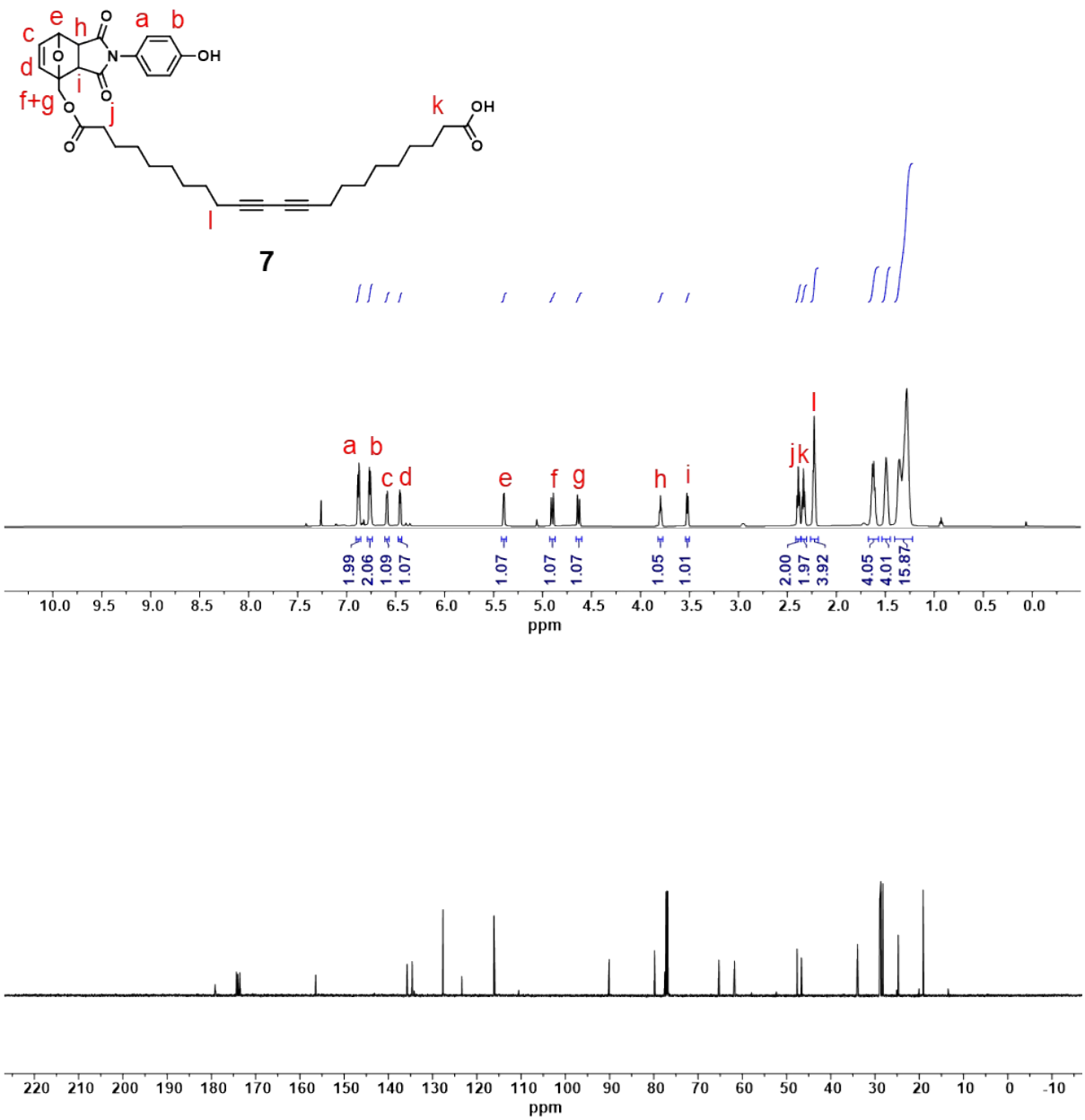


Figure S3. ^{1}H (top, 600 MHz) and ^{13}C (bottom, 150 MHz) NMR spectra of **7** in $CDCl_3$.

