An Alternative Strategy for Adjusting the Association Specificity of Hydrogen-bonded Duplexes

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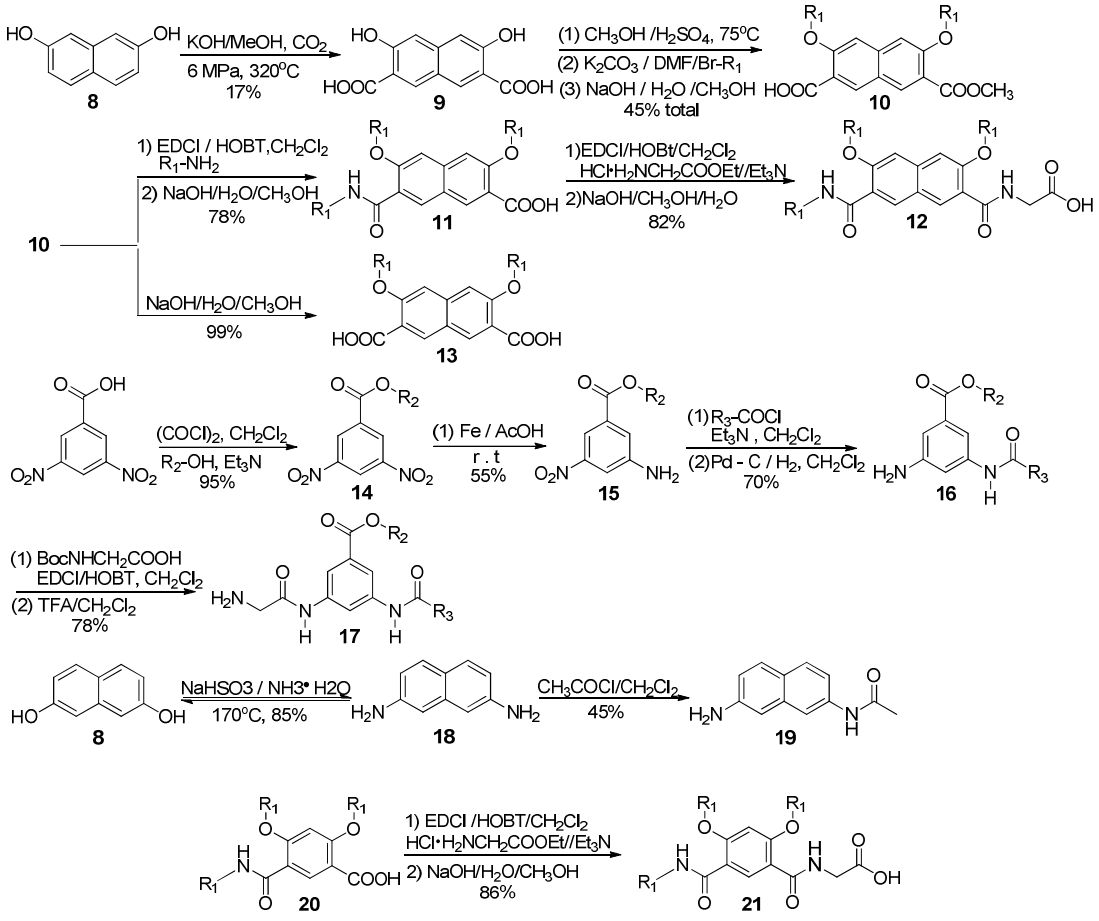
Supporting Information

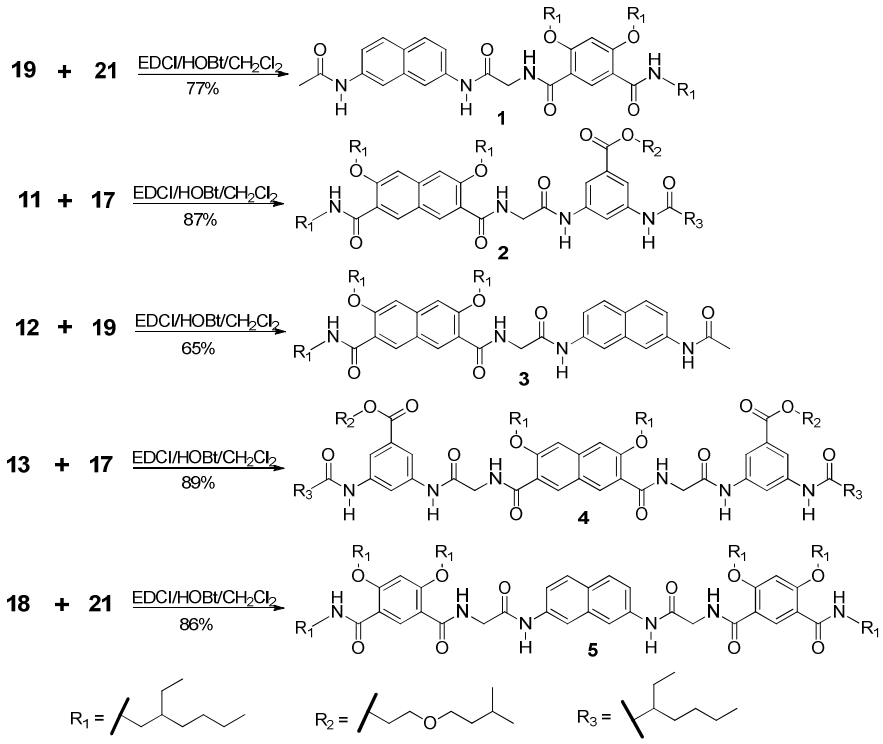
Contents

1. General Information

The ^{1}H NMR and ^{13}C spectra were recorded on Bruker AVANCE AV II- 400 MHz (^{1}H: 400 MHz; ^{13}C: 100 MHz) and Bruker Avance AVANCE AV II- 600 MHz (^{1}H: 600 MHz; ^{13}C: 150 MHz). Chemical shifts are reported in δ values in ppm and coupling constants (J) are denoted in Hz. Multiplicities are denoted as follows: s = singlet, d = doublet, t = triplet, dd = double doulet, and m = multiplet. High resolution mass (HRMS) data were obtained by WATERS Q-TOF Premier. Solvents for extraction and chromatography were reagent grade. CH_2Cl_2 was distilled from CaH_2 and THF was distilled from Na (s) prior to use. $CDCl_3$ and DMSO-d_6 were from Cambridge Isotope Laboratories (CIL).

2. Synthesis and Characterization of New Compounds





Scheme S1. Synthetic route of compounds **1-5**.

3,6-Dihydroxynaphthalene-2,7-dicarboxylic acid (9)[1]. A mixture of 2,7-dihydroxynaphthalene **8** (10.1 g, 62.9 mmol) and KOH (9.5 g, 158.4 mmol) in of CH_3OH (100 mL) was stirred for 4 h in pressure vessel at room temperature. Then 100 mL heat transfer oil was added and heated to 100 ^oC. After removal of CH_3OH in vacuo, the pressure was increased to 6 MPa with CO_2 (g). The reaction was stirred for about 4 h at 310^oC. Then boiled water was added and the mixture was filtered quickly. The aqueous solution was acidified with 1N HCl and filtered. The resulting brown solid was dissolved in acetone and filtered again. Then the filtrate was evaporated under reduced pressure to finally afford **9** (2.6 g, 17%) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 8.617 (s, 2H), 7.831 (s, 2H).

3,6-Bis((2-ethylhexyl)oxy)-7-(methoxycarbonyl)-2-naphthoic acid (10). A mixture of compound **9** (2.0 g, 8.1 mmol), methanol (300 mL) and concentrated sulfuric acid (10 mL) was heated under reflux for 24 h. After cooling to room temperature, the solution was poured into ice water (1000 mL). The precipitate was filtered to give a yellow solid (2.1 g, 95%). A mixture of K_2CO_3 (3.3 g, 23.8 mmol) and the above

yellow solid (1.9 g, 6.8 mmol) in DMF (50 mL) was stirred for 2 h at 80°C. 3-(Bromomethyl)- heptane (2.9 g, 14.9 mmol) was then added and the mixture was stirred for 6 h at 100 °C. The solvent was evaporated under reduced pressure and 1N HCl was added until the pH ≈ 4. The mixture was extracted with ethyl acetate (3×100 mL) and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was purified by column chromatography (eluent: CH_2Cl_2/PE 1:3, v/v) to give a yellow oil (2.9 g, 85%). Hydrolysis in the presence of NaOH at room temperature afforded **10** as a yellow oil (1.8 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.23 (s, 1H), 7.10 (s, 1H), 7.02 (s, 1H), 4.14 (t, *J* = 5.26 Hz, 2H), 3.91 (t, *J* = 9.62 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.03, 10.09, 12.98, 13.06, 21.87, 22.02, 22.96, 27.92, 28.02, 28.67, 29.45, 29.53, 38.14, 51.02, 70.09, 71.44, 104.81, 105.28, 115.29, 120.86, 121.15, 133.18, 135.96, 138.93, 154.95, 157.18, 164.29, 165.38.

7-((2-Ethylhexyl)carbamoyl)-3,6-bis((2-ethylhexyl)oxy)-2-naphthoic acid (11). A solution of compound **10** (125.1 mg, 0.26 mmol), N-(3-dimethylaminopropyl)-N′-ethyl-carbodiimide (EDCI) (59.8 mg, 0.31 mmol) and 1-hydroxy benzotriazole (HOBt) (44.2 mg, 0.33 mmol) in CH_2Cl_2 (30 mL) was stirred at room temperature for 2 h. 2-Ethylhexan-1-amine (40.3 mg, 0.31 mmol) in CH_2Cl_2 (10 mL) was added and stirred in the dark for 24 h. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (eluent: CH_2Cl_2/EA 20:1, v/v) to provide a yellow oil. Hydrolysis with 1N NaOH (9 mL) in methanol (15 mL) for 6 h afforded **11** (108.2 mg, 78%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.91 (s, 1H), 8.83 (s, 1H), 8.79 (s, 1H), 7.88 (t, *J* =5.62 Hz, 1H), 7.19 (s, 1H), 7.14(s, 1H), 4.21 (d, *J* = 9.22 Hz, 2H), 4.13 (dd, *J* = 2.06 Hz, 2H), 3.45 (m, 2H), 1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.79, 10.96, 11.04, 13.99, 14.05, 14.09, 22.89, 28.93, 39.16, 39.59, 43.15, 71.72, 72.41, 105.91, 106.14, 111.55, 116.85, 122.36, 129.86, 135.46, 137.26, 139.33, 155.88, 157.29, 160.31, 164.65, 165.35.

2-(7-((2-Ethylhexyl)carbamoyl)-3,6-bis((2-ethylhexyl)oxy)-2-naphthamido)acetic

acid (12). A mixture of EDCI (53.7 mg, 0.28 mmol), HOBt (37.8 mg, 0.28 mmol) and compound **11** (81.0 mg, 0.14 mmol) in CH_2Cl_2 (20 mL) was stirred under N_2 atmosphere for 2 h. Glycine ethyl ester hydrochloride (29.3 mg, 0.21 mmol) and triethylamine (21.3 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) was added. The above mixture was stirred for 24 h. Purification by column chromatography (eluent: CH_2Cl_2/EA 30:1, v/v) provided a yellowish oil, which was subjected to hydrolysis with 1N NaOH (6 mL) in methanol (15 mL) for 6 h to afford **12** (76.8 mg, 82%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 2H), 8.49 (s, 1H), 7.93 (t, J = 6.12 Hz, 1H), 7.04 (s, 2H), 4.97 (s, 2H), 4.27 (m, 4H), 3.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.78, 9.89, 9.94, 21.68, 22.03, 23.05, 23.27, 23.72, 27.89, 27.96, 28.24, 28.69, 29.55, 29.65, 30.14, 30.91, 38.02, 38.36, 38.56, 42.19, 70.55, 70.89, 104.65, 118.40, 119.52, 120.12, 121.83, 134.45, 137.70, 155.57, 164.26..

3,6-Bis((2-ethylhexyl)oxy)naphthalene-2,7-dicarboxylic acid (13). 1) Compound **10** (1.2 g, 2.5 mmol) was dissolved in methanol (30 mL), to which 2.0 N solution of NaOH (8.0 mmol) was added. The mixture was heated under reflux for 4 h. Methanol was removed in vacuo. The aqueous layer was acidified by addition of concentrated HCl, which was then poured into ethyl acetate (100 mL). The organic layer was washed with distilled H_2O (3 × 50 mL), brine (3 × 50 mL) and dried over Na_2SO_4 and evaporated under reduced pressure to afford **13** (1.2 g, 99.5%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 2H), 7.22 (s, 2H), 4.25 (d, J = 5.53 Hz, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.04, 14.00, 22.89, 28.92, 30.50, 39.13, 72.61, 106.42, 117.69, 122.79, 137.44, 140.35, 156.79, 165.29.

2-(Isopentyloxy)ethyl-3,5-dinitrobenzoate (14). To a solution of 3,5-dinitrobenzoic acid (10.0 g, 47.1 mmol) in CH_2Cl_2 (200 mL) was added oxalyl dichloride (9.1 g, 51.9 mmol) and a drop of DMF as the initiator. The suspension was stirred at room temperature for 2 h and then heated under reflux for 0.5 h. The solvent was evaporated under reduced pressure to give a faint-yellow solid, which was then

dissolved in CH_2Cl_2 (100 mL) and added slowly to a solution of 2-(isopentyloxy) ethanol (5.9 g, 44.8 mmol) and triethylamine (4.8 g, 47.1 mmol) in CH_2Cl_2 (100 mL). After 2 h, the solvent was evaporated, and the residue was dissolved in ethyl acetate (100 ml). The organic solution was washed with H_2O (3 × 60 mL), dried over Na_2SO_4. Evaporation of solvent gave the crude product **14** (13.6 g, 95%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 9.20 (s, 2H), 4.60 (t, *J* = 1.23 Hz, 2H), 3.81 (t, *J* = 1.23 Hz, 2H), 3.56 (t, *J* = 6.45 Hz, 2H), 1.72 (m, 1H), 1.51 (dd, *J* = 6.82 Hz, 2H), 0.90 (d, *J* = 6.47 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.46, 25.03, 38.23, 65.83, 68.08, 69.78, 122.31, 129.41, 133.80, 148.57,162.48.

2-(Isopentyloxy)ethyl-3-amino-5-nitrobenzoate (15). A mixture of compound **14** (0.5 g, 1.9 mmol) and powder Fe (0.5 g, 9.6 mmol) in AcOH (30 mL) was stirred in ice bath for 2 h. After removal of the Fe, the filtrate was concentrated in vacuo and then CH_2Cl_2 was added. The organic layer was extracted with aqueous saturated sodium bicarbonate (3 × 60 mL), dried over Na_2SO_4 and evaporated under reduced pressure to give a solid. Further separation by chromatography (eluent: CH_2Cl_2/EA 4:1, v/v) afforded **15** (0.3 g, 55%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.65 (s, 1H), 7.63 (s, 1H), 4.49 (t, *J* = 4.72 Hz, 2H), 4.15 (s, 2H), 3.76 (t, *J* = 4.86 Hz, 2H), 3.55 (t, *J* = 6.58 Hz, 2H), 1.71 (m, 1H), 1.50 (dd, *J* = 6.72 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.57, 25.07, 38.30, 64.85, 68.39, 69.90, 112.46, 113.59, 120.98, 132.25, 147.94, 149.15, 164.96.

2-(Isopentyloxy)ethyl-3-amino-5-(2-ethylhexanamido)benzoate (16). 2-Ethyl-hexanoyl chloride (0.7 g, 4.0 mmol) was added to the solution of compound **15** (1.0 g, 3.4 mmol) and triethyl amine (0.4 g, 4.1 mmol) in CH_2Cl_2 (30 mL). The mixture was stirred under reflux for 12 h. Water was added and the mixture was stirred for about half an hour. Then the organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography (eluent: CH_2Cl_2/EA 15:1, v/v) to give a yellow solid, which was then reduced by Pd-C (0.3 g) to afford **16** as a yellow solid (0.9 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.17 (s, 1H), 7.14 (s, 1H), 7.10 (s, 1H), 4.43 (t, *J* = 4.83 Hz, 2H), 3.88 (s, 2H),

3.74 (t, J = 4.83 Hz, 2H), 3.53 (t, J = 6.82 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ11.68, 11.89, 13.84, 22.54, 22.73, 24.93, 26.04, 29.47, 29.70, 31.52, 32.42, 38.22, 47.07, 49.94, 64.04, 68.43, 69.75, 131.03, 139.18, 147.48, 166.64, 175.42, 180.13.

2-(Isopentyloxy)ethyl3-(2-aminoacetamido)-5-(2-ethylhexanamido)benzoate (17). A solution of 2-(tert-butoxy-carbonylamino)acetic acid (0.5 g, 2.8 mmol), EDCI (0.6 g, 3.1 mmol) and HOBt (0.4 g, 3.1 mmol) in CH_2Cl_2 (50 mL) was stirred for 2 h at room temperature followed by addition of compound **16** (1.0 g, 2.6 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred in the dark for 24 h. After removal of the solvent, the residue was purified by column chromatography (eluent: PE/EA 12:1, v/v) to give a yellow oil, which was subsequently stirred in the mixed solution of CF_3OOH (5 mL) and CH_2Cl_2 (15 mL) for 3 h to give **17** (0.9 g, 78%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 8.29 (s, 1H), 8.02 (s, 1H), 7.92 (s, 1H), 7.40 (s, 1H), 4.46 (t, J = 4.83 Hz, 2H), 3.76 (t, J = 4.83 Hz, 2H), 3.54 (t, J = 6.82 Hz, 2H), 3.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.95, 12.90, 21.56, 21.75, 23.97, 25.01, 28.70, 31.35, 37.28, 44.05, 48.77, 63.29, 67.42, 68.81, 114.74, 115.08, 115.90, 129.96, 137.24, 138.16, 165.11, 170.77, 174.58.

Naphthalene-2,7-diamine (18). A classic Bucherer synthesis was employed. A mixture of the naphthalene-2,7-diol **8** (1.0 g, 6.3 mmol) and $NaHSO_3$ (1.9 g, 18.7 mmol) in cooled $NH_3{\cdot}H_2O$ (200 mL) was placed in the pressure reactor. The vessel was sealed and heated to 170 ^{o}C and the mixture was stirred for 7 h. The solid was taken up in ethyl acetate and then extracted with 1N HCl. The extracts was made basic with solid KOH. The resulting precipitate was filtered and vacuum dried to afford a tan solid (0.8 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.43 Hz, 2H), 7.21 (s, 2H), 6.62 (dd, J = 7.24 Hz, 2H), 3.69 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.91, 114.87, 122.69, 129.09, 136.65, 144.64.

