Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for

Quadruple hybridization of quinoline-triazole oligomers

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1 Experimental procedures

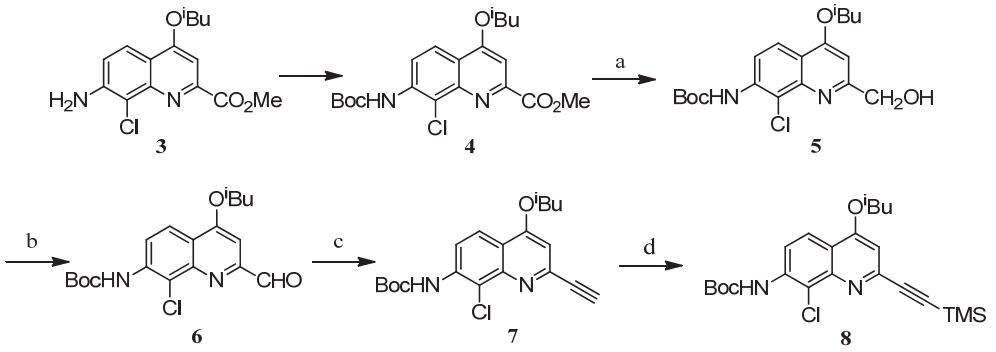
1.1 General methods

All chemicals and solvents were purchased from commercial suppliers and were used without further purification unless otherwise specified. Dichloromethane (DCM) was distilled over CaH_2 prior to use. Column chromatography was carried out on Merck GEDURAN Si60 (40-63 μm).

NMR spectra were recorded on Bruker AVANCE 400 (400 MHz) spectrometers. Chemical shifts were calibrated by $CDCl_3$ (7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR) and by DMSO-d_6 (2.50 ppm for ^{1}H NMR, 39.52 ppm for ^{13}C NMR). All chemical shifts (δ) are quoted in ppm and coupling constants (*J*) are expressed in Hertz (Hz). The following abbreviations are used for convenience in reporting the multiplicity for NMR resonances: s = singlet, d = doublet, t = triplet, and m = multiplet. Data processing was performed with Topspin 2.0 software.

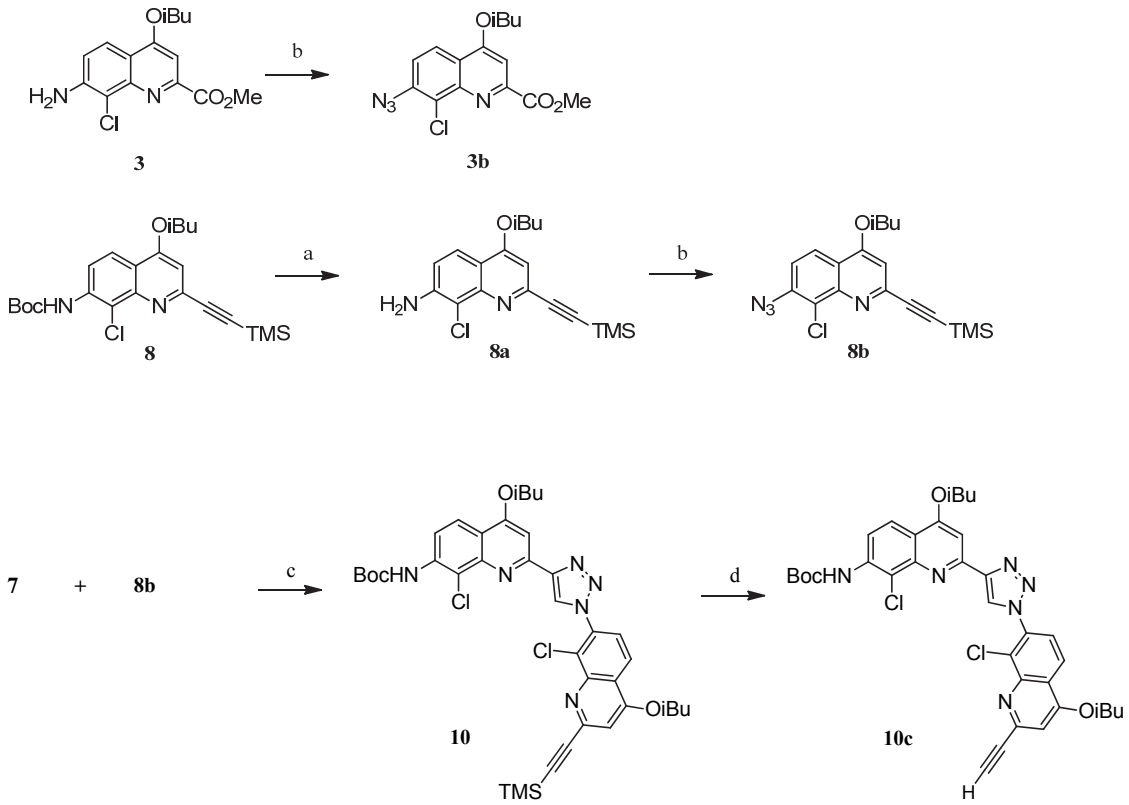
High-resolution electrospray ionization mass spectrometry (ESI-MS) was performed on a micro TOF II instrument featuring a Z spray source with electrospray ionization and modular LockSpray interface.

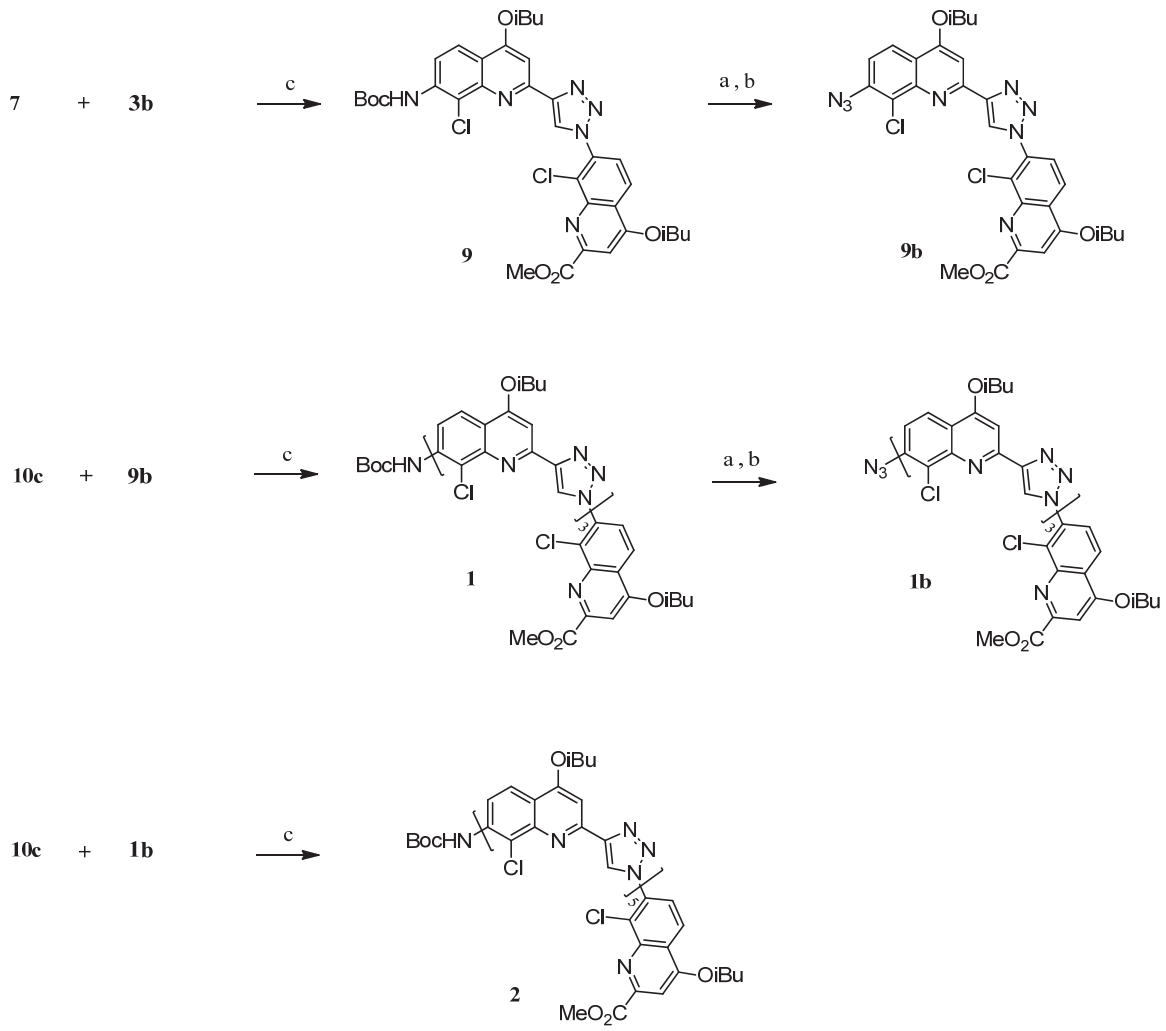
1.2 Synthesis of Monomer



Scheme S1. Synthesis of chloroquinoline monomer **8**: a) $NaBH_4$, THF, reflux; b) MnO_2, DCM, r.t. ; c) Bestmman-Ohira regent, K_2CO_3, MeOH, r.t.; d) CF_3SiMe_3, DMPU, r.t.

1.3 Synthesis of sequences **1** and **2**





Scheme S2. Synthesis of Tetramer and hexamer. a) TFA/DCM, r.t.; b) HCl, $NaNO_2$, NaN_3; c) $CuSO_4$, L-sodium ascorbate, ^{t}BuOH/PhMe; d) $KF{\cdot}2H_2O$, THF.

Compound **3** and compound **4** were prepared accordingly to reference S1.

Compound **5**. A mixture of methyl 7-(tert-butoxycarbonylamino)-4-isobutoxy-8-chloroquinoline-2-carboxylate (1.50 g, 4.0 mmol) and $NaBH_4$ (1.51 g, 40.0 mmol) in THF (20 mL) was stirred at 65°C for 20 min. After that, methanol (8 mL) was added dropwise during 30 min and effervescence was observed. Stirring at 65°C was maintained for further 2 h. The reaction was cooled to room temperature and then evaporated to generate crude solid, which was added DCM (15 mL), washed with water and brine, dried over Na_2SO_4. The solvents were evaporated to give crude product, which was purified by flash chromatography (silica gel) to give the desired products. Eluents: DCM/1% methanol. Yield: 85%. ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.46 (d, J = 8.8 Hz, 1 H), 8.09 (d, J = 9.2 Hz, 1 H), 7.44 (s, 1 H), 6.54 (s, 1 H), 4.84 (s, 2 H), 4.67 (s, 1 H), 3.95 (d, J = 6.4 Hz, 2 H), 2.30-2.24 (m, 1 H), 1.57 (s, 1 H), 1.13 (d, J = 6.4 Hz, 6 H) . ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.5, 161.6, 152.4, 144.1,

137.4, 121.1, 117.7, 117.6, 117.2, 96.9, 75.1, 64.5, 28.4, 28.3, 19.4. ESI-HRMS: m/z calcd for $C_{19}H_{25}ClN_2O_4$ $[M+H]^+$ 381.1581, found 381.1603.

Compound **6**. A solution of compound **5** (1.25 g, 3.3 mmol) in dry methylene chloride (30 mL) was stirred at room temperature with 3.0 g of manganese dioxide. After 8 h, the mixture was filtered off and the solid was washed with methylene chloride. The combined organic phase was concentrated. The pure product was obtained by recrystallization from the mixture of ethyl acetate/hexane. Yield: 95%. ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 10.19 (s, 1 H), 8.63 (d, J = 9.2 Hz , 1 H), 8.18 (d, J = 9.2 Hz, 1 H), 7.49 (s, 1 H), 7.33 (s, 1 H), 4.05 (d, J = 6.4 Hz, 2 H), 2.32-2.26 (m, 1 H), 1.58 (s , 9 H) , 1.14 (d , J = 6.4 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 194.1, 163.2, 154.8, 152.3, 145.7, 138.1, 121.3, 120.4, 119.9, 118.2, 96.4, 82.0, 75.6, 28.4, 28.3, 19.3. ESI-HRMS: m/z calcd for $C_{19}H_{23}ClN_2O_4$ $[M+H]^+$ 379.1425, found 379.1447.

Compound **7**, To a mixture of compound **6** (1.15 g, 3.0mmol) in MeOH (15 mL) was added potassium carbonate (0.83 g, 6.0 mmol) followed by a solution of (1-diazo-2-oxo-propyl)-phosphonic acid dimethyl ester (0.64 g, 3.3 mmol) in MeOH (3 mL) at room temperature and the resulting mixture stirred for 1.5 h. The mixture was then poured into sodium carbonate solution (1 M) and extracted with ethyl acetate and the combined organic extracts washed with brine, dried over Na_2SO_4, and filtered. The solvents were evaporated to give crude product, which was purified by flash chromatography (silica gel) to give the desired products. Eluents: DCM/1% methanol. Yield: 88%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.50 (d, J = 9.2 Hz, 1 H), 8.09 (d, J = 9.2 Hz, 1 H), 7.46 （s, 1 H）, 6.86 （s, 1 H）, 3.96 (d, J = 6.8 Hz, 1 H), 3.21 (s, 1 H), 2.30-2.22 (m, 1 H), 1.56 (s, 9 H), 1.12 (d, J = 6.8 Hz, 1 H), ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.0, 152.3, 145.7, 144.4, 120.8, 118.7, 117.7, 117.2, 103.9, 83.8, 81.7, 77.7, 75.2, 28.4, 28.2, 19.3. ESI-HRMS: m/z calcd for $C_{20}H_{23}ClN_2O_3$ $[M+H]^+$ 375.1475, found 375.1497.

Compound **8**. A mixture of compound **7** (0.82 g, 2.2 mmol) and trifluoromethyltrimethylsilane (0.38g, 0.36 mmol) in DMPU (5 mL) was stirred for 24 h at 40 ℃. The mixture was quenched by adding sat. NH_4Cl and extracted with Et_2O (30 mL × 3). The organic layer was sequentially washed with water (10 mL), brine (10 mL), and dried over $MgSO_4$. After concentration, the residue was purified with SiO_2 column chromatography to afford pure product. Yield: 90%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.48 (d, J = 9.2 Hz, 1 H), 8.07 (d, J = 8.8 Hz, 1 H), 7.46 (s, 1 H), 6.85 (s, 1 H), 3.97 (d, J = 6.4 Hz, 2 H), 2.30-2.20 (m, 1 H), 1.56 (s, 1 H), 1.12 (d, J = 6.8 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.9, 152.4, 145.8, 145.4, 137.7, 120.9, 118.5, 117.7, 117.2, 104.8, 104.3, 95.8, 81.7, 75.3, 28.5, 28.4, 19.5. ESI-HRMS: m/z calcd for $C_{23}H_{31}ClN_2O_3Si$ $[M+H]^+$ 447.1871, found 447.1871.

Compound **3b**. Compound **3** (0.3 g, 0.9 mmol) was dissolved in HCl (18%, 5 mL), and the solution was allowed to cool to -10 °C with ice/salt bath. The solution of $NaNO_2$ (0.09 g, 1.4 mmol) in H_2O (1 mL) was added slowly. After stirring at -10−0 °C for 30 min, a solution of sodium azide (0.09 g, 1.4 mmol) in H_2O (1 mL) was added slowly. The mixture was stirred at room temperature for another 2 h and then was extracted with DCM (30 mL × 3). The combined organic layers were washed with brine (20 mL × 2), dried over Na_2SO_4. After concentration, the residue was purified by flash SiO_2 column chromatography eluting with DCM to afford pure product. Yield: 95%. ^{1}H NMR ($CDCl_3$, 400 MHz): 8.24 (d, J = 8.8 Hz, 1 H), 7.58 (s, 1 H), 7.44 (d, J = 8.8 Hz, 1 H), 4.07-4.06 (s + d, 5 H), 2.33-2.26 (m, 1 H), 1.15 (d, J = 6.8 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.1, 163.3, 150.8, 145.1, 139.1, 123.0, 121.8, 120.6, 119.1, 101.4, 75.7, 53.6, 28.3, 19.3. ESI-HRMS: m/z calcd for $C_{15}H_{15}ClN_4O_3$ $[M+H]^+$ 335.0911, found 335.0905.

