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SUPPLEMENTARY INFORMATION

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# Designing cooperatively folded abiotic uni- and multimolecular helix bundles

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# 1. Supplementary Methods

## 1.1 Nuclear magnetic resonance spectroscopy

NMR spectra were recorded on two different NMR spectrometers: (1) an Avance II NMR spectrometer (Bruker Biospin) with a vertical 7.05 T narrow-bore/ultrashield magnet operating at 300 MHz for $^{1}H$ observation and 75 MHz for $^{13}C$ observation by means of a 5-mm direct BBO H/X probe with Z gradient capabilities; (2) an Avance III NMR spectrometer (Bruker Biospin) with a vertical 16.45 T narrow-bore/ultrashield magnet operating at 700 MHz for $^{1}H$ observation by means of a 5-mm TXI $^{1}H/^{13}C/^{15}N$ probe with Z gradient capabilities. Chemical shifts are described in part per million (ppm, $\delta$) relative to the $^{1}H$ residual signal of the deuterated solvent used. $^{1}H$ NMR splitting patterns with observed first-order coupling are entitled as singlet (s), doublet (d), triplet (t), quartet (q) or broad singlet (bs). Coupling constants (*J*) are reported in hertz. Samples were not degassed. Data processing was achieved with Topspin 2.0 software.

## 1.2 Ion mobility mass spectrometry

*Electrospray ion mobility mass spectrometry* (ESI-IMMS) experiments were performed on an Agilent 6560 DTIMS-Q-TOF spectrometer (Agilent Technologies) equipped with a dual-ESI source operated in positive ion mode. The oligomers were analyzed at a concentration of 100 µM in 1:1 DCM/$CHCl_3$ vol/vol. The syringe pump flow rate was 240 µL $hr^{-1}$. Ion mobility experiments were performed in helium (P = 3.89 torr). The trap entrance grid delta was set to 4 V to improve the softness and the funnels radio frequency amplitudes was set to 200 V to improve the transmission of high m/z ions. The data were analyzed using Agilent MassHunter software (B.07) and IM-MS Browser B.07.01.

## 1.3 X-ray crystallography

Crystallographic data for foldamers **2a** and **1a** were collected at the IECB X-ray facility (UMS 3033 – UMS001) on a Rigaku FR-X rotating anode (3 kW). Data were collected at the copper Kα wavelength with a partial AFC-Kappa goniometer. The X-ray source is equipped with high flux Osmic Varimax mirrors and a Dectris Pilatus 200K hybrid pixel detector. Phi-scans were performed and the Rigaku CrystalClear suite was used to index and integrate the data with a multiscan absorption correction. Crystallographic data for foldamers **3a**, **5a**, **2b** and **4a** were collected at the BM30A (ESRF) beamline. Phi scans were performed and data recorded with a large ADSC Q315r CCD detector. Data were collected at 0.8 Å for **3a** and **5a**, 0.85 Å for **2b** and **4a**, and were processed with the XDS package.[1]

The resolution of these structures requires overcoming difficulties that have more in common with macromolecular crystallography than with small molecule crystallography. This includes small crystal size and weak diffraction intensity, hence the frequent necessary use of synchrotron radiation to collect diffraction data at the limit of atomic resolution (0.9-1.1 Å). Very often, crystals contain a large volume fraction of disordered solvent areas and decorated quinoline monomers exhibit side chain statistical disorder. The structure of **4a** was solved by charge-flipping with Superflip,[2] whereas the five other structures were solved by direct methods using SHELXD included in the SHELXH 2013 module.[3] All

structures were refined by full-matrix least-squares methods using SHELXL,[3] WinGX[4] and the macromolecule graphic interface Coot.[5] Their refinement allowed building of models with R1 values between 10 and 13%. All the refined models are complete with the exception of **4a**, for which a few highly disordered isobutoxy side chains could not be fully built. Owing to the size of the molecules, and the thorough task of controlling bond angles and bond lengths, geometric restraints, generated with program PRODRG,[6] were applied to each model. The SQUEEZE procedure[7] implemented in PLATON was used for all structures in order to treat the regions with highly disordered solvent molecules (mainly chloroform, water, methanol, toluene or *n*-hexane molecules). Every time where solvent or side chain disorder could be modeled with partial occupancy, it was done so. SHELXL SIMU, DELU or RIGU restraints were used in the refinement strategy, when needed, as listed in the cif files. Hydrogen atoms were positioned theoretically on riding positions using AFIX command.

The final cif files were checked using IUCR's checkcif algorithm. Due to the characteristics of the crystals mentioned above (small size, large volume fractions of disordered solvent molecules, side chains disorder, weak diffraction intensity, incompleteness of the data and moderate resolution), a number of A-level and B-level alerts remain in the check cif file. These alerts are explicitly listed below and have been divided into two groups. They are inherent to the data and refinement procedures and do not reflect errors. Rather, they illustrate the limited practicality of the checkcif tool for medium size molecule crystallography.

GROUP 1 ALERTS

PLAT026_ALERT_3_B Ratio Observed / Unique Reflections (too) Low .

PLAT029_ALERT_3_A _diffrn_measured_fraction_theta_full Low ...

PLAT089_ALERT_3_B Poor Data / Parameter Ratio

THETM01_ALERT_3_B The value of sine(theta_max)/wavelength is less than

All these alerts in fact point to the same and unique problem which is the overall weak quality of the data and refinement statistics if compared to that expected for small molecule structures from highly diffracting crystals. They are inherent to the best quality crystals that can be grown from such compounds. Large units cells, especially when several independent molecules are found in the asymmetric unit (for **5a** and **4a**), high fraction volume of disordered solvent and disordered side chain content contribute to low average statistics. Data collection using synchrotron radiation (**3a**, **2b**, **5a** and **4a**) brings the benefit of improving diffraction intensity and collecting at higher resolution, but it also has drawbacks such as radiation damage or beamline data collection geometry which may preclude to collect at high $\theta_{max}$ values and which also limits data completeness as most beam lines are equipped with a single axis goniometer.

GROUP 2 ALERTS

PLAT222_ALERT_3_A Large Non-Solvent H Uiso(max)/Uiso(min) ...

PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds

PLAT234_ALERT_4_A Large Hirshfeld Difference

These A and B alerts are related to geometrical and atomic displacement parameters problems, all concerning side chains and solvent molecules, that result from the way these have been treated (see above) when they have not been squeezed out. As mentioned above, all the models have been restrained using PRODRG. Very often, inspection of residual electron density allowed to build alternate conformations of side chains, but further refinement needed to lower some of the thermal restraints like RIGU SIMU and DELU, in order to take into account disorder.

## 1.4 Experimental procedures

Commercial reagents were purchased from Sigma-Aldrich, Alfa-Aesar or TCI and were used without further purification unless otherwise specified. Tetrahydrofuran (THF) and dichloromethane (DCM) were dried over alumina columns; chloroform, triethylamine (TEA) and diisopropylethylamine (DIPEA) were distilled over calcium hydride ($CaH_2$) prior to use. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel 60-F254 plates and observed under UV light. Column chromatography purifications were carried out on Merck GEDURAN Si60 (40-63 µm). Preparative recycling GPC (gel permeation chromatography) was carried out on a set of 1H, 1.5H, 2.5H and 3H JAIGEL 20*600 mm columns (Japan Analytical Industry) in chloroform containing 0.5~1% ethanol as mobile phase, with a flow rate of 3.5 mL/min. The monitoring UV detector was a UV-600 NEXT. Exact high resolution mass measurements (HRMS) were carried out in the positive ion mode on a TOF spectrometer at the Mass Spectrometry Laboratory at the European Institute of Chemistry and Biology (UMS3033 & US001, IECB), Pessac, France.

**Methyl 4-(*tert*-butoxy)-8-nitroquinoline-2-carboxylate 7**. Methyl 8-nitro-4-oxo-1,4- dihydroquinoline-2-carboxylate[8] **6** (1.00 g, 4.03 mmol) was placed in a round-bottomed flask containing a magnetic stirring bar under $N_2$ atmosphere. The flask was wrapped with aluminum foil to protect from light and AgOAc (3.36 g, 20.15 mmol, 5 equiv) was then added and flushed with $N_2$ for 5 min. DCM (50 mL) was added *via* a syringe and the mixture was stirred vigorously for 5 min at room temperature. Then 2-methyl-2-bromo propane (1.81 mL, 16.12 mmol, 4 equiv.) was added drop-wise over 10 min. The mixture was stirred or 30 min at room temperature, and filtered through a pad of celite into a flask containing saturated aqueous $NaHCO_3$ (50 mL). Celite was washed with using DCM. Organic and aqueous layers were separated. The aqueous layer was one more time back-extracted with DCM (10 mL). The combined organic layers were washed with $H_2O$ (50 mL), brine (50 mL), dried on $Na_2SO_4$, filtered and evaporated to give the crude product **7** with 96% conversion as judged by $^1$H-NMR. Purification by column chromatography on $SiO_2$ eluting with DCM gave pure compound **7** (1.02 g, 83% yield) as a pale yellow solid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 8.43 (dd, $^3J$ = 8.4 Hz, $^3J$ = 1.5 Hz, 1 H), 8.07 (dd, $^3J$ = 7.5 Hz, $^3J$ = 1.5 Hz, 1 H), 7.82 (s, 1 H), 7.61 (dd, $^3J$ = 8.4 Hz, $^3J$ = 7.5 Hz, 1 H), 4.03 (s, 3 H), 1.70 (s, 9 H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.9, 160.6, 150.7, 148.5, 140.4, 127.1, 125.5 (2 C), 124.8, 106.5, 82.6, 53.3, 28.5 ppm. ESI-HRMS, *m/z* calcd $C_{15}H_{17}N_2O_5$ $[M + H]^+$ 305.1137, found 305.1133.

**Methyl 8-amino-4-(tert-butoxy)quinoline-2-carboxylate 8**. Pd/C (150 mg, 10% w/w) was added to a solution of compound **7** (1.5 g, 4.93 mmol) in 50 mL ethyl acetate under a $N_2$ atmosphere. $N_2$ was then exchanged with hydrogen (pressure provided by 2 hydrogen balloons) and the suspension was stirred for 12 h under positive pressure of hydrogen. The reaction mixture was filtered through celite and evaporated under reduced pressure to yield methyl 8-amino-4-(tert-butoxy)quinoline-2-carboxylate **8** as a flashy yellow solid (1.34 g, 99 %). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.68 (s, 1 H), 7.48 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.3 Hz, 1 H), 7.34 (t, $^3J$ = 8.4 Hz, 1 H), 6.91 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.3 Hz, 1 H), 5.10 (s, 2 H), 4.02 (s, 3 H), 1.64 (s, 9 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.5, 160.4, 145.2, 144.9, 138.9, 128.4, 125.5, 110.5 (2 C), 106.3, 81.1, 52.7, 28.7. ESI-HRMS, m/z calcd for $C_{15}H_{19}N_2O_3$ $[M+H]^+$ 275.1390. Found 275.1390.

**Dimer ester QX 10**. Quinolinecarboxylic acid **9** (1.36 g, 4.69 mmol) was converted into its acid chloride using oxalyl chloride as previously described.[8] The acid chloride was dissolved in dry DCM (5 mL) under a $N_2$ atmosphere and added to a solution of 8-amino-4-(tert-butoxy)quinoline- 2-carboxylate **8**, (1.35 g, 4.92 mmol) and N,N-diisopropylethylamine (4.29 mL, 24.6 mmol, 5 equiv.) in dry DCM (5 mL) maintaining an inert gas atmosphere. The reaction was stirred for 12h and then diluted with 50 mL DCM and the organic layer was successively washed with water, saturated aqueous $NaHCO_3$, water and brine (200 mL each). The organic phase was then dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was recrystallized from MeOH/$CHCl_3$ at -18 °C and collected by filtration (2.62 g, 97%). $^1$H NMR (300 MHz, $CDCl_3$) δ 11.89 (s, 1 H), 9.06 (dd, $^3J$ = 7.8, $^4J$ = 1.0 Hz, 1 H), 8.54 (dd, $^3J$ = 8.4, $^4J$ = 1.2 Hz, 1 H), 8.20 (dd, $^3J$ = 7.4, $^4J$ = 1.2 Hz, 1 H), 7.99 – 7.96 (m, 2 H), 7.82 (s, 1 H), 7.69 – 7.59 (m, 2 H), 4.22 (s, 3 H), 4.17 (d, $^3J$ = 6.5 Hz, 2 H), 2.40 – 2.27 (m, 1 H), 1.70 (s, 9 H), 1.17 (d, $^3J$ = 6.7 Hz, 6 H). $^{13}$C NMR (75 MHz, $CDCl_3$) *δ* 167.0, 163.2, 162.4, 160.5, 154.0, 147.9, 147.7, 140.2, 139.4, 134.9, 127.6, 126.6, 125.3, 124.6, 123.4, 118.5, 117.5, 106.5, 100.2, 81.5, 75.7, 53.6, 28.6 (2 C), 28.1, 19.2. ESI-HRMS, m/z calcd for $C_{29}H_{31}N_4O_7$ $[M+H]^+$ 547.2187. Found 547.2176?

**Dimer acid 11**. Crushed LiOH·$H_2O$ (115 mg, 2.68 mmol) was added to a stirring solution of dimer **10** (500 mg, 915 µmol) in 5.5 mL of THF/$H_2O$ (10/1 vol:vol) and the resulting slurry was stirred overnight at room temperature. The excess LiOH was subsequently quenched by adding 5% aqueous citric acid until the mixture became clear (pH ~5). The solution was then transferred to an extracting funnel and extracted with DCM (20 mL x 3). The combined organic layers were washed with water followed by brine. The organic phase was then dried over $MgSO_4$, filtered and evaporated to provide the desired compound as a yellow solid (440 mg, 90%). $^1$H NMR (300 MHz, $CDCl_3$) δ 11.67 (s, 1 H), 9.03 (d, $^3J$ = 7.6 Hz, 1 H), 8.41 (d, $^3J$ = 8.3 Hz, 1 H), 8.24 (d, $^3J$ = 7.6 Hz, 1 H), 7.97 (d, $^3J$ = 8.3 Hz, 1 H), 7.77 (s, 1 H), ), 7.72 (s, 1 H), 7.65 – 7.54 (m, 2 H), 4.08 (d, $^3J$ = 6.3 Hz, 2 H), 2.39 – 2.26 (m, 1 H), 1.69 (s, 9 H), 1.18 (d, $^3J$ = 6.7 Hz, 6 H). $^{13}$C NMR (75 MHz, $CDCl_3$) *δ* 166.6, 163.2, 161.9, 161.1, 153.4, 146.9, 139.1, 139.0, 134.0, 127.4, 127.0, 126.3, 125.4, 124.6, 123.1, 118.7, 117.7, 105.0, 99.7, 81.9, 75.6, 29.7, 28.6, 28.1, 19.2. ESI-HRMS, m/z calcd for $C_{28}H_{29}N_4O_7$ $[M+H]^+$ 533.2031. Found 533.2023.

**Tetramer QXQQ 13**. In an oven dried round-bottomed flask, dimer acid 1**1** (2.60 g, 4.88 mmol) was dissolved in 30 mL of dry DCM under an Argon atmosphere. Then, 1-Chloro-N,N-2-trimethylpropenylamine (1.30 mL, 9.82 mmol) was introduced and the reaction was stirred at room temperature for 2 h. Completion of the reaction was checked by $^1$H NMR. The solvent was then carefully removed and the residue was dried under a high vacuum line to give the corresponding acid chloride as a light yellow solid. This was dissolved in a minimum amount of dry DCM under a $N_2$ atmosphere and transferred to a stirring solution of dimer amine **12** (2.70 g, 5.23 mmol)[8] and N,N-diisopropylethylamine (1.70 mL, 10.0 mmol) in dry DCM (30 mL) at 0°C via a cannula over a period of 30 min. The resulting mixture was stirred at room temperature overnight. The reaction mixture was then diluted with DCM (20 mL) and the organic layer was washed successively with water, saturated aqueous $NaHCO_3$, water, aqueous HCl (0.1 M) and brine (50 mL each). The organic phase was then dried over $MgSO_4$, filtered and rotary evaporated. The crude product was flash chromatographed with DCM/MeOH (99:1 vol/vol) as eluent to yield the desired tetramer **16** as a light yellow solid (4.79 g, 95%). $^1$H NMR (300 MHz, $CDCl_3$) δ 12.32 (s, 1 H), 11.94 (s, 1 H), 11.67 (s, 1 H), 9.15 (dd, $^3J$ = 7.7 Hz, $^4J$ =1.2 Hz, 1 H), 8.57 (dd, $^3J$ = 8.3 Hz, $^4J$ = 1.5 Hz, 1 H), 8.37 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.2 Hz, 1 H), 8.14 (dd, $^3J$ = 7.53, $^4J$ = 1.23, 1 H), 8.06 – 7.99 (m, 3 H), 7.89 (dd, $^3J$ = 8.37, $^4J$ = 1.23, 1

H), 7.75 (t, $^3J$ = 8.16, 1 H), 7.63 – 7.57 (m, 2 H), 7.47 (s, 1 H), 7.39 (dd, $^3J$ = 8.31, $^3J$ = 7.59, 1 H), 7.28 – 7.23 (m, 1 H), 6.89 (s, 1 H), 6.69 (s, 1 H), 4.27 (bs, 2 H), 3.90 (d, $^3J$ = 6.66 Hz, 2 H), 3.85 (d, $^3J$ = 6.66, 2 H), 3.48 (s, 3 H), 2.56 – 2.42 (m, 1 H), 2.39 – 2.24 (m, 2 H), 1.83 (s, 9 H), 1.30 – 1.18 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 164.1, 163.2, 163.1, 162.9, 162.3, 161.6, 161.2, 160.5, 153.6, 150.3, 149.0, 145.7, 145.2, 139.2, 139.1, 139.0, 138.5, 135.2, 134.0, 133.7, 128.0, 127.9, 127.3, 126.5, 125.8, 124.2, 124.0, 123.8, 122.1, 121.9, 117.6, 117.0, 116.9, 116.7, 116.3, 115.9, 102.9, 100.5, 100.2, 97.6, 81.5, 75.7, 75.2, 75.1, 52.3, 28.7, 28.2 (2 C), 28.1, 19.3 (3 C). ESI-HRMS, m/z calcd for $C_{57}H_{58}N_8O_{11}$ $[M+H]^+$ 1031.4298. Found 1031.4287.

**Tetramer acid 14.** Tetramer ester **13** (200 mg, 194 µmol) was dissolved in THF/MeOH (9:1 vol/vol, 10 mL). KOH (871 mg, 15.5 mmol) was added to the stirring solution and the resulting mixture was stirred at room temperature for 30 min. Completion of the reaction was checked by TLC. Excess KOH was subsequently quenched by adding a 5% aqueous citric acid (down to pH ~5). Organic solvents were evaporated. The resulting slurry was diluted with DCM (30 mL) and was washed with brine (30 mL) followed by water (30 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure to obtain the desired acid as a yellow solid (195 mg, 99%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 12.15 (s, 1 H), 11.67 (s, 1 H), 11.40 (s, 1 H), 9.15 (dd, $^3J$ = 7.6 Hz, $^4J$ = 1.4 Hz, 1 H), 8.56 (dd, $^3J$ = 8.3 Hz, $^4J$ = 1.1 Hz, 1 H), 8.47 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.0 Hz, 1 H), 8.12 – 8.08 (m, 3 H), 8.01 (dd, $^3J$ = 8.5 Hz, $^4J$ = 1.1 Hz, 1 H), 7.93 (dd, $^3J$ = 8.5 Hz, $^4J$ = 1.1 Hz, 1 H), 7.76 (t, $^3J$ = 8.0, 1 H), 7.66 – 7.59 (m, 2 H), 7.42 – 7.40 (m, 2 H), 7.27 – 7.22 (m, 1 H), 6.93 (s, 1 H), 6.79 (s, 1 H), 4.25 (bs, 2 H), 3.93 – 3.90 (m, 4 H), 2.55 – 2.44 (m, 1 H), 2.38 – 2.27 (m, 2 H), 1.85 (s, 9 H), 1.30 – 1.17 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 163.6, 163.2, 162.9, 162.8, 162.0, 161.7, 161.3, 160.4, 153.4, 151.0, 148.5, 145.1, 144.8, 139.1, 139.0, 138.4, 137.6, 135.0, 133.4, 133.0, 128.3, 127.9, 127.5, 126.2, 125.9, 124.4, 124.3, 123.7, 122.5, 122.1, 118.2, 118.0, 117.6, 117.3, 116.4, 115.9, 103.7, 100.0, 98.7, 97.6, 81.8, 75.8, 75.6, 75.2, 28.7, 28.2, 28.1, 26.9, 19.3 (3 C). ESI-HRMS, m/z calcd for $C_{72}H_{73}N_{12}O_{12}$ $[M+H]^+$ 1017.4147. Found 1017.4143.

**Tetramer amine 15.** Tetramer **13** (2.12 g, 2.06 mmol) was dissolved in a mixture of EtOAc (200 mL) and ethanol (50 mL) under a $N_2$ atmosphere. Pd/C (10% w/w, 212 mg) and ammonium metavanadate (106 mg) were added to the solution at room temperature. The reaction mixture was then heated to 95°C (bath temperature) and an aqueous solution (10 mL) of ammonium formate (6.55 g, 104 mmol) was added slowly in five intervals (each interval is about 10 minutes). The mixture was further stirred for 24 h at 95°C maintaining the inert atmosphere. Completion of the reaction was checked by $^1$H-NMR of an aliquot. The solution was cooled down to room temperature and then filtered through celite. The filtrate was transferred to an extraction funnel and washed successively with water and brine (each 50 mL). The organic layer was collected, dried over $MgSO_4$, filtered and removed under reduced pressure to yield tetramer amine **15** as a yellow solid (2.03 g, 99%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 12.47 (s, 1 H), 11.98 (s, 1 H), 11.80 (s, 1 H), 9.06 (dd, $^3J$ = 7.6 Hz, $^4J$ = 1.0 Hz, 1 H), 8.43 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.1 Hz, 1 H), 8.05 - 8.00 (m, 3 H), 7.93 (s, 1 H), 7.83 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.1 Hz, 1 H), 7.72 (t, $J$ = 8.1, 1 H), 7.65 (t, $J$ = 8.0, 1 H), 7.54 (dd, $^3J$ = 8.2 Hz, $^4J$ = 1.0 Hz, 1 H), 7.31 (s, 1 H), 7.27 – 7.22 (m, 1 H), 7.02 (t, $^3J$ = 7.9 Hz, 1 H), 6.93 (s, 1 H), 6.69 (s, 1 H), 5.96 (dd, $^3J$ = 7.7 Hz, $^4J$ = 0.9 Hz, 1 H), 4.19 (s, 2 H), 3.91 (d, $^3J$ = 6.5 Hz, 2 H), 3.86 (d, $^3J$ = 6.4 Hz, 2 H), 3.78 (s, 2 H), 3.54 (s, 3 H), 2.52 – 2.41 (m, 1 H), 2.39 – 2.26 (m, 2 H), 1.84 (s, 9 H), 1.26 – 1.20 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 164.3, 164.0, 163.2, 163.0, 162.4, 161.6, 161.5, 160.8, 150.1, 149.8, 148.7, 145.5, 143.2, 139.2, 139.0, 138.3, 136.4, 134.8, 134.1, 133.8, 127.8, 127.5, 127.0, 124.0, 123.0, 122.0, 121.8, 117.2, 116.5, 116.4, 116.3, 116.2, 115.7,

110.0, 109.6, 102.6, 100.3, 98.7, 98.2, 81.7, 75.2, 75.2, 75.1, 52.3, 30.2, 28.7, 28.3, 28.2, 26.9, 19.4 (2 C), 19.3. ESI-HRMS, m/z calcd for $C_{57}H_{61}N_8O_9$ $[M+H]^+$ 1001.4556. Found 1001.4544.

**Dimethyl 4-((4-methoxybenzyl)oxy)pyridine-2,6-dicarboxylate 17.** Dimethyl chelidamate hydrochloride **16**[9] (5.20 g, 21.0 mmol) and $K_2CO_3$ (8.60 g, 62.2 mmol) were suspended in acetone (70 mL) under a $N_2$ atmosphere. 1-(Chloromethyl)-4-methoxybenzene 3.4 mL, 25.1 mmol) was then added and followed by NaI (790 mg, 5.27 mmol). The reaction mixture was heated to reflux for 12 h. After removal of the solvent, EtOAc (100 mL) was added and the suspension was filtered on a sintered glass funnel. The filtrate was then washed with water, dried over $MgSO_4$, filtered and evaporated to dryness. The solid product was then placed on a sintered glass filter funnel (porosity grade 3) and rinsed with petroleum ether followed by cold ether to yield the pure product (5.36 g, 77%). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.89 (s, 2 H), 7.36 (dd, $^3J$ = 8.7 Hz, 2 H), 6.94 (d, $^3J$ = 8.7 Hz, 2 H), 5.16 (s, 2 H), 4.01 (s, 6 H), 3.83 (s, 3 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.8, 165.2, 160.0, 149.8, 129.6, 126.7, 114.9, 114.3, 70.7, 55.3, 53.2. ESI-HRMS, m/z calcd for $C_{17}H_{18}NO_6$ $[M+H]^+$ 332.1129. Found 332.1131

**Methyl 6-(hydroxymethyl)-4-((4-methoxybenzyl)oxy)picolinate 18**. $NaBH_4$ (1.22 g, 32.2 mmol) was added to a stirred solution of compound **17** (5.35 g, 16.1 mmol) in a mixture of DCM (80 mL) and MeOH (100 mL) at 0 ˚C under a $N_2$ atmosphere. The reaction was stirred at 0 ˚C for 30 min and then at room temperature for 2 h. Completion of the reaction was monitored by TLC. The solution was then neutralized with 1 M HCl solution down to pH ~7. The mixture was extracted with DCM (3 x 30 mL). Organic layers were combined, dried over $MgSO_4$ and filtered. The solvent was removed by using a rotary evaporator to yield **18** (4.80 g, 98%). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, $^4J$ = 2.4 Hz, 1 H), 7.34 (d, $^3J$ = 8.7 Hz, 2 H), 7.08 (d, $^4J$ = 2.4 Hz, 1 H), 6.93 (d, $^3J$ = 8.7 Hz, 2 H), 5.11 (s, 2 H), 4.79 (s, 2 H), 3.99 (s, 3 H), 3.83 (s, 3 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.3, 165.5, 162.3, 159.8, 148.5, 129.4, 127.1, 114.1, 111.2, 109.9, 70.1, 64.7, 55.2, 52.9. ESI-HRMS, m/z calcd for $C_{16}H_{18}NO_5$ $[M+H]^+$ 304.1180. Found 304.1182

**Methyl 6-(azidomethyl)-4-((4-methoxybenzyl)oxy)picolinate 19**. To a solution of compound **18** (5.08 g, 16.7 mmol) in dry DMF (100 mL) were successively added $CBr_4$ (8.33 g, 25.1 mmol) and $PPh_3$ (6.59 g, 25.1 mmol) under a $N_2$ atmosphere. The reaction was stirred at room temperature for 1.5 hours under $N_2$. The disappearance of starting material was monitored by TLC. Then, $NaN_3$ (3.27 g, 50.3 mmol) was added to the flask in one portion and the mixture was further stirred for 12 h. Water (80 mL) was added to the reaction mixture which was ten extracted with EtOAc (3 x 50 mL). The organic phases were combined and evaporated. The crude product was purified by silica gel chromatography eluting with DCM/MeOH (400:1 vol/vol) to provide compound **19** (3.86 g, 70%). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, $^4J$ = 2.4 Hz, 1 H), 7.36 (d, $^3J$ = 8.7 Hz, 2 H), 7.15 (d, $^4J$ = 2.4 Hz, 1 H), 6.94 (d, $^3J$ = 8.7 Hz, 2 H), 5.11 (s, 2 H), 4.58 (s, 2 H), 3.99 (s, 3 H), 3.82 (s, 3 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.6, 165.4, 159.9, 158.0, 149.4, 129.5, 126.9, 114.2, 111.6, 111.3, 70.3, 55.5, 55.3, 53.1. ESI-HRMS, m/z calcd for $C_{16}H_{17}N_4O_4$ $[M+H]^+$ 319.1244. Found 319.1247

**6-(azidomethyl)-4-((4-methoxybenzyl)oxy)picolinic acid 20**. Water (20 mL) was added to a stirring solution of compound **19** (800 mg, 2.44 mmol) in THF (20 mL). Ground NaOH (300 mg, 7.5 mmol) was added in one portion and the reaction mixture was stirred for 6 h, i.e. until TLC showed full consumption of starting material. The mixture was then neutralized down to pH ~5 with aqueous citric acid (5% w/vol). Solvents were evaporated. The crude mixture was diluted with ethyl acetate (50 mL) and washed with water (50 mL) followed by brine (50 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated to provide the desired product (710 mg, 93%). $^1$H NMR (300 MHz, $CDCl_3$) δ

7.74 (d, $^4J$ = 2.3 Hz, 1 H), 7.36 (d, $^3J$ = 8.7, 2 H), 7.15 (d, $^4J$ = 2.3 Hz, 1 H), 6.94 (d, $^3J$ = 8.7, 2 H), 5.14 (s, 2 H), 4.48 (s, 2 H), 3.83 (s, 3 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 167.9, 164.2, 159.9, 156.3, 148.4, 129.5, 126.5, 112.7, 114.2, 109.5, 70.7, 55.2, 54.1. ESI-HRMS, m/z calcd for $C_{15}H_{15}N_4O_4$ $[M+H]^+$ 315.1088. Found 315.1091.

**Turn T (22).** Hydrazine (2 mL) was added to a stirred solution of compound **21**[10] (500 mg, 1.18 mmol) in ethanol (10 mL) under a $N_2$ atmosphere. The mixture was then heated to 90 °C for 24 h. The reaction mixture was cooled down to room temperature and water was added to it. The resulting suspension was filtered to yield the pure product which was dried in a desiccator (340 mg, 85%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.19 (s, 2H), 7.83 (s, 2H), 4.17 (d, $^3J$ = 3.5 Hz, 4 H), 3.96 (d, $^3J$ = 6.5 Hz, 4 H), 2.15 - 2.13(m, 2H), 1.08 (d, $^3J$ = 6.7 Hz, 12 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 165.4, 150.9, 123.1, 115.8, 76.3, 28.2, 19.4. ESI-HRMS, m/z calcd for $C_{57}H_{61}N_8O_9$ $[M+H]^+$ 339.2027. Found 339.2029.

**Pentamer YQXQQ 23.** In an oven dried round-bottomed flask, tetramer amine **15** (2.54 g, 2.54 mmol), pyridine **20** (797 mg, 2.54 mmol) and PyBOP (6.54 g, 12.6 mmol) were dissolved in 50 mL anhydrous DCM under an inert atmosphere. *N,N*-diisopropylethylamine (2.5 mL, 14.7 mmol) was then added and the mixture was stirred for 14 days at room temperature maintaining the inert atmosphere. The solution was diluted with 500 mL EtOAc and the organic layer was washed with brine solution (3 x 150 mL), dried over $MgSO_4$, filtered and removed. The product was purified by silica gel chromatography eluting with cyclohexane/EtOAc (7:3 vol/vol) to provide 860 mg (26% yield) of pentamer **23** as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 12.09 (s, 1 H), 11.86 (s, 1 H), 11.82 (s, 1 H), 11.43 (s, 1 H), 8.49-8.45 (m, 2 H), 8.15 (dd, $^3J$ = 7.6 Hz, $^4J$ = 1.0 Hz, 1 H), 8.11 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.0 Hz, 1 H), 8.06 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.1 Hz, 1 H), 8.01 (dd, $^3J$ = 8.2 Hz, $^4J$ = 1.1 Hz, 1 H), 7.99 (dd, $^3J$ = 8.2 Hz, $^4J$ = 1.1 Hz, 1 H), 7.90 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.1 Hz, 1 H), 7.74 (s, 1 H), 7.65 (t, $^3J$ = 8.0, 1 H), 7.55 – 7.49 (m, 3 H), 7.44 (d, $^4J$ = 2.3 Hz, 1 H), 7.39 (s, 1 H), 7.35 – 7.29 (m, 2 H), 7.04 (d, $^3J$ = 8.7 Hz, 2 H), 6.85 (s, 1 H), 6.80 (d, $^4J$ = 2.3 Hz, 1 H), 6.66 (s, 1 H), 5.23 (s, 2 H), 4.41 – 4.36 (m, 1 H), 4.24 – 4.15 (m, 1 H), 3.97 – 3.93 (m, 2 H), 3.88 (s, 3 H), 3.84 (d, $^4J$ = 6.2 Hz, 2 H), 3.40 (s, 3 H), 3.26 (d, $J$ = 15.0 Hz, 1 H), 2.65 (d, $J$ = 15.0 Hz, 1 H), 2.59 – 2.48 (m, 1 H), 2.40 – 2.26 (m, 2 H), 1.86 (s, 9 H), 1.32 – 1.19 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.9, 164.2, 163.4, 163.2, 162.3, 162.1, 161.6, 161.5, 161.0, 160.5, 159.8, 155.7, 151.7, 150.1, 149.8, 149.0, 145.5, 139.1, 138.3, 138.0, 137.8, 134.0, 133.6 (2 C), 129.4, 127.6 (2 C), 127.2, 127.1, 126.7, 123.6, 122.4, 122.0, 121.8, 117.1 (2 C), 117.0, 116.7, 116.4, 116.2 (2 C), 116.1, 114.3, 111.0, 107.6, 102.1, 100.3, 99.5, 98.0, 81.7, 75.4, 75.2, 75.0, 70.3, 55.4, 53.8, 53.4, 52.2, 28.5, 28.3, 28.2, 19.4 (2 C), 19.3. ESI-HRMS, m/z calcd for $C_{72}H_{73}N_{12}O_{12}$ $[M+H]^+$ 1297.5465. Found 1297.5449.

**Pentamer amine 24.** A catalytic amount of Pd/C (10% w/w, 87 mg) and pyridine (27 µL, 0.34 mmol) as a mild catalyst poison to prevent benzyl group hydrogenolysis, were added to a stirred solution of pentamer **23** (873 mg, 673 µmol) in ethyl acetate (50 mL). The mixture was stirred overnight under a hydrogen atmosphere at room temperature. After the reaction had been completed, as checked by $^1$H NMR of an aliquot, the mixture was filtered through celite and the celite was washed with EtOAc (150 mL). The solvent was evaporated and the crude product was purified by silica gel chromatography eluting with MeOH/DCM (1:50 vol/vol) to obtain amine **24** as a yellow solid (713 mg, 83%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 12.06 (s, 1 H), 11.82 (s, 1 H), 11.81 (s, 1 H), 11.43 (s, 1 H), 8.47 – 8.43 (m, 2 H), 8.15 – 8.11 (m, 2 H), 8.06 (dd, $^3J$ = 8.5 Hz, $^4J$ = 1.2 Hz, 1 H), 8.00 – 7.96 (m, 2 H), 7.88 – 7.85 (m, 1 H), 7.73 (s, 1 H), 7.64 (t, $^3J$ = 8.0 Hz, 1 H), 7.54 – 7.48 (m, 3 H), 7.38 (s, 2 H), 7.31– 7.28 (m, 2 H), 7.03 (d, $^3J$ = 8.7 Hz, 2 H), 6.85 (s, 1 H), 6.75 (d, $^4J$ = 2.3 Hz, 1 H), 6.64 (s, 1 H), 5.20 (s, 2 H), 4.40 – 4.35 (m, 1

H), 4.20 – 4.14 (m, 1 H), 3.95 (t, *J* = 6.0 Hz, 2 H), 3.87 (s, 3 H), 3.83 (d, *J* = 6.8 Hz, 2 H), 3.40 (s, 3 H), 2.70 (d, *J* = 15.4 Hz, 1 H), 2.56 – 2.47 (m, 1 H), 2.45 – 2.37 (m, 1 H), 2.40 – 2.23 (m, 2 H), 1.83 (s, 9 H), 1.66 (bs, 2 H), 1.32 – 1.19 (m, 18 H). ESI-HRMS, m/z calcd for $C_{72}H_{75}N_{10}O_{12}$ $[M+H]^+$ 1271.5560. Found 1271.5546.

**Acetylated pentamer 25.** DIPEA (1.30 mL, 7.64 mmol) and acetic anhydride (718 µL, 7.61 mmol) were successively added to a solution of pentamer amine **24** (484 mg, 381 µmol) in dry $CHCl_3$ (8 mL) under a $N_2$ atmosphere. The reaction mixture was stirred at room temperature for 3 h and then the solvent was evaporated. The crude product was purified by silica gel chromatography eluting with cyclohexane/EtOAc (3:2 vol/vol) to provide 464 mg (93% yield) of **25** a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 12.03 (s, 1 H), 11.83 (s, 1 H), 11.83 (s, 1 H), 11.42 (s, 1 H), 8.47 (t, $^3J$ = 8.1 Hz, 2 H), 8.09 – 8.04 (m, 3 H), 8.01 – 7.96 (m, 2 H), 7.87 (dd, $^3J$ = 8.4 Hz, $^4J$ =1.1 Hz, 1 H), 7.70 (s, 1 H), 7.64 (t, $^3J$ = 8.1 Hz, 1 H), 7.55 (d, $^3J$ = 8.0 Hz, 1 H), 7.48 (d, $^3J$ = 8.7 Hz, 2 H), 7.40 (bs, 1 H), 7.37 (s, 1 H), 7.31 – 7.25 (m, 2 H), 7.03 (d, $^3J$ = 8.7 Hz, 2 H), 6.84 (s, 1 H), 6.62 (s, 1 H), 6.60 (d, $^4J$ = 2.3 Hz, 1 H), 6.11 – 6.10 (m, 1 H), 5.22 (s, 2 H), 4.41 – 4.36 (m, 1 H), 4.20 – 4.15 (m, 1 H), 3.98 – 3.81 (m, 9 H), 3.38 (s, 3 H), 2.46 – 2.46 (m, 1 H), 2.40 – 2.27 (m, 2 H), 1.85 (s, 9 H), 1.39 (s, 3 H), 1.33 – 1.18 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 169.0, 166.6, 164.0, 163.5, 163.1, 162.3, 162.0, 161.6, 161.5, 160.9, 160.3, 159.8, 155.7, 151.0, 150.2, 149.8, 148.9, 145.4, 138.9, 138.2, 138.0, 137.7, 133.9, 133.5, 133.3, 133.1, 129.3, 127.5, 127.2, 127.0, 126.8, 123.6, 122.4, 121.9, 121.7, 117.1, 117.1, 117.0, 116.4, 116.2, 116.0, 114.2, 110.9, 108.1, 102.0, 100.2, 99.6, 97.9, 81.9, 75.5, 75.2, 75.0, 70.3, 55.3, 52.1, 43.4, 42.4, 30.1, 28.5, 28.2, 28.2, 26.8, 22.2, 19.4, 19.4, 19.3, 19.3, 19.3, 19.2. ESI-HRMS, m/z calcd for $C_{74}H_{76}N_{10}O_{13}$ $[M+H]^+$ 1313.5666. Found 1313.5653.

**Pentamer acid 26.** Crushed KOH (1.13 g, 20.1 mmol) was added to a stirring solution of pentamer **25** (330 mg, 251 µmol) in THF/MeOH (9:1 vol/vol, 20 mL) and the resulting mixture was stirred at room temperature for 30 min. After completion of the reaction, as checked by TLC, excess KOH was quenched upon adding 5% aqueous citric acid down to pH ~ 5. The organic solvents were evaporated, the slurry was diluted with DCM (30 mL). The organic phase was then washed with brine (30 mL) followed by water (30 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure to yield the desired acid as a yellow solid (305 mg, 93%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.89 (s, 1 H), 11.86 (s, 1 H), 11.46 (s, 1 H), 11.25 (s, 1 H), 8.58 (d, $^3J$ = 7.4 Hz, 1 H), 8.48 (d, $^3J$ = 7.5 Hz, 1 H), 8.12 – 8.06 (m, 4 H), 8.01 (d, $^3J$ = 8.3 Hz, 1 H), 7.92 (d, $^3J$ = 8.5 Hz,1 H), 7.80 (s, 1 H), 7.69 (t, $^3J$ = 8.0, 1 H), 7.56 (d, $^3J$ = 8.0 Hz, 1 H), 7.50 (d, $^3J$ = 8.7 Hz, 2 H), 7.43 (d, $^4J$ = 2.2 Hz, 1 H), 7.34 (s, 1 H), 7.30 (d, $^3J$ = 8.1 Hz, 2 H), 7.04 (d, $^3J$ = 8.7, 2 H), 6.91 (s, 1 H), 6.73 (s, 1 H), 6.62 (d, $^4J$ = 2.1 Hz, 1 H), 6.02 – 5.99 (m, 1 H), 5.21 (s, 2 H), 4.40 – 4.35 (m, 1 H), 4.19 – 4.14 (m, 1 H), 3.99 – 3.78 (m, 9 H), 2.57 – 2.47 (m, 1 H), 2.41 – 2.29 (m, 2 H), 1.86 (s, 9 H), 1.43 (s, 3 H), 1.31 – 1.22 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) 169.0, 166.6, 163.6, 163.5, 163.3, 162.1, 162.0, 161.7, 161.4, 160.8, 160.4, 159.9, 156.0, 150.9, 150.6, 149.9, 148.5, 144.6, 138.1, 137.9, 137.7, 137.5, 133.4, 133.3, 133.0, 132.8, 129.3, 127.7, 127.5 (2 C), 127.0, 126.8, 124.0, 122.3, 122.3, 122.0, 118.1, 117.7, 117.6, 117.0, 117.0, 116.2, 116.1, 116.0, 114.3, 111.0, 108.2, 102.9, 99.4, 98.5, 98.0, 82.3, 75.6, 75.5, 75.3, 70.3, 55.4, 42.6, 29.7, 28.6, 28.2, 28.2, 28.1, 22.3, 19.4, 19.3. ESI-HRMS, m/z calcd for $C_{72}H_{73}N_{12}O_{12}$ $[M+H]^+$ 1299.5515. Found 1299.5518.

**Nonamer Q<u>X</u>QQ<u>Y</u>Q<u>X</u>QQ 5b.** PyBOP (217 mg, 417 µmol) was added to a well stirred solution of pentamer amine **24** (178 mg, 140 µmol), tetramer acid **14** (142 mg, 140 µmol) and DIPEA (242 µL, 1.42 mmol) in anhydrous DCM (10 mL) under an inert atmosphere. The resulting solution was stirred

overnight at room temperature. After completion of the reaction as checked by TLC, the solvent was evaporated. The crude product was purified by silica gel chromatography eluting with cyclohexane/EtOAc (3:2 vol/vol) to provide desired **5b** (120 mg, 38%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 11.57 (s, 1 H), 11.35 (s, 1 H), 11.31 (s, 1 H), 11.02 (s, 1 H), 10.85 (s, 1 H), 10.82 (s, 1 H), 10.50 (s, 1 H), 8.35 (d, $^3J$ = 7.5 Hz, 1 H), 8.29 (dd, $^3J$ = 8.3 Hz, $^4J$ = 1.5 Hz, 1 H), 8.16 – 8.13 (m, 2 H), 7.99 (d, $^3J$ = 7.9 Hz, 1 H), 7.96 (d, $^3J$ = 7.7 Hz, 1 H), 7.91 – 7.87 (m, 2 H), 7.85 – 7.79 (m, 2 H), 7.73 – 7.63 (m, 5 H), 7.57 (s, 1 H), 7.50 (dd, $^3J$ = 7.6 Hz, $^4J$ =1.2 Hz, 1 H), 7.46 (dd, $^3J$ = 7.7 Hz, $^4J$ =1.2 Hz, 1 H), 7.32 – 7.27 (m, 3 H), 7.25 – 7.21 (m, 2 H), 7.17 – 7.07 (m, 5 H), 7.07 – 6.97 (m, 3 H), 6.91 (t, $^3J$ = 8.0 Hz, 1 H), 6.80 (d, $^4J$ =2.2 Hz, 1 H), 6.62 (d, $^4J$ =2.2 Hz, 1 H), 6.58 (s, 1 H), 6.47 (s, 1 H), 6.40 (s, 1 H), 5.93 (s, 1 H), 5.82 (s, 1 H), 5.26 (s, 2 H), 4.13 – 4.02 (m, 2 H), 3.97 – 3.90 (m, 5 H), 3.85 – 3.74 (m, 5 H), 3.70 – 3.63 (m, 3 H), 3.53 (dd, $J$ = 9.0, 7.0 Hz, 1 H), 3.37 (dd, $J$ = 17.7, 3.4 Hz, 1 H), 3.18 (s, 3 H), 2.52 – 2.14 (m, 6 H), 1.78 (s, 9 H), 1.72 (s, 9 H), 1.32 – 1.08 (m, 36 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 165.8, 163.7, 162.7, 162.4, 162.3, 162.1, 162.0, 161.9, 161.8, 161.1, 161.1, 160.6, 160.4, 159.9, 159.7, 159.3, 158.9, 158.4, 154.4, 153.1, 149.6, 149.4, 149.2, 149.0, 148.5, 148.1, 147.7, 144.9, 144.6, 138.5, 138.1, 137.9, 137.9, 137.7, 137.5, 137.1, 133.7, 133.4, 133.3, 133.1, 132.8, 132.6, 132.5, 129.2, 128.2, 127.7, 127.2, 126.8, 126.6, 126.1, 125.9, 125.4, 125.2, 123.8, 123.7, 123.6, 123.4, 121.9, 121.8, 121.7, 121.5, 121.2, 117.0, 117.0, 116.7, 116.6, 116.5, 116.5, 116.3, 116.3, 116.0, 115.9, 115.6, 115.5, 115.4, 114.3, 111.8, 107.4, 102.5, 102.2, 99.9, 99.9, 98.8, 97.9, 97.6, 97.3, 81.4, 81.1, 75.4, 75.0, 74.9, 74.8, 74.7, 70.0, 55.4, 51.9, 42.8, 28.6, 28.6, 28.5, 28.5, 28.1, 28.0, 28.0, 27.9, 19.5, 19.5, 19.5, 19.4, 19.4, 19.4, 19.3, 19.3, 19.2, 19.2, 19.1. ESI-HRMS, m/z calcd for $C_{128}H_{129}N_{18}O_{22}$ $[M+H]^+$ 2270.9562. Found 2270.9533.