N-(7-aminonaphthalen-2-yl)acetamide (19). Acetyl chloride (0.5 g, 6.3 mmol) was added to a mixture of compound **18** (1.0 g, 6.3 mmol), Et_3N (1.0 g, 9.5 mmol) and

CH_2Cl_2 (60 mL) followed by stirring for 20 min at room temperature. After removal of the solvent, the residue was purified by column chromatography (eluent: $CHCl_3/CH_3OH$ 50:1, v/v) to give **19** (0.6 g, 45%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.63(d, *J* = 8.11 Hz, 1H), 7.59 (d, *J* = 8.20 Hz, 1H), 7.24 (s, 1H), 7.17 (dd, *J* = 8.20 Hz, 1H), 6.95 (d, *J* = 2.59 Hz, 1H), 6.87 (dd, *J* = 8.20 Hz, 1H), 3.86 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 24.38, 107.49, 114.05, 116.16, 117.83, 124.98, 128.85, 129.23, 136.83, 138.20, 147.61, 168.91.

5-((2-Ethylhexyl)carbamoyl)-2,4-bis((2-ethylhexyl)oxy)benzoic acid (20)[2]. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.94 (s, 1H), 7.44 (s, 1H), 6.46 (s, 1H), 4.08 (d, *J* = 4.99 Hz, 2H), 4.01 (dd, *J* = 5.51 Hz, 2H), 3.33 (m, 2H), 1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ13.96, 22.57, 25.88, 26.24, 26.77, 28.96, 29.16, 29.20, 29.23,29.32, 29.66, 31.59, 31.71, 31.78, 39.93, 69.85, 70.66, 96.62, 111.21, 138.70, 160.59, 163.55, 164.06, 194.64.

2-(5-((2-Ethylhexyl)carbamoyl)-2,4-bis((2-ethylhexyl)oxy)benzamido)acetic acid (21). A mixture of EDCI (0.8 g, 4.2 mmol), HOBt (0.6 g, 4.3 mmol) and **20** (1.1 g, 2.1 mmol) in CH_2Cl_2 (30 mL) was stirred under N_2 atmosphere for 2 h. Glycine ethyl ester hydrochloride (0.4 g, 2.4 mmol) and triethylamine (0.3 g, 2.5 mmol) in CH_2Cl_2 (10 mL) was added to the above solution followed by stirring for 24 h. After removing the solvent, the residue was purified by column chromatography (eluent: CH_2Cl_2/EA 30:1, v/v) to give a colorless oil. Hydrolysis with 1N NaOH (5.0 mmol) in methanol (30 mL) for 6 h afforded **21** (1.1 g, 86%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.20 (t, *J* = 4.82 Hz, 1H), 7.61 (t, *J* = 5.64 Hz, 1H), 6.49 (s, 1H), 4.29 (d, *J* = 4.82 Hz, 2H), 4.05 (d, *J* = 4.82 Hz, 2H), 3.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.74, 10.76, 10.83, 10.99, 13.99, 14.04, 22.96, 23.01, 23.80, 23.95, 24.22, 28.85, 28.88, 29.00, 30.35, 30.57, 31.08, 38.94, 39.40, 39.48, 42.24, 42.97, 71.79, 72.21, 96.26, 114.23, 114.58, 136.99, 160.57, 160.75, 164.82, 164.92, 172.14.

N^1-(2-((7-acetamidonaphthalen-2-yl)amino)-2-oxoethyl)-N^3-(2-ethylhexyl)-4,6-bis ((2-ethylhexyl)oxy)isophthalamide (1). A mixture of EDCI (120.8 mg, 0.6 mmol), HOBt (89.4 mg, 0.7 mmol) and compound **21** (260.0 mg, 0.4 mmol) in CH_2Cl_2 (25 mL) was stirred under N_2 atmosphere for 2 h. Then compound **19** (84.1 mg, 0.4 mmol) in CH_2Cl_2 (5 mL) was added to the above solution followed by stirring for 24 h at room temperature. After removal of the solvent, the residue was purified by column chromatography (eluent: CH_2Cl_2/CH_3OH 30:1, v/v) to give **1** (250.0 mg, 77%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.99 (s, 1H), 8.52 (s, 1H), 8.46 (t, *J* = 4.92 Hz, 1H), 7.85 (s, 1H), 7.67 (s, 1H), 7.54 (t, *J* = 5.38 Hz, 1H), 7.47 (m, 4H), 6.41 (s,1H), 4.29 (d, *J* = 4.54 Hz, 2H), 3.97 (m, 4H), 3.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.82, 10.83, 10.99, 11.05, 14.00, 14.06,14.09, 14.13, 22.70, 23.02, 23.05, 23.92, 23.98, 24.27, 24.48, 28.93, 28.95, 28.98, 29.06, 29.38, 29.71, 30.53, 30.60, 31.16, 31.94, 39.02, 39.45, 39.61, 42.97, 45.19, 71.84, 72.47, 96.39, 114.09, 115.21, 116.11, 116.60, 119.29, 127.65, 127.98, 128.16, 134.06, 136.09, 136.25, 136.78, 160.67, 160.73, 164.77,165.35, 167.39, 169.16; HRMS (ESI), m/z calcd for $[C_{46}H_{68}N_4O_6+H]^+$ 773.5217; found: 773.5227.

2-(Isopentyloxy)ethyl-3-(2-ethylhexanamido)-5-(2-(7-((2-ethylhexyl)carbamoyl)-3, 6-bis((2-ethylhexyl)oxy)-2-naphthamido)acetamido)benzoate (2). A mixture of EDCI (37.4 mg, 0.2 mmol), HOBt (26.9 mg, 0.2 mmol) and compound **11** (75.6 mg, 0.1 mmol) in CH_2Cl_2 (20 mL) was stirred under N_2 atmosphere for 2 h. Then compound **17** (70.1 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) was added to the above solution, which was stirred for 24 h at room temperature. After removal of the solvent, the residue was purified by column chromatography (eluent: CH_2Cl_2/CH_3OH 40:1, v/v) to give **2** (114.8 mg, 87%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.82 (s, 1H), 8.80 (s, 1H), 8.77 (t, *J* = 5.01 Hz, 1H), 8.12 (s, 1H), 8.04 (s, 1H), 7.96 (s, 1H), 7.94 (t, *J* = 5.76 Hz, 1H), 7.63 (s, 1H), 7.15 (s, 1H), 7.13 (s, 1H), 4.44 (t, *J* = 5.20 Hz, 2H), 4.38 (d, *J* = 4.44 Hz, 2H), 4.14 (m, 4H), 3.73 (t, *J* = 4.59 Hz, 2H), 3.52 (t, *J* = 6.58 Hz, 2H), 3.46 (d, *J* = 4.59 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.79,

10.81, 10.94, 10.98, 11.98, 13.86, 14.00, 14.04, 22.58, 22.73, 23.02, 23.04, 24.09, 24.34, 26.04, 28.94, 28.97, 29.75, 30.69, 32.39, 38.40, 39.11, 39.41, 39.65, 43.19, 45.43, 50.33, 64.29, 68.48, 69.89, 71.66, 72.16, 105.73, 105.83, 116.36, 117.09, 117.36, 120.35, 121.68, 122.84, 131.52, 135.56, 138.56, 138.75, 156.47, 156.71, 165.03, 165.96, 167.55, 174.73; HRMS (ESI), m/z calcd for $[C_{60}H_{94}N_4O_9+H]^+$ 1015.7099; found: 1015.7025.

N^2-(2-((7-acetamidonaphthalen-2-yl)amino)-2-oxoethyl)-N^7-(2-ethylhexyl)-3,6-bis ((2-ethylhexyl)oxy)naphthalene-2,7-dicarboxamide (3). The mixture of EDCI (46.0 mg, 0.3 mmol), HOBt (32.4 mg, 0.3 mmol) and compound **12** (77.0 mg, 0.1 mmol) in CH_2Cl_2 (20 mL) was stirred under N_2 atmosphere for 2 h. Then compound **19** (28.8 mg, 0.2 mmol) in CH_2Cl_2 (15 mL) was added to the above solution, which was stirred for 36 h at room temperature. After removal of the solvent, the residue was purified by column chromatography (eluent: CH_2Cl_2/CH_3OH 50:1/30:1, v/v) to afford **3** (64.2 mg, 65%) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 9.19 (s, 1H), 9.11 (s, 1H), 9.01 (s, 1H), 8.96 (s, 1H), 8.17 (s, 1H), 8.02 (t, *J* = 5.19 Hz, 1H), 7.99 (d, *J* = 9.63 Hz, 1H), 7.93 (s, 1H), 7.78 (s, 2H), 7.76 (s, 1H), 7.19 (s, 2H), 4.71 (s, 2H), 4.17 (d, *J* = 6.39 Hz, 4H), 3.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.81, 10.85, 10.94, 14.02, 14.04, 14.07, 22.67, 22.96, 23.04, 23.10, 23.78, 23.94, 24.11, 24.36, 24.50, 28.93, 28.98, 29.34, 29.68, 30.21, 30.39, 30.61, 30.70, 31.18, 31.91, 38.82, 39.41, 39.58, 43.48, 71.84, 72.77, 106.10, 115.18, 116.26, 120.49, 120.74, 121.70, 122.71, 128.30, 128.53, 134.04, 135.01, 136.85, 138.89, 156.56, 156.87, 165.46, 165.54, 166.80; HRMS (ESI), m/z calcd for $[C_{50}H_{70}N_4O_6+H]^+$ 823.5374; found: 823.5381.

Bis(2-(isopentyloxy)ethyl)-5,5'-((2,2'-((3,6-bis((2-ethylhexyl)oxy)naphthalene-2,7-dicarbonyl)bis(azanediyl))bis(acetyl))bis(azanediyl))bis(3-(2-ethylhexanamido)be-nzoate) (4). A mixture of EDCI (155.3 mg, 0.8 mmol), HOBt (131.5 mg, 1.0 mmol) and compound **13** (153.1 mg, 0.3 mmol) in CH_2Cl_2 (30 mL) was stirred under N_2

atmosphere for 4 h. Then compound **17** (340.1 mg, 0.7 mmol) in CH_2Cl_2 (10 mL) was added to the above solution followed by stirring for 36 h at room temperature. After removal of the solvent, the residue was washed with ethyl acetate (6 × 10 mL) giving **4** (385.2 mg, 89%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 2H), 9.25 (s, 2H), 8.86 (s, 2H), 8.23 (s, 2H), 8.09 (s, 2H), 7.97 (s, 2H), 7.35 (s, 2H), 7.19 (s, 2H), 4.55 (s, 4H), 4.50 (t, *J* = 4.33 Hz, 4H), 4.19 (d, *J* = 5.83 Hz, 4H), 3.79 (t, *J* = 4.95 Hz, 4H), 3.55 (t, *J* = 7.17 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.80, 10.92, 14.02, 22.58, 22.66, 23.03, 24.06, 24.31, 25.03, 28.87, 28.96, 29.33, 29.67, 30.60, 31.90, 38.41, 38.95, 39.40, 39.64, 43.17, 45.38, 64.21, 68.48, 69.87, 71.66, 72.22, 105.72, 117.44, 120.65, 121.58, 122.84, 131.59, 135.27, 138.69, 156.53, 156.63, 165.04, 165.82, 165.89, 167.47; HRMS (ESI), m/z calcd for $[C_{76}H_{114}N_6O_{14}+H]^+$ 1335.8471; found: 1335.8510.

N^1,$N^{1'}$-((naphthalene-2,7-diylbis(azanediyl))bis(2-oxoethane-2,1-diyl))bis(N3-(2-et-hylhexyl)-4,6-bis((2-ethylhexyl)oxy)isophthalamide) (5). The mixture of EDCI (0.1 g, 0.7 mmol), HOBt (0.1 g, 0.7 mmol) and compound **21** (0.2 g, 0.3 mmol) in CH_2Cl_2 (30 mL) was stirred under N_2 atmosphere for 2 h. Then compound **18** (17.8 mg, 0.1 mmol) in CH_2Cl_2 (15 mL) was added to the above solution, which was stirred for 24 h at room temperature and heated under reflux for 6 h. After removal of the solvent, the residue was purified by column chromatography (eluent: CH_2Cl_2/CH_3OH 60:1/40:1, v/v) to afford **5** (134.6 mg, 86%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 2H), 8.46 (t, *J* = 5.62 Hz, 2H), 8.14 (s, 2H), 7.68 (d, *J* = 8.86 Hz, 2H), 7.58 (t, *J* = 5.62 Hz, 2H), 7.44 (d, *J* = 8.86 Hz, 2H), 6.51 (s, 2H), 4.35 (d, *J* = 5.24 Hz, 4H), 4.09 (d, *J* = 5.62 Hz, 4H), 3.41 (d, *J* = 5.62 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.84, 11.01, 11.04, 14.05, 14.09, 23.01, 23.05, 23.97, 24.28, 28.95, 29.04, 29.69, 30.60, 31.16, 39.02, 30.43, 39.62, 42.88, 45.34, 71.78, 72.45, 96.40, 114.20, 115.19, 116.26, 119.14, 127.69, 128.29, 134.31, 136.05, 136.91, 160.60, 160.66, 164.56, 165.30, 167.37; HRMS (ESI), m/z calcd for $[C_{78}H_{122}N_6O_{10}+H]^+$ 1303.9301; found: 1303.9319.

3. Self-assembly of 1 and 2

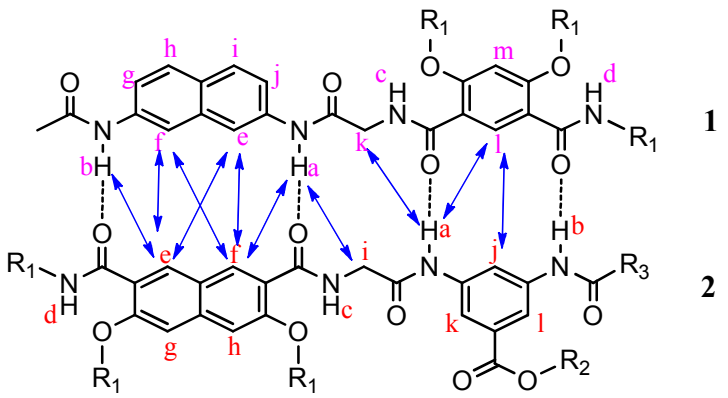


Figure S1. Representation of molecular duplex **1·2**.

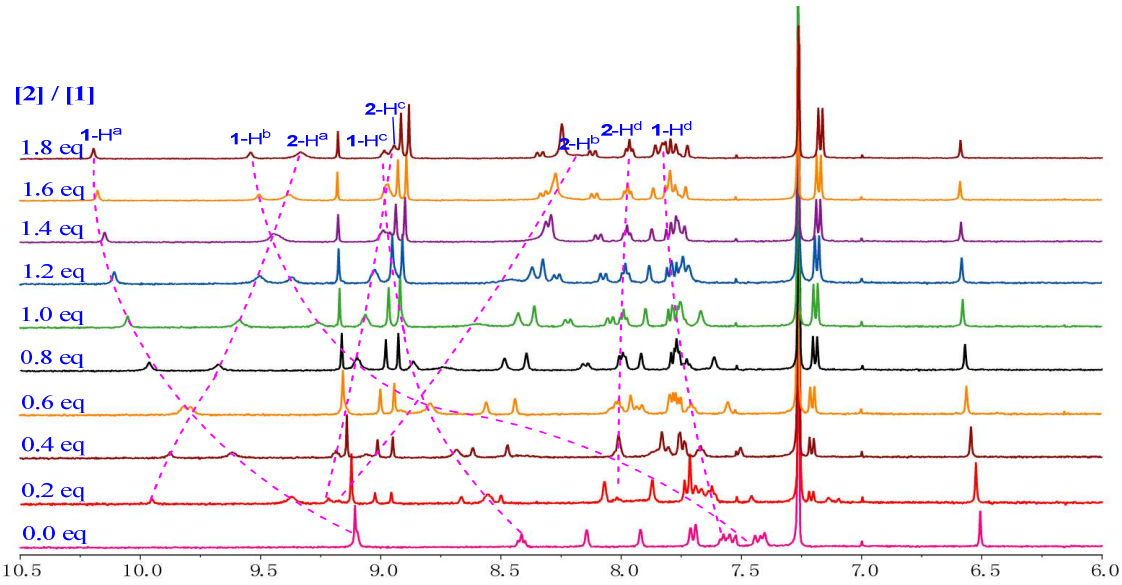
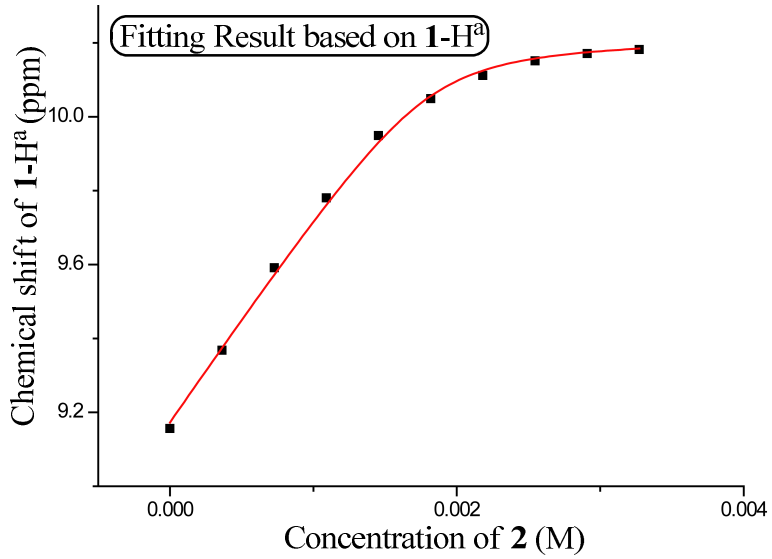


Figure S2. Stacked partial ^{1}H NMR spectra of compound **1** (1.8 mM) when titrated with **2**, from 0 equivalent to 1.8 equivalents in $CDCl_3$ at 298K.