Compound **8b**. Monomer **8** (0.3 g, 0.8 mmol) was dissolved in CH_2Cl_2 (5 mL), and excess TFA (2 mL) was added. The mixture was stirred at room temperature for 3 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (20 mL), washed with saturated $NaHCO_3$, dired over Na_2SO_4 and the evaporated to give amine **8a** as a yellow solid. It was dried in vacuo, and used without further purification. Then, the synthetic procedures are the same as used for synthesis of **3b**. Yield: 91%. ^{1}H NMR($CDCl_3$, 400 MHz): 8.14 (d, J = 8.8 Hz, 1 H), 7.33 (d, J = 9.2 Hz , 1 H), 6.89 (s, 1 H), 3.98 (d, J = 6.4 Hz, 2 H), 2.30-2.22 (m, 1 H), 1.13 (d, J = 6.8 Hz, 6 H) , 0.30 (s, 9 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.9, 146.6, 146.0, 138.7, 121.8, 121.6, 119.1, 117.6, 104.9, 104.5, 96.5, 75.3, 28.3, 19.4, -0.1. ESI-HRMS: m/z calcd for $C_{18}H_{21}ClN_4OSi$ $[M+H]^+$ 373.1251, found 373.1211.

Compound **9**. Compound **7** (296 mg, 0.79 mmol) and compound **3b** (270 mg, 0.8 mmol) were dissolved in a mixture of toluene (5 mL) and tert-butanol (5 mL) and then were degassed with argon. After 30 min, to the solution were added in sequence $CuSO_4$ (12.8 mg, 0.08 mmol) dissolved in water (2 mL) and sodium ascorbate (31.78 mg, 0.16 mmol) dissolved in water (2 mL). The mixture was stirred overnight with protection from light. The solvents were removed under reduced pressure, and the residue was redissolved in DCM, washed with saturated NH_4Cl (20 mL) and brine (20 mL), respectively, and then dried over Na_2SO_4. Solvents were removed under reduced pressure, and the crude product was purified by flash chromatography (SiO_2, gradient DCM/PE to DCM/ethyl acetate = gradient 1/10 to 10/1) to yield **9** (476 mg, 85%) as a pale solid. ^{1}H NMR ($CDCl_3$, 400 MHz) : 9.00 (s, 1 H), 8.47 (d, J = 9.2 Hz, 1 H), 8.41 (d, J = 8.8 Hz, 1 H), 8.15 (d, J = 9.2 Hz,1 H), 7.92 (d, J = 8.8 Hz,1 H), 7.78 (s, 1 H), 7.72 (s, 1 H), 7.46 (s, 1 H), 4.14-4.10 (s + d, 7 H), 2.38-2.30 (m, 2 H), 1.56 (s, 9 H), 1.19-1.15 (d + d, 12 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.9, 163.4, 162.8, 152.4, 152.1, 151.2, 149.1, 145.7, 145.5, 137.4, 136.5, 129.1, 125.8, 125.4, 123.7, 121.9, 121.1, 118.0, 117.8, 117.3, 102.8,

97.9, 81.6, 76.0, 75.4, 53.6, 28.4, 28.3, 19.4, 19.4. ESI-HRMS: m/z calcd for $C_{35}H_{38}Cl_2N_6O_6$ $[M+H]^+$ 709.2308, found 709.2355.

Compound **9b**. Compound **9** (476 mg, 0.67 mmol) was dissolved in CH_2Cl_2 (5 mL), and excess TFA (2 mL) was added. The mixture was stirred at room temperature for 3 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (10 mL), washed with saturated $NaHCO_3$, dried over Na_2SO_4 and the evaporated to give amine **9a** as a yellow solid. It was dried in vacuo, and used without further purification. Then, the synthetic procedures are the same as used for synthesis of **3b**. Yield: 85%. ^1H NMR ($CDCl_3$, 400 MHz) : 9.00 (s, 1 H), 8.41 (d, J = 8.8 Hz, 1 H), 8.22 (d, J = 9.2 Hz, 1 H), 7.90 (d, J = 8.8 Hz, 1 H), 7.83 (s, 1 H), 7.72 (s, 1 H), 7.34 (d, J = 8.8 Hz, 1 H), 4.16-4.12 (d + d, 4 H), 4.10 (s, 3 H), 2.24-2.30 (m, 2 H), 1.18 (d, J = 2.8 Hz, 6 H), 1.17 (d, J = 2.8 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.7, 163.1, 162.6, 152.6, 151.0, 148.6, 146.3, 145.2, 138.3, 136.2, 129.2, 126.1, 125.2, 123.5, 121.6, 121.6, 119.1, 116.6, 102.6, 98.4, 75.8, 75.4, 53.5, 28.2, 28.2, 19.3, 19.3. ESI-HRMS: m/z calcd for $C_{30}H_{28}Cl_2N_8O_6$ $[M+H]^+$ 634.1689, found 634.1702.

Compound **10**. Compound **10** was obtained by a procedure similar to that for Compound **9**, starting with compound **7** (296 mg, 0.79 mmol) and compound **8b** (298 mg, 0.8 mmol). Yield compound **10** (473 mg, 80%) ^1H NMR ($CDCl_3$, 400 MHz): 8.96 (s, 1 H), 8.47 (d, J = 9.2 Hz, 1 H), 8.31 (d, J = 8.8 Hz, 1 H), 8.15 (d, J = 9.2 Hz, 1 H), 7.77-7.76 (s + d, 2 H), 7.46 (s, 1 H), 7.03 (s, 1 H), 4.14 (d, J = 6.4 Hz, 2 H), 4.05 (d, J = 6.4 Hz, 2 H), 2.34-2.32 (m, 2 H), 1.56 (s, 1 H), 1.17 (d, J = 6.8 Hz, 12 H), 0.32 (s, 9 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.8, 161.9, 152.4, 152.2, 149.0, 146.4, 146.0, 145.7, 137.4, 136.3, 128.0, 125.8, 124.1, 122.3, 121.7, 121.1, 118.0, 117.7, 117.3, 106.3, 104.2, 98.0, 97.4, 81.6, 75.6, 75.4, 28.4, 28.4, 28.3, 19.4, 19.4, 0.1. ESI-HRMS: m/z calcd for $C_{30}H_{28}Cl_2N_8O_6$ $[M+H]^+$ 747.7932, found 747.7950.

Compound **10c**. To Compound **10** (473 mg, 0.63 mmol) which was dissolved in THF (5 mL) and methanol (5 mL) was added $KF{\cdot}2H_2O$ (118 mg, 1.26 mmol). It was monitored by TLC, and after stirring at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure. To the residue was added water (10 mL), and the product was extracted with DCM (10 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, DCM/EA: gradient 20/1 to 2/1) to provide **10c** (383 mg, 90%) as a slightly brown solid. ^1H NMR ($CDCl_3$, 400 MHz): 8.98 (s, 1 H), 8.46 (d, J = 9.2 Hz, 1 H), 8.32 (d, J = 8.8 Hz, 1 H), 8.14 (d, J = 9.2 Hz, 1 H), 7.80-7.77 (s + d, 2 H), 7.46 (s, 1 H), 7.05 (s, 1 H), 4.14 (d, J = 6.4 Hz, 2 H), 4.04 (d, J = 6.4 Hz, 2 H), 3.32 (s, 1 H), 2.34-2.31 (m, 2 H), 1.57 (s, 9 H), 1.17 (d, J = 6.8 Hz, 12 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.8, 161.9, 152.4, 152.2, 149.0, 146.4, 146.0, 145.7, 137.4, 136.3, 128.0, 125.8, 124.1, 122.3, 121.7, 121.1, 118.0, 117.7, 117.3, 106.3, 104.2,

98.0, 97.4, 81.6, 75.6, 75.4, 28.4, 28.4, 28.3, 19.4, 19.4. ESI-HRMS: m/z calcd for $C_{35}H_{36}Cl_2N_6O_4$ $[M+H]^+$ 675.2253, found 675.2203.

Sequence **1**. Compound **9b** (220 mg, 0.35 mmol) and compound **10c** (256 mg, 0.38 mmol) were dissolved in a mixture of toluene (10 mL) and tert-butanol (10 mL) and then were degassed with argon. After 30 min, to the solution were added in sequence $CuSO_4$ (16.00 mg, 0.10 mmol) dissolved in water (1 mL) and sodium ascorbate (39.73 mg, 0.20 mmol) dissolved in water (1 mL). The mixture was stirred for 1 day with protection from light. The solvents were removed under reduced pressure, and the residue was redissolved in DCM, washed with saturated NH_4Cl (20 mL) and brine (20 mL), respectively, and then dried over Na_2SO_4. Solvents were removed under reduced pressure, and the crude product was purified by flash chromatography (SiO_2, gradient DCM/PE to DCM/ethyl acetate = gradient 1/10 to 10/1) to yield **9** (330 mg, 55%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) : 9.66 (s, 1 H), 9.56 (s, 2 H), 7.92 (br, 1 H), 7.88 (s, 1 H), 7.84 (s, 1 H), 7.77 (br, 1 H), 7.68 (br, 1 H), 7.59 (s + br, 2 H), 7.49 (s, 1 H), 7.38 (br, 1 H), 7.17 (s, 1 H), 7.06 (br, 1 H), 6.93 (br, 2 H), 4.22 (br, 4 H), 4.09 (s + br, 5 H), 3.94 (br, 2 H), 2.41-2.34 (m, 3 H), 2.17-2.14 (m, 1 H), 1.52 (s, 1 H), 1.25 (d, J = 6.0 Hz, 12 H), 1.20 (d, J = 6.4 Hz, 6 H), 1.07 (d, J = 6.0 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.8, 162.9, 162.8, 162.8, 162.1, 153.1, 152.9, 152.2, 152.0, 150.7, 147.9, 147.4, 144.8, 144.5, 136.9, 135.8, 135.5, 135.4, 128.4, 128.1, 128.0, 127.8, 127.7, 124.2, 123.1, 122.4, 122.0, 121.7, 120.7, 120.6, 120.5, 120.0, 117.2, 117.0, 102.4, 99.8, 99.7, 997.8, 81.4, 76.0, 75.8, 75.2, 53.4, 28.4, 28.2, 19.5, 19.5, 19.4. ESI-HRMS: m/z calcd for $C_{65}H_{64}Cl_4N_{14}O_8Na$ $[M+Na]^+$ 1333.3667, found 1333.3536; m/z calcd for quadruple helix $C_{65}H_{64}Cl_4N_{14}O_8Na_3$ $[4M+3Na]^{3+}$ 1770.8268, found 1770.8147; $C_{260}H_{256}Cl_{16}N_{56}O_{32}Na_2$ $[4M+2Na]^{2+}$ 2644.7457, found 2644.7356.

Compound **1b**. Sequence **1** (330 mg) was dissolved in CH_2Cl_2 (10 mL), and excess TFA (5 mL) was added. The mixture was stirred at room temperature for 3 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (20 mL), washed with saturated $NaHCO_3$, dried over Na_2SO_4 and the evaporated to give amine **9a** as a yellow solid. It was dried in vacuo, and used without further purification. Then, the synthetic procedures are the same as used for synthesis of **3b**. Yield: 55%. ^{1}H NMR ($CDCl_3$, 400 MHz) : 9.63-9.59 (br, 3 H), 7.87 (s, 1 H), 7.85 (s, 1 H), 7.76 (br, 4 H), 7.63 (s, 1 H), 7.55 (s, 1 H), 7.35 (br, 1 H), 7.17 (br, 1 H), 6.94 (br, 2 H), 6.63 (br, 1 H), 4.14-4.10 (m, 11 H), 2.43-2.31 (m, 4 H), 1.25-1.24 (d + d, 12 H), 1.21 (d, J = 6.8 Hz, 6 H), 1.09 (d, J = 6.4 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.0, 162.8, 162.8, 162.0, 152.9, 152.9, 152.5, 150.5, 147.6, 147.3, 147.2, 145.5, 144.6, 144.4, 137.8, 135.6, 130.4, 128.4, 128.2, 127.8, 124.6, 123.0, 122.3, 121.8, 121.6, 120.6, 120.5, 120.3, 118.1, 115.8, 102.3, 99.7, 98.3, 76.0, 75.9, 75.3, 60.5, 53.5, 28.3, 28.2, 19.5, 19.4, 19.3. ESI-HRMS: m/z calcd for $C_{60}H_{44}Cl_4N_{16}O_6$ $[M+H]^+$ 1237.3215, found 1237.3218.

Sequence **2**. Compound **1b** (185 mg, 0.15 mmol) and compound **10c** (108 mg, 0.16 mmol) were dissolved in a mixture of toluene (5 mL) and tert-butanol (5 mL) and then were degassed with argon. After 30 min, to the solution were added in sequence $CuSO_4$ (8.0 mg, 0.05 mmol) dissolved in water (1 mL) and sodium ascorbate (9.9 mg, 0.10 mmol) dissolved in water (1 mL). The mixture was stirred for 2 day with protection from light. The solvents were removed under reduced pressure, and the residue was redissolved in DCM, washed with saturated NH_4Cl (15 mL) and brine (15 mL), respectively, and then dried over Na_2SO_4. Solvents were removed under reduced pressure, and the crude product was purified by flash chromatography (SiO_2, gradient DCM/PE to DCM/ethyl acetate = gradient 1/10 to 10/1) to yield sequence **2** (143 mg, 50%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 9.67 (s, 1 H), 9.63 (s, 2 H), 9.60 (s, 2 H), 7.90 (d, J = 9.6 Hz, 1 H), 7.87 (s, 1 H), 7.81 (s, 1 H), 7.77 (s, 1 H), 7.77 (s, 2 H), 7.70 (d, J = 8.8 Hz, 1 H), 7.65-7.59 (m, 3 H), 7.56 (d, J = 8.8 Hz, 1 H), 7.46 (s, 1 H), 7.31 (d, J = 9.2 Hz, 1 H), 7.13 (s, 1 H), 6.99 (d, J = 8.4 Hz, 1 H), 6.85-6.76 (m, 5 H), 4.28-4.24 (m, 4 H), 4.13-4.00 (m, 11 H), 2.40-2.35 (m, 6 H), 1.52 (s, 9 H), 1.25-1.14 (m, 36 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.3, 165.7, 162.8, 153.1, 152.9, 152.8, 152.8, 152.2, 151.7, 150.6, 147.7, 147.1, 147.1, 144.6, 144.6, 144.4, 138.3, 138.2, 135.7, 135.6, 135.5, 135.4, 130.4, 129.7, 128.5, 128.3, 127.8, 127.6, 126.5, 124.2, 123.0, 122.4, 122.2, 121.9, 121.7, 121.5,120.5, 120.4, 118.6, 117.4, 117.0, 116.3, 102.3, 99.8, 99.7, 99.6, 97.8, 81.2 ,76.0, 75.8, 75.1, 67.2, 60.5, 53.4, 29.8, 29.4, 28.4, 28.3, 28.3, 27.8, 21.2, 19.5, 19.5, 19.4, 19.2, 14.3, 1.1. ESI-HRMS: m/z calcd for $C_{95}H_{90}Cl_6N_{22}O_{10}Na$ $[M+Na]^+$ 1935.5219, found 1935.5430; m/z calcd for quadruple helix $C_{380}H_{360}Cl_{24}N_{88}O_{40}Na_3$ $[4M+3Na]^{3+}$ 2573.0336, found 2573.0343.