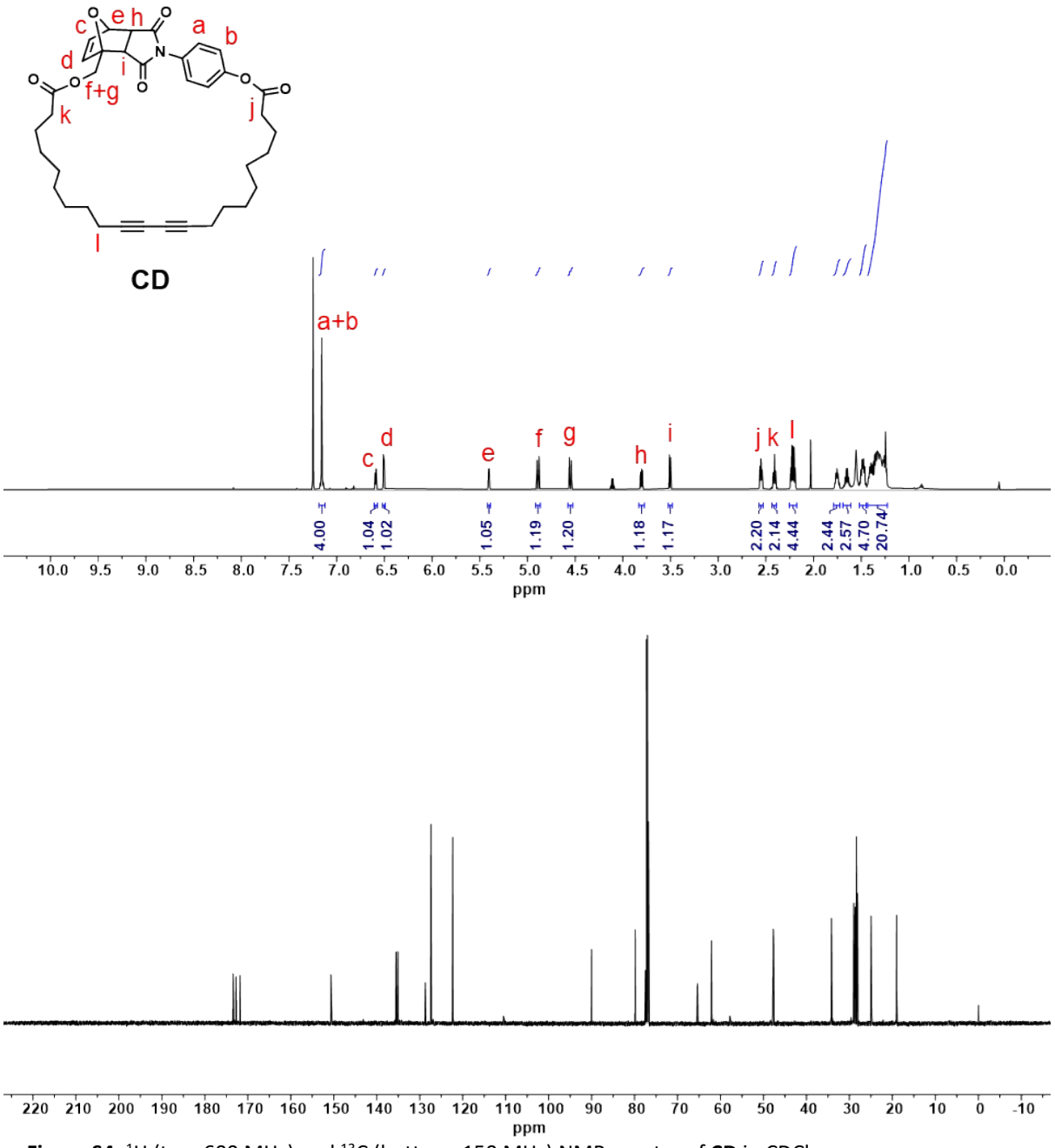


Figure S4. ^{1}H (top, 600 MHz) and ^{13}C (bottom, 150 MHz) NMR spectra of **CD** in $CDCl_3$.

