Supplementary Information

for:

Molecular torsion springs: alteration of helix curvature in frustrated tertiary folds

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1 List of Abbreviations

DCM dichloromethane

DIPEA *N*,*N*-diisopropylethylamine

DMF *N*,*N*-dimethylformamide

DMSO dimethyl sulfoxide

eq. equivalent

Fmoc fluorenylmethoxycarbonyl

MS mass spectrometry

HFIP hexafluroisopropanol

HR-ESI high resolution electrospray ionization

HR-MALDI high resolution matrix-assisted laser desorption/ionization

MeOH methanol

MW microwave

NMP *N*-Methyl-2-pyrrolidone

NMR nuclear magnetic resonance

r. t. room temperature

SPS solid phase synthesis

TEA triethylamine

TFA trifluoroacetic acid

THAP trihydroxy acetophenone

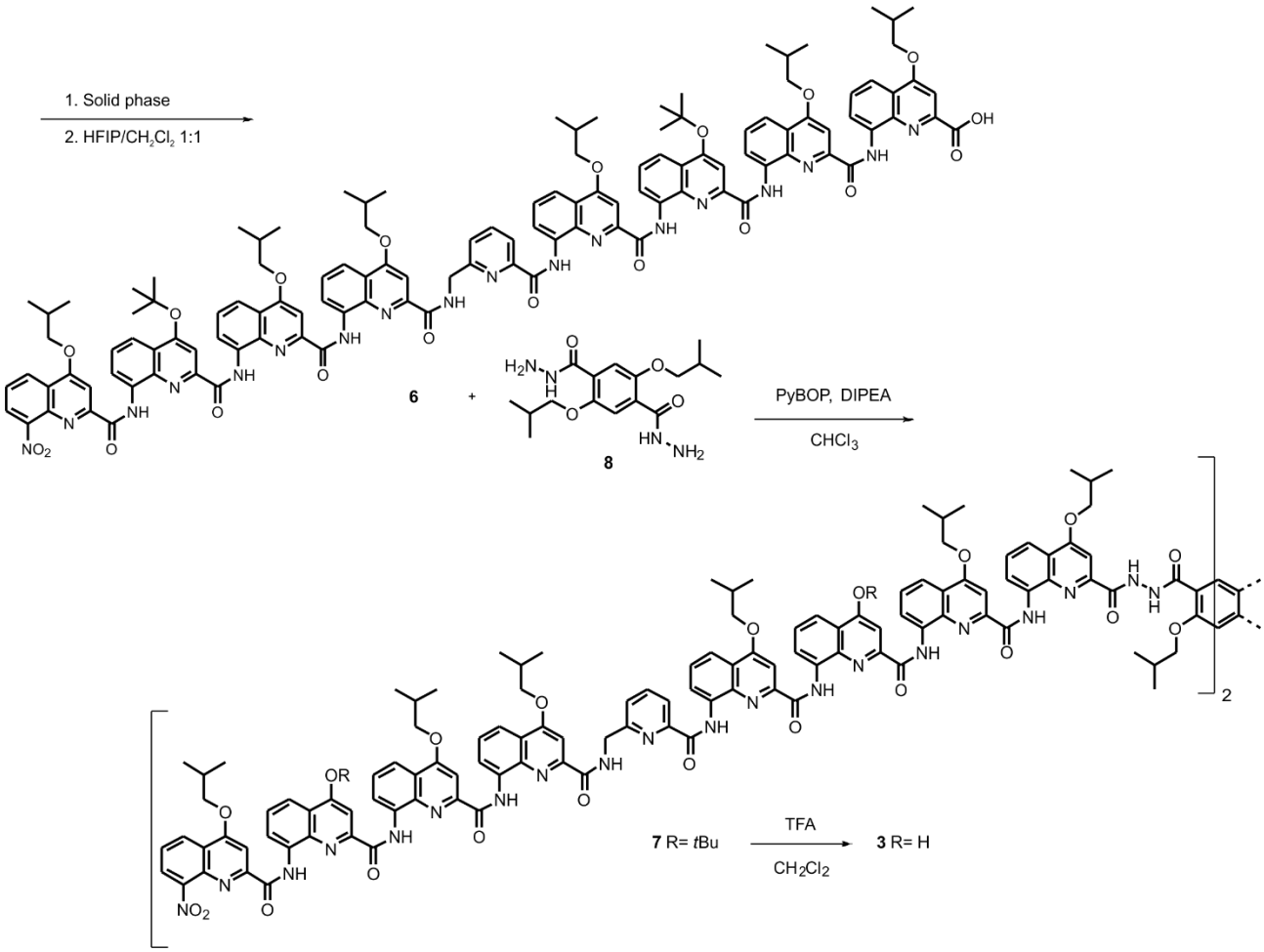
THF tetrahydrofuran

TMS tetramethylsilane

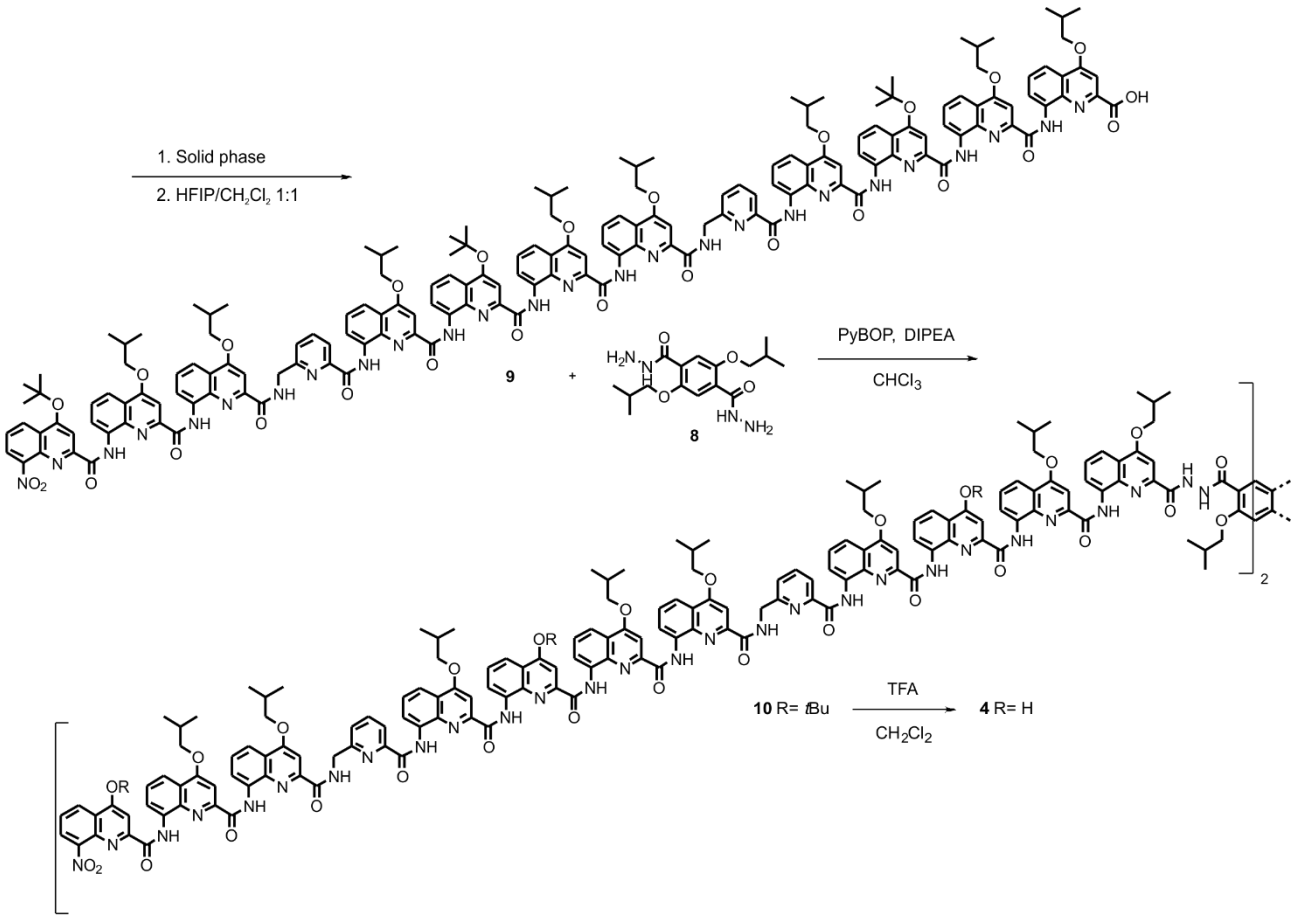
UV/Vis ultraviolet–visible

2 Synthetic Schemes

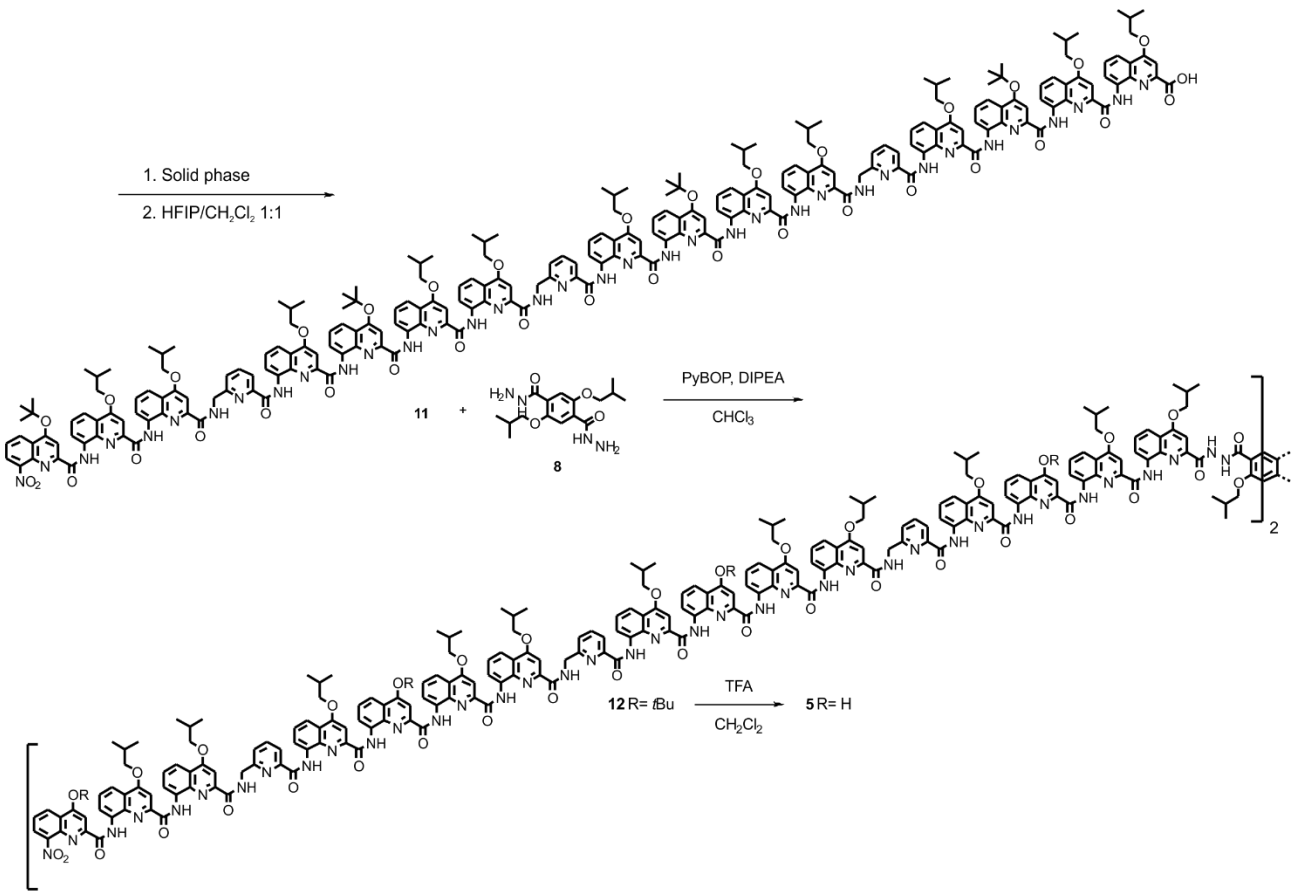
2.1 Synthesis of foldamers



Scheme 1. Synthesis of **3.**



Scheme 2. Synthesis of **4.**



Scheme 3. Synthesis of **5.**

3 Supplementary figures

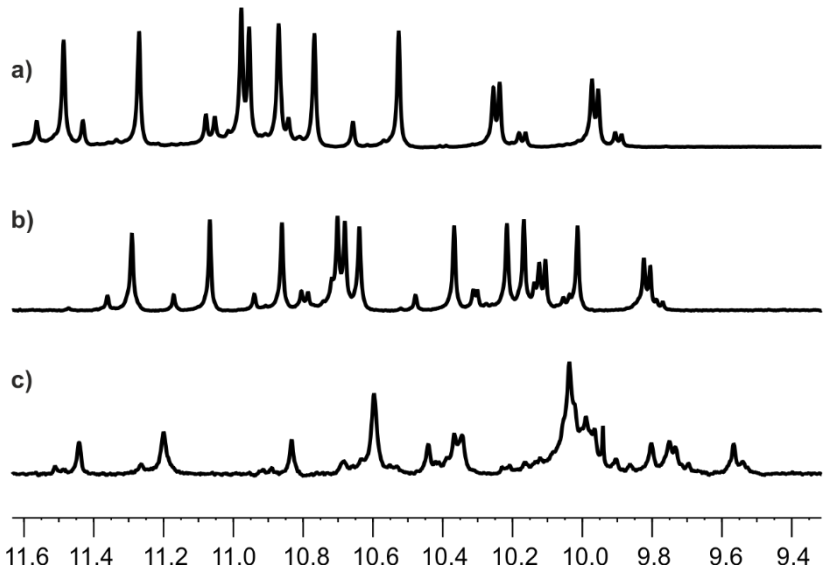


Figure S1. Part of the 500 MHz ^{1}H NMR-spectra of a) **7**, b) **10** and c) **12** at 25 °C in $CDCl_3$ showing the amide proton resonances.