**Decamer YQXQQYQXQQ 4b.** In an oven dried round-bottomed flask, pentamer amine **24** (158 mg, 124 μmol), pentamer acid **26** (161 mg, 124 μmol) and DIPEA (97 μL, 570 μmol) were dissolved in anhydrous DCM (5 mL) under a $N_2$ atmosphere. PyBOP (193 mg, 371 μmol) was added and the mixture was further stirred overnight at room temperature maintaining the inert atmosphere. The solvent was evaporated and the crude product was purified by silica gel chromatography eluting with cyclohexane/EtOAc (1:1 vol/vol) to provide **4b** (216 mg, 68%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 11.53 (s, 1 H), 11.28 (s, 1 H), 11.20 (s, 1 H), 11.06 (s, 1 H), 10.85 (s, 1 H), 10.83 (s, 1 H), 10.65 (s, 1 H), 10.41 (s, 1 H), 8.07 (dd, $^3J$ = 7.6 Hz, $^4J$ = 1.1 Hz, 1 H), 7.99 – 7.95 (m, 3 H), 7.90 (bs, 1 H), 7.88 – 7.84 (m, 2 H), 7.82 – 7.76 (m, 2 H), 7.74 (dd, $^3J$ = 8.9 Hz, $^4J$ = 1.1 Hz, 1 H), 7.72 – 7.65 (m, 5 H), 7.59 (d, $^3J$ = 8.6 Hz, 2 H), 7.53 (s, 1 H), 7.41 – 7.29 (m, 6 H), 7.19 (t, $^3J$ = 8.0 Hz, 1 H), 7.15 – 7.06 (m, 5 H), 7.03 – 6.98 (m, 4 H), 6.96 – 6.90 (m, 2 H), 6.85 (t, $^3J$ = 8.4 Hz, 1 H), 6.67 (d, $^4J$ = 2.2 Hz, 1 H), 6.59 (d, $^4J$ = 2.2 Hz, 1 H), 6.57 (s, 1 H), 6.50 (s, 1 H), 6.38 (s, 1 H), 6.36 (d, $^4J$ = 2.1 Hz, 1 H), 5.89 (s, 1 H), 5.76 (s, 1 H), 5.65 – 5.62 (m, 1 H), 5.21 (s, 2 H), 5.08 – 4.99 (m, 2 H), 4.13 (dd, $^2J$ = 8.8 Hz, $^3J$ = 6.2 Hz, 1 H), 4.08 – 4.03 (m, 1 H), 3.99 – 3.94 (m, 2 H), 3.90 (s, 3 H), 3.83 (s, 3 H), 3.81 – 3.74 (m, 4 H), 3.70 – 3.58 (m, 5 H), 3.28 – 3.21 (m, 1 H), 3.17 (s, 3 H), 2.54 – 2.13 (m, 7 H), 1.99 (d, $^3J$ = 17.4 Hz, 1 H), 1.76 (s, 9 H), 1.74 (s, 9 H), 1.33 (s, 3 H), 1.31 – 1.07 (m, 36 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 168.6, 166.1, 165.6, 163.6, 162.9, 162.6, 162.3, 162.1, 161.9, 161.8, 161.7, 161.4, 161.1, 160.9, 160.6 (2 C), 160.3, 159.8, 159.7 (2 C), 159.0, 158.7, 158.1, 155.4, 154.1, 150.6, 149.8, 149.6, 149.1, 149.0, 148.9, 148.4, 148.1, 147.4, 144.8, 138.4, 137.8, 137.6, 137.5, 137.4, 137.1, 137.0 (2 C), 133.3, 133.0, 132.9, 132.6 (3 C), 132.4, 132.0, 129.2, 128.9, 128.0, 127.3, 127.2, 126.7, 126.4, 126.3, 126.0, 125.8, 125.5, 125.4, 123.5, 123.4, 122.0, 121.9, 121.4 (3 C), 121.2, 117.4, 117.2, 116.8, 116.7, 116.6, 116.4 (2 C), 116.2, 115.9 (2 C), 115.6 (2 C), 115.5 (2 C), 115.3, 114.2, 114.0, 111.7, 110.4, 107.8, 107.1, 102.3, 101.2, 99.8, 99.3, 98.8, 97.7, 97.6, 81.4, 81.3, 75.1, 75.0, 74.8 (2 C), 74.7, 74.6, 70.0, 69.8, 55.3, 55.2,

51.8, 42.8, 41.9, 28.5, 28.3, 28.1, 28.0 (2 C), 27.9, 21.9, 19.5, 19.4 (2 C), 19.3 (2 C), 19.2, 19.1 (3 C). ESI- HRMS, m/z calcd for $C_{145}H_{147}N_{20}O_{24}$ $[M+H]^+$ 2553.0852, $[M+2H]^{2+}$ 1277.0426. Found $[M+H]^+$ 2553.0913 $[M+2H]^{2+}$ 1277.0483.

**Deprotected nonamer QXQQYQXQQ 5a.** TFA (1 mL) was added to a stirred solution of **5b** (50.0 mg, 22.0 µmol) in $CHCl_3$ (3 mL). After complete deprotection (2 h as checked by TLC), all volatiles were evaporated and the crude product was purified by silica gel chromatography eluting with MeOH/DCM (1:10 vol/vol) to provide deprotected nonamer **5a** (30 mg, 67%) as a yellow solid. $^1$H NMR (700 MHz, $CDCl_3$, 273 K) δ 12.08 (s, 1 H), 11.88 (s, 1 H), 11.69 (s, 1 H), 11.38 (s, 1 H), 11.28 (s, 1 H), 11.21 (s, 1 H), 11.00 (s, 1 H), 10.79 (s, 1 H), 10.21 (s, 1 H), 9.85 (s, 1 H), 8.58 (s, 1 H), 8.51 (d, *J* = 8.1 Hz, 1 H), 8.38 – 8.36 (m, 1 H), 8.20 (d, *J* = 7.8 Hz, 1 H), 8.15 - 8.13 (m, 2 H), 8.11 – 8.09 (m, 1 H), 8.06 (s, 1 H), 8.04 (d, *J* = 7.1 Hz, 1 H), 8.01 (d, *J* = 6.8 Hz, 1 H), 7.99 – 7.97 (m, 2 H), 7.94 (d, *J* = 7.5 Hz, 1 H), 7.82 (d, *J* = 8.1 Hz, 1 H), 7.72 (dd, *J* = 8.3, 1.2 Hz, 1 H), 7.65 (d, *J* = 7.5 Hz, 1 H), 7.62 (t, *J* = 7.5 Hz, 1 H), 7.60 – 7.59 (m, 2 H), 7.51 (t, *J* = 7.5 Hz, 1 H), 7.45 – 7.41 (m, 1 H), 7.37 – 7.35 (m, 2 H), 7.32 (s, 1 H), 7.30 – 7.28 (m, 2 H), 7.22 (t, *J* = 7.2 Hz, 1 H), 7.17 – 7.15 (m, 1 H), 7.11 – 7.08 (m, 1 H), 6.96 (s, 1 H), 6.95 (d, *J* = 1.9 Hz, 1 H), 6.64 (s, 1 H), 6.45 (s, 1 H), 5.72 (s, 1 H), 5.42 (s, 1 H). Only the aromatic region is mentioned. The aliphatic region is not reported. It is too difficult to analyze the spectrum as the compound consists of a mixture of three aggregated species. IMS-HRMS, m/z calcd for $C_{112}H_{104}N_{18}O_{21}$ $[M+2H]^{2+}$ 1019.8907. Found 1019.9790. Calcd for $[2M+3H]^{2+}$ 1359.5183. Found 1359.6170.

**Deprotected decamer YQXQQYQXQQ 4a.** TFA (1 mL) was added to a stirred solution of **4b** (65.0 mg, 25.5 µmol) in $CHCl_3$ (3 mL). After complete deprotection (2 h as checked by TLC), all volatiles were evaporated and the crude product was purified by silica gel chromatography eluting with MeOH/DCM (1:10 vol/vol) to provide deprotected decamer **4a** (40 mg, 71%) as a yellow solid. $^1$H NMR (700 MHz, $CDCl_3$, 273 K) δ 12.04 (s, 1 H), 11.54 (s, 1 H), 11.53 (s, 1 H), 11.40 (s, 1 H), 11.17 (s, 1 H), 11.14 (s, 1 H), 11.12 (s, 1 H), 10.98 (s, 1 H), 10.87 (s, 1 H), 9.96 (s, 1 H), 9.69 (s, 1 H), 8.30 (s, 1 H), 8.25 (d, $^3J$ = 7.7 Hz, 1 H), 8.03 – 7.97 (m, 7 H), 7.94 (d, $^3J$ = 7.9 Hz, 1 H), 7.90 (d, $^3J$ = 7.9 Hz, 1 H), 7.88 (d, $^3J$ = 7.9 Hz, 1 H), 7.84 (s, 1 H), 7.77 (d, $^3J$ = 7.8 Hz, 2 H), 7.70 – 7.66 (m, 3 H), 7.63 (d, $^3J$ = 7.4 Hz, 1 H), 7.59 (t, $^3J$ = 7.4 Hz, 1 H), 7.45 (t, $^3J$ = 7.4 Hz, 1 H), 7.40 (t, $^3J$ = 7.8 Hz, 1 H), 7.32 – 7.29 (m, 2 H), 7.22 (s, 1 H), 7.14 (s, 1 H), 7.07 – 7.03 (m, 3 H), 7.00 (s, 1 H), 6.98 (s, 1 H), 6.77 (s, 1 H), 6.70 (t, $^3J$ = 7.3 Hz, 1 H), 6.58 (s, 1 H), 6.55 (d, $^3J$ = 6.7 Hz, 1 H), 6.48 (s, 1 H), 6.09 (bs, 1 H), 5.72 (s, 1 H), 5.26 (s, 1 H), 4.27 (t, $^3J$ = 7.5 Hz, 1 H), 4.24 (bs, 2 H), 4.08 (t, $^3J$ = 7.5 Hz, 1 H), 4.06 – 4.03 (m, 1 H), 3.95 (t, $^3J$ = 6.1 Hz, 1 H), 3.90 – 3.83 (m, 4 H), 3.77 – 3.75 (m, 1 H), 3.71 (bs, 2 H), 3.49 – 3.46 (m, 4 H), 3.37 (t, $^3J$ = 6.8 Hz, 1 H), 2.62 – 2.58 (m, 2 H), 2.48 – 2.48 (m, 2 H), 2.31 – 2.27 (m, 2 H), 2.22 – 2.17 (m, 1 H), 1.42 – 1.06 (m, 39 H). $^{13}$C NMR (75 MHz, $CDCl_3$) *δ* 168.7, 166.2, 165.7, 163.7, 163.0, 162.7, 162.4, 162.2, 162.0, 161.9, 161.8, 161.5, 161.2, 161.0, 160.7 (2 C), 160.4, 159.9, 159.7, 159.1, 158.8, 158.2, 155.4, 154.2, 150.7, 149.9, 149.7, 149.2, 149.1, 149.0, 148.5, 148.2, 147.5, 144.9, 138.5, 137.9, 137.7, 137.6, 137.5, 137.2, 137.1(2 C), 133.4, 133.0, 132.7, 132.6, 132.5, 132.1, 129.3, 129.0, 128.1, 127.4, 127.2, 126.8, 126.5, 126.4, 126.1, 125.9, 125.6, 125.5, 123.6, 123.4, 122.1, 121.9, 121.5 (2 C), 121.2, 117.5, 117.3, 116.9, 116.8, 116.7, 116.5 (2 C), 116.3, 116.0 (2 C), 115.7 , 115.6 (2 C), 115.4, 114.3, 114.1, 111.8, 110.4, 107.9, 107.2, 102.4, 101.3, 99.9, 99.4, 98.9, 97.7 (2 C), 81.5, 81.3, 75.2, 75.1, 74.9 (2 C), 74.8, 74.7, 70.1, 69.9, 55.4, 55.3, 51.9, 42.9, 42.0, 28.6, 28.4, 28.1 (2 C), 28.0 (2 C), 22.0, 19.5 (4 C), 19.4 (3 C), 19.3, 19.2 (2 C), 19.1. IMS-Ms m/z calcd for $C_{121}H_{114}N_{20}O_{22}$ $[3M+4H]^{4+}$ 1651.1424. Found 1651.9090. Calcd for $[2M+3H]^{3+}$ 1467.5711. Found 1468.2520.

**Decamer acid 28.** KOH (362 mg, 6.54 mmol) was added to a stirred solution of decamer **4b** (206 mg, 80.6 µmol) in THF/MeOH (9:1 vol/vol, 15 mL). The reaction was stirred for 30 min at room temperature. Then it was neutralized by adding 5% aqueous citric acid down to pH ~ 5. The organic solvents were evaporated. The crude mixture was taken up in DCM (30 mL) and brine (30 mL). The layers were separated and the organic phase was further washed with water (30 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure to obtain the desired product as a yellow solid (198 mg, 97%). $^1$H NMR (300 MHz, $CDCl_3$, 273 K) δ 11.32 (s, 1 H), 11.19 (s, 1 H), 11.03 (s, 1 H), 10.84 (s, 1 H), 10.81 (s, 1 H), 10.70 (s, 1 H), 10.65 (s, 1 H), 10.35 (s, 1 H), 8.04 – 8.03 (m, 1 H), 8.01 – 8.00 (m, 1 H), 7.99 – 7.96 (m, 1 H), 7.95 (dd, $^3J$ = 8.3 Hz, $^4J$ = 1.3 Hz, 1 H), 7.89 – 7.89 (m, 1 H), 7.86 – 7.84 (m, 2 H), 7.80 (dd, $^3J$ = 8.3 Hz, $^4J$ = 1.1 Hz, 1 H), 7.76 – 7.71 (m, 5 H), 7.68 (td, *J* = 3.4 Hz, *J* = 1.2 Hz, 2 H), 7.65 – 7.64 (m, 1 H), 7.60 (s, 1 H), 7.57 (d, $^3J$ = 8.7 Hz, 2 H), 7.41 – 7.38 (m, 2 H), 7.35 (d, $^3J$ = 8.7 Hz, 2 H), 7.31 (td, *J* = 8.3 Hz, *J* = 1.8 Hz, 2 H), 7.16 (d, $^3J$ = 8.1 Hz, 1 H), 7.14 – 7.04 (m, 6 H), 7.02 – 6.99 (m, 1 H), 6.97 – 6.90 (m, 5 H), 6.84 (t, $^3J$ = 8.0 Hz, 1 H), 6.67 (d, *J* = 2.2 Hz, 1 H), 6.58 (s, 1 H), 6.56 (d, *J* = 2.2 Hz, 1 H), 6.46 (s, 1 H), 6.44 (s, 1 H), 6.36 (d, *J* = 2.2 Hz, 1 H), 5.88 (s, 1 H), 5.72 (s, 1 H), 5.66 (dd, $^3J$ = 6.6 Hz, $^4J$ = 2.3 Hz, 1 H), 5.20 (d, *J* = 2.1 Hz, 2 H), 5.02 (d, *J* = 3.9 Hz, 2 H), 4.14 – 4.09 (m, 1 H), 4.04 – 3.99 (m, 1 H), 3.95 – 3.93 (m, 2 H), 3.89 (s, 3 H), 3.83 (s, 3 H), 3.78 – 3.56 (m, 9 H), 3.27 (dd, *J* = 17.6 Hz, *J* = 3.7 Hz, 1 H), 2.52 – 2.14 (m, 6 H), 1.76 (s, 9 H), 1.74 (s, 9 H), 1.32 (s, 3 H), 1.30 – 1.07 (m, 36 H). $^{13}$C NMR (75 MHz, $CDCl_3$) *δ* 168.7, 166.1, 165.6, 162.9, 162.8, 162.6, 162.2, 162.0, 161.8, 161.7, 161.6 (2 C), 161.5, 160.8, 160.6, 160.5, 160.1, 159.8, 159.7 (2 C), 158.8, 158.7, 158.1, 155.5, 154.2, 150.5, 149.8, 149.6, 149.5, 149.0, 148.8, 148.0, 147.8, 147.4, 144.0, 137.5 (2 C), 137.4 (2 C), 137.0 (2 C), 136.9 (2 C), 132.9, 132.7, 132.6, 132.5 (2 C), 132.3, 132.1, 132.0, 129.2, 128.9, 127.9, 127.4, 127.2, 126.9, 126.3 (2 C), 125.8, 125.7, 125.5 (2 C), 123.9, 123.4, 121.9, 121.7, 121.6, 121.4, 121.3, 117.6, 117.3 (2 C), 117.2, 117.0, 116.6, 116.5, 116.3, 116.2, 115.8, 115.6 (2 C), 115.5, 115.3, 114.2, 114.1, 111.8, 110.5, 107.8, 107.2, 103.0, 101.3, 99.9, 99.2, 98.7, 98.0, 97.7, 97.5, 81.5, 81.4, 75.1 (2 C), 75.0, 74.8, 74.7, 70.0, 69.8, 55.3, 55.2, 42.9, 42.0, 29.6, 28.5, 28.3, 28.1, 28.0 (2 C), 27.9, 23.3, 22.0, 19.4 (2 C), 19.3 (2C), 19.2, 19.1 (3C), 19.0. ESI-HRMS, m/z calcd for $C_{144}H_{145}N_{20}O_{24}$ $[M+H]^+$ 2539.0696, $[M+2H]^{2+}$ 1270.0348. Found $[M+H]^+$ 2539.0773 $[M+2H]^{2+}$ 1270.0414.

**Protected Q<u>X</u>QQ-T-QQ<u>X</u>Q 1b.** In an oven dried round-bottomed flask, the linker 2,5-diisobutoxy-terephthalic acid bis-hydrazide **22** (5.0 mg, 14.7 µmol), tetramer acid **14** (30 mg, 29.5 µmol) and DIPEA (100 µL) were dissolved in anhydrous DCM (5 mL) under an inert atmosphere. PyBOP (46 mg, 88.4 µmol) was added and the reaction mixture was further stirred for 24 h at room temperature maintaining the inert atmosphere. The solvent was evaporated and the crude product was purified by recycling GPC to provide the desired compound (12 mg, 35%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 12.31 (s, 2 H), 11.75 (s, 2 H), 11.45 (s, 2 H), 10.53 (d, $^3J$ = 9.0 Hz, 2 H), 10.43 (d, $^3J$ = 9.0 Hz, 2 H), 9.10 (s, 2 H), 8.57 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.4 Hz, 2 H), 8.44 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.1 Hz, 2 H), 8.17 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.0 Hz, 2 H), 8.13 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.2 Hz, 2 H), 8.07 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.1 Hz, 2 H), 7.92 (bs, 2 H), 7.73 (bs, 2 H), 7.67 – 7.53 (m, 8 H), 7.45 – 7.40 (m, 4 H), 7.31 – 7.27 (m, 2 H), 7.05 (s, 2 H), 6.95 (s, 2 H), 4.33 (bs, 2 H), 4.18 (bs, 2 H), 3.96 – 4.01 (m, 12 H), 2.55 – 2.29 (m, 8 H), 1.60 (s, 18 H), 1.31 – 1.19 (m, 48 H). $^{13}$C NMR (75 MHz, $CDCl_3$) *δ* 163.2, 162.9, 162.8, 162.3, 162.1, 161.3, 160.5, 157.5, 155.5, 153.5, 150.5, 150.4, 149.3, 146.8, 145.3, 139.7, 139.1, 138.6, 138.5, 136.3, 133.7, 133.4, 127.9, 127.6, 126.6, 126.4, 126.2, 124.4, 124.2, 123.8, 122.5, 122.2, 122.0, 118.0, 117.6, 117.4 (2 C), 116.4, 116.0, 115.6, 103.2, 100.2, 98.7, 98.2, 75.7, 75.5, 75.2, 45.8, 28.5 (2 C), 28.4, 28.2, 28.2, 28.1, 19.7, 19.4 (2 C), 19.3. ESI-HRMS, m/z calcd for $C_{128}H_{134}N_{20}O_{24}$ $[M+2H]^{2+}$

1169.0035. Found 1169.0017.

**Deprotected QXQQ-T-QQXQ 1a.** TFA (1 mL) was added to a stirred solution of **1b** (10 mg, 4.27 µmol) in 1 mL $CHCl_3$. After the complete deprotection (3 h), all volatiles were evaporated and the resulting solid was dissolved in DCM (5 mL). This solution was washed with water, aqueous saturated $NaHCO_3$, brine, and then water. The organic phase was dried and evaporated under reduced pressure to provide the desired compound **1a** (9 mg, 94%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 12.11 (s, 2 H), 11.98 (s, 2 H), 10.81 (s, 2 H), 10.50 (bs, 4 H), 10.40 (s, 2 H), 9.50 (d, $^3J$ = 8.0 Hz, 2 H), 8.60 – 8.57 (m, 4 H), 8.39 (dd, $^3J$ = 7.7 Hz, $^4J$ = 1.1 Hz, 2 H), 8.33 – 8.28 (m, 4 H), 8.15 (dd, $^3J$ = 8.4 Hz, $^4J$ = 1.2 Hz, 2 H), 7.95 (t, $^3J$ = 8.1 Hz, 2 H), 7.81 – 7.77 (m, 6 H), 7.67 (t, $^3J$ = 8.0 Hz, 2 H), 7.54 – 7.41 (m, 8 H), 7.00 (s, 2 H), 4.58 – 4.53 (m, 2 H), 4.32 – 4.26 (m, 2 H), 4.17 – 3.96 (m, 10 H), 3.97 – 3.73 (m, 2 H), 2.56 – 2.33 (m, 8 H), 1.41 – 1.15 (m, 48 H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 163.5, 163.3, 163.2, 162.8, 162.6, 162.6, 160.7, 157.1, 155.5, 152.9, 150.7, 150.5, 149.7, 147.8, 145.2, 140.3, 139.5, 139.3, 138.5, 135.3, 134.0, 133.7, 129.7, 128.1, 127.5, 126.7, 126.5, 124.9, 123.6, 123.1, 122.7, 121.6, 121.3, 118.9, 118.7, 117.9, 117.5, 117.4, 115.8, 103.7, 99.6, 99.3, 99.2, 75.7, 75.4, 75.3, 29.7, 29.6, 28.4, 28.3, 28.2, 28.2, 20.1, 19.7, 19.5, 19.4, 19.3, 19.3. ESI-HRMS, m/z calcd for $C_{120}H_{118}N_{20}O_{24}$ $[M+2H]^{2+}$ 1112.9409. Found 1112.9397.

**Protected Q<u>X</u>QQ<u>Y</u>Q<u>X</u>QQ-T-QQ<u>X</u>Q<u>Y</u>QQ<u>X</u>Q 3b.** Nonamer ester **5b** (70 mg, 31 µmol) was dissolved in THF/MeOH (9:1 vol/vol, 10 mL). KOH (138 mg, 2.46 mmol) was added and the resulting mixture was stirred at room temperature for 30 min. After the completion of the reaction as checked by TLC, the solution was neutralized by adding 5% aqueous citric acid down to pH ~ 5. The organic solvents were evaporated. The slurry was taken up in DCM (10 mL) which was then washed with brine (20 mL) followed by water (20 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure to yield the desired acid **27** as a yellow solid. Without further purification, this acid was loaded in an oven dried round-bottomed flask along with 2,5-diisobutoxy-terephthalic acid bis-hydrazide **22** (4.90 mg, 14.5 µmol), and PyBOP (192 mg, 369 µmol) under nitrogen atmosphere. Anhydrous DCM was added followed by DIPEA (50 µL, 294 µmol) and the mixture was further stirred at room temperature for 24 h maintaining the inert atmosphere. After the completion of the reaction as checked by $^1$H NMR of an aliquot, the solvent was evaporated under reduced pressure. The crude product was purified by silica gel chromatography eluting with cyclohexane/EtOAc (4:1 vol/vol) to provide **3b** (45 mg, 64%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 11.51 (s), 11.27 (s), 10.98 (s), 10.88 (s), 10.84 (s), 10.79 (s), 10.48 (s), 10.22 (d, *J* = 9.1 Hz), 9.98 (d, *J* = 9.1 Hz), 8.29 – 8.23 (m), 8.12– 8.08 (m), 7.99 – 7.94 (m), 7.91 – 7.85 (m), 7.80– 7.74 (m), 7.72 – 7.69 (m), 7.67– 7.58 (m), 7.52 – 7.46 (m), 7.42 (d, *J* = 8.4 Hz), 7.37 – 7.28 (m), 7.24 – 7.19 (m), 7.16 – 7.06 (m), 7.02 (d, *J* = 7.5 Hz), 6.98 – 6.93 (m), 6.89 (d, *J* = 8.4 Hz), 6.73 (s), 6.61 (s), 6.58 (s), 6.48 (d, *J* = 2.4 Hz), 6.40 (s), 5.87 (s), 5.81 (s), 5.25 (s), 5.03 (q, *J* = 10.8 Hz), 4.12 – 4.02 (m), 3.96 – 3.76 (m), 3.71 (s, 6H), 3.68 – 3.60 (m), 3.54 – 3.50 (m), 3.27 – 3.28 (m), 2.50 – 2.15 (m), 1.61 (m), 1.45 (s), 1.41 (s), 1.33 – 1.05 (m).(mixture of two diastereomers PP and PM and their ratio is 98: 2, only the major peaks are reported). ESI-HRMS, m/z calcd for $C_{270}H_{274}N_{40}O_{46}$ $[M+2H]^{2+}$ 2408.0278. Found 2408.5261.

**Deprotected helix-turn-helix 3a.** TFA (1 mL) was added to a stirring solution of protected **3b** (30.0 mg, 6.23 µmol) in $CHCl_3$ (3 mL). After the complete deprotection (1 h as checked by TLC), all solvents were evaporated and the crude product was purified by silica gel chromatography eluting with MeOH/DCM (1:10, vol/vol) to provide **3a** (8 mg, 30%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 11.99 (s, 2 H), 11.69 (s, 2 H), 11.50 (s, 2 H), 11.15 (s, 4 H), 10.31 (s, 2 H), 10.24 (s, 2 H), 9.98 (s, 2 H), 9.96 (s, 2 H),

9.95 (s, 2 H), 9.84 (s, 2 H), 9.07 (s, 2 H), 8.66 (s, 2 H), 8.58 (d, *J* = 7.5 Hz, 2 H), 8.51 (d, *J* = 7.5 Hz, 2 H), 8.33 (d, *J* = 7.9 Hz, 2 H), 8.21 (d, *J* = 7.3 Hz, 4 H), 8.15– 8.08 (m, 6 H), 8.02– 7.97 (m, 8 H), 7.89 (t, *J* = 8.8 Hz, 6 H), 7.72 (d, *J* = 7.9 Hz, 2 H), 7.68 – 7.61 (m, 4 H), 7.53 (t, *J* = 7.9 Hz, 2 H), 7.40– 7.29 (m, 8 H), 7.24 – 7.18 (m, 6 H), 7.14 – 7.00 (m, 8 H), 6.94 – 6.73 7.04 (m, 6 H), 6.36 (s, 2 H), 6.10 (s, 2 H), 5.25 (s, 2 H), 4.68 (s, 2 H), 4.28 – 3.61 (m, 24 H), 3.44 – 3.35 (m, 4 H), 3.23 (t, *J* = 7.4 Hz, 2 H), 2.61 – 2.10 (m, 12 H), 1.44 – 0.89 (m, 84 H). ESI-HRMS, m/z calcd for $C_{238}H_{226}N_{40}O_{44}$ $[M+2H]^{2+}$ 2175.8450. Found 2175.8429.

**Protected YQXQQYQXQQ-T-QQXQYQQXQY 2b.** In an oven dried round-bottomed flask, the turn unit 2,5-diisobutoxy-terephthalic acid bis-hydrazide **22** (20.0 mg, 59.1 µmol), decamer acid **28** (300 mg, 118 µmol) and PyBOP (192 mg, 369 µmol) were dissolved in anhydrous DCM (10 mL) under an inert atmosphere. DIPEA (205 µL, 1.21 mmol) was added and the reaction mixture was further stirred for 24 h at room temperature maintaining the inert atmosphere. The solvent was evaporated and the crude product was purified by silica gel chromatography eluting with cyclohexane/EtOAc (4:1 vol/vol) to provide **2b** (99 mg, 31%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 11.48 (s, 2 H), 11.17 (s, 2 H), 10.98 (s, 2 H), 10.86 (s, 2 H), 10.83 (s, 2 H), 10.80 (s, 2 H), 10.63 (s, 2 H), 10.38 (s, 2 H), 10.20 (d, *J* = 9.3 Hz, 2 H), 9.96 (d, *J* = 9.7 Hz, 2 H), 8.10 (d, *J* = 7.5 Hz, 2 H), 7.97 – 7.92 (m, 6 H), 7.88 (d, *J* = 8.3 Hz, 4 H), 7.84 – 7.79 (m, 8 H), 7.76 – 7.68 (m, 8 H), 7.65 – 7.59 (m, 8 H), 7.44 (d, *J* = 7.5 Hz, 2 H), 7.35– 7.31 (m, 10 H), 7.24– 7.16 (m, 4 H), 7.06 – 6.97 (m, 18 H), 6.91 – 6.81 (m, 10 H), 6.71 (s, 2 H), 6.58 (s, 2 H), 6.47 – 6.43 (m, 6 H), 6.28 (d, *J* = 1.8 Hz, 2 H), 5.81 (s, 2 H), 5.73 (s, 2 H), 5.62 – 5.59 (m, 2 H), 4.98 – 4.89 (m, 8 H), 4.14 – 4.02 (m, 4 H), 3.97 – 3.75 (m, 18 H), 3.73 (s, 6 H), 3.66 (s, 6 H), 3.64 – 3.55 (m, 10 H), 3.11 (d, *J* = 14.9 Hz, 2 H), 2.52 – 2.09 (m, 14 H), 1.89 (d, *J* = 16.4 Hz, 2 H), 1.61 (s, 18 H), 1.42 (s, 18 H), 1.34 (s, 6 H), 1.32 – 1.07 (m, 84 H). ESI-HRMS, m/z calcd for $C_{304}H_{310}N_{44}O_{50}$ $[M+3H]^{3+}$ 1794.1134. Found 1794.1138.

**Deprotected helix-turn-helix 2a.** TFA (1 mL) was added to a stirring solution of protected oligomer **2b** (60 mg, 11.2 µmol) in $CHCl_3$ (3 mL). After the complete deprotection (2 h as checked by TLC), all solvents were evaporated and the crude product was purified by silica gel chromatography eluting with MeOH/DCM (1:10 vol/vol) to provide **2a** (20 mg, 38%) as a yellow solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 11.76 (s, 2 H), 11.60 (s, 2 H), 11.41 (s, 2 H), 11.30 (s, 2 H), 10.98 (s, 2 H), 10.77 (s, 2 H), 10.15 (s, 2 H), 9.44 – 9.87 (m, 8 H), 9.73 (s, 2 H), 9.28 (s, 2 H), 8.88 (s, 2 H), 8.53 (d, $^3J$ = 7.6 Hz, 2 H), 8.38 (d, $^3J$ = 7.3 Hz, 2 H), 8.17 – 8.15 (m, 4 H), 8.08 – 7.99 (m, 10 H), 7.96 – 7.92 (m, 4 H), 7.89 – 7.83 (m, 6 H), 7.71 – 7.61 (m, 6 H), 7.56 (d, *J* = 7.0 Hz, 2 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.38 – 7.30 (m, 4 H), 7.22 – 7.20 (m, 6 H), 7.10 – 6.94 (m, 16 H), 6.73 (d, *J* = 6.9 Hz, 4 H), 6.33 (s, 2 H), 6.26 (s, 2 H), 6.01 (s, 2 H), 5.73 (bs, 2 H), 5.14 (s, 2 H), 4.23 – 4.18 (m, 2 H), 4.07 – 4.01 (m, 2 H), 4.00 – 3.68 (m, 24 H), 3.57 – 3.52 (m, 2 H), 3.33 (m, 4 H), 3.25 – 3.08 (m, 2 H), 2.57 – 2.16 (m, 14 H), 1.43 (s, 6 H), 1.40 – 0.86 (m, 84 H). ESI- HRMS, m/z calcd for $C_{256}H_{246}N_{44}O_{46}$ $[M+2H]^{2+}$ 2337.9243. Found 2338.4269.

# 2 Supplementary Tables

**Supplementary Table 1**. Crystallographic data for **1a** and **2a.**

| | **1a** | **2a** |
|---|---|---|
| Formula | C127 H128 N20 O24 | C128 H123 N22 O23 |
| M | 2318.49 | 2337.48 |
| Crystal system | monoclinic | triclinic |
| Space group | P21/c | P-1 |
| a/Å | 17.0411(34) | 19.1113(13) |
| b/Å | 52.1980(104) | 28.614(2) |
| c/Å | 14.9113(30) | 35.750(3) |
| α/° | 90(0) | 71.488(2) |
| β/° | 106.912(30) | 81.839(2) |
| γ/° | 90(0) | 75.011(2) |
| U/Å$^3$ | 12690(5) | 17869(2) |
| T/K | 100 | 291 |
| Z | 4 | 2 |
| ρ/g cm$^{-1}$ | 1.214 | 0.869 |
| size (mm) | 0.2x0.2x0.1 | 0.1x0.1x0.05 |
| λ/Å | 1.54178 | 1.54178 |
| μ/mm$^{-1}$ | 0.702 | 0.501 |
| Total reflections | 50024 | 95633 |
| Unique data | 20107 | 46522 |
| $R_{int}$ | 0.0982 | 0.1130 |
| parameters/restraints | 1578/1901 | 3217/4182 |
| $R_1$/w$R_2$ | 0.1297/0.2888 | 0.1089/0.2663 |
| goodness of fit | 1.330 | 1.058 |
| CCDC # | 1450791 | 1451415 |

**Supplementary Table 2**. Crystallographic data for **3a** and **5a.**

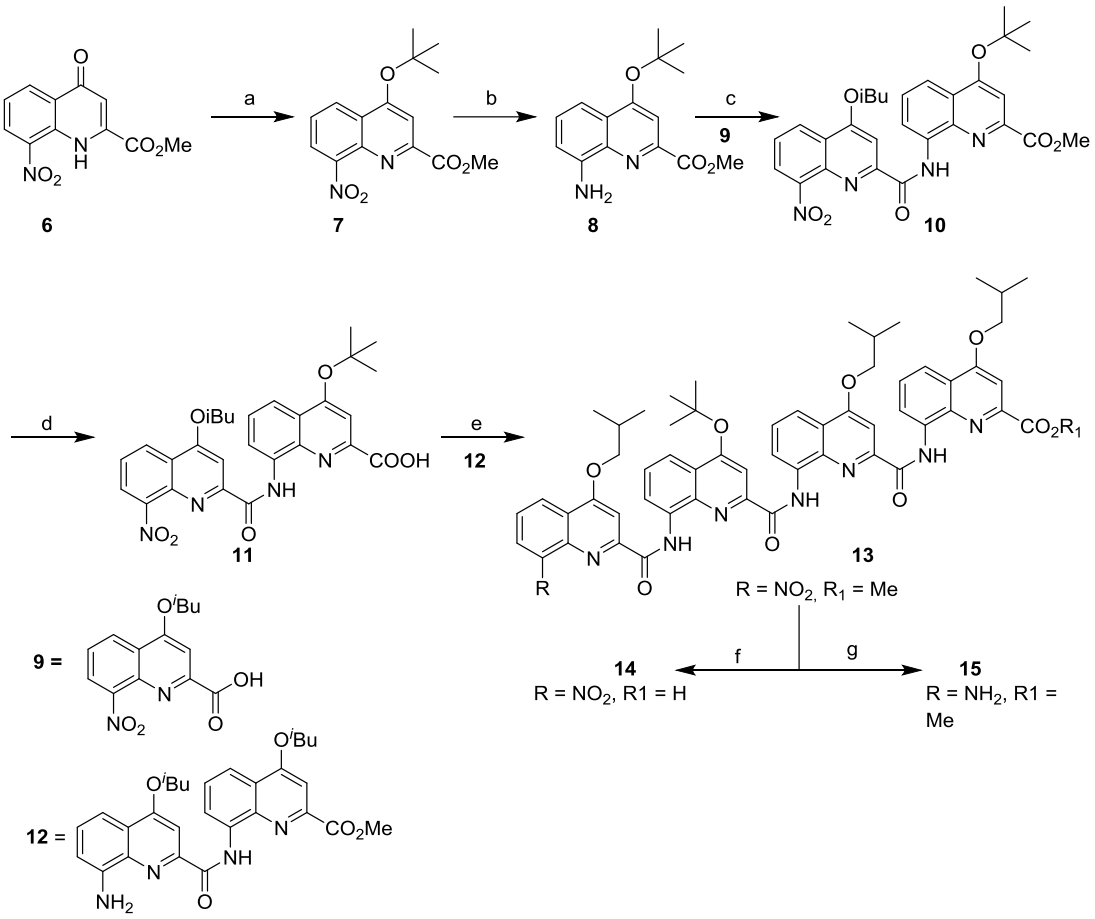
| | **3a** | **5a** |
|---|---|---|
| Formula | C238 H226 N40 O44 | C112 H104 N18 O21 |
| M | 4350.57 | 2038.13 |
| Crystal system | monoclinic | triclinic |
| Space group | P21/n | P1 |
| a/Å | 27.392(6) | 25.286(5) |
| b/Å | 35.870(7) | 26.901(5) |
| c/Å | 28.337(6) | 27.418(6) |
| α/° | 90(0) | 108.71(3) |
| β/° | 90.14(3) | 107.77(3) |
| γ/° | 90(0) | 109.81(3) |
| U/Å$^3$ | 27843(10) | 14717(7) |
| T/K | 100 | 293 |
| Z | 4 | 4 |
| ρ/g cm$^{-1}$ | 1.038 | 0.920 |
| size (mm) | 0.10x0.08x0.05 | 0.07x0.05x0.04 |
| λ/Å | 0.800 | 0.800 |
| μ/mm$^{-1}$ | 0.073 | 0.065 |
| Total reflections | 239455 | 92984 |
| Unique data | 39443 | 51965 |
| $R_{int}$ | 0.0926 | 0.0540 |
| parameters/restraints | 3120/3954 | 5437/7178 |
| $R_1$/w$R_2$ | 0.1048/0.2800 | 0.1021/0.2747 |
| goodness of fit | 1.757 | 0.949 |
| CCDC # | 1451523 | 1451494 |

**Supplementary Table 3**. Crystallographic data for **2b** and **4a.**

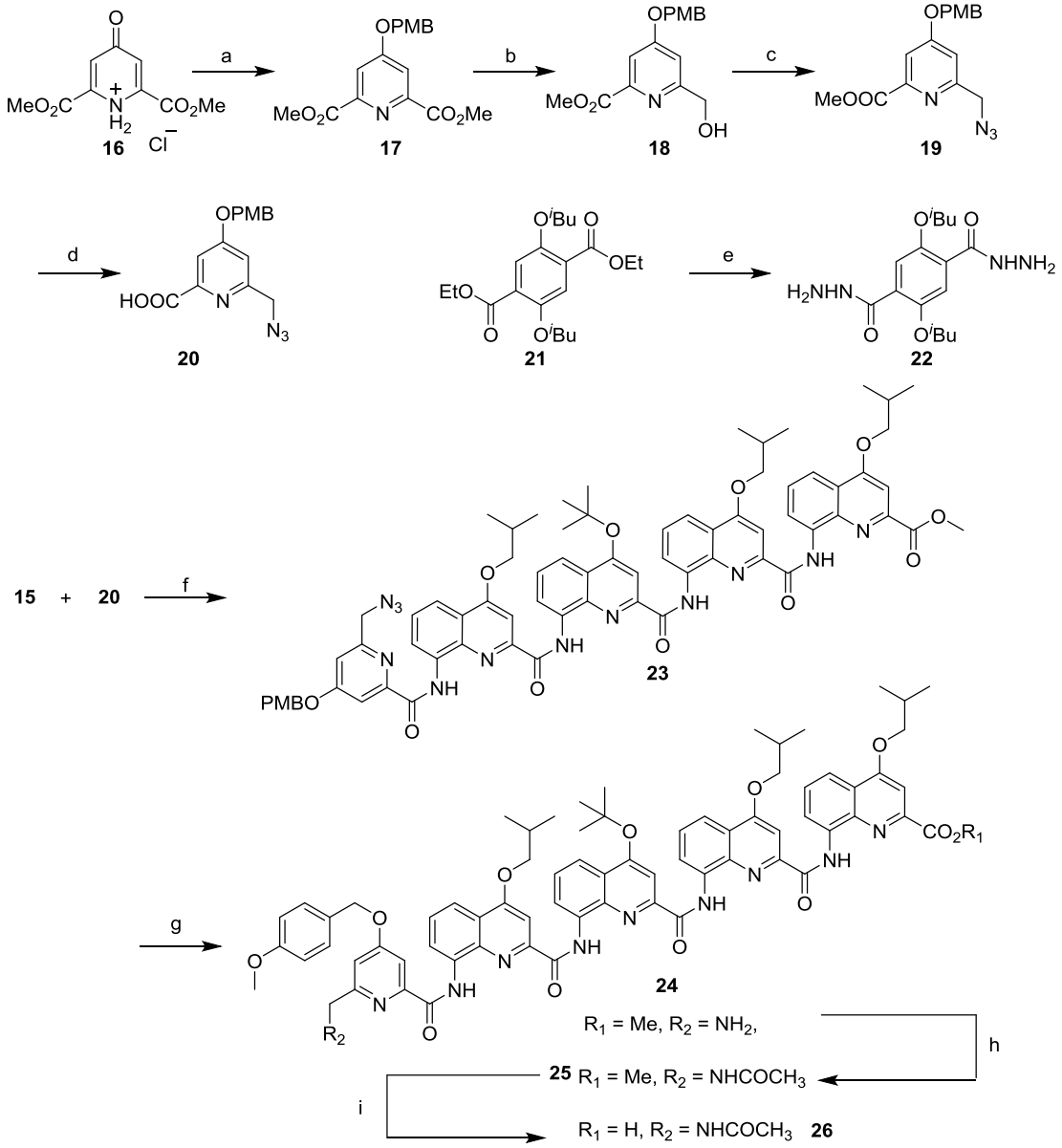
| | **2b** | **4a** |
|---|---|---|
| Formula | C312 H313 N44 O50 Cl24 | C488 H460 CL12 N80 O88<br>(Foldamer : C121H114N20O22) |
| M | 6329.81 | u.a. 2318.49 |
| Crystal system | triclinic | trigonal |
| Space group | P 1 | P3 |
| a/Å | 18.008(4) | 29.3310(41) |
| b/Å | 18.419(4) | 29.3310(41) |
| c/Å | 30.513(6) | 59.1830(118) |
| α/° | 78.68(3) | 90(0) |
| β/° | 88.33(3) | 90(0) |
| γ/° | 65.83(3) | 120(0) |
| U/Å$^3$ | 9039 (4) | 44094(15) |
| T/K | 293 | 291 |
| Z | 1 | 4 |
| ρ/g cm$^{-1}$ | 1.163 | 1.006 |
| size (mm) | 0.05x0.04x0.01 | 0.1x0.05x0.05 |
| λ/Å | 0.8500 | 0.850 |
| μ/mm$^{-1}$ | 0.378 | 0.123 |
| Total reflections | 53409 | 164253 |
| Unique data | 42354 | 60877 |
| $R_{int}$ | 0.040 | 0.0834 |
| parameters/restraints | 4242/8281 | 5836/13234 |
| $R_1$/w$R_2$ | 0.1019/0.2527 | 0.1250/0.2985 |
| goodness of fit | 1.824 | 1.740 |
| CCDC # | 1469843 | 1470116 |