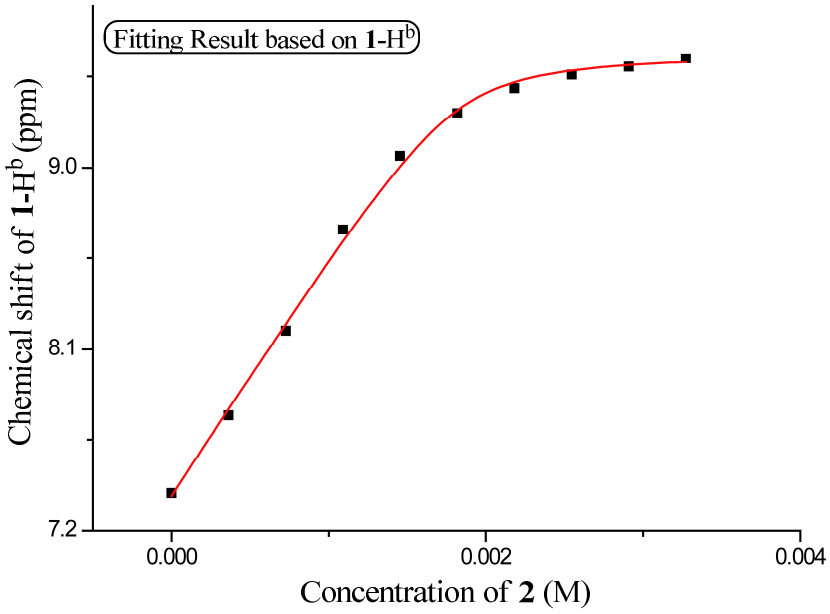
Nonlinear regression analysis is according to the reference 3.



K_a = 19207.58968 ± 6711.06965 M^{-1}

R^2 = 0.99826

Figure S3. Determination of the binding constant of **1**·**2** in $CDCl_3$ at 298K. Fitting result based on **1**-H^a.



K_a = 27902.92365 ± 12764.81351 M^{-1}

R^2 = 0.99763

Figure S4. Determination of the binding constant of **1**·**2** in $CDCl_3$ at 298K. Fitting result based on **1**-H^b.

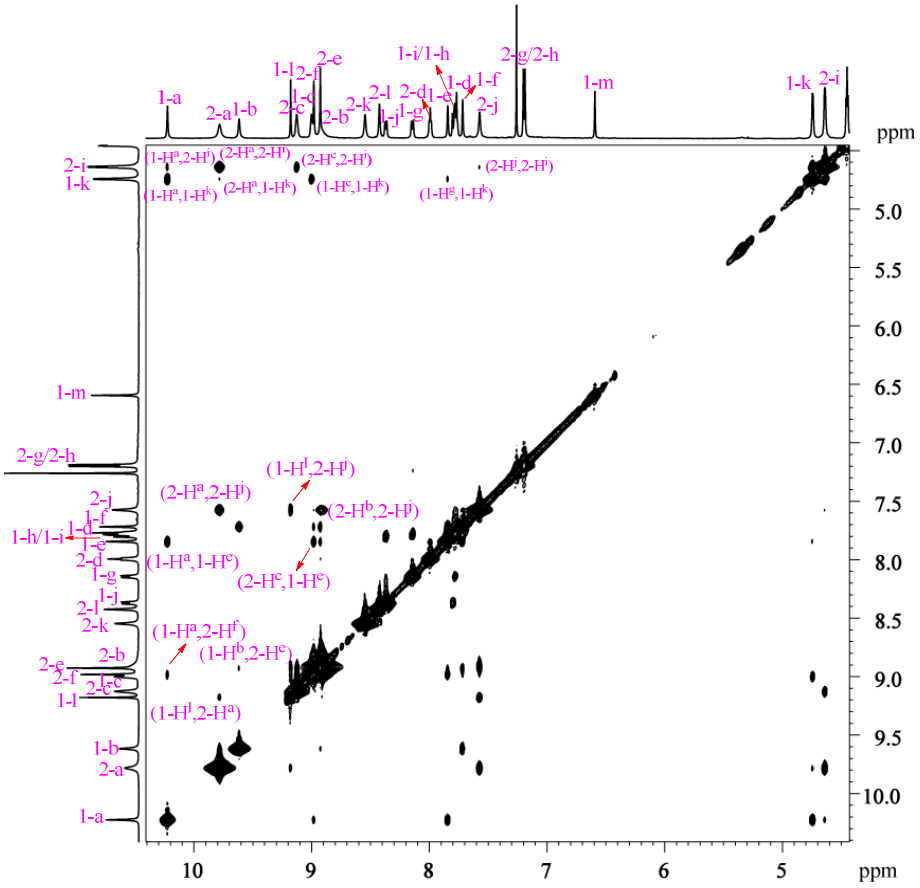


Figure S5. Partial NOESY spectrum of **1·2** (10 mM) in $CDCl_3$ (600 MHz, 298 K).

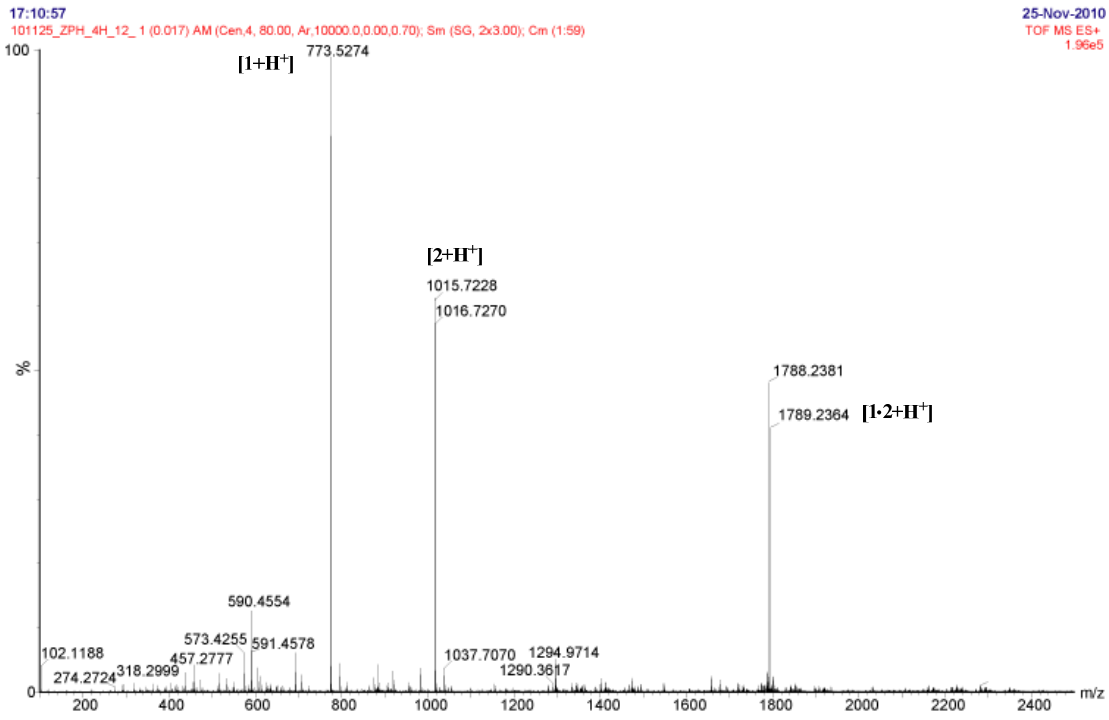


Figure S6. ESI-HRMS spectrum of **1·2** in CH_2Cl_2/CH_3CN (1:3).

4. Self-assembly of 1

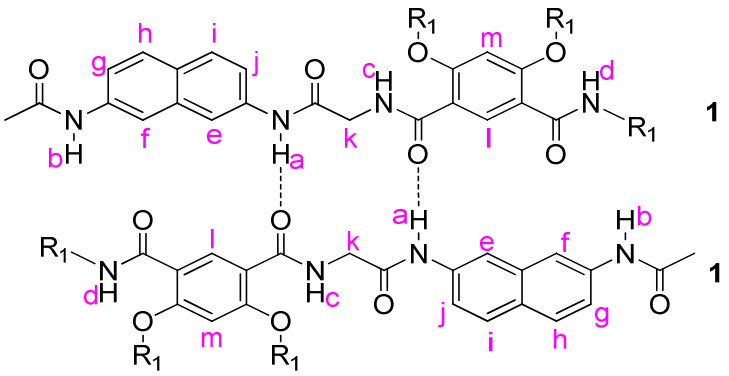


Figure S7. Representation of molecular duplex **1·1**.

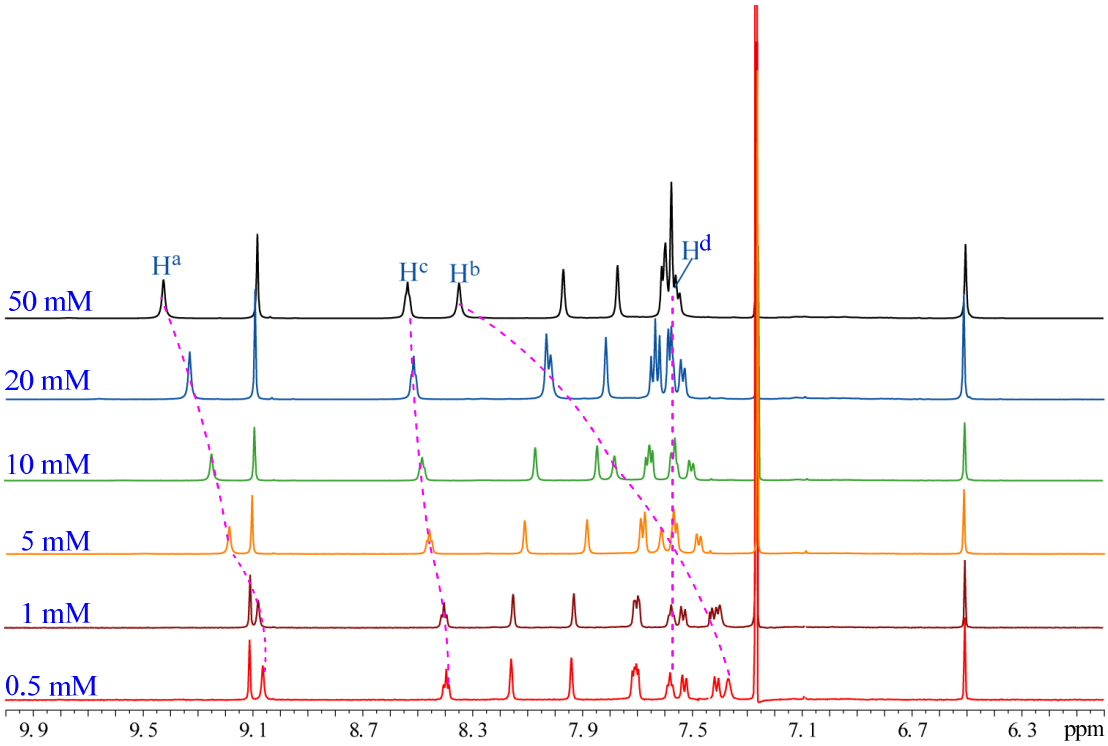
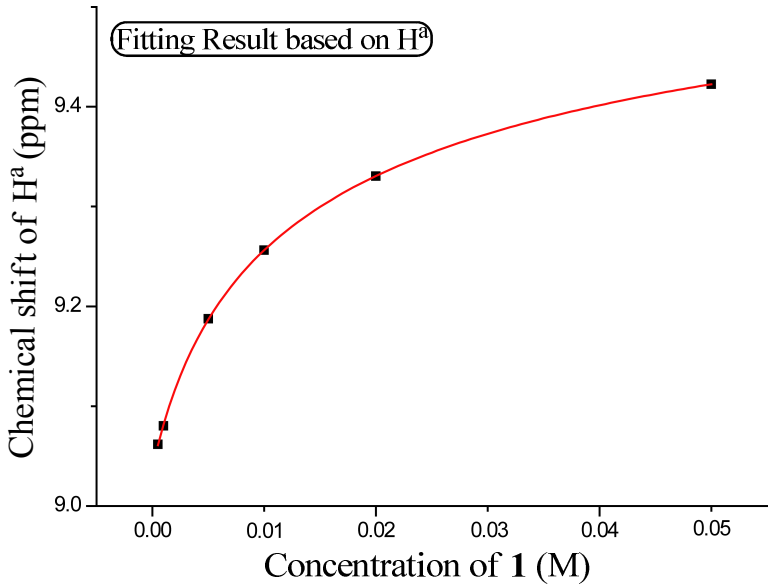


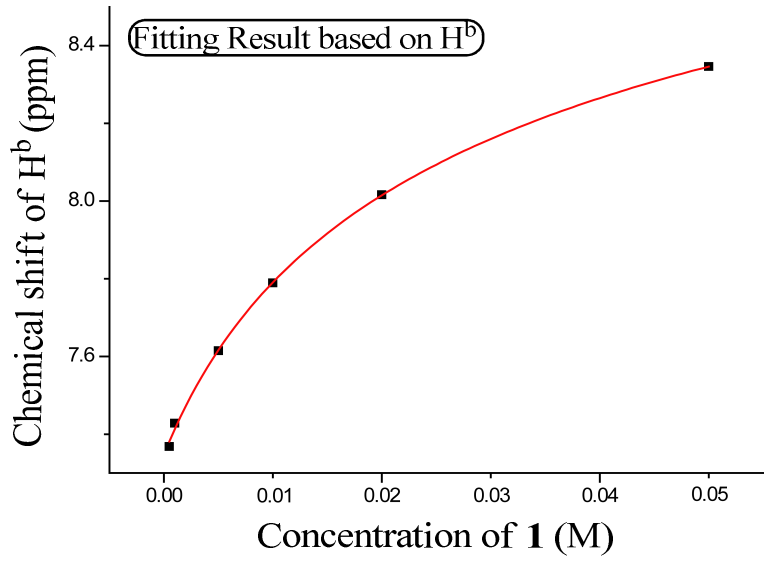
Figure S8. Stacked partial ^{1}H NMR spectra of **1** at different concentrations in $CDCl_3$ at 298 K.



K_{dimer} = 82.66587 ± 1.55085 M^{-1}

R^2 = 0.99996

Figure S9. Determination of the binding constant of **1·1** in $CDCl_3$ at 298K. Fitting result based on H^a.



K_{dimer} = 33.302 ± 3.17859 M^{-1}

R^2 = 0.99901

Figure S10. Determination of the binding constant of **1·1** in $CDCl_3$ at 298K. Fitting result based on H^b.

5. Self-assembly of 2

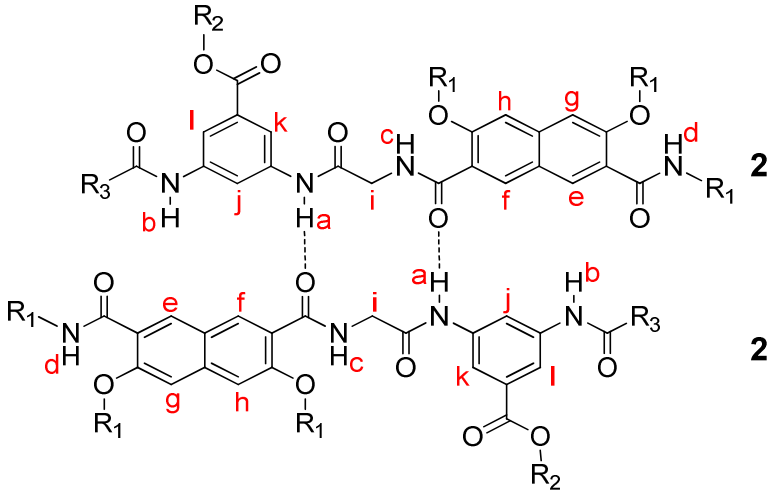


Figure S11. Representation of molecular duplex **2**·**2**

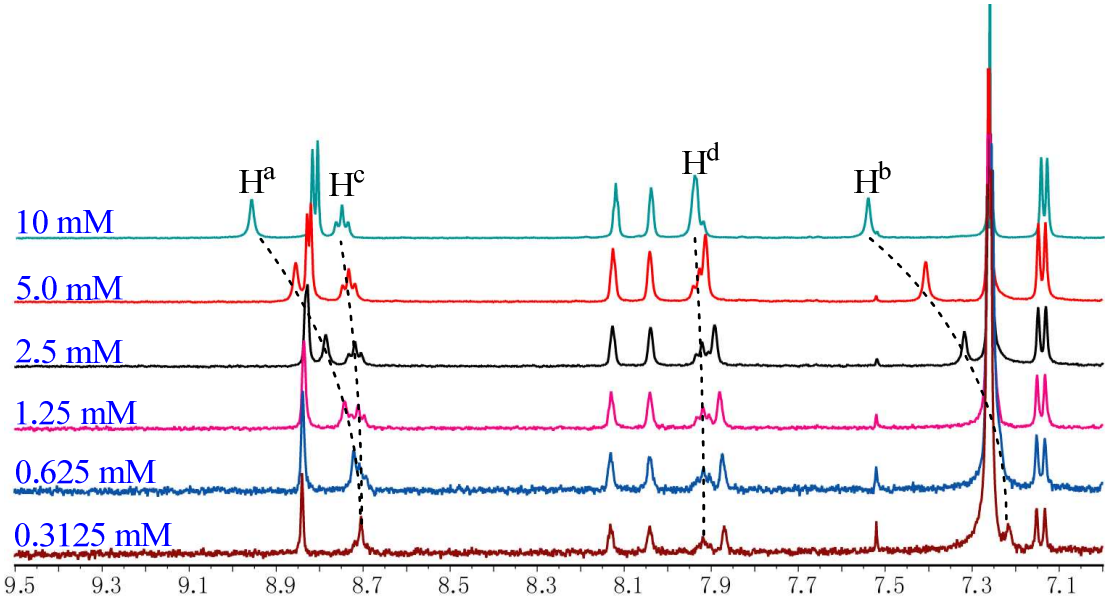
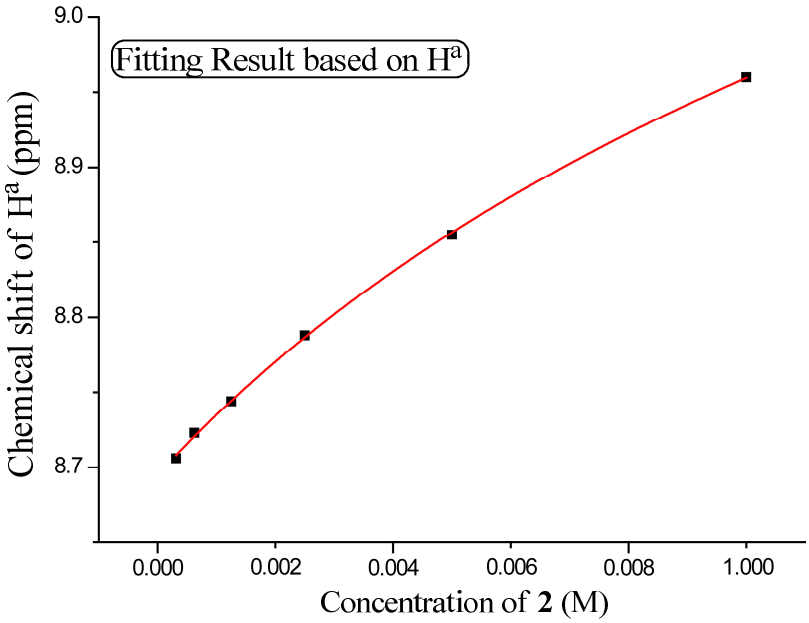


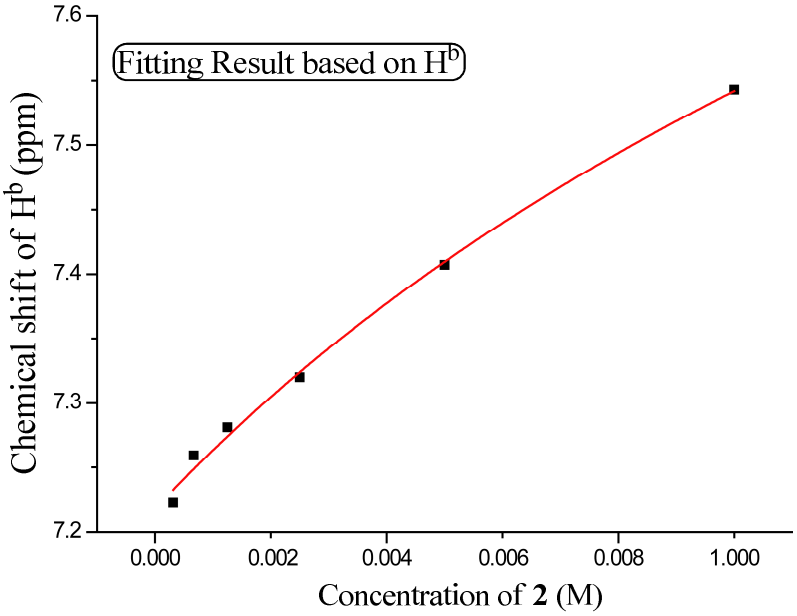
Figure S12. Stacked partial ^{1}H NMR spectra of **2** at different concentrations in $CDCl_3$ at 298 K.