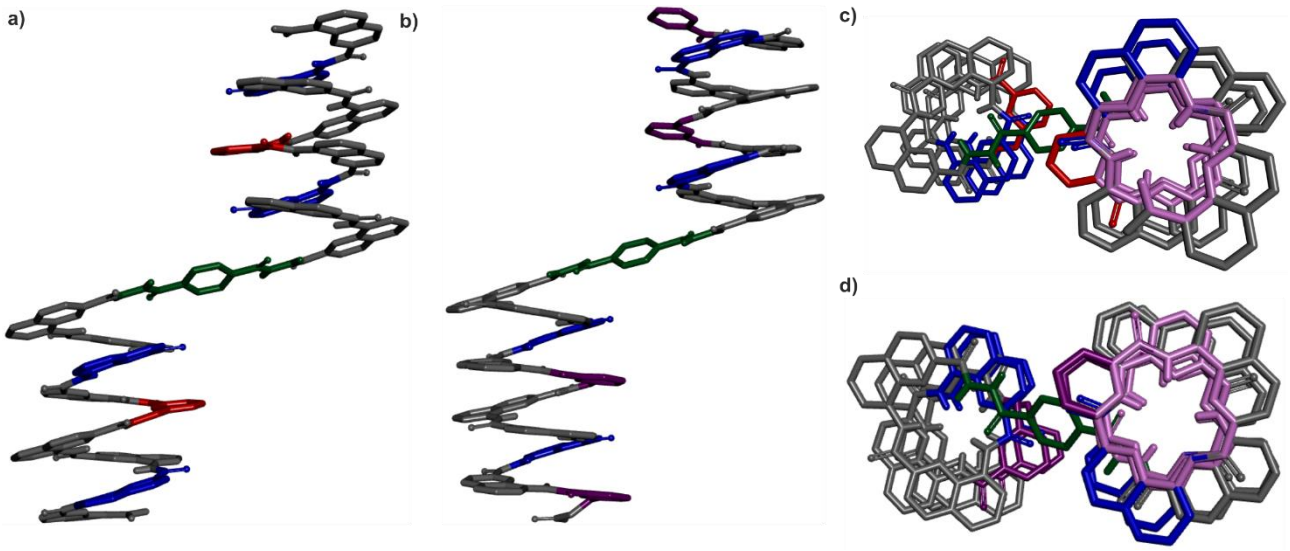


Figure S2. Side-views a) of the crystal structures of protected sequence **7** (new data) and b) of the protected precursor of **2** (from reference 1). The corresponding top-views are shown in c) and d), respectively, where the inner rim of one helix is highlighted in pink. The curvature adopted in these structure corresponds to the preferred curvature, as highlighted by the 15-crown-5 shape of the inner rim. The X units are shown in blue, the Y units in violet and the P units in red tubes. Included solvent molecules, hydrogen atoms and side-chains are omitted for clarity.

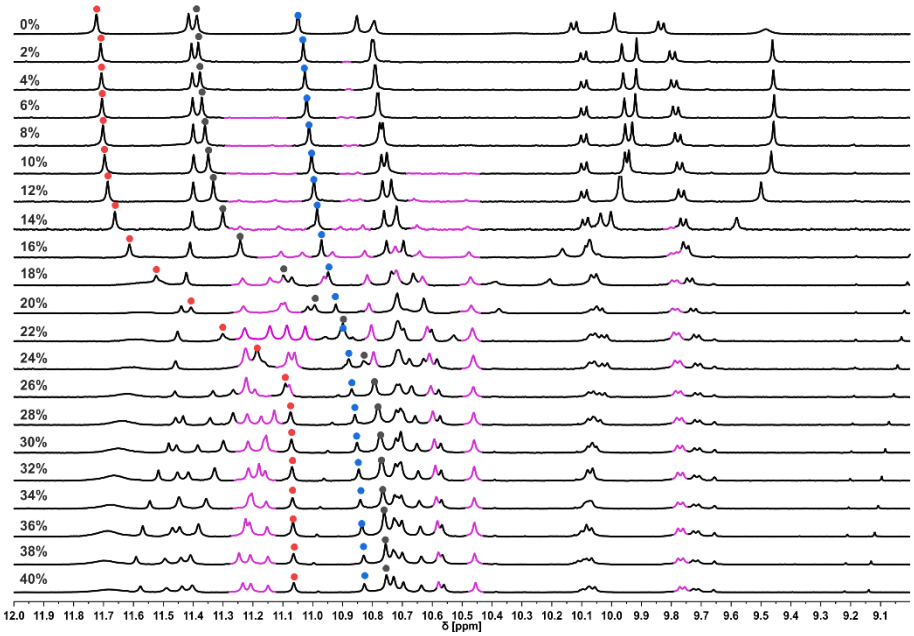


Figure S3. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **3** in $CDCl_3$/DMSO-d_6. The corresponding volume percentages of DMSO-d_6 in $CDCl_3$ are indicated at left. All ^{1}H NMR spectra containing DMSO have been calibrated on the signal corresponding to DMSO at δ = 2.5 ppm. The one containing no DMSO has been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations can be assigned to calibration. The chemical shift variations of the signal marked with a red, black and blue dot are shown in Figure S4; those with a black dot are also shown in Figures 5b & c. The emergence of the disrupted *PM* conformer is highlighted in pink.

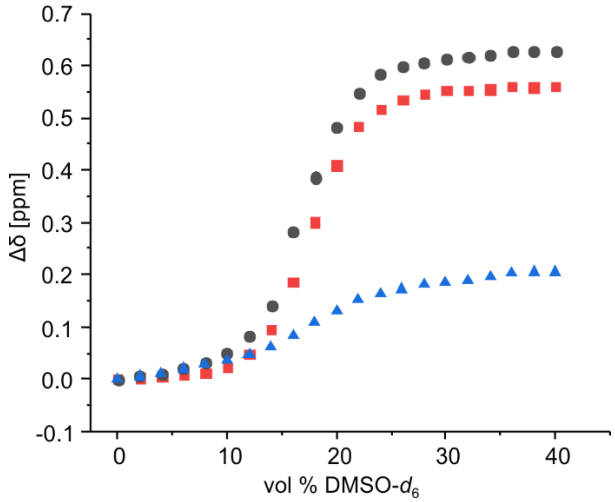


Figure S4. Variation of the chemical shift value of selected ^{1}H NMR signals of **3** upon addition of DMSO-d_6 (signals marked with dots of the same color in Figure S3). The data in black is also shown in Figures 5b & 5c. The inflection occurs near 18.5% of DMSO-d_6.

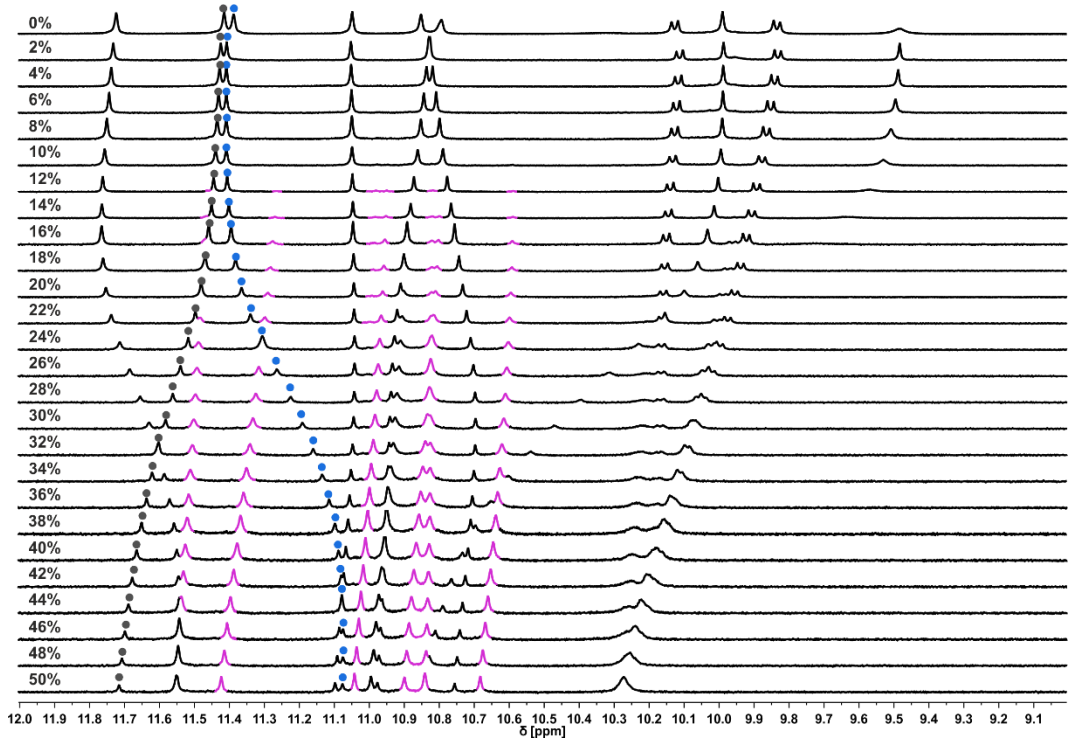


Figure S5. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **3** in $CDCl_3$/pyridine-d_5. The volume percentages of pyridine-d_5 in $CDCl_3$ are indicated at left. All ^{1}H NMR spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. The chemical shift variations of the signals marked with a black and blue dot are shown in Figure S6, those with a blue dot are also shown in Figure 5b. The emergence of the disrupted *PM* conformer is highlighted in pink.

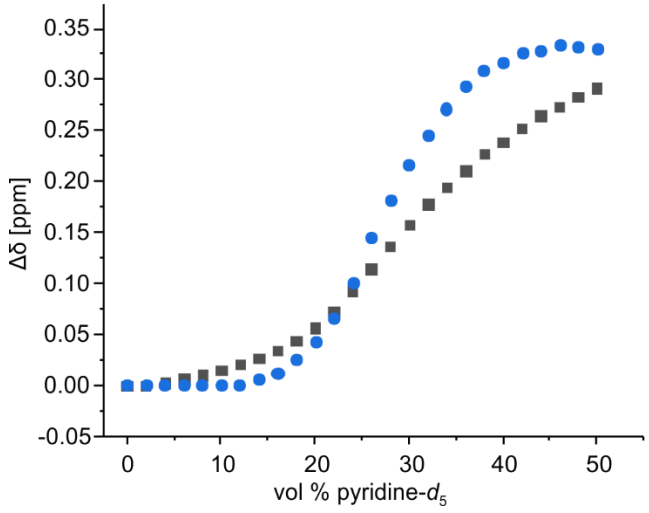


Figure S6. Variations of the chemical shift value of selected ^{1}H NMR signals of sequence **3** upon addition of pyridine-d_5 (signals marked with dots of the same color in Figure S5). The data in blue is also shown in Figure 5b. The inflection occurs near 27.5% of pyridine-d_5.

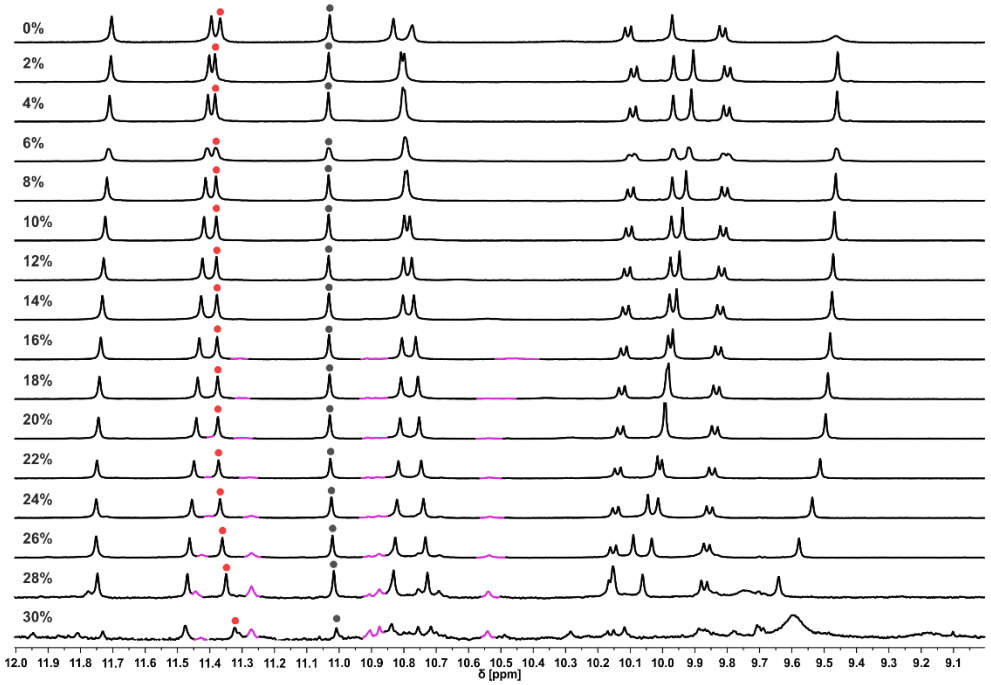


Figure S7. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) resonances of **3** in $CDCl_3$/DMF-d_7. The volume percentages of DMF-$d_7$in $CDCl_3$ are written at left. All ^{1}H NMR spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. The chemical shift variations of the signals marked with a red and black dot are shown in Figure S8, those with a red dot are also shown in Figure 5b. The emergence of the disrupted *PM* conformer is highlighted in pink. The sample precipitated at 32% DMF-d_7.

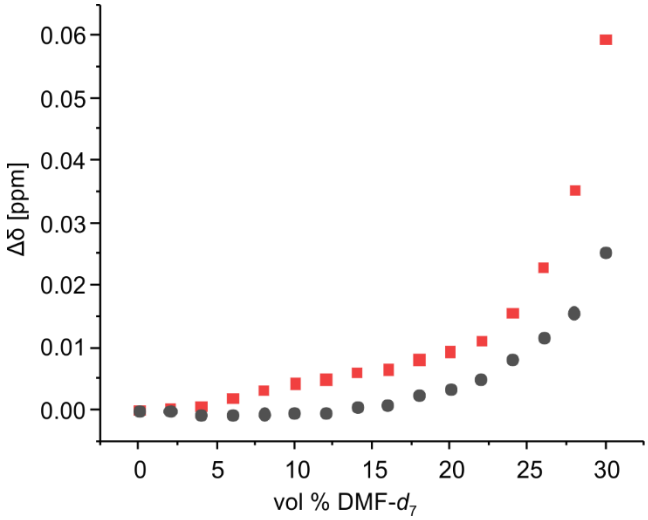


Figure S8. Variations of the chemical shift value of selected ^{1}H NMR signals of **3** on the addition of DMF-d_7 (signals marked with dots of the same color in Figure S7). The curve in red is also shown in Figure 5b. The inflection occurs at > 30% of DMF-d_7

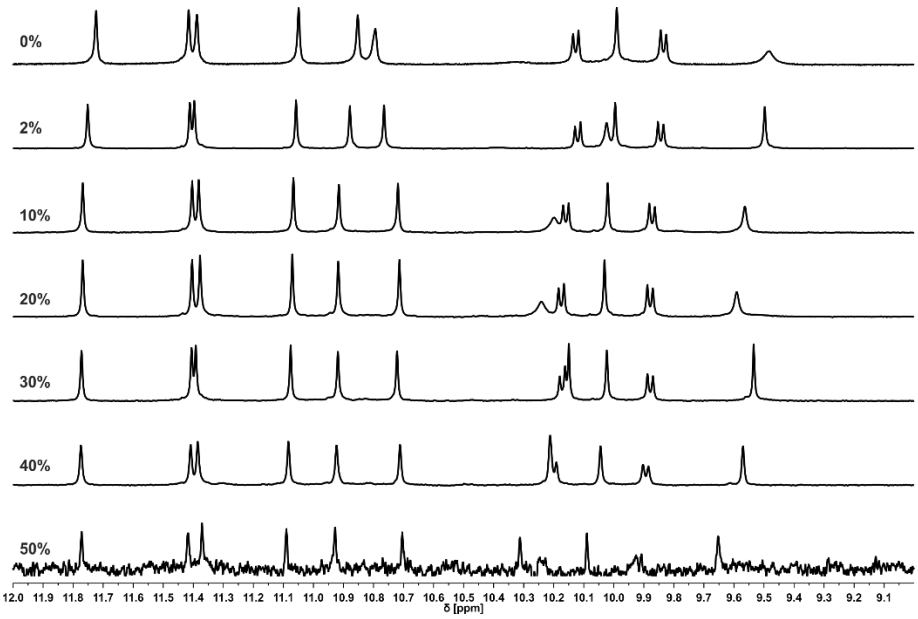


Figure S9. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **3** in $CDCl_3$/methanol-d_3. The volume percentages of methanol-d_3 in $CDCl_3$ are written on the left side of each ^{1}H NMR spectra. All ^{1}H NMR spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. No formation of a second species has been observed. The sample precipitated at 60% methanol-d_3.