# 3 Supplementary Figures

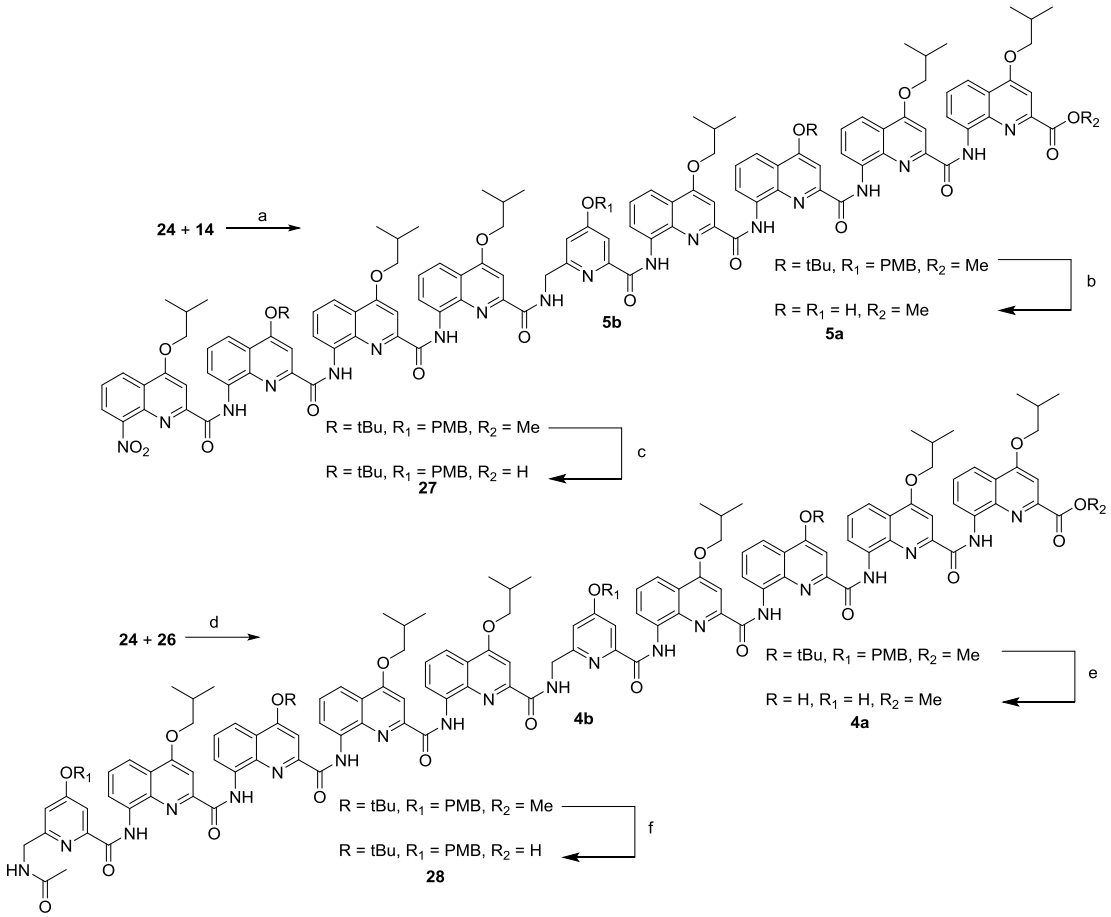
## 3.1 Synthetic Schemes



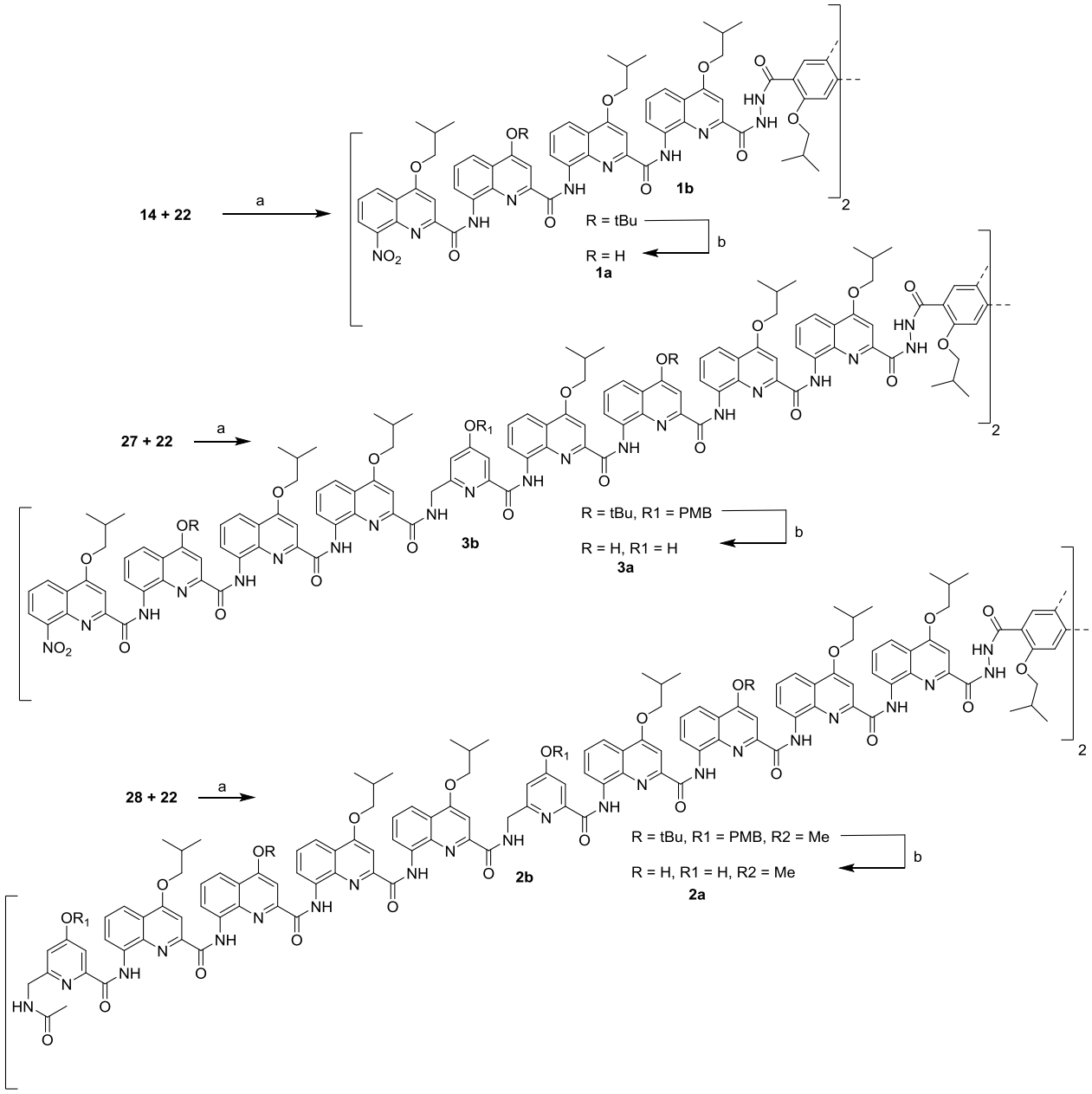

**Supplementary Figure 1:** a) $^{t}$Bu-Br, AgOAC, DCM, 25 ºC, 40 min ; b) Pd/C, $H_2$, 25 ºC, 12 h. c) **9**, 1-Chloro-N,N-2-trimethylpropenylamine, $CHCl_3$, 25 °C, 1 h; DIPEA, $CHCl_3$, 25 °C, 12 h; d) LiOH, THF, $H_2O$, 25 °C, 12 h; e) 1-chloro-N,N-2-trimethylpropenylamine, $CHCl_3$, 25 °C, 2 h; **12**, DIPEA, $CHCl_3$, 25 °C, 12 h; f) Pd/C, $NH_4HCO_2$, $NH_4VO_3$, EtOAc, EtOH, $H_2O$, 95 °C, 24 h; g) NaOH, THF, MeOH, $H_2O$, 25 °C, 12 h;




**Supplementary Figure 2: a)** $K_2CO_3$, NaI, 1-(chloromethyl)-4-methoxybenzene, acetone, reflux, 12 h; b) $NaBH_4$, DCM/MeOH, 25 ºC, 2 h; c) $CBr_4$, $PPh_3$, DMF, 25 ºC,1.5 h; $NaN_3$, 25 ºC, 12 h; d) NaOH, THF/$H_2O$ (10/1, Vol/Vol), 25 ºC, 6 h; e) Hydrazine, 90 °C, 24 h; f) PyBOP, DIPEA, DCM, 25 °C, 12 h; g) $H_2$, 10% Pd/C, pyr, EtOAc, 25 °C, 12 h; h) $Ac_2O$, DIPEA, $CHCl_3$, 25 °C, 3 h; i) KOH, THF, MeOH, 25 °C, 30 min;

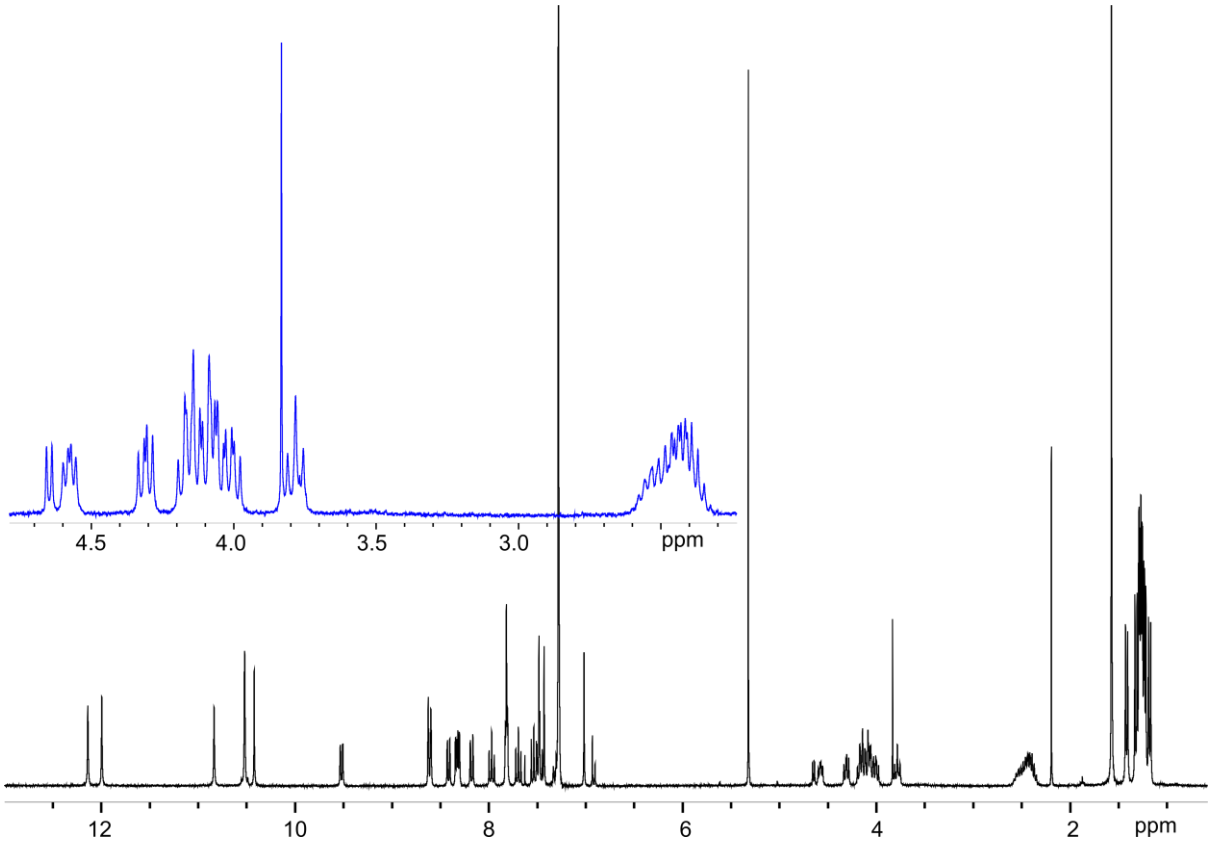



**Supplementary Figure 3.** a) PyBOP, DIPEA, DCM, 25 °C, 12 h; b) TFA, $CHCl_3$, 25 °C, 2 h; c) KOH, THF, MeOH, 25 °C, 30 min; d) PyBOP, DIPEA, DCM, 25 °C, 12 h; e) TFA, $CHCl_3$, 25 °C, 2 h; f) KOH, THF, MeOH, 25 °C, 30 min;

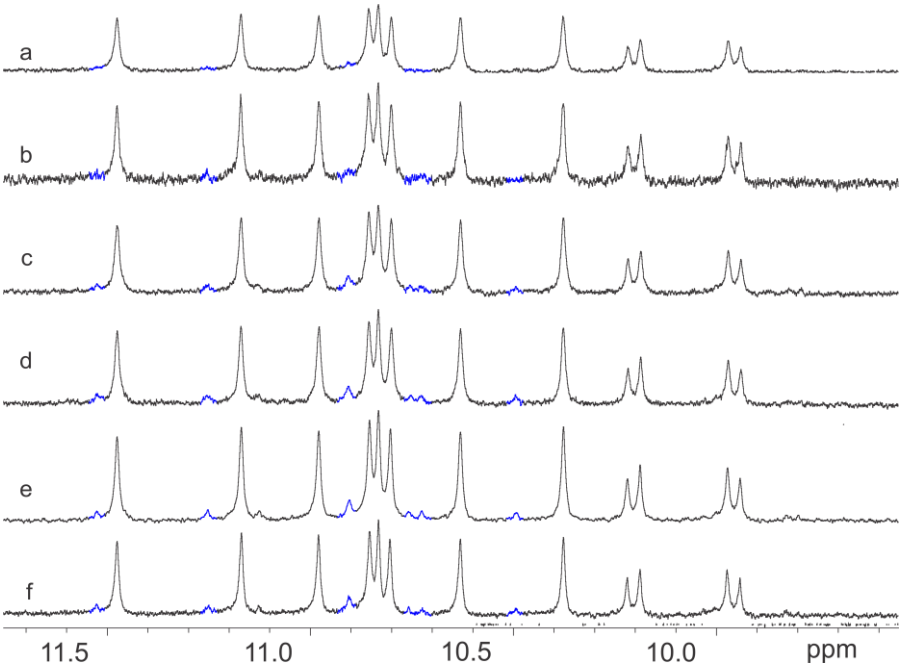



**Supplementary Figure 4.** a) PyBOP, DIPEA, DCM, 25 °C, 24 h; b) TFA, $CHCl_3$, 25 °C, 1 h; c) PyBOP, DIPEA, DCM, 25 °C, 24 h; d) TFA, $CHCl_3$, 25 °C, 2 h.

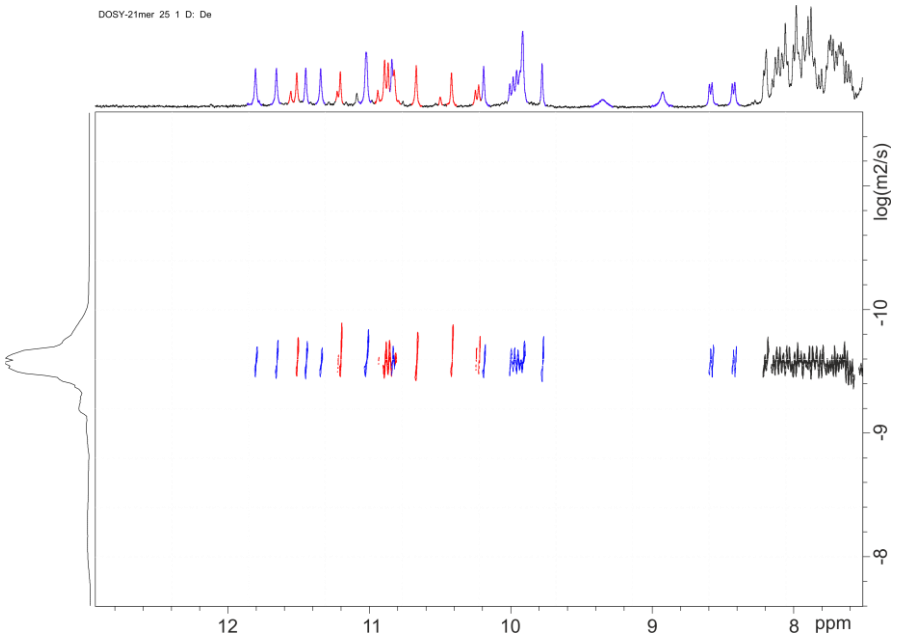
## 3.2 Helix-turn-helix structures (unimolecular bundles)



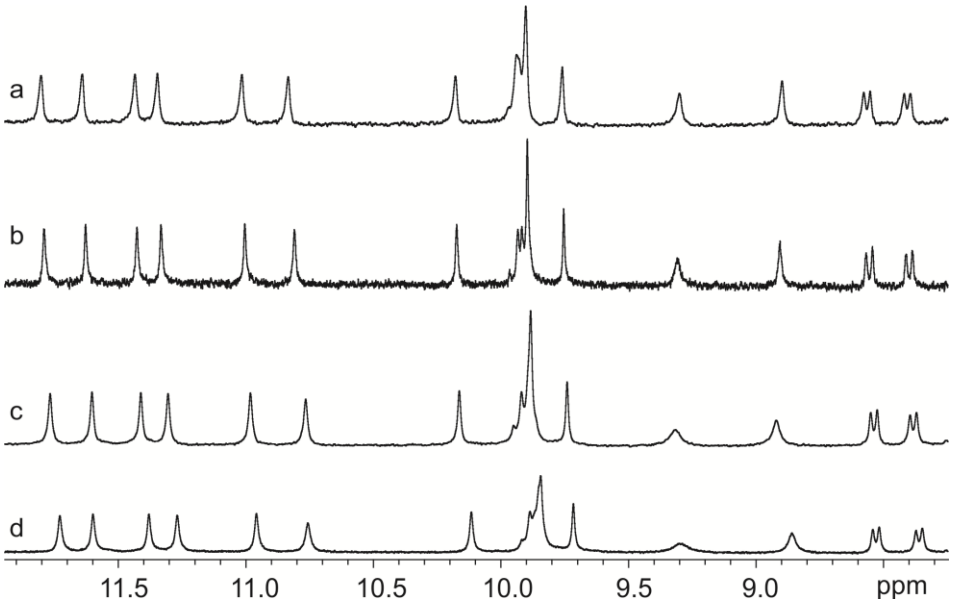

**Supplementary Figure 5.** $^{1}$H NMR spectrum (298 K, 300 MHz) of **1a** in $CDCl_3$. The inset zooms in the aliphatic region showing the anisochronous diastereotopic C*H*$_2$ protons of *i*BuO side chains.



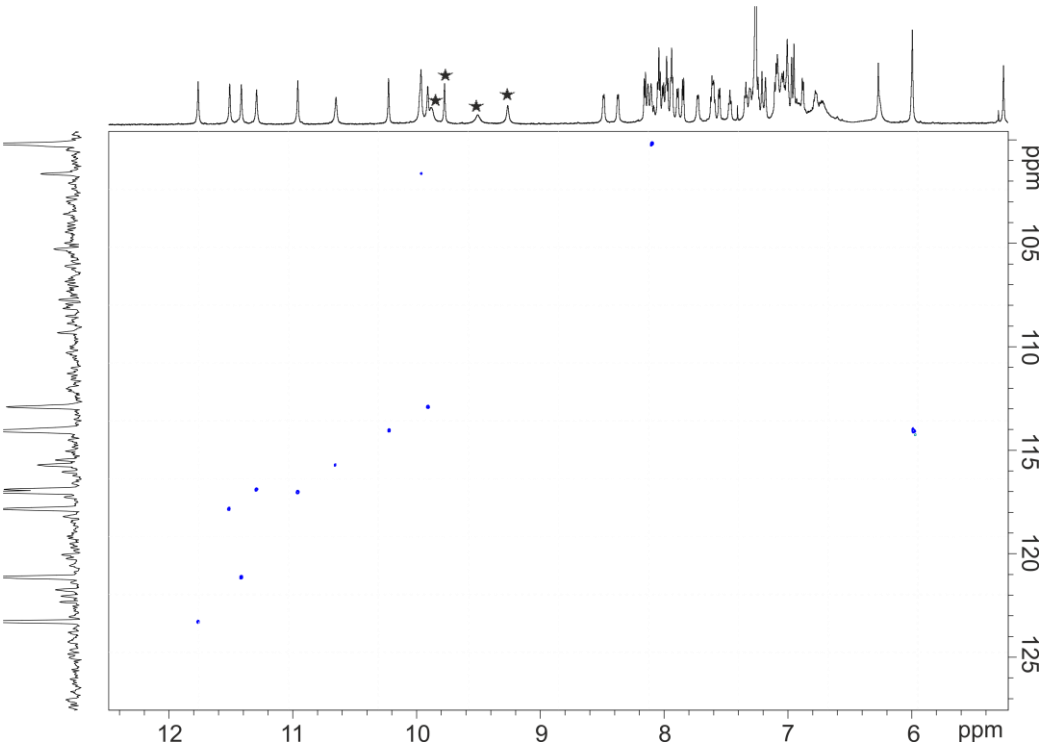

**Supplementary Figure 6.** Evolution of the $^{1}$H NMR spectrum (298 K, 300 MHz) of a freshly dissolved crystal of **2b** in $CDCl_3$ after: (a) 3 min; (b) 15 min; (c) 60 min; (d) 90 min; (e) 2 days; (f) 4 days. Since the crystal is that of the PM conformer, this experiment suggests that the major species in solution is also PM.



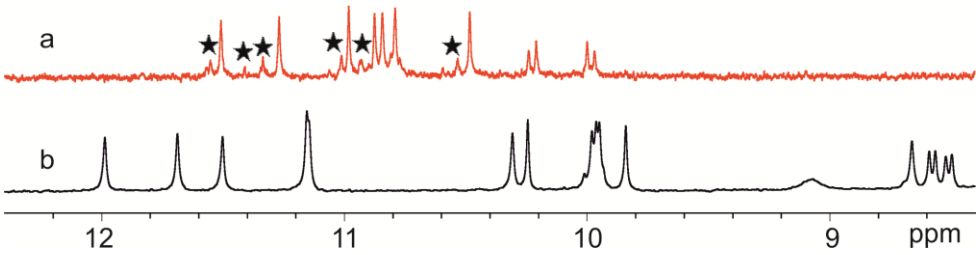

**Supplementary Figure 7.** $^{1}$H NMR DOSY spectrum ($CDCl_3$, 298 K, 400 MHz) of a mixture of **2a** (blue) and **2b** (red). The two species have similar diffusion coefficient, suggesting that **2a** is monomeric.



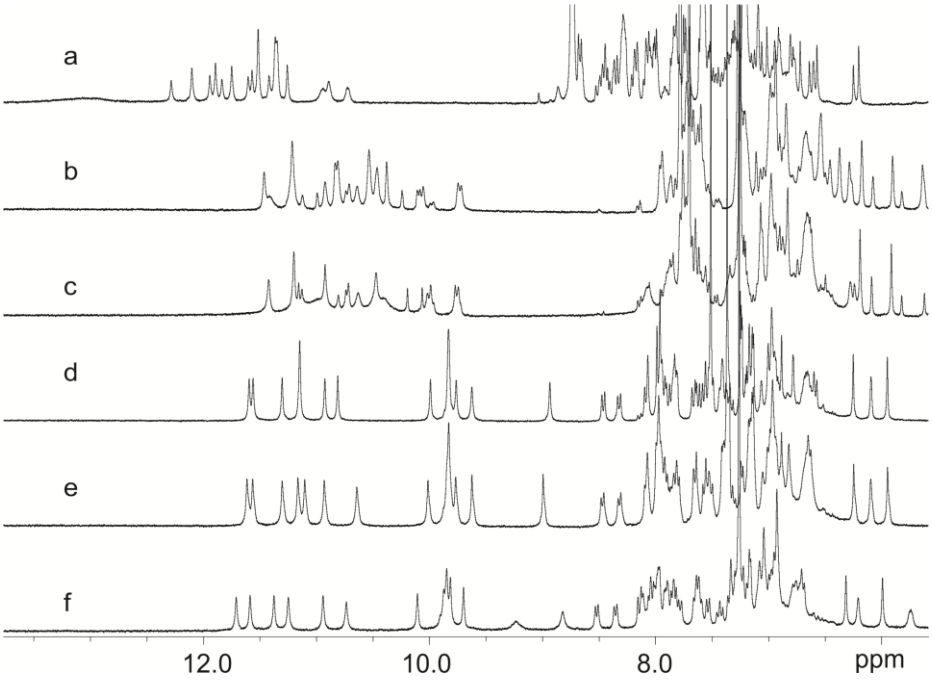

**Supplementary Figure 8.** $^{1}$H NMR spectra of **2a** ($CDCl_3$, 298 K, 300 MHz) at: (a) 2.0 mM (b) 1.5 mM; (c) 1.0 mM; (d) 0.50 mM. The absence of changes is consistent with a monomeric state of **2a** in solution.



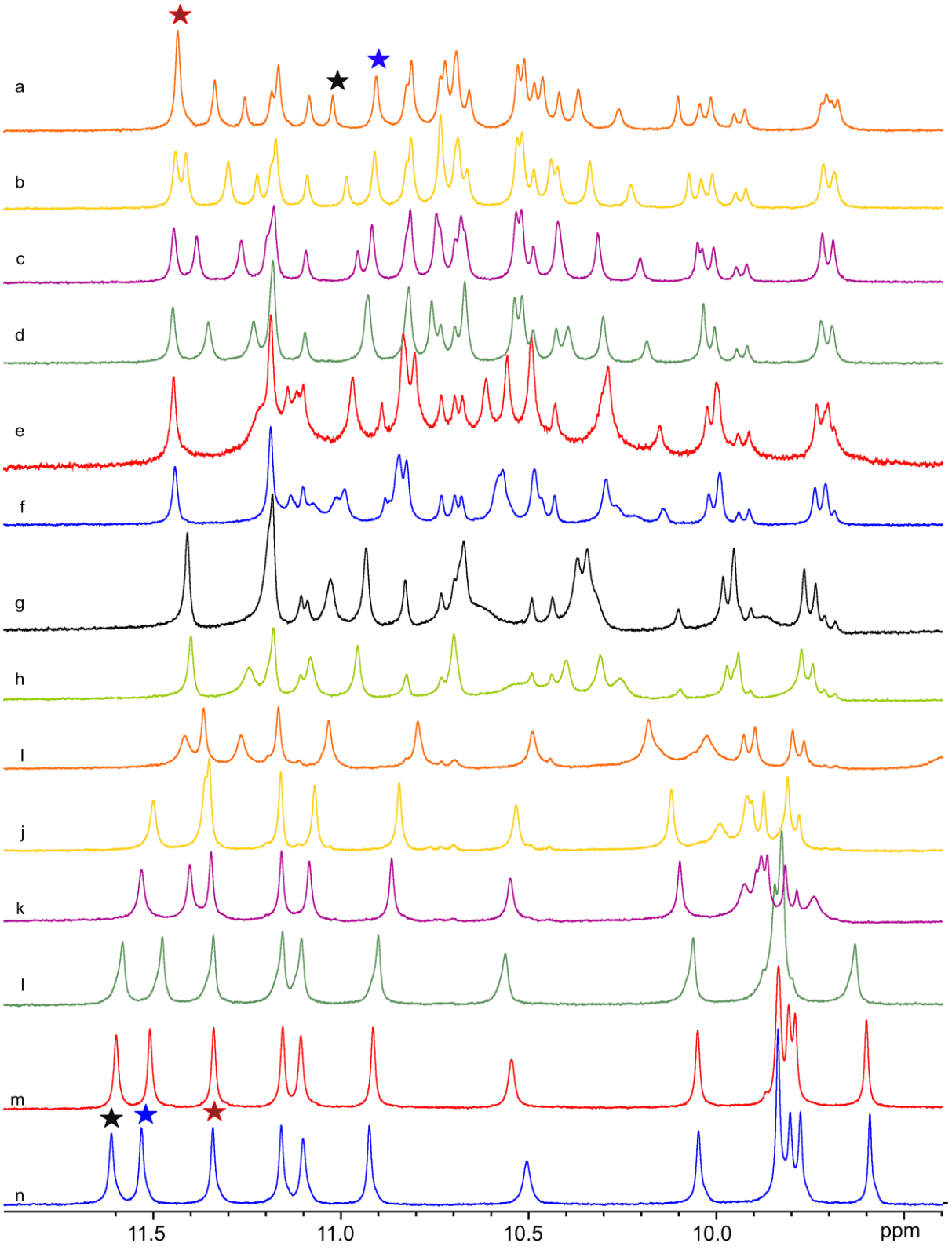

**Supplementary Figure 9.** $^{15}$N-$^{1}$H HSQC NMR spectrum (700 MHz, 298 K) of **2a** in $CDCl_3$. Only NH resonances correlate. Stars indicate the signals of OH protons.



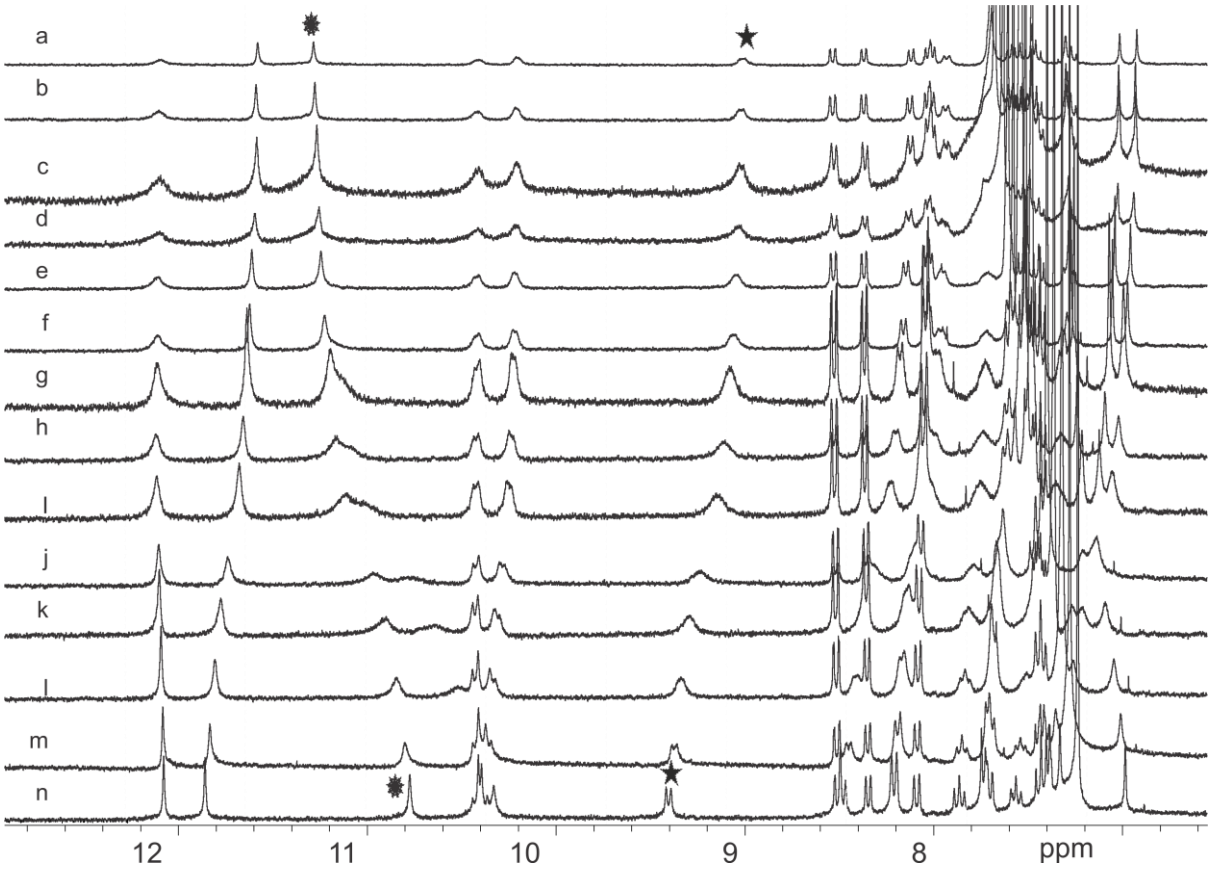

**Supplementary Figure 10.** $^{1}$H NMR spectrum ($CDCl_3$, 298 K, 300 MHz) of: (a) protected **3b;** (b) **3a**. Stars indicate the presence of a second set of peaks in the spectrum of **3b** as a consequence of the coexistence of two diasteromeric *PP*/*MM* and *PM* conformers. Only one conformer prevails in the spectrum of **3a**.



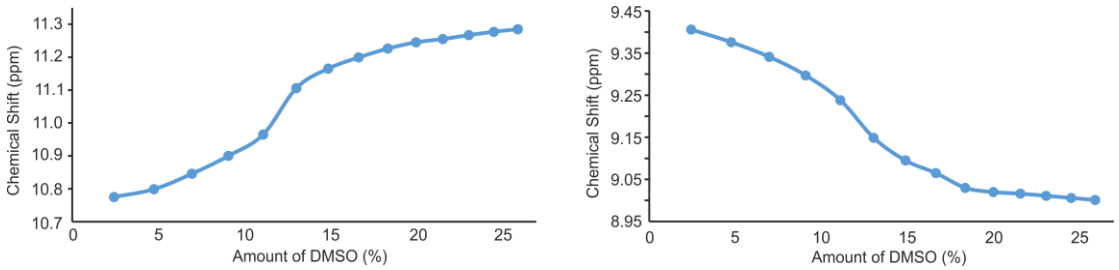

**Supplementary Figure 11.** Effect of polar solvents on the structure of **2a**. $^{1}$H NMR spectra of **2a** in: (a) pure Pyridine-d5; (b) 100:50 $CDCl_3$/DMSO-d6 vol/vol; (c) 100:40 $CDCl_3$/DMSO-d6 vol/vol; (d) 100:20 $CDCl_3$/DMSO-d6 vol/vol; (e) 100:10 $CDCl_3$/DMSO-d6 vol/vol; (f) pure $CDCl_3$.



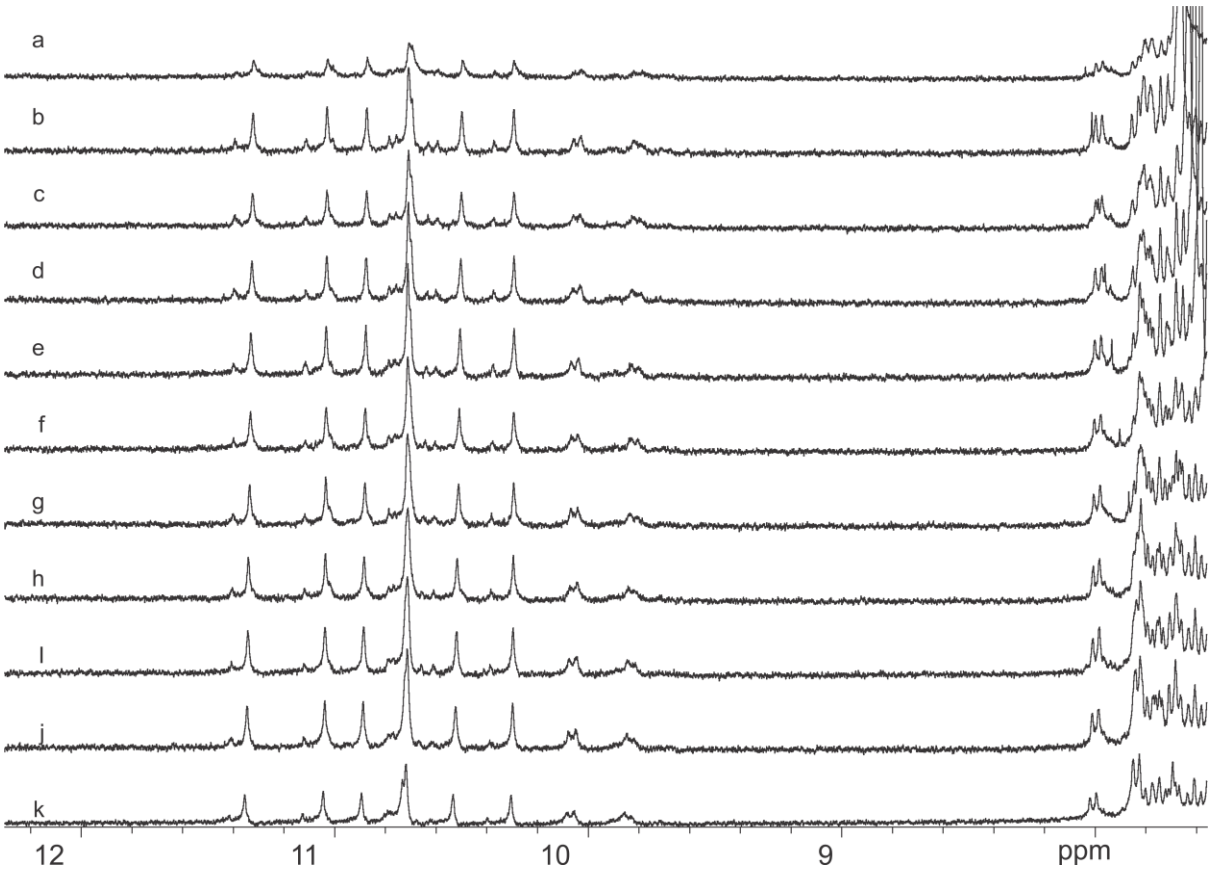

**Supplementary Figure 12.** Part of the $^{1}$H NMR spectra (300 MHz, 323 K) showing amide resonances of **2a** in $CDCl_3$/DMSO-d6. The volume percentages of DMSO-d6 from bottom to top are: 30 (a), 29 (b), 28 (c), 26 (d), 25.4 (e), 25 (f), 24 (g), 23 (h), 22 (i), 21 (j), 20 (k), 18 (l), 17 (m), and 15% (n), respectively. The chemical shift variations of three signals marked with stars are shown in Figure 2f of the manuscript.




**Supplementary Figure 13.** Part of the $^{1}$H NMR spectra (300 MHz, 323 K) of **1a** in $CDCl_3$/DMSO-d6. The volume percentages of DMSO-d6 from bottom to top are: 26 (a), 25 (b), 23 (c), 22 (d), 20 (e), 18 (f), 17 (g), 15 (h), 13 (i), 11 (j), 9 (k), 7 (l), 5 (m), and 2% (n). The chemical shift variations of two signals (marked with stars) are shown in Supplementary Figure 14.



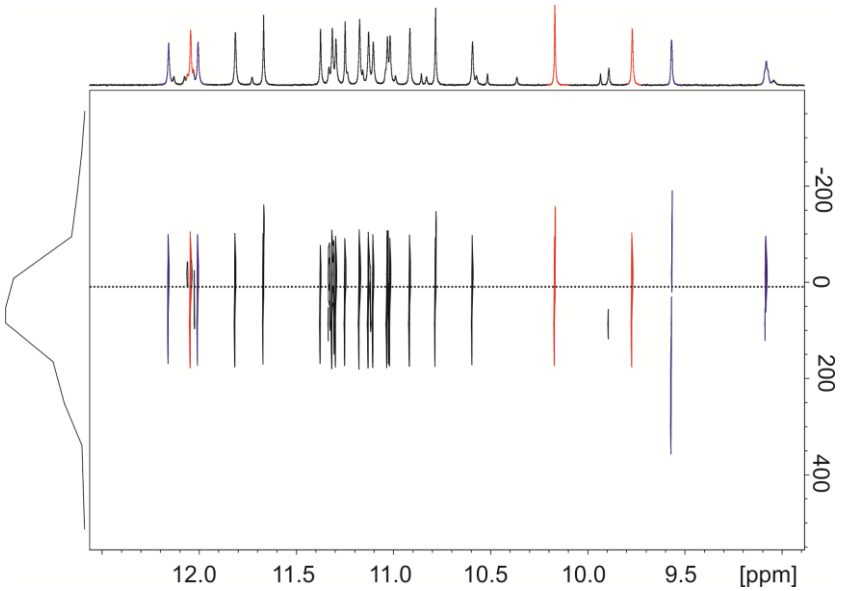

**Supplementary Figure 14**. NMR chemical shift of two amide NH protons of **1a** as a function of the volume percent of DMSO-d6 in $CDCl_3$.



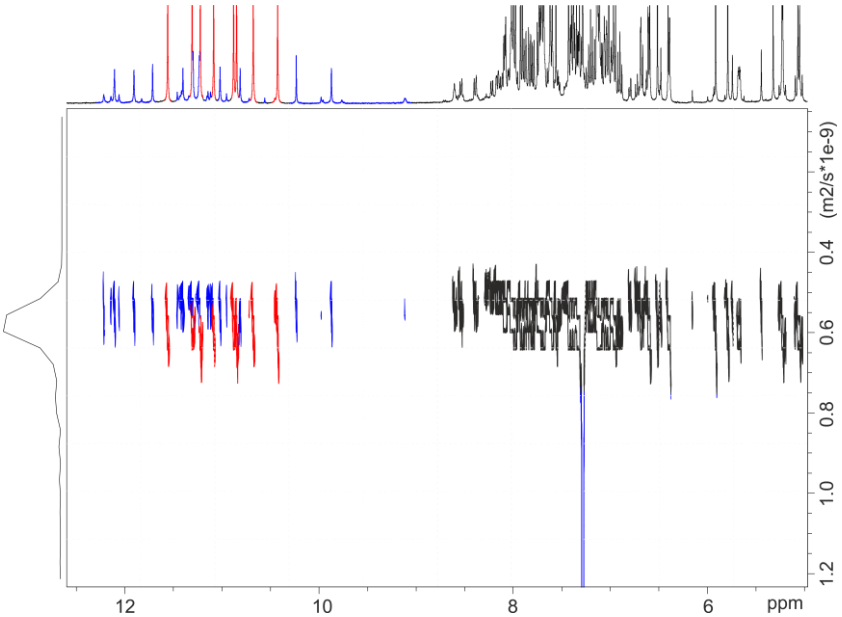

**Supplementary Figure 15.** Part of the $^{1}$H NMR spectra (300 MHz, 323 K) of **2b** in $CDCl_3$/DMSO-d6. The volume percentages of DMSO-d6 from bottom to top are: 27 (a), 26 (b), 25 (c), 23 (d), 22 (e), 20 (f), 18 (g), 17 (h), 15 (i), 13 (j), and 9% (k). The absence of effect of DMSO on the proportion of the *PP*/*MM* and *PM* conformers of **2b** support the hypothesis that the solvent effects observed in the case of **2a** are associated with a structural change and not with a dependence of chemical shifts on the solvent.