2 X-Ray Crystallography

Crystal of compound **1** suitable for X-ray crystallographic analysis was obtained upon recrystallizing the corresponding compounds from DMSO solution.

Crystallographic data of **1** were collected at the Analysis and Testing Center in Huazhong University of Science and Technology (HUST) on a Rigaku MM007 HF rotating anode (0.8 kW). Data were diffracted at the CuKα wavelength, and data-collection strategies were based on Omega scans at 100(2) K. The Rigaku CrystalClear suite version 2.0 was used to index, integrate and scale the data with a multi-scan absorption correction.

The structures were solved by direct methods using SHELXT[S2] and refined against F^2 on all data by full-matrix least squares with SHELXL[S3] following established refinement strategies.[S4] The non-H atoms were refined with anisotropic temperature parameters. All hydrogen atoms, were included into the model at geometrically calculated positions and refined using a riding model. The contribution of the electron density associated with disordered solvent molecules, which could not be modelled with discrete atomic positions were handled using the SQUEEZE[S5] routine in PLATON.[S6,S7] Crystallographic data along with specific details pertaining to the refinement (inclusively addressing CheckCIF alerts) follow. Crystallographic data have been deposited with the CCDC, under deposition numbers CCDC 1937406, compound **1**.

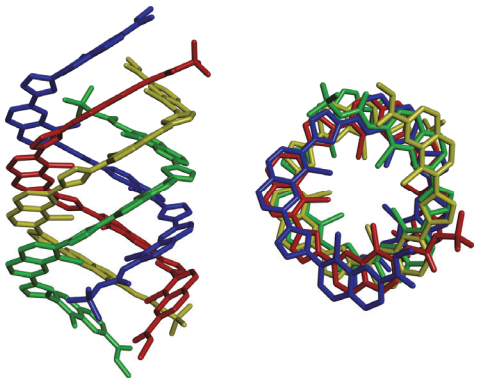


Figure S1. Side and top views of the crystal structure of the **1**. Solvent molecules and isobutoxy residues are omitted for clarity.

Table S1: Crystal data and structure refinement for the compound **1**.

Formula	$C_{67}H_{70}Cl_4N_{14}O_9S$
M	1389.23
Crystal system	triclinic
Space group	P-1
a/Å	20.81810(10)
b/Å	27.55940(10)
c/Å	30.1696(2)
α/°	86.2480(10)
β/°	72.9990(10)
γ/°	81.0640(10)
V/Å^3	16348.33(18)
T /K	100.00(10)
Z	8
ρ/g cm^{-1}	1.129
size (mm)	0.2×0.2×0.2
λ/ Å	1.54184
μ/mm^{-1}	2.014
Independent reflections	35365
measured reflections	118712
parameters/restraints	3477/0
*R*1, *wR*2	0.0689, 0.2186
goodness of fit	1.108

3 Solution studies of aggregation

3.1 Solution studies of sequence **1**

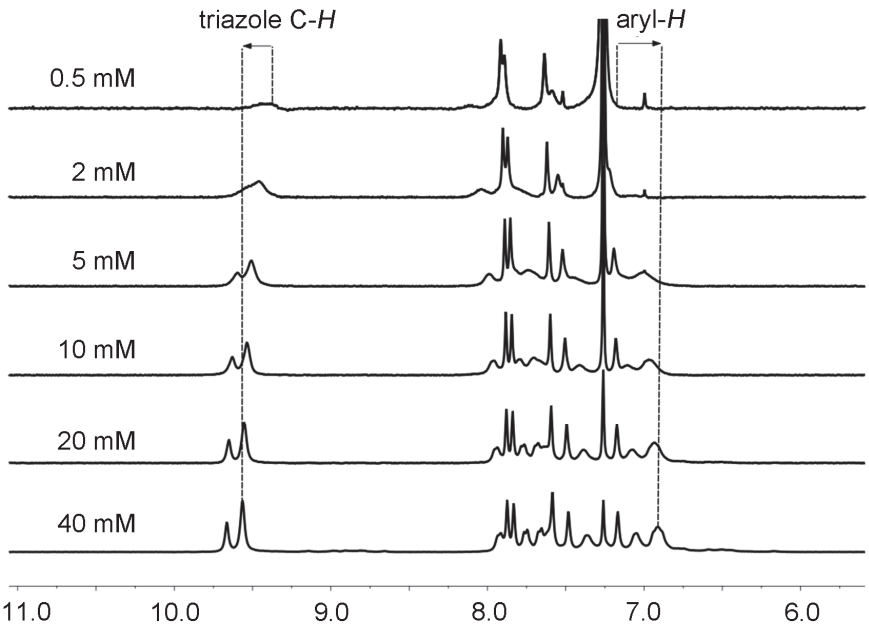


Figure S2. Part of 400 MHz ^{1}H NMR of **1** in various concentration in $CDCl_3$ at 296 K.

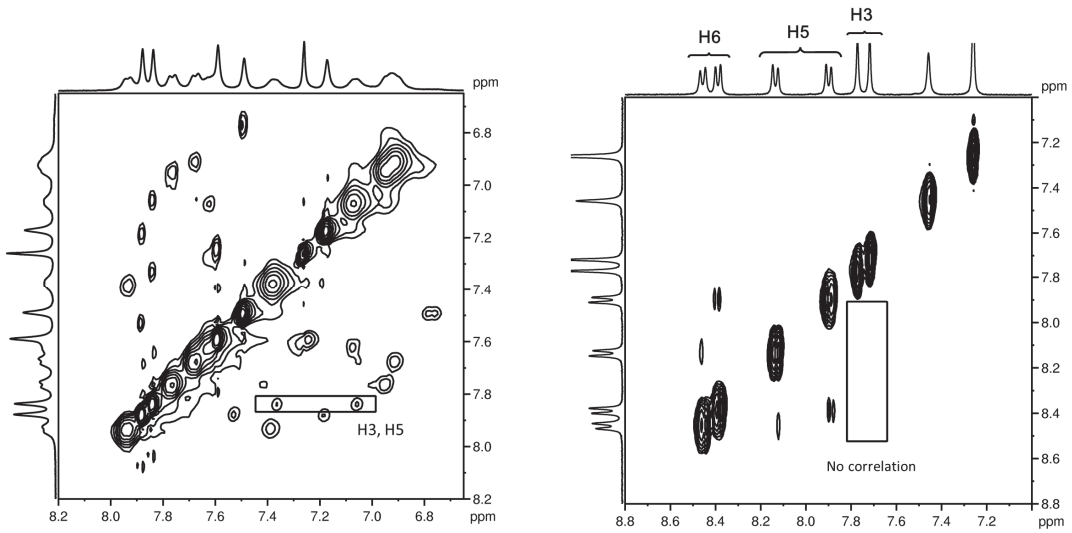


Figure S3. Partial NOESY spectra of **1** (20 mM, left) and **9** (2 mM, right) ($CDCl_3$, 400 MHz). Correlations between H3 and H5 quinoline protons are observed with **1** and not with **9** suggesting that they correspond to intermolecular contacts associated with aggregation of **1**, and not to intramolecular correlations.

Determination of the dimerization constant K_d between single and double helix through NMR chemical shift.

Scheme S3. Schematic diagram of mutual transformation between the single coil and double helix.

For the equilibrium shown in Eq. 1, the dimerization constant is given by Eq. 2.

$$2\,M \rightleftharpoons D \qquad (1)$$

$$K_d = \frac{C_D}{C_M^{\,2}} \qquad (2)$$

Where: C_M = single coil concentration; C_D = double helix concentration
From mass balance,

$$n_M + 2n_D = n_{M0} \qquad (3)$$

Where: n_{M0} = initial number of moles of the monomer.

The observed chemical shifts δ_{obs} at equilibrium in the fast exchange on the time scale is expressed as:

$$\delta_{obs} = \frac{\delta_M \cdot C_M + \delta_D \cdot C_D}{C_{M0}} \qquad (4)$$

Since:

$$C_M + 2C_D = C_{M0} \qquad (5)$$

The observed chemical shifts become:

$$\delta_{obs} = \delta_D + \frac{(\delta_M - \delta_D)\cdot C_M}{C_{M0}} \qquad (6)$$

solving equation (2) and (5),

$$C_M = \frac{-1+\sqrt{1+8K_dC_{M0}}}{4K_d} \qquad (7)$$

Substituting equations (7) into (6),

$$\delta_{obs} = \delta_D + (\delta_M - \delta_D)\cdot\frac{-1+\sqrt{1+8K_dC_{M0}}}{4K_dC_{M0}} \qquad (8)$$

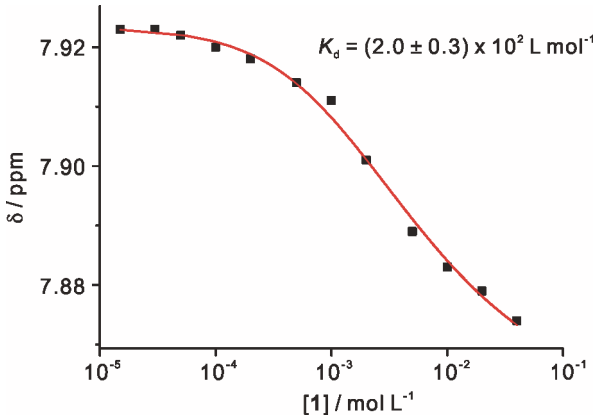


Figure S4. Plots of the chemical shifts (δ) of one of H3 quinoline proton (at 7.923 ppm when **1** at 0.5 mM in Figure S2) versus the logarithm of the concentrations of **1** in $CDCl_3$. The dimerization constant was calculated to be $K_d = 2.0 \times 10^2$ L mol^{-1} based on above equations.

3.2 Solution studies of sequence **2**

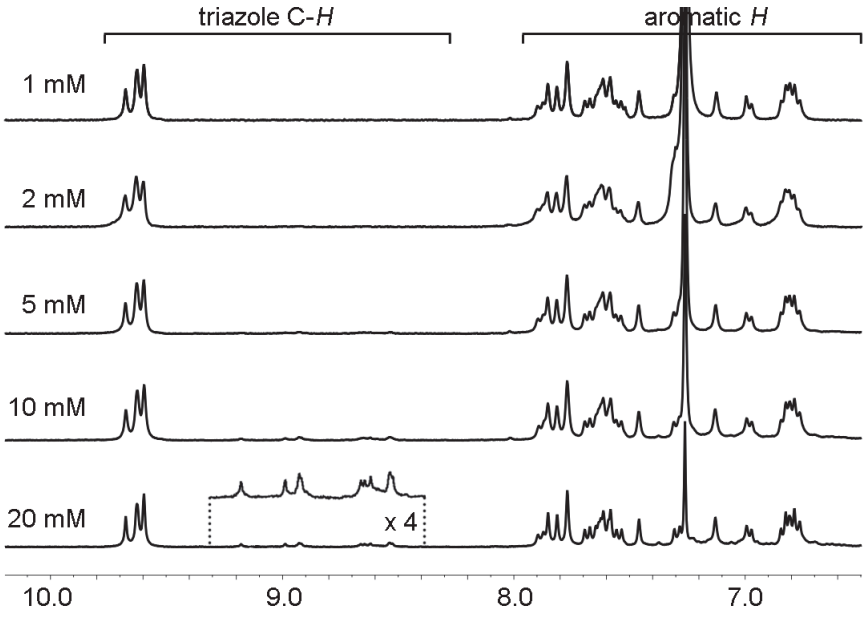
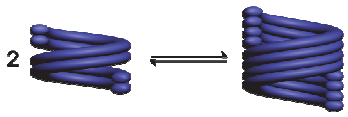


Figure S5. Part of 400 MHz ^{1}H NMR of **2** in various concentration in $CDCl_3$ at 296 K. The tetramerization constant was calculated to be $K_q = 15$ L mol^{-1} in $CDCl_3$ based on equation 14 below.

Determination of the tetramerization constant K_q between double and quadruple helix through NMR integration



Scheme S4. Schematic diagram of mutual transformation between the double helix and quadruple helix.

For the equilibrium shown in Eq. 9, the tetramerization constant is given by Eq. 10.

$$2\,D \rightleftharpoons Q \qquad (9)$$

$$K_q = \frac{C_Q}{C_D{}^2} \qquad (10)$$

where: C_D = double helix concentration; C_Q = quadruple helix concentration

Alternatively,

$$K_q = \frac{n_Q \times V_T}{n_D^2} \qquad (11)$$

where: V_T = total volume of the sample; n_D = number of moles of the double helix; n_Q = number of moles of the quadruple helix

From mass balance,

$$n_D + 2n_Q = {}^{n_{M0}}\!/_{2} \qquad (12)$$

where: n_{M0} = initial number of moles of the monomer

From integration of the NMR spectrum it is possible to obtain the relative ratio of n_D to n_Q molar number, a (Eq. 13).

$$n_D / (n_Q / 2) = a \qquad (13)$$

Substituting equations (12) and (13) into (11),

$$K_q = \frac{(a+4) \times V_T}{8a^2 \times n_{M0}} \qquad (14)$$

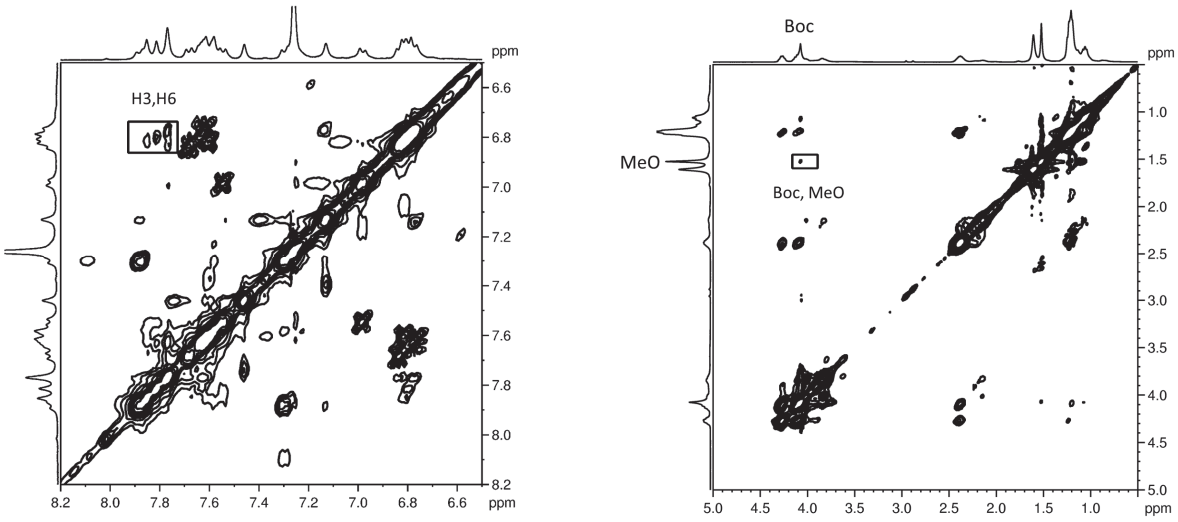


Figure S6. Partial NOESY spectra of **2** ($CDCl_3$, 400 MHz). Correlations between H3 and H6 are observed with **2** suggesting that they correspond to intermolecular contacts associated with aggregation of **2**. The Boc-CH_3 ester correlation in **2** (right) is consistent with a head-to-tail arrangement of a duplex.