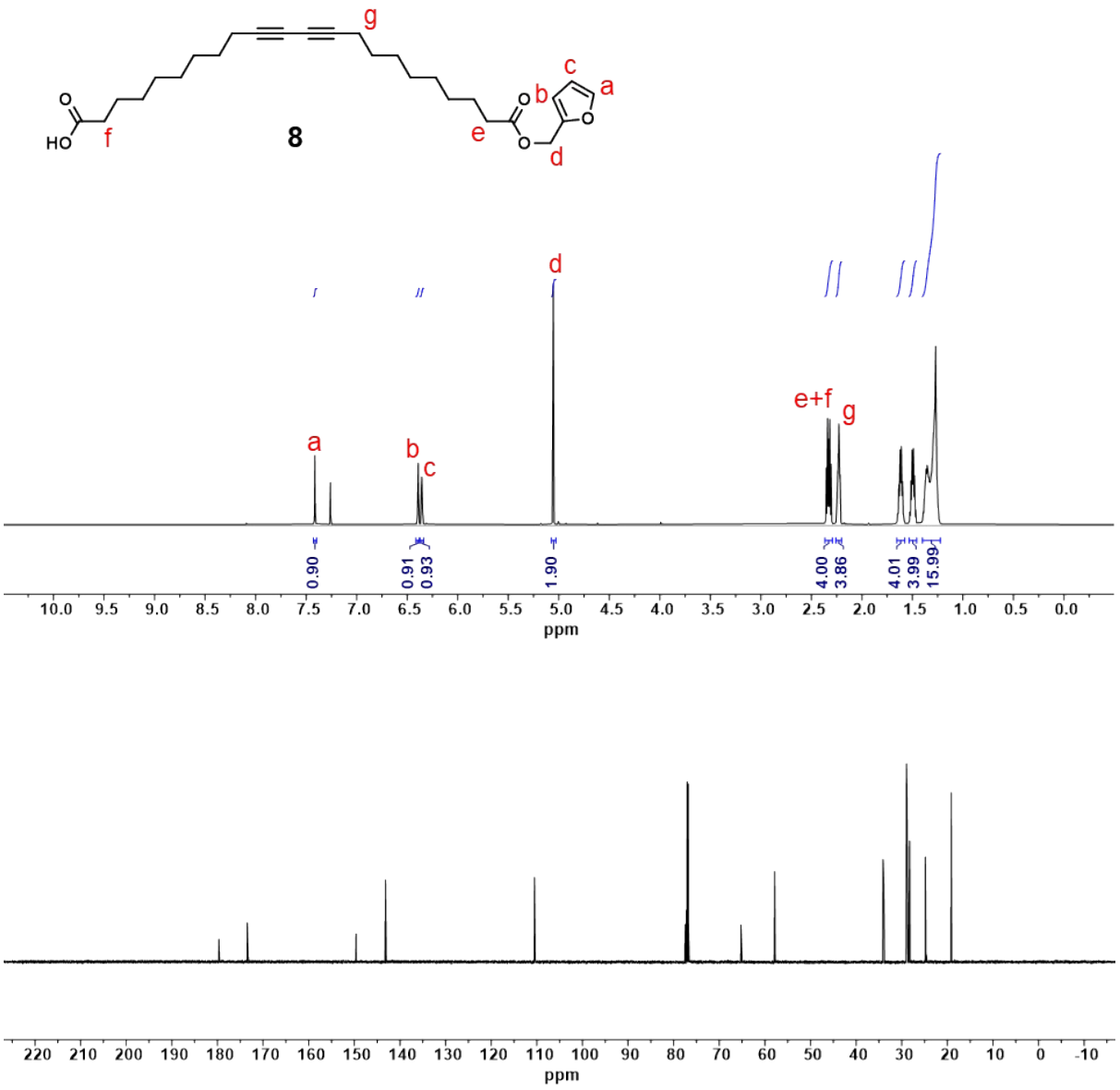


Figure S5. ^{1}H (top, 600 MHz) and ^{13}C (bottom, 150 MHz) NMR spectra of **8** in $CDCl_3$.