## 3.3 Analysis of multimolecular dimeric and trimeric bundles

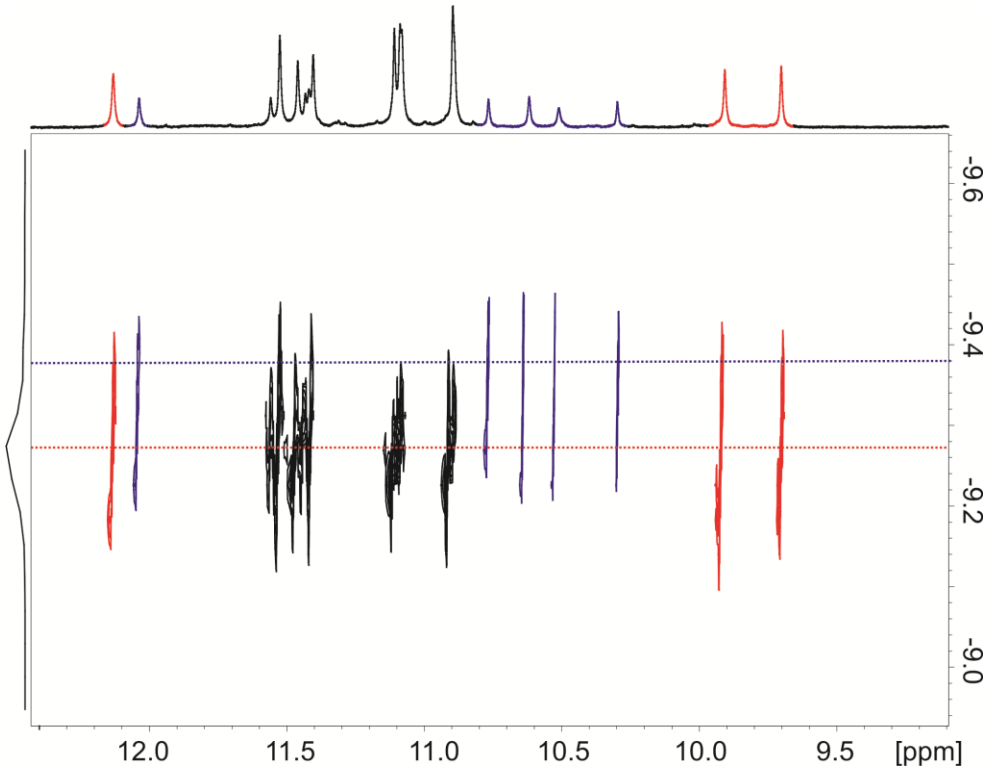
### 3.3.1 Assessing aggregate size



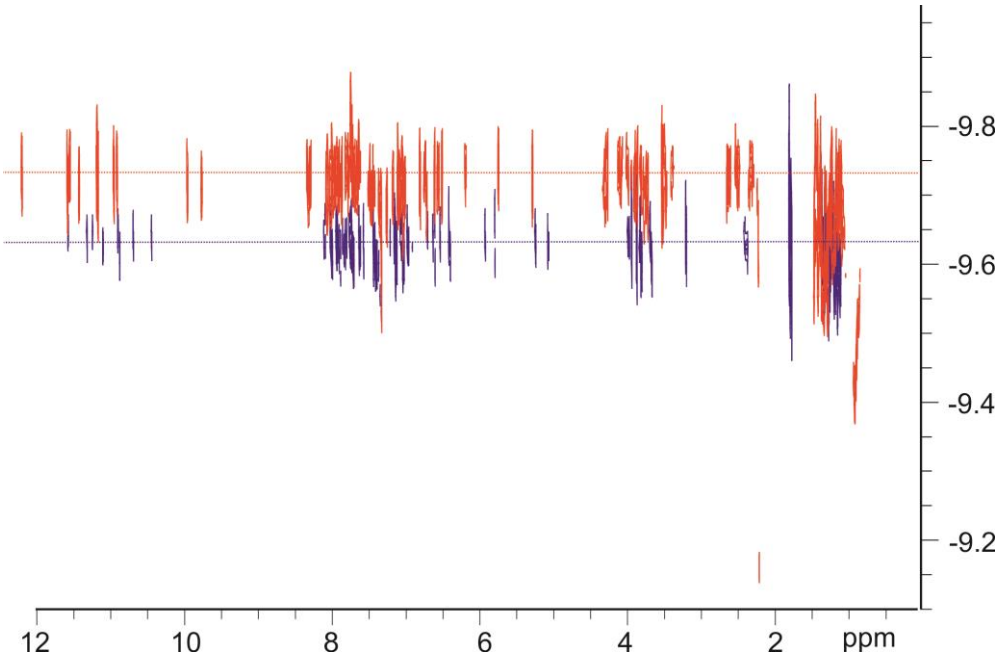

**Supplementary Figure 16.** $^{1}$H NMR DOSY spectrum (1:1 $CDCl_3$/DCM-d2 vol/vol, 298 K, 400 MHz) of **5a**. Selected signals of two distinct aggregates are marked in red and blue, respectively. Identical diffusion coefficients suggest that the two aggregates have the same size.




**Supplementary Figure 17.** $^{1}$H NMR DOSY spectrum ($CDCl_3$, 298 K, 400 MHz) of a mixture of **4b** (red) and **5a** (blue) showing that **5a** has a higher hydrodynamic radius despite its smaller size. This is only possible when **5a** is in aggregated state in solution.

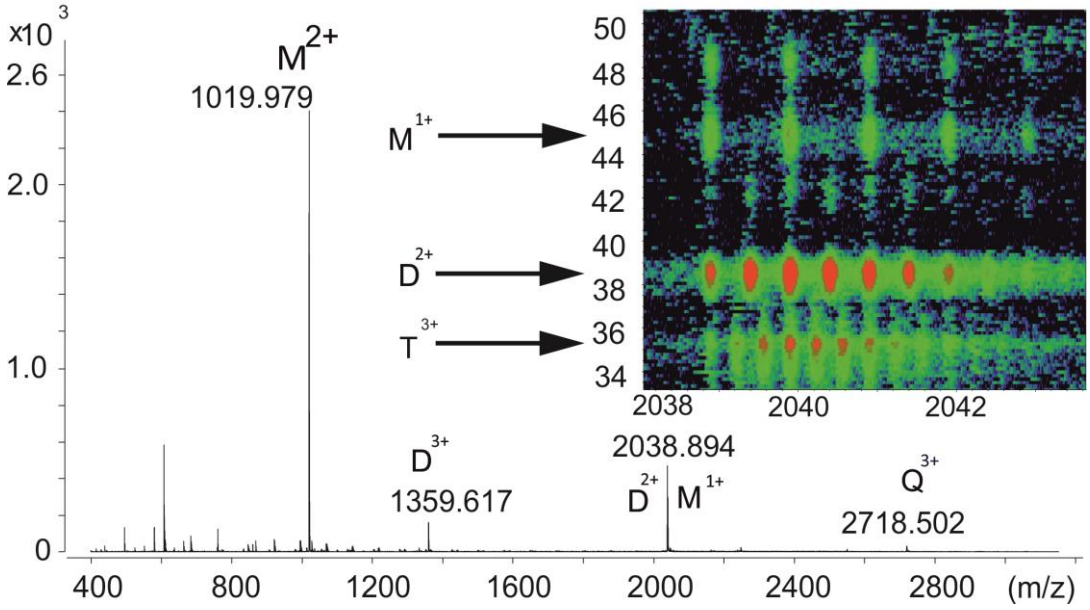



**Supplementary Figure 18.** $^{1}$H NMR DOSY spectrum (1:1 $CDCl_3$/DCM-d2 vol/vol, 298 K, 400 MHz) of **4a**. Selected signals of two distinct aggregates are marked in red and blue respectively. Different diffusion coefficients suggest that the two aggregates have a different size.

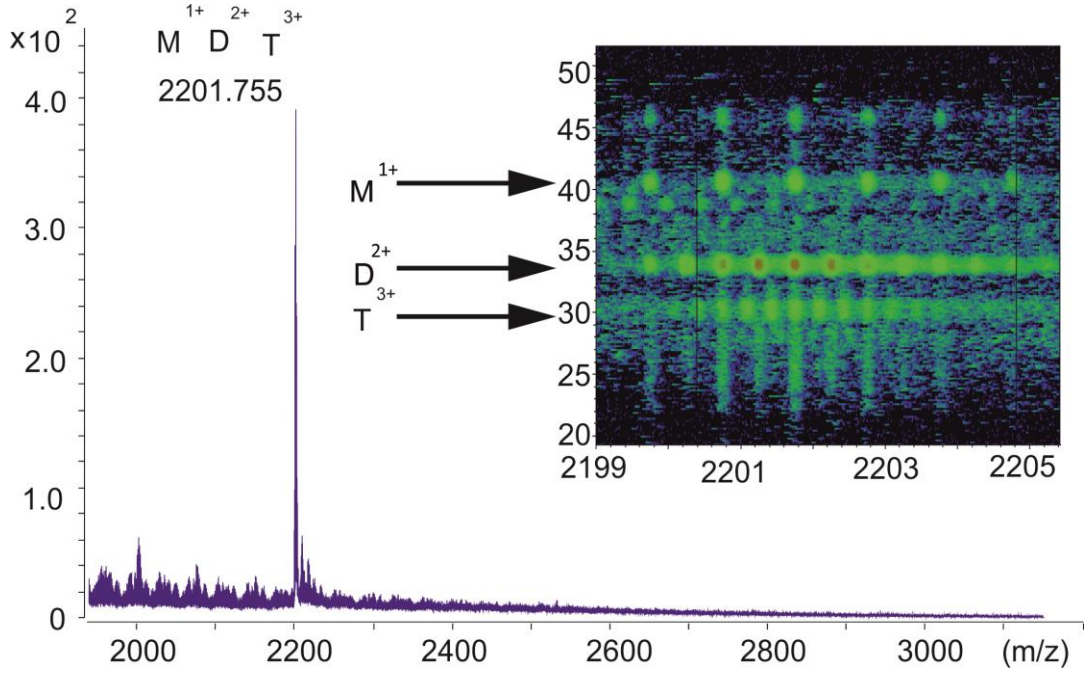



**Supplementary Figure 19.** $^{1}$H NMR DOSY spectrum ($CDCl_3$, 298 K, 400 MHz) of a mixture of **4b** (blue) and **4a** (red) showing that **4a** has a higher hydrodynamic radius despite its smaller size. This is only possible when **4a** is in aggregated state in solution.

### 3.3.2 Assessing aggregate composition by ESI-IMMS

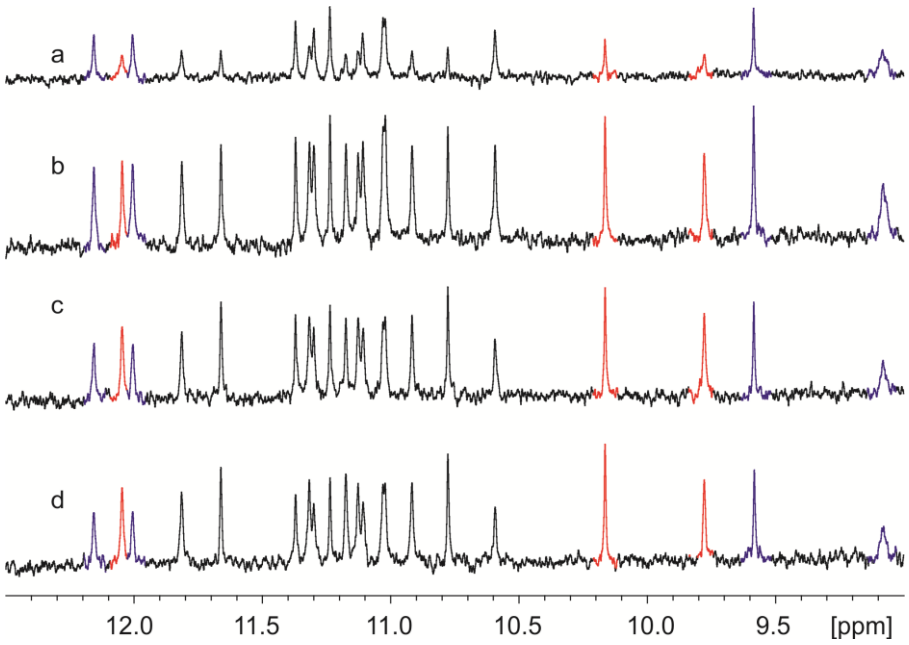



**Supplementary Figure 20.** ESI-IMMS spectrum of **5a** in 1:1 DCM/$CHCl_3$ vol/vol (0.1 mM). Inset: the ion mobility profile of the peak at *m*/*z* = 2038.894 shows it is composed of monomeric (1+), dimeric (2+) and trimeric (3+) species.

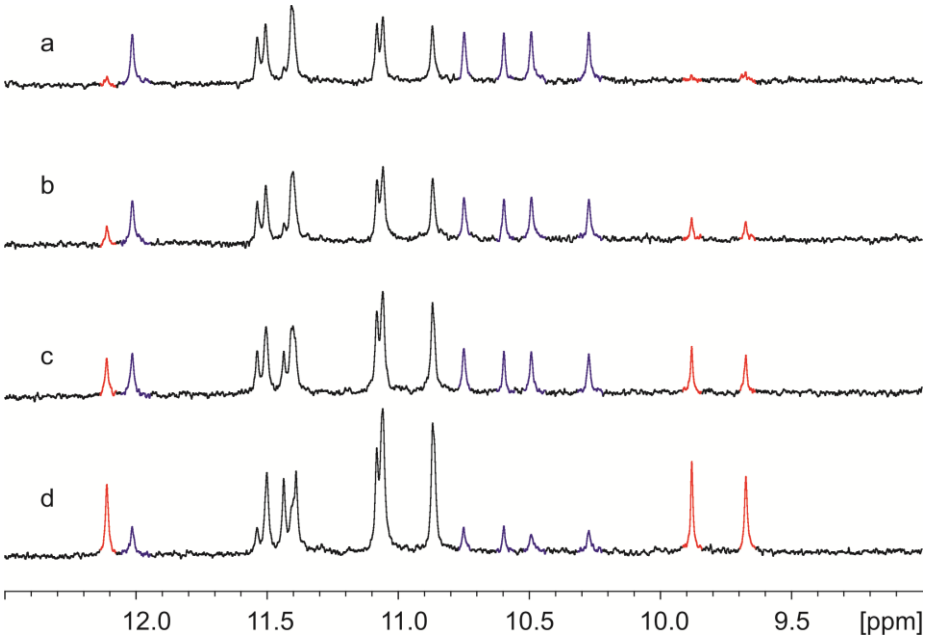



**Supplementary Figure 21.** ESI-IMMS spectrum of **4a** in 1:1 DCM/$CHCl_3$ vol/vol (0.1 mM). Inset: the ion mobility profile of the peak at *m*/*z* = 2201.755 shows it is composed of monomeric (1+), dimeric (2+) and trimeric (3+) species.

### 3.3.3 Assessing aggregate nature by dissolving crystals

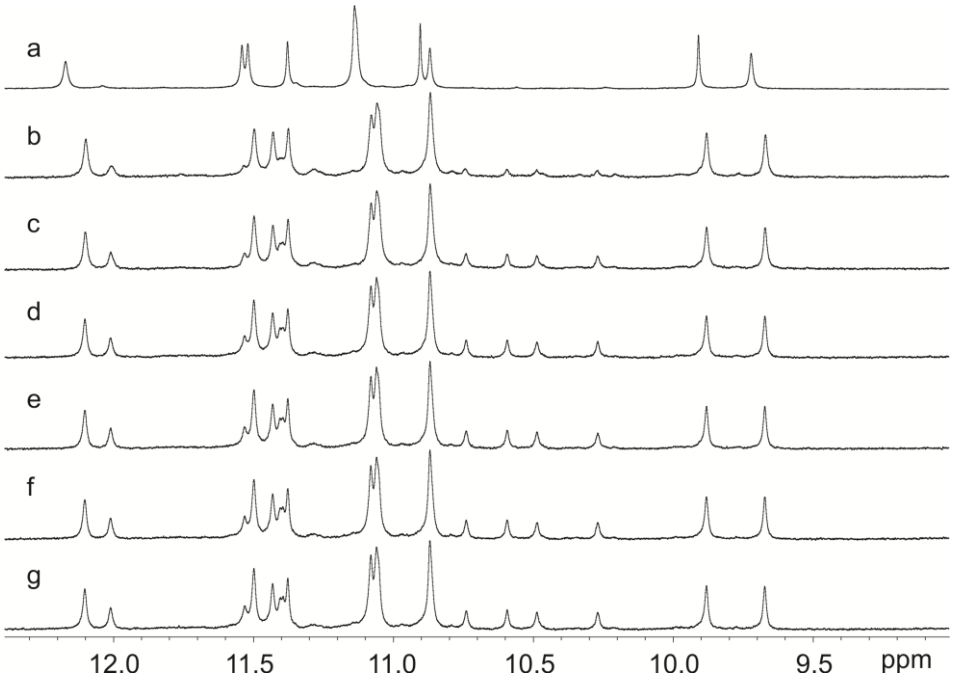



**Supplementary Figure 22.** Evolution of the $^{1}$H NMR spectrum (298 K, 300 MHz) of a freshly dissolved crystal of **5a** grown form chloroform/cyclohexane in 1:1 $CDCl_3$/DCM-d2 vol/vol after: (a) 2 min; (b) 4 min; (c) 6 min; (d) 8 min. This experiment allows to assign the blue signals (*i.e.* the species that is major in pure $CDCl_3$) to the dimeric bundle observed in the solid state.

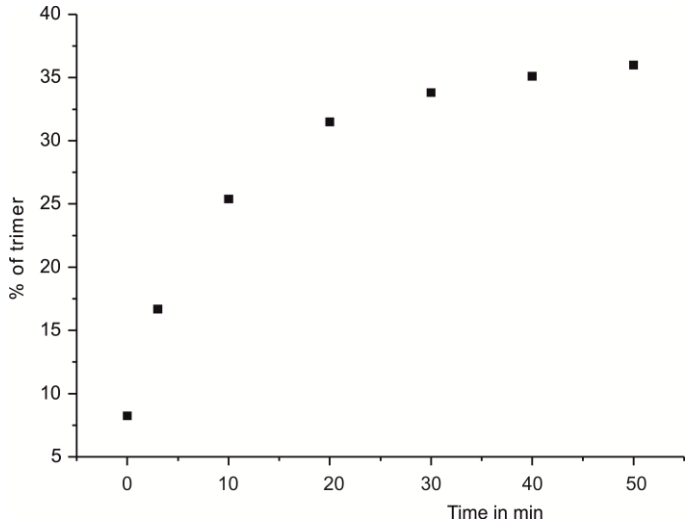



**Supplementary Figure 23.** Evolution of the $^{1}$H NMR spectrum (298 K, 300 MHz) of a freshly dissolved crystal of **4a** grown form DCM/cyclohexane in 1:1 $CDCl_3$/DCM-d2 vol/vol after: (a) 2 min; (b) 4 min; (c) 16 min; (d) 120 min. This experiment allows to assign the blue signals (*i.e.* the species that is major in pure DCM) to the trimeric bundle observed in the solid state. The proportions in d differ from those in Figure 4d because the spectra have been recorded at different concentrations.

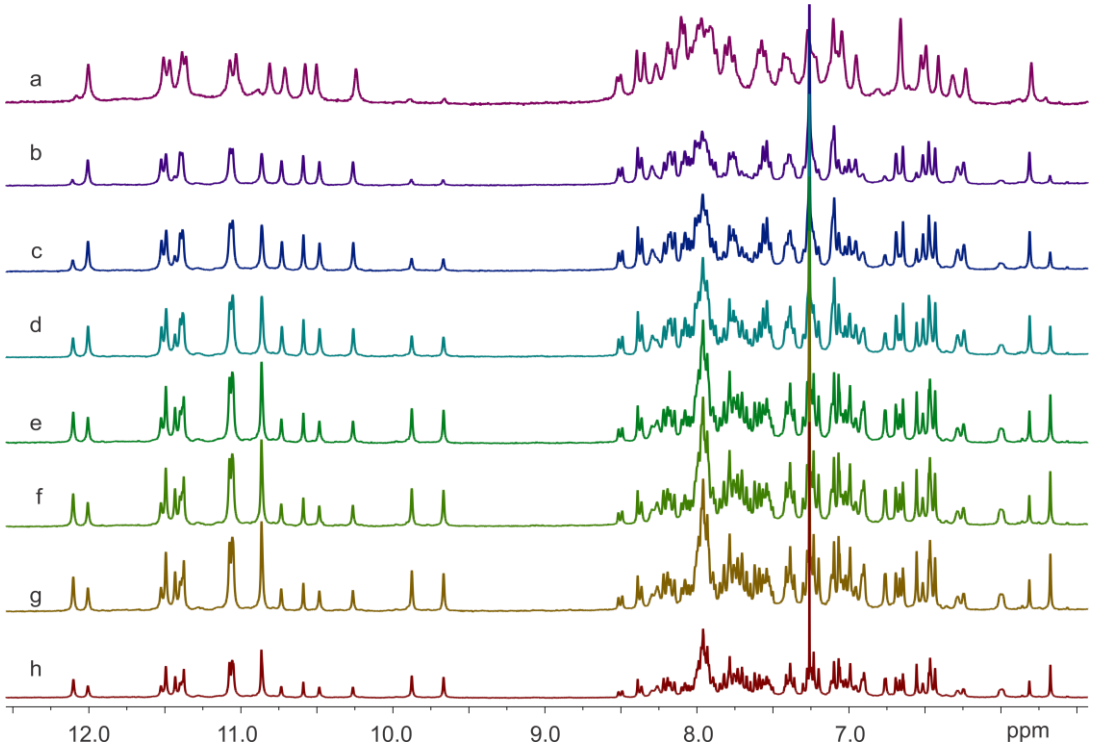
### 3.3.4 Monitoring slow aggregate interconversion



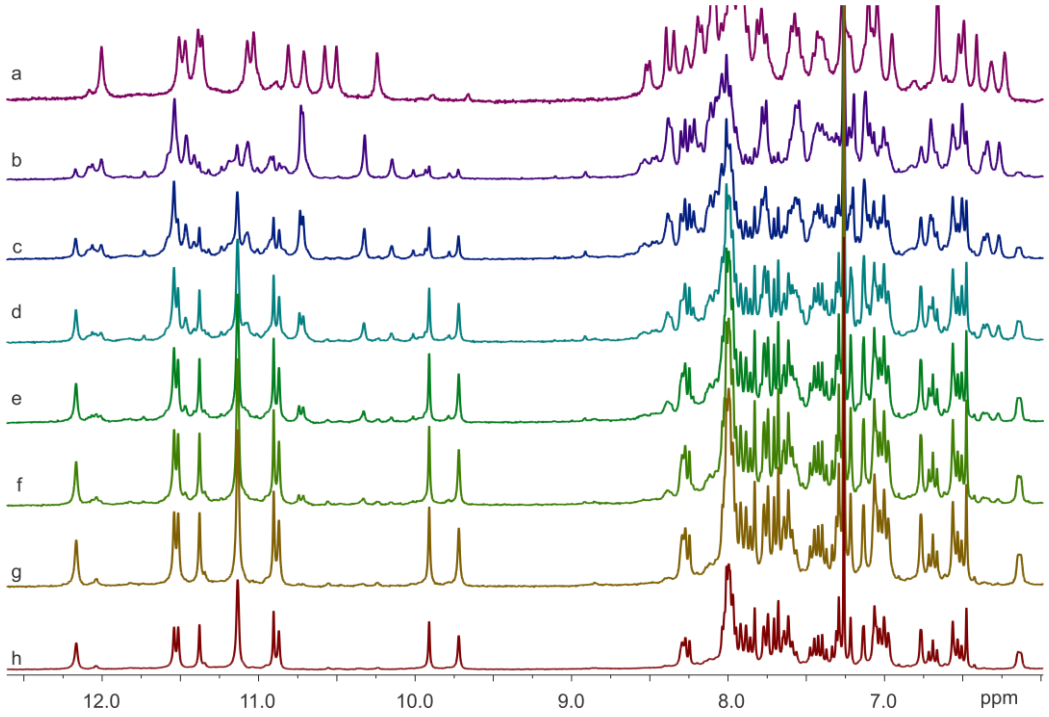

**Supplementary Figure 24.** $^{1}$H NMR spectra (300 MHz, 298 K, 1.5 mM) of **4a:** (a) at equilibrium in $CDCl_3$; (b-g) after evaporating sample (a) and 3 (b), 10 (c), 20 (d), 30 (e), 40 (f) and 50 min (g) after dissolving in 1:1 $CDCl_3$/DCM-d2 vol/vol.



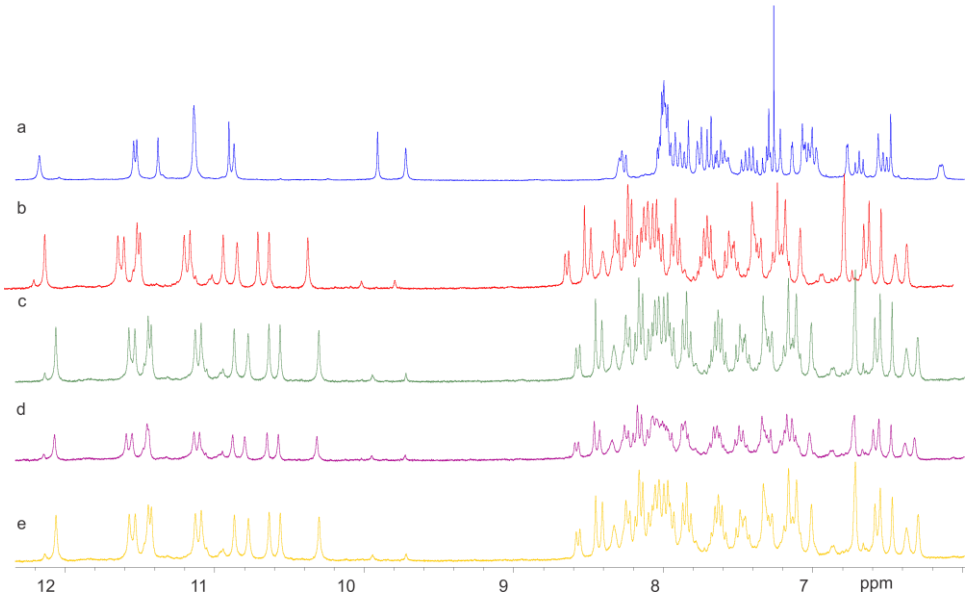

**Supplementary Figure 25.** Proportion of trimer (**4a**)$_3$ as a function of time after dissolving a sample of **4a** at equilibrium in $CHCl_3$ prior to evaporation (thus essentially dimeric) in 1:1 $CDCl_3$/DCM-d2 vol/vol (1.5 mM) as recorded by $^{1}$H NMR (see Supplementary Figure 24).



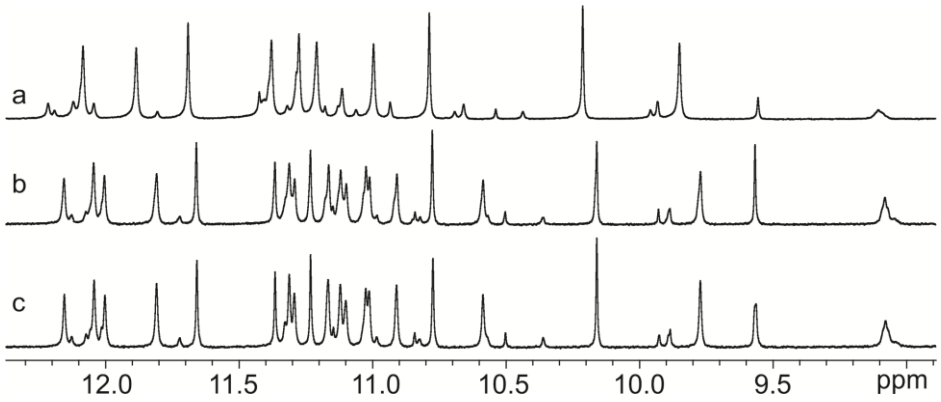

**Supplementary Figure 26.** $^{1}$H NMR spectra (300 MHz, 298 K, 1.5 mM) of **4a:** (a) at equilibrium in DCM-d2; (b-h) after evaporating sample (a) and 2 (b), 10 (c), 20 (d), 60 (e), 90 (f), 120 (g), and 330 min (h) after dissolving in 1:1 $CDCl_3$/DCM-d2 vol/vol.



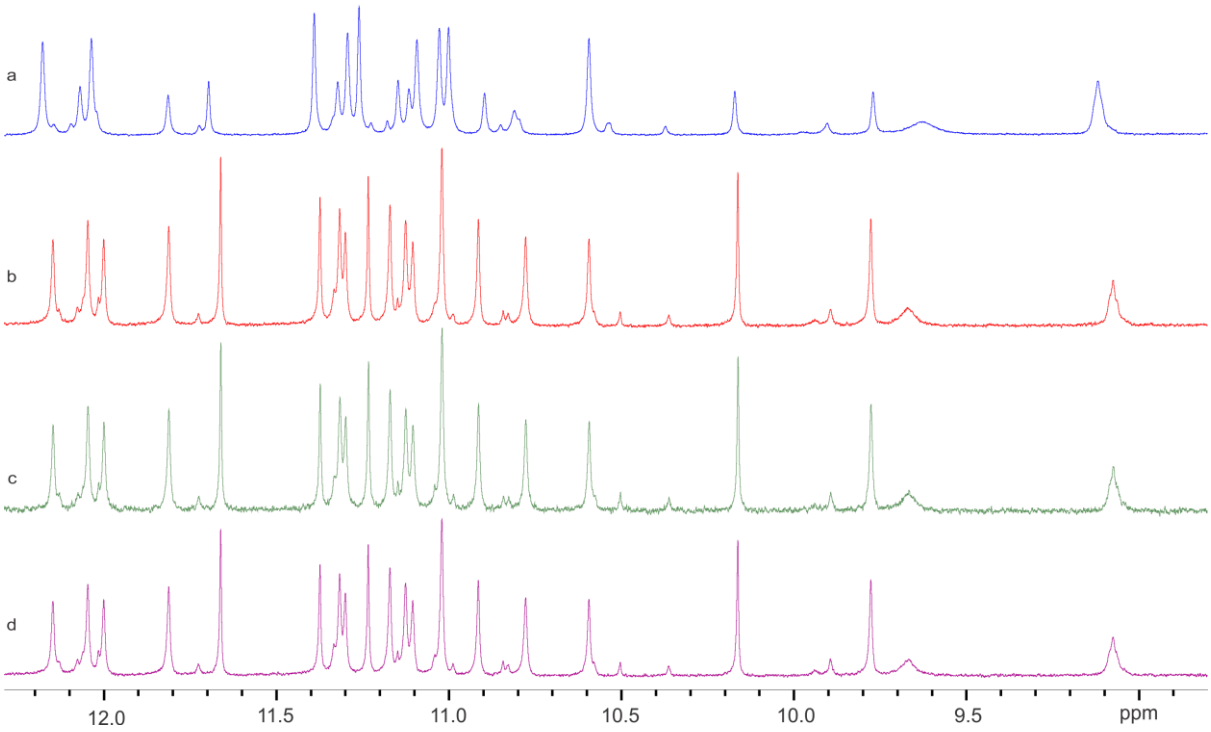

**Supplementary Figure 27.** $^{1}$H NMR spectra (300 MHz, 298 K, 1.5 mM) of **4a:** (a) at equilibrium in DCM-d2; (b-h) after evaporating sample (a) and 2 (b), 10 (c), 20 (d), 30 (e), 40 (f), 65 (h), and 120 min (h) after dissolving it in $CDCl_3$.




**Supplementary Figure 28.** $^{1}$H NMR spectra (300 MHz, 298 K, 1.5 mM) of **4a:** (a) at equilibrium in $CDCl_3$; (b-e) after evaporating sample (a) and 3 (b), 10 (c), 25 (d), and 40 min (e) after dissolving it in DCM-d2.

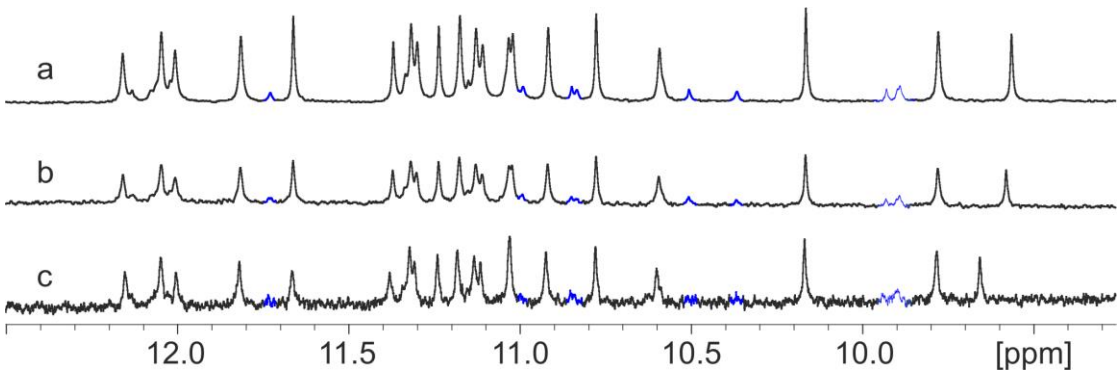



**Supplementary Figure 29.** $^{1}$H NMR spectra (300 MHz, 298 K, 3.0 mM) of **5a:** (a) at equilibrium in $CDCl_3$; (b) after evaporating sample (a) and 15 min after dissolving in 1:1 $CDCl_3$/DCM-d2 vol/vol; (c) after 50 min in 1:1 $CDCl_3$/DCM-d2 vol/vol. The mixture is already at equilibrium in 15 min.

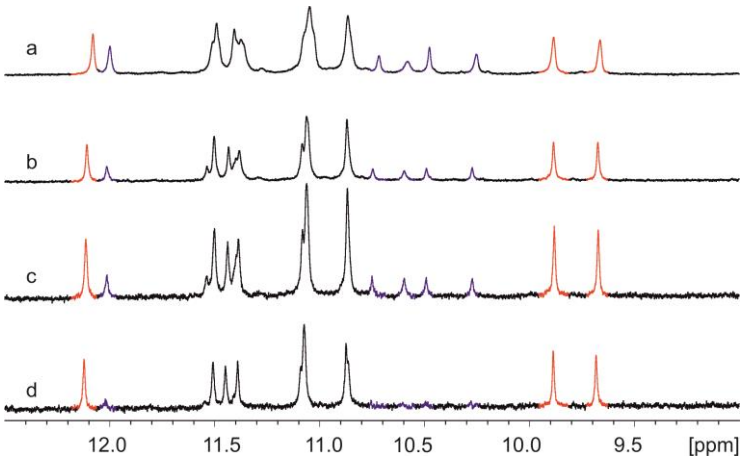



**Supplementary Figure 30.** $^{1}$H NMR spectra (300 MHz, 298 K, 3.0 mM) of **5a**: (a) at equilibrium in DCM-d2; (b) after evaporating sample (a) and 4 min after dissolving it in 1:1 $CDCl_3$/DCM-d2 vol/vol; (c) after 10 min in 1:1 $CDCl_3$/DCM-d2 vol/vol; (d) after 15 min in 1:1 $CDCl_3$/DCM-d2 vol/vol. The mixture is already at equilibrium in 4 min.

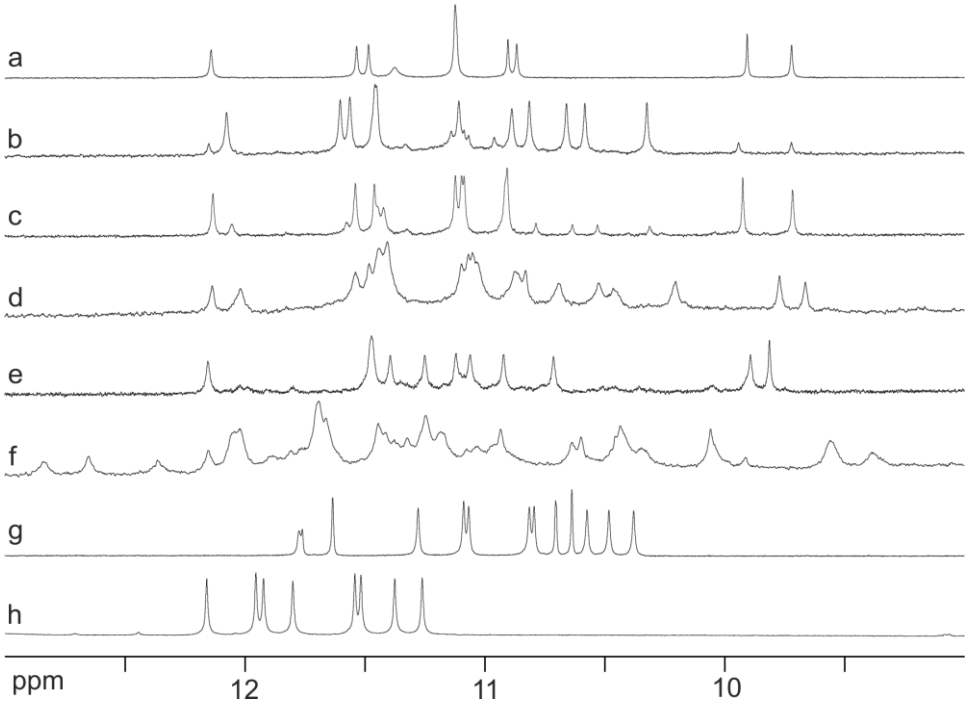
### 3.3.5 Concentration and solvent dependence of aggregation



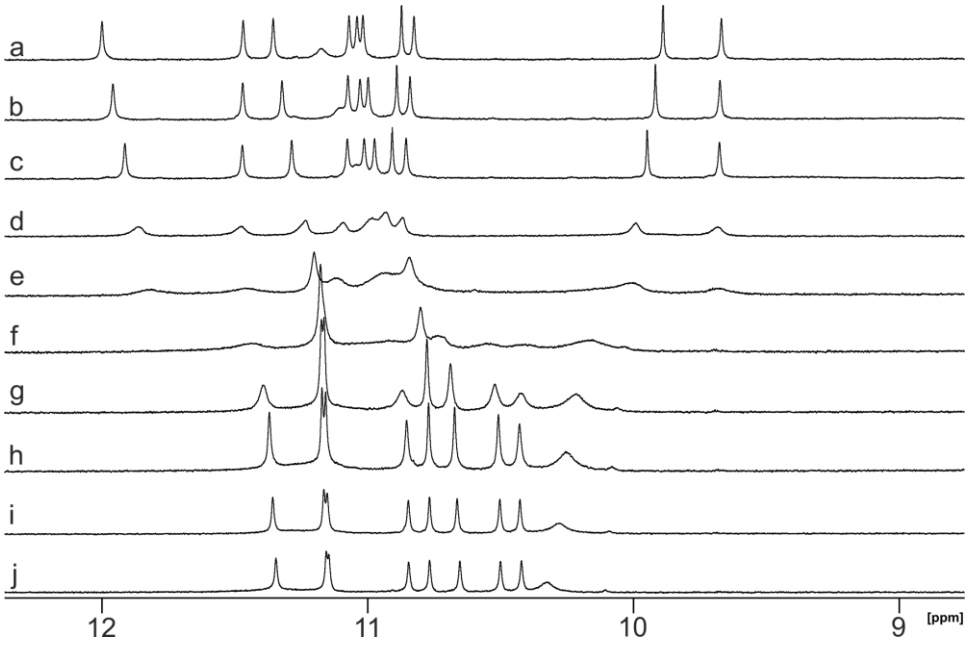

**Supplementary Figure 31.** $^{1}$H NMR spectra (298 K, 300 MHz) of **5a** in 1:1 $CDCl_3$/DCM-d2 vol/vol at: (a) 13.6 mM; (b) 3.40 mM; (c) 1.70 mM. Upon increasing concentration, the relative intensity of the signals marked in blue increases.



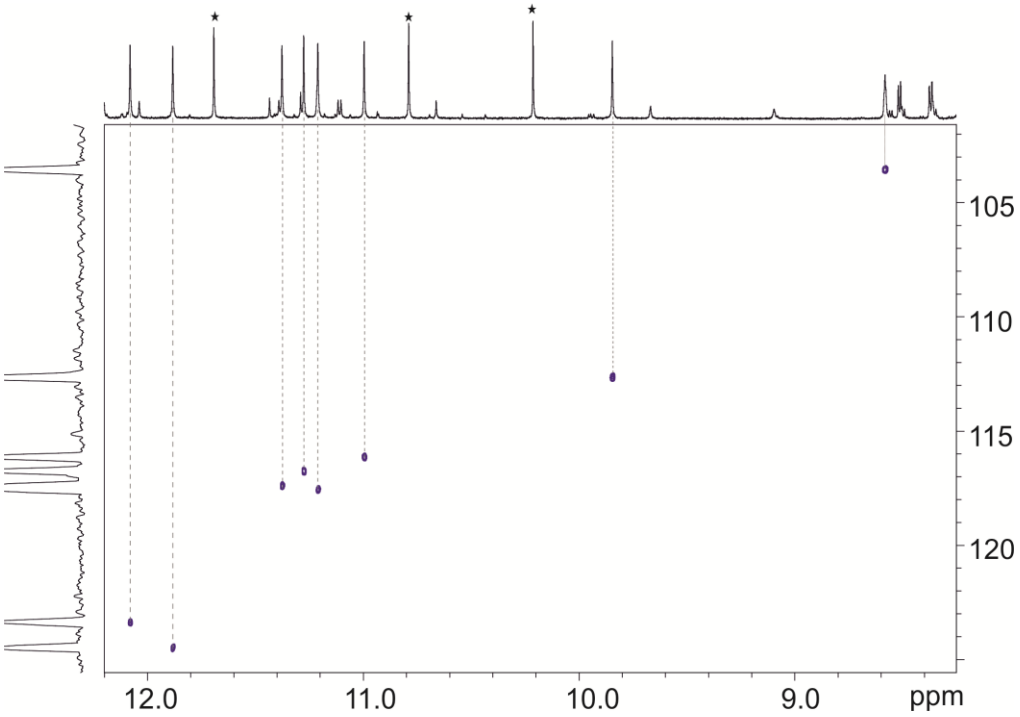

**Supplementary Figure 32:** $^{1}$H NMR spectra (298 K, 300 MHz) of **4a** in 1:1 $CDCl_3$/DCM-d2 vol/vol at: (a) 13.6 mM; (b) 3.40 mM; (c) 1.70 mM; (d) 0.43 mM. The signals marked in red belong to the major species in $CDCl_3$. The signals marked in purple belong to the major species in DCM-d2. Upon increasing concentration, the relative intensity of the signals marked in purple increases.



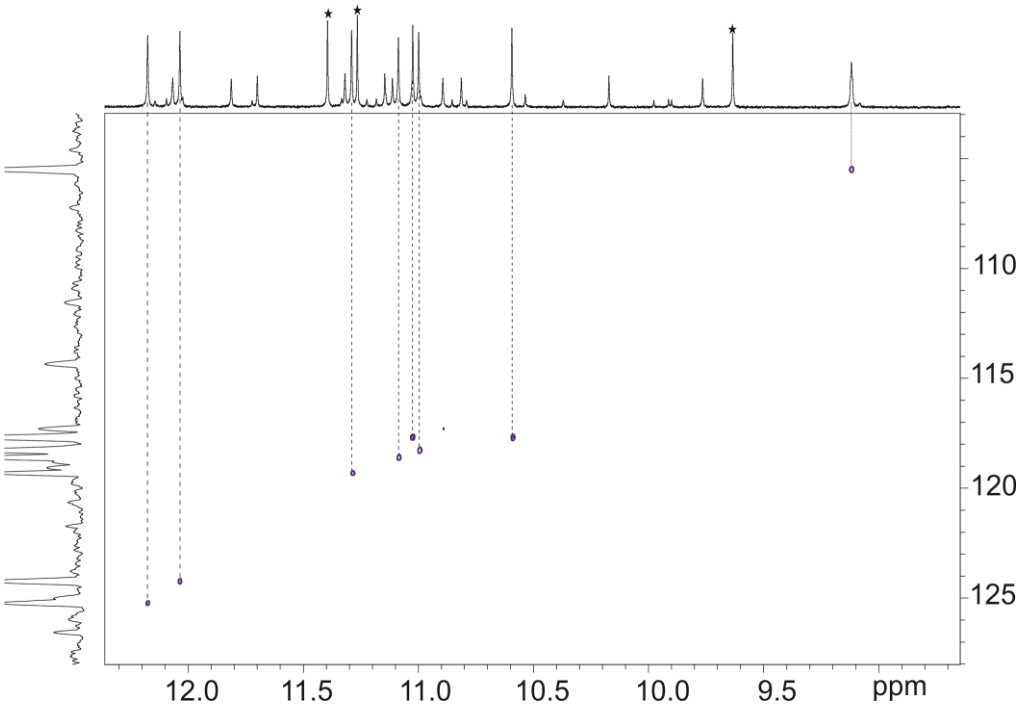

**Supplementary Figure 33:** $^{1}$H NMR spectra (298 K, 300 MHz) of **4a** in different solvents and solvent mixtures. (a) $CDCl_3$ (the dimer prevails); (b) $CD_2Cl_2$ (the trimer dominates) (c) $CDCl_3$/$CD_2Cl_2$ (1/1) (the dimer dominates); (d) $CDCl_3$/$CD_2Cl_2$/$CCl_4$ (1/1/4) (the trimer is enhanced as compared to d); (e) $CDCl_3$/$CD_2Cl_2$/$C_2D_2Cl_4$ (1/1/4) (the dimer is enhanced as compared to d); (f) $CDCl_3$/$CD_2Cl_2$/Toluene-$D_8$ (1/1/4) (more than two species are present); (g) Pyridine-$D_5$ (a monomeric helices prevails); (h) DMSO-$D_6$ (a monomeric helices prevails, see Supplementary Figure 34). Spectra a-f are recorded at 2.5 mM. In the case of $CCl_4$, $C_2D_2Cl_4$ and toluene-$D_8$, spectra cannot be measured in pure solvents because of poor solubility.