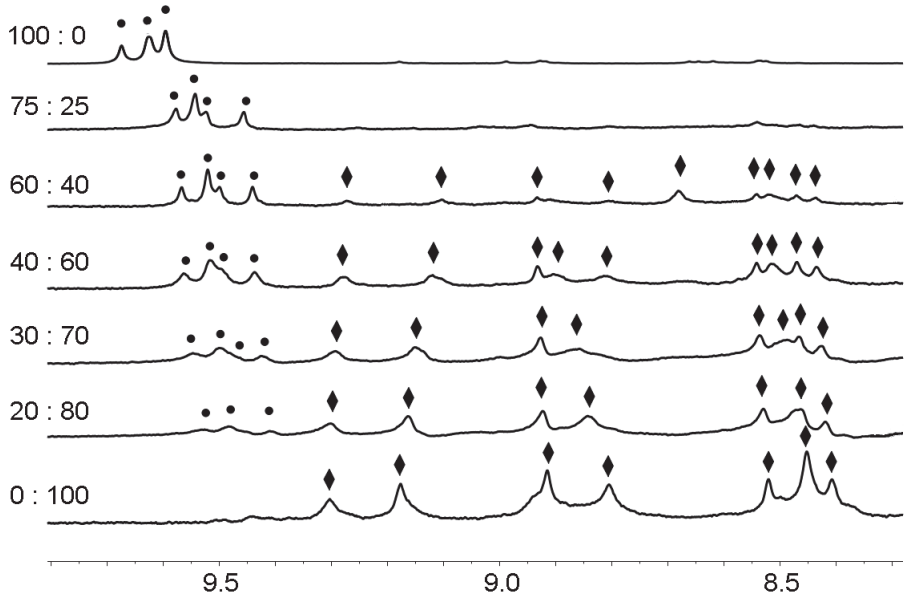


Figure S7. Part of 400 MHz ^{1}H NMR of **2** (1 mM) at 296 K with different ratio of $CDCl_3$/ DMSO-d_6. Triazole signals of the double and quadruple helices are marked with black circles and diamonds, respectively. The tetramerization constants in various solvent mixtures can be calculated based on equation 14 in scheme S4.

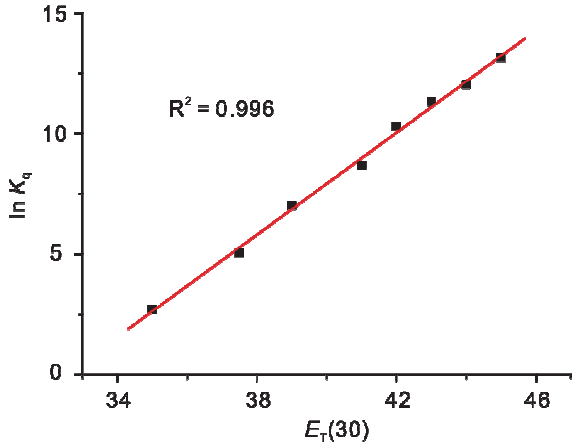


Figure S8. Plot of natural logarithm of equilibrium constants in various solvent mixtures versus solvent polarity (E_T(30), kcal mol^{-1}). E_T(30) values of mixed solvents were determined with mole fractions.

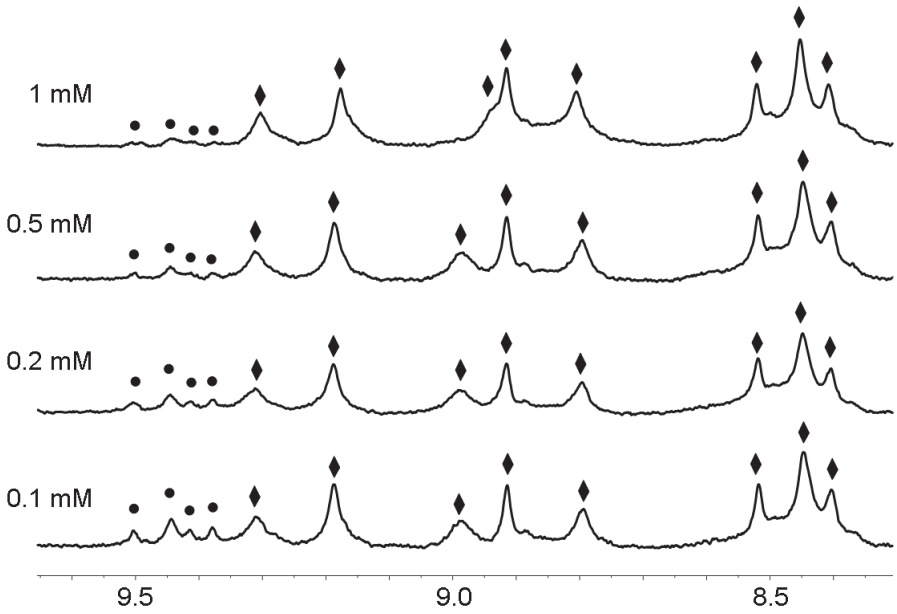


Figure S9. Part of 400 MHz ^{1}H NMR of **2** in various concentration in DMSO-d_6 at 296 K. Triazole signals of the double and quadruple helices are marked with black circles and diamonds, respectively. The tetramerization constant was calculated to be K_q = 5.2 × 10^5 L mol^{-1} based on equation 14 in scheme S4.

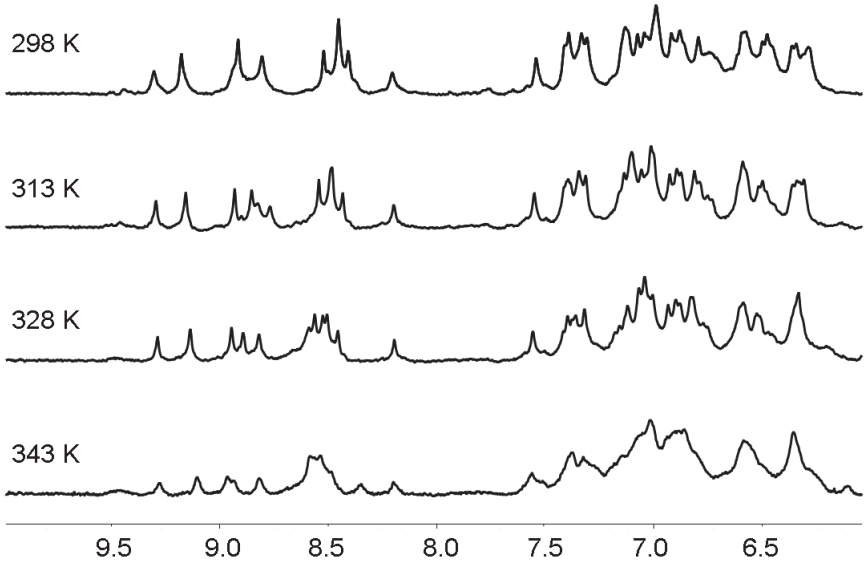


Figure S10. Temperature dependent ^{1}H NMR (400 MHz) of **2** (1 mM) in DMSO-d_6.

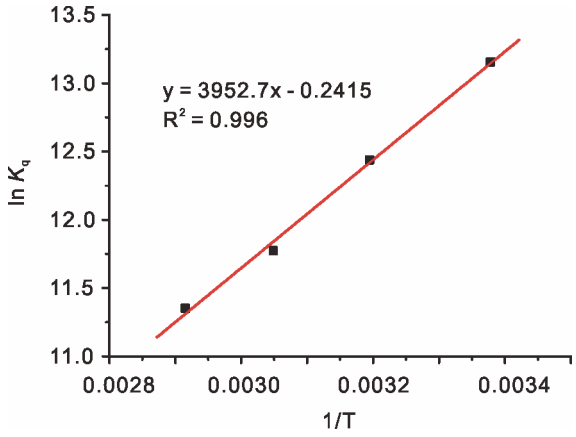


Figure S11. van't Hoff plot of the tetramerization of **2** in DMSO-d_6. Experimental data were fitted to the van't Hoff equation using linear regression analysis (R^2 = 0.996). ΔH and ΔS were determined to be -32.9 KJ · mol^{-1} and -2.0 J · K^{-1}, respectively. ΔG was calculated to be -32.3 KJ · mol^{-1}.

4 Mass spectra

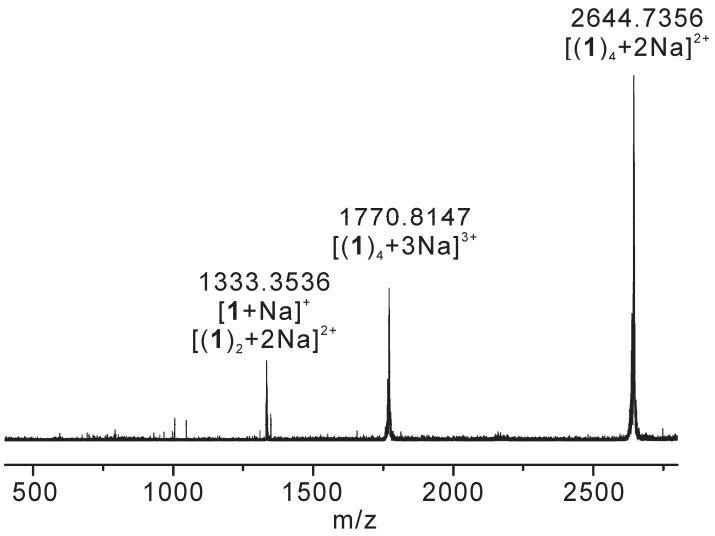


Figure S12. Traces of the high-resolution ESI-MS of sequence **1** corresponding to +1 charged signals for single helical structure, +2 charged signals for double helical structure, and +2 charged and 3+ charged signals for quadruple helix

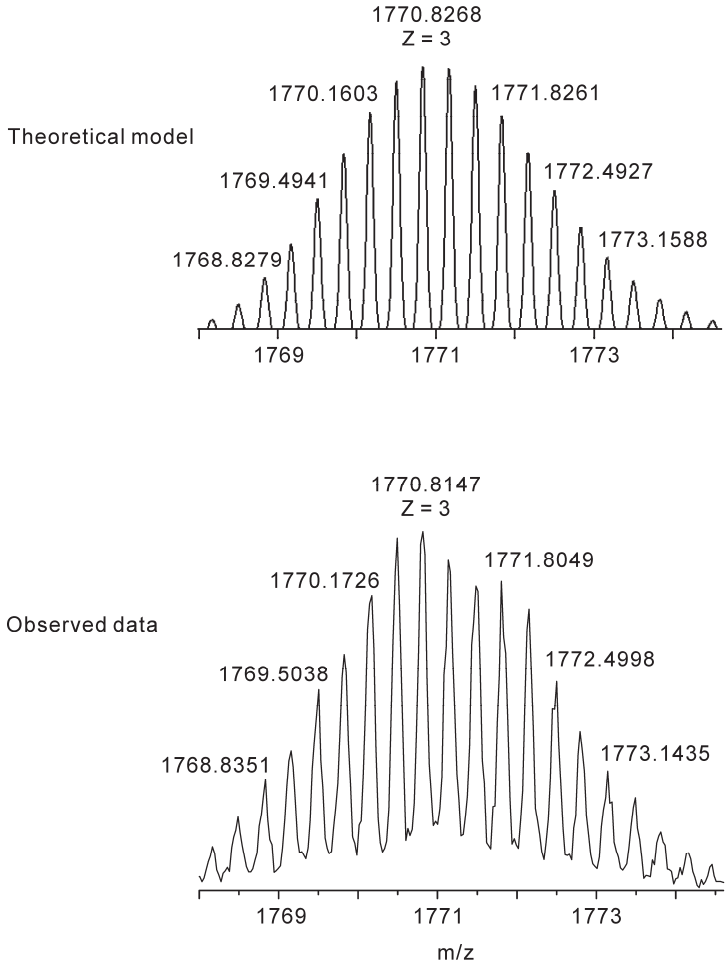


Figure S13. High-resolution ESI-MS data for the +3 peaks of sequence **1**.

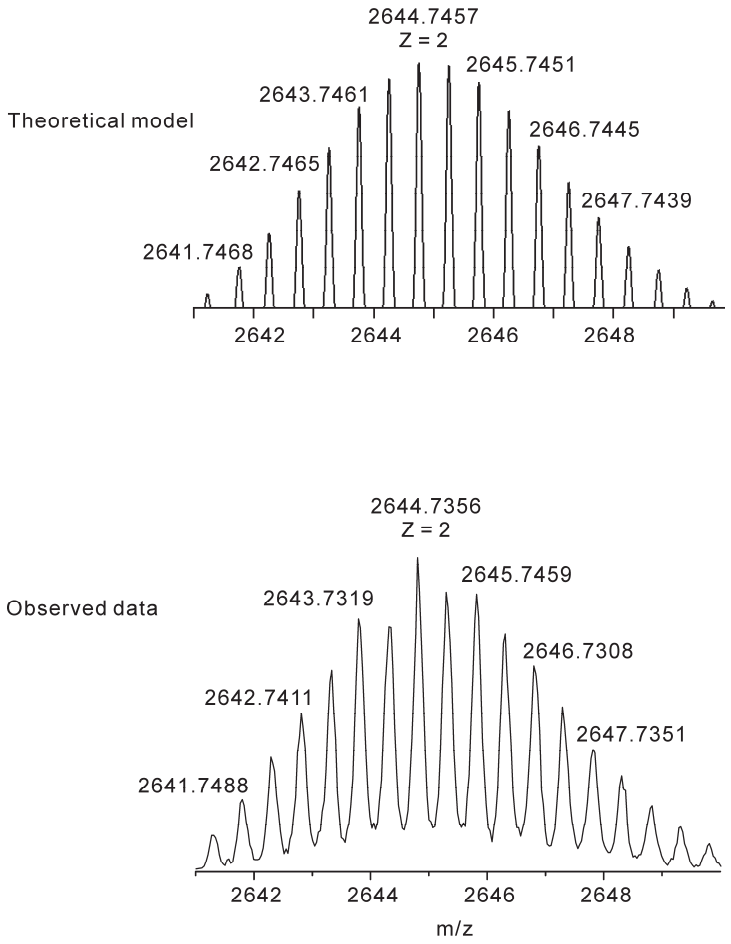


Figure S14. High-resolution ESI-MS data for the +2 peaks of sequence **1**.

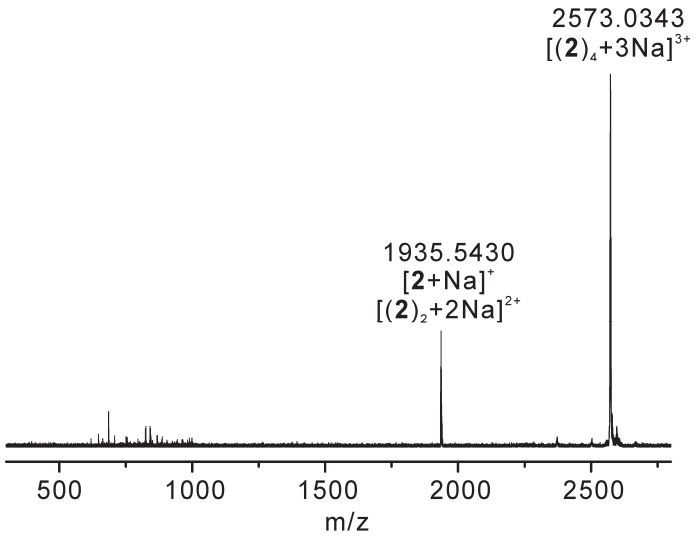


Figure S15. Traces of the high-resolution ESI-MS of sequence **2** corresponding to +1 charged signal for single helical structure, +2 charged signals for double helical structure, and 3+ charged signals for quadruple helix.