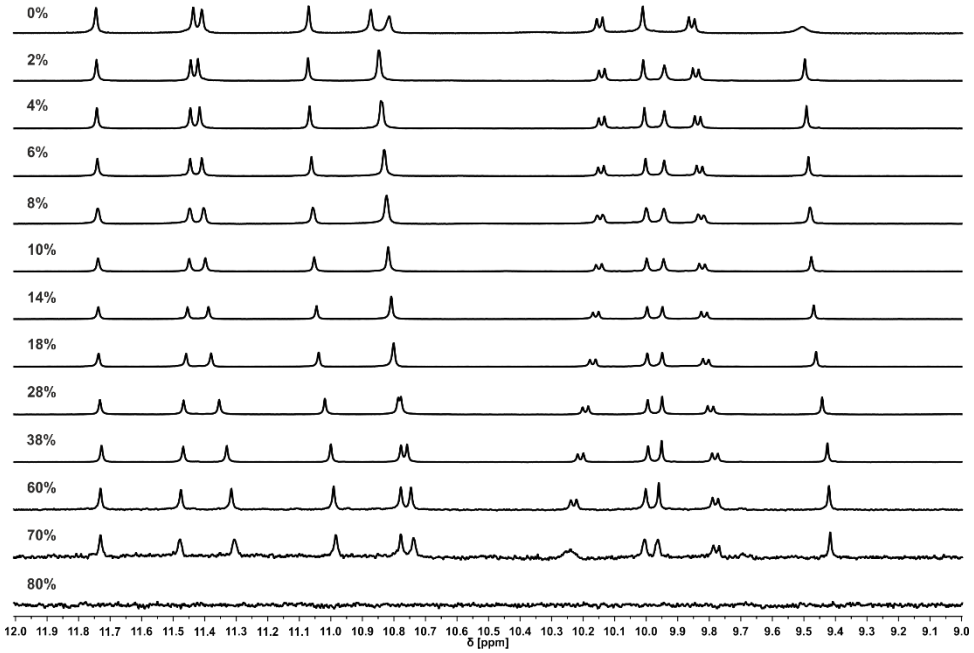


Figure S10. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **3** in $CDCl_3$/acetonitrile-d_3. The volume percentages of acetonitrile-d_3 in $CDCl_3$ are written at left. All ^{1}H NMR spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned. No formation of a second species has been observed. The sample precipitated at 80% acetonitrile-d_3.

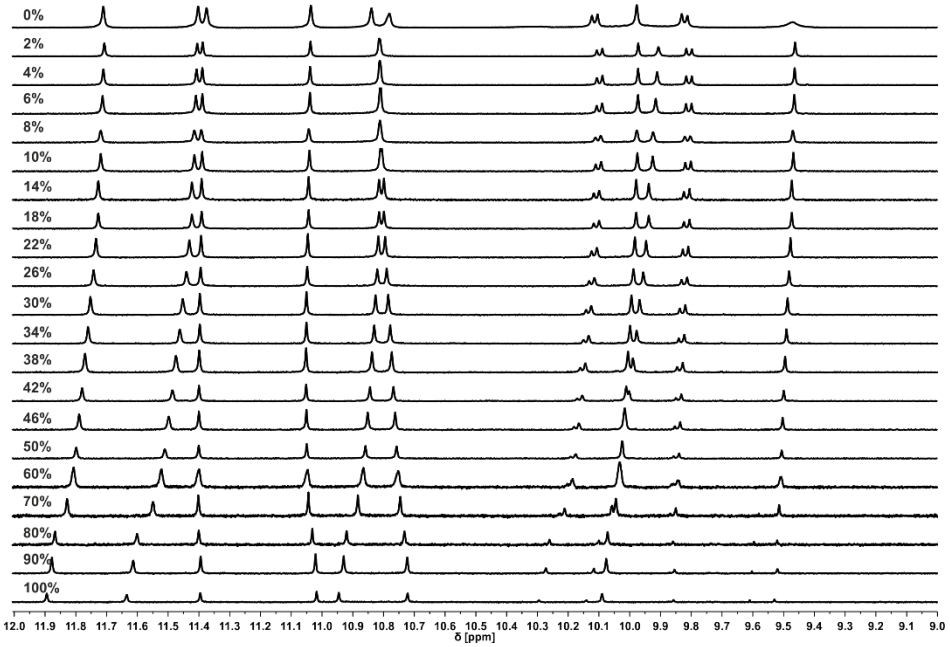


Figure S11. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **3** in $CDCl_3$/acetone-d_6. The volume percentages of acetone-d_6 in $CDCl_3$ are indicated at left. All ^{1}H NMR spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations can be assigned to calibration. No formation of a second species has been observed.

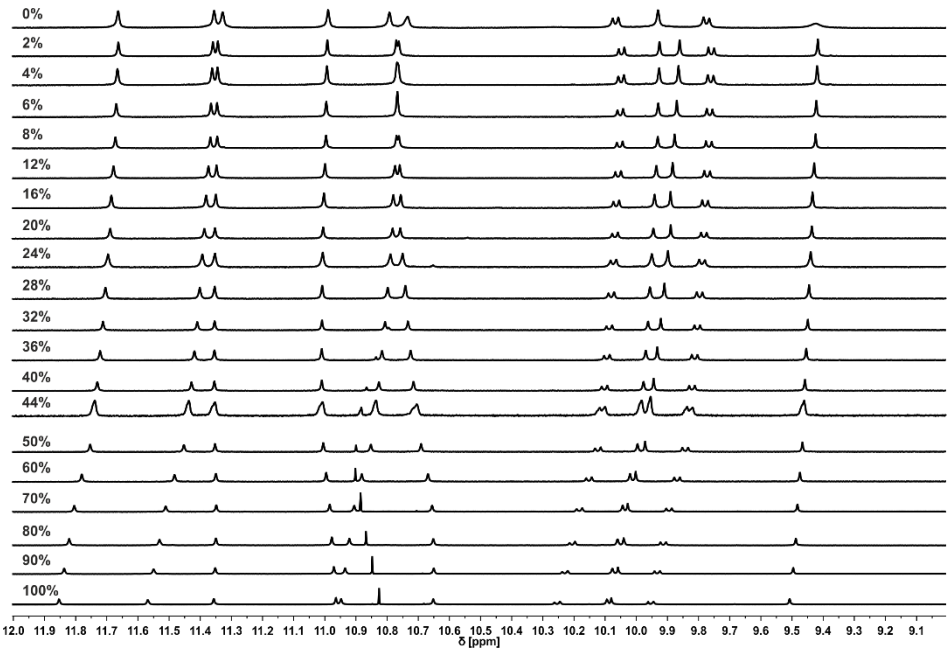


Figure S12. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **3** in $CDCl_3$/tetrahydrofuran-d_8. The volume percentages of tetrahydrofuran-d_8 in $CDCl_3$ are indicated at the left. All spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. No formation of a second species has been observed.

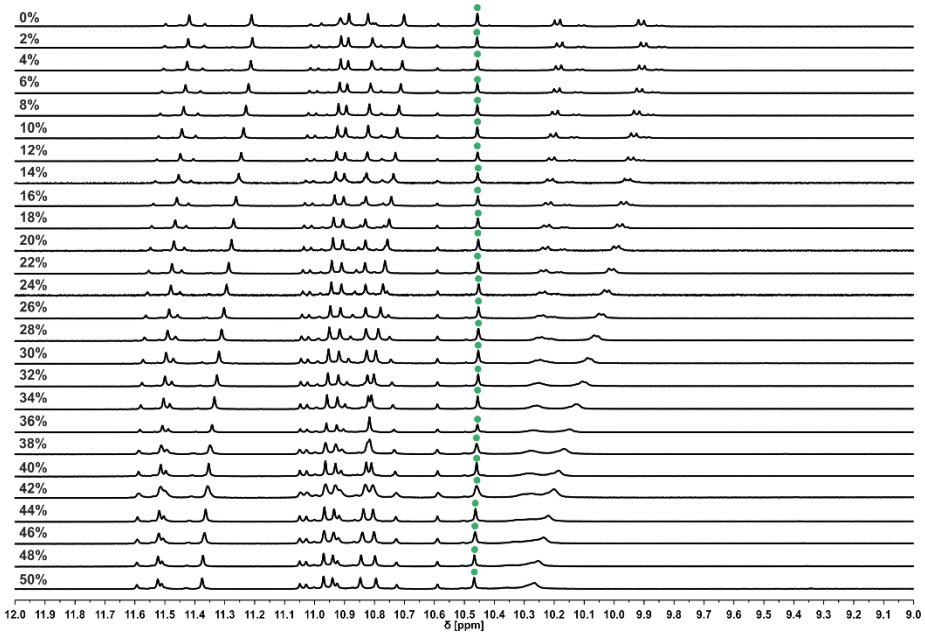


Figure S13. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **7** in $CDCl_3$/pyridine-d_5. The volume percentages of pyridine-$d_5$in $CDCl_3$ are indicated at left. All spectra have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes of some chemical shift variations may be assigned to calibration. The chemical shift variations of the signal marked with a green dot are shown in Figure S15.

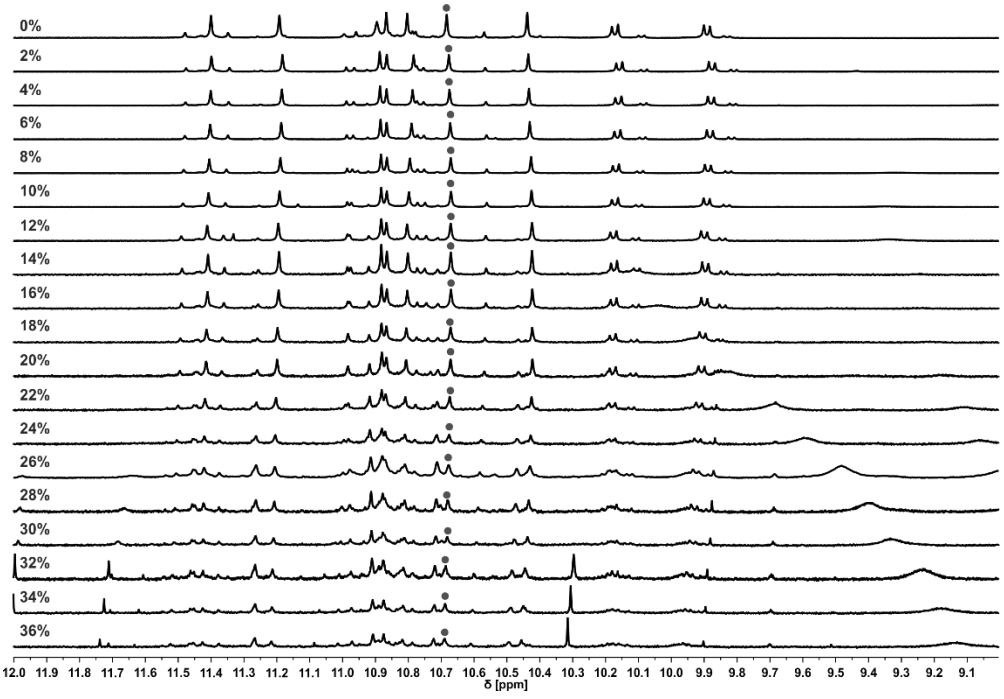


Figure S14. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **7** in $CDCl_3$/DMF-d_7. The volume percentages of DMF-$d_7$in $CDCl_3$ are indicated at left. All ^{1}H NMR have been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. No formation of a second species has been observed. The chemical shift variations of the signal marked with a black dot are shown in Figure S15. The sample precipitated at 38% DMF-$d_7$in solution.

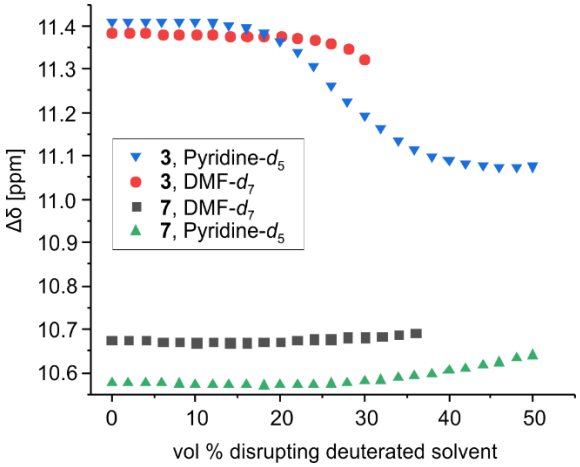


Figure S15. Variation of the chemical shift of selected ^{1}H NMR signals of **3** and its protected precursor **7** in $CDCl_3$ on the addition of disruptive solvents like DMF-d_7 (red and black) and pyridine-d_5 (green and blue). The colors of the data matches those of the dots marked in Figure S5, Figure S7, Figure S13 and Figure S14. The experiment with DMF-d_7 was ended due to precipitation of the sample at 32% (in case of **3**) and 38% (in case of **7**).

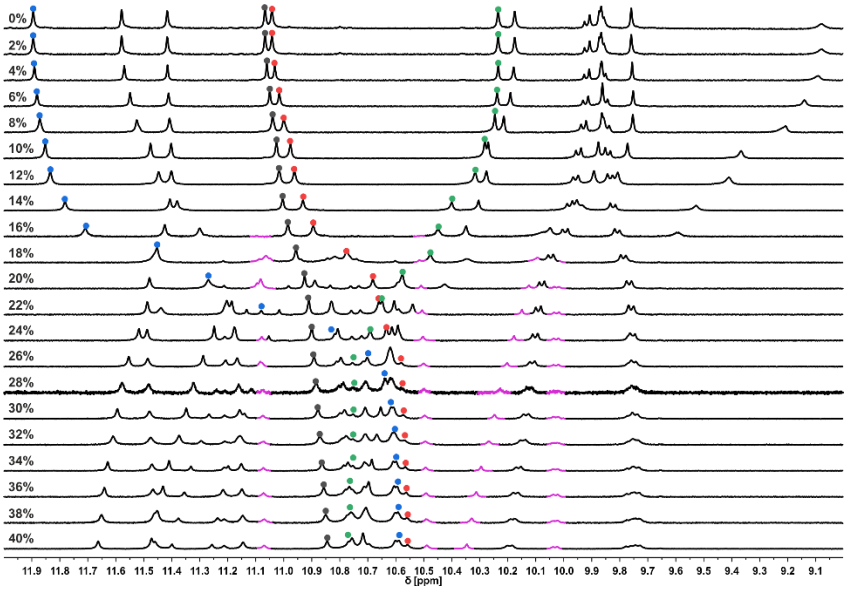


Figure S16. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **1** in $CDCl_3$/DMSO-d_6. The volume percentages of DMSO-d_6 in $CDCl_3$ are indicated at left. All ^{1}H NMR spectra containing DMSO have been calibrated on the signal corresponding to DMSO at δ = 2.5 ppm. The one containing no DMSO has been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. The chemical shift variations of the signal marked with a blue, black, red and green dot are shown in Figure S17, those with a blue dot are also shown in Figure 5c. The emergence of the disrupted *PM* conformer is highlighted in pink.