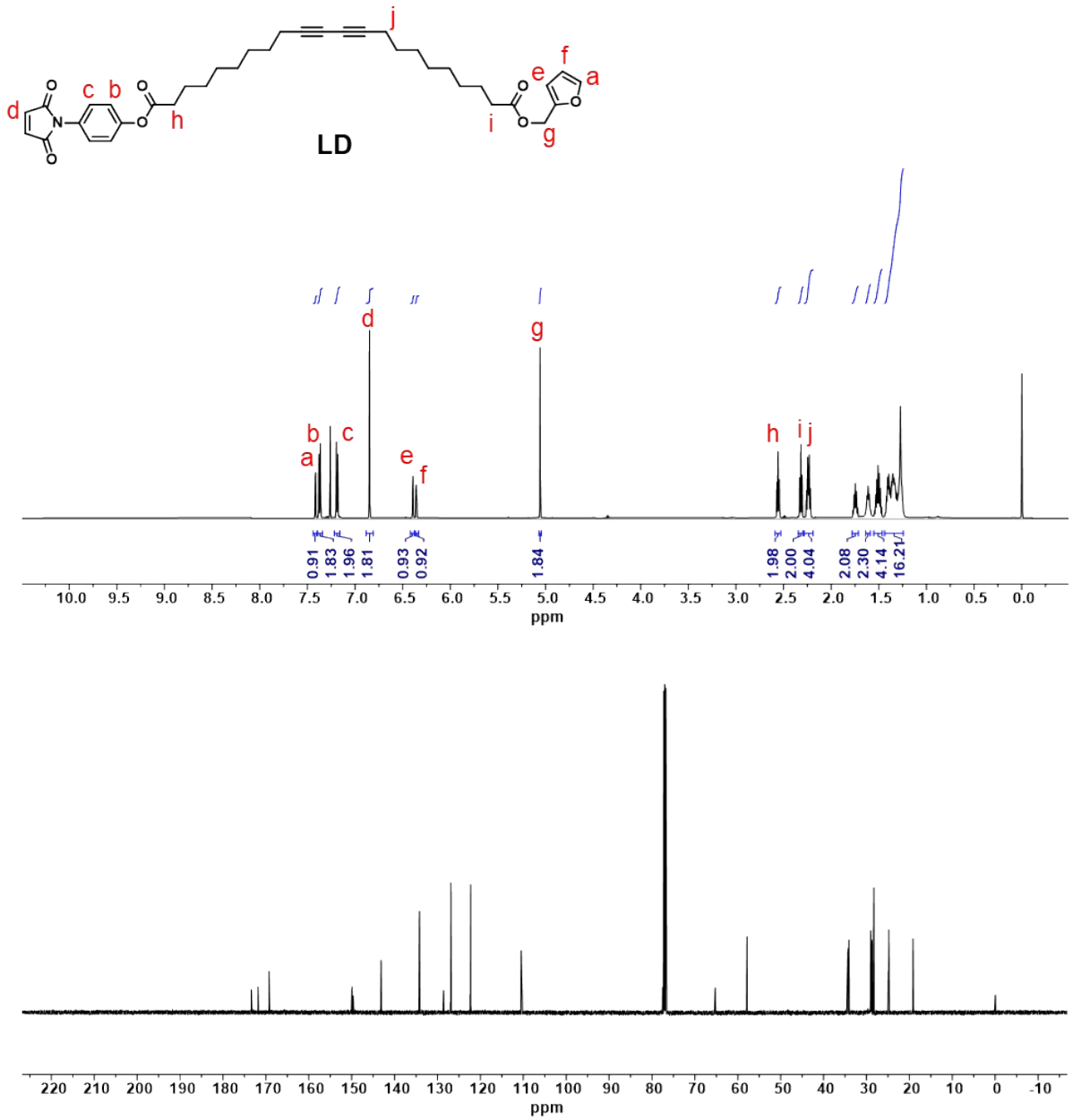


Figure S6. ^{1}H (top, 600 MHz) and ^{13}C (bottom, 150 MHz) NMR spectra of **LD** in $CDCl_3$.

