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 CaH₂ 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 CDCl₃ (7.26 ppm for ¹H NMR, 77.16 ppm for ¹³C NMR) and by DMSO-d₆ (2.50 ppm for ¹H NMR, 39.52 ppm for ¹³C 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) NaBH₄, THF, reflux; b) MnO₂, DCM, r.t.; c) Bestmann-Ohira reagent, K₂CO₃, MeOH, r.t.; d) CF₃SiMe₃, 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, NaNO₂, NaN₃; c) CuSO₄, L-sodium ascorbate, tBuOH/PhMe; d) KF·2H₂O, 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 NaBH₄ (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 Na₂SO₄. 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%. ¹H NMR (CDCl₃, 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). ¹³C NMR (CDCl₃, 100 MHz): δ 162.5, 161.6, 152.4, 144.1,
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%. 

$\delta$ 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). 

$\delta$ 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_{25}ClN_{2}O_{4} [M+H]^+ 381.1581, found 381.1603.

Compound 7. To a mixture of compound 6 (1.15 g, 3.0 mmol) 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$_2$SO$_4$, 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%. 

$\delta$ 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). 

$\delta$ 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_{2}O_{3} 375.1475, found 375.1497.

Compound 8. A mixture of compound 7 (0.82 g, 2.2 mmol) and trifluoromethyltrimethylsilane (0.38 g, 0.36 mmol) in DMPU (5 mL) was stirred for 24 h at 40 °C. The mixture was quenched by adding sat. NH$_4$Cl and extracted with Et$_2$O (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%. 

$\delta$ 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). 

$\delta$ 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$_2$O$_3$Si [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 NaNO₂ (0.09 g, 1.4 mmol) in H₂O (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 H₂O (1 mL) was added slowly. The mixture was stirred at room temperature for another 2 h and then was extracted with DCM (30 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na₂SO₄. After concentration, the residue was purified by flash SiO₂ column chromatography eluting with DCM to afford pure product. Yield: 95%. ¹H NMR (CDCl₃, 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). ¹³C NMR (CDCl₃, 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 C₁₅H₁₅ClN₄O₃ [M+H]+ 335.0911, found 335.0905.