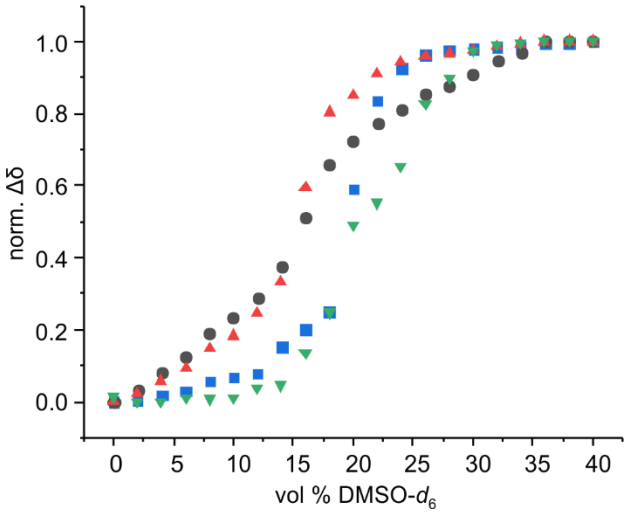


Figure S17. Normalized variation of the chemical shift value of selected ^{1}H NMR signals of **1** upon the addition of DMSO-d_6 (signals marked with dots of the same color in Figure S16). The curve in blue is also shown in Figure 5c. The inflection occurs near 21.5% of DMSO-d_6.

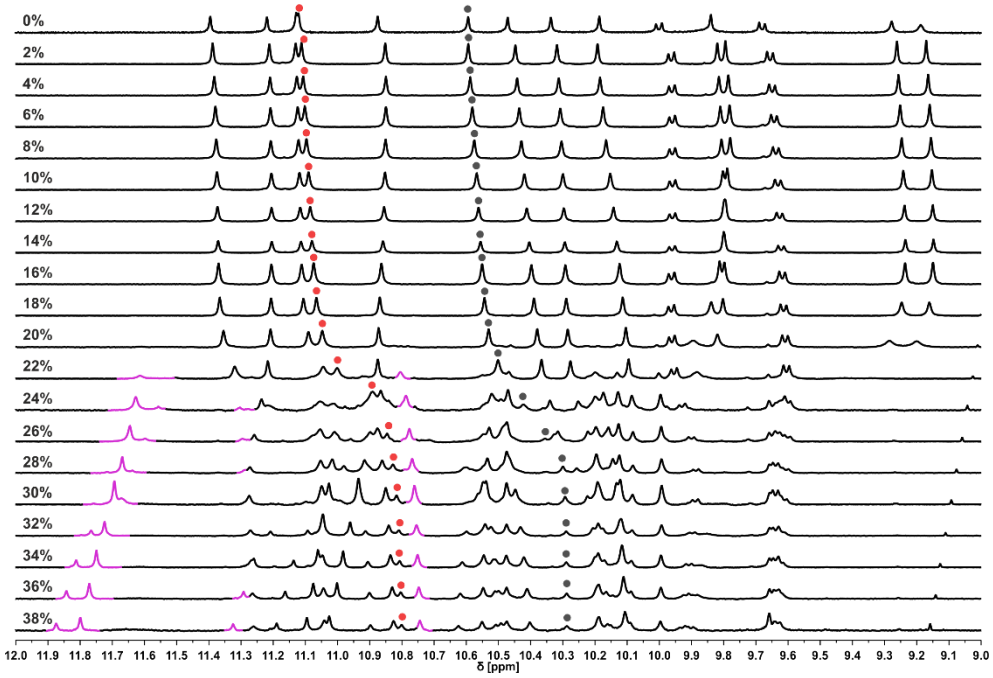


Figure S18. Amide region of the ^{1}H NMR spectra (500 MHz, 25 °C) of **4** in $CDCl_3$/DMSO-d_6. The volume percentages of DMSO-d_6 in $CDCl_3$ are indicated at left. All ^{1}H NMR spectra containing DMSO have been calibrated on the signal corresponding to DMSO at δ = 2.5 ppm. The one containing no DMSO has been calibrated on the signal corresponding to TMS at δ = 0.0 ppm. Minimal changes in some chemical shift variations may be assigned to calibration. The chemical shift variations of the signals marked with a black and red dot are shown in Figure S19, those with a red dot are also shown in Figure 5c. The emergence of the disrupted *PM* conformer is highlighted in pink.

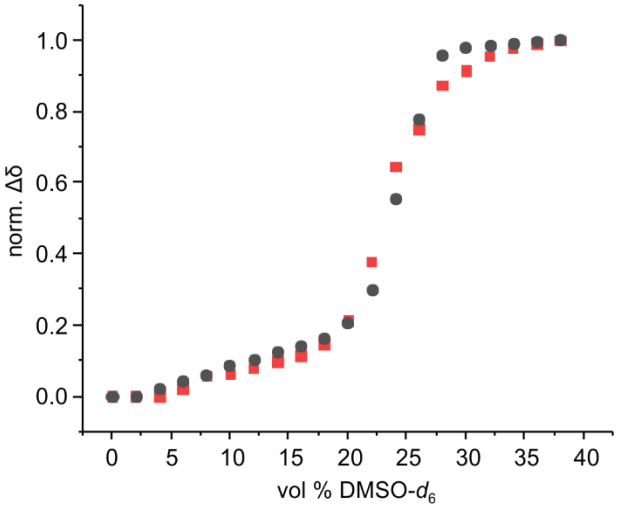


Figure S19. Normalized variation of the chemical shift value of selected ^{1}H NMR signals of **4** on the addition of DMSO-d_6 (signals marked with dots of the same color in Figure S18). The curve in red is also shown in Figure 5c. The inflection occurs near 24.0% of DMSO-d_6.

4 Supplementary methods

4.1 Nuclear magnetic resonance spectroscopy

NMR spectra were recorded on different NMR spectrometers: (I) an Avance II NMR spectrometer (Bruker BioSpin) with a vertical 7.05 T narrow-bore/ultrashield magnet operating at 300 MHz by means of a 5-mm direct BBO H/X probe with Z gradient capabilities; (II) an Avance III HD 400 MHz Bruker BioSpin spectrometer or an Avance III HD 500 MHz Bruker BioSpin spectrometer equipped with a broad band observe 5-mm BB-H&FD CryProbe^{TM} Prodigy. Measurements were performed at 25 °C unless stated otherwise.

Chemical shifts are described in part per million (ppm, δ) relative to the ^{1}H residual signal of the deuterated solvent used unless otherwise noted. Processing was done with MestReNovax64 NMR processing software from Mestrelab Research. ^{1}H NMR splitting patterns with observed first-order coupling are entitled as singlet (s), doublet (d), triplet (t), or broad singlet (bs).

4.2 Solution state ^{1}H NMR studies

For the solvent concentration dependency study a sample was dissolved in $CDCl_3$ (c = 1.2 mM) and the amount of polar solvent in solution was increased stepwise. After an equilibration time of two hours the ^{1}H NMR was recorded after each increase. If a solvent is disruptive a significant change of the chemical shift in the amide region and the formation of a second species is observed, which reflects a conformational transition. The amount of polar solvent in the sample is increased until no further change of the chemical shifts in the amide region and no increase in the formation of a second species is observed.

This experiment has been carried out until 100% or precipitation of the sample in case of solvent at which no formation of a second species has been observed.

The solvents $CDCl_3$ (quality: 99.8 atom % D, containing 0.03vol.% TMS), DMSO-d_6 (quality: 99.9 atom % D), DMF-d_7 (quality: 99.5 atom % D), pyridine-d_5 (quality: ≥99.5 atom % D), methanol-d_3 (quality: 99.8 atom % D), acetonitrile-d_3 (quality: ≥99.8 atom % D), acetone-d_6 (quality: 99.9 atom % D), THF-d_8 (quality: ≥99.5 atom % D, containing 0.03vol.% TMS) have been used.

4.3 X-ray crystallography

The diffraction data for **3** were collected at the FIP (ESRF) beamline using 0.81 Å wavelength and were processed with the XDS package.[2] X-ray diffraction experiments for **7** were performed at the IECB x-

ray facility (CNCR UMS 3033 – INSERM US001) with a Rigaku FRX rotating anode (2.9 kW) diffractometer. CuKα radiation was monochromated with high flux Osmic Varimax HF mirrors for data collection. The x-ray source was equipped with a Dectris Pilatus 200K detector and partial chi goniometer. The data were processed with CrysAlis PRO software [3] with a multiscan absorption correction. All crystals were kept at 100(2) K during data collection. Structures were solved with the ShelXT[4] structure solution program using a dual-space algorithm. Crystal model refinement was performed with ShelXL[5] package using Least Squares minimization implemented in Olex2.[6]

During refinement, anisotropic displacement parameters were used for backbones, some solvent molecules and side chains. The C- and N-bound hydrogen atoms were placed in an idealized position. In **3**, the positions of hydroxy H atoms were established based on hydrogen bond interactions. All H atoms were refined in the riding-model approximation, with $U_{iso}(H)=1.2U_{eq}(CH, CH_2, NH)$, $U_{iso}(H)=1.5U_{eq}(OH, CH_3)$. EADP, DELU and RIGU instructions were employed to model temperature parameters. The geometry of the molecules was improved with DFIX and AFIX commands.

The solvent masking procedure implemented in Olex2[6] was employed to remove severely disordered solvent molecules. The solvent radius was set to 1.2 Å, and the calculated total potential solvent-accessible void volume and electron counts per unit cell were 4656 $Å^3$ and 1132, 2518 Å and 849 for **3** and **7**, respectively.

The final cif files were checked using IUCR's check cif algorithm. Due to the characteristics of the crystal, *i.e.* large volume fractions of disordered solvent molecules, weak diffraction intensity, incompleteness of the data and moderate resolution, A - level and B - level alerts remain in the check cif file. These alerts are inherent to the data and refinement procedures and do not reflect errors. They are explicitly listed below and have been divided into two groups. The first group illustrates the poor quality of the data and refinement statistics compared to that expected for small molecule structures from highly diffracting crystals. The second group is connected to decisions made during refinement and explained below.

Group 1:

PLAT029_ALERT_3_B _diffrn_measured_fraction_theta_full value Low . 0.930

PLAT084_ALERT_3_A High wR2 Value (i.e. > 0.25)

PLAT934_ALERT_3_A Number of (Iobs-Icalc)/Sigma(W) > 10 Outliers

THETM01_ALERT_3_A The value of sine(theta_max)/wavelength is less than 0.550

PLAT023_ALERT_3_A, B Resolution (too) Low [sin(theta)/Lambda < 0.6].

PLAT082_ALERT_2_ B High R1 Value

PLAT098_ALERT_2_B Large Reported Min. (Negative) Residual Density

PLAT220_ALERT_2_B NonSolvent Resd 1 C Ueq(max)/Ueq(min) Range

PLAT230_ALERT_2_B Hirshfeld Test Diff for

PLAT241_ALERT_2_B High 'MainMol' Ueq as Compared to Neighbors

PLAT242_ALERT_2_B Low 'MainMol' Ueq as Compared to Neighbors

PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds

Group 2:

PLAT201_ALERT_2_A Isotropic non-H Atoms in Main Residue(s)

Not all atoms were refined with ADPs

DIFMN02_ALERT_2_B The minimum difference density is < -0.1*ZMAX*1.00

The solvent masking was used to remove severely disordered solvent molecules

PLAT315_ALERT_2_B Singly Bonded Carbon Detected (H-atoms Missing)

Not all H-atoms were localized, but they were used in SFAC calculation

Table S1. Crystal data and refinement details for **3** and **7**.

Identification code	**3**	**7**
Chemical formula	$C_{238}H_{226}N_{40}O_{42}$·7.7($CHCl_3$) solvent*	$C_{254}H_{258}N_{40}O_{42}$·8($CHCl_3$) solvent*
Formula weight	5258.53	5497.93
Crystal system	Orthorhombic	Triclinic
Space group	*P*bcn	*P*-1
Unit cell dimensions (Å, °)	a=25.120 (5)	a=18.2180 (6)
	α=90	α=105.871 (3)
	b=27.450 (6)	b=18.4206 (6)
	β=90	β=95.140 (3)
	c=40.020 (8)	c=29.4522 (10)
	γ=90	γ=114.061 (3)
Volume (Å^3)	27596 (10)	8450.4 (5)
Z	4	1
Density (calculated) (Mg m^{-3})	1.27	1.080
Absorption coefficient (mm^{-1})	0.44	2.29
Crystal size (mm)	0.20 × 0.07 × 0.03	0.20 × 0.07 × 0.03
Completeness	94.1 (up to 25.23°)	99.3 (up to 57.90°)
Reflections collected	233506	85666
Reflections observed [$I > 2\sigma(I)$]	15547	16731
R_{int}	0.049	0.133
Data/parameters/restraints	15863/1343/109	23289/1511/64
Goodness-of-fit on F^2	3.21	1.81
Final R indices [$I > 2\sigma(I)$]	0.1596, 0.5440	0.1624, 0.4515
R indices (all data)	0.1606, 0.5480	0.1777, 0.4671
Largest diff. peak and hole	1.46, -2.24	0.95, -0.58
CCDC #	2213461	2213460

Experiments were carried out at 100 K with Cu *K*a radiation. Absorption was corrected by multi-scan

* Solvent mask was used to remove severely disordered solvent molecules

Table S2. Hydrogen bonds geometry in the crystal structure of **3**. Atom numbers are those of the cif file.

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
O2C-H2C···O7B^{i}	0.84	1.87	2.704 (8)	169
O1C-H1C···O32B^{i}	0.84	1.91	2.742 (7)	173

5 Experimental Procedures

5.1 General methods

Commercial reagents were purchased from Sigma-Aldrich, Alfa-Aesar or TCI and were used without further purification unless otherwise specified. SASRIN resin (100-200 mesh, loading 0.7-1.0 mmol/g) was purchased from Bachem. THF, DCM and toluene were dried over alumina columns (MBRAUN SPS-800 solvent purification system); diisopropylethylamine (DIPEA) was distilled over ninhydrin and then over potassium hydroxide (KOH); chloroform was distilled over calcium hydride (CaH_2) prior to use. Preparative recycling GPC (gel permeation chromatography) was carried out on JAIGEL 20*600 mm columns (Japan Analytical Industry) in chloroform containing 1% ethanol and 0.5% TEA as mobile phase, with a flow rate of 7.5 mL/min. Monitoring by UV detection was carried out at 254 nm, 280 nm, 300 nm and 360 nm. SPS was performed manually under MW irradiation on a CEM Discover (Liberty Bio) oven using an open reaction vessel and an internal optic fiber probe for temperature control. High-resolution electrospray mass spectra were recorded on a Thermo Exactive orbitrap instrument. High-resolution MALDI-TOF mass spectra have been recorded 4800 MALDI-TOF/TOF instrument.

5.2 Solid phase synthesis general protocol

The oligomers **9 &11** were synthesized using SPS on SASRIN resin using previously reported.[7] Quinoline monomers (Fmoc-Q-OH,[7] Fmoc-<u>X</u>-OH,[8] Fmoc-P-OH[9]) were activated as acid chlorides. <u>X</u> refers to the *t*Bu-protected precursors of X.