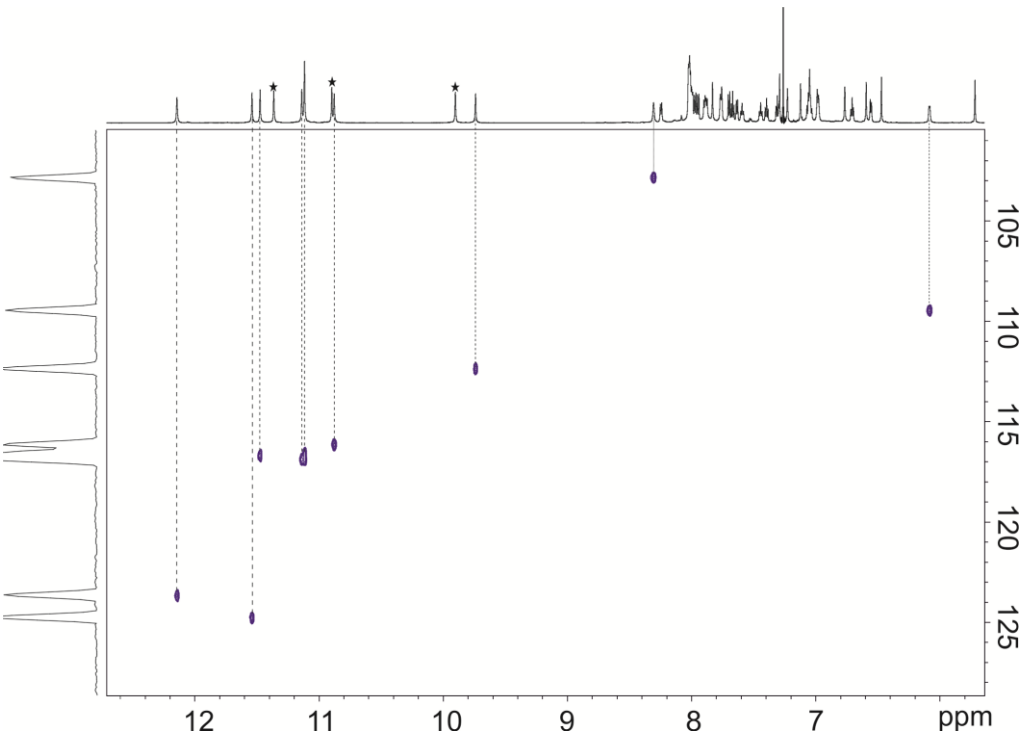

**Supplementary Figure 34:** $^{1}$H NMR spectra (298 K, 300 MHz) of **4a** in $CDCl_3$ following the addition of DMSO-$D_6$: (a)1%; (b) 2% ; (c) 4%; (d) 9%; (e) 13%; (f) 16%; (g) 20%; (h) 23%; (i) 26%, (j) 31%. The initial dimer is progressively dissociated in a monomer. Exchange is relatively fast so average signals are observed. Variations of the monomer/dimer ratio occur over a wide range of solvent proportions.



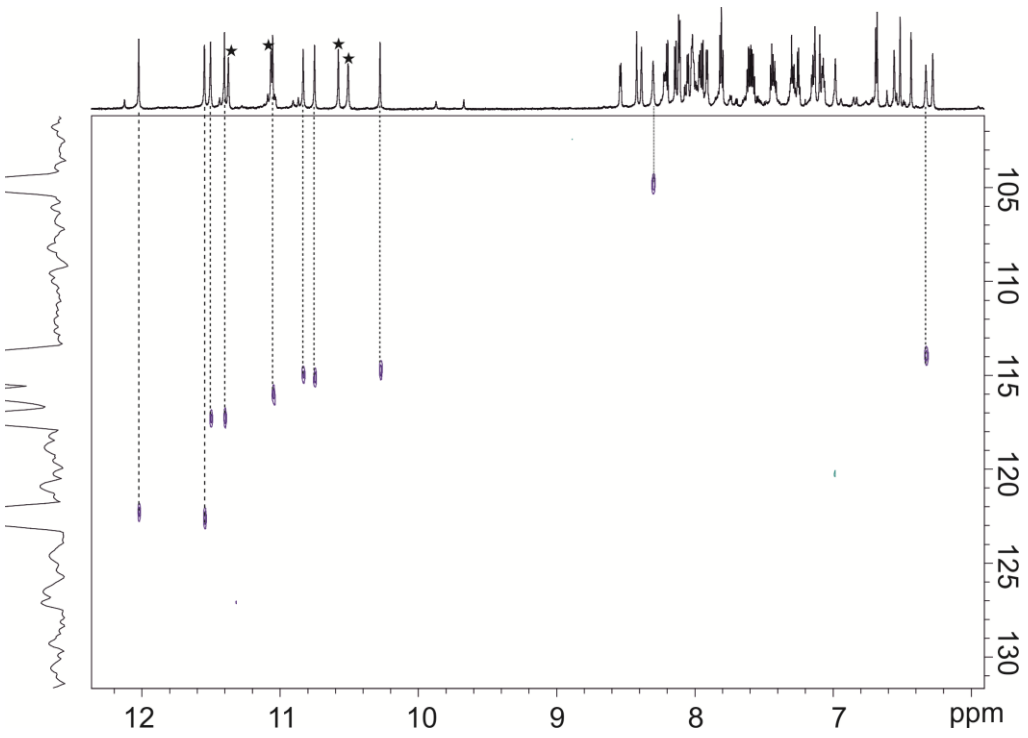

**Supplementary Figure 35.** $^{15}$N-$^{1}$H HSQC (700 MHz, 298 K) of **5a** in $CDCl_3$. Only NH resonances correlate. Stars indicate the signals of OH protons.




**Supplementary Figure 36.** $^{15}N$-$^{1}H$ HSQC (700 MHz, 298 K) of **5a** in DCM-d2. Only NH resonances correlate. Stars indicate the signals of OH protons.

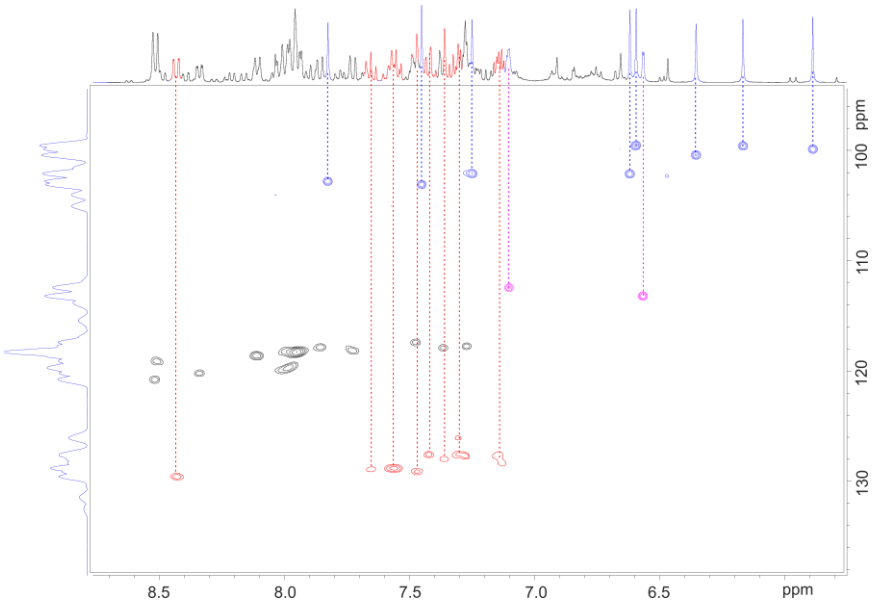



**Supplementary Figure 37.** $^{15}N$-$^{1}H$ HSQC (700 MHz, 298 K) of **4a** in $CDCl_3$. Only NH resonances correlate. Stars indicate the signals of OH protons.

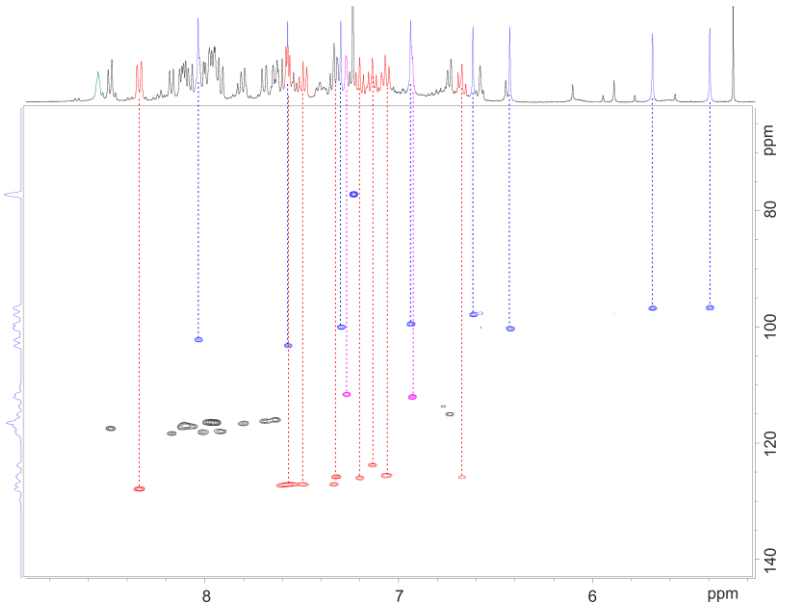



**Supplementary Figure 38.** $^{15}N$-$^{1}H$ HSQC (700 MHz, 298 K) of **4a** in DCM-d2. Only NH resonances correlate. Stars indicate the signals of OH protons.

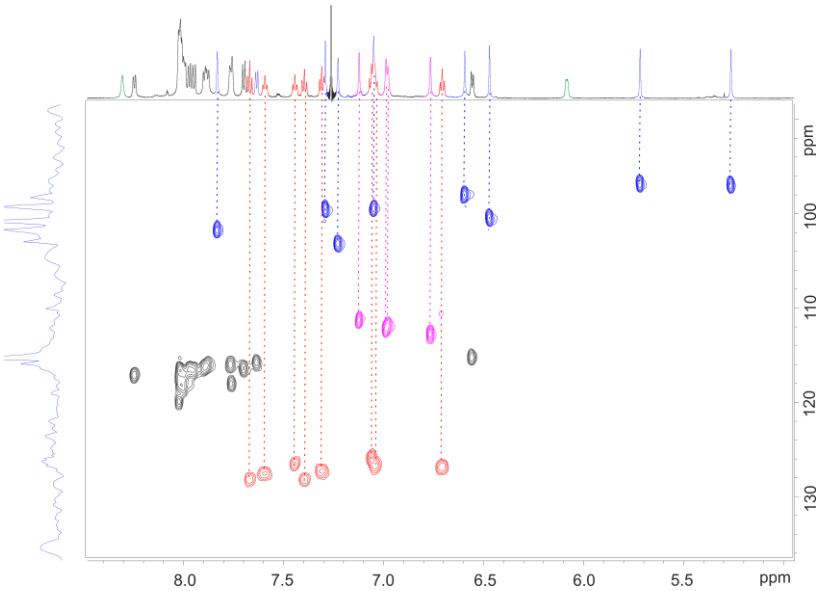
### 3.3.6 Assignment of structures by HSQC and NOE



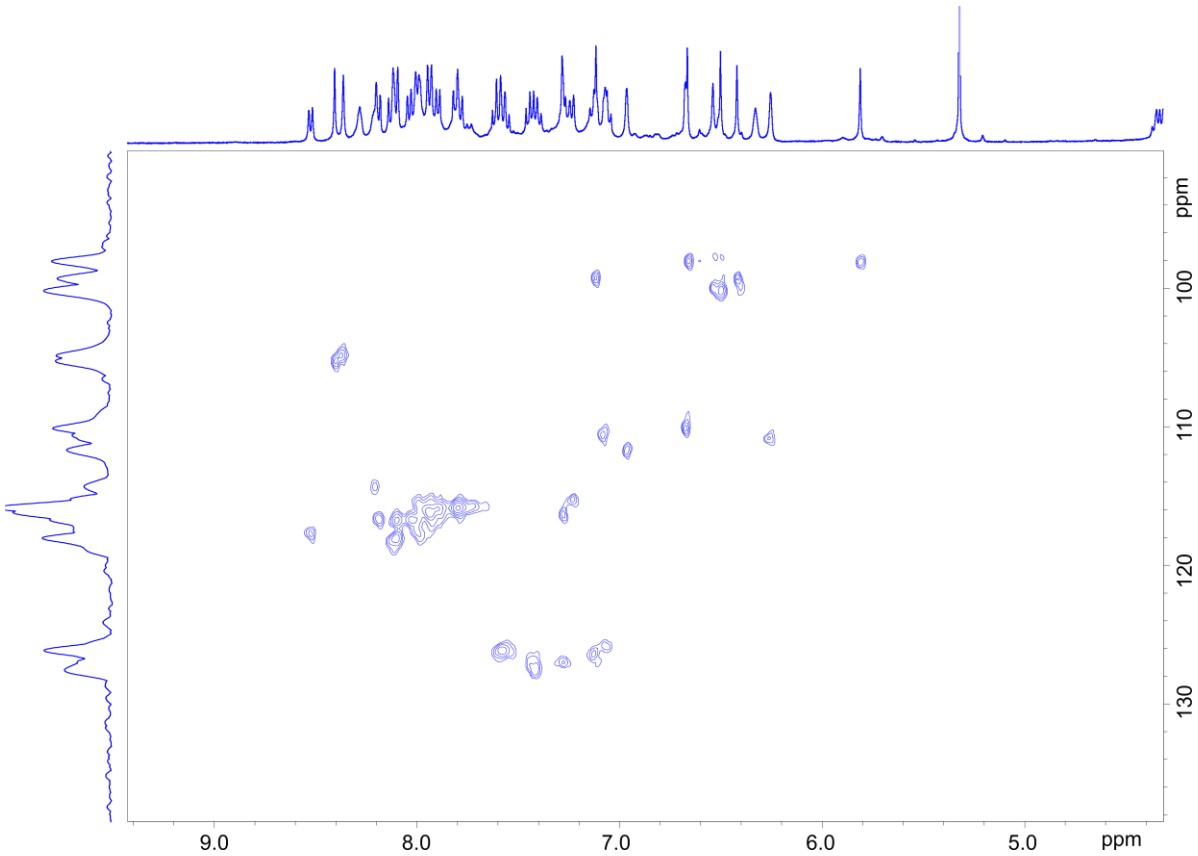

**Supplementary Figure 39.** $^{1}H$-$^{13}C$ HSQC (DCM-d2, 298 K, 400 MHz) of **5a**. Blue signals correspond to quinoline H3 protons. Red signals correspond to quinoline H6 protons. Black signals correspond to quinoline H5 and H7 protons. Pink signals correspond to protons belonging to Y units.



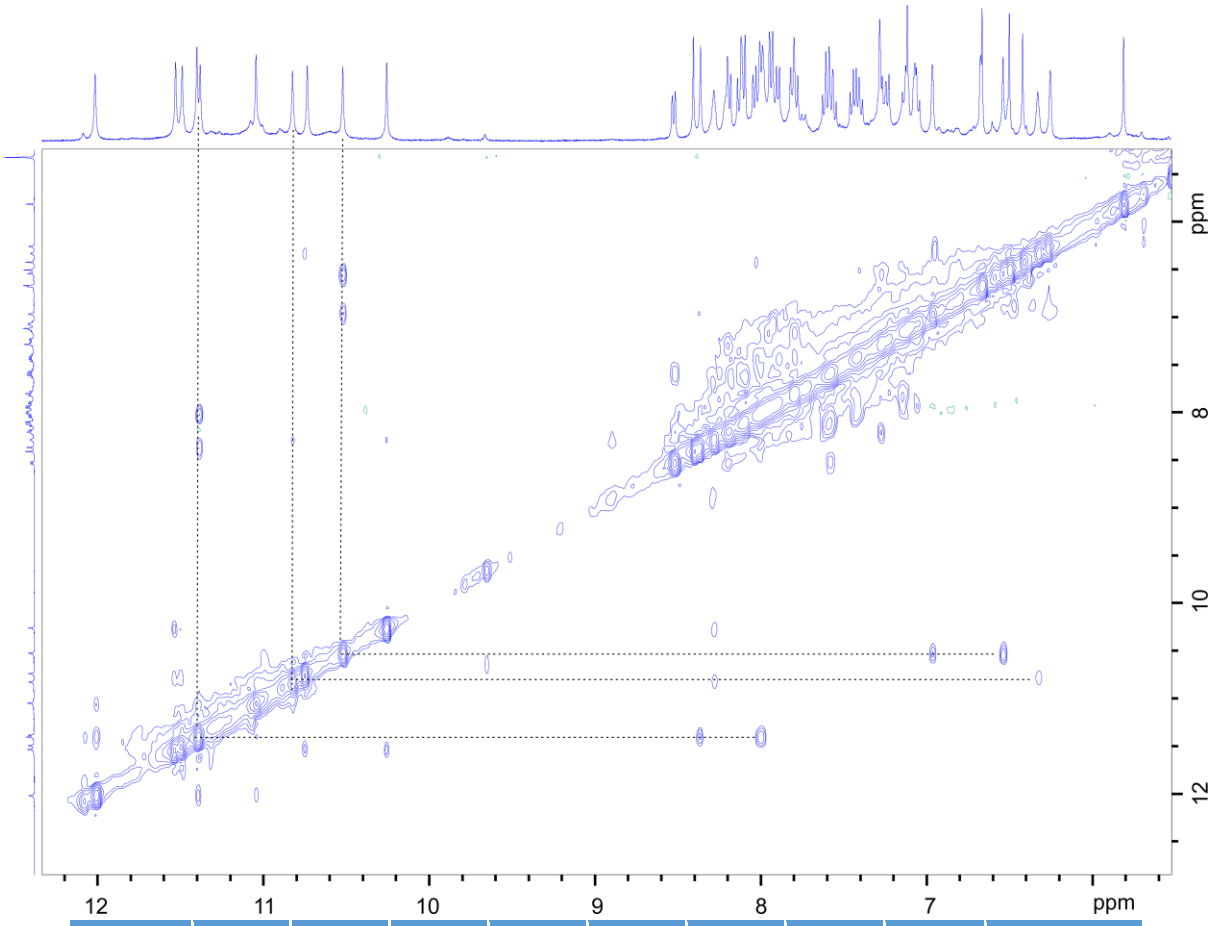

**Supplementary Figure 40.** $^{1}H$-$^{13}C$ HSQC ($CDCl_3$, 298 K, 400 MHz) of **5a**. Blue signals correspond to quinoline H3 protons. Red signals correspond to quinoline H6 protons. Black signals correspond to quinoline H5 and H7 protons. Pink signals correspond to protons belonging to Y units.




**Supplementary Figure 41.** $^{1}H$-$^{13}C$ HSQC ($CDCl_3$, 298 K, 400 MHz) of **4a**. Blue signals correspond to quinoline H3 protons. Red signals correspond to quinoline H6 protons. Black signals correspond to quinoline H5 and H7 protons. Pink signals correspond to protons belonging to Y units.

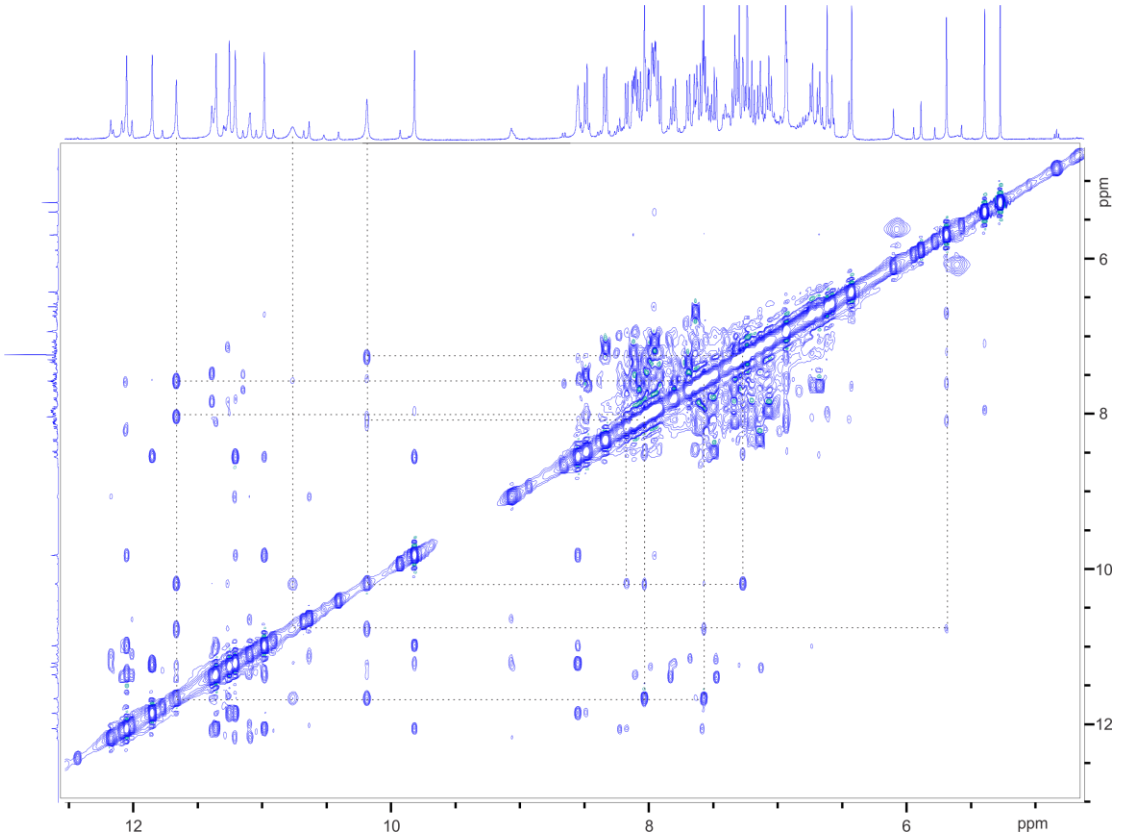



**Supplementary Figure 42.** $^{1}H$-$^{13}C$ HSQC (DCM-d2, 298 K, 400 MHz) of **4a**.



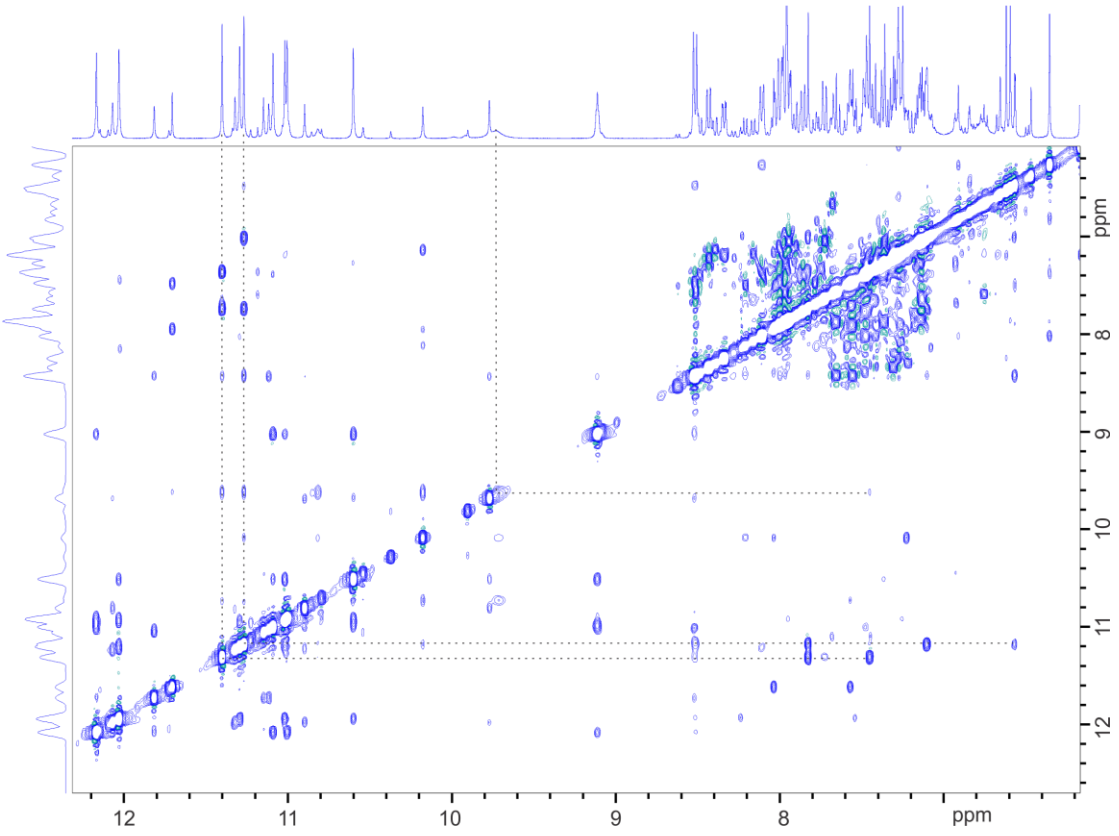

| Protons | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Y**-O<u>H</u> **(10.52)** | | | | | | **Y**-C<u>H</u> (6.97) | **Q**-<u>H3</u> (6.55) | | |
| **Y**-O<u>H</u> **(10.74)** | | | | | | | | **Y**-<u>H3/5</u> (6.33) | NH-COC<u>H</u>$_3$ (1.08) |
| **X**-O<u>H</u> **(11.04)** | **Q**-<u>H5/7</u> (8.51) | **Q**-<u>H3</u> (8.39) | | **Q**-<u>H5/7</u> (8.17) | | | | | |
| **X**-O<u>H</u> **(11.39)** | | | **Q**-<u>H3</u> (8.37) | | **Q**-<u>H5/7</u> (8.00) | **Y**-C<u>H</u> (6.97) | | | |

**Supplementary Figure 43.** *Top:* NOESY spectrum (DCM-d2, 298 K, 400 MHz) of **4a**. *Bottom:* Selection of relevant NOE correlations of **4a** (DCM-d2, 298 K, 400 MHz). Each signal indicated in the left column correlates with all signals indicated in the same line. Assignment to a type of signal (**Y**-O<u>H</u>, **X**-O<u>H</u>, **Q**-<u>H3</u>, **Q**-<u>H5/7</u>…) is established unambiguously, but the exact position in the sequence has not been determined. All correlations are consistent with the parallel trimer observed in the solid state structure of **4a.**



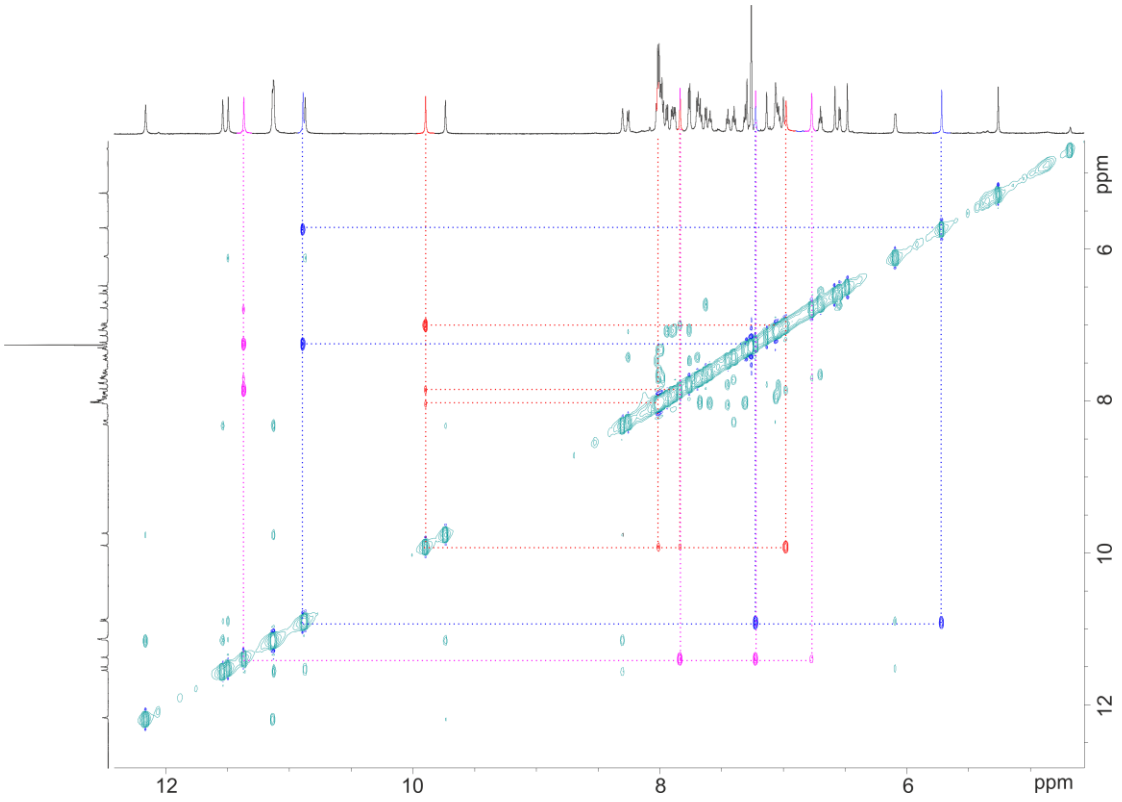

| Protons | | | | Y-CH2 (4.03) | | |
|---|---|---|---|---|---|---|
| **Y**-NH **(8.55)** | | | | | | **Y**-CH2 (4.03) |
| **Y**-OH **(10.19)** | **Q**-H5/7 (8.17) | **Q**-H3 (8.03) | | **Y**-H3/5 (7.27) | | |
| **X**-OH **(10.77)** | | | **Q**-H3 (7.57) | | **Q**-H3 (5.69) | |
| **X**-OH **(11.67)** | | **Q**-H3 (8.03) | **Q**-H3 (7.57) | | | |

**Supplementary Figure 44.** *Top:* NOESY spectrum ($CDCl_3$, 298 K, 400 MHz) of **5a.** *Bottom:* Selection of relevant NOE correlations of **5a** ($CDCl_3$, 298 K, 400 MHz). Each signal indicated in the left column correlates with all signals indicated in the same line. Each signal indicated in the top line correlates with all signals of the same column. Assignment to a type of signal (Y-OH, X-OH, Q-H3, Q-H5/7…) is established unambiguously, but the exact position in the sequence has not been determined. All correlations are consistent with the tilted dimer observed in the solid state structure of **5a**. The correlation highlighted in yellow could not be accounted for in a parallel or an anti-parallel arrangements of the helices.




| Protons | | | | | | |
|---|---|---|---|---|---|---|
| **Y**-CH2 | | **Q**-H3 (7.83) | | **Y**-H3/5 (7.10) | | |
| **X**-OH **(9.73)** | | | **Q**-H3 (7.45) | | | **Q**-H3 (6.35) |
| **Y**-OH **(11.27)** | **Q**-H5/7 (8.51) | **Q**-H3 (7.83) | | **Y**-H3/5 (7.10) | **Y**-H3/5 (6.57) | |
| **X**-OH **(11.40)** | | **Q**-H3 (7.83) | **Q**-H3 (7.45) | | | |

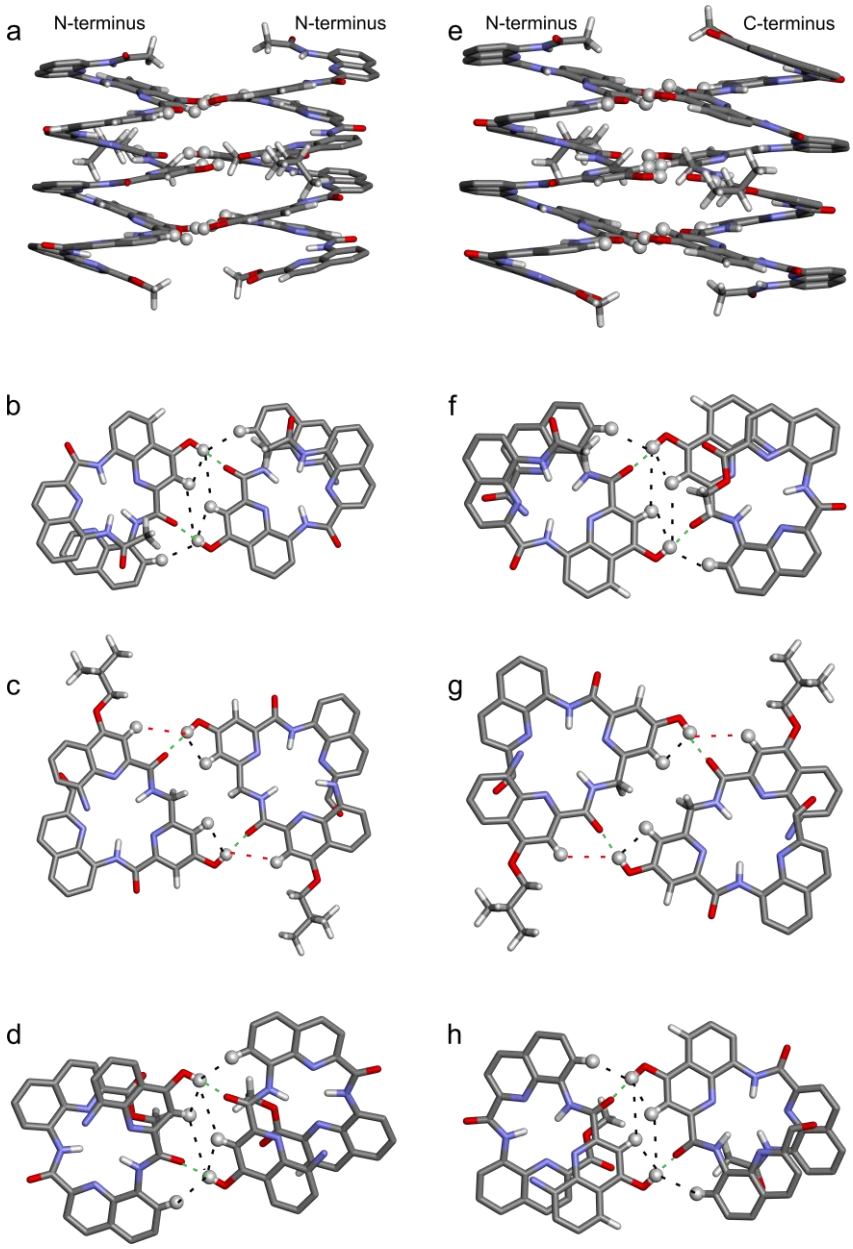
**Supplementary Figure 45.** *Top:* NOESY spectrum (DCM-d2, 298 K, 400 MHz) of **5a**. *Bottom:* Selection of relevant NOE correlations of **5a** (DCM-d2, 298 K, 400 MHz). Each signal indicated in the left column correlates with all signals indicated in the same line. Assignment to a type of signal (Y-OH, X-OH, Q-H3, Q-H5/7…) is established unambiguously, but the exact position in the sequence has not been determined. Correlations highlighted in yellow are incompatible with parallel or antiparallel dimeric structures but compatible with *PP*/*MM* tilted dimeric structures. One the tilted dimeric structure being already attributed to the dominant species in $CDCl_3$ (Supplementary figure 44), the other tilted structure remains the only possible assignment.



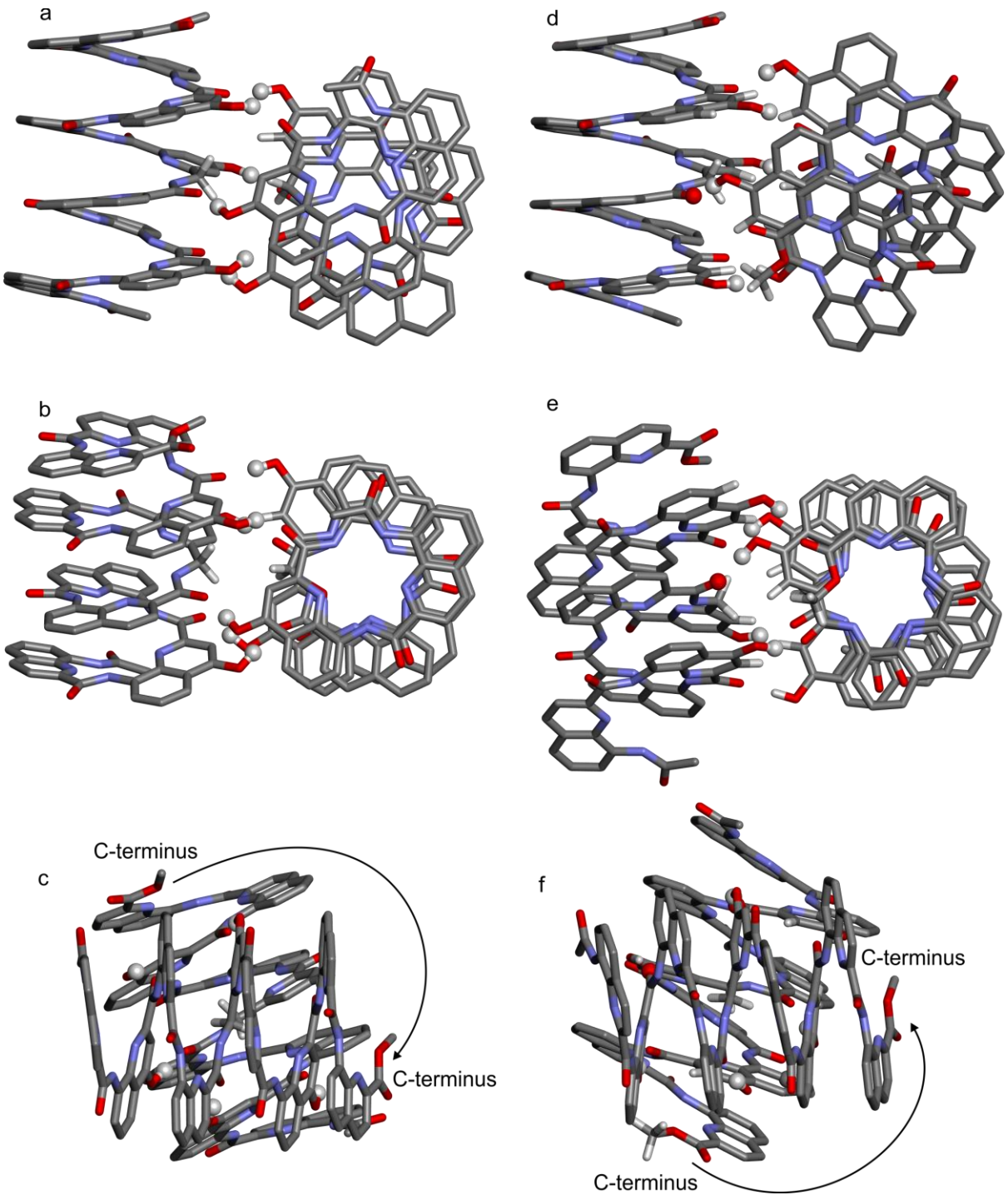

| **Protons** | | | | **Y-**C<u>H2</u> (4.05, 2.62) | | |
|---|---|---|---|---|---|---|
| **Y-**O<u>H</u> **(7.70)** | | | | | Y-<u>H3/5</u> (6.77) | |
| **Y-**O<u>H</u> **(9.90)** | **Q-**<u>H5/7</u> (7.99) | **Q-**<u>H3</u> (7.83) | | **Y-**<u>H3/5</u> (6.98) | | |
| **X-**O<u>H</u> **(10.89)** | **Q-**<u>H5/7</u> (7.99) | | **Q-**<u>H3</u> (7.23) | | | **Q-**<u>H3</u> (5.72) |
| **X-**O<u>H</u> **(11.37)** | | **Q-**<u>H3</u> (7.83) | **Q-**H (7.23) | | Y-<u>H3/5</u> (6.77) | |

**Supplementary Figure 46.** *Top:* NOESY spectrum ($CDCl_3$, 298 K, 400 MHz) of **4a**. *Bottom:* Selection of relevant NOE correlations of **4a** ($CDCl_3$, 298 K, 400 MHz). Each signal indicated in the left column correlates with all signals indicated in the same line. Each signal indicated in the top line correlates with all signals of the same column. Assignment to a type of signal (Y-O<u>H</u>, X-O<u>H</u>, Q-<u>H3</u>, Q-<u>H5/7</u>…) is established unambiguously, but the exact position in the sequence has not been determined. Yellow correlation is not possible for the model compound in bracket. All correlations are compatible with a tilted *PP*/*MM* dimer. Correlations incompatible with parallel PP/MM dimers, parallel PPP/MMM trimers, or both are highlighted in yellow, green or blue, respectively. Correlations incompatible with both parallel PP/MM dimers and antiparallel PM dimers are highlighted in purple. Assignment to a tilted PP/MM dimer is corroborated with the fact that one of the hydroxyl group is upfield shifted, suggesting that it is not hydrogen bonded.

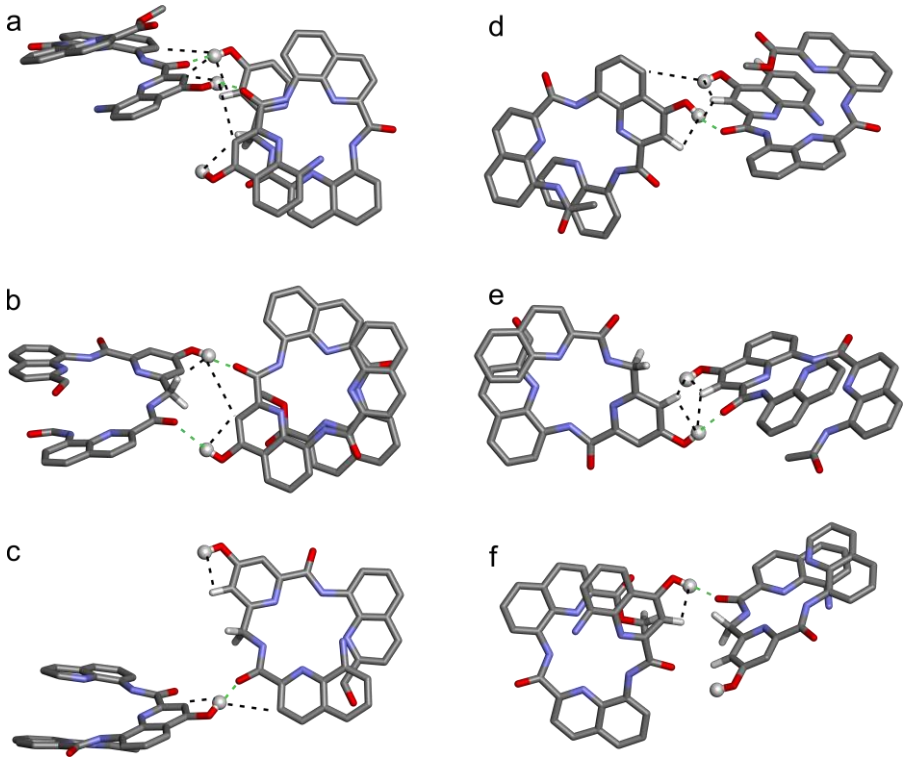
## 3.4 Molecular modelling



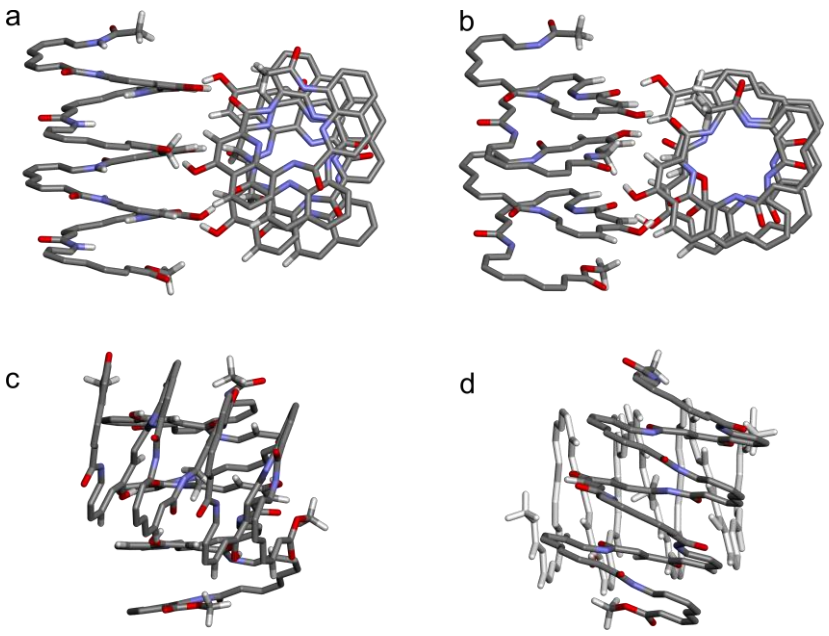

**Supplementary Figure 47.** Energy minimized models of hydrogen bonded dimeric structures of **5a**. a-d show different views of a *PP* parallel dimer (similar to the structure of **3a**). b-d represent fragments showing intermolecular hydrogen bonding. e-h show different views of a *PM* antiparallel dimer. f-h represent fragments showing intermolecular hydrogen bonding. Green dashes indicate hydrogen bonds. Black dashed lines indicate some possible NOE correlations. Red dashed lines focus on NOE correlations of **Y**-OH that are not observed. Instead a correlation between **Y**-OH and the H3 proton of **X** is observed that allows to rule out the existence of the two models shown here. Molecular Models calculation were done using MacroModel version 8.6 (Schrödinger Inc.).Energy minimized structures were initiated from manually pre-organized structures, using MMFs force-field as implemented in this software, 1000 steps of Truncated Newton Conjugate Gradient (TNCG), no implicit solvent and the extended Cutoff option.