K_{dimer} = 17.13675 ± 2.13051 M^{-1}

R^2 = 0.99947

Figure S13. Determination of the binding constant of **2·2** in $CDCl_3$ at 298K. Fitting result based on H^a.



K_{dimer} = 13.0244 ± 8.39111 M^{-1}

R^2 = 0.98922

Figure S14. Determination of the binding constant of **2·2** in $CDCl_3$ at 298K. Fitting result based on H^b.

6. Self-assembly of 3

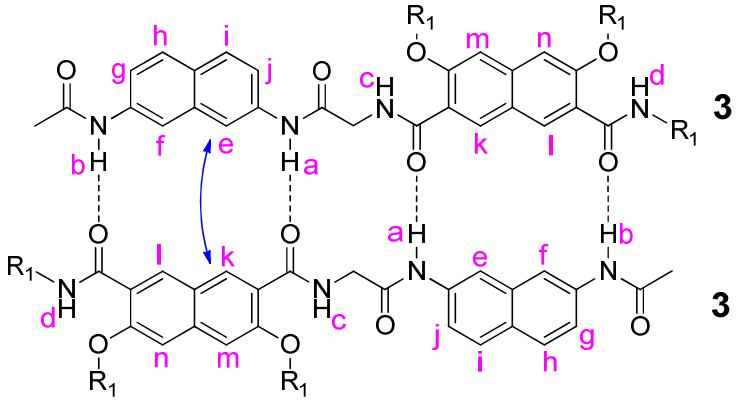


Figure S15. Representation of molecular duplex **3·3**.

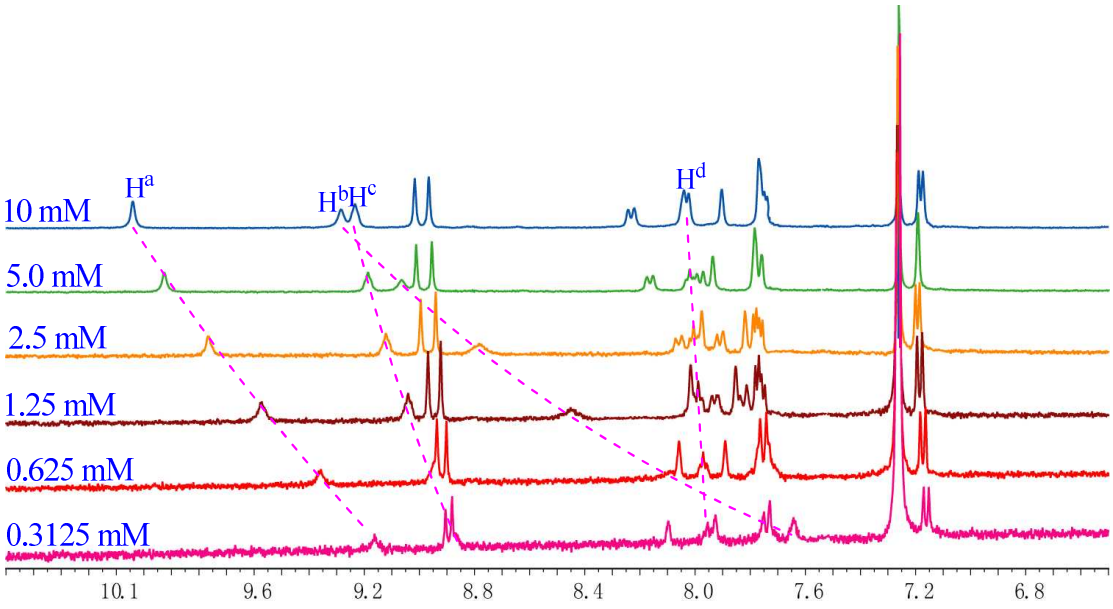
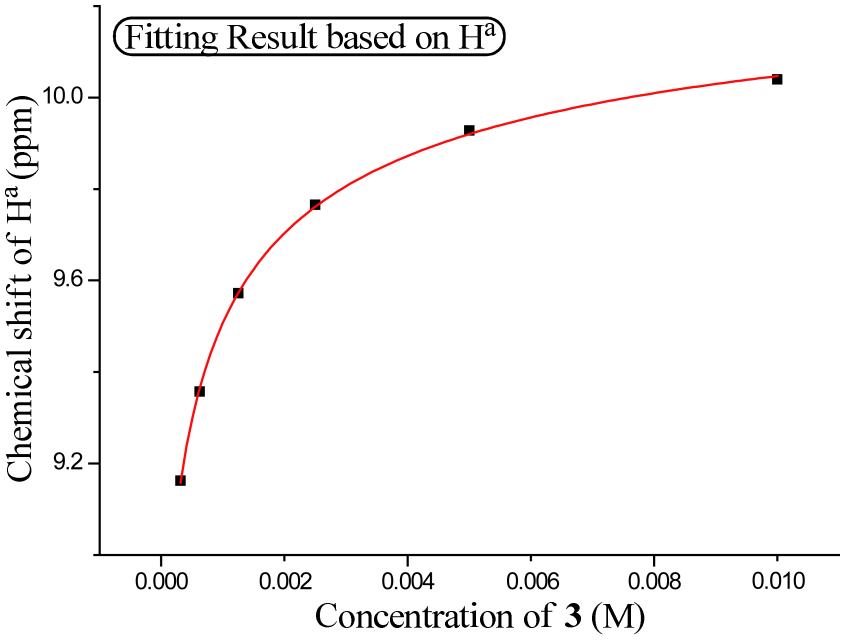


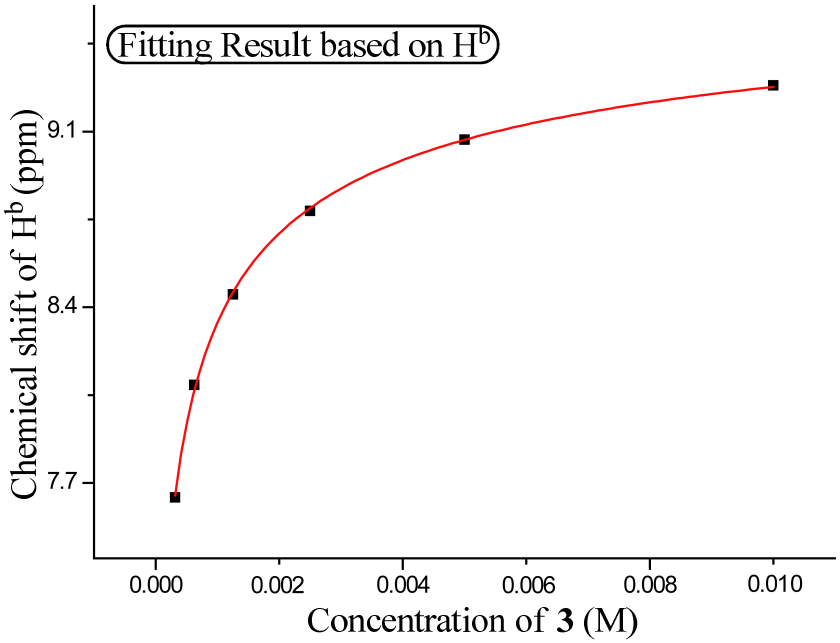
Figure S16. Stacked partial ^{1}H NMR spectra of **3** at different concentrations in $CDCl_3$ at 298 K.



K_{dimer} = 949.22633 ± 132.29769 M^{-1}

R^2 = 0.99939

Figure S17. Determination of the binding constant of **3·3** in $CDCl_3$ at 298K. Fitting result based on H^a.



K_{dimer} = 1551.48779 ± 278.35136 M^{-1}

R^2 = 0.99933

Figure S18. Determination of the binding constant of **3·3** in $CDCl_3$ at 298K. Fitting

result based on H^b.

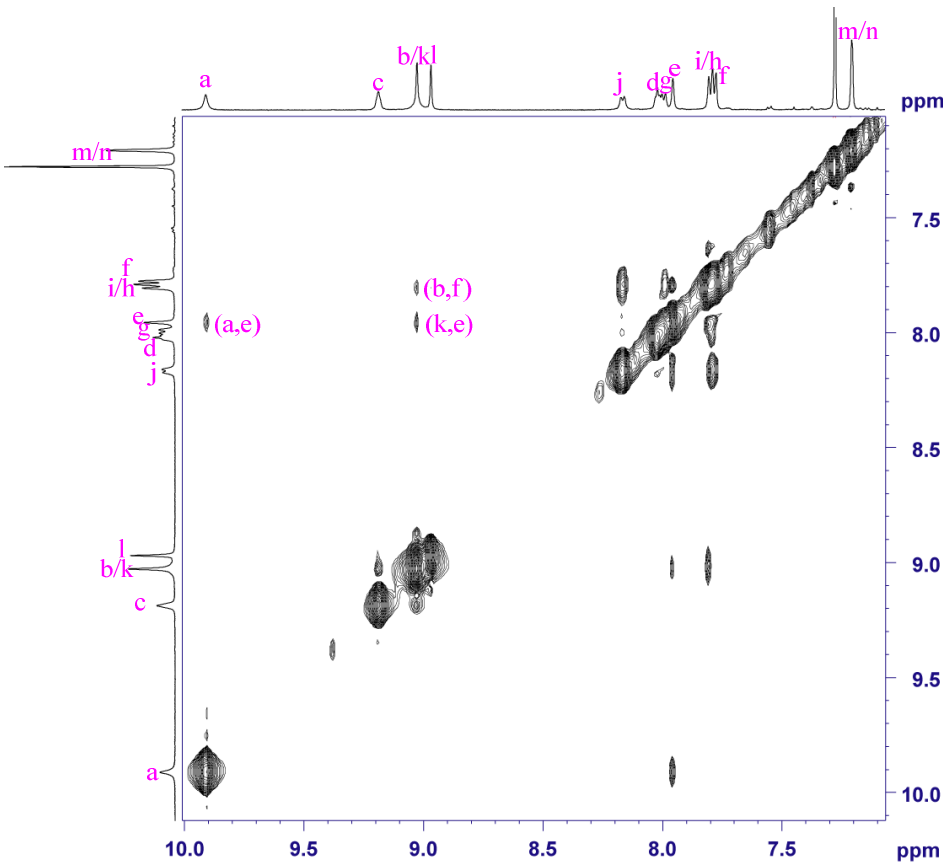


Figure S19. Partial NOESY spectrum of **3** (10 mM) in $CDCl_3$ (600 MHz, 298 K).

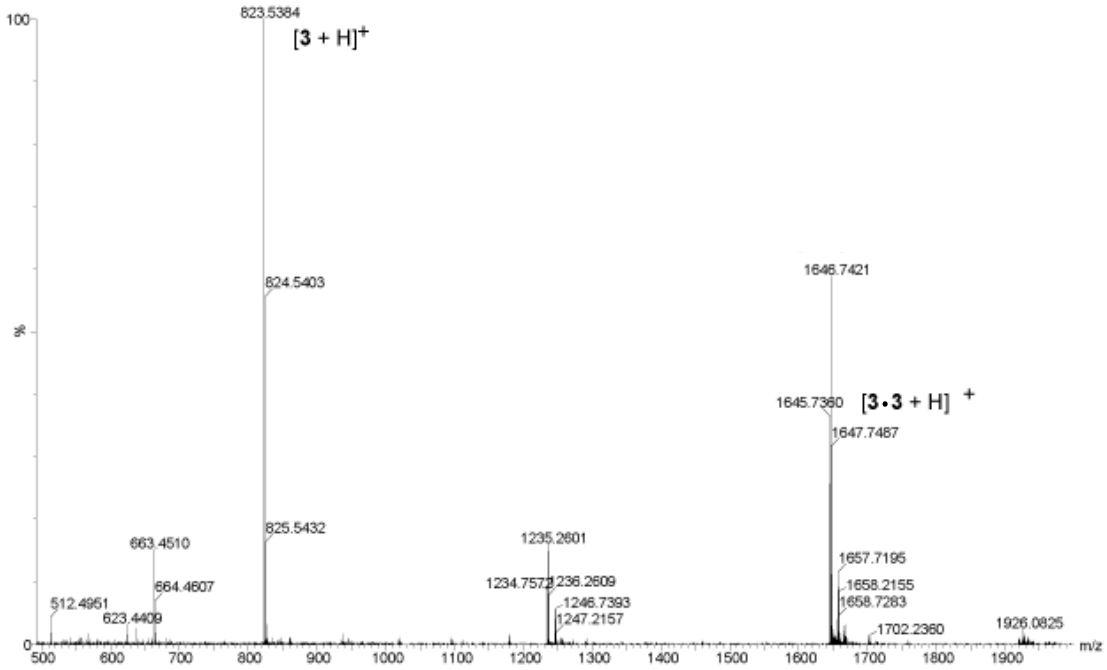


Figure S20. ESI-MS spectrum of **3·3** in CH_2Cl_2/CH_3OH (3:1).

7. ^{1}H NMR titration of 1·1 with 7

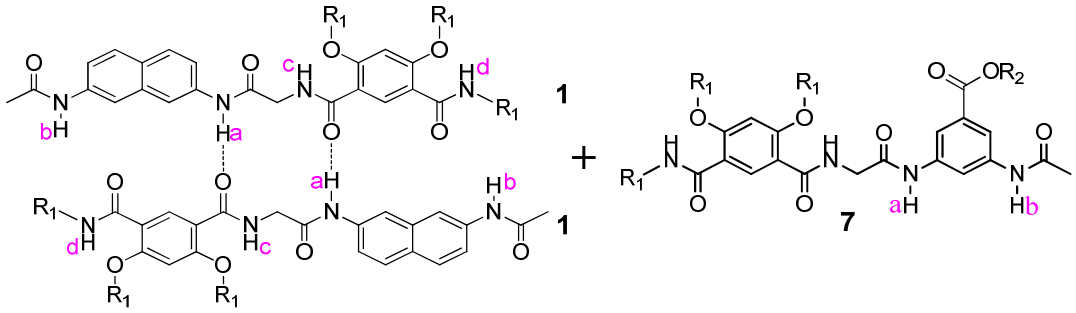


Figure S21. Representation of molecular duplex **1·1** and **7**.