Oligomer **6** was prepared using in situ coupling conditions as follows. [10] Loading of the resin was performed according to previously reported procedures.[7] After swelling of the SASRIN resin (100 mg, 100-200 mesh, loading 0.4616 mmol/g, 46.16 µmol) in DMF for 1 h, the resin was transferred into the MW vessel and washed three times with DMF. For deprotection a 8:2 mixture of DMF/piperidine (2 mL) was added to the resin, and nitrogen was bubbled through the suspension for 3 min. The solution was removed under vacuum, the resin was washed five times with DMF and an 8:2 mixture of DMF/piperidine (2 mL) was added again. After bubbling nitrogen through the suspension for 7 min, the resin was washed five times with DMF and five times with THF. For coupling dry THF (1 mL) and 2,3,5-collidine (5 eq. with respect to the resin-loading) were added to the resin. A mixture of the monomer (2 eq. with respect to the resin-loading) and PPh_3 (4 eq. with respect to the resin-loading) in distilled $CHCl_3$ (1 mL) or dry NMP (1 mL) was prepared. All monomers except Fmoc-P-OH were dissolved in distilled $CHCl_3$, Fmoc-P-OH was dissolved in dry NMP. After the addition of trichloroacetonitrile (4 eq. with respect to the resin-loading), this mixture was added to the resin. Then the reaction mixture was subjected to MW treatment (50 °C, 5 min, 25 W). Then the resin was washed five times with dry THF, then dry THF (4 mL) and 2,3,5-collidine (5 eq. with respect to the resin-loading) were added to

the resin. Again, a mixture of monomer (2 eq. with respect to the resin-loading) and PPh_3 (4 eq. with respect to the resin-loading) in distilled $CHCl_3$ (4 mL) or dry NMP (4 mL) with trichloroacetonitrile was prepared and added to the resin. The reaction mixture was again subjected to MW treatment (50 °C, 5 min, 50 W). After washing with DCM, THF, DMF and DCM, in that order, the resin was kept in a swollen state at 10 °C.

After complete solid phase synthesis, the sequence was cleaved from the resin. Thus, the SASRIN resin (~50 mg) was swelled in DCM for 15 min, HFIP/DCM 1:1 (vol/vol) (6 mL) was added and the mixture was stirred at r.t. for 12 h. The resin was filtered off, and then the solvent was evaporated. The process was repeated until no more foldamer was left on the resin (up to twenty times 12 h).

5.3 Synthesis of oligomers

O_2N-QXQQPQXQQ-OH (**6**) Compound **6** was synthesized using the SPS procedures reported in 5.2 on SASRIN resin (scale: 46.3 µmol). The crude product was purified via precipitation in DCM/MeOH, and the product was obtained as a yellow solid (33%, 15.1 µmol, 30.3 mg). **^{1}H NMR** (300 MHz, $CDCl_3$) δ [ppm] 11.38 (s, 1H), 11.35 (s, 1H), 11.03 (s, 2H), 10.91 (s, 1H), 10.84 (s, 1H), 10.76 (s, 1H), 10.50 (s, 2H), 8.30 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.16 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.13 – 8.07 (m, 2H), 8.01 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.92 – 7.85 (m, 2H), 7.82 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.79-7.74 (m, 3H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H), 7-60-7.59 (m, 1H), 7.46-7.40 (m, 4H), 7.38 (d, *J* = 2.3 Hz, 1H), 7.35 (s, 1H), 7.33-7.24 (m, overlap with residual solvent peak), 7.18 – 7.11 (m, 4H), 7.10 (s, 1H), 7.09-7.05 (m, 1H), 7.04 – 6.96 (m, 2H), 6.91 – 6.84 (m, 1H), 6.63 (s, 1H), 6.49 (s, 1H), 6.45 (s, 1H), 5.99 (s, 1H), 5.76 (s, 1H), 4.68 (s, 2H), 4.14-4.05 (m, 2H), 4.04 – 3.90 (m, 2H), 3.83-3.75 (m, 3H), 3.74-3.65 (m, 2H), 3.56 – 3.47 (m, 2H), 2.55 – 2.14 (m, 5H), 1.79 (s, 9H), 1.73 (s, 9H), 1.31 (d, *J* = 6.7 Hz, 6H), 1.26 (m, 6H), 1.23 – 1.18 (m, 12H), 1.17 (d, *J* = 3.9 Hz, 3H), 1.15 (d, *J* = 5.6 Hz, 6H), 1.11 (d, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 6.7 Hz, 3H). **HRMS** calcd for $C_{119}H_{119}N_{18}O_{20}$ $[M+H]^+$ 2119.8848, found (HR-ESI) 2119.8798.

(O_2N-QXQQPQXQQ)$_2$-T (**7**) Compound **6** (30.3 mg, 14.3 µmol, 1 eq.), 2,6-diisobutoxyterephthalohydrazide (**8**)[1] (2.4 mg, 7.0 µmol, 0.5 eq.) and PyBOP (22.3 mg, 22.8 µmol, 3 eq.) were dissolved in dry $CHCl_3$ under N_2. Then DIPEA (7.3 µL, 22.5 µmol, 3 eq.) was added, and the solution was stirred at r.t. for 1 week. The solvent was removed under vacuum, and the crude was purified via precipitation in DCM/MeOH. The product was recovered as a yellow solid (30.53 mg, 49% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ [ppm] 11.49 (s, 2H), 11.27 (s, 2H), 10.98 (s, 2H), 10.95 (s, 2H), 10.87 (s, 2H), 10.77 (s, 2H), 10.53 (s, 2H), 10.25 (d, *J* = 9.3 Hz, 2H), 9.97 (d, *J* = 9.3 Hz, 2H), 8.28 (dd, *J* = 7.9, 1.5 Hz, 2H), 8.13 (d, *J* = 7.5 Hz, 2H), 8.07 – 8.02 (m, 6H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.91-7.85 (m, 8H), 7.80 – 7.73 (m, 6H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.63 – 7.51 (m, 8H), 7.44 – 7.27 (m, 10H), 7.24-7.19 (m, 4H), 7.14 – 6.96 (m, 18H), 6.90 (t, *J* = 7.8 Hz, 2H), 6.69 (s, 2H), 6.58 (s, 2H), 6.41 (s, 2H), 5.95 (s, 2H), 5.76 (s, 2H), 4.13-4.01 (m, 4H), 3.98-3.89 (m, 4H), 3.89 – 3.74 (m, 10H), 3.69 – 3.61 (m, 4H), 3.57 (t, *J* = 8.4 Hz, 2H), 3.50 (t, *J* = 7.6 Hz, 2H), 3.37 – 3.29 (m, 2H), 2.51-2.41 (m, 2H), 2.39 – 2.17 (m, 10H), 1.86 (d, *J* = 5.2 Hz, 6H), 1.61 (s, 18H), 1.47 (s, 18H), 1.32 (d, *J* = 6.7 Hz, 18H), 1.29 – 1.14 (m, 30H), 1.12 (d, *J* = 6.8 Hz, 6H), 1.07

(d, *J* = 6.7 Hz, 12H), 1.01 (d, *J* = 6.6 Hz, 12H), (mixture of two diastereomers *PP* and *PM* and their ratio is 10:1, only the major peaks are reported). **HRMS** calcd for $C_{254}H_{261}N_{40}O_{42}$ $[M+3H]^{3+}$ 1514.3167, found (HR-ESI) 1514.3261.

(O_2N-QXQQPQXQQ)$_2$-T (**3**) Compound **7** (27.4 mg, 5.9 µmol) was treated with a 50% solution of TFA in CH_2Cl_2 (2 mL) at r.t. for 2 h. The solvent was then removed under vacuum, yielding the product as a yellow solid (24.7 mg, 5.5 µmol, 95%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.80 (s, 2H), 11.49 (s, 2H), 11.47 (s, 2H), 11.12 (s, 2H), 10.90 (s, 4H), 10.18 (d, *J* = 9.0 Hz, 2H), 10.06 (s, 2H), 10.01 (s, 2H), 9.89 (d, *J* = 9.2 Hz, 2H), 9.55 (s, 2H), 8.52 (s, 2H), 8.48 (d, *J* = 7.4 Hz, 2H), 8.45 (d, *J* = 7.5 Hz, 2H), 8.33 (dd, *J* = 7.9, 1.4 Hz, 2H), 8.28 – 8.23 (m, 2H), 8.20 (dd, *J* = 6.8, 2.4 Hz, 2H), 8.18 (dd, *J* = 7.9, 1.1 Hz, 2H), 8.13 – 8.08 (m, 8H), 8.06 (d, *J* = 7.2 Hz, 2H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.96 – 7.93 (m, 6H), 7.91 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.90 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.70- 7.67 (m, 4H), 7.65 – 7.61 (m, 2H), 7.49 – 7.44 (m, 8H), 7.42 – 7.29 (m, 12H), 7.24 (s, 2H), 7.19 – 7.13 (m, 8H), 7.07 - 7.04 (m, 2H), 7.03 (s, 2H), 6.34 (s, 2H), 6.02 (s, 2H), 5.77 (s, 2H), 4.68 (s, 4H), 4.14 (t, *J* = 6.6 Hz, 2H), 4.08 – 3.96 (m, 8H), 3.95 – 3.78 (m, 8H), 3.64 (t, *J* = 6.6 Hz, 2H), 3.54 (t, *J* = 7.3 Hz, 2H), 3.47 (t, *J* = 7.4 Hz, 2H), 2.62 (d, *J* = 15.8 Hz, 2H), 2.52 – 2.44 (m, 2H), 2.43 – 2.27 (m, 16H), 1.38 (d, *J* = 6.7 Hz, 16H), 1.36 – 1.32 (m, 16H), 1.24 – 1.19 (m, 30H), 1.19 – 1.17 (m, 6H), 1.15 (d, *J* = 6.8 Hz, 6H). **HRMS** calcd for $C_{238}H_{228}N_{40}O_{42}$ $[M+2H]^{2+}$ 2158.8462, found (HR-ESI) 2158.8540.

O_2N-XQQPQXQQPQXQQ-OH (**9**) Compound **9** was synthesized using the SPS procedures previously reported[7] on SASRIN resin (scale: 15 µmol). The crude product was purified via precipitation in DCM/MeOH, and the product was obtained as a yellow solid (14.7 mg, 5.1 µmol, 34%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.11 (s, 1H), 11.05 (s, 1H), 10.83 (s, 1H), 10.66 (s, 1H), 10.61 (s, 1H), 10.60 (s, 1H), 10.51 (s, 1H), 10.36 (s, 1H), 10.22 (s, 1H), 10.08 (s, 1H), 10.01 (s, 1H), 8.05 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.97 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.95 (s, 2H), 7.90 (dd, *J* = 7.5, 1.3 Hz, 2H), 7.88 – 7.85 (m, 2H), 7.79 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.74 (ddd, *J* = 8.2, 5.1, 1.3 Hz, 2H), 7.69 (ddd, *J* = 8.1, 4.6, 1.4 Hz, 2H), 7.65 (ddd, *J* = 8.1, 4.3, 1.3 Hz, 2H), 7.62 – 7.59 (m, 2H), 7.58 – 7.55 (m, 2H), 7.51 – 7.46 (m, 4H), 7.44 – 7.40 (m, 2H), 7.36 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.24 – 7.21 (m, 2H), 7.19 – 7.15 (m, 6H), 7.09 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.06 – 7.02 (m, 1H), 7.02 – 6.99 (m, 2H), 6.97 – 6.89 (m, 6H), 6.83 (t, *J* = 7.8 Hz, 1H), 6.80 (ddd, *J* = 7.8, 4.8, 3.5 Hz, 2H), 6.75 (d, *J* = 7.4 Hz, 1H), 6.69 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.69 – 6.62 (m, 2H), 6.51 (s, 1H), 6.48 (s, 1H) 6.32 (s, 1H), 6.23 (s, 1H), 6.17 (s, 1H), 5.64 (s, 1H), 5.39 (s, 1H), 4.07-4.03 (q, *J* = 7.2 Hz, 1H), 3.86 – 3.82 (m, 3H), 3.78 – 3.74 (m, 2H), 3.71 – 3.63 (m, 4H), 3.61 – 3.53 (m, 6H), 3.44 – 3.40 (m, 2H), 3.36 (t, *J* = 7.6 Hz, 1H), 3.16 – 3.09 (m, 2H), 2.88 (s, 6H), 2.81 (s, 6H), 2.36 – 2.28 (m, 2H), 2.25 – 2.20 (m, 2H), 2.19 – 2.09 (m, 3H), 2.08 – 2.01 (m, 1H), 1.97 (s, 1H), 1.95 – 1.90 (m, 1H), 1.64 (s, 10H), 1.62 (s, 10H), 1.58 (s, 10H), 1.22 – 1.14 (m, 7H), 1.10 – 1.02 (m, 13H), 0.99 – 0.94 (m, 4H). **HRMS** calcd for $C_{168}H_{168}N_{26}O_{27}$ $[M+2H]^{2+}$ 1490.6281, found (HR-ESI) 1491.6532.

(O_2N-XQQPQXQQPQXQQ)$_2$-T (**10**) Compound **9** (7.7 mg, 2.6 µmol, 1 eq.), 2,6-diisobutoxyterephthalohydrazide (**8**)[1] (0.4 mg, 1.3 µmol, 0.5 eq.) and PyBOP (0.7 mg, 1.4 µmol, 3 eq.) were

dissolved in dry $CHCl_3$ under N_2. Then DIPEA (0.2 µL, 1.4 µmol, 3 eq.) was added, and the solution was stirred at r.t. for 1 week. The solvent was removed under vacuum, and the crude was purified via GPC. The product was recovered after washing with a 5% citric acid solution, drying over $MgSO_4$ and removal of solvent as a yellow solid (3.75 mg, 23% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.22 (s, 2H), 11.00 (s, 2H), 10.79 (s, 2H), 10.63 (s, 2H), 10.61 (s, 2H), 10.57 (s, 2H), 10.30 (s, 2H), 10.15 (s, 2H), 10.10 (s, 2H), 10.05 (d, *J* = 9.1 Hz, 2H), 9.94 (s, 2H), 9.75 (d, *J* = 9.0 Hz, 2H), 8.01 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.94 (t, *J* = 6.3 Hz, 4H), 7.79 (s, 2H), 7.75 – 7.67 (m, 10H), 7.65 – 7.60 (m, 10H), 7.57 (dd, *J* = 8.0, 1.3 Hz, 4H),7.50 – 7.48 (m, 2H), 7.44 (s, 2H), 7.42 (s, 2H), 7.40 – 7.38 (m, 3H), 7.35-7.31 (t, *J* = 7.3 Hz, 4H), 7.24 (q, *J* = 7.0 Hz, 2H), 7.18 – 7.10 (m, 8H), 7.09 – 7.05 (m, 4H), 7.03 – 6.99 (m, 4H), 6.96 (dd, *J* = 14.4, 7.0 Hz, 4H), 6.91 – 6.82 (m, 6H), 6.82 (s, 2H), 6.79 (q, *J* = 7.3, 6.5 Hz, 4H), 6.73 (dd, *J* = 12.4, 7.0 Hz, 4H), 6.67 (dd, *J* = 12.1, 6.5 Hz, 4H), 6.64– 6.59 (m, 2H), 6.54 (s, 2H), 6.46 (s, 2H), 6.41 (s, 2H), 6.19 (s, 2H), 6.15 (s, 2H), 5.63 (s, 2H), 5.59 (s, 2H), 5.39 (s, 2H), 5.21 – 5.16 (m, 4H), 4.25 – 4.19 (m, 10H), 4.11 – 4.06 (m, 10H), 3.88 – 3.79 (m, 6H), 3.77 – 3.70 (m, 4H), 3.69 – 3.65 (m, 14H), 3.64 – 3.51 (m, 14H), 3.48 – 3.45 (m, 2H), 3.39 (s, 8H), 3.35 – 3.31 (m, 2H), 3.11 – 3.08 (m, 2H), 3.06 – 3.01 (m, 2H), 2.95 – 2.90 (m, 2H), 2.35 – 2.29 (m, 4H), 2.28 – 2.23 (m, 12H), 2.17 – 2.11 (m, 4H), 2.10 (s, 2H), 2.01 (s, 10H), 2.01 (s, 10H), 2.00 (s, 10H), 1.97 (s, 12H), 1.75 (s, 4H), 1.65 – 1.64 (m, 8H), 1.53 (s, 18H), 1.28 (s, 12H), 1.17 – 1.12 (m, 6H), 1.09 – 0.98 (m, 18H), 0.91 (s, 2H), 0.83 – 0.74 (m, 13H). (mixture of two diastereomers *PP* and *PM* and their ratio is 10:1, only the major peaks are reported). **HRMS** calcd for $C_{352}H_{356}N_{56}O_{58}$ $[M+2H]^{2+}$ 3131.3360, found (HR-ESI) 3132.0238.