9. DSC curves of CD (Figure S7).

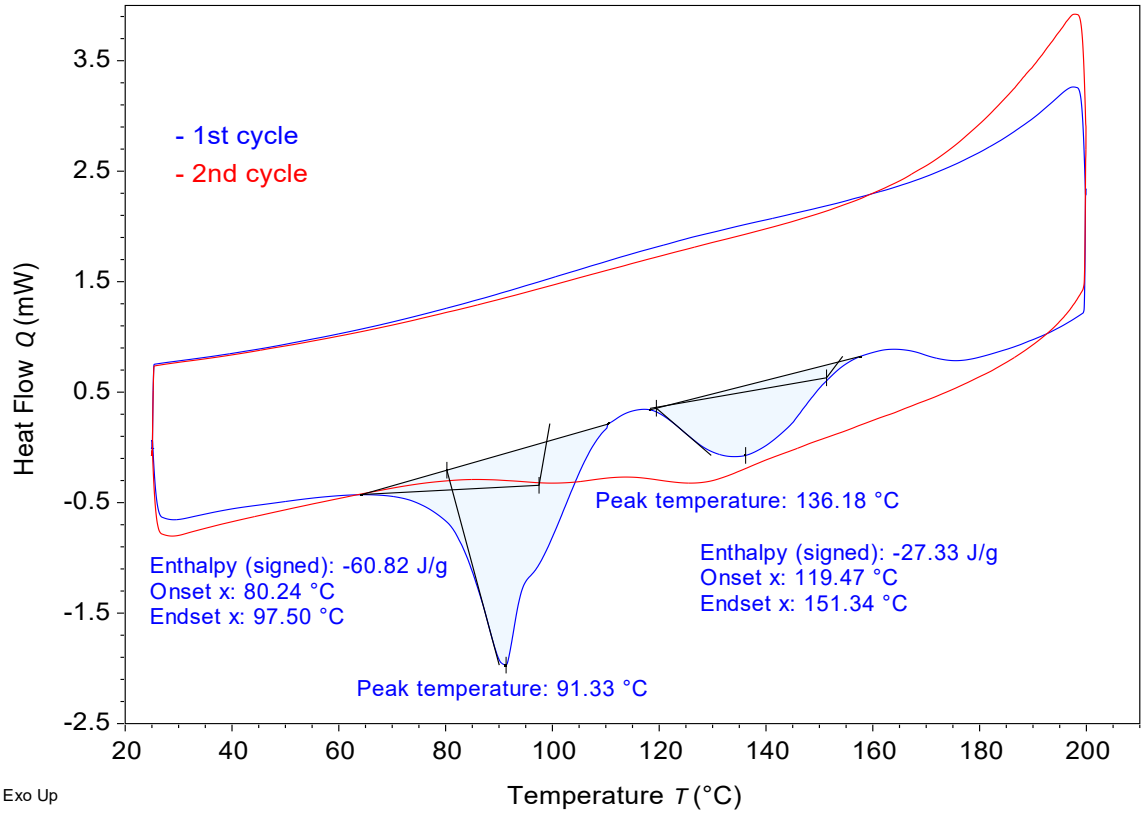


Figure S7. Differential scanning calorimetry (DSC) thermograms of **CD**.

10. Time-dependent UV-vis absorption spectra and Z-average size of rDA reaction followed by UV irradiated CD (Figure S8).