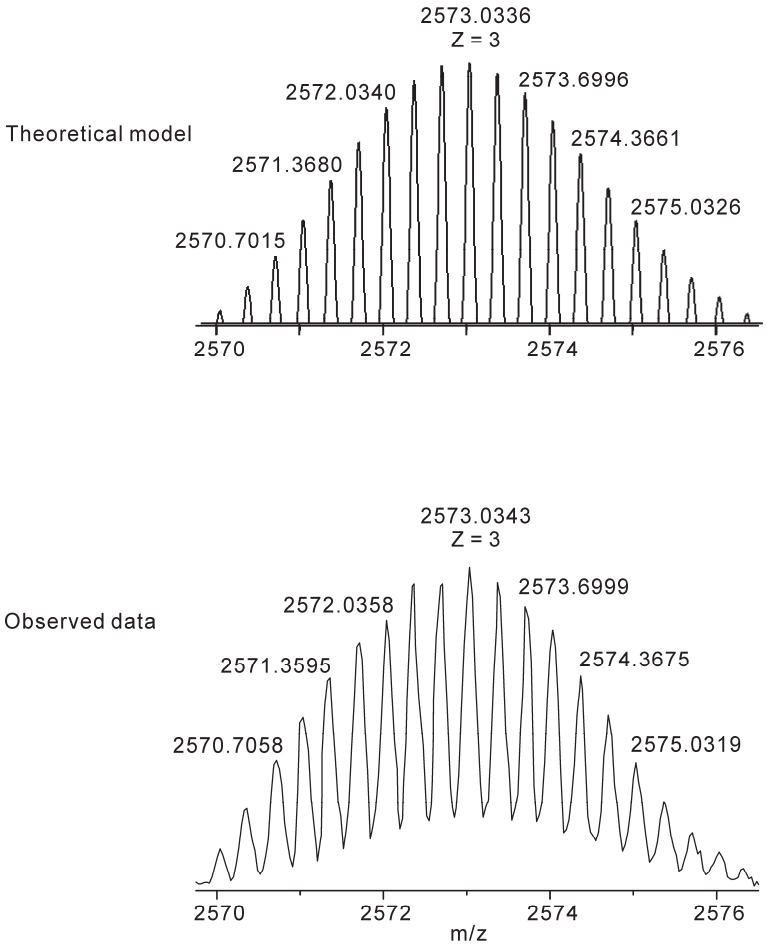


Figure S16. High-resolution ESI-MS data for the +3 peaks of sequence **2**.

5 NMR spectra

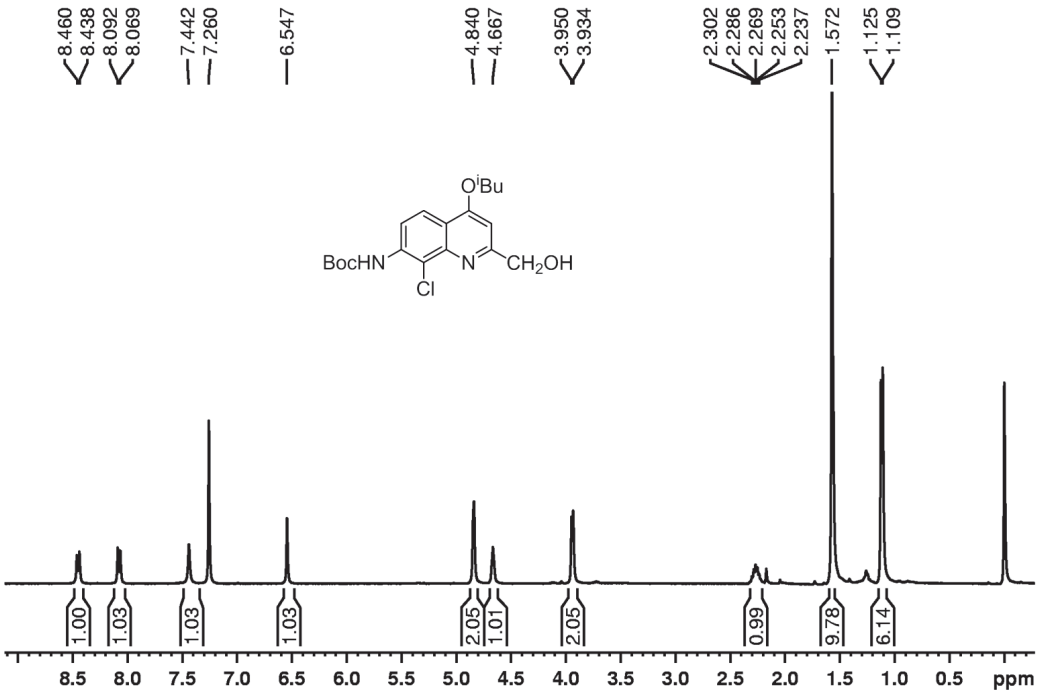


Figure S17. ^{1}H NMR spectrum (400 MHz) of compound **5** in $CDCl_3$.

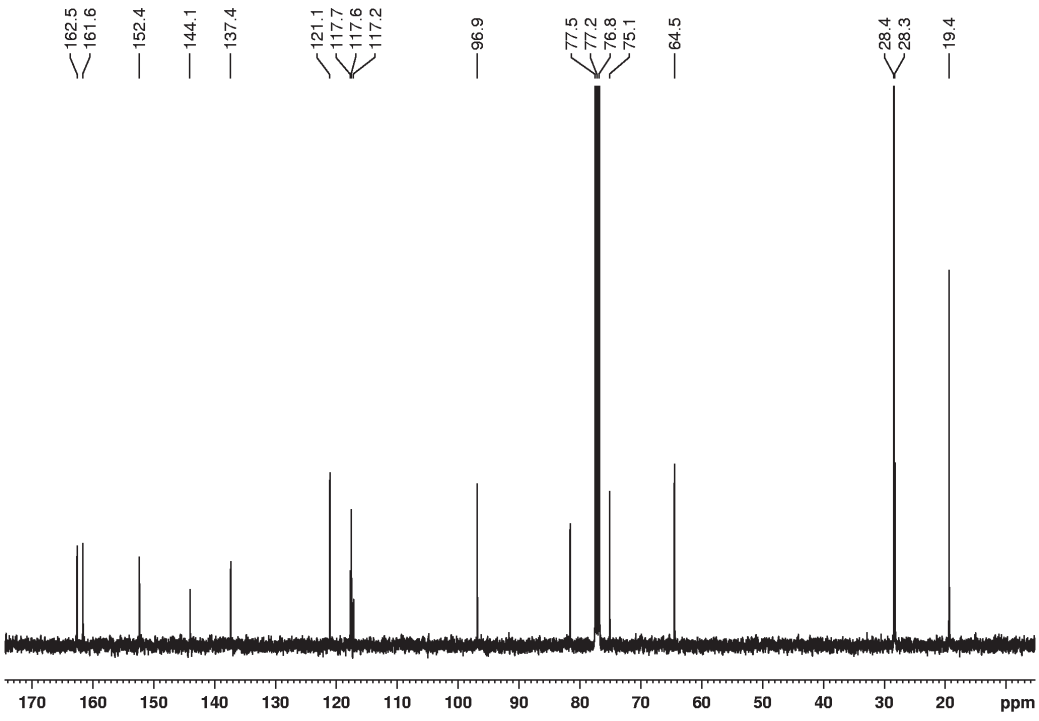


Figure S18. ^{13}C NMR spectrum (100 MHz) of compound **5** in $CDCl_3$.

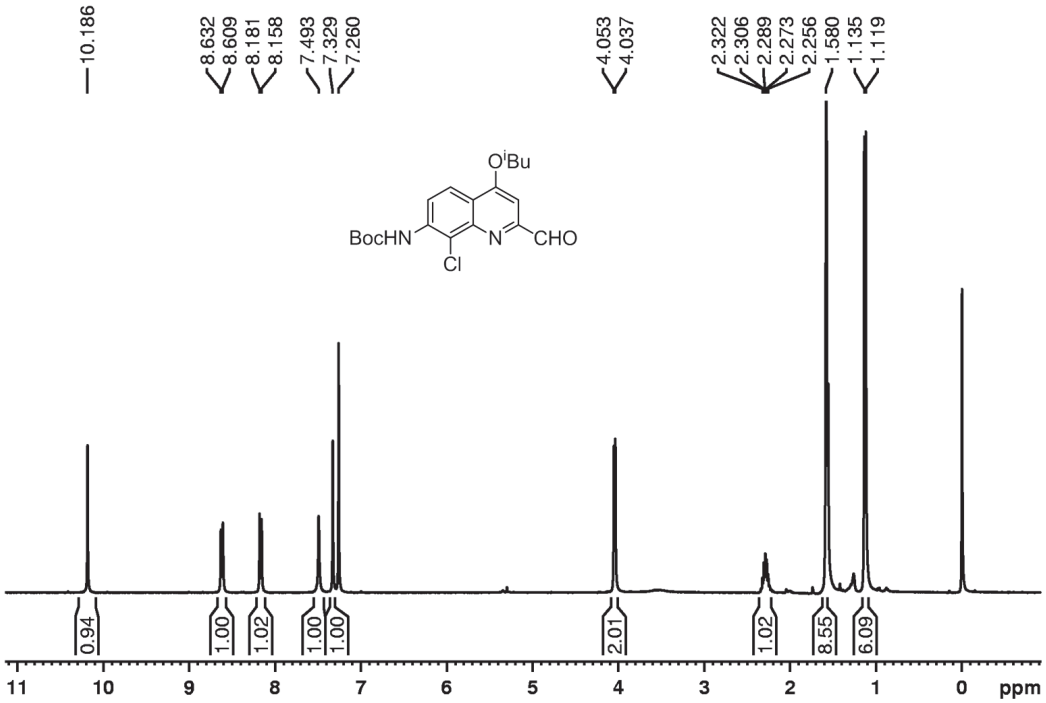


Figure S19. ^{1}H NMR spectrum (400 MHz) of compound **6** in $CDCl_3$.

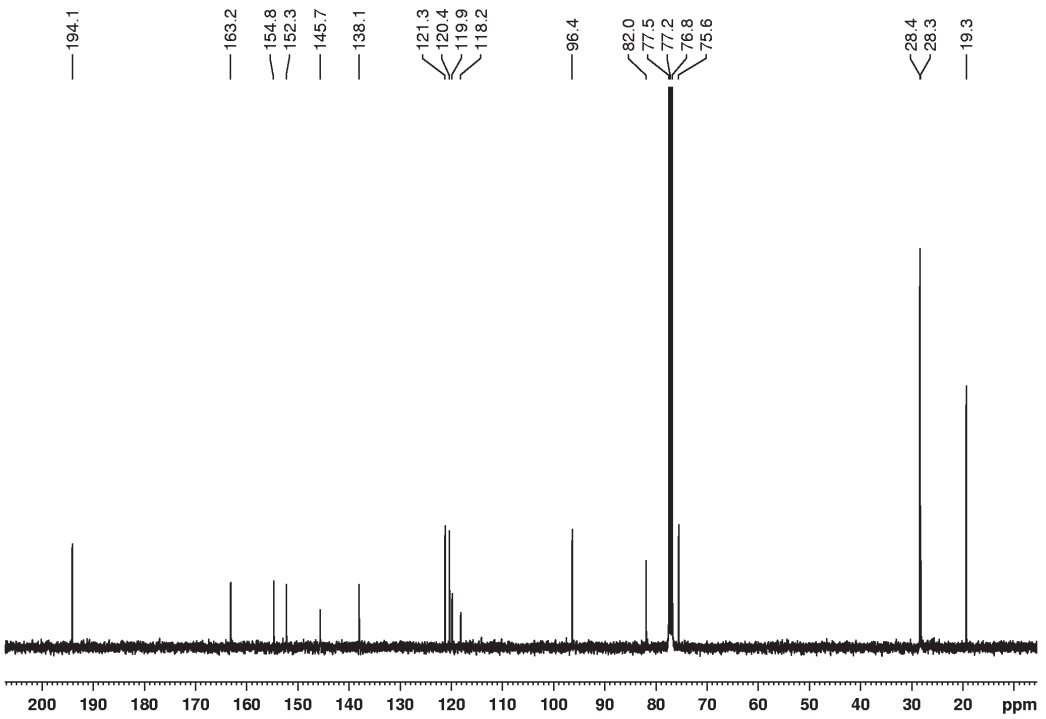


Figure S20. ^{13}C NMR spectrum (100 MHz) of compound **6** in $CDCl_3$.

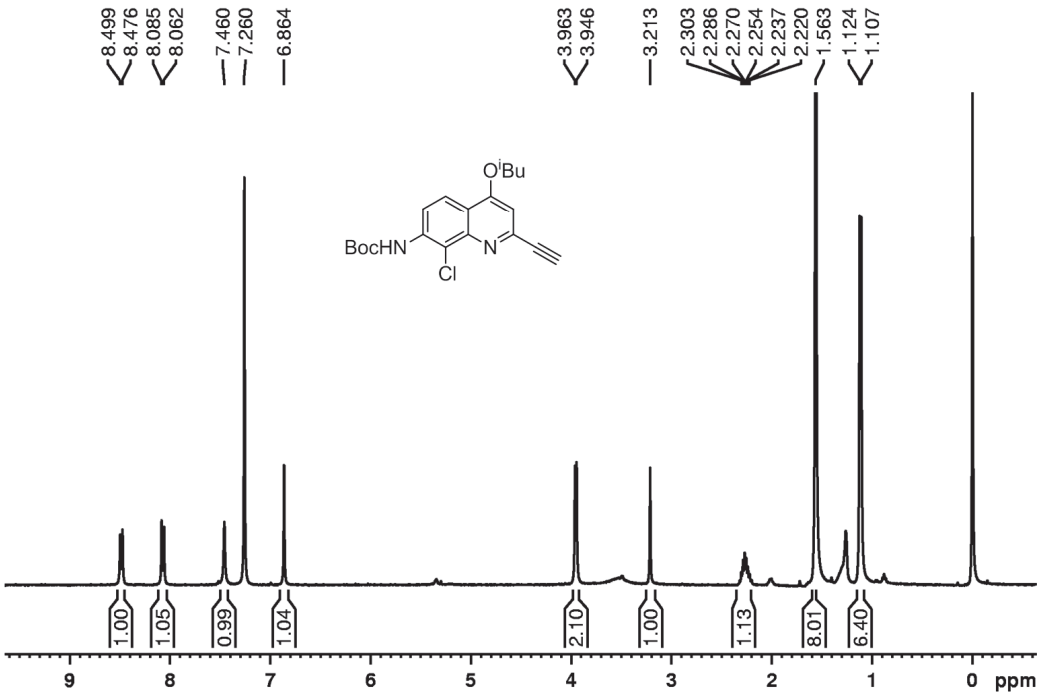


Figure S21. ^{1}H NMR spectrum (400 MHz) of compound **7** in $CDCl_3$.