(O_2N-XQQPQXQQPQXQQ)$_2$-T (**4**) Compound **10** (0.6 mg, 0.1 µmol) was treated with a 50% solution of TFA in CH_2Cl_2 (2 mL) at r.t. for 2 h. The solvent was then removed under vacuum, yielding the product as a yellow solid (quant.). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.40 (s, 2H), 11.22 (s, 2H), 11.13 (s, 2H), 11.12 (s, 2H), 10.88 (s, 2H), 10.60 (s, 2H), 10.47 (s, 2H), 10.34 (s, 2H), 10.19 (s, 2H), 10.00 (d, *J* = 9.0 Hz, 2H), 9.84 (s, 2H), 9.68 (d, *J* = 9.0 Hz, 2H), 9.28 (s, 2H), 9.19 (s, 2H), 8.27 (d, *J* = 7.1 Hz, 2H), 8.21 (d, *J* = 7.2 Hz, 2H), 8.13 (d, *J* = 7.8 Hz, 2H), 8.08 (s, 2H), 8.04 – 8.02 (m, 2H), 8.01 (s, 1H), 7.98 (d, *J* = 6.9 Hz, 2H),7.94 (d, *J* = 7.4 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 7.8 Hz, 2H), 7.79 – 7.76 (m, J = 7.78, 12H), 7.76 – 7.72 (m, J = 7.74, 10H), 7.71 – 7.67 (m, 4H), 7.57 (d, *J* = 7.1 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.40 (s, 1H), 7.37 (d, *J* = 6.9 Hz, 2H), 7.26 – 7.20 (m, 20H), 7.18 (s, 6H), 7.17 – 7.12 (m, 10H), 7.12 – 7.06 (m, 10H), 6.99 (s, 2H), 6.98 (s, 2H), 6.97 – 6.94 (m, 6H), 6.92 – 6.87 (m, 8H), 6.86 – 6.83 (m, J = 6.85, 8H), 6.76 (s, 2H), 6.50 (s, 2H), 6.28 (s, 2H), 5.97 (s, 2H), 5.91 (s, 2H), 5.78 (s, 2H), 5.49 (s. 2H), 3.96 – 3.91 (m, 6H), 3.90 – 3.85 (m, 6H), 3.84 – 3.79 (m, 10H), 3.76 – 3.68 (m, 14H), 3.68 – 3.61 (m, 10H), 3.60 – 3.55 (m, 3H), 3.51 – 3.46 (m, 6H), 3.44 (s, 1H), 3.32 – 3.30 (m, 2H), 2.39 – 2.29 (m, 14H), 2.27 – 2.20 (m, 14H), 2.19 – 2.13 (m, 8H), 2.12 – 2.07 (m, 6H), 2.02 (s, 1H), 2.01 – 2.00 (m, 2H), 1.97 – 1.93 (m, 6H), 1.59 – 1.56 (m, 2H), 1.53 – 1.47 (m, 3H), 1.45 – 1.38 (m, 2H), 1.10 – 1.06 (m, 2H), 1.05 – 1.02 (m, 6H), 0.98 – 0.92 (m, 6H), 0.67 – 0.63 (m, 8H). **HRMS** calcd for $C_{328}H_{306}N_{56}O_{56}$ $[M+2H]^{2+}$ 2963.14, found (HR-ESI) 2963.14; calcd for $C_{328}H_{307}N_{56}O_{56}$ $[M+3H]^{3+}$ 1975.7679, found (HR-ESI) 1975.7618.

O_2N-XQQPQXQQPQXQQPQXQQ-OH (**11**) Compound **11** was synthesized using the SPS procedures previously reported[7] on SASRIN resin(scale: 58 µmol). The crude product was purified via precipitation in DCM/MeOH, and the product was obtained as a yellow solid (33.4 mg, 8.2 µmol, 14.1%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.04 (s, 1H), 10.98 (s, 1H), 10.74 (s, 1H), 10.51 (s, 1H), 10.44 (s, 1H), 10.42 (s, 1H), 10.38 (s, 1H), 10.16 (s, 1H), 10.01 (s, 1H), 10.00 (s, 1H), 9.96 (s, 1H), 9.89 (s, 1H), 9.86 (s, 1H), 9.57 (s, 1H), 8.02 – 8.00 (m, 1H), 7.91 – 7.89 (m, 2H), 7.83 (ddd, *J* = 14.1, 7.3, 1.2 Hz, 3H), 7.76 (s, 1H), 7.73 (dd, *J* = 7.2, 1.1 Hz, 1H), 7.69 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.66 – 7.63 (m, 2H), 7.61 – 7.49 (m, 11H), 7.45 (s, 1H), 7.42 – 7.39 (m, 3H), 7.38 – 7.31 (m, 6H), 7.23 – 7.20 (m, 1H), 7.18 – 7.15 (m, 4H), 7.15 – 7.10 (m, 4H), 7.09-7.05 (qd, *J* = 7.3, 1.3 Hz, 4H), 7.00 (d, *J* = 4.6 Hz, 2H), 6.96 (dd, , *J* = 14.9, 7.4 Hz, 2H), 6.90 – 6.90 (m, 1H), 6.89 – 6.88 (m, 1H), 6.88 – 6.78 (m, 9H), 6.77 – 6.70 (m, 4H), 6.69 – 6.63 (m, 4H), 6.63-6.56 (m, 3H), 6.56 – 6.49 (m, 5H), 6.28 (s, 1H), 6.15 (s, 1H), 6.05 (s, 1H), 5.85 (s, 1H), 5.60 (s, 1H), 5.53 (s, 1H), 5.46 (s, 1H), 5.27 (s, 1H), 5.21 (s, 1H), 4.32 (s, 1H), 3.96 (s, 1H), 3.82 – 3.59 (m, 12H), 3.55 – 3.43 (m, 12H), 3.36 – 3.26 (m, 6H), 3.04 – 3.00 (m, 3H), 2.81 – 2.77 (m, 2H), 2.30 – 2.22 (m, 4H), 2.20 – 1.98 (m, 14H), 1.14 – 1.05 (m, 32H), 1.04 – 0.99 (m, 32H), 0.98 (s, 2H), 0.96 – 0.92 (m, 8H). **HRMS** calcd for $C_{231}H_{230}N_{36}O_{36}$ $[M+2H]^{2+}$ 2041.8631, found (HR-ESI) 2041.8769.

(O_2N-XQQPQXQQPQXQQPQXQQ)$_2$-T (**12**) Compound **11** (11.0 mg, 2.6 µmol, 1 eq.), 2,6-diisobutoxyterephthalohydrazide (**8**)[1] (0.5 mg, 1.3 µmol, 0.5 eq.) and PyBOP (4.2 mg, 8.1 µmol, 3 eq.) were dissolved in dry $CHCl_3$ under N_2. Then DIPEA (1.4 µL, 1.0 µmol, 3 eq.) was added, and the solution was stirred at r.t. for 2 weeks. The solvent was removed under vacuum, and the crude was purified via GPC. The product was recovered after washing with a 5% citric acid solution, drying over $MgSO_4$ and removal of solvent as a yellow solid (2 mg, 0.2 µmol, 9% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.13 (s, 2H), 10.95 (s, 2H), 10.72 (s, 2H), 10.52 (s, 4H), 10.37 (s, 2H), 10.28 (s, 2H), 10.12 (s, 2H), 9.99 – 9.90 (m, 8H), 9.84 (s, 2H), 9.82 (s, 2H), 9.67 (d, *J* = 8.9 Hz, 2H), 9.49 (s, 2H), 7.98 (d, *J* = 7.5 Hz, 2H), 7.87 (dd, *J* = 11.5, 6.7 Hz, 4H), 7.73 – 7.69 (m, 4H), 7.67 – 7.61 (m, 8H), 7.59 – 7.52 (m, 12H), 7.51 – 7.46 (m, 9H), 7.43 – 7.41 (m, 5H), 7.40 – 7.37 (m, 5H), 7.32 – 7.31 (m, 3H), 7.28 – 7.26 (m, 4H), 7.25 – 7.22 (m, 4H), 7.16 – 7.06 (m, 12H), 7.05 – 6.99 (m, 5H), 6.94 – 6.90 (m, 6H), 6.87 – 6.81 (m, 6H), 6.77 – 6.67 (m, 18H), 6.66 – 6.64 (m, 3H), 6.62 – 6.60 (m, 5H), 6.59 – 6.52 (m, 5H), 6.49 – 6.44 (m, 4H), 6.42 – 6.35 (m, 4H), 6.10 (s, 2H), 6.03 (s, 2H), 5.84 (s, 2H), 5.58 (s, 2H), 5.46 (s, 2H), 5.41 (s, 2H), 5.22 (s, 2H), 5.20 (s, 2H), 3.79 – 3.75 (m, 5H), 3.70 – 3.49 (m, 34H), 3.46 – 3.39 (m, 12H), 3.37 – 3.22 (m, 15H), 3.13-3.05 (m, 5H), 2.30 – 2.20 (m, 10H), 2.10 – 2.02 (m, 14H), 1.98 – 1.92 (m, 4H), 1.82 – 1.73 (m, 8H), 1.67 (s, 4H), 1.63 (s, 5H), 1.59 (s, 8H), 1.51 (s, 22H), 1.48 (s, 20H), 1.41 (s, 18H), 1.37 (s, 5H), 1.18 – 1.08 (m, 26H), 1.06 – 1.03 (m, 25H), 1.02 – 0.93 (m, 40H), 0.84 – 0.72 (m, 22H). (mixture of two diastereomers *PP* and *PM* and their ratio is 10:1, only the major peaks are reported). **HRMS** calcd for $C_{478}H_{481}N_{76}O_{74}$ $[M+3H]^{3+}$ 2822.8732, found (HR-ESI) 2823.2296; calcd for $C_{478}H_{482}N_{76}O_{74}$ $[M+4H]^{4+}$ 2117.4067, found (HR-ESI) 2117.6679.

(O_2N-XQQPQXQQPQXQQPQXQQ)$_2$-T (**5**). Compound **12** (2 mg, 0.2 µmol) was treated with a 50% solution of TFA in CH_2Cl_2 (2 mL) at r.t. for 2 h. The solvent was then removed under vacuum, yielding the product as a yellow solid (quant.). **^{1}H NMR** (500 MHz, $CDCl_3$) δ [ppm] 11.28 (s, 1H), 11.13 (s, 2H), 10.98 (s, 2H), 10.82 (s, 3H), 10.80 (s, 2H), 10.37 (d, *J* = 14.0 Hz, 2H), 10.16 (s, 2H), 10.11 (s, 2H), 10.00 (s, 4H), 9.98 (s, 2H), 9.97 (s, 2H), 9.78 (s, 2H), 9.73 (s, 2H), 9.62 (d, *J* = 8.9 Hz, 2H), 9.18 (s, 2H), 8.91 (s, 4H), 8.27 (s, 1H), 8.18 (d, *J* = 6.7 Hz, 2H),8.12 (d, *J* = 6.9 Hz, 2H), 8.06 – 7.94 (m, 4H), 8.00 – 7.97 (m, 1H), 7.94 (d, *J* = 7.5 Hz, 2H), 7.75 – 7.64 (m, 9H), 7.63 – 7.49 (m, 10H), 7.48 – 7.41 (m, 8H), 7.39 – 7.34 (m, 7H), 7.31 – 7.24 (m, overlap with residual solvent peak), 7.16 – 7.09 (m, 11H), 7.08 – 7.01 (m, 10H), 6.95 – 6.89 (m, 8H), 6.87 – 6.84 (m, 10H), 6.81 – 6.78 (m, 10H), 6.76 – 6.70 (m, 9H), 6.66 – 6.60 (m, 10H), 6.45 (s, 2H), 6.41 – 6.37 (m, 2H), 5.93 (s, 2H), 5.86 (s, 2H), 5.83 (s, 2H), 5.71 (s, 2H), 5.66 (s, 2H), 5.57 – 5.49 (m, 4H), 5.42 (s, 2H), 5.33 – 5.26 (m, 10H), 3.96 (d, *J* = 9.5 Hz, 12H), 3.76 – 3.48 (m, 28H), 3.45 – 3.41 (m, 5H), 3.34 (s, 2H), 3.26 (s, 3H), 2.30 – 2.27 (m, 21H), 2.25 – 2.17 (m, 19H), 1.60 – 1.55 (m, 21H), 1.53 – 1.48 (m, 39H), 1.44 – 1.38 (m, 23H), 1.08 – 0.98 (m, 22H), 0.97 – 0.89 (m, 11H), 0.70 – 0.62 (m, 28H). **HRMS** calcd for $C_{446}H_{414}N_{76}O_{76}$ [M] 8017.0969, found (HR-MALDI-TOF, THAP) 8017.1500.