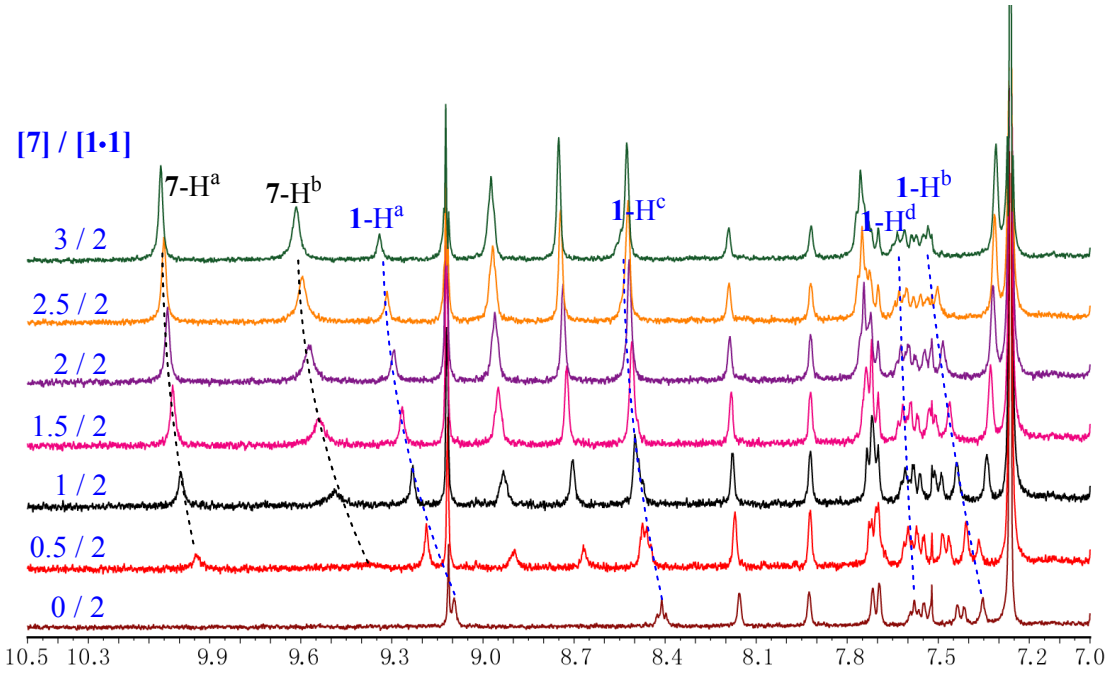
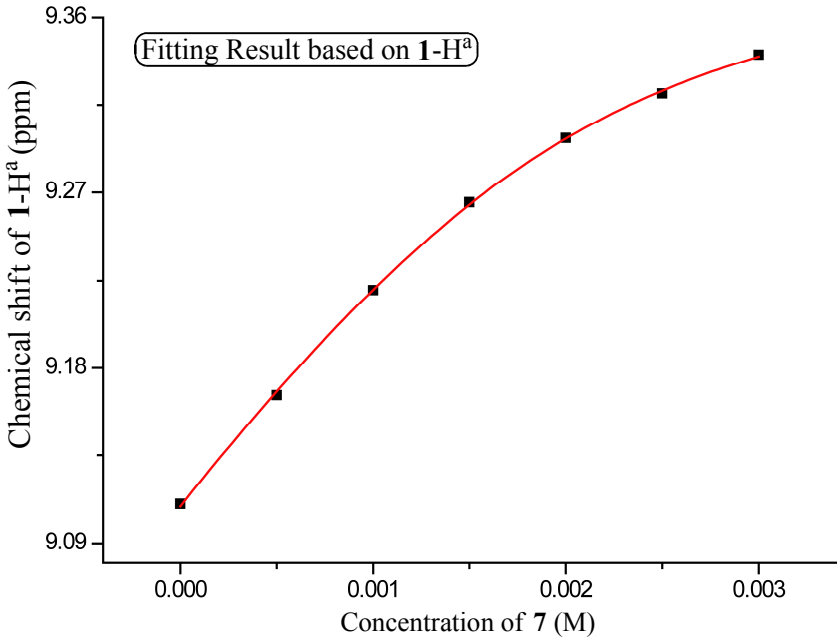


Figure S22. Stacked partial ^{1}H NMR spectra of heterodimer **1·1** (2.0 mM) when titrated with **7**, from 0 equivalent to 1.5 equivalents in $CDCl_3$ at 298K.



$K_a = 964.89801 \pm 82.15376\ M^{-1}$

$R^2 = 0.99969$

Figure S23. Determination of the binding constant of **1·7** in $CDCl_3$ at 298K. Fitting result based on **1**-H^a.

8. ^{1}H NMR titration of 2·2 with 7

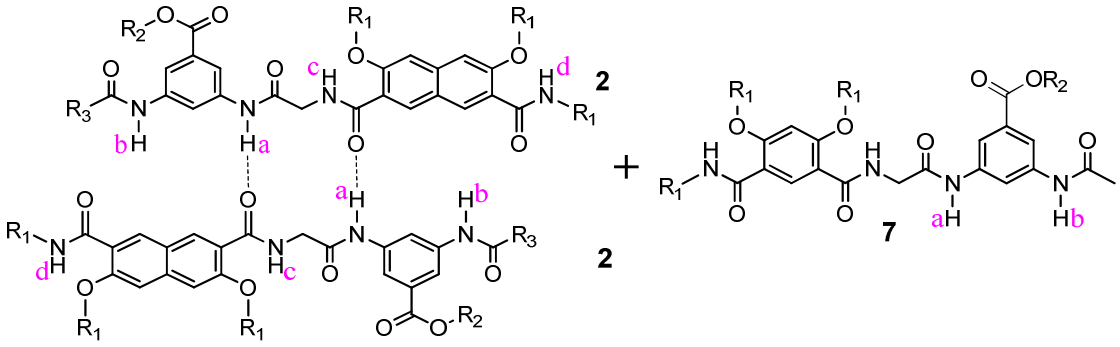


Figure S24. Representation of molecular duplex **2·2** and **7**.

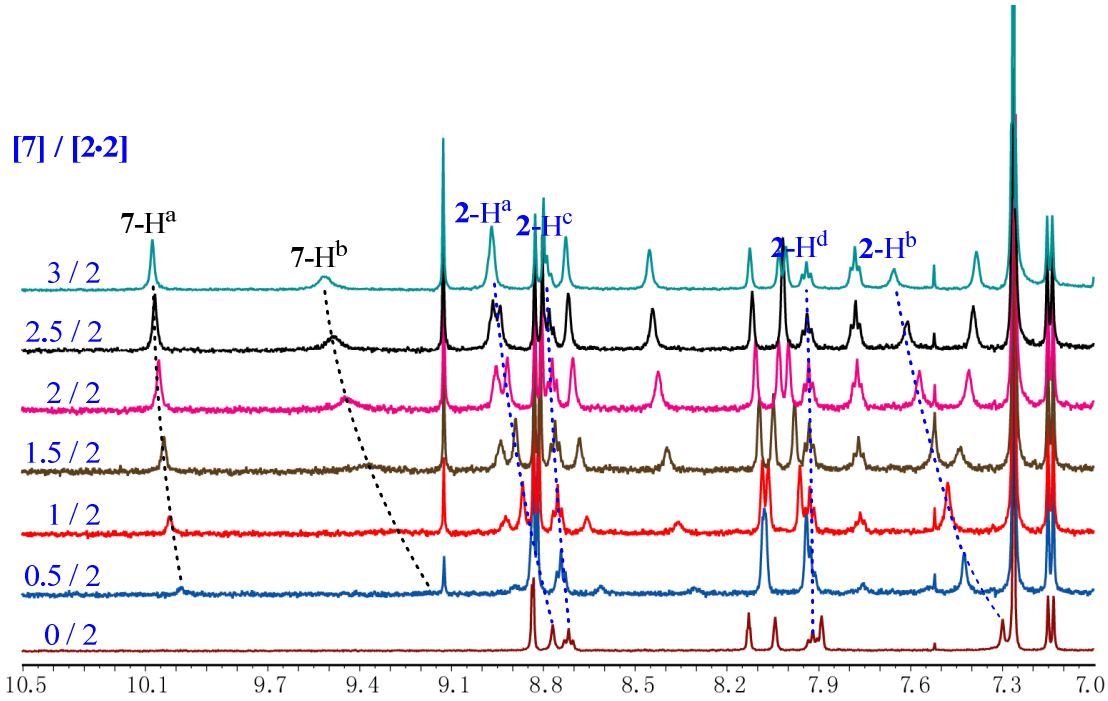
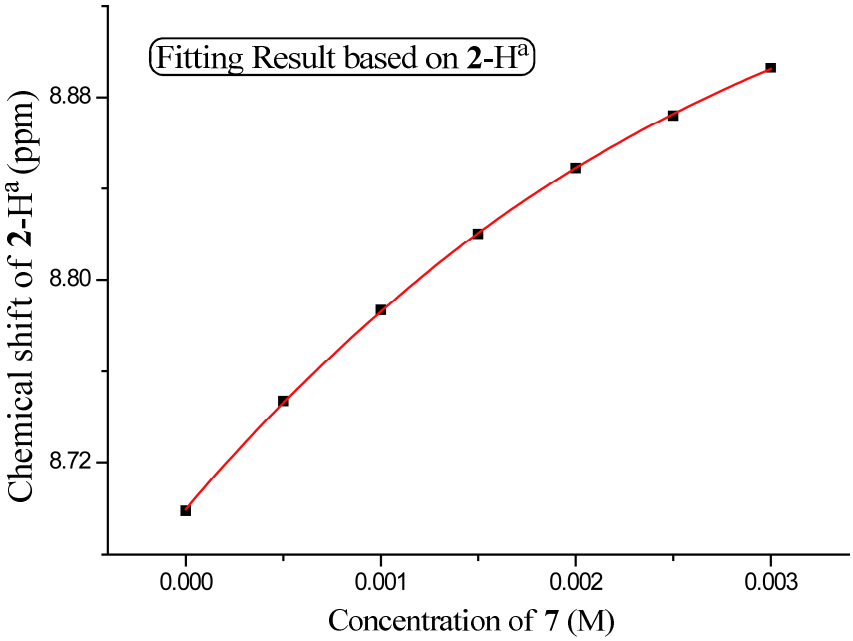


Figure S25. Stacked partial ^{1}H NMR spectra of heterodimer **2·2** (2.0 mM) when titrated with **7**, from 0 equivalent to 1.5 equivalents in $CDCl_3$ at 298K.



$K_a = 679.69679 \pm 74.31216\ M^{-1}$

$R^2 = 0.99985$

Figure S26. Determination of the binding constant of **2·7** in $CDCl_3$ at 298K. Fitting result based on **2**-H^{a}.

9. ^{1}H NMR titration of 1·2 with 7

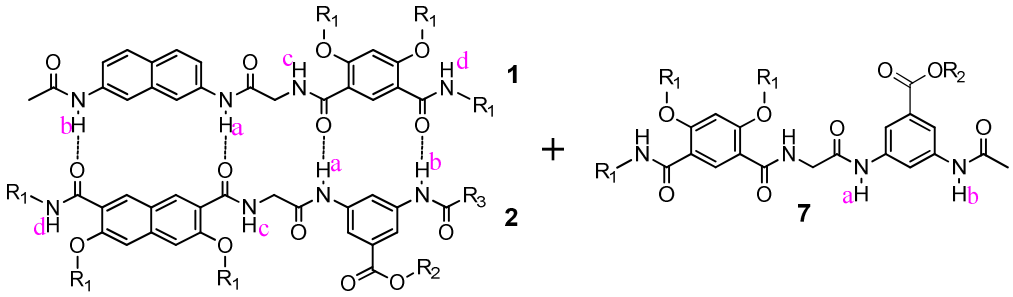


Figure S27. Representation of molecular duplex **1·2** and **7**.

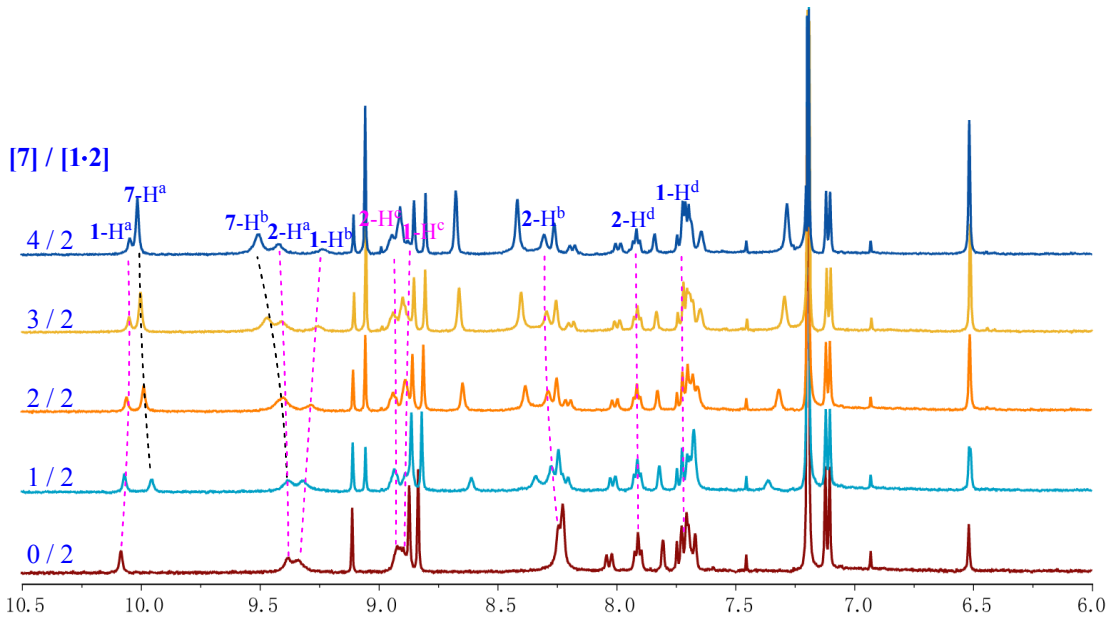


Figure S28. Stacked partial ^{1}H NMR spectra of heterodimer **1·2** (2.0 mM) when titrated with **7**, from 0 equivalent to 2.0 equivalents in $CDCl_3$ at 298K.

10. ^{1}H NMR titration of 3·3 with 7

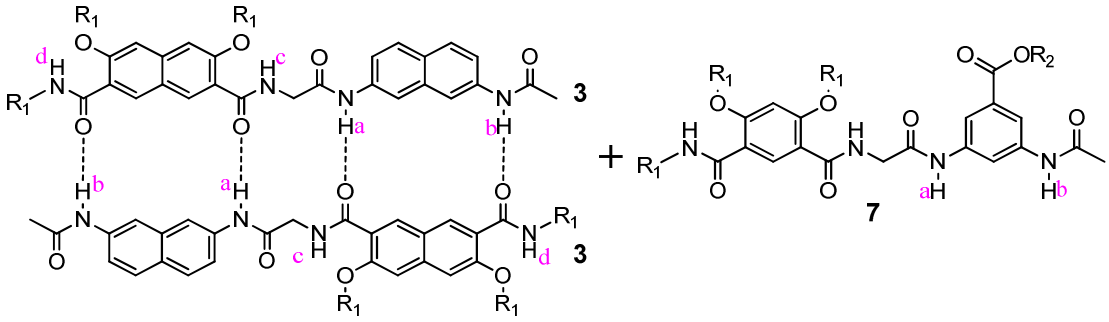


Figure S29. Representation of molecular duplex **3·3** and **7**.

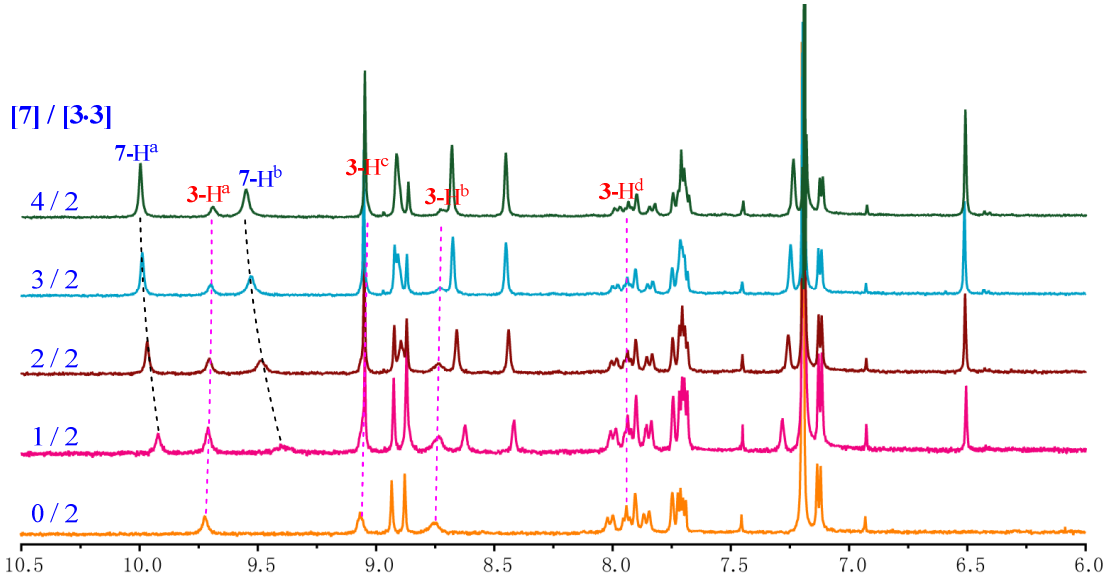


Figure S30. Stacked partial ^{1}H NMR spectra of homodimer **3·3** (2.0 mM) when titrated with **7**, from 0 equivalent to 2.0 equivalents in $CDCl_3$ at 298K.

11. Self-assembly of 4 and 5

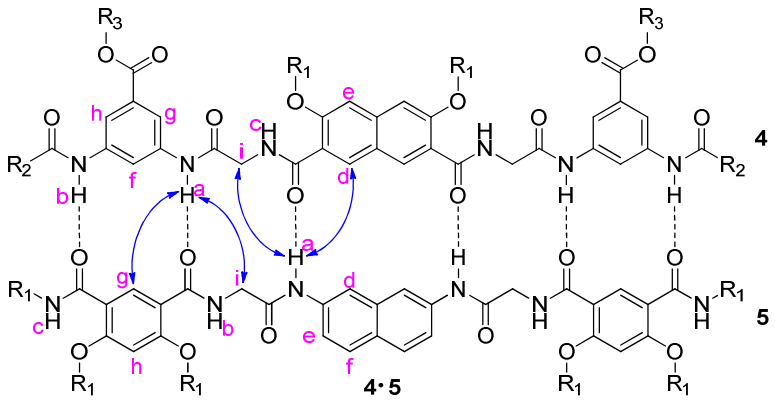


Figure S31. Representation of molecular duplex **4·5**.