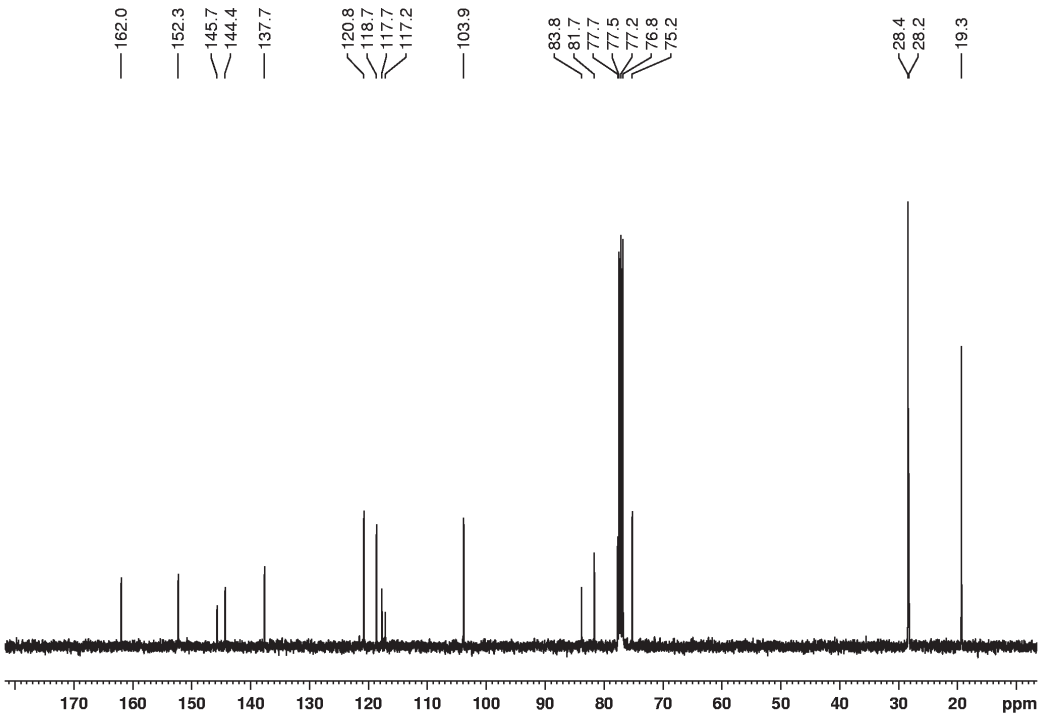


Figure S22. ^{13}C NMR spectrum (100 MHz) of compound **7** in $CDCl_3$.

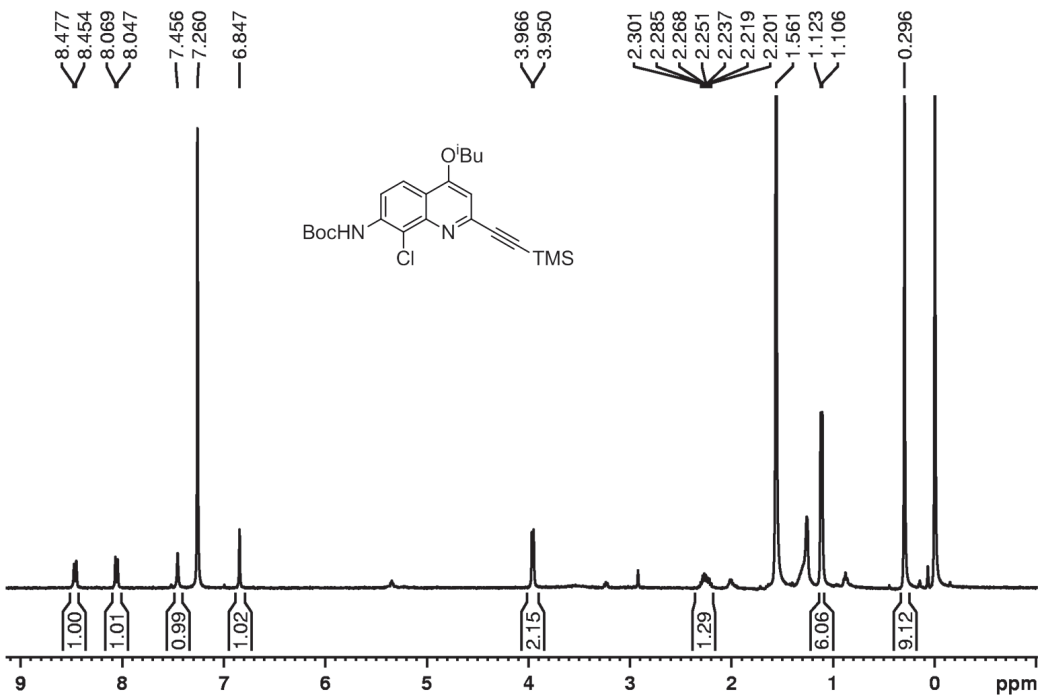


Figure S23. ^{1}H NMR spectrum (400 MHz) of compound **8** in $CDCl_3$.

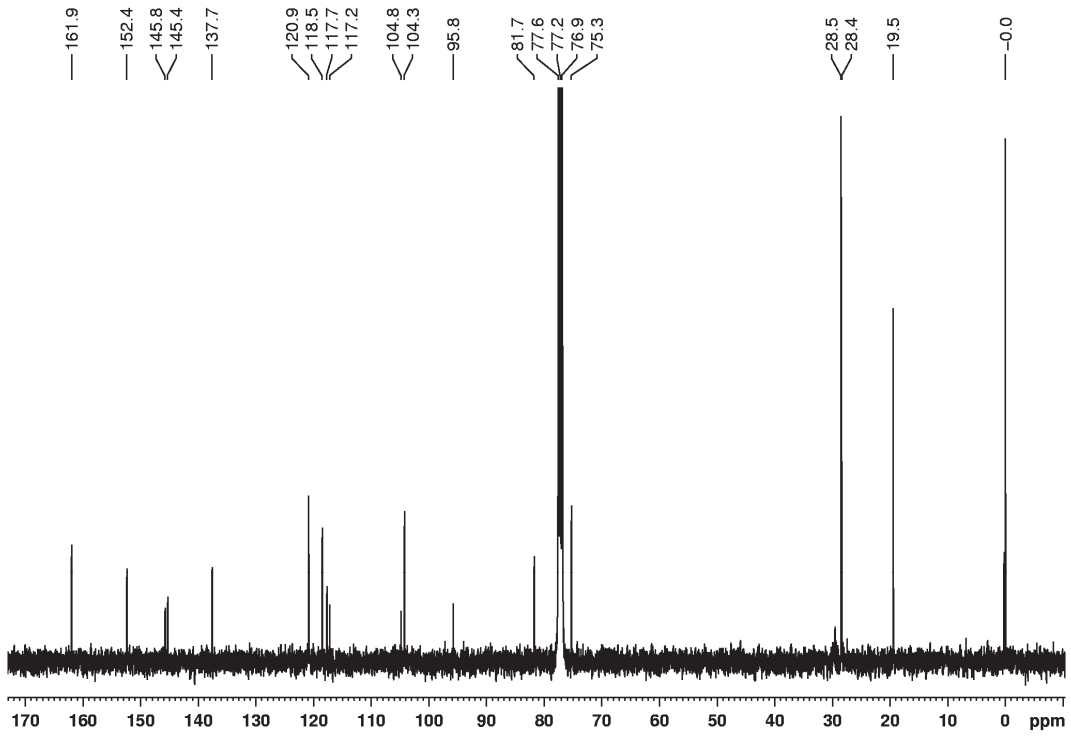


Figure S24. ^{13}C NMR spectrum (100 MHz) of compound **8** in $CDCl_3$.

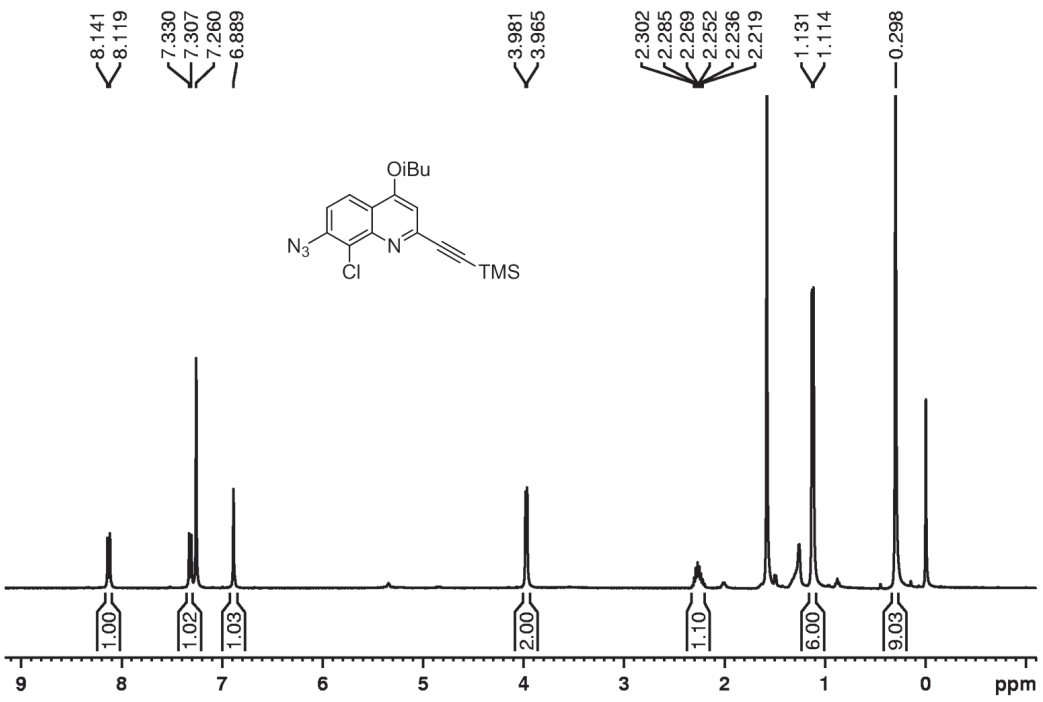


Figure S25. ^{1}H NMR spectrum (400 MHz) of compound **8b** in $CDCl_3$.

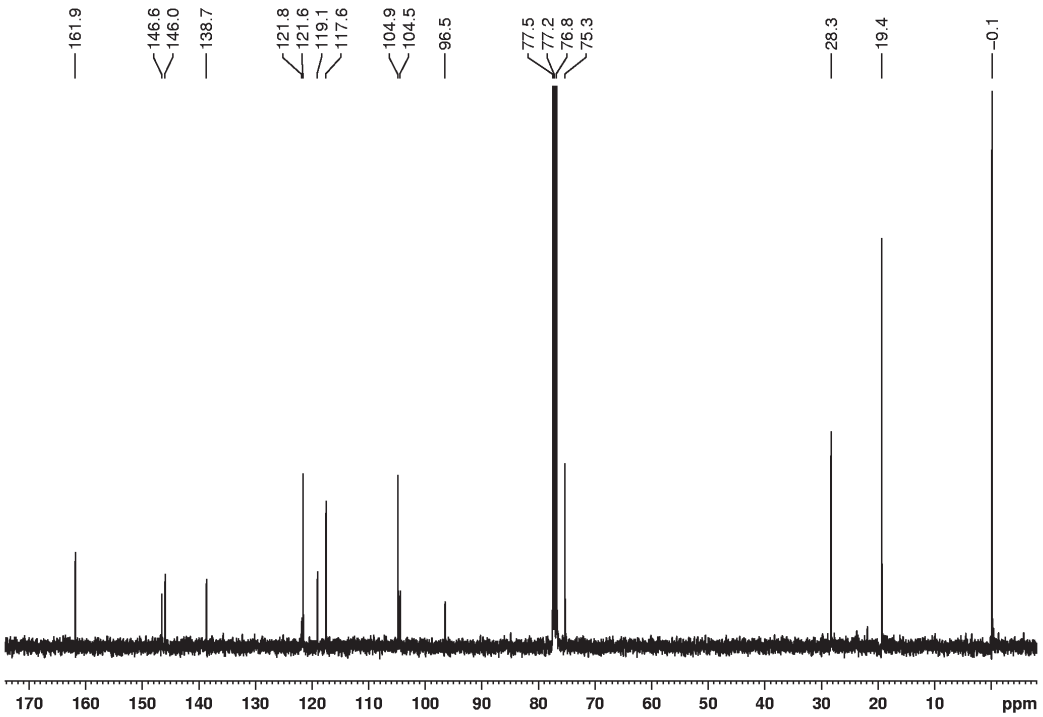


Figure S26. ^{13}C NMR spectrum (100 MHz) of compound **8b** in $CDCl_3$.

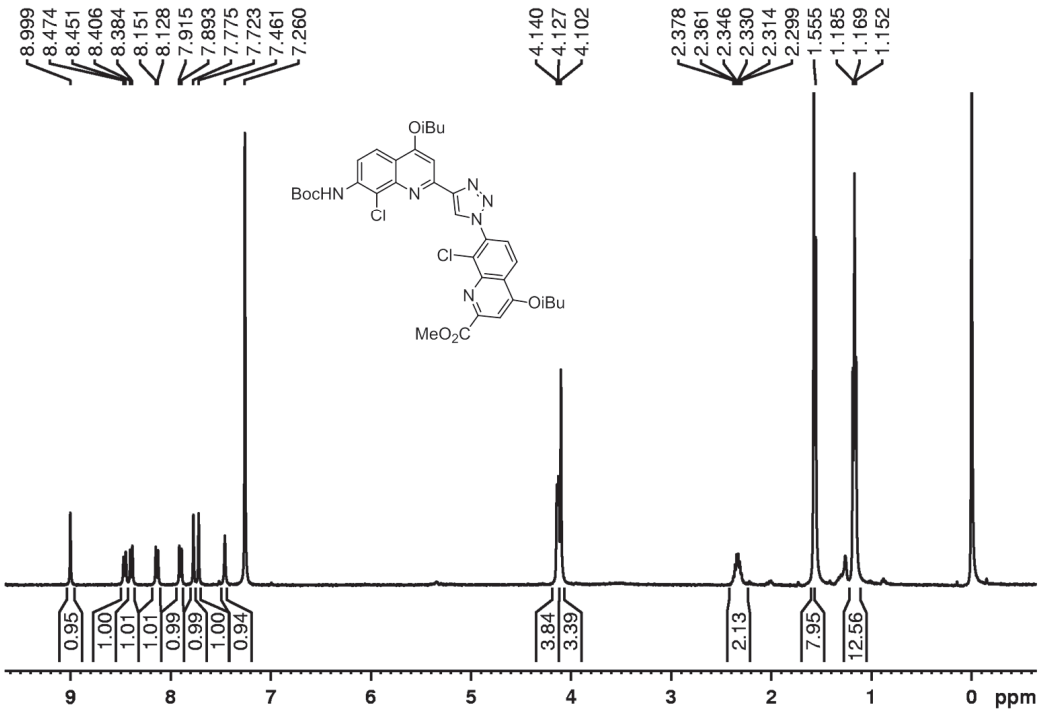


Figure S27. ^{1}H NMR spectrum (400 MHz) of compound **9** in $CDCl_3$.

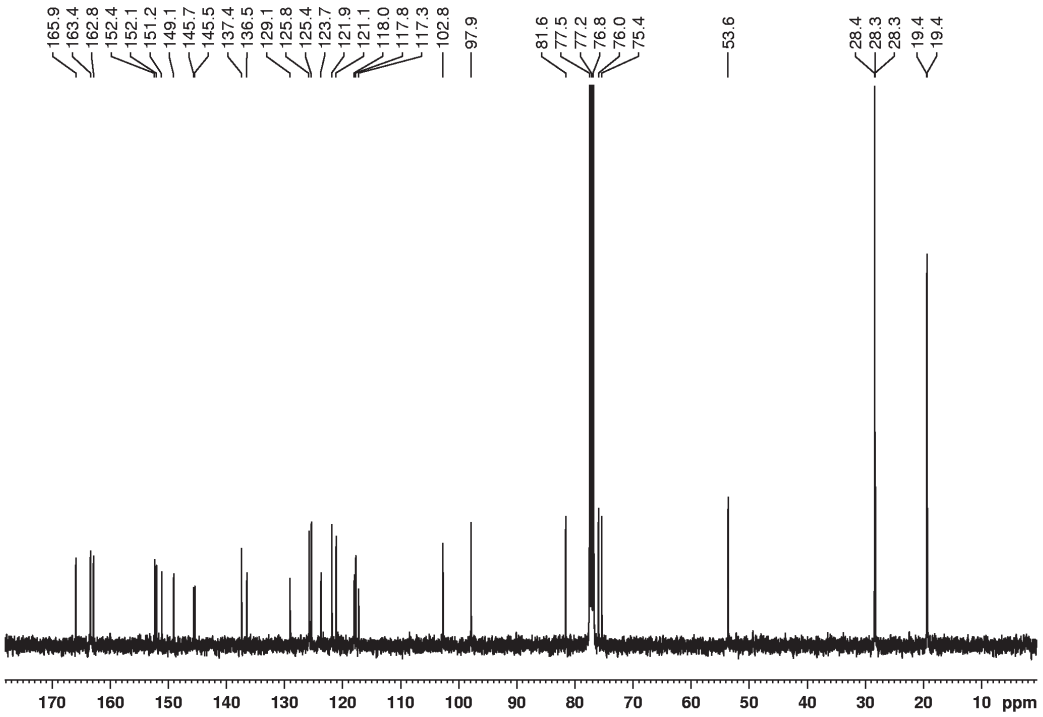


Figure S28. ^{13}C NMR spectrum (100 MHz) of compound **9** in $CDCl_3$.