**Supplementary Figure 48**. Two possible *PP* tilted dimeric structures of **5a**. a-c represent different views of an energy minimized model. d-f represent the tilted dimer observed in the solid state. The model (a, b, c) corresponds to a left-handed 120° tilt with respect to a parallel dimer. The crystal structures (d, e, f) corresponds to a right-handed 120° tilt with respect to a parallel dimer. See also Supplementary Figure 49.

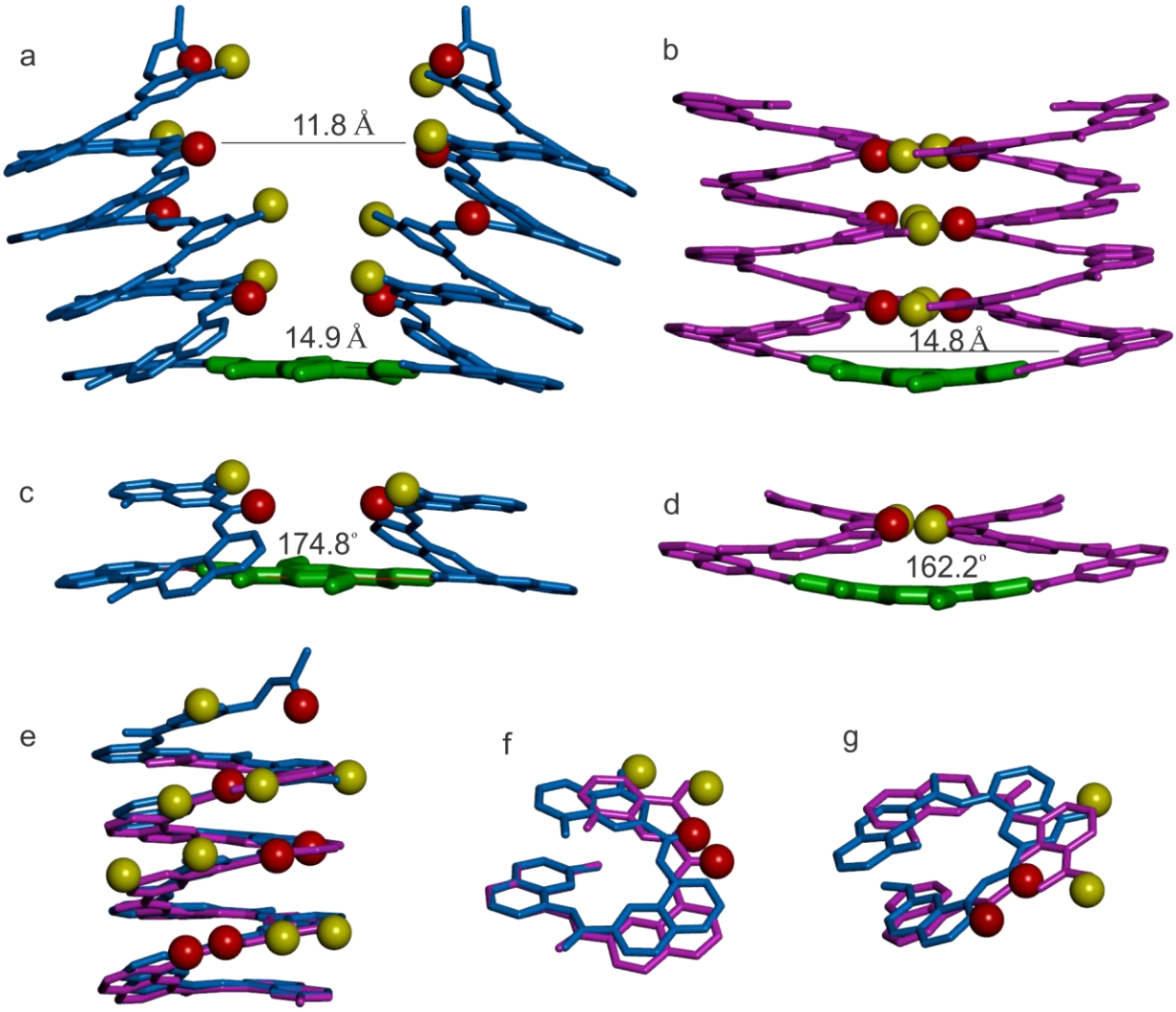



**Supplementary Figure 49**. Interactions within the tilted dimers of **5a** shown in Supplementary Figure 48. (a), (b), (c) depict interactions within the dimer shown in Supplementary Figure 48 (a-f) depict interactions within the dimer shown in Supplementary Figure 48 (d-f). Green dashes indicate hydrogen bonds. Black dashed lines indicate some possible NOE correlations



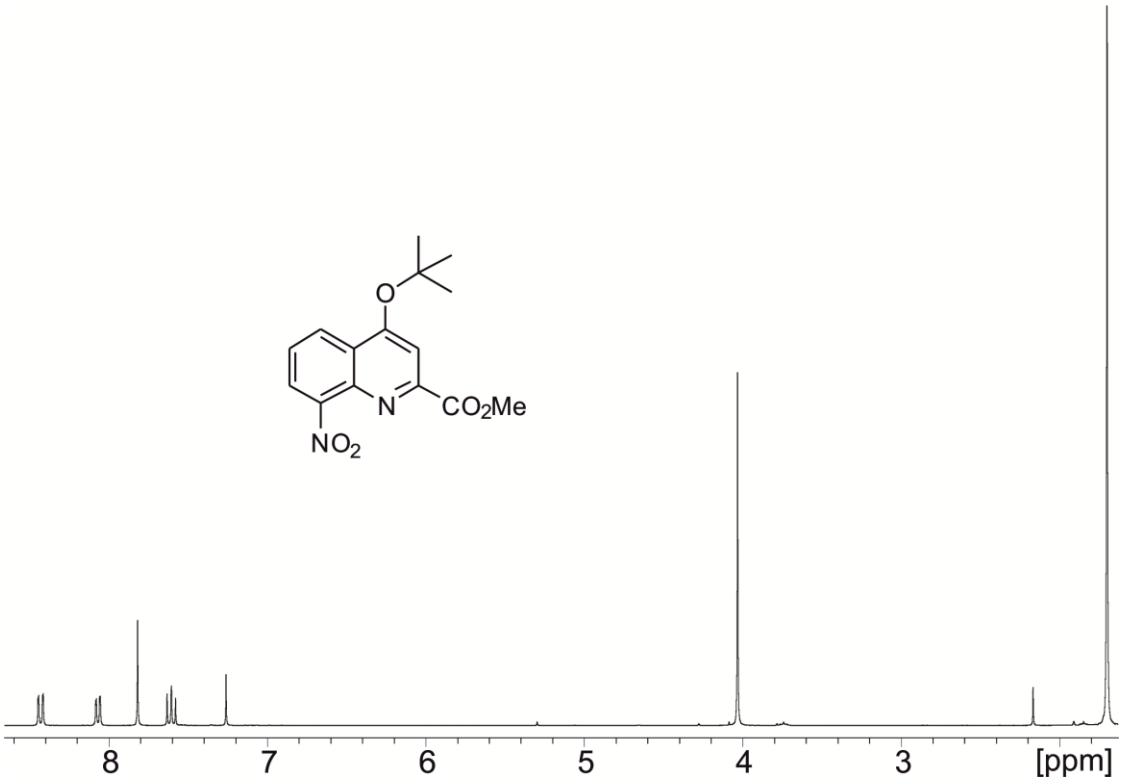

**Supplementary Figure 50.** Different views of the energy minimized model of a hydrogen bonded *PM* tilted dimer of **5a**. For some helices, only the outer rim is shown for clarity. The presence of this dimer in solution is easily ruled out by NMR spectra where it would be expected to show twice as many signals as the other dimers, the two helices being inequivalent.

## 3.5 X-Ray Structures

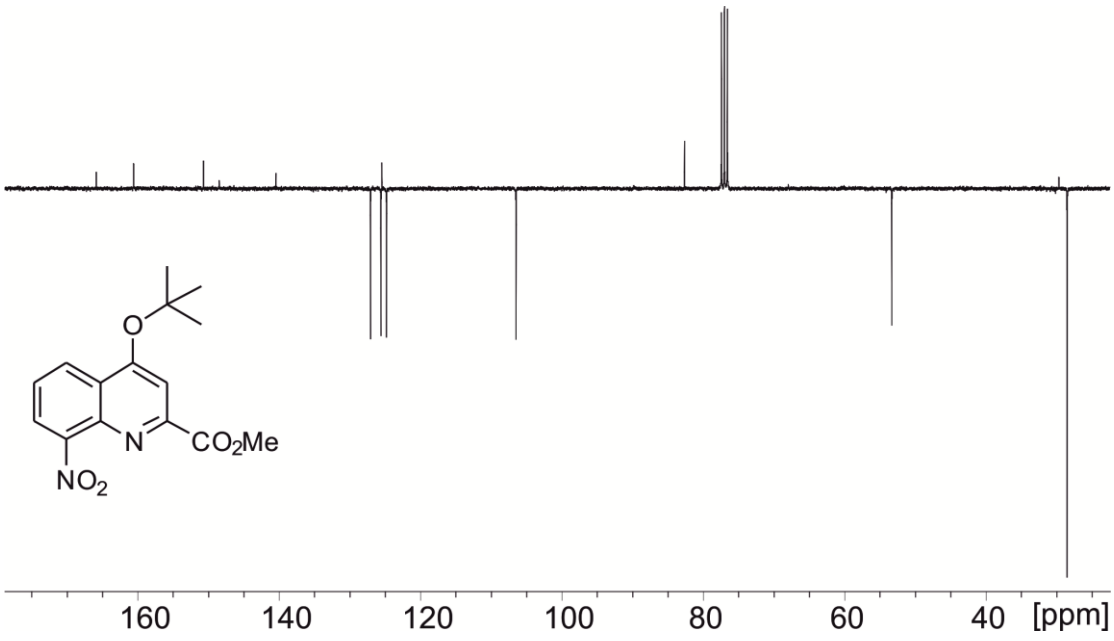



**Supplementary Figure 51.** (a) crystal structure of **2a** in which helices are not hydrogen bonded. (b) crystal structure of **3a** in which helices are hydrogen bonded. Bottom distances are measured between the C2 carbons of the C-terminal quinoline rings of each helix. The top distance is measured between carbonyl oxygen of X3 (left helix, numbering starts from N-terminus) and hydrogen of OH in X3 (right helix, numbering starts from N-terminus). (c) and (d) show the bottom parts of the structures of (a) and (b), respectively. Angles are measured between the C2 carbon of the C-terminal quinoline of one helix, the aromatic C4 carbon of the linker, and the C2 carbon of C-terminal quinoline of the other helix. (e), (f), (g) show different views of the superimposition of a helical segment of **2a** and of a helical segment of **3a.** The C-terminal quinoline rings of each helix have been aligned as can be viewed in f where the three C-terminal quinoline rings are shown. The difference in curvature between the two helices is obvious already by the off-set of the second and third rings counting from the C-terminus. g shows the three N-terminal rings. Red balls and green balls indicate oxygen atoms and hydroxyl protons involved in hydrogen bonds in the folded conformation, respectively.

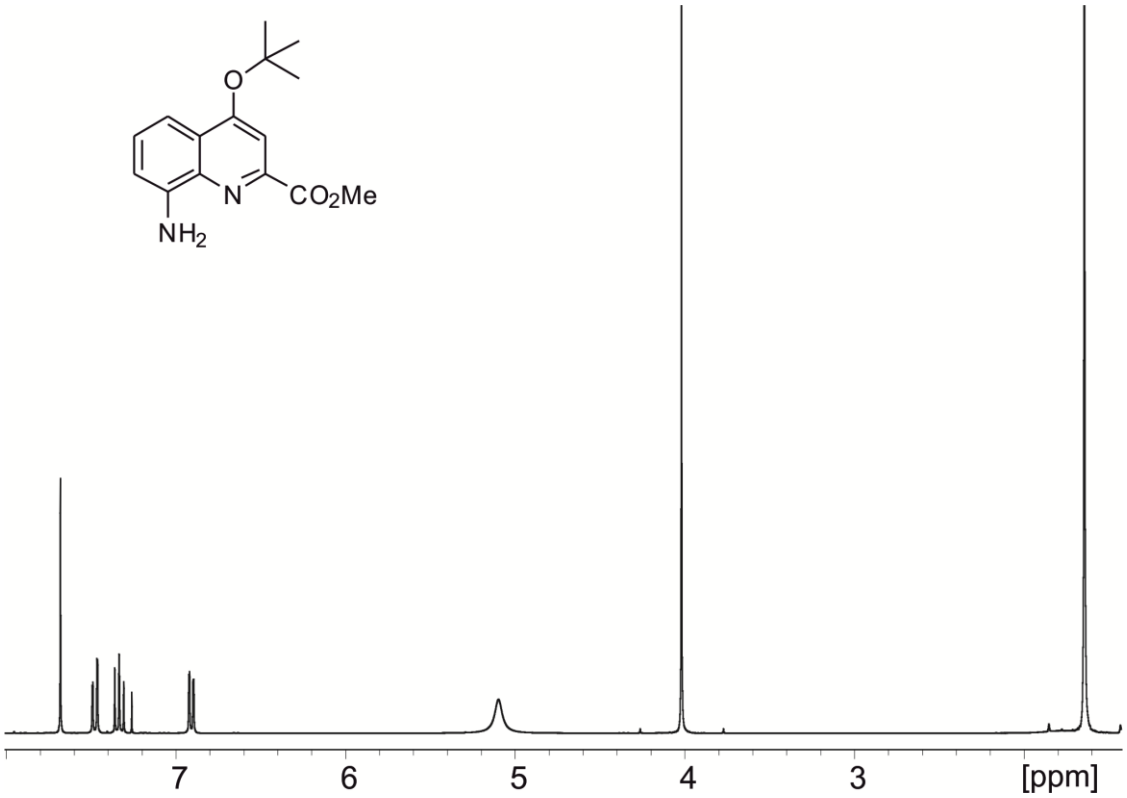
## 3.6 $^{1}$H NMR and $^{13}$C NMR spectra of new compounds