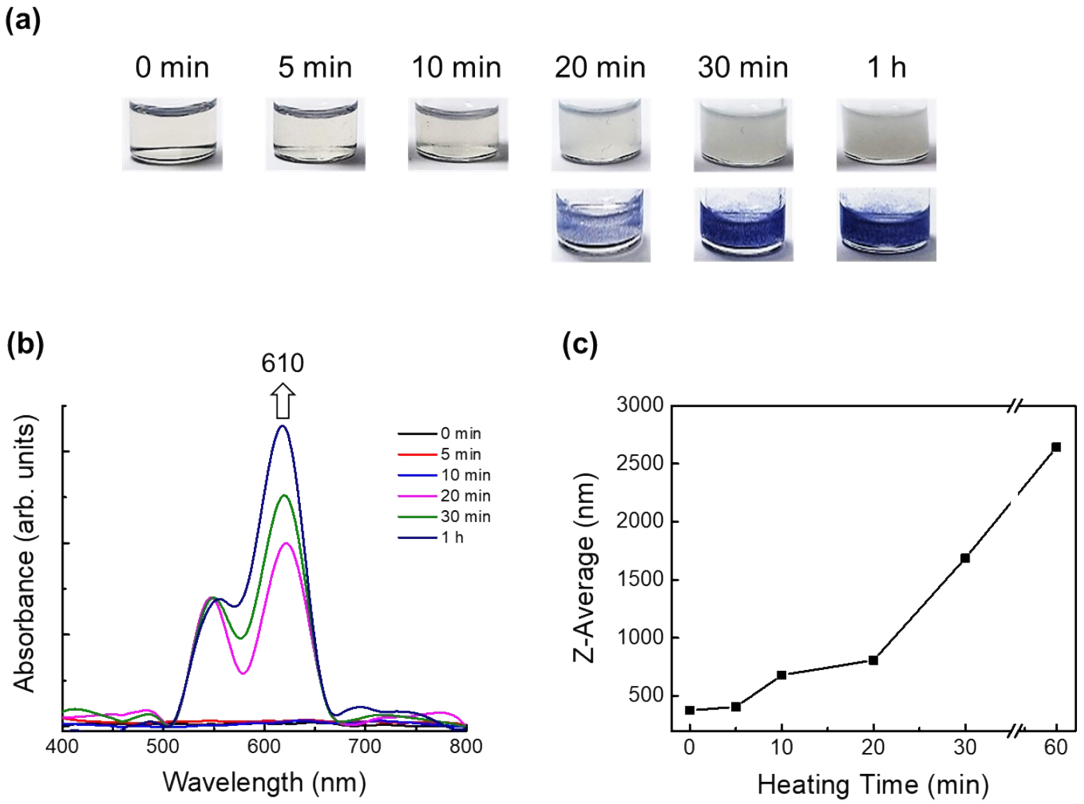


Figure S8. Photographs (a), UV-visible absorption spectra (b) and Z-average size (c) of **CD** solutions in DMF (10 mM) mixed with H_2O (2.5:1, v.v) after incubating at 85 ^oC for the designated times. The heat-treated solutions were irradiated by 254 nm UV (1 mW/cm^2) for 1 min.

11. Optical microscope images of CD after rDA reaction (Figure S9).

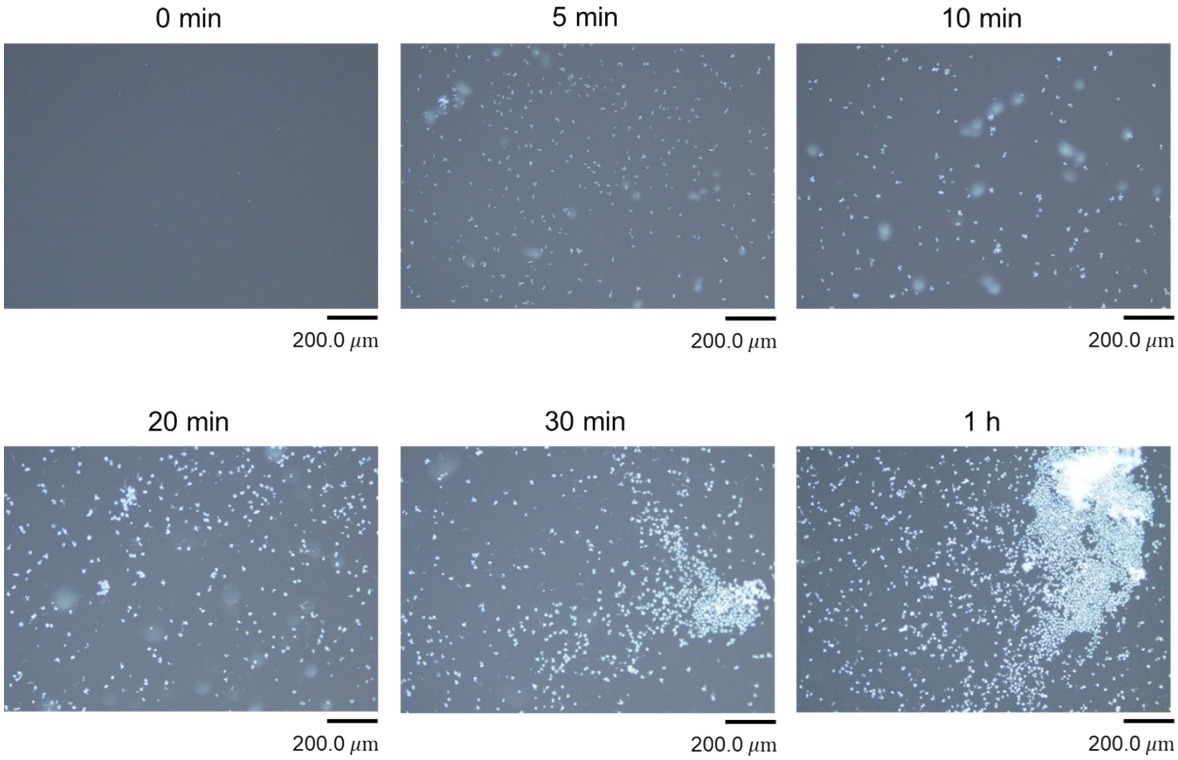


Figure S9. Optical microscope images were captured of **CD** solutions in DMF (10 mM) mixed with H_2O (2.5:1, v/v) following heating at 85 °C for labelled times.