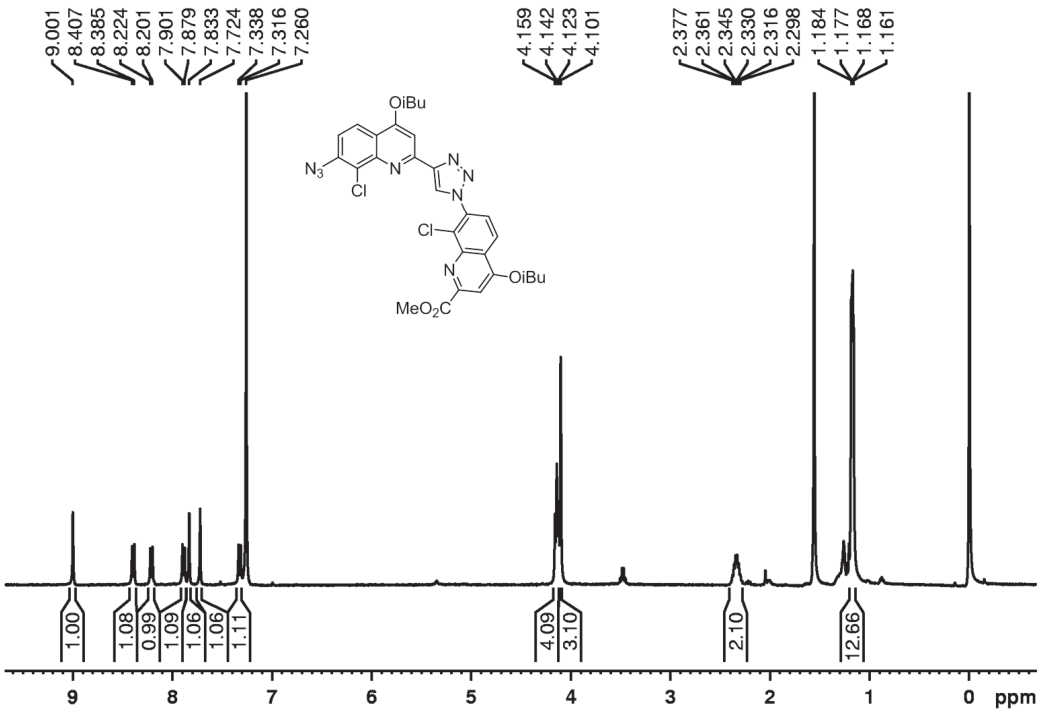


Figure S29. ^{1}H NMR spectrum (400 MHz) of compound **9b** in $CDCl_3$.

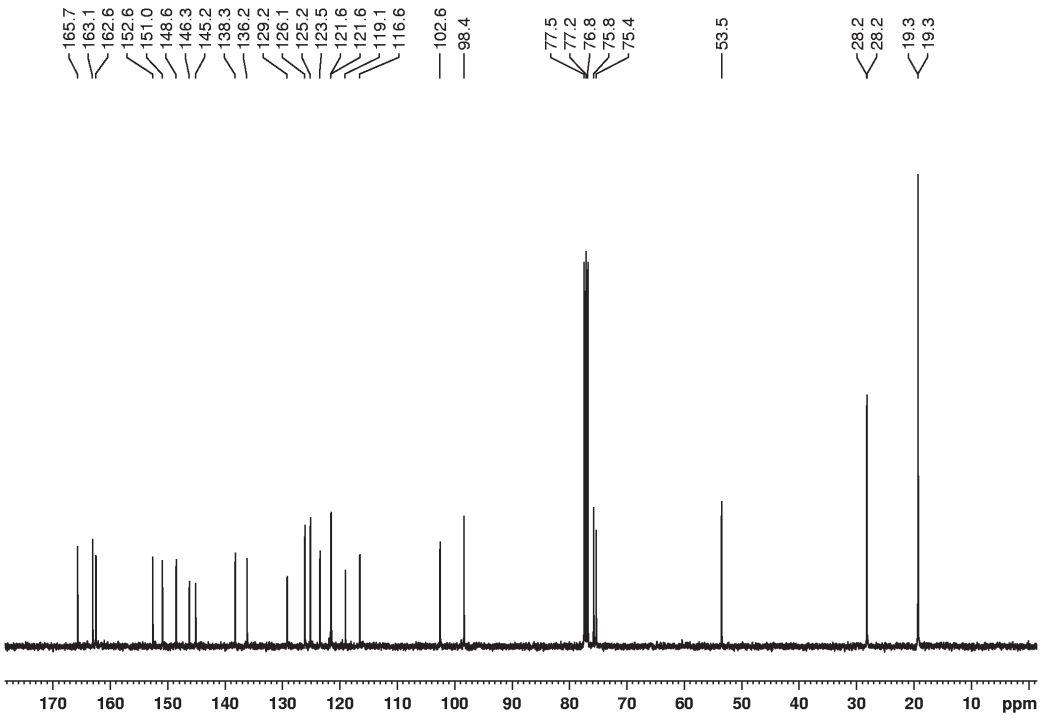


Figure S30. ^{13}C NMR spectrum (100 MHz) of compound **9b** in $CDCl_3$.

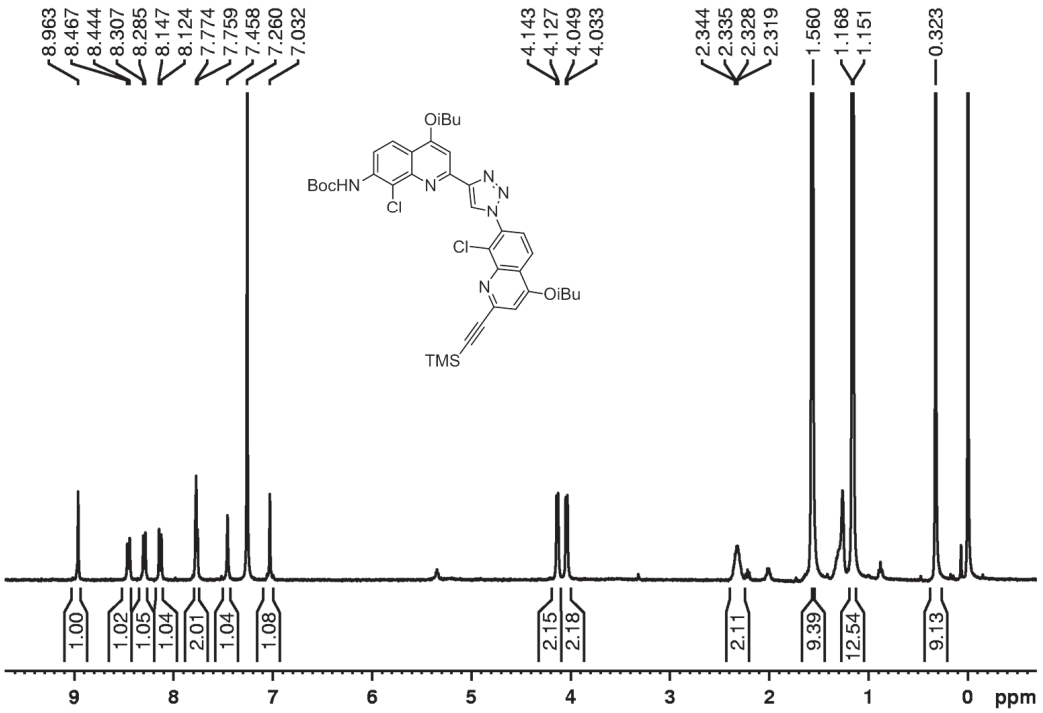


Figure S31. ^{1}H NMR spectrum (400 MHz) of compound **10** in $CDCl_3$.

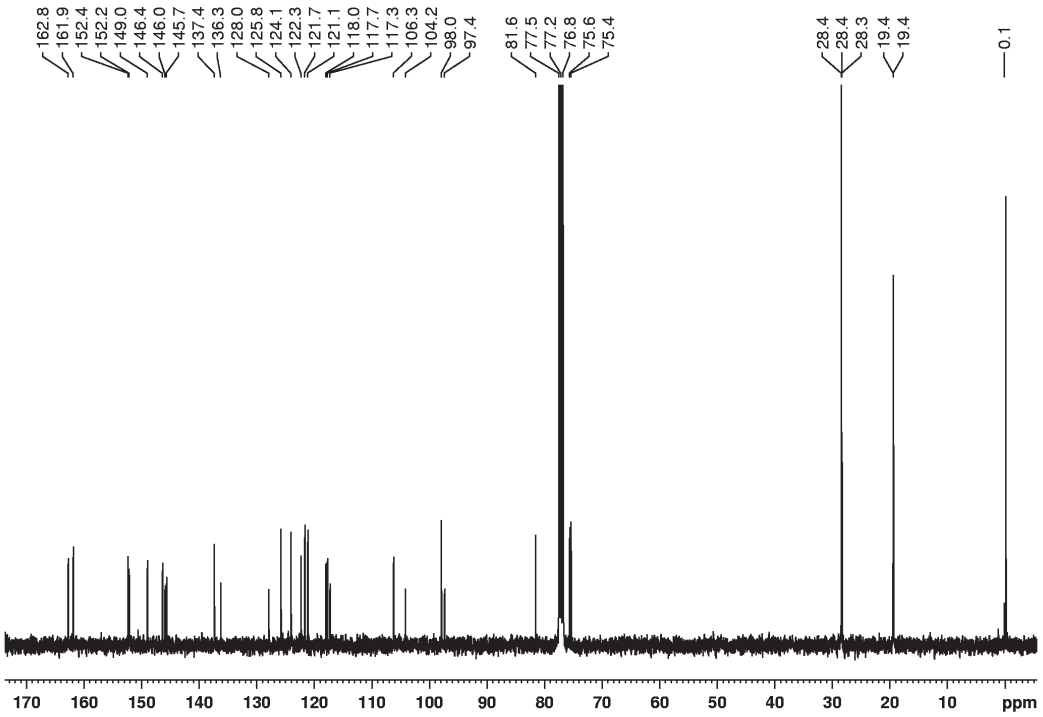


Figure S32. ^{13}C NMR spectrum (100 MHz) of compound **10** in $CDCl_3$.

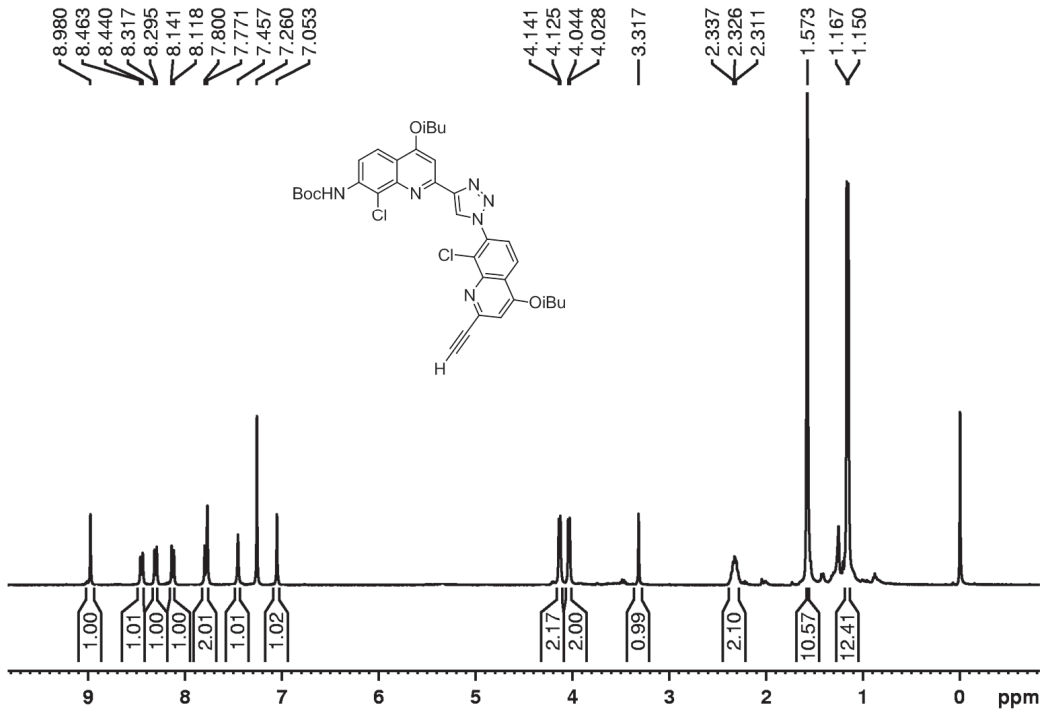


Figure S33. ^{1}H NMR spectrum (400 MHz) of compound **10c** in $CDCl_3$.

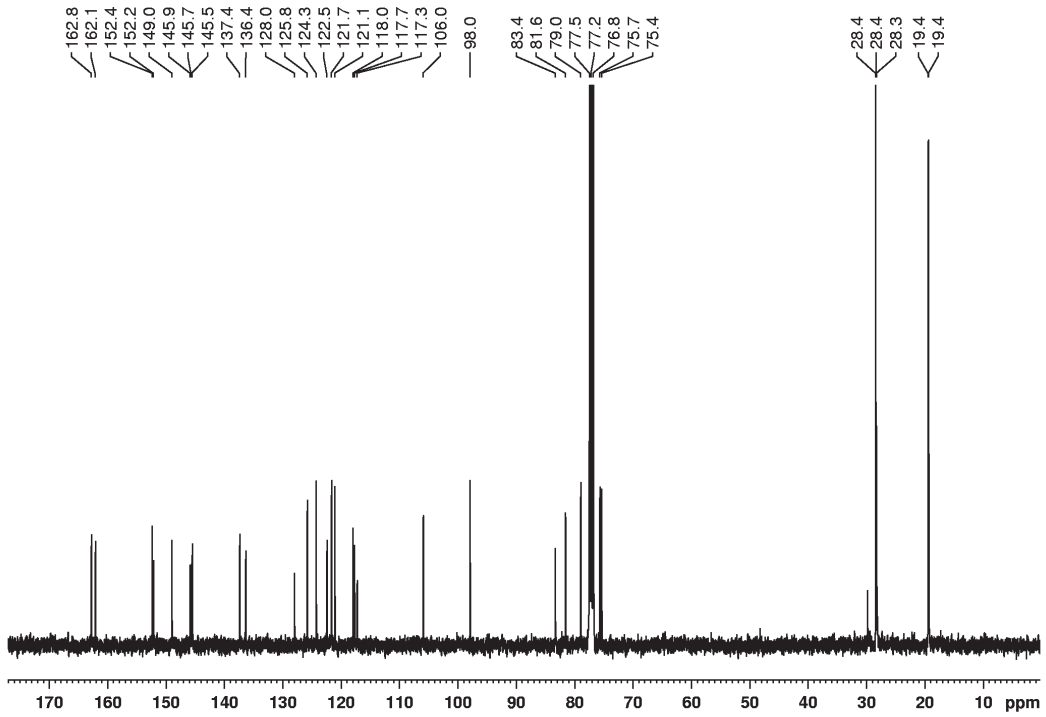


Figure S34. ^{13}C NMR spectrum (100 MHz) of compound **10c** in $CDCl_3$.