6 References

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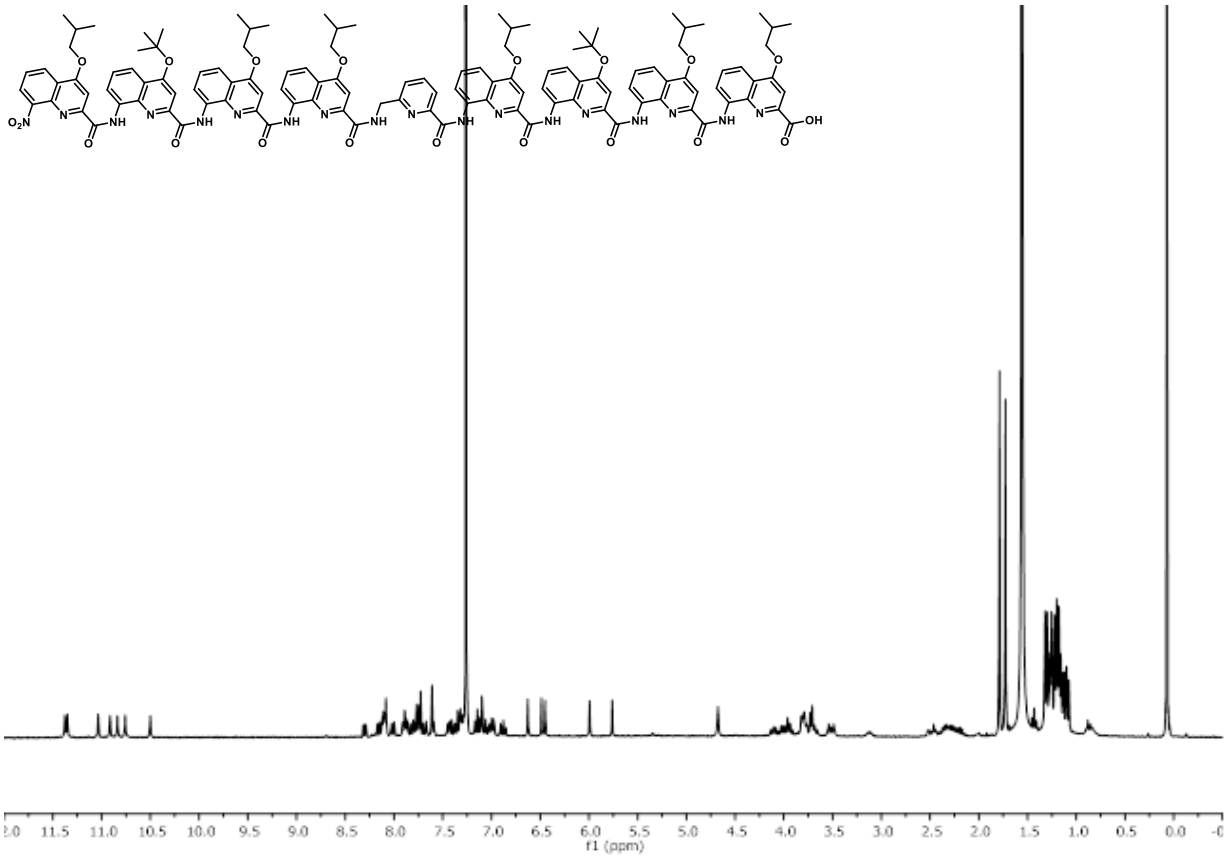
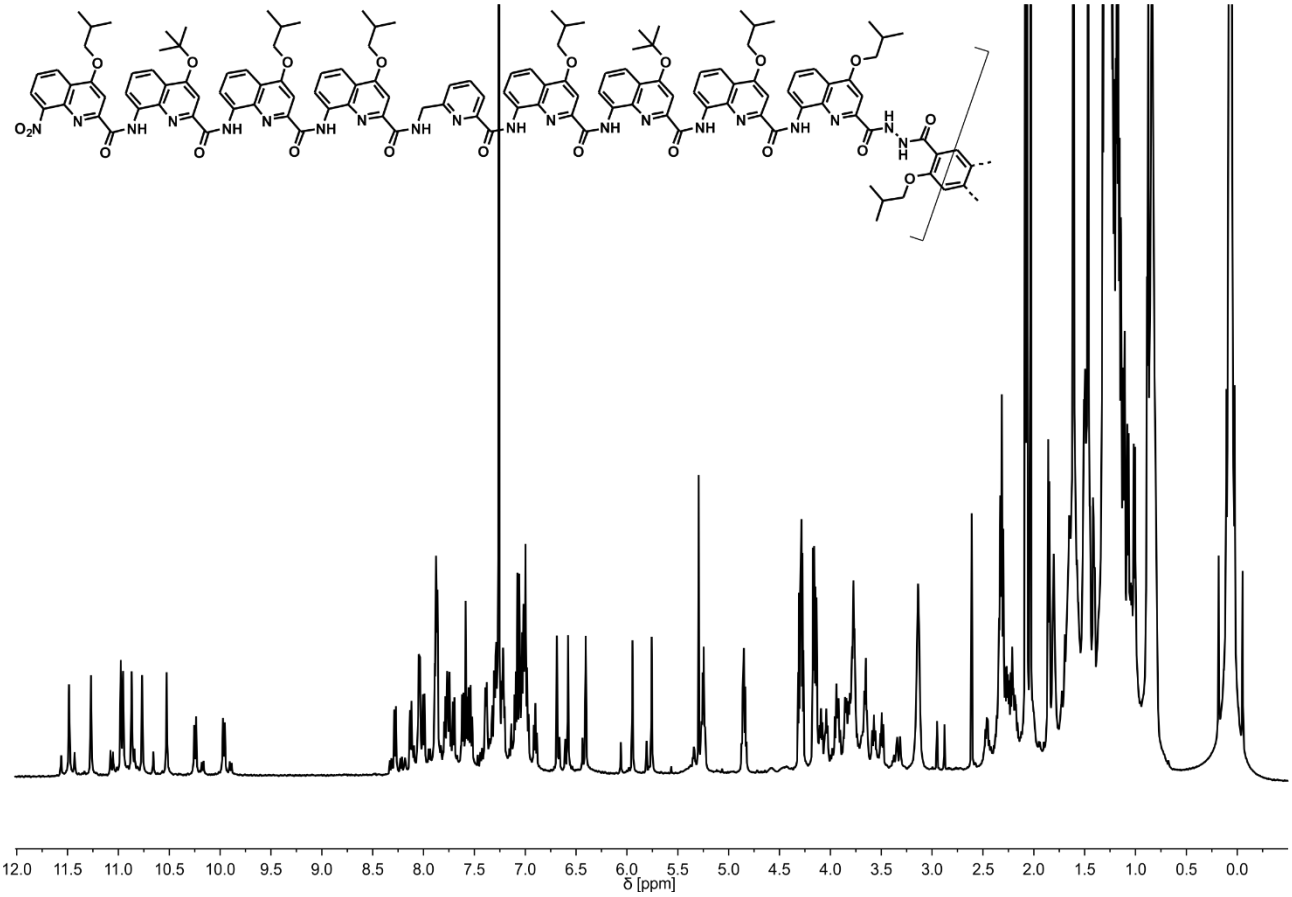
7 ^{1}H NMR spectra of new compounds



^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **6**.



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **7**.

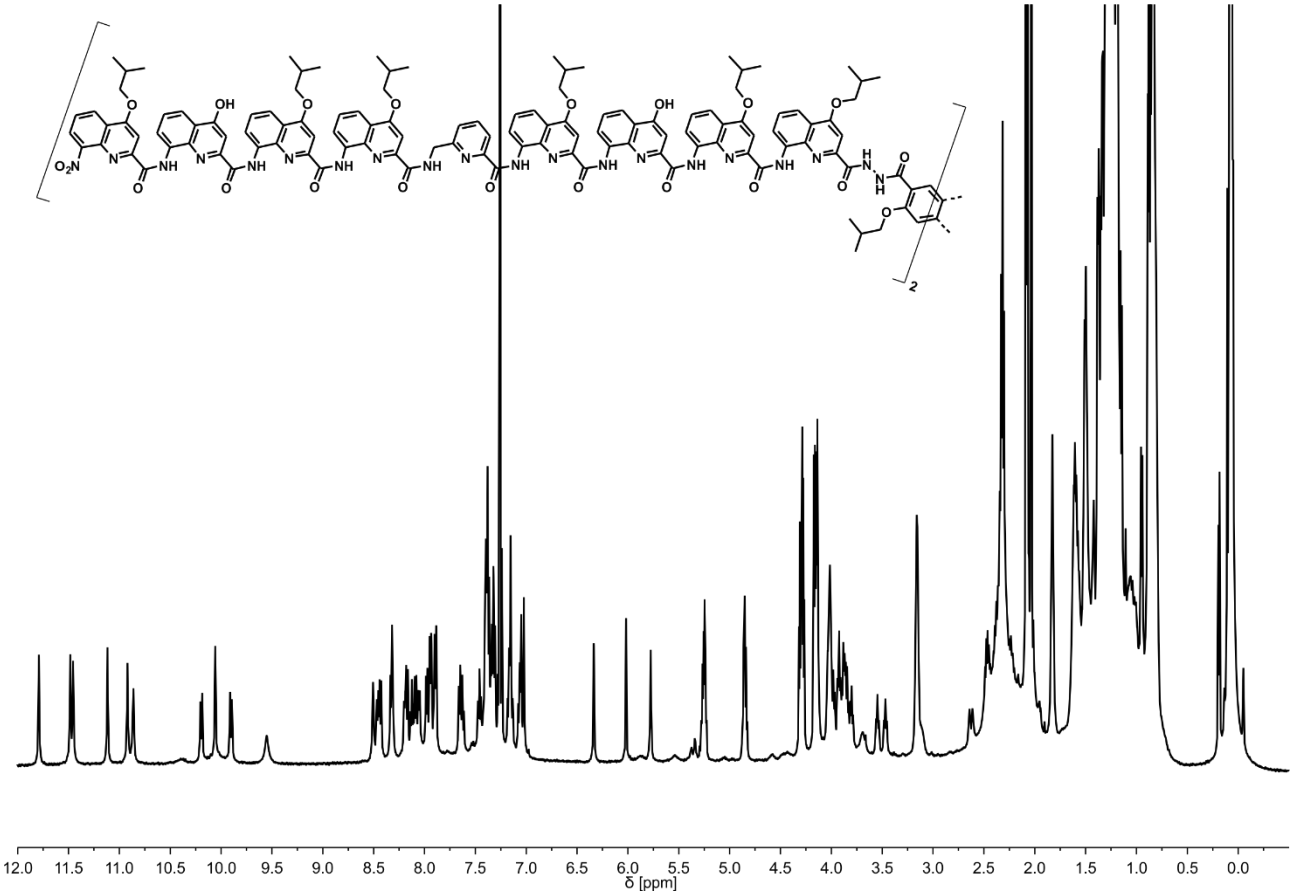
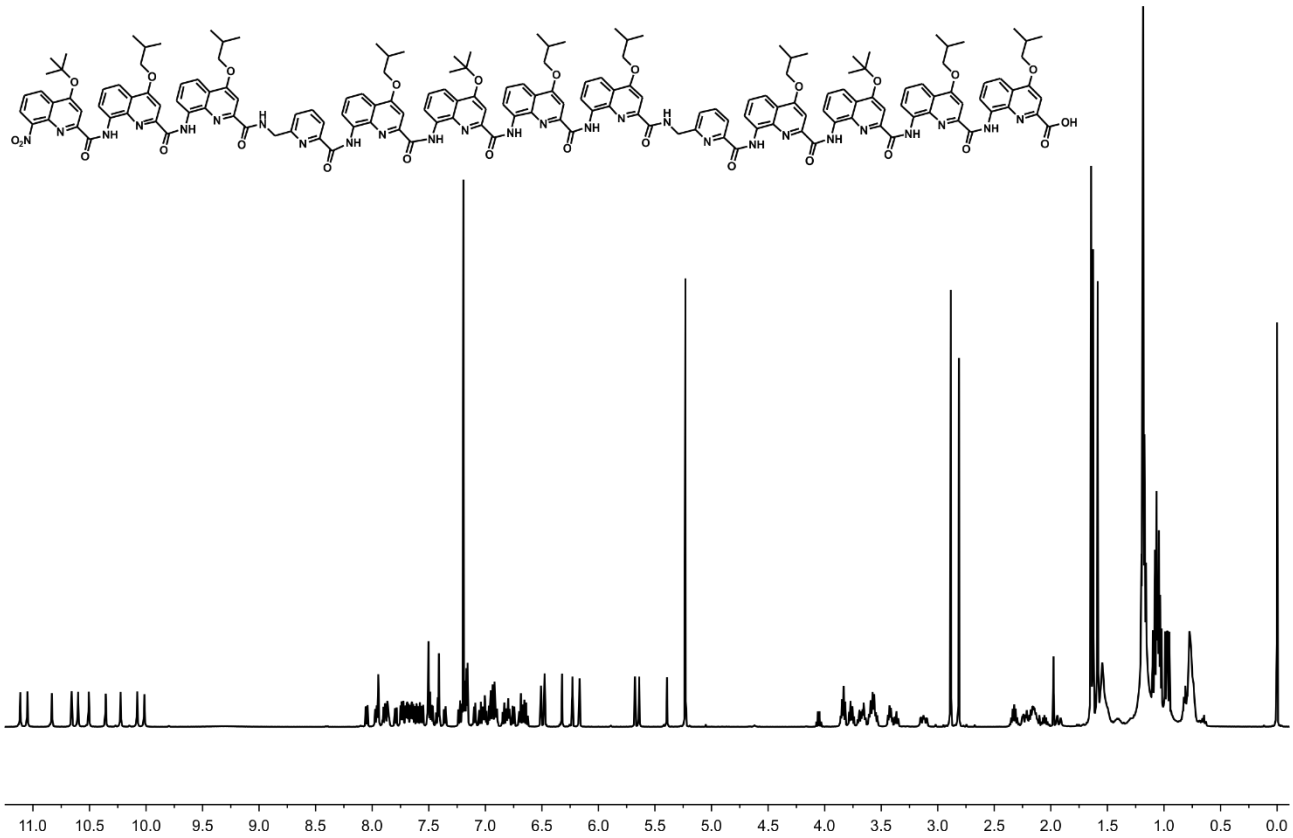
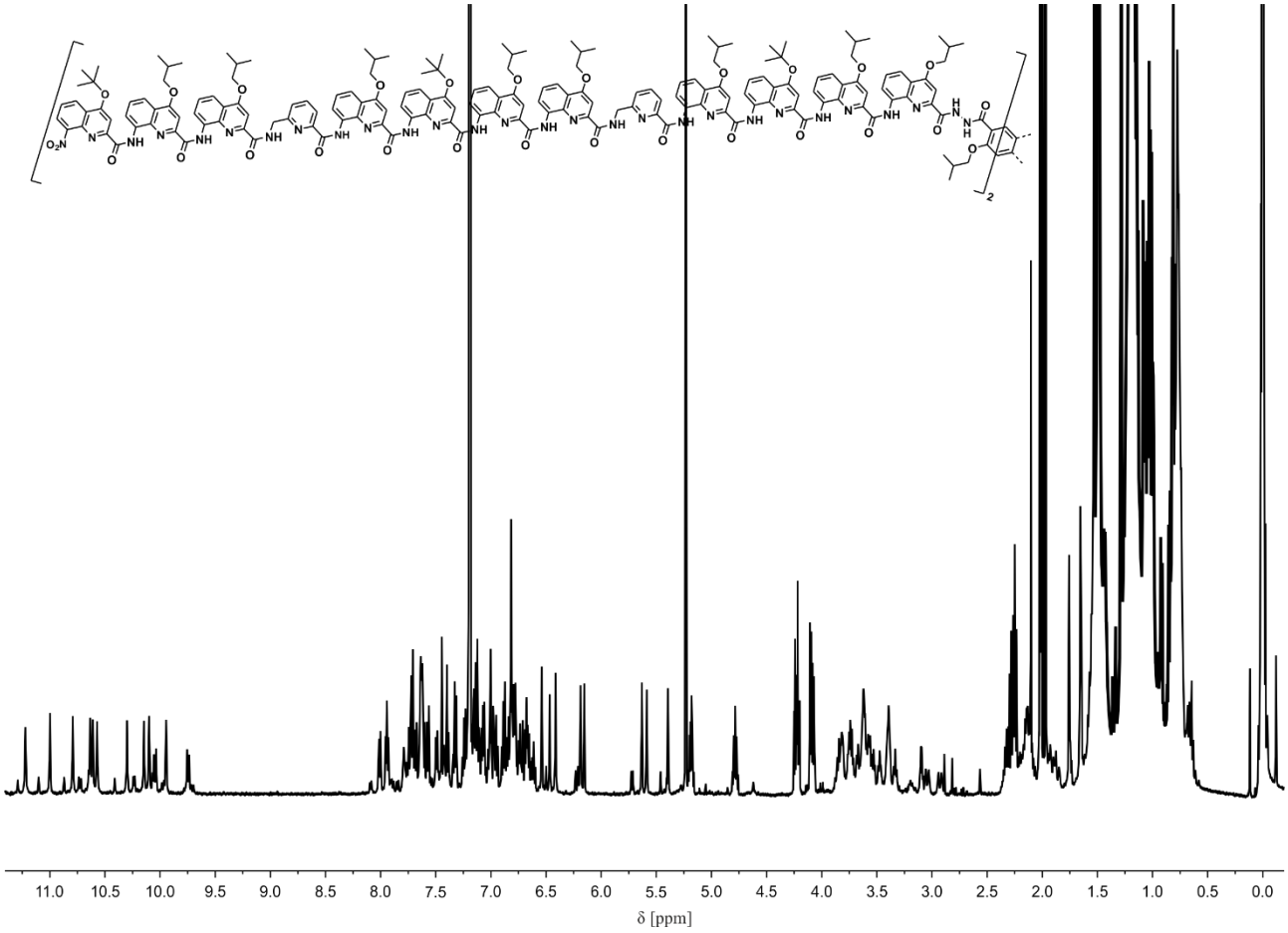