12. SEM images of CD before and after rDA reaction (Figure S10).

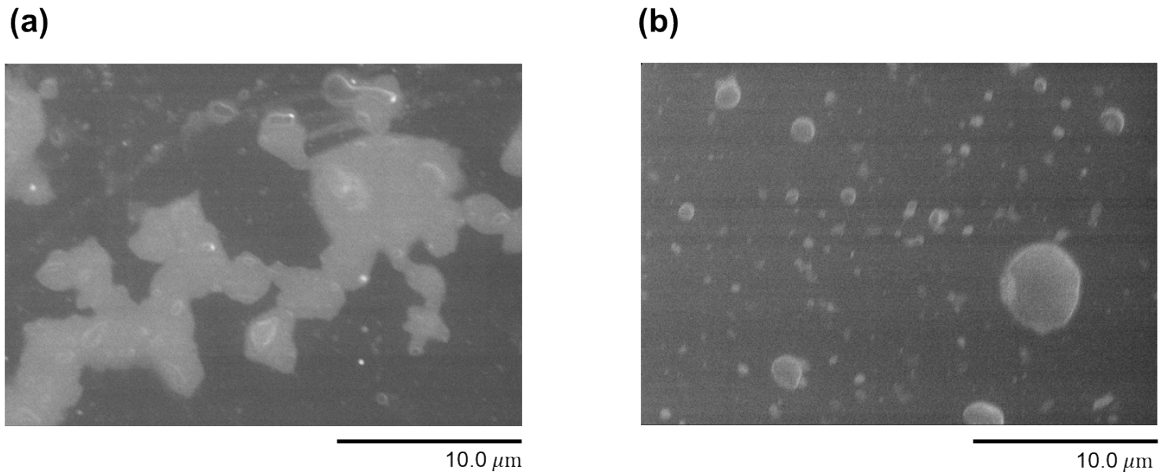


Figure S10. SEM images of the microstructures from **CD** solutions in DMF (10 mM) mixed with H_2O (2.5:1, v/v) before (a) and after (b) heat treatment (85 °C, 30 min).