Compound 8b. Monomer 8 (0.3 g, 0.8 mmol) was dissolved in CH₂Cl₂ (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 CH₂Cl₂ (20 mL), washed with saturated NaHCO₃, dried over Na₂SO₄ 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%. ¹H NMR (CDCl₃, 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). ¹³C NMR (CDCl₃, 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 C₁₈H₂₁ClN₄OSi [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 CuSO₄ (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 NH₄Cl (20 mL) and brine (20 mL), respectively, and then dried over Na₂SO₄. Solvents were removed under reduced pressure, and the crude product was purified by flash chromatography (SiO₂, gradient DCM/PE to DCM/ethyl acetate = gradient 1/10 to 10/1) to yield 9 (476 mg, 85%) as a pale solid. ¹H NMR (CDCl₃, 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). ¹³C NMR (CDCl₃, 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,
Compound 9b. Compound 9 (476 mg, 0.67 mmol) was dissolved in CH₂Cl₂ (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 CH₂Cl₂ (10 mL), washed with saturated NaHCO₃, dried over Na₂SO₄ 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 (CDCl₃, 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). ¹³C NMR (CDCl₃, 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, 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 C₃₀H₂₈Cl₂N₈O₆ [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 (CDCl₃, 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). ¹³C NMR (CDCl₃, 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, 28.3, 19.4, 19.4, 0.1. ESI-HRMS: m/z calcd for C₃₀H₂₈Cl₂N₈O₆ [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·2H₂O (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 Na₂SO₄ and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, DCM/EA: gradient 20/1 to 2/1) to provide 10c (383 mg, 90%) as a slightly brown solid. ¹H NMR (CDCl₃, 400 MHz): 8.98 (s, 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). ¹³C NMR (CDCl₃, 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, 28.3, 19.4, 19.4, 0.1. ESI-HRMS: m/z calcd for C₃₀H₂₈Cl₂N₈O₆ [M+H]⁺ 747.7932, found 747.7950.
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_{2}N_{6}O_{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_{4}Cl (20 mL) and brine (20 mL), respectively, and then dried over Na_{2}SO_{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. ¹H 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). ¹³C NMR (CDCl_{3}, 100 MHz): δ 165.8, 162.9, 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, 124.4, 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_{4}N_{14}O_{8}Na [M+Na]^+ 1333.3667, found 1333.3536; m/z calcd for quadruple helix C_{65}H_{64}Cl_{4}N_{14}O_{8}Na_{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_{2}Cl_{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_{2}Cl_{2} (20 mL), washed with saturated NaHCO_{3}, dried over Na_{2}SO_{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%. ¹H 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). ¹³C NMR (CDCl_{3}, 100 MHz): δ 166.0, 162.8, 162.8, 162.0, 152.9, 152.9, 152.5, 150.5, 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_{4}N_{14}O_{8} [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 CuSO₄ (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 NH₄Cl (15 mL) and brine (15 mL), respectively, and then dried over Na₂SO₄. Solvents were removed under reduced pressure, and the crude product was purified by flash chromatography (SiO₂, gradient DCM/PE to DCM/ethyl acetate = gradient 1/10 to 10/1) to yield sequence 2 (143 mg, 50%) as a white solid. ^1H NMR (CDCl₃, 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). ^13C NMR (CDCl₃, 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, 144.4, 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 C₉₅H₇₀Cl₆N₆₂O₂₉Na [M+Na]^+ 1935.5219, found 1935.5430; m/z calcd for quadruple helix C₃₈₀H₃₆₀Cl₂₂N₁₈₂O₄₀Na₃ [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\textsuperscript{S2} and refined against $F^2$ on all data by full-matrix least squares with SHELXL\textsuperscript{S3} following established refinement strategies.\textsuperscript{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\textsuperscript{S5} routine in PLATON.\textsuperscript{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.

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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.

$$2M \rightleftharpoons D \quad (1)$$

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

Where: $C_M =$ single coil concentration; $C_D =$ double helix concentration

From mass balance,

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

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

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

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

Since:

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

The observed chemical shifts become:

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

solving equation (2) and (5),

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

Substituting equations (7) into (6),

$$\delta_{obs} = \delta_D + \left(\delta_M - \delta_D\right) \cdot \frac{-1 + \sqrt{1 + 8K_dC_{M0}}}{4K_dC_{M0}} \quad (8)$$
Figure S4. Plots of the chemical shifts ($\delta$) 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.

\[
2 \text{ D} \rightleftharpoons \text{ Q} \tag{9}
\]

\[
K_q = \frac{C_Q}{C_D^2} \tag{10}
\]

where: \( C_D \) = double helix concentration; \( C_Q \) = quadruple helix concentration

Alternatively,

\[
K_q = \frac{n_Q \times V_T}{n_D^2} \tag{11}
\]

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,

\[
n_D + 2n_Q = \frac{n_{M0}}{2} \tag{12}
\]

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).

\[
n_D \bigg( \frac{n_Q}{2} \bigg) = a \tag{13}
\]

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

\[
K_q = \frac{(a + 4) \times V_T}{8a^2 \times n_{M0}} \tag{14}
\]
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 $K_q = 5.2 \times 10^5$ 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-<sub>d6</sub>.

Figure S11. van’t Hoff plot of the tetramerization of 2 in DMSO-<sub>d6</sub>. Experimental data were fitted to the van’t Hoff equation using linear regression analysis ($R^2 = 0.996$). $\Delta H$ and $\Delta S$ were determined to be -32.9 KJ·mol$^{-1}$ and -2.0 J·K$^{-1}$, respectively. $\Delta G$ was calculated to be -32.3 KJ·mol$^{-1}$. 
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