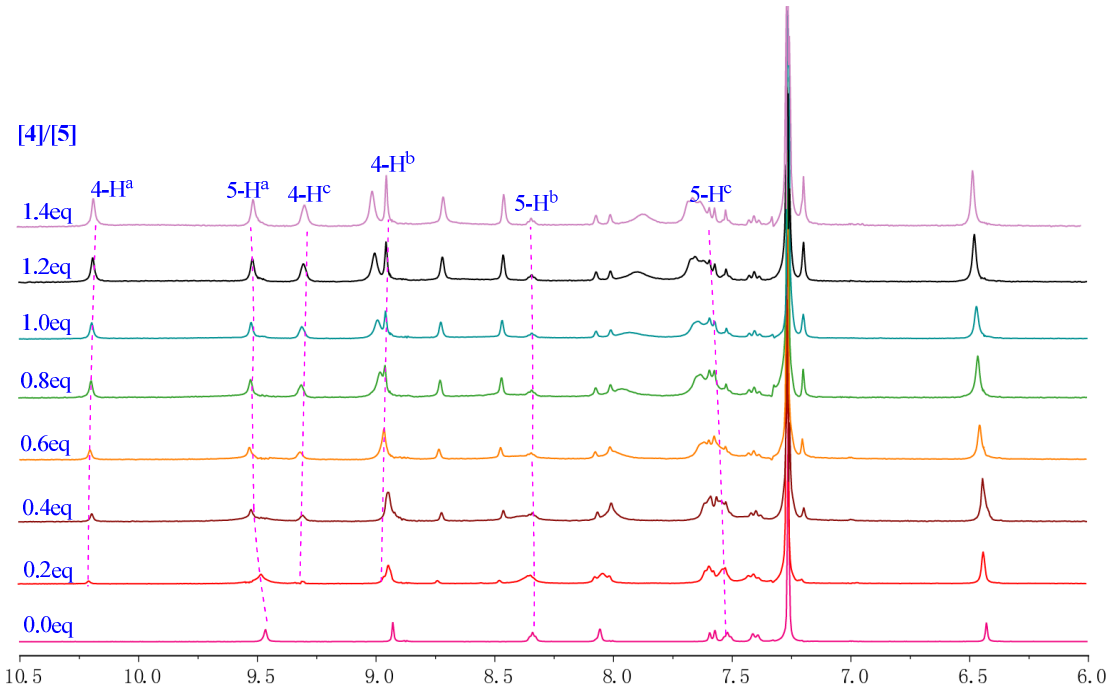
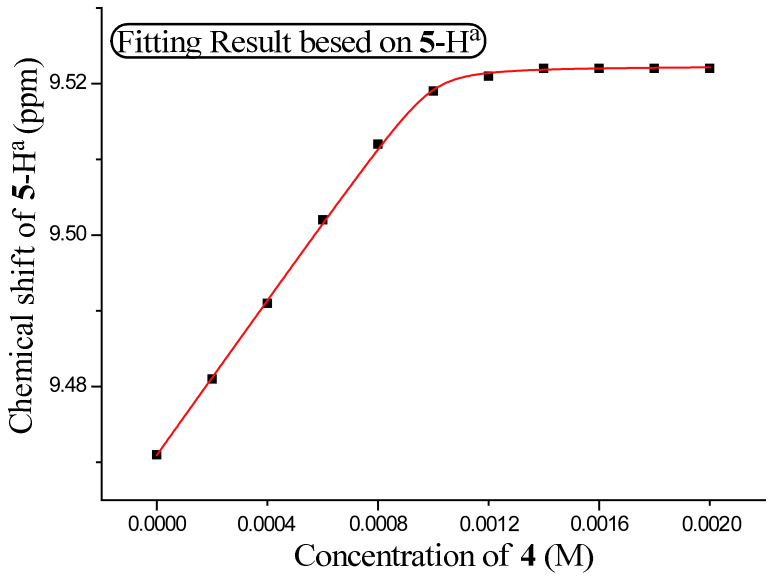


Figure S32. Stacked partial ^{1}H NMR spectra of compound **5** (1.0 mM) when titrated with **4**, from 0 equivalent to 2.0 equivalents in $CDCl_3$-5%DMSO-d_6 at 298K.



$K_a = 241897.68609 \pm 77033.2033\ M^{-1}$

$R^2 = 0.99958$

Figure S33. Determination of the binding constant of **4·5** in $CDCl_3$-5%DMSO-d_6 at 298K. Fitting result based on **5**-H^a.

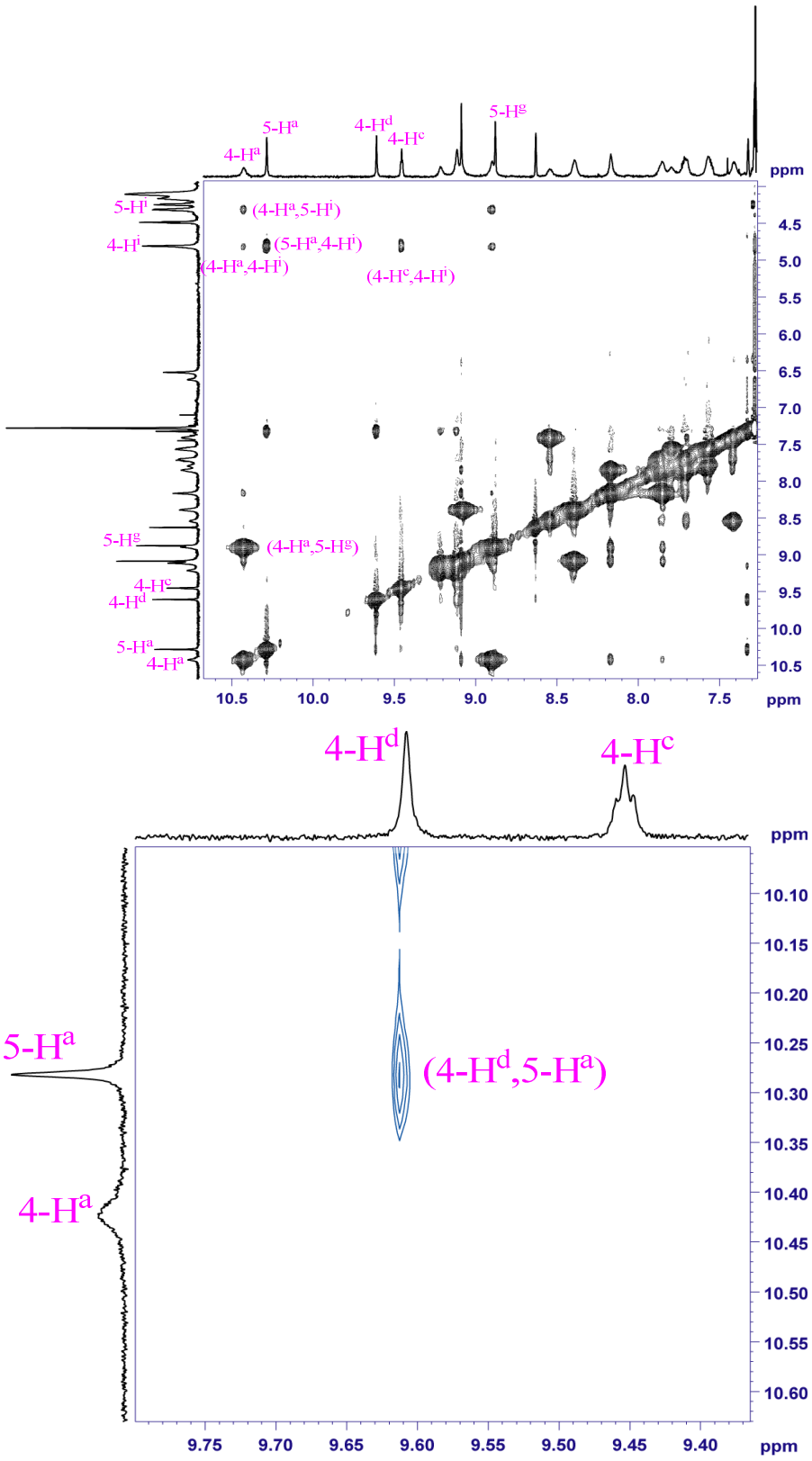


Figure S34. Partial NOESY spectra of **4·5** (5 mM) in $CDCl_3$ (600 MHz, 298K).

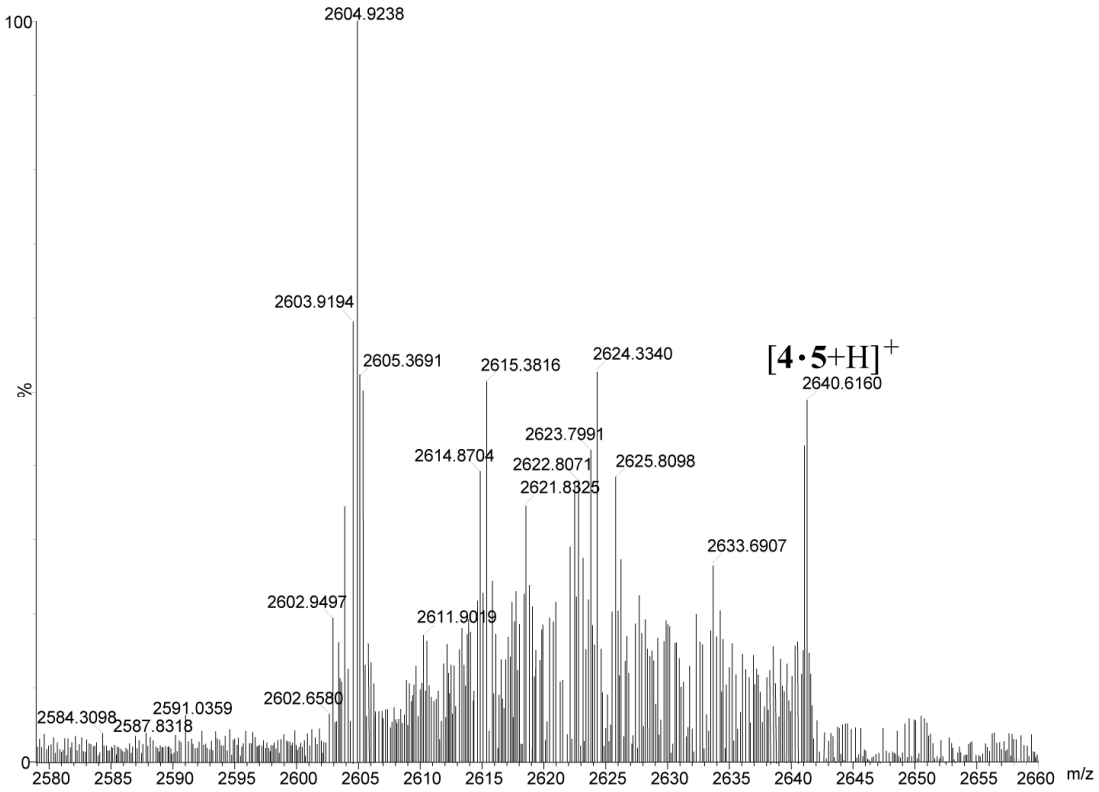


Figure S35. ESI-HRMS spectrum of **4·5** in $CHCl_3/CH_3OH$ (1:1).

12. Self-assembly of 4

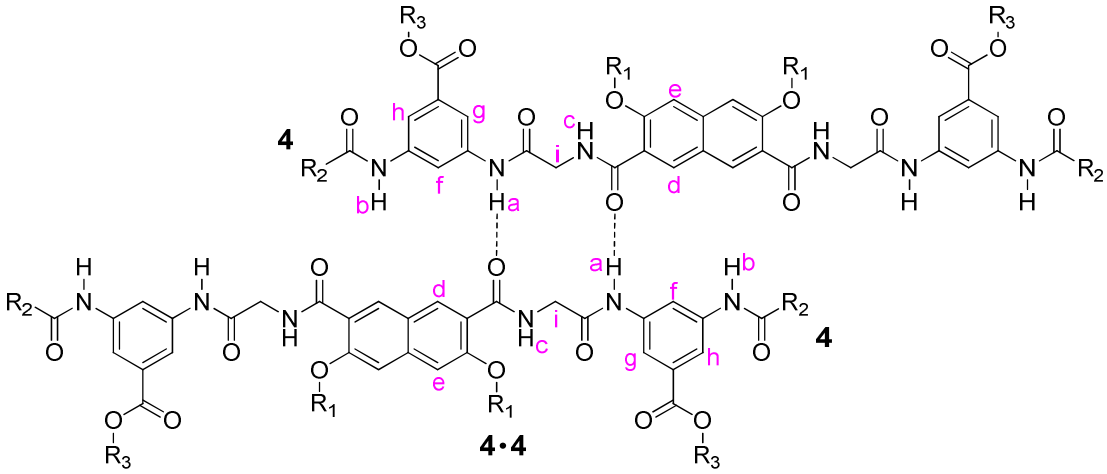


Figure S36. Representation of molecular duplex **4·4**.

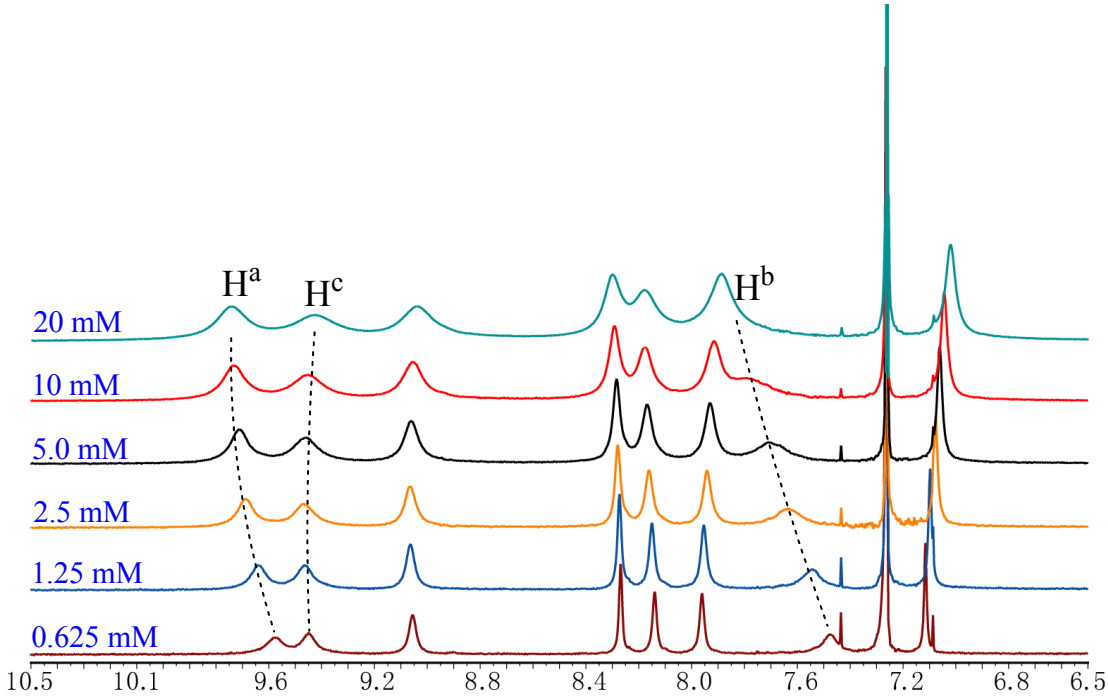
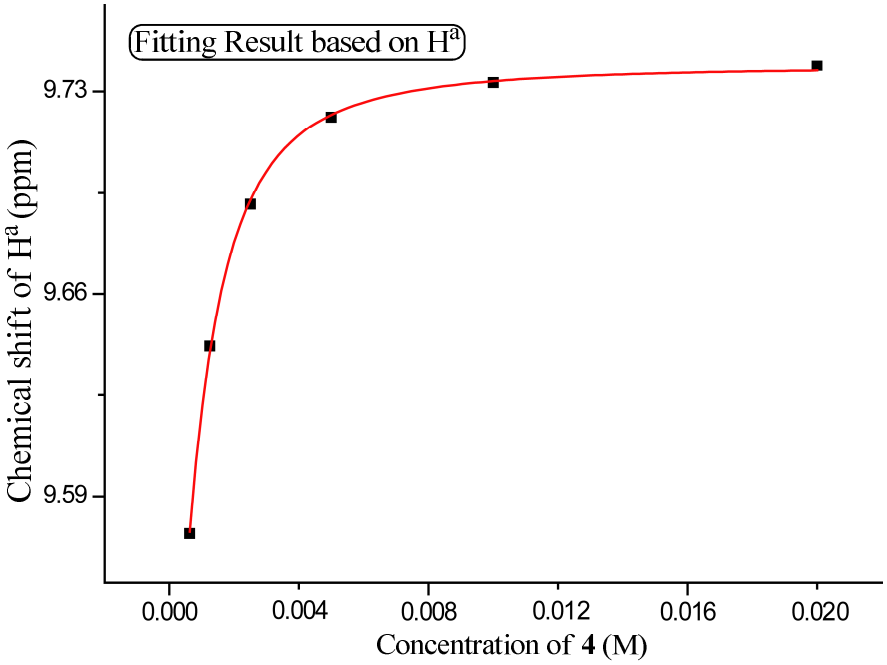


Figure S37. Stacked partial ^{1}H NMR spectra of **4** at different concentrations in $CDCl_3$ at 298 K.



K_{dimer} = 41.64557 ± 2.95682 M^{-1}

R^2 = 0.99962

Figure S38. Determination of the binding constant of **4·4** in $CDCl_3$ at 298K. Fitting result based on H^a.

13. Self-assembly of 5

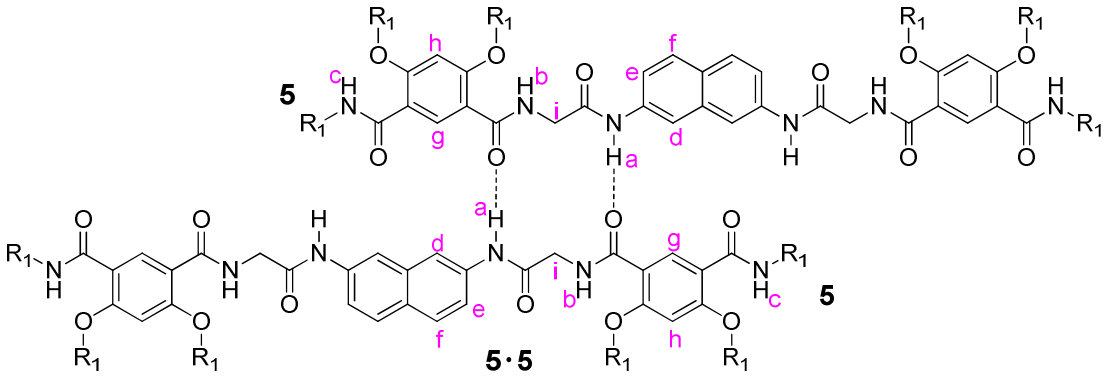


Figure S39. Representation of molecular duplex **5·5**.