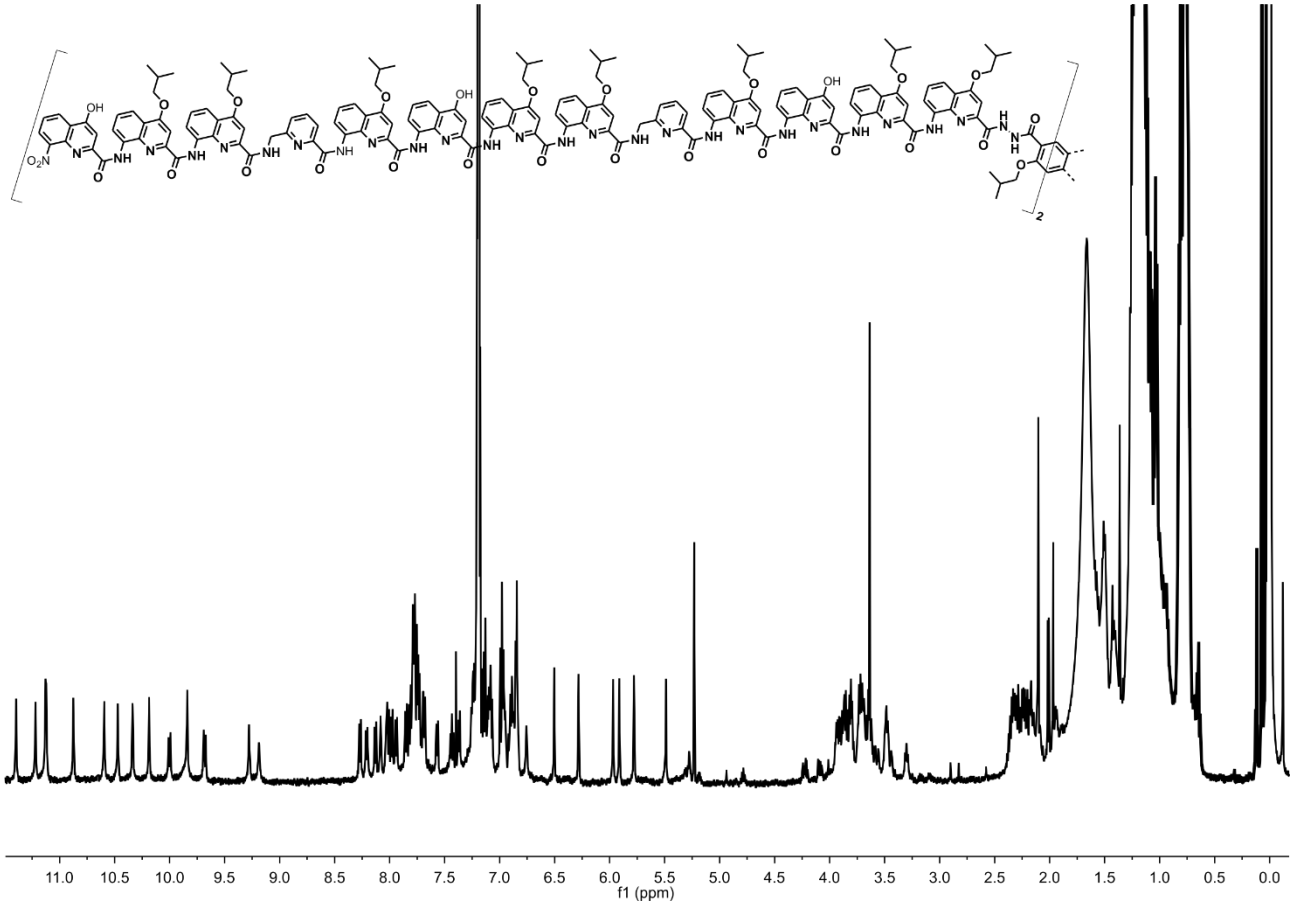
Figure S5: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3**.



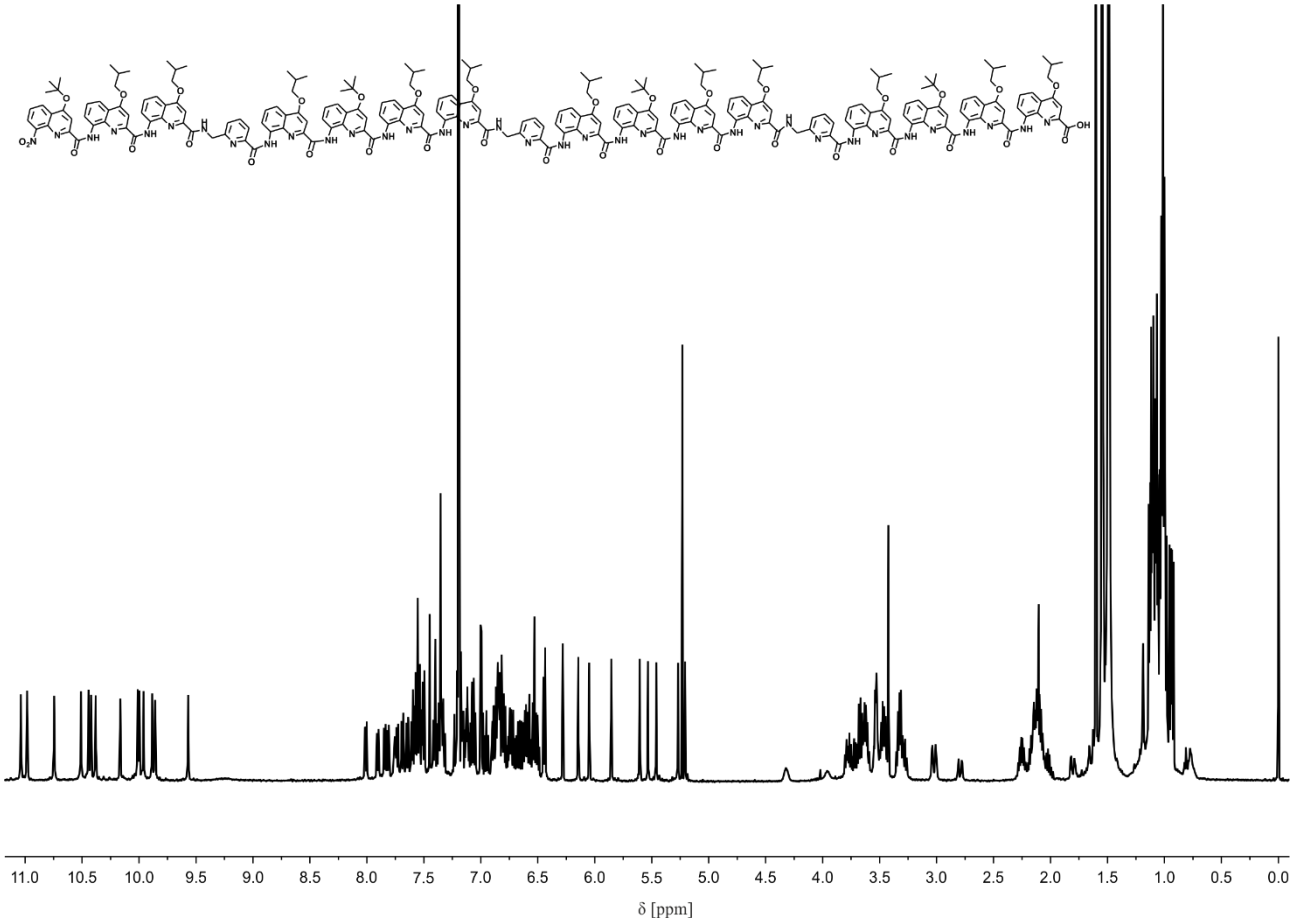
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **9**.



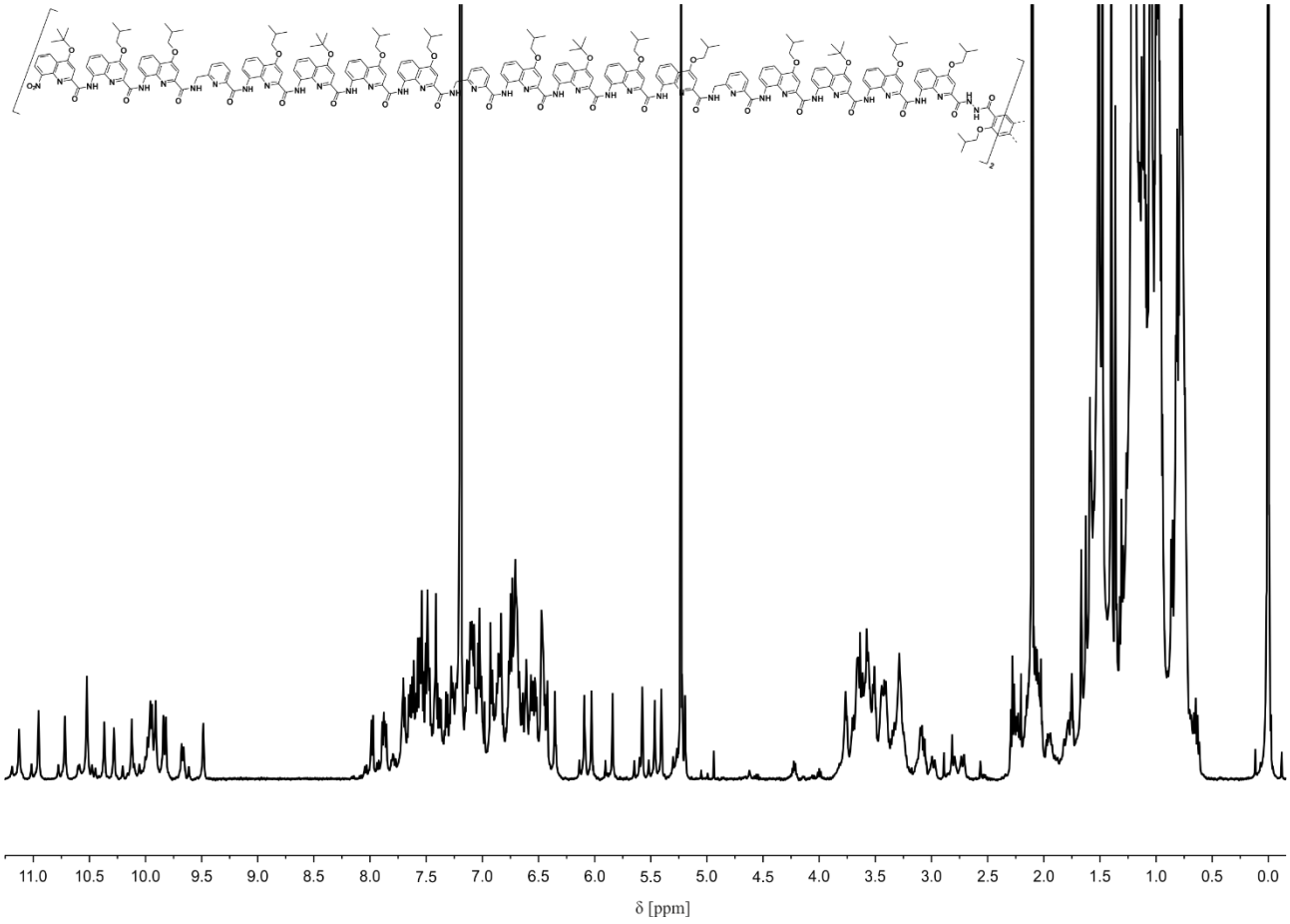
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **10**.



^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **4**.



^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **11**.



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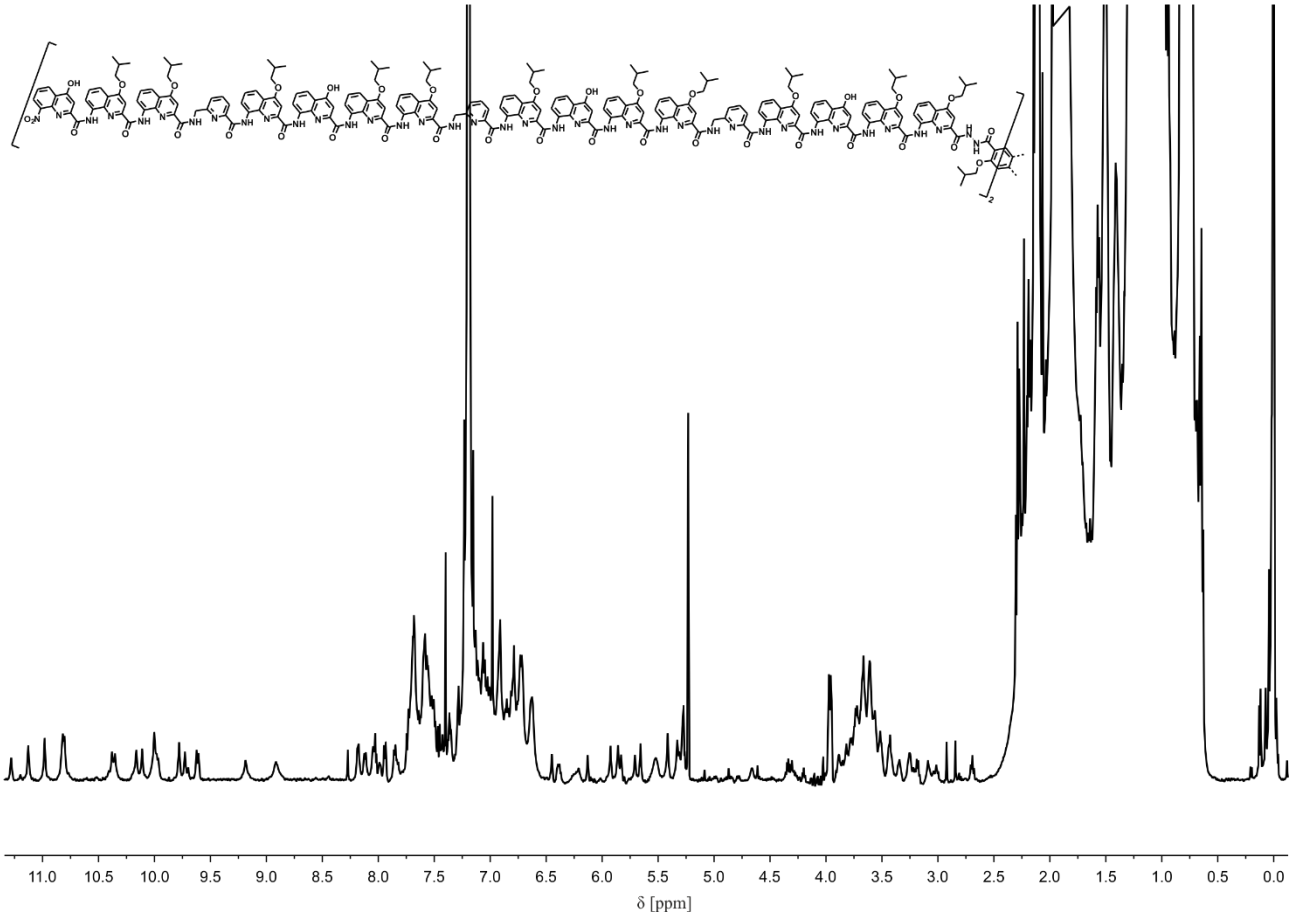

^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **5**.