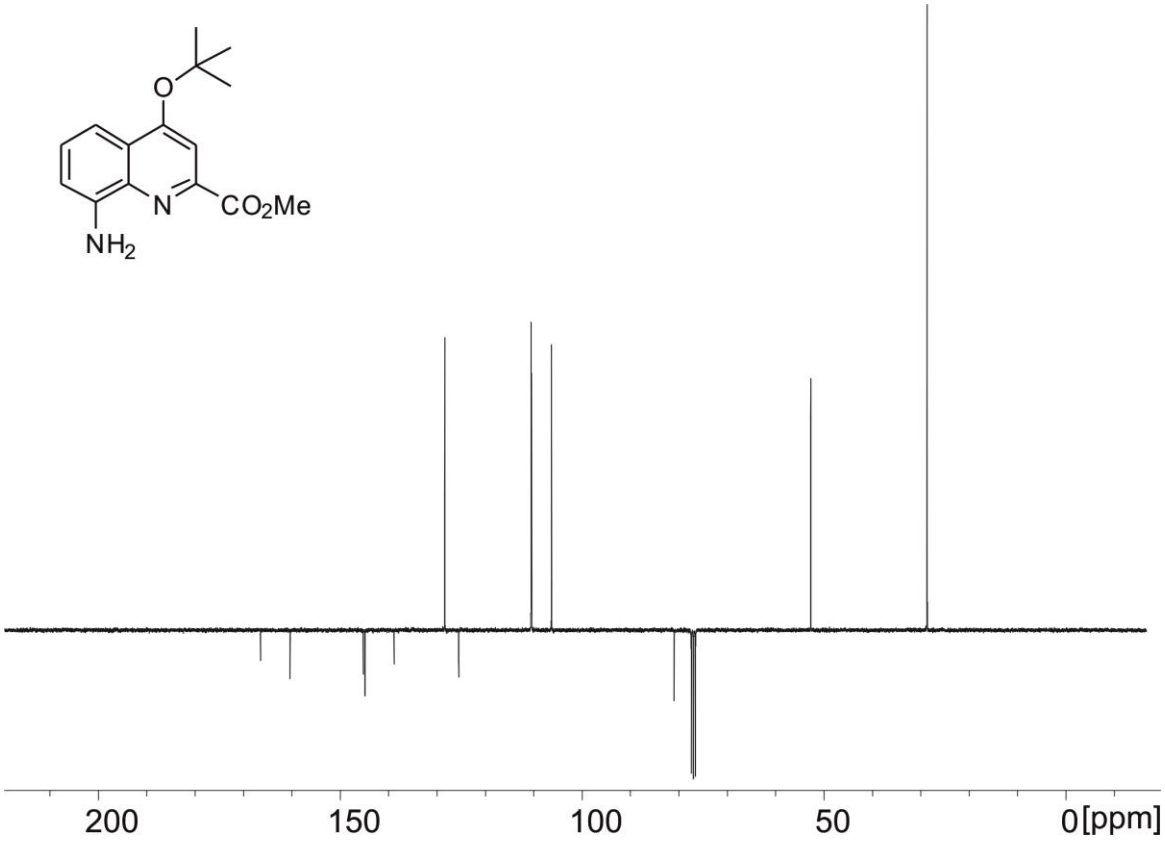

**Supplementary Figure 52:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **7.**



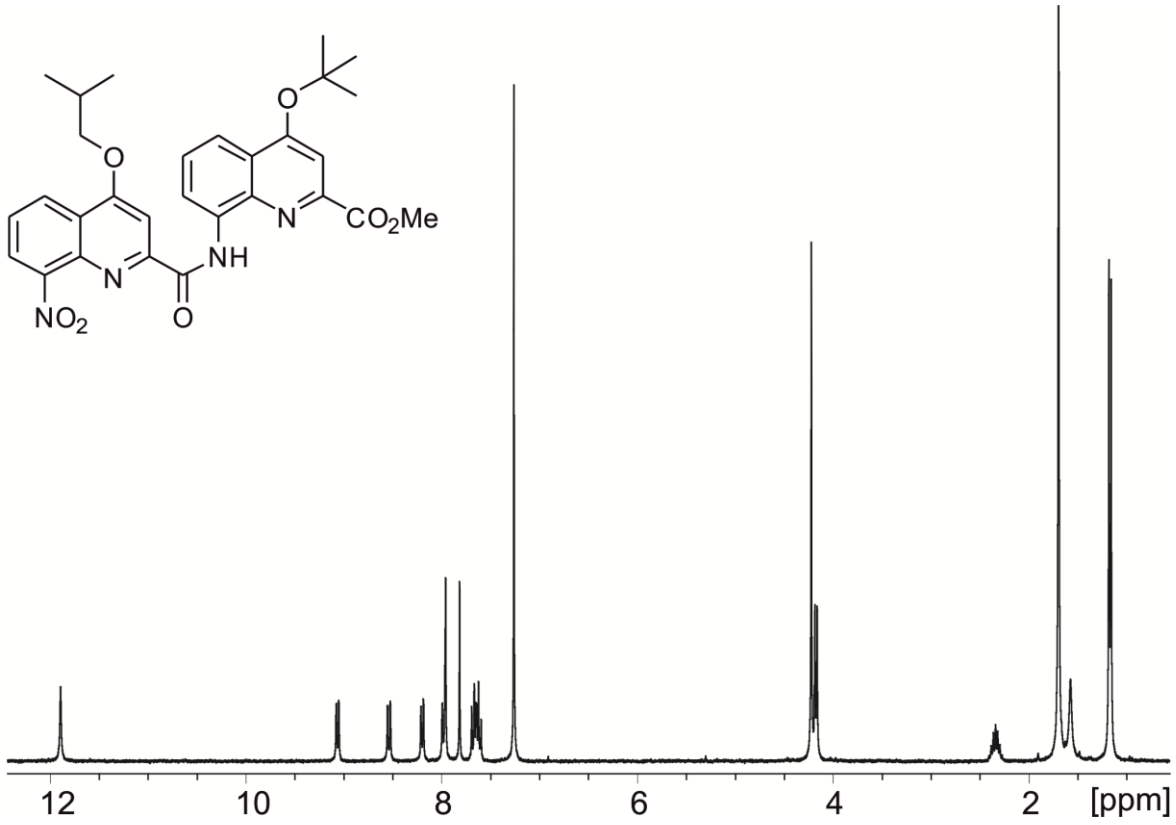

**Supplementary Figure 53:** Jmod $^{13}$C NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **7**.



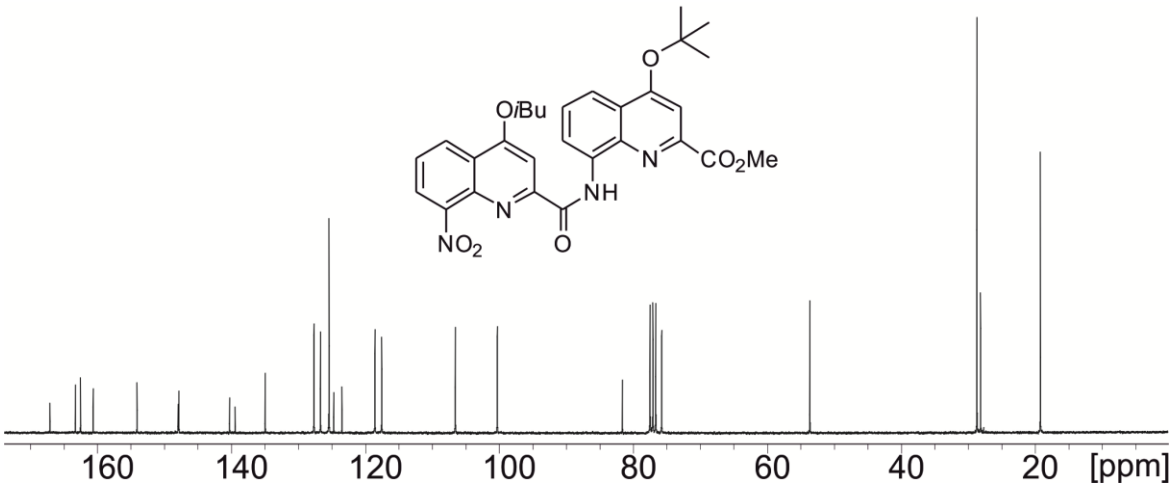

**Supplementary Figure 54:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **8.**



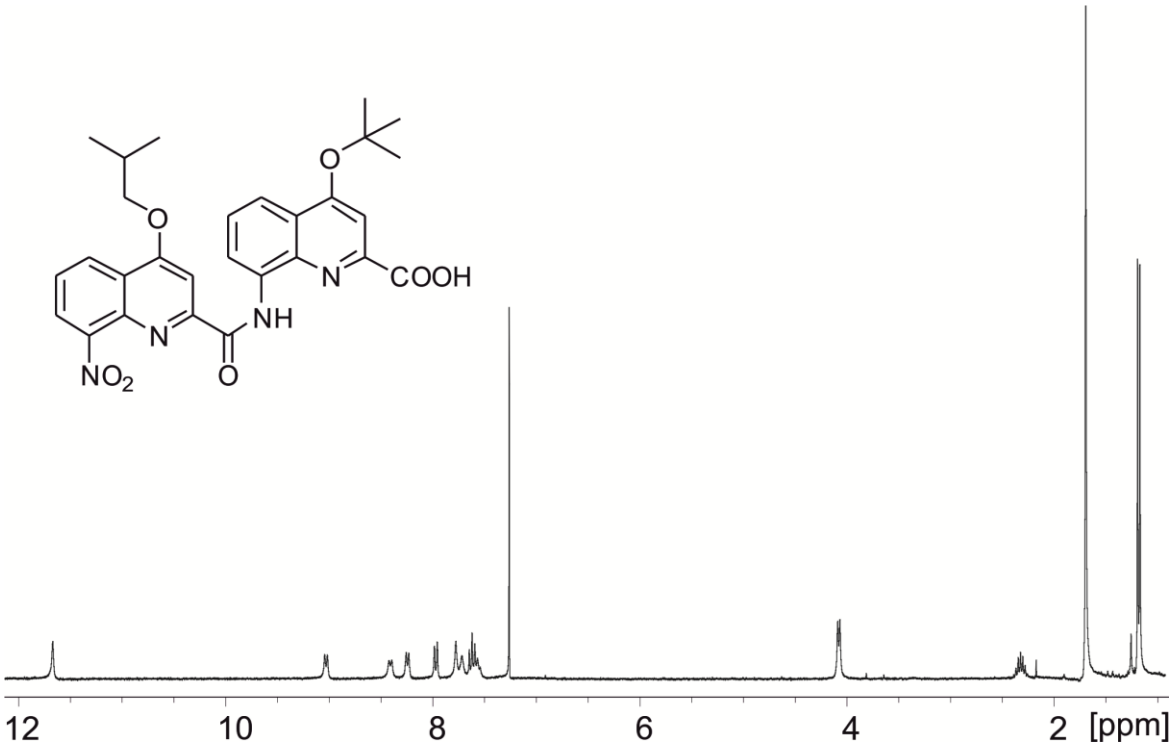

**Supplementary Figure 55:** Jmod $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **8.**



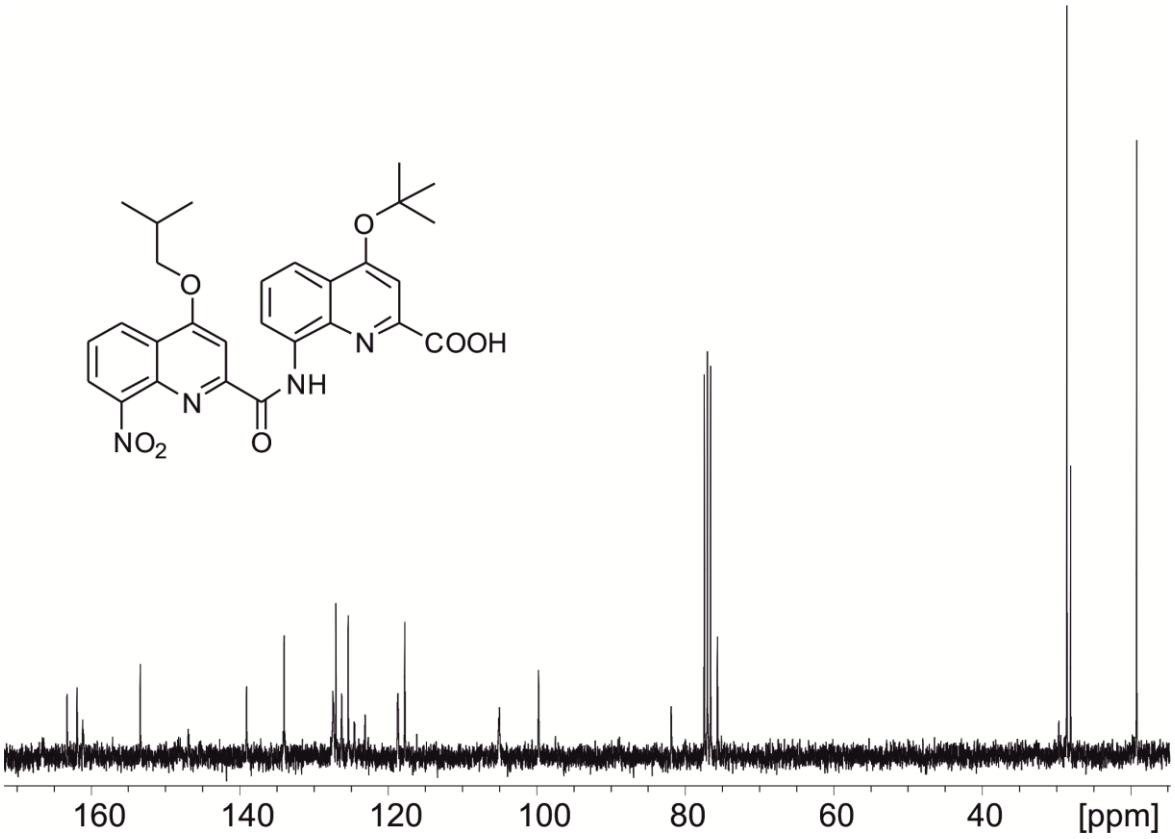

**Supplementary Figure 56:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **10.**



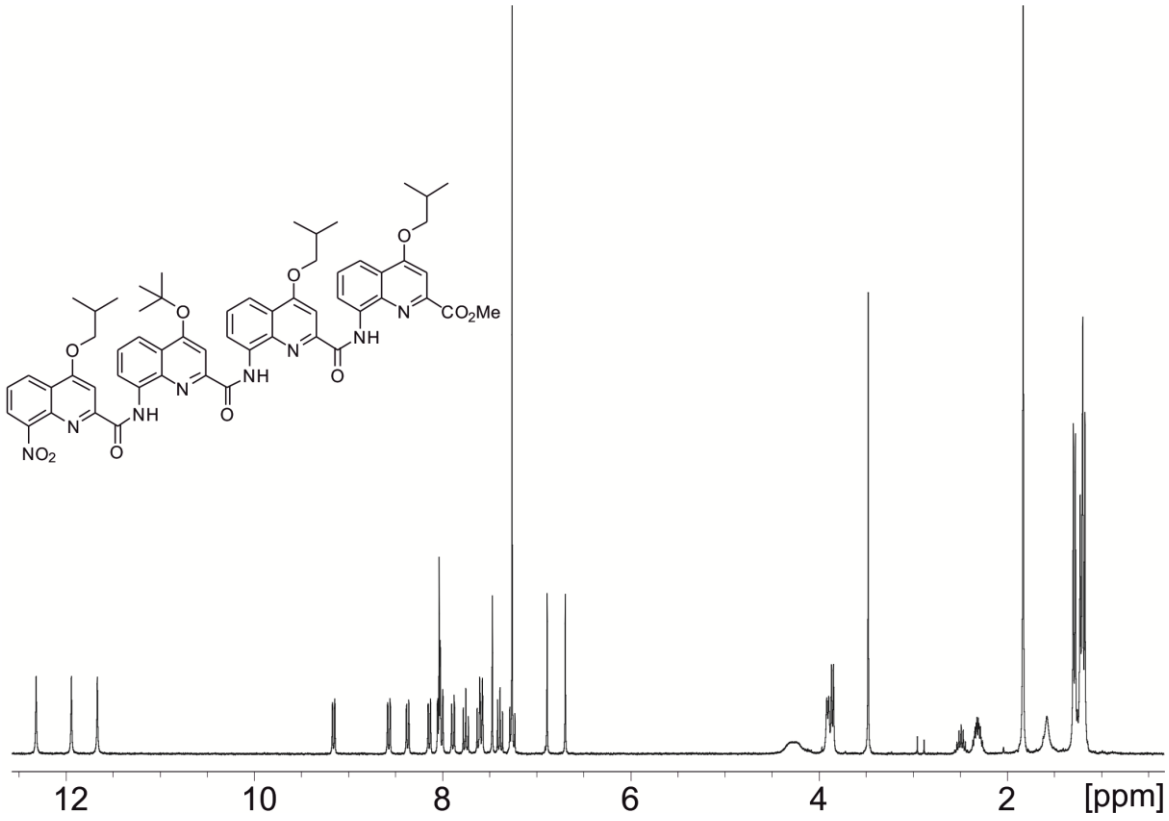

**Supplementary Figure 57:** $^{13}$C NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **10.**



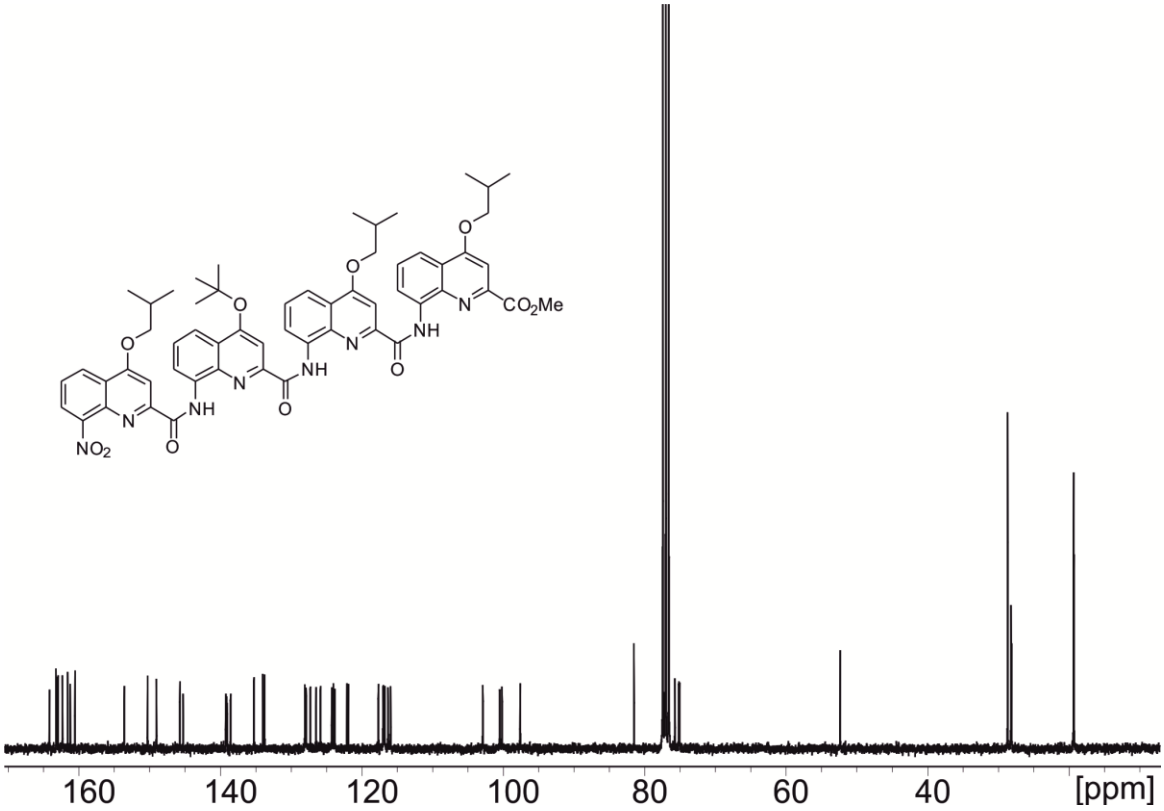

**Supplementary Figure 58:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **11.**



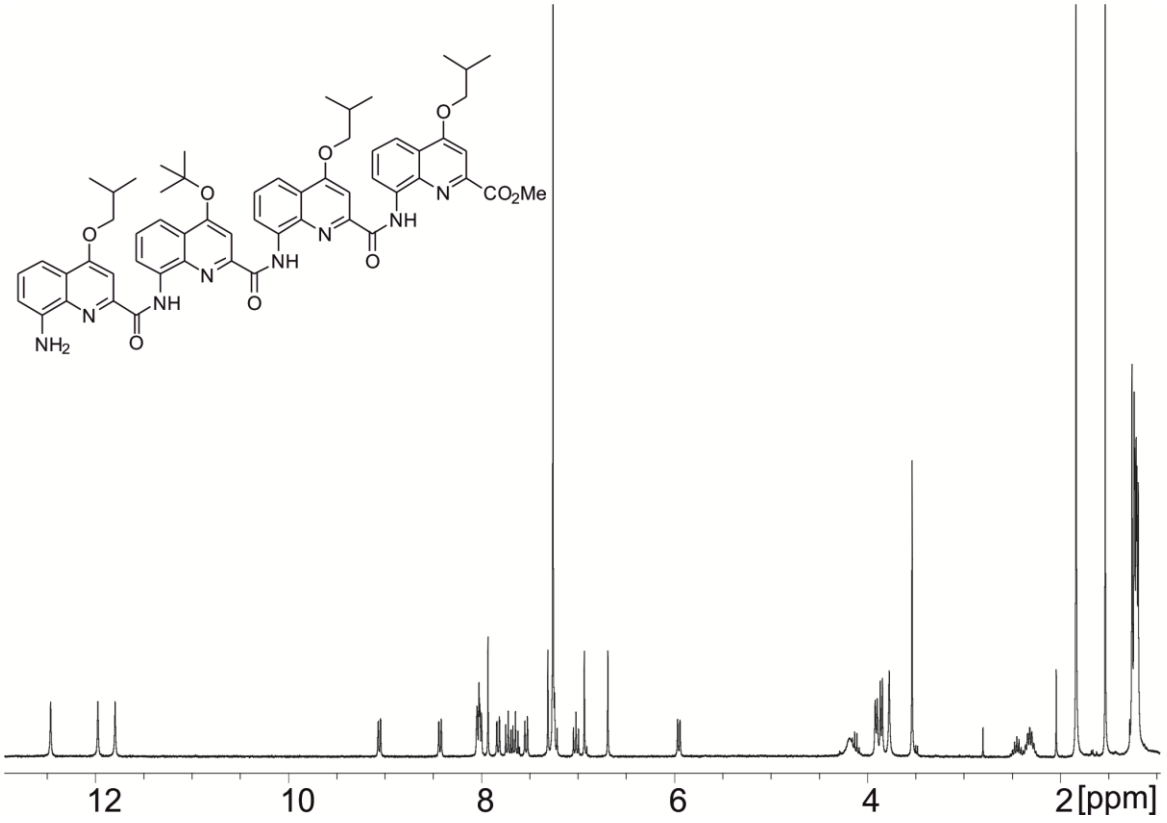

**Supplementary Figure 59:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **11.**



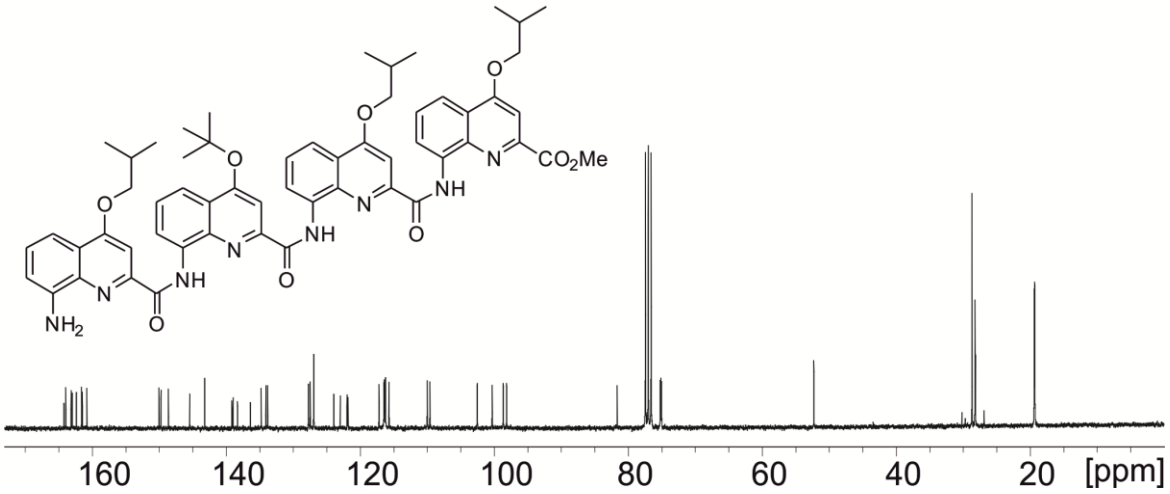

**Supplementary Figure 60:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **13.**



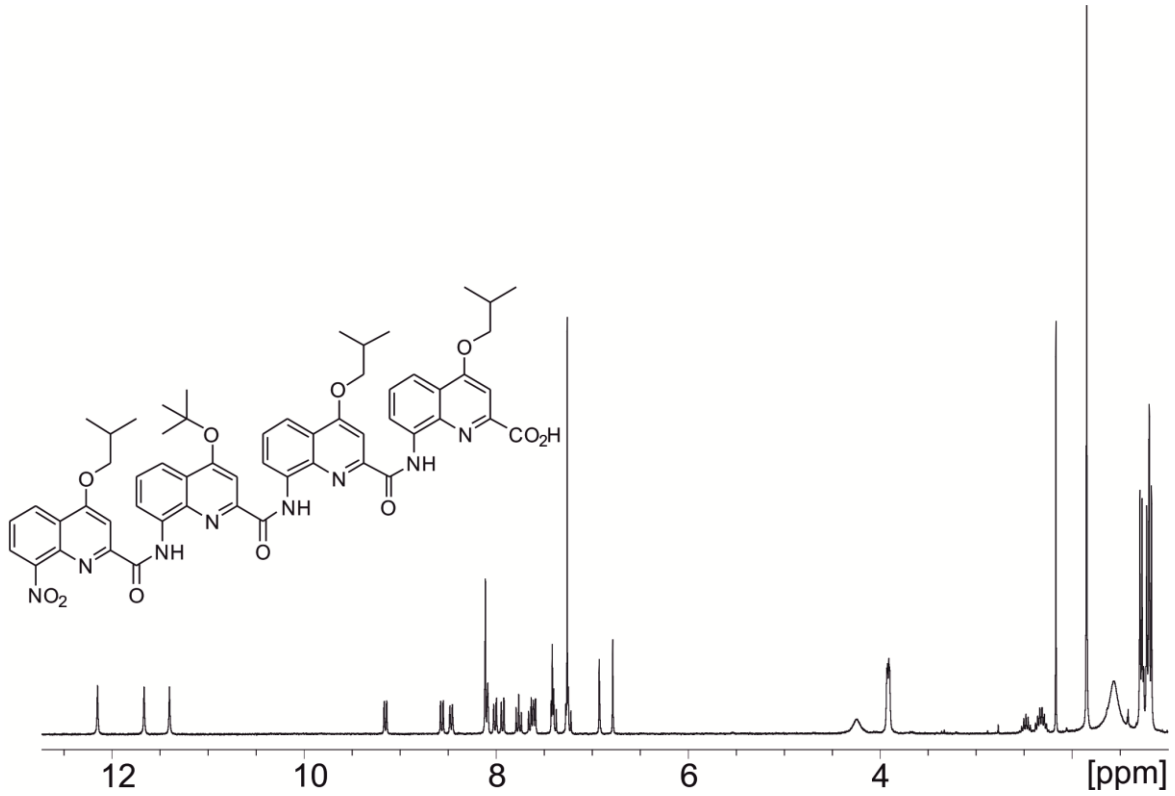

**Supplementary Figure 61:** $^{13}$C NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **13.**



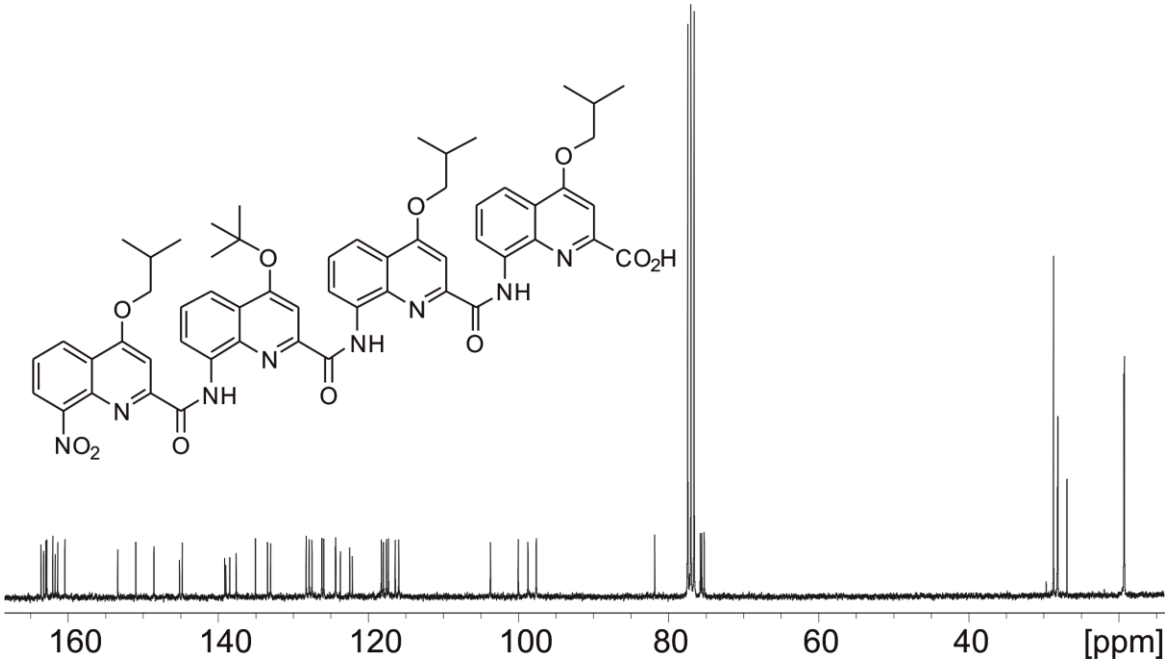

**Supplementary Figure 62:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **15.**



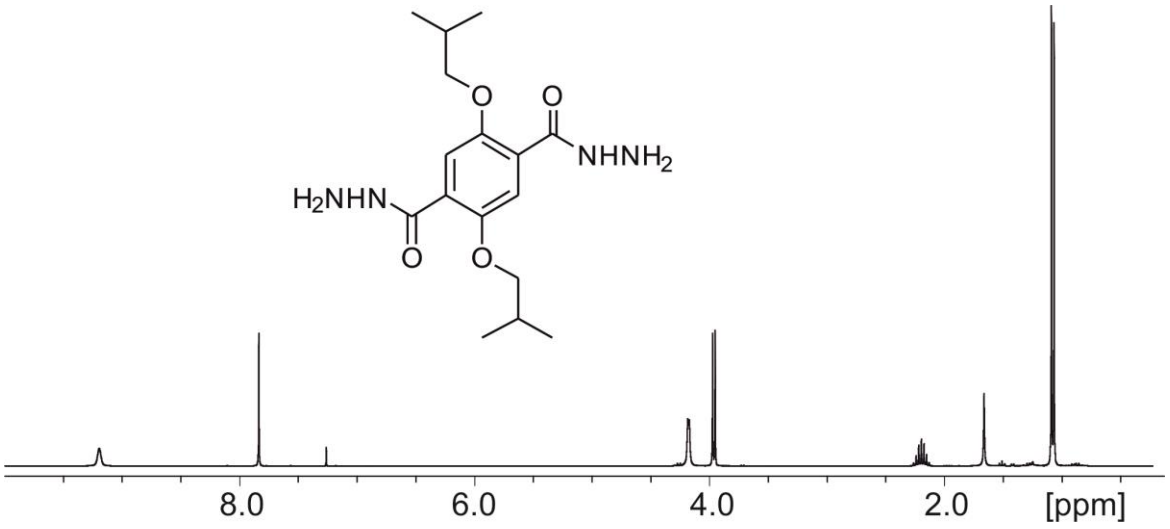

**Supplementary Figure 63:** $^{13}$C NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **15.**



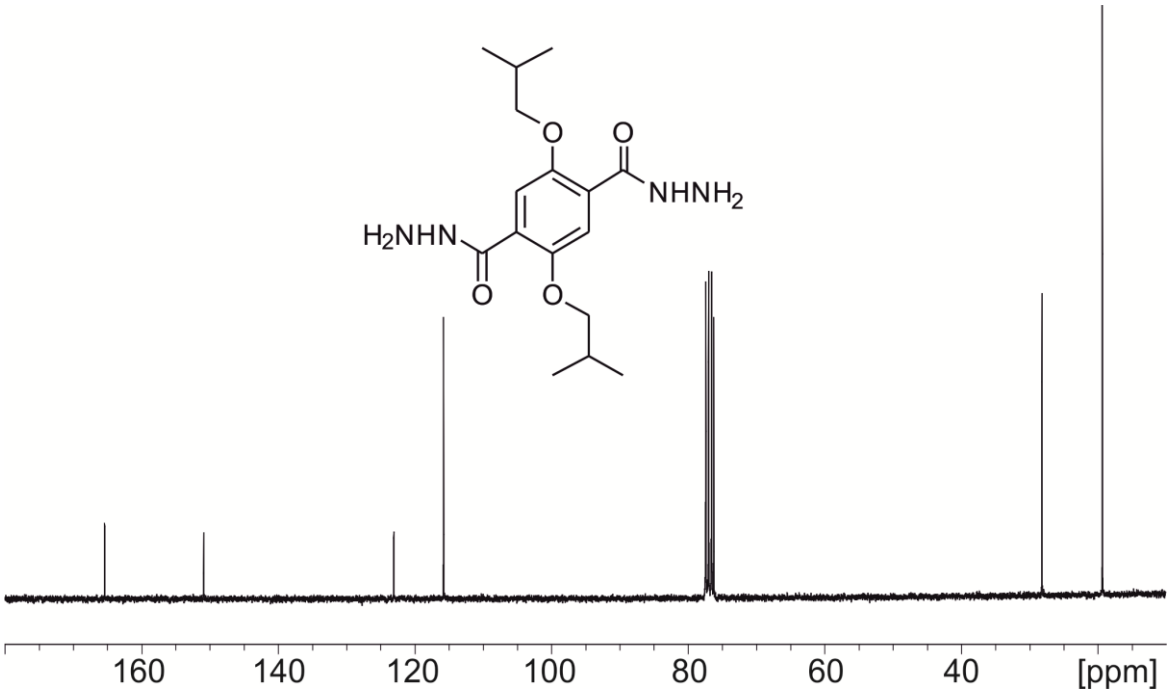

**Supplementary Figure 64:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **14.**



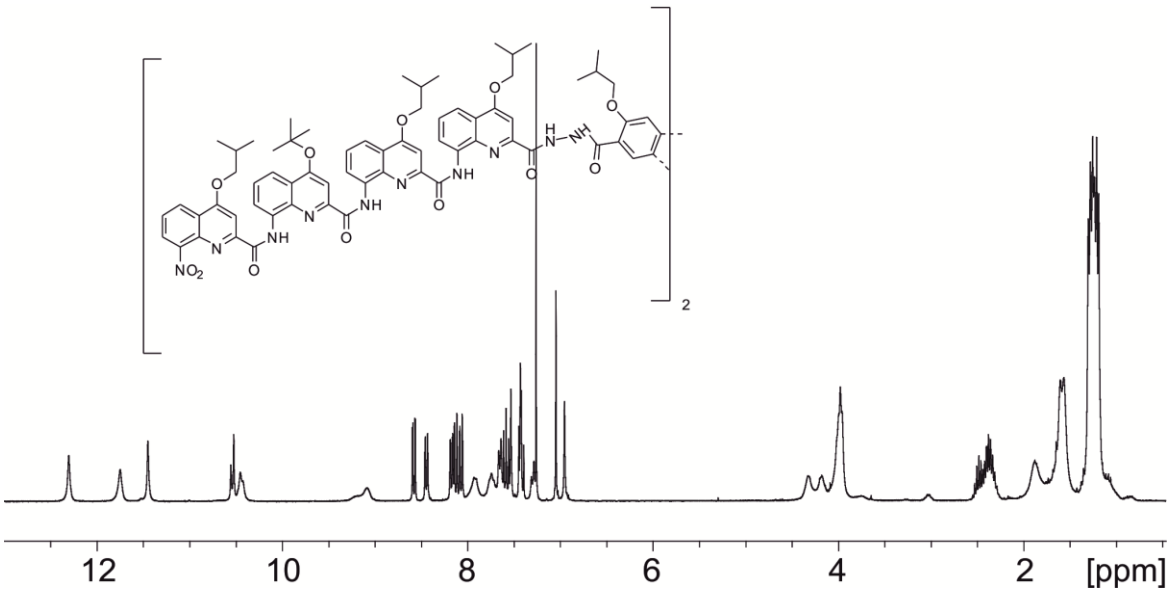

**Supplementary Figure 65:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **14.**



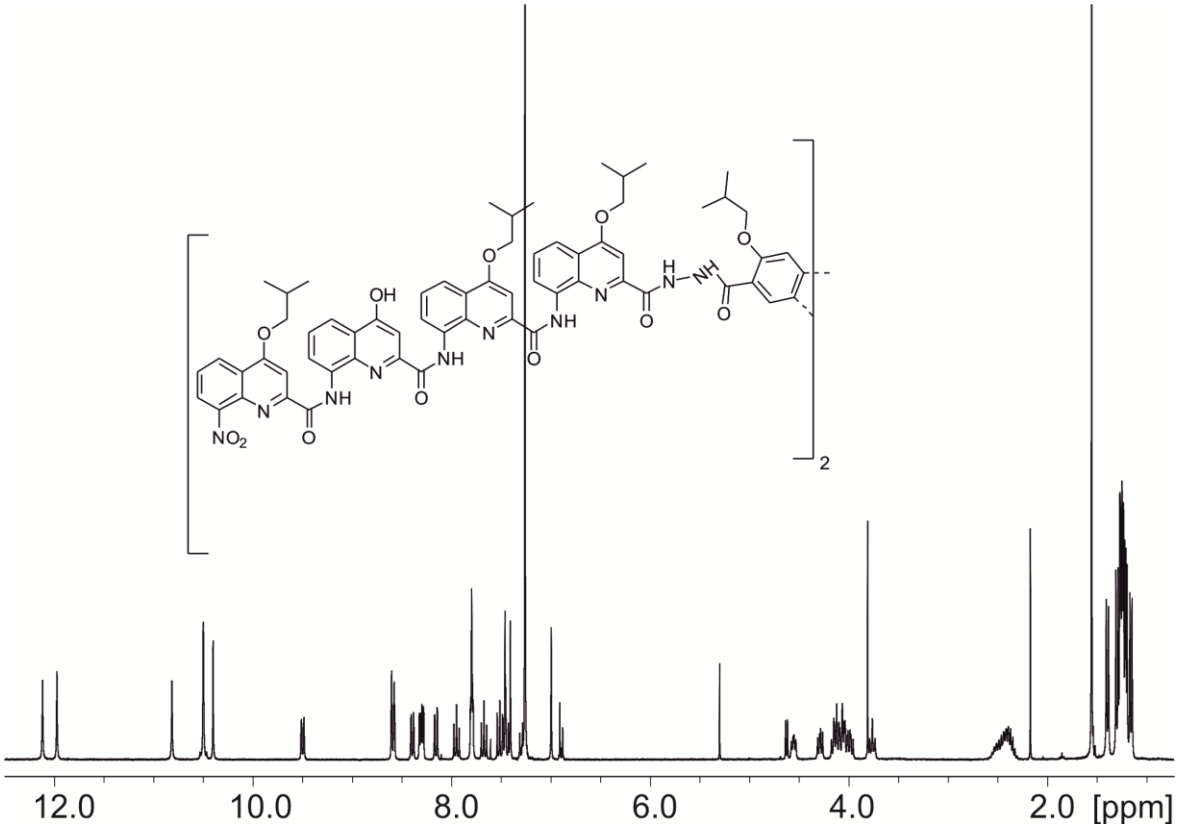

**Supplementary Figure 66:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **22.**



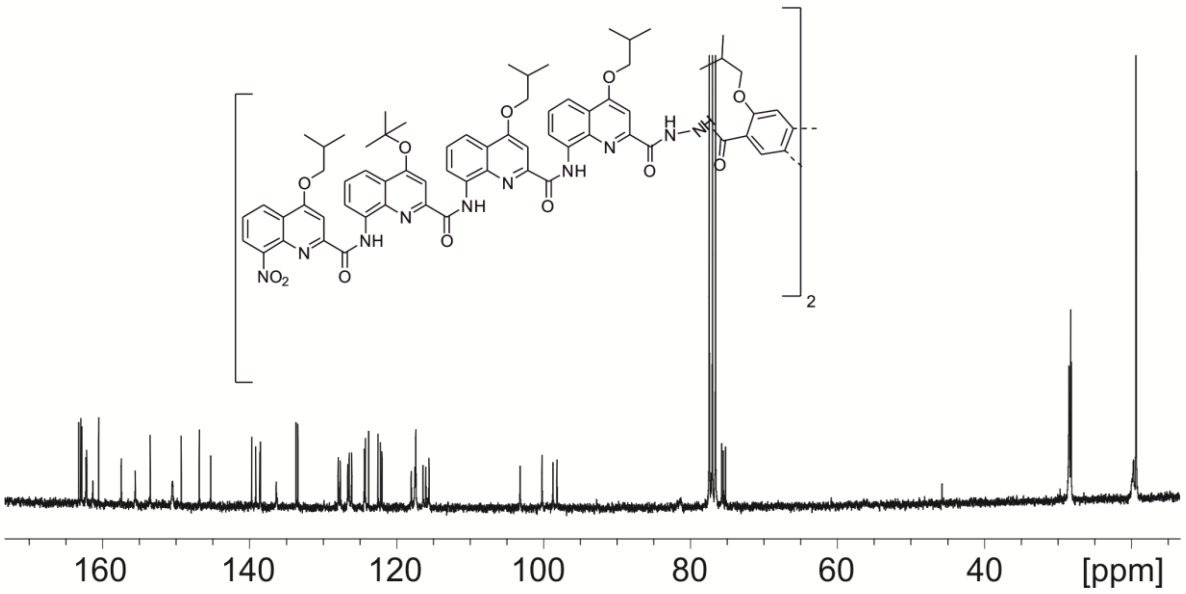

**Supplementary Figure 67:** $^{13}$C NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **22.**



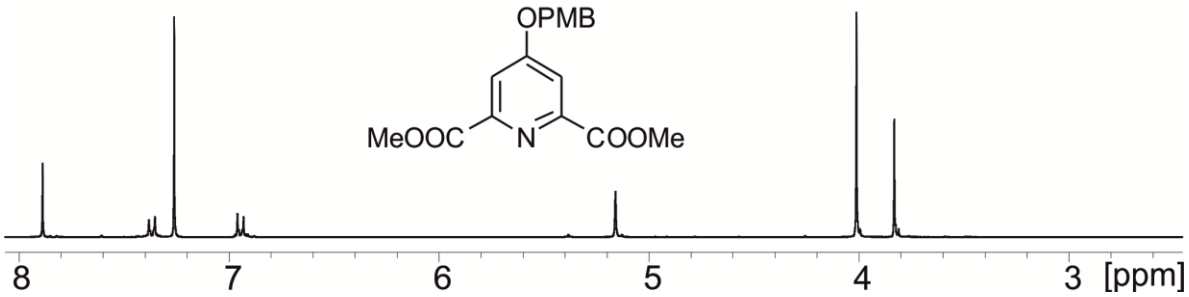

**Supplementary Figure 68:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **1b.**



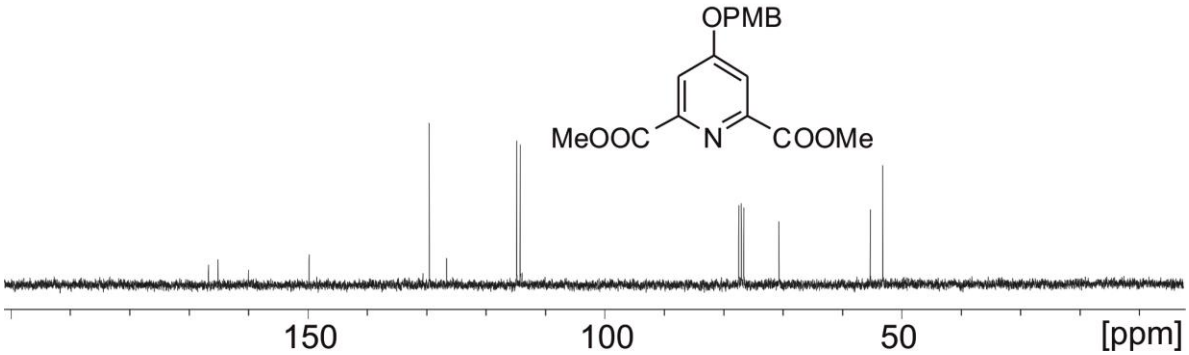

**Supplementary Figure 69:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **1a.**



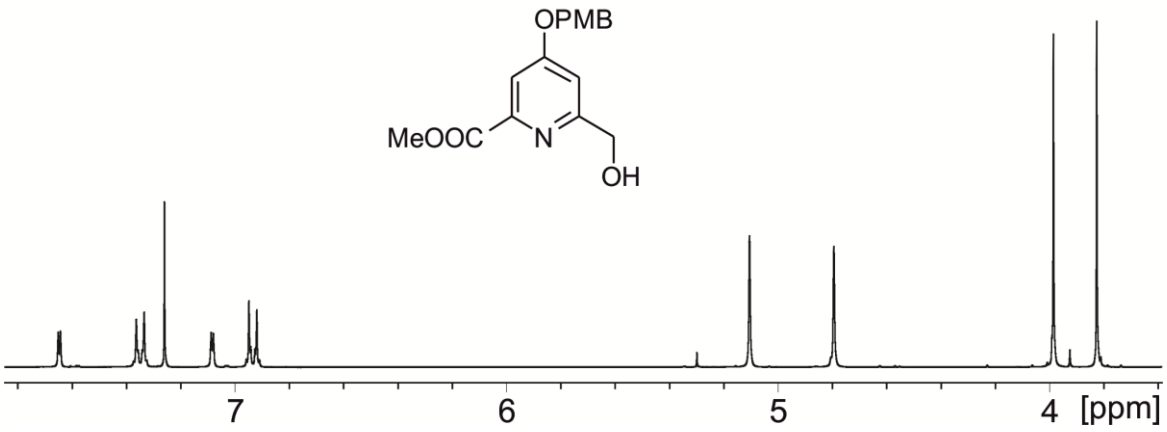

**Supplementary Figure 70:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **1b.**



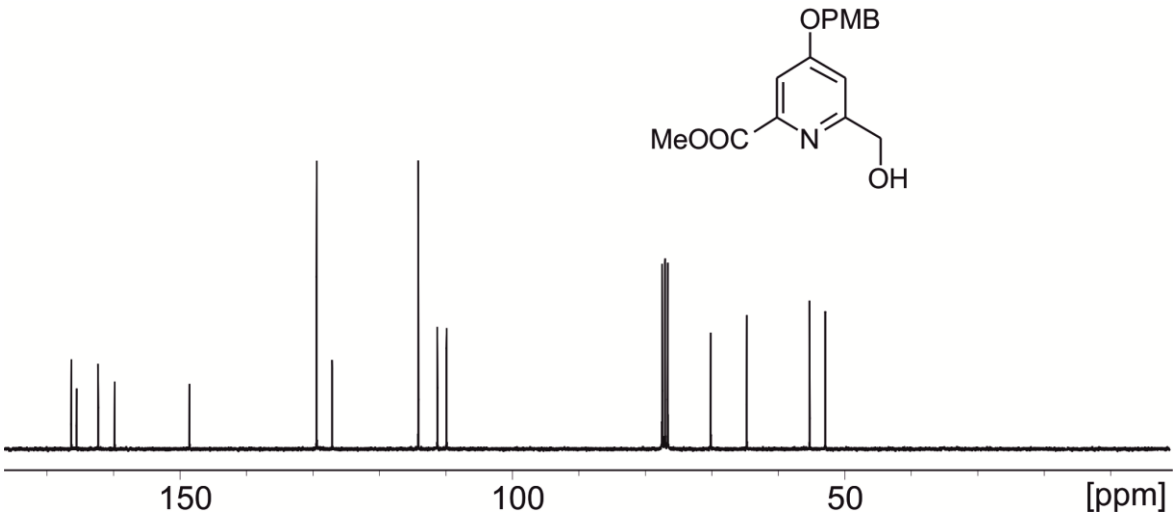

**Supplementary Figure 71:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **17.**



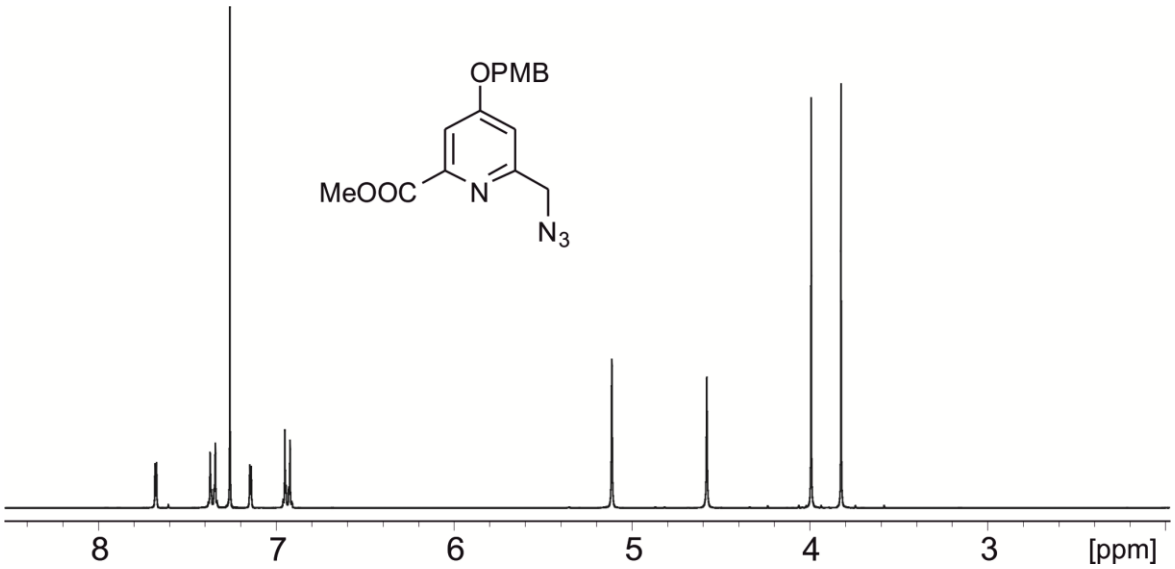

**Supplementary Figure 72:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **17.**



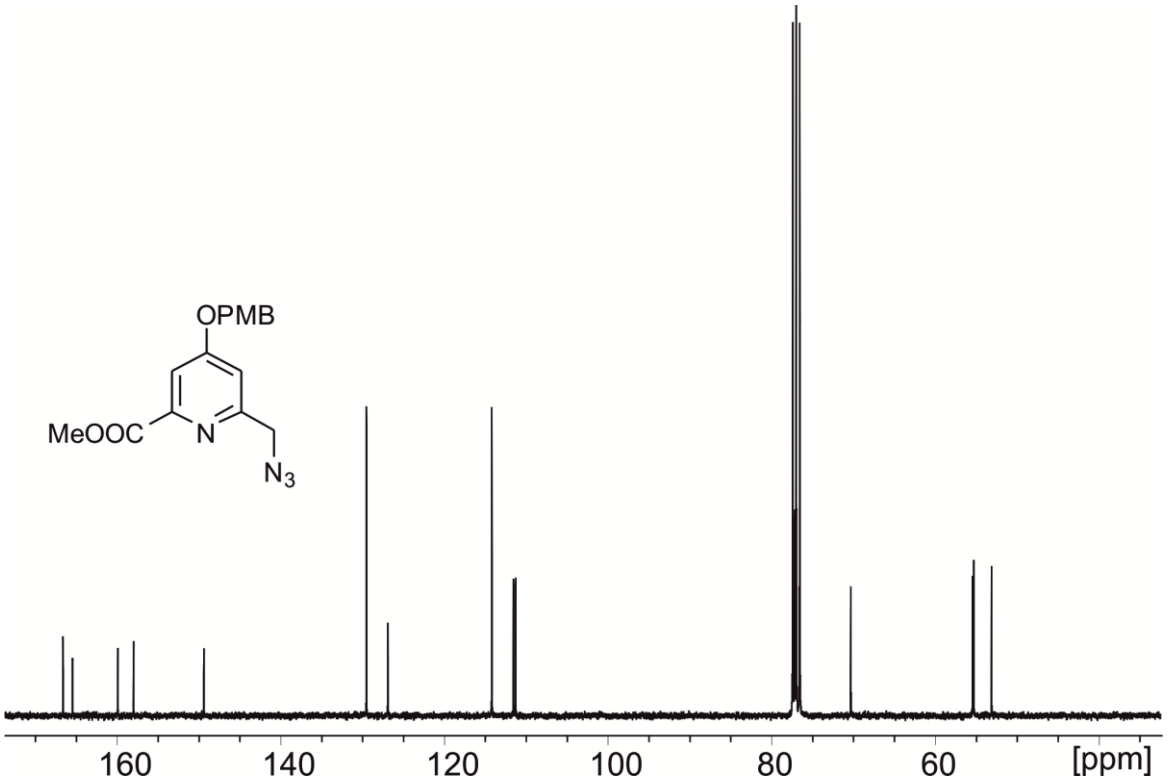

**Supplementary Figure 73:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **18.**



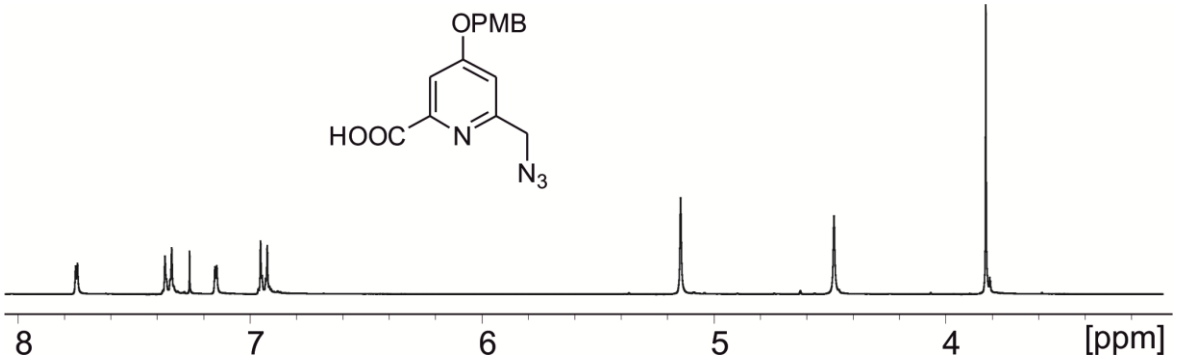

**Supplementary Figure 74:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **18.**



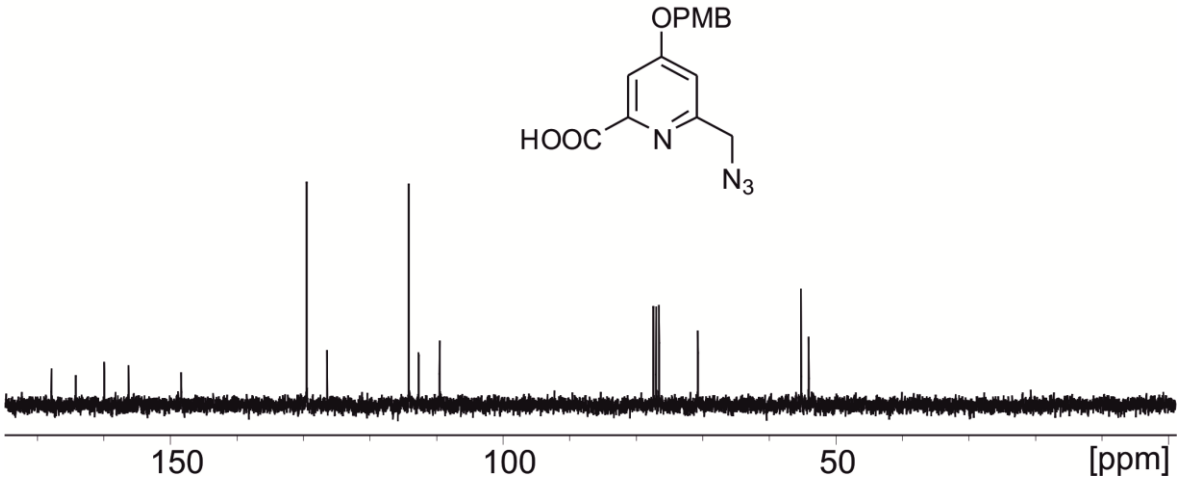

**Supplementary Figure 75:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **19.**



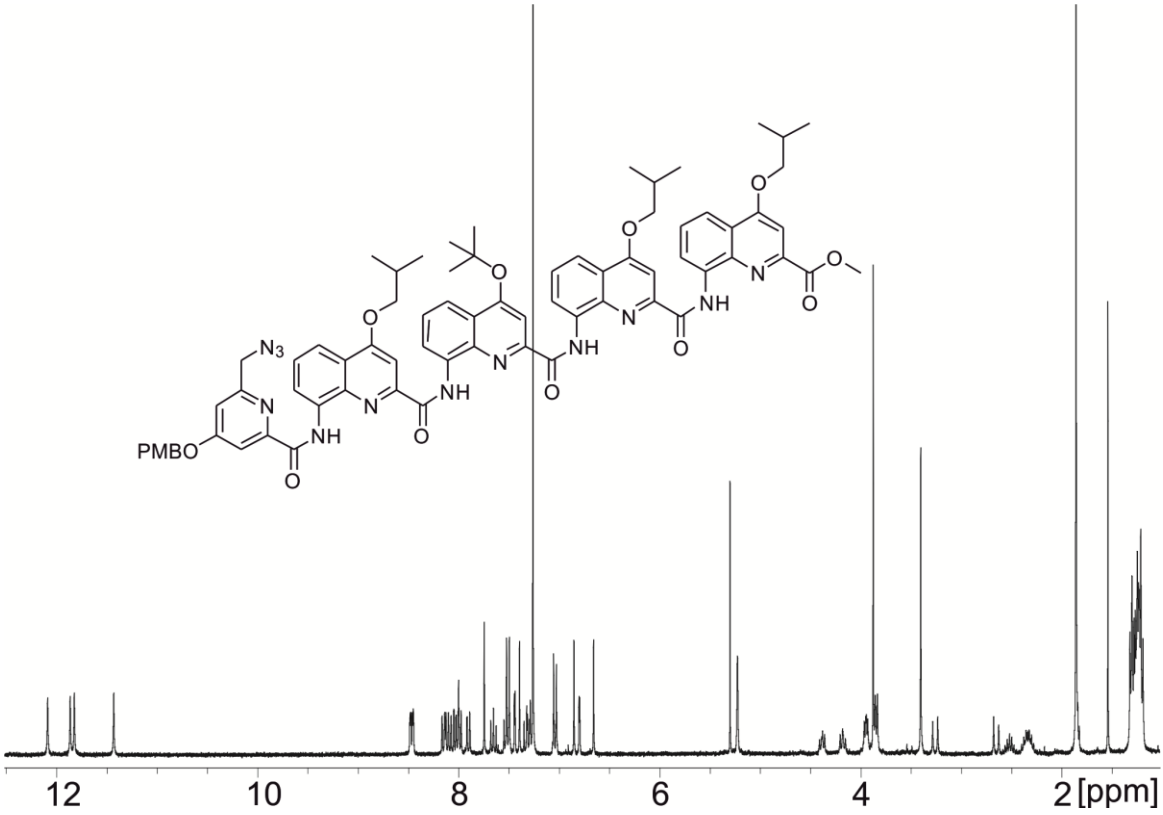