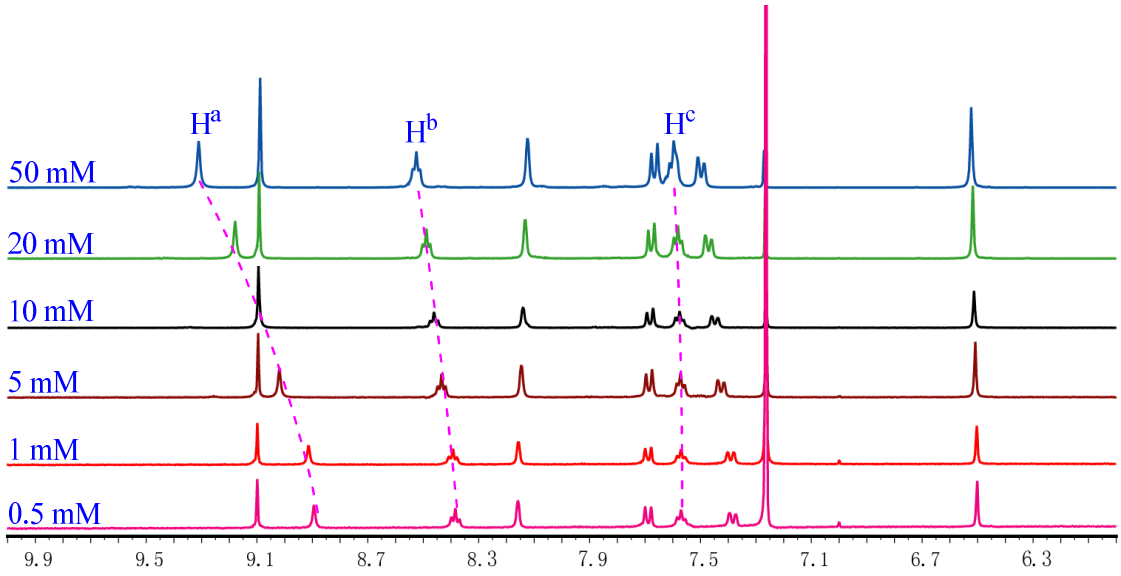
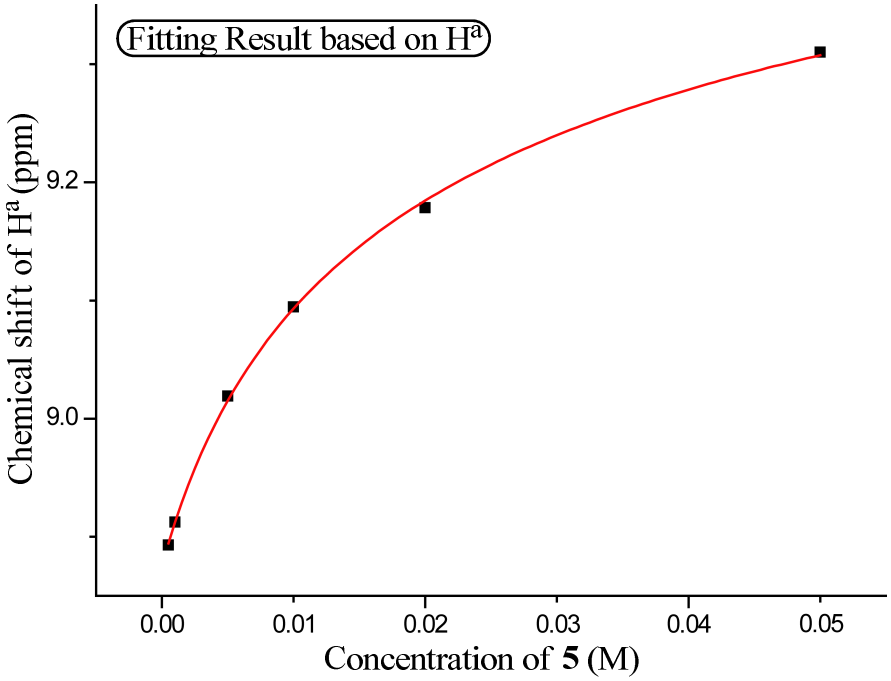


Figure S40. Stacked partial ^{1}H NMR spectra of **5** at different concentrations in $CDCl_3$ at 298 K.



K_{dimer} = 51.99114 ± 4.29852 M^{-1}

R^2 = 0.99921

Figure S41. Determination of the binding constant of **5·5** in $CDCl_3$ at 298K. Fitting result based on H^a.

14. Molecular Modeling of 1·2

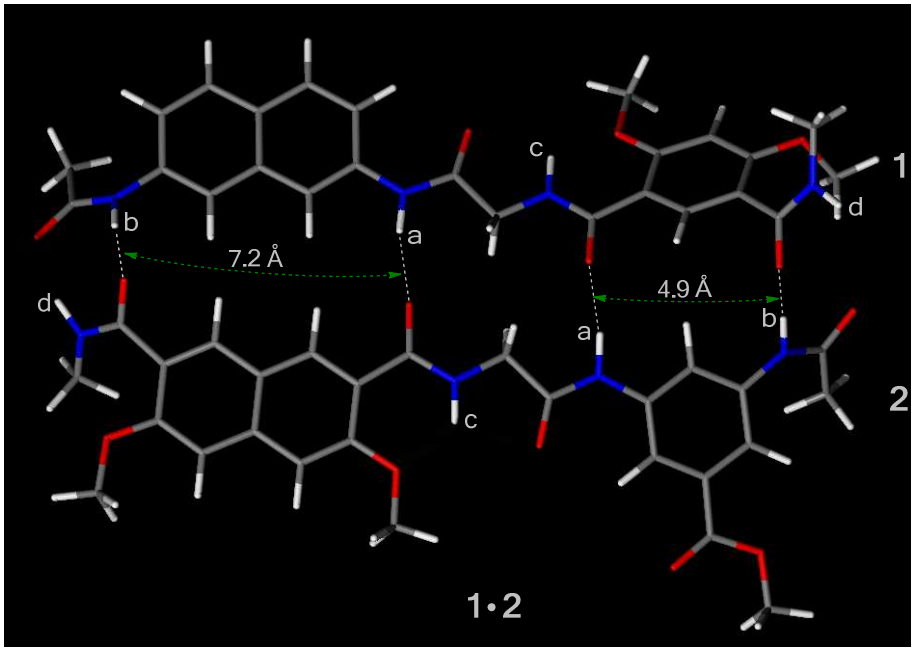


Figure 42. Optimized structure of heterodimer **1·2** obtained by DFT calculation at the

B3LYP/6-31G** level.[4] Substituents replaced with methyl groups for simplicity.

Table S1. Atomic Coordinates for the Optimized Structure of the heterodimer **1·2**.

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	2.975410	-3.361096	-0.085668
2	6	3.043473	-4.783951	-0.140124
3	6	4.266637	-5.405916	-0.222193
4	6	5.480885	-4.672987	-0.252876
5	6	5.411590	-3.244021	-0.207008
6	6	4.142114	-2.617427	-0.129951
7	6	6.756879	-5.290930	-0.311902
8	6	7.914183	-4.546405	-0.320853
9	6	7.850612	-3.126151	-0.302601
10	6	6.618566	-2.500844	-0.247493
11	7	9.020105	-2.322108	-0.262240
12	7	1.751711	-2.666890	0.043474
13	6	10.087921	-2.299641	-1.115153
14	6	10.215477	-3.380797	-2.171822
15	8	10.943955	-1.411929	-1.027399
16	6	-4.335477	-2.826136	0.350036
17	6	-4.604074	-3.977156	-0.431335
18	6	-5.913077	-4.458728	-0.533848
19	6	-6.955225	-3.851727	0.171839
20	6	-6.696873	-2.765252	1.025353
21	6	-5.395868	-2.258717	1.057927
22	8	-8.216591	-4.364147	0.020124
23	8	-3.554963	-4.552107	-1.078449
24	6	-7.731565	-2.048143	1.842437
25	6	-3.019197	-2.108091	0.453425
26	8	-7.792033	-0.811153	1.833616
27	7	-8.570016	-2.766422	2.631182
28	8	-2.985967	-0.938612	0.881207
29	7	-1.893549	-2.752189	0.098320
30	6	-8.529274	-4.180194	2.972369
31	6	-0.600072	-2.115068	0.177574
32	8	0.187946	-4.333472	-0.307411
33	6	0.485948	-3.168384	-0.053818
34	6	2.839583	3.801061	0.579758
35	6	2.727204	2.370016	0.683590
36	6	3.895803	1.642409	0.766111
37	6	5.173302	2.239118	0.722657

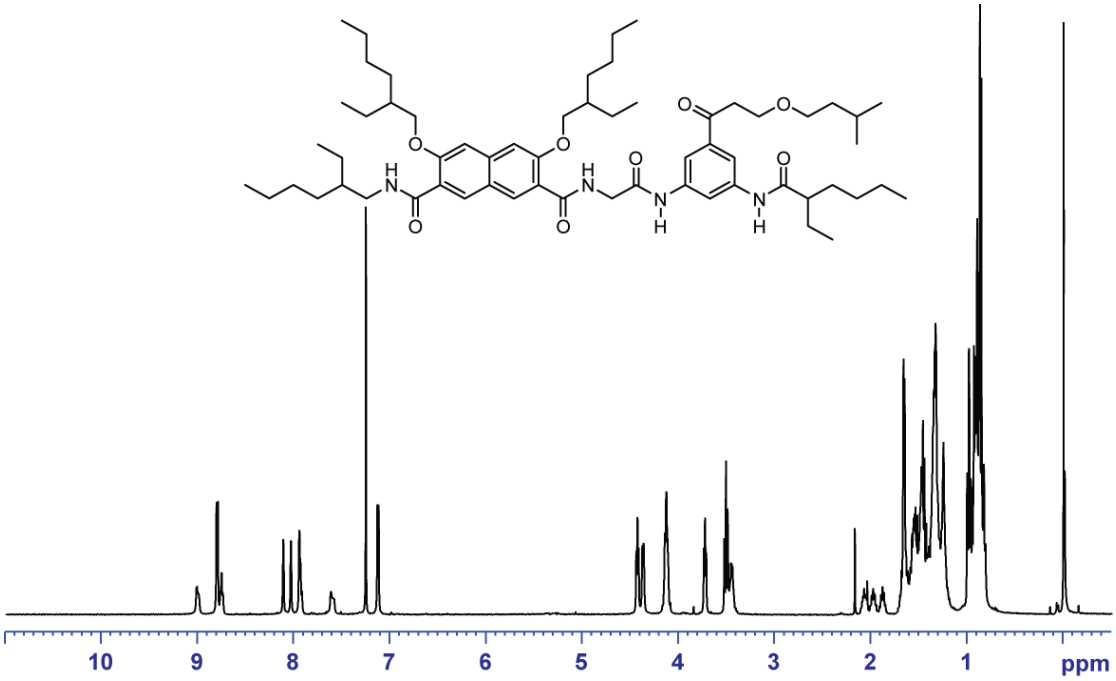
38	6	5.275985	3.657109	0.609508
39	6	4.078583	4.415974	0.549444
40	6	6.356315	1.468698	0.748766
41	6	7.608325	2.030316	0.619768
42	6	7.708413	3.458692	0.577157
43	6	6.567562	4.245262	0.566494
44	8	8.975060	3.955166	0.580471
45	8	1.668494	4.494856	0.506742
46	6	8.743916	1.041128	0.573852
47	6	1.454736	1.561877	0.687288
48	7	9.739392	1.167318	-0.330779
49	8	8.685007	0.044991	1.317991
50	6	9.815319	2.060118	-1.475728
51	6	-4.789867	3.798273	-0.254213
52	6	-4.577160	2.443320	0.028310
53	6	-5.647367	1.542426	-0.053756
54	6	-6.930570	1.968727	-0.409436
55	6	-7.151818	3.324399	-0.675374
56	6	-6.077169	4.219804	-0.606257
57	7	-7.958627	0.996936	-0.428150
58	7	-3.326572	1.893874	0.365309
59	6	-8.897430	0.717857	-1.390822
60	6	-9.004145	1.631667	-2.598878
61	1	-7.911796	0.290922	0.313451
62	8	-9.634616	-0.259545	-1.271844
63	6	-2.111361	2.510142	0.439161
64	6	-0.974868	1.515911	0.696356
65	8	-1.899484	3.711441	0.303457
66	1	-3.319964	0.884813	0.525370
67	6	-6.259977	5.674934	-0.884507
68	8	-5.379123	6.509436	-0.823262
69	8	-7.536994	5.981329	-1.222913
70	7	0.280552	2.219650	0.739727
71	8	1.498711	0.317157	0.653577
72	1	1.821322	-1.666458	0.234412
73	1	8.986214	-1.517040	0.380320
74	6	9.155180	5.364885	0.602068
75	6	1.685324	5.911178	0.360648
76	6	-7.776860	7.369213	-1.495508
77	6	-9.094060	-3.584743	-0.821631
78	6	-3.767774	-5.720117	-1.868465
79	1	2.126861	-5.354685	-0.119171
80	1	4.310538	-6.491400	-0.258798
81	1	4.089464	-1.532426	-0.107809

82	1	6.812106	-6.376321	-0.325447
83	1	8.880750	-5.037357	-0.314258
84	1	6.575508	-1.417253	-0.243548
85	1	10.838126	-2.986241	-2.975238
86	1	10.720674	-4.257263	-1.752469
87	1	9.250418	-3.705614	-2.566424
88	1	-6.161483	-5.300031	-1.167302
89	1	-5.185200	-1.387268	1.666366
90	1	-9.235966	-2.179731	3.117480
91	1	-1.910609	-3.709692	-0.235644
92	1	-8.738948	-4.295777	4.039565
93	1	-9.252408	-4.763571	2.395628
94	1	-7.534406	-4.581261	2.775802
95	1	-0.459769	-1.627507	1.147111
96	1	-0.493957	-1.323035	-0.574014
97	1	3.808875	0.566012	0.859655
98	1	4.151626	5.493818	0.468845
99	1	6.288677	0.393207	0.864391
100	1	6.642971	5.325518	0.530471
101	1	10.356421	0.350169	-0.358120
102	1	10.206253	1.492044	-2.324211
103	1	8.827260	2.440474	-1.743588
104	1	10.474411	2.913206	-1.288438
105	1	-3.981158	4.512423	-0.202670
106	1	-5.479553	0.489942	0.147396
107	1	-8.142605	3.689302	-0.907421
108	1	-9.468685	1.059506	-3.402541
109	1	-9.652376	2.484637	-2.372001
110	1	-8.037911	2.023879	-2.923670
111	1	-0.969285	0.768472	-0.102424
112	1	-1.165287	0.959098	1.621782
113	1	0.246307	3.232378	0.684609
114	1	10.232942	5.527248	0.632791
115	1	8.740937	5.837909	-0.296944
116	1	8.694209	5.811793	1.490869
117	1	0.638696	6.209072	0.302311
118	1	2.160138	6.392741	1.223172
119	1	2.205815	6.206174	-0.557522
120	1	-8.835777	7.442061	-1.743436
121	1	-7.545029	7.980373	-0.619672
122	1	-7.162317	7.710207	-2.332487
123	1	-10.074065	-4.058266	-0.750412
124	1	-9.163060	-2.539982	-0.504960
125	1	-8.747395	-3.618871	-1.861095

126	1	-2.783639	-6.002747	-2.241347
127	1	-4.180882	-6.536462	-1.265830
128	1	-4.434847	-5.510966	-2.712081

B3LYP/6-31+G** optimized Cartesian coordinates are listed. The total electronic energy (HF) was calculated to be -3505.4785968 hartree.

15. ^{1}H NMR and ^{13}C NMR Spectra of 1-5



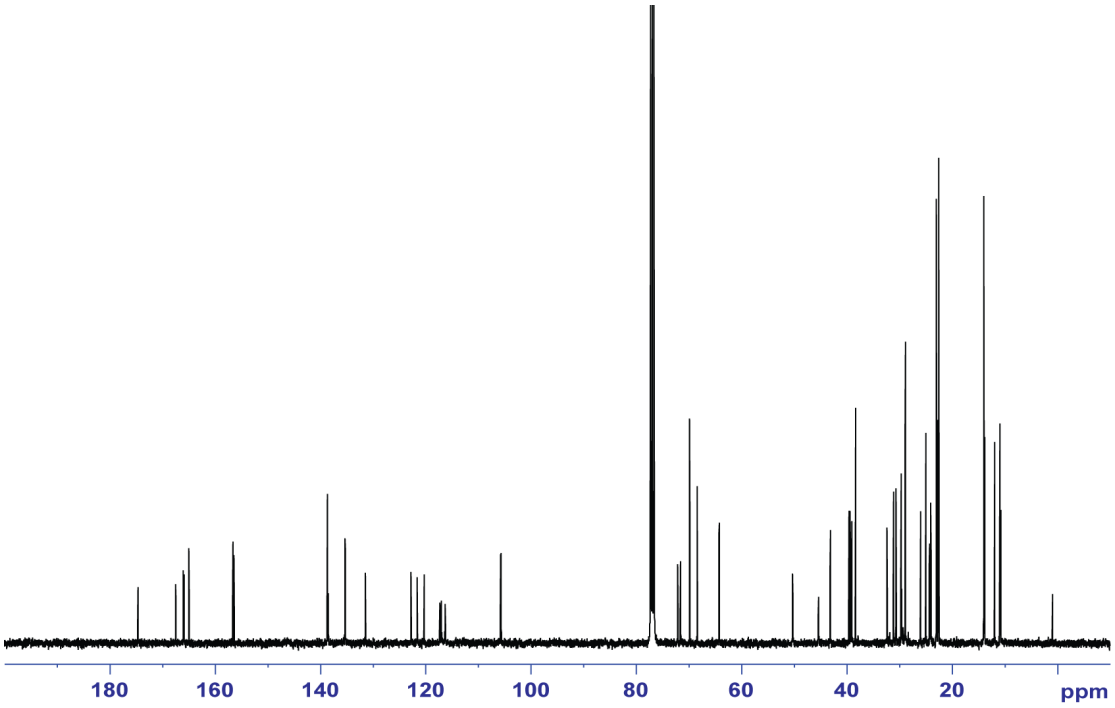
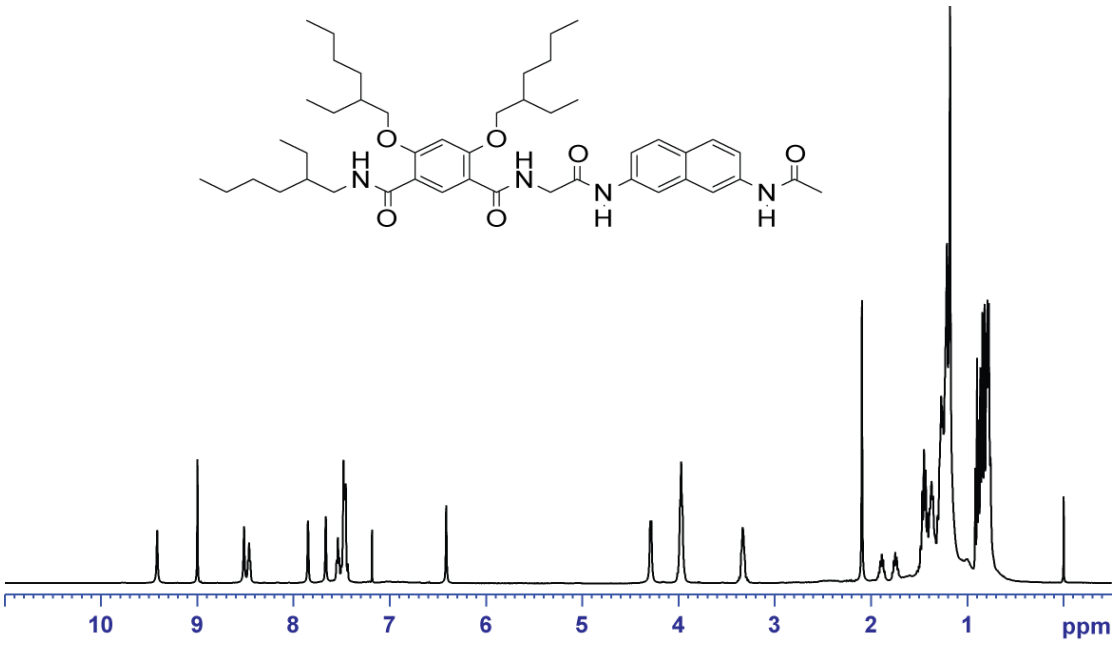


Figure S43. ^{1}H NMR and ^{13}C NMR spectra of **1**.