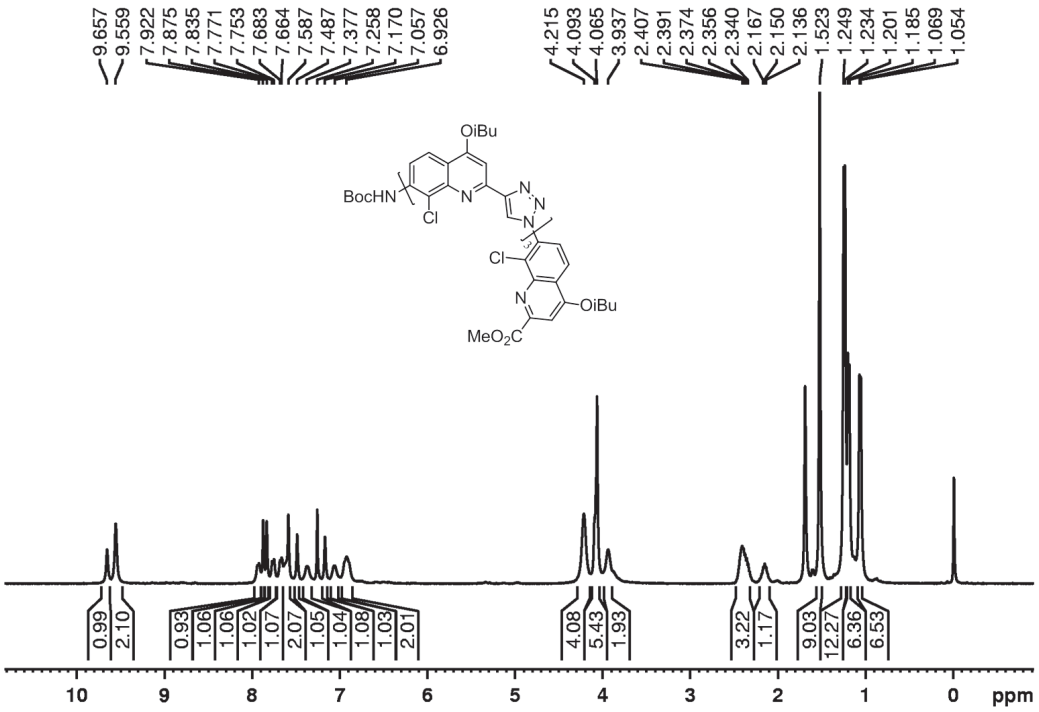


Figure S35. ^{1}H NMR spectrum (400 MHz) of tetramer **1** in $CDCl_3$.

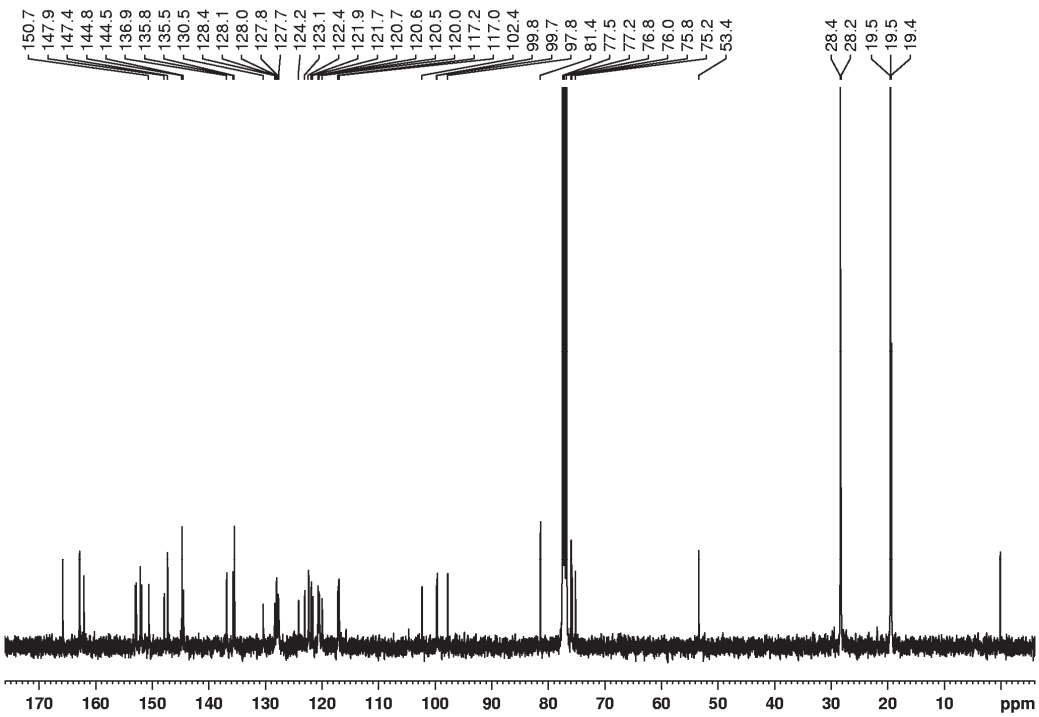


Figure S36. ^{13}C NMR spectrum (100 MHz) of tetramer **1** in $CDCl_3$.

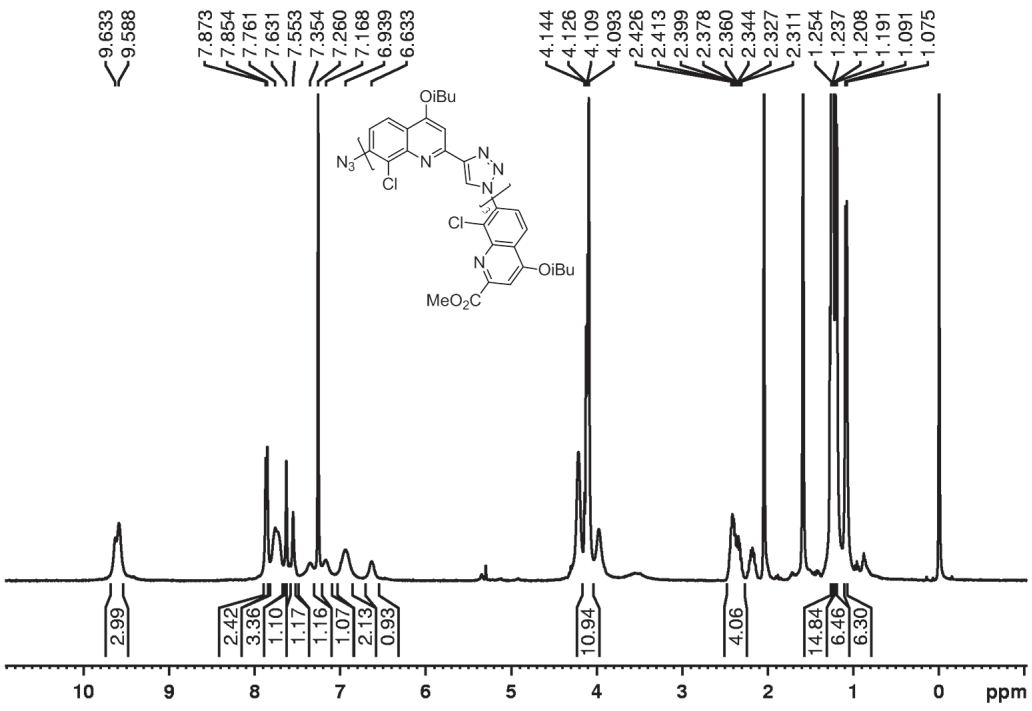


Figure S37. ^{1}H NMR spectrum (400 MHz) of compound **1b** in $CDCl_3$.

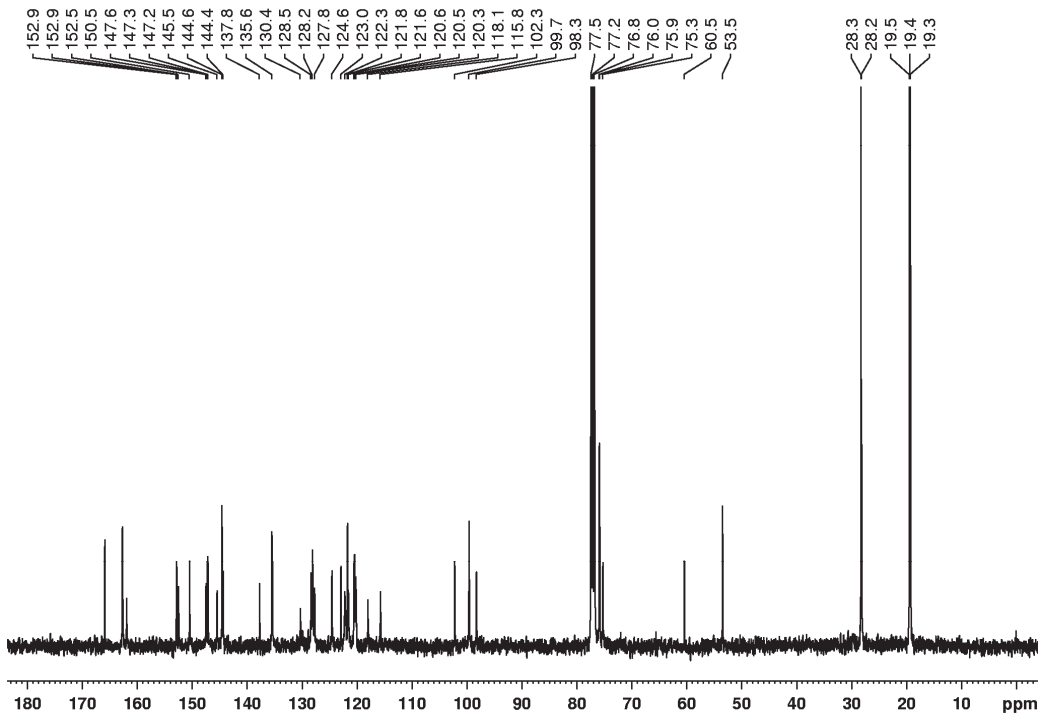


Figure S38. ^{13}C NMR spectrum (100 MHz) of compound **1b** in $CDCl_3$.

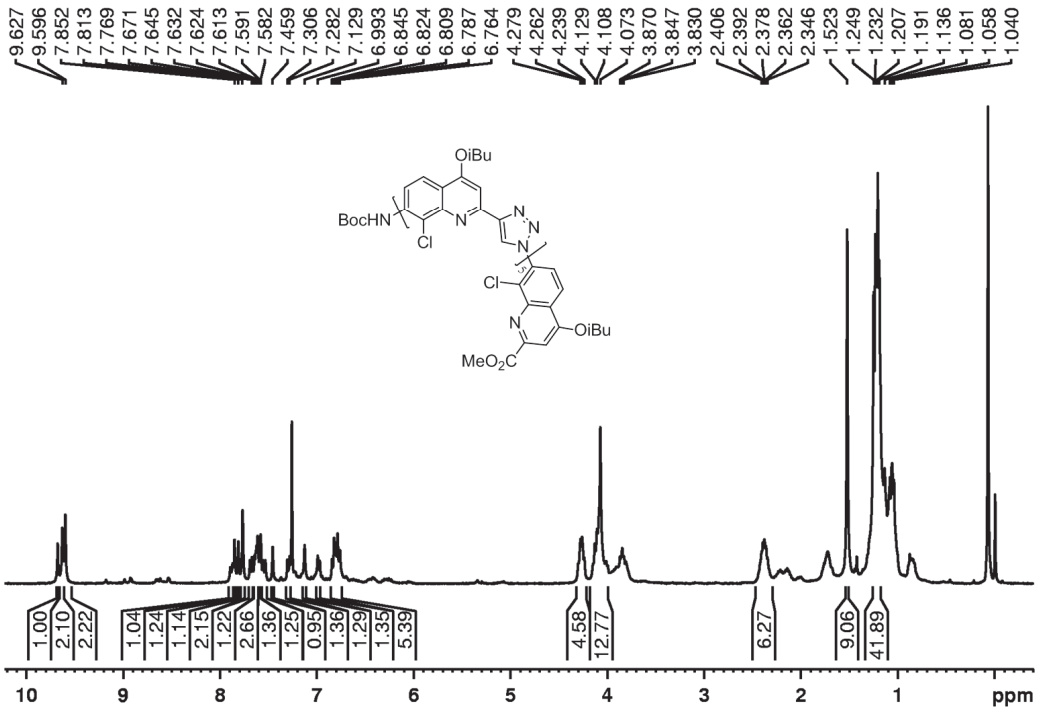


Figure S39. ^{1}H NMR spectrum (400 MHz) of hexamer **2** in $CDCl_3$.

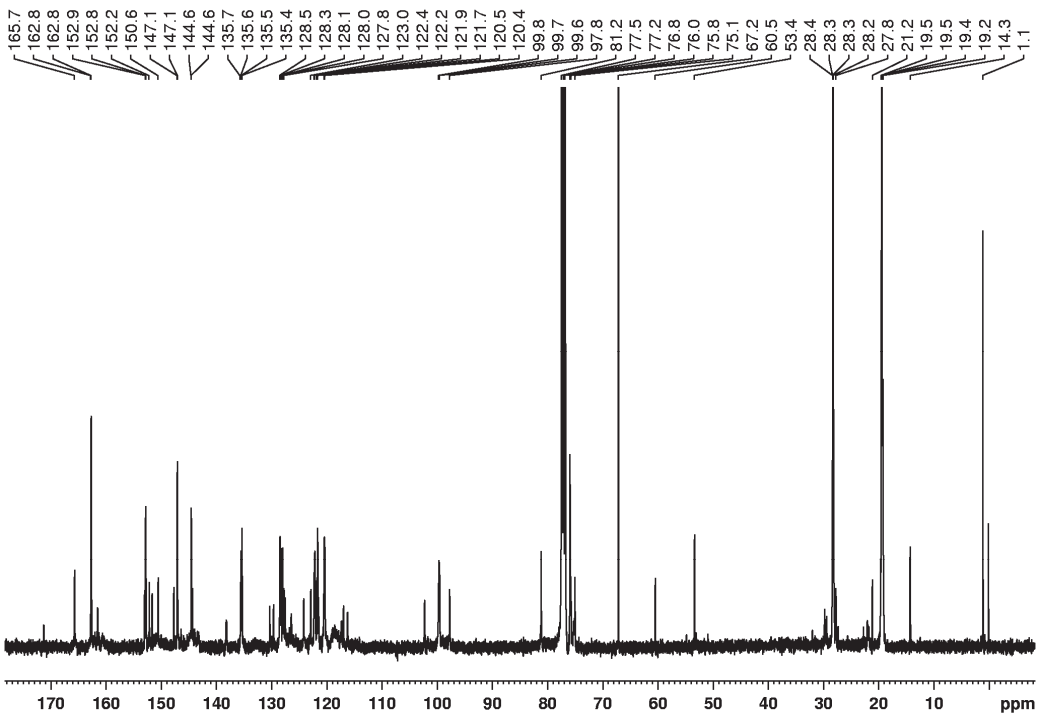


Figure S40. ^{13}C NMR spectrum (100 MHz) of hexamer **2** in $CDCl_3$.

6 References

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