**Supplementary Figure 76:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **19.**



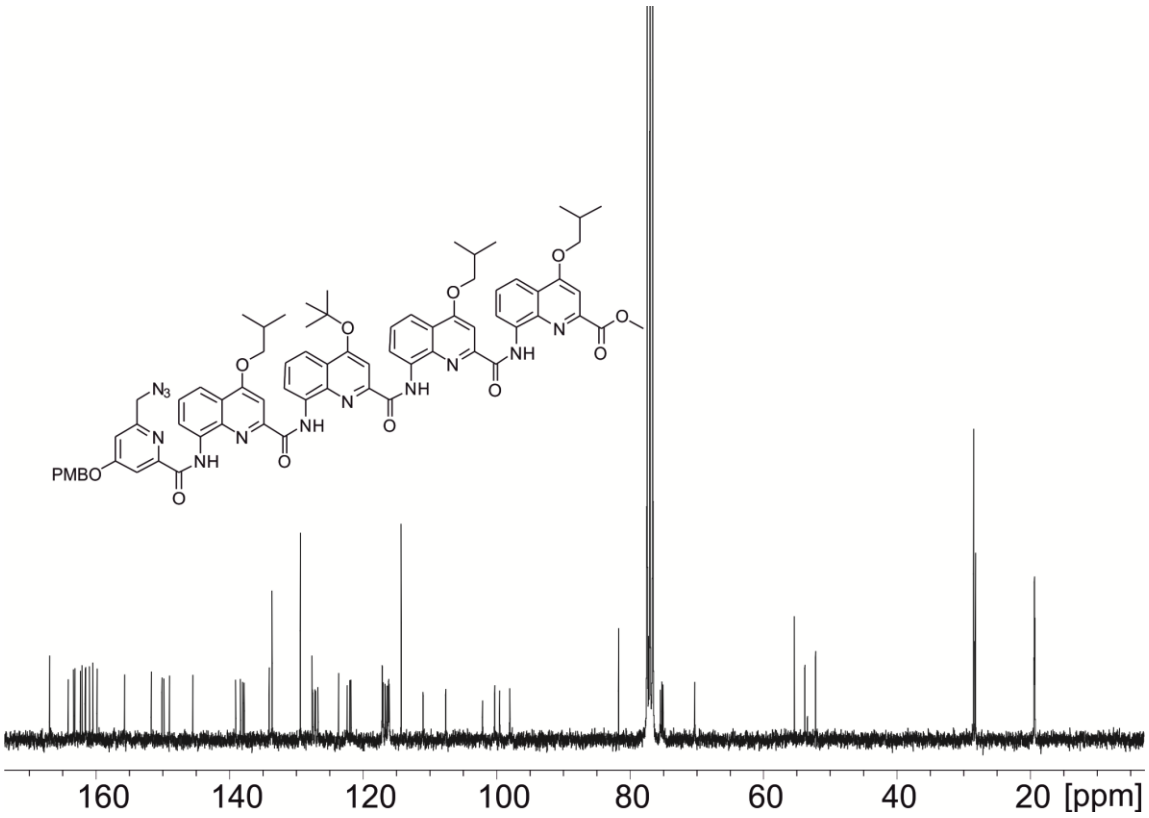

**Supplementary Figure 77:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **20.**



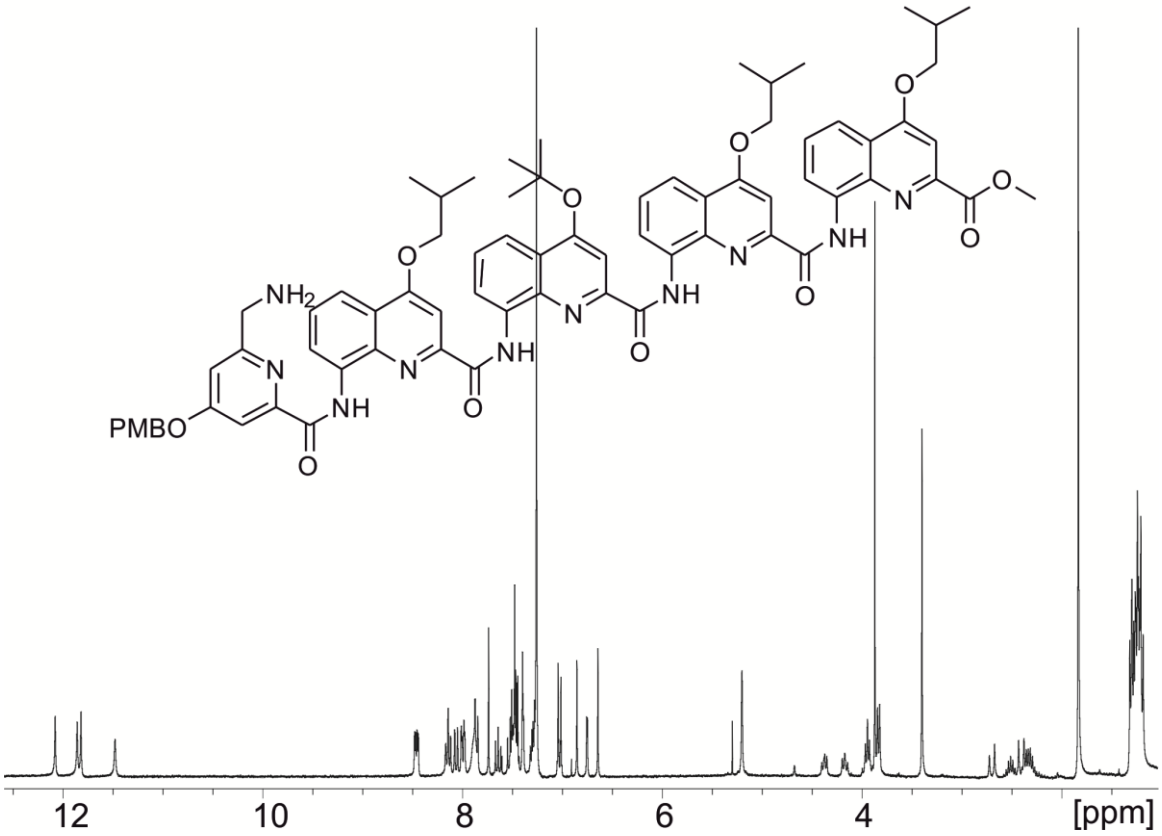

**Supplementary Figure 78:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **20.**



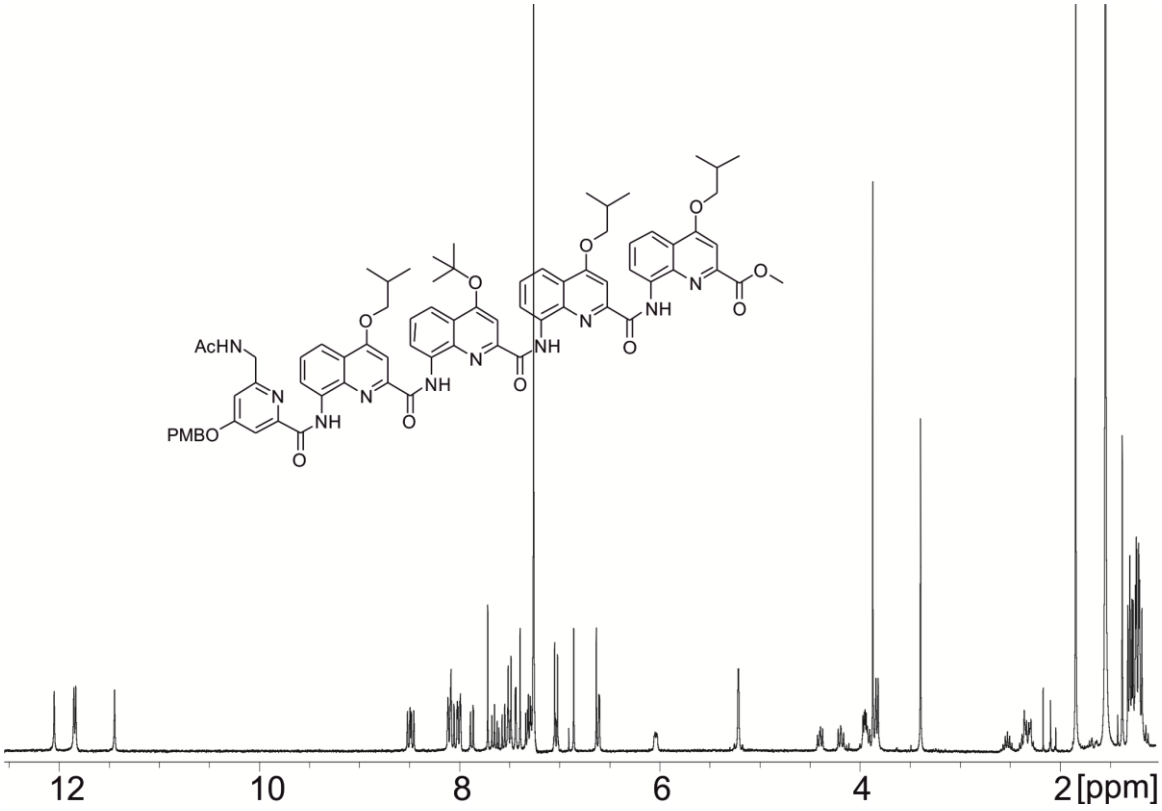

**Supplementary Figure 79:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **23.**



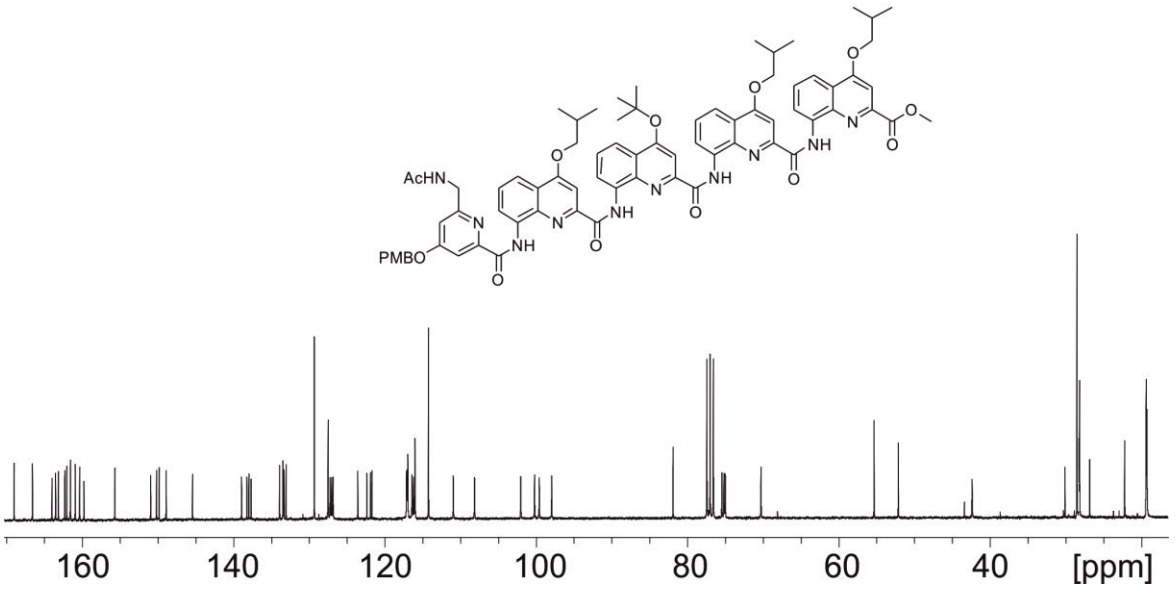

**Supplementary Figure 80:** $^{13}$C NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **23.**



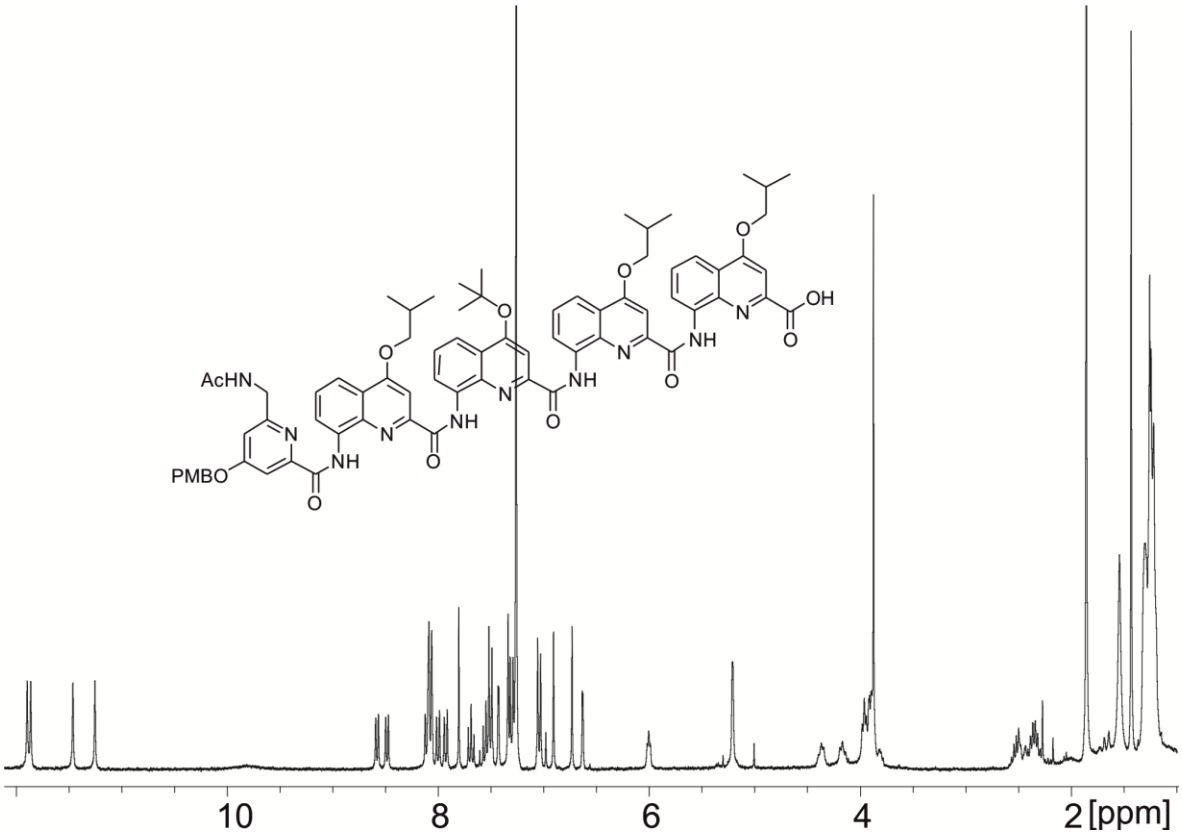

**Supplementary Figure 81:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **24.**



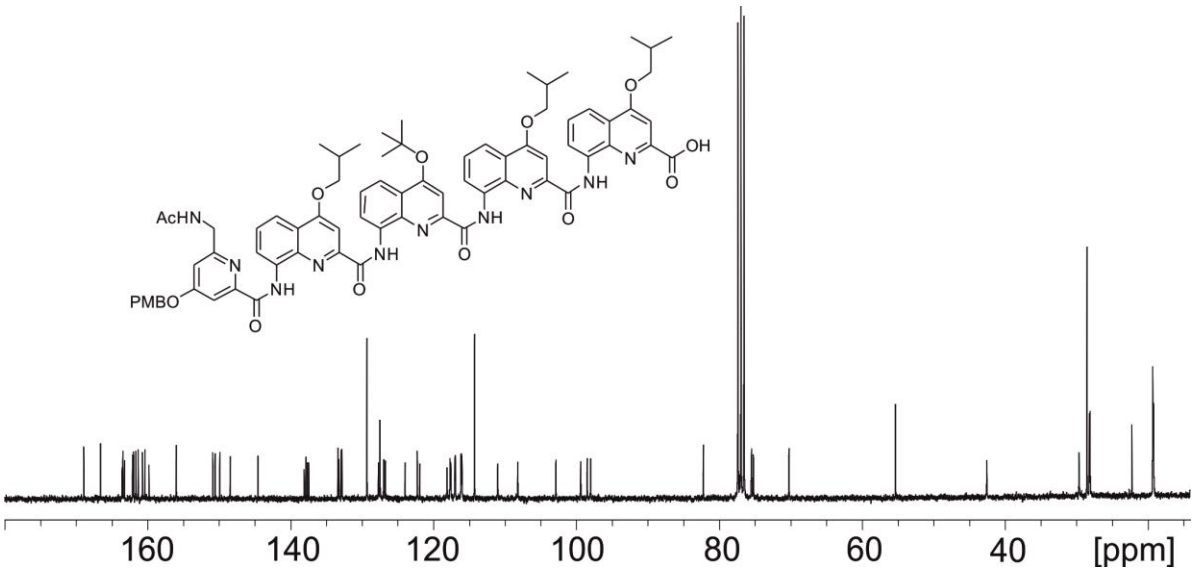

**Supplementary Figure 82:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **25.**



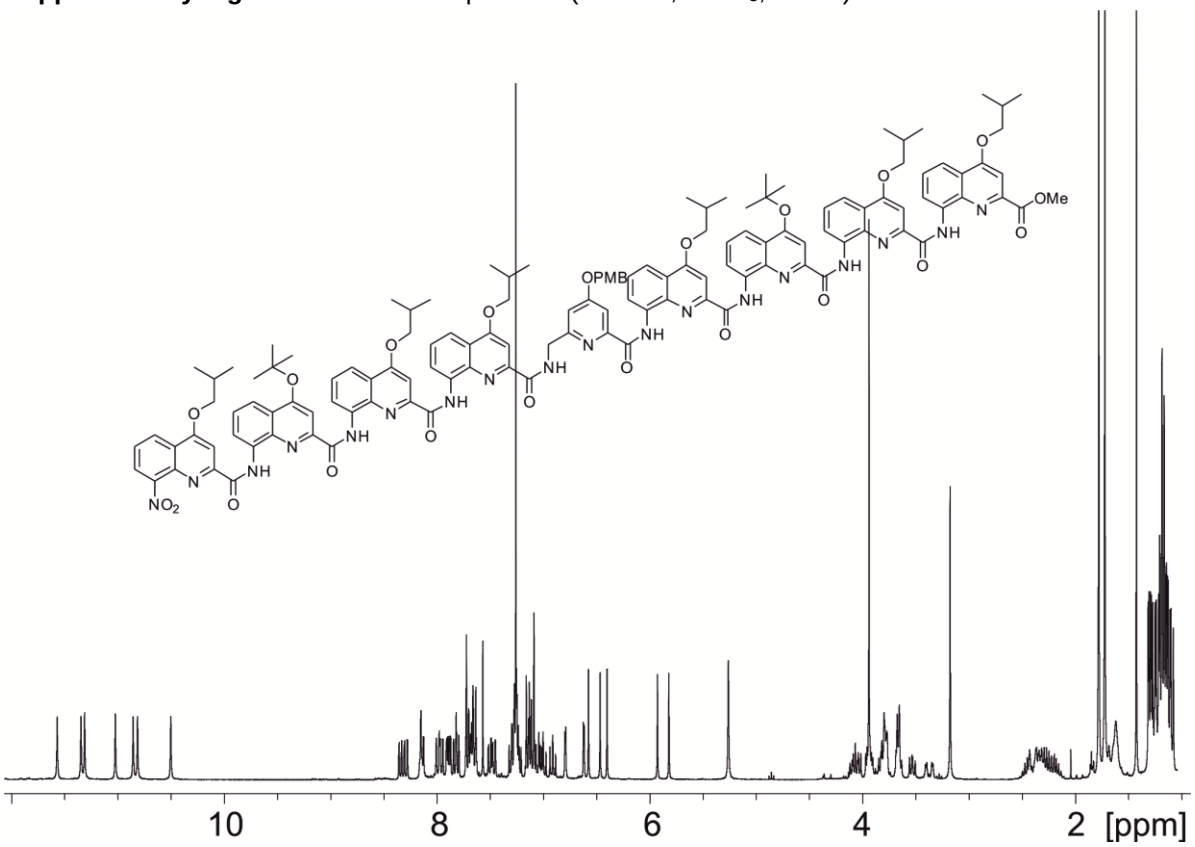

**Supplementary Figure 83:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **25.**



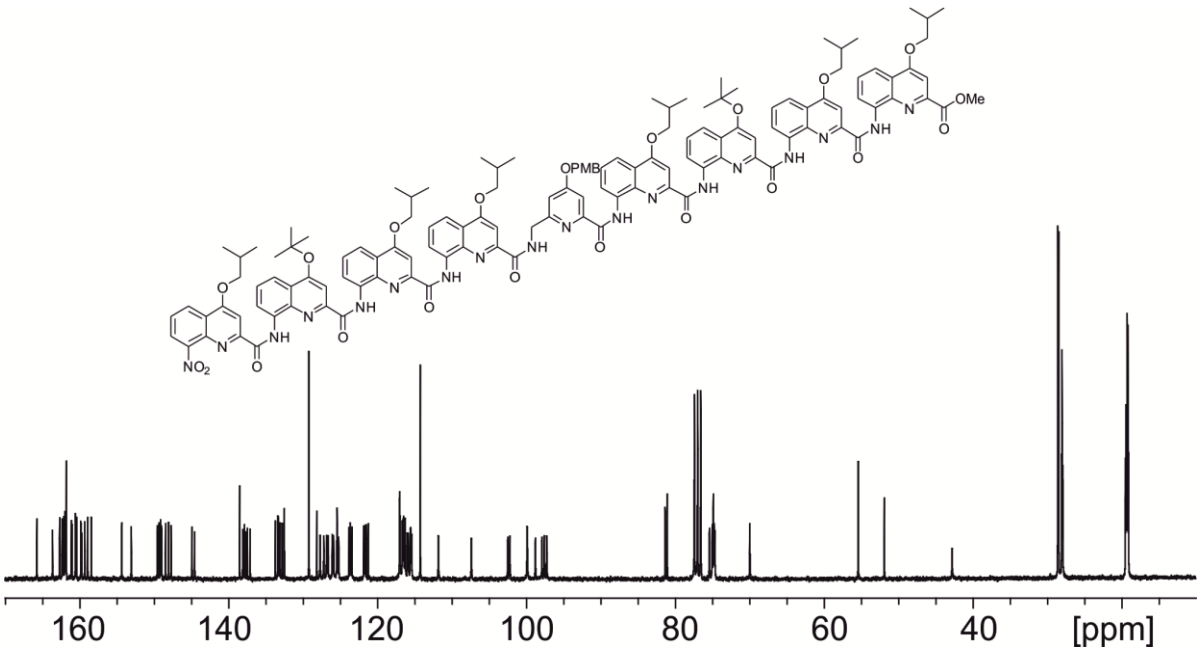

**Supplementary Figure 84:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **26.**



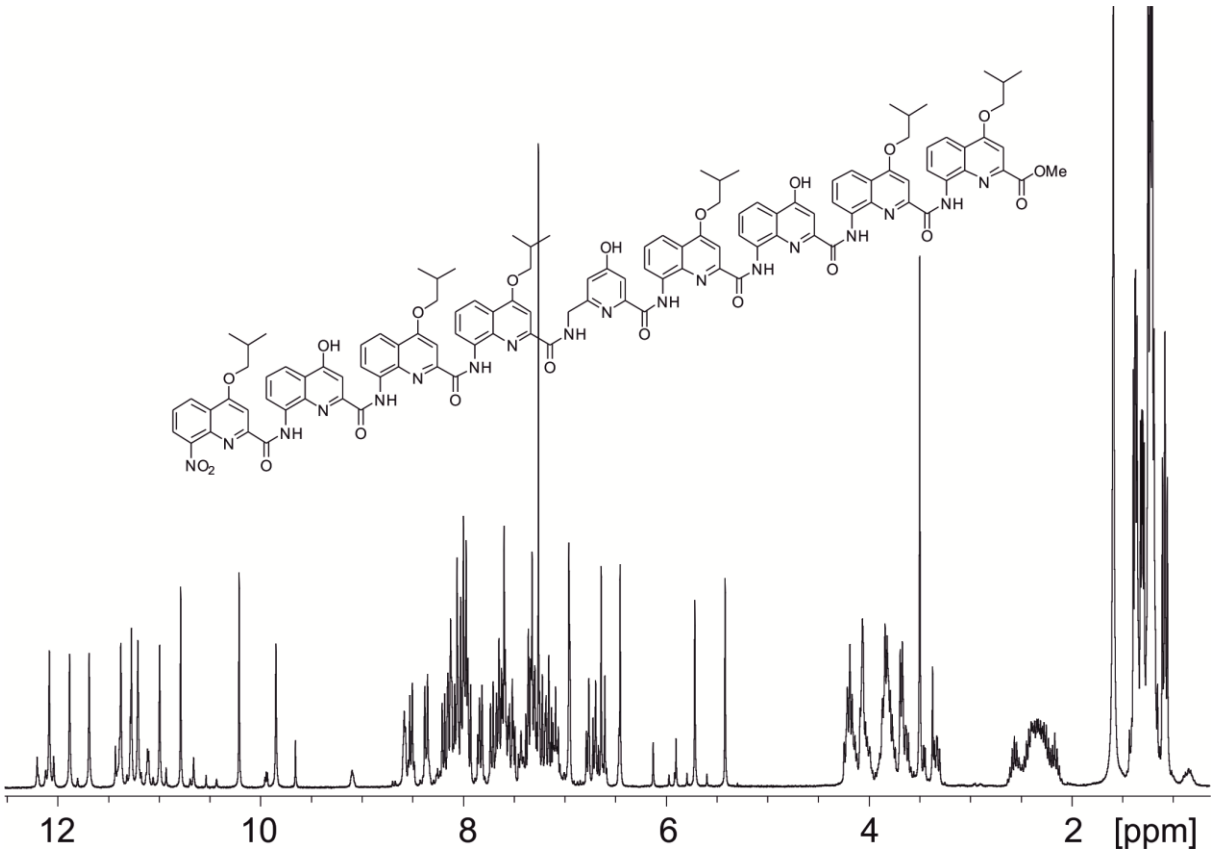

**Supplementary Figure 85:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **26.**



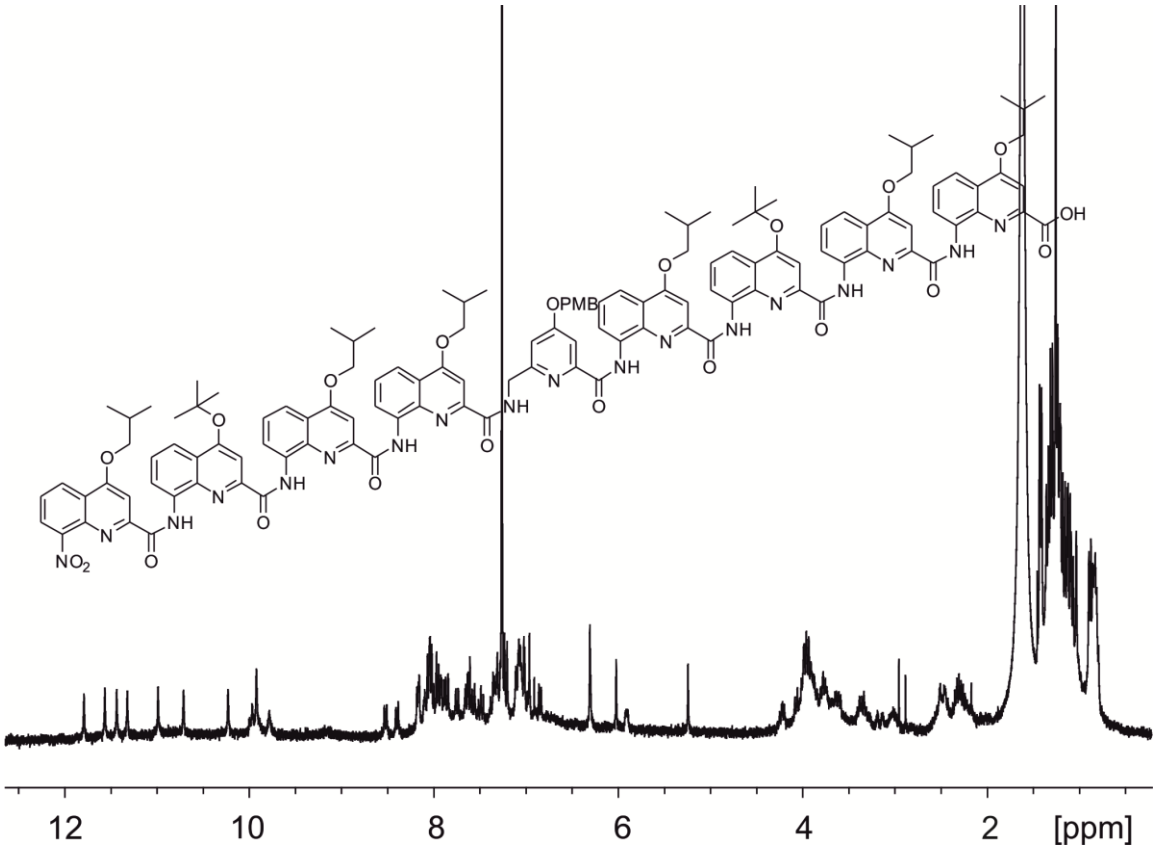

**Supplementary Figure 86:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **5b.**



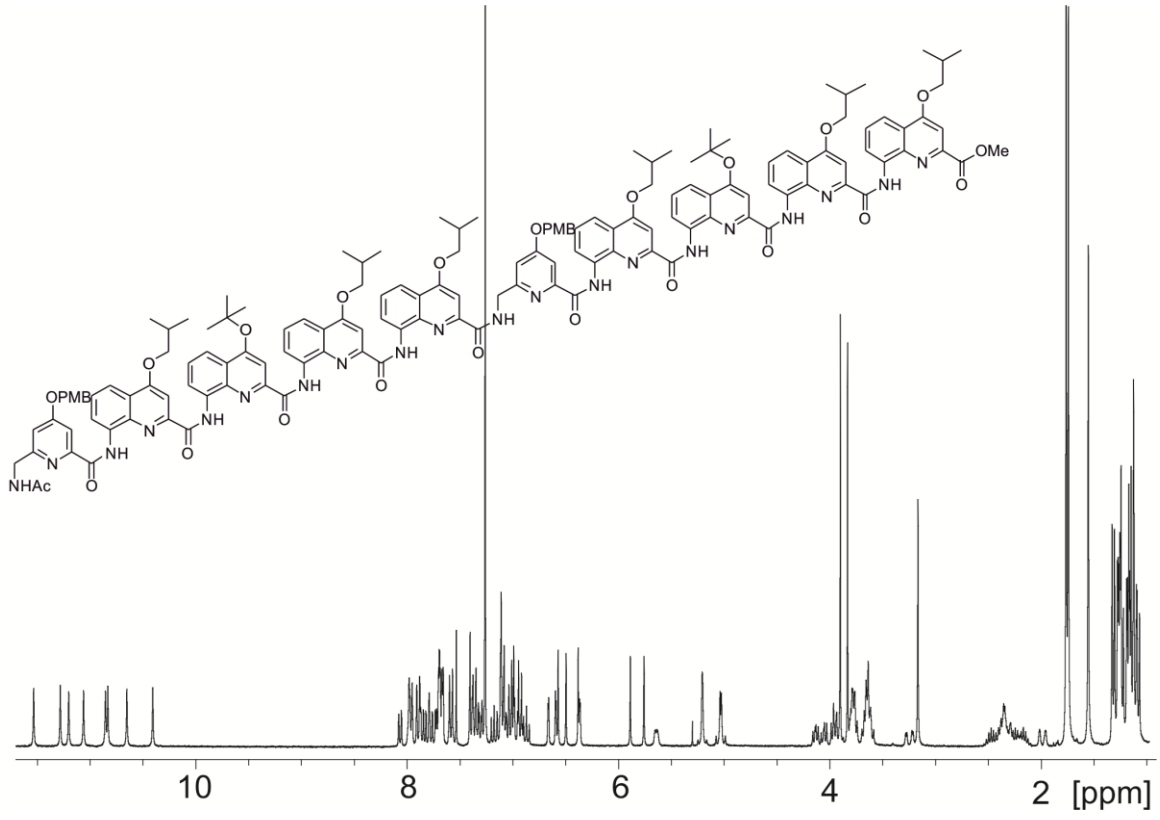

**Supplementary Figure 87:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **5b.**



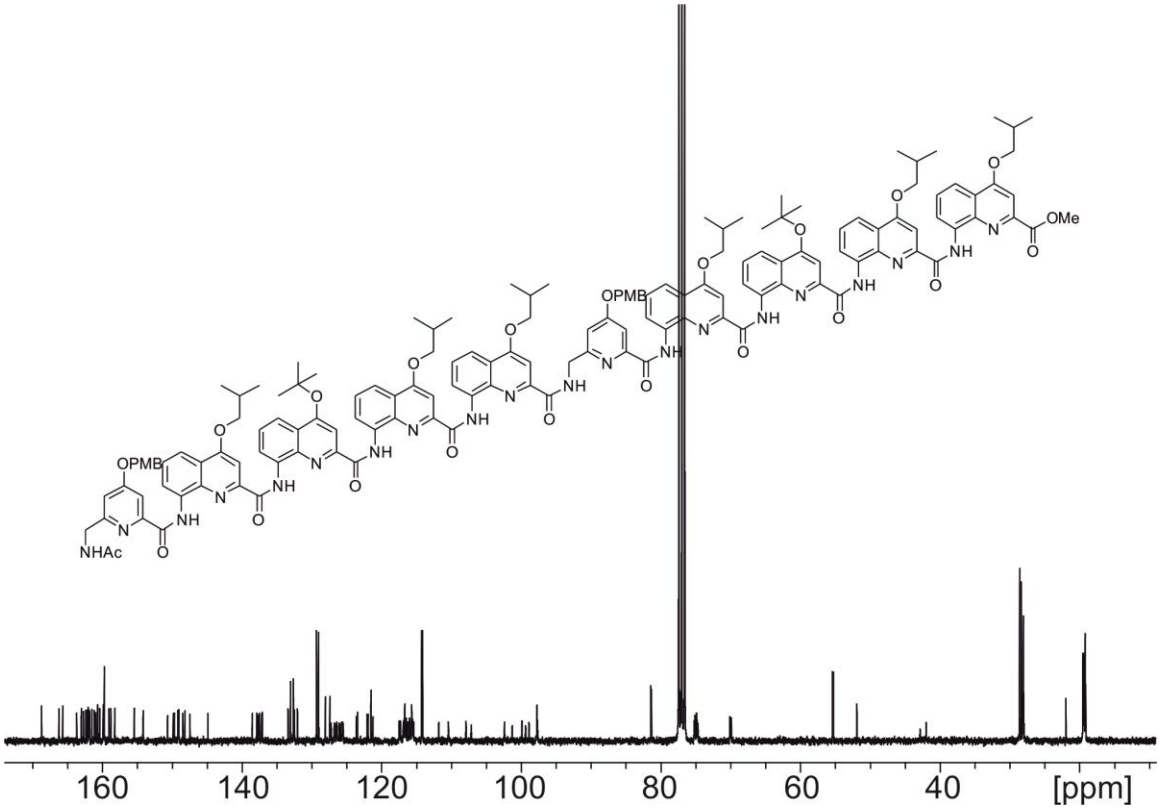

**Supplementary Figure 88:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **5a.**



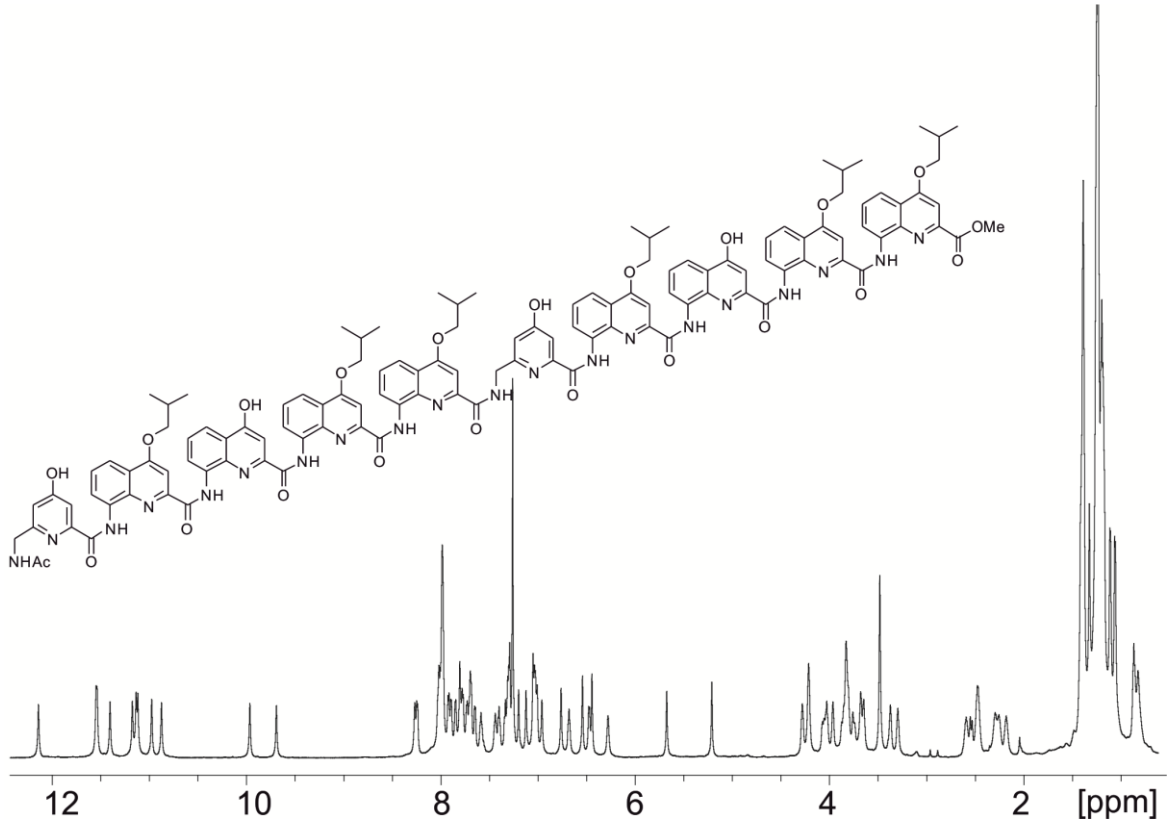

**Supplementary Figure 89:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **27.**



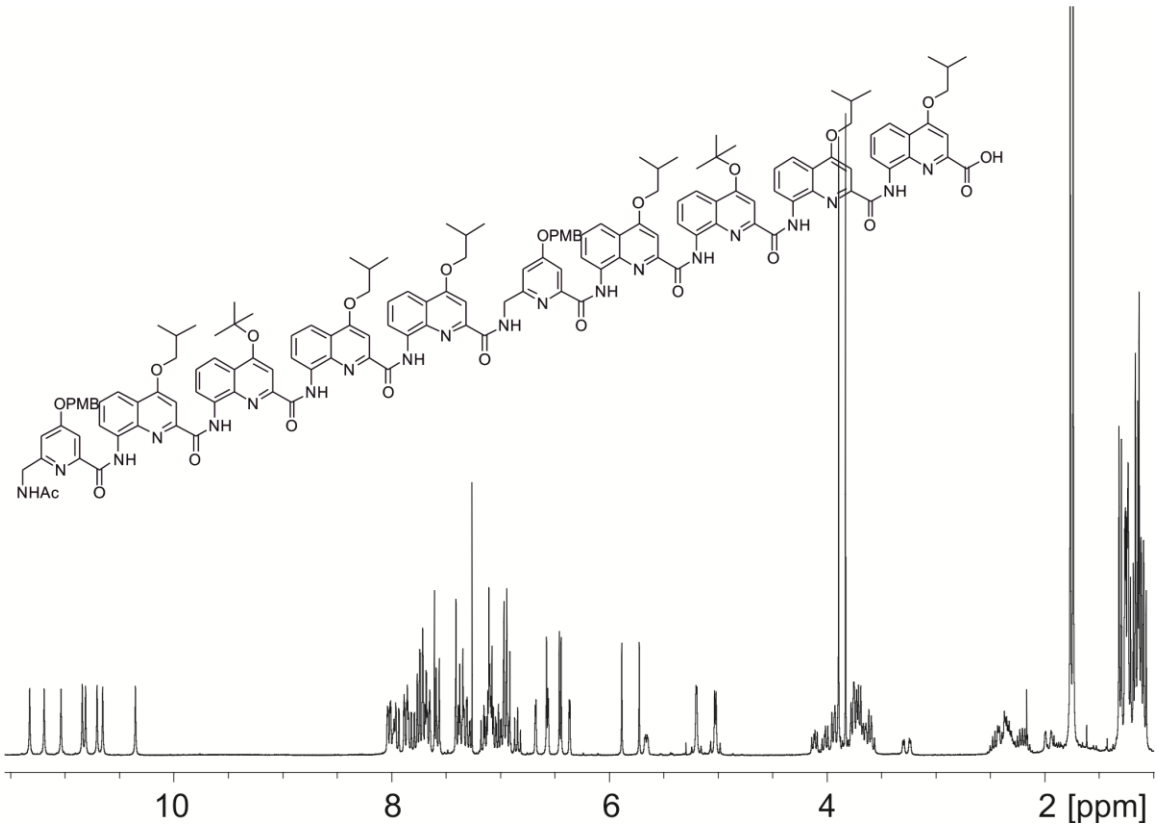

**Supplementary Figure 90:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **4b.**



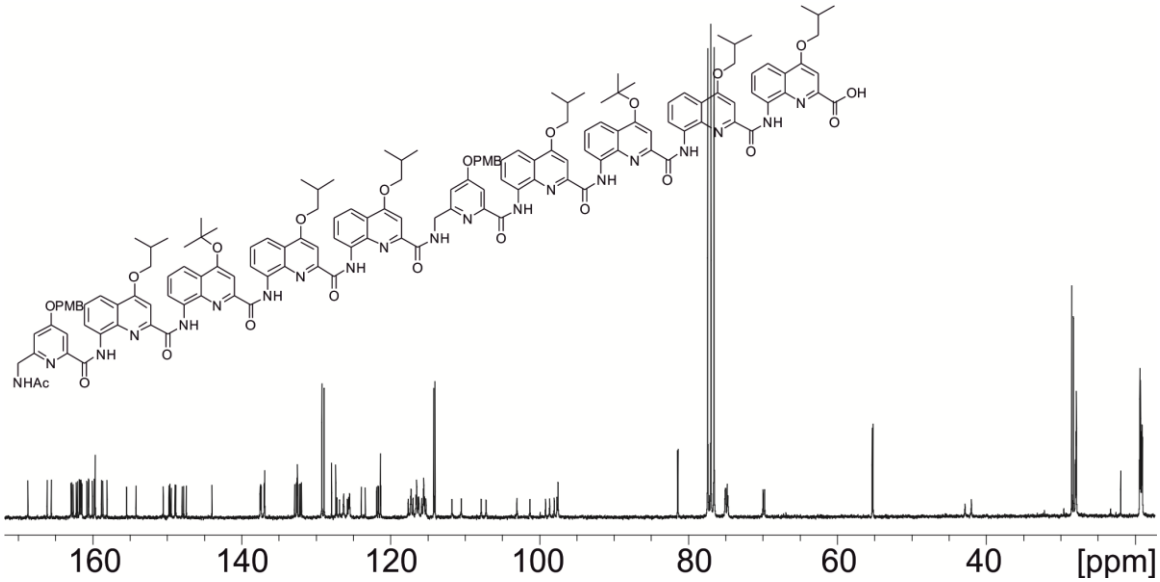

**Supplementary Figure 91:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **4b.**



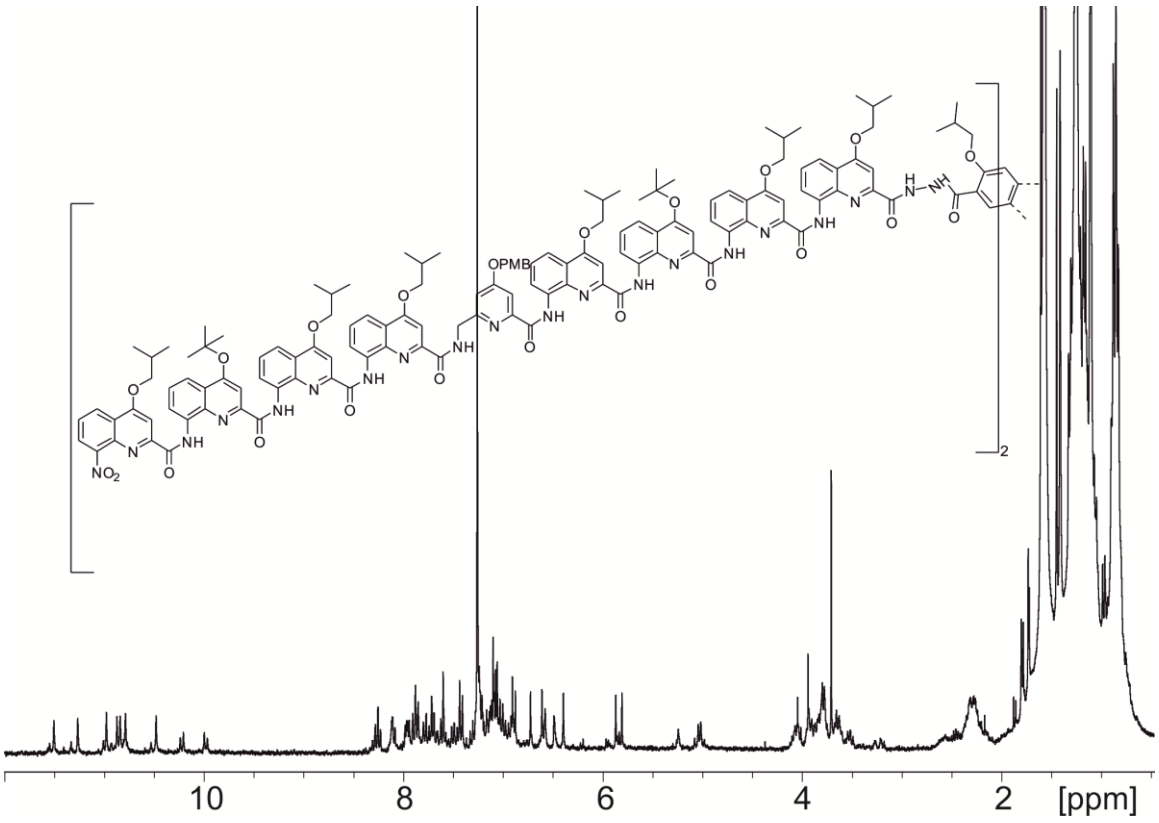

**Supplementary Figure 92:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **4a.**



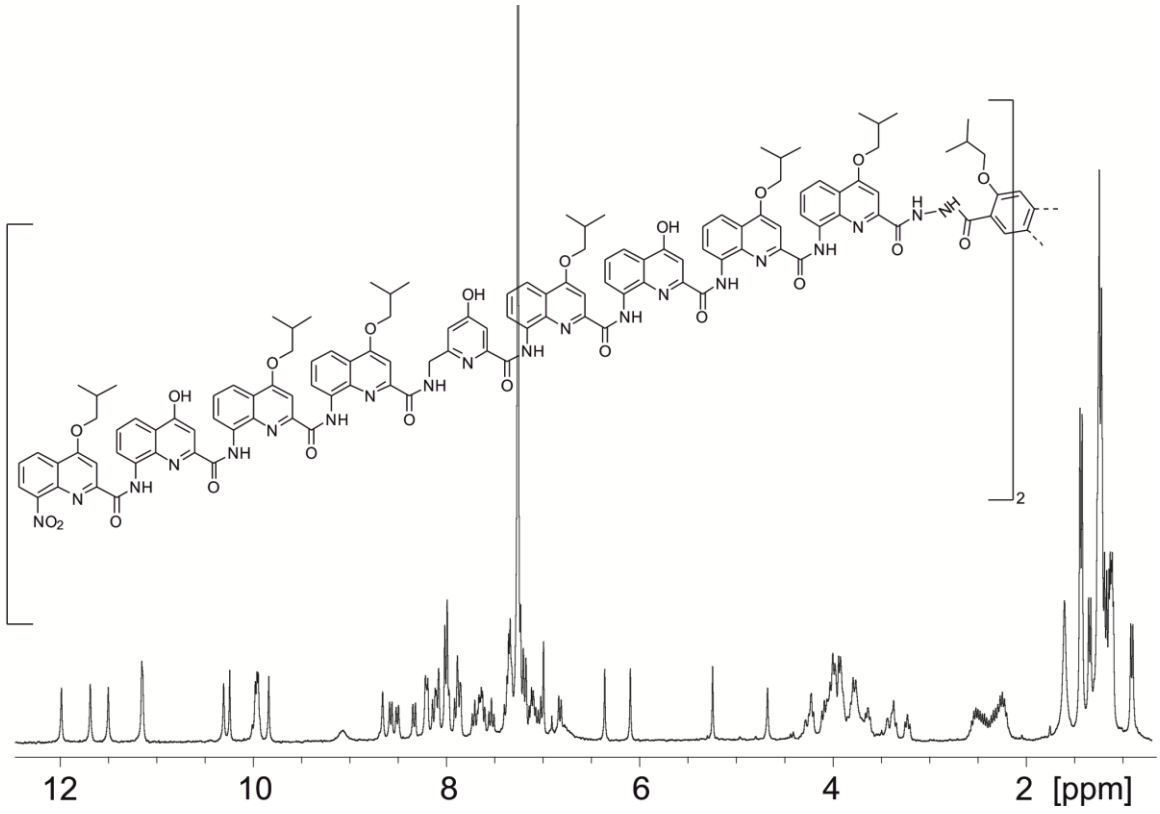

**Supplementary Figure 93:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **28.**



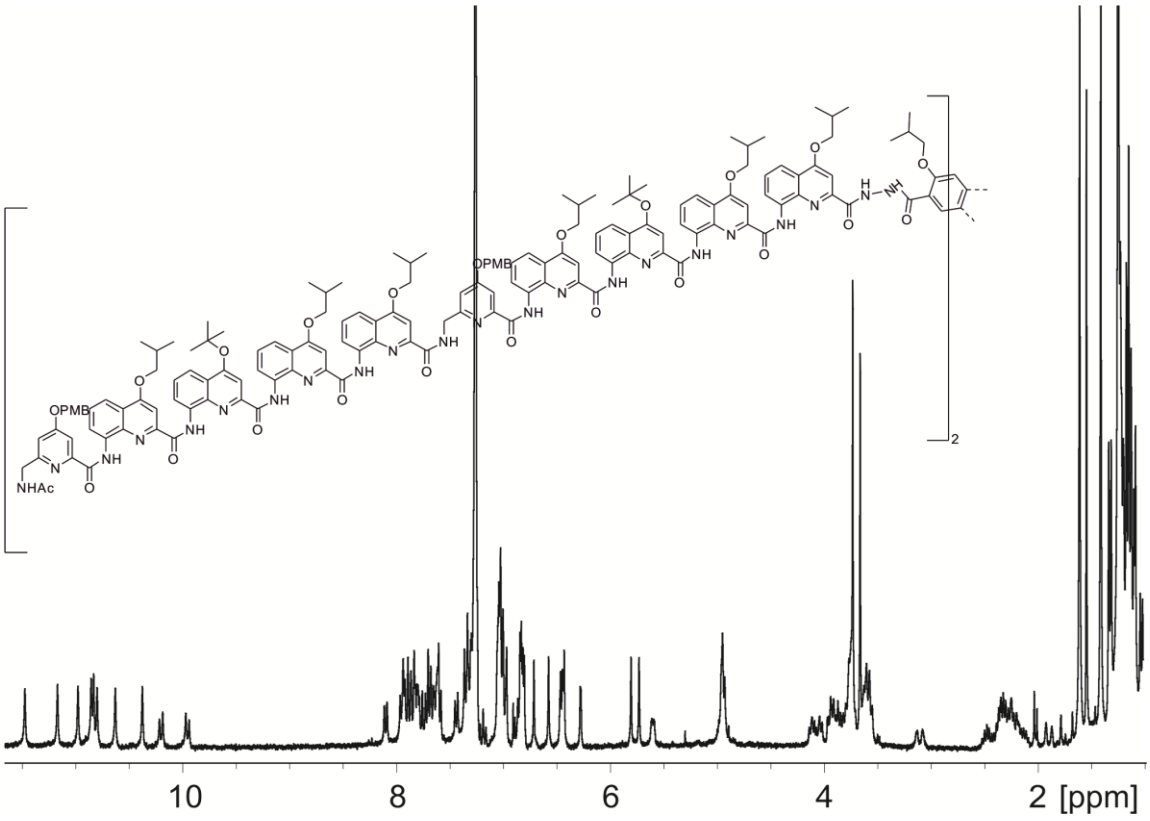

**Supplementary Figure 94:** $^{13}C$ NMR spectrum (75 MHz, $CDCl_3$, 298 K) of **28.**



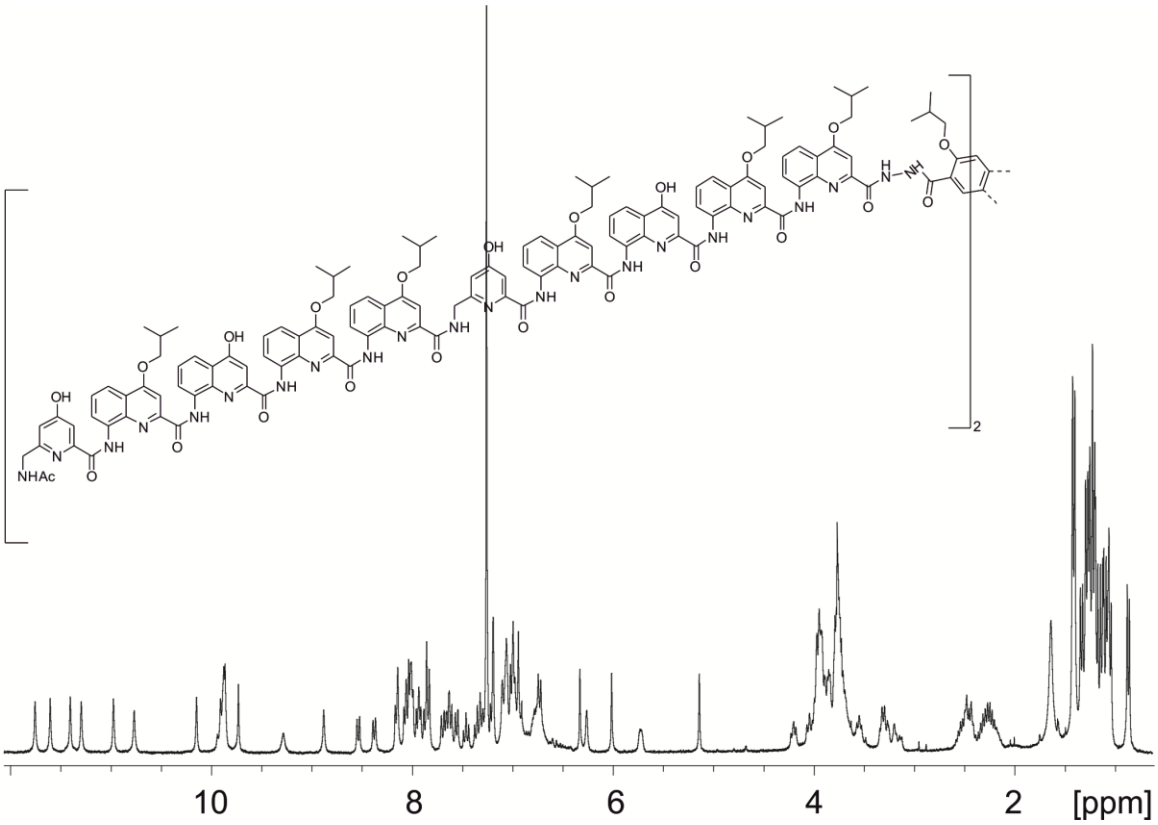

**Supplementary Figure 95:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **3b.**




**Supplementary Figure 96:** $^{1}H$ NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **3a.**




**Supplementary Figure 97:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **2b.**




**Supplementary Figure 98:** $^{1}$H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of **2a.**

# 4 Supplementary Videos

**Supplementary Video 1:** Views of the helix-turn-helix **3a**.
**Supplementary Video 2:** Views of the trimeric bundle (**4a**)$_3$ observed in $CD_2Cl_2$
**Supplementary Video 3:** Views of the dimeric bundle (**5a**)$_2$ observed in $CDCl_3$

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