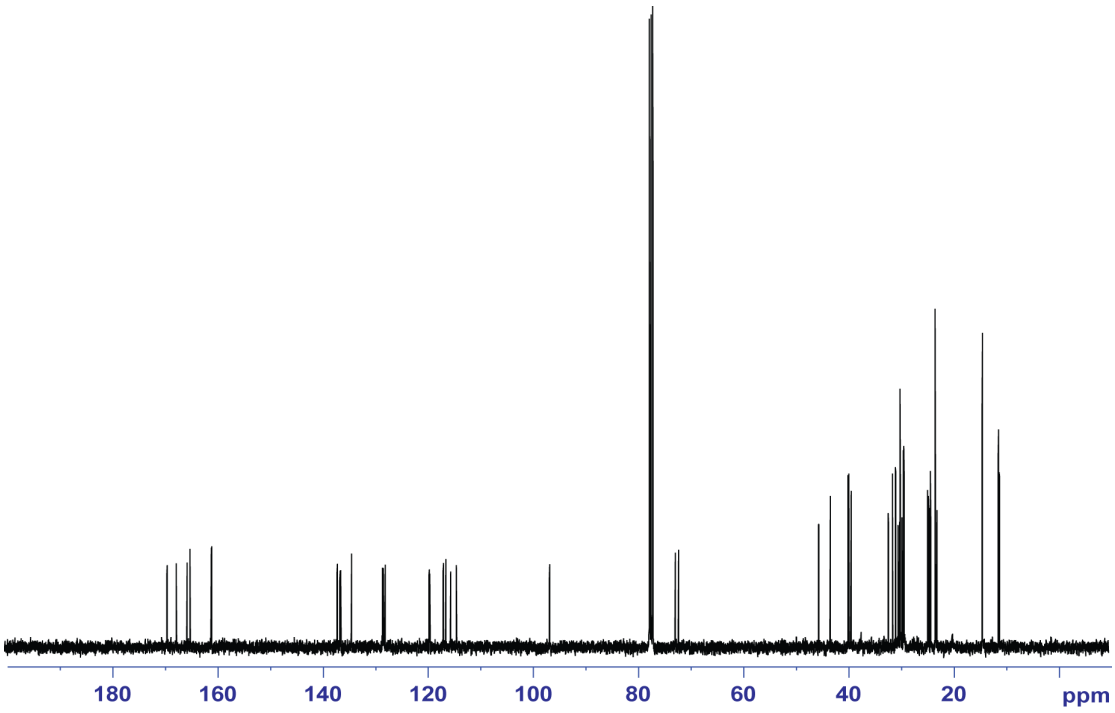
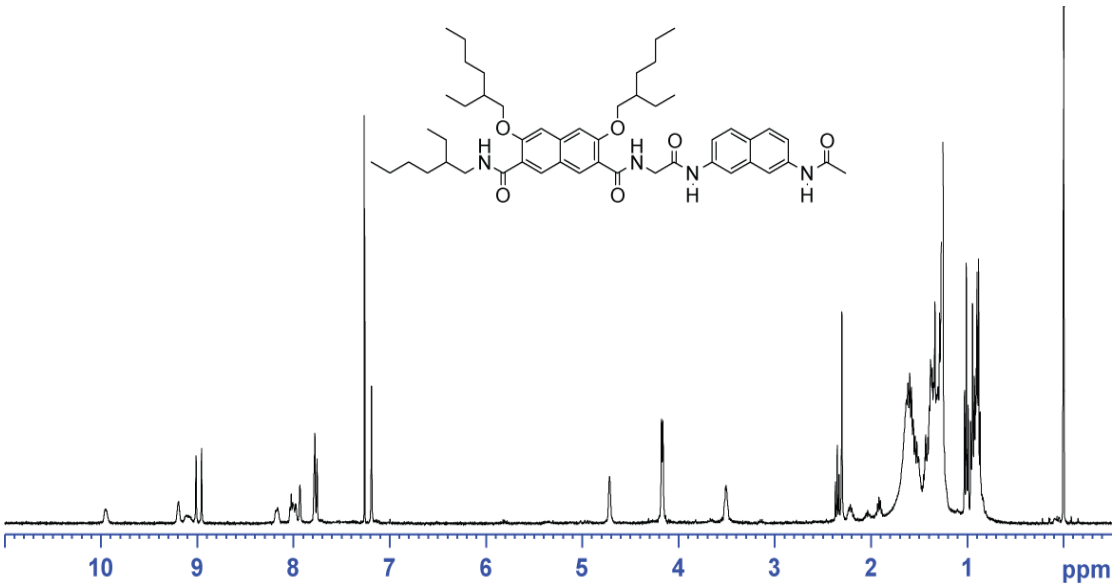


Figure S44. ^{1}H NMR and ^{13}C NMR spectra of **2**.



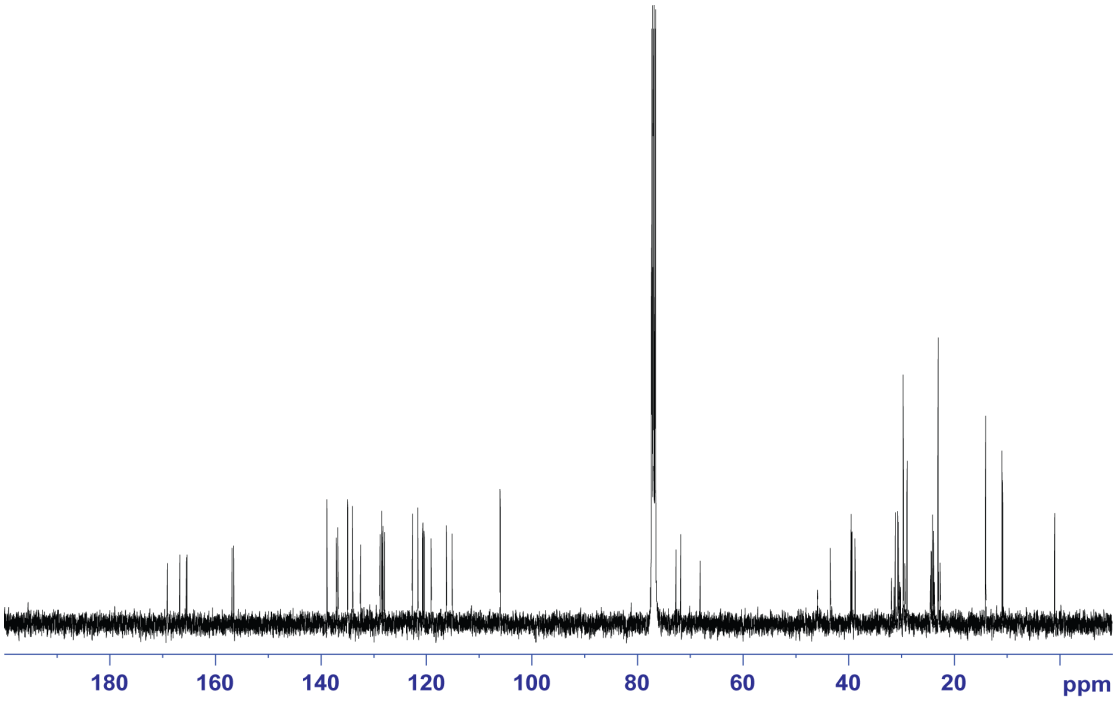
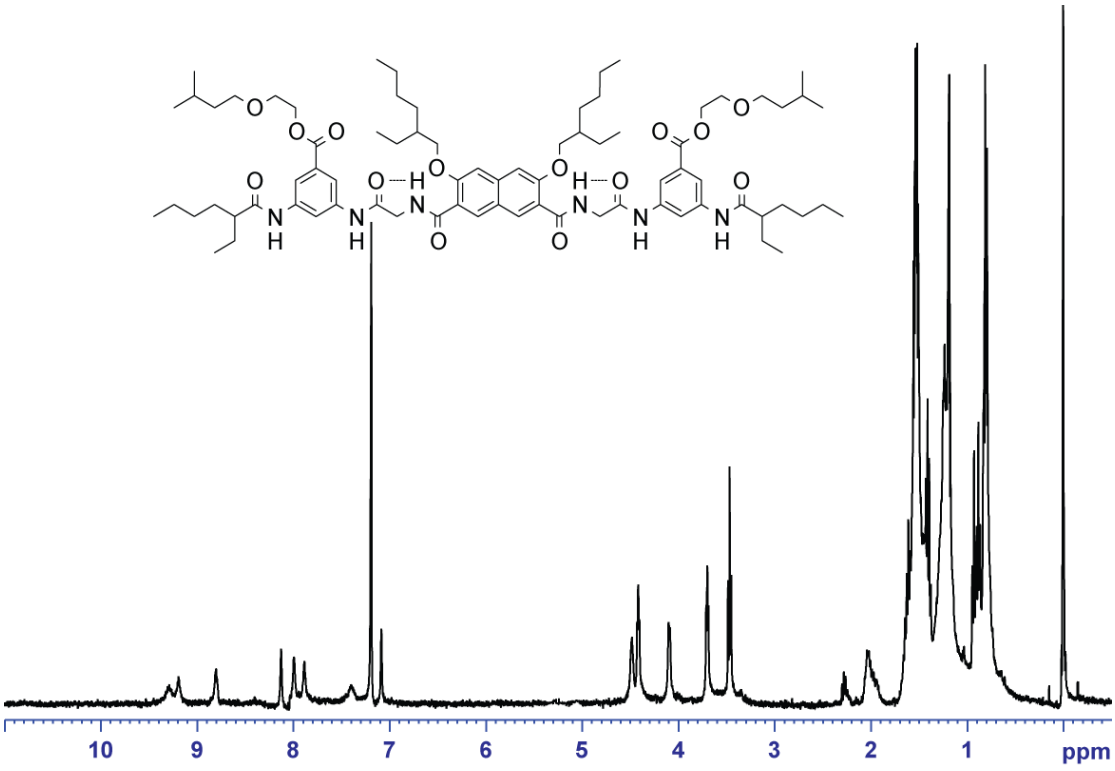


Figure S45. ^{1}H NMR and ^{13}C NMR spectra of **3**.



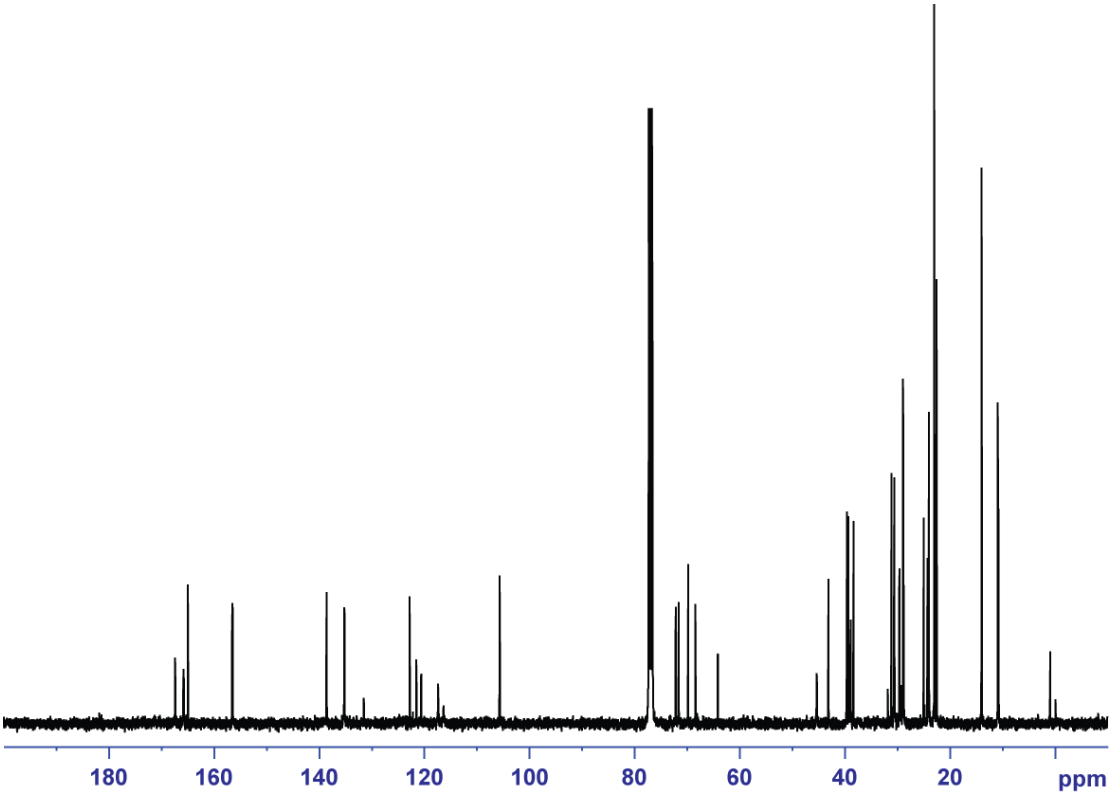
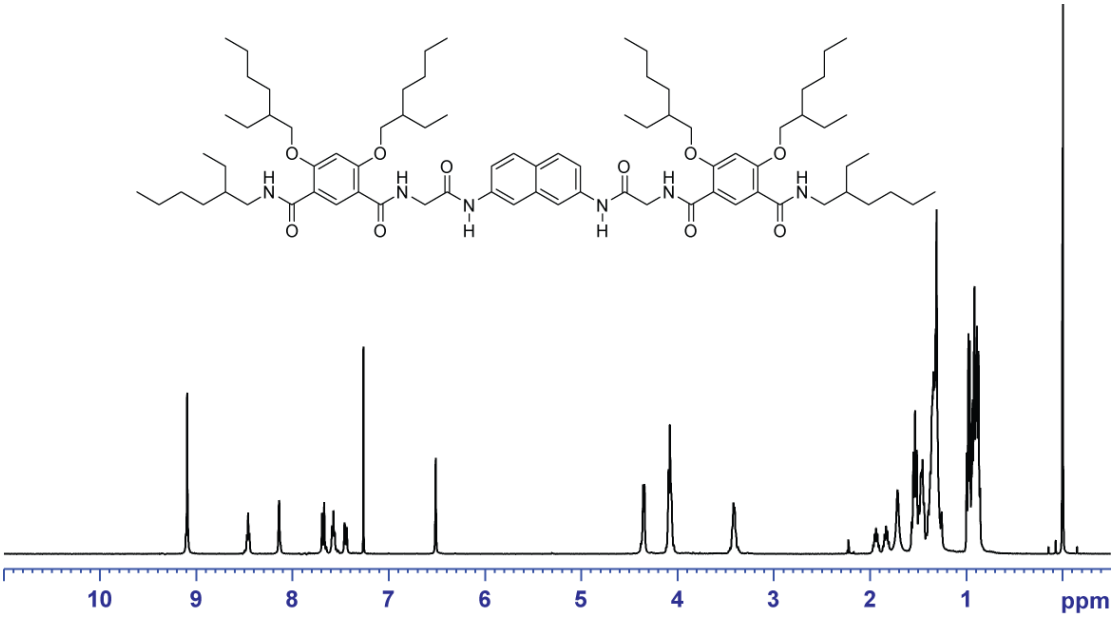


Figure S46. ^{1}H NMR and ^{13}C NMR spectra of **4**.



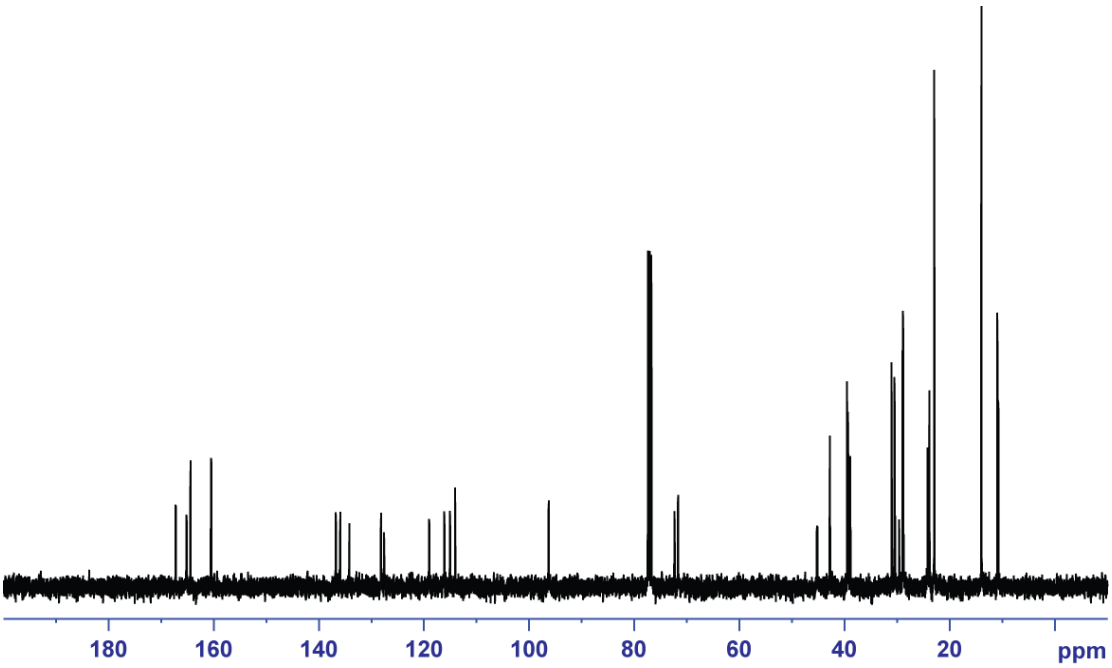


Figure S47. ^{1}H NMR and ^{13}C NMR spectra of **5**.

16. References

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