13. UV-vis spectra and photographs of polydiacteylene-immobilized filter papers upon exposure to thiols (Figure S11).

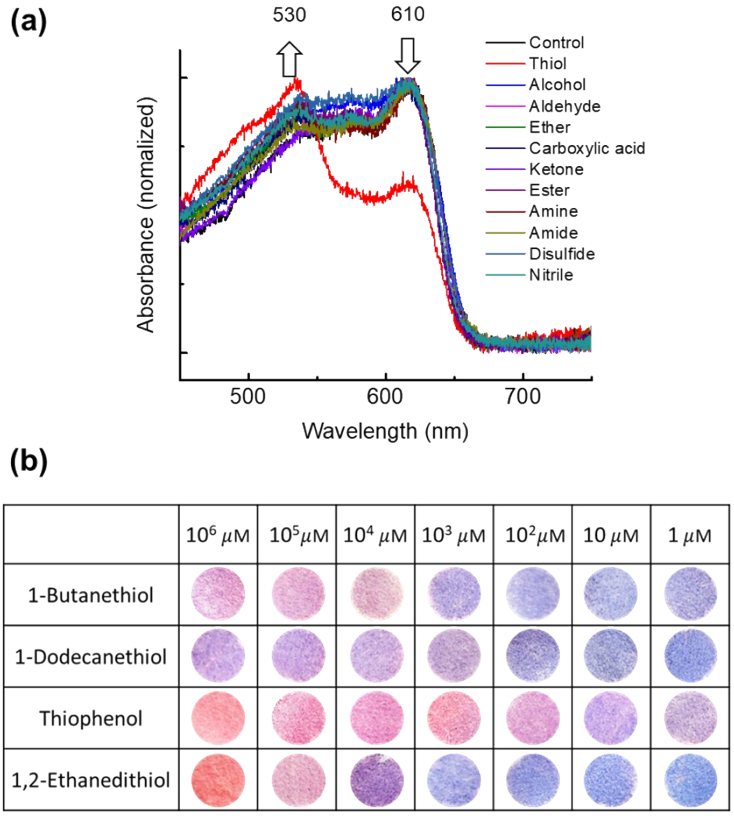


Figure S11. (a) UV-visible absorption spectra of polydiacetylene-coated filter papers upon exposure to various compounds (10 mM in hexane-EtOH mixture (2:1, v/v)). Compounds: thiol (butanethiol), alcohol (butanol), aldehyde (butyraldehyde), ether (dibutyl ether), carboxylic acid (butyric aicd), ketone (butanone), ester (butyl acetate), amine (butylamine), amide (butyramide), disulfide (dibutyl disulfide), nitrile (butyronitrile). (b) Colorimetric response of the polydiacetylene-immobilized filter papers upon exposure to thiols. The polydiacetylene-coated filter papers used for the sensor study were prepared by drop-casting of heat-treated (85 ^{o}C, 30 min) CD solutions followed by 254 nm UV irradiation (1 mW/cm^2, 1 min).

14. ^{1}H NMR spectra of CD after exposure to butanethiol (Figure S12).

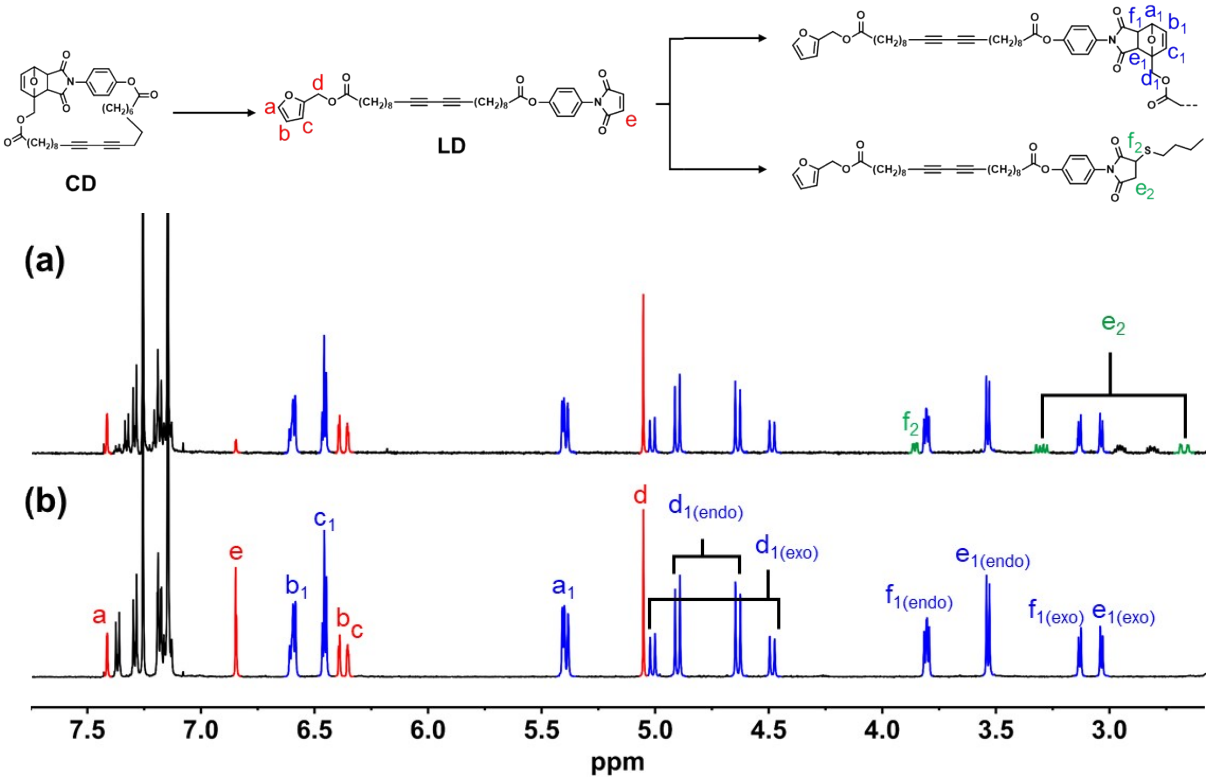


Figure S12. (a) ^{1}H NMR spectrum of a heat treated **CD** sample after exposure to butanethiol (10 mM). (b) ^{1}H NMR spectrum of a heat treated **CD** sample obtained without exposure to butanethiol (10 mM).